Enantioselective Multi-Component Reactions: Conjunctive Coupling and Related Processes

GABRIEL JORDAN LOVINGER

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Gabriel Jordan Lovinger

Advisor: Professor James P. Morken, Ph.D.

Abstract: This dissertation details the discovery, development, and mechanistic exploration of several enantioselective processes involving organoboronic esters. The first chapter will discuss electrophile-induced metallate rearrangement reactions, the fundamental reactivity that underlies much of the subsequently discussed work. The second chapter details the discovery and mechanistic study of the metal-induced metallate rearrangement reaction and the multi-component conjunctive coupling reaction manifold and related reactions it enables. The factors that govern the competition between metal-induced metallate rearrangement versus transmetallation will be explored. The third chapter will discuss efforts to understand and overcome the initial limitations of the conjunctive coupling reaction including halide inhibition of palladium catalysis and the inability to engage other organometallic reagents such as organomagnesium nucleophiles, and how this allowed the development of a more general reaction. The fourth chapter discusses the development of an enantioselective triamine–nickel-catalyzed conjunctive coupling reaction of alkyl electrophiles as well as a related nickel-promoted radical-polar crossover reaction and the mechanistic features leading to one reaction manifold or the other. A related enantioselective diamine–nickel-catalyzed tandem radical addition cross coupling reaction of alkyl iodides, alkenylboron reagents, and alkyl- or arylzinc reagents will also be discussed. The fifth chapter will cover the discovery of a diamine–nickel-catalyzed

enantioselective carbozincation reaction of alkenylboron compounds which produces enantioenriched α-boryl alkylzinc reagents. The mechanistic investigations undertaken and application of these species in a variety of stereospecific transformation will be discussed along with the preliminary discovery and optimization of a diphosphine-Pd-catalyzed stereoconvergent Negishi cross-coupling reaction of racemic α-boryl alkylzinc reagents.

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To my parents and sister: thank you for a lifetime of love and support

To Kaya: this work would not have been possible without you.

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LIST OF ABBREVIATIONS

Å: angstrom
Ac: acetyl
Acac: acetylacetonyl
Ad: adamantly
atm: atmospheres
$B_2(pin)_2$: bis(pinacolato)diboron
9-BBN: 9-borabicyclo(3.3.1)nonane
BINAP: 2,2'-bis(diphenylphosphino)-1,1'-binaphthyl
Bn: benzyl
Bz: benzoyl
*t*Bu-XPhos: 2-di-*tert*-butylphosphino-2′,4′,6′-triisopropylbiphenyl
cat: catechol
CH_2Cl_2: dichloromethane
cod: 1,5-cyclooctadiene
conv: conversion
Cy: cyclohexyl
dan: 1,8-diaminonaphthalene
DART: direct analysis in real time
dba: dibenzylideneacetone
D*t*BuPF: 1,1'-bis(di-*tert*-butylphosphino) ferrocene
DCE: 1,2-dichloroethane
DFT: density functional theory
DI: deionized
DIBAL-H: diisobutylaluminum hydride
DMA: N,N-dimethylacetamide
DMAP: 4-dimethylaminopyridine
DME: dimethoxyethane
DMF: N,N-dimethylformamide
DCyPF: 1,1'-bis(dicyclohexylphosphino) ferrocene
DPPF: 1,1'-bis(diphenylphosphino) ferrocene
DPPF: 1,1'-bis(diphenylphosphino) ferrocene
$DPPF \cdot PdCl_2$: 1,1′-bis(diphenylphosphino) ferrocene]dichloropalladium(II)
dr: diastereomeric ratio
ee: enantiomeric excess
er: enantiomeric ratio
es: enantiospecificity
ESI: electrospray ionization
EtOAc: ethyl acetate
Eq: equation
equiv: equivalents
GC: gas chromatography
h: hour(s)
HOMO: highest occupied molecular orbital
HRMS: high resolution mass Spectrometry
HPLC: high performance liquid chromatography
Hz: hertz
HSA: hydroxylamine-*O*-sulfonic acid
IR: infared spectroscopy
IPA: isopropanol
LiTMP: lithium 2,2,6,6-tetramethylpiperidide
LDA: lithium diisopropylamide
MeCN: acetonitrile
LUMO: lowest unoccupied molecular orbital
min: minutes
M: molar
MTBE: methyl *t*butyl ether
MS: molecular sieves
NBS: *N*-bromosuccinimide
nbd: norbornadiene
NMR: nuclear magnetic resonance
neo: neopentyl glycol
NR: no reaction
NHC: *N*-heterocyclic carbine
pin: pinacol
$Pd(OAc)_2$: palladium (II) acetate
pmb: *p*-methoxybenzyl
PMA: phosphomolybdic acid
PyBox: pyridine bis(oxazoline)
ppm: parts per million
rr: regioisomeric ratio
rac: racemic
Ruphos: 2-dicyclohexylphosphino-2′,6′-
rt: room temperature

SFC: supercritical fluid chromatography
SPhos: 2-dicyclohexylphosphino-2′,6′-Dimethoxybiphenyl
TBAF: tetrabutylammonium fluoride
TBS: *t*-butyldimethylsilyl
TEMPO: 2,2,6,6-tetramethyl-1-piperidinyloxy free radical
TFA: trifluoroacetate
TLC: thin layer chromatography
TMS: trimethylsilyl
Ts: *p*-toluenesulfonyl
diisopropoxybiphenyl
TADDOL: 2,2-dimethyl-α,α,α',α'-tetraaryl-1,3-dioxolane-4,5-dimethanol
TBDPS: *t*-butyldiphenylsilyl
temp: temperature
TES: triethylsilyl
Tf: *p*-trifluoromethylsulfonyl
THF: tetrahydrofuran
TMEDA: *N,N,N',N*-Tetramethylenediamine
tol: toluene
UV: ultraviolet

Chapter One

Electrophile-Induced 1,2-Metallate Rearrangement Reactions

1.1 Introduction

The preparation of natural products and pharmaceuticals relies on the ability of chemists to orchestrate a series of reactions to construct and functionalize carbon frameworks. Thus, methods that enable new or non-obvious bond formations, especially in a modular and stereocontrolled manner, are of paramount importance.[1] In this context, organoboron compounds are some of the most broadly utilized and synthetically versatile reagents in organic synthesis.[2] The widespread use of these compounds is due, in part, to their low toxicity, wide availability, ready preparation from chemical feedstocks such as alkenes, and their ability to engage in a large variety of stereoselective or stereospecific transformations. Indeed, the ability to replace boron stereospecifically by oxygen, nitrogen, halogen, zinc, and carbon-based functional groups among others, means that the development of methods to prepare even a single enantioenriched organoboron structural motif provides access to an array of diverse enantioenriched compounds.

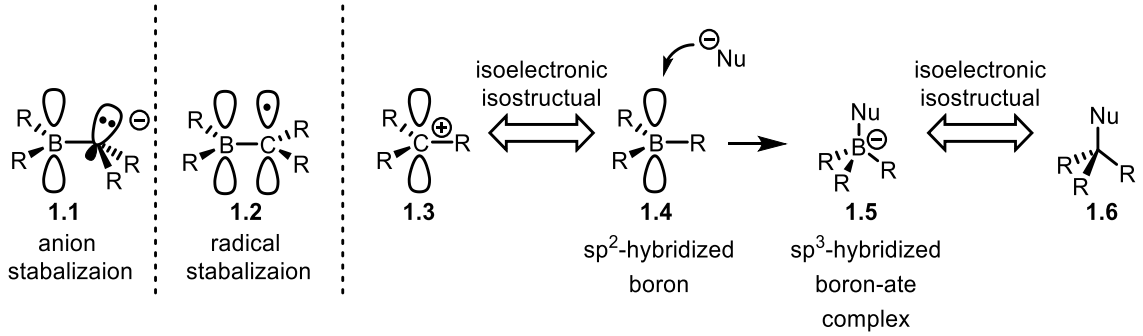
In contrast to the enormous research effort dedicated to the introduction of the boron moiety into organic molecules (hydroboration, protoboration, Miyaura borylation, C-H borylation, diboration, conjugate borylation, etc) and the replacement of this moiety with other functional groups (*vide supra*), the use of boron to orchestrate reactivity within a

[1] (a) Mohr, J. T.; Krout, M. R.; Stoltz, B. M. *Nature* **2008**, *455*, 323. (b) Trost, B. M. *J. Org. Chem.* **2014**, 79, 9913. (c) Enders, D.; Jaeger, K.-E. *Asymmetric Synthesis with Chemical and Biological Methods*; 1st ed.; Wiley-VCH, **2007**.
[2] Hall, D. G. *Boronic Acids* (Wiley-VHC, Weinheim, Germany, 2011).

molecular framework has not been as well explored. Strategies that utilize a boron-based functional group to forge new bonds in a non-destructive manner introduce opportunities for subsequent product diversification. In principle, this allows boron to act as a unique directing group, enabling reactivity to increase structural complexity while expanding rather than decreasing the types of products that can be prepared.

As depicted in Scheme 1.1, the ability of boron to mediate a diverse set of reactivities stems from its unique electronic structure and bonding behavior. Unlike carbon, which possesses four valence electrons, boron has only three and thus often bonds to three groups to form neutral species with trigonal planar geometry. This six-electron valence shell configuration results in a boron atom possessing an empty p orbital which lies orthogonal to the trigonal sp^2 plane, making these species isoelectronic and isostructural to carbocations (**1.3** versus **1.4**). The electron-deficient boron atom is thus capable of accepting two-electrons to achieve a full valence octet. The incomplete octet can therefore lead to intramolecular orbital interactions that stabilize species such as an α-boryl anion (**1.1**) or radical (**1.2**) in which electron density on an adjacent atom is delocalized into the empty p orbial of boron. The trigonal planar geometry of boron also renders the p orbital sterically accessible to nucleophilic attack and thus enables organoboron species to bond to two-electron donors to form boron-ate species (**1.4** to **1.5**) which are isoelectronic and

Scheme 1.1. Electronic structure of boron leads to stabalizing interactions and boron-ate formation



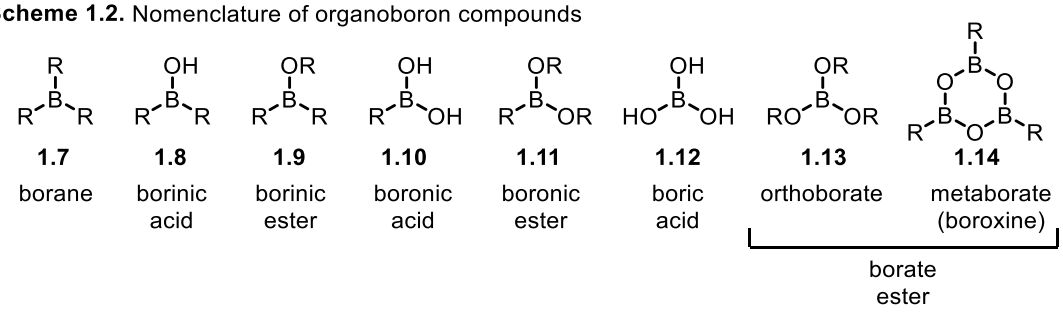
isostructural with neutral carbonaceous structures (**1.6**).

While boron-ate complexes are generally drawn with a formal negative charge on boron, this is merely a convention as the difference in Pauling electronegativity values between boron (2.04) and the atoms to which it is attached generally results in bond polarization away from boron. When the atoms attached to boron are main group elements such as carbon (2.55), oxygen (3.04), or nitrogen (3.04), electron density lies primarily on these atoms. The ability of boron to stabilize nucleophiles through covalent bonding while allowing these species to retain much of their electron density enables boron-ate complexes to engage in a wide range of reactions through 1,2-metallate rearrangement.

The reactivity of organoboron compounds is strongly influenced by the ligands to which boron is attached, enabling organoboron species to be tuned through ligand design. In accordance with the importance of boron ligands in determining reactivity, the nomenclature of these species is defined in terms of the nature and number of these ligands (Scheme 1.2).

Outside the realm of boron-based catalysts, boron's ability to stabilize high energy intermediates and mediate reactivity in the context of enantioselective catalysis has not been extensively exploited (a subject which will be explored throughout the following chapters of this thesis), the homologation of organoboron compounds is one area of research where an inherent reactivity mode of boron, 1,2-metallate rearrangement, has been

Scheme 1.2. Nomenclature of organoboron compounds



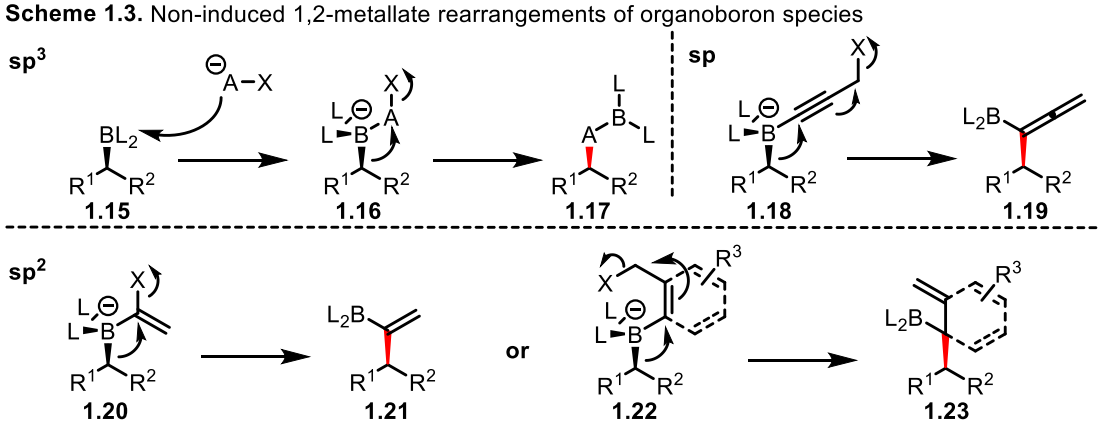
extensively employed. 1,2-Metallate rearrangement reactions of organoboron compounds have a rich history, full of elegant synthetic transformations, which offers fundamental inspiration for the development of new synthesis methods. The exploration of these transformations from a mechanistic and historical perspective will be the focus of this chapter.

1.2 Background

1.2.1 Non-Electrophile-Induced 1,2-Metallate Rearrangement

1,2-Metallate rearrangement is a reactivity mode of organoboron compounds that stems from the ability of boron to bond to two-electron donors. When a three-coordinate organoboron species accepts a nucleophile, the resulting four-coordinate boron-ate species can participate in a 1,2-metallate rearrangement in which one of the electron-rich groups on boron can migrate to an adjacent electrophilic site (hereafter referred to simply as a terminus of migration). Most commonly, the migrating group is carbon-based and the adjacent terminus of migration is a main group atom such as carbon, oxygen, or nitrogen with an appended leaving group (Scheme 1.3). In this case, the displacement of the leaving group X accompanies the formation of a new carbon-heteroatom or carbon-carbon bond.

Scheme 1.3. Non-induced 1,2-metallate rearrangements of organoboron species



This general mode of reactivity enables organoboron species to be readily transformed into a wide variety of other functional groups. When the terminus of migration is a carbon atom, a new carbon-carbon bond is formed and the boron functional group is retained in the product. While 1,2-metallate rearrangements are most commonly observed for species with sp^3-hybridized termini of migration, examples of 1,2-metallate rearrangement with sp^2 and sp-hybridized carbon groups also exist (Scheme 1.3). The examples depicted thus far are all cases of spontaneous or non-induced 1,2-metallate rearrangements in which the boron-ate intermediates engage in bond-making and bond breaking without the aid of an external activating agent.

1.2.2 Electrophile-Induced 1,2-Metallate Rearrangement

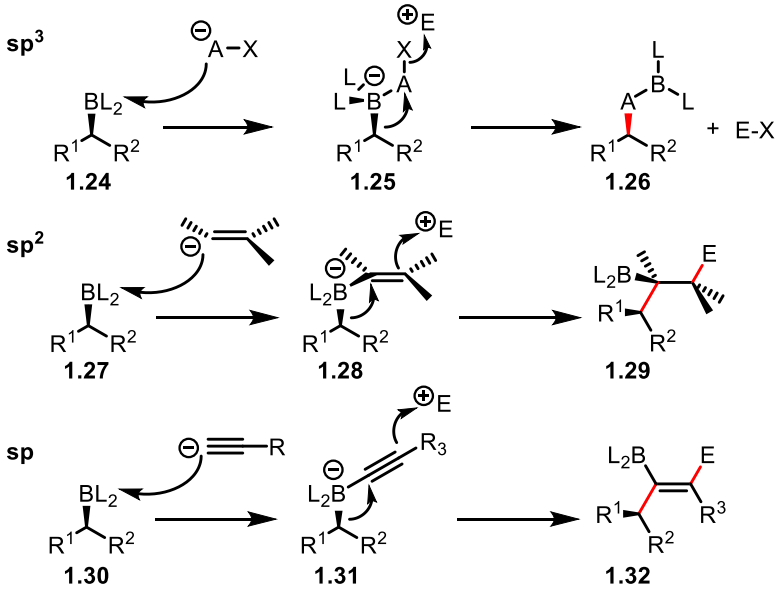
In cases where a boron-ate complex is formed which does not undergo a spontaneous rearrangement, an external electrophilic activator may be added to induce rearrangement. This situation occurs for boron-ate complexes without a good leaving group or, more frequently, for boron-ate complexes with no leaving group but with an sp^2- or sp-hybridized ligand (Scheme 1.4). In this second case, interaction of the π system with an electrophilic reagent can precipitate 1,2-metallate rearrangement, simultaneously forging a new carbon-carbon bond, while incorporating the electrophilic reagent and retaining the valuable boron functional group. In some instances the electrophilic component is subsequently eliminated, thus constituting a traceless activation strategy for carbon-carbon bond formation. The electrophile-induced rearrangement of unsaturated systems allows for the stereoselective formation of multiple bonds and thus represents an efficient strategy to rapidly construct complex carbon frameworks while incorporating valuable functional

groups.

While electrophile-induced 1,2-metallate rearrangement reactions of organoboron compounds have been known for almost as long as the 1,2-metallate rearrangement itself, this intriguing class of reaction has been far less studied than its non-induced counterpart.

This review aims to provide a historical and mechanistic perspective with which to understand 1,2-metallate rearrangement reactions mediated by electrophilic reagents and

Scheme 1.4. Electrophile-Induced 1,2-metallate rearrangements of organoboron compounds



catalysts while highlighting the enormous potential of this underexplored class of reactions. Limited examples of 1,2-metallate rearrangements involving atoms other than boron, such as copper, aluminum, and other metals will also be covered. The reactions discussed can be generally organized into three categories according to the hybridization of the terminus of migration involved (sp^3, sp^2, sp). Within each general grouping, the discussion will be organized according to the nature of the electrophilic activator employed to promote the reaction, including: (a) non-induced, (b) Lewis acid-induced, (c) carbon electrophile-induced, (d) proton-induced, (e) selenium-induced, (f) boron-induced, (g)

radical-induced, (h) halogen-induced, or the manner in which activation occurs: (i) heteroatom activation-induced. Since multiple excellent review exist on the topic, examples of non-induced 1,2-metallate rearrangement reactions will be limited to those required for historical and mechanistic discussion.

1.3 sp^3-Hybridized Terminus of Migration

1.3.1 Non-Induced Rearrangements to sp^3-Hybridized Heteroatoms

Historically, the importance of organoboron compounds has stemmed primarily from their ability to engage in carbon-boron to carbon-heteroatom substitution reactions. The ability to transform orbanoboron compounds into a wide variety of other functional groups makes methods that selectively introduce this moiety into molecular scaffolds uniquely versatile strategies to build structural complexity without sacrificing functional group diversity.

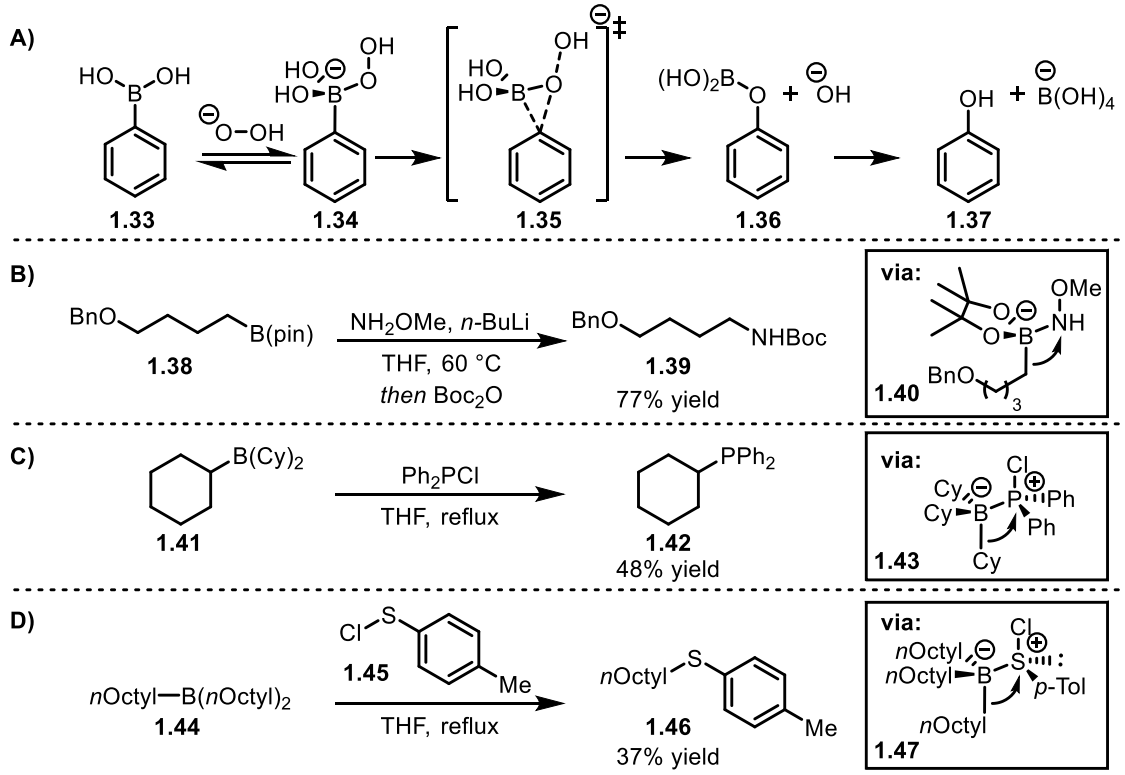
The oxidation of organoboron compounds to their corresponding alcohols is the most broadly utilized class of boron-to-heteroatom replacement reaction. In conjunction with the development of hydroboration, boron oxidation allows the conversion of alkenes to a wide variety of alcohols. The oxidation of phenylboronic acid[3] and butylboronic acid[4] by alkaline hydrogen peroxide, first developed in the 1930's, is likely the earliest example of a reaction involving 1,2-metallate rearrangement, though the nature of the mechanism would not be well understood until Kuvila's seminal mechanistic studies in the 1950's[5] (Scheme 1.5.A) This method of preparing alcohols from boronic acids and boranes was

[3] Ainley A. D.; Challenger, F. *J. Chem. Soc.* **1930**, 2171.
[4] Snyder H. K.; Kuck, J. A.; Johnson, J. R. *J. Am. Chem. Soc*. 1938, 60, 105.
[5] (a) Kuivila, H. G. *J. Am. Chem. Soc.* **1954**, 76, 870. (b) Kuivila, H. G. armour, A. G. *J. Am. Chem. Soc.* **1957**, 76, 5659. (c) Kuivila, H. G. *J. Am. Chem. Soc*. **1955**, 77, 4014.

later extended to boronic esters[6] by H. C. Brown in 1987.

In addition to oxidation, amination of boranes[7] and boronic esters[8] is well established as a method to prepare synthetically valuable alkyl and aryl amines (Scheme 1.5.B). The replacement of boron with phosphorous (Scheme 1.5.C) and sulfur (Scheme 1.5.D), though uncommon, has been demonstrated by Harpp[9] for alkyl boranes and is believed to proceed through a mechanism involving 1,2-metallate rearrangement as the key carbon-heteroatom bond forming event. The weak nucleophilicity of *para*-tolylsulfenylchloride and chlorodiphenyl phosphine towards boron likely contributes to difficulty of these reactions

Scheme 1.5. Carbon-boron to carbon-heteroatom or carbon-carbon substitution reations



[6] (a) Brown, H. C.; Snyder, C.; Rad, B. C. S.; Zweifel, G. *Tetrahedron* **1986**, 42, 5505. (b) Evans, D. A.; Weber, A. E. *J. Am. Chem. Soc.* **1987**, 109, 7151.
[7] (a) Kabalka, G. W.; Sastry, K. A. R.; McCollum, G. W.; Yoshioka, H. *J. Org. Chem*. **1981**, 46, 4296. (b) Brown, H. C.; Midland M. M.; Levy, A. B. *J. Am. Chem. Soc.*, **1973**, 95, 2394.
[8] (a) Mlynarski, S. N.; Karns, A. S.; Morken, J. P. *J. Am. Chem. Soc*. **2012**, 134, 16449. (b) Edelstein, E. K.; Grote, A. C.; Palkowitz, M. D.; Morken, J. P. *Syn. Lett.* **2018**, 29, 1749.
[9] Draper, P. M.; Chan, T. H.; Harpp, D. N. *Tetrahedron Lett.* **1970**, 11, 1687.

which have not been well explored and remain limited to trialkyl boranes. Extending these reactions to alkyl boronic esters would considerably improve their utility in organic synthesis and provide a convenient method to prepare enantioenriched chiral phosphine and sulfur-containing compounds. Reactions to replace boron with other functional groups such as halides[10], selenium[11], and metals[12] are known but proceed by different mechanisms and are thus outside the scope of this review.

1.3.2 Non-Induced Rearrangements to C(sp^3)-Hybridized Termini

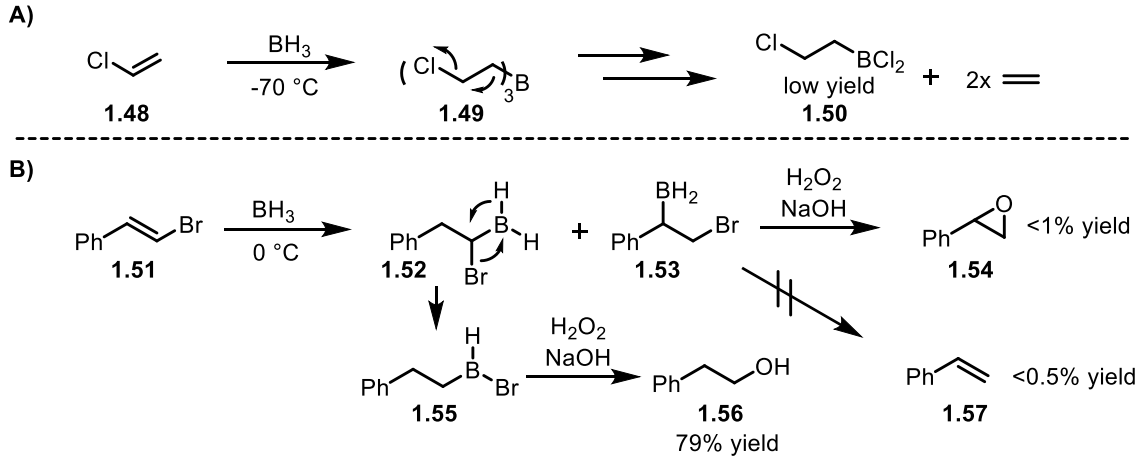
In 1958, Hawthorn and Dupont reported that treatment of vinyl chloride with borane at -80 ˚C and subsequent warming of the reaction solution to room temperature resulted in a violent reaction from which only a small amount of β-chloroethylboron dichloride (**1.50**) was recovered.[13] The authors concluded that hydroboration occurs selectively at the β-position of vinyl chloride, initially producing β-chloroethyl borane (**1.49**) which undergoes rapid thermal decomposition upon warming (Scheme 1.6.A). Subsequently, through careful product analysis Snyder and Pasto demonstrated that hydroboration of alkenyl bromides and chlorides occurs predominantly at the α-position but that these initial products are prone to undergo subsequent 1,2-metallate rearrangements in which a hydride on boron migrates to the α-boryl carbon (Scheme 1.6.B).[14] The authors suggested the

[10] (a) Brown, H. C.; De Lue, N. R.; Kabalka, G. W.; Hedgecock, H. C. Jr. *J. Am. Chem. Soc*. **1976**, 98, 1290. (b) Matteson, D. S.; Mendoza, A. *J. Organomet. Chem*. **1978**, 156, 149. (c) Lane, C. F.; Brown, H. C. *J. Am. Chem. Soc*. **1970**, 92, 7212. (d) Larouche-Gauthier, R.; Elford, T. G.; Aggarwal, V. K. *J. Am. Chem. Soc*. **2011**, 133, 16794. (e) Sandford, C.; Rasappan, R.; Aggarwal, V. K. *J. Am. Chem. Soc.* **2015**, 137, 10100.
[11] Arase, A.; Masuda, Y. *Chem. Lett.* **1976**, 1115.
[12] (a) Michaelis, A.; Bechker, P. *Chem. Ber*. **1882**, 15, 180. (b) Kondo, K.; Murahashi, S. *Tetrahedron Lett.* **1979**, 20, 1237.
[13] Hawthorne, M. F.; Dupont, J. A. *J. Am. Chem. Soc.* **1958**, 80, 5830.
[14] Pasto, D. J.; Snyder, Sr. R. *J. Org. Chem.* **1966**, 31, 2773.

earlier work reported by Hawthorn and Dupont likely occurred through a similar α-selective hydroboration and rearrangement/thermal decomposition.

Thus, Hawthorn and Dupont's inauspicious report likely constitutes the earliest 1,2-metallate rearrangement reaction of an α-haloboronate. This initial work was quickly followed in 1962 when Pasto observed that the hydroboration of ene thiol ethers resulted

Scheme 1.6. Early examples of 1,2-hydride rearrangement

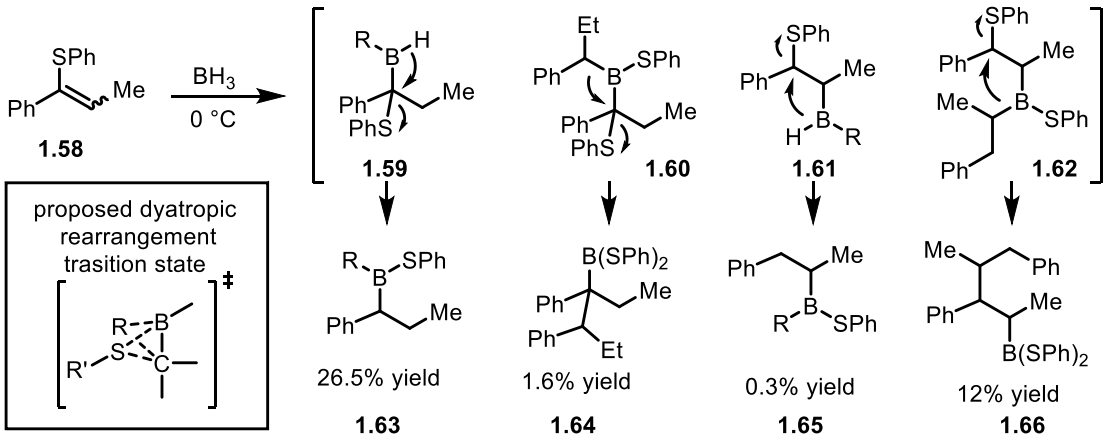


in the formation of various products consistent with 1,2 and 1,3-hydride or alkyl transfer (Scheme 1.7).[15] The authors found that hydroboration regioselectivity favored the product in which boron resides on the same carbon as the phenyl thiol group and hydride transfer was found to proceed more rapidly than alkyl transfer. In a following report[16] the author proposed a possible dyatropic transition state (inset) involving the concerted transfer of sulfur from carbon to boron and a hydride from boron to carbon.

It was not until a report by Matteson in 1963 on the 1,2-metallate rearrangement reaction of α-bromo boronic esters and Grignard reagents that a firm mechanistic understanding of this class of reaction was established.[17] Using a series of competition experiments and the

[15] Pasto, D. J. *J. Am. Chem. Soc*. **1962**, 84, 4991.
[16] Pasto, D. J.; Miesel, J. L. *J. Am. Chem. Soc.* **1963**, 85, 2118.
[17] Matteson, D. S.; Mah, R. W. H. *J. Am. Chem. Soc*. **1963**, 85, 2599.

Scheme 1.7. Early example of 1,2-rearrangement with α-thio leaving group

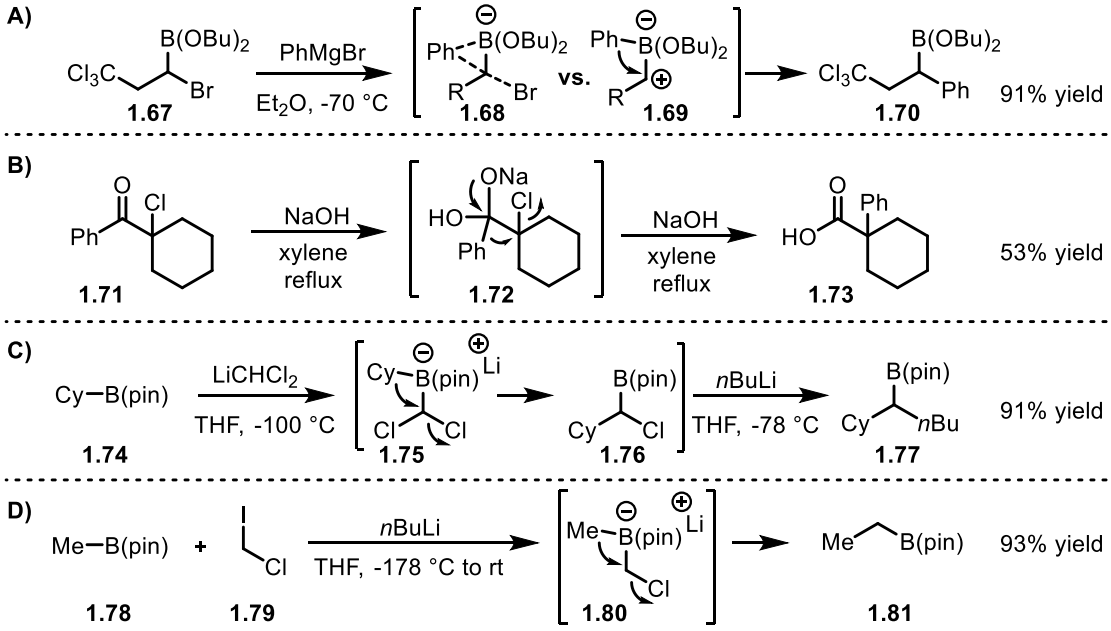


reaction of independently synthesized intermediates, Matteson demonstrated that the substitution proceeds in a concerted fashion from an initially formed boron-ate species not by direct S_N2 or by an initial C-Br ionization (S_N1) (Figure 1.8.A). Interestingly, in this seminal report Matteson did not refer to earlier reports of 1,2-metallate rearrangement reactions but cited instead the semipinacol rearrangement of chlorocyclohexylphenyl ketone (**1.71**) as a mechanistically related reaction (Scheme 1.8.B).[18]

While initial reports of nucleophilic substitution of α-halo boronic esters were mechanistically intriguing, their synthetic value was limited as methods to prepare this class of compound by radical bromination,[19] hydrohalogenation,[20] and hydroboration[21] were often inefficient and cumbersome. Matteson subsequently demonstrated a simple route to these compounds by using $LiCHCl_2$, generated *in situ* from *n*BuLi and dichloromethane. The two-step homologation and nucleophilic displacement reaction sequence allowed access to a broad variety of structures (Scheme 1.8.C).[22] In addition,

[18] Stevens, C. I.; Farkas, E., *J. Am Chem. Soc*. **1952**, 74, 5352.
[19] Matteson, D. S. *J. Am. Chem. Soc.* **1960**, 82, 4228.
[20] Matteson, D. S.; Schaumberg, G. D. *J. Org. Chem.* **1966**, 31, 726.
[21] Pasto, D. J.; Hickman, J.; Cheng, T.-C. *J. Am. Chem. Soc.* **1968**, 90, 6259.
[22] Matteson, D. S.; Majumdar, D. *J. Am. Chem. Soc.* **1980**, 102, 7588.

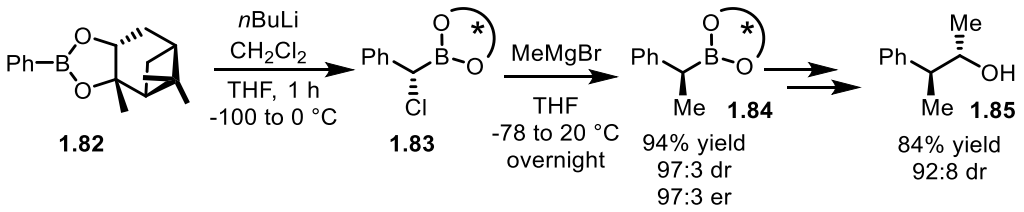
Scheme 1.8. Matteson's mechanistic studies and synthetic improvements



using $LiCH_2Cl$ allowed the direct homologation of boronic esters (Scheme 1.8.D).[23]

Matteson later demonstrated the potential of this homologation method for the stereoselective synthesis of functionalized carbon chains. By utilizing boronic esters incorporating an enantiomerically enriched pinane diol ligand he was able to demonstrate that homologation with $LiCHCl_2$, followed by treatment with Grignard reagents resulted in the formation of enantioenriched boronic ester products in excellent yields (Scheme 1.9). These products could be re-subjected to the reaction sequence to iteratively construct compounds with multiple contiguous stereocenters. While this approach has a broad scope

Scheme 1.9. Stereoselective 1,2-rearrangement reactions of organoboron compounds



[23] Sadhu, K. M.; Matteson, D. S. *Organometallics* **1985**, 4, 1687.

and has been applied to the stereoselective synthesis of natural products, being particularly useful for the preparation of chiral α-amido boronic esters,[24] it suffers from the limitation that a stoichiometric chiral director must be incorporated into the boronic ester substrate. This substrate-controlled method of boronic ester homologation is somewhat cumbersome if the preparation of multiple diasteriomers of a product is required, since a multistep diol deprotection/reprotection sequence is necessary.

An alternative strategy was developed by Hoppe[25] who demonstrated that an enantioenriched organolithium reagent can be generated by enantioselective lithiation of carbamate **1.86** in the presence of (-)-sparteine; subsequent borylation of this intermediate affords the corresponding boronic ester **1.88** with high enantioselectivity (Scheme 1.10.A). Treatment of intermediate **1.88** with isopropyl magnesium chloride led to the formation of boronic ester **1.90** *via* stereospecific 1,2-metallate rearrangement (**1.89**). In contrast to Matteson's substrate control strategy, this reagent control strategy allows the sense of chirality at each step of carbon chain extension to be controlled by the incorporation of a chiral nucleophile.

Building on work by Lee[26] and Stevens[27] who pioneered the use of sulfur[28] and nitrogen ylides as homologating reagents for organoboranes, Aggarwal has demonstrated that chiral sulfur ylides can be used as stoichiometric chiral reagents in the homologation of boranes (Scheme 1.10.B).[29] This method is restricted to boranes though it has been generalized

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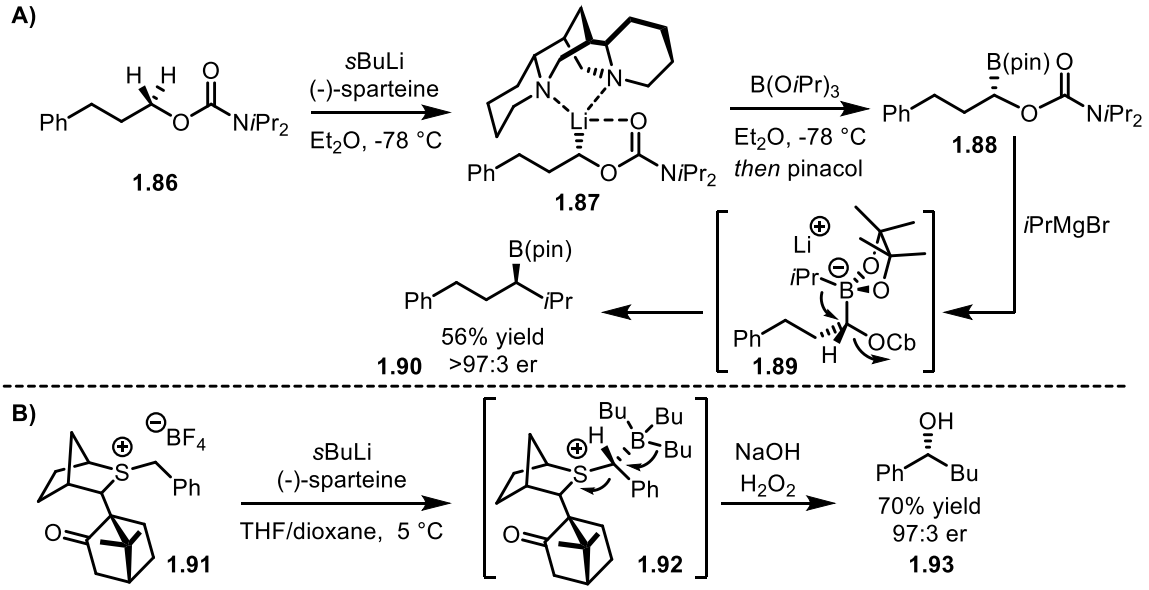
[24] Matteson, D. S. *Med. Res. Rev.* **2008,** 28, 233.
[25] Beckmann, E.; Desai, V.; Hoppe, D. *Synlett* **2004**, 13, 2275.
[26] (a) Tufariello, J. J.; Lee, L. T. C. *J. Am. Chem. Soc.* **1966**, 88, 4757. (b) Tufariello, J. J.; Lee, L. T. C.; Wojtkowski, P. *J. Am. Chem. Soc.* **1967**, 89, 6804.
[27] Musker, W. K.; Stevens, R. R. *Tetrahedron Lett.* **1967**, 11, 995.
[28] (a) For a review on sulfur ylids, see: Corey, E. J.; Chaykovsky, M, *J. Am. Chem. Soc.* **1965**, 87, 1353.
[29] (a) Aggarwal, V. K.; Fang, G. U.; Schmidt, A. T. *J. Am. Chem. Soc*. **2005**, 127, 1643. (b) Aggarwal, B. K.; Harvey, J. N; Robiette, R. *Angew. Chem. Int. Ed*. **2005**, 44, 5468.

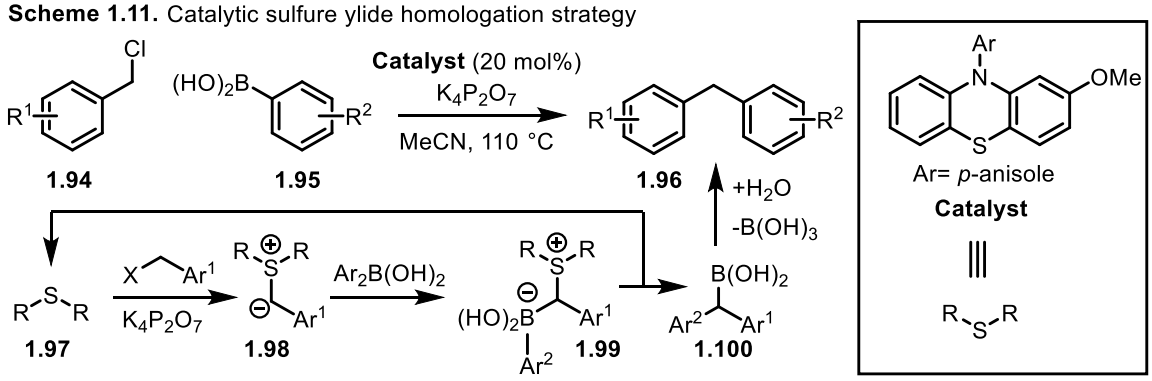
Scheme 1.10. Stereoselective 1,2-rearrangement reactions of organoboron compounds



somewhat to engage 9-BBN substrates.

Recently, Huang has demonstrated that under basic conditions in the presence of a sulfide catalysts, benzyl halides and aryl boronic acids can be coupled (Scheme 1.11).[30] The authors proposed a mechanism in which sulfur ylide **1.98** is catalytically generated from sulfide catalyst **1.97** by nucleophilic substitution and deprotonation, and after reacting with aryl boronic ester **1.95** to form boron-ate **1.99**, undergoes 1,2-metallate rearrangement to furnish secondary boronic ester **1.100**. Under basic conditions the doubly benzylic

Scheme 1.11. Catalytic sulfure ylide homologation strategy

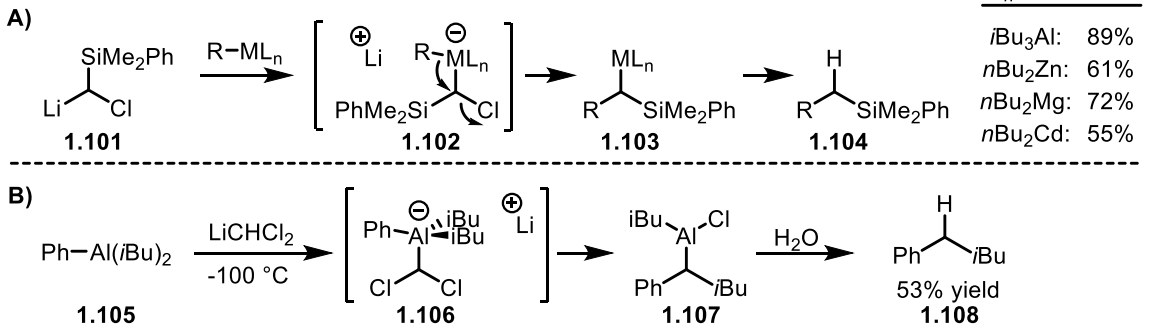


[30] He, Z.; Song, F.; Sun, h.; Huang, Y. *J. Am. Chem. Soc.* **2018**, 140, 2693.

boronic ester **1.100** undergoes protodeboration to furnish diarylmethyl product **1.96**.

It is worth noting that 1,2-metallate rearrangement reactions involving the displacement of a leaving group at an sp^3-hybridized carbon are known for atoms other than boron, including aluminum, zinc[31], magnesium, and cadmium. In 1988, Negishi reported that alkylaluminum, zinc, magnesium, and cadmium substrates, when treated with homologation reagent **1.101**, are converted to diorganometallic intermediates **1.103**, which could undergo protodemetallation (Scheme 1.12.A).[32] Kinetic analysis of the reaction of *i*Bu_3Al or Me_3Al with **1.101** showed first-order kinetics, indicating a 1,2-rearrangement mechanism rather than pathways involving direct nucleophilic displacement of the chloride of **1.101** by an alkylaluminum nucleophile (S_N2), or the formation of a carbene from **1.101** and subsequent insertion into R-MLn reagents. Finally, ^1H NMR analysis showed that upon mixing Me_3Al and **1.101**, the Me signal for Me_3Al at -1.03 ppm initially shifted to -1.24 ppm (the protons of $LiAlMe_4$ appear at -1.33) before slowly shifting back to -1.02 ppm over the course of several hours. This observation is consistent with the formation of a tetracoordinate aluminum-ate species, followed by rearrangement to form a neutral tricoordinate aluminum species. In a following report, Negishi demonstrated that other

Scheme 1.12. Homologation reactions of metals other than boron

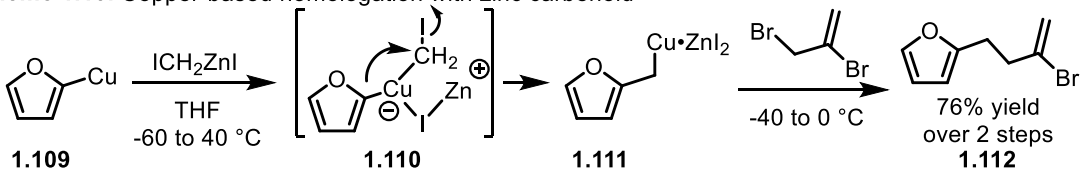


[31] For a review on sp^3-hybridized organozinc carbenoid homologation reactions, see: Marek, I. *Tetrahedron* **2002**, 58, 9463.
[32] Negishi, E.; Akiyoshi K. *J. Am. Chem. Soc.* **1988**, 110, 646.

organometallic reagents such as $Cp_2Zr(nBu)_2$, $Cp_2Hf(nBu)_2$, Ph_3V, Ph_2Cr, and $Mn(nBu)_2$ could react analogously with lithium carbenoid **1.101**.[33] Alkyltitanium, iron, cobalt, nickel, and copper species gave low yields (9-39% yield) of rearrangement product, resulting instead in homocoupling of organolithium reagent as the predominately product.

An example of an organocopper-based rearrangement utilizing the carbenoid reagent iodomethylzinc iodide was reported by Knochel (Scheme 1.13).[34] It was proposed that upon addition of 2-furylcopper **1.109** to a solution of iodomethylzinc iodide, 1,2-

Scheme 1.13. Copper-based homologation with zinc carbenoid



rearrrangement of 1,1-dimetallic intermediate **1.110** occurred, forming organocopper intermediate **1.111** which then underwent alkylation with allylbromide to give alkene **1.112** in 76% yield over two steps. A variety of other heterocyclic, carbocyclic, and alkyl organocopper reagents participated in the reaction as well sulfur and nitrogen-based nucleophiles.

1.3.3 Lewis Acid-Induced Rearrangements to C(sp^3)-Hybridized Termini

In contrast to the examples described thus far in which 1,2-rearrangement occurs spontaneously, some 1,2-metallate rearrangements employ the addition of a reagent to promote rearrangement. In situations where inherent reactivity is low due to the poor leaving group ability of the α-boryl heteroatom, a stoichiometric additive can enhance

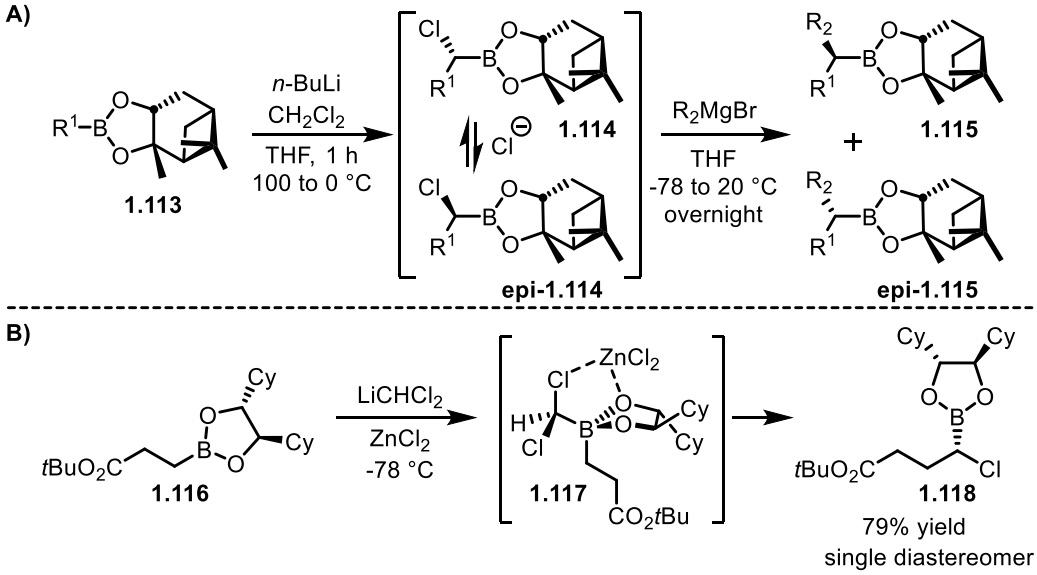
[33] Negishi, E.; Akiyoshi, K.; O'Connor, B.; Takagi, K.; Wu, G. *J. Am. Chem. Soc.* **1989**, 111, 3089.
[34] Knochel, P.; Jeong, N.; Rozema, M. J.; Yeh, M. C. P. *J. Am. Chem. Soc.* **1989**, 111, 6474.

reactivity. For 1,2-rearrangement reactions involving the displacement of a leaving group, Lewis acid additives are the most commonly employed promoters. Early reports by Matteson noted that the use of excess Grignard reagent often enhanced the efficiency of homologation reactions, presumably due to the increased concentration of endogenous $MgBr_2$. This effect was later studied by Matteson in more depth in the context of chiral diol directed homologation reactions. The addition of $ZnCl_2$ was found to enhance both yields and enantioselectivities (Scheme 1.14.A).[35] The role of $ZnCl_2$ in these cases is twofold: (1) association of chloride anion formed during the reaction (**1.113** to **1.115**) with zinc is proposed to form aggregates such as $ZnCl_2 \cdot LiCl$ that sequester chloride anion, thus minimizing epimerization of α-chloroboronic ester intermediates (**1.114** versus **epi-1.114**) by a degenerate 1,2-rearrangement with LiCl, (2), Lewis acid coordination to the α-boryl chloride leaving group of **1.114** enhances the rate of the subsequent 1.2-metallate rearrangement with organomagnesium nucleophile, thus minimizing the time in which the intermediate product **1.114** may epimerize by the previously mentioned process. This information was used to improve the synthetic procedure which was subsequently applied to the preparation of several small molecular targets.[36] Another role of $ZnCl_2$ in this class of reaction is to chelate between the chiral diol ligand and one of the chloride leaving groups, thereby enhancing the structural rigidity of the two diastereomeric transition states leading to enhanced stereoinduction.[37] (Scheme 1.14.B).

In a total synthesis of (S)-(−)-*N*-acetylcolchinol reported by Kocienski, the author demonstrated that a chiral lithiated carbamate could react directly with aryl pinacol boronic

[35] Matteson, D. S.; Erdik, E. *Organometallics* **1983**, 2, 1083.
[36] Matteson, D. S.; Sadhu, K. M. *J. Am. Chem. Soc*. **1983**, 105, 2077.
[37] Hiscox, W. C.; Matteson, D. S. *J. Organomet. Chem*. **2000**, 614, 314.

Scheme 1.14. Stereoselective $ZnCl_2$-induced 1,2-rearrangements

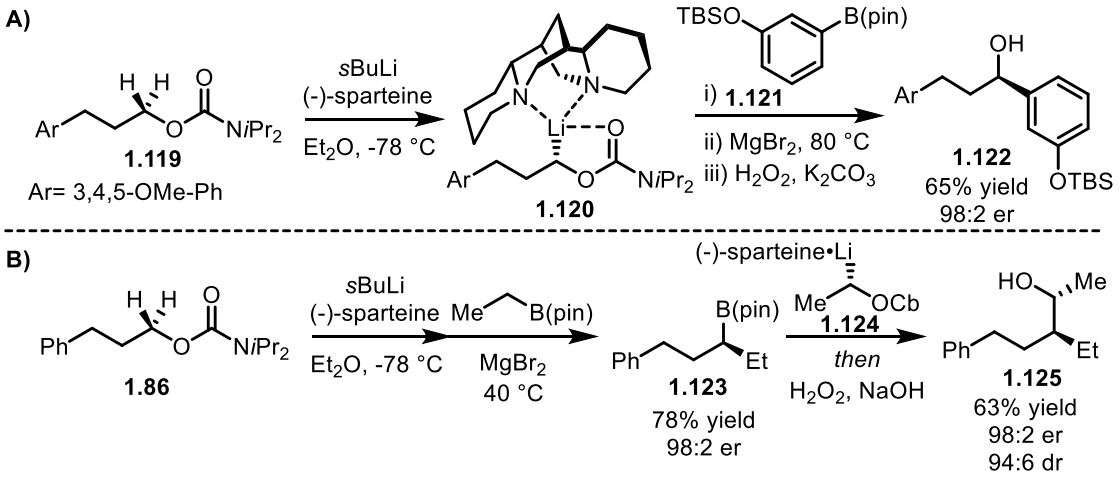


ester **1.119** (Scheme 1.15.A) to afford chiral secondary alcohol **1.122** with excellent enantioenrichment after oxidation.[38] In contrast to the two-step approach reported by Hoppe, in which an isolated boronic ester intermediate undergoes spontaneous rearrangement when treated with a Grignard reagent, in this case rearrangement required exchange of solvent, addition of magnesium bromide, and heating to 80 °C. This one-pot lithiation-borylation strategy was subsequently improved and generalized by Aggarwal who attributed the need for additional Lewis acidic $MgBr_2$ to the poor leaving group ability of the carbamate group (Scheme 1.15.B).[39] This approach was also demonstrated to be effective for consecutive homologations (**1.123** to **1.125**), enabling an iterative approach to building up functionalized carbon chains in which each stereocenter is controlled by the selection of the enantiomer of lithiated carbamate employed.

While Aggarwal initially found that the use of sterically hindered or electron-deficient

[38] Besong, G.; Jarowicki, K.; Kocienski, P. J.; Sliwinski, E.; Boyle, T. F. *Org. Biomol. Chem.* **2006**, 4, 2193.
[39] Stymiest, J. L.; Dutheuil, G.; Mahmood, A.; Aggarwal, V. K. *Angew. Chem. Int. Ed.* **2007**, 119, 7635.

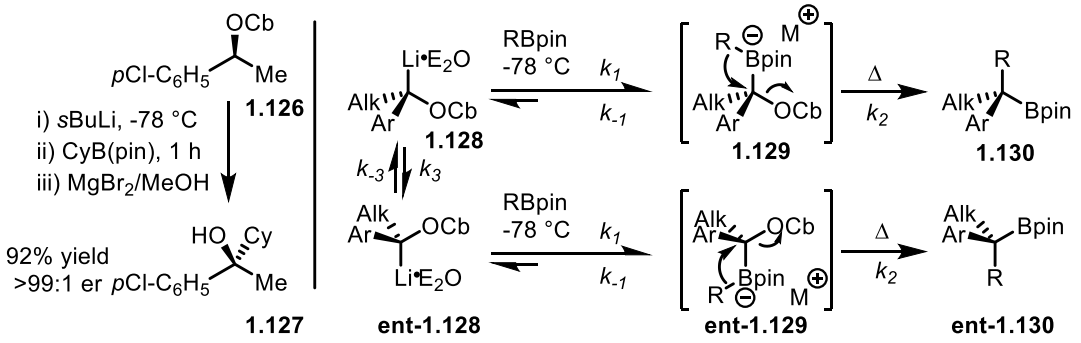
Scheme 1.15. Lithiation-borylation reactions involving $MgBr_2$-induced 1,2-rearrangements



carbamates resulted in reduced enantioselectivity in lithiation-borylation reactions[40] an in-depth study of the role of $MgBr_2$ in promoting reactivity and suppressing undesired processes was subsequently undertaken by the same authors. This led to the development of a strategy utilizing $MgBr_2$ and methanol to convert tertiary carbamates to fully substituted enantioenriched products (Scheme 1.16).[41] Using a variety of trapping experiments, it was determined that enantioenriched lithiated carbamate **1.126** undergoes racemization when the reaction with an organoboronic ester is slow. This situation was most pronounced when sterically hindered boronic esters were employed. Furthermore it was observed that the formation of boron-ate species **1.129** is a reversible process. The authors concluded that when the sterically bulky lithiated carbamate **1.128** is reacted with a sterically hindered boronic ester the rate of boron-ate formation (k_1) and the rate of rearrangement (k_2) are diminished relative to the rate of epimerization (k_3) while the rate of boron-ate reversion to lithiated carbamate **1.128** (k_{-1}) is increased. By adding a 1 M solution of $MgBr_2$ in MeOH after addition of an organoboronic ester to lithiated carbamate

[40] Stymiest, J. L.; Bagutski, V..; French, R. S.; Aggarwal, V. K. *Nature* **2008**, 456, 778.
[41] Bagutski, V.; French, R. M.; Aggarwal, V. K. *Angew. Chem. Int. Ed*. **2010**, 49, 5142.

Scheme 1.16. Mechanistic study of lithiation-borylation reactions of tertiary carbamates

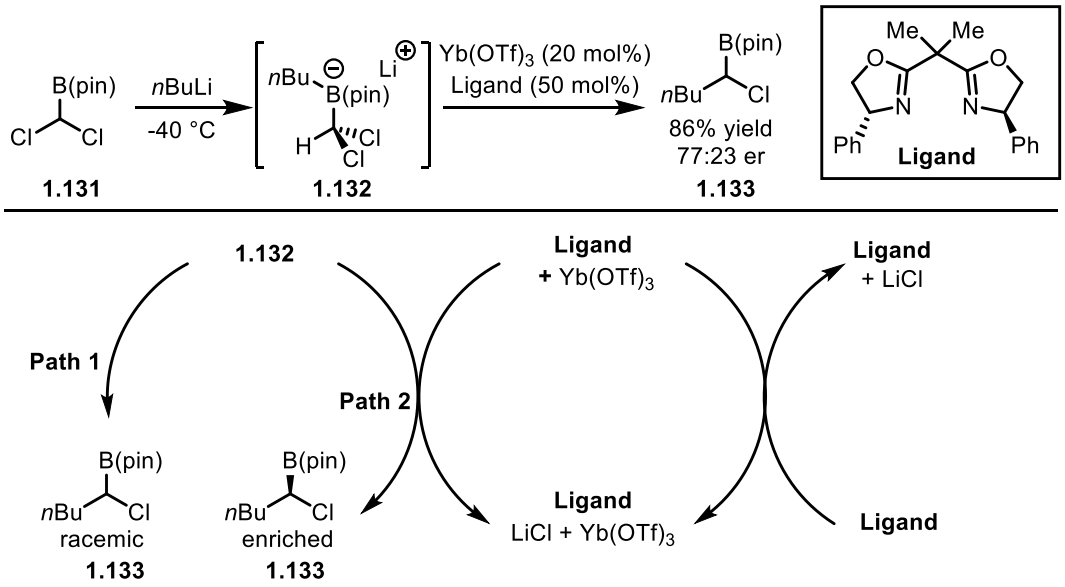


1.128 excellent yields and enantioselectivities were observed. The authors proposed that $MgBr_2$ enhances the rate of rearrangement (k_2) relative to the rate (k_{-1}) of reforming lithiated carbamate **1.128**, and that MeOH is capable of rapidly protonating any lithiated carbamate present in the reaction solution.

In addition to the substrate and reagent control strategies for stereoselective organoboronate rearrangements pioneered by Matteson and Hoppe/Aggarwal respectively, an intriguing example of enantioselective rearrangement reaction controlled by a chiral Lewis acid catalyst was reported by Jadhav (Scheme 1.17).[42] In a brief report, the authors demonstrated that addition of *n*BuLi to 1,1-dichloromethylboronic pinacol ester **1.131**, followed by addition of a Lewis acid and chiral bis-oxazoline ligand, resulted in the formation of enantioenriched α-chloroalkylboronic ester **1.133**. A survey of several combinations of Lewis acids and chiral bis-oxazoline ligands resulted in the identification of $Yb(OTf)_3$ and PhBox ligand (inset) as an effective catalyst combination. Unfortunately, the enantioselectivies obtained for this reaction were somewhat low when catalytic amounts of Lewis acid and chiral ligand were used. A combination of 20 mol% $Yb(OTf)_3$ and 50 mol% PhBOX resulted in the formation of product in 86% yield with 77:23 er. By

[42] Jadhav, P. K.; Man, H.-W. *J. Am. Chem. Soc.* **1997**, 119, 846.

Scheme 1.17. Catalytic enantioselective chiral Lewis acid-catalyzed 1,2-rearrangement

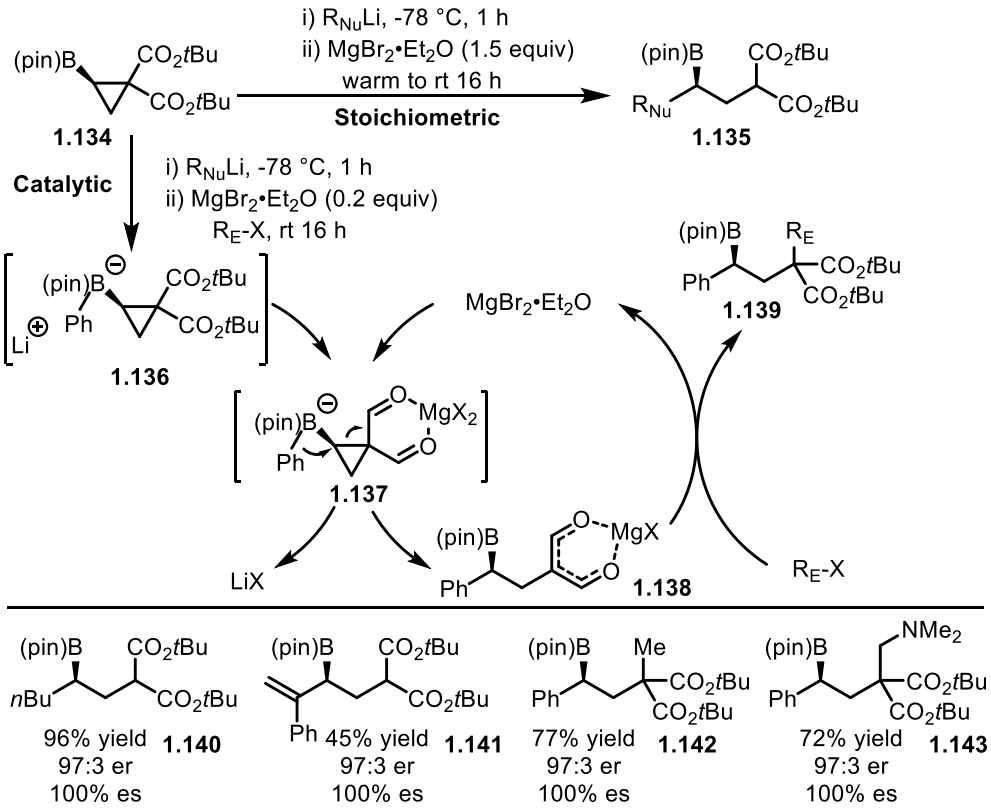


increasing the amount of $Yb(OTf)_3$ to 30 mol% and employing 5.0 equivalents of ligand, the enantioselectivity could be improved to 94:6 er. The authors attributed low product enantioenrichment to the existence of a competing background reaction catalyzed by unligated $Y(OTf)_3$ and LiCl (Path 1). Despite the clear limitations of the reported method, it provides a proof of concept that a catalytic amount of a chiral Lewis acid can discriminate between the two enantiotopic leaving groups of a boron-ate complex, facilitating an enantioselective 1,2-metallate rearrangement to furnish an enantioenriched α-chloroboronic ester.

Aggarwal recently demonstrated that stoichiometric or catalytic amounts of $MgBr_2$ can facilitate the stereospecific 1,2-metallate rearrangement-ring opening of chiral donor-acceptor type cyclopropyl boronic pinacol esters to furnish enantioenriched γ-boryl malonates (Scheme 1.18).[43] The ring-opening-protonation reaction utilizes stoichiometric $MgBr_2$ (**1.134** to **1.135**) and is proposed to proceed by the addition of an organolithium

[43] Gregson, C. H. U.; Ganesh, V.; Aggarwal, V. K. *Org. Lett.* **2019**, 21, 3412.

Scheme 1.18. Stereospecific $MgBr_2$-catalyzed 1,2-rearrangement of DA-cyclopropylboronic esters



nucleophile to chiral cyclopropyl ester **1.134**, forming boron-ate complex **1.136**, which then associates with $MgBr_2$, forming **1.137**. **1.137** Then undergoes a stereospecific 1,2-metallate rearrangement to form enolate intermediate **1.138** which is protonated either *in situ* or during workup. While the cyclopropane ring strain provides a significant driving force, the authors argue that it is the Lewis acid coordination to the dicarbonyl moiety and the resulting anionic charge stabilization that enables 1,2-metallate rearrangement to occur. The reaction proceeds with both alkyl and aryl migrating groups. Notably, alkenyl groups also participate in this rearrangement reaction, generating valuable enantioenriched allylic boronic esters. Due to $MgBr_2$ sequestration with intermediate **1.138** 1.5 equivalents of $MgBr_2$ were required to obtain optimal yields in the rearrangement-protonation reaction. However, the addition of two equivalents of electrophile (MeI, allylBr, and Eschenmoser's

salt) subsequent to formation of boron-ate allowed the reaction to be run as a catalytic three-component process, utilizing 20 mol% $MgBr_2$. The electrophilic trapping of enolate **1.138** presumably facilitates turnover of $MgBr_2$. While only three examples of this three-component reaction were reported, they represent rare examples of a stereospecific 1,2-metallate rearrangement reaction promoted by catalytic amounts of a Lewis acid.

In addition to Lewis acids such as $ZnCl_2$, $Yb(OTf)_3$, and $MgBr_2$, TMSOTf has been found to enhance the leaving group ability of α-boryl heteroatoms. Aggarwal has reported that the addition of TMSOTf enables the lithiation-borylation strategy originally developed for *O*-linked carbamates, to be extended to *N*-linked carbamates (Scheme 1.19).[44] The authors found that the previously developed lithiation-borylation conditions utilizing $MgBr_2$ were not effective for Boc-protected benzylamine **1.144,** presumably due to the poorer leaving group ability of the *N*-linked carbamoyl group compared to the *O*-linked group. The stoichiometric addition of TMSOTf was found to promote rearrangement of intermediate boron-ate species **1.146**, which can be generated from *N*-linked carbamate **1.144** upon enantioselective deprotonation and trapping with a trialkylborane.[45] Interestingly, it was observed that both trapping of lithiated benzylamine **1.145** by trialkylborane as well as the subsequent 1,2-rearrangement proceeded with inversion, resulting in a net stereoretentive lithiation-borylation process. The enhanced ability of TMSOTf to promote 1,2-rearrangement relative to $MgBr_2$ can likely be attributed to the greater oxophilicity of TMSOTf leading to greater charge stabilization during the 1,2-rearrangment step (inset, Scheme 1.19). The inability to engage less reactive boronic ester

[44] Coldham, I.; Patel, J. J.; Raimbault, S.; Whittaker, D. T. E.; Adams, H.; Fang, G. Y.; Aggarwal, V. K. *Org. Lett.* **2008**, 10, 141.
[45] (a) Park, Y. S.; Boys, M. L.; Beak, P. *J. Am. Chem. Soc*. **1996**, 118, 3757. (b) Faibish, N. C.; Park, Y. S.; Lee, S.; Beak, P. *J. Am. Chem. Soc*. **1997**, 119, 11561.

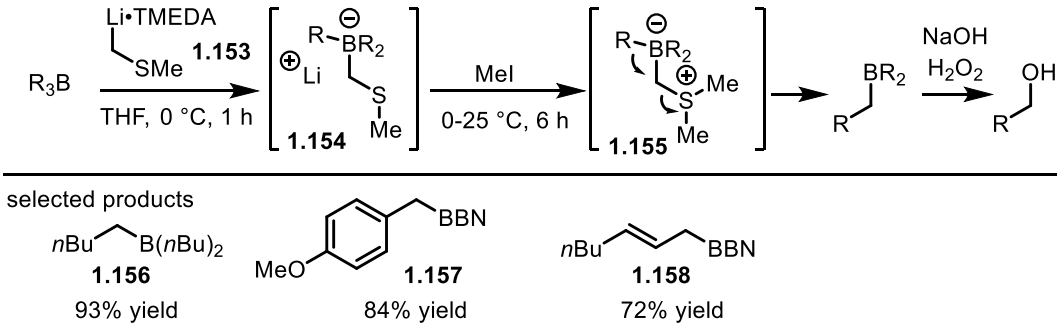
starting materials limited the substrate scope to trialkyl boranes, but good yields and selectivities were obtained for several benzylic carbamates (**1.148** to **1.150**). Additionally, it was demonstrated that Boc-protected pyrrolidine and indoline substrates could be engaged effectively (**1.151** and **1.152**), suggesting this method may be applicable as a late-state diversification strategy.

1.3.4 Proton- and Carbon-Electrophile-Induced Rearrangements

In addition to Lewis acid-induced rearrangements of α-halo organoboronic esters, the covalent activation of organoboron compounds with α-heteroatom substituents by carbon-based electrophiles or Brønsted acids has also been demonstrated. An excellent example of the potential advantages offered by an electrophile-induced rearrangement strategy in comparison to analogous spontaneous rearrangement reactions is illustrated by a report by Negishi on the homologation reaction of boranes utilizing α-lithiated thioether **1.153** and methyl iodide (Scheme 1.20).[46] The authors found that treatment of trialkylboranes with **1.153** resulted in the formation of α-thioorganoboron-ate complex **1.154**. In contrast to the reaction of trialkyl boranes with sulfur ylides, boron-ate **1.154** did not undergo spontaneous rearrangement at 0 ˚C and could be observed using ^{1}H NMR spectroscopy. Addition of an electrophilic reagent such as methyl iodide to the otherwise stable boron-ate species was found to promote the formation of the corresponding homologated borane. The authors proposed that the electrophilic reagent alkylates the sulfur atom (**1.154** to **1.155**), thereby increasing its leaving group ability and precipitating 1,2-rearrangement of the boron-ate complex. Perhaps owing to the greater nucleophilicity and smaller steric profile of α-

[46] Negishi, E.; Yoshida, T.; Silveira, A.; Chiou, B. L. *J. Org. Chem.* **1975**, 40, 814.

Scheme 1.20 Methyl iodide-induced 1,2-rearrangement of α-boryl thioether



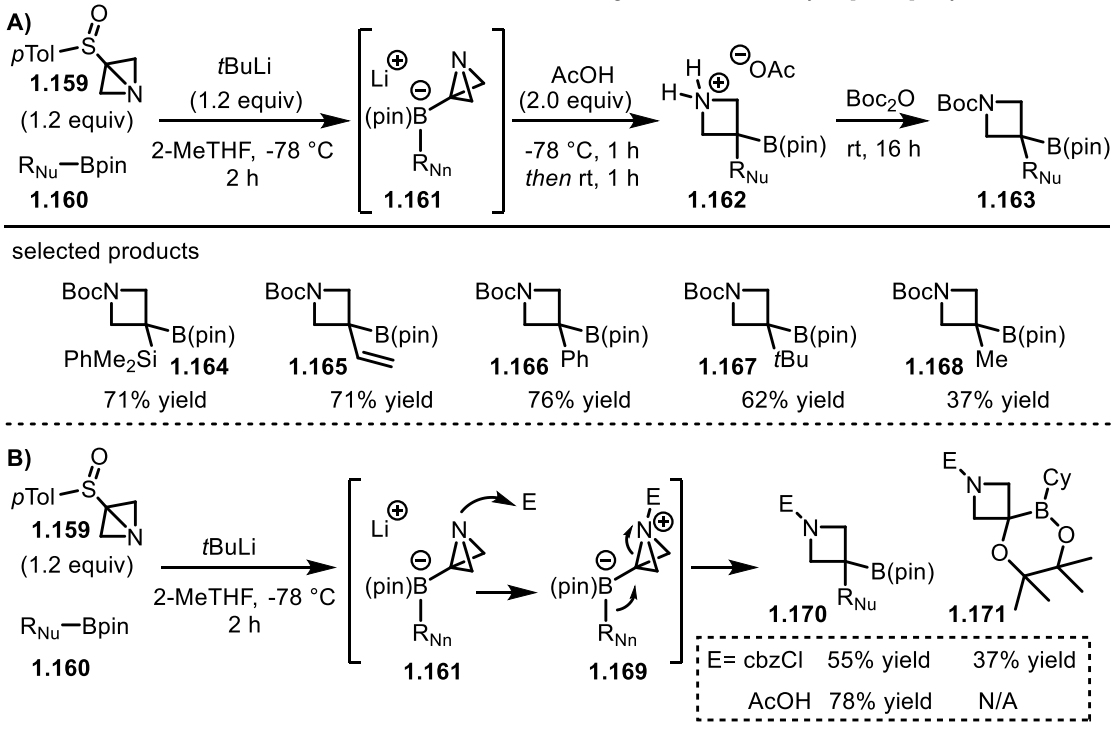
lithiated thioether **1.153** relative to the corresponding sulfur ylide, this method of one-carbon homologation of boranes was found to be less sensitive to steric factors than the corresponding method using sulfur ylides. Additionally, because the boron-ate formation and 1,2-metallate rearrangement steps are decoupled in the electrophile-induced strategy, undesired multiple homologation products were not observed. This method was found to be effective for a variety of primary (**1.156**) and secondary (**1.157**) alkylboranes, as well as aryl- and alkenyl-9-BBN substrates, the latter granting first-ever access to stereochemically defined allylic-9-BBN reagents **1.158**.

Aggarwal has recently reported a proton-induced 1,2-metallate rearrangement reaction of strained azabicyclo[1.1.0]butane-derived boron-ate complexes to produce substituted azetadines (Scheme 1.21.A).[47] The authors found that, in contrast to boron-ate complexes derived from boronic esters and lithiated epoxides[48] or aziridines,[49] boron-ate complex **1.161** did not undergo spontaneous rearrangement despite the considerable ring strain build into the azabicyclo[1.1.0]butyl group. The persistence of **1.161** was attributed to the poor leaving group ability of a secondary alkyl amine anion relative to a primary alkoxy or Boc-protected amine. It was found that after the formation of **1.161**, the addition of two

[47] Fawcett, A.; Murtaza, A.; Gregson, C. H. U.; Aggarwal, V. K. *J. Am. Chem. Soc.* **2019**, 141, 4573.
[48] Vedrenne, E.; Wallner, O. A. Vitale, M.; Schmidt, F.; Aggarwal, V. K. *Org. Lett.* **2009**, 11, 165.
[49] Schmidt, F.; Keller, F.; Vedrenne, E.; Aggarwal, V. K. *Angew. Chem. Int. Ed*. **2009**, 48, 1149.

equivalents of acetic acid induced 1,2-rearrangement and furnished azetedine boronic ester **1.162**. This isolable salt could then be used in further transformations such as acylation or Buchwald–Hartwig cross-coupling. This reaction was found to be general with respect to the nature of the boronic ester groups that could be engaged. Aryl-, alkyl-, and alkenylboronic pinacol esters could be successfully employed, though primary alkylboronic esters result in somewhat reduced yields. Interestingly, dimethylphenylsilylboronic ester was successfully employed in the reaction, furnishing geminal diorganometallic **1.164**. Notably, carbon-based electrophiles such as benzyl chloroformate, while effective at inducing rearrangement resulted in an inseparable mixture of products resulting from both carbon and oxygen migration (Scheme 1.21.B). This result is consistent with a scenario in which electrophilic activation of boron-ate **1.161** produces an activated complex **1.169** in which the steric and electronic nature of the electrophile (proton versus acyl) control the relative orientation of the B-C and B-O bond

Scheme 1.21. Heteroatom activation-induced 1,2-rearrangements of azabicyclo[1.1.0]butylborates

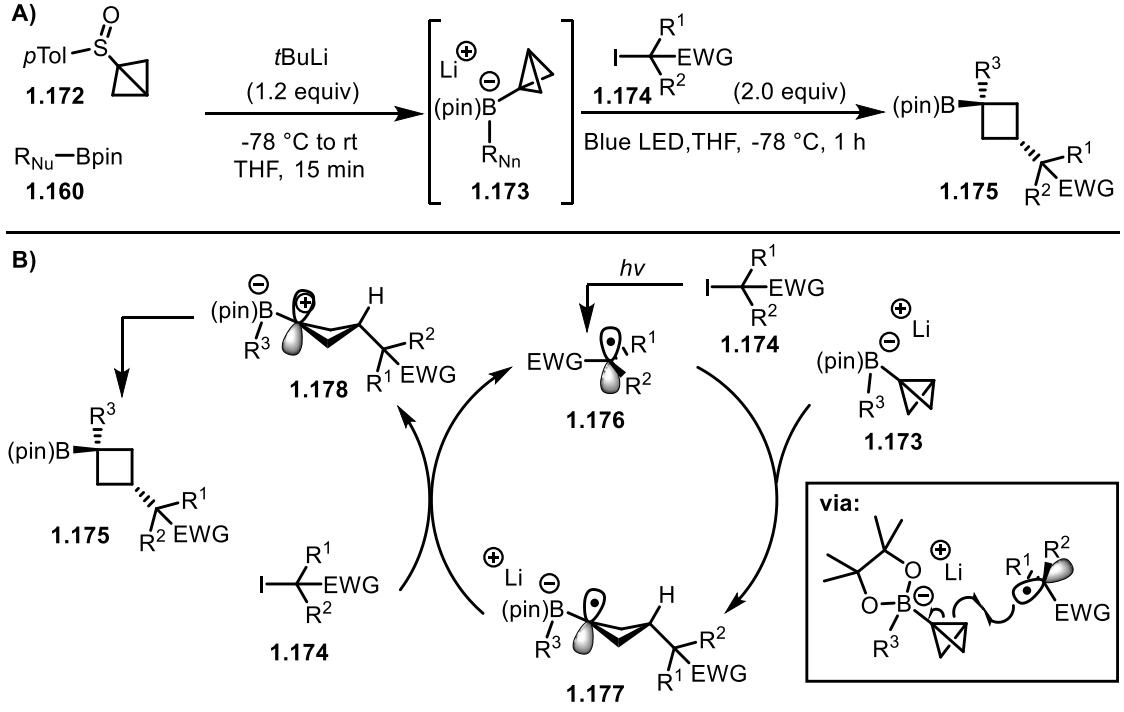


with respect to the $\sigma^*_{C\text{-}N}$ orbital. The ability of the activating agent to control carbon versus oxygen migration highlights the potential of the electrophile-induced rearrangement strategy to tune the chemoselectivity of 1,2-metallate rearrangement reactions.

1.3.5 Radical-Induced Rearrangements

Inspired by recently developed radical-induced 1,2-metallate rearrangement reactions of alkenylboron-ate complexes (discussed in section 1.4.8), Aggarwal recently reported the first example of a radical-induced 1,2-metallate rearrangement reaction involving the rupture of a C-C σ-bond (Scheme 1.22.A).[50] Employing a similar strain release approach as in the previous proton-induced rearrangement reaction of azabicyclo[1.1.0]butyl boron-ate complexes, the authors found that electrophilic carbon-centered radicals were capable

Scheme 1.22. Aggarwal's radical-induced 1,2-rearrangement of strained bicyclobutyl boron-ate complexes



[50] Silvi, M.; Aggarwal, V. K. *J. Am. Chem. Soc.* **2019**, 141, 9511.

of inducing the rearrangement reaction of strained bicyclobuty boron-ate complexes **1.173**, thereby furnishing substituted cyclobutane products **1.175**. While products were obtained in racemic form, the reaction was found to take place with a high degree of diastereoselectivity in most cases. As depicted in Scheme 1.22.B, the authors proposed that the reaction proceeds by a pathway which is mechanistically aligned with radical-polar crsossover reactions of alkenylboron-ate complexes in which radical addition (inset) generates an α-boryl radical species **1.177** which undergoes single-electron oxidation to form zwiterionic species **1.178**. Intermediate **1.178** subsequently rearranges, producing product **1.175**. The prospect of generalizing this approach to C-C σ-bond difunctionalization reactions of less strained substrate classes promises to provide access to diverse aliphatic organoboron compounds.

1.4 sp^2-Hybridized Terminus of Migration

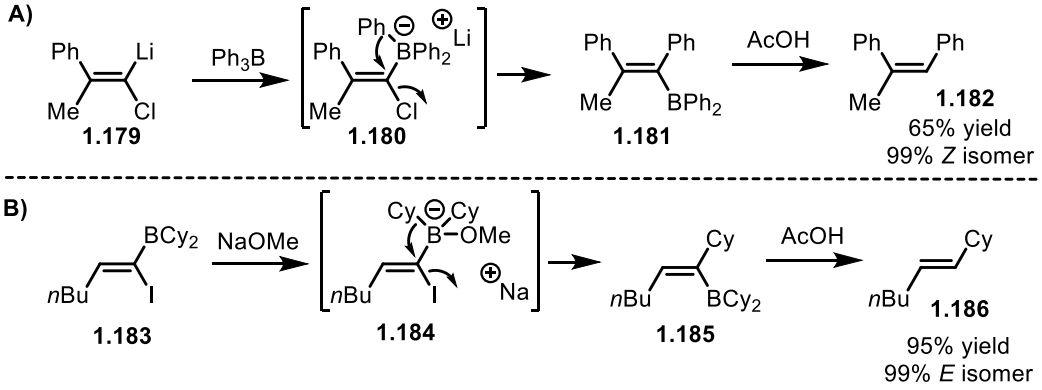
1.4.1 Non-Induced Rearrangements

In 1967, Merkle reported that treatment of triphenylborane with 1-chloro alkenyllithium **1.179** and subsequent protonolysis with acetic acid resulted in the isolation of *Z* alkene **1.182** (Scheme 1.23.A).[51] The authors proposed a mechanism in which initially formed boron-ate complex **1.180** undergoes 1,2-rearrangement displacing a chloride leaving group with inversion at the adjacent sp^2-hybridized carbon. In the same year, Zweifel reported a similar reaction in which treatment of 1-iodo hexenylborane **1.183** with sodium methoxide resulted in the formation of *E* olefin **1.186** after protonolysis with acetic acid (Scheme

[51] (a) Köbrich, G.; Merkle, H. R. *Angew, Chem. Int. Ed*. **1967**, 6, 74. (b) Köbrich, G.; Merkle, H. R. *Chem. Ber*. **1967**, 100. 3371.

1.23.B). [52] While the concerted nucleophilic displacement of a leaving group at an sp^2-hybridized carbon may seem unusual, such mechanisms are known for alkenyl and aryl[53] halides, as well as for acyl[54] transfer reactions. Following these initial publications, Zweifel

Scheme 1.23. First examples of non-induced 1,2-rearrangements of alkenyl boronates



demonstrated that 1,2-rearrangement in this class of reaction, as with reactions involving sp^3-hybridized termini of migration, occurs with retention at the migrating carbon and inversion at the terminus of migration (Scheme 1.24.A).[55] Corey subsequently demonstrated that this type of reaction might serve as a stereospecific approach to constructing chiral prostaglandins (Scheme 1.24.B).[56] Negishi further demonstrated the potential synthetic utility of this method for the general and stereoselective preparation of *trans-trans* dienes by a sequence of stereoselective hybroborations, stereospecific 1,2-rearrangement, and protodeboration (Scheme 1.24.C).[57]

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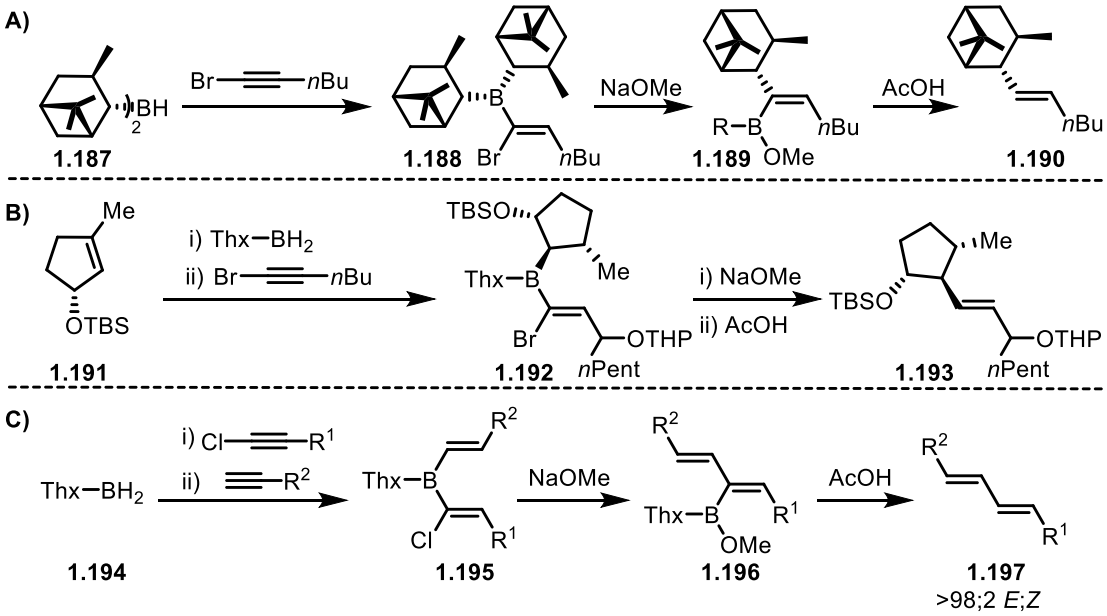
[52] Lucchini, V.; Modena, G.; Pasquato, L. *J. Am. Chem. Soc*. **1993**, 115, 4527. (b) Glukhovtsev, M. N.; Pross, A.; Radom, L. *J. Am. Chem. Soc.* **1994**, 116, 5961. (c) Lucchini, V.; Modena, G.; Pasquato, L. *J. Am. Chem. Soc.* **1995**, 117, 2297. (d) Okayama, T.; Takino, T.; Sato, K.; Ochiai, M. *J. Am. Chem. Soc.* **1998**, 120, 2275. (e) Bach, R. D.; Baboul, A. G.; Schlegel, H. B. *J. Am. Chem. Soc.* **2001**, 123, 5787.
[53] (a) Sun, H.; DiMagno, S. *Angew. Chem. Int. Ed.* **2006**, 45, 2720. (b) Neumann, C. N.; Hooker, J. M.; Ritter, T. *Nature* **2016**, 534, 369. (c) Neumann, C. N.; Ritter, T. *Acc. Chem. Res.* **2017**, 50, 2822. (d) Kwan, E. E.; Zeng, Y.; Besser, H. A.; Jacobsen, E. N. *Nat. Chem.* **2018**, 10, 917.
[54] (a) Williams, A. *Acc. Chem. Res*. **1989**, 22, 387. (b) Curran, T. P.; Farrar, C. R.; Niazy, O.; Williams, A. *J. Am. Chem. Soc.* **1980**, 102, 6828. (c) Chrystiuk, E.; Williams, A. *J. Am. Chem. Soc.* **1987**, 109, 3040.
[55] G. Zweifel, G.; Fisher, R. P.; Snow, J. T.; Whitney, C. C. *J. Am. Chem. Soc*. **1971**, 93, 6309.
[56] Corey, E. J.; Ravindranathan, T. *J. Am. Chem. Soc*. **1972**, 94, 4013.
[57] Negishi, E.; Yoshida, T. *J. Chem. Soc. Chem. Commun*. **1973**, 606.

Scheme 1.24. Early reports of non-induced 1,2-rearrangement reactions



In addition to 1,2-metallate rearrangement reactions of alkenylboron species, similar non-induced reactions have been reported for copper,[58] aluminum,[59] lithium,[60] zirconium[61] and zinc.[62] Of these, copper-based rearrangement reactions have been the most commonly employed in organic synthesis.[63]

1.4.2 Lewis Acid-Induced Rearrangements to C(sp^2)-Hybridized Termini

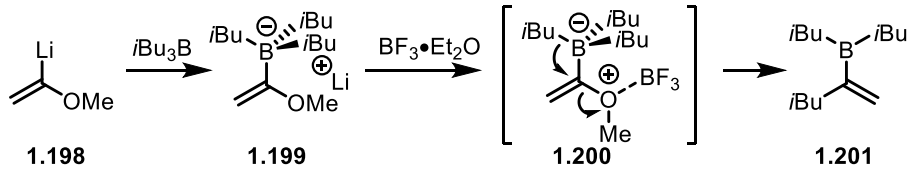
In 1978, Levy reported that the addition of $BF_3 \cdot Et_2O$ to alkenylboron-ate complexes such as **1.199** (derived from trialkylboranes and lithiated methyl vinyl ether **1.198**) could be successfully used as a means to prepare α-substituted alkenylboranes **1.201** (Scheme

[58] (a) Posner, G. H.; Loomis, G. L.; Sawaya, H. S. *Tetrahedron Lett*. **1975**, 1373. (b) Fujisawa, T. Kurita, Y. Kawashima, M.; Sato, T. *Chemistry Letters*, **1982**, 1641. (c) Kocienski, P.; Wadman, S. *J. Am. Chem. Soc.* **1989**, 11, 2363. (d) Kocienski, P.; Barber, C.; *Pure Appl. Chem*. **1990**, 62, 1933.
[59] Miller, J. A. *J. Org. Chem.* **1989**, 54, 998.
[60] Duraisamy, M.; Walborsky, H. M. *J. Am. Chem. Soc.*, **1984**, 106, 5035.
[61] (a) Sastry, G. N.; Jemmis, E. D. *J. Organomet. Chem.* **1990**, 388, 289. (b) Mintz, E. A.; A. S. Ward, *J. Organomet. Chem*. **1986**, 306, C52. 24. (c) Erker, G.; Petrenz, R. *J. Chem. Soc. Chem. Commun.* **1989**, 345.
[62] Harada, T.; Hara, D.; Hattori, K; Oku, A. *Tetrahedron Lett*. **1988**, 29, 3821.
[63] (a) Fujisawa, T. Kurita, Y. Kawashima, M.; Sato, T. *Chem. Lett.* **1982**, 1641. (b) Kocienski, P.; Wadman, S. *J. Am. Chem. Soc.* **1989**, 11, 2363. (c) Kocienski, P.; Barber, C. *Pure Appl. Chem.* **1990**, 62, 1933.

1.25).[64]

Soderquist subsequently demonstrated that the same type of boron-ate complexes are stable under ambient temperatures but when activated with TMSCl readily rearrange

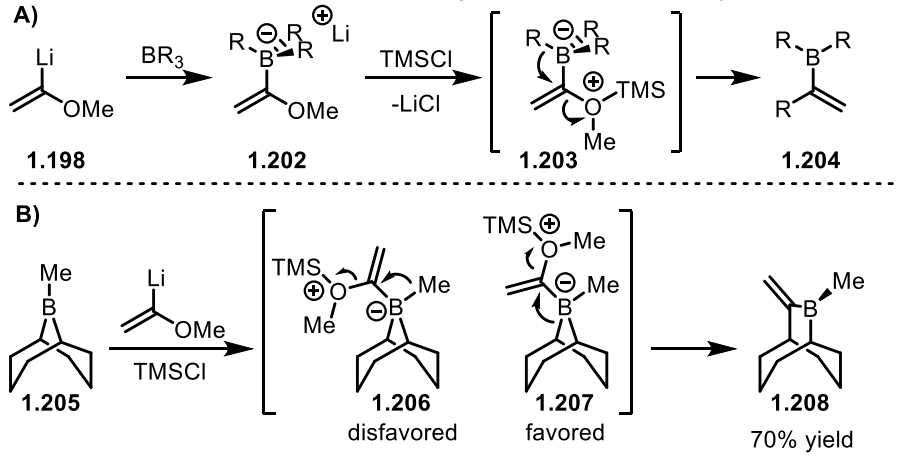
Scheme 1.25. BF_3-induced 1,2-rearrangement reaction of alkenyl boron-ate complex



1.198 **1.199** **1.200** **1.201**

(Scheme 1.26.A).[65] The use of 9-alkyl-BBN reagents in place of other trialkyboranes was found to lead exclusively to the ring expanded product **1.208.** The authors attribute this outcome to unfavorable steric interaction between the activated methoxy leaving group in the boron-ate conformer leading to alkyl migration compared to ring expansion (**1.206** versus **1.207**) (Scheme 1.26.B).

Scheme 1.26. TMSCl-induced 1,2-rearrangement reaction of alkenyl boron-ate complexes



[64] Levy, A. B.; Schwartz, S. J.; Wilson N.; Christie, B. *J. Organomet. Chem.* **1978**, 156, 123.
[65] Soderquist, J. A.; Rivera, I. *Tetrahedron Lett.* **1989**, 30, 3919.

1.4.3 Halogen-Induced Rearrangements

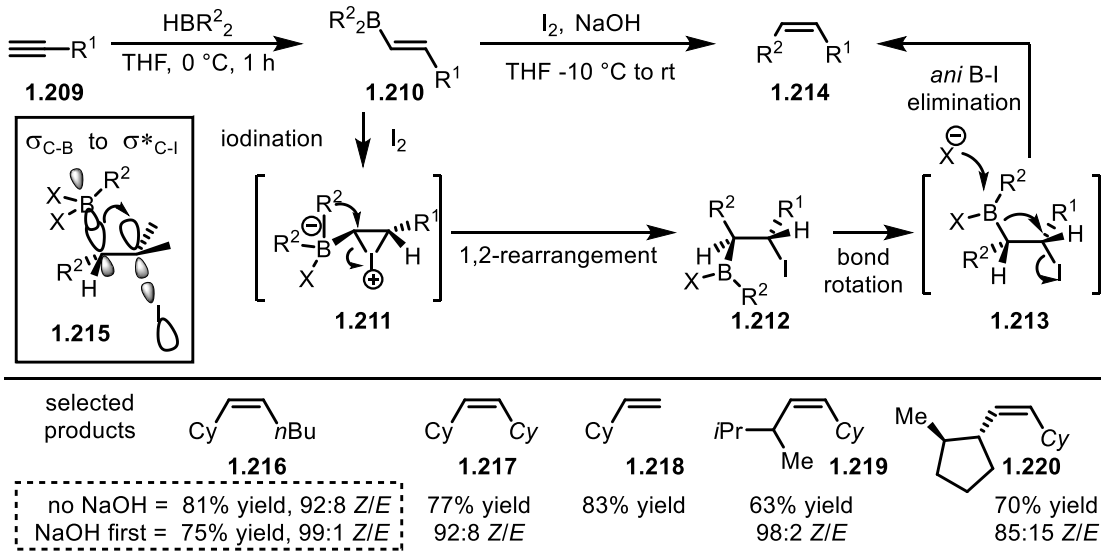
In cases where the sp^2-hybridized carbon attached to boron lacks a leaving group, rearrangement can be induced with the addition of an electrophilic activating agent which interacts with the π-system, inducing rearrangement. This mode of activation, in contrast to a leaving group activation strategy, results in the incorporation of the electrophilic component into the reaction product and thus offers the opportunity to construct multiple bonds simultaneously. In cases where the electrophilic component undergoes elimination subsequent to rearrangement, the sequence of electrophilic activation, rearrangement, and elimination constitutes a boron-mediated coupling of two organic fragments with a traceless electrophilic activator. For cases where elimination does not occur, the predominately stereospecific nature of 1,2-metallate rearrangements, combined with the potential for concomitant addition of nucleophile and electrophile across the double bond presents the possibility of stereoinduction by facially-selective alkene activation.

1.4.3.1 Zweifel-Evans Olefination

The first example of an electrophile-induced boronate rearrangement to an sp^2-hybridized carbon was reported by Zweifel in 1967 (Scheme 1.27).[66] In this seminal report, the authors noted that the addition of iodine to a THF solution of alkenylborane **1.210** and sodium hydroxide resulted in the formation of *Z*-alkene **1.214** in high yields and isomeric purity. In the IR spectrum the absorption band associated with the alkene double bond (1604 cm^{-1}) of **1.210** disappeared upon adding a stoichiometric amount of iodine. Additionally, ^1H NMR analysis of an organoborane-iodine solution of alkenylboron **1.210**

[66] Zweifel, G.; Arzoumanian, H.; Whitney, C. C. *J. Am. Chem. Soc.* **1967**, 89, 3652.

Scheme 1.27. Zweifel's seminal report of *Z*-selective, iodine-induced olefination



(R^1= *n*Bu, R^2=Cy) revealed that 1-cyclohexyl-1-hexene was formed in 81% yield and 92:8 *Z*/*E* selectivity during the iodination step before workup, but that addition of NaOH to the boronate solution prior to addition of iodine resulted in superior *Z*/*E* selectivity. The authors proposed a mechanism in which alkenylborane **1.210** is activated by iodine and a Lewis base (iodide or hydroxide) to form boron-ate complex **1.211**, which then undergoes 1,2-metallate rearrangement to produce β-iodo borane **1.212**. Upon base-assisted *anti* boron-iodide elimination, compound **1.212** furnishes *Z*-alkene **1.214**. The transformation was found to be relatively general, furnishing mono-, di-, and trisubstituted alkenes. This method was later demonstrated to be stereoretentive with respect to the migrating carbon.[67] The stereospecific nature of *anti* B-I elimination is a product of the stereochemical requirements to achieve $\sigma_{C\text{-}B}$ to $\sigma^*_{C\text{-}B}$ electron donation (inset, **1.215**).

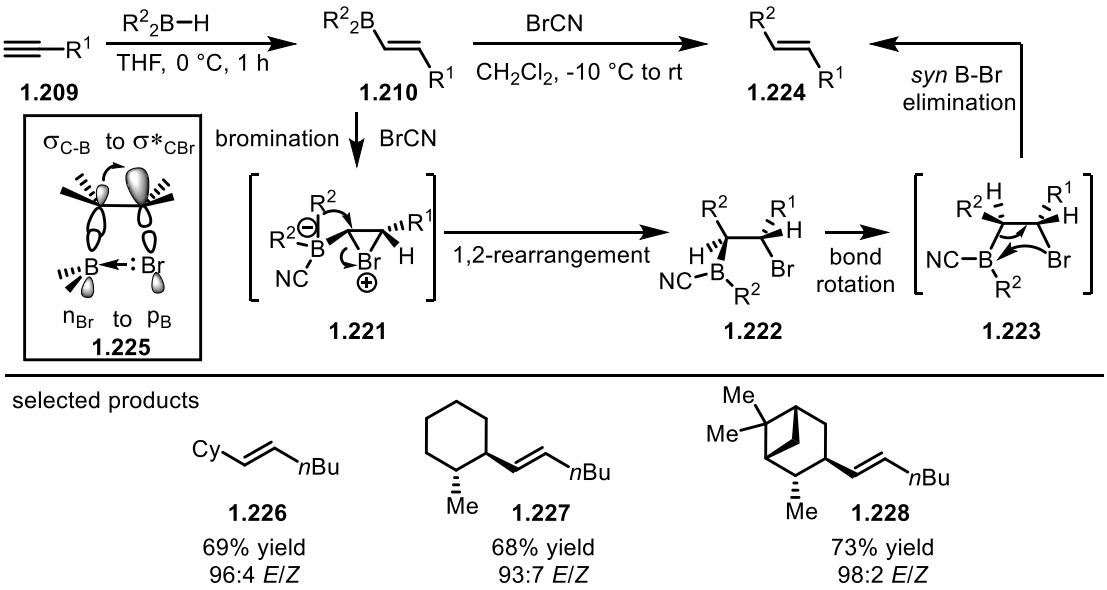
In a subsequent report, Zweifel demonstrated that by excluding base, switching from THF to dichloromethane solvent, and changing the activating reagent to cyanogen bromide

[67] See reference 55.

or cyanogen iodide rather than iodine, *E*-alkenes could be prepared exclusively (Scheme 1.28).[68] The authors proposed that without addition of exogenous base or coordinating solvent, the electron-withdrawing cyano group attached to boron enhances β-halogen coordination to the empty p orbital on boron resulting in predominately *syn* elimination (**1.223 to 1.224**). This hypothesis is consistent with a simple orbital analysis (inset, **1.225**).

The Zweifel olefination reaction of boranes was later improved by Levy who, recognizing the synthetic limitations imposed by the need to access intermediate boron-

Scheme 1.28. *E*-selective cyanogen bromide-induced olefination reaction



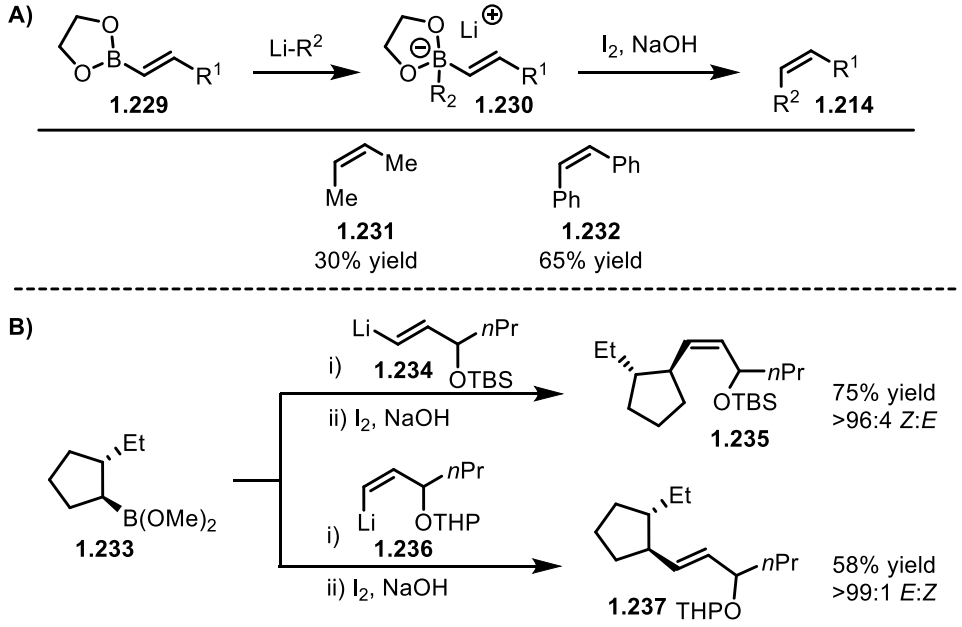
ate complexes such as **1.221** by hydroboration of alkynes with dialkylboranes, demonstrated that the addition of alkenyllithium nucleophiles to trialkylboranes, followed by treatment with iodine was effective for the *Z*-selective preparation of trisubstituted alkenes.[69]

In 1976, Matteson[70] and Evans[71] independently reported that the Zweifel olefination

[68] Zweifel, G.; Fisher, R. P.; Snow, J. T.; Whitney, C. C. *J. Am. Chem. Soc.* **1972**, 94, 6560.
[69] Levy, A. B.; LaLima, N. J. *J. Org. Chem*. **1978**, 43, 1279.
[70] Matteson, D. S.; Jesthi, P. K. *J. Organomet. Chem.* **1976**, 110, 25.
[71] (a) Evans, D. A.; Thomas, R. C.; Walker, J. A. *Tetrahedron Lett*. **1976**, 17, 1427. (b) Evans, D. A.;

method could be performed using boronic esters (Scheme 1.29). In contrast to Zweifel's original approach which involved generating alkenylboranes by hydroboration of alkynes and direct treatment with iodine alone or iodine and sodium hydroxide, Matteson found that the treatment of an alkenylboronic glycol esters with methyl or phenyllithium resulted in the clean formation of boron-ate complex **1.230** which was capable of undergoing iodination, 1.2-rearrangement, and hydroxide promoted *anti* elimination to furnish *Z*-alkenes **1.214**. Taking the same approach, Evans demonstrated that both *Z* and *E* alkene products (**1.235** and **1.237**) could be selectively obtained by employing either *E* or *Z* alkenyllithium reagents (**1.234** and **1.236**), respectively. The ability to employ organoboronic esters, which are more stable than boranes, has greatly expanded the utility of the Zweifel–Evans olefination reaction, negating the need to waste two alkyl fragments and precluding the possibility of competing migrating groups, which can be a problem with

Scheme 1.29. Iodine-induced olefination reactions involving boronic ester-derived ate complexes

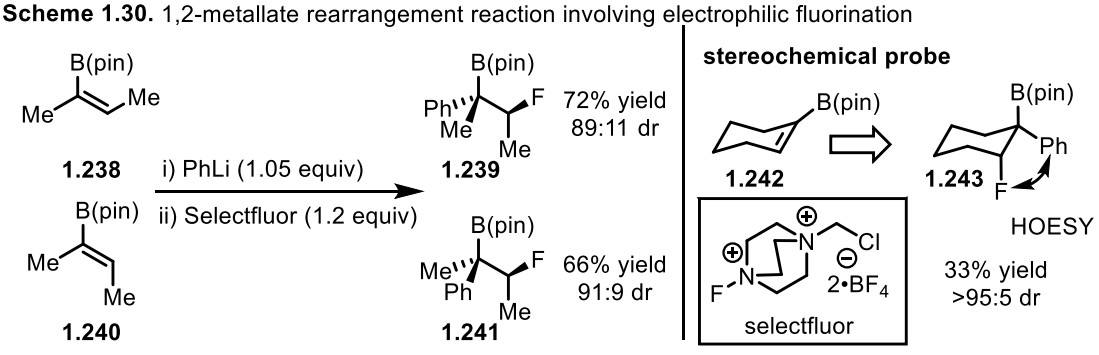


Crawford, T. C.; Thomas, R. C.; Walker, J. A. *J. Org. Chem.* **1976**, 41, 3947.

mixed boranes. The generality and utility of this method has been expanded considerably to include the preparation of monosubstituted and trisubstituted alkenes, as well as dienes, ketones, alkynes, vinylsulfides, and has been shown to be efficient with organolithium, organomagnesium, and organocerium[72] nucleophiles.[73]

While the Zweifel–Evans olefination reaction involves the formation of β-halo boron intermediates, these species are not generally isolable, owing to their rapid decomposition by boron-halide elimination. An intriguing example of the preparation of β-fluoro boronic esters was reported by Aggarwal in a communication on the selenium-induced 1,2-metallate rearrangement reaction of alkenylboron-ate complexes (discussed in the following section of this chapter regarding selenium-induced rearrangements) (Scheme 1.30).[74] The authors found that upon stepwise treatment with phenylithium and electrophilic fluorinating agent Selectfluor, *cis* or *trans* isobutenylboronic esters **1.238** and **1.240** were readily transformed into β-fluoroboronic esters **1.239** and **1.241** respectively (Scheme 1.30.A). Interestingly, the electrophilic fluorine-induced rearrangement reaction was shown to proceed by an unusual *syn* migration in which the electrophile and migrating

Scheme 1.30. 1,2-metallate rearrangement reaction involving electrophilic fluorination



[72] Music, A.; Hoarau, C.; Hilgert, N.; Zischka F.; Didier, D. *Angew .Chem. Int. Ed.* **2019**, 58, 1188.
[73] For an excellent review on Zweifel-Evans olefination and its application in organic synthesis, see: Armstrong, R. J.; Aggarwal, V. K. *Synthesis*, **2017**, 49, 3323.
[74] Armstrong, R. J.; Sandford, C.; Garcı´a-Ruiz C.; Aggarwal V. K. *Chem. Commun.* **2017**, 53, 4922.

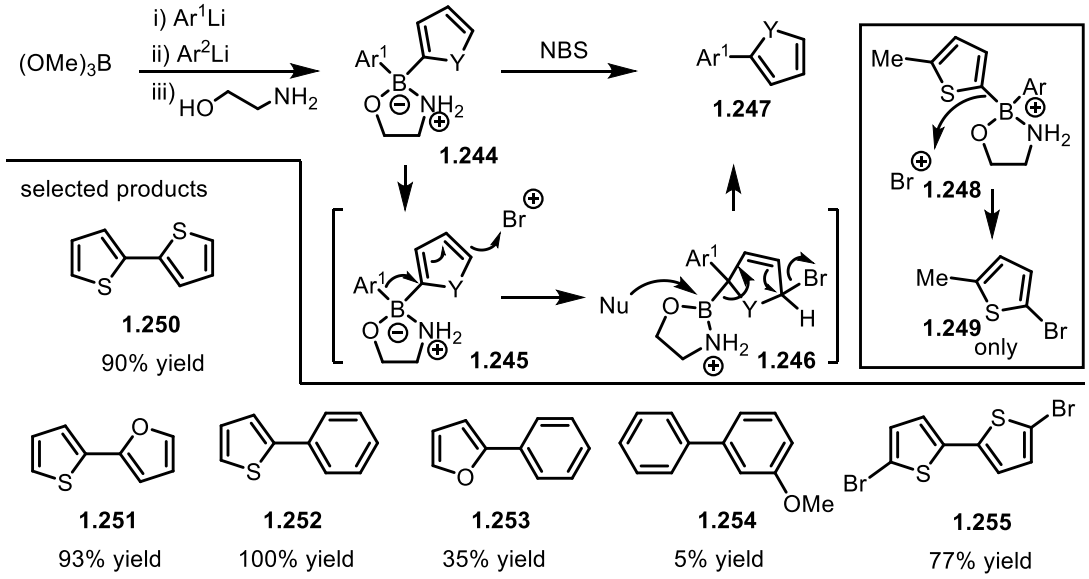
group add across the same face of the π-bond (Scheme 1.30.B). The authors proposed that, in contrast to the iodonium- and bromonium activation mode employed in Zweifel–Evans olefination reactions, the cationic nature of the fluorine electrophile promotes *syn* migration.

1.4.3.2 Halogen-Induced Arylation Reactions

While Zweifel–Evans olefination involves activation of the isolated π-bond of an alkenylboron reagent, presumably *via* the intermediacy of an iodonium or bromonium species (Scheme 1.27 and 1.28), halogen-induced rearrangement reactions are known for extended unsaturated systems such as arenes and heteroarenes as well. In the same year that Matteson and Evans reported iodine-promoted 1,2-metallate rearrangements of alkenylboron-ate complexes, Davies reported the halogen-induced 1,2-metallate rearrangement of diaryl ethanolamine boron-ate complex **1.224**, furnishing heterocycle-containing biaryls (Scheme 1.31).[75] In this and a subsequent report, Davies demonstrated that a variety of air-stable diarylboron-ate complexes, accessed by stepwise aryl nucleophile addition to trimethoxy or triisopropoxy borate followed by treatment with ethanolamine, could readily participate in a boron-mediated, NBS-induced aryl-aryl coupling reaction.[76] The proposed mechanism involves bromination of the most electron-rich heteroaromatic group at the 5-position, thereby inducing a 1,2-metallate rearrangement (**1.245** to **1.246**) which is followed by nucleophile-promoted bromo-boryl elimination (**1.246** to **1.247**). Consistent with the proposed mechanism, it was observed that when the 5-position of the heteroaromatic group was substituted, only halodeborylation occurred

[75] Davies, G. M.; Davies, P. S.; Paget, W. E.; Wardleworth, J. M. *Tetrahedron Lett*. **1976**, 10, 795.
[76] Pelter, A.; Williamson, H.; Davies, G. M. *Tetrahedron Lett*. **1984**, 4, 453.

Scheme 1.31. Davies' boron-mediated, halogen-induced biaryl coupling reaction

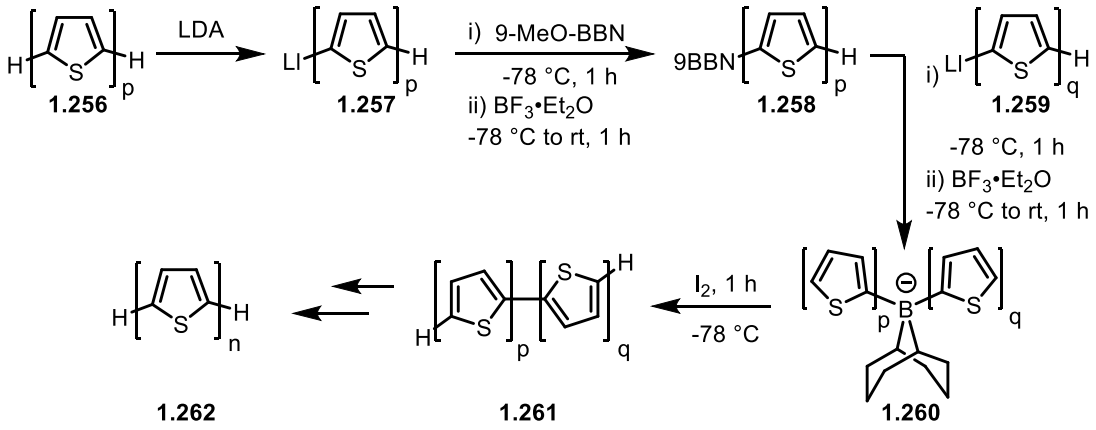


(inset, **1.248** to **1.249**). Additionally, unsymmetrically substituted boron-ate complexes resulted in mixed biaryl products with no symmetrical biaryl products observed, pointing to the intramolecular nature of the mechanism. It was also noted that the reaction was regiospecific with the new carbon-carbon bond always occurring at the positions formerly attached to boron. A variety of symmetrical and mixed biaryls could be accessed in this way, though attempts to couple two non-heterocyclic aromatic groups failed (**1.254**).

In a following report, Kagan demonstrated that a lithiation-borylation strategy utilizing thiophene monomers or oligomers could be employed to prepare bis-aryl-9-BBN-derived ate complexes **1.260** which, upon treatment with iodine, furnished extended polythiophene oligomers (Scheme 1.32).[77] This approach to polythiophene oligomer construction is interesting as it can be performed iteratively and oligomer size can, in principle, be precisely controlled.

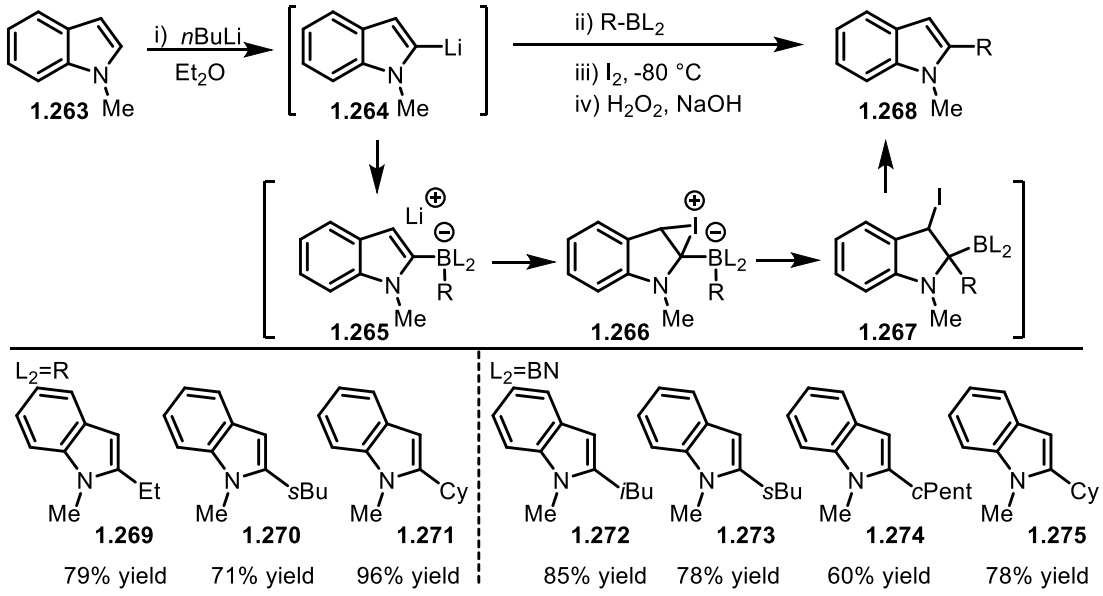
[77] Kagan, J.; Arora, S. K. *Tetrahedron Lett.* **1983**, 24, 4043.

Scheme 1.32. Kagan's boron-mediated, iodine-induced thiophene oligimerization strategy



Levy expanded the scope of halide-induced heteroaromatic functionalization reactions to include the regiospecific alkylation of indoles utilizing alkylboranes and *in situ* generated 2-lithio *N*-methyl indoles. (Scheme 1.33).[78] A similar mechanism to the Zweifel–Evans olefination was proposed. It was found that both trialkylborane and 9-alkyl-BBN reagents were competent in the reaction. Interestingly, this approach allows the one-pot

Scheme 1.33. Levy's boron-mediated, iodine-induced indole alkylation reation



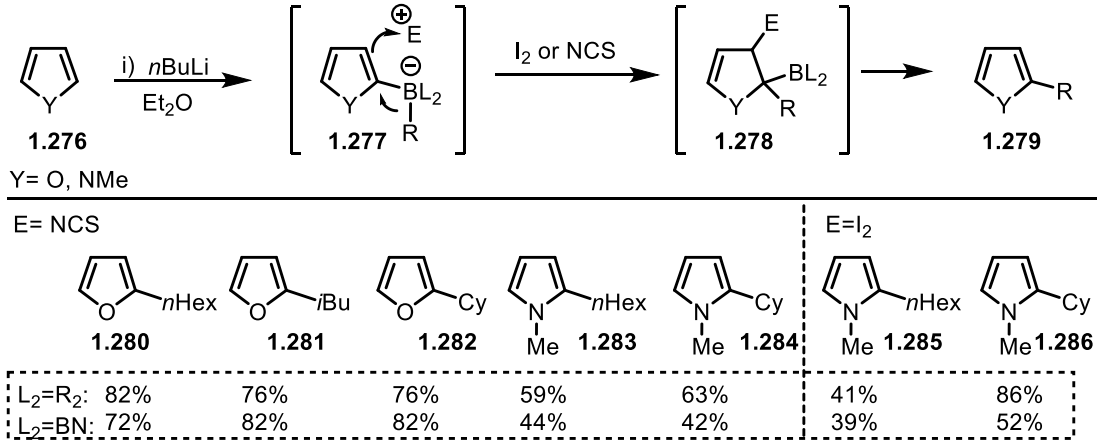
[78] Levy, A. B. *J. Org. Chem.* **1978**, 43, 4684.

diversification of the indole core with regioselectivity complementary to traditional electrophilic alkylation of indoles, which favors substitution at the more nucleophilic 3- rather than 2-position.

Levy subsequently extended this boron-mediated electrophile-induced regioselective heterocycle alkylation methodology to include pyrroles and furan (Scheme 1.34).[79] A variety of electrophilic reagents were investigated and iodine and NCS were found to be optimal. Similar to the previous report, electrophilic activation was proposed to result in halogenation at the 3-position of the heterocyclic ring, before B-I elimination. In contrast to the indole and pyrrole-derived boron-ate complexes, furan-derived complexes produced only low yields of alkylated products upon treatment with iodine, but reacted smoothly upon treatment with NCS. The authors noted that the choice of electrophilic activator is crucial though no mechanistic rationale was proposed.

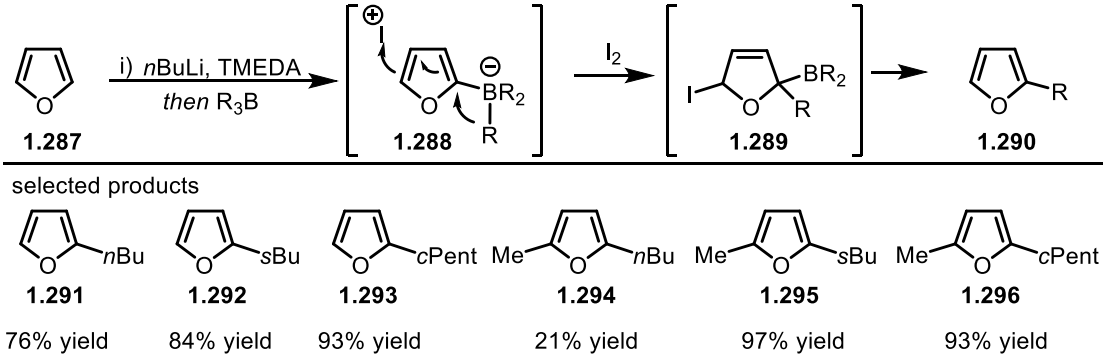
Interestingly, a contemporaneous report by Suzuki found that 2-lithio furan participated efficiently in regioselective alkylation with trialkyboranes utilizing iodine as the electrophilic activator (Scheme 1.35).[80] While it is not clear why iodine was found to be

Scheme 1.34. Levy's boron-mediated, halogen-induced 2-alkylation of furan and *N*-methyl pyrrole



[79] Marinelli, E. R.; Levy, A. B. *Tetrahedron Lett*. **1979**, 25, 2313.
[80] Akimoto, I.; Suzuki, A. *Synth*esis **1979**, 146.

Scheme 1.35. Suzuki's boron-mediated, iodine-induced 2-alkylation of furans



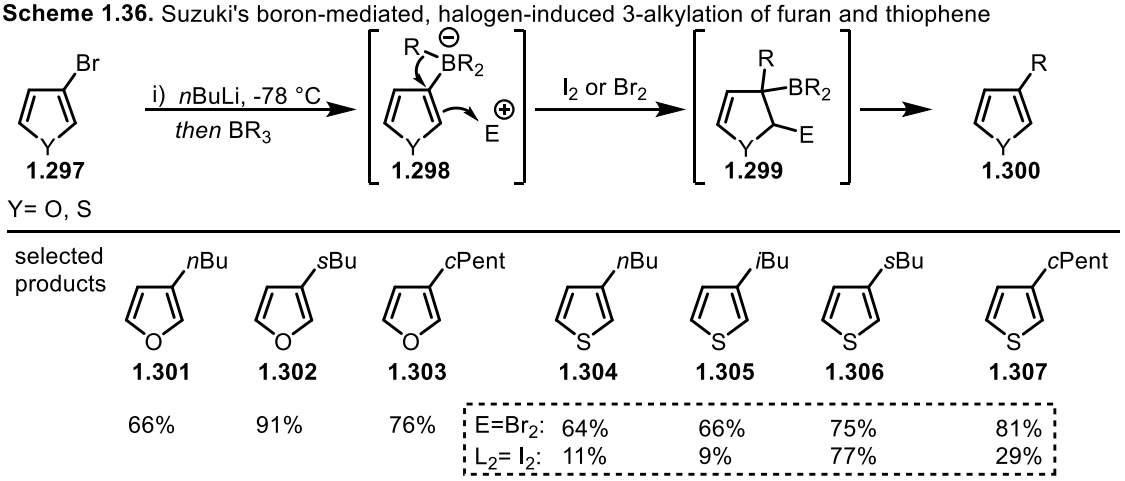
effective in this case whereas it was not in Levy's report, the use of TMEDA during the lithiation step in Suzuki's method may enhance the nucleophilicity of boron-ate **1.288** by lithium cation binding. Notably, Suzuki found that 5-methylfuran was an effective substrate, furnishing 2,5-dialkyl furan products (**1.294**, **1.295**, **1.296**). Like Levy, Suzuki extended this method to the reaction of trialkylboranes with lithiated thiophene and 1-methyl pyrroles.[81]

Suzuki later demonstrated that 3-alkyl furans were accessible using this method, by lithium-halogen exchange with 3-bromofuran **1.297** (Scheme 1.36).[82] In this case, the authors proposed that electrophilic activation occurs at the 2-position (**1.298**). It was observed that more substituted alkyl migrating groups appeared to result in higher yields, perhaps due to the greater nucleophilicity of these species. Iodine was found to be an effective electrophilic activator for furan but bromine was found to be more effective for reactions involving 3-lithiothiophene.

Research into the Zweifel–Evans olefination and related processes lay relatively dormant for several decades until it was reinvestigated by Aggarwal. In 2014, Aggarwal reported that enantioenriched secondary and tertiary boronic esters could be engaged in

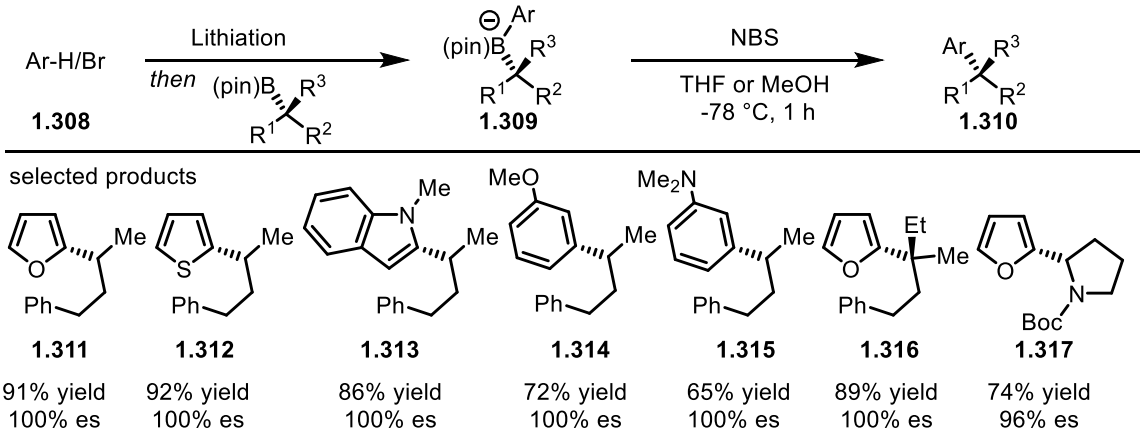
[81] Sotoyama, T.; Hara, S.; Suzuki, A. *Bull. Chem. Soc. Jpn.* **1979**, 52, 1865.
[82] Itaru, A.; Masahiro, S.; Suzuki, A. *Bull. Chem. Soc. Jpn*. **1981**, 54, 1587.

Scheme 1.36. Suzuki's boron-mediated, halogen-induced 3-alkylation of furan and thiophene



stereospecific halogen-induced arylation reactions, and he showed that these arylation reactions could utilize a wide range of lithiated aromatics (Scheme 1.37).[83] This approach allows the coupling of alkyl boronic esters, including tertiary boronic esters (**1.316**), to afford products with quaternary stereocenters that are challenging to obtain through metal-catalyzed cross-coupling. The authors found the transformation to be general with respect to the aromatic moiety, proceeding in high yield with complete retention of enantiomeric purity for a range of heterocycles (**1.313-1.313**, **1.316, 1.317**) and electron-rich aromatic rings (**1.314** and **1.315**). The reaction is proposed to proceed by an S_EAr pathway in which

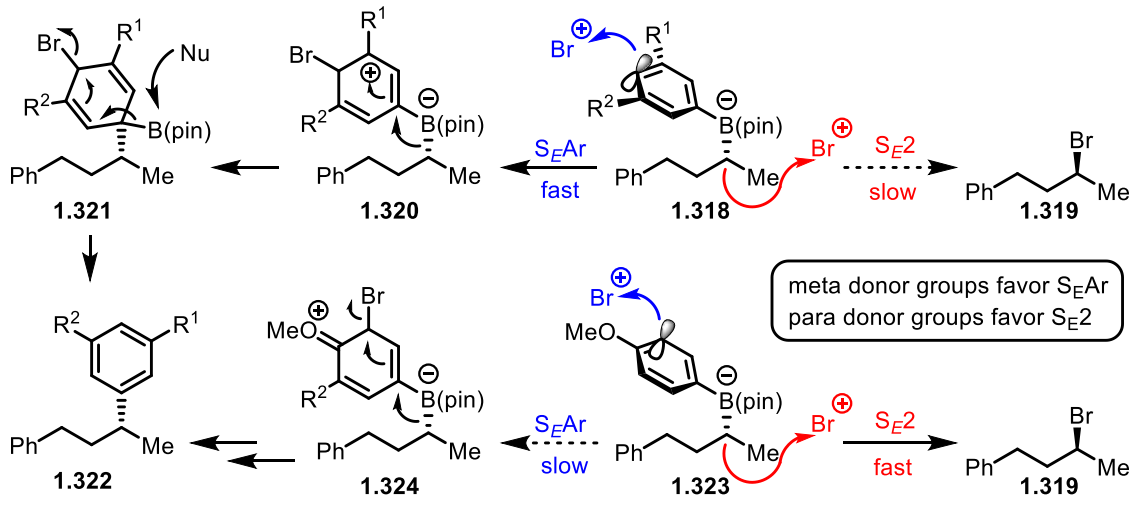
Scheme 1.37. Aggarwal's stereospecific halogen-induced arrylation of enantioenriched boronic esters



[83] Bonet, A.; Odachowski, M.; Leonori, D.; Essafi, S.; Aggarwal, V. K. *Nat. Chem.* **2014**, 6, 584.

bromination of the arene at the *para* or *ortho* position induces 1,2-metallate rearrangement (Scheme 1.38). Consistent with this proposal, for less electron-rich or less sterically hindered aromatics, the use of MeOH in place of THF for the addition of NBS was found to improve yields of coupled product, presumably due to the stabilization of charged intermediates. For some substrates, particularly those with poor electron-donating groups or substituents at the *para* position, low yields of coupled product were observed, with an invertive S_E2 bromination pathway predominating. Aggarwal had previously developed the S_E2 pathway as a method to stereospecifically functionalize boronic esters.[84] The authors proposed that the boron-ate substituent on the aromatic ring acts as an electron-donating group and, when the aromatic ring is electronically consonant with this group such that electron-density is maximized at the *para* and *ortho* positions, the S_EAr mechanism (in blue) will be fast, outcompeting the invertive S_E2 pathway (in red). In contrast, when the electron-density at the *para* and *ortho* positions of the aromatic ring is

Scheme 1.38. Mechanistic proposal: S_EAr competition with S_E2



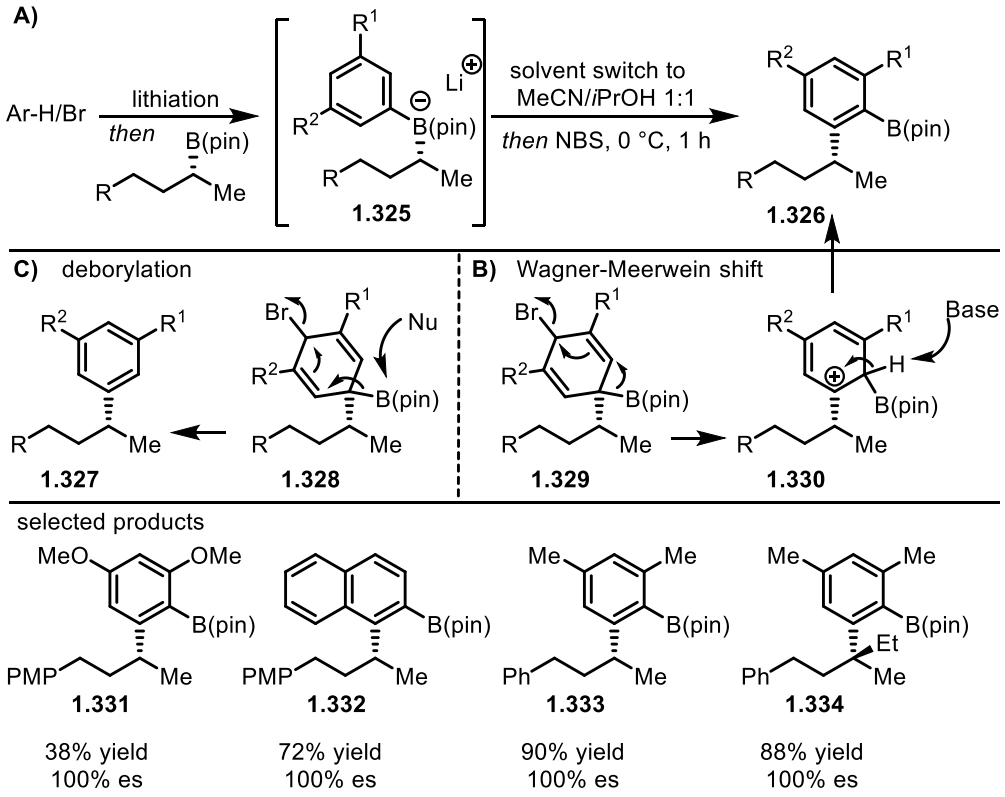
[84] a) Feeney, K.; Berionni, G.; Mayr, H.; Aggarwal, V. K. *Org. Lett.* **2015**, 17, 2614. (b) Mohiti, M.; Rampalakos, C.; Feeney, K.; Leonori, D.; Aggarwal, V. K. *Chem. Sci.* **2014**, 5, 602. (c) Larouche-Gauthier, R.; Elford, T. G.; Aggarwal, V. K. *J. Am. Chem. Soc.* **2011**, 133, 16794.

not maximized, or the *ortho* position is substituted, the S_EAr pathway is slow relative to the S_E2 pathway, leading to the predominant formation of bromination product **1.319**.

Aggarwal has investigated the mechanistic aspects of this reaction in more detail using a combination of DFT calculations, *in situ* IR analysis, and structure-activity relationship studies with a variety of alkylboronic esters and arylithium reagents.[85] Using DFT calculations, the authors found that for the productive S_EAr mechanism, bromination of the aromatic ring and 1,2-metallate rearrangement occurs simultaneously *via* a single transition state. It was also found that increasing electron density on the aromatic ring, as previously proposed, decreases the energetic barrier for the S_EAr pathway but does not significantly affect the S_E2 pathway. Conversely, increasing steric hindrance at the sp^3-hybridized carbon adjacent to boron decreased the barrier for the S_E2 pathway but does not significantly affect the S_EAr pathway. It was also found that, while less general, DDQ can be used in place of NBS as an electrophilic activator, inducing 1,2-metallate rearrangement. The mechanistic details of this observation will be discussed in more detail in the following section of this chapter focused on radical-induced rearrangements. In the same report, Aggarwal observed that when a solvent exchange was performed (THF to MeCN/*i*PrOH) prior to NBS addition, rearrangement products could be obtained wherein the boron was retained in the product **1.326** (Scheme 1.39.A). The authors attributed the formation of this product to a Wagner–Meerwein shift/deprotonation pathway (Scheme 1.39.B). The switch to a more polar solvent (MeCN versus THF) may help stabilize the positive charge that develops in the Wagner–Meerwein shift, while the use of a less nucleophilic yet more basic alcohol (*i*PrOH versus MeOH) may facilitate deprotonation over nucleophilic attack of

[85] Odachowski, M.; Bonet, A.; Essafi, S.; Conti-Ramsden, P.; Harvey, J. N. Leonori, D.; Aggarwal, V. K. *J. Am. Chem. Soc.* **2016**, 138, 9521.

Scheme 1.39. NBS-induced arylation-boryl rearrangement reaction of enantionriched alkyl boroic esters

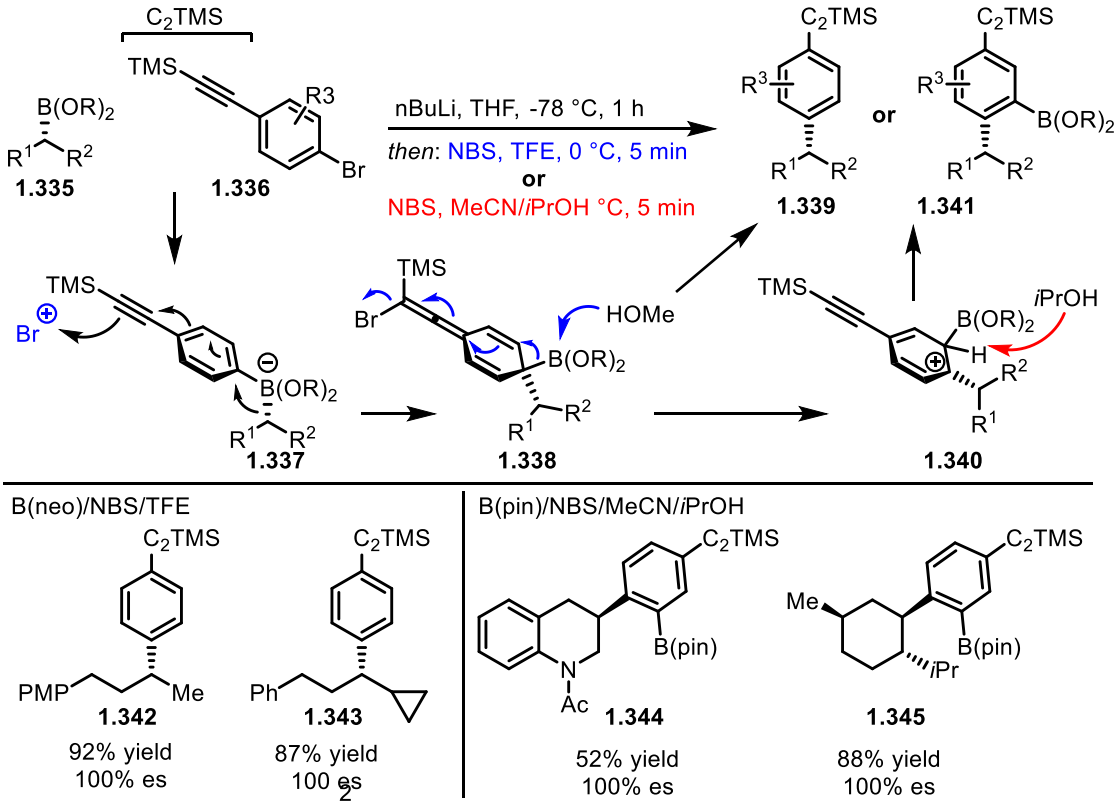


boron leading to the competing B-Br elimination pathway (Scheme 1.39.C).

Aggarwal has demonstrated that enantiospecific arylation of alkylboronic esters can be extended to more electron-poor rings with the incorporation of an alkyne substituent at the *para* position of the aromatic ring (Scheme 1.40).[86] In this case, the sterically accessible, electron-rich alkyne moiety acts as an auxiliary site of electrophilic activation for NBS, facilitating 1,2-metallate rearrangement to the aromatic ring through electronic conjugation (**1.227** to **1.338**). The authors found that by utilizing the smaller neopentyl ligands on boron, the boron-halide elimination pathway leading to the formation of coupled product **1.339** was favored. When the ligand on boron was changed to pinacol and an acetonitrile/*i*PrOH solvent system was used, the previously described Wagner–Meerwein

[86] Ganesh, V.; Odachowski, M.; Aggarwal, V. K. *Angew. Chem. Int. Ed.* **2017**, 56, 9752.

Scheme 1.40. NBS-induced stereospecific arylation of boronic esters using 4-alkynyl aromatic nucleophiles



shift predominated, furnishing coupled product **1.341** in which the valuable boron functional handle is retained. The substrate scope was found to be broad with respect to enantioenriched secondary and tertiary boronic esters, and excellent enantiospecificity was observed in all cases. While the need to incorporate an alkyne moiety as an axillary site of activation is not a completely general solution, the products were shown to be synthetically versatile.

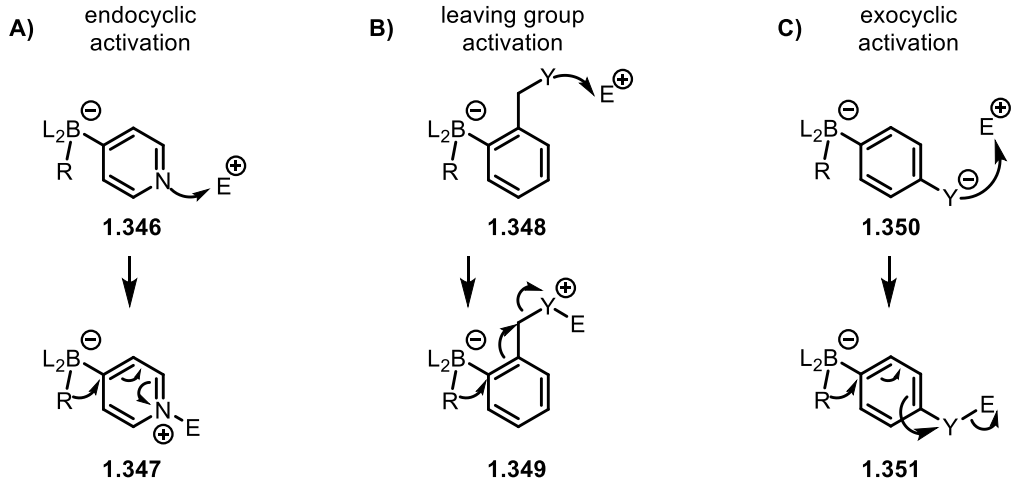
1.4.4 Heteroatom Activation-Induced Arylation

For boron-ate complexes attached to aromatic systems in which a heteroatom is present, either within the ring or adjacent to it, the possibility of inducing rearrangement by heteroatom activation with an electrophilic agent presents itself. Unlike the halogen-

induced rearrangements previously discussed, the electrophilic reagent does not interact directly with the π-system, but rather induces rearrangement by covalent modification of a heteroatom. This activation can take the form of increasing a heterocycle's ability to stabilize charge (Scheme 1.41.A.), activation of a benzylic heteroatom leaving group (Scheme 1.41.B), or can involve the intermediate installation of a leaving group (Scheme 1.41.C).

One of the earliest examples of this reactivity mode was described by Ishikura in a report detailing that a variety of electrophilic agents, including Lewis acids, acyl halides, and anhydrides could be used to induce the rearrangement reaction of trialkylborane-derived 4-pyridyl boron-ate complexes (Scheme 1.42.A).[87] Not only did this report firmly establish the compatibility of boron-ate complexes with a variety of electrophilic activating agents, it also provided proof of concept that electron-poor aromatic systems which are ineffective substrates for the halogen-induced arylation methods previously discussed, can be successfully engaged by an alternative mode of activation. As depicted in Scheme

Scheme 1.41. Modes of heteroatom activation-induced 1,2-rearrangements



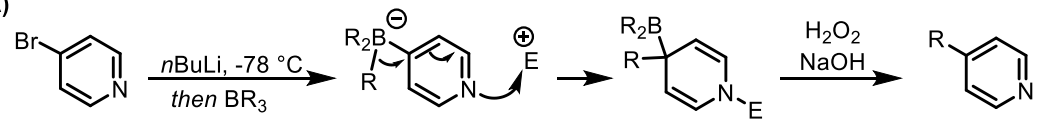
[87] Ishikura, M.; Terashima, M. *Heterocycles* **1986**, 24, 2793.

1.42.B the reaction was proposed to proceed *via* a 1,2-metallate rearrangement precipitated by electrophilic activation of the pyridine nitrogen[88] (**1.356** to **1.357**) followed by elimination of the boron and electrophile moiety during oxidative workup. When the reaction mixture of boron-ate **1.356** and acyl chloride was directly subjected to silica gel purification without oxidative workup, diene **1.359** was isolated in 10% yield along with 44% of the expected coupled pyridine product. The authors proposed that **1.359** is the product of protodeboration of intermediate **1.358**, lending some support for their proposed mechanism.

This reaction has been improved by the Aggarwal group, which has demonstrated a stereospecific reaction with enantioenriched boronic esters lithiated pyridines, quinolones,

Scheme 1.42. Ishikura's electrophilic activation strategy for pyridine alkylation

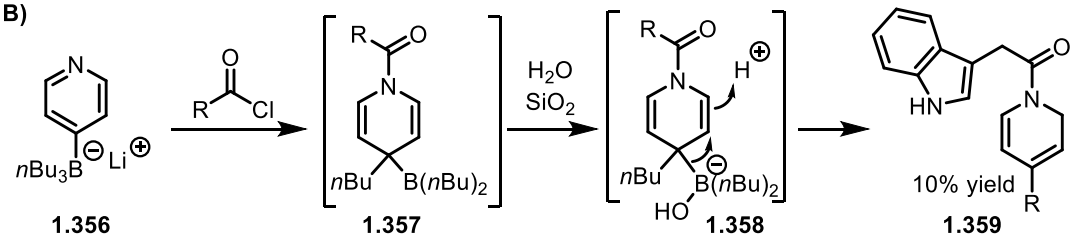
A)



1.352 **1.353** **1.354** **1.355**

entry	R_3B	$E^{\oplus}$	yield (%)	entry	R_3B	$E^{\oplus}$	yield (%)
1	nBu$_3$B	BF_3•Et_2O	58	7	nBu$_3$B	PhCOCl	40
2	nBu$_3$B	$B(OMe)_3$	38	8	sBu$_3$B	BF_3•Et_2O	48
3	nBu$_3$B	$AlCl_3$	20	9	sBu$_3$B	$TiCl_4$	44
4	nBu$_3$B	$TiCl_4$	45	10	nBu$_3$B	$(CF_3CO)_2O$	45
5	nBu$_3$B	$(CF_3CO)_2O$	56	11	nHex$_3$B	BF_3•Et_2O	59
6	nBu$_3$B	$(CH_3CO)_2O$	33	12	Cy$_3$B	BF_3•Et_2O	26

B)



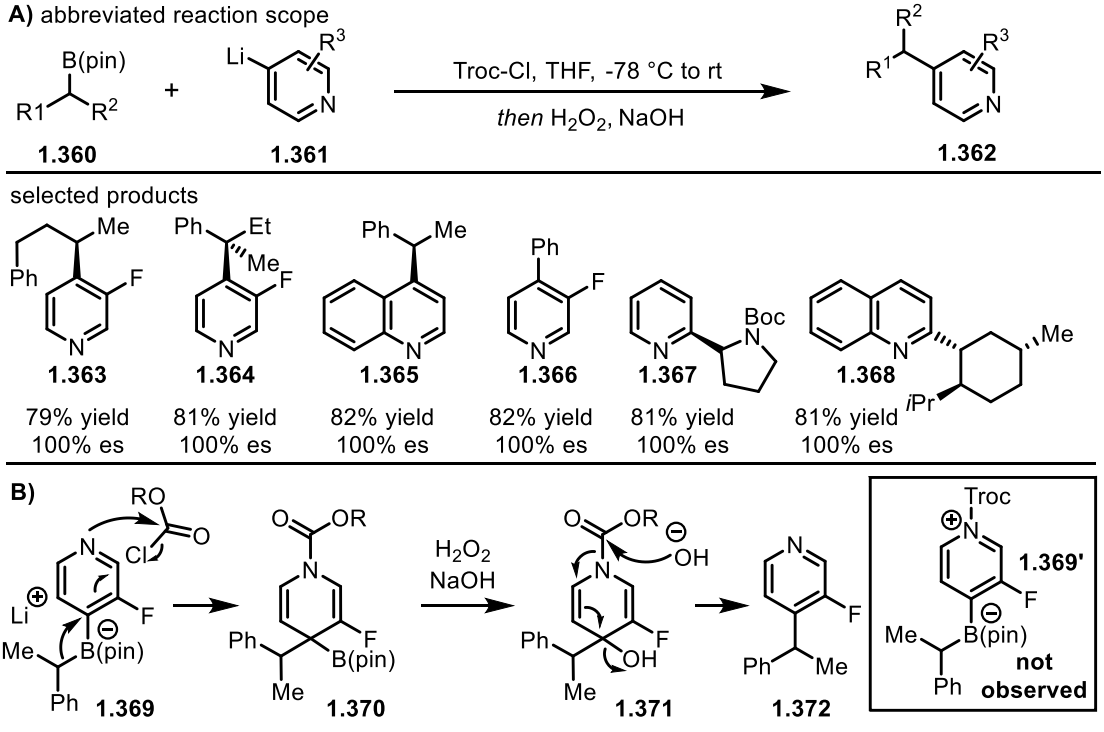
1.356 **1.357** **1.358** **1.359**

[88] Charette, A. B.; Bull, J. A.; Mousseau, J. J.; Pelletier, G. *Chem. Rev.* **2012**, 112, 2642.

and isoquinolines (Scheme 1.43)[89] Troc-chloride was found to be a broadly effective activating agent. Using ^{11}B NMR and *in situ* IR monitoring, the intermediacy of **1.369** and **1.370** was confirmed while the pyridine-activated complex **1.369** was not observed, suggesting a rapid concomitant activation-1,2-metallate rearrangement. Rearomatization of intermediated **1.370** was proposed to occur by oxidation of boron and nucleophilic deacylation (**1.370** to **1.372**).

In a subsequent publication, Aggarwal demonstrated that lithiated benzyl amine-derived boron-ate complexes **1.374** can be engaged in a 1,2-metallate rearrangement/*anti* S_N2' elimination and subsequent 1,3-borotropic shift sequence (**1.374** to **1.376**) when treated consecutively with acyl chloride and sodium tetraphenylborate (Scheme 1.44.A).[90] This overall transformation involves three stereospecific processes: a stereoretentive 1,2-

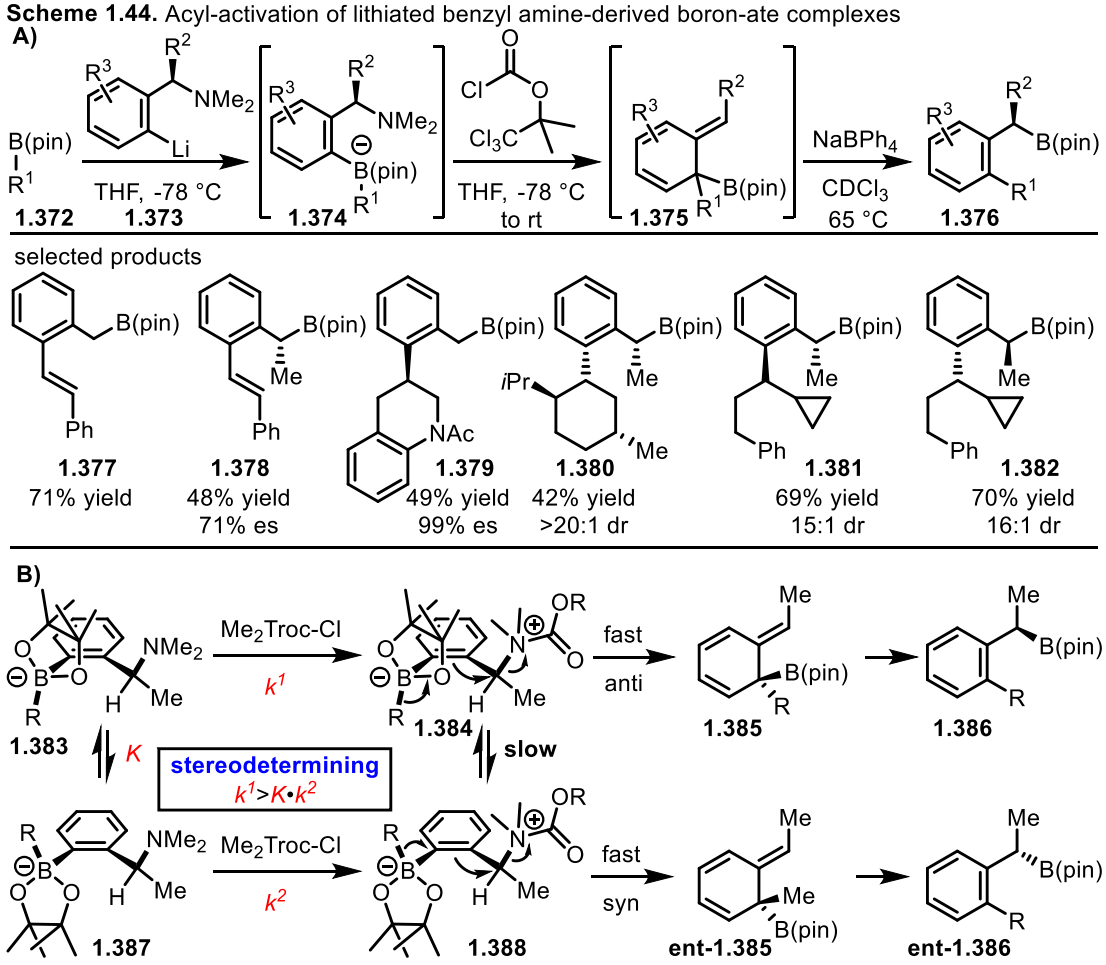
Scheme 1.43. Acyl chloride-induced pyridine functionalization of boronic esters



[89] Llaveria, J.; Leonori, D.; Aggarwal, V. K. *J. Am. Chem. Soc.* **2015**, 137, 10958.
[90] Aichhorn, S.; Bigler, R.; Myers, E. L.; Aggarwal, V. K. *J. Am. Chem. Soc*. **2017**, 139, 9519.

metallate rearrangement, a stereospecific *anti* S_N2' elimination, and a 1,3-borotropic rearrangement. The net stereoretentive *anti* S_N2' elimination/1,3-borotropic rearrangement sequence is proposed to proceed by a stereodetermining acylation (**1.383** to **1.384**) with rapid subsequent 1,2-rearrangement which precludes interconversion of acylated intermediates **1.384** and **1.388** (Scheme 1.44.B). Allylboron intermediate **1.385** could be detected by NMR and, while not easily isolated, could participate in a Cope rearrangement, protodeborylation, and stereospecific allylation reactions *in situ*. Subsequent reports have also shown these compounds to be competent in Diel–Alder[91] reactions and palladium-

Scheme 1.44. Acyl-activation of lithiated benzyl amine-derived boron-ate complexes

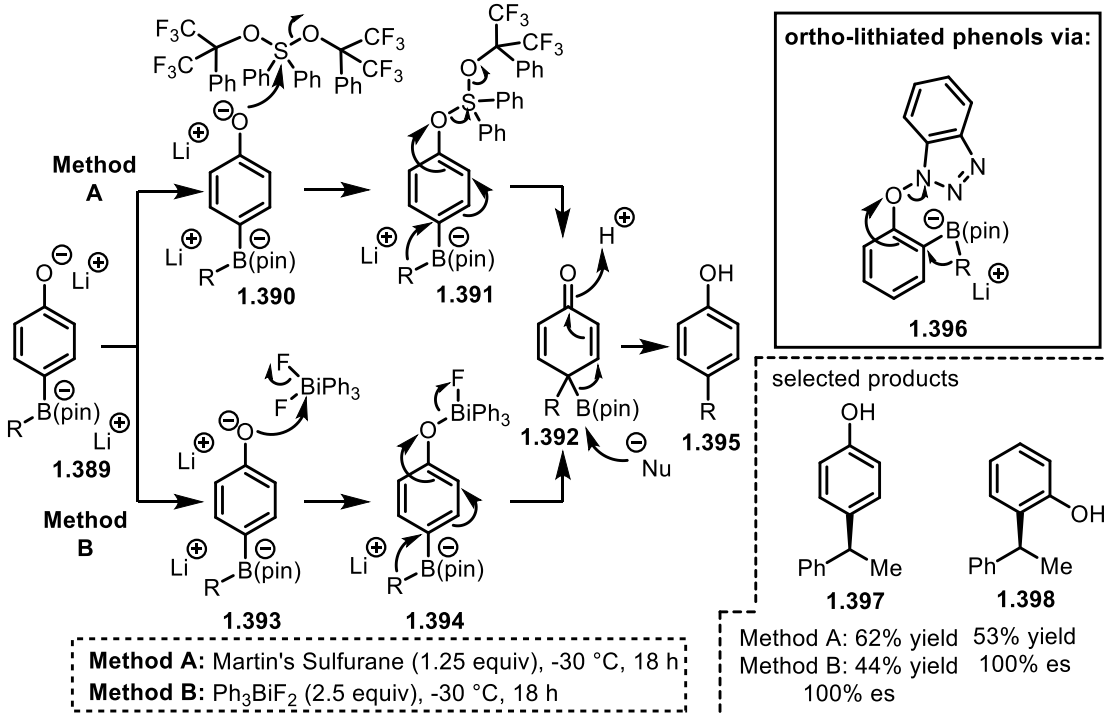


[91] Tillin, C.; Bigler, R.; Calo-Lapido, R.; Collins, B. S. L.; Noble, A.; Aggarwal, V. K. *Synlett* **2019**, 30, 449.

catalyzed cross-coupling.[92] A similar reaction has been reported using lithiated aryl hydrazines.[93]

Aggarwal has extended the concept of heteroatom-activation-induced organoboronic ester arylation to the synthesis of phenols (Scheme 1.45).[94] When boron-ate complexes **1.389** derived from boronic esters and lithiated phenols were treated with Martin's sulfurane, or triphenylbismuth difluoride, coupled phenol products **1.395** could be obtained in synthetically useful yields. The use of Martin's sulfurane, in general, resulted in higher yields and was used to further explore the substrate scope for this transformation. While dianionic boron-ate complex **1.389** successfully participated in the reaction, the use of *ortho*-phenoxides resulted in poor yields of the desired products. The authors attributed

Scheme 1.45. Activation of phenol substituted boron-ate complexes



[92] Rubial, B.; Collins, B. S. L.; Bigler, R.; Aichhorn, S.; Noble, A.; Aggarwal, V. K. *Angew. Chem. Int. Ed.* **2019**, 58, 1366.
[93] Ganesh, V.; Noble, A.; Aggarwal, V. K. *Org. Lett.* **2018**, 20, 6144.
[94] Wilson, C. M.; Ganesh, V.; Noble, A.; Aggarwal, V. K. *Angew. Chem. Int. Ed.* **2017**, 56, 16318.

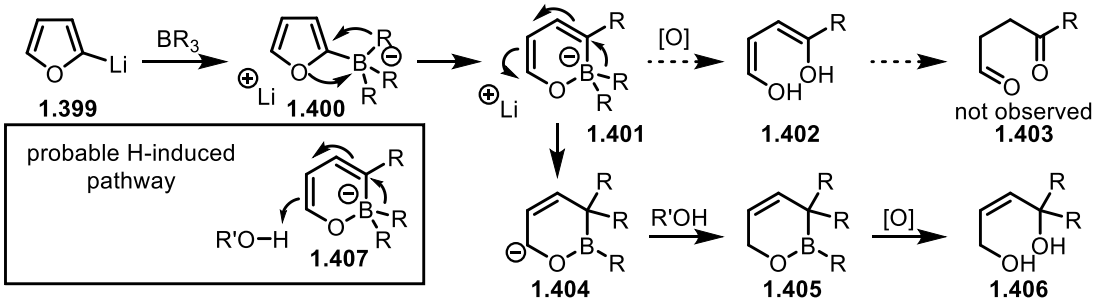
the inhibited activation of *ortho*-phenoxy substrate to steric hindrance by the adjacent boron-ate group. It was found that by pre-activating *ortho*-bromophenol substrates with a benzotriazole group, the boron-ate complex **1.396** (inset) formed upon lithium-halogen exchange and treatment with boronic esters underwent spontaneous rearrangement upon warming to room temperature.

1.4.5 Proton-Induced Rearrangements

Contemporaneous with reports by Zweifel and Levy of halogen-induced arylation reactions of furan- and pyrrole-derived boron-ate complexes, Suzuki studied an unusual rearrangement reaction of 2-lithiated furan-derived boron-ate complexes (Scheme 1.46).[95] The authors envisioned that 1,4-ketoaldehyde **1.403** might be conveniently accessed from 2-lithiated furan **1.399** and trialkylboranes. The authors imagined that a spontaneous dyatropic 1,2-metallate rearrangement of *in situ* generated boron-ate complex **1.400** would form borinic ester ate complex **1.401**, which would be oxidized to form the desired dicarbonyl product **1.403** by tautomerization of diol **1.402**. Unexpectedly, the sole product observed upon treatment of 2-lithiated furan **1.399** and various trialkylboranes was dialkylborinic ester **1.405** which was obtained in high yield as an isolable solid. Crossover experiments confirmed that the alkyl transfer from boron occurred in an intramolecular fashion, and independent preparation of **1.405** and oxidation to unsaturated diol **1.406** confirmed the identity of **1.405**. The formation **1.405** was rationalized as occurring by a second spontaneous rearrangement of **1.401** to form an unusual α-oxy anion **1.404**, which would be protonated upon workup. The formation of high-energy intermediate **1.404** seems

[95] Suzuki, A.; Miyaura, N.; Itoh, M. *Tetrahedron* **1971**, 27, 2775.

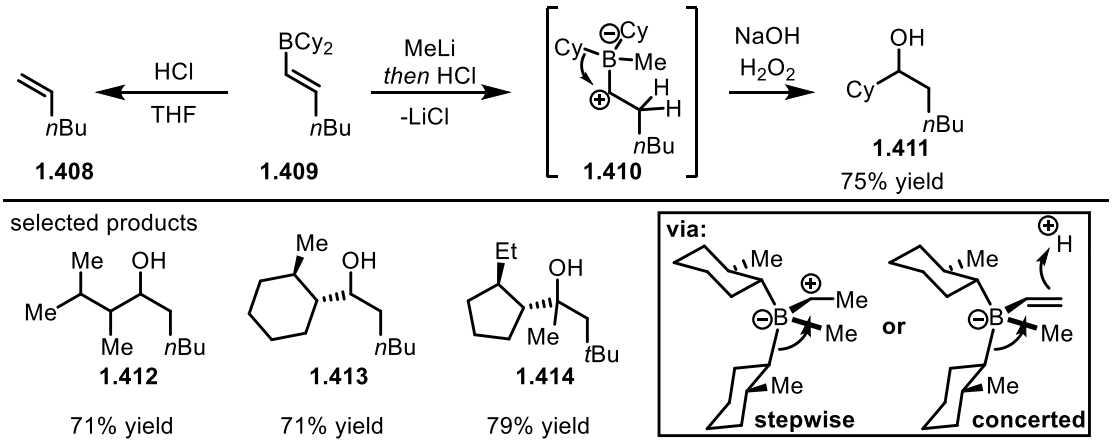
Scheme 1.46. Suzuki's probable proton-induced alkylation/ring opening of furan



somewhat unlikely and a subsequent report by Levy proposed an alternative mechanism in which borinic ester ate complex **1.407** (inset) undergoes proton-induced 1,2-rearrangement upon workup.[96]

Zweifel reported a proton-induced rearrangement reaction of alkenylboranes which furnishes secondary and tertiary alcohols (Scheme 1.47).[97] The authors observed that treatment of alkenylborane **1.409** with hydrochloric acid resulted in substantial protodeborylation to form hexene (**1.408**). In contrast, if **1.409** was treated sequentially with methyllithium, hydrochloric acid, and alkaline hydrogen peroxide, secondary alcohol **1.411** was obtained in 75% yield. The authors proposed that protonation of the boron-ate complex derived from methyllithium and alkenylborane **1.409** occurs at the alkene,

Scheme 1.47. Zweifel's proton-induced rearrangement of alkylboron-ate complexes

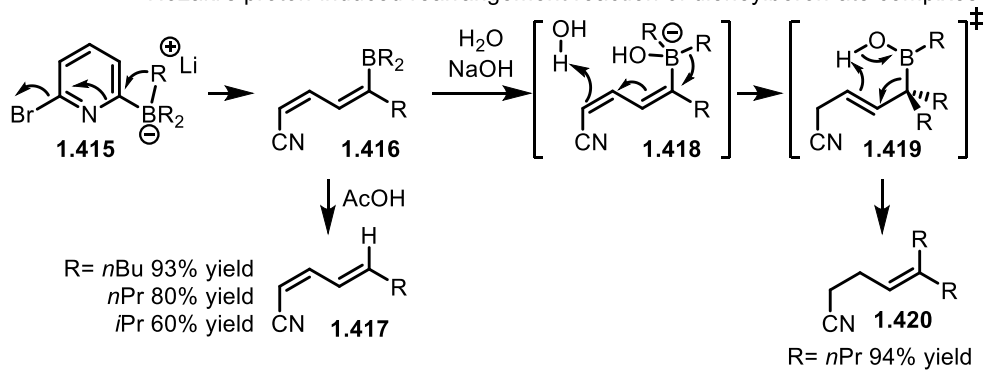


[96] Levy, A. B.; Schwartz, S. J *Tetrahedron Lett*. **1976**, 26, 2201.
[97] Zweifel, G.; Fisher, R. P. *Synthesis* **1974**, 339.

generating a zwiterionic intermediate **1.410** which rapidly rearranges to form an alkylborane; subsequently oxidation then gives alcohol **1.411**. The authors noted that methyl migration was not observed and that chiral alkyl fragments migrated with retention of configuration. The authors did not comment on the diastereoselectivity of these reactions other than to note that products **1.413** and **1.414** were obtained as a mixture of stereoisomers. This is perhaps not surprising given the proposed stepwise mechanism, though it is possible that a concerted mechanism might suffer from poor alkene facial discrimination (inset).

Nozaki reported a stereospecific alkylative cleavage of the pyridine ring of 2-bromo-6 lithiopyridine by trialkylboranes to form isomerically pure nitrile-substituted dienes **1.417** or alkene-containing alkyl nitriles **1.420** (Scheme 1.48).[98] The authors found that treatment of 2-bromo-6 lithiopyridine with trialkylborane resulted in the formation of alkenylborane

Scheme 1.48. Nozaki's proton-induced rearrangement reaction of dieneylboron-ate complxes



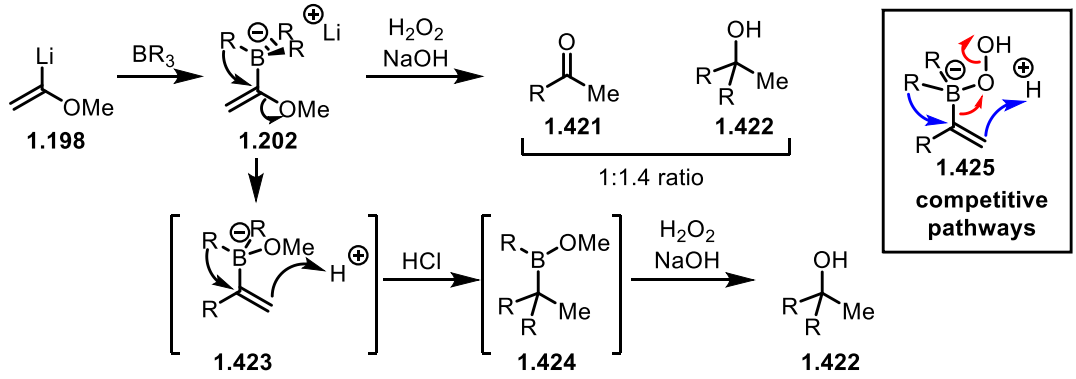
1.416, which was not isolated but could be spectroscopically detected. Protodeborylation of **1.416** with glacial acetic acid resulted the formation of isomerically pure **1.417**. The authors propose **1.416** is formed by a concerted alkyl rearrangement/ring cleavage and bromide elimination of *in situ* generated ate-complex **1.415**. Treatment of **1.416** with

[98] Utimoto, K.; Sakai, N.; Obayashi, M.; Nozaki, H. *Tetrahedron* **1976**, 32, 769.

aqueous sodium hydroxide was found to result in the formation of trisubstituted alkene **1.420**, which was attributed to the proton-induced 1,2-metallate rearrangement of dienylboron-ate complex **1.418** and subsequent protodeborylation *via* a 6-membered transition state **1.419**.[99] Protonation at the distal alkene rather than the alkene proximal to boron was rationalized to occur because of the ability of the nitrile substituent to stabilize negative charge buildup.

Levy reported a proton-induced 1,2-metallate rearrangement that enables the preparation of tertiary alcohols from α-methoxy vinyllithium **1.198** and trialkylboranes (Scheme 1.49).[100] The authors found that after the *in situ* formation of boron-ate complex **1.202**, rearrangement occurred upon warming, and after treatment with alkaline hydrogen peroxide, led to the formation of a mixture of dialkyl ketones **1.421** and tertiary alcohols

Scheme 1.49. Levy's preparation of tertiary alcohols by a proton-induced double migration reaction



1.422. The unexpected formation of **1.422** was attributed to a proton-induced 1,2-metallate rearrangement pathway which competes with boron oxidation (inset, **1.425**). It was found that the product ratio could be controlled by varying the workup conditions.[101] When the unpurified reaction solution of **1.423** was treated at low temperature with hydrochloric

[99] For an analogous protodeborylation see: Brown, H. C.; Nambu, H. *J. Am. Chem. Soc.* **1970**, 92, 1761.
[100] Levy, A. B.; Schwartz, S. J. *Tetrahedron Lett.* **1976**, 26, 2201.
[101] See reference 64.

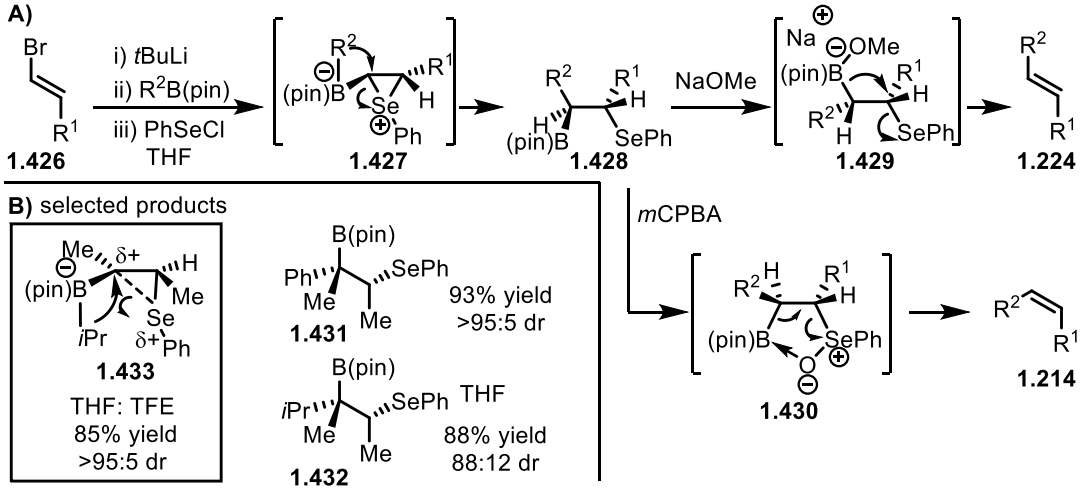
acid, exclusive formation of tertiary alcohol **1.422** was observed, while addition of ethanol as cosolvent immediately prior to oxidation led to the clean formation of methyl ketone product **1.421**. The quantitative yield of ketone **1.421** suggested that hydrogen bonding may promote displacement of the methoxy leaving group of boron-ate complex **1.202** while not promoting protonation of the subsequently formed alkenylboron-ate **1.423.**

1.4.6 Borane, Selenium and Sulfur-Induced Rearrangements

1,2-metallate rearrangement reactions of alkenylboron-ate complexes in which the electrophilic activator is a main group element other than carbon or halogen are uncommon, yet some notable examples exist. Aggarwal recently demonstrated that PhSeCl can act as an alternative to electrophilic halogen sources for the Zweifel–Evans-type olefination reaction of organoboronic esters (Scheme 1.50.A).[102] The mechanism, as proposed in this and a subsequent report,[103] involves the formation of a zwitterionic seleniranium ion **1.427** which undergoes stereospecific 1,2-rearrangement/ring opening to furnish isolable β-selenoboronic ester intermediates **1.428**. These intermediates were shown to be capable of undergoing *anti* elimination when treated with sodium methoxide or *syn*-elimination upon oxidation of the selenium moiety with the electrophilic oxidant *m*CPBA, leading to *E* or *Z* alkenes **1.224** and **1.214** respectively. Interestingly, when an α-substituted alkenylboron-ate substrate was employed with an isopropyl migrating group, lower diastereoselectivity was observed for the β-selenoboronic ester intermediates **1.432** (Scheme 1.50.B). The low diastereoselectivity observed in this case was attributed to a competitive *syn* elimination pathway (inset, **1.433**) Consistent with this mechanistic

[102] Armstrong, R. J.; García-Ruiz, C.; Myers, E. L.; Aggarwal, V. K. *Angew. Chem. Int. Ed.*, **2017**, 56, 786.
[103] See reference 74.

Scheme 1.50. Aggarwal's selenium-induced olefination reaction

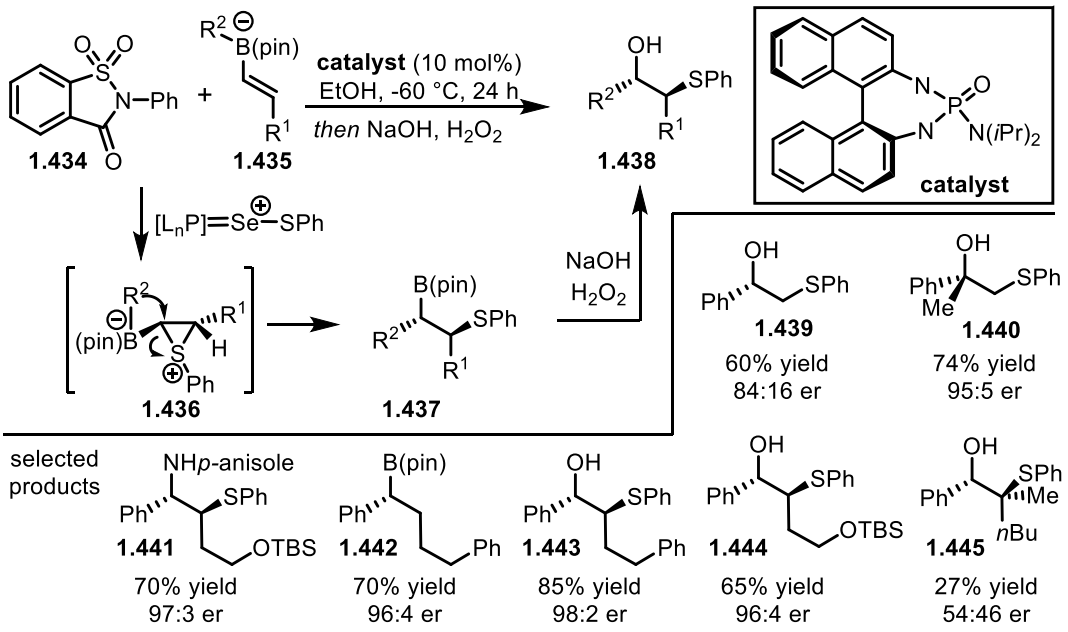


proposal, changing the reaction solvent from THF to the more polar THF:TFE solvent system overturned the diastereoselectivity such that the opposite diastereomer of **1.432** was obtained in 85% yield and >95:5 dr (inset).

Denmark has recently established an enantio- and diastereoselective Lewis base-catalyzed carbosulfenylation reaction of alkenylboronic esters (Scheme 1.51).[104] By subjecting *in situ* generated prochiral alkenylboron-ate complexes **1.435** to a chiral selenium-based catalyst, sulfenium ion transfer occurs and delivers enantioenriched boronic ester products **1.437**, which were isolated as the corresponding alcohol **1.438** in most cases. The mechanism is proposed to procced by the formation of a thiiranium ion intermediate **1.436**, which undergoes stereospecific opening by a 1,2-metallate rearrangement. This rearrangement reaction was shown to apply to mono-, di, and trisubstituted alkenylboronic ester substrates. The use of vinyl and terminally disubstituted alkenylboronic ester substrates resulted in diminished enantioselectivity and yield. This is likely due to poor matching of the steric profiles of the catalyst and substrate, which might

[104] Tao, Z.; Robb, K. A.; Panger, J. L.; Denmark, S. E. *J. Am. Chem. Soc.* **2018**, 140, 15621.

Scheme 1.51. Denmark's catalytic enantioselective 1,2-metallate rearrangement by sulfenium ion catalysis

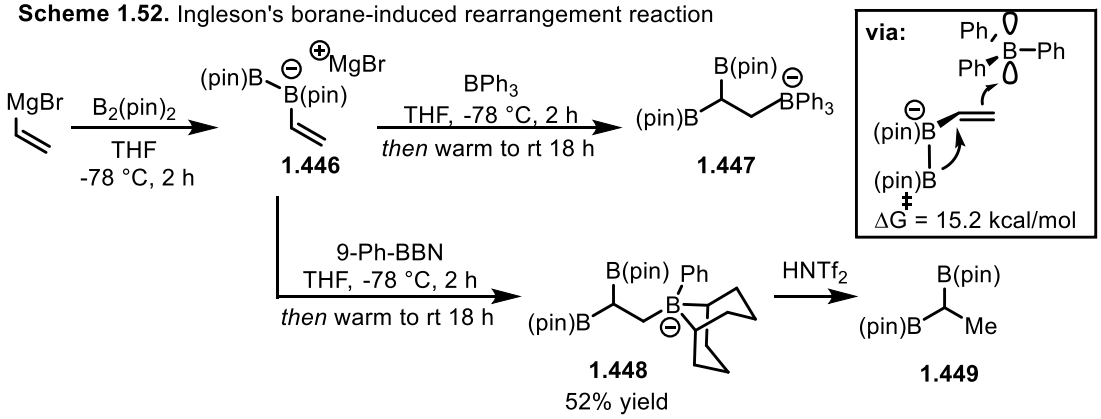


be remedied by catalyst modification. In addition to oxidation, the authors also demonstrated a variety of transformations of the β-borylthioether products, including amination (**1.441)**, and C-S cleavage (**1.442**) in high yield.

Ingleson has recently reported a borane-induced 1,2-metallate rearrangement reaction of bis(pinacolato)diboron-derived vinylboron-ate complex **1.446** to furnishing tris boronate products (Scheme 1.52).[105] This unusual reaction is proposed to involve the interaction of the π-acidic p orbital of triphenyl borane with the electron-rich π-bond of the vinylboron-ate. Based on DFT calculations, rearrangement is proposed to proceed *via* a concerted asynchronous transition state with a relatively low barrier (inset). 9-Ph-BBN was also found to be an effective electrophilic activating agent (**1.446** to **1.448**), and protodeborylation of the 9-BBN moiety facilitated the formation of geminal diboron product **1.449**. The reaction was found to be strongly inhibited by terminal alkene substitution thus limiting the substrate scope to **1.447** and **1.449**. While the substrate scope

[105] Fasano, V.; Cid, J.; Procter, R. J.; Ross, E. Ingleson, M. J. *Angew. Chem. Int. Ed*. **2018**, 130, 13477.

Scheme 1.52. Ingleson's borane-induced rearrangement reaction



of this transformation is currently limited the mechanistic implications of a Lewis acid-induced 1,2-metallate rearrangement by direct interaction with an α-boryl π-system are intriguing. The prospect of rendering the reaction enantioselective and catalytic with the introduction of a proper chiral borane catalyst and a compatible stoichiometric electrophilic reagent capable of turning over the initially formed borane adduct is intriguing.

1.4.7 Carbon Electrophile-Induced Rearrangements

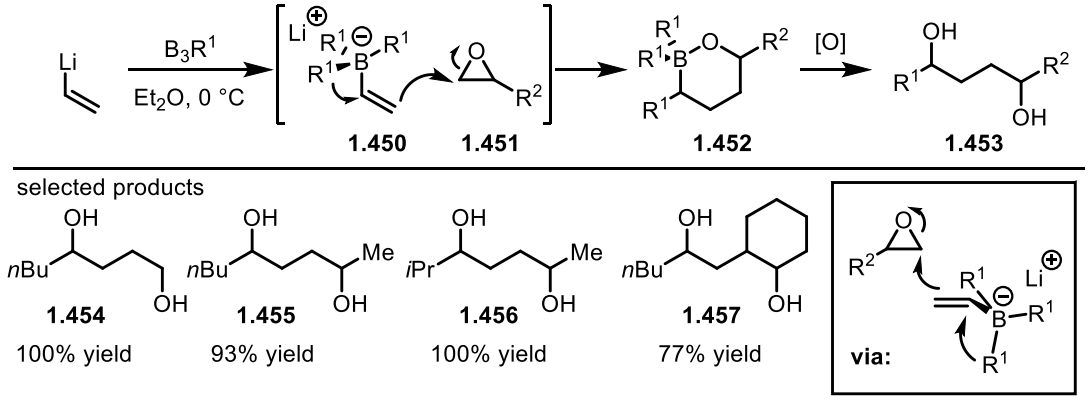
While less common than halogen-induced rearrangement reactions, carbon-based electrophiles are also known to induce 1,2-metallate rearrangements of boron-ate complexes adjacent to sp^2-hybridized systems. These reactions can be roughly divided into two categories: those involving isolated alkenes and those involving aromatic systems.

1.4.7.1 Rearrangements of Alkenyl Substrates

An early study by Utimoto reported a 1,2-metallate rearrangement reaction of vinyl trialkylborane-derived ate complexes with epoxides (Scheme 1.53).[106] This multi-component reaction merges three simple starting materials in a procedurally simple

[106] Utimoto, K.; Uchida, K.; Nozaki, H. *Tetrahedron Lett*. **1973**, 45, 4527.

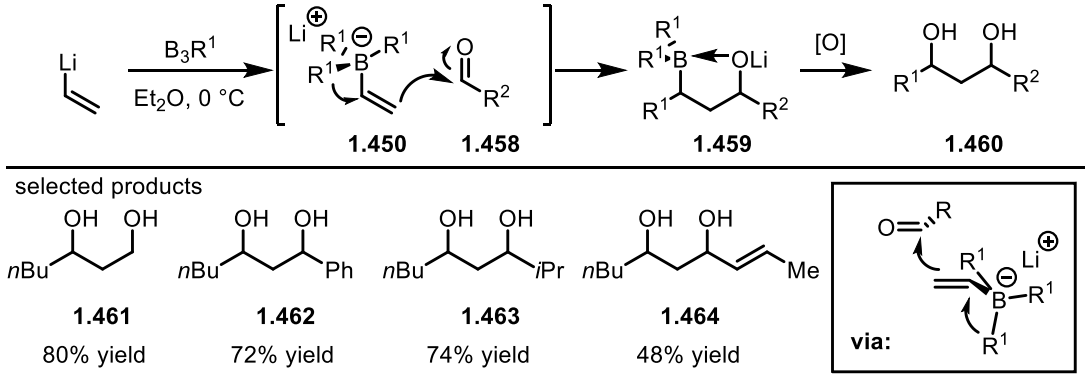
Scheme 1.53. Utimoto's three-component 1,4-diol synthesis by epoxide-induced rearrangement



fashion, furnishing products **1.452** with a 1,4-difunctional pattern which, upon oxidation, grant access to valuable 1,4-diols (**1.454** through **1.457**).

In a subsequent report, Utimoto demonstrated that various aldehydes **1.458** could be similarly engaged, granting access to 1,3-diol products **1.460** in high yield after oxidative workup (Scheme 1.54).[107] Low diastereoselectivity was observed in these reactions, with

Scheme 1.54. Utimoto's three-component 1,3-diol synthesis by aldehyde-induced rearrangement

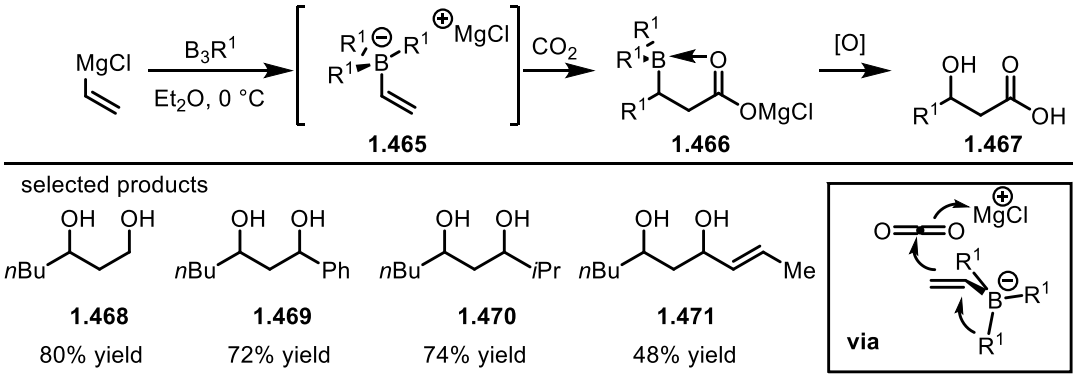


the majority giving between 1:1 and 64:36 dr.

Deng later expanded the scope of carbon-based electrophiles to CO_2 by employing simple Grignard reagent-derived vinylboron-ate complexes **1.465**, thus producing β-hydroxy carboxylic acids **1.467** upon oxidative workup (Scheme 1.55).[108]

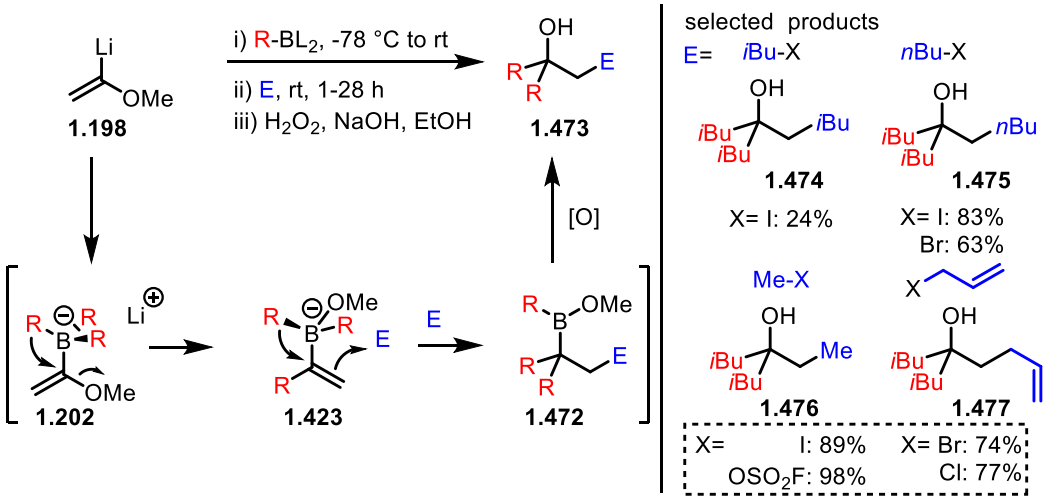
[107] Utimoto, K.; Uchida, K.; Nozaki, H. *Tetrahedron*, **1977**, *33*, 1949.
[108] Deng, M.-Z.; Lu, D. A.; Xu, W.-H. *J. Chem. Soc. Chem. Commun.* **1985**, 1478.

Scheme 1.55. Deng's three-component β-hydroxy carboxylic acid synthesis by CO_2-induced rearrangement



Levy further expanded the scope of electrophiles to include alky halides (Scheme 1.56).[109] In the same report where the proton-induced rearrangement reaction of α-methoxy vinyllithium-derived boron-ate complexes was demonstrated (*vide supra*), Levy found that the addition of various alkyl halides led to rearrangement of *in situ* generated alkenylboron-

Scheme 1.56. Levy's three-component alkyl electrophile-induced rearrangement reaction

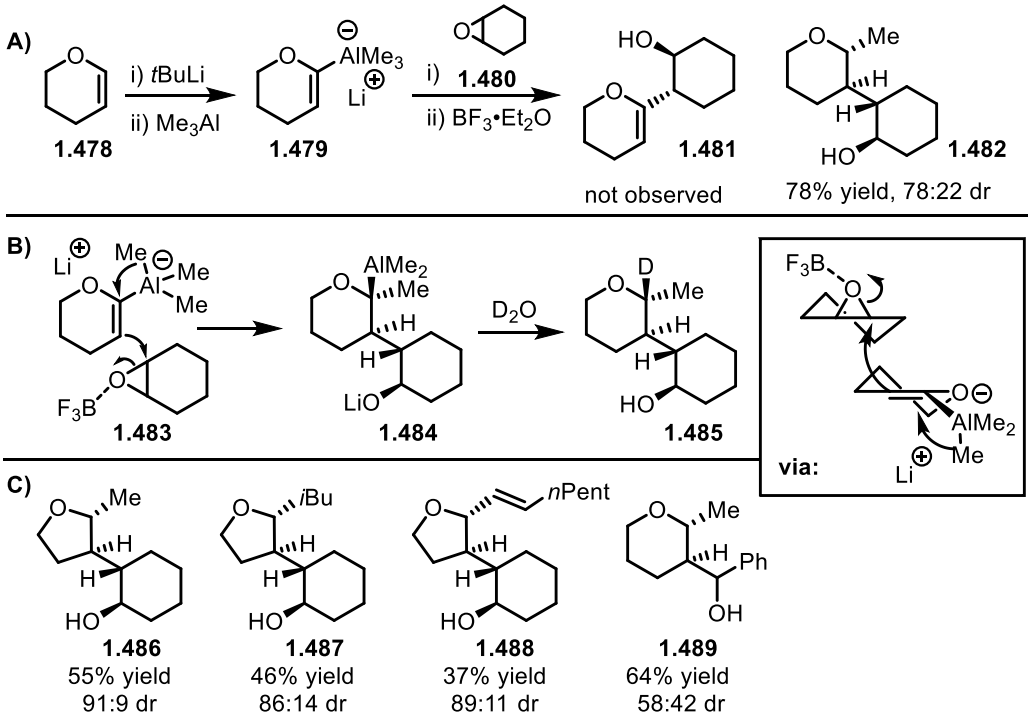


ate complex **1.423** and produced tertiary borinic esters **1.472**, which were isolated as the corresponding alcohol after oxidation. The transformation was found to effectively engage various primary alkyl electrophiles (**1.475**, **1.476**, **1.477**) though more sterically hindered electrophiles such as isobutyl iodide led to diminished yields (**1.474**).

[109] See reference 64.

1,2-Metallate rearrangements promoted by carbon electrophiles are not limited to alkenylboranes. Alexakis reported a similar reaction of aluminum-ate complexes with epoxides and aldehydes (Scheme 1.57.A).[110] When aluminum-ate nucleophile **1.479** was treated with epoxide **1.480** in the presence $BF_3{\cdot}Et_2O$, the expected direct addition product **1.481** was not observed but instead product **1.482** was obtained in high yield as a separable mixture two diastereomers. Deuterium labeling experiments (Scheme 1.57.B) as well as crystallographic analysis of the relative stereochemistry of the major diastereomer of **1.482**

Scheme 1.57. Alexakis' alkenylaluminum-based epoxide and aldehyde-induced rearrangement reaction



suggests the reaction proceeds by a mechanism similar to those reported for related boron-based systems (inset). As depicted in Scheme 1.57.C, reactions utilizing 2-lithiated dihydrofuran generally resulted in high diastereoselectivity (**1.486**, **1.487**, **1.488**). The addition of $BF_3{\cdot}Et_2O$ was found to be essential to promote the desired reaction. Aldehydes

[110] Alexakis, A. ; Hanaizi, J.; Jachiet, D. ; Normant, J.-F.; Toupet, L. *Tetrahedron Lett.* **1990**, 31, 1271.

proved to be competent electrophiles, resulting in somewhat diminished diastereoselectivity (**1.489**), but the use of alky halide electrophiles resulted in complex mixtures of products**.**

While reports of multi-component reactions involving carbon electrophile-induced 1,2-rearrangements are relatively rare, perhaps owing to the synthetic limitations of using borane and aluminum reagents, these reactions enable synthetically powerful C-C bond formations. The prospect of developing this class of transformation by employing boronic esters and using catalytic chiral Lewis acid to exercise stereocontrol presents an intriguing avenue for investigation.

1.4.7.2 Rearrangements of Aromatic Substrates

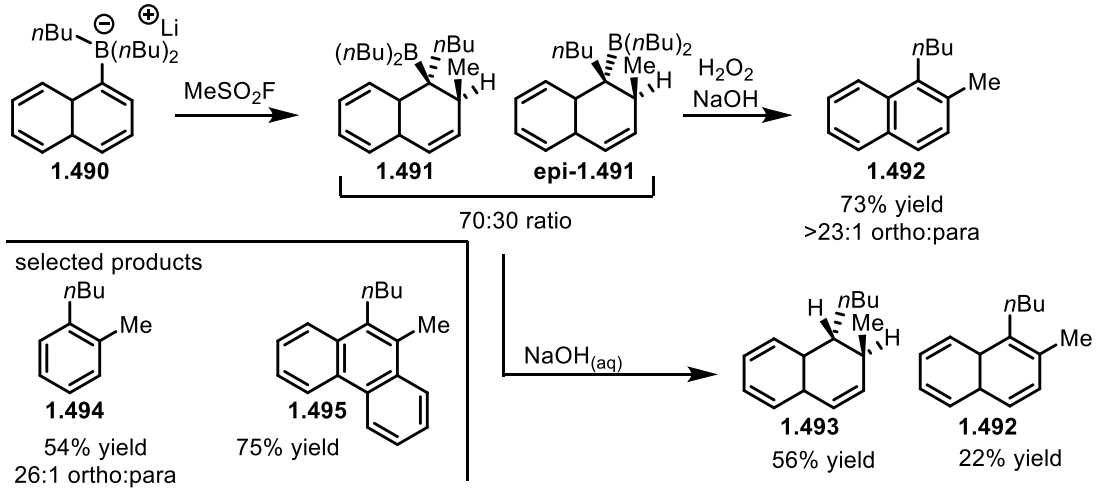
In addition to rearrangement reactions involving alkenyl organometallics and alkyl electrophiles, which can be thought of as analogous to enolate alkylations, related transformation are also known for some aromatic π-system.

Negishi reported an aromatic substitution reaction of aryltrialkylboron-ate complexes with methyl fluorosulfonate which enabled the preparation of *ortho*-dialkyl-substituted aromatic compounds in moderate to good yields (Scheme 1.58).[111] The authors proposed a mechanistic scenario in which intermolecular electrophilic aromatic substitution by methyl fluorosulfonate precedes intramolecular nucleophilic trapping**.** Oxidizing a reaction solution of 1-napthylboron-ate complex **1.490** and methyl fluorosulfonate resulted in the formation of *ortho*-dialkyl naphthalene product **1.492** in high yield. The excellent *ortho*:*para* selectivity observed was attributed to attractive electrostatic interaction

[111] Negishi, E.; Merrill, R. E. *J. Chem. Soc. Chem. Commun.* **1974**, 860.

between the boron-ate moiety and methyl fluorosulfonate. Treatment of the same reaction solution with aqueous base resulted in the formation of a mixture of aromatic and dihydroaromatic compounds **1.493** and **1.492**. This result was attributed to the formation of a mixture of *syn* and *anti*-addition products **1.491** and **epi-1.491** respectively, the former of which undergoes stereoretentive protodeborylation to form **1.493** while the latter

Scheme 1.58. Negishi's methyl fluorosulphonate-induced regiospecific aromatic dialkylation



undergoes rapid dehydroboration forming **1.492**. A phenanthryl and a simple phenyl tributylboron-ate complex were successfully engaged in this reaction (**1.494** and **1.495)**. Considering the substantial resonance stabilization energy of benzene (32 kcal/mole)[112] the formation of **1.494** is particularly remarkable.

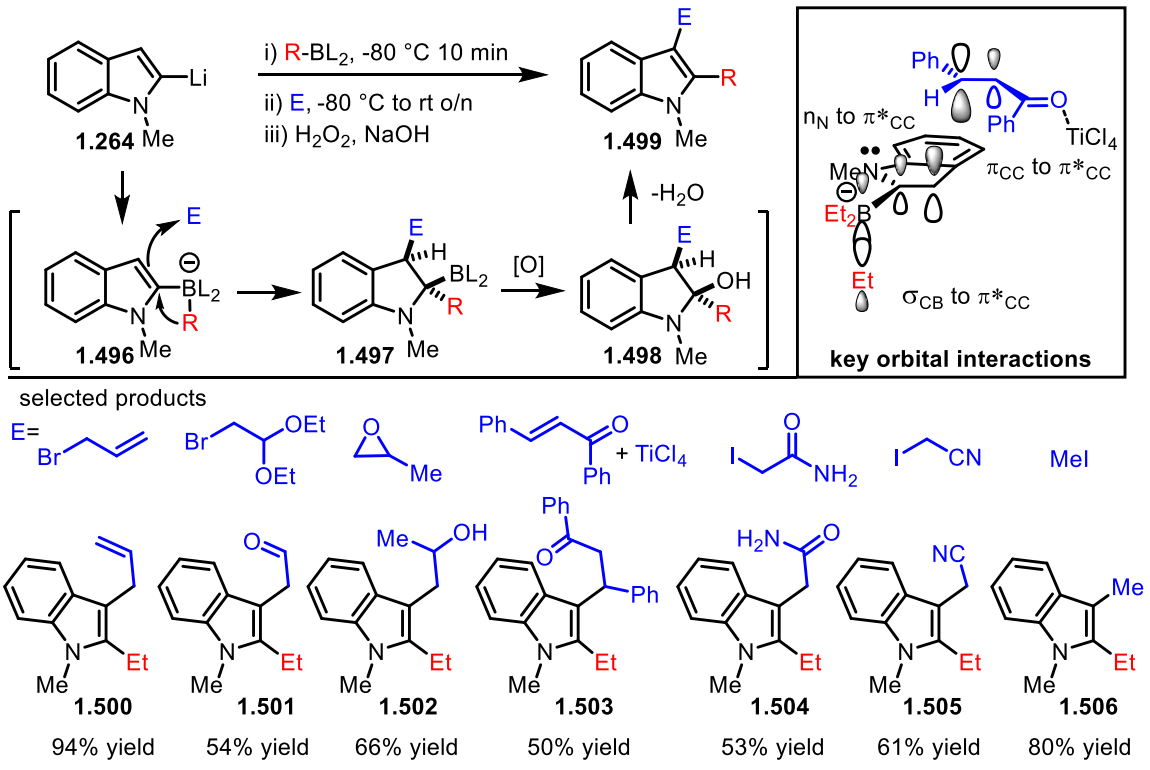
The vast majority of carbon-electrophile-induced rearrangement reactions of aromatic systems involve indole-derived boron-ate complexes. This is likely due to the considerable research interest associated with the preparation of indole derivatives as well as the greater nucleophilicity and lower resonance stabilization energy of these systems.

In a continuation of an earlier study of the halogen-induced rearrangement reaction of

[112] Cyrański, M. K. *Chem. Rev.* **2005**, 105, 3773.

indole-derived boron-ate complexes (*vide supra*), Levy reported a one-pot method for the 2,3-dialkylation of *N*-methyl indole **1.264** (Scheme 1.59).[113] The procedure developed involves lithiation of indole, consecutive treatment with trialkyl borane and a variety of electrophiles, followed by oxidation to furnish 1-methyl, 2,3-dialkyl indole **1.499**. The electrophile scope was found to be quite broad, including alkyl halides (**1.500**, **1.501**, **1.504**, **1.505**, **1.506**), epoxides (**1.502**), as well as chalcone (**1.503**). Considering the key indole π to chalcone π* orbital interactions involved in the formation of **1.503** (inset) we see that the attacking π-orbital of the indole molecule is highly polarized towards the terminal carbon due both to the neighboring nitrogen lone pair as well as hyperconjugation from the neighboring σ_{CB} orbital. Additionally, the antibonding π* orbital of chalcone is highly polarized towards the terminal alkene position, which is enhanced by the inductive

Scheme 1.59. Levy's electrophile-induced three-component indole dialkylation



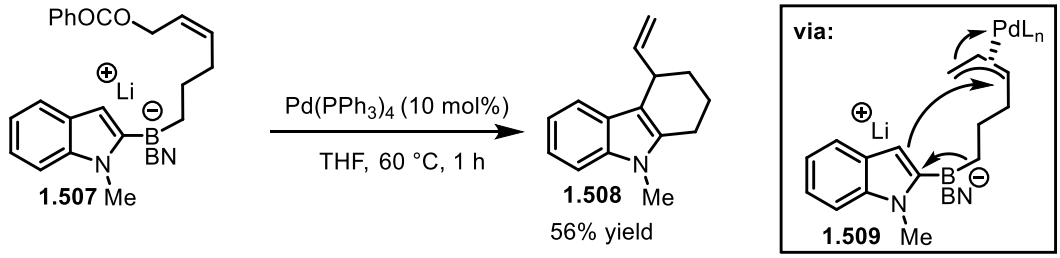
[113] Levy, A. B. *Tetrahedron Lett.* **1979**, 42, 4021.

influence of Lewis acidic $TiCl_4$. This substrate in particular suggests that the use of chiral Lewis acid catalysis might provide a means of rendering this conjugate addition reaction stereoselective.

Over a decade after Levy's seminal investigation, Ishikura reported a series of studies detailing the catalytic allylation reaction of indole-derived boron-ate complexes (Scheme 1.60).[114] The reported palladium-catalyzed intramolecular annulation reaction was proposed to involve oxidative addition of Pd^0 to allyl carbonate (**1.507**), generating an electrophilic palladium π-allyl (inset, **1.509**) which induces 1,2-metallate rearrangement of the pendant indole nucleophile to furnish annulated product **1.508**. Notably the primary alkyl group migrated in preference to the BBN secondary bridgehead carbon. This type of metal-catalyzed rearrangement reaction is distinct from the metal-induced rearrangements that will be discussed in chapter 2 of this dissertation as palladium does not directly interact with the π-system of the boron-ate but rather serves to catalytically generate a highly electrophilic carbon-based species which induces 1,2-rearrangement.

Building on this initial work, Ishikura later extended the scope of the reaction to the intramolecular alkylation of *N*-methyl indole utilizing propargyl carbonate electrophiles,[115]

Scheme 1.60. Ishikura's intramolecular palladium-catalyzed indole allylation

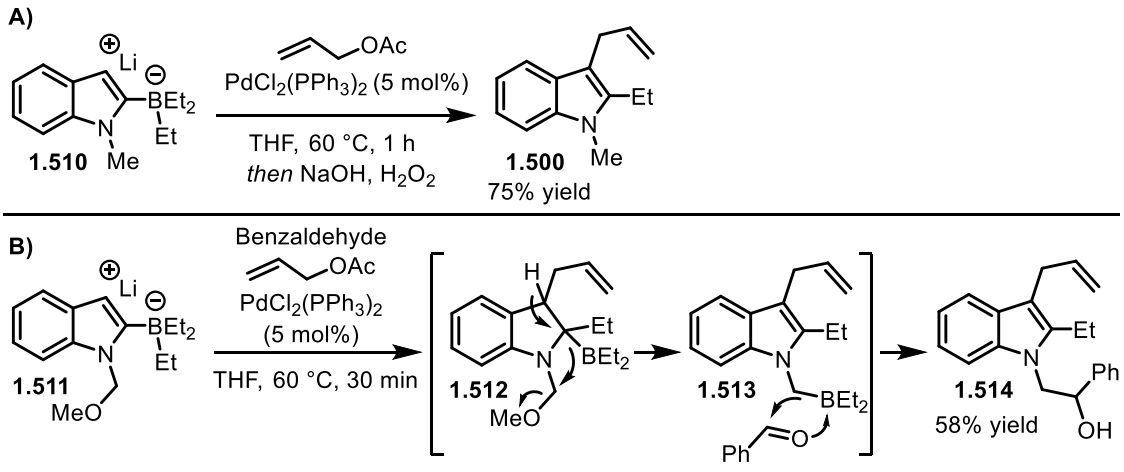


[114] Ishikura, M.; Terashima, M.; Okamura, K.; Date, T. *J. Chem. Soc. Chem. Commun.* **1991**, 1219.
[115] Ishikura, M.; Agata, I. *Heterocycles* **1996**, 43, 1591.

and allyl epoxides, carbonates, and acetates (Scheme 1.61.A).[116] In a later report, Ishikura developed a four-component coupling reaction of trialkylboranes, lithiated indole, allyl electrophiles, and aldehyde electrophile (Scheme 1.61.B).[117] The key to this transformation was the incorporation of a methoxy leaving group on the *N*-methyl indole component which allowed a borotropic shift to occur during deborylative rearomatization **1.512** to **1.513**). Nucleophilic attack of **1.513** on an equivalent of aldehyde furnishes the final product **1.514**. Notably, this palladium-catalyzed reaction could be performed in just 30 minutes without the need for oxidative workup.

With precedent for the palladium-catalyzed allylation of indole-derived boron-ate complexes established, Ready has recently rendered this transformation enantio- and diastereoselective utilizing enantioenriched Pd-(*S*)-BINAP and Pd-(*S*)-H_8-BINAP catalysts (Scheme 1.62), catalysts 1 and 2 respectively), and significantly improving the synthetic utility of the transformation by utilizing aryl- and alkyboronic pinacol esters

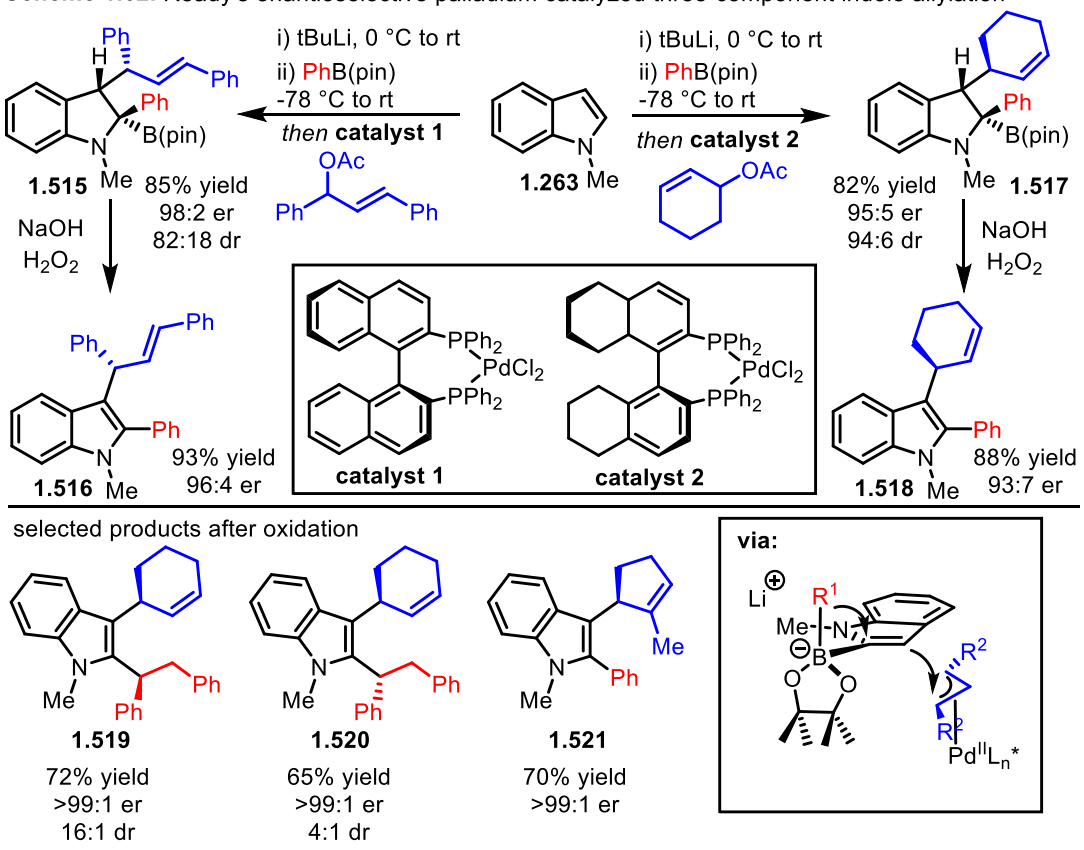
Scheme 1.61. Ishikura's intramolecular palladium catalyzed indole alkylation



[116](a) Ishikura, M.; Kato, H. *Tetrahedron* **2002**, *58*, 9838. (b) Ishikura, M.; Ida, W.; Yanada, K. *Tetrahedron* **2006**, 62, 1015.
[117] Ishikura, M.; Kate, H.; Ohnuki, N. *Chem. Commun.* **2002**, 3, 220.

rather than boranes.[118] Due to the improved stability of boronic esters relative to boranes, indolineboronic ester products **1.516** and **1.518** could be isolated, demonstrating this method's capacity to generate three contiguous stereocenters with excellent enantioselectivity and good-to-excellent diastereoselectivity. The proposed mechanism for this reaction is analogous to Ishikura's proposal, though a stepwise outer-sphere attack of the indoleboron-ate complex on the electrophilic palladium π-allyl species was favored rather than a concerted mechanism. A simplified stereochemical model which is consistent with the observed enantio- and diasteroselectivity can be visualized as depicted in Scheme 1.62 (inset). Ready has applied this method to the preparation of indolines with quaternary

Scheme 1.62. Ready's enantioselective palladium catalyzed three-component indole allylation

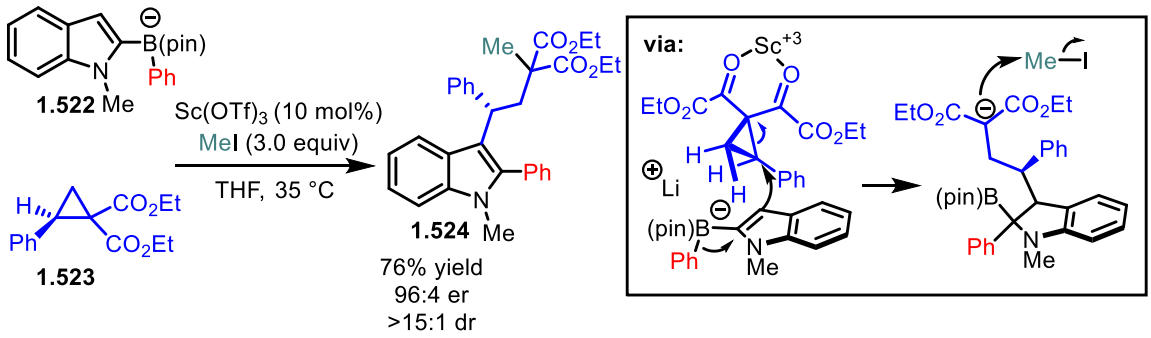


[118] Panda, S.; Ready, J. M. *J. Am. Chem. Soc.* **2017**, 139, 6038.

stereocenters at the indole 3-position.[119]

Recently, Studer demonstrated that donor-acceptor cyclopropanes, when activated with catalytic amounts of Lewis acid, are sufficiently electrophilic to activate indole-derived boron-ate complexes.[120] As depicted in Scheme 1.63 scandium triflate is proposed to activate donor-acceptor cyclopropane **1.523** by carbonyl binding, rendering the strained ring sufficiently electrophilic to enable nucleophilic attack by the indoleboron-ate **1.522**, thus generating a malonate anion which can then react with an alkyl electrophile to turn over the catalytic cycle (inset). Notably, this reaction represents an overall four-component coupling of boronic esters, lithiated indoles, donor-acceptor type cyclopropanes, and alkyl halides. When enantioenriched cyclopropane **1.523** was employed in this reaction, product **1.524** was obtained in high enantio- and diasteroenrichment, allowing a plausible stereochemical model to be proposed (insert) in which invertive cyclopropane ring-rupture and *anti* 1,2-rearrangement occurs in a stereospecific fashion, with the large boron and phenyl groups directed away from one another. While the use of chiral enantioenriched cyclopropane substrates currently enables access non-racemic products, the use of a chiral Lewis acid might enable achiral cyclopropanes to be engaged in an enantioselective

Scheme 1.63. Studer's scandium-catalyzed four-component coupling



[119] Panda, S.; Ready, J. M. *J. Am. Chem. Soc.* **2018**, 140, 13242.
[120] Das, S.; Daniliuc, C. G.; Studer, A. *Angew. Chem. Int. Ed*. **2018**, 57, 4053.

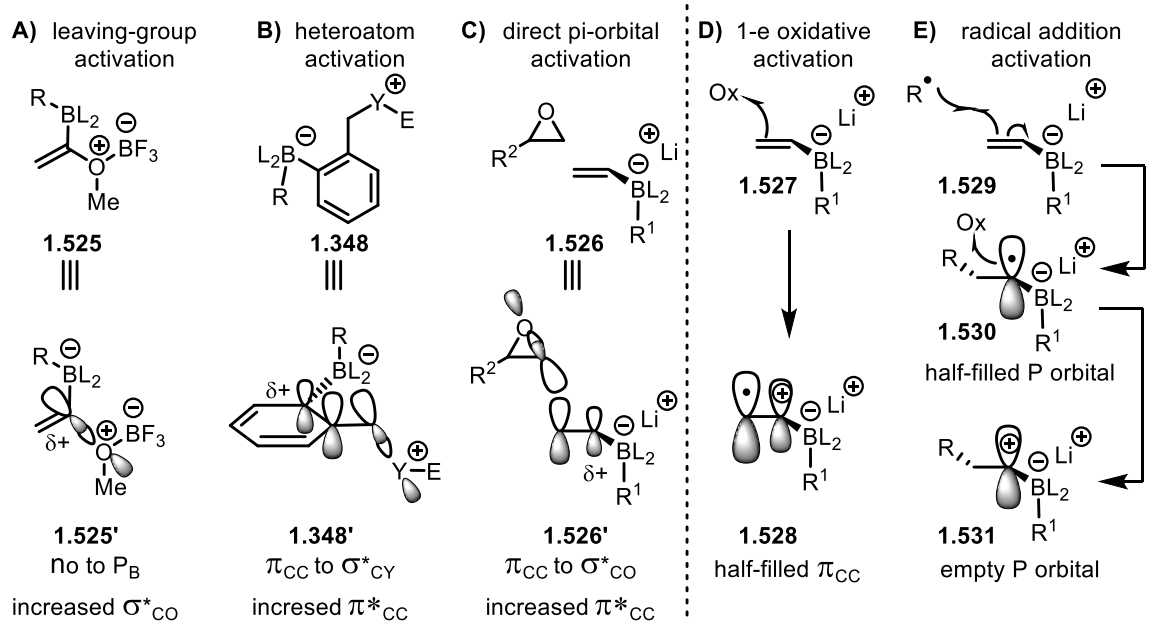
fashion.

1.4.8 Radical-Induced Rearrangements

A mechanistic requirement common across all electrophile-induced rearrangement reactions is that an electrophilic species must reduce the electron density at the terminus of migration adjacent to boron for rearrangement to occur. At one extreme, a stepwise rearrangement reaction such as Zweifel's proposal for the proton-induced rearrangement of alkenylboron-ate complexes (*vide supra*) can occur, where an empty p orbital adjacent to boron is formed and accepts the migrating group with its pair of electrons. For concerted rearrangements, it is an antibonding orbital adjacent to boron that accepts electrons.

Modes of electrophilic activation are varied but generally involve: (1) direct through-bond induction, as in the case of leaving group activation (Scheme 1.64.A), (2) activation of a π-system by hyperconjugation in the case of heteroatom activation (Scheme 1.64.B); or (3) direct electrophilic interaction with the π-system to which the terminus of migration belongs (Scheme 1.64.C). Recently, new mechanisms for 1,2-metallate rearrangement have been proposed involving one-electron processes (Scheme 1.64.D and E). While similar to the previous two-electron activation modes in that they reduce electron density at the terminus of migration, they are mechanistically distinct. Due to hyperconjugation from a four-coordinate boron moiety to an adjacent unsaturated-system, such π-bonds are electron-rich and may, in principle, undergo single-electron oxidation to furnish a radical cation species such as **1.527** (Scheme 1.64.D) which, in principle, are prone to 1,2-metallate rearrangement. A second possible radical activation mode involves an initial radical addition to the electron-rich π-bond adjacent to boron, thus generating an alpha-

Scheme 1.64. Modes of 2-electron electrophilic activation and radical activation: orbital analysis

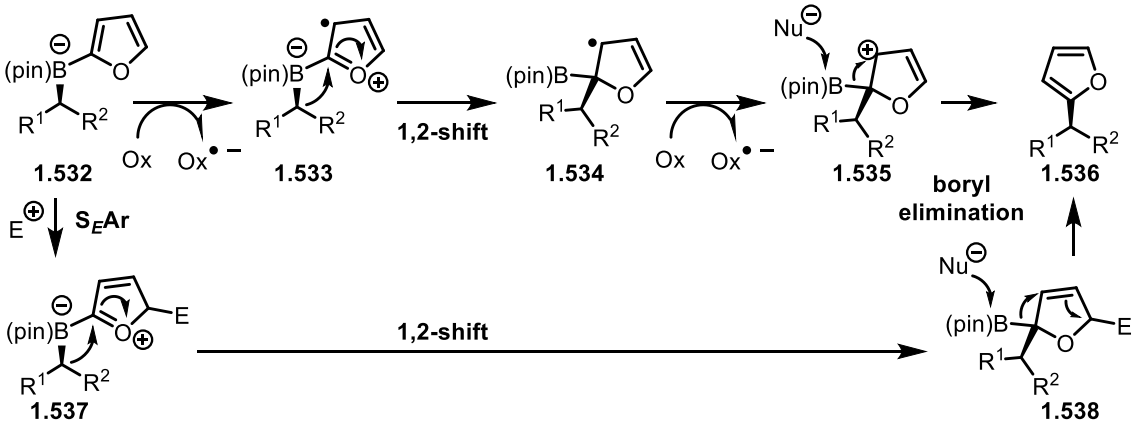


boryl radical species **1.530** (Scheme 1.64.E), which may undergo subsequent single-electron oxidation, to furnish zwitterion **1.531** which may undergo 1,2-metallate rearrangement. In contrast to two-electron activation modes, radical-induced rearrangement reactions have only recently been reported.

As previously alluded to, in 2016 Aggarwal reported that DDQ, like NBS, serves as a competent electrophilic activator in the electrophile-induced arylation of enantioenriched alkylboronic esters.[121] NBS was found to be the more generally applicable reagent as DDQ was observed to promote the oxidative cleavage of benzylic and tertiary boron-ate complexes to the corresponding radical species. This observation prompted the authors to consider the one-electron pathway (**1.532** to **1.536**) depicted in Scheme 1.65. This mechanistic scenario was ultimately discarded based on DFT modeling which suggested single-electron oxidation should occur at the B-C(sp^3) bond rather than the adjacent unsaturated furyl ring. Additionally, the stereospecific nature of successful couplings and

[121] See reference 85.

Scheme 1.65. Aggarwal's proposal for single electron oxidation-induced rearrangement versus S_EAr

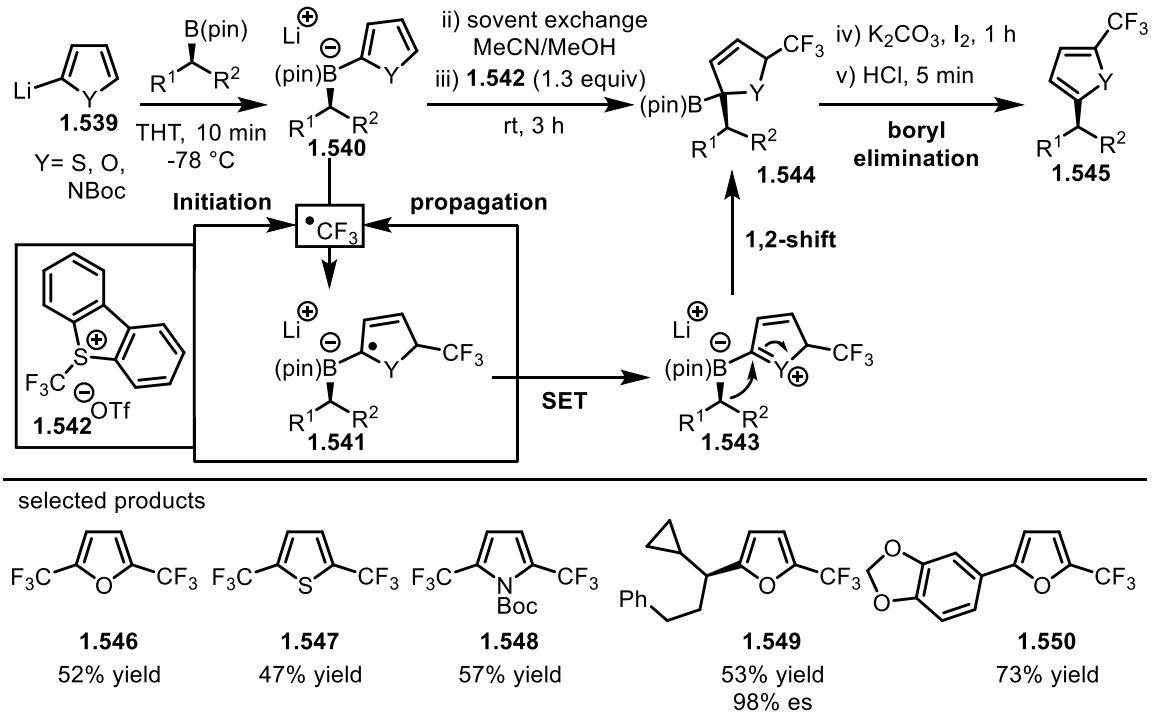


the lack of cyclopropane ring opening for substrates containing a cyclopropane at the β-boryl position were cited as evidence against an oxidative radical coupling mechanism. The favored two-electron S_EAr pathway (bottom of Scheme 1.65) was also found to be consistent with the 2-electron electrophilic character of DDQ which is reported to be comparable to tropylium ion.[122]

While a radical pathway was not found to be operative in this initial report, it appears to have provided inspiration for a following report from the same group on the enantiospecific trifluoromethyl radical-induced three component reaction of boronic esters with furans (Scheme 1.66).[123] A variety of furan-, thiophene-, and pyrrole-derived boron-ate complexes were found to react with trifluoromethyldibenzothiophenium salt **1.542** (Umemoto's reagent) to furnish trifluoromethylated intermediate **1.544** which, upon treatment with iodine and base followed by acidic workup, underwent deborylative rearomatization to produce coupled product **1.545**. Support for the mechanistic scenario depicted in Scheme 1.66 was provided by EPR detection of trifluoromethyl radicals utilizing the spin trap *N-tert*-butyl-α-phenylnitrone (PBN), control experiments

[122] Guo, X.; Mayr, H. *J. Am. Chem. Soc*. **2013**, 135, 12377.
[123] Wang, Y.; Noble, A.; Sandford, C.; Aggarwal, V. K. *Angew. Chem. Int. Ed.* **2017**, 56, 1810.

Scheme 1.66. Aggarwal's CF_3 radical-induced three component reaction of boronic esters with furans

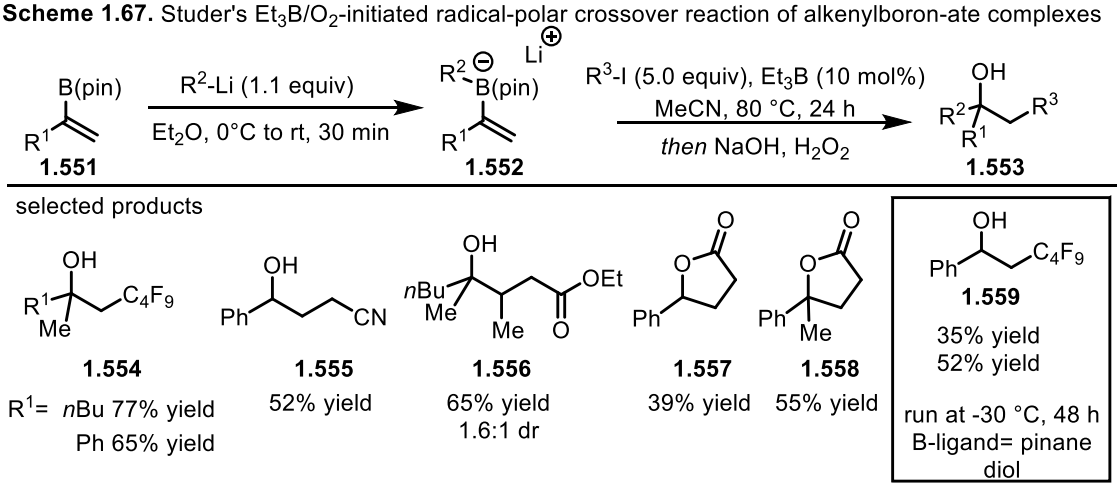


demonstrating that radical generation required both reagent **1.542** and boron-ate complex **1.540**, and the observation of reaction inhibition in the presence of radical trap PBN. Addition of a CF_3 radical (likely generated by single-electron transfer (SET) from a sacrificial amount of boron-ate **1.540** to reagent **1.542**) to boron-ate complex **1.540** at the 5 position of furan produces α-boryl radical **1.541**. Radical intermediate **1.541** then undergoes single-electron oxidation by reagent **1.542** to generate zwiterionic intermediate **1.543** and propagate the radical chain. Finally, 1,2-metallate rearrangement of **1.543** generates isolable allylic boronate intermediate **1.544** which was generally converted to the corresponding aromatic heterocycle **1.545** by boryl elimination.

A contemporaneous report by Studer investigated a related three-component coupling of alkenylboron-ate complexes with a variety of electrophiles (Scheme 1.67).[124] The authors

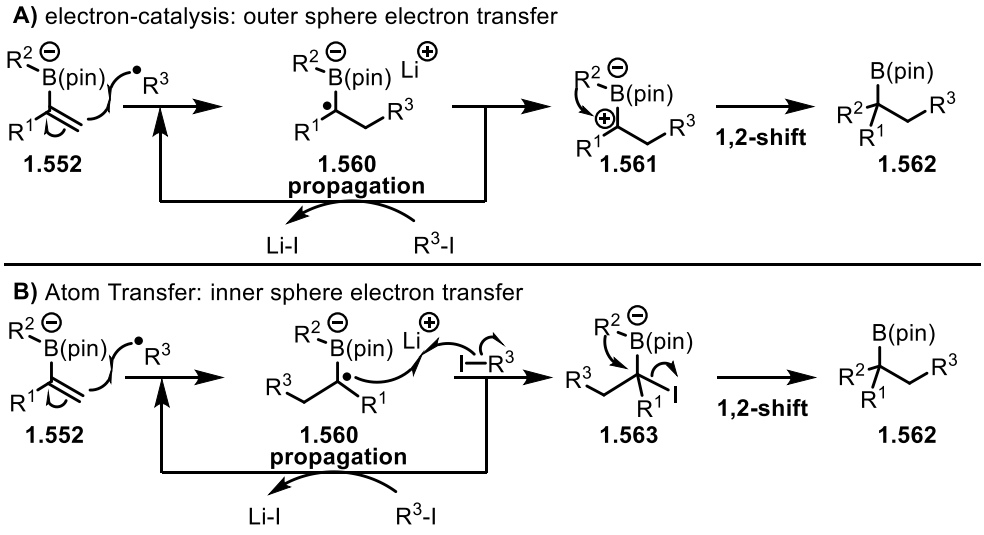
[124] Kischkewitz, M.; Okamoto, K.; Mück,-Lichtenfeld, C.; Studer, A. *Science* **2017**, 355, 936.

Scheme 1.67. Studer's Et_3B/O_2-initiated radical-polar crossover reaction of alkenylboron-ate complexes



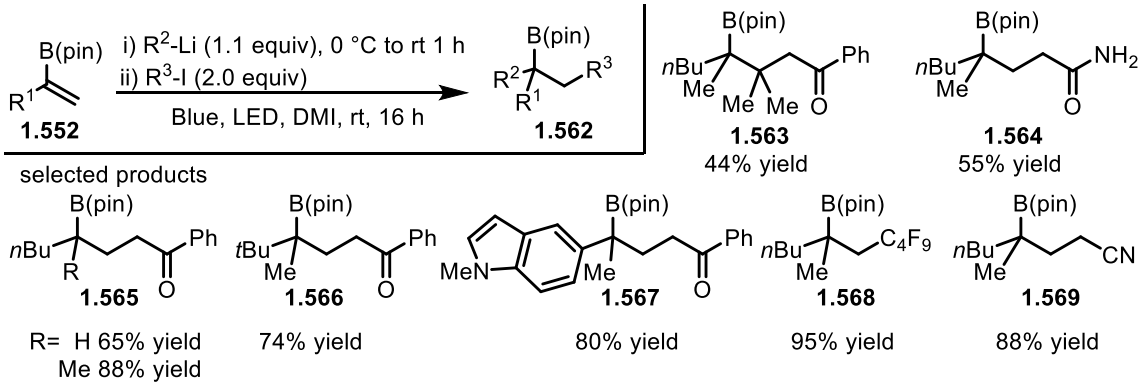
found that in the presence of adventitious oxygen, the addition of triethylborane to a solution of alkenylboron-ate complex **1.552** and various electron-deficient alkyl electrophiles resulted in the formation of alkylboronic pinacol esters which were generally oxidized to the corresponding alcohol for ease of isolation. A variety of secondary and tertiary alcohols incorporating perfluoroalkyl (**1.554**), methyl nitrile (**1.555**), and ester (**1.556**) functionality could be prepared in this manner, with lactone products **1.557** and **1.558** generated by treatment of the corresponding ester with catalytic acid. Notably, when (+)-vinylboronic pinanediol ester was employed in the reaction at low temperature for prolonged reaction time, a degree of stereocontrol was observed (inset, **1.559**). In agreement with Agarwal's mechanistic proposal, Studer proposed an oxygen/borane initiated radical-polar crossover mechanism involving outer-sphere electron transfer (Scheme 1.68.A). A mechanistically related inner-sphere atom transfer pathway (Scheme 1.68.B) was computationally found to be kinetically feasible but experimentally this pathway was found to be less probable based on the observation of product when Togni's reagent was employed as a CF_3 radical source; this reagent should not be capable of participating in an atom transfer pathway.

Scheme 1.68. Two potential reaction mechanisms for radical-induced 1,2-metallate rearangement



Shortly after this report, Aggarwal[125] and Morken[126] independently reported similar radical-induced multi-component reactions. Aggarwal found that blue light could serve as an efficient radical initiator to promote the formation of primarily tertiary alkylboronic esters in excellent yield (Scheme 1.69). The radical nature of the reaction mechanism was supported by the observation that radical scavengers such as 2,2,6,6-tetramethyl piperidine 1-oxide (TEMPO) and 1,1-diphenylethylene, inhibited the reaction. UV-Vis absorption studies indicated that light serves as a radical initiator by homolyzing the carbon-iodine

Scheme 1.69. Aggarwal's photo-initiated radical-polar crossover reaction of alkenylboron-ate complexes



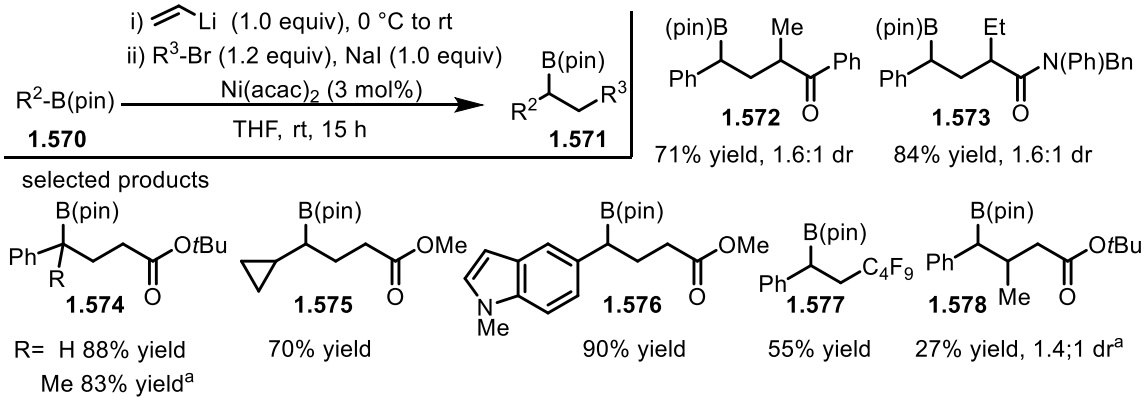
[125] Silvi, M.; Sandford, C.; Aggarwal, V. K. *J. Am. Chem. Soc.* **2017**, 139, 5736.
[126] Lovinger, G. J.; Morken, J. P. *J. Am. Chem. Soc.* **2017**, 139, 17293.

bond of the electrophile. For some electrophiles, it was found that the addition of a ruthenium photosensitizer was required to achieve high yields; this was attributed to either poor initiation or slow chain propagation.

In a study by Morken investigating the enantioselective triamine–nickel-catalyzed conjunctive coupling of alkenylboron-ate complexes and alkyl electrophile, which will be discussed in detail in chapter 4 of this dissertation, it was observed that for electron-deficient alkyl electrophiles 3 mol% nickel salt served as an efficient radical initiator to promote radical-polar crossover reactions at room temperature (Scheme 1.70). The reaction was found to be general, granting access to various functionalized alkylboronic esters in high yield. The use of radical probe substrates, radical trapping agents, and deuterium labeling experiments supported the radical nature of the reaction.

Renaud subsequently reported a similar radical-polar crossover reaction initiated by triethylborane and di-*tert*-butylhyponitrile at elevated temperatures (Scheme 1.71).[127] Interestingly, borinic ester **1.583**, the product of oxygen migration, was observed when *tert*-butyllithium was employed as a nucleophile, consistent with the trapping of an α-boryl

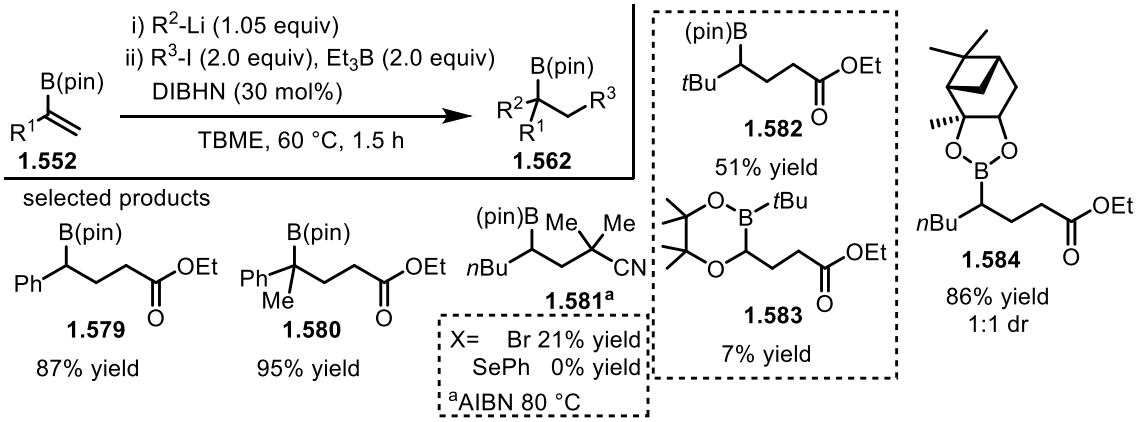
Scheme 1.70. Morken's nickel-initiated radical-polar crossover reaction of alkenylboron-ate complexes



[a]reaction conducted by addition of PhLi to alkenylB(pin).

[127] Tappin, N. D. C.; Gnägi-Lux, M.; Renaud, P. *Chem. Eur. J.* **2018**, 24, 11498.

Scheme 1.71. Renaud's Et_3B/DIBHN-initiated radical-polar crossover reaction of alkenylboron-ate complexes



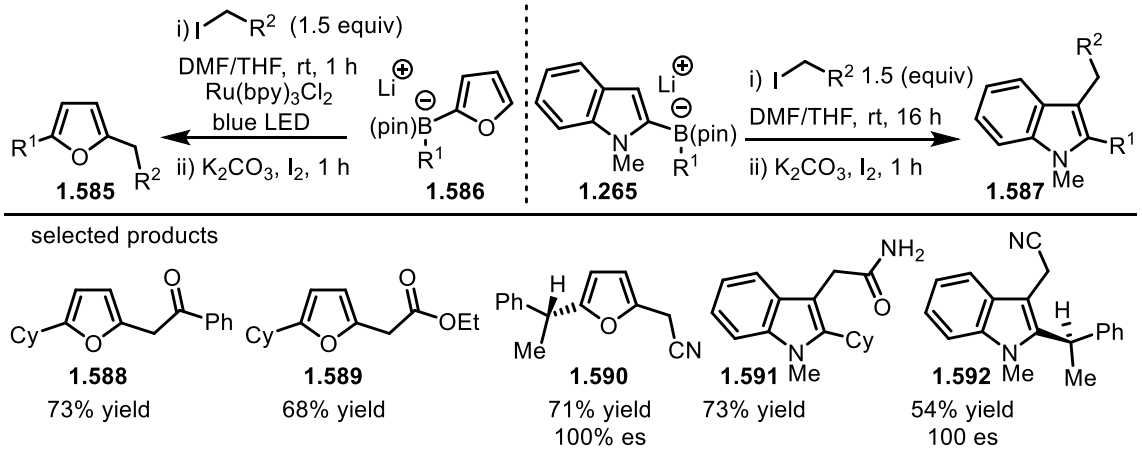
cationic intermediate. In contrast to Studer's report, the use of (+)-vinylboronic acid pinanediol ester did not result in any observable stereoinduction (**1.584**) likely owing to the higher temperatures employed (60 ˚C versus -30 ˚C). For substrate **1.581** the lack of reactivity of an alkyl selenide electrophile compared to the bromide electrophile was taken as evidence against an atom transfer mechanism as selenium and bromine have similar rates of atom transfer but alkyl bromides are more easily reduced.

Aggarwal subsequently applied his photo-initiated radical-polar crossover strategy to the three-component reaction of lithiated furan-derived boron-ate complexes (Scheme 1.72). [128] In the same report it was found that lithiated indole-derived boron-ate complexes **1.265** could participate in a similar overall transformation by a polar S_N2 pathway presumably proceeding by the same mechanism reported by Levy in his related reaction utilizing trialkylboranes (*vide supra*).

Adopting visible light initiation conditions, Studer has demonstrated that enantioenriched alkylboronic esters can engage in stereospecific radical-induced rearrangement reactions (Scheme 1.73.A).[129] Consistent with the predominantly

[128] Silvi, M; Schrof, R.; Noble, A.; Aggarwal, V. K. *Chem. Eur. J.* **2018**, *24*, 4279.
[129] Gerleve, C.; Kischkewitz, M.; Studer, A. *Angew. Chem. Int. Ed*. **2018**, 57, 2331.

Scheme 1.72. Aggarwal's three-component difunctionalization reactions of furan and indole



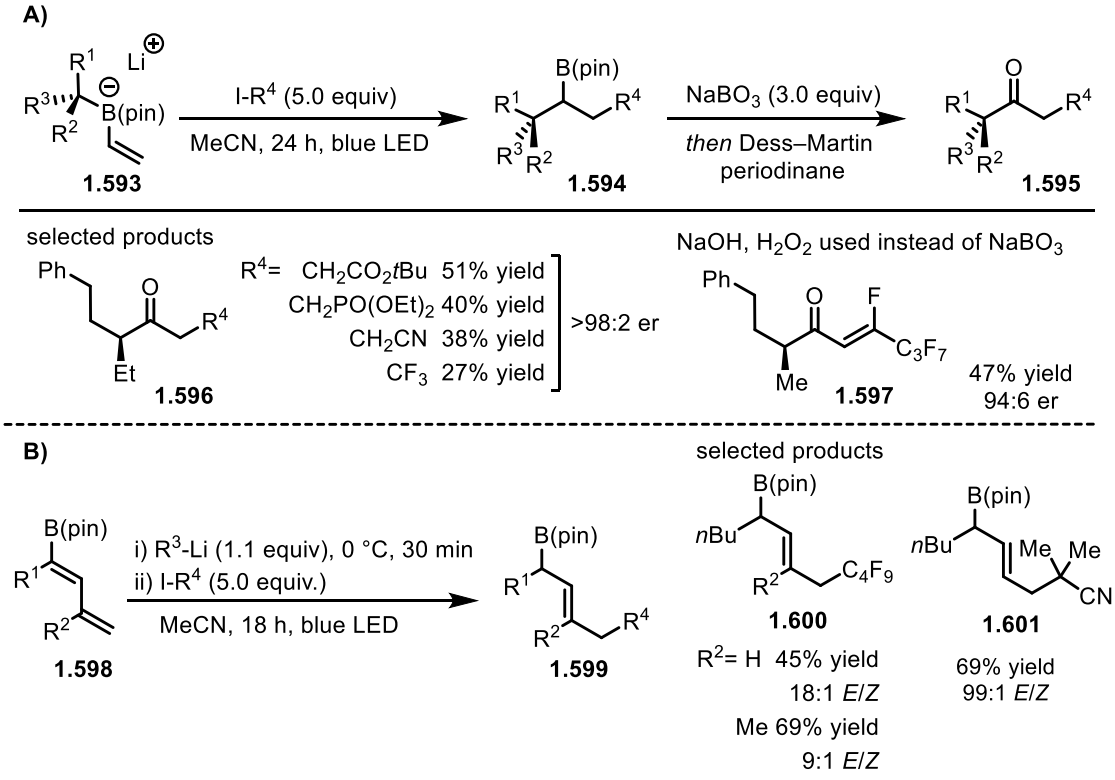
stereoretentive nature of 1,2-metallate rearrangement reactions, the use of enantioenriched boronic ester starting materials led to products with excellent enantioenrichment. Low diastereoselectivy was observed in these reactions due to the non-selective nature of radical addition. By subjecting these products to a one-pot two-fold oxidation (**1.594** to **1.595**), enantioenriched α-chiral ketones could be obtained, thus obviating the limitation of poor diastereoselectivity. For boronic ester products incorporating perfluoroalkyl electrophiles, replacing sodium perborate oxidation with alkali hydrogen peroxide oxidation was found to produce fluorinated α,β-unsaturated ketones (**1.596** to **1.597**).

By employing dienenylboronic ester substrates Studer has expanded the types of products that can be accessed by radical-induced rearrangement reactions to di- and trisubstituted allylboronic esters (Scheme 1.73.B).[130] While *E*/*Z* selectivity was found to be somewhat substrate dependent, many reactions were found to produce good to excellent *E*-selectivity.

Shi has recently demonstrated that by engaging alkenylboron-ate complexes **1.446** (generated from bispinacolato diboron and alkenyl Grignard reagents) using photoredox

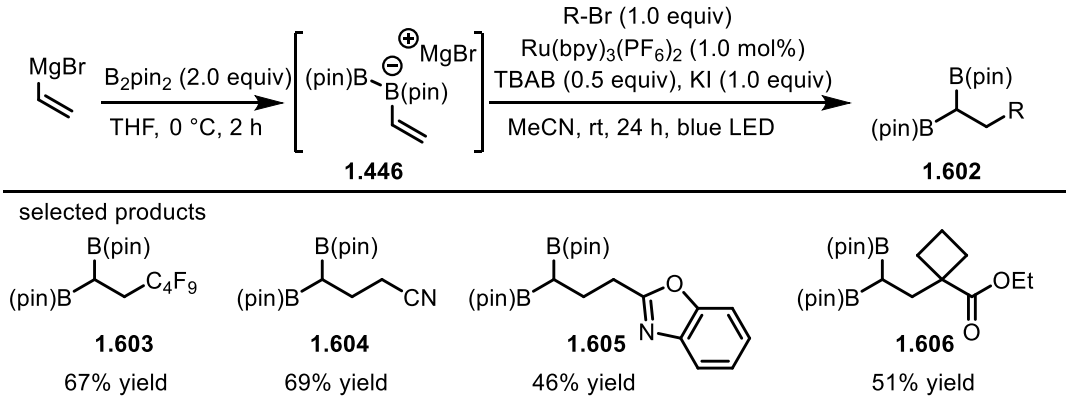
[130] Kischkewitz, M.; Gerleve, C.; Studer, A. *Org. Lett.* **2018**, 20, 3666.

Scheme 1.73. Application of radical-polar crossover reaction to α-chiral-ketones and allylboronic esters



initiation conditions, diverse germinal diboron products **1.602** can be obtained (Scheme 1.74).[131] The reaction demonstrates excellent functional group compatibility due to the mild condition employed, thus allowing the preparation of germinal diboron reagents incorporating labile functional groups that might otherwise be challenging to prepare.

Scheme 1.74. Shi's preparation of geminal bis pinacol boronic esters



[131] Zhao, B.; Li, Z.; Wu, Y.; Wang, Y.; Qian, J.; Yuan, Y.; Shi, Z. *Angew. Chem. Int. Ed.* **2019**, 58, 1.

While research into radical-induced 1,2-metallate rearrangement reactions is still in its infancy, the three-component reactions that have been develop thus far collectively represent a powerful strategy for the construction of complex and diverse functionalized carbon frameworks in a modular and rapid manor. The prospect of extending the types of electrophiles that can be employed in these processes and rendering this class of transformation enantioselective is both synthetically appealing and mechanistically compelling.

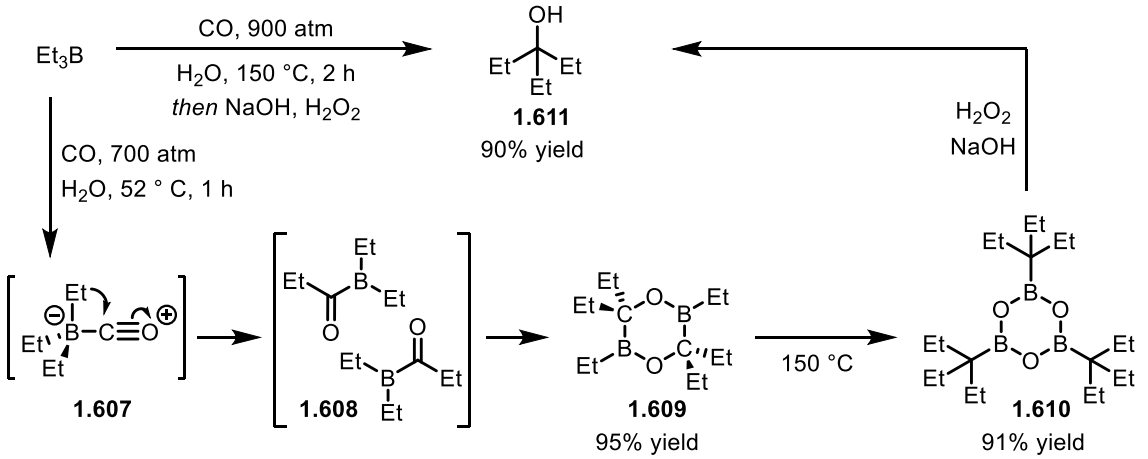
1.5 sp-Hybridized Terminus of Migration

1.5.1 Non-Induced Rearrangements

In 1962, while working at DuPont's Experimental Station Laboratory, Hillman reported a carbonylation reaction of trialkylboranes and carbon monoxide which produced tertiary alcohols after oxidation (Scheme 1.75).[132] Based on the independent preparation of various isolable intermediates a plausible mechanism was proposed in which coordination of carbon monoxide to a trialkylborane forms zwiterionic boron-ate complex **1.607** which undergoes alkyl migration, generating dialkyl acylborane **1.608**. Compound **1.608** then undergoes dimerization involving the migration of a second alkyl group from boron to the adjacent carbon, forming dimeric borinic ester **1.609**. It was found that **1.609** could be prepared in excellent yields if the reaction was run at a lower temperatures and that upon heating it readily converted to boroxine **1.610**, which could be converted to tertiary alcohol **1.611** upon oxidation. Subsequent studies found that by running reactions in the presence

[132] Hillman, M. E. D. *J. Am. Chem. Soc.* **1962**, 84, 4715.

Scheme 1.75. Hillman's seminal discovery of borane carbonylation

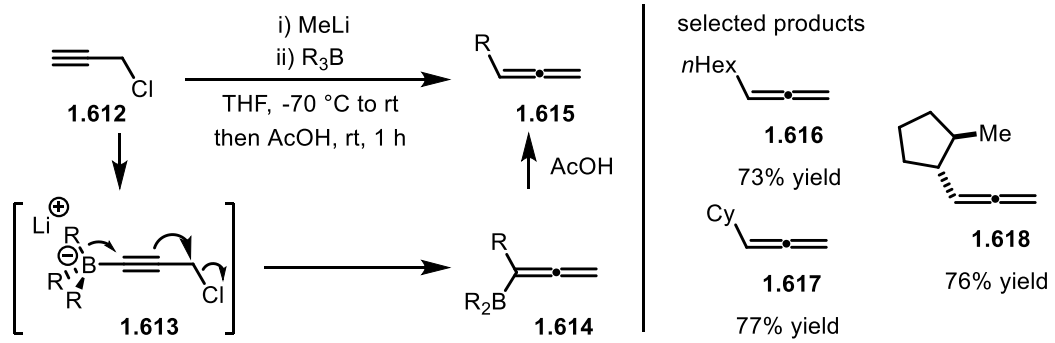


of excess ethylene glycol or by addition of ethylene glycol to boroxine products, isolable boronic esters could be obtained.[133] Addition of aldehydes to the reaction was later found to facilitate the formation of secondary alcohols after alkaline hydrolysis.[134] The aldehyde was proposed to intercept dialkyl acylborane **1.608** by a 1,3-dipolar addition reaction which furnished an isolable 5-membered borinic ester product, which upon alkaline hydrolysis, furnished secondary alcohols. Carbonylation of boranes was later studied by Brown[135] and has been extensively reviewed[136]

Zweifel later found that alkynylboron-ate complexes (**1.613**), prepared from lithiated propargylic chloride and trialkylboranes, readily underwent spontaneous 1,2-metallate rearrangement to furnish allenylboranes **1.614**. These intermediates could be converted to the corresponding allene (**1.615**) upon treatment with acetic acid (Scheme 1.76).[137] In a

[133] Hillman, M. E. D. *J. Am. Chem. Soc*. **1963**, 85, 982.
[134] Hillman, M. E. D. *J. Am. Chem. Soc*. **1963**, 85, 1626.
[135] (a) Brown, H. C.; Negishi, E. *J. Am. Chem. Soc.* **1967**, 89, 5477. (b) Brown, H. C.; Negishi. E. *Chem. Commun.* **1968**, 594. (c) Brown, H. C. Negishi, E. *J. Am. Chem. Soc.* **1967**, 89, 5478. (d) Brown. H. C.; Dickason, W. C. *J. Am. Chem. Soc.* **1969**, 91, 1226.
[136] (a) Brown. H, C., "Boranes in Organic Chemistry," Cornell University Press, Ithaca, New York, **1972**; (b) Cragg, G. M. L., "Organoboranes in Organic Synthesis," Marcel Dekker, New York, **1973**. (b) Brown, H. C., *Accounts Chem. Res*. **1969** 2, 65. (c) Negishi, E. *Intra-Sci. Chem. Rept.* **1973,** 81.
[137] Leung, T.; Zweifel, G. *J. Am. Chem. Soc.* **1974**, 96, 5620.

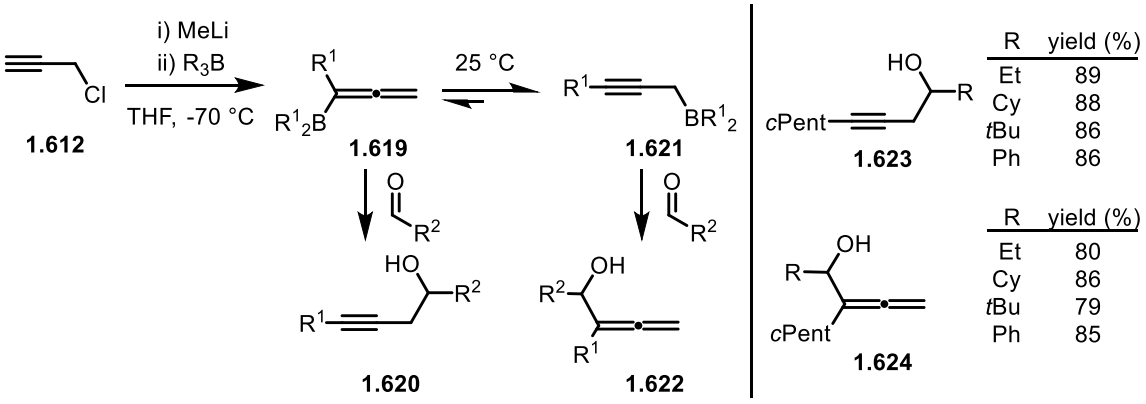
Scheme 1.76. Zweifel's preparation of allenes from propargyl chloride



subsequent report, Zweifel found that the allenylborane products **1.619**, initially formed from propargyl chloride **1.612** and trialkylborane, reacted efficiently with aldehydes at low temperature to furnish homopropargyl alcohols **1.620** (Scheme 1.77**)**. [138] By warming the reaction solution to room temperature before addition of the aldehyde electrophile the authors found that allenyl alcohols **1.622** could be obtained in high yields. This temperature dependent product selectivity was attributed to the borotropic rearrangement of allenylborane **1.619** to the thermodynamically favored propargylborane isomer **1.621**. By controlling the temperature at which aldehyde addition was conducted, excellent yields of >99% isomerically pure homo propargylic or allenyl alcohol could be obtained.

Midland later improved the utility and generality of this type of reaction by

Scheme 1.77. Allenylation and homopropargylation of aldehydes by temperature controlled isomerization

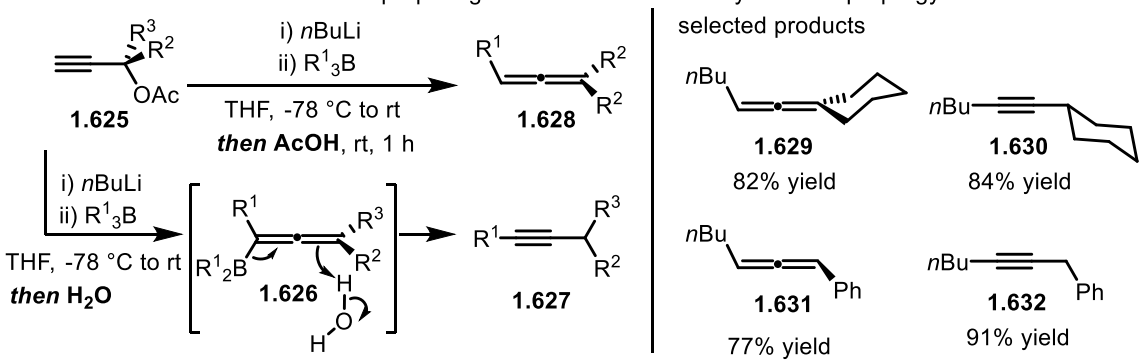


R	yield (%)
Et	89
Cy	88
*t*Bu	86
Ph	86

R	yield (%)
Et	80
Cy	86
*t*Bu	79
Ph	85

[138] Zweifel, G.; Backlund, S. J.; Leung, T. *J. Am. Chem. Soc.* **1978**, 100, 5561.

Scheme 1.78. Midland's method of preparing allenes and internal alkynes from propargyl acetates



demonstrating that propargyl acetate (**1.625**) rather than chloride reagents could be used to obtain trisubstituted allene products (**1.628**) (Scheme. 1.78).[139] The authors also demonstrated that internal alkyne products (**1.627**) could be obtained by utilizing water rather than acetic acid to facilitate protodeborylation.

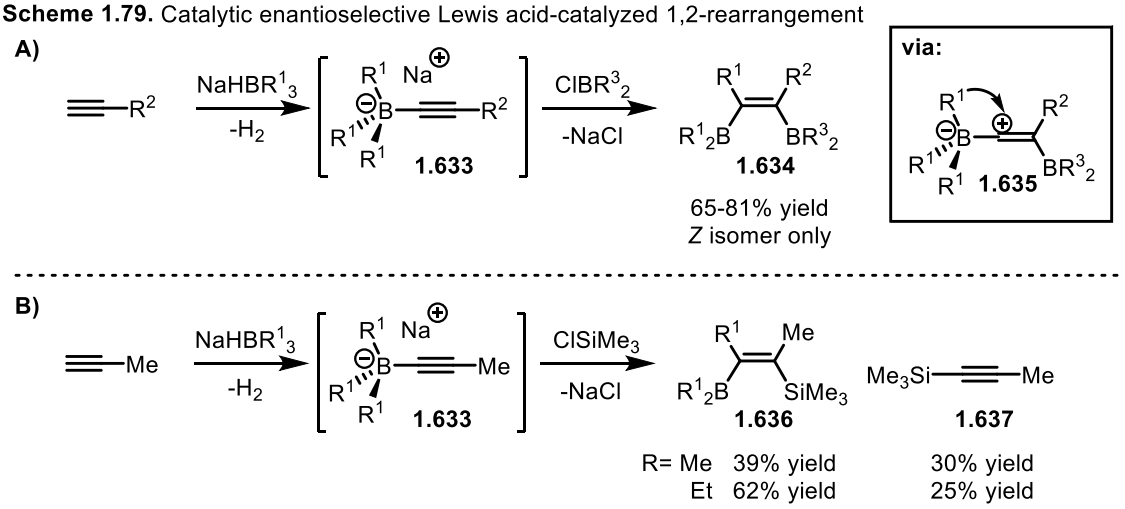
1.5.2 Boron-, Silicon-, Phosphorous-, and Sulfur-Induced Rearrangements

In 1965, Binger reported that the addition of dialkyl chloroboranes to trialkylborane-derived ate complexes **1.633** resulted in the formation of 1,2-bis boryl alkene **1.634** in high yield with excellent *E*/*Z* selectivity (Scheme 1.79.A).[140] While the proposed mechanism involves the addition of boron-ate complex to dialkyl chloroborane to generate a vinyl cation (inset, **1.635**), given the excellent isomeric purity observed, it seems plausible that attack of the alkyne moiety on dialky chloroborane occurs concomitantly with migration of an alkyl group from boron to the adjacent carbon. Zweifel later reported a similar transformation utilizing alkynylboron-ate complexes with an alkenyl migrating group and $BF_3{\cdot}Et_2O$ as the electrophilic activator.[141] The authors proposed that the excellent *Z*-

[139] Midland, M. M. *J. Org. Chem.* **1977**, 42, 2650.
[140] Binger, P.; Köster, R. *Tetrahedron Lett.* **1965**, 6, 1901.
[141] Zweifel, G; Backlund, S. J. *J. Organomet. Chem.* **1978**, 156, 159.

selectivity observed in this case might be due to a concerted rather than stepwise mechanism in which $BF_3 \cdot Et_2O$ coordination to the electron-rich alkyne triggers intramolecular transfer of an alkenyl group. Binger later demonstrated that trimethylsilyl chloride is also capable of inducing the 1,2-metallate rearrangement of alkynylboron-ate complexes, producing β-silyl alkenylboranes (Scheme 1.79.B).[142] The products were again obtained with high *Z* alkene isomeric purity, suggesting a similar mechanism to the previous report might be operative. In this case, a competitive transmetallation reaction

Scheme 1.79. Catalytic enantioselective Lewis acid-catalyzed 1,2-rearrangement

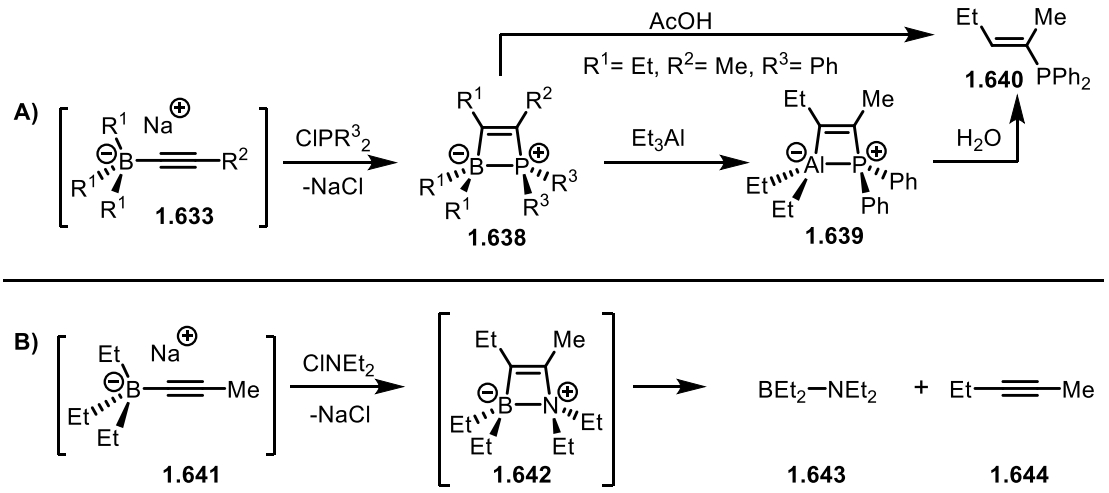


was observed forming alkynylsilane **1.637.** Consistent with the generally poor migrating aptitude of methyl groups in 1,2-metallate rearrangement reactions of organoboronates, it was found that by switching from a trimethyl- to a triethylborane-derived ate complexes, the product ratio of rearrangement to transmetallation could be improved .

Binger later found that diorganochlorophosphines were competent electrophilic activators of alkynylboron-ate complexes and that the phosphaboretene products **1.638** thus obtained could be readily converted to alkenyl phosphines **1.640** by direct protodeborylation or by transmetallation with triethylaluminum (**1.638** to **1.639**) followed

[142] Binger, P.; Köster, R. *Synthesis* **1973**, 5, 309.

Scheme 1.80. Preperation of organo-1,2-phosphaboretenes by chlorophosphine-induced rearrangement

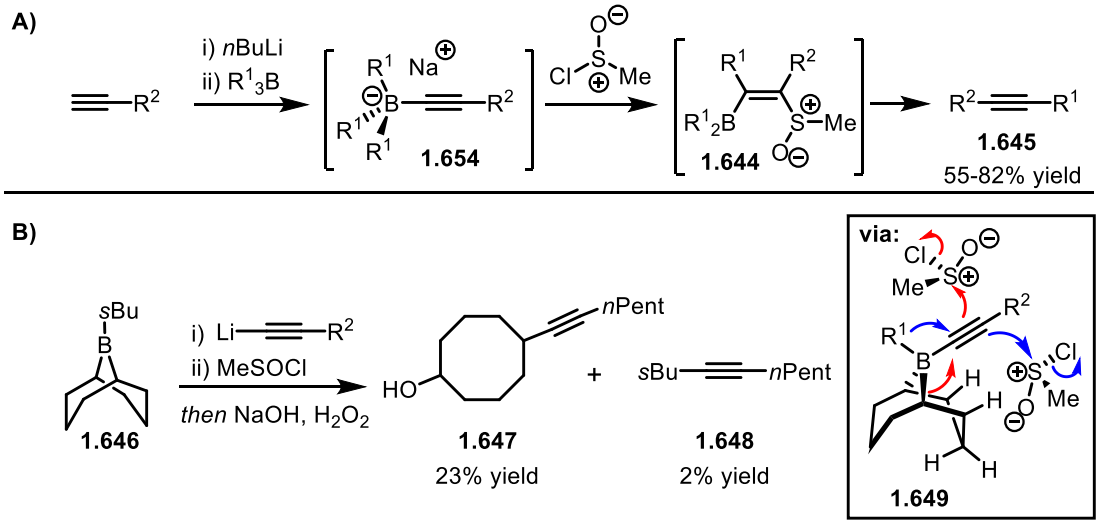


by protodemetallation (Scheme 1.80.A).[143] Use of diethylchloroamine was found to directly produce a mixture of internal alkyne and aminoborane products (Scheme 1.80.B). In this case the authors proposed a similar mechanism involving a less persistent intermediate **1.642**.

The same year Binger reported silicon-induced rearrangement reactions of alkynylboron-ate complexes, Nozaki found that methyl sulfonyl chloride acts as a traceless activating agent, facilitating the conversion of alkynylboron-ate complexes to internal alkynes by a sulfur-induced 1,2-metallate rearrangement/boron-sulfur elimination sequence (Scheme 1.81.A).[144] Interestingly, the authors noted that the use of B-alkyl-9-borabicyclo[3.3.l]nonane-derived boron-ate complexes, resulted in the predominate migration of one of the carbons of the BBN ring in contrast to the general behavior of BBN as a non-migrating group (Scheme 1.81.B). Based on this behavior, the authors proposed a reaction model (inset, **1.649**) in which the electrophile approaches the alkyne predominately from the top face due to steric repulsion with the BBN moiety and migration

[143] Binger, P.; Köster, R. *J. Organomet. Chem.* **1974**, 73, 205.
[144] Naruse, M.; Utimoto, K.; Noaaki, H. *Tetrahedron Lett.* **1973,** 21, 1647.

Scheme 1.81. Nozaki's internal alkyne synthesis by methyl sulfonyl chloride-induced 1,2-rearrangement



and electrophilic attack occur in an *anti* orientation across the alkyne.

Related alkynylboron-ate complex rearrangement reactions induced by chalcogen halide electrophiles including PhSCl, PhSeBr, Ph/BuTeBr, have been reported by Heves.[145] Heves has reported a similar sulfur-induced rearrangement reactions of trialkylalkynyl aluminum-ate complexes.[146]

1.5.3 Proton-Induced Rearrangements

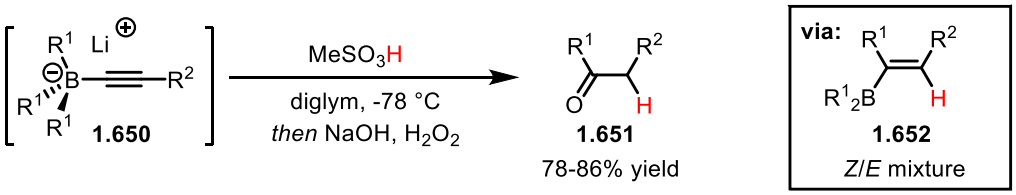
In the same report where Binger discussed the boron-induced rearrangement of alkynylboron-ate complexes (*vide supra*), he also noted that exposure of these compounds to hydrochloric acid resulted in a similar rearrangement, producing alkenylboron compounds as an equimolar mixture of *E* and *Z* isomers. The same behavior was noted in subsequent reports, though the yields obtained were not specified and the conditions employed in these reactions were not well defined.[147] It seems that the lack of

[145] Gerard, J.; Bietlot, E.; Heves, L. *Tetrahedron Lett.* **1998**, 39, 8735.
[146] Debuigne, A.; Gérard, J.; Heves, L. *Tetrahedron Lett*. **1999**, 40, 5943.
[147] Binger, P.; Benedikt, G.; Rotermund, G. W.; Koster, R. *Liebigs Ann. Chem*. **1968**, 717, 21.

stereospecificity in these reactions may have initially discouraged further studies.

Nearly a decade after the initial report by Binger, Pelter disclosed a procedure for the preparation of alkyl ketones by a proton-induced 1,2-metallate rearrangement reaction of alkynyl boron-ate complexes followed by oxidation with alkaline hydrogen peroxide (Scheme 1.82).[148] The authors noted that this procedure obviates the synthetic limitation

Scheme 1.82. Pelter's preperation of ketones and alkenylboranes by proton-induced rearrangement

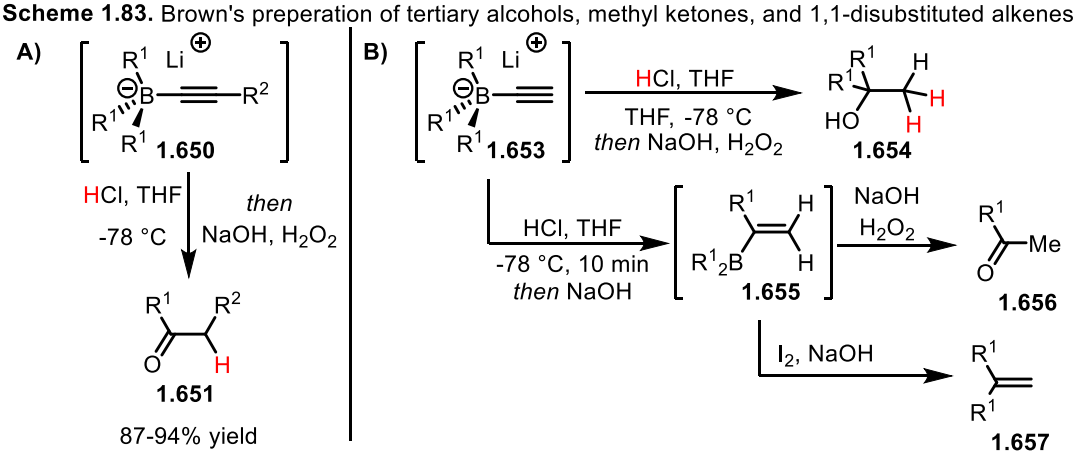


of initially obtaining a mixture of *E* and *Z* alkenylborane products (inset) while providing a general method of preparing ketones.

Brown later investigated this reaction as a means of preparing Markovnikov alkenyl- and alkylboranes.[149] After demonstrating an improved preparation of alkyl ketones (Scheme 1.83.A) the authors noted that the use of lithium acetylide in place of substituted lithiated alkynes resulted in poor yields of the desired ketone product (**1.656**) due to a second protonation and rearrangement of the intermediary alkenylborane, thus producing tertiary alcohols **1.654**. The authors found that after treatment with acid, addition of base at low temperature before warming the reaction solution to room temperature facilitated the preparation of alkenylborane products **1.655** which could be readily converted to the corresponding methyl ketones **1.656** or 1,1-disubstituted alkene **1.657** (Scheme 1.83.B). Following Pelter's report, Suzuki investigated a similar proton-induced rearrangement reaction, demonstrating that the use of propionic acid at low temperatures facilitated a

[148] Pelter, A.; Harrison, C. R.; Kirpatric, D. *J. Chem. Soc. Chem. Commun*. **1973**, 544.
[149] Brown, H. C.; Levy, A. B.; Midland, M. M. *J. Am. Chem. Soc.***1975**, 17, 5017.

Scheme 1.83. Brown's preperation of tertiary alcohols, methyl ketones, and 1,1-disubstituted alkenes



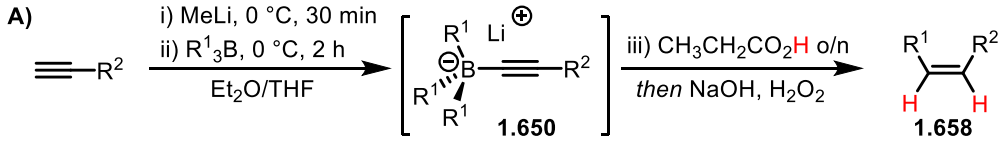
rearrangement and protodeborylation thereby yielding internal and terminal alkenes from lithiated alkynes and borane reagents (Scheme 1.84.A).[150] By studying the effect of migrating group identity on the *Z*/*E* selectivity of the reaction (entry 1-4) the authors concluded that more sterically bulky migrating groups resulted in higher *Z*-selectivity. By utilizing thexyl dialkylborane reagents (entry 5-8) in place of simple trialkylboranes, the authors found generally high *Z*-selectivities could be achieved with less dependence on the nature of the migrating group. Based on this data, the authors proposed a mechanism (Scheme 1.84.B) in which initial protonation of alkynylboron-ate complex **1.650** produces a linear vinylic carbocation **1.659** which can access two bent conformations **1.660** and **1.661**. These intermediates lead to *Z* and *E* alkenes **1.658** and **1.663** respectively by 1,2-metallate rearrangement and spereospecific protodeborylation of the corresponding alkenylborane intermediates. A more sterically hindered boron moiety is proposed to destabilize bent vinyl cation **1.661** relative to **1.660** thus resulting in the observed *Z*-selectivity.

By studying the nature of the migrating group and proton source used, Pelter

[150] Miyaura, N.; Yoshinari, M.; Itoh, M.; Suzuki, A. *Tetrahedron* **1974**, 15, 2961.

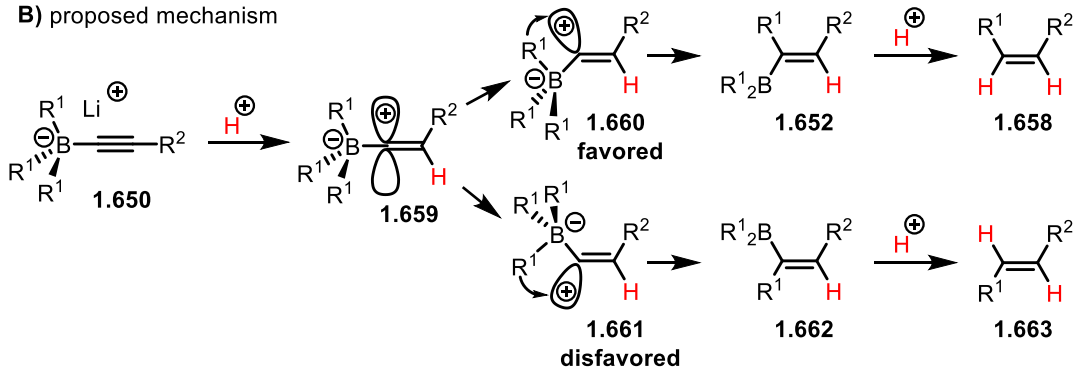
subsequently suggested that the mechanism involved in the proton-induced rearrangement reactions of alkynylboron-ate complexes may be somewhat more nuanced than Suzuki's initial proposal.[151] The authors observed that reactions involving a phenyl migrating group resulted in substantially higher *Z* product selectivity than those involving a cyclohexyl group (inset) (Scheme 1.85). The authors found that the nature of the proton source used

Scheme 1.84. Suzuki's preperation of *Z* alkenes by proton-induced rearrangement



entry	R^1	R^2	yield	temp (°C)	*Z*/*E*	entry	$R^1{}_2B$-Thx	R^2	yield	temp (°C)	*Z*/*E*
1	*n*Bu	Ph	73	0	74:26	5[a]	*i*Bu	Ph	56	0	86:14
2	*i*Bu	Ph	78	0	54:46	6[a]	*i*Bu	Ph	74	-70	97:3
3	*s*Bu	Ph	75	0	81:19	7[a]	*n*Bu	Ph	81	-70	98:2
4	*n*Bu	Me	77	0	72:28	8[a]	Er	Ph	82	-70	95:5

a) dialkyl thexyl borane used in place of $R^1{}_3B$

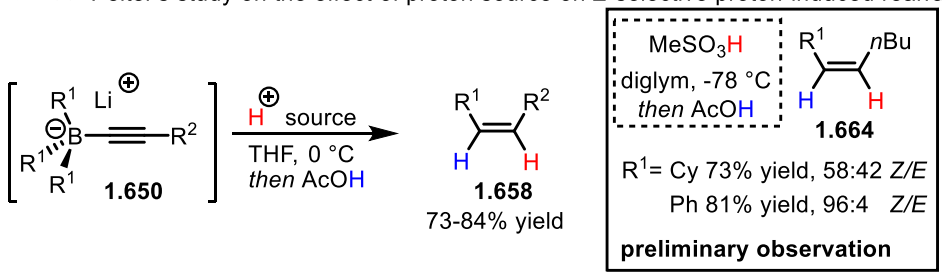


also effected *Z*/*E* selectivity with propionic acid favoring higher *Z*-selectivity while methanesulfonic acid was found to result in higher *E*-selectivity (entry 1 and 2 or 6 and 7). Counter to Suzuki's mechanistic proposal the use of very sterically hindered tri-thexylborane with an *n*-butyl substituted alkyne resulted in predominantly *E*-selectivity

[151] Pelter, A.; Harrison, C. R.; Subrahmanyam, C.; Kirkpatrick, D. *J. Am. Chem. Soc., Perkin Trans. 1.* **1976**, 2435.

