Nonracemic Organoboronates by Transition Metal-Catalyzed C-C and C-Si Bond Forming Reactions

Author: Adam Anthony Szymaniak

NONRACEMIC ORGANOBORONATES BY TRANSITION METAL-CATALYZED C-C AND C-Si BOND FORMING REACTIONS

Adam Anthony Szymaniak

A dissertation

submitted to the Faculty of

the department of Chemistry

in partial fulfillment

of the requirements for the degree of

Doctor of Philosophy

Boston College
Morrissey College of Arts and Sciences
Graduate School

June 2018

NONRACEMIC ORGANOBORONATES BY TRANSITION METAL-CATALYZED C-C AND C-Si BOND FORMING REACTIONS

Adam Anthony Szymaniak

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

ABSTRACT: This dissertation will describe the development of three transition metal-catalyzed syntheses of nonracemic organoboronates. The first chapter explains the development of a palladium-catalyzed enantiotopic-group-selective cross-coupling of geminal bis(boronates) with alkenyl electrophiles. This process enables the synthesis of highly valuable nonracemic disubstituted allylic boronates. Chapter two describes a palladium-induced 1,2-metallate rearrangement of vinylboron "ate" complexes. The newly developed process incorporates an alternative route for the transmetallation step of Suzuki-Miyaura cross-couplings. Lastly, an enantioselective platinum-catalyzed hydrosilylation of alkenyl boronates is disclosed. This reaction enables the synthesis of nonracemic geminal silylboronates for the divergent synthesis of functionalized stereocenters.

TABLE OF CONTENTS

Dedicated to:

My family and girlfriend for their continuous support and love.

My parents: Greg and Beth Szymaniak

My brother and wife: Aleks and Kate Szymaniak

My brother, wife, and beautiful children: Justin and Aileen, Evan, Alice, Annemarie,

Elsie Szymaniak

My wonderful girlfriend: Rachel Patchel

ACKNOWLEDGEMENTS

I would like to most importantly thank my advisor, Professor James P. Morken. I could not have asked for a more-ideal advisor to work for. His breath of chemistry knowledge always amazed me and his passion for chemistry always motivated me to be the best chemist I can. He was there to help you whenever needed, but also allowed you to be an independent chemist; I will always be grateful for that.

I have to thank the Morken lab, past and present. I could not be any prouder to say I worked in the Morken lab. I have to specifically thank Bowman Potter for being my mentor and shaping me into the chemist I am today. Matteo Chierchia, for being a great mentee and working on a project with me that didn't quite make it to "high er." The "conjunctive-team" for working on the first report and all the subsequent projects together. Chenlong Zhang, for being an awesome mentee and working hard on the hydrosilylation project. I also have to thank specific people who helped me in the Morken lab: Meredith Eno, Liang Zhang, Ryan Coombs, and Chris Schuster. I most definitely have to thank the "315C" group (Matteo, Jesse, and Lu) for making our side of the lab fun to work in, with countless laughs (and for reading my thesis). In addition to the Morken lab, I have to thank the BC chemistry department for all the support and help throughout the years.

Lastly, I have to thank my family. They have loved and supported me throughout my PhD career, and I couldn't be any more grateful for that. Spending time with my family, my beautiful nephew and nieces helped so much. I also have to thank my amazing girlfriend, Rachel. She's always there for me and helped me through the hardest and most stressful part of graduate school; finding a job. I can't express enough gratitude for that.

LIST OF ABBREVIATIONS

Nu: nucleophile

LG: leaving group

H^+: acid

LDA: lithium disopropylamine

TBAF: tetrabutyl ammonium fluoride

R: group

X: halogen

M: metal

E^+: electrophile

$Pd_2(dba)_3$: tris(dibenzylideneacetone)dipalladium

(*S*)-MeO-MOP: (*S*)-(+)-2-(Diphenylphosphino)-2′-methoxy-1,1′-binaphthyl

er: enantiomeric ratio

(*S*, *R*)-PPFA: (*S*)-*N*,*N*-Dimethyl-1-[(*R*)-2-(diphenylphosphino)ferrocenyl]ethylamine

$Pd(OAc)_2$: palladium (II) acetate

9-BBN: 9-Borabicyclo[3.3.1]nonane

$Ni(cod)_2$: Bis(1,5-cyclooctadiene)nickel(0)

TBS: *tert*-butyldimethylsilyl

THF: tetrahydrofuran

$Pd[(P^tBu)_3]_2$: bis(tri-*tert*-butylphosphino)palladium (0)

Bpin: pinacol derived boronate

NMR: nuclear magnetic resonance spectroscopy

DFT: density functional theory

LUMO: lowest unoccupied molecular orbital

L: ligand

Ar: aryl

Equiv.: equivalents

TADDOL: tetra-aryl dioxolane diol

r.t.: room temperature

$Pd(PPh_3)_4$: tetrakis(triphenylphosphine) palladium (0)

$C(sp^2)$: sp^2 hybridized carbon

$Cu(NCMe)_4PF_6$:

Tetrakis(acetonitrile)copper(I) hexafluorophosphate

E-X: electrophile

Xantphos: 4,5-Bis(diphenylphosphino)-9,9-dimethylxanthene

Quinox-P: (*R*,*R*)-(–)-2,3-Bis(*tert*-butylmethylphosphino)quinoxaline

B_2pin_2: bis(pinacolato)diboron

Bneo: neopentyl diol derived boronate

DCM: dichloromethane

DME: dimethoxyethane

NHC: *N*-heterocyclic carbene

G: group

$Pt(acac)_2$: Platinum(II) acetylacetonate

(R)-DTBM Segphos: (*R*)-(−)-5,5′-Bis[di(3,5-di-*tert*-butyl-4-methoxyphenyl)phosphino]-4,4′-bi-1,3-benzodioxole, [(4*R*)-(4,4′-bi-1,3-benzodioxole)-5,5′-diyl]bis[bis(3,5-di-*tert*-butyl-4-methoxyphenyl)phosphine]