(entry 7). Simply changing the alkyne substituent from *n*-butyl to phenyl was found to invert the observed selectivity (entry 7 and 8). The authors did not propose a mechanistic explanation for these effects but noted "the attack by protic acids even on simple alkynes

Scheme 1.85. Pelter's study on the effect of proton source on *Z*-selective proton-induced rearrangement



entry	R^1	R^2	proton source	*Z/E*	entry	R^1	R^2	proton source	*Z/E*
1	*n*Bu	*n*Bu	$EtCO_2H$	62:38	5	*n*Bu	Ph	$MeSO_3H$	56:44
2	*n*Bu	*n*Bu	$MeSO_3H$	42:58	6[a]	Thex	*n*Bu	$EtCO_2H$	29:71
3[a]	*n*Bu	*n*Bu	$EtCO_2H$	39:61	7[a]	Thex	*n*Bu	$MeSO_3H$	21:79
4	*n*Bu	Ph	$EtCO_2H$	77:23	8[a]	Thex	Ph	$EtCO_2H$	97:3

a) Reaction conducted at -78 °C.

is very complex, and may well depend on the proton source" citing an earlier study.[152]

Related proton-induced rearrangement reactions of trialkylcyanoboron-ate complexes which produce ketone products have also been studied.[153]

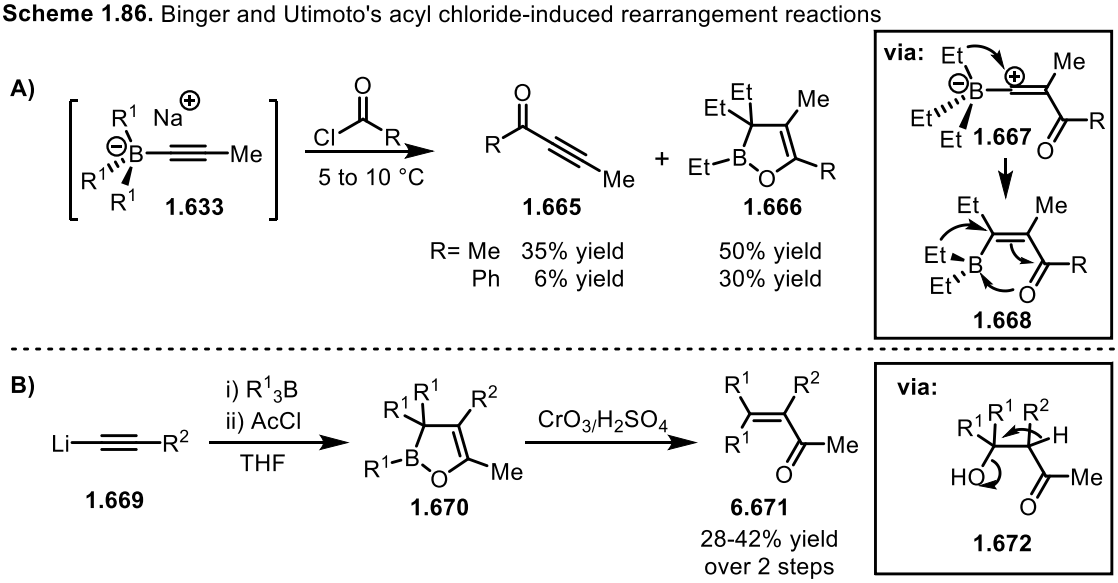
While this class of reaction has received little recent interest, perhaps owing to the synthetic limitations imposed by the use of boranes, the possibility of rendering this class of reaction highly selective utilizing the boronic esters and various acid reagents and catalysts available today presents a potentially powerful approach for the synthesis of diverse products.

[152] Bentley, T. W. *Ann. Reports (B)*, **1974**, 127.
[153] Pelter, A.; Hutchings, M. G.; Smith, K. *J. Chem. Soc., Perkin Trans. I*, **1975**, 142.

1.5.4 Carbon-Electrophile-Induced Rearrangements

In 1967, Binger reported that the acylation of alkynylboron-ate complexes resulted in the formation of a mixture of alkynyl ketone **1.665** and cyclic 2-oxa-3-borolene **1.666**, the products of direct alkyne transfer and acyl electrophile-induced rearrangement/cyclization respectively. (Scheme 1.86.A).[154] Utimoto later revisited this process as a means of preparing α,β-unsaturated ketones from lithium trialkylboron-ate complexes, noting that cyclic 2-oxa-3-borolenes **1.670** are remarkably resistant to oxidation by molecular oxygen and alkaline hydrogen peroxide, necessitating the use of Jones reagent (Scheme 1.86.B).[155] While products were obtained in modest yields, the modular three-component construction of α,β-unsaturated ketones represents and appealingly synthetic transformation which might be improved upon. The use of boronic esters in place of boranes for example might facilitate an increase in isolated yields due to greater product stability and allow two

Scheme 1.86. Binger and Utimoto's acyl chloride-induced rearrangement reactions



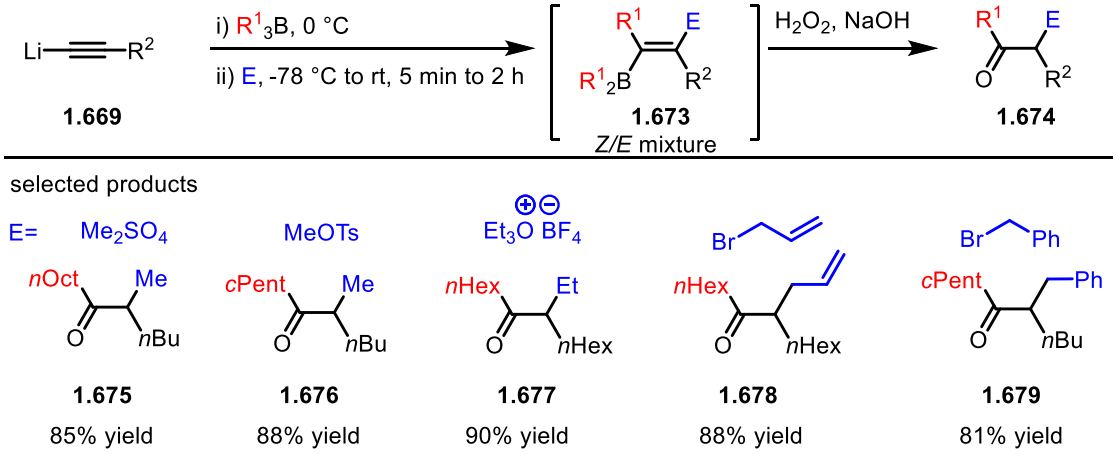
[154] Binger P. *Angew. Chem. Int. Ed.* **1967**, 84.
[155] (a) Naruse, M.; Tomita, T.; Utimoto, K.; Nozaki, H. *Tetrahedron lett.* **1973**, 14 795. (b) Naruse, M.; Tomita, T.; Utimoto, K.; Nozaki, H. *Tetrahedron* **1974**, 30, 835.

different β-substituents to be stereoselectively introduced by two controlled stepwise rearrangements. Similar acyl electrophile-induced rearrangement of trialkylcyanoborates have been subsequently reported and reviewed.[156]

Pelter later investigated the use of alkynylboron-ate complexes as enolate equivalents in a series of alkylation reactions with various alkyl, allyl, and benzyl electrophiles (Scheme 1.87).[157] The reaction was found to be high-yielding for a variety of substrates, granting rapid access to various alkyl ketones in a modular manner. It was found upon protodeborylation of alkenylborane **1.673** that this intermediate is formed as a 70:30 mixture of geometric isomers suggesting a non-stereospecific 1,2-metallate rearrangement, consistent with proton-induced rearrangement reactions of alkynylboron-ate complexes.

In a subsequent report, Pelter demonstrated that when specific primary alkyl halides with α-electron withdrawing groups were employed in the previously reported alkyl halide-

Scheme 1.87. Pelter's preparation of alkyl ketones by alkyl halide-induced rearrangement



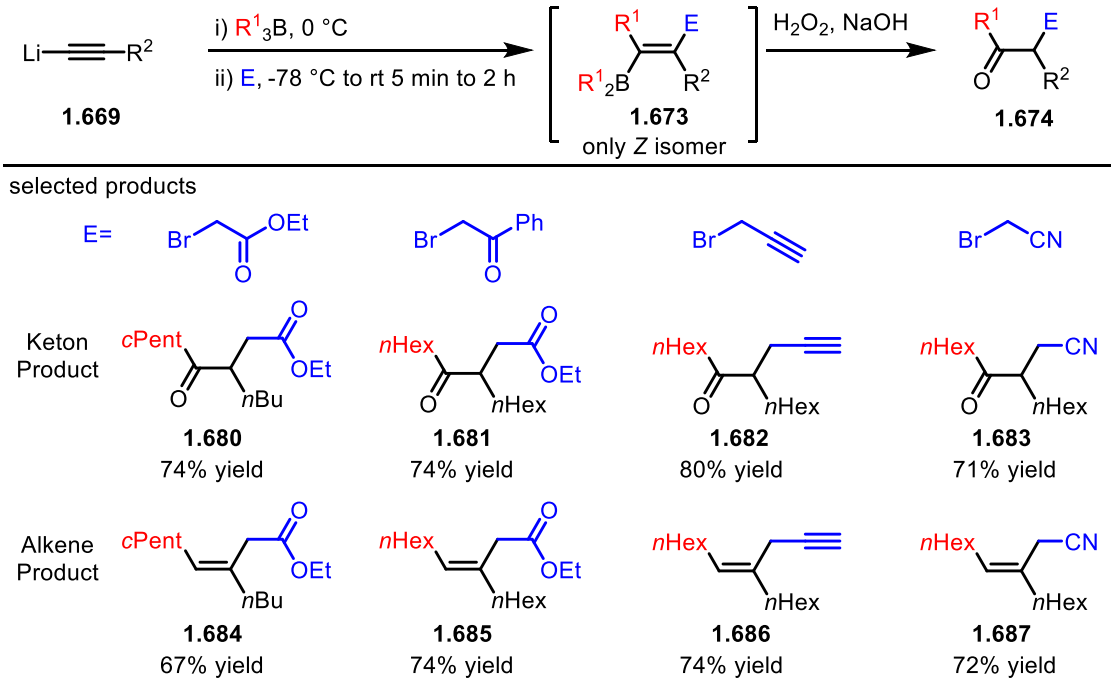
[156] (a) Pelter, A.; Smith, K.; Hutchings, M. G.; Rowe, K. *J. Chem. Soc. Perkin Trans. I*, **1975**, 129. (b) Pelter, A.; Smith, K.; Hutchings, M. G.; Rowe, K. *J. Chem. Soc. Perkin Trans. I*, **1975**, 138. (c) Kabalka, G. W.; *Synth. Commun.* **1979**, 607. (d) Bryson, T. A.; Reichel, C. J. *Tetrahedron Lett.* **1980**, 2381. (e) Brown, H. C.; Sikorski, J. A.; Kulkarni, S. U. ; Lee, H. D. *J. Org. Chem.* **1980**, 45, 4542. (f) Garst, M. E.; Bonfiglio, J. N. *Tetrahedron Lett.* **1981**, 22, 2075.

[157] See reference 148.

induced rearrangement reaction, stereochemically defined trisubstituted alkenylboranes could be obtained (Scheme 1.88).[158] Acidic or basic oxidative workup of the initially formed alkenylborane products (**1.673**) enabled 1,4-dicarbonyl (**1.680** through **1.683**) or stereodefined trisubstituted alkenes (**1.684** through **1.687**) to be readily prepared in a net three component coupling.

In a subsequent in-depth report utilizing computational calculations and chemical probes, Pelter proposed that alkylation reactions of alkynylboron-ate complexes proceed

Scheme 1.88. Pelter's synthesis of ketons and stereochemically-defined trisubstituted alkenes

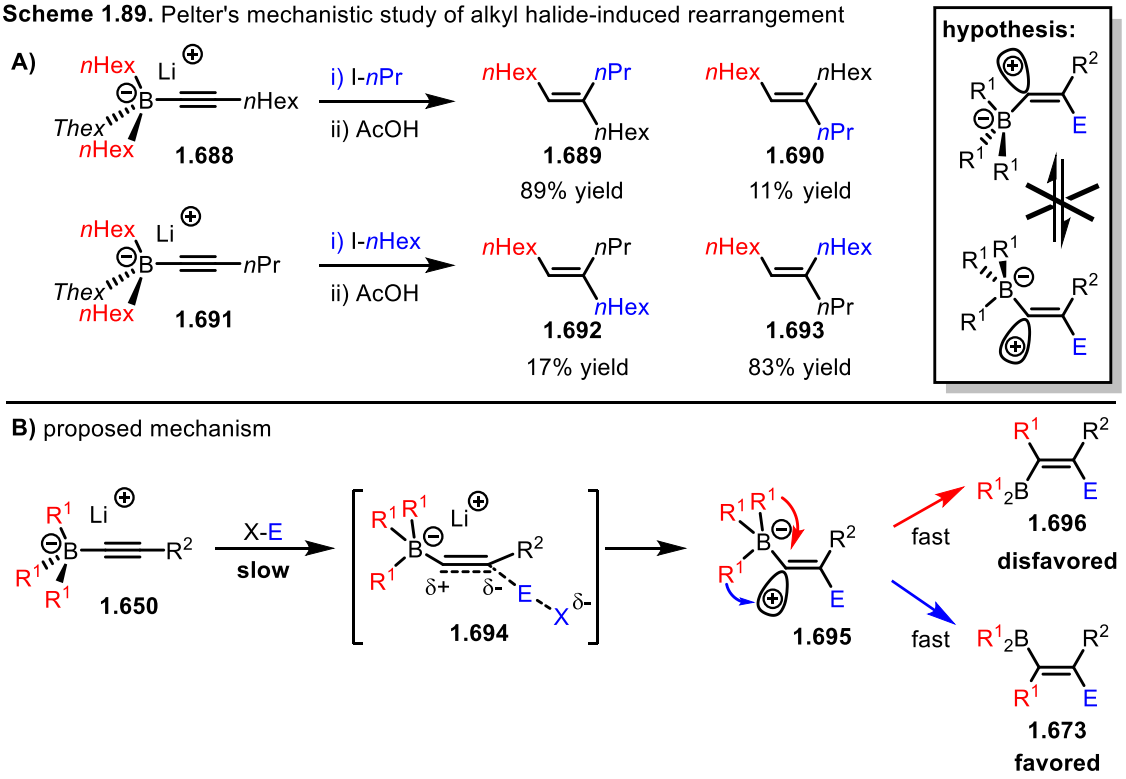


by a stepwise mechanism involving a bent cationic intermediate which is formed subsequent to electrophilic attack on the alkyne π-bond.[159] In an elegantly designed experiment depicted in Scheme 1.89.A, the authors demonstrated that electrophile and migrating group predominantly add to the same side of the alkyne moiety regardless of

[158] Pelter, A.; Gould, K. J.; Harrision, C. R. *Tetrahedron Lett*. **1975**, 16, 3327.
[159] Pelter, A.; Bentley, T. W.; Harrison, C. R.; Subrahmanyam, C.; Laub, R. J. *J. Chem. Soc. Perkin Trans. 1*, **1976**, 2419.

their identity, a result which is consistent with a kinetically controlled process and is inconsistent with a mechanism involving equilibrating vinyl cationic species (inset) as previously proposed by Suzuki (*vide supra*). As depicted in Scheme 1.89.B the authors proposed that kinetic control arises from the rate limiting formation of a bent alkyne transition state **1.694** in which the boron is bends away from the incoming electrophile and that the subsequently formed bent vinyl cation **1.695** then undergoes a rapid 1,2-metallate

Scheme 1.89. Pelter's mechanistic study of alkyl halide-induced rearrangement



rearrangement either to the convex side of the terminus of migration, forming the major product **1.673**, or to the concave side, leading to the minor geometric isomer **1.696**.

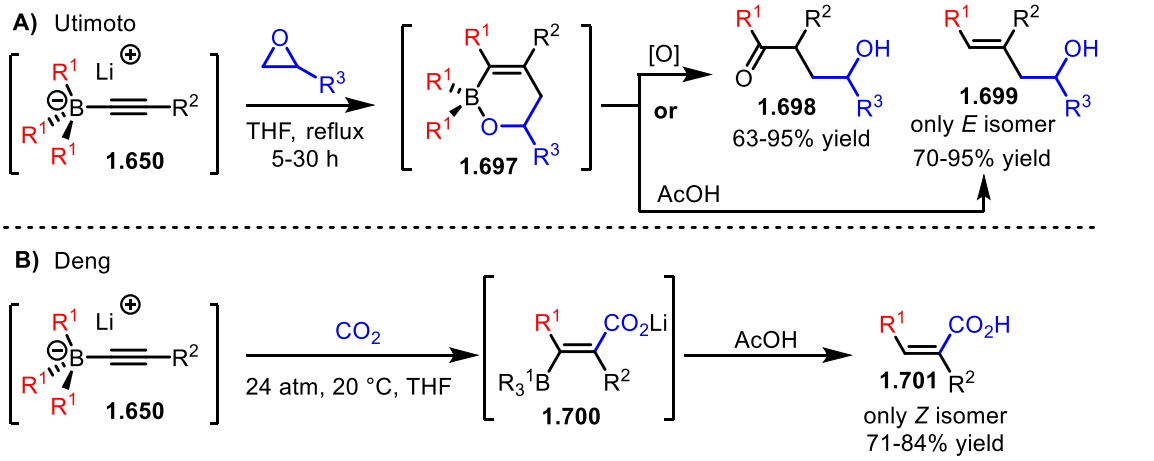
Pelter later expanded the scope of products that could be obtained utilizing this method to include terminal 1,1-disubstituted olefins through the use of dihalomethyl electrophiles which undergo a double migration and borotropic rearrangement.[160] Related reactions of

[160] Pelter, A.; Harrison, C. R *J. Chem. Soc. Chem. Commun.* **1974**, 828.

alkynylboron-ate complexes with benzylhalide electrophiles have been reported by Deng.[161]

Paralleling an earlier report of the reaction of alkenylboron-ate complexes with epoxides (*vide supra*) to furnish 1,4-diols, Utimoto reported that alkynylboron-ate complexes can engage in a similar reaction, granting access to γ-hydroxy ketones **1.698** or stereodefined trisubstituted β-hydroxy alkenes **1.699** (Scheme 1.90.A).[162] The mechanistic

Scheme 1.90. Modular access to γ-hydroxy ketones, homoallyl alcohols, and α,β-unsaturated carboxylates



reason alkene products are obtained as the pure *E* isomer was not discussed.

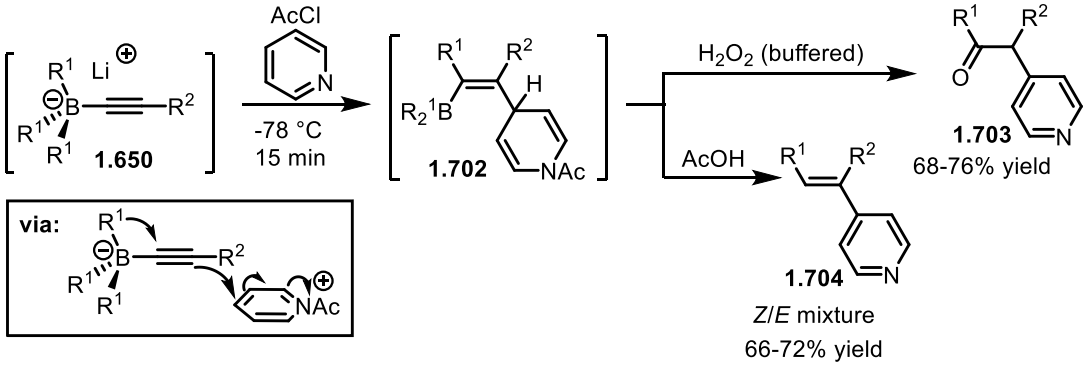
Deng later developed an efficient method of preparing stereodefined α,β-unsaturated carboxylic acids (**1.701**) by the reaction of alkynylboraon-ate complexes with carbon dioxide (Scheme 1.90.B).[163] While the nature of the rearrangement transition state was not discussed, products were obtained as single *Z* isomers, suggesting this reaction may involve a stereospecific 1,2-metllate rearrangement.

Pelter later discovered alkynylboron-ate complexes can participate in highly regioselective S_NAr reactions with pyridine in the presence of acyl chloride, furnishing

[161] Chen, Y.; Deng, M.-Z. *Heteroatom Chem*. **1994**, 5, 391.
[162] Naruse, M.; Utimoto, K.; Nozaki, K. *Tetrahedron* **1974**, 30, 3037.
[163] Deng, M.-Z.; Tang, Y.; Xu, W. *Tetrahedron Lett*. **1984**, *25*, 1797.

either α-pyridyl ketones **1.703** or 4-alkenyl pyridines **1.704** depending on the subsequent workup conditions (Scheme 1.91). [164] The authors proposed that acyl chloride activates pyridine through the formation of acyl pyridinium chloride which is then attacked by the alkyne π-bond (inset). While alkenyl pyridine products were obtained as a reported 65:35 mixture of *Z* and *E* isomers, suggesting a non-stereospecific stepwise mechanism, the

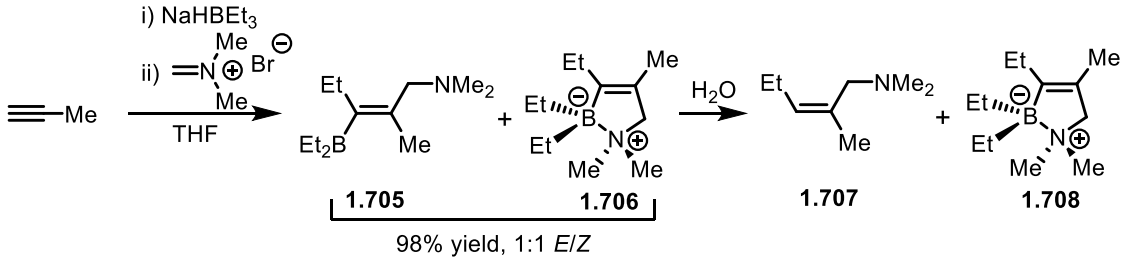
Scheme 1.91. Pelter's regioselective pyridine functionalization



modular, rapid, and highly regioselective nature of this pyridine functionalization reaction make it synthetically appealing.

Binger demonstrated that other charged unsaturated electrophiles, specifically dimethyl iminium bromide, are capable of inducing 1,2-metallate rearrangement reactions (Scheme 1.92),[165] Upon formation of alkynylboron-ate and treatment with iminium electrophile, a mixture of *E* and *Z* alkenylborane products (**1.705** and **1.706**) was obtained, the former of

Scheme 1.92. Three-component conjugate addition to iminium electrophile by 1,2-rearrangement

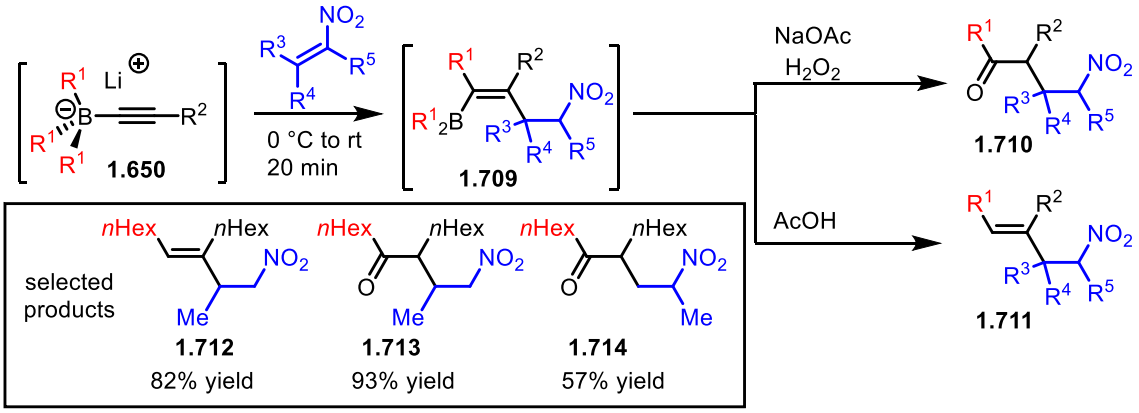


[164] Pelter, A.; Gould, K. J. *J. Chem. Soc. Chem. Commun.* **1974**. 347.
[165] Binger, P.; Köster, R. *Chem. Ber.* **1975**, 108, 395.

which readily underwent prododeborylation, while the later proved to be surprisingly stable.

Pelter later demonstrated that neutral Michael acceptors such as nitroalkenes are sufficiently electrophilic to induce the rearrangement reaction of alkynylboron-ate complexes, producing γ-nitro ketones **1.710** or β-nitro trisubstituted alkenes **1.711** (Scheme 1.93).[166] The reaction was found to be efficient for a range alky migrating groups

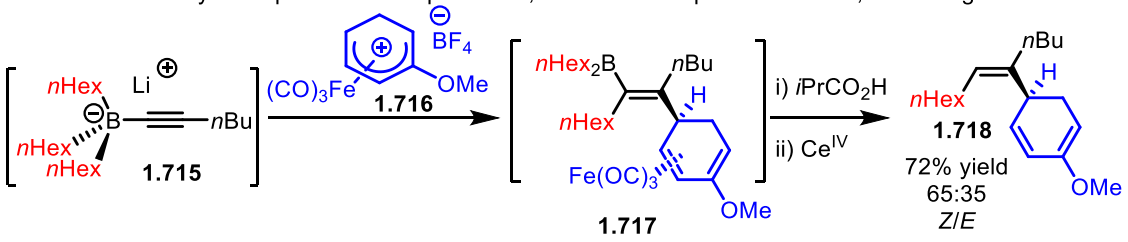
Scheme 1.93. Modular synthesis of γ-nitro ketones and trisubsituted β-nitro alkenes by 1,2-rearrangement



and nitroalkene substitution patterns.

In what is likely the earliest example of an induced rearrangement reaction involving a metal-activated alkene electrophile, Pelter demonstrated that a cationic η^5 dienyliron complex **1.716** can be used to produce trisubstituted alkenes (Scheme 1.94).[167] While the reaction required discrete preparation of the stoichiometric dienyliron electrophile and the

Scheme 1.94. Early example of a metal-promoted, carbon electrophile-induced 1,2-rearrangement reaction

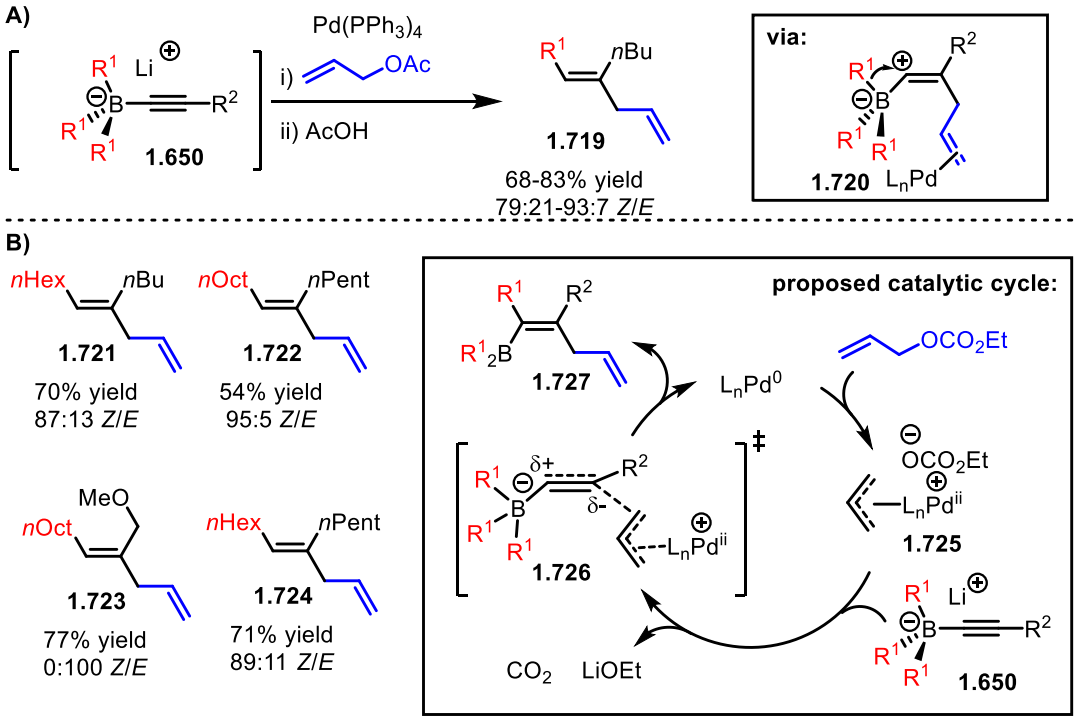


[166] Pelter, A.; Hughes, L. *J. Chem. Soc. Chem. Commun*. **1977**, 913.
[167] Pelter A.; Gould, K. J.; Kane-Maguire, A. P. *J. Chem. Soc. Chem. Commun.* **1974**, 1029.

alkene product was obtained as mixture of *E*/*Z* isomers, this reaction represents an intriguing example of a base-metal complex promoted rearrangement reaction that conceivably might inspire the development of related iron-catalyzed processes.

In 1989, Deng reported the first transition metal-catalyzed allylation reaction of alkynylboron-ate complexes, providing a method of preparing trisubstituted 1,4-dienes in moderate to good yield and *E*/*Z* selectivity (Scheme 1.95.A).[168] Observation of both product alkene isomers was rationalized by the authors as arising from a non-stereospecific mechanism involving the formation of an α-boryl vinyl cation **1.720** (inset) in which the four-coordinate boron bends preferentially towards the palladium-bound allyl substituent preceding 1,2-migration. It is unclear whether or not this work influenced the development of related palladium-catalyzed allylation reactions of indole-derived boron-ate complexes

Scheme 1.95. Deng's Pd-catalyzed allyl electrophile-induced 1,2-rearrangement reactions



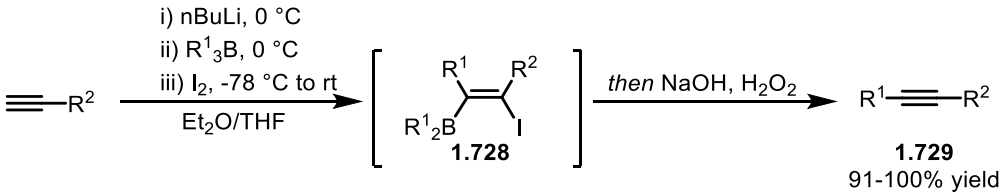
[168] Deng, M.-Z..; Zhang, H.-Q. *Acta. Chimica. Sinica.* **1989**, 47, 499.

reported two years later by Ishikura (*vide supra*). A year later Deng reported that the use of allyl carbonate rather than acetate electrophiles led to improved *E*/*Z* product selectivity (Scheme 1.95B). [169] The authors proposed a catalytic cycle involving a bent alkyne transition state, though no mechanistic discussion was offered (inset). A possible explanation for the bent alkyne transition state proposed is that an attractive interaction between the negatively charged four-coordinate boron moiety and the cationic allyl-palladium electrophile exists. This reaction was later applied by the same author to the synthesis of stereodefined dienes, in this case products were obtained as single isomers.[170] Murakami later demonstrated that triaryl borane-derived ate complexes could be similarly engaged in allylation reactions catalyzed by palladium-phosphine complexes.[171]

1.5.5 Halogen-Induced Rearrangements

Following Zweifel's discovery of the halogen-induced olefination reaction of trialkylboranes, the same author demonstrated that iodine is similarly capable of promoting alkynylation reactions producing internal alkynes in excellent yield (Scheme 1.96).[172] The authors proposed that this reaction proceeds by the intermediacy of vicinally disubstituted intermediate **1.728** which readily undergoes elimination upon treatment with base. This

Scheme 1.96. Zweifel's halide-induced alkynylation reaction



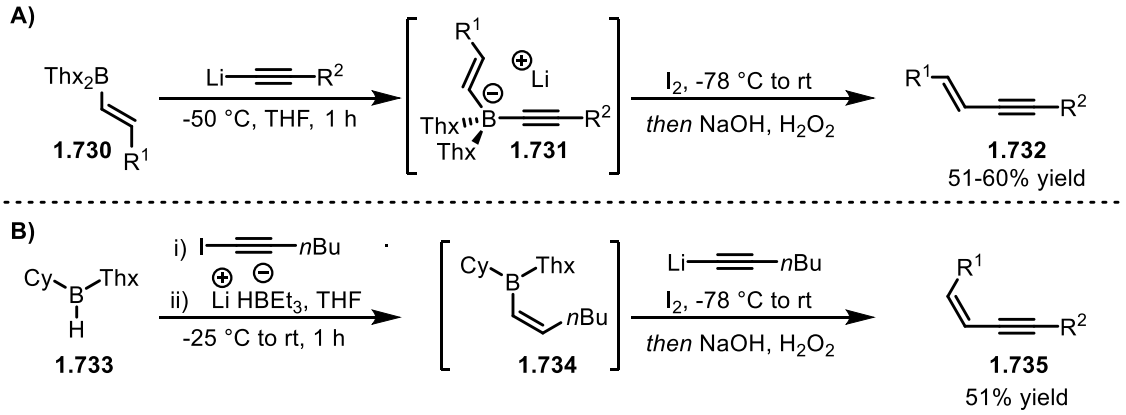
[169] Chen, Y; Li, N.-S.; Deng, M.-Z. *Tetrahedron Lett*. **1990**, 31, 2405.
[170] Chen, Y; Li, Deng, M.-Z; Ning, S. *Chin. Sci. Bull.* **1991**, 36, 570.
[171] Ishida, N.; Shinmoto, T.; Sawano, S.; Miura, T.; Murakami, M. *Bull. Chem. Soc. Jpn.* **2010**, 83, 1380.
[172] Suzuki, A.; Miyaura, N.; Abiko, S.; Itoh, M.; Brown, H. C.; Sinclair, J. A.; Midland, M. M. *J. Am. Chem. Soc.* **1973**, 95, 3080.

reaction was subsequently extended to the preparation of terminal alkynes through the use of lithium acetylide-ethyelene diamine complex.[173]

Negishi later demonstrated that this approach could grant access to enynes by the use of *E*[174] or *Z*[175] alkenylboranes (Scheme 1.97.A/B). Notably, a variation of Zweifel's non-induced rearrangement reaction of α-halo alkenylboranes involving a hydride migrating group was employed to prepare isomerically pure *Z* alkenylborane **1.734**.

Despite the wide variety of valuable products made available in a rapid and modular manor utilizing electrophile-induced rearrangement reactions of alkynylboron-ate complexes, there has been no further development of this process in recent years. Given the general instability of boranes it is perhaps unsurprising that these synthesis methods have not found widespread adoption, yet as can be seen with the recent resurgence in

Scheme 1.97. Negishi's preparation of *E* and *Z* eneynes by iodine-induced 1,2-rearrangement



interest regarding electrophile-induced rearrangement reactions of aryl- and alkenylboronic esters, reinvestigation of these systems employing modern synthetic techniques and reagents offers the potential for the development of synthetically useful and

[173] Midland, M.; Sinclair, J. A.; Brown, H. C. *J. Org. Chem.* **1974**, 39, 731.
[174] Negishi, E.; Lew, G.; Yoshida, T. *J. Chem. Soc. Chem. Commun.* **1973**, 874.
[175] Negishi, E.; Williams, R. M.; Lew, G.; Yoshida, T. J. *Oganomet. Chem*. **1975**, 92, C4.

mechanistically interesting transformations.

1.6 Conclusion and Future Outlook

The ability of organoboron compounds to mediate 1,2-metallate rearrangement reactions makes these compound exceptionally versatile synthetic intermediates, capable of undergoing reactions that construct complex molecular scaffolds from simple starting materials, while enabling subsequent product diversification. The ability of a wide range of electrophilic compounds to induce rearrangement reactions of diverse boron-ate species represents a general design strategy for the development of new methods to access valuable synthetic motifs, often in a modular manner. While the stereospecific nature of many of these transformations has enabled the elaboration of enantioenriched alkylboronic esters as well as the preparation of stereodefined alkene isomers, the potential of rendering these transformations enantioselective and catalytic has only recently been realized. A resurgence in interest in this class of reaction, combined with modern synthesis techniques and knowledge promises to spark the development of new and powerful transformations capable of addressing challenging synthesis problems while contributing to fundamental scientific knowledge.

Chapter Two

Metal-Induced Metallate Rearrangement: Three-Component Conjunctive Coupling and Mechanistic Studies

2.1 Introduction

The advent of enantioselective catalysis utilizing transition metal complexes has revolutionized organic synthesis, enabling the efficient construction of complex organic molecules with unprecedented efficiency. The general principles governing enantioinduction and catalytic activity for a range of catalyst structures and reactions have been established thanks to the pioneering work of many luminaries in the field of enantioselective catalysis including Knowles, Noyori, Sharpless, as well as the pioneering contributions of Heck, Negishi, Suzuki, and others in the field of catalytic cross-coupling reactions utilizing transition metal complexes.

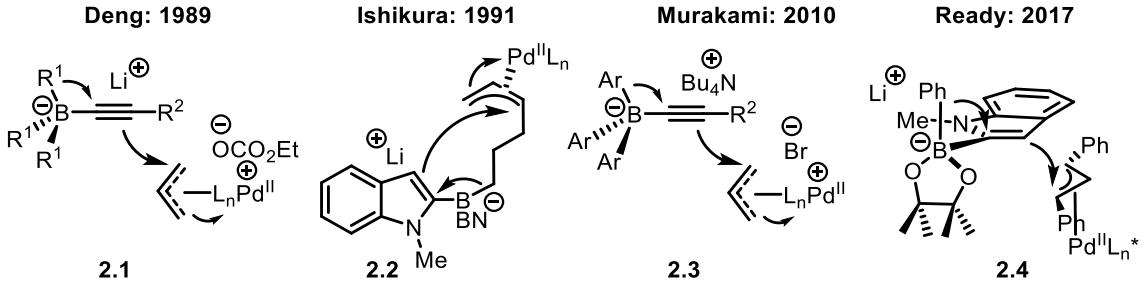
Thanks to the large number of powerful chemical transformations which have been developed using transition metal complexes, the field of chemical synthesis has largely moved beyond the question of whether any arbitrary molecular structure can be made, to pusuing the development of methods which enable structures to be made with increasing efficiency and stereocontrol, utilizing readily available starting materials.

In this vein, the development of enantioselective multicomponent coupling reactions which enable diverse product motifs to be prepared efficiently, in a modular fashion from simple and readily available chemical building blocks is at the forefront of modern chemical synthesis and catalysis.

As discussed in chapter one of this dissertation, many electrophilic species are capable

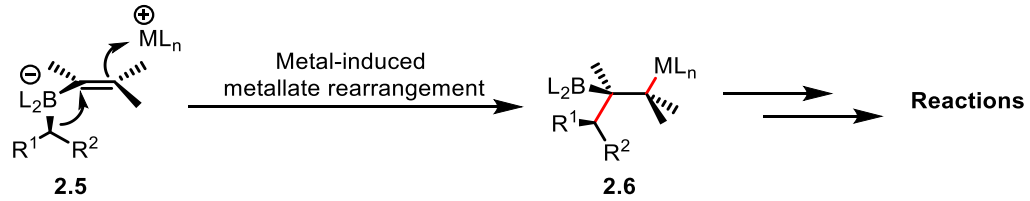
of inducing the metallate rearrangement reaction of organometallic ate complexes. Of those processes described, a small subset involve the catalytic use of electrophilic allylpalladium complexes to promote metallate rearrangement by an outer sphere mechanism (Scheme 2.1).[1] In this section, the limited reported examples of 1,2-metallate rearrangement

Scheme 2.1. Outer sphere rearrangement reactions catalyzed by palladium complexes



reactions in which a transition metal species directly induces rearrangement by an inner sphere mechanism will be discussed (Scheme 2.2). The inner sphere activation of boron-ate complexes has significant mechanistic and synthetic consequences. In contrast to the outer sphere mechanism shown above in which palladium acts as an auxiliary electrophilic activator, an inner sphere metal-induced metallate rearrangement reaction is capable of generating an alkyl metal species **2.6** which, in principle, can be engaged in a diverse set of synthetic transformations which are known to involve the intermediacy of a carbon-

Scheme 2.2. Inner sphere 1,2-metallate rearrangement promoted by electrophilic organometallic complex



[1] For a review on reactions involving alkynylboron–ate allylation reactions catalyzed by organopalladium complexes, see: (a) Fukushima, M.; Takushima, D.; Satomura, H. Onodera, G.; Kimura, M. *Chem. Eur. J.* **2012**, 18, 8019.

metal bond. Not only can this transformation enable a powerful new class of multicomponent reactions — indeed the process forges multiple bonds while retaining a valuable boron functional group — but it might be rendered catalytic in transition metal activator and through the use of chiral ligands enable stereocontrol. In the context of catalytic reactions employing transition metal complexes, this metal-induced metallate rearrangement represents a virtually unexplored elementary reaction.

2.2 Background

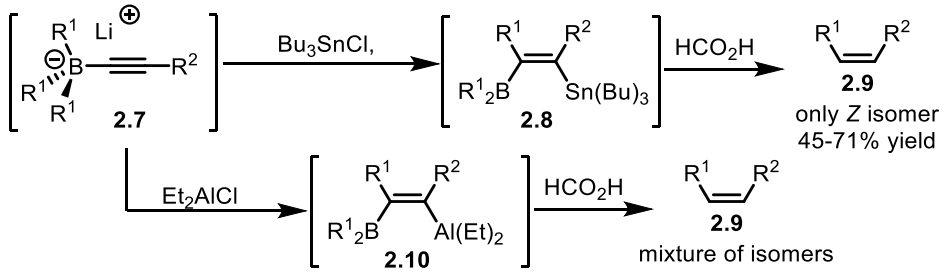
2.2.1 1,2-Metallate Rearrangements Involving Transition Metal Electrophiles

2.2.1.1 Rearrangement of Organoboronates

Aligned with previous reports of rearrangement reactions of alkynylboron-ate complexes induced by electrophilic silicon-, sulfur-, nitrogen-, and boron-halide species, (see chapter one) Hooz reported a 1,2-metallate rearrangement reaction of borane-derived alkynylboron-ate complexes induced by tributyltin chloride or diethylaluminum chloride (Scheme 2.3).[2] The authors found that while the organostannane-induced reaction appeared to proceed stereospecifically (based on isolation of isomerically pure *Z*-alkene product **2.09** upon protodemetallation of proposed intermediate **2.10**) the corresponding organoalane-induced reaction appeared to proceed nonstereospecifically, producing an *E*/*Z* isomeric product mixture. To further support the proposed formation of **2.10**, the authors treated the reaction mixture containing putative intermediate **2.10** with Negishi's sulfur-based

[2] Hooz, J.; Mortimer, R. *Tetrahedron Lett*. **1976**, 17, 805.

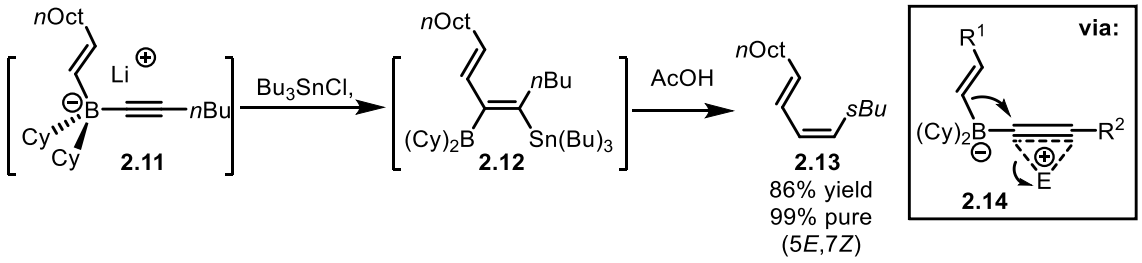
Scheme 2.3. Hooz's synthesis of di- and trisubstituted olefins by metal chloride-induced rearrangement



organoboron homologating reagent[3] and indeed observed the expected trisubstituted alkene upon subsequent protodemetallation. Shortly after this report Zweifel described a similar transformation utilizing alkenyl migrating groups as a means of preparing isomerically well-defined dienes (Scheme 2.4).[4] The authors, proposed that the reaction involves a stereospecific trialkylstannane-induced rearrangement (inset). Subsequently, Wrackmyer studied vicinal diorganometallic species such as **2.12** in more detail[5] and their preparation and reactivity was explored by Wang.[6]

Contemporaneous with his studies on the Bu_3SnCl-induced rearrangement reaction,

Scheme 2.4. Zwefel's synthesis of di- and trisubstituted olefins by $SnBu_3Cl$-induced rearrangement

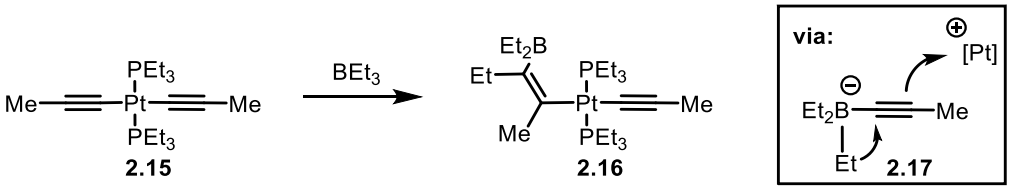


[3] Neglshi, E.; Yoshida, T.; Sllveira, A. Jr.; Chlou, B. L. *J. Org. Chem.* **1975**, 40, 814.
[4] Zweifel, G.; Backlund, S. J. *J. Organomet. Chem*. **1978**, 156, 159.
[5] (a) Wrackmeyer, B.; Bihlmayer, C.; Schilling, M. *Chem. Ber*. **1983**, 116, 3182. (b) Wrackmeyer, B.; Kehr, G.; Wilbold, S.; Boese, R. *Chemistry of Heterocyclic Compounds* **1999**, 35, 1041. (c) Wrackmeyer, B.; Kehr, G.; Wettinger, D. *Inorganica Chim. Acta.* **1994**, 220, 161. (d) Wrackmeyer, B. *Coordin. Chem. Rev.* **1995**, 145, 125.
[6] (a) Wang, K. K.; Chu, K.-H. *J. Org. Chem.* **1984**, 49, 5175. (b) Chu, K.-H.; Wang, K. K. *J. Org. Chem.* **1986,** 51, 767. (c) Wang, K. K.; Chu, K.-H.; Lin, Y.; Chen, J.-H. *Tetrahedron* **1989**, 45, 1105.

Wrackmyer demonstrated that trialkylboranes react with platinum acetylides (**2.15**) to form alkenylplatinum complexes (**2.16**) in which the boron moiety was incorporated (Scheme 2.5).[7] The authors attributed the formation of this product to a platinum-induced metallate rearrangement of boron-ate complex **2.17** (inset) which is formed *in situ* from abstraction of an alkyne ligand from platinum by the trialkylborane.

As described in chapter one, halogen-induced arylation reactions of alkylboron-ate complexes are only efficient for electron-rich arenes. To expand the scope of the aryl

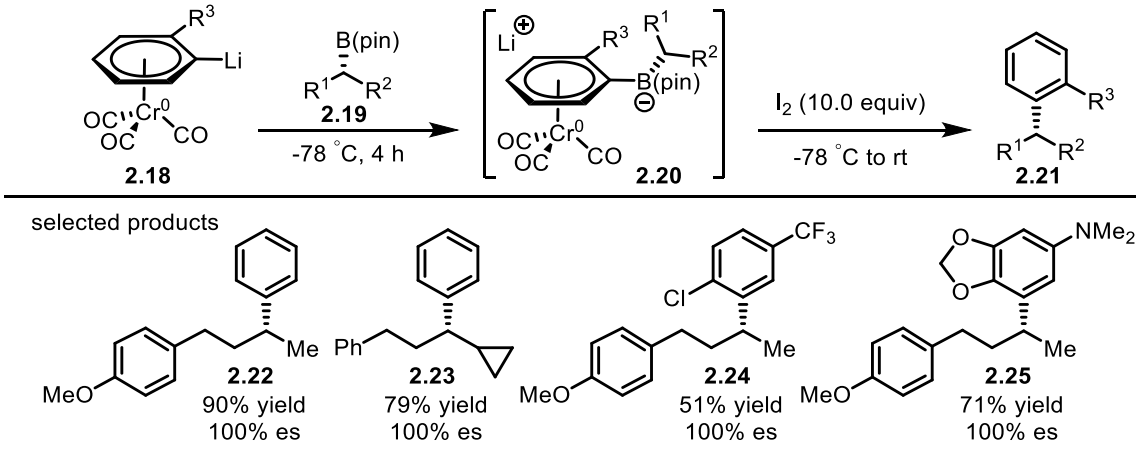
Scheme 2.5. Platinum-induced 1,2-metallate rearrangement reaction of alkynylboron-ate complexes



groups that can be employed, Aggarwal has developed a variety of stoichiometric activation strategies tailored to specific substrate classes such as pyridines, alkyne-substituted arenes, phenols, and benzyl amines. Adding to the number of organometallic species known to mediate the 1,2-metallate rearrangement reaction of boron-ate complexes, Aggarwal recently reported an oxidant-triggered rearrangement reaction of boron-ate-substituted arenes bound to tricarbonyl chromium complexes (Scheme 2.6).[8] This method is general with respect to the aryl groups that can be engaged. Conceptually, the chromium atom associates with the arene π-system acting as an auxiliary site of oxidative activation. The proposed mechanism of this reaction is depicted in Scheme 2.7. Starting from **2.20**,

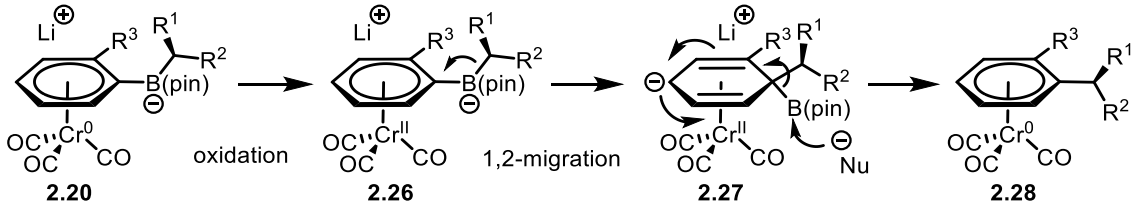
[7] Sebald, A.; Wrackmeyer, B. *J. Chem. Soc. Chem. Commun.* **1983**, 309.
[8] Bigler, R.; Aggarwal, V. K. *Angew. Chem. Int. Ed.* **2018**, 57, 1082.

Scheme 2.6. Aggarwal's oxidant-triggered $Cr(CO)_3$-induced metallate rearrangement



oxidation of the Cr(0) moiety to Cr(II) complex **2.26** precipitates 1,2-metallate rearrangement, furnishing dearomatized intermediate **2.27** which, for the use of a methyl migrating group, was crystallographically characterized. Dearomatized intermediate **2.27** is then proposed to undergo a nucleophile-induced reductive deborylation furnishing aryl

Scheme 2.7. Proposed mechanism for oxident-triggered $Cr(CO)_3$-induced metallate rearrangement



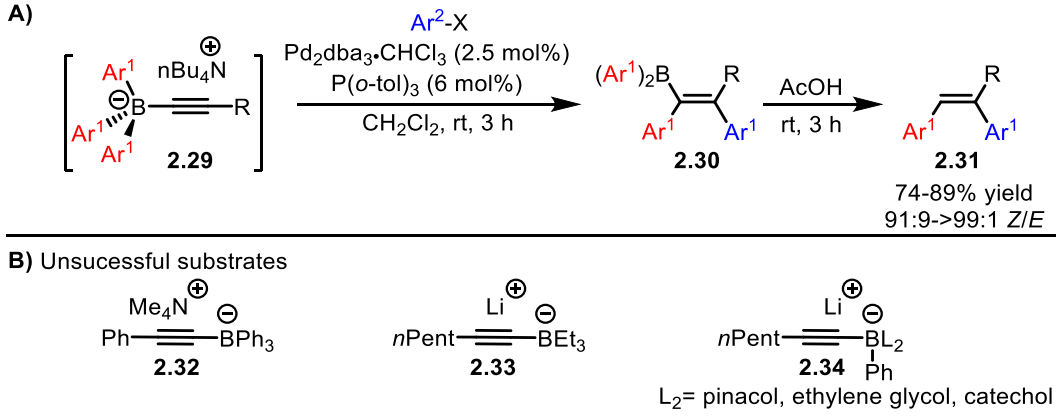
chromium complex **2.28**. In practice, the presence of excess I_2 oxidant facilities decomplexation of Cr(0) from the arene product. In principle, this strategy might be rendered catalytic in chromium tricarbonyl.

The metal-induced metallate rearrangement reactions mentioned thus far involve the use of a stoichiometric organometallic activating agent. In principle, any one of these reactions might be rendered catalytic if the organometallic intermediate formed upon 1,2-metallate rearrangement were to engaged in a subsequent functionalization reaction that

released an organic product and allowed the organometallic activating agent to be regenerated. Outside of the conjunctive coupling reactions which will be discussed shortly, only a handful of examples of catalytic reactions potentially involving such a mechanism have been reported. Interestingly none of the examples predating the work described in the body of this dissertation are reported by the authors to proceed by the metal-induced metallate rearrangement mechanism, though none conclusively excluded the mechanism.

In 2007, Murakami reported that triarylborane-derived alkynylboron-ate complexes undergo regiospecific diarylation with aryl halide electrophiles catalyzed by phosphine–palladium complexes (Scheme 2.8.A). The reaction produced *Z*-alkenes (**2.31**) selectively, which is consistent with *syn* addition of the aryl groups across the triple bond.[9] While a wide variety of aryl electrophiles could be engaged and various alkyne substituents could be accommodated, reaction of phenyl-substituted substrate (**2.32**) was unsuccessful (Scheme 2.8.B). Additionally, the nature of the migrating group, the cationic counterion (**2.33**), and the ligand on boron (**2.34**) proved to be essential factors controlling the success

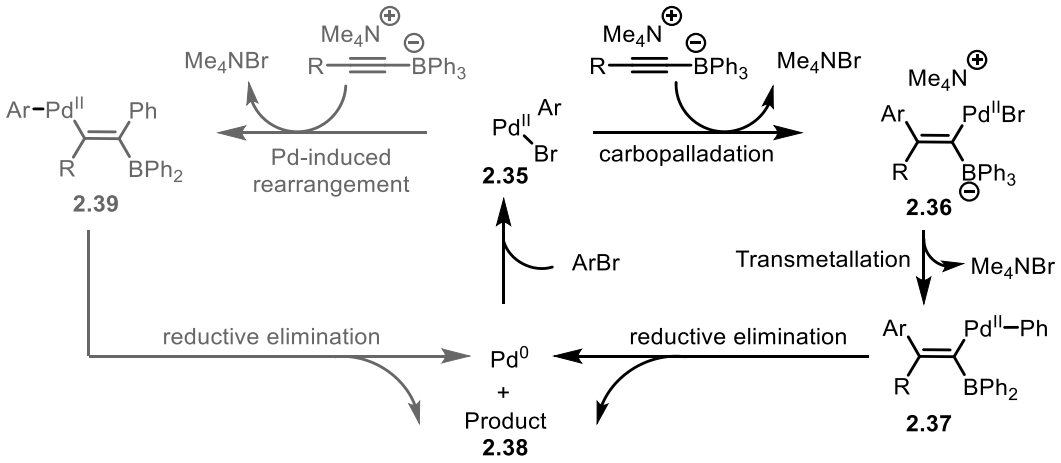
Scheme 2.8. Murakami's preparation of trisubstituted alkenes from alkynylboron-ate complexes



[9] Ishida, N.; Miura, T.; Murakami, M. *Chem. Commun.* **2007**, 4381.

of the reaction. To account for the stereochemical outcome, the authors proposed a carbopalladation mechanism, while parenthetically acknowledging that an alternative palladium-induced rearrangement pathway (grey) may be possible (Scheme 2.9). Both mechanistic proposals involve the oxidative addition of an aryl bromide electrophile by a Pd(0) species to generate an electrophilic arylpalladium complex **2.35**. Along one path,

Scheme 2.9. Murakami's mechanistic proposals

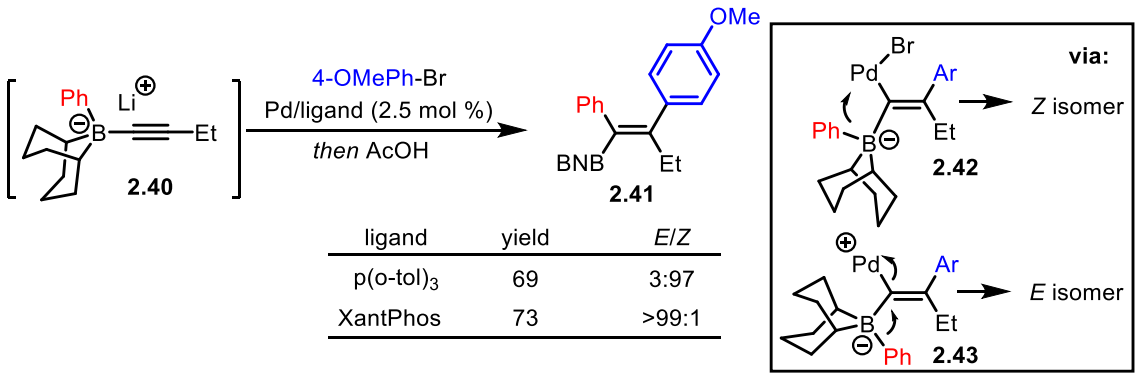


carbopalladation of an alkynylboron-ate complex produces α-boryl alkenyl–Pd(II) species **2.36** which then react by intramolecular transmetallation from boron to palladium, generating **2.37**. Reductive elimination of this species then produces the observed product **2.38** as well as a reduced palladium species capable of re-entering the catalytic cycle. Alternatively, arylpalladium complex **2.35** can induce the 1,2-metallate rearrangement of an alkynylboron-ate complex to furnish **2.39**, which then undergoes reductive elimination to produce the observed product as well as a reduced palladium complex. A mechanistic rationale for why the carbopalladation mechanism would be favored over the palladium-induced pathway was not offered, though crossover experiments did rule out mechanisms involving intermolecular aryl transfer. The authors attributed the formation of a minor

amount of *E*-olefin product to a competing invertive reductive elimination from **2.36**.[10] It is worth noting that electrophile-induced 1,2-metallate rearrangement reactions of alkynylboron-ate complexes are known to produce both *E*- and *Z*-alkene isomers or proceed non-stereospecifically. [11] Thus, the experimental data available appears inconclusive with respect to ruling out any of the possible mechanisms proposed.

Murakami further developed this reaction, reporting that it could be performed with trialkylborane-derived ate complexes,[12] and could operate with 2-bromopyridine-*N*-oxide electrophiles. [13] Interestingly, when 9-BBN-derived alkynylboron-ate complexes were employed in the reaction, the authors noted the *E*-alkene product isomer was predominantly formed rather than the *Z*-alkene as in previous reports (Scheme 2.10).[14] The authors found that the *E*/*Z* selectivity of the reaction could be controlled by choice of the ligand on palladium, with the bulky monodentate tri(*o*-tolyl)phosphine favoring *E*-alkene formation,

Scheme 2.10. Murakami's *E*- or *Z*-selective synthesis of trisubstituted alkenes



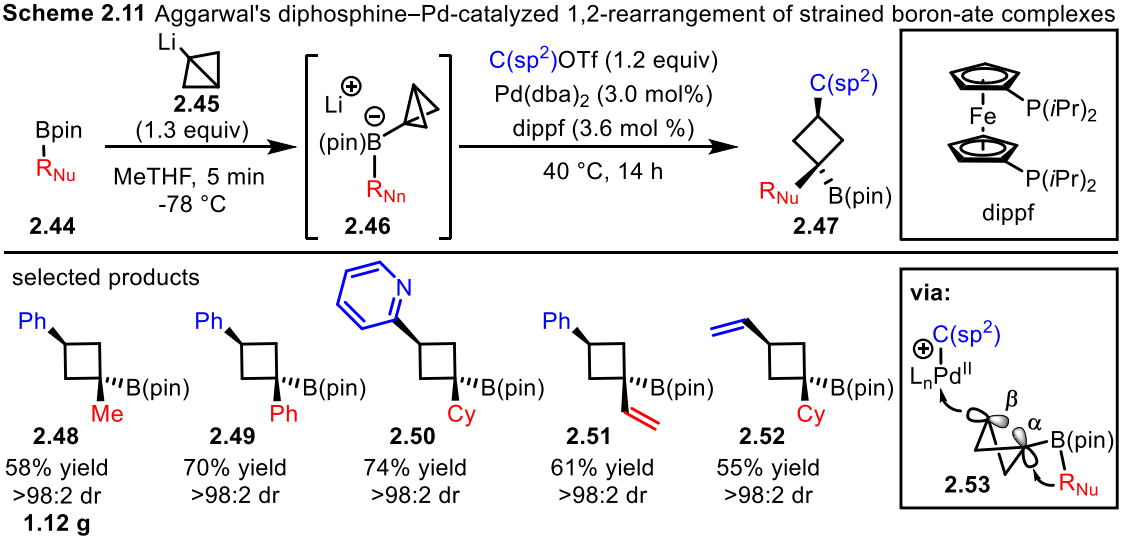
ligand	yield	*E*/*Z*
$p(o\text{-tol})_3$	69	3:97
XantPhos	73	>99:1

[10] (a) Köbrich, G.; Merkle, H. R. *Angew. Chem. Int. Ed*. **1967**, 6, 74. (b) Köbrich, G.; Merkle, H. R. *Chem. Ber*. **1967**, 100, 3371. See section 1.4 of chapter one of this dissertation for discussion.
[11] See section 1.5 of chapter one of this dissertation for examples and discussion.
[12] Ishida, N.; Narumi, M.; Murakami, M. *Org. Lett.* **2008**, 10, 1279.
[13] Ishida, N.; Ikemoto, W.; Narumi, M.; Murakami, M. *Org. Lett.* **2011**, 13, 3008.
[14] (a) Ishida, N.; Shimamoto, Y.; Murakami, M. *Org. Lett.* **2009**, 11, 5434. (b) Ishida, N.; Shimamoto, Y.; Murakami, M. *Org. Lett.* **2010**, 12, 3179.

while the wide bite-angle diphosphine XantPhos was observed to favor formation of the *Z*-alkene. The authors proposed that the reaction proceeds by a carbopalladation mechanism and that the choice of ligand determines the olefin isomer formed by promoting either the intramolecular transmetallation pathway (**2.42**, inset) followed by retentive reductive elimination or by an invertive displacement pathway (**2.43**, inset) producing the observed *E* isomer of product.

In 2019, Aggarwal reported that boron-ate complexes bearing a strained carbocyclic ring can be activated by a catalytic amount of palladium-diphosphine complex, thereby inducing a stereospecific 1,2-metallate rearrangement reaction tha produces substituted cyclobutane products (Scheme 2.11) [15] Inspired by the prospect of developing a diphosphine–palladium-catalyzed multicomponent reaction that operates by activating C–C σ-bonds rather than C–C π-bonds, the authors sought a strategy to overcome the

Scheme 2.11 Aggarwal's diphosphine–Pd-catalyzed 1,2-rearrangement of strained boron-ate complexes



[15] Fawcett, A.; Biberger, T.; Aggarwal, V. K. *Nat. Chem.* **2019**, 11, 117.

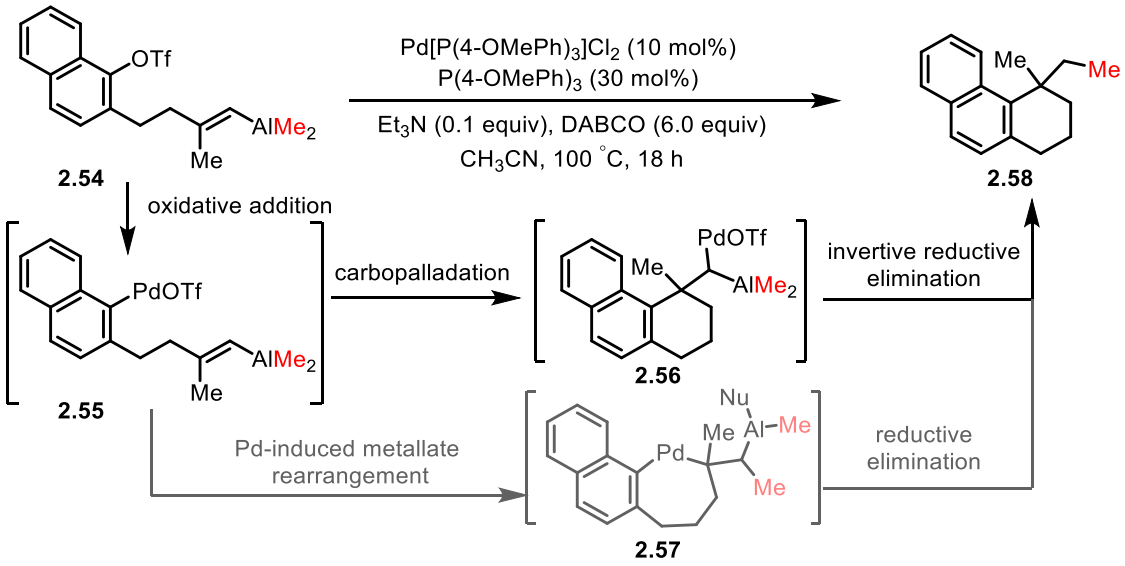
generally poor propensity of such bonds to react with Pd-complexes.[16] Targeting a ground-state destabilization strategy, the authors reasoned that using a bicyclo[1.1.0] butane carbocyclic moiety, a compound that possesses substantial ring strain (~66 Kcal/mol),[17] might promote reaction of a C–C σ-bond with the catalyst (**2.53**, inset). This strategy proved successful and the reaction was shown to be quite general with respect to the electrophiles and migrating groups which could be employed (**2.48** through **2.52**). If this strategy can be extended to less strained substrates it might enable a powerful new set of transformations to be developed for the activation of C–C σ-bonds. The possibility of rendering related transformations enantioselective is an intriguing prospect.

2.2.1.2 Rearrangement of Organoalanes

While far less common than 1,2-metallate rearrangement reactions involving organoboron-ate complexes, as discussed in chapter one, rearrangement reactions involving organoaluminum-ate complexes are also known. In 2004 Fillion reported that a catalytic quantity of palladium-diphosphine complex was sufficient to promote the intramolecular 1,2-ligand migration of dialkylalkenylalane compounds containing an aryltriflate moiety (Scheme 2.12).[18] While the authors discussed the possibility that this reaction might operate by way of a palladium-induced metallate rearrangement mechanism (grey pathway) they proposed that an alternative carbopalladation mechanism was more

[16] Crabtree, R. H. *Angew. Chem. Int. Ed.* **1993**, 32, 789.
[17] Khoury, P. R., Goddard, J. D.; Tam, W. *Tetrahedron* **2004**, 60, 8103.
[18] Fillion, E.; Carson, R. J.; Trépanier, V. E.; Goll, J. M.; Remorova, A. A. *J. Am. Chem. Soc.* **2004**, 126, 15354.

Scheme 2.12. Fillion's diphosphine–Pd-catalyzed 1,2-ligand migration of organoalanes



likely operative for the reactions studied. Both mechanisms involve initial oxidative addition of a palladium-based catalyst to **2.54**, forming intermediate **2.55**. From this intermediate the potential reaction pathways diverge, either involving: (1) a sequence of carbopalladation to form geminal diorganometallic intermediate **2.56**, followed by an invertive reductive displacement (elimination) of the covalently bound palladium moiety and proto-dealumination to form observed product **2.58**, or (2) palladium-induced 1,2-metallate rearrangement of **2.55** to form vicinal diorganometallic intermediate **2.57**, followed by stereoretentive reductive elimination and proto-dealumination to form **2.58**. The authors cited the yield enhancement observed for aryl triflate substrates with a 2,6-disubstitution pattern (such as **2.54**) as evidence in support of the carbopalladation mechanism but did not provide conclusive evidence disproving the palladium-induced rearrangement mechanism. Additionally, the authors noted that without such a 2,6-disubstitution pattern, complex product mixtures containing structures which might be

derived from both mechanisms are obtained. A subsequent study in 2009 by the same authors provided more mechanistic insight and several more examples of this reaction, but did not provide conclusive data excluding the palladium-induced metallate rearrangement mechanism.[19] These appear to be the sole reports of an aluminum-based metallate rearrangement reaction promoted by an organometallic complex.

In spite of the clear potential of metal-induced metallate rearrangement reactions to enble a general strategy to access reactive intermediates capable of forming synthetically useful bonds in a modular manner, this area has remained virtually unexplored for decades. The lack of synthetic examples, combined with the paucity of experimental mechanistic information has no doubt contributed to a lack of research interest. In the realm of catalytic reactions, previous to the work detailed below, metal-induced metallate rearrangement was restricted to the realm of discounted mechanistic pathways. Of the few catalytic reactions that may plausibly operate by this mechanism none are enantioselective.

2.2.2 Proposal for Metal-Induced Metallate Rearrangement and the Conjunctive Coupling Process

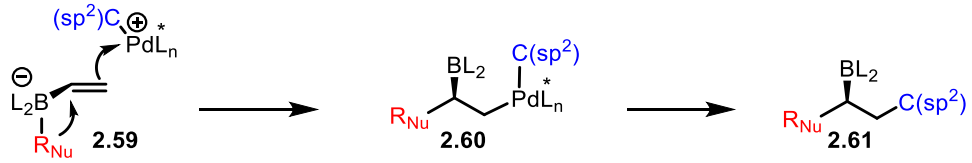
As demonstrated by the examples in chapter one, stoichiometric electrophile-induced rearrangement reactions represent a versatile approach for the construction of diverse synthetically useful structures. The examples above suggest that an organometallic complex might catalyze a three-component coupling of an organoboronic ester, an

[19] Fillion, E.; Tre´panier, V. E´.; Heikkinen, J. J.; Remorova, A. A.; Carson, R. J.; Goll, J. M.; Seed, A. *Organometallics* **2009**, 28, 3527.

organometallic nucleophile, and an organic electrophile, enabling a versatile approach for the construction of multiple synthetically useful carbon–carbon, or even carbon–heteroatom bonds.

Initially drawing mechanistic inspiration from the early work of Zwiefel and Evans on the halogen-induced olefination reaction, we considered whether the stoichiometric electrophilic activating agent I_2 employed in these reactions could be replaced with a catalytic π-acidic transition metal complex (Scheme 2.13). If so, a metal-induced metallate rearrangement would enable the generation of β-metallated chiral boronic ester intermediate **2.60**. The use of chiral ligands on the catalyst transition metal might conceivably rendered this elementary step enantioselective by controlling facial selectivity in alkene binding. While a host of competing pathways such electrophilic quenching, proto-demetallation, or β-hydride/β-boryl elimination might intervene, we imagined that if the catalyst were pre-loaded with a carbon ligand reductive elimination from **2.60** would furnish enantioenriched boronic ester product **2.61**. Because the overall transformation is

Scheme 2.13. Mechanistic hypothesis for conjunctive cross-coupling



reminiscent of a cross-coupling reaction but involves the merger of two nucleophiles as well as an electrophile it is referred to as a conjunctive cross-coupling (hereafter referred to simply as a conjunctive coupling).

In this chapter, the initial development and mechanistic study of this reaction will be discussed along with an exploration of the factors controlling the balance between the

metal-induced metallate rearrangements and competing transmetallation reactions. A subsequent extension of the reaction manifold to the generation of products with fully-substituted stereogenic carbon centers, as well as an example of how the mechanistic understanding gained in these studies can enable the development of other synthetically useful transformations will also be briefly touched on.

2.3 Development of Conjunctive Coupling[20]

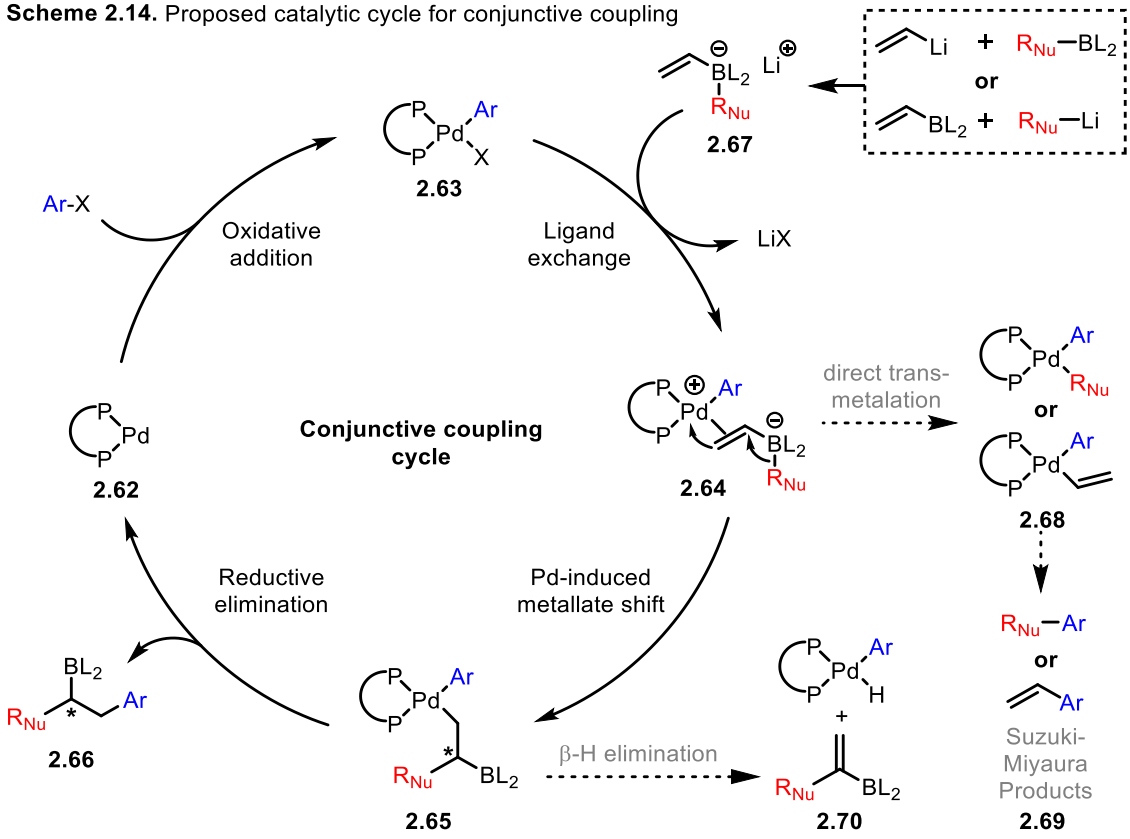
2.3.1 Proposed Catalytic Cycle

As a starting point for the development of the proposed catalytic conjunctive coupling, we hypothesized that if such a process were to work it might operate by a catalytic cycle such as depicted in Scheme 2.14. Oxidative addition of phosphine-bound Pd(0) complex **2.62** to an electrophile produces oxidized Pd(II) intermediate **2.63**. Ligand dissociation of the anion bound to **2.63** and coordination of the vinylboron-ate complex **2.67** generates **2.64**. The highly electrophilic nature of the cationic palladium complex will then induce a 1,2-metallate rearrangement to furnish alkylpalladium intermediate **2.65** which will undergo reductive elimination to produce the desired product as well as reduced palladium species **2.62** which can re-engage in the catalytic cycle. To prevent undesired side reactions such as direct transmetallation from vinyl-bound palladium complex **2.64** (to form Suzuki-Miyaura products **2.69)** and β–H or β–boryl elimination from palladated species **2.65**, we hypothesized that several reaction parameters would have to be carefully selected. First,

[20] Zhang, L.; Lovinger, G. J.; Edelstein, E. K.; Szymaniak, A. A.; Chierchia, M. P.; Morken, J. P. *Science* **2016**, 351, 70.

we hypothesized that aryl triflates would serve as an ideal class of electrophile to undergo facile oxidative addition and the non-coordinating nature of the triflate anion would serve to facilitate the formation of cationic palladium species **2.64**. In terms of the phosphine ligand employed, we imagined that an electron-rich, wide bite angle diphosphine would likely facilitate oxidative addition [21] while promoting reductive elimination. [22] The chelating nature of such a ligand should retard undesired β-elimination processes from **2.65** by preventing the formation of an open coordination cite on palladium. Initial experiments

Scheme 2.14. Proposed catalytic cycle for conjunctive coupling

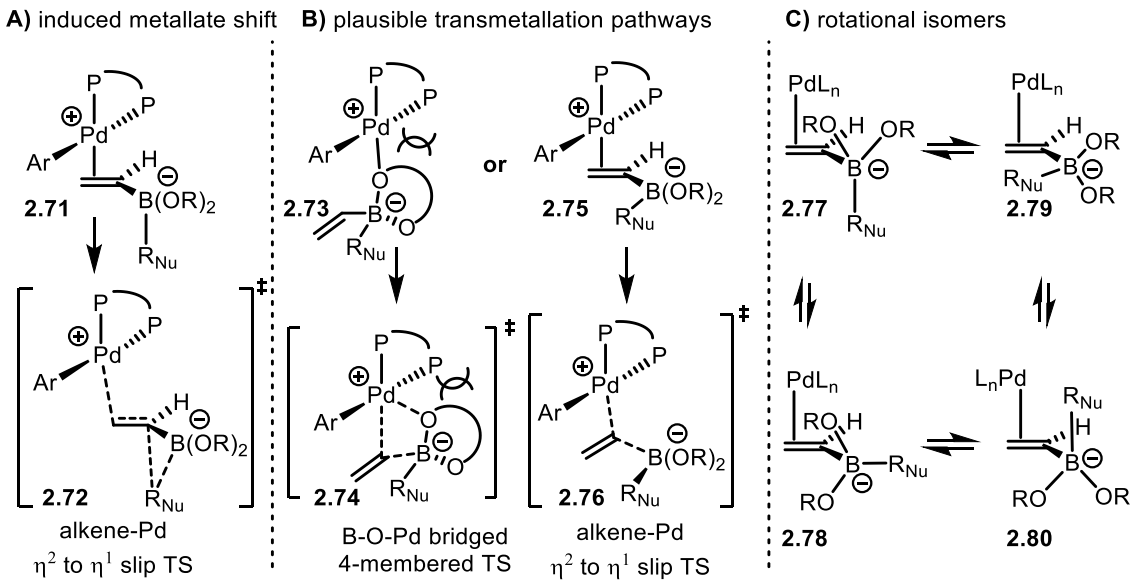


[21] Littke, A. F.; Fu, G. C. *Angew, Chem. Int. Ed*. **2002**, 41, 4176.
[22] Shekhar, S. L.; Hartwig, J. F. *J. Am. Chem. Soc*. **2004**, 126, 13016. (b) Dicosimo, R.; Whitesides, G. M. *J. Am. Chem. Soc.* **1982**, 104, 3601. (c) Komiya, S.; Abe, Y.; Yamamoto, A.; Yamamoto, T. *Organometallics* **1983**, 2, 1466. (d) Tatsumi, K.; Nakamura, A.; Komiya, S.; Yamamoto, A.; Yamamoto, T. *J. Am. Chem. Soc*. **1984**, 106, 8181.

utilizing PhOTf, a vinylboron-ate complex (vinyl–B(pin) + *n*BuLi), $Pd(OAc)_2$ and various mono- and bidentate phospine ligands revealed that only ferrocene-based bisphosphine ligands such as 1,1-bis(diphenylphosphino)ferrocene (DPPF) and 1,1-bis(dicyclohexyl) phosphinoferrocene (DCyPF) produced appreciable yields of the desired conjunctive product. The use of monodentate ligands as well as non-ferrocene-based diphosphine ligands resulted in the observation of cross-coupled Suzuki products (as depicted in Scheme. 2.14). Notably β-hydride elimination products were not observed during the course of reaction development. Instead, the Suzuki-Miyaura cross-coupling reaction arising from direct transmetallation from the boron-ate complex to the palladium catalyst was observed to be the main competing reaction. While the mechanistic details of the metal-induced metallate rearrangement and transmetallation reactions will be discussed in more detail in the following sections, Scheme 2.15 provides a summary of some key points. First, a simplified analysis of the steric and electronic requirements for the key palladium-induced metallate rearrangement reveals that it likely involves a palladium-bound olefin complex **2.71** in which the catalyst ligand set and the alkene are orthogonal to one another The corresponding transition state **2.72** involves η^2 to η^1 slippage of palladium to the terminal alkene position with concomitant migration of a group on boron to the adjacent polarized carbon atom. Second, while the mechanism of transmetallation is not well understood in general relative to other elementary reactions such as oxidative addition, there are likely two main possibilities: (1) transmetallation proceeds, from a pinacol oxygen-bound palladium species **2.73** through a 4-membered pentacoordinate transition state **2.74**, or (2) transmetallation proceeds from an alkene-bound palladium species **2.75**

through an open transition state **2.76** involving an η^2 to η^1 slippage of palladium to the internal alkene position. A third key point is that, while the metallate rearrangement transition state **2.72** requires the migrating group to be located in an *anti*-periplanar orientation relative to palladium, in principle, transmetallation may proceed from multiple rotational isomers of the vinylboron-ate complex (Scheme 2.15.C). Thus, it is perhaps not surprising that the course of the reaction (Suzuki-Miyaura or conjunctive coupling) was found to be highly dependent on the phosphine ligand structure employed, as this would be expected to strongly influence the ease with which the diphosphine-palladium complex

Scheme 2.15. Metal-induced metallate rearrangement versus transmetallation



can access the internal versus terminal alkene positions and might control alkenylboron-ate complex rotational isomer populations.

While the diol ligand on boron was found to have a subsidiary influence on the reaction, with both pinacol and neopentyl glycol esters producing substantial amounts of the desired product, the use of neopentyl boronic esters was found to result in higher

enantioselectivities as detailed below.

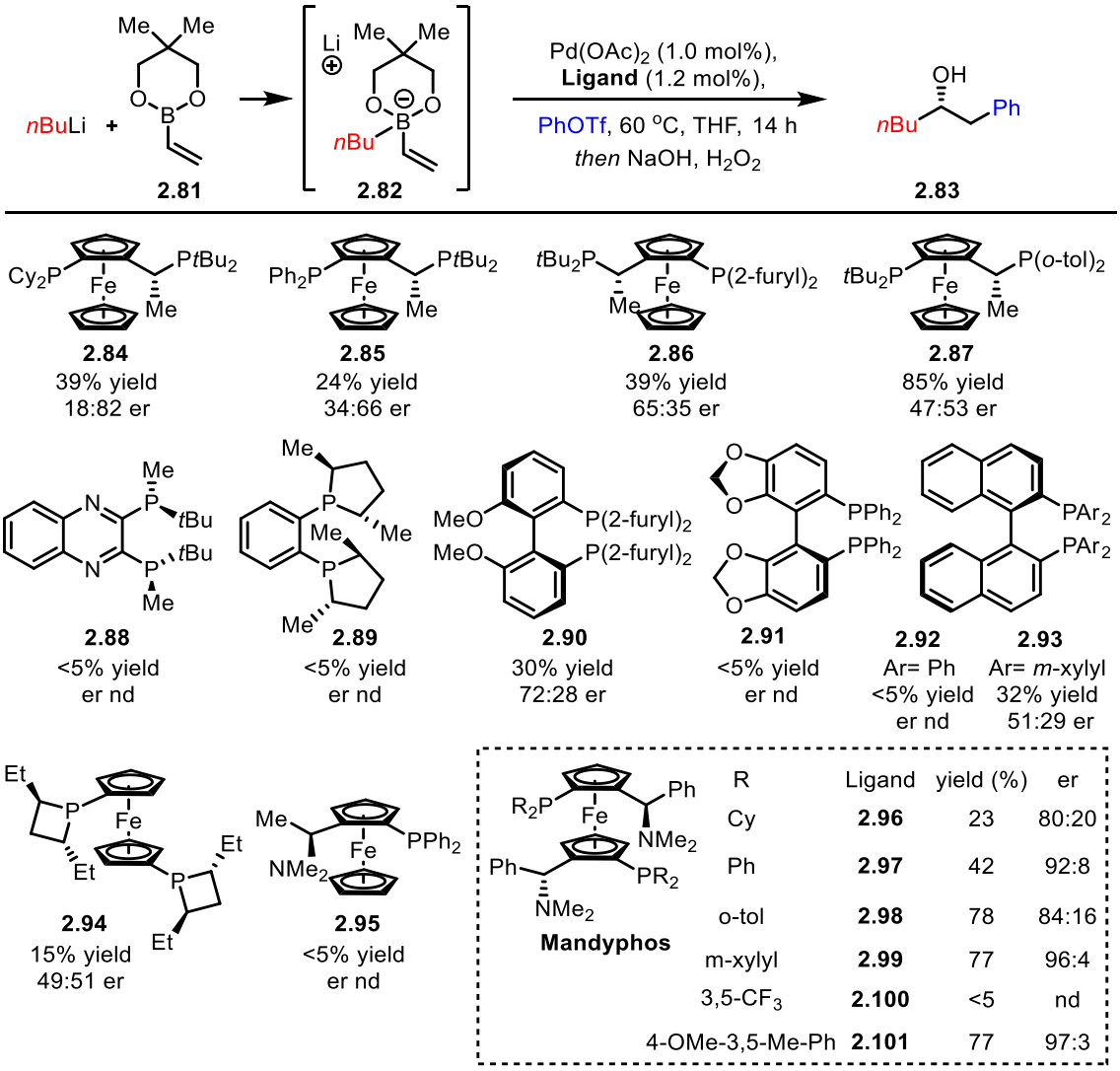
2.3.2 Investigation of Phosphine Ligand Structure

Following an initial assessment of reactivity with achiral ligands, various chiral diphosphine ligands were investigated (Scheme 2.16). The use of chiral monodentate ligands was explored but uniformly failed to produce appreciable yields of the conjunctive product. JosiPhos ligands (**2.84** through **2.87**) were found to produce the desired product in moderate enantioselectivity but low yield (**2.84**) or low enantioselectivity with excellent yield (**2.87)**. Non-ferrocene-based diphosphine ligands with a small bite angle such as QuinoxP* (**2.88**) and DuPhos (**2.89**) were not effective in promoting the desired reaction but instead promoted the Suzuki reaction as indicated by the observation by ^{1}H NMR of styrene in the unpurified reaction mixture. Axially chiral biphenyl and binapthyl ligands (**2.90** through **2.93**) gave low yields and enantioselectivities. The MandyPhos[23] ligand class was found to be exceptionally effective at promoting the conjunctive coupling reaction, producing the highest yields and enantioselectivities observed for any of the ligands tested. Ligand **2.101** bearing the most electron-rich and sterically hindered aryl groups on phosphine was most effective, producing the desired producte in 77% isolated yield and 97:3 er. Conversely, the ligand bearing the most electron-deficient aryl substituents **2.100** was the only ligand that did not produce any appreciable product. Substitution on the phosphine aryl rings appears to improve the yield of the reaction (**2.97** vs. **2.98**, **2.99**,

[23] (a) Hayashi, T.; Yamamoto, A.; Hojo, M.; Ito, Y. *J. Chem. Soc., Chem. Commun*. **1989**, 495. (b) Almena Perea, J. J.; Lotz, M.; Knochel, P. *Tetrahedron: Asymmetry* **1999**, 10, 375.

2.101): while *meta*-disubstitution[24] appears to improve the enantioselectivity of the reaction, *ortho*-substitution appears to decrease enantioselectivity. C_2-symmetric ligand **2.94** bearing chiral substituents on the phosphine groups gave low yields of the desired product in essentially racemic form. To probe whether the dimethyl amine substituent

Scheme 2.16. Investigation of diphosphine ligand structures



[24] Trabesinger, G.; Albinati, A.; Feiken, N.; Kunz, R. W.; Pregosin, P. S.; Tschoerner, M. *J. Am. Chem. Soc.* **1997**, 119, 6315.

common to the Mandyphos class of ligand may participate in binding to palladium (*P*,*N*-binding mode) non-C_2-symmetric *P*,*N*-type ligand **2.95** was tested in the reaction. The ineffectiveness of this ligand suggests that the *P*,*N*-binding mode, at least for phosphorous and nitrogen substituents on the same ferrocene ring, is unlikely.

The high degree of specificity of the reaction with respect to ligand structure is consistent with the previously mentioned mechanistic hypothesis for metal-induced metallate rearrangement and transmetallation (Scheme 2.15). According to this analysis, the reason the MandyPhos ligand class is superior at promoting the metallate rearrangement compared to monodentate ligands and those with smaller bite angles may be that the palladium atom in the catalytically active MandyPhos complexes is less sterically accessible. As such, it may be more energetically favorable for the palladium center to bind the vinyl group of the substrate rather than the sterically hindered pinacol oxygen (**2.73** to **2.74**). Additionally, a more sterically hindered ligand set on the palladium-center will penalize the η^2 to η^1 slippage of palladium to the internal alkene position (transmetallation) (**2.75** to **2.76**) but conversely will favor the η^2 to η^1 slippage of palladium to the unsubstituted terminal vinyl position involved in the rearrangement mechanism (**2.71** to **2.72**). Notably, due to the formation of a stronger Pd–C(sp^2) bond transmetallation is likely a more thermodynamically favored process than metallate rearrangement that formers a weaker Pd-C(sp^3) bond.

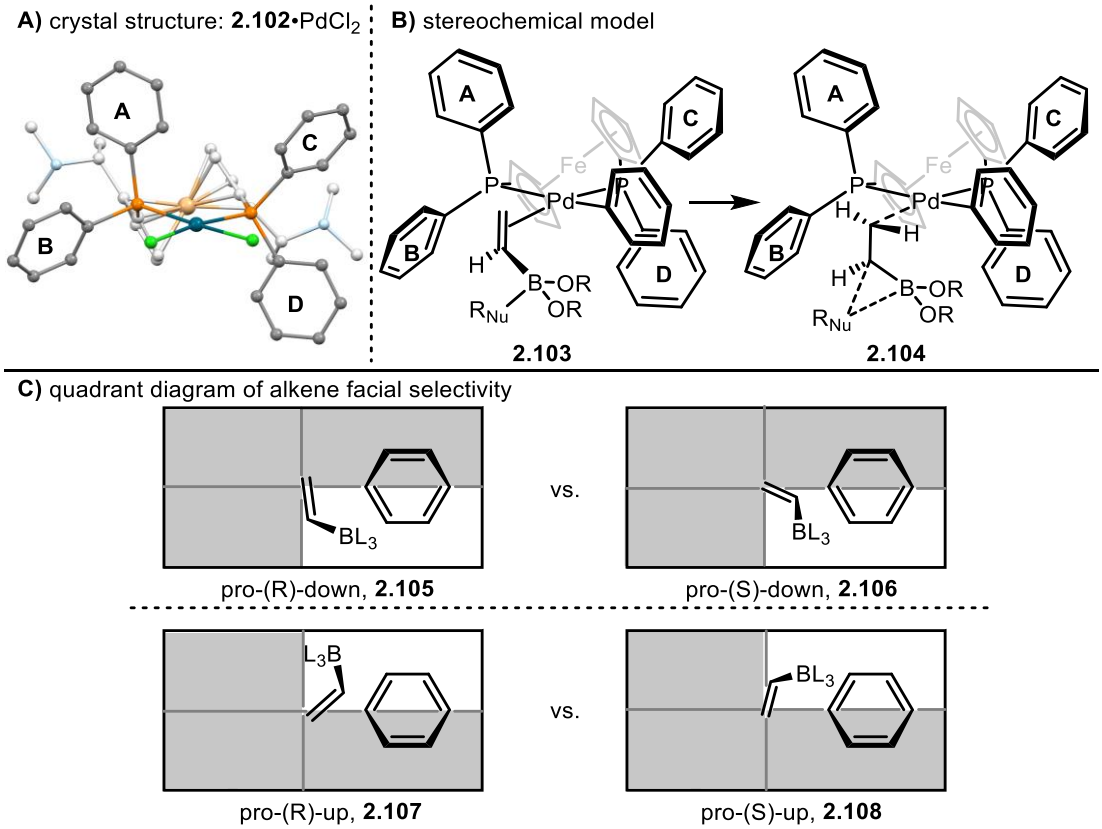
With the aim of developing a greater understanding of the aspects of ligand and substrate structure leading to the high enantioselectivies observed for the MandyPhos ligands, we examined a crystal structure of **2.102**·$PdCl_2$ reported by Ito and Hayashi

(Scheme 2.16.A).[25] The ligand structure of this palladium-complex differs from the MandyPhos ligand **2.101** only in the substitution of a methyl for a phenyl group on the ferrocenyl substituents. Based on the mechanistic proposal for conjunctive coupling, after oxidative addition of this complex to PhOTf and ligand association of a vinylboron-ate complex, a ground state palladium-alkene complex **2.103** should be formed (Scheme 2.16.B). The facial selectivity and relative orientation of the vinylboron-ate will be governed by steric interactions between the four-coordinate boron moiety and the pseudo-axial and pseudo-equatorial diarylphosphine substituents of the 6-membered metallocycle of the catalyst. The subsequent 1,2-metallate rearrangement is expected to be an early starting-material-like transition state involving minimal structural rearrangement based on the calculated exothermic nature of the reaction, as well as computational modeling of this structure (detailed below). Considering a simplified quadrant diagram[26] analysis of this model (2.16.C), in which darker shading corresponds to a larger degree of steric repulsion, the forward projecting aryl rings (A and B) on the left of the catalyst will occupy these left quadrants while the steric occupation of the right two quadrants will be controlled by the relative steric impact of the aryl rings (C and D) behind the aryl group attached to palladium. While the rotational orientation and steric profile of the aryl substituents on phosphine (2- or 3,5-disubstitution, unsubstituted, etc) may substantially modulate the canting of the aryl group attached to palladium and thus tune the specific model invoked

[25] (a) Hayashi, T.; Yamamoto, A.; Hojo, M.; Ito, Y. *J. Chem. Soc. Chem. Commun.* **1989**, 495. (b) Hayashi, T.; Yamamoto, A.; Hojo, M.; Kishi, K.; Ito, Y.; Nishioka, E.; Miura, H.; Yanagi, K. *J. Organomet. Chem.* **1989**, 370, 129.
[26] Gladysz, J. A.; Boone, B. J.; *Angew. Chem. Int. Ed.* **1997**, 36, 550.

for a particular MandyPhos catalyst, two main scenarios present themselves to explain the observed stereochemical outcomes of conjunctive reactions in which the (R) enantiomer of product is formed when the (S) enantiomer of catalyst is used in the reaction. (1) If the aryl group attached to palladium cants forward to occupy the upper right quadrant due to the steric influence of psudo-equitorial ring C (top two quadrant diagrams: **2.105**/**2.106**) then the pro-(R)-down alkene binding-mode **2.105** would be expected to be lower in energy as the alkene of this boron-ate complex lies along the unoccupied vertical axis which is orthogonal to the square plane formed by the palladium catalyst. The pro-(S)-down alkene binding mode **2.106**, in contrast, resides in an orientation which is largely coplanar with the square plane of the catalyst and thus involves penalizing steric interactions.

Scheme 2.16. Crystal structure and plausible stereochemical model



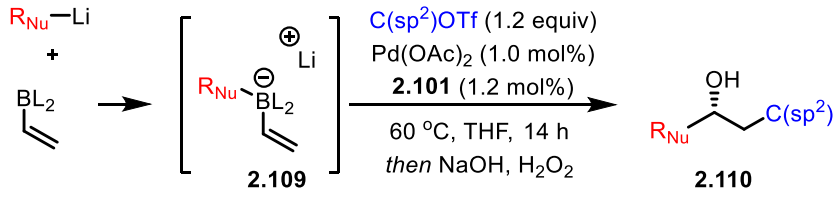
Additionally, migration from the pro-(R)-down structure **2.105** can occur in such a manner that the migrating group is not in proximity to the adjacent pseudo-equatorial arene (B). (2) If the aryl group attached to palladium is canted forward to occupy the lower right quadrant (bottom two quadrant diagrams: **2.107**/**2.108**) then the rationale for the energetic difference between pro-(R)/(S) alkene binding modes is somewhat more subtle. Because the upper left quadrant is occupied by a psudo-axial aryl group (A) which does not project forward as much as the corresponding psudo-equatorial aryl group (B), the pro-(R)-up alkene binding-mode (**2.107**) can reside in a largely orthogonal orientation with respect to the square plane of the catalyst without incurring a substantial steric interaction with the upper left quadrant (A ring). This orientation allows the large four-coordinate boron substituent to project up and away from the aryl group on palladium, thus minimizing overall steric interactions between the vinylboron-ate and catalyst complexes. In contrast, the pro-(S)-up alkene binding-mode (**2.108**) similarly benefits from a smaller steric interaction with the upper left-hand quadrant but orients the large boron-ate substituent to the right where it experiences penalizing steric interactions with the proximal aryl group on palladium. Therefore it appears that, as is experimentally observed, the steric profile of the electrophile, ligand on boron, and the aryl substituents on the diphosphine ligand employed in the conjunctive reaction all strongly influence the degree of enantioselectivity in this process.

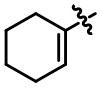
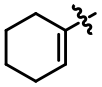
2.3.3 Optimization of Conditions

We then explored the impact of various reaction parameters including the nature of the

migrating group, the ligand on boron, and the type of electrophile employed in the reaction (Table 2.1). While both neopentyl and pinacol boronic esters were found to be effective for reactions employing either alky or aryl migrating groups (entries 1-4) use of the neopentyl ligand resulted in reproducibly higher enatioselectivity. Conversely, when alkenyl rather than aryl electrophiles were employed in the reaction, the use of pinacol rather than neopentyl glycol boronic esters was found to result in higher enantioselectivity (entries 5 and 6). The observed matching/mismatching behavior between boron ligand and electrophile is consistent with the stereochemical model advanced above in which the stereochemical profile of the active catalyst that binds to the vinylboron-ate complex depends strongly on the electrophile.

Table 2.1. Effect of migrating group, ligand on boron, and electrophile[a]



entry	R_m	L_2	$C(sp^2)$	er
1	Bu	pin	Ph	85:15
2	Bu	neo	Ph	98:2
3	Ph	pin	Ph	93:7
4	Ph	neo	Ph	98:2
5	Ph	neo		82:18
6	Ph	pin		97:3

[a] Enantiomer ratio (er) was determined using SFC analysis.

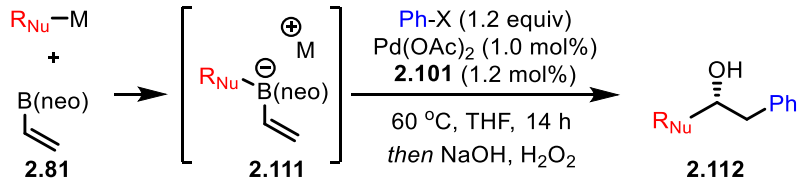
2.3.4 Effect of Halides on Reaction Outcome

While aryl and alkenyl organotriflate electrophiles are readily prepared from the corresponding phenols, ketones, or aldehydes, we were interested to investigate what other classes of electrophiles might be engaged in conjunctive coupling (Table 2.2). Using the less electrophilic phenyl mesylate electrophile (entry 2), the reaction did not produce appreciable amounts of the desired product. Chlorobenzene (entry 5) was similarly unreactive as phenyl mesylate in the reaction, while the use of iodo- and bromobenzene (entries 3 and 4) resulted in low yields of the desired product but with excellent enantioselectivities. While the lack of product formation when employing phenyl mesylate and chlorobenzene was consistent with the difficulty of engaging these substrates in oxidative addition, the low yields observed with iodo- and bromobenzene suggested to us that halide anions may inhibit the reaction. The common halide scavenging agent silver triflate was employed in a reaction with chlorobenzene (entry 6) in an attempt to combat halide inhibition of catalysis if this were indeed occurring. Based on ^{11}B NMR analysis of the reaction solution, we found that the vinylboron-ate complex starting material decomposes quickly upon exposure to silver triflate, thus invalidating this as a possible approach to circumvent halide inhibition of catalysis while at the same time revealing the reactivity of boron-ate complexes to redox active metals.

It is important to note that while the boron-ate complexes utilized for the optimization of this reaction were prepared *in situ* from the addition of *n*-Bu- or phenyllithium reagents to a vinylboronic ester reagent, the same complex can be prepared by the addition of

vinyllithium to the corresponding alkyl- and phenylboronic ester reagents. Envisioning that such an approach might increase the utility of conjunctive coupling by enabling it to engage a wide range of commercially available and readily prepared organoboronic esters utilizing a single vinyl organometallic reagent, we next investigated the use of vinyl Grignard reagents (entries 8 and 9). These reactions did not produce appreciable amounts of the desired product. Somewhat surprisingly, reactions employing vinyllithium prepared by the

Table 2.2. Effects of electrophile and halide content on conjunctive coupling[a]

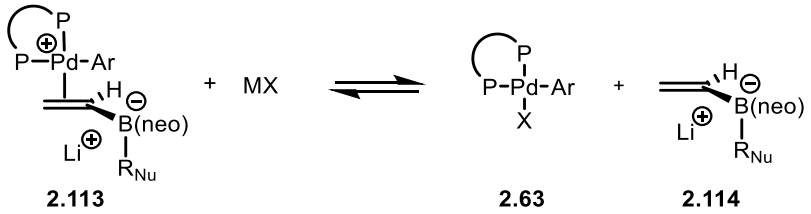


entry	X	R_{Nu}	M	additive	Yield (%)	R_{Nu}
1	OTf	*n*Bu	Li	-	77	98:2
2	OMs	*n*Bu	Li	-	<5	na
3	I	*n*Bu	Li	-	9	96:4
4	Br	*n*Bu	Li	-	9	96:4
5	Cl	*n*Bu	Li	-	<5	na
6	Cl	*n*Bu	Li	AgOTf (1.2 equiv)	<5	na
7	OTf	Ph	Li	-	84	97:3
8[b]	OTf	Ph	MgBr	-	<5	na
9[b]	OTf	Ph	MgCl	-	<5	na
10[c]	OTf	Ph	Li	-	<5	na
11	OTf	*n*Bu	Li	LiBr (1 mol%)	41	98:2
12	OTf	*n*Bu	Li	LiI (1 mol%)	13	98:2
13[d]	OTf	*n*Bu	Li	LiI (1 mol%)	69	98:2

[a]Yields are of purified material. Enantiomer ratio (er) was determined using SFC analysis. [b]Boron-ate complex prepared by addition of vinyl Grignard reagent to phenylboronic neopenyl ester. [c]Vinyllithium prepared from vinyl bromide and *tert*-butyllithium. [d]$Pd(OAc)_2$ (5 mol%) and **2.101** (6 mol%) were employed.

lithium-halogen exchange [27] of vinyl bromide and *tert*-butyllithium were similarly unsuccessful (entry 10). Considering that, in principle, the boron-ate complex prepared in this case should be identical to the one obtained when phenyllithium was added to vinylboronic ester (entry 7) we suspected that the LiBr generated during the preparation of vinyllithium[28] might have an inhibitory effect on the reaction. To understand how halide anions might be have such a deleterious effect on the reaction we considered the proposed catalytic cycle (Scheme 2.14). If the formation of a cationic palladium complex is indeed essential to allow binding of a vinylboron-ate complex to occur and to induce 1,2-metallate rearrangement, then as depicted in Scheme 2.17 the presence of coordinating halide anions in the reaction media might lead to the formation of a neutral halide-bound palladium complex **2.63** incapable of promoting the reaction. When aryl halide electrophiles are employed in the reaction, halide-bound palladium complex **2.63** is directly formed

Scheme 2.17. Hypothesis for halide inhibition of conjunctive coupling catalyzed by Pd–complexs



2.113 **2.63** **2.114**

after oxidative addition, thus the small amount of product formed with iodo- and bromobenzene suggests some degree of reversibility to palladium-halide binding. The observation that use of organometallic nucleophile containing endogenous halide anions

[27] (a) Wittig, G.; Pockels, U.; Dröge, H. *Ber. Dtsch. Chem. Ges.* **1938**, 71, 1903. (b) Gilman, H.; Langham, W.; Jacoby, A. L. *J. Am. Chem. Soc.* **1939**, 61, 106. Reviews: (c) G. Bailey, W. F.; Patricia, J. J. *J. Organomet. Chem.* **1988**, 352, 1. (d) Seyferth, D. *Organometallics* **2006**, 25, 2.

[28] (a) Corey, E. J.; Beames, D. J. *J. Am. Chem. Soc.* **1972**, 94, 7210. (b) Kluge, H. F.; Untch, K. G.; Fried, J. H. *J. Am. Chem. Soc.* **1972**, 94, 7827. (c) Neumann, H.; Seebach, D. *Tetrahedron Lett.* **1976**, 52, 4839.

completely inhibits the reaction is also consistent with this hypothesis as the harmful halide anions would be present in high concentration from the beginning of the reaction instead of being slowly generated during the course of the reaction. We investigated this hypothesis further by adding exogenous lithium halide salts to reactions employing otherwise efficient reaction conditions and found even 1 mol% halide impurity was sufficient to strongly inhibit the reaction (Table 2.2, entries 11 and 12). By increasing catalyst loading from 1 to 5 mol%, much of the product yield could be recovered (entry 13). However, because metal halide impurities are present in stoichiometric quantities from Grignard reagents and organolithium nucleophiles produced by lithium-halogen exchange, this did not provide a general solution. Thus, with the goal of enabling the conjunctive coupling to have a broad substrate scope employing readily accessible organoboronic ester starting materials we next investigated methods of preparing vinyllithium with low hlide content.

2.3.5 Preparation of Vinyllithium With Low Halide Content

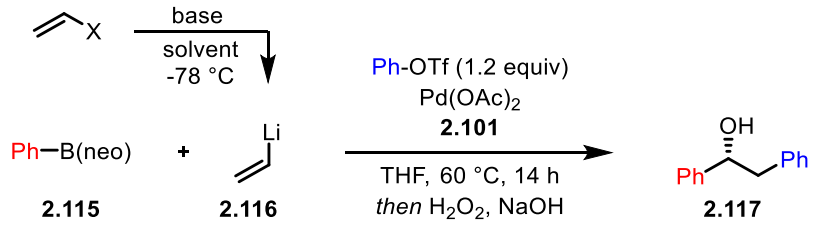
While halide-free vinyllithium can be readily prepared from the lithium-tin[29] exchange reaction between tetravinyltin and *n*-BuLi, the toxicity of organotin compounds prompted us to develop an alternative method (Table 2.3). We initially attempted to remove LiBr from vinyllithium prepared by lithium-halogen exchange (vinyl bromide plus *tert*-butyllithium) but filtration proved unsuccessful owing to the high degree of solubility of LiBr in THF solvent (entry 1). Reducing the polarity of the reaction media by employing Et_2O in place of THF, while facilitating the visible precipitation of some LiBr from the

[29] Seyferth, D.; Weiner, M. A. *J. Am. Chem. Soc.* **1961**, 83, 3583.

reaction solution, was similarly unsuccessful in producing a reagent which was effective in conjunctive coupling (entry 2). Reasoning that removal of lithium halide impurities by filtration was unlikely to be a productive strategy we next attempted to prepare vinyllithium utilizing reagents which, in principle, would not lead to the generation of lithium halide coproduct. In contrast to *t*BuLi, *n*BuLi can undergo lithium-halogen exchange but not a subsequent elimination reaction (producing LiX). Thus, in principle one equivalent of *n*BuLi can be used in place of two equivalents of *t*BuLi to generate halide-free organolithium nucleophiles.[30] When this strategy was attempted with *n*BuLi and vinyl bromide, vinyllithium was formed inefficiently (assessed by titration and/or trapping with benzaldehyde) and the resulting reaction solution was not effective in conjunctive coupling (entry 3). While vinyl iodide is known to undergo lithium-halogen exchange more readily than vinyl bromide,[31] we were initially reticent to use this reagent as the butyl iodide side product formed during the exchange reaction would also be more prone to elimination which would both destroy vinyl lithium and produce LiI. By recognizing that vinyl iodide is sufficiently reactive to undergo lithium-halogen exchange in a fully hydrocarbon solvent media and that the vinyllithium product formed is quite insoluble in this solvent, we developed a procedure which generates vinyllithium as a solid precipitate while facilitating starting material and organohalide side product removal by simple filtration. Use of vinyllithium generated in this manner resulted in substantial product formation when employed in a conjunctive coupling (entry 4). The lower yield observed for conjunctive

[30] Lau, K. S. Y.; Schlosser, M. *J. Org. Chem.* **1978**, 43, 1595.
[31] (a) Cooke, M. P. *J. Org. Chem.* **1984**, 49, 1144. (b) Reich, H. J.; Phillips, N. H.; Reich, I. L. *J. Am. Chem. Soc.* **1985**, 107, 4101.

Table 2.3. Preperation of vinyllithium with low halide content



2.115 **2.116** **2.117**

entry	X	base (equiv)	solvent mixture	Pd/L loading (%)	yield (%)	er
1	Br	*t*BuLi (2.0)	THF/ pentane	1	<5	na
2	Br	*t*BuLi (2.0)	Et_2O/ pentane	1	<5	na
3	Br	*n*BuLi (1.0)	Et_2O/ hexane	1	<5	na
4	I	*n*BuLi (1.0)	pentane/ hexane	1	40	nd
5	I	*n*BuLi (1.0)	pentane/ hexane	5	69	98:2
6_a	I	*n*BuLi (1.0)	pentane/ hexane	2	84	98:2

[a] Yeilds are of purified material. Enantiomer ratio (er) was determined by SFC analysis. [b]Vinyllithium was recrystalized.

coupling employing this vinyllithium reagent is consistent with the generation of a small amount of LiI during reagent preparation. This was confirmed by the increase in yield observed when increased catalyst loading was employed in a conjunctive coupling with this reagent (entry 5). We found that the purity of the vinyllithium produced using the procedure mentioned above could be improved by recrystallization at low temperature in ether, and that use of this reagent was highly effective in conjunctive coupling reactions employing 2 mol% catalyst loading (entry 6).

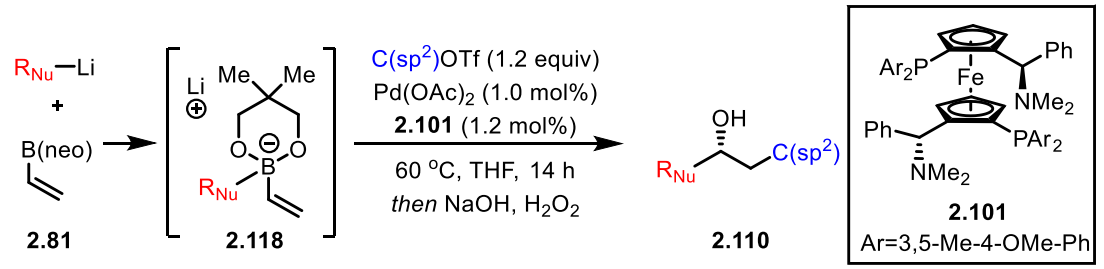
2.4 Substrate Scope and Utility of Conjunctive Coupling

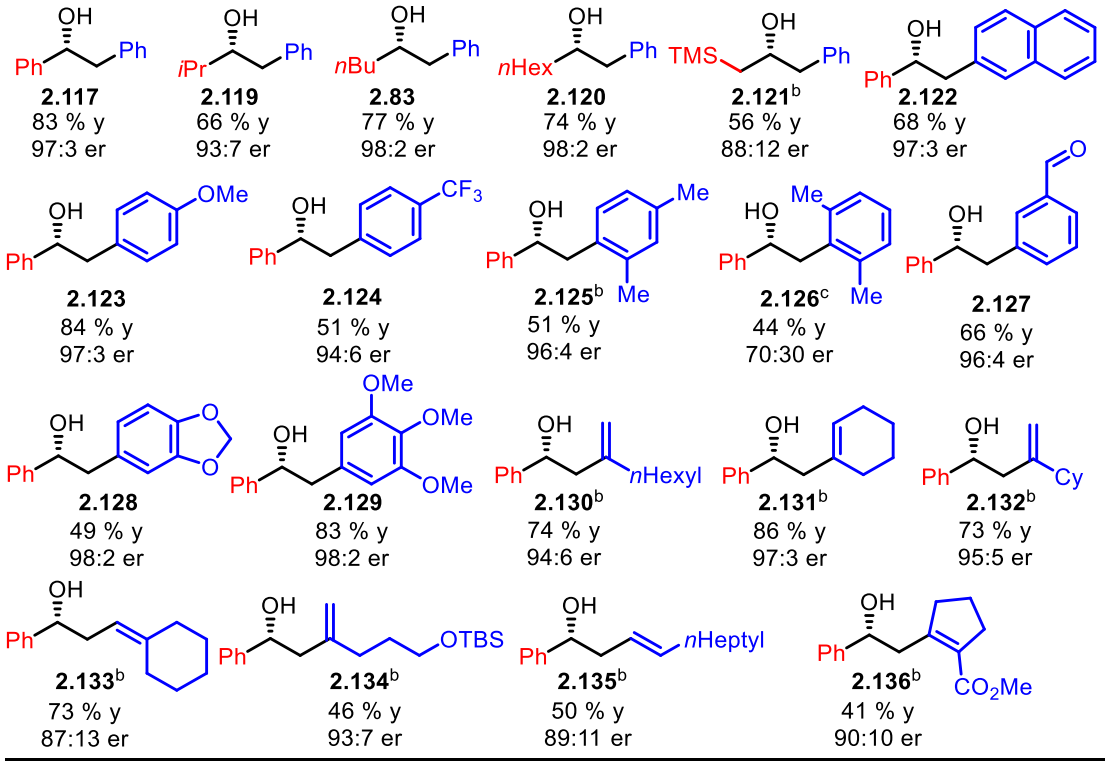
With multiple methods of generating the boron-ate species employed in conjunctive coupling in hand we next investigated the substrate scope of this reaction.

2.4.1 Scope of Conjunctive Coupling with Vinylboronic Esters

We first assessed the scope of the reaction employing commercially available organolithium reagents with various aryl and alkenyl triflate electrophiles (Scheme 2.18). Both aryl and alkyl migrating groups participated well in conjunctive coupling reactions (**2.117** through **2.12**). Use of both electron-rich and electron-poor aryl triflate reagents was similarly effective (**2.123** and **2.124**). While some degree of steric hindrance in the electrophile component was found to be well accommodated by the reaction (**2.125**), the presence of two *ortho* substituents on the aryl ring of the electrophile was found to reduce both the yield and enantioselectivity of the reaction (**2.126**). Notably, while the use of organolithium reagents is often associated with poor functional group compatibility, conjunctive couplings were found to be compatible with electrophiles with labile functional groups such as an aldehyde (**2.127**). As previously noted, the use of pinacol boronic esters in place of neopentyl boronic esters facilitated reactions employing alkenyl electrophiles (**2.130** through **2.136**), providing optimal yield and enantioselectivity for conjunctive coupling. Notably, scrambling of alkenyl electrophile *E*/*Z* geometry was not observed in these reactions, thus allowing the alkene geometry of the desired product to be determined by the choice of alkenyl electrophile substrate. Of note, the products obtained utilizing alkenyl electrophile can be readily mapped onto polyketide structures and as such

Scheme 2.18. Substrate scope: vinylboronic ester and alkyl- or aryllithium nucleophiles[a]





[a]Yeilds are of purified material and are an average of at least two experiments. Enantiomer ration (er) was determined by SFC analysis. [b]VInylB(pin) was used instead of vinylB(neo). [c]Reaction was performed at 80 °C.

conjunctive coupling represents a potentially powerful approach to access polyketide-type structures in a modular manner from simple starting materials.

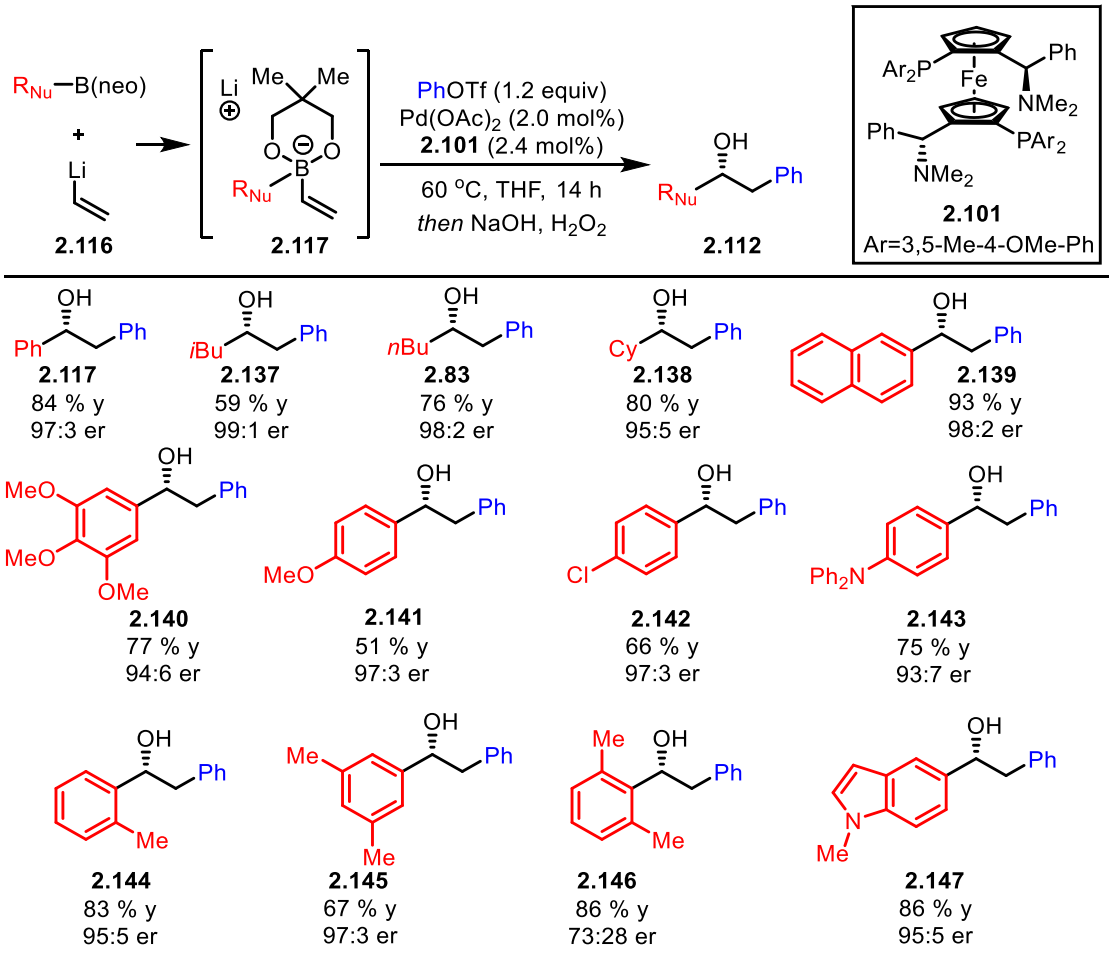
The number of commercially available organolithium nucleophiles with low halide content is quite limited and the preparation of such reagents is synthetically demanding. Therefore we were interested to know if the vinyllithium that we had prepared as detailed

above, could serve as a general synthetic reagent enabling a much wider variety of migrating groups to be employed in the reaction.

2.4.2 Scope of Conjunctive Coupling with Vinyllithium

As can be seen in Scheme 2.19, conjunctive coupling reactions employing vinyllithium with low halide content were equally effective as those employing commercially available organolithium reagents (**2.117** and **2.83** in Scheme 2.18/2.19). Secondary alkyl migrating

Scheme 2.19. Substrate scope: vinyllithium and alkyl- or arylboronic ester reagents[a]



[a]Yeilds are of purified material and are an average of at least two experiments. Enntiomer ratio (er) was determined by SFC analysis.

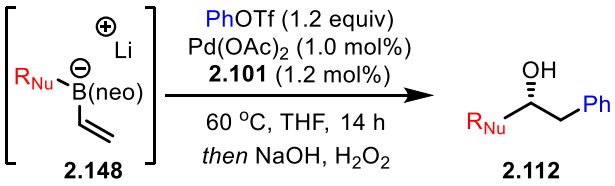
groups as well as various functionalized aryl groups worked well in the reaction (**2.138** through **2.147**). As demonstrated by the high yields obtained when mono- or disubstituted aryl migrating groups (**2.144** and **2.145** respectively) are employed, the reaction is relatively insensitive to sterically hindered migrating groups, though enantioselectivity was diminished when the very sterically hindered 2,6-methylphenyl migrating group (**2.146**) was employed in the reaction. An *N*-methyl indole migrating group participated smoothly in the reaction (**2.147**), suggesting that more complex heterocycle-containing structures might be readily accessible using conjunctive coupling.

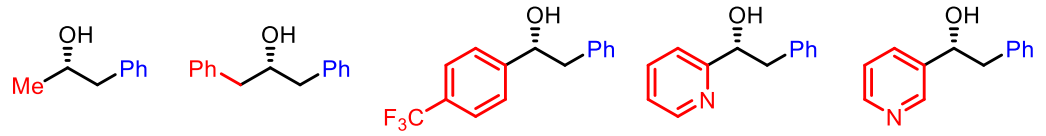
2.4.3 Initial Synthetic Limitation of Conjunctive Coupling

The diversity of products accessible using conjunctive coupling is quite broad, encompassing structures incorporating aromatic groups of diverse electronic and steric profile (as either nucleophile or electrophile) and possessing either aryl- or alkyl-substituted stereogenic carbon centers. Yet, this initial conjunctive coupling method was found to have some synthetic limitations that are worthy of note and which will hopefully inspire the development of future improvements to this class of reaction (Scheme 2.20). In contrast to the majority of primary and secondary alkyl migrating groups, methyl (**2.149**) and benzyl (**2.150**) groups did not participate well in the reaction. While the origin of poor yield in these cases was not fully evaluated, some observations are worthy of note. First, methyl is generally considered a poor migrating group in related 1,2-metallate rearrangement reactions.[32] Additionally, the small steric profile of this migrating group

[32] Bottoni, A.; Lombardo, M.; Neri, A. Trombini, C. *J. Org. Chem.* **2003**, 68, 3397.

Scheme 2.20. Challenging reactions[a]





2.149	**2.150**[b]	**2.151**	**2.152**[b]	**2.153**[b]
32 % y	20 % y	20 % y	<5 % y	<5 % y
er nd	er nd	er nd	er nd	er nd

[a]Yields are of purified material. [b]Yields are based on ^{1}H NMR analysis against an internal standard.

may make it more challenging for the associated vinylboron-ate-catalyst complex to achieve the *anti*-periplanar orbital alignment required for the metal-induced metallate rearrangement to occur (illustrated in brief in Scheme 2.15 and discussed in more depth in section 2.6.2.1 through 2.6.2.3). The benzyl migrating group may suffer from an increased propensity to undergo deleterious transmetallation or protodeborylation processes. Electron-deficient aromatic (**2.151**) and heteroaromatic groups (**2.152** and **2.153**) also proved to be challenging substrates to engage in the reaction.

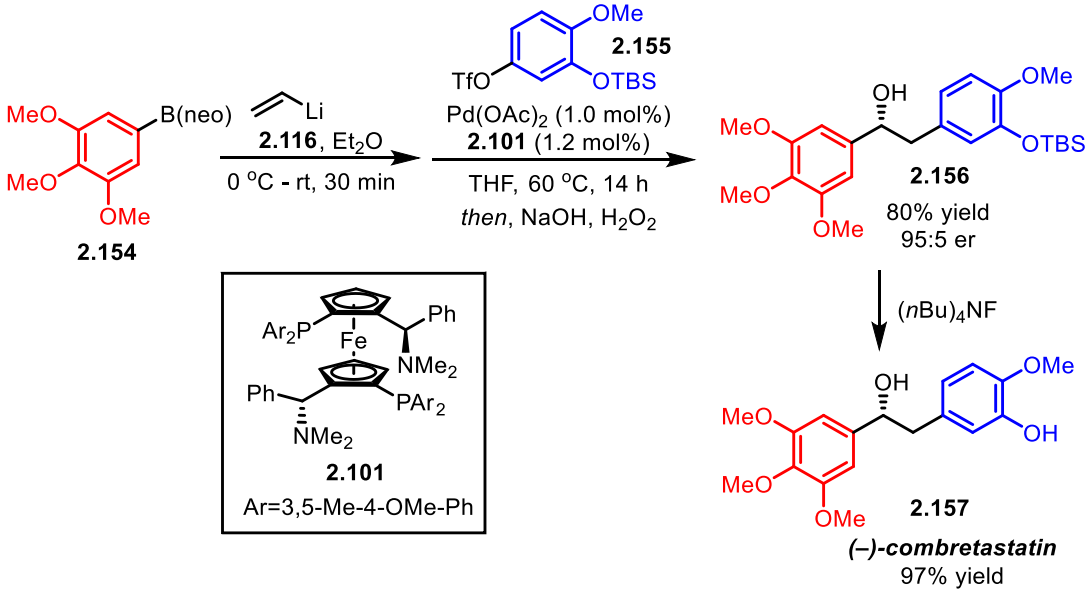
2.4.4 Utility of Conjunctive Coupling for Natural Product Synthesis

In an effort to demonstrate the potential synthesis utility of conjunctive coupling we prepared (—)-combretastatin[33] (**2.157**), a member of a family of cytotoxic stilbene-derived natural products known to bind β-tubulin (Scheme 2.21). The desired natural product could

[33] Pettit, G. R.; Cragg, G. M.; Herald, D. L.; Schmidt, J. M.; Lohavanijaya, P. *Can. J. Chem.* **1982**, 60, 1374.

be prepared in good yield and enantioselectivity in two steps from readily prepared aryl boronic ester **2.154** and aryl triflate **2.155**. While a variety of synthesis approaches have been reported for the preparation of members of the combretastatin family,[34] conjunctive coupling offers the distinct advantage that it engages different starting materials in a convergent and modular manner. In comparison to the two step conjunctive coupling/oxidation and deprotection sequence detailed below (78% yield overall yield) a representative previous synthesis of Combretastatin employed 6 linear steps starting from trimethoxy benzaldehyde (65% yield). [35] Conceivably, the convergent nature of conjunctive coupling might allow the reaction to serve as an ideal strategy for the construction of libraries of small molecule analogues of pharmaceuticals. This could be particularly enabling as it offers the same modular logic to molecular construction as cross-

Scheme 2.21. Synthesis of (–)-combretastatin using conjunctive coupling[a]



[a] Yeilds are of purified material. Enantiomer ratio (er) was determined by SFC analysis.

[34] Singh, R.; Kaur, H.; *Synthesis*, **2009**, 2009, 2471.
[35] Ramacciotti, A.; Fiaschi, R.; Napolitano, E. *Tetrahedron: Asymmetry*, **1996**, 7, 1101.

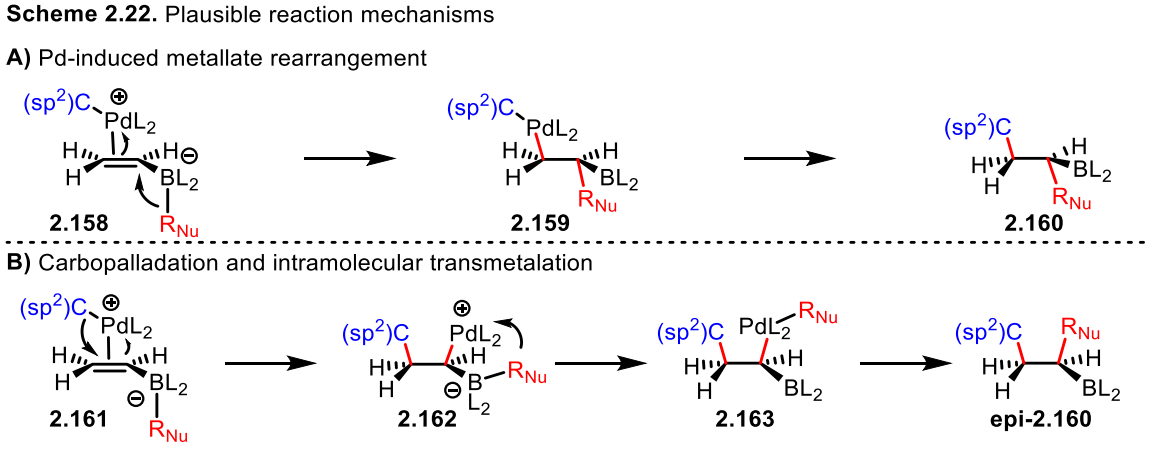
coupling but with the possibility of accessing more complex enantioenriched structures.

2.5 Mechanistic Studies

2.5.1 Potential Mechanisms

While we hypothesized that the conjunctive coupling reaction most likely proceeds by a 1,2-rearrangement pathway (Scheme 2.22.A), we recognized that alternative mechanistic scenarios were possible. One such possibility is that the reaction may involve an initial carbopalladation of the vinylboron-ate complex (**2.161** to **2.162**), followed by intramolecular transmetallation (**2.162** to **2.163**), and then stereoretentive reductive elimination (**2.163** to **epi-2.160**) (Scheme 2.22.B). In contrast to the 1,2-metallate rearrangement pathway (**2.158** to **2.160**) which involves a net *anti*-addition of the migrating group and electrophile across the double bond, the second pathway would result in the overall *syn*-addition of the migrating group and electrophile across the double bond (**2.160** versus **epi-2.160**). Due to the diastereomeric relationship between these two structures, a deuterium labeling experiment was conducted to distinguish between these two mechanistic possibilities.

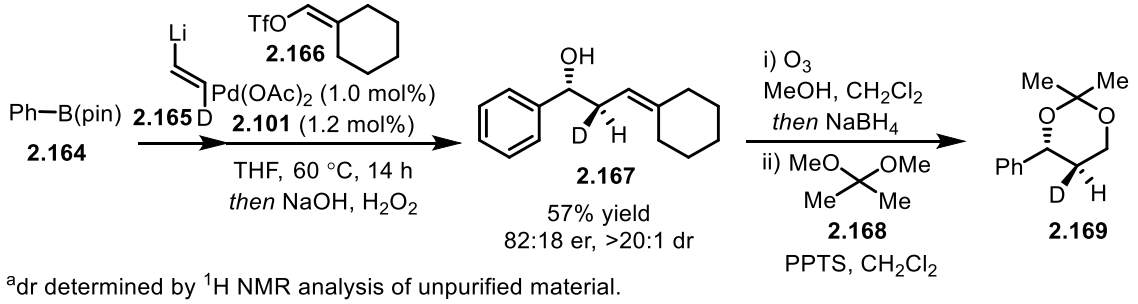
Scheme 2.22. Plausible reaction mechanisms



2.5.2 Deuterium-Labeling Experiment and Computational Modeling

To distinguish between the two mechanistic scenarios described above, the deuterium-labeling experiment depicted in Scheme 2.23 was conducted. When t*rans*-deuterium labeled vinyllithium **2.165** was employed in a conjunctive coupling of alkenyl triflate **2.166** and phenylboronic pinacol ester **2.164**, only one product diastereomer was observed by analysis using ^{1}H NMR. The relative stereochemical outcome of the reaction was confirmed through ^{1}H NMR analysis of the coupling constants of the product **2.169** obtained after ozonolysis, reduction, and acetonide protection. This result is consistent with

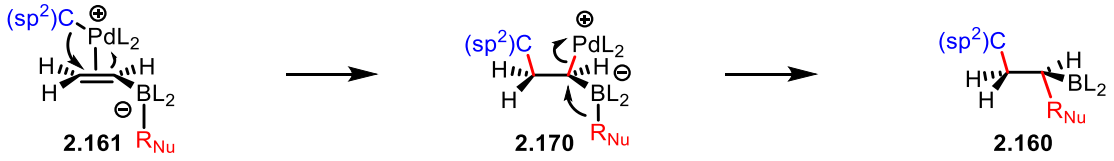
Scheme 2.23. Deuterium labeling experiment to probe the diastereoselectivity of the reaction[a]



[a]dr determined by ^{1}H NMR analysis of unpurified material.

the stereochemical outcome expected for the 1,2-metallate rearrangement mechanism and is inconsistent with the carbopalladation mechanism (Scheme 2.22.B). A third mechanistic possibility that could not be ruled out based on the deuterium labeling experiment is depicted in Scheme 2.24. In this mechanistic scenario, carbopalladation of the vinylboron-ate complex produces an α-boryl alkylpalladium species **2.170** in the same fashion as the previous carbopalladation mechanism, but this step is then followed by a reductive displacement (elimination) of palladium to furnish product **2.161** with the same relative stereochemistry as would be formed by the 1,2-metallate pathway.

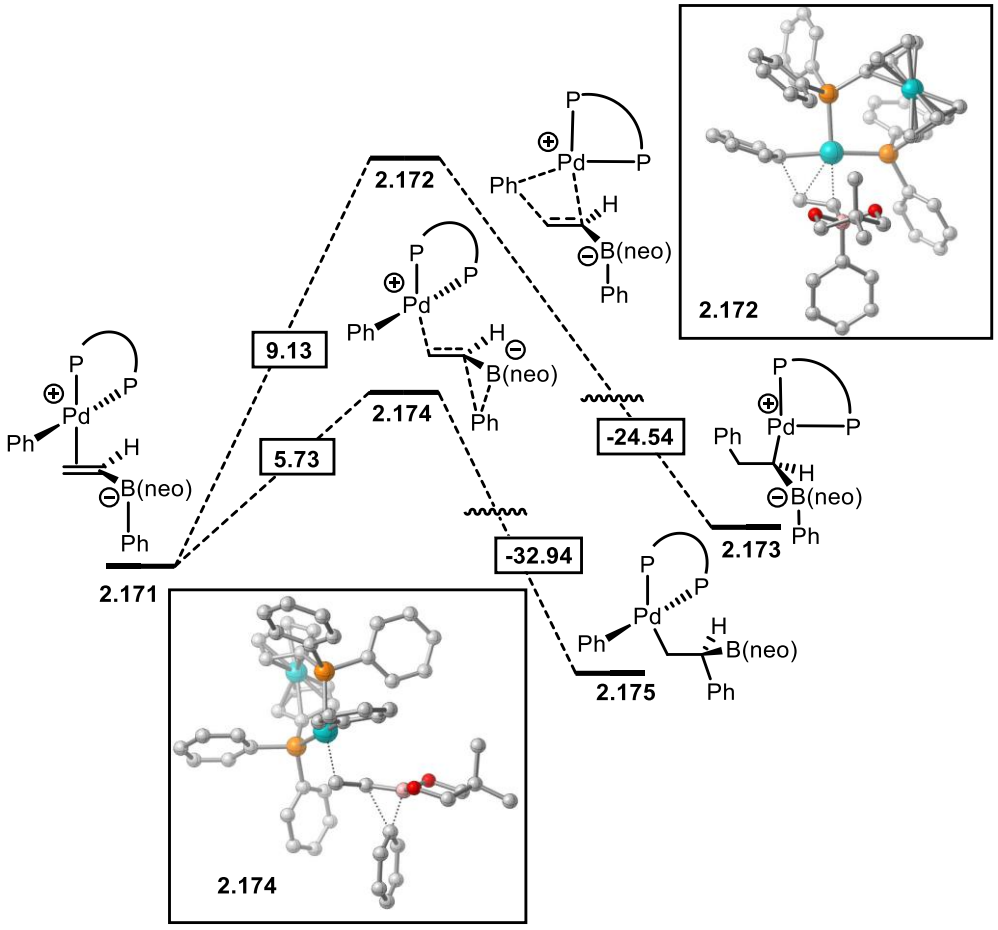
Scheme 2.24. Alternative carbopalladation pathway involving an invertive reductive elimination



While this third mechanistic possibility was not excluded in the isotope labeling study detailed above, we subsequently performed computational calculations to shed light on whether the palladium-induced metallate rearrangement or carbopalladation mechanism are more energetically feasible. Employing the BP86/def2-SVP functional and basis set for geometry optimization and M06/def2-TZVPP to perform single point energy calculations, the energetic reaction profile for metal-induced metallate rearrangement and carbopalladation steps were compared (Scheme 2.25). Starting from boron-ate complex **2.171** in a conformation that positions the migrating group and palladium in anti-orientation, the palladium-induced metallate rearrangement reaction was found to proceed by a transition state **2.174** with a low energetic barrier of 5.73 kcal/mol. This transition state involves a shifting of palladium to the less sterically hindered terminal vinyl carbon (η^2 to an η^1 bonding mode) while the vinyl group and ligand sets on palladium remain in an orthogonal orientation. In contrast, because of the orbital requirements involved in carbopalladation, transition state **2.174** involves a much larger 9.13 kcal/mol barrier in which the palladium shifts to the more sterically crowded internal vinyl carbon (η^2 to an η^1) with a largely coplanar orientation, further exacerbating steric clashes between the ligand set on palladium and on boron. Assuming that reductive elimination from **2.175** relative to **2.173** is not a prohibitively high-energy process, because both of the alternative mechanisms to the metal-induced metallate rearrangement initially proceed by

carbopalladation transition state **2.172**, demonstrating that the carbopalladation step is energetically unfavorable compared to palladium-induced metallate rearrangement is sufficient to rule out both alternative mechanisms.

Scheme 2.25. DFT calculations to probe palladium-induced rearrangement and carbopalladation pathways[a]



[a]Phosphine ligand is dppf. Optimized geometries calculated with DFT (BP86/Def2-SVP;PCM solvent model with THF). ΔG values are in kcal/mol, calculated with DFT (M06/def2-TZVPP//BP86/def2-SVP; PCM solvent model with THF). Hydrogen atoms removed from structures for clarity.

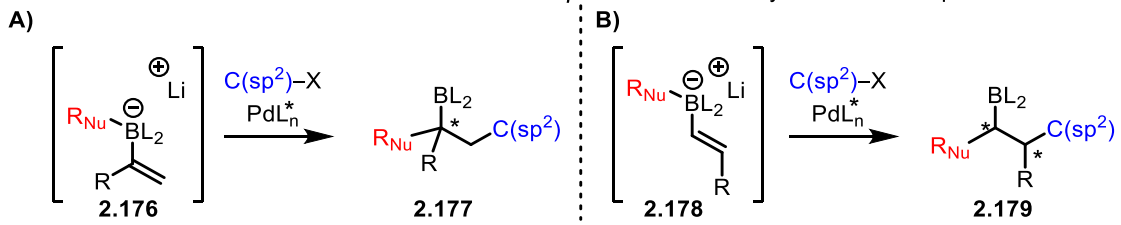
2.6 Application of Substituted Alkenylboron Reagents to Conjunctive Coupling

Considering the large degree of structural complexity that the conjunctive coupling reaction can construct in a single step, we wondered if the use of boron-ate complexes with

alkene substitution could enable the construction of more challenging product structures such as those containing fully-substituted stereocenters (Scheme 2.26.A) or even multiple stereocenters (Scheme 2.26.B).

Considering mechanistically related alkene nucleopalladation reactions[36] for which increasing alkene substitution strongly decreases reactivity, we were not sure if more substituted alkenylboron-ate complexes could be efficiently engaged in conjunctive

Scheme 2.26. Substituted boronic esters from α- or β-substituted alkenylboron-ate complexes

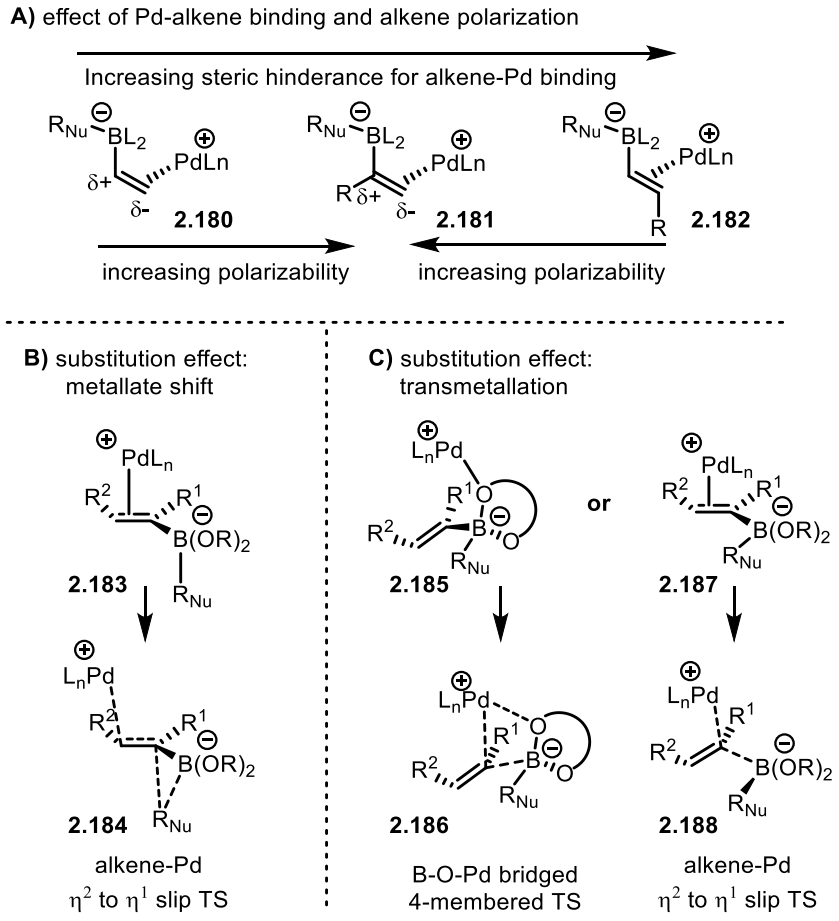


couplings. Marshalling the mechanistic understanding established in preliminary studies, we considered how alkene substitution might affect the reaction (Scheme 2.27). We first considered how alkene-substitution might affect the relative position of binding of a palladium complex as well as how the intrinsic as well as induced alkene polarization[37] might be altered (Scheme 2.27.A). α-Alkene substitution would be expected to penalize alkene binding to palladium thus destabilizing the ground state palladium-olefin complex **2.181**, while at the same time shifting the position of palladium-binding towards the terminal position so as to minimize steric repulsion. This shift of palladium to the terminal position would be expected to lead to a greater degree of alkene polarization which is in concert with the natural polarization pattern and which is further reinforced by the α-

[36] Hegedus, L. S.; Williams, R. E.; McGuire, M. A.; Hayashi, T. *J. Am. Chem. Soc.* **1980**, 102, 4973.
[37] Stone, A. J. *Inorg. Chem.* **1981**, 20, 563.

substituent which can stabilize positive charge buildup at the α-carbon. Conversely, the β-alkene substitution pattern would be expected to more severely impair alkene binding while also decreasing the natural pattern of alkene polarization (**2.182**). In terms of the palladium-induced 1,2-metallate rearrangement transition state (Scheme 2.28.B), it appears clear that for β-substituted alkenylboron-ate complexes the shift of palladium to the terminal alkene carbon will involve additional strain relative to the corresponding ground state, and therbye lead to a higher reaction barrier relative to the corresponding reaction employing an unsubstituted alkenylboron-ate complex. For an α-substituted alkenylboron-ate complex, the shifting of palladium to the terminal position involves relief of steric interactions

Scheme 2.27. Effects of alkene substitution



between the α-substituent and the palladium–complex. Considering the effect of alkene substitution on possible competing transmetallation pathways (Scheme 2.28.C) it is possible to see that both substitution patterns will impair alkene binding and thus may help to favor a mechanism involving pinacol oxygen coordination to a palladium complex (**2.185** versus **2.187**). In either transmetallation mechanism, the α-substitution pattern would be expected to impair transmetallation due to increasing steric repulsion as the palladium-complex moves to that position, while the β-substitution pattern would not be expected to substantially penalize the rate of the reaction.

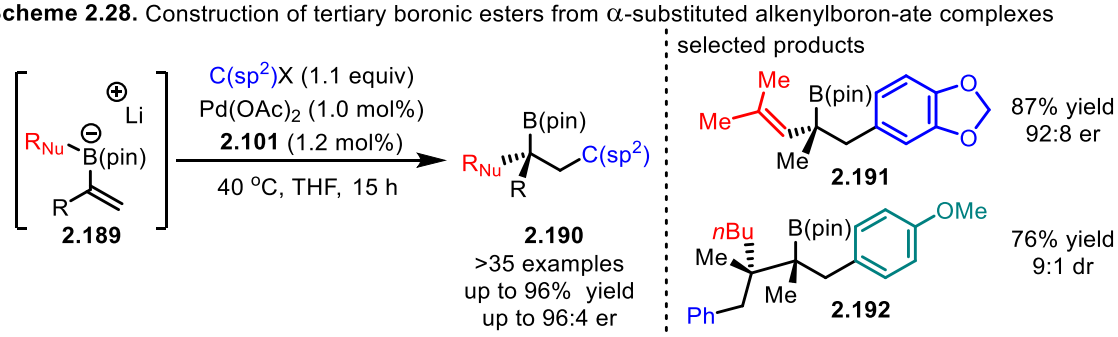
While the experimental details of the development of a conjunctive coupling reaction employing α-substituted alkenylboron reagents and producing products with valuable fully-substituted stereocenters is beyond the scope of this dissertation, a brief description of the reaction system as well as calculated reaction barriers for the metallate rearrangement reactions of vinyl- versus isopropenylboron-ate complexes is warranted.

2.6.1 α-Substituted Alkenylboron Reagents: Computational Aspects[38]

With the mechanistic features mentioned above in mind, the reaction of α-substituted alkenylboron-ate complexes was successfully developed by Liang Zhang and Jesse Myhill. This reaction grants modular access to diverse structures containing fully-substituted stereogenic carbon centers and a large array of useful functional groups (Scheme 2.28). Notably, because the product of a conjunctive coupling is a boronic ester and thus can serve as the starting material for a second conjunctive coupling, in principle, it should be possible

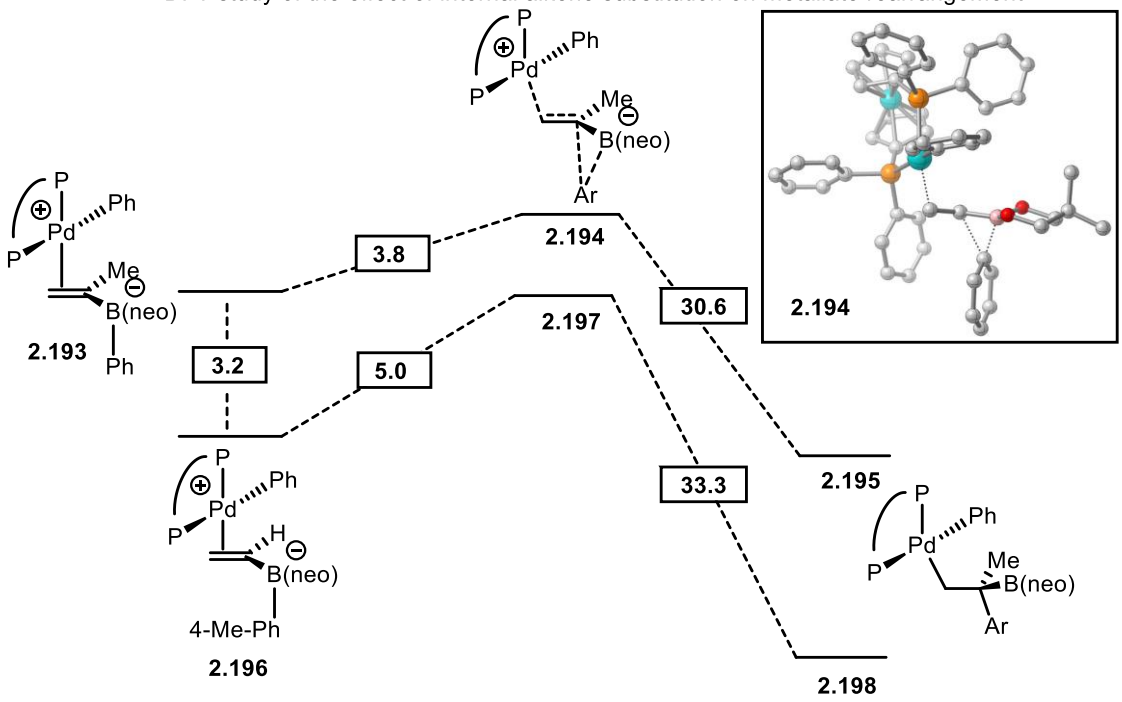
[38] Myhill, J. A.; Zhang, L.; Lovinger, G. J.; Morken, J. P. *Angew. Chem. Int. Ed*. **2018**, 57, 12799.

Scheme 2.28. Construction of tertiary boronic esters from α-substituted alkenylboron-ate complexes



to perform iterative couplings in which the molecular building blocks as well as absolute stereochemistry at each newly formed stereogenic carbon center can be controlled. This report provided the first example of the iterative application of conjunctive couplings in the context of the construction of two contiguous fully-substituted stereocenters (**2.192**). Utilizing reaction progress kinetic analysis, Jesse Myhill determined that oxidative addition is the turnover-limiting step in the conjunctive coupling catalytic cycle, a result which is consistent with the low kinetic barrier calculated for the palladium-induced metallate rearrangement reaction of both vinyl- and isopropenylboron-ate complexes (Scheme 2.29). These calculations confirm that, while α-substitution on the alkene of the boron-ate complex leads to ground state destabilization (**2.196** versus **2.193**) this does not disproportionately destabilize the corresponding transition state**.** The fact that α-substituted alkenylboron-ate complexes participate smoothly in conjunctive couplings without increased amounts of Suzuki-Miyaura product observed relative to the use of vinylboron-ate complexes suggests that, as discussed above, α-alkene substitution likely penalizes transmetallation to an equal or larger degree as metallate rearrangement.

Scheme 2.29. DFT study of the effect of internal alkene substitution on metallate rearrangement[a]



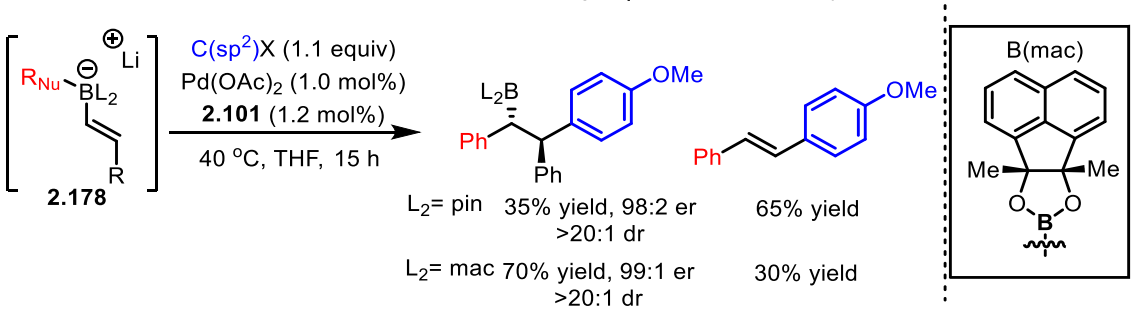
[a]Ligand on Pd is dppf. Optimized geometries calculated using DFT (BP86/Def2-SVP;PCM solvent model with THF). ΔG values are in kcal/mol, calculated using DFT (M06/def2-TZVPP//BP86/def2-SVP;SMD solvent model with THF). Hydrogen atoms removed from structures for clarity.

2.6.2 Alkene Substitution Effects on Metallate Rearrangement Versus Transmetallation

Suzuki-Miyaura cross-coupling is the main competing reaction to conjunctive coupling in most cases, this stems from a competition between the transmetallation and metal-induced metallate rearrangement reactions. While for vinyl- and α-substituted alkenylboron-ate complexes, this competition can be made to favor the metallate rearrangement pathway by judicious choice of conditions and catalytic diphosphine ligand, my colleagues found that for β-substituted alkenylboron-ate complexes, the Suzuki-

Miyaura reaction predominated in most cases (Scheme 2.30).[39] While my colleagues were able to discover that employing the methylated acenaphthoquinone (mac) diol ligand (inset) on boron rather than pinacol ligand substantially improved yields of conjunctive coupling product, this synthetically useful solution lacked an experimentally validated or computationally supported mechanistic foundation that might lead to further methodological improvements. Seeing the pronounced preference of β-substituted

Scheme 2.30. Enantio- and diastereoselective coupling of β-substituted alkenylboron-ate complexes



alkenylboron-ate complexes to undergo transmetallation as an opportunity to investigate the fundamental mechanistic details of this reaction we conducted the following computational studies.

2.6.2.1 Alkene- Versus Oxygen-Bound Palladium Complexes: Conformation and Ligand Effects

Despite the enormous importance of transmetallation as one of a small collection of organometallic elementary reactions, many aspects of this process remain poorly understood. Perhaps owing to the importance of the Suzuki-Miyaura cross-coupling

[39] Myhill, J. A.; Wilhelmsen, C. A.; Zhang, L.; Morken, J. P. *J. Am. Chem. Soc*. **2018**, 140, 15181.

reaction, transmetallation from boron to palladium has been the focus of numerous mechanistic studies; however these studies have largely been concerned with determining the role of oxygen-based activating agents such as hydroxide anions in promoting these reactions.[40] While the specific details vary based on the system investigated, it is generally agreed upon that under typical Suzuki-Miyaura coupling conditions of aryl organoboronates, transmetallation proceeds through a B–O–Pd linked species which is formed by addition of a Pd–OH (palladium hydroxo) species to a three-coordinate organoboron species.[41] Remarkably, experimental data enabling a detailed mechanistic picture of pre-transmetallation species as well as the nature of transmetallation transition states has only come to light in the last few years.[42] While the complexity of these studies would require detailed explanation, a few key points can be extracted which are helpful in considering the mechanistic possibilities discussed below. (1) Sterically hindered or chelating phosphine ligands on palladium preclude the formation of a B–O–Pd pre-transmetallation complex, thus necessitating ligand dissociation, (2) transmetallation of B–O–Pd pre-transmetallation complexes requires a coordinatively unsaturated palladium species such that the use of a chelating diphosphine ligands such as DPPF slows the rate of transmetallation four-fold relative to Ph_3P,[40b] the chelating diphosphine having to dissociate before transmetallation can occur. The need to generate a coordinatively

[40] (a) Matos, K.; Soderquist, J. A. *J. Org. Chem.* **1998**, 63, 461. (b) Carrow, B. P.; Hartwig, J. F. *J. Am. Chem. Soc.* **2011**, 133, 2116. (c) Amatore, C.; Jutand, A.; Le Duc, G. *Chem. Eur. J.* **2013**, 19, 10082. (d) Schmidt, A. F.; Kurokhtina, A. A. *Kinet. Catal.* **2012**, 53, 714.
[41] For an review, see: Lennox, A. J. J.; Lloyd-Jones, G. C. *Angew. Chem. Int. Ed.* **2013**, 52, 7362.
[42] (a) Thomas, A. A.; Denmark, S. E. *Science* **2016**, 352, 329. (b) Thomas, A. A.; Wang, H.; Zahrt, A. F.; Denmark, S. E. *J. Am. Chem. Soc.* **2017**, 139, 3805. (c) Thomas, A. A.; Zahrt, A. F.; Delaney, C. P.; Denmark, S. E. *J. Am. Chem. Soc.* **2018**, 140, 4401.

unsaturated palladium species has been previously proposed in related studies involving the transmetallation of arylsilanolates.[43]

Despite this wealth of recently gained mechanistic knowledge about the transmetallation of aryl boronic esters utilizing oxygen activating agents, the nature of transmetallation in the conjunctive coupling cannot be immediately explained using this data. First, conjunctive coupling employs a pre-formed boron-ate complex which is activated by a carbon rather than oxygen-based nucleophile, precluding the formation of a B–O-Pd species. Secondly, anhydrous conditions are employed in the reaction, precluding formation of a Pd-OH species. An additional complicating factor is that for conjunctive coupling reactions transmetallation often involves transfer of an alkenyl rather than aryl group. The experimental studies mentioned above have focused on the transfer of aryl groups but alkenyl groups may have alternative modes of transmetallation available to them involving a stabilizing η^2 interaction with palladium which is not sterically favorable for aryl groups.[44]

In considering this information, we imagined several mechanistic scenarios for transmetallation under conjunctive coupling reaction conditions that we loosely organized into those involving some form of B–O-Pd linker (Scheme 2.31.A) and those that involve

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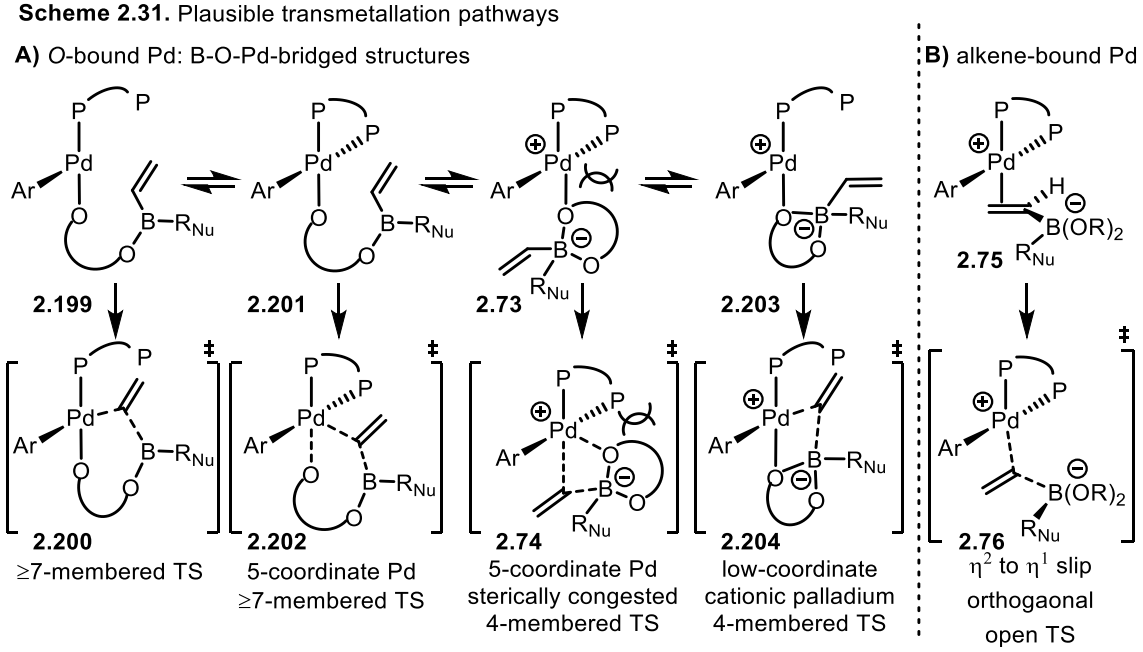
[43] Tymonko, S. A.; Smith, R. C.; Ambrosi, A.; Ober, M. H.; Wang, H.; Denmark, S. E. *J. Am. Chem. Soc.* **2015**, 137, 6200.

[44] For theoretical studies on B-to-Pd transmetallation of a vinyl group, see: (a) Braga, A. A. C.; Morgon, N. H.; Ujaque, G.; Maseras, F. *J. Am. Chem. Soc.* **2005**, 9298. (b) Braga, A. A. C.; Morgon, N. H.; Ujaque, G.; Lledós, A.; Maseras, F. *J. Organomet. Chem.* **2006**, 691, 4459. For a related studies involving vinylstannanes, see: (c) Álvarez, R.; Faza, O. N.; de Lera, A. R.; Cárdenas, D. J. *Adv. Synth. Catal.* **2007**, 349, 887. (d) Casado, A. L.; Espinet, P.; Gallego, A. M.; Marinez-Iladuya, J. M. *Chem. Comm.* **2001**, 339. For a review on the mechanisms of the still reaction see: (e) Espinet, P.; Echavarren, A. M. *Angew. Chem. Int. Ed.* **2004**, 43, 4704. (see page 4721 for relevant discussion of open associative transmetallation)

an alkene-Pd interaction (Scheme 2.31.B). In terms of initially assessing the likelihood of these different pathways: pinacol-bound palladium complex **2.73** would be expected to suffer from substantial steric penalties between the ligand set on boron and the ligand set on palladium. Additionally the donating oxygen in this case is an L-type ligand rather than an X-type ligand, and as such is more aligned with coordination from an ether rather than from the hydroxyl group normally invoked in Suzuki-Miyaura cross-coupling reactions. The strained 4-membered penta-coordinate palladium metallocyclic transition state **2.74** that arises from this ground state complex would be expected to be energetically demanding. Some degree of steric penalty might be relieved in ground state complex **2.73** if a pinacol oxygen on boron were to dissociate to form **2.201**, though the corresponding transition state **2.202** would still possess an unfavorable penta-coordinate configuration and would involve additional entropic penalties due to its medium ring size. Phosphine ligand dissociation from **2.201** might conceivably open up a coordination site on palladium

Scheme 2.31. Plausible transmetallation pathways



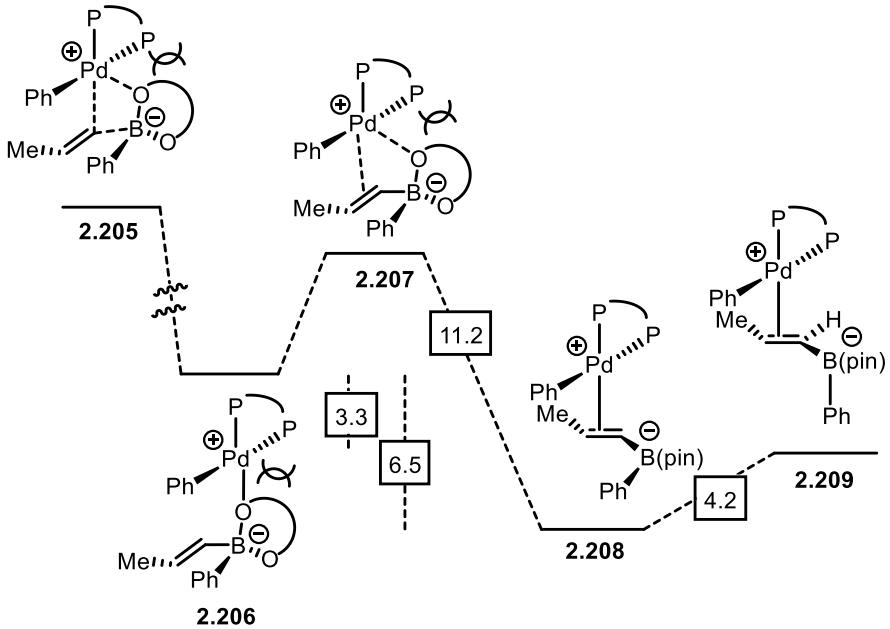
and facilitate transmetallation, though transition state **2.200** would still involve an entropically unfavorable medium ring sized. Finally, dissociation of a phosphine ligand from palladium species **2.73** might facilitate binding to a pinacol oxygen in the ground state, while simultaneously facilitating the subsequent transmetallation transition state **2.204**. One note against this potential mechanism is that dissociation of a chelating diphosphine from an already electron-deficient cationic palladium complex is likely energetically unfavorable.

In contrast to the previously discussed pathways that possess some combination of penalizing steric interaction, high-energy penta-coordinate palladium, unfavorable entropic requirements, or involve the generation of destabilized low-coordinate cationic palladium species, a plausible alternative pathway not involving a Pd-O interaction is depicted in Scheme 2.31.B. Ground state complex **2.75** possesses a geometrically flexible η^2 coordination mode between palladium and the vinylboron-ate complex that allows a minimization of steric interactions. Additionally, the acyclic transition state **2.76** proceeding from this ground state involves minimal geometric reorganization.

Theoretical studies on the transmetallation of vinylboronic esters and vinylstannanes predict that these organometallic reagents likely proceed by this latter mode of transmetallation (open associative transmetallation) under normal Suzuki-Miyaura[42a,42b] and Stille[42c-42e] cross-coupling conditions respectively. Additionally, the experimental observation that the catalyst resting state in conjunctive coupling reactions is a Pd^0-vinylboron-ate complex[36] is also strongly indicates that an alkene-Pd rather than an O-Pd coordination mode is energetically preferred.

To probe if our preliminary qualitative analysis is supported by theoretical calculations we first investigated the energetic profile for the interconversion between alkene-Pd (**2.209**) and O-Pd (**2.206**) complexes for *trans*-propenylboronic pinacol ester (Scheme 2.32). Starting from complex **2.209** possessing the *anti*-periplanar orientation of migrating group relative to palladium (required for the metallate rearrangement pathway), we observed that rotation of the boron-ate alkene substituent to form **2.208** leads to a 4.2 kcal/mol stabilization. This is attributed to the relatively narrow pinacol ligand structure in which methyl groups project along the axis formed by the boron and migrating group but do not extend as far along the lateral axis. Thus rotation relieves steric interactions between the forward projecting pinacol methyl groups and the ligand set on palladium. This reorganization is both stabilizing and orients the pinacol oxygen such that complex

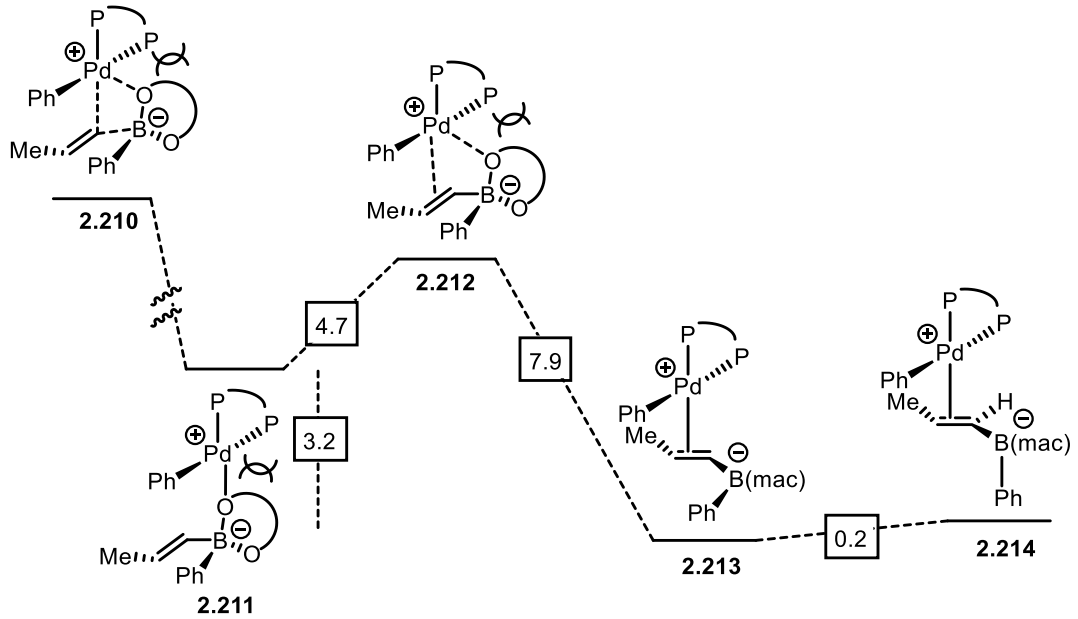
Scheme 2.32. Energy profile of alkene- or oxygen-bound palladium for pinacol ligand



[a]Phosphine ligand is dppf. Optimized geometries calculated with DFT (BP86/Def2-SVP;PCM solvent model with THF). ΔG values are in kcal/mol, calculated using DFT (M06/def2-TZVPP//BP86/def2-SVP ;PCM solvent model with THF). Hydrogen atoms removed from structures for clarity.

2.208 can proceed through a 4-membered transition state **2.207** involving a penta-coordinate palladium center, to *O*-bound palladium complex **2.206**. Preliminary attempts to find a transmetallation transition state structure proceeding from **2.206** were unsuccessful. While **2.206** has previously been proposed as a potential ground state leading to transmetallation in conjunctive couplings,[36] this ground state structure is 6.5 kcal/mol less stable than alkene bound structure **2.208** and accessing this ground state does not appear to be an energetically favorable process, involving a 11.2 kcal/mol barrier. Investigating the corresponding energy profile for alkenylboron-ate complexes possessing the mac ligand, we saw similar overall behavior, though the *O*-bound Pd-complex **2.211** is somewhat less destabilized by 3.2 kcal/mol relative to alkene-bound Pd-complex **2.213**. This smaller energetic difference appears to be entirely due to the ability of the relatively

Scheme 2.33. Energy profile of Alkene- or oxygen-bound palladium for mac ligand



[a]Phosphine ligand is dppf. Optimized geometries calculated with DFT (BP86/Def2-SVP;PCM solvent model with THF). ΔG values are in kcal/mol, calculated using DFT (M06/def2-TZVPP//BP86/def2-SVP ;PCM solvent model with THF). Hydrogen atoms removed from structures for clarity.

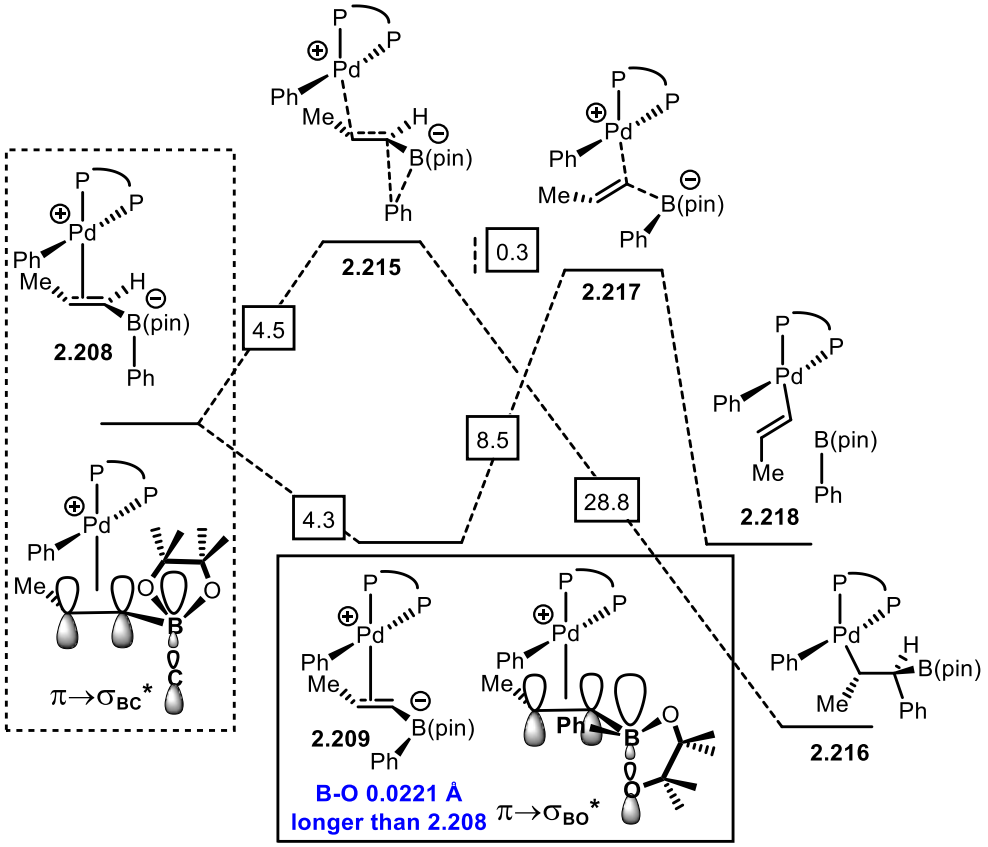
wide mac ligand to destabilizing the twisted conformation of **2.213**. Given that the implementation of the mac ligand in place of the pinacol ligand has been shown to lead to an increase in formation of metallate rearrangement relative to transmetallation product this result is somewhat surprisingly; the mac ligand does not appear to substantially destabilize the *O*-bound palladium complex which has been proposed to lead to transmetallation. Counterintuitively this ground state is if anything more readily accessible due to the destabilization of the twisted grounds state structure **2.213**. This result suggested to us that perhaps transmetallation occurs by an alternative pathway that is destabilized by the inability of an alkenyl–Bmac reagent to achieve a twisted conformation.

2.6.2.2 Alkene- Versus Oxygen-Bound Palladium Complexes: Implications for Transmetallation

Considering the large influence the mac ligand appears to have on the relative energies of alkene-bound palladium complexes we next looked at transmetallation pathways proceeding from these species. As discussed in the previous section, transmetallation may occur from an alkene-bound palladium complex by a transition state involving slippage of the palladium center from an η^2 to an η^1 coordination mode. A search of possible transition states located a single lowest energy structure possessing a twisted boron-ate to alkene orientation. As can be seen in Scheme 2.34, for *trans*-propenylboronic pinacol esters the palladium-induced metallate rearrangement transition state **2.215** is slightly higher in energy than transmetallation transition state **2.217**. This result is consistent with the experimentally observed conjunctive to Suzuki-Miyaura product distribution for

alkenylboronic pinacol esters in which transmetallation is preferred. In considering why the transmetallaition transition state **2.217** is lower in energy than the metallate rearrangement transition state **2.215** it is important to remember that these are early transition states involving a relatively small degree of geometric reorganization. As such, the energetic stabilization arising from rotation of the boron-ate alkene substituent (**2.208** to **2.209**) appears to contribute to stabilization of the transition state proceeding from this stabilized ground state. Due to orbital alignment requirements the metallate rearrangement transition state **2.215** cannot adopt a more stable boron-ate rotational orientation. In

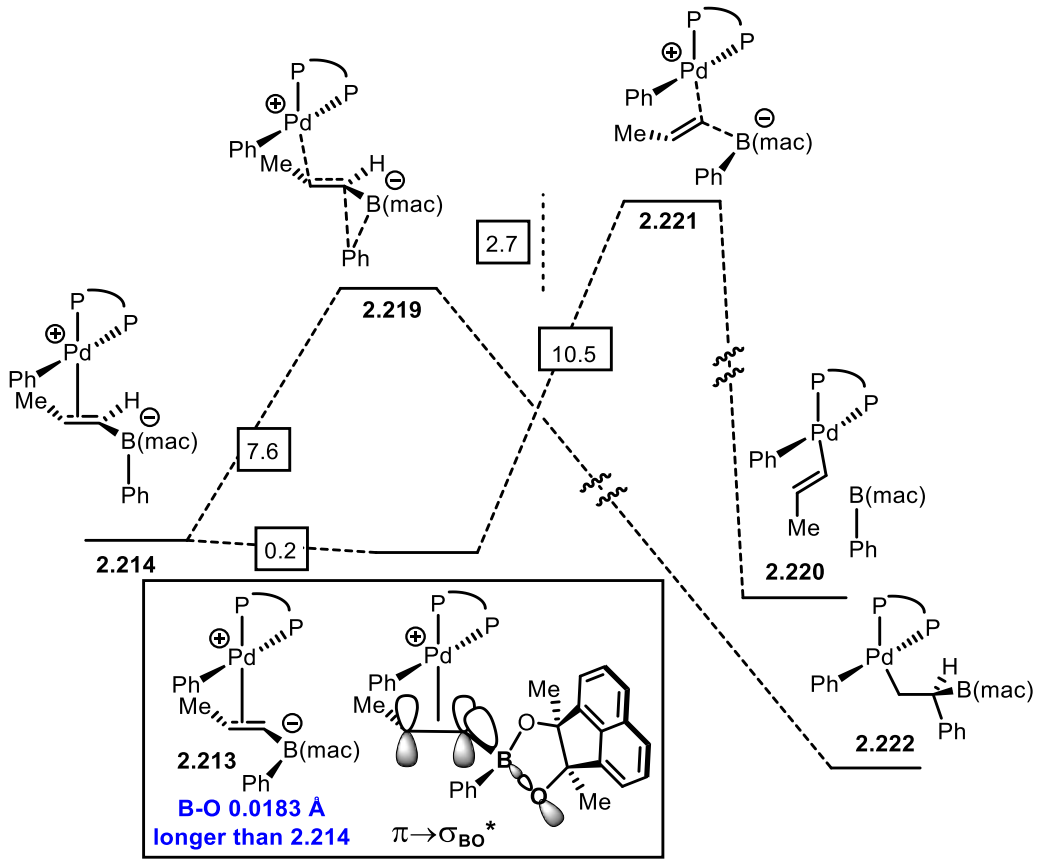
Scheme 2.34. Trans-propenylboronic pinacol ester: metallate rearrangement versus transmetallation



[a]Phosphine ligand is dppf. Optimized geometries calculated with DFT (BP86/Def2-SVP;PCM solvent model with THF). ΔG values are in kcal/mol, calculated using DFT (M06/def2-TZVPP//BP86/def2-SVP ;PCM solvent model with THF). Hydrogen atoms removed from structures for clarity.

considering the origin of the stabilizing influence of the twisted boron-ate rotational isomer it is worthy of note that in addition to relieving steric interactions of the forward-projecting methyl groups of the pinacol ligand with the ligand set on palladium, it appears likely that this orientation benefits from a stabilizing orbital alignment of empty B–O antibonding orbitals with the filled alkene π-bond (inset, **2.209**). This hypothesis is supported by the observation of a lengthening of the B–O bonds upon rotation, consistent with donation from the C–C π to B–O σ*. Looking at the analogous reaction profile for the mac rather than pinacol ester we find that the transmetallation transition state **2.221** is now higher than

Scheme 2.35. Effect of mac ligand: metallate rearrangement verses transmetallation



[a]Phosphine ligand is dppf. Optimized geometries calculated with DFT (BP86/Def2-SVP;PCM solvent model with THF). ΔG values are in kcal/mol, calculated using DFT (M06/def2-TZVPP//BP86/def2-SVP ;PCM solvent model with THF). Hydrogen atoms removed from structures for clarity.

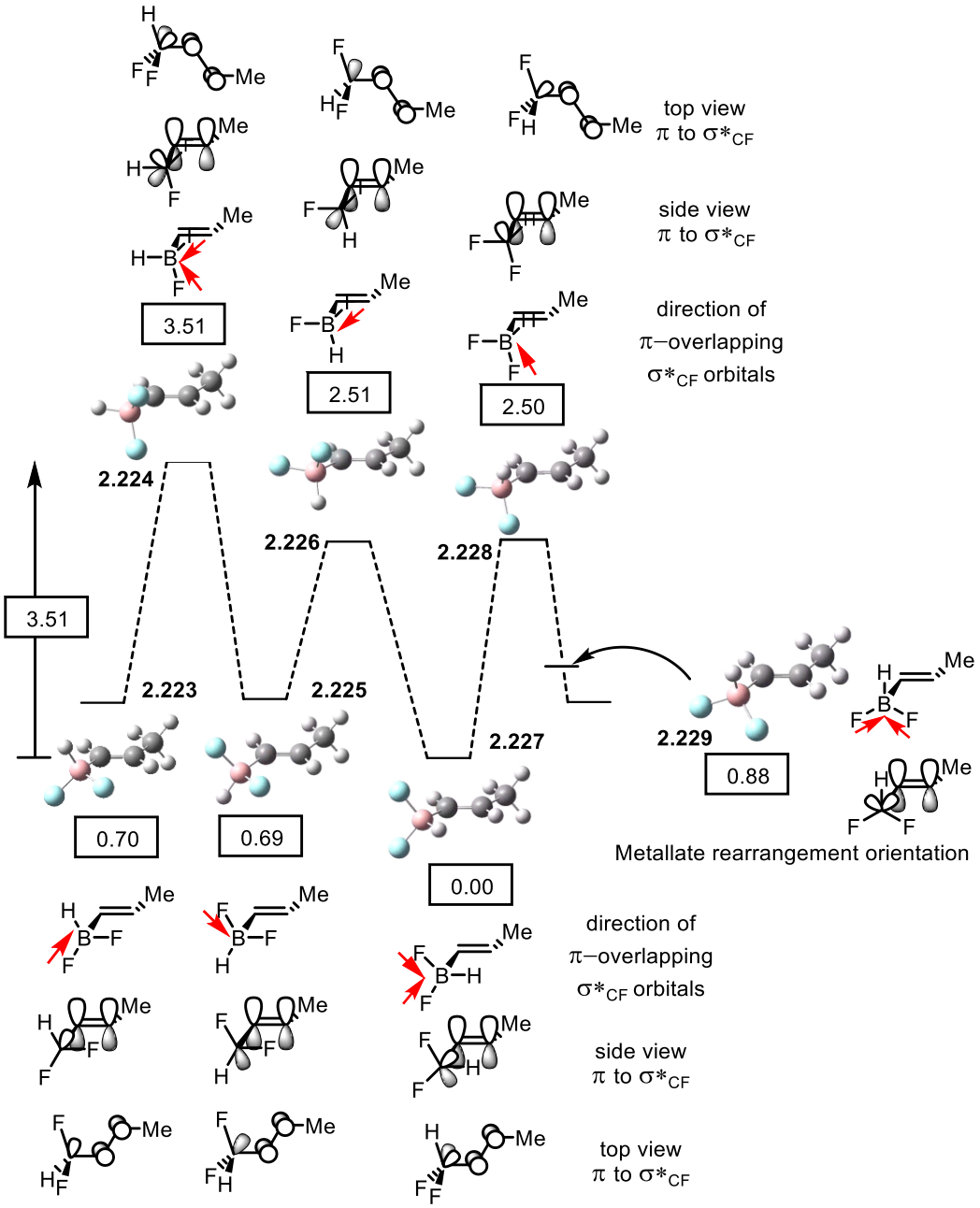
the metallate rearrangement transition state **2.219** (Scheme 2.35). This result is also in qualitative agreement with the observed increase in formation of conjunctive coupling rather than Suzuki-Miyaura product upon implementation of the mac rather than pinacol ester ligand. The lack of ground state stabilization upon boron-ate rotation (**2.214** to **2.213**) appears to translate to a substantial increase in the barrier to transmetallation. The lack of stabilization upon rotation of the boron ligand set appears to be due both to the relatively wide mac ligand structure as well as less stabilizing orbital interactions as indicated by the smaller degree of B–O bond elongation upon rotation (**2.214** to **2.213**).

2.6.2.3 Probe of Alkenylboron-Ate Conformation

To probe the inherent steric and electronic factors that govern the rotational orientation of alkenylboron-ate complexes without complicating steric interactions between the boron and palladium ligand sets we targeted the model system depicted in Scheme 2.36. When a B–F antibonding orbital (highlighted by red arrow) is pointed to the outside of the filled alkene π-orbital there is minimal orbital overlap, leading to energy maxima (**2.224**, **2.226**, **2.228**). These orientations also involve two gauche interactions between the alkeneyl hydrogen and either an H and an F atom (**2.226** and **2.228**) or two F atoms (**2.224**). The global maximum (**2.224**) occurs when both factors are maximized (both antibonding orbitals oriented outwards and both F atoms gauche to the alkenyl H atom). Conversely, when a B–F antibonding orbital is pointed to the inside of the filled alkene π-orbital there is maximum orbital overlap, leading to energy minima (**2.223**, **2.225**, **2.227**). These orientations also involve one eclipsing interaction between the alkenyl hydrogen and either

an F atom (**2.223** and **2.225**) or an H atom (**2.227**). The global energy minimum **2.227** occurs when both antibonding orbitals are optimally overlapping the alkene π-system and

Scheme 2.36. 360 degree scan of boron-ate rotation[a]



[a]Optimized geometries calculated with DFT (b3lyp/6-311++g(d,p);PCM solvent model with THF). ΔG values are in kcal/mol calculated with DFT (M06/def2-TZVPP//b3lyp/6-311++g(d,p);PCM solvent model with THF). σ^*_{CF} orbitals which are orthoganoal to π system are not depicted.

the eclipsing interactions are minimized. Notably, the lowest energy conformation **2.227** corresponds to the orientation found in the lowest energy transmetallasion transition states described above, while structure **2.229** corresponds the ground state structure leading to metallate rearrangement.

While more exhaustive theoretical exploration of possible transmetallation pathways involving oxygen dissociation from boron or phosphine dissociation from palladium is warranted, the present work provides a plausible fundamental model capable of explaining the observed competition between conjunctive coupling and Suzuki-Miyaura coupling. This model suggests that rationally designing diol ligand structures for boron and diphosphine ligands on palladium which control the relative orientation of the boron-ate migrating group substituent may lead to more efficient conjunctive coupling reactions.

2.7 Extension of Metal-Induced Metallate Rearrangement to Other Reactions

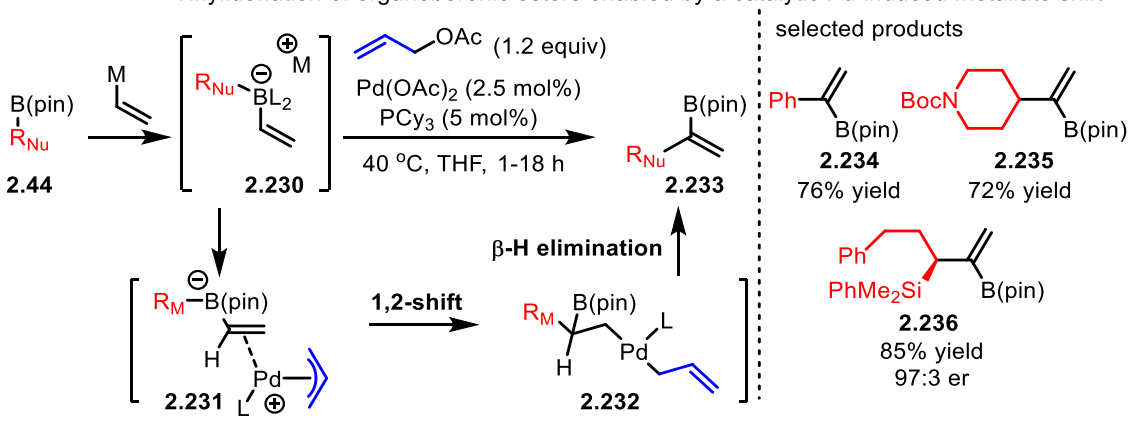
2.7.1 Vinylidenation of Organoboronic Esters[45]

Because the metal-induced metallate rearrangement operates as an alternative elementary reaction to transmetallation, it offers the potential to enable the development of new transformations beyond conjunctive coupling. In principle, the alkylpalladium intermediate generated upon 1,2-metallate rearrangement might be diverted to a wide range of alternative processes. As a preliminary demonstration of this potential, we recently reported a monophosphine–palladium-catalyzed vinylidenation reaction of organoboronic esters (Scheme 2.37). In an attempt to extend the conjunctive coupling reaction manifold

[45] Aparece, M. D.; Gao, C.; Lovinger, G. J. Morken, J. P. *Angew. Chem. Int. Ed.* **2019**, 58, 592.

to engage allyl electrophiles my coworkers found that only low yields of the desired conjunctive product could be obtained. The difficulty of promoting the conjunctive coupling of allyl electrophiles likely arises from the fact that after oxidative addition the η^3 coordination mode of the allyl group occupies multiple coordination sites on the palladium center; a coordination site is necessary for binding and activation of a boron-ate complex. It was found that by employing monodentate phosphine ligands in place of bidentate phosphine ligands, α-substituted alkenylboron product **2.233** could be efficiently produced.

Scheme 2.37. Vinylidenation of organoboronic esters enabled by a catalytic Pd-induced metallate shift



This product is consistent with β-hydride elimination from the intermediate alkylpalladium species (**2.232**) expected after 1,2-metallate rearrangement. This method represents the only direct conversion of an organoboronic ester starting material to the corresponding vinylidenation product. While this method provides ready access to a valuable class of synthetic building block, it also represents experimental evidence for the metal-induced metallate rearrangement, as product **2.233** is not accessible by the alternative carbopalladation mechanisms discussed in Section 2.5. Because the reaction is enabled by a palladium–monophosphine rather than diphosphine-complex as the previous conjunctive couplings, we decided to exmine the potential mechanism for this catalytic process in more

detail.

2.7.2 Computational Study

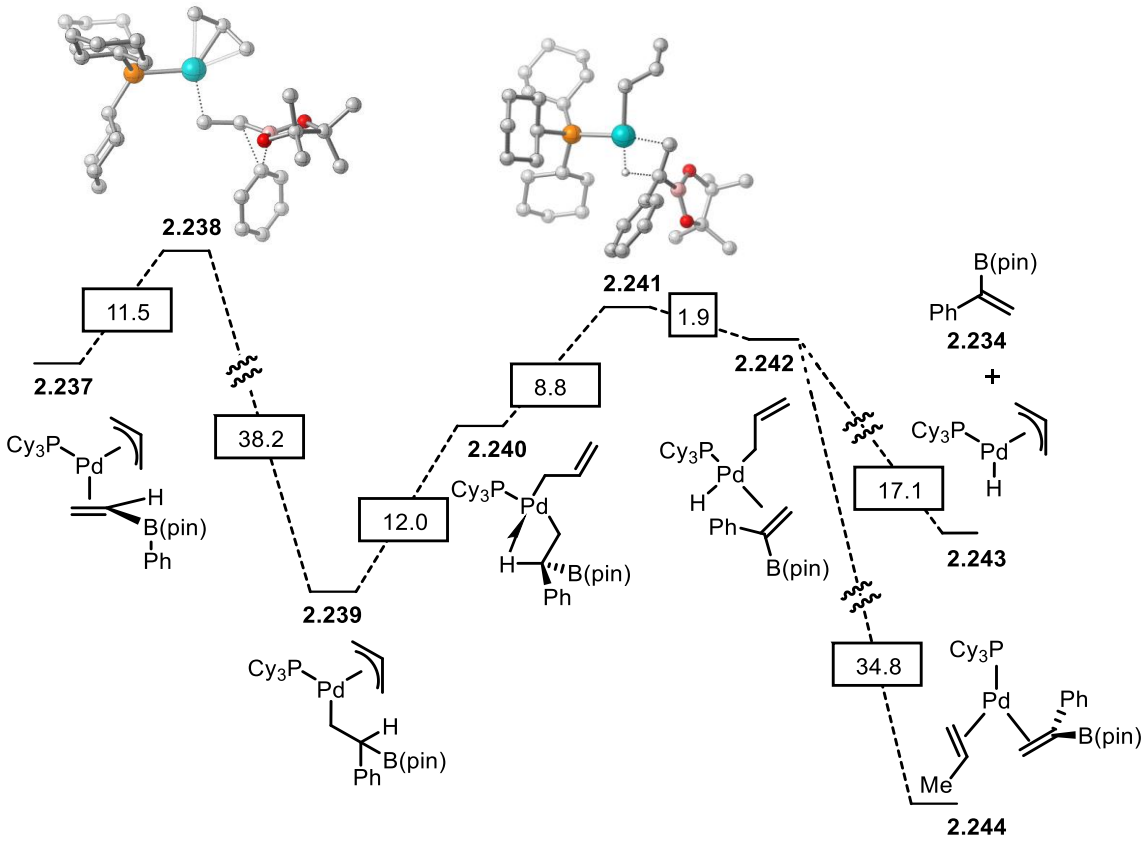
Analysis of the reaction was conducted on a complex between (η^3-allyl)Pd(PCy_3) and vinylphenylboron-ate complex **2.237** by the use of density functional theory. The competing pathway involving a bis(phosphine)Pd(η^1-allyl) is much higher in energy. As depicted in Scheme 2.38, a metallate shift (rearrangement) promoted by (PCy_3)Pd(η^3-allyl) occurs *via* transition state **2.238** with an activation barrier of 11.5 kcal/mo1 furnishing alkyl palladium intermediate **2.239**. Notably, this barrier is higher than those involved in conjunctive cross-coupling reactions employing diphosphine ligands (approximately 5 kcal/mol Scheme 2.25, 2.29, 2.34). The fact that the reaction is successful, many reactions being complete in 1 h, is consistent with the fact that oxidative addition is the turnover limiting step in mechanistically related conjunctive coupling reactions. An important feature of the allyl ligand in complex **2.239** is that it can adopt a stabilizing η^3-bonding mode or an η^1-bonding mode, thereby providing an open coordination site for an agostic interaction[46] with the substrate β-hydrogen (to give **2.240**). This change in bonding mode is 12 kcal/mol uphill and is followed by an 8.8 kcal/mol β-hydride elimination *via* transition state **2.241**. While the β-hydride elimination is an endothermic process, it is followed by exothermic processes including: (1) displacement of the alkenylboron as the allyl group reassumes the η^3-bonding mode to furnish **2.243**, (2) or reductive elimination of the hydride

[46] For a recent review of agostic interactions, see: M. Brookhart, M. L. H. Green, G. Parkin, *Proc. Natl. Acad. Sci.* USA **2007**, 104, 6908.

and allyl group to furnish **2.244**.

Interestingly allyl acetate serves two purposes in this reaction without being incorporated into the product: (1) it acts as an oxidant for palladium allowing it to achieve the electrophilic Pd(II) state required to induce metallate rearrangement while simultaneously serving as an LX-type bidentate ligand, and (2) it acts as a stoichiometric

Scheme 2.38. DFT reaction profile of vinylidenation: metal-induced metallate shift/β-H elimination[a]



[a]Phosphine ligand is PCy_3. Optimized geometries calculated with DFT (BP86/Def2-SVP;PCM solvent model with THF). ΔG values are in kcal/mol, calculated with DFT (PBE0-D3BJ/def2-TZVPP//BP86/ def2-SVP;SMD solvent model with THF). Hydrogen atoms removed from structures for clarity.

oxidant/hydride acceptor, enabling catalytic turnover.

The mechanistic information gained from this study adds to a more generalized understanding of how the metal-induced 1,2-metallate rearrangement might be utilized to

enable new catalytic processes. It specifically suggests that new ligand designs (monodentate versus bidentate, stable versus fluxional, L/L versus L/X) are key design features to explore that may unlock new reaction pathways.

2.8 Conclusion

The discovery and mechanistic investigation of the diphosphine–palladium-catalyzed conjunctive coupling reaction forms a foundation for the development of further catalytic enantioselective multi-component reactions that employing other coupling partners. The competition between transmetallation and metal-induced-metallate rearrangement provides a unique opportunity to study the detailed role of conformational and stereoelectronic effects that govern these two processes and sheds light on modes of transmetallation that may be operative in other catalytic reactions. The metal-induced 1,2-metallate rearrangement represents a previously unexplored mechanistic pathway that can be applied to other systems and may serve as a general elementary reaction that could be employed in the design of diverse catalytic processes.

2.9 Experimental

2.9.1 General Information

Note: NMR spectra of compounds included in the following sections have been previously published and can be accessed online. ^{1}H NMR spectra were recorded on either a Varian Gemini-500 (500 MHz), Varian Gemini-600 (600 MHz), or Varian Inova-500 (500 MHz) spectrometer. Chemical shifts are reported in ppm with the solvent resonance as the internal standard ($CDCl_3$: 7.24 ppm). Data are reported as follows: chemical shift, integration, multiplicity (s = singlet, d = doublet, t = triplet, q = quartet, p = pentet, m = multiplet), and coupling constants (Hz). ^{13}C NMR spectra were recorded on either a Varian Gemini-500 (125 MHz), Varian Gemini-600 (150 MHz) or a Varian Inova-500 (125 MHz) spectrometer with complete proton decoupling. Chemical shifts are reported in ppm with the solvent resonance as the internal standard. ^{11}B NMR spectra were recorded on a Varian Gemini-500 (128 MHz) or Varian Gemini-600 (160 MHz) spectrometer. ^{19}F NMR spectra were recorded on a Varian Gemini-500 (470 MHz) spectrometer. Infrared (IR) spectra were recorded on a Bruker alpha-P Spectrometer. Frequencies are reported in wavenumbers (cm^{-1}) as follows: strong (s), broad (br), medium (m), and weak (w). Optical rotations were measured on a Rudolph Analytical Research Autopol IV Polarimeter. High-resolution mass spectrometry (DART) was performed at the Mass Spectrometry Facility, Boston College, Chestnut Hill, MA. Liquid chromatography was performed using forced flow (flash chromatography) on silica gel (SiO_2, 230 x 450 Mesh) purchased from Silicycle. Thin layer chromatography (TLC) was performed on 25 μm silica gel glass backed plates from Silicycle. Visualization was performed using ultraviolet light (254 nm), ceric

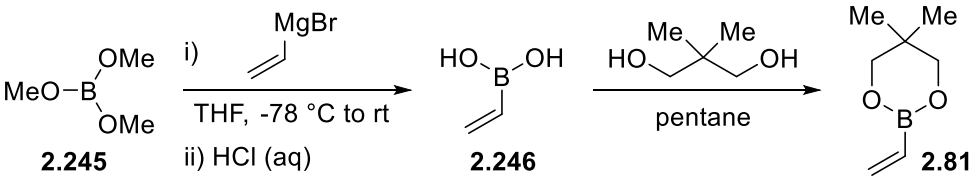
ammonium molybdate (CAM) in ethanol or phosphomolybdic acid, and cerium(IV) sulfate in ethanol with sulfuric acid (Seebach).

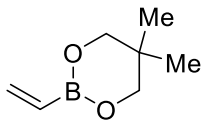
Analytical supercritical fluid chromatography (SFC) was performed on a TharSFC Method Station II equipped with Waters 2998 Photodiode Array Detector with isopropanol or methanol as the modifier.

All reactions were conducted in oven- or flame-dried glassware under an inert atmosphere of nitrogen or argon. Tetrahydrofuran (THF), diethyl ether (Et_2O), dichloromethane (DCM) and toluene were purified using Pure Solv MD-4 solvent purification system, from Innovative Technology, Inc., by passing the solvent through two activated alumina columns after purging with argon. Palladium (II) acetate, (S_p,S_p)-**2.101**, and 1,1′-Bis(dicyclohexyl-phosphino)ferrocene were purchased from Strem Chemicals, Inc. and used without further purification. Vinyl boronic acid pinacol ester was purchased from Combi Blocks and used without further purification. Boronic acids were purchased from Aldrich and used without further purification. Neopentyl glycol was purchased from Aldrich and used without further purification. 4-methoxyphenyltrifluoromethanesulfonate and 2-naphthyl trifluoromethanesulfonate were purchased from Aldrich and used without further purification. Phenyl triflluoromethanesulfonate and Trifluoromethansulfonic anhydride were purchased from Oakwood Chemicals and used without further purification. All other reagents were purchased from either Aldrich, Alfa Aesar or Acros and used without further purification.

2.9.2 Experimental Information

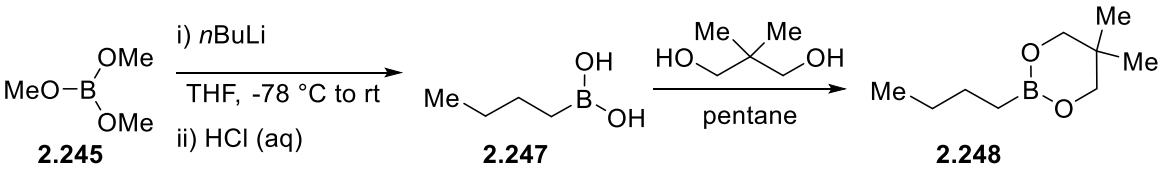
2.9.2.1 Procedures for Preparation of Boronic Esters



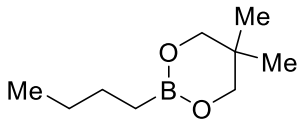


5,5-Dimethyl-2-vinyl-1,3,2-dioxaborinane (2.81). To an oven-dried 250 mL round bottom flask with magnetic stir bar under N_2 was added trimethylborate (**2.245**) (9.95 g, 95.80 mmol, 1.78 equiv) and 50 mL of THF. The flask was allowed to cool to -78˚C and vinylmagnesium bromide (60 mL, 0.90 M, 54 mmol, 1.0 equiv) was added over 2 h by syringe pump. After addition of vinylmagnesium bromide the solution was allowed to warm to room temperature and stir for 8 h, after which a 1 M aqueous solution of HCl (30 mL) was added followed by 25 mL of deionized water and the solution was allowed to stir at room temperature for 2 h. The product was extracted from solution with 6 x 50 mL of Et_2O and the combined organic layers were washed with 50 mL of deionized water, and 50 mL of brine, dried wtih Na_2SO_4, filtered with Et_2O, and the solvent was removed under reduced pressure. The resulting oil (**2.246**) was subjected to the general procedure for the preparation of boronic esters and the unpurified product was purified by vacuum distillation (under house vac) while being heated to 83 ˚C. The

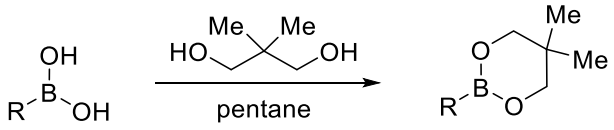
product was isolated as clear colorless oil (5.81 g, 77 % yield). All spectral data was in accord with the literature.[47]



2.245 **2.247** **2.248**

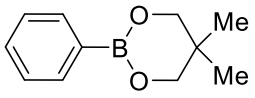


2-Butyl-5,5-dimethyl-1,3,2-dioxaborinane (2.248). To an oven-dried 250 mL round bottom flask with magnetic stir bar under N_2 was added trimethylborate (**2.245**) (11.21 g, 106.8 mmol, 1.78 equiv) and 50 mL of THF. The flask was allowed to cooled to -78˚C and *n*BuLi (23.72 mL, 2.53M, 60 mmol, 1.0 equiv) was added over 2 h by syringe pump. After addition of *n*BuLi the solution was allowed to warm to room temperature and stir for 8 h, after which a 1 M aqueous solution of HCl (30 ml) was added and the solution was allowed to stir at room temperature for 2 h. The product was extracted from solution with 4 x 20 mL of Et_2O and the combined organic layers were washed with brine, dried with Na_2SO_4, filtered with Et_2O and the solvent was removed under reduced pressure. The resulting oil (**2.247**) was subjected to the general procedure for preparation of boronic esters. The product was isolated as clear colorless oil (5.26 g, 52% yield). All spectral data was in accord with the literature.[48]

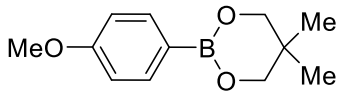


[47] Kaminsky, L.; Wilson, R. J.; Clark, D. A. *Org. Lett.* **2015**, 17, 3126.
[48] Blakemore, P. R.; Marsden, S. P.; Vater, H. D. *Org. Lett.* **2006**, 8, 773.

General Procedure for the Preparation of Boronic Esters: To an oven-dried round bottom flask with magnetic stir bar was added boronic acid (1.0 equiv) and pentane. The suspension was allowed to cool to 0˚C and 2,2-dimethyl-1,3-propanediol (neopentyl glycol) (1.05 equiv) was added neat and the solution was allowed to warm to room temperature and stir for 3 h. If a water layer was observed it was removed and the resulting pentane solution was dried with Na_2SO_4, filtered with Et_2O, and the solvent was removed under reduced pressure. The resulting residue was purified on silica gel (plug with CH_2Cl_2 as the eluent).



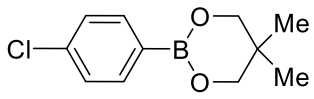
5,5-Dimethyl-2-phenyl-1,3,2-dioxaborinane (2.164). Preparted according to the general procedure above with phenylboronic acid (0.268 g, 22.0 mmol), neopenty glycol (2.41 g, 23.1 mmol, 1.05 equiv), and pentane (60 mL). The resulting white solid (4.18 g, quantitative yield) was used without further purification. All spectral data was in accord with the literature.[49] This compound is commercially available [CAS: 5123-13-7].



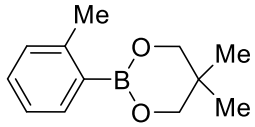
2-(4-Methoxyphenyl)-5,5-dimethyl-1,3,2-dioxaborinane (2.249). Prepared according to the general procedure above with 4-methoxyphenylboronic acid (0.4559 g, 3.0 mmol, 1.0 equiv), neopentyl glycol (0.328 g, 3.15 mmol, 1.05 equiv) and pentane (9.0 mL). The unpurified residue was

[49] Tobisu, M.; Kinuta, H.; Kita, Y.; Rémond, E.; Chatani, N. *J. Am. Chem. Soc.* **2012**, 134, 115.

purified on a silica gel plug with CH_2Cl_2 to afford the product as white solid (0.650 g, 98%). All spectral data was in accord with the literature.[50]

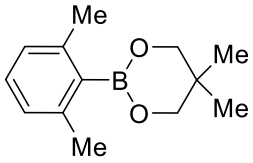


2-(4-Chlorophenyl)-5,5-dimethyl-1,3,2-dioxaborinane (2.250). Prepared according to the general procedure above with 4-chlorophenylboronic acid (0.4691 g, 3.0 mmol, 1.0 equiv), neopentyl glycol (0.328 g, 3.15 mmol, 1.05 equiv), and pentane (9 mL). The unpurified residue was purified on a silica gel plug with CH_2Cl_2 to afford the product as white solid (0.667 g, 99% yield). All spectral data was in accord with the literature.[51]

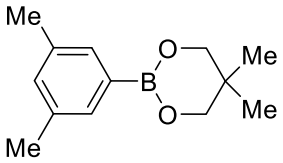


5,5-Dimethyl-2-(*o*-tolyl)-1,3,2-dioxaborinane (2.251). Prepared according to the general procedure above with *o*-tolylboronic acid (0.4079 g, 3.0 mmol, 1.0 equiv), neopentyl glycol (0.328 g, 3.15 mmol, 1.05 equiv), and pentane (9.0 mL). The unpurified residue was purified on a silica gel plug with CH_2Cl_2 to afford the product as colorless oil (0.611 g, quantitative yield). All spectral data was in accord with the literature.[52]

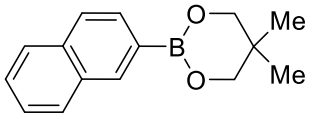
[50] Rosen, B. M.; Huang, C.; Percec, V. *Org. Lett.* **2008**, 10, 2597.
[51] Zhao, Y.; Snieckus, V. *Angew. Chem. Int. Ed.* **2014**, 356, 1527.
[52] Ukai, K.; Aoki, M.; Takaya, J.; Iwasawa, N. *J. Am. Chem. Soc.* **2006**, 128, 8706.



2-(2,6-Dimethylphenyl)-5,5-dimethyl-1,3,2-dioxaborinane (2.252). Prepared according to the general procedure above with 2,6-dimethylphenylboronic acid (0.4499 g, 3.0 mmol, 1.0 equiv), neopentyl glycol (0.328 g, 3.15 mmol, 1.05 equiv), and pentane (9.0 mL). The unpurified residue was purified on a silica gel plug with CH_2Cl_2 to afford the product as white solid (0.558 g, 85%). **^{1}H NMR** (600 MHz, $CDCl_3$) δ 7.09 (1H, t, *J* = 7.8 Hz), 6.93 (2H, d, *J* = 7.8 Hz), 3.78 (4H, s), 2.38 (6H, s), 1.09 (6H, s). **^{13}C NMR** (150 MHz, $CDCl_3$) δ 140.58, 128.59, 126.48, 77.37, 77.16, 76.95, 72.38, 31.79, 22.40, 22.37. **^{11}B NMR** (192 MHz, $CDCl_3$) δ 26.25. **IR** (neat) ν_{max} 3056.7 (w), 2960.3 (w), 2931.5 (w), 1596.3 (w), 1475.0 (m), 1455.3 (m), 1292.4 (s), 1246.2 (m), 1029.0 (w), 768.6 (m), 694.3 (m), 699.1 (m) cm^{-1}. **HRMS** (DART) for $C_{13}H_{20}BO_2$ $[M+H]^+$ calculated: 219.1556, found: 219.1557.

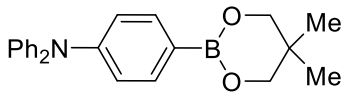


2-(3,5-Dimethylphenyl)-5,5-dimethyl-1,3,2-dioxaborinane (2.253). Prepared according to the general procedure above with 3,5-dimethylphenylboronic acid (0.4499 g, 3.0 mmol, 1.0 equiv), neopentyl glycol (0.328 g, 3.15 mmol, 1.05 equiv), and pentane (9.0 mmol). The unpurified residue was purified on a silica gel plug with CH_2Cl_2 to afford the product as white solid (0.479 g, 73%). All spectral data was in accord with the literature.[48]

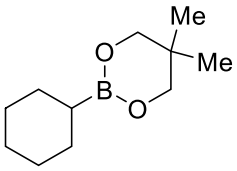


5,5-Dimethyl-2-(naphthalen-2-yl)-1,3,2-dioxaborinane (2.254). Prepared according to the general procedure above with

2-napthylboronic acid (2.00 g, 11.6 mmol, 1.0 equiv), neopentyl glycol (1.27 g, 12.18 mmol, 1.05 equiv), and pentane (100.0 mL). The unpurified residue was purified on a silica gel plug with CH_2Cl_2 to afford the product as white solid (2.79 g, quantitative yield). All spectral data was in accord with the literature. [48]

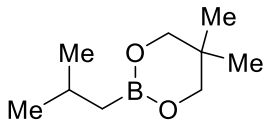


4-(5,5-Dimethyl-1,3,2-dioxaborinan-2-yl)-*N*,*N*-diphenylaniline (2.255). Prepared according to the general procedure above with 4-(diphenylamino)phenylboronic acid (0.4935 g, 1.7 mmol, 1 equiv), neopentyl glycol (0.187 g, 1.79 mmol, 1.05 equiv), and pentane (10 mL). The unpurified residue was purified on a silica gel plug with CH_2Cl_2 to afford the product as white solid (0.466 g, 77%). All spectral data was in accord with the literature.[53]

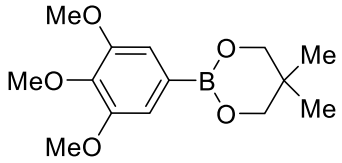


2-Cyclohexyl-5,5-dimethyl-1,3,2-dioxaborinane (2.256). Prepared according to the general procedure above with cycylohexylboronic acid (1.98 g, 15.5 mmol, 1.0 equiv), neopentyl glycol (1.70 g, 16.28 mmol, 1.0 equiv), and pentane (100 mL). The unpurified residue was purified on a silica gel plug with CH_2Cl_2 to afford the product as colorless oil (3.00 g, 99% yield). All spectral data was in accord with the literature.[54]

[53] Goodall, W.; Williams, J. A. *Chem. Commun.* **2001**, 23, 2514.
[54] Bose, S. K.; Fucke, K.; Liu, L.; Steel, P. G.; Marder, T. B. *Angew. Chem. Int. Ed.* **2014**, 53, 1799.

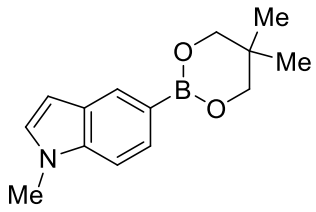


2-Isobutyl-5,5-dimethyl-1,3,2-dioxaborinane (2.257). Prepared according to the general procedure above with (2-methylpropyl)boronic acid (0.3058 g, 3.0 mmol, 1.0 equiv), neopentyl glycol (0.328 g, 3.15 mmol, 1.05 equiv), and pentane (9.0 mL). The unpurified residue was purified on a silica gel plug with CH_2Cl_2 to afford the product as colorless oil (0.398 g, 78% yield). All spectral data was in accord with the literature.[55]



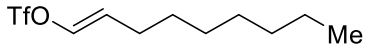
5,5-Dimethyl-2-(3,4,5-trimethoxyphenyl)-1,3,2-dioxaborinane (2.258). Prepared according to the general procedure above with 3,4,5-trimethoxyphenylboronic acid (1.91 g, 9.0 mmol, 1.0 equiv), neopentyl glycol (0.984 g, 9.45 mmol, 1.05 equiv), and pentane (100.0 mL). The unpurified residue was purified on a silica gel plug with CH_2Cl_2 to afford the product as white solid (2.52 g, quantitative yield). **^{1}H NMR** (600 MHz, $CDCl_3$) δ 7.04 (2H, s), 3.89 (6H, s), 3.87 (3H, s), 3.76 (4H, s), 1.02 (6H, s). **^{13}C NMR** (150 MHz, $CDCl_3$) δ 152.78, 140.34, 110.31, 72.32, 60.75, 56.02, 31.86, 21.89. **^{11}B NMR** (160 MHz, $CDCl_3$) δ 26.49. **IR** (neat) ν_{max} 29589.0 (w), 2936.7 (w), 2889.3 (w), 1576.9 (m), 1477.2 (m), 1337.3 (s), 1229.9 (s), 1123.4 (s), 1004.0 (m), 688.1 (m) cm^{-1}. **HRMS** (DART) for $C_{14}H_{22}BO_5$ $[M+H]^+$ calculated: 281.1560, found: 281.1551.

[55] Barsamian, A. L.; Wu, A.; Blakemore, P. R. *Org. Biomol. Chem.* **2015**, 13, 3781.



5-(5,5-Dimethyl-1,3,2-dioxaborinan-2-yl)-1-methyl-1*H*-indole (2.259). Prepared according to the general procedure above with (1-methyl-1H-indol-5-yl)boronic acid (0.500 g, 2.772 mmol, 1.0 equiv), neopentyl glycol (0.306 g, 2.910 mmol, 1.05 equiv), and pentane (100.0 mL). The unpurified residue was purified on a silica gel plug with CH_2Cl_2 to afford the product as white solid (0.4739 g, 70 % yield). **^{1}H NMR** (500 MHz, $CDCl_3$) δ 8.12 (1H, s), 7.65 (1H, d, *J* = 7.0 Hz), 7.29 (1H, d, *J* = 7.0 Hz), 7.00 (1H, d, *J* = 2.5 Hz), 6.48 (1H, d, *J* = 2.5 Hz), 3.78 (4H, s), 3.77 (3H, s), 1.02 (6H, s). **^{13}C NMR** (150 MHz, $CDCl_3$) δ 138.65, 128.85, 128.40, 127.87, 127.07, 108.577, 101.79, 72,52, 32.97, 32.13, 22.16. **^{11}B NMR** (160 MHz, $CDCl_3$) δ 27.15. **IR** (neat) ν_{max} 2960.4 (w), 2939.3 (w), 2895.9 (w), 2874.6 (w), 1608.0 (w), 1513.9 (w),1 4.78.8 (w), 1333.1 (m), 1304.9 (s), 1271.5 (m), 1245.4 (m), 1185.2 (m), 1118.03 (m), 717.99 (w), 692.0 (w), 678.88 (w) cm^{-1}. **HRMS** (DART) for $C_{14}H_{19}BNO_2$ $[M+H]^+$ calculated: 244.1509, found: 244.1519.

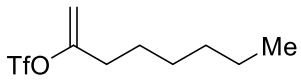
2.9.2.2 Procedures for Preparation of Alkenyl and Aryl Trifluoromethanesulfonates



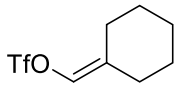
***(E)*-Non-1-en-1-yl trifluoromethanesulfonate (2.260).** The title compound was prepared according to a literature procedure with slight modification.[56] In an Ar-filled glove box, CsF (5.01 g, 33.0 mmol, 3.0 equiv) and *N*-

[56] McCammant, M. S.; Liao, L.; Sigman, M. S. *J. Am. Chem. Soc.* **2013**, 135, 4167.

Phenyl-bis(trifluoromethanesulfonimide) (7.86 g, 22.0 mmol, 2.0 equiv) were placed in a large pressure vessel and sealed. Outside the glovebox the flask was briefly opened and a solution of 1-nonen-1-yl trimethylsilyl ether[57] (95/5 mixture of *E*/*Z* isomers, 2.36 g, 11 mmol, 1.0 equiv) in dimethoxyethane (30 mL) was added. After addition the pressure vessel was quickly sealed with a screw cap. The solution was allowed to stir vigorously at room temperature for 4 h after which the pressure was released and the mixture was diluted with pentane (100 mL), washed twice with water and once with brine, dried with Na_2SO_4, filtered and concentrated under reduced pressure. The unpurified oil was purified by silica gel chromatography (100% pentane) to afford the title compound as clear colorless oil (1.51 g, 50% yield). All spectral data was in accord with the literature.[58]

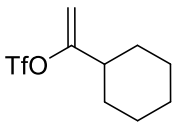


Oct-1-en-2-yl trifluoromethanesulfonate (2.261). The title compound was prepared according to the procedure reported in the literature.[59] All spectral data was in accord with the literature.

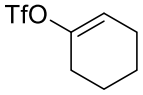


Cyclohexylidenemethyl trifluoromethanesulfonate (2.166). The title compound was prepared according to the procedure reported in the literature.[60] All spectral data was in accord with the literature.

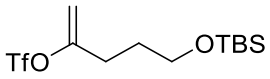
[57] Matsuzawa, S.; Horiguchi, Y.; Nakamura, E.; Kuwajima, I. *Tetrahedron* **1989**, 45, 349.
[58] Shirakawa, W.; Imazaki, Y.; Hayashi, T. *Chem. Commun.* **2009**, 34, 5088.
[59] Takai, K.; Sakogawa, K.; Kataoka, Y.; Oshima, K.; Utimoto, K. *Org. Synth*. **1995**, 72, 180.
[60] Stang, P. J.; Treptow, W. *Synthesis* **1980**, 1980, 283.



1-Cyclohexylvinyl trifluoromethanesulfonate (2.262). The title compound was prepared according to the procedure reported in the literature.[61] All spectral data was in accord with the literature.



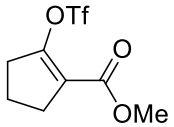
Cyclohex-1-en-1-yl trifluoromethanesulfonate (2.263). The title compound was prepared according to the procedure reported in the literature. All spectral data was in accord with the literature.[62]



5-((*tert*-Butyldimethylsilyl)oxy)pent-1-en-2-yl trifluoromethanesulfo-nate (2.264). Prepared following a published procedure with slight modification.[55] 4-Pentyn-1-ol (1.44 mL, 15.5 mmol, 1.0 equiv) was placed in a flame-dried round bottom flask and allowed to dissolve in dry pentane (15 mL). The solution was allowed to cool to – 40 ˚C and triflic acid (2.5 mL, 27.8 mmol, 1.6 equiv) was added dropwise with stirring. The mixture was allowed to stir for 10 min at -40 ˚C and allowed to warm to room temperature over 30 min. The mixture was quenched with water (10 mL), the product was extracted with diethyl ether and the combined ether solution washed with a saturated aquious solution of sodium bicarbonate and brine. The unpurified mixture was dried over Na_2SO_4, concentrated under reduced pressure and filtered through a plug of neutral alumina with CH_2Cl_2. The resulting triflate, obtained as clear yellow oil (1.84 g, 7.8 mmol, 1 equiv) was placed in a flame dried round

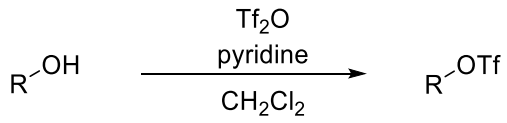
[61] Al-huniti, M. H.; Lepore, S. D. *Org. Lett.* **2014**, 16, 4154.
[62] Lim, B. Y.; Jung, B. E.; Cho, C. G. *Org. Lett.* **2014**, 16, 4492.

bottom flask with imidazole (1.10 g, 16 mmol, 2 equiv) and allowed to dissolved in CH_2Cl_2 (20 mL). The solution was flushed with N_2 and allowed to cool to 0 °C. *tert*-Butyldimethylsilyl chloride (1.18 g, 7.8 mmol, 1.0 equiv) was added as a solution in CH_2Cl_2 (10 mL). The mixture was allowed to stir at room temperature for 2 h after which a 1 M aqueous solution of HCl (5 mL) were added. The product was extracted with CH_2Cl_2 and washed with a saturated aquious solution of sodium bicarbonate and brine, dried with Na_2SO_4, filtered, and concentrated under reduced pressure. The unpurified mixture was purified by silica gel chromatography (1% ethyl acetate in hexane) to afford the title compound as colorless oil (2.10 g, 40 % yield over two steps). **^{1}H NMR** (600 MHz, $CDCl_3$) δ 5.11 (1H, d, J = 3.0 Hz), 4.95 (1H, d, J = 3.0 Hz), 3.65 (2H, t, J = 6.0 Hz), 2.44 (2H, t, J = 7.8 Hz), 1.75 (2H, q, J = 6.6 Hz), 0.89 (9H, s), 0.05 (6H, s). **^{13}C NMR** (125 MHz, CDC_3) δ 156.9, 104.4, 61.4, 30.6, 29.3, 25.7, 18.4, -5.3. **IR** (neat) ν_{max} 2995.9 (s), 2931.6 (s), 2894.4 (s), 2859.8 (s), 1671.0 (s), 1473.0 (s), 1253.3 (s), 1209.3 (s), 1141.1 (s), 1104.7 (s), 945.0 (s), 835.9 (s), 776.7 (s), 611.56 (s) cm^{-1}. **HRMS** (DART) for: $C_{12}H_{24}F_3O_4S_1Si_1$ $[M+H]^+$: calculated: 349.1117, found: 349.1114.

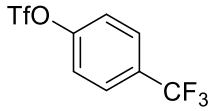


5-Hydroxypent-1-en-2-yl trifluoromethanesulfonate (2.265). The title compound was prepared according to the procedure reported in the literature.[63] All spectral data was in accord with the literature.

[63] Logan, A. W. J.; Parker, J. S.; Hallside, M. S.; Burton, J. W. *Org. Lett.* **2012**, 14, 2940.

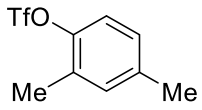


General Procedure for the Synthesis of Aryl Trifluoromethanesulfonates: Aryl Trifluoromethansulfonates were made according to literature procedure with slight modification.[64] To a solution of the corresponding phenol and pyridine in CH_2Cl_2 at 0 ˚C, a solution of trifluoromethanesulfonic anhydride in CH_2Cl_2 was added dropwise. The mixture was then allowed to warm to room temperature and stir for 1 h. The mixture was diluted with Et_2O, quenched with a 3 M solution of aqueous HCl and washed successively with a saturated solution of aqueous $NaHCO_3$ and brine. The solution was dried with Na_2SO_4, filtered with Et_2O, and the solvent was removed under reduced pressure. The residue was purified by silica gel chromatography to afford aryl trifluoromethanesulfonates.

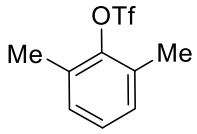


4-(Trifluoromethyl)phenyl trifluoromethanesulfonate (2.266). Prepared according to the general procedure above with 4-trifluoromethylphenol (0.630 g, 3.8 mmol, 1.0 equiv), trifluoromethanesulfonic anyhydride (0.774 mL, 4.6 mmol, 1.21 equiv), pyridine (0.615 mL, 7.6 mmol, 2.0 equiv), and CH_2Cl_2 (6.0 mL). The unpurified residue was purified by silica gel chromatography (10% ethyl acetate in hexanes) to afford the product as colorless oil (1.180 g, 98% yield). All spectral data was in accord with the literature.[65]

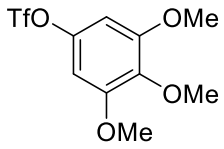
[64] Goossen, L. J.; Linder, C.; Rodríguez, N.; Lange, P. P. *Chem. Eur. J.* **2009**, 15, 9336.
[65] Gill, D.; Hester, A. J.; Lloyd-Jones, G. C. *Org. Biomol. Chem.* **2004**, 2, 2547.



2,4-Dimethylphenyl trifluoromethanesulfonate (2.267). Prepared according to the general procedure above with 2,4-dimethylphenol (0.906 mL, 7.5 mmol, 1.0 equiv), trifluoromethanesulfonic anhydride (1.50 mL, 9.0 mmol, 1.2 equiv), pyridine (1.2 mL, 15.0 mmol), and CH_2Cl_2 (13.0 mL). The unpurified residue was purified by silica gel chromatography (5% ethyl acetate in hexanes) to afford the product as colorless oil (1.680 g, 88% yield). All spectral data was in accord with the literature.[66]



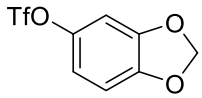
2,6-Dimethylphenyl trifluoromethanesulfonate (2.268). Prepared according to the general procedure above with 2,6-dimethylphenol (0.611 g, 5.0 mmol, 1.0 equiv), trifluoromethanesulfonic anhydride (1.0 mL, 6.0 mmol, 1.2 equiv), pyridine (0.809 mL, 10.0 mmol), and CH_2Cl_2 (8.0 mL). The unpurified residue was purified by silica gel chromatography (17% ethyl acetate in hexanes) to afford the product as yellow oil (1.124 g, 88% yield). All spectral data was in accord with the literature.[67]



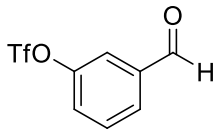
3,4,5-Trimethoxyphenyl trifluoromethanesulfonate (2.269). Prepared according to the general procedure above with 3,4,5-trimethoxyphenol (0.921 g, 5.0 mmol, 1.0 equiv), trifluoromethanesulfonic anhydride (1.0 mL, 6.0 mmol, 1.2 equiv), pyridine (0.809 mL,

[66] Radivoy, G.; Alonso, F.; Yus, M. *Tetrahedron* **1999**, 55, 14479.
[67] Mori, H.; Matsuo, T.; Yoshioka, Y.; Katsumura, S. *J. Org. Chem.* **2006**, 71, 9004.

10.0 mmol), and CH_2Cl_2 (8.0 mL). The unpurified residue was purified by silica gel chromatography (20% ethyl acetate in hexanes) to afford the product as off-white solid (1.552 g, 98% yield). All spectral data was in accord with the literature.[68]



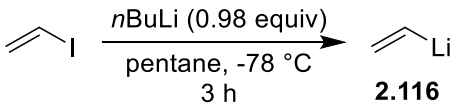
Benzo[*d*][1,3]dioxol-5-yl trifluoromethanesulfonate (2.270). Prepared according to the general procedure above with sesamol (1.04 g, 7.5 mmol, 1.0 equiv), trifluoromethansulfonic anhydride (1.5 mL, 9.0 mmol, 1.2 equiv), pyridine (1.2 mL, 15.0 mmol), and CH_2Cl_2 (13.0 mL). The unpurified residue was purified by silica gel chromatography (5% ethyl acetate in hexanes) to afford the product as colorless oil (1.89 g, 94%). All spectral data as in accord with the literature.[69]



3-Formylphenyl trifluoromethanesulfonate (2.271). Prepared according to the general procedure above with 3-hydroxybenzaldehyde (916 mg, 7.5 mmol, 1.0 equiv), trifluoromethanesulfonic anhydride (1.5 mL, 9.0 mmol, 1.2 equiv), pyridine (1.2 mL, 15.0 mmol), and CH_2Cl_2 (10 mL). The unpurified residue was purified by silica gel chromatography (10% ethyl acetate in hexanes) to afford the product as colorless oil (1.47 g, 77% yield). All spectral data was in accord with the literature.[60]

[68] Macmillan, D.; Anderson, D. W. *Org. Lett.* **2004**, 6, 4659.
[69] Echavarren, A. M.; Stille, J. K. *J. Am. Chem. Soc.* **1987**, 109, 5478.

2.9.2.3 Procedure for Preparation of Vinyllithium from Vinyl Iodide



2.116

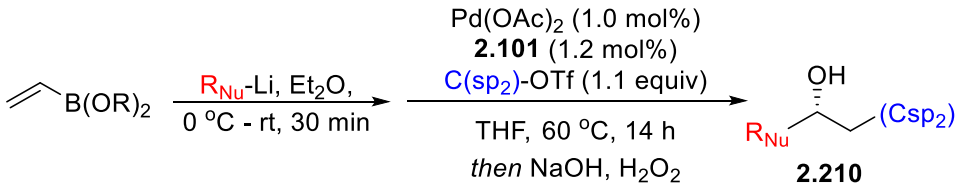
To an oven-dried 250 mL round bottom flask with magnetic stir bar in an Ar-filled glovebox was added vinyl iodide (12.1670 g, 76.6611 mmol, 1.00 equiv) and pentane (35 mL). The flask was sealed with a rubber septa, removed from the glovebox, allowed to cool to -78 ˚C under argon, and maintained at this temperature while *n*BuLi (29.7 mL, 75.1410 mmol, 0.98 equiv) was added by syringe pump over two h. Vinyllithium formation was observed as a white suspension in the flask within 2-3 min of initial *n*BuLi addition. Upon completion of slow addition, the solution was allowed to stir for an additional hour at between -50 and -78 ˚C. The vinyllithium suspension was transferred by cannula in two portions to an oven-dried Schlenck filter under argon and filtered, washed with pentane, and dried in the following manner: After transfer of the first half of the vinyllithium suspension in pentane, the pentane was removed under positive pressure by slightly reducing the pressure in the bottom chamber of the filter while maintaining constant positive pressure of argon in the upper portion of the filter. (Caution, positive pressure must be maintained at all times in the top chamber to prevent air from entering the schlenk filter and reacting with the pyrophoric vinyllithium). After the pentane was removed, a white powdery layer of solid vinyllithium was observed on top of the Schlenk filter frit. The second half of the vinyllithium suspension was transferred and the pentane removed in the same manner. To ensure thorough removal of soluble impurities (*n*-BuLi, *n*BuI, vinyl

iodide) the white powdery pad of vinyllithium left after initial filtration was rinsed three times with 20 mL of dried, distilled, and degassed pentane by adding the pentane to the top chamber of the Schlenk filter and agitating the vinyllithium for two min and removal of pentane as described above. The solid vinyllithium was then dried for 15 min under positive pressure of argon by reducing the pressure in the bottom chamber of the filter while maintaining positive pressure in the upper chamber of the filter. The receiving 250 mL round bottom flask with pentane washes was replaced by quick-switch with an oven-dried 100 mL 2-neck round bottom flask under argon. The solid vinyllithium was dissolved using 48 mL of diethyl ether and was rinsed into the receiving flask by reducing the pressure of the lower chamber of the filter as described above. The resulting clear yellow solution was titrated using BHT with 1,10-phenanthroline in THF and the yield (72.82 mmol, 95 % yield) was calculated based on the measured molarity (1.58 M) and the measured volume of the solution upon transfer to a single-necked 100 mL round bottom flask (At this point the vinyllithium can be used directly in a conjunctive coupling with 5 mol % catalyst loading and the coupling product can be obtained in 69% yield, 98:2 er).

The freshly prepared solution of vinyllithium (1.58 M) was immediately recrystallized three times from diethyl ether by allowing the solution to cool to -45 ˚C over 1 h using a Cryocool and maintaining this temperature overnight (10 h) and then reducing the temperature to -78 ˚C for 6 h using a dry ice acetone bath. Solid vinyllithium was observed to form as clear, glassy, crystals. After the recrystallization period the supernatant diethyl ether was removed, and the round bottom flask was allowed to warm to room temperature, and 10 mL of fresh diethyl ether was added to the flask. The recrystallization was repeated

two more times, resulting in an overall 47 % yield of vinyllithium, evaluated as before, as a clear, nearly colorless solution in diethyl ether.

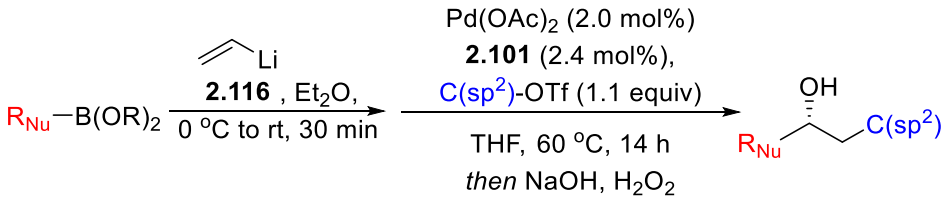
2.9.2.4 General Procedures for Conjunctive Coupling



Method A:

To an oven-dried 2-dram vial equipped with a magnetic stir bar in an Ar-filled glovebox was added vinylboronic ester (0.30 mmol, 1.00 equiv) and diethyl ether (0.3 mL). The vial was sealed with a septum cap, and removed from the glovebox. The vial was allowed to cool to 0 ˚C, and an alkyl/aryllithium solution (0.30 mmol, 1.0 equiv) was added. The vial was allowed to warm to room temperature and stir for 30 min. The solvent was carefully removed under reduced pressure, and the vial was brought back into the glovebox. To a separate oven-dried 2-dram vial equipped with a magnetic stir bar in the glovebox was added $Pd(OAc)_2$ (0.003 mmol, 0.01 equiv), (S_p,S_p)-**2.101** (0.0036 mmol, 0.012 equiv), and THF (0.3 mL). The $Pd(OAc)_2$/(S_p,S_p)-**2.101** solution was allowed to stir for 20 min at room temperature. Then the $Pd(OAc)_2$/(S_p,S_p)-**2.101** solution was transferred into the vial, followed by THF (0.9 mL), and aryl/vinyl triflate (0.33 mmol, 1.10 equiv). The vial was sealed with a polypropylene cap, taped, and brought out of the glovebox where it was allowed to stir at 60 ˚C for 14 h. The resulting mixture was allowed to cool to room temperature, filtered through a silica gel plug with diethyl ether, and concentrated under

reduced pressure. The mixture was diluted with THF (3 mL), allowed to cool to 0 ˚C, a 3 M aquious solution of NaOH (2 mL) was added, followed by 30% H_2O_2 (1.0 mL), dropwise. The mixture was allowed to warm to room temperature and stir for 4 h. The mixture was allowed to cool to 0 ˚C and a saturated solution of aqueous $Na_2S_2O_3$ (3 mL) was added dropwise. The mixture was allowed to warm to room temperature and the product was extracted from the aqueous layer with ethyl acetate (3 x 20 mL). The combined organic layers were dried with Na_2SO_4, filtered, and concentrated under reduced pressure, and subsequently purified by silica gel chromatography to afford the desired product.

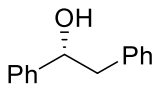


Method B:

To an oven-dried 2-dram vial equipped with a magnetic stir bar in an Ar-filled glovebox was added alkyl/arylboronic ester (0.30 mmol, 1.0 equiv) and diethyl ether (0.3 mL). The vial was sealed with a septum cap, and removed from the glovebox. The vial was allowed to cool to 0˚C, and a vinyllithium solution (0.30 mmol, 1.0 equiv) was added. The vial was allowed to warm to room temperature and stir for 30 min. The solvent was carefully removed under reduced pressure, and the vial was brought back into the glovebox. To a separate oven-dried 2-dram vial equipped with a magnetic stir bar in the glovebox was added $Pd(OAc)_2$ (0.006 mmol, 0.02 equiv), (S_p,S_p)-**2.101** (0.0072 mmol, 0.024 equiv), and THF (0.6 mL). The $Pd(OAc)_2$/(S_p,S_p)-**2.101** solution was allowed to stir for 20 min at room

temperature. The $Pd(OAc)_2$/(S_p,S_p)-**2.101** solution was transferred into the vial, followed by THF (0.6 mL), and aryl/vinyl triflate (0.33 mmol, 1.10 equiv) was added. The vial was sealed with a polypropylene cap, taped, and brought out of the glovebox where it was allowed to stir at 60 ˚C for 14 h. The resulting mixture was allowed to cool to room temperature, filtered through a silica gel plug with diethyl ether, and concentrated under reduced pressure. The mixture was diluted with THF (3 mL), allowed to cool to 0 ˚C, and a 3 M aquious solution of NaOH (2 mL) was added, followed by 30% H_2O_2 (1.0 mL), dropwise. The mixture was allowed to warm to room temperature, and was allowed to stir for 4 h. The mixture was allowed to cool to 0 ˚C and a satirated solution of aqueous $Na_2S_2O_3$ (3 mL) was added dropwise. The mixture was allowed to warm to room temperature and the product was extracted from the aqueous layer with ethyl acetate (3 x 20 mL). The combined organic layers were dried with Na_2SO_4, filtered, and concentrated under reduced pressure, and subsequently purified by silica gel chromatography to afford the desired products.

2.9.2.5 Characterization of Conjunctive Coupling Products and Determination of Stereochemical Identity



(R)*-1,2-Diphenylethan-1-ol (2.117).** The reaction was performed according to the general procedure ***(Method A) with vinylboronic pinacol ester (**2.81**) (42.0 mg, 0.30 mmol, 1.00 equiv), phenyllithium (0.167 mL, 1.9M in dibutyl ether, 0.30 mmol, 1.00 equiv), phenyltrifluoromethanesulfonate (74.60 mg, 0.33 mmol, 1.10 equiv),

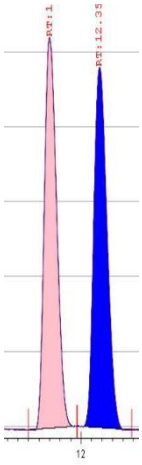
palladium (II) acetate (0.670 mg, 0.003 mmol, 0.010 equiv), (S_p,S_p)-**2.101** (3.80 mg, 0.0036 mmol, 0.012 equiv) in THF (1.2 mL, 0.25 M). The unpurified mixture was purified by silica gel chromatography (5% ethyl acetate in hexanes, stain in CAM) to afford white solid (49.37 mg, 83% yield). **^{1}H NMR** (600 MHz, $CDCl_3$) δ 7.26-7.21 (4H, m), 7.20-7.15 (3H, m), 7.14-7.0 (1H, m), 7.10-7.07 (2H, m), 4.78 (1H, ddd, *J* = 6.6, 4.2, 2.4 Hz), 2.93 (1H, dd, *J* = 13.8, 4.8 Hz), 2.87 (1H, dd, *J* = 14.4, 9.0 Hz), 1.84 (1H, br s). **^{13}C NMR** (150 MHz, $CDCl_3$) δ 143.95, 138.17, 129.66, 128.66, 128.56, 127.76, 126.77, 126.04, 75.49, 46.25. **HRMS** (DART) for $C_{14}H_{13}$ $[M+H-H_2O]^+$ calculated: 181.1017, found: 181.1021. **$[\alpha]^{20}_D$**: +11.787 (*c* 0.635, $CHCl_3$, *l* =50 mm) (lit: **$[\alpha]^{20}_D$** = +12.5 (*c* 1.01, $CHCl_3$, 98:2 er).[70]

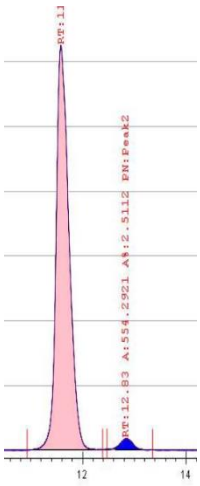
Determination of Stereochemical Identity: Racemic compound was prepared according to the general procedure (***Method A***) with 4,4,5,5-tetramethyl-2-vinyl-1,3,2-dioxaborolane, and $Pd(OAc)_2$ (5 mol%) and 1,1′-Bis(dicyclohexyl-phosphino)ferrocene (6 mol%) as the catalyst. Absolute stereochemistry was determined by single crystal X-ray diffraction.

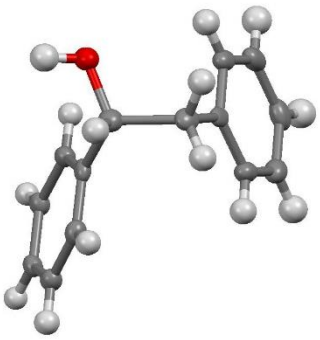
SFC (Chiracel OD-H, 5% IPA, 3 mL/min, 100 bar, 35 °C, 210-270 nm) – analysis of (R)-1,2-diphenylethan-1-ol

Racemic Material Standard Conditions Crystal Structure

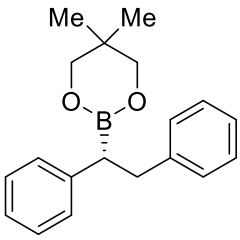
[70] Guo, J.; Chen, J.; Lu, Z. *Chem. Commun.* **2015**, 51, 5725.





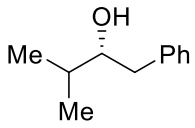


Peak No	% Area	Area	RT (min)	Peak No	% Area	Area	RT (min)
1	50.2599	8450.5728	11.4	1	97.4888	21518.079	11.58
2	49.7401	8363.1658	12.35	2	2.5112	554.2921	12.83
Total:	100	16813.7386		Total:	100	22072.3711	



(R)*-2-(1,2-Diphenylethyl)-5,5-dimethyl-1,3,2-dioxaborinane (2.272).** The reaction was performed according to the general procedure ***(Method A) without oxidation step with 5,5-dimethyl-2-vinyl-1,3,2-dioxaborinane (**2.81**) (42.0 mg, 0.30 mmol, 1.00 equiv), phenyllithium (0.167 mL, 1.9M in dibutyl ether, 0.30 mmol, 1.00 equiv), phenyltrifluoromethanesulfonate (74.60 mg, 0.33 mmol, 1.10 equiv), palladium (II) acetate (0.670 mg, 0.003 mmol, 0.010 equiv), (S_p,S_p)-**2.101** (3.80 mg, 0.0036 mmol, 0.012 equiv) in THF (1.2 mL, 0.25 M). The unpurified mixture was purified by silica gel chromatography (30% CH_2Cl_2 in pentane, stain in CAM) to afford colorless solid (67.0 mg, 76% yield). **^{1}H NMR** (600 MHz, $CDCl_3$) δ 7.25-7.24 (4H, m), 7.24-7.19 (2H, m), 7.16 (2H, d, J = 7.85 Hz), 7.14-7.10 (2H, m), 3.53 (4H, s), 3.19 (1H, dd, J = 13.2, 9.6 Hz), 2.92 (1H, dd, J = 13.8, 7.2 Hz), 2.57 (1H, t, J = 7.2 Hz), 0.79 (6H, s). **^{11}B NMR** (160 MHz, $CDCl_3$)

δ 29.47. **^{13}C NMR** (150 MHz, $CDCl_3$) δ 143.96, 142.55, 128.98, 128.42, 128.40, 128.19, 125.71, 125.31, 72.27, 38.52, 31.79, 21.88. **IR** (neat) ν_{max} 3081.9 (w), 3025.2 (w), 2960.3 (w), 1599.6 (w), 1475.8 (m), 1376.3 (m), 1279.3 (m), 1199.7 (s), 1069.8 (s), 770.6 (m), 696.9 (s), 524.5 (m), 493.4 (m) cm^{-1}. **HRMS** (DART) for $C_{19}H_{24}BO_2$ $[M+H]^+$ calculated: 295.1869, found: 295.1872. **$[\alpha]^{20}_D$**: -48.214 (*c* 2.975, $CHCl_3$, *l* =50 mm).

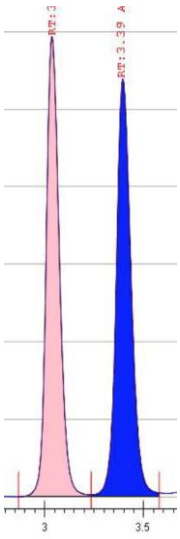


(R)*-3-Methyl-1-phenylbutan-2-ol (2.119).** The reaction was performed according to the general procedure **(*Method A) with 5,5-dimethyl-2-vinyl-1,3,2-dioxaborinane (**2.81**) (42.0 mg, 0.30 mmol, 1.0 equiv), isopropyllithium (0.441 mL, 0.68M in pentane, 0.30 mmol, 1.0 equiv), phenyltrifluoromethanesulfonate (74.60 mg, 0.33 mmol, 1.1 equiv), palladium (II) acetate (0.670 mg, 0.003 mmol, 0.01), (S_p,S_p)-**2.101** (3.80 mg, 0.0036 mmol, 0.012 equiv) in THF (1.2 mL, 0.25 M). The unpurified mixture was purified by silica gel chromatography (30% CH_2Cl_2 in hexanes) to afford yellow oil. (32.5 mg, 66% yield). **^{1}H NMR** (600 MHz, $CDCl_3$) δ 7.30 (2H, t, *J* = 7.2 Hz), 7.21-7.24 (3H, m), 3.57-3.59 (1H, m), 2.84 (1H, dd, *J* = 13.8, 3.0 Hz), 2.32 (1H, dd, *J* = 13.2, 9.0 Hz,), 1.77-1.72 (1H, m), 1.42 (1H, d, *J* = 3.6 Hz), 0.99 (3H, s), 0.98 (3H, s). **^{13}C NMR** (150 MHz, $CDCl_3$) δ 139.39, 129.59, 128.82, 126.62, 77.72, 41.02, 33.37, 19.16, 17.64. **IR** (neat) ν_{max} 3241 (br), 3027 (w), 2957 (m), 2927 (m), 2981 (m), 1494 (m), 1467 (m), 1031 (m), 995 (s) 741 (m), 698 (s) cm^{-1}. **HRMS** (DART) for $C_{11}H_{20}NO$ $[M+NH_4]^+$: calculated: 182.1545, found: 182.1547. **$[\alpha]^{20}_D$**: +15.74 (*c* 0.535, $CHCl_3$, *l* = 50 mm).

Determination of Stereochemical Identity: Racemic compound was prepared according to the general procedure ***(Method A)*** with 4,4,5,5-tetramethyl-2-vinyl-1,3,2-dioxaborolane, and $Pd(OAc)_2$ (5 mol%) and 1,1'-Bis(dicyclohexyl-phosphino)ferrocene (6 mol%) as the catalyst. Absolute stereochemistry was assigned by analogy (see products **2.83, 2.117,** and **2.120**).

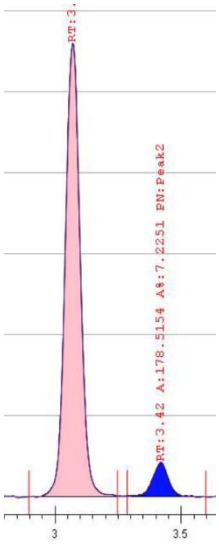
SFC (Chiracel OD-H, 5% IPA, 3 mL/min, 100 bar, 35°C, 210-270 nm) – analysis of (R)-3-methyl-1-phenylbutan-2-ol.

Racemic Material

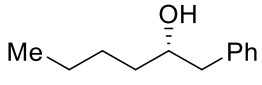


Peak No	% Area	Area	RT (min)
1	49.2988	5449.2883	3.04
2	50.7012	5604.3147	3.39
Total:	100	11053.603	

Standard Conditions



Peak No	% Area	Area	RT (min)
1	92.7749	2292.2693	3.07
2	7.2251	178.5154	3.42
Total:	100	2470.7847	



(S)*-1-Phenylhexan-2-ol (2.83).** The reaction was performed according to the general procedure ***(Method A) with 5,5-dimethyl-

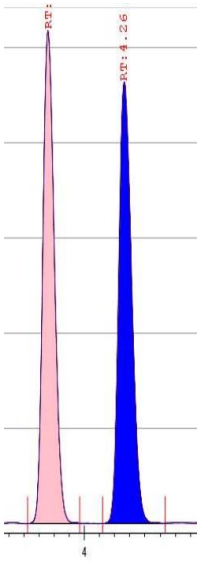
2-vinyl-1,3,2-dioxaborinane (**2.81**) (42.0 mg, 0.30 mmol, 1.00 equiv), *n*-butyllithium (0.120 mL, 2.5M in hexanes, 0.30 mmol, 1.00 equiv), phenyltrifluoromethanesulfonate (74.60 mg, 0.33 mmol, 1.10 equiv), palladium (II) acetate (0.670 mg, 0.003 mmol, 0.010 equiv), (S_p,S_p)-**2.101** (3.80 mg, 0.0036 mmol, 0.012 equiv) in THF (1.2 mL, 0.25 M). The unpurified mixture was purified by silica gel chromatography (50% CH_2Cl_2 in pentane, stain in CAM) to afford colorless oil (39.5 mg, 74 % yield). **^{1}H NMR** (600 MHz, $CDCl_3$) δ 7.30 (2H, t, *J* = 7.2 Hz), 7.24-7.18 (3H, m), 3.80 (1H, dddd, *J* = 12.6, 8.4, 4.8 Hz), 2.82 (1H, dd, *J* = 13.2, 4.2 Hz), 2.63 (1H, dd, *J* = 13.2, 8.4 Hz). 1.56-1.28 (6H, m), 0.90 (3H, t, *J* = 7.2 Hz). **^{13}C NMR** (150 MHz, $CDCl_3$) δ 138.80, 129.57, 128.69, 126.57, 72.84, 44.20, 36.68, 28.08, 22.85, 14.21. **HRMS** (DART) for $C_{12}H_{17}$ $[M+H-H_2O]^+$ calculated: 161.1330, found: 161.1335. **$[\alpha]^{20}_D$**: +14.786 (*c* 0.510, $CHCl_3$, *l* =50 mm). (lit: **$[\alpha]^{28}_D$**: +6.3, *c* 1.0, $CHCl_3$, 68:32 er).[71]

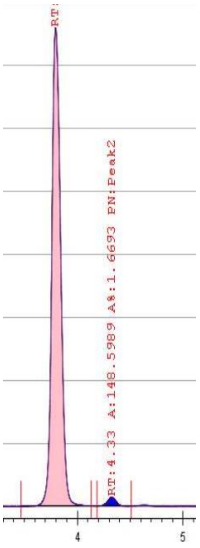
Determination of Stereochemical Identity: Racemic compound was prepared according to the general procedure (***Method A***) with 4,4,5,5-tetramethyl-2-vinyl-1,3,2-dioxaborolane, and $Pd(OAc)_2$ (5 mol%) and 1,1′-Bis(dicyclohexyl-phosphino)ferrocene (6 mol%) as the catalyst. Absolute stereochemistry was determined by comparison to the literature.[67]

SFC (Chiracel OD-H, 5% IPA, 3 mL/min, 100 bar, 35 °C, 210-270 nm) – analysis of (R)-1,2-diphenylethan-1-ol

Racemic Material Standard Conditions

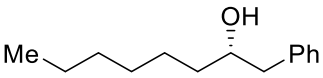
[71] Ema, T.; Ura, N.; Yoshii, M.; Korenaga, T.; Sakai, T. *Tetrahedron* **2009**, 65. 9583.





Peak No	% Area	Area	RT (min)
1	49.8946	5442.8203	3.76
2	50.1054	5465.8191	4.26
Total:	100	10908.6394	

Peak No	% Area	Area	RT (min)
1	98.3307	8753.1054	3.79
2	1.6693	148.5989	4.33
Total:	100	8901.7043	



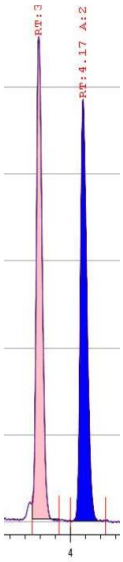
(S)*-1-Phenyloctan-2-ol (2.120).** The reaction was performed according to the general procedure ***(Method A) with 5,5-dimethyl-2-vinyl-1,3,2-dioxaborinane (**2.81**) (42.0 mg, 0.30 mmol, 1.00 equiv), hexyllithium (0.130 mL, 2.3M in hexanes, 0.30 mmol, 1.00 equiv), phenyltrifluoromethanesulfonate (74.60 mg, 0.33 mmol, 1.10 equiv), palladium (II) acetate (0.670 mg, 0.003 mmol, 0.010 equiv), (S_p,S_p)-**2.101** (3.80 mg, 0.0036 mmol, 0.012 equiv) in THF (1.2 mL, 0.25 M). The unpurified mixture was purified by silica gel chromatography (50% CH_2Cl_2 in pentane, stain in CAM) to afford white solid (47.0 mg, 76% yield. **HRMS** (DART) for $C_{14}H_{26}NO$ $[M+NH_4]^+$ calculated: 224.2014, found:

224.2016. $[\alpha]^{20}_{D}$: +11.444 (*c* 1.645, $CHCl_3$, *l* =50 mm). (lit: $[\alpha]^{20}_{D}$: +8.222 (*c* 2.043, $CHCl_3$, *l* = 50 mm 96:4 er). All spectral data was in accord with the literature.[72]

Determination of Stereochemical Identity: Racemic compound was prepared according to the literature. Absolute stereochemistry was determined by comparison to the literature.[68]

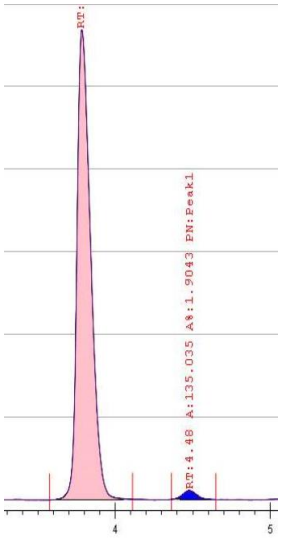
SFC (Chiracel OD-H, 3% IPA, 5 mL/min, 100 bar, 35 °C, 210-270 nm) – analysis of (S)-1-phenyloctan-2-ol

Racemic Material



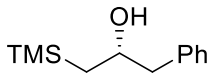
Peak No	% Area	Area	RT (min)
1	50.7244	2991.7195	3.58
2	49.2756	2906.2689	4.17
Total:	100	5897.9884	

Standard Conditions



Peak No	% Area	Area	RT (min)
1	98.0957	6956.0252	3.78
2	1.9043	135.035	4.48
Total:	100	7091.0602	

[72] Mlynarski, S. N.; Schuster, C. H.; Morken, J. P. *Nature* **2014**, 505, 386.

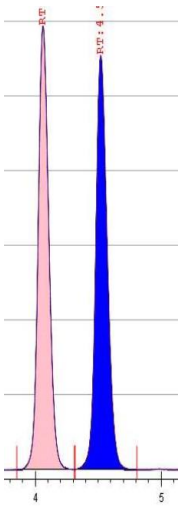


(R)*-1-Phenyl-3-(trimethylsilyl)propan-2-ol (2.121).** The reaction was performed according to the general procedure ***(Method A) with vinylboronic acid pinacol ester (46.20 mg, 0.30 mmol, 1.00 equiv), (trimethylsilyl)methyllithium (0.300 mL, 1.0M in pentane, 0.30 mmol, 1.00 equiv), phenyltrifluoromethanesulfonate (74.6 mg, 0.33 mmol, 1.10 equiv), palladium (II) acetate (0.670 mg, 0.003 mmol, 0.010 equiv), (S_p,S_p)-**2.101** (3.80 mg, 0.0036 mmol, 0.012 equiv) in THF (1.2 mL, 0.25 M). The unpurified mixture was purified by silica gel chromatography (5% ethyl acetate in pentane, stain in CAM) to afford colorless oil (35.20 mg, 56% yield). **^{1}H NMR** (600 MHz, $CDCl_3$) δ 7.30 (2H, t, J = 7.2 Hz), 7.24-7.18 (3H, m), 3.98 (1H, ddd, J = 13.2, 13.2, 9.0 Hz), 2.84 (1H, dd, J = 13.8, 4.2 Hz), 2.63 (1H, dd, J = 13.2, 7.8 Hz), 1.44 (1H, br s), 0.96-0.86 (2H, m), 0.06 (9H, s). **^{13}C NMR** (150 MHz, $CDCl_3$) δ 138.98, 129.56, 128.73, 126.63, 71.08, 47.70, 25.99, -0.57. **IR** (neat) ν_{max} 3582.1 (br), 3441.2 (br) 3062.7 (w), 3028.2 (w), 2951.4 (w), 2917.7 (w), 1495.6 (w), 1454.0 (w), 1247.0 (s), 1076.0 (m), 1056.2 (m), 1018.7 (m), 854.8 (s), 837.4 (s), 743.8 (s), 698.5 (s) cm^{-1}. **HRMS** (DART) for $C_{12}H_{24}NOSi$ $[M+NH_4]^+$ calculated: 226.1627, found 226.1622. **$[\alpha]^{20}_D$**: +3.850 (*c* 1.135, $CHCl_3$, *l* =50 mm).

Determination of Stereochemical Identity: Racemic compound was prepared according to the general procedure (***Method A***) with 4,4,5,5-tetramethyl-2-vinyl-1,3,2-dioxaborolane, and $Pd(OAc)_2$ (5 mol%) and 1,1′-Bis(dicyclohexylphosphino)ferrocene (6 mol%) as the catalyst. Absolute stereochemistry was assigned by analogy (see products **2.83, 2.117,** and **2.120**).

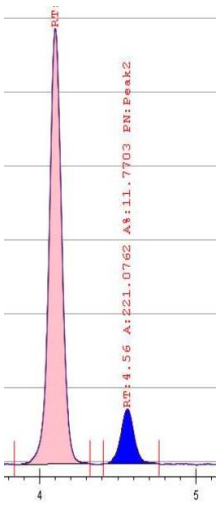
SFC (Chiracel OD-H, 2% IPA, 3 mL/min, 100 bar, 35 °C, 210-270 nm) – analysis of (R)-1-phenyl-3-(trimethylsilyl)propan-2-ol.

Racemic Material

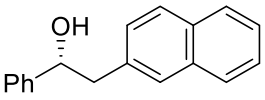


Peak No	% Area	Area	RT (min)
1	49.9308	3484.2905	4.06
2	50.0692	3493.9499	4.52
Total:	100	6978.2404	

Standard Conditions



Peak No	% Area	Area	RT (min)
1	88.2297	1657.1827	4.1
2	11.7703	221.0762	4.56
Total:	100	1878.2589	



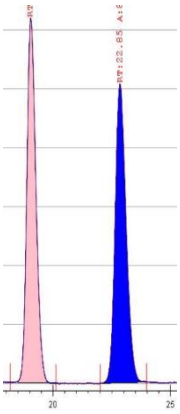
(R)*-2-(Naphthalen-2-yl)-1-phenylethan-1-ol (2.122).** The reaction was performed according to the general procedure ***(Method A) with 5,5-dimethyl-2-vinyl-1,3,2-dioxaborinane (**2.81**) (42.0 mg, 0.30 mmol, 1.00 equiv), phenyl lithium (0.167 mL, 1.9M in dibutyl ether, 0.30 mmol, 1.00 equiv), 2-naphthyltrifluoromethanesulfonate (91.20 mg, 0.33 mmol, 1.10 equiv), palladium (II) acetate (0.670 mg, 0.003 mmol, 0.010 equiv), (S_p,S_p)-**2.101** (3.8 mg, 0.0036 mmol, 0.012 equiv) in THF (1.2 mL, 0.25 M). The unpurified mixture was purified by silica gel chromatography (50% CH_2Cl_2 in pentane, stain in CAM) to afford white solid (50.70 mg, 68% yield). **^{1}H NMR** (600 MHz, $CDCl_3$) δ 7.81 (1H, d, J = 6.6 Hz), 7.78 (1H, d, J = 8.4

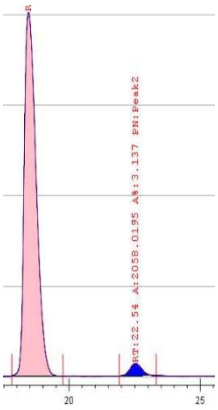
Hz), 7.48-7.42 (2H, m), 7.38 (2H, d, *J* = 7.2 Hz) 7.30-7.26 (4H, m) 4.99 (1H, ddd, *J* = 7.8, 4.2, 2.4 Hz), 3.20 (1H, dd, *J* = 14.4, 4.8 Hz), 3.15 (1H, dd, *J* = 13.8, 9.0 Hz), 1.99 (1H, d, *J* = 3.0 Hz). **^{13}C NMR** (150 MHz, $CDCl_3$) δ 143.94, 135.68, 133.67, 132.48, 128.61, 128.27, 128.23, 127.92, 127.80, 127.79, 127.71, 126.20, 126.05, 125.69, 75.37, 46.42. **IR** (neat) ν_{max} 3365.3 (br), 3056.4 (w), 3029.5 (w), 2912.3 (w), 1631.0 (w), 1528.0 (w), 1454.0 (w), 1199.7 (w), 1055.4 (m), 1012.9 (m), 811.1 (s), 747.7 (m), 724.3 (m), 699.4 (s) 478.4 (m) cm^{-1}. **HRMS** (DART) for $C_{18}H_{15}$ $[M+H-H_2O]^+$ calculated: 231.1174, found 231.1167. **$[\alpha]^{20}_D$**: -2.8194 (*c* 0.770, $CHCl_3$, *l* =50 mm).

Determination of Stereochemical Identity: Racemic compound was prepared according to the general procedure (***Method A***) with 4,4,5,5-tetramethyl-2-vinyl-1,3,2-dioxaborolane, and $Pd(OAc)_2$ (5 mol%) and 1,1′-Bis(dicyclohexyl-phosphino)ferrocene (6 mol%) as the catalyst. Absolute stereochemistry was assigned by analogy (see products **2.83**, **2.117**, and **2.120**).

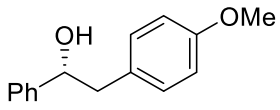
SFC (Chiracel OD-H, 10% IPA, 3 mL/min, 100 bar, 35 °C, 210-270 nm) – analysis of (R)-2-(naphthalen-2-yl)-1-phenylethan-1-ol.

Racemic Material Standard Conditions





Peak No	% Area	Area	RT (min)	Peak No	% Area	Area	RT (min)
1	50.215	8280.1194	19.03	1	96.863	63545.7182	18.44
2	49.785	8209.2224	22.85	2	3.137	2058.0195	22.54
Total:	100	16489.3418		Total:	100	65603.7377	



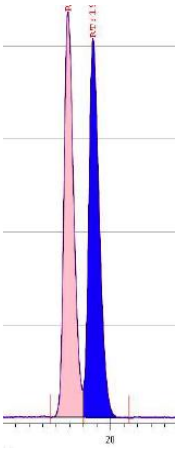
(R)*-2-(4-Methoxyphenyl)-1-phenylethan-1-ol (2.123).** The reaction was performed according to the general procedure (Method A***) with 5,5-dimethyl-2-vinyl-1,3,2-dioxaborinane (**2.81**) (42.0 mg, 0.30 mmol, 1.00 equiv), phenyl lithium (0.167 mL, 1.9M in dibutyl ether, 0.30 mmol, 1.00 equiv), 4-methoxyphenyl trifluoromethanesulfonate (84.5 mg, 0.33 mmol, 1.10 equiv), palladium (II) acetate (0.67 mg, 0.003 mmol, 0.01 equiv), and (S_p,S_p)-**2.101** (3.8 mg, 0.0036 mmol, 0.012 equiv) in THF (1.2 mL, 0.25 M). The unpurified mixture was purified by silica gel chromatography (10% ethyl acetate in hexanes) to afford colorless oil (57.4 mg, 84% yield). **^{1}H NMR** (600 MHz, $CDCl_3$) δ 7.34-7.31 (4H, m), 7.28-7.24 (1H, m), 7.09 (2H, d, J = 9.0 Hz), 6.83 (2H, d, J = 8.4 Hz), 4.84 (1H, ddd, J = 7.8, 4.8, 2.4 Hz), 3.78 (3H, s), 2.98 (1H, dd, J = 13.8, 4.8 Hz), 2.91 (1H, dd, J= 14.4, 9.0 Hz), 1.97 (1H, s); **^{13}C NMR** (150 MHz, $CDCl_3$) δ 158.6, 144.0, 130.6, 130.1, 128.6, 127.7, 126.0, 114.1, 75.6, 55.4, 45.3; **IR** (neat) ν_{max} 3407.9 (br), 2999.5 (m), 2834.9 (m), 1611.0 (m), 1583.6 (w), 1510.0 (s), 1453.3 (m),

1242.4 (s), 1176.6 (m), 1031.5 (s), 820.1 (m), 699.1 (s) cm^{-1}; **HRMS** (DART) for: $C_{15}H_{15}O_1$ $[M+H-H_2O]^+$: calculated: 211.1123, found: 211.1130. **$[\alpha]_D^{20}$**: 4.081 (*c* 1.470, $CHCl_3$, *l* = 50 mm).

Determination of Stereochemical Identity: Racemic compound was prepared according to the general procedure (***Method A***) with 4,4,5,5-tetramethyl-2-vinyl-1,3,2-dioxaborolane, and $Pd(OAc)_2$ (5 mol%) and 1,1′-Bis(dicyclohexyl-phosphino)ferrocene (6 mol%) as the catalyst. Absolute stereochemistry was assigned by analogy (see products **2.83**, **2.117**, and **2.120**).

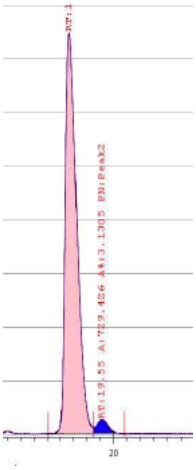
SFC (Chiracel OD-H, 5% IPA, 3 mL/min, 100 bar, 35 °C, 210-270 nm) – analysis of (R)-2-(4-methoxyphenyl)-1-phenylethan-1-ol

Racemic Material

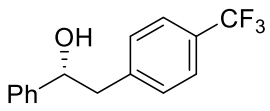


Peak No	% Area	Area	RT (min)
1	49.8369	5531.1911	18.43
2	50.1631	5567.3946	19.35
Total:	100	11098.5857	

Standard Conditions



Peak No	% Area	Area	RT (min)
1	96.8695	22571.4586	18.31
2	3.1305	729.426	19.55
Total:	100	23300.8846	

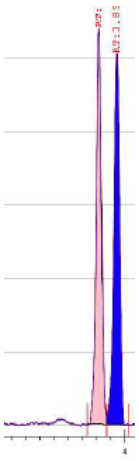


(R)*-1-Phenyl-2-(4-(trifluoromethyl)phenyl)ethan-1-ol (2.124).** The reaction was performed according to the general procedure (Method A***) with 5,5-dimethyl-2-vinyl-1,3,2-dioxaborinane (**2.81**) (42.0 mg, 0.30 mmol, 1.00 equiv), phenyl lithium (0.167 mL, 1.9M in dibutyl ether, 0.30 mmol, 1.00 equiv), 4-(trifluoromethyl)phenyl trifluoromethanesulfonate (**2.266**) (97.1 mg, 0.33 mmol, 1.10 equiv), palladium (II) acetate (0.67 mg, 0.003 mmol, 0.01 equiv), and (S_p,S_p)-**2.101** (3.8 mg, 0.0036 mmol, 0.012 equiv) in THF (1.2 mL, 0.25 M). The unpurified mixture was purified by silica gel chromatography (5% ethyl acetate in hexanes) to afford colorless oil (40.9 mg, 51% yield). **^{1}H NMR** (600 MHz, $CDCl_3$) δ 7.52 (2H, d, J = 8.4 Hz), 7.36-7.27 (6H, m), 4.90 (1H, ddd, *J* = 8.4, 5.4, 3.0 Hz), 3.08 (1H, dd, *J* = 13.2, 7.2 Hz), 3.05 (1H, dd, *J*= 13.2, 5.4 Hz), 1.92 (1H, s). **^{13}C NMR** (150 MHz, $CDCl_3$) δ 143.6, 142.4, 130.1, 129.2, 128.9, 128.7, 128.1, 126.0, 125.4 (q, *J* = 3.5 Hz), 75.3, 45.7. **IR** (neat) ν_{max} 3343.5 (br), 2928.8 (w), 1618.3 (w), 1494.5 (m), 1417.9 (m), 1322.6 (s), 1237.4 (m), 1161.6 (m), 1119.4 (s), 1108.1 (s), 1019.1 (m), 841.8 (m), 700.1 (m), 650.7 (m) cm^{-1}. **HRMS** (DART) for: $C_{15}H_{12}F_3$ $[M+H-H_2O]^+$: calculated: 249.0891, found: 249.0900. **$[\alpha]_D^{20}$**: 5.360 (*c* 1.535, $CHCl_3$, *l* = 50 mm).

Determination of Stereochemical Identity: Racemic compound was prepared according to the general procedure (***Method A***) with 4,4,5,5-tetramethyl-2-vinyl-1,3,2-dioxaborolane, and $Pd(OAc)_2$ (5 mol%) and 1,1′-Bis(dicyclohexyl-phosphino)ferrocene (6 mol%) as the catalyst. Absolute stereochemistry was assigned by analogy (see products **2.83**, **2.117**, and **2.120**).

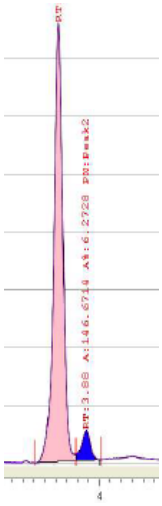
SFC (Chiracel OD-H, 5% IPA, 3 mL/min, 100 bar, 35 °C, 210-270 nm) – analysis of (R)-1-phenyl-2-(4-(trifluoromethyl)phenyl)ethan-1-ol

Racemic Material

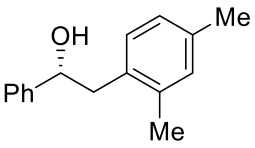


Peak No	% Area	Area	RT (min)
1	50.473	557.993	3.64
2	49.527	547.5345	3.89
Total:	100	1105.5275	

Standard Conditions



Peak No	% Area	Area	RT (min)
1	93.7272	2191.5358	3.63
2	6.2728	146.6714	3.88
Total:	100	2338.2072	



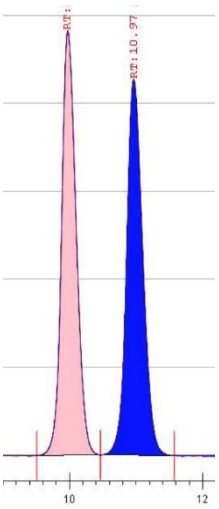
(R)*-2-(2,4-Dimethylphenyl)-1-phenylethan-1-ol (2.125).** The reaction was performed according to the general procedure ***(Method A, slight modification at 80 °C) with 5,5-dimethyl-2-vinyl-1,3,2-dioxaborinane (**2.81**) (42.0 mg, 0.30 mmol, 1.0 equiv), phenyllithium (0.167 mL, 1.9M in dibutyl ether, 0.30 mmol, 1.0 equiv), 2,4-dimethylphenyl trifluoromethanesulfonate (**2.267**) (83.90 mg, 0.33 mmol, 1.1 equiv), palladium (II) acetate (0.670 mg, 0.003 mmol, 0.01 equiv), (S_p,S_p)-**2.101** (3.80 mg, 0.0036 mmol, 0.012) in THF (1.2 mL, 0.25 M). The unpurified mixture was purified by silica gel chromatography (40% CH_2Cl_2 in hexanes) to

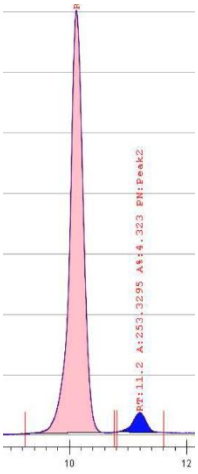
afford colorless oil. (34.6 mg, 51% yield). **^{1}H NMR** (600 MHz, $CDCl_3$) δ 7.33-7.37 (4H, m), 7.27 (1H, t, *J* = 7.2 Hz), 7.04 (1H, d, *J* = 7.8 Hz), 6.98 (1H, s), 6.95 (1H, d, *J* = 7.8 Hz), 4.86-4.86 (1H, m), 3.00 (1H, dd, *J* = 14.4, 4.2 Hz), 2.94 (1H, dd, *J* = 13.8, 9.0 Hz), 2.29 (3H, s), 2.26 (3H, s), 1.92 (1H, d, *J* = 2.4 Hz); **^{13}C NMR** (150 MHz, $CDCl_3$) δ 144.4, 136.8, 136.5, 133.3, 131.5, 130.4, 128.6, 127.7, 126.9, 125.9, 74.6, 43.2, 21.1, 19.7 **IR** (neat) ν_{max} 3418 (br), 3027 (w), 3004 (w), 2921 (m), 2856 (w), 1493 (w), 1451 (m), 1026 (s), 805 (s), 699 (s), 567 (m) cm^{-1}; **HRMS** (DART): for $C_{16}H_{17}$ $[M+H-H_2O]^+$: calculated: 209.1330, found: 209.1329. **$[\alpha]^{20}_D$**: + 3.99 (*c* 0.450, $CHCl_3$, *l* = 50 mm).

Determination of Stereochemical Identity: Racemic compound was prepared according to the general procedure ***(Method A)*** with 4,4,5,5-tetramethyl-2-vinyl-1,3,2-dioxaborolane, and $Pd(OAc)_2$ (5 mol%) and 1,1'-Bis(dicyclohexyl-phosphino)ferrocene (6 mol%) as the catalyst. Absolute stereochemistry was assigned by analogy (see products **2.83**, **2.117**, and **2.120**).

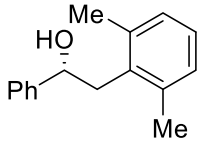
SFC (Chiracel OJ-H, 5% IPA, 3 mL/min, 100 bar, 35°C, 210-270 nm) – analysis of (R)-2-(2,4-dimethylphenyl)-1-phenylethan-1-ol.

Racemic Material Standard Conditions





Peak No	% Area	Area	RT (min)	Peak No	% Area	Area	RT (min)
1	50.3811	7320.6585	9.97	1	95.677	5606.6891	10.12
2	49.6189	7209.9062	10.97	2	4.323	253.3295	11.2
Total:	100	14530.5647		Total:	100	5860.0186	



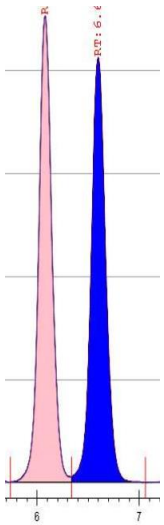
(R)*-2-(2,6-Dimethylphenyl)-1-phenylethan-1-ol (2.126).** The reaction was performed according to the general procedure ***(Method A) with 5,5-dimethyl-2-vinyl-1,3,2-dioxaborinane (**2.81**) (42.0 mg, 0.30 mmol, 1.00 equiv), phenyllithium (0.167 mL, 1.9M in dibutyl ether, 0.30 mmol, 1.00 equiv), 2,6-dimethylphenyl trifluoromethanesulfonate (**2.268**) (83.90 mg, 0.33 mmol, 1.10 equiv), palladium (II) acetate (0.670 mg, 0.003 mmol, 0.010 equiv), (S_p,S_p)-**2.101** (3.80 mg, 0.0036 mmol, 0.012 equiv) in THF (1.2 mL, 0.25 M). The unpurified mixture was purified by silica gel chromatography (30% CH_2Cl_2 in pentane, stain in CAM) to afford white solid (50.50 mg, 44% yield. **^{1}H NMR** (600 MHz, $CDCl_3$) δ 7.38-7.32 (4H, m), 7.30-7.26 (1H, m), 7.07-7.00 (3H, m), 4.91 (1H, ddd, J = 7.8 4.8, 1.8 Hz). 3.15 (1H, dd, J = 13.8, 9.0 Hz), 2.98 (1H, dd, J = 13.8, 4.8 Hz), 2.31 (6H, s), 1.85 (1H, d, J = 2.4 Hz). **^{13}C NMR** (150 MHz, $CDCl_3$) δ 144.64, 137.58, 135.07, 128.58, 128.53, 127.70, 126.64, 125.70, 74.19, 39.96,

20.55. **IR** (neat) ν_{max} 3534.5 (br), 3416.7 (br), 3064.4 (w), 3027.0 (w), 2956.3 (w), 2921.1 (w), 1550.7 (w), 1493.0 (m), 1379.0 (m), 1049.2 (w), 1024.6 (m), 758.0 (s), 700.2 (s) cm^{-1}. **HRMS** (DART) for $C_{16}H_{17}$ $[M+H-H_2O]^+$ calcualted: 209.1330, found: 209.1332. **$[\alpha]^{20}_D$**: +1.419 (*c* 0.435, $CHCl_3$, *l* =50 mm).

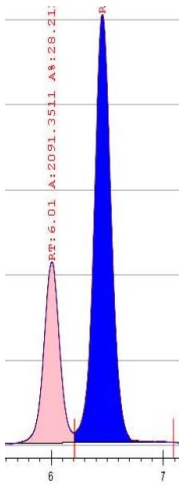
Determination of Stereochemical Identity: Racemic compound was prepared according to the general procedure (***Method A***) with 4,4,5,5-tetramethyl-2-vinyl-1,3,2-dioxaborolane, and $Pd(OAc)_2$ (5 mol%) and 1,1′-Bis(dicyclohexylphosphino)ferrocene (6 mol%) as the catalyst. Absolute stereochemistry was assigned by analogy (see products **2.83**, **2.117**, and **2.120**).

SFC (Chiracel OD-H, 8% IPA, 3 mL/min, 150 bar, 35 °C, 210-270 nm) – analysis of (R)-2-(2,6-dimethylphenyl)-1-phenylethan-1-ol.

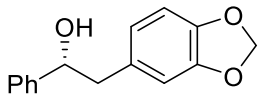
Racemic Material



Standard Conditions



Peak No	% Area	Area	RT (min)	Peak No	% Area	Area	RT (min)
1	49.905	8107.1524	6.08	1	28.2137	2091.3511	6.01
2	50.095	8138.0096	6.6	2	71.7863	5321.1889	6.46
Total:	100	16245.162		Total:	100	7412.54	



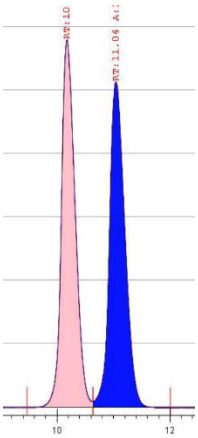
(R)*-2-(Benzo[*d*][1,3]dioxol-5-yl)-1-phenylethan-1-ol (2.128).** The reaction was performed according to the general procedure ***(Method A) with 5,5-dimethyl-2-vinyl-1,3,2-dioxaborinane (**2.81**) (42.0 mg, 0.30 mmol, 1.0 equiv), phenyllithium (0.167 mL, 1.9M in dibutyl ether, 0.30 mmol, 1.0 equiv), benzo[d][1,3]dioxol-5-yl trifluoromethanesulfonate (**2.270**) (88.50 mg, 0.33 mmol, 1.1 equiv), palladium (II) acetate (0.67 mg, 0.003 mmol), (S_p,S_p)-**2.101** (3.8 mg, 0.0036 mmol) in THF (1.2 mL, 0.25 M). The unpurified mixture was purified by silica gel chromatography (5% EtOAc in hexanes) to afford white solid. (35.6 mg, 49% yield). **^{1}H NMR** (600 MHz, $CDCl_3$) δ 7.33 (4H, d, J = 4.8 Hz), 7.25-7.29 (1H, m), 6.72 (1H, d, J = 7.8 Hz), 6.68 (1H, d, J = 1.2 Hz), 6.62 (1H, dd, J = 8.4, 1.8 Hz), 5.91 (2H, s), 4.82 (1H, dd, J = 7.8, 4.2 Hz), 2.94 (1H, dd, J = 13.8, 4.2 Hz), 2.88 (1H, dd, J = 13.8, 8.4 Hz,), 1.99 (1H, brs,); **^{13}C NMR** (150 MHz, $CDCl_3$) δ 147.9, 146.5, 143.9, 131.9, 128.6, 127.8, 126.0, 122.6, 110.0, 108.4, 101.1, 75.6, 45.9; **IR** (neat) ν_{max} 3411 (br), 3062 (w), 3028 (w), 2919 (m), 1607 (w), 1501 (s), 1440 (s), 1243 (s), 1187 (m), 1187 (m), 1036 (s), 928 (s), 699 (s), 537 (m) cm^{-1}; **HRMS** (DART): for $C_{15}H_{13}O_2$ $[M+H-H_2O]^+$: calculated: 225.0915, found: 225.0916. **$[\alpha]^{20}_D$**: + 1.35 (*c* 1.025, $CHCl_3$, *l* = 50 mm).

Determination of Stereochemical Identity: Racemic compound was prepared according to the general procedure ***(Method A)*** with 4,4,5,5-tetramethyl-2-vinyl-1,3,2-dioxaborolane,

$Pd(OAc)_2$ (5 mol%) and 1,1'-Bis(dicyclohexyl-phosphino)ferrocene (6 mol%) as the catalyst. Absolute stereochemistry was assigned by analogy (see products **2.83**, **2.117**, and **2.120**).

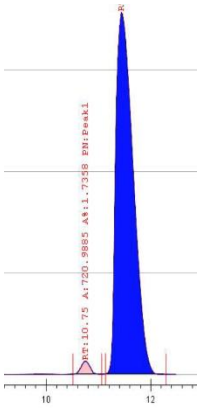
SFC (Chiracel OJ-H, 8% IPA, 3 mL/min, 100 bar, 35°C, 210-270 nm) – analysis of (R)-2-(benzo[d][1,3]dioxol-5-yl)-1-phenylethan-1-ol.