Piv: pivalate

$Pt(dba)_3$: tris(dibenzylideneacetone)platinum

(*S*,*S*,*R*)-Mandyphos: (S_P,S'_P)-1,1′-Bis[bis(4-methoxy-3,5-dimethylphenyl)phosphino]-2,2′-bis[(*R*)-α-(dimethylamino)benzyl]ferrocene

LTMP: lithium 2,2,6,6-tetramethylpiperidide

$Rh(cod)_2Cl_2$: Chloro(1,5-cyclooctadiene)rhodium(I) dimer

HBpin: pinacolborane

dppb: diphenylphosphinobutane

DCE: 1,2-dichloroethane

DMF: *N,N*-dimethylformamide

TMEDA: tetramethylethylenediamine

CPME: cyclopentyl methyl ether

ICy: 1,3-Dicyclohexylimidazolium

$Pd(dppf)Cl_2$·DCM: [1,1′Bis(diphenylphosphino)ferrocene]dichloropalladium(II), complex with dichloromethane

SFC: supercritical fluid chromatography

n.d.: not determined

(*R,R*)-Me-BPE: (+)-1,2-Bis[(2*R*,5*R*)-2,5-dimethylphospholano]ethane

(*S*)-^{i}Pr-Phox: (4*S*)-2-[2-(diphenylphosphino)phenyl]-4,5-dihydro-5,5-dimethyl-4-(1-methylethyl)-oxazole

(*R*)-MeO-Biphep: (R)-(+)-2,2'-Bis(diphenylphosphino)-6,6'-dimethoxy-1,1'-biphenyl

(*R*)-*p*-tol-BINAP: (*R*)-(+)-2,2′-Bis(di-*p*-tolylphosphino)-1,1′-binaphthyl

(*R,R*)-WalPhos: (R)-(+)-1-[(R)-2-(2'-Diphenylphosphinophenyl)ferrocenyl]ethyldiphenylphosphine

(*R,R*)-TaniaPhos: (R_P)-1-[(*R*)-α-(Dimethylamino)-2-(diphenylphosphino)benzyl]-2-diphenylphosphinoferrocene

JosiPhos: (*R*)-1-[(S_P)-2-(Dicyclohexylphosphino)ferrocenylethyl]diphenylphosphine

MTBE: methyl *tert*-butyl ether

MeCN: acetonitrile

DiBAL-H: diisobutylaluminum hydride

AcOH: acetic acid

3,5-xylyl: 3,5-dimethylphenyl

p-tolyl: 4-methylphenyl

$PdCl_2(MeCN)_2$: bis(acetonitrile)dichloropalladium

RuPhos: 2-Dicyclohexylphosphino-2′,6′-diisopropoxybiphenyl

Bdan: diaminonaphthalene derived boronate

NBS: *N*-bromosuccinimide

TCCA: Trichloroisocyanuric acid

S_E2: bimolecular electrophilic substitution

L_n: ligands

P(*o*-tol)$_3$: tri(2-methylphenyl)phosphine

$Pd((p\text{-}OMeC_6H_4)_2Cl_2$: bis(4-methoxyphenyl)dichloropalladium

P(*p*-$OMeC_6H_4)_3$: tri(4-methoxyphenyl)phosphine

DABCO: 1,4-diazabicyclo[2.2.2]octane

Tf: trifluoromethanesulfonate

(*S,S*)-Me-DuPhos: (+)-1,2-Bis[(2*S*,5*S*)-2,5-dimethylphospholano]benzene

Ts: tosylate

Ms: mesylate

PPTS: Pyridinium *p*-toluenesulfonate

DIPEA: diisopropylethylamine

TBSCl: chloro-*tert*-butyldimethylsilane

*m*CPBA: *meta*-chloroperbenzoic acid

$[Ni(methallyl)Cl]_2$: methallylnickel chloride dimer

[PdCl(π-allyl)]: Allylpalladium(II) chloride dimer

(*S,S*)-Ph-BPE: (+)-1,2-Bis((2*S*,5*S*)-2,5-diphenylphospholano)ethane

XPhos: 2-Dicyclohexylphosphino-2′,4′,6′-triisopropylbiphenyl

Y: group

Cb: 2,2-diisopropylcarbamoyl

(+)/(-)-sp: (+)/(-) sparteine

Li(+)-sp: lithium-sparteine complex

MOM: methoxy methyl ether

TIB: 2,4,6-triisopropylbenzoate

BOX: bis(oxazoline)

$Ir[dF(CF_3]ppy]_2(dtbbpy)PF_6$: [4,4′-*Bis*(1,1-dimethylethyl)-2,2′-bipyridine-*N*1,*N*1′]*bis*[3,5-difluoro-2-[5-(trifluoromethyl)-2-pyridinyl-*N*]phenyl-C]iridium(III) hexafluorophosphate

LEDs: light-emitting diodes

DG: directing group

Imid.: imidazolium

$Rh(acac)(CO)_2$: (Acetylacetonato)dicarbonylrhodium(I)