Racemic Material

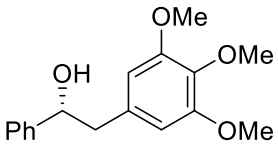


Peak No	% Area	Area	RT (min)
1	50.088	19597.5824	10.18
2	49.912	19528.6842	11.04
Total:	100	39126.2666	

Standard Conditions



Peak No	% Area	Area	RT (min)
1	1.7358	720.9885	10.75
2	98.2642	40816.235	11.44
Total:	100	41537.2235	



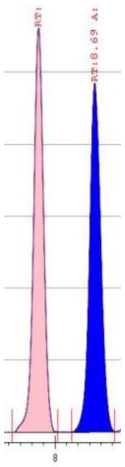
***(R)*-1-Phenyl-2-(3,4,5-trimethoxyphenyl)ethan-1-ol (2.129).** The reaction was performed according to the general procedure *(**Method A**)* with 5,5-dimethyl-2-vinyl-1,3,2-dioxaborinane (**2.81**) (42.0 mg, 0.30 mmol, 1.00 equiv), phenyl lithium (0.167 mL, 1.9M in dibutyl ether, 0.30 mmol, 1.00 equiv), 3,4,5-trimethoxyphenyl trifluoromethanesulfonate (**2.269**). (104.4 mg, 0.33 mmol, 1.10 equiv), palladium (II) acetate (0.670 mg, 0.003 mmol, 0.010 equiv),

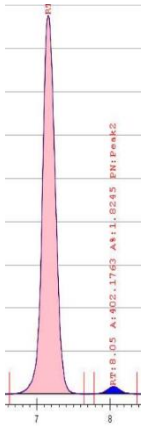
(S_p,S_p)-**2.101** (3.80 mg, 0.0036 mmol, 0.012 equiv) in THF (1.2 mL, 0.25 M). The unpurified mixture was purified by silica gel chromatography (15-20% ethyl acetate in pentane, stain in CAM) to afford white solid (75.20 mg, 87% yield). **^{1}H NMR** (600 MHz, $CDCl_3$) δ 7.37-7.30 (4H, m), 7.28-7.24 (1H, m), 6.35 (2H, s), 4.86 (1H, dd, 8.4, 5.4 Hz), 3.81 (3H, s), 3.78 (6H, s), 2.96 (1H, dd, *J* = 13.8, 5.4 Hz), 2.90 (1H, dd, *J* = 13.2, 7.8 Hz), 2.07 (1H, br s). **^{13}C NMR** (150 MHz, $CDCl_3$) δ 153.26, 143.82, 136.83, 133.64, 128.52, 127.74, 126.05, 106.52, 75.30, 60.95, 56.16, 46.53. **IR** (neat) ν_{max} 3446.9 (br), 3027.2 (w), 2937.9 (w), 2837.3 (w), 1589.0 (m), 1506.9 (m), 1454.5 (m), 1421.1 (m), 1333.8 (w), 1236.7 (m), 1122.1 (s), 1041.9 (w), 1007.9 (m), 701.5 (m) cm^{-1}. **HRMS** (DART) for $C_{17}H_{19}O_3$ $[M+H-H_2O]^+$ calcualted: 271.1334, found: 271.1345. **$[\alpha]^{20}_D$**: +6.128 (*c* 2.890, $CHCl_3$, *l* =50 mm).

Determination of Stereochemical Identity: Racemic compound was prepared according to the general procedure (***Method A***) with 4,4,5,5-tetramethyl-2-vinyl-1,3,2-dioxaborolane, and $Pd(OAc)_2$ (5 mol%) and 1,1′-Bis(dicyclohexylphosphino)ferrocene (6 mol%) as the catalyst. Absolute stereochemistry was assigned by analogy (see products **2.83**, **2.117**, and **2.120**).

SFC (Chiracel OD-H, 10% MeOH, 3 mL/min, 150 bar, 35 °C, 210-270 nm) – analysis of (R)-1-phenyl-2-(3,4,5-trimethoxyphenyl)ethan-1-ol.

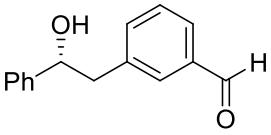
Racemic Material Standard Conditions





Peak No	% Area	Area	RT (min)
1	50.5474	6748.707	7.71
2	49.4526	6602.5431	8.69
Total:	100	13351.2501	

Peak No	% Area	Area	RT (min)
1	98.1755	21641.2099	7.15
2	1.8245	402.1763	8.05
Total:	100	22043.3862	



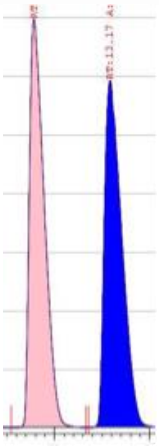
(*R*)-3-(2-Hydroxy-2-phenylethyl)benzaldehyde (2.127). The reaction was performed according to the general procedure (***Method A***) with 4,4,5,5-tetramethyl-2-vinyl-1,3,2-dioxaborolane (46.2 mg, 0.30 mmol, 1.00 equiv) phenyl lithium (0.167 mL, 1.9M in dibutyl ether, 0.30 mmol, 1.00 equiv), 3-formylphenyl trifluoromethanesulfonate. (**2.271**) (83.9 mg, 0.33 mmol, 1.10 equiv), palladium (II) acetate (0.670 mg, 0.003 mmol, 0.01 equiv), (S_p,S_p)-**2.101** (3.80 mg, 0.0036 mmol, 0.012 equiv) in THF (1.2 mL, 0.25 M). The unpurified mixture was purified by silica gel chromatography (20% EtOAc in Hexanes) to afford colorless oil (45 mg, 66% yield). **^{1}H NMR** (600 MHz, $CDCl_3$) δ 9.97 (1H, s), 7.48-7.70 (2H, m), 7.46-7.26 (6H, m), 4.94 (1H, t, J = 6.5 Hz), 3.12-3.10 (2H, m), 1.98 (1H, s). **^{13}C NMR** (125 MHz, $CDCl_3$) δ 192.4, 143.5, 139.3, 136.5, 135.8, 130.6, 129.0, 128.5, 127.9, 125.8, 75.2, 45.4. **IR** (neat) ν_{max} 3423.5 (br), 3062.1 (s), 3029.5 (s), 2922.1 (m), 2850.5 (s), 1691.3 (s), 1603.0 (d), 1451.7 (s), 1241.1 (s), 1143.8 (s), 1048.0 (s), 698.8 (s) cm^{-1}. **HRMS** (DART) for:

$C_{15}H_{18}N_1O_1$ $[M+NH_4]^+$: calculated: 244.1339, found: 244.1338. **$[\alpha]_D^{20}$**: +3.63 (*c* 0.84, $CHCl_3$, *l* =50 mm).

Determination of Stereochemical Identity: Racemic compound was prepared according to the general procedure (***Method A***) with 4,4,5,5-tetramethyl-2-vinyl-1,3,2-dioxaborolane, and $Pd(OAc)_2$ (5 mol%) and 1,1′-Bis(dicyclohexylphosphino)ferrocene (6 mol%) as the catalyst. Absolute stereochemistry was assigned by analogy (see products **2.83**, **2.117**, and **2.120**).

SFC (Chiracel AS-H, 7% IPA, 3 mL/min, 100 bar, 35 °C, 210-270 nm) – analysis of (R)-3-(2-hydroxy-2-phenylethyl)benzaldehyde.

Racemic Material



Peak Info			
Peak No	% Area	Area	RT (min)
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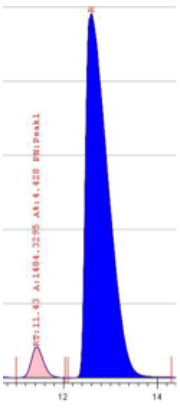
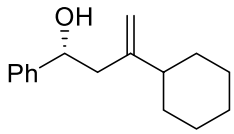
2	50.0872	15144.4606	13.17
Total:	100	30236.1906	

Standard Conditions



Peak Info			
Peak No	% Area	Area	RT (min)
1	4.428	1484.3295	11.43
2	95.572	32037.2605	12.6
Total:	100	33521.59	

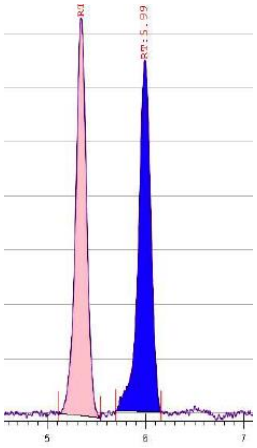


(R)*-3-Cyclohexyl-1-phenylbut-3-en-1-ol (2.132).** The reaction was performed according to the general procedure (Method A***) with 4,4,5,5-tetramethyl-2-vinyl-1,3,2-dioxaborolane (46.2 mg, 0.30 mmol, 1.00 equiv), phenyl lithium (0.167 mL, 1.9M in dibutyl ether, 0.30 mmol, 1.00 equiv), 1-cyclohexylvinyl trifluoromethanesulfonate (**2.262**) (85.2 mg, 0.33 mmol, 1.10 equiv), palladium (II) acetate (0.67 mg, 0.003 mmol, 0.01 equiv), and (S_p,S_p)-**2.101** (3.8 mg, 0.0036 mmol, 0.012 equiv) in THF (1.2 mL, 0.25 M). The unpurified mixture was purified by silica gel chromatography (5% ethyl acetate in hexane) to afford colorless oil (50.2 mg, 73% yield). **^{1}H NMR** (600 MHz, $CDCl_3$) δ 7.38-7.32 (4H, m), 7.27-7.24 (1H, m), 4.93 (1H, t, J = 1.2 Hz), 4.88 (1H, d, J = 0.6 Hz), 4.77 (1H, ddd, J = 10.2, 3.6, 2.4 Hz), 2.50 (1H, ddd, J = 13.8, 3.6, 1.2 Hz), 2.36 (1H, dd, J= 13.2, 9.0 Hz), 2.20 (1H, s), 1.88-1.75 (5H, m), 1.70-1.67 (1H, m), 1.29-1.05 (5H, m). **^{13}C NMR** (150 MHz, $CDCl_3$) δ 152.0, 144.3, 128.5, 127.6, 126.0, 111.1, 71.9, 46.1, 44.0, 32.9, 32.4, 27.0, 26.8, 26.5. **IR** (neat) ν_{max} 3390.4 (br), 2932.5 (s), 2851.3 (m), 1639.0 (m), 1493.6 (m), 1449.2 (m), 1028.4 (m), 888.1 (m), 755.2 (m), 699.0 (s), 556.4 (m) cm^{-1}. **HRMS** (DART) for: $C_{16}H_{21}$ $[M+H-H_2O]^+$: calculated: 213.1643, found: 213.1641. **$[\alpha]_D^{20}$**: +44.267 (*c* 2.140, $CHCl_3$, *l* = 50 mm).

Determination of Stereochemical Identity: Racemic compound was prepared according to the general procedure (***Method A***) with 4,4,5,5-tetramethyl-2-vinyl-1,3,2-dioxaborolane, and $Pd(OAc)_2$ (5 mol%) and 1,1′-Bis(dicyclohexyl-phosphino)ferrocene (6 mol%) as the catalyst. Absolute stereochemistry was assigned by analogy (see products **2.83**, **2.117**, and **2.120**).

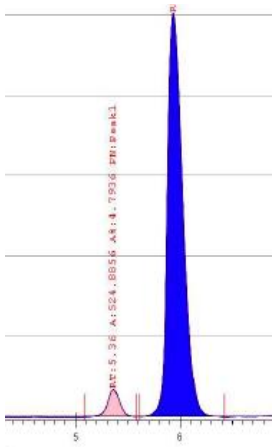
SFC (Chiracel OD-H, 5% IPA, 3 mL/min, 100 bar, 35 °C, 210-270 nm) – analysis of (R)-3-cyclohexyl-1-phenylbut-3-en-1-ol

Racemic Material

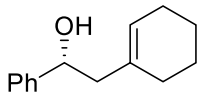


Peak No	% Area	Area	RT (min)
1	50.0769	284.402	5.34
2	49.9231	283.5282	5.99
Total:	100	567.9302	

Standard Conditions



Peak No	% Area	Area	RT (min)
1	4.7936	524.8856	5.36
2	95.2064	10424.8768	5.93
Total:	100	10949.7624	



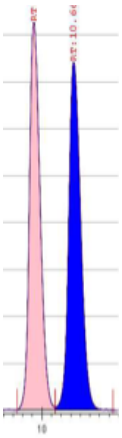
(R)*-2-(Cyclohex-1-en-1-yl)-1-phenylethan-1-ol (2.131)**. The reaction was performed according to the general procedure (Method A***) with 4,4,5,5-tetramethyl-2-vinyl-1,3,2-dioxaborolane (46.2 mg, 0.30 mmol, 1.00 equiv) phenyl lithium (0.167 mL, 1.9M in dibutyl ether, 0.30 mmol, 1.00 equiv), cyclohex-1-en-1-yl trifluoromethanesulfonate (**2.263**) (76.0 mg, 0.33 mmol, 1.10 equiv), palladium (II) acetate (0.670 mg, 0.003 mmol, 0.01 equiv), (S_p,S_p)-**2.101** (3.80 mg, 0.0036 mmol, 0.012 equiv) in THF (1.2 mL, 0.25 M). The unpurified mixture was purified by silica gel chromatography (30% CH_2Cl_2 in pentane) to afford colorless oil (52.3 mg, 86% yield). **^{1}H NMR** (600 MHz, $CDCl_3$) δ 7.39-7.34 (3H, m), 7.28-7.23 (1H, m), 5.60 (1H, s), 4.76 (1H, dd, *J* = 9.0, 4.2 Hz), 2.36 (1H, m), 2.30 (1H, dd, *J* = 18.8, 9.6 Hz), 2.17 (1H, s), 2.09-2.05

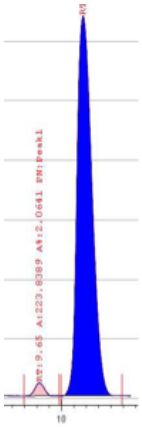
(3H, m), 1.94-1.92 (1H, m), 1.68-1.64 (2H, m), 1.61-1.57 (2H, m). **^{13}C NMR** (125 MHz, CDC_3) δ 144.5, 134.6, 128.5, 127.4, 125.9, 125.9, 71.4, 49.1, 28.4, 25.5, 23.0, 22.4. **IR** (neat) ν_{max} 3406.1 (br), 3028.27 (m), 2922.0 (s), 2922.5 (s), 2855.4 (s), 2833.9 (s), 1493.2 (s) 1451.1 (m), 1050.2 (m), 1006.6 (s), 753.4 (m), 699.0 (s), 547.2 (s) cm^{-1}. **HRMS** (DART) for: $C_{14}H_{17}$ $[M+H-H_2O]^+$: calculated: 185.1330, found: 185.1329. **$[\alpha]_D^{20}$**: +72.35 (*c* 0.74, $CHCl_3$, *l* =50 mm).

Determination of Stereochemical Identity: Racemic compound was prepared according to the general procedure (***Method A***) with 4,4,5,5-tetramethyl-2-vinyl-1,3,2-dioxaborolane, $Pd(OAc)_2$ (5 mol%) and 1,1′-Bis(dicyclohexylphosphino)ferrocene (6 mol%) as the catalyst. Absolute stereochemistry was assigned by analogy (see products **2.83**, **2.117**, and **2.120**).

SFC (Chiracel OD-H, 5% IPA, 3 mL/min, 100 bar, 35 °C, 210-270 nm) – analysis of (R)-2-(cyclohex-1-en-1-yl)-1-phenylethan-1-ol.

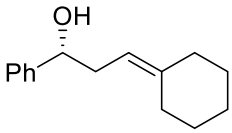
Racemic Material Standard Conditions





Peak Info			
Peak No	% Area	Area	RT (min)
1	49.6784	6384.9152	9.83
2	50.3216	6467.5726	10.66
Total:	100	12852.4878	

Peak Info			
Peak No	% Area	Area	RT (min)
1	2.0641	223.8389	9.65
2	97.9359	10620.284	10.35
Total:	100	10844.1229	



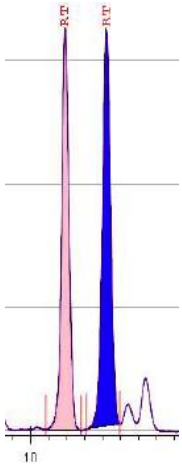
(R)*-3-Cyclohexylidene-1-phenylpropan-1-ol (2.133)**. The reaction was performed according to the general procedure (Method A***) with 4,4,5,5-tetramethyl-2-vinyl-1,3,2-dioxaborolane (46.2 mg, 0.30 mmol, 1.00 equiv), phenyl lithium (0.167 mL, 1.9M in dibutyl ether, 0.30 mmol, 1.00 equiv), cyclohexylidenemethyl trifluoromethanesulfonate (**2.2166**) (80.6 mg, 0.33 mmol, 1.10 equiv), palladium (II) acetate (0.67 mg, 0.003 mmol, 0.01 equiv), and (S_p,S_p)-**2.101** (3.8 mg, 0.0036 mmol, 0.012 equiv) in THF (1.2 mL, 0.25 M). The unpurified mixture was purified by silica gel chromatography (3 % ethyl acetate in hexane) to afford colorless oil (48.5 mg, 75% yield). **^{1}H NMR** (600 MHz, $CDCl_3$) δ 7.36-7.31 (4H, m), 7.26-7.23 (1H, m), 5.01 (1H, t, J = 7.8 Hz), 4.65 (1H, ddd, *J* = 7.8, 4.8, 3.0 Hz), 2.48 (1H, ddd, *J* = 14.4, 7.8, 7.8 Hz), 2.41 (1H, ddd, *J*= 12.6, 6.0, 6.0 Hz), 2.11-2.07 (4H, m), 2.01 (1H, t, *J* = 3.0 Hz), 1.53-1.49 (4H, m), 1.44-1.36 (2H, m); **^{13}C NMR** (150 MHz, $CDCl_3$) δ 144.4, 144.3, 128.5, 127.5, 126.1, 116.4, 74.2, 37.5, 29.1, 28.8, 28.0, 27.0. **IR** (neat) ν_{max} 3343.5 (br), 2923.4 (s), 2851.6 (m), 1494.2

(m), 1447.4 (m), 1266.0 (m), 1232.4 (m), 1027.8 (m), 849.9 (m), 758.2 (m), 698.8 (s), 551.8 (m) cm^{-1}. **HRMS** (DART) for: $C_{15}H_{19}$ $[M+H-H_2O]^+$: calculated: 199.1487, found: 199.1496. $[\alpha]_D^{20}$: +41.066 (*c* 0.540, $CHCl_3$, *l* = 50 mm).

Determination of Stereochemical Identity: Racemic compound was prepared according to the general procedure (***Method A***) with 4,4,5,5-tetramethyl-2-vinyl-1,3,2-dioxaborolane, and $Pd(OAc)_2$ (5 mol%) and 1,1′-Bis(dicyclohexyl-phosphino)ferrocene (6 mol%) as the catalyst. Absolute stereochemistry was assigned by analogy (see products **2.83**, **2.117**, and **2.120**).

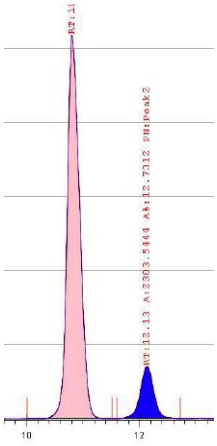
SFC (Chiracel OD-H, 5% IPA, 3 mL/min, 100 bar, 35 °C, 210-270 nm) – analysis of (R)-3-cyclohexylidene-1-phenylpropan-1-ol

Racemic Material

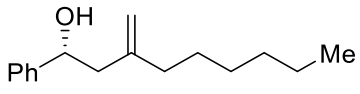


Peak No	% Area	Area	RT (min)
1	47.2345	4658.0381	10.96
2	52.7655	5203.4843	12.11
Total:	100	9861.5224	

Standard Conditions



Peak No	% Area	Area	RT (min)
1	87.2688	15790.1342	10.8
2	12.7312	2303.5444	12.13
Total:	100	18093.6786	

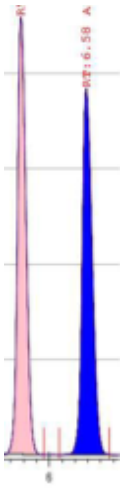


(R)*-3-Methylene-1-phenylnonan-1-ol (2.130)**. The reaction was performed according to the general procedure (Method A***) with 4,4,5,5-tetramethyl-2-vinyl-1,3,2-dioxaborolane (46.2 mg, 0.30 mmol, 1.00 equiv) phenyl lithium (0.167 mL, 1.9M in dibutyl ether, 0.30 mmol, 1.00 equiv), oct-1-en-2-yl trifluoromethanesulfonate (**2.261**) (85.9 mg, 0.33 mmol, 1.10 equiv), palladium (II) acetate (0.670 mg, 0.003 mmol, 0.01 equiv), (S_p,S_p)-**2.101** (3.80 mg, 0.0036 mmol, 0.012 equiv) in THF (1.2 mL, 0.25 M). The unpurified mixture was purified by silica gel chromatography (30% CH_2Cl_2 in pentane) to afford colorless oil (60.0 mg, 86% yield). **^{1}H NMR** (600 MHz, $CDCl_3$) δ 7.39-7.34 (4H, m), 7.29-7.26 (1H, m), 4.94 (1H, s), 4.91 (1H, s), 4.80 (1H, dd, *J* = 1.8, 9.6 Hz), 2.47 (1H, ddd, *J* = 13.8, 4.20 Hz), 2.40 (1H, ddd, *J* = 14.9, 9.6 Hz), 2.17 (1H, d, *J* = 1.8 Hz), 2.08 (1H, t, *J* = 7.8 Hz), 1.51-1.42 (2H, m), 1.34-1.26 (6H, m), 0.90 (3H, t, *J* = 6.6). **^{13}C NMR** (125 MHz, $CDCl_3$) δ 146.7, 144.24, 128.5, 127.6, 125.9, 125.9, 112.9, 71.7, 46.9, 35.9, 31.9, 30.5, 29.2, 29.2, 27.8, 22.8, 14.2. **IR** (neat) ν_{max} 3383.7 (w), 2955.3 (s), 2924.0 (s), 2854.0 (s), 1493.7 (s), 1454.3 (m), 1041.5 (m), 968.8 (s), 755.9 (s), 699.1 (s) cm^{-1}. **HRMS** (DART) for: $C_{16}H_{23}$ $[M+H-H_2O]^+$: calculated: 215.1800, found: 215.1801. **[α]$_D^{20}$**: +36.69 (*c* 1.23, $CHCl_3$, *l* =50 mm).

Determination of Stereochemical Identity: Racemic compound was prepared according to the general procedure (***Method A***) with 4,4,5,5-tetramethyl-2-vinyl-1,3,2-dioxaborolane, and $Pd(OAc)_2$ (5 mol%) and 1,1′-Bis(dicyclohexylphosphino)ferrocene (6 mol%) as the catalyst. Absolute stereochemistry was assigned by analogy (see products **2.83**, **2.117**, and **2.120**).

SFC (Chiracel OD-H, 5% IPA, 3 mL/min, 100 bar, 35 °C, 210-270 nm) – analysis of (R)-3-methylene-1-phenylnonan-1-ol.

Racemic Material



Peak Info			
Peak No	% Area	Area	RT (min)
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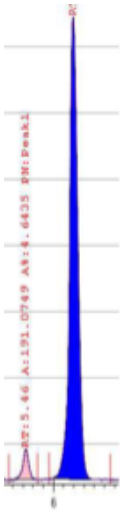
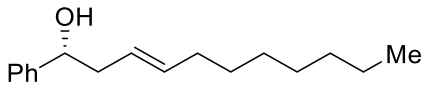
2	49.5693	4158.4116	6.58
Total:	100	8389.0811	

Standard Conditions



Peak Info			
Peak No	% Area	Area	RT (min)
1	4.6435	191.0749	5.46
2	95.3565	3923.7903	6.39
Total:	100	4114.8652	



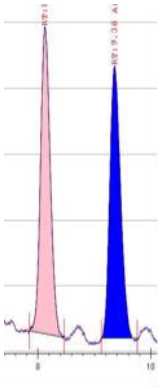
(R,E)*-1-Phenylundec-3-en-1-ol (2.135)**. The reaction was performed according to the general procedure (Method A***) with 4,4,5,5-tetramethyl-2-vinyl-1,3,2-dioxaborolane (46.2 mg, 0.30 mmol, 1.00 equiv) phenyl lithium (0.167 mL, 1.9M in dibutyl ether, 0.30 mmol, 1.00 equiv), (*E*)-non-1-en-1-yl trifluoromethanesulfonate (**2.260**) (90.5 mg, 0.33 mmol, 1.10 equiv), palladium (II) acetate (0.670 mg, 0.003 mmol, 0.01 equiv), (S_p,S_p)-**2.101** (3.80 mg, 0.0036 mmol, 0.012 equiv) in THF (1.2 mL, 0.25 M). The unpurified mixture was purified by silica gel chromatography (30% CH_2Cl_2 in pentane) to afford colorless oil (39.9 mg, 54% yield). **^{1}H NMR** (600 MHz, $CDCl_3$) δ 7.35-7.345 (4H, m), 7.28-7.26 (1H, m), 5.58 (1H,

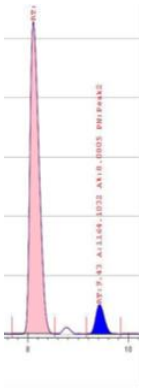
ddd, J = 14.4, 6.6 Hz), 5.40 (1H, ddd, J = 15.6, 7.2 Hz), 4.69-4.67 (1H, m), 2.47 (1H, ddd, J = 10.8, 5.4 Hz), 2.41 (1H, ddd, J = 14.4, 7.8 Hz), 2.07 (1H, s), 2.02 (2H, q, J = 7.2 Hz), 1.37-1.21 (10H, m), 0.89 (3H, t, J = 7.2 Hz,). **^{13}C NMR** (125 MHz, $CDCl_3$) δ 144.2, 135.5, 128.5, 127.5, 126.0, 125.5, 73.6, 43.0, 32.8, 33.0, 29.6, 29.3, 29.3, 14.3. **IR** (neat) ν_{max} 3389.8 (w), 3065.9 (s), 3029.0 (s), 2925.9 (s), 2855.9 (s), 1643.6 (s), 1453.3 (m), 1049.7 (m), 889.7 (s), 698.0 (s) cm^{-1}. **HRMS** (DART) for: $C_{17}H_{25}$ $[M+H-H_2O]^+$: calculated: 229.1956, found: 229.1953**.** **$[\alpha]_D^{20}$**: +26.66 (*c* 0.36, $CHCl_3$, *l* =50 mm).

Determination of Stereochemical Identity: with 4,4,5,5-tetramethyl-2-vinyl-1,3,2-dioxaborolane $Pd(OAc)_2$ (5 mol%) and 1,1′-Bis(dicyclohexylphosphino)ferrocene (6 mol%) as the catalyst. Absolute stereochemistry was assigned by analogy (see products **2.83**, **2.117**, and **2.120**).

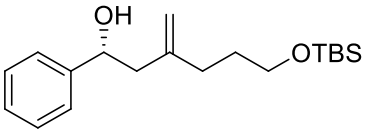
SFC (Chiracel OD-H, 5% IPA, 3 mL/min, 100 bar, 35 °C, 210-270 nm) – analysis of (R,E)-1-phenylundec-3-en-1-ol.

Racemic Material Standard Conditions





Peak Info				Peak Info			
Peak No	% Area	Area	RT (min)	Peak No	% Area	Area	RT (min)
1	50.3629	557.0803	8.12	1	91.9195	13242.1375	8.11
2	49.6371	549.0516	9.36	2	8.0805	1164.1032	9.43
Total:	100	1106.1319		Total:	100	14406.2407	



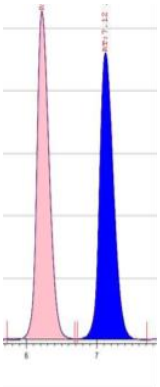
(R)*-6-(*tert*-Butyldimethylsilyloxy)-3-methylene-1-phenylhexan-1-ol (2.134)**. The reaction was performed according to the general procedure (Method A***) with 4,4,5,5-tetramethyl-2-vinyl-1,3,2-dioxaborolane (46.2 mg, 0.30 mmol, 1.00 equiv) phenyl lithium (0.167 mL, 1.9M in dibutyl ether, 0.30 mmol, 1.00 equiv), 5-((*tert*-butyldimethylsilyl)oxy)pent-1-en-2-yl trifluoromethanesulfonate (**2.264**) (115.0 mg, 0.33 mmol, 1.10 equiv), palladium (II) acetate (0.670 mg, 0.003 mmol, 0.01 equiv), (S_p,S_p)-**2.101** (3.80 mg, 0.0036 mmol, 0.012 equiv) in THF (1.2 mL, 0.25 M). The unpurified mixture was purified by silica gel chromatography (3% ethyl acetate in hexanes) to afford clear colorless oil (43.3 mg, 45% yield). **^{1}H NMR** (600 MHz, $CDCl_3$) δ 7.39-7.31 (4H, m), 7.28-7.22 (1H, m), 4.95 (1H, s), 4.92 (1H, s), 4.81 (1H, dd, J = 9.5, 4.1 Hz), 3.63 (2H, t, J = 6.4), 2.37 (1H, dd, J = 14.1, 4.0 Hz), 2.41 (1H, dd, J = 14.1, 9.5 Hz), 2.16-2.12 (3H, m), 1.74-1.64 (2H, m), 0.90 (9H, s), 0.05 (6H, s). **^{13}C NMR** (125 MHz, $CDCl_3$) δ 146.2, 144.2, 128.6, 127.6, 125.9, 113.1,

71.7, 62.8, 47.1, 32.1, 31.0, 47.1, 32.1, 31.0, 26.1, 18.52, -5.1. **IR** (neat) ν_{max} 3438.3(br), 2952.8 (s), 2929.3 (s), 2886.0 (m), 2856.5 (s), 1644.4 (s), 1492.5 (m), 1454.1 (s), 1254.3 (s), 1101.3 (s), 835.4 (s), 775.2 (s), 699.2 (s) cm^{-1}. **HRMS** (DART) for: $C_{19}H_{31}O_1Si_1$ $[M+H-H_2O]^+$: calculated: 303.2144, found: 303.2154. **$[\alpha]_D^{20}$**: +22.00 (*c* 0.26, $CHCl_3$, *l* =50 mm).

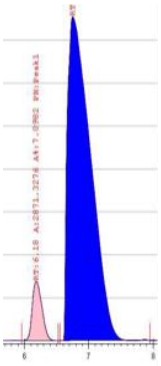
Determination of Stereochemical Identity: Racemic compound was prepared according to the general procedure (***Method A***) with 4,4,5,5-tetramethyl-2-vinyl-1,3,2-dioxaborolane $Pd(OAc)_2$ (5 mol%) and 1,1′-Bis(dicyclohexylphosphino)ferrocene (6 mol%) as the catalyst. Absolute stereochemistry was assigned by analogy (see products **2.83**, **2.117**, and **2.120**).

SFC (Chiracel OD-H, 5% IPA, 3 mL/min, 100 bar, 35 °C, 210-270 nm) – analysis of 6-((tert-butyldimethylsilyl)oxy)-3-methylene-1-phenylhexan-1-ol.

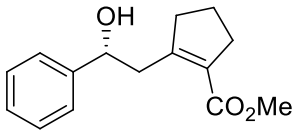
Racemic Material



Standard Conditions



Peak Info				Peak Info			
Peak No	% Area	Area	RT (min)	Peak No	% Area	Area	RT (min)
1	50.0691	3171.9339	6.22	1	7.0982	2871.3276	6.18
2	49.9309	3163.182	7.12	2	92.9018	37580.4402	6.75
Total:	100	6335.1159		Total:	100	40451.7678	

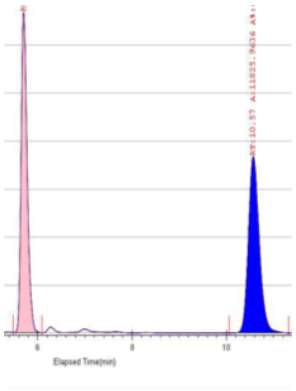


(*R*)-methyl 2-(2-Hydroxy-2-phenylethyl)cyclopent-1-enecarboxylate (2.136). The reaction was performed according to the general procedure (***Method A***) with 4,4,5,5-tetramethyl-2-vinyl-1,3,2-dioxaborolane (46.2 mg, 0.30 mmol, 1.00 equiv) phenyl lithium (0.167 mL, 1.9M in dibutyl ether, 0.30 mmol, 1.00 equiv), 5-hydroxypent-1-en-2-yl trifluoromethanesulfonate (**2.265**) (90.5 mg, 0.33 mmol, 1.10 equiv), palladium (II) acetate (0.670 mg, 0.003 mmol, 0.01 equiv), (S_p,S_p)-**L1.101** (3.80 mg, 0.0036 mmol, 0.012 equiv) in THF (1.2 mL, 0.25 M). Oxidation was performed at pH 7 over 24 h. A phosphate buffer solution was used instead of a 3 M solution of aqueous NaOH. The unpurified mixture was purified by silica gel chromatography (40% CH_2Cl_2 in Hexanes) to afford colorless oil (39.9 mg, 54% yield). **^{1}H NMR** (600 MHz, $CDCl_3$) δ 7.40 (2H, d, J = 12 Hz), 7.34 (2H, t, J = 6.0 Hz,7.27-7.24 (1H, m), 4.91 (1H, m), 3.75 (3H, s), 3.11 (1H, dd, J = 13.2, 3.9 Hz), 2.79 (1H, dd, J= 13.3, 3.9 Hz), 2.66-2.62 (2H, m), 2.54-2.48 (1H, m), 2.32-2.25 (1H, m) 1.81 (2H, q, J = 7.6 Hz). **^{13}C NMR** (125 MHz, $CDCl_3$) δ 168.0, 157.0, 145.0, 130.3, 128.4, 127.4, 125.6, 125.6, 73.32, 51.6, 40.37, 39.36, 33.60, 21.74. **IR** (neat) ν_{max} 3451.0 (br), 2952.0 (s), 2924.9 (s), 2854.8 (s), 1705.3 (s), 1636.0 (s), 1434.7 (m), 1266.5 (m), 1198.3 (s), 1116.4 (s), 1054.1 (s), 768.6 (s), 701.9 (s) cm^{-1}. **HRMS** (DART) for: $C_{15}H_{17}O_2$ $[M+H-H_2O]^+$: calculated: 229.1230, found: 229.1229. $[\boldsymbol{\alpha}]_D^{20}$: +73.65 (*c* 0.68, $CHCl_3$, *l* =50 mm).

Determination of Stereochemical Identity: Racemic compound was prepared according to the general procedure (***Method A***) with 4,4,5,5-tetramethyl-2-vinyl-1,3,2-dioxaborolane, and $Pd(OAc)_2$ (5 mol%) and 1,1′-Bis(dicyclohexylphosphino)ferrocene (6 mol%) as the catalyst. Absolute stereochemistry was assigned by analogy (see products **2.83**, **2.117**, and **2.120**).

SFC (Chiracel OD-H, 5% IPA, 3 mL/min, 100 bar, 35 °C, 210-270 nm) – Methyl (R)-2-(2-hydroxy-2-phenylethyl)cyclopent-1-ene-1-carboxylate.

Racemic Material



Peak Info

Peak No	% Area	Area	RT (min)
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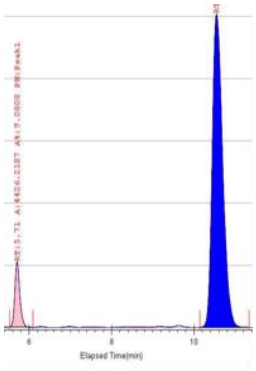
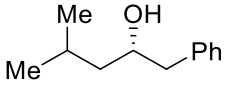
2	49.764	11825.9636	10.57
Total:	100	23764.0851	

Standard Conditions



Peak Info

Peak No	% Area	Area	RT (min)
1	9.0808	4426.2187	5.71
2	90.9192	44316.2386	10.55
Total:	100	48742.4573	



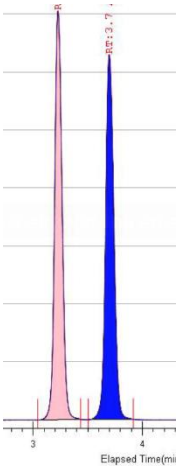
(S)*-4-Methyl-1-phenylpentan-2-ol (2.137).** The reaction was performed according to the general procedure (Method B***) with 2-isobutyl-5,5-dimethyl-1,3,2-dioxaborinane (**2.81**) (51.0 mg, 0.30 mmol, 1.00 equiv),

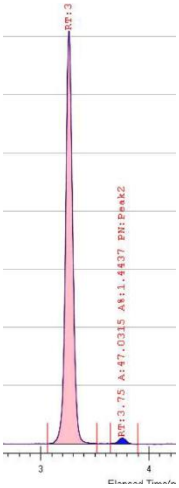
vinylllithium (0.211 mL, 1.42M in Et_2O, 0.30 mmol, 1.00 equiv), phenyltrifluoromethanesulfonate (74.60 mg, 0.33 mmol, 1.10 equiv), palladium (II) acetate (1.34 mg, 0.006 mmol, 0.02 equiv), (S_p,S_p)-**2.101** (7.60 mg, 0.0072 mmol, 0.024 equiv) in THF (1.2 mL, 0.25 M). The unpurified mixture was purified by silica gel chromatography (40% CH_2Cl_2 in hexanes) to afford colorless oil. (31.6 mg, 59% yield). **^{1}H NMR** (600 MHz, $CDCl_3$) δ 7.30 (2H, t, *J* = 7.2 Hz), 7.20-7.24 (3H, m), 3.87-3.89 (1H, m), 2.80 (1H, dd, *J* = 13.2, 3.6 Hz), 2.61 (1H, dd, *J* = 13.2, 8.4 Hz), 1.78-1.85 (1H, m), 1.41-1.48 (2H, m), 1.27-1.31 (1H, m), 0.93 (3H, d, *J* = 6.6 Hz), 0.90 (3H, d, *J* = 8.4 Hz); **^{13}C NMR** (150 MHz, $CDCl_3$) δ 138.8, 129.6, 128.7, 126.6, 70.9, 46.2, 44.8, 24.8, 23.6, 22.2; **IR** (neat) ν_{max} 3387 (br), 3027 (w), 2953 (m), 2921 (m), 2868 (w), 2362 (w), 1512 (w), 1466 (m), 1346 (w), 1136 (w), 1078 (m), 1019 (m), 743 (s), 697 (s), 603 (w) cm^{-1}. **HRMS** (DART) for $C_{12}H_{17}$ $[M+H-H_2O]^+$: calculated: 161.1330, found: 161.1337. **$[\alpha]^{20}_D$**: +4.736 (*c* 0.285, $CHCl_3$, *l* = 50 mm).

Determination of Stereochemical Identity: Racemic compound was prepared according to the general procedure ***(Method B)*** with $Pd(OAc)_2$ (5 mol%) and 1,1'-Bis(dicyclohexylphosphino)ferrocene (6 mol%) as the catalyst. Absolute stereochemistry was assigned by analogy (see products **2.83**, **2.117**, and **2.120**).

SFC (Chiracel OD-H, 5% IPA, 3 mL/min, 100 bar, 35°C, 210-270 nm) – analysis of (*S*)*-4-methyl-1-phenylpentan-2-ol.*

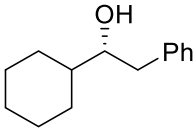
Racemic Material Standard Conditions





Peak No	% Area	Area	RT (min)
1	50.2125	6624.2856	3.23
2	49.7875	6568.2136	3.7
Total:	100	13192.4992	

Peak No	% Area	Area	RT (min)
1	98.5563	3210.702	3.26
2	1.4437	47.0315	3.75
Total:	100	3257.7335	



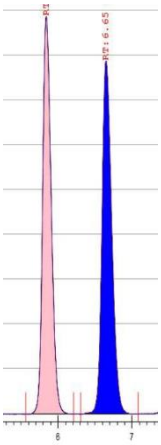
(R)*-1-Cyclohexyl-2-phenylethan-1-ol (2.138)**. The reaction was performed according to the general procedure (Method B***) with 2-cyclohexyl-5,5-dimethyl-1,3,2-dioxaborinane (**2.256**) (58.8 mg, 0.30 mmol, 1.00 equiv), vinyl lithium (0.210 mL, 1.42 M in Et_2O, 0.30 mmol, 1.00 equiv), phenyltrifluoromethanesulfonate (74.60 mg, 0.33 mmol, 1.10 equiv), palladium (II) acetate (1.30 mg, 0.0060 mmol, 0.020 equiv), (S_p,S_p)-**2.101** (7.60 mg, 0.0072 mmol,0.024 equiv) in THF (1.20 mL, 0.25 M). The unpurified mixture was purified by silica gel chromatography (5% ethyl acetate in hexanes, stain in CAM) to afford white solid (49.2 mg, 80% yield). **^{1}H NMR** (600 MHz, $CDCl_3$) δ 7.31-7.28 (2H, m), 7.23-7.18 (3H, m), 3.57 (1H, ddd, J = 9.6, 6.0, 3.6 Hz), 2.87 (1H, dd, J = 13.2, 3.0 Hz), 2.58 (1H, dd, J = 13.2, 9.0 Hz), 1.92-1.88 (1H, m), 1.80-1.62 (3H, m), 1.70-1.64 (1H, m), 1.44-1.38 (2H, m), 1.28-

1.04 (5H, m). **^{13}C NMR** (150 MHz, $CDCl_3$) δ 139.39, 129.53, 128.72, 126.51, 76.95, 43.35, 40.95, 29.49, 28.16, 26.71, 26.47, 26.33. **IR** (neat) ν_{max} 3327.3 (br), 3024.8 (w), 2923.1 (s), 2852.3 (m), 1493.7 (w), 1444.5 (w), 1401.3 (m), 1085.0 (w), 1059.6 (m), 1001.9 (m), 749.5 (s), 698.2 (s) cm^{-1}. **HRMS** (DART) for $C_{14}H_{24}NO$ $[M+NH_4]^+$ calculated: 222.1858, found: 222.1858. **$[\alpha]^{20}_D$**: +23.326 (*c* 1.445, $CHCl_3$, *l* =50 mm).

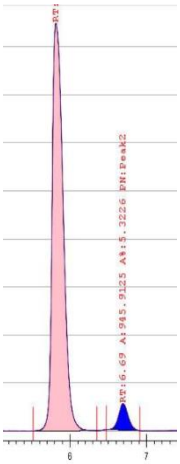
Determination of Stereochemical Identity: Racemic compound was prepared according to the general procedure (***Method B***) with $Pd(OAc)_2$ (5 mol%) and 1,1′-Bis(dicyclohexylphosphino)ferrocene (6 mol%) as the catalyst. Absolute stereochemistry was assigned by analogy (see products **2.83**, **2.117**, and **2.120**).

SFC (Chiracel OD-H, 5% IPA, 3 mL/min, 100 bar, 35 °C, 210-270 nm) – analysis (R)-1-cyclohexyl-2-phenylethan-1-ol.

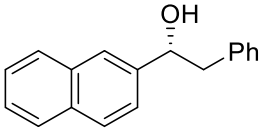
Racemic Material



Standard Conditions



Peak No	% Area	Area	RT (min)	Peak No	% Area	Area	RT (min)
1	49.9353	7108.9938	5.84	1	94.6774	16825.8605	5.81
2	50.0647	7127.4132	6.65	2	5.3226	945.9125	6.69
Total:	100	14236.407		Total:	100	17771.773	

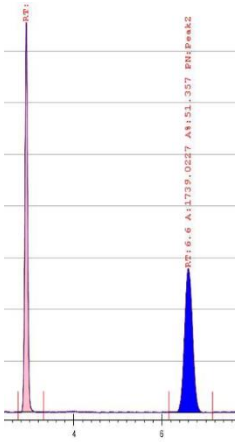


(R)*-1-(Naphthalen-2-yl)-2-phenylethan-1-ol (2.139)**. The reaction was performed according to the general procedure (Method B***) with 5,5-dimethyl-2-(naphthalen-2-yl)-1,3,2-dioxaborinane (**2.254**) (72.0 mg, 0.30 mmol, 1.00 equiv), vinyl lithium (0.210 mL, 1.42 M in Et_2O, 0.30 mmol, 1.00 equiv), phenyltrifluoromethanesulfonate (74.60 mg, 0.33 mmol, 1.10 equiv), palladium (II) acetate (1.30 mg, 0.0060 mmol, 0.020 equiv), (S_p,S_p)-**2.101** (7.60 mg, 0.0072 mmol,0.024 equiv) in THF (1.20 mL, 0.25 M). The unpurified mixture was purified by silica gel chromatography (15% ethyl acetate in hexanes, stain in CAM) to afford white solid (69.0 mg, 93% yield). **^{1}H NMR** (600 MHz, $CDCl_3$) δ7.84-7.78 (4H, m), 7.51-7.45 (3H, m), 7.29 (2H, t, *J* = 7.2 Hz), 7.23-7.20 (3H, m), 5.06 (1H, dd, *J* = 7.8, 4.2 Hz), 3.13 (1H, dd, *J* = 13.2, 4.8 Hz). 3.06 (1H, dd, *J* = 14.4, 9.0 Hz), 2.04 (1H, br s). **^{13}C NMR** (150 MHz, $CDCl_3$) δ 141.38, 138.14, 133.47, 133.19, 129.72, 128.75, 128.38, 128.16, 127.87. 126.86, 126.31, 126.03, 124.79, 124.28, 75.63, 46.21. **IR** (neat) ν_{max} 3529.1 (br), 3461.9 (br), 3057.9 (w), 3025.9 (w), 2914.8 (w), 1601.1 (w), 1494.2 (w). 1360.6 (w), 1077.5 (w), 1043.3 (m), 893.2 (m), 818.4 (s), 743.5 (s), 727.6 (s), 698.7 (s), 481.6 (s) cm^{-1}. **HRMS** (DART) for $C_{18}H_{15}$ $[M+H-H_2O]^+$ calculated: 231.1174, found: 231.1170. $[\alpha]^{20}_D$: -2.515 (*c* 1.340, $CHCl_3$, *l* =50 mm).

Determination of Stereochemical Identity: Racemic compound was prepared according to the general procedure (***Method B***) with $Pd(OAc)_2$ (5 mol%) and 1,1′-Bis(dicyclohexylphosphino)ferrocene (6 mol%) as the catalyst. Absolute stereochemistry was assigned by analogy (see products **2.83**, **2.117**, and **2.120**).

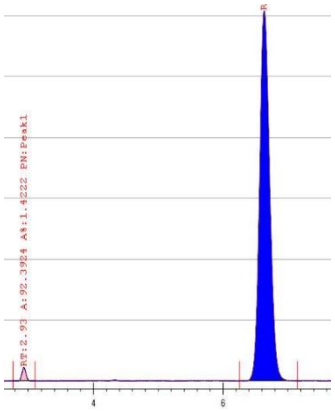
SFC (Chiracel ODR-H, 15% MeOH, 3 mL/min, 100 bar, 35 °C, 210-270 nm) – analysis (R)-1-(naphthalen-2-yl)-2-phenylethan-1-ol.

Racemic Material

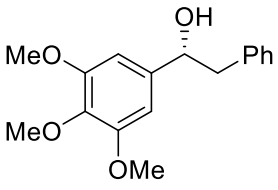


Peak No	% Area	Area	RT (min)
1	48.643	1647.1222	2.92
2	51.357	1739.0227	6.6
Total:	100	3386.1449	

Standard Conditions



Peak No	% Area	Area	RT (min)
1	1.4222	92.3924	2.93
2	98.5778	6404.1044	6.63
Total:	100	6496.4968	



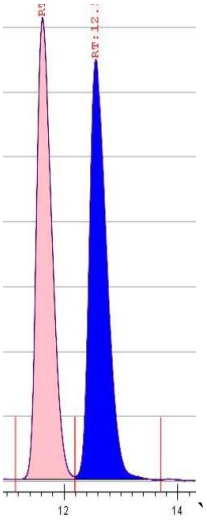
(R)*-2-Phenyl-1-(3,4,5-trimethoxyphenyl)ethan-1-ol (2.140).** The reaction was performed according to the general procedure ***(Method B) with 2-(3,4,5-trimethoxyphenyl)-5,5-dimethyl-1,3,2-dioxaborinane (**2.258**) (84.0 mg, 0.30 mmol, 1.00 equiv), vinyl lithium (0.210 mL, 1.42 M

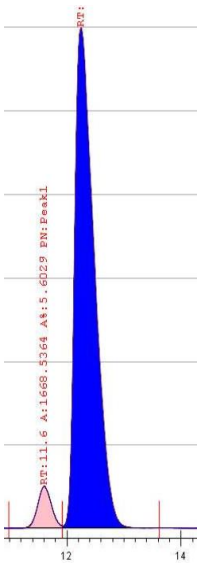
in Et_2O, 0.30 mmol, 1.00 equiv), phenyltrifluoromethanesulfonate (74.60 mg, 0.33 mmol, 1.10 equiv), palladium (II) acetate (1.30 mg, 0.0060 mmol, 0.020 equiv), (S_p,S_p)-**2.101** 1 (7.60 mg, 0.0072 mmol, 0.024 equiv) in THF (1.20 mL, 0.25 M). The unpurified mixture was purified by silica gel chromatography (10% ethyl acetate in hexanes, stain in CAM) to afford white solid (66.70 mg, 77% yield). **^{1}H NMR** (600 MHz, $CDCl_3$) δ 7.31-7.28 (2H, m), 7.24-7.21 (1H, m), 7.20-7.17 (2H, m), 6.54 (2H, s), 4.82 (1H, t, J = 6.6 Hz), 3.82 (9H, s), 3.00 (1H, dd, J = 13.2, 5.4 Hz), 2.96 (1H, dd, J = 13.8, 8.4 Hz), 1.94 (1H, d, J = 1.8 Hz). **^{13}C NMR** (150 MHz, $CDCl_3$) δ 153.32, 139.66, 138.05, 137.38, 129.67, 128.65, 126.80, 102.91, 75.63, 60.99, 56.23, 46.26. **IR** (neat) ν_{max} 3462.0 (br), 2939.3 (w), 2836.6 (w), 1592.2 (m), 1506.7 (m), 1456.5 (m), 1326.3 (m), 1233.5 (m), 1125.3 (s), 1007.6 (s), 701.3 (w) cm^{-1}. HRMS (DART) for $C_{17}H_{19}O_3$ $[M+H-H_2O]^+$ calculated: 271.1334, found: 271.1327. **$[\alpha]^{20}_D$**: -1.373 (*c* 0.510, $CHCl_3$, *l* =50 mm).

Determination of Stereochemical Identity: Racemic compound was prepared according to the general procedure (*Method B*) with $Pd(OAc)_2$ (5 mol%) and 1,1′-Bis(dicyclohexylphosphino)ferrocene (6 mol%) as the catalyst. Absolute stereochemistry was assigned by analogy (see products **2.83**, **2.117**, and **2.120**).

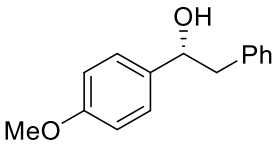
SFC (Chiracel ODR-H, 6% MeOH, 3 mL/min, 100 bar, 35 °C, 210-270 nm) – analysis of (R)-2-phenyl-1-(3,4,5-trimethoxyphenyl)ethan-1-ol.

Racemic Material Standard Conditions





Peak No	% Area	Area	RT (min)	Peak No	% Area	Area	RT (min)
1	49.3717	13286.3101	11.62	1	5.6029	1668.5364	11.6
2	50.6283	13624.4834	12.56	2	94.3971	28111.3344	12.25
Total:	100	26910.7935		Total:	100	29779.8708	



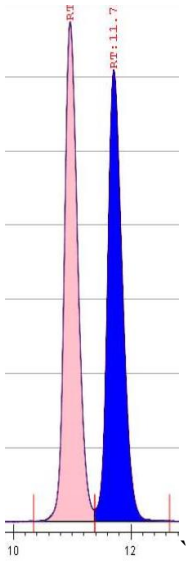
(R)*-1-(4-Methoxyphenyl)-2-phenylethan-1-ol (2.141)**. The reaction was performed according to the general procedure ***(Method B) with 2-(4-methoxyphenyl)-5,5-dimethyl-1,3,2-dioxaborinane (2.249) (66.0 mg, 0.30 mmol, 1.00 equiv), vinyl lithium (0.210 mL, 1.42 M in Et_2O, 0.30 mmol, 1.00 equiv), phenyltrifluoromethanesulfonate (74.60 mg, 0.33 mmol, 1.10 equiv), palladium (II) acetate (1.30 mg, 0.0060 mmol, 0.020 equiv), (S_p,S_p)-**2.101** (7.60 mg, 0.0072 mmol, 0.024 equiv) in THF (1.20 mL, 0.25 M). The unpurified mixture was purified by silica gel chromatography (40% CH_2Cl_2 in pentane, stain in CAM) to afford white solid (59.60 mg, 87% yield). **^{1}H NMR** (600 MHz, $CDCl_3$) δ 7.31-7.24 (4H, m), 7.23-7.21 (1H, m), 7.17 (2H, d, J = 6.6 Hz), 6.87 (2H, d, J = 9.0 Hz), 4.84 (1H, t, 6.6 Hz), 3.80 (3H, s), 3.02-2.96 (2H, m), 1.92 (1H, br s). **^{13}C NMR** (150 MHz, $CDCl_3$) δ 159.21,

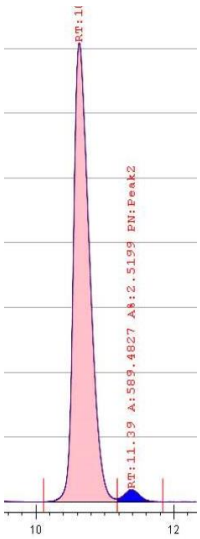
138.29, 136.14, 129.63, 128.60, 127.29, 126.68, 113.91, 75.11, 55.42, 46.15. **IR** (neat) ν_{max} 3389.0 (br), 3002.2 (w), 2918.0 (w), 2835.9 (w), 1611.4 (m), 1512.2 (s), 1454.2 (w), 1302.3 (w), 1246.0 (s), 1157.1 (m), 1032.9 (m). 831.9 (m), 699.4 (m) cm^{-1}. **HRMS** (DART) for $C_{15}H_{15}O$ $[M+H-H_2O]^+$ calculated: 211.1123, found: 211.1123. **$[\alpha]^{20}_D$**: -2.0386 (*c* 1.275, $CHCl_3$, *l* =50 mm).

Determination of Stereochemical Identity: Racemic compound was prepared according to the general procedure (***Method B***) with $Pd(OAc)_2$ (5 mol%) and 1,1′-Bis(dicyclohexylphosphino)ferrocene (6 mol%) as the catalyst. Absolute stereochemistry was assigned by analogy (see products **2.83**, **2.117**, and **2.120**).

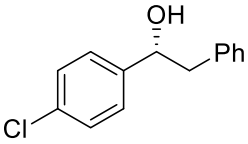
SFC (Chiracel OD-H, 8% IPA, 3 mL/min, 100 bar, 35 °C, 210-270 nm) – analysis of (R)-1-(4-methoxyphenyl)-2-phenylethan-1-ol.

Racemic Material Standard Conditions





Peak No	% Area	Area	RT (min)	Peak No	% Area	Area	RT (min)
1	49.8119	10639.7812	10.97	1	97.4801	22803.3883	10.63
2	50.1881	10720.1395	11.71	2	2.5199	589.4827	11.39
Total:	100	21359.9207		Total:	100	23392.871	



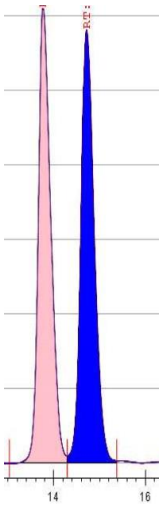
(R)*-1-(4-Chlorophenyl)-2-phenylethan-1-ol (2.142).** The reaction was performed according to the general procedure ***(Method B) with 2-(4-chlorophenyl)-5,5-dimethyl-1,3,2-dioxaborinane (**2.250**) (67.30 mg, 0.30 mmol, 1.00 equiv), vinyl lithium (0.176 mL, 1.72 M in Et_2O, 0.30 mmol, 1.00 equiv), phenyltrifluoromethanesulfonate (74.60 mg, 0.33 mmol, 1.10 equiv), palladium (II) acetate (1.30 mg, 0.0060 mmol, 0.020 equiv), (S_p,S_p)-**2.101** (7.60 mg, 0.0072 mmol, 0.024 equiv) in THF (1.20 mL, 0.25 M). The unpurified mixture was purified by silica gel chromatography (30% CH_2Cl_2 in pentane, stain in CAM) to afford colorless oil (46.40 mg, 66% yield). **^{1}H NMR** (600 MHz, $CDCl_3$) δ 7.30-7.20 (7H, m), 7.13 (2H, d, 6.0 Hz), 4.84 (1H, ddd, *J* = 8.4, 5.4, 3.0 Hz), 2.97 (1H, dd, *J* = 13.8, 4.8 Hz), 2.92 (1H, dd, *J* = 13.8, 8.4 Hz), 1.95 (1H, d, 2.4 Hz). **^{13}C NMR** (150 MHz, $CDCl_3$) δ 142.34, 137.65, 133.36,

129.64, 128.73, 128.65, 127.43, 126.91, 74.78, 46.24. **IR** (neat) ν_{max} 3389.5 (br), 3085.1 (w), 3062.2 (w), 3027.9 (w), 2851.4 (w), 1600.0 (w), 1492.5 (m), 1453.6 (w), 1089.4 (m), 1013.2 (m), 827.6 (m), 745.7 (m). 699.7 (s), 544.76 (s) cm^{-1}. **HRMS** (DART) for $C_{14}H_{12}Cl$ $[M+H-H_2O]^+$ calcualted: 215.0628, found: 215.0636. **$[\alpha]^{20}_D$**: -8.716 (*c* 1.845, $CHCl_3$, *l* =50 mm).

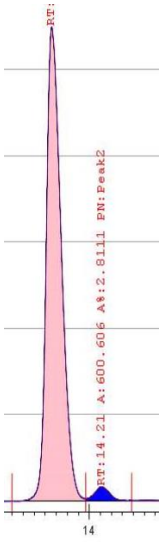
Determination of Stereochemical Identity: Racemic compound was prepared according to the general procedure (***Method B***) with $Pd(OAc)_2$ (5 mol%) and 1,1′-Bis(dicyclohexylphosphino)ferrocene (6 mol%) as the catalyst. Absolute stereochemistry was assigned by analogy (see products **2.83**, **2.117**, and **2.120**).

SFC (Chiracel OD-H, 6% IPA, 3 mL/min, 100 bar, 35 °C, 210-270 nm) – analysis (R)-1-(4-chlorophenyl)-2-phenylethan-1-ol.

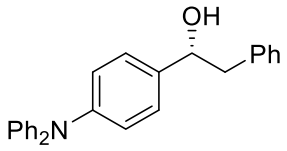
Racemic Material



Standard Conditions



Peak No	% Area	Area	RT (min)	Peak No	% Area	Area	RT (min)
1	49.0709	11621.9899	13.76	1	97.1889	20764.8334	13.31
2	50.9291	12062.0942	14.72	2	2.8111	600.606	14.21
Total:	100	23684.0841		Total:	100	21365.4394	



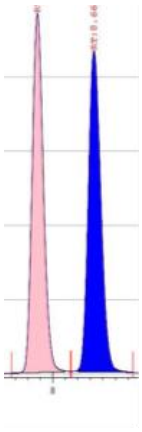
(R)*-1-(4-(Diphenylamino)phenyl)-2-phenylethan-1-ol (2.143)**. The reaction was performed according to the general procedure (Method B***) with 4-(5,5-dimethyl-1,3,2-dioxaborinan-2-yl)-*N*,*N*-diphenylaniline (**2.255**) (107.18 mg, 0.30 mmol, 1.00 equiv), vinyl lithium (0.176 mL, 1.72 M in Et_2O, 0.30 mmol, 1.00 equiv), phenyltrifluoromethanesulfonate (75.60 mg, 0.33 mmol, 1.10 equiv), palladium (II) acetate (1.30 mg, 0.006 mmol, 0.02 equiv), (S_p,S_p)-**2.101** (7.60 mg, 0.0072 mmol, 0.024 equiv) in THF (1.20 mL, 0.25 M). The unpurified mixture was purified by silica gel chromatography (40% CH_2Cl_2 in hexanes) to afford white solid (81.0 mg, 75% yield). **^{1}H NMR** (600 MHz, $CDCl_3$) δ 7.33-7.31 (2H, m), 7.26-7.22 (10H, m), 7.09-7.06 (5H, m), 7.02-7.00 (2H, m), 4.87-4.84 (1H, m), 3.06 (1H, dd, *J* = 13.6, 4.6 Hz), 3.01 (1H, dd, *J* = 13.6, 8.8 Hz), 1.91 (1H, s). **^{13}C NMR** (150 MHz, $CDCl_3$) δ 147.9, 147.4, 138.3, 138.1, 129.7, 129.4, 128.7, 127.0, 126.8, 124.3, 124.3, 124.2, 122.9, 75.2, 46.1. **IR** (neat) ν_{max} 3383.1 (br), 3061.3 (m), 2922.1 (w), 2854.4(w), 1589.0 (s), 1508.9 (s), 1314.1 (m), 1277.3 (s), 752.2 (s), 696.0 (s) cm^{-1}. **HRMS** (DART) for: $C_{26}H_{22N}N_1$ [M+H-H_2O]$^+$: calculated: 348.1752, found: 348.1763. [**α**]$_D^{20}$: -7.79 (*c* 0 .43, $CHCl_3$, *l* =50 mm).

Determination of Stereochemical Identity: Racemic compound was prepared according to the general procedure (***Method B***) with $Pd(OAc)_2$ (5 mol%) and 1,1′-

Bis(dicyclohexylphosphino)ferrocene (6 mol%) as the catalyst. Absolute stereochemistry was assigned by analogy (see products **2.83**, **2.117**, and **2.120**).

SFC (Chiracel OD-H, 5% IPA, 3 mL/min, 100 bar, 35 °C, 210-270 nm) – analysis of (R)-1-(4-(diphenylamino)phenyl)-2-phenylethan-1-ol.

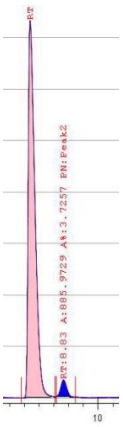
Racemic Material



Peak Info

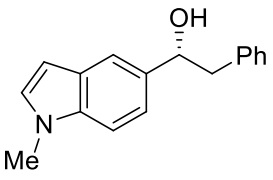
Peak No	% Area	Area	RT (min)
1	50.0189	6007.4743	7.75
2	49.9811	6002.9239	8.66
Total:	100	12010.3982	

Standard Conditions



Peak Info

Peak No	% Area	Area	RT (min)
1	96.2743	22893.8564	7.7
2	3.7257	885.9729	8.83
Total:	100	23779.8293	



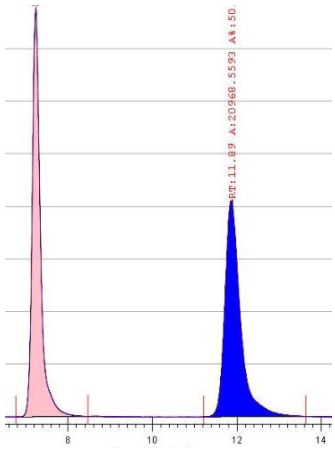
(R)*-1-(1-Methyl-1H-indol-5-yl)-2-phenylethanol (2.147)**. The reaction was performed according to the general procedure (Method B***) with 5-(5,5-dimethyl-1,3,2-dioxaborinan-2-yl)-1-methyl-1*H*-indole (**2.259**) (75.20 mg, 0.30 mmol, 1.00 equiv), vinyl lithium (0.210 mL, 1.42 M in Et_2O, 0.30 mmol, 1.00 equiv), phenyltrifluoromethanesulfonate (74.60 mg, 0.33

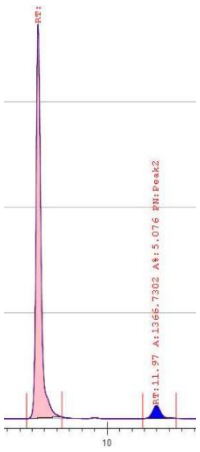
mmol, 1.10 equiv), palladium (II) acetate (1.30 mg, 0.0060 mmol, 0.020 equiv), (S_p,S_p)-**2.101** (7.60 mg, 0.0072 mmol, 0.024 equiv) in THF (1.20 mL, 0.25 M). The unpurified mixture was purified by silica gel chromatography (15% ethyl acetate in hexanes, stain in CAM) to afford white solid (64.8 mg, 86% yield). **^{1}H NMR** (500 MHz, $CDCl_3$) δ 7.61 (1H, s), 7.630-7.21 (7H, m), 7.04 (1H, d, J = 3.0 Hz), 6.45 (1H, d, J = 3.0 Hz), 4.99 (1H, t, J = 7.0 Hz), 3.78 (3H, s), 3.09 (2H, d, J = 7.0 Hz), 1.93 (1H, br s). **^{13}C NMR** (150 MHz, $CDCl_3$) δ 138.83, 136.45, 135.12, 129.62, 129.38, 128,49, 128.48, 126.47, 119.99, 118.41, 109.30, 101.15, 76.21, 46.42, 32.97. **IR** (neat) ν_{max} 2960.4 (w), 3383.6 (w), 3025.8 (w), 2919.9 (w), 1512.4 (m), 1451.7 (w), 1244.5 (w), 1030.9 (w), 721.5 (s), 699.7 (s) cm^{-1} . **HRMS** (DART) for $C_{12}H_{18}NO$ $[M+H]^+$ calculated: 252.1379 found: 252.13884. **$[\alpha]_D^{20}$**: -10.328 (*c* 2.08, $CHCl_3$, l =50 mm).

Determination of Stereochemical Identity: Racemic compound was prepared according to the general procedure (***Method B***) with $Pd(OAc)_2$ (5 mol%) and 1,1′-Bis(dicyclohexylphosphino)ferrocene (6 mol%) as the catalyst. Absolute stereochemistry was assigned by analogy (see products **2.83**, **2.117**, and **2.120**).

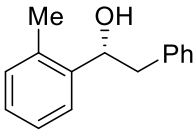
SFC (Chiracel OJ-H, 30% IPA, 3 mL/min, 100 bar, 35 °C, 210-270 nm) – analysis of (R)-1-(1-methyl-1H-indol-5-yl)-2-phenylethanol.

Racemic Material Standard Conditions





Peak No	% Area	Area	RT (min)	Peak No	% Area	Area	RT (min)
1	49.8909	20877.2269	7.23	1	94.924	25558.6592	7.23
2	50.1091	20968.5593	11.89	2	5.076	1366.7302	11.97
Total:	100	41845.7862		Total:	100	26925.3894	



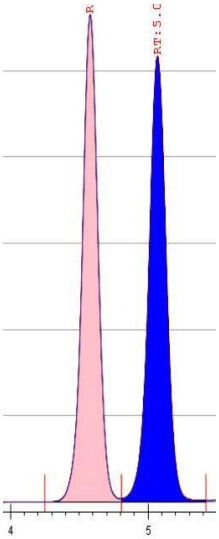
(R)*-2-Phenyl-1-(o-tolyl)ethan-1-ol (2.144)**. The reaction was performed according to the general procedure ***(Method B) with 5,5-dimethyl-2-(o-tolyl)-1,3,2-dioxaborinane (**2.251**). (61.20 mg, 0.30 mmol, 1.00 equiv), vinyl lithium (0.176 mL, 1.72 M in Et_2O, 0.30 mmol, 1.00 equiv), phenyltrifluoromethanesulfonate (74.60 mg, 0.33 mmol, 1.10 equiv), palladium (II) acetate (1.30 mg, 0.0060 mmol, 0.010 equiv), (S_p,S_p)-**2.101** (7.60 mg, 0.0072 mmol, 0.012 equiv) in THF (1.20 mL, 0.25 M). The unpurified mixture was purified by silica gel chromatography (2% ethyl acetate in pentane, stain in CAM) to afford white solid (57.6 mg, 90% yield). **^{1}H NMR** (600 MHz, $CDCl_3$) δ 7.60 (1H, d, *J* = 7.8 Hz), 7.36 (2H, t, *J* = 6.6 Hz), 7.33-7.24 (5H, m), 7.18 (1H, d, *J*= 7.2 Hz), 5.17 (1H, ddd, *J* = 5.4, 3.6, 1.8 Hz), 3.06 (1H, dd, *J* = 14.4, 4.8 Hz), 2.97 (1H, dd, *J* = 13.8, 9.0 Hz), 2.33 (3H, s), 1.96 (1H, br s). **^{13}C NMR** (150 MHz, $CDCl_3$) δ 142.17, 138.49, 134.49, 130.41, 129.58, 128.66, 127.43, 126.74, 126.48, 125.37, 71.85, 45.15, 19.12. **IR** (neat) ν_{max} 3384.9 (br), 3061.3 (w), 2920.4

(w), 2859.95 (w), 1603.1 (w), 1494.1 (m), 1454.0 (m), 1076.0 (m), 1038.8 (m), 755.1 (s). 738.2 (m), 698.4 (s) cm^{-1}. **HRMS** (DART) for $C_{15}H_{15}$ $[M+H-H_2O]^+$ calculated: 195.1174, found: 195.1181. $[\alpha]^{20}_D$: +30.812 (*c* 1.760, $CHCl_3$, *l* =50 mm).

Determination of Stereochemical Identity: Racemic compound was prepared according to the general procedure (***Method B***) with $Pd(OAc)_2$ (5 mol%) and 1,1′-Bis(dicyclohexylphosphino)ferrocene (6 mol%) as the catalyst. Absolute stereochemistry was assigned by analogy (see products **2.83**, **2.117**, and **2.120**).

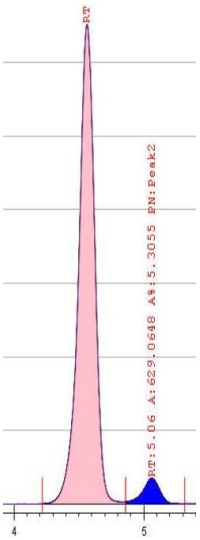
SFC (Chiracel OJ-H, 10% IPA, 3 mL/min, 100 bar, 35 °C, 210-270 nm) – analysis (R)-2-phenyl-1-(o-tolyl)ethan-1-ol.

Racemic Material

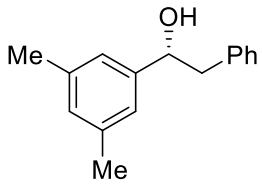


Peak No	% Area	Area	RT (min)
1	49.4517	8989.9843	4.58
2	50.5483	9189.3254	5.07
Total:	100	18179.3097	

Standard Conditions



Peak No	% Area	Area	RT (min)
1	94.6945	11227.6762	4.56
2	5.3055	629.0648	5.06
Total:	100	11856.741	

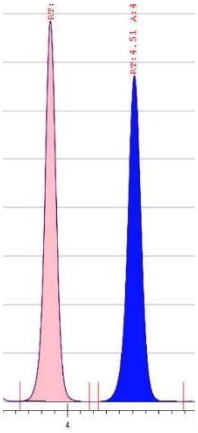


***(R)*-1-(3,5-Dimethylphenyl)-2-phenylethan-1-ol (2.145)**. The reaction was performed according to the general procedure **(*Method B*)** with 2-(3,5-dimethylphenyl)-5,5-dimethyl-1,3,2-dioxaborinane (65.4 mg, 0.30 mmol) (**2.253**), vinylllithium (0.211 mL, 1.42M in Et_2O, 0.30 mmol), phenyltrifluoromethanesulfonate (74.60 mg, 0.33 mmol), palladium (II) acetate (1.34 mg, 0.006 mmol), (S_p,S_p)-**2.101** (7.60 mg, 0.0072 mmol) in THF (1.2 mL, 0.25 M). The unpurified mixture was purified by silica gel chromatography (40% CH_2Cl_2 in hexanes) to afford colorless oil. (45.4 mg, 67% yield). **^{1}H NMR** (600 MHz, $CDCl_3$) δ 7.34 (2H, t, *J* = 7.2 Hz), 7.25-7.28 (3H, m,), 7.02 (2H, s), 6.96 (1H, s), 4.84 (1H, dd, *J* = 9.0, 4.2 Hz,), 3.05 (1H, dd, *J* = 14.4, 4.8 Hz,), 2.98 (1H, dd, *J* = 14.4, 9.6 Hz,), 2.36 (6H, s), 1.98 (1H, s). **^{13}C NMR** (150 MHz, $CDCl_3$) δ 144.0, 138.5, 138.1, 129.6, 129.3, 128.6, 126.7, 123.8, 75.5, 46.2, 21.4. **IR** (neat) ν_{max} 3404 (br), 3060 (w), 3026 (w), 2941 (m), 2859 (w), 2361 (w), 1603 (m), 1453 (m), 1180 (w), 1051 (m), 849 (s), 748 (m), 698 (s), 507 (m) cm^{-1}. **HRMS** (DART): for $C_{16}H_{17}$ $[M+H-H_2O]^+$: calculate: 209.1330, found: 209.1320. **$[\alpha]^{20}_D$**: +10.24 (*c* 2.835, $CHCl_3$, *l* = 50 mm).

Determination of Stereochemical Identity: Racemic compound was prepared according to the general procedure ***(Method B)*** with $Pd(OAc)_2$ (5 mol%) and 1,1'-Bis(dicyclohexylphosphino)ferrocene (6 mol%) as the catalyst. Absolute stereochemistry was assigned by analogy (see products **2.83**, **2.117**, and **2.120**).

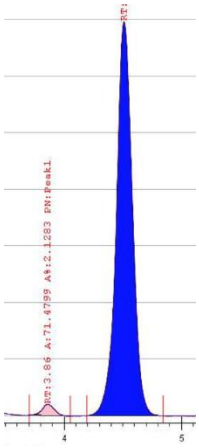
SFC (Chiracel OJ-H, 10% IPA, 3 mL/min, 100 bar, 35°C, 210-270 nm) – analysis of (R)-1-(3,5-dimethylphenyl)-2-phenylethan-1-ol.

Racemic Material

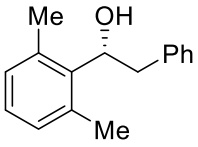


Peak No	% Area	Area	RT (min)
1	49.8529	4861.1049	3.87
2	50.1471	4889.7919	4.51
Total:	100	9750.8968	

Standard Conditions



Peak No	% Area	Area	RT (min)
1	2.1283	71.4799	3.86
2	97.8717	3287.0332	4.51
Total:	100	3358.5131	



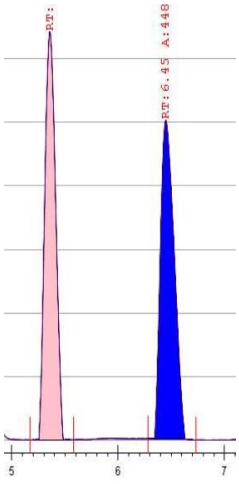
(R)*-1-(2,6-Dimethylphenyl)-2-phenylethan-1-ol (2.146)**. The reaction was performed according to the general procedure (Method B***) with 2-(2,6-dimethylphenyl)-5,5-dimethyl-1,3,2-dioxaborinane (**2.252**) (65.4 mg, 0.30 mmol, 1.00 equiv), vinyl lithium (0.210 mL, 1.42 M in Et_2O, 0.30 mmol, 1.00 equiv), phenyltrifluoromethanesulfonate (74.60 mg, 0.33 mmol, 1.10 equiv), palladium (II) acetate (1.30 mg, 0.0060 mmol, 0.020 equiv), (S_p,S_p)-**2.101** (7.60 mg, 0.0072 mmol,0.024 equiv) in THF (1.20 mL, 0.25 M). The unpurified mixture was purified by silica gel chromatography (40% CH_2Cl_2 in pentane, stain in CAM) to afford white solid (50.50 mg, 74% yield). **^{1}H NMR** (600 MHz, $CDCl_3$) δ 7.31 (2H, t, J = 6.6 Hz), 7.26-7.20 (3H, m),

7.17 (1H, t, *J* = 7.2 Hz), 7.00 (2H, d, *J* = 7.8 Hz), 5.32 (1H, ddd, *J* = 7.8 4.8, 1.8 Hz). 3.22 (1H, dd, *J* = 13.8, 9.0 Hz), 3.01 (1H, dd, *J* = 13.8, 5.4 Hz), 2.43 (6H, s), 1.83 (1H, d, *J* = 2.4 Hz). **^{13}C NMR** (150 MHz, $CDCl_3$) δ 138.90, 138.80, 136.24, 129.55, 129.52, 128.65, 127.30, 126.66, 72.00, 42.33, 20.96. **IR** (neat) ν_{max} 3549.2 (br), 3429.9 (br), 3062.1 (w), 3025.8 (w), 2925.0 (w), 2864.5 (w), 1601.8 (w), 1495.1 (m), 1468.0 (m), 1453.1 (w), 1045.3 (m) 769.9 (s), 752.6 (s), 700.0 (s) cm^{-1}. **HRMS** (DART) for $C_{16}H_{17}$ $[M+H-H_2O]^+$ calculated: 209.1330, found: 209.1323. **$[\alpha]^{20}_D$**: -6.573 (*c* 1.660, $CHCl_3$, *l* =50 mm).

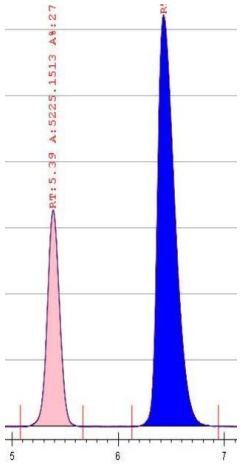
Determination of Stereochemical Identity: Racemic compound was prepared according to the general procedure (***Method B***) with $Pd(OAc)_2$ (5 mol%) and 1,1′-Bis(dicyclohexylphosphino)ferrocene (6 mol%) as the catalyst. Absolute stereochemistry was assigned by analogy (see products **2.83**, **2.117**, and **2.120**).

SFC (Chiracel OJ-H, 10% IPA, 3 mL/min, 100 bar, 35 °C, 210-270 nm) – analysis (R)-1-(2,6-dimethylphenyl)-2-phenylethan-1-ol.

Racemic Material Standard Conditions



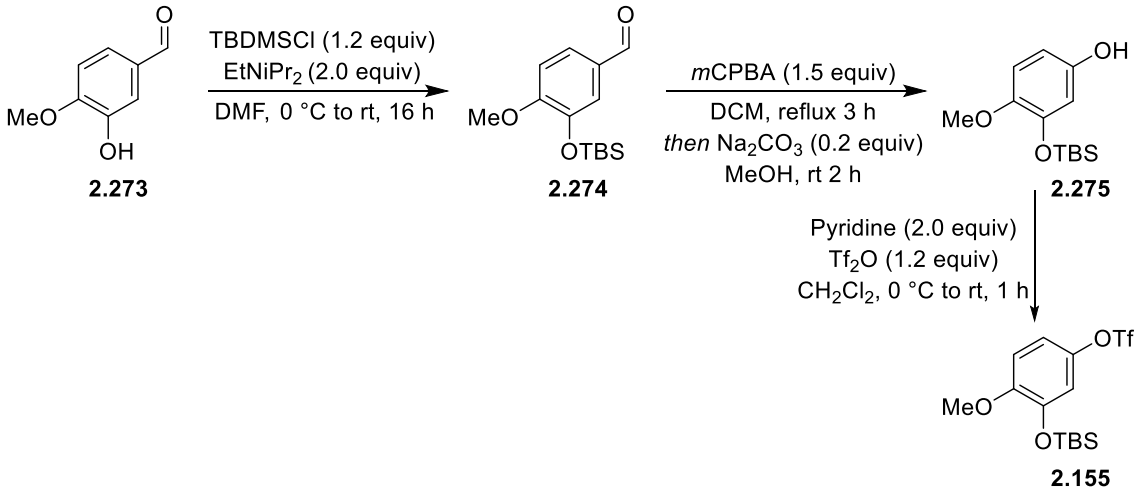
Peak No	% Area	Area	RT (min)
1	50.288	4540.9221	5.36
2	49.712	4488.9112	6.45
Total:	100	9029.8333	

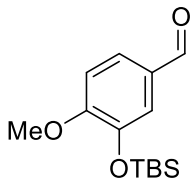


Peak No	% Area	Area	RT (min)
1	27.1761	5225.1513	5.39
2	72.8239	14001.8745	6.43
Total:	100	19227.0258	

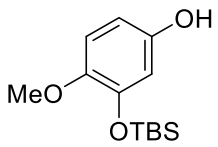
2.9.2.6 (-)-Combretastatin Synthesis (2.157)

Preparation of aryl triflate electrophile: 3-(*tert*-Butyldimethylsilyloxy)-4-methoxy phenyl trifluoromethanesulfonate (2.1550).





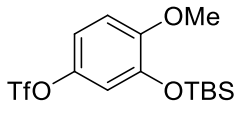
3-((*tert*-Butyldimethylsilyl)oxy)-4-methoxybenzaldehyde (2.274). To an oven-dried 100 mL round bottom flask equipped with a magnetic stir bar was added Isovanillin (**2.273**) (4.12 g, 28.29 mmol, 1.0 equiv) and *N,N*-dimethylformamide (30 mL). The solution was allowed to cool to 0˚C under a nitrogen atmosphere, and *N,N*-diisopropylethylamine (6.83 g, 52.82 mmol, 2.0 equiv) was added and the solution was allowed to sire at 0 ˚C for 10 min. To the cooled solution was added *tert*-butyldimethylsilyl chloride (4.7565 g, 31.56 mmol, 1.2 equiv) as a 1 M solution in THF over 30 min by syringe pump. The solution was allowed to warm to room temperature and stir for 12 h. The solution was diluted with diethyl ether, washed with water and brine, and dried with Na_2SO_4. After removing solvent under reduced pressure the residue was purified by silica gel chromatography (10% EtOAc in hexane) and the product was obtained as colorless oil (6.89 g, 99% yield). All spectral data was in accord with the literature.[73]



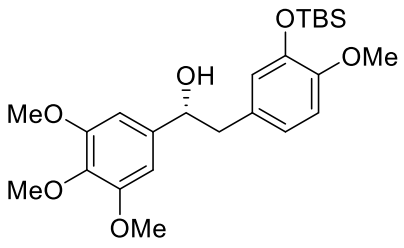
3-((*tert*-Butyldimethylsilyl)oxy)-4-methoxyphenol (2.275). To an oven-dried 250 mL round bottom flask equipped with a magnetic stir bar was added TBS-protected Isovanillin (**2.274**) (6.89 g, 25.99 mmol, 1.0 equiv) and anhydrous CH_2Cl_2 (103 mL), the solution was allowed to cool to 0 ˚C and placed under nitrogen. To this cooled solution was added 3-chloroperbenzoic acid (13.45 g, 38.98, 1.5 equiv), the solution was allowed to refluxed for 3 h, the resulting solution was

[73] Ramana. Reddy, M. V.; Mallireddigari, M. R.; Cosenza, S. C.; Pallela, V. R.; Iqbal, N. M.; Robell, K. A.; Kang, A. D.; Reddy, E. P. *J. Med. Chem.* **2008**, 51, 86.

washed twice with a saturated solution of aqueous $NaHCO_3$. The organic phase was dried over anhydrous $MgSO_4$ and the solvent was removed under reduced pressure. The resulting residue was dissolved in methanol (150 mL), and to this solution was added Na_2CO_3 (0.64 g, 5.19 mmol, 0.2 equiv). The mixture was allowed to stir at room temperature for 2 h, after which the solution was quenched with a saturated aqueous solution of NH_4Cl and the product was extracted with CH_2Cl_2 (4x45 mL). The combined organic layers were dried over Na_2SO_4, filtered through a neutral alumina pad, and concentrated under reduced pressure. The resulting residue was used in next step without further purification.



3-(*tert*-Butyldimethylsilyloxy)-4-methoxyphenyl trifluoromethanesulfonate (2.155). The residue from the last step (**2.275**) was subjected to the general procedure for preparation of aryl triflates to afford the product (8.1837 g, 97% yield). (81% overall yield over three steps). **^{1}H NMR** (600 MHz, $CDCl_3$) δ 6.84-6.80 (2H, m), 6.85 (1H, d, J = 2.4 Hz), 3.80 (3H, s), 0.97 (9H, s), 0.15 (6H, s). **^{13}C NMR** (150 MHz, $CDCl_3$) δ 151.2, 146.1, 142.8, 122.2, 120.0, 117.9, 114.5, 114.2, 112.0, 56.0, 25.8, 18.6, -4.5. **IR** (neat) ν_{max} 2932.6 (w), 1603.6 (m), 1505.0 (s), 1419.9 (m), 1181.4 (s), 1107.9 (s), 882.2 (m), 826.9 (s), 802.1 (s), 693.6 (m), 599.4 (m), 505.6 (s) cm^{-1}. **HRMS** (DART) for $C_{14}H_{22}F_3O_5S_1Si_1$ $[M+H]^+$ calculated: 387.0909, found: 387.0908.



(R)*-2-(3-((*tert*-Butyldimethylsilyl)oxy)-4-methoxyphenyl)-1-(3,4,5-trimethoxyphenyl)ethan-1-ol (2.156)**. The reaction was performed according to the general procedure ***(Method B) with 5,5-dimethyl-2-(3,4,5-trimethoxyphenyl)-1,3,2-dioxaborinane (**2.154**) (84.0 mg, 0.30 mmol, 1.00 equiv), vinyllithium (0.190 mL, 1.59 M in Et_2O, 0.30 mmol, 1.00 equiv), 3-((*tert*-butyldimethylsilyl)oxy)-4-methoxyphenyl trifluoromethanesulfonate (**2.155**) (139.0 mg, 0.36 mmol, 1.20 equiv), palladium (II) acetate (0.67 mg, 0.0030 mmol, 0.010 equiv), (S_p,S_p)-**2.101** (3.80 mg, 0.0036 mmol, 0.012 equiv) in THF (1.20 mL, 0.25 M). The unpurified mixture was purified by silica gel chromatography (15-25% ethyl acetate in hexanes, stain in CAM) to afford colorless oil (107.0 mg, 80% yield). **^{1}H NMR** (600 MHz, $CDCl_3$) δ 6.76 (1H, d, *J* = 7.8 Hz), 6.71-6.66 (2H, m), 6.53 (2H, s), 4.73 (t, *J* = 5.4 Hz), 3.82 (6H, s), 3.81 (3H, s), 3.76 (3H, s), 2.90 (1H, dd, *J* = 13.8, 4.8 Hz), 2.84 (1H, dd, 13.8, 8.4 Hz), 2.02 (1H, br s), 0.97 (9H, s), 0.11 (6H, d, *J* = 3.0 Hz). **^{13}C NMR** (150 MHz, $CDCl_3$) δ 153.32, 149.98, 145.14, 139.68, 137.34, 130.44, 122.78, 122.32, 112.33, 103.0, 75.62, 60.98, 56.25, 55.70, 45.42, 25.87, 18.59, -4.48. **$[\alpha]^{20}_D$**: -6.772 (*c* 0.502, $CHCl_3$, *l* =50 mm). lit: **$[\alpha]^{20}_D$**: -8.51 (*c* 2.4, $CHCl_3$).[74] All spectral data was in accord with the literature.[70]

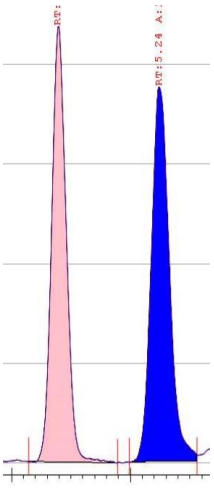
Determination of Stereochemical Identity: Racemic compound was prepared according to the general procedure (***Method B***) with $Pd(OAc)_2$ (5 mol%) and 1,1′-

[74] Ramacciotti, A.; Fiaschi, R.; Napolitano, E.*Tetrahedron: Asymmetry* **1996**, 7, 1101.

Bis(dicyclohexylphosphino)ferrocene (6 mol%) as the catalyst. Absolute stereochemistry was assigned by analogy (see products **2.83**, **2.117**, and **2.120**).

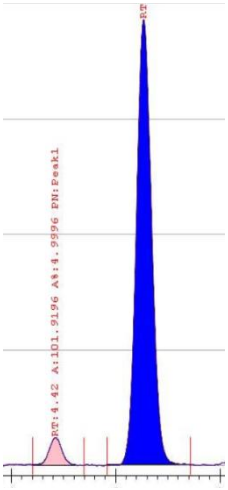
SFC (Chiracel ODR-H, 10% MeOH, 3 mL/min, 100 bar, 35 °C, 210-270 nm) – analysis of (R)-2-(3-((tert-butyldimethylsilyl)oxy)-4-methoxyphenyl)-1-(3,4,5-trimethoxyphenyl)ethan-1-ol.

Racemic Material

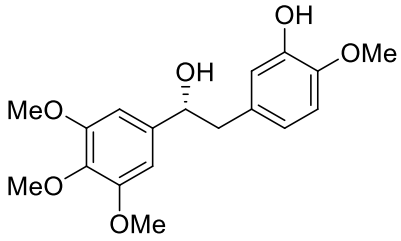


Peak No	% Area	Area	RT (min)
1	48.2262	1848.99	4.39
2	51.7738	1985.0084	5.24
Total:	100	3833.9984	

Standard Conditions



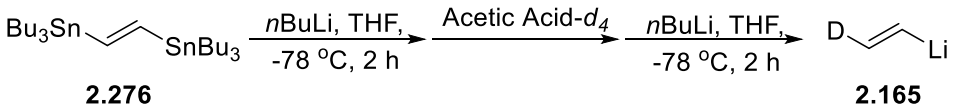
Peak No	% Area	Area	RT (min)
1	4.9996	101.9196	4.42
2	95.0004	1936.6484	5.27
Total:	100	2038.568	



***(-)*-Combretastatin (2.157)**. Combretastatin was prepared according to the reported procedure to afford

the desired product in 97 % yield. $[\alpha]^{20}_{D}$: -5.458 (*c* 0.795, $CHCl_3$, *l* =50 mm). All spectral data was in accord with previous reports.[70]

2.9.2.7 Deuterium-labeling Experiment

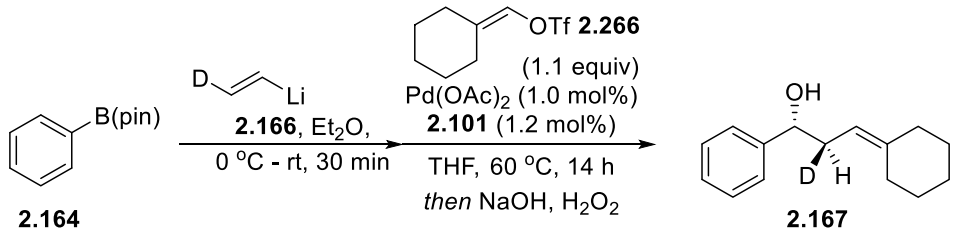


2.276 **2.165**

Procedure for the Preparation of trans-deuterium-labeled vinyl lithium (2.165). The *trans*-deuterium labeled vinyllithium was prepared according to the literature procedure with modification.[75] To an oven-dried 25 mL round bottom flask equipped with a magnetic stir bar in an Ar-filled glovebox was added bis(tributylstannyl)ethylene (1.818 g, 3.00 mmol, 1.0 equiv), and THF (3 mL). The flask was sealed with a rubber septum, and removed from glovebox. The flask was allowed to cool to -78˚C , and *n*-butyllithium (3.30 mmol, 1.1 equiv) was added dropwise. The flask was allowed to stir for an additional 2 h at -78 ˚C. Then acetic acid-d_4 was added dropwise at -78˚C. The mixture was allowed to warm to room temperature and was quenched with a saturated solution of aquious Na_2CO_3. The product was extracted from the aqueous layer with hexanes (3 x 20 mL). The combined organic layers were dried over Na_2SO_4, filtered through a neutral alumina pad, and concentrated under reduced pressure. The resulting residue was used in the next step

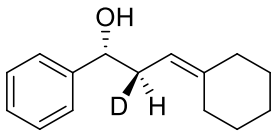
[75] Hughes, R. P.; Trujillo, H. A.; Egan J. W. Jr.; Rheingold, A. L. *J. Am. Chem. Soc*. **2000**, 122, 2261.

without further purification. The resulting residue from the last step was brought into an Ar-filled glovebox and transferred into an oven-dried 25 mL round bottom flask equipped with a magnetic stir bar, diluted with THF (3 mL), sealed with a rubber septum, and removed from glovebox. The flask was allowed to cool to -78˚C, and *n*-butyllithium (3.00 mmol, 1.0 equiv) was added dropwise. The flask was allowed to stir for an additional 2 h at -78˚C. Upon completion, the *trans*-deuterium labeled vinyllithium solution was allowed to warm to room temperature, was titrated with BHT and 1,10-phenanthroline in THF, and used in conjunctive cross coupling.



Procedure for the Conjunctive Cross Coupling with trans-Deuterium-Labeled Vinyl Lithium. To an oven-dried 2-dram vial equipped with a magnetic stir bar in an Ar-filled glovebox was added 4,4,5,5-tetramethyl-2-phenyl-1,3,2-dioxaborolane (**2.164**) (61.2 mg, 0.30 mmol, 1.0 equiv) and diethyl ether (0.3 mL). The vial was sealed with a septum cap, and removed from the glovebox. The vial was allowed to cool to 0˚C, and *trans*-deuterium labeled vinyllithium solution (0.30 mmol, 1.0 equiv) was added. The vial was allowed to warm to room temperature and stir for 30 min. Over this period, white solid formed. Pentane (2 mL) was added to the mixture by syringe, and the white solid was allowed to settle to the bottom of the vial. The clear supernatant was removed by syringe. The resulting white solid was suspended in pentane (3 mL), the white solid was allowed to settle down

to the bottom of the vial, and the clear supernatant was removed by syringe. The pentane wash process was repeated three times. Then, the solvent was carefully removed under reduced pressure, and the vial was brought back into the glovebox. A separated oven-dried 2-dram vial equipped with a magnetic stir bar in the glovebox was charged with $Pd(OAc)_2$ (0.67 mg, 0.003 mmol, 0.01 equiv), (S_p,S_p)-**2.101** (3.80 mg, 0.0036 mmol, 0.012 equiv) and THF (0.6 mL). The $Pd(OAc)_2$/(S_p,S_p)-**2.101** solution was allowed to stir for 20 min at room temperature. The $Pd(OAc)_2$/(S_p, S_p)-**2.101** solution was transferred into the vial, followed by THF (0.6 mL), and cyclohexylidenemethyl trifluoromethanesulfonate (**2.266**) (80.6 mg, 0.33 mmol, 1.10 equiv) was added. The vial was sealed with a polypropylene cap, taped, and brought out of the glovebox where it was allowed to stir at 60 ˚C for 14 h. The resulting mixture was allowed to cool to room temperature, was filtered through a silica gel plug with diethyl ether, and was concentrated under reduced pressure. The mixture was diluted with THF (3 mL), allowed to cool to 0˚C and a 3 M solution of aquious NaOH (2 mL) was added, followed by 30% H_2O_2 (1.0 mL), dropwise. The mixture was allowed to warm to room temperature, and stir for 4 h. The mixture was allowed to cool to 0 ˚C and a saturated solution of aqueous $Na_2S_2O_3$ (3 mL) was added dropwise. The mixture was allowed to warm to room temperature and the product was extracted from the aqueous layer with ethyl acetate (3 x 20 mL). The combined organic layers were dried over Na_2SO_4, filtered, concentrated under reduced pressure, and subsequently purified by silica gel chromatography (5% ethyl acetate in hexanes) to afford the desired product as colorless oil (37.2 mg, 57% yield).

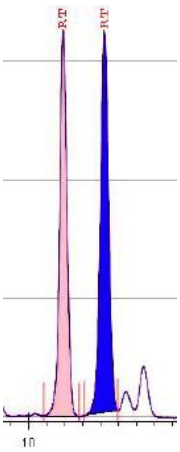


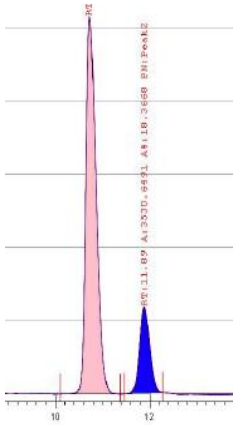
(1*R*,2*R*)-3-Cyclohexylidene-1-phenylpropan-2-*d*-1-ol (2.168). **^{1}H NMR** (500 MHz, $CDCl_3$) δ 7.35-7.31 (4H, m), 7.26-7.23 (1H, m), 5.09 (1H, d, *J* = 7.5 Hz), 4.64 (1H, d, *J* = 5.5 Hz), 2.46 (1H, t, *J* = 7.5 Hz), 2.13-2.05 (4H, m), 2.01 (1H, s), 1.52-1.46 (4H, m), 1.45-1.35 (2H, m). **^{13}C NMR** (100 MHz, $CDCl_3$) δ 144.4, 144.3, 128.5, 127.5, 126.1, 116.3, 74.2, 37.5, 29.1, 28.8, 28.0, 27.0. **IR** (neat) ν_{max} 3358.7 (br), 2923.1 (s), 2851.4 (m), 1493.1 (m), 1446.7 (m), 1343.0 (m), 1233.2 (m), 1025.2 (m), 849.3 (m), 755.9 (m), 697.7 (s), 546.8 (m) cm^{-1}. **HRMS** (DART) for: $C_{15}H_{18}D_1$ $[M+H-H_2O]^+$: calculated: 200.1550, found: 200.1551. **$[\alpha]_D^{20}$** : +40.061 (*c* 0.640, $CHCl_3$, *l* = 50 mm).

Determination of Stereochemical Identity: Racemic compound was prepared according to the general procedure (***Method A***) with 4,4,5,5-tetramethyl-2-vinyl-1,3,2-dioxaborolane, and $Pd(OAc)_2$ (5 mol%) and 1,1′-bis(dicyclohexyl-phosphino)ferrocene (6 mol%) as the catalyst. Absolute stereochemistry was assigned by analogy (see products **2.83**, **2.117**, and **2.120**).

SFC (Chiracel OD-H, 5% IPA, 3 mL/min, 100 bar, 35 °C, 210-270 nm) – analysis of (1R,2R)-3-cyclohexylidene-1-phenylpropan-2-d-1-ol

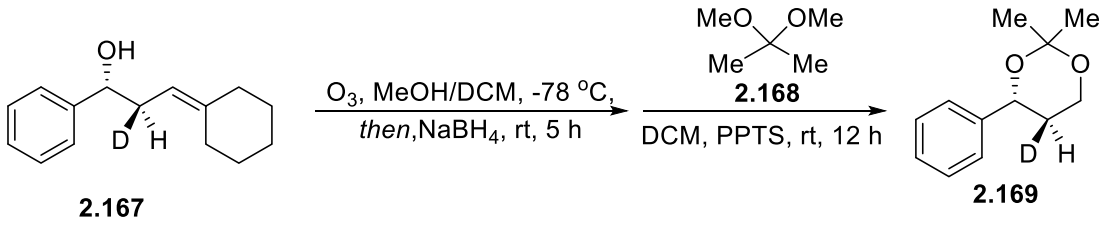
Racemic Material Standard Conditions





Peak No	% Area	Area	RT (min)	Peak No	% Area	Area	RT (min)
1	47.2345	4658.0381	10.96	1	81.6332	15692.3394	10.72
2	52.7655	5203.4843	12.11	2	18.3668	3530.6491	11.89
Total:	100	9861.5224		Total:	100	19222.9885	

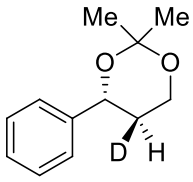
Proof of Stereochemistry: (1*R*,2*R*)-3-cyclohexylidene-1-phenylpropan-2-*d*-1-ol was ozonized, reduced, and cyclized as an acetonide by the sequence shown below. Relative stereochemistry was determined by measuring the coupling constants.



To an oven-dried 6-dram vial equipped with a magnetic stir bar was added (1*R*,2*R*)-3-cyclohexylidene-1-phenylpropan-2-d-1-ol (**34**) (38.2 mg, 0.18 mmol, 1.00 equiv), dichloromethane (3.0 mL), and methanol (3.0 mL). The mixture was allowed to cool to -78 ˚C, and O_3 was allowed to bubble through the mixture until the solution turned blue. Then sodium borohydride (200 mg, 5.3 mmol, 29.4 equiv) was added, and the mixture was

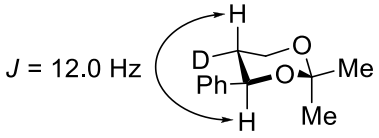
allowed to warm to room temperature and stir for 5 h. Upon completion, the mixture was quenched with water, the product was extracted from the aqueous layer with ethyl acetate (3 x 20 mL). The combined organic layers were dried over Na_2SO_4, filtered, concentrated under reduced pressure, and subsequently purified by silica gel chromatography (30 % ethyl acetate in hexane) to afford (1*R*,2*R*)-1-phenylpropane-2-*d*-1,3-diol as colorless oil (19.5 mg, 71% yield).

To an oven-dried 6-dram vial equipped with a magnetic stir bar was added (1*R*,2*R*)-1-phenylpropane-2-*d*-1,3-diol (19.5 mg, 0.13 mmL, 1.00 equiv), 2,2-dimethoxypropane (0.3 mL), and dichloromethane (2.0 mL). The mixture was allowed to cool to 0 ˚C, and pyridinium *p*-toluenesulfonate (3.3 mg, 0.013 mmol, 0.10 equiv) was added. The mixture was allowed to warm to room temperature and stir for 12 h. Upon completion, the mixture was concentrated under reduced pressure, and subsequently purified using silica gel chromatography (5 % ethyl acetate in hexane) to afford (4*R*,5*R*)-2,2-dimethyl-4-phenyl-1,3-dioxane-5-*d* as colorless oil (20.6 mg, 82% yield).



(4*R*,5*R*)-2,2-Dimethyl-4-phenyl-1,3-dioxane-5-*d* (S-30). ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.38-7.32 (4H, m), 7.27-7.24 (1H, m), 4.91 (1H, d, *J* = 12.0 Hz), 4.13 (1H, t, *J* = 12.6 Hz), 3.91 (1H, dd, *J* = 11.4, 4.8 Hz), 1.88 (1H, dt, *J* = 12.6, 5.4 Hz), 2.01 (1H, s), 1.57 (3H, s), 1.49 (3H, s). **^{13}C NMR** (150 MHz, $CDCl_3$) δ 142.6, 128.6, 127.8, 126.1, 99.0, 71.6, 60.3, 30.3, 19.4. **IR** (neat) ν_{max} 2992.2 (m), 2938.2 (m), 2866.1 (m), 1452.7 (m), 1378.4 (s), 1368.5 (s), 1223.1 (m), 1195.6 (s), 1163.6

(m), 949.2 (m), 886.8 (s), 698.4 (s), 520.8 (m) cm^{-1}. **HRMS** (DART) for: $C_{12}H_{16}D_1O_2$ $[M+H]^+$: calculated: 194.1291, found: 194.1289.



anti relative stereochemistry was determined

by measuring the coupling constant

2.9.3 Computational Information

2.9.3.1 DFT Calculations to Probe Palladium-Induced Rearrangement and Carbopalladation Pathways: Scheme 2.25

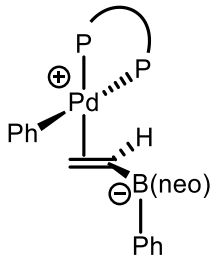
All calculations were performed using the Gaussian09 package of programs.[76] Geometry optimizations were carried out with the density functional BP86 in conjunction with the def2-SVP[77] basis set in tetrahydrofuran as solvent using the IEFPCM model.[78] Very tight convergence criteria and an ultrafine integration grid were applied. Stationary points were assessed through vibrational analysis and Gibbs free energy corrections were performed

[76] Frisch, M. J.; Trucks, G. W.; Schlegel, H. B.; Scuseria, G. E.; Robb, M. A.; Cheeseman, J. R.; Scalmani, G.; Barone, V.; Mennucci, B.; Petersson, G. A.; Nakatsuji, H.; Caricato, M.; Li, X.; Hratchian, H. P.; Izmaylov, A. F.; Bloino, J.; Zheng, G.; Sonnenberg, J. L.; Hada, M.; Ehara, M.; Toyota, K.; Fukuda, R.; Hasegawa, J.; Ishida, M.; Nakajima, T.; Honda, Y.; Kitao, O.; Nakai, H.; Vreven, T.; Montgomery, Jr., J. A.; Peralta, J. E.; Ogliaro, F.; Bearpark, M.; Heyd, J. J.; Brothers, E.; Kudin, K. N.; Staroverov, V. N.; Kobayashi, R.; Normand, J.; Raghavachari, K.; Rendell, A.; Burant, J. C.; Iyengar, S. S.; Tomasi, J.; Cossi, M.; Rega, N.; Millam, J. M.; Klene, M.; Knox, J. E.; Cross, J. B.; Bakken, V.; Adamo, C.; Jaramillo, J.; Gomperts, R.; Stratmann, R. E.; Yazyev, O.; Austin, A. J.; Cammi, R.; Pomelli, C.; Ochterski, J. W.; Martin, R. L.; Morokuma, K.; Zakrzewski, V. G.; Voth, G. A.; Salvador, Page S-75 Myhill, Zhang, Lovinger, and Morken Supplementary Information P.; Dannenberg, J. J.; Dapprich, S.; Daniels, A. D.; Farkas, Ö.; Foresman, J. B.; Ortiz, J. V.; Cioslowski, J.; Fox, D. J. Gaussian 09, Revision D.01, Gaussian, Inc., Wallingford CT, **2009**.

[77] (a) Weigend, F.; Ahlrichs, R. *Phys. Chem. Chem. Phys*. **2005**, 7, 3297.; (b) Weigend, F. *Phys. Chem. Chem. Phys.* **2006**, 8, 1057.

[78] Scalmani, G.; Frisch, M. J. *J. Chem. Phys*. **2010**, 132, 114110. Huang et al., Supporting Information, page S354.

under standard conditions (298.15 K, 1.0 atm). Intrinsic Reaction Coordinate (IRC)[79] calculations were performed on transition state sturctures followed by subsequent optimization of the end points with the previously mentioned optimization method. Gibbs free energies have been assessed through single point calculations with the density functional M06[80] applying the larger def2-TZVPP[73] basis set, followed by addition of thermal corrections obtained at the level of geometry optimization (denoted as M06/def2-TZVPP//BP86/def2-SVP). The diphosphine ligand employed in these calculations is 1,1'-Bis(diphenylphosphino)ferrocene.



2.171

BP86 Optimization and Frequency Calculation:
Thermal correction to Gibbs Free Energy= 0.775274 a.u.
Lowest frequency= 9.86 cm^{-1}
M06 Single Point Calculation:
Electronic Energy= -4299.19708 a.u.

0 1

Fe	3.16444400	-1.95644500	-1.47969500
P	0.19012800	-2.09405900	0.13290700
P	2.17655300	1.05504800	-0.13719500
C	1.82873100	-2.84696900	-0.24908600
C	3.07226000	-2.57552700	0.45266600
C	4.13413500	-3.27387100	-0.21879700
C	3.56977000	-3.97711600	-1.33697600
C	2.15547100	-3.72247900	-1.36321400
C	2.90295900	0.04373100	-1.48513500
C	4.30163400	-0.28011300	-1.71003200
C	4.38627600	-1.08388000	-2.89919900
C	3.05859600	-1.26272800	-3.42089900
C	2.13998700	-0.57136400	-2.55757500

[79] (a) Page, M.; McIver Jr., J. W. *J. Chem. Phys*. **1988**, 88, 922. (b) Page, M.; Doubleday Jr., C.; McIver Jr., J. W. *J. Chem. Phys*. **1990**, 93, 5634.
[80] Zhao, Y.; Truhlar, D. G. *Acc. Chem. Res*. **2008**, 41, 157.

C	-0.84941400	-2.75995500	-1.24672500
C	-1.02397600	-4.15537000	-1.41975500
C	-1.76430200	-4.64727500	-2.50676800
C	-2.33953000	-3.75387000	-3.43126200
C	-2.18600100	-2.36926500	-3.25271200
C	-1.44859500	-1.86965800	-2.16219600
C	-0.37182300	-3.06682400	1.61980600
C	-1.69930900	-3.54029800	1.73582200
C	-2.12605300	-4.18787600	2.90942600
C	-1.23751500	-4.37263400	3.98251900
C	0.08451400	-3.90396100	3.87692400
C	0.51313300	-3.25209400	2.70814200
C	3.51074000	1.09887900	1.14430200
C	4.73190500	1.77579000	0.91950100
C	5.74435500	1.75245200	1.89453900
C	5.54938100	1.05924100	3.10316000
C	4.33465400	0.39148400	3.33812700
C	3.32001400	0.41514800	2.36493400
C	2.22433200	2.75072900	-0.89232500
C	1.97671700	2.91427900	-2.27407400
C	1.99507000	4.19559300	-2.85299800
C	2.26514500	5.32588000	-2.06182200
C	2.50462900	5.16997400	-0.68476600
C	2.47452900	3.89335400	-0.09885700
H	5.19486900	-3.24710200	0.06309900
H	4.12322900	-4.58375700	-2.06592700
H	5.30704200	-1.51235100	-3.31691700
H	2.78505700	-1.84950800	-4.30758700
H	-0.58112500	-4.86279800	-0.70118900
H	-2.91971700	-4.14124600	-4.28389600
H	-1.39801500	-0.78028300	-2.00564700
H	-2.41008600	-3.41545800	0.90504300
H	-1.57370300	-4.88165800	4.89953200
H	1.55248300	-2.89629200	2.64734000
H	4.89363100	2.33328700	-0.01596900
H	6.34358200	1.04611800	3.86614100
H	2.36162800	-0.09656400	2.55254300
H	1.77610200	2.03975200	-2.91107600
H	2.28649500	6.32845800	-2.51759000
H	2.64471300	3.79028100	0.98350000
C	0.05254700	2.22464300	1.54941800
C	-0.56640200	3.30454300	0.88957700
C	0.58562600	2.43624500	2.84058700
C	-0.64923800	4.56873900	1.50587200

H	-1.01596300	3.16361700	-0.10220400
C	0.50801300	3.70407800	3.45469400
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C	-0.10993500	4.77666400	2.78786600
H	-1.14423700	5.39761500	0.97332300
H	0.93164800	3.84501600	4.46309300
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H	-1.89394400	-5.73404400	-2.63151100
H	-2.65512800	-1.66293300	-3.95487800
H	2.70909800	6.05007600	-0.05493400
H	6.69126600	2.28315400	1.70788700
H	4.17044700	-0.14458500	4.28597900
H	-3.16335600	-4.55148200	2.97944200
H	0.79117600	-4.04589300	4.70992800
H	3.19981000	-1.92367300	1.32471200
H	1.04876200	-0.53362400	-2.67273700
Pd	0.09241000	0.33325700	0.72507700
C	-2.36877100	-0.12446500	0.76381000
H	-2.33768000	-1.17812900	0.42263600
B	-3.44972100	0.77016000	-0.06150400
O	-3.27139000	0.57820400	-1.53023800
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H	-5.22809800	1.01265700	-2.13828900
H	-3.94465900	1.17699500	-3.38524400
C	-4.08808400	2.86380100	-1.98820000
C	-5.21465300	3.61078500	-2.72058600
H	-5.18927400	4.69893300	-2.49364600
H	-5.12118700	3.49906600	-3.82283400
H	-6.21642100	3.22904500	-2.42675100
C	-2.71820400	3.41397200	-2.42353300
H	-2.59466000	3.34658500	-3.52650900
H	-2.59789200	4.48007300	-2.13321400
H	-1.89792200	2.83373500	-1.95632500
C	-4.85749500	0.03919900	0.47722700
C	-5.40213900	-1.10617200	-0.15471500
C	-5.53874300	0.52126600	1.62229700
C	-6.57252000	-1.73165300	0.31797500
H	-4.89789600	-1.50919000	-1.05047900
C	-6.71045300	-0.09072800	2.10522100

H	-5.13461300	1.40922800	2.13928500
C	-7.23315800	-1.22451900	1.45292600
H	-6.97432300	-2.61889800	-0.20087500
H	-7.22152500	0.31571300	2.99480500
H	-8.14940600	-1.71005300	1.82788300
C	-1.77824700	0.11792200	2.00046000
H	-1.95050100	1.08240600	2.50272900
H	-1.42703400	-0.70637100	2.65052100
H	5.14366000	0.01170600	-1.07079600
H	1.45227500	-4.09887700	-2.11491700

1 4 1.0 5 1.0 8 1.0 9 1.0 10 1.0 13 1.0
2 4 1.0 14 1.0 20 1.0
3 9 1.0 26 1.0 32 1.0 75 1.0
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7 8 1.5 39 1.0
8 111 1.0
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10 11 1.5 110 1.0
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13 74 1.0
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18 19 1.5 67 1.0
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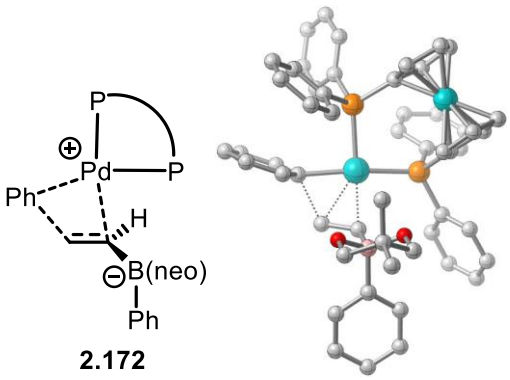

2.172

BP86 Optimization and Frequency Calculation:
Thermal correction to Gibbs Free Energy= 0.776132 a.u.
Lowest frequency= 272.50 cm^{-1}
M06 Single Point Calculation:
Electronic Energy= -4299.183376 a.u.

0 1

Fe	-1.70597200	1.74152500	2.50870400
P	0.31880600	1.88174300	-0.23617800
P	-2.29902300	-0.64386800	-0.00237900
C	0.00763400	2.20492400	1.53544800
C	0.27135100	1.20902000	2.55652000
C	-0.11240300	1.75963400	3.82607500
C	-0.60594700	3.09333000	3.60763300
C	-0.53538000	3.37663300	2.19921800
C	-2.82908400	0.45758800	1.38742700
C	-2.94349000	0.12741200	2.79434200
C	-3.46162500	1.27675800	3.48492100
C	-3.67571100	2.32244400	2.52101300
C	-3.28331300	1.82802900	1.22854200
C	-0.80400400	3.04644200	-1.15518000
C	-0.69253100	4.44878000	-0.99730700
C	-1.54036700	5.31396500	-1.70845500
C	-2.49653700	4.79446100	-2.60214000
C	-2.59386400	3.40516400	-2.78747100
C	-1.74952200	2.53797800	-2.06911600
C	1.93446200	2.75394700	-0.53262900
C	2.31282000	3.06816900	-1.85881300
C	3.50969900	3.75836400	-2.11358500
C	4.34158000	4.14530800	-1.04665100
C	3.97503100	3.82683700	0.27275200

C	2.78130800	3.12805100	0.53108200
C	-2.51988000	-2.31003800	0.78524400
C	-3.58085300	-3.18210600	0.46357000
C	-3.70043900	-4.42331200	1.11553400
C	-2.76795700	-4.80496300	2.09548100
C	-1.69930800	-3.94580100	2.41061900
C	-1.56835600	-2.71334800	1.74976800
C	-3.78907300	-0.48840800	-1.10631800
C	-5.08641000	-0.34677100	-0.55747100
C	-6.20595200	-0.23092800	-1.39836200
C	-6.04750400	-0.25103500	-2.79675300
C	-4.76313900	-0.38902100	-3.35023900
C	-3.64129300	-0.50642000	-2.50913700
H	-0.05858100	1.24310100	4.79350500
H	-1.00173100	3.77029600	4.37661800
H	-3.64025800	1.34694900	4.56617500
H	-4.04600600	3.33390500	2.73488100
H	0.07564600	4.87225600	-0.33188200
H	-3.15614800	5.47581500	-3.16254500
H	-1.81893300	1.45018300	-2.22153600
H	1.66041800	2.78832100	-2.70243600
H	5.27647600	4.69301200	-1.24488500
H	2.50812100	2.87651500	1.56593200
H	-4.32186300	-2.89850700	-0.29829500
H	-2.86822300	-5.77481600	2.60805000
H	-0.71210800	-2.06107400	1.98328700
H	-5.22467900	-0.32499600	0.53454300
H	-6.92652500	-0.15630400	-3.45380600
H	-2.63995200	-0.61863400	-2.94792000
C	-0.18554200	-2.35408200	-1.85034200
C	-0.88347800	-2.48212900	-3.07473100
C	-0.05226200	-3.49696600	-1.02509200
C	-1.48517700	-3.70218900	-3.43627900
H	-0.93436700	-1.63072000	-3.77344600
C	-0.65384800	-4.71374100	-1.38872000
H	0.57857700	-3.43319700	-0.12500200
C	-1.37898200	-4.82204000	-2.59137500
H	-2.02965300	-3.77726300	-4.39189000
H	-0.54142300	-5.59093300	-0.73101600
H	-1.84136200	-5.77996500	-2.87848000
H	-7.20923000	-0.12166700	-0.95678000
H	-1.44633400	6.40294000	-1.57126200
H	-3.32669700	2.98829000	-3.49607200
H	-4.62890600	-0.40423900	-4.44336900

H	-4.53359700	-5.09478700	0.85342400
H	-0.95431800	-4.23982800	3.16664600
H	3.79027800	3.99903700	-3.15124800
H	4.62302300	4.12313000	1.11300300
H	0.72265400	0.22755400	2.36308200
H	-3.32377800	2.38656600	0.28476300
Pd	-0.01239400	-0.41941800	-0.89943400
C	2.14039200	-0.52143400	-1.29684000
H	2.34232900	0.48752700	-1.69791300
B	3.11292900	-1.03426500	-0.07552800
O	2.80368800	-2.45690000	0.26056900
O	2.98204900	-0.17758300	1.13523800
C	3.77480900	-0.62703200	2.21228000
H	4.86707000	-0.54881400	1.96658300
H	3.59544300	0.03756900	3.09206300
C	3.58633100	-2.95843500	1.32166300
H	4.66888400	-3.01129600	1.03104600
H	3.26275300	-4.00410200	1.54515200
C	3.48629500	-2.10197000	2.61702800
C	4.53887600	-2.57439600	3.63331500
H	4.37247900	-3.63534400	3.92135600
H	5.56802100	-2.49449100	3.22118500
H	4.50033400	-1.96761000	4.56422700
C	2.07809100	-2.22454300	3.22278200
H	1.85713300	-3.27309300	3.51856900
H	1.96656700	-1.58446100	4.12461300
H	1.31730200	-1.91310500	2.47999600
C	4.62303200	-0.90749700	-0.77136900
C	5.18523300	-1.97341100	-1.51769800
C	5.37883200	0.28966600	-0.70991400
C	6.43401400	-1.86292100	-2.15855000
H	4.62350500	-2.92177800	-1.58801600
C	6.63009200	0.41648400	-1.34404200
H	4.97009600	1.14545600	-0.14512000
C	7.16496800	-0.66229200	-2.07366300
H	6.84272200	-2.71644300	-2.72644800
H	7.19330500	1.36270800	-1.27100000
H	8.14361400	-0.56822700	-2.57310900
C	1.63695200	-1.45101200	-2.25819600
H	1.42917900	-1.12522100	-3.29322500
H	2.00544400	-2.48419900	-2.17979600
H	-2.67981600	-0.83317800	3.25290700
H	-0.87019600	4.30289000	1.71718700

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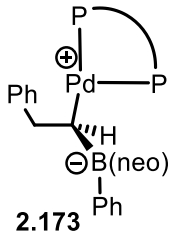

2.173

BP86 Optimization and Frequency Calculation:
Thermal correction to Gibbs Free Energy= 0.776199 a.u.
Lowest frequency= 6.47 cm^{-1}
M06 Single Point Calculation:
Electronic Energy= -4299.222555 a.u.

0 1

Fe	-1.94668900	1.71501500	2.47369400
P	0.22037800	1.86455700	-0.21553100
P	-2.28191800	-0.80427900	0.09478600
C	-0.22694300	2.22413600	1.52244700
C	0.05632700	1.30627500	2.60908700

C	-0.40167900	1.90622200	3.83123700
C	-0.96461400	3.19268500	3.51763400
C	-0.86361800	3.39614300	2.09717700
C	-2.97587100	0.30737300	1.39665800
C	-3.08198800	0.03477400	2.81449300
C	-3.68003200	1.17848000	3.44861300
C	-3.94816000	2.16481100	2.43600200
C	-3.50786500	1.63931800	1.17061000
C	-0.93012900	2.89770100	-1.24678500
C	-0.91623800	4.31058300	-1.15857500
C	-1.78965600	5.07901500	-1.94624300
C	-2.67439900	4.45083000	-2.84341500
C	-2.67492700	3.05013800	-2.95593500
C	-1.80469200	2.27909000	-2.16313500
C	1.79380300	2.82620200	-0.43613100
C	2.21942100	3.16213400	-1.74291400
C	3.39859400	3.89925900	-1.93940700
C	4.16738200	4.30917500	-0.83402600
C	3.75457800	3.96899400	0.46604000
C	2.57671100	3.22602900	0.66703000
C	-2.50687400	-2.46260400	0.90848800
C	-3.62567100	-3.29293400	0.67975700
C	-3.72683700	-4.54036800	1.32233600
C	-2.71848700	-4.97065700	2.20313700
C	-1.60041400	-4.14865000	2.43482000
C	-1.49152800	-2.90724100	1.78479700
C	-3.63130000	-0.77515100	-1.17980000
C	-4.98537500	-0.52373600	-0.85670400
C	-5.96819300	-0.52782600	-1.86208400
C	-5.61300400	-0.78336100	-3.19953300
C	-4.26923100	-1.03537500	-3.52847900
C	-3.28364800	-1.02844700	-2.52508100
H	-0.35176800	1.45064800	4.82906200
H	-1.42580400	3.88813400	4.23178000
H	-3.87666000	1.28568100	4.52368900
H	-4.38624200	3.15825200	2.60084100
H	-0.20578900	4.81820900	-0.48789000
H	-3.35397000	5.05666600	-3.46354100
H	-1.79542100	1.18249800	-2.25799800
H	1.62103400	2.85478000	-2.61605800
H	5.08981200	4.89133300	-0.98747700
H	2.26689200	2.95982300	1.68789400
H	-4.42271800	-2.97265700	-0.00807600
H	-2.80019700	-5.94848500	2.70362800

H	-0.59920700	-2.28363000	1.95114600
H	-5.27656100	-0.32205100	0.18566500
H	-6.38464800	-0.78294900	-3.98571400
H	-2.23168800	-1.22175100	-2.79077000
C	0.84335600	-2.06048500	-2.62678000
C	0.17450800	-2.27276100	-3.85907000
C	0.41389600	-2.79554400	-1.48472300
C	-0.84166500	-3.23280300	-3.97044600
H	0.48884500	-1.69929800	-4.74694700
C	-0.62720300	-3.74987800	-1.60632400
H	1.02873100	-2.75448100	-0.55782100
C	-1.24501600	-3.97971400	-2.84192400
H	-1.32479000	-3.40692400	-4.94565300
H	-0.93125800	-4.33044700	-0.72189500
H	-2.03896100	-4.73728300	-2.93519400
H	-7.01909800	-0.32969300	-1.59738600
H	-1.77157800	6.17748100	-1.86524400
H	-3.35064500	2.54932600	-3.66686600
H	-3.98202400	-1.23502000	-4.57297500
H	-4.60291900	-5.18027100	1.13023400
H	-0.80023300	-4.47864700	3.11589500
H	3.71689800	4.15641300	-2.96210900
H	4.35273200	4.28358300	1.33600900
H	0.56012200	0.33864800	2.48951900
H	-3.56812300	2.15145400	0.20167900
Pd	0.06338200	-0.40212500	-0.65921400
C	2.12255300	-0.40361300	-1.19136000
H	2.45386700	0.63674500	-1.36203900
B	3.05268500	-1.00021700	0.04203700
O	2.74419100	-2.42028300	0.39753100
O	2.91419200	-0.13236300	1.24719400
C	3.69132300	-0.56880600	2.33912900
H	4.78715100	-0.50778800	2.10418700
H	3.51049900	0.11275600	3.20573700
C	3.49389400	-2.91304300	1.48905400
H	4.58055100	-2.98570300	1.22282400
H	3.14906200	-3.94952300	1.72078300
C	3.37667800	-2.03163400	2.76502200
C	4.39820300	-2.50232800	3.81297100
H	4.20768100	-3.55463800	4.11726800
H	5.43738000	-2.44716500	3.42256400
H	4.34905700	-1.87691100	4.73085600
C	1.95272000	-2.11379100	3.33730300
H	1.68889800	-3.15480600	3.62398500

H	1.83911000	-1.47130100	4.23702700
H	1.22607300	-1.77065800	2.57426400
C	4.58388500	-0.88103500	-0.60921500
C	5.20758000	-1.96592900	-1.27534000
C	5.30524200	0.33907000	-0.57310100
C	6.48189100	-1.85008200	-1.86511600
H	4.67951700	-2.93501800	-1.31823800
C	6.58053800	0.47024800	-1.15471400
H	4.84955500	1.20712800	-0.06557200
C	7.17584100	-0.62683600	-1.80735400
H	6.93879200	-2.71850500	-2.37008400
H	7.11563200	1.43391900	-1.10187600
H	8.17336000	-0.52894400	-2.26703900
C	2.05266200	-1.13948700	-2.53957500
H	2.01371700	-0.43115300	-3.39518200
H	2.97842000	-1.74560500	-2.69457300
H	-2.75717300	-0.88543900	3.31592500
H	-1.23294600	4.27133400	1.54940800

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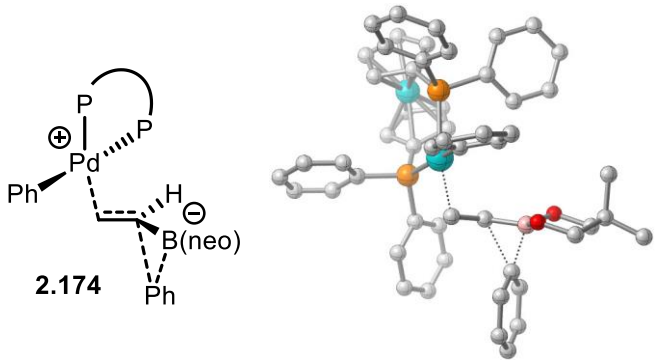

2.174

BP86 Optimization and Frequency Calculation:
Thermal correction to Gibbs Free Energy= 0.774952 a.u.
Lowest frequency= -275.96 cm^{-1}
M06 Single Point Calculation:
Electronic Energy= -4299.187622 a.u.

0 1

Fe	3.36702200	1.23350000	-1.89087900
P	0.74962400	2.08980000	0.12852000
P	1.99606100	-1.37954000	-0.09743000
C	1.71235300	2.29420900	-1.41802400
C	1.47784900	1.48729100	-2.60429100
C	2.42487100	1.88230800	-3.61049700
C	3.24804500	2.92753000	-3.06462100
C	2.81453000	3.18940500	-1.71844400
C	3.43981600	-0.49153000	-0.82319000
C	4.03066500	-0.68483900	-2.13537200
C	5.13083100	0.23005000	-2.27335300
C	5.23677100	0.99426300	-1.06066200
C	4.19760100	0.56068200	-0.16567200
C	1.80286600	2.83136000	1.46469800
C	2.16753300	4.19824200	1.46454700
C	2.96479000	4.72018000	2.49752900
C	3.39561100	3.88964700	3.54924000
C	3.02148400	2.53474300	3.56832900
C	2.22782500	2.00911700	2.53213300
C	-0.56218600	3.39376200	-0.07460400
C	-1.13765500	4.01164100	1.06065300
C	-2.15226200	4.97304800	0.91143700
C	-2.60767700	5.33008300	-0.37003700
C	-2.04553000	4.71629900	-1.50353500
C	-1.03239500	3.75236500	-1.35895100
C	1.41357500	-2.39972600	-1.53198400

C	2.18987700	-3.45553400	-2.06374500
C	1.73442500	-4.17629300	-3.18131600
C	0.50245000	-3.85201400	-3.77994400
C	-0.27731000	-2.80758700	-3.25328400
C	0.17396600	-2.08808700	-2.13190500
C	2.84491800	-2.61766900	1.00415200
C	4.01746200	-2.26950400	1.71279300
C	4.62848700	-3.19090700	2.58219600
C	4.07976600	-4.47341600	2.75483900
C	2.91083500	-4.82593200	2.05689000
C	2.29232500	-3.90536200	1.19402000
H	2.51895800	1.44078600	-4.61132300
H	4.08544600	3.42228700	-3.57457700
H	5.76133600	0.34317500	-3.16533500
H	5.96245900	1.79340200	-0.85973000
H	1.81275600	4.86631400	0.66419300
H	4.01561700	4.30342800	4.36025100
H	1.92460400	0.94772600	2.54690600
H	-0.77727000	3.76178600	2.07104900
H	-3.39949000	6.08687600	-0.48500800
H	-0.59772000	3.28643800	-2.25674500
H	3.15355900	-3.72144100	-1.60181500
H	0.14781100	-4.42016500	-4.65453500
H	-0.44907800	-1.28511500	-1.70172800
H	4.47295700	-1.27687300	1.58286900
H	4.56152200	-5.19664600	3.43187300
H	1.36930500	-4.19324800	0.66941000
C	-0.40005400	-1.94192000	1.69950400
C	-0.02274900	-2.11535200	3.05246700
C	-1.13816800	-2.97342200	1.08014300
C	-0.36721900	-3.28336400	3.76188600
H	0.55018600	-1.33016700	3.57491200
C	-1.47538900	-4.14772500	1.78395300
H	-1.47150300	-2.86689900	0.03765400
C	-1.09312400	-4.30852700	3.12776500
H	-0.06229100	-3.39089000	4.81650300
H	-2.05305500	-4.93795200	1.27562700
H	-1.36287100	-5.22394400	3.67936500
H	5.54461800	-2.90208600	3.12169700
H	3.24497300	5.78545000	2.48453100
H	3.34226200	1.88214300	4.39553200
H	2.46860200	-5.82640600	2.18683400
H	2.34661100	-4.99793800	-3.58592200
H	-1.24773600	-2.55234000	-3.70649100

H	-2.58595300	5.44818000	1.80550100
H	-2.39292500	4.99151500	-2.51207500
H	0.71986700	0.69947900	-2.70201500
H	3.99810200	0.97696800	0.83006300
Pd	0.11257900	-0.17661500	0.78400900
C	-2.49401300	0.46572600	0.26343200
H	-2.23124500	1.27746300	-0.44167100
B	-3.65142700	-0.45215000	-0.22042500
O	-4.04062200	-1.58706100	0.57794100
O	-3.82286200	-0.59146100	-1.65393100
C	-5.03727400	-1.19917800	-2.05889500
H	-5.90112300	-0.50579400	-1.88326100
H	-4.98730500	-1.37992500	-3.15809500
C	-5.24729100	-2.22030700	0.19794100
H	-6.12860800	-1.58090800	0.46856800
H	-5.34407000	-3.16519800	0.78168500
C	-5.32084800	-2.53244900	-1.31991400
C	-6.73125200	-3.03145600	-1.67575600
H	-6.81965800	-3.23843500	-2.76410900
H	-6.96966800	-3.97385700	-1.13716000
H	-7.50954000	-2.28414700	-1.40952600
C	-4.26805400	-3.58861400	-1.70530300
H	-4.43751800	-4.53994000	-1.15661600
H	-4.30902700	-3.81215800	-2.79323700
H	-3.24585600	-3.23289400	-1.46805900
C	-4.53916900	1.00122900	0.34693300
C	-5.10928300	1.01303300	1.63937100
C	-4.96646300	1.97098000	-0.58692400
C	-6.10751300	1.94200300	1.98017500
H	-4.77053400	0.26972500	2.38021400
C	-5.96222500	2.90784200	-0.25100900
H	-4.52602800	1.97406500	-1.59803400
C	-6.53610300	2.89472800	1.03403300
H	-6.55511100	1.92684300	2.98795100
H	-6.29296700	3.65194800	-0.99466500
H	-7.31499800	3.62768000	1.30032900
C	-1.81605000	0.51185600	1.53177400
H	-1.58057000	1.51099100	1.94880400
H	-2.17196500	-0.19343900	2.30185000
H	3.68140300	-1.38987400	-2.89929100
H	3.26560400	3.91489100	-1.03061400

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7 8 1.5 39 1.0
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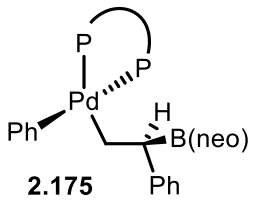

2.175

BP86 Optimization and Frequency Calculation:
Thermal correction to Gibbs Free Energy= 0.776828 a.u.
Lowest frequency= 12.95 cm^{-1}
M06 Single Point Calculation:
Electronic Energy= -4299.241986 a.u.

0 1

Fe	3.16264800	1.44418600	-1.95926000
P	0.43007400	2.06793500	0.01996300
P	2.11962100	-1.19147400	0.01339800
C	1.38564300	2.31326100	-1.53099900
C	1.25617800	1.43024100	-2.67788300
C	2.15197000	1.88769900	-3.70457200
C	2.83885600	3.05115600	-3.21140000

C	2.37087400	3.32100200	-1.87805300
C	3.45421300	-0.19083600	-0.78190000
C	4.05293400	-0.39648800	-2.08771700
C	5.02986700	0.63537600	-2.30584600
C	5.05222500	1.48575300	-1.14691200
C	4.08130900	0.98897000	-0.20840300
C	1.43075100	2.91374900	1.34131400
C	1.71393200	4.29934500	1.30934300
C	2.47371900	4.89417400	2.33133800
C	2.94720400	4.11815500	3.40618300
C	2.65204400	2.74468200	3.45863100
C	1.89643900	2.14711500	2.43273200
C	-0.93988200	3.30829300	-0.21429400
C	-1.55416300	3.91095100	0.90828600
C	-2.58363600	4.85281300	0.73903100
C	-3.02154800	5.20034400	-0.55104700
C	-2.42787300	4.59432200	-1.67252600
C	-1.39580200	3.65342100	-1.50698400
C	1.78229900	-2.42802700	-1.33137700
C	2.69713600	-3.45274400	-1.66430900
C	2.42857500	-4.32368000	-2.73483100
C	1.24868100	-4.17777600	-3.48817300
C	0.33187300	-3.16319700	-3.16074200
C	0.59414800	-2.29830600	-2.08266100
C	3.09875100	-2.18561100	1.25263200
C	4.29428400	-1.69084100	1.82247900
C	4.98632200	-2.43271500	2.79729200
C	4.49844700	-3.68225700	3.21633700
C	3.30957200	-4.18271400	2.65542900
C	2.61044500	-3.44089600	1.68820800
H	2.30266000	1.41380300	-4.68352100
H	3.61098200	3.62034400	-3.74632300
H	5.63444700	0.76444300	-3.21357600
H	5.67669500	2.37859000	-1.01014400
H	1.32224700	4.92596900	0.49291700
H	3.53731600	4.58855900	4.20873100
H	1.65126700	1.07104200	2.47143600
H	-1.21107100	3.66463900	1.92534900
H	-3.82541900	5.94184300	-0.68201700
H	-0.93193800	3.19743600	-2.39542500
H	3.62616800	-3.57222800	-1.08504600
H	1.04205700	-4.85990600	-4.32819000
H	-0.13407000	-1.51787200	-1.80030900
H	4.70491000	-0.72329800	1.49927700

H	5.04305200	-4.26521000	3.97612500
H	1.67601800	-3.84491700	1.27076000
C	-0.41341500	-1.96698000	1.70409300
C	-0.22043600	-2.01294200	3.10915700
C	-0.88441200	-3.14994700	1.08571900
C	-0.47086400	-3.18151600	3.85570700
H	0.13245200	-1.11514800	3.64549300
C	-1.14061800	-4.32329000	1.82571600
H	-1.05618400	-3.17178000	-0.00142600
C	-0.93327800	-4.34712500	3.21683000
H	-0.30478300	-3.17874500	4.94656100
H	-1.50585700	-5.22602200	1.30672200
H	-1.13425200	-5.26217000	3.79779300
H	5.91870900	-2.02957500	3.22415500
H	2.69002600	5.97371000	2.29197400
H	3.00498200	2.13301900	4.30397700
H	2.91524500	-5.16053700	2.97481000
H	3.14797300	-5.12023500	-2.98341000
H	-0.59692800	-3.04713700	-3.74082800
H	-3.04550600	5.31790100	1.62429900
H	-2.76320500	4.85986800	-2.68792800
H	0.59862900	0.55363300	-2.73551700
H	3.84210500	1.44084200	0.76260900
Pd	-0.00372000	-0.20780600	0.72078300
C	-3.00859900	0.46461600	0.18708400
H	-2.57076500	1.02204500	-0.66961100
B	-3.65896800	-0.86423700	-0.42103000
O	-4.07045500	-1.87422900	0.41514300
O	-3.91908100	-0.89375600	-1.77962000
C	-4.81869000	-1.87986100	-2.30628700
H	-5.85811200	-1.48350900	-2.23749600
H	-4.58312900	-2.00587900	-3.38526700
C	-4.88659600	-2.94998200	-0.06448200
H	-5.94989600	-2.70101900	0.15648900
H	-4.62860100	-3.85430300	0.52805100
C	-4.72413000	-3.23550800	-1.57503300
C	-5.87330300	-4.14950800	-2.03981000
H	-5.79503100	-4.36115200	-3.12702600
H	-5.84351100	-5.12338000	-1.50715400
H	-6.86635600	-3.68914900	-1.85219900
C	-3.36740100	-3.90428900	-1.87265000
H	-3.26374900	-4.85864400	-1.31552900
H	-3.27212100	-4.12928100	-2.95565800
H	-2.51671400	-3.25328300	-1.58914900

C	-4.27287600	1.24071300	0.59892500
C	-4.74108200	1.26172000	1.93421100
C	-5.04842600	1.91347200	-0.37813400
C	-5.92833700	1.93278700	2.27990700
H	-4.16421700	0.74497100	2.71650500
C	-6.23472700	2.58447600	-0.03659600
H	-4.70587000	1.91023000	-1.42571300
C	-6.68295900	2.59890000	1.29765900
H	-6.26618700	1.93419700	3.32951100
H	-6.81195600	3.10510100	-0.81853600
H	-7.61198500	3.12584800	1.56887000
C	-1.97653300	0.30407600	1.31946200
H	-1.85941400	1.27042200	1.86040500
H	-2.32483500	-0.43968100	2.06189400
H	3.78842600	-1.19176000	-2.79507100
H	2.72867900	4.12850300	-1.22789000

1 4 1.0 5 1.0 8 1.0 9 1.0 13 1.0
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5 6 1.5 73 1.0
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7 8 1.5 39 1.0
8 111 1.0
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21 22 1.5 45 1.0
22 23 1.5 71 1.0
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30 31 1.5 70 1.0
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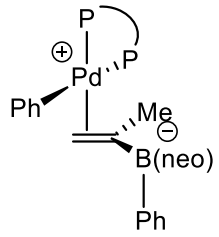
2.9.3.2 DFT Calculations: Application of Substituted Alkenylboron Reagents to Conjunctive Coupling: Scheme 2.29

All calculations were performed using the Gaussian09 package of programs.[72] Geometry optimizations were carried out with the density functional BP86 in conjunction with the def2-SVP[73] basis set in tetrahydrofuran as solvent using the IEFPCM model.[74] Very tight convergence criteria and an ultrafine integration grid were applied. Stationary points were assessed through vibrational analysis and Gibbs free energy corrections were performed under standard conditions (298.15 K, 1.0 atm). Intrinsic Reaction Coordinate (IRC)[75] calculations were performed on transition state sturctures followed by subsequent optimization of the end points with the previously mentioned optimization method. Gibbs free energies have been assessed through single point calculations with the density functional M06[76] applying the larger def2-TZVPP[73] basis set, followed by addition of thermal corrections obtained at the level of geometry optimization (denoted as M06/def2-TZVPP//BP86/def2-SVP). The diphosphine ligand employed in these calculations is 1,1'-Bis(diphenylphosphino)ferrocene.



2.193

BP86 Optimization and Frequency Calculation:
Thermal correction to Gibbs Free Energy = 0.799271 au
M06 Single Point Calculation:
Electronic Energy: -4338.4916 au

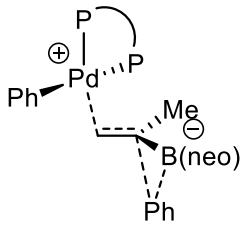
0 1

Fe	3.55870300	0.50254500	-2.01676400
P	1.41844400	2.01623000	0.13845700
P	1.61474500	-1.66790000	-0.11119900
C	2.32127800	1.99728100	-1.45139600
C	1.80016100	1.32537200	-2.63161200
C	2.77296500	1.44434600	-3.68131200
C	3.89629000	2.18221700	-3.16940100
C	3.62618800	2.52890500	-1.80017200
C	3.19417200	-1.18262400	-0.93665400
C	3.59779000	-1.52261500	-2.29084800

C	4.90694800	-0.97757600	-2.52190400
C	5.32806600	-0.29551600	-1.32965500
C	4.27865900	-0.40899200	-0.35304500
C	2.70433200	2.22901000	1.46432800
C	3.52017700	3.38365200	1.52014800
C	4.47394700	3.53159100	2.54127800
C	4.61162300	2.54114400	3.53202500
C	3.78716800	1.40337200	3.50054400
C	2.83883500	1.24902200	2.47221900
C	0.66603700	3.71778900	0.16420400
C	0.16318900	4.22695300	1.38510600
C	-0.44569600	5.49224800	1.43160700
C	-0.56170000	6.26521400	0.26152600
C	-0.06213100	5.76709700	-0.95437300
C	0.54713400	4.50001800	-1.00570400
C	0.76371700	-2.59001800	-1.47323400
C	1.26380800	-3.81691100	-1.96874500
C	0.62695700	-4.45424000	-3.04739400
C	-0.50930800	-3.87523100	-3.64367400
C	-1.01336600	-2.65827000	-3.15316100
C	-0.38119900	-2.02118400	-2.07050000
C	2.18517900	-2.99478200	1.06161800
C	3.38389100	-2.84005500	1.79514900
C	3.78950100	-3.82015000	2.71816300
C	3.00567700	-4.96865200	2.92289600
C	1.81040600	-5.12862400	2.19997000
C	1.39883200	-4.14957400	1.27979900
H	2.68421300	1.01913000	-4.68959400
H	4.81856400	2.41592200	-3.71786500
H	5.47175400	-1.04656900	-3.46106000
H	6.27150000	0.24939800	-1.19349200
H	3.39863600	4.18451200	0.77406900
H	5.35468000	2.66379800	4.33578800
H	2.19013600	0.35730400	2.45107100
H	0.26255500	3.64157500	2.31386800
H	-1.03991100	7.25662700	0.29903000
H	0.93501700	4.12179200	-1.96417200
H	2.15394600	-4.27873300	-1.51388000
H	-1.00548800	-4.37889400	-4.48833000
H	-0.78941100	-1.07926500	-1.66579200
H	4.02170500	-1.95732300	1.64661300
H	3.32562700	-5.73767300	3.64368000
H	0.45502200	-4.28762500	0.73336300
C	-0.75645700	-1.56353100	1.69476700

C	-0.40841200	-1.56401100	3.06473900
C	-1.64389800	-2.54521300	1.21908800
C	-0.93898200	-2.53079700	3.94246500
H	0.28174200	-0.80464700	3.47100000
C	-2.16727800	-3.51765600	2.09671700
H	-1.95748800	-2.55455600	0.16714100
C	-1.81885400	-3.51591800	3.45822800
H	-0.65705700	-2.51073600	5.00831800
H	-2.86481700	-4.27670500	1.70551300
H	-2.23329200	-4.27537900	4.14085900
H	4.72968300	-3.68315500	3.27558200
H	5.10673000	4.43279500	2.56907300
H	3.87541900	0.63151300	4.28112200
H	1.18606300	-6.02320500	2.35214300
H	1.02281700	-5.41042200	-3.42471400
H	-1.90891900	-2.20088300	-3.60062500
H	-0.83056200	5.87620200	2.38955400
H	-0.14365700	6.36821000	-1.87389400
H	0.83634800	0.80454500	-2.69600000
H	4.29246100	0.03950500	0.64799300
Pd	0.08458200	-0.01739500	0.65427400
C	-2.49119300	1.00530800	-0.12227300
B	-3.91918400	0.23571300	-0.29839000
O	-4.10032900	-0.88283400	0.64295200
O	-4.11712900	-0.18775800	-1.71167600
C	-5.33348500	-0.87093200	-1.92681600
H	-6.21123900	-0.18834700	-1.77287400
H	-5.37204500	-1.20634200	-2.99167800
C	-5.30435200	-1.59070600	0.46398200
H	-6.19044300	-0.95489200	0.73411100
H	-5.31116200	-2.46187300	1.16274100
C	-5.51621600	-2.09854000	-0.99189400
C	-6.94177500	-2.65592100	-1.13774300
H	-7.13508800	-2.99920400	-2.17746400
H	-7.10335000	-3.52647000	-0.46524300
H	-7.70783300	-1.89038500	-0.88736800
C	-4.48607000	-3.18414500	-1.34873700
H	-4.54686700	-4.04614500	-0.64940200
H	-4.65475900	-3.57003600	-2.37776700
H	-3.45807300	-2.77398700	-1.30600800
C	-4.95642000	1.50678400	0.09115800
C	-5.32947200	1.75413900	1.43452200
C	-5.49972900	2.36848800	-0.89187300
C	-6.20529400	2.79959500	1.78356400

H	-4.92555200	1.09758200	2.22459000
C	-6.37713900	3.41915800	-0.55951500
H	-5.23643500	2.19802000	-1.95090200
C	-6.73220700	3.64066800	0.78453000
H	-6.47959700	2.96207300	2.83995500
H	-6.78896500	4.06773300	-1.35155600
H	-7.41602600	4.46321600	1.05193600
C	-1.81775600	1.12811400	1.10818100
H	-1.27870000	2.06966600	1.32510300
H	-2.26945800	0.62943800	1.98148000
H	2.99868600	-2.08381600	-3.01742000
H	4.30668300	3.07030800	-1.13176700
C	-2.07064600	1.82866600	-1.30642400
H	-2.90789400	2.49936100	-1.59640300
H	-1.17070700	2.44963600	-1.14433300
H	-1.92782600	1.17001900	-2.19071600



2.194

BP86 Optimization and Frequency Calculation:
Thermal correction to Gibbs Free Energy = 0.800098 au
M06 Single Point Calculation:
Electronic Energy: -4337.69 au

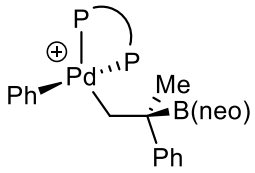
0 1

Fe	4.37349000	-1.09066600	-0.12419600
P	1.08406200	-2.00255400	-0.06472200
P	2.13784800	1.53389800	0.04413000
C	2.83581100	-2.28602700	0.42322000
C	3.46799400	-1.69069800	1.58968700
C	4.84703800	-2.09754800	1.61232300
C	5.08470000	-2.93618000	0.46948900
C	3.85430400	-3.05933700	-0.26445300
C	3.69613700	0.76400700	-0.55778300
C	5.03070400	0.83645700	0.00928000
C	5.91801100	0.08159700	-0.83409300
C	5.15395500	-0.45862900	-1.92560700
C	3.78655300	-0.04426400	-1.76249500
C	0.98028500	-2.76950200	-1.74869700

C	1.23849600	-4.14225000	-1.97579500
C	1.16736100	-4.67164200	-3.27566300
C	0.83398200	-3.84077100	-4.36202600
C	0.56559200	-2.47832800	-4.14426800
C	0.63550300	-1.94633900	-2.84370700
C	0.20226400	-3.23159500	1.02712400
C	-0.85262000	-4.03958500	0.54229200
C	-1.56009900	-4.89048000	1.41108100
C	-1.22839100	-4.94749000	2.77532700
C	-0.18239200	-4.14617600	3.26787800
C	0.52450200	-3.29331700	2.40329800
C	2.51146000	1.99721600	1.79926800
C	3.50107500	2.94875100	2.13973900
C	3.76139600	3.24909300	3.48806500
C	3.03401900	2.61097100	4.51010500
C	2.03943300	1.67365600	4.18020700
C	1.77796900	1.37135400	2.83150900
C	2.19913300	3.16275500	-0.85411800
C	2.65833200	3.21470500	-2.19018800
C	2.67185500	4.43147400	-2.89434700
C	2.22856500	5.61308900	-2.27465800
C	1.76533500	5.56795400	-0.94786000
C	1.74475100	4.35257000	-0.24259900
H	5.59238500	-1.79271400	2.35868100
H	6.04619300	-3.38474500	0.18621200
H	6.98972900	-0.07787400	-0.65508300
H	5.53779000	-1.10087100	-2.72919000
H	1.48653900	-4.80647400	-1.13309100
H	0.77658300	-4.25975700	-5.37915300
H	0.40957000	-0.88098600	-2.66415000
H	-1.12503500	-4.01880500	-0.52374700
H	-1.78297100	-5.61469800	3.45385300
H	1.33840400	-2.67617800	2.81255600
H	4.06396500	3.47017600	1.34996900
H	3.23782400	2.85225400	5.56538200
H	0.98964100	0.64680100	2.56349100
H	3.01876900	2.30287300	-2.68997600
H	2.24323700	6.56722800	-2.82505000
H	1.36522600	4.33417400	0.78950900
C	-0.83355800	2.06848300	-0.21282700
C	-1.12663500	2.64962800	-1.46744100
C	-1.16886600	2.80005300	0.94957100
C	-1.71888800	3.92422500	-1.55886000
H	-0.89056800	2.10710000	-2.39820200

C	-1.76362500	4.07540900	0.86191600
H	-0.96472200	2.38266000	1.94962000
C	-2.03617600	4.64602300	-0.39394200
H	-1.93449000	4.35477800	-2.55119000
H	-2.01601500	4.62292500	1.78566400
H	-2.49848000	5.64385400	-0.46470600
H	3.03727500	4.45351800	-3.93346300
H	1.37022500	-5.74177700	-3.44030100
H	0.29407500	-1.82463300	-4.98806900
H	1.41062500	6.48642500	-0.45387000
H	4.53504600	3.99124900	3.74126200
H	1.45758000	1.17962100	4.97420700
H	-2.37773600	-5.51145700	1.01272900
H	0.08877400	-4.18346000	4.33496300
H	2.99062600	-1.01569200	2.31178800
H	2.94911600	-0.31372900	-2.41939100
Pd	0.12861300	0.25837200	-0.10830200
C	-2.79700100	-0.28211000	0.59564300
B	-4.17026100	0.39092000	0.26025800
O	-4.35104700	0.97473300	-1.05008000
O	-4.87148300	1.05120600	1.34350500
C	-6.20713200	1.42664000	1.06184400
H	-6.86923000	0.52218200	1.01644700
H	-6.57787600	2.05386600	1.90627100
C	-5.67888000	1.34313400	-1.36961400
H	-6.31018100	0.43142100	-1.54144600
H	-5.66203500	1.90821100	-2.33079400
C	-6.35562000	2.20549800	-0.27116100
C	-7.84802500	2.37890500	-0.59996600
H	-8.36418400	2.97216800	0.18555500
H	-7.98512200	2.91416000	-1.56436100
H	-8.36777200	1.39969200	-0.68003700
C	-5.66818100	3.57949800	-0.16887200
H	-5.76160400	4.14133900	-1.12345600
H	-6.12974600	4.19574500	0.63309400
H	-4.58886200	3.47137700	0.05608800
C	-4.68615400	-1.32376200	0.18612400
C	-4.69118900	-2.00472500	-1.05155500
C	-5.39911900	-1.89677700	1.26228800
C	-5.40007300	-3.20738400	-1.21905500
H	-4.13709400	-1.57417400	-1.90171100
C	-6.10757700	-3.10410600	1.10611200
H	-5.42144600	-1.37745000	2.23454600
C	-6.10806200	-3.76499000	-0.13594700

H	-5.40059200	-3.71537700	-2.19797600
H	-6.66476400	-3.52904900	1.95772200
H	-6.65906600	-4.71135100	-0.26115300
C	-1.83374300	-0.66987600	-0.41799600
H	-1.56134200	-1.74106000	-0.36370400
H	-2.11475400	-0.37083000	-1.44556800
H	5.31078400	1.34938400	0.93742300
H	3.72002900	-3.61444000	-1.20053900
C	-2.50054500	-0.65602800	2.02640300
H	-1.95552300	-1.61819500	2.12985900
H	-1.84104200	0.14111800	2.43757300
H	-3.40555300	-0.65998500	2.66086800



2.195

BP86 Optimization and Frequency Calculation:
Thermal correction to Gibbs Free Energy = 0.802532 au
M06 Single Point Calculation:
Electronic Energy: -4338.5376 au

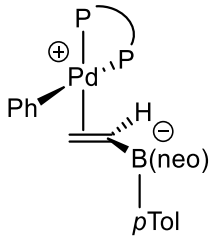
0 1

Fe	4.25830600	-1.09387100	0.34723300
P	0.96403700	-1.96326000	-0.14297800
P	2.07364700	1.55051400	0.10432000
C	2.61932900	-2.25187400	0.61549200
C	3.04123600	-1.65633000	1.87248900
C	4.38513500	-2.08713000	2.14965100
C	4.80896500	-2.94446100	1.07605900
C	3.72910300	-3.05291700	0.13186700
C	3.71367500	0.77327000	-0.22113200
C	4.92560100	0.82304400	0.57578500
C	5.93188000	0.03445800	-0.08342100
C	5.36382900	-0.50533800	-1.28901300
C	3.99964600	-0.05805900	-1.37886100
C	1.16866400	-2.58932200	-1.87987600
C	1.49956000	-3.93214300	-2.17852200
C	1.66052500	-4.34481800	-3.51257200
C	1.48623200	-3.42620200	-4.56484000

C	1.14368900	-2.09311900	-4.27883600
C	0.98300800	-1.67857900	-2.94391300
C	-0.00367300	-3.33557700	0.67295900
C	-0.94610000	-4.11149000	-0.04010600
C	-1.68266400	-5.11819500	0.60981600
C	-1.49717100	-5.36181700	1.98120600
C	-0.57338400	-4.58513600	2.70345500
C	0.16451500	-3.57927900	2.05649100
C	2.23501500	2.13340300	1.85992900
C	3.17486600	3.11189800	2.26018100
C	3.26909400	3.49704400	3.60893700
C	2.42491800	2.91493200	4.57323900
C	1.48062800	1.94917300	4.18334100
C	1.38459700	1.56399000	2.83352400
C	2.25318400	3.12480400	-0.87971600
C	2.84489200	3.09088400	-2.16356300
C	2.94085700	4.25852000	-2.94073500
C	2.44563400	5.47930600	-2.44913000
C	1.84784500	5.52060000	-1.17734200
C	1.74665000	4.35360200	-0.39997000
H	4.98888800	-1.78744800	3.01646200
H	5.79655400	-3.41449200	0.97632100
H	6.94998900	-0.14500000	0.28739400
H	5.86989100	-1.16827000	-2.00325700
H	1.61868400	-4.66691700	-1.36699100
H	1.60979000	-3.75392800	-5.60932200
H	0.69919900	-0.63732200	-2.70794200
H	-1.10169900	-3.94460700	-1.11639000
H	-2.07263900	-6.15317100	2.48709800
H	0.88847000	-2.98944200	2.63905100
H	3.83157900	3.58591300	1.51396500
H	2.49949200	3.22116200	5.62881100
H	0.63521500	0.81774700	2.51726000
H	3.24706200	2.14826400	-2.56459300
H	2.52445100	6.39534200	-3.05604700
H	1.26457000	4.40410800	0.58704800
C	-0.91768400	2.08250700	-0.49355600
C	-1.14672500	2.56971500	-1.80528500
C	-1.27858700	2.93552900	0.57897400
C	-1.68507200	3.85062400	-2.03740600
H	-0.89765200	1.93934400	-2.67617700
C	-1.81503300	4.22079000	0.35399800
H	-1.12682200	2.60950000	1.62166800
C	-2.01508100	4.68893900	-0.95686400

H	-1.84295600	4.19741400	-3.07298100
H	-2.07605000	4.86029200	1.21451800
H	-2.43180100	5.69376000	-1.13476900
H	3.41125900	4.21132400	-3.93601100
H	1.91912500	-5.39311400	-3.73148800
H	0.99390600	-1.37123000	-5.09726400
H	1.45066500	6.46958600	-0.78307300
H	4.00557000	4.25988900	3.90798800
H	0.80922700	1.49675100	4.93026200
H	-2.40950600	-5.71319400	0.03495700
H	-0.41960600	-4.76467900	3.77959300
H	2.44784400	-0.96930800	2.48945300
H	3.28734300	-0.32720200	-2.16987200
Pd	0.02866900	0.27965000	-0.21985400
C	-3.00196800	-0.59737100	0.47136100
B	-4.16693800	0.50251000	0.28483400
O	-4.52176400	0.92202200	-0.97754800
O	-4.90447200	0.86262800	1.39679600
C	-6.19245200	1.47041800	1.24040800
H	-6.95634100	0.66104900	1.17448200
H	-6.40524000	2.05018200	2.16488400
C	-5.77856900	1.57101200	-1.20694400
H	-6.52724500	0.79039200	-1.47707500
H	-5.65735600	2.23287300	-2.09165900
C	-6.29046600	2.38553400	0.00200200
C	-7.76392100	2.76628200	-0.23360000
H	-8.16630200	3.33956700	0.62818900
H	-7.86692600	3.40510000	-1.13610600
H	-8.40413500	1.86979200	-0.37567100
C	-5.44041900	3.65398100	0.20502200
H	-5.50284500	4.31561500	-0.68425300
H	-5.79937800	4.22973100	1.08441100
H	-4.37066000	3.41548900	0.36600200
C	-3.90984100	-1.84307600	0.28294500
C	-4.28213300	-2.27197000	-1.01877900
C	-4.45570500	-2.56158200	1.37540900
C	-5.14153300	-3.36520700	-1.21759900
H	-3.89241700	-1.72963800	-1.89288700
C	-5.31758400	-3.65661700	1.18020000
H	-4.20420400	-2.26628300	2.40408200
C	-5.66646000	-4.06879200	-0.11734200
H	-5.40564400	-3.66881300	-2.24421600
H	-5.71719800	-4.19396000	2.05618800
H	-6.34132300	-4.92631200	-0.27071700

C	-1.89389700	-0.56665100	-0.62950800
H	-1.67312100	-1.61009000	-0.93835700
H	-2.25565900	-0.03632100	-1.53341300
H	5.04516400	1.34403100	1.53349500
H	3.75701600	-3.61561000	-0.80901000
C	-2.41427400	-0.54465400	1.89950500
H	-1.75449900	0.34133700	1.98830700
H	-3.19715000	-0.45389700	2.67944800
H	-1.80422300	-1.44641100	2.12024800



2.196

BP86 Optimization and Frequency Calculation:
Thermal correction to Gibbs Free Energy = 0.797698 au
M06 Single Point Calculation:
Electronic Energy: -4338.495172 au

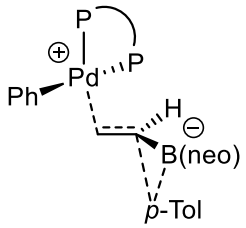
0 1

Fe	3.19626000	-1.71447600	1.88270000
P	0.47931900	-2.16997200	-0.10872300
P	2.25105300	1.09515000	0.10001500
C	1.39391700	-2.50772300	1.43906200
C	1.29810200	-1.65827800	2.61507200
C	2.17995800	-2.18486200	3.61968900
C	2.82391100	-3.35341900	3.08363800
C	2.34382000	-3.56205200	1.74441600
C	3.52755800	-0.02821800	0.80864400
C	4.16328200	0.06835800	2.11183200
C	5.10579300	-1.01003100	2.23247700
C	5.06767300	-1.78112400	1.02053500
C	4.09754700	-1.18697500	0.14112200
C	1.39223600	-3.08756500	-1.43743500
C	1.52300300	-4.49621600	-1.41366500
C	2.21492500	-5.16218000	-2.43948200
C	2.77112600	-4.43441400	-3.50826900
C	2.62817300	-3.03681100	-3.55149700

C	1.94094900	-2.36781000	-2.52201900
C	-1.03613900	-3.22751000	0.09565900
C	-1.70810100	-3.73807300	-1.03980600
C	-2.88250600	-4.49517800	-0.89044800
C	-3.40124800	-4.75265200	0.39087600
C	-2.73913900	-4.24865800	1.52428400
C	-1.56617300	-3.48764300	1.38027600
C	1.81614400	2.16381100	1.54598000
C	2.76564600	3.03907800	2.12495300
C	2.43511100	3.78368200	3.26968700
C	1.15843800	3.66068300	3.84960200
C	0.20794600	2.80242300	3.27119800
C	0.52975500	2.06220100	2.11875300
C	3.28608200	2.19174300	-0.98725700
C	4.33073500	1.64184300	-1.76420500
C	5.09098700	2.45992500	-2.61856400
C	4.81956000	3.83627700	-2.70738600
C	3.77792100	4.38900700	-1.94110500
C	3.01121500	3.57420000	-1.09123200
H	2.35134900	-1.75039400	4.61326300
H	3.57750200	-3.96684800	3.59524200
H	5.72385900	-1.22319300	3.11471900
H	5.65200400	-2.68648800	0.80995500
H	1.06624500	-5.08123900	-0.60026800
H	3.30762000	-4.96025700	-4.31378800
H	1.82101900	-1.27190800	-2.55991900
H	-1.30521800	-3.56367600	-2.05001600
H	-4.32069800	-5.34777700	0.50570100
H	-1.05874500	-3.10072300	2.27728400
H	3.76758300	3.14378300	1.68044800
H	0.90309900	4.24273500	4.74926800
H	-0.23592800	1.41635400	1.65502700
H	4.56735200	0.56942000	-1.70242500
H	5.41850900	4.47752100	-3.37329300
H	2.19053600	4.02048800	-0.51087500
C	0.13231200	1.98069400	-1.81282400
C	0.66261000	1.98171500	-3.12273000
C	-0.47579300	3.15191800	-1.32417100
C	0.58003600	3.13276100	-3.93099800
H	1.14767800	1.07982500	-3.53321100
C	-0.54646800	4.30782700	-2.12978400
H	-0.93032400	3.16684000	-0.32451200
C	-0.02215400	4.30335900	-3.43397500
H	0.99404300	3.11136800	-4.95279600

H	-1.02969000	5.21538900	-1.73115500
H	-0.08506700	5.20617500	-4.06294100
H	5.90462600	2.01528800	-3.21335800
H	2.31291300	-6.25882600	-2.40740200
H	3.04707100	-2.46170000	-4.39211600
H	3.55356200	5.46541600	-2.00581400
H	3.18110800	4.46316700	3.71144300
H	-0.79819800	2.70918600	3.70713400
H	-3.39324400	-4.88750900	-1.78391200
H	-3.13555100	-4.44928700	2.53219900
H	0.67323500	-0.76052800	2.70795800
H	3.81963700	-1.56521600	-0.85076800
Pd	0.23195800	0.19780600	-0.80822700
C	-2.26161600	-0.07810900	-0.49378900
H	-2.16833900	-0.99168700	0.12600000
B	-3.32907400	0.97238000	0.11673800
O	-3.43053700	2.24694600	-0.61701500
O	-3.11243900	1.19003400	1.57244600
C	-4.07882400	2.04381200	2.14909700
H	-5.09350600	1.56407600	2.13774700
H	-3.81626300	2.20956700	3.22221300
C	-4.39369300	3.12718900	-0.08409900
H	-5.43054000	2.71738000	-0.21960200
H	-4.35345500	4.08808000	-0.65216800
C	-4.19703200	3.41937100	1.43155300
C	-5.42202700	4.17780400	1.96981700
H	-5.32418600	4.37817200	3.05910900
H	-5.54172200	5.15936900	1.46149300
H	-6.36005800	3.60181700	1.81564100
C	-2.92429500	4.25214500	1.66251700
H	-2.96509600	5.21338700	1.10543700
H	-2.79319400	4.49076600	2.74043600
H	-2.02555200	3.69808300	1.32854400
C	-4.68406100	0.01202100	-0.15584600
C	-5.42368200	0.10312100	-1.36069700
C	-5.14154400	-0.93178600	0.79301000
C	-6.56930800	-0.67625000	-1.59262500
H	-5.09045600	0.81752100	-2.13386100
C	-6.28859700	-1.71750200	0.56998100
H	-4.58701300	-1.04393100	1.74109700
C	-7.02872000	-1.60368200	-0.62726700
H	-7.12328700	-0.56771200	-2.54203100
H	-6.61906700	-2.43710400	1.33975000
C	-1.74994200	-0.18896100	-1.79083400

H	-1.50914300	-1.17576400	-2.23187000
H	-1.95392700	0.60913400	-2.52334400
H	3.94344600	0.81775200	2.88135600
H	2.66899700	-4.35905900	1.06483400
C	-8.27518800	-2.42741300	-0.86963800
H	-8.27424500	-2.88473000	-1.88188200
H	-8.37811300	-3.24312800	-0.12555200
H	-9.19372700	-1.80273100	-0.80519200



2.197

BP86 Optimization and Frequency Calculation:
Thermal correction to Gibbs Free Energy = 0.79765 au
M06 Single Point Calculation:
Electronic Energy: -4338.487107 au

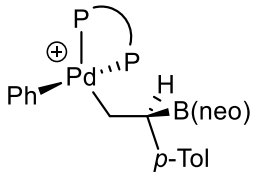
0 1

Fe	3.17849300	1.55517700	-2.02453900
P	0.58798000	2.13343900	0.12087700
P	2.26791500	-1.15116200	-0.07596800
C	1.42944100	2.41369200	-1.48199600
C	1.23560600	1.54892600	-2.63433100
C	2.06973600	2.02974900	-3.70118200
C	2.78213800	3.18549000	-3.22669500
C	2.39181000	3.43043900	-1.86429900
C	3.53821800	-0.11250200	-0.91852700
C	4.06420800	-0.27300500	-2.26225000
C	5.02725600	0.76810400	-2.49697500
C	5.11113300	1.57971100	-1.31366800
C	4.19449700	1.04881700	-0.34060200
C	1.61565700	3.03130800	1.37960300
C	1.79895000	4.43338200	1.33586800
C	2.57948100	5.07797400	2.31072800
C	3.17369700	4.33509600	3.34831200
C	2.97995900	2.94422800	3.41167100
C	2.20349500	2.29659000	2.43309700
C	-0.88100700	3.26617300	-0.01628200

C	-1.48939300	3.77916200	1.15372300
C	-2.62374600	4.60394200	1.06419200
C	-3.16609500	4.92872300	-0.19193500
C	-2.57023200	4.41985300	-1.35942300
C	-1.43793000	3.59055500	-1.27436300
C	1.75462600	-2.29584400	-1.44140700
C	2.63791200	-3.25956400	-1.98111200
C	2.23145300	-4.06871800	-3.05623500
C	0.94322500	-3.92382000	-3.60504600
C	0.05744700	-2.97381700	-3.06755900
C	0.45862200	-2.16825100	-1.98642000
C	3.32801700	-2.22425100	1.01495000
C	4.50054500	-1.71470400	1.61789500
C	5.26641600	-2.51628200	2.48353000
C	4.87434600	-3.83795100	2.75786200
C	3.70680200	-4.35108800	2.16496500
C	2.93452200	-3.55127400	1.30584700
H	2.16551500	1.57415400	-4.69552800
H	3.52165800	3.76587400	-3.79448300
H	5.57997200	0.93015800	-3.43195700
H	5.74007400	2.47003900	-1.18175700
H	1.31494400	5.03091600	0.54750700
H	3.77982000	4.84433100	4.11426100
H	2.04063500	1.20633500	2.48387200
H	-1.06280900	3.55488800	2.14436300
H	-4.05238600	5.57889900	-0.26049700
H	-0.97926700	3.20410200	-2.19764800
H	3.64786800	-3.38252000	-1.55946500
H	0.62851400	-4.55900500	-4.44829000
H	-0.24750100	-1.44348200	-1.54541900
H	4.83414500	-0.68809300	1.40688800
H	5.47709400	-4.46697000	3.43209600
H	2.01611100	-3.96487900	0.86321700
C	0.03103800	-1.94864700	1.85526700
C	0.52486800	-1.99907100	3.18070000
C	-0.62525000	-3.09096600	1.34772500
C	0.37114200	-3.15428200	3.97323400
H	1.04221200	-1.12657900	3.61550200
C	-0.76964100	-4.25236000	2.13478700
H	-1.05398200	-3.07967200	0.33545500
C	-0.27409500	-4.29012300	3.45052900
H	0.76284500	-3.16446700	5.00435400
H	-1.28691000	-5.13122100	1.71436900
H	-0.39416900	-5.19622800	4.06666300

H	6.18006800	-2.10257000	2.93947800
H	2.71767200	6.16985000	2.26379200
H	3.42871400	2.35807900	4.22905700
H	3.38703500	-5.38412000	2.37468000
H	2.92690900	-4.81741800	-3.46785600
H	-0.95739200	-2.85841600	-3.47810200
H	-3.08292200	4.99845500	1.98442500
H	-2.98561000	4.67180100	-2.34812600
H	0.57772100	0.67104700	-2.67180300
H	4.00900300	1.46777200	0.65659600
Pd	0.26916300	-0.18004000	0.84080800
C	-2.36070600	0.07247900	0.23544400
H	-2.17786900	0.89989600	-0.47630500
B	-3.35913100	-1.00411900	-0.27807600
O	-3.62857900	-2.16695800	0.53274300
O	-3.42957400	-1.20582900	-1.71445900
C	-4.53426000	-1.97538200	-2.15721700
H	-5.48664100	-1.39322000	-2.04861700
H	-4.40371600	-2.17962500	-3.24567800
C	-4.73013900	-2.95324300	0.12091100
H	-5.69452100	-2.41933100	0.33000900
H	-4.73998800	-3.88682300	0.73054300
C	-4.68925700	-3.31310500	-1.38749600
C	-6.00798300	-3.99247700	-1.79278400
H	-6.01431900	-4.23982400	-2.87629100
H	-6.15704900	-4.94136900	-1.23380400
H	-6.88435800	-3.33983000	-1.59002900
C	-3.49707000	-4.24167100	-1.68466100
H	-3.57999200	-5.19232200	-1.11515000
H	-3.45032900	-4.49665800	-2.76546100
H	-2.53990600	-3.75768000	-1.40604000
C	-4.45745100	0.32006400	0.20067500
C	-5.09282900	0.29404300	1.46339300
C	-4.96468700	1.20470300	-0.77472800
C	-6.21949500	1.08725300	1.72465400
H	-4.70003400	-0.37480100	2.24738500
C	-6.09306000	2.00421100	-0.51342100
H	-4.48160000	1.24820400	-1.76532500
C	-6.74348800	1.96037700	0.73919100
H	-6.70778200	1.03382700	2.71323700
H	-6.47955600	2.67740800	-1.29793700
C	-1.75508200	0.23029700	1.53240200
H	-1.68207100	1.25631300	1.94340700
H	-2.03917300	-0.51227000	2.29730300

H	3.76016500	-1.04216700	-2.98232100
H	2.78278000	4.22684500	-1.21940700
C	-7.95738500	2.81394700	1.03052500
H	-7.79312900	3.46421400	1.91671500
H	-8.21633000	3.46607100	0.17268700
H	-8.84590900	2.18678500	1.26037000



2.198

BP86 Optimization and Frequency Calculation:
Thermal correction to Gibbs Free Energy = 0.7978 au
M06 Single Point Calculation:
Electronic Energy = -4338.540288 au

0 1

Fe	-3.11905800	-1.75877100	-1.95497700
P	-0.32049700	-2.07806600	0.00305500
P	-2.37927200	0.96063300	0.04477900
C	-1.25058500	-2.42208500	-1.54391800
C	-1.23142400	-1.52279300	-2.68529400
C	-2.07655500	-2.07333500	-3.70925800
C	-2.62262000	-3.31058700	-3.21947400
C	-2.11717500	-3.53331100	-1.89113000
C	-3.59241000	-0.17812600	-0.75985000
C	-4.21249500	-0.02925300	-2.06322000
C	-5.06620100	-1.16333000	-2.29103100
C	-4.98964500	-2.02208300	-1.14054100
C	-4.07945500	-1.42745900	-0.19802900
C	-1.20774600	-3.04670400	1.32140400
C	-1.31619900	-4.45649300	1.28181500
C	-1.99440300	-5.14680600	2.30121300
C	-2.55922200	-4.44141500	3.38062000
C	-2.43740300	-3.04211400	3.44032300
C	-1.76365200	-2.34966200	2.41709200
C	1.18631600	-3.14381000	-0.24362200
C	1.89057100	-3.64370000	0.87669300
C	3.02993600	-4.44800800	0.70324500
C	3.48805600	-4.75850800	-0.58933600
C	2.80195000	-4.25550200	-1.70879200
C	1.66014400	-3.45207400	-1.53900500

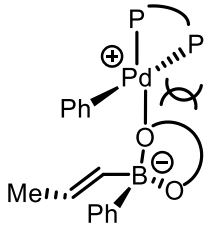
C	-2.19669400	2.24691800	-1.28321900
C	-3.22401500	3.16733900	-1.59151400
C	-3.06548900	4.08001800	-2.64912600
C	-1.88418800	4.07967800	-3.41426900
C	-0.85636000	3.16898100	-3.11186000
C	-1.00915000	2.26295500	-2.04656100
C	-3.45721000	1.81616400	1.30461900
C	-4.58675400	1.18154600	1.87057100
C	-5.34813200	1.82278600	2.86491200
C	-4.99679900	3.10945800	3.30783100
C	-3.87507600	3.74922600	2.75025100
C	-3.10685900	3.10884800	1.76315400
H	-2.28757400	-1.61389800	-4.68395900
H	-3.32887600	-3.96078300	-3.75309800
H	-5.65366600	-1.35153200	-3.19965600
H	-5.50824900	-2.98150900	-1.01242800
H	-0.85096700	-5.02445900	0.46102100
H	-3.08481800	-4.98588200	4.18119400
H	-1.65390500	-1.25178800	2.46102200
H	1.53384900	-3.42698900	1.89588600
H	4.37903300	-5.39195200	-0.72377500
H	1.12672900	-3.07531900	-2.42553000
H	-4.15462100	3.17249700	-1.00261500
H	-1.76358800	4.79428400	-4.24399100
H	-0.19493900	1.56488400	-1.78373900
H	-4.89102400	0.18141700	1.52942000
H	-5.59558300	3.61302100	4.08346500
H	-2.22644100	3.62207200	1.34827800
C	0.06539200	2.00717000	1.72310100
C	-0.12810600	2.01207400	3.12890200
C	0.39853100	3.24384000	1.12072400
C	-0.00848000	3.19127800	3.89116000
H	-0.37672300	1.07375400	3.65425100
C	0.51922300	4.42910900	1.87582700
H	0.56516900	3.29874600	0.03409500
C	0.31513000	4.41055400	3.26756000
H	-0.16924100	3.15479900	4.98221700
H	0.77661300	5.37466600	1.36850400
H	0.41176800	5.33481500	3.86055900
H	-6.22713200	1.31089800	3.28852400
H	-2.07468800	-6.24466200	2.25619200
H	-2.86249600	-2.48375800	4.28934600
H	-3.58791500	4.75781500	3.08780900
H	-3.87207000	4.79473500	-2.87812900

H	0.07372400	3.16699600	-3.70142900
H	3.56188400	-4.83469300	1.58691300
H	3.15160500	-4.49450800	-2.72597400
H	-0.67906700	-0.57628100	-2.74104300
H	-3.78752800	-1.85843000	0.76812800
Pd	-0.14854500	0.22652100	0.71702600
C	2.88059800	-0.03361000	0.05636700
H	2.46611500	-0.59500400	-0.80952400
B	3.36193300	1.38608800	-0.49924800
O	3.66514500	2.39977900	0.37821700
O	3.59701800	1.50648900	-1.85783900
C	4.37759900	2.60782300	-2.34367700
H	5.45536400	2.32775700	-2.29476100
H	4.12189600	2.75305400	-3.41568000
C	4.34516200	3.58289200	-0.05797800
H	5.43224200	3.45100800	0.14794800
H	3.98912100	4.42540900	0.57380900
C	4.13801800	3.91208800	-1.55436300
C	5.17354600	4.96838700	-1.98342000
H	5.06103500	5.21831900	-3.05946300
H	5.04136800	5.90811500	-1.40675500
H	6.21352000	4.61369500	-1.82230700
C	2.71254700	4.43641200	-1.81849000
H	2.50719900	5.34849100	-1.22025600
H	2.58390600	4.69525500	-2.89045100
H	1.94212500	3.68264600	-1.56141100
C	4.23941000	-0.68248800	0.37549700
C	4.79617600	-0.66688600	1.67465600
C	5.02251800	-1.26058700	-0.65355600
C	6.06626700	-1.21309900	1.93296100
H	4.22599600	-0.21701500	2.50214300
C	6.29022700	-1.80403700	-0.39439800
H	4.62315600	-1.28230600	-1.68068900
C	6.84148200	-1.79590500	0.90755300
H	6.46697200	-1.18246100	2.96081700
H	6.86678200	-2.24935300	-1.22350000
C	1.89252200	-0.03891000	1.23908000
H	1.92709000	-1.02473200	1.75467100
H	2.17453100	0.72710500	1.98668900
H	-4.04102500	0.79786600	-2.76269000
H	-2.37542200	-4.38011000	-1.24370400
C	8.19692100	-2.40780900	1.18808000
H	8.60442000	-2.06921800	2.16211500
H	8.14191000	-3.51866700	1.22280500

H 8.93418000 -2.15013800 0.39898400

2.9.3.3 DFT Calculations: Alkene- Versus Oxygen-Bound Palladium: Conformation, Ligand Effects, and Implications for Transmetallation: Scheme 2.32, 2.33, 2.34, 2.35

All calculations were performed using the Gaussian09 package of programs.[72] Geometry optimizations were carried out with the density functional BP86 in conjunction with the def2-SVP[73] basis set in tetrahydrofuran as solvent using the IEFPCM model.[74] Very tight convergence criteria and an ultrafine integration grid were applied. Stationary points were assessed through vibrational analysis and Gibbs free energy corrections were performed under standard conditions (298.15 K, 1.0 atm). Intrinsic Reaction Coordinate (IRC)[75] calculations were performed on transition state sturctures followed by subsequent optimization of the end points with the previously mentioned optimization method. Gibbs free energies have been assessed through single point calculations with the density functional M06[76] applying the larger def2-TZVPP[73] basis set, followed by addition of thermal corrections obtained at the level of geometry optimization (denoted as M06/def2-TZVPP//BP86/def2-SVP). The diphosphine ligand employed in these calculations is 1,1'-Bis(diphenylphosphino)ferrocene.



2.206

BL_2 = B(pin)

BP86 Optimization and Frequency Calculation:
Thermal correction to Gibbs Free Energy= 0.826525 a.u.
Lowest frequency= 12.15 cm^{-1}
M06 Single Point Calculation:
Electronic Energy= -4377.788136 a.u.

0 1

C	-3.20021500	1.08259200	2.67961900
C	-3.12354600	1.46363400	1.38082600
H	-2.71607600	2.48292300	1.20241200
H	-3.62479000	0.08239800	2.90519200
B	-3.63418700	0.67354600	0.05434200
O	-4.41617000	1.56330400	-0.86064000
O	-2.36704800	0.36667900	-0.83583000
C	-4.65612600	-0.57503400	0.40573100
C	-4.58759100	-1.90303500	-0.07738100
C	-5.81492900	-0.25879000	1.16899600
C	-5.60431200	-2.85018600	0.16477000
H	-3.71125400	-2.21549800	-0.66336100
C	-6.83766200	-1.19029100	1.42376200
H	-5.92116700	0.76278800	1.57247100
C	-6.73917700	-2.50050200	0.91688500
H	-5.50319400	-3.87328600	-0.23604800
H	-7.71886700	-0.89377100	2.01882400
H	-7.53616300	-3.23846600	1.10874400
C	-2.80644700	1.89174600	3.88945500
H	-3.67388700	2.05091200	4.57036800
H	-2.03132300	1.37683600	4.50098600
H	-2.40806300	2.89010600	3.61105000
C	-3.75689200	1.84991900	-2.08099700
C	-2.66791500	0.69644300	-2.22293400
C	-1.39814600	1.15252400	-2.94921300
H	-0.68067100	0.30945200	-3.03422800
H	-1.63911200	1.48573300	-3.98028200
H	-0.89660400	1.98681200	-2.42599000
C	-3.22512500	-0.54734100	-2.94192900
H	-2.50223300	-1.38058700	-2.84346600
H	-4.18452700	-0.87674500	-2.50138300
H	-3.38126300	-0.35424400	-4.02326900
C	-3.13861500	3.26141700	-1.99982800
H	-2.70487900	3.60116600	-2.96354600
H	-3.94063000	3.97341700	-1.71613700
H	-2.35419000	3.31271400	-1.22333200
C	-4.79969300	1.84999100	-3.21797500
H	-4.32867400	2.00322900	-4.21234000
H	-5.38176500	0.90912600	-3.24128500
H	-5.51535500	2.68200700	-3.05214500
H	-2.80217800	-5.68254900	0.56564600
C	-2.32262600	-4.70637300	0.38983200
H	-2.02103200	-5.04972200	-1.74177000

H	-2.49823800	-4.05840700	2.46395500
C	-1.88446500	-4.35358900	-0.89773400
C	-2.14859300	-3.80021500	1.45126400
H	1.02844900	-6.28279800	1.70969600
C	1.34820700	-5.25732800	1.95299000
C	-1.26268000	-3.10622600	-1.12254500
C	-1.52833000	-2.55699100	1.22938700
H	1.80951300	-5.71733100	4.03293500
C	1.78113800	-4.94064800	3.25246300
H	0.93574500	-4.53115700	-0.04526200
C	-1.08136900	-2.19897200	-0.06047800
H	-0.91686200	-2.86502100	-2.13834100
C	1.30708100	-4.26866600	0.95572300
H	-1.39639800	-1.86780400	2.07900800
C	2.17191700	-3.62379800	3.54961200
C	1.72007000	-2.94739400	1.23967400
C	3.13471200	-4.18094500	-2.99283600
C	2.56045300	-3.66330800	-4.16829400
H	3.81079600	-5.04894900	-3.04306100
H	2.78177100	-4.12747800	-5.14225200
H	2.50792300	-3.35973100	4.56475300
C	2.85569700	-3.59222200	-1.74722800
C	1.70320000	-2.55178400	-4.09414500
C	2.14465200	-2.63443500	2.55117900
Pd	-0.28066200	-0.33049300	-0.20545500
C	1.41613900	-1.96792100	-2.84783600
C	1.98418600	-2.48149300	-1.66316000
H	3.32828800	-3.99927700	-0.84059800
H	1.24821100	-2.13851800	-5.00783500
P	1.67520800	-1.60864400	-0.05524600
H	0.72829300	-1.10919400	-2.78597100
H	0.24813300	0.17492600	2.42116700
H	0.73448200	0.27737900	4.87670500
H	2.46317200	-1.61507000	2.80929500
C	0.74434700	1.06213600	2.84916400
C	1.01624500	1.12187000	4.22858400
C	3.33400500	-0.83108400	0.19869200
P	0.75110900	1.97807500	0.17754200
C	1.09822700	2.13116700	1.99695500
H	-1.01240900	3.85810900	1.71586000
H	4.50147600	-1.55612100	-1.62124800
H	2.01552700	0.91939900	-2.51413400
C	4.48342500	-0.99261700	-0.68177800
C	-0.78424700	4.32937500	0.74880200

C	1.63817100	2.25801700	4.77431500
C	3.76420700	0.01142200	1.30353000
C	3.76420700	0.01142200	1.30353000
C	0.03401800	3.66123900	-0.19028300
H	3.14162900	0.36481300	2.13372100
H	1.85236300	2.30724800	5.85361300
C	-1.29727000	5.60742600	0.46717000
C	2.68736300	1.56826200	-1.93867600
H	-1.92903500	6.11445400	1.21349300
C	2.37552800	2.18325900	-0.65814100
C	0.32114200	4.29910700	-1.41937200
Fe	3.95954800	0.96356400	-0.47394800
C	1.69573600	3.28296800	2.56173500
C	1.97034500	3.34075900	3.93859600
H	0.96726900	3.80688600	-2.16233700
C	-1.00664800	6.23440900	-0.75721500
C	-0.19681300	5.57547700	-1.69918400
C	5.58632100	-0.26408000	-0.12065200
C	5.14565500	0.35225500	1.09933500
C	4.02923300	1.93225300	-2.30015000
H	-1.40819200	7.23649200	-0.97569300
H	0.04170500	6.05950500	-2.65957300
H	1.93175800	4.15287300	1.93015800
C	3.54495700	2.94515300	-0.25661000
H	4.56511500	1.59874300	-3.19847600
H	2.44116500	4.24197900	4.36221000
H	6.58517100	-0.17300500	-0.56748200
H	5.74521200	1.00074000	1.75159600
C	4.55621500	2.77903200	-1.26478400
H	3.66254700	3.51764400	0.67087800
H	5.56851600	3.20336700	-1.23079900

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100 112 1.0

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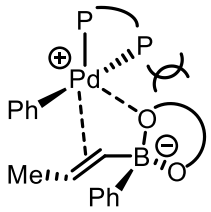

2.207

BL_2 = B(pin)

BP86 Optimization and Frequency Calculation:
Thermal correction to Gibbs Free Energy= 0.82999 a.u.
Lowest frequency= -60.89 cm^{-1}
M06 Single Point Calculation:
Electronic Energy= -4377.785551 a.u.

0 1

C	-2.41321700	0.01624500	2.59937000
C	-2.46296900	0.77834000	1.46964000
H	-1.98439900	1.77558500	1.54024700
H	-2.95349700	-0.95053900	2.58430300
B	-3.37453000	0.49676900	0.14258500
O	-3.86117500	1.79518000	-0.39749100
O	-2.49073600	-0.01799300	-0.99841000
C	-4.62920400	-0.51791700	0.50594600

C	-4.76293600	-1.84307200	0.02795500
C	-5.66826300	-0.05372600	1.35545200
C	-5.86650700	-2.65693300	0.35941600
H	-3.97289600	-2.24941800	-0.62337200
C	-6.77689200	-0.84943300	1.69656200
H	-5.60919900	0.97388300	1.75661800
C	-6.88355400	-2.16239400	1.19545700
H	-5.93254200	-3.68506300	-0.03684200
H	-7.56546700	-0.44718100	2.35608000
H	-7.74987000	-2.79249500	1.45797800
C	-1.78472700	0.36463000	3.91799200
H	-2.56683600	0.41505200	4.70980300
H	-1.06916900	-0.41691100	4.25982700
H	-1.25344100	1.33695800	3.89463800
C	-4.00835800	1.68152700	-1.80551000
C	-2.84022000	0.64987400	-2.22875700
C	-1.59900700	1.37272600	-2.77214700
H	-0.78527200	0.63608900	-2.92788900
H	-1.79249000	1.86488800	-3.74719600
H	-1.24017900	2.13639100	-2.05864500
C	-3.28432300	-0.40093300	-3.26526800
H	-2.43198800	-1.06705100	-3.51634800
H	-4.10448600	-1.03429700	-2.87836700
H	-3.62451900	0.07658400	-4.20853800
C	-3.85414200	3.08839900	-2.41401800
H	-3.89023500	3.06609600	-3.52353000
H	-4.69085800	3.72745800	-2.06223400
H	-2.91089800	3.57135000	-2.09678800
C	-5.42548500	1.17142700	-2.17146900
H	-5.59697600	1.16952600	-3.26828200
H	-5.61789400	0.15440600	-1.78278800
H	-6.17112700	1.85224500	-1.71035700
H	-2.57327200	-5.81146700	0.96660300
C	-2.11938500	-4.82049000	0.80525300
H	-2.40187100	-4.85520600	-1.35585200
H	-1.69290800	-4.48447700	2.91758000
C	-2.02219800	-4.28623800	-0.49103100
C	-1.62696700	-4.07923500	1.89453200
H	1.59373100	-6.32156200	1.40659100
C	1.96795400	-5.30761000	1.61856500
C	-1.45460100	-3.01119600	-0.69760000
C	-1.02763000	-2.82231700	1.68528500
H	2.98354200	-5.88769800	3.45804300
C	2.74160000	-5.06449300	2.76733700

H	1.02500200	-4.46539700	-0.14107100
C	-0.95866000	-2.26718700	0.39004400
H	-1.42060600	-2.60102500	-1.71587600
C	1.65435000	-4.25950100	0.73746500
H	-0.60896300	-2.28200400	2.54848600
C	3.20035500	-3.76220900	3.02965500
C	2.13141600	-2.95080600	0.98077100
C	2.62404300	-3.92460700	-3.48651000
C	1.77240700	-3.40360600	-4.47826100
H	3.31637300	-4.74656300	-3.72795900
H	1.79328500	-3.81889500	-5.49818700
H	3.80463200	-3.55662600	3.92737900
C	2.60154300	-3.39847500	-2.18327100
C	0.89457800	-2.35270600	-4.16122000
C	2.90068800	-2.71302700	2.14248100
Pd	-0.25707000	-0.35692500	0.19006900
C	0.86460900	-1.83245200	-2.85527700
C	1.71410700	-2.34702500	-1.85521100
H	3.28421800	-3.80859000	-1.42365700
H	0.22304300	-1.93793800	-4.92923900
P	1.71984000	-1.55021300	-0.17818400
H	0.16550100	-1.02118600	-2.59649100
H	1.02475400	0.17566600	2.61973500
H	2.02687500	0.42199400	4.90577700
H	3.28438400	-1.70730400	2.36400600
C	1.42865800	1.14915700	2.94577600
C	1.98941700	1.28966100	4.22855200
C	3.34594300	-0.67207300	-0.24713400
P	0.66334500	2.00097800	0.35757900
C	1.36752700	2.24809600	2.06135700
H	-1.15258600	3.60498500	2.14173300
H	4.13932500	-1.25309000	-2.30305900
H	1.44639700	1.11773500	-2.58700300
C	4.29146200	-0.72895700	-1.35277200
C	-1.08213100	4.12782300	1.17607100
C	2.48817700	2.53565100	4.64577900
C	3.95415600	0.15163300	0.78574900
C	-0.28044900	3.60200300	0.13625200
H	3.50199000	0.43398300	1.74375900
H	2.92561600	2.64862200	5.65033600
C	-1.77402500	5.33896000	1.00648100
C	2.17991500	1.77982900	-2.11167400
H	-2.38931800	5.73116000	1.83150800
C	2.07960700	2.32623000	-0.76792200

C	-0.18748900	4.32429700	-1.07568400
Fe	3.73091400	1.18665900	-0.94178800
C	1.85121300	3.50368400	2.49932700
C	2.41278800	3.64286900	3.78009700
H	0.44574900	3.95245600	-1.89500800
C	-1.67908200	6.04654900	-0.20461000
C	-0.88248800	5.53543200	-1.24375600
C	5.45015000	0.04092700	-0.99534200
C	5.24459000	0.58099400	0.31956600
C	3.41234700	2.23544100	-2.69299900
H	-2.22085500	6.99643400	-0.33610700
H	-0.79169000	6.08474200	-2.19425600
H	1.77669800	4.38522200	1.84409300
C	3.26693200	3.13132600	-0.54536400
H	3.78819500	1.97046700	-3.68997600
H	2.78919200	4.62562100	4.10555200
H	6.32704600	0.20963600	-1.63437100
H	5.93482700	1.23674300	0.86644600
C	4.08143800	3.06541100	-1.72820500
H	3.52324100	3.66652300	0.37688400
H	5.06193800	3.54292300	-1.85710500

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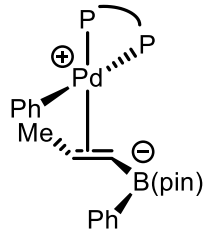

2.208

BP86 Optimization and Frequency Calculation:
Thermal correction to Gibbs Free Energy= 0.826749 a.u.
Lowest frequency= 9.09 cm^{-1}
M06 Single Point Calculation:
Electronic Energy= -4377.800205 a.u.

0 1

C	-1.73908600	-0.12959300	-2.44237900
C	-2.07162200	-0.82869600	-1.28164800
H	-1.72403700	-1.88240600	-1.25775600
H	-2.23184800	0.84969500	-2.57671300
B	-3.34446900	-0.52802300	-0.24189100
O	-4.30055600	-1.66329800	-0.48530900
O	-2.93945800	-0.69445800	1.19057900
C	-4.15172800	0.86766600	-0.57570300
C	-4.31474000	1.90955600	0.36886400
C	-4.81398700	1.04625600	-1.81840900
C	-5.08245600	3.06064100	0.10164900
H	-3.82742900	1.80585400	1.35200100
C	-5.58014000	2.19139700	-2.10762900
H	-4.74203200	0.25347700	-2.58367200
C	-5.71758400	3.20999900	-1.14496100
H	-5.18721300	3.84597300	0.87007500
H	-6.07897300	2.28999400	-3.08713200
H	-6.31928200	4.10799600	-1.36325300

C	-1.14082000	-0.69134100	-3.70948500
H	-1.95382800	-0.83518700	-4.45724100
H	-0.41382500	0.00713800	-4.17537400
H	-0.65488900	-1.67262200	-3.55366900
C	-4.37767500	-2.50184900	0.66690100
C	-3.88636300	-1.54960400	1.84513200
C	-3.18525400	-2.28359400	2.99937400
H	-2.86892800	-1.55310400	3.77375800
H	-3.86680200	-3.01391800	3.48474900
H	-2.28254900	-2.82360900	2.65579600
C	-5.04746800	-0.71609700	2.43474000
H	-4.62977000	0.05747000	3.11229400
H	-5.62152500	-0.19765000	1.64285300
H	-5.74777900	-1.34176500	3.02682500
C	-3.45124400	-3.71978700	0.47565800
H	-3.56126900	-4.47287100	1.28432400
H	-3.69765500	-4.21014400	-0.48868300
H	-2.39121800	-3.40630600	0.43221200
C	-5.82658200	-3.00136600	0.80877400
H	-5.96477500	-3.59266200	1.73905000
H	-6.54787800	-2.16164400	0.81332300
H	-6.08003900	-3.65817100	-0.04995500
H	-1.26454000	5.69802000	-3.28514900
C	-1.04323600	4.72951600	-2.80843200
H	-2.44009400	5.02598500	-1.16081700
H	0.41841700	4.13007200	-4.31307400
C	-1.69721000	4.35448300	-1.62171600
C	-0.10521000	3.85276500	-3.38323600
H	2.19852700	6.19228100	-1.24203800
C	2.66991900	5.22493400	-1.00741100
C	-1.42131800	3.11184800	-1.01291400
C	0.17577100	2.61507800	-2.77171200
H	4.64694100	5.83201000	-1.69685800
C	4.03781300	5.02331200	-1.26290600
H	0.81798600	4.37181300	-0.27617900
C	-0.48640200	2.22838300	-1.58374600
H	-1.96616200	2.83664000	-0.09974500
C	1.88843000	4.19554200	-0.45670000
H	0.92125200	1.95239100	-3.24342300
C	4.62160100	3.78216100	-0.95803500
C	2.47032600	2.94629000	-0.13453700
C	0.06012300	4.09899000	3.58258600
C	-1.15929600	3.50404900	3.95512100
H	0.42593700	4.99324200	4.11171000

H	-1.75496400	3.93195300	4.77705100
H	5.69271900	3.60988900	-1.14872700
C	0.82345700	3.55026000	2.53825600
C	-1.61318300	2.36246700	3.27262800
C	3.84611300	2.75220700	-0.39588500
Pd	0.00135400	0.33992600	-0.91708400
C	-0.86287000	1.81512300	2.21513200
C	0.36409800	2.40709400	1.84332400
H	1.78557600	4.01340900	2.27163600
H	-2.56517300	1.88750100	3.55697100
P	1.42471800	1.57656400	0.57069100
H	-1.25969900	0.92936100	1.68756800
H	2.47410400	0.24471500	-2.16374900
H	4.66795700	0.37708600	-3.36041000
H	4.33311000	1.79891300	-0.15077800
C	3.14968300	-0.62679400	-2.17099600
C	4.38472500	-0.55226300	-2.84207300
C	2.60991000	0.70542200	1.69096400
P	1.10925400	-1.88269500	-0.65635600
C	2.76326800	-1.80919500	-1.50248800
H	1.08028200	-3.03603700	-3.40392100
H	1.76339500	1.19949400	3.74492600
H	-0.37056000	-1.25075700	2.00522600
C	2.53577700	0.70677000	3.14346300
C	0.60183300	-3.76766700	-2.73418200
C	5.24814900	-1.66088100	-2.85078800
C	3.77306200	-0.08945100	1.32751200
C	0.48469600	-3.49644900	-1.35025200
H	4.10736400	-0.32809800	0.31105300
H	6.21606400	-1.60437100	-3.37341100
C	0.14323100	-4.98464100	-3.26501500
C	0.53375800	-1.85760200	2.15410300
H	0.24521600	-5.17993800	-4.34425800
C	1.40910000	-2.32679000	1.09170800
C	-0.08766500	-4.47647800	-0.51052800
Fe	2.45016500	-1.19334500	2.39075100
C	3.62718600	-2.92940300	-1.54223700
C	4.86512100	-2.84999000	-2.20137900
H	-0.16549000	-4.29685700	0.57212000
C	-0.43395800	-5.95207500	-2.42177500
C	-0.54269500	-5.69613400	-1.04446500
C	3.63540000	-0.06341700	3.65273700
C	4.39927700	-0.54995100	2.53768900
C	1.05402300	-2.33856700	3.40303400

H	-0.79066800	-6.90735400	-2.83802300
H	-0.98204900	-6.45122400	-0.37369600
H	3.32576200	-3.87956800	-1.07494900
C	2.46253200	-3.11130400	1.71107500
H	0.63299500	-2.13110700	4.39549300
H	5.53077500	-3.72746200	-2.21734400
H	3.83702700	-0.26688900	4.71274500
H	5.28866900	-1.19157700	2.59167300
C	2.23846000	-3.10826400	3.13179600
H	3.30389900	-3.59520100	1.20053300
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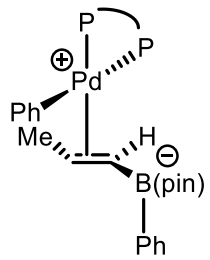

2.209

BP86 Optimization and Frequency Calculation:
Thermal correction to Gibbs Free Energy= 0.826005 a.u.
Lowest frequency= 12.63 cm^{-1}
M06 Single Point Calculation:
Electronic Energy= -4377.792814 a.u.

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Fe	2.80051800	-1.90332400	1.98244800
P	0.11995000	-2.07334600	-0.13252000
P	2.29505600	0.92994300	0.06863300
C	0.93779000	-2.46247000	1.46066900
C	0.89223100	-1.57433800	2.61026800
C	1.64419400	-2.17921100	3.67429500
C	2.15325500	-3.43884300	3.20360100
C	1.71956400	-3.62412100	1.84526000
C	3.39152800	-0.32781000	0.85909700
C	3.97344300	-0.24653200	2.18960900
C	4.76582200	-1.42490600	2.40718700
C	4.68884500	-2.24410200	1.22958200
C	3.84372200	-1.58008500	0.27437500
C	1.06880200	-3.00335100	-1.43072600
C	1.17309000	-4.41446200	-1.42415300
C	1.90151500	-5.07798900	-2.42605900
C	2.52141000	-4.34562300	-3.45597200
C	2.40567500	-2.94512100	-3.48370400
C	1.68216000	-2.27929300	-2.47734900
C	-1.41749300	-3.11971700	0.01169500
C	-2.00480400	-3.71238400	-1.13049500
C	-3.17467000	-4.48198200	-1.01347300
C	-3.77525400	-4.67054800	0.24406500
C	-3.20195900	-4.07861600	1.38315600
C	-2.03288000	-3.30585400	1.27004100
C	2.14170600	2.15898700	1.44532200
C	3.25489500	2.92242400	1.86979900

C	3.14369600	3.78720700	2.97129200
C	1.92561300	3.89201100	3.66741700
C	0.81760800	3.13400500	3.25240700
C	0.92101200	2.27651600	2.14171000
C	3.47716400	1.74402100	-1.11776500
C	4.39763400	0.96841800	-1.85850100
C	5.27993500	1.58040600	-2.76677900
C	5.25972900	2.97466800	-2.94352200
C	4.34128700	3.75209900	-2.21609500
C	3.44840400	3.14323600	-1.31854700
H	1.82006700	-1.74022900	4.66509000
H	2.79100000	-4.12998000	3.77067300
H	5.31099100	-1.66733200	3.32900200
H	5.16400400	-3.22392000	1.08921500
H	0.66567700	-5.00484600	-0.64573600
H	3.08623100	-4.86972400	-4.24305800
H	1.58720500	-1.18008800	-2.49765500
H	-1.54270600	-3.58669600	-2.12196800
H	-4.69010300	-5.27697100	0.33542700
H	-1.59946700	-2.84713900	2.17140100
H	4.21723800	2.84046000	1.34191300
H	1.83972100	4.56742100	4.53317300
H	0.04495300	1.69697800	1.80413500
H	4.44503200	-0.12173400	-1.72596300
H	5.95714000	3.45452200	-3.64829700
H	2.72180600	3.76587600	-0.77550800
C	0.24400800	2.22983500	-1.61335200
C	0.80556700	2.35752700	-2.90324600
C	-0.26848800	3.38060500	-0.97988000
C	0.84423900	3.60715900	-3.55220000
H	1.22163400	1.47797200	-3.42258000
C	-0.20712400	4.63561400	-1.62096700
H	-0.76754300	3.29945300	-0.00379400
C	0.34451500	4.75411300	-2.90945700
H	1.27765400	3.68148800	-4.56327200
H	-0.61340400	5.52418200	-1.10960500
H	0.37905500	5.73395200	-3.41265500
H	5.99300800	0.95940200	-3.33178400
H	1.97775100	-6.17665800	-2.40626900
H	2.87499200	-2.36481200	-4.29352600
H	4.30961900	4.84458400	-2.35204900
H	4.01678700	4.37869600	3.28913500
H	-0.13771000	3.21259800	3.79390800
H	-3.61612500	-4.93908000	-1.91311600

H	-3.66521600	-4.21855500	2.37259500
H	0.38034500	-0.60462500	2.64645600
H	3.56792300	-1.97423900	-0.71119100
Pd	0.10831300	0.34526600	-0.78201100
C	-2.29580900	0.02704800	-0.90172200
H	-2.37354400	-1.07366600	-0.82211100
B	-3.33158900	0.78626800	0.10873800
O	-3.21158300	2.25166400	0.22902500
O	-3.27204100	0.29043900	1.50403600
C	-4.74054200	0.30798600	-0.67501200
C	-5.29496300	1.06875600	-1.73442300
C	-5.40996600	-0.89277600	-0.33450800
C	-6.46988400	0.67351500	-2.40115300
H	-4.79714800	2.00923000	-2.02939300
C	-6.58573600	-1.30361500	-0.99325800
H	-5.00085100	-1.51111100	0.48303100
C	-7.12308300	-0.51885300	-2.03106500
H	-6.88287700	1.29690600	-3.21288300
H	-7.08801500	-2.24051100	-0.69670700
H	-8.04337300	-0.83441700	-2.55018800
C	-1.78347400	0.47902700	-2.12195700
H	-1.91115300	1.55236300	-2.34170800
H	3.81742500	0.56340600	2.91145300
H	1.97171600	-4.47935200	1.20694200
C	-1.54950700	-0.37281200	-3.34904000
H	-2.46165100	-0.33919500	-3.98836600
H	-0.71349900	0.00849100	-3.97191200
H	-1.35428500	-1.43565600	-3.10323600
C	-5.16438900	0.88299000	2.90845300
H	-5.88032400	0.70777100	2.08354600
H	-5.06420200	-0.06755000	3.47365800
H	-5.59654900	1.64131900	3.59499700
C	-2.81783400	1.39192200	3.58200200
H	-3.14274800	2.14835700	4.32640300
H	-2.78187600	0.40606700	4.09110400
H	-1.78707700	1.63538200	3.26073600
C	-5.24063400	3.17356500	1.20389700
H	-5.73762800	3.51688500	2.13524200
H	-5.18300900	4.03914500	0.51095200
H	-5.87922200	2.40672600	0.72701500
C	-2.98433900	3.81459100	2.03899600
H	-3.00716400	4.66423500	1.32489600
H	-3.39201000	4.17454000	3.00670000
H	-1.92456800	3.53504500	2.18977700

C	-3.77450400	1.30120600	2.37665900
C	-3.80904500	2.64791000	1.46435000

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78 79 1.0 80 1.0 81 1.0
79 117 1.0
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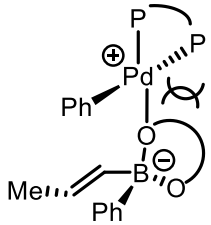

2.211

BL_2 = B(mac)

BP86 Optimization and Frequency Calculation:
Thermal correction to Gibbs Free Energy= 0.871386 a.u.
Lowest frequency= 14.66 cm^{-1}
M06 Single Point Calculation:
Electronic Energy= -4682.52658 a.u.

0 1

Fe	-4.19689700	-1.09137100	-1.39297100
P	-1.22737300	-2.00795700	0.03882200
P	-2.30033300	1.54169800	-0.13847100
C	-2.54839900	-2.23241700	-1.21495700
C	-2.55098000	-1.54786300	-2.49796200
C	-3.72894500	-1.94453100	-3.21809200
C	-4.45937100	-2.87581600	-2.40149900
C	-3.73820200	-3.06316200	-1.17193600
C	-3.90162100	0.66880200	-0.44222500
C	-4.74732400	0.86145500	-1.61160700
C	-5.92103300	0.04889300	-1.45808500
C	-5.82408800	-0.65175000	-0.20819800
C	-4.58550200	-0.28188300	0.42114900
C	-2.04102700	-2.36538100	1.67312900
C	-2.57123300	-3.64068200	1.97955800
C	-3.19504400	-3.87314000	3.21712800
C	-3.28285100	-2.84268900	4.17188000
C	-2.73580800	-1.57960500	3.88699600
C	-2.11546400	-1.34461100	2.64600300
C	-0.27554900	-3.59649200	-0.20103600
C	0.53128900	-4.10497300	0.84252300
C	1.17896900	-5.34311000	0.70110200
C	1.04640300	-6.08385900	-0.48712000
C	0.26813400	-5.57291700	-1.54026600
C	-0.39104400	-4.33798400	-1.39927700
C	-2.22507500	2.58198300	-1.67290300
C	-3.06047100	3.70936700	-1.84420800
C	-3.04576400	4.42360700	-3.05500100
C	-2.21024800	4.01563800	-4.11075600
C	-1.38548600	2.88825600	-3.95157500
C	-1.39189000	2.17853500	-2.73795900
C	-2.77381100	2.72914800	1.21668200
C	-3.64926600	2.32470300	2.25017800
C	-3.99155400	3.21109300	3.28698300
C	-3.47194600	4.51623100	3.30355000
C	-2.59753600	4.92550000	2.28129600
C	-2.24090100	4.03899000	1.25181900

H	-4.03018300	-1.57782800	-4.20812600
H	-5.42060900	-3.34165400	-2.65639900
H	-6.73609300	-0.04063200	-2.18836700
H	-6.55003200	-1.37371300	0.18838600
H	-2.48199400	-4.46626000	1.25666400
H	-3.76713500	-3.02969800	5.14331000
H	-1.67560700	-0.35708500	2.42627900
H	0.65380900	-3.53719100	1.77653200
H	1.55384800	-7.05567000	-0.59392500
H	-1.01181900	-3.96201300	-2.22651500
H	-3.73256800	4.03207600	-1.03471300
H	-2.20198300	4.57773400	-5.05786100
H	-0.73064700	1.30711400	-2.60531600
H	-4.08475000	1.31651400	2.25433600
H	-3.74618500	5.21277000	4.11151900
H	-1.53780500	4.37334900	0.47508600
C	0.37397300	2.21434400	0.58386700
C	0.52556900	2.45138200	1.96667600
C	0.78565600	3.20457100	-0.32787800
C	1.09381000	3.65440200	2.42699400
H	0.21431900	1.69175300	2.70097900
C	1.35477800	4.41059600	0.13472500
H	0.66274000	3.05979700	-1.41081700
C	1.50643800	4.64078300	1.51287300
H	1.21341800	3.81721400	3.51049200
H	1.67692700	5.17197200	-0.59458300
H	1.94680400	5.58409500	1.87371700
H	-4.67713200	2.87553400	4.08102000
H	-3.60782100	-4.86976900	3.43999900
H	-2.78284900	-0.77230800	4.63436900
H	-2.17858000	5.94401700	2.28481000
H	-3.69727500	5.30370600	-3.17352000
H	-0.72757900	2.56069300	-4.77165000
H	1.79720900	-5.72739600	1.52757400
H	0.16183100	-6.14085100	-2.47819700
H	-1.78924600	-0.83851800	-2.84369500
H	-4.21529600	-0.68253000	1.37205000
Pd	-0.31176200	0.35350000	0.09982200
C	1.79517800	-0.98132200	2.43375300
H	0.81365700	-1.46453100	2.22513400
B	2.75514500	-0.69721200	1.15984900
O	1.89539000	-0.17475500	-0.05283200
O	3.24875100	-1.98830200	0.59033200
C	3.99000900	0.31865300	1.53606100

C	3.99102400	1.71400200	1.29879700
C	5.12163400	-0.20274000	2.21574700
C	5.05341000	2.54306000	1.71065700
H	3.13913700	2.16594400	0.76761600
C	6.18676400	0.61247100	2.64314800
H	5.17079300	-1.28888000	2.40480500
C	6.15773800	1.99717700	2.39065000
H	5.01818500	3.62541200	1.49874100
H	7.04797800	0.16627200	3.16995500
H	6.99012200	2.64301900	2.71726200
C	2.06688200	-0.76445800	3.74280500
H	3.03283500	-0.28334000	3.99872200
H	-4.52122000	1.50428100	-2.46981700
H	-4.05784900	-3.69477800	-0.33430800
C	1.19900600	-1.12316300	4.92140600
H	1.71877400	-1.83069400	5.60706400
H	0.95899900	-0.22848800	5.54027700
H	0.24272000	-1.59170300	4.60886300
C	3.29838600	-3.16053200	-1.50667000
H	3.51932300	-3.08349100	-2.59077600
H	3.98327000	-3.91827100	-1.07321000
H	2.26349600	-3.52551000	-1.37351400
C	1.50985100	-0.98823400	-2.33216100
H	0.86343300	-0.11481400	-2.56024900
H	2.00544800	-1.29017300	-3.27645500
H	0.86886000	-1.82423600	-1.99465900
C	3.51438900	-1.82422800	-0.78459100
C	2.54261600	-0.60565900	-1.27213000
C	3.51970400	0.43914300	-1.83865100
C	4.85208600	-0.03247900	-1.71440100
C	3.30536300	1.66246200	-2.46349400
C	4.92893100	-1.30205500	-1.09228700
C	5.99572600	0.69265300	-2.17055600
C	4.42877300	2.41247100	-2.93262600
H	2.29173400	2.06873300	-2.59955200
C	6.17844300	-1.87882500	-0.89714400
C	7.26721300	0.07267700	-1.95982800
C	5.74032000	1.95492000	-2.79233100
H	4.24948800	3.38487700	-3.42017300
C	7.34276400	-1.17540300	-1.33736800
H	6.28718100	-2.86252200	-0.41222200
H	8.18616600	0.58451600	-2.28997500
H	6.58208300	2.56269100	-3.16333700
H	8.33198900	-1.63651900	-1.18084900

1 4 1.0 5 1.0 8 1.0 9 1.0 10 1.0 13 1.0
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6 7 1.5 38 1.0
7 8 1.5 39 1.0
8 95 1.0
9 10 1.0 13 1.0
10 11 1.5 94 1.0
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13 74 1.0
14 15 1.5 19 1.5
15 16 1.5 42 1.0
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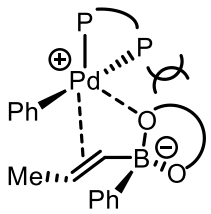

2.212

BL_2 = B(mac)

BP86 Optimization and Frequency Calculation:
Thermal correction to Gibbs Free Energy= 0.873402 a.u.
Lowest frequency= -60.66 cm^{-1}
M06 Single Point Calculation:
Electronic Energy= -4682.521044 a.u.

0 1

Fe	4.04080400	0.99403700	-1.63087900
P	1.34483000	2.02438900	0.22189900
P	2.18456800	-1.60352700	-0.25591100
C	2.49131700	2.20478200	-1.20242000
C	2.28554700	1.55650100	-2.48745200
C	3.37256200	1.91936100	-3.35424200
C	4.25225000	2.79317600	-2.62633200
C	3.71495700	2.97906000	-1.30591400
C	3.77537700	-0.79241600	-0.72804800
C	4.46898300	-0.96410100	-1.99652100
C	5.69085000	-0.21082100	-1.94660600
C	5.77302400	0.43132700	-0.66440800
C	4.60006900	0.08214700	0.09010200
C	2.39808200	2.41520600	1.70415700
C	2.96168700	3.69730200	1.90634100
C	3.78323800	3.94582400	3.01905200
C	4.04338000	2.92370000	3.95102800
C	3.46988200	1.65337400	3.77069800
C	2.64847500	1.40295100	2.65594400
C	0.39111400	3.62498500	0.04890700
C	-0.19213200	4.24845400	1.17660200
C	-0.85849400	5.47902100	1.05047200
C	-0.95449300	6.10916100	-0.20288700
C	-0.38196100	5.49676600	-1.33083200
C	0.28447500	4.26412200	-1.20776500
C	1.78185000	-2.47506700	-1.84416000
C	2.52421900	-3.59325900	-2.28964400

C	2.24747600	-4.17425600	-3.53944100
C	1.23832700	-3.64208500	-4.36270500
C	0.50289700	-2.52495600	-3.92991800
C	0.77135200	-1.94985500	-2.67522500
C	2.80870200	-2.96105200	0.85795600
C	3.85160100	-2.70672600	1.77738900
C	4.31910200	-3.72387200	2.62857400
C	3.75800700	-5.01094300	2.56859300
C	2.71567600	-5.27034200	1.66100600
C	2.23508400	-4.25302900	0.82007100
H	3.51765800	1.56601000	-4.38356600
H	5.19151600	3.22147000	-3.00091800
H	6.41883000	-0.11942500	-2.76357100
H	6.57384100	1.10151800	-0.32523200
H	2.74795800	4.51412600	1.19986600
H	4.68447800	3.12266500	4.82432500
H	2.18620400	0.41079600	2.51921400
H	-0.10553200	3.78920600	2.17283700
H	-1.47278600	7.07618600	-0.29926200
H	0.74139500	3.81174500	-2.10052200
H	3.32708600	-4.01336600	-1.66514300
H	1.02525600	-4.09953400	-5.34167100
H	0.18468100	-1.08573400	-2.32322200
H	4.31965100	-1.71402300	1.83203200
H	4.13021400	-5.80980100	3.22932200
H	1.40127800	-4.46958600	0.13576100
C	-0.31514600	-2.17492700	0.92854700
C	-0.11209100	-2.68083900	2.22954400
C	-1.06645500	-2.93370100	0.01107100
C	-0.69134600	-3.90338600	2.62006400
H	0.50712400	-2.12880800	2.95348400
C	-1.61880000	-4.17430000	0.39374600
H	-1.24564700	-2.56206000	-1.00697400
C	-1.44023600	-4.65967300	1.70040800
H	-0.54021200	-4.27023300	3.64851900
H	-2.20349700	-4.75414600	-0.33926500
H	-1.88014900	-5.62404700	2.00115500
H	5.13455700	-3.50572500	3.33620200
H	4.21845000	4.94767700	3.16137500
H	3.65274500	0.85286400	4.50459300
H	2.26152700	-6.27241300	1.61013200
H	2.82972600	-5.04792300	-3.87238200
H	-0.28770600	-2.09983700	-4.56806100
H	-1.30089700	5.94911000	1.94283900

H	-0.44680100	5.98123800	-2.31796800
H	1.45212700	0.89024100	-2.74094400
H	4.36214900	0.44692100	1.09641700
Pd	0.38211200	-0.30707900	0.46938200
C	-1.44633400	0.93783600	2.17140100
H	-0.92133400	1.91046100	2.08160900
B	-2.65843100	0.66249000	1.11109100
O	-2.06402100	0.13852600	-0.20402800
O	-3.23345500	1.98107600	0.69653700
C	-3.81486500	-0.31820900	1.75281100
C	-4.10082600	-1.62466300	1.29426200
C	-4.58656200	0.14143900	2.85253600
C	-5.09379600	-2.43049600	1.88776500
H	-3.52404800	-2.02006300	0.44405200
C	-5.58201500	-0.64688000	3.45759400
H	-4.40254300	1.15721500	3.24595100
C	-5.84126600	-1.94532300	2.97571000
H	-5.28580200	-3.44497900	1.49795700
H	-6.16112500	-0.25022700	4.30952000
H	-6.61921400	-2.57073200	3.44497600
C	-1.17063600	0.21922300	3.29700400
H	-1.74081500	-0.71752700	3.45157600
H	4.11260400	-1.55129600	-2.85045000
H	4.17604400	3.57148200	-0.50647400
C	-0.23995700	0.58511100	4.41649200
H	-0.81211000	0.69171500	5.36626400
H	0.51018800	-0.21412600	4.61291400
H	0.30066600	1.53411300	4.22903000
C	-3.50969100	3.29711200	-1.28756700
H	-3.82245000	3.29561900	-2.35196400
H	-4.15715100	4.01678300	-0.74466600
H	-2.46622700	3.65976500	-1.21767700
C	-1.73571600	1.21174900	-2.36020100
H	-1.15996700	0.34887500	-2.75308400
H	-2.23661200	1.69374200	-3.22375900
H	-1.02348600	1.93403500	-1.91686700
C	-3.65168000	1.90999000	-0.64516100
C	-2.74471000	0.73382900	-1.31514200
C	-3.77644600	-0.22479400	-1.93087500
C	-5.08713000	0.20740700	-1.60035300
C	-3.62955700	-1.37142500	-2.70496500
C	-5.09319800	1.39912400	-0.83375700
C	-6.27306600	-0.48202500	-1.99954400
C	-4.79822700	-2.08105600	-3.12615000

H	-2.63591300	-1.74745800	-2.99799400
C	-6.31332200	1.92490000	-0.42419500
C	-7.51293200	0.08648200	-1.56893700
C	-6.08650900	-1.66181400	-2.78691900
H	-4.67437900	-2.99027700	-3.73737800
C	-7.51846600	1.25271500	-0.80000900
H	-6.36724400	2.84420900	0.18153500
H	-8.46291900	-0.40056100	-1.84430600
H	-6.96342000	-2.23757800	-3.12631400
H	-8.48396900	1.67312000	-0.47317000

1 4 1.0 5 1.0 8 1.0 9 1.0 10 1.0 13 1.0
2 4 1.0 14 1.0 20 1.0
3 9 1.0 26 1.0 32 1.0 75 1.0
4 5 1.0 8 1.0
5 6 1.5 73 1.0
6 7 1.5 38 1.0
7 8 1.5 39 1.0
8 95 1.0
9 10 1.0 13 1.0
10 11 1.5 94 1.0
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12 13 1.5 41 1.0
13 74 1.0
14 15 1.5 19 1.5
15 16 1.5 42 1.0
16 17 1.5 66 1.0
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19 44 1.0
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23 24 1.5 46 1.0
24 25 1.5 72 1.0
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26 27 1.5 31 1.5
27 28 1.5 48 1.0
28 29 1.5 69 1.0
29 30 1.5 49 1.0
30 31 1.5 70 1.0
31 50 1.0
32 33 1.5 37 1.5
33 34 1.5 51 1.0

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35 36 1.5 52 1.0
36 37 1.5 68 1.0
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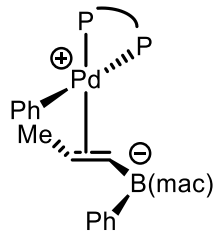

2.213

BP86 Optimization and Frequency Calculation:
Thermal correction to Gibbs Free Energy= 0.872342 a.u.
Lowest frequency= 12.14 cm^{-1}
M06 Single Point Calculation:
Electronic Energy= -4682.532667 a.u.

0 1

Fe	-3.18465300	1.27213000	2.44481700
P	-1.59219500	2.00725100	-0.48654700
P	-2.18829200	-1.48749900	0.61527100
C	-1.97324100	2.36695200	1.26763800
C	-1.21813700	1.78948500	2.36759700
C	-1.78554000	2.26575300	3.59826900
C	-2.88291100	3.13834500	3.27843700
C	-3.00305100	3.21083600	1.84733100
C	-3.39275400	-0.58951600	1.68466400
C	-3.44771400	-0.62881100	3.13728400
C	-4.54430400	0.19353100	3.56760500
C	-5.17770000	0.74734600	2.40302700
C	-4.47504500	0.27440400	1.24110500
C	-3.17654400	2.26978200	-1.42198500
C	-3.82359900	3.52788500	-1.45234900
C	-5.01838700	3.69577900	-2.17245200
C	-5.57387400	2.61750500	-2.88663000
C	-4.92598100	1.37032100	-2.88268300
C	-3.73369100	1.19880600	-2.15536800
C	-0.65826600	3.54990500	-0.96364500
C	-0.64226100	3.99749800	-2.30528900
C	0.06916900	5.15398400	-2.66586700

C	0.77387100	5.88408000	-1.69189700
C	0.75768000	5.45154900	-0.35463100
C	0.04811700	4.29234700	0.00831300
C	-1.06975300	-2.24870000	1.87742800
C	-1.53435300	-3.26892200	2.74133800
C	-0.68867700	-3.80004700	3.72967600
C	0.62543000	-3.31664800	3.86934000
C	1.08852600	-2.29990500	3.01707700
C	0.24910300	-1.76532200	2.02222900
C	-3.23875900	-2.89599200	0.00031900
C	-4.56632300	-2.65520500	-0.42120800
C	-5.36151500	-3.70507800	-0.91383200
C	-4.84489200	-5.01002900	-0.98821600
C	-3.52350300	-5.25627000	-0.57533100
C	-2.72213300	-4.20844700	-0.09226600
H	-1.45393900	1.98746200	4.60720400
H	-3.53994300	3.64046300	4.00104100
H	-4.82689300	0.38727100	4.61083800
H	-6.03022900	1.43918700	2.39634400
H	-3.38423400	4.39050100	-0.92801100
H	-6.50713700	2.75430800	-3.45537000
H	-3.22314100	0.22120800	-2.15556900
H	-1.20859300	3.45504100	-3.07820500
H	1.32955900	6.79198500	-1.97445400
H	0.03279600	3.97548800	1.06177400
H	-2.56107700	-3.65409500	2.64480700
H	1.28907300	-3.73659300	4.64174700
H	0.64446500	-0.97637900	1.35689900
H	-4.99861300	-1.64641700	-0.36041500
H	-5.47017600	-5.83337200	-1.36827200
H	-1.68425700	-4.41745400	0.20470800
C	-0.54871700	-2.25125200	-1.66349600
C	-1.39305800	-2.64863000	-2.72470900
C	0.43944500	-3.14599700	-1.21107200
C	-1.23364700	-3.90590200	-3.33850500
H	-2.18868400	-1.97869900	-3.09171200
C	0.59222800	-4.40926200	-1.82078100
H	1.12400700	-2.86281900	-0.39947200
C	-0.23876500	-4.79265500	-2.88751600
H	-1.89702800	-4.19162600	-4.17148800
H	1.38053000	-5.08906300	-1.45819900
H	-0.11222600	-5.77681600	-3.36674800
H	-6.39491400	-3.49787600	-1.23405800
H	-5.51397700	4.67942200	-2.18275200

H	-5.34458500	0.52515700	-3.45127500
H	-3.10473000	-6.27323700	-0.63415700
H	-1.06048900	-4.59676500	4.39324500
H	2.11617600	-1.91709100	3.11326600
H	0.06685700	5.48800500	-3.71542800
H	1.29563400	6.02219200	0.41878400
H	-0.37029800	1.10084400	2.26268000
H	-4.70298800	0.54941300	0.20396300
Pd	-0.80671500	-0.32696800	-0.95924600
C	1.19009400	0.67307600	-1.76497400
H	0.92926200	1.74830100	-1.71412600
B	2.60055900	0.34146800	-0.94149500
O	2.44082700	0.51152100	0.54347000
O	3.47435700	1.49761000	-1.34057300
C	3.31274500	-1.08419500	-1.34446800
C	3.63158800	-2.07233900	-0.38137000
C	3.71179900	-1.35977200	-2.67751900
C	4.29762500	-3.26697200	-0.71780000
H	3.35337100	-1.88469500	0.66924600
C	4.37107500	-2.55129300	-3.03525000
H	3.51363000	-0.61103000	-3.46510500
C	4.66725400	-3.51533800	-2.05263900
H	4.53377000	-4.00783600	0.06533100
H	4.66356400	-2.72819700	-4.08461500
H	5.18808800	-4.44845000	-2.32511300
C	0.62636000	-0.01997800	-2.83146700
H	1.03037300	-1.02734700	-3.03401000
H	-2.75727800	-1.17301900	3.79211600
H	-3.76482800	3.77806100	1.29905700
C	-0.19348600	0.54973500	-3.96222600
H	0.46715800	0.69639000	-4.84675200
H	-0.99458400	-0.14713700	-4.28602700
H	-0.64692200	1.52873600	-3.71649400
C	4.37991200	3.45471200	-0.28573200
H	4.96990200	3.84734600	0.56783500
H	4.90124200	3.74371500	-1.22220100
H	3.38291100	3.93898100	-0.28937500
C	2.85061500	2.38786200	2.00393400
H	2.30293300	1.87972200	2.82514800
H	3.61821800	3.04427400	2.46276900
H	2.12751600	3.01908300	1.45210600
C	4.23747700	1.92652800	-0.23410200
C	3.47052100	1.33946300	1.07321400
C	4.55570200	0.52652200	1.80093100

C	5.74030500	0.50198000	1.02069100
C	4.54718200	-0.14786500	3.01786900
C	5.62262400	1.25751700	-0.17276600
C	6.92297800	-0.20611000	1.39598600
C	5.72029800	-0.85738300	3.42846900
H	3.66072600	-0.14136000	3.67327000
C	6.70052600	1.29348800	-1.05034300
C	8.01874500	-0.14049400	0.47883800
C	6.87729300	-0.89859700	2.64732100
H	5.70698900	-1.39013700	4.39377100
C	7.89535500	0.58547800	-0.70842900
H	6.65153500	1.85539000	-1.99726400
H	8.95920600	-0.66693700	0.71110100
H	7.75990100	-1.46110000	2.99411100
H	8.74889300	0.61891800	-1.40566800

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7 8 1.5 39 1.0
8 95 1.0
9 10 1.0 13 1.0
10 11 1.5 94 1.0
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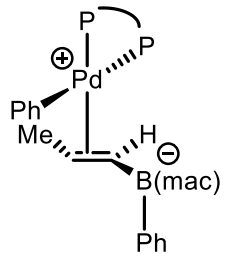

2.214

BP86 Optimization and Frequency Calculation:
Thermal correction to Gibbs Free Energy= 0.870623 a.u.
Lowest frequency= 10.59 cm^{-1}
M06 Single Point Calculation:
Electronic Energy= -4682.530606 a.u.

0 1

Fe	3.51747400	-1.42480200	2.25153700
P	1.20214600	-2.09191000	-0.17184200
P	2.70840200	1.27611900	0.25467200
C	1.87728500	-2.32943700	1.51525100
C	1.51960400	-1.47666900	2.63665900
C	2.23726700	-1.93352400	3.79414200
C	3.03397600	-3.06672400	3.40905000
C	2.81509600	-3.32114700	2.01093100
C	3.92323100	0.24694000	1.18847000
C	4.31657500	0.42358100	2.57761600
C	5.28981400	-0.58249900	2.90083400
C	5.51226300	-1.38740000	1.73191000
C	4.67429300	-0.88768300	0.67571700
C	2.45896100	-2.82386300	-1.32726000
C	2.82300500	-4.19025700	-1.27346000

C	3.78054000	-4.70653100	-2.16290800
C	4.37554900	-3.87214700	-3.12774900
C	4.00458200	-2.51865400	-3.20413600
C	3.05083400	-1.99887100	-2.30980200
C	-0.12127800	-3.40604000	-0.19187200
C	-0.44160400	-4.10205000	-1.38088400
C	-1.45354300	-5.07710100	-1.38619400
C	-2.16076100	-5.37012400	-0.20655200
C	-1.85404600	-4.67672000	0.97740200
C	-0.84373600	-3.69907300	0.98665600
C	2.13186600	2.42363600	1.58827800
C	3.00754500	3.37952300	2.15565000
C	2.58277700	4.18416300	3.22598800
C	1.28521100	4.03680500	3.74895800
C	0.41193700	3.08776600	3.19108300
C	0.82808400	2.28909200	2.10987100
C	3.84638700	2.32658800	-0.77810300
C	4.97482300	1.75077500	-1.40453300
C	5.82811900	2.53560700	-2.20051200
C	5.56978600	3.90590000	-2.37729400
C	4.44389300	4.48379600	-1.76440600
C	3.58129500	3.70043300	-0.97971500
H	2.20155800	-1.47722100	4.79205200
H	3.71831100	-3.62601400	4.06083100
H	5.75830000	-0.72614100	3.88348700
H	6.18045600	-2.25567300	1.66030700
H	2.34246100	-4.86439600	-0.54783800
H	5.12139900	-4.28162700	-3.82716100
H	2.75671300	-0.93719200	-2.37122400
H	0.10893700	-3.89560400	-2.31182300
H	-2.95134300	-6.13689800	-0.21086700
H	-0.61728100	-3.16652600	1.92238200
H	4.02966300	3.49633600	1.76427200
H	0.95349000	4.66457000	4.59090700
H	0.13333000	1.55966400	1.65864200
H	5.20628700	0.68462900	-1.26973900
H	6.24337800	4.52208700	-2.99366500
H	2.69192800	4.16516800	-0.52869400
C	0.70373700	2.15938000	-1.71385100
C	1.39938100	2.38254800	-2.92284600
C	-0.09156000	3.19732600	-1.18718800
C	1.29052000	3.61248400	-3.60039200
H	2.03809000	1.59439400	-3.35545400
C	-0.18139600	4.43675600	-1.85492500

H	-0.68592700	3.03331000	-0.27782700
C	0.50363600	4.64817100	-3.06490200
H	1.83340900	3.76079600	-4.54846600
H	-0.80927900	5.23643200	-1.42788600
H	0.42109000	5.61324600	-3.59047700
H	6.70508000	2.06988100	-2.67736600
H	4.05727700	-5.77119400	-2.10672100
H	4.45371400	-1.86174600	-3.96542000
H	4.22559800	5.55436500	-1.90303600
H	3.27305300	4.92702000	3.65586000
H	-0.60443100	2.97056500	3.59750200
H	-1.68694300	-5.61221500	-2.32017000
H	-2.40298000	-4.89744000	1.90640100
H	0.83029000	-0.62397700	2.59460000
H	4.59679900	-1.31644700	-0.33085000
Pd	0.81135900	0.28201800	-0.85974500
C	-1.44542300	-0.48415200	-1.29529300
H	-1.32834900	-1.57983000	-1.19929800
B	-2.72605300	0.07486100	-0.45132300
O	-2.88355800	1.54965900	-0.37984300
O	-2.73031900	-0.36348400	0.97564800
C	-3.92037600	-0.66059300	-1.35719100
C	-4.52515900	-0.00115000	-2.45567600
C	-4.33154700	-1.99260000	-1.10633100
C	-5.50699800	-0.62357400	-3.24887700
H	-4.22669300	1.03735900	-2.68057900
C	-5.31125200	-2.62962200	-1.89201300
H	-3.87717900	-2.53797700	-0.26150100
C	-5.90521900	-1.94552900	-2.96941300
H	-5.96842900	-0.07677900	-4.08908900
H	-5.61565800	-3.66545400	-1.66378800
H	-6.67343600	-2.43883800	-3.58794900
C	-0.87377400	0.05664300	-2.45005000
H	-1.16734000	1.08773200	-2.70918500
H	3.92247800	1.17884000	3.26722700
H	3.30438100	-4.10599200	1.42184500
C	-0.31865100	-0.73532100	-3.61141000
H	-1.12597900	-0.87686400	-4.36626700
H	0.50628300	-0.20214000	-4.12852200
H	0.03867600	-1.74101700	-3.31324200
C	-2.92508000	0.74585400	3.09810200
H	-3.51881100	1.44755800	3.71867000
H	-2.87207700	-0.22416000	3.63519800
H	-1.89128900	1.13419600	3.00853900

C	-3.14415700	3.16480900	1.38732700
H	-3.22603000	3.98531500	0.64423000
H	-3.73104200	3.45652600	2.28221900
H	-2.07852900	3.07735800	1.67630900
C	-3.54576000	0.53180300	1.71232300
C	-3.65726700	1.85963200	0.76748400
C	-5.16232300	1.96651900	0.46544200
C	-5.86135000	0.91608600	1.11199800
C	-5.88351300	2.88304300	-0.29197400
C	-5.00330600	0.05317500	1.84012500
C	-7.27741800	0.74149400	1.03180400
C	-7.30292600	2.73647500	-0.39005200
H	-5.38400400	3.71256000	-0.81880400
C	-5.56067400	-1.02570900	2.51844100
C	-7.81987200	-0.37516800	1.74251600
C	-7.99135400	1.70207400	0.24825600
H	-7.87090000	3.46574600	-0.99124700
C	-6.97580500	-1.22555200	2.46053600
H	-4.93529900	-1.72841600	3.09315100
H	-8.90617000	-0.56263300	1.71995100
H	-9.08642700	1.62126700	0.14846100
H	-7.41284400	-2.08172100	3.00079600

1 4 1.0 5 1.0 8 1.0 9 1.0 10 1.0 13 1.0
2 4 1.0 14 1.0 20 1.0
3 9 1.0 26 1.0 32 1.0 75 1.0
4 5 1.0 8 1.0
5 6 1.5 73 1.0
6 7 1.5 38 1.0
7 8 1.5 39 1.0
8 95 1.0
9 10 1.0 13 1.0
10 11 1.5 94 1.0
11 12 1.5 40 1.0
12 13 1.5 41 1.0
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19 44 1.0
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27 28 1.5 48 1.0
28 29 1.5 69 1.0
29 30 1.5 49 1.0
30 31 1.5 70 1.0
31 50 1.0
32 33 1.5 37 1.5
33 34 1.5 51 1.0
34 35 1.5 65 1.0
35 36 1.5 52 1.0
36 37 1.5 68 1.0
37 53 1.0
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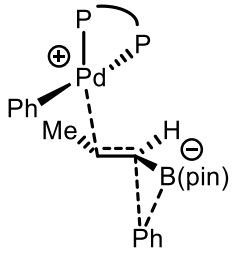

2.215

BP86 Optimization and Frequency Calculation:
Thermal correction to Gibbs Free Energy= 0.826051 a.u.
Lowest frequency= -254.92 cm^{-1}
M06 Single Point Calculation:
Electronic Energy= -4377.785654 a.u.

0 1

Fe	-2.84336700	1.78743500	2.07715400
P	-0.23716200	2.04597100	-0.14542000
P	-2.34726200	-0.98427500	0.09430700
C	-1.01256400	2.39016500	1.48352900
C	-0.90326400	1.48384600	2.61445200
C	-1.61992500	2.05534700	3.72094300
C	-2.17094800	3.31338600	3.29496600
C	-1.79824300	3.52940800	1.92279000
C	-3.45918300	0.21555800	0.95293000
C	-3.98062800	0.10484600	2.30473800

C	-4.77931800	1.26809300	2.57720200
C	-4.76589400	2.10715500	1.41064300
C	-3.95251300	1.47082900	0.40948000
C	-1.26527500	2.95675800	-1.39705600
C	-1.44189500	4.36016600	-1.36366100
C	-2.23225700	5.00080300	-2.33315900
C	-2.84351600	4.25322600	-3.35737600
C	-2.65621000	2.86117100	-3.41241300
C	-1.87032400	2.21822300	-2.43840200
C	1.25897700	3.15826500	-0.02829500
C	1.77309200	3.82175400	-1.16657300
C	2.92346000	4.62367100	-1.06742700
C	3.57801300	4.77508800	0.16790900
C	3.07589000	4.11583600	1.30415200
C	1.92696100	3.31166100	1.20828400
C	-2.11621700	-2.25162500	1.42786000
C	-3.18126300	-3.07012700	1.87064300
C	-2.98684500	-3.97710200	2.92636300
C	-1.73141900	-4.07341300	3.55517300
C	-0.66894600	-3.26214600	3.12085700
C	-0.85927700	-2.35964300	2.05881800
C	-3.53580500	-1.80998400	-1.07989500
C	-4.53602600	-1.06204300	-1.74198400
C	-5.40699100	-1.68186300	-2.65603500
C	-5.29461400	-3.05780400	-2.92045100
C	-4.29762700	-3.80781100	-2.27172400
C	-3.41858800	-3.19003900	-1.36615400
H	-1.74502500	1.59611600	4.71034900
H	-2.79565700	3.98307400	3.90107100
H	-5.28819700	1.48739700	3.52528400
H	-5.26191400	3.08127000	1.30716600
H	-0.94305500	4.96422400	-0.59013700
H	-3.45777500	4.75948600	-4.11878800
H	-1.71698800	1.12562900	-2.47695900
H	1.26795300	3.72641700	-2.14013500
H	4.47743200	5.40615400	0.24494400
H	1.55008100	2.80113500	2.10759600
H	-4.16949300	-3.00027300	1.39023400
H	-1.58128600	-4.78488300	4.38258800
H	-0.02245800	-1.73647800	1.69896500
H	-4.65438500	0.01232400	-1.54113200
H	-5.98160700	-3.54433900	-3.63096800
H	-2.63360400	-3.79023500	-0.88228700
C	-0.24589000	-2.20352000	-1.69014800

C	-0.72835700	-2.27189900	-3.01868300
C	0.21385300	-3.39937800	-1.09293800
C	-0.74402100	-3.48825000	-3.72955800
H	-1.10353100	-1.36426300	-3.52136000
C	0.18832700	-4.62079300	-1.79771200
H	0.61738300	-3.38940200	-0.06922800
C	-0.28815100	-4.67128000	-3.12028000
H	-1.12126600	-3.50857600	-4.76575000
H	0.55459100	-5.53805300	-1.30668000
H	-0.30045400	-5.62459800	-3.67320000
H	-6.18335200	-1.08195900	-3.15709800
H	-2.36446800	6.09365400	-2.29256800
H	-3.11874900	2.26996000	-4.21832000
H	-4.19473600	-4.88556200	-2.47460100
H	-3.82324500	-4.61131700	3.26051800
H	0.31720000	-3.33355600	3.60549500
H	3.30691700	5.13556900	-1.96428600
H	3.58024000	4.22681000	2.27707400
H	-0.37644100	0.52131900	2.61058700
H	-3.72164200	1.88406500	-0.58023300
Pd	-0.18577000	-0.34842700	-0.79695700
C	2.53458600	0.06595200	-0.62301800
H	2.55120500	1.16299400	-0.49362600
B	3.52865900	-0.68784300	0.31968500
O	3.54552100	-2.12684700	0.43171600
O	3.91579600	-0.12855000	1.60559200
C	4.63863600	-0.06730800	-0.94116100
C	4.99754600	-0.87798500	-2.04031000
C	5.38161000	1.11087700	-0.70346100
C	6.10775300	-0.55878800	-2.84313000
H	4.40693000	-1.78336900	-2.25877400
C	6.48674100	1.44287500	-1.50905200
H	5.10658200	1.75863800	0.14539800
C	6.85653100	0.60500300	-2.57897400
H	6.38938300	-1.21648900	-3.68239900
H	7.06481500	2.35906700	-1.30192800
H	7.72184200	0.86235800	-3.21134400
C	1.81006200	-0.39455400	-1.77450000
H	1.97631100	-1.46315100	-1.99702500
H	-3.78078500	-0.71493300	3.00470300
H	-2.09260900	4.39100100	1.31170400
C	1.73914300	0.44468800	-3.04332600
H	2.71676800	0.40039500	-3.57994900
H	0.96571700	0.07155800	-3.74647400

H	1.53153000	1.51421000	-2.83573200
C	5.31608400	-0.86835200	3.43772800
H	6.22084900	-0.62956600	2.84660400
H	5.07473900	0.01904000	4.05942500
H	5.55354600	-1.70792300	4.12458700
C	2.85119900	-1.34172800	3.39450400
H	2.95908300	-2.09928200	4.19849900
H	2.63433800	-0.36281300	3.86907500
H	1.98072200	-1.61428700	2.76542300
C	5.82036900	-2.61242000	1.14405200
H	6.46656200	-2.96359300	1.97486500
H	5.87708100	-3.35819800	0.32460300
H	6.22728000	-1.65626300	0.76052700
C	3.85142900	-3.79829600	2.14865700
H	4.04660400	-4.61179100	1.41917400
H	4.37850600	-4.05489300	3.09140700
H	2.76245900	-3.77923200	2.34697500
C	4.12287000	-1.20635900	2.53197300
C	4.34779000	-2.46235400	1.57987600

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8 95 1.0
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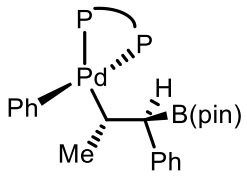

2.216

BP86 Optimization and Frequency Calculation:
Thermal correction to Gibbs Free Energy= 0.82722 a.u.
Lowest frequency= 14.11 cm^{-1}
M06 Single Point Calculation:
Electronic Energy= -4377.839897 a.u.

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Fe	3.86004200	-1.71097600	-0.05806200
P	0.33377100	-1.98675800	0.08203000
P	2.11686500	1.21757700	0.09243400
C	2.07148100	-2.56794300	0.41648800
C	2.82568500	-2.23966800	1.61337300
C	4.07639300	-2.94787400	1.57088800
C	4.11407300	-3.71401000	0.35510900
C	2.88329600	-3.49003600	-0.35431200
C	3.60125800	0.26497700	-0.41194200
C	4.85541700	0.03617500	0.28123800
C	5.66544100	-0.83157400	-0.53107500
C	4.93252400	-1.14487700	-1.72870300
C	3.66346200	-0.47331600	-1.66181500
C	-0.12470400	-3.16918700	-1.28173700
C	-1.10328500	-4.17536500	-1.13660900
C	-1.43395700	-5.00920900	-2.22189400
C	-0.78689200	-4.85588500	-3.45973400
C	0.18535300	-3.84994000	-3.61493900
C	0.50284900	-3.00510300	-2.53944100
C	-0.46307100	-2.75581700	1.58627700
C	-0.09519600	-4.05329400	2.01989100
C	-0.68148500	-4.61560400	3.16520800
C	-1.64051800	-3.89021900	3.89885500
C	-2.00524300	-2.60032000	3.48013700

C	-1.41634300	-2.03389200	2.33279600
C	2.25206900	1.33473400	1.94500400
C	3.31471500	2.02381800	2.57583800
C	3.39106200	2.08489100	3.97772100
C	2.40109400	1.47147100	4.76874400
C	1.32866300	0.80578900	4.15055500
C	1.25278100	0.74336200	2.74640800
C	2.60838500	2.95335400	-0.36425100
C	1.90006100	4.03904200	0.20069400
C	2.25372300	5.36151300	-0.11226600
C	3.31213700	5.62001400	-1.00355900
C	4.01134700	4.54626400	-1.58079900
C	3.66256300	3.21997900	-1.26378400
H	4.87473000	-2.88520200	2.32231200
H	4.94532200	-4.34464900	0.01229600
H	6.66045100	-1.21326400	-0.26535600
H	5.27120600	-1.80123000	-2.54124300
H	-1.61810200	-4.31135500	-0.17394400
H	-1.04466000	-5.51269300	-4.30558500
H	1.23446000	-2.19487100	-2.68333500
H	0.65671200	-4.62918600	1.45777600
H	-2.09997200	-4.33313100	4.79690500
H	-1.71984900	-1.02255800	2.02641200
H	4.08119100	2.53018700	1.96858400
H	2.46185400	1.52208600	5.86749900
H	0.40708400	0.23174100	2.25964500
H	1.07158800	3.85166000	0.90246300
H	3.58969300	6.65784400	-1.24753400
H	4.22389900	2.38770400	-1.71523900
C	-0.05953800	1.93825900	-2.04786300
C	0.62409800	1.82253100	-3.28328700
C	-0.76393500	3.14256200	-1.80754100
C	0.61495800	2.86565500	-4.23295200
H	1.17755200	0.89907700	-3.52666600
C	-0.77068800	4.19035000	-2.75021500
H	-1.34688500	3.25832600	-0.88007600
C	-0.08080400	4.05910700	-3.96964200
H	1.15544900	2.73896300	-5.18662200
H	-1.32879500	5.11670100	-2.53047000
H	-0.08926300	4.87650900	-4.70916600
H	1.69734700	6.19675500	0.34245700
H	-2.20454400	-5.78607300	-2.09342300
H	0.68960500	-3.71122800	-4.58449800
H	4.84068900	4.73799600	-2.28043400

H	4.22701200	2.62023100	4.45567700
H	0.54254000	0.33418100	4.76086600
H	-0.38690100	-5.62698600	3.48817000
H	-2.75592900	-2.02208100	4.04120500
H	2.49876600	-1.56707400	2.41575600
H	2.86317900	-0.51550300	-2.41141700
Pd	0.01056100	0.33473400	-0.77270000
C	-3.02833700	-0.33943700	-0.46690300
H	-2.69959600	-1.27986100	0.02530100
B	-3.27488900	0.76457500	0.65135400
O	-3.36711700	2.11959300	0.39031300
O	-3.55062800	0.46263700	1.97491500
C	-4.43386300	-0.62934000	-1.02377100
C	-5.14231500	0.33386800	-1.78355300
C	-5.06746400	-1.87032100	-0.78104200
C	-6.42784300	0.06360100	-2.28306600
H	-4.67304300	1.30934300	-1.98766300
C	-6.35613500	-2.14338600	-1.27526300
H	-4.53462400	-2.63782300	-0.19502300
C	-7.04391900	-1.17686000	-2.03060700
H	-6.95475500	0.82994200	-2.87509800
H	-6.82337300	-3.12089800	-1.07135100
H	-8.05192800	-1.38861800	-2.42202700
C	-2.00581600	0.09102500	-1.55845500
H	-2.26945400	1.12549400	-1.85103100
H	5.12737600	0.42412500	1.27057800
H	2.61151800	-3.93439500	-1.31906500
C	-2.05112100	-0.77347000	-2.82059300
H	-3.03905300	-0.69393900	-3.33214800
H	-1.28189200	-0.45573500	-3.55560200
H	-1.88961100	-1.84831100	-2.60825400
C	-3.99603600	2.76399700	1.54588100
C	-3.71920200	1.71949300	2.71260200
C	-2.40738900	1.98201800	3.46562200
H	-2.47574000	2.89028200	4.09722100
H	-2.19033000	1.12081000	4.12908700
H	-1.55355700	2.10163700	2.76976400
C	-4.87039700	1.54318400	3.70663200
H	-4.59409500	0.78584000	4.46812500
H	-5.08208600	2.49457700	4.23638300
H	-5.79772000	1.20307700	3.20829600
C	-5.48809500	2.91942000	1.21032600
H	-6.03526900	3.44716000	2.01701000
H	-5.58863200	3.51399800	0.28009500

H	-5.97162200	1.93697300	1.03901100
C	-3.35675400	4.13950200	1.74948800
H	-3.58593500	4.79052700	0.88165100
H	-3.76255600	4.63008300	2.65792300
H	-2.25675700	4.07342300	1.84708500

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8 95 1.0
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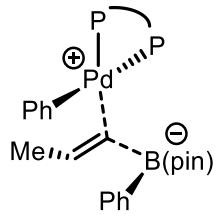

2.217

BP86 Optimization and Frequency Calculation:
Thermal correction to Gibbs Free Energy= 0.824402 a.u.
Lowest frequency= -177.39 cm^{-1}
M06 Single Point Calculation:
Electronic Energy= -4377.784302 a.u.

0 1

C	-2.31598000	-0.35719900	-2.63111200
C	-2.00207500	-0.74967900	-1.34534900
H	-1.88048600	-1.84932200	-1.26557500
H	-2.43234500	0.72295700	-2.83984700
B	-3.32067700	-0.47552200	0.01351300
O	-4.23133600	-1.58883400	-0.21678900
O	-2.69959900	-0.71215000	1.31181500
C	-4.11432900	0.92871600	-0.19568200
C	-4.24828100	1.86294800	0.85932100
C	-4.86324200	1.18979100	-1.36848400
C	-5.07354100	2.99985100	0.75358900
H	-3.69217600	1.68582900	1.79407700
C	-5.69125400	2.32033800	-1.49261200
H	-4.81407400	0.47477100	-2.20764700
C	-5.80044200	3.23527600	-0.42733800
H	-5.15139200	3.70543000	1.59826200
H	-6.26251900	2.48717800	-2.42157000
H	-6.45009700	4.12158300	-0.51742800
C	-2.58201200	-1.25098900	-3.80546500
H	-1.84125200	-1.06446000	-4.61691800
H	-2.55336100	-2.32573500	-3.53837300
H	-3.57304200	-1.01883000	-4.25669700
C	-4.16874000	-2.53404800	0.86141600
C	-3.45731600	-1.70810500	2.02679100
C	-2.50069800	-2.53829900	2.89418200
H	-2.04309200	-1.89357300	3.67325800
H	-3.03974600	-3.35936500	3.41155400

H	-1.68282900	-2.98061100	2.29449600
C	-4.46890400	-0.99441500	2.94912100
H	-3.91710000	-0.31029300	3.62646900
H	-5.19120400	-0.38758600	2.36920700
H	-5.03529500	-1.71131400	3.57866800
C	-3.36217900	-3.76272900	0.40356800
H	-3.36982500	-4.57377800	1.16090700
H	-3.81475800	-4.16018800	-0.52799900
H	-2.30958600	-3.50577200	0.18397700
C	-5.60314100	-2.98494200	1.18889000
H	-6.26923900	-2.12462900	1.39126600
H	-6.02267400	-3.54045900	0.32444400
H	-5.62305800	-3.66295700	2.06793900
H	-1.82685600	5.48520900	-3.18838400
C	-1.53305000	4.54364100	-2.69659600
H	-2.59180000	4.97877800	-0.84290200
H	-0.37837500	3.81432000	-4.39822400
C	-1.95885700	4.25932100	-1.38848400
C	-0.72510200	3.60934800	-3.37142200
H	1.61212500	6.38765800	-1.21111300
C	2.12782800	5.41427600	-1.20857100
C	-1.58730300	3.05133700	-0.75923600
C	-0.35381000	2.40663100	-2.74019600
H	3.76498100	6.09162800	-2.47899300
C	3.32970600	5.24879900	-1.91897300
H	0.62029400	4.48816200	0.04094100
C	-0.79034700	2.10117800	-1.42689000
H	-1.94292400	2.86006800	0.26234700
C	1.56965000	4.34120200	-0.49316700
H	0.27926300	1.69580400	-3.29773700
C	3.97020300	3.99774900	-1.90960600
C	2.21282700	3.08248200	-0.46656000
C	0.56094000	3.98162400	3.75071300
C	-0.61033600	3.37719100	4.24429400
H	1.00176900	4.84518700	4.27372100
H	-1.09161200	3.76759300	5.15511900
H	4.91253000	3.85225900	-2.46142300
C	1.17720900	3.48321000	2.59032200
C	-1.16370600	2.27591200	3.56885400
C	3.41732800	2.92354500	-1.19021100
Pd	-0.16584100	0.27912200	-0.70483600
C	-0.55799900	1.77864700	2.39940600
C	0.61984700	2.37911000	1.90328700
H	2.10061000	3.95657000	2.22230400

H	-2.08059000	1.79760100	3.94804500
P	1.45972300	1.63011900	0.42865900
H	-1.02117500	0.92612700	1.86927900
H	1.96833900	0.16324200	-2.41862000
H	3.77234100	0.19931600	-4.16075300
H	3.94455600	1.95934600	-1.19338500
C	2.60747400	-0.72290500	-2.57299000
C	3.62057100	-0.70448300	-3.54987400
C	2.95355600	0.89898200	1.24324400
P	1.01902900	-1.87193700	-0.51928800
C	2.39146000	-1.87172600	-1.78067600
H	-0.11759500	-2.96680700	-3.00043500
H	2.66021000	1.43496100	3.43536400
H	0.32384500	-1.14090600	2.43357400
C	3.27395300	0.96265000	2.65966900
C	-0.19231000	-3.76132100	-2.24091600
C	4.42930000	-1.83711200	-3.74644000
C	4.02636200	0.15545200	0.60162000
C	0.26954700	-3.52638500	-0.92469000
H	4.08782500	-0.11161700	-0.46030400
H	5.22338400	-1.82486500	-4.50977500
C	-0.72371200	-5.01162600	-2.59743100
C	1.24938600	-1.72404300	2.34417600
H	-1.07478700	-5.18130100	-3.62772000
C	1.81435500	-2.20847000	1.09519800
C	0.18126600	-4.56546800	0.02699100
Fe	3.11338900	-0.97078400	2.01844300
C	3.19170200	-3.01628200	-2.00641600
C	4.21020200	-2.99365300	-2.97433400
H	0.53778300	-4.40278500	1.05545900
C	-0.80112200	-6.04531100	-1.64493100
C	-0.34763100	-5.81871500	-0.33433800
C	4.51856500	0.27767100	2.87421400
C	4.98430100	-0.21621400	1.60793800
C	2.11872700	-2.12435800	3.41534000
H	-1.21310200	-7.02719600	-1.92677400
H	-0.40176200	-6.62261000	0.41692000
H	3.00758800	-3.94171400	-1.43869800
C	3.03928700	-2.91643000	1.42314900
H	1.97985500	-1.88675800	4.47824200
H	4.82995200	-3.89028400	-3.13411400
H	5.01096600	0.13416000	3.84521100
H	5.89541500	-0.80463200	1.43675300
C	3.21963600	-2.85705100	2.84906300

H 3.72899700 -3.38708100 0.71203500
H 4.07062400 -3.27431900 3.40397400

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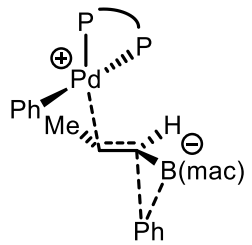

2.219

BP86 Optimization and Frequency Calculation:
Thermal correction to Gibbs Free Energy= 0.868451 a.u.
Lowest frequency= -313.53 cm^{-1}
M06 Single Point Calculation:
Electronic Energy= -4682.516377 a.u.

0 1

Fe	-3.73906400	1.35017100	2.20025800
P	-1.38735400	2.06601700	-0.20481700
P	-2.79724200	-1.33032700	0.26382700
C	-2.11529100	2.29445200	1.46672200
C	-1.74764600	1.46765100	2.60405100
C	-2.49271200	1.91695300	3.74769500
C	-3.31792900	3.02096700	3.33803500
C	-3.08848500	3.26299800	1.93900200
C	-4.08177000	-0.35977800	1.16769700
C	-4.49108900	-0.51600400	2.55296000
C	-5.49528500	0.47142800	2.84040000
C	-5.72161400	1.24414300	1.64992700
C	-4.85345800	0.74321300	0.61837200
C	-2.64161600	2.75185100	-1.39108900
C	-3.07560600	4.09795000	-1.34880300
C	-4.03368800	4.56590000	-2.26430500
C	-4.56089000	3.70235400	-3.24283700
C	-4.12084400	2.36886800	-3.30706600
C	-3.16566000	1.89782900	-2.38762300
C	-0.11246900	3.43296900	-0.17334900
C	0.18138100	4.20076000	-1.32392000
C	1.16978700	5.20005300	-1.28397700
C	1.88016100	5.44816300	-0.09639300
C	1.59839700	4.68637100	1.05186700
C	0.61238400	3.68532700	1.01489400
C	-2.16018700	-2.42607400	1.61780500
C	-2.97173300	-3.41875900	2.21522000
C	-2.47996300	-4.19121800	3.28131800
C	-1.17653800	-3.97809700	3.76713700
C	-0.36416500	-2.99471800	3.17678400
C	-0.84975600	-2.22684300	2.10248700
C	-3.86121600	-2.47377600	-0.75202700
C	-5.04051200	-1.99725000	-1.36872500
C	-5.82350100	-2.84725000	-2.17018400
C	-5.44239800	-4.18610700	-2.36567600
C	-4.26638400	-4.66590200	-1.76220100

C	-3.47604700	-3.81666800	-0.96935300
H	-2.45558800	1.47448700	4.75185000
H	-4.02612300	3.56858400	3.97420000
H	-5.98321500	0.62409800	3.81228400
H	-6.41259400	2.09148700	1.54896500
H	-2.65002800	4.79538800	-0.61093300
H	-5.30816400	4.07375000	-3.96186800
H	-2.81413300	0.85230500	-2.43653000
H	-0.37325600	4.03293400	-2.25990700
H	2.65150200	6.23376000	-0.06550300
H	0.40608300	3.09987100	1.92391000
H	-3.99471500	-3.59226100	1.84671700
H	-0.79288100	-4.58270200	4.60410200
H	-0.20481300	-1.47121400	1.62188300
H	-5.36705200	-0.95790100	-1.21940800
H	-6.05953900	-4.85362700	-2.98783500
H	-2.54922600	-4.20488700	-0.52144400
C	-0.68030400	-2.12645400	-1.73808100
C	-1.28603500	-2.33317700	-3.00000300
C	0.09876200	-3.17536500	-1.19818100
C	-1.11919400	-3.54399600	-3.70118300
H	-1.90250800	-1.54033900	-3.45698400
C	0.25553200	-4.39341200	-1.89172000
H	0.62064300	-3.04091000	-0.23875500
C	-0.35053000	-4.58364600	-3.14692400
H	-1.59899800	-3.67407300	-4.68576100
H	0.86910000	-5.19549000	-1.44781800
H	-0.21999900	-5.53277400	-3.69183400
H	-6.74202300	-2.45781200	-2.63752100
H	-4.36501900	5.61539600	-2.21710600
H	-4.51737700	1.69001700	-4.07837900
H	-3.95304100	-5.71110000	-1.91302900
H	-3.12095800	-4.96302100	3.73621500
H	0.65767500	-2.82539500	3.55059200
H	1.38082400	5.79051300	-2.18965200
H	2.14771200	4.87186400	1.98845700
H	-1.03648900	0.63211800	2.58095700
H	-4.76823000	1.15021100	-0.39709600
Pd	-0.92067300	-0.28412900	-0.85377300
C	1.67277900	0.57703900	-0.85779000
H	1.50078700	1.64153000	-0.62277000
B	2.80390200	-0.09202500	-0.03529100
O	3.10336000	-1.50172700	-0.12213500
O	3.11554900	0.35929900	1.30529800

C	3.69793900	0.85552500	-1.27889800
C	4.18274000	0.20309500	-2.43420100
C	4.18006600	2.14964000	-0.98118100
C	5.16472100	0.80310300	-3.24215000
H	3.79862300	-0.79876800	-2.68806600
C	5.15714800	2.75857400	-1.78943900
H	3.79967400	2.67573700	-0.08980900
C	5.65412200	2.08480000	-2.92150800
H	5.55071700	0.27170800	-4.12786300
H	5.53427200	3.76336500	-1.53638200
H	6.41871400	2.55999900	-3.55741300
C	0.94584500	0.06365400	-1.99089900
H	1.27960500	-0.94488800	-2.29007200
H	-4.08588900	-1.24530300	3.26431500
H	-3.59361200	4.02543800	1.33409400
C	0.65068300	0.93624600	-3.20271600
H	1.58278200	1.08459100	-3.79861500
H	-0.09521400	0.46572200	-3.87700600
H	0.27970000	1.94373200	-2.92695200
C	3.59991300	-0.82647800	3.34113200
H	4.28451500	-1.53036900	3.85582100
H	3.59340200	0.12502600	3.91217700
H	2.57281300	-1.24233200	3.36743600
C	3.63632300	-3.17611000	1.52423600
H	3.64052100	-3.96481400	0.74383900
H	4.33730300	-3.48501600	2.32580400
H	2.61282500	-3.12219800	1.94538400
C	4.03956300	-0.55452400	1.89942100
C	4.04303700	-1.83817300	0.89996000
C	5.48140500	-1.88163400	0.36398700
C	6.23917400	-0.83032900	0.93911700
C	6.09994300	-2.73667000	-0.54106200
C	5.48165000	-0.03180600	1.83315300
C	7.61798900	-0.59813300	0.64631200
C	7.48019500	-2.52975300	-0.85463500
H	5.55053700	-3.56297200	-1.02055500
C	6.10256700	1.03940000	2.46595900
C	8.22974500	0.50855500	1.31514500
C	8.22802200	-1.49722900	-0.28410500
H	7.96766600	-3.21029300	-1.57194800
C	7.48372800	1.29569700	2.19527100
H	5.55469100	1.69233500	3.16461600
H	9.29223600	0.73845100	1.13188800
H	9.29022500	-1.37051400	-0.55055400

H 7.97320000 2.14509000 2.69955100

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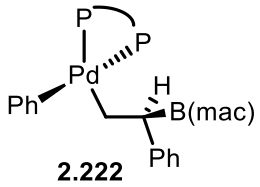

2.222

BP86 Optimization and Frequency Calculation:
Thermal correction to Gibbs Free Energy= 0.86992 a.u.
Lowest frequency= 8.75 cm^{-1}
M06 Single Point Calculation:
Electronic Energy= a.u.

0 1

Fe	-3.46127200	1.29067200	2.39963000
P	-1.19278000	2.03976400	-0.09767000
P	-2.77588800	-1.28059400	0.23126800
C	-1.82817900	2.19457200	1.62503500
C	-1.44534700	1.28134200	2.68817600
C	-2.10036800	1.69415400	3.89925700
C	-2.88526400	2.86275600	3.60518400
C	-2.72000900	3.17883700	2.21155200
C	-3.96597100	-0.32591800	1.27722900
C	-4.29529900	-0.55784400	2.67225200
C	-5.21896600	0.45930600	3.09498200
C	-5.47591400	1.32606000	1.97744100
C	-4.70503400	0.85392100	0.85828600
C	-2.50217300	2.81962100	-1.16594900
C	-2.91234600	4.16647300	-1.02629500
C	-3.91652600	4.69544700	-1.85554700
C	-4.51577300	3.89274600	-2.84440000
C	-4.10133400	2.55910400	-3.00544000
C	-3.09951200	2.02793300	-2.17251700
C	0.09670800	3.39517900	-0.04959400
C	0.32033600	4.25178100	-1.15212700
C	1.31012300	5.24928300	-1.09534500
C	2.09637700	5.40410700	0.06013400
C	1.88754000	4.55105600	1.15893800
C	0.89712400	3.55550900	1.10570100
C	-2.21811400	-2.55276600	1.46582900
C	-3.08204700	-3.56472200	1.94424600
C	-2.64643400	-4.46435800	2.93234900
C	-1.34643100	-4.35973700	3.46071600
C	-0.48125000	-3.35691100	2.98968100
C	-0.91187200	-2.46369100	1.99122300

C	-3.94493500	-2.25887400	-0.84588700
C	-5.17360200	-1.71276800	-1.28250200
C	-6.02203200	-2.44285300	-2.13470200
C	-5.65896500	-3.73175600	-2.56204400
C	-4.43619400	-4.28135400	-2.13715000
C	-3.58102300	-3.55048700	-1.29491500
H	-2.03167400	1.18864400	4.87156600
H	-3.52645700	3.40515900	4.31296300
H	-5.63498600	0.56750800	4.10560500
H	-6.12237800	2.21367800	1.98069200
H	-2.43228100	4.81850200	-0.28039400
H	-5.29911300	4.31178300	-3.49580800
H	-2.76373000	0.98283100	-2.29508100
H	-0.28902500	4.15342600	-2.06338100
H	2.86964500	6.18726500	0.10452900
H	0.74836500	2.89760600	1.97550000
H	-4.10428100	-3.65087800	1.54417900
H	-1.00668900	-5.06281400	4.23765400
H	-0.23175100	-1.68905800	1.59589800
H	-5.48798300	-0.71330300	-0.94899300
H	-6.32640000	-4.30624100	-3.22401200
H	-2.62185400	-3.99288900	-0.98591600
C	-0.64074300	-2.05595200	-1.87379700
C	-1.22128200	-2.20301000	-3.15902200
C	0.06907500	-3.16894000	-1.35969600
C	-1.09830600	-3.39707100	-3.89691700
H	-1.78860100	-1.36911800	-3.60703100
C	0.18816800	-4.37070900	-2.08813000
H	0.55616200	-3.10438700	-0.37486800
C	-0.39402300	-4.49186600	-3.36330300
H	-1.56229600	-3.47206000	-4.89511400
H	0.74800200	-5.21711600	-1.65470300
H	-0.29609800	-5.42817900	-3.93684500
H	-6.97762800	-1.99965200	-2.45789700
H	-4.22747900	5.74516800	-1.73278100
H	-4.55455000	1.92718300	-3.78547600
H	-4.13676300	-5.28852500	-2.46807600
H	-3.32905700	-5.24968100	3.29423900
H	0.53739900	-3.27427700	3.40019300
H	1.46401900	5.91045100	-1.96298600
H	2.49859500	4.66105800	2.06886700
H	-0.78315000	0.41423600	2.57216800
H	-4.66084000	1.32633600	-0.13096000
Pd	-0.83413700	-0.25340600	-0.89767800

C	2.10574800	0.79266600	-1.27805300
H	1.79232100	1.74105100	-0.79778200
B	2.70408800	-0.11712100	-0.12508900
O	3.11539400	-1.42700500	-0.29375600
O	2.98538100	0.37881900	1.13756600
C	3.31059700	1.14052400	-2.17011900
C	3.91424500	0.17241100	-3.00891400
C	3.86149600	2.44317600	-2.16578800
C	5.01610100	0.49761600	-3.81828500
H	3.51492900	-0.85395700	-3.02208200
C	4.96839200	2.77112100	-2.97023500
H	3.40744000	3.21366600	-1.52104300
C	5.55050200	1.79986600	-3.80393400
H	5.46542000	-0.27523800	-4.46343100
H	5.37556000	3.79541300	-2.94686000
H	6.41573600	2.05422300	-4.43718200
C	0.91589800	0.19087800	-2.07379300
H	1.24598400	-0.78574700	-2.47863200
H	-3.89018200	-1.35876900	3.30204100
H	-3.21653600	4.00206000	1.68431600
C	0.47140200	1.06301900	-3.25406200
H	1.31001900	1.24583900	-3.96767200
H	-0.34278100	0.57763500	-3.83213800
H	0.10416700	2.06109000	-2.93465000
C	2.98360300	-0.87479300	3.21112600
H	3.50941600	-1.62939300	3.82876800
H	2.92093800	0.06503900	3.79623400
H	1.94997600	-1.22568200	3.02203300
C	3.28224000	-3.19619600	1.35657100
H	3.39316200	-3.95407300	0.55509900
H	3.82041300	-3.56345700	2.25280900
H	2.20472000	-3.11124200	1.59725700
C	3.72344300	-0.61562200	1.90139500
C	3.85077200	-1.86196100	0.88025000
C	5.34756200	-1.93919000	0.57163600
C	6.03071400	-0.93928700	1.30905300
C	6.07579600	-2.78271400	-0.25833900
C	5.16458000	-0.14763400	2.10524400
C	7.44451100	-0.75059400	1.25742700
C	7.49447200	-2.61414900	-0.33360300
H	5.58752200	-3.56850600	-0.85618600
C	5.70308500	0.87100000	2.88185100
C	7.97181500	0.30343600	2.06828000
C	8.16949300	-1.63497600	0.39822900

H	8.07124200	-3.28272000	-0.99287700
C	7.11772600	1.08296900	2.85099400
H	5.06917600	1.51620200	3.51058200
H	9.05644700	0.49902700	2.07146500
H	9.26421200	-1.53899100	0.31451000
H	7.54407700	1.89160800	3.46634800

1 4 1.0 5 1.0 8 1.0 9 1.0 13 1.0
2 4 1.0 14 1.0 20 1.0 75 1.0
3 9 1.0 26 1.0 32 1.0
4 5 1.0 8 1.0
5 6 1.5 73 1.0
6 7 1.5 38 1.0
7 8 1.5 39 1.0
8 95 1.0
9 10 1.0 13 1.0
10 11 1.5 94 1.0
11 12 1.5 40 1.0
12 13 1.5 41 1.0
13 74 1.0
14 15 1.5 19 1.5
15 16 1.5 42 1.0
16 17 1.5 66 1.0
17 18 1.5 43 1.0
18 19 1.5 67 1.0
19 44 1.0
20 21 1.5 25 1.5
21 22 1.5 45 1.0
22 23 1.5 71 1.0
23 24 1.5 46 1.0
24 25 1.5 72 1.0
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26 27 1.5 31 1.5
27 28 1.5 48 1.0
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31 50 1.0
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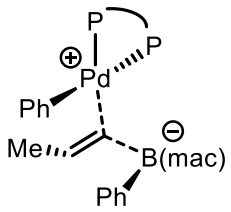

2.221

BP86 Optimization and Frequency Calculation:
Thermal correction to Gibbs Free Energy= 0.869699 a.u.
Lowest frequency= -164.76 cm^{-1}
M06 Single Point Calculation:
Electronic Energy= -4682.513324 a.u.

0 1

Fe	-3.37786100	1.38594000	2.31195300
P	-1.46880000	1.99563800	-0.45903200
P	-2.24776200	-1.42173700	0.62933900
C	-2.03006700	2.42756000	1.23063800
C	-1.40822400	1.87638500	2.42369900
C	-2.09447100	2.40143600	3.57180900
C	-3.13789900	3.27624600	3.10814300
C	-3.10352300	3.30090600	1.67053900
C	-3.53801100	-0.49847200	1.58047400
C	-3.72135200	-0.49654000	3.02227200
C	-4.84110800	0.34826300	3.33508700
C	-5.36367800	0.87682800	2.10548700
C	-4.56612000	0.36621800	1.02329000
C	-2.94696000	2.25734800	-1.56067700
C	-3.54624100	3.52958100	-1.71449200
C	-4.65493900	3.69622300	-2.56190600
C	-5.16854400	2.60099700	-3.28170900
C	-4.56491200	1.33795800	-3.15440000
C	-3.46002500	1.16838500	-2.29939600
C	-0.48010700	3.50861300	-0.91028200
C	-0.20392100	3.77477800	-2.27199300
C	0.52310900	4.91789400	-2.64393700
C	0.98842300	5.81160300	-1.66155200
C	0.72047400	5.55433900	-0.30607000
C	-0.00762000	4.40972200	0.06943600
C	-1.29032900	-2.21502600	2.00489300

C	-1.88042300	-3.17989700	2.85544400
C	-1.14510400	-3.73699100	3.91539500
C	0.18548200	-3.33693100	4.13931200
C	0.77612700	-2.37845800	3.29819200
C	0.04538500	-1.81789800	2.23372800
C	-3.26599600	-2.81444000	-0.07913700
C	-4.51443900	-2.54010700	-0.68359400
C	-5.27272300	-3.57225000	-1.26370000
C	-4.79650400	-4.89474500	-1.25006000
C	-3.55225500	-5.17496600	-0.65859500
C	-2.78922300	-4.14479900	-0.08287500
H	-1.87711400	2.15320100	4.61901300
H	-3.85943700	3.81132700	3.73997400
H	-5.21175300	0.57178300	4.34432400
H	-6.20460600	1.57576200	2.00565300
H	-3.13453100	4.40339100	-1.18571600
H	-6.03312300	2.73640500	-3.95069600
H	-2.97895100	0.18017600	-2.20065600
H	-0.58073400	3.09597800	-3.05288600
H	1.55534900	6.70951100	-1.95383900
H	-0.22507300	4.23203300	1.13347100
H	-2.92031400	-3.50214100	2.69058400
H	0.76272300	-3.77789800	4.96750000
H	0.53120600	-1.08095800	1.56864000
H	-4.91424500	-1.51620900	-0.70135000
H	-5.39243600	-5.70420900	-1.70072200
H	-1.81046700	-4.38232700	0.35776000
C	-0.38784000	-2.22179600	-1.52225100
C	-1.09780900	-2.56030600	-2.70081800
C	0.44318800	-3.20423300	-0.94783900
C	-0.96278000	-3.82998100	-3.29484700
H	-1.76950800	-1.82656900	-3.17731200
C	0.57523000	-4.47983200	-1.53701800
H	1.01185000	-2.98619700	-0.03333400
C	-0.12343600	-4.79839700	-2.71341100
H	-1.52165400	-4.06136000	-4.21715100
H	1.24065700	-5.22391700	-1.06878800
H	-0.01586100	-5.79321300	-3.17547600
H	-6.24541800	-3.33725300	-1.72452300
H	-5.11480300	4.69162800	-2.66784300
H	-4.94952700	0.47851300	-3.72584200
H	-3.16412600	-6.20581300	-0.64679500
H	-1.61513400	-4.48937700	4.56848800
H	1.82032900	-2.06810400	3.45845900

H	0.72339000	5.11324400	-3.70939900
H	1.07391900	6.25149800	0.47012900
H	-0.57340200	1.16417700	2.43230900
H	-4.69725000	0.62069000	-0.03561600
Pd	-0.67808700	-0.31592600	-0.80694200
C	1.06249200	0.45157400	-1.87548400
H	1.15104300	1.55066500	-1.75882200
B	2.65389800	-0.04057500	-0.91742200
O	2.44267600	0.12668600	0.51527800
O	3.51704200	1.05622800	-1.34837000
C	3.23931700	-1.48594600	-1.36718000
C	3.65411400	-2.41755700	-0.38422800
C	3.54202900	-1.80726200	-2.71129100
C	4.31464300	-3.61453200	-0.72119800
H	3.45892700	-2.18459900	0.67571400
C	4.19923600	-2.99945900	-3.06600000
H	3.27085300	-1.09672600	-3.51095100
C	4.58745100	-3.91417900	-2.06819100
H	4.62212000	-4.31653200	0.07243800
H	4.41835100	-3.21481300	-4.12547600
H	5.10409400	-4.84959800	-2.33981600
C	0.99935800	0.07228200	-3.20163700
H	0.87668200	-1.00209400	-3.43666000
H	-3.09665100	-1.02786100	3.74969800
H	-3.79340000	3.85762200	1.02474300
C	1.12001400	0.96393500	-4.40170100
H	1.39127700	2.00395800	-4.13419100
H	1.87494500	0.56602500	-5.11577900
H	0.16130900	0.98242300	-4.97009100
C	3.96632800	3.24830900	-0.44359000
H	4.41719200	3.81475000	0.39654000
H	4.50476600	3.52935400	-1.37227000
H	2.90863300	3.55831400	-0.55576000
C	2.46336500	2.14374700	1.85409400
H	1.94874300	1.62135800	2.68682700
H	3.09353900	2.94301300	2.29398400
H	1.69271800	2.61303400	1.21274300
C	4.07840400	1.73460000	-0.23146100
C	3.29655100	1.13956000	1.05504900
C	4.40989400	0.51632800	1.91102400
C	5.65001000	0.62731600	1.23208100
C	4.38256600	-0.10291500	3.15583600
C	5.53691300	1.30509100	-0.00755500
C	6.88177500	0.11666900	1.74404900

C	5.60151100	-0.61995800	3.69904600
H	3.44751600	-0.20032500	3.73104200
C	6.67473300	1.47048600	-0.78880000
C	8.03619400	0.30552500	0.92079500
C	6.81911600	-0.52366800	3.02205900
H	5.57483100	-1.11158800	4.68535700
C	7.92158400	0.96017200	-0.30783200
H	6.63437500	1.98112600	-1.76443100
H	9.01634400	-0.06840200	1.25942200
H	7.73645600	-0.93787300	3.47169200
H	8.82232800	1.09222400	-0.92949400

1 4 1.0 5 1.0 8 1.0 9 1.0 10 1.0 13 1.0
2 4 1.0 14 1.0 20 1.0 75 1.0
3 9 1.0 26 1.0 32 1.0 75 1.0
4 5 1.0 8 1.0
5 6 1.5 73 1.0
6 7 1.5 38 1.0
7 8 1.5 39 1.0
8 95 1.0
9 10 1.0 13 1.0
10 11 1.5 94 1.0
11 12 1.5 40 1.0
12 13 1.5 41 1.0
13 74 1.0
14 15 1.5 19 1.5
15 16 1.5 42 1.0
16 17 1.5 66 1.0
17 18 1.5 43 1.0
18 19 1.5 67 1.0
19 44 1.0
20 21 1.5 25 1.5
21 22 1.5 45 1.0
22 23 1.5 71 1.0
23 24 1.5 46 1.0
24 25 1.5 72 1.0
25 47 1.0
26 27 1.5 31 1.5
27 28 1.5 48 1.0
28 29 1.5 69 1.0
29 30 1.5 49 1.0
30 31 1.5 70 1.0
31 50 1.0
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33 34 1.5 51 1.0
34 35 1.5 65 1.0
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112 115 1.5 116 1.0
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114 118 1.5 119 1.5
115 119 1.5 120 1.0
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119 124 1.0
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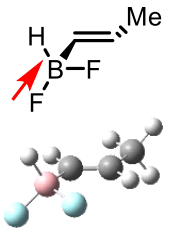
2.9.3.4 Probe or Alkenylboron-Ate Conformation: Scheme 2.38

All calculations were performed using the Gaussian09 package of programs.[72] A dihedral scan of boron-ate complex **2.223** was performed with the density functional B3LYP in conjunction with the 6-311++G(d,p) bases set in tetrahydrofuran as solvent using the IEFPCM model[81] and the input keyword "opt=modredundant" and scan angle specification: "D 4 1 3 15 S 72 5.000". The default convergence criteria and integration grid were applied. Gibbs free energies were assessed through single point calculations with the density functional M06 applying the larger def2-TZVPP[73b] basis set, followed by addition of thermal corrections obtained from frequency calculations performed under standard conditions (298.15 K, 1.0 atm) at the same level of theory as the dihedral scan (denoted as M06/def2-TZVP//B3LYP/6-311++G(d,p).