Psi: pounds per square inch

NMO: *N*-Methylmorpholine-*N*-Oxide

$(nBu)_4NRuO_4$: tetrabutylammonium perruthenate

S_E': gamma-selective electrophilic substitution

rr: regioisomeric ratio

HNE: human neutrophil elastase

μm: micromolar

"F^+": electrophilic fluorine

B_2cat_2: bis(catecholato)diboron

(*S*)-MonoPhos: (*S*)-(+)-(3,5-Dioxa-4-phosphacyclohepta[2,1-a;3,4-

a′]dinaphthalen-4-yl)dimethylamine

(*R*)-SiPhos: (11a*R*)-(+)-10,11,12,13-Tetrahydrodiindeno[7,1-de:1′,7′-fg][1,3,2]dioxaphosphocin-5-dimethylamine

(*R*)-Quinap: (R)-(+)-1-(2-diphenylphosphino-1-naphthyl)isoquinoline

ent: enantiomer

3M: 3 molar

Boc_2O: Di-*tert*-butyl dicarbonate

P*: chiral phosphine ligand

R_f: retention factor

MHz: megahertz

l: path length

$[\alpha]^{20}_{D:}$: optical rotation

ESI+: electrospray ionization

DART: direct analysis in real time

IR: infrared spectroscopy

HRMS: high resolution mass spectroscopy

CHAPTER 1

Development of an Enantiotopic-Group-Selective Cross-Coupling of Geminal Bis(Boronates) with Alkenyl Halides

1.1 Introduction

The synthesis of alkyl organoboronates has become a widely-studied area of synthetic organic chemistry, with regards to the synthesis of nonracemic and even racemic organoboronates. There are a plethora of methods being developed to target these compounds such as borylation of halides, borylation of π-systems, C-H borylation, amongst many of other technologies.[1] Organoboronates attract this much attention due to the organoboronate having the ability to be transformed into a wide variety of functional groups, as well as participate in metal-catalyzed reactions. In this respect, Suzuki-Miyaura cross-couplings have become one of the most widely used organometallic reactions.[2] The utility of this reaction has also grown exponentially in the pharmaceutical industry for the construction of advanced pharmaceutical intermediates of biological significance.[2]

---

[1] Fernandez, E.; Whiting, A. *Synthesis and Applications of Organoboron Compounds* **2015**, Springer, New York, *49*, pp. 331. ISBN 978-3319130538

[2] a) Miyaura, N.; Suzuki, A. *Chem. Rev.* **1995**, *95*, 2457-2483 b) Yasuda, N.; King, A. O. *Topic Organomet. Chem.* **2004**, *6*, 205-245 c) Torborg, C.; Beller, M. *Adv. Synth. Catal.* **2009**, *351*, 3027-3043 d) Budaran, V. L.; Shuttleworth, P. S.; Clark, J. H.; Luque, R. *Current Organic Synthesis* **2010**, *7*, 614-627 e)

The ability to expand Suzuki-Miyaura cross-couplings into the realm of asymmetric catalysis could potentially have a large impact in synthetic organic chemistry and its development is highly desirable. Typical enantioselective Suzuki-Miyaura cross-couplings involve the synthesis of chiral biaryl compounds, which are used for the synthesis of chiral phosphine ligands and natural products.[3] The ability to employ the enantioselective Suzuki-Miyaura reaction for the cross-coupling of alkyl organoboronates would be a significance advance. This chapter will discuss approaches to enantioselective Suzuki-Cross coupling reactions and the development of an enantiotopic-group-selective cross-coupling of geminal bis(boronates) for the synthesis of nonracemic allylic boronates.

1.2 Background

1.2.1 Enantioselective Suzuki-Miyaura Cross-Couplings and Asymmetric Catalysis with Geminal Bis(Boronates)

The synthesis of organoboronates has received much attention from the synthetic organic chemistry community. This stems from the fact that, depending on the nature of the organoboronate ligands, these molecules can be stable to air and moisture. In addition to stability, organoboronates possess inherent reactivity. Upon activation by addition of a nucleophile to their vacant *p*-orbital, the newly formed organoboron "ate" complex can react with electrophiles. In one example (Scheme 1.1), activation of the organoboronate by addition of a nucleophile with an appended leaving group will promote a 1,2-migration

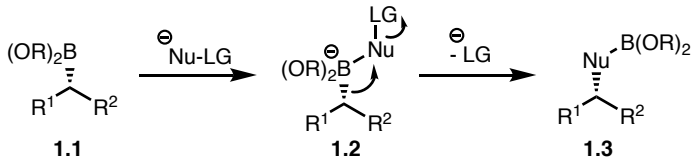
---

Suzuki, A. *Angew. Chem. Int. Ed.* **2011**, *50*, 6723-6737 f) Navarro, O.; Maluenda, I. *Molecules* **2015**, *20*, 7528-7557

[3] a) Ma, Y. –N.; Yang, S. –D. *Chem. Eur. J.* **2015**, *21,* 6673-6677 and references within b) Hassan, J.; Sevignon, M.; Gozzi, C.; Schulz, E.; Lemaire, M. *Chem. Rev.* **2002**, *102*, 1359-1460 c) Linton, E. C.; Morgan, B. J.; Kozlowski, M. C. *Chem. Soc. Rev.* **2009**, *38*, 3193-3207

of the carbon-boron bond to displace the leaving group and produce a new carbon-nucleophile bond.[4] An important feature of the 1,2-migration of organoboron "ate" complexes is that if the organoboronate is nonracemic, the 1,2-rearrangement occurs with stereoretention at the migrating carbon.

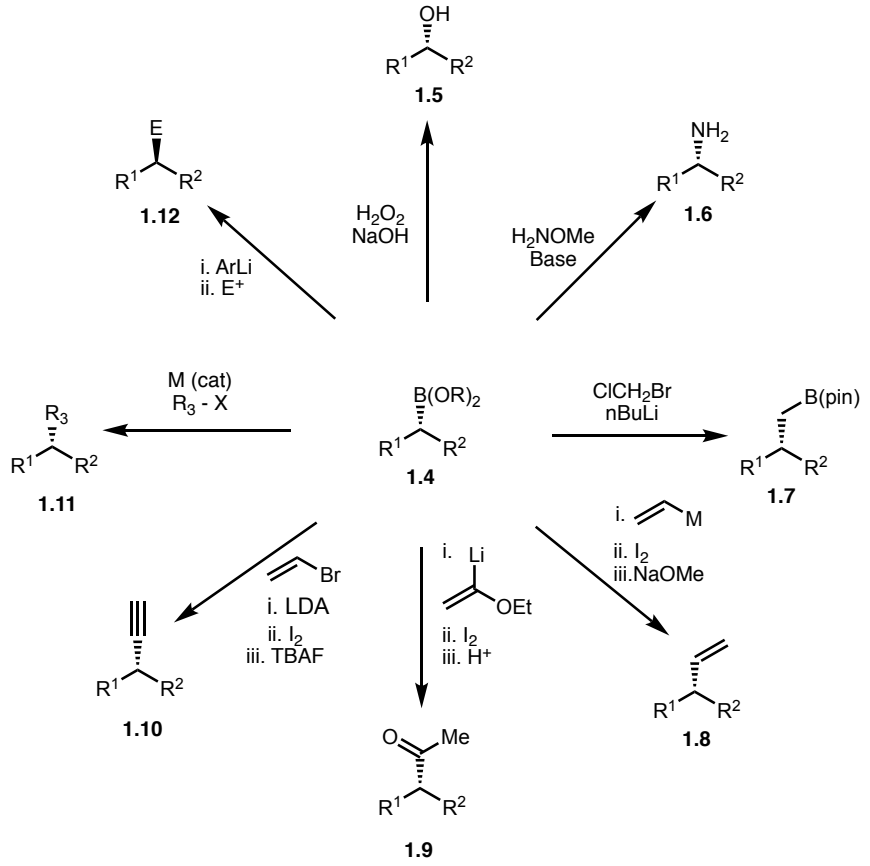
Scheme 1.1 Stereoretentive 1,2-Migration of Organoboron "Ate" Complexes



This type of reactivity occurs with a wide variety of nucleophiles and therefore allows heteroatoms and π-systems to be incorporated into products.[5] Stereospecific 1,2-metallate shifts enable oxidation (**1.5**) and amination (**1.6**) of organoboronates while the Matteson homologation (**1.7**) can extend the functional organoboron handle by a one-carbon homologation. A variety of olefination reactions have been reported, such as the Zweifel olefination (**1.8**), as well as an alkynylation by Aggarwal (**1.10**).[5a] A wide variety of stereospecific cross-couplings (**1.11**) of organoboronates have been also developed[5b], and a stereoinvertive electrophilic displacement (**1.12**) of organoboron "ate" complexes has been developed by Aggarwal.[5a] These examples show the versatile reactivity of organoboron "ate" complexes, and highlight the powerful methods by which organoboronates can be further functionalized. The versatility of organoboronates has inspired synthetic chemists to develop methods for their synthesis in a nonracemic fashion.

[4] Matteson, D. S. *Stereodirected Synthesis with Organoboranes.* Springer, Berlin, **1995**, 48-92.
[5] a) Sandford, C.; Aggarwal, V. K. *Chem. Commun.* **2017**, *53*, 5481-5494 b) Rygus, J. P. G.; Crudden, C. M. *J. Am. Chem. Soc.* **2017**, *139*, 18124-18137

Scheme 1.2 Reactions of Organoboron "Ate" Complexes



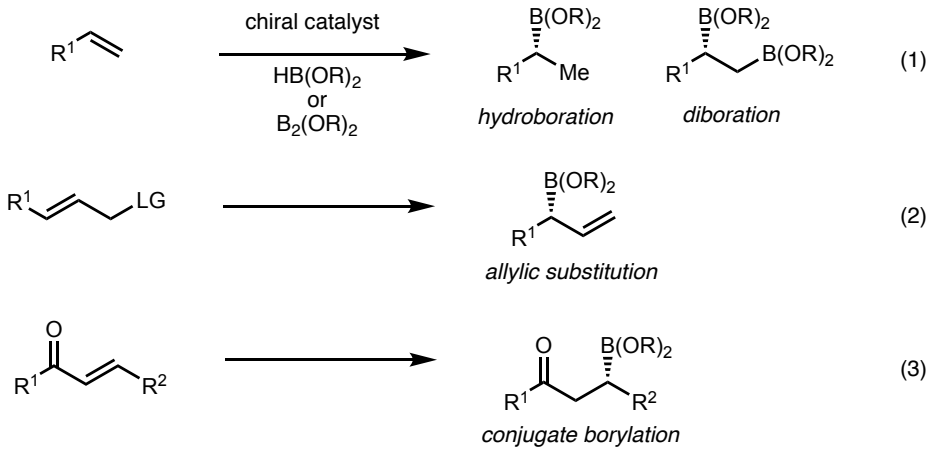
Potentially inspired by the Nobel Prize winning hydroboration of alkenes[6], the development of catalytic methods for the synthesis of nonracemic organoboronates has largely focused on the addition of boron reagents across π-systems. Specific examples of these reactions include but are not limited to the metal-catalyzed asymmetric hydroboration and diboration of alkenes (Scheme 1.3, eq. 1), allylic substitution (Scheme 1.3, eq. 2), and conjugate borylation (Scheme 1.3, eq. 3).[7] In contrast to this approach, the synthesis of nonracemic organoboronates by the Suzuki-Miyaura cross-couplings is underdeveloped.