2.223

Frequency Calculation:
Thermal correction to Gibbs Free Energy = 0.055386 au
Single Point Calculation:
Electronic Energy = -342.645565885 au

-1 1

C	-0.34455900	-0.48554900	0.30255900
H	-0.59231400	-1.52351700	0.55791800
B	1.19827900	-0.05727200	0.42325700
C	-1.37434000	0.29714600	-0.04318100
H	-1.17045500	1.33853700	-0.29764400

[81] Scalmani, G.; Frisch, M. J. *J. Chem. Phys*. **2010**, 132, 114110.

C	-2.82224400	-0.11215900	-0.12404000
H	-3.44947400	0.49322800	0.54251500
H	-3.22335100	0.02768200	-1.13571800
H	-2.95530300	-1.16310900	0.14936400
F	2.02774600	-0.95228800	-0.39325300
F	1.41969800	1.28855100	-0.08753000
H	1.61936800	-0.10945500	1.58229900

1 2 1.0 3 1.0 4 2.0
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3 10 1.0 11 1.0 12 1.0
4 5 1.0 6 1.0
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6 7 1.0 8 1.0 9 1.0
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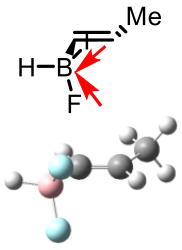

2.224

Frequency Calculation:
Thermal correction to Gibbs Free Energy = 0.056310 au
Single Point Calculation:
Electronic Energy = -342.642013118 au

-1 1

C	-0.36915000	-0.02929400	0.67180100
H	-0.76010200	-0.08837600	1.69458700
B	1.23557000	-0.00908600	0.46664100
C	-1.29263400	0.01901700	-0.29710900
H	-0.96164600	0.07817500	-1.33654700
C	-2.78726300	-0.00301700	-0.11231300
H	-3.25876400	0.88795700	-0.54554000
H	-3.24082900	-0.86662800	-0.61484800

H	-3.05680200	-0.04812200	0.94705000
F	1.67425100	-1.15566500	-0.33491900
F	1.65228100	1.17654100	-0.28535900
H	1.85578300	-0.02569500	1.53032200

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4 5 1.0 6 1.0
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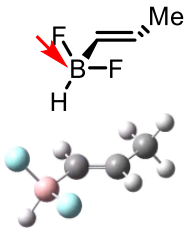

2.225

Frequency Calculation:
Thermal correction to Gibbs Free Energy = 0.055380 au
Single Point Calculation:
Electronic Energy = -342.645576647 au

-1 1

C	-0.34459200	0.48574600	0.29997600
H	-0.59193700	1.52391900	0.55499200
B	1.19790100	0.05674100	0.42163300
C	-1.37508700	-0.29691600	-0.04383900
H	-1.17183500	-1.33854100	-0.29799500
C	-2.82290000	0.11257300	-0.12297400
H	-3.22558000	-0.02756000	-1.13404300
H	-3.44940300	-0.49254800	0.54453100
H	-2.95569600	1.16360500	0.15025200
F	1.41961200	-1.28939300	-0.08718900
F	2.02973200	0.95273800	-0.39133000
H	1.61632900	0.10891300	1.58179600

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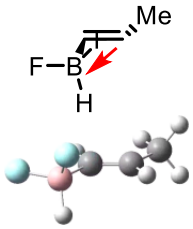

2.226

Frequency Calculation:
Thermal correction to Gibbs Free Energy = 0.056109 au
Single Point Calculation:
Electronic Energy = -342.643400713 au

-1 1

C	-0.34989000	0.42442400	0.00097200
H	-0.49096200	1.40466000	-0.47132100
B	1.15668500	-0.01030800	0.37962800
C	-1.46471000	-0.28489000	0.21671000
H	-1.38043000	-1.26471500	0.69358600
C	-2.87009100	0.12774200	-0.13572400
H	-3.33767100	-0.58432500	-0.82718500
H	-3.51374400	0.16357500	0.75235100
H	-2.88745000	1.11546300	-0.60572600
F	1.53214600	-1.25648300	-0.29002700
F	2.08919600	1.00959300	-0.10103600
H	1.34290500	-0.16476800	1.58797800

1 2 1.0 3 1.0 4 2.0
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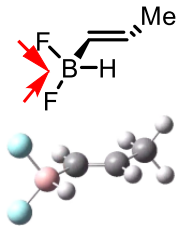

2.227

Frequency Calculation:
Thermal correction to Gibbs Free Energy = 0.054496 au
Single Point Calculation:
Electronic Energy = -342.645794965 au

-1 1

C	-0.35885700	0.01558600	-0.27994400
H	-0.45009500	0.03686100	-1.37426300
B	1.11747700	-0.00005000	0.34870900
C	-1.50625200	-0.00273300	0.40906500
H	-1.45310200	-0.02483500	1.49993800
C	-2.89977000	0.00227600	-0.16230000
H	-3.46367400	-0.88569000	0.14949500
H	-3.47341400	0.86979000	0.18697700
H	-2.88248600	0.02557400	-1.25569600
F	1.85414600	-1.17234000	-0.13518400
F	1.87902800	1.16056600	-0.12364300
H	1.12608700	-0.00625900	1.57852100

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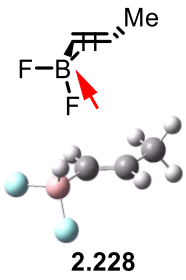

2.228

Frequency Calculation:
Thermal correction to Gibbs Free Energy = 0.056100 au
Single Point Calculation:
Electronic Energy = -342.643418806 au

-1 1

C	-0.34964200	-0.42705300	0.00524600
H	-0.49257400	-1.41444200	-0.45136200
B	1.15731500	0.00923300	0.37990500
C	-1.46330300	0.28700300	0.21099500
H	-1.37736700	1.27384800	0.67285300
C	-2.86949900	-0.12872300	-0.13444900
H	-3.51222300	-0.15173000	0.75473200
H	-3.33696400	0.57449700	-0.83494600
H	-2.88845100	-1.12270400	-0.59097300
F	2.09021600	-1.00825800	-0.10537200
F	1.52854800	1.25793800	-0.28673400
H	1.34679900	0.15988100	1.58837500

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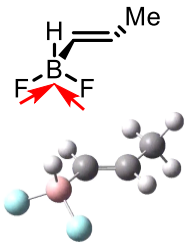

2.229

Frequency Calculation:
Thermal correction to Gibbs Free Energy = 0.054762 au
Single Point Calculation:
Electronic Energy = -342.644657835 au

-1 1

C	-0.34479200	-0.47621900	0.14153900
H	-0.53528400	-1.55459500	0.07463700
B	1.17599100	-0.02336300	0.40306500
C	-1.42328500	0.31393300	0.06936800
H	-1.28525400	1.39452100	0.14499600
C	-2.84964500	-0.13392700	-0.11788200
H	-3.48407700	0.18207800	0.72000200
H	-3.29321400	0.30226100	-1.02170100
H	-2.91713100	-1.22276600	-0.20023100
F	2.08462000	-0.97307100	-0.24794200
F	1.45644700	1.28137100	-0.18445300
H	1.47173500	0.01789100	1.60037500

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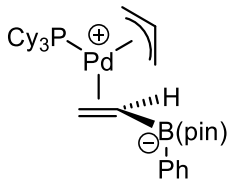
2.9.3.5 DFT Calculations: Vinylidenation of Organoboronic Esters: Scheme 2.38

All calculations were performed using the Gaussian09 package of programs.[72] Geometry optimizations were carried out with the density functional BP86 in conjunction with the def2-SVP[73] basis set in tetrahydrofuran as solvent using the IEFPCM model.[77] Very tight convergence criteria and an ultrafine integration grid were applied. Stationary points were assessed through vibrational analysis and Gibbs free energy corrections were performed under standard conditions (298.15 K, 1.0 atm). Intrinsic Reaction Coordinate (IRC)[75] calculations were performed followed by subsequent optimization of the end points with the previously mentioned optimization method. Gibbs free energies have been assessed through single point calculations with the density functional PBE0-D3BJ[82] applying the larger def2-TZVPP[73] basis set and the SMD[83] solvent model, followed by addition of thermal corrections obtained at the level of geometry optimization (denoted as PBE0-D3BJ /def2-TZVPP$_{THF(SMD)}$//BP86/def2-SVP)$_{THF(PCM)}$).



2.237

BP86 Optimization and Frequency Calculation:
Sum of electronic and thermal Free Energies= -2011.429186 a.u.
Thermal correction to Gibbs Free Energy= 0.762606 a.u.
Lowest frequency= 10.50 cm^{-1}
PB86-D3BJ Single Point Calculation:
Electronic Energy= -2012.066354 a.u.

0 1

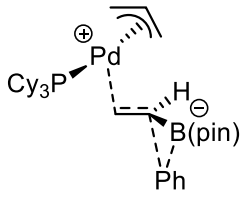
Pd	-0.17409600	-0.19458400	-1.22661400
P	-2.20033500	-0.06592900	0.04400200
C	0.85358400	-1.38468900	0.34876300
C	1.91998000	-1.12473700	-0.51759300
H	2.08596300	-1.89746500	-1.29368300
H	0.30476200	-2.34417400	0.32440700
H	0.79296800	-0.82078500	1.29493800
B	3.20096400	-0.15251300	-0.15041400

[82] (a) Grimme, S.; Ehrlich, S.; Goerigk, L. *J. Comp. Chem*. **2011**, 32, 1456. (b) Adamo, C.; Barone, V. *J. Chem. Phys.* **1999**, 110, 6158.
[83] Marenich, A. V.; Cramer, C. J.; Truhlar, D. G. *J. Phys. Chem. B.* **2009**, 113, 6378.

O	3.60523300	0.76157200	-1.25444400
O	2.97223300	0.73590600	1.02039700
C	4.34136900	-1.31327800	0.20826900
C	4.65671600	-1.65276600	1.54642900
C	5.02520800	-2.02774600	-0.80698400
C	5.61172000	-2.63862200	1.86182500
H	4.14490800	-1.10770300	2.35842600
C	5.98479600	-3.01452400	-0.50907000
H	4.81252200	-1.79369000	-1.86570500
C	6.28191900	-3.32622100	0.83168600
H	5.83897200	-2.87255600	2.91630400
H	6.50639100	-3.54415400	-1.32485400
H	7.03126300	-4.09879600	1.07166100
C	1.20050900	0.00112900	-3.01919400
H	1.76161400	0.88455900	-2.66878000
H	1.82417000	-0.84529100	-3.34330800
C	-1.04138000	0.99900700	-2.84839200
H	-0.66387800	2.00409400	-2.59335000
H	-2.11407200	0.94082900	-3.09029900
C	-0.15776900	0.03337500	-3.40341000
H	-0.58032700	-0.82219500	-3.96098500
C	-2.37233000	-0.56353000	1.86088500
C	-2.12373300	-2.06208000	2.15331200
C	-1.52773600	0.32370200	2.80597900
H	-3.44679100	-0.35870200	2.07712600
C	-2.39926700	-2.39165200	3.63378700
H	-1.07121800	-2.32055400	1.91592800
H	-2.75832300	-2.70145500	1.50644400
C	-1.78756700	-0.02164200	4.28534600
H	-0.44824900	0.18736100	2.57612800
H	-1.74471500	1.39762100	2.63553800
C	-1.56100700	-1.51352900	4.57630900
H	-2.19551100	-3.46856900	3.81743200
H	-3.48177500	-2.23657700	3.84890300
H	-1.13812500	0.60692400	4.93180900
H	-2.83835800	0.24724500	4.54167600
H	-1.80148000	-1.74224900	5.63698700
H	-0.48202600	-1.75522500	4.44006800
C	-2.94402400	1.68404100	-0.03761900
C	-4.15899100	1.98239700	0.87293300
C	-1.88410600	2.79931900	0.12759600
H	-3.29886700	1.72227900	-1.09433300
C	-4.75596500	3.37043000	0.55962300
H	-3.84074700	1.96029400	1.93881900

H	-4.94725600	1.21088500	0.76398600
C	-2.47541400	4.18491000	-0.19156100
H	-1.50426300	2.80054900	1.17300000
H	-1.00308400	2.59467700	-0.51263900
C	-3.70741200	4.48804800	0.67685600
H	-5.61369400	3.56632300	1.23873400
H	-5.17175300	3.36084800	-0.47419300
H	-1.69676400	4.96526300	-0.05143200
H	-2.76363200	4.21972900	-1.26771300
H	-4.15187700	5.46702200	0.39538600
H	-3.39019900	4.58248800	1.74088900
C	-3.44535000	-1.13639200	-0.91495300
C	-2.79887900	-2.43715800	-1.45342000
C	-4.79925300	-1.44772900	-0.23546700
H	-3.65364900	-0.48762400	-1.79895900
C	-3.74795700	-3.18738000	-2.40609400
H	-2.53307000	-3.10377800	-0.60286600
H	-1.84177900	-2.19594600	-1.96545900
C	-5.74321900	-2.20386500	-1.19360400
H	-4.62982700	-2.07164200	0.66955400
H	-5.29642300	-0.51980900	0.11108500
C	-5.10052100	-3.48826400	-1.74027200
H	-3.26440500	-4.12594200	-2.75295500
H	-3.91565000	-2.56647100	-3.31633100
H	-6.69518000	-2.43489800	-0.66868300
H	-6.00975700	-1.53455100	-2.04381500
H	-5.78523200	-3.98860700	-2.45856000
H	-4.94552800	-4.20699000	-0.90285700
C	3.24525200	2.09116500	0.66016400
C	4.12666400	1.95242500	-0.65989500
C	3.95763300	2.79163100	1.82997500
H	4.24680600	3.83196500	1.56849800
H	3.27861100	2.84081000	2.70748400
H	4.86702600	2.24130300	2.13962400
C	1.90608000	2.80841300	0.38805300
H	1.25737900	2.70563000	1.28220000
H	2.02840900	3.89143700	0.17514800
H	1.38105800	2.33372000	-0.46635200
C	3.97004800	3.11033000	-1.65869400
H	4.28328400	4.07727500	-1.21120700
H	4.60942000	2.92738000	-2.54803300
H	2.92459000	3.21097600	-2.01019100
C	5.63037200	1.77353300	-0.34488100
H	6.15581100	1.46958600	-1.27432200

H	6.09636800	2.71186000	0.02236100
H	5.79424500	0.97971800	0.40985100



2.238

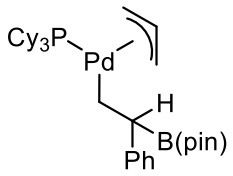
BP86 Optimization and Frequency Calculation:
Sum of electronic and thermal Free Energies = -2011.421128 a.u.
Thermal correction to Gibbs Free Energy= 0.760387 a.u.
Lowest frequency: -329.77 cm^{-1}
PB86-D3BJ Single Point Calculation:
Electronic Energy: -2012.045885 a.u.

0 1

Pd	-0.43759900	-0.66064900	1.08696200
P	-2.39669400	-0.05291400	-0.07687300
C	0.89064400	0.76112900	0.15292700
C	2.11278300	0.55549900	0.89027900
H	2.14429900	1.00971800	1.89806300
H	0.38032900	1.73456900	0.29271600
H	0.92977200	0.46276800	-0.91243100
B	3.43018700	-0.08407400	0.38511700
O	4.37329900	-0.68914900	1.29320700
O	3.52691400	-0.75009100	-0.89415300
C	3.72086700	1.70170400	0.17464500
C	3.57665100	2.28246700	-1.10385700
C	4.40289300	2.43146300	1.17245600
C	4.13747300	3.53863500	-1.39455200
H	3.03176200	1.73058600	-1.88795300
C	4.95766200	3.69499800	0.89363800
H	4.52058000	1.99400500	2.17886000
C	4.82837800	4.25089500	-0.39329100
H	4.03491200	3.96940600	-2.40475100
H	5.49349500	4.24942700	1.68226900
H	5.26084400	5.24001100	-0.61568000
C	0.99840800	-1.80310800	2.35717900
H	1.34724900	-2.53138000	1.60506600
H	1.79006400	-1.30316300	2.93311000
C	-1.38192700	-2.41874100	2.10445800

H	-1.18446400	-3.21002600	1.36052500
H	-2.40821500	-2.38207100	2.50287800
C	-0.31780300	-1.88988900	2.88042600
H	-0.55605900	-1.35188400	3.81670400
C	-2.53716800	1.43132700	-1.24009300
C	-2.31319200	2.78142400	-0.51799800
C	-1.62013900	1.32133500	-2.48114200
H	-3.59389600	1.40770400	-1.59532500
C	-2.49642100	3.97422400	-1.47647800
H	-1.28539500	2.80475900	-0.09338700
H	-3.00600800	2.88780800	0.34160700
C	-1.81048500	2.51908400	-3.43209200
H	-0.55997400	1.27836100	-2.15216600
H	-1.81520400	0.37787600	-3.03090200
C	-1.59011000	3.85902300	-2.71228800
H	-2.29807900	4.92268900	-0.93206600
H	-3.56096400	4.01835600	-1.80383600
H	-1.11920600	2.42074200	-4.29681000
H	-2.84260400	2.49230600	-3.85202900
H	-1.77067500	4.70791200	-3.40674100
H	-0.52489700	3.93419600	-2.39448700
C	-2.95137800	-1.55872500	-1.09356200
C	-4.09388600	-1.35422400	-2.11477500
C	-1.75565300	-2.28213500	-1.76093300
H	-3.33040100	-2.23334100	-0.28952500
C	-4.52145600	-2.69415200	-2.74908600
H	-3.75557700	-0.66633800	-2.92128000
H	-4.97361300	-0.87347200	-1.64078200
C	-2.18775800	-3.61924800	-2.39087100
H	-1.31821500	-1.63209400	-2.55109200
H	-0.94743100	-2.44206800	-1.01487800
C	-3.33575600	-3.42803200	-3.39600600
H	-5.32405000	-2.51294600	-3.49646900
H	-4.96924500	-3.34202400	-1.96062600
H	-1.31536600	-4.10287800	-2.88104800
H	-2.51752500	-4.31300000	-1.58313700
H	-3.66349900	-4.40849000	-3.80437900
H	-2.96707200	-2.83480300	-4.26446500
C	-3.79856200	0.17748300	1.18876100
C	-3.31252500	0.88588400	2.47711700
C	-5.11652500	0.81531300	0.69233300
H	-4.01729000	-0.88172100	1.46317100
C	-4.39255700	0.86192200	3.57466900
H	-3.05155000	1.94294800	2.24633600

H	-2.37496600	0.41072000	2.83716300
C	-6.19650900	0.79288300	1.79398900
H	-4.93150300	1.87071700	0.39295700
H	-5.49880300	0.29608100	-0.20975600
C	-5.71456800	1.47538200	3.08439100
H	-4.02401300	1.39714600	4.47642500
H	-4.57035700	-0.19288900	3.88804000
H	-7.12253100	1.27878300	1.41727600
H	-6.46698200	-0.26524800	2.01577900
H	-6.49351900	1.40479400	3.87413200
H	-5.56391700	2.56235800	2.88975000
C	4.50098600	-1.80566800	-0.79045400
C	5.34568800	-1.39398600	0.49679000
C	5.31182800	-1.86515400	-2.09292200
H	6.11886800	-2.62528800	-2.03213300
H	4.64635900	-2.14517400	-2.93603500
H	5.76781000	-0.88558400	-2.33344100
C	3.74528400	-3.13646400	-0.59920400
H	3.02373900	-3.26316100	-1.43250300
H	4.42612200	-4.01274300	-0.59726900
H	3.17424400	-3.13581200	0.35087200
C	5.87860500	-2.57554100	1.31866800
H	6.56286400	-3.20899700	0.71640200
H	6.44901900	-2.19670800	2.19229900
H	5.05637900	-3.20969900	1.70203600
C	6.51269900	-0.44327200	0.15794000
H	6.92557200	-0.03092000	1.10168200
H	7.33268900	-0.96605300	-0.37634200
H	6.17459400	0.40867200	-0.46393200



2.239

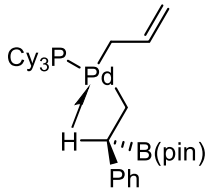
BP86 Optimization and Frequency Calculation:
Sum of electronic and thermal Free Energies= -2011.476634 a.u.
Thermal correction to Gibbs Free Energy= 0.762371 a.u.
Lowest frequency= 9.33 cm^{-1}
PB86-D3BJ Single Point Calculation:
Electronic Energy: -2012.108684 a.u.

0 1

P	2.07776100	0.06804600	0.09698600
C	-0.91348600	1.01251400	-0.75338400
C	-2.42805000	0.94154900	-1.09118100
H	-2.56146900	0.87768000	-2.19146300
H	-0.50697200	1.97692000	-1.13392100
H	-0.79689200	1.03262900	0.35170200
B	-3.16840400	-0.31470600	-0.46498300
O	-4.16831200	-1.00613800	-1.12347100
O	-2.94715300	-0.79224000	0.81641500
C	-3.16598400	2.20661600	-0.64026700
C	-3.22861000	2.57976600	0.72547200
C	-3.79315400	3.05669900	-1.58172100
C	-3.88607200	3.75425200	1.13036600
H	-2.75747600	1.93081000	1.48093700
C	-4.45409300	4.23238900	-1.18110100
H	-3.75923700	2.78798800	-2.65121900
C	-4.50263400	4.58858700	0.17860200
H	-3.92097700	4.01940700	2.19997900
H	-4.93205100	4.87567300	-1.93818300
H	-5.01811000	5.50947000	0.49551500
C	-0.96333300	-1.24631700	-2.97574700
H	-1.63605800	-1.92897200	-2.42760300
H	-1.47507800	-0.53588900	-3.64466700
C	1.11789800	-2.49726300	-2.46333600
H	0.62057300	-3.17044600	-1.74428800
H	2.16367700	-2.73077800	-2.70868200
C	0.36157500	-1.67457200	-3.31372400
H	0.87628800	-1.18379300	-4.16147500
Pd	0.38541600	-0.49191200	-1.46213800
C	1.92693900	-0.95071700	1.67996600
C	0.66685000	-0.59760300	2.50299100
C	1.94430100	-2.46363200	1.36186700
H	2.81950400	-0.71400200	2.30156900
C	0.58940600	-1.44373800	3.78973900
H	-0.24191300	-0.77668400	1.88582900
H	0.65727100	0.48038600	2.76929700
C	1.86889900	-3.31335600	2.64409600
H	1.07323500	-2.69333700	0.70726900
H	2.84912100	-2.73535200	0.77703200
C	0.63641000	-2.95110900	3.48900200
H	-0.33568200	-1.18800300	4.35068900
H	1.44197900	-1.17515500	4.45575700
H	1.85722400	-4.39335100	2.38037200
H	2.79169500	-3.14951100	3.24741600

H	0.62664200	-3.53648200	4.43412100
H	-0.28422000	-3.23919500	2.93188200
C	3.91241200	-0.07718100	-0.42684600
C	4.90842700	-0.49271800	0.68138200
C	4.13719200	-0.93024800	-1.69186000
H	4.15192800	0.97495800	-0.70634400
C	6.36624600	-0.39372700	0.18704100
H	4.70500100	-1.54263300	0.98908600
H	4.78200800	0.13085000	1.58983800
C	5.59274100	-0.83406600	-2.18671400
H	3.89549800	-1.99285900	-1.46450300
H	3.43264200	-0.61660000	-2.48990100
C	6.59530700	-1.22192000	-1.08748100
H	7.05749400	-0.71958000	0.99455500
H	6.60849500	0.67440800	-0.01922800
H	5.72947700	-1.47623200	-3.08388000
H	5.79613100	0.21087500	-2.51740300
H	7.63900600	-1.09725000	-1.44932800
H	6.47473600	-2.30361400	-0.84706900
C	1.99830300	1.86599900	0.68239800
C	2.91176700	2.26191900	1.86321300
C	2.19035900	2.85361800	-0.49299900
H	0.94206400	1.96836200	1.01912500
C	2.63823800	3.71277300	2.31080900
H	3.97797300	2.17882000	1.55393500
H	2.77689800	1.57335500	2.72403700
C	1.91751200	4.30469500	-0.05264200
H	3.23692400	2.78669100	-0.87033200
H	1.53238200	2.57330300	-1.34233200
C	2.79165600	4.70692800	1.14742400
H	3.31909400	3.98379600	3.14696600
H	1.60266100	3.77766800	2.71710500
H	2.08694600	4.99634500	-0.90630800
H	0.84235400	4.40374200	0.22168000
H	2.54151100	5.73696400	1.48247300
H	3.85965700	4.73308500	0.82886600
C	-4.03771800	-1.71454200	1.14645700
C	-4.56926800	-2.14191300	-0.29006900
C	-5.06641400	-0.91296400	1.96064300
H	-5.48450300	-0.07079400	1.37354300
H	-5.90393700	-1.55296400	2.30369200
H	-4.56795100	-0.48940600	2.85587900
C	-3.47829400	-2.86103200	1.99111100
H	-2.63123000	-3.36788400	1.49144700

H	-3.11835600	-2.46926700	2.96395300
H	-4.26533100	-3.61443500	2.19997400
C	-6.08793200	-2.30624300	-0.39280900
H	-6.36401200	-2.58814000	-1.42923700
H	-6.44474600	-3.10936400	0.28422700
H	-6.62144600	-1.37022000	-0.14109600
C	-3.86442300	-3.38549900	-0.85467700
H	-4.17907000	-4.30854900	-0.32764200
H	-4.12707900	-3.49422800	-1.92625300
H	-2.76192700	-3.29905100	-0.77861400



2.240

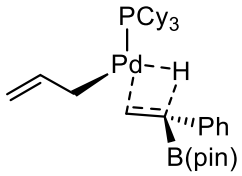
BP86 Optimization and Frequency Calculation:
Sum of electronic and thermal Free Energies= -2011.462496 a.u.
Thermal correction to Gibbs Free Energy= 0.756593 a.u.
Lowest frequency= 6.32 cm^{-1}
PB86-D3BJ Single Point Calculation:
Electronic Energy= -2012.08376 a.u.

0 1

P	-2.00307200	-0.06951300	0.30498500
C	1.70895900	0.43005400	-2.02248600
C	2.17933100	0.72811300	-0.59448900
H	1.32024700	0.44177100	0.13765900
H	1.77925200	1.29127100	-2.71605500
H	2.12850400	-0.48632900	-2.48348700
B	3.31360200	-0.31653500	-0.19664900
O	4.66025700	-0.03972800	-0.21597800
O	3.02045800	-1.61758800	0.15220200
C	2.52701300	2.17675200	-0.29854200
C	3.42754900	2.88589100	-1.12783600
C	1.98991500	2.84852100	0.82294200
C	3.77819000	4.21685900	-0.84355100
H	3.86407200	2.38328600	-2.00557900
C	2.33935300	4.17985900	1.11144900
H	1.27942200	2.31817000	1.47887500
C	3.23615100	4.87161500	0.27790700

H	4.48262300	4.74716200	-1.50482500
H	1.90229800	4.68071100	1.99044900
H	3.50888400	5.91592900	0.49870200
C	-1.04937800	-0.12593300	-3.09404700
H	-0.93417300	0.89702700	-3.51475100
H	-2.12314500	-0.34875100	-2.94388200
Pd	-0.15526900	0.09587800	-1.20619600
C	-3.18298600	1.40315600	0.19479200
C	-2.46738600	2.72637500	0.55222900
C	-3.81283200	1.50888400	-1.21356200
H	-3.99844700	1.23505200	0.93450800
C	-3.41242700	3.93810600	0.43103200
H	-1.59762500	2.85856000	-0.13319000
H	-2.05227300	2.68641900	1.58129100
C	-4.77066400	2.71019600	-1.32209200
H	-2.99475600	1.62294000	-1.95869800
H	-4.34735000	0.57191600	-1.47913300
C	-4.06288400	4.02578600	-0.95914800
H	-2.85427400	4.87175300	0.66037500
H	-4.21073600	3.85415000	1.20432600
H	-5.19077600	2.76377700	-2.34992400
H	-5.63668700	2.55488900	-0.63776800
H	-4.77615100	4.87749300	-1.00056900
H	-3.27598600	4.23831200	-1.71902000
C	-3.10263300	-1.62448900	0.31914100
C	-4.56859400	-1.44198300	0.77473200
C	-3.04616700	-2.39796000	-1.01681600
H	-2.59280400	-2.26220700	1.07966700
C	-5.29310200	-2.79987700	0.87868400
H	-5.10825800	-0.80381900	0.03989100
H	-4.62283500	-0.91277700	1.74802600
C	-3.77028900	-3.75298300	-0.91367300
H	-3.52588900	-1.78839800	-1.81639700
H	-1.99047400	-2.53900700	-1.33039800
C	-5.22421200	-3.58735100	-0.44035700
H	-6.35051800	-2.63841600	1.18204700
H	-4.82353700	-3.40118200	1.69121500
H	-3.73621000	-4.27557600	-1.89430800
H	-3.22148500	-4.40429700	-0.19440900
H	-5.71266200	-4.57939700	-0.32551300
H	-5.80340000	-3.04257900	-1.22156900
C	-1.36179700	0.00790200	2.09004600
C	-2.41614100	0.08802600	3.21502600
C	-0.35315500	-1.12829000	2.37806000

H	-0.78539100	0.96305200	2.09371000
C	-1.75094900	0.26648600	4.59517800
H	-3.01410600	-0.85082200	3.22655800
H	-3.13189800	0.91760300	3.03248500
C	0.30871100	-0.95920300	3.75927500
H	-0.88081200	-2.10957700	2.34923300
H	0.42279400	-1.17224100	1.58351300
C	-0.73455800	-0.85078000	4.88379600
H	-2.53007500	0.29947200	5.38752900
H	-1.23332500	1.25299200	4.62480700
H	1.00144500	-1.80710200	3.95067700
H	0.93686600	-0.03862100	3.74986800
H	-0.23534400	-0.67845900	5.86198300
H	-1.27523200	-1.82118200	4.97567100
C	4.28680500	-2.36479800	0.15731600
C	5.35869700	-1.20533800	0.34504700
C	-0.88975500	-2.34660800	-4.31188900
H	-0.31589600	-3.03976100	-4.94901000
H	-1.89223400	-2.67741000	-3.98832800
C	-0.38424700	-1.14233800	-3.93904100
H	0.62518500	-0.87817000	-4.30964200
C	4.38880100	-3.07169500	-1.20289400
H	5.29111400	-3.71268700	-1.26177000
H	3.49814000	-3.71636600	-1.34414500
H	4.42068200	-2.34449700	-2.03924800
C	4.24225500	-3.39229900	1.28926500
H	3.45545100	-4.14514000	1.08051100
H	5.21076800	-3.92690700	1.37089200
H	4.01628700	-2.92250300	2.26507400
C	5.64891900	-0.87649300	1.81753500
H	6.24314200	-1.67590700	2.30364500
H	6.23001800	0.06614100	1.86918900
H	4.71368900	-0.73352700	2.39535200
C	6.66602600	-1.40377500	-0.42371200
H	7.33769300	-0.53902700	-0.24878800
H	7.19041200	-2.31723700	-0.07600200
H	6.49538600	-1.48878900	-1.51351200



2.241

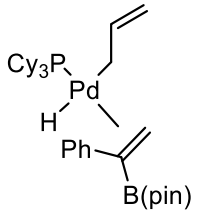
BP86 Optimization and Frequency Calculation:
Sum of electronic and thermal Free Energies= -2011.446985
Thermal correction to Gibbs Free Energy= 0.756808
Lowest frequency= -448.75 cm^{-1}
PB86-D3BJ Single Point Calculation:
Electronic Energy= -2012.069914

0 1

P	-1.78410600	-0.13134400	0.33212000
C	1.69374900	0.72000200	-2.36219300
C	2.14737200	0.88291700	-1.00611300
H	0.95248600	0.24694900	0.10354100
H	1.45278700	1.60734200	-2.97133000
H	2.01776700	-0.16993100	-2.92486300
B	3.11460400	-0.24506700	-0.45998500
O	4.18919700	0.01588400	0.36088700
O	3.01617600	-1.57079100	-0.83151000
C	2.31037700	2.26991300	-0.42686800
C	2.63813600	3.36707400	-1.25775100
C	2.22050300	2.50290800	0.96695300
C	2.85438100	4.64877100	-0.71859900
H	2.74541400	3.21412400	-2.34284200
C	2.43832200	3.77860500	1.50844700
H	1.96209600	1.66428100	1.63350500
C	2.75432500	4.86239100	0.66628000
H	3.10914800	5.48433800	-1.39040600
H	2.35719400	3.93039700	2.59689400
H	2.92229200	5.86561100	1.08935500
C	-1.19087600	0.15322800	-3.04160800
H	-1.15665400	1.22274900	-3.34621000
H	-2.23869000	-0.12177300	-2.81912700
Pd	-0.02784800	0.20674600	-1.19427700
C	-2.94966600	1.35485800	0.39412900
C	-2.20636900	2.62878000	0.85997800
C	-3.65100400	1.61740600	-0.95767200
H	-3.73022500	1.10891600	1.14962200
C	-3.14899800	3.84651500	0.92708600
H	-1.37259500	2.83442300	0.14922300
H	-1.73675000	2.47386800	1.85384400
C	-4.60981100	2.82001800	-0.87195400
H	-2.87700100	1.82115500	-1.72823700
H	-4.20146500	0.71584300	-1.30064700
C	-3.87691000	4.08820000	-0.40511300
H	-2.57183500	4.74817400	1.22631700

H	-3.90262200	3.67790300	1.73080900
H	-5.08855700	2.98791600	-1.86101900
H	-5.43522300	2.58598300	-0.16036000
H	-4.58749800	4.93782400	-0.31008700
H	-3.13371600	4.38584700	-1.18023100
C	-2.87611600	-1.68582400	0.20148900
C	-4.34417700	-1.54393200	0.66843100
C	-2.81755400	-2.36681900	-1.18168600
H	-2.36711100	-2.37470800	0.91603000
C	-5.05169500	-2.91486500	0.68833800
H	-4.88983400	-0.86692900	-0.02568700
H	-4.40580200	-1.07852700	1.67323400
C	-3.51682800	-3.73821600	-1.15782400
H	-3.31908000	-1.71763700	-1.93346000
H	-1.76407500	-2.46514600	-1.51731700
C	-4.97229500	-3.62283700	-0.67432300
H	-6.11109100	-2.78384400	0.99912700
H	-4.57581600	-3.55711800	1.46499300
H	-3.47689000	-4.19949300	-2.16840800
H	-2.95602900	-4.42291300	-0.48001500
H	-5.44597100	-4.62690100	-0.61666000
H	-5.56047700	-3.04231400	-1.42219600
C	-1.14192500	-0.24552600	2.11574000
C	-2.20166200	-0.23795000	3.23912900
C	-0.17197600	-1.43275000	2.30393900
H	-0.53597900	0.68584700	2.20448300
C	-1.53824500	-0.20055800	4.63128200
H	-2.82523800	-1.15714600	3.16748600
H	-2.89311900	0.62437000	3.13223800
C	0.48791800	-1.40755500	3.69611100
H	-0.72587000	-2.39264600	2.18689100
H	0.60216600	-1.41685700	1.50606300
C	-0.55709500	-1.36803400	4.82367900
H	-2.32073900	-0.21412500	5.42072600
H	-0.99259400	0.76401300	4.74833600
H	1.15232800	-2.29088300	3.81358100
H	1.14441900	-0.51022700	3.77062900
H	-0.05753400	-1.29701600	5.81412500
H	-1.12614000	-2.32639900	4.82857500
C	4.25951600	-2.23515900	-0.42446700
C	4.80214900	-1.26979500	0.71826700
C	-1.08635500	-1.90657600	-4.54234900
H	-0.55360900	-2.47801900	-5.32066200
H	-2.01878800	-2.34841900	-4.14947300

C	-0.60996900	-0.71756100	-4.08580200
H	0.32805500	-0.35156500	-4.54919600
C	5.16479000	-2.27755100	-1.66584300
H	6.10857900	-2.82280200	-1.46483400
H	4.63105600	-2.80249900	-2.48352100
H	5.41754600	-1.25839400	-2.02176600
C	3.92690800	-3.65523100	0.03732100
H	3.53877600	-4.24532100	-0.81738900
H	4.83486600	-4.16585200	0.41864200
H	3.15863500	-3.66133800	0.83329600
C	4.28788400	-1.63096700	2.11943200
H	4.75246600	-2.56394400	2.49619400
H	4.54289200	-0.81119400	2.82081400
H	3.18706800	-1.75884600	2.12855300
C	6.32148500	-1.09010300	0.74211700
H	6.60218800	-0.38707800	1.55234000
H	6.82725400	-2.05714000	0.94042600
H	6.70402700	-0.68114500	-0.21201300



2.242

BP86 Optimization and Frequency Calculation:
Sum of electronic and thermal Free Energies= -2011.448913 a.u.
Thermal correction to Gibbs Free Energy= 0.757938 a.u.
Lowest frequency= 7.85 cm^{-1}
PB86-D3BJ Single Point Calculation:
Electronic Energy= -2012.074021 a.u.

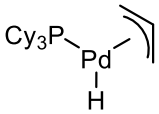
0 1

P	-1.74990600	-0.18219400	0.29071800
C	1.79926200	0.93705800	-2.30970100
C	2.28110200	1.00343400	-0.98207500
H	0.78431500	-0.08189000	0.37791600
H	1.48824900	1.84532800	-2.84981800
H	2.06639200	0.07047200	-2.93378000
B	3.12883800	-0.22207600	-0.46895000
O	4.03721700	-0.14661400	0.56919700
O	3.14411300	-1.45054600	-1.11016700

C	2.37153200	2.31977700	-0.25869000
C	2.54930000	3.53085400	-0.97206600
C	2.34778200	2.38951900	1.15724000
C	2.68346300	4.75997300	-0.30172900
H	2.60639900	3.51072100	-2.07168500
C	2.48465900	3.61393500	1.82832500
H	2.20924300	1.46127900	1.73170700
C	2.65020200	4.80951400	1.10236000
H	2.82355800	5.68456600	-0.88490600
H	2.45871100	3.63704100	2.92990000
H	2.75576600	5.77139600	1.62910100
C	-1.01880200	0.62468100	-2.90819100
H	-0.91806600	1.72586300	-3.02292500
H	-2.08120200	0.38712200	-2.71691800
Pd	0.13003100	0.27866100	-1.03901400
C	-2.74562300	1.39772600	0.58434500
C	-1.91549100	2.45436500	1.35068000
C	-3.31361200	2.01542500	-0.71281200
H	-3.60290900	1.09530100	1.22762400
C	-2.74159500	3.72409100	1.63700200
H	-1.01953700	2.71518000	0.74170600
H	-1.53254200	2.04322600	2.30782800
C	-4.16015400	3.26721400	-0.41343600
H	-2.46808100	2.29759800	-1.37549600
H	-3.91766900	1.27374700	-1.27646600
C	-3.34798900	4.32091100	0.35670500
H	-2.10344600	4.47355900	2.15317100
H	-3.56193400	3.47050800	2.34766600
H	-4.54748200	3.69191900	-1.36481000
H	-5.05357700	2.97592600	0.18597900
H	-3.98185100	5.20063500	0.60172800
H	-2.52741000	4.69745300	-0.29628000
C	-2.98661900	-1.55467800	-0.18273600
C	-4.47103600	-1.28752500	0.16073800
C	-2.85573300	-2.06581300	-1.63131900
H	-2.64337500	-2.38655100	0.47554100
C	-5.32113500	-2.55585500	-0.05980000
H	-4.86157600	-0.47253400	-0.48788100
H	-4.58791300	-0.94016800	1.20752600
C	-3.69476500	-3.33921700	-1.84518700
H	-3.20932500	-1.27928900	-2.33303000
H	-1.78988100	-2.24644200	-1.88359900
C	-5.17260400	-3.10762500	-1.48735900
H	-6.38708900	-2.33340200	0.16405700

H	-5.00466000	-3.33515900	0.67135500
H	-3.59771100	-3.68120700	-2.89834300
H	-3.28469400	-4.15967100	-1.21168300
H	-5.75403900	-4.04827400	-1.60046900
H	-5.61237400	-2.37981000	-2.20775900
C	-1.27446500	-0.71202300	2.05180600
C	-2.43095400	-0.79828700	3.07198500
C	-0.45128300	-2.01846500	2.06265100
H	-0.58819700	0.10684400	2.36736000
C	-1.90363300	-1.11666400	4.48645700
H	-3.13788200	-1.60251600	2.76791900
H	-3.01475300	0.14577100	3.09773100
C	0.07098300	-2.34414200	3.47518200
H	-1.08172200	-2.86634400	1.70867100
H	0.39443900	-1.93072000	1.34630400
C	-1.06915300	-2.40711500	4.50501300
H	-2.75664200	-1.19226300	5.19512000
H	-1.27689500	-0.26617600	4.84063100
H	0.63233800	-3.30324000	3.45572500
H	0.80108200	-1.56040600	3.78164300
H	-0.66358800	-2.59277000	5.52313000
H	-1.72951400	-3.27335500	4.26866600
C	4.30612200	-2.19250400	-0.61857200
C	4.59541700	-1.48571500	0.77624700
C	-1.07583900	-1.13890300	-4.75454300
H	-0.59148200	-1.58848800	-5.63738400
H	-2.02919200	-1.58858800	-4.42792200
C	-0.51611400	-0.08385400	-4.10456000
H	0.43498800	0.29714800	-4.52624400
C	5.43142000	-1.98839500	-1.64655000
H	6.33609600	-2.57345200	-1.38584500
H	5.07673600	-2.32684600	-2.64100200
H	5.71679200	-0.92034300	-1.73109700
C	3.93939000	-3.67525700	-0.52468500
H	3.73739500	-4.07594000	-1.53877700
H	4.77550900	-4.25967600	-0.08865100
H	3.03580900	-3.83845400	0.09248100
C	3.82722700	-2.11413000	1.94840100
H	4.22986700	-3.11211600	2.21357400
H	3.92171900	-1.45751500	2.83669300
H	2.74922300	-2.22090000	1.71473300
C	6.07722100	-1.34284100	1.13118900
H	6.18043900	-0.82512100	2.10635600
H	6.55656300	-2.33902100	1.22262700

H	6.62801200	-0.75462400	0.37309500



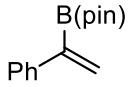
2.243

BP86 Optimization and Frequency Calculation:
Sum of electronic and thermal Free Energies= -1291.949553 a.u.
Thermal correction to Gibbs Free Energy= 0.485799 a.u.
Lowest frequency= 20.32 cm^{-1}
PB86-D3BJ Single Point Calculation:
Electronic Energy= -1292.292616 a.u.

0 1

P	0.22329200	-0.09158800	-0.01429300
H	-0.88834400	-2.27483500	1.28085700
C	-2.99169000	0.93112800	1.76144300
H	-3.25188500	1.72948600	1.04938000
H	-2.50092200	1.25445900	2.69566700
Pd	-1.57586600	-0.83314400	1.26447200
C	-0.26391300	-0.05060600	-1.83780400
C	-0.56215000	-1.46462800	-2.38813000
C	-1.48010900	0.87751100	-2.06394800
H	0.60554000	0.36399500	-2.39666400
C	-0.98084000	-1.41749800	-3.87059900
H	-1.37859600	-1.92066900	-1.78233200
H	0.32092200	-2.12763700	-2.27313600
C	-1.89435200	0.92549200	-3.54674200
H	-2.32906000	0.50018000	-1.44957900
H	-1.26639600	1.90364800	-1.69572000
C	-2.17830100	-0.48077000	-4.09946200
H	-1.21536000	-2.44458400	-4.22524700
H	-0.11786400	-1.06588200	-4.48213600
H	-2.78540600	1.57940800	-3.66602100
H	-1.07864600	1.39788200	-4.14147600
H	-2.43074800	-0.43044400	-5.18088000
H	-3.07462100	-0.90067400	-3.58740400
C	1.03202900	1.59284500	0.36084600
C	1.60754300	2.35703400	-0.85468000
C	0.13283500	2.51995300	1.20716100
H	1.89183300	1.29936000	1.00807600
C	2.36224100	3.62648700	-0.41050000
H	0.77694300	2.65439100	-1.53284800
H	2.28274300	1.70960500	-1.45079100

C	0.88319600	3.79282200	1.64218500
H	-0.76699400	2.80301500	0.61555200
H	-0.24521200	1.97003400	2.09368200
C	1.47403100	4.54851100	0.44040200
H	2.74363300	4.16648500	-1.30430400
H	3.25871400	3.32936200	0.18127300
H	0.20146300	4.45270100	2.22156800
H	1.70718500	3.50886000	2.33718000
H	2.05060300	5.43503200	0.78294600
H	0.64325800	4.94053300	-0.19091300
C	1.68276800	-1.28910100	0.06316800
C	2.86862100	-1.00892300	-0.88441500
C	2.17730900	-1.47471100	1.51554300
H	1.20808200	-2.25048000	-0.24078800
C	3.92944600	-2.12526700	-0.79261300
H	3.34533300	-0.04163800	-0.60784400
H	2.52399600	-0.90385400	-1.93539000
C	3.24302900	-2.58343600	1.60836600
H	2.61701000	-0.52002600	1.88715900
H	1.31371700	-1.70803000	2.17482000
C	4.41916400	-2.32634800	0.65117900
H	4.78281300	-1.88961700	-1.46501100
H	3.48856800	-3.07717500	-1.16841300
H	3.60494700	-2.67171600	2.65574500
H	2.77070900	-3.56096700	1.35741200
H	5.14981600	-3.16275600	0.69957000
H	4.96731200	-1.41348400	0.98123300
C	-3.27140200	-1.43401600	2.49185800
H	-3.77399000	-2.40075200	2.33055300
H	-2.87658700	-1.27373400	3.51188300
C	-3.65530700	-0.31164800	1.69332600
H	-4.33895100	-0.49000100	0.84154700

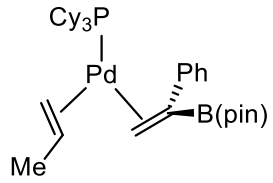


2.234

BP86 Optimization and Frequency Calculation:
Sum of electronic and thermal Free Energies= -719.54371 a.u.
Thermal correction to Gibbs Free Energy= 0.250332 a.u.
Lowest frequency= 15.86 cm^{-1}
PB86-D3BJ Single Point Calculation:
Electronic Energy= -719.7869279 a.u.

0 1

C	-1.01977000	2.57674800	-0.52467200
C	-0.97936700	1.23981000	-0.26946000
H	-1.96777900	3.12746200	-0.65759300
H	-0.08952800	3.15955100	-0.62310600
B	0.44343800	0.57464000	-0.13763600
O	0.66925200	-0.70753200	0.31803800
O	1.60597600	1.25120600	-0.45103200
C	-2.23160500	0.44502300	-0.10550200
C	-3.39429300	1.01438000	0.47460400
C	-2.30332000	-0.90240700	-0.54127200
C	-4.58275800	0.27664200	0.59507800
H	-3.35606000	2.04700500	0.85708800
C	-3.49393700	-1.63935100	-0.42681500
H	-1.41014400	-1.37212000	-0.97910400
C	-4.64030400	-1.05424400	0.14063100
H	-5.46902200	0.74141100	1.05665800
H	-3.52520500	-2.68204000	-0.78223500
H	-5.57152600	-1.63494900	0.23762600
C	2.73115200	0.45019600	0.03970100
C	2.09471100	-1.00347200	0.13066700
C	3.12433400	1.02765900	1.40885000
H	4.01854600	0.52123500	1.82401900
H	3.36089000	2.10450800	1.29227700
H	2.29753100	0.93667400	2.14188000
C	3.89223300	0.58552400	-0.94756400
H	4.25841000	1.63219500	-0.95376400
H	4.73786000	-0.06851300	-0.65176900
H	3.58851200	0.32445700	-1.97895400
C	2.21278800	-1.80152700	-1.17731100
H	3.25658400	-2.12411600	-1.36411600
H	1.58020200	-2.70923200	-1.10623900
H	1.86728600	-1.20953900	-2.04869500
C	2.57565000	-1.84731900	1.31274500
H	2.06368000	-2.83083700	1.30339800
H	3.66731700	-2.03166300	1.24428700
H	2.36034700	-1.36004700	2.28238800



2.244

BP86 Optimization and Frequency Calculation:
Sum of electronic and thermal Free Energies= -2011.502052 a.u.
Thermal correction to Gibbs Free Energy= 0.765673 a.u.
Lowest frequency= 11.72 cm^{-1}
PB86-D3BJ Single Point Calculation:
Electronic Energy= -2012.137166 a.u.

0 1

C	-1.50639500	0.77985700	-2.34131700
C	-0.96372800	0.64431500	1.55237800
C	-2.12035000	1.01668300	0.79647500
C	-0.11544400	-1.12823400	-3.33785900
H	-2.41312300	0.15015300	-2.34911800
H	-0.35567000	1.40217200	2.07272800
H	-0.30869200	-1.11258400	-4.43532500
H	-1.68733300	1.86876600	-2.33028200
H	-0.94466000	-0.35200700	2.02416500
H	-0.82846600	-1.84708500	-2.88441400
C	-4.01217000	-2.28378300	0.53156700
C	-5.06320300	-1.26637700	-0.08582400
C	-3.29558300	-3.13068300	-0.53282200
H	-2.45207200	-3.67160500	-0.05858200
H	-3.97574600	-3.87989700	-0.98555700
H	-2.88148100	-2.49760400	-1.34295900
C	-4.56553700	-3.18878300	1.63649400
H	-5.38223300	-3.83195900	1.24916700
H	-3.76102700	-3.85221800	2.01397200
H	-4.95320300	-2.60410900	2.49226700
C	-6.15600800	-0.84281200	0.91047400
H	-6.71893900	0.01285000	0.48613600
H	-6.87425500	-1.66417900	1.10679900
H	-5.71960000	-0.51870900	1.87663800
C	-5.69881800	-1.71038300	-1.40558800
H	-6.28504700	-2.64202100	-1.26672900
H	-6.39252900	-0.92535900	-1.76969900
H	-4.94007100	-1.88598000	-2.19156800
B	-3.12551600	-0.14718300	0.49647200

O	-3.02139900	-1.38848700	1.12004700
O	-4.23874200	-0.08548400	-0.33740600
H	0.90877500	-1.53477300	-3.20840100
Pd	-0.40096000	0.42505100	-0.50233500
P	1.86382500	-0.23608100	-0.05934600
C	3.10327500	0.56186100	-1.25070100
C	2.74955200	2.04586300	-1.52365900
C	4.61806100	0.44581300	-0.95762700
H	2.89257700	-0.00162600	-2.19225500
C	3.56948500	2.61108400	-2.69820800
H	2.96027200	2.64624500	-0.61097400
H	1.66044900	2.14921600	-1.71222800
C	5.45030700	1.00034100	-2.13273200
H	4.85731900	1.03284900	-0.04315700
H	4.91489500	-0.59978500	-0.74503200
C	5.08129100	2.45677600	-2.46006700
H	3.30828300	3.67909200	-2.86240800
H	3.28601400	2.07281000	-3.63236700
H	6.53369000	0.91768200	-1.89680900
H	5.27775500	0.36384300	-3.03143400
H	5.65384200	2.81272700	-3.34400100
H	5.38445800	3.10918100	-1.60873800
C	1.95538200	-2.10632700	-0.36428800
C	3.31004300	-2.78065700	-0.68144200
C	1.18787000	-2.87716000	0.73724100
H	1.33929900	-2.18365400	-1.28841500
C	3.11251700	-4.26697400	-1.04563200
H	3.99484200	-2.70905300	0.19152300
H	3.81378600	-2.26376600	-1.52426300
C	1.01252000	-4.36309900	0.37017800
H	1.74134800	-2.80990300	1.70087100
H	0.19558900	-2.40676200	0.90737600
C	2.35899100	-5.03396300	0.05267600
H	4.09979900	-4.73774600	-1.24466800
H	2.53757200	-4.33330900	-1.99821900
H	0.49541300	-4.89547700	1.19783900
H	0.34477600	-4.44208400	-0.51837300
H	2.20423700	-6.09240400	-0.24987200
H	2.98352500	-5.06148300	0.97572100
C	2.45088500	0.06033000	1.71758100
C	3.70372500	-0.68426400	2.23492200
C	2.56461600	1.57159400	2.03086300
H	1.57852700	-0.32556500	2.29590800
C	3.91199800	-0.43155700	3.74328300

H	4.60236500	-0.34286300	1.67877700
H	3.61724000	-1.77501600	2.05527800
C	2.76564700	1.82204700	3.53733100
H	3.43421600	1.99450000	1.47986800
H	1.66836900	2.11515600	1.66353100
C	3.99388000	1.06774500	4.07331100
H	4.82913500	-0.95718300	4.08772100
H	3.06328800	-0.88436900	4.30617600
H	2.86241200	2.91266700	3.72963700
H	1.85620100	1.48573100	4.08664800
H	4.09527300	1.21825300	5.17005700
H	4.91472400	1.49544200	3.61318400
C	-2.46946500	2.46041400	0.57714200
C	-1.78374700	3.50927400	1.24922400
C	-3.52344300	2.84630100	-0.29677900
C	-2.11592600	4.85893900	1.04843900
H	-0.97516900	3.26811900	1.95583100
C	-3.85740900	4.19626300	-0.49649100
H	-4.09068200	2.06268900	-0.81807300
C	-3.15567900	5.21699900	0.17047500
H	-1.55802400	5.63982300	1.59132200
H	-4.68106000	4.45254500	-1.18350800
H	-3.41851900	6.27547200	0.01395200
C	-0.26749400	0.26174800	-2.75392400
H	0.50495500	0.98556000	-3.07214400

Chapter Three

Pd-Catalyzed Conjunctive Coupling Between Grignard Reagent-Derived Boron-Ate Complexes and C(sp^2) Halides or Triflates: NaOTf as a Grignard Reagent Activator and Halide Scavenger

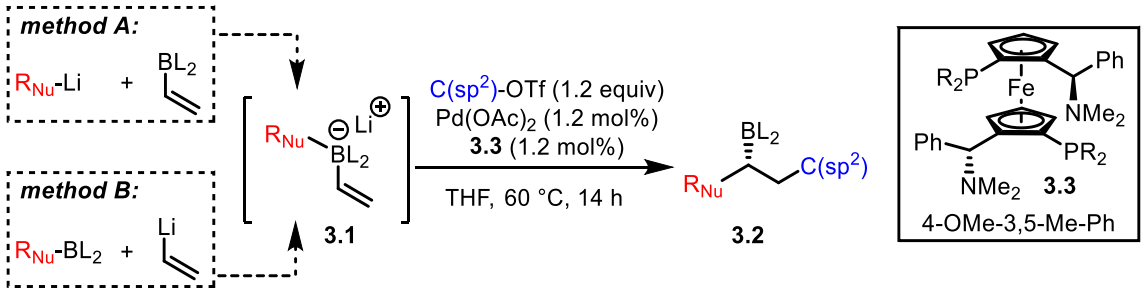
3.1 Introduction

Enantioenriched organoboron compounds are important intermediates in organic synthesis that can be converted to a broad array of chiral structures by mild stereospecific reactions.[1] For this reason, intense efforts have been directed toward the construction of these compounds in an enantioselective fashion. While ground breaking work by Brown established the utility of chiral organoboranes[2], organoboronic esters have become the preferred class of boron reagents in contemporary enantioselective synthesis because of their near ideal balance of stability and reactivity. With these reagents, powerful stoichiometric enantioselective homologation reactions have enabled a broad array of C−C and C−heteroatom bond forming reactions directly from the organoboronic ester starting materials.[3] Similarly, many catalytic processes have been developed that provide access to

[1] For reviews, see: (a) Brown, H. S.; Singaram, B. *Acc. Chem. Res*. **1988**, 21, 287. (b) Organoboranes for Synthesis; Ramachandran, P. V., Brown, H. C., Eds.; American Chemical Society: Washington, D.C., **2001**; ACS Symposium Series 783. (c) Stereodirected Synthesis with Organoboranes; Matteson, D. S., Ed.; Springer: New York, **1995**. (d) Leonori, D.; Aggarwal, V. K. *Acc. Chem. Res*. **2014**, 47, 3174.
[2]) (a) Brown, H. C.; Ramachandran, P. V. *Pure Appl. Chem*. **1991**, 63, 307. (b) Brown, H. C.; Ramachandran, P. V. *Acc. Chem. Res*. **1992**, 25, 16.
[3] (a) Negishi, E.; Idacavage, M. *J. Org. React*. **1985**, 33, 1. (b) Aggarwal, V. K.; Fang, G. Y.; Ginesta, X.; Howells, D. M.; Zaja, M. *Pure Appl. Chem.* **2006**, 78, 215. (c) Leonori, D.; Aggarwal, V. K. *Top. Organomet. Chem*. **2015**, 49, 271.

chiral organoboronic esters from simple building blocks.[4] In this vein, the conjunctive coupling reaction discussed in chapter two of this dissertation (Scheme **3.1**) is an exceptionally versatile method to produce enantiomerically enriched alkylboronic esters in an efficient fashion.[5] Because the alkenylboron-ate complex **3.1** is generated *in situ* from the reaction of appropriate organoboronic esters and organolithium compounds, conjunctive coupling represents a three-component reaction that merges simple starting

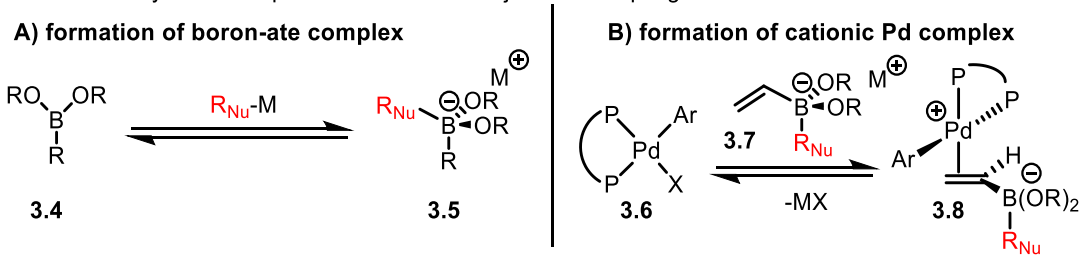
Scheme 3.1. Diphosphine–Pd-catalyzed conjunctive coupling reaction



materials to generate chiral organoboronic ester products. Initial efforts to enhance the operational utility of conjunctive coupling by reengineering it to employ readily available and functional-group-tolerant Grignard reagents in place of organolithium compounds, and to extend the substrate scope from C(sp^2) triflate electrophiles to common and inexpensive C(sp^2) halide electrophiles were unsuccessful. Because the mechanistic hypothesis for the conjunctive reaction, as proposed and explored in chapter two of this dissertation, depends on the successful generation of two key intermediates, (1) anionic boron-ate complex **3.5**,

[4] For reviews, see: (a) Hall, D. G.; Lee, J. C. H.; Ding, J. *Pure Appl. Chem*. **2012**, 84, 2263. (b) Neeve, E. C.; Geier, S. J.; Mkhalid, I. A. I.; Westcott, S. A.; Marder, T. B. *Chem. Rev*. **2016**, 116, 9091. (c) Ferris, G. E.; Mlynarski, S. N.; Morken, J. P. Diborane Compounds (Update 2012). In Science of Synthesis; Bode, J. W., Ed.; Thieme, **2012**; Vol. 3, p 227.
[5] Zhang, L.; Lovinger, G. J.; Edelstein, E. K.; Szymaniak, A. A.; Chierchia, M. P.; Morken, J. P. *Science* **2016**, 351, 70.

Scheme 3.2. Key reactive species involved in conjunctive coupling



and (2) cationic palladium complex **3.8** (Scheme 3.2.A/B), we suspected that a more in-depth understanding of the factors determining the formation and reactivity of these species might enable us to overcome the initially encountered limitations of the conjunctive coupling reaction manifold.

This chapter explores the mechanistic challenges associated with extending the conjunctive coupling reaction in the directions mentioned above and presents an effective solution that enables broadly useful reactions with aryl halides, and allows the use of Grignard reagent-derived ate complexes.

3.2 Background

3.2.1 Enhancing Grignard Reagent Nucelophilicity Utilizing Additives

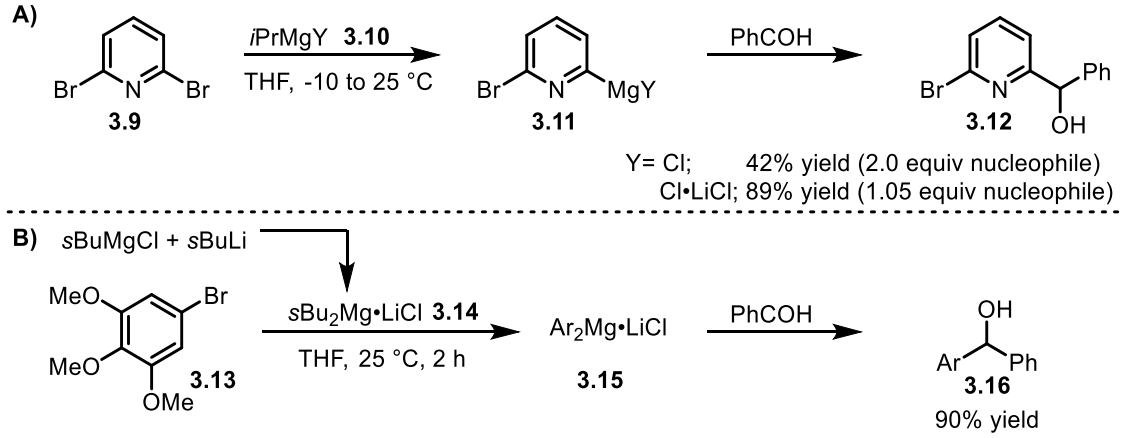
Organomagnesium compounds are among the most widely employed organometallic reagents in organic synthesis[6] and have been utilized extensively as nucleophiles and cross-coupling reagents.[7] Organomagnesium and organolithium reagents are sometimes treated as interchangeable organometallic nucleophiles in organic synthesis, yet Grignard reagents are often less reactive. The decreased nucleophilicity of these species is due to the greater

[6] Seyferth, D. *Organometallics* **2009**, 28, 1598.
[7] Knappke, C. E. I.; Wangelin, A. J. V. *Chem. Soc. Rev.* **2011**, 40, 4948.

covalent character of the carbonmagnesium bond relative to the carbon–lithium bond. Grignard reagents thus have greater functional group compatibility than their organolithium counterparts, yet this lower reactivity can also lead to diminished yields and undesired side reactions. Additionally, the preparation of Grignard reagents can be challenging. While lithium-halogen exchange is a fast process that occurs even at extremely low temperatures, the corresponding magnesium-halogen exchange reaction is considerably slower, often requiring elevated temperatures that can lead to decomposition during reagent preparation.

Various strategies have been developed to enhance the rate of magnesium-halogen exchange and increase the nucleophilicity of Grignard reagents. The Knochel group has pioneered the use of simple metal salt additives such as LiCl to enhance the rate of magnesium-halogen exchange reactions of aryl halides at low temperature, allowing the preparation of Grignard reagents containing sensitive functional groups (Figure 3.3.A).[8] In addition to the use of the "turbo Grignard" reagent *i*PrMgCl·LiCl to enhance the rate

Scheme 3.3. Knochel's turbo-Grignard method to enhance Mg-halogen exchange reactions



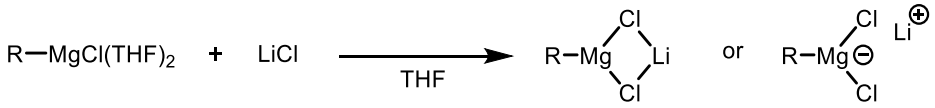
[8] Krasovskiy, A.; Knochel, P. *Angew. Chem. Int. Ed.* **2004**, 43, 3333.

of magnesium-halogen exchange reactions, the Knochel group has demonstrated that the magnesium-ate reagent *s*Bu_2Mg·LiCl, generated by the addition of *s*BuLi to *s*BuMgCl, is efficient at promoting the formation of even very electron-rich Grignard reagents (Figure 3.3.B).[9] While the exact mechanistic origin for the enhanced reactivity of these higher-order magnesium reagents is not precisely understood, it is generally believed to arise from a combination of increased solubility and altered aggregation state.

The use of LiCl has been specifically studied in some detail and it is proposed to break up higher order organomagnesium aggregates leading to the formation of more reactive monomeric species with greater nucleophilicity (Figure 3.4).[10]

Addition of LiCl to amido magnesium halide Hauser bases has similarly been found to form mixed Mg/Li amides R_2NMgCl·LiCl referred to as "turbo Hauser bases".[11] These

Scheme 3.4. Proposed origin of "turbo-Grignard" effect to enhance Mg-halogen exchange reactions



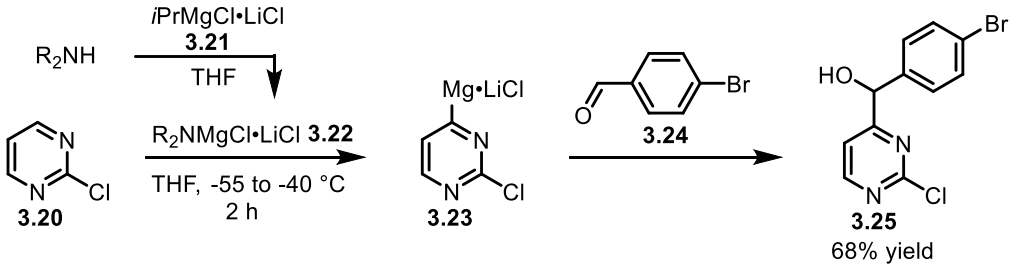
3.17 **3.18** **3.19**

reagents can also be conveniently generated by addition of the turbo Grignard reagent to amines (Scheme 3.5). These reagents are used as non-nucleophilic bases for metallation of aromatic and heteroaromatic substrates to form the corresponding Grignard reagents (**3.20** to **3.23**).

---

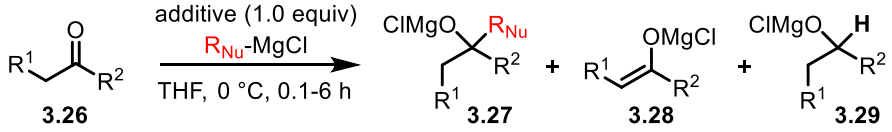
[9] Krasovskiy, A.; Straub, B. F.; Knochel, P. *Angew Chem. Int. Ed.* **2006**, 45, 159.
[10] Schnegelsberg, C.; Bachmann, S.; Kolter, M.; Auth, T.; John, M.; Stalke, D.; Koszinowski, K. *Chem. Eur. J.* **2016**, 22, 7752.
[11] (a) Krasovskiy, A.; Krasovskaya, V.; Knochel, P. *Angew. Chem., Int. Ed.* **2006**, 45, 2958. (b) Lin, W.; Baron, O.; Knochel, P. *Org. Lett.* **2006**, 8, 5673. (c) Neufed, R.; Teuteberg, T. L.; Herbst-Irmer, R.; Mata, R. A.; Stalke, D. *J. Am. Chem. Soc.* **2016**, 138, 4796.

Scheme 3.5. Generation of "turbo Hauser base" and use in low temperature metallation reactions

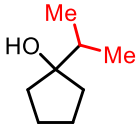
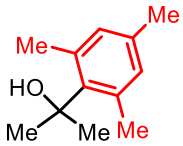
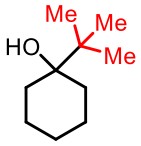
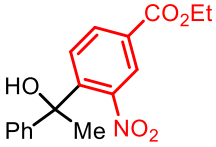


Lanthanide(III) salts have been found to enhance the reactivity of Grignard reagents towards direct nucleophilic addition to ketones over competing reactions such as enolization and reduction[12] (by β-hydride transfer) but the generally poor solubility[13] of

Scheme 3.6. Knochel's lanthanide salt additives enhance Grignard reagent addition to ketones



selected products

nucleophile	*i*PrMg•LiCl	ArMgBr•LiCl	*t*BuMg•LiCl	ArMgCl•LiCl
product				
	3.30	**3.31**	**3.32**	**3.33**
	yield	yield	yield	yield
no additive	3% yield	22% yield	4% yield	0% yield
$CeCl_3$	72% yield	57% yield	-	0% yield
$LnCl_3$•LiCl[a]	92-94% yield	69-71% yield	92-93% yield	73% yield

[a]Ln=La, Ce, Nd

[12] A) Imamoto, T.; Sugiyura, Y.; Takiyama, N. *Tetrahedron Lett*. **1984**, 25, 4233. (b) Imamoto, T.; Takiyama, N.; Nakamura, K. *Tetrahedron Lett*. **1985**, 26, 4763. (c) Imamoto, T.; Sugiyura, Y.; Takiyama, N.; Hatojima, T.; Kamiya, Y. *J. Am. Chem. Soc*. **1989**, 111, 4392. (d) Schumann, H.; Glanz, M.; Gottfriedsen, J.; Dechert, S. Wolff, D. *Pure Appl. Chem*. **2001**, 73, 279.
[13] Novikov, Y. Y.; Sampson, P. *Org. Lett*. **2003**, 5, 2263.

these Lewis acidic species has limited their effectiveness.[14] Knochel found that the addition of LiCl to lanthanides salts increased their solubility in organic solvents and improved the nucleophilic substitution reaction between sterically hindered Grignard reagents and ketones (Figure 3.6).[15] While it appears likely that LiCl has dual purposes, to both increase the solubility and Lewis acidity of the $LnCl_3$ Lewis acid (Lewis base activation of Lewis Acid) as well as to increase the nucleophilicity of the Grignard reagent, the relative importance of the two roles was not explored. The authors further demonstrated that even a catalytic amount of $LnCl_3 \cdot 2LiCl$ (10 mol%) was sufficient to promote the addition of Grignard reagents to nonactivated imines.

3.2.2 Halide Inhibition and the Role of Cationic Pd in Catalytic Reactions

Because the electronic structure and steric environment of transition metal complexes are strongly influenced by the ligands to which the metal atom is bound, the ability to control the ligand environment of such complexes is essential in determining reaction outcomes ranging from chemo- and regioselectivity to overall reaction rate and enantioselectivity.

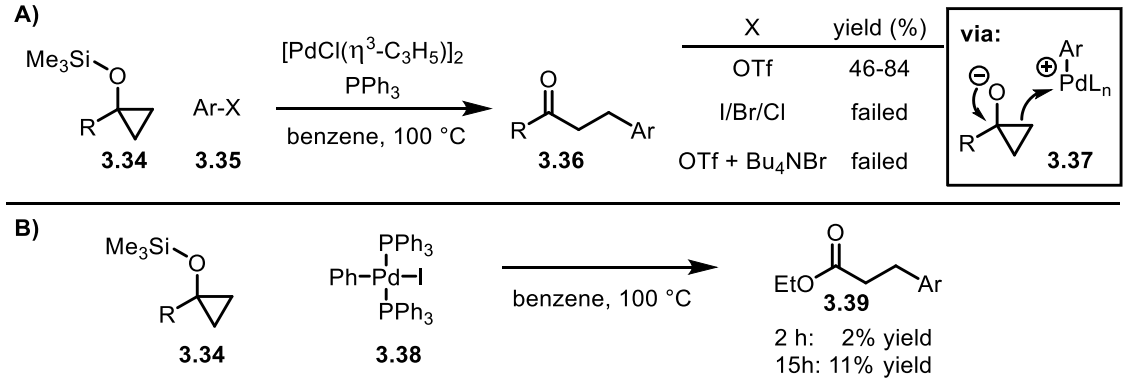
For reactions involving the formation of cationic catalytic species, this general phenomena is particularly important as cationic and neutral transition metal complexes often exhibit distinct reactivity.[16] One aspect of this general phenomena can be seen in the

[14] a) Kobayashi, S.; Sugiura, M.; Lam, H. W. L. *Chem. Rev*. **2002**, 102, 2227. (b) Kobayashi, K.; Manabe, K. *Acc. Chem. Res*. **2002**, 25, 209.
[15] Krasovskiy, A.; Kopp, F.; Knochel, P. *Angew Chem. Int. Ed.* **2006**, 45, 497.
[16] (a) For a review on cationic complexes of Ni and Pd in C-C bond forming reactions of olefins see Mecking, S. *Coord. Chem. Rev.* **2000**, 203, 325. (b) for a review on gycosylation reactions catalyzed by cationic transition metal complexes see: McKay, M. J.; Nguyen, H. M. *ACS Catal*. **2012**, 2, 8, 1563.

ability of halide anions to inhibit reactions catalyzed by cationic palladium species. For example, Kuwajima reported that halide anions are capable of inhibiting the arylation reaction of siloxycyclopropane reagents (Figure 3.7.A).[17] The authors found that when aryl electrophiles with coordinating leaving groups such as aryl halides were employed in place of aryl triflate electrophiles, the reaction was strongly inhibited. Consistent with the hypothesis that coordinating halide anions inhibit the formation of the cationic palladium species involved in cyclopropane ring opening (inset), the authors found that reactions employing aryl triflates were strongly inhibited by the addition of $(n\text{Bu})_4\text{Br}$. Stoichiometric experiments employing discreetly prepared oxidative addition adduct **3.38** further support the hypothesis that halide binding to palladium strongly inhibits catalysis (Figure 3.7.B).

The development of the Heck reaction is one area in which the role of cationic and neutral palladium complexes, and the halide inhibition of catalysis, has been extensively explored.[18] Following pioneering work by Shibasaki[19] and Overman[20] in the development

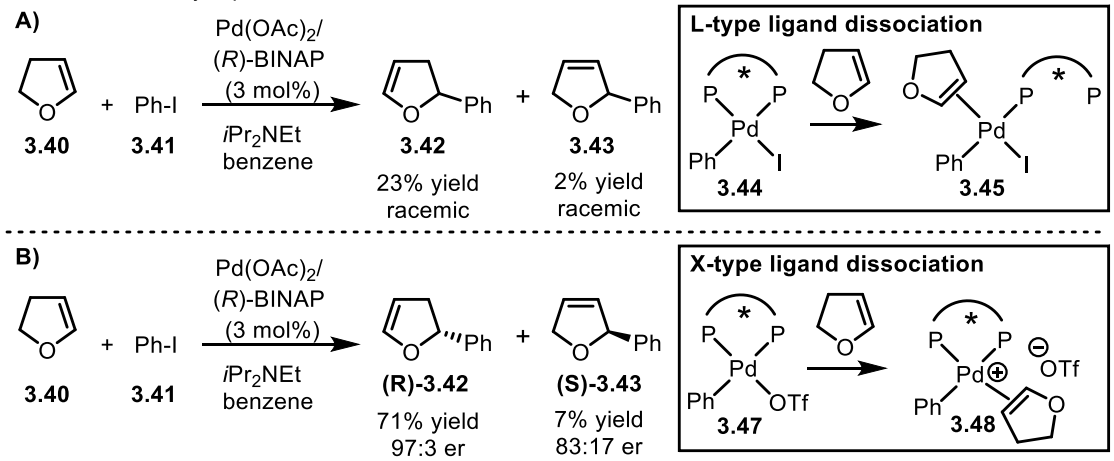
Scheme 3.7. Halide inhibition of arylation reactions of siloxycyclopropanes with aryl triflates electrophiles



[17] Aoki, S.; Fujimura, T.; Nakamura, E.; Kuwajima, I. *J. Am. Chem. Soc.* **1988**, 110, 3298.
[18] For a review on the role of cationic vs. neutral palladium complexes in the Heck reaction see: Ruan, J.; Xiao, J. *Acc. Chem. Res*. **2011**, 44, 614.
[19] Sato, Y.; Sodeoka, M.; Shibasaki, M. *J. Org. Chem.* **1989**, 54, 4738.
[20] Carpenter, N. E.; Kucera, D. J.; Overman, L. E. *J. Org. Chem*. **1989**, 54, 5846.

of the enantioselective Heck reaction, Hayashi demonstrated that by utilizing aryl triflates instead of aryl iodide electrophiles both the yield and enantioselectivity of the arylation of dihydrofuran **3.40** could be drastically improved (Figure 3.8.A versus 3.8.B).[21] This dramatic difference in reactivity and enantioselectivity was proposed to arise from the differing abilities of iodide and triflate anions to dissociate from the metal, forming coordinatively unsaturated palladium species that are capable of engaging in alkene binding. When more coordinating iodide anions are present in the reaction, the authors proposed that dissociation of a phosphine ligand is required to allow alkene biding to occur,

Scheme 3.8. Early reports on the effect of neutral versus cationic Pd in the Heck reaction

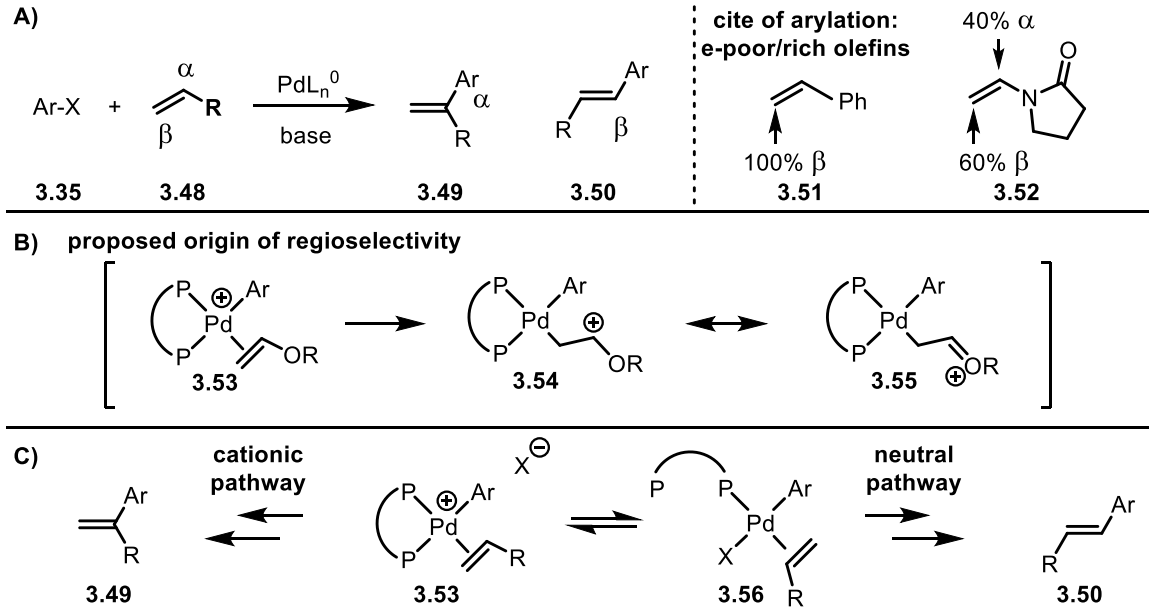


thus leading to lower yields and a lack of stereoinduction (inset, Figure 3.8.A). In contrast, when aryl triflates are employed, the noncoordinating nature of the triflate anion facilitates the formation of a coordinatively unsaturated cationic palladium species, capable of binding alkene substrates more efficiently, and leading to a greater influence from the non-dissociated chiral phosphine ligand set (inset, Figure 3.8.B).

[21] Ozawa, F.; Kubo, A.; Hayash, T. *J. Am. Chem. Soc.* **1991**, 113, 1417.

In addition to the effect on catalyst efficiency, regioselectivity in Heck reactions has also been found to strongly depend on the formation of cationic versus neutral palladium species. While electron-poor alkenes are known to undergo arylation reactions with excellent regioselectivity for the terminal β position, the use of electron-rich alkenes has been shown to lead to poor regioselectivity (Figure 3.9.A).[22] While the origin of regiocontrol in the Heck reaction has been shown to depend on a number of factors including the electronics of the aromatic electrophile and ligands employed,[23] the ability of electron-rich alkenes to stabilize positive charge buildup at the α-position of the alkene is believed to facilitate migratory insertion of the aryl group on palladium to this position (Figure 3.9.B).[24] This natural alkene polarization is enhanced by the binding of such

Scheme 3.9. Site-selectivity in Heck reaction: electronic effect and cationic vs. neutral reaction pathways



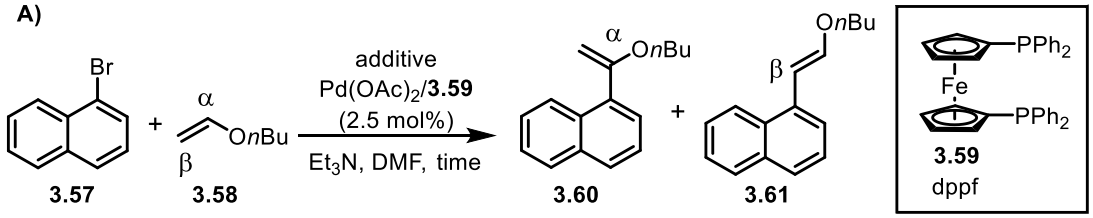
[22] See reference 11
[23] Daves, G. D.; Hallberg, A. *Chem. Rev.* **1989**, 89, 1433.
[24] Chen, C.; Luo, S.; Jordan. R. F. *J. Am. Chem. Soc*. **2010**, 132, 5273.

alkenes to electron-poor cationic palladium complexes[25], thus leading to enhanced selectivity for α-arylation of electron-rich alkenes (Figure 3.9.C).[26] With this mechanistic rationale in mind, various approaches have been developed to enhance the reactivity and selectivity of Heck reactions by promoting the formation of cationic palladium species.

Following early efforts by Larock utilizing silver salts to promote the formation of cationic palladium in Heck reactions of aryl iodides,[27] Cabri demonstrated that the addition of thallium acetate is capable of dramatically improving both the rate and selectivity for the α-arylation of electron-rich alkenes with aryl bromide electrophiles (Figure 3.10.A).[28] As with the use of silver salts, thallium salts are proposed to facilitate the formation of cationic palladium by salt metathesis, sequestering halide anions by the formation of insoluble salts which precipitate from solution (inset, figure 3.10.B).

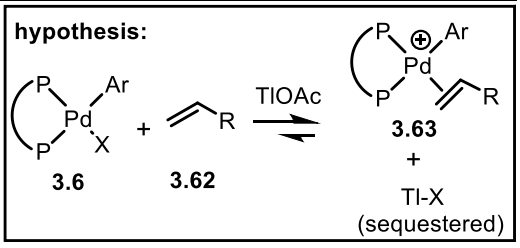
Scheme 3.10. Early reports on the effect of neutral vs. cationic Pd in the Heck reaction

A)



B)

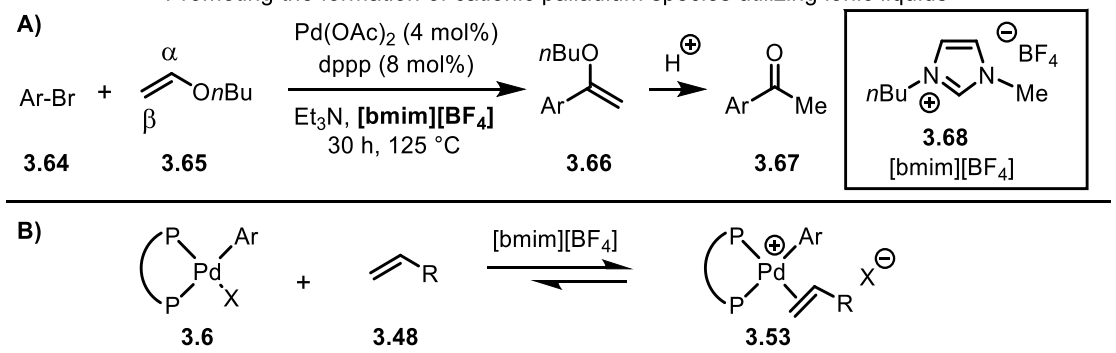
entry	additive	time	conversion (%)	α/β ratio
1	none	18 h	>99	61/39
2	$AgNO_3$	24 h	48	>99/1
3	AgOTf	24 h	68	>99/1
4	TlOAc	48 min	>99	>99/1



[25] Henriksen, S. T.; Norrby, P.-O.; Kaukoranta, P.; Andersson, P. G. *J. Am. Chem. Soc*. **2008**, 130, 10414.
[26] Deeth, R. J.; Smith, A.; Brown, J. M. *J. Am. Chem. Soc.* **2004**, 126, 7144.
[27] (a) Larock, R. C.; Gong, W. H.; Baker, B. E.*Tetrahedron Lett.* **1989**, 30, 2603. (b) Larock, R. C.; Gong, W. H. *J. Org. Chem*. **1990**, 55, 407.
[28] Cabri, W.; Candiani, I.; Bedeschi, A.; Santi, R. *Tetrahedron Lett*. **1991**, 32, 1753.

Due to the cost of utilizing stoichiometric silver and the undesirable toxicity of thallium salts, alternative strategies have been devised for the α-selective arylation of electron-rich olefines. Xiao demonstrated that by utilizing highly polar reaction media, specifically ionic liquids, α-arylation of electron-rich olefins with aryl bromides could be achieved without the need for stoichiometric silver or thallium additives (Figure 3.11.A).[29] The ionic liquid

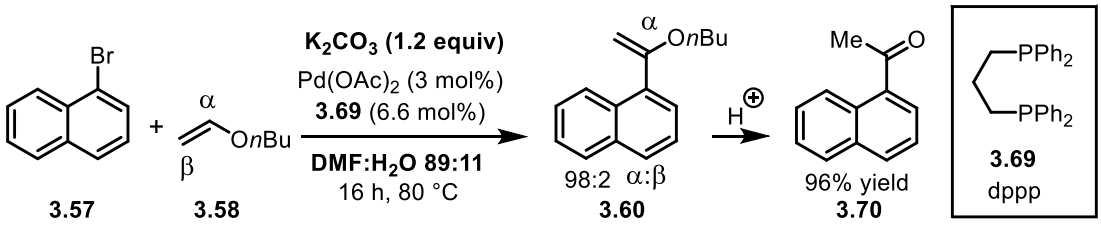
Scheme 3.11. Promoting the formation of cationic palladium species utilizing ionic liquids



was proposed to stabilize the formation of ionic species, thus facilitating the formation of cationic palladium (Figure 3.11.B).

Hallberg found that substitution of triethylamine base with potassium carbonate as well as the addition of water as a polar solvent additive facilitated excellent yields and selectivities for arylation of electron-rich alkenes with aryl bromide electrophiles without

Scheme 3.12. Silver and thalium-free conditions utilizing polar solvent system and potassium carbonate

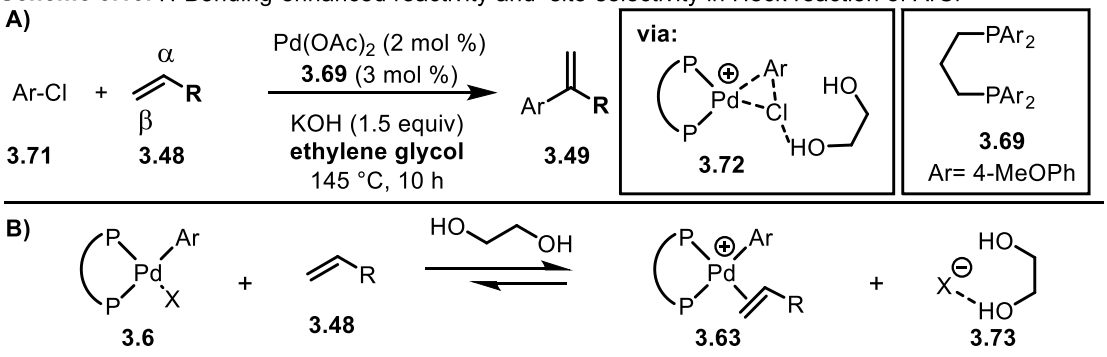


[29] Hyder, Z.; Mo J.; Xiao, J. *Adv. Synth. Catal.* **2006**, 348, 1699.

the need for silver or thallium salts (Figure 3.12).[30] While the exact role of the potassium carbonate relative to trimethylamine in promoting the reaction was not addressed by the authors, it is plausible that ionic binding between potassium and bromide ions facilitates the formation of cationic palladium.

In addition to stoichiometric halide scavenging agents and polar reaction media, the use of hydrogen bonding additives and solvent have been reported as effective strategies to promote the formation of cationic palladium species. Following initial studies demonstrating that the addition of the cationic hydrogen bond donor $HNEt_3$ drastically improves the rate of Heck reactions compared to the use of ionic liquids[31], Xiao discovered that employing ethylene glycol similarly led to rate acceleration, enabling even relatively unreactive aryl chloride electrophiles to be used (Figure 3.13).[32] Empirical observation as well as density functional theory calculations performed by the authors support ethylene glycol playing dual roles as a hydrogen bond donor capable of accelerating oxidative

Scheme 3.13. H-Bonding-enhanced reactivity and site-selectivity in Heck reaction of ArCl



[30] Vallin, S. A.; Larhed, M.; Hallberg, A. *J. Org. Chem*. **2001**, 66, 4340.
[31] Mo, J.; Xiao, J. *Angew. Chem, Int. Ed.* **2006**, 45, 4152.
[32] Ruan, J.; Iggo, J. A.; Berry, N. G.; Xiao, J. *J. Am. Chem. Soc*. **2010**, 132, 16689.

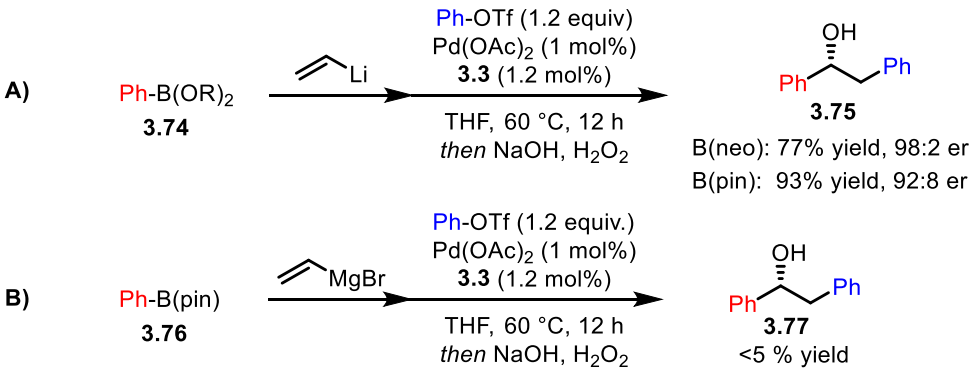
addition of the palladium(0) catalyst to aryl chlorides (inset, Figure 3.13.A), as well as a halide abstractor, facilitating the formation of cationic palladium species (Figure 3.13.B).

3.3 Challenges in Conjunctive Coupling[33]

3.3.1 Boron-Ate Complexes Derived from Grignard Reagents

As previously alluded to, while conjunctive coupling is efficient and highly selective, the initial implementation required halide-free organolithium-derived boron-ate complexes. Because trace amounts of lithium halide salts often arise during the course of lithium-halogen exchange reactions (by elimination), obtaining halide-free organolithium reagents is technically demanding. With a goal of extending the conjunctive cross-coupling reaction to readily accessible starting materials that may have greater functional group compatibility than organolithium reagents, we investigated reactions of boron-ate complexes derived from commercially available Grignard reagents. As depicted in Scheme 3.14, when halide free vinyllithium was replaced with commercial vinylmagnesium

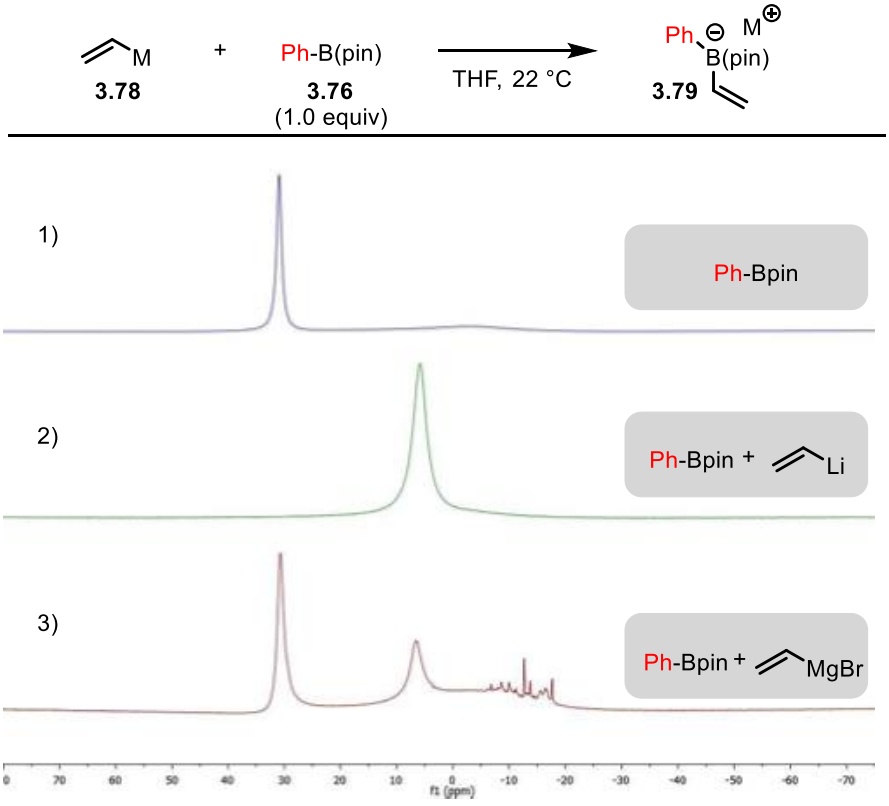
Scheme 3.14. Comparison of conjunctive coupling with vinyllithium versus vinylmagnesium bromide



[33] Lovinger, G. J.; Aparece, M. D.; Morken, J. P. *J. Am. Chem. Soc.* **2017** 139, 3153.

bromide in THF for construction of the boron-ate complex from PhB(pin), the conjunctive coupling reaction failed to deliver appreciable amounts of product. To learn about underlying reasons for the difference in reactivity between the lithium- and magnesium-based reagents, the reaction of the vinyl metal reagents and PhB(pin) was analyzed by ^{11}B NMR spectroscopy. As depicted in Figure 3.15, the reaction between halide-free vinyllithium and PhB(pin) leads to the rapid disappearance of the resonance for PhB(pin) (δ = 30.9 ppm) and appearance of a new resonance at δ = 5.8 ppm consistent with efficient formation of a four-coordinate boron species (eq. 1 versus 2).[34] In contrast, the analogous

Scheme 3.15. ^{11}B NMR analysis of reaction between vinyl metal reagents and PhB(pin)



[34] For ^{11}B NMR of four-coordinate pinacol boron-ate complexes, see: Wrackmeyer, B. *Annu. Rep. NMR Spectrosc*. **1988**, 20, 61.

reaction with vinylmagnesium bromide provides ca. 20% conversion to the putative boron-ate complex (eq. 3). While formation of boron-ate complexes from Grignard reagents has not been studied in significant detail previously, extant reports describing the reaction between Grignard reagents and α-haloboronates[35] imply that access to boron-ate complexes as transient reactive intermediates is feasible; however, a report by Blakemore[36] suggests that formation of Grignard reagent-derived boron-ate complexes may be more difficult than the analogous reactions of lithium derivatives, as observed here. Thus, one significant challenge to employing Grignard reagents in conjunctive couplings may arise from their diminished nucleophilicity, and hence diminished ability to generate the requisite boron-ate complexes, as compared to organolithium reagents.

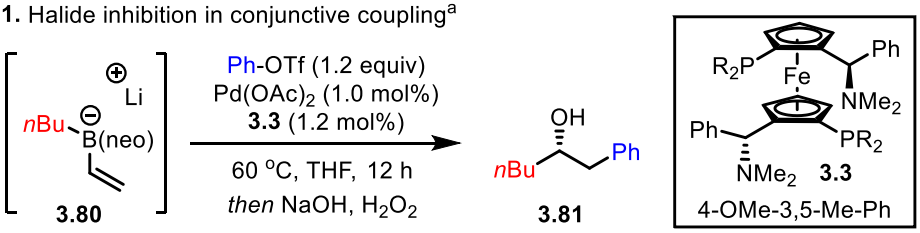
3.3.2 Inhibition by Halide Salts

While inefficient boron-ate complex formation with vinylmagnesium bromide accounts for diminished efficiency of conjunctive cross-coupling with the magnesium- versus lithium-based process, the lack of any conjunctive coupling product at all, even when ca. 20% boron-ate complex was generated from the Grignard reagent, suggests other effects might also be operative. In particular, the above-mentioned observation that conjunctive couplings are ineffective with lithium halide-containing boron-ate complexes, and that conjunctive couplings are much less effective with aryl and alkenyl halides, suggested that halide ions might inhibit the catalytic process. To probe the inhibitory effect of halides on

[35] Brown, H. C.; De Lue, N. R.; Yamamoto, Y.; Maruyama, K.; Kasahara, T.; Murahashi, S.; Sonoda, A. *J. Org. Chem.* **1977**, 42, 4088.
[36] Blakemore, P. R.; Marsden, S. P.; Vater, H. D. *Org. Lett*. **2006**, 8, 773.

conjunctive coupling, the experiments in Table 3.1 were conducted. Relative to the standard reaction conditions with 1 mol% catalyst loading and halide free boron-ate complex (entry 1, vinyllithium obtained from tetravinylstannane by Li–Sn exchange[37] or from vinyl iodide and *n*BuLi, followed by recrystallization from ether[38]), addition of 1 mol% LiI leads to a significant erosion of conjunctive coupling efficiency (entries 1 and

Table 3.1. Halide inhibition in conjunctive coupling[a]



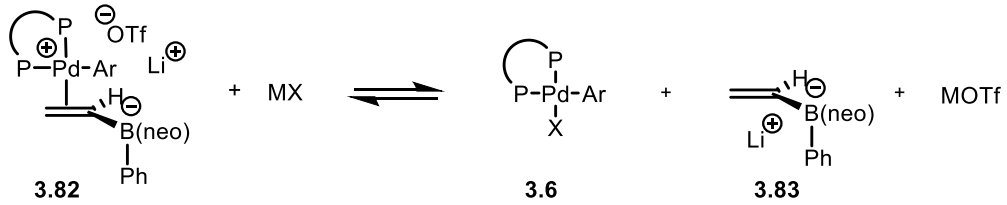
entry	alteration	yield (%)[b]	er[c]
1	none	77	98:2
2	1 mol% LiI	13	98:2
3	1 mol% LiBr	41	98:2
4	1 mol% LiCl	40	98:2
5	1 mol% (nBu)$_4$NCl	31	98:2
6	1 mol% LiI, 5 mol% catalyst	69	98:2
7	PhCl instead of PhOTf	<5	nd
8	PhBr instead of PhOTf	9	96:4
9	PhI instead of PhOTf	9	96:4
10	100 mol% LiBr	23	78:22
11	100 mol% (nBu)$_4$NBr	19	92:8

[a]The ate complex was prepared by addition of *n*-butyllithium to vinylB(neo) and the conjunctive coupling was conducted at 0.17 M. [b]Yield represents isolated yield of purified material. [c]Enantiomer ratio (er) determined by SFC analysis.

[37] Seyferth, D.; Weiner, M. A. *J. Am. Chem. Soc.* **1961**, 83, 3583.
[38] Shinokubo, H.; Miki, H.; Yokoo, T.; Oshima, K.; Utimoto, K. *Tetrahedron* **1995**, 51, 11681.

2), but an otherwise high level of enantioselectivity. The observation that the inhibitory effect of 1 mol% LiI is somewhat ameliorated by conducting the reaction with 5 mol% $Pd(OAc)_2$/Mandyphos (**3.3)** (entry 6) suggests that the effect may be due to interaction of LiI and a catalytically active complex. Considering the inhibitory effect of LiI, it is unsurprising that conjunctive cross-coupling of aryl halide electrophiles are inefficient even when lithium halide-free boron-ate complexes are employed (entries 7, 8, and 9): conjunctive coupling itself releases lithium halide as a direct product of the reaction. The halide inhibition observed in conjunctive coupling reactions is consistent with the proposed reaction mechanism wherein π-bonding between a cationic transition metal complex and the reacting boron-ate complex is a necessary prerequisite. In this scenario, it is plausible that halide ions outcompete the olefin for binding to palladium (Figure 3.16), thereby leading to reaction inhibition. In related stoichiometric processes, the presence of halide ions has been shown to inhibit carbopalladation of alkenes by sequestering cationic

Scheme 3.16. Hypothesis for the origin of halide inhibition of conjunctive coupling



3.82 **3.6** **3.83**

palladium complexes.[39] Similarly, while catalytic Heck[40], Stille[41], and other[42] reactions often exhibit acceleration due to the presence of halide ions, this effect is generally traced to an acceleration of oxidative addition. When oxidative addition is not the slow step of catalysis, halide anions may sequester catalytic species off cycle, acting as inhibitors.[43] Indeed, as discussed in the background to this chapter, halide inhibition of catalysis has been documented in the case of catalytic Heck reactions and catalytic activation/cross-coupling of cyclopropanes.

3.4 Studied on the Effects of Additives and Solvent on Conjunctive Coupling

3.4.1 Effect of Additives on Boron-Ate Complex Formation from Grignard Reagents and Subsequent Conjunctive Coupling

The above-described studies suggested to us that development of a strategy for effective boron-ate complex formation and concomitant removal of halide ions from the reaction medium might enable conjunctive coupling reactions with Grignard reagents and also allow the use of organohalide electrophiles. We reasoned that efficient construction of boron-ate complexes from Grignard reagents might be facilitated by the addition of

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[39] (a) Kawataka, F.; Shimizu, I.; Yamamoto, A. *Bull. Chem. Soc. Jpn*. **1995**, 68, 654. (b) Kayaki, Y.; Shimizu, I.; Yamamoto, A. *Chem. Lett*. **1995**, 24, 1089. (c) Amatore, C.; Carre, E.; Jutand, A.; M´ 'Barki, M. A.; Meyer, G. *Organometallics* **1995**, 14, 5605. (d) Amatore, C.; Godin, B.; Jutand, A.; Lemaître, F. *Chem. Eur. J*. **2007**, 13, 2002. (e) Amatore, C.; Godin, B.; Jutand, A.; Lemaître, F. *Organometallics* **2007**, 26, 1757.

[40] (a) Jeffrey, T. *J. Chem. Soc. Chem. Commun*. **1984**, 1287. (b) Jeffrey, T. *Tetrahedron Lett*. **1985**, 26, 2667. (c) Grigg, R.; Stevenson, P.; Worakun, T. *Tetrahedron* **1988**, 44, 2033. (d) Andersson, C.-M.; Hallberg, A. *J. Org. Chem*. **1988**, 53, 2112.

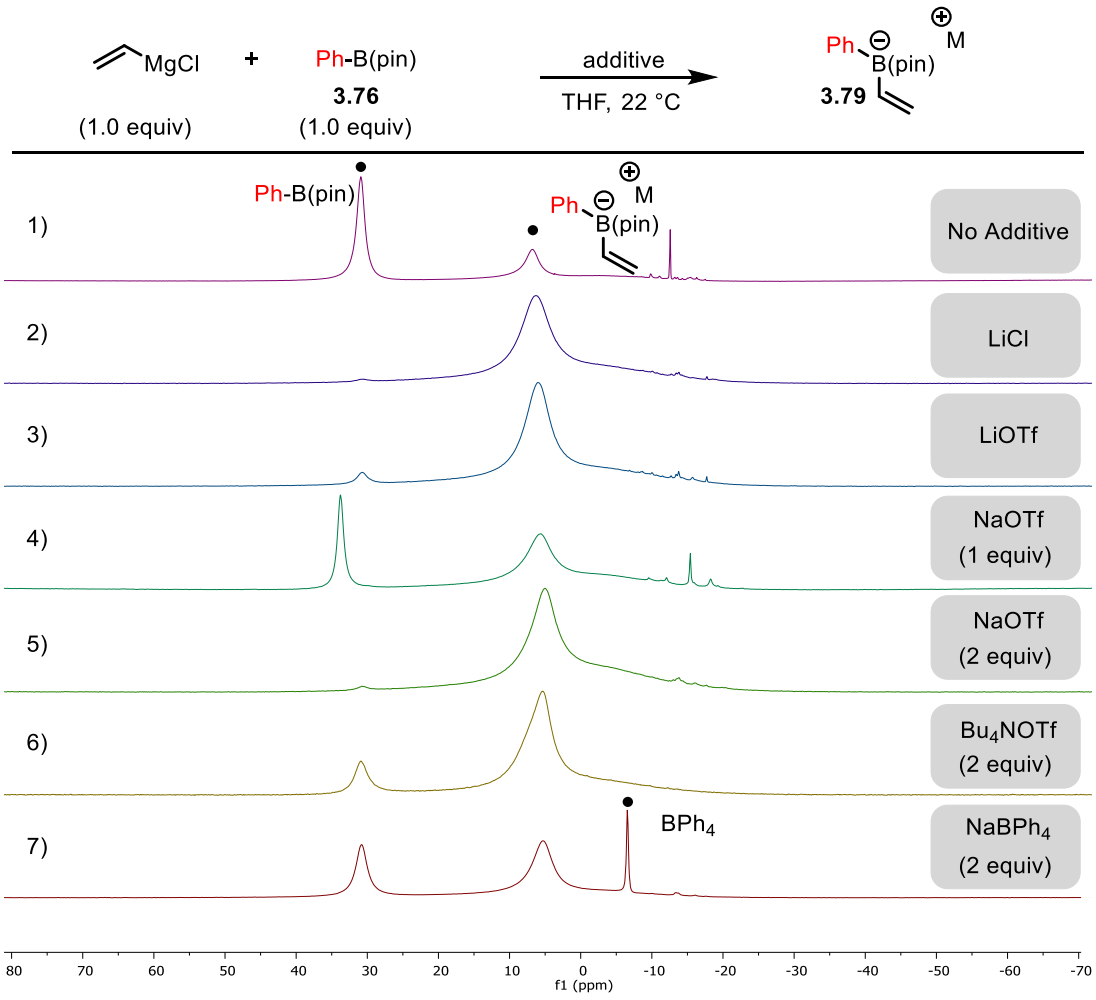
[41] (a) Scott, W. J.; Crisp, G. T.; Stille, J. K. *J. Am. Chem. Soc*. **1984**, 106, 4630. (b) Scott, W. J.; Stille, J. K. *J. Am. Chem. Soc*. **1986**, 108, 3033. (c) Scott, W. J.; McMurry, J. E. *Acc. Chem. Res.* **1988**, 21, 47.

[42] Beletskaya, I. P. *J. Organomet. Chem*. **1983**, 250, 511.

[43] Jutand, A. Appl. *Organomet. Chem*. **2004**, 18, 574.

appropriate additives that enhance the reactivity of magnesium-based reagents. Along these lines we first examined the capacity of LiCl to facilitate boron-ate complex formation. As previously discussed, studies by Knochel have shown that lithium chloride increases the reactivity of Grignard reagents in Mg-halogen exchange reactions and increases the reactivity of Hauser bases. While we considered that addition of LiCl would likely compound the problem of halide inhibition in catalytic conjunctive coupling reactions, it would nonetheless reveal the capacity for additives to enhance boron-ate complex formation. As depicted in Scheme 3.17, when vinylmagnesium chloride was added to PhBpin in THF in the presence of one equivalent of LiCl, complete conversion to the boron-ate complex was observed by ^{11}B NMR analysis (entry 1 versus 2). Unsurprisingly, the resulting complex was unreactive in conjunctive coupling. It is worth noting that unlike LiCl, LiBr was ineffective at promoting boron-ate complex formation (data not shown), highlighting the subtlety of the observed activating effect (see experimental section for full list of additives tested). In an effort to uncover additives that are less likely to inhibit conjunctive coupling reactions, we studied the capacity for other weakly basic metal salts to promote boron-ate complex formation. It was found that both LiOTf and NaOTf can effect boron-ate complex formation (entries 3, 4), although the later ion pair is less effective and requires 2 equivalents to achieve >95% conversion (entry 5). In terms of mechanistic features, it is worth noting the effectiveness of Bu_4NOTf in facilitating conversion to the boron-ate complex (entry 6). While NaOTf has been proposed

Scheme 3.17. ^{11}B NMR of reactions between vinylMgCl and PhB(pin) in the presence of additives



to activate Grignard reagents by halide abstraction to generate RMgOTf,[44] the lack of Lewis acidity of Bu_4NOTf suggests that the ability of additives to facilitate boron-ate complex formation stems predominantly from the Lewis basicity of the triflate as opposed to either halide abstraction or Lewis acid activation of the boronic ester reagent through pinacol oxygen to Lewis acid donation.[45] Although, it should be noted that $NaBPh_4$, a

[44] (a) Kendall, A. J.; Salazar, C. A.; Martino, P. F.; Tyler, D. R. O*rganometallics* **2014**, 33, 6171. (b) Reetz, M. T.; Harmat, N.; Mahrwald, R. *Angew. Chem., Int. Ed*. **1992**, 31, 342.
[45] (a) Corey, E. J.; Barnes-Seeman, D.; Lee, T. W. *Tetrahedron: Asymmetry* **1997**, 8, 3711. (b) Midland, M. J. *Org. Chem.* **1998**, 63, 914. (c) Rauniyar, V.; Hall, D. G. *J. Am. Chem. Soc.* **2004**, 126, 4518.

nonbasic Lewis acid, also promotes boron-ate complex formation (entry 7), albeit less effectively than Bu_4NOTf. This observation suggests that Lewis acid association may play a beneficial but less significant role in promoting association between the boronic ester and Grignard reagent. To minimize halide inhibition of catalysis we considered that cations that are able to ion pair with halide anions might serve as scavenging agents and facilitate catalysis. While AgOTf was considered as a potential candidate for such a strategy, addition of AgOTf was found to rapidly decompose the halide free lithium-derived boron-ate complex as determined by ^{11}B NMR analysis. We speculated that nonredox active cationic metals whose halide salts are either insoluble or tightly ion-paired in THF solvent might be introduced as metal triflates and, upon anion exchange, act as effective scavengers. Along these lines, while the solubility of LiCl in THF has received attention,[46] the solubility of other metal halides has not been reported. To aid in the interpretation of reaction outcomes, the solubility of a series of metal salts in THF solvent was measured. In these experiments, 1−3 g of anhydrous salt was stirred in 21 mL of anhydrous tetrahydrofuran for 24 h at room temperature. The solution was allowed to stand undisturbed overnight, the supernatant then filtered to remove remaining non-dissolved salt, and a 10 mL portion of the solution evaporated to constant weight. Using this procedure, the data in Table 3.2 was collected.

Considering the remarkable difference in solubility between NaOTf and NaCl, as well as the ability of NaOTf to promote boron-ate complex formation from Grignard reagents, this additive was examined in conjunctive coupling reactions that employ

[46] Krasovskiy, A.; Knochel, P. *Synthesis* **2006**, 5, 890.

Table 3.2. Solubility of metal salts in anhydrous THF solvent[a]

salt	solubility (mg/mL)	solubility (M)
LiCl	49.5	1.12
LiBr	388	4.47
LiOTf	473	3.03
NaCl	0.20	0.0036
NaCl (1:1 THF:DMSO)[b]	0.32	0.0055
NaBr	0.15	0.0015
NaOTf	220	1.30
NaOTf (1:1 THF:DMSO)[b]	289	1.68
KCl	0.30	0.0039
KBr	0.30	0.0022
KOTf	4.0	0.0213
$MgCl_2$	40.6	0.427
$Mg(OTf)_2$	4.4	0.014

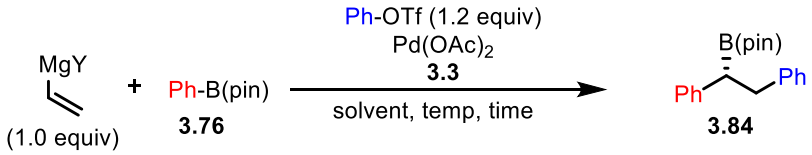
[a]See text for procedural details. [b]For these entries, saturated concentration determined by slowly adding salt to solvent until the solution remained turbid.

vinylmagnesium chloride. Notably, NaOTf [47] is a commercially available and inexpensive salt. Optimization of the reaction of the boron-ate complex derived from vinylmagnesium bromide and phenylboronic pinacol ester with phenyl triflate (Table 3.3) illustrated that while LiCl (entry 2) and LiOTf (entry 3) are capable of facilitating boron-ate formation (*vide supra*) they do not facilitate the subsequent coupling reaction. In contrast, the addition of KOTf facilitated product formation with two equivalents being more effective than one equivalent (entry 4 and 5) and three equivalents (entry 6) not providing a substantial further

[47] Surya Prakash, G. K.; Mathew, T. *e-EROS Encyclopedia of Reagents for Organic Synthesis* **2010**, DOI: 10.1002/ 047084289X.rn01137

improvement. While both KOTf and NaOTf were found to be effective when either vinylmagnesium bromide or chloride were employed, the combination of NaOTf with vinylmagnesium chloride was found to produce the most consistently high yield and enantioselectivity (entry 9 and 10, see full optimization table in the experimental section). The addition of DMSO as a polar cosolvent was found to provide an increase in yield and enantioselectivty relative to THF, though reactions were found to proceed more slowly, requiring 24 rather than <14 h to reach completion (entry 11 and 12). Notably, as with THF, two equivalents of NaOTf was found to be essential with THF:DMSO solvent system. This level of selectivity and reaction efficiency is comparable to that obtained with boron-ate complexes prepared from halide-free vinyllithium reagents.

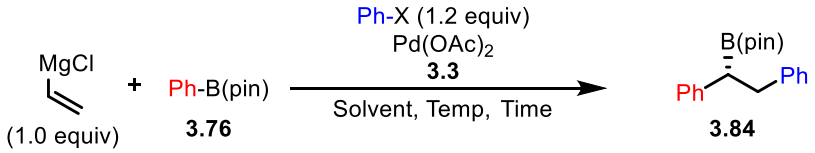
Table 3.3 Optimization of coupling between Grignard-derived boron-ate complexes and aryl triflates



entry	additive	Y	[Pd] (mol%)	solvent	temp (°C)	time (h)	yield (mol%)	er
1	NA	Br	3.0	THF	60	14	0	na
2	LiCl (1.0 equiv)	Br	3.0	THF	60	14	0	na
3	LiOTf (1.0 equiv)	Br	3.0	THF	60	14	0	na
4	KOTf (1.0 equiv)	Br	3.0	THF	40	14	10	94:6
5	KOTf (2.0 equiv)	Br	3.0	THF	40	14	64	92:8
6	KOTf (3.0 equiv)	Br	3.0	THF	40	14	65	92:8
7	NaOTf (2.0 equiv)	Br	3.0	THF	40	14	58	94:6
9	KOTf (2.0 equiv)	Cl	2.0	THF	24	14	63	93:7
10	NaOTf (2.0 equiv)	Cl	3.0	THF	24	14	75	93:7
11	NaOTf (2.0 equiv)	Cl	3.0	THF	40	14	72	94:6
12	**NaOTf (2.0 equiv)**	**Cl**	**3.0**	**THF:DMSO 1:1**	**40**	**24**	**81**	**96:4**
13	NaOTf (1.0 equiv)	Cl	3.0	THF:DMSO 1:1	40	24	45	97:3

In addition to its ability to facilitate the reaction of Grignard reagent-derived boron-ate complexes with aryl or alkenyl triflates, the apparent halide-scavenging ability of NaOTf[48] can also enable the reaction of aryl bromide electrophiles. When bromobenzene electrophile was employed in a conjunctive coupling in place of phenyl triflate, under otherwise identical conditions (Table 3.3, entry 11 versus. Table 3.4, entry 1), product yield decreased from 72% to 4%. Raising the reaction temperature from 40 ˚C to 60 ˚C led to only a minor improvement in yield (entry 2). When an additional equivalent of NaOTf was added, the yield increased from 4% to 33% and when the reaction was run in pure DMSO

Table 3.4 Optimization of coupling between Grignard-derived boron-ate complexes and aryl bromides



Entry	Additive	X	cat (mol%)	Solvent	Temp (°C)	Time (h)	yield (%)	er
1	NaOTf (2.0 equiv)	Br	3.0	THF	40	14	4	94:6
2	NaOTf (2.0 equiv)	Br	3.0	THF	60	14	8	94:6
3	NaOTf (3.0 equiv)	Br	3.0	THF	40	14	33	94:6
4	NaOTf (3.0 equiv)	Br	3.0	THF	60	14	30	92:8
5	NaOTf (3.0 equiv)	Br	3.0	DMSO	40	14	80	94:6
6	**NaOTf (3.0 equiv)**	**Br**	**3.0**	**THF:DMSO 1:1**	**60**	**24**	**84**	**97:3**
7	NaOTf (3.0 equiv)	Br	2.0	THF:DMSO 1:1	60	24	83	95:5
8	NaOTf (3.0 equiv)	Br	1.0	THF:DMSO 1:1	60	24	54	96:4
9	NaOTf (3.0 equiv)	Br	1.0	THF:DMSO 1:1	70	24	69	95:5
10	NaOTf (3.0 equiv)	Br	2.0	THF:DMSO 1:3	60	24	84	97:3
11	NaOTf (3.0 equiv)	Br	2.0	THF:DMSO 1:3	70	24	80	96:4
12	NaOTf (3.0 equiv)	I	3.0	THF:DMSO 1:1	60	24	81	97:3

[48] For examples of halide abstraction by NaOTf, see: From LnRuCl (a) Quebatte, L.; Scopelliti, R.; Severin, K. *Eur. J. Inorg. Chem.* **2005**, 3353. From LnI(III)Cl: (b) Brantley, J. N.; Samant, A. V.; Toste, F. D. *ACS Cent. Sci.* **2016**, 2, 341. LnAuCl: (c) Serra, D.; Moret, M.-E.; Chen, P. *J. Am. Chem. Soc*. **2011**, 133, 8914. LnPdCl: (d) Delis, J. G. P.; Groen, J. H.; Vrieze, K.; van Leeuwen, P. W. N. M.; Veldman, N.; Spek, A. L. *Organometallics* **1997**, 16, 551.

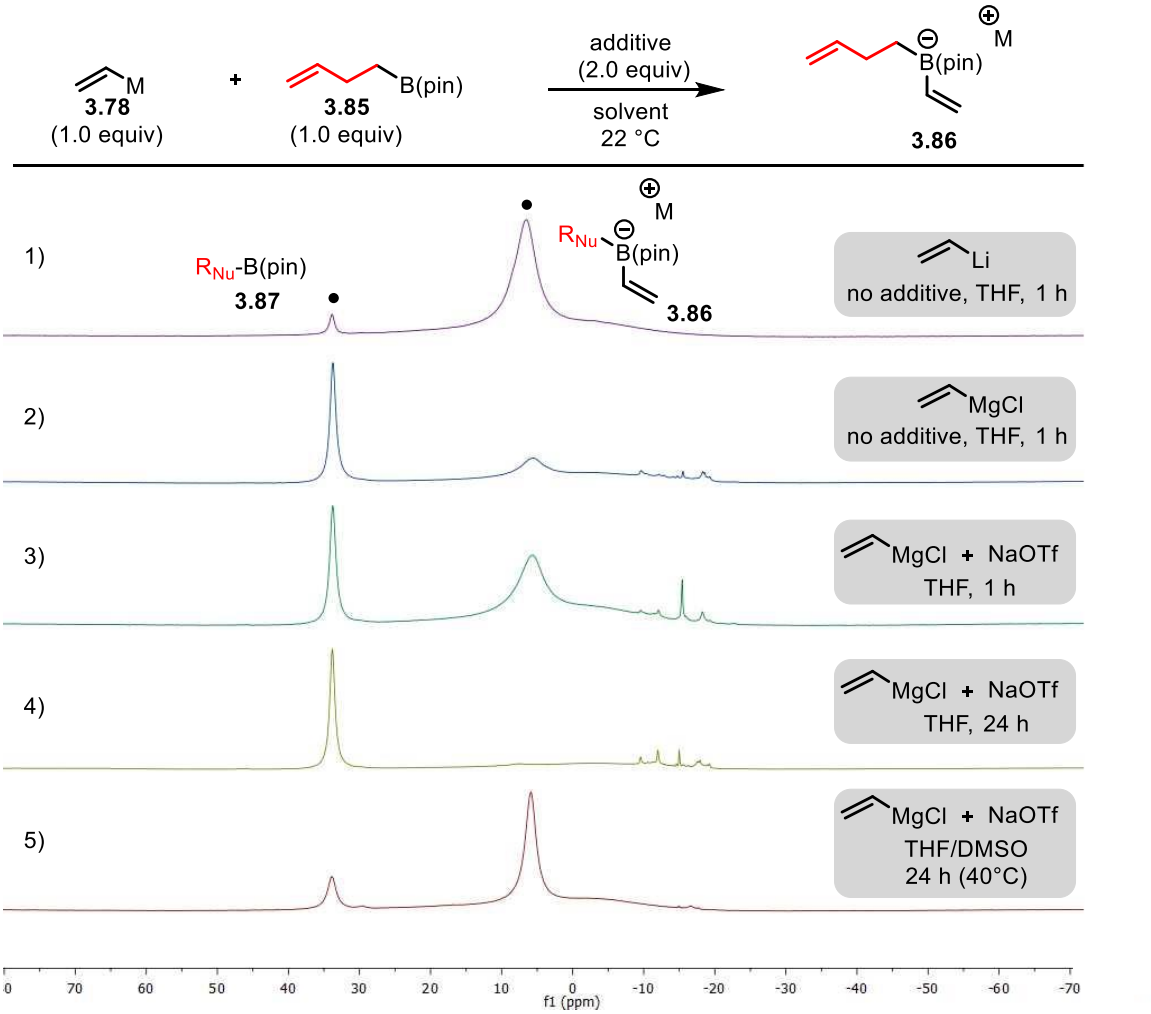
the yield further improved to 80% (entry 5). Optimal levels of yield and enantioselectivity were achieved by increasing the reaction temperature to 60 ˚C while employing a 1:1 THF:DMSO solvent system (entry 6). Importantly, aryl iodides behaved similarly to aryl bromides under the same reaction conditions (entry 12). Notably, catalyst loading could be decreased from 3% to 2% with almost no loss in yield and enantioselectivity (entry 7 and 10). Decreasing the catalyst loading further to 1% led to a decrease in yield to 54% (entry 8), though this could be remedied (69% yield) by increasing the reaction temperature to 70˚C (entry 9).

3.4.2 Formation and Stability of Boron-Ate Complexes: Solvent Effects

While we found that NaOTf facilitates formation of boron-ate complexes from aryl and vinyl Grignard reagents and can enable conjunctive coupling of these species, two features remained challenging. First, even with the addition of NaOTf, formation of boron-ate complexes from Grignard reagents and alkylboronic esters was not efficient (ca. 50% conversion to boron-ate complex). Second, whereas the Li-based boron-ate complexes possess excellent long-term stability in solution, the Mg-based reagents lack stability over a time course comparable to a typical catalytic reaction. These aspects were probed by ^{11}B NMR (Scheme 3.18). When 3-butenylB(pin) was reacted with vinyllithium, the derived boron-ate complex **3.86** formed immediately (eq. 1) and was stable even after 24 h at room temperature (not shown). In contrast, even with the addition of NaOTf, vinyl magnesium chloride only converted ca. 50% of the alkylB(pin) substrate to the derived boron-ate complex after 1 h (eq. 3). Furthermore this complex was not stable, and largely converted

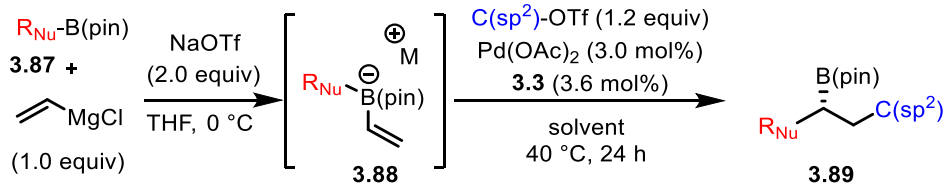
back to three-coordinate boron species (mixture of 3-butenylB(pin) and vinylB(pin)) after standing for 24 h (eq. 4). Considering that the polarity and/or coordinating ability of the reaction medium might enhance the stability of boron-ate complexes, we examined complexation reactions in different solvents. Most effective was the inclusion of DMSO as a cosolvent: as depicted in eq. 5, the reaction of vinylmagnesium chloride with the alkylB(pin) substrate and NaOTf in THF/DMSO (1:1) solvent mixture proceeds in high conversion and furnishes a boron-ate complex that persisted with little

Scheme 3.18. ^{11}B NMR of reactions between vinyl metal reagents and 3-butenylB(pin)



change even after 24 h at room temperature (data not shown) or 40 °C . This observation is expected to aid in the development of practical conjunctive coupling reactions, and may also prove useful in the design of other boron-based processes.[49] That the increased stability of Grignard reagent-derived boron-ate complexes of alkylboron species in the presence of DMSO cosolvent translates to increased reaction yield can be ascertained by examining the data in Table 3.5. Across a small selection of boronic esters and electrophiles, comparison of conjunctive couplings in either THF solvent or THF/DMSO (1:1) revealed that conjunctive couplings with the alkyl–B(pin) derivative are ineffective in THF solvent, whereas in THF/DMSO a reasonable yield and enantioselectivity were

Table 3.5. Effect of solvent on catalytic conjunctive coupling reactions[a]



entry	R_{Nu}	Ar	solvent	Yield (%)[c]	er[c]
1	3-butenyl	Ph	THF	<5	n/a
2	3-butenyl	Ph	THF/DMSO	73	91:9
3	Ph	Ph	THF	72	94:6
4	Ph	Ph	THF/DMSO	81	96:4
5	Ph	*p*-MeO-Ph	THF	78	92:8
6	Ph	*p*-MeO-Ph	THF/DMSO	89	98:2
7	Ph	*p*-CF_3-Ph	THF	67	75:25
8	Ph	*p*-CF_3-Ph	THF/DMSO	85	95:5

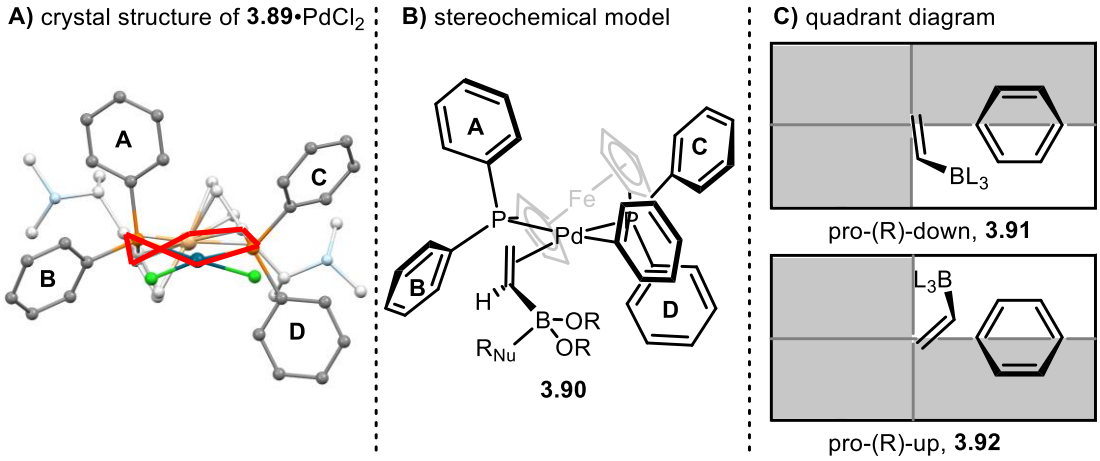
[a]Reactions conducted as described in the text and conjunctive coupling was conducted at 0.17 M. [b]Yields represents isolated yields of purified material. [c]Enantiomer ratio (er) determined by SFC analysis of boronic ester.

[49] Armstrong, R. J.; Niwetmarin, W.; Aggarwal, V. K. *Org. Lett.* **2017**, 19, 2762.

obtained (entries 1 and 2). Notably, use of the more polar THF/DMSO solvent medium also resulted in improvements to the yields and enantioselectivities observed for the reaction of arylB(pin) reagents (entry 3 through 8). While the increase in yields observed in these cases are less substantial than when alkylboronic esters are employed, the inclusion of DMSO cosolvent consistently resulted in substantially enhanced enantioselectivities relative to the use of THF alone.

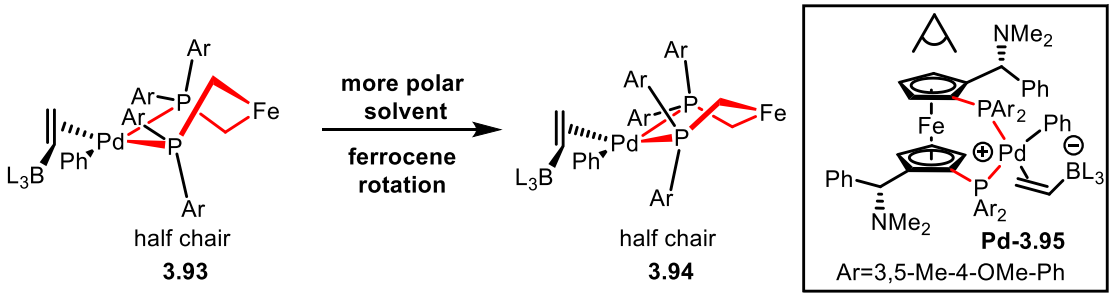
Because enantioselectivity represents the energy difference between transition states ($\Delta\Delta G^{\ddagger}$), barring complicating factors (such as differing rates of background reaction), this experimental data can be correlated with structural changes to the substrate-catalyst activated complex as a function of external stimuli such as solvent polarity. Considering the catalyst structure and plausible stereochemical model previously discussed in chapter two of this dissertation (Scheme 3.19.A/B) it is apparent that the relative position of the pseudo axial/equatorial aryl groups on phosphorous are what primarily dictate facial selectivity of alkene binding according to a simplified quadrant diagram (Scheme. 3.16.C). While a detailed analysis of how the relative reorientation of aryl groups might lead to stabilization of the two Pro-(R) alkene binding modes (**3.91** and **3.92**) or destabilization of the corresponding Pro-(S) binding modes is somewhat complex, an understanding of the mechanism by which solvent polarity might plausibly change catalyst structure could provide insight that informs catalyst design. In this vein, one possible explanation is that the relative orientation or twist of the cyclopentadienyl rings of ferrocene results in twisting of the catalyst metallocyclic core (Scheme 3.19, highlighted in red), reorienting the pseudo axial/equatorial aryl groups (**3.93** to **3.94**, Scheme 3.20). As depicted in Scheme 3.21, a

Scheme 3.19. Polarity-controlled allosteric change to catalyst structure and plausible stereochemical model



simple analysis of the dipole moments present in alkene-catalyst complexes **3.96** and **3.97** allows such a structural change upon increasing solvent polarity to be rationalized in terms of net dipole stabilization leading to reorientation of the cyclopentadienyl ferrocene rings of these structures. As assessed by qualitative analysis of dipole vectors and confirmed by density functional calculations (described in chapter two of this dissertation), the net dipole of **3.96** is oriented from left to right (Scheme 3.21.B, highlighted in purple). This is largely

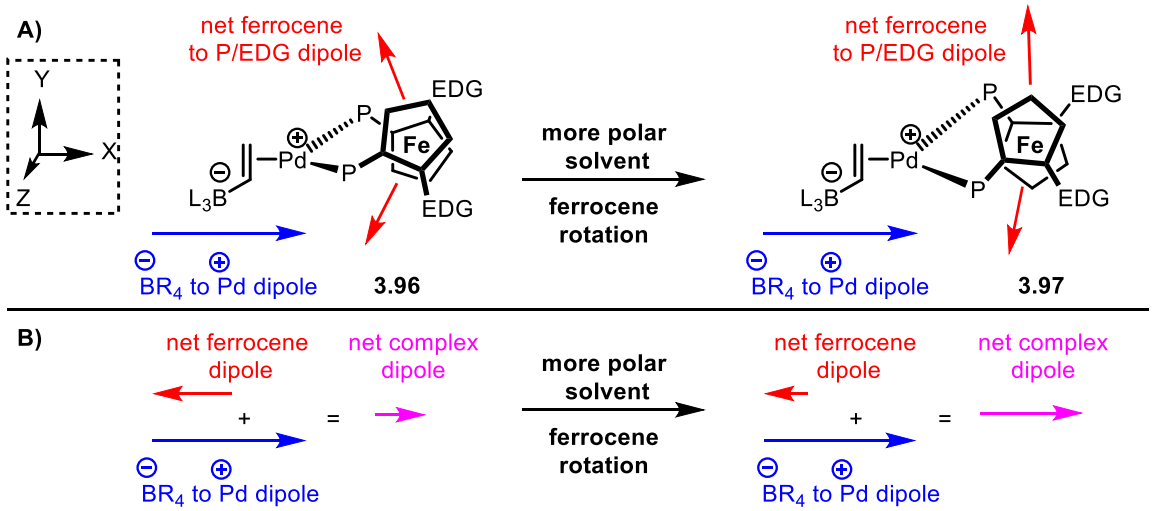
Scheme 3.20. Plausible polarity-controlled, structural change to catalyst metallacycle



determined by the net position of the negatively charged boron-ate complex to the electropositive iron and cationic palladium atoms (Scheme 3.21.A, dipole component highlighted in blue). As depicted in Scheme 3.21.A, the individual dipole components of each cyclopentadienyl ring (highlighted in red) of ferrocene can be visualized as the net

vector of the phosphorous and benzyldimethylamine (EDG) substitutes. Because of the C_2 symmetric nature of the ferrocene moiety, the Y and Z components of these dipoles are in opposition and cancel out. The X components of these vectors are in concert and thus add together, generating a net ferrocene dipole moment from right to left which is in opposition to the larger boron-ate to Pd vector. Thus, stabilization of the global dipole moment of

Scheme 3.21. Plausible polarity-controlled, dipole-driven change in catalyst structure



the substrate-catalyst complex **3.96** might stabilize a structural reorientation of the ferrocene rings such that the oppositional ferrocene dipole moment is minimized (Scheme 3.21.B).

It is worth noting that this analysis is consistent with a maximization of the net electric field of the substrate-catalyst complex along the direction of electron flow involved in the metal-induced metallate rearrangement transition state which should lead to transition state stabilization.[50] While this phenomena is a well-known transition state stabilizing effect for

[50] Welborn, V. V.; Pestana, L. R.; Head-Gordon, T. *Nature Catalysis* **2018,** 1, 649.

enzymes,[51] it has not been well explored in the context of designing catalysts for organic synthesis.[52] As such, a study of the effect of dipole/electric field optimization through ligand design for conjunctive coupling may serve as an interesting opportunity to expand scientific understanding of this phenomena as well as a means to improve the conjunctive coupling reaction manifold. Overall, the data presented in the above two sections argues for the use of NaOTf additive and THF/DMSO solvent mixture for effective and general catalytic conjunctive couplings of Grignard-reagent derived boron-ate complexes. We therefore surveyed these conditions across a range of substrates.

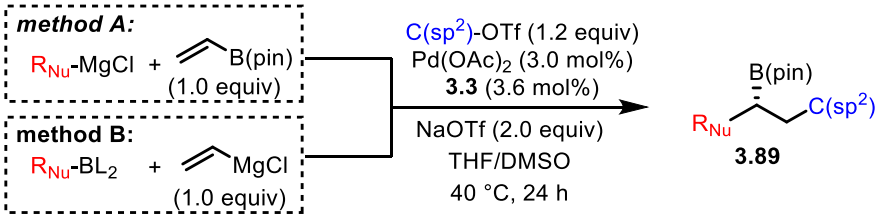
3.5 Substrate Scope

3.5.1 Scope of Conjunctive Coupling with Grignard Reagent-Derived Ate Complexes

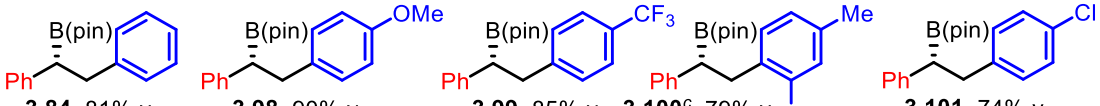
With effective conditions established to employ Grignard reagent-derived boron-ate complexes in conjunctive couplings, the scope of the catalytic enantioselective transformation was assessed. As depicted in Scheme 3.22, it was found that the Mg-based system allows conjunctive couplings with a range of aromatic carbocycles, heterocycles and olefinic organotriflate electrophiles. Of note, an aldehyde group attached to the electrophile survives the reaction intact (**3.102**), an observation that points to the buffering effect the boron atom imposes on the precursor nucleophilic Grignard reagent. Other labile functional groups such as a nitriles (**3.111**), an amide (**3.118**) esters (**3.119**, **3.126**), an acetal

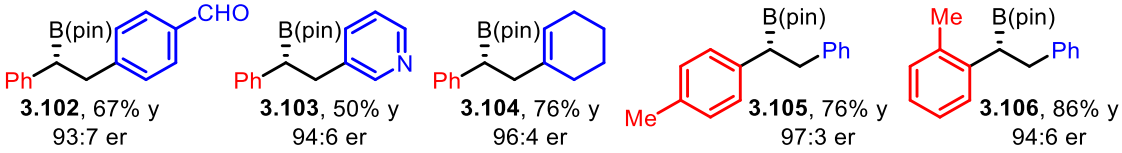
[51] Fried, S. D.; Boxer, S. G. *Annu. Rev. Biochem.* **2017**, 86, 387.
[52] Che, F; Gray, J. T.; Ha, S.; Kruse, N.; Scott, S. L.; McEwen, J.-S.*ACS Catal.* **2018**, 8, 5153.

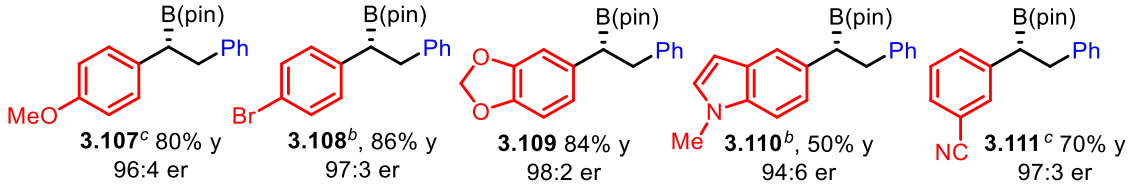
Scheme 3.22. Conjunctive coupling between Grignard-derived boron-ate complexes and organotriflates[a]

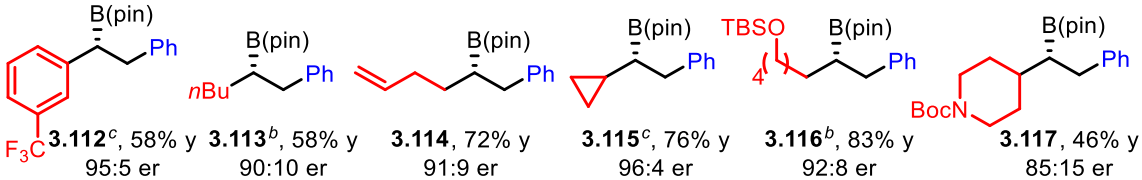


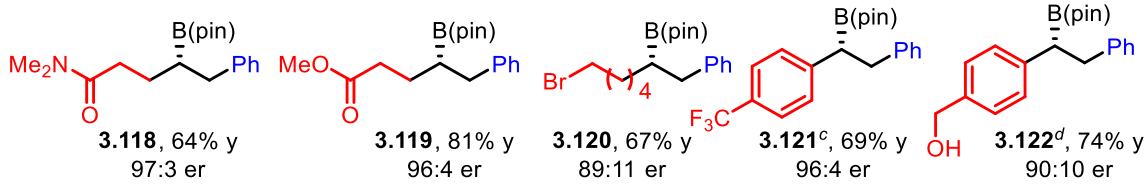
method B:

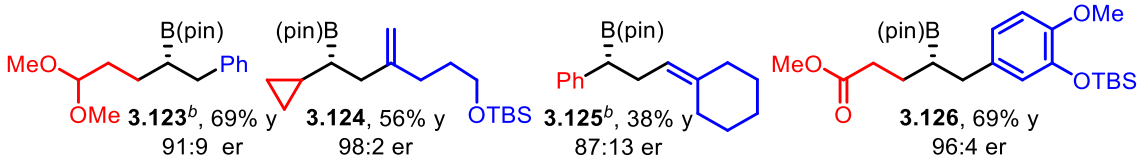




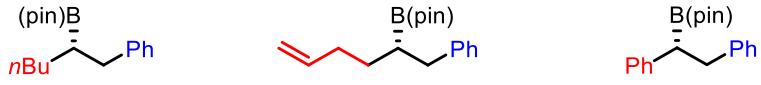








method A:



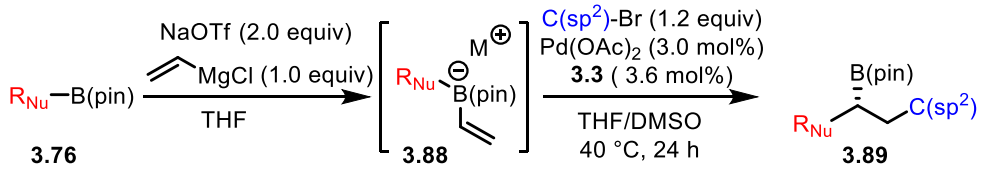
[a]Conjunctive coupling was conducted at 0.17 M. Yields represent isolated yields of purified material. Both the yield and the enantiomer ratio (er) represent the average value for two experiments. [b]Product isolated as the derived alcohol. [c]Reaction conducted at 60 °C. [d]Solvent= THF, (2.0 equiv) of nucleophile employed.

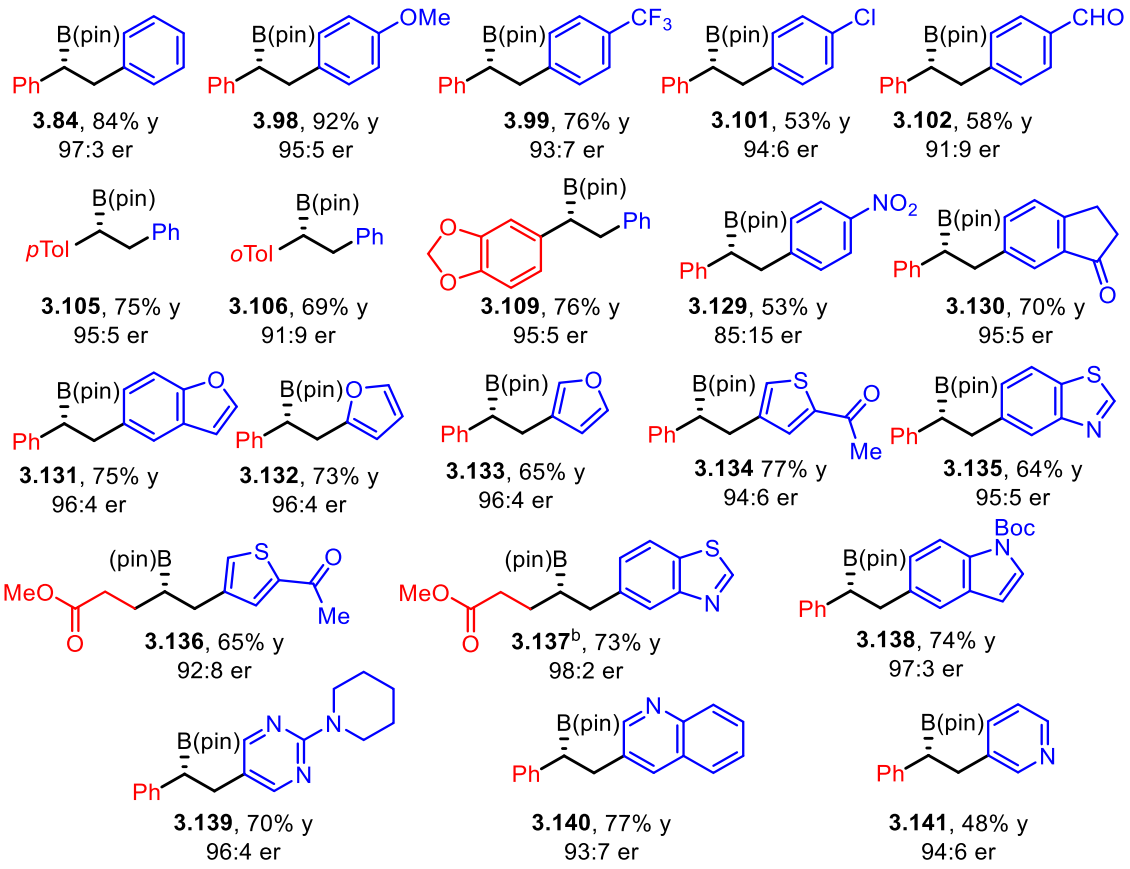
(**3.123**), a primary alkyl bromide (**3.120**), and an unprotected alcohol (**3.122**) (employing two equivalents of nucleophile) all survive boron-ate complex formation and conjunctive coupling, furnishing products in good yield and enantioselectivity. It is worth noting that electron-deficient migrating groups such as a *para*-trifluoromethylphenyl group can be employed successfully (**3.121**) with the current conditions whereas the previously reported reaction conditions furnished low yields of this product.[53] Lastly, it should be pointed out that conjunctive couplings involving vinyl–B(pin) and alkyl or aryl Grignard reagents (method A) were also effective.

A survey of the substrate scope involving organobromide electrophiles is depicted in Scheme 3.23. Of note, as found during optimization (Table 3.3/3.4), the yield and enantioselectivity with this substrate class parallels that observed when using organotriflate electrophiles so long as an added equivalent of NaOTf is included in the reaction. We were able to demonstrate the compatibility of these reactions with furan (**3.132**, **3.133**), thiophene (**3.134, 3.136**), quinolone (**3.135**), pyridine (**3.141**), pyrimidine (**3.139**), indole (**3.138**), benzofuran (**3.131**), benzothiazole (**3.135, 3.136**), and other functionalized organic bromides, suggesting that a large collection of targets may ultimately be available from conjunctive couplings, even when the corresponding organotriflate electrophile is not readily available. It should be noted that under the current conditions, alkenyl bromides are significantly less effective than alkenyl triflate electrophiles (i.e., substrate **3.104**, Scheme 3.22 was prepared in 34% yield, 94:6 er from the alkenyl bromide versus 76% yield, 96:4 er from the corresponding organotriflate electrophile).

[53] See reference 5.

Scheme 3.23. Conjunctive coupling between Grignard-derived boron-ate complexes and organobromides[a]





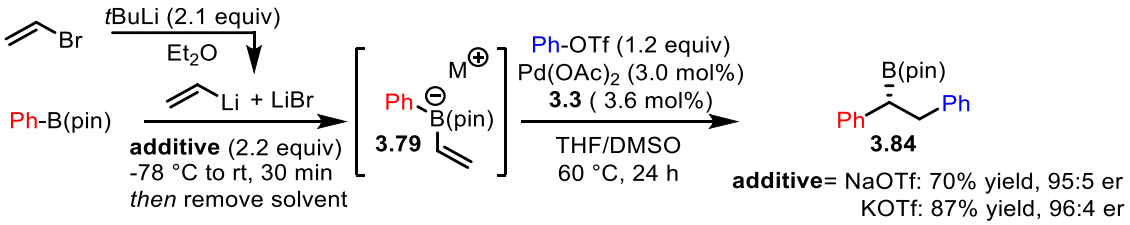
[a]Conjunctive coupling was conducted at 0.17 M. Yields represent isolated yields of purified material. Both the yield and the enantiomer ratio (er) represent the average value for two experiments. [b]Reaction conducted at 55 °C.

3.5.2 Conjunctive Coupling with C(sp^2) Triflates and Li-Based Boron-Ate Complexes Derived from Li-Halogen Exchange

In addition to enabling reactions of Grignard reagent-derived boron-ate complexes and aryl triflate or halide electrophiles, we imagined that the halide-scavenging ability of

NaOTf might enable the direct use of organolithium reagents generated by lithium-halogen exchange (i.e., without removal of lithium halide byproducts). Thus, vinyllithium, prepared by treatment of vinyl bromide with two equivalents of *tert*-butyllithim was directly added to PhB(pin) in the presence of either NaOTf or KOTf (Scheme 3.24). The derived boron-ate complex was then engaged in conjunctive coupling with PhOTf. While addition of NaOTf was effective, we found that KOTf performs somewhat better as a LiBr

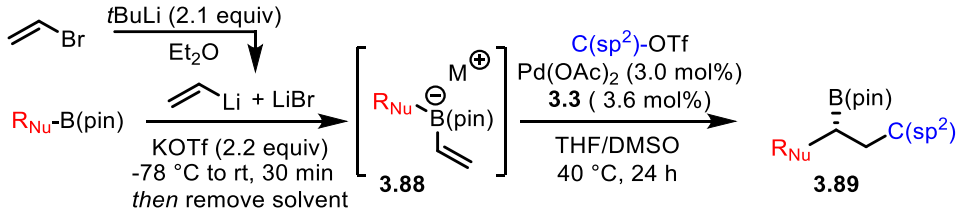
Scheme 3.24. Additive effect: coupling with halide-containing organolithium-derived boron-ate complexes[a]

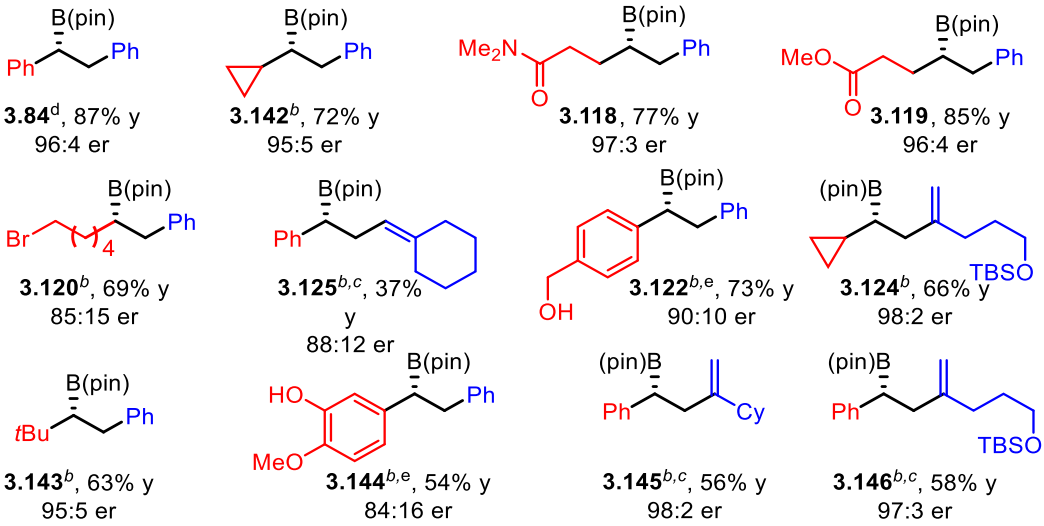


[a]Conjunctive coupling was conducted at 0.17 M. Yields represent isolated yields of purified material. Both the yield and the enantiomer ratio (er) represent the average value for two experiments.

scavenger in these reactions. The substrate scope for this set of conditions was similarly broad as the previously described methods employing Grignard nucleophiles. Notably, the use of NaOTf provided higher selectivity when alkenyl triflate electrophiles were employed (Scheme 3.25). While the mechanistic rationale for the improved yields observed utilizing KOTf with aryl organotriflate electrophiles and NaOTf with alkenyl organotriflate electrophiles is not clear, this empirical guide facilitated the preparation of products incorporating a sterically hindered *tert*-butyl migrating group **3.143** as well as groups containing labile **3.118**, **3.119**, **3.120** and even protic **3.122** functionality (a second equivalent was employed in this later case).

Scheme 3.25. Conjunctive coupling with halide-containing organolithium-derived boron-ate complexes[a]





[a]Conjunctive coupling was conducted at 0.17 M. Yields represent isolated yields of purified material. Both the yield and the enantiomer ratio (er) represent the average value for two experiments. [b]Product isolated as the derived alcohol. [c]NaOTf was employed in place of KOTf and the solvent was THF. [d]Reaction conducted at 60 °C. [e](2.0 equiv) of nucleophile weas employed.

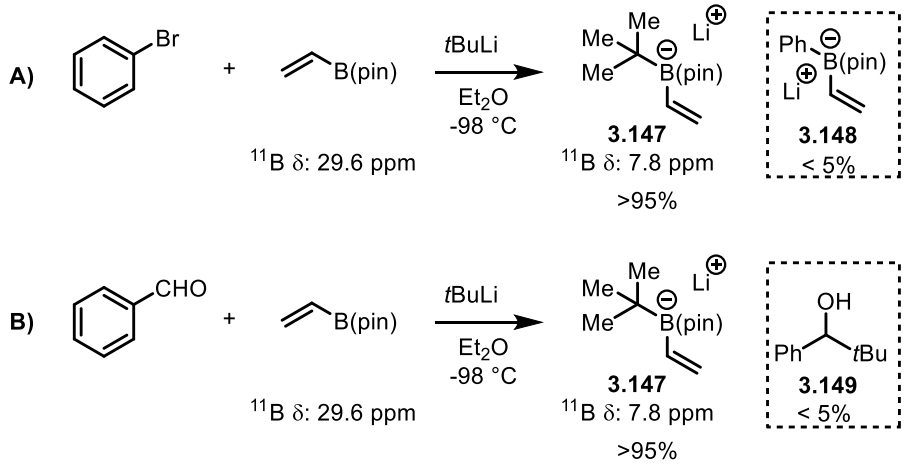
3.6 Functional Group Compatibility in Conjunctive Coupling

3.6.1 Boron-Buffered Nucleophilicity by Kinetic Trapping

Aspects of the functional group tolerance exhibited during the course of catalytic conjunctive coupling reactions are informative and merit comment. The examples in Scheme 3.22 reveal a range of functional groups — either attached to the electrophile or the boron-ate complex — that are compatible with catalytic conjunctive coupling reactions. While the compatibility of functional groups attached to the electrophile (i.e., product **3.102**) can be anticipated because of the modest basicity and nucleophilicity of boron-ate

complexes,[54] the ability to assemble functionalized boron-ate complexes by reacting functionalized boronic esters with organometallic compounds (Grignard and organolithium reagents) is less anticipated.[55] For example, effective production of compounds 3**.118**, **3.119**, **3.120** in Scheme 3.25 indicates that amides, esters, and alkyl halides survive treatment with organolithium reagents. Observing this, we considered that this functional group compatibility likely arises from the boronic ester's ability to act as both a kinetic and thermodynamic trap, thus serving to protect against direct reaction of strong nucleophiles with labile functional groups. We expected this feature of boron-ate complex formation might allow conjunctive couplings to be conducted as a three-component reaction without the need to pre-generate the boron-ate complex *in situ* before introduction of the electrophile and the catalyst. To probe the speed with which boron-ate complex formation

Scheme 3.26. Nucleophile trapping competition experiments

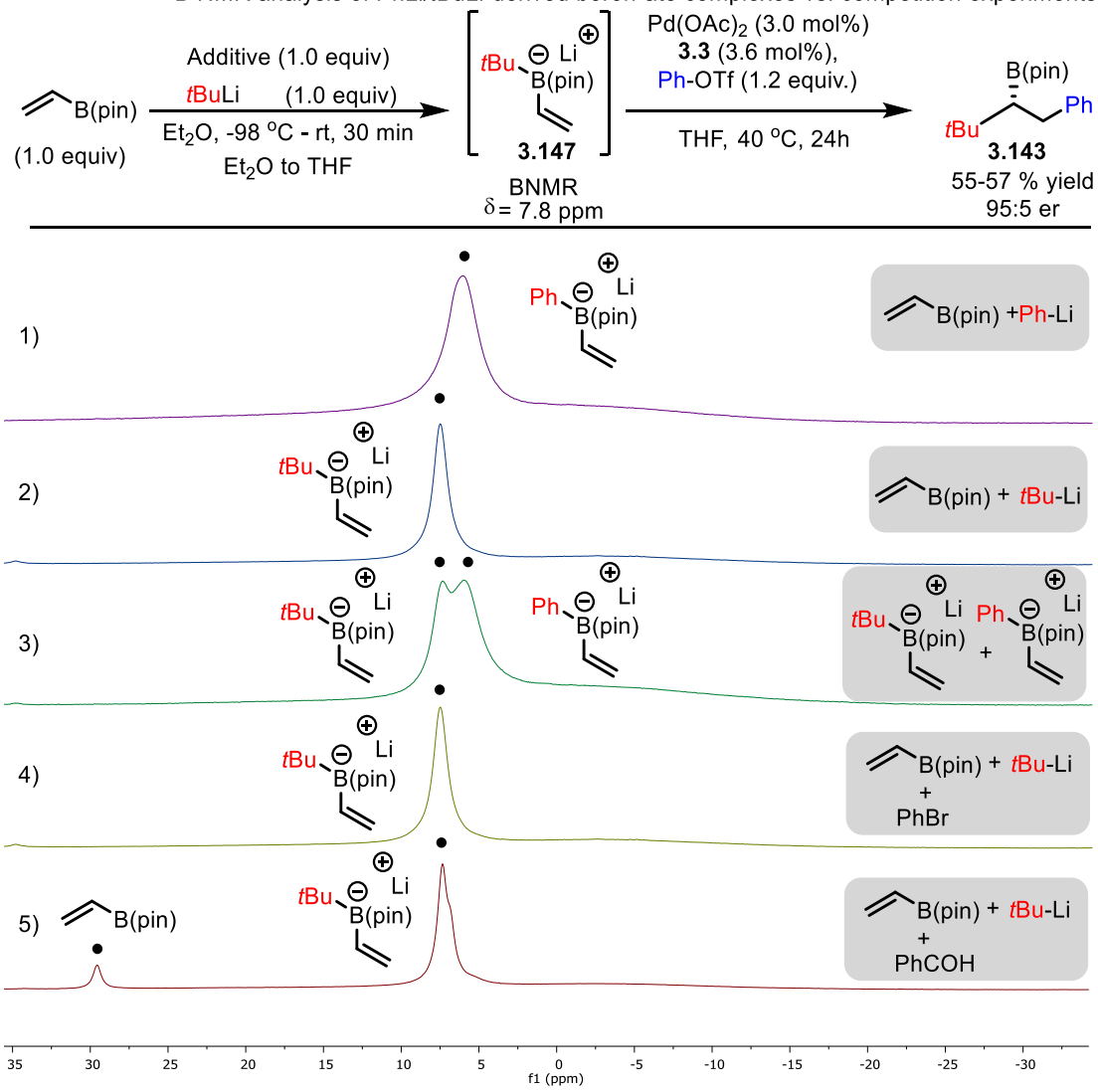


[54] (a) Feeney, K.; Berionni, G.; Mayr, H.; Aggarwal, V. K. *Org. Lett*. **2016**, 17, 2614. (b) Berionni, G.; Leonov, A. I.; Mayer, P.; Ofial, A. R.; Mayr, H. *Angew. Chem. Int. Ed*. **2015**, 54, 2780.

[55] For addition of alkyllithium reagents to B(pin) derivatives bearing esters and amides, see: (a) Odachowski, M.; Bonet, A.; Essafi, S.; Conti-Ramsden, P.; Harvey, J. N.; Leonori, D.; Aggarwal, V. K. *J. Am. Chem. Soc.* **2016**, 138, 9521. (b) Armstrong, R. J.; García-Ruiz, C.; Myers, E. L.; Aggarwal, V. K. *Angew. Chem. Int. Ed*. **2017**, 56, 786. (c) Wang, Y.; Noble, A.; Myers, E. L.; Aggarwal, V. K. *Angew. Chem. Int. Ed.* **2016**, 55, 4270. Review: (d) Matteson, D. J. *J. Organomet. Chem*. **1999**, 581, 51.

occurs relative to reactions of organometallic reagents with other functional groups, we conducted more challenging competition experiments (Scheme 3.26). In the first, a mixture of vinyl–B(pin) and bromobenzene was treated with *tert*-butyllithium at −98 °C in ether (scheme 3.26.A); the solvent was then removed and the ^{11}B NMR in THF was collected. In this experiment, the ^{11}B NMR resonance corresponding to vinylB(pin) (δ 29.6 ppm) was replaced with a resonance at 7.8 ppm corresponding to boron-ate complex **3.147**; a

Scheme 3.27 ^{11}B NMR analysis of PhLi/*t*BuLi-derived boron-ate complexes vs. competition experiments

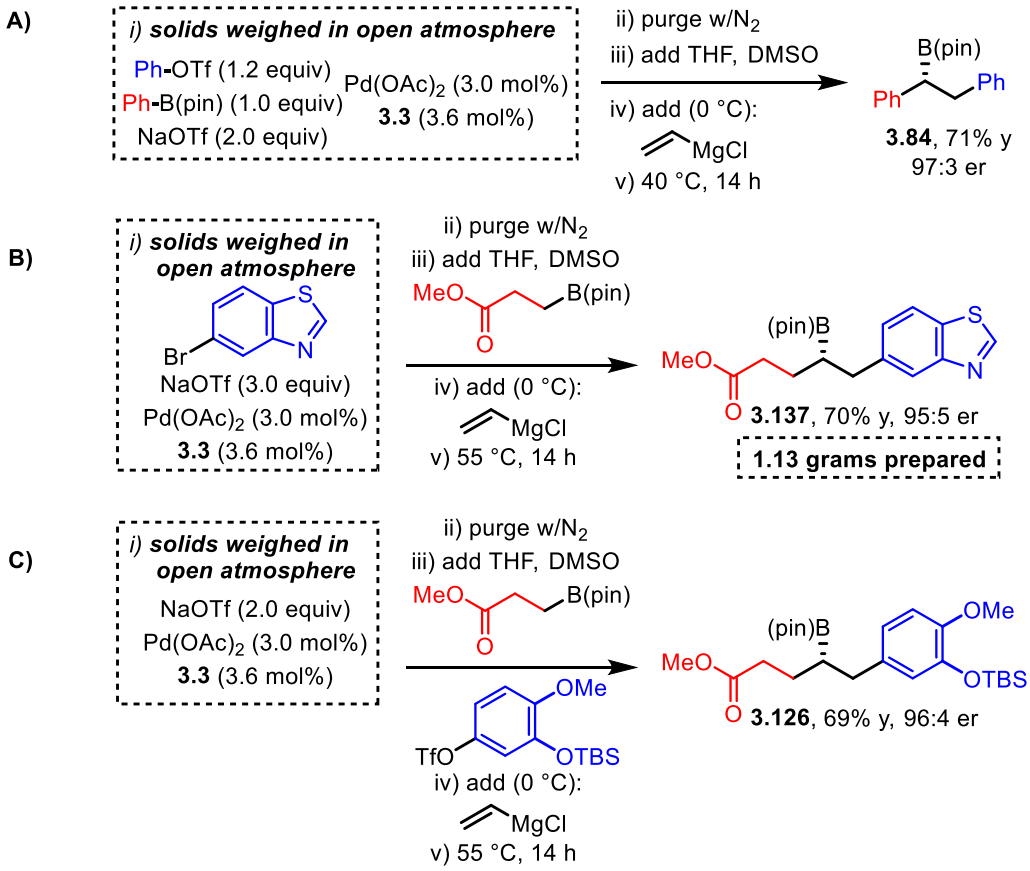


resonance at 5.8 ppm corresponding to the formation of **3.148** by addition of PhLi (generated by Li/Br exchange) to vinylB(pin) was not observed (see Scheme 3.27, eq. 1 through 4). Thus, addition of *tert*-butyllithium to vinylB(pin) appears to outcompete Li−Br exchange. When this reaction solution was subjected to conjunctive coupling, the desired product was isolated in comparable yield (57%) to the previously optimized reaction. Similarly, we found that addition of *tert*-butyllithium to vinylB(pin) also outcompeted addition to benzaldehyde (Scheme 3.26.B). Subjecting this reaction solution to conjunctive coupling conditions also resulted in the formation of the desired products (55% yield) (eq. 5, scheme 3.27).

3.6.2 Glovebox-Free and Preparative Scale Procedure

To probe the capacity for conjunctive couplings to be conducted without the aid of a glovebox, as a three-component assembly without preformation of boron-ate complexes, and on preparative scale, we examined the reactions shown in Scheme 3.28. In these experiments, the solid reagents were weighed in the open atmosphere, combined and transferred to a dried flask, and then the headspace of the reaction vessel was purged with dry nitrogen gas. After addition of liquid reagents and solvent, the flask was cooled to 0 °C, the Grignard reagent was added, and the reaction was allowed to proceed at the indicated temperature overnight. With this straightforward procedure, the derived conjunctive coupling products were obtained in good yield and enantioselectivity. As depicted in Scheme 3.28.B, the reaction can be operated in this manner even on preparative scale and provides functionalized products in a practical fashion. Lastly, this procedure applies

Scheme 3.28 Glovebox-free procedure to conduct conjunctive couplings as a three-component assembly



regardless of whether the substrates are both solids (3.28.A), both liquids (3.28.C), or one of each (3.28.B).

3.7 Conclusion

We have identified that key challenges associated with the use of Grignard reagent-derived boron-ate complexes arise from a combination of ineffective boron-ate complex formation and inhibition of conjunctive coupling reactions by the presence of halide ions. The latter problem contributes to the diminished reactivity of organohalide electrophiles in conjunctive couplings as well. The addition of NaOTf or KOTf largely counteracts these

problems and provides a convenient and broad-scoped catalytic conjunctive coupling process. We anticipate that these reactions may find use in organic synthesis and that the utility of alkali metal triflates may find use in the development of other catalytic processes involving boron reagents.

3.8 Experimental

3.8.1 General Information

Note: NMR spectra of compounds included in the following sections have been previously published and can be accessed online. ^{1}H NMR spectra were recorded on either a Varian Gemini-500 (500 MHz), Varian Gemini-600 (600 MHz), or Varian Inova-500 (500 MHz) spectrometer. Chemical shifts are reported in ppm with the solvent resonance as the internal standard ($CDCl_3$: 7.24 ppm). Data are reported as follows: chemical shift, integration, multiplicity (s = singlet, d = doublet, t = triplet, q = quartet, p = pentet, m = multiplet, app = apparent), and coupling constants (Hz). ^{13}C NMR spectra were recorded on either a Varian Gemini-500 (125 MHz), Varian Gemini-600 (150 MHz) or a Varian Inova-500 (125 MHz) spectrometer with complete proton decoupling. Chemical shifts are reported in ppm with the solvent resonance as the internal standard ($CDCl_3$: 77.24 ppm). Chemical shifts are reported in ppm using phosphoric acid as the external standard (H_3PO_4: 0.0 ppm). ^{11}B NMR spectra were recorded on a Varian Gemini-500 (128 MHz) spectrometer. Chemical shifts are reported in ppm using boron trifluoride diethyl etherate as the external standard ($BF{\cdot}OEt_2$: 0.0 ppm). ^{19}F NMR spectra were recorded on a Varian Gemini-500 (470 MHz) spectrometer. Infrared (IR) spectra were recorded on a Bruker alpha-P Spectrometer. Frequencies are reported in wavenumbers (cm^{-1}) as follows: strong (s), broad (br), medium (m), and weak (w). Optical rotations were measured on a Rudolph Analytical Research Autopol IV Polarimeter and the values reported are averages of seven measurements. High-resolution mass spectrometry (DART) was performed at the Mass Spectrometry Facility, Boston College, Chestnut

Hill, MA. Liquid chromatography was performed using forced flow (flash chromatography) on silica gel (SiO_2, 230 x 450 Mesh, purchased from Silicycle) either manually or using an automated column (Biotage). Thin layer chromatography (TLC) was performed on 25 μm silica gel aluminum backed plates from Silicycle. Visualization was performed using ultraviolet light (254 nm), ceric ammonium molybdate (CAM) in ethanol or phosphomolybdic acid, and cerium(IV) sulfate in ethanol with sulfuric acid (Seebach).

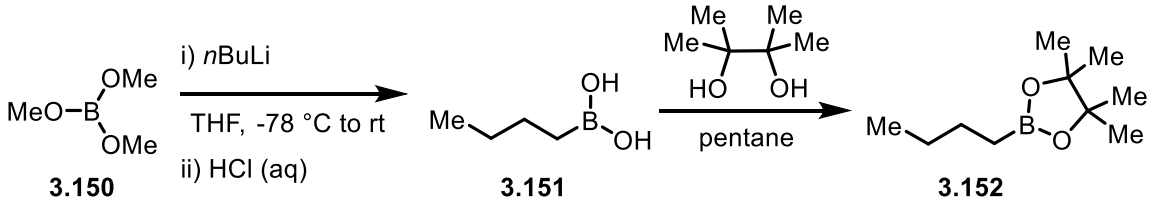
Analytical supercritical fluid chromatography (SFC) was performed on a TharSFC Method Station II equipped with Waters 2998 Photodiode Array Detector with isopropanol or methanol as the modifier.

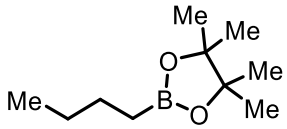
Tetrahydrofuran (THF), diethyl ether (Et_2O), dichloromethane (DCM) and toluene were purified using Pure Solv MD-4 solvent purification system, from Innovative Technology, Inc., by passing the solvent through two activated alumina columns after purging with argon. Palladium (II) acetate, (S_p,S_p)-**3.3**, 1,1′-Bis(dicyclohexyl-phosphino)ferrocene, and 1,1′-Bis(diisopropylphosphino)ferrocene were purchased from Strem Chemicals, Inc. and used without further purification. Pinacol was purchased from Aldrich. All pinacol esters were purchased from Combi Blocks, Okwood Chemicals, or Frontier Scientific and used without further purification. All Organobromides were purchased from Combi Blocks, Okwood Chemicals, or Frontier Scientific and used without further purification. Phenyl trifluoromethanesulfonate, 4-methoxyphenyltrifluoro methanesulfonate, and trifluoromethane-sulfonic anhydride were purchased from Oakwood Chemicals and used without further purification. All other reagents were

purchased from either Aldrich, Alfa Aesar or Acros and used without further purification.

3.8.2 Experimental Information

3.8.2.1 Procedures for Preparation of Boronate Esters

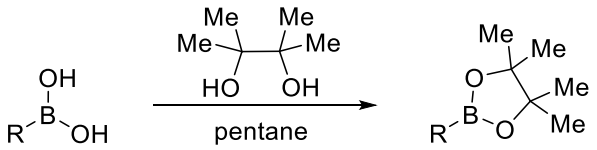




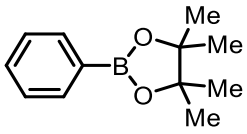
2-Butyl-4,4,5,5-tetramethyl-1,3,2-dioxaborolane (3.152). To an oven-dried 250 mL round bottom flask with magnetic stir bar under N_2 was added trimethylborate (11.21 g, 106.8 mmol, 1.78 equiv) and 50 mL of tetrahydrofuran. The flask was allowed to cool to -78 ˚C and *n*BuLi (23.72 mL, 2.53 M, 60 mmol, 1.0 equiv) was added over 2 h by syringe pump. After addition of *n*BuLi the solution was allowed to warm to room temperature and stir for 8 h, after which a 1 M solution of aquious HCl (30 mL) was added and the solution was allowed to stir at room temperature for 2 h. The product was extracted from solution with 4 x 20 mL of diethyl ether and the combined organic layers were washed with brine, dried with Na_2SO_4, filtered with diethyl ether and the solvent was removed *in vacuo*. The resulting oil (**3.151)** was subjected to the general procedure for preparation of boronate esters above.

The product was isolated as clear, colorless oil (5.26 g, 52 % yield). All spectral data was in accord with the literature.[56]

General Procedure for the Preparation of Boronate Esters



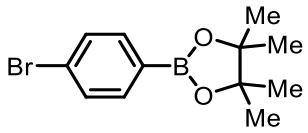
To an oven-dried round bottom flask with magnetic stir bar was added boronic acid (1.0 equiv) and pentane. The suspension was allowed to cool to 0 ˚C and 2,3-dimethylbutane-2,3-diol (pinacol) (1.05 equiv) was added neat and the solution was allowed to warm to room temperature and stir for 3 h. If a water layer was observed it was removed and the resulting pentane solution was dried with with Na_2SO_4, filtered with diethyl ether, and the solvent was removed *in vacuo*. The resulting residue was purified on silica gel (plug with CH_2Cl_2 as the eluent).



5,5-Dimethyl-2-phenyl-1,3,2-dioxaborinane (3.76). Preparted according to the general procedure above with phenylboronic acid (0.268 g, 22.0 mmol, 1.0 equiv), pinacol (2.41 g, 23.1 mmol, 1.05 equiv), and pentane (60 mL). The resulting white solid (4.18 g, quantitative yield) was used without further

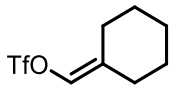
[56] Yamamoto, Y.; Fujikawa, R.; Umemoto, T.; Miyaura, N. *Tetrahedron* **2004**, 60, 10695.

purification. All spectral data was in accord with the literature.[57] This compound is commercially available [CAS: 24388-23-6].



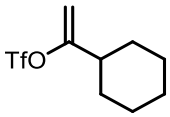
2-(4-Bromophenyl)-4,4,5,5-tetramethyl-1,3,2-dioxaborolane (3.153). Prepared according to the general procedure above with 4-bromophenylboronic acid (1.00 g, 5.0 mmol, 1.0), pinacol (0.620 g, 5.25 mmol, 1.05), and pentane (15 mL). The resulting white solid (1.19 g, 84% yield) was used without further purification. All spectral data was in accord with the literature.[58] This compound is commercially available [CAS: 68716-49-4].

3.8.2.2 Procedures for Preparation of Alkenyl and Aryl Trifluoromethanesulfonates

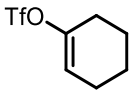


Cyclohexylidenemethyl trifluoromethanesulfonate (3.154). The title compound was prepared according to the procedure reported in the literature.[59] All spectral data was in accord with the literature.[60]

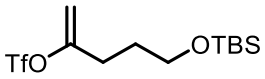
[57] Clary, J. W.; Rettenmaier, T. J.; Snelling, R.; Bryks, W.; Banwell, J.; Wipke, W. T.; Singaram, B. *J. Org. Chem.* **2011**, 76, 9602.
[58] Zhu, W.; Ma, D. *Org. Lett.* **2006**, 8, 261.
[59] Stang, P. J.; Treptow, W. *Synthesis* **1980**, 4, 283.
[60] Al-huniti, M. H.; Lepore, S. D. *Org. Lett*. **2014**, 16, 4154.



1-Cyclohexylvinyl trifluoromethanesulfonate (3.155). The title compound was prepared according to the procedure reported in the literature.[59] All spectral data was in accord with the literature.[60]

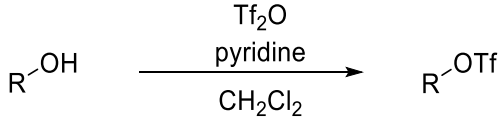


Cyclohex-1-en-1-yl trifluoromethanesulfonate (3.156). The title compound was prepared according to the procedure reported in the literature.[59] All spectral data was in accord with the literature.[60]



5-((*tert*-Butyldimethylsilyl)oxy)pent-1-en-2-yl trifluoromethanesulfo-nate (3.157). The title compound was prepared according to the procedure reported in the literature.[61] All spectral data was in accord with the literature.

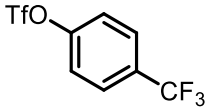
General Procedure for the Synthesis of Aryl Trifluoromethanesulfonates



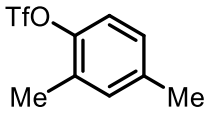
Aryl trifluoromethanesulfonates were made according to literature procedure with slight modification.[62] To a solution of the corresponding phenol and pyridine in CH_2Cl_2 at 0 ˚C, a solution of trifluoromethanesulfonic anhydride in CH_2Cl_2 was added dropwise. The mixture was then allowed to warm to room temperature and stir for 1 h. The mixture was

[61] Zhang, L.; Lovinger, G. J.; Edelstein, E. K.; Szymaniak, A. A.; Chierchia, M. P.; Morken, J. P. *Science* **2016**, 351, 70.
[62] Goosen, L. J.; Linder, C.; Rodríguez, N.; Lange, P. P. *Chem. Eur. J.* **2009**, 15, 9336.

diluted with Et_2O, quenched with a 3 M solution of aquious HCl and washed successively with a saturated solution of aqueous $NaHCO_3$ and brine. The solution was dried over Na_2SO_4, filtered with Et_2O, and the solvent was removed *in vacuo*. The residue was purified by silica gel chromatography to afford aryl trifluoromethanesulfones.



4-(Trifluoromethyl)phenyl trifluoromethanesulfonate (3.158). Prepared according to the general procedure above with 4-trifluoromethylphenol (0.630 g, 3.8 mmol, 1.0 equiv), trifluoromethanesulfonic anyhydride (0.774 mL, 4.6 mmol, 1.21 equiv), pyridine (0.615 mL, 7.6 mmol, 2.0 equiv), and CH_2Cl_2 (6.0 mL). The unpurified residue was purified by silica gel chromatography (10% ethyl acetate/Hexanes) to afford the product as colorless oil (1.180 g, 98% yield). All spectral data was in accord with the literature.[63]



2,4-Dimethylphenyl trifluoromethanesulfonate (3.159). Prepared according to the general procedure above with 2,4-dimethylphenol (0.906 mL, 7.5 mmol, 1.0 equiv), trifluoromethanesulfonic anhydride (1.50 mL, 9.0 mmol, 1,2 equiv), pyridine (1.2 mL, 15.0 mmol, 2.0 equiv), and CH_2Cl_2 (13.0 mL). The unpurified residue was purified by silica gel chromatography (5% ethyl acetate/Hexanes) to afford the product as colorless oil (1.680 g, 88% yield). All spectral data was in accord with the literature.[64]

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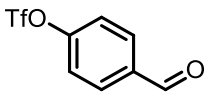
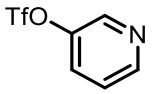
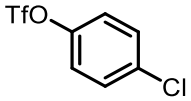
[63] Gill, D.; Hester, A. J.; Lloyd-Jones, G. C. *Org. Biomol. Chem.* **2004**, 4, 2547.
[64] Radivoy, G.; Alonso, F.; Yus, M. *Tetrahedron* **1999**, 55, 14479.



4-Formylphenyl trifluoromethanesulfonate (3.160). Prepared according to the general procedure above with 4-hydroxybenzaldehyde (0.488 g, 4.0 mmol, 1.0 equiv), trifluoromethanesulfonic anhydride (0.81 mL, 4.8 mmol, 1.2 equiv), pyridine (0.65 mL, 8.0 mmol, 2.0 equiv), and CH_2Cl_2 (7.0 mL). Following quenching, extraction, drying, and concentrating *in vacuo*, the unprurified residue was passed through a Celite pad, which was washed with copious amounts of CH_2Cl_2, to afford the product as colorless oil (0.60 g, 60% yield); the product decomposes upon exposure to silica gel. All spectral data was in accord with the literature.[65]



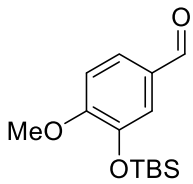
Pyridin-3-yl trifluoromethanesulfonate (3.161). Prepared according to the general procedure above with 3-hydroxypyridine (0.380 g, 4.0 mmol, 1.0 equiv), trifluoromethanesulfonic anhydride (0.81 mL, 4.8 mmol, 1.2 equiv), pyridine (0.65 mL, 8.0 mmol, 1.2 equiv), and CH_2Cl_2 (20.0 mL). The reaction was quenched with water (20 mL) instead of HCl. Following quenching, extraction, drying, and concentrating *in vacuo*, the unpurified residue was purified by silica gel chromatography (30% ethylacetate/Hexanes) to afford the product as yellow oil (0.69 g, 76% yield). All spectral data was in accord with the literature.[65]



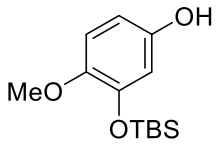
4-Chlorophenyl trifluoromethanesulfonate (3.162). Prepared according to the general procedure above with 4-chlorophenol (0.514 g, 4.0 mmol, 1.0 equiv), trifluoromethanesulfonic anhydride (0.81 mL, 4.8 mmol, 1.2 equiv),

[65] Echavarren, A. M.; Stille, J. K. *J. Am. Chem. Soc.* **1987**, 109, 5478.

pyridine (0.65 mL, 8.0 mmol, 2.0 equiv), and CH_2Cl_2 (7.0 mL). The unpurified residue was purified by silica gel chromatography (30% ethyl acetate/Hexanes) to afford the product as colorless oil (0.877 g, 84% yield). All spectral data was in accord with the literature.[66]



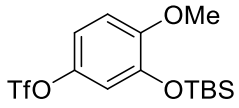
3-((*tert*-Butyldimethylsilyl)oxy)-4-methoxybenzaldehyde (3.163). To an oven-dried 100 mL round bottom flask equipped with a magnetic stir bar was added Isovanillin (**3.164**) (4.12 g, 28.29 mmol, 1.0 equiv) and *N,N*-dimethylformamide (30 mL). The solution was allowed to cool to 0 ˚C under a nitrogen atmosphere, and *N,N*-diisopropylethylamine (6.83 g, 52.82 mmol, 2.0 equiv) was added and the solution was allowed to stir for 10 min. To the cooled solution was added *tert*-butyldimethylsilyl chloride (4.7565 g, 31.56 mmol, 1.2 equiv) as a 1 M solution in THF over 30 min by syringe pump. The solution was allowed to warm to room temperature and stir for 12 h. The solution was diluted with diethyl ether, washed with water and brine, and dried with Na_2SO_4. After removing solvent under reduced pressure the residue was purified by silica gel chromatography (10% EtOAc in hexane) and the product was obtained as colorless oil (6.89 g, 99% yield). All spectral data was in accord with the literature.[67]



3-((*tert*-Butyldimethylsilyl)oxy)-4-methoxyphenol (3.165). To an oven-dried 250 mL round bottom flask equipped with a magnetic stir

[66] Murai, N.; Yonaga, M.; Tanaka, K. *Org. Lett.* **2012**, 14, 1278.
[67] Ramana. Reddy, M. V.; Mallireddigari, M. R.; Cosenza, S. C.; Pallela, V. R.; Iqbal, N. M.; Robell, K. A.; Kang, A. D.; Reddy, E. P. *J. Med. Chem.* **2008**, 51, 86.

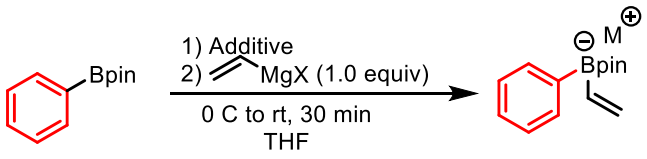
bar was added TBS-protected Isovanillin (**3.163**) (6.89 g, 25.99 mmol, 1.0 equiv) and anhydrous CH_2Cl_2 (103 mL), the solution was allowed to cool to 0 °C and was placed under nitrogen. To this cooled solution was added 3-chloroperbenzoic acid (13.45 g, 38.98, 1.5 equiv), the solution was refluxed for 3 h, and the resulting solution was washed twice with a saturated aqueous solution of $NaHCO_3$. The organic phase was dried over anhydrous $MgSO_4$ and the solvent was removed under reduced pressure. The resulting residue was dissolved in methanol (150 mL), and to this solution was added Na_2CO_3 (0.64 g, 5.19 mmol, 0.2 equiv). The mixture was allowed to stir at room temperature for 2 h, after which the solution was quenched with a saturated solution of aqueous NH_4Cl and extracted with CH_2Cl_2 (4x45 mL). The combined organic layers were dried over Na_2SO_4, filtered through a neutral alumina pad, and concentrated under reduced pressure. The resulting residue was used in next step without further purification.



3-(*tert*-Butyldimethylsilyloxy)-4-methoxyphenyl trifluoromethanesulfonate (3.166). The residue from the last step (**3.165**) was subjected to the general procedure for preparation of aryl triflates to afford the product (8.1837 g, 97% yield). (81% overall yield over three steps). **^{1}H NMR** (600 MHz, $CDCl_3$) δ 6.84-6.80 (2H, m), 6.85 (1H, d, J = 2.4 Hz), 3.80 (3H, s), 0.97 (9H, s), 0.15 (6H, s). **^{13}C NMR** (150 MHz, $CDCl_3$) δ 151.2, 146.1, 142.8, 122.2, 120.0, 117.9, 114.5, 114.2, 112.0, 56.0, 25.8, 18.6, -4.5. **IR** (neat) ν_{max} 2932.6 (w), 1603.6 (m), 1505.0 (s), 1419.9 (m), 1181.4 (s), 1107.9 (s), 882.2 (m), 826.9 (s), 802.1 (s), 693.6 (m), 599.4 (m), 505.6 (s) cm^{-1}. **HRMS** (DART) for $C_{14}H_{22}F_3O_5S_1Si_1$ $[M+H]^+$ calculated: 387.0909, found: 387.0908.

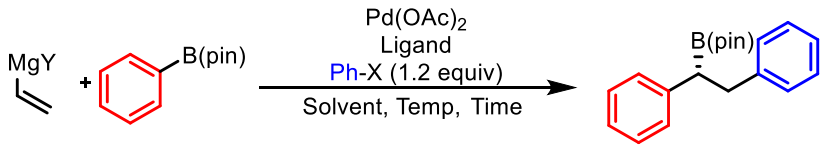
3.8.2.3 ^{11}B NMR Analysis of Boron "Ate" Formation with Various Additives

"Standard" indicates no improvement vs. no additive. Ratios of PhBpin: boron-ate are estimates based on ^{11}B NMR.



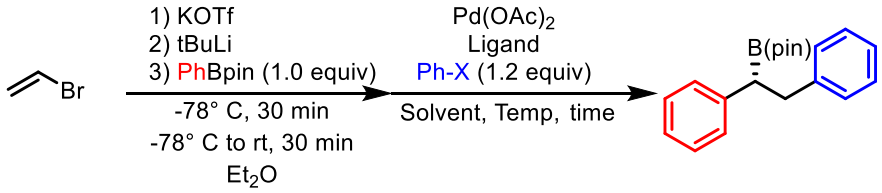
Entry	X	Additive	Ate:PhBpin
1	Br/Cl	none	Standard
2	**Br/Cl**	**LiCl (1 equiv)**	**>95:5**
3	Br	LiBr (1 equiv)	Standard
4	**Br/Cl**	**LiOTf (1 equiv)**	**>95:5**
5	**Br/Cl**	**NBu_4OTf (2 equiv)**	**85:15**
6	Br	$Mg(OTf)_2$ (2 equiv)	Standard
7	Br	$Sc(OTf)_3$ (2 equiv)	Standard
8	Br/Cl	$NaBPh_4$ (2 equiv)	~40:60
9	Br	$Yb(OTf)_3$ (2 equiv)	Standard
10	Br	KPF_6 (2 equiv)	~70:30
11	Br	KNO_3 (2 equiv)	~70:30
12	Br	KOAc (2 equiv)	~60:40
13	Br	K_3PO_4 (2 equiv)	~20:80
14	Br	K_2CO_3 (2 equiv)	20:80
15	**Br/Cl**	**KOTf (2 equiv)**	**>95:5**
16	**Br/Cl**	**NaOTf (2 equiv)**	**>95:5**
17	Br	KOTf:LiOTf (1:1 equiv)	60:40
18	Br/Cl	CaOTf (2 equiv)	standard
19	Br/Cl	$Eu(OTf)_3$ (2 equiv)	~50:50

3.8.2.4 Optimization of Conjunctive Coupling with Vinyl Grignard Reagent



Entry	Additive	Y	X	cat (mol%)	Solvent	Temp (°C)	Time (h)	yield (%)	er
1	NA	Br	OTf	3.0	THF	60	14	0	NA
2	LiCl (1.0 equiv)	Br	OTf	3.0	THF	60	14	0	NA
3	LiOTf (1.0 equiv)	Br	OTf	3.0	THF	60	14	0	NA
4	KOTf (1.0 equiv)	Br	OTf	3.0	THF	40	14	10	94:6
5	KOTf (2.0 equiv)	Br	OTf	3.0	THF	40	14	64	92:8
6	KOTf (3.0 equiv)	Br	OTf	3.0	THF	40	14	65	92:8
7	NaOTf (2.0 equiv)	Br	OTf	3.0	THF	40	14	58	94:6
8	KOTf (2.0 equiv)	Cl	OTf	3.0	THF	60	14	34	89:11
9	KOTf (2.0 equiv)	Cl	OTf	2.0	THF	24	14	63	93:7
10	NaOTf (2.0 equiv)	Cl	OTf	3.0	THF	60	14	66	92:8
11	NaOTf (2.0 equiv)	Cl	OTf	3.0	THF	24	14	75	93:7
12	NaOTf (2.0 equiv)	Cl	OTf	3.0	THF	40	14	72	94:6
13	NaOTf (1.0 equiv)	Cl	OTf	3.0	THF:DMSO 1:1	40	24	45	97:3
14	**NaOTf (2.0 equiv)**	**Cl**	**OTf**	**3.0**	**THF:DMSO 1:1**	**40**	**24**	**81**	**96:4**
15	NaOTf (2.0 equiv)	Cl	Br	3.0	THF	40	14	4	94:6
16	NaOTf (2.0 equiv)	Cl	Br	3.0	THF	60	14	8	94:6
17	NaOTf (3.0 equiv)	Cl	Br	3.0	THF	40	14	33	94:6
18	NaOTf (3.0 equiv)	Cl	Br	3.0	THF	60	14	30	92:8
19	NaOTf (3.0 equiv)	Cl	Br	3.0	DMSO	40	14	80	94:6
20	**NaOTf (3.0 equiv)**	Cl	Br	**3.0**	**THF:DMSO 1:1**	**60**	**24**	**84**	**97:3**
21	NaOTf (3.0 equiv)	Cl	Br	2.0	THF:DMSO 1:1	60	24	8	95:5
22	NaOTf (3.0 equiv)	Cl	Br	1.0	THF:DMSO 1:1	60	24	54	96:4
23	NaOTf (3.0 equiv)	Cl	Br	1.0	THF:DMSO 1:1	70	24	69	95:5
24	NaOTf (3.0 equiv)	Cl	Br	2.0	THF:DMSO 1:3	60	24	84	97:3
25	NaOTf (3.0 equiv)	Cl	Br	2.0	THF:DMSO 1:3	70	24	80	96:4

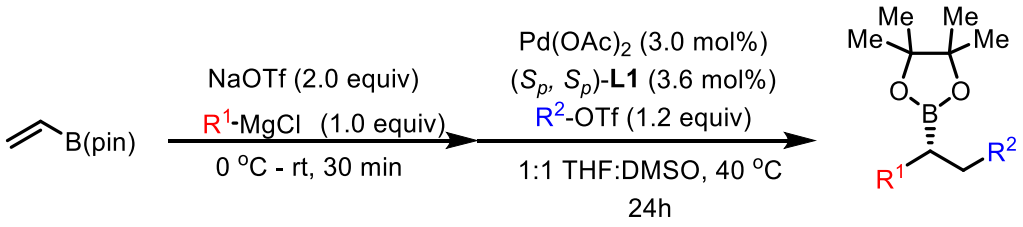
3.8.2.5 Optimization of Conjunctive Coupling with Vinyllithium



Entry	Additive	X	cat (mol%)	Solvent	Temp (°C)	Time (h)	yield (%)	er
1	KOTf (1.0 equiv)	OTf	3.0	THF	60	14	75	94:6
2	KOTf (2.0 equiv)	OTf	3.0	THF	60	14	77	94:6
3	NaOTf (2.0 equiv)	OTf	3.0	THF	60	14	70	95:5
4	KOTf (3.0 equiv)	OTf	3.0	THF	60	14	56	94:6
5	**KOTf (2.2 equiv)**	**OTf**	**3.0**	**1:1 DMSO:THF**	**60**	**18**	**87**	**96:4**
6	KOTf (2.2 equiv)	OTf	3.0	1:1 DMSO:THF	40	18	53	97:3
7	NaOTf (1.0 equiv)	OTf	3.0	1:1 DMSO:THF	60	18	62	96:4
8	KOTf (1.1 equiv)	OTf	3.0	1:1 DMSO:THF	60	18	72	95:5
9	KOTf (1.0. equiv)	Br	3.0	1:1 DMSO:THF	60	14	14	93:7
10	KOTf (2.0 equiv)	Br	3.0	1:1 DMSO:THF	60	14	55	96:4

3.8.2.6 General Procedures for Conjunctive Coupling

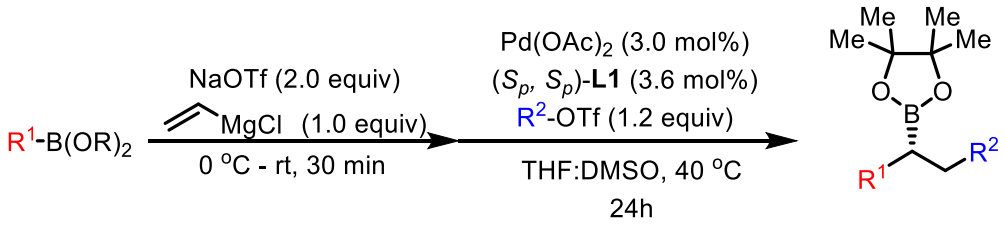
Method A:



In a glovebox under argon an oven-dried 2-dram vial equipped with a magnetic stir bar was charged with 4,4,5,5-tetramethyl-2-vinyl-1,3,2-dioxaborolane (0.30 mmol, 1.00 equiv), sodium trifluoromethanesulfonate (0.60 mmol, 2.00 equiv), and tetrahydrofuran (0.5 mL),

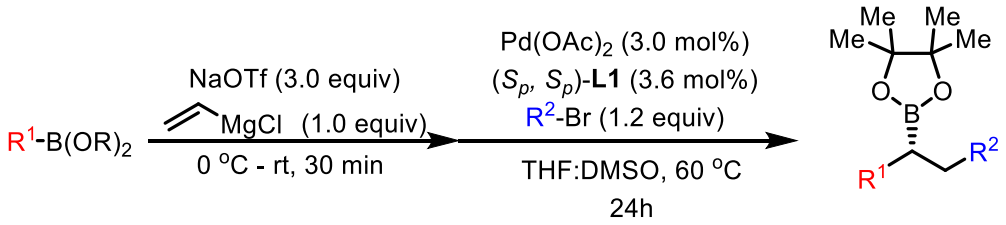
sealed with a septum cap, and removed from the glovebox. Under positive nitrogen pressure the vial was allowed to cool to 0 ºC, and organomagnesium chloride solution in tetrahydrofuran (0.30 mmol, 1.0 equiv) was added dropwise. The vial was allowed to warm to room temperature and stir for 30 min before being brought back into the glovebox. In the glovebox a second oven-dried 2-dram vial equipped with a magnetic stir bar was charged with $Pd(OAc)_2$ (0.90 mL, 0.01 M in dimethyl sulfoxide, 0.009 mmol, 0.03 equiv), and (S_p,S_p)-**3.3** (0.0108 mmol, 0.036 equiv). The $Pd(OAc)_2$/(S_p,S_p)-**3.3** solution was allowed to stir for 15 min at room temperature. The $Pd(OAc)_2$/(S_p,S_p)-**3.3** solution was then transferred into the vial, followed by tetrahydrofuran (0.2 mL) (used to rinse the $Pd(OAc)_2$/(S_p,S_p)-**3.3** vial), and aryl/vinyl trifluoromethanesulfonate (0.36 mmol, 1.20 equiv). The vial was sealed with a polypropylene cap, taped, and brought out of the glovebox where it was allowed to stir at 40 ºC for 24 h. To the resulting mixture was added water (10 mL) and the product was extracted from the aqueous layer with ethyl acetate (3 x 20 mL). The combined organic layers were dried over Na_2SO_4, concentrated under reduced pressure, filtered through a silica gel plug with diethyl ether, reconcentrated, and subsequently purified by silica gel chromatography to provide the desired products.

Method B:



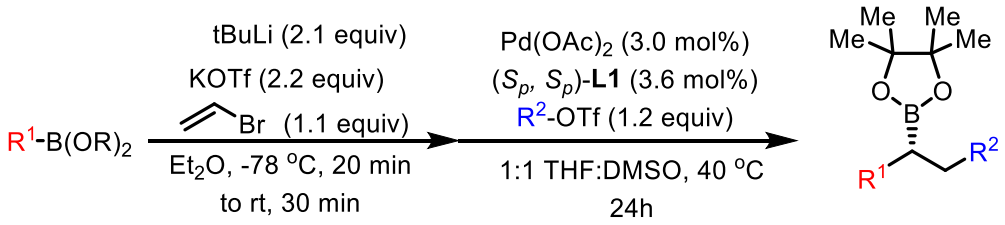
In a glovebox under argon an oven-dried 2-dram l equipped with a magnetic stir bar was charged with boronate (0.30 mmol, 1.00 equiv), sodium trifluoromethanesulfonate (0.60 mmol, 2.00 equiv), and tetrahydrofuran (0.5 mL), sealed with a septum cap, and removed from the glovebox. Under positive nitrogen pressure the vial was allowed to cool to 0 ºC and vinylmagnesium chloride solution in tetrahydrofuran (0.30 mmol, 1.0 equiv) was added dropwise. The vial was allowed to warm to room temperature and stir for 30 min before being brought back into the glovebox. In the glovebox a second oven-dried 2-dram vial equipped with a magnetic stir bar was charged with $Pd(OAc)_2$ ((0.90 mL, 0.01 M in dimethyl sulfoxide, 0.009 mmol, 0.03 equiv), and (S_p,S_p)-**3.3** (0.0108 mmol, 0.036 equiv.). The $Pd(OAc)_2$/(S_p,S_p)-**3.3** solution was allowed to stir for 15 min at room temperature. The $Pd(OAc)_2$/(S_p,S_p)-**3.3** solution was then transferred into the vial, followed by tetrahydrofuran (0.2 mL) (used to rinse the $Pd(OAc)_2$/(S_p,S_p)-**3.3** vial), and aryl/vinyl trifluoromethanesulfonate (0.36 mmol, 1.20 equiv). The vial was sealed with a polypropylene cap, taped, and brought out of the glovebox where it was allowed to stir at 40 ºC for 24 h. To the resulting mixture was added water (10 mL) and the aqueous layer was extracted with ethyl acetate (3 x 20 mL). The combined organic layers were dried over Na_2SO_4, concentrated under reduced pressure, filtered through a silica gel plug with diethyl ether, reconcentrated, and subsequently purified by silica gel chromatography to provide the desired products.

Method C:



In a glovebox under argon an oven-dried 2-dram vial equipped with a magnetic stir bar was charged with boronate (0.30 mmol, 1.00 equiv), sodium trifluoromethanesulfonate (0.60 mmol, 2.00 equiv), and tetrahydrofuran (0.5 mL), sealed with a septum cap, and removed from the glovebox. Under positive nitrogen pressure the vial was allowed to cool to 0 ºC, and vinylmagnesium chloride solution in tetrahydrofuran (0.30 mmol, 1.0 equiv) was added dropwise. The vial was allowed to warm to room temperature and stir for 30 min before being brought back into the glovebox. In the glovebox a second oven-dried 2-dram vial equipped with a magnetic stir bar was charged with $Pd(OAc)_2$ ((0.90 mL, 0.01 M in dimethyl sulfoxide, 0.009 mmol, 0.03 equiv), and (S_p,S_p)-**3.3** (0.0108 mmol, 0.036 equiv). The $Pd(OAc)_2$/(S_p,S_p)-**3.3** solution was allowed to stir for 15 min at room temperature. The $Pd(OAc)_2$/(S_p,S_p)-**3.3** solution was then transferred into the vial, followed by tetrahydrofuran (0.2 mL) (used to rinse the $Pd(OAc)_2$/(S_p,S_p)-**3.3** vial), and arylbromide (0.36 mmol, 1.20 equiv). The vial was sealed with a polypropylene cap, taped, and brought out of the glovebox where it was allowed to stir at 60 ºC for 24 h. To the resulting mixture was added water (10 mL) and the product was extracted from the aqueous layer with ethyl acetate (3 x 20 mL). The combined organic layers were dried over Na_2SO_4, concentrated under reduced pressure, filtered through a silica gel plug with diethyl ether, reconcentrated, and subsequently purified by silica gel chromatography to provide the desired products.

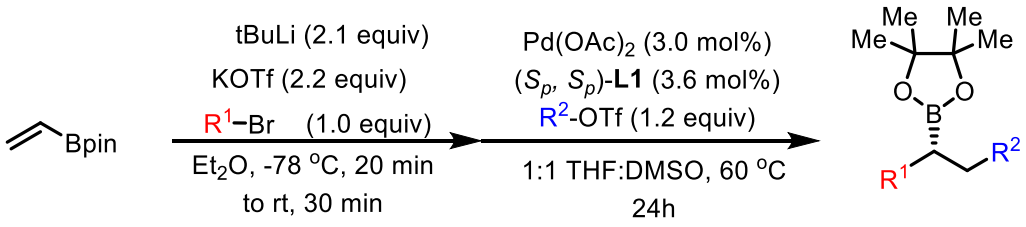
Method D:



In a glovebox under argon an oven-dried 2-dram vial equipped with a magnetic stir bar was charged with potassium trifluoromethanesulfonate (0.66 mmol, 2.20 equiv), and diethyl ether (0.5 mL), and sealed with a septum cap. A 1 mL syringe was charged with (0.33 mmol, 1.1 equiv) of vinylbromide solution in ether and was pierced through the septa of the 2-dram vial. An oven-dried 1-dram vial was then charged with boronate (0.30 mmol, 1.00 equiv) and diethyl ether (0.3 mL) and a 1 mL syringe with diethyl ether (0.40 mL) meant for rinsing was similarly pierced through the top of the 1-dram vial. The vials with corresponding syringes were removed from the glovebox and placed under positive nitrogen pressure. The 2-dram vial with potassium trifluoromethanesulfonate and diethyl ether was allowed to cool to -78 ºC, and *t*-BuLi solution in hexanes (0.63 mmol, 2.10 equiv) was added dropwise. The vial was allowed to stir at -78 ºC, for 30 min after which the boronate solution contained in the 1-dram vial was added by syringe to the reaction dropwise. The 1-dram vial was then rinsed with diethyl ether (0.40 mL) and this solution was added to the 2-dram vessel. The vessel was then allowed to warm to room temperature and stir for 20 min. The solution was then evaporated to dryness under reduced pressure and was brought back into the glovebox. In the glovebox the residue in the vessel was allowed to re-dissolved in tetrahydrofuran (0.70 mL). A second oven-dried 2-dram vial equipped with a magnetic stir bar was charged with $Pd(OAc)_2$ ((0.90 mL, 0.01 M in

dimethyl sulfoxide, 0.009 mmol, 0.03 equiv), and (S_p,S_p)-**3.3** (0.0108 mmol, 0.036 equiv). The $Pd(OAc)_2$/(S_p,S_p)-**3.3** solution was allowed to stir for 15 min at room temperature. The $Pd(OAc)_2$/(S_p,S_p)-**3.3** solution was then transferred into the vial, followed by tetrahydrofuran (0.2 mL) (used to rinse the $Pd(OAc)_2$/(S_p,S_p)-**3.3** vial), and aryl/vinyl trifluoromethanesulfonate (0.36 mmol, 1.20 equiv). The vial was sealed with a polypropylene cap, taped, and brought out of the glovebox where it was allowed to stir at 40 ºC for 24 h. To the resulting mixture was added water (10 mL) and the product was extracted from the aqueous layer with ethyl acetate (3 x 20 mL). The combined organic layers were dried over Na_2SO_4, concentrated under reduced pressure, filtered through a silica gel plug with diethyl ether, reconcentrated, and subsequently purified by silica gel chromatography to provide the desired products.

Method E:

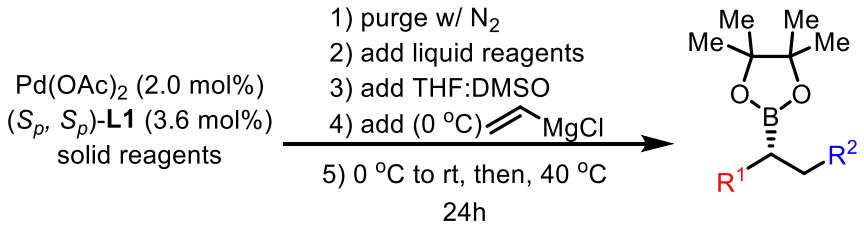


In a glovebox under argon an oven-dried 2-dram vial equipped with a magnetic stir bar was charged with potassium trifluoromethanesulfonate (0.63 mmol, 2.10 equiv), organobromide (0.33 mmol, 1.1 equiv) and diethyl ether (0.5 mL), and sealed with a septum cap. The vials was removed from the glovebox and placed under positive nitrogen pressure. The 2-dram vial was allowed to cool to -78 ºC, and *t*-BuLi solution in hexanes (0.63 mmol, 2.10 equiv) was added dropwise. The vial was allowed to stir at -78 ºC, for 30

min after which the boronate (0.3 mmol, 1.0 equiv) was added by syringe to the reaction. The vessel was then allowed to warm to room temperature and stir for 20 min. The solution was then evaporated to dryness under reduced pressure and was brought back into the glovebox. In the glovebox the residue in the vessel was re-dissolved in tetrahydrofuran (0.70 mL). A second oven-dried 2-dram vial equipped with a magnetic stir bar was charged with $Pd(OAc)_2$ ((0.90 mL, 0.01 M in dimethyl sulfoxide, 0.009 mmol, 0.03 equiv), and (S_p,S_p)-**3.3** (0.0108 mmol, 0.036 equiv). The $Pd(OAc)_2$/(S_p,S_p)-**3.3** solution was allowed to stir for 15 min at room temperature. The $Pd(OAc)_2$/(S_p,S_p)-**3.3** solution was then transferred into the vial, followed by tetrahydrofuran (0.2 mL) (used to rinse the $Pd(OAc)_2$/(S_p,S_p)-**3.3** vial), and aryl/vinyl trifluoromethanesulfonate (0.36 mmol, 1.20 equiv). The vial was sealed with a polypropylene cap, taped, and brought out of the glovebox where it was allowed to stir at 60 ºC for 24 h. To the resulting mixture was added water (10 mL) and the product was extracted from the aqueous layer with ethyl acetate (3 x 20 mL). The combined organic layers were dried over Na_2SO_4, concentrated under reduced pressure, filtered through a silica gel plug with diethyl ether, reconcentrated, and subsequently purified by silica gel chromatography to provide the desired products.

3.8.2.7 Procedure for Experiment Conducted Outside of the Glovebox

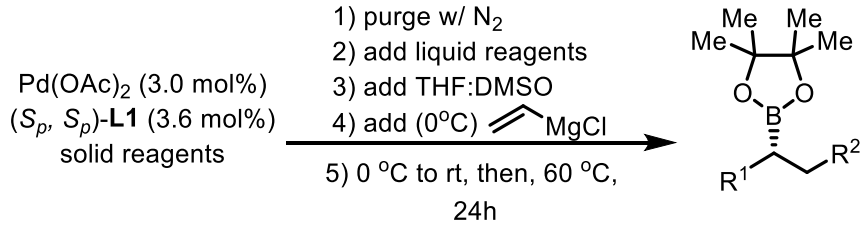
Method F: (without the aid of a glovebox)



In a hood an oven-dried 2-dram vial equipped with a magnetic stir bar was charged with all the solid reagents including: sodium trifluoromethanesulfonate (0.60 mmol, 2.00 equiv), $Pd(OAc)_2$ (0.009 mmol, 0.03 equiv), (S_p,S_p)-**3.3** (0.0108 mmol, 0.036 equiv), and (if they were solids) aryl/vinyl trifluoromethanesulfonate (0.36 mmol, 1.20 equiv), and boronate (0.3 mmol, 1.0 equiv). The vial was then sealed with a polypropylene cap and the atmosphere in the vial was exchanged with nitrogen by three two-minute cycles. The vial was then placed under positive nitrogen pressure and the liquid reagents were added if there were any, followed by tetrahydrofuran (0.6 mL) and dimethyl sulfoxide (0.9 mL). The solution was allowed to stir for 15 min at room temperature until the solution became homogeneous after which the reaction was allowed to cool to 0 ºC in an icebath and vinylmagnesium chloride solution in tetrahydrofuran (0.30 mmol, 1.0 equiv) was added dropwise. The vial was allowed to warm to room temperature before being sealed with tape and heated at 40 ºC for 24 h. To the resulting mixture was added water (10 mL) and the aqueous layer was extracted with ethyl acetate (3 x 20 mL). The combined organic layers were dried over Na_2SO_4, concentrated under reduced pressure, filtered through a silica gel

plug with diethyl ether, reconcentrated, and subsequently purified by silica gel chromatography to provide the desired products.

Method G: (without the aid of a glovebox)



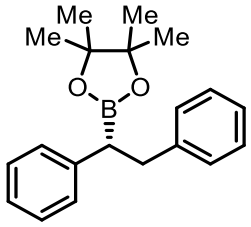
In a hood an oven-dried 2-dram vial equipped with a magnetic stir bar was charged with all the solid reagents including: sodium trifluoromethanesulfonate (0.90 mmol, 3.00 equiv), $Pd(OAc)_2$ (0.009 mmol, 0.03 equiv), (S_p,S_p)-**3.3** (0.0108 mmol, 0.036 equiv), and (if they were solids) aryl bromide (0.36 mmol, 1.20 equiv), and boronate (0.3 mmol, 1.0 equiv). The vial was then sealed with a polypropylene cap and the atmosphere in the vial was exchanged with nitrogen by three two-minute cycles. The vial was then placed under positive nitrogen pressure and the liquid reagents were added if there were any, followed by tetrahydrofuran (0.6 mL) and dimethyl sulfoxide (0.9 mL). The solution was allowed to stir for 15 min at room temperature until the solution became homogeneous after which the reaction was allowed to cool to 0 ºC in an icebath and vinylmagnesium chloride solution in tetrahydrofuran (0.30 mmol, 1.0 equiv) was added dropwise. The vial was allowed to warm to room temperature before being sealed with tape and heated at 60 ºC for 24 h. To the resulting mixture was added water (10 mL) and the product was extracted from the

aqueous layer with ethyl acetate (3 x 20 mL). The combined organic layers were dried over Na_2SO_4, concentrated under reduced pressure, filtered through a silica gel plug with diethyl ether, reconcentrated, and subsequently purified by silica gel chromatography to provide the desired products.

3.8.2.8 General Method for Oxidation of Boronic Ester Products:

Note: Where appropriate, boronic ester products were oxidized. In these cases, the procedure used was the same as that described in the corresponding method A/B/C/D/E/F/G but with the modification that: After the reaction was completed the mixture was filtered through a silica gel plug with diethyl ether, concentrated under reduced pressure, and diluted with tetrahydrofuran (3 mL). The unpurified mixture was allowed to cool to 0 ºC and a 3 M solution of aqueous NaOH (2 mL) was added, followed by 30% H_2O_2 (1.0 mL), dropwise. The mixture was allowed to warm to room temperature, and stir for 3 h. The mixture was allowed to cool to 0 ºC and a saturated solution of aqueous $Na_2S_2O_3$ (3 mL) was added dropwise. After warming to room temperature the product was extracted from the aqueous layer with ethyl acetate (3 x 20 mL). The combined organic layers were dried over Na_2SO_4, concentrated under reduced pressure, and subsequently purified by silica gel chromatography to provide the desired products.

3.8.2.9 Characterization of Conjunctive Coupling Products and Determination of Stereochemical Identity



(R)-2-(1,2-Diphenylethyl)-4,4,5,5-tetramethyl-1,3,2-dioxaborolane (3.84). The reaction was performed according to the general procedure (***Method A)*** with 4,4,5,5-tetramethyl-2-vinyl-1,3,2-dioxaborolane (**3.76**) (46.2 mg, 0.30 mmol, 1.00 equiv), sodium trifluoromethanesulfonate (103.2 mg, 0.60 mmol, 2.00 equiv), phenylmagnesium chloride (0.17 mL, 1.77 M in tetrahydrofuan, 0.30 mmol, 1.00 equiv), phenyl trifluoromethanesulfonate (81.4 mg, 0.36 mmol, 1.20 equiv), palladium (II) acetate (0.9 mL, 0.01 M in dimethyl sulfoxide, 0.009 mmol, 0.030 equiv), (S_p,S_p)-**3.3** (11.37 mg, 0.0108 mmol). The unpurified product was purified by automated silica gel chromatography (Biotage 1% → 5% ethyl acetate in hexanes, stained in CAM) to afford white solid (74.9 mg, 81% yield).

(***Method B)*** with 4,4,5,5-tetramethyl-2-phenyl-1,3,2-dioxaborolane (**3.76**) (61.2 mg, 0.30 mmol, 1.00 equiv) sodium trifluoromethanesulfonate (103.2 mg, 0.60 mmol, 2.00 equiv), vinylmagnesium chloride (0.20 mL, 1.53 M in tetrahydrofuran, 0.30 mmol, 1.00 equiv), phenyl trifluoromethanesulfonate (81.4 mg, 0.36 mmol, 1.20 equiv), palladium (II) acetate (0.9 mL, 0.01 M in dimethyl sulfoxide, 0.009 mmol, 0.030 equiv), (S_p,S_p)-**3.3** (11.37 mg, 0.0108 mmol, 0.036 equiv). The unpurified product was purified by automated silica gel

chromatography (Biotage 1% → 5% ethyl acetate in hexanes, stained in CAM) to afford white solid (74.9 mg, 81% yield).

(***Method C)*** with 4,4,5,5-tetramethyl-2-phenyl-1,3,2-dioxaborolane (**3.76**) (61.2 mg, 0.30 mmol, 1.00 equiv), sodium trifluoromethanesulfonate (154.9 mg, 0.90 mmol, 3.00 equiv), vinylmagnesium chloride (0.20 mL, 1.53 M in tetrahydrofuran, 0.30 mmol, 1.00 equiv bromobenzene (81.4 mg, 0.36 mmol, 1.20 equiv), palladium (II) acetate (0.9 mL, 0.01 M dimethyl sulfoxide, 0.009 mmol, 0.030 equiv), (S_p,S_p)-**3.3** (11.37 mg, 0.0108 mmol, 0.036 equiv). The unpurified product was purified by automated silica gel chromatography (Biotage 1% → 5% ethyl acetate in hexanes, stained in CAM) to afford white solid (77.7 mg, 84% yield).

(Method D) with 4,4,5,5-tetramethyl-2-phenyl-1,3,2-dioxaborolane (**3.76**) (61.2 mg, 0.30 mmol, 1.00 equiv). potassium trifluoromethanesulfonate (118.5 g, 0.63 mmol, 2.10 equiv), vinylbromide (0.25 mL, 1.32 M in diethy ether, 0.33 mmol, 1.10 equiv), phenyl trifluoromethanesulfonate (81.4 mg, 0.36 mmol, 1.20 equiv), palladium (II) acetate (0.9 mL, 0.01 M dimethyl sulfoxide, 0.009 mmol, 0.030 equiv), (S_p,S_p)-**3.3** (11.37 mg, 0.0108 mmol, 0.036 equiv). The unpurified product was purified by automated silica gel chromatography (Biotage 1% → 5% ethyl acetate in hexanes, stained in CAM) to afford white solid (80.4 mg, 87% yield).

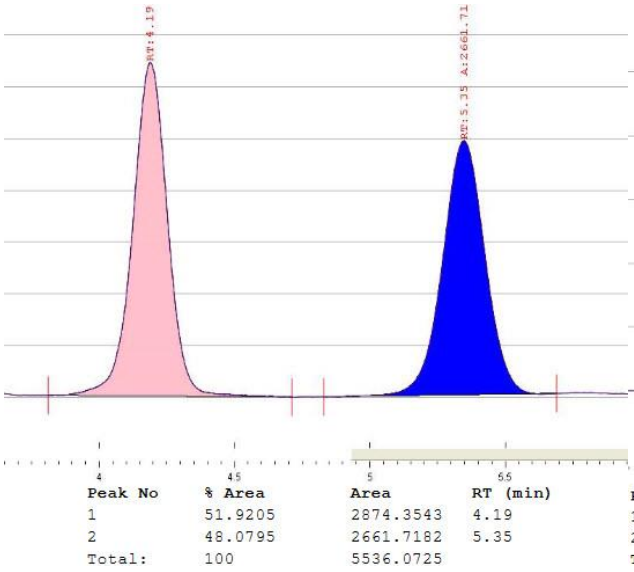
(Method F) with 4,4,5,5-tetramethyl-2-phenyl-1,3,2-dioxaborolane (**3.76**) (61.2 mg, 0.30 mmol, 1.00 equiv), sodium trifluoromethanesulfonate (103.2 mg, 0.60 mmol, 2.00 equiv), vinylmagnesium chloride (0.20 mL, 1.53 M in tetrahydrofuran, 0.30 mmol, 1.00 equiv), phenyl trifluoromethanesulfonate (81.4 mg, 0.36 mmol, 1.20 equiv), palladium (II) acetate (0.9 mL, 0.01 M dimethyl sulfoxide, 0.009 mmol, 0.030 equiv), (S_p,S_p)-**3.3** (11.37 mg, 0.0108 mmol, 0.036 equiv). The unpurified product was purified by automated silica gel chromatography (Biotage 1% → 5% ethyl acetate in hexanes, stained in CAM) to afford white solid (65.6 mg, 71% yield).

^{1}H NMR (600 MHz, $CDCl_3$) δ 7.31 – 7.17 (m, 10H), 3.21 (dd, *J* = 13.5, 9.8 Hz, 1H), 3.02 (dd, *J* = 13.5, 6.9 Hz, 1H), 2.74 (dd, *J* = 9.8, 6.9 Hz, 1H), 1.17 (s, 6H), 1.16 (s, 6H). **^{11}B NMR** (160 MHz, $CDCl_3$) δ 33.00. ^{13}C NMR (151 MHz, $CDCl_3$) δ 142.78 , 141.95 , 129.09 , 128.61 , 128.53 , 128.23 , 125.95 , 125.59 , 83.60 , 39.07 , 34.64 , 24.80 , 24.72. **IR** (neat) ν_{max} 2977.30 (w), 2929.44 (w), 1493.68 (w), 1452.33 (w), 1361.52 (s), 1325.25 (s), 1140.53 (s), 967.43 (w), 853.72 (w), 761.56 (w), 698.98 (s), 528.85 (w) cm^{-1}. **HRMS** (DART) for $C_{20}H_{26}BO_2$ $[M+H]^+$ calculated: 309.2026, found: 309.2025. $[\alpha]^{20}_D$: -49.358 (*c* 3.69, $CHCl_3$, *l* =50 mm).

Determination of Stereochemical Identity: Racemic compound was prepared according to the general procedure (***Method B, run at 60 ºC***) with $Pd(OAc)_2$ (5 mol%) and 1,1′-Bis(dicyclohexylphosphino)ferrocene (6 mol%) as the catalyst. Absolute stereochemistry was assigned by analogy (see product **3.127** and **3.134**).

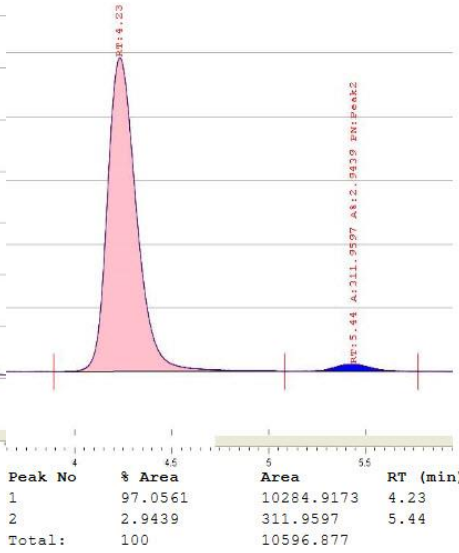
SFC (Chiracel OJ-H, 1% IPA, 3 mL/min, 100 bar, 35 °C, 210-270 nm) – analysis of (R)-2-(1,2-diphenylethyl)-4,4,5,5-tetramethyl-1,3,2-dioxaborolane.

Racemic Material

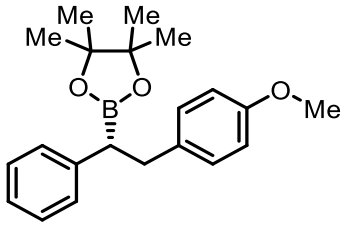


Peak No	% Area	Area	RT (min)
1	51.9205	2874.3543	4.19
2	48.0795	2661.7182	5.35
Total:	100	5536.0725	

Standard Conditions



Peak No	% Area	Area	RT (min)
1	97.0561	10284.9173	4.23
2	2.9439	311.9597	5.44
Total:	100	10596.877	



(*R*)-2-(2-(4-Methoxyphenyl)-1-phenylethyl)-4,4,5,5-tetramethyl-1,3,2-dioxaborolane (3.98). The reaction was performed according to the general procedure ***(Method B)*** with 4,4,5,5-tetramethyl-2-phenyl-1,3,2-dioxaborolane (**3.76**) (61.2 mg, 0.30 mmol, 1.00 equiv), sodium trifluoromethanesulfonate (103.2 mg, 0.60 mmol, 2.00 equiv), vinylmagnesium chloride (0.20 mL, 1.53 M in tetrahydrofuran, 0.30 mmol, 1.00 equiv), 4-methoxyphenyl trifluoromethanesulfonate (92.2 mg, 0.36 mmol, 1.20 equiv), palladium (II) acetate (0.90 mL, 0.01 M in dimethyl sulfoxide, 0.009 mmol, 0.030 equiv), (S_p,S_p)-**3.3** (11.37 mg, 0.0108 mmol, 0.036 equiv). The unpurified product

was purified by automated silica gel chromatography (Biotage 1% → 5% ethyl acetate in hexanes, stained in CAM) to afford white solid (91.3 mg, 90% yield).

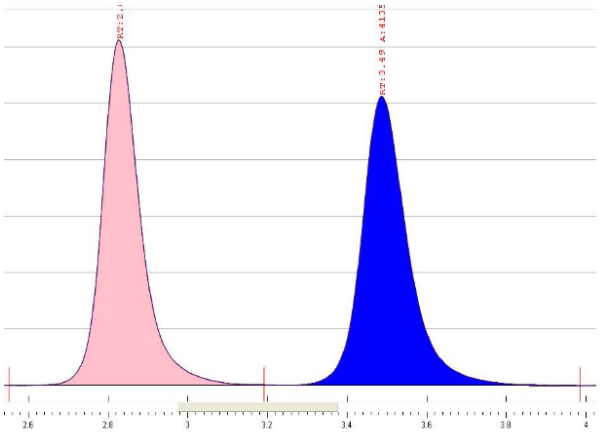
(Method C) with 4,4,5,5-tetramethyl-2-phenyl-1,3,2-dioxaborolane (**3.76**) (61.2 mg, 0.30 mmol, 1.00 equiv), sodium trifluoromethanesulfonate (154.9 mg, 0.90 mmol, 3.00 equiv), vinylmagnesium chloride (0.20 mL, 1.53 M in tetrahydrofuran, 0.30 mmol, 1.00 equiv), 4-bromoanisole (67.3 mg, 0.36 mmol, 1.20 equiv), palladium (II) acetate (0.90 mL, 0.01 M in dimethyl sulfoxide, 0.009 mmol, 0.030 equiv), (S_p,S_p)-**3.3** (11.37 mg, 0.0108 mmol, 0.036 equiv). The unpurified product was purified by automated silica gel chromatography (Biotage 1% → 5% ethyl acetate in hexanes, stained in CAM) to afford white solid (93.4 mg, 92% yield).

^{1}H NMR (600 MHz, $CDCl_3$) δ 7.26 – 7.20 (m, 4H), 7.14 – 7.10 (m, 1H), 7.08 (d, J = 8.6 Hz, 2H), 6.75 (d, J = 8.6 Hz, 2H), 3.75 (s, 3H), 3.08 (dd, J = 13.6, 9.7 Hz, 1H), 2.89 (dd, J = 13.6, 6.9 Hz, 1H), 2.63 (dd, J = 9.6, 7.0 Hz, 1H), 1.11 (s, 6H), 1.10 (s, 6H). **^{11}B NMR** (128 MHz, $CDCl_3$) δ 32.97. **^{13}C NMR** (151 MHz, $CDCl_3$) δ 157.92, 142.83, 134.07, 129.95, 128.59, 128.48, 125.52, 113.62, 83.53, 55.38, 38.14, 34.91, 24.78, 24.73. **IR** (neat) ν_{max} 3060.40 (w), 3025.37 (w), 2976.85 (m), 2932.81 (w), 2834.43 (w), 1611.11 (m), 1510.56 (s), 1360.56 (s), 1324.02 (s), 1243.26 (s), 1139.26 (s), 1034.86 (m), 967.45 (m), 829.03 (m), 700.16 (s) cm^{-1}. **HRMS** (DART) for $C_{21}H_{28}BO_3$ $[M+H]^+$: calculated: 339.21315, found: 339.21403. $[\alpha]_D^{20}$ = – 46.292 (*c* 1.73, $CHCl_3$, *l* = 50 mm).

Determination of Stereochemical Identity: Racemic compound was prepared according to the general procedure (***Method B, run at 60 ºC***) with $Pd(OAc)_2$ (5 mol%) and 1,1′-Bis(dicyclohexylphosphino)ferrocene (6 mol%) as the catalyst. Absolute stereochemistry was assigned by analogy (see product **3.127** and **3.134**).

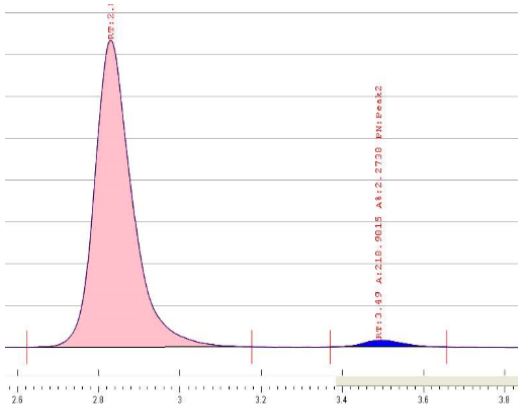
SFC (Chiracel OJ-H, 5% IPA, 3 mL/min, 100 bar, 35 °C, 210-270 nm) – analysis of (R)-2-(2-(4-methoxyphenyl)-1-phenylethyl)-4,4,5,5-tetramethyl-1,3,2-dioxaborolane.

Racemic Material

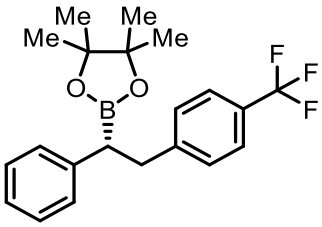


Peak No	% Area	Area	RT (min)
1	49.9893	4134.1383	2.83
2	50.0107	4135.9048	3.49
Total:	100	8270.0431	

Standard Conditions



Peak No	% Area	Area	RT (min)
1	97.7262	9411.7889	2.83
2	2.2738	218.9815	3.49
Total:	100	9630.7704	



(*R*)-4,4,5,5-Tetramethyl-2-(1-phenyl-2-(4-(trifluoromethyl) phenyl) ethyl)-1,3,2-dioxaborolane (3.99). The reaction was performed according to the general procedure ***(Method B)*** with 4,4,5,5-tetramethyl-2-phenyl-1,3,2-dioxaborolane (**3.76**) (61.2 mg, 0.30 mmol, 1.00 equiv), sodium trifluoromethanesulfonate (103.2 mg, 0.60 mmol,

2.00 equiv), vinylmagnesium chloride (0.20 mL, 1.53 M in tetrahydrofuran, 0.30 mmol, 1.00 equiv), 4-(trifluoromethyl)phenyl trifluoromethanesulfonate (**3.158**) (105.9 mg, 0.36 mmol, 1.20 equiv), palladium (II) acetate (0.90 mL, 0.01 M in dimethyl sulfoxide, 0.009 mmol, 0.030 equiv), (S_p,S_p)-**3.3** (11.37 mg, 0.0108 mmol, 0.036 equiv). The unpurified product was purified by automated silica gel chromatography (Biotage 1% → 5% ethyl acetate in hexanes, stained in CAM) to afford colorless oil (95.9 mg, 85% yield).

(Method C) with 4,4,5,5-tetramethyl-2-phenyl-1,3,2-dioxaborolane (**3.76**) (61.2 mg, 0.30 mmol, 1.00 equiv), sodium trifluoromethanesulfonate (154.9 mg, 0.90 mmol, 3.00 equiv), vinylmagnesium chloride (0.20 mL, 1.53 M in tetrahydrofuran, 0.30 mmol, 1.00 equiv), 4-bromobenzotrifluoride (81.0 mg, 0.36 mmol, 1.20 equiv), palladium (II) acetate (0.90 mL, 0.01 M in dimethyl sulfoxide, 0.009 mmol, 0.030 equiv), (S_p,S_p)-**3.3** (11.37 mg, 0.0108 mmol, 0.036 equiv). The unpurified product was purified by automated silica gel chromatography (Biotage 1% → 5% ethyl acetate in hexanes, stained in CAM) to afford colorless oil (85.8 mg, 76% yield).

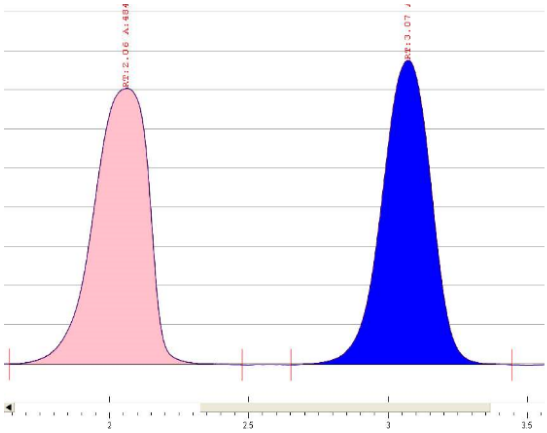
^{1}H NMR (600 MHz, $CDCl_3$) δ 7.46 (d, J = 8.0 Hz, 2H), 7.29 – 7.23 (m, 4H), 7.21 (d, J = 6.9 Hz, 2H), 7.15 (t, J = 7.2 Hz, 1H), 3.20 (dd, J = 13.6, 9.3 Hz, 1H), 3.00 (dd, J = 13.6, 7.3 Hz, 1H), 2.66 (dd, J = 8.9, 7.6 Hz, 1H), 1.12 (s, 6H), 1.12 (s, 6H). **^{11}B NMR** (128 MHz, $CDCl_3$) δ 32.68. **^{13}C NMR** (151 MHz, $CDCl_3$) δ 146.14, 142.11, 129.37, 128.66, 128.59, 128.33 (partially buried, q, $^2J_{C–F}$ = 32.2 Hz), 125.85, 125.14 (q, $^3J_{C–F}$ = 3.7 Hz), 124.62 (q, $^1J_{C–F}$ = 271.7 Hz), 83.80, 38.81, 34.38, 24.76, 24.74. **IR** (neat) ν_{max} 3061.55 (w), 3025.45

(w), 2979.30 (m), 2932.67 (w), 1362.99 (m), 1321.35 (s), 1162.23 (m), 1139.06 (s), 1120.38 (s), 1066.83 (s), 842.37 (m), 700.83 (m) cm^{-1}. **HRMS** (DART) for $C_{21}H_{28}BF_3NO_2$ $[M+NH_4]^+$: calculated: 394.21652, found: 394.21675. $[\alpha]_D^{20} = -41.075$ (*c* 2.58, $CHCl_3$, *l* = 50 mm).

Determination of Stereochemical Identity: Racemic compound was prepared according to the general procedure (***Method B, run at 60 ºC***) with $Pd(OAc)_2$ (5 mol%) and 1,1′-Bis(dicyclohexylphosphino)ferrocene (6 mol%) as the catalyst. Absolute stereochemistry was assigned by analogy (see product **3.127** and **3.134**).

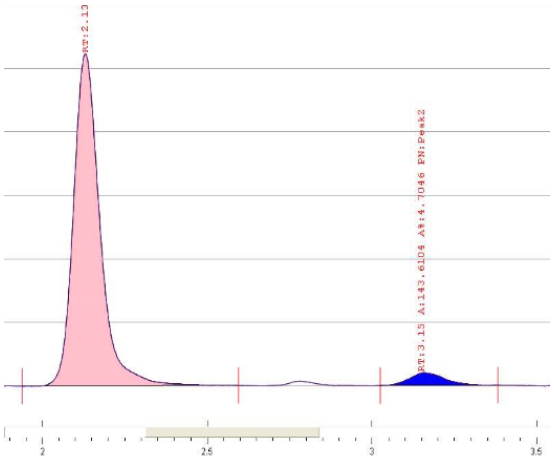
SFC (Chiracel OJ-H, 1% IPA, 3 mL/min, 100 bar, 35 °C, 210-270 nm) – analysis of (R)-4,4,5,5-tetramethyl-2-(1-phenyl-2-(4-(trifluoromethyl)phenyl)ethyl)-1,3,2-dioxaborolane.

Racemic Material

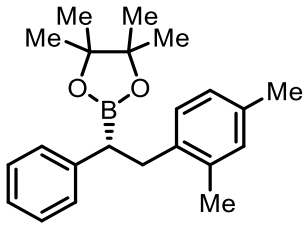


Peak No	% Area	Area	RT (min)
1	50.3616	4843.2255	2.06
2	49.6384	4773.6823	3.07
Total:	100	9616.9078	

Standard Conditions



Peak No	% Area	Area	RT (min)
1	95.2954	2908.9488	2.13
2	4.7046	143.6104	3.15
Total:	100	3052.5592	

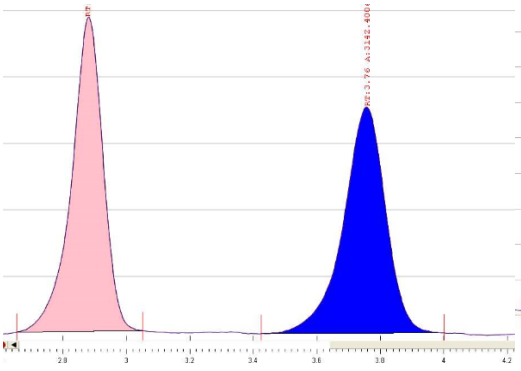


(*R*)-2-(2-(2,4-Dimethylphenyl)-1-phenylethyl)-4,4,5,5-tetramethyl-1,3,2-dioxaborolane (3.100). The reaction was performed according to the general procedure ***(Method B, with the modification: the reaction was run at 60 ºC instead of 40 ºC)*** with 4,4,5,5-tetramethyl-2-phenyl-1,3,2-dioxaborolane (**3.76**) (61.2 mg, 0.30 mmol, 1.00 equiv), sodium trifluoromethanesulfonate (103.2 mg, 0.60 mmol, 2.00 equiv), vinylmagnesium chloride (0.20 mL, 1.53 M in tetrahydrofuran, 0.30 mmol, 1.00 equiv), 2,4-dimethylphenyl trifluoromethanesulfonate (**3.159**) (91.5 mg, 0.36 mmol, 1.20 equiv), palladium (II) acetate (0.90 mL, 0.01 M in dimethyl sulfoxide, 0.009 mmol, 0.030 equiv), (S_p,S_p)-**3.3** (11.37 mg, 0.0108 mmol, 0.036 equiv). The unpurified product was purified by silica gel chromatography (0% → 20% ethyl acetate in hexanes, stained in CAM) to afford colorless oil (71.1 mg, 70% yield). **^{1}H NMR** (500 MHz, $CDCl_3$) δ 7.24 (d, J = 3.9 Hz, 4H), 7.16 – 7.09 (m, 1H), 7.04 (d, J = 7.7 Hz, 1H), 6.90 (s, 1H), 6.85 (d, J = 7.6 Hz, 1H), 3.11 (dd, J = 13.7, 10.1 Hz, 1H), 2.85 (dd, J = 13.8, 6.2 Hz, 1H), 2.62 (dd, J = 9.8, 6.2 Hz, 1H), 2.24 (s, 3H), 2.22 (s, 3H), 1.11 (s, 6H), 1.10 (s, 6H). **^{11}B NMR** (128 MHz, $CDCl_3$) δ 32.79. **^{13}C NMR** (126 MHz, $CDCl_3$) δ 143.21, 137.00, 136.23, 135.36, 131.05, 129.28, 128.63, 128.53, 126.35, 125.57, 83.60, 35.95, 33.27, 24.86, 24.74, 21.12, 19.57. **IR** (neat) ν_{max} 3082.50 (w), 3057.14 (w), 3023.76 (w), 2976.78 (m), 2926.55 (m), 2863.88 (w), 1600.81 (w), 1493.07 (m), 1451.70 (m), 1359.49 (s), 1324.47 (s), 1141.37 (s), 967.98 (m), 853.68 (m), 700.02 (m) cm^{-1}. **HRMS** (DART) for $C_{22}H_{30}BO_2$ $[M+H]^+$: calculated: 337.2339, found: 337.2337. $[\alpha]_D^{20}$ = – 22.542 (*c* 1.02, $CHCl_3$, *l* = 50 mm).

Determination of Stereochemical Identity: Racemic compound was prepared according to the general procedure (***Method B, run at 60 ºC***) with $Pd(OAc)_2$ (5 mol%) and 1,1′-Bis(diisopropylphosphino)ferrocene (6 mol%) as the catalyst. Absolute stereochemistry was assigned by analogy (see product **3.127** and **3.134**).

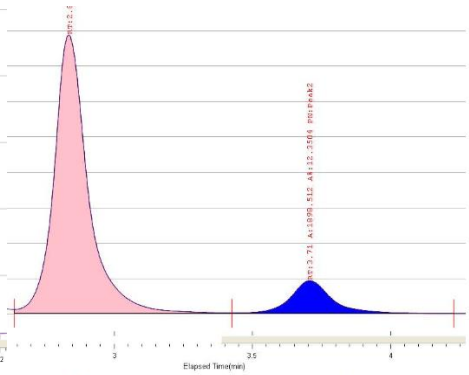
SFC (Chiracel OJ-H, 2% IPA, 3 mL/min, 100 bar, 35 °C, 210-270 nm) – analysis of (R)-2-(2-(2,4-dimethylphenyl)-1-phenylethyl)-4,4,5,5-tetramethyl-1,3,2-dioxaborolane.

Racemic Material

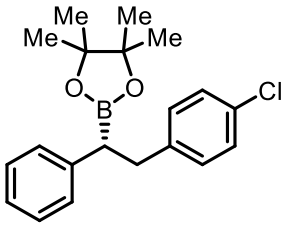


Peak No	% Area	Area	RT (min)
1	50.8958	3257.0512	2.88
2	49.1042	3142.4006	3.76
Total:	100	6399.4518	

Standard Conditions



Peak No	% Area	Area	RT (min)
1	87.6496	13473.5164	2.84
2	12.3504	1898.512	3.71
Total:	100	15372.0284	



(*R*)-2-(2-(4-Chlorophenyl)-1-phenylethyl)-4,4,5,5-tetramethyl-1,3,2-dioxaborolane (3.101). The reaction was performed according to the general procedure *(**Method B**)* with 4,4,5,5-tetramethyl-2-phenyl-1,3,2-dioxaborolane (**3.76**) (61.2 mg, 0.30 mmol, 1.00 equiv), sodium trifluoromethanesulfonate (103.2 mg, 0.60 mmol, 2.00 equiv),

vinylmagnesium chloride (0.20 mL, 1.53 M in tetrahydrofuran, 0.30 mmol, 1.00 equiv), 4-chlorophenyl trifluoromethanesulfonate (**3.162**) (93.8 mg, 0.36 mmol, 1.20 equiv), palladium (II) acetate (0.90 mL, 0.01 M in dimethyl sulfoxide, 0.009 mmol, 0.030 equiv), (S_p,S_p)-**3.3** (11.37 mg, 0.0108 mmol, 0.036 equiv). The unpurified product was purified by silica gel chromatography (0% → 20% CH_2Cl_2 in hexanes, stained in CAM) to afford white solid (77.1 mg, 75% yield).

(Method C) with 4,4,5,5-tetramethyl-2-phenyl-1,3,2-dioxaborolane (**3.76**) (61.2 mg, 0.30 mmol, 1.00 equiv), sodium trifluoromethanesulfonate (154.9 mg, 0.90 mmol, 3.00 equiv), vinylmagnesium chloride (0.20 mL, 1.53 M in tetrahydrofuran, 0.30 mmol, 1.00 equiv), 1-bromo-4-chlorobenzene (68.9 mg, 0.36 mmol, 1.20 equiv), palladium (II) acetate (0.90 mL, 0.01 M in dimethyl sulfoxide, 0.009 mmol, 0.030 equiv), (S_p,S_p)-**3.3** (11.37 mg, 0.0108 mmol, 0.036 equiv). The unpurified product was purified by silica gel chromatography (0% → 20% CH_2Cl_2 in hexanes, stained in CAM) to afford white solid (54.5 mg, 53% yield).

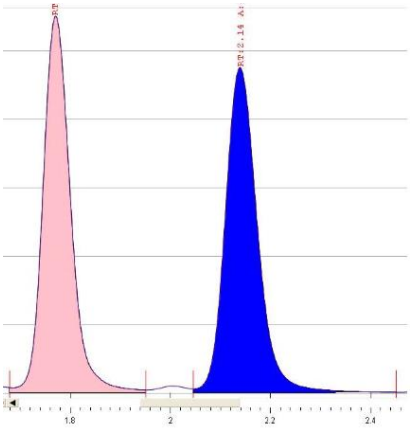
^{1}H NMR (500 MHz, $CDCl_3$) δ 7.23 – 7.09 (m, 7H), 7.06 (d, J = 8.4 Hz, 2H), 3.09 (dd, J = 13.6, 9.3 Hz, 1H), 2.89 (dd, J = 13.6, 7.2 Hz, 1H), 2.60 (dd, J = 9.2, 7.4 Hz, 1H), 1.10 (s, 6H), 1.10 (s, 6H). **^{11}B NMR** (128 MHz, $CDCl_3$) δ 32.68. **^{13}C NMR** (126 MHz, $CDCl_3$) δ 142.31, 140.41, 131.64, 130.42, 128.59, 128.57, 128.28, 125.72, 83.69, 38.33, 34.57, 24.77, 24.76. **IR** (neat) ν_{max} 3062.99 (w), 3028.92 (w), 2992.58 (m), 2974.97 (m), 2926.86 (w), 2866.56 (w), 2854.54 (w), 1599.48 (w), 1491.98 (m), 1451.90 (m), 1361.24 (s),

1325.22 (m), 1137.88 (s), 840.95 (m), 698.86 (s), 526.61 (m) cm^{-1}. **HRMS** (DART) for $C_{20}H_{28}BClNO_2$ $[M+NH_4]^+$: calculated: 360.19016, found: 360.18982. $[\alpha]_D^{20} = -51.441$ (*c* 2.55, $CHCl_3$, *l* = 50 mm).

Determination of Stereochemical Identity: Racemic compound was prepared according to the general procedure (***Method C, run at 60 ºC***) with $Pd(OAc)_2$ (5 mol%) and 1,1′-Bis(diisopropylphosphino)ferrocene (6 mol%) as the catalyst. Absolute stereochemistry was assigned by analogy (see product **3.127** and **3.134**).

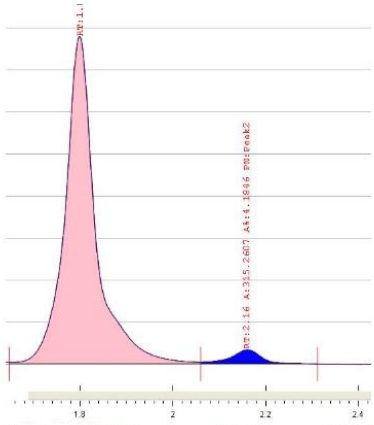
SFC (Chiracel OJ-H, 10% IPA, 3 mL/min, 100 bar, 35 °C, 210-270 nm) – analysis of (R)-2-(2-(4-chlorophenyl)-1-phenylethyl)-4,4,5,5-tetramethyl-1,3,2-dioxaborolane.

Racemic Material

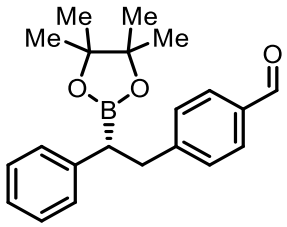


Peak No	% Area	Area	RT (min)
1	49.8972	4165.2611	1.77
2	50.1028	4182.4299	2.14
Total:	100	8347.691	

Standard Conditions



Peak No	% Area	Area	RT (min)
1	95.8154	7218.5232	1.8
2	4.1846	315.2607	2.16
Total:	100	7533.7839	



(*R*)-4-(2-Phenyl-2-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)ethyl) benzaldehyde (3.102). The reaction was performed according to the general procedure ***(Method B)*** with 4,4,5,5-tetramethyl-2-phenyl-1,3,2-dioxaborolane (**3.76**) (61.2 mg, 0.30 mmol, 1.00 equiv), sodium trifluoromethanesulfonate (103.2 mg, 0.60 mmol, 2.00 equiv), vinylmagnesium chloride (0.20 mL, 1.53 M in tetrahydrofuran, 0.30 mmol, 1.00 equiv), 4-formylphenyl trifluoromethanesulfonate (**3.160**) (91.5 mg, 0.36 mmol, 1.20 equiv), palladium (II) acetate (0.90 mL, 0.01 M in dimethyl sulfoxide, 0.009 mmol, 0.030 equiv), (S_p, S_p)-**3.3** (11.37 mg, 0.0108 mmol, 0.036 equiv.). The unpurified product was purified by silica gel chromatography (0% → 50% → 100% CH_2Cl_2 in hexanes, stained in CAM) to afford white solid (74.6 mg, 74% yield).

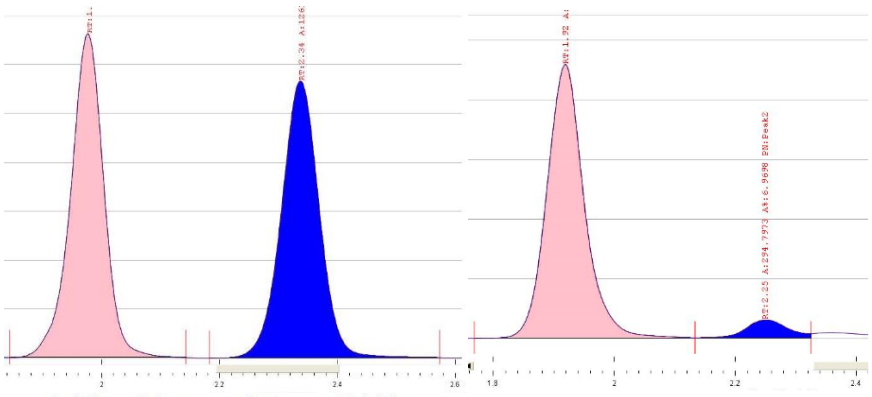
(Method C) with 4,4,5,5-tetramethyl-2-phenyl-1,3,2-dioxaborolane (**3.76**) (61.2 mg, 0.30 mmol, 1.00 equiv), sodium trifluoromethanesulfonate (154.9 mg, 0.90 mmol, 3.00 equiv), vinylmagnesium chloride (0.20 mL, 1.53 M in tetrahydrofuran, 0.30 mmol, 1.00 equiv), 4-bromobenzaldehyde (66.6 mg, 0.36 mmol, 1.20 equiv), palladium (II) acetate (0.90 mL, 0.01 M in dimethyl sulfoxide, 0.009 mmol, 0.030 equiv), (S_p, S_p)-**3.3** (11.37 mg, 0.0108 mmol, 0.036 equiv). The unpurified product was purified by silica gel chromatography (0% → 50% → 100% CH_2Cl_2 in hexanes, stained in CAM) to afford white solid (58.5 mg, 58% yield).

^{1}H NMR (500 MHz, $CDCl_3$) δ 9.92 (s, 1H), 7.71 (d, *J* = 8.0 Hz, 2H), 7.30 (d, *J* = 8.0 Hz, 2H), 7.25 – 7.20 (m, 2H), 7.18 (d, *J* = 6.9 Hz, 2H), 7.13 (app t, *J* = 7.2 Hz, 1H), 3.21 (dd, *J* = 13.5, 9.3 Hz, 1H), 3.01 (dd, *J* = 13.5, 7.5 Hz, 1H), 2.66 (app t, *J* = 8.1 Hz, 1H), 1.11 (s, 6H), 1.10 (s, 6H). **^{11}B NMR** (128 MHz, $CDCl_3$) δ 33.00. **^{13}C NMR** (126 MHz, $CDCl_3$) δ 192.23, 149.53, 141.97, 134.63, 129.82, 129.73, 128.61, 128.55, 125.83, 83.78, 39.18, 34.24, 24.74, 24.72. **IR** (neat) ν_{max} 3059.19 (w), 3025.78 (w), 2977.21 (m), 2929.43 (w), 2861.26 (w), 2826.64 (w), 2733.18 (w), 1698.39 (s), 1604.87 (m), 1361.01 (s), 1326.41 (s), 1139.63 (s), 844.14 (m), 701.29 (m), 538.21 (m) cm^{-1}. **HRMS** (DART) for $C_{21}H_{26}BO_3$ $[M+H]^+$: calculated: 337.1975, found: 337.1981. $[\alpha]_D^{20}$ = – 57.821 (*c* 2.62, $CHCl_3$, *l* = 50 mm).

Determination of Stereochemical Identity: Racemic compound was prepared according to the general procedure (***Method C, run at 60 ºC***) with $Pd(OAc)_2$ (5 mol%) and 1,1′-Bis(diisopropylphosphino)ferrocene (6 mol%) as the catalyst. Absolute stereochemistry was assigned by analogy (see product **3.127** and **3.134**).

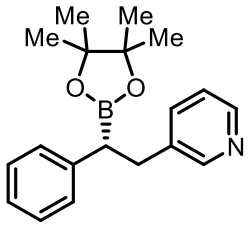
SFC (Chiracel OJ-H, 10% IPA, 3 mL/min, 100 bar, 35 °C, 210-270 nm) – analysis of (R)-4-(2-phenyl-2-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)ethyl)benzaldehyde.

Racemic Material Standard Conditions



Peak No	% Area	Area	RT (min)
1	50.5587	1289.8685	1.98
2	49.4413	1261.3593	2.34
Total:	100	2551.2278	

Peak No	% Area	Area	RT (min)
1	93.0302	3934.8527	1.92
2	6.9698	294.7973	2.25
Total:	100	4229.65	



(*R*)-3-(2-Phenyl-2-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)ethyl) pyridine (3.102). The reaction was performed according to the general procedure ***(Method B)*** with 4,4,5,5-tetramethyl-2-phenyl-1,3,2-dioxaborolane (**3.76**) (61.2 mg, 0.30 mmol, 1.00 equiv), sodium trifluoromethanesulfonate (103.2 mg, 0.60 mmol, 2.00 equiv), vinylmagnesium chloride (0.20 mL, 1.53 M in tetrahydrofuran, 0.30 mmol, 1.00 equiv), 3-pyridyl trifluoromethanesulfonate (**3.161**) (81.8 mg, 0.36 mmol, 1.20 equiv), palladium (II) acetate (0.90 mL, 0.01 M in dimethyl sulfoxide, 0.009 mmol, 0.030 equiv), (S_p, S_p)-**3.3** (11.37 mg, 0.0108 mmol, 0.036 equiv). The unpurified product was purified by silica gel chromatography (0% → 50% → 100% CH_2Cl_2 in hexanes, stained in CAM) to afford pink oil (47.3 mg, 51% yield).

(Method C) with 4,4,5,5-tetramethyl-2-phenyl-1,3,2-dioxaborolane (**3.76**) (61.2 mg, 0.30 mmol, 1.00 equiv), sodium trifluoromethanesulfonate (154.9 mg, 0.90 mmol, 3.00 equiv),

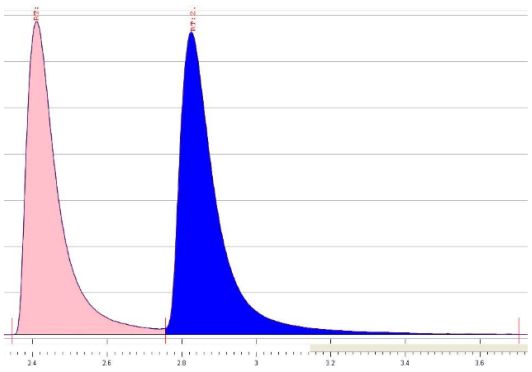
vinylmagnesium chloride (0.20 mL, 1.53 M in tetrahydrofuran, 0.30 mmol, 1.00 equiv), 3-bromopyridine (56.9 mg, 0.36 mmol, 1.20 equiv), palladium (II) acetate (0.90 mL, 0.01 M in dimethyl sulfoxide, 0.009 mmol, 0.030 equiv), (S_p, S_p)-**3.3** (11.37 mg, 0.0108 mmol, 0.036 equiv). The unpurified product was purified by silica gel chromatography (0% → 50% → 100% CH_2CH_2 in hexanes, stained in CAM) to afford pink oil (45.5 mg, 49% yield).

^{1}H NMR (500 MHz, $CDCl_3$) δ 8.38 (s, 1H), 8.34 (d, J = 3.3 Hz, 1H), 7.41 (d, J = 7.8 Hz, 1H), 7.26 – 7.18 (m, 2H), 7.16 (d, J = 7.1 Hz, 2H), 7.13 – 7.05 (m, 2H), 3.11 (dd, J = 13.7, 9.2 Hz, 1H), 2.90 (dd, J = 13.7, 7.4 Hz, 1H), 2.59 (app t, J = 8.3 Hz, 1H), 1.10 (s, 6H), 1.09 (s, 6H). **^{11}B NMR** (128 MHz, $CDCl_3$) δ 32.81. **^{13}C NMR** (126 MHz, $CDCl_3$) δ 150.34, 147.24, 141.87, 137.25, 136.54, 128.64, 128.59, 125.87, 123.19, 83.81, 36.08, 34.37, 25.03, 24.73. **IR** (neat) ν_{max} 3083.23 (w), 3058.15 (w), 3025.24 (w), 2977.72 (m), 2929.39 (w), 2861.19 (w), 1600.02 (w), 1574.63 (w), 1493.42 (m), 1478.78 (m), 1451.31 (m), 1422.39 (m), 1364.27 (s), 1328.41 (s), 1141.17 (s), 968.05 (m), 853.25 (m), 701.71 (m) cm^{-1}. **HRMS** (DART) for $C_{19}H_{25}BNO_2$ $[M+H]^+$: calculated: 310.1978, found: 310.1990. $[\alpha]_D^{20}$ = – 39.247 (*c* 1.76, $CHCl_3$, *l* = 50 mm).

Determination of Stereochemical Identity: Racemic compound was prepared according to the general procedure (***Method B, run at 60 ºC***) with $Pd(OAc)_2$ (3 mol%), (S_p, S_p)-**3.3** (1.8 mol%), and (R_p, R_p)-**3.3** (1.8 mol%) as the catalyst. Absolute stereochemistry was assigned by analogy (see product **3.127** and **3.134**).

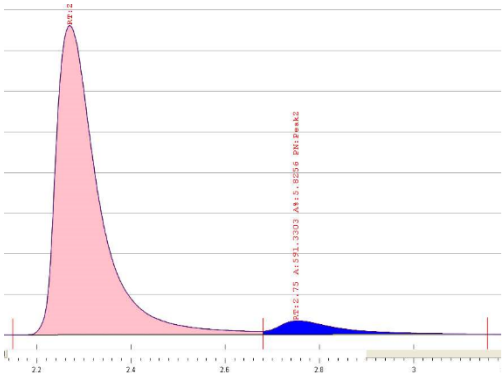
SFC (Chiracel OJ-H, 4% MeOH, 3 mL/min, 100 bar, 35 °C, 210-270 nm) – analysis of (R)-3-(2-phenyl-2-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)ethyl)pyridine.

Racemic Material

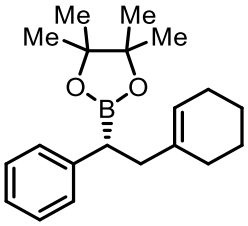


Peak No	% Area	Area	RT (min)
1	47.4152	4045.2841	2.41
2	52.5848	4486.3369	2.83
Total:	100	8531.621	

Standard Conditions

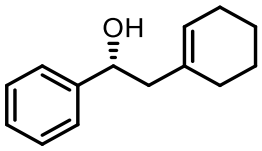


Peak No	% Area	Area	RT (min)
1	94.1744	9559.2412	2.27
2	5.8256	591.3303	2.75
Total:	100	10150.5715	



(*R*)-2-(2-(Cyclohex-1-en-1-yl)-1-phenylethyl)-4,4,5,5-tetramethyl-1,3,2-dioxaborolane (3.104) The reaction was performed according to general procedure (***Method B)*** with 4,4,5,5-tetramethyl-2-phenyl-1,3,2-dioxaborolane (**3.76**) (61.2 mg, 0.30 mmol, 1.00 equiv) sodium trifluoromethanesulfonate (103.2 mg, 0.60 mmol, 2.00 equiv), vinylmagnesium chloride (0.20 mL, 1.53 M in tetrahydrofuran, 0.30 mmol, 1.00 equiv), cyclohex-1-en-1-yl trifluoromethanesulfonate (**3.156**) (82.9 mg, 0.36 mmol, 1.20 equiv), palladium (II) acetate (0.9 mL, 0.01 M in dimethyl sulfoxide, 0.009 mmol, 0.030 equiv), (S_p, S_p)-**3.3** (11.37 mg, 0.0108 mmol, 0.036 equiv). The unpurified product was purified by automated silica gel chromatography (Biotage 1% →5% ethyl acetate in hexanes, stained

in CAM) to afford white solid (71.2 mg, 76% yield). **^{1}H NMR** (600 MHz, $CDCl_3$) δ 7.25 – 7.19 (m, 4H), 7.13 – 7.08 (m, 1H), 5.42 (s, 1H), 2.56 (dd, *J* = 10.5, 5.9 Hz, 1H), 2.49 (app t, 1H), 2.22 (dd, *J* = 13.7, 5.6 Hz, 1H), 2.02 – 1.83 (m, 4H), 1.63 – 1.42 (m, 4H), 1.17 (s, 6H), 1.15 (s, 6H). **^{11}B NMR** (160 MHz, $CDCl_3$) δ 32.89. **^{13}C NMR** (151 MHz, $CDCl_3$) δ 143.42 , 137.42 , 128.48 , 128.41 , 125.32 , 121.77 , 83.43 , 41.14 , 30.86 , 28.84 , 25.46 , 24.86 , 24.82 , 23.26 , 22.77. **IR** (neat) ν_{max} 2976.74 (w), 2925.87 (w), 1359.22 (m), 1323.98 (m), 1141.45 (m), 969.45 (w), 850.07 (w), 699.65 (m) cm^{-1}. **HRMS** (DART) for $C_{20}H_{30}BO_2$ $[M+H]^+$ calculated: 313.23388, found: 313.23507. $[\alpha]^{20}_D$: -6.100 (*c* 1.215, $CHCl_3$, *l* =50 mm).

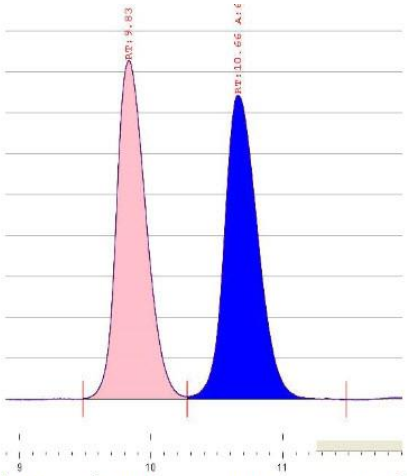


(*R*)-2-(Cyclohex-1-en-1-yl)-1-phenylethan-1-ol (3.104-OH) Product **3.104** was oxidized according to ***General Method for Oxidation of Boronic Ester Products.*** All spectral data was in accord with the literature.[61]

Determination of Stereochemical Identity: Racemic compound was prepared according to the general procedure (***Method B, run at 60 ºC***) with $Pd(OAc)_2$ (5 mol%) and 1,1′-Bis(dicyclohexylphosphino)ferrocene (6 mol%) as the catalyst. Absolute stereochemistry was assigned by analogy (see product **3.127** and **3.134**).

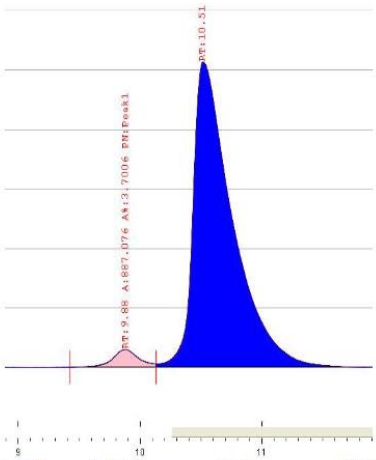
SFC (Chiracel OJ-H, 1% IPA, 3 mL/min, 100 bar, 35 °C, 210-270 nm) – analysis of (R)-2-(cyclohex-1-en-1-yl)-1-phenylethan-1-ol.

Racemic Material

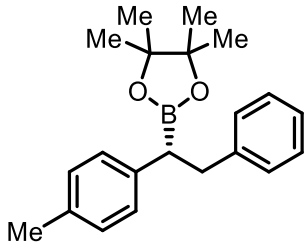


Peak No	% Area	Area	RT (min)
1	49.6784	6384.9152	9.83
2	50.3216	6467.5726	10.66
Total:	100	12852.4878	

Standard Conditions



Peak No	% Area	Area	RT (min)
1	3.7006	887.076	9.88
2	96.2994	23083.9786	10.51
Total:	100	23971.0546	

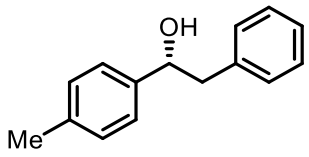


(*R*)-4,4,5,5-Tetramethyl-2-(2-phenyl-1-(p-tolyl)ethyl)-1,3,2-Dioxa-borolane (3.105). The reaction was performed according to the general procedure ***(Method B)*** with 4,4,5,5-tetramethyl-2-(p-tolyl)-1,3,2-dioxaborolane (65.4 mg, 0.30 mmol, 1.00 equiv), sodium trifluoromethanesulfonate (103.2 mg, 0.60 mmol, 2.00 equiv), vinylmagnesium chloride (0.20 mL, 1.53 M in tetrahydrofuran, 0.30 mmol, 1.00 equiv), phenyl trifluoromethanesulfonate (81.4 mg, 0.36 mmol, 1.20 equiv) palladium (II) acetate (0.90 mL, 0.01 M in dimethyl sulfoxide, 0.009 mmol, 0.030 equiv), (S_p,S_p)-**3.3** (11.37 mg, 0.0108 mmol, 0.036 equiv). The unpurified product was purified by silica gel chromatography

(0% → 30% CH_2Cl_2 in hexanes, stained in CAM) to afford white solid (78.3 mg, 81% yield).

(Method C) with 4,4,5,5-tetramethyl-2-(p-tolyl)-1,3,2-dioxaborolane (65.4 mg, 0.30 mmol, 1.00 equiv), sodium trifluoromethanesulfonate (154.9 mg, 0.90 mmol, 3.00 equiv), vinylmagnesium chloride (0.20 mL, 1.53 M in tetrahydrofuran, 0.30 mmol, 1.00 equiv), bromobenzene (56.5 mg, 0.36 mmol, 1.20 equiv), palladium (II) acetate (0.90 mL, 0.01 M in dimethyl sulfoxide, 0.009 mmol, 0.030 equiv), (S_p,S_p)-**3.3** (11.37 mg, 0.0108 mmol, 0.036 equiv). The unpurified product was purified by silica gel chromatography (0% → 30% CH_2Cl_2 in hexanes, stained in CAM) to afford white solid (75.4 mg, 78% yield).

^{1}H NMR (500 MHz, $CDCl_3$) δ 7.30 – 7.21 (m, 4H), 7.21 – 7.14 (m, 3H), 7.10 (d, J = 7.8 Hz, 2H), 3.17 (dd, J = 13.4, 10.0 Hz, 1H), 2.98 (dd, J = 13.5, 6.8 Hz, 1H), 2.69 (dd, J = 9.8, 6.9 Hz, 1H), 2.33 (s, 3H), 1.14 (s, 6H), 1.13 (s, 6H). **^{11}B NMR** (128 MHz, $CDCl_3$) δ 32.91. **^{13}C NMR** (126 MHz, $CDCl_3$) δ 142.04, 139.64, 134.89, 129.24, 129.07, 128.43, 128.19, 125.89, 83.49, 39.26, 34.09, 24.79, 24.70, 21.20. **IR** (neat) ν_{max} 3085.45 (w), 3060.29 (w), 3025.44 (w), 2977.10 (m), 2924.49 (w), 2861.47 (w), 1603.87 (w), 1510.16 (m), 1359.23 (s), 1321.39 (s), 1140.06 (s), 967.33 (m), 855.65 (m), 815.57 (m), 698.19 (s), 537.31 (m) cm^{-1}. **HRMS** (DART) for $C_{21}H_{28}BO_2$ $[M+H]^+$: calculated: 323.21823, found: 323.21907. $[\alpha]_D^{20}$ = – 41.664 (*c* 3.50, $CHCl_3$, *l* = 50 mm).

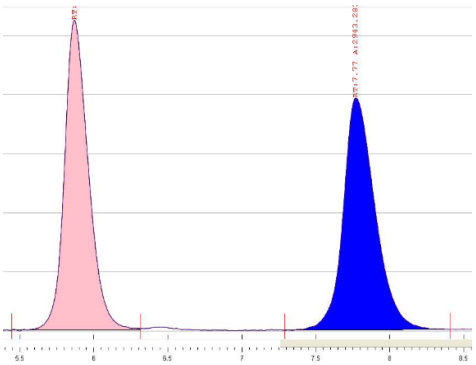


(R)*-2-Phenyl-1-(p-tolyl)ethan-1-ol (3.105-OH).** Product **3.105** was oxidized according to ***General Method for Oxidation of Boronic Ester Products. All spectral data was in accord with the literature.[68]

Determination of Stereochemical Identity: Racemic compound was prepared according to the general procedure (***Method B, run at 60 ºC***) with $Pd(OAc)_2$ (5 mol%) and 1,1′-Bis(diisopropylphosphino)ferrocene (6 mol%) as the catalyst. Absolute stereochemistry was assigned by analogy (see product **3.127** and **3.134**).

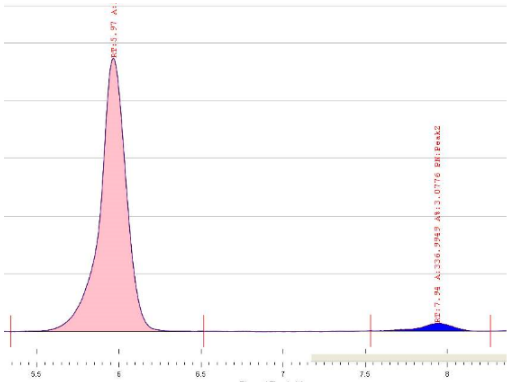
SFC (Chiracel OJ-H, 10% IPA, 3 mL/min, 100 bar, 35 °C, 210-270 nm) – analysis of (R)-2-phenyl-1-(p-tolyl)ethan-1-ol.

Racemic Material



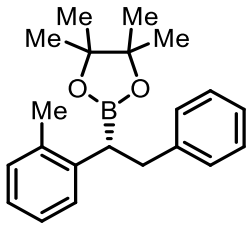
Peak No	% Area	Area	RT (min)
1	50.1383	2959.6156	5.87
2	49.8617	2943.2838	7.77
Total:	100	5902.8994	

Standard Conditions



Peak No	% Area	Area	RT (min)
1	96.9224	10612.8941	5.97
2	3.0776	336.9949	7.94
Total:	100	10949.889	

[68] Zhou, C.; Wang, Z. *Synthesis* **2005**, 10, 1649.

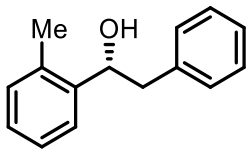


(*R*)-4,4,5,5-Tetramethyl-2-(2-phenyl-1-(o-tolyl)ethyl)-1,3,2-dioxaborolane (3.106). The reaction was performed according to the general procedure ***(Method B)*** with 4,4,5,5-tetramethyl-2-(o-tolyl)-1,3,2-dioxaborolane (65.4 mg, 0.30 mmol, 1.00 equiv), sodium trifluoromethanesulfonate (103.2 mg, 0.60 mmol, 2.00 equiv), vinylmagnesium chloride (0.20 mL, 1.53 M in tetrahydrofuran, 0.30 mmol, 1.00 equiv), phenyl trifluoromethanesulfonate (81.4 mg, 0.36 mmol, 1.20 equiv), palladium (II) acetate (0.90 mL, 0.01 M in dimethyl sulfoxide, 0.009 mmol, 0.030 equiv), (S_p,S_p)-**3.3** (11.37 mg, 0.0108 mmol, 0.036 equiv). The unpurified product was purified by silica gel chromatography (0% → 20% CH_2Cl_2 in hexanes, stained in CAM) to afford white solid (86.3 mg, 89% yield).

(Method C) with 4,4,5,5-tetramethyl-2-(o-tolyl)-1,3,2-dioxaborolane (65.4 mg, 0.30 mmol, 1.00 equiv), sodium trifluoromethanesulfonate (154.9 mg, 0.90 mmol, 3.00 equiv), vinylmagnesium chloride (0.20 mL, 1.53 M in tetrahydrofuran, 0.30 mmol, 1.00 equiv), bromobenzene (56.5 mg, 0.36 mmol, 1.20 equiv), palladium (II) acetate (0.90 mL, 0.01 M in dimethyl sulfoxide, 0.009 mmol, 0.030 equiv), (S_p,S_p)-**3.3** (11.37 mg, 0.0108 mmol, 0.036 equiv). The unpurified product was purified by silica gel chromatography (0% → 20% CH_2Cl_2 in hexanes, stained in CAM) to afford white solid (68.6 mg, 71% yield).

^{1}H NMR (500 MHz, $CDCl_3$) δ 7.40 (d, J = 7.6 Hz, 1H), 7.29 – 7.22 (m, 4H), 7.22 – 7.16 (m, 2H), 7.15 (d, J = 7.0 Hz, 1H), 7.10 (app t, J = 7.3 Hz, 1H), 3.21 (dd, J = 12.7, 9.0 Hz,

1H), 3.02 – 2.87 (m, 2H), 2.31 (s, 3H), 1.17 (s, 12H). **^{11}B NMR** (128 MHz, $CDCl_3$) δ 33.00. **^{13}C NMR** (126 MHz, $CDCl_3$) δ 142.16, 141.23, 136.29, 130.39, 129.05, 128.21, 128.14, 126.16, 125.93, 125.46, 83.49, 38.85, 30.42, 24.79, 24.77, 20.18. **IR** (neat) ν_{max} 3060.95 (w), 3026.24 (w), 2976.72 (m), 2928.80 (w), 2860.41 (w), 1601.71 (w) 1492.63 (m), 1453.84 (m), 1356.48 (s), 1322.40 (s), 1139.82 (s), 967.09 (m), 852.83 (m), 727.68 (s), 698.05 (s) cm^{-1}. **HRMS** (DART) for $C_{21}H_{28}BO_2$ $[M+H]^+$: calculated: 323.21823, found: 323.21834. $[\alpha]_D^{20} = -28.296$ (*c* 3.07, $CHCl_3$, *l* = 50 mm).

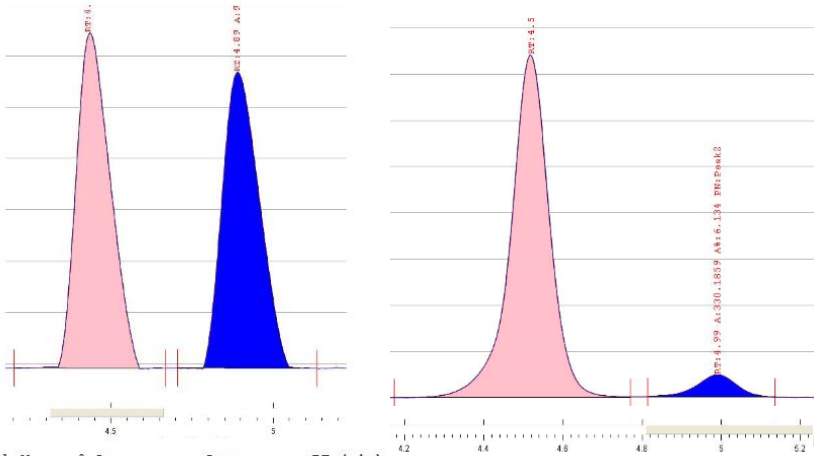


(R)*-2-Phenyl-1-(o-tolyl)ethan-1-ol (3.106-OH).** Product **3.106** was oxidized according to ***General Method for Oxidation of Boronic Ester Products. All spectral data was in accord with the literature.[61]

Determination of Stereochemical Identity: Racemic compound was prepared according to the general procedure (***Method B, run at 60 ºC***) with $Pd(OAc)_2$ (5 mol%) and 1,1′-Bis(diisopropylphosphino)ferrocene (6 mol%) as the catalyst. Absolute stereochemistry was assigned by analogy (see product **3.127** and **3.134**).

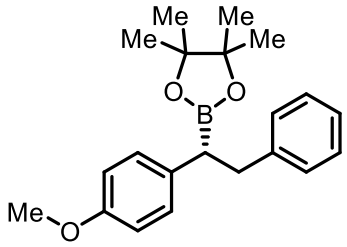
SFC (Chiracel OJ-H, 10% IPA, 3 mL/min, 100 bar, 35 °C, 210-270 nm) – analysis (R)-2-phenyl-1-(o-tolyl)ethan-1-ol.

Racemic Material Standard Conditions



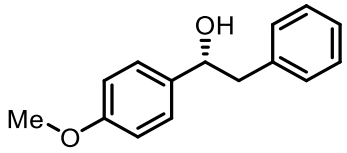
Peak No	% Area	Area	RT (min)
1	50.9739	943.0438	4.43
2	49.0261	907.009	4.89
Total:	100	1850.0528	

Peak No	% Area	Area	RT (min)
1	93.866	5052.7199	4.52
2	6.134	330.1859	4.99
Total:	100	5382.9058	



(*R*)-2-(1-(4-Methoxyphenyl)-2-phenylethyl)-4,4,5,5-tetramethyl-1,3,2-dioxaborolane (3.107). The reaction was performed according to general procedure (***Method B)*** with 2-(4-methoxyphenyl)-4,4,5,5-tetramethyl-1,3,2-dioxaborolane (70.23 mg, 0.30 mmol, 1.00 equiv), sodium trifluoromethanesulfonate (103.2 mg, 0.60 mmol, 2.00 equiv), vinylmagnesium chloride (0.20 mL, 1.53 M in tetrahydrofuran, 0.30 mmol, 1.00 equiv), phenyl trifluoromethanesulfonate (81.4 mg, 0.36 mmol, 1.20 equiv), palladium (II) acetate (0.9 mL, 0.01 M in dimethyl sulfoxide, 0.009 mmol, 0.030 equiv), (S_p,S_p)-**3.3** (11.37 mg, 0.0108 mmol, 0.036). The unpurified product was purified by automated silica gel chromatography (Biotage 1% → 5% ethyl acetate in hexanes, stained in CAM) to afford white solid (91.3 mg, 90% yield). **^{1}H NMR** (600 MHz, $CDCl_3$) δ 7.21 (t, *J* = 7.3 Hz, 1H), 7.19 – 7.11 (m, 3H), 6.80 (d, *J* = 8.7 Hz, 1H), 3.77 (s,

1H), 3.11 (dd, *J* = 13.5, 9.7 Hz, 1H), 2.92 (dd, *J* = 13.5, 7.0 Hz, 1H), 2.62 (dd, *J* = 9.6, 7.1 Hz, 1H), 1.11 (s, 3H), 1.11 (s, 3H). **^{11}B NMR** (160 MHz, $CDCl_3$) δ 32.75. **^{13}C NMR** (126 MHz, $CDCl_3$) δ 157.67 , 142.01 , 134.76 , 129.48 , 129.08 , 128.19 , 125.88 , 113.97 , 83.51 , 55.36 , 39.36 , 33.56 , 24.80 , 24.72. **IR** (neat) ν_{max} 3337.49 (br), 3027.54 (w), 2976.97 (w), 1607.00 (w), 1508.51 (s), 1360.39 (m), 1322.59 (m), 1242.35 (s), 1139.13 (s), 1034.72 (m), 966.96 (m). 828.44 (m), 697.81 (m), 541.36 (m) cm^{-1}. **HRMS** (DART) for $C_{21}H_{27}BO_3$ $[M+NH_4]^+$ calculated: 356.23970, found: 356.23969. $[\alpha]^{20}_D$: -49.358 (*c* 3.69, $CHCl_3$, *l* =50 mm).

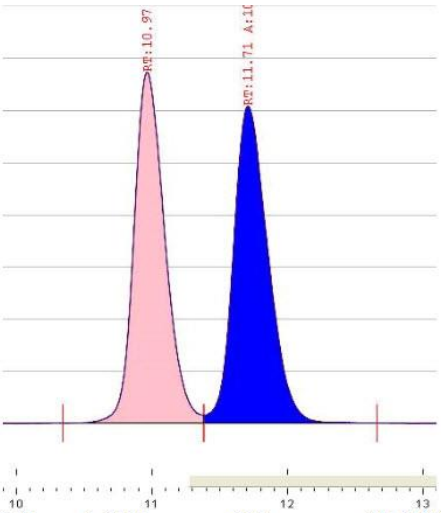


(R)*-1-(4-Methoxyphenyl)-2-phenylethan-1-ol (3.107-OH).** Product **3.107** was oxidized according to ***General Method for Oxidation of Boronic Ester Products. All spectral data was in accord with the literature.[61]

Determination of Stereochemical Identity: Racemic compound was prepared according to the general procedure (***Method B, run at 60 ºC***) with $Pd(OAc)_2$ (5 mol%) and 1,1′-Bis(dicyclohexylphosphino)ferrocene (6 mol%) as the catalyst. Absolute stereochemistry was assigned by analogy (see product **3.127** and **3.134**).

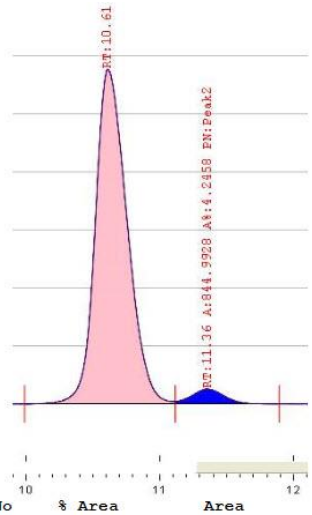
SFC (Chiracel OD-H, 8% IPA, 3 mL/min, 100 bar, 35 °C, 210-270 nm) – analysis of (R)-1-(4-methoxyphenyl)-2-phenylethan-1-ol.

Racemic Material

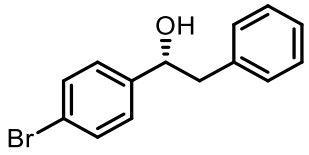


Peak No	% Area	Area	RT (min)
1	16.0614	2799.2453	7.02
2	83.9386	14629.1852	8.28
Total:	100	17428.4305	

Standard Conditions



Peak No	% Area	Area	RT (min)
1	95.7542	19056.8183	10.61
2	4.2458	844.9928	11.36
Total:	100	19901.8111	



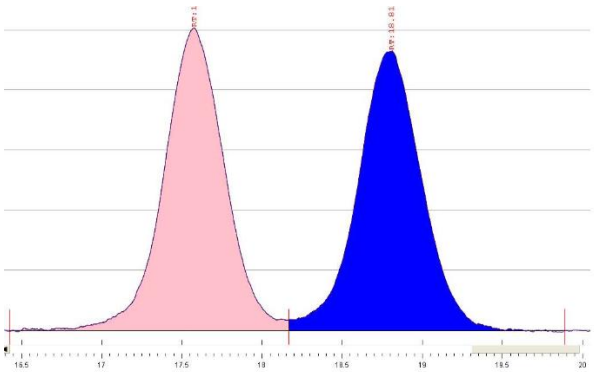
(*R*)-1-(4-Bromophenyl)-2-phenylethan-1-ol (3.108-OH). The reaction was performed according to the general procedure ***(Method B)*** with 4,4,5,5-tetramethyl-2-(4-bromophenyl)-1,3,2-dioxaborolane (**3.153**) (84.9 mg, 0.30 mmol, 1.00 equiv), sodium trifluoromethanesulfonate (103.2 mg, 0.60 mmol, 2.00 equiv), vinylmagnesium chloride (0.20 mL, 1.53 M in tetrahydrofuran, 0.30 mmol, 1.00 equiv), phenyl trifluoromethanesulfonate (81.4 mg, 0.36 mmol, 1.20 equiv) palladium (II) acetate (0.90 mL, 0.01 M in dimethyl sulfoxide, 0.009 mmol, 0.030 equiv), (S_p,S_p)-**3.3** (11.37 mg, 0.0108 mmol, 0.036 equiv). Unpurified product **3.108** was oxidized according to ***General Method for Oxidation of Boronic Ester Products.*** The unpurified product was purified by silica gel chromatography (0% → 20% → 50% CH_2Cl_2 in hexanes, stained in CAM) to afford

colorless oil (75.9 mg, 91% yield). **^{1}H NMR** (500 MHz, $CDCl_3$) δ 7.45 (d, *J* = 8.4 Hz, 2H), 7.29 (app t, *J* = 7.3 Hz, 2H), 7.24 (d, *J* = 7.3 Hz, 1H), 7.20 (d, *J* = 8.2 Hz, 2H), 7.15 (d, *J* = 6.8 Hz, 2H), 4.84 (dd, *J* = 8.2, 5.1 Hz, 1H), 2.99 (dd, *J* = 13.6, 5.0 Hz, 1H), 2.93 (dd, *J* = 13.6, 8.3 Hz, 1H), 2.01 (s, 1H). **^{13}C NMR** (126 MHz, $CDCl_3$) δ 142.94, 137.68, 131.66, 129.71, 128.80, 127.85, 126.99, 121.53, 74.87, 46.26. **IR** (neat) ν_{max} 3373.67 (m, br), 3084.72 (w), 3060.88 (w), 3027.32 (m), 2918.60 (m), 1591.86 (m), 1488.45 (s), 1453.70 (m), 1070.49 (s), 1044.49 (m), 1009.03 (s), 822.90 (s), 744.58 (s), 699.39 (s), 543.23 (s) cm^{-1}. **HRMS** (DART) for $C_{14}H_{12}Br$ $[M+H-H_2O]^+$: calculated: 259.01224, found: 259.01212. $[\alpha]_D^{20}$ = – 3.182 (*c* 2.28, $CHCl_3$, *l* = 50 mm).

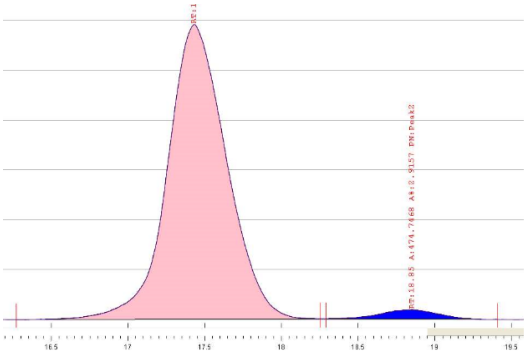
Determination of Stereochemical Identity: Racemic compound was prepared according to the general procedure (***Method B, run at 60 ºC***) with $Pd(OAc)_2$ (5 mol%) and 1,1′-Bis(diisopropylphosphino)ferrocene (6 mol%) as the catalyst. Absolute stereochemistry was assigned by analogy (see product **3.127** and **3.134**).

SFC (Chiracel OD-H, 6% IPA, 3 mL/min, 100 bar, 35 °C, 210-270 nm) – analysis (R)-1-(4-bromophenyl)-2-phenylethan-1-ol.

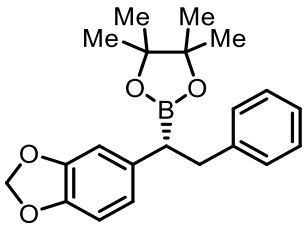
Racemic Material Standard Conditions



Peak No	% Area	Area	RT (min)
1	50.7049	2678.072	17.58
2	49.2951	2603.6058	18.81
Total:	100	5281.6778	



Peak No	% Area	Area	RT (min)
1	97.0843	15807.6836	17.43
2	2.9157	474.7468	18.85
Total:	100	16282.4304	



(*R*)-2-(1-(Benzo[d][1,3]dioxol-5-yl)-2-phenylethyl)-4,4,5,5-tetramethyl-1,3,2-dioxaborolane (3.109). The reaction was performed according to the general procedure ***(Method B)*** with 2-(benzo[d][1,3]dioxol-5-yl)-4,4,5,5-tetramethyl-1,3,2-dioxaborolane (74.4 mg, 0.30 mmol, 1.00 equiv), sodium trifluoromethanesulfonate (103.2 mg, 0.60 mmol, 2.00 equiv), vinylmagnesium chloride (0.20 mL, 1.53 M in tetrahydrofuran, 0.30 mmol, 1.00 equiv), phenyl trifluoromethanesulfonate (81.4 mg, 0.36 mmol, 1.20 equiv), palladium (II) acetate (0.90 mL, 0.01 M in dimethyl sulfoxide, 0.009 mmol, 0.030 equiv), (S_p,S_p)-**3.3** (11.37 mg, 0.0108 mmol, 0.036 equiv). The unpurified

product was purified by automated silica gel chromatography (Biotage 1% → 10% ethyl acetate in hexanes, stained in CAM) to afford white solid (91.9 mg, 87% yield).

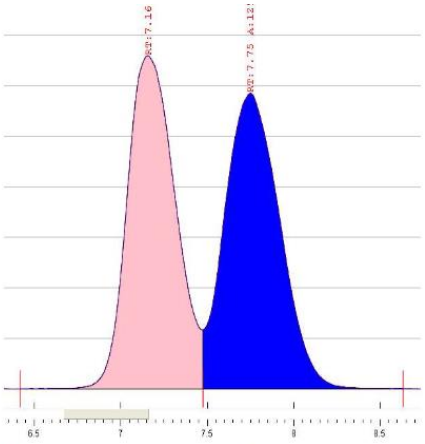
(Method C) with 2-(benzo[d][1,3]dioxol-5-yl)-4,4,5,5-tetramethyl-1,3,2-dioxaborolane (74.4 mg, 0.30 mmol, 1.00 equiv), sodium trifluoromethanesulfonate (154.9 mg, 0.90 mmol, 3.00 equiv), vinylmagnesium chloride (0.20 mL, 1.53 M in tetrahydrofuran, 0.30 mmol, 1.00 equiv), bromobenzene (56.5 mg, 0.36 mmol, 1.20 equiv), palladium (II) acetate (0.90 mL, 0.01 M in dimethyl sulfoxide, 0.009 mmol, 0.030 equiv), (S_p, S_p)-**3.3** (11.37 mg, 0.0108 mmol, 0.036 equiv). Purification by automated silica gel chromatography (Biotage 1% → 10% ethyl acetate in hexanes, stained in CAM) to afford white solid (80.3 mg, 76% yield).

^{1}H NMR (600 MHz, $CDCl_3$) δ 7.20 (app t, J = 7.6 Hz, 2H), 7.15 (d, J = 7.4 Hz, 2H), 7.12 (app t, J = 7.2 Hz, 1H), 6.75 (d, J = 1.4 Hz, 1H), 6.68 (d, J = 8.0 Hz, 1H), 6.64 (dd, J = 8.0, 1.4 Hz, 1H), 5.89 (s, 2H), 3.07 (dd, J = 13.5, 9.5 Hz, 1H), 2.89 (dd, J = 13.5, 7.2 Hz, 1H), 2.58 (dd, J = 9.2, 7.4 Hz, 1H), 1.11 (s, 6H), 1.10 (s, 6H). **^{11}B NMR** (128 MHz, $CDCl_3$) δ 32.82. **^{13}C NMR** (151 MHz, $CDCl_3$) δ 147.71, 145.51, 141.80, 136.59, 129.08, 128.24, 125.97, 121.46, 109.12, 108.37, 100.87, 83.63, 39.43, 34.24, 24.82, 24.75. **IR** (neat) ν_{max} 3063.47 (w), 3027.13 (w), 2977.09 (m), 2925.36 (m), 2897.27 (m), 1486.69 (s), 1370.75 (s), 1327.09 (s), 1241.03 (s), 1142.13 (s), 1040.12 (s), 937.94 (m), 861.96 (m), 810.61 (m), 699.61 (m) cm^{-1}. **HRMS** (DART) for $C_{21}H_{26}BO_4$ $[M+H]^+$: calculated: 353.19241, found: 353.19152. $[\alpha]_D^{20}$ = – 53.108 (*c* 1.79, $CHCl_3$, *l* = 50 mm).

Determination of Stereochemical Identity: Racemic compound was prepared according to the general procedure (***Method B, run at 60 ºC***) with $Pd(OAc)_2$ (5 mol%) and 1,1′-Bis(dicyclohexylphosphino)ferrocene (6 mol%) as the catalyst. Absolute stereochemistry was assigned by analogy (see product **3.127** and **3.134**).

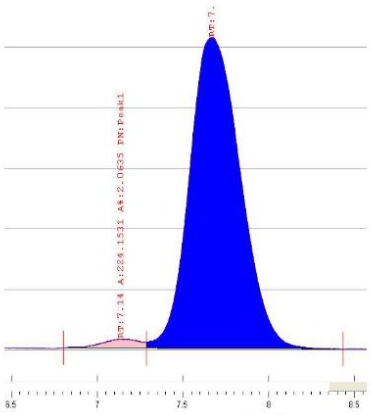
SFC (Chiracel OJ-H, 0% IPA, 3 mL/min, 100 bar, 35 °C, 210-270 nm) – analysis of (R)-2-(1-(benzo[d][1,3]dioxol-5-yl)-2-phenylethyl)-4,4,5,5-tetramethyl-1,3,2-dioxaborolane.

Racemic Material

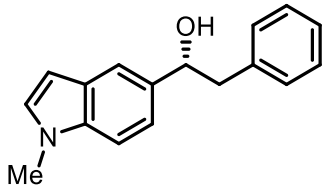


Peak No	% Area	Area	RT (min)
1	49.6278	12782.896	7.16
2	50.3722	12974.6567	7.75
Total:	100	25757.5527	

Standard Conditions



Peak No	% Area	Area	RT (min)
1	2.0635	224.1531	7.14
2	97.9365	10638.5433	7.67
Total:	100	10862.6964	



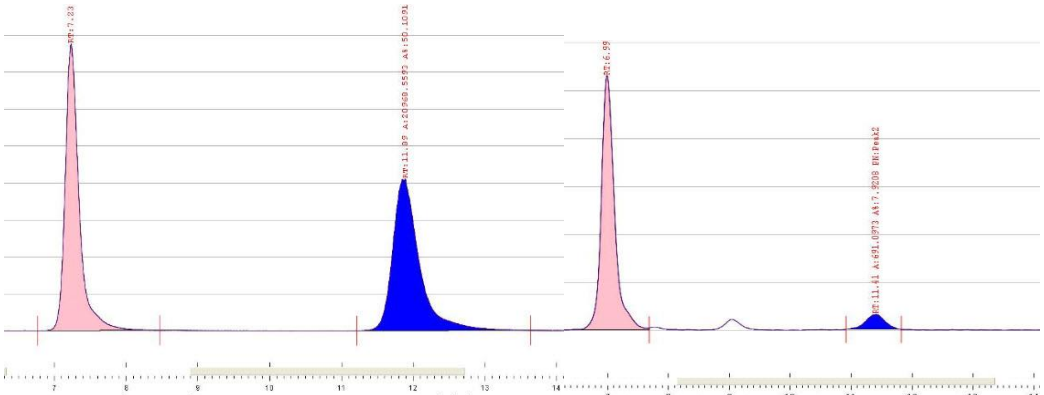
(*R*)-1-(1-Methyl-1H-indol-5-yl)-2-phenylethan-1-ol (3.110-OH). The reaction was performed according to general procedure ***(Method B)*** with 1-methyl-5-(4,4,5,5-tetramethyl-

1,3,2-dioxaborolan-2-yl)-1H-indole (77.1 mg, 0.30 mmol, 1.00 equiv), sodium trifluoromethanesulfonate (103.2 mg, 0.60 mmol, 2.00 equiv), vinylmagnesium chloride (0.20 mL, 1.53 M in tetrahydrofuran, 0.30 mmol, 1.00 equiv), phenyl trifluoromethanesulfonate (81.4 mg, 0.36 mmol, 1.20 equiv), palladium (II) acetate (0.9 mL, 0.01 M in dimethyl sulfoxide, 0.009 mmol, 0.030 equiv), (S_p,S_p)-**3.3** (11.37 mg, 0.0108 mmol. 0.036). Unpurified product **3.110** was oxidized according to ***General Method for Oxidation of Boronic Ester Products.*** The unpurified product was purified by automated silica gel chromatography (Biotage 1% → 20% ethyl acetate in hexanes, stained in CAM) to afford white solid (37.7 mg, 50% yield). All spectral data was in accord with the literature.[6]

Determination of Stereochemical Identity: Racemic compound was prepared according to the general procedure (***Method B, run at 60 ºC***) with $Pd(OAc)_2$ (5 mol%) and 1,1′-Bis(dicyclohexylphosphino)ferrocene (6 mol%) as the catalyst. Absolute stereochemistry was assigned by analogy (see product **3.127** and **3.134**).

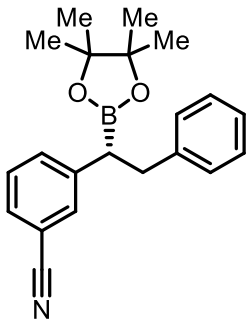
SFC (Chiracel OJ-H, 30% IPA, 3 mL/min, 100 bar, 35 °C, 210-270 nm) – analysis of (R)-1-(1-methyl-1H-indol-5-yl)-2-phenylethan-1-ol.

Racemic Material Standard Conditions



Peak No	% Area	Area	RT (min)
1	49.8909	20877.2269	7.23
2	50.1091	20968.5593	11.89
Total:	100	41845.7862	

Peak No	% Area	Area	RT (min)
1	92.0792	8034.0038	6.99
2	7.9208	691.0973	11.41
Total:	100	8725.1011	



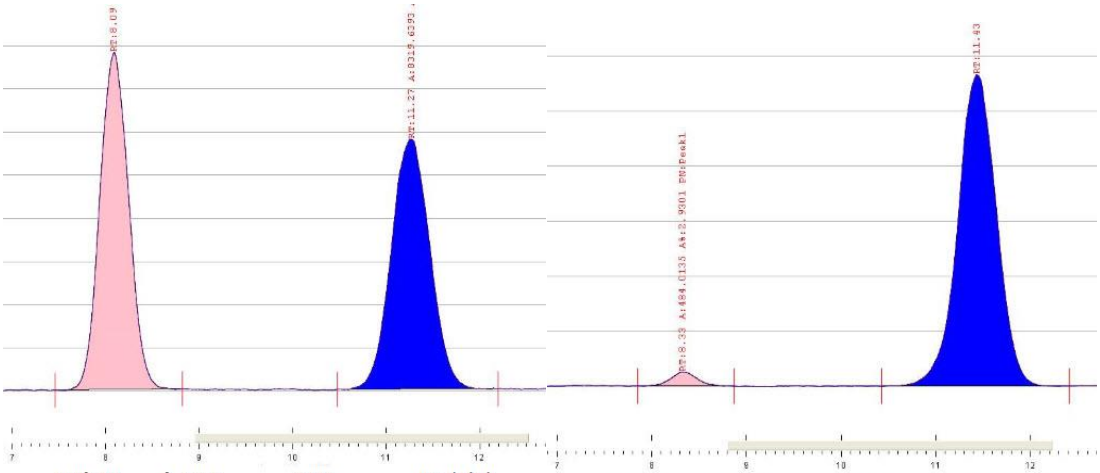
(*R*)-3-(2-Phenyl-1-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)ethyl) benzonitrile (3.111). The reaction was performed according to general procedure ***(Method B)*** with 3-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)benzonitrile (68.7 mg, 0.30 mmol, 1.00 equiv), sodium trifluoromethanesulfonate (103.2 mg, 0.60 mmol, 2.00 equiv), vinylmagnesium chloride (0.20 mL, 1.53M in tetrahydrofuran, 0.30 mmol, 1.00 equiv), phenyl trifluoromethanesulfonate (81.4 mg, 0.36 mmol, 1.20 equiv), palladium (II) acetate (0.9 mL, 0.01 M in dimethyl sulfoxide, 0.009 mmol, 0.030 equiv), (S_p, S_p)-**3.3** (11.37 mg, 0.0108 mmol). The unpurified product was purified by automated silica gel chromatography (Biotage 1% → 5% ethyl acetate in hexanes, stained in CAM) to afford white solid (69.9 mg, 70% yield). **^{1}H NMR** (600 MHz, $CDCl_3$) δ 7.49 (app t, *J* = 1.5 Hz, 1H), 7.40 (app dd, *J* = 7.8, 1.6 Hz, 2H), 7.30 (app t, 1H), 7.20 (app t, *J* = 7.4 Hz, 2H), 7.16 – 7.07 (m, 3H), 3.13 (dd, *J* = 13.6, 8.8 Hz, 1H), 2.91 (dd, *J* = 13.6, 7.8 Hz, 1H), 2.70 (app t, *J* = 8.3 Hz, 1H), 1.12 (s, 6H), 1.11 (s, 6H). **^{11}B NMR** (160 MHz,

$CDCl_3$) δ 32.59. **^{13}C NMR** (151 MHz, $CDCl_3$) δ 144.25, 140.80, 133.35, 132.16, 129.43, 129.16, 128.94, 128.36, 126.27, 119.37, 112.40, 84.00, 38.64, 34.37, 24.77, 24.70. **IR** (neat) ν_{max} 3027.61 (w), 2931.10 (w), 2228.22 (w), 1599.68 (w), 1579.48 (w), 1480.71 (w), 1359.55 (m), 1332.50 (m), 1139.37 (w), 969.24 (w), 859.19 (w). 798.94 (w), 699.91 (s) cm^{-1}. **HRMS** (DART) for $C_{21}H_{28}BO_3N_2$ $[M+NH_4]^+$ calculated: 351.22438, found: 351.22411. $[\alpha]^{20}_D$: -57.715 (*c* 2.83, $CHCl_3$, *l* =50 mm).

Determination of Stereochemical Identity: Racemic compound was prepared according to the general procedure (***Method B, run at 60***) with $Pd(OAc)_2$ (5 mol%) and 1,1′-Bis(dicyclohexylphosphino)ferrocene (6 mol%) as the catalyst. Absolute stereochemistry was assigned by analogy (see product **3.127** and **3.134**).

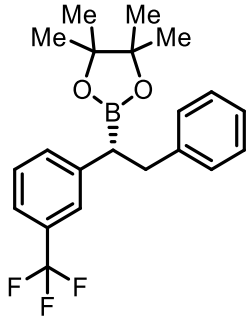
SFC (Chiracel OJ-H, 1% IPA, 3 mL/min, 100 bar, 35 °C, 210-270 nm) – analysis of (R)-3-(2-phenyl-1-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)ethyl)benzonitrile.

Racemic Material Standard Conditions



Peak No	% Area	Area	RT (min)
1	50.1611	8373.4164	8.09
2	49.8389	8319.6393	11.27
Total:	100	16693.0557	

Peak No	% Area	Area	RT (min)
1	2.9301	484.0135	8.33
2	97.0699	16034.4013	11.43
Total:	100	16518.4148	



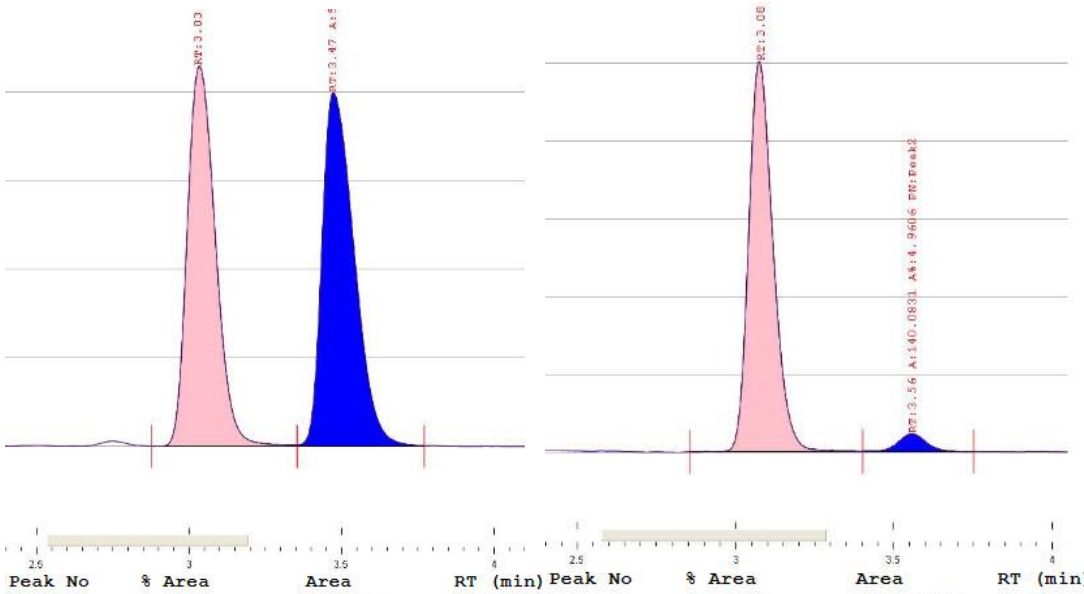
(*R*)-4,4,5,5-Tetramethyl-2-(2-phenyl-1-(3-(trifluoromethyl)phenyl)ethyl) -1,3,2-dioxaborolane (3.112). The reaction was performed according to general procedure ***(Method B, with the modification that the reaction was run at 60 ºC instead of 40 ºC)*** with 4,4,5,5-tetramethyl-2-(3-(trifluoromethyl)phenyl)-1,3,2-dioxaborolane (81.6 mg, 0.30 mmol, 1.00 equiv), sodium trifluoromethanesulfonate (103.2 mg, 0.60 mmol, 2.00 equiv), vinylmagnesium chloride (0.20 mL, 1.53 M in tetrahydrofuran, 0.30 mmol, 1.00 equiv), phenyl trifluoromethanesulfonate (81.4 mg, 0.36 mmol, 1.20 equiv), palladium (II) acetate (0.9 mL, 0.01 M in dimethyl sulfoxide, 0.009 mmol, 0.030 equiv), (S_p, S_p)-**3.3** (11.37 mg, 0.0108 mmol, 0.036). The unpurified product was purified by automated silica gel chromatography (Biotage 1% → 5% ethyl acetate in hexanes, stained in CAM) to afford white solid (65.5 mg, 58% yield**). ^{1}H NMR** (500 MHz, $CDCl_3$) δ 7.49 (s, 1H), 7.41 – 7.36 (m, 2H), 7.36 – 7.30 (m, 1H), 7.26 – 7.18 (m, 2H), 7.17

– 7.11 (m, 3H), 3.15 (dd, J = 13.5, 9.5 Hz, 1H), 2.95 (dd, J = 13.5, 7.2 Hz, 1H), 2.80 – 2.68 (m, 1H), 1.12 (s, 6H), 1.10 (s, 6H). **^{11}B NMR** (160 MHz, $CDCl_3$) δ 32.79. **^{13}C NMR** (126 MHz, $CDCl_3$) δ 143.77 , 141.27 , 132.15 , 130.75 (q, J = 31.8 Hz), 129.05 , 128.87 , 128.36 , 126.20 , 125.41 (q, J = 3.8 Hz), 124.56 (q, J = 272.3 Hz), 122.51 (q, J = 3.9 Hz), 83.91 , 38.97 , 34.69 , 24.81 , 24.67. **IR** (neat) ν_{max} 2979.24 (w), 2929.51 (w), 1370.49 (m), 1328.10 (s), 1162.98 (m), 1140.73 (s), 1075.10 (w), 6.98.96 (w) cm^{-1}. **HRMS** (DART) for $C_{21}H_{25}BF_3O_2$ $[M+H]^+$ calculated: 377.19, found: 377.1915. $[\alpha]^{20}_D$: -34.893 (*c* 1.720, $CHCl_3$, *l* =50 mm).

Determination of Stereochemical Identity: Racemic compound was prepared according to the general procedure (***Method B, run a t60 ºC***) with $Pd(OAc)_2$ (5 mol%) and 1,1′-Bis(dicyclohexylphosphino)ferrocene (6 mol%) as the catalyst. Absolute stereochemistry was assigned by analogy (see product **3.127** and **3.134**).

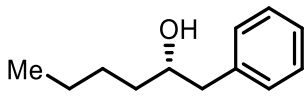
SFC (Chiracel ODR-H, 1% IPA, 3 mL/min, 100 bar, 35 °C, 210-270 nm) – analysis of (R)-4,4,5,5-tetramethyl-2-(2-phenyl-1-(3-(trifluoromethyl)phenyl)ethyl)-1,3,2-dioxaborolane.

Racemic Material Standard Conditions



Peak No	% Area	Area	RT (min)
1	48.6367	5493.607	3.03
2	51.3633	5801.5807	3.47
Total:	100	11295.1877	

Peak No	% Area	Area	RT (min)
1	95.0394	2683.8159	3.08
2	4.9606	140.0831	3.56
Total:	100	2823.899	

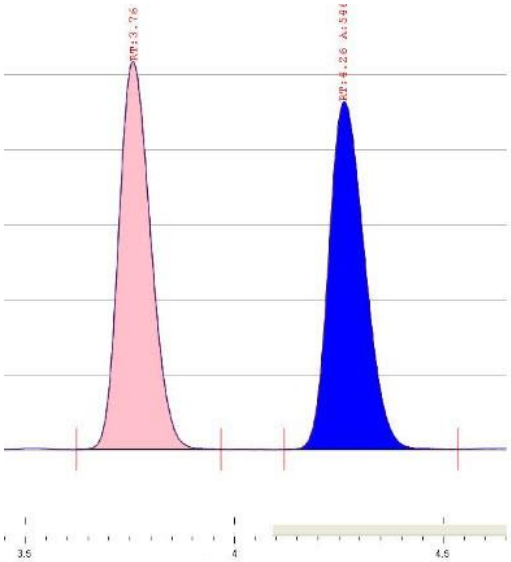


(S)*-1-Phenylhexan-2-ol (3.127-OH).** The reaction was performed according to general procedure ***(Method B) with 2-butyl-4,4,5,5-tetramethyl-1,3,2-dioxaborolane () (55.2 mg, 0.30 mmol, 1.00 equiv), sodium trifluoromethanesulfonate (103.2 mg, 0.60 mmol, 2.00 equiv), vinylmagnesium chloride (0.20 mL, 1.53 M in tetrahydrofuran, 0.30 mmol, 1.00 equiv), phenyl trifluoromethanesulfonate (81.4 mg, 0.36 mmol, 1.20 equiv), palladium (II) acetate (0.9 mL, 0.01 M in dimethyl sulfoxide, 0.009 mmol, 0.030 equiv), (S_p,S_p)-**3.3** (11.37 mg, 0.0108 mmol, 0.036). Unpurified product **3.127** was oxidized according to ***General Method for Oxidation of Boronic Ester Products.*** The unpurified product was purified by automated silica gel chromatography (Biotage 1% → 5% ethyl acetate in hexanes, stained in CAM) to afford colorless oil (31.0 mg, 58% yield). All spectral data was in accord with the literature.[61]

Determination of Stereochemical Identity: Racemic compound was prepared according to the general procedure **(*Method B, run at 60 ºC*)** with $Pd(OAc)_2$ (5 mol%) and 1,1′-Bis(dicyclohexylphosphino)ferrocene (6 mol%) as the catalyst. Absolute stereochemistry was assigned by analogy (see product **3.127** and **3.134**).

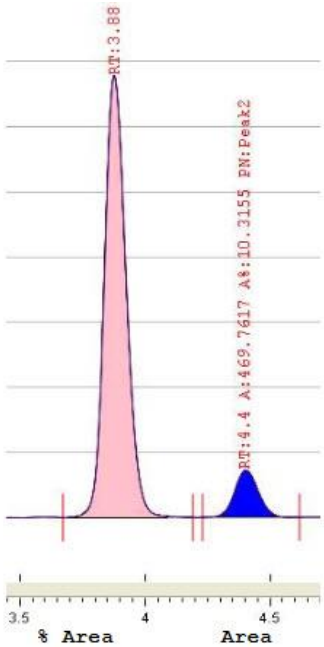
SFC (Chiracel OD-H, 5% IPA, 3 mL/min, 100 bar, 35 °C, 210-270 nm) – analysis of (S)-1-phenylhexan-2-ol.

Racemic Material

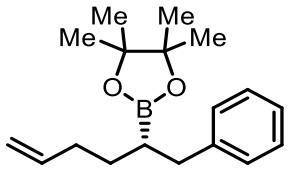


Peak No	% Area	Area	RT (min)
1	49.8946	5442.8203	3.76
2	50.1054	5465.8191	4.26
Total:	100	10908.6394	

Standard Conditions



Peak No	% Area	Area	RT (min)
1	89.6845	4084.1825	3.88
2	10.3155	469.7617	4.4
Total:	100	4553.9442	

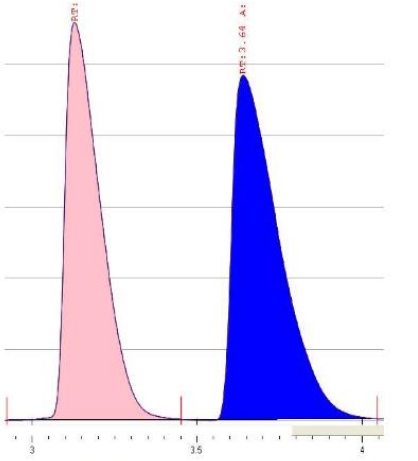


(*S*)-4,4,5,5-Tetramethyl-2-(1-phenylhex-5-en-2-yl)-1,3,2-dioxaborolane (3.128). The reaction was performed according to the general procedure ***(Method B)*** with 2-(3-buten-1-yl)-4,4,5,5-tetramethyl-1,3,2-dioxaborolane (54.6 mg, 0.30 mmol, 1.00 equiv), sodium trifluoromethanesulfonate (103.2 mg, 0.60 mmol, 2.00 equiv), vinylmagnesium chloride (0.20 mL, 1.53 M in tetrahydrofuran, 0.30 mmol, 1.00 equiv), phenyl trifluoromethanesulfonate (81.4 mg, 0.36 mmol, 1.20 equiv), palladium (II) acetate (0.90 mL, 0.01 M in dimethyl sulfoxide, 0.009 mmol, 0.030 equiv), (S_p,S_p)-**3.3** (11.37 mg, 0.0108 mmol, 0.036 equiv). The unpurified product was purified by automated silica gel chromatography (Biotage 1% → 4% ethyl acetate in hexanes, stained in CAM) to afford colorless oil (62.7 mg, 73% yield). **^{1}H NMR** (600 MHz, $CDCl_3$) δ 7.24 – 7.17 (m, 4H), 7.13 (app t, J = 7.1 Hz, 1H), 5.78 (dddd, J = 16.9, 10.2, 6.7, 6.7 Hz, 1H), 4.98 (dd, J = 17.1, 1.8 Hz, 1H), 4.91 (dd, J = 10.2, 1.1 Hz, 1H), 2.71 (dd, J = 13.6, 8.7 Hz, 1H), 2.66 (dd, J = 13.6, 7.5 Hz, 1H), 2.14 – 2.00 (m, 2H), 1.58 – 1.43 (m, 2H), 1.43 – 1.35 (m, 1H), 1.15 (s, 6H), 1.12 (s, 6H). **^{11}B NMR** (128 MHz, $CDCl_3$) δ 33.82. **^{13}C NMR** (151 MHz, $CDCl_3$) δ 142.36, 139.16, 129.07, 128.24, 125.81, 114.61, 83.21, 37.44, 33.58, 30.63, 25.56, 25.01, 24.93. **IR** (neat) ν_{max} 3063.58 (w), 3026.57 (w), 2977.20 (m), 2925.82 (m), 2855.22 (w), 1729.94 (w), 1380.67 (s), 1318.76 (s), 1143.00 (s), 908.95 (m), 860.66 (m), 743.50 (m), 698.71 (m) cm^{-1}. **HRMS** (DART) for $C_{18}H_{31}BNO_2$ $[M+NH_4]^+$: calculated: 304.24478, found: 304.24478. $[\alpha]_D^{20}$ = – 3.876 (*c* 1.84, $CHCl_3$, *l* = 50 mm).

Determination of Stereochemical Identity: Racemic compound was prepared according to the general procedure (***Method B, run at 60 ºC***) with $Pd(OAc)_2$ (5 mol%) and 1,1′-Bis(dicyclohexylphosphino)ferrocene (6 mol%) as the catalyst. Absolute stereochemistry was assigned by analogy (see product **3.127** and **3.134**).

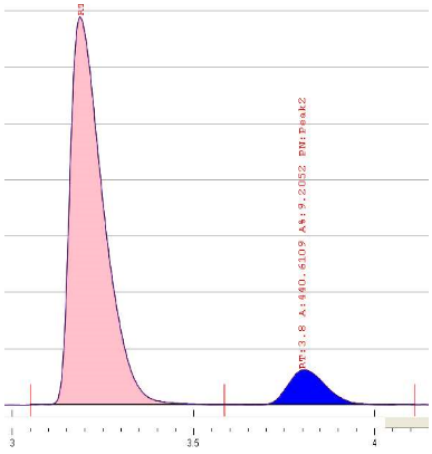
SFC (Chiracel ODR-H, 1% IPA, 3 mL/min, 100 bar, 35 °C, 210-270 nm) – analysis (S)-4,4,5,5-tetramethyl-2-(1-phenylhex-5-en-2-yl)-1,3,2-dioxaborolane.

Racemic Material

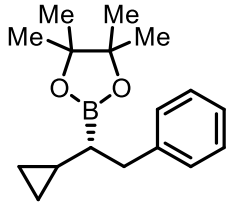


Peak No	% Area	Area	RT (min)
1	46.717	8238.0355	3.13
2	53.283	9395.8698	3.64
Total:	100	17633.9053	

Standard Conditions



Peak No	% Area	Area	RT (min)
1	90.7948	4345.9488	3.19
2	9.2052	440.6109	3.8
Total:	100	4786.5597	



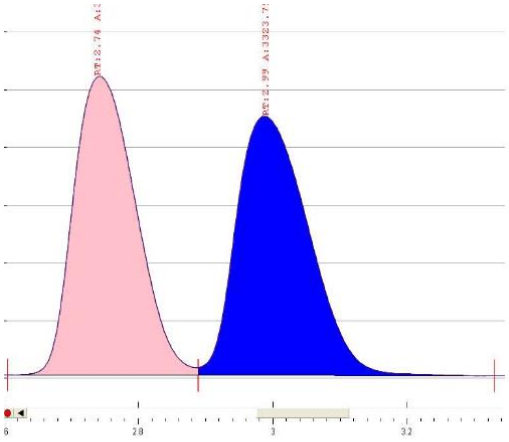
(*R*)-2-(1-Cyclopropyl-2-phenylethyl)-4,4,5,5-tetramethyl-1,3,2-dioxaboro lane (3.115). The reaction was performed according to the general procedure ***(Method B)*** with 2-cyclopropyl-4,4,5,5-tetramethyl-1,3,2-dioxaborolane (50.4 mg, 0.30 mmol, 1.00 equiv), sodium

trifluoromethanesulfonate (103.2 mg, 0.60 mmol, 2.00 equiv), vinylmagnesium chloride (0.20 mL, 1.53 M in tetrahydrofuran, 0.30 mmol, 1.00 equiv), phenyl trifluoromethanesulfonate (81.4 mg, 0.36 mmol, 1.20 equiv), palladium (II) acetate (0.90 mL, 0.01 M in dimethyl sulfoxide, 0.009 mmol, 0.030 equiv), (S_p,S_p)-**3.3** (11.37 mg, 0.0108 mmol, 0.036 equiv). The unpurified product was purified by automated silica gel chromatography (Biotage 1% → 5% ethyl acetate in hexanes, stained in CAM) to afford colorless oil (62.1 mg, 76% yield). **^{1}H NMR** (500 MHz, $CDCl_3$) δ 7.23 – 7.17 (m, 4H), 7.14 – 7.09 (m, 1H), 2.85 – 2.74 (m, 2H), 1.14 (s, 6H), 1.12 (s, 6H), 0.79 – 0.67 (m, 2H), 0.44 – 0.34 (m, 2H), 0.16 – 0.11 (m, 1H), 0.03 – -0.02 (m, 1H). **^{11}B NMR** (128 MHz, $CDCl_3$) δ 33.49. **^{13}C NMR** (151 MHz, $CDCl_3$) δ 142.60, 129.09, 128.17, 125.72, 83.21, 37.89, 31.51, 24.92, 24.86, 12.87, 5.52, 3.82. **IR** (neat) ν_{max} 3074.67 (w), 3027.59 (w), 2977.93 (m), 2928.94 (w), 2855.57 (w), 1603.16 (w), 1377.91 (s), 1320.03 (s), 1216.53 (m), 1142.57 (s), 977.86 (m), 865.02 (m), 744.32 (m), 698.31 (s) cm^{-1}. **HRMS** (DART) for $C_{17}H_{26}BO_2$ $[M+H]^+$: calculated: 273.20258, found: 273.20328. $[\alpha]_D^{20}$ = – 10.575 (*c* 2.89, $CHCl_3$, *l* = 50 mm).

Determination of Stereochemical Identity: Racemic compound was prepared according to the general procedure (***Method B, run at 60 ºC***) with $Pd(OAc)_2$ (5 mol%) and 1,1′-Bis(dicyclohexylphosphino)ferrocene (6 mol%) as the catalyst. Absolute stereochemistry was assigned by analogy (see product **3.127** and **3.134**).

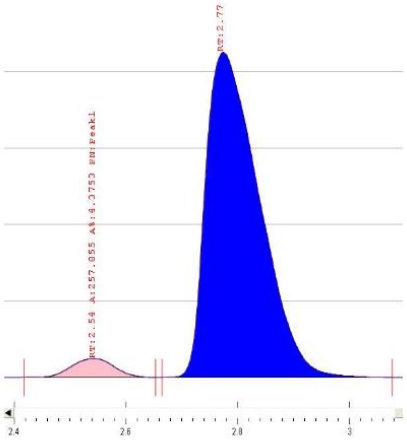
SFC (Chiracel ODR-H, 1% IPA, 3 mL/min, 100 bar, 35 °C, 210-270 nm) – analysis (R)-2-(1-cyclopropyl-2-phenylethyl)-4,4,5,5-tetramethyl-1,3,2-dioxaborolane.

Racemic Material

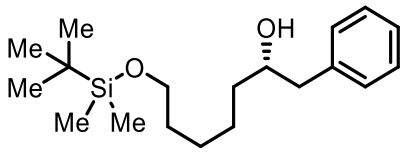


Peak No	% Area	Area	RT (min)
1	49.8436	3303.0686	2.74
2	50.1564	3323.7975	2.99
Total:	100	6626.8661	

Standard Conditions



Peak No	% Area	Area	RT (min)
1	4.3753	257.855	2.54
2	95.6247	5635.5716	2.77
Total:	100	5893.4266	



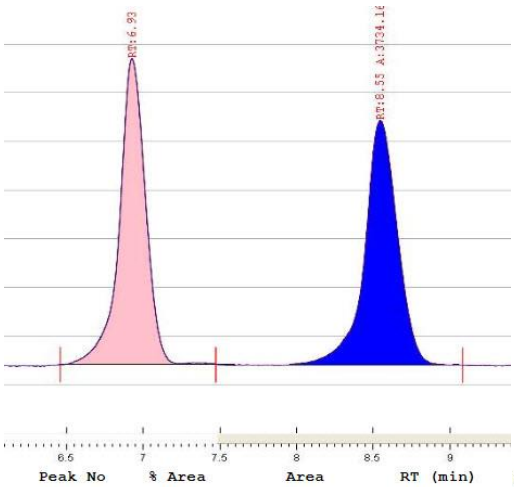
(*S*)-7-((*tert*-Butyldimethylsilyl)oxy)-1-phenylheptan-2-ol (3.116-OH). The reaction was performed according to general procedure ***(Method B)*** with *tert*-butyldimethyl((5-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)pentyl)oxy)silane (98.6 mg, 0.30 mmol, 1.00 equiv), sodium trifluoromethanesulfonate (103.2 mg, 0.60 mmol, 2.00 equiv), vinylmagnesium chloride (0.20 mL, 1.53 M in tetrahydrofuran, 0.30 mmol, 1.00 equiv), phenyl trifluoromethanesulfonate (81.4 mg, 0.36 mmol, 1.20 equiv), palladium (II) acetate (0.9 mL, 0.01 M in dimethyl sulfoxide, 0.009 mmol, 0.030 equiv), (S_p,S_p)-**3.3** (11.37 mg, 0.0108 mmol, 0.036). Unpurified product **3.116** was oxidized

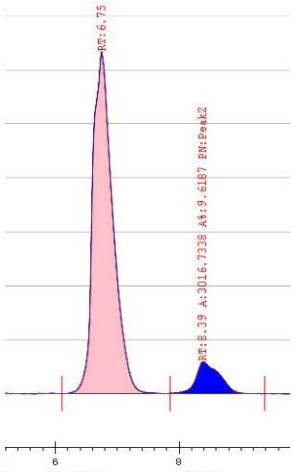
according to ***General Method for Oxidation of Boronic Ester Products.*** The unpurified product was purified by automated silica gel chromatography (Biotage 1% → 20% ethyl acetate in hexanes, stained in CAM) to afford colorless oil (80.3 mg, 83% yield). **^{1}H NMR** (600 MHz, $CDCl_3$) δ 7.33 – 7.27 (m, 2H), 7.23 – 7.17 (m, 3H), 3.87 – 3.73 (m, 1H), 3.59 (t, *J* = 6.6 Hz, 2H), 2.81 (dd, *J* = 13.6, 4.2 Hz, 1H), 2.63 (dd, *J* = 13.6, 8.4 Hz, 1H), 1.56 – 1.45 (m, 6H), 1.40 – 1.28 (m, 3H), 0.88 (s, 9H), 0.03 (s, 6H). **C^{13} NMR** (151 MHz, $CDCl_3$) δ 138.83, 129.63, 128.78, 126.66, 72.85, 63.42, 44.31, 37.07, 33.06, 26.22, 26.10, 25.80, 18.60, -5.02. **IR** (neat) ν_{max} 3410.16 (br), 2928.75 (s), 2856.29 (s), 1253.25 (m), 1094.72 (m), 832.61 (m), 773.80 (m), 698.82 (m) cm^{-1}. **HRMS** (DART) for $C_{19}H_{34}O_2Si$ $[M+H]^+$ calculated: 323.2406, found: 323.2418. $[\alpha]^{20}_D$: +5.549 (*c* 1.135, $CHCl_3$, *l* =50 mm).

Determination of Stereochemical Identity: Racemic compound was prepared according to the general procedure **(*Method E, run at 60 ºC*)** with $Pd(OAc)_2$ (5 mol%) and 1,1′-Bis(dicyclohexylphosphino)ferrocene (6 mol%) as the catalyst. Absolute stereochemistry was assigned by analogy (see product **3.127** and **3.134**).

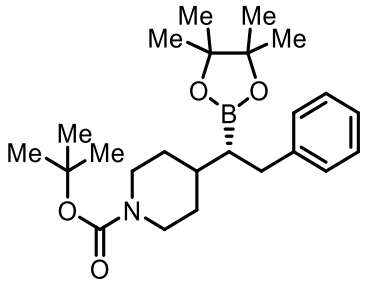
SFC (Chiracel OD-H, 5% IPA, 3 mL/min, 100 bar, 35 °C, 210-270 nm) – analysis of (S)-7-((tert-butyldimethylsilyl)oxy)-1-phenylheptan-2-ol.

Racemic Materia Standard Conditions





Peak No	% Area	Area	RT (min)	Peak No	% Area	Area	RT (min)
1	50.0389	3739.9901	6.93	1	90.3813	28346.3254	6.75
2	49.9611	3734.1684	8.55	2	9.6187	3016.7338	8.39
Total:	100	7474.1585		Total:	100	31363.0592	



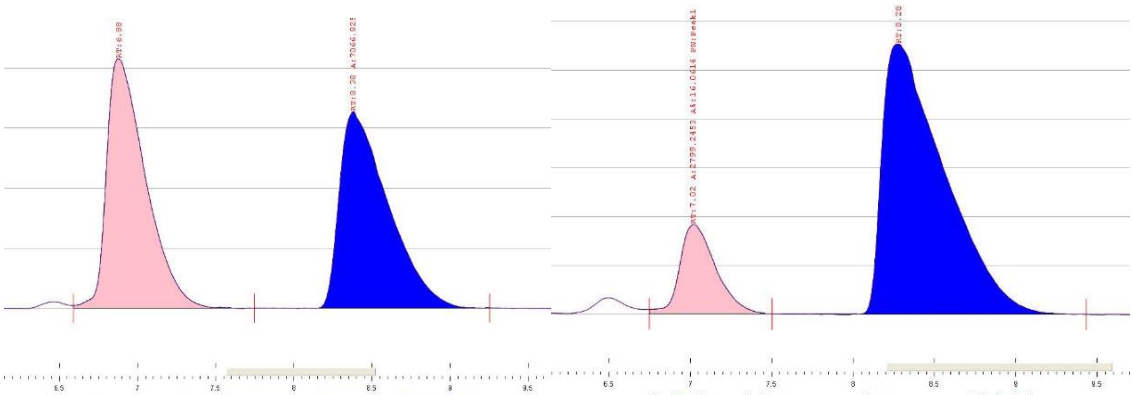
tert*-Butyl (*R*)-4-(2-phenyl-1-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)ethyl)piperidine-1-carboxylate (3.117).** The reaction was performed according to the general procedure ***(Method B) with *tert*-butyl 4-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)piperidine-1-carboxylate (70.2 mg, 0.30 mmol, 1,00 equiv), sodium trifluoromethanesulfonate (103.2 mg, 0.60 mmol, 2.00 equiv), vinylmagnesium chloride (0.20 mL, 1.53 M in tetrahydrofuran, 0.30 mmol, 1.00 equiv), phenyl trifluoromethanesulfonate (81.4 mg, 0.36 mmol, 1.20 equiv), palladium (II) acetate (0.9 mL, 0.01 M in dimethyl sulfoxide, 0.009 mmol, 0.030 equiv), (S_p,S_p)-**3.3** (11.37 mg, 0.0108 mmol, 0.036). The unpurified product was purified by automated silica gel chromatography (Biotage 1% →10% ethyl acetate in hexanes, stained in CAM) to afford white solid (42.9 mg, 46% yield). **^{1}H NMR** (600 MHz, $CDCl_3$) δ 7.23 – 7.14 (m, 4H), 7.11 (app t, J = 7.1 Hz, 1H), 4.25 – 3.90 (m, 2H), 2.75 (dd, J = 13.5, 6.4 Hz, 1H), 2.63 (m, 3H),

1.79 – 1.63 (m, 2H), 1.58 – 1.49 (m, 1H), 1.42 (s, 9H), 1.32 (ddd, *J* = 10.6, 6.4, 6.4 Hz, 1H), 1.29 – 1.21 (m, 2H), 1.08 (s, 6H), 1.03 (s, 6H). **^{13}C NMR** (151 MHz, $CDCl_3$) δ 155.10, 142.24, 129.04, 128.26, 125.87, 83.28, 79.30, 44.65, 38.29, 34.99, 32.24, 31.19, 28.67, 25.04, 24. **IR** (neat) ν_{max} 2975.99 (w), 2930.24 (w), 2853.01 (w), 1690.68 (s), 1417.52 (m), 1364.98 (m), 1243.51 (m), 1164.62 (s), 1142.25 (s), 864.31 (w), 698.70 (w) cm^{-1}. **HRMS** (DART) for $C_{24}H_{38}BNO_4$ $[M+H]^+$ calculated: 416.29721, found: 416.29674. $[\alpha]^{20}_D$: -3.644 (*c* 3.065, $CHCl_3$, *l* =50 mm).

Determination of Stereochemical Identity: Racemic compound was prepared according to the general procedure ***(Method B, run at 60 ºC)*** with $Pd(OAc)_2$ (5 mol%) and 1,1′-Bis(dicyclohexylphosphino)ferrocene (6 mol%) as the catalyst. Absolute stereochemistry was assigned by analogy (see product **3.127** and **3.134**).

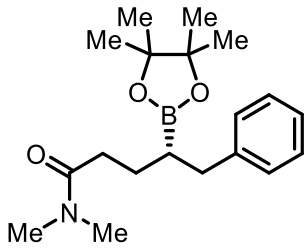
SFC (Chiracel ODR-H, 3% IPA, 3 mL/min, 100 bar, 35 °C, 210-270 nm) – analysis of (R)-4-(2-phenyl-1-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)ethyl)piperidine-1-carboxylate.

Racemic Material Standard Conditions



Peak No	% Area	Area	RT (min)
1	50.5596	7226.7896	6.88
2	49.4404	7066.8253	8.38
Total:	100	14293.6149	

Peak No	% Area	Area	RT (min)
1	16.0614	2799.2453	7.02
2	83.9386	14629.1852	8.28
Total:	100	17428.4305	



(*S*)-*N*,*N*-Dimethyl-5-phenyl-4-(4,4,5,5-tetramethyl-1,3,2-dioxaboro lan-2-yl)pentanamide (3.118). The reaction was performed according to general procedure ***(Method B)*** with *N*,*N*-dimethyl-3-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)propanamide (68.1 mg, 0.30 mmol, 1.00 equiv), sodium trifluoromethanesulfonate (103.2 mg, 0.60 mmol, 2.00 equiv), vinylmagnesium chloride (0.20 mL, 1.53M in tetrahydrofuran, 0.30 mmol, 1.00 equiv), phenyl trifluoromethanesulfonate (81.4 mg, 0.36 mmol, 1.20 equiv), palladium (II) acetate (0.9 mL, 0.01 M in dimethyl sulfoxide, 0.009 mmol, 0.030 equiv), (S_p,S_p)-**3.3** (11.37 mg, 0.0108 mmol, 0.036). The unpurified product was purified by automated silica gel chromatography (Biotage 1% → 5 → 10% ethyl acetate in hexanes, stained in CAM) to afford colorless oil (63.6 mg, 64% yield).

(Method D) with N,N-dimethyl-3-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)propanamide (68.1 mg, 0.30 mmol, 1.00 equiv), potassium trifluoromethanesulfonate

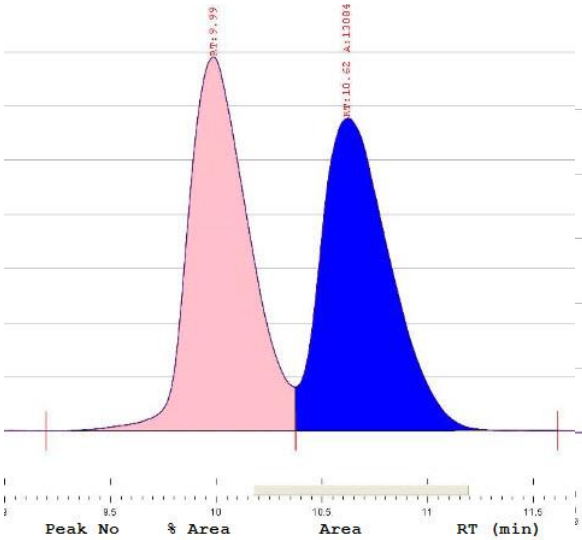
(118.5 g, 0.63 mmol, 2.10 equiv), vinylbromide (0.25 mL, 1.32 M in diethyl ether, 0.33 mmol, 1.10 equiv), phenyl trifluoromethanesulfonate (81.4 mg, 0.36 mmol, 1.20 equiv), palladium (II) acetate (0.9 mL, 0.01 M dimethyl sulfoxide, 0.009 mmol, 0.030 equiv), (S_p,S_p)-**3.3** (11.37 mg, 0.0108 mmol, 0.036). The unpurified product was purified by automated silica gel chromatography (Biotage 1% → 5 → 10% ethyl acetate in hexanes, stained in CAM) to afford colorless oil (76.5 mg, 77% yield).

^{1}H NMR (600 MHz, $CDCl_3$) δ 7.23 – 7.15 (m, 4H), 7.13 – 7.08 (m, 1H), 2.93 (s, 3H), 2.89 (s, 3H), 2.74 (dd, *J* = 13.7, 8.4 Hz, 1H), 2.65 (dd, *J* = 13.7, 7.7 Hz, 1H), 2.39 – 2.28 (m, 1H), 2.30 – 2.22 (m, 1H), 1.78 – 1.66 (m, 2H), 1.36 (p, *J* = 8.1 Hz, 1H), 1.14 (s, 6H), 1.12 (s, 6H). **^{11}B NMR** (160 MHz, $CDCl_3$) δ 33.41. **^{13}C NMR** (126 MHz, $CDCl_3$) δ 173.27, 142.08, 129.04, 128.25, 125.85, 83.28, 37.41, 35.51, 33.33, 26.73, 25.76, 25.01, 24.95. **IR** (neat) ν_{max} 2976.10 (w), 2927.55 (w), 1643.88 (s), 1380.86 (m), 1320.38 (m), 11141.62 (s), 700.02 (w) cm^{-1}. **HRMS** (DART) for $C_{19}H_{31}BNO_3$ $[M+H]^+$ calculated: 332.23970, found: 332.24058. $[\alpha]^{20}_D$: -8.9656 (*c* 1.010, $CHCl_3$, *l* =50 mm).

Determination of Stereochemical Identity: Racemic compound was prepared according to the general procedure (***Method B, run at 60 ºC***) with $Pd(OAc)_2$ (5 mol%) and 1,1′-Bis(dicyclohexylphosphino)ferrocene (6 mol%) as the catalyst. Absolute stereochemistry was assigned by analogy (see product **3.127** and **3.134**).

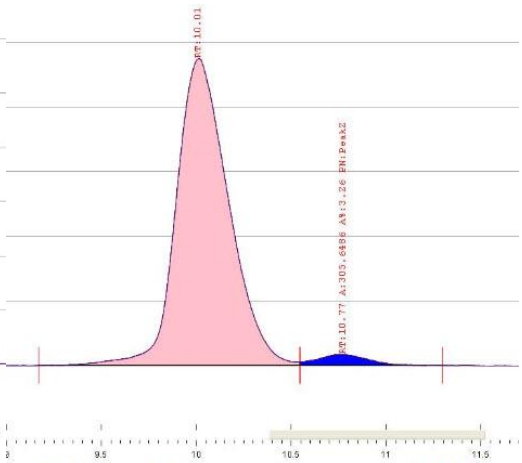
SFC (Chiracel OD-H, 3% MeOH, 3 mL/min, 100 bar, 35 °C, 210-270 nm) – analysis of (S)-N,N-dimethyl-5-phenyl-4-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)pentanamide.

Racemic Material

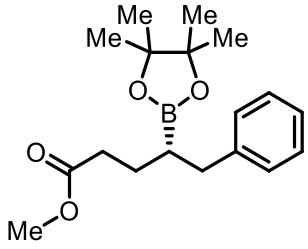


Peak No	% Area	Area	RT (min)
1	51.126	13687.032	9.99
2	48.874	13084.1678	10.62
Total:	100	26771.1998	

Standard Conditions



Peak No	% Area	Area	RT (min)
1	96.74	9070.0641	10.01
2	3.26	305.6486	10.77
Total:	100	9375.7127	



Methyl (*S*)-5-phenyl-4-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)pentanoate (3.119). The reaction was performed according to general procedure (***Method B)*** with methyl 3-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)propanoate (64.2 mg, 0.30 mmol, 1.00 equiv), sodium trifluoromethanesulfonate (103.2 mg, 0.60 mmol, 2.00 equiv), vinylmagnesium chloride (0.20 mL, 1.53 M in tetrahydrofuran, 0.30 mmol, 1.00 equiv), phenyl trifluoromethanesulfonate (81.4 mg, 0.36 mmol, 1.20 equiv), palladium (II) acetate (0.9 mL, 0.01 M in dimethyl sulfoxide, 0.009 mmol, 0.030 equiv), (S_p,S_p)-**3.3** (11.37 mg, 0.0108 mmol, 0.036 equiv). The unpurified product was purified by

automated silica gel chromatography (Biotage 1% → 5 → 10% ethyl acetate in hexanes, stain in CAM) to afford colorless solid (77.3 mg, 81% yield).

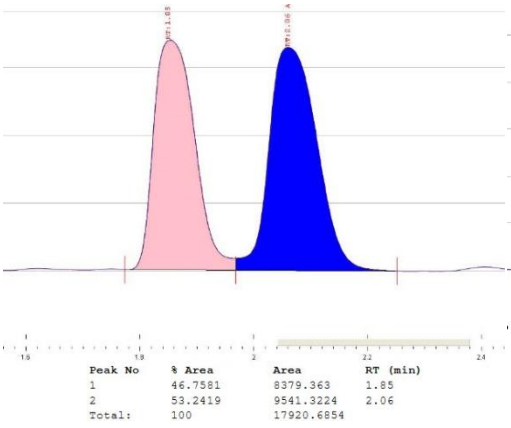
(Method D) with methyl 3-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)propanoate (64.2 mg, 0.30 mmol, 1.00 equiv), potassium trifluoromethanesulfonate (118.5 g, 0.63 mmol, 2.10 equiv), vinylbromide (0.25 mL, 1.32 M in diethyl ether, 0.33 mmol, 1.10 equiv), phenyl trifluoromethanesulfonate (81.4 mg, 0.36 mmol, 1.20 equiv), palladium (II) acetate (0.9 mL, 0.01 M dimethyl sulfoxide, 0.009 mmol, 0.030 equiv), (S_p,S_p)-**3.3** (11.37 mg, 0.0108 mmol, 0.036 equiv). The unpurified product was purified by automated silica gel chromatography (Biotage 1% → 5 → 10% ethyl acetate in hexanes, stained in CAM) to afford colorless solid (81.1 mg, 85% yield).

^{1}H NMR (600 MHz, $CDCl_3$) δ 7.23 – 7.19 (m, 2H), 7.19 – 7.15 (m, 2H), 7.15 – 7.10 (m, 1H), 3.62 (s, 3H), 2.73 (dd, *J* = 13.7, 8.4 Hz, 1H), 2.64 (dd, *J* = 13.7, 7.6 Hz, 1H), 2.42 – 2.22 (m, 2H), 1.72 (q, *J* = 7.9 Hz, 2H), 1.35 (p, *J* = 7.8 Hz, 1H), 1.15 (s, 6H), 1.12 (s, 6H). **^{11}B NMR** (160 MHz, $CDCl_3$) δ 33.67. **^{13}C NMR** (151 MHz, $CDCl_3$) δ 174.25, 141.88, 129.05, 128.29, 125.94, 83.38, 51.63, 37.21, 33.75, 26.25, 25.43, 24.99, 24.92. **IR** (neat) ν_{max} 2977.22 (w), 2929.20 (w), 1737.15 (s), 1381.23 (m), 1320.47 (m), 1213.06 (m), 1132.14 (s), 699.57 (w) cm^{-1}. **HRMS** (DART) for $C18H_{28}BO_4$ $[M+H]^+$ calculated: 319.2081, found: 319.2095. $[\alpha]^{20}_D$: -8.385 (*c* 2.555, $CHCl_3$, *l* =50 mm).

Determination of Stereochemical Identity: Racemic compound was prepared according to the general procedure (***Method B, run at 60 ºC***) with $Pd(OAc)_2$ (5 mol%) and 1,1′-Bis(dicyclohexylphosphino)ferrocene (6 mol%) as the catalyst. Absolute stereochemistry was assigned by analogy (see product **3.127** and **3.134**).

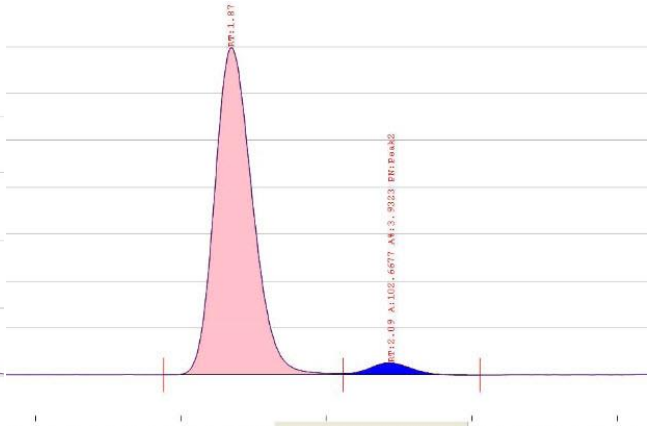
SFC (Chiracel ODR-H, 5% IPA, 3 mL/min, 100 bar, 35 °C, 210-270 nm) – analysis of methyl (S)-5-phenyl-4-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)pentanoate.

Racemic Material

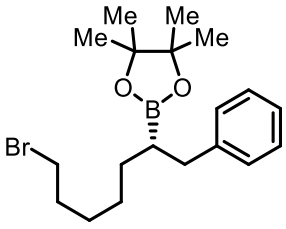


Peak No	% Area	Area	RT (min)
1	46.7581	8379.363	1.85
2	53.2419	9541.3224	2.06
Total:	100	17920.6854	

Standard Conditions



Peak No	% Area	Area	RT (min)
1	96.0677	2508.1964	1.87
2	3.9323	102.6677	2.09
Total:	100	2610.8641	



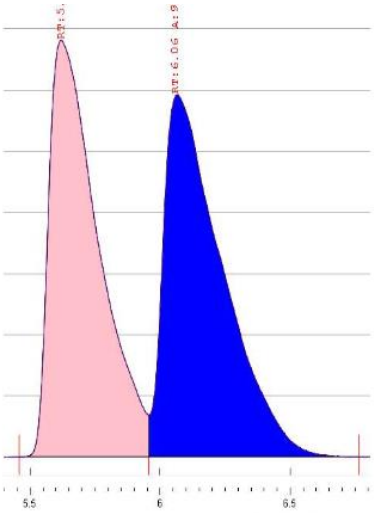
(*S*)-2-(7-Bromo-1-phenylheptan-2-yl)-4,4,5,5-tetramethyl-1,3,2-dioxaborolane (3.120). The reaction was performed according to the general procedure ***(Method B)*** with 2-(5-bromopentyl)-4,4,5,5-tetramethyl-1,3,2-dioxaborolane (83.1 mg,

0.30 mmol, 1.00 equiv), sodium trifluoromethanesulfonate (103.2 mg, 0.60 mmol, 2.00 equiv), vinylmagnesium chloride (0.20 mL, 1.53 M in tetrahydrofuran, 0.30 mmol, 1.00 equiv), phenyl trifluoromethanesulfonate (81.4 mg, 0.36 mmol, 1.20 equiv), palladium (II) acetate (0.90 mL, 0.01 M in dimethyl sulfoxide, 0.009 mmol, 0.030 equiv), (S_p,S_p)-**3.3** (11.37 mg, 0.0108 mmol, 0.036 equiv). The unpurified product was purified by automated silica gel chromatography (Biotage 1% → 5% ethyl acetate in hexanes, stain in CAM) to afford colorless oil (76.6 mg, 67% yield). **^{1}H NMR** (600 MHz, $CDCl_3$) δ 7.22 (app t, J = 7.5 Hz, 2H), 7.18 (d, J = 7.0 Hz, 2H), 7.12 (app t, J = 7.2 Hz, 1H), 3.36 (t, J = 6.9 Hz, 2H), 2.70 (dd, J = 13.6, 8.5 Hz, 1H), 2.63 (dd, J = 13.6, 7.3 Hz, 1H), 1.81 (app p, J = 7.2 Hz, 2H), 1.48 – 1.26 (m, 7H), 1.15 (s, 6H), 1.12 (s, 6H). **^{11}B NMR** (128 MHz, $CDCl_3$) δ 33.86. **^{13}C NMR** (151 MHz, $CDCl_3$) δ 144.84, 131.48, 130.68, 128.25, 85.65, 39.96, 36.53, 35.34, 33.49, 30.98, 30.87, 28.44, 27.45, 27.37. **IR** (neat) ν_{max} 3025.93 (w), 2977.04 (m), 2927.75 (m), 2854.50 (m), 1454.40 (m), 1380.74 (m), 1319.26 (m), 1142.84 (s), 966.64 (m), 861.78 (m), 746.57 (m), 699.08 (m) cm^{-1}. **HRMS** (DART) for $C_{19}H_{34}BBrNO_2$ $[M+NH_4]^+$: calculated: 398.1866, found: 398.1847. $[\alpha]_D^{20}$ = – 6.243 (*c* 2.92, $CHCl_3$, *l* = 50 mm).

Determination of Stereochemical Identity: Racemic compound was prepared according to the general procedure (***Method B, run at 60 ºC***) with $Pd(OAc)_2$ (5 mol%) and 1,1′-Bis(dicyclohexylphosphino)ferrocene (6 mol%) as the catalyst. Absolute stereochemistry was assigned by analogy (see product **3.127** and **3.134**).

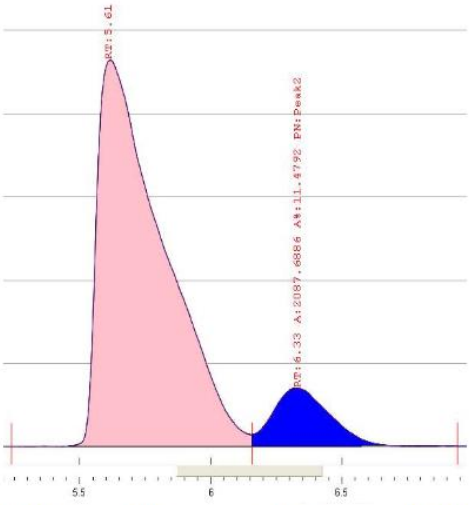
SFC (Chiracel ODR-H, 2% IPA, 3 mL/min, 100 bar, 35 °C, 210-270 nm) – analysis (S)-2-(7-bromo-1-phenylheptan-2-yl)-4,4,5,5-tetramethyl-1,3,2-dioxaborolane.

Racemic Material

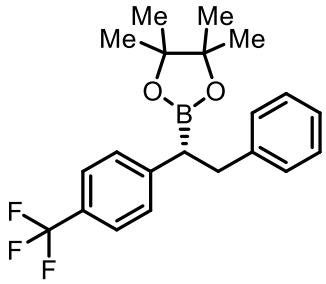


Peak No	% Area	Area	RT (min)
1	49.0818	8953.338	5.62
2	50.9182	9288.3425	6.06
Total:	100	18241.6805	

Standard Conditions

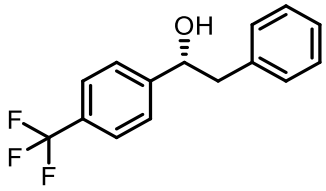


Peak No	% Area	Area	RT (min)
1	88.5208	16098.9933	5.61
2	11.4792	2087.6886	6.33
Total:	100	18186.6819	



(*R*)-4,4,5,5-Tetramethyl-2-(2-phenyl-1-(4-(trifluoromethyl) phenyl) ethyl)-1,3,2-dioxaborolane (3.121). The reaction was performed according to general procedure (***Method B, with the modification that the reaction was run at 60 ºC instead of 40 ºC)*** with 4,4,5,5-tetramethyl-2-(4-(trifluoromethyl)phenyl)-1,3,2-dioxaborolane (81.6 mg, 0.30 mmol, 1.00 equiv), sodium trifluoromethanesulfonate (103.2 mg, 0.60 mmol, 2.00 equiv), vinylmagnesium chloride (0.20 mL, 1.53 M in tetrahydrofuran, 0.30 mmol, 1.00 equiv), phenyl trifluoromethanesulfonate (81.4 mg, 0.36 mmol, 1.20 equiv), palladium (II)

acetate (0.9 mL, 0.01 M in dimethyl sulfoxide, 0.009 mmol, 0.030 equiv), (S_p,S_p)-**3.3** (11.37 mg, 0.0108 mmol, 0.036). The unpurified product was purified by automated silica gel chromatography (Biotage 1% → 5% ethyl acetate in hexanes, stained in CAM) to afford white solid (77.9 mg, 69% yield). **^{1}H NMR** (600 MHz, $CDCl_3$) δ 7.49 (d, *J* = 8.1 Hz, 2H), 7.33 (d, *J* = 8.1 Hz, 2H), 7.23 – 7.19 (m, 2H), 7.17 – 7.12 (m, 3H), 3.17 (dd, *J* = 13.6, 9.2 Hz, 1H), 2.96 (dd, *J* = 13.6, 7.4 Hz, 1H), 2.76 (app t, 1H), 1.12 (s, 6H), 1.11 (s, 6H). **^{11}B NMR** (160 MHz, $CDCl_3$) δ 32.59. **^{13}C NMR** (151 MHz, $CDCl_3$) δ 147.07, 141.26, 129.01, 128.88, 128.36, 127.90 (q, *J* = 32.2 Hz), 126.20, 125.41 (q, *J* = 3.8 Hz), 124.68 (q, *J* = 271.7 Hz), 83.90, 38.70, 34.77, 24.80, 24.72. **IR** (neat) ν_{max} 2979.33 (w), 2931.73 (w), 1616.08 (w), 1370.55 (w), 1321.35 (m), 1161.97 (w), 1135.95 (m), 1109.00 (m), 1067.27 (m), 843.69 (w), 698.28 (m) cm^{-1}. **HRMS** (DART) for $C_{21}H_{25}BF_3O_2$ $[M+H]^+$ calculated: 377.19, found: 377.1898. $[\alpha]^{20}_D$: -42.814 (*c* 3.20, $CHCl_3$, *l* =50 mm).



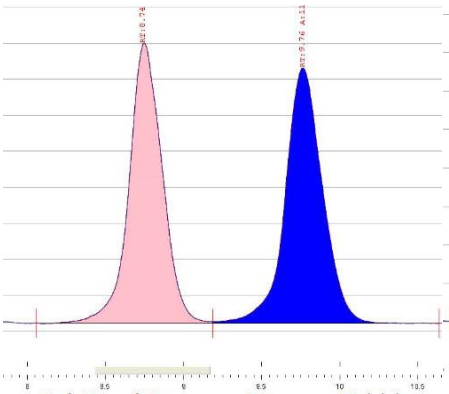
(*R*)-2-Phenyl-1-(4-(trifluoromethyl)phenyl)ethan-1-ol (3.121-OH). Product **3.121** was oxidized according to ***General Method for Oxidation of Boronic Ester Products.*** **^{1}H NMR** (600 MHz, $CDCl_3$) δ 7.59 (d, *J* = 8.2 Hz, 2H), 7.45 (d, *J* = 8.1 Hz, 2H), 7.31 (app t, *J* = 7.5 Hz, 2H), 7.25 (app t, 1H), 7.17 (app d, *J* = 7.1 Hz, 2H), 4.96 – 4.91 (m, 1H), 3.03 (dd, *J* = 13.7, 4.7 Hz, 1H), 2.95 (dd, *J* = 13.7, 8.7 Hz, 1H), 2.09 – 2.01 (m, 1H). **^{13}C NMR** (151 MHz, $CDCl_3$) δ 147.86, 137.48, 129.97 (q, *J* = 32.1 Hz), 129.72, 128.89, 127.13, 126.39, 125.54 (q, *J* = 3.7 Hz), 124.38 (q, *J* = 271.9 Hz), 74.87, 46.36. **IR** (neat) ν_{max} 3327.52 (br), 2920.13 (w), 1325.74 (s), 1153.77 (m), 1120.51 (s), 1066.42 (s), 832.69 (w), 737.84 (w),

701.37 (w) cm^{-1}. **HRMS** (DART) for $C_{15}H_{12}F$ $[M+H-H_2O]^+$ calculated: 249.0891, found: 249.0881. $[\alpha]^{20}_D$: +7.565 (*c* 1.465, $CHCl_3$, *l* =50 mm).

Determination of Stereochemical Identity: Racemic compound was prepared according to the general procedure (***Method B, run at 60 ºC***) with $Pd(OAc)_2$ (5 mol%) and 1,1′-Bis(dicyclohexylphosphino)ferrocene (6 mol%) as the catalyst. Absolute stereochemistry was assigned by analogy (see product **3.127** and **3.134**).

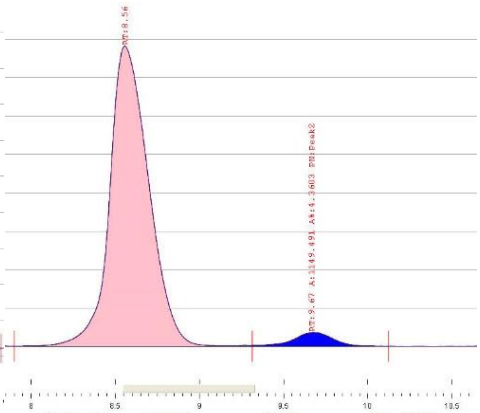
SFC (Chiracel OD-H, 5% IPA, 3 mL/min, 100 bar, 35 °C, 210-270 nm) – analysis of (R)-2-phenyl-1-(4-(trifluoromethyl)phenyl)ethan-1-ol.

Racemic Material

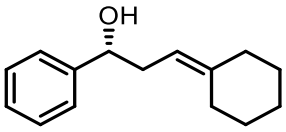


Peak No	% Area	Area	RT (min)
1	49.4338	11552.877	8.74
2	50.5662	11817.539	9.76
Total:	100	23370.416	

Standard Conditions



Peak No	% Area	Area	RT (min)
1	95.6397	25212.8832	8.56
2	4.3603	1149.491	9.67
Total:	100	26362.3742	



***(R)*-3-Cyclohexylidene-1-phenylpropan-1-ol (3.125-OH).** The reaction was performed according to the general procedure

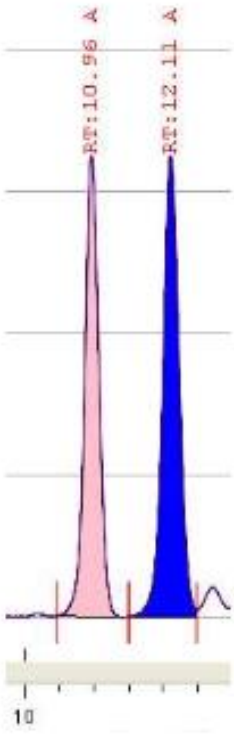
*(**Method B**)* with 4,4,5,5-tetramethyl-2-phenyl-1,3,2-dioxaborolane (**3.76**) (61.2 mg, 0.30 mmol, 1.00 equiv), sodium trifluoromethanesulfonate (103.2 mg, 0.60 mmol, 2.00 equiv), vinylmagnesium chloride (0.20 mL, 1.53 M in tetrahydrofuran, 0.30 mmol, 1.00 equiv), cyclohexylidenemethyl trifluoromethanesulfonate (**3.154**) (87.9 mg, 0.36 mmol, 1.20 equiv), palladium (II) acetate (0.90 mL, 0.01 M in dimethyl sulfoxide, 0.009 mmol, 0.030 equiv), (S_p,S_p)-**3.3** (11.37 mg, 0.0108 mmol, 0.036 equiv). Unpurified product **3.125** was oxidized according to ***General Method for Oxidation of Boronic Ester Products.*** The unpurified product was purified by silica gel chromatography (0% → 20% ethyl acetate in hexanes, stained in CAM) to afford a colorless oil (26.6 mg, 41% yield).

(***Method D, with the modification that NaOTf was used instead of KOTf***) with sodium trifluoromethanesulfonate (113.6 mg in 0.50 mL diethyl ether, 0.66 mmol, 2.20 equiv), vinylbromide (0.34 mL, 0.96 M in diethyl ether, 0.33 mmol, 1.10 equiv), *t*BuLi (0.35 mL, 1.78 M in hexanes, 0.63 mmol, 2.10 equiv), 4,4,5,5-tetramethyl-2-phenyl-1,3,2-dioxaborolane (**3.76**) (61.2 mg in 0.30 mL diethyl ether + 0.4 mL diethyl ether rinse, 0.30 mmol, 1.00 equiv), cyclohexylidenemethyl trifluoromethanesulfonate (**3.154**) (87.9 mg, 0.36 mmol, 1.20 equiv), palladium (II) acetate (0.90 mL, 0.01 M in THF, 0.009 mmol, 0.030 equiv), (S_p,S_p)-**3.3** (11.37 mg, 0.0108 mmol, 0.036 equiv). Unpurified product **3.125** was oxidized according to ***General Method for Oxidation of Boronic Ester Products.*** The unpurified product was purified by silica gel chromatography (0% → 20% ethyl acetate in hexanes, stained in CAM) to afford colorless oil (24.0 mg, 37% yield). All spectral data was in accord with the literature.[61]

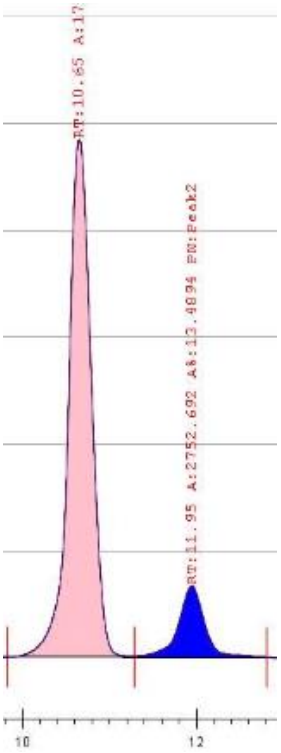
Determination of Stereochemical Identity: Racemic compound was prepared and reported previously[61] with 4,4,5,5-tetramethyl-2-vinyl-1,3,2-dioxaborolane, and $Pd(OAc)_2$ (5 mol%) and 1,1′-Bis(dicyclohexylphosphino) ferrocene (6 mol%) as the catalyst. Absolute stereochemistry was assigned by analogy (see product **3.127** and **3.134**).

SFC (Chiracel OD-H, 5% IPA, 3 mL/min, 100 bar, 35 °C, 210-270 nm) – analysis of (R)-3-cyclohexylidene-1-phenylpropan-1-ol

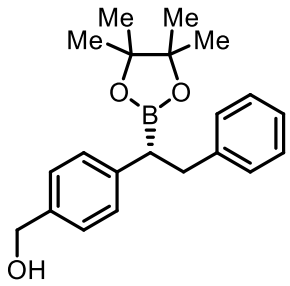
Racemic Material



Standard Conditions



Peak No	% Area	Area	RT (min)	Peak No	% Area	Area	RT (min)
1	46.2512	4641.7789	10.96	1	86.5106	17653.659	10.65
2	53.7488	5394.2368	12.11	2	13.4894	2752.692	11.95
Total:	100	10036.0157		Total:	100	20406.351	



(*R*)-(4-(2-Phenyl-1-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl) ethyl)phenyl)methanol (3.122). The reaction was performed according to the general procedure (***Method B)*** with (4-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)phenyl)methanol (70.2 mg, 0.30 mmol, 1,00 equiv), sodium trifluoromethanesulfonate (103.2 mg, 0.60 mmol, 2.00 equiv), vinylmagnesium chloride (0.20 mL, 1.53 M in tetrahydrofuran, 0.30 mmol, 1.00 equiv), phenyl trifluoromethanesulfonate (81.4 mg, 0.36 mmol, 1.20 equiv), palladium (II) acetate (0.9 mL, 0.01 M in dimethyl sulfoxide, 0.009 mmol, 0.030 equiv), (S_p,S_p)-**3.3** (11.37 mg, 0.0108 mmol, 0.036 equiv). The unpurified product was purified by automated silica gel chromatography (Biotage 1% → 10% ethyl acetate in hexanes, stained in CAM) to afford white solid (75.1 mg, 74% yield).

(*Method D*) with (4-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)phenyl)methanol (70.2 mg, 0.30 mmol, 1,00 equiv), potassium trifluoromethanesulfonate (118.5 g, 0.63 mmol, 2.10 equiv), vinylbromide (0.25 mL, 1.32 M in diethy ether, 0.33 mmol, 1.10 equiv), phenyl trifluoromethanesulfonate (81.4 mg, 0.36 mmol, 1.20 equiv), palladium (II) acetate (0.9 mL, 0.01 M dimethyl sulfoxide, 0.009 mmol, 0.030 equiv), (S_p,S_p)-**3.3** (11.37 mg, 0.0108 mmol, 0.036 equiv). The unpurified product was purified by automated silica gel

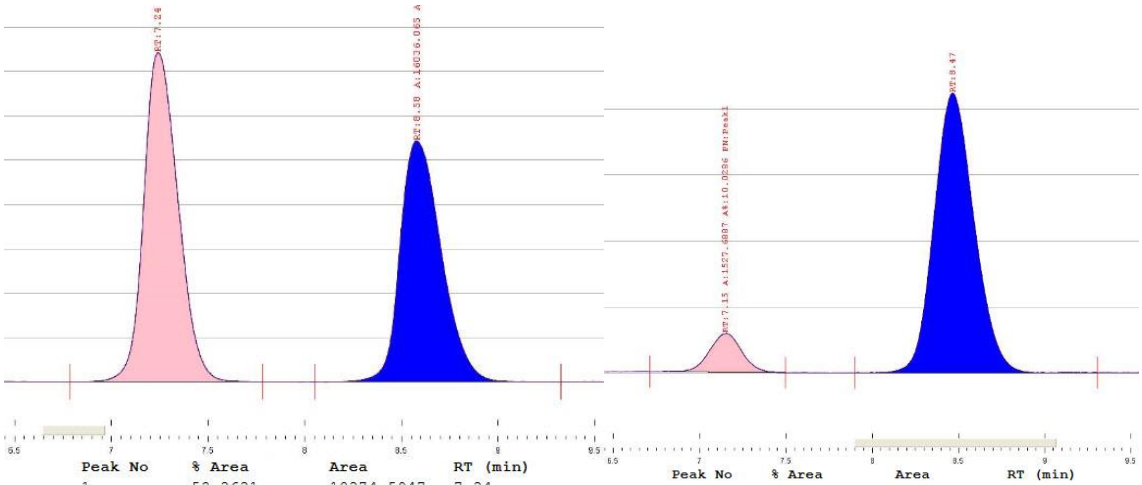
chromatography (Biotage 1% → 10% ethyl acetate in hexanes, stained in CAM) to afford white solid (74.1 mg, 73% yield).

^{1}H NMR (600 MHz, $CDCl_3$) δ 7.25 – 7.14 (m, 8H), 7.12 (app t, *J* = 7.1 Hz, 1H), 4.62 (d, *J* = 5.3 Hz, 2H), 3.13 (dd, *J* = 13.5, 9.6 Hz, 1H), 2.93 (dd, *J* = 13.5, 7.1 Hz, 1H), 2.67 (dd, *J* = 9.3, 7.3 Hz, 1H), 1.59 (app t, *J* = 5.6 Hz, 1H), 1.09 (s, 6H), 1.09 (s, 6H). **^{11}B NMR** (160 MHz, $CDCl_3$) δ 32.87. **^{13}C NMR** (151 MHz, $CDCl_3$) δ 142.37, 141.83, 138.09, 129.07, 128.82, 128.26, 127.43, 125.99, 83.66, 65.57, 39.07, 34.39, 24.82, 24.74. **IR** (neat) ν_{max} 3412.74 (br), 2976.75 (w), 2928.81 (w), 2863.18 (w), 1360.14 (m), 1325.38 (s), 1139.99 (s), 967.34 (w), 854.84 (w), 742.70 (w), 698.84 (w) cm^{-1}. **HRMS** (DART) for $C_{21}H_{26}BO_2$ $[M+ H-H_2O]^+$ calculated: 321.2026, found: 321.2017. $[\alpha]^{20}_D$: -43.381 (*c* 3.18, $CHCl_3$, *l* =50 mm).

Determination of Stereochemical Identity: Racemic compound was prepared according to the general procedure (***Method B**, run at 60 ºC*) with $Pd(OAc)_2$ (5 mol%) and (S_p,S_p)-**3.3** (1.8 mol%), and (R_p,R_p)-**3.3** (1.8 mol%) as the catalyst. Absolute stereochemistry was assigned by analogy (see product **3.127** and **3.134**).

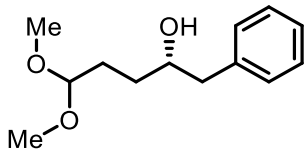
SFC (Chiracel AD-H, 10% IPA, 3 mL/min, 100 bar, 35 °C, 210-270 nm) – analysis of (R)-(4-(2-phenyl-1-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)ethyl)phenyl)methanol.

Racemic Material Standard Conditions



Peak No	% Area	Area	RT (min)
1	53.2621	18274.5947	7.24
2	46.7379	16036.065	8.58
Total:	100	34310.6597	

Peak No	% Area	Area	RT (min)
1	10.0286	1527.6887	7.15
2	89.9714	13705.5946	8.47
Total:	100	15233.2833	



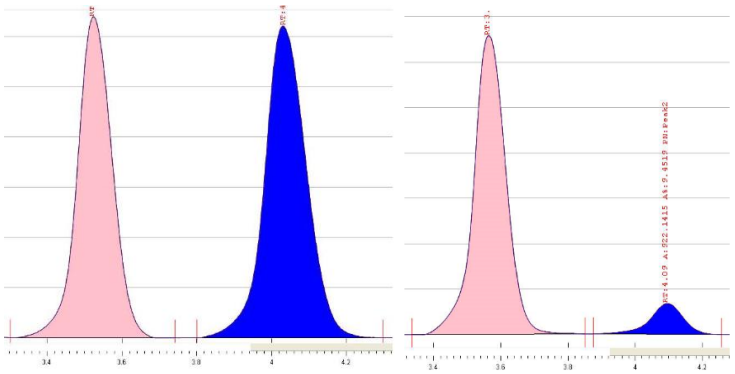
(*S*)-5,5-Dimethoxy-1-phenylpentan-2-ol (3.123-OH). The reaction was performed according to the general procedure ***(Method B)*** with 4,4,5,5-tetramethyl-2-(3,3-dimethoxypropyl)-1,3,2-dioxaborolane (69.0 mg, 0.30 mmol, 1.00 equiv), sodium trifluoromethanesulfonate (103.2 mg, 0.60 mmol, 2.00 equiv), vinylmagnesium chloride (0.20 mL, 1.53 M in tetrahydrofuran, 0.30 mmol, 1.00 equiv), phenyl trifluoromethanesulfonate (81.4 mg, 0.36 mmol, 1.20 equiv) palladium (II) acetate (0.90 mL, 0.01 M in dimethyl sulfoxide, 0.009 mmol, 0.030 equiv), (S_p,S_p)-**3.3** (11.37 mg, 0.0108 mmol, 0.036 equiv). Unpurified product **3.123** was oxidized according to ***General Method for Oxidation of Boronic Ester Products.*** The unpurified product was purified by automated silica gel chromatography (Biotage 1% → 20% ethyl acetate in hexanes, stained in CAM) to afford colorless oil (49.0 mg, 73% yield). **^{1}H NMR** (600 MHz, $CDCl_3$) δ 7.30 (app t, *J* = 7.4 Hz, 2H), 7.24 – 7.19 (m, 3H), 4.38 (app t, *J* = 5.5 Hz, 1H), 3.82 (dddd, *J* = 8.4, 8.4, 4.3, 4.3 Hz, 1H), 3.32 (s,

3H), 3.32 (s, 3H), 2.79 (dd, J = 13.6, 4.7 Hz, 1H), 2.69 (dd, J = 13.6, 8.1 Hz, 1H), 2.17 (s, 1H), 1.81 (dddd, J = 14.4, 9.0, 6.0, 6.0 Hz, 1H), 1.72 (dddd, J = 15.0, 9.0, 6.0, 6.0 Hz, 1H), 1.63 (dddd, J = 15.0, 13.2, 9.0, 3.6 Hz, 1H), 1.52 (dddd, J = 18.0, 9.0, 9.0, 6.0 Hz, 1H). **^{13}C NMR** (151 MHz, $CDCl_3$) δ 138.76, 129.57, 128.68, 126.58, 104.82, 72.57, 53.22, 52.96, 44.31, 31.76, 29.17. **IR** (neat) ν_{max} 3453.77 (m, br), 3026.59 (w), 2935.82 (s), 2830.25 (m), 1495.30 (m), 1453.48 (m), 1385.15 (m), 1362.68 (m), 1127.88 (s), 1055.47 (s), 961.97 (m), 744.01 (s), 700.87 (s) cm^{-1}. **HRMS** (DART) for $C_{13}H_{19}O_2$ $[M+H–H_2O]^+$: calculated: 207.1385, found: 207.1379. $[\alpha]_D^{20}$ = + 7.783 (*c* 2.14, $CHCl_3$, *l* = 50 mm).

Determination of Stereochemical Identity: Racemic compound was prepared according to the general procedure (***Method B, run at 60 ºC***) with $Pd(OAc)_2$ (3 mol%), (S_p,S_p)-**3.3** (1.8 mol%), and (R_p,R_p)-**3.3** (1.8 mol%) as the catalyst. Absolute stereochemistry was assigned by analogy (see product **3.127** and **3.134**).

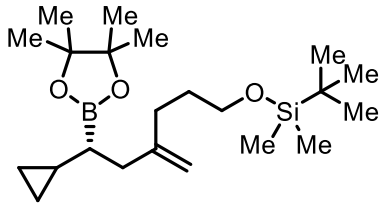
SFC (Chiracel OD-H, 10% IPA, 3 mL/min, 100 bar, 35 °C, 210-270 nm) – analysis of (S)-5,5-dimethoxy-1-phenylpentan-2-ol.

Racemic Material Standard Conditions



Peak No	% Area	Area	RT (min)
1	46.3381	4158.5954	3.52
2	53.6619	4815.868	4.03
Total:	100	8974.4634	

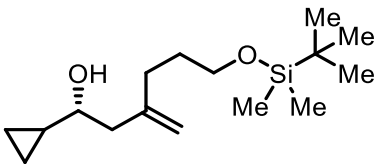
Peak No	% Area	Area	RT (min)
1	90.5481	8834.0367	3.56
2	9.4519	922.1415	4.09
Total:	100	9756.1782	



(*R*)-*tert*-Butyl((6-cyclopropyl-4-methylene-6-(4,4,5,5-tetramethy l-1,3,2-dioxaborolan-2-yl)hexyl)oxy) dimethylsilane (3.124). The reaction was performed according to general procedure (***Method B, with the modification that tetrahydrofuran was used instead of 1:1 dimethyl sulfoxide:tetrahydrofuran)*** with 2-cyclopropyl-4,4,5,5-tetramethyl-1,3,2-dioxaborolane (50.4 mg, 0.30 mmol, 1.00 equiv), sodium trifluoromethanesulfonate (103.2 mg, 0.60 mmol, 2.00 equiv), vinylmagnesium chloride (0.20 mL, 1.53M in tetrahydrofuran, 0.30 mmol, 1.00 equiv), 5-((*tert*-butyldimethylsilyl)oxy)pent-1-en-2-yl trifluoromethanesulfonate (125.3 mg, 0.36 mmol, 1.20 equiv), palladium (II) acetate (0.9 mL, 0.01 M in dimethyl sulfoxide, 0.009 mmol, 0.030 equiv), (S_p,S_p)-**3.3** (11.37 mg, 0.0108 mmol, 0.036 equiv). The unpurified product was purified by automated silica gel chromatography (Biotage 1% → 5% ethyl acetate in hexanes, stained in CAM) to afford colorless oil (66.2 mg, 56% yield).

(Method D, with the modification that tetrahydrofuran was used instead of 1:1 dimethyl sulfoxide:tetrahydrofuran) with 2-cyclopropyl-4,4,5,5-tetramethyl-1,3,2-dioxaborolane (50.4 mg, 0.30 mmol, 1.00 equiv), potassium trifluoromethanesulfonate (118.5 g, 0.63 mmol, 2.10 equiv), vinylbromide (0.25 mL, 1.32 M in diethy ether, 0.33 mmol, 1.10 equiv), 5-((*tert*-butyldimethylsilyl)oxy)pent-1-en-2-yl trifluoromethanesulfonate (125.3 mg, 0.36 mmol, 1.20 equiv), palladium (II) acetate (0.9 mL, 0.01 M in tetrahydrofuran, 0.009 mmol, 0.030 equiv), (S_p,S_p)-**3.3** (11.37 mg, 0.0108 mmol, 0.036 equiv). The unpurified product was purified by automated silica gel chromatography (Biotage 1% → 10% ethyl acetate in hexanes, stained in CAM) to afford colorless oil (78.1 mg, 66% yield).

^{1}H NMR (600 MHz, $CDCl_3$) δ 4.70 (s, 1H), 4.66 (s, 1H), 3.57 (dddd, J = 6.6, 1.6 Hz, 2H), 2.27 – 2.14 (m, 2H), 2.01 (app t, J = 7.7 Hz, 2H), 1.69 – 1.53 (m, 2H), 1.20 (s, 12H), 0.87 (s, 9H), 0.71 – 0.61 (m, 1H), 0.61 – 0.54 (m, 1H), 0.44 – 0.31 (m, 2H), 0.12 (dddd, J = 9.3, 5.0 Hz, 1H), 0.05 – -0.03 (m, 7H). **^{11}B NMR** (160 MHz, THF-d_8) δ 33.55. **^{13}C NMR** (151 MHz, $CDCl_3$) δ 155.10, 142.24, 129.04, 128.26, 125.87, 83.28, 79.30, 45.08, 44.21, 38.29, 34.99, 32.21, 31.17, 28.67, 25.04, 24.95. **IR** (neat) ν_{max} 2928.91 (w), 1378.20 (w), 1319.33 (w), 1144.04 (m), 1099.98 (m), 834.98 (m), 774.57 (w) cm^{-1}. **HRMS** (DART) for $C_{22}H_{44}BO_3Si$ $[M+H]^+$ calculated: 395.3179, found: 395.319397 $[\alpha]^{20}_D$: -12.203 (c = 1.360, $CHCl_3$, l =50 mm).

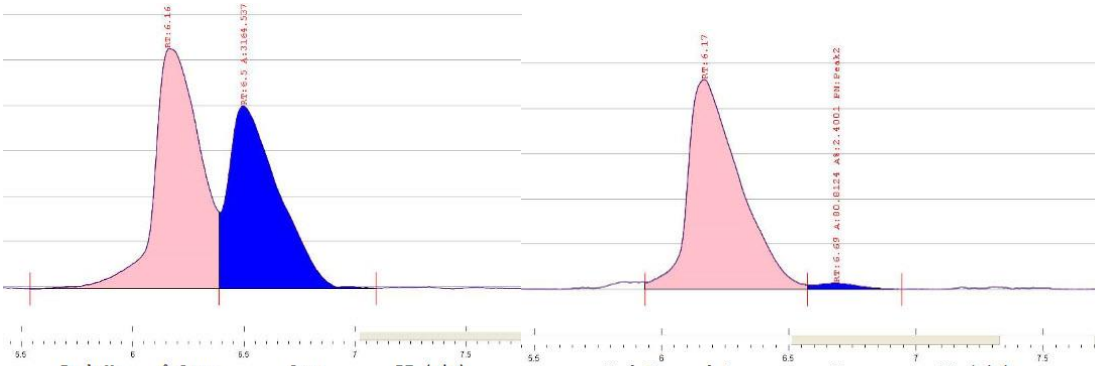


(*R*)-6-((*tert*-Butyldimethylsilyl)oxy)-1-cyclopropyl-3-methylenehexan-1-ol (3.124-OH). Product **3.124** was oxidized according to ***General Method for Oxidation of Boronic Ester Products.*** **^{1}H NMR** (600 MHz, $CDCl_3$) δ 4.88 – 4.85 (m, 1H), 4.85 – 4.82 (m, 1H), 3.59 (dddd, *J* = 10.1, 6.3, 3.7, 1.6 Hz, 2H), 2.99 (ddd, *J* = 9.3, 3.3 Hz, 1H), 2.38 (dd, *J* = 14.0, 3.3 Hz, 1H), 2.23 (app dd, 1H), 2.12 – 2.01 (m, 2H), 1.76 (s, 1H), 1.70 – 1.58 (m, 2H), 0.91 – 0.83 (m, 10H), 0.54 – 0.44 (m, 2H), 0.36 – 0.29 (m, 1H), 0.21 – 0.14 (m, 1H), 0.04 – -0.00 (m, 6H). **^{13}C NMR** (151 MHz, $CDCl_3$) δ 146.54, 112.39, 74.11, 62.89, 44.55, 32.26, 31.14, 26.17, 18.55, 17.72, 3.13, 2.51, -5.06. **IR** (neat) ν_{max} 3390.94 (br), 3077.98 (w), 2928.92 (s), 2856.84 (s), 1471.51 (w), 1254.11 (m), 1100.10 (s), 834.26 (s), 774.57 (m) cm^{-1}. **HRMS** (DART) for $C_{16}H_{31}BOSi$ $[M+H-H_2O]^+$ calculated: 267.2144, found: 267.2153 $[\alpha]^{20}_D$: -4.404 (*c* 2.050, $CHCl_3$, *l* =50 mm).

Determination of Stereochemical Identity: Racemic compound was prepared according to the general procedure (***Method B, run at 60 ºC***) with $Pd(OAc)_2$ (5 mol%) and 1,1′-Bis(dicyclohexylphosphino)ferrocene (6 mol%) as the catalyst. Absolute stereochemistry was assigned by analogy (see product **3.127** and **3.134**).

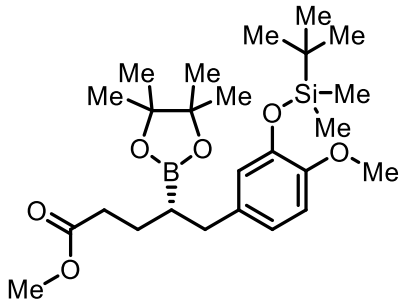
SFC (Chiracel OD-H, 1% IPA, 3 mL/min, 100 bar, 35 °C, 210-270 nm) – analysis of R)-6-((tert-butyldimethylsilyl)oxy)-1-cyclopropyl-3-methylenehexan-1-ol.

Racemic Material Standard Conditions



Peak No	% Area	Area	RT (min)
1	54.4908	3789.088	6.16
2	45.5092	3164.5373	6.5
Total:	100	6953.6253	

Peak No	% Area	Area	RT (min)
1	97.5999	3286.2517	6.17
2	2.4001	80.8124	6.69
Total:	100	3367.0641	



Methyl (*S*)-5-(3-((*tert*-butyldimethylsilyl)oxy)-4-methoxyphenyl)-4-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)pentanoate (3.126). The reaction was performed according to general procedure (***Method B)*** with methyl 3-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)propanoate (64.2 mg, 0.30 mmol, 1.00 equiv), sodium trifluoromethanesulfonate (103.2 mg, 0.60 mmol, 2.00 equiv), vinylmagnesium chloride (0.20 mL, 1.53 M in tetrahydrofuran, 0.30 mmol, 1.00 equiv), 3-((*tert*-butyldimethylsilyl)oxy)-4-methoxyphenyl trifluoromethanesulfonate (**3.166**) (139.1 mg, 0.36 mmol, 1.20 equiv), palladium (II) acetate (0.9 mL, 0.01 M in dimethyl sulfoxide, 0.009 mmol, 0.030 equiv), (S_p,S_p)-**3.3** (11.37 mg, 0.0108 mmol, 0.036 equiv). The unpurified product was purified by automated silica gel chromatography (Biotage 1% → 5 →10% ethyl acetate in hexanes, stain in CAM) to afford white solid (99.0 mg, 69% yield).

(Method F) with with methyl 3-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)propanoate (64.2 mg, 0.30 mmol, 1.0 equiv), vinylmagnesium chloride (0.20 mL, 1.53M in tetrahydrofuran, 0.30 mmol, 1.00 equiv), 3-((*tert*-butyldimethylsilyl)oxy)-4-methoxyphenyl trifluoromethanesulfonate (**3.166**) (139.1 mg, 0.36 mmol, 1.20 equiv), palladium (II) acetate (0.9 mL, 0.01 M dimethyl sulfoxide, 0.009 mmol, 0.030 equiv), (S_p,S_p)-**3.3** (11.37 mg, 0.0108 mmol, 0.036 equiv). The unpurified product was purified by automated silica gel chromatography (Biotage 1% → 5 →10% ethyl acetate in hexanes, stained in CAM) to afford white solid (99.0 mg, 69% yield).

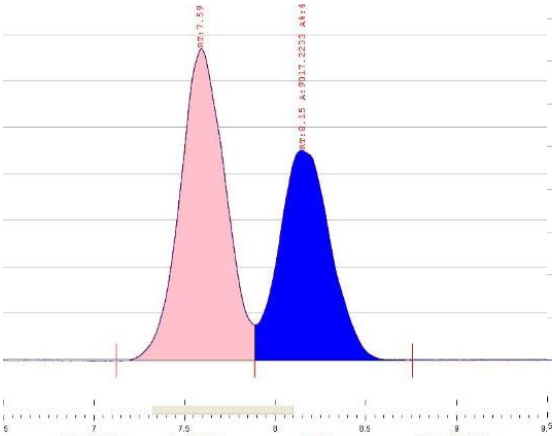
^{1}H NMR (600 MHz, $CDCl_3$) δ 6.72 – 6.67 (m, 3H), 3.73 (s, 3H), 3.61 (s, 3H), 2.63 (dd, *J* = 13.8, 8.2 Hz, 1H), 2.51 (dd, *J* = 13.8, 7.8 Hz, 1H), 2.39 – 2.22 (m, 2H), 1.71 – 1.63 (m, 2H), 1.27 (app p, *J* = 8.0 Hz, 1H), 1.16 (s, 6H), 1.14 (s, 6H), 0.96 (s, 9H), 0.11 (s, 6H). **^{11}B NMR** (160 MHz, $CDCl_3$) δ 33.73. **^{13}C NMR** (151 MHz, $CDCl_3$) δ 174.30, 149.26, 144.82, 134.60, 122.05, 121.87, 112.19, 83.36, 55.82, 51.62, 36.37, 33.81, 26.12, 25.97, 25.52, 25.05, 24.97, 18.66, -4.41, -4.42. **IR** (neat) ν_{max} 2929.47 (w), 2857.37 (w), 1738.36 (s), 1509.32 (s), 1317.69 (m), 1140.73 (s), 987.08 (m), 838.67 (s), 782.09 (m) cm^{-1}. **HRMS** (DART) for $C_{25}H_{44}BO_{6Si}$ $[M+H]^+$ calculated: 479.3, found: 479.2983. $[\alpha]^{20}_D$: -7.689 (*c* 1.865, $CHCl_3$, *l* =50 mm).

Determination of Stereochemical Identity: Racemic compound was prepared according to the general procedure (***Method B****, run at 60 ºC*) with $Pd(OAc)_2$ (5 mol%) and 1,1′-

Bis(dicyclohexylphosphino)ferrocene (6 mol%) as the catalyst. Absolute stereochemistry was assigned by analogy (see product **3.127** and **3.134**).

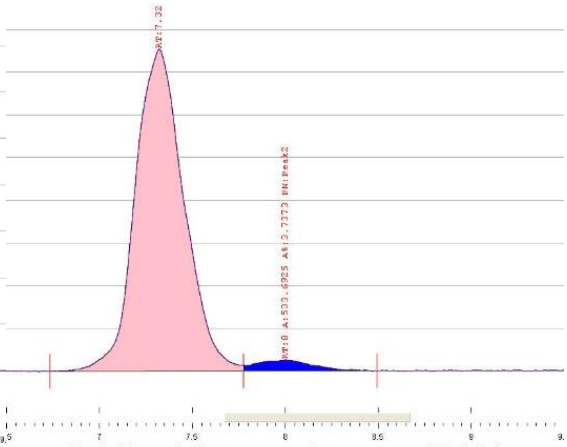
SFC (Chiracel OJ-H, 1% IPA, 3 mL/min, 100 bar, 35 °C, 210-270 nm) – analysis of methyl (S)-5-(3-((tert-butyldimethylsilyl)oxy)-4-methoxyphenyl)-4-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)pentanoate.

Racemic Material

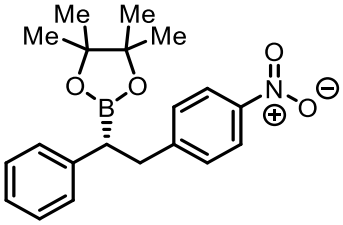


Peak No	% Area	Area	RT (min)
1	56.4852	11704.9976	7.59
2	43.5148	9017.2233	8.15
Total:	100	20722.2209	

Standard Conditions



Peak No	% Area	Area	RT (min)
1	96.2627	13746.3978	7.32
2	3.7373	533.6925	8
Total:	100	14280.0903	



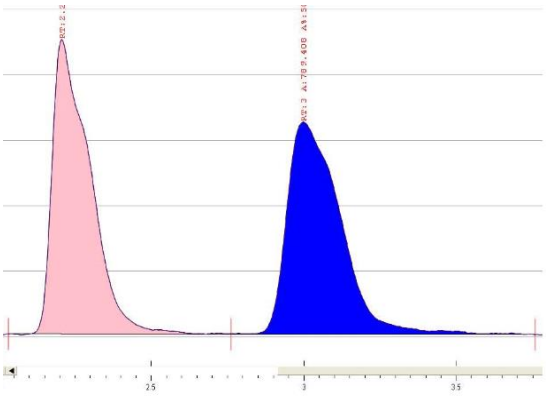
(*R*)-4,4,5,5-Tetramethyl-2-(2-(4-nitrophenyl)-1-phenylethyl)-1,3,2-dioxaborolane (3.129). The reaction was performed according to the general procedure ***(Method C)*** with 4,4,5,5-tetramethyl-2-phenyl-1,3,2-dioxaborolane (**3.76**) (61.2 mg, 0.30 mmol, 1.00 equiv), sodium trifluoromethanesulfonate (154.9 mg,

0.90 mmol, 3.00 equiv), vinylmagnesium chloride (0.20 mL, 1.53 M in tetrahydrofuran, 0.30 mmol, 1.00 equiv), 4-bromonitrobenzene (72.7 mg, 0.36 mmol, 1.20 equiv), palladium (II) acetate (0.90 mL, 0.01 M in dimethyl sulfoxide, 0.009 mmol, 0.030 equiv), (S_p,S_p)-**3.3** (11.37 mg, 0.0108 mmol, 0.036 equiv). The unpurified product was purified by silica gel chromatography (30% → 60% → 100% CH_2Cl_2 in hexanes, stained in CAM) to afford yellow solid (59.6 mg, 56% yield). **^{1}H NMR** (600 MHz, $CDCl_3$) δ 8.12 (d, *J* = 8.6 Hz, 2H), 7.34 (d, *J* = 8.5 Hz, 2H), 7.31 (app t, *J* = 7.6 Hz, 2H), 7.27 – 7.18 (m, 3H), 3.31 (dd, *J* = 13.6, 8.7 Hz, 1H), 3.10 (dd, *J* = 13.6, 7.8 Hz, 1H), 2.71 (app t, *J* = 8.2 Hz, 1H), 1.21 (s, 6H), 1.19 (s, 6H). **^{11}B NMR** (128 MHz, $CDCl_3$) δ 31.17. **^{13}C NMR** (151 MHz, $CDCl_3$) δ 149.97, 146.48, 141.58, 129.84, 128.70, 128.57, 125.99, 123.47, 83.90, 38.82, 34.20, 24.77, 24.75. **IR** (neat) ν_{max} 2973.89 (m), 2928.27 (w), 1600.99 (m), 1514.68 (s), 1344.29 (s), 1137.89 (s), 963.97 (m), 847.21 (s), 703.28 (s) cm^{-1}. **HRMS** (DART) for $C_{20}H_{25}BNO_4$ $[M+H]^+$: calculated: 354.1877, found: 354.1892. $[\alpha]_D^{20}$ = – 56.087 (*c* 2.10, $CHCl_3$, *l* = 50 mm).

Determination of Stereochemical Identity: Racemic compound was prepared according to the general procedure (***Method C, run at 60 ºC***) with $Pd(OAc)_2$ (5 mol%) and 1,1′-Bis(diisopropylphosphino)ferrocene (6 mol%) as the catalyst. Absolute stereochemistry was assigned by analogy (see product **3.127** and **3.134**).

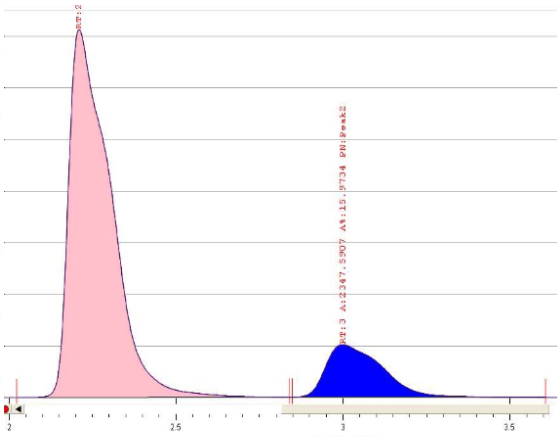
SFC (Chiracel OJ-H, 8% IPA, 3 mL/min, 100 bar, 35 °C, 210-270 nm) – analysis of (R)-4,4,5,5-tetramethyl-2-(2-(4-nitrophenyl)-1-phenylethyl)-1,3,2-dioxaborolane.

Racemic Material

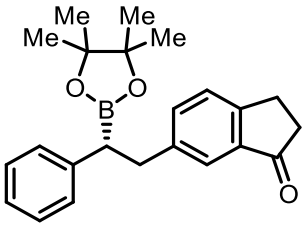


Peak No	% Area	Area	RT (min)
1	49.4108	771.0201	2.21
2	50.5892	789.408	3
Total:	100	1560.4281	

Standard Conditions



Peak No	% Area	Area	RT (min)
1	84.0266	12349.2825	2.21
2	15.9734	2347.5907	3
Total:	100	14696.8732	



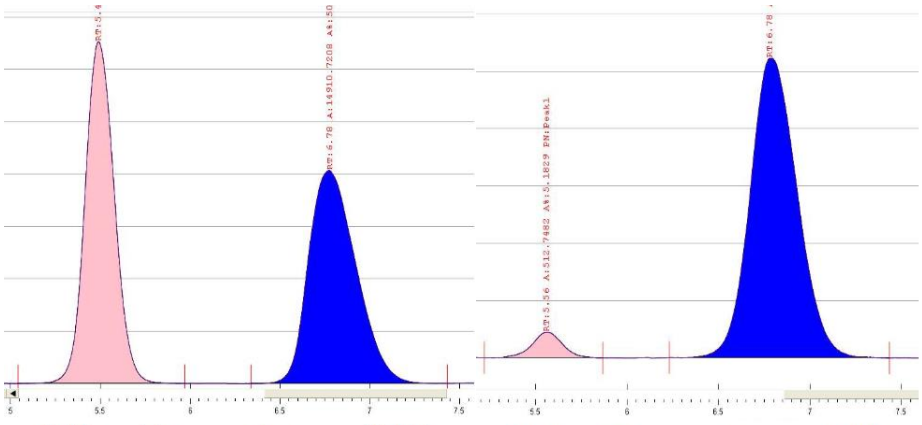
(*R*)-6-(2-Phenyl-2-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl) ethyl)-2,3-dihydro-1H-inden-1-one (3.130). The reaction was performed according to the general procedure ***(Method C)*** with 4,4,5,5-tetramethyl-2-phenyl-1,3,2-dioxaborolane (**3.76**) (61.2 mg, 0.30 mmol, 1.00 equiv), sodium trifluoromethanesulfonate (154.9 mg, 0.90 mmol, 3.00 equiv), vinylmagnesium chloride (0.20 mL, 1.53 M in tetrahydrofuran, 0.30 mmol, 1.00 equiv), 6-bromoindanone (76.0 mg, 0.36 mmol, 1.20 equiv), palladium (II) acetate (0.90 mL, 0.01 M in dimethyl sulfoxide, 0.009 mmol, 0.030 equiv), (S_p,S_p)-**3.3** (11.37 mg, 0.0108 mmol, 0.036 equiv). The unpurified product was purified by automated silica gel chromatography (Biotage 1% →40% ethyl acetate in hexanes, stained in CAM) to afford white solid (90.2 mg, 83% yield). **^{1}H NMR** (500 MHz, $CDCl_3$) δ 7.59 (s, 1H), 7.35 (dd, *J* = 7.8, 1.6 Hz, 1H), 7.28 (d, *J* = 7.8 Hz, 1H), 7.24 – 7.16 (m, 4H), 7.10 (app t, *J*

= 7.0 Hz, 1H), 3.20 (dd, *J* = 13.5, 9.3 Hz, 1H), 3.04 (app t, *J* = 5.8 Hz, 2H), 2.96 (dd, *J* = 13.5, 7.1 Hz, 1H), 2.66 – 2.59 (m, 3H), 1.11 (s, 12H). **^{11}B NMR** (128 MHz, $CDCl_3$) δ 32.58. **^{13}C NMR** (126 MHz, $CDCl_3$) δ 207.13, 153.04, 142.25, 141.46, 137.23, 135.90, 128.56, 128.54, 126.32, 125.70, 123.85, 83.70, 38.56, 36.73, 34.81, 25.61, 24.76, 24.73. **IR** (neat) ν_{max} 3024.40 (w), 2976.54 (m), 2926.69 (m), 2862.22 (w), 1707.07 (s), 1361.02 (s), 1325.34 (s), 1279.18 (m), 1139.02 (s), 967.44 (m), 840.00 (m), 757.28 (m), 700.39 (s) cm^{-1}. **HRMS** (DART) for $C_{23}H_{28}BO_3$ $[M+H]^+$: calculated: 363.21315, found: 363.21350. $[\alpha]_D^{20}$ = – 61.409 (*c* 3.37, $CHCl_3$, *l* = 50 mm).

Determination of Stereochemical Identity: Racemic compound was prepared according to the general procedure (***Method C, run at 60 ºC***) with $Pd(OAc)_2$ (5 mol%) and 1,1′-Bis(diisopropylphosphino)ferrocene (6 mol%) as the catalyst. Absolute stereochemistry was assigned by analogy (see product **3.127** and **3.134**).

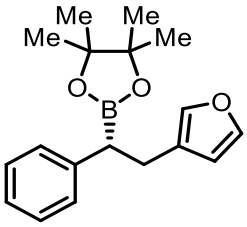
SFC (Chiracel OJ-H, 5% IPA, 3 mL/min, 100 bar, 35 °C, 210-270 nm) – analysis of (R)-6-(2-phenyl-2-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)ethyl)-2,3-dihydro-1H-inden-1-one.

Racemic Material Standard Conditions



Peak No	% Area	Area	RT (min)
1	49.8	14791.8907	5.49
2	50.2	14910.7208	6.78
Total:	100	29702.6115	

Peak No	% Area	Area	RT (min)
1	5.1829	512.7482	5.56
2	94.8171	9380.2646	6.78
Total:	100	9893.0128	



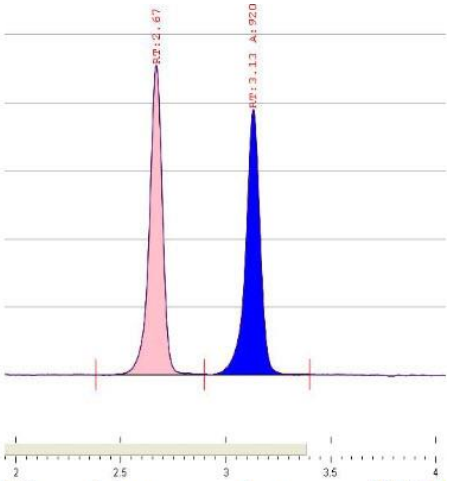
(*R*)-2-(2-(Furan-3-yl)-1-phenylethyl)-4,4,5,5-tetramethyl-1,3,2-dioxa borolane (3.133). The reaction was performed according to general procedure (***Method C)*** with 4,4,5,5-tetramethyl-2-phenyl-1,3,2-dioxaborolane (**3.76**) (61.2 mg, 0.30 mmol, 1.00 equiv), sodium trifluoromethanesulfonate (154.9 mg, 0.90 mmol, 3.00 equiv), vinylmagnesium chloride (0.20 mL, 1.53 M in tetrahydrofuran, 0.30 mmol, 1.00 equiv), 3-bromofuran (52.9 mg, 0.36 mmol, 1.20 equiv), palladium (II) acetate (0.9 mL, 0.01 M in dimethyl sulfoxide, 0.009 mmol, 0.030 equiv), (S_p,S_p)-**3.3** (11.37 mg, 0.0108 mmol, 0.036 equiv). The unpurified product was purified by automated silica gel chromatography (Biotage 1% →5% ethyl acetate in hexanes, stained in CAM) to afford white solid (71.4 mg, 65% yield). **^{1}H NMR** (600 MHz, $CDCl_3$) δ 7.29 – 7.22 (m, 5H), 7.18 – 7.12 (m, 2H), 6.22 (s, 1H), 2.98 (dd, *J* = 14.4, 9.5 Hz, 1H), 2.75 (dd, *J* = 14.4, 7.0 Hz, 1H), 2.59 (dd, *J* = 9.3, 7.1 Hz, 1H), 1.15 (s, 6H), 1.14 (s, 6H). **^{11}B NMR** (160 MHz, THF-d_8) δ 32.78. **^{13}C NMR** (151 MHz, $CDCl_3$) δ 142.73, 142.52, 139.55, 128.56, 128.51, 125.66, 124.75, 111.55, 83.65, 33.46, 28.03,

24.80, 24.75. **IR** (neat) ν_{max} 2977.58 (w), 2930.86 (w), 1493.42. (w), 1451.59.88 (w), 1351.13 (w), 1325.48 (s), 1140.24 (s), 1023.50 (m), 966.20 (m), 872.27 (m), 850.44 (m). 775.04 (m), 700.20 (m) cm^{-1}. **HRMS** (DART) for $C_{18}H_{24}BO_3$ $[M+H]^+$ calculated: 299.18185, found: 299.18238. $[\alpha]^{20}_D$: -35.466 (*c* 1.550, $CHCl_3$, *l* =50 mm).

Determination of Stereochemical Identity: Racemic compound was prepared according to the general procedure (***Method C, run at 60 ºC***) with $Pd(OAc)_2$ (5 mol%) and 1,1′-Bis(dicyclohexylphosphino)ferrocene (6 mol%) as the catalyst. Absolute stereochemistry was assigned by analogy (see product **3.127** and **3.134**).

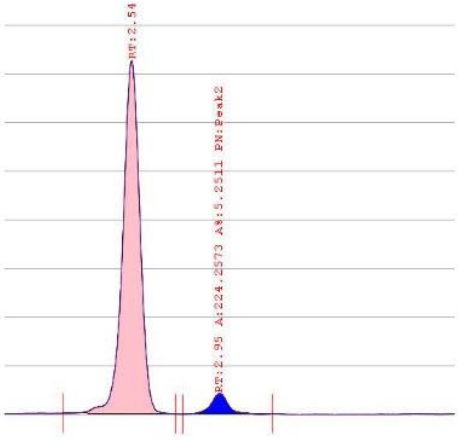
SFC (Chiracel OJ-H, 1% IPA, 3 mL/min, 100 bar, 35 °C, 210-270 nm) – analysis (R)-2-(2-(furan-3-yl)-1-phenylethyl)-4,4,5,5-tetramethyl-1,3,2-dioxaborolane.

Racemic Material

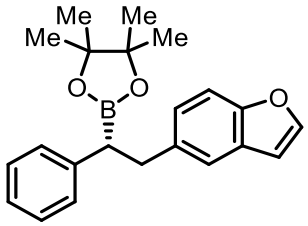


Peak No	% Area	Area	RT (min)
1	51.6531	983.5679	2.67
2	48.3469	920.6134	3.13
Total:	100	1904.1813	

Standard Conditions



Peak No	% Area	Area	RT (min)
1	94.7489	4046.431	2.54
2	5.2511	224.2573	2.95
Total:	100	4270.6883	

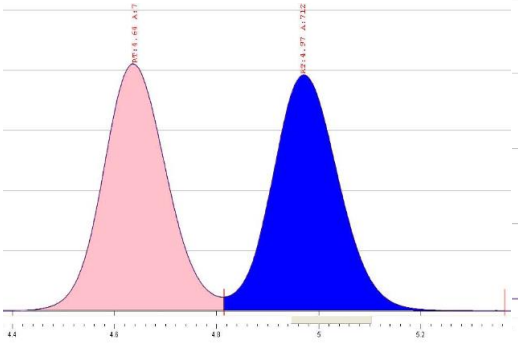


(*R*)-2-(2-(Benzofuran-5-yl)-1-phenylethyl)-4,4,5,5-tetramethyl-1,3,2-dioxaborolane (3.131). The reaction was performed according to the general procedure *(**Method C**)* with 4,4,5,5-tetramethyl-2-phenyl-1,3,2-dioxaborolane (**3.76**) (61.2 mg, 0.30 mmol, 1.00 equiv), sodium trifluoromethanesulfonate (154.9 mg, 0.90 mmol, 3.00 equiv), vinylmagnesium chloride (0.20 mL, 1.53 M in tetrahydrofuran, 0.30 mmol, 1.00 equiv), 5-bromobenzofuran (70.9 mg, 0.36 mmol, 1.20 equiv), palladium (II) acetate (0.90 mL, 0.01 M in dimethyl sulfoxide, 0.009 mmol, 0.030 equiv), (S_p,S_p)-**3.3** (11.37 mg, 0.0108 mmol, 0.036 equiv). The unpurified product was purified by automated silica gel chromatography (Biotage 0% →10% ethyl acetate in hexanes, stained in CAM) to afford colorless oil (79.4 mg, 76% yield). **^{1}H NMR** (500 MHz, $CDCl_3$) δ 7.52 (s, 1H), 7.39 (s, 1H), 7.33 (d, J = 8.5 Hz, 1H), 7.28 – 7.18 (m, 4H), 7.11 (d, J = 8.2 Hz, 2H), 6.63 (s, 1H), 3.24 (dd, J = 13.2, 10.1 Hz, 1H), 3.04 (dd, J = 13.4, 6.8 Hz, 1H), 2.70 (dd, J = 9.0, 7.0 Hz, 1H), 1.08 (s, 6H), 1.06 (s, 6H). **^{11}B NMR** (128 MHz, $CDCl_3$) δ 33.20. **^{13}C NMR** (126 MHz, $CDCl_3$) δ 153.78, 145.05, 142.81, 136.41, 128.59, 128.52, 127.42, 125.61, 125.57, 121.20, 110.87, 106.57, 83.55, 38.96, 35.34, 24.74, 24.73. **IR** (neat) ν_{max} 3058.01 (w), 3024.78 (w), 2976.61 (m), 2929.75 (m), 2859.41 (w), 1467.87 (m), 1360.28 (s), 1323.53 (s), 1139.59 (s), 1031.41 (m), 968.33 (m), 850.72 (m), 765.57 (m), 734.35 (m), 700.04 (s) cm^{-1}. **HRMS** (DART) for $C_{22}H_{26}BO_3$ $[M+H]^+$: calculated: 349.1975, found: 349.1980. $[\alpha]_D^{20}$ = – 43.515 (*c* 3.495, $CHCl_3$, *l* = 50 mm).

Determination of Stereochemical Identity: Racemic compound was prepared according to the general procedure (***Method C, run at 60 ºC***) with $Pd(OAc)_2$ (5 mol%) and 1,1′-Bis(diisopropylphosphino)ferrocene (6 mol%) as the catalyst. Absolute stereochemistry was assigned by analogy (see product **3.127** and **3.134**).

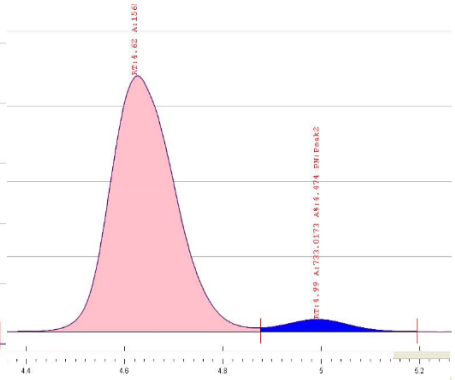
SFC (Chiracel OJ-H, 5% IPA, 3 mL/min, 100 bar, 35 °C, 210-270 nm) – analysis (R)-2-(2-(benzofuran-5-yl)-1-phenylethyl)-4,4,5,5-tetramethyl-1,3,2-dioxaborolane.

Racemic Material

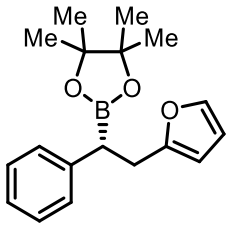


Peak No	% Area	Area	RT (min)
1	50.0183	7132.5765	4.64
2	49.9817	7127.3546	4.97
Total:	100	14259.9311	

Standard Conditions



Peak No	% Area	Area	RT (min)
1	95.526	15650.8875	4.62
2	4.474	733.0173	4.99
Total:	100	16383.9048	



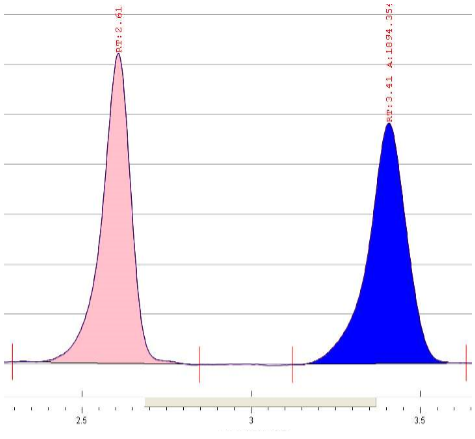
(*R*)-2-(2-(Furan-2-yl)-1-phenylethyl)-4,4,5,5-tetramethyl-1,3,2-dioxaboro lane (3.132). The reaction was performed according to the general procedure ***(Method C)*** with 4,4,5,5-tetramethyl-2-phenyl-1,3,2-dioxaborolane (**3.76**) (61.2 mg, 0.30 mmol, 1.00 equiv), sodium trifluoromethanesulfonate (154.9 mg, 0.90 mmol, 3.00 equiv), vinylmagnesium chloride (0.20 mL, 1.53 M in tetrahydrofuran, 0.30 mmol, 1.00 equiv), 2-bromofuran (52.9 mg, 0.36

mmol, 1.20 equiv), palladium (II) acetate (0.90 mL, 0.01 M in dimethyl sulfoxide, 0.009 mmol, 0.030 equiv), (S_p,S_p)-**3.3** (11.37 mg, 0.0108 mmol, 0.036 equiv). The unpurified product was purified by automated silica gel chromatography (Biotage 1% →5% Ethyl acetate in hexanes, stained in CAM) to afford white solid (65.3 mg, 73% yield). **^{1}H NMR** (600 MHz, $CDCl_3$) δ 7.29 – 7.20 (m, 5H), 7.17 – 7.11 (m, 1H), 6.22 (dd, *J* = 3.1, 1.8 Hz, 1H), 5.94 (dd, *J* = 3.2, 0.9 Hz, 1H), 3.19 (dd, *J* = 15.1, 9.9 Hz, 1H), 2.95 (dd, *J* = 15.1, 6.6 Hz, 1H), 2.75 (dd, *J* = 9.9, 6.6 Hz, 1H), 1.17 (s, 6H), 1.14 (s, 6H). **^{11}B NMR** (128 MHz, $CDCl_3$) δ 32.64. **^{13}C NMR** (151 MHz, $CDCl_3$) δ 155.81, 142.31, 140.85, 128.58, 128.42, 125.73, 110.19, 105.53, 83.70, 31.22, 24.77, 24.74 (methine C adjacent to B not observed). **IR** (neat) ν_{max} 3026.86 (w), 2977.47 (m), 2928.74 (w), 2854.97 (w), 1599.24 (m), 1360.95 (s), 1326.42 (s), 1140.45 (s), 1008.03 (m), 967.54 (m), 850.12 (m), 729.28 (m), 699.69 (s) cm^{-1}. **HRMS** (DART) for $C_{18}H_{24}BO_3$ $[M+H]^+$: calculated: 299.18185, found: 299.18327. $[\alpha]_D^{20}$ = – 30.982 (*c* 1.19, $CHCl_3$, *l* = 50 mm).

Determination of Stereochemical Identity: Racemic compound was prepared according to the general procedure (***Method C, run at 60 ºC***) with $Pd(OAc)_2$ (5 mol%) and 1,1′-Bis(diisopropylphosphino)ferrocene (6 mol%) as the catalyst. Absolute stereochemistry was assigned by analogy (see product **3.127** and **3.134**).

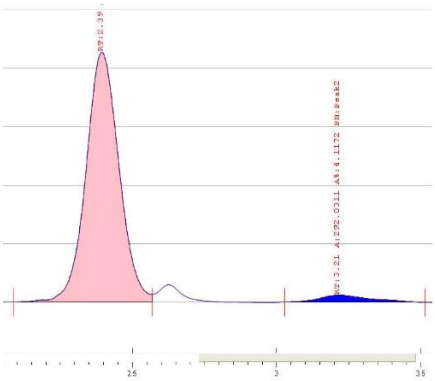
SFC (Chiracel OJ-H, 1% IPA, 3 mL/min, 100 bar, 35 °C, 210-270 nm) – analysis (R)-2-(2-(furan-2-yl)-1-phenylethyl)-4,4,5,5-tetramethyl-1,3,2-dioxaborolane.

Racemic Material

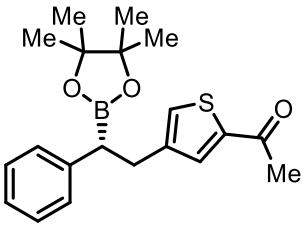


Peak No	% Area	Area	RT (min)
1	49.6198	1865.7639	2.61
2	50.3802	1894.3546	3.41
Total:	100	3760.1185	

Standard Conditions



Peak No	% Area	Area	RT (min)
1	95.8828	6800.8486	2.39
2	4.1172	292.0311	3.21
Total:	100	7092.8797	



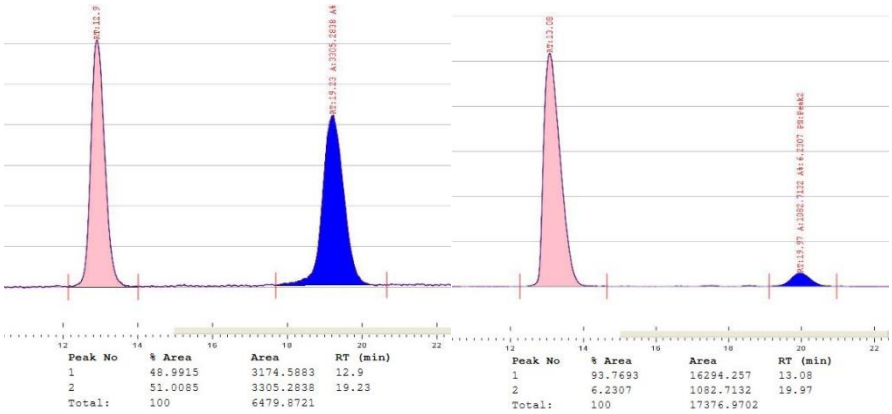
(*R*)-1-(4-(2-Phenyl-2-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl) ethyl)thiophen-2-yl)ethan-1-one (3.134). The reaction was performed according to general procedure (***Method C)*** with 4,4,5,5-tetramethyl-2-phenyl-1,3,2-dioxaborolane (**3.76**) (61.2 mg, 0.30 mmol, 1.00 equiv.), sodium trifluoromethanesulfonate (154.9 mg, 0.90 mmol, 3.00 equiv), vinylmagnesium chloride (0.20 mL, 1.53 M in tetrahydrofuran, 0.30 mmol, 1.00 equiv), 1-(4-bromothiophen-2-yl)ethan-1-one (73.8 mg, 0.36 mmol, 1.20 equiv), palladium (II) acetate (0.9 mL, 0.01 M dimethyl sulfoxide, 0.009 mmol, 0.030 equiv), (S_p,S_p)-**3.3** (11.37 mg, 0.0108 mmol, 0.036 equiv). The unpurified product was purified by automated silica gel chromatography (Biotage 1% →5% ethyl acetate in hexanes, stained in CAM) to afford off-white solid (82.3 mg, 77% yield). **^{1}H NMR** (600 MHz, $CDCl_3$) δ 7.44 (app d, *J* = 1.3 Hz, 1H), 7.26 (app t, *J* = 7.6 Hz, 2H), 7.20 (app d, *J* = 6.9 Hz, 3H), 7.15 (app t, *J* = 6.9 Hz, 1H), 3.15 (dd, *J* = 14.2, 9.3 Hz, 1H), 2.93 (dd, *J* =

14.2, 7.2 Hz, 1H), 2.63 (dd, *J* = 9.2, 7.2 Hz, 1H), 2.48 (s, 3H), 1.14 (s, 6H), 1.13 (s, 6H). **^{11}B NMR** (160 MHz, $CDCl_3$) δ 32.59. **^{13}C NMR** (151 MHz, $CDCl_3$) δ 190.91, 143.93, 143.62, 142.06, 134.28, 130.11, 128.64, 128.54, 125.87, 83.76, 33.93, 33.43, 26.89, 24.76, 24.74. **IR** (neat) ν_{max} 2975.69 (w), 2933.00 (w), 1661.22. (s), 11356.74 (s), 1324.69 (s), 1138.00 (s), 848.18 (m), 764.63 (w), 700.66 (m) cm^{-1}. **HRMS** (DART) for $C_{20}H_{25}BO_3S$ $[M+H]^+$ calculated: 357.16957, found: 357.16935. $[\alpha]^{20}_D$: -40.579 (*c* 3.890, $CHCl_3$, *l* =50 mm).

Determination of Stereochemical Identity: Racemic compound was prepared according to the general procedure (***Method C****, run at 60 ºC*) with $Pd(OAc)_2$ (5 mol%) and 1,1′-Bis(dicyclohexylphosphino)ferrocene (6 mol%) as the catalyst. Absolute stereochemistry was assigned by analogy (see product **3.127** and **3.134**).

SFC (Chiracel OJ-H, 1% IPA, 3 mL/min, 100 bar, 35 °C, 210-270 nm) – analysis of (R)-1-(4-(2-phenyl-2-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)ethyl)thiophen-2-yl)ethan-1-one.

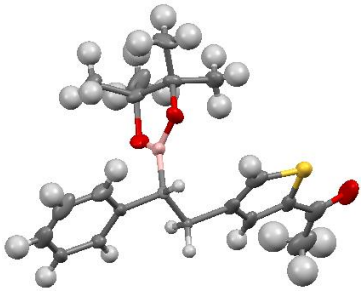
Racemic Material Standard Conditions

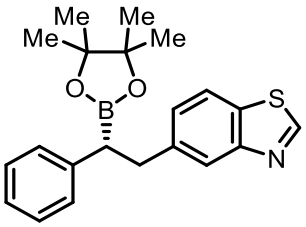


Peak No	% Area	Area	RT (min)
1	48.9915	3174.5883	12.9
2	51.0085	3305.2838	19.23
Total:	100	6479.8721	

Peak No	% Area	Area	RT (min)
1	93.7693	16294.257	13.08
2	6.2307	1082.7132	19.97
Total:	100	17376.9702	

Crystal Structure





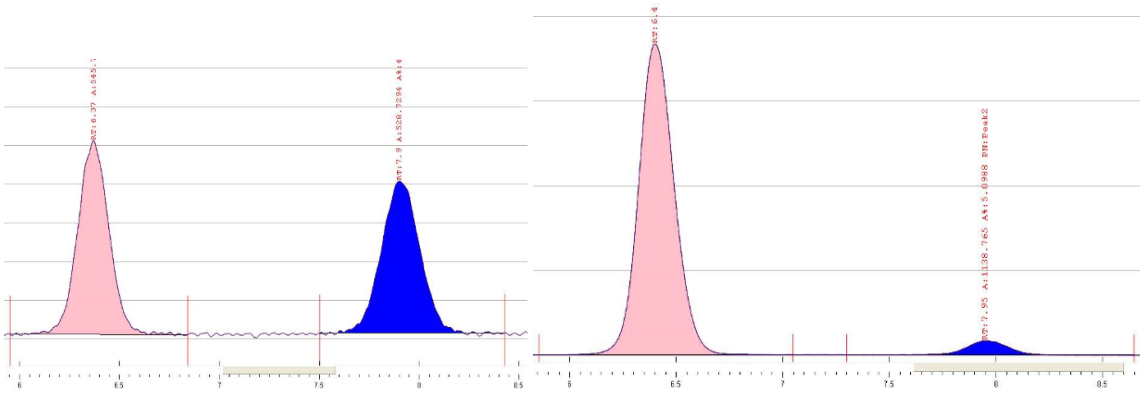
(*R*)-5-(2-Phenyl-2-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl) ethyl)benzo[d]thiazole (3.135). The reaction was performed according to the general procedure *(**Method C**)* with 4,4,5,5-tetramethyl-2-phenyl-1,3,2-dioxaborolane (**3.76**) (61.2 mg, 0.30 mmol, 1.00 equiv), sodium trifluoromethanesulfonate (154.9 mg, 0.90 mmol, 3.00 equiv), vinylmagnesium chloride (0.20 mL, 1.53 M in tetrahydrofuran, 0.30 mmol, 1.00 equiv), 5-bromobenzothiazole (77.1 mg, 0.36 mmol, 1.20 equiv), palladium (II) acetate (0.90 mL, 0.01 M in dimethyl sulfoxide, 0.009 mmol, 0.030 equiv), (S_p,S_p)-**3.3** (11.37 mg, 0.0108 mmol, 0.036 equiv). The unpurified product was purified by automated silica gel chromatography (Biotage 0% →50% CH_2Cl_2 in hexanes, stained in CAM) to

afford colorless oil (71.2 mg, 65% yield). **^{1}H NMR** (500 MHz, $CDCl_3$) δ 8.94 (s, 1H), 7.96 (s, 1H), 7.79 (d, *J* = 8.2 Hz, 1H), 7.29 – 7.21 (m, 5H), 7.14 (app hept, *J* = 3.7 Hz, 1H), 3.34 (dd, *J* = 13.5, 9.3 Hz, 1H), 3.12 (dd, *J* = 13.6, 7.2 Hz, 1H), 2.74 (dd, *J* = 9.0, 7.5 Hz, 1H), 1.12 (s, 6H), 1.11 (s, 6H). **^{11}B NMR** (128 MHz, $CDCl_3$) δ 33.00. **^{13}C NMR** (126 MHz, $CDCl_3$) δ 153.97, 153.58, 142.34, 140.49, 131.14, 128.55, 128.52, 127.18, 125.65, 123.67, 121.31, 83.65, 38.78, 34.90, 24.72, 24.68**. IR** (neat) ν_{max} 3060.66 (w), 3025.02 (w), 2976.11 (m), 2928.50 (m), 2860.23 (w), 1440.95 (s), 1359.88 (s), 1324.95 (s), 1139.88 (s), 969.17 (m), 845.81 (s), 700.65 (s) cm^{-1}. **HRMS** (DART) for $C_{21}H_{25}BNO_2S$ $[M+H]^+$: calculated: 366.16990, found: 366.17111. $[\alpha]_D^{20}$ = – 41.788 (*c* 3.77, $CHCl_3$, *l* = 50 mm).

Determination of Stereochemical Identity: Racemic compound was prepared according to the general procedure (***Method C, run at 60 ºC***) with $Pd(OAc)_2$ (5 mol%) and 1,1′-Bis(diisopropylphosphino)ferrocene (6 mol%) as the catalyst. Absolute stereochemistry was assigned by analogy (see product **3.127** and **3.134**).

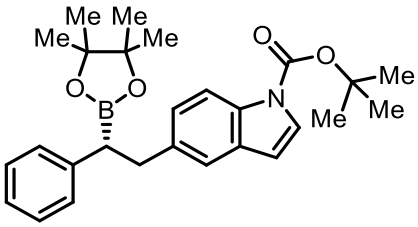
SFC (Chiracel OD-H, 10% IPA, 3 mL/min, 100 bar, 35 °C, 210-270 nm) – analysis (R)-5-(2-phenyl-2-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)ethyl)benzo[d]thiazole.

Racemic Material Standard Conditions



Peak No	% Area	Area	RT (min)
1	50.7936	545.7844	6.37
2	49.2064	528.7294	7.9
Total:	100	1074.5138	

Peak No	% Area	Area	RT (min)
1	94.9012	21195.3246	6.4
2	5.0988	1138.765	7.95
Total:	100	22334.0896	



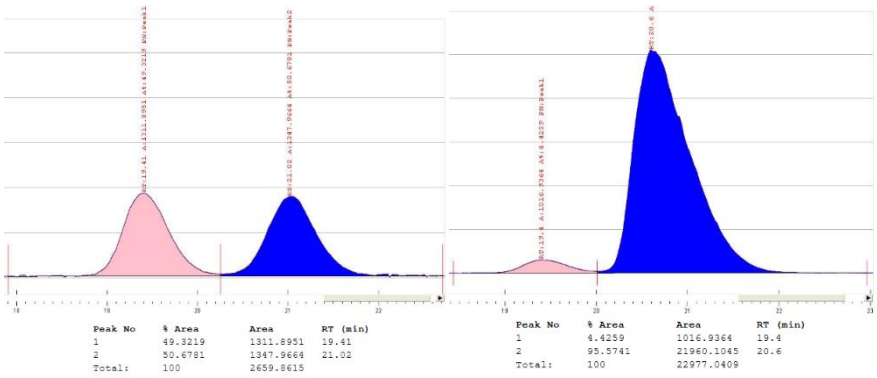
tert*-Butyl (*R*)-5-(2-phenyl-2-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)ethyl)-1H-indole-1-carboxylate (3.138).** The reaction was performed according to the general procedure ***(Method C) with 4,4,5,5-tetramethyl-2-phenyl-1,3,2-dioxaborolane (**3.76**) (61.2 mg, 0.30 mmol, 1.00 equiv), sodium trifluoromethanesulfonate (154.9 mg, 0.90 mmol, 3.00 equiv), vinylmagnesium chloride (0.20 mL, 1.53 M in tetrahydrofuran, 0.30 mmol, 1.00 equiv), *t*-butyl 5-bromoindole-1-carboxylate (106.6 mg, 0.36 mmol, 1.20 equiv), palladium (II) acetate (0.90 mL, 0.01 M in dimethyl sulfoxide, 0.009 mmol, 0.030 equiv), (S_p,S_p)-**3.3** (11.37 mg, 0.0108 mmol, 0.036 equiv). The unpurified product was purified by automated silica gel chromatography (Biotage 0% →50% CH_2Cl_2 in hexanes, stained in CAM) to afford white solid (105.1 mg, 78% yield). **^{1}H NMR** (600 MHz, $CDCl_3$) δ 8.01 (s, 1H), 7.55 (s, 1H), 7.39 (s, 1H), 7.31 – 7.25 (m, 4H), 7.21 – 7.11 (m, 2H), 6.48 (d, J = 3.7 Hz, 1H), 3.29 (dd, J = 13.5, 9.8 Hz, 1H), 3.07 (dd, J = 13.5, 6.8 Hz, 1H), 2.75 (dd, J = 9.7, 6.8 Hz,

1H), 1.67 (s, 9H), 1.13 (s, 6H), 1.12 (s, 6H). **^{11}B NMR** (128 MHz, $CDCl_3$) δ 32.64. **^{13}C NMR** (151 MHz, $CDCl_3$) δ 149.96, 142.88, 136.31, 133.81, 130.68, 128.57, 128.47, 125.90, 125.60, 125.50, 121.00, 114.79, 107.34, 83.51, 38.92, 35.17, 28.38, 24.75, 24.73 (quaternary C of *tert*-butyl group not observed). **IR** (neat) ν_{max} 2976.84 (w), 2931.15 (m), 1730.38 (s), 1469.06 (m), 1369.70 (s), 1348.51 (s), 1325.08 (s), 1255.59 (m), 1217.42 (m), 1162.60 (s), 1128.89 (s), 1082.05 (m), 1023.09 (m), 764.85 (m), 700.63 (m) cm^{-1}. **HRMS** (DART) for $C_{27}H_{35}BNO_4$ $[M+H]^+$: calculated: 448.26591, found: 448.26791. $[\alpha]_D^{20}$ = – 39.460 (*c* 4.03, $CHCl_3$, *l* = 50 mm).

Determination of Stereochemical Identity: Racemic compound was prepared according to the general procedure (***Method C, run at 60 ºC***) with $Pd(OAc)_2$ (5 mol%) and 1,1′-Bis(diisopropylphosphino)ferrocene (6 mol%) as the catalyst. Absolute stereochemistry was assigned by analogy (see product **3.127** and **3.134**).

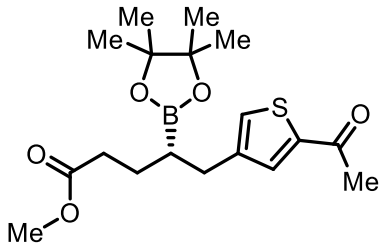
SFC (Chiracel OD-H, 2% IPA, 3 mL/min, 100 bar, 35 °C, 210-270 nm) – analysis tert-butyl (R)-5-(2-phenyl-2-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)ethyl)-1H-indole-1-carboxylate.

Racemic Material Standard Conditions



Peak No	% Area	Area	RT (min)
1	49.3219	1311.8951	19.41
2	50.6781	1347.9664	21.02
Total:	100	2659.8615	

Peak No	% Area	Area	RT (min)
1	4.4259	1016.9364	19.4
2	95.5741	21960.1045	20.6
Total:	100	22977.0409	



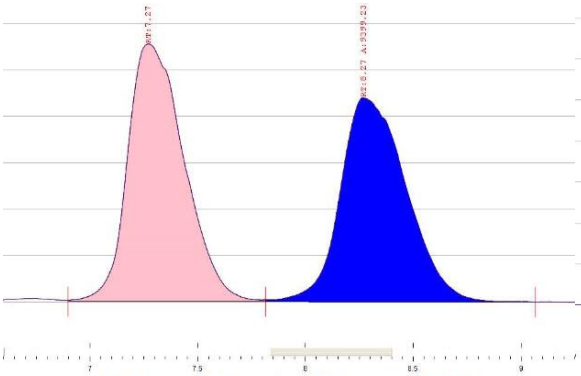
Methyl (*S*)-5-(5-acetylthiophen-3-yl)-4-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)pentanoate (3.136). The reaction was performed according to general procedure (***Method C)*** with methyl 3-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)propanoate (64.2 mg, 0.30 mmol, 1.00 equiv), sodium trifluoromethanesulfonate (154.9 mg, 0.90 mmol, 3.00 equiv), vinylmagnesium chloride (0.20 mL, 1.53 M in tetrahydrofuran, 0.30 mmol, 1.00 equiv), 1-(4-bromothiophen-2-yl)ethan-1-one (73.8 mg, 0.36 mmol, 1.20 equiv), palladium (II) acetate (0.9 mL, 0.01 M in dimethyl sulfoxide, 0.009 mmol, 0.030 equiv), (S_p,S_p)-**3.3** (11.37 mg, 0.0108 mmol, 0.036 equiv). The unpurified product was purified by automated silica gel chromatography (Biotage 1% →5% ethyl acetate in hexanes, stained in CAM) to afford white solid (71.4 mg, 65% yield). **^{1}H NMR** (600 MHz, $CDCl_3$) δ 7.52 (s, 1H), 7.26 (s, 1H), 3.63 (s, 3H), 2.73 (dd, *J* = 14.4, 8.8 Hz, 1H), 2.65 (dd, *J* = 14.4, 6.9 Hz, 1H), 2.49 (s, 3H), 2.42 – 2.23 (m, 2H), 1.73 (q, *J* = 7.7 Hz, 2H), 1.32 (p, *J* = 7.5 Hz, 1H), 1.14 (s, 6H), 1.13 (s, 6H). **^{11}B NMR** (128 MHz, $CDCl_3$) δ 33.49. **^{13}C NMR** (151 MHz, $CDCl_3$) δ 190.95, 174.11, 144.18, 143.67, 134.19, 130.04, 83.58, 51.73, 33.54, 31.67, 26.98, 26.28, 24.98, 24.97, 24.72. **IR**

(neat) ν_{max} 2976.61 (w), 2927.68 (w), 1734.68 (s), 1662.98 (s), 1417.13 (m), 1371.65 (m), 1270.26 (m), 1140.38 (s) cm^{-1}. **HRMS** (DART) for $C_{18}H_{28}BO_5S$ $[M+H]^+$ calculated: 367.1751, found: 367.176. $[\alpha]^{20}_D$: +2.173 (*c* 1.900, $CHCl_3$, *l* =50 mm).

Determination of Stereochemical Identity: Racemic compound was prepared according to the general procedure (***Method C, run at 60 ºC***) with $Pd(OAc)_2$ (5 mol%) and (S_p, S_p)-L1 (1.8 mol%), and (R_p, R_p)-L1 (1.8 mol%) as the catalyst. Absolute stereochemistry was assigned by analogy (see product **3.127** and **3.134**).

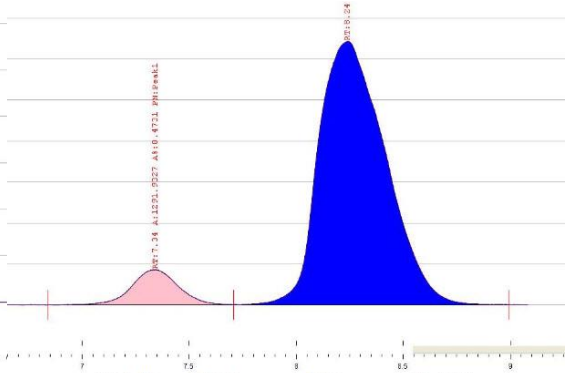
SFC (Chiracel OJ-H, 1% IPA, 3 mL/min, 100 bar, 35 °C, 210-270 nm) – analysis of methyl (S)-5-(5-acetylthiophen-3-yl)-4-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)pentanoate.

Racemic Material

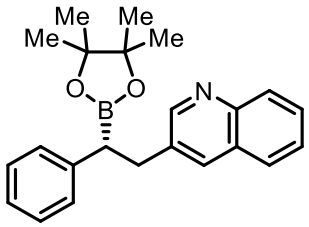


Peak No	% Area	Area	RT (min)
1	51.9467	10160.8085	7.27
2	48.0533	9399.2393	8.27
Total:	100	19560.0478	

Standard Conditions



Peak No	% Area	Area	RT (min)
1	8.4731	1291.9327	7.34
2	91.5269	13955.5406	8.24
Total:	100	15247.4733	

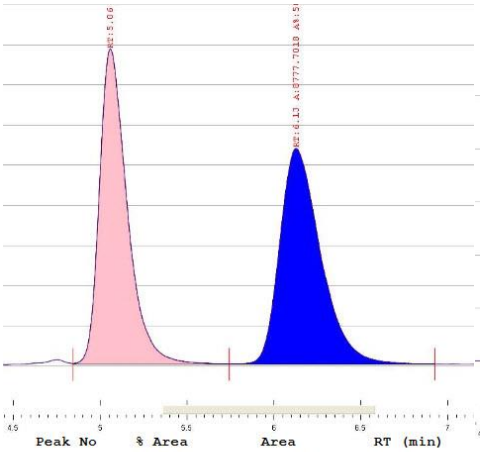


(*R*)-3-(2-Phenyl-2-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl) ethyl)quinolone (3.140). The reaction was performed according to general procedure (***Method C)*** with 4,4,5,5-tetramethyl-2-phenyl-1,3,2-dioxaborolane (61.2 mg, 0.30 mmol, 1.00 equiv), sodium trifluoromethanesulfonate (154.9 mg, 0.90 mmol, 3.00 equiv), vinylmagnesium chloride (0.20 mL, 1.53 M in tetrahydrofuran, 0.30 mmol, 1.00 equiv), 3-bromoquinoline (74.5 mg, 0.36 mmol, 1.20 equiv), palladium (II) acetate (0.9 mL, 0.01 M in dimethyl sulfoxide, 0.009 mmol, 0.030 equiv), (S_p,S_p)-**3.3** (11.37 mg, 0.0108 mmol, 0.036). The unpurified product was purified by automated silica gel chromatography (Biotage 2% →20% ethyl acetate in hexanes, stained in CAM) to afford white solid (82.9 mg, 77% yield). **^{1}H NMR** (500 MHz, $CDCl_3$) δ 8.75 (d, *J* = 1.8 Hz, 1H), 8.05 (app d, *J* = 8.4 Hz, 1H), 7.87 (app s, 1H), 7.69 (app d, *J* = 8.2 Hz, 1H), 7.62 (app t, *J* = 7.7 Hz, 1H), 7.47 (app t, *J* = 7.5 Hz, 1H), 7.25 (app t, 4H), 7.15 (app t, *J* = 6.5 Hz, 1H), 3.34 (dd, *J* = 13.8, 9.1 Hz, 1H), 3.12 (dd, *J* = 13.9, 7.3 Hz, 1H), 2.75 (app t, 1H), 1.11 (s, 12H). **^{11}B NMR** (160 MHz, $CDCl_3$) δ 32.86. **^{13}C NMR** (126 MHz, $CDCl_3$) δ 152.59, 146.96, 141.91, 134.94, 134.63, 129.30, 128.70, 128.68, 128.64, 128.17, 127.50, 126.57, 125.93, 83.84, 36.27, 34.42, 24.80, 24.74. **IR** (neat) ν_{max} 2976.63 (m), 2929.93 (w), 1726.48 (w), 1493.83 (m), 1327.42 (m), 1141.06 (s), 967.37 (w), 849.21 (w), 751.75 (w), 701.56 (w) cm^{-1}. **HRMS** (DART) for $C_{23}H_{27}BNO_2$ $[M+ H]^+$ calculated: 360.21348, found: 360.21532. $[\alpha]^{20}_D$: -46.5119 (*c* 3.18, $CHCl_3$, *l* =50 mm).

Determination of Stereochemical Identity: Racemic compound was prepared according to the general procedure (***Method C, run at 60 ºC***) with $Pd(OAc)_2$ (5 mol%) and 1,1′-Bis(dicyclohexylphosphino)ferrocene (6 mol%) as the catalyst. Absolute stereochemistry was assigned by analogy (see product **3.127** and **3.134**).

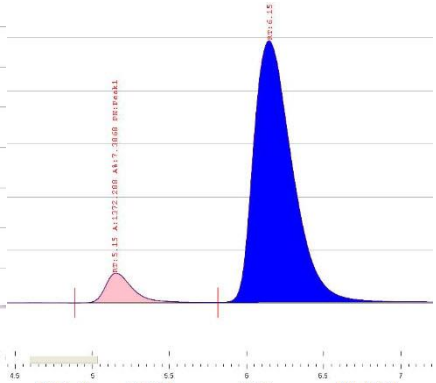
SFC (Chiracel OJ-H, 7% IPA, 3 mL/min, 100 bar, 35 °C, 210-270 nm) – analysis of (R)-3-(2-phenyl-2-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)ethyl)quinolone.

Racemic Material

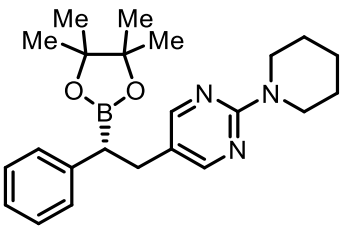


Peak No	% Area	Area	RT (min)
1	49.8916	8739.7127	5.06
2	50.1084	8777.7018	6.13
Total:	100	17517.4145	

Standard Conditions



Peak No	% Area	Area	RT (min)
1	7.3868	1372.288	5.15
2	92.6132	17205.1935	6.15
Total:	100	18577.4815	



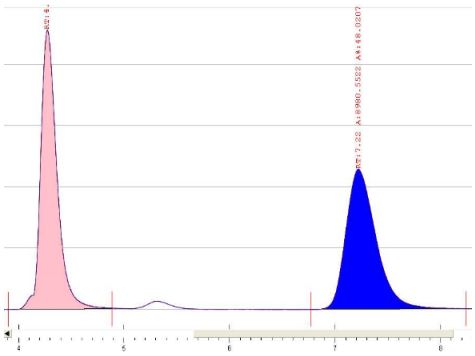
(*R*)-5-(2-Phenyl-2-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)ethyl)-2-(piperidin-1-yl)pyrimidine (3.139). The reaction was performed according to the general procedure ***(Method C)*** with 4,4,5,5-tetramethyl-2-phenyl-1,3,2-dioxaborolane (**3.76**) (61.2 mg, 0.30 mmol, 1.00 equiv), sodium trifluoromethanesulfonate

(154.9 mg, 0.90 mmol, 3.00 equiv), vinylmagnesium chloride (0.20 mL, 1.53 M in tetrahydrofuran, 0.30 mmol, 1.00 equiv), 5-bromo-2-(piperidin-1-yl)pyrimidine (87.2 mg, 0.36 mmol, 1.20 equiv), palladium (II) acetate (0.90 mL, 0.01 M in dimethyl sulfoxide, 0.009 mmol, 0.030 equiv), (S_p,S_p)-**3.3** (11.37 mg, 0.0108 mmol, 0.036 equiv). The unpurified product was purified by automated silica gel chromatography (Biotage 0% →15% ethyl acetate in hexanes, stained in CAM) to afford white solid (83.8 mg, 71% yield). **^{1}H NMR** (500 MHz, $CDCl_3$) δ 8.04 (s, 2H), 7.21 (app t, J = 7.6 Hz, 2H), 7.18 – 7.14 (m, 2H), 7.11 (app t, J = 7.3 Hz, 1H), 3.71 – 3.65 (m, 4H), 2.91 (dd, J = 14.1, 8.5 Hz, 1H), 2.72 (dd, J = 14.1, 7.9 Hz, 1H), 2.50 (app t, J = 8.2 Hz, 1H), 1.61 (p, J = 5.7 Hz, 2H), 1.54 (app p, J = 5.6 Hz, 4H), 1.14 (s, 6H), 1.13 (s, 6H). **^{11}B NMR** (128 MHz, $CDCl_3$) δ 32.75. **^{13}C NMR** (126 MHz, $CDCl_3$) δ 161.03, 158.01, 141.92, 128.66, 128.64, 125.82, 121.64, 83.76, 45.19, 34.53, 32.58, 25.85, 25.09, 24.82, 24.79. **IR** (neat) ν_{max} 3348.31 (w, br), 2977.12 (m), 2931.39 (m), 2853.55 (m), 1604.14 (s), 1498.41 (s), 1444.64 (s), 1361.24 (s), 1328.15 (s), 1140.94 (s), 946.09 (m), 851.03 (m), 755.50 (m), 699.52 (s), 673.07 (m) cm^{-1}. **HRMS** (DART) for $C_{23}H_{33}BN_3O_2$ $[M+H]^+$: calculated: 394.26658, found: 394.26775. $[\alpha]_D^{20}$ = – 20.812 (*c* 3.78, $CHCl_3$, *l* = 50 mm).

Determination of Stereochemical Identity: Racemic compound was prepared according to the general procedure (***Method C, run at 60 ºC***) with $Pd(OAc)_2$ (5 mol%) and (S_p,S_p)-**3.3** (1.8 mol%), and (R_p,R_p)-**3.3** (1.8 mol%) as the catalyst. Absolute stereochemistry was assigned by analogy (see product **3.127** and **3.134**).

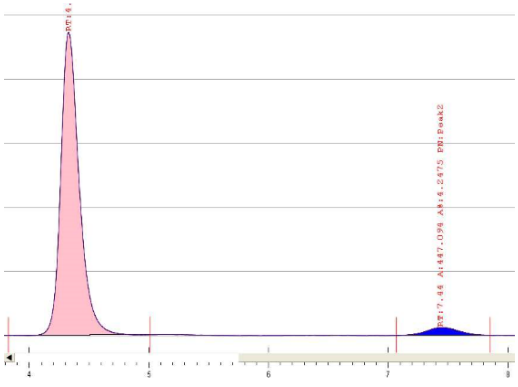
SFC (Chiracel OJ-H, 5% IPA, 3 mL/min, 100 bar, 35 °C, 210-270 nm) – analysis (R)-5-(2-phenyl-2-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)ethyl)-2-(piperidin-1-yl)pyrimidine.

Racemic Material

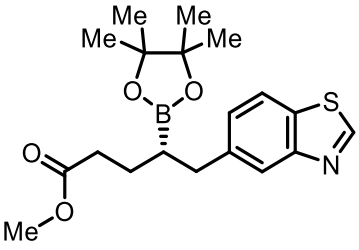


Peak No	% Area	Area	RT (min)
1	51.9793	9720.859	4.27
2	48.0207	8980.5522	7.22
Total:	100	18701.4112	

Standard Conditions



Peak No	% Area	Area	RT (min)
1	95.7525	10078.9185	4.33
2	4.2475	447.094	7.44
Total:	100	10526.0125	



Methyl (*S*)-5-(benzo[d]thiazol-5-yl)-4-(4,4,5,5-tetramethyl-1,3,2 -dioxaborolan-2-yl)pentanoate (3.137). The reaction was performed according to general procedure ***(Method C, with modification: reaction conducted at 55˚C)*** with methyl 3-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)propanoate (64.2 mg, 0.30 mmol, 1.00 equiv), sodium trifluoromethanesulfonate (154.9 mg, 0.90 mmol, 3.00 equiv), vinylmagnesium chloride (0.20 mL, 1.53 M in tetrahydrofuran, 0.30 mmol, 1.00 equiv), 5-bromobenzo[d]thiazole (77.1 mg, 0.36 mmol, 1.20 equiv), palladium (II) acetate (0.9 mL, 0.01 M in dimethyl sulfoxide, 0.009 mmol, 0.030 equiv), (S_p,S_p)-**3.3** (11.37 mg, 0.0108

mmol. 0.036 equiv). The unpurified product was purified by automated silica gel chromatography (Biotage 1% →5% ethyl acetate in hexanes, stained in CAM) to afford white solid (82.2 mg, 73% yield).

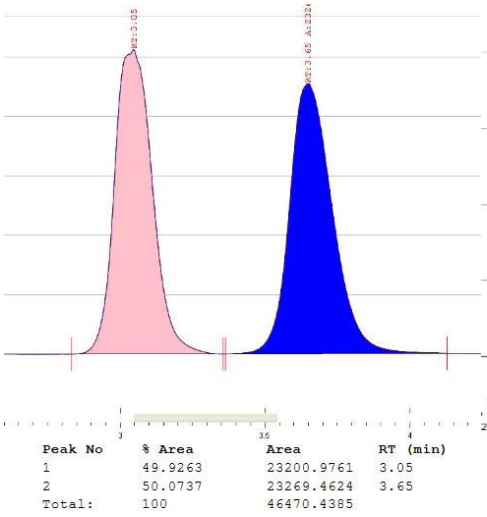
(Method G) with methyl 3-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)propanoate (64.2 mg, 0.30 mmol, 1.00 equiv), sodium trifluoromethanesulfonate (154.9 mg, 0.90 mmol, 3.00 equiv), vinylmagnesium chloride (0.20 mL, 1.53M in tetrahydrofuran, 0.30 mmol, 1.00 equiv), phenyl trifluoromethanesulfonate (81.4 mg, 0.36 mmol, 1.20 equiv), palladium (II) acetate (0.9 mL, 0.01 M dimethyl sulfoxide, 0.009 mmol, 0.030 equiv), (S_p,S_p)-**3.3** (11.37 mg, 0.0108 mmol, 0.036 equiv). The unpurified product was purified by automated silica gel chromatography (Biotage 1% →5% ethyl acetate in hexanes, stained in CAM) to afford white solid (82.2 mg, 73% yield).

^{1}H NMR (600 MHz, $CDCl_3$) δ 8.91 (s, 1H), 7.93 (s, 1H), 7.79 (d, *J* = 8.2 Hz, 1H), 7.28 (d, *J* = 9.7 Hz, 1H), 3.60 (s, 3H), 2.91 (dd, *J* = 13.7, 8.2 Hz, 1H), 2.78 (dd, *J* = 13.7, 7.7 Hz, 1H), 2.38 (ddd, *J* = 15.7, 8.0, 8.0 Hz, 1H), 2.29 (ddd, *J* = 15.9, 7.9, 7.9 Hz, 1H), 1.73 (app q, *J* = 7.8 Hz, 2H), 1.40 (app q, *J* = 7.7 Hz, 1H), 1.14 (s, 6H), 1.11 (s, 6H). **^{11}B NMR** (160 MHz, $CDCl_3$) δ 33.51. **^{13}C NMR** (151 MHz, $CDCl_3$) δ 174.14, 154.01, 153.73, 140.47, 131.23, 127.13, 123.73, 121.50, 83.48, 51.63, 37.09, 33.67, 26.12, 25.72, 24.97, 24.95. **IR** (neat) ν_{max} 2977.05 (w), 2929.89 (w), 1734.75 (s), 1440.78 (m), 1380.71 (m), 1319.51 (m), 1141.49 (s), 846.47 (m) cm^{-1}. **HRMS** (DART) for $C_{19}H_{26}BNO_4S$ $[M+H]^+$ calculated: 376.1754, found: 376.1753. $[\alpha]^{20}_D$: -7.957 (*c* 2.075, $CHCl_3$, *l* =50 mm).

Determination of Stereochemical Identity: Racemic compound was prepared according to the general procedure (***Method C, run at 60 ºC***) with $Pd(OAc)_2$ (5 mol%) and (S_p,S_p)-**3.3** (1.8 mol%), and (R_p, R_p)-**3.3** (1.8 mol%) as the catalyst as the catalyst. Absolute stereochemistry was assigned by analogy (see product **3.127** and **3.134**).

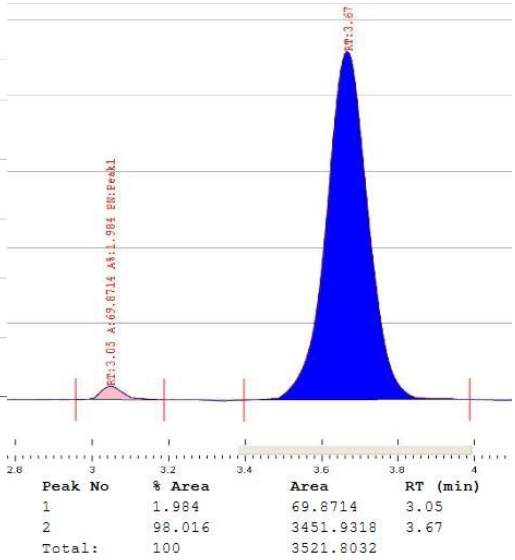
SFC (Chiracel OJ-H, 6% IPA, 3 mL/min, 100 bar, 35 °C, 210-270 nm) – analysis of methyl (S)-5-(benzo[d]thiazol-5-yl)-4-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)pentanoate.

Racemic Material

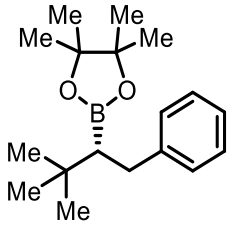


Peak No	% Area	Area	RT (min)
1	49.9263	23200.9761	3.05
2	50.0737	23269.4624	3.65
Total:	100	46470.4385	

Standard Conditions

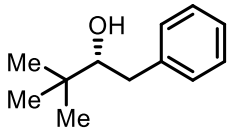


Peak No	% Area	Area	RT (min)
1	1.984	69.8714	3.05
2	98.016	3451.9318	3.67
Total:	100	3521.8032	



(*R*)-2-(3,3-Dimethyl-1-phenylbutan-2-yl)-4,4,5,5-tetramethyl-1,3,2-dioxaborolane (3.143). The reaction was performed according to general procedure ***(Method D, with modification:tetrahydrofuran was used instead of 1:1 dimethyl sulfoxide:tetrahydrofuran)*** 2-(*tert*-

butyl)-4,4,5,5-tetramethyl-1,3,2-dioxaborolane (55.2 mg, 0.30 mmol, 1.00 equiv), potassium trifluoromethanesulfonate (124.2 mg, 0.66 mmol, 2.20 equiv), vinylbromide (0.25 mL, 1.32 M in diethyl ether, 0.33 mmol, 1.10 equiv), phenyl trifluoromethanesulfonate (81.4 mg, 0.36 mmol, 1.20 equiv), palladium (II) acetate (0.9 mL, 0.01 M in tetrahydrofuran, 0.009 mmol, 0.030 equiv), (S_p,S_p)-**3.3** (11.37 mg, 0.0108 mmol, 0.036 equiv). The unpurified product was purified by automated silica gel chromatography (Biotage 1% →5% ethyl acetate in hexanes, stained in CAM) to afford colorless oil (54.5 mg, 63% yield). **^{1}H NMR** (500 MHz, $CDCl_3$) δ 7.22 – 7.16 (m, 4H), 7.13 – 7.04 (m, 1H), 2.81 (dd, *J* = 13.1, 4.3 Hz, 1H), 2.58 (app t, *J* = 13.0 Hz, 1H), 1.27 (dd, *J* = 12.9, 4.3 Hz, 1H), 1.05 (app s, 6H), 1.02 (app d, *J* = 1.8 Hz, 9H), 0.97 (app s, 6H). **^{11}B NMR** (160 MHz, THF-d_8) δ 33.37. **^{13}C NMR** (126 MHz, $CDCl_3$) δ 142.98 , 129.31 , 128.17 , 125.68 , 83.02 , 39.02 , 33.25 , 32.43 , 29.83 , 25.27 , 24.79. **IR** (neat) ν_{max} 2954.51 (w), 2867.96 (w), 1370.54 (w), 1318.21 (w), 1141.93 (w), 698.09 (w) cm^{-1}. **HRMS** (DART) for $C18H_{33}BO_2N$ $[M+NH_4]^+$ calculated: 306.2604, found: 306.2607. $[\alpha]^{20}_D$: 21.987 (*c* 0.825, $CHCl_3$, *l* =50 mm).



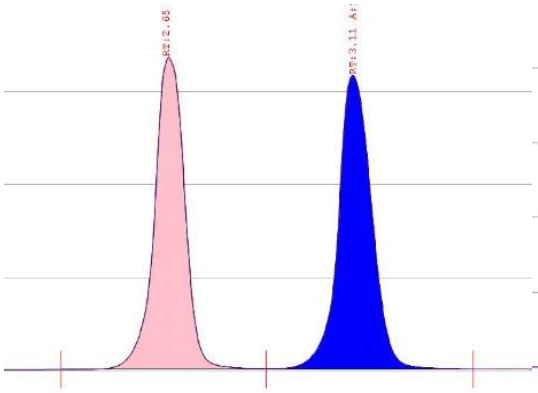
(*R*)-3,3-Dimethyl-1-phenylbutan-2-ol (3.143-OH). Product **3.143** was oxidized according to ***General Method for Oxidation of Boronic Ester Products.*** All spectral data was in accord with the literature[69]

[69] Miller, S. P.; Morgan, J. B.; Nepveux, F. J.; Morken, J. P. *Org. Lett.* **2004**, 6, 131.

Determination of Stereochemical Identity: Racemic compound was prepared according to the general procedure ***(Method D, with modification: tetrahydrofuran was used instead of 1:1 dimethyl sulfoxide:tetrahydrofuran and the temperature was increased from 40 ºC to 60 ºC)*** with $Pd(OAc)_2$ (5 mol%) and 1,1′-Bis(dicyclohexylphosphino)ferrocene (6 mol%) as the catalyst. Absolute stereochemistry was assigned by analogy (see product **3.127** and **3.134**).

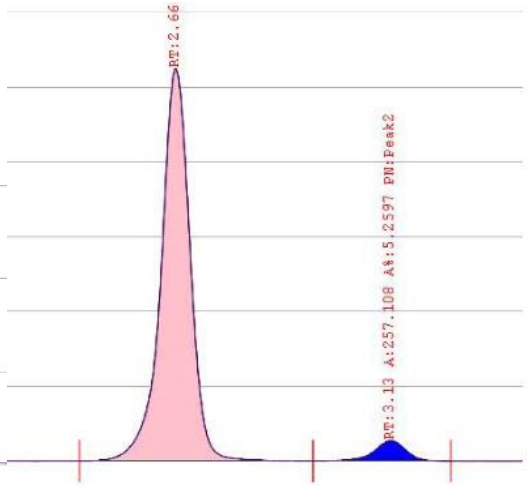
SFC (Chiracel OD-H, 5% IPA, 3 mL/min, 100 bar, 35 °C, 210-270 nm) – analysis of (R)-3,3-dimethyl-1-phenylbutan-2-ol.

Racemic Material

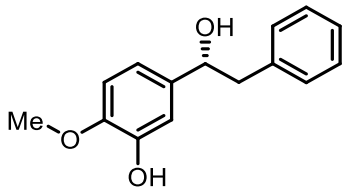


Peak No	% Area	Area	RT (min)
1	49.0071	8705.8842	2.65
2	50.9929	9058.6536	3.11
Total:	100	17764.5378	

Standard Conditions



Peak No	% Area	Area	RT (min)
1	94.7403	4631.1385	2.66
2	5.2597	257.108	3.13
Total:	100	4888.2465	

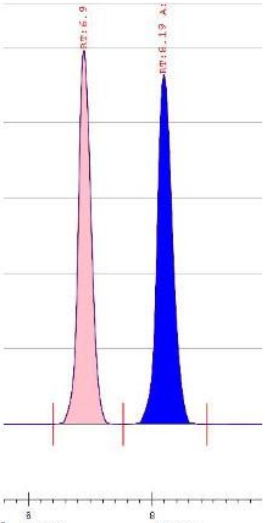


(*R*)-5-(1-Hydroxy-2-phenylethyl)-2-methoxyphenol (3.144-OH). The reaction was performed according to the general procedure: ***(Method E, with the modification: tetrahydrofuran was used instead of 1:1 dimethyl sulfoxide:tetrahydrofuran and 3.15 equiv. of t-BuLi was used rather than 2.1 equiv.)*** with 5-bromo-2-methoxyphenol (67.0 mg, .33 mmol, 1.10 equiv), potassium trifluoromethanesulfonate (118.5 g, 0.63 mmol, 2.10 equiv), *tert*-butyllithium (055 mL, 1.71 M in hexanes, 0.945 mmol, 3.15 equiv) 4,4,5,5-tetramethyl-2-vinyl-1,3,2-dioxaborolane (46.2 mg, 0.30 mmol, 1.00 equiv), phenyl trifluoromethanesulfonate (81.4 mg, 0.36 mmol, 1.20 equiv), palladium (II) acetate (0.9 mL, 0.01 M in tetrahydrofuran, 0.009 mmol, 0.030 equiv), (S_p,S_p)-**3.3** (11.37 mg, 0.0108 mmol, 0.036 equiv). Unpurified product **3.144** was oxidized according to ***General Method for Oxidation of Boronic Ester Products.*** The unpurified product was purified by automated silica gel chromatography (Biotage 1% →20% ethyl acetate in hexanes, stained in CAM) to afford white solid (39.6 mg, 54% yield). **^{1}H NMR** (600 MHz, $CDCl_3$) δ 7.28 (app t, J = 7.5 Hz, 2H), 7.25 – 7.13 (m, 3H), 6.96 (s, 1H), 6.79 (app t, J = 8.3 Hz, 1H), 5.60 (s, 1H), 4.79 (app t, 2H), 3.87 (s, 3H), 3.07 – 2.86 (m, 2H), 1.86 (s, 1H). **^{13}C NMR** (151 MHz, $CDCl_3$) δ 146.23, 145.83, 138.39, 137.50, 129.70, 128.70, 126.77, 117.79, 112.47, 110.65, 75.24, 56.24, 46.17. **IR** (neat) ν_{max} 3426.24 (br), 2935.77 (w), 1594.29 (w), 1509.07 (w), 1270.34 (m), 1126.70 (w), 1028.30 (w) cm^{-1}. **HRMS** (DART) for $C_{15}H_{15}O_2$ $[M+H-H_2O]^+$ calculated: 227.1072, found: 227.1084. $[\alpha]^{20}_D$: -3.400 (*c* 0.735, $CHCl_3$, *l* =50 mm).

Determination of Stereochemical Identity: Racemic compound was prepared according to the general procedure ***(Method E, with the modification: tetrahydrofuran was used instead of 1:1 dimethyl sulfoxide:tetrahydrofuran, 3.15 equiv of t-BuLi was used rather than 2.1 equiv. and the temperature was increased from 40 ºC to 60 ºC)*** with $Pd(OAc)_2$ (5 mol%) and 1,1′-Bis(dicyclohexylphosphino)ferrocene (6 mol%) as the catalyst. Absolute stereochemistry was assigned by analogy (see product **3.127** and **3.134**).

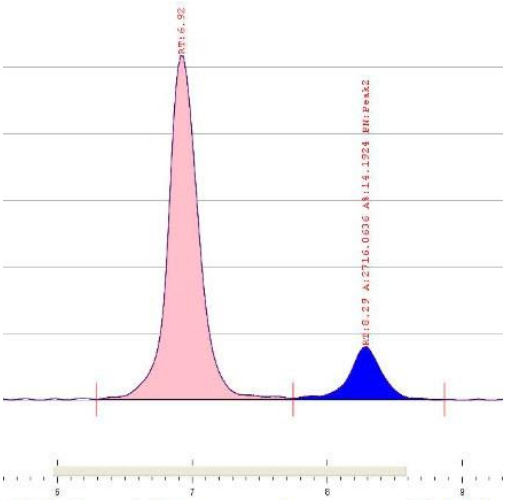
SFC (Chiracel OD-H, 20% IPA, 3 mL/min, 100 bar, 35 °C, 210-270 nm) – analysis of (R)-5-(1-hydroxy-2-phenylethyl)-2-methoxyphenol.

Racemic Material

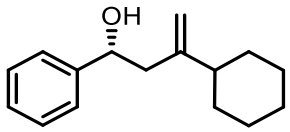


Peak No	% Area	Area	RT (min)
1	47.2195	14543.5227	6.9
2	52.7805	16256.2706	8.19
Total:	100	30799.7933	

Standard Conditions



Peak No	% Area	Area	RT (min)
1	85.8076	16421.428	6.92
2	14.1924	2716.0636	8.29
Total:	100	19137.4916	

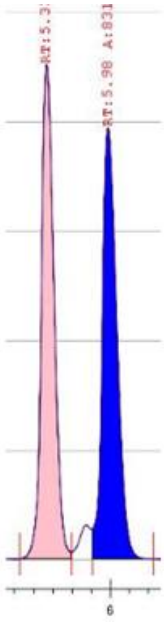


(R)*-3-Cyclohexyl-1-phenylbut-3-en-1-ol (3.145-OH).** The reaction was performed according to the general procedure (Method D, with the modification: NaOTf was used instead of KOTf***) with sodium trifluoromethanesulfonate (113.6 mg in 0.50 mL diethyl ether, 0.66 mmol, 2.20 equiv), vinylbromide (0.34 mL, 0.96 M in diethyl ether, 0.33 mmol, 1.10 equiv), *t*BuLi (0.35 mL, 1.78 M in hexanes, 0.63 mmol, 2.10 equiv), 4,4,5,5-tetramethyl-2-phenyl-1,3,2-dioxaborolane (**3.76**) (61.2 mg in 0.30 mL diethyl ether + 0.4 mL diethyl ether rinse, 0.30 mmol, 1.00 equiv), 1-cyclohexylvinyl trifluoromethanesulfonate **(3.155)** (93.0 mg, 0.36 mmol, 1.20 equiv), palladium (II) acetate (0.90 mL, 0.01 M in THF, 0.009 mmol, 0.030 equiv), (S_p,S_p)-**3.3** (11.37 mg, 0.0108 mmol, 0.036 equiv). Unpurified product **3.145** was oxidized according to ***General Method for Oxidation of Boronic Ester Products.*** The unpurified product was purified by silica gel chromatography (0% → 20% ethyl acetate in hexanes, stained in CAM) to afford colorless oil (38.5 mg, 56% yield). All spectral data was in accord with the literature.[61]

Determination of Stereochemical Identity: Racemic compound was prepared and reported previously[61] with 4,4,5,5-tetramethyl-2-vinyl-1,3,2-dioxaborolane, and $Pd(OAc)_2$ (5 mol%) and 1,1′-Bis(dicyclohexylphosphino) ferrocene (6 mol%) as the catalyst. Absolute stereochemistry was assigned by analogy (see product **3.127** and **3.134**).

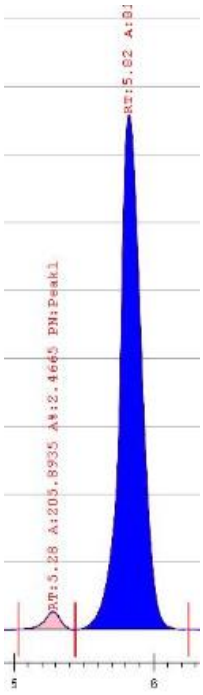
SFC (Chiracel OD-H, 5% IPA, 3 mL/min, 100 bar, 35 °C, 210-270 nm) – analysis of (R)-3-cyclohexyl-1-phenylbut-3-en-1-ol.

Racemic Material

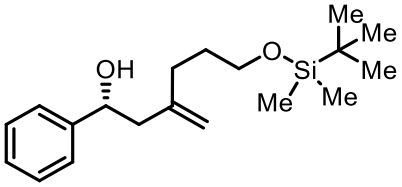


Peak No	% Area	Area	RT (min)
1	49.9523	8295.3259	5.33
2	50.0477	8311.1554	5.98
Total:	100	16606.4813	

Standard Conditions



Peak No	% Area	Area	RT (min)
1	2.4665	205.8935	5.28
2	97.5335	8141.7545	5.82
Total:	100	8347.648	



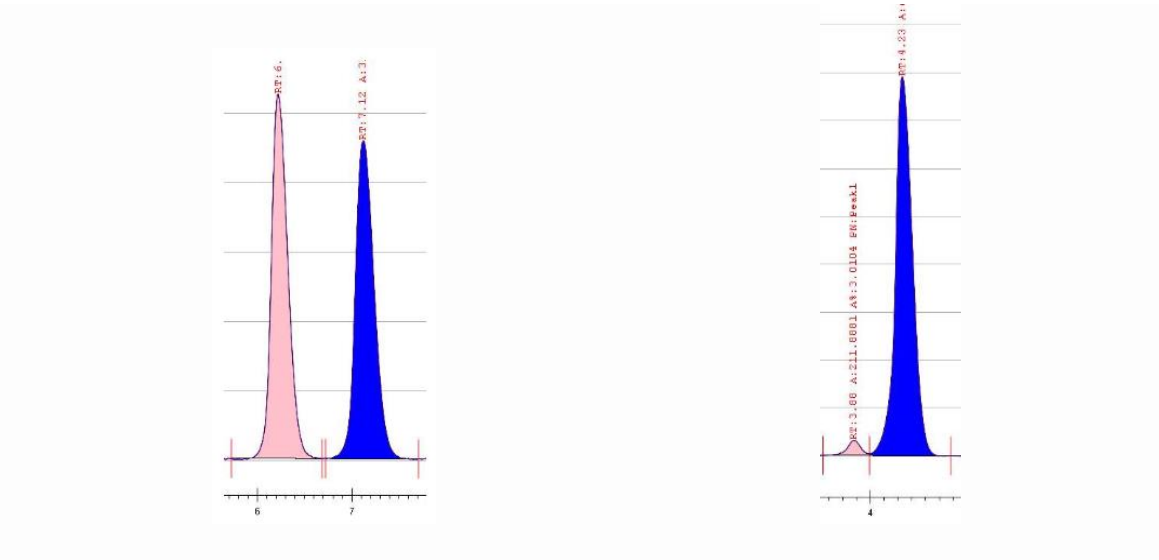
_(R)_-6-(_tert_-Butyldimethylsilyloxy)-3-methylene-1-phenyl hexan-1-ol (3.146-OH). The reaction was performed according to the general procedure (***Method D, with the modification: NaOTf was used instead of KOTf***) with sodium trifluoromethanesulfonate (113.6 mg in 0.50 mL diethyl ether, 0.66 mmol, 2.20 equiv), vinylbromide (0.34 mL, 0.96 M in diethyl ether, 0.33 mmol, 1.10 equiv), *t*BuLi (0.35 mL, 1.78 M in hexanes, 0.63 mmol, 2.10 equiv), 4,4,5,5-tetramethyl-2-phenyl-1,3,2-

dioxaborolane (**3.76**) (61.2 mg in 0.30 mL diethyl ether + 0.4 mL diethyl ether rinse, 0.30 mmol, 1.00 equiv), 5-((*tert*-butyldimethylsilyl)oxy)pent-1-en-2-yl trifluoromethanesulfonate (**3.157**) (125.4 mg, 0.36 mmol, 1.20 equiv), palladium (II) acetate (0.90 mL, 0.01 M in tetrahydrofuran, 0.009 mmol, 0.030 equiv), (S_p,S_p)-**3.3** (11.37 mg, 0.0108 mmol, 0.036 equiv). Unpurified product **3.146** was oxidized according to ***General Method for Oxidation of Boronic Ester Products.*** The unpurified product was purified by silica gel chromatography (0% → 20% EtOAc in hexanes, stained in CAM) to afford yellow oil (53.1 mg, 55% yield). All spectral data was in accord with the literature.[61]

Determination of Stereochemical Identity: Racemic compound was prepared and reported previously[61] with 4,4,5,5-tetramethyl-2-vinyl-1,3,2-dioxaborolane, and $Pd(OAc)_2$ (5 mol%) and 1,1′-Bis(dicyclohexylphosphino) ferrocene (6 mol%) as the catalyst. Absolute stereochemistry was assigned by analogy (see product **3.127** and **3.134**).

SFC (Chiracel OD-H, 5% IPA, 3 mL/min, 100 bar, 35 °C, 210-270 nm) – analysis of 6-(tert-butyldimethylsilyloxy)-3-methylene-1-phenylhexan-1-ol.

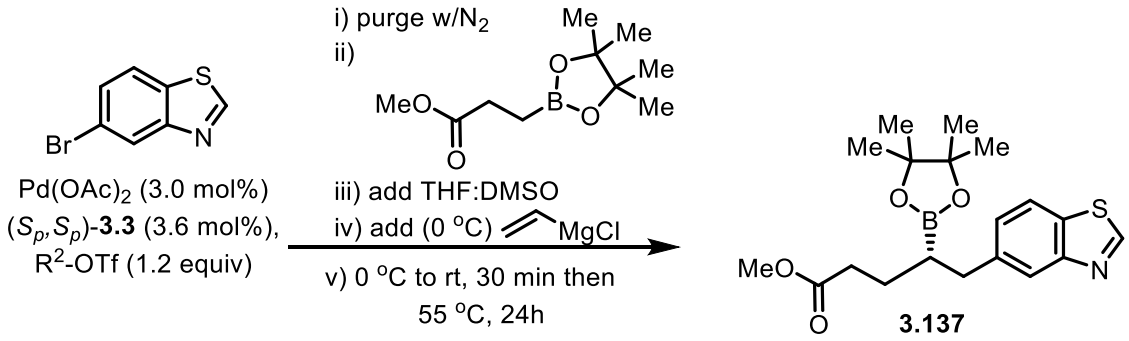
Racemic Material Standard Conditions



Peak No	% Area	Area	RT (min)
1	50.0691	3171.9339	6.22
2	49.9309	3163.182	7.12
Total:	100	6335.1159	

Peak No	% Area	Area	RT (min)
1	3.0104	211.8881	3.88
2	96.9896	6826.5322	4.23
Total:	100	7038.4203	

3.8.2.9 Procedure for Gram-Scale Experiment Conducted Outside of the Glovebox



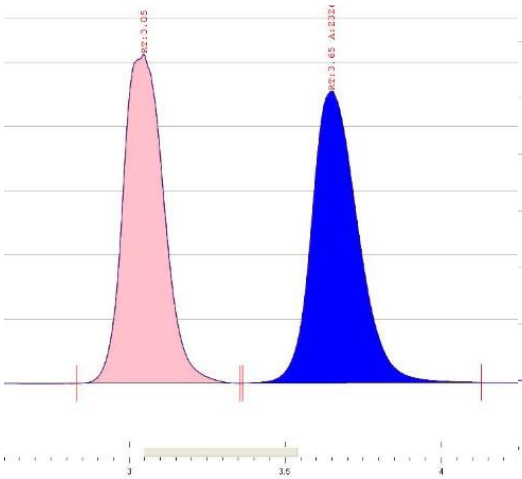
In a hood an oven-dried 50 mL round bottom flask equipped with a magnetic stir bar was charged with all the solid reagents including: sodium trifluoromethanesulfonate (2.3175 g, 12.9 mmol, 3.00 equiv), $Pd(OAc)_2$ (0.0289 g, 0.129 mmol, 0.03 equiv), (S_p,S_p)-**3.3** (0.1630

g, 0.1548 mmol, 0.036 equiv), and 5-bromobenzo[d]thiazole (1.1047 g, 5.16 mmol, 1.2 equiv). The vial was then sealed with a rubber septa and the atmosphere in the vial was exchanged with nitrogen by three two-minute cycles. The vial was then placed under positive nitrogen pressure and methyl 3-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)propanoate (0.9205 g, 4.3 mmol, 1.0 equiv) was added followed by tetrahydrofuran (4.36 mL) and dimethyl sulfoxide (7.17 mL). The solution was allowed to stir for 15 min at room temperature until the solution became homogeneous, after which the reaction was allowed to cool to 0 ºC in an ice bath and vinylmagnesium chloride solution (4.3 mmol, 1.0 equiv., 1.53 M in tetrahydrofuran (Sigma-Aldrich), 2.81 mL) was added dropwise. The vial was allowed to warm to room temperature before being sealed with tape and heated at 55 ºC for 24 h. To the resulting mixture was added water (30 mL) and the product was extracted from the aqueous layer with ethyl acetate (4 x 50 mL). The combined organic layers were dried over Na_2SO_4, concentrated under reduced pressure, filtered through a silica gel plug with diethyl ether, reconcentrated, and subsequently The unpurified product was purified by automated silica gel chromatography (Biotage 1% →20% ethyl acetate in hexanes, stained in CAM) to afford white solid (1.1296g, 70% yield)

Determination of Stereochemical Identity: Racemic compound was prepared according to the general procedure ***(Method B, with the modification: the reaction was run at 55 ºC instead of 60 ºC)*** with $Pd(OAc)_2$ (5 mol%) and (S_p,S_p)-**3.3** (1.8 mol%), and (R_p,R_p)-**3.3** (1.8 mol%) as the catalyst Absolute stereochemistry was assigned by analogy (see product **3.127** and **3.134**).

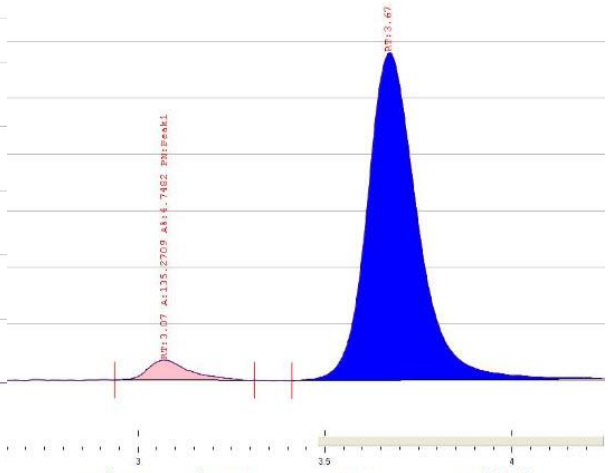
SFC (Chiracel OJ-H, 6% IPA, 3 mL/min, 100 bar, 35 °C, 210-270 nm) – analysis of methyl (S)-5-(benzo[d]thiazol-5-yl)-4-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)pentanoate.

Racemic Material



Peak No	% Area	Area	RT (min)
1	49.9263	23200.9761	3.05
2	50.0737	23269.4624	3.65
Total:	100	46470.4385	

Standard Conditions



Peak No	% Area	Area	RT (min)
1	4.7482	135.2709	3.07
2	95.2518	2713.6338	3.67
Total:	100	2848.9047	

Chapter Four

Catalytic Enantioselective Multi-Component Reactions of Alkenylboron Reagents and C(sp^3) Electrophiles: Conjunctive Coupling, Radical Addition/Coupling and Related Radical-Polar Crossover Reactions

4.1 Introduction

While most research in the field of catalytic cross-coupling[1] has focused on the construction of C(sp^2)−C(sp^2) bonds, largely relying on palladium complexes, recent advances have expanded the scope of cross-coupling methods to include C(sp^2)−C(sp^3) and C(sp^3)−C(sp^3) couplings.[2] The latter class of C−C bonds are often difficult to forge using traditional catalytic cross-coupling methods due to mechanistic considerations such as challenging oxidative addition, slow transmetalation, and facile β-hydride elimination. The growing success of cross-coupling reactions utilizing nickel complexes has made it apparent that this class of catalyst is capable of constructing C(sp^2)–C(sp^3) and C(sp^3)–C(sp^3) bonds while engaging challenging or poorly reactive classes of electrophiles.

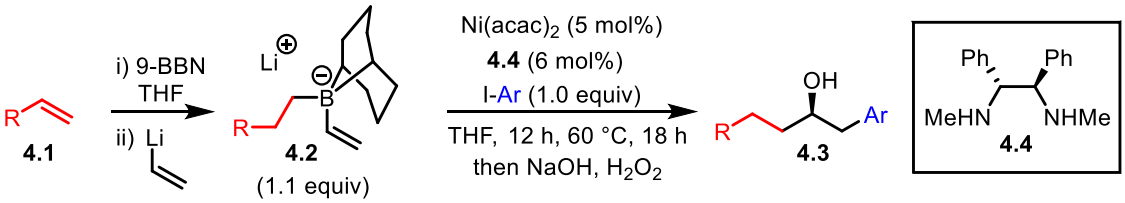
The ability of nickel complexes to mediate the formation of radical species in particular has enabled the development of a wide variety of versatile cross-coupling methods. Yet harnessing these reactive intermediates and particularly controlling enantioselectivity in such transformations is an active area of research with many unsolved challenges. In the context of multi-component reactions, the ability of nickel-based catalysts to mediate both radical and two-electron processes opens up the potential to design reactions that harness

[1] For a comprehensive overview of catalytic cross-coupling, see: de Meijere, A. Diederich, F., Eds. Metal-Catalyzed Cross- Coupling Reactions, 2nd ed.; Wiley-VCH: Weinheim, Germany, **2004**; Vols. 1 and 2.
[2] For recent reviews see: (a) Choi, J.; Fu, G. C. *Science* **2017**, 356, 152. (b) Fu, G. C. *ACS Cent. Sci*. **2017**, 3, 692.

both radical and polar reactivity modes to rapidly construct complex molecular frameworks, potentially with the ability to exercise stereocontrol.

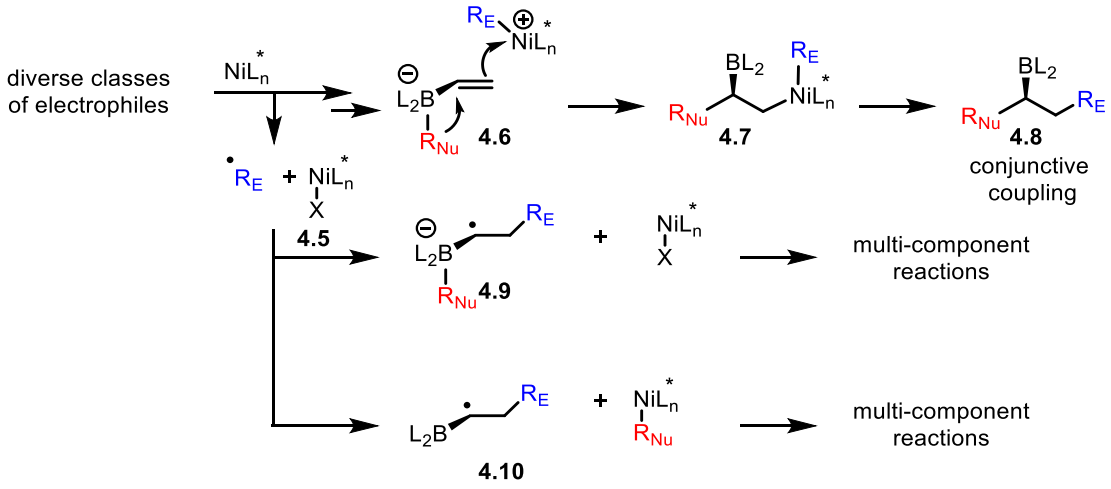
Preliminary studies conducted by my coworkers[3] established that the nickel complex of diamine **4.4** is capable of engaging aryl iodide electrophiles and alkyl–9BBN-derived

Scheme 4.1. Conjunctive coupling: 9-BBN-derived ate complexes/aryl iodides catalyzed by a Ni complex



boron-ate complexes **4.2** in an enantioselective conjunctive coupling, generating products similar to those produced by the palladium-based systems previously discussed in chapters two and three of this dissertation (Scheme 4.1). We imagined that if the ability of a nickel-based catalyst to generate radical intermediates could be harnessed we might be able to engineer a conjunctive coupling reaction which could engage diverse electrophile classes

Scheme 4.2. Potential multicomponent reactions utilizing Ni-based catalysts with alkenylboron reagents



[3] Chierchia, M.; Law, C.; Morken, J. P. *Angew. Chem. Int. Ed.* **2017**, 56, 11870.

including sp^3-hybridized electrophiles (Scheme 4.2). Additionally, the ability of alkenyl boron reagents to act as radical acceptors might facilitate the generation of α-boryl intermediates (**4.9** and **4.10**) which might participate in related multi-component process.

4.2 Background

4.2.1 Mechanistic Aspects of Nickel in Catalytic Coupling Reactions

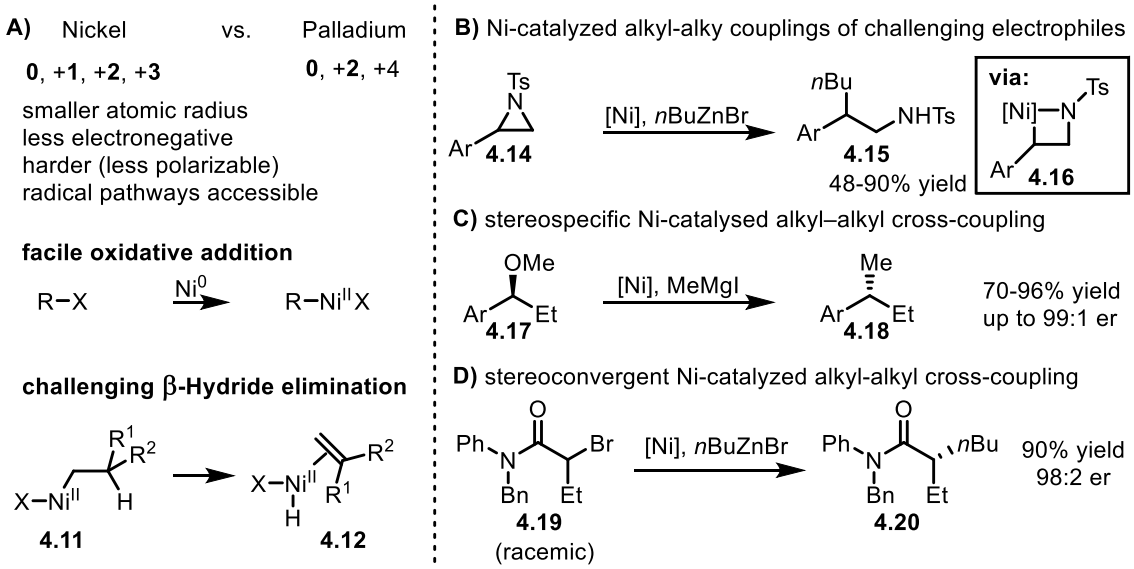
Catalytic reactions utilizing palladium complexes have been heavily investigated, leading to an in-depth mechanistic understanding of this class of catalyst which has enabled the development of a suit of powerful transformations.[4] More recently the use of nickel complexes in cross-coupling reactions has attracted increasing interest.[5] While arguably initially viewed as simply a cheaper alternative to palladium-based catalysts, the use of nickel-based catalysts has revolutionized the field of cross-coupling, enabling challenging bond forming reactions and engaging classes of electrophiles traditionally considered to be unreactive.

In comparison to palladium, nickel can readily access even as well as odd oxidation states, facilitating the generation of radical intermediates and enabling reaction pathways usually inaccessible to palladium-based catalysts (Scheme 4.3.A). Additionally, nickel is less electronegative than palladium, thus nickel-based catalysts generally engage in facile oxidative addition (a process that reduced electron density on the metal center) relative to

[4](a) Seechurn, C. C. C. J.; Kitching, M. O.; Colacot, T. J.; Snieckus, V. *Angew. Chem. Int. Ed*. **2012**, 51, 5062. (b) Roya, D.; Uozumi, Y. *Adv. Synth. Catal*. **2018**, 360, 602.
[5]For excellent reviews on homogeneous nickel catalysis, see: (a) Ananikov, V. P. *ACS Catal.* **2015**, 5, 1964. (b) Tasker, S. Z.; Standley, E. A.; Jamison, T. F. *Nature* **2014**, 509, 299.

palladium-based catalysts.[6] Additionally, β-hydride elimination tends to be slower for nickel complexes due to the higher energy barrier for Ni–carbon bond rotation prior to β-hydride elimination.[7] Taken together, the ability of nickel-based catalysts to engage in facile oxidative addition and their resistance to non-productive β–hydride elimination decomposition pathways has enabled the development of new transformations involving alkylnickel intermediates which engage challenging electrophiles such as aziridines[8] and benzyl methyl ethers, forging valuable $C(sp^3)$–$C(sp^3)$ bonds (Scheme 4.3.B[9]/C[10]). In addition to being able to engage in stereospecific and stereoselective transformations[11], pioneering work by the Fu group has established that nickel complexes are capable of

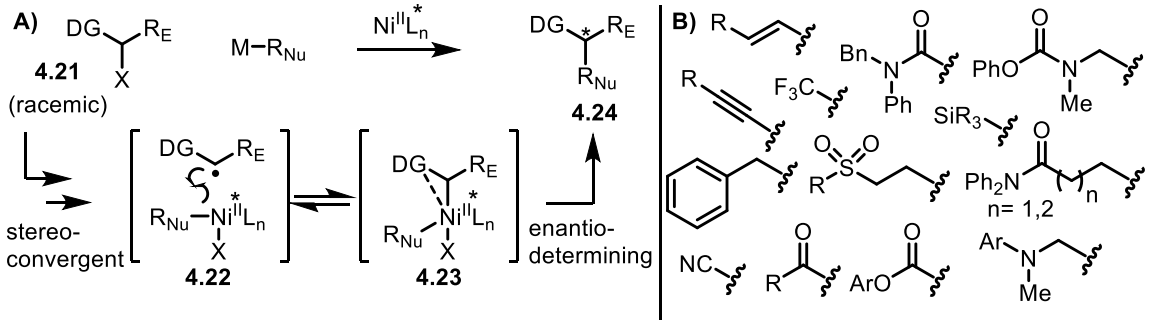
Scheme 4.3. Mechanistic aspects of Ni vs. Pd and application in cross-coupling reactions



[6]Tsou, T. T.; Kochi, J. K. *J. Am. Chem. Soc.* **1979**, 101, 6319.
[7]Lin, B.-L.; Liu, L.; Fu, Y.; Luo, S.-W.; Chen, Q.; Guo, Q.-X. *Organometallics*, **2004**, 23, 2114.
[8] Lin, B. L., Clough, C. R.; Hillhouse, G. L. *J. Am. Chem. Soc*. **2002**, 124, 2890.
[9] Huang, C.-Y.; Doyle, A. G. *J. Am. Chem. Soc.* **2012**, 134, 9541.
[10] Taylor, B. L. H.; Swift, E. C.; Waetzig, J. D.; Jarvo, E. R. *J. Am. Chem. Soc.* **2011**, 133, 389.
[11] For recent reviews, see: (a) Cherney, A. H.; Kadunce, N. T.; Reisman, S. E. *Chem. Rev.* **2015**, 115, 9587. (b) Tollefson, E. J.; Hanna, L. E.; Jarvo, E. R. *Acc. Chem. Res.* **2015**, 48, 2344.

catalyzing the stereoconvergent couplings of racemic alkyl electrophiles (Scheme 4.3.D).[12] As depicted in Scheme 4.4.A, this class of reaction is believed to proceed by way of a stereoablative oxidative addition of a chiral racemic electrophile **4.21** to generate a prochiral radical species **4.22**, followed by an enantiodetermining recombination/reductive elimination (**4.22** to **4.24**). While the reversibility of the radical trapping step (**4.22** to **4.23**) is supported by computational evidence in related systems,[13] a thorough mechanistic investigation, particularly with respect to the role of electrophile directing group, has

Scheme 4.4. Fu's stereoconvergent coupling reactions utilizing various directing group

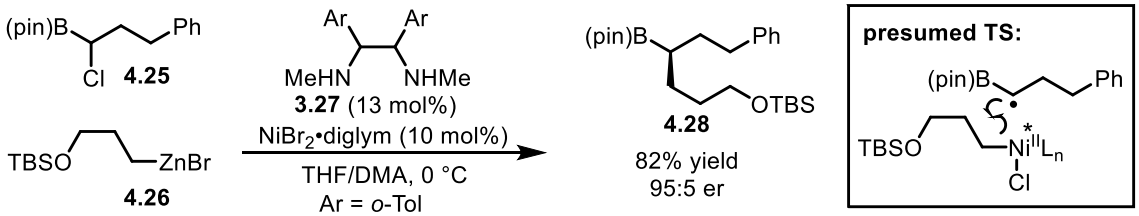


yet to be conducted. A common feature of all of the reactions reported thus far is the need to have a directing group present within the electrophile. While a large number of functional groups have been demonstrated to act as effective directing groups for stereoconvergent couplings,[14] (Scheme 4.4.B) the high degree of substrate specificity observed has hampered the general use of this method in organic synthesis. In 2016, Fu demonstrated that a simple pinacol boronic ester could act as a directing group in the enantioconvergent coupling of α-halo boronic pinacol esters with alkylzinc nucleophiles

[12] See reference 2.
[13] Gutierrez, O.; Tellis, J. C.; Primer, D. N.; Molander, G. A.; Kozlowski, M. C. *J. Am. Chem. Soc.* **2015**, 137, 4896.
[14] See reference 2.

(Scheme 4.5).[15] The ability of a pinacol ester to act as a directing group in this class of reaction is consistent with previous reports, detailed below, investigating the ability of boron moieties to stabilize radicals and to act as carbonyl isosteres. This method represent a very general synthesis route to access enantioenriched alkylboronic esters. Importantly,

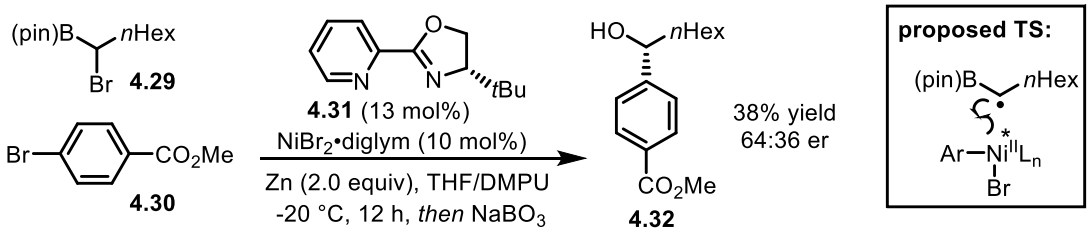
Scheme 4.5. Fu's use of boronic pinacol ester as a directing group in stereoconvergent coupling reactions



this report also established the functional group compatibility of alkyzinc nucleophiles with boronic esters.

Related to Fu's report, Martin recently disclosed an efficient reductive coupling of aryl bromide electrophiles with α-bromo boronic esters (Scheme 4.6).[16] The authors demonstrated that, while somewhat less efficient, a modest degree of enantiocontrol could be exerted through the use of chiral pyOx ligand **4.31**. The same group recently disclosed a bipryridine–Ni-catalyzed reductive coupling of α-chloro boronic esters with unactivated

Scheme 4.6. Martin's example of asymmetric umpolung reductive arylation of bromoalkyl boronic esters



[15] Schmidt, J.; Choi, J.; Liu, A. T.; Slusarczyk, M.; Fu, G. C. *Science* **2016**, 354, 1265.
[16] Sun, S.-Z.; Martin, R. *Angew. Chem. Int. Ed*. **2018**, 57, 3622.

olefins.[17] These reports further established the utility of boronic esters as a directing/radical stabilizing group in coupling reactions involving α-boryl radical intermediates.

4.2.2 Dicarbofunctionalization Reactions Involving Radial Addition

In contrast to cross-coupling reactions, catalytic intermolecular alkene difunctionalization reactions offer the potential to construct multiple bonds in one step. Dicarbofunctionalization reactions in particular have attracted significant interest[18] as a potential strategy to assemble complex carbon frameworks, though few enantioselective variations have been reported.[19] While the vast majority of reports have employed a carbometallation/cross-coupling strategy,[20] primarily focusing on the construction of $C(sp^2)$–$C(sp^3)$ bonds, the use of a radical addition/cross-coupling approach has been demonstrated as an effective strategy facilitating the formation of $C(sp^3)$–$C(sp^3)$ bonds.[21]

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[17] Sun, S.-Z.; Börjesson, M.; Martin-Montero, R; Martin, R. *J. Am. Chem. Soc*. **2018**, 140, 12765.

[18] For recent reviews, see: (a) R. K. Dhungana, S. KC, P. Basnet, P. R. Giri, *Chem. Rec.* **2018**, 18, 1314 (b) J.-S. Zhang, L. Liu, T. Chen, L.-B. Han, *Chem. Asian J.* **2018**, 13, 227. (c) K. H. Jensen, M. S. Sigman, *Org. Biomol. Chem.,* **2008**, 6, 4083.

[19]For enantioselective intermolecular dicarbofunctionalization by carbometallation cross coupling, see (a) Stokes, B. J.; Liao, L.; de Andrade, A. M.; Wang, Q.; Sigman, M. S. *Org. Lett.* **2014**, 16, 4666. (b) Wu, X.; Lin, H.-C.; Li, M.-L.; Li, L.-L.; Han, Z.-Y.; Gong, L.-Z. *J. Am. Chem. Soc.* **2015**, 137, 13476. (c) Anthony, D.; Lin, Q.; Baudet, J.; Diao, T. *Angew. Chem. Int. Ed*. **2019**, 58, 3198.

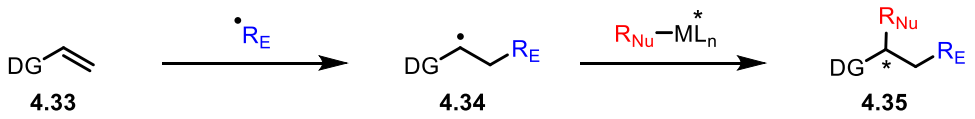
[20] For selected examples of intermolecular olefin dicarbofunctionalization by carbometallation/cross-coupling, see: (a) Derosa, J.; van der Puyl, V. A.; Tran, V. T.; Liu, M.; Engle, K. M. *Chem. Sci*. **2018**, 9, 5278. (b) Derosa, J.; Tran, V. T.; Boulous, M. N.; Chen, J. S.; Engle, K. M. *J. Am. Chem. Soc.* **2017**, 139, 10657. (c) Shrestha, B.; Basnet, P.; Dhungana, R. K.; KC, S.; Thapa, S.; Sears, J. M.; Giri, R. *J. Am. Chem. Soc.* **2017**, 139, 10653. (d) Derosa, J.; Kleinmans, R.; Tran, V. T.; Karunananda, M. K.; Wisniewski, S. R.; Eastgate, M. D.; Engle, K. M. *J. Am. Chem. Soc.* **2018**, 140, 17878. (e) Basnet, P.; KC, S.; Dhungana, R. K.; Shrestha, B.; Boyle, T. J.; Giri, R. *J. Am. Chem. Soc.* **2018**, 140, 15586. (f) Thapa, S.; Dhungana, R. K.; Thapa-Magar, R.; Shrestha, B.; KC, S.; Giri, R. *Chem. Sci.* **2018**, 9, 904. (g) Li, W.; Boon, J. K.; Zhao, Y. *Chem. Sci.* **2018**, 9, 600. (h) Gao, P.; Chen, L.-A.; Brown. M. K. *J. Am. Chem. Soc.* **2018**, 140, 10653.

[21] For selected examples of intermolecular dicarbofunctionalization by radical cascade/cross-coupling, see: (a) Guo, L.; Tu, H.; Zhu, S.; Chu, L. *Org. Lett.* **2019**, 21, 4771. (b) Klauck, F. J. R.; Yoon, H.; James, M. J.; Lautens, M.; Glorius, F. *ACS Catal.* **2019**, 9, 236. (c) KC, S.; Dhungana, R.; Shrestha, B.; Thapa, S.; Khanal, N.; Basnet, P.; Lebrun, R.; Giri, R. *J. Am. Chem. Soc.* **2018**, 140, 9801. (d) García-Domínguez, A..; Li, Z.; Nevado, C. *J. Am. Chem. Soc.* **2017**, 139, 6835. (e) Qin, T.; Cornella, J.; Li, C.; Malins, L. R.;

Enantioselective radical addition/cross-coupling reactions offer an approach to the generation of prochiral radical intermediates which is complementary to enantioconvergent cross-couplings (Scheme 4.7). While this type of multicomponent reaction offers the potential to rapidly construct complex molecular scaffolds in a modular manner, potentially allowing the formation of multiple contiguous stereocenters, it also involves significant

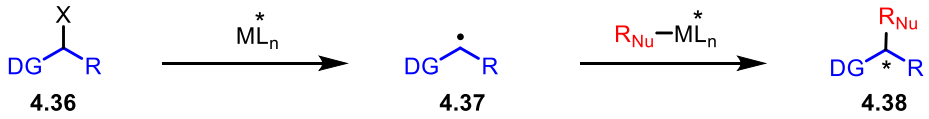
Scheme 4.7. Comparision of stereoselective radical addition/coupling vs. stereoconvergent cross-coupling

A) stereoselective radical addition/cross-coupling



4.33 **4.34** **4.35**

B) stereoconvergent cross-coupling

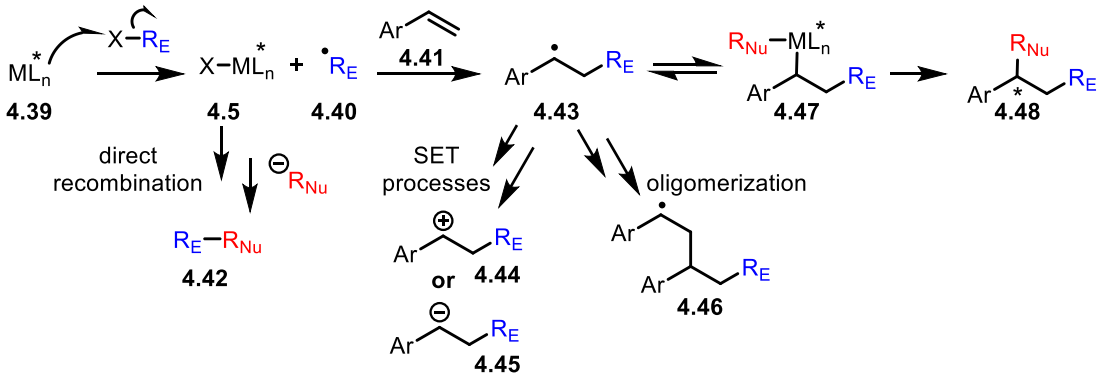


4.36 **4.37** **4.38**

additional mechanistic complications compared to cross-coupling reactions. As depicted in Scheme 4.8, in addition to the challenges faced by cross-coupling reactions such as radical generation (**4.39** to **4.40**) and enantioselective radical-catalyst recombination/ reductive elimination (**4.40** to **4.42**), radical addition/cross-coupling reactions require the orchestration of distinct radical addition (to alkene acceptor) and radical-catalyst recombination steps for two different radical species (**4.40** and **4.43**). Additionally a variety of side reactions must be avoided such as direct recombination with the metal center (**4.40** to **4.42**), single electron transfer pathways (**4.43** to **4.44**/**4.45**) and radical chain processes such as oligomerization or polymerization (**4.43** to **4.46**). The difficulty of controlling the

Edwards, J. T.; Kawamura, S.; Maxwell, B. D.; Eastgate, M. D.; Baran, P. S. *Science* **2016**, *352*, 801. (f) Gu, J.-W.; Min, Q.-Q.; Yu, L.-C.; Zhang, X. *Angew. Chem. Int. Ed.* **2016**, 55, 1227.

Scheme 4.8. Schematic of some potential challenges associated with radical addition/coupling reactions

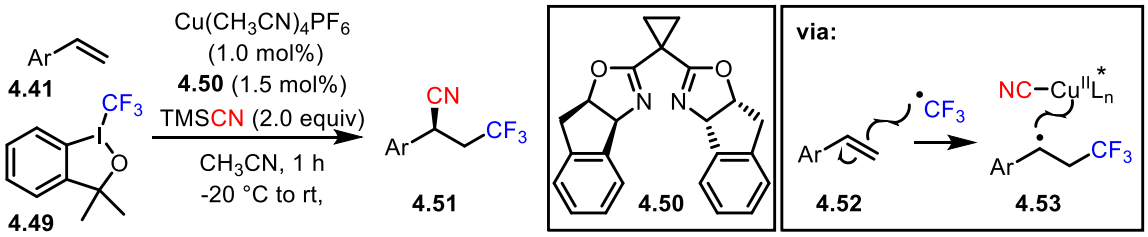


rates of a series of reactions involving reactive radical species, while suppressing multiple undesired side reactions, and attempting to exercising enantiocontrol is perhaps the reason that enantioselective dicarbofunctionalization reactions involving C(sp^3) electrophiles are rare.

Building on pioneering reports by the Buchwald group[22] on enantioselective bisoxazoline–Cu(I)-catalyzed intramolecular alkene oxytrifluoromethylation, the Liu group disclosed an enantioselective bisoxazoline–Cu(I)-catalyzed intermolecular cyanotrifluoromethylation reaction of aryl-substituted alkenes (Scheme 4.9).[23] Based on mechanistic studies, the authors proposed that the reaction is initiated by a single-electron transfer process between CF_3 reagent **4.49** and a catalytic Cu(I) species and proceeds by radical addition and recombination of the subsequently formed benzylic radical species **4.52** with a chiral Cu(II)-cynide species (**4.53)**. The same group subsequently reported a mechanistically similar catalytic enantioselective intermolecular trifluoromethyl-arylation

[22] (a) Zhu, R.; Buchwald, S. L. *Angew. Chem. Int. Ed.* **2013**, 52, 12655. (b) Zhu, R.; Buchwald, S. L. *J. Am. Chem. Soc*. **2015**, 137, 8069.
[23] Wang, F.; Wang, D.; Wan, X.; Wu, L.; Chen, p.; Liu, G. *J. Am. Chem. Soc*. **2016**, 138, 15547.

Scheme 4.9. Enantioselective diamine–Cu-catalyzed cyanotrifluoromethylation of alkenes by radical process



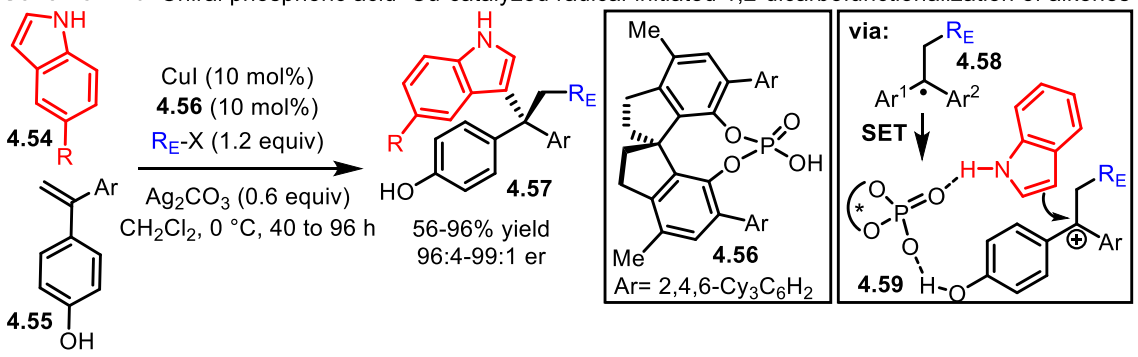
reaction of aryl-substituted alkenes[24] and has extended this reaction to engage tertiary carbon-centered radicals, thus forming fully substituted quaternary stereogenic carbon centers.[25]

Building on their own seminal report of chiral phosphoric acid–Cu(I)-catalyzed alkene intramolecular aminotrifluoromethylation,[26] the Xiu-Yuan Liu group recently demonstrated that a similar chiral phosphoric acid–Cu(I)-catalyst system is capable of promoting the alkyl arylation reaction of diaryl-substituted alkene **4.55** (Scheme 4.10).[27] Supported by a study of the mechanism and origin of enantioinduction utilizing density functional theory calculations, the authors proposed that rather than proceeding by recombination of tertiary radial **4.58** to copper followed by reductive elimination, the observed product **4.57** is formed by nucleophilic attack on a diaryl carbocation species **4.59** generated by single electron transfer from radical species **4.58**.

While copper-based catalysts have been the most well explored in the context of enantioselective radical-addition/cross-coupling reactions, the Zhang group recently reported an intriguing enantioselective 1,2-difunctionalization reaction of 1,3-butadiene

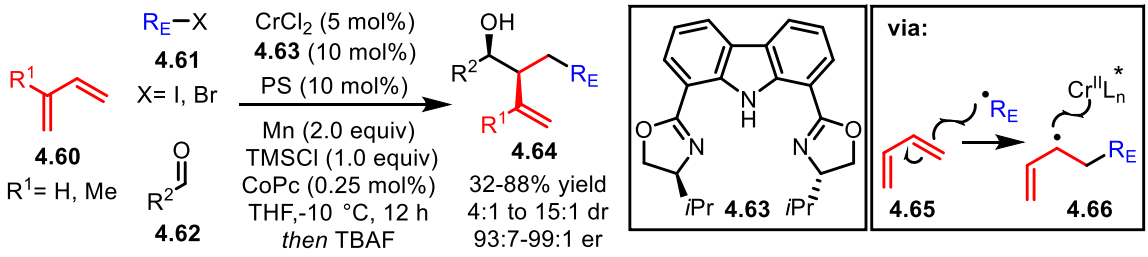
[24] Wu, L.; Wang, F.; Wan, X.; Wang, D.; Chen, P.; Liu, G. *J. Am. Chem. Soc*. **2017**, 139, 2904.
[25] Wu, L.; Wang, F.; Chen, P.; Liu, G. *J. Am. Chem. Soc*. **2019**, 141, 1887.
[26] Lin, J.-S.; Dong, X.-Y.; Li, T.-T.; Jiang, N.-C.; Tan, B.; Liu, X.-Y. *J. Am. Chem. Soc*. **2016**, 138, 9357.
[27] Lin, J.-S.; Li, T.-T.; Liu, J.-R.; Jiao, G.-Y.; Gu, Q.-S.; Cheng, J.-T.; Guo, Y.-L.; Hong, X.; Liu X.-Y. *J. Am. Chem. Soc*. **2019**, 141, 1074.

Scheme 4.10. Chiral phosphoric acid–Cu-catalyzed radical-initiated 1,2-dicarbofunctionalization of alkenes



catalyzed by chiral chromium complexes (Scheme 4.11). Taking inspiration from Takai's stoichiometric chromium-mediated three-component coupling of 1,3-diene with alkyl iodide electrophiles, and aldehydes,[28] the authors found that by employing chiral carbazole-based bisoxazoline ligand **4.63** along with Cr(II) chloride, the reaction could be rendered catalytic as well as enantio- and diastereoselective. Based primarily on literature precedent the authors proposed that sub-stoichiometric cobalt phthalocyanine initiates radical

Scheme 4.11. Enantioselective 1,2-difunctionalization of 1,3-butadiene by alkylation/carbonyl allylation



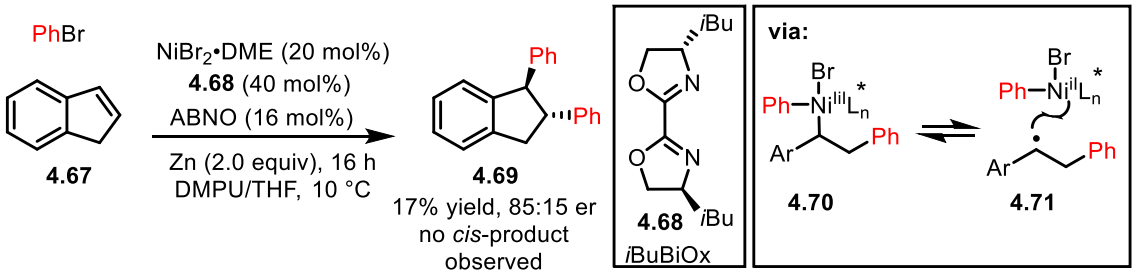
formation from electrophile **4.61**, this radical then adds to 1,3-butadiene (inset, **4.65**) to form an allylic radical (inset, **4.66)** which recombines with the a chromium complex and, after isomerization to form the terminal allylchromium species (not shown), engages in an allylation reaction to generate enantioenriched homoallylalcohol **4.64**.

While proceeding by a polar β-migratory insertion rather than a radical addition

[28] Takai, K.; Matsukawa, N.; Takahashi, A.; Fujii, T. *Angew. Chem. Int. Ed*. **1998**, 37, 152.

pathway, the Diao group has recently reported an enantioselective BiOx–Ni-catalyzed homodiarylation reaction of aryl-substituted alkenes which is proposed to involve radical intermediates (Scheme 4.12).[29] Following observations of minor bisbenzyl dimer side products consistent with radical-radical recombination, the authors conducted a probed of the relative stereochemistry of the reaction with indene **4.67** as the substrate. While the formation of the cis-diarylated product would be expected if a polar β-migratory insertion/reductive elimination mechanism was operative, only the corresponding *trans*-

Scheme 4.12. BiOx–Ni-catalyzed asymmetric reductive homodiarylation of vinyl arenes



product **4.69** was observed. Consistent with a previous computational study by Molander and Kozlowski on a related system,[30] this result was attributed by the authors to the ability of the benzylic nickel species **4.70** obtained after β-migratory insertion to reversibly form benzyl radial 4.71. While several dicarbofunctionalizations reactions capable of forming two C(sp^3)–C(sp^3) bonds have been developed,[31] to the best of our knowledge, no enantioselective variants have been reported to date.

[29] See reference 19c.
[30] See reference 13.
[31] For a recent review, see: (a) Dhungana, R. K.; KC, S.; Basnet, P.; Giri, R. *Chem. Rec*. **2018**, 18, 1314. (b) References cited above.

4.2.3 α-Boryl Radical Intermediates in Organic Synthesis

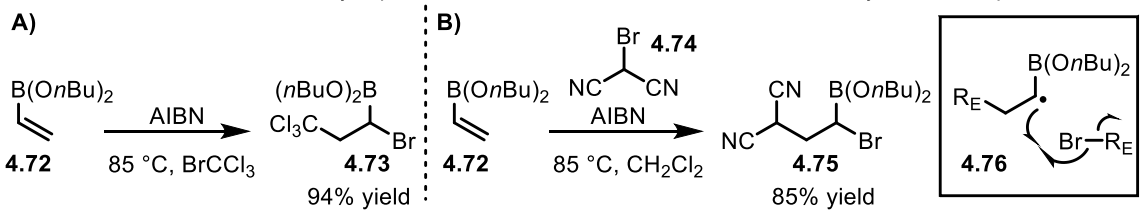
As illustrated by the examples discussed above, the vast majority of dicarbofunctionalization reactions, and indeed alkene difunctinoalization reactions in general, utilize aryl-substituted alkene substrates capable of stabilizing radical and organometallic intermediates (the difunctionalization of 1,3-butadiene being a notable exception). While aryl groups are ubiquitous in natural products, pharmaceuticals, and agrochemicals, the use of a synthetically diversifiable functional handle in place of an aryl group might expand the diversity of products that can be obtained utilizing this approach.

While the use of boranes and boronic esters as radical stabilizing group has not been heavily employed in the development of synthesis methods, ample evidence exists that α-boryl radicals can participate in a variety of radical processes.

Pioneering work by Matteson developing synthesis routes to α-halo boronic esters established that vinylboronic esters can participate in atom transfer radical addition (ATRA) reactions with bromotrichloromethane and tetrachloromethane electrophiles using azobisisobutyronitrile (AIBN) as a chemical initiator (Scheme 4.13.A).[32] The relatively small radical transfer constant ($3x10^{-3}$) that was experimentally observed for the reaction of alkenylboron reagent **4.72** and carbon tetrachloride was proposed by the authors to provide evidence that the intermediate radical species (inset, **4.76**), generated upon radical addition, is stabilized by carbon-boron π-bonding. Due to the ability of α-boryl radical **4.76** to undergo oligomerization reactions, solvent quantities of electrophile were employed to ensure the formation of **4.73**. A subsequent report by the same authors extended this

[32] Matteson, D. S. *J. Am. Chem. Soc*. **1960**, 82, 4228.

Scheme 4.13. Matteson's early reports of atom transfer radical addition of alkenylboron compounds



reaction to employ bromomalononitrile as an electrophile (Scheme 4.13.B).[33]

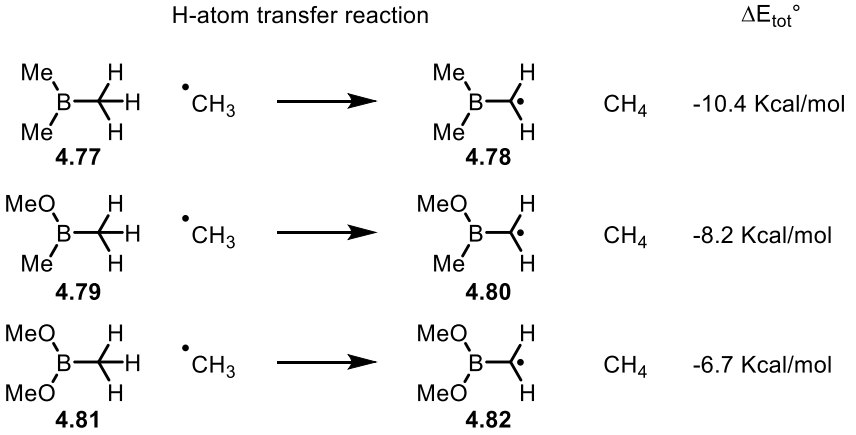
The boron atom of vinylboranes is known to participate in strong π-bonding due to the ability of the boron p orbital to accept electron density from an adjacent π-system.[34] The same effect enables boron to stabilize an unpaired electron on an adjacent atom. Studies of the hydrogen atom abstraction reactions of bromine radicals with triethyl borane indicate a radical stabilization energy of 14.5 kcal/mol relative to a secondary propyl radical.[35] Competition experiments indicated that H-abstraction by bromine radicals from triethyl borane is at least 5 times faster than for toluene. Theoretical studies on the $H_2BCH_2^{\bullet}$ radical utilizing UHF/6-31G[36] and MP4SDTQ/6-31G*[37] level of theory indicate a stabilization energy of 11 kcal/mol and 9.7 kcal/mole respectively.

Utilizing low temperature EPR spectroscopy, the Walton group established that the barriers to internal rotation for several α-boryl radical species (generated by bromine abstraction from α-bromo boronic esters, radical addition to vinylboronic esters, and hydrogen abstraction from alkyboronic esters), is 3 ± 1 kcal/mol.[38] Computational calculations conducted by the same group on the hydrogen transfer reaction of simple

[33] Matteson, D. S.; Schaumberg, G. D. *J. Org. Chem*. **1966**, 31, 726.
[34] D. S. Matteson, *Prog. Boron. Chem*. **1970**, 3, 1176.
[35] Grotewold, J.; Lissi, E. A.; Scaiano, J. C. J. *Organomet. Chem*. **1969**, 19, 431.
[36] Pasto, D. J.; Krasnansky, R.; Zercher, C. *J. Org. Chem*. **1987**, 52, 3062.
[37] Coolidge, M. B.; Borden, W. T. *J. Am. Chem. Soc*. **1988**, 110, 2298.
[38] Walton, J.; McCarroll, A. J.; Chen, Q.; Carboni, B.; Nziengui, R. *J. Am. Chem. Soc*. **2000**, 122, 5455.

methyl-substituted boron compounds with methyl radial (Scheme 4.14) indicate that increasing the number of oxygen substituents on boron decreases the radical stabilization energy. This is consisted with increasing oxygen lone pair donation into the boron p orbital thereby decreasing the ability of this orbital to stabilize the adjacent radical.

Scheme 4.14. Computaionally calculated energies of H-transfer for model -boryl radical species



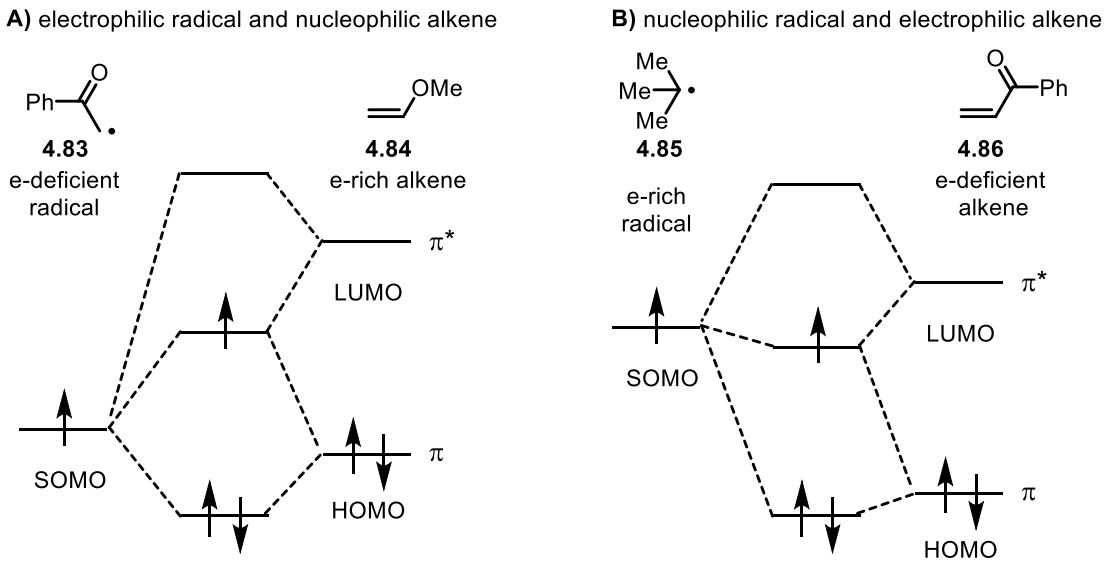
The rates and chemoselectivites of radical addition reactions to alkenes is often strongly influenced by polar effects in the substrate and as such the proper choice of radical and alkene is essential to ensure an efficient reaction.[39] This general phenomenon is explained by frontier molecular orbital interaction between the radical SOMO and the LUMO or HOMO of the alkene reagent (Scheme 4.15).[40] Maximum orbital interactions and thus transition state stabilization occurs when either (1) SOMO-HOMO interaction is maximized: an electron-deficient radical species with adjacent electron withdrawing/

[39] (a) Citterio, A.; Minisci, F.; Porta, O.; Sesana, G. *J. Am. Chem. Soc*. **1977**, 99, 7960. (b) Giese, B.; Meixner, J. *Angew. Chem. Int. Ed.* **1979**, 18, 154. (c) Pryor, W. A.; Lin, T. A.; Stanley, J. P.; Henderson, R. W. *J. Am. Chem. Soc.* **1973**, 95, 6993. (d) Tedder, J. M. *Angew. Chem. Int. Ed*. **1982**, 18, 401.
[40] For reviews, see: (a) Fleming, I.; Frontier Orbitals and Organic Chemical Reactions, Wiley, New York **1976**. (b) Giese; B. *Angew. Chem., Int. Ed*. **1983**, 22, 771. For a theoretical treatment, see: Houk, K. N.; Paddon-Row, M. N.; Spellmeyer, D. C.; Rondan, N. G.; Nagase, S. *J. Org. Chem*. **1986**, 51, 2874.

resonance stabilizing groups interacts with an electron-rich alkene (Scheme 4.15.A) or (2) when SOMO-LUMO interaction is maximized: an electron-rich radical interacts with an electron-deficient alkene (Scheme 4.15.B).

Because the empty boron p orbital can accept electron density from an adjacent π-system alkenylboron reagents are electron-deficient alkenes which are polarity-matched with nucleophilic radicals. This polarity matching effect has been experimentally observed for radical addition reactions to alkenylboronic esters. As depicted in Scheme 4.16, the

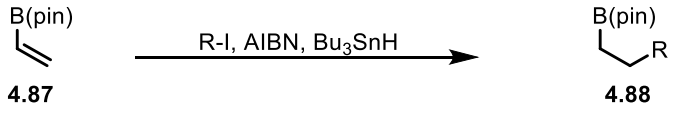
Scheme 4.15. Qualitative diagram of frontier molecular orbital interactions of radical additions to alkenes



Carboni group observed that while *tert*-butyl radicals, generated from *tert*-butyl iodide and AIBN/Bu_3SnH, reacted smoothly with vinylboronic pinacol ester (74% yield), cyclohexyl radicals reacted poorly (15% yield), while *n*-butyl radicals were not observed to form any desired product.[41] This result is consistent with the decreasing nucleophilicity of less substituted alkyl radicals (tertiary > secondary > primary). As depicted in Scheme 4.17,

[41] Guennouni, N.; Lhermitte, F.; Cochard, S.; Carboni, B. *Tetrahedron* 51, **1995**, 6999.

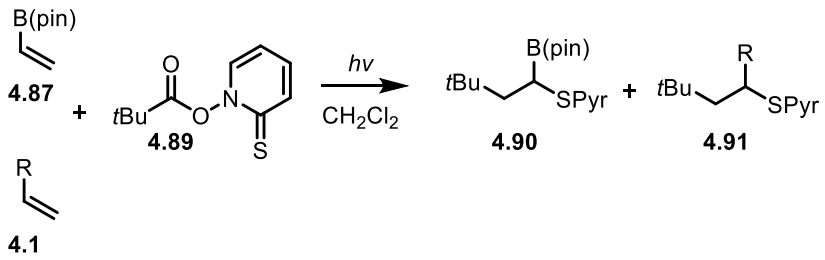
Scheme 4.16. Impact of alkyl radical substitution on radical additions to vinylboronic pinacol ester



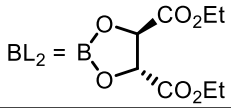
R	yield (%)
*t*Bu	75
Cy	15
*n*Bu	0

competition experiments conducted in the same report between vinylboronic pinacol ester and various alkenes **4.1** with *O*-acyl thione **4.89** resulted in mixtures of atom transfer radical addition products **4.90** and **4.91**, the ratio of which depended on the electronic nature of the alkene substituted R. The authors reported that vinylboronic pinacol ester reacted much more efficiently than styrene (entry 1) but that when R substituents

Scheme 4.17. Comparision of pinacol boronic ester to other electron withdrawing groups in radical additions



entry	R	yield (%): **4.90**/**4.91**
1	Ph	100/0
2	BL_2	28/72
3	CO_2NMe_2	20/80
4	CO_2Me	4/96



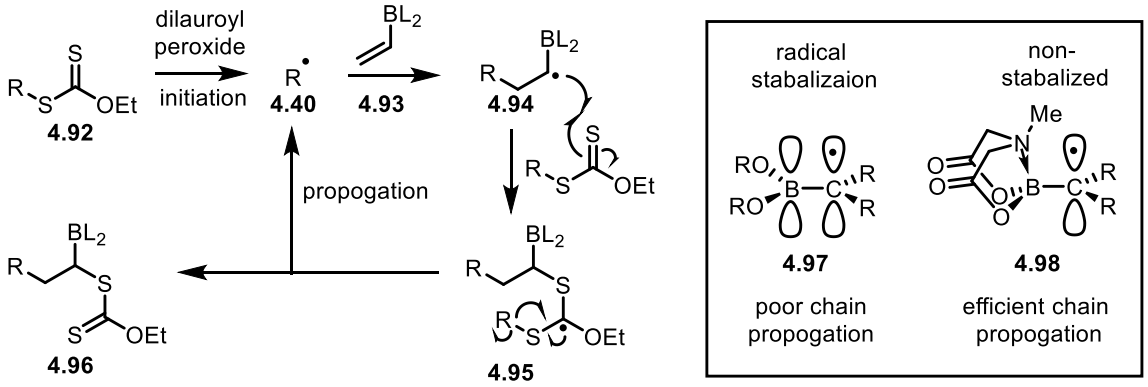
more electron withdrawing than B(pin) were employed the product ratio was inverted (entries 2-4). Related reactions involving heteroatom-centered radical addition to alkynylboron compounds to generate alkenyl α-boryl radical intermediates have been reported by Carboni.[42]

It is worth noting that because atom transfer radical addition reactions of alkenes are radical chain processes that involve both radical addition and propagation steps, reactions

[42] Lhermitte, F.; Carboni, B. *Synlett* **1996**, 4, 377.

involving an efficient radical addition but in which a subsequent propagation step, such as atom abstraction, is inefficient will overall be inefficient reactions.[43] An excellent example of this phenomena in the context of the atom transfer radical addition reaction of alkenylboron reagents was recently reported by the Zard group (Scheme 4.18).[44] In two previous reports the authors found that the atom transfer radical addition reaction of xanthates **4.92** and alkenylboronic pinacol ester reagents was inefficient relative to the analogous reaction with allylboronic pinacol ester.[45] The authors attributed the poor overall reactivity to slow radical chain propagation from α-boryl radical **4.94** to radical **4.40** *via* **4.95**. The authors hypothesized that by utilizing vinylboronic MIDA esters instead of

Scheme 4.18. Zard's appraoch to enhance α-boryl radical propogation by radical destabaliztion



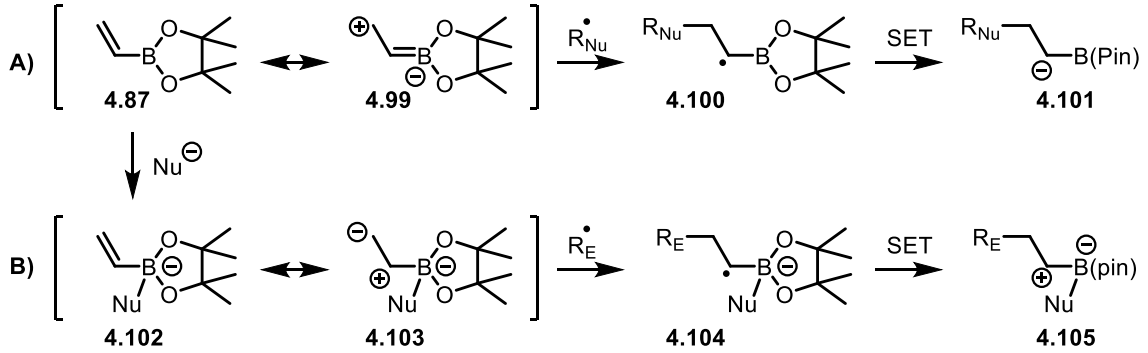
vinylboronic pinacol esters α-boryl radical species might be destabilized, thus promoting efficient chain propagation (inset, **4.97** and **4.98**). The proposed strategy proved to be effective, facilitating the preparation of a diverse scope of alkylboronic MIDA esters.

A final point that must be made in any discussion of boron's ability to mediate radical

[43] Studer, A.; Curran, D. P. *Angew. Chem. Int. Ed*. **2016**, 55, 58.
[44] Quiclet-Sire, B.; Zard, S. Z. *J. Am. Chem. Soc*. **2015**, 137, 6762.
[45] (a) Lopez-Ruiz, H.; Zard, S. Z. *Chem. Commun*. **2001**, 2618. (b) Heinrich, M. R.; Sharp, L.; Zard, S. Z. *Chem. Commun*. **2005**, 3077.

reactions is that unlike other functional groups such as nitriles or amines (electron withdrawing and donating respectively) the boronic ester moiety is capable of switching from being an electron-withdrawing to an electron donating group depending on the hybridization of boron. Thus, boronic esters can be used to modulate the polarity and thus reactivity of alkenes and radicals using the addition of nucleophile as a switch (Scheme 4.19). As briefly discussed in chapter one of this dissertation in the context of radical-polar crossover reactions, α-boryl alkyl radical ate complexes **4.104** are proposed to readily

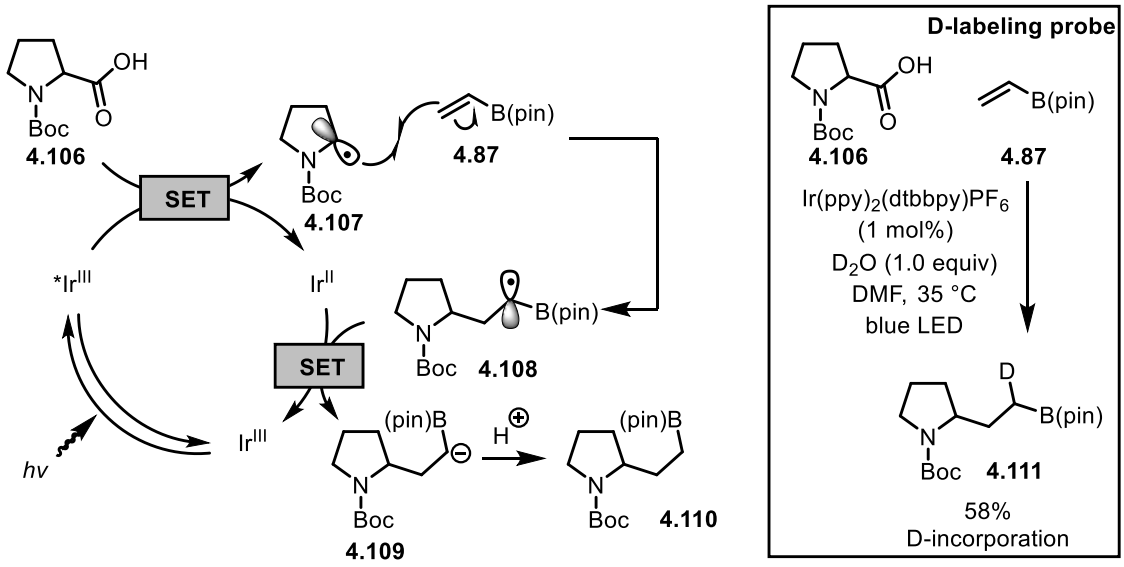
Scheme 4.19. Nucleophile-induced alkene polarization change and controle of single-electron transfer



undergo single-electron transfer to the corresponding cationic species **4.105**. Conversely, one might imagine that an alpha-boryl radical species **4.100** possessing an sp^2-hybridized boronic ester might undergo single-electron transfer to form the corresponding α-boryl anion **4.101**. In a report detailing the visible-light-mediated decarboxylative radical addition reaction of vinylboronic pinacol ester, Agarwall proposed that α-boryl anions are formed during the course of the reaction (Scheme 4.20).[46] The authors conducted a deuterium-labeling experiment (inset, **4.106** to **4.111**) which provides some experimental evidence in support of this mechanistic proposal.

[46] Noble, A.; Mega, R. S.; Pflästerer, D.; Myers, E. L.; Aggarwal, V. K. *Angew. Chem. Int. Ed.*, **2018**, 2155.

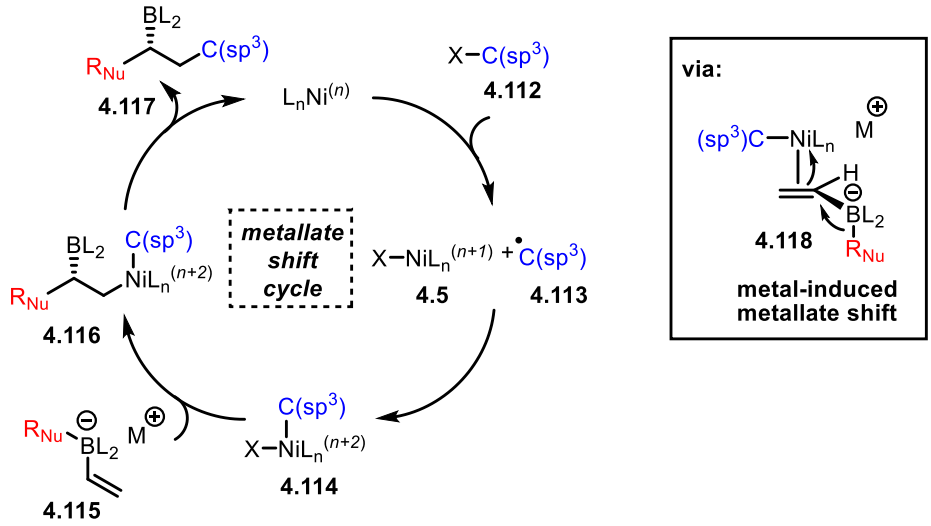
Scheme 4.20. Aggarwal's visible light mediated decarboxylative radical addition to alkenylboronic esters



4.3 Proposal for PyBox–Ni-Catalyzed Enantioselective Conjunctive Coupling with C(sp^3) Electrophiles[47]

As a starting point for reaction development we hypothesized that the conjunctive

Scheme 4.21. Prospective mechanisms for conjunctive coupling of C(sp^3) electrophiles with Ni complexes



[47] Lovinger, G. J.; Morken, J. P. *J. Am. Chem. Soc.* **2017**, 139, 17293.

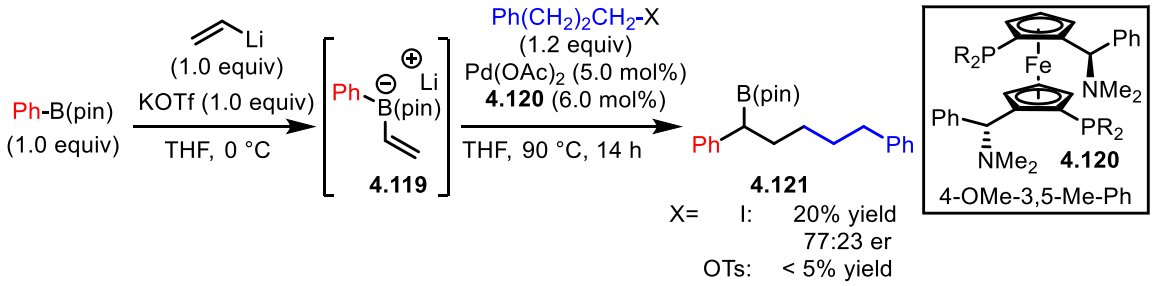
coupling of alkyl electrophiles might proceed by a similar mechanism to the previously discussed conjunctive coupling reactions of C(sp^2) electrophiles, only differing in that oxidative addition would likely proceed by way of a radical pathway (Scheme 4.21).

4.4 Reaction Development

4.4.1 Initial Experiments with a Palladium-Based Catalyst System

We began our investigation by assessing the capacity of the previously developed palladium-based catalyst system to promote conjunctive coupling of primary alkyl halides. Initial reactions of phenylboronic ester-derived boron-ate complex **4.119** and 1-iodo-3-phenylpropane with $Pd(OAc)_2$ and Mandypohs ligand **4.120** (Scheme 4.22) were unsuccessful. We found that by increasing the temperature employed in the reaction from 60 to 90 °C and by adding an equivalent of KOTf as a halide scavenging agent the desired

Scheme 4.22. Initial test reactions utilizing palladium-based catalyst system

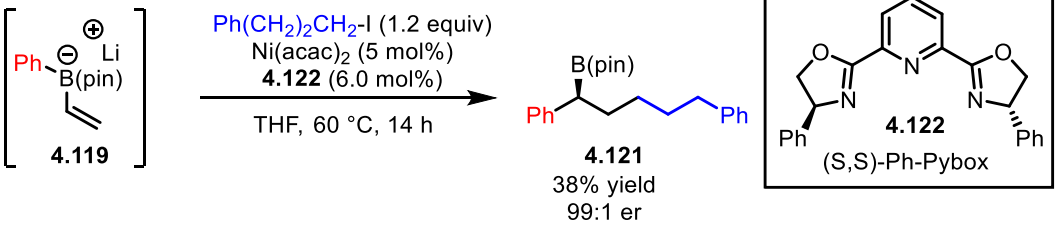


product **4.121** was isolated in 20% yield, though with poor enantioenrichment. Attempts to employ alkyl triflate or tosylate electrophiles so as to prevent possible halide inhibition of catalysis were unsuccessful. We observed alkyl tosylates to be unreactive while alkyl triflates facilitated the decomposition of vinylboron-ate complex **4.119** by alkylation of a pinacol oxygen.

4.4.2 Initial Experiments with a Nickel-Based Catalyst System

With the initial encouraging result that conjunctive coupling product **4.121** could be formed with a palladium-based catalyst utilizing an alkyl electrophile, albeit in low yield and enantioenrichment, we next investigated nickel-based catalysts (Scheme 4.23). Subjecting boron-ate complex **4.119** to 1-iodo-3-phenylpropane and a catalyst solution

Scheme 4.23. Initial test reaction utilizing nickel-based catalyst system



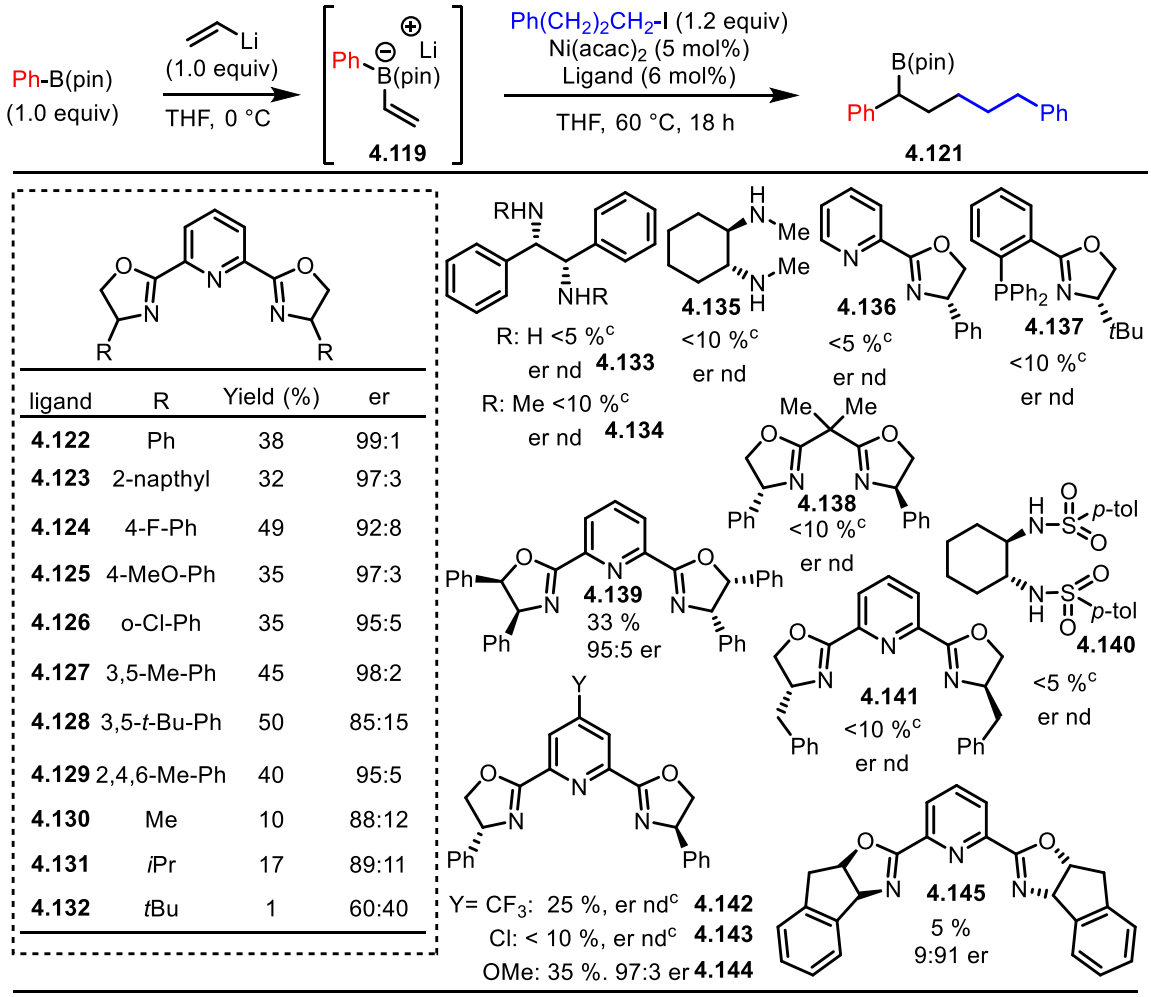
consisting of $Ni(acac)_2$ and Phenyl Pybox ligand **4.122** we observed that the desired conjunctive coupling product was formed in an encouraging 38% yield and 99:1 er. This result suggested to us that reaction development utilizing a nickel-based catalyst was a productive line of investigation.

4.4.3 Ligand Investigation with a Nickel-Based Catatlyst System

Employing the previously described reaction conditions, we investigated a variety chiral ligand structures (Scheme 4.24). We found that diamines **4.134**,[48] the optimal ligand for diamine–Ni-catalyzed conjunctive coupling of aryl iodide electrophiles, was ineffective in the current reaction employing alkyl electrophiles. Other diamine ligands (**4.133**, **4.135**,

[48] For selected enantioselective Ni-catalyzed cross-coupling with Ni/diamine catalysts, see: (a) Wilsily, A.; Tramutola, F.; Owston, N. A.; Fu, G. C. *J. Am. Chem. Soc*. **2012**, 134, 5794. (b) Lu, Z.; Wilsily, A.; Fu, G. C. *J. Am. Chem. Soc*. **2011**, 133, 8154. (c) Saito, B.; Fu, G. C. *J. Am. Chem. Soc*. **2007**, 129, 9602.

Scheme 4.24. Effect of ligand structures[a]



ligand	R	Yield (%)	er
4.122	Ph	38	99:1
4.123	2-napthyl	32	97:3
4.124	4-F-Ph	49	92:8
4.125	4-MeO-Ph	35	97:3
4.126	o-Cl-Ph	35	95:5
4.127	3,5-Me-Ph	45	98:2
4.128	3,5-*t*-Bu-Ph	50	85:15
4.129	2,4,6-Me-Ph	40	95:5
4.130	Me	10	88:12
4.131	*i*Pr	17	89:11
4.132	*t*Bu	1	60:40

[a] Yields represent isolated yields of purified material. [b]Determined by chiral SFC analysis. [c]Determined by ^{1}H NMR versus an internal standard.

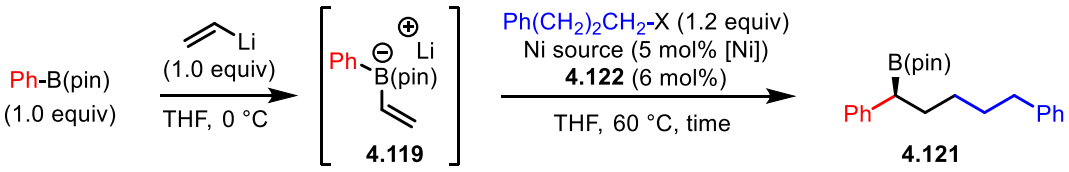
4.140) proved to be equally ineffective at promoting the desired reaction. A survey of other bidentate ligands indicated that bis(oxazoline) **4.136**, phosphine-oxazoline **4.137**, and pyridyl-oxazoline **4.136** are ineffective ligand scaffolds. Examining tridentate Pybox ligands more closely, we found that both the yield and enantioselectivity of these reactions was strongly dependent on the nature of the substituents on the oxazoline ring, with alky-substituted ligands (Me: **4.130**, *i*Pr: **4.131**, *t*Bu: **4.132**, Benzyl: **4.141**) performing poorly. In contrast, the use of aryl-substituted Pybox ligands generally resulted in more favorable

yields and enantioselectivities. We then investigated if the electronic nature of the aryl substituent substantially effects the course of the reaction. Relative to phenyl Pybox **4.122** we found that a more electron-rich 4-methoxy phenyl substituent (**4.125**) did not improve the yield or enantioselectivity of the reaction. Interestingly, the use of a 4-fluoro phenyl substituent Pybox ligand (**4.124**) appeared to improve the yield of the reaction but resulted in a substantial decrease in enantioselectivity. We found that ligands with *ortho*-substituted aromatic rings did not perform better than phenyl-Pybox (**4.126** and **4.129**). In contrast, 3,5-dimethyl phenyl Pybox (**4.127**) and 3,5-*tert*-butyl phenyl-Pybox (**4.128**) ligands both led to increased yields of the desired produced (45% and 50% yield respectively versus 38% for Ph-Pybox) thought the more sterically-hindered ligand resulted in a substantial decreased in enantioselectivity.

4.4.4 Optimization of Conditions

It is worth noting that subsequent to the experiments mentioned above, a survey of sources of $Ni(acac)_2$ revealed that employing $Ni(acac)_2$ from Sigma Aldrich, Strem, or Acros rather than Combi-Blocks resulted in a slightly improved yield of product **4.121** (49% vs. 38% yield) which we attributed to reagent quality. Thus, employing Ph-Pybox ligand **4.122**, various reaction parameters were investigated. First, the impact of the electrophile counterion and the nickel salt employed were assessed (Table 4.1). In contrast to 1-iodo-3-phenylpropane (entry 1), the corresponding bromide (entry 2), chloride (entry 3), and tosylate (entry 4) electrophiles proved to be ineffective coupling partners. The use of nickel pre-catalysts other than $Ni(acac)_2$ generally resulted in inferior yields of product

Table 4.1. Effect of electrophile anion, nickel source, and catalyst preperation[a]



entry	X	Ni source	time (h)	Yield (%)[a]	er[b]
1	I	$Ni(acac)_2$	18	49	98:2
2	Br	$Ni(acac)_2$	18	23	98:2
3	Cl	$Ni(acac)_2$	18	<5[c]	nd
4	OTs	$Ni(acac)_2$	18	0[c]	na
5	I	$NiCl_2$	18	0[c]	na
6	I	$Ni(OTf)_2$	18	0[c]	na
7	I	$NiBr_2$•glym	18	<5[c]	nd
8	I	$NiCl_2$•glym	18	35	99:1
9	I	$[MethallylNiC]_2$	18	51	98:2
10[d]	I	$[MethallylNiC]_2$	15	55	99:1
11[d,e]	I	$[MethallylNiC]_2$	15	70	99:1
12[f]	I	$Ni(acac)_2$	15	<10[c]	na

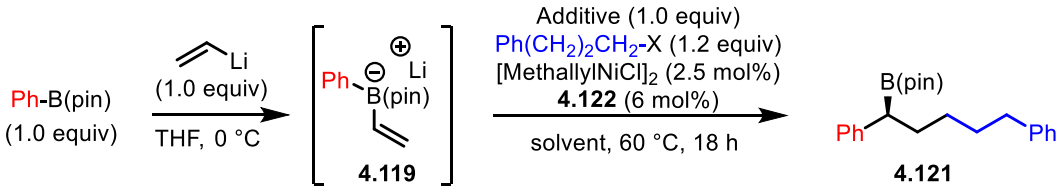
[a] Yields represent isolated yields of purified material. [b]Determined by SFC analysis. [c]Determined by ^1H NMR versus an internal standard. [d]1.5 h catalyst complexation time instead of 0.5 h. [e](R,R)-3,5-Me-Ph-Pybox used instead of (S,S)-Ph-Pybox. [f]no ligand added to reaction.

(entries 5-8). Methallyl nickel chloride dimer proved to be a superior pre-catalyst in terms of yield and reaction reproducibility (entry 9). We found that allowing the ligand and nickel pre-catalyst to complex for 1.5 h rather than 30 min resulted in a slight increase in the yield of the reaction. Utilizing these conditions and employing ligand **4.127** in place of Ph-Pybox **4.122** resulted in a yield of 70% with 99:1 er (entry 11). A control experiment employing $Ni(acac)_2$ alone (entry 12) confirmed the essential role of the triamine ligand in promoting the formation of the desired product.

We found the addition of polar cosolvents such as acetonitrile, dimethylformamide, and

trifluorotoluene resulted in diminished yields relative to pure tetrahydrofuran (entries 1-4) (Table 4.2). Assessing the effect of several additives, we found that the reaction appeared to be inhibited by the introduction of chloride anions (entries 5 and 6). In contrast, LiOH, a common impurity in organolithium reagents arising from contamination with moister, inhibited the reaction to a lesser degree (entry 7). The addition of NaI to a reaction

Table 4.2. Effect of additives and solvent[a]



entry	X	additive	solvent	yield (%)[a]	er[b]
1	I	none	THF	49	98:2
2	I	none	THF:ACN 1:1	26	99:1
3	I	none	THF:DMA 1:1	25	nd
4	I	none	THF:$PHCF_3$	<10[c]	nd
5	I	LiCl	THF	<10[c]	nd
6	I	$(n\text{Bu})_4\text{Cl}$	THF	<10[c]	nd
7	I	LiOH	THF	37	99:1
8	Br	none	THF	23	98:2
9	Br	NaI	THF	47	99:1
10	Cl	NaI	THF	0[c]	na

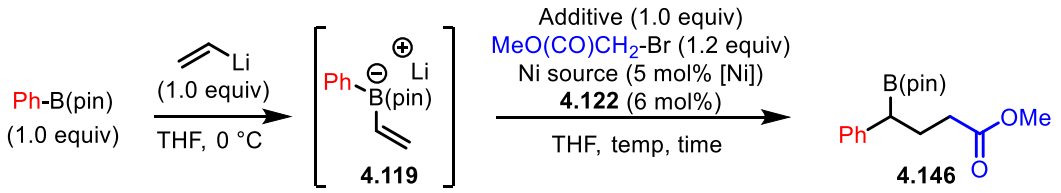
[a] Yields represent isolated yields of purified material. [b]Determined by SFC analysis.
[c]Determined by ^{1}H NMR versus an internal standard.

employing 1-bromo-3-phenylpropane (entry 9) resulted in a reaction that was nearly as effective as that employing the corresponding alkyl iodide electrophile (entry 1).

In contrast to the highly enantioselective reaction observed when 1-iodo-3-phenylpropane was employed as an electrophile, as seen in Table 4.3, when α-

bromomethyl acetate was employed, the reaction furnished racemic product (entries 1). Unlike reactions employing alkyl halide electrophiles without adjacent electon withdrawing groups, reactions employing α-bromomethyl acetate were efficient in the absence of ligand and, with addition of NaI, furnished racemic product **4.146** in outstanding yield (entries 2 and 3). The reaction was found to be relatively insensitive to reaction temperature (entries 2, 3, 4). The reaction also produced an appreciable, though substantially diminished yield of the desired product when conducted without $Ni(acac)_2$

Table 4.3. Effect of additives and solvent[a]



entry	Ni source	additive	temp (°C)	yield (%)[a]	er[b]
1[c]	$Ni(acac)_2$	none	60	34	50:50
2[d]	$Ni(acac)_2$	NaI	rt	92	50:50
3	$Ni(acac)_2$	NaI	rt	84	50:50
4	$Ni(acac)_2$	NaI	0	51	50:50
5	none	NaI	rt	36	50:50
6[e]	$Ni(acac)_2$	NaI	rt	91	50:50
7[e,f]	$Ni(acac)_2$	NaI	rt	92	50:50

[a] Yields represent isolated yields of purified material. [b]Determined by SFC analysis. [c](R,R)-3,5-Me-Ph-Pybox used instead of (S,S)-Ph-Pybox. [d]Reaction conducted without ligand. [e]3 mole% $Ni(acac)_2$ employed. [f]Reaction conducted in the dark.

(entry 5). Finally, the reaction was found to be effective when conducted with 3 mol% $Ni(acac)_2$ (entry 6). Also of note, rigorous exclusion of light was not found to inhibit the reaction (entry 7).

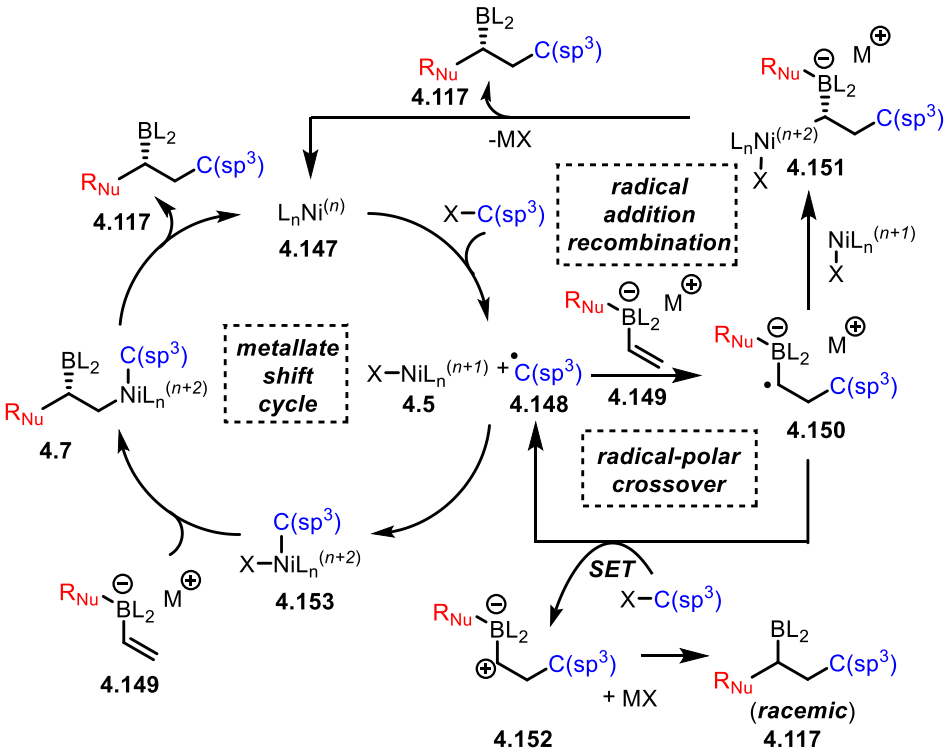
The marked difference in reactivity and selectivity when using 1-iodo-3-phenylpropane

versus α-bromomethyl acetate suggested that the operative mechanisms for these reactions are likely different. In particular, the noted insensitivity of the reaction with α-bromomethyl acetate to temperature, and its ability to proceed in the absence of nickel and ligand, suggested that radical processes were likely operative. The fact that the reaction was much more efficient with the addition of $Ni(acac)_2$ and could be conducted in the dark suggested that $Ni(acac)_2$ might be serving as an initiator. In light of reports by Studer[49] and Aggarwal[50] on radical-polar crossover reactions that were published during the course of the mechanistic studies detailed in the following section of this dissertation, we suspected that radical processes might intervene in the triamine–Ni-catalyzed conjunctive coupling reactions of particular substrates. We considered three mechanistic scenarios as plausible reaction pathways (Scheme 4.25), with all involving initial halogen atom abstraction[51] to convert the $C(sp^3)$ halide to a carbon-centered radical **4.149** and nickel complex **4.5**. In one direction, following the precedent of Studer and Aggarwal, reaction of the carbon-centered radical with the olefinic boron-ate complex **4.149** might deliver α-boryl radical **4.150**, which undergoes single-electron transfer with the organohalide substrate thereby regenerating the carbon-centered radical and delivering transient carbocation **4.152**; cation **4.152** would be expected to undergo 1,2-metallate shift and thus deliver racemic reaction product **4.117**. Formation of enantiomerically enriched reaction product **4.117** could occur by one of two routes. In one pathway, recombination of the initially generated carbon-centered radical **4.148** with Ni-complex **4.5** might deliver complex **4.153**, a compound that

[49] Kischkewitz, M.; Okamoto, K.; Mück-Lichtenfeld, C.; Studer, A. *Science* **2017**, 355, 936.
[50] Silvi, M.; Sandford, C.; Aggarwal, V. K. *J. Am. Chem. Soc.* **2017**, 139, 5736.
[51] Jahn, U. *Top. Curr. Chem*. **2011**, 320, 323.

could engage in an enantioselective metal-induced metallate rearrangement similar to previously described Pd and Ni complexes. Alternatively, aligned with recent observations by Fu on cross-coupling of α-halo boronic esters, α-boryl radical **4.150** might reengage Ni-complex **4.5** to furnish α-boryl alkylnickel complex **4.151**; subsequent intramolecular transmetalation and reductive elimination (or invertive reductive displacement) would furnish non-racemic product **4.117**. Following the above-described mechanistic proposals, substrates that would furnish an electrophilic radical would be more prone to react with an electron-rich vinylboron-ate complex **4.149**[52] and undergo the radical chain process described by the radical-polar crossover cycle. Substrates leading to non-stabilized radicals

Scheme 4.25. Prospective mechanisms for conjunctive coupling of C(sp^3) electrophiles with Ni complexes[a]



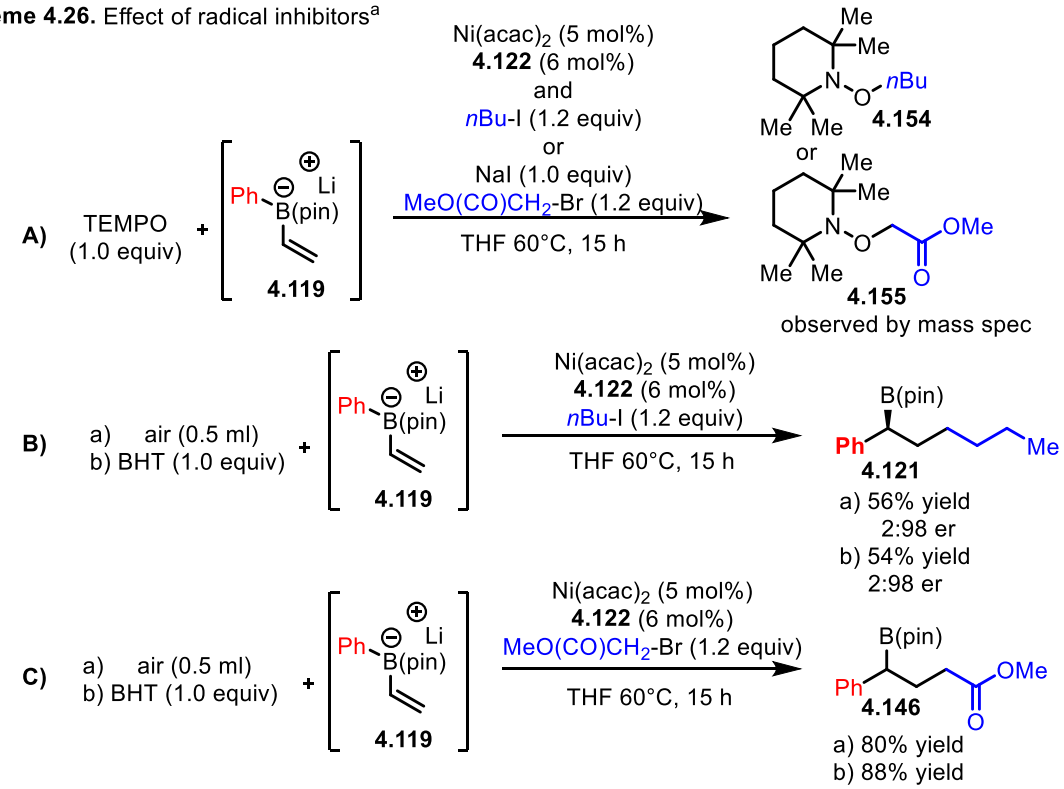
[52] See reference 40b.

could favor the metallate shift cycle since nickel complex **4.5** would be expected to rapidly recombine with the initially formed radical, or these substrates might engage in the radical addition/recombination cycle since single-electron transfer from **4.150** to an alkyl halide might be impeded by the redox potential of the non-activated electrophile.