---

[6] Herbert C. Brown - Nobel Lecture: From Little Acorns to Tall Oaks - from Boranes through Organoboranes". *Nobelprize.org.* Nobel Media AB **2014**. Web. 12 Mar 2018. <http://www.nobelprize.org/nobel_prizes/chemistry/laureates/1979/brown-lecture.html>

[7] a) Collins, B. S. L.; Wilson, C. M.; Myers, E. L.; Aggarwak, V. K. *Angew. Chem. Int. Ed.* **2017**, *56*, 11700-11733 b) Calow, A. D. J.; Whiting, A. *Org. Biomol. Chem.* **2012**, *10*, 5485-5497 c) Schiffner, J. A.; Muther, K.; Oestreich, M. *Angew. Chem. Int. Ed.* **2010**, *49*, 1194-1196

Scheme 1.3 General Methods for the Catalytic, Enantioselective Synthesis of Organoboronates



Typically, employing Suzuki-Miyaura cross-couplings for asymmetric catalysis consumes the organoboron reagent in the process of forming a new carbon stereocenter. Such is the case in pioneering work done by Buchwald and coworkers for the construction of functionalized nonracemic biaryls through an enantioselective Suzuki-Miyaura cross-coupling (Scheme 1.4, eq. 1).[8] Numerous other groups further advanced the synthesis of nonracemic biaryls through enantioselective Suzuki-Miyaura cross-couplings.[3] Willis and coworkers developed an enantioselective desymmetrization of bis(alkenyl) triflates through a Suzuki-Miyaura cross-coupling with aryl boronic acids (Scheme 1.4, eq. 2).[9] The reaction occurred with good yields and enantioselectivity. Lastly, Fu and coworkers pioneered a stereoconvergent enantioselective alkyl-alkyl Suzuki-Miyaura cross-coupling that uses nickel-catalysis to produce hydrocarbons in good yields and enantioselectivity (Scheme 1.4, eq. 3).[10]

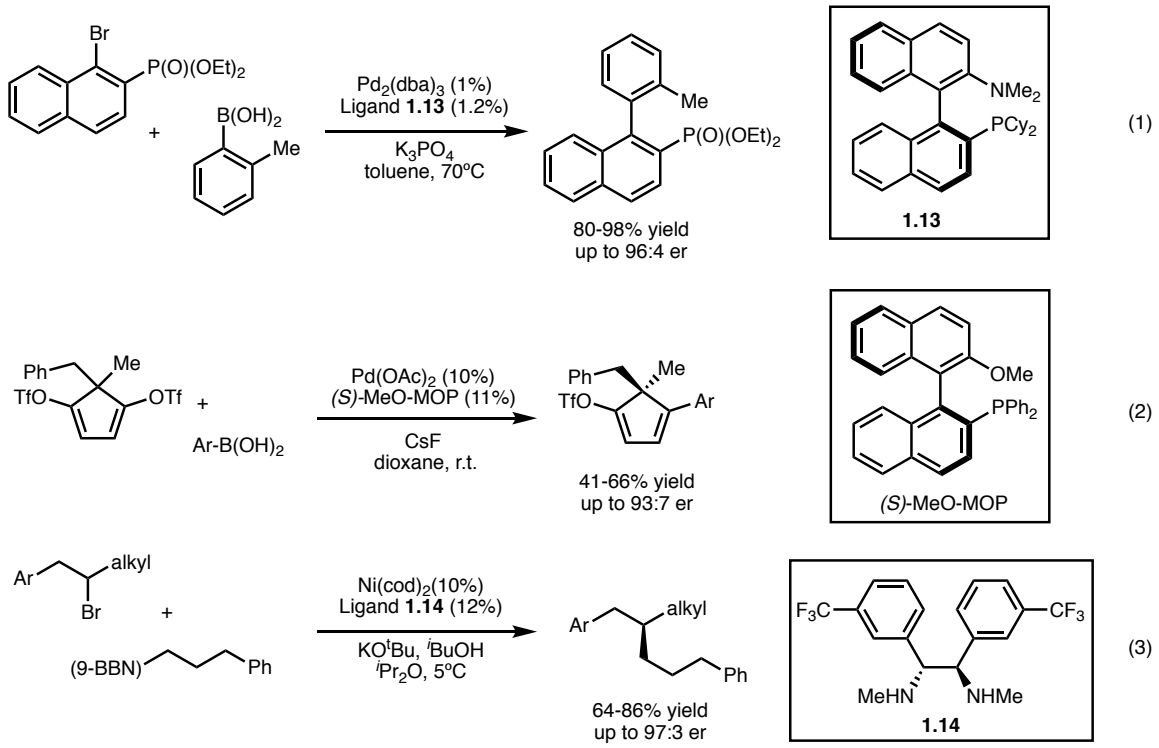
---

[8] a) Yin, J.; Buchwald, S. L. *J. Am. Chem. Soc.* **2000**, *122*, 12051-12052 b) For the first reported synthesis on nonracemic biaryls see: Crepy, K. V. L.; Cammidge, A. N. *Chem. Commun.* **2000**, 1723-1724

[9] Powell, L. H. W.; Claverie, C. K.; Watson, S. J.; Willis, M. C. *Angew. Chem. Int. Ed.* **2004**, *43*, 1249-1251