4.5 Mechanistic Investigation

To determine which of the potential pathways mentioned above was most likely operative for each of the two conjunctive coupling reactions investigated, we conducted a series of mechanistic experiments. First, we examined reactions of both activated and unactivated electrophiles in the presence of TEMPO (Scheme 4.26.A). Addition of one

Scheme 4.26. Effect of radical inhibitors[a]

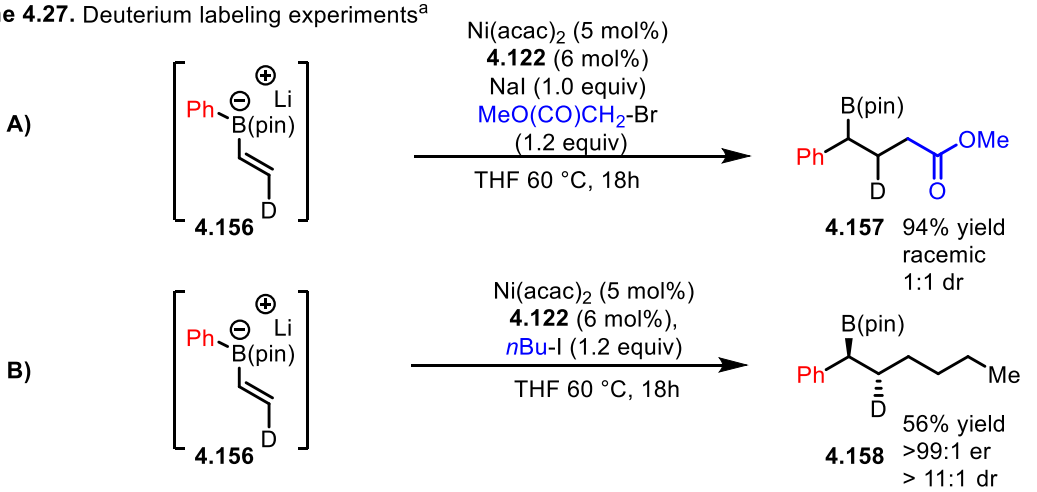


[a] Yields represent isolated yields of purified material. Enantiomeric ratio (er) determined by SFC analysis.

equivalent of the radical scavenger was sufficient to inhibit these reactions. TEMPO-electrophile adducts were detected by mass spectrometry, thereby suggesting that radicals are indeed involved in the reaction of these substrates. Reactions involving either 1-iodo-3-phenylpropane (Scheme 4.26.B) or α-bromomethyl acetate (Scheme 4.26.C) proceeded smoothly upon exposure to air or in the presence of an equivalent of the radical inhibitor BHT, suggesting these reactions are reasonably robust.

Consistent with the non-stereospecific nature of the radical-polar crossover mechanism, conjunctive coupling between an isotopically labeled boron-ate complex **4.119** furnished the reaction product as a mixture of diastereomers (Scheme 4.27.A). The enantioselective conjunctive coupling of iodobutane was observed to be a stereospecific process (Scheme 4.27.B), thus the radical addition/recombination pathway was ruled out. Notably, radical intermediates still appear to intervene in the enantioselective reactions of non-activated alkyl halides as indicated by the ring-opening and ring-closing reactions in Scheme 4.28.A/B. With an understanding of the operative mechanisms that can intervene in

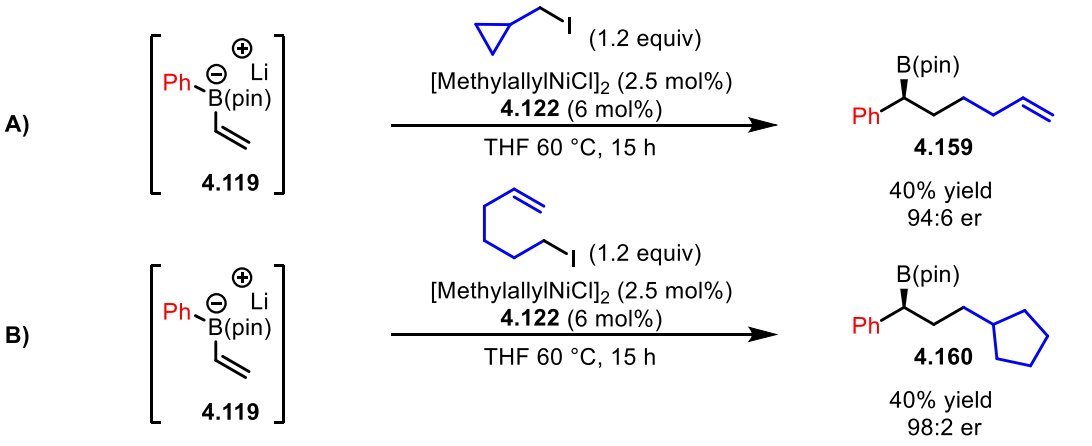
Scheme 4.27. Deuterium labeling experiments[a]



[a] Yields represent isolated yields of purified material. Enantiomeric ratio (er) determined by SFC analysis.

conjunctive coupling reactions with Ni-based catalysts, we set out to investigate more fully which classes of C(sp^3) electrophiles take part in the radical-polar crossover pathway and which instead engage in enantioselective conjunctive coupling by the metal-induced metallate shift pathway.

Scheme 4.28. Radical clock experiments[a]



[a]Yields represent isolated yields of purified material. Enantiomeric ratio (er) determined by SFC analysis.

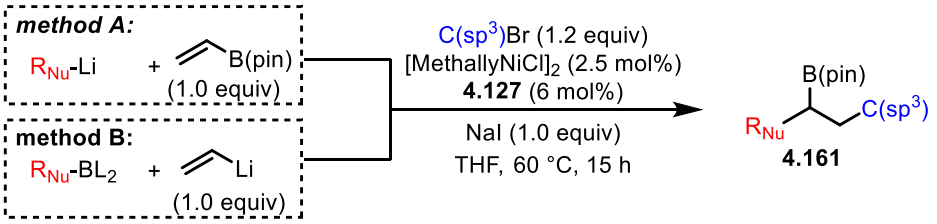
4.6 Synthetic Scope

Using the observed enantioselectivity of a specific conjunctive coupling reaction as as an indicator of the reaction mechanism by which it proceeds, we surveyed a variety of primary and secondary alkyl halide electrophiles (Scheme 4.29). Based on this information we concluded that whereas primary and secondary alkyl halides can engage in conjunctive coupling by the metallate shift pathway (**4.162** and **4.163**) and electron-withdrawing groups can be accommodated without a change in mechanism (**4.164**), the presence of a single electron-withdrawing conjugating group is sufficient to render the reaction non-selective. Thus, alkyl halides bearing an adjacent ester (products: **4.165**, **4.146**, **4.170**, **4.171**), ketone

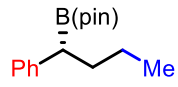
(products: **4.167** and **4.168**), or amide (product **4.169**) result in high yielding but non-enantioselective reactions. We hypothesized that do to the electrophilic character of the intermediate radical species, these electrophiles react preferentially with the electron-rich alkene of a boron-ate complex rather than recombining with the Ni-complex. A fluorinated alkyl halide (product **4.166**) also appears to react by the radical-polar crossover pathway. Notably, with activated substrates the reaction could be conducted at room temperature, without ligand, and utilizing just 3 mol% $Ni(acac)_2$. Consistent with the likely role of nickel as a radical initiator in these reactions, the nature of the nickel salt employed impacted the yield, with $Ni(acac)_2$ being particularly effective. It is worth noting that, as with previous conjunctive coupling reactions, the boron-ate complexes employed in these reactions were equally effective when generated from vinyllithium nucleophile and an organoboronic ester (Method B) as when prepared from vinylboronic pinacol ester and the corresponding organolithium reagent (Method A).

The scope of the enantioselective conjunctive coupling reaction employing unactivated primary and secondary organohalides was further examined (Scheme 4.30). In addition to 1-iodo-3-phenylpropane, iodobutane (product: **4.174**) and iodoethane (product: **4.162**) also engage in the reaction, suggesting that no directing group effect assists the stereocontrol observed for this process. β-Branched electrophiles (products: **4.180**, **4.181**, **4.182**) and cyclic secondary electrophiles (**4.183**, **4.184**, **4.192**) were also successfully engaged in the reaction, though the use of iodocyclohexane produced low yield of the conjunctive coupling product (**4.163**, Scheme **4.29**). Electron-rich (product: **4.187**), electron-poor (products: **4.186** and **4.188**), sterically hindered (product: **4.185**), and heterocyclic

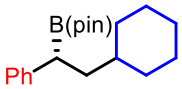
Scheme 4.29. Impact of substrate functionality on conjunctive coupling with C(sp^3) electrophiles



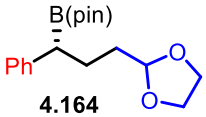
method B:



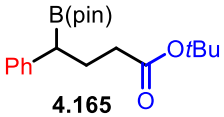
4.162[a]
71% yield, 94:6 er



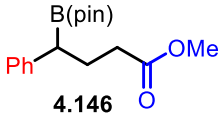
4.163[b]
35% yield, 83:17 er



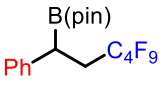
4.164
35% yield, 96:4 er



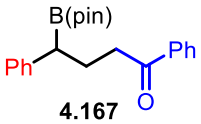
4.165
86% yield, 50:50 er
(88 % yield)



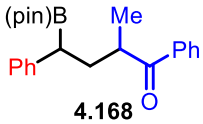
4.146
92% yield 50:50 er
(91% yield)



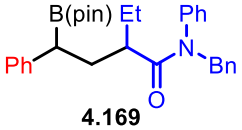
4.166
56% yield, 50:50 er
(91% yield)



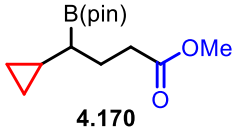
4.167
53% yield. 50:50 er



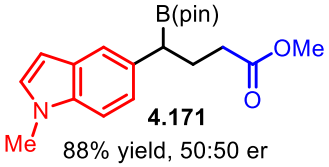
4.168
72% yield, 51:49 er
1:6 dr
(71% yield)



4.169
83 % yield, 51:49 er
1:6 dr
(84% yield)

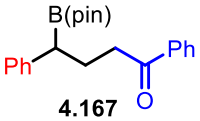


4.170
73% yield, 50:50 er
(70% yield)

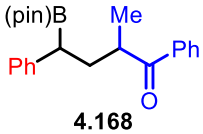


4.171
88% yield, 50:50 er
(90% yield)

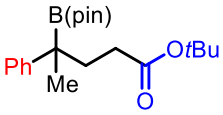
method A:



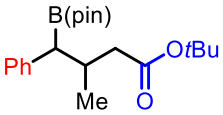
4.167
54% yield, 50:50 er



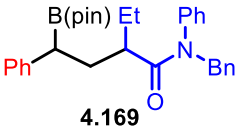
4.168
70% yield, 51:49 er
1:6 dr



4.172
84% yield, 50:50 er
(83% yield)



4.173
27% yield, 50:50 er
1.4:1 dr

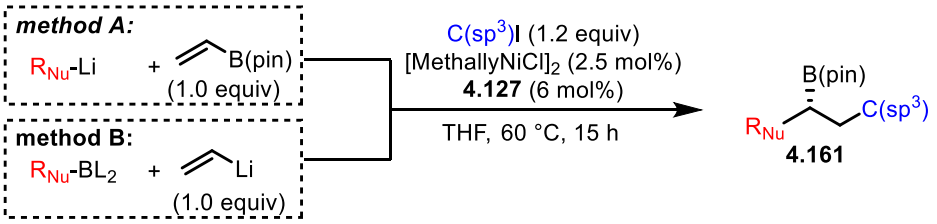


4.169
85% yield, 51:49 er
1:6 dr

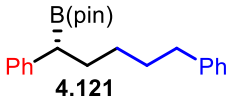
[a]Data for compounds **4.162-4.164** from reactions that employed 5 mol% [(methallyl)NiCl]2 and 6 mol% **4.127**, others are for 5 mol% $Ni(acac)_2$ and 6 mol% **4.127.** Yields in parentheses are for reactions that are ligand-free andemploy 3 mol% $Ni(acac)_2$ at 22 °C. All yields represent isolated product obtained after chromatographic purification. Enantiomeric ratio (er) determined by SFC analysis. Products **4.162-4.164** are derived from the alkyl iodide, whereas the others employed the organobromide and 1 equiv of NaI. [b]Product isolated as the derived alcohol after peroxide oxidation.

(products: **4.191**, **4.192**, **4.193**) migrating groups were also successfully employed in the reaction. It is worth noting that the reaction is compatible with labile functional groups

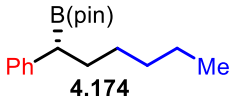
Scheme 4.30. Triamine–Ni-catalyzed enantioselective conjunctive coupling with C(sp^3) electrophiles[a]



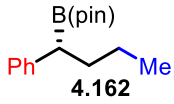
method B:



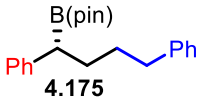
4.121
70% yield
99:1 er



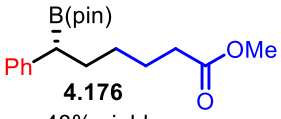
4.174
66% yield
98:2 er



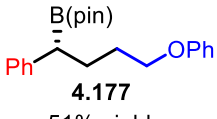
4.162
71% yield
6:94 er



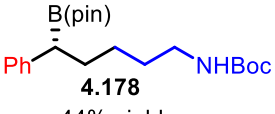
4.175
62% yield
99:1 er



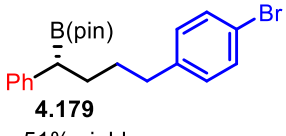
4.176
48% yield
99:1 er



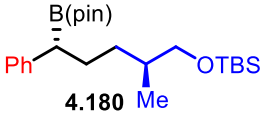
4.177
51% yield
98:2 er



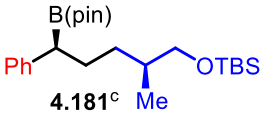
4.178
44% yield
98:2 er



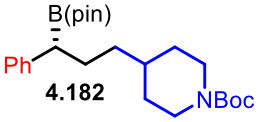
4.179
51% yield
98:2 er



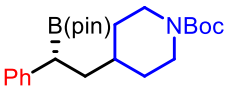
4.180
73% yield
>20:1 dr



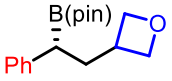
4.181[c]
72% yield
>20:1 dr



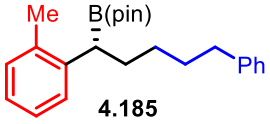
4.182
57% yield
98:2 er



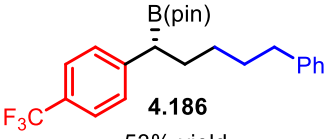
4.183[b]
47% yield
93:7 er



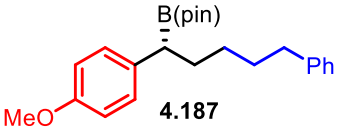
4.184
49% yield
92:8 er



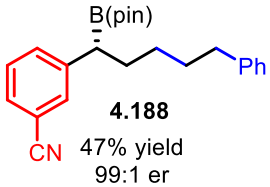
4.185
64% yield
94:6 er



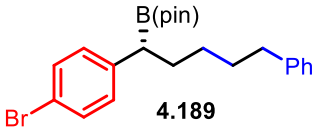
4.186
53% yield
99:1 er



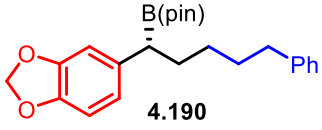
4.187
52% yield
98:2 er



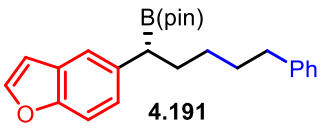
4.188
47% yield
99:1 er



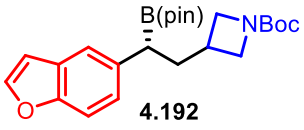
4.189
62% yield
98:2 er



4.190
53% yield
98:2 er

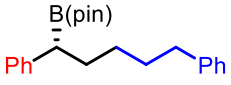


4.191
67% yield
98:2 er

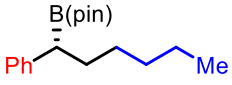


4.192
43% yield
95:5 er

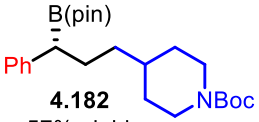
method A:



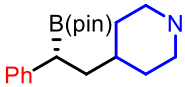
4.121
67% yield
99:1 er



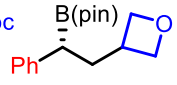
4.174
65% yield
98:2 er



4.182
57% yield
98:2 er



4.183
47% yield
93:7 er



4.184
44% yield
92:8 er

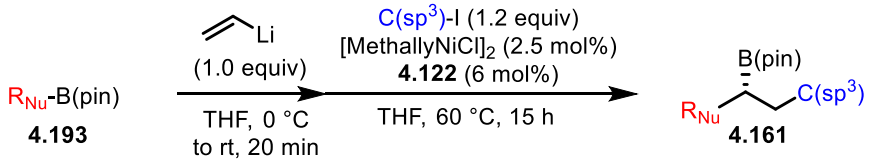
[a]All yields represent isolated product obtained after chromatographic purification. Enantiomeric ratio (er) determined by SFC analysis. [b]Product isolated as the derived alcohol after peroxide oxidation. [c](S,S)-**4.122** employed as ligand.

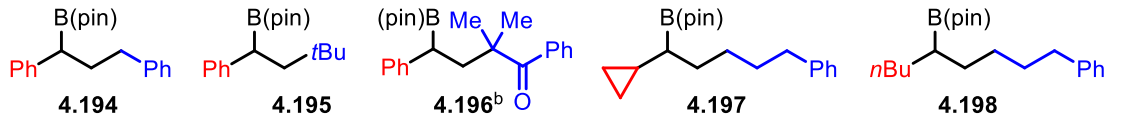
such as methyl esters (product: **4.176**) and nitriles (product: **4.188**), free carbamate NH groups (product: **4.178**), and TBS-protected alcohols (products: **4.180**, **4.181**). Also of note, it is possible to selectively couple to C(sp^3)-hybridized iodide electrophiles in the presence of an C(sp^2)-hybridized bromide functional group (products: **4.179**, **4.189**). Notably, electrophiles with labile β-substituents (product: **4.177**) were observed to survive the reaction without undergoing elimination.

Several substrates proved quite challenging for this reaction (Scheme 4.31). Reactions employing boron-ate complexes derived from alkylboronic esters did not produce desired product successfully, but instead the corresponding alkylboronic esters were recovered (**4.197**, **4.198**). We attribute this to a competing direct transmetallation pathway by which the vinyl group of the boron-ate complex is transferred to the catalyst. Additionally, the use of tertiary electrophiles (**4.195**, **4.196**) was not productive (likely due to challenging radical recombination with either the catalytic Ni-complex or the alkenylboron-ate species. Finally benzyl electrophiles did not work well in the reaction (**4.194**).

Despite these specific limitations, the catalytic enantioselective three-component reaction represents a versatile method of constructing enantioenriched boronic ester products with benzylic stereogenic carbon centers. Additionally, the mechanistic information uncovered in this study adds to a more thorough understanding of both the metal-induced metallate rearrangement and reveales how radical processes such as the radical-polar crossover reaction can intervene, depending on the electronic nature of the electrophile. Additionally, the ability to use a small amount of a chemically stable, inexpensive, and commercially available nickel salt to promote the radical-polar crossover

Scheme 4.31. Challenging substrates[a]





[a]Yields determined by ^{1}H NMR versus an internal standard. [b]employed organobromide electrophile and 1 equivalent of NaI.

reaction represents a synthetically appealing and complementary approach to Studer[53] and Renaud's[54] borane initiated processes and Aggarwal's[55] photoinitiated approach.

4.7 Enantioselective Radical Addition/Coupling Reaction of Alkenylboron Reagents, Alky Iodides, and Organozinc Reagents[56]

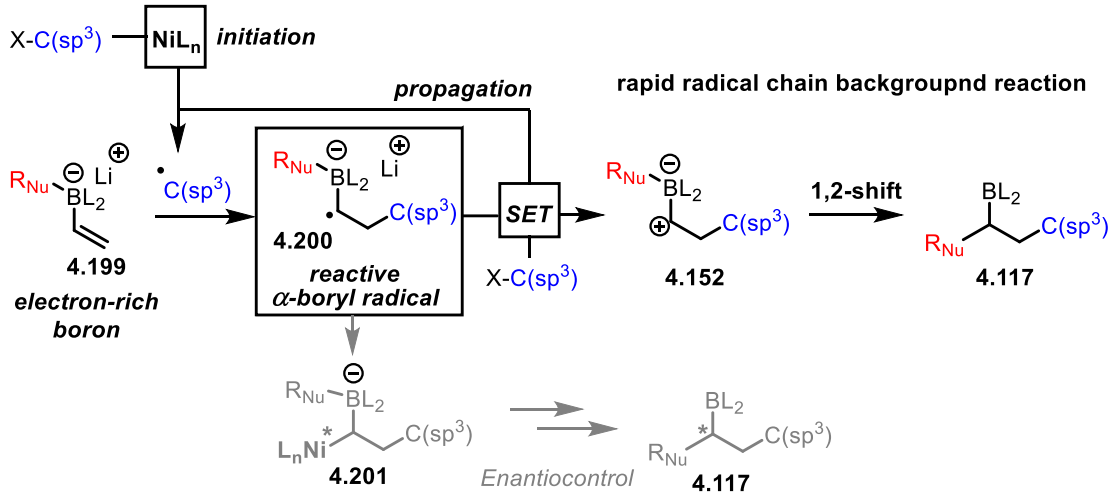
As noted in the previous study, a limitation to the broad application of conjunctive coupling of C(sp^3) electrophiles to the construction of enantioenriched boronic esters is the difficulty of engaging alkyl migrating groups, thus limiting the substrate scope to compounds possessing benzylic stereogenic carbon centers. Additionally, highly hindered tertiary electrophiles could not be engaged successfully. In considering these synthetic limitations and the competing reactions that intervene in these cases we were inspired to address these shortcomings through an alternate enantioselective process involving the

[53] Kischkewitz, M.; Okamoto, K.; Mück-Lichtenfeld, C.; Studer, A. *Science* **2017**, 355, 936.
[54] Tappin, N. D. C.; Gnägi-Lux, M.; Renaud, P. *Chem. Eur. J.* **2018**, 24, 11498.
[55] Silvi, M.; Sandford, C.; Aggarwal, V. K. *J. Am. Chem. Soc.* **2017**, 139, 5736.
[56] Chierchia, M.; Lovinger, G. J.[+]; Xu, P.[+]; Morken, J. P. *Angew. Chem. Int. Ed.* **2019**, 58, 14245. ([+] these authors contributed equally).

catalytic generation and capture of α-boryl radical intermediates.

As discussed above, the Ni-initiated radical-polar crossover reaction (Scheme 4.32) is a highly efficient approach to generating alkylboron compounds and can engage both aryl and alkyl migrating groups but does not provide a means to readily control product stereochemistry. While we had entertained the possibility that a stereoselective mechanism

Scheme 4.32. Difficulty of engaging catalytically generated α-boryl radicals in an enantioselective manifold

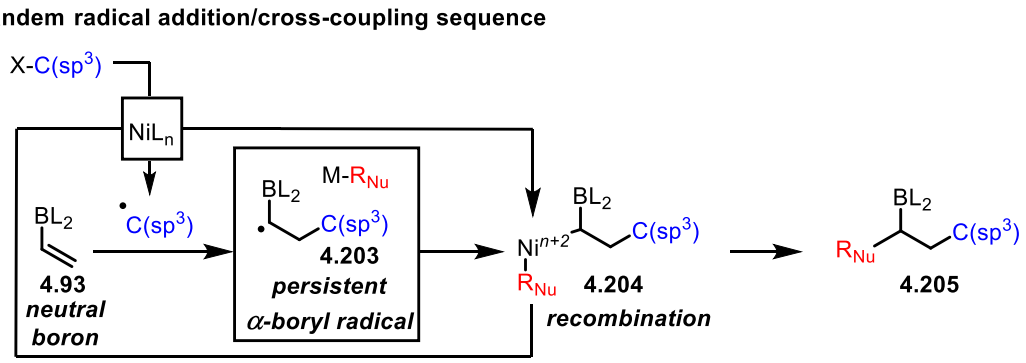


involving generation of α-boryl radical **4.200** and subsequent recombination (**4.201**)/reductive elimination to form product **4.117** might be feasible in some instances, we experimentally disproved this as an operating mechanism. A critical impediment to catalyst-based stereocontrol in the radical process proposed is that SET from the α-boryl radical **4.200** to an alkyl halide molecule likely outcompetes recombination of this species with the Ni complex, and thus the Ni complex operates as an initiator not a catalyst.

To address this mechanistic obstacle, we targeted formation of a neutral α-boryl radical **4.203** (Scheme 4.33) that would be stabilized and less prone to engage in a SET radical propagation reaction. If the intermediate radical were to instead react with the Ni complex

furnishing α-boryl alkylnickel complex **4.204**, then catalyst-based stereocontrol might be established.

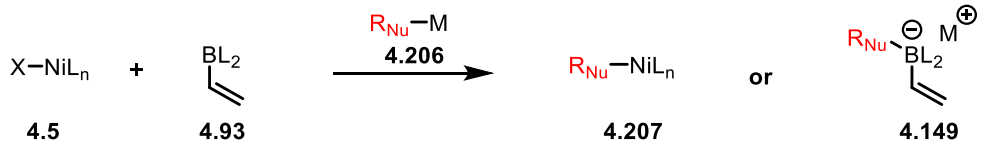
Scheme 4.33. Strategy to engage catalytically generated α-boryl radicals in enantioselective coupling



4.7.1 Optimization of Enantioselective Radical Addition/Cross-Coupling Reaction

To begin our investigation of the radical addition/cross-coupling process proposed in Scheme 4.33, we first attempted to identify an appropriate stoichiometric organometallic reagent capable of transmetallating with a Ni-based catalyst, but which will not react directly with three-coordinate vinylboron reagents (Scheme 4.34). Organolithium nucleophiles efficiently form boron-ate complexes and were thus discounted. While Grignard reagents are less nucleophilic than organolithium reagents, as discussed in chapter three of this dissertation, they do covert vinylboronic pinacol ester to the corresponding ate complex to some extent. As discussed in the introduction to this chapter, Fu and Martin have demonstrated that alkyl- and arylzinc reagents do not directly react

Scheme 4.34. Competition between nucleophilic addition to boron or nickel



with alkylboronic pinacol esters and we found that, despite being somewhat more electrophilic, vinylboronic pinacol ester was similarly unreactive with these reagents.

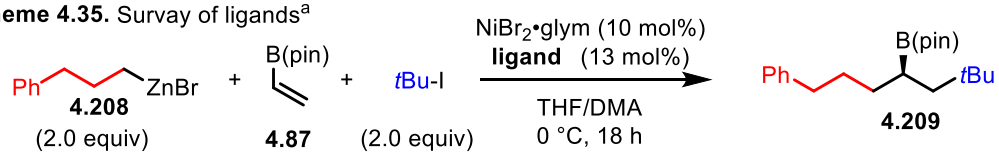
With regard to the electrophilic component of the reaction, we hypothesized that an electron-rich alkyl radical would most efficiently add to an electron-deficient alkenylboronic ester. We also imagined that employing a sterically-hindered radical species might suppress direct radical combination with Ni-based species. Thus, *tert*-butyl iodide was selected for initial studies.

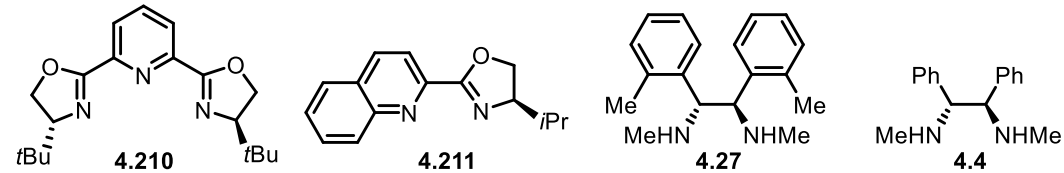
In terms of initial reaction conditions such as solvent and temperature, we considered that the conditions employed by Fu and Martin in radical-based cross-coupling reactions of α-halo boronic esters would likely serve as an effective starting point as these reactions are proposed to involve generation and selective recombination of an α-boryl radical similar to **4.293** with a Ni-based catalyst.

4.7.2 Optimization of the Ligand on Nickel

As depicted in Scheme 4.35, we surveyed a variety of bidentate and tridentate nitrogen-based ligands employing *tert*-butyl iodide, alkylzinc bromide **4.208**, and vinylboronic pinacol ester. Both tridentate and bidentate ligands were found to be competent in promoting the desired reaction with modest to good yield and enantioselectivity. While *ortho*-tolyl-substituted diamine **4.27** previously employed by Fu, provided the highest enantioselectivity, diamine **4.4** proved to be the most effective ligand in terms of both yield and enantioselectivity of the three-component reaction product **4.209**.

Scheme 4.35. Survay of ligands[a]



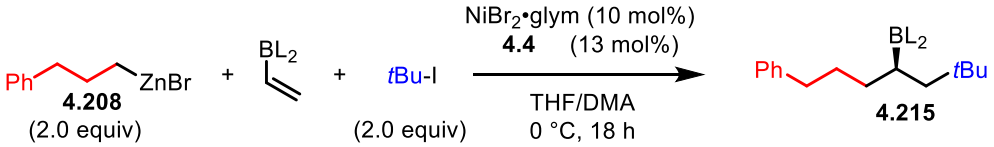


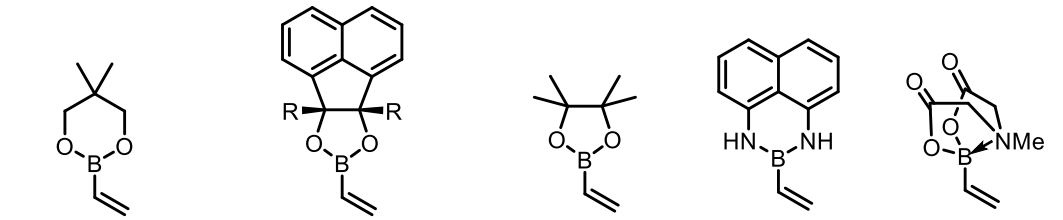
[a] Yields are of isolated and purified material. Enantiomer ratio (er) determined by SFC analysis.

4.7.3 Optimization of the Ligand on Boron

We next investigated the effect of varying the vinylboron reagents employed in the reaction (Scheme 4.36). Of the reagents studied, electron-rich four-coordinate vinylboronic MIDA ester **4.218** was the only one which did not produce significant amounts of the desired product **4.215**. This observation is consistent with the mechanistic hypothesis that an electron-deficient vinylboron reagent is more prone to engage in radical addition reactions with nucleophilic radicals and is less likely to engage in radical chain or SET processes. While the interplay of the steric and electronic properties of these ligand and their impact on the reaction are not entirely clear, it is worth noting that using vinylboronic diamine **4.218** produced the highest yielding reaction. While this is not the most

Scheme 4.36. Survay of ligands on boron reagent[a]





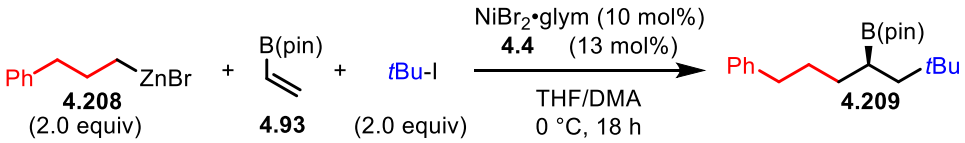
[a] Yields represent isolated yields of purified material. Enantiomer ratio (er) determined by SFC analysis.

electrophilic boron reagent due the strong donating ability of the amine groups, the α-boryl radical species formed from this reagent upon radical addition is likely the least sterically-hindered do to the flat aromatic ligand structure of this reagent. Of the vinylboron reagents tested, vinylboronic pinacol ester proved to be the most effective coupling partner overall.

4.7.4 Control Experiments and Optimization of the Organozinc Nucleophile

We next conducted control experiments (Table 4.4). Both nickel and ligand were found to be essential (entries 2 and 3). The desired product was not formed when either *tert*-butyl bromide (entry 4) or *n*-butyl iodide (entry 5) were employed in the reaction. Notably, we found that in contrast to alkylzinc iodide prepared by zinc insertion reaction (entry 6), alkylzinc chloride reagents prepared by addition of the corresponding organolithium reagent to zinc dichloride (entry 7) provided the desired product with slightly decreased yield but with improved enantioselectivity. This effect appears to be due to the activation

Table 4.4. Control experiments and optimization of organozinc reagent



entry	modification	yield (%)[a]	er[b]
1	none	71	87:13
2	no $NiBr_2$•glym	<5	na
3	no ligand	<5	na
4	*t*Bu-Br	<5	na
5	*n*Bu-I	<5	na
6		75	86:14
7		54	95:5
8		55	95:5

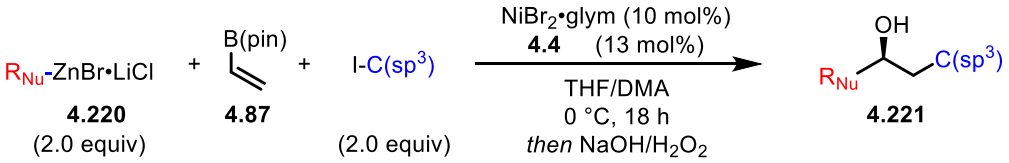
[a] Yields represent isolated yields of purified material. Both the yield and the enantiomer ratio (er) represent the average value for two experiments. [b]Enantiomer ratio (er) Determined by SFC analysis.

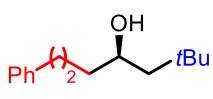
of the organozinc nucleophiles by LiCl as addition of LiCl to reactions employing alkylzinc bromide reagents (entry 8) proved similarly effective.

4.7.5 Substrate Scope of Intermolecular Reaction

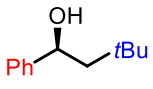
With a preliminary understanding of what typed of reagents productively participate in the radical addition/cross-coupling reaction we next assessed the substrate scope of the transformation (Scheme 4.37). Consistent with the generally excellent functional group compatibility of organozinc nucleophiles, a range of functional groups such as an ether (product: **4.224**), a protected alcohol (product: **4.226**), or amino (product: **4.233**) group were well tolerated under the reaction conditions employed. That methylzinc bromide could be employed (product: **4.225**) is noteworthy as methyl-substituted carbon

Scheme 4.37. Substrate scope of intermolecular radical addition/cross-coupling reaction

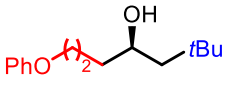




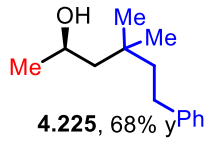
4.222, 55% y
95:5 er



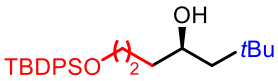
4.223, 70% y
97:3 er



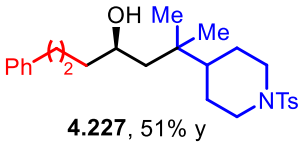
4.224, 68% y
94:6 er



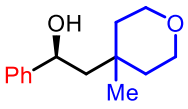
4.225, 68% y
88:12 er



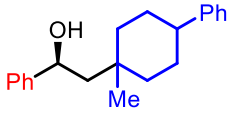
4.226, 70% y
92:8 er



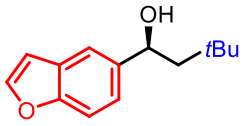
4.227, 51% y
91:9 er



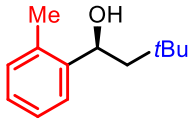
4.228, 73% y
96:4 er



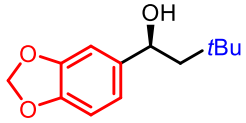
4.229, 52% y (2.8:1 dr)
95:5 er (major)



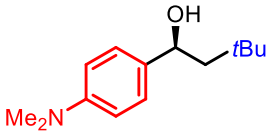
4.230, 52% y
98:2 er



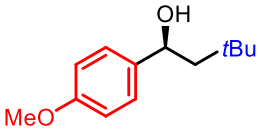
4.231, 32% y
92:8 er



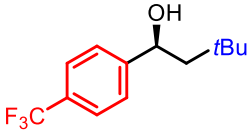
4.232, 66% y
96:4 er



4.233, 46% y
91:9 er



4.234, 63% y
95:5 er



4.235, 56% y
97:3 er

[a] Yields represent isolated yields of purified material. Both the yield and the enantiomer ratio (er) represent the average value for two experiments. [b]Enantiomer ratio (er) determined by SFC analysis.

stereocenters are ubiquitous in natural products[57] but thus far have proven challenging to access using the conjunctive coupling reaction manifold. Notably, arylzinc reagents could be used in place of alkylzinc reagents under the same reaction conditions, providing enantiomerically enriched benzylic boronic ester intermediates. In terms of the

[57] Claraz, A.; Sahoo, G.; Berta, D.; Madarász, A.; Pápai, I.; Pihko, P. M. *Angew. Chem. Int. Ed*. **2016**, 55, 669.

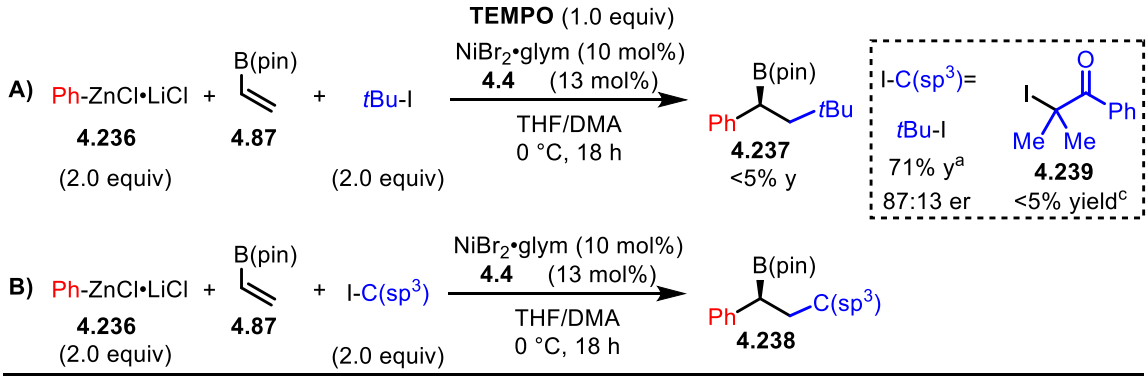
electrophilic partner, carbon scaffolds with oxygen- and nitrogen-based functional groups were successfully engaged (products: **4.227**, **4.228**). For substrate **4.229**, where a quaternary stereogenic carbon center is formed in the radical addition step, a modest degree of substrate-controlled diastereoselectivity was observed.

4.7.6 Mechanistic Investigations

With a goal of learning more about the mechanistic features that underpin this three-component reaction we conducted a series of experiments. As shown in Scheme 4.38.A, addition of one equivalent of TEMPO completely suppressed formation of desired product **4.237**, suggesting the intermediacy of radical species. If radical species are indeed involved in the mechanism of this process, then the polarity of such radicals might strongly influence the course of the reaction. Attempting to probe this hypothesis, we subjected tertiary α-iodo ketone electrophile **4.239** to the reaction (inset, Scheme 4.38.B). In contrast to *tert*-butyl iodide, use of this reagent, which should form a more electrophilic radical species upon C-I homolysis, did not result in appreciable product formation.

Assuming radicals are involved in the productive reaction mechanism for this process, the previously noted inability to employ primary iodide electrophiles in the reaction could be due to a less facile C–I halogen abstraction, or it could be due to competitive side reactions with this substrate class such as a polar S_N2-type oxidative addition that might not lead to the formation of a primary radical species but rather produce direct cross-coupling or homo-coupling products. To probe these possibilities, we conducted a reaction of 1-iodo-3-phenylpropane and alkylzinc reagent **4.240** in the absence of vinylboronic

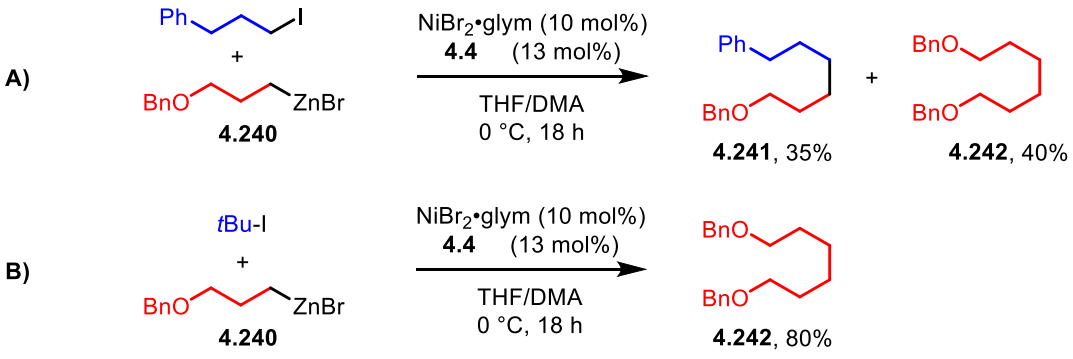
Scheme 4.38. Reaction with TEMPO radical inhibitor and probing the electronic nature of the electrophile



[a] Yields represent isolated yields of purified material. Both the yield and the enantiomer ratio (er) represent the average value for two experiments. [b] Enantiomer ratio determined by SFC analysis. [c]Yields determined by ^{1}H NMR versus an internal standard.

pinacol ester (Scheme 4.39.A). The observation of both cross-coupled (**4.241**) and homo-coupled[58] (**4.242**) products suggested to us that primary alkyl iodides can indeed undergo oxidative addition with the catalytic Ni complex employed in this reaction. Notably, when the same reaction is conducted with *tert*-butyl iodide, the homo-coupling product is formed exclusively (Scheme 4.39.B) This result is consistent with our initial hypothesis that use of

Scheme 4.39. Probe of competitive cross-coupling and homo-coupling background reactions[a]

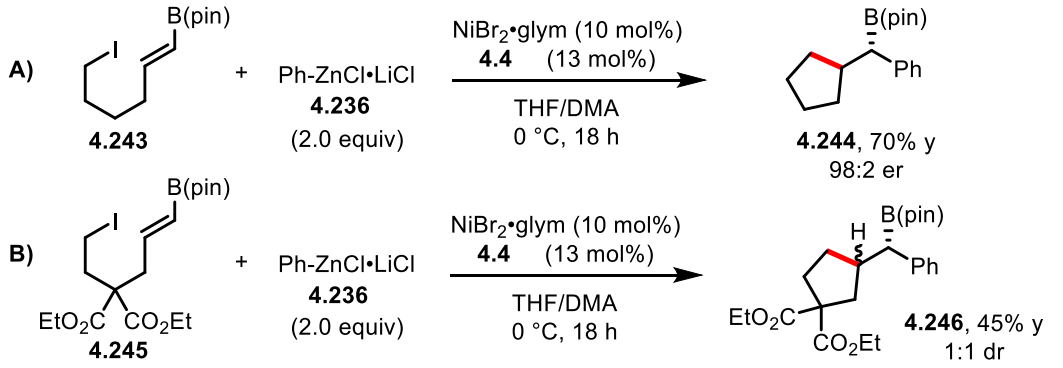


[a]Yields determined by ^{1}H NMR versus an internal standard.

[58] For a review on catalytic oxidative coupling of two nucleophiles, see: Liu, R C.; Zhang, H.; Shi, W.; Lei, A. *Chem. Rev.* **2011**, 111, 1780. For related catalytic homocoupling of organometallic reagents, see: a) Jin, L.; Zhang, H.; Li, P.; Sowa Jr, J. R.; Lei, A. *J. Am. Chem. Soc.* **2009**, 131, 9892. (b) Lei, A.; Zhang, X. *Org. Lett.* **2002**, 4, 2285. (c) Lei, A.; Zhang, X. *Tetrahedron Lett.* **2002**, 43, 2525.

a tertiary electrophile might inhibit radical addition to nickel species relative to alkenylboron species. To determine the reason primary alkyl iodide electrophiles do not participate in the radical addition/coupling reaction we conducted the reactions depicted in Scheme 4.40. As shown in Scheme 4.40.A, reaction of substrate **4.243** and PhZnCl·LiCl in the presence of Ni/**4.4** resulted in efficient cyclization/coupling to give product **4.244** with excellent enantioselectivity.[59] Employing the same reaction conditions with substrate **4.245** resulted in the formation of a 1:1 diastereomer mixture of product **4.246**. Taken together, these results indicate that the cyclization of the primary iodide is likely a radical

Scheme 4.40. Cyclization probe substrates[a]



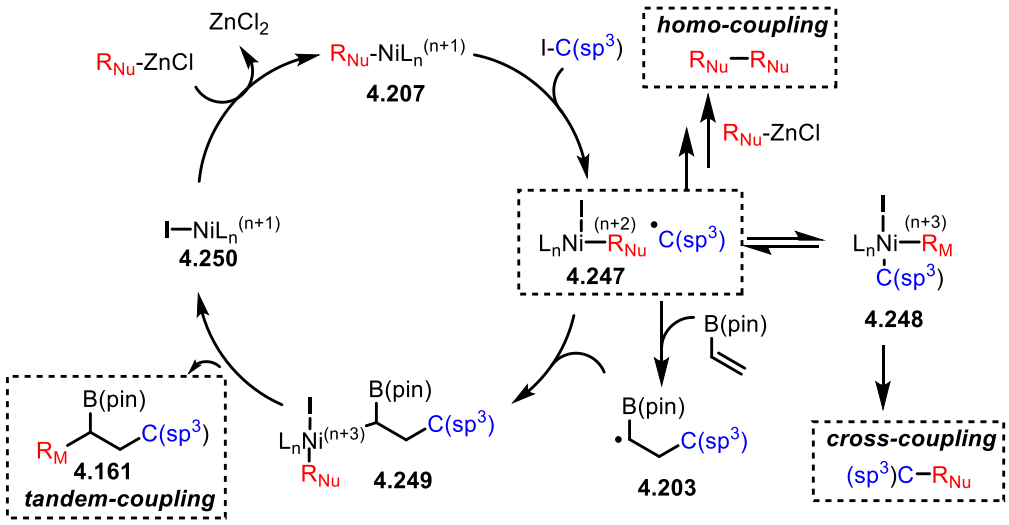
[a] Yields are of isolated and purified material. Both the yield and the enantiomer ratio (er) represent the average value for two experiments. Enantiomer ratio (er) determined by SFC analysis.

[59] For aligned radical cyclization/cross-coupling reactions, see: (a) Wakabayashi, K.; Yorimitsu, H.; Oshima, K. *J. Am. Chem. Soc.* **2001**, 123, 5374. (b) Phapale, V. B.; Buñuel, E.; García-Iglesias, M.; Cárdenas, D. J. *Angew. Chem. Int. Ed.* **2007**, 46, 8790. (c) Thapa, S.; Basnet, P.; Giri, R. *J. Am. Chem. Soc*. **2017**, 139, 5700. (d) KC, S.; Basnet, P.; Thapa, S.; Shrestha, B.; Giri, R. *J. Org. Chem.* **2018**, 83, 2920. (e) Kuang, Y.; Wang, X.; Anthony, D.; Diao, T. *Chem. Commun.* **2018**, 54, 2558. (f) Jin, Y.; Wang, C. *Chem. Sci*. **2019**, 10, 1780. (g) Yan, C. S.; Peng, Y.; Xu, X. B.; Wang, Y. W. *Chem. Eur. J.* **2012**, 18, 6039. (h) Yu, X.; Yang, T.; Wang, S.; Xu, H.; Gong, H. *Org. Lett.* **2011**, 13, 2138. (i) Jiang, B.; Liu, J. X.; Wei, Y.; Shi, M. *Org. Lett.* **2018**, 20, 6229. For selected enantioselctive cyclization/cross-coupling reactions, see: (j) Wang, K.; Ding, Z.; Zhou, Z.; Kong, W. *J. Am. Chem. Soc.* **2018**, 140, 12364. (k) Yasui, Y.; Kamisaki, H.; Takemoto, Y. *Org. Lett.* **2008**, 10, 3303. (l) Tian, Z.-X.; Qiao, J.-B.; Xu, G.-L.; Pang, X.; Qi, L.; Ma, W. Y.; Zhao, Z.-Z.; Duan, J.; Du, Y.-F.; Su, P.; Liu, X.-Y.; Shu, X.-Z. *J. Am. Chem. Soc.* **2019**, 141, 7637. (m) You, W.; Brown, M. K. *J. Am. Chem. Soc.* **2015**, 137, 14578. (n) Cong, H.; Fu, G. C. *J. Am. Chem. Soc.* **2014**, 136, 3788. (o) Jin, Y.; Wang, C. *Angew. Chem. Int. Ed.* **2019**, 58, 6722. (p) Souillart, L.; Parker, E.; Cramer, N. *Angew. Chem. Int. Ed.* **2014**, 53, 3001. (q) Xu, T.; Ko, H. M. Savage, N. A.; Dong, G. *J. Am. Chem. Soc.* **2012**, 134, 20005. (r) Liu, L.; Ishida, N.; Murakami, M. *Angew. Chem. Int. Ed.* **2012**, 51, 2485.

process as the reaction in Scheme 4.40.B would be expected to proceed diastereoselectivity if this reaction were to occur by oxidative addition and subsequent stereospecific migratory insertion. Collectively, the experiments described above suggested to us that the three-component reaction likely occurs by a radical addition/cross-coupling mechanism.

While it is difficult to rigorously exclude every competing mechanism that may operate in this catalytic process, one plausible catalytic cycle that is consistent with the experimental evidence detailed above is depicted in Scheme 4.41. This proposal involves halide abstraction from the alkyl halide by a alkyl–Ni(I) complex **4.207** to furnish a Ni(II) species **4.247** along with a carbon-centered radical. Subsequent to addition of this radical to vinylB(pin) to generate α-boryl radical species **4.203**, recombination of this species with Ni(II) complex **4.247** will generate α-boryl alkyl–Ni(III) complex **4.249**, that then can undergo reductive elimination, delivering the tandem radical addition/cross-coupling product **4.161** along with a Ni(I) iodide complex **4.250**. Transmetallation between the organozinc reagent and **4.249** then regenerates the starting alkyl–Ni(I) complex **4.207.** This cycle accounts for the homo-coupling and cross-coupling products that are observed in the absence of vinyl–B(pin) as well as the observation that enantioselectivity in the formation of product is dependent upon the nature of the R_{Nu} group employed in the reaction. Finally, this catalytic cycle and the experiments above suggest a requirement for effective intermolecular reactions: subsequent to formation of a carbon-centered radical by halide abstraction by a Ni complex on the alkyl iodide, capture of the radical by the vinylboronic ester must outcompete direct cross-coupling that arises from recombination of the Ni complex with the radical center.

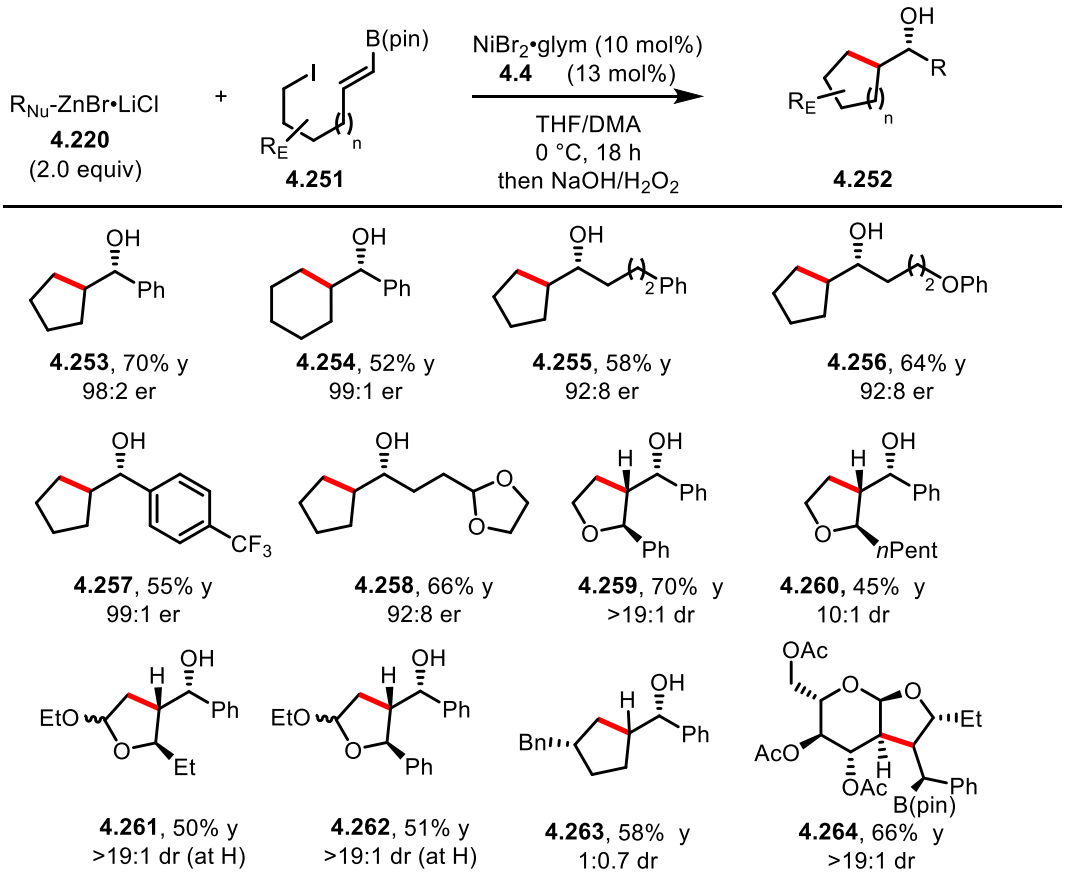
Scheme 4.41. Prospective mechanism for radical addition/cross-coupling catalyzed by Ni complexes



4.7.7 Substrate Scope of Intramolecular Reaction

While we initially employed the intramolecular cyclization reaction described in Scheme 4.40 as a mechanistic probe, upon considering the potential synthesis value of this process we realized it might offer the distinctive feature of forging two C–C bonds while generating an exocyclic boron-substituted stereogenic carbon center in an enantioselective fashion. Investigating the substrate scope of this process, we found that it could readily be applied to the construction of both five- and six-membered ring systems (Scheme 4.42, products: **4.253** to **2.258**). By employing a combination of substrate-based stereocontrol in the ring closure, along with catalyst-based control of the boron-substituted stereogenic carbon center, the overall transformation may be used to obtain complex cyclic structures efficiently. With these considerations, we explored a number of additional substrates using this intramolecular cyclization/cross-coupling sequence. We found that the reaction could

Scheme 4.42. Intramolecular radical cyclization/cross-coupling reaction



[a] Yields represent isolated yields of purified material and both the yield and the enantiomer ratio (er) represent the average value for two experiments. Enantiomer ratio (er) determined by SFC analysis. Unless otherwise indicated R_{Nu}-ZnBr•LiCl (**2.220**) obtained by addtion fo R_{Nu}-Li to $ZnCl_2$. [b]RNu-ZnBr employed: reaction conducted in DMA solvent at room temperature. [c]Due to the instability of the coresponding alocohl, this product was isolated as the organoboronic ester.

be carried out to readily construct substituted monocyclic (products: **4.259** to **4.263**) and bicyclic products (product: **4.264**) with sensitive functional groups and often with excellent diastereoselectivity.

4.8 Conclusion

In conclusion, we have developed two highly enantioselective three-component

reactions catalyzed by nickel complexes which employ alkenylboron reagents and unactivated alkyl electrophiles, as well as a highly efficient non-enantioselective radical-polar crossover reaction employing activated electrophiles. Collectively, these three multi-component reactions are capable of transforming simple commercially available building blocks into diverse enantioenriched alkylboronic ester products which can be transformed into functionalized C(sp^3)-rich carbon frameworks. Research in this area of chemistry is ongoing and the mechanistic insights which have been gained in these studies promises to enable the development of powerful new transformations in organich synthesis which harness the potential of boron to mediate both polar and radical processes.

4.9 Experimental

4.9.1 General Information

Note: NMR spectra of compounds included in the following sections have been previously published and can be accessed online. ^{1}H NMR spectra were recorded on either a Varian Gemini-500 (500 MHz), Varian Gemini-600 (600 MHz), or Varian Inova-500 (500 MHz) spectrometer. Chemical shifts are reported in ppm with the solvent resonance as the internal standard ($CDCl_3$: 7.26 ppm). Data are reported as follows: chemical shift, integration, multiplicity (s = singlet, d = doublet, t = triplet, q = quartet, p = pentet, m = multiplet, app = apparent), and coupling constants (Hz). ^{13}C NMR spectra were recorded on either a Varian Gemini-500 (125 MHz), Varian Gemini-600 (150 MHz) or a Varian Inova-500 (125 MHz) spectrometer with complete proton decoupling. Chemical shifts are reported in ppm with the solvent resonance as the internal standard ($CDCl_3$: 77.24 ppm). ^{11}B NMR spectra were recorded on a Varian Gemini-500 (128 MHz) spectrometer. Chemical shifts are reported in ppm using boron trifluoride diethyl etherate as the external standard ($BF_3{\cdot}O(C_2H_5)_2$: 0.0 ppm). Infrared (IR) spectra were recorded on a Bruker alpha-P Spectrometer. Frequencies are reported in wavenumbers (cm^{-1}) as follows: strong (s), broad (br), medium (m), and weak (w). Optical rotations were measured on a Rudolph Analytical Research Autopol IV Polarimeter and the values reported are averages of seven measurements. High-resolution mass spectrometry (DART) was performed at the Mass Spectrometry Facility, Boston College, Chestnut Hill, MA. Liquid chromatography was performed using forced flow (flash chromatography) on silica gel (SiO_2, 230 x 450 Mesh, purchased from Silicycle) either manually or using an automated column. Thin layer

chromatography (TLC) was performed on 25 μm silica gel aluminum backed plates from Silicycle. Visualization was performed using ultraviolet light (254 nm), ceric ammonium molybdate (CAM) in ethanol or phosphomolybdic acid, and cerium(IV) sulfate in ethanol with sulfuric acid (Seebach).

Analytical supercritical fluid chromatography (SFC) was performed on a TharSFC Method Station II equipped with Waters 2998 Photodiode Array Detector with isopropanol or methanol as the modifier.

Tetrahydrofuran (THF), diethyl ether (Et_2O), dichloromethane (DCM) and toluene were purified using Pure Solv MD-4 solvent purification system, from Innovative Technology, Inc., by passing the solvent through two activated alumina columns after purging with argon. Vinyllithium was prepared according to the reported procedure. (*R*,*R*)/(*S*,*S*)-3,5-dimethyl-phenyl-pybox **4.127** was prepared according to the reported procedure[60] Methylallylnickel chloride dimer, and (-)-2,6-Bis[(4*R*)-4-phenyl-2-oxazolin-2-yl]pyridine (*R*,*R*)-Ph-Pybox (*R*,*R*)-**4.122** were purchased from Strem Chemicals, Inc. and used without further purification. (-)-2,6-Bis[(4*S*)-4-phenyl-2-oxazolin-2-yl]pyridine (*S*,*S*)-Ph-Pybox (*S*,*S*)-**4.122** was purchased from Combi-Blocks and used without further purification. Pinacol was purchased from Aldrich. All pinacol esters were purchased from Combi-Blocks, Okwood Chemicals, or Frontier Scientific and used without further purification except for PhB(pin) which was prepared according to the reported procedure. Organobromides and iodides were purchased from Combi-Blocks, Oakwood Chemicals,

[60] Eno, M. S.; Lu, A.; Morken, J. P. *J. Am. Chem. Soc.* **2016**, 138, 7824.

Frontier Scientific, or Sigma Aldrich and used without further purification. *N*,*N*-dimethyl acetamide (DMA) was purchased from Sigma Aldrich, distilled over 4Å molecular sieves under reduced pressure and stored under argon atmosphere. Nickel(II) dibromide·glyme was purchased from STREM. (S,S)-*N*,*N*′-dimethyl-1,2-diphenylethane-1,2- diamine (*S*,*S*)-**4.4** (as well as (*R*,*R*)-**4.4** and racemic **4.4**) was synthesized from the corresponding commercially available (*S*,*S*)-1,2-diphenylethylenediamine (Oakwood Chemicals) following literature methods.[61] All other reagents were purchased from either Aldrich, Alfa Aesar or Acros and were used without further purification.

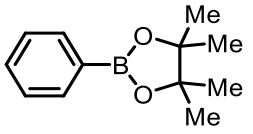
4.9.2 Experimental Information

4.9.2.1 PyBox–Ni-Catalyzed Enantioselective Conjunctive Coupling with C(sp^3) Electrophiles: A Radical-Ionic Mechanistic Dichotomy

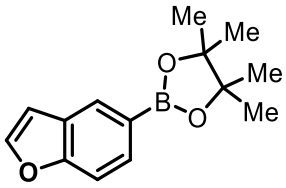
4.9.2.1.1 Procedures for Preparation of Boronic Esters

General Procedure for the Preparation of Boronate Esters. To an oven-dried round bottom flask with magnetic stir bar was added boronic acid (1.0 equiv) and pentane. The suspension was allowed to cool to 0 ºC and 2,3-dimethylbutane-2,3-diol (pinacol) (1.05 equiv) was added neat and the reaction solution was allowed to warm to room temperature and stirred for 3 h. If a water layer was observed it was removed and the resulting pentane solution was dried with Na_2SO_4, filtered with diethyl ether, and the solvent was removed *in vacuo*. The resulting residue was purified on silica gel (plug with CH_2Cl_2 as the eluent).

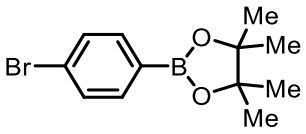
[61] V. F. Kuznetsov, G. R. Jefferson, G. P. A. Yap, H. Alper, *Organometallics* **2002**, 21, 4241.



5,5-Dimethyl-2-phenyl-1,3,2-dioxaborinane (4.265). Prepared according to the general procedure above with phenylboronic acid (0.268 g, 22.0 mmol, 1.0 equiv), pinacol (2.41 g, 23.1 mmol, 1.05 equiv), and pentane (60 mL). The resulting white solid (4.18 g, quantitative yield) was used without further purification. All spectral data was in accord with the literature. This compound is commercially available [CAS: 24388-23-6].



2-(Benzofuran-5-yl)-4,4,5,5-tetramethyl-1,3,2-dioxaborolane (4.266). Prepared according to the general procedure above with benzofuran-5-ylboronic acid (0.750 g, 4.63 mmol, 1 equiv), pinacol (0.575 g, 4.86 mmol,1.05 equiv), and pentane (75 mL). The resulting white solid (1.074 g, 95% yield) was used without further purification. All spectral data was in accord with the literature.[62] This compound is commercially available [CAS: 519054-55-8].



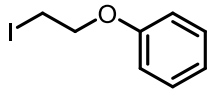
2-(4-Bromophenyl)-4,4,5,5-tetramethyl-1,3,2-dioxaborolane (4.267). Prepared according to the general procedure above with 4-bromophenylboronic acid (1.00 g, 5.0 mmol, 1.0 equiv),

[62] Clary, J. W.; Rettenmaier, T. J.; Snelling, R.; Bryks, W.; Banwell, J.; Wipke, W. T.; Singaram, B. *J. Org. Chem.* **2011**, 76, 9602.

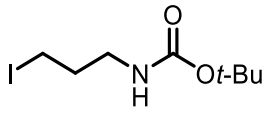
pinacol (0.620 g, 5.25 mmol, 1.05 equiv), and pentane (15 mL). The resulting white solid (1.19 g, 84% yield) was used without further purification. All spectral data was in accord with the literature.[63] This compound is commercially available [CAS: 68716-49-4].

4.9.2.1.2 Procedures for Preparation of Alkyl Iodides

General Procedure for the Preparation of Alkyl Iodides from Alkyl Bromides. To an oven-dried round bottom flask with magnetic stir bar was added sodium iodide (5.0 equiv), and alkyl bromide (1.0 equiv) and acetone. The suspension was allowed to reflux for 24 h. After the specified time, the reaction solution was allowed to cool to room temperature, was filtered through a cotton plug to remove insoluble salts, to the filtrate was added water and the product was extracted from this mixture with diethyl ether (4x) and the collected organic phase was dried with Na_2SO_4, filtered with diethyl ether, and the solvent was removed *in vacuo*. The resulting residue was purified on silica gel or alumina.



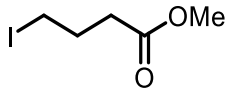
(2-Iodoethoxy)benzene (4.268) Prepared according to the general procedure. (95% yield), All spectral data was in accord with the literature.[64]



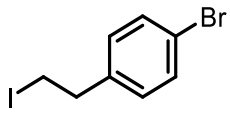
***tert*-Butyl (3-iodopropyl)carbamate (4.269).** Prepared according to

[63] Zhu, W.; Ma, D. *Org. Lett.* **2006**, 8, 261.
[64] Cahiez, Gerard; Gager, Oliver; Moyeux, Alban; Delacroix, T. *Adv. Synth. Catal.* **2012**, 354, 8, 1519.

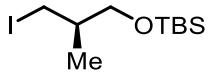
the literature procedure (89% yield) All spectral data was in accord with the literature.[65]



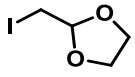
Methyl 4-iodobutanoate (4.270). Prepared according to the general procedure (76% yield). All spectral data was in accord with the literature.[66]



1-Bromo-4-(2-iodoethyl)benzene (4.271). Prepared according to the general procedure (81% yield). All spectral data was in accord with the literature.[67]



(*R*)-t*ert*-Butyl(3-iodo-2-methylpropoxy)dimethylsilane (4.272). Prepared according to the general procedure (83% yield). All spectral data was in accord with the literature.[68]



2-(Iodomethyl)-1,3-dioxolane (4.273). Prepared according to the literature procedure (87% yield).[69] All spectral data was in accord with the literature.[70]

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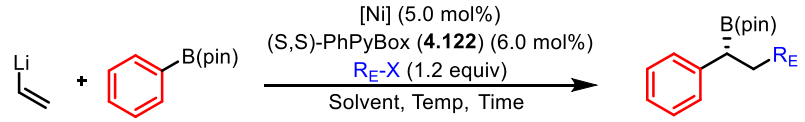
[65] Ensch, C.; Hesse, M. *Helv. Chim. Acta*. **2002**, 85, 1659.
[66] Olah, G.A.; Karpeles, R.; Narang, S.C. *Synthesis* **1982**, 963.
[67] Moriya, T.; Yoneda, S.; Kawana, K.; Ikeda, Reiko; Konakahara, T.; Sakai, N. *J. Org. Chem.* **2013**, 78, 10642.
[68] Kraft, P.; Tochtermann, W. *Liebigs Annalen* **1995**, 1409.
[69] Synder, S. A.; Brucks, A. P.; Treitler, D. S.; Moga, I. *J. Am. Chem. Soc.* **2012**, 134, 17714.
[70] Pudleiner, Heinz, Laatsch, H. *Liebigs Annalen der Chemie* **1990**, 423.

4.9.2.1.3 Procedures for the Synthesis of Vinyllithium from Tetravinyltin

Lithium-Tin Exchange: To an oven-dried 250 mL round bottom flask equipped with a stir bar in an Ar-filled glovebox was added tetravinyltin (5.67 g, 25.0 mmol, 1.0 equiv) and pentane (100 mL).The reaction flask was sealed with a rubber septum, removed from the glovebox, and allowed to cool to 0 ℃. Under N_2, *n*BuLi (18.9 mL. 2.65 M in hexanes, 2.0 equiv) was added by syringe pump over an hour. Vinyllithium formation was observed as white suspension in the reaction flask within 2-3 min of initial *n*BuLi addition. Upon completion of slow addition at 0 ℃, the flask was allowed to warm to room temperature and stir for 2 h. The reaction flask was then sealed, and returned to an Ar-filled glovebox. The vinyllithium suspension was vacuum filtered through a fritted funnel and the solid vinyllithium was consecutively washed with pentane (3x 30 mL), then dried under reduced pressure. Caution should be taken with the pentane filtrate, as organotin waste is toxic and is to be disposed of accordingly. Caution should be taken with the dry vinyllithium, as it is a very fine powder and pyrophoric. The solid vinyllithium was dissolved in THF (approximately 40 mL) and then filtered through acrodisc syringe filters to afford the vinyllithium solution in quantitative yield as pale yellow solution which is stored under Ar in the freezer of the glovebox. The molarity of the solution is determined by titration with BHT in the presence of 1,10- phenanthroline and generally ranges from 1.3 – 1.9 M.

Note: Freshly titrated good quality (clear or pale yellow and particulate free) *n*BuLi was used to afford the vinyllithium solution as pale yellow solution. Older bottles of *n*BuLi that have turned darker yellow and cloudy will afford vinyllithium as a dark yellow or orange solution in THF.

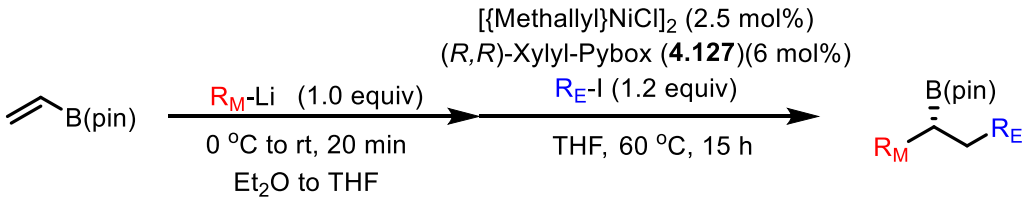
4.9.2.1.4 Optimization of Conjunctive Coupling with Unactivated and Activated Electrophiles



Entry	R_E	X	Ni source	Additive	Solvent	Temp (°C)	Time (h)	yield (%)	er
1	-$(CH_2)_3$Ph	I	NiCl	none	THF	60	18	0	NA
2	-$(CH_2)_3$Ph	I	$Ni(OTf)_2$	none	THF	60	18	0	NA
3	-$(CH_2)_3$Ph	I	$NiBr_2$(glym)	none	THF	60	18	<5	ND
4	-$(CH_2)_3$Ph	I	$NiCl_2$(glym)	none	THF	60	18	35	1:99
5	-$(CH_2)_3$Ph	I	$Ni(acac)_2$	none	THF	60	18	49	2:98
6	-$(CH_2)_3$Ph	I	[MethallylNiCl]$_2$	none	THF	60	18	51	2:98
7	-$(CH_2)_3$Ph	Br	$Ni(acac)_2$	none	THF	60	18	23	2:98
8	-$(CH_2)_3$Ph	Cl	Ni(acac)2	none	THF	60	18	<5	ND
9	-$(CH_2)_3$Ph	OTs	$Ni(acac)_2$	none	THF	60	18	0	NA
10	-$(CH_2)_3$Ph	Br	$Ni(acac)_2$	NaI	THF	60	18	47	1:99
11	-$(CH_2)_3$Ph	Cl	$Ni(acac)_2$	NaI	THF	60	18	0	NA
12	-$(CH_2)_3$Ph	I	$Ni(acac)_2$	LiCl	THF	60	18	<10	ND
13	-$(CH_2)_3$Ph	I	$Ni(acac)_2$	nBu$_4$Cl	THF	60	18	<10	ND
14	-$(CH_2)_3$Ph	I	$Ni(acac)_2$	LiOH	THF	60	18	37	1:99
15	-$(CH_2)_3$Ph	I	$Ni(acac)_2$	none	THF:ACN (1:1)	60	18	26	ND
16	-$(CH_2)_3$Ph	I	$Ni(acac)_2$	none	THF: DMA (1:1)	60	18	25	ND
17	-$(CH_2)_3$Ph	I	$Ni(acac)_2$	none	THF: $PhCF_3$	60	18	<10	ND
18[a]	-$(CH_2)_3$Ph	I	[MethallylNiCl]$_2$	none	THF	60	15	55	1:99
19[a,b]	**-$(CH_2)_3$Ph**	**I**	**[MethallylNiCl]$_2$**	**none**	**THF**	**60**	**15**	**70**	**99:1**
20	-CH_2(CO)OMe	Br	$Ni(acac)_2$	none	THF	rt	15	34	50:50
21	-CH_2(CO)OMe	Br	$Ni(acac)_2$	NaI	THF	60	15	92	50:50
22	-CH_2(CO)OMe	Br	$Ni(acac)_2$	NaI	THF	rt	15	84	50:50
23	-CH_2(CO)OMe	Br	Ni(acac)2	NaI	THF	0	15	51	50:50
24	-CH_2(CO)OMe	Br	none	none	THF	rt	15	25	50:50
25	-CH_2(CO)OMe	Br	none	NaI	THF	rt	15	36	50:50
26[c]	-CH_2(CO)OMe	Br	[MethallylNiCl]$_2$	NaI	THF	rt	15	48	50:50
27[c]	**-CH_2(CO)OMe**	**Br**	**$Ni(acac)_2$**	**NaI**	**THF**	**rt**	**15**	**91**	**50:50**
28[d]	-CH_2(CO)OMe	Br	$Ni(acac)_2$	NaI	THF	rt	15	92	50:50

a= 1.5 h catalyst complexation time instead of 0.5 h.
b= (R,R)-3,5-Me-Ph-Pybox used instead of (S,S)-Ph-pybox
c= 3 mol% $Ni(acac)_2$
d= reaction conducted in the dark

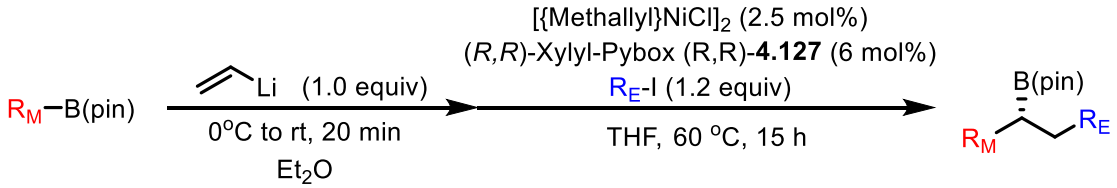
4.9.2.1.5 General Procedures for Conjunctive Coupling



Method A: (migrating group introduced as organolithium reagent, using unactivated alkyl iodide electrophiles)

In a glovebox under argon, an oven-dried 2-dram vial equipped with a magnetic stir bar was charged with (*R*,*R*)-3,5-dimethylphenyl-Pybox **(*R*,*R*)-Xylyl-Pybox (*R*,*R*)-4.127** (7.7 mg, 0.018 mmol, 0.06 equiv), methallylnickel chloride dimer (1 mL of 0.0075 M stock solution in THF prepared with sonication, 0.0075 mmol, 0.025 equiv) and this catalyst solution was allowed to stir for 1.5 h at room temperature. In the glovebox, a second oven-dried 2-dram vial equipped with a magnetic stir bar was charged with 4,4,5,5-tetramethyl-2-vinyl-1,3,2-dioxaborolane **4.87** (46.2 mg, 0.30 mmol, 1.00 equiv), and diethyl ether (0.5 mL), sealed with a septum cap, and removed from the glovebox. Under positive nitrogen pressure, the vial was allowed to cool to 0 ºC, and organolithium solution (0.30 mmol, 1.0 equiv) was added dropwise. The vial was allowed to warm to room temperature and stir for 20 min. The solution was then evaporated to dryness under reduced pressure and was brought back into the glovebox. In the glovebox, the residue in the vessel was re-dissolved in tetrahydrofuran (0.70 mL). To the vial was added alkyl iodide (0.36 mmol, 1.20 equiv) followed by the methallylnickel chloride dimer/**(*R*,*R*)-Xylyl-Pybox (*R*,*R*)-4.127** solution, and tetrahydrofuran (0.2 mL) (used to rinse the catalyst vial). The vial was sealed with a

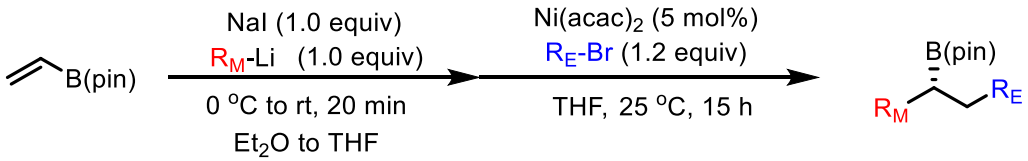
polypropylene cap, taped, and brought out of the glovebox where it was allowed to stir at 60 ºC for 15 h. The resulting solution was allowed to cool to room temperature, filtered through a silica gel plug with diethyl ether, concentrated under reduced pressure, and subsequently purified by silica gel chromatography to provide the observed products.



Method B: (migrating group introduced as boronic ester, using unactivated alkyl iodide electrophiles)

In a glovebox under argon, an oven-dried 2-dram vial equipped with a magnetic stir bar was charged with (*R*,*R*)-3,5-dimethylphenyl-Pybox **(*R*,*R*)-Xylyl-Pybox (*R*,*R*)-4.127** (7.7 mg, 0.018 mmol, 0.06 equiv), methallylnickel chloride dimer (1 mL of 0.0075 M stock solution in THF prepared with sonication, 0.0075 mmol, 0.025 equiv) and this catalyst solution was allowed to stir for 1.5 h at room temperature. In the glovebox, a second oven-dried 2-dram vial equipped with a magnetic stir bar was charged with boronate (0.30 mmol, 1.00 equiv), and tetrahydrofuran (0.5 mL), sealed with a septum cap, and removed from the glovebox. Under positive nitrogen pressure, the vial was allowed to cool to 0 ºC, and vinyllithium solution in tetrahydrofuran (0.30 mmol, 1.0 equiv) was added dropwise. The vial was allowed to warm to room temperature and stir for 20 min before being brought back into the glovebox. To the vial was added alkyl iodide (0.36 mmol, 1.20 equiv) followed by the methallylnickel chloride dimer/**(*R*,*R*)-Xylyl-Pybox (*R*,*R*)-4.127** solution,

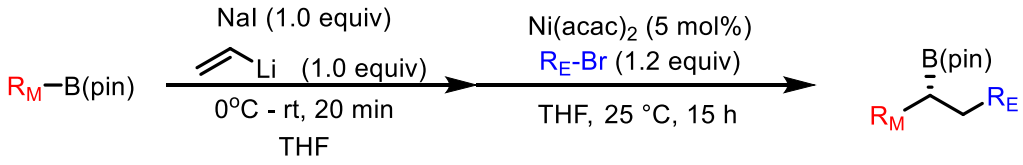
and tetrahydrofuran (0.2 mL) (used to rinse the catalyst vial). The vial was sealed with a polypropylene cap, taped, and brought out of the glovebox where it was allowed to stir at 60 ºC for 15 h. The resulting solution was allowed to cool to room temperature, filtered through a silica gel plug with diethyl ether, concentrated under reduced pressure, and subsequently purified by silica gel chromatography to provide the observed products.



Method C: (migrating group introduced as organolithium reagent, using activated alkyl bromide electrophiles)

In the glovebox, an oven-dried 2-dram vial equipped with a magnetic stir bar was charged with sodium iodide (44.9 mg, 0.3 mmol, 1.0 equiv), 4,4,5,5-tetramethyl-2-vinyl-1,3,2-dioxaborolane **4.87** (46.2 mg, 0.30 mmol, 1.00 equiv), and diethyl ether (0.5 mL), sealed with a septum cap, and removed from the glovebox. Under positive nitrogen pressure, the vial was allowed to cool to 0 ºC, and organolithium solution (0.30 mmol, 1.0 equiv) was added dropwise. The vial was allowed to warm to room temperature and stir for 20 min. The solution was then evaporated to dryness under reduced pressure and was brought back into the glovebox. In the glovebox, the residue in the vessel was redissolved in tetrahydrofuran (0.70 mL). To the vial was added alkyl bromide (0.36 mmol, 1.20 equiv) followed by nickel acetylacetonate (1 mL of 0.015 M stock solution in THF prepared with sonication, 0.015 mmol, 0.05 equiv), and tetrahydrofuran (0.2 mL) (used to rinse the nickel

solution vial). The vial was sealed with a polypropylene cap, taped, and brought out of the glovebox where it was allowed to stir at 25 ºC for 15 h. The resulting solution was allowed to cool to room temperature, filtered through a silica gel plug with diethyl ether, concentrated under reduced pressure, and subsequently purified by silica gel chromatography to provide the observed products.



Method D: (migrating group introduced as boronic ester, using activated alkyl bromide electrophiles)

In the glovebox, an oven-dried 2-dram vial equipped with a magnetic stir bar was charged with sodium iodide (44.9 mg, 0.3 mmol, 1.0 equiv), boronate (0.30 mmol, 1.00 equiv), and diethyl ether (0.5 mL), sealed with a septum cap, and removed from the glovebox. Under positive nitrogen pressure, the reaction vial was allowed to cool to 0 ºC, and vinyllithium solution in tetrahydrofuran (0.30 mmol, 1.0 equiv) was added dropwise. The vial was allowed to warm to room temperature and stir for 20 min before being brought back into the glovebox. To the vial was added alkyl bromide (0.36 mmol, 1.20 equiv) followed by nickel acetylacetonate (1 mL of 0.015 M stock solution in THF prepared with sonication, 0.015 mmol, 0.05 equiv), and tetrahydrofuran (0.2 mL) (used to rinse the catalyst vial). The vial was sealed with a polypropylene cap, taped, and brought out of the glovebox where it was allowed to stir at 25 ºC for 15 h. The resulting solution was allowed

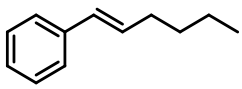
to cool to room temperature, filtered through a silica gel plug with diethyl ether, concentrated under reduced pressure, and subsequently purified by silica gel chromatography to provide the observed products.

4.9.2.1.6 General Method for Oxidation of Boronic Ester Products:

Note: Where appropriate, boronic ester products were oxidized. In these cases, the procedure used was the same as that described in the above method but with the modification that: the unpurified or purified boronic ester product was diluted with tetrahydrofuran (3 mL). (While we have never experienced any adverse events working with hydrogen peroxide, due to its potential danger, a blast shield was placed in front of the reaction vessel.) The unpurified mixture was allowed to cool to 0 ºC and a 3 M solution of aqueous NaOH (2 mL) and 30% H_2O_2 (1.0 mL) were added dropwise. The reaction mixture was allowed to warm to room temperature and stir for 3 h. The reaction mixture was allowed to cool to 0 ºC and a saturated solution of aqueous $Na_2S_2O_3$ (3 mL) was added dropwise. After warming to room temperature the product was extracted from the aqueous layer with ethyl acetate (3 x 20 mL). The combined organic layers were dried over Na_2SO_4, concentrated under reduced pressure, and subsequently purified by silica gel chromatography to provide the desired products.

4.9.2.1.7 Deuterium-Labeling Experiments

The *trans*-deuterium labeled vinyllithium was prepared according to the literature procedure[14]. To an oven-dried 25 mL round bottom flask equipped with a magnetic stir bar in the glovebox was added bis(tributylstannyl)ethylene (1.818 g, 3.00 mmol, 1.0 equiv), and THF (3 mL), sealed with rubber septum, and removed from glovebox. The reaction flask was allowed to cool to -78 0 ºC, and *n*-butyllithium (3.30 mmol, 1.1 equiv) was added dropwise. The reaction flask was allowed to stir for 2 h at -78 0 ºC. Then acetic acid-d_4 was added dropwise at -78 0 ºC. The reaction mixture was allowed to warm to room temperature and quenched with a saturated solution of aqueous sodium bicarbonate. The product was extracted from the aqueous layer with hexane (3 x 20 mL). The combined organic layers were dried over Na_2SO_4, filtered through a neutral alumina pad, and concentrated under reduced pressure. The resultant residue from the last step was brought into the glovebox without further purification and transferred into an oven-dried 25 mL round bottom flask equipped with a magnetic stir bar, diluted with THF (3 mL), sealed with a rubber septum, and removed from glovebox. The flask was allowed to cool to -78 0 ºC, and *n*-butyllithium (3.00 mmol, 1.0 equiv) was added dropwise. The reaction flask was allowed to stir for an additional 2 h at -78 0 ºC. Upon completion, the *trans*-deuterium labeled vinyllithium solution was allowed to warm to room temperature, titrated, and used in conjunctive cross couplings.

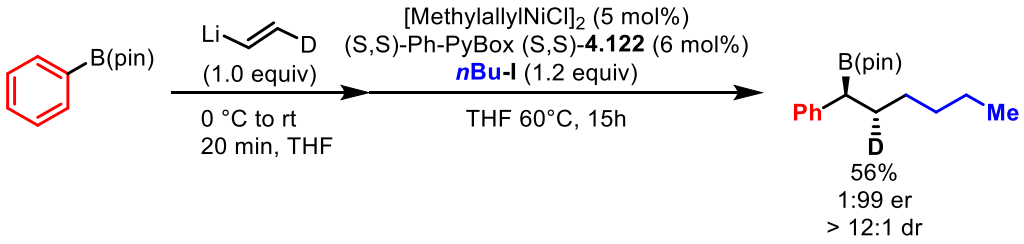


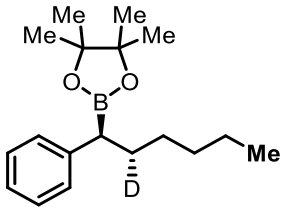
(*E*)-Hex-1-en-1-ylbenzene (4.274). A 25 mL oven-dried round bottom flask with stirbar was charged with K_2CO_3 (0.2116 g, 1.531 mmol, 1.0 equiv), $Pd(OAc)_2$ (0.0172 g, 0.077 mmol, 0.05 equiv), PPh_3 (0.0803 g, 0.306 mmol, 0.2 equiv), PhOTf (0.3462 g, 1.531 mmol, 1.0 equiv), (*E*)-2-(hex-1-en-1-yl)-5,5-dimethyl-1,3,2-dioxaborinane, *n*-hexyl-B(neo)[71] (0.4503 g, 2.29 mmol, 1.5 equiv), and was purged with nitrogen. To the round bottom flask was added 3 mL of dried and degassed DMF, a reflux condenser was attached to the round bottom flask and the reaction was allowed to stir at 90 ºC overnight. In the morning the reaction was allowed to cool to room temperature and the DMF was removed with three aqueous washes, and the resulting reaction solution was dried with Na_2SO_4, concentrated under reduced pressure, and purified by automated silica gel chromatography (Biotage 1% → 3% ethyl acetate in hexanes) to afford colorless oil (283.3 mg, 77% yield). All spectral data was in accord with the literature.[72]

[71] For representative procedure to prepare the pinacol ester see (a) Edelstein, E. K.; Namirembe, S.; Morken, J. P. *J. Am. Chem. Soc.* **2017**, 139, 5027. For characterization data of the neopentyl ether see (b) Althaus, M.; Mahmood, A.; Suarez, J. R.; Thomas, S. P.; Aggarwal, V. K. *J. Am. Chem. Soc.* **2010**, 132, 5922.

[72] Cahiez, G.; Gager, O.; Buendia, J.; Patinote, C. *Chem. Eur. J.* **2012**, 5860.

Procedure for the Conjunctive Coupling with *Trans*-Deuterium-Labeled Vinyllithium with Unactivated Electrophile.



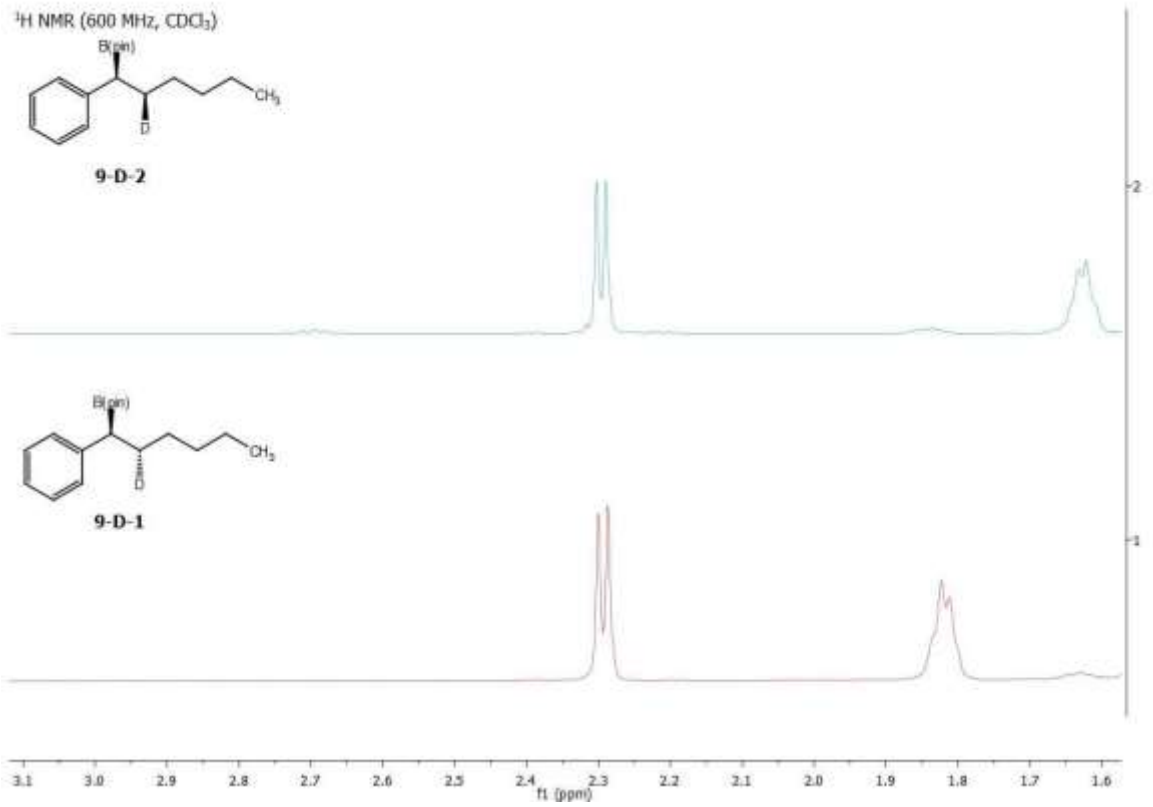


4,4,5,5-Tetramethyl-2-((1*S*,2*S*)-1-phenylhexyl-2-d)-1,3,2-dioxaboro lane (4.158). The reaction was performed according to the general procedure (***Method B***) with 4,4,5,5-tetramethyl-2-phenyl-1,3,2-dioxaborolane (**4.265**) (61.2 mg, 0.30 mmol, 1.00 equiv), *trans*-deuterium-labeled vinyllithium (0.54 mL, 0.56 M in tetrahydrofuan, 0.30 mmol, 1.00 equiv), *n*-butyl iodide (66.2 mg, 0.36 mmol, 1.2 equiv), 2,6-bis[(4*S*)-phenyl-2-oxazolin-2-yl]pyridine **(*S*,*S*)-4.122** (6.6 mg, 0.018 mmol, 0.018 equiv), methallyl nickel chloride dimer (2.2 mg, 0.0075 mmol, 0.025 equiv, 0.0075 M stock solution in THF prepared with sonication). The unpurified product was purified by automated silica gel chromatography (Biotage 1% → 2% ethyl acetate in hexanes, stained in CAM) to afford clear oil (48.6 mg, 56 % yield). **^{1}H NMR** (600 MHz, $CDCl_3$) δ 7.28 – 7.23 (m, 2H), 7.23 – 7.18 (m, 2H), 7.15 – 7.08 (m, 1H), 2.29 (d, *J* = 8.2 Hz, 1H), 1.88 – 1.73 (m, 1H), 1.67 – 1.59 (m, 0.08H), 1.32 – 1.23 (m, 6H), 1.21 (s, 6H), 1.19 (s, 6H), 0.88 – 0.80 (m, 3H). **^{11}B NMR** (160 MHz, $CDCl_3$) δ 33.08. **^{13}C NMR** (151 MHz, $CDCl_3$) δ 143.73, 128.56, 128.41, 125.25, 83.42, 32.38 (t, *J*=19.3), 32.03, 29.08, 24.86, 24.80, 22.77,

14.27, (C-B not observed). **IR** (neat) ν_{max} 2976.85 (w), 2957.24 (w), 2924.16 (m), 2856.34 (w), 1452.51 (w), 1358.78 (m), 1272.09 (w), 1214.14 (w), 114.46 (s), 968.62 (m), 851.40 (w), 700.42 (m) cm^{-1}. **HRMS** (DART) for $C_{18}H_{28}DBO_2$ $[M+NH_4]^+$: calculated: 290.2402, found: 290.2406. $[\alpha]_D^{20}$ = +15.858 (*c* 1.02, $CHCl_3$, *l* = 50 mm).

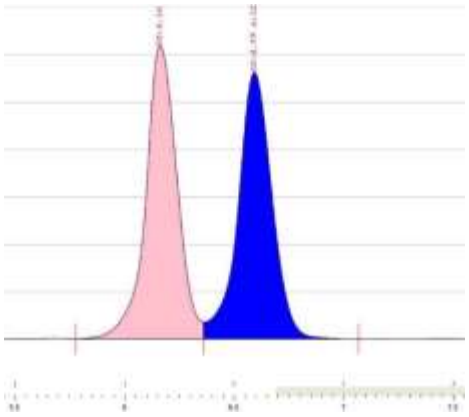
Determination of Stereochemical Identity: A stereoisomer mixture was prepared by mixing the R and S enantiomer products of reactions run according to the general procedure (***Method B***) with [methallylNiCl]$_2$ (2.5 mol%) and (*S,S*)-Ph-Pybox **(*S*,*S*)-4.122** (3.0 mol%), or (*R,R*)-Ph-Pybox **(*R*,*R*)-4.122** (3.0 mol%) as the catalyst. [Note: non-deuterium-labeled stereoisomer mixture of product **4.174** was used]. Absolute stereochemistry was assigned by analogy (see product **4.192**) and by comparison to authentic sample **4.158** of known configuration. Product was oxidized according to ***General Method for Oxidation of Boronic Ester Products.***

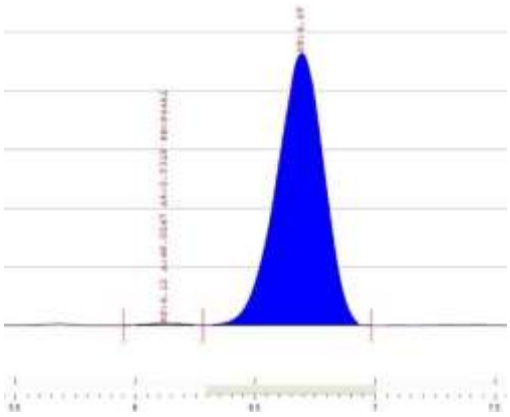
Diastereoselectivity was determined by ^1H NMR.



SFC (Chiracel OD-H, 5% IPA, 3 mL/min, 100 bar, 35 °C, 210-270 nm) – analysis of(1S,2S)-1-phenylhexan-2-d-1-ol.

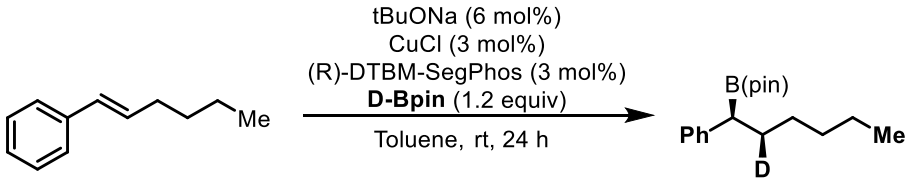
Stereoisomer mixture Standard Conditions

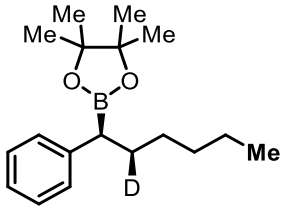




Peak No	% Area	Area	RT (min)	Peak No	% Area	Area	RT (min)
1	50.3224	12276.9642	6.16	1	0.5318	68.0267	6.12
2	49.6776	12119.6412	6.59	2	99.4682	12723.5991	6.69
Total:	100	24396.6054		Total:	100	12791.6258	

Procedure for the Preparation of Authentic Deuterium-Labeled Product.





4,4,5,5-Tetramethyl-2-((1*S*,2*R*)-1-phenylhexyl-2-d)-1,3,2-dioxaboro lane (epi-4.158). The reaction was performed according to the literature procedure[73] with *trans*-1-phenyl-1-hexene (160.3 mg, 1.0 mmol, 1.00 equiv), sodium *tert*-butoxide (5.77 mg, 0.06 mmol, 0.06 equiv), copper (I) chloride (2.97 mg, 0.030 mmol,

[73] Noh, D.; Yoon, S. K.; Won, J.; Lee, J. Y.; Yun. *J. Chem. An Asian J.* **2011**, 1967.

0.03 equiv), (*R*)-DTBM-SegPhos (35.39 mg, 0.030 mmol, 0.03 equiv), 4,4,5,5-tetramethyl-1,3,2-dioxaborolane-2-d[74] and toluene. The unpurified product was purified by automated silica gel chromatography (Biotage 1% → 2% ethyl acetate in hexanes, stained in CAM) to afford a clear oil (39.5 mg, 45 % yield).

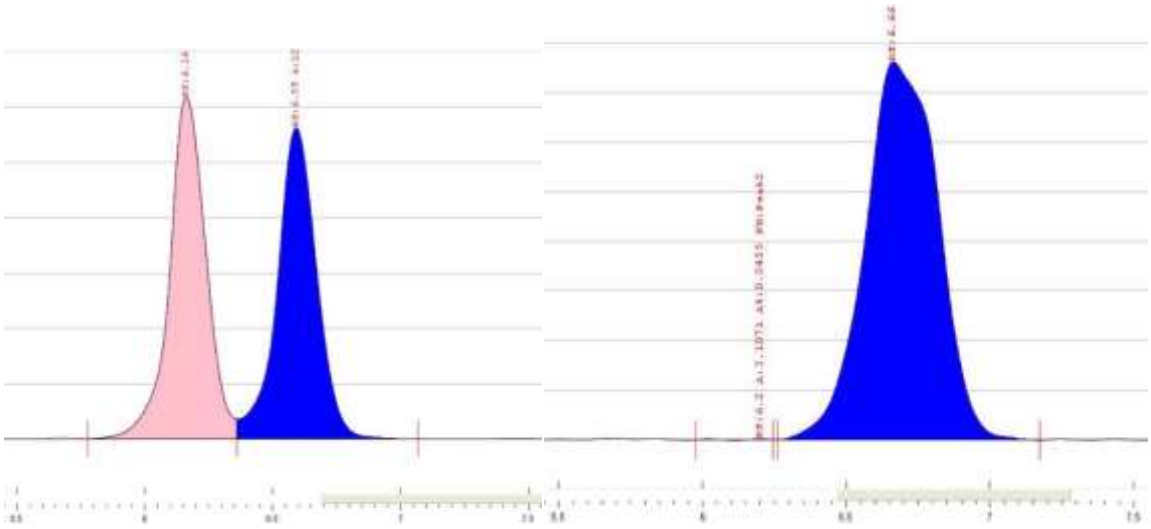
^{1}HNMR (600 MHz, $CDCl_3$) δ 7.28 – 7.23 (m, 2H), 7.23 – 7.18 (m, 2H), 7.15 – 7.10 (m, 1H), 2.30 (d, *J* = 7.8 Hz, 1H), 1.88 – 1.80 (m, 0.08H), 1.69 – 1.57 (m, 1H), 1.31 – 1.24 (m, 6H), 1.21 (s, 6H), 1.19 (s, 6H), 0.90 – 0.81 (m, 3H). **^{11}B NMR** (160 MHz, $CDCl_3$) δ 33.091. **^{13}C NMR** (151 MHz, $CDCl_3$) δ 143.75, 128.56, 128.42, 125.25, 83.43, 32.39 (t, *J*=19.4), 32.04, 29.10, 24.86, 24.80, 22.78, 14.28, 14.27. **IR** (neat) ν_{max} 2976.79 (w), 2957.24 (w), 2921.65 (m), 2856.55 (w), 1492.73 (w), 1452.09 (w), 1358.89 (m), 1321.01 (s), 1269.92 (w), 1214.06 (w), 1141.76 (s), 966.38 (m), 849.52 (m), 699.89 (m) cm^{-1}. **HRMS** (DART) for $C_{18}H_{28}DBO_2$ $[M+NH_4]^+$: calculated: 290.2402, found: 290.2406. $[\alpha]_D^{20}$ = –18.651 (*c* 2.60, $CHCl_3$, *l* = 50 mm).

Determination of Stereochemical Identity: [Note: non-deuterium-labeled stereoisomer mixture of **4.174** was used]. Absolute stereochemistry was assigned by analogy.[73] Product was oxidized according to ***General Method for Oxidation of Boronic Ester Products.***

SFC (Chiracel OD-H, 5% IPA, 3 mL/min, 100 bar, 35 °C, 210-270 nm) – analysis of (1S,2R)-1-phenylhexan-2-d-1-ol.

Stereoisomer Mixture Standard Conditions

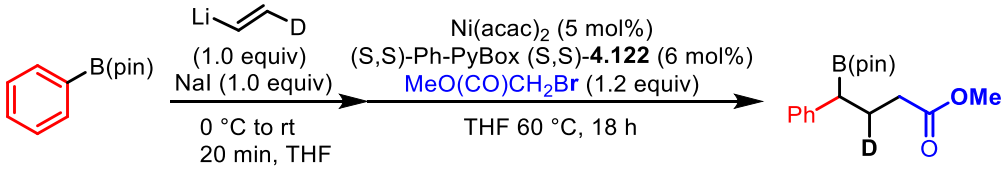
[74] Ely, R. J.; Morken, J. P. *J. Am. Chem. Soc.* **2010**, 132, 2534.

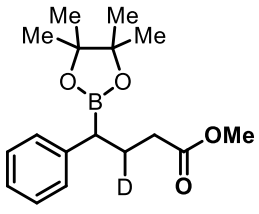


Peak No	% Area	Area	RT (min)
1	50.3224	12276.9642	6.16
2	49.6776	12119.6412	6.59
Total:	100	24396.6054	

Peak No	% Area	Area	RT (min)
1	0.0455	3.1071	6.2
2	99.9545	6821.4348	6.66
Total:	100	6824.5419	

Procedure for the Conjunctive Coupling with *Trans*-Deuterium-Labeled Vinyllithium with Activated Electrophile.

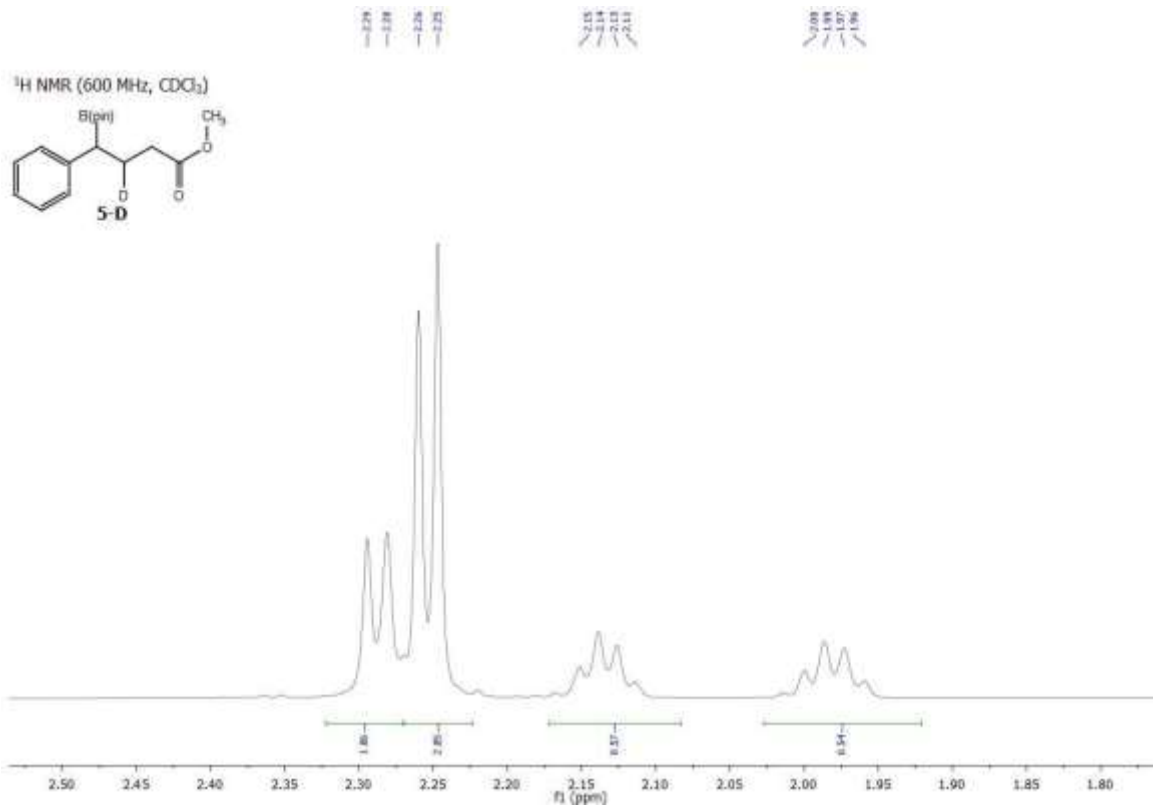




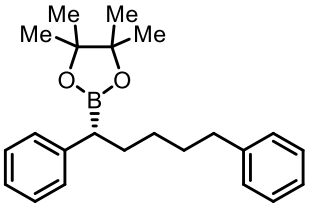
Methyl 4-phenyl-4-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)butan oate-3-d (4.157). The reaction was performed according to the general procedure (***Method D, with the modification that Ni/Ligand catalyst solution was used as in Method A)*** with 4,4,5,5-tetramethyl-2-phenyl-1,3,2-dioxaborolane (**4.265**) (61.2 mg, 0.30 mmol,

1.00 equiv), *trans*-deuterium-labeled vinyllithium (0.54 mL, 0.56 M in tetrahydrofuan, 0.30 mmol, 1.00 equiv), sodium iodide (44.9 mg, 0.30 mmol, 1.00 equiv), methyl 2-bromoacetate (55.1 mg, 0.36 mmol, 1.2 equiv), 2,6-bis[(4*S*)-phenyl-2-oxazolin-2-yl]pyridine (*S*,*S*)-**4.122** (6.6 mg, 0.018 mmol, 0.018 equiv), nickel acetylacetonate (3.9 mg, 0.015 mmol, 0.05 equiv, 0.015 M stock solution in THF prepared with sonication). The unpurified product was purified by automated silica gel chromatography (Biotage 1% → 4% ethyl acetate in hexanes, stained in CAM) to afford clear oil (86.1 mg, 94 % yield). **^{1}H NMR** (600 MHz, $CDCl_3$) δ 7.25 (t, *J* = 7.5 Hz, 2H), 7.18 (d, *J* = 7.5 Hz, 2H), 7.13 (t, *J* = 7.3 Hz, 1H), 3.62 (s, 3H), 2.29 (d, *J* = 8.0 Hz, 1H), 2.25 (d, *J* = 7.8 Hz, 2H), 2.13 (aap q, *J* = 7.5 Hz, 0.57H), 1.98 (ap q, *J* = 8.1 Hz, 0.54H), 1.21 (s, 6H), 1.18 (s, 6H). **^{11}B NMR** (160 MHz, $CDCl_3$) δ 32.88. **^{13}C NMR** (151 MHz, $CDCl_3$) δ 174.19, 142.27, 128.66, 128.58, 125.67, 83.61, 51.56, 33.53, 31.71 (C-B), 27.46 (t, *J*= 19.7 Hz), 24.82, 24.75. **IR** (neat) ν_{max} 2977.57 (w), 2950.58 (w), 1735.91 (s), 1436.23 (w), 1358.53 (s), 1320.93 (s), 1270.50 (m), 1196.67 (m), 1166.01 (m), 1139.15 (s), 1031.49 (w), 967.61 (m), 847.94 (m), 766.74 (w), 700.67 (s), 578.37 (w), 514.17 (w) cm^{-1}. **HRMS** (DART) for $C_{17}H_{24}DBO_4$ $[M+H]^+$: calculated: 306.1987, found: 306.1979.

Determination of Stereochemical Identity: *Diastereoselectivity was assigned by ^{1}H NMR analysis.*



4.9.2.1.8 Characterization of Conjunctive Coupling Products and Determination of Stereochemical Identity



(R)-2-(1,5-Diphenylpentyl)-4,4,5,5-tetramethyl-1,3,2-dioxaborolane (4.121). The reaction was performed according to the general procedure (***Method A)*** with 4,4,5,5-tetramethyl-2-vinyl-1,3,2-dioxaborolane **4.87** (46.2 mg, 0.30 mmol, 1.00 equiv), phenyllithium (0.16 mL, 1.9 M in dibutyl ether, 0.3 mmol, 1.0 equiv), (3-iodopropyl)benzene (88.6 mg, 0.36 mmol, 1.2 equiv), (*R*,*R*)-3,5-dimethylphenyl-Pybox

(*R*,*R*)-Xylyl-Pybox (*R*,*R*)-4.127 (7.7 mg, 0.018 mmol, 0.06 equiv), methallylnickel chloride dimer (2.2 mg, 0.0075 mmol, 0.025 equiv, 0.0075 M stock solution in THF prepared with sonication). The unpurified product was purified by automated silica gel chromatography (Biotage 1% → 2% ethyl acetate in hexanes, stained in CAM) to afford clear oil (73.6 mg, 70 % yield).

(***Method B)*** with 4,4,5,5-tetramethyl-2-phenyl-1,3,2-dioxaborolane (**4.265**) (61.2 mg, 0.30 mmol, 1.00 equiv), vinyllithium (0.19 mL, 1.58 M in tetrahydrofuran, 0.30 mmol, 1.00 equiv), (3-iodopropyl)benzene (88.6 mg, 0.36 mmol, 1.2 equiv), (*R*,*R*)-3,5-dimethylphenyl-Pybox **(*R*,*R*)-Xylyl-Pybox** (*R*,*R*)-**4.127** (7.7 mg, 0.018 mmol, 0.06 equiv), methallylnickel chloride dimer (2.2 mg, 0.0075 mmol, 0.025 equiv, 0.0075 M stock solution in THF prepared with sonication). The unpurified product was purified by automated silica gel chromatography (Biotage 1% → 2% ethyl acetate in hexanes, stained in CAM) to afford clear oil (70.4 mg, 67 % yield).

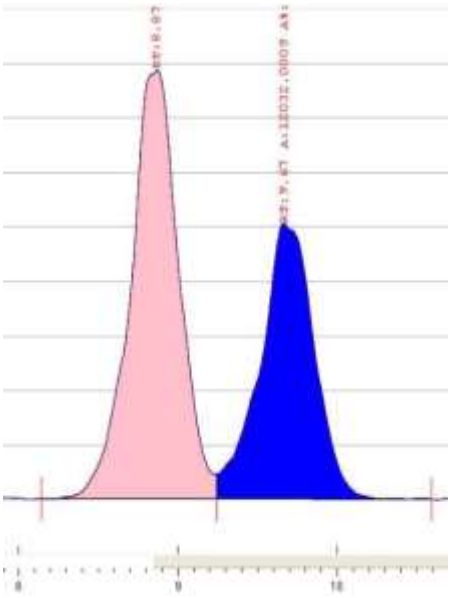
^{1}H NMR (600 MHz, $CDCl_3$) δ 7.28 – 7.24 (m, 4H), 7.23 – 7.20 (m, 2H), 7.18 – 7.12 (m, 4H), 2.63 – 2.53 (m, 2H), 2.31 (app t, J = 7.9 Hz, 1H), 1.95 – 1.83 (m, 1H), 1.73 – 1.67 (m, 1H), 1.66 – 1.59 (m, 2H), 1.38 – 1.30 (m, 2H), 1.20 (s, 6H), 1.17 (s, 6H). **^{11}B NMR** (160 MHz, $CDCl_3$) δ 33.21. **^{13}C NMR** (151 MHz, $CDCl_3$) δ 143.60, 143.02, 128.61, 128.56, 128.46, 128.40, 125.73, 125.32, 83.45, 36.03, 32.73, 32.61 (C-B, partially buried), 31.66, 29.16, 25.03, 24.84, 24.79. **IR** (neat) ν_{max} 2976.93 (m), 2928.64 (m), 2855.88 (m), 1493.81 (w), 1452.64 (w), 1359.31 (s), 1321.55 (s), 1142.41 (s), 966.88 (m), 849.87 (m), 699.07 (s)

cm^{-1}. **HRMS** (DART) for $C_{23}H_{31}BO_2$ $[M+H]^+$ calculated: 351.2495, found: 351.2508. $[\alpha]^{20}_D$: –11.778 (*c* 2.430, $CHCl_3$, *l* =50 mm).

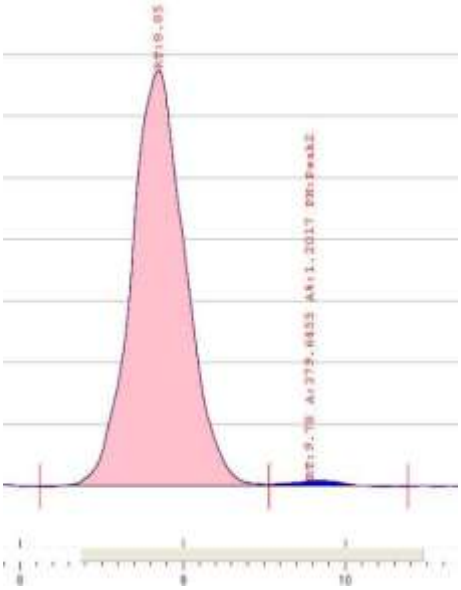
Determination of Stereochemical Identity: A stereoisomer mixture was prepared by mixing the R and S enantiomer products of reactions run according to the general procedure (***Method B***) with [{methallyl}NiCl]$_2$ (2.5 mol%) and (*S,S*)-Ph-Pybox (S,S)-**4.122** (3.0 mol%), or (*R,R*)-Ph-Pybox (R,R)-**4.122** (3.0 mol%) as the catalyst. Absolute stereochemistry was assigned by analogy (see products: **4.192** and **epi-4.158**).

SFC (Chiracel OJ-H, 2% IPA, 3 mL/min, 100 bar, 35 °C, 210-270 nm) – analysis of (R)-2-(1,5-diphenylpentyl)-4,4,5,5-tetramethyl-1,3,2-dioxaborolane.

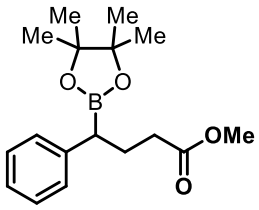
Stereoisomer mixture



Standard Conditions



Peak No	% Area	Area	RT (min)	Peak No	% Area	Area	RT (min)
1	58.142	16712.7717	8.87	1	98.7983	31212.6504	8.85
2	41.858	12032.0009	9.67	2	1.2017	379.6455	9.78
Total:	100	28744.7726		Total:	100	31592.2959	



Methyl 4-Phenyl-4-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)butan oate (4.146). The reaction was performed according to general (***Method C)*** with 4,4,5,5-tetramethyl-2-vinyl-1,3,2-dioxaborolane **4.87** (46.2 mg, 0.30 mmol, 1.00 equiv), phenyllithium (0.16 mL, 1.9 M in dibutyl ether, 0.3 mmol, 1.0 equiv), sodium iodide (44.9 mg, 0.30 mmol, 1.00 equiv) methyl 2-bromoacetate (55.1 mg, 0.36 mmol, 1.2 equiv), nickel acetylacetonate (3.9 mg, 0.015 mmol, 0.05 equiv, 0.015 M stock solution in THF prepared with sonication). The unpurified product was purified by automated silica gel chromatography (Biotage 1% → 4% ethyl acetate in hexanes, stained in CAM) to afford clear oil (83.9 mg, 92 % yield).

(***Method D)*** with 4,4,5,5-tetramethyl-2-phenyl-1,3,2-dioxaborolane (**4.265**) (61.2 mg, 0.30 mmol, 1.00 equiv), vinyllithium (0.19 mL, 1.58 M in tetrahydrofuran, 0.30 mmol, 1.00 equiv), sodium iodide (44.9 mg, 0.30 mmol, 1.00 equiv), methyl 2-bromoacetate (55.1 mg, 0.36 mmol, 1.2 equiv), nickel acetylacetonate (3.9 mg, 0.015 mmol, 0.05 equiv, 0.015 M stock solution in THF prepared with sonication). The unpurified product was purified by automated silica gel chromatography (Biotage 1% → 4% ethyl acetate in hexanes, stained in CAM) to afford colorless oil (83.9 mg, 92 % yield).

(***Method D, with the modification that Ni/Ligand catalyst solution was used as in Method A)*** with 4,4,5,5-tetramethyl-2-phenyl-1,3,2-dioxaborolane (**4.265**) (61.2 mg, 0.30 mmol, 1.00 equiv), vinyllithium (0.19 mL, 1.58 M in tetrahydrofuran, 0.30 mmol, 1.00 equiv), sodium iodide (44.9 mg, 0.30 mmol, 1.00 equiv), methyl 2-bromoacetate (55.1 mg, 0.36 mmol, 1.2 equiv), (*R*,*R*)-3,5-dimethylphenyl-Pybox **(*R*,*R*)-Xylyl-Pybox** (*R*,*R*)-**4.127** (7.7 mg, 0.018 mmol, 0.06 equiv), nickel acetylacetonate (3.9 mg, 0.015 mmol, 0.05 equiv, 0.015 M stock solution in THF prepared with sonication). The unpurified product was purified by automated silica gel chromatography (Biotage 1% → 5% ethyl acetate in hexanes, stained in CAM) to afford colorless oil (83.0 mg, 91 % yield).

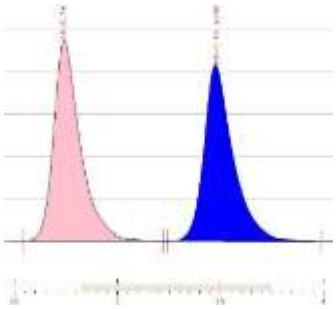
^{1}H NMR (600 MHz, $CDCl_3$) δ 7.25 (t, *J* = 7.4 Hz, 2H), 7.18 (d, *J* = 7.3 Hz, 2H), 7.13 (t, *J* = 7.3 Hz, 1H), 3.62 (s, 3H), 2.32 – 2.23 (m, 3H), 2.15 (app dq, *J* = 15.3, 7.5 Hz, 1H), 2.05 – 1.95 (m, 1H), 1.21 (s, 6H), 1.18 (s, 6H). **^{11}B NMR** (160 MHz, $CDCl_3$) δ 32.79. **^{13}C NMR** (151 MHz, $CDCl_3$) δ 174.18, 142.27, 128.66, 128.58, 125.67, 83.61, 51.56, 33.61, 31.79 (C-B), 27.81, 24.82, 24.75. **IR** (neat) ν_{max} 2977.25 (w), 1735.87 (s), 1436.52 (w), 1436.52 (w), 1362.93 (s), 1362.93 (s), 1321.94 (s), 1248.52 (m), 1211.20 (m), 1138.65 (s), 966.67 (m), 848.19 (m), 764.65 (w), 700.54 (s), 517.68 (w) cm^{-1}. **HRMS** (DART) for $C_{17}H_{25}BO_4$ $[M+H]^+$: calculated: 305.1924, found: 305.1938.

Determination of Stereochemical Identity: A stereoisomer mixture was prepared according to the general procedure (***Method D***) with nickel acetylacetonate (3.9 mg, 0.015

mmol, 0.05 equiv, 0.015 M stock solution in THF prepared with sonication).

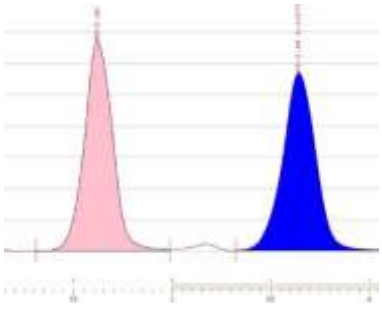
SFC (Chiracel OJ-H, 1% IPA, 3 mL/min, 100 bar, 35 °C, 210-270 nm) – analysis of methyl 4-phenyl-4-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)butanoate.

Stereoisomer Mixture

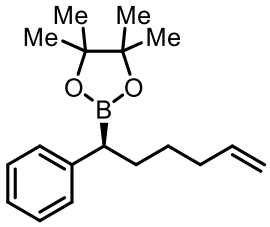


Peak No	% Area	Area	RT (min)
1	50.7883	8522.3145	2.74
2	49.2117	8257.7461	3.48
Total:	100	16780.0606	

Standard Conditions



Peak No	% Area	Area	RT (min)
1	50.0166	13288.6804	2.62
2	49.9834	13279.8692	3.64
Total:	100	26568.5496	



(*S*)-4,4,5,5-Tetramethyl-2-(1-phenylhex-5-en-1-yl)-1,3,2-dioxaborolane (4.159). The reaction was performed according to general (***Method B, with the modification that: (S,S)-Ph-Pybox (S,S)-4.122 rather than* (*R,R*)-Xylyl-Pybox (*R,R*)-4.127 was used***)** with 4,4,5,5-tetramethyl-2-phenyl-1,3,2-dioxaborolane (**4.264**) (61.2 mg, 0.30 mmol, 1.00 equiv), vinyllithium (0.19 mL, 1.58 M in tetrahydrofuran, 0.30 mmol,

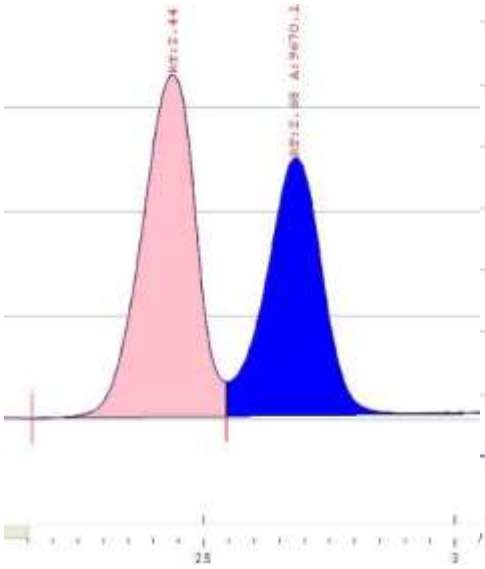
1.00 equiv), (iodomethyl)cyclopropane (65.52 mg, 0.36 mmol, 1.2 equiv), 2,6-Bis[(4*S*)-phenyl-2-oxazolin-2-yl]pyridine (S,S)-**4.122** (6.6 mg, 0.018 mmol, 0.018 equiv), nickel acetylacetonate (3.9 mg, 0.015 mmol, 0.05 equiv, 0.015 M stock solution in THF prepared with sonication). The unpurified product was purified by automated silica gel chromatography (Biotage 1% → 5% ethyl acetate in hexanes, stained in CAM) to afford colorless oil (34.3 mg, 40 % yield). **^{1}H NMR** (600 MHz, $CDCl_3$) δ 7.24 (d, *J* = 8.6 Hz, 2H), 7.20 (d, *J* = 7.2 Hz, 2H), 7.12 (t, *J* = 7.2 Hz, 1H), 5.78 (ddd, *J* = 16.9, 10.2, 6.6 Hz, 1H), 4.97 (dd, 1H), 4.90 (dd, *J* = 17.2, 1.3 Hz, 1H), 2.30 (app t, *J* = 7.9 Hz, 1H), 2.10 – 1.98 (m, *J* = 7.2 Hz, 2H), 1.90 – 1.78 (m, 1H), 1.66 (dddd, *J* = 21.2, 13.4, 8.2, 6.0 Hz, 1H), 1.39 – 1.34 (m, 3H), 1.20 (s, 6H), 1.18 (s, 6H). **^{11}B NMR** (160 MHz, $CDCl_3$) δ 33.08. **^{13}C NMR** (151 MHz, $CDCl_3$) δ 143.51, 139.18, 128.58, 128.46, 125.34, 114.44, 83.48, 77.45, 77.24, 77.03, 34.00, 32.44 (C-B, partially buried), 32.34, 28.82, 24.86, 24.81. **IR** (neat) ν_{max} 2977.32 (w), 2928.25 (w), 2856.29 (w), 1451.81 (w), 1322.29 (s), 1271.74 (w), 1215.28 (w), 1143.03 (s), 966.82 (w), 909.73 (w), 850.10 (w), 700.53 (s) cm^{-1}. **HRMS** (DART) for $C_{18}H_{27}BO_2$ $[M+H]^+$ calculated: 287.2182 found: 287.2194. $[\alpha]^{20}_D$: +11.477 (*c* 0.555, $CHCl_3$, *l* =50 mm).

Determination of Stereochemical Identity: A stereoisomer mixture was prepared by mixing the R and S enantiomer products of reactions run according to the general procedure (***Method B***) with nickel acetylacetonate (3.9 mg, 0.015 mmol, 0.05 equiv 0.015 M stock solution in THF prepared with sonication) and (*S,S*)-Ph-Pybox (S,S)-**4.122** (3.0 mol%), or (*R,R*)-Ph-Pybox (R,R)-**4.122** (3.0 mol%) as the catalyst. Absolute stereochemistry was

assigned by analogy (see products: **4.192** and **epi-4.158**).

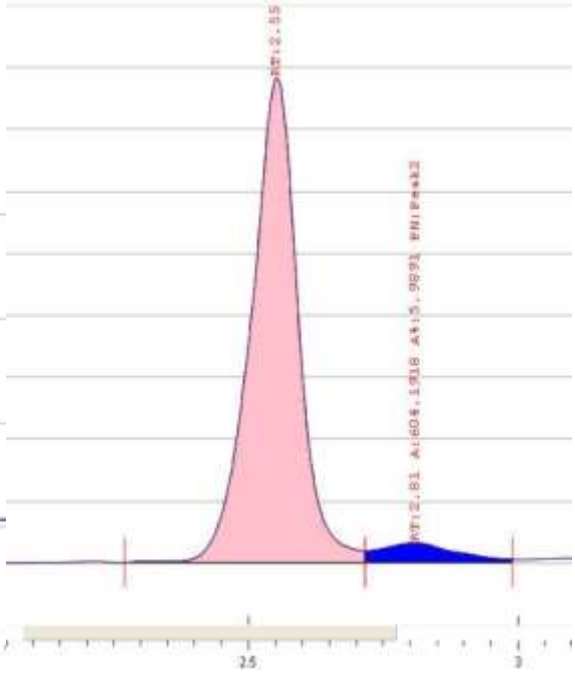
SFC (Chiracel OJ-H, 1% IPA, 3 mL/min, 100 bar, 35 °C, 210-270 nm) – analysis of (S)-4,4,5,5-tetramethyl-2-(1-phenylhex-5-en-1-yl)-1,3,2-dioxaborolane

Stereoisomer Mixture

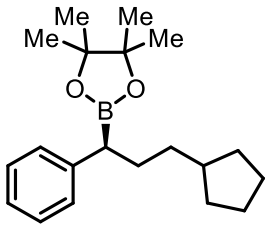


Peak No	% Area	Area	RT (min)
1	55.7633	12189.8132	2.44
2	44.2367	9670.1191	2.68
Total:	100	21859.9323	

Standard Conditions



Peak No	% Area	Area	RT (min)
1	94.0109	9483.9554	2.55
2	5.9891	604.1918	2.81
Total:	100	10088.1472	



(*S*)-2-(3-Cyclopentyl-1-phenylpropyl)-4,4,5,5-tetramethyl-1,3,2-

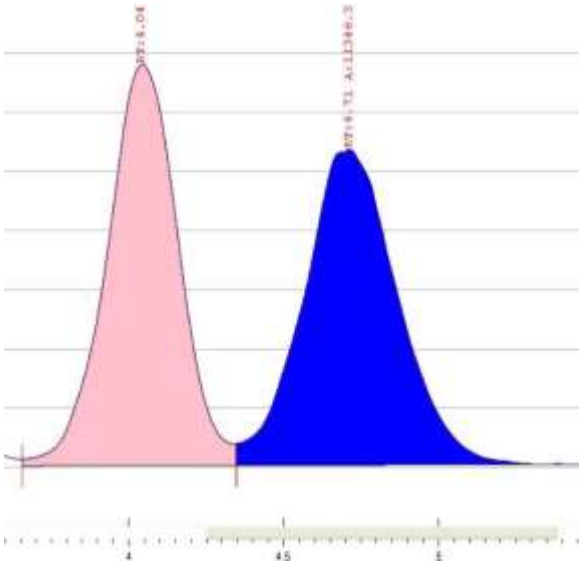
dioxa borolane (4.160). The reaction was performed according to general (***Method B, with the modification that: NaI added as in procedure D, and (S,S)-Ph-Pybox (S,S)-4.122 rather than* (*R*,*R*)-Xylyl-Pybox (R,R)-4.127 was used***)** with 4,4,5,5-tetramethyl-2-phenyl-1,3,2-dioxaborolane (**4.265**) (61.2 mg, 0.30 mmol, 1.00 equiv), vinyllithium (0.19 mL, 1.58 M in tetrahydrofuran, 0.30 mmol, 1.00 equiv), sodium iodide (44.9 mg, 0.30 mmol, 1.00 equiv) 6-bromohex-1-ene (58.7 mg, 0.36 mmol, 1.2 equiv), 2,6-Bis[(4*S*)-phenyl-2-oxazolin-2-yl]pyridine (*S*,*S*)-**4.122** (6.6 mg, 0.018 mmol, 0.018 equiv), nickel acetylacetonate (3.9 mg, 0.015 mmol, 0.05 equiv, 0.015 M stock solution in THF prepared with sonication). The unpurified product was purified by automated silica gel chromatography (Biotage 1% → 5% ethyl acetate in hexanes, stained in CAM) to afford colorless oil (37.7 mg, 40 % yield). **^{1}H NMR** (600 MHz, $CDCl_3$) δ 7.19 (t, *J* = 9.3, 7.4 Hz, 2H), 7.15 (d, *J* = 6.8 Hz, 2H), 7.07 (d, *J* = 7.1 Hz, 1H), 2.22 (app t, *J* = 8.0 Hz, 1H), 1.79 (app dq, *J* = 15.9, 8.0 Hz, 1H), 1.72 – 1.64 (m, 2H), 1.64 – 1.55 (m, 1H), 1.55 – 1.45 (m, 2H), 1.46 – 1.38 (m, 2H), 1.26 – 1.18 (m, 3H), 1.15 (s, 6H), 1.13 (s, 6H), 1.05 – 0.91 (m, 2H). **^{11}B NMR** (160 MHz, $CDCl_3$) δ 33.08. **^{13}C NMR** (151 MHz, $CDCl_3$) δ 143.77, 128.55, 128.42, 125.25, 83.43, 40.38, 36.13, 32.92, 32.87, 31.93, 25.40, 24.88, 24.80. (C-B carbon not observed) **IR** (neat) ν_{max} 2976.51 (w), 2929.62 (m), 2859.77 (w), 1492.33 (w), 1452.32 (w), 1370.05 (s), 1322.09 (s), 1143.30 (s), 966.83 (w), 849.78 (w), 700.49 (m) cm^{-1}. **HRMS** (DART) for $C_{20}H_{31}BO_2$ $[M+H]^+$ calculated: 332.2761 found: 332.276. $[\alpha]^{20}_D$: +15.285 (*c* 0.555, $CHCl_3$, *l* =50 mm).

Determination of Stereochemical Identity: A stereoisomer mixture was prepared by

mixing the R and S enantiomer products of reactions run according to the general procedure (***Method B***) with nickel acetylacetonate (3.9 mg, 0.015 mmol, 0.05 equiv, 0.015 M stock solution in THF prepared with sonication) and (*S,S*)-Ph-Pybox (*S,S*)-**4.122** (3.0 mol%), or (*R,R*)-Ph-Pybox (*R,R*-**4.122** (3.0 mol%) as the catalyst. Absolute stereochemistry was assigned by analogy (see products: **4.192** and **epi-4.158**).

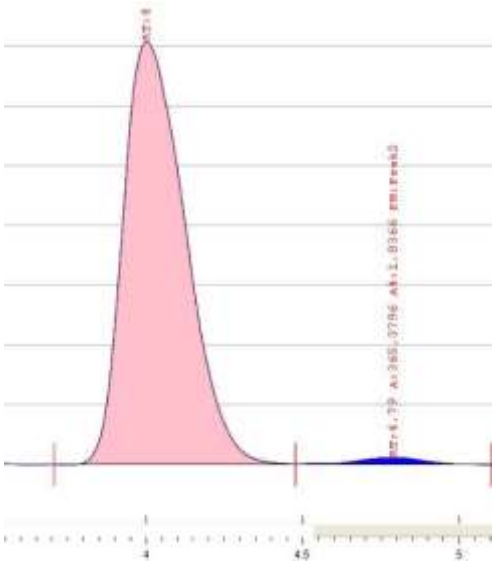
SFC (Chiracel AD-H, 1% IPA, 3 mL/min, 100 bar, 35 °C, 210-270 nm) – analysis of (S)-2-(3-cyclopentyl-1-phenylpropyl)-4,4,5,5-tetramethyl-1,3,2-dioxaborolane.

Stereoisomer Mixture

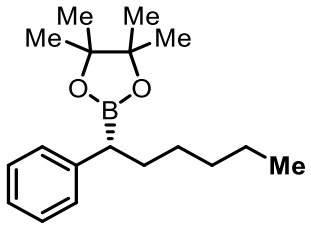


Peak No	% Area	Area	RT (min)
1	49.0455	10921.2322	4.04
2	50.9545	11346.3165	4.71
Total:	100	22267.5487	

Standard Conditions



Peak No	% Area	Area	RT (min)
1	98.1634	19528.5794	4
2	1.8366	365.3796	4.79
Total:	100	19893.959	



(*R*)-4,4,5,5-Tetramethyl-2-(1-phenylhexyl)-1,3,2-dioxaborolane (4.174). The reaction was performed according to the general procedure (***Method A)*** with 4,4,5,5-tetramethyl-2-vinyl-1,3,2-dioxaborolane **4.87** (46.2 mg, 0.30 mmol, 1.00 equiv), phenyllithium (0.16 mL, 1.9 M in dibutyl ether, 0.3 mmol, 1.0 equiv), *n*-butyl iodide (66.2 mg, 0.36 mmol, 1.2 equiv), (*R*,*R*)-3,5-dimethylphenyl-Pybox **(*R*,*R*)-Xylyl-Pybox (*R*,*R*)-4.127** (7.7 mg, 0.018 mmol, 0.06 equiv), methallyl nickelchloride dimer (2.2 mg, 0.0075 mmol, 0.025 equiv, 0.0075 M stock solution in THF prepared with sonication). The unpurified product was purified by automated silica gel chromatography (Biotage 1% → 2% ethyl acetate in hexanes, stained in CAM) to afford colorless oil (57.1 mg, 66 % yield).

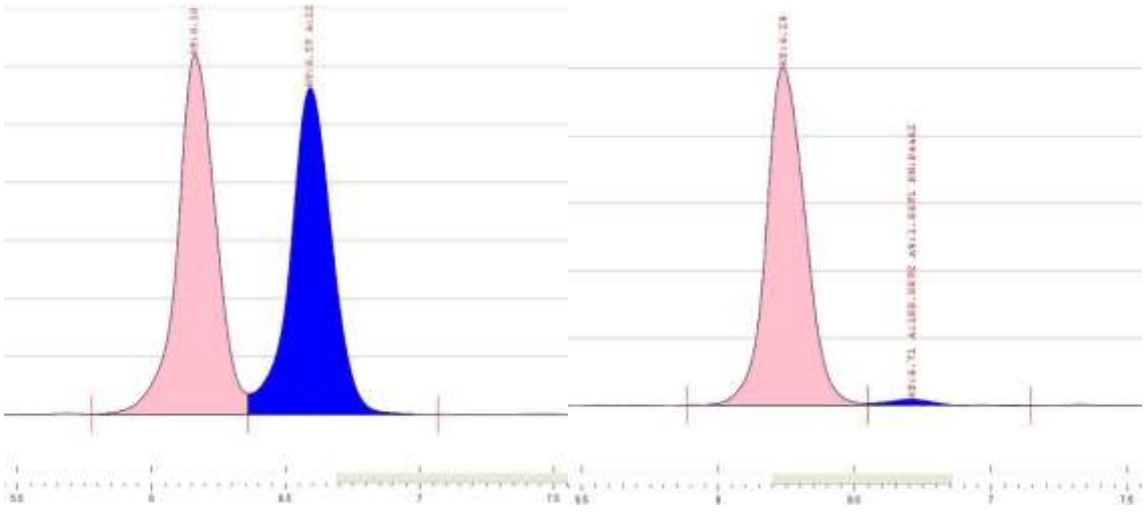
(***Method B)*** with 4,4,5,5-tetramethyl-2-phenyl-1,3,2-dioxaborolane (**4.265**) (61.2 mg, 0.30 mmol, 1.00 equiv), vinyllithium (0.19 mL, 1.58 M in tetrahydrofuran, 0.30 mmol, 1.00 equiv), *n*-butyl iodide (66.2 mg, 0.36 mmol, 1.2 equiv), (*R*, *R*)-3,5-dimylthylphenyl-Pybox **(*R*,*R*)-Xylyl-Pybox** (*R*,*R*)-**4.127** (7.7 mg, 0.018 mmol, 0.06 equiv), methallylnickel chloride dimer (2.2 mg, 0.0075 mmol, 0.025 equiv, 0.0075 M stock solution in THF prepared with sonication). The unpurified product was purified by automated silica gel chromatography (Biotage 1% → 2% ethyl acetate in hexanes, stained in CAM) to afford colorless oil (56.2 mg, 65 % yield).

^{1}H NMR (600 MHz, $CDCl_3$) δ 7.27 – 7.22 (m, 2H), 7.22 – 7.17 (m, 2H), 7.14 – 7.09 (m, 1H), 2.29 (app t, *J* = 7.9 Hz, 1H), 1.88 – 1.77 (m, 1H), 1.69 – 1.58 (m, 1H), 1.30 – 1.23 (m, 6H), 1.20 (s, 6H), 1.18 (s, 6H), 0.90 – 0.80 (m, 3H). **^{11}B NMR** (160 MHz, $CDCl_3$) δ 32.98. **^{13}C NMR** (151 MHz, $CDCl_3$) δ 143.73, 128.55, 128.41, 125.25, 83.41, 32.78, 32.67 (C-B, partially buried), 32.06, 29.18, 24.85, 24.79, 22.77, 14.27. **IR** (neat) ν_{max} 2976.84 (w), 2957.34 (w), 2926.51 (m), 2886.44 (w), 1452.67 (w), 1360.16 (m), 1320.78 (s), 1270.08 (w), 1215.13 (w), 1142.21 (s), 966.89 (w), 851.09 (m), 700.09 (m) cm^{-1}. **HRMS** (DART) for $C_{18}H_{29}BO_2$ $[M+NH_4]^+$: calculated: 306.2607, found: 306.2607. $[\alpha]_D^{20}$ = –16.962 (*c* 1.47, $CHCl_3$, *l* = 50 mm).

Determination of Stereochemical Identity: A stereoisomer mixture was prepared by mixing the R and S enantiomer products of reactions run according to the general procedure (***Method B***) with [{methallyl}NiCl]$_2$ (2.5 mol%) and (*S,S*)-Ph-Pybox (*S,S*)-**4.122** (3.0 mol%), or (*R,R*)-Ph-Pybox (*R,R*)-**4.127** (3.0 mol%) as the catalyst. Absolute stereochemistry was assigned by analogy (see products: **4.192** and **epi-4.158**. Product was oxidized according to ***General Method for Oxidation of Boronic Ester Products.***

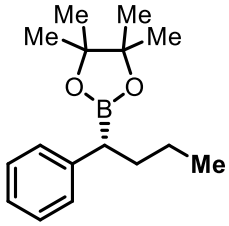
SFC (Chiracel OD-H, 5% IPA, 3 mL/min, 100 bar, 35 °C, 210-270 nm) – analysis of (R)-1-phenylhexan-1-ol.

Stereoisomer mixture Standard Conditions



Peak No	% Area	Area	RT (min)
1	50.3224	12276.9642	6.16
2	49.6776	12119.6412	6.59
Total:	100	24396.6054	

Peak No	% Area	Area	RT (min)
1	98.1309	9916.8484	6.24
2	1.8691	188.8892	6.71
Total:	100	10105.7376	



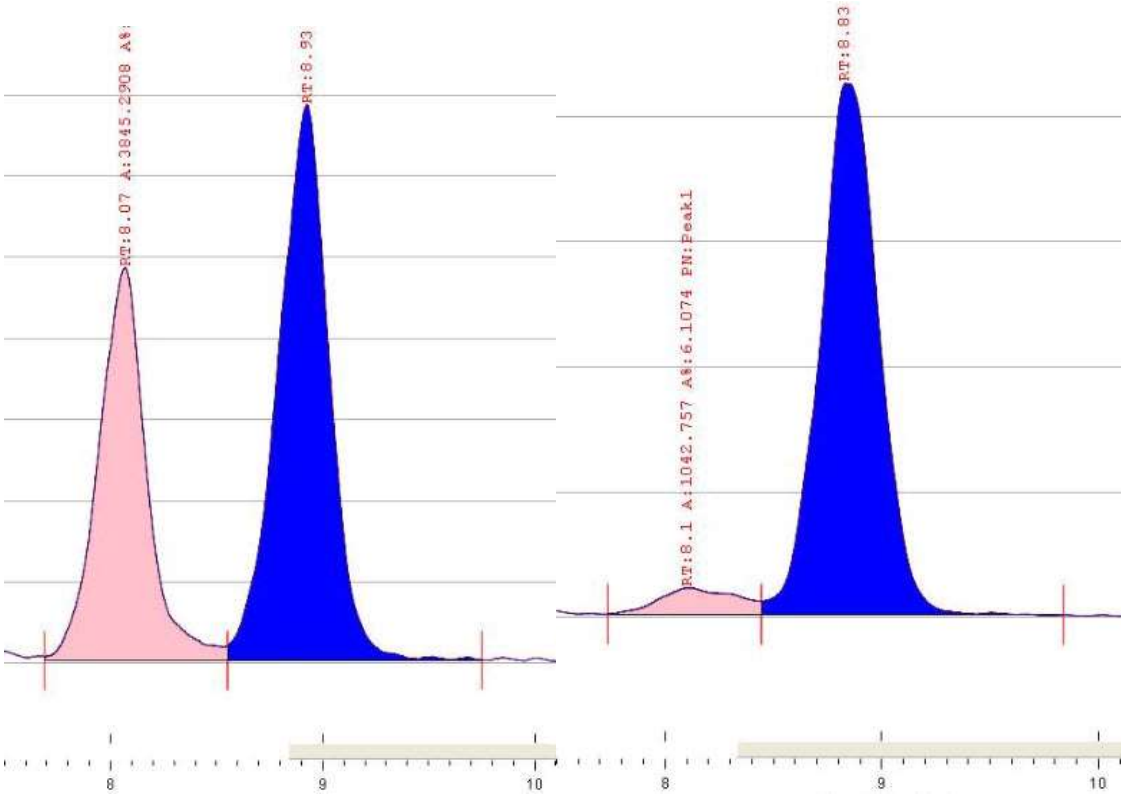
(*R*)-4,4,5,5-Tetramethyl-2-(1-phenylbutyl)-1,3,2-dioxaborolane (4.162). The reaction was performed according to general (***Method B)*** with 4,4,5,5-tetramethyl-2-phenyl-1,3,2-dioxaborolane (**4.265**) (61.2 mg, 0.30 mmol, 1.00 equiv), vinyllithium (0.19 mL, 1.58 M in tetrahydrofuran, 0.30 mmol, 1.00 equiv), iodoethane (56.1 mg, 0.36 mmol, 1.2 equiv), (*R*,*R*)-3,5-dimethylphenyl-Pybox **(*R*,*R*)-Xylyl-Pybox** (*R*,*R*)-**4.127** (7.7 mg, 0.018 mmol, 0.06 equiv), methallyl nickelchloride dimer (2.2 mg, 0.0075 mmol, 0.025 equiv, 0.0075 M stock solution in THF prepared with sonication). The unpurified product was purified by automated silica gel chromatography (Biotage 1% → 3% ethyl acetate in hexanes, stained in CAM) to afford colorless oil (55.4 mg, 71 % yield.

^{1}H NMR (600 MHz, $CDCl_3$) δ 7.26 (d, *J* = 9.1 Hz, 2H), 7.21 (d, *J* = 7.0 Hz, 2H), 7.13 (t, *J* = 7.2 Hz, 1H), 2.33 (app t, *J* = 8.0 Hz, 1H), 1.83 (app dq, *J* = 15.6, 7.9 Hz, 1H), 1.64 (app dq, *J* = 13.1, 7.7 Hz, 1H), 1.35 – 1.26 (m, 2H), 1.22 (s, 6H), 1.20 (s, 6H), 0.90 (t, *J* = 7.4 Hz, 3H). **^{11}B NMR** (160 MHz, $CDCl_3$) δ 33.28. **^{13}C NMR** (151 MHz, $CDCl_3$) δ 143.69, 128.60, 128.42, 125.27, 83.44, 35.03, 32.42 (C-B), 24.86, 24.81, 22.59, 14.34. **IR** (neat) ν_{max} 2976.50 (w), 29227.98 (w), 2859.86 (w), 1452.69 (w), 1369.82 (m), 1321.29 (m), 1248.61 (w), 1143.00 (m), 966.25 (w), 848.93 (w), 700.38 (w) cm^{-1}. **HRMS** (DART) for $C_{26}H_{25}BO_2$ $[M+NH_4]^+$ calculated: 278.2291, found: 278.2292. $[\alpha]^{20}_D$: –14.699 (*c* 0.55, $CHCl_3$, *l* =50 mm).

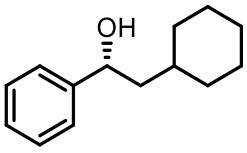
Determination of Stereochemical Identity: A stereoisomer mixture was prepared by mixing the R and S enantiomer products of reactions run according to the general procedure (***Method B***) with [{methallyl}NiCl]$_2$ (2.5 mol%) and (*S,S*)-Ph-Pybox (*S,S*)-**4.122** (3.0 mol%), or (*R,R*)-Ph-Pybox (*R,R*)-**4.122** (3.0 mol%) as the catalyst. Absolute stereochemistry was assigned by analogy (see products: **4.192** and **epi-4.158**). Product was oxidized according to ***General Method for Oxidation of Boronic Ester Products.***

SFC (Chiracel OJ-H, 1% IPA, 3 mL/min, 100 bar, 35 °C, 210-270 nm) – analysis of (R)-1-phenylbutan-1-ol.

Stereoisomer Mixture Standard Conditions



Peak No	% Area	Area	RT (min)	Peak No	% Area	Area	RT (min)
1	39.9638	3845.2908	8.07	1	6.1074	1042.757	8.1
2	60.0362	5776.6429	8.93	2	93.8926	16030.8632	8.83
Total:	100	9621.9337		Total:	100	17073.6202	



(*R*)-2-Cyclohexyl-1-phenylethan-1-ol (4.163-OH). The reaction was performed according to the general procedure (***Method B)*** with 4,4,5,5-tetramethyl-2-phenyl-1,3,2-dioxaborolane (**4.265**) (61.2 mg, 0.30 mmol, 1.00 equiv), vinyllithium (0.19 mL, 1.58 M in tetrahydrofuran, 0.30 mmol, 1.00 equiv), iodocyclohexane (75.6 mg, 0.36 mmol, 1.2 equiv), (*R*,*R*)-3,5-dimethylphenyl-Pybox **(*R*,*R*)-Xylyl-Pybox** (*R*,*R*)-**4.127** (7.7 mg, 0.018 mmol, 0.06 equiv), methallylnickel chloride dimer (2.2 mg, 0.0075 mmol, 0.025

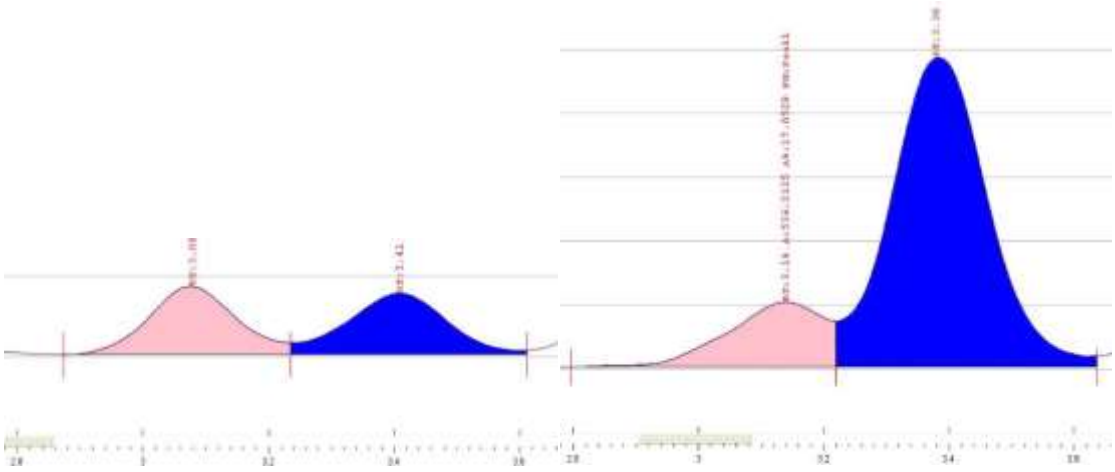
equiv, 0.0075 M stock solution in THF prepared with sonication). The unpurified product **5** was oxidized according to ***General Method for Oxidation of Boronic Ester Products.*** and was purified by automated silica gel chromatography (Biotage 1% → 5% ethyl acetate in hexanes, stained in CAM) to afford colorless oil (mg, 56 % yield). All spectral data was in accord with the literature.[75]

Determination of Stereochemical Identity: A stereoisomer mixture was prepared by mixing the R and S enantiomer products of reactions run according to the general procedure (***Method B***) with [{methallyl}NiCl]$_2$ (2.5 mol%) and (*S,S*)-Ph-Pybox (*S*,*S*)-**4.122** (3.0 mol%), or (*R,R*)-Ph-Pybox (*R*,*R*)-**4.122** (3.0 mol%) as the catalyst. Absolute stereochemistry was assigned by analogy (see products: **4.192** and **epi-4.158**). Product was oxidized according to ***General Method for Oxidation of Boronic Ester Products.***

SFC (Chiracel OD-H, 10% IPA, 3 mL/min, 100 bar, 35 °C, 210-270 nm) – analysis of (R)-4-(2-hydroxy-2-phenylethyl)piperidine-1-carboxylate.

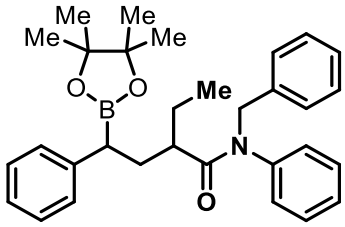
Stereoisomer Mixture Standard Conditions

[75] Tlahuext-Aca, A.; Garza-Sanchez, R. A.; Glorius, F. *Angew. Chem. Int. Ed.* **2017**, 56, 3078.



Peak No	% Area	Area	RT (min)
1	49.3953	825.4074	3.08
2	50.6047	845.6181	3.41
Total:	100	1671.0255	

Peak No	% Area	Area	RT (min)
1	17.0528	536.2135	3.14
2	82.9472	2608.2259	3.38
Total:	100	3144.4394	

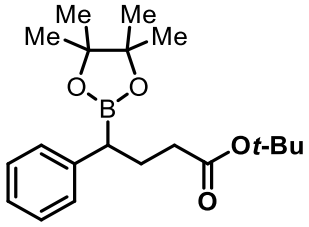


N*-Benzyl-2-ethyl-*N*,4-diphenyl-4-(4,4,5,5-tetramethyl-1,3,2-dioxa borolan-2-yl)butanamide (4.169).** The reaction was performed according to general (Method C)*** with 4,4,5,5-tetramethyl-2-vinyl-1,3,2-dioxaborolane (**4.265**) (46.2 mg, 0.30 mmol, 1.00 equiv), phenyllithium (0.16 mL, 1.9 M in dibutyl ether, 0.3 mmol, 1.0 equiv), sodium iodide (44.9 mg, 0.30 mmol, 1.00 equiv) *N*-benzyl-2-bromo-*N*-phenylbutanamide (119.6 mg, 0.36 mmol, 1.2 equiv), nickel acetylacetonate (3.9 mg, 0.015 mmol, 0.05 equiv, 0.015 M stock solution in THF prepared with sonication). The unpurified product was purified by automated silica gel chromatography (Biotage 2% → 15% ethyl acetate in hexanes, stained in CAM) to afford colorless oil (123.3 mg, 85 % yield).

(***Method D)*** with4,4,5,5-tetramethyl-2-phenyl-1,3,2-dioxaborolane (**4.265**) (61.2 mg, 0.30 mmol, 1.00 equiv), vinyllithium (0.19 mL, 1.58 M in tetrahydrofuran, 0.30 mmol, 1.00 equiv), sodium iodide (44.9 mg, 0.30 mmol, 1.00 equiv), *N*-benzyl-2-bromo-*N*-phenylbutanamide (119.6 mg, 0.36 mmol, 1.2 equiv), nickel acetylacetonate (3.9 mg, 0.015 mmol, 0.05 equiv, 0.015 M stock solution in THF prepared with sonication). The unpurified product was purified by automated silica gel chromatography (Biotage 2% → 15% ethyl acetate in hexanes, stained in CAM) to afford colorless oil (120.4 mg, 83 % yield)

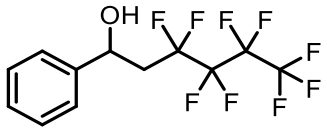
^{1}H NMR (600 MHz, $CDCl_3$) δ 7.27 – 6.97 (m, 14.28H), 6.82 – 6.77 (m, 1.24H), 4.97 (d, *J* = 14.2 Hz, 0.73H), 4.91 (d, *J* = 14.1 Hz, 0.29H), 4.78 (d, *J* = 14.2 Hz, 0.49H), 4.73 (d, *J* = 14.2 Hz, 0.75H), 2.45 (dd, *J* = 10.6, 5.7 Hz, 0.57H), 2.29 – 2.22 (m, 1.19H), 2.22 – 2.14 (m, 0.58H), 2.13 – 2.06 (m, 0.79H), 2.04 – 1.96 (m, 1.36H), 1.94 – 1.86 (m, 0.59H), 1.67 – 1.57 (m, 0.88H), 1.55 – 1.45 (m, 1.26H), 1.42 – 1.33 (m, 0.66H), 1.15 (s, 3.77H), 1.11 (s, 2.53H), 1.09 (s, 2.43H), 1.06 (s, 3.56H), 0.78 (t, *J* = 7.4 Hz, 2.02H), 0.72 (t, *J* = 7.4 Hz, 1.29H). **^{11}B NMR** (160 MHz, $CDCl_3$) δ 32.70. **^{13}C NMR** (151 MHz, $CDCl_3$) δ 176.11, 175.39, 142.63, 142.30, 142.17, 142.05, 138.06, 129.46, 129.15, 129.10, 129.06, 128.87, 128.77, 128.47, 128.44, 128.40, 128.34, 128.33, 128.31, 127.58, 127.52, 127.34, 125.21, 83.41, 83.35, 53.24, 53.20, 42.63, 42.05, 34.73, 32.58, 30.51, 29.87, 29.68 (C-B), 29.57 (C-B), 26.26, 24.89, 24.87, 24.67, 24.64, 24.54, 12.24, 11.81. **IR** (neat) ν_{max} 3061.12 (w), 3027.77 (w), 2973.41 (m), 2929.56 (w), 1650.24 (s), 1594.94 (m), 1493.88 (m), 1398.84

(m), 1358.76 (m), 1319.87 (m), 1269.90 (m), 1166.10 (m), 1006.55 (w), 848.36 (w), 698.53 (s) cm^{-1}. **HRMS** (DART) for $C_{31}H_{38}BNO_3$ $[M+H]^+$: calculated: 484.3023, found: 484.3031.



tert*-Butyl 4-phenyl-4-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan -2-yl)butanoate (4.165).** The reaction was performed according to general (Method D)*** with 4,4,5,5-tetramethyl-2-phenyl-1,3,2-dioxaborolane (**4.265**) (61.2 mg, 0.30 mmol, 1.00 equiv), vinyllithium (0.19 mL, 1.58 M in tetrahydrofuran, 0.30 mmol, 1.00 equiv), sodium iodide (44.9 mg, 0.30 mmol, 1.00 equiv), *tert*-butyl 2-bromoacetate (70.2 mg, 0.36 mmol, 1.2 equiv), nickel acetylacetonate (3.9 mg, 0.015 mmol, 0.05 equiv, 0.015 M stock solution in THF prepared with sonication). The unpurified product was purified by automated silica gel chromatography (Biotage 1% → 6% ethyl acetate in hexanes, stained in CAM) to afford colorless oil (91.4 mg, 88 % yield). **^{1}H NMR** (600 MHz, $CDCl_3$) δ 7.25 (t, J = 7.5 Hz, 2H), 7.18 (d, J = 7.0 Hz, 2H), 7.13 (t, J = 7.3 Hz, 1H), 2.29 (t, J = 7.5 Hz, 1H), 2.21 – 2.04 (m, 3H), 1.99 – 1.89 (m, 1H), 1.42 (s, 9H), 1.21 (s, 6H), 1.18 (s, 6H). **^{11}B NMR** (160 MHz, $CDCl_3$) δ 33.08. **^{13}C NMR** (151 MHz, $CDCl_3$) δ 173.21, 142.57, 128.72, 128.56, 125.60, 83.57, 80.10, 35.11, 31.79 (C-B), 28.33, 28.03, 24.85, 24.78. **IR** (neat) ν_{max} 2977.13 (m), 2929.38 (w), 1727.23 (s), 1453.63 (w), 1366.87 (s), 1322.81 (s), 1254.24 (w), 1214.95 (w), 1140.18 (s), 967.26 (w), 849.59 (m), 765.15 (w), 701.23 (m) cm^{-1}. **HRMS** (DART) for

$C_{20}H_{31}BO_4$ $[M+H]^+$ calculated: 347.2394, found: 347.2379.



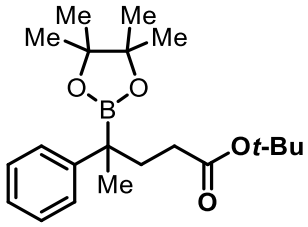
3,3,4,4,5,5,6,6,6-Nonafluoro-1-phenylhexan-1-ol (4.166-OH).

The reaction was performed according to general (***Method D, with the modification that no NaI was added)*** with 4,4,5,5-tetramethyl-2-phenyl-1,3,2-dioxaborolane (**4.265**) (61.2 mg, 0.30 mmol, 1.00 equiv), vinyllithium (0.19 mL, 1.58 M in tetrahydrofuran, 0.30 mmol, 1.00 equiv), 1,1,1,2,2,3,3,4,4-nonafluoro-4-iodobutane (124.5 mg, 0.36 mmol, 1.2 equiv), nickel acetylacetonate (3.9 mg, 0.015 mmol, 0.05 equiv, 0.015 M stock solution in THF prepared with sonication). The unpurified product **4.166** was oxidized according to ***General Method for Oxidation of Boronic Ester Products.*** and was purified by automated silica gel chromatography (Biotage 1% → 3% ethyl acetate in hexanes, stained in CAM) to afford colorless oil (57.2 mg, 56 % yield). All spectral data was in accord with the literature.[76]

(***Method D, with the modification that no NaI was added and that Ni/Ligand catalyst solution was used as in Method A)*** with 4,4,5,5-tetramethyl-2-phenyl-1,3,2-dioxaborolane (**4.264**) (61.2 mg, 0.30 mmol, 1.00 equiv), vinyllithium (0.19 mL, 1.58 M in tetrahydrofuran, 0.30 mmol, 1.00 equiv), 1,1,1,2,2,3,3,4,4-nonafluoro-4-iodobutane (124.5 mg, 0.36 mmol, 1.2 equiv), (*R*,*R*)-3,5-dimylthylphenyl-Pybox **(*R*,*R*)-Xylyl-Pybox** (R,R)-

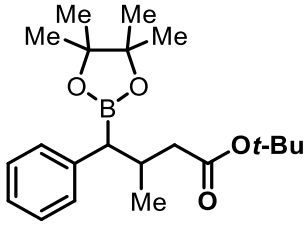
[76] Kischkewitz, M.; Okamoto, K.; Mück-Lichtenfeld, C.; Studer, A. *Science*. **2017**, 355, 936.

4.127 (7.7 mg, 0.018 mmol, 0.06 equiv), nickel acetylacetonate (3.9 mg, 0.015 mmol, 0.05 equiv, 0.015 M stock solution in THF prepared with sonication). The unpurified product **5** was oxidized according to ***General Method for Oxidation of Boronic Ester Products.*** and was purified by automated silica gel chromatography (Biotage 1% → 5% ethyl acetate in hexanes, stained in CAM) to afford colorless oil (56.1 mg, 55 % yield). All spectral data was in accord with the literature.[76]



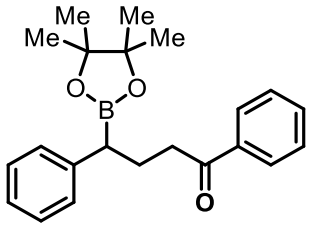
tert*-Butyl 4-phenyl-4-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl) pentanoate (4.172).** The reaction was performed according to general (Method C)*** with 4,4,5,5-tetramethyl-2-(prop-1-en-2-yl)-1,3,2-dioxaborolane (50.4 mg, 0.30 mmol, 1.00 equiv), phenyllithium (0.16 mL, 1.9 M in dibutyl ether, 0.3 mmol, 1.0 equiv), sodium iodide (44.9 mg, 0.30 mmol, 1.00 equiv) *tert*-butyl 2-bromoacetate (70.2 mg, 0.36 mmol, 1.2 equiv), nickel acetylacetonate (3.9 mg, 0.015 mmol, 0.05 equiv, 0.015 M stock solution in THF prepared with sonication). The unpurified product was purified by automated silica gel chromatography (Biotage 2% → 15% ethyl acetate in hexanes, stained in CAM) to afford colorless oil (91.1 mg, 84% yield). **^{1}H NMR** (600 MHz, $CDCl_3$) δ 7.33 – 7.24 (m, 4H), 7.14 (t, *J* = 7.0 Hz, 1H), 2.20 – 1.97 (m, 4H), 1.41 (s, 9H), 1.34 (s, 3H), 1.21 (s, 6H), 1.19 (s, 6H). **^{11}B NMR** (160 MHz, $CDCl_3$) δ 33.57. **^{13}C NMR** (151 MHz, $CDCl_3$) δ 173.80, 146.21, 128.33, 127.08, 125.44, 83.60, 80.00, 34.32, 31.83, 30.52, 29.81 (C-B), 28.29,

24.75, 21.26. **IR** (neat) ν_{max} 2976.32 (w), 2930.81 (s), 2872.79 (w), 1726.88 (s), 1458.61 (w), 1367.04 (m), 1312.27 (m), 1142.96 (s), 1104.00 (m), 965.68 (w), 847.57 (m), 765.96 (w), 699.30 (m) cm^{-1}. **HRMS** (DART) for $C_{21}H_{33}BO_4$ $[M+H]^+$ calculated: 361.255, found: 361.2558.



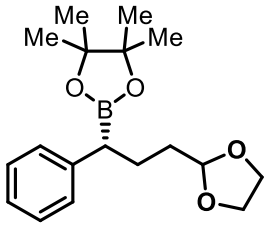
tert*-Butyl 3-methyl-4-phenyl-4-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)butanoate (4.173).** The reaction was performed according to general (Method C)*** with (*E*)-4,4,5,5-tetramethyl-2-(prop-1-en-1-yl)-1,3,2-dioxaborolane (50.4 mg, 0.30 mmol, 1.00 equiv), phenyllithium (0.16 mL, 1.9 M in dibutyl ether, 0.3 mmol, 1.0 equiv), sodium iodide (44.9 mg, 0.30 mmol, 1.00 equiv) *tert*-butyl 2-bromoacetate (70.2 mg, 0.36 mmol, 1.2 equiv), nickel acetylacetonate (3.9 mg, 0.015 mmol, 0.05 equiv, 0.015 M stock solution in THF prepared with sonication). The unpurified product was purified by automated silica gel chromatography (Biotage 1% → 4% ethyl acetate in hexanes, stained in CAM) to afford colorless oil (29.3 mg, 27 % yield). **^{1}H NMR** (600 MHz, $CDCl_3$) δ 7.28 – 7.17 (m, 4H), 7.17 – 7.10 (m, 1H), 2.53 – 2.35 (m, 1.69H), 2.23 – 2.13 (m, 1.16H), 2.13 – 2.02 (m, 1.15H), 1.74 (dd, *J* = 14.7, 10.2 Hz, 0.8H), 1.45 (s, 3.65H), 1.39 (s, 5.21H), 1.21 (s, 2.55H), 1.19 (s, 3.37H), 1.18 (s, 2.38H), 1.16 (s, 3.35H), 1.07 (d, *J* = 6.5 Hz, 1.99H), 0.82 (d, *J* = 6.6 Hz, 1.38H). **^{11}B NMR** (160 MHz, $CDCl_3$) δ 32.77. **^{13}C NMR** (151 MHz, $CDCl_3$) δ 173.09, 172.74, 141.43, 141.21, 129.78, 129.35, 128.54,

128.36, 125.74, 125.70, 83.55, 83.54, 80.21, 80.02, 42.59, 42.08, 40.12 (C-B), 39.44 (C-B), 33.51, 33.32, 30.55, 29.92, 28.39, 28.34, 24.88, 24.78, 20.11, 18.98. **IR** (neat) ν_{max} 2976.70 (m), 2930.08 (w), 1725.63 (s), 1453.76 (w), 1364.48 (s), 1320.60 (s), 1139.87 (s), 970.71 (m), 850.09 (m), 702.50 (m) cm^{-1}. **HRMS** (DART) for $C_{21}H_{33}BO_4$ $[M+H]^+$ calculated: 361.255, found: 361.2548.



1,4-Diphenyl-4-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)butan-1-one (4.167). The reaction was performed according to general (***Method D)*** with 4,4,5,5-tetramethyl-2-phenyl-1,3,2-dioxaborolane (**4.265**) (61.2 mg, 0.30 mmol, 1.00 equiv), vinyllithium (0.19 mL, 1.58 M in tetrahydrofuran, 0.30 mmol, 1.00 equiv), sodium iodide (44.9 mg, 0.30 mmol, 1.00 equiv), 2-bromo-1-phenylethan-1-one (71.7 mg, 0.36 mmol, 1.2 equiv), nickel acetylacetonate (3.9 mg, 0.015 mmol, 0.05 equiv, 0.015 M stock solution in THF prepared with sonication). The unpurified product was purified by automated silica gel chromatography (Biotage 1% → 4% ethyl acetate in hexanes, stained in CAM) to afford colorless oil (55.7 mg, 53 % yield). **^{1}H NMR** (600 MHz, $CDCl_3$) δ 7.89 (d, *J* = 8.3 Hz, 2H), 7.52 (t, *J* = 7.4 Hz, 1H), 7.41 (t, *J* = 7.8 Hz, 2H), 7.27 (t, *J* = 7.6 Hz, 2H), 7.22 (d, *J* = 7.1 Hz, 2H), 7.16 (t, *J* = 7.2 Hz, 1H), 2.97 – 2.84 (m, 2H), 2.40 (dd, *J* = 69.5, 7.4 Hz, 1H), 2.28 (dddd, *J* = 13.6, 9.2, 6.6 Hz, 1H), 2.11 (dddd, *J* = 13.3, 8.9, 4.5 Hz, 1H), 1.23 (s, 6H), 1.20 (s, 6H). **^{11}B NMR** (160 MHz, $CDCl_3$) δ 32.98. **^{13}C NMR** (151 MHz,

$CDCl_3$) δ 200.59, 142.60, 137.19, 132.99, 128.72, 128.66, 128.63, 128.27, 125.68, 83.65, 38.19, 31.91 (C-B), 27.45, 24.88, 24.81. **IR** (neat) ν_{max} 2976.30 (w), 2930.18 (w), 1682.25 (s), 1598.12 (w), 1492.21 (w), 1448.85 (w), 1360.59 (w), 1320.16 (s), 1271.34 (m), 1213.36 (m), 1139.31 (s), 966.76 (m), 848.82 (m), 744.50 (m), 699.05 (s), 577.83 (w), 517.26 (w) cm^{-1}. **HRMS** (DART) for $C_{22}H_{27}BO_3$ $[M+H]^+$ calculated: 351.2132, found: 351.2146.



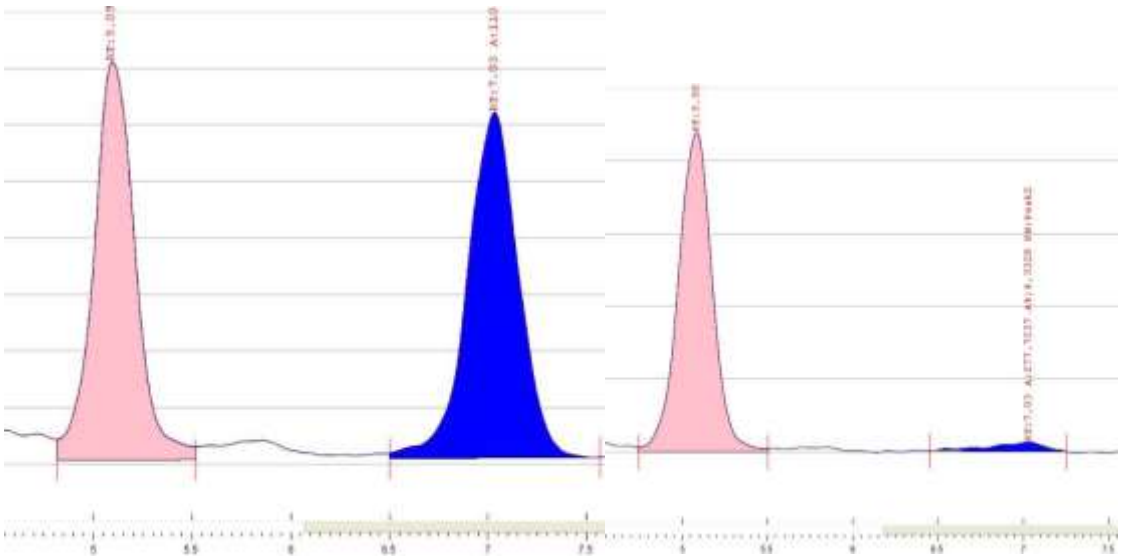
(*R*)-2-(3-(1,3-Dioxolan-2-yl)-1-phenylpropyl)-4,4,5,5-tetramethyl-1,3,2-dioxaborolane (4.164). The reaction was performed according to general (***Method B)*** with 4,4,5,5-tetramethyl-2-phenyl-1,3,2-dioxaborolane (**4.265**) (61.2 mg, 0.30 mmol, 1.00 equiv), vinyllithium (0.19 mL, 1.58 M in tetrahydrofuran, 0.30 mmol, 1.00 equiv), 2-(Iodomethyl)-1,3-dioxolane (**4.272**) (77.0 mg, 0.36 mmol, 1.2 equiv), (*R*, *R*)-3,5-dimethylphenyl-Pybox **(*R*,*R*)-Xylyl-Pybox** (*R*,*R*)-**4.127** (7.7 mg, 0.018 mmol, 0.06 equiv), methallylnickel chloride dimer (2.2 mg, 0.0075 mmol, 0.025 equiv, 0.0075 M stock solution in THF prepared with sonication). The unpurified product was purified by automated silica gel chromatography (Biotage 1% → 10% ethyl acetate in hexanes, stained in CAM) to afford colorless oil (33.4 mg, 35 % yield). **^{1}H NMR** (600 MHz, $CDCl_3$) δ 7.24 (t, *J* = 7.5 Hz, 2H), 7.19 (d, *J* = 7.1 Hz, 2H), 7.12 (t, *J* = 7.2 Hz, 1H), 4.83 (app t, *J* = 4.8 Hz, 1H), 3.97 – 3.89 (m, 2H), 3.85 – 3.76 (m, 2H), 2.31 (app t, *J* = 8.0 Hz, 1H), 1.96 (dddd,

J = 13.1, 10.8, 7.6, 5.7 Hz, 1H), 1.78 (dddd, *J* = 13.7, 10.0, 6.7, 4.4 Hz, 1H), 1.63 (dddd, *J* = 13.8, 8.5, 4.2 Hz, 2H), 1.20 (s, 6H), 1.18 (s, 6H). **^{11}B NMR** (160 MHz, $CDCl_3$) δ 32.93. **^{13}C NMR** (151 MHz, $CDCl_3$) δ 143.04, 128.64, 128.51, 125.46, 104.83, 83.53, 65.00, 33.58, 32.30 (C-B), 27.10, 24.86, 24.81. **IR** (neat) ν_{max} 2976.79 (w), 2928.40 (w), 2880.19 (w), 1452.77 (w), 1370.20 (m), 1322.90 (m), 121486 (w), 1141.87 (s), 1031.73 (w), 967.81 (w), 900.38 (w), 848.68 (w), 701.84 (w) cm^{-1}. **HRMS** (DART) for $C_{18}H_{27}BO_4$ $[M+NH_4]^+$ calculated: 336.2346. found: 336.2362. $[\alpha]^{20}_D$: 11.845 (*c* 1.11, $CHCl_3$, *l* =50 mm).

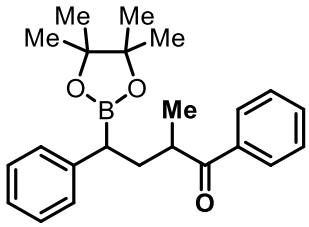
Determination of Stereochemical Identity: A stereoisomer mixture was prepared by mixing the R and S enantiomer products of reactions run according to the general procedure (***Method B***) with [{methallyl}NiCl]$_2$ (2.5 mol%) and (*S,S*)-Ph-Pybox (*S*,*S*)-**4.122** (3.0 mol%), or (*R,R*)-Ph-Pybox (*R*,*R*)-**4.127** (3.0 mol%) as the catalyst. Absolute stereochemistry was assigned by analogy (see products: **4.192** and **epi-4.158**).

SFC (Chiracel OJ-H, 2% IPA, 3 mL/min, 100 bar, 35 °C, 210-270 nm) – analysis of (R)-2-(3-(1,3-dioxolan-2-yl)-1-phenylpropyl)-4,4,5,5-tetramethyl-1,3,2-dioxaborolane.

Stereoisomer Mixture Standard Conditions



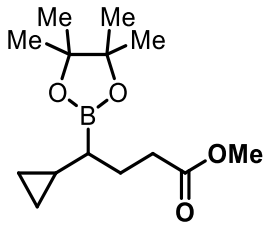
Peak No	% Area	Area	RT (min)	Peak No	% Area	Area	RT (min)
1	48.3646	10330.1872	5.09	1	95.6672	6132.1182	5.08
2	51.6354	11028.811	7.03	2	4.3328	277.7237	7.03
Total:	100	21358.9982		Total:	100	6409.8419	



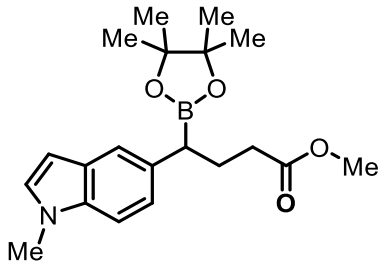
2-Methyl-1,4-diphenyl-4-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)butan-1-one (4.168). The reaction was performed according to general (***Method C)*** with 4,4,5,5-tetramethyl-2-vinyl-1,3,2-dioxaborolane (46.2 mg, 0.30 mmol, 1.00 equiv), phenyllithium (0.16 mL, 1.9 M in dibutyl ether, 0.3 mmol, 1.0 equiv), sodium iodide (44.9 mg, 0.30 mmol, 1.00 equiv) 2-bromo-1-phenylpropan-1-one (76.7 mg, 0.36 mmol, 1.2 equiv), nickel acetylacetonate (3.9 mg, 0.015 mmol, 0.05 equiv 0.015 M stock solution in THF prepared with sonication). The unpurified product was purified by automated silica gel chromatography (Biotage 1% → 4% ethyl acetate in hexanes, stained in CAM) to afford colorless oil (77.6 mg, 71 % yield).

(***Method D)*** with4,4,5,5-tetramethyl-2-phenyl-1,3,2-dioxaborolane (**4.265**) (61.2 mg, 0.30 mmol, 1.00 equiv), vinyllithium (0.19 mL, 1.58 M in tetrahydrofuran, 0.30 mmol, 1.00 equiv), sodium iodide (44.9 mg, 0.30 mmol, 1.00 equiv), 2-bromo-1-phenylpropan-1-one (76.7 mg, 0.36 mmol, 1.2 equiv), nickel acetylacetonate (3.9 mg, 0.015 mmol, 0.05 equiv 0.015 M stock solution in THF prepared with sonication). The unpurified product was purified by automated silica gel chromatography (Biotage 1% → 4% ethyl acetate in hexanes, stained in CAM) to afford colorless oil (78.7 mg, 72 % yield).

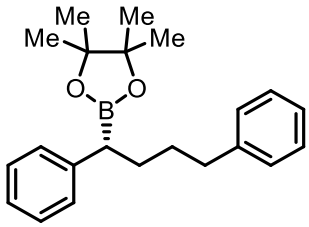
^{1}H NMR (600 MHz, $CDCl_3$) δ 7.96 (d, *J* = 7.7 Hz, 0.55H), 7.74 (d, *J* = 7.7 Hz, 1.43H), 7.59 (t, *J* = 7.3 Hz, 0.36H), 7.55 (t, *J* = 7.3 Hz, 0.78H), 7.48 (t, *J* = 7.6 Hz, 0.52H), 7.44 – 7.38 (m, 1.44H), 7.39 – 7.33 (m, 1.45H), 7.33 – 7.28 (m, 1.49H), 7.26 (t, *J* = 6.7 Hz, 1.18H), 7.21 – 7.10 (m, 0.86H), 3.54 – 3.46 (m, 0.34H), 3.41 – 3.33 (m, 0.78H), 2.59 – 2.40 (m, 1.36H), 2.25 (m, 0.95H), 1.94 – 1.78 (m, 1.44H), 1.30 – 1.19 (m, 15H). **^{11}B NMR** (160 MHz, $CDCl_3$) δ 32.79. **^{13}C NMR** (151 MHz, $CDCl_3$) δ 204.58, 204.31, 142.77, 142.29, 136.93, 136.50, 132.93, 132.82, 128.98, 128.67, 128.66, 128.62, 128.59, 128.57, 128.50, 125.84, 125.59, 83.62, 77.45, 77.24, 77.03, 39.64, 38.87, 36.53, 36.38, 30.52, 30.28 (C-B), 29.89, 29.68 (C-B), 24.87, 24.81, 24.78, 24.76, 17.88, 15.87. **IR** (neat) ν_{max} 2975.78 (w), 2931.31 (w), 1681.84 (s), 1597.62 (w), 1448.78 (w), 1359.12 (s), 1322.35 (s), 1253.81 (m), 1227.45 (m), 1141.45 (s). 968.94 (s), 848.87 (m), 701.99 (s) cm^{-1}. **HRMS** (DART) for $C_{23}H_{29}BO_3$ $[M+H]^+$: calculated: 365.2288, found: 365.2309.



Methyl 4-cyclopropyl-4-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl) butanoate (4.170). The reaction was performed according to general (***Method D)*** with 2-cyclopropyl-4,4,5,5-tetramethyl-1,3,2-dioxaborolane (50.4 mg, 0.30 mmol, 1.00 equiv), vinyllithium (0.19 mL, 1.58 M in tetrahydrofuran, 0.30 mmol, 1.00 equiv), sodium iodide (44.9 mg, 0.30 mmol, 1.00 equiv), methyl 2-bromoacetate (55.1 mg, 0.36 mmol, 1.2 equiv), nickel acetylacetonate (3.9 mg, 0.015 mmol, 0.05 equiv, 0.015 M stock solution in THF prepared with sonication). The unpurified product was purified by silica gel chromatography (1% → 3% ethyl acetate in hexanes, stained in CAM) to afford colorless oil (56.3 mg, 70 % yield). **^{1}H NMR** (600 MHz, cdcl$_3$) δ 3.64 (s, 3H), 2.41 – 2.31 (m, 2H), 1.87 – 1.74 (m, 2H), 1.23 (s, 12H), 0.66 – 0.56 (m, 1H), 0.46 – 0.28 (m, 3H), 0.11 – -0.01 (m, 2H). **^{11}B NMR** (160 MHz, $CDCl_3$) δ 33.41. **^{13}C NMR** (151 MHz, cdcl$_3$) δ 174.54, 83.26, 51.59, 33.86, 28.36 (C-B), 26.94, 25.01, 24.87, 12.36, 5.54, 3.68. **IR** (neat) ν_{max} 2978.34 (w), 2931.38 (w), 1737.90 (s), 1436.63 (w), 1371.38 (m), 1318.16 (s), 1252.75 (m), 1214.17 (m), 1142.36 (s), 1015.15 (w), 968.34 (w), 847.98 (w) cm^{-1}. **HRMS** (DART) for $C_{14}H_{25}BO_4$ $[M+H]^+$: calculated: 269.1924, found: 269.1931.



Methyl 4-(1-methyl-1H-indol-5-yl)-4-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)butanoate (4.171). The reaction was performed according to the general procedure (***Method D)*** with 1-methyl-5-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)-1H-indole (77.1 mg, 0.30 mmol, 1.00 equiv), vinyllithium (0.19 mL, 1.58 M in tetrahydrofuran, 0.30 mmol, 1.00 equiv), sodium iodide (44.9 mg, 0.30 mmol, 1.00 equiv), methyl 2-bromoacetate (55.1 mg, 0.36 mmol, 1.2 equiv), nickel acetylacetonate (3.9 mg, 0.015 mmol, 0.05 equiv, 0.015 M stock solution in THF prepared with sonication). The unpurified product was purified by automated silica gel chromatography (Biotage 2% → 12% ethyl acetate in hexanes, stained in CAM) to afford colorless oil (96.5 mg, 90 % yield). **^{1}H NMR** (600 MHz, $CDCl_3$) δ 7.42 (s, 1H), 7.21 (d, *J* = 8.4 Hz, 1H), 7.09 – 7.05 (m, 1H), 6.98 (d, *J* = 3.0 Hz, 1H), 6.39 (d, *J* = 3.0 Hz, 1H), 3.73 (s, 3H), 3.61 (s, 3H), 2.37 (dd, *J* = 9.0, 6.9 Hz, 1H), 2.27 (app t, *J* = 7.8 Hz, 1H), 2.19 (app dq, *J* = 14.6, 7.8, 7.3 Hz, 1H), 2.10 – 1.98 (m, 1H), 1.22 (s, 6H), 1.18 (s, 6H). **^{11}B NMR** (128 MHz, $CDCl_3$) δ 33.08. **^{13}C NMR** (151 MHz, $CDCl_3$) δ 174.46, 135.48, 132.84, 128.97, 128.82, 122.79, 120.46, 109.27, 100.66, 83.44, 51.49, 33.68, 32.94, 31.52 (C-B), 28.50, 24.83, 24.81. **IR** (neat) ν_{max} 2976.15 (w), 1735.19 (s), 1488.99 (w), 1445.50 (w), 1362.04 (m), 1319.39 (m), 1246.00 (m), 1142.65 (s), 967.93 (w), 848.38 (w), 723.63 (w) cm^{-1}. **HRMS** (DART) for $C_{20}H_{28}BNO_4$ $[M+H]^+$: calculated: 358.219, found: 358.219.

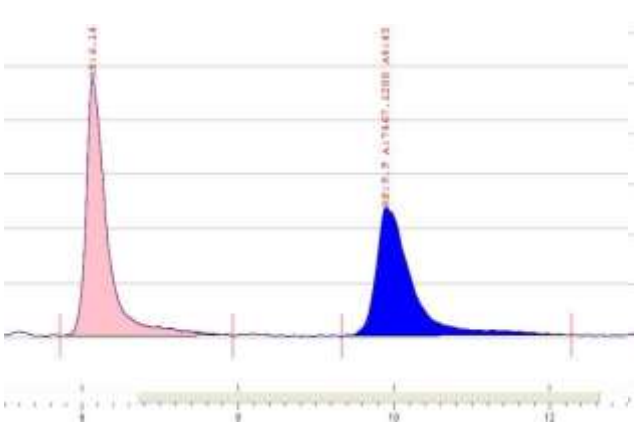


(*R*)-2-(1,4-Diphenylbutyl)-4,4,5,5-tetramethyl-1,3,2-dioxaborolane (4.175). The reaction was performed according to the general procedure (***Method B)*** with 4,4,5,5-tetramethyl-2-phenyl-1,3,2-dioxaborolane (**4.265**) (61.2 mg, 0.30 mmol, 1.00 equiv), vinyllithium (0.19 mL, 1.58 M in tetrahydrofuran, 0.30 mmol, 1.00 equiv), (2-iodoethyl)benzene (835 mg, 0.36 mmol, 1.2 equiv), (*R*,*R*)-3,5-dimethylphenyl-Pybox **(*R*,*R*)-Xylyl-Pybox** (*R*,*R*)-**4.127** (7.7 mg, 0.018 mmol, 0.06 equiv), methallylnickel chloride dimer (2.2 mg, 0.0075 mmol, 0.025 equiv, 0.0075 M stock solution in THF prepared with sonication). The unpurified product was purified by automated silica gel chromatography (Biotage 1% → 3% ethyl acetate in hexanes, stained in CAM) to afford colorless oil (62.6 mg, 62 % yield). **^{1}H NMR** (600 MHz, $CDCl_3$) δ 7.28 – 7.23 (m, 4H), 7.23 – 7.19 (m, 2H), 7.18 – 7.11 (m, 4H), 2.70 – 2.55 (m, 2H), 2.35 (app t, *J* = 7.9, 2.0 Hz, 1H), 1.96 – 1.88 (m, 1H), 1.74 (dddd, *J* = 15.5, 13.1, 7.4, 1.9 Hz, 1H), 1.66 – 1.57 (m, 2H), 1.22 (s,6H), 1.20 (s,6H). **^{11}B NMR** (160 MHz, $CDCl_3$) δ 33.23. **^{13}C NMR** (151 MHz, $CDCl_3$) δ 143.39, 142.89, 128.58, 128.57, 128.47, 128.41, 125.75, 125.36, 83.49, 36.16, 32.51, 32.44 (C-B, partially buried), 31.29, 24.87, 24.81. **IR** (neat) ν_{max} 2976.90 (m), 2928.91 (m), 2856.90 (w), 1600.99 (w), 1493.94 (m), 1452.47 (m), 1360.79 (s), 1321.34 (s), 1142.01 (s), 966.67 (m), 966.67 (m), 890.02 (m), 747.65 (m), 699.05 (s) cm^{-1}. **HRMS** (DART) for $C_{22}H_{29}BO_2$ $[M+H]^+$: calculated: 337.2339, found: 337.2349. $[\alpha]_D^{20} = -23.479$ (*c* 2.05, $CHCl_3$, *l* = 50 mm).

Determination of Stereochemical Identity: A stereoisomer mixture was prepared by mixing the R and S enantiomer products of reactions run according to the general procedure (***Method B***) with [{methallyl}NiCl]$_2$ (2.5 mol%) and (*S,S*)-Ph-Pybox (*S,S*)-**4.122** (3.0 mol%), or (*R,R*)-Ph-Pybox (*R,R*)-**4.122** (3.0 mol%) as the catalyst. Absolute stereochemistry was assigned by analogy (see products: **4.192** and **epi-4.158**).

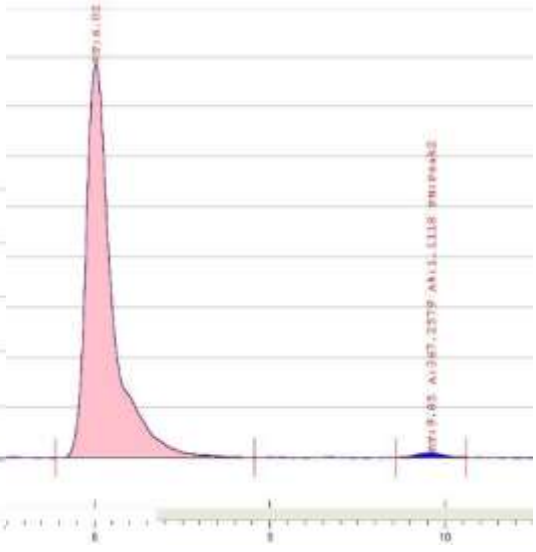
SFC (Chiracel OJ-H, 2% IPA, 3 mL/min, 100 bar, 35 °C, 210-270 nm) – analysis of (R)-2-(1,4-diphenylbutyl)-4,4,5,5-tetramethyl-1,3,2-dioxaborolane.

Stereoisomer mixture

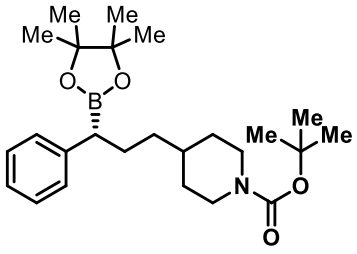


Peak No	% Area	Area	RT (min)
1	54.1469	8817.7517	6.14
2	45.8531	7467.1288	9.9
Total:	100	16284.8805	

Standard Conditions



Peak No	% Area	Area	RT (min)
1	98.8882	32664.4299	6.02
2	1.1118	367.2579	9.85
Total:	100	33031.6878	



tert*-Butyl (*R*)-4-(3-phenyl-3-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)propyl)piperidine-1-carboxylate (4.182).** The reaction was performed according to the general procedure (Method A)*** with 4,4,5,5-tetramethyl-2-vinyl-1,3,2-dioxaborolane (**4.87**) (46.2 mg, 0.30 mmol, 1.00 equiv), Phenyllithium (0.16 mL, 1.9 M in dibutyl ether, 0.3 mmol, 1.0 equiv), *tert*-butyl 4-(iodomethyl)piperidine-1-carboxylate (117.1 mg, 0.36 mmol, 1.2 equiv), (*R*,*R*)-3,5-dimethylphenyl-Pybox **(*R*,*R*)-Xylyl-Pybox** (*R*,*R*)-**4.127** (7.7 mg, 0.018 mmol, 0.06 equiv), methallylnickel chloride dimer (2.2 mg, 0.0075 mmol, 0.025 equiv, 0.0075 M stock solution in THF prepared with sonication). The unpurified product was purified by automated silica gel chromatography (Biotage 1% → 7% ethyl acetate in hexanes, stained in CAM) to afford colorless oil (73.4 mg, 57 % yield).

(***Method B)*** with 4,4,5,5-tetramethyl-2-phenyl-1,3,2-dioxaborolane (**4.265**) (61.2 mg, 0.30 mmol, 1.00 equiv), vinyllithium (0.19 mL, 1.58 M in tetrahydrofuran, 0.30 mmol, 1.00 equiv), *tert*-butyl 4-(iodomethyl)piperidine-1-carboxylate (117.1 mg, 0.36 mmol, 1.2 equiv), (*R*,*R*)-3,5-dimethylphenyl-Pybox **(*R*,*R*)-Xylyl-Pybox** (*R*,*R*)-**4.127** (7.7 mg, 0.018 mmol, 0.06 equiv), methallylnickel chloride dimer (2.2 mg, 0.0075 mmol, 0.025 equiv, 0.0075 M stock solution in THF prepared with sonication). The unpurified product was purified by automated silica gel chromatography (Biotage 1% → 7% ethyl acetate in

hexanes, stained in CAM) to afford colorless oil (72.1 mg, 56 % yield).

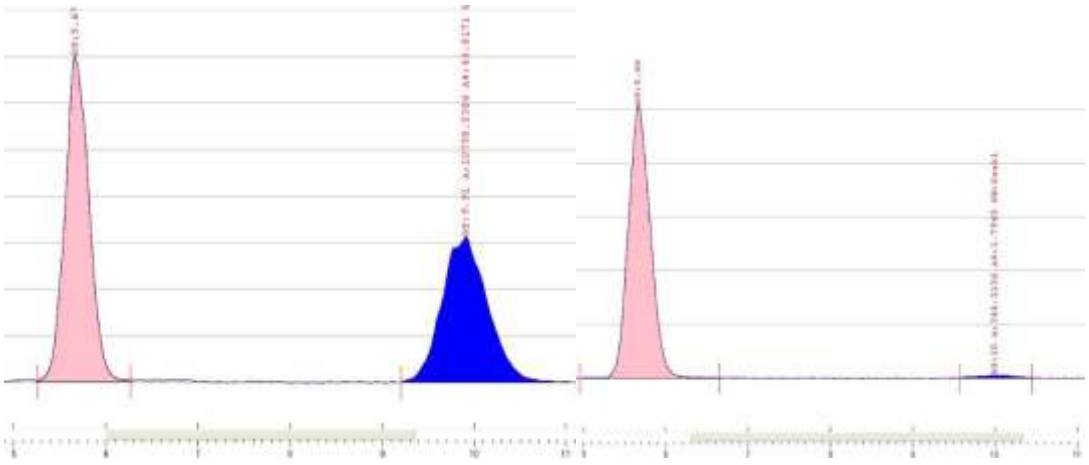
^{1}H NMR (600 MHz, $CDCl_3$) δ 7.27 – 7.21 (m, 2H), 7.21 – 7.16 (m, 2H), 7.15 – 7.09 (m, 1H), 4.03 (s, 2H), 2.64 (s, 2H), 2.25 (q, *J* = 7.9, 7.5 Hz, 1H), 1.85 (dddd, *J* = 12.9, 7.9 Hz, 1H), 1.72 – 1.56 (m, 3H), 1.44 (s, 9H), 1.39 – 1.30 (m, 1H), 1.26 – 1.21 (m, 2H), 1.20 (s, 6H), 1.18 (s, 6H), 1.04 (pt, *J* = 11.8, 6.3 Hz, 2H). **^{11}B NMR** (160 MHz, $CDCl_3$) δ 33.18. **^{13}C NMR** (151 MHz, $CDCl_3$) δ 155.10, 143.38, 128.49, 128.47, 125.37, 83.49, 79.30, 44.14, 36.28, 36.23, 32.59 (C-B, partially buried), 32.35, 29.80, 28.69, 24.87, 24.77. **IR** (neat) ν_{max} 2976.03 (m), 2925.59 (m), 2851.19 (w), 1691.33 (s), 1420.74 (m), 1364.06 (s), 1321.84 (m), 1275.32 (m), 1142.64 (s), 966.19 (m), 850.00 (m), 767.94 (m), 701.33 (m) cm^{-1}. **HRMS** (DART) for $C_{25}H_{40}BNO_4$ $[M+H]^+$: calculated: 430.3129, found: 430.3142 $[\alpha]_D^{20}$ = –9.724 (*c* 2.50, $CHCl_3$, *l* = 50 mm).

Determination of Stereochemical Identity: A stereoisomer mixture was prepared by mixing the R and S enantiomer products of reactions run according to the general procedure (***Method B***) with [{methallyl}NiCl]$_2$ (2.5 mol%) and (*S,S*)-Ph-Pybox (S,S)-**4.122** (3.0 mol%), or (*R,R*)-Ph-Pybox (*R,R*)-**4.122** (3.0 mol%) as the catalyst. Absolute stereochemistry was assigned by analogy (see products: **4.192** and **epi-4.158**).

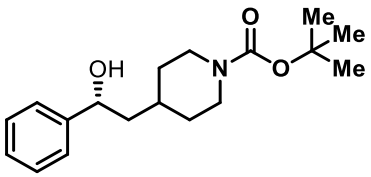
SFC (Chiracel OJ-H, 2% IPA, 3 mL/min, 100 bar, 35 °C, 210-270 nm) – analysis of tert-butyl (R)-4-(3-phenyl-3-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)propyl)piperidine-1-carboxylate.

Stereoisomer Mixture

Standard Conditions



Peak No	% Area	Area	RT (min)	Peak No	% Area	Area	RT (min)
1	54.1829	12722.6112	5.67	1	98.2037	18823.7583	5.66
2	45.8171	10758.2386	9.91	2	1.7963	344.3136	10
Total:	100	23480.8498		Total:	100	19168.0719	



tert*-Butyl (*R*)-4-(2-hydroxy-2-phenylethyl)piperidine-1-carboxylate (4.183-OH).** The reaction was performed according to the general procedure (Method A)*** with 4,4,5,5-tetramethyl-2-vinyl-1,3,2-dioxaborolane (**4.87**) (46.2 mg, 0.30 mmol, 1.00 equiv), phenyllithium (0.16 mL, 1.9 M in dibutyl ether, 0.3 mmol, 1.0 equiv), *tert*-butyl 4-iodopiperidine-1-carboxylate (112.0 mg, 0.36 mmol, 1.2 equiv), (*R*,*R*)-3,5-dimethylphenyl-Pybox **(*R*,*R*)-Xylyl-Pybox** (*R*,*R*)-**4.127** (7.7 mg, 0.018 mmol, 0.06 equiv), methallylnickel chloride dimer (2.2 mg, 0.0075 mmol, 0.025 equiv, 0.0075 M stock solution in THF prepared with sonication). The unpurified product **4.183** was oxidized according to ***General Method for Oxidation of Boronic Ester Products.*** and was purified

by automated silica gel chromatography (Biotage 1% → 10% ethyl acetate in hexanes, stained in CAM) to afford colorless oil (43.1 mg, 47 % yield). All spectral data was in accord with the literature.[77]

(***Method B)*** with 4,4,5,5-tetramethyl-2-phenyl-1,3,2-dioxaborolane (**4.265**) (61.2 mg, 0.30 mmol, 1.00 equiv), vinyllithium (0.19 mL, 1.58 M in tetrahydrofuran, 0.30 mmol, 1.00 equiv), *tert*-butyl 4-iodopiperidine-1-carboxylate (112.0 mg, 0.36 mmol, 1.2 equiv), (*R*,*R*)-3,5-dimethylphenyl-Pybox **(*R*,*R*)-Xylyl-Pybox** (*R*,*R*)-**4.127** (7.7 mg, 0.018 mmol, 0.06 equiv), methallylnickel chloride dimer (2.2 mg, 0.0075 mmol, 0.025 equiv, 0.0075 M stock solution in THF prepared with sonication). The unpurified product **4.183** was oxidized according to ***General Method for Oxidation of Boronic Ester Products.*** and was purified by automated silica gel chromatography (Biotage 1% → 10% ethyl acetate in hexanes, stained in CAM) to afford colorless oil (43.1 mg, 47 % yield). All spectral data was in accord with the literature.[77] $[\alpha]_D^{20}$ = +8.133 (*c* 0.85, $CHCl_3$, l = 50 mm).

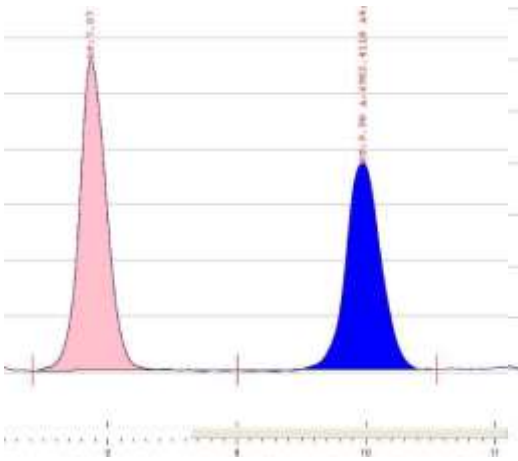
Determination of Stereochemical Identity: A stereoisomer mixture was prepared by mixing the R and S enantiomer products of reactions run according to the general procedure (***Method B***) with [{methallyl}NiCl]$_2$ (2.5 mol%) and (*S,S*)-Ph-Pybox (*S,S*)-**4.122** (3.0 mol%), or (*R,R*)-Ph-Pybox (R,R)-**4.122** (3.0 mol%) as the catalyst. Absolute stereochemistry was assigned by analogy (see products: **4.192** and **epi-4.158**). Product was

[77] Orjales, A.; Mosquera, R.; Toledo, A.; Pumar, M. C.; García, N.; Cortizo, L.; Labeaga, L.; Innerárity, A. *J. Med. Chem.* **2003**, 46, 5512.

oxidized according to ***General Method for Oxidation of Boronic Ester Products.***

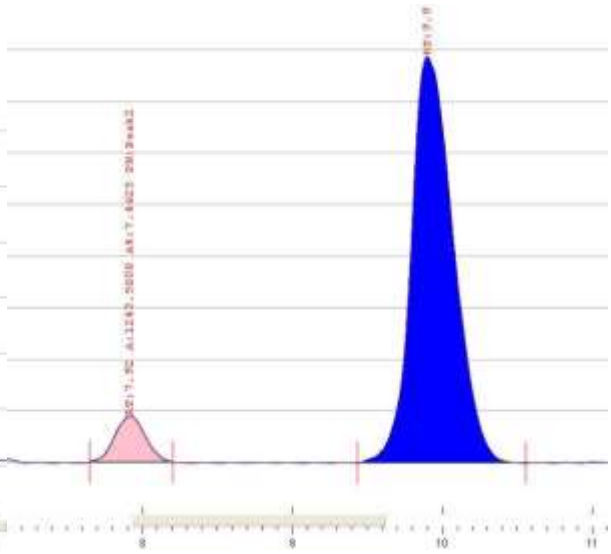
SFC (Chiracel OD-H, 10% IPA, 3 mL/min, 100 bar, 35 °C, 210-270 nm) – analysis of (R)-4-(2-hydroxy-2-phenylethyl)piperidine-1-carboxylate.

Stereoisomer Mixture

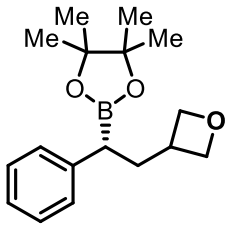


Peak No	% Area	Area	RT (min)
1	53.9742	8188.2259	7.87
2	46.0258	6982.4118	9.98
Total:	100	15170.6377	

Standard Conditions



Peak No	% Area	Area	RT (min)
1	7.4625	1243.5808	7.92
2	92.5375	15420.7231	9.9
Total:	100	16664.3039	



(*R*)-4,4,5,5-Tetramethyl-2-(2-(oxetan-3-yl)-1-phenylethyl)-1,3,2-dioxaboro

lane (4.184). The reaction was performed according to the general procedure (***Method A)***

with 4,4,5,5-tetramethyl-2-vinyl-1,3,2-dioxaborolane (**4.87**) (46.2 mg, 0.30 mmol, 1.00 equiv), phenyllithium (0.16 mL, 1.9 M in dibutyl ether, 0.3 mmol, 1.0 equiv), 3-iodooxetane (66.2 mg, 0.36 mmol, 1.2 equiv), (*R*,*R*)-3,5-dimethylphenyl-Pybox **(*R*,*R*)-Xylyl-Pybox** (*R*,*R*)-**4.127** (7.7 mg, 0.018 mmol, 0.06 equiv), methallylnickel chloride dimer (2.2 mg, 0.0075 mmol, 0.025 equiv, 0.0075 M stock solution in THF prepared with sonication). The unpurified product was purified by automated silica gel chromatography (Biotage 1% → 10% ethyl acetate in hexanes, stained in CAM) to afford colorless oil (42.4 mg, 49 % yield).

(***Method B)*** with 4,4,5,5-tetramethyl-2-phenyl-1,3,2-dioxaborolane (**4.265**) (61.2 mg, 0.30 mmol, 1.00 equiv), vinyllithium (0.19 mL, 1.58 M in tetrahydrofuran, 0.30 mmol, 1.00 equiv), 3-iodooxetane (66.2 mg, 0.36 mmol, 1.2 equiv), (*R*,*R*)-3,5-dimethylphenyl-Pybox **(*R*,*R*)-Xylyl-Pybox** (*R*,*R*)-**4.127** (7.7 mg, 0.018 mmol, 0.06 equiv), methallylnickel chloride dimer (2.2 mg, 0.0075 mmol, 0.025 equiv, 0.0075 M stock solution in THF prepared with sonication). The unpurified product was purified by automated silica gel chromatography (Biotage 1% → 10% ethyl acetate in hexanes, stained in CAM) to afford colorless oil (38.0 mg, 44 % yield).

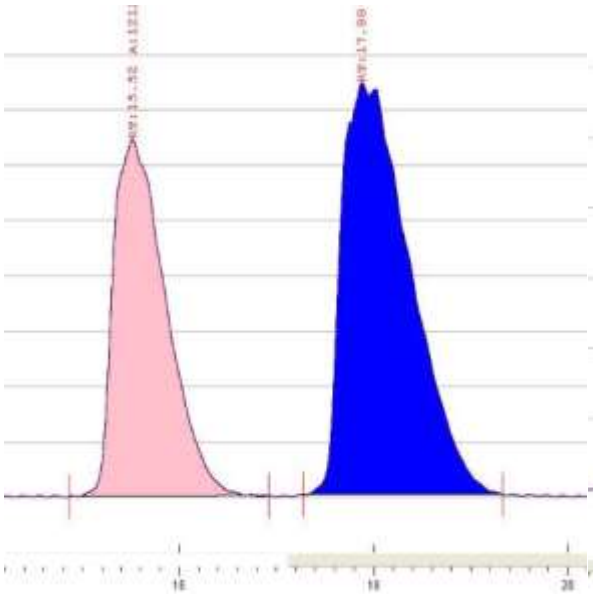
^{1}H NMR (600 MHz, $CDCl_3$) δ 7.24 (app t, *J* = 7.6 Hz, 2H), 7.17 – 7.10 (m, 3H), 4.71 (dd, *J* = 7.9, 5.9 Hz, 1H), 4.57 (dd, *J* = 7.8, 6.0 Hz, 1H), 4.40 (app t, *J* = 6.2 Hz, 1H), 4.21 (app t, *J* = 6.3 Hz, 1H), 2.99 – 2.84 (m, 1H), 2.23 – 2.13 (m, 2H), 2.09 – 1.98 (m, 1H), 1.21 (s, 6H), 1.19 (s, 6H). **^{11}B NMR** (160 MHz, $CDCl_3$) δ 33.08. **^{13}C NMR** (151 MHz, $CDCl_3$) δ

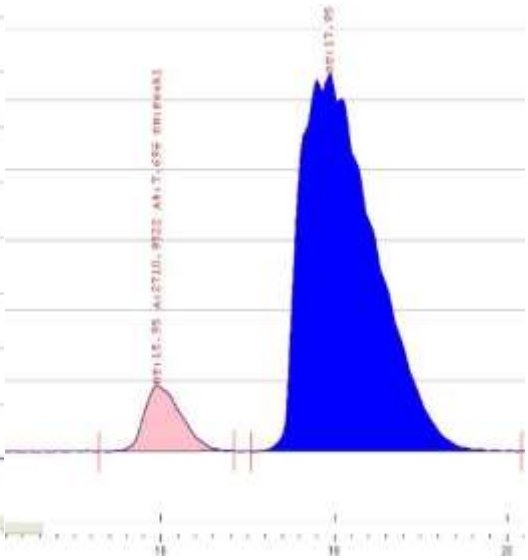
142.42, 128.63, 128.56, 125.73, 83.69, 77.86, 77.82, 36.78, 35.15, 30.41 (C-B), 24.82, 24.81. **IR** (neat) ν_{max} 2976.11 (m), 2929.92 (m), 2862.93 (m), 1492.64 (w), 1451.74 (w), 1361.08 (s), 1323.31 (s), 967.98 (m), 967.98 (m), 848.61 (m), 702.23 (m) cm^{-1}. **HRMS** (DART) for $C_{17}H_{25}BO_3$ $[M+H]^+$: calculated: 289.1975, found: 289.1973. $[\alpha]_D^{20} = -21.978$ (*c* 1.60, $CHCl_3$, l = 50 mm).

Determination of Stereochemical Identity: A stereoisomer mixture was prepared by mixing the R and S enantiomer products of reactions run according to the general procedure (***Method B***) with [{methallyl}NiCl]$_2$ (2.5 mol%) and (*S,S*)-Ph-Pybox (*S*,*S*)-**4.122** (3.0 mol%), or (*R,R*)-Ph-Pybox (*R*,*R*)-**4.122** (3.0 mol%) as the catalyst. Absolute stereochemistry was assigned by analogy (see products: **4.192** and **epi-4.158**).

SFC (Chiracel OD-H, 1% IPA, 3 mL/min, 100 bar, 35 °C, 210-270 nm) – analysis of *(R)-4,4,5,5-tetramethyl-2-(2-(oxetan-3-yl)-1-phenylethyl)-1,3,2-dioxaborolane.*

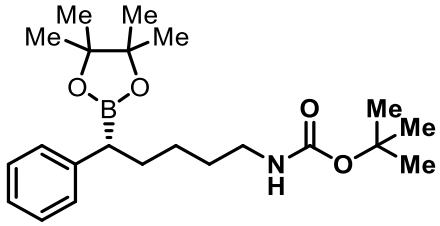
Stereoisomer Mixture Standard Conditions





Peak No	% Area	Area	RT (min)
1	39.8593	12129.068	15.52
2	60.1407	18300.6273	17.88
Total:	100	30429.6953	

Peak No	% Area	Area	RT (min)
1	7.696	2710.9522	15.95
2	92.304	32514.5236	17.95
Total:	100	35225.4758	



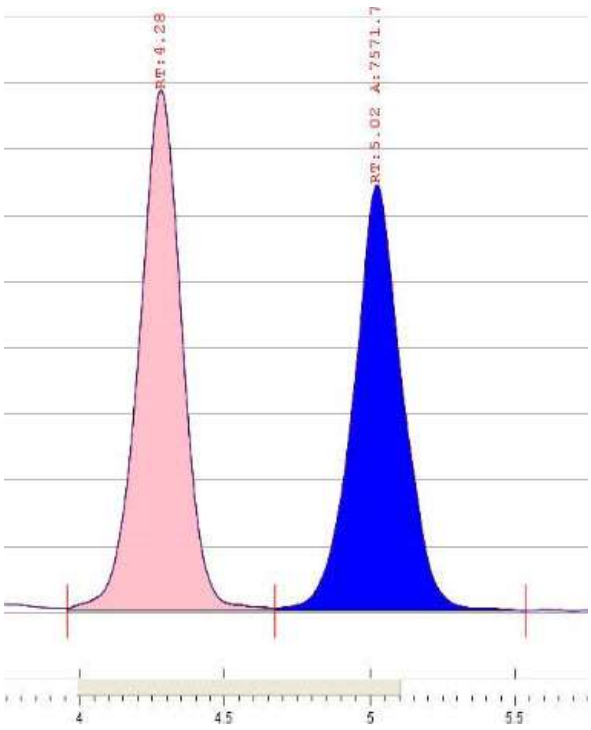
tert*-Butyl (*R*)-(5-phenyl-5-(4,4,5,5-tetramethyl-1,3,2-dioxa borolan-2-yl)pentyl)carbamate (4.178).** The reaction was performed according to general (Method B)*** with 4,4,5,5-tetramethyl-2-phenyl-1,3,2-dioxaborolane (**4.265**) (61.2 mg, 0.30 mmol, 1.00 equiv), vinyllithium (0.19 mL, 1.58 M in tetrahydrofuran, 0.30 mmol, 1.00 equiv), *tert*-butyl (2-iodoethyl)carbamate (**4.268**) (97.6 mg, 0.36 mmol, 1.2 equiv), (*R*,*R*)-3,5-dimethylphenyl-Pybox **(*R*,*R*)-Xylyl-Pybox** (*R*,*R*)-**4.127** (7.7 mg, 0.018 mmol, 0.06 equiv), methallylnickel chloride dimer (2.2 mg, 0.0075 mmol, 0.025 equiv, 0.0075 M stock solution in THF prepared with sonication). The

unpurified product was purified by automated silica gel chromatography (Biotage 1% → 15% ethyl acetate in hexanes, stained in CAM) to afford colorless oil (50.6 mg, 44 % yield). **^{1}H NMR** (600 MHz, $CDCl_3$) δ 7.27 – 7.21 (m, 2H), 7.18 (d, *J* = 7.9 Hz, 2H), 7.14 – 7.09 (m, 1H), 4.50 (br, s, 1H), 3.16 – 2.91 (br, m, 2H), 2.28 (t, *J* = 7.9 Hz, 1H), 1.84 (dq, *J* = 15.7, 7.9 Hz, 1H), 1.64 (dq, *J* = 15.5, 7.8 Hz, 1H), 1.50 – 1.44 (m, 2H), 1.42 (s, 9H), 1.33 – 1.24 (m, 3H), 1.20 (s, 6H), 1.18 (s, 6H). **^{11}B NMR** (160 MHz, $CDCl_3$) δ 33.18. **^{13}C NMR** (151 MHz, $CDCl_3$) δ 156.11, 143.31, 128.52, 128.48, 125.39, 83.51, 79.13, 40.58, 32.50 (C-B, partially buried), 32.29, 30.05, 28.64, 26.54, 24.84, 24.78. **IR** (neat) ν_{max} 3356.66 (br, w), 2976.46 (m), 2930.18 (m), 2861.92 (w), 1696.08 (s), 1514.07 (m), 1452.67 (m), 1364.90 (m), 1321.92 (m), 1270.17 (m), 1248.95 (m), 1167.26 (m), 1142.41 (m), 967.36 (w), 849.59 (w), 701.64 cm^{-1}. **HRMS** (DART) for $C_{22}H_{36}BNO_4$ $[M+H]^+$: calculated: 390.2816, found: 390.2832. $[\alpha]_D^{20}$ = – 8.332 (*c* 2.105, $CHCl_3$, *l* = 50 mm).

Determination of Stereochemical Identity: A stereoisomer mixture was prepared by mixing the R and S enantiomer products of reactions run according to the general procedure (***Method B***) with [{methallyl}NiCl]$_2$ (2.5 mol%) and (*S,S*)-Ph-Pybox (S,S)-**4.122** (3.0 mol%), or (*R,R*)-Ph-Pybox (*R,R*)-**4.122** (3.0 mol%) as the catalyst. Absolute stereochemistry was assigned by analogy (see products: **4.192** and **epi-4.158**).

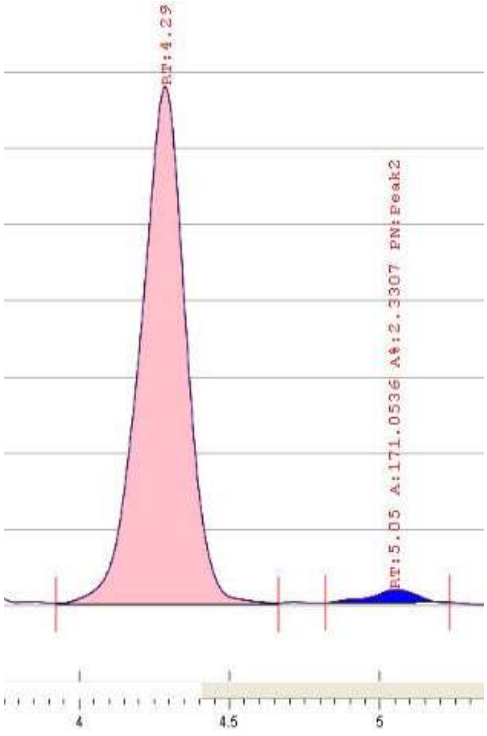
SFC (Chiracel OJ-H, 3% IPA, 3 mL/min, 100 bar, 35 °C, 210-270 nm) – analysis of tert-butyl (R)-(5-phenyl-5-(4,4,5,5-tetramethyl-1,3,2-dioxa borolan-2-yl)pentyl)carbamate.

Stereoisomer Mixture

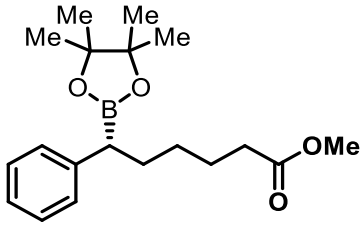


Peak No	% Area	Area	RT (min)
1	51.7854	8132.498	4.28
2	48.2146	7571.7225	5.02
Total:	100	15704.2205	

Standard Conditions



Peak No	% Area	Area	RT (min)
1	97.6693	7168.022	4.29
2	2.3307	171.0536	5.05
Total:	100	7339.0756	



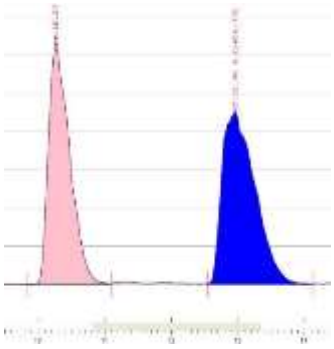
Methyl (*R*)-6-phenyl-6-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)hexanoate (4.176). The reaction was performed according to general (***Method B***) with 4,4,5,5-tetramethyl-2-phenyl-1,3,2-dioxaborolane (**4.265**) (61.2 mg, 0.30 mmol, 1.00 equiv), vinyllithium (0.19 mL, 1.58 M in tetrahydrofuran, 0.30 mmol, 1.00 equiv), methyl 4-iodobutanoate (**4.269**) (82.1 mg, 0.36 mmol, 1.2 equiv), (*R*,*R*)-3,5-

dimethylphenyl-Pybox **(*R*,*R*)-Xylyl-Pybox** (*R*,*R*)-**4.127** (7.7 mg, 0.018 mmol, 0.06 equiv), methallylnickel chloride dimer (2.2 mg, 0.0075 mmol, 0.025 equiv, 0.0075 M stock solution in THF prepared with sonication). The unpurified product was purified by automated silica gel chromatography (Biotage 2% → 12% ethyl acetate in hexanes, stained in CAM) to afford colorless oil (45.9 mg, 48 % yield). **^{1}H NMR** (600 MHz, $CDCl_3$) δ 7.27 – 7.21 (m, 2H), 7.21 – 7.16 (m, 2H), 7.17 – 7.09 (m, 1H), 3.63 (s, 3H), 2.33 – 2.22 (m, 3H), 1.89 – 1.80 (m, 1H), 1.71 – 1.55 (m, 3H), 1.36 – 1.21 (m, 2H), 1.20 (s, 6H), 1.18 (s, 6H). **^{11}B NMR** (160 MHz, $CDCl_3$) δ 33.08. **^{13}C NMR** (151 MHz, $CDCl_3$) δ 174.39, 143.33, 128.54, 128.47, 125.37, 83.49, 51.61, 34.22, 32.36 (C-B, partially buried), 32.32, 28.92, 25.15, 24.85, 24.78. **IR** (neat) ν_{max} 2977.07 (w), 2930.68 (w), 1737.02 (s), 1436.45 (w), 1360.52 (s), 1320.46 (m), 1248.56 (s), 1196.86 (s), 966.84 (m), 848.59 (s), 700.99 (s) cm^{-1}. **HRMS** (DART) for $C_{19}H_{29}BO_4$ $[M+H]^+$: calculated: 333.2237, found: 333.2242. $[\alpha]_D^{20}$ = –15.173 (*c* 2.18, $CHCl_3$, *l* = 50 mm).

Determination of Stereochemical Identity: A stereoisomer mixture was prepared by mixing the R and S enantiomer products of reactions run according to the general procedure (***Method B***) with [{methallyl}NiCl]$_2$ (2.5 mol%) and (*S,S*)-Ph-Pybox (*S*,*S*)-**4.122** (3.0 mol%), or (*R,R*)-Ph-Pybox (*R*,*R*)-**4.122** (3.0 mol%) as the catalyst. Absolute stereochemistry was assigned by analogy (see products: **4.192** and **epi-4.158**).

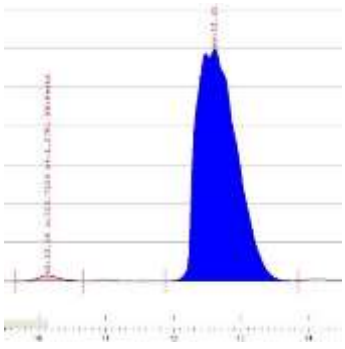
SFC (Chiracel OD-H, 1% IPA, 3 mL/min, 100 bar, 35 °C, 210-270 nm) – analysis of methyl (R)-6-phenyl-6-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)hexanoate.

Stereoisomer Mixture

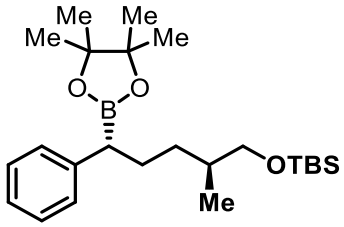


Peak No	% Area	Area	RT (min)
1	47.148	13940.2449	10.27
2	52.852	15626.772	12.96
Total:	100	29567.0169	

Standard Conditions



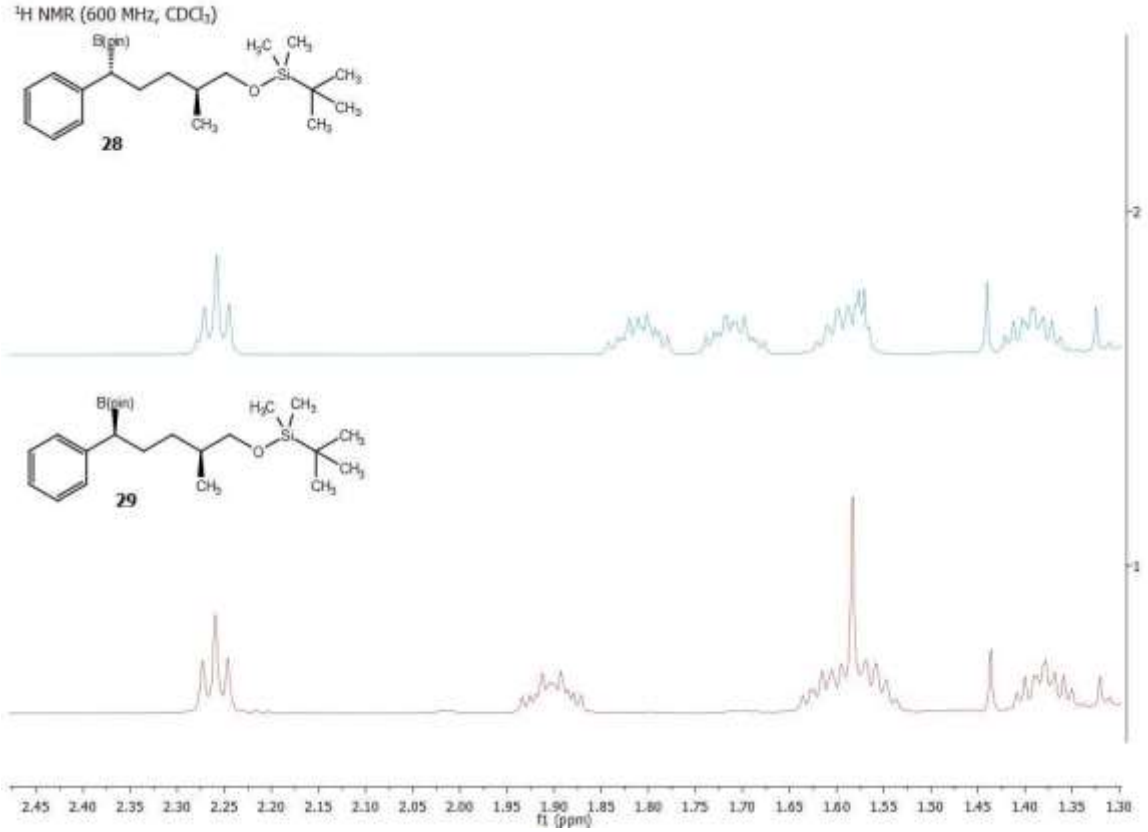
Peak No	% Area	Area	RT (min)
1	1.2781	326.7126	10.14
2	98.7219	25235.8903	12.61
Total:	100	25562.6029	

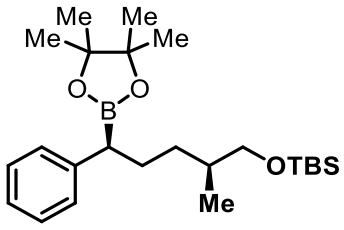


tert*-Butyldimethyl(((2*S*,5*R*)-2-methyl-5-phenyl-5-(4,4,5,5-tetra methyl-1,3,2-dioxaborolan-2-yl)pentyl)oxy)silane (4.180).** The reaction was performed according to general (Method B)*** with 4,4,5,5-tetramethyl-2-phenyl-1,3,2-dioxaborolane (**4.265**) (61.2 mg, 0.30 mmol, 1.00 equiv), vinyllithium (0.19 mL, 1.58 M in tetrahydrofuran, 0.30 mmol, 1.00 equiv), (*R*)-*tert*-butyl(3-iodo-2-methylpropoxy)dimethylsilane (**4.271**) (113.1 mg, 0.36 mmol, 1.2 equiv), (*R*,*R*)-3,5-dimethylphenyl-Pybox **(*R*,*R*)-Xylyl-Pybox** (*R*,*R*)-**4.127** (7.7 mg, 0.018 mmol, 0.06 equiv), methallylnickel chloride dimer (2.2 mg, 0.0075 mmol, 0.025 equiv, 0.0075 M stock solution in THF prepared with sonication). The unpurified product was purified by

automated silica gel chromatography (Biotage 1% → 10% ethyl acetate in hexanes, stained in CAM) to afford colorless oil (91.7 mg, 73 % yield). **^{1}H NMR** (600 MHz, $CDCl_3$) δ 7.25 (t, *J* = 7.5 Hz, 2H), 7.21 (d, *J* = 7.0 Hz, 2H), 7.13 (t, *J* = 7.2 Hz, 1H), 3.41 (dd, *J* = 9.7, 6.0 Hz, 1H), 3.32 (dd, *J* = 9.7, 6.7 Hz, 1H), 2.26 (app t, *J* = 7.9 Hz, 1H), 1.81 (dddd, *J* = 16.4, 8.0, 5.4 Hz, 1H), 1.71 (dddd, *J* = 12.8, 7.8, 4.9 Hz, 1H), 1.64 – 1.54 (m, 1H), 1.43 – 1.35 (m, 1H), 1.21 (s, 6H), 1.19 (s, 6H), 1.08 – 0.96 (m, 1H), 0.88 (s, 9H), 0.84 (d, *J* = 6.7 Hz, 3H), 0.02 (s, 6H). **^{11}B NMR** (160 MHz, $CDCl_3$) δ 33.05. **^{13}C NMR** (151 MHz, $CDCl_3$) δ 143.63, 128.58, 128.43, 125.29, 83.44, 68.69, 36.09, 33.15, 33.02 (C-B), 30.26, 26.22, 24.87, 24.82, 18.59, 16.88, -5.10, -5.11. **IR** (neat) ν_{max} 2954.68 (w), 2928.33 (w), 2856.04 (w), 1462.38 (w), 1369.88 (m), 1321.60 (m), 1252.64 (w), 1143.00 (m), 1090.24 (m), 968.21 (w), 835.33 (s), 774.02 (m), 700.12 (m), 667.74 (m) cm^{-1}. **HRMS** (DART) for $C_{24}H_{43}BO_3Si$ $[M+H]^+$ calculated: 419.3153, found: 419.3138. $[\alpha]^{20}_D$: –15.008 (*c* 1.715, $CHCl_3$, *l* =50 mm).

Determination of Stereochemical Identity: Electrophile was purchased as a single enantiomer of the above specified configuration. Diastereoselectivity was assigned by ^{1}H NMR analysis. Absolute stereochemistry of the α-boryl stereocenter was assigned by analogy (see products: **4.192** and **epi-4.158**).

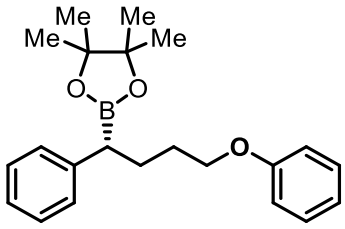




tert*-Butyldimethyl(((2*S*,5*S*)-2-methyl-5-phenyl-5-(4,4,5,5-tetra methyl-1,3,2-dioxaborolan-2-yl)pentyl)oxy)silane (4.181).** The reaction was performed according to general (Method B)*** with 4,4,5,5-tetramethyl-2-phenyl-1,3,2-dioxaborolane (**4.265**) (61.2 mg, 0.30 mmol, 1.00 equiv), vinyllithium (0.19 mL, 1.58 M in tetrahydrofuran, 0.30 mmol, 1.00 equiv), (*R*)-*tert*-butyl(3-iodo-2-methylpropoxy)dimethylsilane (**4.271**) (113.1 mg, 0.36 mmol, 1.2 equiv), (*R*,*R*)-3,5-dimethylphenyl-Pybox **(*S*,*S*)-Xylyl-Pybox** (*S*,*S*)-**4.127** (7.7 mg, 0.018 mmol, 0.06 equiv),

methallylnickel chloride dimer (2.2 mg, 0.0075 mmol, 0.025 equiv 0.0075 M stock solution in THF prepared with sonication). The unpurified product was purified by automated silica gel chromatography (Biotage 1% → 10% ethyl acetate in hexanes, stained in CAM) to afford colorless oil (90.4 mg, 72 % yield). **^{1}H NMR** (600 MHz, $CDCl_3$) δ 7.24 (t, *J* = 7.5 Hz, 2H), 7.20 (d, *J* = 7.2 Hz, 2H), 7.12 (t, *J* = 7.2 Hz, 1H), 3.41 (dd, *J* = 9.7, 5.7 Hz, 1H), 3.32 (dd, *J* = 9.7, 6.7 Hz, 1H), 2.26 (app t, *J* = 8.0 Hz, 1H), 1.90 (dddd, *J* = 19.5, 8.4, 4.9 Hz, 1H), 1.65 – 1.51 (m, 2H), 1.38 (dddd, *J* = 12.8, 10.9, 5.1 Hz, 1H), 1.21 (s, 6H), 1.19 (s, 6H), 1.09 – 0.99 (m, 2H), 0.90 – 0.83 (m, 12H), 0.00 (s, 6H). **^{11}B NMR** (160 MHz, $CDCl_3$) δ 33.37. **^{13}C NMR** (151 MHz, $CDCl_3$) δ 143.66, 128.55, 128.44, 125.29, 83.44, 68.62, 36.14, 33.25, 32.98 (C-B, partially buried), 30.43, 26.19, 24.90, 24.80, 18.56, 16.99, -5.13, -5.14. **IR** (neat) ν_{max} 2954.52 (w), 2928.19 (w), 2856.11 (w), 1462.79 (w), 1360.12 (m), 1321.67 (w), 1143.23 (m), 1091.19 (m), 835.69 (s), 700.30 (m), 668.18 (m) cm^{-1}. **HRMS** (DART) for $C_{24}H_{43}BO_3Si$ $[M+H]^+$ calculated: 419.3153, found: 419.3138. $[\alpha]^{20}_D$: +7.372 (*c* 1.55, $CHCl_3$, *l* =50 mm).

Determination of Stereochemical Identity: Electrophile was purchased as a single enantiomer of the above specified configuration. Diastereoselectivity was assigned by ^{1}H NMR analysis (see above). Absolute stereochemistry of the α-boryl stereocenter was assigned by analogy (see products: **4.192** and **epi-4.158**).

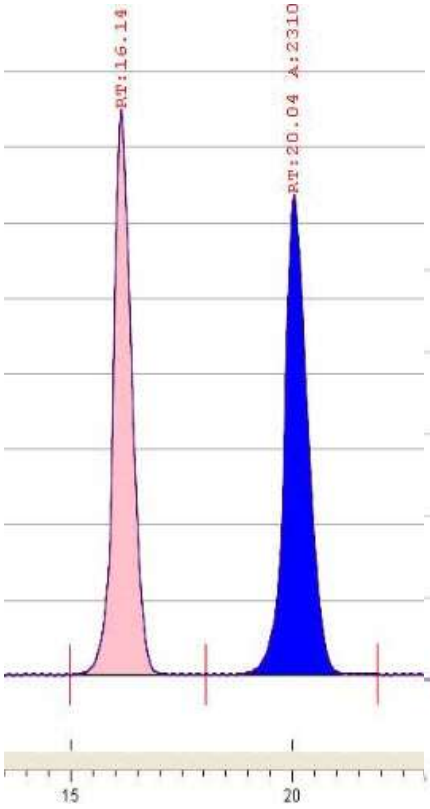


(*R*)-4,4,5,5-Tetramethyl-2-(4-phenoxy-1-phenylbutyl)-1,3,2-dioxa borolane (4.177) The reaction was performed according to general (***Method B)*** with 4,4,5,5-tetramethyl-2-phenyl-1,3,2-dioxaborolane (**4.265**) (61.2 mg, 0.30 mmol, 1.00 equiv), vinyllithium (0.19 mL, 1.58 M in tetrahydrofuran, 0.30 mmol, 1.00 equiv), (2-iodoethoxy)benzene (**4.267**) (89.3 mg, 0.36 mmol, 1.2 equiv), (*R*,*R*)-3,5-dimethylphenyl-Pybox **(*R*,*R*)-Xylyl-Pybox** (*R*,*R*)-**4.127** (7.7 mg, 0.018 mmol, 0.06 equiv), methallylnickel chloride dimer (2.2 mg, 0.0075 mmol, 0.025 equiv, 0.0075 M stock solution in THF prepared with sonication). The unpurified product was purified by automated silica gel chromatography (Biotage 1% →6% ethyl acetate in hexanes, stained in CAM) to afford colorless oil (44.4 mg, 42 % yield). **^{1}H NMR** (600 MHz, $CDCl_3$) δ 7.30 – 7.17 (m, 6H), 7.16 – 7.09 (m, 1H), 6.93 – 6.86 (m, 1H), 6.88 – 6.82 (m, 2H), 3.91 (aap t, *J* = 6.4 Hz, 2H), 2.35 (dd, *J* = 7.8, 3.4 Hz, 1H), 2.07 – 1.94 (m, 1H), 1.87 – 1.66 (m, 3H), 1.20 (s, 6H), 1.17 (s, 6H). **^{11}B NMR** (160 MHz, $CDCl_3$) δ 32.98. **^{13}C NMR** (151 MHz, $CDCl_3$) δ 159.27, 143.09, 129.55, 128.60, 128.55, 125.50, 120.61, 114.70, 83.57, 68.01, 32.26 (C-B), 29.12, 29.04, 24.87, 24.80. **IR** (neat) ν_{max} 2977.08 (w), 2933.85 (w), 2867.83 (W), 1600.18 (m), 1495.95 (m), 1370.27 (m), 1323.18 (m), 1244.69 (m), 1142.7 (m), 966.82 (w), 849.15 (w), 753.40 (m), 692.22 (m) cm^{-1}. **HRMS** (DART) for $C_{22}H_{29}BO_3$ $[M+H]^+$ calculated: 353.2288, found: 353.2302. $[\alpha]^{20}_D$: -11.290 (*c* 1.503, $CHCl_3$, *l* =50 mm).

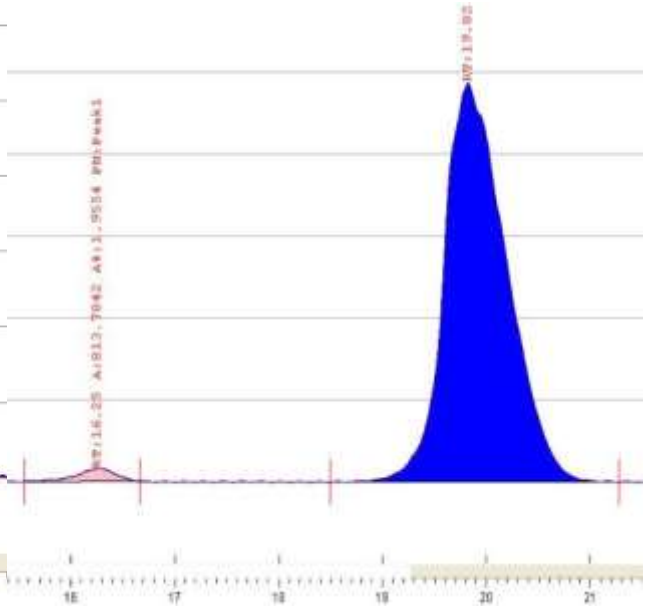
Determination of Stereochemical Identity: A stereoisomer mixture was prepared by mixing the R and S enantiomer products of reactions run according to the general procedure (***Method B***) with [{methallyl}NiCl]$_2$ (2.5 mol%) and (*S,S*)-Ph-Pybox (*S,S*)-**4.122** (3.0 mol%), or (*R,R*)-Ph-Pybox (*R,R*)-**4.122** (3.0 mol%) as the catalyst. Absolute stereochemistry was assigned by analogy (see products: **4.192** and **epi-4.158**). Product was oxidized according to ***General Method for Oxidation of Boronic Ester Products.***

SFC (Chiracel OD-H, 10% IPA, 3 mL/min, 100 bar, 35 °C, 210-270 nm) – analysis of (R)-4-phenoxy-1-phenylbutan-1-ol.

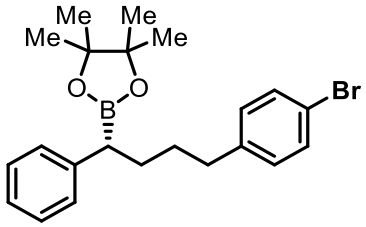
Stereoisomer Mixture



Standard Conditions



Peak No	% Area	Area	RT (min)	Peak No	% Area	Area	RT (min)
1	48.4338	21698.313	16.14	1	1.9554	813.7842	16.25
2	51.5662	23101.6692	20.04	2	98.0446	40803.0901	19.82
Total:	100	44799.9822		Total:	100	41616.8743	



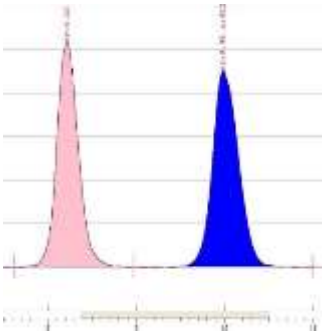
(*R*)-2-(4-(4-Bromophenyl)-1-phenylbutyl)-4,4,5,5-tetramethyl-1,3,2-dioxaborolane (4.179). The reaction was performed according to general (***Method B)*** with 4,4,5,5-tetramethyl-2-phenyl-1,3,2-dioxaborolane (**4.265**) (61.2 mg, 0.30 mmol, 1.00 equiv), vinyllithium (0.19 mL, 1.58 M in tetrahydrofuran, 0.30 mmol, 1.00 equiv), 1-bromo-4-(2-iodoethyl)benzene (111.9 mg, 0.36 mmol, 1.2 equiv), (*R*,*R*)-3,5-dimethylphenyl-Pybox **(*R*,*R*)-Xylyl-Pybox** (*R*,*R*)-**4.127** (7.7 mg, 0.018 mmol, 0.06 equiv), methallylnickel chloride dimer (2.2 mg, 0.0075 mmol, 0.025 equiv, 0.0075 M stock solution in THF prepared with sonication). The unpurified product was purified by automated silica gel chromatography (Biotage 1% → 3% ethyl acetate in hexanes, stained in CAM) to afford colorless oil (62.7 mg, 51 % yield). **^{1}H NMR** (600 MHz, $CDCl_3$) δ 7.38 – 7.33 (m, 2H), 7.29 – 7.21 (m, 2H), 7.21 – 7.17 (m, 2H), 7.16 – 7.11 (m, 1H), 7.03 – 6.97 (m, 2H), 2.62 – 2.49 (m, 2H), 2.32 (app t, *J* = 7.9 Hz, 1H), 1.94 – 1.80 (m, 1H), 1.75 – 1.64 (m, 1H), 1.62 – 1.53 (m, 2H), 1.21 (s, 6H), 1.19 (s, 6H). **^{11}B NMR** (160 MHz, $CDCl_3$) δ 33.28. **^{13}C NMR** (151 MHz, $CDCl_3$) δ 143.23, 141.78, 131.44, 130.35, 128.56, 128.51, 125.44, 119.46, 83.53, 35.49, 32.41 (C-B, partially buried), 32.30, 31.04, 24.87, 24.80. **IR** (neat) ν_{max} 2977.23 (w), 2930.13 (w), 2857.43 (w), 1488.27 (m), 1451.76 (w), 1369.29 (m), 1322.18 (m), 1142.37 (s), 1010.96 (w), 701.35 (m) cm^{-1}. **HRMS** (DART) for $C_{22}H_{28}BBrO_2$

$[M+NH_4]^+$ calculated: 432.1709, found: 432.1729. $[\alpha]^{20}_D$: –19.320 (*c* 1.48, $CHCl_3$, *l* =50 mm).

Determination of Stereochemical Identity: A stereoisomer mixture was prepared by mixing the R and S enantiomer products of reactions run according to the general procedure (***Method B***) with [{methallyl}NiCl]$_2$ (2.5 mol%) and (*S,S*)-Ph-Pybox (*S,S*)-**4.122** (3.0 mol%), or (*R,R*)-Ph-Pybox (*R,R*)-**4.122** (3.0 mol%) as the catalyst. Absolute stereochemistry was assigned by analogy (see products: **4.192** and **epi-4.158**).

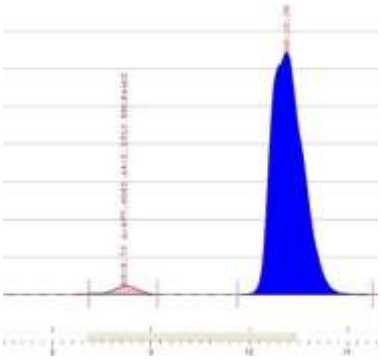
SFC (Chiracel AD-H, 2% IPA, 3 mL/min, 100 bar, 35 °C, 210-270 nm) – analysis of (R)-2-(4-(4-bromophenyl)-1-phenylbutyl)-4,4,5,5-tetramethyl-1,3,2-dioxaborolane.

Stereoisomer Mixture

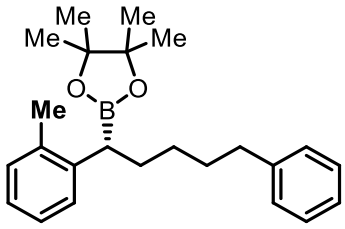


Peak No	% Area	Area	RT (min)
1	48.5077	8694.1096	8.22
2	51.4923	9229.0447	9.98
Total:	100	17923.1543	

Standard Conditions



Peak No	% Area	Area	RT (min)
1	2.2913	697.6045	8.73
2	97.7087	29747.6486	10.38
Total:	100	30445.2531	

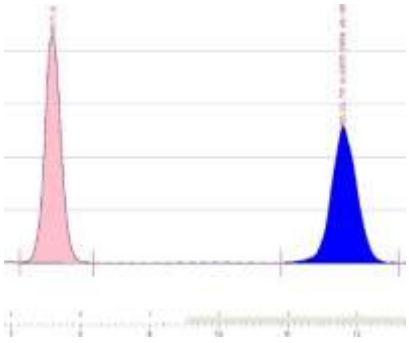


(*R*)-4,4,5,5-Tetramethyl-2-(5-phenyl-1-(o-tolyl)pentyl)-1,3,2-dioxa borolane (4.185). The reaction was performed according to general (***Method B)*** with 4,4,5,5-tetramethyl-2-(o-tolyl)-1,3,2-dioxaborolane (65.4 mg, 0.30 mmol, 1.00 equiv), vinyllithium (0.19 mL, 1.58 M in tetrahydrofuran, 0.30 mmol, 1.00 equiv), (3-iodopropyl)benzene (88.6 mg, 0.36 mmol, 1.2 equiv), (*R*,*R*)-3,5-dimethylphenyl-Pybox **(*R*,*R*)-Xylyl-Pybox** (*R*,*R*)-**4.127** (7.7 mg, 0.018 mmol, 0.06 equiv), methallylnickel chloride dimer (2.2 mg, 0.0075 mmol, 0.025 equiv, 0.0075 M stock solution in THF prepared with sonication). The unpurified product was purified by automated silica gel chromatography (Biotage 1% → 2% ethyl acetate in hexanes, stained in CAM) to afford colorless oil (69.9 mg, 64 % yield). **^{1}H NMR** (600 MHz, $CDCl_3$) δ 7.27 (q, *J* = 7.5 Hz, 5H), 7.24 – 7.10 (m, 6H), 7.07 (t, *J* = 7.4 Hz, 1H), 2.61 (ddd, *J* = 11.0, 6.3, 5.2 Hz, 2H), 2.53 (app t, *J* = 7.8 Hz, 1H), 1.97 – 1.87 (m, 1H), 1.75 – 1.61 (m, 3H), 1.46 – 1.36 (m, 2H), 1.22 (s, 4H), 1.19 (s, 4H). **^{11}B NMR** (160 MHz, $CDCl_3$) δ 33.47. **^{13}C NMR** (151 MHz, $CDCl_3$) δ 143.00, 142.02, 136.12, 130.28, 128.61, 128.39, 127.90, 126.10, 125.72, 125.13, 83.36, 36.04, 32.29, 31.79, 29.34, 28.22 (C-B), 24.89, 24.76, 20.37. **IR** (neat) ν_{max} 2976.96 (m), 2929.65 (m), 2856.59 (w), 1489.71 (w), 1454.12 (w), 1370.20 (m), 1321.35 (m), 1143.18 (s), 967.07 (w), 850.07 (w), 731.09 (m), 698.62 (m) cm^{-1}. **HRMS** (DART) for $C_{24}H_{33}BO_2$ $[M+H]^+$: calculated: 365.2652, found: 365.2667. $[\alpha]_D^{20}$ = –8.172 (*c* 2.01, $CHCl_3$, *l* = 50 mm).

Determination of Stereochemical Identity: A stereoisomer mixture was prepared by mixing the R and S enantiomer products of reactions run according to the general procedure (***Method B***) with [{methallyl}NiCl]$_2$ (2.5 mol%) and (*S,S*)-Ph-Pybox (*S*,*S*)-**4.122** (3.0 mol%), or (*R,R*)-Ph-Pybox (*R*,*R*)-**4.122** (3.0 mol%) as the catalyst. Absolute stereochemistry was assigned by analogy (see products: **4.192** and **epi-4.158**).

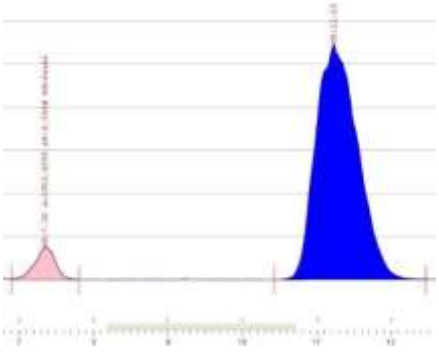
SFC (Chiracel OJ-H, 2% IPA, 3 mL/min, 100 bar, 35 °C, 210-270 nm) – analysis of (R)-4,4,5,5-tetramethyl-2-(5-phenyl-1-(o-tolyl)pentyl)-1,3,2-dioxa borolane.

Stereoisomer Mixture

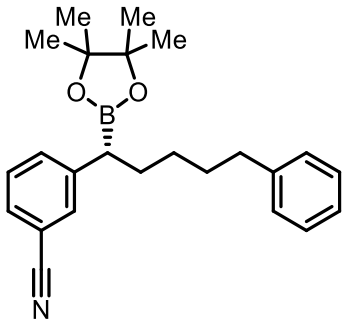


Peak No	% Area	Area	RT (min)
1	51.5313	7080.0157	7.6
2	48.4687	6659.2484	11.79
Total:	100	13739.2641	

Standard Conditions



Peak No	% Area	Area	RT (min)
1	6.3566	2923.4595	7.35
2	93.6434	43067.7162	11.23
Total:	100	45991.1757	



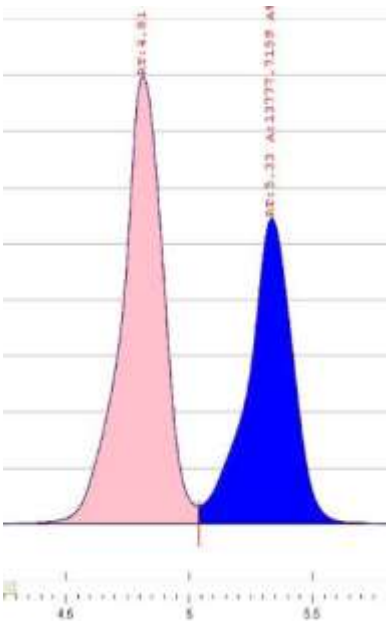
(*R*)-3-(5-Phenyl-1-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl) pentyl)benzonitrile (4.188). The reaction was performed according to general (***Method B)*** with 3-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)benzonitrile (68.7 mg, 0.30 mmol, 1.00 equiv), vinyllithium (0.19 mL, 1.58 M in tetrahydrofuran, 0.30 mmol, 1.00 equiv), (3-iodopropyl)benzene (88.6 mg, 0.36 mmol, 1.2 equiv), (*R*,*R*)-3,5-dimethylphenyl-Pybox **(*R*,*R*)-Xylyl-Pybox** (*R*,*R*)-**4.127** (7.7 mg, 0.018 mmol, 0.06 equiv), methallylnickel chloride dimer (2.2 mg, 0.0075 mmol, 0.025 equiv, 0.0075 M stock solution in THF prepared with sonication). The unpurified product was purified by automated silica gel chromatography (Biotage 1% → 3% ethyl acetate in hexanes, stained in CAM) to afford colorless oil (52.8 mg, 47 % yield). **^{1}H NMR** (600 MHz, $CDCl_3$) δ 7.50 (s, 1H), 7.45 – 7.40 (m, 2H), 7.33 (t, *J* = 7.7 Hz, 1H), 7.26 (t, *J* = 7.6 Hz, 2H), 7.19 – 7.11 (m, 3H), 2.63 – 2.51 (m, 2H), 2.33 (app t, *J* = 7.9 Hz, 1H), 1.87 (dddd, *J* = 13.6, 9.7, 7.8, 6.1 Hz, 1H), 1.72 – 1.57 (m, 3H), 1.32 – 1.25 (m, 2H), 1.19 (s, 6H), 1.17 (s, 6H). **^{11}B NMR** (160 MHz, $CDCl_3$) δ 32.79. **^{13}C NMR** (151 MHz, $CDCl_3$) δ 145.22, 142.69, 133.21, 132.04, 129.22, 129.15, 128.58, 128.44, 125.83, 119.52, 112.42, 83.86, 35.89, 32.37, (C-B not observed), 31.44, 28.84, 24.80, 24.77. **IR** (neat) ν_{max} 2978.88 (w), 2930.31 (m), 2855.99 (w), 2228.99 (w), 1481.16 (w), 1454.39 (w), 1370.93 (m), 1327.91 (m), 1141.98 (m), 967.77 (w), 859.74 (w), 847.75 (w), 747.37 (w), 699.42 (w) cm^{-1}. **HRMS** (DART) for

$C_{24}H_{30}BNO_2$ $[M+NH_4]^+$: calculated: 393.2713, found: 393.2729. $[\alpha]_D^{20} = -11.791$ (*c* 1.565, $CHCl_3$, *l* = 50 mm).

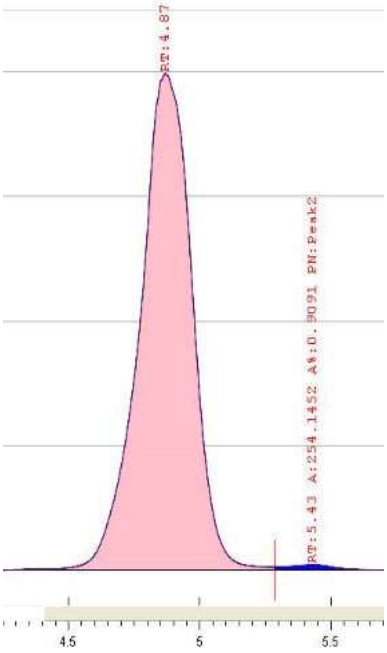
Determination of Stereochemical Identity: A stereoisomer mixture was prepared by mixing the R and S enantiomer products of reactions run according to the general procedure (***Method B***) with [{methallyl}NiCl]$_2$ (2.5 mol%) and (*S,S*)-Ph-Pybox (*S,S*)-**4.122** (3.0 mol%), or (*R,R*)-Ph-Pybox (*R,R*)-**4.127** (3.0 mol%) as the catalyst. Absolute stereochemistry was assigned by analogy (see products: **4.192** and **epi-4.158**).

SFC (Chiracel OJ-H, 5% IPA, 3 mL/min, 100 bar, 35 °C, 210-270 nm) – analysis of (R)-3-(5-phenyl-1-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl) pentyl)benzonitrile.

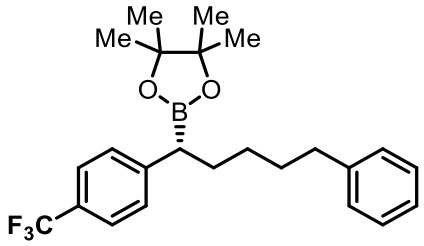
Stereoisomer Mixture



Standard Conditions



Peak No	% Area	Area	RT (min)	Peak No	% Area	Area	RT (min)
1	57.825	18890.2602	4.81	1	99.0909	27700.1247	4.87
2	42.175	13777.7159	5.33	2	0.9091	254.1452	5.43
Total:	100	32667.9761		Total:	100	27954.2699	



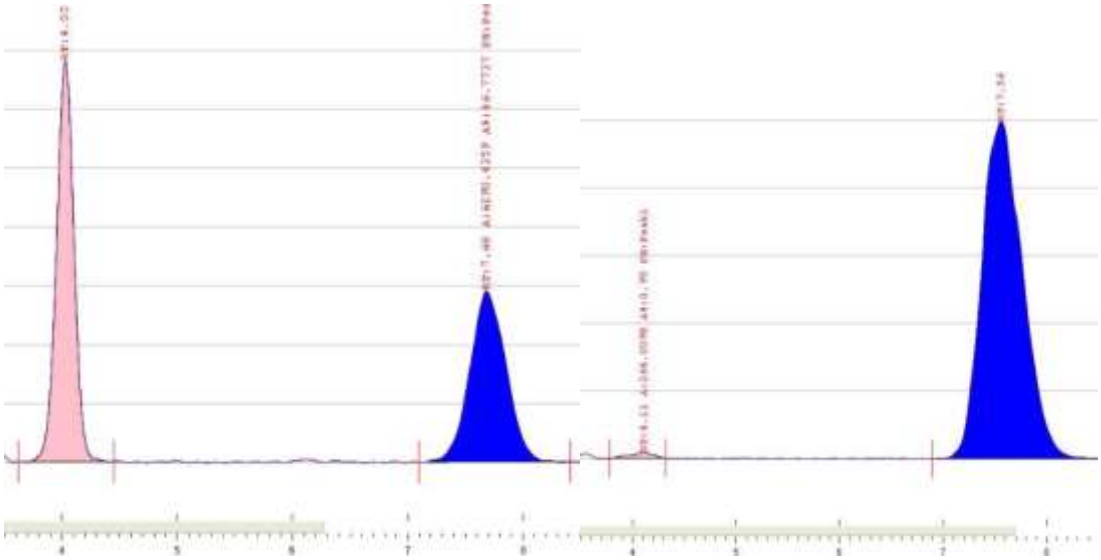
(*R*)-4,4,5,5-Tetramethyl-2-(5-phenyl-1-(4-(trifluoromethyl)phenyl)pentyl)-1,3,2-dioxaborolane (4.186) The reaction was performed according to general (***Method B)*** with 4,4,5,5-tetramethyl-2-(4-(trifluoromethyl)phenyl)-1,3,2-dioxaborolane (81.6 mg, 0.30 mmol, 1.00 equiv), vinyllithium (0.19 mL, 1.58 M in tetrahydrofuran, 0.30 mmol, 1.00 equiv), (3-iodopropyl)benzene (88.6 mg, 0.36 mmol, 1.2 equiv), (*R*,*R*)-3,5-dimethylphenyl-Pybox **(*R*,*R*)-Xylyl-Pybox** (*R*,*R*)-**4.127** (7.7 mg, 0.018 mmol, 0.06 equiv), methallylnickel chloride dimer (2.2 mg, 0.0075 mmol, 0.025 equiv, 0.0075 M stock solution in THF prepared with sonication). The unpurified product was purified by automated silica gel chromatography (Biotage 1% → 2% ethyl acetate in hexanes, stained in CAM) to afford colorless oil (66.5 mg, 53 % yield). **^{1}H NMR** (600 MHz, $CDCl_3$) δ 7.51 (d, *J* = 8.1 Hz, 2H), 7.31 (d, *J* = 8.0 Hz, 2H), 7.26 (t, *J* = 7.5 Hz, 2H), 7.20 – 7.10 (m, 3H), 2.64 – 2.53 (m, 2H), 2.38 (app t, *J* = 7.9 Hz, 1H), 1.90 (app dq, *J* = 14.0, 8.0 Hz, 1H), 1.70 (app dq, *J* = 15.5, 8.0 Hz, 1H), 1.66 – 1.60 (m, 2H), 1.36 – 1.29 (m, 2H), 1.20 (s, 6H), 1.18 (s, 6H). **^{11}B NMR** (160 MHz, $CDCl_3$) δ 33.28. **^{13}C NMR** (151 MHz, $CDCl_3$) δ 147.98, 142.81, 128.77, 128.59, 128.42, 127.66 (q, *J*= 31.7 Hz), 125.8, 125.36 (q, *J*=3.8 Hz), 124.6 (q, *J*=271.2

Hz), 83.74, 35.93, 32.72 (C-B), 32.43, 31.52, 28.95, 24.81, 24.77. **IR** (neat) ν_{max} 2978.67 (w), 2929.78 (m), 2857.46 (w), 1616.74 (w), 1370.83 (m), 1322.06 (s), 1162.15 (s), 1120.30 (s), 1067.89 (s), 1017.96 (w), 851.27 (m), 746.87 (w), 698.54 (m) cm^{-1}. **HRMS** (DART) for $C_{24}H_{30}BF_3O_2$ $[M+NH_4]^+$ calculated: 436.2635, found: 436.2657. $[\alpha]^{20}_D$: – 11.281 (*c* 2.17, $CHCl_3$, *l* =50 mm).

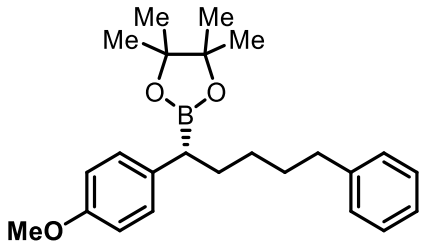
Determination of Stereochemical Identity: A stereoisomer mixture was prepared by mixing the R and S enantiomer products of reactions run according to the general procedure (***Method B***) with [{methallyl}NiCl]$_2$ (2.5 mol%) and (*S,S*)-Ph-Pybox (S,S)-**4.122** (3.0 mol%), or (*R,R*)-Ph-Pybox (*R,R*)-**4.122** (3.0 mol%) as the catalyst. Absolute stereochemistry was assigned by analogy (see products: **4.192** and **epi-4.158**).

SFC (Chiracel OJ-H, 2% IPA, 3 mL/min, 100 bar, 35 °C, 210-270 nm) – analysis of (R)-4,4,5,5-tetramethyl-2-(5-phenyl-1-(4-(trifluoromethyl) phenyl)pentyl)-1,3,2-dioxaborolane.

Stereoisomer Mixture Standard Conditions



Peak No	% Area	Area	RT (min)	Peak No	% Area	Area	RT (min)
1	53.2263	7158.221	4.03	1	0.95	264.0098	4.11
2	46.7737	6290.4359	7.68	2	99.05	27526.251	7.56
Total:	100	13448.6569		Total:	100	27790.2608	



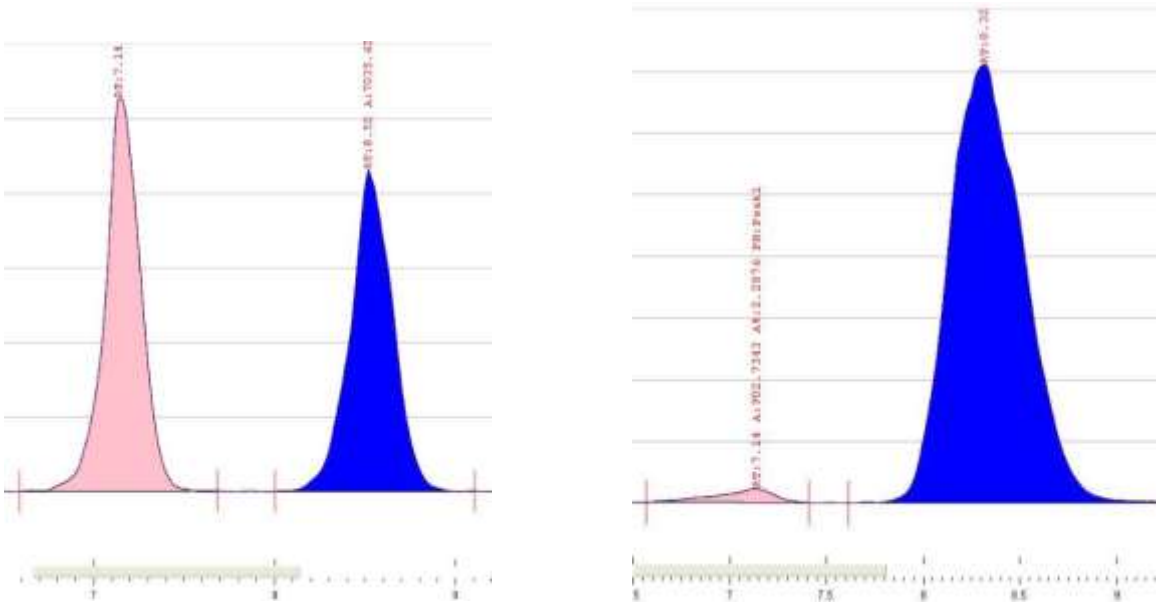
(*R*)-2-(1-(4-Methoxyphenyl)-5-phenylpentyl)-4,4,5,5-tetrameth yl-1,3,2-dioxaborolane (4.187). The reaction was performed according to general (***Method B)*** with 2-(4-methoxyphenyl)-4,4,5,5-tetramethyl-1,3,2-dioxaborolane (70.2 mg, 0.30 mmol, 1.00 equiv), vinyllithium (0.19 mL, 1.58 M in tetrahydrofuran, 0.30 mmol, 1.00 equiv), (3-iodopropyl)benzene (88.6 mg, 0.36 mmol, 1.2 equiv), (*R*,*R*)-3,5-dimethylphenyl-Pybox **(*R*,*R*)-Xylyl-Pybox** (*R*,*R*)-**4.127** (7.7 mg, 0.018 mmol, 0.06 equiv), methallylnickel chloride dimer (2.2 mg, 0.0075 mmol, 0.025 equiv, 0.0075 M stock solution in THF prepared with sonication). The unpurified product was purified by

automated silica gel chromatography (Biotage 1% → 4% ethyl acetate in hexanes, stained in CAM) to afford colorless oil (59.3 mg, 52 % yield). **^{1}H NMR** (600 MHz, $CDCl_3$) δ 7.26 (t, *J* = 7.6 Hz, 2H), 7.20 – 7.10 (m, 5H), 6.82 (d, *J* = 8.6 Hz, 2H), 3.79 (s, 3H), 2.64 – 2.52 (m, 2H), 2.25 (app t, *J* = 7.9 Hz, 1H), 1.84 (app dq, *J* = 15.9, 7.9 Hz, 1H), 1.69 – 1.57 (m, 3H), 1.37 – 1.29 (m, 3H), 1.20 (s, 6H), 1.18 (s, 6H). **^{11}B NMR** (160 MHz, $CDCl_3$) δ 33.37. **^{13}C NMR** (151 MHz, $CDCl_3$) δ 157.48, 143.03, 135.56, 129.39, 128.60, 128.38, 125.71, 113.91, 83.38, 55.37, 36.03, 32.98, 31.65, 31.51 (C-B, partially buried), 29.08, 24.83, 24.79. **IR** (neat) ν_{max} 2976.87 (w), 2928.58 (m), 2855.67 (w), 1606.57 (w), 1505.97 (s), 1454.56 (w), 1359.19 (m), 1320.72 (m), 1245.46 (s), 1142.45 (s), 1037.27 (m), 967.58 (w), 828.89 (m), 699.18 (m) cm^{-1}. **HRMS** (DART) for $C_{24}H_{33}BO_3$ $[M+H]^+$: calculated: 398.2866, found: 398.287. $[\alpha]_D^{20}$ = –8.605 (*c* 1.94, $CHCl_3$, *l* = 50 mm).

Determination of Stereochemical Identity: A stereoisomer mixture was prepared by mixing the R and S enantiomer products of reactions run according to the general procedure (***Method B***) with [{methallyl}NiCl]$_2$ (2.5 mol%) and (*S,S*)-Ph-Pybox (*S*,*S*)-**4.122** (3.0 mol%), or (*R,R*)-Ph-Pybox (*R*,*R*)-**4.122** (3.0 mol%) as the catalyst. Absolute stereochemistry was assigned by analogy (see products: **4.192** and **epi-4.158**).

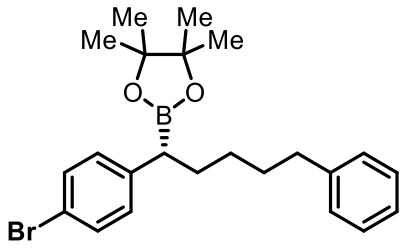
SFC (Chiracel OJ-H, 4% IPA, 3 mL/min, 100 bar, 35 °C, 210-270 nm) – analysis of (R)-2-(1-(4-methoxyphenyl)-5-phenylpentyl)-4,4,5,5-tetrameth yl-1,3,2-dioxaborolane.

Stereoisomer Mixture Standard Conditions



Peak No	% Area	Area	RT (min)
1	50.853	7279.838	7.14
2	49.147	7035.6214	8.52
Total:	100	14315.4594	

Peak No	% Area	Area	RT (min)
1	2.2876	902.7343	7.14
2	97.7124	38558.8822	8.32
Total:	100	39461.6165	



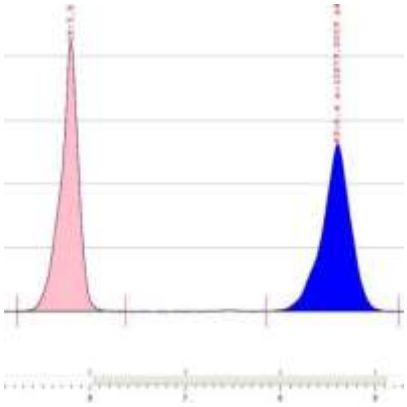
(*R*)-2-(1-(4-Bromophenyl)-5-phenylpentyl)-4,4,5,5-tetramethyl-1,3,2-dioxaborolane (4.189). The reaction was performed according to general (***Method B)*** with 2-(4-bromophenyl)-4,4,5,5-tetramethyl-1,3,2-dioxaborolane (**4.266**) (84.9 mg, 0.30 mmol, 1.00 equiv), vinyllithium (0.19 mL, 1.58 M in tetrahydrofuran, 0.30 mmol, 1.00 equiv), (3-iodopropyl)benzene (88.6 mg, 0.36 mmol, 1.2 equiv), (*R*,*R*)-3,5-dimethylphenyl-Pybox **(*R*,*R*)-Xylyl-Pybox** (*R*,*R*)-**4.127** (7.7 mg, 0.018 mmol, 0.06 equiv), methallylnickel chloride dimer (2.2 mg, 0.0075 mmol, 0.025 equiv, 0.0075 M stock solution in THF prepared with sonication). The unpurified product was

purified by automated silica gel chromatography (Biotage 1% → 3% ethyl acetate in hexanes, stained in CAM) to afford colorless oil (79.9 mg, 62 % yield). **^{1}H NMR** (600 MHz, c $CDCl_3$) δ 7.36 (d, *J* = 8.2 Hz, 2H), 7.26 (t, *J* = 7.6 Hz, 2H), 7.19 – 7.11 (m, 3H), 7.08 (d, *J* = 8.3 Hz, 2H), 2.64 – 2.51 (m, 2H), 2.26 (app t, *J* = 7.9 Hz, 1H), 1.85 (app dq, *J* = 15.3, 7.8 Hz, 1H), 1.69 – 1.56 (m, 3H), 1.34 – 1.25 (m, 2H), 1.19 (s, 6H), 1.17 (s, 6H). **^{11}B NMR** (160 MHz, $CDCl_3$) δ 32.98. **^{13}C NMR** (151 MHz, $CDCl_3$) δ 142.84, 142.63, 131.46, 130.30, 128.57, 128.40, 125.75, 119.02, 83.58, 77.45, 77.24, 77.03, 35.94, 32.50, 32.02 (C-B), 31.52, 28.93, 24.81, 24.77. **IR** (neat) ν_{max} 2978.88 (w), 2930.31 (m), 2855.99 (w), 2228.99 (w), 1481.16 (w), 1454.39 (w), 1370.93 (m), 1327.91 (m), 1141.98 (m), 967.77 (w), 859.74 (w), 847.75 (w), 747.37 (w), 699.42 (w) cm^{-1}. **HRMS** (DART) for $C_{23}H_{30}BBrO_2$ $[M+NH_4]^+$ calculated: 446.1866, found: 446.1871. $[\alpha]^{20}_D$: –16.972 (*c* 2.575, $CHCl_3$, *l* =50 mm).

Determination of Stereochemical Identity: A stereoisomer mixture was prepared by mixing the R and S enantiomer products of reactions run according to the general procedure (***Method B***) with [{methallyl}NiCl]$_2$ (2.5 mol%) and (*S,S*)-Ph-Pybox (S,S)-**4.122** (3.0 mol%), or (*R,R*)-Ph-Pybox (*R*,*R*)-**4.122**(3.0 mol%) as the catalyst. Absolute stereochemistry was assigned by analogy (see products: **4.192** and **epi-4.158**).

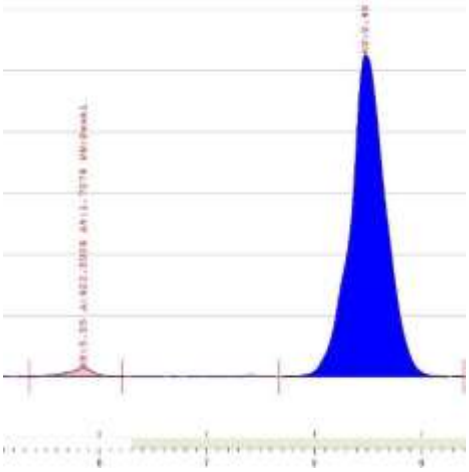
SFC (Chiracel OJ-H, 5% IPA, 3 mL/min, 100 bar, 35 °C, 210-270 nm) – analysis of (R)-2-(1-(4-bromophenyl)-5-phenylpentyl)-4,4,5,5-tetramethyl-1,3,2-dioxaborolane.

Stereoisomer Mixture

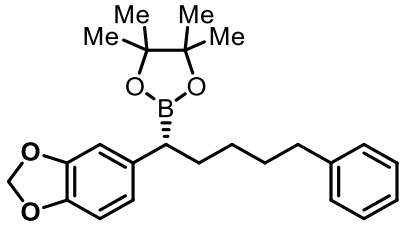


Peak No	% Area	Area	RT (min)
1	50.3518	11034.001	5.8
2	49.6482	10879.8059	8.6
Total:	100	21913.8069	

Standard Conditions



Peak No	% Area	Area	RT (min)
1	1.7074	423.8004	5.85
2	98.2926	24397.3066	8.48
Total:	100	24821.107	



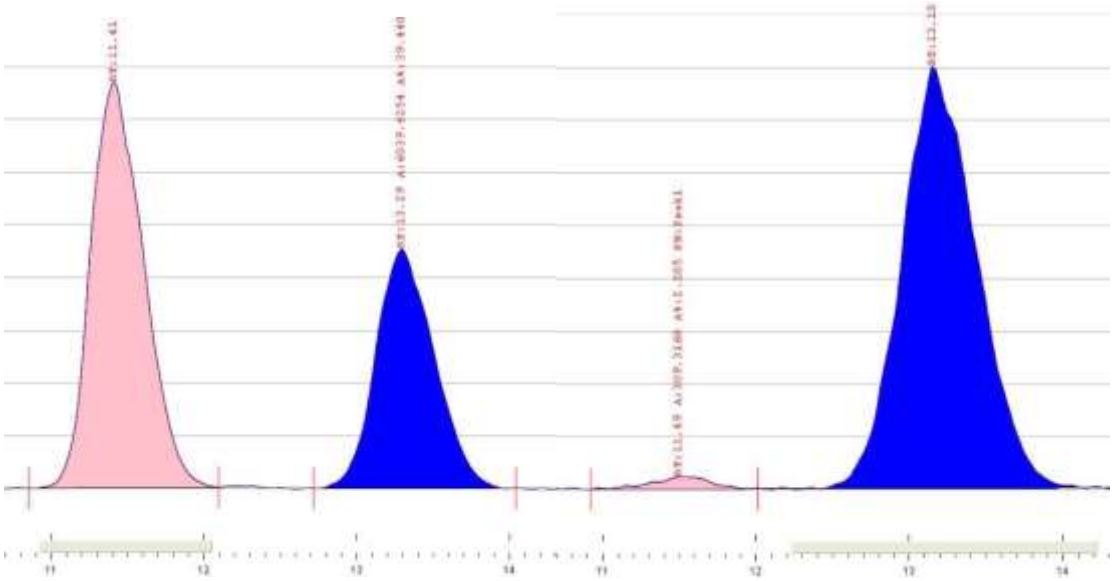
(*R*)-2-(1-(Benzo[d][1,3]dioxol-5-yl)-5-phenylpentyl)-4,4,5,5-tetramethyl-1,3,2-dioxaborolane (4.190). The reaction was performed according to general (***Method B)*** with 2-(benzo[d][1,3]dioxol-5-yl)-4,4,5,5-tetramethyl-1,3,2-dioxaborolane (74.4 mg, 0.30 mmol, 1.00 equiv), vinyllithium (0.19 mL, 1.58 M in tetrahydrofuran, 0.30 mmol, 1.00 equiv), (3-iodopropyl)benzene (88.6 mg, 0.36 mmol, 1.2 equiv), (*R*,*R*)-3,5-dimethylphenyl-Pybox **(*R*,*R*)-Xylyl-Pybox** (*R*,*R*)-**4.127** (7.7 mg, 0.018 mmol, 0.06 equiv), methallylnickel chloride dimer (2.2 mg, 0.0075 mmol, 0.025 equiv, 0.0075 M stock solution in THF prepared with sonication). The unpurified product was purified by automated silica gel chromatography (Biotage 1% → 3% ethyl acetate in

hexanes, stained in CAM) to afford colorless oil (63.1 mg, 53 % yield. **^{1}H NMR** (600 MHz, $CDCl_3$) δ 7.26 (t, *J* = 7.4 Hz, 2H), 7.19 – 7.11 (m, 3H), 6.74 (s, 1H), 6.71 (d, *J* = 7.9 Hz, 1H), 6.64 (d, *J* = 7.9 Hz, 1H), 5.93 – 5.89 (m, 2H), 2.63 – 2.52 (m, 2H), 2.22 (app t, *J* = 7.9 Hz, 1H), 1.82 (app dq, *J* = 15.7, 7.8 Hz, 1H), 1.67 – 1.59 (m, 3H), 1.35 – 1.28 (m, 3H), 1.20 (s, 6H), 1.18 (s, 6H). **^{11}B NMR** (160 MHz, $CDCl_3$) δ 33.08. **^{13}C NMR** (151 MHz, $CDCl_3$) δ 147.66, 145.31, 143.00, 137.43, 128.61, 128.39, 125.73, 121.32, 109.02, 108.31, 100.81, 83.47, 77.45, 77.24, 77.03, 36.02, 33.05, 32.17 (C-B), 31.63, 29.00, 24.85, 24.80. **IR** (neat) ν_{max} 3376.48 (Br, w), 2977.46 (w), 2929.72 (m), 2858.08 (w), 1604.59 (w), 1486.94 (m), 1442.28 (m), 1371.86 (m), 1325.71 (m), 1142.83 (m), 1038.87 (m), 932.10 (m), 851.06 (m), 811.02 (m), 699.44 (w) cm^{-1}. **HRMS** (DART) for $C_{24}H_{31}BO_4$ $[M+H]^+$: calculated: 395.2394, found: 395.2381. $[\alpha]_D^{20}$ = –8.605 (*c* 1.90, $CHCl_3$, *l* = 50 mm).

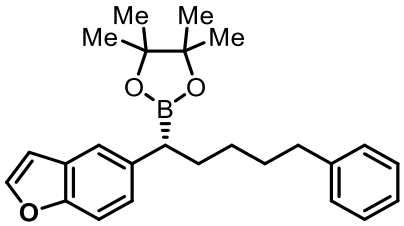
Determination of Stereochemical Identity: A stereoisomer mixture was prepared by mixing the R and S enantiomer products of reactions run according to the general procedure (***Method B***) with [{methallyl}NiCl]$_2$ (2.5 mol%) and (*S,S*)-Ph-Pybox (*S*,*S*)-**4.122** (3.0 mol%), or (*R,R*)-Ph-Pybox (*R*,*R*)-**4.122** (3.0 mol%) as the catalyst. Absolute stereochemistry was assigned by analogy (see products: **4.192** and **epi-4.158**).

SFC (Chiracel OJ-H, 2% IPA, 3 mL/min, 100 bar, 35 °C, 210-270 nm) – analysis of (R)-2-(1-(benzo[d][1,3]dioxol-5-yl)-5-phenylpentyl)-4,4,5,5-tetramethyl-1,3,2-dioxaborolane.

Stereoisomer Mixture Standard Conditions



Peak No	% Area	Area	RT (min)	Peak No	% Area	Area	RT (min)
1	60.5592	9273.2178	11.41	1	2.205	309.3168	11.49
2	39.4408	6039.4254	13.29	2	97.795	13718.8293	13.15
Total:	100	15312.6432		Total:	100	14028.1461	



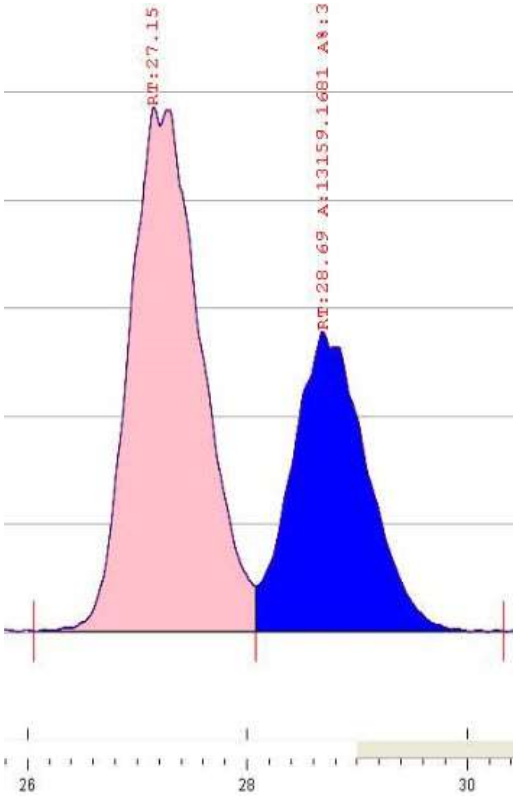
(*R*)-2-(1-(Benzofuran-5-yl)-5-phenylpentyl)-4,4,5,5-tetra methyl-1,3,2-dioxaborolane (4.191). The reaction was performed according to general (***Method B)*** with 2-(benzofuran-5-yl)-4,4,5,5-tetramethyl-1,3,2-dioxaborolane (**4.265**) (73.2 mg, 0.30 mmol, 1.00 equiv), vinyllithium (0.19 mL, 1.58 M in tetrahydrofuran, 0.30 mmol, 1.00 equiv), (3-iodopropyl)benzene (88.6 mg, 0.36 mmol, 1.2 equiv), (*R*,*R*)-3,5-dimethylphenyl-Pybox **(*R*,*R*)-Xylyl-Pybox** (*R*,*R*)-**4.127** (7.7 mg, 0.018 mmol, 0.06 equiv), methallylnickel chloride dimer (2.2 mg, 0.0075 mmol, 0.025 equiv,

0.0075 M stock solution in THF prepared with sonication). The unpurified product was purified by automated silica gel chromatography (Biotage 1% → 3% ethyl acetate in hexanes, stained in CAM) to afford colorless oil (78.5 mg, 67 % yield). **^{1}H NMR** (600 MHz, $CDCl_3$) δ 7.59 – 7.55 (m, 1H), 7.43 (s, 1H), 7.40 (d, *J* = 8.5 Hz, 1H), 7.26 (t, *J* = 7.5 Hz, 2H), 7.19 – 7.11 (m, 4H), 6.71 (s, 1H), 2.65 – 2.52 (m, 2H), 2.40 (app t, *J* = 7.9 Hz, 1H), 1.93 (app dq, *J* = 15.4, 8.1 Hz, 1H), 1.74 (app dq, *J* = 15.6, 7.8 Hz, 1H), 1.69 – 1.60 (m, 2H), 1.41 – 1.32 (m, 2H), 1.21 (s, 6H), 1.18 (s, 6H). **^{11}B NMR** (160 MHz, $CDCl_3$) δ 33.08. **^{13}C NMR** (151 MHz, $CDCl_3$) δ 153.53, 144.95, 143.01, 137.97, 128.60, 128.38, 127.71, 125.72, 125.14, 120.54, 111.13, 106.72, 83.45, 36.01, 33.25, 32.29 (C-B), 31.65, 29.08, 24.84, 24.79. **IR** (neat) ν_{max} 2976.66 (w), 2929.82 (m), 2855.44 (w), 1465.09 (w), 1370.40 (m), 1321.37 (m), 1260.78 (w), 1143.70 (m), 1031.70 (w), 968.22 (w), 849.11 (w), 739.84 (w), 698.97 (w) cm^{-1}**. HRMS** (DART) for $C_{25}H_{31}BO_3$ $[M+NH_4]^+$ calculated: 408.271, found: 408.2729. $[\alpha]^{20}_D$: –16.857 (*c* 1.11, $CHCl_3$, *l* =50 mm).

Determination of Stereochemical Identity: A stereoisomer mixture was prepared by mixing the R and S enantiomer products of reactions run according to the general procedure (***Method B***) with [{methallyl}NiCl]$_2$ (2.5 mol%) and (*S,S*)-Ph-Pybox (*S*,*S*)-**4.122** (3.0 mol%), or (*R,R*)-Ph-Pybox (*R*,*R*)-**4.122** (3.0 mol%) as the catalyst. Absolute stereochemistry was assigned by analogy (see products: **4.192** and **epi-4.158**).

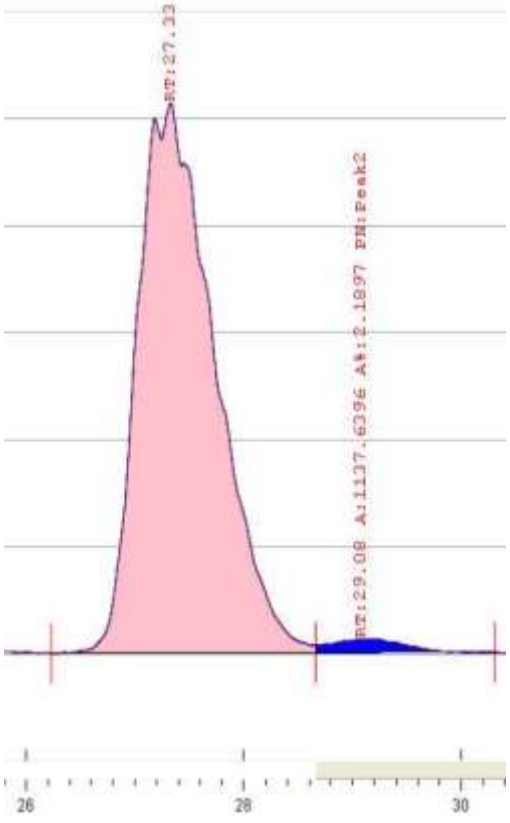
SFC (Chiracel OD-H, 2% IPA, 3 mL/min, 100 bar, 35 °C, 210-270 nm) – analysis of (R)-2-(1-(benzofuran-5-yl)-5-phenylpentyl)-4,4,5,5-tetra methyl-1,3,2-dioxaborolane.

Stereoisomer Mixture

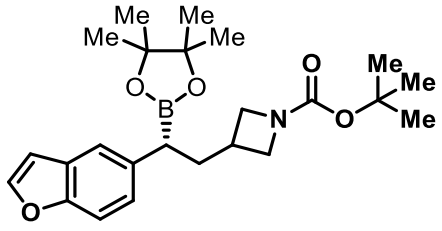


Peak No	% Area	Area	RT (min)
1	62.5591	21987.3255	27.15
2	37.4409	13159.1681	28.69
Total:	100	35146.4936	

Standard Conditions



Peak No	% Area	Area	RT (min)
1	97.8103	50817.4588	27.33
2	2.1897	1137.6396	29.08
Total:	100	51955.0984	



tert*-Butyl (*R*)-3-(2-(benzofuran-5-yl)-2-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)ethyl)azetidine-1-carboxylate (4.192).** The reaction was performed according to general (Method B)*** with 2-(benzofuran-5-yl)-4,4,5,5-

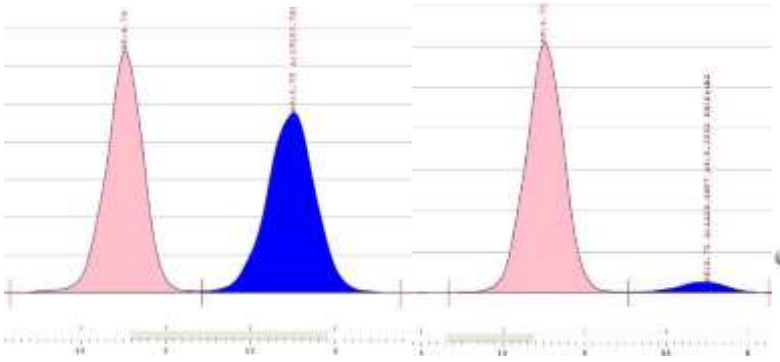
tetramethyl-1,3,2-dioxaborolane **(4.265)** (73.2 mg, 0.30 mmol, 1.00 equiv), vinyllithium (0.19 mL, 1.58 M in tetrahydrofuran, 0.30 mmol, 1.00 equiv), *tert*-butyl 3-iodoazetidine-1-carboxylate (101.9 mg, 0.36 mmol, 1.2 equiv), (*R*,*R*)-3,5-dimethylphenyl-Pybox **(*R*,*R*)-Xylyl-Pybox** (*R*,*R*)-**4.127** (7.7 mg, 0.018 mmol, 0.06 equiv), methallylnickel chloride dimer (2.2 mg, 0.0075 mmol, 0.025 equiv, 0.0075 M stock solution in THF prepared with sonication). The unpurified product was purified by automated silica gel chromatography (Biotage 3% → 14% ethyl acetate in hexanes, stained in CAM) to afford colorless oil (55.1 mg, 43 % yield). **^{1}H NMR** (600 MHz, $CDCl_3$) δ 7.57 (d, *J* = 1.8 Hz, 1H), 7.38 (d, *J* = 8.4 Hz, 1H), 7.35 (d, *J* = 1.7 Hz, 1H), 7.09 (d, *J* = 1.8 Hz, 1H), 7.07 (d, *J* = 1.8 Hz, 1H), 6.68 (s, 1H), 3.94 (app t, *J* = 8.4 Hz, 1H), 3.81 (app t, *J* = 8.4 Hz, 1H), 3.58 (dd, *J* = 8.4, 5.7 Hz, 1H), 3.42 (dd, *J* = 8.5, 5.7 Hz, 1H), 2.40 (app dtd, *J* = 16.0, 8.0, 2.2 Hz, 1H), 2.30 (dd, *J* = 9.0, 6.8 Hz, 1H), 2.11 (app dq, *J* = 14.7, 7.5 Hz, 1H), 1.96 (app dq, *J* = 15.9, 8.2 Hz, 1H), 1.77 – 1.61 (m, 1H), 1.41 (s, 9H), 1.21 (s, 6H), 1.19 (s, 6H). **^{11}B NMR** (160 MHz, $CDCl_3$) δ 32.964. **^{13}C NMR** (151 MHz, $CDCl_3$) δ 156.58, 153.69, 145.20, 127.89, 125.01, 120.68, 111.40, 106.66, 83.74, 79.27, 77.45, 77.24, 77.03, 55.00, 54.28, 37.94, 30.55, 30.04 (C-B, partially buried), 29.93, 28.63, 28.52, 24.85. **IR** (neat) ν_{max} 2975.41 (m), 291.09 (w), 2876.82 (w), 1700.49 (s), 1400.76 (s), 1365.36 (s), 1325.07 (m), 1257.42 (w), 1142.00 (s), 1031.99 (w), 859.53 (w), 771.02 (w), 740.72 (w) cm^{-1}. **HRMS** (DART) for $C_{24}H_{34}BNO_5$ $[M+H]^+$: calculated: 428.2608, found: 428.2629. $[\alpha]_D^{20}$ = –33.569 (*c* 1.45, $CHCl_3$, *l* = 50 mm).

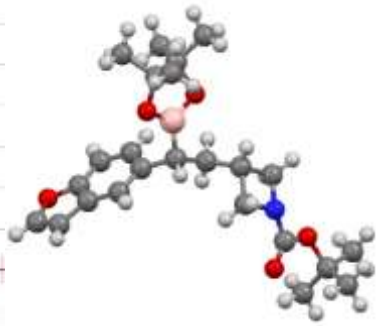
Determination of Stereochemical Identity: A stereoisomer mixture was prepared by

mixing the R and S enantiomer products of reactions run according to the general procedure (***Method B***) with [{methallyl}NiCl]$_2$ (2.5 mol%) and (*S,S*)-Ph-Pybox (*S,S*)-**4.122** (3.0 mol%), or (*R,R*)-Ph-Pybox (*R,R*)-**4.122** (3.0 mol%) as the catalyst. Absolute stereochemistry was assigned by analogy (**epi-4.158**) and by the crystal structure below.

SFC (Chiracel OJ-H, 5% IPA, 3 mL/min, 100 bar, 35 °C, 210-270 nm) – analysis of tert-butyl (R)-3-(2-(benzofuran-5-yl)-2-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)ethyl)azetidine-1-carboxylate.

Stereoisomer Mixture | Standard Conditions | Crystal Structure





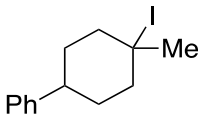
Peak No	% Area	Area	RT (min)
1	50.5254	19564.1246	4.76
2	49.4655	19153.704	5.75
3	0.0091	3.5152	8.15
Total:	100	38721.3438	

Peak No	% Area	Area	RT (min)
1	94.6498	19931.6331	4.75
2	5.3502	1126.6687	5.75
Total:	100	21058.3018	

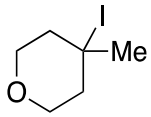
4.9.2.2 Enantioselective Radical Addition/Coupling Reaction of Alkenylboron Reagents, Alky Iodides, and Organozinc Reagents

4.9.2.2.1 Procedure for Preparation of Tertiary Alkyl Iodides

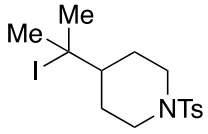
The corresponding tertiary alcohol (1.0 equiv) and sodium iodide (2.0 equiv) were dissolved in acetonitrile and allowed to cool to 0º C. Methanesulfonic acid (2.0 equiv) was added dropwise to the reaction mixture, which was then allowed to warm to room temperature and stir for 30 min. Minimizing light exposure, the mixture was then concentrated on a rotary evaporator, redissolved in diethyl ether and washed with a saturated aqueous solution of $NaHCO_3$ followed by a wash with a saturated solution of aquious $Na_2S_2O_3$. The organic layer was dried over $MgSO_4$ and concentrated. Purification by silica gel chromatography was generally carried out rapidly (prolonged residence on the stationary phase resulted in H-I elimination). The compounds were stored in a freezer in the dark under N_2 atmosphere.



(4-Iodo-4-methylcyclohexyl)benzene (4.275). The title compound was obtained through the general procedure from the corresponding alcohol 1-methyl-4-phenylcyclohexan-1-ol (1.08 g, 5.7mmol). The product was isolated by silica gel chromatography (pentane, stain in CAM) to afford white solid (1.4 g, 82% yield). **^{1}H NMR** (500 MHz, $CDCl_3$) δ 7.42-7.17 (m, 5H), 2.51 (tt, *J* = 12.4, 3.8 Hz, 1H), 2.29-2.23 (m, 2H), 2.19 (s, 3H), 2.10-1.98 (m, 2H), 1.88 (dd, *J* = 14.2, 3.7 Hz, 2H), 1.07 (ddd, *J* = 15.4, 12.4, 3.6 Hz, 2H).**^{13}C NMR** (126 MHz, $CDCl_3$) δ 146.7, 128.6, 127.1, 126.3, 58.6, 46.1, 43.7, 39.6, 32.8. **IR** (neat) ν_{max} 2952.20 (m), 2905.07 (m), 2853.6 (m), 1463.3 (w), 1441.3 (w), 1102.4 (s), 1013.6 (s), 979.7 (s), 775.6 (s), 614.3 (s), 476.6 (s). **HRMS** (DART) for $C_{13}H_{17}$ $(M+H-HI)^+$: Calc'd: 173.1325, found: 173.1318.

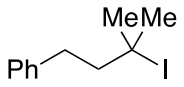


4-Iodo-4-methyltetrahydro-2*H*-pyran (4.276). The title compound was obtained through the general procedure from the corresponding alcohol 1-methyl-4-phenylcyclohexan-1-ol (780 mg, 6.7 mmol). The product was isolated by silica gel chromatography (1% ethyl acetate in pentane, stain in CAM) to afford clear yellow oil (986 mg, 67% yield). Clear yellow liquid. **^{1}H NMR** (500 MHz, $CDCl_3$) δ 3.95-3.88 (m, 2H), 3.77-3.69 (m, 2H), 2.15 (s, 3H), 2.03 (dd, *J* = 14.7, 2.3 Hz, 2H), 1.31 (ddd, *J* = 15.1, 10.8, 4.4 Hz, 2H). **^{13}C NMR** (126 MHz, $CDCl_3$) δ 66.4, 52.9, 44.9, 39.1. **IR** (neat) ν_{max} 2952.2 (m), 2905.0 (m), 2853.6 (m), 1463.3 (w), 1441.3 (w), 1102.4 (s), 1013.6 (s), 979.7 (s), 775.6 (s), 614.3 (s), 476.6 (s). **HRMS** (DART) for $C_6H_{22}OI$ $(M+H)^+$: Calc'd: 226.9922, found: 226.9927.



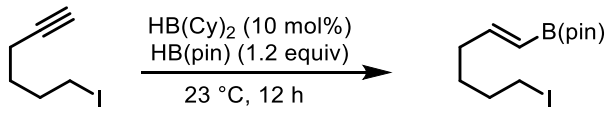
4-(2-Iodopropan-2-yl)-1-tosylpiperidine (4.277). The title compound was synthesized from the corresponding alcohol (2-(1-tosylpiperidin-4-yl)propan-2-ol) which was obtained in turn through standard procedures starting from commercially available ethyl isonipecotate. All spectral data was in accord with the literature.[78]

[78] Soulard, V.; Villa, G.; Vollmar, D. P. *J. Am. Chem. Soc.* **2018**, 140, 155.



(3-Iodo-3-methylbutyl)benzene (4.278). The title compound was synthesized from the corresponding alcohol 2-methyl-4-phenylbutan-2-ol. All spectral data was in accord with the literature. [79]

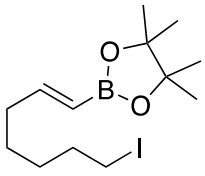
4.9.2.2.2 Procedure for Preparation of Cyclizing Substrates



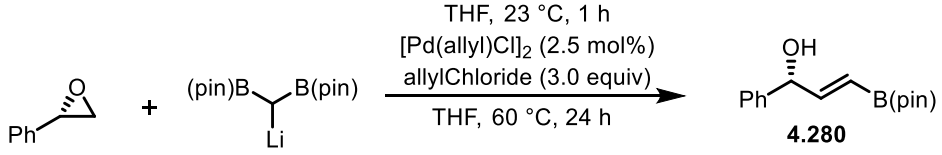
(*E*)-2-(6-Iodohex-1-en-1-yl)-4,4,5,5-tetramethyl-1,3,2-dioxaborolane (4.243). In the glovebox a 2 dram vial was charged with neat 4,4,5,5-tetramethyl-1,3,2-dioxaborolane (2.88 g, 22.5 mmol, 1.2 equiv) and dicyclohexylborane (333.9 mg, 1.87 mmol, 0.10 equiv). The vial was allowed to cool inside the glovebox freezer for 30 min and 6-iodohex-1-yne (3.90 g, 18.8 mmol, 1.0 equiv) was added to the cold mixture. The vial was sealed and the mixture was allowed to warm to room temperature and stir for 12 h. The reaction mixture was quenched by bubbling air through the solution for 2 h at room temperature to oxidize the dicyclohexylborane. The resulting mixture was diluted with hexane, washed with water, dried over Na_2SO_4, and filtered. The solvent was evaporated under reduced pressure and the residue was purified by silica gel chromatography with 2% ethyl acetate in hexanes as eluent (5.32 g, 84% yield). All spectra for the isolated product were in accord

[79] Zhao, S.; Mankad, N. P. *Angew. Chem. Int. Ed.* **2018**, 57, 5867.

with the literature. [80]

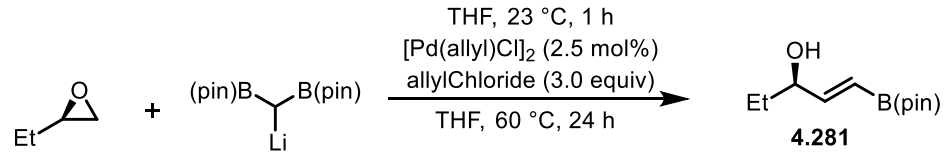


(*E*)-2-(7-Iodohept-1-en-1-yl)-4,4,5,5-tetramethyl-1,3,2-dioxaborolane (4.279) was synthesized using the same procedure as for substrate **4.242** from 7-Iodohept-1-yne. The unpurified product was isolated by silica gel chromatography (2% ethyl acetate in hexanes, stain in CAM), as colorless oil (78% yield). **^{1}H NMR** (600 MHz, $CDCl_3$) δ 6.59 (dt, *J* = 17.9, 6.4 Hz, 1H), 5.42 (dt, *J* = 17.9, 1.4 Hz, 1H), 3.16 (t, *J* = 7.1 Hz, 2H), 2.15 (q, *J* = 6.6 Hz, 2H), 1.81 (p, *J* = 7.1 Hz, 2H), 1.47-1.34 (m, 4H), 1.25 (s, 12H). **^{13}C NMR** (151 MHz, $CDCl_3$) δ 154.0, 83.2, 35.6, 33.5, 30.2, 27.2, 24.9, 6.9. **IR** (neat) ν_{max} 2974.1 (w), 2926.4 (w), 2853.3 (w), 1636.4 (m), 1359.4 (s), 1317.2 (s), 1143.0 (s), 994.9 (w), 969.2 (w), 848.5 (w). **HRMS** (DART) for $C_{13}H_{25}BO_2I$ $(M+H)^+$: Calc'd: 351.0987, found: 351.0967.

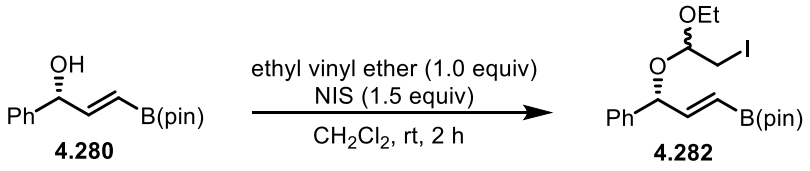


(*R*,*E*)-1-Phenyl-3-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)prop-2-en-1-ol (4.280) was generated from commercial (*S*)-styrene oxide following the method reported by Meek.[81] All spectral data matched previously published results.[81]

[80] N. Guennouni, F. Lhermitte, S. Cochard, B. Carboni, *Tetrahedron* **1995**, 51, 6999.
[81] S. A. Murray, E. C. M. Luc, S. J. Meek, *Org. Lett.* **2018**, 20, 469.

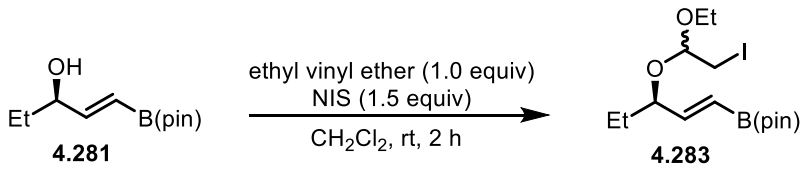


(*R,E*)-1-(4,4,5,5-Tetramethyl-1,3,2-dioxaborolan-2-yl)pent-1-en-3-ol (4.281) was generated from commercial (*R*)-1,2-epoxybutanestyrene (434 mg, 6.00 mmol, 1.0 equiv) following the method reported by Meek.[81] The product was isolated by silica gel chromatography (15% ethyl acetate in hexanes, stain in CAM) as colorless oil (1.27 g, 77 % yield). **^{1}H NMR** (600 MHz, $CDCl_3$) δ 6.59 (dd, *J* = 18.1, 5.3 Hz, 1H), 5.60 (d, *J* = 18.1 Hz, 1H), 4.06 (s, 1H), 1.77 (s, 1H), 1.55 (dt, *J* = 21.1, 14.3, 7.4 Hz, 2H), 1.25 (s, 11H), 0.92 (t, *J* = 7.5 Hz, 3H).**^{13}C NMR** (151 MHz, $CDCl_3$) δ 155.1, 117.7, 83.4, 75.1, 29.5, 24.8, 9.7. **IR** (neat) ν_{max} 3432.2 (br), 2974.1 (w), 2928.7 (w), 2874.5 (w), 1640.5(m), 1356.0 (s), 1317.8 (s), 1142.4 (s), 997.0 (m), 965.7 (m), 898.8 (m), 647.3 (w). **HRMS** (DART) for $C_{11}H_{25}BNO_3$ $(M+NH_4)^+$: Calc'd: 230.1922, found: 230.1926. **$[\alpha]_D^{20}$** = -12.40 (*c* 1.0, $CHCl_3$, *l* = 50 mm).

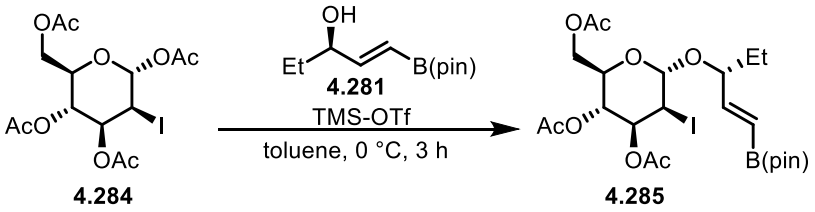


2-((*3R,E*)-3-(1-Ethoxy-2-iodoethoxy)-3-phenylprop-1-en-1-yl)-4,4,5,5-tetramethyl-1,3,2-dioxaborolane (4.282). A mixture of **4.280** (156.1 mg, 0.6 mmol, 1.0 equiv) and

ethyl vinyl ether (43.3 mg, 0.6 mmol, 1.0 equiv) in CH_2Cl_2 (10 mL) was added to a suspension of *N*-iodosuccinimide (202.5 mg, 0.9 mmol, 1.5 equiv) in CH_2Cl_2 (10 mL) at 0 °C over 5 min. After stirring at room temperature for 2 h, water (10 mL) was added, and the stirring was continued for an hour. The layers were separated and the product was extracted from the aqueous layer with CH_2Cl_2 (2×15 mL). The combined organic extracts were washed with brine (20 mL), dried with Na_2SO_4, filtered, and concentrated under reduced pressure. Purification by silica gel chromatography (10% ethyl acetate in hexanes, stain in CAM) afforded **4.282** as a 1:1 mixture of diastereomers (clear yellow oil, 0.21 g, 77% yield).**^{1}H NMR** (500 MHz, $CDCl_3$) δ 7.36-7.26 (m, 10H), 6.66 (ddd, *J* = 39.0, 18.0, 5.8 Hz, 2H), 5.69 (t, *J* = 19.2, 19.2 Hz, 2H), 5.14 (dd, *J* = 18.9, 5.8 Hz, 2H), 4.78 (t, *J* = 5.5, 5.5 Hz, 1H), 4.56 (t, 1H), 3.79-3.69 (m, 2H), 3.60-3.52 (m, 3H), 3.43 (dq, *J* = 9.0, 7.1, 7.1, 6.9 Hz, 1H), 3.23-3.18 (m, 4H), 1.86-1.84 (m, 2H), 1.25 (d, *J* = 6.7 Hz, 24H), 1.20 (t, *J* = 7.0, 7.0 Hz, 3H), 1.13 (t, *J* = 7.0, 7.0 Hz, 3H). **^{13}C NMR** (151 MHz, $CDCl_3$) δ 152.0, 151.6, 140.4, 139.5, 128.6, 128.5, 128.2, 127.9, 127.7, 127.1, 100.2, 99.4, 83.5, 83.4, 80.1, 79.8, 68.0, 61.7, 61.2, 25.7, 24.9, 24.9, 24.9, 15.2, 15.1, 5.9, 5.6. **IR** (neat) ν_{max} 2973.5 (m), 2925.1 (w), 1636.7 (m), 1352.8 (s), 1323.0 (s), 1266.5 (w), 1141.2 (s), 1107.9 (m), 1055.3 (m), 994.4 (s), 968.5 (s), 847.3 (m), 759.1 (m), 698.2 (m), 658.9 (w). **HRMS** (DART) for $C_{19}H_{32}BNO_4I$ $(M+NH_4)^+$: Calc'd: 476.1464, found: 476.1463.

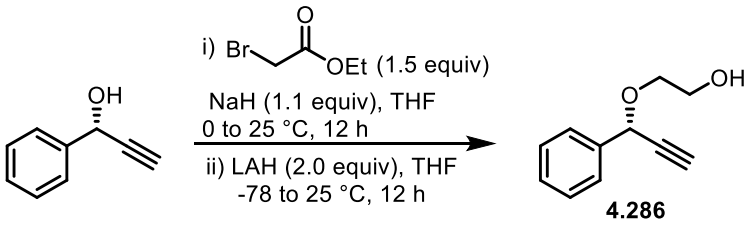


2-((*3R,E*)-3-(1-Ethoxy-2-iodoethoxy)pent-1-en-1-yl)-4,4,5,5-tetramethyl-1,3-dioxolane (4.283) was synthesized using the same procedure for the synthesis of **4.282** using **4.281** (200 mg, 0.94 mmol, 1.0 equiv**)** as starting material. The product consisting of a 1:1 inseparable mixture of diastereomers was isolated by silica gel chromatography (10% ethyl acetate in hexanes, stain in CAM) as clear yellow oil (240 mg, 62% yield). **^{1}H NMR** (500 MHz, $CDCl_3$) δ 6.46 (ddd, *J* = 45.5, 18.1, 7.1 Hz, 2H), 5.58 (dd, *J* = 18.2, 2.9 Hz, 2H), 4.59 (dt, *J* = 14.7, 5.6, 5.6 Hz, 2H), 3.99 (q, *J* = 6.7, 6.7, 6.7 Hz, 1H), 3.88 (q, *J* = 6.5, 6.5, 6.5 Hz, 1H), 3.69-3.44 (m, 4H), 3.20 (dt, *J* = 5.0, 2.9, 2.9 Hz, 4H), 1.70-1.50 (m, 5H), 1.32-1.24 (m, 24H), 1.22 (t, *J* = 7.0, 7.0 Hz, 3H), 1.17 (t, *J* = 7.0, 7.0 Hz, 3H), 0.92 (t, *J* = 7.5, 7.5 Hz, 6H). **^{13}C NMR** (151 MHz, $CDCl_3$) δ 153.1, 152.4, 100.9, 99.6, 83.5, 83.4, 81.2, 80.5, 62.2, 61.5, 28.2, 27.8, 25.0, 24.9, 24.9, 24.8, 15.3, 15.0, 9.8, 9.7, 6.3, 6.3. **IR** (neat) ν_{max} 2972.9 (m), 2927.8 (w), 2874.6 (w), 1639.6 (m), 1365.7 (s), 1323.9 (s), 1141.9 (s), 1101.4 (s), 1047.4 (s), 998.4 (s), 968.6 (s), 847.9 (m), 648.5 (w), 577.4 (w). **HRMS** (DART) for $C_{15}H_{32}BNO_4I$ $(M+NH_4)^+$: Calc'd: 428.1464, found: 428.1467.



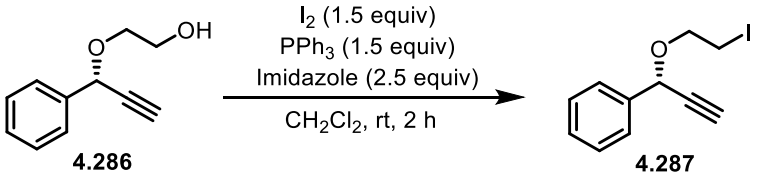
(2*R*,3*R*,4*S*,5*S*,6*S*)-2-(Acetoxymethyl)-5-iodo-6-(((*R*,*E*)-1-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)pent-1-en-3-yl)oxy)tetrahydro-2*H*-pyran-3,4-diyl diacetate (4.285) was synthesized starting from (2*R*,3*S*,4*S*,5*R*,6*R*)-6-(acetoxymethyl)-3-iodotetrahydro-2*H*-pyran-2,4,5-triyl triacetate (**4.284**) (1.07 g, 2.34 mmol, 1.1 equiv) and **4.281** (452 mg, 2.13 mmol, 1.0 equiv) following the method described by Wan.[82] The unpurified product was isolated by silica gel chromatography (30% ethyl acetate in hexanes, UV) to afford white solid (1.12 g, 86% yield). **^{1}H NMR** (500 MHz, $CDCl_3$) δ 6.33 (dd, *J* = 18.1, 7.2 Hz, 1H), 5.59 (d, *J* = 18.1 Hz, 1H), 5.37 (t, *J* = 9.8 Hz, 1H), 5.16 (s, 1H), 4.66 (dd, *J* = 9.5, 4.3 Hz, 1H), 4.50 (d, *J* = 4.3 Hz, 1H), 4.21 (dd, *J* = 12.2, 5.0 Hz, 1H), 4.16-4.12 (m, 1H), 4.08-4.05 (m, 1H), 3.99 (q, *J* = 6.8 Hz, 1H), 2.11 (s, 3H), 2.08 (s, 3H), 2.06 (s, 3H), 1.72-1.50 (m, 4H), 1.28 (d, *J* = 2.5 Hz, 13H), 0.93 (t, *J* = 7.4 Hz, 3H). **^{13}C NMR** (151 MHz, $CDCl_3$) δ 170.8, 169.9, 169.7, 150.4, 98.7, 98.6, 83.6, 80.8, 69.4, 69.2, 67.9, 62.5, 30.4, 28.1, 25.0, 24.9, 24.8, 21.1, 20.9, 20.8, 10.2. **IR** (neat) ν_{max} 2973.9 (m), 2933.1 (m), 1744.3 (s), 1641.1 (m), 1453.5 (w), 1366.3 (m), 1328.9 (w), 1222.2 (s), 1142.9 (s), 1114.6 (s), 1030.7 (s). **HRMS** (DART) for $C_{23}H_{40}BNOI$ $(M+NH_4)^+$: Calc'd: 628.1785, found: 628.1779. **$[\alpha]_D^{20}$** = 47.39 (*c* 1.0, $CHCl_3$, *l* = 50 mm).

[82] H. Wang, J. Tao, X. Cai, W. Chen, Y. Zhao, Y. Xu, W. Yao, J. Zeng, Q. Wan, *Chem. Eur. J.* **2014**, 20, 17319.



(*R*)-2-((1-Phenylprop-2-yn-1-yl)oxy)ethan-1-ol (4.286). Commercial (*R*)-1-phenylprop-2-yn-1-ol (981.0 mg, 7.42 mmol, 1.0 equiv) was added dropwise to a suspension of sodium hydride (217.6 mg, 8.16 mmol, 90% purity, 1.1 equiv) in THF (6 mL) at 0 °C. The mixture was allowed to warm to room temperature and stirred for 1 h. After the mixture was allowed to cool to 0 °C, ethyl 2-bromoacetate (1.86 g, 11.13 mmol, 1.5 equiv) was added dropwise to the mixture. The mixture was allowed to warm to room temperature and stir for 12 h. The reaction mixture was quenched with a saturated solution of aqueous NH_4Cl (10 mL) and the product was extracted with Et_2O (3 x 20 mL). The combined organic layers were then dried with anhydrous Na_2SO_4. After filtration, the material was concentrated under reduced pressure. The corresponding unpurified ether product was dissolved in THF (20 mL) and added dropwise to a solution of LAH in THF (1 M, 15.0 mL) at −78 °C under a nitrogen atmosphere. The reaction was allowed to warm to room temperature and stir for 12 h, after which it was allowed to cool to 0ºC and quenched by careful addition of H_2O (1.0 mL) and then a 3 M solution of aqueous NaOH (3.0 mL). After stirring at room temperature for 20 min $MgSO_4$ was added to the reaction mixture and the suspension was filtered through celite. The solvent was removed in vacuo and the unpurified product was purified by silica gel chromatography (20% ethyl acetate in hexanes) to obtain **4.284** (0.78 g, 44% yield over two steps) as colorless oil. All spectral data is in accord with the

literature.[83]

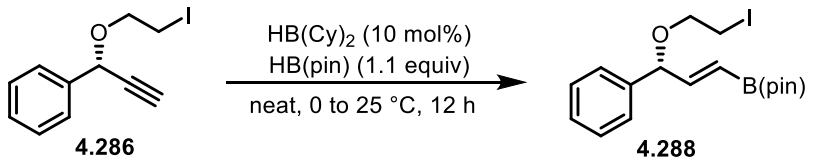


4.286 4.287

(*R*)-(1-(2-Iodoethoxy)prop-2-yn-1-yl)benzene (4.287). A solution of triphenylphosphine (1.03 g, 3.92 mmol, 1.5 equiv) and iodine (0.99 g, 3.92 mmol, 1.5 equiv) in dichloromethane (20 mL) was allowed to stir for 10 min at ambient temperature. Imidazole (0.44 g, 6.53 mmol, 2.5 equiv) was added to the resulting mixture. After a 10 min stir, **4.286** (0.46 g, 2.61 mmol) was added and the resulting mixture was allowed to stir for 2 h. The mixture was quenched by the addition of a saturated solution of aqueous sodium metabisulfite (10 mL). The aqueous and organic layers were separated followed by extraction of the product from the aqueous layer with dichloromethane (3 x 20 mL). The combined organic extracts were dried with Na_2SO_4 and concentrated under reduced pressure. The resulting residue was purified by silica gel chromatography (5% ethyl acetate in hexanes) to afford **4.285** (0.45 g, 60% yield) as light yellow oil. **^{1}H NMR** (500 MHz, $CDCl_3$) δ 7.56-7.54 (m, 2H), 7.44-7.32 (m, 3H), 5.28 (d, *J* = 2.2 Hz, 1H), 3.95-3.89 (m, 1H), 3.84-3.77 (m, 1H), 3.31-3.28 (m, 2H), 2.69 (d, *J* = 2.2 Hz, 1H). **^{13}C NMR** (151 MHz, $CDCl_3$) δ 137.7, 128.8, 128.7, 127.5, 81.1, 76.4, 71.4, 68.9, 2.5. **IR** (neat) ν_{max} 3284.2 (m), 3059.1 (w), 3027.0 (w), 2914.6 (w), 2850.9 (w), 1491.4 (w), 1451.3 (m), 1261.2 (m),

[83] J. Bucher, T. Wurm, K. S. Nalivela, M. Rudolph, F. Rominger, A. S. K. Hashmi *Angew. Chem. Int. Ed.* **2014**, 53, 3854.

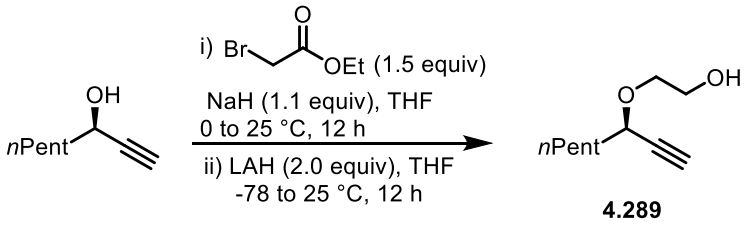
1189.5 (w), 1170.2 (w), 1094.3 (s), 1054.1 (s), 1027.2 (m), 990.3 (m), 740.0 (m), 696.4 (s), 652.8 (s). **HRMS** (DART) for $C_{11}H_{12}OI$ $(M+H)^+$: Calc'd: 286.9927, found: 286.9929.



4.286 **4.288**

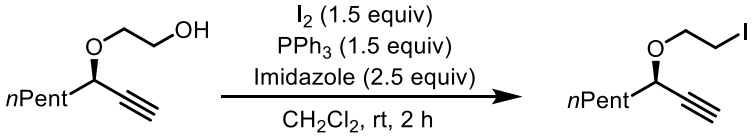
(*R*,*E*)-2-(3-(2-Iodoethoxy)-3-phenylprop-1-en-1-yl)-4,4,5,5-tetramethyl-1,3,2-dioxaborolane (4.288). In the glovebox a 2-dram vial is charged with neat dicyclohexylborane (19.1 mg, 0.11 mmol, 0.1 equiv), 4,4,5,5-tetramethyl-1,3,2-dioxaborolane (164.5 mg, 1.30 mmol, 1.18 equiv) and **4.287** (306.4 mg, 1.1 mmol, 1.0 equiv) was added at 0 °C and the mixture was allowed to stir for 12 h at room temperature. The mixture was quenched by bubbling air through the solution with a tube pump for 2 h at room temperature to oxidize the dicyclohexylboryl group. The resulting mixture was diluted with hexane, washed with water, dried with anhydrous Na_2SO_4, and filtered. The solvent was evaporated under reduced pressure and the residue was purified by silica gel chromatography (5% ethyl acetate in hexanes, stain in CAM) to afford the title compound (0.25 g, 56% yield) as colorless yellow oil. **^{1}H NMR** (500 MHz, $CDCl_3$) δ 7.37-7.27 (m, 5H, 6.66 (dd, *J* = 18.0, 5.8 Hz, 1H), 5.70 (d, *J* = 17.8 Hz, 1H), 4.86 (d, *J* = 5.7 Hz, 1H), 3.79-3.71 (m, 2H), 3.67-3.63 (m, 1H), 3.28-3.24 (m, 2H), 1.87-1.84 (m, 1H), 1.25 (s, 12H). **^{13}C NMR** (151 MHz, $CDCl_3$) δ 151.9, 140.1, 128.7, 128.0, 127.2, 84.0, 83.5, 69.5, 24.9, 3.0. **IR** (neat) ν_{max} 2974.2 (w), 1637.3 (m), 1355.7 (s), 1355.7 (s), 1265.3 (w), 1142.6 (s), 1106.9 (w), 995.4 (w), 969.3 (w), 847.8 (m), 669.2 (m). **HRMS** (DART) for $C_{17}H_{23}BO_3I$

$(M+H)^+$: Calc'd: 413.0779, found: 413.0788. **$[\alpha]_D^{20}$**= 19.11 (*c* 1.0, $CHCl_3$, *l* = 50 mm).



4.289

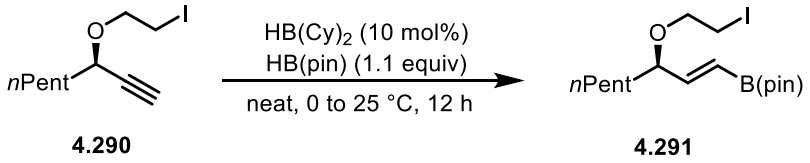
(*R*)-2-(Oct-1-yn-3-yloxy)ethan-1-ol (4.289) was synthesized using the same procedure for the synthesis of **4.286**, using commercially available (*R*)-oct-1-yn-3-ol. The product was isolated by silica gel chromatography (20% ethyl acetate in hexanes, stain in CAM) to afford colorless oil (37% yield over two steps). **^{1}H NMR** (500 MHz, $CDCl_3$) δ 4.08 (td, *J* = 6.7, 6.6, 2.0 Hz, 1H), 3.88-3.83 (m, 1H), 3.80-3.75 (m, 2H), 3.56-3.51 (m, 1H), 2.45 (t, *J* = 1.9, 1.9 Hz, 1H), 1.93 (t, *J* = 6.3, 6.3 Hz, 1H), 1.81-1.69 (m, 2H), 1.50-1.44 (m, 2H), 1.36-1.31 (m, 4H), 0.91 (t, *J* = 7.0, 7.0 Hz, 3H). **^{13}C NMR** (151 MHz, $CDCl_3$) δ 83.0, 74.0, 70.2, 70.1, 62.1, 35.7, 31.6, 25.0, 22.7, 14.1. **IR** (neat) ν_{max} 3423.7 (br), 3306.2 (m), 2950.9 (s), 2927.2 (s), 2858.8 (m), 1460.8 (w), 1333.3 (w), 1105.5 (s), 1070.6 (m), 657.9 (w), 629.3 (w). **HRMS** (DART) for $C_{10}H_{19}O_2$ $(M+H)^+$: Calc'd: 171.1380, found: 171.1376.



4.289 **4.290**

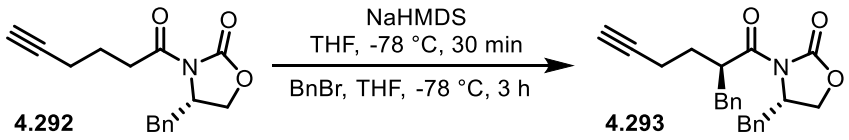
(*R*)-3-(2-Iodoethoxy)oct-1-yne (2.490) was synthesized using the same procedure for the synthesis of **4.287**. All spectral data is in accord with the literature.[84]

[84] H. Iwamoto, Y. Ozawa, K. Kubota, H. Ito, *J. Org. Chem*. **2017**, 82, 10563.



4.290 **4.291**

2-((*R*,*E*)-3-(2-Iodoethoxy)oct-1-en-1-yl)-4,4,5-trimethyl-1,3,2-dioxaborolane (4.291) was synthesized using the same procedure for the synthesis of **4.288**. Isolated by silica gel chromatography (10% ethyl acetate in hexanes, stain CAM) to afford the product as clear yellow oil (60% yield). **^{1}H NMR** (500 MHz, $CDCl_3$) δ 6.42 (dd, *J* = 18.1, 6.6 Hz, 1H), 5.57 (d, *J* = 18.1 Hz, 1H), 3.77-3.71 (m, 2H), 3.58-3.46 (m, 1H), 3.21 (t, *J* = 7.0, 7.0 Hz, 2H), 1.59-1.38 (m, 4H), 1.33-1.22 (d, 16H), 0.87 (t, 3H). **^{13}C NMR** (151 MHz, $CDCl_3$) δ 153.2, 83.4, 82.5, 69.7, 35.2, 31.9, 25.2, 24.9, 22.7, 14.2, 3.4. **IR** (neat) ν_{max} 2973.9 (w), 2953.2 (w), 2926.2 (m), 2855.6 (w), 1639.1 (m), 1464.4 (w), 1356.5 (s), 1327.2 (s), 1265.6 (m), 1142.9 (s), 1107.2 (m), 1107.2 (m), 998.2 (m), 968.8 (m), 848.5 (m). **HRMS** (DART) for $C_{16}H_{34}BNO_3I$ $(M+NH_4)^+$: Calc'd: 426.1671, found: 426.1669. **$[\alpha]_D^{20}$** = 26.05 (*c* 1.0, $CHCl_3$, *l* = 50 mm).



4.292 **4.293**

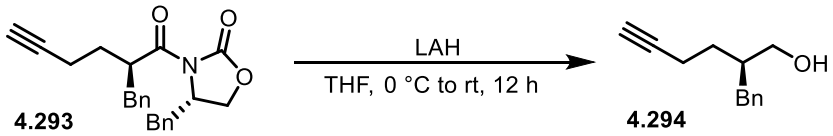
(*S*)-4-Benzyl-3-(hex-5-ynoyl)oxazolidin-2-one (4.292) was synthesized using reported method. All spectral data is in accord with the literature.[85]

[85] C. R. Moyes, R. Berger, S. D. Goble, B. Harper, D.-M. Shen, L. Wang, A. Bansal, P. N. Brown, A. S. Chen, K. H. Dingley, J. Di Salvo, A. Fitzmaurice, L. N. Gichuru, D. Hrenuik, A. L. Hurley, N. Jochnowitz,

(*S*)-4-Benzyl-3-((*R*)-2-benzylhex-5-ynoyl)oxazolidin-2-one (4.293). In a flame-dried round bottom flask, under an atmosphere of N_2, a solution of sodium bis(trimethylsilyl)amide (11.6 mL, 1.00 M in THF, 11.6 mmol, 1.75 equiv) was further diluted with THF (20 mL) and allowed to cool to -78 °C. To it was added a solution of (4*S*)-4-benzyl-3-hex-5-ynoyl-oxazolidin-2-one (**4.292**) (1.8 g, 6.63 mmol, 1.0 equiv) in THF (10 mL) by syringe over 10 min. After stirring for 30 min, benzylbromide (3.40 g, 19.9 mmo, 3.0 equiv) was added neat. The solution was then allowed to stir at -78 °C for 2.5 h at which point the reaction was quenched with a 0.5 M aqueous solution of HCl. The product was extracted with ethyl acetate (50 mL x 2) and the combined organic extracts were washed with water (100 mL), brine (100 mL) and dried with anhydrous Na_2SO_4. The solution was concentrated under reduced pressure and the residue was purified by silica gel chromatography (15% ethyl acetate in hexanes, UV active) to afford the product as colorless oil (1.41 g, 59% yield). **^{1}H NMR** (600 MHz, $CDCl_3$) δ 7.34-7.16 (m, 8H), 7.12-7.03 (m, 2H), 4.66-4.62 (m, 1H), 4.39-4.30 (m, 1H), 4.13 (t, *J* = 8.4 Hz, 1H), 4.07 (dd, *J* = 9.0, 2.6 Hz, 1H), 3.13-3.00 (m, 2H), 2.79 (dd, *J* = 13.4, 7.5 Hz, 1H), 2.46 (dd, *J* = 13.4, 9.6 Hz, 1H), 2.25-2.22 (m, 2H), 2.06-1.99 (m, 1H), 1.94-1.93 (m, 1H), 1.78-1.70 (m, 1H). **^{13}C NMR** (151 MHz, $CDCl_3$) δ 175.4, 153.1, 138.6, 135.3, 129.5, 129.5, 129.0, 128.5, 127.4, 126.7, 83.4, 69.2, 66.0, 55.3, 43.8, 38.8, 37.8, 30.1, 16.6. **IR** (neat) ν_{max} 3284.2 (m), 3059.2 (w), 3025.4 (w), 2921.6 (m), 2856.9 (w), 1772.4 (s), 1691.1 (s), 1385.3 (s), 1348.1 (s), 1239.9 (s), 1210.1 (s), 1193.1 (s), 739.9 (s). **HRMS** (DART) for $C_{23}H_{24}NO3$ $(M+H)^+$:

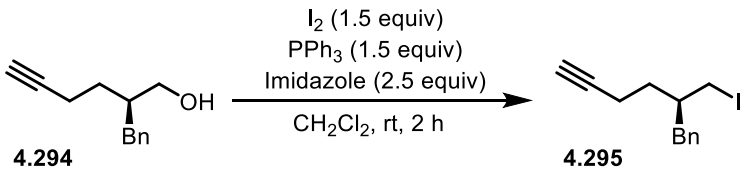
S. Mistry, H. Nagabukuro, G. M. Salituro, A. Sanfiz, A. S. Stevenson, K. Villa, B. Zamlynny, M. Struthers, S. D. Edmondson, *J. Med. Chem.* **2014**, 57, 1437.

Calc'd: 362.1751, found: 362.1761. $[\alpha]_D^{20}$ = 18.20 (*c* 1.0, $CHCl_3$, *l* = 50 mm).



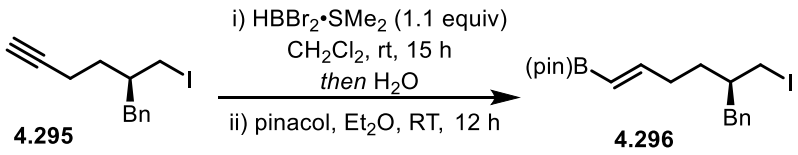
4.293 **4.294**

(*R*)-2-Benzylhex-5-yn-1-ol (4.294). To a solution of LAH (220.5 mg, 5.8 mmol, 3.0 equiv) in THF (30 mL) was added a solution of **4.293** (0.70 g, 1.94 mmol, 1.0 equiv) in 20 mL THF at -78 °C. The mixture was allowed to warm to room temperature over the course of a several hours and stir for 12 h. The mixture was allowed to cool to 0 ºC and H_2O (0.6 mL) was carefully added, followed by a 3 M solution of aqueous NaOH (0.6 mL). The suspension was allowed to stir at room temperature for 20 min after which $MgSO_4$ was added. The resulting mixture was filtered through a pad of celite and concentrated in vacuo. The unpurified product was purified by silica gel chromatography (15% ethyl acetate in hexanes) to afford **4.294** (0.25 g, 68% yield) as colorless oil. **^{1}H NMR** (500 MHz, $CDCl_3$) δ 7.32-7.27 (m, 2H), 7.23-7.21 (m, 3H), 3.63-3.53 (m, 2H), 2.67 (d, *J* = 7.3 Hz, 2H), 2.30-2.27 (m, 2H), 2.02-1.97 (m, 2H), 1.72-1.57 (m, 2H), 1.31 (td, *J* = 5.6, 5.6, 2.2 Hz, 1H). **^{13}C NMR** (151 MHz, $CDCl_3$) δ 140.4, 129.3, 128.5, 126.2, 84.5, 68.8, 64.3, 41.6, 37.5, 29.7, 16.4. **IR** (neat) ν_{max} 3288.6 (m), 3023.4 (w), 3025.4 (w), 2921.3 (m), 1600.8 (w), 1493.5 (m), 1451.5 (m), 1029.0 (s), 981.9 (s), 736.3 (s), 699.3 (s), 631.8 (s), 493.4 (w). **HRMS** (DART) for $C_{13}H_{17}O$ $(M+H)^+$: Calc'd:189.1274, found: 189.1268. $[\alpha]_D^{20}$ = 1.19 (*c* 1.0, $CHCl_3$, *l* = 50 mm).



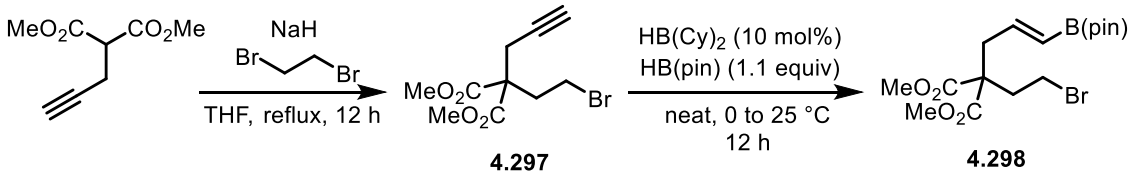
4.294 **4.295**

(*R*)-(2-(Iodomethyl)hex-5-yn-1-yl)benzene (4.295). A solution of triphenylphosphine (0.53 g, 2.0 mmol, 1.54 equiv) and iodine (0.51 g, 2.0 mmol, 1.54 equiv) in dichloromethane (5 mL) was allowed to stir for 10 min at ambient temperature. Imidazole (0.23 g, 3.3 mmol, 2.54 equiv) was added to the resulting mixture. After stirring for 10 min, **4.294** (.25 g, 1.3 mmol, 1.0 equiv) was added and the resulting mixture was allowed to stir for 2 h. The mixture was quenched by the addition of a saturated solution of aqueous sodium metabisulfite solution (5 mL). The aqueous and organic layers were separated and the product was extracted from the aqueous layer with dichloromethane (3 x 10 mL). The combined organic extracts were dried over Na_2SO_4 and concentrated under reduced pressure. The resulting residue was purified by flash chromatography (5% ethyl acetate in hexane, stain in CAM) to afford the title compound (0.3 g, 75%) as light yellow oil. **^{1}H NMR** (500 MHz, $CDCl_3$) δ 7.34-7.31 (m, 2H), 7.28-7.24 (m, 3H), 3.27 (dd, *J* = 10.3, 3.1 Hz, 1H), 3.16 (dd, *J* = 10.2, 2.9 Hz, 1H), 2.71 (dd, *J* = 13.8, 4.1 Hz, 1H), 2.56 (dd, *J* = 13.8, 7.6 Hz, 1H), 2.37-2.19 (m, 2H), 2.00 (t, *J* = 2.6, 2.6 Hz, 1H), 1.71-1.56 (m, 3H). **^{13}C NMR** (151 MHz, $CDCl_3$) δ 139.5, 129.3, 128.6, 126.5, 83.4, 69.3, 40.2, 39.1, 33.1, 15.9, 15.5. **IR** (neat) ν_{max} 3290.6 (m), 3058.8 (w), 2920.0 (m), 2851.4 (w), 1601.0 (w), 1493.7 (m), 1451.2 (m), 1220.8 (m), 735.9 (s), 699.1 (s), 634.9 (s), 491.3 (w). **HRMS** (DART) for $C_{13}H_{16}I$ $(M+H)^+$: Calc'd: 299.0291, found: 299.0292. **$[\alpha]_D^{20}$** = -45.02 (*c* 1.0, $CHCl_3$, *l* = 50 mm).



4.295 **4.296**

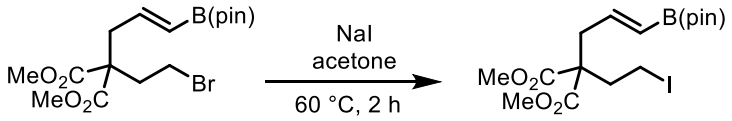
(*R*,*E*)-2-(5-Benzyl-6-iodohex-1-en-1-yl)-4,4,5,5-tetramethyl-1,3,2-dioxaborolane (4.296). To a solution of **4.295** (0.30 g, 1.0 mmol, 1.0 equiv) in 10 mL of anhydrous dichloromethane was added 1.1 mL of a 1.0 M solution of $HBBr_2•SMe_2$ (1.1 mmol. 1.1 equiv) in dichloromethane. After 15 h at room temperature, the mixture was allowed to cool to 0 ºC and water (5 mL) was slowly added. The product was extracted from the aqueous phase with 2 x 20 mL of ether. Pinacol (0.12 g, 1.0 mmol, 1.0 equiv) was added to the combined organic phases and the solution was allowed to stir for 12 h at room temperature. The reaction mixture is concentrated under reduced pressure, and purified by silica gel chromatography (5% ethyl acetate in hexane, stain in CAM) to afford **4.296** (0.35 g, 82%) as colorless oil. **^{1}H NMR** (500 MHz, $CDCl_3$) δ 7.33-7.26 (m, 2H), 7.24-7.19 (m, 3H), 6.63 (dt, *J* = 17.9, 6.4, 6.4 Hz, 1H), 5.49 (d, *J* = 17.9 Hz, 1H), 3.23 (dd, *J* = 10.0, 4.2 Hz, 1H), 3.13 (dd, *J* = 10.0, 3.7 Hz, 1H), 2.67 (dd, *J* = 13.8, 5.5 Hz, 1H), 2.55 (dd, *J* = 13.8, 8.4 Hz, 1H), 2.30-2.21 (m, 1H), 2.18-2.11 (m, 1H), 1.59-1.46 (m, 2H), 1.46-1.37 (m, 1H), 1.29 (s, 12H). **^{13}C NMR** (151 MHz, $CDCl_3$) δ 153.4, 139.7, 129.2, 128.5, 126.4, 83.2, 40.4, 39.9, 33.1, 32.8, 24.9, 15.9. **IR** (neat) ν_{max} 3022.6 (m), 2974.1 (m), 2923.5 (w), 1636.3 (m), 1452.0 (w), 1396.3 (m), 1360.6 (s), 1320.1 (s), 1143.0 (s), 999.4 (w), 969.5 (w), 848.7 (w), 738.3 (w), 699.7 (m). **HRMS** (DART) for $C_{19}H_{29}BO_2I$ $(M+H)^+$: Calc'd: 427.1300, found: 427.1315. **$[\alpha]_D^{20}$** = -18.64 (*c* 1.0, $CHCl_3$, *l* = 50 mm).



Dimethyl(*E*)-2-(2-bromoethyl)-2-(3-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)allyl)malonate (4.298). Sodium hydride (260 mg, 10.75 mmol, 1.15 equiv) was placed in a flame dried round bottom flask under Ar atmosphere and was allowed to dissolve in 10 mL of THF. The flask was allowed to cool to 0 ºC and a solution of dimethyl 2-prop-2-ynylpropanedioate (1.59 g, 9.34 mmol, 1.0 equiv) in 10 mL of THF was added dropwise. The mixture was allowed to stir for 20 min at 0 ºC after which neat 1,2-dibromoethane (5.27 g, 28.03 mmol, 3.0 equiv) was added. The mixture was allowed to reflux for 12 h. The suspension was then allowed to cool to 0 ºC and the reaction was quenched with a saturated solution of aqueous NH_4Cl (10 mL). The organic layer was extracted with ethyl acetate three times, washed with brine, dried over sodium sulfate and concentrated under reduced pressure. The unpurified material (**4.297**) was filtered through a silica plug with 20% ethyl acetate in hexanes and carried to the next step.

Inside an argon filled glovebox a 4 dram vial was charged with neat 4,4,5,5-tetramethyl-1,3,2-dioxaborolane (637.32 mg, 5.00 mmol, 1.15 equiv) and dicyclohexylborane (77.13 mg, 0.43 mmol, 0.10 equiv). The vial was placed inside the glove box freezer to cool for 30 min. Dimethyl-2-(2-bromoethyl)-2-prop-2-ynyl-propanedioate (**4.297)** (1.20 g, 4.33 mmol, 1.0 equiv) was added to the cool suspension and the vial was then sealed and allowed to stir for 12 h at room temperature. Finally, the reaction mixture was quenched by bubbling air through the solution for 2 h at room temperature to oxidize the

dicyclohexylborane. The resulting mixture was diluted with diethyl ether, washed with water, dried over Na_2SO_4, and filtered. The solvent was evaporated under reduced pressure and the residue was purified by silica gel chromatography (10% ethyl acetate in hexanes, stain in $KMnO_4$) to afford the product **4.298** as colorless oil (862 mg, 49% yield). **^{1}H NMR** (600 MHz, $CDCl_3$) δ 6.35 (dt, *J* = 17.7, 7.2 Hz, 1H), 5.53 (dt, *J* = 17.7, 1.2 Hz, 1H), 3.74 (s, 6H), 3.34 (t, 2H), 2.76 (dd, *J* = 7.2, 1.3 Hz, 2H), 2.45 (t, 2H), 1.25 (s, 12H). **^{13}C NMR** (151 MHz, $CDCl_3$) δ 170.7, 146.1, 121.9, 83.5, 57.5, 52.9, 40.1, 36.4, 27.2, 24.9. **IR** (neat) ν_{max} 2975.4 (w), 1732.4 (s), 1637.6 (w), 1436.1 (w), 1390.7 (m), 1362.6 (m), 1268.9 (m), 1166.2 (m), 998.4 (w), 970.4 (w), 643.0 (w). **HRMS** (DART) for $C_{16}H_{26}BIO_6$ $(M+H)^+$: Calc'd: 405.1079, found: 405.1075.



4.298 **4.299**

Dimethyl(*E*)-2-(2-iodoethyl)-2-(3-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)allyl)malonate (4.299). To a round bottom flask containing **4.298** (400 mg, 0.99 mmol, 1.0 equiv) was added a solution of sodium iodide (592.04 mg, 3.95 mmol, 4.0 equiv) in acetone (22 mL). The reaction mixture was allowed to reflux for 2 h. The mixture was allowed to cool to room temperature, diluted with diethyl ether (100 mL), and washed with water and brine. The organic layer was dried with Na_2SO_4, and concentrated under reduced pressure. The product was isolated after silica gel chromatography (10% ethyl acetate in hexanes, stain in CAM) as clear yellow oil (395 mg, 89% yield). **^{1}H NMR** (600 MHz,

$CDCl_3$) δ 6.34 (dt, *J* = 17.7, 7.2 Hz, 1H), 5.52 (d, *J* = 17.7 Hz, 1H), 3.73 (s, 6H), 3.14-3.00 (m, 2H), 2.73 (d, *J* = 7.2 Hz, 2H), 2.52-2.38 (m, 2H), 1.25 (s, 12H). **^{13}C NMR** (151 MHz, $CDCl_3$) δ 170.47, 146.12, 83.43, 59.05, 52.85, 39.82, 37.97, 24.88, 2.42. **IR** (neat) ν_{max} 2975.24 (br), 1732.1 (s), 1637.31 (w), 1436.06 (w), 1390.18 (m), 1324.55 (m), 1143.48 (m), 997.73 (w), 970.29 (w), 848.74 (w). **HRMS** (DART) for $C_{16}H_{26}BIO_6$ $(M+H)^+$: Calc'd: 453.0940, found: 453.0949.

4.9.2.2.3 Procedures for the Preparation of Organozinc Reagents: Alkylzinc bromide Synthesis by Zinc Insertion into C-Br Bond.

A 20 mL vial was charged with zinc powder (1.26 g, 19.31 mmol, 2.50 equiv) and a stir bar. The vial was capped with a PTFE-lined pierceable screwcap and the system was allowed to stir at 80 °C under high vacuum for 2 h. The vial was then allowed to cool to room temperature and backfilled with N_2. At this point the vial was brought into an Ar filled glove box, and a solution of iodine (95.84 mg, 0.38 mmol, 0.02 equiv) in DMA (1 mL) was added to the reaction flask and the suspension was allowed to stir until the red color subsided. In turn, alkyl bromide (7.60 mmol, 1.00 equiv) and an additional 4 mL of DMA were added. The vial was capped with a Teflon screwcap, taped and the suspension was allowed to stir at 80 °C for 12 h. Next, the mixture was allowed to cool to room temperature, brought inside the glovebox and filtered through a syringe filter (pore-size: 0.45 μM, PTFE). The resulting organozinc solution was titrated following the Knochel

method (I_2 in a 0.5 M THF solution of LiCl).[86] The solutions could be stored in a freezer under inert atmosphere for several weeks without deleterious effects. **Note:** for the three component cross-coupling reactions (**Procedure A**, see below) the alkylzinc bromide solution (0.4 mmol, 2.0 equiv) was transferred under inert atmosphere into a flame dried vial containing LiCl (35.6 mg, 0.84 mmol, 4.20 equiv) in 0.5 mL of THF. The mixture was stirred vigorously for 1 h at room temperature prior to being used in the cross-coupling reaction.

Organozinc Chloride synthesis by addition of organolithium reagents to $ZnCl_2$.

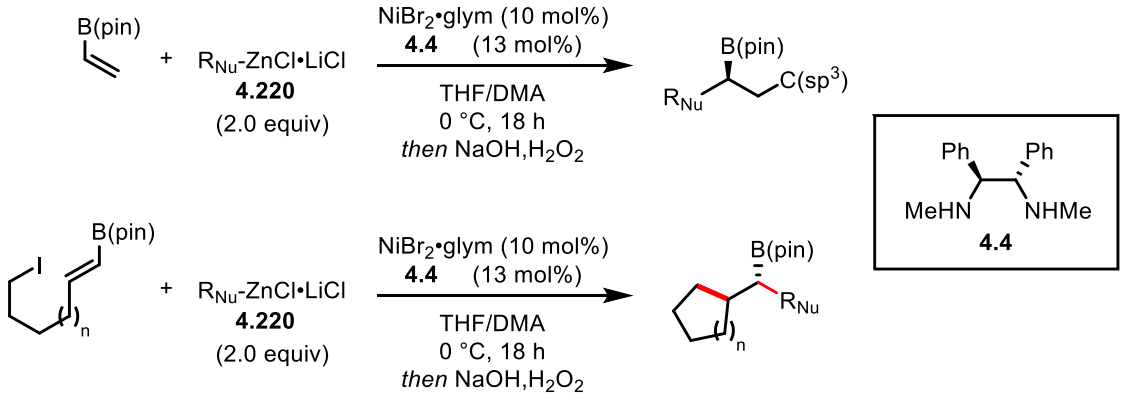
Organolithium reagents were generated by lithium-halogen exchange with *tert*-butyllithium using the following procedure: aryl bromide or alkyl iodide (1.0 mmol) was placed in a flame-dried 20 mL vial under N_2 atmosphere and dissolved with 5 mL of dry diethyl ether. The vial was sealed with a pierceable PTFE-lined cap and a septum was taped over it (this second septum was backfilled with N_2 to create a buffer zone to prevent air from entering the vial). The solution was allowed to cool to -78 ºC and *tert*-butyllithium (1.18 mL, 1.7 M, 2.0 equiv) was added dropwise. The solution was allowed to stir at -78°C for 30-40 min after which time a solution of $ZnCl_2$ in THF was added (2.4 mL, 0.5 M, 1.2 equiv). The mixture was allowed to warm to room temperature and stirred for 45 min after which time the solvent was carefully removed under vacuum using a Schlenck line. The concentrated residue was brought inside an argon filled glovebox and redissolved in 2 mL

[86] Krasovskiy, A.; Knochel, P. *Synthesis* **2006**, 5, 890.

of THF. The resulting solution was titrated following literature procedure.[87] **Note**: phenyllithium and methyllithium solutions purchased from commercial sources (Sigma Aldrich) were added to $ZnCl_2$ solutions in THF (0.5 M, 1.2 equiv) at 0 ºC, stirred for 45 min, and used directly in the reaction.

4.9.2.2.4. Representative Procedure for Cross-Coupling

Procedure A, for the three component cross-coupling (alkyl- or arylZnX) and two component cyclization/cross-coupling with aryl ZnX reagents.



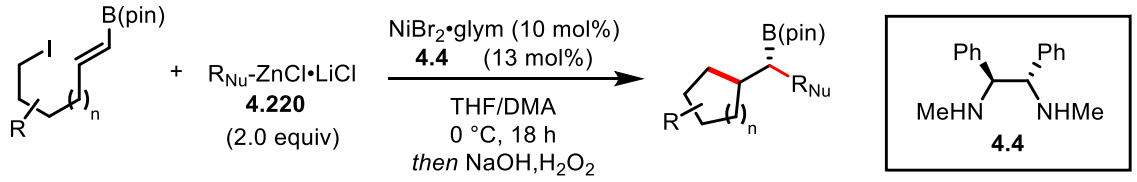
In an argon-filled glovebox, an oven-dried 2 dram vial equipped with a magnetic stir bar was charged with $NiBr_2$•glyme (6.17 mg, 0.02 mmol, 0.1 equiv), (*S*,*S*)-*N*,*N*-dimethyl-1,2-diphenyl-ethane-1,2-diamine (*S,S*)-**4.4** (6.25 mg, 0.026 mmol, 0.13) and dissolved in 1.0 mL of THF. The catalyst solution was stirred for 1 h at ambient temperature. Vinylboronic

[87] Krasovskiy, A.; Knochel, P. *Synthesis* **2006**, 5, 0890.

acid pinacol ester (30.80 mg, 0.20 mmol, 1.00 equiv) and alkyl iodide (0.40 mmol, 2.00 equiv), or cyclizing alkenylboron substrate (0.20 mmol, 1.00 equiv) were added to the catalyst solution (alternatively, the reactants could be weighed out in a separate vial and the catalyst solution added to the latter). At this point, THF and DMA were added so as to reach a final volume (taking into account the volume of the organozinc solution) of 2.00 mL of THF and 0.40 mL DMA. The vial was sealed with a PTFE-lined pierceable cap, taped, and brought outside the glovebox where it was placed in a CryoCool set at 0 ºC. The vial was allowed to cool for 20-30 min before addition of the organozinc solution (0.40 mmol, 2.00 equiv) (***Note:*** for the three component reactions with alkylZnBr reagents, the organozinc reagent was stirred with LiCl (35.6 mg, 0.84 mmol, 4.20 equiv), in 0.50 mL of THF for 1 h at room temperature before addition). The puncture hole was taped over and the reaction mixture was stirred at 0 ºC for 18 h. Oxidation was then carried out by adding 0.50 mL of 30% H_2O_2 and 0.50 mL of a 3.0 M solution of aqueous NaOH to the cold reaction mixture (the vial was vented to prevent pressure build-up). The mixture was stirred vigorously for 2-3 h and allowed to slowly warm to room temperature. At this point the reaction mixture was allowed to cool to 0 ºC once more and the oxidation was quenched by addition of 0.50 mL of a saturated solution of aqueous $Na_2S_2O_3$ .The product was extracted from the organic layer four times with ethyl acetate, dried with $MgSO_4$ and concentrated under reduced pressure. The unpurified product was purified by silica gel chromatography. **Note**: In order to isolate the boronic ester product prior to oxidation, the work-up was carried out by adding 0.30 mL of a saturated solution of aqueous NH_4Cl to the reaction mixture at 0 ºC. The mixture was then transferred to a separatory funnel using

ethyl acetate, and the organic layer was washed with brine, dried with $MgSO_4$, and concentrated. The unpurified product was then purified by silica gel chromatography.

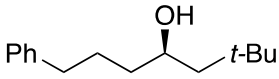
Procedure B, for intramolecular cyclization/cross-coupling reactions using alkylZnBr.



In an argon-filled glovebox, an oven-dried 2 dram vial equipped with a magnetic stirrer was charged with $NiBr_2$•glyme (6.17 mg, 0.02 mmol, 0.10 equiv), (*S,S*)-*N,N*-dimethyl-1,2-diphenyl-ethane-1,2-diamine (*S,S*)-**4.4** (6.25 mg, 0.026 mmol,) and dissolved in 1.0 mL of DMA. The catalyst solution was allowed to stir for 1 h at ambient temperature. The cyclizing alkenylboron substrate (0.20 mmol, 1.00 equiv) was added to the catalyst solution (alternatively, the substrated could be weighed out in a separate vial and the catalyst solution added to the latter). DMA was added so as to reach a final volume (taking into account the volume of the organozinc solution) of 2.00 mL. The vial was sealed with a PTFE-lined pierceable cap, taped, and brought outside the glovebox where it was placed in an ice-bath. The vial was allowed to cool for a few min before addition of the organozinc solution (0.40 mmol, 0.20 equiv). The puncture hole was taped over and the reaction mixture was taken off the ice bath and allowed to stir at room temperature for 18 h. Finally, the mixture was allowed to cool to 0 ºC and 0.30 mL of a saturated solution of aqueous NH_4Cl were added. The mixture was then transferred to a separatory funnel using ethyl

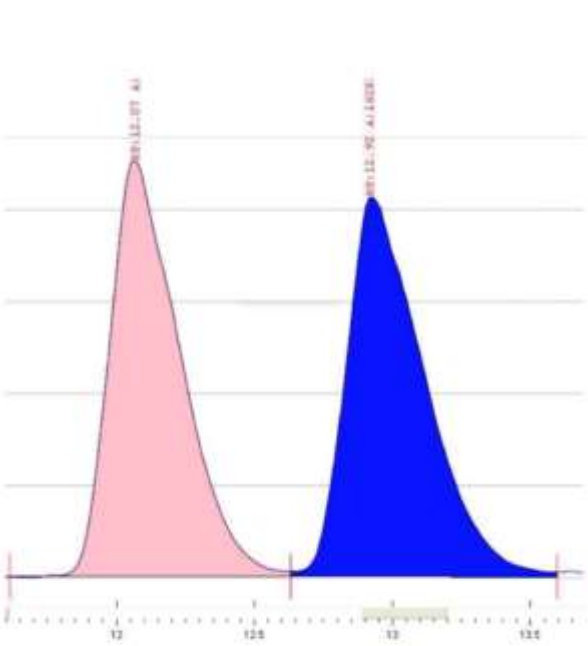
acetate and the organic layer was washed with brine, dried over $MgSO_4$, and concentrated. The unpurified product could then be isolated as the boronic ester by silica gel chromatography, or redissolved in 1.0 mL of THF and oxidized following the method outlined in **procedure B**.

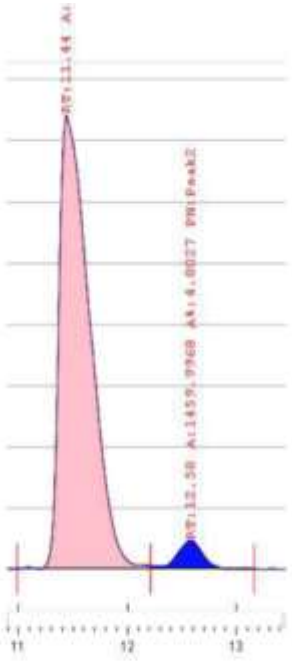
4.9.2.2.5 Procedures and Characterization for Cross-Coupling Product



(*R*)-6,6-Dimethyl-1-phenylheptan-4-ol (**4.222**) The reaction was performed according to general **procedure A** with vinylboronic acid pinacol ester (30.8 mg, 0.20 mmol, 1.0 equiv), *tert*-butyl iodide (73.6 mg, 0.40 mmol, 2.0 equiv), and (3-phenylpropyl)zinc bromide•LiCl solution in DMA (0.24 mL, 1.68 M, 0.4 mmol, 2.0 equiv), in a mixture of THF/DMA (2.00 mL THF and 0.40 mL DMA overall) using $NiBr_2$•glyme (6.17 mg, 0.020 mmol, 0.10 equiv) and (*S*,*S*)-**4.4** (6.25 mg, 0.026 mmol, 0.13 equiv) as catalyst. The unpurified mixture was purified by silica gel chromatography (10% ethyl acetate in hexanes, stain in CAM) to afford the product as colorless oil (24.3 mg, 55% yield). **^{1}H NMR** (500 MHz, $CDCl_3$) δ 7.29-7.26 (m, 3H), 7.19-7.18 (m, 2H), 3.80-3.75 (m, 1H), 2.67-2.60 (m, 2H), 1.82-1.69 (m, 1H), 1.7-1.60 (m, 1H), 1.52-1.42 (m, 2H), 1.38-1.30 (m, 2H), 0.95 (s, 9H). **^{13}C NMR** (151 MHz, $CDCl_3$) δ 142.56, 128.55, 128.44, 125.87, 69.64, 51.49, 39.33, 36.04, 30.41, 30.30, 27.59. **IR** (neat) ν_{max} 3358.9 (br), 3023.7 (w), 2945.4 (s), 2931.7 (s), 2859.3 (m), 1602.2 (w), 1494.4 (m), 1452.2 (m), 1362.2 (m), 1089.6 (m), 746.89 (m), 697.6 (s). **HRMS** (DART) for $C_{15}H_{28}NO$ $(M+NH_4)^+$: Calc'd: 238.2165,

found: 238.2166. $[\alpha]_D^{20} = 8.60$ (*c* 1.0, $CHCl_3$, *l* = 50 mm).



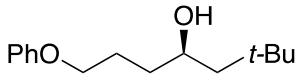


Peak Info				Peak Info			
Peak No	% Area	Area	RT (min)	Peak No	% Area	Area	RT (min)
1	49.58	16011.8643	12.07	1	95.1973	28939.5308	11.44
2	50.42	16283.1295	12.92	2	4.8027	1459.9968	12.58
Total:	100	32294.9938		Total:	100	30399.5276	

Determination of Stereochemical Identity: Racemic compound was prepared according to the **general procedure A** with racemic **4.4** as ligand. Absolute stereochemistry was assigned analogy (see product **4.223** and **4.253**).

SFC (Chiracel AD-H, 2% IPA, 3 mL/min, 100 bar, 35 °C, 210-289 nm)-analysis of **(*R*)-6,6-Dimethyl-1-phenylheptan-4-ol**.

Racemic Material Enantioenriched Material

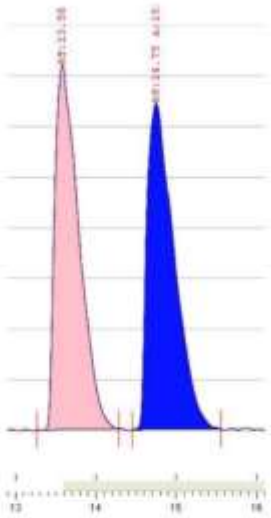


(*R*)-6,6-Dimethyl-1-phenoxyheptan-4-ol (4.224). The reaction was performed according to general **procedure A** with vinylboronic acid pinacol ester (30.8 mg, 0.20 mmol, 1.0 equiv), *tert*-butyl iodide (73.6 mg, 0.40 mmol, 2.0 equiv), and (3-phenoxypropyl)zinc bromide•LiCl solution in DMA (0.360 mL, 1.1 M, 0.4 mmol, 2.0 equiv), in a mixture of THF/DMA (2.00 mL THF and 0.40 mL DMA overall) using $NiBr_2$•glyme (6.17 mg, 0.020 mmol, 0.10 equiv) and (*S*,*S*)-**4.4** (6.25 mg, 0.026 mmol, 0.13 equiv) as catalyst. The unpurified mixture was purified by silica gel chromatography (20% ethyl acetate in hexanes, stain in CAM) to afford the product as colorless oil (33.1 mg, 70% yield). **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.32-7.21 (m, 2H), 6.99-6.84 (m, 3H), 4.08-3.91 (m, 2H), 3.91-3.75 (m, 1H), 2.00-1.76 (m, 2H), 1.71-1.55 (m, 2H), 1.40 (d, J = 5.1 Hz, 2H), 0.98 (s, 9H). **^{13}C NMR** (126 MHz, $CDCl_3$) δ 159.0, 129.6, 120.8, 114.6, 69.2, 68.1, 51.5, 36.4, 30.4, 30.3, 25.7. **IR** (neat) ν_{max} 3394.5 (br), 2947.5 (m), 1598.8 (m), 1495.5 (m), 1471.1 (m), 1360.4 (w), 1247.9 (s), 1034.4 (w), 757.1 (m), 690.7 (m). **HRMS** (DART) for $C_{15}H_{25}O_2$ $(M+H)^+$: Calc'd: 237.18491, found: 237.18571. **$[\alpha]_D^{20}$** = -6.898 (*c* 1.0, $CHCl_3$, *l* = 50 mm).

Determination of Stereochemical Identity: Racemic compound was prepared according to the **general procedure A** with racemic **4.4** as ligand. Absolute stereochemistry was assigned analogy (see product **4.223** and **4.253**).

SFC (Chiracel AD-H, 1% IPA, 3 mL/min, 100 bar, 35 °C, 210-289 nm)-analysis of **(*R*)-6,6-Dimethyl-1-phenoxyheptan-4-ol**.

Racemic Material



Peak No	% Area	Area	RT (min)
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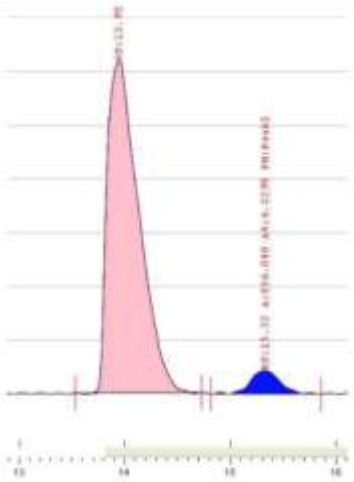
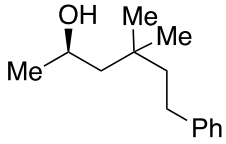
2	50.2412	15106.0982	14.75
Total:	100	30067.1482	

Enantioenriched Material



Peak No	% Area	Area	RT (min)
1	93.7702	12885.1701	13.95
2	6.2298	856.048	15.33
Total:	100	13741.2181	



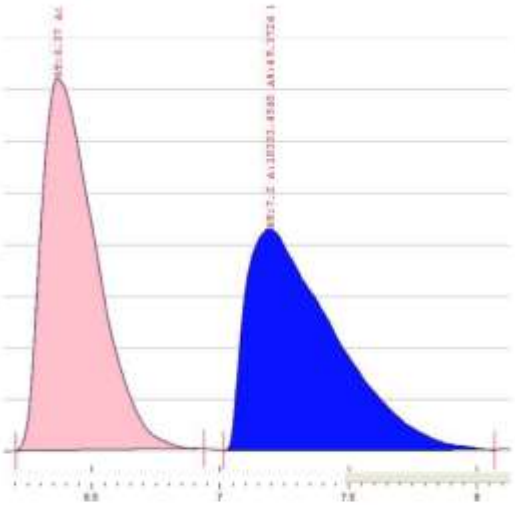
(*R*)-4,4-Dimethyl-6-phenylhexan-2-ol (4.225). The reaction was performed according to general **procedure A** with vinylboronic acid pinacol ester (30.8 mg, 0.20 mmol, 1.0 equiv), (3-iodo-3-methylbutyl)benzene (109.7 mg, 0.40 mmol, 2.0 equiv), and methylzinc chloride•LiCl solution in THF (1.01 mL, 0.40 M, 0.40 mmol, 2.0 equiv) (**Note:** the organozinc reagent was obtained by addition of commercial MeLi (130 µL, 3.1 M in DME, 0.4 mmol, 2.0 equiv) to $ZnCl_2$ in THF (880 µL, 0.5 M, 0.44 mmol, 2.2 equiv). After allowing to stir for 30 min at room temperature additional LiCl (18.7 mg,

0.44 mmol, 2.2 equiv) was added to improve yield and selectivity of the reaction), in a mixture of THF/DMA (2.00 mL THF and 0.40 mL DMA overall) using $NiBr_2$•glyme (6.17 mg, 0.020 mmol, 0.10 equiv) and (*S*,*S*)-**4.4** (6.25 mg, 0.026 mmol, 0.13 equiv) as catalyst. The unpurified mixture was purified by silica gel chromatography (10% ethyl acetate in hexanes, stain in CAM) to afford the product as colorless oil (48.9 mg, 55% yield). **^{1}H NMR** (600 MHz, $CDCl_3$) δ 7.30-7.23 (m, 2H), 7.21-7.14 (m, 3H), 4.03-4.00 (m, 1H), 2.65-2.50 (m, 2H), 1.65-1.52 (m, 2H), 1.50 (dd, *J* = 14.5, 7.9 Hz, 1H), 1.41 (dd, *J* = 14.6, 2.9 Hz, 1H), 1.22 (d, *J* = 6.2 Hz, 3H), 1.02 (s, 3H), 1.01 (s, 3H). **^{13}C NMR** (151 MHz, $CDCl_3$) δ 143.5, 128.5, 125.7, 65.7, 51.0, 45.3, 33.1, 30.9, 27.9, 27.8, 26.3. **IR** (neat) ν_{max} 3363.6 (br), 3023.3 (w), 2955.9 (s), 2924.5 (s), 2863.2 (m), 1494.9 (m), 1467.25 (m), 1259.0 (m), 1072.9 (s), 1051.5 (s), 1029.7 (s), 737.7 (s) 697.4 (s). **HRMS** (DART) for $C_{14}H_{26}NO$ $(M+NH_4)^+$: Calc'd: 224.2007, found: 224.2009. **$[\alpha]_D^{20}$** = 11.80 (*c* 1.0, $CHCl_3$, *l* = 50 mm).

Determination of Stereochemical Identity: Racemic compound was prepared according to the **general procedure A** with racemic **4.4** as ligand. Absolute stereochemistry was assigned analogy (see product **4.223** and **4.253**).

SFC (Chiracel AS-H, 1% IPA, 3 mL/min, 100 bar, 35 °C, 210-289 nm)-analysis of **(*R*)-4,4-Dimethyl-6-phenylhexan-2-ol.**

Racemic Material Enantioenriched Material



Peak Info			
Peak No	% Area	Area	RT (min)
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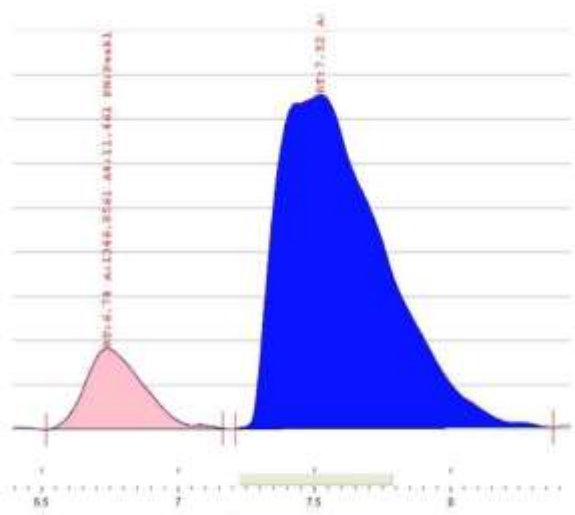
2	49.3726	10333.4565	7.2
Total:	100	20929.526	



Peak Info			
Peak No	% Area	Area	RT (min)
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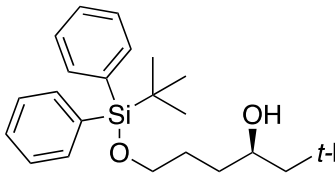
2	88.539	10404.7458	7.52
Total:	100	11751.6019	



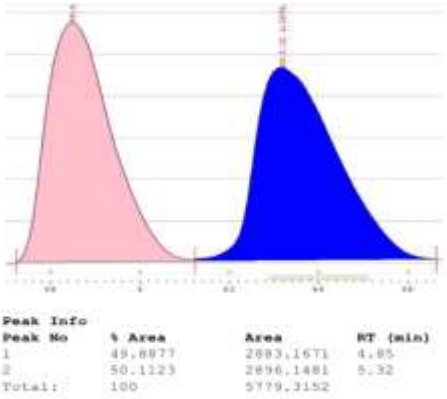
(*R*)-1-((*tert*-Butyldiphenylsilyl)oxy)-6,6-dimethylheptan-4-ol (4.226). The reaction was performed according to general **procedure A** with vinylboronic acid pinacol ester (30.8 mg, 0.20 mmol, 1.0 equiv), *tert*-butyl iodide (73.6 mg, 0.40 mmol, 2.0 equiv), and (3-((*tert*-butyldiphenylsilyl)oxy)propyl)zinc bromide•LiCl solution in DMA (0.425 mL, 0.94 M, 0.4 mmol, 2.0 equiv), in a mixture of THF/DMA (2.00 mL THF and 0.40 mL DMA overall) using $NiBr_2$•glyme (6.17 mg, 0.020 mmol, 0.10 equiv) and *(S,S)*-**4.4** (6.25 mg, 0.026 mmol, 0.13 equiv) as catalyst. The unpurified mixture was purified by silica gel chromatography (10% ethyl acetate in hexanes, stain in CAM) to afford the product as colorless oil (56 mg, 70% yield). **^{1}H NMR** (500 MHz, $CDCl_3$) δ 7.69-

7.67 (m, 3H), 7.48-7.36 (m, 5H), 3.82-3.76 (m, 1H), 3.71-3.68 (m, 2H), 1.83 (s, 1H), 1.73-1.61 (m, 2H), 1.60-1.47 (m, 2H), 1.42 -1.32 (m, 2H), 1.06 (s, 9H), 0.97 (s, 9H).. **^{13}C NMR** (151 MHz, $CDCl_3$) δ 135.7, 135.7, 133.9, 133.9, 129.8, 127.8, 69.3, 64.3, 51.4, 36.6, 30.4, 30.3, 28.9, 27.0, 19.3. **IR** (neat) ν_{max} 3385.9 (br), 3067.8 (w), 3047.8 (w), 2948.0 (s), 2928.7 (s), 2856.3 (s), 1471.1 (m), 1426.3 (m), 1388.8 (m), 1108.8 (s), 700.3 (s), 613.0 (m), 504.4 (s). **HRMS** (DART) for $C_{25}H_{39}O_2Si$ $(M+H)^+$: Calc'd: 399.2714, found: 399.2723. **$[\alpha]_D^{20}$** = -3.60 (*c* 1.0, $CHCl_3$, *l* = 50 mm).

Determination of Stereochemical Identity: Racemic compound was prepared according to the **general procedure A** with racemic **4.4** as ligand. Absolute stereochemistry was assigned analogy (see product **4.223** and **4.253**).

SFC (Chiracel OJ-H, 3% IPA, 3 mL/min, 100 bar, 35 °C, 210-289 nm)-analysis of **(*R*)-1-((*tert*-Butyldiphenylsilyl)oxy)-6,6-dimethylheptan-4-ol.**

Racemic Material Enantioenriched Material



Peak Info				
Peak No	% Area	Area	RT (min)	
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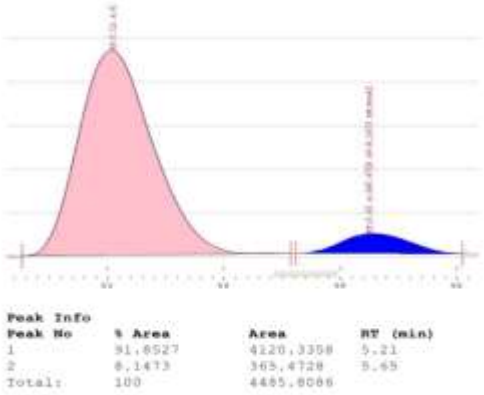
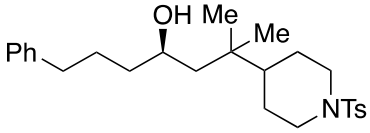
Total:	100	5779.3152		



Peak Info			
Peak No	% Area	Area	RT (min)
1	91.6527	4120.3358	5.21
2	8.1473	365.4728	5.65
Total:	100	4485.8086	



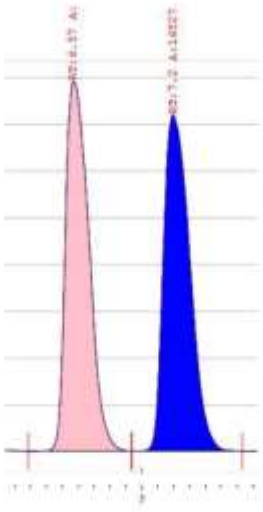
(*R*)-6-Methyl-1-phenyl-6-(1-tosylpiperidin-4-yl)heptan-4-ol (4.227). The reaction was performed according to general **procedure A** with vinylboronic acid pinacol ester (30.8 mg, 0.20 mmol, 1.0 equiv), 4-(2-iodopropan-2-yl)-1-tosylpiperidine (162.92 mg, 0.40 mmol, 2.0 equiv), and (3-phenylpropyl)zinc bromide•LiCl solution in DMA (0.24 mL, 1.68 M, 0.4 mmol, 2.0 equiv), in a mixture of THF/DMA (2.00 mL THF and 0.40 mL DMA overall) using $NiBr_2$•glyme (6.17 mg, 0.020 mmol, 0.10 equiv) and (*S*,*S*)-**4.4** (6.25 mg, 0.026 mmol, 0.13 equiv) as catalyst. The unpurified mixture was purified by silica gel chromatography (20% ethyl acetate in hexanes, stain in CAM) to afford the product as white solid (48.9 mg, 55% yield). **^{1}H NMR** (500 MHz, $CDCl_3$) δ 7.65-7.63(m, 2H), 7.33-7.26 (m, 4H), 7.19-7.17 (m, 3H), 3.84 (apparent d, *J* = 11.2 Hz, 2H), 3.70-3.67 (m, 1H), 2.69-2.55 (m, 2H), 2.43 (s, 3H), 2.20-1.99 (m, 2H), 1.79-1.58 (m, 4H), 1.45-1.25 (m, 6H), 1.11-1.07 (m, 2H), 0.87 (s, 3H), 0.84 (s, 3H). **^{13}C NMR** (126 MHz, $CDCl_3$) δ 143.5, 142.3, 133.2, 129.6, 128.5, 128.4, 127.9,

125.9, 69.0, 47.3, 47.2, 44.7, 39.6, 35.9, 34.7, 27.5, 26.1, 25.3, 25.1, 21.6. **IR** (neat) ν_{max} 3541.5 (br), 3023.0 (m), 2926.1 (s), 2850.8 (m), 1715.6 (w), 1596.4 (w), 1493.2 (m),1464.6 (s), 1450.4 (s), 1353.5 (s), 1334.5 (s), 1303.2 (s), 1054.5 (s), 930.8 (s), 862.3 (s), 813.0 (s), 724.1 (s), 698.9 (s), 649.2 (s), 573.8 (s). **HRMS** (DART) for $C_{26}H_{38}NO_3S$ $(M+H)^+$: Calc'd: 444.2565, found: 444.2567. $\mathbf{[\alpha]_D^{20}} = 4.60$ (*c* 1.0, $CHCl_3$, *l* = 50 mm).

Determination of Stereochemical Identity: Racemic compound was prepared according to the **general procedure A** with racemic **4.4** as ligand. Absolute stereochemistry was assigned analogy (see product **4.223** and **4.253**).

SFC (Chiracel OJ-H, 15% IPA, 3 mL/min, 100 bar, 35 °C, 210-289 nm)-analysis of **(*R*)-6-Methyl-1-phenyl-6-(1-tosylpiperidin-4-yl)heptan-4-ol.**

Racemic Material Enantioenriched Material



Peak Info			
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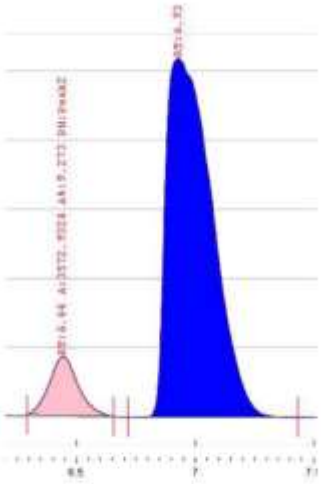
2	50.6156	16527.6547	7.2
Total:	100	32653.2625	



Peak Info			
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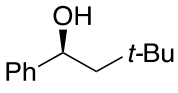
Total:	100	38530.4235	



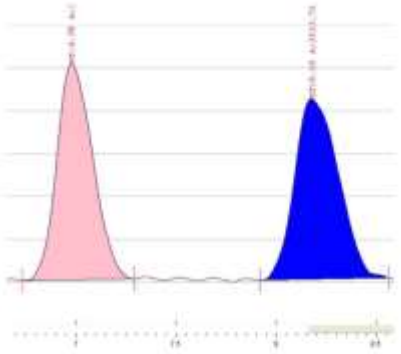
(*S*)-3,3-Dimethyl-1-phenylbutan-1-ol (4.223). The reaction was performed according to general **procedure A** with vinylboronic acid pinacol ester (30.8 mg, 0.20 mmol, 1.0 equiv), *tert*-butyl iodide (73.6 mg, 0.40 mmol, 2.0 equiv), and phenylzinc chloride solution in THF (1.0 mL, 0.4 M, 0.4 mmol, 2.0 equiv), in a mixture of THF/DMA (2.00 mL THF and 0.40 mL DMA overall) using $NiBr_2$•glyme (6.17 mg, 0.020 mmol, 0.10 equiv) and (*S*,*S*)-**4.4** (6.25 mg, 0.026 mmol, 0.13 equiv) as catalyst. The unpurified mixture was purified by silica gel chromatography (10% ethyl acetate in hexanes, stain in CAM) to afford the product as white solid (25.1 mg, 70% yield). **HRMS** (DART) for $C_{26}H_{38}NO_3S$ $(M+H-H_2O)^+$: Calc'd: 161.1321, found: 161.1325. $[\alpha]_D^{20}$ = -52.39 (*c* = 0.5, $CHCl_3$, *l* = 50 mm). (lit: $[\alpha]D^{20}$ = -71.2 (*c* 1.9, THF, *l* = 100mm, ≤ 99% *ee*, (*S*)-enantiomer)). All spectral

data was in accord with the literature. [88]

Determination of Stereochemical Identity: Racemic compound was prepared according to the **general procedure A** with racemic **4.4** as ligand. Absolute stereochemistry was assigned analogy (see product **4.223** and **4.253**).

SFC (Chiracel ODR-H, 1% IPA, 3 mL/min, 100 bar, 35 °C, 210-289 nm)-analysis of **(*S*)-3,3-Dimethyl-1-phenylbutan-1-ol.**

Racemic Material



Peak Info

Peak No	% Area	Area	RT (min)
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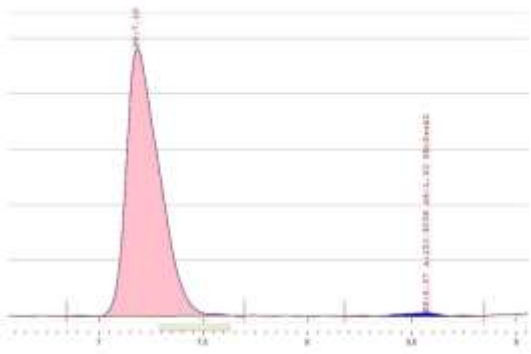
2	50.6564	3213.7248	8.18
Total:	100	6344.1668	

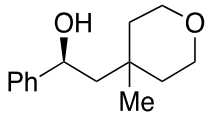
Enantioenriched Material



Peak Info

Peak No	% Area	Area	RT (min)
1	98.57	10575.7422	7.18
2	1.43	153.4258	8.57
Total:	100	10729.168	

[88] Scholz, R.; Hellmann, G.; Rohs, S.; Özdemir, D.; Raabe, G.; Vermeeren, C.; Gais, H.-J. *Eur. J. Org. Chem*. **2010**, 4588.

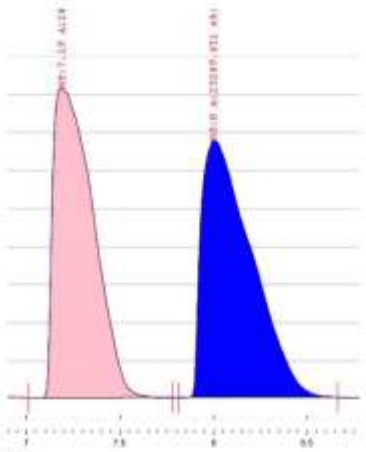


(*S*)-2-(4-Methyltetrahydro-2*H*-pyran-4-yl)-1-phenylethan-1-ol (4.228). The reaction was performed according to general **procedure A** with vinylboronic acid pinacol ester (30.8 mg, 0.20 mmol, 1.0 equiv), 4-iodo-4-methyltetrahydro-2*H*-pyran (90.0 mg, 0.40 mmol, 2.0 equiv), and phenylzinc chloride solution in THF (1.0 mL, 0.4 M, 0.4 mmol, 2.0 equiv), in a mixture of THF/DMA (2.00 mL THF and 0.40 mL DMA overall) using $NiBr_2$•glyme (6.17 mg, 0.020 mmol, 0.10 equiv.) and (*S*,*S*)-**4.4** (6.25 mg, 0.026 mmol, 0.13 equiv) as catalyst. The unpurified mixture was purified by silica gel chromatography (20% ethyl acetate in hexanes, stain in CAM) to afford the product as colorless oil (32.2 mg, 73% yield). **^{1}H NMR** (600 MHz, $CDCl_3$) δ 7.36-7.35 (m, 3H), 7.29-7.26 (m, 2H), 4.90 (dd, *J* = 8.8, 3.5 Hz, 1H), 3.84-3.70 (m, 1H), 3.71-3.59 (m, 2H), 1.91 (dd, *J* = 14.7, 8.7 Hz, 1H), 1.75-1.58 (m, 3H), 1.56-1.44 (m, 2H), 1.37-1.30 (m, 1H), 1.26 (s, 1H), 1.14 (s, 3H). **^{13}C NMR** (151 MHz, $CDCl_3$) δ 146.4, 128.8, 127.7, 125.8, 71.8, 64.1, 64.0, 51.5, 38.5, 38.4, 31.0, 24.5. **IR** (neat) ν_{max} 3410.3 (br), 2950.7 (s), 2919.2 (s), 2853.8 (s), 1452.7 (m), 1102.3 (s), 1060.0 (m), 1036.0 (m), 1017.1 (m), 699.3 (m). **HRMS** (DART) for C14H19O $(M+H-H_2O)^+$: Calc'd: 203.1424, found: 203.1430. **$[\alpha]_D^{20}$** = 40.78 (*c* 0.5, $CHCl_3$, *l* = 50 mm).

Determination of Stereochemical Identity: Racemic compound was prepared according to the **general procedure A** with racemic **4.4** as ligand. Absolute stereochemistry was assigned analogy (see product **4.223** and **4.253**).

SFC (Chiracel OJ-H, 5% IPA, 3 mL/min, 100 bar, 35 °C, 210-289 nm)-analysis of **(*S*)-2-(4-Methyltetrahydro-2*H*-pyran-4-yl)-1-phenylethan-1-ol.**

Racemic Material



Peak Info

Peak No	% Area	Area	RT (min)
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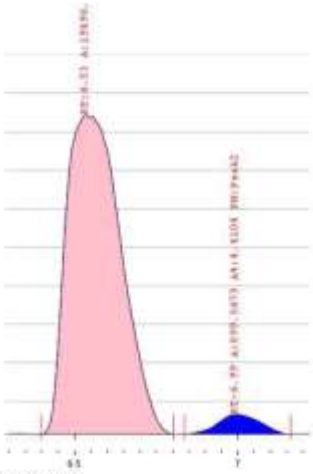
2	51.0988	25249.631	8
Total:	100	49413.3685	

Enantioenriched Material



Peak Info

Peak No	% Area	Area	RT (min)
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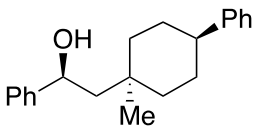
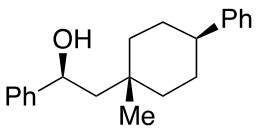
2	4.4104	899.5675	6.99
Total:	100	20396.4592	



and



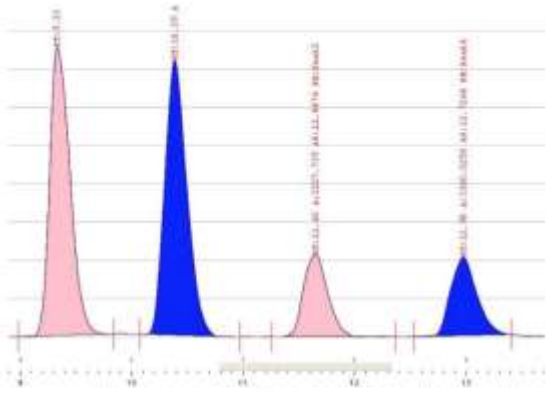
(*S*)-2-((1*S*,4*R*)-1-Methyl-4-phenylcyclohexyl)-1-phenylethan-1-ol (4.229 and **4.229')**. The reaction was performed according to general **procedure A** with vinylboronic acid pinacol ester (30.8 mg, 0.20 mmol, 1.0 equiv), (4-iodo-4-methylcyclohexyl)benzene (120.1 mg, 0.40 mmol, 2.0 equiv), and phenylzinc chloride solution in THF (1.0 mL, 0.4 M, 0.4 mmol, 2.0 equiv), in a mixture of THF/DMA (2.00 mL THF and 0.40 mL DMA overall) using $NiBr_2$•glyme (6.17 mg, 0.020 mmol, 0.10 equiv) and (*S*,*S*)-**4.4** (6.25 mg, 0.026 mmol, 0.13 equiv) as catalyst. The

unpurified mixture was purified by silica gel chromatography (10% ethyl acetate in hexanes, stain in CAM) to afford the product as colorless oil consisting of a 1:2.7 mixture of diastereomers (30.6 mg, 52% yield). The diastereomeric ratio was determined by ^{1}H NMR integration. **^{1}H NMR** (500 MHz, $CDCl_3$) δ 7.44-7.34 (m, 13H), 7.34-7.26 (m, 12H), 7.26-7.16 (m, 11H), 4.97 (dd, *J* = 8.4, 2.9 Hz, 1H, minor diastereomer), 4.88 (dd, *J* = 8.2, 3.2 Hz, 3H, major diastereomer), 2.55-2.37 (m, 5H), 2.00 (m, 4H), 1.94-1.85 (m, 4H), 1.84-1.52 (m, 32H), 1.39-1.24 (m, 9H), 1.14 (s, 3H), 1.09 (s, 9H). **^{13}C NMR** (151 MHz, $CDCl_3$) δ 147.7, 147.6, 146.8, 146.8, 128.7, 128.7, 128.4, 128.4, 127.6, 127.5, 127.0, 126.9, 126.0, 126.0, 125.9, 72.4, 71.8, 55.4, 45.2, 44.7, 44.4, 39.1, 38.7, 38.7, 38.6, 32.8, 32.4, 30.5, 29.9, 29.8, 29.8, 29.7, 22.3. **IR** (neat) ν_{max} 412.6 (br), 2919.3 (m), 2857.4 (w), 1491.2 (w), 1053.4 (w), 718.5 (m), 697.2 (s), 533.78 (w). **HRMS** (DART) for $C_{15}H_{25}O_2$ $(M+H-H_2O)^+$: Calc'd: 277.1951, found: 277.1951.

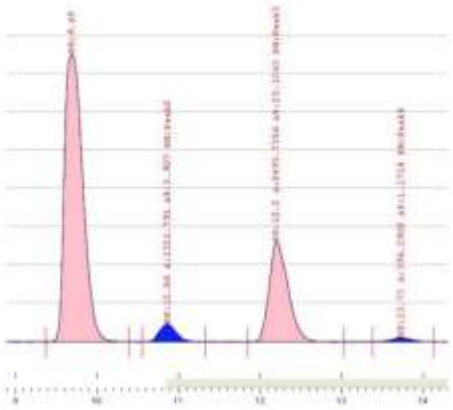
Determination of Stereochemical Identity: Racemic compound was prepared according to the **general procedure A** with racemic **4.4** as ligand. Absolute stereochemistry was assigned analogy (see product **4.223** and **4.253**).

SFC (Chiracel OJ-H, 4% IPA, 3 mL/min, 100 bar, 35 °C, 210-289 nm)-analysis of **(*S*)-2-(1-Methyl-4-phenylcyclohexyl)-1-phenylethan-1-ol**.

Racemic Material Enantioenriched Material

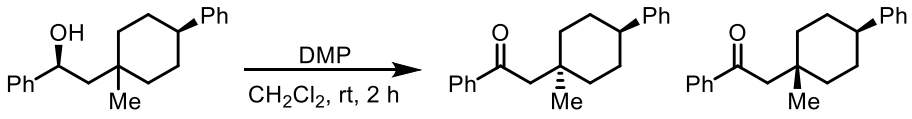


Peak No	% Area	Area	RT (min)
1	36.764	9533.1123	9.33
2	38.062	9869.7005	10.39
3	12.4476	3227.739	11.65
4	12.7264	3300.0258	12.98
Total:	100	25930.5776	

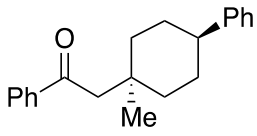


Peak No	% Area	Area	RT (min)
1	69.8153	23619.2332	9.69
2	3.907	1321.791	10.86
3	25.1063	8493.7356	12.2
4	1.1714	396.2900	13.73
Total:	100	33831.0506	

The stereochemical configuration was determined by COSY and NOESY analysis of compound **SI-25** which was isolated as a single stereoisomer from the mixture obtained after oxidation of product **4.300**.



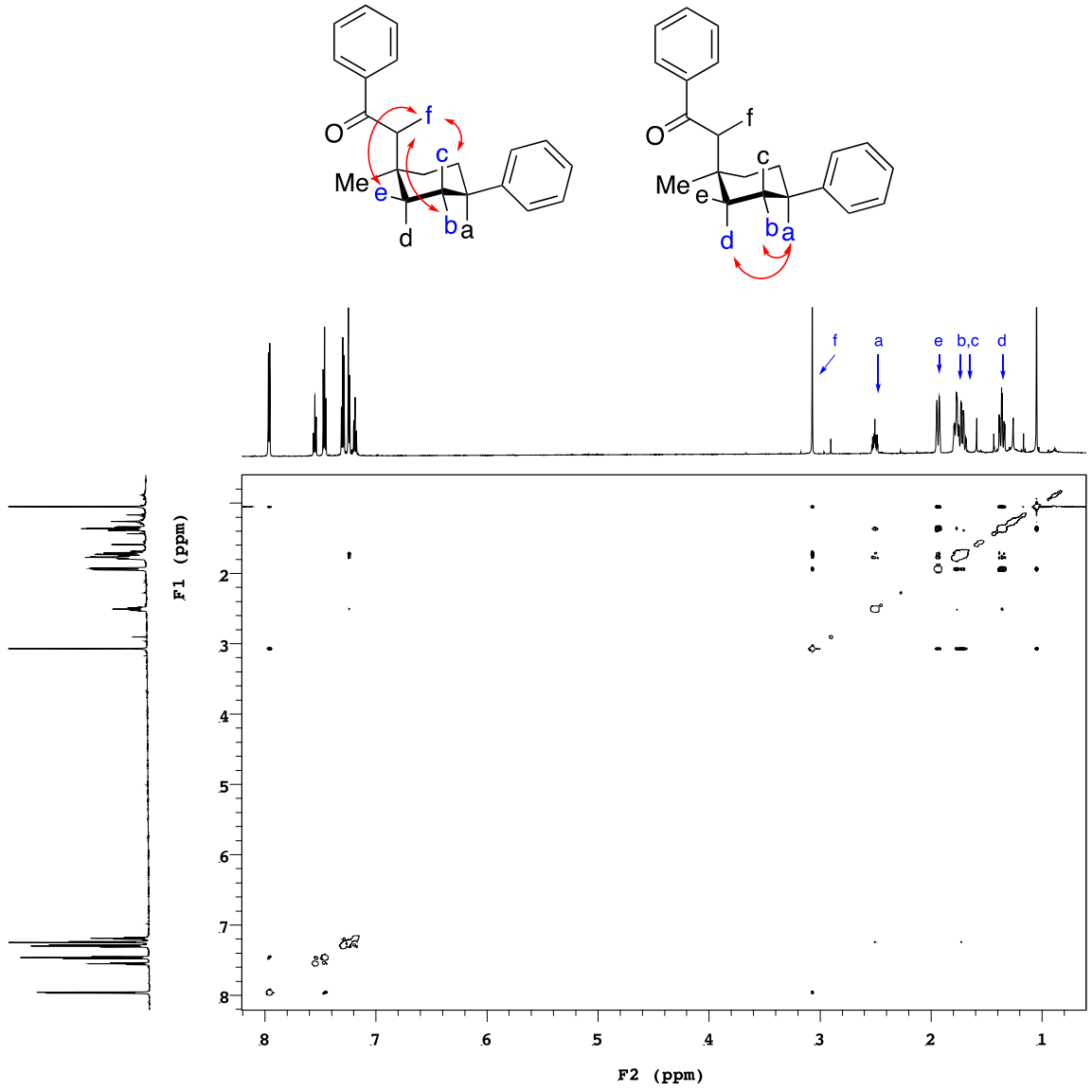
4.229/4.229' **4.300** 2.7:1 dr

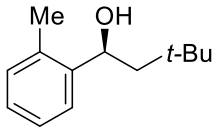


2-((1*S*,4*S*)-1-Methyl-4-phenylcyclohexyl)-1-phenylethan-1-one (4.300) Diastereomeric mixture **4.229** (40.7 mg, 0.14 mmol, 1.0 equiv) was placed in a vial equipped with a stir barr, and was allowed to dissolve in 5 mL of dichloromethane. Sodium

bicarbonate (47 mg, 0.56 mmol, 4.0 equiv) was added to the solution followed by Dess-Martin periodinane (88.0 mg, 0.21 mmol, 1.5 equiv) and the mixture was allowed to stir at room temperature for 2 h. The reaction was quenched with a 10% solution of aqueous sodium thiosulfate (2 mL) followed by a saturated solution of aqueous sodium bicarbonate (2 mL). The product was extracted from the organic layer twice with dichloromethane and twice with diethyl ether, the combined organic layers were dried with $MgSO_4$ and concentrated in vacuo. The major diastereomer was isolated by silica gel chromatography (1-5% ethyl acetate in pentanes, UV) as colorless oil (22 mg, 55% yield). **^{1}H NMR** (600 MHz, $CDCl_3$(600 MHz, Chloroform-*d*) δ 7.99-7.94 (m, 2H), 7.58-7.52 (m, 1H), 7.46 (t, *J* = 7.7 Hz, 2H), 7.30 (t, *J* = 7.6 Hz, 2H), 7.26-7.23 (m, 2H), 7.21-7.17 (m, 1H), 3.07 (s, 2H), 2.51 (tt, *J* = 12.0, 4.1 Hz, 1H), 1.94 (app. d, *J* = 11.3 Hz, 2H), 1.82 – 1.66 (m, 4H), 1.36 (td, *J* = 13.4, 4.1 Hz, 2H), 1.05 (s, 3H). **^{13}C NMR** (151 MHz, $CDCl_3$) δ 201.1, 147.2, 139.0, 132.7, 128.5, 128.3, 128.3, 128.2, 128.1, 126.8, 125.9, 44.1, 42.6, 38.6, 33.6, 29.9, 29.8. **IR** (neat) ν_{max} 3056.3 (w), 3023.3 (w), 2921.7 (s), 2858.7 (s), 1686.2 (s), 1671.2 (s), 1596.3 (w), 1447.0 (m), 1375.0 (m), 1252.8 (m), 750.0 (s), 728.2 (s). **HRMS** (DART) for $C_{13}H_{19}$ $(M+H-H_2O)^+$: Calc'd: 175.1481, found: 175.1473

Relevant NOESY correlations are illustrated below.





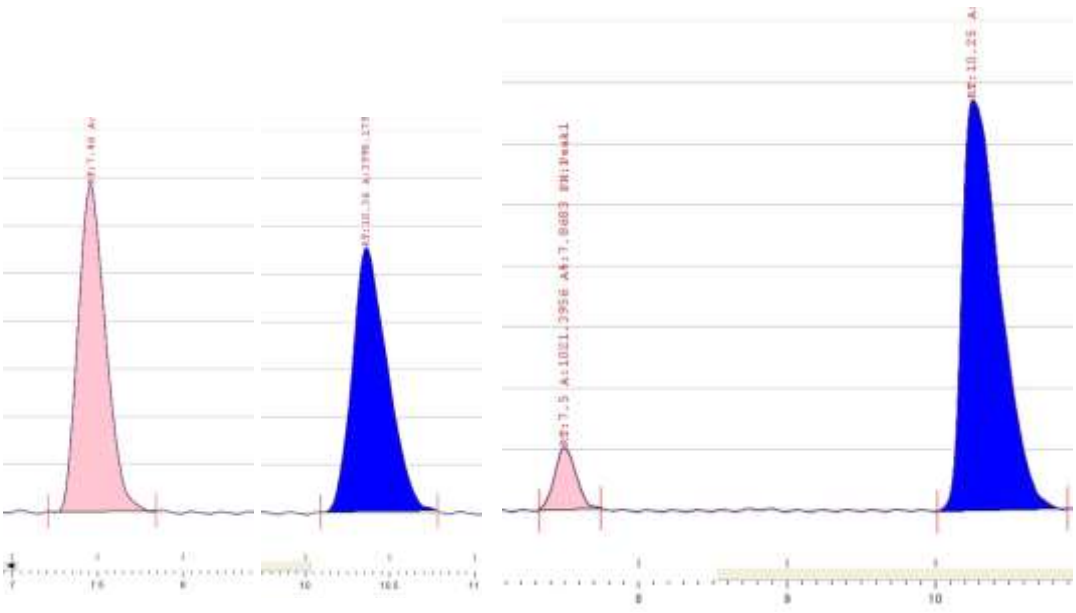
(*S*)-3,3-Dimethyl-1-(o-tolyl)butan-1-ol (4.231) The reaction was performed according to the general **procedure A** with vinylboronic acid pinacol ester (30.8 mg, 0.20 mmol, 1.0 equiv), *tert*-butyl iodide (73.6 mg, 0.40 mmol, 2.0 equiv), and (*o*-tolyl)

zinc chloride (0.89 mL, 0.45 M, 0.4 mmol, 2.0 equiv), in a mixture of THF/DMA (2.00 mL THF and 0.40 mL DMA overall) using $NiBr_2$•glyme (6.17 mg, 0.020 mmol, 0.10 equiv) and (*S*,*S*)-**4.4** (6.25 mg, 0.026 mmol, 0.13 equiv) as catalyst. The unpurified mixture was purified by silica gel chromatography (10% ethyl acetate in hexanes, stain in CAM) to afford the product as colorless oil (27.6 mg, 56% yield). **^{1}H NMR** (500 MHz, $CDCl_3$) δ 7.50 (d, *J* = 7.7, 1.5 Hz, 1H), 7.23 (t, *J* = 7.4, 7.4 Hz, 1H), 7.17-7.11 (m, 2H), 5.10 (dt, *J* = 9.3, 2.9, 2.9 Hz, 1H), 2.34 (s, 3H), 1.68 (dd, *J* = 14.9, 9.1 Hz, 1H), 1.58 (dt, *J* = 3.5, 1.2 Hz, 1H), 1.51 (dd, *J* = 14.8, 1.4 Hz, 1H), 1.04 (s, 9H). **^{13}C NMR** (151 MHz, $CDCl_3$) δ 144.8, 133.8, 130.5, 127.1, 126.5, 125.3, 68.8, 52.1, 30.9, 30.4, 19.3. **IR** (neat) ν_{max} 2953.0 (m), 2922.3 (s), 2850.9 (w), 1462.4 (w), 1363.0 (w), 1337.35 (w), 1079.7 (w), 1026.27 (w), 425.5 (w). **HRMS** (DART) for $C_{13}H_{19}$ $(M+H-H_2O)^+$: Calc'd: 175.1481, found: 175.1473. **$[\alpha]_D^{20}$** = 17.00 (*c* 0.20, $CHCl_3$, *l* = 50 mm).

Determination of Stereochemical Identity: Racemic compound was prepared according to the **general procedure A** with racemic **4.4** as ligand. Absolute stereochemistry was assigned analogy (see product **4.223** and **4.253**).

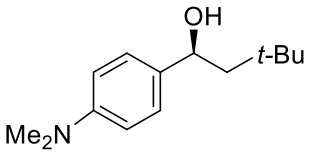
SFC (Chiracel ODR-H, 1% IPA, 3 mL/min, 100 bar, 35 °C, 210-289 nm)-analysis of **(*S*)-1-(4-Methoxyphenyl)-3,3-dimethylbutan-1-ol.**

Racemic Material Enantioenriched Material



Peak No	% Area	Area	RT (min)
1	49.0177	3844.1176	7.46
2	50.9823	3998.1798	10.36
Total:	100	7842.2974	

Peak No	% Area	Area	RT (min)
1	7.8683	1021.3956	7.5
2	92.1317	11959.7606	10.25
Total:	100	12981.1562	



(*S*)-1-(4-(Dimethylamino)phenyl)-3,3-dimethylbutan-1-ol

(4.233) The reaction was performed according to the general **procedure A** with vinylboronic acid pinacol ester (30.8 mg, 0.20 mmol, 1.0 equiv), *tert*-butyl iodide (73.6 mg, 0.40 mmol, 2.0 equiv), and (4-(dimethylamino)phenyl) zinc chloride (1.11 mL, 0.36 M, 0.4 mmol, 2.0 equiv), in a mixture of THF/DMA (2.00 mL THF and 0.40 mL DMA overall) using $NiBr_2$•glyme (6.17 mg, 0.020 mmol, 0.10 equiv) and (*S*,*S*)-**4.4** (6.25 mg, 0.026 mmol, 0.13 equiv) as catalyst. The unpurified mixture was purified by silica gel chromatography (20% ethyl acetate in hexanes, stain in CAM) to afford the product as colorless oil (20.4 mg, 46% yield). **^{1}H NMR** (500 MHz, $CDCl_3$) δ 7.23 (d, 2H), 6.72 (d,

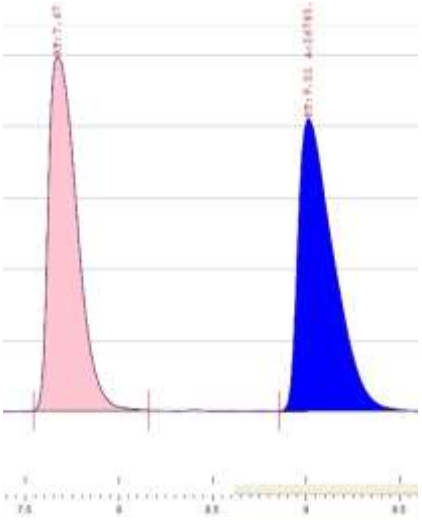
2H), 4.74 (dd, J = 8.3, 4.1 Hz, 1H), 2.95 (s, 6H), 1.82-1.74 (m, 1H), 1.63-1.54 (m, 2H), 0.97 (s, 9H). **^{13}C NMR** (151 MHz, $CDCl_3$) δ 150.3, 134.6, 127.0, 112.8, 72.4, 52.5, 40.8, 30.5, 30.4. **IR** (neat) ν_{max} 3256.4 (br), 2947.6 (m), 2915.3 (w), 2882.2 (w), 2027.4 (w), 1614.0 (m), 1521.8 (m), 1468.3 (w), 1360.7 (w), 1348.2 (w), 1224.4 (w), 1059.5 (w), 1018.6 (w), 988.7 (w), 819.1 (w). **HRMS** (DART) for $C_{14}H_{22}N$ $(M+H-H_2O)^+$: Calc'd: 204.1747, found: 204.1743. **$[\alpha]_D^{20}$** = 28.98 (*c* 0.35, $CHCl_3$, *l* = 50 mm).

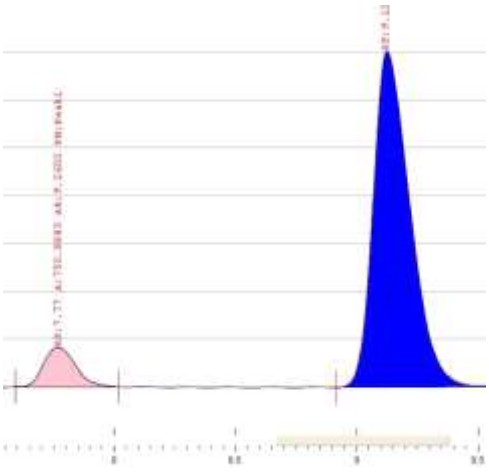
Determination of Stereochemical Identity: Racemic compound was prepared according to the **general procedure A** with racemic **4.4** as ligand. Absolute stereochemistry was assigned analogy (see product **4.223** and **4.253**).

SFC (Chiracel OJ-H, 5% IPA, 3 mL/min, 100 bar, 35 °C, 210-289 nm)-analysis of **(*S*)-1-(4-(Dimethylamino)phenyl)-3,3-dimethylbutan-1-ol.**

Racemic Material

Enantioenriched Material





Peak No	% Area	Area	RT (min)
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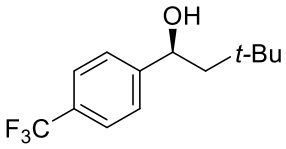
2	50.6972	26745.8883	9.01
Total:	100	52756.1957	

Peak No	% Area	Area	RT (min)
1	9.2602	750.8843	7.77
2	90.7398	7357.8656	9.12
Total:	100	8108.7499	



(*S*)-3,3-Dimethyl-1-(4-(trifluoromethyl)phenyl)butan-1-ol (4.235). The reaction was performed according to the general **procedure A** with vinylboronic acid pinacol ester (30.8 mg, 0.20 mmol, 1.0 equiv), *tert*-butyl iodide (73.6 mg, 0.40 mmol, 2.0 equiv), and 4-(trifluoromethyl)phenylzinc chloride (0.52 mL, 0.77 M, 0.4 mmol, 2.0 equiv), in a mixture of THF/DMA (2.00 mL THF and 0.40 mL DMA overall) using $NiBr_2$•glyme (6.17 mg, 0.020 mmol, 0.10 equiv) and (*S*,*S*)-**4.4** (6.25 mg, 0.026 mmol, 0.13 equiv) as catalyst. The unpurified mixture was purified by silica gel chromatography (10% ethyl acetate in hexanes, stain in CAM) to afford the product as colorless oil (27.6 mg, 56% yield). **^{1}H NMR** (500 MHz, $CDCl_3$) δ 7.60 (d, J = 8.0 Hz, 2H), 7.46 (d, J = 8.0 Hz, 2H), 4.91 (d, J = 8.0 Hz, 1H), 1.77– 1.71 (m, 2H), 1.56 (dd, J = 14.7, 3.1 Hz, 1H), 1.02

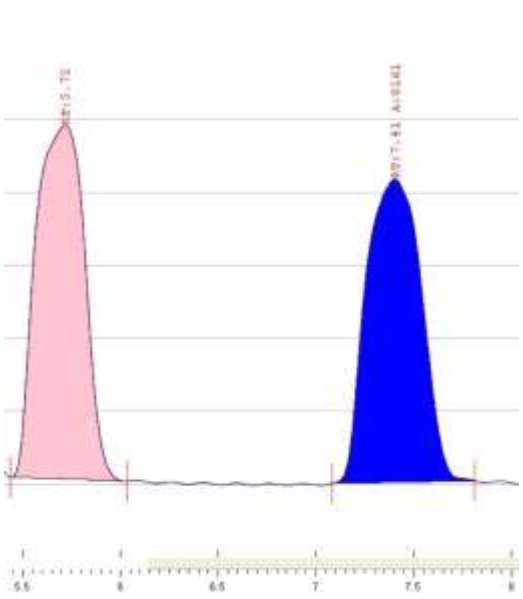
(s, 9H). **^{13}C NMR** (151 MHz, $CDCl_3$) δ 150.5, 126.1, 125.6, 125.6, 125.6, 125.6, 72.1, 53.3, 30.8, 30.3. **IR** (neat) ν_{max} 3396.7 (br), 2952.3 (m), 2866.9 (w), 1324.8 (s), 1164.2 (m), 1126.6 (m), 1067.7 (m), 1016.6 (w), 843.7 (w). **HRMS** (DART) for $C_{13}H_{16}F_3$ $(M+H-H_2O)^+$: Calc'd: 229.1199, found: 229.1204. **$[\alpha]_D^{20}$** = 28.66 (*c* 0.30, $CHCl_3$, *l* = 50 mm).

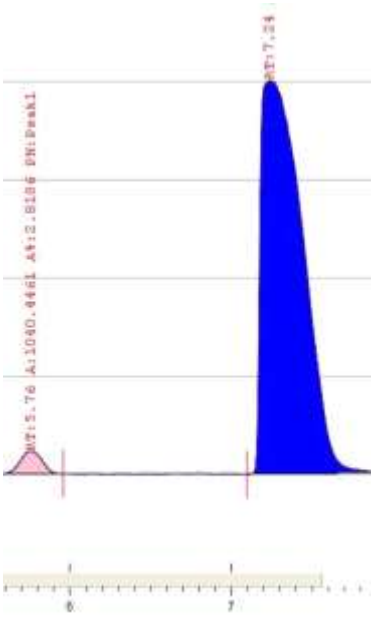
Determination of Stereochemical Identity: Racemic compound was prepared according to the **general procedure A** with racemic **4.4** as ligand. Absolute stereochemistry was assigned analogy (see product **4.223** and **4.253**).

SFC (Chiracel OJ-H, 1% IPA, 3 mL/min, 100 bar, 35 °C, 210-289 nm)-analysis of **(*S*)-3,3-Dimethyl-1-(4-(trifluoromethyl)phenyl)butan-1-ol**

Racemic Material

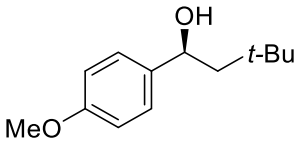
Enantioenriched Material





Peak No	% Area	Area	RT (min)
1	50.6036	8360.4958	5.72
2	49.3964	8161.0401	7.41
Total:	100	16521.5359	

Peak No	% Area	Area	RT (min)
1	2.8186	1040.4461	5.76
2	97.1814	35873.3607	7.24
Total:	100	36913.8068	



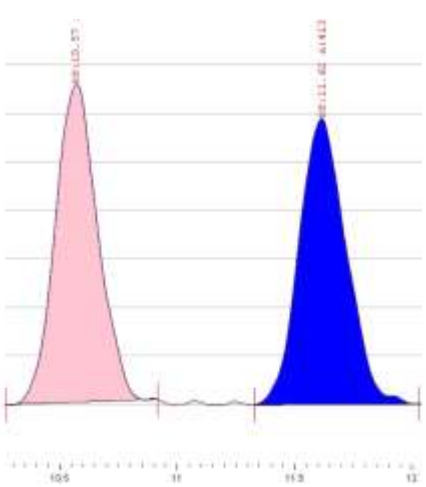
(*S*)-1-(4-Methoxyphenyl)-3,3-dimethylbutan-1-ol (4.234). The reaction was performed according to the general **procedure A** with vinylboronic acid pinacol ester (30.8 mg, 0.20 mmol, 1.0 equiv), *tert*-butyl iodide (73.6 mg, 0.40 mmol, 2.0 equiv), and (4-methoxyphenyl)zinc chloride (0.23 mL, 1.74 M, 0.4 mmol, 2.0 equiv), in a mixture of THF/DMA (2.00 mL THF and 0.40 mL DMA overall) using $NiBr_2$•glyme (6.17 mg, 0.020 mmol, 0.10 equiv) and (*S*,*S*)-**4.4** (6.25 mg, 0.026 mmol, 0.13 equiv) as catalyst. The unpurified mixture was purified by silica gel chromatography (10% ethyl acetate in hexanes, stain in CAM) to afford the product as colorless oil (26.2 mg, 63% yield). **^{1}H NMR** (500 MHz, $CDCl_3$) δ 7.28-7.26 (m, 2H), 6.90-6.83 (d, *J* = 8.6 Hz, 2H), 4.79 (dt, *J* =

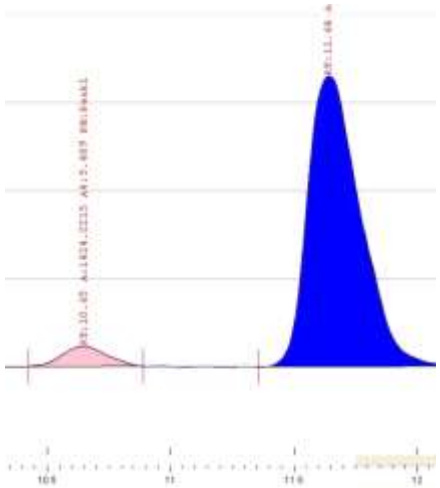
7.9, 3.8 Hz, 1H), 3.80 (s, 3H), 1.77 (dd, J = 14.3, 8.1 Hz, 1H), 1.60 (dd, 2H), 0.97 (s, 9H). **^{13}C NMR** (151 MHz, $CDCl_3$) δ 159.1, 138.8, 127.2, 114.0, 72.2, 55.4, 52.9, 30.6, 30.3. **IR** (neat) ν_{max} 3408.8 (br), 2948.4 (m), 2864.8 (w), 2833.9 (w), 1610.5 (w), 1510.3 (s), 1244.4 (s), 1173 (m), 1035.3 (m), 830.6 (m), 587.3 (w). **HRMS** (DART) for $C_{13}H_{19}O$ $(M+H-H_2O)^+$: Calc'd: 191.1430, found: 191.1420. **$[\alpha]_D^{20}$** = 39.72 (*c* 0.59, $CHCl_3$, *l* = 50 mm).

Determination of Stereochemical Identity: Racemic compound was prepared according to the **general procedure A** with racemic **4.4** as ligand. Absolute stereochemistry was assigned analogy (see product **4.223** and **4.253**).

SFC (Chiracel OJ-H, 2% IPA, 3 mL/min, 100 bar, 35 °C, 210-289 nm)-analysis of **(S)-1-(4-Methoxyphenyl)-3,3-dimethylbutan-1-ol .**

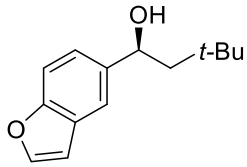
Racemic Material Enantioenriched Material





Peak No	% Area	Area	RT (min)
1	49.9828	4128.837	10.57
2	50.0172	4131.6767	11.62
Total:	100	8260.5137	

Peak No	% Area	Area	RT (min)
1	5.489	1424.2215	10.65
2	94.511	24522.3855	11.64
Total:	100	25946.607	



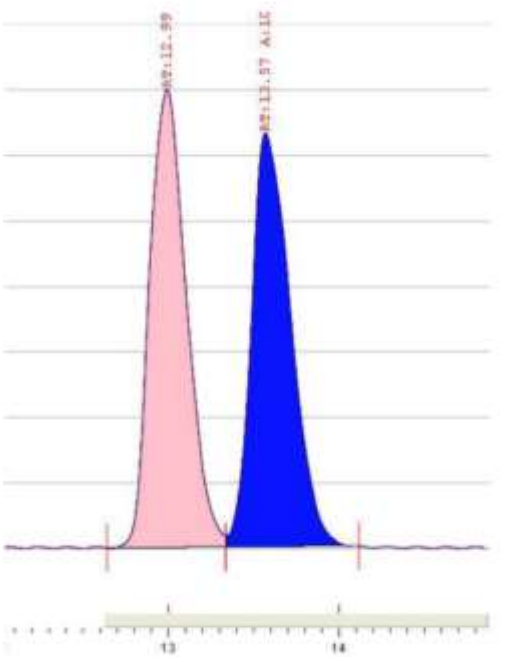
(*S*)-1-(Benzofuran-5-yl)-3,3-dimethylbutan-1-ol (4.230). The reaction was performed according to general **procedure A** with vinylboronic acid pinacol ester (30.8 mg, 0.20 mmol, 1.0 equiv), *tert*-butyl iodide (73.6 mg, 0.40 mmol, 2.0 equiv), and (3- benzofuran-5-ylzinc chloride solution in THF (1.0 mL, 0.4 M, 0.4 mmol, 2.0 equiv), in a mixture of THF/DMA (2.00 mL THF and 0.40 mL DMA overall) using $NiBr_2$•glyme (6.17 mg, 0.020 mmol, 0.10 equiv) and (*S*,*S*)-**4.4** (6.25 mg, 0.026 mmol, 0.13 equiv) as catalyst. The unpurified mixture was purified by silica gel chromatography (10% ethyl acetate in hexanes, UV active) to afford the product as colorless oil (23.1 mg, 52% yield).**^{1}H NMR** (600 MHz, $CDCl_3$) δ 7.62 (d, *J* = 2.1 Hz, 1H), 7.59 (s, 1H), 7.47 (d, *J* = 8.5 Hz, 1H), 7.29 (dd, *J* = 8.5, 1.5 Hz, 1H), 6.75 (d, *J* = 2.2 Hz, 1H), 4.93 (dd, *J* = 8.9, 3.3 Hz, 1H), 1.82 (dd, *J* = 14.5, 8.3 Hz, 1H), 1.74 (s, 1H), 1.66 (dd, *J* = 14.5, 3.7 Hz, 1H), 1.00

(s, 9H). **^{13}C NMR** (151 MHz, $CDCl_3$) δ 154.5, 145.6, 141.4, 127.6, 122.54, 118.5, 111.5, 106.8, 72.8, 53.4, 30.7, 30.4. **IR** (neat) ν_{max} 3377.6 (br), 2948.9 (s), 2864.0 (m), 1466.2 (m), 1362.9 (m), 1158.8 (m), 1106.2 (m), 767.5 (m), 747.2 (m), 734.3 (m), 699.5 (m). **HRMS** (DART) for $C_{14}H_{17}O$ $(M+H-H_2O)^+$: Calc'd: 201.1274, found: 201.1268. **$[\alpha]_D^{20}$** = -47.687 (*c* 1.0, $CHCl_3$, *l* = 50 mm).

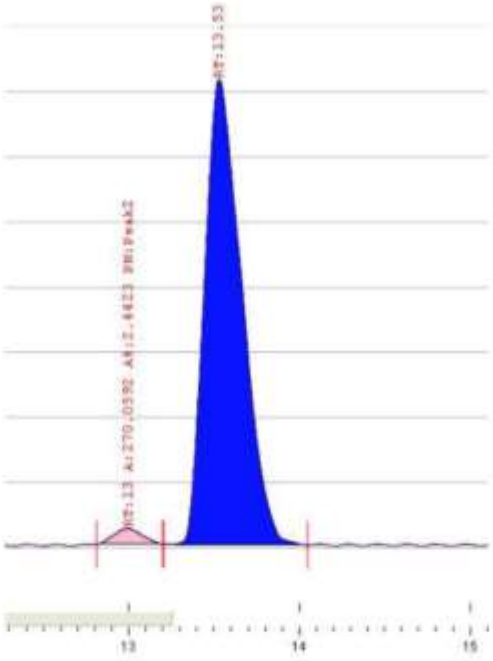
Determination of Stereochemical Identity: Racemic compound was prepared according to the **general procedure A** with racemic **4.4** as ligand. Absolute stereochemistry was assigned analogy (see product **4.223** and **4.253**).

SFC (Chiracel OJ-H, 2% IPA, 3 mL/min, 100 bar, 35 °C, 210-289 nm)-analysis of **(S)-1-(Benzofuran-5-yl)-3,3-dimethylbutan-1-ol**.

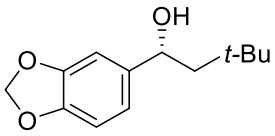
Racemic Material Enantioenriched Material



Peak No	% Area	Area	RT (min)
1	50.839	10492.7555	12.99
2	49.161	10146.4396	13.57
Total:	100	20639.1951	



Peak No	% Area	Area	RT (min)
1	2.4423	270.0592	13
2	97.5577	10787.3117	13.53
Total:	100	11057.3709	



(*S*)-1-(Benzo[d][1,3]dioxol-5-yl)-3,3-dimethylbutan-1-ol (4.232).

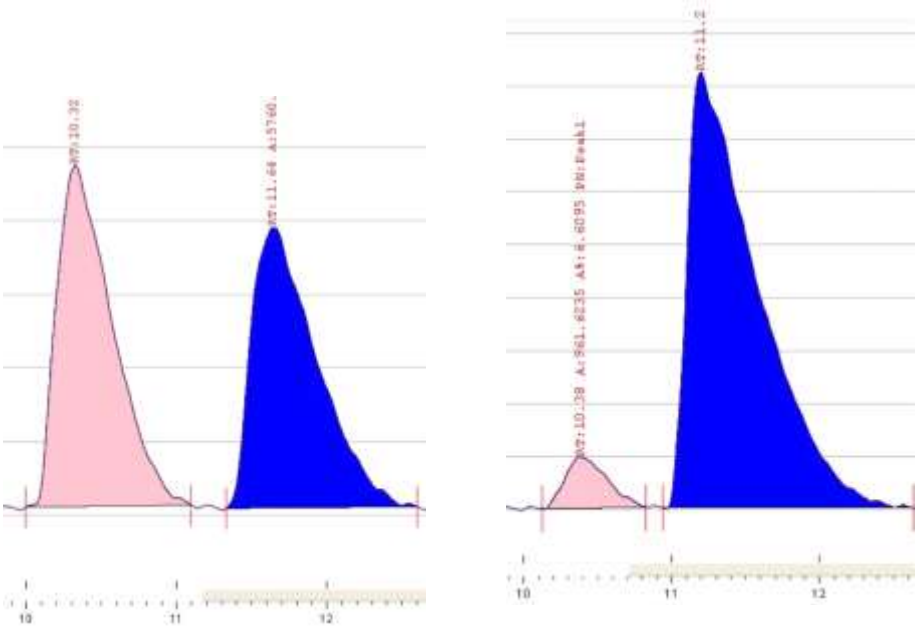
The reaction was performed according to the general **procedure A** with vinylboronic acid pinacol ester (30.8 mg, 0.20 mmol, 1.0 equiv), *tert*-butyl iodide (73.6 mg, 0.40 mmol, 2.0 equiv), and (benzo[d][1,3]dioxol-5-yl) zinc bromide•LiCl (1.11 mL, 0.36 M, 0.4 mmol, 2.0 equiv), in a mixture of THF/DMA (2.00 mL THF and 0.40 mL DMA overall) using $NiBr_2$•glyme (6.17 mg, 0.020 mmol, 0.10 equiv) and (*R*,*R*)-**4.4** (6.25 mg, 0.026 mmol, 0.13 equiv) as catalyst. The unpurified mixture was purified by silica gel chromatography (10% ethyl acetate in hexanes, stain in CAM) to afford the product as colorless oil (29.3 mg, 66%

yield). **^{1}H NMR** (500 MHz, $CDCl_3$) δ 6.93-6.86 (s, 1H), 6.80-6.74(m, 2H), 5.94 (s, 2H), 4.74 (dd, *J* = 8.2, 3.9 Hz, 1H), 1.74 (dd, *J* = 14.4, 8.2 Hz, 1H), 1.64 (s, 1H), 1.57 (dd, *J* = 14.4, 3.9 Hz, 1H), 0.97 (s, 9H). **^{13}C NMR** (151 MHz, $CDCl_3$) δ 147.9, 146.9, 140.8, 119.2, 108.2, 106.5, 101.1, 72.5, 53.0, 30.6, 30.5, 30.3. **IR** (neat) ν_{max} 3378.6 (br), 2948.8 (s), 2901.2 (m), 1502.1 (m), 1485.9 (s), 1440.4 (m), 1363.4 (w), 1243.2 (s), 1039.5 (s), 934.0 (w), 810.7 (w). **HRMS** (DART) for $C_{13}H_{17}O_2$ $(M+H-H_2O)^+$: Calc'd: 205.1223, found: 205.1219. **$[\alpha]_D^{20}$** = 31.17 (*c* 0.34, $CHCl_3$, *l* = 50 mm).

Determination of Stereochemical Identity: Racemic compound was prepared according to the **general procedure A** with racemic **4.4** as ligand. Absolute stereochemistry was assigned analogy (see product **4.223** and **4.253**).

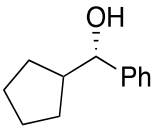
SFC (Chiracel AS-H, 1% IPA, 3 mL/min, 100 bar, 35 °C, 210-289 nm)-analysis of **(*S*)-1-(Benzo[d][1,3]dioxol-5-yl)-3,3-dimethylbutan-1-ol.**

Racemic Material Enantioenriched Material



Peak No	% Area	Area	RT (min)
1	50.8722	5964.8104	10.32
2	49.1278	5760.2832	11.64
Total:	100	11725.0936	

Peak No	% Area	Area	RT (min)
1	6.6095	961.6235	10.38
2	93.3905	13587.4501	11.2
Total:	100	14549.0736	



(*S*)-Cyclopentyl(phenyl)methanol (4.253). The reaction was performed according to general **procedure A** with (*E*)-2-(6-iodohex-1-en-1-yl)-4,4,5,5-tetramethyl-1,3,2-dioxaborolane (67.2 mg, 0.20 mmol, 1.0 equiv), and phenylzinc chloride solution in THF (1.00 mL, 0.4 M, 0.4 mmol, 2.0 equiv), in a mixture of THF/DMA (2.00 mL THF and 0.40 mL DMA overall) using $NiBr_2$•glyme (6.17 mg, 0.020 mmol, 0.10 equiv) and (*S*,*S*)-**4.4** (6.25 mg, 0.026 mmol, 0.13 equiv) as catalyst. The unpurified mixture was purified by silica gel chromatography (10% ethyl acetate in hexanes, stain in CAM) to afford the product as colorless oil (24.6 mg, 70% yield). **HRMS** (DART) for C12H15 $(M+H-H_2O)^+$: Calc'd: 159.1166, found: 151.1168. $[\alpha]_D^{20}$ = -51.03 (*c* = 1.0, $CHCl_3$, *l* = 50

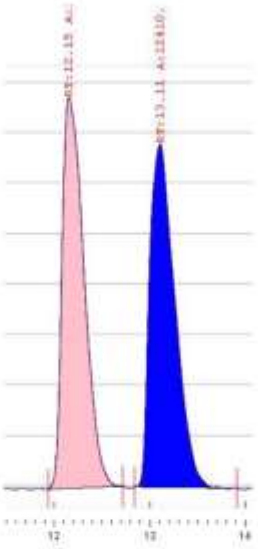
mm (lit:$[\alpha]_D^{20}$ = - 40.08 (*c* 0.8, $CHCl_3$, 78% *ee*, (*S*)-enantiomer)). All spectral data was in accord with the literature.[89]

Determination of Stereochemical Identity: Racemic compound was prepared according to the **general procedure A** with racemic **4.4** as ligand. Absolute stereochemistry was assigned by comparison with the optical rotation reported in the literature for the same compound.[89] The stereochemical assignment was found to be in accord with product **4.223** (determined through X-ray crystallography).

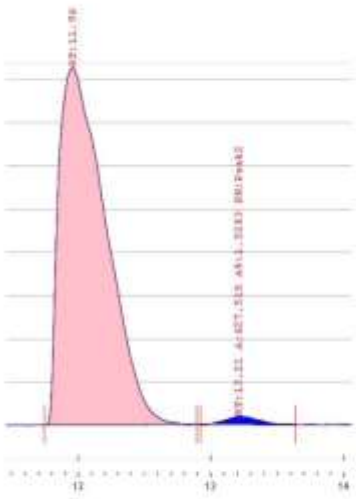
SFC (Chiracel OJ-H, 2% IPA, 3 mL/min, 100 bar, 35 °C, 210-289 nm)-analysis of **(*S*)-Cyclopentyl(phenyl)methanol.**

Racemic Material Enantioenriched Material

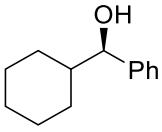
[89] Morris, D. J.; Hayes, A. M.; Wills, M. *J. Org. Chem*. **2006**, 7035.



Peak Info			
Peak No	% Area	Area	RT (min)
1	49.8135	12317.9168	12.15
2	50.1865	12410.1565	13.11
Total:	100	24728.0733	



Peak Info			
Peak No	% Area	Area	RT (min)
1	98.4757	40539.7235	11.96
2	1.5243	627.515	13.21
Total:	100	41167.2385	



(*R*)-Cyclohexyl(phenyl)methanol (4.254). The reaction was performed according to general **procedure A** with (*E*)-2-(7-iodohept-1-en-1-yl)-4,4,5,5-tetramethyl-1,3,2-dioxaborolane (70.0 mg, 0.20 mmol, 1.0 equiv), and phenylzinc chloride solution in THF (1.00 mL, 0.4 M, 0.4 mmol, 2.0 equiv), in a mixture of THF/DMA (2.00 mL THF and 0.40 mL DMA overall) using $NiBr_2$•glyme (6.17 mg, 0.020 mmol, 0.10 equiv) and (*R*,*R*)-**4.4** (6.25 mg, 0.026 mmol, 0.13 equiv) as catalyst. The unpurified mixture was purified by silica gel chromatography (10% ethyl acetate in hexanes, stain in CAM) to afford the product as colorless oil (19.0 mg, 52% yield). **HRMS** (DART) for $C_{13}H_{17}$ $(M+H-H_2O)^+$: Calc'd: 173.1325, found: 173.1329. $[\alpha]_D^{20} = 28.27$ (*c* = 0.29, $CHCl_3$, *l* = 50 mm (lit: $[\alpha]_D^{20} = -21.4$ (*c* 1.01, $CHCl_3$, 91% *ee*, (*S*)-enantiomer)). All spectral data was in accord

with the literature.[90]

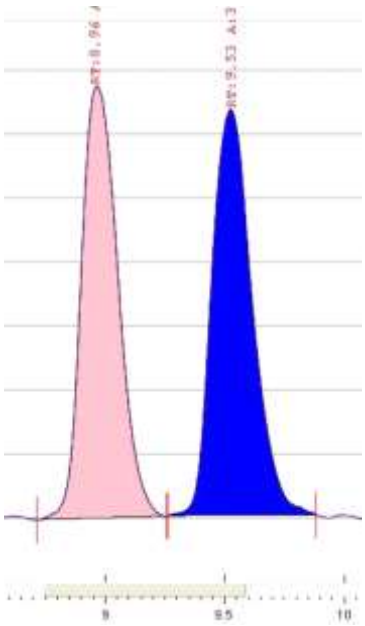
Determination of Stereochemical Identity: Racemic compound was prepared according to the **general procedure A** with racemic **4.4** as ligand. Absolute stereochemistry was assigned analogy (see product **4.223** and **4.253**) and comparison of optical rotation reported in the literature for the same compound.[90]

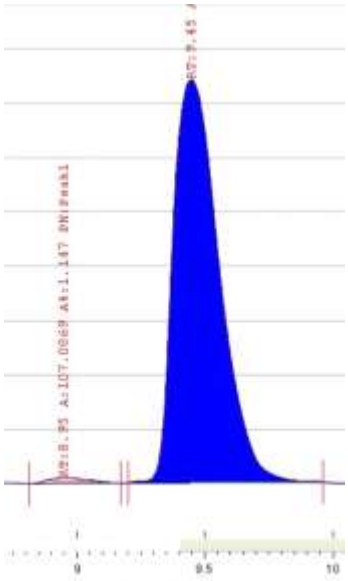
SFC (Chiracel OJ-H, 3% IPA, 3 mL/min, 100 bar, 35 °C, 210-289 nm)-analysis of **(*S*)-Cyclohexyl(phenyl)methanol.**

Racemic Material

Enantioenriched Material

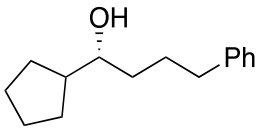
[90] Arenas, I.; Boutureira, O.; Matheu, M. I.; Díaz Y.; Castillón, S. *Eur. J. Org. Chem*. **2015**, 3666.





Peak No	% Area	Area	RT (min)
1	49.1136	3580.9512	8.96
2	50.8864	3710.2034	9.53
Total:	100	7291.1546	

Peak No	% Area	Area	RT (min)
1	1.147	107.0869	8.95
2	98.853	9229.2502	9.45
Total:	100	9336.3371	



(*R*)-1-Cyclopentyl-4-phenylbutan-1-ol (4.255). The reaction was performed according to general **procedure B** with (*E*)-2-(6-iodohex-1-en-1-yl)-4,4,5,5-tetramethyl-1,3,2-dioxaborolane (67.2 mg, 0.20 mmol, 1.0 equiv), and (3-phenylpropyl)zinc bromide solution in DMA (0.24 mL, 1.68 M, 0.4 mmol, 2.0 equiv), with (2.00 mL THF and 0.40 mL DMA overall) using $NiBr_2$•glyme (6.17 mg, 0.020 mmol, 0.10 equiv) and (*S*,*S*)-**4.4** (6.25 mg, 0.026 mmol, 0.13 equiv) in DMA (2.40 mL). The unpurified mixture was purified by silica gel chromatography (10% ethyl acetate in hexanes, stain in CAM) to afford the product as colorless oil (25.3 mg, 58% yield). **^{1}H NMR** (500 MHz, $CDCl_3$) δ 7.29-7.26 m, 2H), 7.20-7.18(m, 3H), 3.43 (td, J = 8.0, 3.2 Hz, 1H), 2.72-2.53 (m,

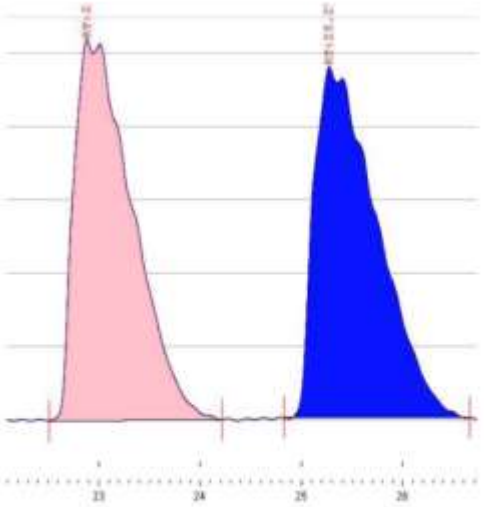
2H), 1.89-1.50 (m, 10H), 1.46-1.28 (m, 2H), 1.29 -1.15 (m, 1H).**^{13}C NMR** (151 MHz, $CDCl_3$) δ 142.6, 128.5, 128.4, 125.8, 75.9, 46.5, 36.1, 35.9, 29.3, 28.6, 27.7, 25.8, 25.7. **IR** (neat) ν_{max} 3357.1 (br), 3082.2 (w), 3057. 3022.8 (w), 2938.7 (s), 2861.2 (s), 1494.2 (m), 1450.8 (m), 1094.4 (m), 1053.8 (m), 1028.9 (m), 920.6 (m), 800.8 (s), 746.5 (s). **HRMS** (DART) for $C_{15}H_{21}$ $(M+H-H_2O)^+$: Calc'd: 201.1634, found: 201.1638. **$[\alpha]_D^{20}$** = -5.66 (*c* 1.0, $CHCl_3$, *l* = 50 mm).

Determination of Stereochemical Identity: Racemic compound was prepared according to the **general procedure A** with racemic **4.4** as ligand. Absolute stereochemistry was assigned analogy (see product **4.223** and **4.253**).

SFC (Chiracel OJ-H, 2% IPA, 3 mL/min, 100 bar, 35 °C, 210-289 nm)-analysis of **(*R*)-1-Cyclopentyl-4-phenylbutan-1-ol.**

Racemic Material

Enantioenriched Material



Peak Info			
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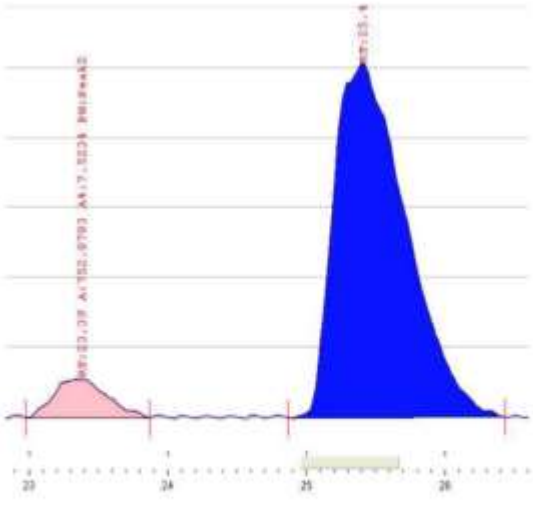

Peak Info			
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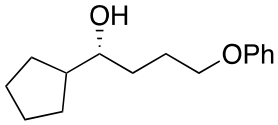


(*R*)-1-Cyclopentyl-4-phenoxybutan-1-ol (4.256). The reaction was performed according to general **procedure B** with (*E*)-2-(6-iodohex-1-en-1-yl)-4,4,5,5-tetramethyl-1,3,2-dioxaborolane (67.2 mg, 0.20 mmol, 1.0 equiv), and (3-phenoxypropyl)zinc bromide solution in DMA (0.360 mL, 1.1 M, 0.4 mmol, 2.0 equiv), with (2.00 mL THF and 0.40 mL DMA overall) using $NiBr_2$•glyme (6.17 mg, 0.020 mmol, 0.10 equiv) and (*S*,*S*)-**4.4** (6.25 mg, 0.026 mmol, 0.13 equiv) in DMA (2.40 mL). The unpurified mixture was purified by silica gel chromatography (15% ethyl acetate in hexanes, stain in CAM) to afford the product as colorless oil (30.1 mg, 64% yield). **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.39-7.18 (m, 2H), 7.05-6.76 (m, 3H), 4.00 (ddd, *J* = 5.8, 3.0 Hz, 2H), 3.59-3.35 (m, 1H), 2.14-1.43 (m, 12H), 1.43-1.30 (m, 1H), 1.27-1.17 (m, 1H).**^{13}C**

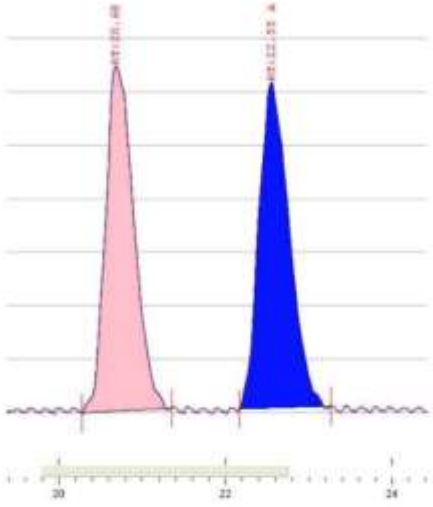
NMR (126 MHz, $CDCl_3$) δ 159.1, 129.6, 120.8, 114.7, 75.8, 68.1, 46.7, 33.0, 29.3, 28.8, 25.9, 25.8 (one diastereotopic carbon peak not observed). **IR** (neat) ν_{max} 3408.7 (Br), 2946.9 (m), 2865.0 (m), 1598.1 (w), 1495.6 (m), 1299.5 (w), 1244.0 (s), 1040.7 (w), 1012.4 (w), 752.3 (m), 690.7 (m). **HRMS** (DART) for $C_{15}H_{23}O_2$ $(M+H)^+$: Calc'd: 235.1694, found: 235.1704. $\mathbf{[\alpha]_D^{20}}$ = 4.159 (*c* 1.0, $CHCl_3$, *l* = 50 mm).

Determination of Stereochemical Identity: Racemic compound was prepared according to the **general procedure A** with racemic **4.4** as ligand. Absolute stereochemistry was assigned analogy (see product **4.223** and **4.253**).

SFC (Chiracel OJ-H, 4% IPA, 3 mL/min, 100 bar, 35 °C, 210-289 nm)-analysis of **(*R*)-1-Cyclopentyl-4-phenoxybutan-1-ol.**

Racemic Material

Enantioenriched Material



Peak No	% Area	Area	RT (min)
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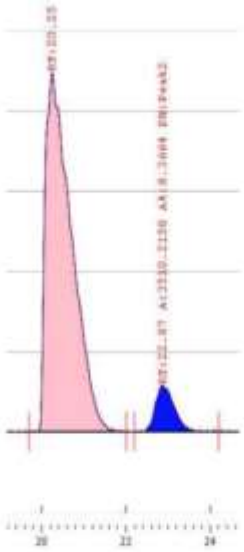

Peak No	% Area	Area	RT (min)
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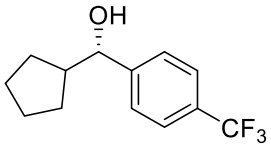
2	8.3664	3510.2158	22.87
Total:	100	41955.9008	



(*S*)-Cyclopentyl(4-(trifluoromethyl)phenyl)methanol (4.257). The reaction was performed according to general **procedure A** with (*E*)-2-(6-iodohex-1-en-1-yl)-4,4,5,5-tetramethyl-1,3,2-dioxaborolane (67.2 mg, 0.20 mmol, 1.0 equiv), and 4-(trifluoromethyl)phenyl zinc chloride solution in THF (0.52 mL, 0.77 M, 0.4 mmol, 2.0 equiv), in a mixture of THF/DMA (2.00 mL THF and 0.40 mL DMA overall) using $NiBr_2$•glyme (6.17 mg, 0.020 mmol, 0.10 equiv) and (*S*,*S*)-**4.4** (6.25 mg, 0.026 mmol, 0.13 equiv) as catalyst. The unpurified mixture was purified by silica gel chromatography (10% ethyl acetate in hexanes, stain in CAM) to afford the product as colorless oil (27.0 mg, 55% yield). **^{1}H NMR** (500 MHz, $CDCl_3$) δ 7.59 (d, *J* = 7.9 Hz, 2H), 7.46 (d, *J* = 7.8 Hz, 2H), 4.50 (d, *J* = 8.2 Hz, 1H), 2.18 (h, *J* = 8.9, 8.9, 8.9, 8.3, 8.3 Hz, 1H), 1.93 (dd, *J* = 3.3, 1.2 Hz, 1H), 1.85 (h, td, *J* = 12.4, 12.2, 7.3 Hz, 1H), 1.71-1.55 (m, 3H), 1.55-1.45 (m, 2H),

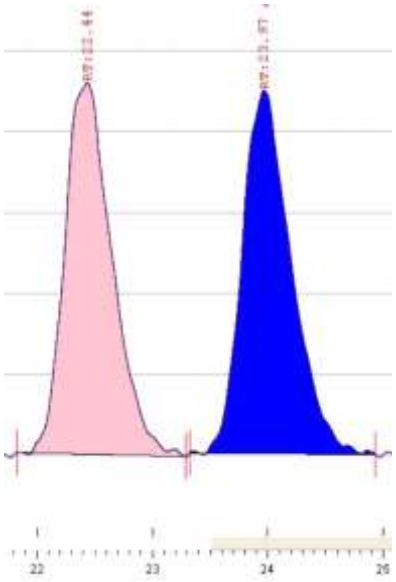
1.43-1.36 (m, 1H), 1.22-1.14 (m, 1H). **^{13}C NMR** (151 MHz, $CDCl_3$) δ 148.5, 126.9, 125.4, 125.4, 125.4, 125.4, 78.4, 47.9, 29.5, 29.2, 25.6, 25.5. **IR** (neat) ν_{max} 3374.5 (br), 2953.1 (w), 2867.0 (w), 1618.6 (w), 1417.4 (w), 1323.9 (s), 1162.2 (m), 1123.4 (s), 1065.9 (s), 1016.1 (w), 836.9 (w), 758.6 (w). **HRMS** (DART) for $C_{13}H_{14}F_3$ $(M+H-H_2O)^+$: Calc'd: 227.1042, found: 227.1048. **$[\alpha]_D^{20}$** = -29.83 (*c* 1.00, $CHCl_3$, *l* = 50 mm).

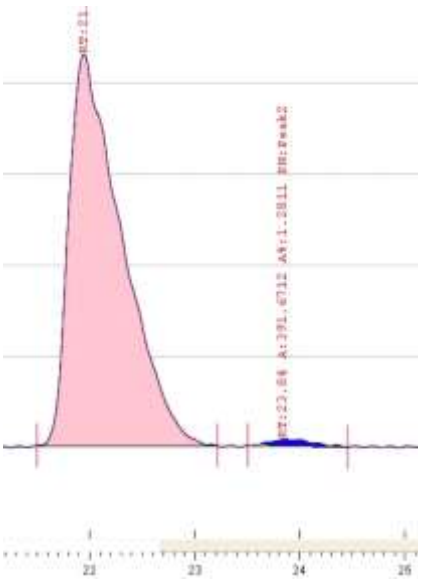
Determination of Stereochemical Identity: Racemic compound was prepared according to the **general procedure A** with racemic **4.4** as ligand. Absolute stereochemistry was assigned analogy (see product **4.223** and **4.253**).

SFC (Chiracel AD-H, 1% IPA, 3 mL/min, 100 bar, 35 °C, 210-289 nm)-analysis of **(*S*)-Cyclopentyl(4-(trifluoromethyl)phenyl)methanol.**

Racemic Material

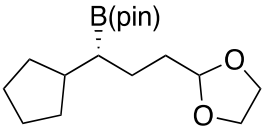
Enantioenriched Material





Peak No	% Area	Area	RT (min)
1	49.6834	6573.1351	22.44
2	50.3166	6656.9053	23.97
Total:	100	13230.0404	

Peak No	% Area	Area	RT (min)
1	98.7189	30182.1448	21.94
2	1.2811	391.6712	23.84
Total:	100	30573.816	



(*R*)-2-(1-Cyclopentyl-3-(1,3-dioxolan-2-yl)propyl)-4,4,5,5-tetramethyl-1,3,2-dioxaborolane (4.258). The reaction was performed according to general **procedure B** with (*E*)-2-(6-iodohex-1-en-1-yl)-4,4,5,5-tetramethyl-1,3,2-dioxaborolane (67.2 mg, 0.20 mmol, 1.0 equiv), and (2-(1,3-dioxolan-2-yl)ethyl)zinc bromide solution in DMA (0.330 mL, 1.23 M, 0.4 mmol, 2.0 equiv), with (2.00 mL THF and 0.40 mL DMA overall) using $NiBr_2$•glyme (6.17 mg, 0.020 mmol, 0.10 equiv) and (*S*,*S*)-**4.4** (6.25 mg, 0.026 mmol, 0.13 equiv) in DMA (2.40 mL). ***Note:*** product was isolated and characterized as the boronic ester prior to oxidation since the corresponding alcohol was prone to decomposition. The unpurified mixture was purified by silica gel chromatography (15% ethyl acetate in hexanes, stain in CAM) to afford the product as

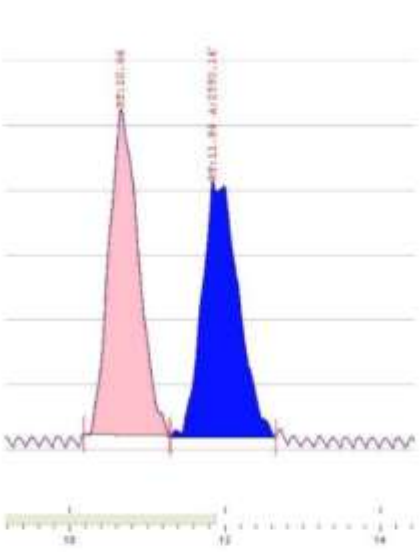
colorless oil (40.8 mg, 66% yield). **^{1}H NMR** (600 MHz, $CDCl_3$)) δ 4.83 (t, *J* = 4.8 Hz, 1H), 3.99-3.91 (m, 2H), 3.87-3.78 (m, 2H), 1.88-1.77 (m, 2H), 1.77-1.64 (m, 2H), 1.62-1.54 (m, 4H), 1.53-1.40 (m, 3H), 1.24 (s, 12H), 1.17-1.05 (m, 2H), 0.96-0.85 (m, 1H). **^{13}C NMR** (151 MHz, $CDCl_3$) δ 104.9, 83.0, 65.0, 42.0, 33.9, 32.6, 32.2, 25.4, 25.3, 25.1, 25.0. **IR** (neat) ν_{max} 2974.1 (m), 2943.9 (m), 2864.7 (m), 1455.5 (w), 1378.4 (m), 1316.5 (m), 1213.3 (w), 1143.8 (s), 1033.6 (w), 966.8 (w), 842.5 (w). **HRMS** (DART) for $C_{17}H_{32}BO_4$ $(M+H)^+$: Calc'd:311.2388, found: 311.2386. **$[\alpha]_D^{20}$** = 6.67 (*c* 1.0, $CHCl_3$, *l* = 50 mm).

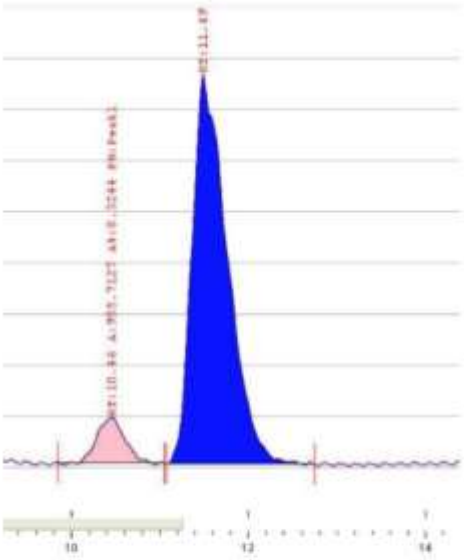
Determination of Stereochemical Identity: Racemic compound was prepared according to the **general procedure A** with racemic **4.4** as ligand. Absolute stereochemistry was assigned analogy (see product **4.223** and **4.253**). ***Note:*** the analysis of stereochemistry was performed on the corresponding TBDPS protected silyl ether. The boronic ester (both the enriched sample and the racemate) was oxidized under standard conditions and the unpurified alcohol was promptly protected with TBDPS-Cl following standard procedures.

SFC (Chiracel AD-H, 1% IPA, 3 mL/min, 100 bar, 35 °C, 210-289 nm)-analysis of **(*R*)-1-Cyclopentyl-3-(1,3-dioxolan-2-yl)propan-1-ol**.

Racemic Material

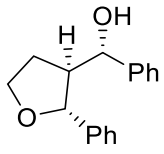
Enantioenriched Material





Peak No	% Area	Area	RT (min)
1	50.5782	2653.8255	10.66
2	49.4218	2593.1472	11.84
Total:	100	5246.9727	

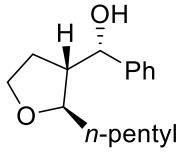
Peak No	% Area	Area	RT (min)
1	8.3244	955.7127	10.46
2	91.6756	10525.088	11.49
Total:	100	11480.8007	



(*S*)-Phenyl((*2R*,*3R*)-2-phenyltetrahydrofuran-3-yl)methanol (4.259). The reaction was performed according to the general **procedure A** with (*R,E*)-2-(3-(2-iodoethoxy)-3-phenylprop-1-en-1-yl)-4,4,5,5-tetramethyl-1,3,2-dioxaborolane (82.8 mg, 0.20 mmol, 1.0 equiv), and phenylzinc chloride solution in THF (1.00 mL, 0.4 M, 0.4 mmol, 2.0 equiv), in a mixture of THF/DMA (2.00 mL THF and 0.40 mL DMA overall) using $NiBr_2$•glyme (6.17 mg, 0.020 mmol, 0.10 equiv) and (*S*,*S*)-**4.4** (6.25 mg, 0.026 mmol, 0.13 equiv) as catalyst. The unpurified mixture was purified by silica gel chromatography (10% ethyl acetate in hexanes, stain in CAM) to afford the product as white solid (35.8 mg, 70% yield). **^{1}H NMR** (500 MHz, $CDCl_3$) δ 7.33-7.22 (m, 8H), 7.10 (d, *J* = 6.8 Hz, 2H),

4.72 (d, J = 6.6 Hz, 2H), 4.11 (q, J = 8.1, 8.1, 8.1 Hz, 1H), 4.00 (q, J = 8.0, 8.1, 8.1 Hz, 1H), 2.53-2.48 (m, 1H), 2.26 (m, 2H), 2.05-1.95 (m, 1H). **^{13}C NMR** (151 MHz, $CDCl_3$) δ 143.4, 142.6, 128.6, 128.4, 127.9, 127.4, 126.4, 126.1, 82.6, 74.0, 68.3, 55.3, 27.5. **IR** (neat) ν_{max} 3400.0 (br), 3081.8 (w), 3058.3 (w), 2921.4 (w), 2872.1 (w), 1600.9 (w), 1491.9 (m), 1452.0 (m), 1059.6 (m), 1040.6 (m), 1024.8 (m), 756.3 (m), 699.3 (s). **HRMS** (DART) for $C_{17}H_{19}O_2$ $(M+H)^+$: Calc'd: 255.1380, found: 255.1383 **$[\alpha]_D^{20}$** = 23.05 (*c* 0.85, $CHCl_3$, *l* = 50 mm).

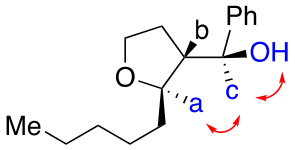
Determination of Stereochemical Identity: In order to assign the stereochemical configuration of the title compound, the substrate was first protected with TBSCl through standard methods. All spectra for the resulting TBS-ether was found to match that obtained for compound **4.302** for which the stereochemical configuration has been determined through NOESY correlation (see below).

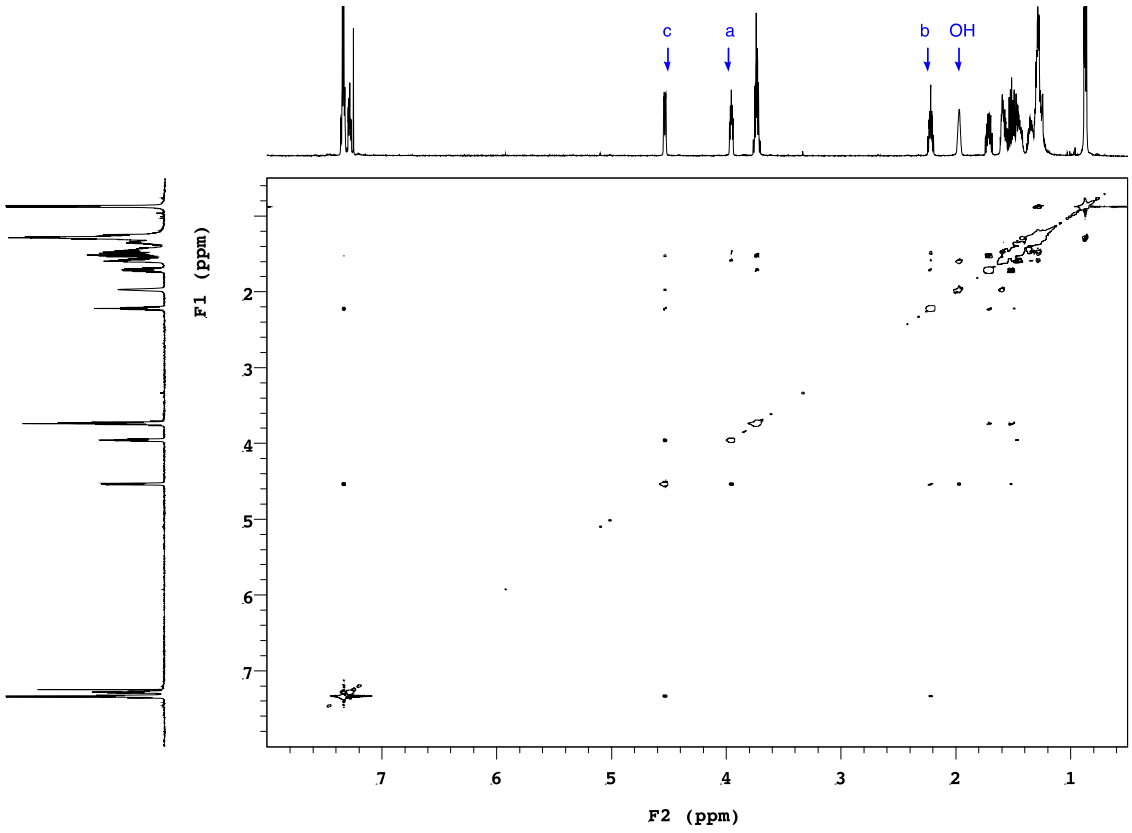


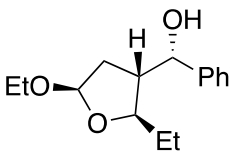
(*S*)-((*2R*,*3R*)-2-Pentyltetrahydrofuran-3-yl)(phenyl)methanol (4.260). The reaction was performed according to the general **procedure A** with (*R*,*E*)-2-(3-(2-iodoethoxy)oct-1-en-1-yl)-4,4,5,5-tetramethyl-1,3,2-dioxaborolane (81.6 mg, 0.20 mmol, 1.0 equiv), and phenylzinc chloride solution in THF (1.00 mL, 0.4 M, 0.4 mmol, 2.0 equiv), in a mixture of THF/DMA (2.00 mL THF and 0.40 mL DMA overall) using $NiBr_2$•glyme (6.17 mg, 0.020 mmol, 0.10 equiv) and (*S*,*S*)-**4.4** (6.25 mg, 0.026 mmol, 0.13 equiv) as

catalyst. The unpurified mixture was purified by silica gel chromatography (10% ethyl acetate in hexanes, stain in CAM) to afford the product as colorless oil (17.6 mg, 45% yield). **^{1}H NMR** (500 MHz, $CDCl_3$) δ 7.33-7.23 (m, 5H), 4.52 (dd, 1H), 3.96-3.92 (m, 1H), 3.74-3.70 (m, 2H), 2.23-2.17 (m, 1H), 1.94 (d, J = 3.4 Hz, 1H), 1.73-1.63 (m, 1H), 1.60-1.36 (m, 4H), 1.32-1.12 (m, 5H), 0.86 (t, J = 6.5, 6.5 Hz, 3H). **^{13}C NMR** (151 MHz, $CDCl_3$) δ 143.9, 128.7, 128.0, 126.7, 82.6, 77.5, 66.7, 51.4, 36.0, 32.1, 30.1, 26.2, 22.8, 14.2. **IR** (neat) ν_{max} 3407.6 (br), 3061.1 (w), 3027.4 (w), 2951.6 (s), 2925.5 (s), 2855.4 (s), 1452.7 (w), 1074.5 (m), 1034.4 (m), 904.6 (w), 761.9 (m), 700.8 (s). **HRMS** (DART) for $C_{16}H_{25}O_2$ $(M+H)^+$: Calc'd: 249.1849, found: 249.1848 **$[\alpha]_D^{20}$** = 31.80 (*c* 0.64, $CHCl_3$, *l* = 50 mm).

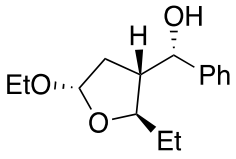
Determination of Stereochemical Identity: The stereochemistry of the carbon skeleton was assigned through NOESY correlation analysis. The absolute configuration at the B(pin)/OH containing stereocenter was assigned by analogy (see product **4.223** and **4.253**). Relevant NOESY correlations are illustrated below.







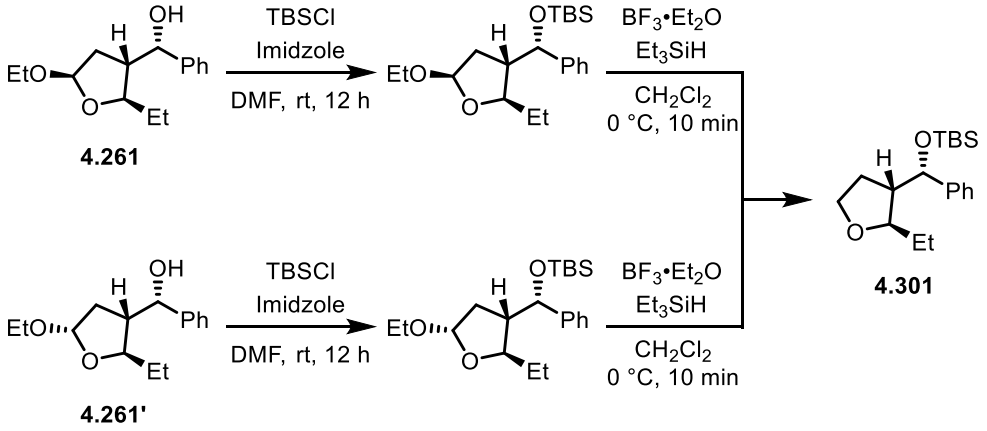
and

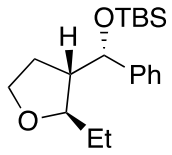


(*1S*)-((*2R*,*3R*)-5-Ethoxy-2-ethyltetrahydrofuran-3-yl)(phenyl)methanol (4.261 an 4.261'). The reaction was performed according to the general **procedure A** with 2-((3*R,E*)-3-(1-ethoxy-2-iodoethoxy)pent-1-en-1-yl)-4,4,5,5-tetramethyl-1,3,2-dioxaborolane (82.0 mg, 0.20 mmol, 1.0 equiv), and phenylzinc chloride solution in THF (1.00 mL, 0.4 M, 0.4 mmol, 2.0 equiv), in a mixture of THF/DMA (2.00 mL THF and 0.40 mL DMA overall) using $NiBr_2$•glyme (6.17 mg, 0.020 mmol, 0.10 equiv) and (*S*,*S*)-**4.4** (6.25 mg, 0.026 mmol, 0.13 equiv) as catalyst. The unpurified mixture was purified by silica gel chromatography (10% ethyl

acetate in hexanes, stain in CAM) to afford the product as colorless oil (25.0 mg, 50% yield). The product was obtained as a pair of separable diastereomers. *Diastereomer 1:* **^{1}H NMR** (500 MHz, $CDCl_3$) 7.37-7.36 (m, 2H), 7.33-7.30 (m, 2H), 7.23-7.19 (m, 1H), 5.12 (d, *J* = 4.6 Hz, 1H), 4.90 (d, *J* = 4.3 Hz, 1H), 4.12 (q, *J* = 5.1, 5.1, 4.9 Hz,1H), 4.05 (s, 1H), 3.82 (dq, *J* = 9.3, 7.2, 7.2, 7.1 Hz, 1H), 3.50 (dq, *J* = 9.2, 9.2, 6.1, 6.1 Hz, 1H), 2.28-2.25 (m, 1H), 2.20 (ddd, *J* = 13.3, 11.1, 4.9 Hz, 1H), 1.88 (dd, *J* = 13.5, 2.2 Hz, 1H), 1.26-1.21 (m, 5H), 0.66 (t, *J* = 7.4, 7.4 Hz, 3H). **^{13}C NMR** (151 MHz, $CDCl_3$) δ 143.6, 128.4, 127.3, 126.1, 102.7, 79.9, 75.4, 62.2, 49.4, 37.7, 28.9, 15.2, 9.5. **IR** (neat) ν_{max} 3423.0 (br), 3059.3 (w), 3026.7 (w), 2968.8 (m), 2920.7 (s), 2873.5 (m), 1492.0 (w), 1452.3 (m), 1202.9 (w), 1082.4 (s), 1072.3 (s), 979.0 (s), 758.2 (w), 701.0 (s). **HRMS** (DART) for $C_{15}H_{21}O_3$ (M+H)+: Calc'd: 249.1485, found: 249.1483. **$[\alpha]_D^{20}$** = 22.40 (*c* 1.00, $CHCl_3$, *l* = 50 mm). *Diastereomer 2:* **^{1}H NMR** (500 MHz, $CDCl_3$) δ 7.33-7.25 (m, 5H), 4.99 (d, *J* = 2.9 Hz, 1H), 4.51 (dd, *J* = 8.5, 3.0 Hz, 1H), 4.03 (ddd, *J* = 9.5, 6.3, 3.7 Hz, 1H), 3.72 (dq, *J* = 9.4, 7.1, 7.1, 7.0 Hz, 1H), 3.36 (dq, *J* = 9.6, 7.2, 7.1, 7.1 Hz, 1H), 2.55-2.46 (m, 1H), 1.90 (d, *J* = 3.4 Hz, 1H), 1.74-1.63 (m, 3H), 1.57 (ddd, *J* = 13.5, 8.6, 6.9 Hz, 1H), 1.14 (t, *J* = 7.1, 7.1 Hz, 3H), 0.99 (t, *J* = 7.4, 7.4 Hz, 3H). **^{13}C NMR** (151 MHz, $CDCl_3$) δ 143.6, 128.7, 128.1, 126.5, 103.2, 103.2, 85.2, 77.9, 62.4, 49.5, 37.3, 31.1, 15.3, 11.1. **IR** (neat) ν_{max} 3433.0 (br), 2968.7 (m), 2927.1 (m), 2872.2 (m), 1452.9 (m), 1372.2 (w), 1343.9 (w), 1309.5 (w), 1190.3 (w), 1092.5 (s), 1064.9 (s), 1023.0 (s), 971.8 (s), 760.1 (w), 701.4 (s), 624.9 (w). **HRMS** (DART) for $C_{15}H_{21}O_3$ $(M+H)^+$: Calc'd: 249.1485, found: 249.1490. **$[\alpha]_D^{20}$**= -108.38 (*c* 1.00, $CHCl_3$, *l* = 50 mm).

Determination of Stereochemical Identity: The transformations below were carried out on the isolated compounds **4.261** and **4.261'** separately in order to assess the stereochemistry of the isolated compounds. Upon reduction all spectral data of the two separate products was found to be identical. The stereochemical assignment was determined through NOESY correlation analysis of the resulting products. The absolute configuration at the B(pin)/silyl ether containing stereocenter was assigned by analogy (see product **4.223** and **4.253**).

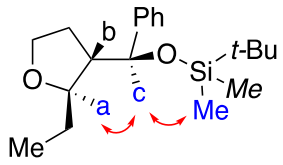


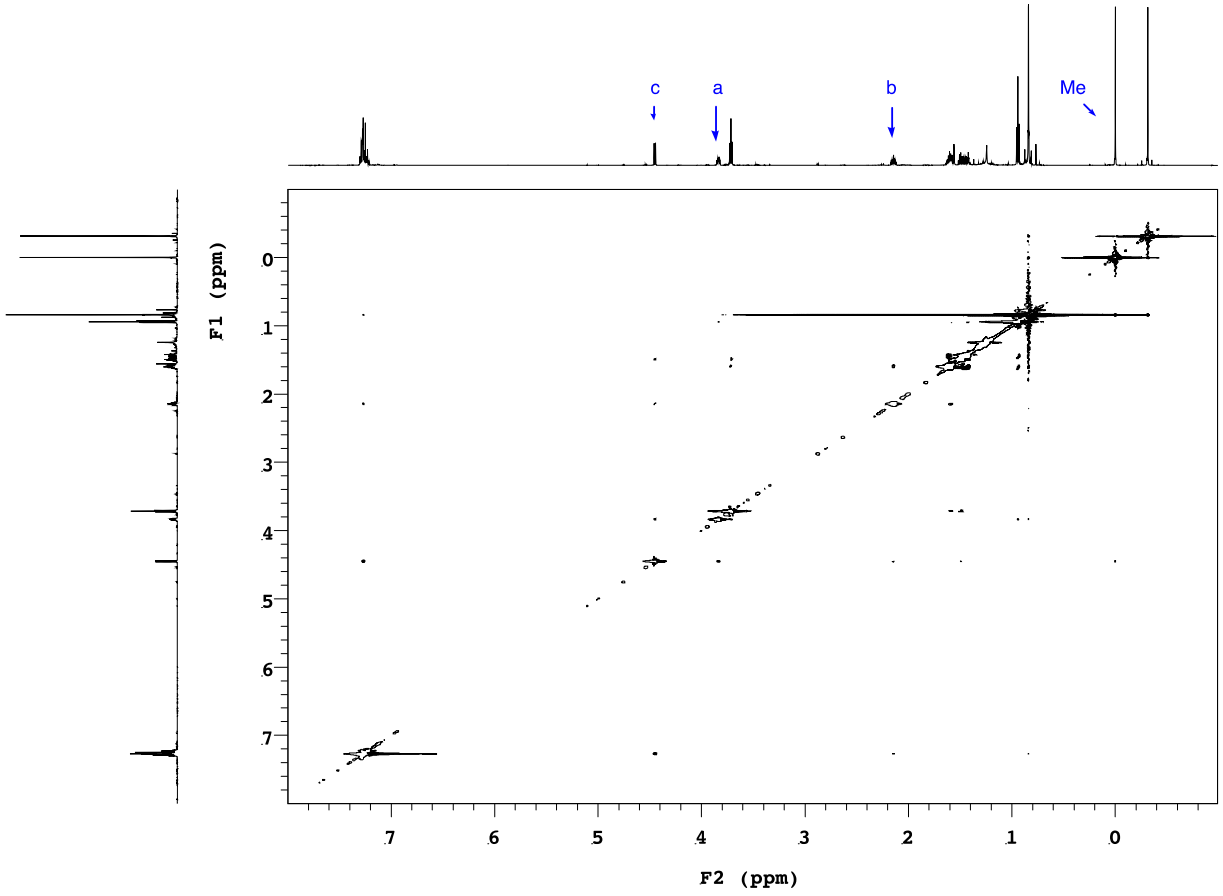


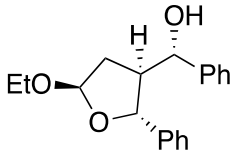
***tert*-Butyl((*S*)-((*2R,3S*)-2-ethyltetrahydrofuran-3-yl)(phenyl)methoxy)dimethylsilane (4.301)**. Compound **4.261** (12 mg, 0.048 mmol, 1.0 equiv) was dissolved in anhydrous DMF (4 mL), followed by addition of imidazole (9.8 mg, 0.14 mmol, 3.0 equiv), and TBSCl (5.9 mg, 0.072 mmol, 1.5 equiv). The resulting mixture was allowed to stir overnight at room temperature, diluted with diethyl ether, washed twice with water and

brine, dried with Na_2SO_4, filtered, and concentrated under reduced pressure. The unpurified mixture is filtered through silica gel (3% ethyl in hexanes). The resulting mixture was allowed to dissolved in CH_2Cl_2 (5 mL) and triethylsilane (17.5 μL, 0.1 mmol) was added, followed by dropwise addition of BF_3•Et_2O (6.8 μL, 0.055 mmol) at 0 °C. The mixture was stirred for 10 min at the same temperature, then a saturated solution of aqueous sodium bicarbonate solution (5 mL) was added, and the product was extracted from the mixture with CH_2Cl_2 (3×10 mL). The combined extracts were dried with anhydrous sodium sulfate and concentrated in vacuo. Purification by silica gel chromatography provided **4.301** (8.2 mg, 93% over two steps) as colorless oil. **^{1}H NMR** (500 MHz, $CDCl_3$) δ 7.31-7.19 (m, 5H), 4.45 (d, *J* = 8.5 Hz, 1H), 3.84 (ddd, *J* = 8.3, 5.8, 3.7 Hz, 1H), 3.72 (t, *J* = 6.7, 6.7 Hz, 2H), 2.17-2.12 (m, 1H), 1.65-1.55 (m, 2H), 1.53-1.39 (m, 2H), 0.95 (t, *J* = 7.4, 7.4 Hz, 3H), 0.84 (s, 9H), 0.00 (s, 3H), -0.31 (s, 3H). **^{13}C NMR** (151 MHz, $CDCl_3$) δ 144.4, 128.2, 127.5, 126.9, 84.0, 78.4, 67.0, 52.7, 30.2, 29.0, 25.9, 18.2, 10.8, -4.4, -4.8. **IR** (neat) ν_{max} 2953.9 (s), 2926.3 (s), 2853.9 (s), 1460.2 (w), 1251.7 (m), 1107.9 (m), 1080.2 (m), 851.6 (s), 836.2 (s), 775.0 (s). **HRMS** (DART) for $C_{19}H_{33}O_2Si$ $(M+H)^+$: Calc'd: 321.2244, found: 321.2232. **$[\alpha]_D^{20}$** = -42.66 (*c* 0.38, $CHCl_3$, *l* = 50 mm).

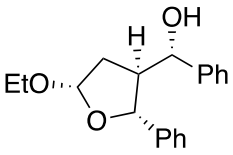
Relevant NOESY correlations are illustrated below.







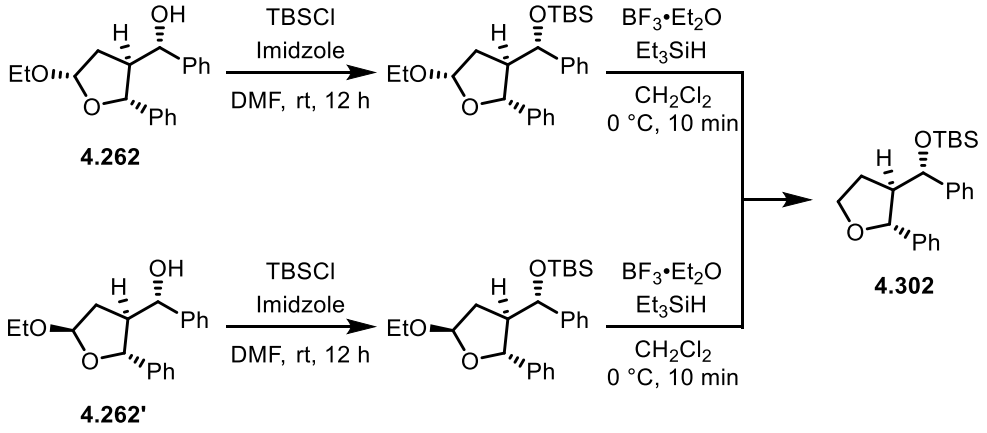
and

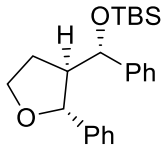


(*1S*)-((*2R*,*3S*)-5-Ethoxy-2-phenyltetrahydrofuran-3-yl)(phenyl)methanol (4.262 and 4.62') . The reaction was performed according to the general **procedure A** with 2-((*3R*,*E*)-3-(1-ethoxy-2-iodoethoxy)-3-phenylprop-1-en-1-yl)-4,4,5,5-tetramethyl-1,3,2-dioxaborolane (91.6 mg, 0.20 mmol, 1.0 equiv), and phenylzinc chloride solution in THF (1.00 mL, 0.4 M, 0.4 mmol, 2.0 equiv), in a mixture of THF/DMA (2.00 mL THF and 0.40 mL DMA overall)

using $NiBr_2$•glyme (6.17 mg, 0.020 mmol, 0.10 equiv) and (*S*,*S*)-**4.4** (6.25 mg, 0.026 mmol, 0.13 equiv) as catalyst. The unpurified mixture was purified by silica gel chromatography (10% ethyl acetate in hexanes, stain in CAM) to afford the product as colorless oil (30.4 mg, 51% yield). The product is a pair of separable diastereomers. *Diastereomer 1 (up):* **^{1}H NMR** (500 MHz, $CDCl_3$) δ 7.36-7.23 (m, 9H), 7.23-7.18 (m, 1H), 5.34 (d, *J* = 4.9 Hz, 1H), 5.12 (d, *J* = 5.8 Hz, 1H), 4.94 (t, *J* = 4.9, 4.9 Hz, 1H), 3.99 (d, *J* = 5.8 Hz, 1H), 3.93-3.86 (m, 1H), 3.61-3.58 (m, 1H), 2.58-2.54 (m, 1H), 2.12-2.07 (m, 1H), 2.01 (dd, *J* = 14.0, 3.2 Hz, 1H), 1.30 (td, *J* = 7.1, 7.1, 1.2 Hz, 3H). **^{13}C NMR** (151 MHz, $CDCl_3$) δ 144.1, 142.3, 128.7, 128.4, 127.8, 127.2, 126.0, 126.0, 103.3, 103.3, 82.1, 82.1, 73.3, 62.6, 54.1, 33.3, 15.2. **IR** (neat) ν_{max} 3424.6 (br), 3060.1 (w), 3029.2 (w), 2971.0 (w), 2923.0 (w), 1492.5 (w), 1452.4 (w), 1197.7 (w), 1097.0 (m), 1046.2 (s), 1022.8 (s), 759.1 (w), 699.6 (s). **HRMS** (DART) for $C_{19}H_{26}NO_3$ $(M+NH_4)^+$: Calc'd: 316.1907, found: 316.1906. **$[\alpha]_D^{20}$** = 72.04 (*c* 1.00, $CHCl_3$, *l* = 50 mm). *Diastereomer 2 (down):* **^{1}H NMR** (500 MHz, $CDCl_3$) δ 7.27-7.15 (m, 10H), 5.18 (d, *J* = 5.2 Hz, 1H), 4.91 (d, *J* = 8.9 Hz, 1H), 4.69 (s, 1H), 3.84 (dq, *J* = 9.8, 7.2, 7.1, 7.1 Hz, 1H), 3.47 (dq, *J* = 9.8, 7.1, 7.1, 7.1 Hz, 1H), 2.74-2.69 (m, 1H), 2.32 (ddd, *J* = 12.9, 11.4, 5.3 Hz, 1H), 1.99-1.94 (m, 2H), 1.23 (t, *J* = 7.1, 7.1 Hz, 3H). **^{13}C NMR** (151 MHz, $CDCl_3$) δ 143.1, 142.3, 128.4, 128.2, 127.7, 127.4, 127.2, 125.9, 103.7, 84.1, 77.3, 77.0, 76.8, 72.7, 62.8, 53.4, 34.3, 15.1. **IR** (neat) ν_{max} 3434.9 (br), 3059.9 (w), 3027.7 (w), 2972.1 (w), 2923.4 (w), 1492.4 (w), 1453.4 (w), 1190.9 (w), 1094.9 (m), 1041.2 (m), 974.1 (m), 908.4 (w), 754.9 (w), 700.6 (s). **HRMS** (DART) for $C19H26NO_3$ $(M+NH_4)^+$: Calc'd: 316.1907, found: 316.1894. **$[\alpha]_D^{20}$** = 57.75 (*c* 1.00, $CHCl_3$, *l* = 50 mm).

Determination of Stereochemical Identity: The transformation below were carried out on the isolated compounds **4.262** and **4.262'** separately in order to assess the stereochemistry of the isolated compounds. Upon reduction all spectral data of the two separate products was found to be identical. The stereochemical assignment was determined through NOESY correlation analysis of the resulting products. The absolute configuration at the B(pin)/silyl ether containing stereocenter was assigned by analogy (see product **4.223** and **4.253**).

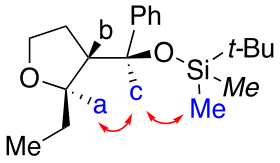


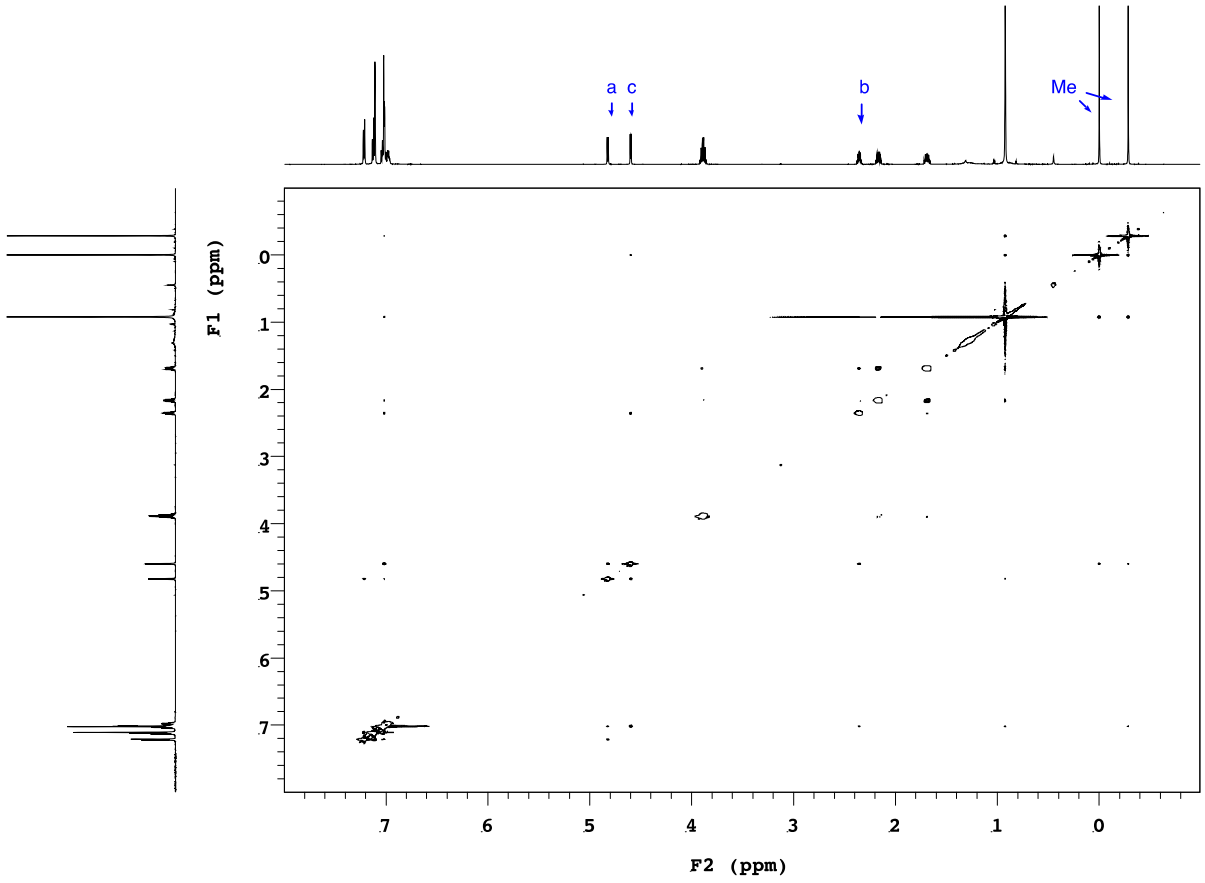


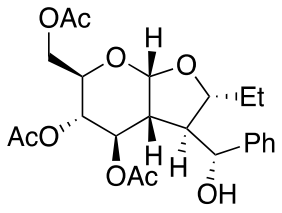
***tert*-Butyldimethyl((*S*)-phenyl((*2R,3R*)-2-phenyltetrahydrofuran-3-yl)methoxy)silane (4.302).** The title compound was generated through the same procedure used to synthesize **4.301** and isolated by silica gel chromatography (10% ethyl acetate in hexanes, stain in CAM) to afford the product as colorless oil (17.0 mg, 81% yield). **^{1}H NMR** (500 MHz, $CDCl_3$) δ 7.28-7.21 (m, 8H), 7.15-7.14 (m, 2H), 4.68 (dd, *J* = 15.2, 5.9 Hz, 2H), 4.08 (td, *J* = 7.8, 7.7, 6.1 Hz, 1H), 3.97 (td, *J* = 8.0, 7.9, 6.4 Hz, 1H), 2.43-2.40

(m, 1H), 2.33-2.27 (m, 1H), 1.95-1.89 (m, 1H), 0.93 (s, 9H), 0.08 (s, 3H), -0.25 (s, 3H). **^{13}C NMR** (151 MHz, $CDCl_3$) δ 144.2, 143.0, 128.4, 128.2, 127.4, 127.4, 126.6, 126.3, 82.5, 82.4, 74.3, 74.3, 68.5, 57.0, 27.4, 26.0, 18.3, -4.1, -4.2, -4.8, -4.8. **IR** (neat) ν_{max} 3026.5 (w), 2880.3 (w), 2853.3 (w), 1452.1 (w), 1250.7 (w), 1060.6 (m), 1003.2 (w), 834.1(s), 773.9 (m), 698.4 (s). **HRMS** (DART) for $C_{23}H_{33}O_2Si$ $(M+NH_4)^+$: Calc'd: 386.2515, found: 386.2510. **$[\alpha]_D^{20}$** = -49.60 (*c* 0.90, $CHCl_3$, *l* = 50 mm).

NOESY was carried out in C_6D_6. Relevant NOESY correlations are illustrated below.







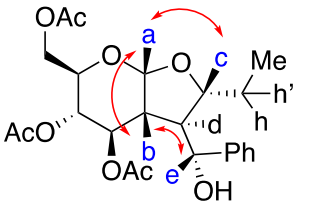
(2*R*,3*R*,3a*R*,4*R*,5*S*,6*R*,7a*S*)-6-(Acetoxymethyl)-2-ethyl-3-((*R*)-hydroxy(phenyl)methyl)hexahydro-4*H*-furo[2,3-*b*]pyran-4,5-diyl diacetate (4.263).

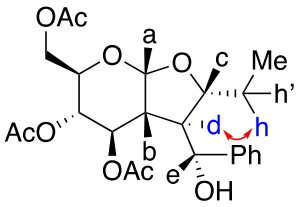
The reaction was performed according to general **procedure A** with (2*R*,3*R*,4*S*,5*S*,6*S*)-2-(acetoxymethyl)-5-iodo-6-(((*R*,*E*)-1-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)pent-1-

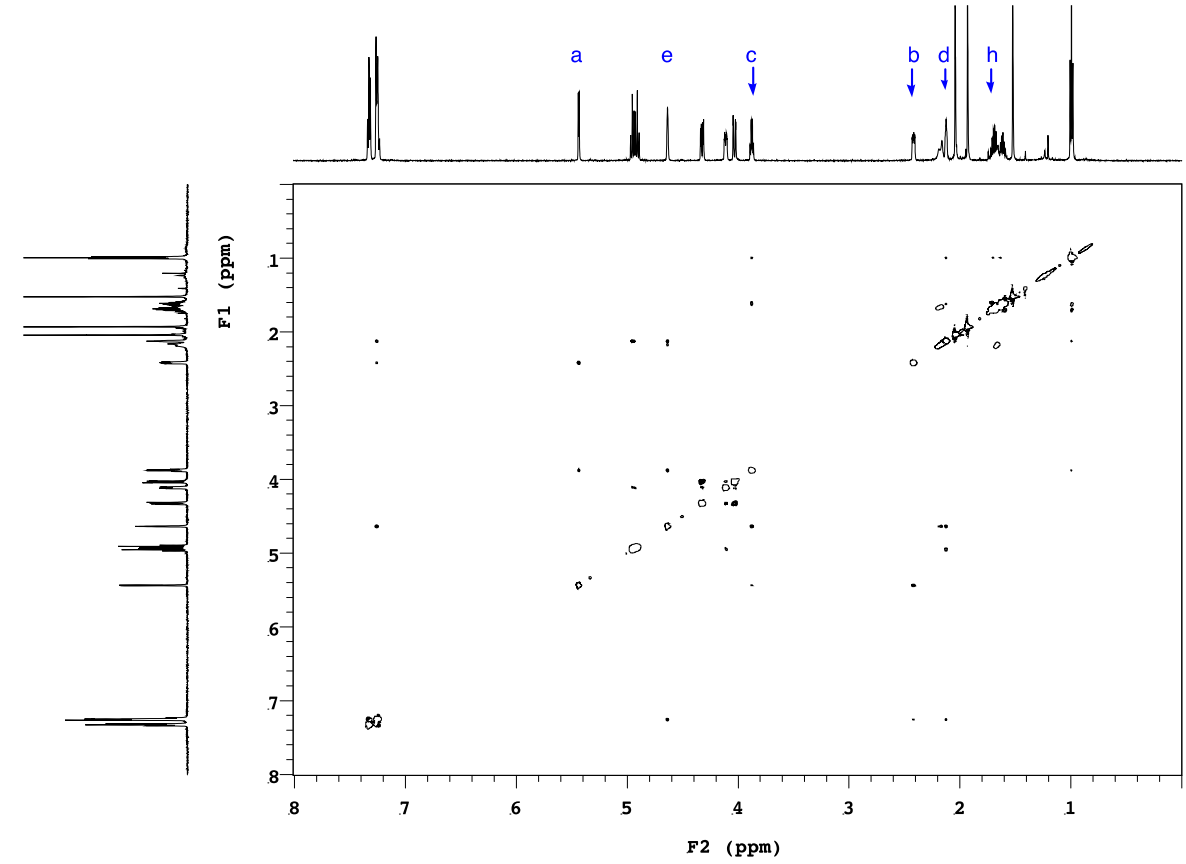
en-3-yl)oxy)tetrahydro-2*H*-pyran-3,4-diyl diacetate (122.1 mg, 0.20 mmol, 1.0 equiv), and phenylzinc chloride solution in THF (1.00 mL, 0.4 M, 0.4 mmol, 2.0 equiv), in a mixture of THF/DMA (2.00 mL THF and 0.40 mL DMA overall) using $NiBr_2$•glyme (6.17 mg, 0.020 mmol, 0.10 equiv) and (*R*,*R*)-**4.4** (6.25 mg, 0.026 mmol, 0.13 equiv) as catalyst. ^{1}H NMR of the boronic ester isolated prior to oxidation indicated a 5:1 diastereomeric ratio in the reaction product. ***Note:*** the oxidation was carried out under buffered conditions by using pH 7 phosphate buffer solution (0.50 mL) in place of a 3 M solution of aqueous NaOH, and the oxidation was allowed to proceed for 12 h. The unpurified mixture was purified by silica gel chromatography (30% ethyl acetate in hexanes, stain in CAM) to afford the product as a single diastereomer. White solid (59.6 mg, 66% yield). **^{1}H NMR** (600 MHz, $CDCl_3$) δ 7.37-7.30 (m, 2H), 7.27-7.22 (m, 3H), 5.44 (d, *J* = 4.6 Hz, 1H), 5.00-4.88 (m, 2H), 4.64-4.63 (m, 1H), 4.33 (dd, *J* = 12.3, 4.2 Hz, 1H), 4.11 (ddd, *J* = 9.6, 4.3, 2.2 Hz, 1H), 4.03 (dd, *J* = 12.3, 2.2 Hz, 1H), 3.88 (q, *J* = 6.1 Hz, 1H), 2.42 (ddd, *J* = 9.0, 4.6, 1.8 Hz, 1H), 2.17-2.09 (m, 2H), 2.05 (s, 3H), 1.93 (s, 3H), 1.75-1.56 (m, 2H), 1.53 (s, 3H), 1.00 (t, *J* = 7.4 Hz, 3H). **^{13}C NMR** (151 MHz, $CDClz_3$) δ 171.0, 170.8, 169.7, 143.0, 128.7, 127.7, 125.6, 100.8, 79.4, 74.3, 73.7, 69.5, 68.2, 62.2, 54.5, 43.1, 28.8, 20 .9, 20.7, 20.5, 10.3. **IR** (neat) ν_{max} 3506.0 (br), 2960.8 (m), 2931.6 (m), 2876.70 (w), 1744.4 (s), 1451.8 (m), 1230.9 (s), 1036.4 (s), 795.2 (w) 763.7 (w). **HRMS** (DART) for $C_{23}H_{34}NO_9$ $(M+NH_4)^+$: Calc'd 468.2228:, found: 468.2248. **$[\alpha]_D^{20}$** = 78.38 (*c* 0.5, $CHCl_3$, *l* = 50 mm).

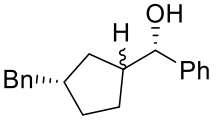
Determination of Stereochemical Identity: The stereochemistry of the carbon skeleton was assigned through NOESY correlation analysis. The absolute configuration at the

B(pin)/OH containing stereocenter was assigned by analogy (see product **4.223** and **4.253**). Relevant NOESY correlations are illustrated below (assignment of the ^{1}H NMR shifts was aided by COSY analysis. The COSY spectrum is included along with the other spectral data).



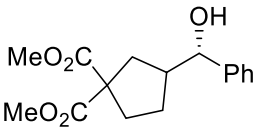






(*1S*)-((*3S*)-3-Benzylcyclopentyl)(phenyl)methanol (4.264). The

reaction was performed according to the general **procedure A** with (*R*,*E*)-2-(5-benzyl-6-iodohex-1-en-1-yl)-4,4,5,5-tetramethyl-1,3,2-dioxaborolane (85.2 mg, 0.20 mmol, 1.0 equiv), and phenylzinc chloride solution in THF (1.00 mL, 0.4 M, 0.4 mmol, 2.0 equiv), in a mixture of THF/DMA (2.00 mL THF and 0.40 mL DMA overall) using $NiBr_2$•glyme (6.17 mg, 0.020 mmol, 0.10 equiv) and (*S*,*S*)-**4.4** (6.25 mg, 0.026 mmol, 0.13 equiv) as catalyst. The unpurified mixture was purified by silica gel chromatography (10% ethyl acetate in hexanes, stain in CAM) to afford the product as colorless oil (30.9 mg, 58% yield). The product is a diastereomeric mixture (d.r. = 1.2:1) **^{1}H NMR** (500 MHz, $CDCl_3$) δ 7.34 (m, 8H), 7.30-7.24 (m, 7H), 7.19-7.12 (m, 7H), 4.43 (d, *J* = 8.2 Hz, 1H), 4.38 (d, *J* = 8.5 Hz, 1H), 2.68-2.56 (m, 5H), 2.43-2.38 (m, 2H), 2.32-2.23 (m, 2H), 2.14-2.08 (m, 1H), 1.88-1.66 (m, 8H), 1.63-1.43 (m, 5H), 1.39-1.14 (m, 5H), 0.97 (q, *J* = 11.1, 11.1, 11.1 Hz, 1H). **^{13}C NMR** (151 MHz, $CDCl_3$) δ 144.3, 144.3, 142.1, 142.0, 128.9, 128.8, 128.5, 128.3, 128.3, 127.7, 127.7, 126.7, 126.6, 125.8, 125.8, 79.3, 79.2, 47.4, 46.3, 42.4, 42.3, 42.1, 41.3, 37.0, 35.1, 32.9, 31.7, 29.6, 28.1. **IR** (neat) ν_{max} 3022.8 (w), 2922.3 (w), 2852.0 (w), 1492.5 (m), 1450.5 (m), 1028.6 (w), 741.5 (m), 697.0 (s), 599.3 (w), 542.1 (w), 479.9 (m). **HRMS** (DART) for $C_{19}H_{21}$ $(M+H-H_2O)^+$: Calc'd: 249.1638, found: 249.1627. **Note**: the product was obtained as a mixture of diastereomers and an optical rotation was not obtained

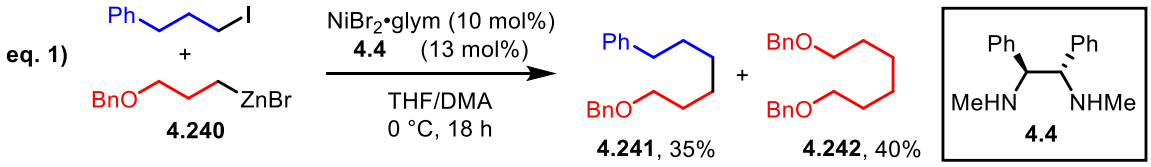


Dimethyl 3-((*S*)-hydroxy(phenyl)methyl)cyclopentane-1,1-dicarboxylate (4.246-OH). The reaction was performed according to general **procedure**

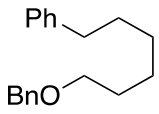
A dimethyl (*E*)-2-(2-iodoethyl)-2-(3-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)allyl)malonate (90.4 mg, 0.20 mmol, 1.0 equiv), and phenylzinc chloride solution in THF (1.00 mL, 0.4 M, 0.4 mmol, 2.0 equiv), in a mixture of THF/DMA (2.00 mL THF and 0.40 mL DMA overall) using $NiBr_2$•glyme (6.17 mg, 0.020 mmol, 0.10 equiv) and (*S*,*S*)-**4.4** (6.25 mg, 0.026 mmol, 0.13 equiv) as catalyst. ***Note:*** the oxidation was carried out under buffered conditions by using pH 7 phosphate buffer solution (0.50 mL) in place of a 3 M solution of aqueous NaOH, and the oxidation was allowed to proceed for 12 h. The unpurified mixture was purified by silica gel chromatography (30% ethyl acetate in hexanes, stain in CAM) to afford the product as colorless oil (36.0 mg, 62% yield).

^{1}H NMR (600 MHz, C_6D_6) δ 7.15-7.12 (m, 2H), 7.10-7.04 (m, 6H), 7.04-6.99 (m, 2H), 4.18 (d, *J* = 7.1 Hz, 1H), 4.11 (d, *J* = 6.7 Hz, 1H), 3.27 (s, 3H), 3.24 (s, 3H), 3.22 (s, 3H), 3.19 (s, 3H), 2.70-2.62 (m, 1H), 2.41-2.36 (m, 1H), 2.35-2.29 (m, 3H), 2.25-2.19 (m, 2H), 2.19-2.12 (m, 1H), 2.12-2.05 (m, 1H), 1.83-1.73 (m, 1H), 1.73-1.63 (m, 1H), 1.35 (s, 1H), 1.35-1.29 (m, 3H), 0.39 (s, 1H). **^{13}C NMR** (151 MHz, $CDCl_3$) δ 173.3, 173.1, 172.9, 172.8, 144.0, 143.8, 128.6, 128.5, 127.80, 127.8, 126.4, 126.3, 77.9, 77.7, 60.2, 60.1, 52.9, 52.8, 52.8, 52.8, 46.9, 46.8, 37.2, 37.2, 34.2, 34.0, 28.8, 28.3. **IR** (neat) ν_{max} 3522.2 (br), 3026.2 (w), 1726.3 (s), 1492.2 (w), 1267.0 (m), 1197.0 (w), 1158.7 (w), 1102.6 (w), 763.8 (w), 702.4 (w). **HRMS** (DART) for $C_{16}H_{19}O_5$ $(M+H)^+$: Calc'd: 291.1227, found: 291.1226. **Note**: the product was obtained as a mixture of diastereomers and an optical rotation was not obtained. The diastereomeric ratio was determined by the integration of the ^{1}H NMR in C_6D_6.

4.9.2.2.6 Background Reaction Experiments

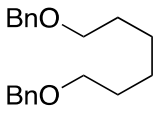


Equation (1). In an argon-filled glovebox, an oven-dried 2 dram vial equipped with a magnetic stirrer was charged with $NiBr_2$•glyme (6.17 mg, 0.02 mmol, 0.1 equiv), (*S,S*)-*N,N'*-dimethyl-1,2-diphenyl-ethane-1,2-diamine (*S,S*)-**4.4** (6.25 mg, 0.026 mmol, 0.13 equiv) and dissolved in 2.0 mL of THF. The catalyst solution was stirred for 1 h at ambient temperature. **(3-Iodopropyl)benzene** (98.4 mg, 0.40 mmol, 1.0 equiv) was added to the catalyst solution. The vial was sealed with a PTFE-lined pierceable cap, taped, and brought outside the glovebox where it was placed in a CryoCool set at 0 ºC. The vial was allowed to cool for 30 min before addition of **(3-(benzyloxy)propyl)zinc bromide** solution (0.410 mL, 0.97 M 0.40 mmol, 1.0 equiv). The puncture hole was taped over and the reaction mixture was allowed to stir at 0 ºC for 18 h. The reaction was quenched with a saturated solution of aqueous NH_4Cl (0.40 mL), diluted with diethyl ether and washed with water and brine sequentially. The organic layer was dried over magnesium sulfate and concentrated. The unpurified material was then subjected to silica gel chromatography.

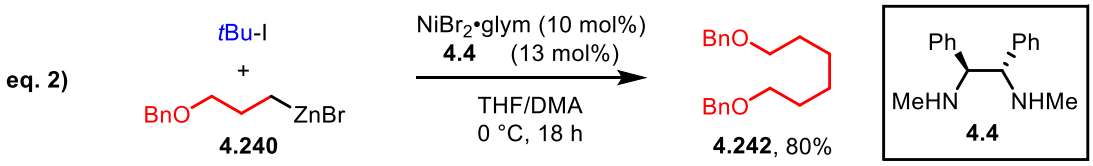


(6-(Benzyloxy)hexyl)benzene (4.241). The product of the reaction was

isolated by silica gel chromatography (25% CH_2Cl_2 in hexane, stain in CAM) as colorless oil (37.8 mg, 35% yield). **^{1}H NMR** (600 MHz, $CDCl_3$) δ 7.36-7.34 (m, 4H), 7.32-7.23 (m, 3H), 7.20-7.13 (m, 3H), 4.50 (s, 2H), 3.46 (t, J = 6.6 Hz, 2H), 2.84-2.53 (m, 2H), 1.69-1.55 (m, 4H), 1.45-1.34 (m, 4H). **^{13}C NMR** (151 MHz, $CDCl_3$) δ 142.9, 138.8, 128.5, 128.5, 128.4, 127.7, 127.6, 125.7, 73.0, 70.6, 36.0, 31.6, 29.8, 29.3, 26.2. **IR** (neat) ν_{max} 3082.6 (w), 3060.2 (w), 3024.1 (w), 2925.8 (s), 2851.7 (s), 1494.1 (m), 1452.2 (m), 1360.8 (m), 1202.6 (s), 734.2 (s), 696.4 (s). **HRMS** (DART) for $C_{19}H_{25}O$ $(M+H)^+$: Calc'd: 269.1900 , found: 269.1901.



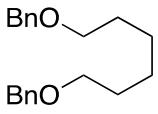
1,6-bis(Benzyloxy)hexane (4.242) was isolated by silica gel chromatography (40% CH_2Cl_2 in hexane, stain in CAM) as colorless oil (24.1 mg, 40% yield based on 0.50 equiv of starting material). All spectral data were in accord with the literature.[91]



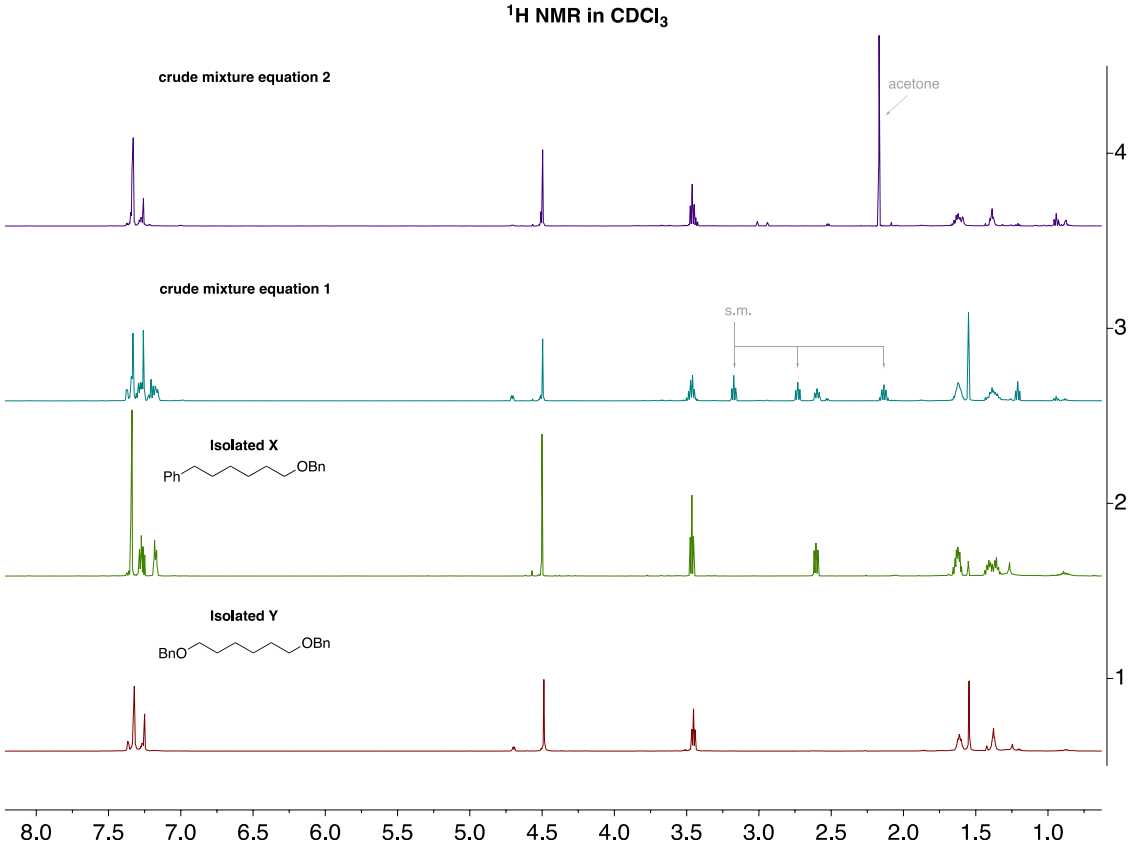
Equation (2). The experiment was carried out following the same procedure as for equation (1) by replacing **(3-iodopropyl)benzene** with ***t*-butyl iodide** (73.6 mg, 0.40

[91] Mash, E. A.; Kantor, L.; Liza, T. A.; Waller, S. C. *Synth. Commun.* **1997**, 27, 507.

mmol, 1.00 equiv).



1,6-bis(Benzyloxy)hexane (4.242) was isolated by silica gel chromatography (40% CH_2Cl_2 in hexane, stain in CAM) as a colourless oil (47.8 mg 80% yield based on 0.50 equiv of starting material) All spectral data were in accord with the literature.[91]



Comparison of the ^{1}H NMR for the unpurified mixtures from eq. (1) and eq.(2) with the corresponding isolated products ^{1}H NMR spectra for reference. The starting material (s.m.) corresponds to unreacted (3-iodopropyl)benzene.

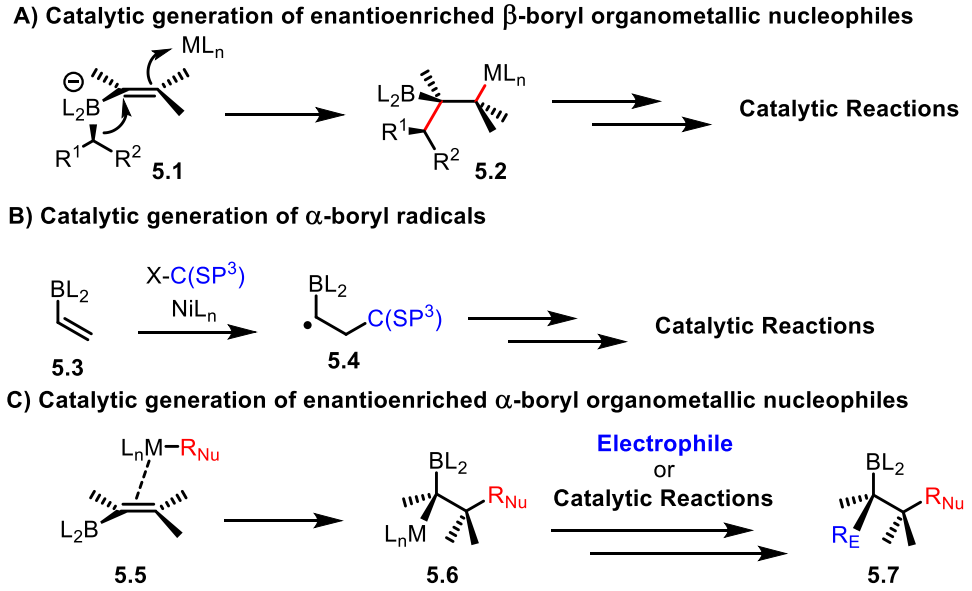
Chapter Five

Formation of Enantioenriched α-Boryl Alkylzinc Reagents Enabled by Enantioselective Carbometallation of Vinylboron Reagents

5.1 Introduction

As discussed in the preceding chapters of this dissertation, the ability of boron to stabilize various reactive intermediates can be used as a productive strategy to engineer enantioselective catalytic multicomponent reactions capable of accessing versatile enantioenriched alkylboronic ester products. The ability of boron to reversibly bond to nucleophilic species and mediate 1,2-metallate rearrangement reactions has enabled the development of enantioselective diphosphine–Pd- and triamine–Ni-catalyzed conjunctive couplings of aryl/alkenyl and alkyl electrophiles respectively as well as Ni-initiated radical-polar crossover reactions (Scheme 5.1.A). The ability of a trivalent boronic ester to

Scheme 5.1. Catalytic generation of reactive boron-containing intermediates



stabilize α-boryl radical intermediates has facilitated the development of an enantioselective diamine–Ni-catalyzed radical addition/coupling reaction of vinylboronic pinacol ester with alkyl halides and alkyl- or arylzinc halides (Scheme 5.1.B).

In this chapter, the ability of a trivalent boronic ester to stabilize α-boryl organometallic intermediates will be shown to enable the development of a catalytic, enantioselective carbometallation reaction (Scheme 5.1.C). The enantioenriched geminal diorganometallic reagents that this process produces will be shown to react with diverse electrophilic species. The carbometallation-electrophile trapping sequence will be shown to constitute a class of enantioselective multicomponent reactions capable of forging multiple bonds, while retaining a valuable boron functional group for further synthetic manipulation.

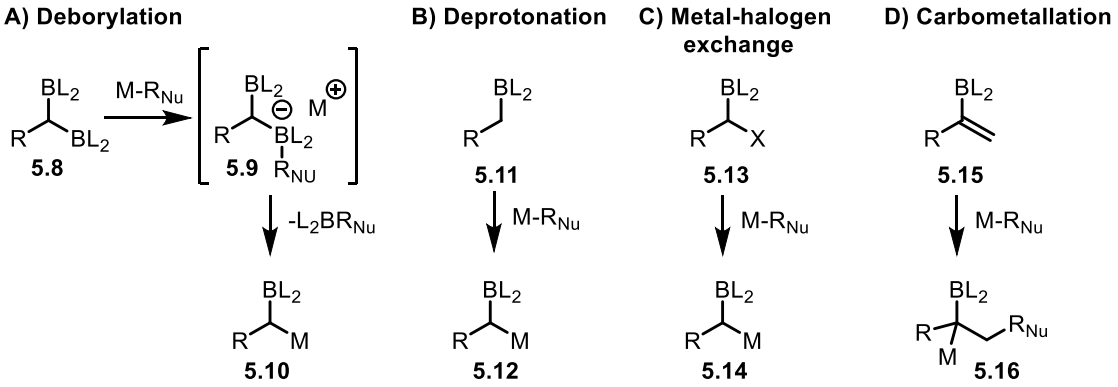
5.2 Background

5.2.1 α-Boryl Organometallic Reagents

Geminal diorganometallic nucleophiles, particularly those bearing a boron functional group, are versatile reagents in organic synthesis. The preparation and reactivity of various types, including α-boryl lithium, zinc, copper, zirconium, and silicon reagents, as well as homo and hetero geminal diboron species are known (Scheme 5.2). Perhaps the earliest example of these species was reported by H. C. Brown, who noted that geminal diboron compounds readily undergo protodeborylation in the presence of sodium hydroxide base.[1] While the exact nature of the α-boryl anion generated upon deborylation of geminal diboron compounds was not well understood, the deborylative approach of generating α-

[1] Brown, H. C.; Zweifel, G. *J. Am. Chem. Soc*. **1961**, 83, 3834.

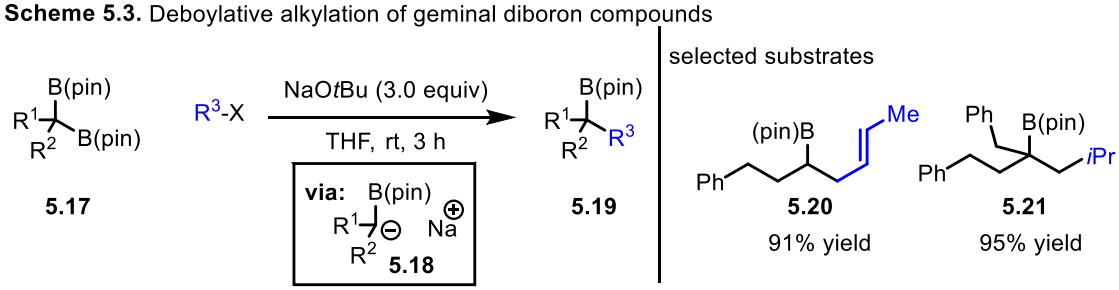
Scheme 5.2. Methods employed to access α-boryl organometallic species



boryl organometallic species has attracted considerable research interest[2] owing to the ease of preparation of these species and their ability to participate in various C–C bond forming reactions. Our group reported a deborylative alkylation of geminal diboronic pinacol esters (**5.17**) that proceeds under mild conditions to furnish a variety of alkylboronic ester products (Scheme 5.3).[3]

α-Boryl silicon reagents have attracted somewhat less research interest, perhaps owing to the lower degree of reactivity these species demonstrate relative to other germinal

Scheme 5.3. Deboylative alkylation of geminal diboron compounds



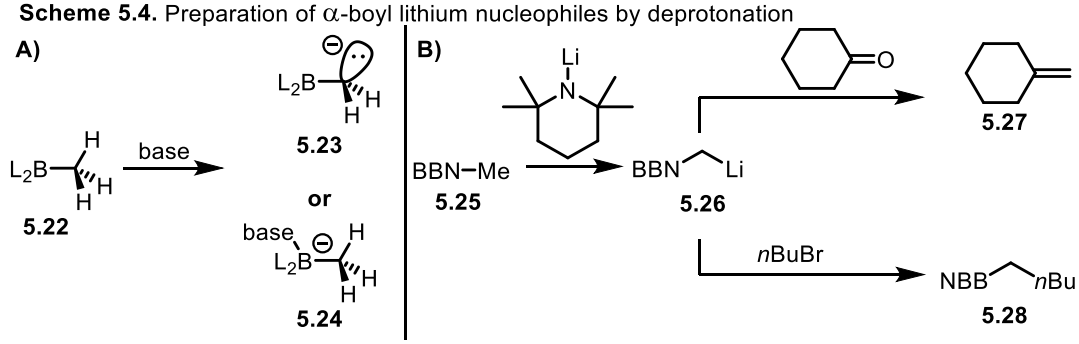
[2] (a) Cainelli, G.; Bello, G. D.; Zubiana, G. *Tetrahedron Lett*. **1965**, 38, 3429. (b) Zweifel, G.; Avzoumanian, H. *Tetrahedron Lett*. **1966**, 25, 2535. (c) Zweifel, G.; Arzoumanian, H. *J. Am. Chem. Soc*. **1967**, 89, 291. (d) Matteson, D. S.; Thomas, J. R. *J. Organomet. Chem.* **1970**, 24, 263. (e) Zweifel, G.; Fisher, R. P.; Horng, A. *Synthesis*, **1973**, 37. (f) Mukaiyama, T.; Murakami, M.; Oriyama, T.; Yamaguchi, M. *Chem. Lett.* **1981**, 1193.

[3] Hong, K.; Liu, X.; Morken, J. P. *J. Am. Chem. Soc.* **2014**, 136, 10581.

diorganometallic species.[4] A notable exception is α-boryl allylsilanes which have been employed as allylating reagents.[5]

In addition to deboylative metallation of geminal diboron compounds, deprotonation of alkylboranes[6] and boronic esters[7] (Scheme 5.4) has been developed as an approach to generate α-boyl organolithium nucleophiles. While α-boryl protons are acidified due to the presence of the adjacent Lewis acidic boron moiety, reaction of base by nucleophilic addition to the empty p orbital of boron is possible and can complicate a deprotonation

Scheme 5.4. Preparation of α-boyl lithium nucleophiles by deprotonation



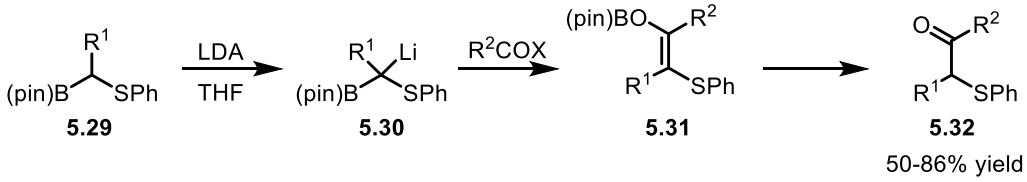
[4] For some non-catalytic methods of preparing these species, see: (a) Bootwicha, T.; Feilner, J. M.; Myers, E. L.; Aggarwal, V. K. *Nat. Chem*. **2017**, 9, 896. (b) Barsamian, A. L.; Wu, Z.; Blakemore, P. R. *Org. Biomol. Chem*. **2015**, 13, 3781. For recent catalytic and enantioselective methods, see: (c) Meng, F.; Jang, H.; Hoveyda, A. H. *Chem. Eur. J*. **2013**, 19, 3204. (d) Szymaniak, A. A.; Zhang, C.; Coombs, J. R.; Morken, J. P. *ACS Catal*. **2018**, 8, 2897.

[5] (a) Shimizu, M.; Kitagawa, H.; Kurahashi, T.; Hiyama, T. *Angew. Chem. Int. Ed*. **2001**, 40, 4283. (b) Carosi, L.; Lachance, H.; Hall, D. G. *Tetrahedron Lett*. **2005**, 8981. (c) Aggarwal, V. K.; Binanzer, M.; de Ceglie, M. C.; Gallanti, M.; Glasspoole, B. W.; Kendrick, S. J. F.; Sonawane, R. P.; Vazquez-Romero, A.; Webster, M. P. *Org. Lett*. **2011**, 13, 1490.

[6] (a) Rathke, M. W.; Kow, R. *J. Am. Chem. Soc*. **1972**, 94, 6854. (b) Kow, R.; Rathke, M. W. *J. Am. Chem. Soc.* **1973**, 95, 2715. (c) Pelter, A.; Singaram, B.; Williams, L.; Wilson, J. W. *Tetrahedron Lett*. **1983**, 24, 623. (d) Pelter, A.; Singaram, B.; Wilson, J. W. *Tetrahedron Lett*. **1983**, 24, 631. (e) Garad, . V.; Pelter, A.; Singaram, B.; Wilson, J. W. *Tetrahedron Lett*. **1983**, 24, 637. (f) Wilson, J. W. J. *Organomet. Chem*. **1980**,186, 297. (g) Pelter, A.; Williams, L.; Wilson, J. W. *Tetrahedron Lett*. **1983**, 24, 627. (h) Pelter, A.; Singaram, B.; Wilson, J. W. *Tetrahedron Lett*. **1983**, 24, 635. (i) Pelter, A.; Buss, D.; Pitchford, A. *Tetrahedron Lett*. **1985**, 26, 5093. (j) Pelter, A.; Buss, D.; Colclough, E. *J. Chem. Soc. Chem. Commun*. **1987**, 297. (k) Pelter, A.; Smith, K.; Elgendy, S.; Rowlands, M. *Tetrahedron Lett*. **1989**, 30, 5643, 5647.

[7] (a) Matteson, D. S.; Moody, R. J. *Organometallics* **1982**, 1, 20. (b) Matteson, D. S.; Moody, R. J. *J. Am. Chem. Soc.* **1977**, 99, 3196. (c) Matteson, D. S.; Arne, K. H. *Organometallics,* **1982**, 1, 280. (d) Matteson, D. S.; Majumdar, D. *Organometallics* **1983**, 2, 230.

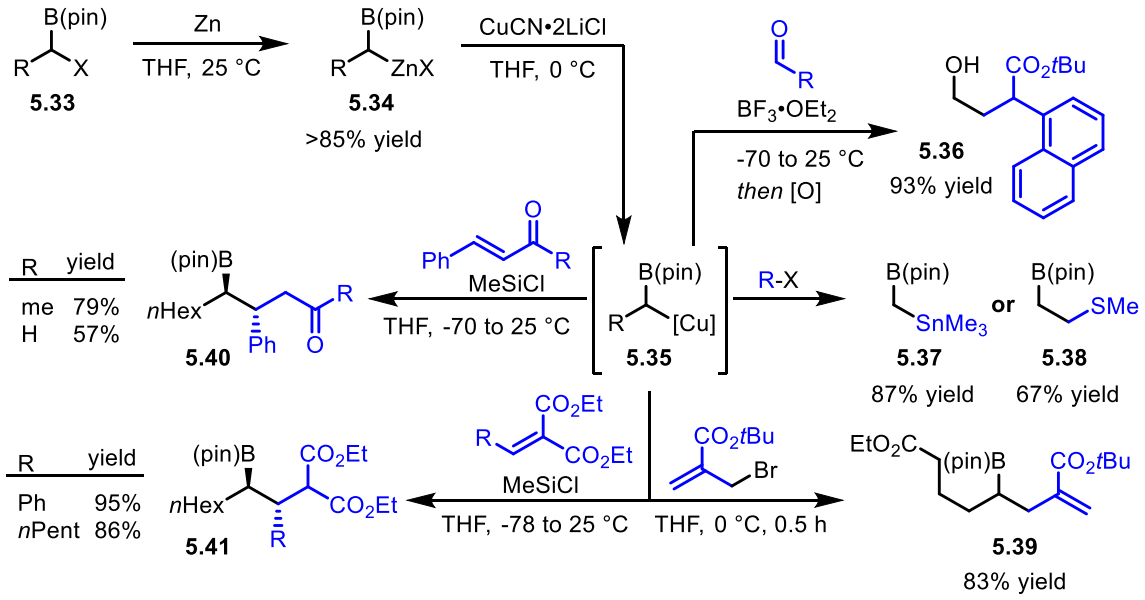
Scheme 5.5. Preparation of boron enolates by acylation of α-boryl alkyllithium nucleophiles



approach to α-boryl lithium reagents (Scheme 5.4.A). To disfavor the formation of Lewis base-Lewis acid adducts **5.24**, sterically hindered bases such as LiTMP or LDA, or sterically hindered ligands on boron such as a mesityl substituent are often employed in these reactions. α-Boryl organolithium reagents have been demonstrated to participate in alkylation and boron-Wittig olefination reactions (Scheme 5.4.B) and have been used to access boron-enolate nucleophiles (Scheme 5.5).

Knochel reported that α-boryl zinc reagents can be readily prepared from α-halo boronic esters by zinc insertion (Scheme 5.6).[8] These reagents were shown to participate in a wide

Scheme 5.6. Knochel's seminal report on the preperation of α-boryl zinc reagents



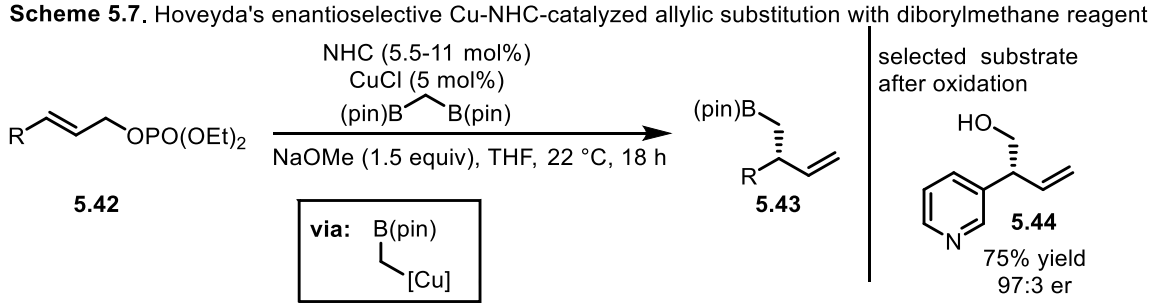
[8] Knochel, P. *J. Am. Chem. Soc.* **1990**, 112, 7431.

variety of CuCN-mediated reactions such as carbonyl addition (product **5.36**), electrophilic stannylation (**5.37**) and alkylation **(5.38**), allylation to form functionalized homoallyl boronic ester **5.39**, and diastereoselective conjugate addition reactions with α,β-unsaturated aldehydes, ketones (**5.40**) and esters (**5.41**). The same author later demonstrated that diethylzinc could be used in place of zinc metal for the preparation of α-boryl diorganozinc reagents.[9]

In addition to stoichiometric methods of generating α-boryl alkylcopper species, catalytic methods of accessing these species have also been developed. Hoveyda reported that an enantioenriched NHC–Cu complex can catalyze the efficient site- and enantioselective addition of commercially available di-B(pin)–methane to allylic phosphates **5.42** (Scheme 5.7).[10] This method furnishes versatile boron-containing products **5.43** which can be readily modified. The utility of this method for organic synthesis was showcased by its application to a short total synthesis of rhopaloic acid A.

Suzuki demonstrated a CuCN-mediated reacting of α-boryl alkylzinc reagents with propargyl tosylates to enabled the preparation of homoallenylboron reagents

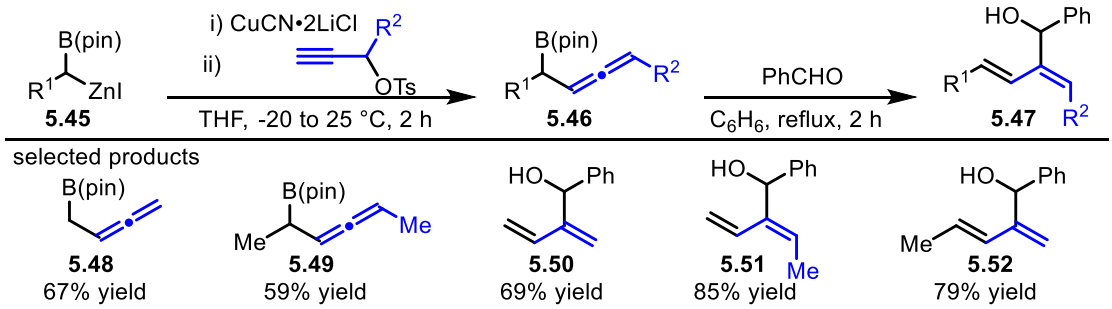
Scheme 5.7. Hoveyda's enantioselective Cu-NHC-catalyzed allylic substitution with diborylmethane reagent



[9] Rozema, M. J.; Sidduri, A. R.; Knochel, P. *J. Org. Chem.* **1992**, 57, 1956.
[10] Shi, Y.; Hoveyda, A. H. *Angew. Chem. Int. Ed.* **2016**, 55, 3455.

(Scheme 5.8).[11] These reagents were shown to participate in efficient allylation reactions with benzaldehyde to furnish dienyl allylic alcohols **5.47**. Suzuki also reported a CuCN-mediated direct addition reaction of α-boryl alkylzinc reagents to aldehydes, enabling the

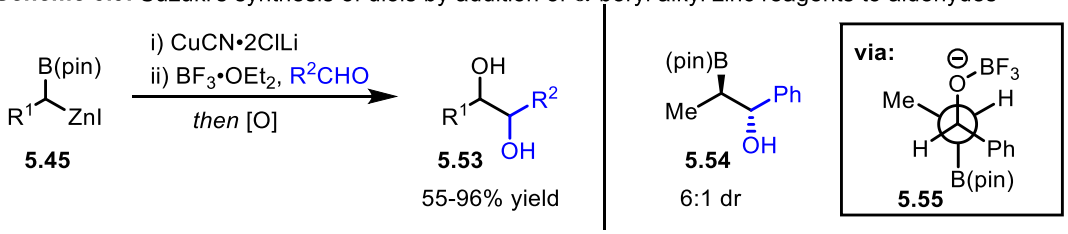
Scheme 5.8. Suzuki's CuCN mediated allenylation of α-boryl zinc reagent and preperation of dienes



preparation diol products **5.53** (Scheme 5.9).[12] Notably, the authors found that the initial products, β-hydroxy boronic ester products **5.54**, were stable and could be isolated. The reaction was found to proceed in a diastereoselective fashion, which was rationalized as occurring by an addition reaction that minimizes torsional interactions as in Newman projection **5.55** (inset).

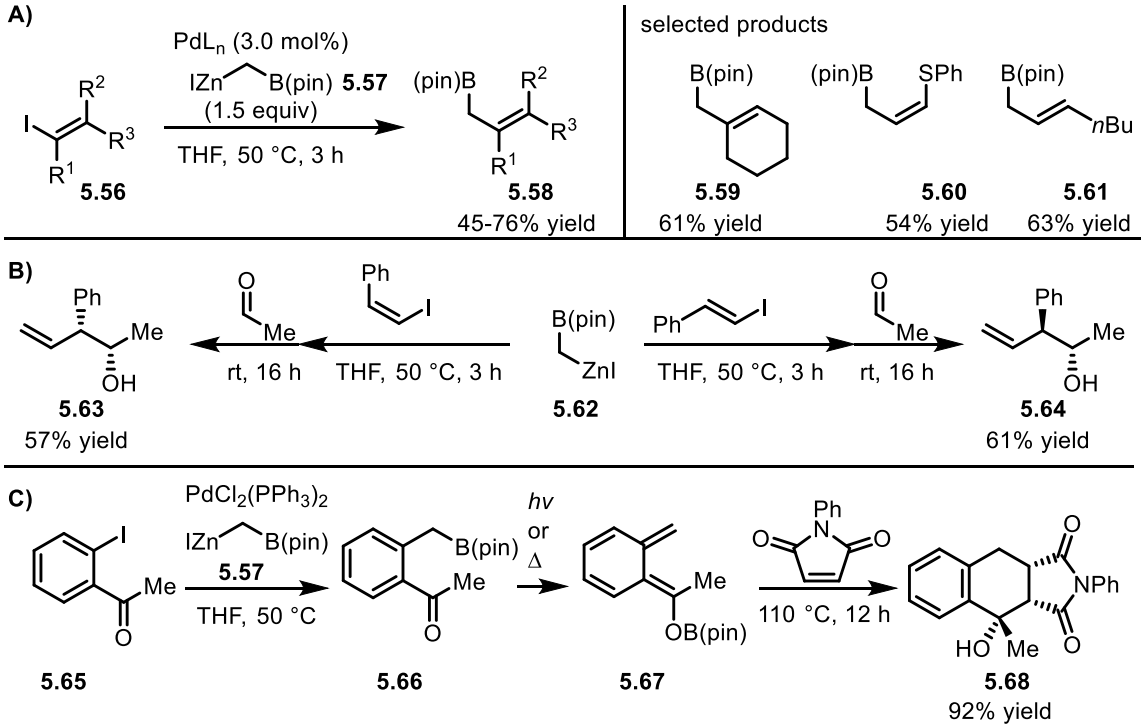
Suzuki also demonstrated that allylboronic pinacol esters can be produced by the cross-coupling of α-boryl alkylzinc reagent **5.57** with alkenyl halides (Scheme 5.10.A).[13] Notably, the authors demonstrated that the configuration of the alkenyl halides is

Scheme 5.9. Suzuki's synthesis of diols by addition of α-boryl alkyl zinc reagents to aldehydes



[11] Gridnev, I.; Kanai, G.; Miyaura, N.; Suzuki, A. *J. Organomet. Chem*. **1994**, 481, C4.
[12] Sakai, M.; Saito, S.; Kanas, G.; Suzuki, A.; Miyaura, N. *Tetrahedron* **1996**, 52, 915.
[13] Watanabe, T.; Miyaura, N.; Suzuki, A. *J. Organomet. Chem*. **1993**, 444, C1.

Scheme 5.10. Suzuki's catalyzed synthesis of allylboronic esters and *ortho*-acylbenzyl boronic ester



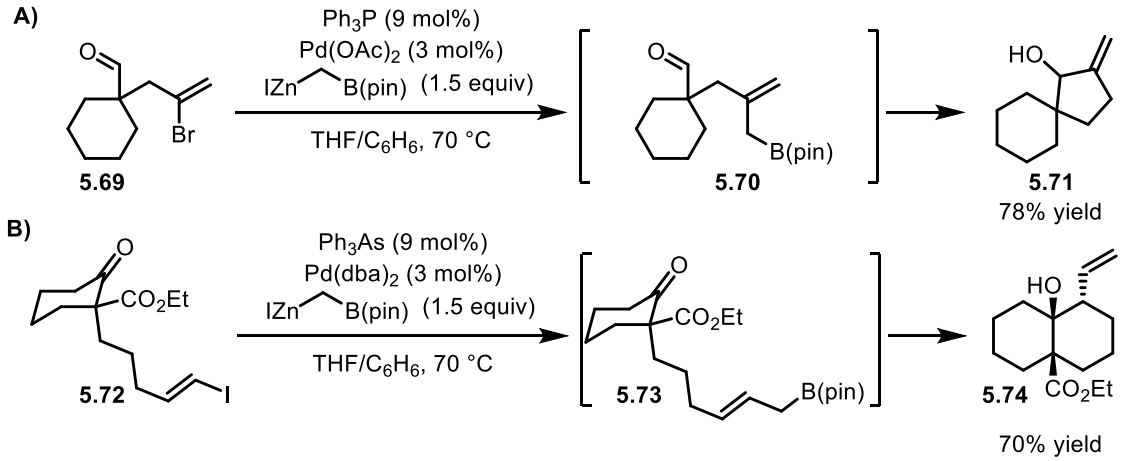
maintained during the reaction, thus granting access to stereochemically well-defined allylboron reagents (Scheme 5.10.B). The same authors demonstrated that *ortho*-quinodimethane reagents such as **5.67**, which have been studied for their use in Diels-Alder reactions[14], can be readily prepared by coupling α-boryl alkylzinc reagents with *ortho*-acyliodoarenes followed by photo or thermal isomerization (Scheme 5.10.C).[15]

Suzuki later reported that carbocyclic structures including spirocycles and fused ring systems, can be prepared by a cross-coupling and *in situ* carbonyl allylation strategy (Scheme 5.11.A/B).[16]

In addition to α-boryl lithium, zinc, and copper reagents, α-boryl alkylzirconium

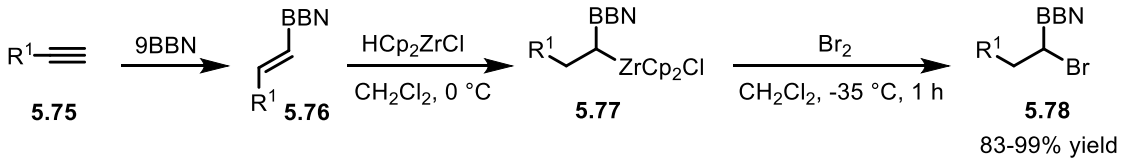
[14] Jefford, C. W.; Bernardinelli, G.; Wang, Y.; Spellmeyer, D. C.; Buda, A.; Houk K. N. *J. Am. Chem. Soc*. **1992**, 114, 1157
[15] Kanai, G.; Miyaura, N.; Suzuki, A. *Chem. Lett*. **1993**, 845.
[16] Watanabe, T.; Sakai, M.; Miyaura, N.; Suzuki, A. *J. Chem. Soc. Chem. Commun*. **1994**, 467.

Scheme 5.11. Use of α-boryl zinc nucleophile to prepare allyl boronic ester



reagents have been prepared and shown to participate in direct and copper-mediated reactions. Schwartz initially described the preparation of α-boryl alkylzirconium reagent by hydrozirconation of hexenyl-9-BBN.[17] Shrebnik later reported that hydrozirconation can be used as a means of generating α-boryl alkylzirconium reagent which can be readily converted to the corresponding α-halo borane **5.78** (Scheme 5.12).[18] Shrebnik then

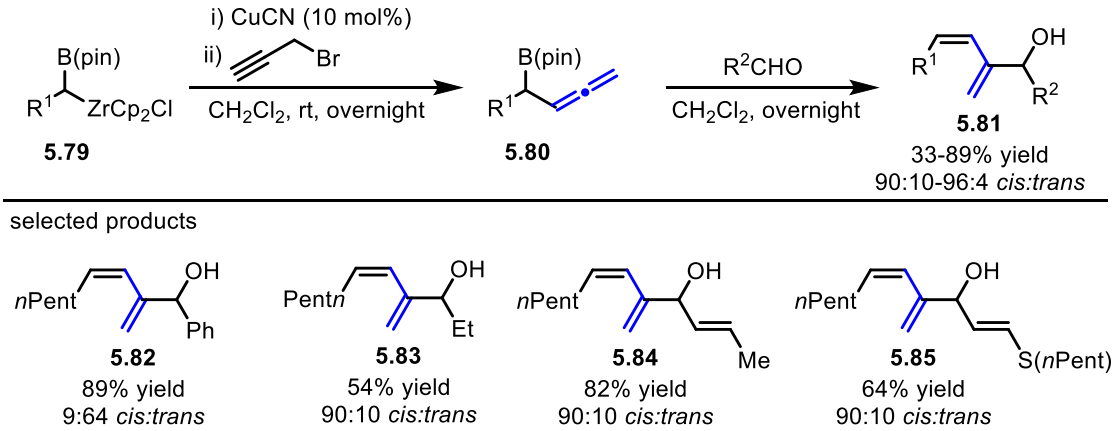
Scheme 5.12. Srebnik's preperation and bromination of α-boryl zirconium reagents



demonstrated that α-boryl alkylzirconium reagents can be used to prepare allenylboron reagents and that these reagents can be used to synthesize isomerically enriched dienyl and trienyl allylic alcohols (Scheme 5.13).[19] α-Boryl alkylzirconium reagents have also been

[17] Hartner, F. W. Jr.; Schwartz, J. *J. Am. Chem. Soc*. **1981**, 103, 4979.
[18] Zheng, B.; Srebnik, M. *Tetrahedron Lett*. **1993**, 34, 4133.
[19] Zheng, B.; Srebnik, M. *J. Org. Chem*. **1995**, 60, 486.

Scheme 5.13. Srebnik's catalytic allenylation of α-boryl zirconium reagents to access dienes and trienes



demonstrated to participate in copper-catalyzed conjugate addition[20] and acylation[21] reactions, and have been used in the preparation of small-molecule natural products.[22]

α-Boryl organometallic species have been shown to be versatile reagents in organic synthesis, participating in a wide variety of stoichiometric and catalytic reactions, and granting access to diverse product classes. If this class of reagent could be prepared in an enantioselective fashion and participate in reactions in an enantiospecific manner then it might constitute a powerful chiral building block. Yet, apart from enantioenriched geminal hetero diboron reagents, little is known about the configurational stability of these compounds. Indeed, information about the configurational stability of stereodefined organometallic nucleophiles is somewhat limited in general.

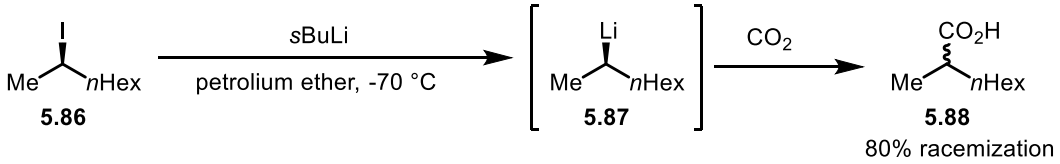
[20] Pereira, S.; Srebnik, M. *Tetrahedron Lett*. **1995**, 36, 1805.
[21] Zheng, B.; Srebnik, M. *Tetrahedron Lett*. **1995**, 36, 5665.
[22] Deloux, L.; Srebnik, M. *Tetrahedron Lett*. **1996**, 37, 2735.

5.2.2 Stoichiometric Preparation Stereodefined Organometallic Reagents

5.2.2.1 Li-Substituted Stereogenic Carbon Centers

Stereodefined organometallic compounds containing a Li-substituted stereogenic carbon are the most prevalent and well-studied class of chiral organometallic reagents.[23] Owing to the highly ionic character of the carbon-lithium bond, these compounds generally possess a low degree of configurational stability. An early study by Letsinger on the formation and carbonylation of non-stabilized 1-methylheptyllithium (**5.87**), obtained from lithium halogen exchange with (-)-2-iodooctane **5.86** at -70˚C, found that a large degree of

Scheme 5.14. Low configurational stability of alkyllithium reagents obtained via Li-I exchange

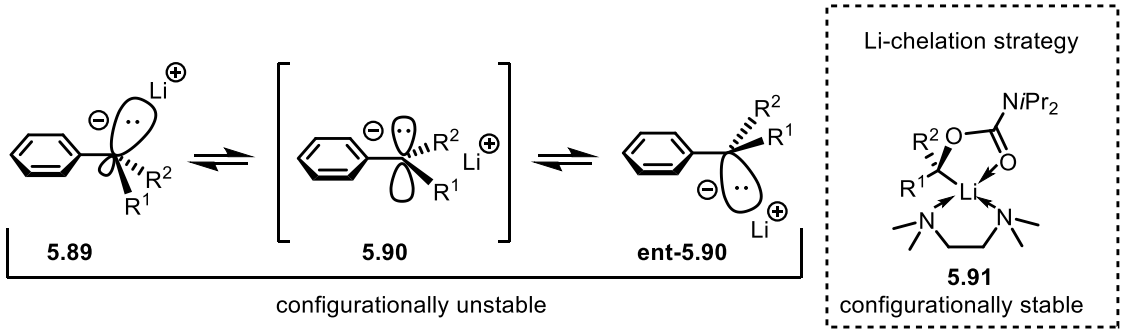


racemization occurred.[24] Owing to this low degree of configurational stability, studies of compounds possessing Li-substituted stereogenic carbon centers have generally focused

[23] a) Topics in Stereochemistry – Stereochemical Aspects of Organolitium Compoundss (Gawley, R. E.; Siegel, J. S. Vol. 26, VHCA, Wiley-VCH, **2010**. (b) Basu, A.; Thayumanavan, S. *Angew. Chem. Int. Ed.* **2002**, 41, 716.
[24] Letsinger, R. L. *J. Am. Chem. Soc.* **1950**, 72, 4842.

on stabilized species such as heteroatom-substituted[25] alkyl, benzylic[26], and allylic[27] organolithium reagents with intra- and/or intermolecular coordinating groups. While the presence of a π-bond adjacent to a Li-substituted carbon atom leads to thermodynamic anion stabilization due to resonance, the same effect leads to greater anion planarization[28] and solvent separation of carbon and lithium ions, thus facilitating stereomutation by migration of lithium from one enantiotopic face of carbon to the other (**5.89** to **ent-5.90**; Figure **5.15**). Hoppe and Beak found that the *N,N'*-dialkylcarbomoyloxy group, originally designed to enhance the kinetic acidity of benzylic substrates towards deprotonation-

Scheme 5.15. Mechanism of stereomutation for chiral organolithium compounds/Li-chelate stabilization



[25] a) Cohen, T.; Lin, M.-T *J. Am. Chem. Soc*. **1984**, 106, 1130. (b) Still, W. C.; Sreekumar, C. *J. Am. Chem. Soc.* **1980**, 102, 1201. (c) Hoppe, D.; Hintze, F.; Tebben, P. *Angew. Chem. Int. Ed.* **1990**, 29, 1422. (d) Rychnovsky, S. D.; Mickus, D. E. *Tetrahedron Lett.* **1989**, 30, 3011. (e) Kapeller, D. C.; Brecker, L.; Hammerschmidt, F. *J. Org. Chem.* **2009**, 74, 2380. (f) Schlosser, M.; Limat, D. *J. Am. Chem. Soc.* **1995**, 12342. (g) Gawley, R. E.; Zhang, Q. *J. Am. Chem. Soc.* **1993**, 115, 7515. (h) Kapeller, D. C.; Hammerschmidt, F. *Chem. Euro. J.* **2009**, 15, 5729. (i) O'Brien, P.; Warren, S. *J. Chem. Soc. Perkin Trans.* **1**, **1996**, 2467. (j) Hoffmann, R. W.; Ruhland, T.; Bewersdorf, M. J. Chem. Soc. Chem. Commun. **1991**, 195. Kapeller, D. C.; Hammerschmidt, F. J. Am. Chem. Soc. **2008**, 130, 2329.

[26] (a) Clayden, J.; Helliwell, M.; Pink, J. H.; Westlund, N. *J. Am. Chem. Soc.* **2001**, 123, 12449. (b) Hoffmann, R. W.; Rühl, T.; Chemla, F.; Zahneisen, T. *Liebigs. Ann. Chem.* **1992**, 719. (c) Peoples, P. R. Grutzner, J. B. *J. Am. Chem. Soc.* **1980**, 102, 4709. (d) Hoppe, I.; Marsch, M.; Harms, K.; Boche, G.; Hoppe, D. *Angew, Chem. Int, Ed.* **1995**. 34, 2158.

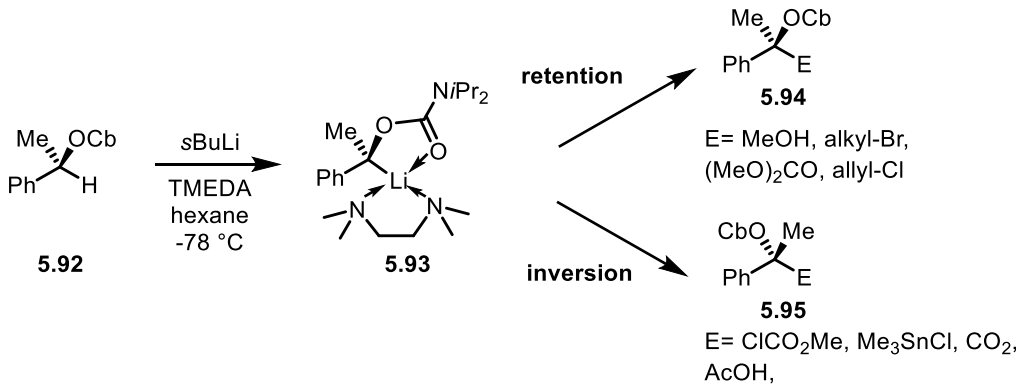
[27] Hoppe, D. *Synthesis* **2009**, 43.

[28] Zarges, W.; Marsch, M.; Harms, K., Koch, W., Frenking, G.; Boche, G. *Chem Ber.* **1991**, 124, 543. (b) Rein, K.; Goicoechea-Pappas, M.; Anklekar, T. V.; Hart, G. C.; Smith, G. A.; Gawley. R. E. *J. Am Chem. Soc.* **1989**, 111, 2211. (c) Meyers, A. I.; Guiles, J.; Warmus, J. S.; Gonzales, M. A. *Tetrahedron Lett.* **1991**, 32, 550.

lithiation[29], also enhances the configurational stability of organolithium compounds by lithium coordination (inset, Figure 5.15).[30] This internal lithium chelation, as well as coordination from chelating diamines such as TMEDA are proposed to retard intra and intermolecular Li migration.

In an early study, Hoppe found that configurationally stable lithiated benzylic carbamate **5.93** could be obtained from the corresponding enantioenriched benzylic carbamate by deprotonation with *s*-BuLi at low temperature in non-polar solvent and in the presence of

Scheme 5.16. Electrophile-dependent stereochemical outcome for benzyllithium electrophile trapping



a chelating diamine TMEDA (Figure 5.16).[31] Such species were confirmed to be configurationally stable based on their ability to undergo highly stereospecific reactions with electrophiles, producing enantioenriched products. In this and subsequent studies it was found that electrophilic trapping can proceed stereoretentively or invertively depending on the nature of the electrophile employed.[32]

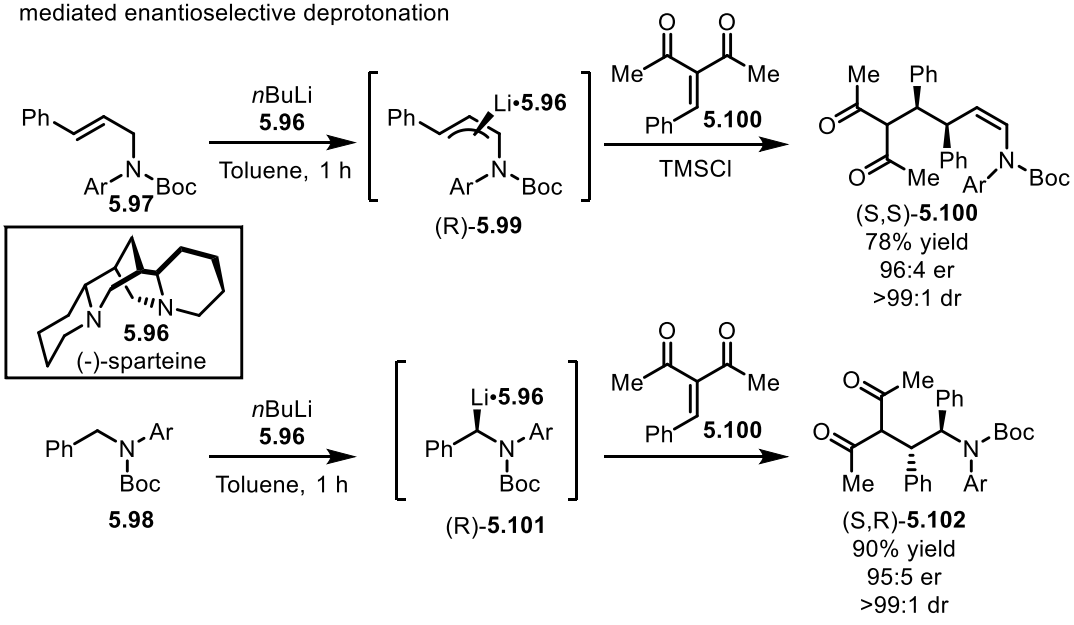
---

[29] (a) Beak, P.; McKinney, B. G. *J. Am. Chem. Soc.* **1977**, 99, 5213. (b) Hoppe, D.; Brönneke, A. *Tetrahedron Lett.* **1983**, 24, 1687. (c) Hoppe, D.; Brönneke, A. *Synthesis* **1982**, 1045.
[30] Hoffmamt, R. W.; Lanz. J.; Metternich, R.; Tarara, G.; Hoppe, D. *Angew. Chem. Int. Ed.* **1987**, 99, 119.
[31] Hoppe, D.; Carstens, A.; Kämer, T. *Angew. Chem. Int. Ed.* **1990**, 29. 1424.
[32] (a) Carstens, A.; Hoppe, D. *Tetrahedron* **1994**, 50, 6097. (b) Hammerschmidt, F. A.; Völlenkle, H. *Chem. Eur. J.* **1997**, 1728.

In addition to stereoretentive deprotonation of enantiomerically enriched molecules, enantioenriched organolithium reagents can also be accessed by stereoselective deprotonation of prochiral substrates mediated by chiral diamine ligands such as (-)-sparteine.[33] Beak demonstrated the utility of this approach for the stoichiometric preparation of configurationally stable allylic and benzylic organolithium compounds **5.99** and **5.101** as well as their use in diastereoselective conjugate addition reactions (Scheme 5.17).[34]

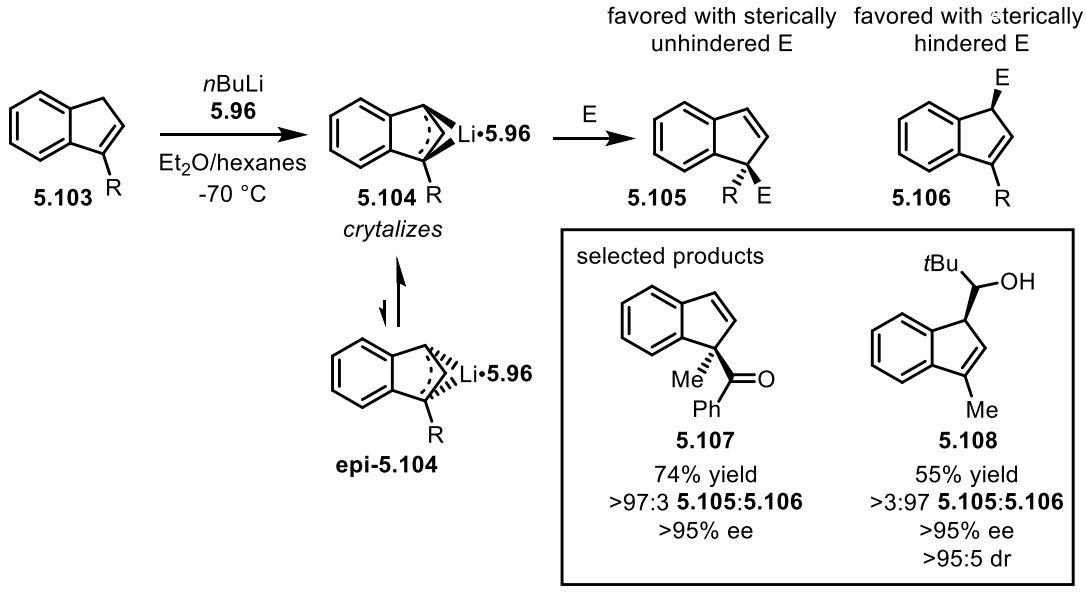
Hoppe later demonstrated that the presence of (-)-spartein during the formation of non-heteroatom-stabilized 1-substituted chiral lithiated indene **5.104** (Scheme 5.18) leads to the preferential crystallization of one diastereomer of lithium-diamine adduct over the other (**5.104** versus **epi-5.104)**, facilitating the formation of enantioenriched products upon

Scheme 5.17. Access to enantioenriched allylic and benzylic organolithium nucleophilic by (-)-sparteine-mediated enantioselective deprotonation



[33] Hoppe, D.; Hense, T. *Angew. Chem. Int. Ed*. **1997**, 36, 2282.
[34] Curtis, M. D.; Beak, P. *J. Org. Chem.* **1999**, 64, 2996.

Scheme 5.18. Acess to enantioenriched lithiated indene **5.104** by crystalization with (-)-sparteine

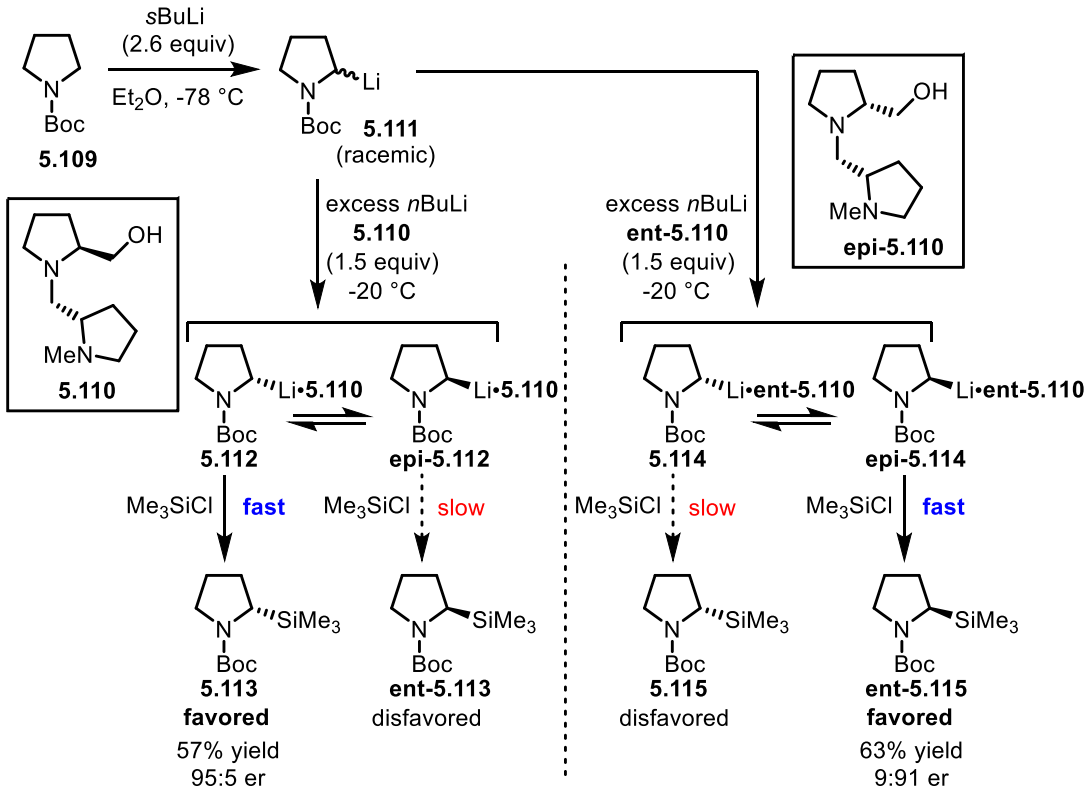


electrophilic trapping.[35] The enantio- and regioselectivity of these reactions was found to be excellent, with less sterically hindered electrophiles leading to bond formation at the more sterically hindered allylic carbon (**5.107**), while more sterically hindered electrophiles reacted at the less substituted position (**5.108**).

In addition to (-)-spartein-promoted kinetic deprotonation-lithiation and physical resolution by crystallization, Colhan demonstrated that stoichiometric chiral ligands can be used to promote the dynamic kinetic resolution of racemic 2-lithiated pyrroles (Figure. 5.19).[36] The half-life for racemization of *N*-Boc-2-lithiated pyrrole **5.111** in Et_2O has been determined to be 12.6 h and 26 min at -22 ˚C and -5 ˚C respectively.[37] The authors thus found that upon consecutive addition of chiral amino alcohol ligand **5.110** and TMSCl to

[35] Hoppe, I.; Marsch, M.; Harms, K.; Boche, G.; Hoppe, D. *Angew. Chem. Int. Ed.* **1995**, 34, 2158.
[36] Coldham, I.; Dufour, S.; Hazell, T. F. N.; Patel, J. J.; Sanchez-Jimenez, G. *J. Am. Chem. Soc.* **2006**, 128, 10943.
[37] Ashweek, N. J.; Brandt, P.; Coldham, I.; Dufour, S.; Gawley, R. E.; Haeffner, F.; Klein, R.; Sanchez-Jimenez, G. *J. Am. Chem. Soc*. **2005**, 127, 449.

Scheme 5.19. Dynamic kinetic resolution of *N*-Boc-2-lithiopyrrolidine using chiral aminoalcohols



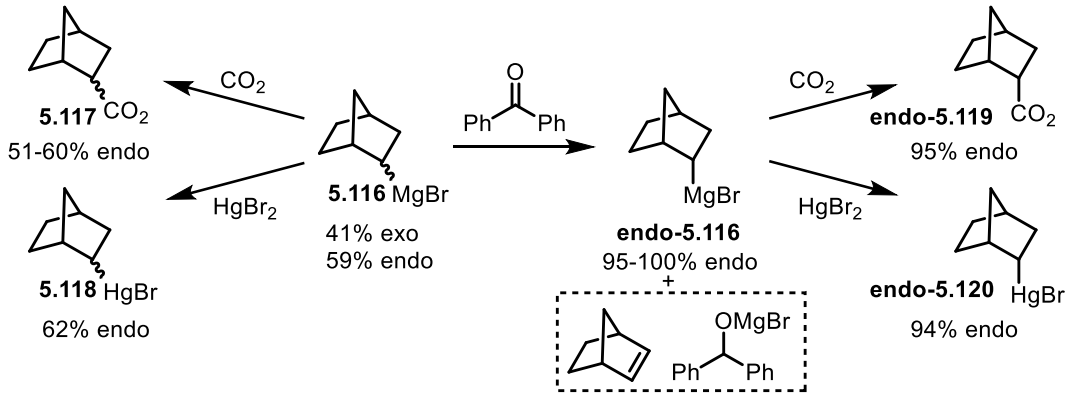
racemic **5.111,** α–amino silane **5.113** was obtained with significant enantioenrichment. This outcome was attributed to the formation of an interconverting mixture of diastereomeric complexes **5.112** and **epi-5.112,** one of which reacts faster with the added Me_3SiCl electrophile. The addition of excess *n*BuLi was found to be essential to ensure efficient raceimization of the Li-substituted stereogenic carbon center. By employing epimeric amino alcohol ligand **epi-5.110** the authors found that the opposite enantiomer of product could be obtained.