[10] Saito, B.; Fu, G. C. *J. Am. Chem. Soc.* **2008**, *130*, 6694-6695

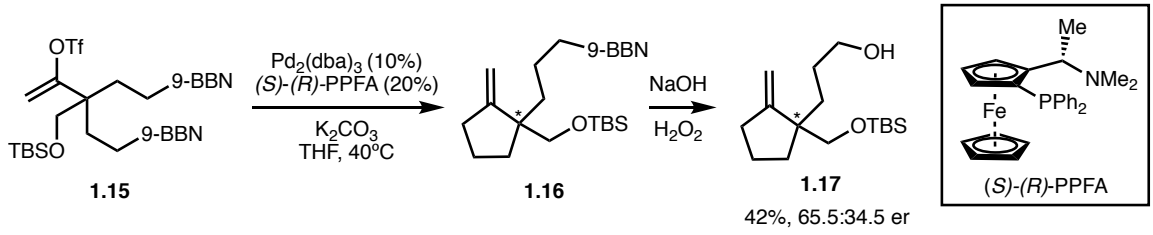
Scheme 1.4 Examples of Enantioselective Suzuki-Miyaura Cross-Couplings



Our group was interested in developing an enantioselective Suzuki-Miyaura cross-coupling which would furnish a versatile boron-containing stereocenter. This idea is conceptually related to pioneering work done by Shibasaki and coworkers on the cross-coupling of prochiral bis(boranes), as well as Shibata, Endo and coworkers on the cross-coupling of geminal bis(boronates). Shibasaki and coworkers reported the first example of an enantioselective intramolecular Suzuki-Miyaura cross-coupling of bis(borane) **1.15** to furnish cyclopentylidene alcohol **1.17** after oxidation (Scheme 1.5).[11] Although the yield and enantioselectivity were modest, this pioneering example showed the potential for an enantioselective Suzuki-Miyaura cross-coupling while still retaining an organoborane in the product for further functionalization.

[11] Cho, S. Y.; Shibasaki, M. *Tetrahedron: Asymmetry* **1998**, *9*, 3751-3754

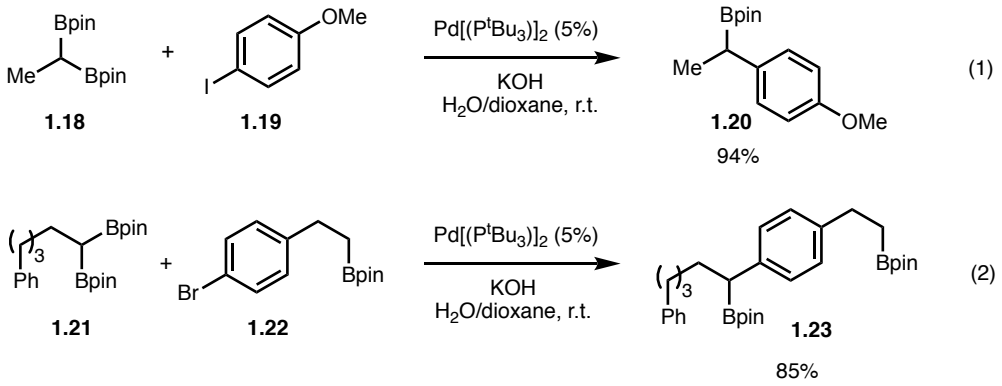
Scheme 1.5 First Example of an Enantioselective Intramolecular Suzuki-Miyaura Cross-Coupling



Work done by Shibata, Endo and coworkers on the cross-coupling of geminal bis(boronates) extended this concept further. As depicted in Scheme 1.6 (eq. 1), subjecting geminal bis(boronate) **1.18** to a palladium-catalyzed cross-coupling with *p*-iodoanisole **1.19** resulted in the mono- cross-coupled benzylic boronate **1.20**.[12] The reaction occurred with good yield over a short reaction time under mild conditions. The efficiency of this cross-coupling of an alkyl organoboronate at room temperature over two hours was quite surprising. Typically, palladium-catalyzed Suzuki-Miyaura cross-couplings of alkyl organoboronates require more forcing conditions. The remarkable reactivity of geminal bis(boronates) is exemplified by the competitive cross-coupling of geminal bis(boronate) **1.21** and electrophile **1.22**, a compound containing an appended mono-alkyl organoboronate (Scheme 1.6, eq. 2). Subjecting these partners to the same reaction conditions resulted in exclusive cross-coupling of the geminal bis(boronate) moiety as depicted in product **1.23**. This result clearly demonstrates that geminal bis(boronates) have enhanced reactivity in Suzuki-Miyaura cross-couplings relative to mono-alkyl organoboronates.

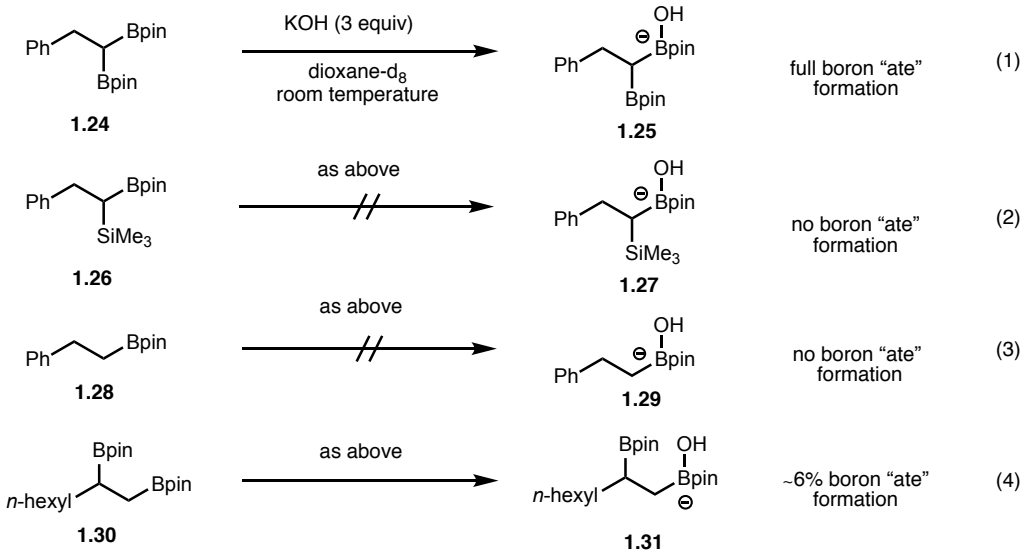
[12] Ohkubo, T.; Hirokami, M.; Endo, K.; Shibata, T. *J. Am. Chem. Soc.* **2010**, *132*, 11033-11035

Scheme 1.6 Palladium-Catalyzed Cross-Coupling of Geminal Bis(Boronates)



Shibata, Endo and coworkers carried out ^{11}B-NMR experiments to probe the reactivity of geminal bis(boronates) depicted in Scheme 1.7. Geminal bis(boronate) **1.24** showed full formation of the boron "ate" complex **1.25** by ^{11}B-NMR (Scheme 1.7, eq. 1). The silicon analogue, geminal silylboronate **1.26,** showed no formation of the boron "ate" complex (Scheme 1.7, eq. 2). Additionally, mono-alkyl organoboronate **1.28** showed no boron "ate" complex formation (Scheme 1.7, eq. 3), consistent with the result of the competition experiment in Scheme 1.6 (eq. 2). Lastly, vicinal bis(boronate) **1.30** displayed some boron "ate" complex formation (Scheme 1.7, eq. 4); however, conversion was much less than geminal bis(boronate) **1.24**. These data show that the enhanced reactivity of geminal bis(boronates) in cross-couplings may come from the enhanced formation of boron "ate" complexes, which are required for transmetallation

Scheme 1.7 ^{11}B-NMR experiments of Organoboron "Ate" Complex Formation of Various Organoboronates

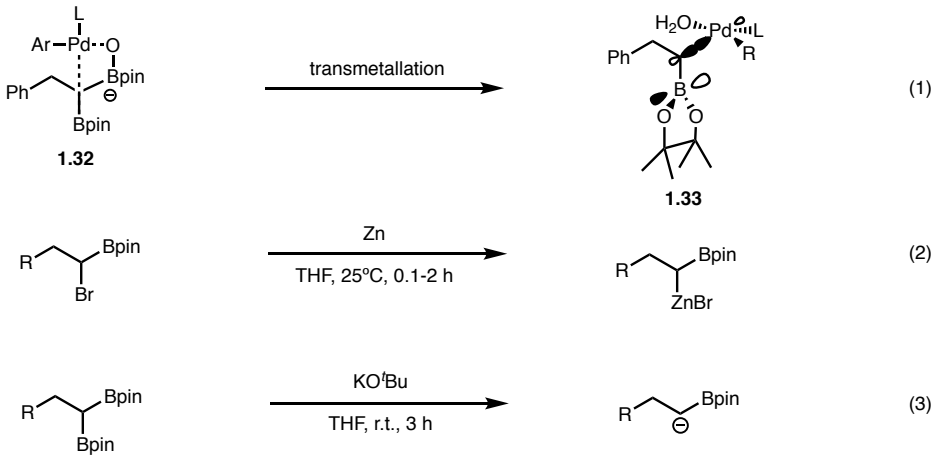


Shibata and Endo employed DFT to calculate the geminal bis(boronate) LUMO maps; this shows a large LUMO distribution around the B-B moiety resulting in assistance of the neighboring boron for boron "ate" complex formation. Alternatively, a driving force for the transmetallation step might be the formation of α-boryl palladium intermediate **1.33** (Scheme 1.8, eq. 1). By allowing hyperconjugation of the carbon-palladium bond into the vacant *p*-orbital on the adjacent boron, the α-boryl group may be a stabilizing feature.[13] This stabilizing feature is conceptually similar to the zinc insertion into α-haloboronates as studied by Knochel (Scheme 1.8, eq. 2).[14] Knochel hypothesized that the remarkably easy zinc insertion reflects upon the participation of the organoboronate group for the formation of the organometallic. Related to boronate stabilization observed with geminal bis(boronates) in cross-coupling reactions, Morken and coworkers studied the deborylative

[13] Leonori, D.; Aggarwal, V. K. *Angew. Chem. Int. Ed.* **2015**, *54,* 1082-1096
[14] Knochel, P. *J. Am. Chem. Soc.* **1990**, *112*, 7431-4433

formation of α-boryl anions (Scheme 1.8, eq. 3).[15] Treatment of geminal bis(boronates) with potassium *tert*-butoxide under mild conditions allowed for the formation of an α-boryl anion. The α-boryl anion was stabilized sufficiently where the species could be observed by ^{13}C-NMR. The formed α-boryl anion was then trapped with a variety of electrophiles. These two examples, in addition to the cross-coupling of geminal bis(boronates), attest to the stabilizing feature of α-boryl organometallic species. This stabilizing feature can be considered a driving force for organometallic reactions, and also might govern regioselectivity for the formation of an α-boryl metal intermediate.