5.2.2.2 Mg-Substituted Stereogenic Carbon Centers

Due to the greater covalent character of the magnesium-carbon bond relative to the

lithium-carbon bond, Grignard reagents, in principle, should demonstrate greater configurational stability than the corresponding organolithium reagents. Yet, stereodefined organometallic compounds containing a Mg-substituted stereogenic carbon center have been much less studied than their lithium counterparts. An early report by Jensen and Nakamaye established that endo-norbornylmagnesium bromide (**endo-5.116**) could be generated in a stereoselective fashion by kinetic resolution.[38] Exploiting the greater reactivity of **exo-5.116** towards the reduction of benzophenone, the authors found they

Scheme 5.20. Kinetic resolution of diastereomeric norbornylmagnesium reagents

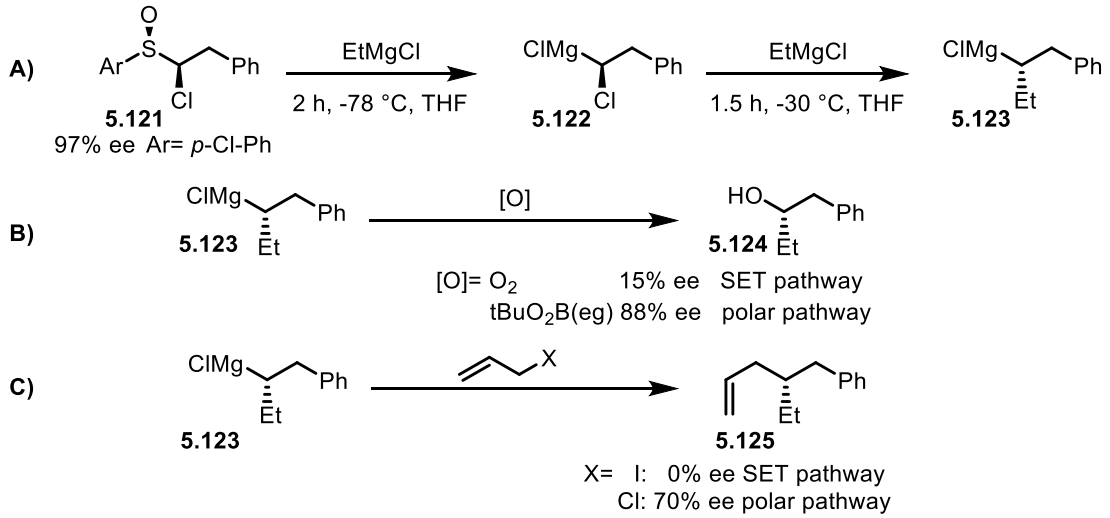


could generate nearly pure samples of **endo-5.116** which could be studied by ^{1}H NMR and trapped stereoretentively with carbon dioxide and mercury dibromide to furnish stereodefined products **endo-5.119** and **endo-5.120** respectively. Consistent with earlier ^{1}H NMR studies of by Whitesides[39] which established that secondary organomagnesium reagents undergo slow inversion at low temperature, the authors found that the equilibrium composition of **endo-** and **exo-5.116** was reestablished upon allowing a sample of **endo-5.116** to stand at room temperature for one day.

[38] Jensen, F. R.; Nakamaye, K. L. *J. Am. Chem. Soc.* **1966**, 88, 3437.
[39] Whitesides, G. M.; Roberts, J. D. *J. Am. Chem. Soc.* **1965**, 87, 4878.

Because enantioenriched organomagnesium compounds cannot be prepared from enantioenriched alkyl halides by treatment with magnesium metal or most magnesium-halide/magnesium-sulfoxide exchange reactions due to stereoablative single electron transfer processes and unfavorable thermodynamics respectively, access to this class of compounds has remained relatively restricted.[40] Hoffmann developed a straightforward method of generating one enantioenriched organomagnesium reagent by a sequence of magnesium sulfoxide exchange and carbenoid homologation of chiral α-chlorosulfoxide **5.121** with excess EtMgCl at low temperature (Figure 5.21).[41] Secondary alkyl Grignard reagent **5.123** was found to undergo a first-order racemization process at -10˚C with a half-life of 5 h.[42] The enantiospecificity of electrophilic trapping reactions of **5.123** was found to depend strongly on the identity of the electrophilic reagent employed and this behavior

Scheme 5.21. Stereochemical outcome of Mg-sulfoxide exchange and subsequent electrophile trapping



[40] Hoffmann, R. W. *Chem. Soc. Rev*. **2003**, 32, 225.
[41] Hoffmann, R. W.; Hölzer, B.; Knopff, O.; Harms, K. *Angew. Chem. Int. Ed*. **2000**, 39, 3072.
[42] (a) Hoffmann, R. W.; Hölzer, B.; Knopff, O. *Org. Lett*. **2001**, 3, 1945. (b) Hoffmann, R. W.; Hölzer, B. *Chem. Commun*. **2001**, 491. (c) Hoffmann, R. W.; Hölzer, B. *J. Am. Chem. Soc*. **2002**, 4204. (d) Hoffmann, R. W.; Hölzer, B. *Chem. Commmun*, **2003**, 732.

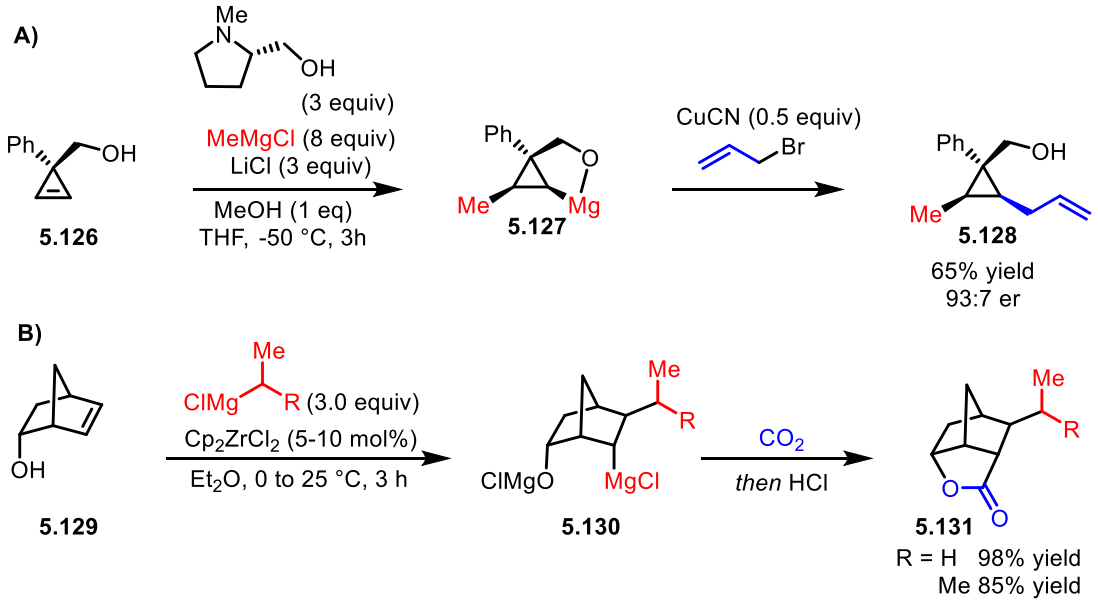
was attributed to the propensity of electrophiles to engage in single electron transfer (SET) or polar addition mechanisms (Figure 5.21.B/C).

In addition to kinetic resolution and stereospecific sulfoxide-magnesium exchange, stereospecific carbomagnesiation reactions provide a general strategy for the preparation of enantioenriched compounds containing a Mg-substituted stereogenic carbon center. In general unactivated carbon–carbon π-bonds do not readily react with organomagnesium and organozinc reagents, thus this class of reaction, though a potentially powerful approach to generating versatile stereodefined organometallic reagents, has generally been restricted to reactions with alkynes and highly strained cyclopropene substrates, often with electron withdrawing or directing groups.[43] While transition-metal complexes based on copper and iron have been found to catalyze such reactions, as will be described in the section that follows on Zn-substituted stereogenic carbon centers, the classes of substrates that can be engaged have largely remained restricted to substituted cyclopropene rings.

Two examples of stereoselective carbomagnesiation reactions are depicted in Scheme 5.22. Fox reported a chiral amino alcohol-promoted carbomagnesiation of cyclopropene **5.126** (Scheme 5.22.A).[44] The authors found that addition of various electrophiles including proton, I_2, CO_2, DMF, $(PhS)_2$ and allybromide with copper cyanide as catalyst subsequent to the carbomagnsiation reaction afforded cyclopropane products such as **5.128** with excellent enantiomeric purity as a single diastereomer. While reactions utilizing MeMgCl were found to result in high yields and enantioselectivities, the use of other

[43] For an excellent review on transition-metal-catalyzed intermolecular carbomagnesiation and carbozincation please see Murakami, K.; Yorimitsu, H. *Beilstein J. Org. Chem*. **2013**, 9, 278.
[44] Liu, X.; Fox, J. M. *J. Am. Chem. Soc*. **2006**, 128, 5600.

Scheme 5.22. Alcohol-promoted and Zr-catalyzed carbomagnesiation and stereospecific electrophile trap



organomagnesium reagents resulted in substantially diminished enantioselectivities. Hoveyda and Morken reported a regio- and stereoselective zirconocene dichloride-catalyzed carbomagnesation of alkene **5.129** (Scheme 5.22.B).[45] Notably this reaction proceeds with relatively unstrained 5-membered cyclic alkenes. The authors found that the alcohol group of **5.129** acts as an internal Lewis base, dramatically enhancing the reactivity and selectivity of the reaction such that less reactive secondary alkyl Grignard reagents could be used. The authors demonstrated that organomagnesium intermediate **5.130** is likely formed by an invertive Zr-to-Mg transmetallation and that **5.130** can be stereospecifically functionalized with CO_2 to form **5.131**.

5.2.2.3 Zn-Substituted Stereogenic Carbon Centers

Organozinc compounds are versatile reagents in organic synthesis. Due to the greater

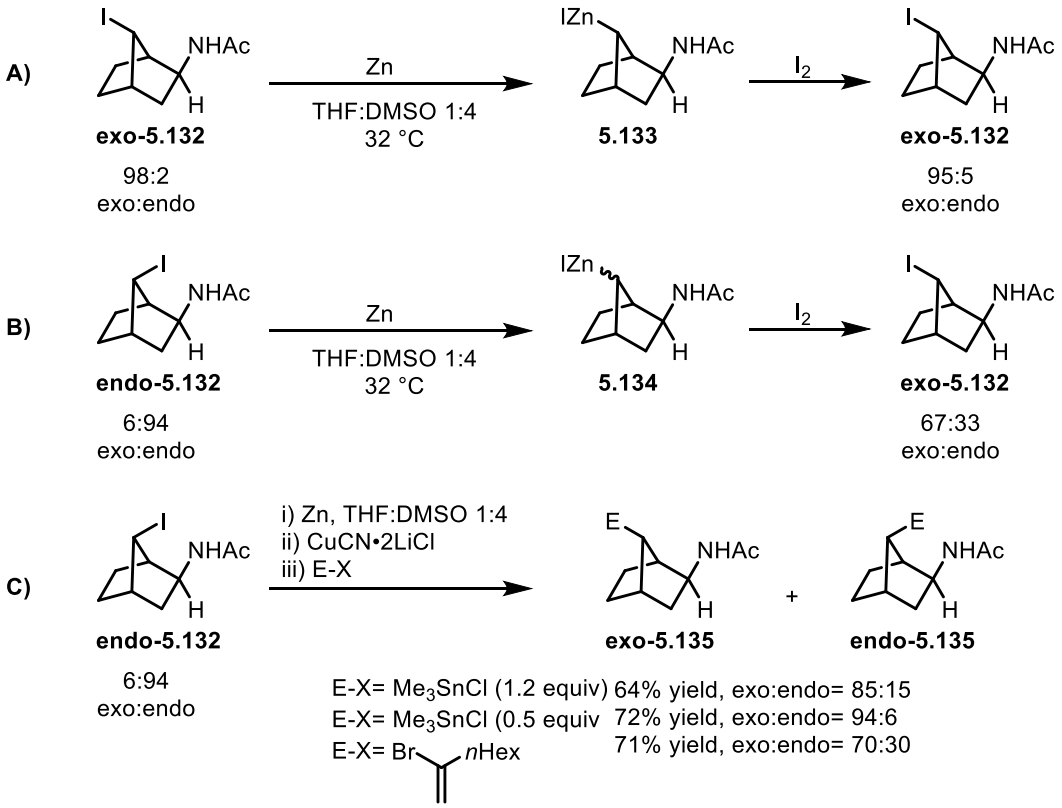
[45] Hoveyda, A. H.; Morken, J. P.; Houri, A. F.; Xu, Z. *J. Am. Chem. Soc*. **1992**, 114, 6692.

covalent character of the carbon–zinc bond, organozinc reagents serve as functional group tolerant nucleophiles in reactions such as cross-couplings and conjugate additions. Perhaps owing to the limited synthesis methods known for the preparation of compounds containing zinc-substituted stereogenic carbon centers, the configurational stability of such compounds has not been well studied. The limited reports available have generally focused on cyclic molecules bearing other stereogenic carbon centers, or on compounds with elements of strain that complicate a thorough understanding of the configurational stability and reactivity of these compounds.

One of the earliest studies concerning the generation and reactivity of stereodefined organozinc compounds was reported by Knochel in 1994 (Figure 5.23.A/B).[46] In the report, the authors found that treatment of exo- and endo-norbornyl iodide electrophiles **exo-5.132** (Scheme 5.23.A) and **endo-5.132** (Scheme 5.23.B) with zinc metal followed by treatment with iodine, resulted in the formation of secondary iodide compound **exo-5.132** with predominately exo configuration. The fact that the reaction of exo- and endo-**5.132** resulted in alkyl iodide products with different ratios of endo:exo diastereomers was interpreted as an indication that zinc insertion into the carbon–iodine bond is a stereospecific process as is the subsequent electrophilic trapping with iodine. While the degree of stereospecificity of Zn insertion, the rate of stereomutation of Zn-substituted stereogenic carbon centers, and the degree of stereospecificity involved in electrophilic trapping of these organometallic intermediates was not extensively explored, the ratio of exo:endo products

[46] Duddu, R.; Eckhardt, M.; Furlong, M.; Knoess, H. P.; Berger, S.; Knochel. P. *Tetrohedron* **1994**, 50, 2415.

Scheme 5.23. Knochel's seminal study on the configurational stability of organozinc reagents

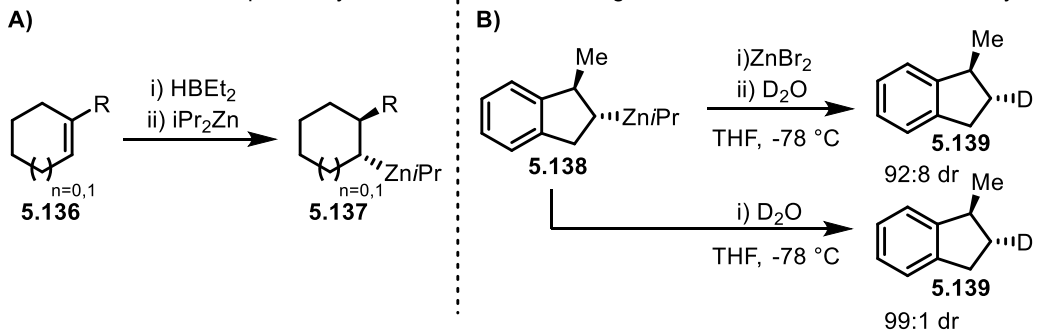


observed for electrophile trapping experiments was found to depend on electrophile identity and concentration Figure (5.23.C).

Knochel later reported a highly diastereoselective method of preparing secondary organozinc compounds by a sequence of highly regio- and diastereoselective hydroboration of cyclic trisubstituted alkenes followed by stereoretentive boron-to-zinc transmetallation (Figure 5.24.A).[47] A subsequent publication by the same authors more thoroughly explored the configurational stability of these compounds and their ability to

[47] Boudier, A.; Hupe, E.; Knochel, P. *Angew. Chem. Int. Ed*. **2000**, 39, 2294.

Scheme 5.24. Stereospecific hydroboration/B-Zn exchange and errosion of diastereoselectivity with $ZnBr_2$

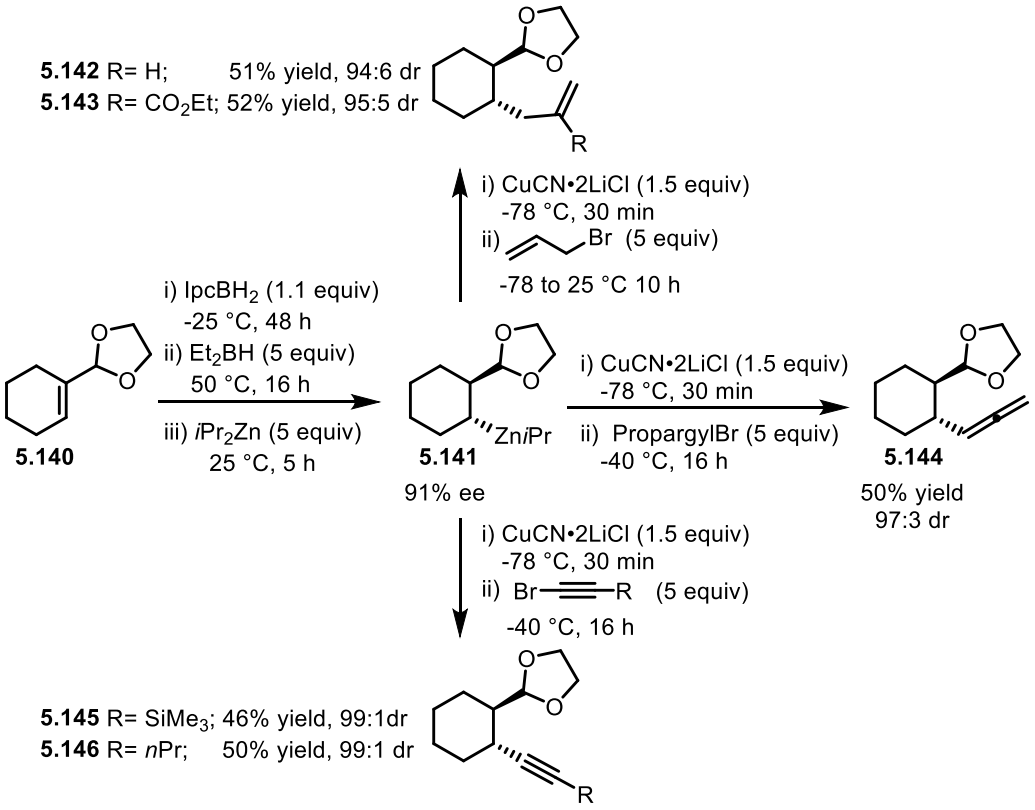


engage in stereospecific electrophile trapping reactions (Figure 5.24.B).[48] The authors found, by deuterium trapping experiments, that a small degree of erosion of dr was observed when $ZnBr_2$ was added to the reaction solution (Figure 5.24.B), but that a secondary alkylzinc species such as **5.138** appeared to be quite configurationally stable even at elevated temperatures. The potential role of the adjacent methyl-substituted stereogenic carbon center in reinforcing the configuration of the zinc-substituted stereogenic carbon was not thoroughly explored. The presence of an adjacent methyl stereocenter might destabilize the transition state involved in epimerization thus leading to kinetic stabilization (persistence). Alternatively, because epimerization of the Zn-substituted stereogenic center would lead to the formation of the contra-thermodynamic diasteriomer of **5.137/5.138**, even if such stereomutation were kinetically accessible, the configuration of the Zn-substituted center might be maintained due to dynamic configurational stability.

In the same and subsequent reports the authors found that utilizing enantioenriched hydroboration reagent (-)-$IpcBH_2$ enabled this method to be rendered enantioselective,

[48] Boudier, A.; Darcel, C.; Flachsmann, F.; Micouin, L.; Oestreich, M.; Knochel, P. *Chem. Eur. J.* **2000**, 6, 2748.

Scheme 5.25. Enantioselective reactions by asymmetric hydroboration/B-Zn exchange sequence

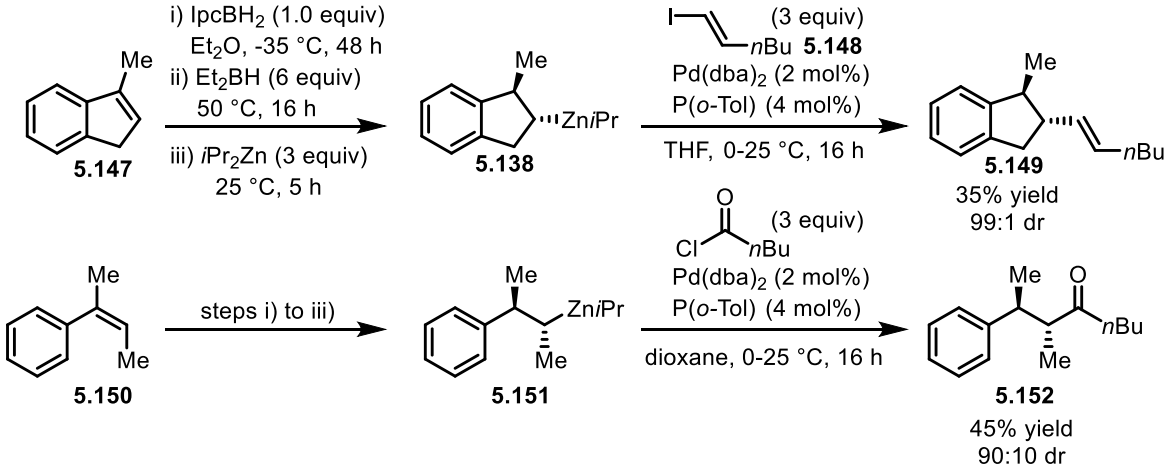


facilitating the preparation of enantioenriched alkylzinc nucleophiles such as **5.141** which were demonstrated to participate in a variety of copper-promoted coupling reactions with allylic, alkynyl, and propargylic bromide electrophiles (Figure 5.25).[49] This approach was also demonstrated to be an effective method of preparing enantioenriched organozinc nucleophiles which participate in stereospecific cross-coupling and acylation reactions catalyzed by phosphine-ligated palladium complexes (Figure 5.26).

Reike reported an elegantly designed ^{1}H NMR study of the configurational stability of non-stabilized secondary organozinc compounds which found that such Zn-substituted

[49] Hupe, E.; Knochel, P. *Angew. Chem. Int. Ed.* **2001**, 40, 3022.

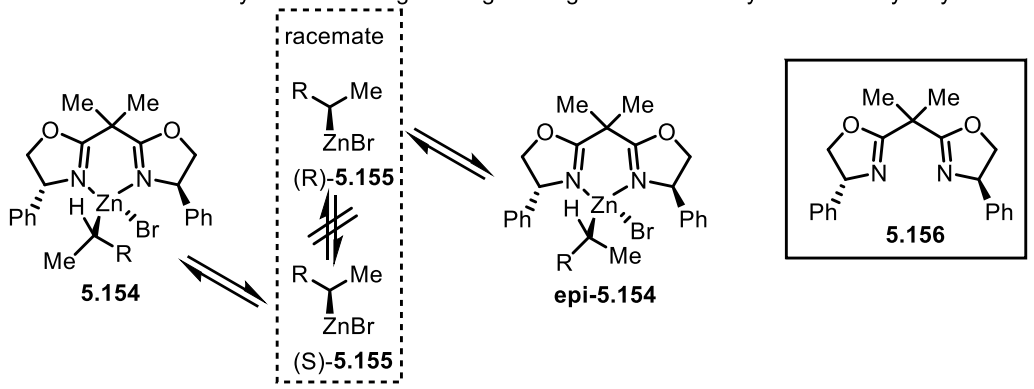
Scheme 5.26. Enantioselective preperation and coupling of cyclic and acyclic organozinc nucleophiles



stereogenic carbon centers are configurationally stable at room temperature.[50] The ability of an enantioenriched chiral bis(oxazoline) ligand **5.156** to convert the enantiomers of the chiral compound **5.155** into diastereomeric complexes **5.154** and **epi-5.154** which can be distinguished by ^{1}H NMR, was utilized to determine the rate of raceimization of **5.155**.

Håkannson has reported an intriguing method of preparing enantioenriched indenyl organozinc complex **5.159** utilizing total spontaneous resolution by crystallization (Scheme 5.28).[51] By exploiting the stereochemical lability of benzylic/allylic organozinc

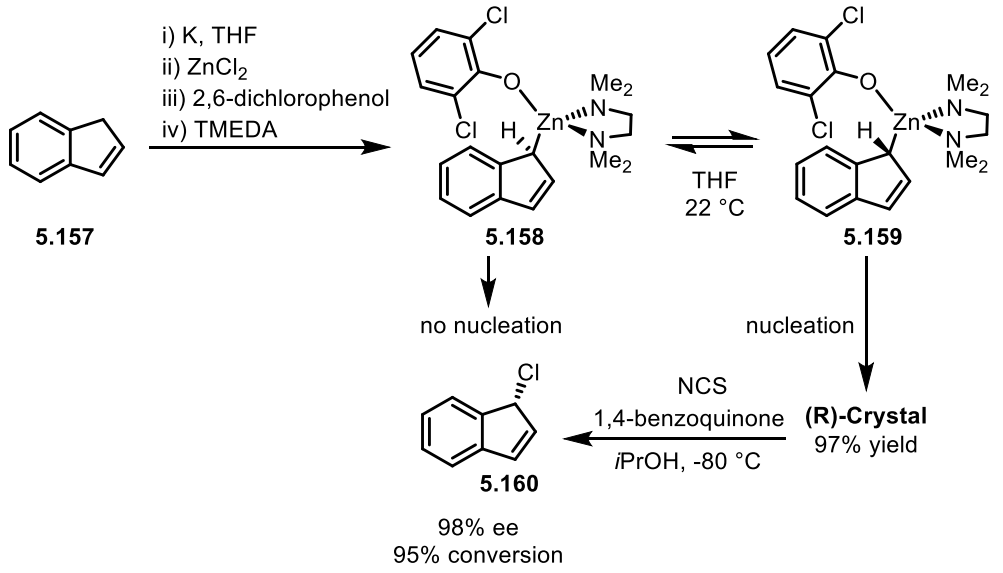
Scheme 5.27. NMR study demonstrating the high configurational stability of secondary alkylzinc reagents.



[50] Guijarro, A.; Rieke, R. D. *Angew. Chem. Int. Ed.* **2000**, 39, 1475.
[51] Olsson, S.; Lennartson, A.; Håkansson, M. *Chem. Eur. J.* **2013**, 19, 12415.

compound **5.158** in solution, combined with the greater propensity of the homo-dimers of this compound to undergo crystallization, enantioenriched crystalline samples of **5.159** were prepared. The authors found that while **5.159** racemized quickly in a THF solution at low temperature, by carefully controlling the conditions in which crystalline samples of **5.159** were quenched with the chlorinating reagent NCS, enantioenriched benzylic chloride **5.160** could be formed with nearly perfect enantiospecificity. Notably, the use of the radical

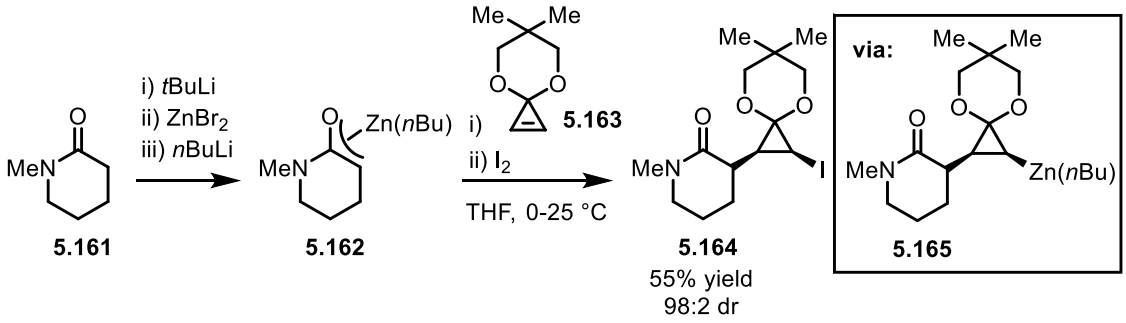
Scheme 5.28. Asymmetric synthesis of enantiopure organozinc reagents and enantiospecific chlorination.



inhibitor 1,4-benzoquinone as well as protic solvents was found to be essential to ensure the highest degree of enantiospecificity. This report demonstrates that while π-systems adjacent to a zinc-substituted stereogenic carbon center provide thermodynamic stabilization, they simultaneously reduce the configurational stability of such compounds.

While the zinc enolates of esters and amides such as **5.161** generally exhibit low reactivity towards carbozincation of unactivated alkenes, Nakamura has demonstrated that these compounds are capable of reacting efficiently with strained cyclopropenone acetal

Scheme 5.29. Diastereoselective cis-addition of zincated amides to cyclopropene **5.163**.

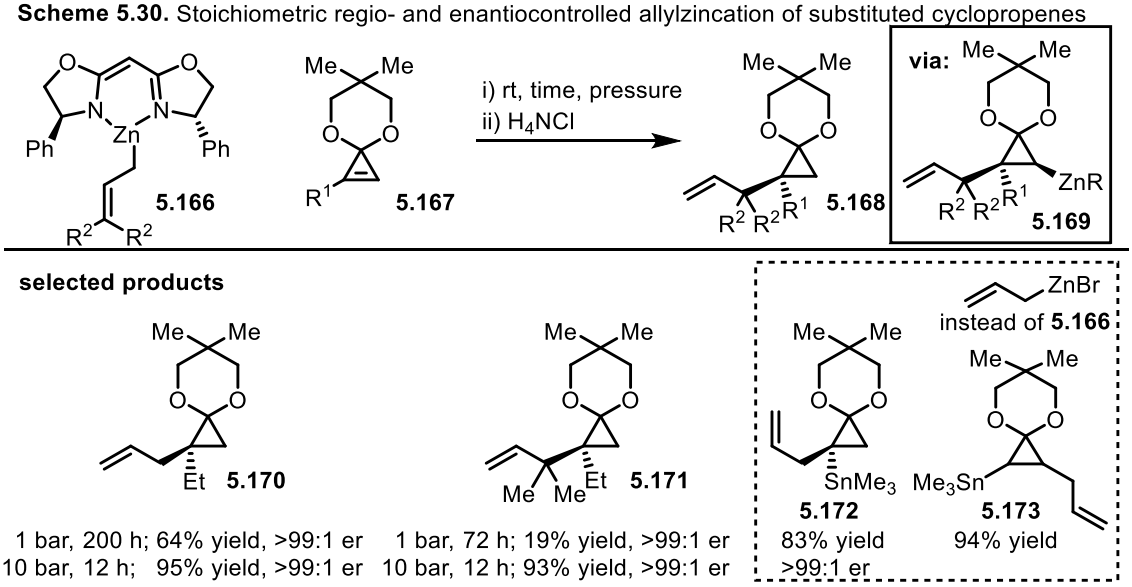


5.163 (Scheme 5.29).[52] The authors demonstrated that zincated lactam **5.162** could react in a diastereospecific manner to produce cyclopropylzinc species **5.165** which exhibited sufficient configurational stability such that the derived alkyl iodide **5.164** could be isolated with excellent diastereomeric enrichment. This reaction appears to be driven primarily by relief of strain in converting **5.163** to **5.165**, while the configurational stability of **5.165** appears to be consistent with the simple unactivated alkylzinc reagents previously described by Reiki.

Nakamura later demonstrated that allylzincation of substituted cyclopropenone acetals with chiral bis(oxazoline)-allylzinc reagents **5.166** can be used as a means to stoichiometrically prepare enantio- and diastereoenriched cyclopropylzinc reagents (Scheme 5.30).[53] While the stereochemical stability of the intermediate alkyzinc species **5.169** (inset) formed before protonation was not investigated, the authors noted an intriguing rate acceleration when the reaction was run under elevated pressure (1 bar versus 10 bar). The authors also noted that the inherent regioselectivity of the allylzincation of trimethylstannane-substituted cyclopropane substrates favored formation of the

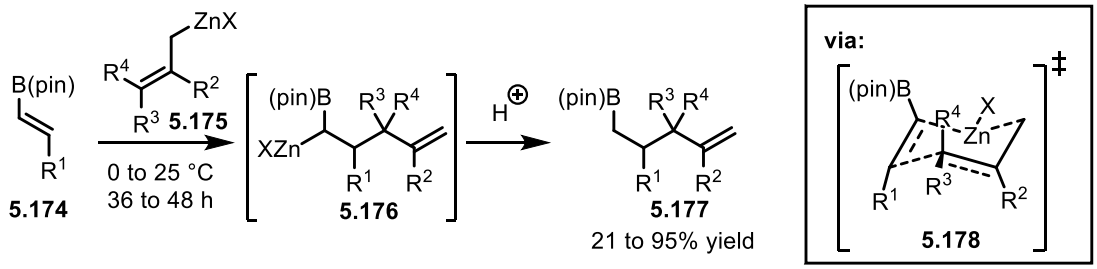
[52] Nakamura, E.; Kubota, K. *J. Org. Chem.* **1997**, 62, 792.
[53] Nakamura, M.; Inoue, T.; Sato, A.; Nakamura, E. *Org. Lett.* **2000**, 2, 2193.

Scheme 5.30. Stoichiometric regio- and enantiocontrolled allylzincation of substituted cyclopropenes



regioisomer **5.173** in which an α-stannyl alkylzinc intermediate is formed, while use of chiral zinc reagent **5.166** inverted this regioselectivity (**5.172** verses **5.173**, inset) due to steric factors. The inherent regioselectivity of the reaction was attributed to the ability of the trialkylstannane moiety to stabilize negative charge buildup on an adjacent carbon. This stabilizing effect was later exploited by the same authors to expand the alkene substrate classes that can be engaged in allylzincation reactions from strained cyclopropenes to alkenylboron reagents (Scheme 5.31).[54] The initially formed α-boryl alkylzinc products

Scheme 5.31. Nakamura's stoichiometric regioselective allylzincation of alkenyl boron reagents

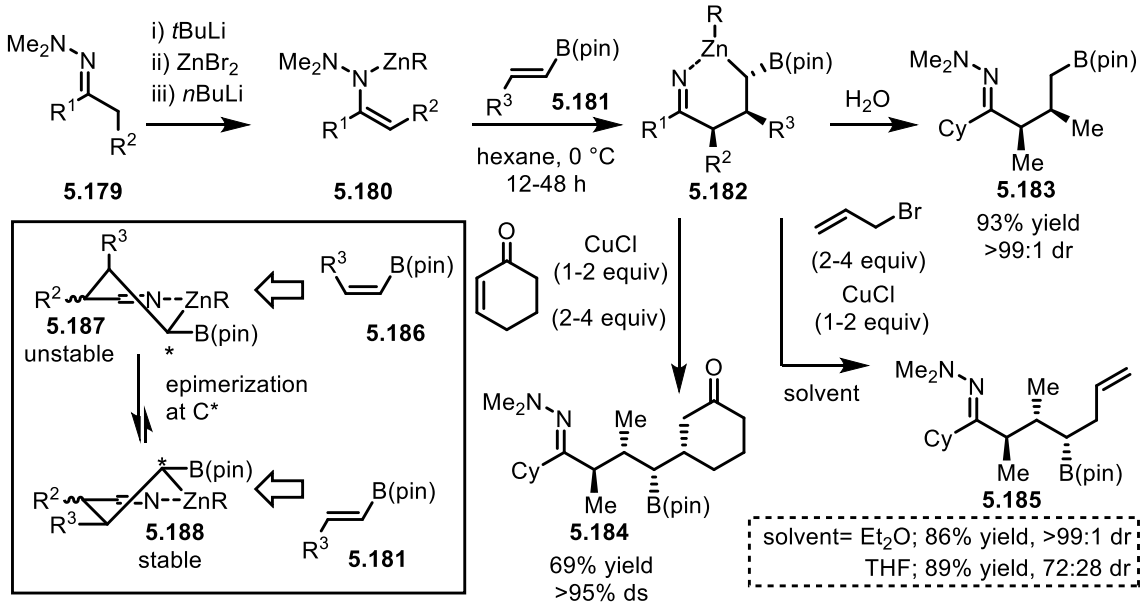


[54] Nakamura, M.; Hara, K.; Hatakeyama, T.; Nakamura E. *Org. Lett.* **2001**, 3, 3137.

5.176 generated during these reactions were isolated as the corresponding protonated species **5.177** in generally high yield (>80% yield) when diorganozinc nucleophiles (X= *n*Bu) were employed in the reaction. DFT calculations were used to support the involvement of a key 6-memebered transition state **5.178** (inset) in which the empty p orbital on boron facilitates charge stabilization.

As depicted in Scheme 5.32 the Nakamura group has demonstrated in subsequent studies that zincated hydrazine nucleophiles can engage in diastereoselective addition reactions to alkenylboronic esters and that the α-boryl alkylzinc bimetallic intermediates **5.182** thus generated can be engaged in stereospecific electrophile trapping reactions.[55] These reports not only lend further evidence that a boron moiety can facilitate

Scheme 5.32. Diastereoselective addition of zincated hydrazones to alkenylboronates and electrophile trap



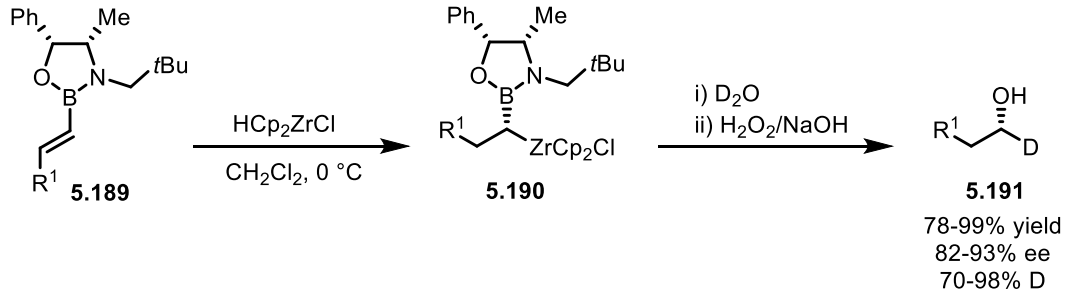
[55] (a) Nakamura, M.; Hara, K.; Fukudome, H.; Nakamura, E. *J. Am. Chem. Soc*. **2004**, 126, 14344. (b) Hatakeyama, T.; Nakamura, M.; Nakamura, E. *J. Am. Chem. Soc.* **2008**, 130, 15688.

carbometallation reactions of unstrained acyclic alkenes but that factors such as solvent polarity can play a role in the stereospecificity of trapping reactions of stereochemically well-defined α-boryl alkyl organometallic reagents (see bottom right hand corner dotted inset for **5.185**). The authors found that under the reaction conditions employed, epimerization of the α-boryl zinc-substituted stereogenic carbon center occurred readily and was primarily controlled by the conformational stability of the 6-membered chelate structure of the product (**5.187** versus **5.188**, inset). Thus the Zn-substituted stereogenic carbon centers of these compounds do not possess persistent configurational stability but rather exhibits dynamic configurational stability which is imposed by the other stereogenic carbon centers in these molecules.

5.2.2.4 Zr-Substituted Stereogenic Carbon Centers

In what is perhaps the earliest example of an enantioselective hydrozirconation reaction Shrebnik reported that reacting Schwartz's reagent with alkenylboron **5.189** bearing an enantioenriched chiral amino alcohol ligand resulted in the formation of enantioenriched α-boryl alkylzirconium intermediates **5.190** which could be trapped stereospecifically with

Scheme 5.33. Srebnik's diastereoselective hydrozirconation-deuteriation of alkenyl boronates



deuterated water (Scheme 5.33).[56] Upon oxidation, the deuterated primary alcohols were shown to possess a high degree of deuterium content and enantioenrichment. It is unclear from the available data if α-boryl alkylzirconium species such as **5.190** possess static configurational stability (persistence) or if the presence of the chiral diamine ligand on boron reinforces the configuration of the zirconium-substituted α-boryl stereogenic carbon center (dynamically stable) by destabilizing the alternative diastereomeric geminal diorganometallic species.

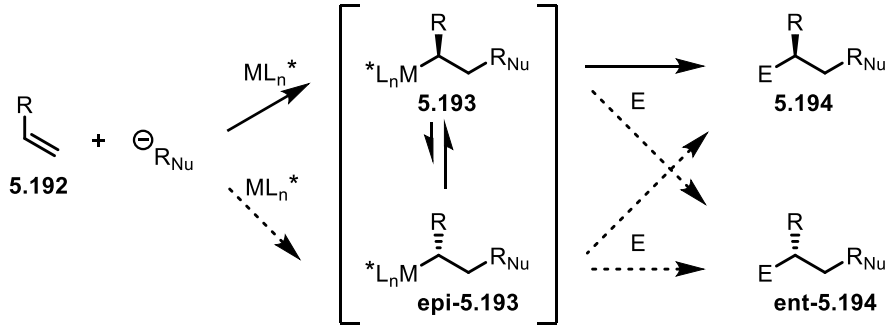
5.2.3 Catalytic Generation of Stereodefined Organometallic Nucleophiles as Catalytic Intermediates

In addition to the stoichiometric preparation of stereodefined organometallic reagents, these species are also generated in catalytic reactions in which they exist as transient intermediates. The vast majority of these reactions involve the use of transition metal complexes which, during the course of the reaction, are bonded to the metal-substituted stereogenic carbon center. Because stereochemically-defined organometallic intermediates are generated in catalytic quantities and are subsequently consumed to turn over the catalytic cycle, these species need only be configurationally stable over a relatively short period of time relative to stoichiometrically-prepared reagents. Additionally, for reactions where the catalytic transition metal complex employed in the reaction possesses chiral ligands, the epimerization of the metal-substituted stereogenic carbon center involves the generation of a diastereomeric organometallic complexes of inequivalent thermodynamic

[56] Pereira, S.; Srebnik, M. *Tetrahedron Lett*. **1994**, 35, 6247.

stability and which may react with electrophilic species at dissimilar rates. For example, Scheme 5.34. depicts a hypothetical example of an enantioselective carbometallation-electrophile trapping reaction in which an enantioenriched organometallic species **5.193** is generated as a catalytic intermediate. As is the case for stoichiometrically prepared enantioenriched organometallic reagents, the overall stereochemical outcome of the reaction depends on the initial enantioselectivity of the conjugate addition reaction (**5.192** to **5.193** or **epi-5.193** as well as the stereospecificity of the electrophilic trapping step (**5.193** to **5.194** or **epi-5.194**). Unlike related stoichiometric cases, organometallic intermediates **5.193** and **epi-5.193** are diastereomers by virtue of the chiral ligands on the

Scheme 5.34. Possible stereochemical scenario for catalytically-generated chiral organometallic species

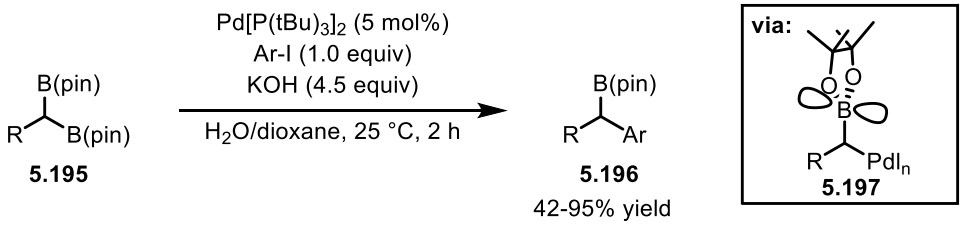


catalyst and thus the rate of reaction of these species with electrophiles is inequivalent. In one scenario the presence of the chiral ligand on the catalytic intermediate **5.193** may enforce kinetic stereochemical stability (persistence) by destabilizing the transition state for epimerization (**5.193** to **epi-5.193**) leading to a non-Curtin Hammett situation. Conversely, in a Curtin Hammett scenario where the rate of electrophile trapping is slow relative to epimerization, the ligands on the metal centers of **5.193** and **epi-5.193** will cause electrophilic trapping to proceed by diastereomeric transition states, thus providing enantioselectivity in the reaction without enforcing the stereochemical stability of the chiral

organometallic intermediates involved in the reaction.

Of the reactions reported to generate species with metal-substituted stereogenic carbon centers as catalytic intermediates, those that involve α-boryl organometallic species are of particular interest and will serves as a focus for the current discussion. Catalytic cross-coupling of geminal diboron reagents with aryl[57], alkenyl[58], and allyl[59] electrophiles employing palladium-phosphine complexes has attracted interest recently and provides a means of accessing α-boryl palladium species as catalytic intermediates. In his seminal report on the cross-coupling of geminal diboron reagents (Scheme 5.35),[56a] Shibata attributed the ease of transmetallation and lack of competitive β-hydride elimination observed for this class of coupling partner relative to other alkylboronic esters to the

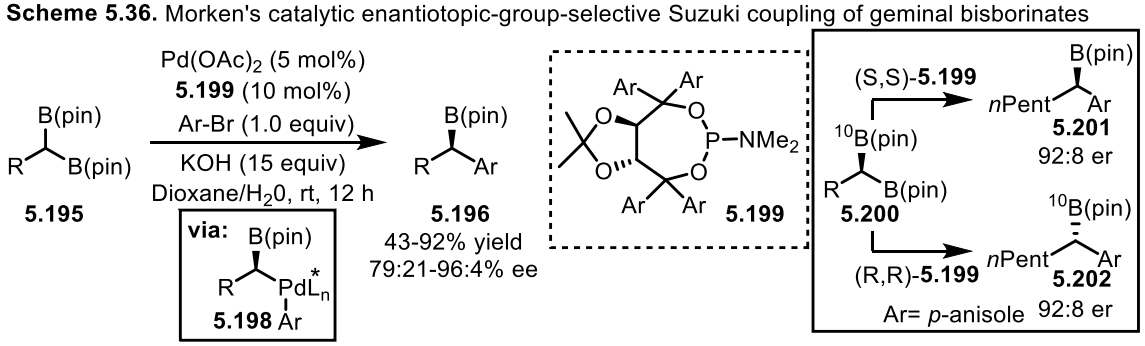
Scheme 5.35. Shibata's seminal Pd-diphosphine-catalyzed Suzuki-Miyaura Coupling of 1,1-diboron reagents



stabilizing influence of the p orbital of boron in key catalytic intermediate **5.197** (inset). Our group has reported a related enantioselective Suzuki-Miyaura cross-couplings of geminal diboron reagents (Scheme 5.36).[56c] $^{11}B/^{10}B$ Isotope labeling experiments (inset) support a mechanism in which transmetallation occurs enantioselectively and the enantioenriched α-boryl alkylpalladium species (**5.198**, inset) formed during the reaction

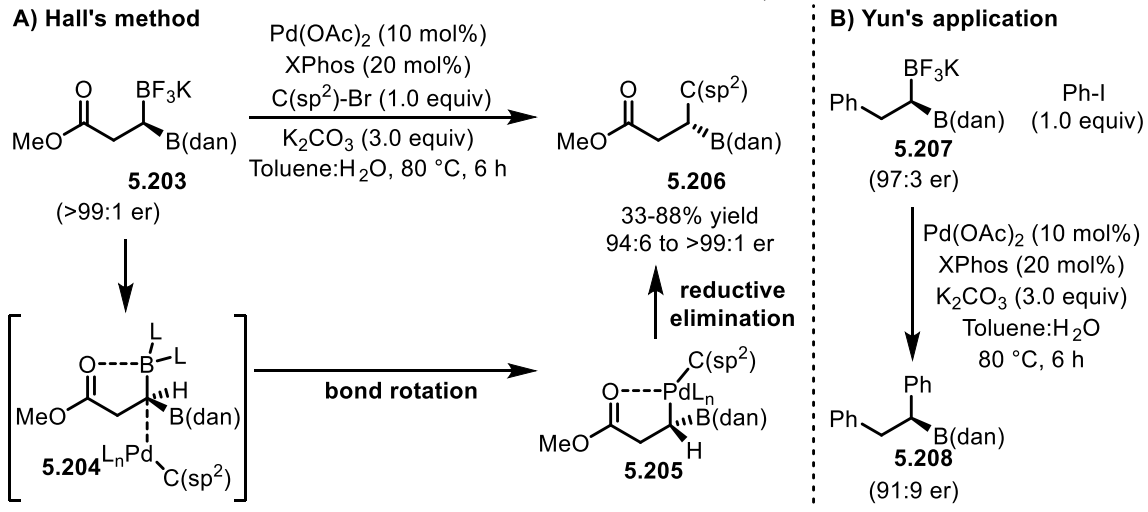
[57] (a) Endo, K.; Ohkubo, T.; Hirokami, M.; Shibata, T. *J. Am. Chem. Soc.* **2010**, 132, 11033. (b) Endo, K.; Ishioka, T.; Ohkubo, T.; Shibata, T. *J. Org. Chem*. **2012**, 77, 7223. (c) Sun, C; Potter, B.; Morken, J. P. *J. Am. Chem. Soc.* **2014**, 136, 6534.
[58] Potter, B.; Szymaniak, A. A.; Edelstein, E. K.; Morken, J. P. *J. Am. Chem. Soc*. **2014**, 136, 17918.
[59] Endo, K.; Ohkubo, T.; Ishioka, T.; Shibata, T. *J. Org. Chem*. **2012**, 77, 4826.

Scheme 5.36. Morken's catalytic enantiotopic-group-selective Suzuki coupling of geminal bisborinates



is configurationally stable over the amount of time required for reductive elimination to occur. Hall has reported a stereospecific Suzuki cross-coupling of enantioenriched geminal hetero diboron reagents (Scheme 5.37.A).[60] Because the Pd-phosphine catalyst employed in these reactions is achiral, the high degree of stereospecificity observed indicates that the α-boryl alkylpalladium intermediate **5.205** formed during the course of the reaction is configurationally persistent. Yun reported that the coupling reaction of a related enantioenriched hetero geminal diboron reagent **5.207** under the same reaction conditions

Scheme 5.37. Hall's stereospecific Suzuki coupling of enantioenriched γ-carbonyl geminal diboron reagents

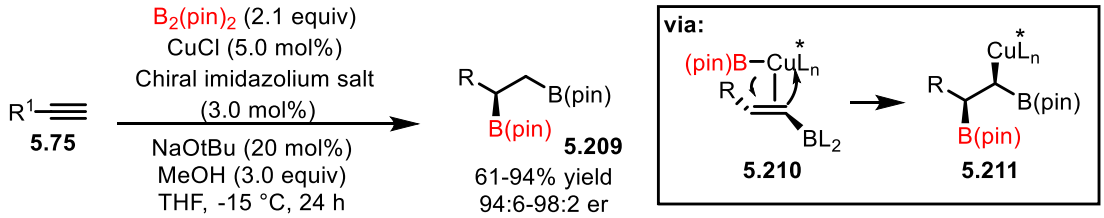


[60] Lee, J.; McDonald, R.; Hall, D. *Nat. chem.* **2011**, 894.

proceeds with significant erosion of enantioenrichment (Scheme 5.37.B).[61] Whether the lower degree of stereospecificity in this coupling is due to a competition between invertive versus retentive transmetallation mechanisms or due to a lower degree of configurational stability of the α-boryl alkylpalladium intermediate formed before reductive elimination was not discussed.

A pioneering study by Hoveyda on the enantioselective NHC–Cu-catalyzed double protoboration of terminal alkynes to furnish enantioenriched 1,2-diboron compounds **5.209** has demonstrated that α-boryl alkylcopper species such as **5.211** (inset) can be catalytically generated (Scheme 5.38).[62] In combination with subsequent reports on the NHC–Cu-catalyzed protoboration of aryl-[63] and silyl-substituted[64] alkenes, the same authors concluded that the directing ability of various groups for the formation of α-R alkylcopper species occurs in the order R = B(pin) > aryl > silyl > alkenyl. While the stereochemical stability of the α-boryl alkylcopper catalytic intermediate **5.211** was not directly probed, related benzylic alkylcopper species were shown to undergo highly stereospecific retentive protonation reactions suggesting these species do not racemize before catalytic turnover by

Scheme 5.38. Hoveyda's enantioselective NHC-Cu-catalyzed double boron additions to terminal alkynes

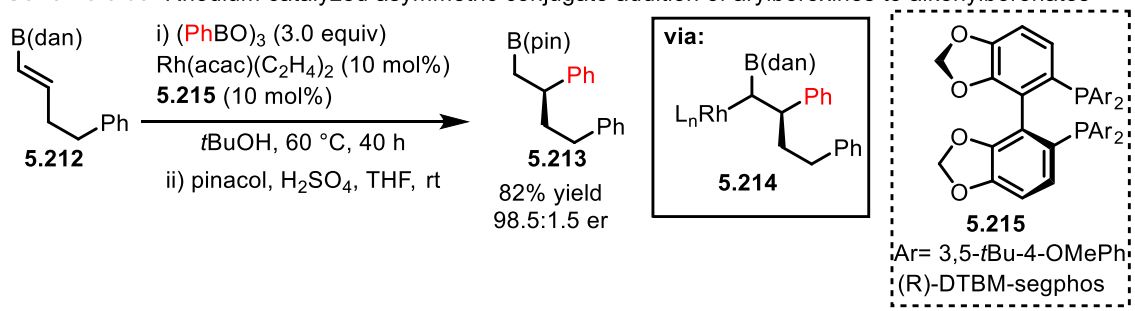


[61] Feng, X.; Jeon, H.; Yun, J. *Angew. Chem., Int. Ed*. **2013**, 52, 3989.
[62] Lee, Y.; Jang, H.; Hoveyda, A. H. *J. Am. Chem. Soc*. **2009**, 131, 18234.
[63] (a) Lee, Y.; Hoveyda, A. H. *J. Am. Chem. Soc.* **2009**, 131, 3160. (b) Corbern, R.; Mszar, N. W.; Hoveyda, A. H. *Angew. Chem. Int. Ed*. **2011**, 50, 7079.
[64] See reference 4c.

reacting with a proton source.[62] Related enantioenriched benzylic copper species generated in the diphosphine-Cu-catalyzed hydroboration reactions of styrenes have also been shown to undergo highly stereospecific transmetallation with HB(pin) to furnish enantioenriched benzylic boronic esters.[65]

Hayashi has reported an enantioselective diphosphine–rhodium-catalyzed conjugate addition of arylboroxine nucleophiles to alkenylboron reagents (Scheme 5.39).[66] The reaction is proposed to proceed *via* an enantioenriched α-boryl rhodium intermediate 5.214

Scheme 5.39. Rhodium catalyzed asymmetric conjugate addition of arylboroxines to alkenylboronates

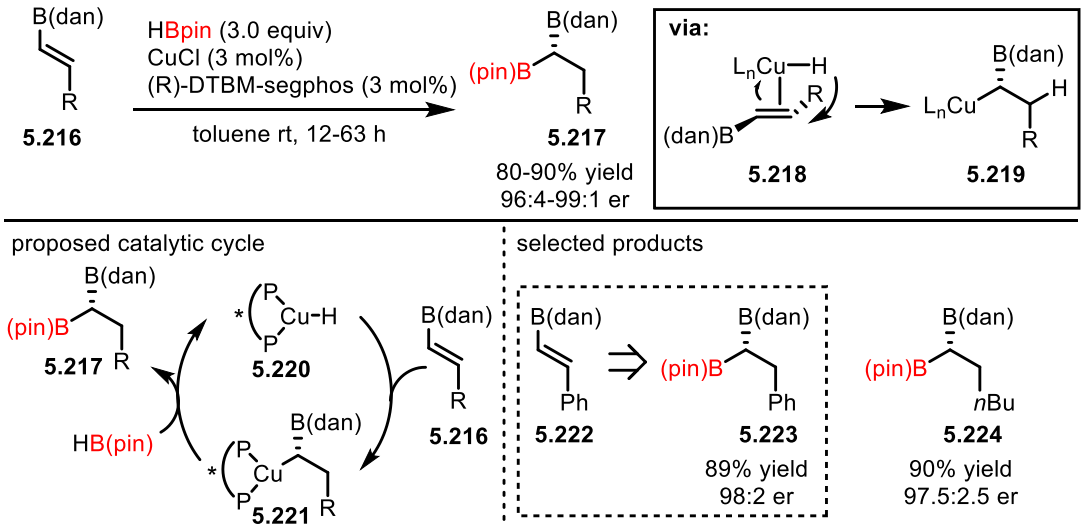


(inset) though the configurational stability of the Rh-substituted stereogenic center was not investigated.

Yun has reported a diphosphine–Cu-catalyzed hydroboration of alkenylboron reagents which allows access to enantioenriched germinal diboron compounds (Scheme 5.40).[67] The ability of the boron substituent to direct the regioselectivity of Cu-H addition (**5.216** to **5.217**, inset) is exemplified by the efficient preparation of β-phenyl geminal diboron compound **5.223**. The same authors later reported an enantioselective diphosphine–Cu-catalyzed hydroallylation reaction of alkenylboron reagents (Scheme 5.41). The reaction

[65] Noh, D.; Chea, H.; Ju, J.; Yun, J. *Angew. Chem. Int. Ed.* **2009**, 48, 6062.
[66] Sasaki, K.; Hayashi, T. *Angew. Chem. Int. Ed*. **2010**, 49, 8145
[67] Feng, X.; Jeon, H.; Yun, J. *Angew. Chem. Int. Ed*. **2013**, 52, 3989.

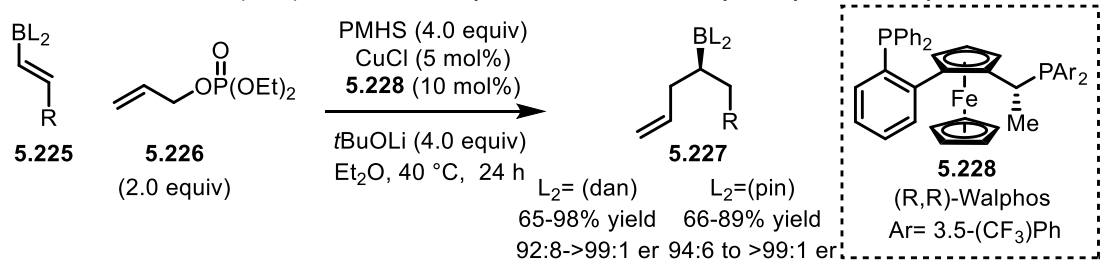
Scheme 5.40. Yun's diphosphine-Cu-H-catalyzed enantioselective hydroboration of alkenyl B(dan)



mechanism was proposed to be the same as the previously reported hydroboration reaction, differing only in the nature of the electrophile employed in the reaction. A ferrocene-based Walphos ligand **5.228** was found to be superior in terms of yield and enantioselectivity to the previously employed DTBM-Segphos diphospine and both diamine (dan) and pinacol boronic ester reagents could be efficiently engaged in the reaction.

Meek has reported a mechanistically related diphosphine–Cu-catalyzed boryl conjugate addition reaction to vinylboronic pinacol ester in which the α-boryl alkylcopper intermediates generated are trapped with aldehyde electrophiles to furnish β-hydroxy

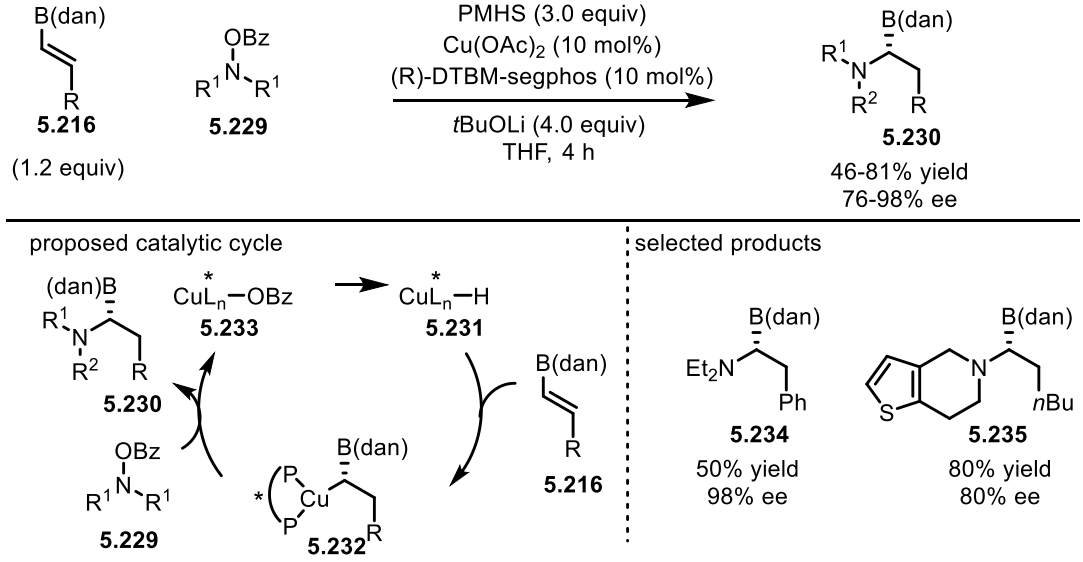
Scheme 5.41. Yun's Diphosphine-Cu-H-catalyzed enantioselective hydroallylation alkenyl boronates



boronic ester products.[68] The same authors reported an enantioselective diphosphine-Cu-catalyzed deborylative addition reaction of germinal diboron reagents to aldehydes which invoked the intermediacy of an α-boryl alkylcopper catalytic intermediate.[69]

Miura and Hirano have reported an enantioselective diphosphine–Cu-catalyzed hydroamination reaction of alkenylboron reagents which produces enantioeriched α-amino boron compounds (Scheme 5.42).[70] In line with related hydroamination reactions[71] involving copper-hydride addition to alkenyl substrates, the authors proposed a catalytic cycle in which electrophilic amination of α-boryl copper species **5.232** with a nitrogen-based electrophile **5.229** facilitates catalytic turnover. This report demonstrates that

Scheme 5.42. Hirano/Miura's Cu-diphosphine-catalyzed enantioselective hydroamination of alkenyl B(dan)

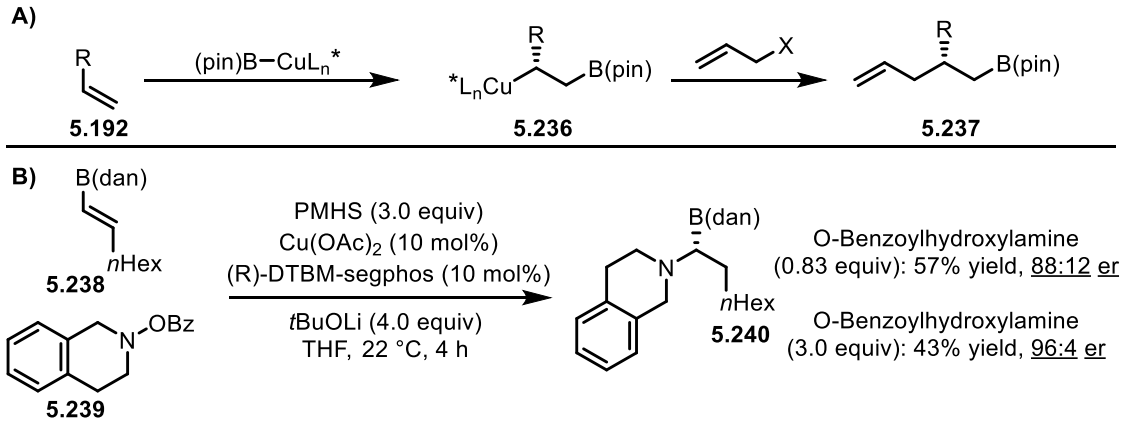


[68] Green, J. C.; Joannou, M. V.; Murray, S. A.; Zanghi, J. M.; Meek. S. J. *ACS Catal*. **2017**, 7, 4441.
[69] Joannou, M. V.; Moyer, B. S.; Meek, S. J. *J. Am. Chem. Soc*. **2015**, 137, 6176.
[70] Nishikawa, D. Hirano, K.; Miura, M. *J. Am. Chem. Soc*. **2015**, 137, 15620.
[71] (a) Miki, Y.; Hirano, K.; Satoh, T.; Miura, M. *Angew. Chem. Int. Ed.* **2013**, 52, 10830. (b) Miki, Y.; Hirano, K.; Satoh, T.; Miura, M. *Org. Lett*. **2014**, 16, 1498. (c) Hirano, K.; Miura, M. *Pure Appl. Chem.* **2014**, 86, 291. (d) Zhu, S.; Niljianskul, N.; Buchwald, S. L. *J. Am. Chem. Soc*. **2013**, 135, 15746. (e) Zhu, S.; Buchwald, S. L. *J. Am. Chem. Soc*. **2014**, 136, 15913. (f) Niljianskul, N.; Zhu, S.; Buchwald, S. L. *Angew. Chem. Int. Ed*. **2015**, 54, 1638. (g) Shi, S.-L.; Buchwald, S. L. *Nat. Chem*. **2015**, 7, 38. (h) Yang, Y.; Shi, S.-L.; Niu, D.; Liu, P.; Buchwald, S. L. *Science* **2015**, 349, 62.

enantioenriched α-boryl copper nucleophiles can engage in stereospecific amination, granting access to products which are of interest as pharmacophores in proteasome inhibitors[72] and as chiral building blocks in organic synthesis.[73] The influence of the chiral ligand on copper in maintaining the stereochemical integrity of the copper-substituted stereogenic carbon center during the course of the reaction was not discussed.

Hoveyda has recently reported the most detailed investigation to date into the mechanistic intricacies of reactions involving the generation of copper-substituted stereogenic carbon centers.[74] As a representative case study the author focused on the diphosphine–Cu-catalyzed allyl-boron addition reaction depicted in Scheme 5.43.A. While the complexity of the study warrants detailed consideration, a few of the key points

Scheme 5.43. Hoveyda's in-depth mechanistic study of Cu-substituted stereogenic carbon centers



[72] (a) Bross, P. F.; Kane, R.; Farrell, A. T.; Abraham, S.; Benson, K.; Brower, M. E.; Bradley, S.; Gobburu, J. V.; Goheer, A.; Lee, S.-L.; Leighton, J.; Liang, C. Y.; Lostritto, R. T.; McGuinn, W. D.; Morse, L. A.; Verbois, S. L.; Williams, G.; Wang, Y.-C.; Pazdur, R. *Clin. Cancer Res*. **2004**, 10, 3954. (b) Kupperman, E.; Lee, E. C.; Cao, Y.; Bannerman, B.; Fitzgerald, M.; Berger, A.; Yu, J.; Yang, Y.; Hales, P.; Bruzzese, F.; Liu, J.; Blank, J.; Garcia, K.; Tsu, C.; Dick, L.; Fleming, P.; Yu, L.; Manfredi, M.; Rolfe, M.; Bolen, J. *Cancer Res*. **2010**, 70, 1970. (c) Rentsch, A.; Landsberg, D.; Brodmann, T.; Bülow, L.; Girbig, A.-K.; Kalesse, M. *Angew. Chem., Int. Ed*. **2013**, 52, 5450.

[73] (a) Ohmura, T.; Awano, T.; Suginome, M. *J. Am. Chem. Soc*. **2010**, 132, 13191. (b) Awano, T.; Ohmura, T.; Suginome, M. *J. Am. Chem. Soc*. **2011**, 133, 20738.

[74] Lee, J.; Radomkit, S.; Torker, S.; del Pozo, J.; Hoveyda, A. H. *Nat. Chem*. **2018**, 10, 99.

uncovered can be briefly mentioned. First, increasing the concentration of the electrophile present in the reaction resulted in improved enantioselectivity. This was found to be due to the ability to avoid diastereoselective Cu-H elimination processes from **5.236** and/or the ability of achiral Cu–boryl intermediates to be converted to allyl–B(pin) rather than participate in the catalytic cycle by adding to an alkene substrate. Secondly, the authors demonstrated that lower alkene concentration and/or higher chiral ligand concentration minimize the formation of achiral Cu–alkyl species which contribute to erosion in enantioselectivity. Thirdly, the use of less reactive allylphenyl carbonate electrophiles was found to improve the enantioselectivcity of the reaction by enhancing the chemoselective Cu–H elimination of achiral Cu–alkyl species. The mechanistic features found in this study were shown to apply to other reactions proposed to involve the intermediacy of species with Cu-substituted stereogenic carbon centers such as the enantioselective hydroamination reaction of alkenylboron reagents (Scheme 5.43.B).

Several examples of reactions involving the catalytic generation of α-boryl alkylnickel complexes as catalytic intermediates were discussed in chapter four of this dissertation.[75]

[75] (a) Schmidt, J.; Choi, J.; Liu, A. T.; Slusarczyk, M.; Fu, G. C. *Science* **2016**, 354, 1265. (b) Sun, S.-Z.; Martin, R. *Angew. Chem. Int. Ed*. **2018**, 57, 3622. (c) Sun, S.-Z.; Börjesson, M.; Martin-Montero, R; Martin, R. *J. Am. Chem. Soc*. **2018**, 140, 12765. (d) Chierchia, M.; Lovinger, G. J.; Xu, P.; Morken, J. P. *Angew. Chem. Int. Ed*. **2019**, 58, 1.

5.2.4 Catalytic Generation of Stereodefined Organometallic Nucleophiles as Stoichiometric Products

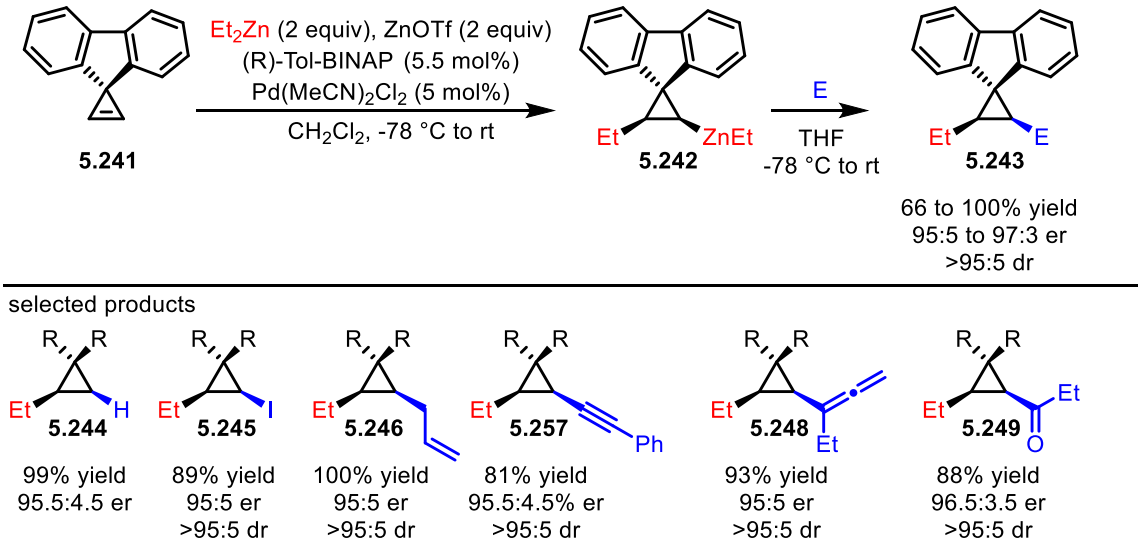
As indicated in the previous section, the catalytic generation of stereodefined organometallic species as catalytic intermediates can offer certain advantages over stoichiometric methods of preparation such as 1) obviating the need to prepare stereodefined (enantioenriched) starting materials and 2) potentially minimizing racemization processes as stereodefined organometallic species are generated and rapidly consumed during the course of a single reaction cycle. Conversely, catalytic reactions must contend with the limitation that the reaction conditions and reagents employed in both the generation and consumption of organometallic intermediates must be mutually compatible.

A complementary strategy to the previously mentioned approaches is one in which a catalyst converts a prochiral starting material into an enantioenriched stoichiometric organometallic product which can then be converted to a wide range of structures by means of stereospecific reactions with electrophiles. Because the catalytic generation of the enantioenriched organometallic species and the electrophilic trapping event occur separately, the electrophilic reagents and conditions employed in the trapping step can be entirely orthoganol to those used in the enantioselective catalytic reaction.

While this strategy has not been well explored, one good example of its use is the catalytic enantioselective carbozincation of cyclopropene substrates. Adding to the body of literature concerned with enantioselective addition reactions to cyclopropenes,[76] Lautens

[76] Marek, I.; Simaan, S.; Masarwa, A. *Angew. Chem., Int. Ed.* **2007**, 46, 7364. (b) Rubin, M.; Rubina, M.; Gevorgyan, V. *Chem. Rev*. **2007**, 107, 3117. (c) Rubin, M.; Rubina,M.; Gevorgyan, V. *Synthesis* **2006**, 1221. (d) Fox, J. M.; Yan, N. *Curr. Org. Chem*. **2005**, 9, 719. (e) Nakamura, M.; Isobe, H.; Nakamura, E. *Chem. Rev*. **2003**, 103, 1295.

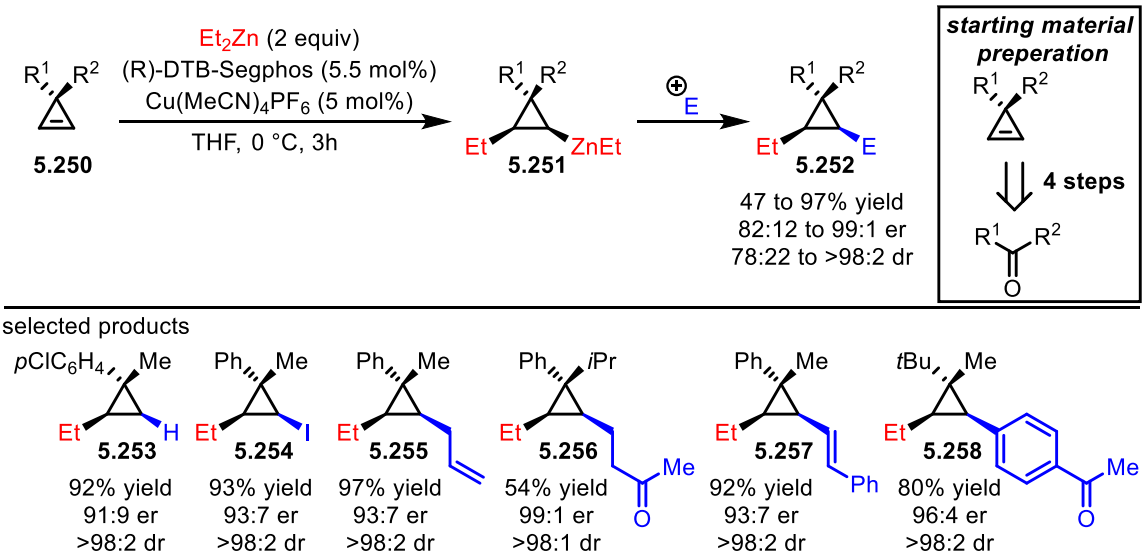
Scheme 5.44. Enantioselective Pd-diphosphine-catalyzed carbozincation-stereospecific elctrophile trap



reported the enantio- and diastereoselective diphosphine–Pd-catalyzed carbozincation of diaryl cyclopropene **5.241** (Scheme 5.44).[77] While the authors found the reaction was only highly enantioselective with cyclopropene substrate **5.241**, they found that a wide variety of electrophiles could be engaged in a stereospecific fashion, leading to diverse products in high yield, with excellent enantio- and diastereoselectivity. Marek subsequently reported a related enantio- and diasteroselective diphosphine–Cu-catalyzed carbozincation of cyclopropene substrates (Scheme 5.45).[78] While the use of diorganozinc nucleophiles other than diethylzinc resulted in diminished enantioselectvities, the authors demonstrated that the reaction could accommodate a wider range of cyclopropene substituents and that the enantioenriched organozinc nucleophile products could be trapped by a range of electrophilic species with excellent stereospecificity. While these and related reports of carbometallation of cyclopropenes provide an inspiring proof of concept, they have been

[77] Kramer, K.; Leong, P.; Lautens, M. *Org. Lett*. **2011**, 13, 819.
[78] D. S. Müller and I. Marek, *J. Am. Chem. Soc.* **2015**, 137, 15414.

Scheme 5.45. Enantioselective diphosphine-Cu-catalyzed carbozincation-stereospecific electrophile trap

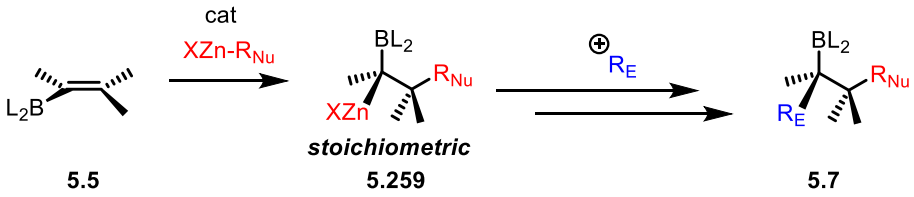


limited to the use of highly strained cyclopropene substrates that are not commercially available and require multistep preparation to access. If this approach could be applied to a more general alkene substrate class a wide range of product motifs other than substituted cyclopropanes might be accessed.

5.3 Proposal for the Catalytic Enantioselective Carbozincation of Alkenylboron Reagents to Prepare Enantioenriched α-Boryl Alkylzinc Nucleophiles

As demonstrated by the examples above, α-boryl alkyl organometallic species are versatile reagents capable of generating diverse products by engaging in stoichiometric and catalytic reactions with a range of electrophilic species. We hoped to access these reagents catalytically and enantioselectively, expecting that if these species were sufficiently configurationally stable so as to engage in stereospecific transformations, they might serve as versatile chiral organometallic reagents, facilitating the formation of diverse product structures in a modular manner (Scheme 5.46).

Scheme 5.46. Catalytic generation of stoichiometric enantioenriched α-boryl alkylzinc nucleophiles

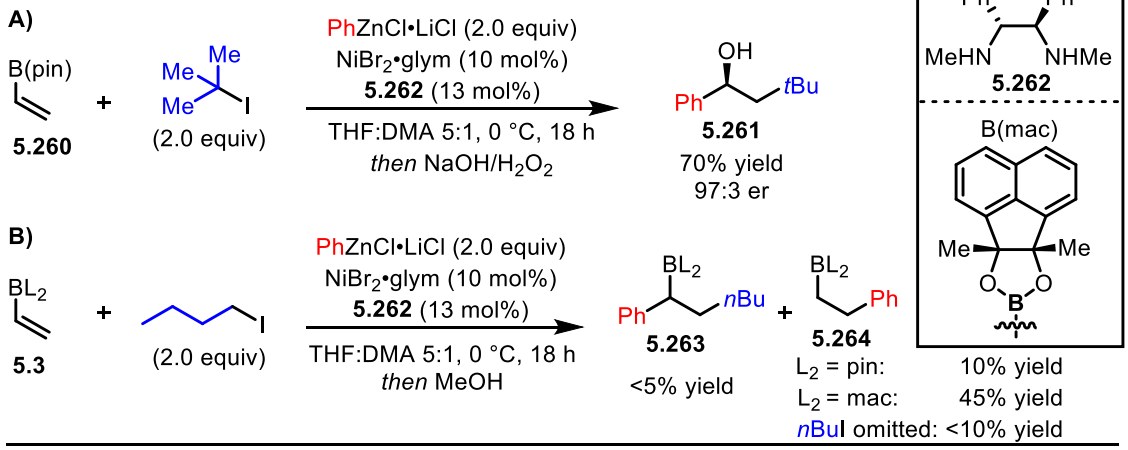


In this chapter, the discovery, development, and mechanistic study of an enantioselective catalytic carbozincation reaction of alkenylboron reagents is discussed.

5.4 Initial Discovery and Mechanistic Probes

During the course of developing the enantioselective diamine–Ni-catalyzed radical addition-coupling reaction described in the second half of chapter four (Scheme 5.47.A), we observed that, in contrast to the use of tertiary alkyl iodide electrophiles, when primary alkyl iodide electrophiles were employed in the reaction no appreciable formation of the desired product **5.263** was observed (Scheme 5.47.B). We attributed this outcome to a fast recombination of primary alkyl radical with the diamine–Ni catalyst complex, which

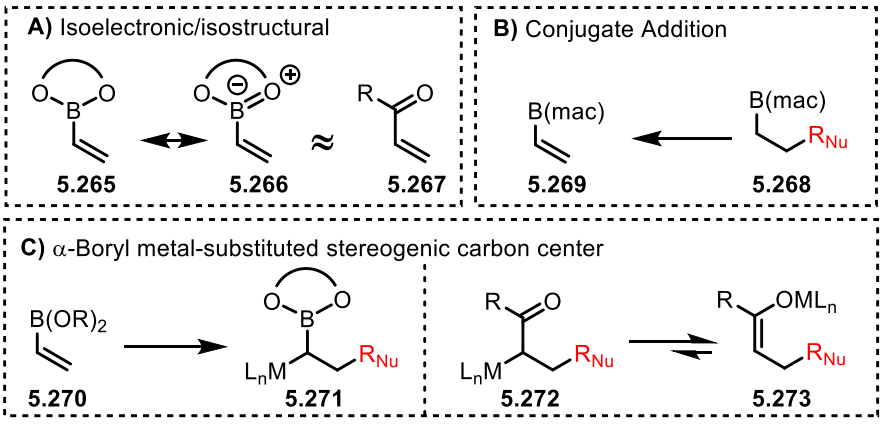
Scheme 5.47. Initial discovery[a]



[a] Yields are of purified material.

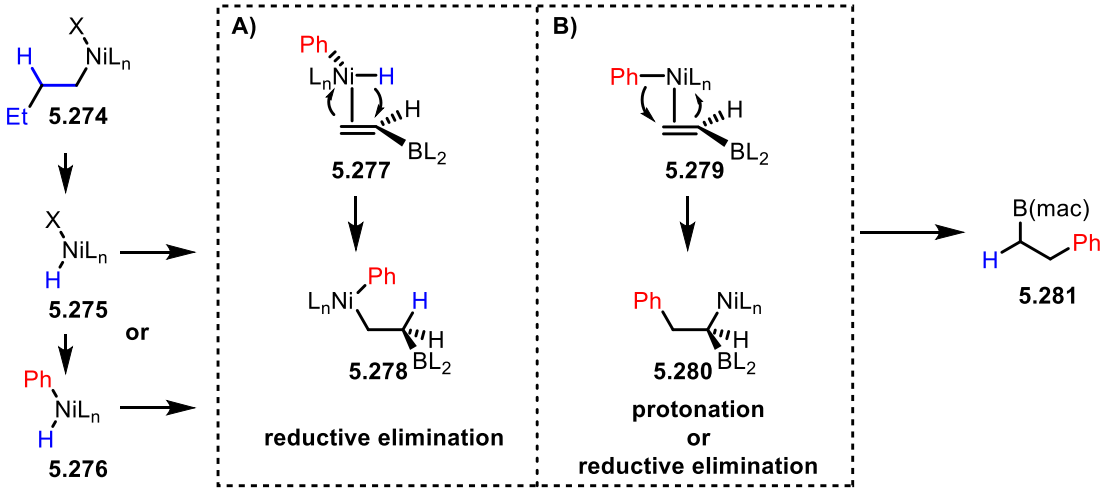
outcompetes radical addition to an alkenylboron reagent. Despite this inauspicious result, careful analysis of the reaction mixture revealed the formation of a small amount of linear product **5.264** in which the arylzinc nucleophile was incorporated with opposite regioselectivity to the expected radical addition/coupling product. Preliminarily we found that we could increase the amount of product **5.264** by employing vinyl–B(mac) rather than vinyl–B(pin) as the substrate. Additionally, we found that, while the *n*BuI electrophile was not incorporated into product **5.264**, omitting this reagent resulted in a substantial reduction in product formation. Recognizing the isoelectronic and isostructural relationship that exists between a vinylboronic ester and an α,β-unsaturated ester (Scheme 5.48.A) we hypothesized that product **5.26**4 might be the product of a diamine–Ni-catalyzed conjugate addition/protonation reaction of a vinylboronic pinacol ester substrate with an arylzinc nucleophile (Scheme 5.48.B). Importantly, such a mechanism would involve the generation of an α-boryl metal-substituted stereogenic carbon center (**5.271**, Scheme 5.48.C). We reasoned that such a species would be more configurationally stable than the corresponding α-metallated ester intermediate (Scheme 5.48.C) and thus might be engaged

Scheme 5.48. Mechanistic hypothesis: addition to form α-Boryl metal-substituted stereogenic center



in stereospecific substitution reactions. We first sought to determine the origin of the proton source that is delivered to the intermediate and facilitates catalytic turnover from a putative α-boryl alkylnickel species. While a large number of mechanistic possibilities can be imagined, we hypothesized that the reaction likely proceeds by one of two main pathways: (1) a hydride addition mechanism (Scheme 5.49.A) in which a nickel hydride **5.275** or **5.276,** generated by reductive elimination from an alkylnickel species **5.274,** adds selectively at the internal alkene carbon (**5.277** to **5.278**) with catalyst turnover occurring by reductive elimination; or (2) a phenyl addition mechanism (Scheme 5.49.B) in which the α-boryl alkylnickel species **5.280** thus generated is turned over by reductive elimination (with a hydride on Ni) or by protonation with an adventitious proton source in solution.

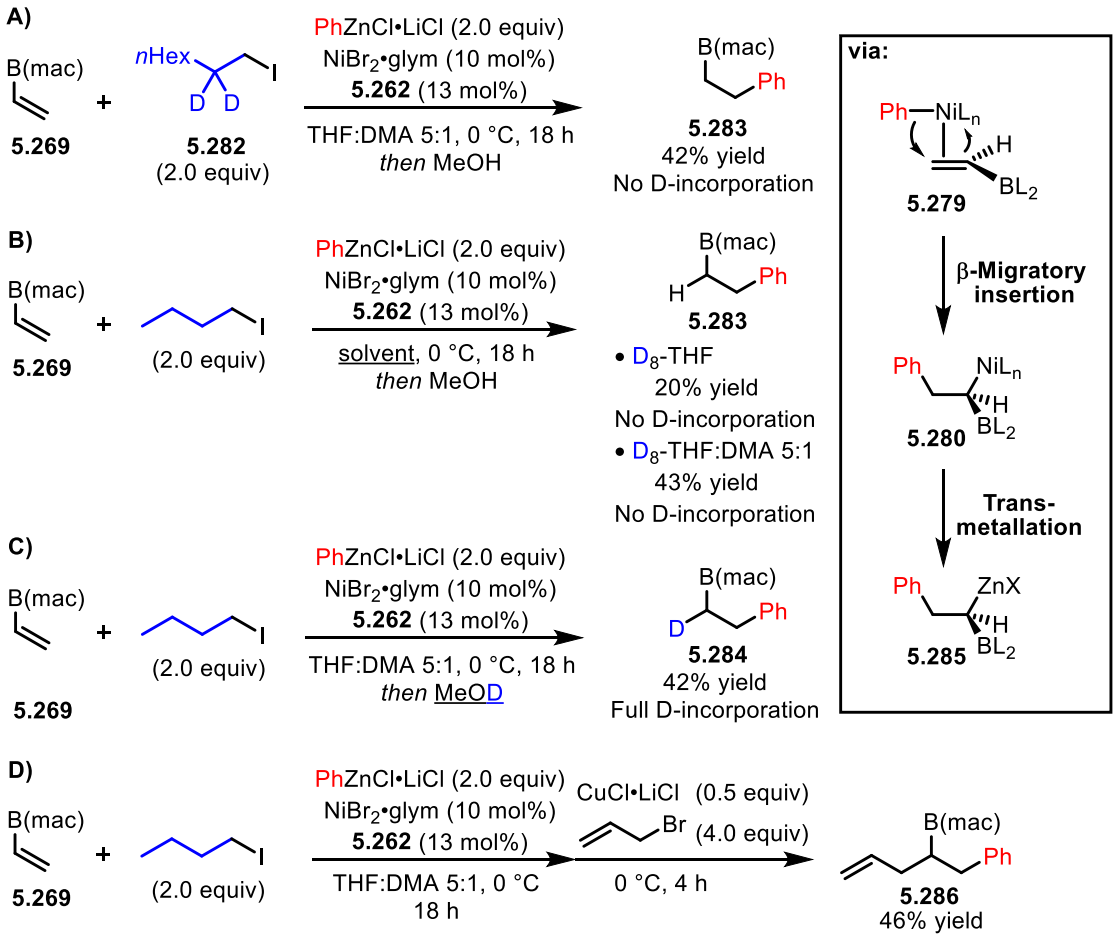
Scheme 5.49. Mechanistic hypothesis: formation of β-phenyl product **5.281**[a]



The observation that *n*BuI appears to be required for catalytic turnover suggested to us that a hydride addition mechanism in which *n*BuI acts as both an oxidant and hydride source might be the more likely pathway. To test this hypothesis my colleague Chenlong Zhang prepared a deuterium labeled alkyl iodide **5.282** and subjected it to the reaction (Scheme

5.50.A). The lack of deuterium incorporation in the product disproved a hydride addition mechanism. To test if the solvent might be acting as a source of protons we ran test reactions in both rigorously dried D8-THF:DMA 5:1 and D8-THF solvent systems (Scheme 5.50.B). Both reactions resulted in normal levels of yield but with no deuterium incorporation, thus excluding solvent or adventitious moisture as the source of protons responsible for catalytic turnover. These results suggested the possibility that the observed product might be formed during reaction workup by the protonation of an α-boryl alkyl

Scheme 5.50. Mechanistic probe of proton source as origin of catalytic turnover[a]



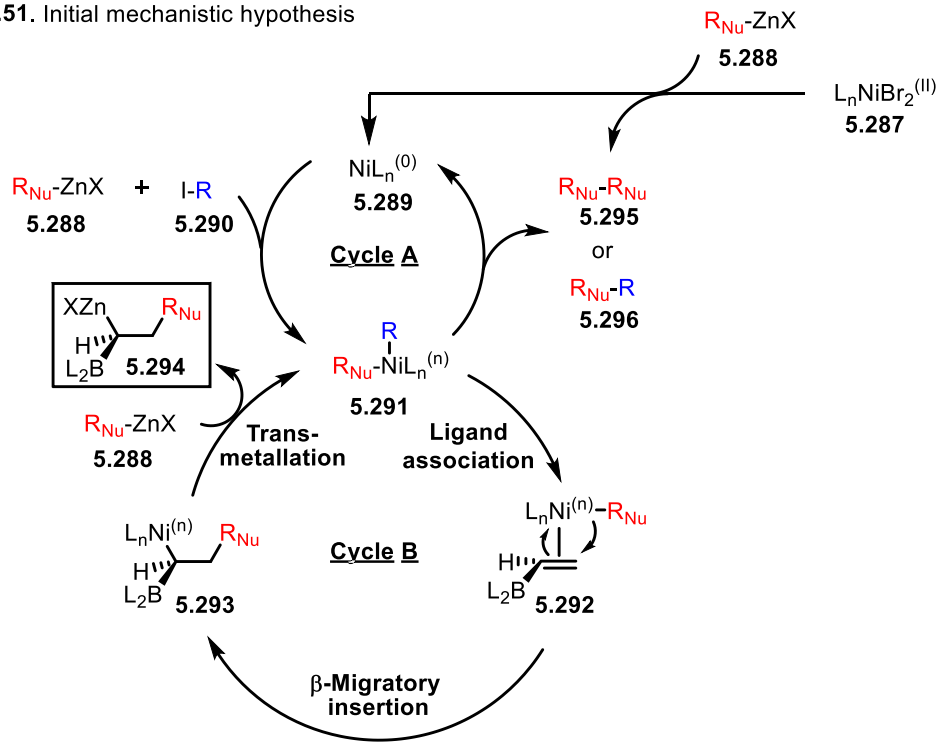
[a] Yields determined by ^{1}H NMR againsts 2,4,6-treimethoxybenzene internal standard.

metal species with MeOH. As depicted in Scheme 5.50.C, quenching a reaction run under otherwise standard conditions with deuterated methanol resulted in full deuterium incorporation into the observed conjugate addition product **5.284**. That the yield of the product was substantially higher than the catalyst loading suggested to us that the α-boryl alkyl species being quenched at the end of the reaction was not an α-boryl alkylnickel species, but rather an α-boryl alkylzinc species (inset, Scheme 5.50). This hypothesis was further supported by the observation that allylation product **5.286** (Scheme 5.50.D) could be obtained in similar yields as the corresponding protonation product **5.283** when allyl bromide and CuCl were added at the end of the reaction. While reaction mechanisms involving catalytic turnover by a second transmetallation from a nickel catalyst to an organozinc nucleophile are uncommon, a few examples have been reported[79] and the phenomenon is of considerable interest in palladium-catalyzed Negishi coupling reactions.[80] If such a reaction took place, we imagined it might operate by a catalytic cycle as depicted in Scheme 5.51. Starting from an Ni(0) species **5.289** (generated from a $NiBr_2$ pre-catalyst **5.287** by transmetallation with organozinc nucleophile and reductive elimination) oxidative addition with alkyl halide and transmetallation with organozinc nucleophile would produce organonickel complex **5.291**. Ligand association of vinylboronic ester would form Ni–olefin complex **5.292** which would then undergo β-

[79] (a) Vaupel, A.; Knochel, P. *Tet. Lett*. **1994**, 35, 8349. (b) Vettel, S.; Vaupel, A.; Knochel, P. *J. Org. Chem.* **1996**, 61, 7473. (c) Wang, J.; Meng, Ge.; Xie, K.; Li, L.; Sun, H.; Huang, Z. *ACS Catal*. **2017**, 7, 7421.

[80] (a) Perez-Temprano, M. H.; Nova, A. Casares, J. A.; Espinet, P. *J. Am. Chem. Soc.* **2008**, 130, 10518. (b) Liu, Q.; Lan, Y.; Liu, J.; Li, G.; Wu, Y.-D.; Lei, A. J. Am. Chem. Soc. **2009**, 131, 10201. (c) Jin, L.; Lei, A. *Org. Biomol. Chem*. **2012**, 10, 6817. (d) del Pozo, J.; Salas, G.; lvarez, R. A.; Casares, J. A.; Espinet, P. *Organometallics* **2016**, 35, 3604.

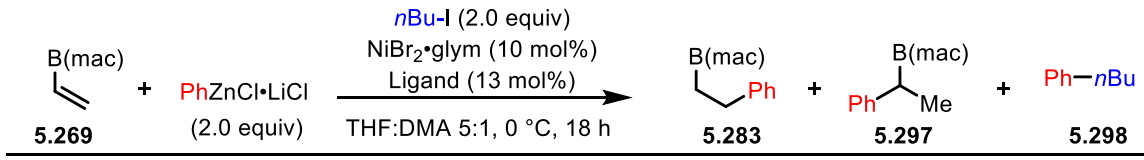
Scheme 5.51. Initial mechanistic hypothesis

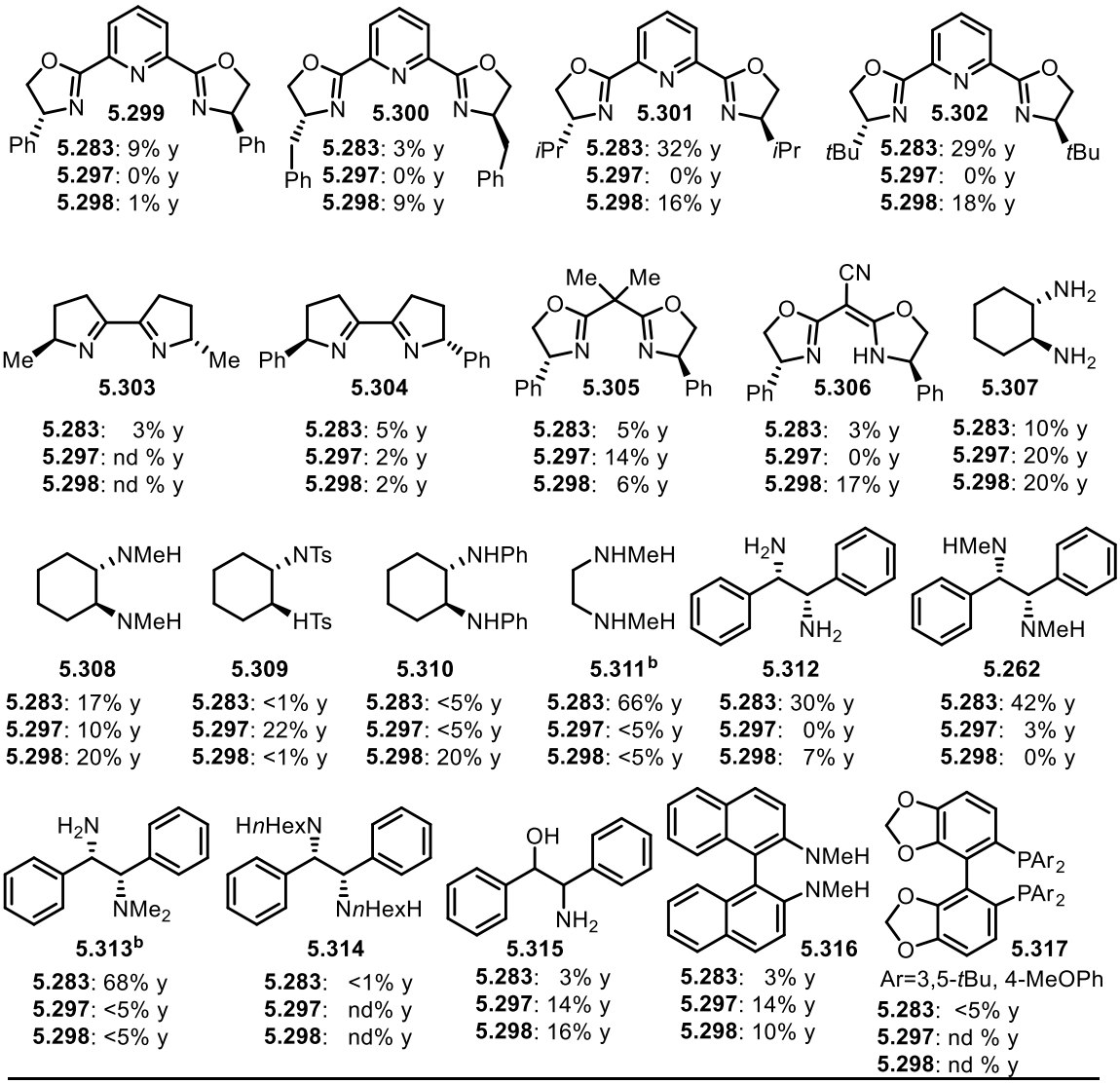


migratory insertion to form α-boryl alkylnickel intermediate **5.293**. Transmetallation of **5.293** with an equivalent of organozinc nucleophile would then produce α-boryl alkylzinc product **5.294** as well as regenerate organonickel complex **5.291** which might reengage in the catalytic cycle. This proposal would explain why the reaction appears to require an alkyl halide though it is not incorporated into the observed product. The alkyl halide would thus serves as an oxidant to initially form the active catalytic species **5.291** from a reduced Ni(0) species or reform it if **5.291** were to undergo a undesired side reaction such as reductive elimination to produce cross-coupling or homocoupling products **5.296** or **5.295** respectively.

With this initial mechanistic hypothesis in mind we next surveyed a variety of ligands on nickel to assess the influence of the ligand structure on reaction outcome (Scheme 5.52).

Scheme 5.52. Effect of ligand structures on Nickel on product distribution yield[a]





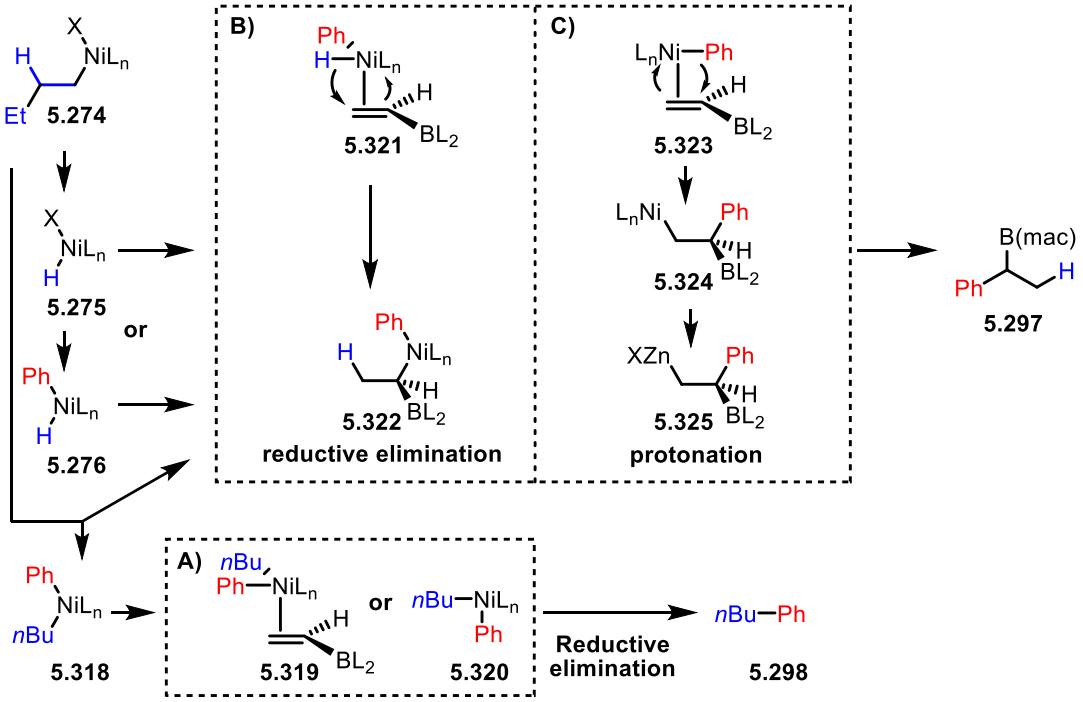
[a] Yields determined by ^{1}H NMR against 2,4,6-trimethoxybenzene internal standard. nd = not determined.
[b] THF:DMSO 5:1 solvent system employed.

While catalytic complexes derived from aryl (**5.299**) and benzyl (**5.300**) pybox ligands demonstrated a low degree of reactivity, the use of alkyl-substituted pybox ligands (**5.301**

and **5.302**) resulted in higher yields of the desired product **5.283** but also produced substantial amounts of cross-coupling product **5.298**. Use of box ligands **5.303** through **5.306** did not result in substantial product formation, though ligand **5.305** did promote the formation of opposite regioisomeric product **5.297**. Use of cyclohexyl diamines **5.297** through **5.310** resulted in variable levels of reactivity but poor product selectivity. Notably, a reaction employing *N*-tosyl ligand **5.309** selectivity promoted the formation of opposite regioisomeric product **5.297**. *N*,*N*'-dimethyl ethylene diamine **5.311** was very effective at promoting the selective formation of the desired product and diphenyl ethylene diamine **5.312** also demonstrated a high degree of product selectivity albeit with diminished reactivity. The addition of methyl substituents to the nitrogens of the diphenyl ethylene diamine ligand structure appeared to increase catalytic reactivity and product selectivity (**5.262)**, as did the addition of two methyl groups to one nitrogen (**5.313**). Increasing the size of the alkyl substituents to hexyl groups (**5.314**) essentially inhibited the desired reaction. Other ligand classes such an amino alcohol **5.315**, a diaryl amine **5.316**, and a diphosphine **5.317** resulted in undesirable product selectivities or reduced reactivity.

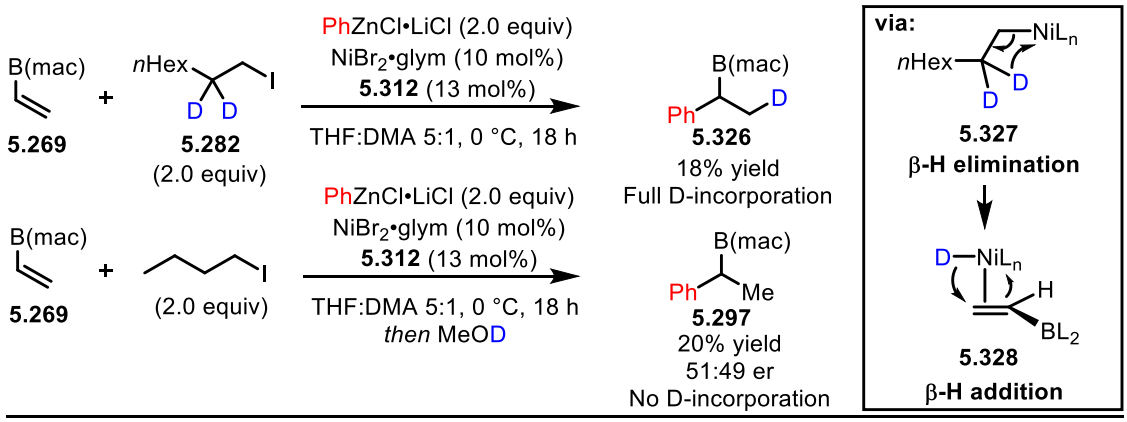
With the hope of gaining mechanistic insight that might allow us to promote the formation of the desired product **5.283** while suppressing the formation of opposite regioisomeric product **5.297** and cross-coupling product **5.298**, we considered the potential reaction pathway that might be leading to the formation of these side products (Scheme 5.53). As depicted in Scheme 5.53.A, we hypothesized that the formation of cross-coupling product **5.298** likely requires the formation of a Ni(II) or Ni(III) intermediate which may undergo reductive elimination either unaided (**5.320**) or may be promoted by the binding

Scheme 5.53. Mechanistic hypothesis: formation of α-phenyl product **5.297** and cross-coupling product[a]



of a π-acidic vinylboronic ester ligand (**5.319**). Additionally, we envisioned that regioisomeric product **5.297** might be formed either by (1) a β-migratory insertion of a hydride to the terminal vinyl position, or a phenyl addition to the internal vinyl position, followed by reductive elimination (Scheme 5.53.B) or, (2) analogously to the proposed mechanism for the formation of desired product **5.283**, by a mechanism involving β-migratory insertion of a phenyl group to the α-boryl carbon of the vinylboronic ester substrate followed by transmetallation (Scheme 5.53.C). To interrogate these mechanistic possibilities we first ran a reaction employed deuterium-labeled alkyl iodide **5.282** in a reaction with *N*,*N*'-tosyl ligand **5.309**. We observed full deuterium incorporation into the product, suggesting that the reaction to form **5.297** proceeds by a mechanism involving β-hydride elimination to form a nickel–hydride species which participates in β-hydride addition (inset, Scheme 5.54) and reductive elimination. When *n*BuI was used under the

Scheme 5.54. Mechanistic probes for the origen of oposit regioisomer of product[a]



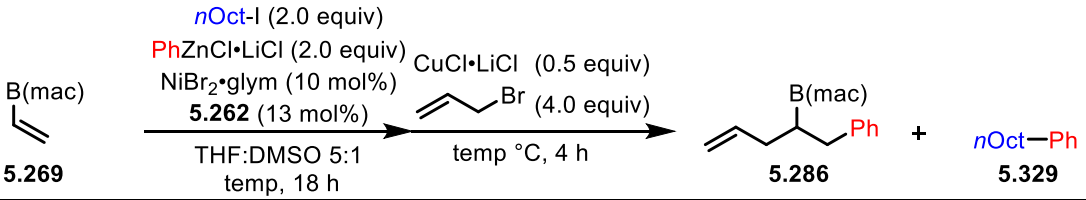
[a] Yields determined by ^{1}H NMR against internal standard. nd = not determined.

same reaction conditions and the reaction was quenched with deuterated methanol no deuterium incorporation into product **5.297** was observed, disproving the formation of a β-boryl alkylzinc species **5.325**. The fact that we obtained product **5.297** as a racemate suggests that either the catalyst derived from the *N,N'*-tosyl ligand **5.309** employed in these reactions engages in a non-enantioselective β-migratory insertion or that a racemization pathway exist for an organometallic intermediate bearing a metal-substituted stereogenic center. This later possibility might arise due to slow reductive elimination from an α-boryl alkylnickel intermediate.

Because cross-coupling between organozinc nucleophile and alkyl iodide reagent is likely a competitive process to the desired carbozincation reaction, leading to the consumption of nucleophile and reduction of catalytically competent higher oxidation state organonickel species to catalytically inactive Ni(0) species, we next sought to assess the extent to which this process occurs. While the initial survey of ligands conducted in Scheme 5.52 indicated that the appropriate choice of diamine ligand could suppress the formation of cross-coupling product, we sought to more accurately assess this process

using the higher molecular weight *n*Octly-I reagent which would lead to the formation of the higher boiling *n*Octyl-Ph cross-coupling product. We found that while a significant amount of *n*Octyl-Ph was produced in a reaction conducted at 0°C, lowering the reaction temperature to -20°C strongly inhibited the formation of this product, while the amount of α-boryl alkylzinc product was unaffected. While further decreasing the reaction temperature to -40 °C completely suppressed the formation of cross-coupling product, it

Scheme 5.55. Effect of temperature on the amount of cross-coupling versus carbometallation product[a]



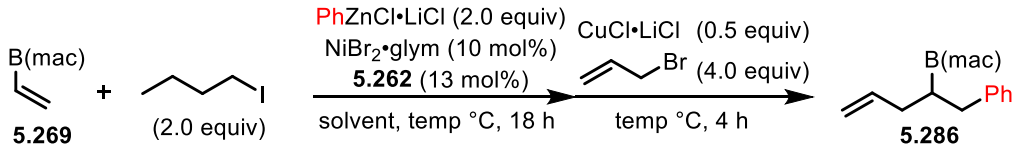
entry	temp (°C)	yield **5.286** (%)	yield **5.329** (%)
1	0	42	34
2	-20	45	12
3	-40	18	<5

[a] Yields determined by ^{1}H NMR against 2,4,6-trimethoxybenzene internal standard.

also led to a substantial decrease in the formation of the desired product, a limitation which we attribute to the use of *n*Octyl-I in place of shorter chain alkyl iodide reagents as will be discussed shortly.

With some of the mechanistic aspects leading to deleterious side reactions elucidated and strategies for the suppression of these species outlined, we next sought to determine if the putative α-boryl alkylzinc product might be formed in an enantioselective manner, and if so, if this species might be trapped in an enantiospecific fashion. To investigate this possibility, we conducted experiments to trap the putative α-boryl alkylzinc product with allyl bromide and copper chloride (Scheme 5.56). We observed that the product was

Scheme 5.56. Survey of temperature and solvent effects[a]



entry	temp (°C)	solvent	yield (%)	er
1	0	THF:DMA 5:1	46	53:47
2	0	THF:DMSO 5:1	56	57:43
3	-20	THF	23	nd
4	-20	THF:DMF 5:1	29	60:40
5	-20	THF:CPSO 5:1	<5	nd
6	-20	THF:HMPA 5:1	<5	nd
7	-20	THF:DBSO 5:1	<5	nd
8	-20	THF:DMSO 5:1	50	75:25
9	-30	THF:DMSO 5:1	36	82:18

[a] Yields determined by ^{1}H NMR against 2,4,6-trimethoxybenzene internal standard. nd = not determined. DBSO = dibutyl sulfoxideCPSO = cyclopentyl sulfoxide.

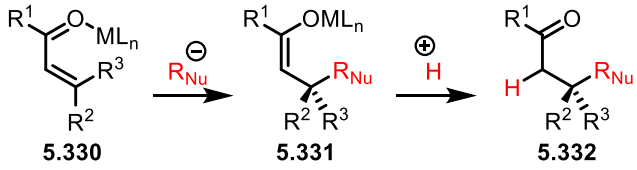
slightly enantioenriched (entry 1). By employing DMSO rather than DMA as a cosolvent we found that the yield and enantioenrichment of product **5.286** could be improved slightly (entry 2). The use of THF alone or other solvent systems resulted in inferior results (entries 3 through 7). Lowering the reaction temperature resulted in a substantial increase in the enantioenrichment of product **5.286** (entries 2, 8, 9).

In an effort to further improve the enantioselectivity of the transformation, we next considered the mechanistic events that might contribute to or erode the enantiomeric enrichment of allyl trap product **5.286**. While the enantioenrichment of products generated by many enantioselective reactions depends on a single enantioselective step (such as for an enantioselective Lewis acid-catalyzed conjugate addition reaction (Scheme 5.57.A), we imagined that for the enantioselective carbozincation-electrophile trap reaction under

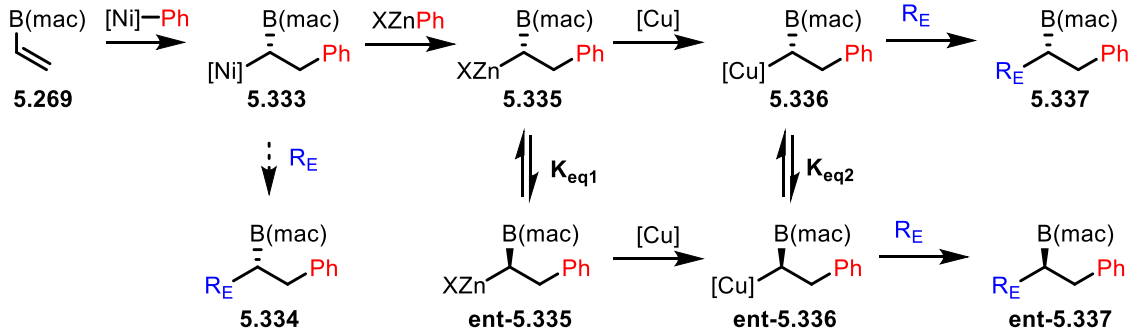
investigation, the enantioenrichment of the final product is likely the composite of multiple stereoselective and stereospecific processes and is influenced by the degree to which intermediates may engage in racemization. As depicted in Scheme 5.57.B, the enantioenrichment of the product obtained after electrophilic trapping is dependent on: (1) the initial enantioselectivity of the diamine–Ni-catalyzed β-migratory insertion (**5.269** to **5.333**), (2) the stereospecificity of transmetallation from α-boryl alkylnickel intermediate **5.335** to α-boryl alkylzinc intermediate **5.335**, (3) the stereospecificity of transmetallation from α-boryl alkylzinc intermediate **5.335** to α-boryl alkylcopper intermediate **5.336**, (4) the degree to which **5.333** and **5.336** undergo racemization during the course of these steps, and (5) the stereospecificity of the electrophile trapping step (**5.336** to **5.337**). Because information about the stereochemical stability of α-boryl alkylzinc compounds, to the best of our knowledge, has not been reported, we next probed the speed with which these compounds undergo racemization (Scheme 5.58). By allowing samples of α-boryl

Scheme 5.57. Possible sources of errosion of er: transmetallation, electrophilic traping, and racemization

A) enantioselective conjugate addition



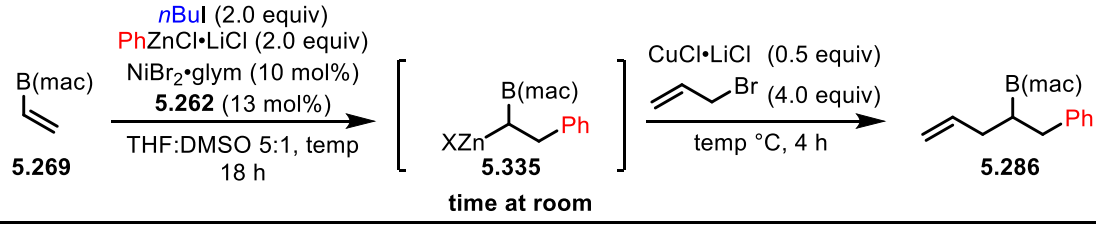
B) enantioselective carbozincation/electrophile trapping



alkylzinc product generated *in situ* at -20˚C to warm and stir at room temperature for variable amounts of time before being cooled to -20 ˚C and trapped with allyl bromide/CuCl, we observed a substantial erosion of enantiomeric enrichment of product as a function of time. The racemization of these compounds appears to be relatively slow, requiring more than three hours at room temperature to fully racemize. Notably, this set of experiments rules out the possibility that the enantioenrichment of allyl trap product **5.286** is due to a stereoconvergent reaction of α-boryl alkylzinc product catalyzed by an enantioenriched nickel-diamine or copper-diamine complex formed *in situ*. It is also noteworthy that the α-boryl alkylzinc product **5.335** appears to be chemically stable for prolonged periods of time at room temperature (entry 5).

We next probed the degree to which racemization of α-boryl alkylzinc product **5.335** might be occurring at low temperature during the course of the reaction (Scheme 5.59). Varying the reaction time employed before the allyl trap was performed for reactions at -

Scheme 5.58. Racemization of α-boryl alkyl zinc intermediate upon warming to room temperature[a]



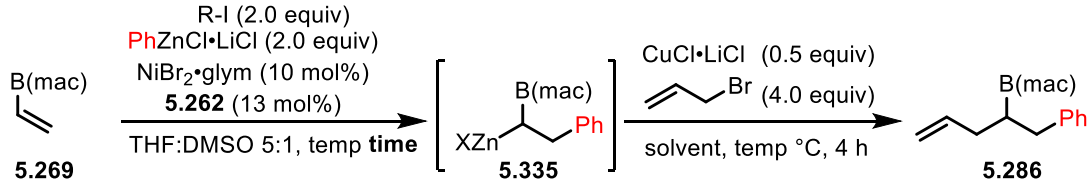
entry	time at rt before E trap	yield (%)	er
1	0	46	75:25
2	5 min	48	72:28
3	1 h	47	55:45
4	3 h	46	53:47
5	4 days	43	50:50

[a] Yields determined by ^{1}H NMR against 2,4,6-trimethoxybenzene internal standard. Enantiomer ratio (er) determined by SCF analysis.

20˚C, we observed that shorter reaction times resulted in the isolation of samples of product with higher enantioenrichment (entries 1 versus 2), suggesting that racemization is occurring during the course of the reaction. By lowering the reaction temperature from -20˚C to -30˚C, racemization appeared to slow substantially as indicated by the lack of erosion of enantioenrichment of products obtained from reactions run for 5 versus 18 hours (entries 3 versus 4). These results indicate that by lowering the reaction temperature to -30˚C or lower, racemization of α-boryl alkylzinc intermediates may be arrested such that this process no longer diminishes the enantioenrichment of the products. Importantly, the configurational stability of α-boryl alkylzinc species at -30˚C was independent of the identify of alkyl iodide employed in the reaction and persisted even after extended reaction times (entries 5 and 6).

While the experiments in Scheme 5.59 demonstrate that α-boryl alkylzinc species **5.335**

Scheme 5.59. Racemization of α-boryl alkyl zinc intermediate during reactions at various temperatures[a]

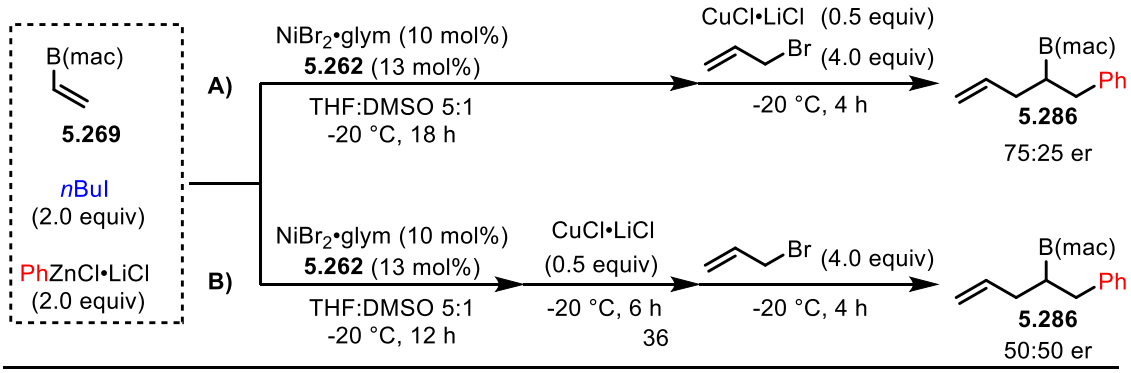


entry	R-I	temp (°C)	reaction time (h)	yield (%)	er
1	*n*BuI	-20	6	19	84:16
2	*n*BuI	-20	18	62	77:13
3	MeI	-30	5	9	86:14
4	MeI	-30	18	22	84:16
5	*n*BuI	-30	26	29	81:19
6	*n*BuI	-30	36	32	81:19

[a] Yields determined by ^{1}H NMR against 2,4,6-trimethoxybenzene internal standard. Enantiomer ratio (er) determined by SCF analysis.

can undergo racemization and that this process can be slowed at low temperature, as indicated in Scheme 5.57, the racemiztion of α-boryl alkylcopper intermediates generated in the allyl trap step may also contribute to the erosion of product enantioenrichment. We imagined two scenarios, (1) α-boryl alkylcopper species racemize less quickly than α-boryl alkylzinc species such that this process is not a significant source of erosion of product enantioenrichment, or (2) α-boryl alkylcopper species racemize more quickly, in which case additional optimization of the conditions used for the allyl trapping step might be required. To probe this question, the two experiments depicted in Scheme 5.60 were conducted. In contrast to a control reaction in which α-boryl alkylzinc product was allowed to form for 18 hours followed by CuCl-catalyzed allyl bromide trap, producing **5.286** with significant enantioenrichment (Scheme 5.60.A), when a solution of CuCl was added after 12 hours and allowed to stir for 6 hours before the addition of allyl bromide, **5.286** was obtained in racemic form (Scheme 5.60.B). This indicates that the racemization of *in situ*-generated α-boryl alkylcopper species is faster than for α-boryl alkylzinc species. Efforts

Scheme 5.60. Role of CuCl in promoting the racemization of α-boryl alkyl zinc intermediate[a]

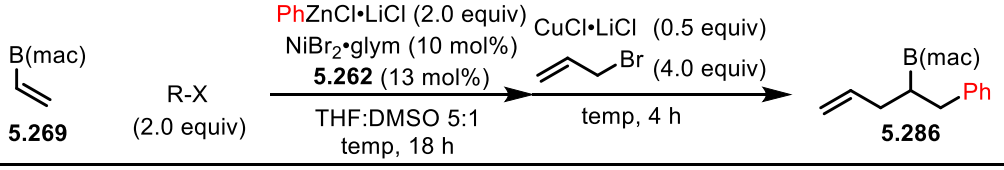


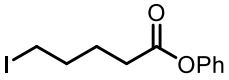
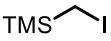
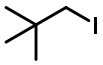
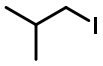
[a] Yields determined by ^{1}H NMR against 2,4,6-trimethoxybenzene internal standard. Enantiomer ratio (er) determined by SCF analysis.

towards combatting the erosion of product enantioenrichment due to the racemization of α-boryl alkylcopper intermediates by the use of lower amounts of CuCl and modulation of the solvent polarity employed in the trapping step are currently underway.

With an initial understanding of the racemization processes of α-boryl organometallic intermediates that lead to erosion in product enantioenrichment established, and preliminary strategies to combat these processes outlined (lower reaction temperatures employed in the carbozincation step, lower amounts of CuCl, higher amounts of allyl bromide electrophile, and lower solvent polarity employed in the electrophile trapping step) we next sought to understand the factors controlling the enantioselectivity of the diamine–Ni-catalyzed β-migratory insertion step as well as the α-boryl alkylnickel to α-boryl alkylzinc transmetallation step. We initiated these investigations by probing the effect of the alkyl iodide reagent on the reaction (Scheme 5.61). While reactions employing *n*BuI at 0 and -20°C were effective (entries 1 and 2), reactions employing *n*BuBr (entry 3), electrophilic perflorobutyl iodide (entry 4), a primary alkyl iodide with coordinating ester group (entry 5), and sterically hindered electrophiles (entries 6, 7, and 8) were far less effective in terms of the yield of the reaction. Notably, decreasing the size of the alkyl iodide reagent employed in the reaction from *n*-heptyl iodide to methyl iodide (entries 9, 10, 2, 11, 12, 13) led to an increase in the enantioselectivity of the reaction. The enantioselectivity could be further improved by lowering the reaction temperature from -20 to -40°C (entries 13, 14, 15). The observation that the nature of the electrophilic reagent employed in the reaction appears to directly impact enantioselectivity implied to us that this reagent might not simply be serving as an oxidant, facilitating the reentry of reduced

Scheme 5.61. Effect of alkyl halide on yield and enantioselectivity[a]



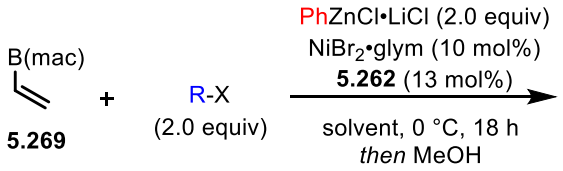
entry	temp (°C)	R-X	yield (%)	er
1	0	*n*Bu-I	56	53:47
2	-20	*n*Bu-I	42	75:25
3	-20	*n*Bu-Br	0	nd
4	-20	I-C_4F_9	0	nd
5	-20		11	nd
6	-20		7	nd
7	-20		9	nd
8	-20		17	74:26
9	-20	*n*Hept-I	38	74:26
10	-20	*n*Pent-I	24	73:27
11	-20	*n*Pr-I	31	73:27
12	-20	Et-I	37	78:22
13	-20	Me-I	51	81:19
14	-30	Me-I	54	85:15
15	-40	Me-I	54	87:13

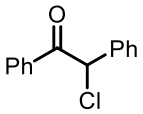
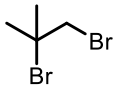
[a] Yields determined by ^{1}H NMR against 2,4,6-trimethoxybenzene internal standard. Enantiomer ratio (er) determined by SCF analysis.

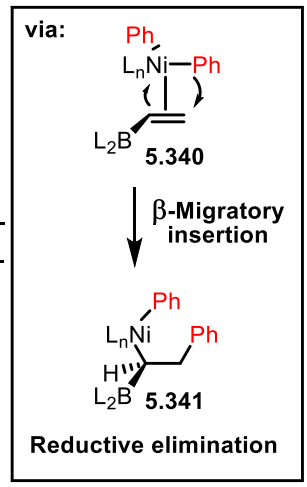
Ni(0) species into the catalytic cycle, but might be serving as an X-type ligand on the active catalytic species which engages in the β-migratory insertion step. This hypothesis is consonant with the observation that the use of alkyl halides such as those depicted in

Scheme 5.62, which are known to promote the formation of NiX_2[81], were not competent for the desired reaction but instead led to the formation of diarylated product **5.345** as well as a substantial amount of biphenyl **5.346.** To further probe the mechanistic hypothesis that the reaction under investigation is promoted by a catalytic species bearing organic fragments from both electrophile and nucleophile we conducted the reactions depicted in

Scheme 5.62. Mechanistic probes for the role of R-X[a]



R-X	solvent	yield (%) **5.338**	er **5.338**	yield (%) **5.339**
	THF:DMA=5:1	20	88:12	90
	THF:DMSO=5:1	23	67:23	50



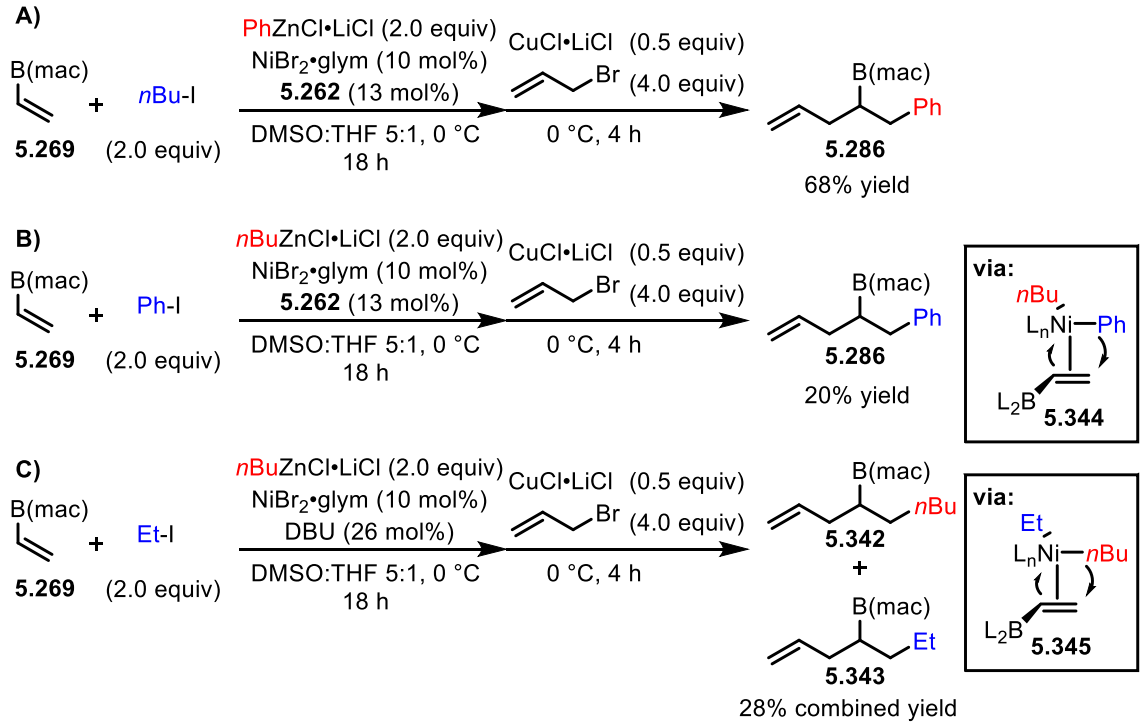
[a] Yields determined by ^{1}H NMR against 2,4,6-trimethoxybenzene internal standard. Enantiomeric ratio (er) determined by SFC analysis.

Scheme 5.63. Because putative catalytic species **5.351** can be generated by the combination of a ligated nickel precatalyst with *n*BuI and PhZnX or *n*BuZnX and PhI the use of either reagent combination should lead to the same product **5.289**. This outcome was found to be the case in practice (Scheme 5.63.A/B). The incorporation of a phenyl group into the product using both reagent combinations suggests that both reactions proceed *via* common intermediate **5.344** in which the phenyl group migrates preferentially. Furthermore, as

[81] (a) Iles, L; Okabe, J.; Yoshika, N.; Nakamura, E. *Org. Lett.* **2010**, 12, 2838. (b) Matsumoto, A.; Ilies, L.; Nakamura, E. *J. Am. Chem.* Soc. **2011**, 133, 6557. (c) Jin, L.; Liu, C.; Liu, J.; Hu, F.; Lan, U. Batsanov, A. S.; Howard, J. A. K.; Marder, T. B.; Lei, A. *J. Am. Chem. Soc*. **2009**, 131, 16656.

depicted in Scheme 5.63.C, when a crossover experiment was conducted employing EtI and *n*BuZnCl, a mixture of products was obtained in which both the Et and *n*Bu groups (groups with similar propensities to participate in β-migratory insertion) were incorporated into the product. Not only does this experiment support the hypothesis that the carbozincation reaction likely proceeds by a diorganonickel species **5.345**, but it also highlights the potential of this method to engage alkylzinc nucleophiles. It is mechanistically interesting to note that the lower efficiency of the combination of PhI with *n*BuZnX (Scheme 5.63.B) is consistent with the fact that, in contrast to the reaction employing *n*BuI and PhZnX (Scheme 5.63.A) which can proceed by a redox neutral catalytic cycle (Scheme 5.64.A), the use of PhI with *n*BuZnX involves a less efficient catalytic cycle requiring reductive elimination of a nickel dibutyl intermediate **5.354** before

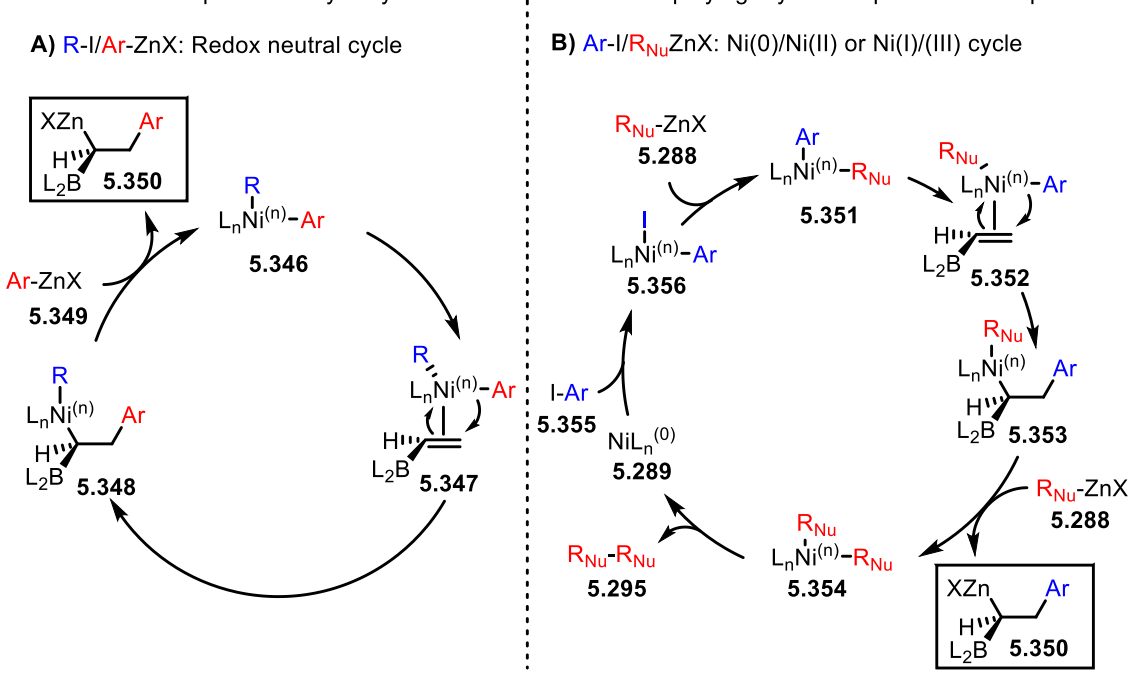
Scheme 5.63. Mechanistic probes to test the hypothesis that R-I serves as X-type ligand on Ni[a]



[a] Yields determined by ^{1}H NMR against 2,4,6-trimethoxybenzene internal standard.

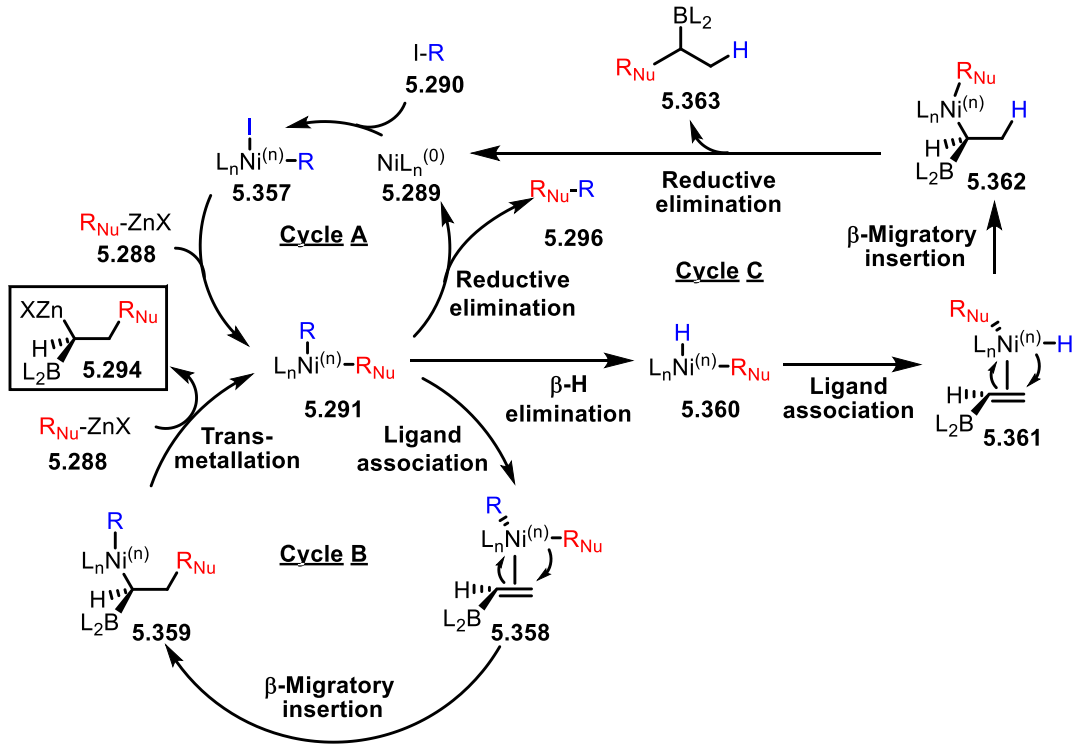
oxidative addition to PhI and transmetallation to *n*BuZnX can regenerate **5.351** (Scheme 5.64.B). The second reagent combination, while less atom economical, might be useful for more precious aryl halides if an inexpensive sacrificial organozinc nucleophile can be employed. With the proceeding mechanistic information in hand we propose a more

Scheme 5.64. Proposed catalytic cycles for carbozinaction employing aryl electrophile or nucleophile



detailed mechanistic scenario for the carbozincation reaction (Scheme 5.65) in which three competing catalytic cycles are connected *via* a common diorganonickel catalytic intermediate **5.291**. Cycle A is both responsible for the generation of key catalytic intermediate **5.291** as well as for the deleterious reductive elimination pathway that produces cross-coupling product **5.296**. Cycle B is a redox neutral cycle which produces desired α-boryl alkylzinc product **5.294** by a transmetallation step which also regenerates the active catalytic species **5.291**. Cycle C is a second deleterious catalytic pathway that occurs when catalytic intermediate **5.291** engages in a β-hydride elimination to form a

Scheme 5.65. Proposed catalytic cycle with competing β-H elimination-addition process

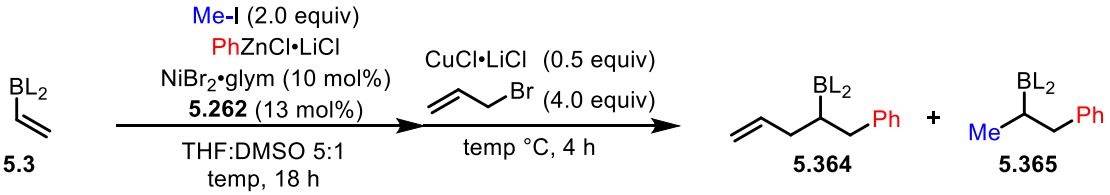


nickel hydride species **5.360**; **5.361** can react by hydride addition and reductive elimination steps to generate a Ni(0) species **5.289** which can reengage in cycle A to regenerate diorganonickel complex **5.291**. Because all three cycles appear to intersect *via* **5.291**, inhibiting reductive elimination and β-hydride elimination pathways is key to promoting the desired carbozincation reaction. This mechanistic proposal is consistent with the observation that lowering the temperature at which the reaction is conducted appears to strongly inhibit the formation of cross-coupling product (Scheme 5.55) and that the use of MeI, which precludes the β-hydride elimination pathway (Cycle C), also leads to higher yield and enantioselectivity at low temperature (Scheme 5.61, entries 9 to 12 versus 13).

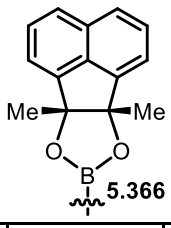
5.5 Survey of Ligand Structure on Boron

Employing our optimal conditions (THF:DMSO 5:1, MeI, at low temperature) we next investigated the role that the ligand structure on boron has on the reaction (Scheme 5.66). During this study we observed the formation α-boryl methyl product **5.365** in addition to the expected allyl-trap product **5.364**. Previous experiments had not revealed such an α-boryl alkylation product, likely because longer-chain alkyl iodide reagents were employed in the reaction. Quantification of the yield and enantioselectivity of allyl trap product **5.364** and α-boryl methyl product **5.365** employing the mac ligand **5.366** on boron revealed that lowering the reaction temperature from -20 to -40˚C strongly suppressed the formation of **5.365**. Notably, we found that at -20˚C α-boryl methyl product **5.365** was substantially more enantioenriched than the corresponding allyl trap product **5.364**. This situation was even more apparent when the ligand on boron employed in the reaction was changed from mac (**5.366)** to hydrogenated acenaphthoquinone (hac) (**5.367**). In this case, not only was the α-boryl methyl product formed as the major product of the reaction but it was much more enantioenriched (97:3 er) compared to the allyl trap product (79:21 er). Across a range of ligand structures, the highest yield and enantioselectivity of allyl trap product was obtained utilizing the mac ligand on boron. Notably, in every instance where we obtained sufficient quantities of α-boryl methyl product such that the enantioenrichment could be assessed, it was found to be 11-18 er units more enantioenriched than the corresponding allyl trap product. We hypothesized that the two most likely mechanistic scenarios leading to the formation of α-boryl methyl product **5.365** were: (1) an α-boryl–Ni–Me intermediate might undergo competitive reductive elimination rather than transmetallation to form α-

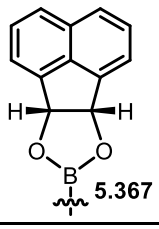
Scheme 5.66. Effect of ligand structures on boron[a]



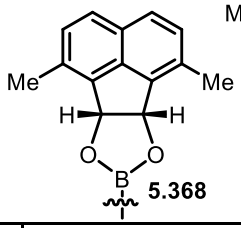
L_2 =



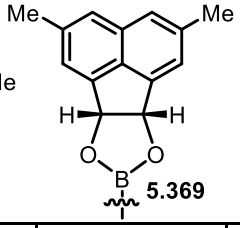
5.366



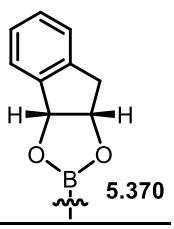
5.367



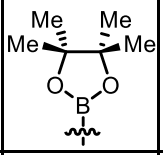
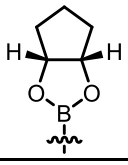
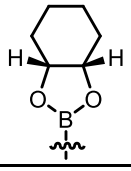
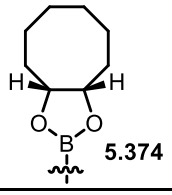
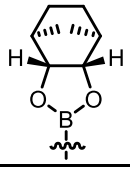
5.368



5.369



5.370

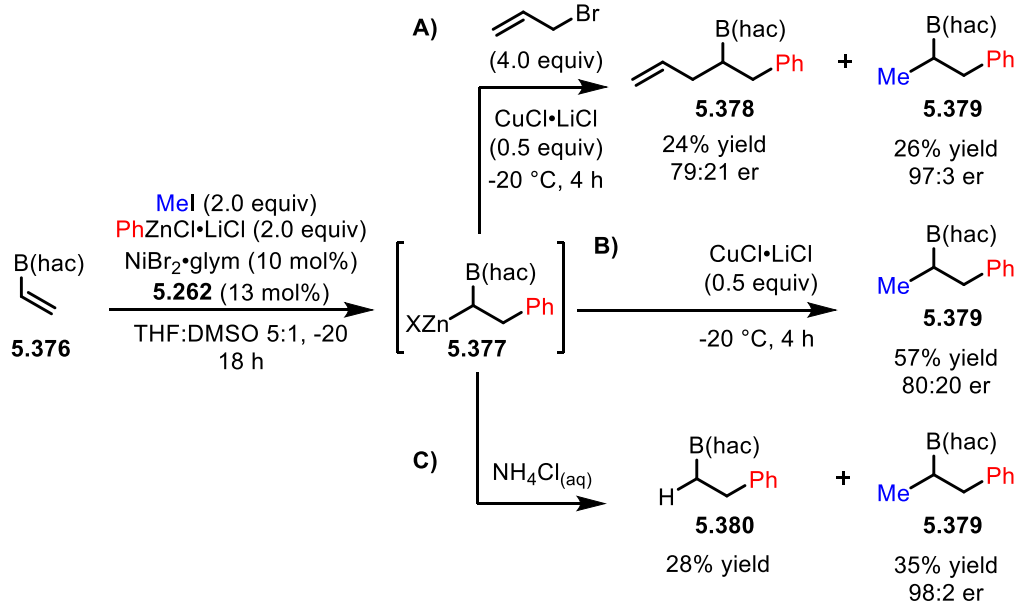
5.364:-20 °C	51% y 79:21 er	24% y 79:21 er	24% y 76:24 er	16% y 78:22 er	
-30 °C	51% y 85:15 er				22% y 88:12 er
-40 °C	42% y 88:12 er	8% y 89:11 er			
5.365:-20 °C	11% y 90:10 er	26% y 97:3 er	8% y er nd	<5% y er nd	
-30 °C	yield nd er nd				7% y er nd
-40 °C	6% y er nd	<5% yield er nd			
L_2 =	**5.271** 	**5.372** 	**5.373** 	 **5.374**	**5.375** 
5.364:-20 °C	27% y 60:40 er	41% y 76:24 er	13% y 68:32 er	26% y 71:29 er	
-30 °C					41% y 83:17 er
5.365:-20 °C	2% y er nd	12% y 89:11 er	21% y 86:14 er	12% y 88:12 er	

[a] Yields determined by ^{1}H NMR against 2,4,6-trimethoxybenzene internal standard. nd = not determined. Enantiomer ratio (er) determined by SCF analysis.

boryl alkylzinc product, or (2) that *in situ*-generated α-boryl alkylzinc product might directly (or upon transmetallation with CuCl) react with MeI. To probe if the α-boryl methyl product could be formed by the nucleophilic substitution of MeI with α-boryl

alkylzinc or copper species a reaction was conducted in which CuCl but no allyl bromide was added at the end of the reaction (Scheme 5.68.B). In this case α-boryl methyl product was formed in a yield equivalent to the combined yield of allyl-trap product and α-boryl methyl product (Scheme 5.68.A), suggesting that α-boryl alkylzinc or copper species can react with MeI *in situ* to generate methyl product **5.379**. Notably, under these conditions product **5.379** was obtained with a substantially lower level of enantioenrichment. This result suggested to us that the formation of α-boryl methyl product might proceed by two mechanisms with different degrees of stereoselectivity/stereospecificity. As depicted in Scheme 5.68.C, when a reaction was quenched with a proton source rather than CuCl, α-boryl methyl product was obtained in similar yield and enantioselectivity as when a CuCl-promoted allyl bromide trap was employed. While this set of experiments does not

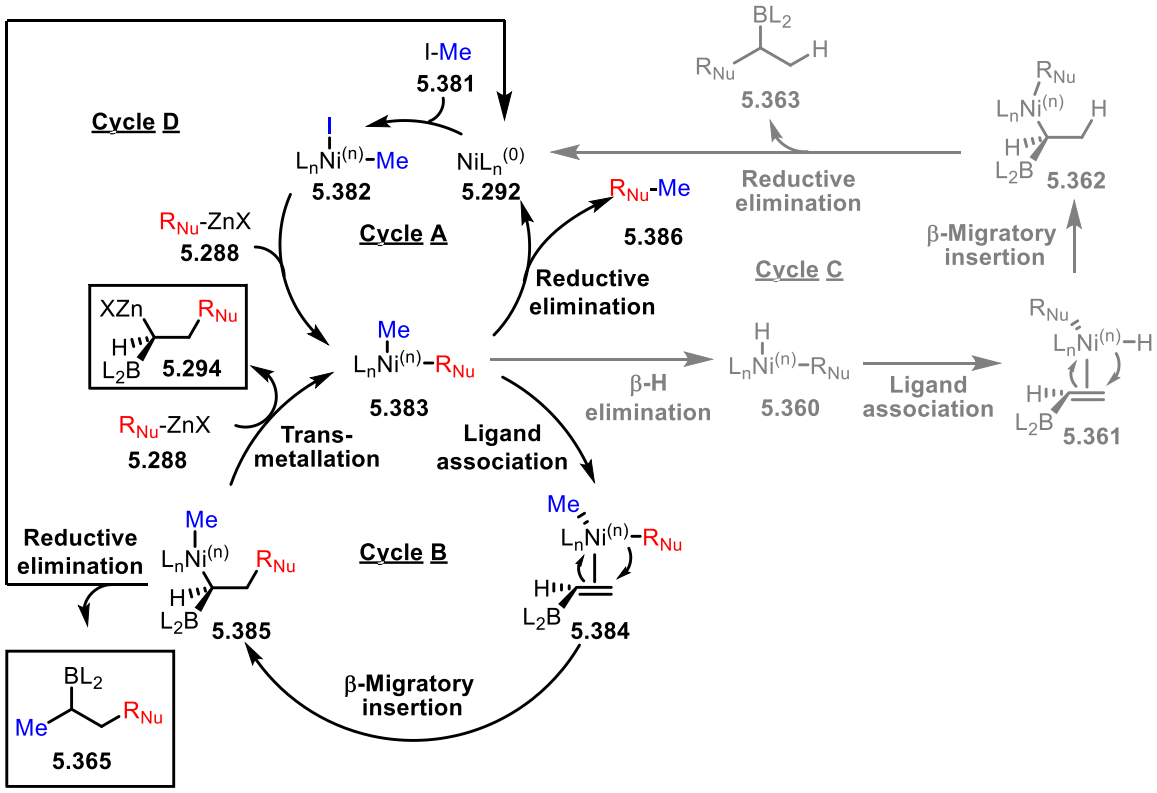
Scheme 5.68. Mechanistic probes for of the origin of methylation product **5.379**[a]



[a] Yields determined by ^{1}H NMR against 2,4,6-trimethoxybenzene internal standard. nd = not determined. Enantiomer ratio (er) determined by SCF analysis.

completely rule out the possibility that α-boryl alkylzinc nucleophiles may react with MeI in a much more stereospecific fashion than the corresponding α-boryl alkycopper species, we believe that these results are most consistent with a mechanistic scenario in which α-boryl methyl product **5.379** is formed by a reductive elimination pathway (Scheme 5.69). Combining this information with the previously proposed mechanism we obtain an overall mechanistic scenario in which the previously noted β-hydride elimination pathway (cycle C) is no longer relevant due to the use of MeI but a new reductive elimination pathway (cycle D) proceeding from α-boryl–Ni–Me complex **5.385** competes with the transmetallation step that produces α-boryl alkylzinc product **5.394**. The fact that Cycle D does not appear to operate when longer chain alkyl iodide reagents are employed in the

Scheme 5.69. Proposed catalytic cycle and competing reductive elimination processes when MeI is used



reaction might be explained by the difficulty of canting[82] a sterically hindered boron-substituted secondary alkyl group towards a larger butyl rather than methyl group during reductive elimination. Given the importance of methyl-substituted stereogenic carbon centers in natural products and pharmaceutical compounds, this highly enantioselective competitive aryl-methylation reaction of vinylboronic esters might be further developed into a useful reaction in its own right. Furthermore, if this reaction could be generalized to engage alkyl halide reagents other than MeI, it might provide a general strategy to obtain enantioenriched alkylboronic esters.

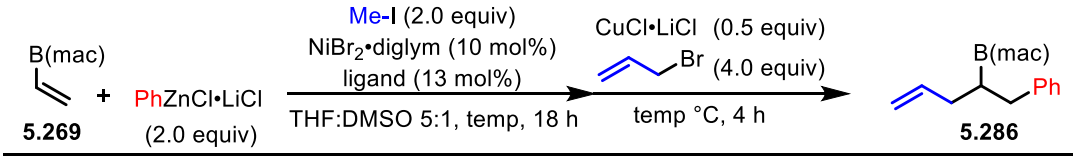
5.6 Survey of Ligand Structure on Nickel

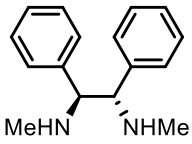
While our initial survey of ligand structures (Scheme 5.52) identified *N*,*N*'-dimethyl ethylene diamine **5.311** and *N*,*N*'-dimethyl diphenylethylene diamine **5.262** as effective ligand structures in terms of yield and product selectivity, we were interested to know if further ligand modifications could improve the enantioselectivity of the carbozincation-allyl bromide trap reaction. For ligand **5.262** an enantioselectivity of 88:12 er at -40˚C was obtained and this could be improved to 91:9 er by adding a small amount of DMF to the solvent system (which appeared to improve the homogeneity of the reaction at low temperature). Increasing the catalyst loading to 20 mol% resulted in an increase of yield to 65% while maintaining the same level of enantioselectivity (92:8 er). Decreasing the reaction temperature further to -45˚C while increasing the catalyst loading to 20% resulted

[82] Organotransition Metal Chemistry: From Bonding to Catalysis. Hartwig J. F. 1964, University of Science Books, Mill Vally, Calefornia.

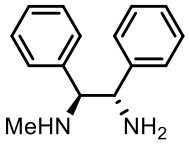
in a further increase to the enantioselectiviy of the reaction (50% yield, 94:6 er). While

Scheme 5.70. Effect of diamine ligand structures[a]

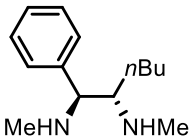




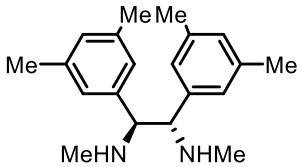
5.262
-20 °C, 51% y, 79:21 er
-30 °C, 54% y, 85:15 er
-40 °C, 42% y, 88:12 er
-40 °C, 38% y, 91:9 er[b]
-40 °C, 65% y, 92:8 er[b,c]
-45 °C, 50% y, 94:6 er[b,c]



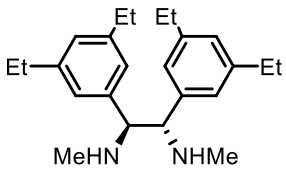
5.387
3% y, er nd



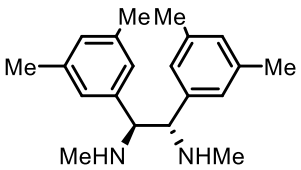
5.388
25% y, 55:45 er



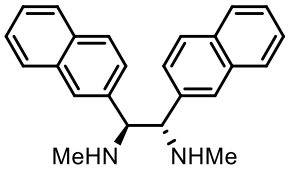
5.389
56% y, 65:35 er



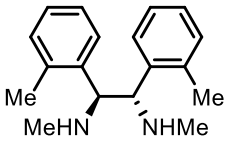
5.390
-20 °C, 27% y, 71:29 er



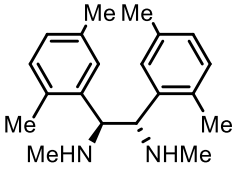
5.391
16% y, 74:26 er[d]



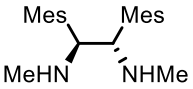
5.392
-40 °C, 42% y, 82:18 er



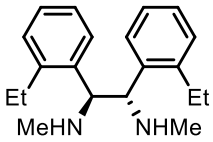
5.393
-20 °C, 42% y, 82:18 er
-40 °C, 38% y, 91:9 er



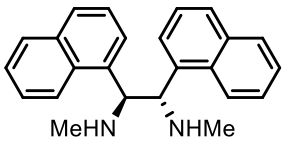
5.394
32% y, 82:18 er



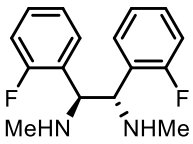
5.395
25% y, 71:26 er



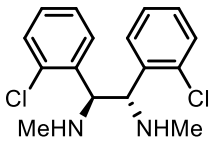
5.396
34% y, 84:16 er
36% y, 91:9 er



5.397
-20 °C, 44% y, 76:24 er
-40 °C, 27% y, 85:15 er



5.398
0% y, er nd



5.399
30% y, 92:8 er
25% y, 95:5 er[b]

[a] Yields determined by ^{1}H NMR against 2,4,6-trimethoxybenzene internal standard. nd = not determined. Enantiomer ratio (er) determined by SCF analysis. [b]10:1:1 THF:DMSO:DMF solvent system employed. [c]20% catalyst loading employed. [d]*n*BuI employed in place of MeI.

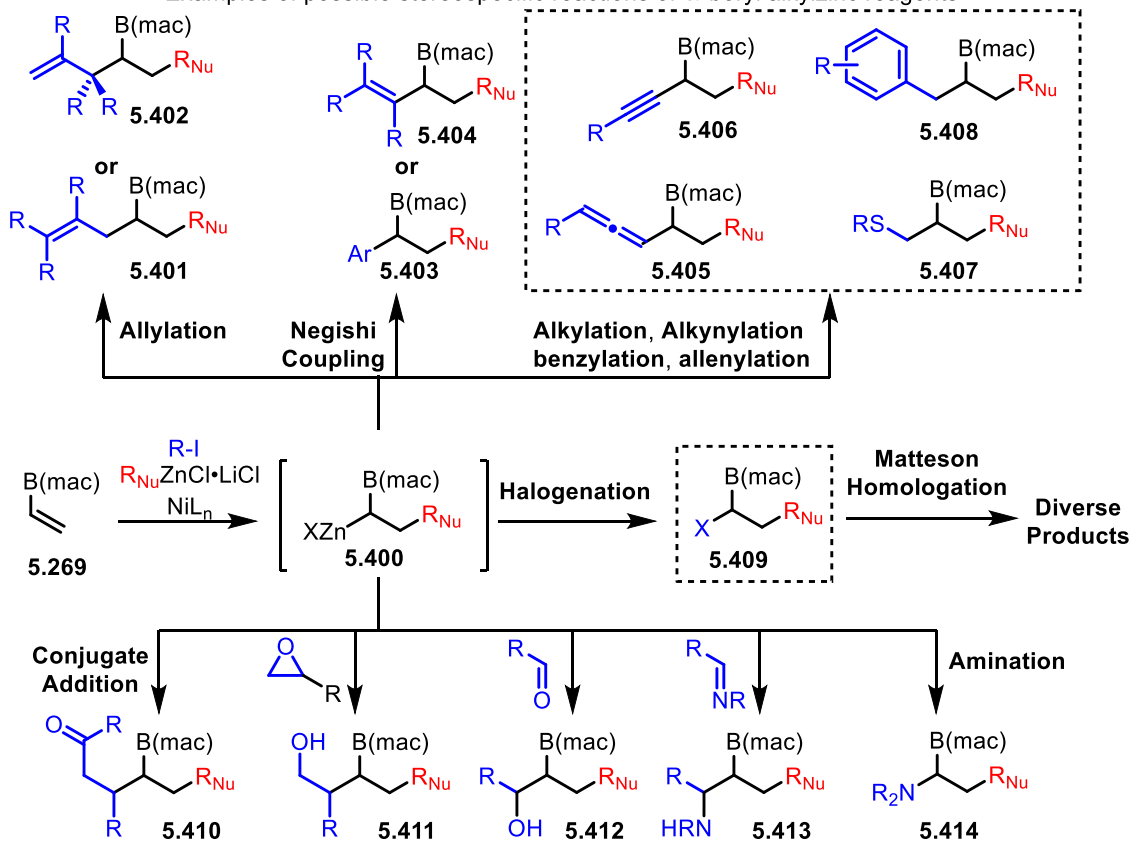
mono methylated ligand **5.387** demonstrated good reactivity at 0 ˚C (68% yield), at -20˚C only trace product was observed. Substitution of an *n*Bu group for a Ph group in the ligand backbone (**5.388**) resulted in a substantial decrease in yield and selectivity. *Meta* substitution on the aromatic rings of the ligand structure led to a decrease in the enantioselectivty of the reaction (**5.389** to **5.392)**. The presence of a single methyl or ethyl *ortho* substituents on the aromatic rings of the catalyst appeared to enhance the enantioselectivity of the reaction (**5.393**, **5.394**, **5.396**), though the use of di-*ortho* substituted mesityl ligand **5.395** resulted in low yield and enantioselectivity. 1-Napthyl ligand **5.397** was also less effective in terms of yield and enantioselectivy than *ortho*-tolyl ligand **5.393**. We then attempted to probe if varying the steric and electronic nature of the *ortho* aryl substituent from an alkyl to a halide might lead to an increase in the efficiency of the reaction. While *ortho*-fluorophenyl ligand **5.398** was completely ineffective in promoting the desired reaction, the use of *ortho*-chlorophenyl ligand **5.399** led to an increase in enantioselectivity relative to **5.262** (92:8 er versus 88:12 er), which could be further improved to 95:5 er by employing the previously mentioned THF:DMSO:DMF modification to the solvent system. We anticipate that further modification to reaction conditions and catalyst structure will lead to improvements in the yield and enantioselectivity of this reaction.

5.7 Substrate Scope

Because α-boryl and benzyl alkylzinc reagents have been demonstrated to react with a wide range of electrophiles we imagined that the enantiomerically-enriched reagents

described above might grant access to a variety of valuable product motifs (Scheme 5.71). Therefore, while we continued in our effort to optimize the yield and enantioselectivity of the carbozincation-allyl trap reaction we surveyed the substrate scope with respect to the electrophile and nucleophile classes that can be engaged.

Scheme 5.71. Examples of possible stereospecific reactions of α-boryl alkylzinc reagents

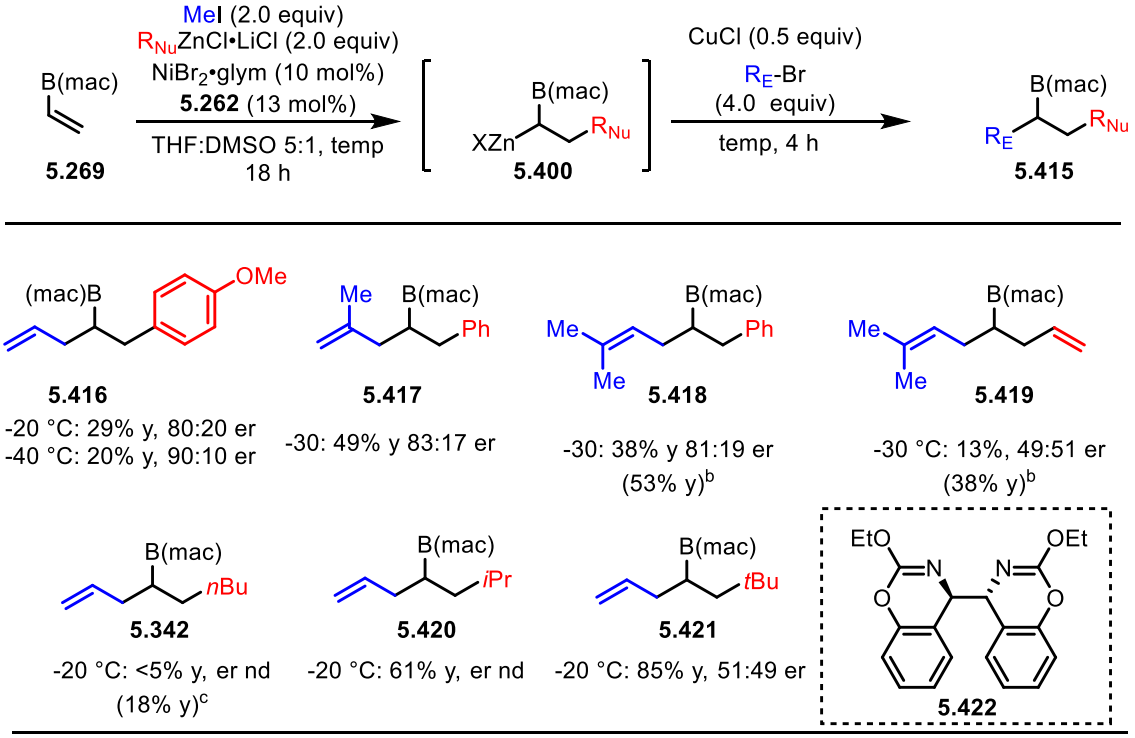


5.7.1 Survey of Scope with Respect to Nucleophile and Allyl Electrophile

The reaction can accommodate the use of an electron-rich para-methoxyphenylzinc chloride nucleophile, producing product **5.416** with comparable enantioenrichment relative to the analogous reaction employing phenylzinc chloride nucleophile (Scheme 5.70). We attribute the somewhat diminished yield obtained in this case to the presence of LiBr

(generated from the nucleophile preparation that employs Li-Br exchange with PhBr and *t*BuLi, followed by transmetallation with $ZnCl_2$) which we have observed to inhibit the reaction. Nucleophile preparation employing Zn insertion rather than Li-Br exchange should address this issue. Comparable levels of yield and enantioselectivity can be obtained employing allylbromide electrophiles with various substitution pattern (**5.417**, **5.418**). Employing a vinylzinc nucleophile in the reaction resulted in a diminished yield and loss of enantioselectivity (**5.419**). We found the yield of this reaction could be somewhat improved using achiral ligand **5.311** (yields in parenthesis). The diminished yield and enantioselectivity of the reaction employing vinylzinc nucleophile is likely due to the

Scheme 5.72. Initial survey of substrate scope with respect to nucleophile and allyl electrophile



[a] Yields determined by ^{1}H NMR against 2,4,6-trimethoxybenzene internal standard. Enantiomer ratio (er) determined by SCF analysis. [b]Racemic reaction conditions employed [*n*BuI (2.0 equiv), PhZnCl (2.0 equiv), $NiBr_2$•glym (10%), N,N'-dimethyl ethylene diamine **5.311** (13%), THF:DMSO 5:1, 0° C, 18 h. [c]Racemic conditions employed with **5.422** (20%) as ligand at 0° C.

difference in the steric profile of this nucleophile relative to an aryl group and might be accommodated by ligand modification.

We next investigated if alkyl nucleophiles could be engaged in the reaction. While we found that *n*BuZnCl could be employed in the carbozinaction-allyl trap reaction using the achiral amine ligand DBU (Scheme 5.63.C), reactions employing this nucleophile with chiral diamine ligand **5.262** were substantially lower yielding (**5.342**). The yield of this reaction could be somewhat improved by employing diamine ligand **5.422** at 0˚C, though the rate of racemization of α-boryl alkylzinc nucleophile at this temperature precluded a determination of the enantioselectivity of this process. We attributed this result to a more challenging β-migratory insertion step with an alky-Ni rather than Ph-Ni catalyst complex as well as the greater amount of deleterious decomposition pathways of vinyl–B(mac) observed in these reactions (likely occurring from transmetallation of the vinylboron reagent upon activation by the more nucleophilic *n*BuZnCl rather than PhZnCl). In contrast to the low yield obtained employing *n*BuZnCl, we obtained a higher yield of product when employing *i*PrZnCl and *t*BuZnCl nucleophiles (product **5.420** and **5.421**). The stark difference in reactivity between primary alkyzinc nucleophiles and secondary/tertiary nucleophiles, as well as the lack of enantioenrichment in the case of product **5.421** suggests that these products may be formed by a different mechanism involving the formation of a secondary or tertiary alkyl radicals, which, by radical addition and reduction processes, leads to the formation of α-boryl alkylzinc products in a non-enantioselective fashion.

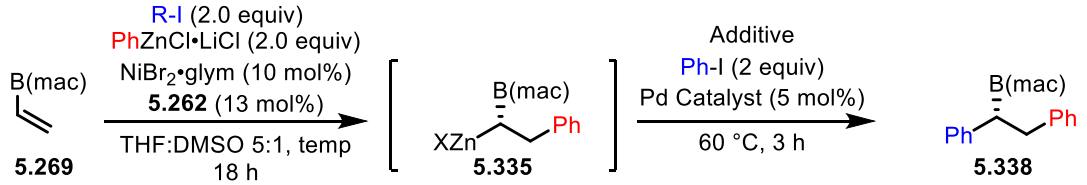
With the reactivity of various nucleophilic species established we next turned our attention to assessing if enantioenriched α-boryl alkylzinc reagents can participate in

stereospecific reactions beyond allylation.

5.7.2 Diphosphine–Pd-Catalyzed Negishi Coupling of α-Boryl Alkylzinc Nucleophiles

A brief assessment of the Negishi coupling reaction of α-boryl alkylzinc reagents with PhI employing achiral diphosphine–Pd complexes demonstrated that this transformation can occur in a stereospecific fashion (Scheme 5.73). The use of elevated temperatures for the coupling step was found to be superior to the use of lower temperatures with respect to yield and enantioselectivity, suggesting that the rate of the coupling reaction is more strongly accelerated by increase in temperature than the accompanying racemization process. While we found that the use of MeI rather than *n*BuI at -20°C led to an increase in product enantioenrichment (entry 1 and 2), a much lower yield was obtained. The

Scheme 5.73. Diphosphine–Pd-catalyzed Negishi coupling of α-boryl alkylzinc intermediate[a]



entry	R-I	temp (°C)	additive	Pd Catalyst	yield (%)	er
1	*n*BuI	-20	none	$(Ph_3P)_3PdCl_2$	42	62:38
2	MeI	-20	none	$(Ph_3P)_3PdCl_2$	10	69:31
3	*n*BuI	-20	LiCl (2.0 equiv)	$(Ph_3P)_3PdCl_2$	45	71:29
4[b]	MeI	-30	LiCl (2.0 equiv)	$(Ph_3P)_3PdCl_2$	36	79:21
5[b]	MeI	-30	LiCl (2.0 equiv)	$Pd(OAc)_2$ + SPhos	41	76:24
6[b]	MeI	-30	LiCl (2.0 equiv)	$Pd(OAc)_2$ + RuPhos	34	77:23
7[b]	MeI	-30	LiCl (2.0 equiv)	$Pd(OAc)_2$ + PCy_3	29	79:21
8[b]	MeI	-30	LiCl (2.0 equiv)	$Pd(OAc)_2$ + $P(O\text{-}Tol)_3$	16	83:17

[a] Yields determined by ^1H NMR against 2,4,6-trimethoxybenzene internal standard. Enantiomer ratio (er) determined by SCF analysis. [b]1.0 equiv of MeI rather than 2.0 equiv.

enantioenrichment of product could be improved by addition of LiCl to the coupling step (entries 1 versus 3). We hypothesized that residual MeI from the carbizincation reaction might inhibit the Negishi coupling step by competitively reacting with the Pd–diphosphine catalyst. Consistent with this hypothesis when the carbozincation step was conducted at -30 °C employing 1.0 rather than 2.0 equivalents of MeI, the yield of the reaction was improved from 10% to 36% with a further improvement of product enantioenrichemt. Varying the nature of the phosphine ligand employed in the coupling step (entries 4 through 8) did not lead to a substantial improvement in the yield or enantioenrichment of the product. The yield and enantioselectivity of the carbozincation-Negishi cross-coupling sequence will be further refined by merging the use of LiCl and lower amounts of MeI in the coupling step with improvements to the carbozincation step described above (improved ligand design, lower temperature, THF:DMF:DMSO solvent system).

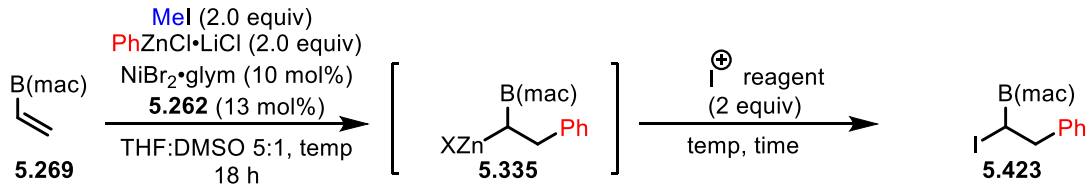
5.7.3 Halogenation of α-Boryl Alkylzinc Nucleophiles

In addition to CuCl-catalyzed allylation and diphophine–Pd-catalyzed Negishi coupling reaction, we were interested to know if enantioenriched α-boryl alkylzinc nucleophiles might be halogenated. If this reaction were to occur and proceed in a stereospecific fashion, the carbozincation-halogenation reaction sequence would constitute a general and modular entry point into the manifold of stereospecific 1,2-metallate rearrangement reactions of enantioenriched α-halo boronic ester compounds.[83] When preliminary experiments were

[83] Matteson, D. S. Boronic Acids: Preparation, Applications in Organic Synthesis and Medicine, D. G. Hall, Ed. (Wiley–VCH, **2005**), chap. 8.

conducted at -20 ˚C employing 20% catalyst loading with ligand **5.262** for the carbozincation step and I_2 or NIS iodination reagents for the halogenation step, good yields of α-iodo alkylboronic ester product **5.423** were obtained but with low levels of enantioenrichment (entries 1 and 2). Reducing the temperature at which the carbozincation and trapping steps were conducted from -20 to -30˚C resulted in an increase in product enantioenrichment (entries 2 and 3). The reproducibility of the reaction with respect to product enantioenrichment could be improved by quenching the reaction at low temperature with aqueous sodium thiosulfate rather than directly passing the reaction

Scheme 5.74. Halogenation of α-boryl alkylzinc intermediate[a]



entry	temp	Electrophile	work up conditions	I⊕ trap time (h)	yield (%)	er
1[b]	-20	I_2	silica gel	2	77	55:45
2[b]	-20	NIS	silica gel	2	64	59:41
3[b]	-30	NIS	silica gel	2	65	73:27
4[b]	-30	NIS	$Na_2S_2O_{3(aq)}$	2	53	74:26
5[b]	-40	NIS	$Na_2S_2O_{3(aq)}$	2	44	84:15
6[b]	-40	NIS	H_2O	2	51	80:20
7	-40	NIS	$Na_2S_2O_{3(aq)}$	1	35	84:15
8[c]	-40	NIS	$Na_2S_2O_{3(aq)}$	1	39	85:15
9[c,d]	-40	NIS	$Na_2S_2O_{3(aq)}$	1	51	50:50
10[c,d,e]	-40	NIS	$Na_2S_2O_{3(aq)}$	1	>5	na
11[c,d,e,]	-40	I_2	$Na_2S_2O_{3(aq)}$	1	29	49:51
12[c,e]	-40	I_2	$Na_2S_2O_{3(aq)}$	1	39	85:15

[a] Yields determined by ^{1}H NMR against 2,4,6-trimethoxybenzene internal standard. Enantiomer ratio (er) determined by SCF analysis. [b]20% catalyst loading was employed. [c]Electrophile was added at -78 °C. [d]THF:DMF:DMSO (10:1:1) solvent system used. [e]rxn diluted (0.08 to 0.05 M) with Et_2O before addition of electrophile.

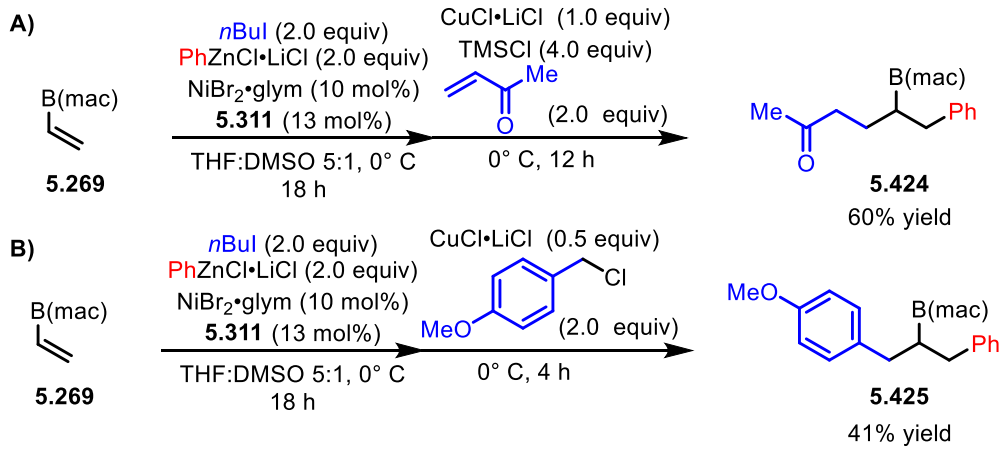
solution through a silica gel plug (entries 3 and 4). This beneficial effect may be due to the reduction of electrophilic species in the reaction solution, such as I_2 which can participate in non-stereospecific halogenation upon warming during workup; further the addition of water may solvate iodide anions thereby preventing them from racemizing the product by a degenerate metallate rearrangement. Decreasing the temperature at which the carbozincation reaction was conducted to -40 ˚C led to a further increase in product enantioenrichment to 84:16 er (entry 5), while quenching the reaction with water rather than saturated aqueous sodium thiosulfate led to a decrease in product enantioenrichment to 80:20 er (etnry 6). Decreasing the Ni-diamine catalyst loading from 20 to 10% resulted in a decrease in yield but did not affect product enantioenrichement (entries 5 versus 7) while cooling the reaction solution from -40 ˚C to -78 ˚C before addition of NIS led to a slight improvement in the reproducibility of the reaction (entry 8) and levels of yield and enantioenrichment which are similar to the corresponding carbozincation-allyl trap sequence (Scheme 5.70). The use of the three solvent system of THF:DMF:DMSO (10:1:1), which we found to be beneficial in the carbozincation-allyl trap reaction sequence, in this sequence resulted in improved yields of product but without detectable levels of enantioenrichment (entry 9). Attempts to counteract the apparent deleterious effects of DMF on the halogenation step by diluting a reaction with Et_2O before addition of NIS were unsuccessful, likely owing to the poor solubility of NIS at -78 to -40˚C in this less polar reaction solution (entry 10). The use of I_2, which has greater solubility in Et_2O, again resulted in the product being formed as a racemate (entry 11). The restoration of enantioselectivity upon conducting this same reaction sequence without the addition of

DMF in the carbozincation step confirms the deleterious effect of this solvent on the enantiospecificity of the halogenation step (entry 12). Further improvements to product yield and enantioenrichment are currently being explored by utilizing higher catalyst loading and employing the *ortho*-substituted diamine ligands which we have found lead to enhanced enantioselectivies in the carbozincation-allyl trapping sequence.

5.7.4 Benzylation and Conjugate Addition of α-Boryl Alkylzinc Nucleophiles

With the feasibility of engaging enantioenriched α-boryl alkylzinc nucleophiles in stereospecific allylation, Negishi cross-coupling, and halogenation reactions established, we next assessed if these organometallic compounds could participate in other reactions. Utilizing the achiral diamine ligand *N*,*N*'-dimethyl ethylene diamine **5.311** we found that *in situ* generated α-boryl alkylzinc nucleophiles participate smoothly in conjugate addition (Scheme 5.75.A) and benzylation reactions (5.76.B). Notably the conjugate addition of α-boryl alkylzinc nucleophiles grants access to products such as **5.424** with a valuable 1,4-

Scheme 5.75. Benzylation and conjugate addition of α-boryl alkylzinc nucleophiles[a]



[a] Yields are of purified material.

difunctionalization pattern. If α,β-unsaturated esters can be engaged in this reaction, that would grant access to enantioenriched lactones and lactams upon boron oxidation/amination and acid-catalyzed condensation. The benzylation of α-boryl alkyzinc nucleophiles is a potentially powerful method of preparing enantioenriched dibenzyl alcohols and amines that would be challenging to prepare using traditional methods such as enantioselective ketone reduction (or benzyl nucleophile addition to an aldehyde) and reductive amination (or benzyl nucleophile addition to an aldimine) respectively. We anticipate many other valuable products can be accessed utilizing this one-pot carbozincation-electrophile trapping approach.

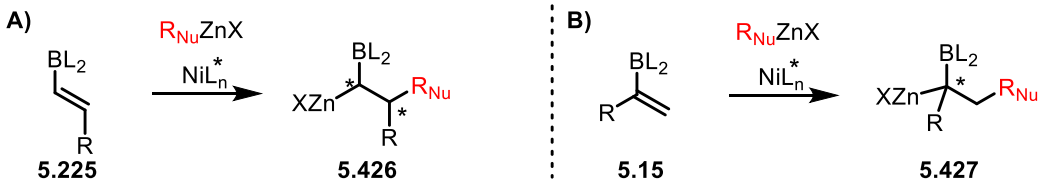
5.8 Future Directions

While the mechanistic insights gained during the development of the present diamine–Ni-catalyzed enantioselective carbozincation reaction has broad implications for the development of further enantioselective multicomponent processes, some specific near-term innovations that we anticipate are described below.

5.8.1 Carbozincation of Substituted Alkenylboron Reagents

If terminally substituted alkenylboron reagents could be engaged in the enantioselective carbozincation reaction, this would facilitate the rapid and modular construction of diverse products bearing adjacent stereogenic carbon centers (Scheme 5.76.A). Such reactions might be able to employ a combination of catalyst and substrate control to preparing all four stereoisomers of product. While the configuration of the non-labile β-boryl

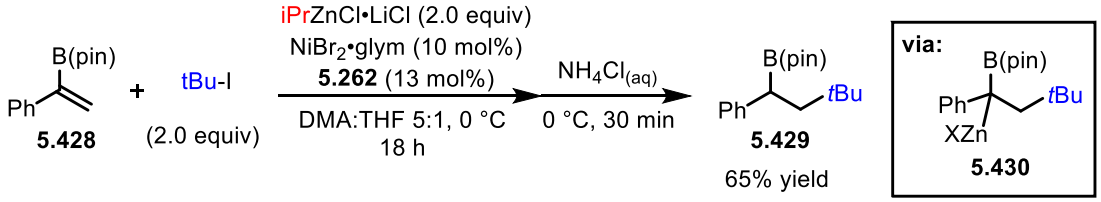
Scheme 5.76. Preperation of more higly substituted α-boryl alkylzinc nucleophiles[a]



stereogenic carbon center of **5.426** would be set by the carbozincation step, the configuration of the Zn-substituted α-boryl stereogenic carbon center might be either retained or inverted depending on the conditions employed in the electrophile trapping step.

If 1,1-disubstituted alkenylboron reagents could be successfully employed in carbozincation-electrophile trapping reactions this would grant access to products bearing fully-substituted stereogenic carbon centers (Scheme 5.76.B). The feasibility of preparing fully-substituted α-boryl alkylzinc nucleophiles finds support in the mechanistic probe depicted in Scheme 5.77. We observed that by employing *i*PrZnCl nucleophile and *t*BuI electrophile, 1-phenyl vinylboronic ester reagent **5.428** was converted to secondary alkylboronic ester product **5.429** upon protic workup. The intermediacy of α-boryl alkylzinc reagent **5.430** (inset) in this reaction is supported by the observation that if D_2O rather than NH_4Cl is used to quench the reaction, full deuterium incorporation into **5.429** is observed. While this reaction likely operates by a non-stereoselective radical addition-reduction mechanism (*via* an α-boryl radical species), the ability to access functionalized alkylzinc nucleophiles in a modular manner is potentially valuable. Additionally, the

Scheme 5.77. Preperation of more higly substituted α-boryl alkylzinc nucleophiles



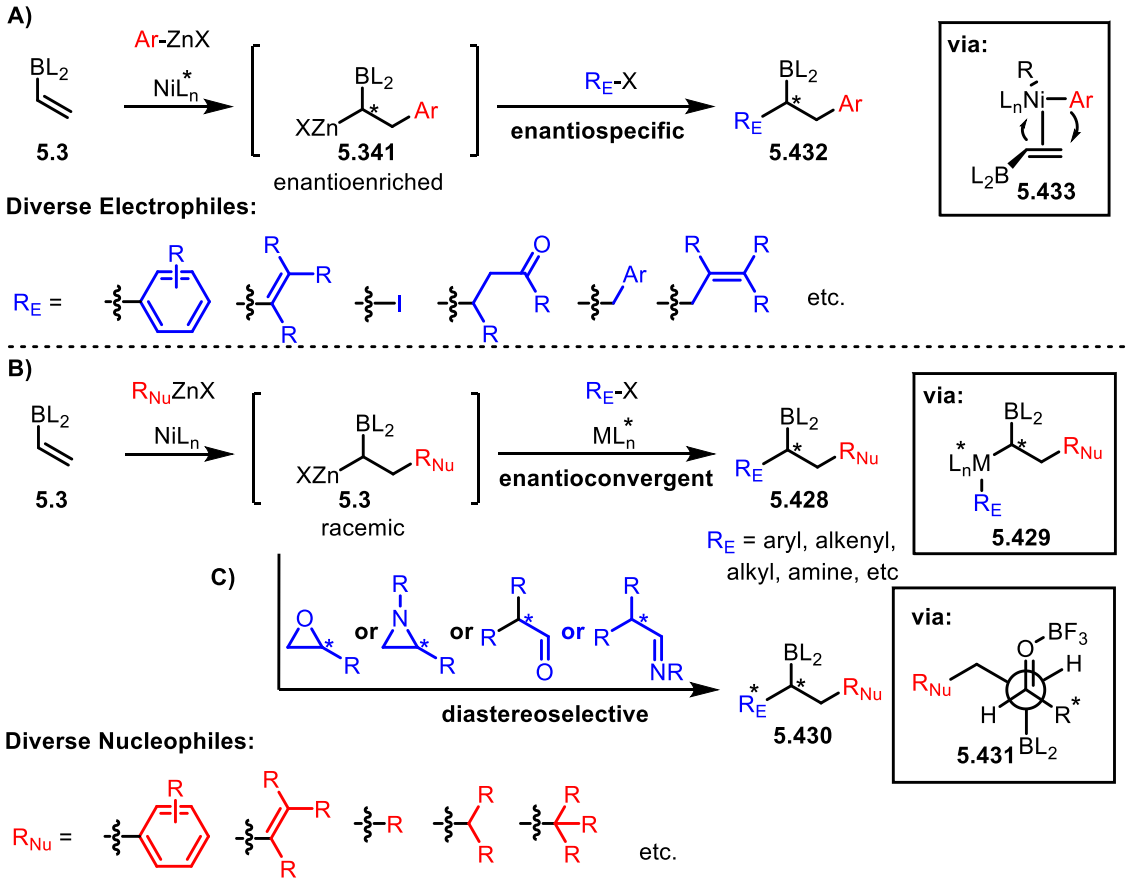
stereochemical lability of such compounds might be exploited to enable the preparation of enantioenriched products utilizing a stereoconvergent dynamic kinetic resolution approach.

5.8.2 Dynamic Kinetic Resolution of α-Boryl Alkylzinc Nucleophiles

We have demonstrated that the enantioselective preparation of α-boryl alkylzinc nucleophiles can enable this class of compounds to serves as versatile enantioenriched organometallic intermediates, capable of engaging a wide variety of electrophilic species (Scheme 5.78.A). While the reaction is also capable of employing diverse nucleophiles, including aryl, alkenyl, and primary, secondary and tertiary alkylzinc species, non-aryl-based reagents cannot currently be engaged in an enantioselective fashion. While the different steric and electronic profile of alkenyl nucleophiles can likely be accommodated by altering the ligand structure and conditions employed in the reaction, engaging alkyl nucleophile will likely entail additional fundamental challenges. Primary alkylzinc nucleophiles demonstrate sufficiently low reactivity that appreciable levels of product formation only occur at temperatures at which α-boryl alkylzinc product racemization is rapid. For secondary and tertiary alkylzinc nucleophiles, alternative radical-based pathways appear to intervene, producing α-boryl alkylzinc products efficiently but in racemic fashion.

A potentially powerful complementary approach to enantioselective carbozincation-stereospecific electrophile trapping would be to prepare α-boryl alkylzinc nucleophiles in a racemic fashion and then subject these *in situ*-generated organometallic intermediates to

Scheme 5.78. Improved nucleophile generality enabled by stereoconvergent coupling of α-boryl alkylzinc



stereoconvergent coupling reactions (Scheme 5.78.B). Because the stereoselectivity of the overall transformation is determined in the second step of the reaction sequence, the carbozincation step can be optimized to maximize yield without regard to stereoselectivity or racemization, thus drastically expanding the types of nucleophiles that can be engaged. Additionally, in contrast to the narrow substrates scope traditionally associated with stereoconvergent coupling reactions of secondary organometallic reagents[84], this approach should grant access to a wide range of products. Because the second stereoconvergent coupling step involves the formation of a stereocenter distal from the previously

[84] Cherney, A. H.; Kadunce, N. T.; Reisman, S. E. *Chem. Rev.* **2015**, 115, 9587.

incorporated nucleophile group, the yield and enantioselectivity of the reaction should be relatively insensitive to the nature of the nucleophiles employed in this reaction. Furthermore, the boron functional group can increase the lability of the Zn-substituted stereogenic carbon center, promoting the stereomutation required for such a strategy, while enabling subsequent product diversification by the numerous known functional group transformations of boron.[85] Finally, unlike traditional enantioconvergent couplings of secondary alkyl organometallics, which require substrates to bear two groups of substantially different size to ensure high enantioselectivity, our proposed strategy can modulate the ligand set on boron to tune the enantioselectivity of the transformation without limiting the generality of the products that can be accessed.

As depicted in Scheme 5.78.C, racemic secondary α-boryl alkylzinc nucleophiles might also be used as versatile nucleophilic reagents in diastereoselective reactions with readily available enantioenriched electrophiles such as epoxides, aziridines, aldehydes, and imines, furnishing enantioenriched 1,2 and 1,3 diols, amino alcohols and diamine products after oxidation or amination of the boronic ester moiety.

To probe the feasibility of a carbozincation-stereoconvergent coupling strategy we carefully designed the model system depicted in Scheme 5.79. To highlight the potential of this method to utilize alkyl nucleophiles that cannot be successfully engaged in an enantioselective fashion employing the previously described approach we employed vinylboronic pinacol ester, *t*BuZnCl nucleophile, *n*BuI electrophile, $NiBr_2$•glym, and the achiral diamine ligand *N*,*N*'-Me-ethylene diamine (**5.311**). Taking inspiration from a report

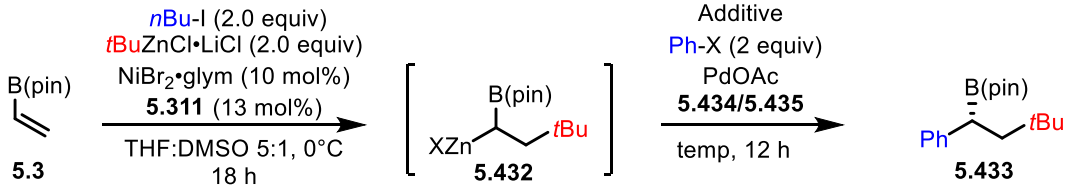
[85] Sanford, C.; Aggarwal, V. K. *Chem. Commun*. **2017**, 53, 5481.

by Knochel describing the enantioselective coupling of α-methylbenzyl Grignard reagents with alkenyl bromide electrophiles, we chose to employ $Pd(OAc)_2$ and ferrocene-based diphosphine Mandyphos ligand (**5.434**) as the precatalyst combination for the second coupling step of the sequence.[86] Based on reports of the beneficial role of metal halide additive such as $ZnBr_2$ in enantioselective coupling reactions of secondary organometallic reagents[82,87], as well as our own observation that the addition of CuCl accelerates the rate of racemization of α-boryl alkylzinc reagents, (Scheme 5.60) (a mechanistic requirement for a dynamic kinetic resolution of such a reagent, barring racemization of the α-boryl alkylpalladium catalytic complex before reductive elimination) CuCl was employed as a co-catalyst. Employing 50% CuCl co-catalyst, and 0.5% Pd-diphosphine catalyst at 0˚C, we obtained 51% yield of the desired carbozincation-Negishi coupling product **5.433** with 75:25 er. Decreasing the amount of CuCl to 30% and increasing the amount of Pd-diphosphine to 2% resulted in a slight decrease in yield to 46% but an increased in the enantioenrichment of the desired product to 80:20 er (entry 2). Decreasing the amount of CuCl further to 5% led to a further decrease in yield but without substantially altering product enantioenrichment. (entry 3). Decreasing the reaction temperature from 0 to -20˚C, employing 30% CuCl and 2% Pd-diphosphine led to an increase in yield to 68% yield while maintaining product enantioenrichment (entry 4). Changing the aromatic groups of the diphosphine ligand employed in the reaction from phenyl to 4-methoxy-3,5-dimethylphenyl Mandyphos ligand (**5.435**) utilizing the conditions employed in entry 2,

[86] Schwink, L.; Knochel, P. *Chem. Eur. J*. **1998**, 4, 950.
[87] a) Cross, G.; Vriesema, B. K.; Boven, G.; Kellogg, R. M.; Bolhuis, F. van *J. Organomet. Chem.* **1989**, 370, 357. (b) Hayashi, T.; Hagihara, T.; Katsuro, Y.; Kumada, M. *Bull. Chem. Soc. Jpn.* **1983**, 56, 363.

the yield of the reaction increased from 46 to 84% yield with a slight decrease in enantioenrichment from 80:20 to 75:25 er (entry 5). Control reactions demonstrated that CuCl appears to be essential for the reaction to proceed efficiently (entry 6) and addition of ZnCl2 in place of CuCl was ineffective at promoting the desired reaction. Switching from a THF:DMSO 5:1 to THF:DMF:DMSO 10:1:1 solvent system did not improve the reaction (entries 8 versus 5). Decreasing the temperature at which the Negishi coupling step is conducted from 0 to -40 ºC strongly suppressed product formation (entry 9). When the electrophile employed in the reaction was changed from iodobenzene to bromobenzene

Scheme 5.79. Stereoconvergent Negishi coupling of α-boryl alkylzinc nucleophiles[a]



entry	temp (°C)	X	CuCl•LiCl (mol%)	$Pd(OAc)_2$ (mol%)	**Ligand** (mol%)	yield (%)	er
1	0	I	50	0.5	**5.434** 0.6	51	75:25
2	0	I	30	2	**5.434** 2.4	46	80:20
3	0	I	5	2	**5.434** 2.4	37	81:19
4	-20	I	30	2	**5.434** 2.4	68	80:20
5	0	I	30	2	**5.435** 2.4	84	75:25
6	0	I	0	2	**5.435** 2.4	<5	NA
7[b]	0	I	0	2	**5.435** 2.4	<10	NA
8[c]	0	I	30	2	**5.435** 2.4	84	75:25
9	-40	I	30	2	**5.435** 2.4	<10	NA
10	0	Br	30	2	**5.435** 2.4	54	92:8
11	0	OTf	30	2	**5.435** 2.4	44	94:6

[a] Yields are of isolated material. Enantiomer ratio (er) determined by SCF analysis. Ligand **5.434** is (S_P,S_P)-1,1'-Bis[(*R*)-(dimethylamino)phenylmethyl]-2,2'-bis(diphenylphosphino)ferrocene (Mandyphos SL-M001-1). Ligand **5.435** is (R_P,R_P)-1,1'-Bis[bis(4-methoxy-3,5-dimethylphenyl)phosphino]-2,2'-bis[(*S*)-(dimethyl amino)benzyl]ferrocene. [b] $ZnCl_2$ (1.0 equiv) employed in place of CuCl•LiCl additive. [c] THF:DMF:DMSO 5:1:1 solvent system employed.

the yield of the reaction decreased from 84 to 54% but the enantioselectivity of the reaction improved from 75:25 to 92:8 er (entry 5 versus 10). When phenyl triflate was employed rather than iodobenzene the yield of the reaction similarly decreased but the enantioselectivity of the reaction was further increased to 94:6 er (entry 10).

While further optimization is currently underway to improve the yield and enantioselectivity of this transformation, as well as to uncover its mechanistic underpinnings, it is clear from these preliminary results that this carbozincation-enantioconvergent coupling approach represents a potentially powerful method for the modular construction of enantioenriched alkylboronic ester products.

5.9 Conclusion

We have developed a highly enantioselective carbozincation reaction catalyzed by nickel-diamine complexes which employs alkenylboron reagents and arylzinc nucleophiles to produce enantioenriched α-boryl alkylzinc nucleophiles. This new class of enantioenriched organometallic building block shows excellent configurational stability below -30˚C and can react with diverse electrophilic reagents in a stereospecific manner. When conducted in a one-pot fashion, the carbozincation-electrophile trapping reaction sequence constitutes a three-component coupling which is capable of transforming simple chemical building blocks into diverse enantioenriched alkylboronic ester products which can be transformed into functionalized C(sp^3)-rich carbon frameworks. Research in this area of chemistry is ongoing and the mechanistic insights which have been gained in these studies promise to enable the development of powerful new transformations which harness

the potential of boron to mediate the formation of anionic species and facilitate stereoconvergent processes.

5.10 Experimental

5.10.1 General Information

^{1}H NMR spectra were recorded on either a Varian Gemini-500 (500 MHz), Varian Gemini-600 (600 MHz), or Varian Inova-500 (500 MHz) spectrometer. Chemical shifts are reported in ppm with the solvent resonance as the internal standard ($CDCl_3$: 7.26 ppm). Data are reported as follows: chemical shift, integration, multiplicity (s = singlet, d = doublet, t = triplet, q = quartet, p = pentet, m = multiplet, app = apparent), and coupling constants (Hz). ^{13}C NMR spectra were recorded on either a Varian Gemini-500 (125 MHz), Varian Gemini-600 (150 MHz) or a Varian Inova-500 (125 MHz) spectrometer with complete proton decoupling. Chemical shifts are reported in ppm with the solvent resonance as the internal standard ($CDCl_3$: 77.24 ppm). ^{11}B NMR spectra were recorded on a Varian Gemini-500 (128 MHz) spectrometer. Chemical shifts are reported in ppm using boron trifluoride diethyl etherate as the external standard ($BF_3{\cdot}O(C_2H_5)_2$: 0.0 ppm). Infrared (IR) spectra were recorded on a Bruker alpha-P Spectrometer. Frequencies are reported in wavenumbers (cm^{-1}) as follows: strong (s), broad (br), medium (m), and weak (w). Optical rotations were measured on a Rudolph Analytical Research Autopol IV Polarimeter and the values reported are averages of seven measurements. High-resolution mass spectrometry (DART) was performed at the Mass Spectrometry Facility, Boston College, Chestnut Hill, MA. Liquid chromatography was performed using forced flow (flash chromatography) on silica gel (SiO_2, 230 x 450 Mesh, purchased from Silicycle) either manually or using an automated column (Biotage). Thin layer chromatography (TLC) was performed on 25 μm silica gel aluminum backed plates from Silicycle.

Visualization was performed using ultraviolet light (254 nm), ceric ammonium molybdate (CAM) in ethanol or phosphomolybdic acid, and cerium(IV) sulfate in ethanol with sulfuric acid (Seebach).

Analytical chiral supercritical fluid chromatography (SFC) was performed on a TharSFC Method Station II equipped with Waters 2998 Photodiode Array Detector with isopropanol or methanol as the modifier.

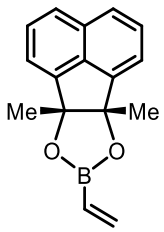
Tetrahydrofuran (THF), diethyl ether (Et_2O), dichloromethane (DCM) and toluene were purified using Pure Solv MD-4 solvent purification system, from Innovative Technology, Inc., by passing the solvent through two activated alumina columns after purging with argon. The ligand employed in Scheme **5.52** were purchased from Sigma Aldrich and Strem chemicals. Vinylboronic pinacol esters was purchased from Combi-Blocks and was used without further purification. Allylic bromides, Iodobenzene, and 4-methoxy phenyl bromide were purchased from Sigma Aldrich. Alkyl iodide electrophiles were purchased from Oakwood Chemicals and used without purification. VinylZnCl nucleophile was prepared by transmetallation of vinyllithium (prepared according to the reported procedure[88]) with $ZnCl_2$ according to the general reaction procedures below. All other alkyl iodide electrophiles were purchased from Oakwood Chemicals, Sigma Aldrich, or Acros and used without further purification. Dimethyl sulfoxide (DMSO was purchased from Acros and used without purification. *N*,*N*-dimethyl formamide (DMF) was purchased from Sigma Aldrich and used without purification. *N*,*N*-dimethyl acetamide (DMA) was

[88] Zhang, L.; Lovinger, G. J.; Edelstein, E. K.; Szymaniak, A. A.; Chierchia, M. P.; Morken, J. P. *Science* **2016**, *351*, 70.

purchased from Sigma Aldrich, distilled over 4Å molecular sieves under reduced pressure and stored under argon atmosphere. Nickel(II) dibromide·glyme was purchased from Strem. (*S*,*S*)-*N*,*N*′-dimethyl 1,2-diphenylethane-1,2-diamine (*S*,*S*)-**5.262** (as well as (*R*,*R*)-**5.262**) was synthesized from the corresponding commercially available (*S*,*S*)-1,2-diphenylethylenediamine (Oakwood Chemicals) following literature methods.[89] The diamine ligands in Scheme 5.70 were prepared according to the reported literature procedure. All other reagents were purchased from either Aldrich, Alfa Aesar or Acros and were used without further purification.

5.10.2 Experimental Information

5.10.2.1 Procedures for Preparation of Vinyl–B(mac) and Vinyl–B(hac)

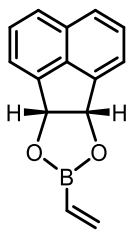


6b,9a-Dimethyl-8-vinyl-6b,9a-dihydroacenaphtho[1,2-d][1,3,2] dioxaborole (5.269). Vinyl–B(mac) was prepared according to the literature procedure.[90] To a solution of potassium vinyltrifluoroborate (343.9 mg, 2.57 mmol, 1.0 equiv) in a 50% solution of acetonitrile/water (5 mL) was added sequentially open to air at room temperature: 1,2-dimethylacenaphthylene-1,2-diol (550 mg, 2.57 mmol, 1.0 equiv), imidazole (524.3 mg, 7.70 mmol, 3.0 equiv), and $FeCl_3$ (20.8 mg, 0.128 mmol, 0.05 equiv). The reaction was allowed to stir for 30 min, then filtered through a plug of silica gel with Et_2O and concentrated. The unpurified material was

[89] V. F. Kuznetsov, G. R. Jefferson, G. P. A. Yap, H. Alper, *Organometallics* **2002**, 21, 4241.
[90] J. A. Myhill, C. A. Wilhelmsen, L. Zhang, and J. P. Morken, *J. Am. Chem. Soc*. **2018**, 140, 15181.

purified by silica gel chromatography to afford the desired product (0.591 g, 2.364 mmol, 92% yield).

^{1}H NMR (500 MHz, $CDCl_3$) δ 7.81 (dd, J = 7.8, 1.1 Hz, 2H), 7.73 – 7.54 (m, 4H), 6.15 (dd, J = 19.6, 4.1 Hz, 1H), 5.99 (dd, J = 13.7, 4.1 Hz, 1H), 5.84 (dd, J = 19.6, 13.7 Hz, 1H), 1.84 (s, 6H). **^{13}C NMR** (126 MHz, $CDCl_3$) δ144.68, 137.32, 137.31, 134.72, 131.36, 128.48, 125.29, 119.49, 91.95, 22.10. **IR** (neat) ν_{max} 3061.55(w), 2972.95(w), 1618.14(m), 1432.59(s), 1373.13(m), 1328.09(s), 1314.88(s), 1248.84(s), 1116.15(s), 872.70(s), 805.21(s) cm^{-1}. **HRMS** (DART) for $C_{16}H_{16}BO_2$ $[M+H]^+$ calculated: 251.12379, found: 251.12445.



8-Vinyl-6b,9a-dihydroacenaphtho[1,2-d][1,3,2]dioxaborole (5.376). Vinyl–B(hac) was prepared according to the literature procedure.[91] To a solution of potassium vinyltrifluoroborate (0.3439 mg, 2.57 mmol, 1.0 equiv) in a 50% solution of acetonitrile/water (5 mL) was added sequentially open to air at room temperature: 1,2-dihydroacenaphthylene-1,2-diol (0.4786 g, 2.57 mmol, 1.0 equiv), imidazole (524.3 mg, 7.70 mmol, 3.0 equiv), and $FeCl_3$ (0.0208 mg, 0.128 mmol, 0.05 equiv). The reaction was allowed to stir at 30 min, then filtered through a plug of silica gel with Et_2O and concentrated. The unpurified material was purified by silica gel chromatography to afford the desired product (65% yield).

[91] Myhill, J. A.; Wilhelmsen, C. A.; Zhang, L.; Morken, J. P. *J. Am. Chem. Soc*. **2018**, 140, 15181.

^{1}H NMR (400 MHz, $CDCl_3$) 7.81 (d, J = 8.1 Hz, 2H), 7.65 (d, J = 6.9 Hz, 2H), 7.59 (dd, J = 8.1, 6.9 Hz,2H), 6.25 – 6.11 (m, 3H), 6.01 (dd, J = 13.7, 4.1 Hz, 1H), 5.85 (dd, J = 19.5, 13.7 Hz, 1H). **^{13}C NMR** (101 MHz, $CDCl_3$) δ 140.72, 137.85, 136.77, 131.46, 128.37, 125.65, 121.85, 82.72, 16.08. **IR** (neat) ν_{max} 3005.72(w), 2990.99(w), 2962.02(w), 1616.47(m), 1425.05(m), 1330.02(m), 1275.36(s), 1260.69(s), 979.23(w), 750.20(s) cm^{-1}. **HRMS** (DART) for $C_{14}H_{11}BO_2$ $[M+H]^+$ calculated: 222.08466, found: 222.08385.

5.10.2.2 General Procedure A: Preparation of Organozinc Chloride Nucleophiles:

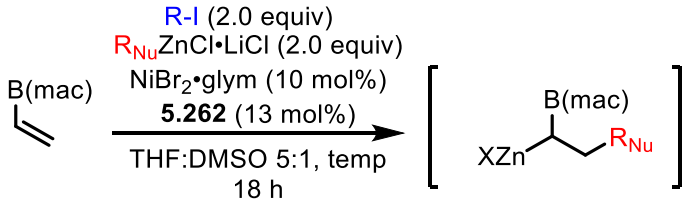
Commercial organolithium reagents were purchased from Sigma Aldrich and were converted to the corresponding organozinc nucleophile by dropwise addition of organolithium nucleophile (1.0 equiv) to a solution of $ZnCl_2$ in THF (0.66 M, 1.2 equiv) at 0 ºC. The reaction solution was allowed to stir at room temperature for 45 min, and was used directly in reactions.

5.10.2.3 General Procedure B: Preparation of Organozinc Chloride Nucleophiles:

Organolithium reagents were prepared by lithium-halogen exchange with *tert*-butyllithium using the following procedure: aryl bromide (1.0 mmol) was placed in a flame-dried 20 mL vial under N_2 atmosphere and dissolved with 5 mL of dry diethyl ether. The vial was sealed with a pierceable PTFE-lined cap and a septum was taped over it (this second septum was backfilled with N_2 to create a buffer zone to prevent air from entering the vial). The

solution was allowed to cool to -78 ºC and *tert*-butyllithium (1.18 mL, 1.7 M, 2.0 equiv) was added dropwise. The solution was allowed to stir at -78°C for 30-40 min after which a solution of $ZnCl_2$ in THF was added (2.4 mL, 0.5 M, 1.2 equiv). The mixture was allowed to warm to room temperature and stir for 45 min after which the solvent was carefully removed under vacuum using a Schlenck line. The concentrated residue was brought inside an argon filled glovebox and redissolved in 2 mL of THF. The resulting solution was titrated following literature procedure.[92]

5.10.2.4 General Procedures for Carbozincation Reaction:

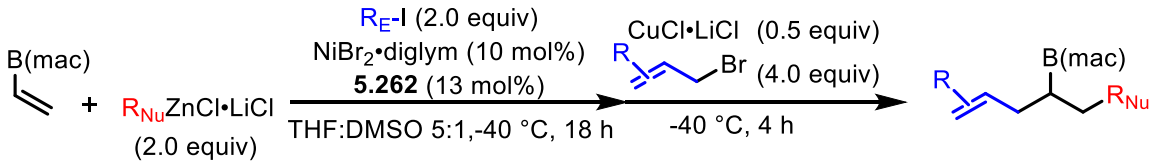


In an argon-filled glovebox, an oven-dried 2 dram vial equipped with a magnetic stir bar was charged with $NiBr_2$•glyme (0.0062 g, 0.02 mmol, 0.10 equiv), (*S,S*)-*N,N*'-dimethyl-1,2-diphenyl-ethane-1,2-diamine (*S,S*)-**5.262** (0.0063 g, 0.026 mmol, 0.13 equiv) and THF 0.67 mL. The catalyst solution was allowed to stir for 1.5 h at ambient temperature. In an argon-filled glovebox a second oven-dried 2 dram vial with magnetic stir bar was charged with (6b,9a)-6b,9a-dimethyl-8-vinyl-6b,9a-dihydroacenaphtho[1,2-d][1,3,2] dioxaborole (0.050 g, 0.2 mmol, 1.00 equiv), the catalyst solution (0.67 mL), and alkyl iodide (0.40 mmol, 2.0 equiv). THF and DMSO were added to the vial so as to reach a final volume

[92] Krasovskiy, A.; Knochel, P. *Synthesis* **2006**, 5, 0890.

(taking into account the volume of the organozinc solution) of 2.08 mL of THF and 0.42 mL DMSO (2.5 mL, 0.08 M, 5:1 THF:DMSO). The vial was sealed with a PTFE-lined pierceable cap, taped, and brought outside the glovebox where it was placed under positive nitrogen pressure and was allowed to cool to -10 ºC (brine ice bath). The nitrogen inlet was then removed, the puncture hole was sealed with tape, and the reaction mixture was placed in a CryoCool set at -40 ºC and allowed to stir for 20-30 min before addition of the organozinc solution (0.40 mmol, 2.00 equiv). The reaction mixture was allowed to stirred at -40 ºC for 18 h.

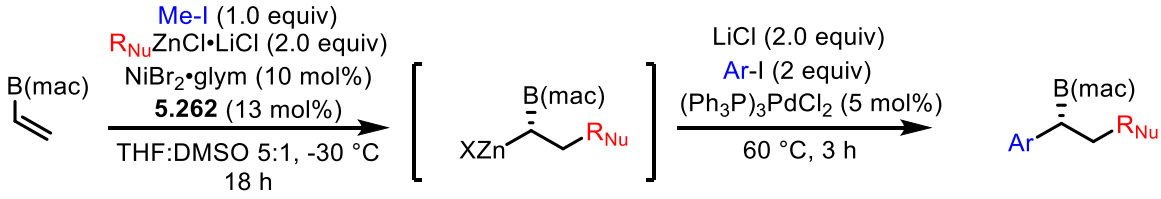
5.10.2.5 General Procedures for Carbozincation-Allyl Trap:



The carbozincation step of the reaction sequence was conducted according to ***General Procedures for Carbozincation Reaction (Section 5.10.2.4).*** At the end of the carbozincation step allyl bromide and a THF solution of CuCl•2LiCl (0.10 mmol, 0.5 equiv) were added sequentially to the cold reaction solution. The reaction was allowed to stir at -40 ºC for 2-4 h. At the end of this time, 0.30 mL of a saturated solution of aqueous NH_4Cl was added to the reaction and this mixture was allowed to warm to room temperature while stirring. The mixture was then transferred to a separatory funnel using ethyl acetate, and the organic layer was washed with brine, dried over Na_2SO_4,

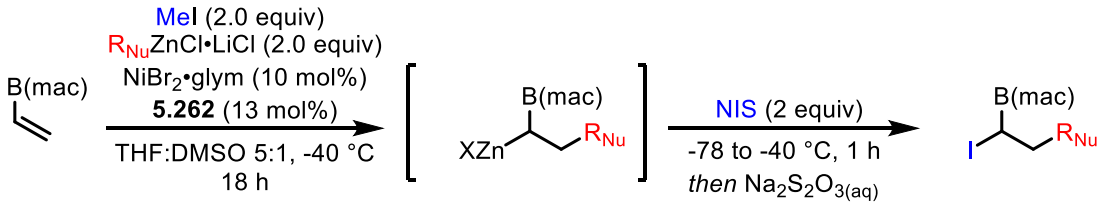
concentrated under reduced pressure, filtered through a silica gel plug with diethyl ether, reconcentrated, and subsequently purified by silica gel chromatography to provide the desired product.

5.10.2.6 General Procedures for Carbozincation-Negishi Cross-Coupling:



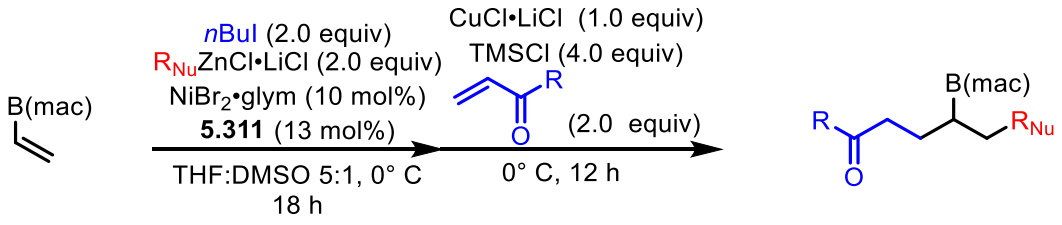
The carbozincation step of the reaction sequence was conducted according to ***General Procedures for Carbozincation Reaction (Section 5.10.2.4)***, with the modification that the reaction was conducted at -30 rather than -40 °C and employed 1.0 rather than 2.0 equivalents of MeI. To the cold solution containing α-boryl alkylzinc nucleophile was added ArI (0.4 mmol, 2.0 equiv) and a THF solution of LiCl (0.4 mmol, 2.0 equiv) and $(Ph_3P)_3PdCl_2$ (0.01 mmol, 0.05 equiv). The reaction was allowed to warm to room temperature while stirring and was then allowed to warm to 60 °C for 3 h. The mixture was then allowed to cool to room temperature and was transferred to a separatory funnel using ethyl acetate, and the organic layer was washed with brine, dried over Na_2SO_4, concentrated under reduced pressure, filtered through a silica gel plug with diethyl ether, concentrated, and subsequently purified by silica gel chromatography to provide the desired product.

5.10.2.7 General Procedures for Carbozincation-Iodination:



The carbozincation step of the reaction sequence was conducted according to ***General Procedures for Carbozincation Reaction (Section 5.10.2.4)***. At the end of the carbozincation step the reaction solution was allowed to cool to -78 ºC and a solution of NIS in THF (1 mL, 1 M solution, 0.4 mmol, 2.0 equiv) was added dropwise to the solution. The reaction was allowed to warm to -40 ºC and stir at that temperature for 1-2 h. 0.30 mL of a saturated aqueous solution of $Na_2S_2O_3$ was then added to the reaction, which was then allowed to stir at -40 ºC for 30 min. While still cold the reaction was filtered through a silica gel plug with diethyl ether, reconcentrated, and subsequently purified by silica gel chromatography to provide the desired products.

5.10.2.8 General Procedures for Carbozincation-Conjugate Addition:



The carbozincation step of the reaction sequence was conducted according to ***General Procedures for Carbozincation Reaction (Section 5.10.2.4)*** with the modification that the reaction was conducted at 0 ˚C rather than -40˚C and employed *n*BuI and ligand **5.311**

rather than MeI and ligand **5.262**. At the end of the carbozincation step Michael acceptor (0.4 mmol, 2.0 equiv), TMSCl (0.8 mmol, 4.0 equiv), and a THF solution of CuCl•2LiCl (0.20 mmol, 1.0 equiv) were added sequentially to the cold reaction. The reaction was allowed to stir at 0 ºC for 12 h. A saturated solution of aqueous NH_4Cl (0.30 mL) was then added to the reaction and the mixture was allowed to warm to room temperature while stirring. The mixture was then transferred to a separatory funnel using ethyl acetate, and the organic layer was washed with brine, dried over Na_2SO_4, concentrated under reduced pressure, filtered through a silica gel plug with diethyl ether, reconcentrated, and subsequently purified by silica gel chromatography to provide the desired products.

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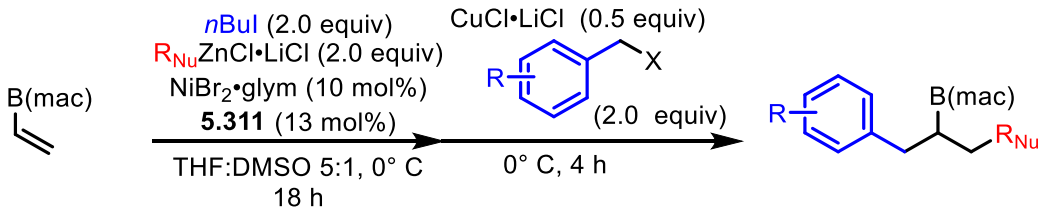
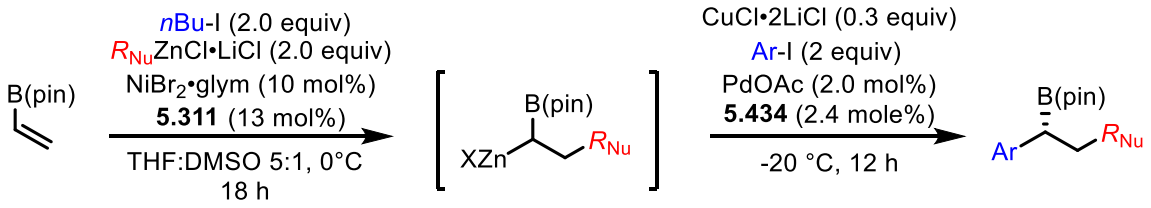
5.10.2.9 General Procedures for Carbozincation-Benzylation:



Carbozincation–benzylation reactions were conducted according to ***General Procedures for Carbozincation-Allyl Trap Reaction (Section 5.10.2.5)*** but employing benzyl halide, *n*BuI, and ligand **5.311** in place of: allyl bromide, MeI, and ligand **5.262**.

5.10.2.10 General Procedures for Stereoconvergent Negishi Cross-Coupling:

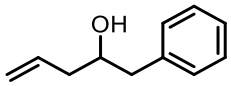


The carbozincation step of the reaction sequence was conducted according to ***General Procedures for Carbozincation Reaction (Section 5.10.2.4)*** with the modification that the reaction was conducted at 0 ˚C rather than -40 ˚C and employed *n*BuI and ligand **5.311** rather than MeI and ligand **5.262**. In an argon-filled glovebox, an oven-dried 2-dram vial equipped with a magnetic stir bar was charged with $Pd(OAc)_2$ (0.004 mmol, 0.02 equiv), (S_p,S_p)-**5.434** (0.0024 mmol, 0.024 equiv), and THF (0.2 mL). The $Pd(OAc)_2$/(S_p,S_p)-**5.434** solution was allowed to stir for 20 min at room temperature. At the end of the carbozincation step the reaction solution was allowed to cool to -20˚C and aryl iodide (0.4 mmol, 2.0 equiv), a THF solution of CuCl•2LiCl (0.15 M, 0.06 mmol, 0.3 equiv), and the $Pd(OAc)_2$/(S_p,S_p)-**5.434** solution were added sequentially to the cold solution. The reaction was allowed to stir at -20 ºC for 12 h. A saturated solution of aqueous NH_4Cl (0.30 mL) was then added to the reaction and the mixture was allowed to warm to room temperature while stirring. The mixture was then transferred to a separatory funnel using ethyl acetate, and the organic layer was washed with brine, dried over Na_2SO_4, concentrated under reduced pressure, filtered through a silica gel plug with diethyl ether, reconcentrated, and subsequently purified by silica gel chromatography to provide the desired products.

5.10.2.11 General Method for Oxidation of Boronic Ester Products*:*

Note: Where appropriate, boronic ester products were oxidized. In these cases, the procedure used was the same as that described in the corresponding method of preparation but with the modification that: After the reaction was completed the mixture was filtered through a silica gel plug with diethyl ether, concentrated under reduced pressure, and diluted with tetrahydrofuran (3 mL). The unpurified mixture was allowed to cool to 0 ºC and a 3 M solution of aqueous NaOH (2 mL) was added, followed by 30% H_2O_2 (1.0 mL), dropwise. The mixture was allowed to warm to room temperature and stir for 3 h. The reaction was allowed to cool to 0 ºC and a saturated solution of aqueous $Na_2S_2O_3$ (3 mL) was added dropwise. After warming to room temperature the product was extracted from the aqueous layer with ethyl acetate (3 x 20 mL). The combined organic layers were dried over Na_2SO_4, concentrated under reduced pressure, and subsequently purified by silica gel chromatography to provide the desired products.

5.10.2.12 Characterization of Carbozincation-Electrophile Trap Reactions and Determination of Stereochemical Identity



1-Phenylpent-4-en-2-ol (5.286-OH). The reaction was performed according to the ***General Procedures for Carbozincation-Allyl Trap (Section 5.10.2.5)*** *with* 6b,9a)-6b,9a-dimethyl-8-vinyl-6b,9a-dihydroacenaphtho[1,2-d][1,3,2] dioxaborole (0.050 g, 0.2 mmol, 1.00 equiv), PhZnCl•LiCl **[**prepared according

to ***General Procedure A: Preparation of Organozinc Chloride Nucleophiles (Section 5.10.2.2)*** using PhLi (0.22 mL, 1.81 M (Bu_2O), $ZnCl_2$ (0.0599 g, 0.44 mmol, 2.2 equiv)**]**, $NiBr_2$•glyme (0.0062 g, 0.02 mmol, 0.10 equiv), (*S*,*S*)-*N*,*N*'-dimethyl-1,2-diphenyl-ethane-1,2-diamine (*S,S*)-**5.262** (0.0063 g, 0.026 mmol, 0.13 equiv). MeI (0.40 mmol, 2.00 equiv), Allyl bromide (0.0968 g, 0.80 mmol, 4.00 equiv), CuCl (0.0098 g, 0.10 mmol, 0.50 equiv), LiCl (0.0085 g, 0.2 mmol, 1.0 equiv). The unpurified product was subjected to oxidation according to ***General Method for Oxidation of Boronic Ester Products (Section 5.10.2.11)***. The oxidized reaction mixture was purified by automated silica gel chromatography (Biotage 1% → 5% ethyl acetate in hexanes, stained in CAM) to afford colorless oil (0.0162 g, 50% yield). All spectral data was in accord with the literature.[93]

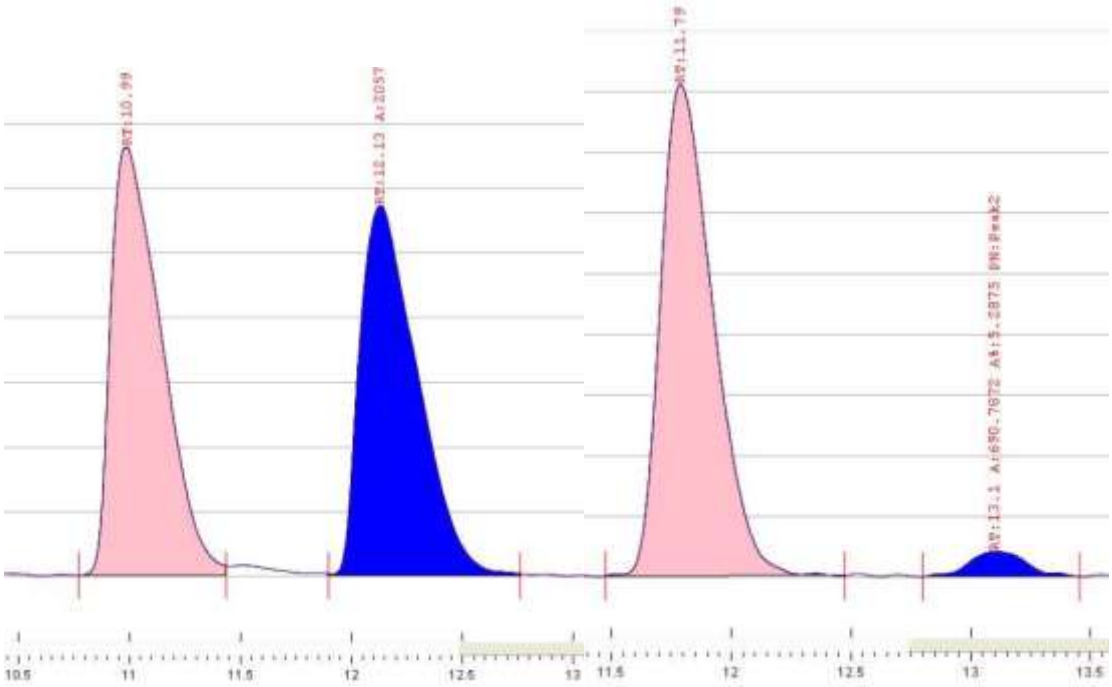
Determination of Stereochemical Identity: Racemic compound was prepared according to the ***General Procedures for Carbozincation-Allyl Trap (Section 5.10.2.5)*** *(with the modification: reaction run at 0˚C, with nBuI)* with $NiBr_2$•glyme (10 mol%) and *N*,*N*'-dimethyl ethane ligand **5.311** (13 mol%) as the catalyst. Absolute stereochemistry is not yet assigned.

SFC (Chiracel OJ-H, 1% IPA, 3 mL/min, 100 bar, 35 °C, 210-270 nm) – analysis of 1-phenylpent-4-en-2-ol.

[93] Lin, M.-H.; Lin, W.-C.; Liu, H.-J.; Chuang, T.-H. *J. Org. Chem*. **2013**, 78, 1278.

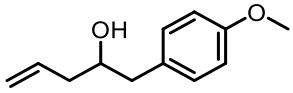
Racemic Material

Standard Conditions



Peak No	% Area	Area	RT (min)
1	50.3549	20872.548	10.99
2	49.6451	20578.3073	12.13
Total:	100	41450.8553	

Peak No	% Area	Area	RT (min)
1	94.7125	12373.7306	11.79
2	5.2875	690.7872	13.1
Total:	100	13064.5178	



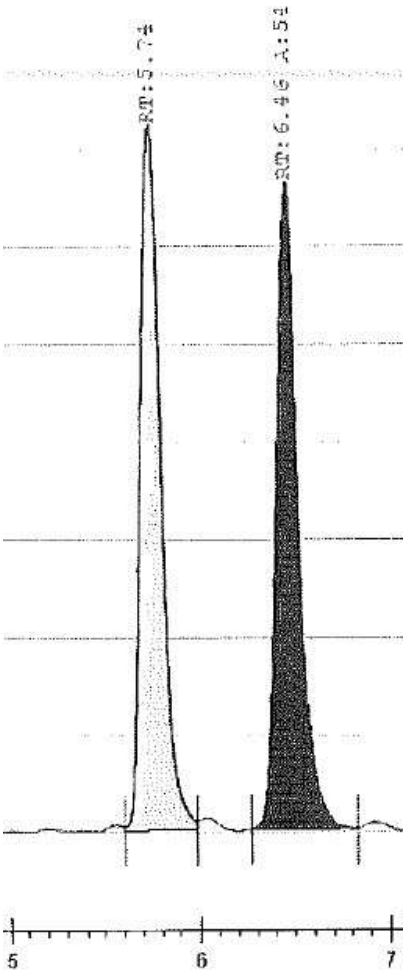
1-(4-Methoxyphenyl)pent-4-en-2-ol (5.416-OH). The reaction was performed according to the ***General Procedures for Carbozincation-Allyl Trap (Section 5.10.2.5)*** *with* 6b,9a)-6b,9a-dimethyl-8-vinyl-6b,9a-dihydroacenaphtho[1,2-d][1,3,2] dioxaborole (0.050 g, 0.2 mmol, 1.00 equiv), 4-MeOPhZnCl•LiCl **[**prepared according to ***General Procedure B: Preparation of Organozinc Chloride Nucleophiles (Section 5.10.2.3)*** using 4-MeOPhLi (0.4 mmol, 2.00 equiv)**]**, $ZnCl_2$ (0.0599 g, 0.44 mmol, 2.2 equiv)], $NiBr_2$•glyme (0.0062 g, 0.02 mmol, 0.10

equiv), (*S,S*)-*N,N*'-dimethyl-1,2-diphenyl-ethane-1,2-diamine (*S,S*)-**5.262** (0.0063 g, 0.026 mmol, 0.13 equiv). MeI (0.40 mmol, 2.00 equiv), Allyl bromide (0.0968 g, 0.80 mmol, 4.00 equiv), CuCl (0.0098 g, 0.10 mmol, 0.50 equiv), LiCl (0.0085 g, 0.2 mmol, 1.0 equiv). The unpurified product was subjected to oxidation according to ***General Method for Oxidation of Boronic Ester Products (Section 5.10.2.11)***. The oxidized reaction mixture was purified by automated silica gel chromatography (Biotage 1% → 5% ethyl acetate in hexanes, stained in CAM) to afford colorless oil (0.0077 g, 20% yield). All spectral data was in accord with the literature.[89]

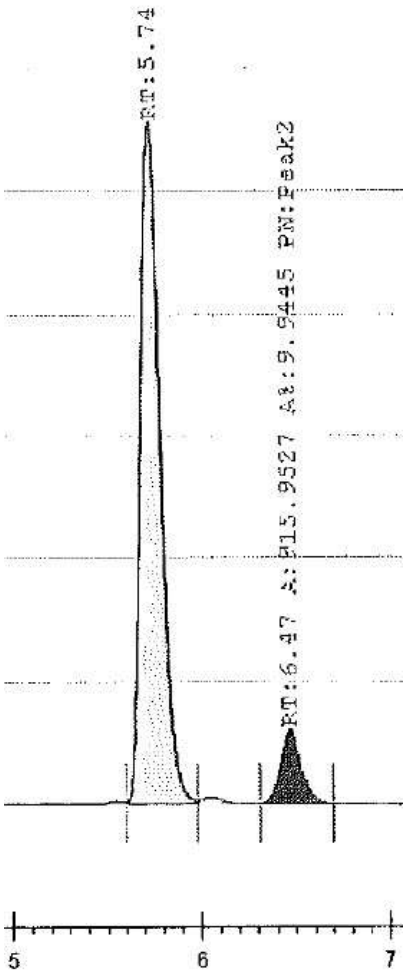
Determination of Stereochemical Identity: Racemic compound was prepared according to the ***General Procedures for Carbozincation-Allyl Trap (Section 5.10.2.5)*** *(with the modification: reaction run at 0˚C, with n*BuI) with $NiBr_2$•glyme (10 mol%) and *N,N*'-dimethyl ethane ligand **5.311** (13 mol%) as the catalyst. Absolute stereochemistry is not yet assigned.

SFC (Chiracel OJ-H, 5% IPA, 3 mL/min, 100 bar, 35 °C, 210-270 nm) – analysis of 1-(4-methoxyphenyl)pent-4-en-2-ol.

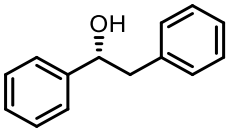
Racemic Material



Standard Conditions



Peak No	% Area	Area	RT (min)	Peak No	% Area	Area	RT (min)
1	49.9524	5468.9111	5.74	1	90.0555	8294.6761	5.74
2	50.0476	5479.3302	6.46	2	9.9445	915.9527	6.47
Total:	100	10948.2413		Total:	100	9210.6288	



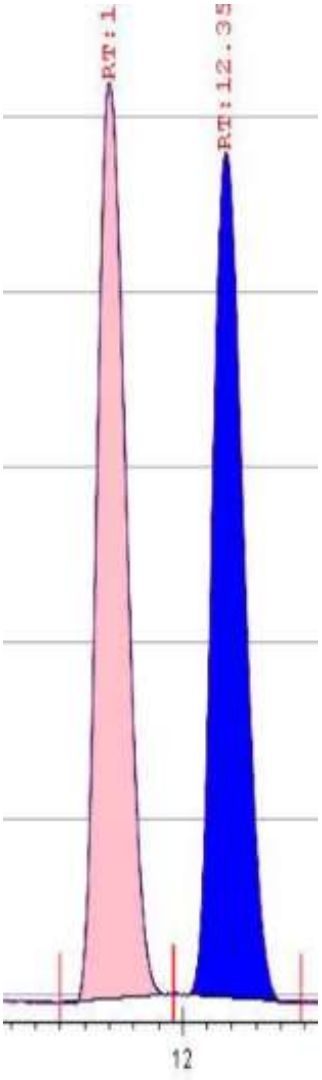
(R)-1,2-Diphenylethan-1-ol (5.338-OH). The reaction was performed

according to the ***General Procedures for Carbozincation-Negishi Cross-Coupling (Section 5.10.2.6)*** *with* 6b,9a)-6b,9a-dimethyl-8-vinyl-6b,9a-dihydro acenaphtho[1,2-d][1,3,2] dioxaborole (0.050 g, 0.2 mmol, 1.00 equiv), PhZnCl•LiCl **[**prepared according to ***General Procedure A: Preparation of Organozinc Chloride Nucleophiles (Section 5.10.2.2)*** using PhLi (0.22 mL, 1.81 M (Bu_2O), $ZnCl_2$ (0.0599 g, 0.44 mmol, 2.2 equiv)**]**, $NiBr_2$•glyme (0.0062 g, 0.02 mmol, 0.10 equiv), (*S*,*S*)-*N*,*N*'-dimethyl-1,2-diphenyl-ethane-1,2-diamine (*S,S*)-**5.262** (0.0063 g, 0.026 mmol, 0.13 equiv). MeI (0.20 mmol, 1.00 equiv), Iodobenzene (0.0816 g, 0.80 mmol, 4.00 equiv), $(Ph_3P)_3PdCl_2$ (0.007 g, 0.01 mmol, 0.05 equiv)., LiCl (0.0085 g, 0.2 mmol, 1.0 equiv). The unpurified product was subjected to oxidation according to ***General Method for Oxidation of Boronic Ester Products (Section 5.10.2.11)***. The oxidized reaction mixture was purified by automated silica gel chromatography (Biotage 1% → 5% ethyl acetate in hexanes, stained in CAM) to afford colorless oil (0.0162 g, 50% yield). All The unpurified product was purified by automated silica gel chromatography (Biotage 1% → 5% ethyl acetate in hexanes, stained in CAM) to afford white solid (0.0064 g, 16% yield). All spectral data was in accord with the literature.[85]

Determination of Stereochemical Identity: Racemic compound was prepared according to the general procedure ***General Procedures for Carbozincation-Negishi Cross-Coupling (Section 5.10.2.6)*** *(with the modification: reaction run at 0°C, with nBuI*) with $NiBr_2$•glyme (10 mol%) and *N*,*N*'-dimethyl ethane ligand **5.311** (13 mol%) as the catalyst. Absolute stereochemistry was assigned by comparison to the literature.[85]

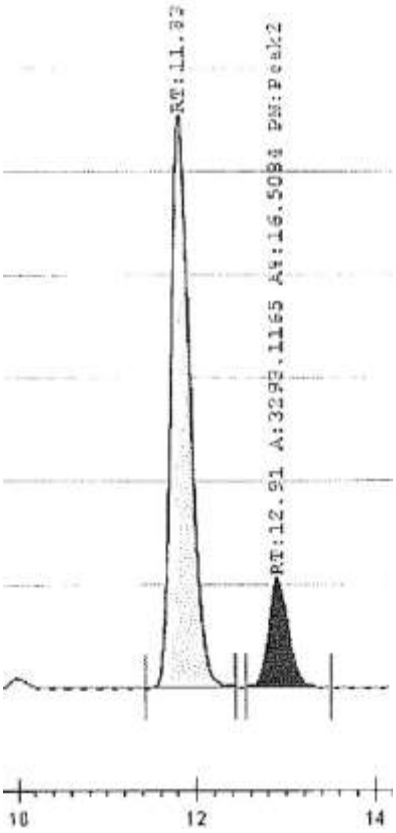
SFC (Chiracel OD-H, 5% IPA, 3 mL/min, 100 bar, 35 °C, 210-270 nm) – analysis of (R)-1,2-diphenylethan-1-ol.

Racemic Material

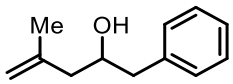


Peak No	% Area	Area	RT (min)
1	50.2599	8450.5728	11.4
2	49.7401	8363.1658	12.35
Total:	100	16813.7386	

Standard Conditions



Peak No	% Area	Area	RT (min)
1	83.4916	16655.0632	11.83
2	16.5084	3293.1165	12.91
Total:	100	19948.1797	



4-Methyl-1-phenylpent-4-en-2-ol (5.417-OH). The reaction was performed according to the general procedure ***General Procedures for Carbozincation-Allyl Trap (Section 5.10.2.5)*** *with* 6b,9a)-6b,9a-dimethyl-8-vinyl-6b,9a-dihydroacenaphtho[1,2-d][1,3,2] dioxaborole (0.050 g, 0.2 mmol, 1.00 equiv), PhZnCl•LiCl **[**prepared according to ***General Procedure A: Preparation of Organozinc Chloride Nucleophiles (Section 5.10.2.2)*** using PhLi (0.22 mL, 1.81 M (Bu_2O), ZnCl2 (0.0599 g, 0.44 mmol, 2.2 equiv)**]**, $NiBr_2$•glyme (0.0062 g, 0.02 mmol, 0.10 equiv), (*S*,*S*)-*N*,*N*'-dimethyl-1,2-diphenyl-ethane-1,2-diamine (*S,S*)-**5.262** (0.0063 g, 0.026 mmol, 0.13 equiv). MeI (0.40 mmol, 2.00 equiv), 3-bromo-2-methylprop-1-ene (0.108 g, 0.80 mmol, 4.00 equiv), CuCl (0.0098 g, 0.10 mmol, 0.50 equiv), LiCl (0.0085 g, 0.2 mmol, 1.0 equiv). The unpurified product was subjected to oxidation according to ***General Method for Oxidation of Boronic Ester Products (Section 5.10.2.11)***. *The oxidized reaction mixture was* purified by automated silica gel chromatography (Biotage 1% → 5% ethyl acetate in hexanes, stained in CAM) to afford colorless oil (0.0173 g, 49% yield). All spectral data was in accord with the literature.[94]

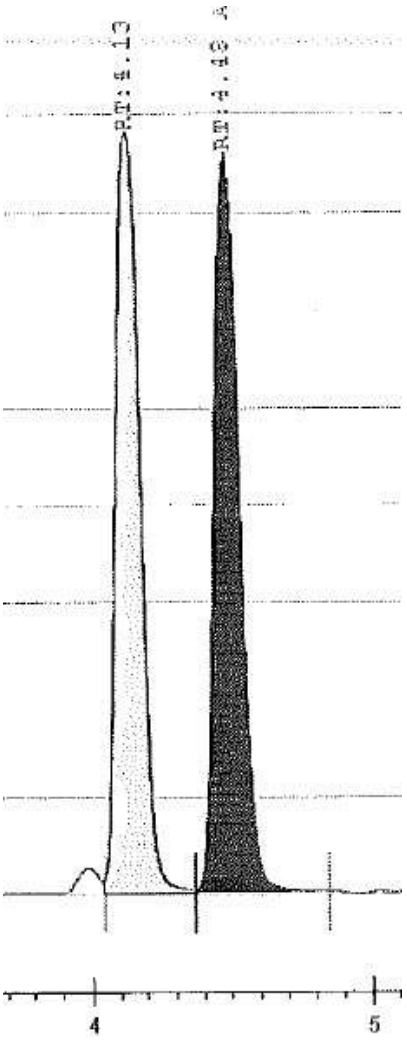
Determination of Stereochemical Identity: Racemic compound was prepared according to the ***General Procedures for Carbozincation-Allyl Trap (Section 5.10.2.5)*** *(with the modification: reaction run at 0˚C, with nBuI*) with $NiBr_2$•glyme (10 mol%) and *N*,*N*'-

[94] Kandur, W. V.; Richert, K. J.; Rieder, C. J.; Thomas, A. M.; Hu, C.; Ziller, J. W.; Woerpel, K. A. *Org. Lett*. **2014**, 16, 2650

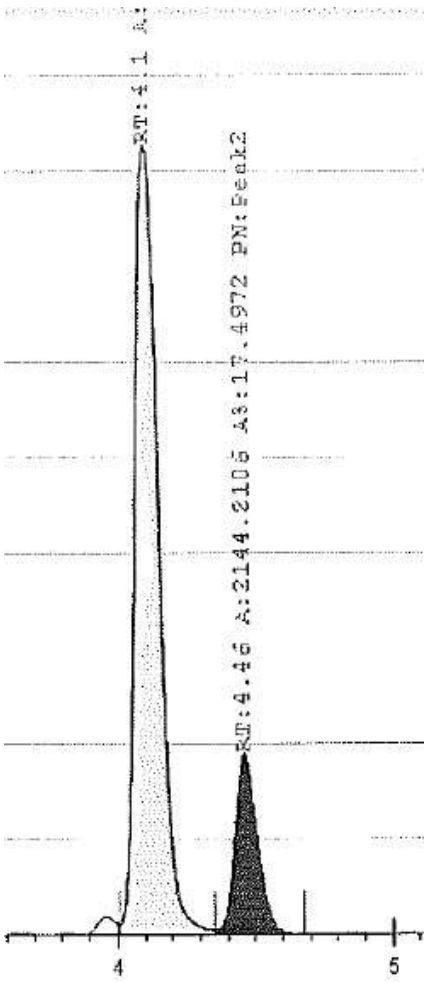
dimethyl ethane ligand **5.311** (13 mol%) as the catalyst. Absolute stereochemistry is not yet assigned.

SFC (Chiracel OD-H, 5% IPA, 3 mL/min, 100 bar, 35 °C, 210-270 nm) – analysis of 4-methyl-1-phenylpent-4-en-2-ol.

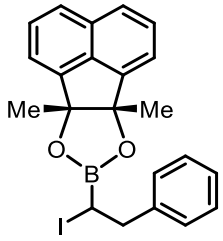
Racemic Material



Standard Conditions



Peak No	% Area	Area	RT (min)	Peak No	% Area	Area	RT (min)
1	49.5134	9470.897	4.13	1	82.5028	10110.3712	4.1
2	50.4866	9657.0654	4.48	2	17.4972	2144.2106	4.46
Total:	100	19127.9624		Total:	100	12254.5818	



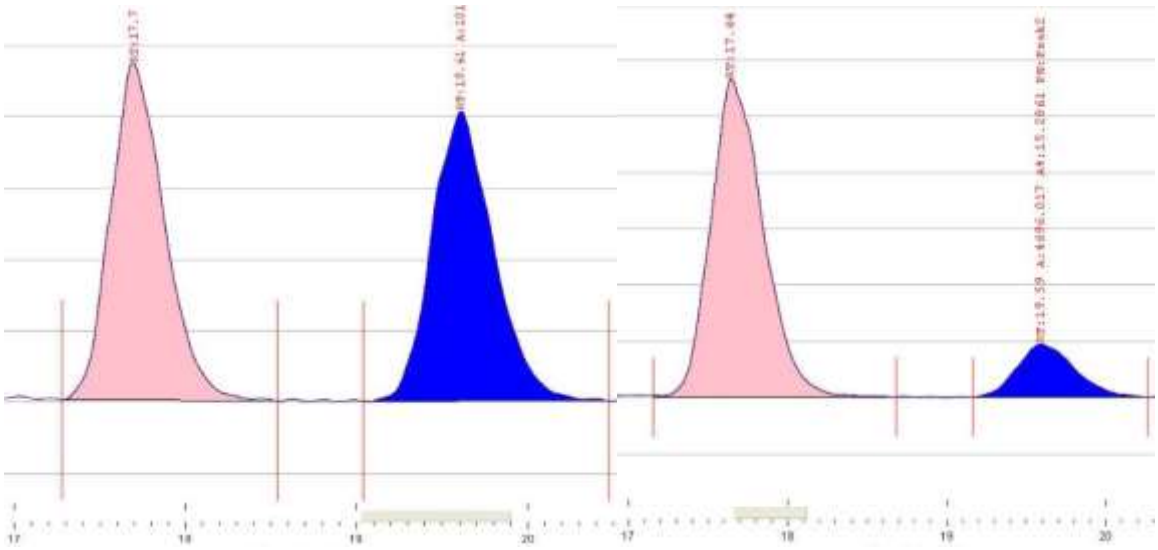
(6b,9a)-8-(1-Iodo-2-phenylethyl)-6b,9a-dimethyl-6b,9a-dihydroacenaphtho[1,2-d][1,3,2]dioxaborole (5.423). The reaction was performed according to the ***General Procedures for Carbozincation-Iodination (Section 5.10.2.7)*** *with* 6b,9a)-6b,9a-dimethyl-8-vinyl-6b,9a-dihydroacenaphtho[1,2-d][1,3,2] dioxaborole (0.050 g, 0.2 mmol, 1.00 equiv), PhZnCl•LiCl **[**prepared according to ***General Procedure A: Preparation of Organozinc Chloride Nucleophiles (Section 5.10.2.2)*** using PhLi (0.22 mL, 1.81 M (Bu_2O), $ZnCl_2$ (0.0599 g, 0.44 mmol, 2.2 equiv)**]**, $NiBr_2$•glyme (0.0062 g, 0.02 mmol, 0.10 equiv), (*S,S*)-*N,N*'-dimethyl-1,2-diphenyl-ethane-1,2-diamine (*S,S*)-**5.262** (0.0063 g, 0.026 mmol, 0.13 equiv). MeI (0.40 mmol, 2.00 equiv), *N*-iodosuccinimide (0.0899 g, 0.80 mmol, 2.00 equiv), The unpurified product was purified by automated silica gel chromatography (Biotage 1% → 5% ethyl acetate in hexanes, stained in CAM) to afford colorless oil (0.0354 g, 39% yield). **^{1}H NMR** (500 MHz, $CDCl_3$) δ 7.79 (dd, *J* = 10.8, 8.2 Hz, 2H), 7.64 – 7.59 (m, 1H), 7.58 – 7.53 (m, 2H), 7.47 (d, *J* = 6.9 Hz, 1H), 7.01 – 6.96 (m, 1H), 6.92 (d, *J* = 4.4 Hz, 4H), 3.26 (dd, *J* = 9.5, 7.8 Hz, 1H), 3.14 (dd, *J* = 13.6, 9.5 Hz, 1H), 3.04 (dd, *J* = 13.6, 7.8 Hz, 1H), 1.75 (s, 6H). **^{11}B NMR** (160 MHz, $CDCl_3$) δ 34.37. ^{13}C NMR (126 MHz, $CDCl_3$) δ 144.26, 144.14, 140.87, 135.03, 131.54, 128.67, 128.67, 128.62, 128.38, 127.23, 126.68, 125.58, 119.79, 119.71, 92.78, 41.38, 21.89, 21.58 (carbon adjacent to boron not observed). **IR** (neat) ν_{max} 3004.85 (w), 2930.78 (w), 2836.63 (w),

1700.93 (s), 1632.53 (w), 1603.43 (m), 1502.41 (w), 1483.31 (w), 1251.55 (m), 1231.78 (m), 1159.95 (m), 886.33 (m), 851.71 (m), 484.00 (w) cm^{-1}. **HRMS** (DART) for $C_{22}H_{21}BO_2I$ $[M+H]^+$ calculated: 455.06738, found: 455.06634. $[\alpha]^{20}_D$: 0.4588 (*c* 1.454, $CHCl_3$, *l* =50 mm).

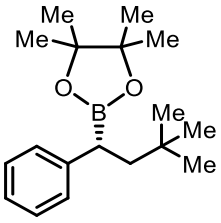
Determination of Stereochemical Identity: Racemic compound was prepared according to ***General Procedures for Carbozincation-Iodination (Section 5.10.2.7)*** *(with the modification: reaction run at 0˚C, with nBuI*) with $NiBr_2$•glyme (10 mol%) and *N,N*'-dimethyl ethane ligand **5.311** (13 mol%) as the catalyst. Absolute stereochemistry is not yet assigned.

SFC (Chiracel OD-H, 5% IPA, 3 mL/min, 100 bar, 35 °C, 210-270 nm) – analysis of (6b,9a)-8-(1-iodo-2-phenylethyl)-6b,9a-dimethyl-6b,9a-dihydroacenaphtho[1,2-d] [1,3,2]dioxaborole.

Racemic Material Standard Conditions



Peak No	% Area	Area	RT (min)	Peak No	% Area	Area	RT (min)
1	50.5207	10367.2705	17.7	1	84.7139	26024.7515	17.64
2	49.4793	10153.5551	19.61	2	15.2861	4696.017	19.59
Total:	100	20520.8256		Total:	100	30720.7685	



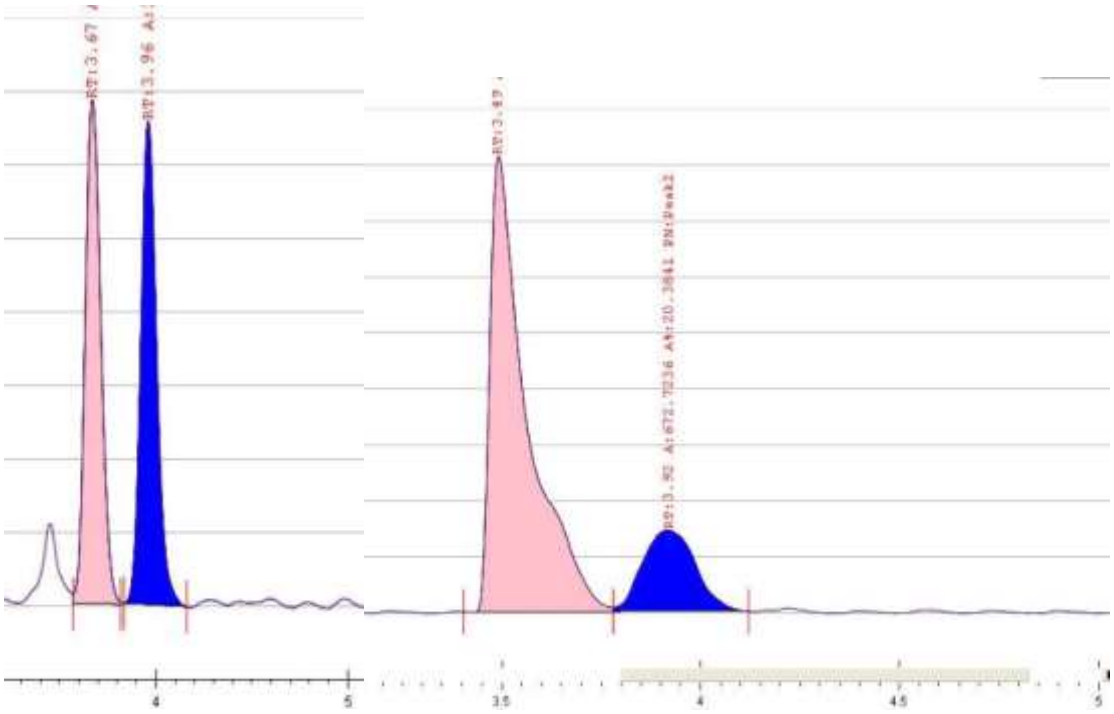
(R)-2-(3,3-Dimethyl-1-phenylbutyl)-4,4,5,5-tetramethyl-1,3,2 dioxa borolane (5.433). The reaction was performed according to the general procedure ***General Procedures for Stereoconvergent Negishi Cross-Coupling (Section 5.10.2.10)*** *with* 6b,9a)-6b,9a-dimethyl-8-vinyl-6b,9a-dihydroacenaphtho[1,2-d][1,3,2] dioxaborole (0.050 g, 0.2 mmol, 1.00 equiv), PhZnCl•LiCl **[**prepared according to ***General Procedure A: Preparation of Organozinc Chloride Nucleophiles (Section 5.10.2.2)*** using PhLi (0.22 mL, 1.81 M (Bu_2O), $ZnCl_2$ (0.0599 g, 0.44 mmol, 2.2 equiv)**]**, $NiBr_2$•glyme (0.0062 g, 0.02 mmol, 0.10 equiv), *N*,*N*'-dimethylethylene **5.311** (0.0023 g, 0.026 mmol, 0.13 equiv). *n*BuI (0.0736 g, 0.40 mmol, 2.00 equiv), $Pd(OAc)_2$ (0.00089 g, 0.002 mmol, 0.02 equiv), (S_p,S_p)-Mandyphos M001-1 ligand **5.434** (0.0039 g, 0.0048 mmol, 0.024 equiv), Iodobenzene (0.0816 g, 0.80 mmol,

4.00 equiv). The unpurified product was purified by automated silica gel chromatography (Biotage 1% → 5% ethyl acetate in hexanes, stained in CAM) to afford colorless, crystalline solid (0.039g, 64% yield). **^{1}H NMR** (500 MHz, $CDCl_3$) δ 7.26 – 7.22 (m, 4H), 7.15 – 7.07 (m, 1H), 2.40 (dd, *J* = 10.0, 3.7 Hz, 1H), 2.04 (dd, *J* = 13.3, 10.0 Hz, 1H), 1.51 (dd, *J* = 13.3, 3.8 Hz, 1H), 1.15 (s, 3H), 1.14 (s, 3H), 0.91 (s, 9H).**^{11}B NMR** (160 MHz, $CDCl_3$) δ 33.98. **^{13}C NMR** (126 MHz, $CDCl_3$) 145.05, 128.44, 128.41, 125.16, 83.41, 46.76, 31.59, 29.90, 28.63, 24.79, 24.66.**IR** (neat) ν_{max} 2920.03 (m), 2850.95 (w), 1476.2 (w), 1363.41 (s), 1345.97 (s), 1205.50 (m), 1137.76 (s), 966.19 (m), 861.38 (m), 836.59 (m), 771.04 (m), 746.58 (m), 699.87 (s), 608.13 (w), 577.57 (w), 531.03 (w) cm^{-1}. **HRMS** (DART) for $C_{18}H_{30}BO_2$ $[M+H]^+$ calculated: 289.23334, found: 289.23401. $[\alpha]^{20}_D$: -8.159 (*c* 2.01, $CHCl_3$, *l* =50 mm).

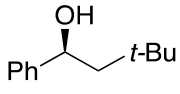
Determination of Stereochemical Identity: Racemic compound was prepared according to the ***General Procedures for Stereoconvergent Negishi Cross-Coupling (Section 5.10.2.10) (****with the modification: reaction run at 0˚C, with nBuI*) with $NiBr_2$•glyme (10 mol%) and *N*,*N*'-dimethyl ethane diamine ligand **5.311** (13 mol%) as the catalyst. Absolute stereochemistry was assigned by comparison to the literature.[95] *SFC (Chiracel OJ-H, 1% IPA, 3 mL/min, 100 bar, 35 °C, 210-270 nm) – analysis of (R)-2-(3,3-dimethyl-1-phenylbutyl)-4,4,5,5-tetramethyl-1,3,2-dioxaborolane*

Racemic Material Standard Conditions

[95] Chierchia, M.; Lovinger, G. J.[+]; Xu, P. [+]; Morken, J. P. *Angew. Chem. Int. Ed*. **2019**, 58, 14245.



Peak No	% Area	Area	RT (min)	Peak No	% Area	Area	RT (min)
1	50.6946	1943.6206	3.67	1	79.6159	2627.5112	3.49
2	49.3054	1890.36	3.96	2	20.3841	672.7236	3.92
Total:	100	3833.9806		Total:	100	3300.2348	

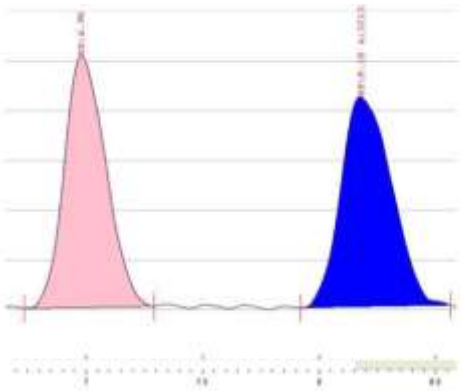


(S)-2-(3,3-Dimethyl-1-phenylbutyl)-4,4,5,5-tetramethyl-1,3,2 dioxa borolane (5.433-OH). The reaction was performed according to the general procedure ***General Procedures for Stereoconvergent Negishi Cross-Coupling (Section 5.10.2.10)*** *with* 6b,9a)-6b,9a-dimethyl-8-vinyl-6b,9a-dihydroacenaphtho[1,2-d][1,3,2] dioxaborole (0.050 g, 0.2 mmol, 1.00 equiv), PhZnCl•LiCl **[**prepared according to ***General Procedure A: Preparation of Organozinc Chloride Nucleophiles (Section 5.10.2.2)*** using PhLi (0.22 mL, 1.81 M (Bu_2O), $ZnCl_2$ (0.0599 g, 0.44 mmol, 2.2 equiv)**]**, $NiBr_2$•glyme (0.0062 g, 0.02 mmol, 0.10 equiv), *N*,*N*'-dimethylethylene **5.311** (0.0023 g, 0.026 mmol, 0.13 equiv). *n*BuI

(0.0736 g, 0.40 mmol, 2.00 equiv), $Pd(OAc)_2$ (0.00089 g, 0.002 mmol, 0.02 equiv), (R_p,R_p)-Mandyphos M004-2 ligand **5.435** (0.0051 g, 0.0048 mmol, 0.024 equiv), Iodobenzene (0.0816 g, 0.80 mmol, 4.00 equiv). The unpurified product was purified by automated silica gel chromatography (Biotage 1% → 5% ethyl acetate in hexanes, stained in CAM) to afford colorless, colorless oil (0.0157g, 44% yield). All spectral data was in accord with the literature. [96]

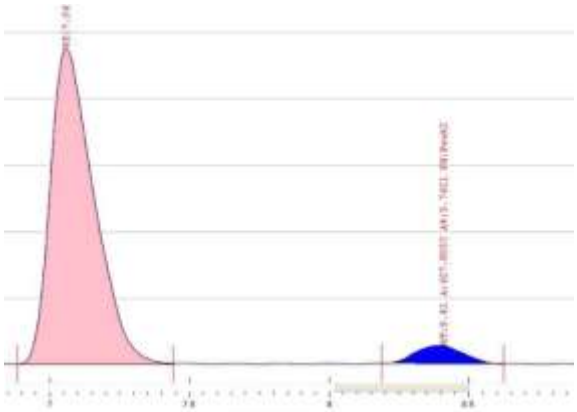
SFC (Chiracel ODR-H, 1% IPA, 3 mL/min, 100 bar, 35 °C, 210-289 nm)-analysis of **(*R*)-3,3-Dimethyl-1-phenylbutan-1-ol.**

Racemic Material



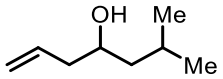
Peak No	% Area	Area	RT (min)
1	49.3436	3130.442	6.98
2	50.6564	3213.7248	8.18
Total:	100	6344.1668	

Enantioenriched Material

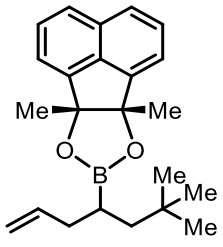


Peak No	% Area	Area	RT (min)
1	94.2379	10267.632	7.06
2	5.7621	627.8053	8.41
Total:	100	10895.4373	

[96] Scholz, R.; Hellmann, G.; Rohs, S.; Özdemir, D.; Raabe, G.; Vermeeren, C.; Gais, H.-J. *Eur. J. Org. Chem*. **2010**, 4588.



6-Methylhept-1-en-4-ol (5.420-OH). The reaction was performed according to the ***General Procedures for Carbozincation-Allyl Trap (Section 5.10.2.5)*** with 6b,9a)-6b,9a-dimethyl-8-vinyl-6b,9a-dihydroacenaphtho[1,2-d] [1,3,2] dioxaborole (0.050 g, 0.2 mmol, 1.00 equiv), *i*PrZnCl•LiCl **[**prepared according to ***General Procedure A: Preparation of Organozinc Chloride Nucleophiles (Section 5.10.2.2)*** using *i*PrLi (0.4 mmol, 0.4 equiv), $ZnCl_2$ (0.0599 g, 0.44 mmol, 2.2 equiv)**]**, $NiBr_2$•glyme (0.0062 g, 0.02 mmol, 0.10 equiv), (*S*,*S*)-*N*,*N*'-dimethyl-1,2-diphenyl-ethane-1,2-diamine (*S,S*)-**5.262** (0.0063 g, 0.026 mmol, 0.13 equiv). MeI (0.40 mmol, 2.00 equiv), Allyl bromide (0.0968 g, 0.80 mmol, 4.00 equiv), CuCl (0.0098 g, 0.10 mmol, 0.50 equiv), LiCl (0.0085 g, 0.2 mmol, 1.0 equiv). The unpurified product was subjected to oxidation according to ***General Method for Oxidation of Boronic Ester Products (Section 5.10.2.11)***. The oxidized reaction mixture was purified by automated silica gel chromatography (Biotage 1% → 5% ethyl acetate in hexanes, stained in CAM) to afford colorless oil (0.0156 g, 61% yield). All spectral data was in accord with the literature.[97]



(6b,9a)-8-(6,6-Dimethylhept-1-en-4-yl)-6b,9a-dimethyl-6b,9a-dihydroacenaphtho[1,2-d][1,3,2]dioxaborole (5.421). The reaction was performed according to the general procedure ***General Procedures for Carbozincation-Allyl Trap (Section 5.10.2.5*)** with 6b,9a)-6b,9a-dimethyl-8-vinyl-6b,9a-dihydroacenaphtho[1,2-d][1,3,2] dioxaborole (0.050 g, 0.2 mmol,

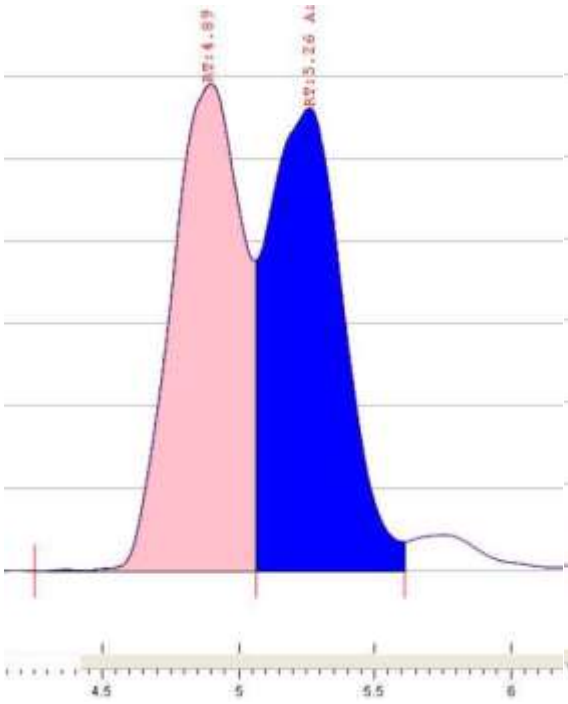
[97] Wipf, P.; Graham, T. H. *J. Org. Chem.* **2003**, 68, 8798.

1.00 equiv), *i*PrZnCl•LiCl **[**prepared according to ***General Procedure A: Preparation of Organozinc Chloride Nucleophiles (Section 5.10.2.2)*** using *tBu*Li (0.4 mmol, 0.4 equiv), $ZnCl_2$ (0.0599 g, 0.44 mmol, 2.2 equiv)**]**, $NiBr_2$•glyme (0.0062 g, 0.02 mmol, 0.10 equiv), (*S*,*S*)-*N*,*N*'-dimethyl-1,2-diphenyl-ethane-1,2-diamine (*S*,*S*)-**5.262** (0.0063 g, 0.026 mmol, 0.13 equiv). MeI (0.40 mmol, 2.00 equiv), allyl bromide (0.0968 g, 0.80 mmol, 4.00 equiv), CuCl (0.0098 g, 0.10 mmol, 0.50 equiv), LiCl (0.0085 g, 0.2 mmol, 1.0 equiv). The unpurified product was purified by automated silica gel chromatography (Biotage 1% → 5% ethyl acetate in hexanes, stained in CAM) to afford colorless oil (0.0592 g, 85% yield). **^{1}H NMR** (500 MHz, $CDCl_3$) δ 7.76 (d, *J* = 8.0 Hz, 2H), 7.62 – 7.47 (m, 4H), 5.62 – 5.46 (m, 1H), 4.63 (d, 1H), 4.55 (d, 1H), 2.03 – 1.87 (m, 2H), 1.76 (s, 6H), 1.50 – 1.36 (m, 1H), 1.17 – 1.09 (m, 1H), 1.09 – 0.99 (m, 1H), 0.64 (s, 9H). **^{11}B NMR** (160 MHz, $CDCl_3$) δ 35.25. **^{13}C NMR** (126 MHz, $CDCl_3$) δ 145.06, 145.01, 138.10, 135.02, 131.40, 128.54, 125.26, 125.23, 119.49, 114.93, 91.86, 91.79, 46.39, 38.06, 30.97, 29.63, 22.08, 22.06, 19.62.**IR** (neat) ν_{max} 3042.75 (w), 2948.95 (m), 1450.87 (w), 1378.56 (m), 1303.18 (m), 1232.76 (w), 1199.45 (w), 1114.85 (m), 1076.87 (m), 909.74 (w), 823.45 (m), 775.65 (s), 633.21 (w) cm^{-1}. **HRMS** (DART) for $C_{23}H_{30}BO_2$ $[M+H]^+$ calculated: 349.23334, found: 349.23290.

Determination of Stereochemical Identity: *Racemic compound was prepared according to the general procedure* ***General Procedures for Carbozincation-Allyl Trap (Section 5.10.2.5)*** *(with the modification: reaction run at 0˚C, with nBuI) with $NiBr_2$•glyme (10 mol%) and N,N'-dimethyl ethane diamine ligand* ***5.311*** *(13 mol%) as the catalyst.*

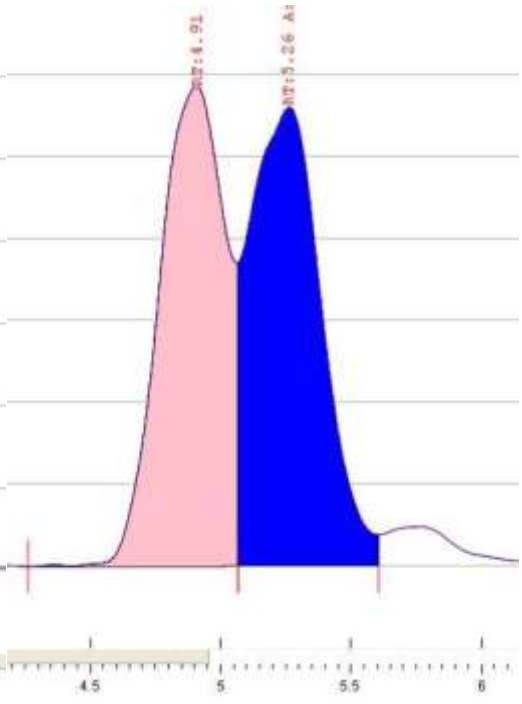
SFC (Chiracel AD-H, 1% IPA, 3 mL/min, 100 bar, 35 °C, 210-270 nm) – analysis of (6b,9a)-8-(6,6-dimethylhept-1-en-4-yl)-6b,9a-dimethyl-6b,9a-dihydroacenaphtho[1,2-d][1,3,2]dioxaborole.

Racemic Material

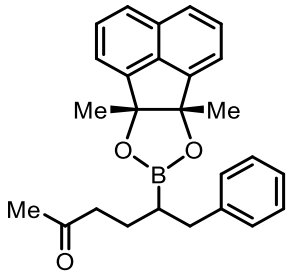


Peak No	% Area	Area	RT (min)
1	49.5587	21276.0061	4.89
2	50.4413	21654.924	5.26
Total:	100	42930.9301	

Standard Conditions

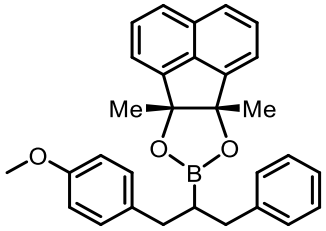


Peak No	% Area	Area	RT (min)
1	48.8551	20553.9601	4.91
2	51.1449	21517.2911	5.26
Total:	100	42071.2512	



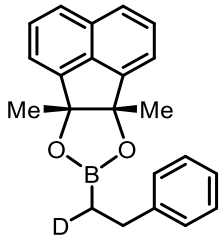
5-((6bR,9aS)-6b,9a-Dimethyl-6b,9a-dihydroacenaphtho[1,2-d][1,3,2]dioxaborol-8-yl)-6-phenylhexan-2-one (5.424). The reaction was performed according to the ***General Procedures for Carbozincation-Conjugate Addition (Section 5.10.2.8)*** with 6b,9a)-6b,9a-dimethyl-8-vinyl-6b,9a-dihydroacenaphtho[1,2-d][1,3,2] dioxaborole (0.050 g, 0.2 mmol, 1.00 equiv), PhZnCl•LiCl **[**prepared according to ***General Procedure A: Preparation of Organozinc Chloride Nucleophiles (Section 5.10.2.2)*** using PhLi (0.4 mmol, 0.4 equiv), $ZnCl_2$ (0.0599 g, 0.44 mmol, 2.2 equiv)**]**, $NiBr_2$•glyme (0.0062 g, 0.02 mmol, 0.10 equiv), *N*,*N*'-dimethylethylene **5.311** (0.0023 g, 0.026 mmol, 0.13 equiv), *n*BuI (0.0736 g, 0.40 mmol, 2.00 equiv), but-3-en-2-one (0.0280 g, 0.40 mmol, 4.00 equiv), CuCl (0.0196 g, 0.20 mmol, 1.00 equiv), LiCl (0.017 g, 0.4 mmol, 2.0 equiv), trimethylsilyl chloride (0.0869 g, 0.80 mmol, 4.0 equiv). The unpurified product was purified by automated silica gel chromatography (Biotage 1% → 10% ethyl acetate in hexanes, stained in CAM) to afford colorless oil (0.04779 g, 60% yield). **^{1}H NMR** (600 MHz, $CDCl_3$) ^{1}H NMR (500 MHz, $cdcl_3$) δ 7.80 (dd, *J* = 8.2, 5.0, 0.7 Hz, 2H), 7.63 – 7.56 (m, 2H), 7.53 (d, *J* = 7.0, 0.8 Hz, 1H), 7.48 (d, *J* = 7.0, 0.7 Hz, 1H), 7.00 – 6.88 (m, 5H), 2.62 (qd, *J* = 13.4, 7.9 Hz, 2H), 2.22 (td, *J* = 7.4, 2.9 Hz, 2H), 1.91 (s, 3H), 1.72 (s, 3H), 1.70 (s, 3H), 1.64 – 1.58 (m, 2H), 1.30 – 1.21 (m, 1H).**^{11}B NMR** (160 MHz, $CDCl_3$) δ 34.66. **^{13}C NMR** (126 MHz, $CDCl_3$) δ 209.11, 144.93, 144.90, 141.58, 134.80, 131.54, 128.73, 128.65, 128.62, 128.07, 125.72, 125.39, 125.35, 119.59, 119.58, 92.02, 91.97, 43.07, 37.59, 29.87, 25.69, 25.18, 22.11, 22.03.**IR** (neat) ν_{max} 3023.85 (w), 2970.23 (w), 2925.67 (w), 2854.57 (w), 1711.78 (s), 1378.95 (br), 1173.35 (m), 1115.03 (s), 1076.32 (s), 824.83 (s), 777.65 (s),

748.30 (m), 699.87 (m), 574.16 (w) cm^{-1}. **HRMS** (DART) for $C_{26}H_{28}BO_3$ $[M+H]^+$ calculated: 399.21260, found: 399.21188.



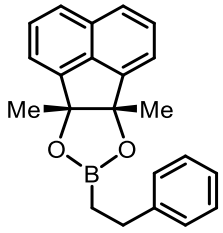
(6bR,9aS)-8-(1-(4-Methoxyphenyl)-3-phenylpropan-2-yl)-6b,9a-dimethyl-6b,9a-dihydroacenaphtho[1,2-d][1,3,2] dioxa borole (5.425). The reaction was performed according to the ***General Procedures for Carbozincation-Benzylation (5.10.2.9)*** with 6b,9a)-6b,9a-Dimethyl-8-vinyl-6b,9a-dihydroacenaphtho[1,2-d][1,3,2] dioxaborole (0.050 g, 0.2 mmol, 1.00 equiv), PhZnCl•LiCl **[**prepared according to ***General Procedure A: Preparation of Organozinc Chloride Nucleophiles (Section 5.10.2.2)*** using PhLi (0.22 mL, 1.81 M (Bu_2O), $ZnCl_2$ (0.0599 g, 0.44 mmol, 2.2 equiv)**]**, $NiBr_2$•glyme (0.0062 g, 0.02 mmol, 0.10 equiv), (*S*,*S*)-*N*,*N*'-dimethyl-1,2-diphenyl-ethane-1,2-diamine (*S,S*)-**5.262** (0.0063 g, 0.026 mmol, 0.13 equiv), *n*BuI (0.0736 g, 0.40 mmol, 2.00 equiv) 4-methoxybenzyl chloride (0.1253 g, 0.80 mmol, 4.00 equiv), CuCl (0.0098 g, 0.10 mmol, 0.50 equiv), LiCl (0.0085 g, 0.2 mmol, 1.0 equiv). The unpurified product was purified by automated silica gel chromatography (Biotage 1% → 10% ethyl acetate in hexanes, stained in CAM) to afford colorless oil (0.0368 g, 41% yield). **^{1}H NMR** (500 MHz, $CDCl_3$) δ 7.84 – 7.78 (m, 2H), 7.63 – 7.54 (m, 2H), 7.49 – 7.41 (m, 2H), 7.02 – 6.92 (m, 5H), 6.82 – 6.75 (m, 2H), 6.45 – 6.39 (m, 2H), 3.69 (s, 3H), 2.73 – 2.52 (m, 4H), 1.62 (s, 3H), 1.59 (s, 3H).**^{11}B NMR** (160 MHz, $CDCl_3$) δ 34.37. **^{13}C NMR** (126 MHz, $CDCl_3$) δ 157.61, 144.93, 144.89, 141.83, 134.89, 133.77, 131.51, 129.58, 128.77, 128.61, 128.59, 128.06, 125.68, 125.23, 119.54, 119.52, 113.44, 110.20, 91.90, 55.30, 37.70, 36.85, 29.93, 22.03.**IR** (neat)

ν_{max} 3024.50 (w), 2976.18 (w), 2925.17 (w), 2850.40 (w), 1609.12 (w), 1508.84 (m), 1377.77 (m), 1299.39 (m), 1242.15 (s), 1173.79 (m), 1114.76 (m), 1076.53 (m), 1035.81 (w), 824,05 (m), 776,99 (m), 699.35 (m), 507.76 (w) cm^{-1}. **HRMS** (DART) for $C_{30}H_{33}BO_3$ $[M+NH_4]^+$ calculated: 466.2548, found: 466.25540



(6b,9a)-6b,9a-Dimethyl-8-(2-phenylethyl-1-d)-6b,9a-dihydroace naphtho[1,2-d][1,3,2]dioxaborole (5.284). The reaction was performed according to the general procedure (***General Procedures for Carbozincation Reaction (Section 5.10.2.4)*** *(with the modification that N,N'-dimethyl formamide and nBuI was used in place of dimethyl sulfoxide and MeI and the reaction was conducted ate 0 ˚ C)* with 6b,9a)-6b,9a-dimethyl-8-vinyl-6b,9a-dihydroacenaphtho[1,2-d][1,3,2] dioxaborole (0.050 g, 0.2 mmol, 1.00 equiv), PhZnCl•LiCl **[**prepared according to ***General Procedure A: Preparation of Organozinc Chloride Nucleophiles (Section 5.10.2.2)*** using PhLi (0.22 mL, 1.81 M (Bu_2O), $ZnCl_2$ (0.0599 g, 0.44 mmol, 2.2 equiv)**]**, $NiBr_2$•glyme (0.0062 g, 0.02 mmol, 0.10 equiv), (*S*,*S*)-*N*,*N*'-dimethyl-1,2-diphenyl-ethane-1,2-diamine (*S,S*)-**5.262** (0.0063 g, 0.026 mmol, 0.13 equiv), *n*BuI (0.0736 g, 0.40 mmol, 2.00 equiv) with a workup by addition of MeOD (0.3 mL) to the reaction solution before allowing the reaction to warm to room temperature and stir for 30 min. The unpurified product was purified by automated silica gel chromatography (Biotage 1% → 3% ethyl acetate in hexanes, stained in CAM) to afford crystalline solid (0.0277 g, 42% yield). **^{1}H NMR** (500 MHz, $CDCl_3$) δ 7.84 – 7.78 (m, 2H),

7.65 – 7.59 (m, 2H), 7.58 – 7.53 (m, 2H), 7.17 – 7.12 (m, 2H), 7.12 – 7.05 (m, 3H), 2.70 (d, J = 8.3 Hz, 2H), 1.77 (s, 6H), 1.09 (t, J = 8.2 Hz, 1H). **^{11}B NMR** (160 MHz, $CDCl_3$) δ 34.66. **^{13}C NMR** (126 MHz, $CDCl_3$) δ 144.99, 144.44, 134.88, 131.59, 128.69, 128.29, 128.11, 125.61, 125.46, 119.64, 92.00, 30.15, 22.26, 12.85. **IR** (neat) ν_{max} 3023.25 (w), 2971.21 (w), 2926.69 (w), 2857.52 (w), 1494.48 (w), 1452.37 (w), 1362.65 (m), 1303.70 (m), 1262.42 (w), 1172.08 (w), 1115.03 (m), 1076.80 (m), 965.70 (w), 885.60 (w), 823.88 (m), 776.51 (s), 745.04 (m), 697.65 (m) cm^{-1}. **HRMS** (DART) for $C_{22}H_{21}BO_2D$ $[M+H]^+$ calculated: 330.1776, found: 330.177.



(6bR,9aS)-6b,9a-Dimethyl-8-phenethyl-6b,9a-dihydroacenaphtho[1,2-d][1,3,2]dioxaborole (5.283). The reaction was performed according to the general procedure (***General Procedures for Carbozincation Reaction (Section 5.10.2.4)*** *(with the modification that N,N'-dimethyl formamide and nBuI was used in place of dimethyl sulfoxide and MeI and the reaction was conducted ate 0° C) with* 6b,9a)-6b,9a-dimethyl-8-vinyl-6b,9a-dihydroacenaphtho[1,2-d][1,3,2] dioxaborole (0.050 g, 0.2 mmol, 1.00 equiv), PhZnCl•LiCl **[**prepared according to ***General Procedure A: Preparation of Organozinc Chloride Nucleophiles (Section 5.10.2.2)*** using PhLi (0.22 mL, 1.81 M (Bu_2O), $ZnCl_2$ (0.0599 g, 0.44 mmol, 2.2 equiv)**]**, $NiBr_2$•glyme (0.0062 g, 0.02 mmol, 0.10 equiv), (*S,S*)-*N,N*'-dimethyl-1,2-diphenyl-ethane-1,2-diamine (*S,S*)-**5.262** (0.0063 g, 0.026 mmol, 0.13 equiv). *n*BuI (0.0736 g, 0.40 mmol, 2.00 equiv), with a protic workup by addition of a solution of aqueous NH_4Cl (0.3 mL) to the reaction before allowing the reaction to warm

to room temperature and stir for 30 min. The unpurified product was purified by automated silica gel chromatography (Biotage 1% → 3% ethyl acetate in hexanes, stained in CAM) to afford crystalline solid (0.0277 g, 43% yield). **^{1}H NMR** (500 MHz, $CDCl_3$) δ 7.82 (d, *J* = 8.2 Hz, 2H), 7.62 (t, 2H), 7.56 (d, *J* = 7.0 Hz, 2H), 7.18 – 7.12 (m, 2H), 7.12 – 7.05 (m, 3H), 2.70 (t, 2H), 1.77 (s, 6H), 1.11 (t, 2H). **^{11}B NMR** (160 MHz, $CDCl_3$) δ 34.66. **^{13}C NMR** (126 MHz, CDCl3) δ 144.99, 144.45, 134.88, 131.59, 128.68, 128.29, 128.11, 125.61, 125.46, 119.64, 92.00, 30.23, 22.26, 13.16. **IR** (neat) ν_{max} 3023.22 (w), 2970.12 (w), 2926.62 (w), 2855.92 (w), 1494.32 (w), 1452.22 (w), 1368.26 (m), 1302.19 (m), 1172.00 (w), 1114.39 (m), 1075.62 (m), 965.59 (w), 889.62 (w), 824.08 (m), 776.34 (m), 749.63 (m), 697.36 (m) cm^{-1}. **HRMS** (DART) for $C_{22}H_{22}BO_2$ $[M+H]^+$ calculated: 329.17099, found: 329.17074.