Scheme 1.8 α-Boryl Stabilized Organometallic Compounds and Related Species

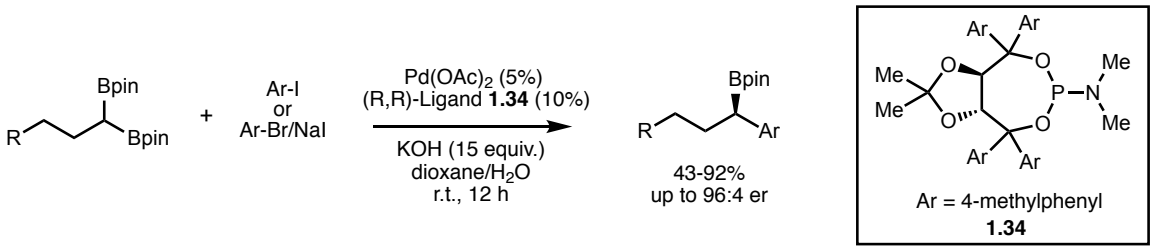


With the reactivity of geminal bis(boronates) towards palladium-catalyzed cross-couplings understood, our group wondered whether this reaction could be accomplished in an enantioselective fashion. This mode of reactivity would in fact constitute an enantioselective Suzuki-Miyaura cross-coupling which produces a new boron-containing carbon stereocenter for further functionalization. Employing a TADDOL-based phosphoramidite ligand, a palladium catalyst and aryl electrophiles, Morken and coworkers

[15] Hong, K.; Liu, X.; Morken, J. P. *J. Am. Chem. Soc.* **2014**, *136*, 10581-10584

were able to develop an enantiotopic-group-selective cross-coupling of geminal bis(boronates) (Scheme 1.9).[16] This method was shown to be quite broad with respect to different functionality on the geminal bis(boronate) and the aryl electrophile. In addition to a broad scope, the cross-coupling occurred with good yields and enantioselectivity.

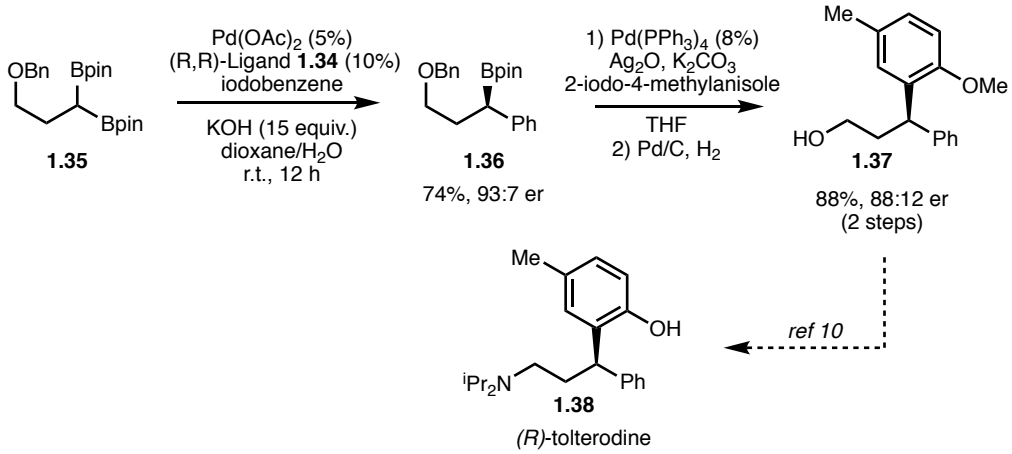
Scheme 1.9 Enantiotopic-Group-Selective Cross-Coupling of Geminal Bis(Boronates) with Aryl Electrophiles



The utility of this cross-coupling was demonstrated by a formal synthesis of pharmaceutically-relevant *(R)*-tolterodine, a drug marketed by Pfizer for the treatment of overactive bladder (Scheme 1.10). After cross-coupling of the geminal bis(boronate) **1.35** with iodobenzene, a stereospecific cross-coupling of benzylic boronate (**1.36**) developed by Crudden was employed.[17] Subsequent benzyl deprotection furnished alcohol **1.37**, a known precursor[18] for the synthesis of *(R)*-tolterodine.

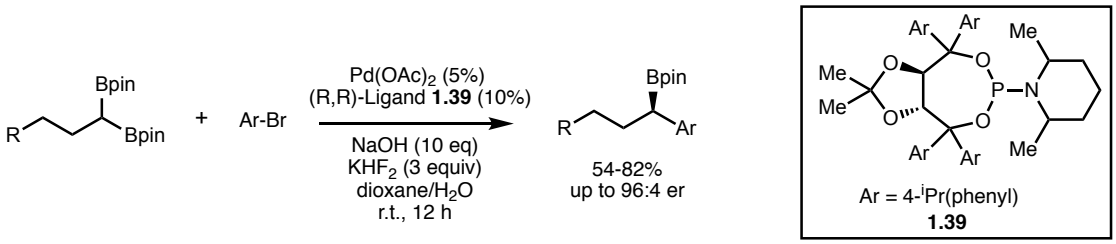
[16] Sun, C.; Potter, B.; Morken, J. P. *J. Am. Chem. Soc.* **2014**, *136*, 6534-6537
[17] Imao, D.; Glasspoole, B. W.; Laberge, V. S.; Crudden, C. M. *J. Am. Chem. Soc.* **2009**, *131*, 5024
[18] Jonsson, N. A.; Spark, B. A.; Mikiver, L.; Moses, P. Nilvebrant, L.; Glas, G. U.S. Patent 5,382,600 A1, 1995

Scheme 1.10 Formal Synthesis of *(R)*-tolterodine



The cross-coupling of geminal bis(boronates) with aryl electrophiles was further developed by Hall and coworkers (Scheme 1.11).[19] The subsequent work employed slightly different reactions conditions and a different TADDOL-derived phosphoramidite ligand. The modified reaction conditions produced comparable yields and enantioselectivity as the first report.

Scheme 1.11 Hall Conditions for Cross-Coupling of Geminal Bis(Boronates)

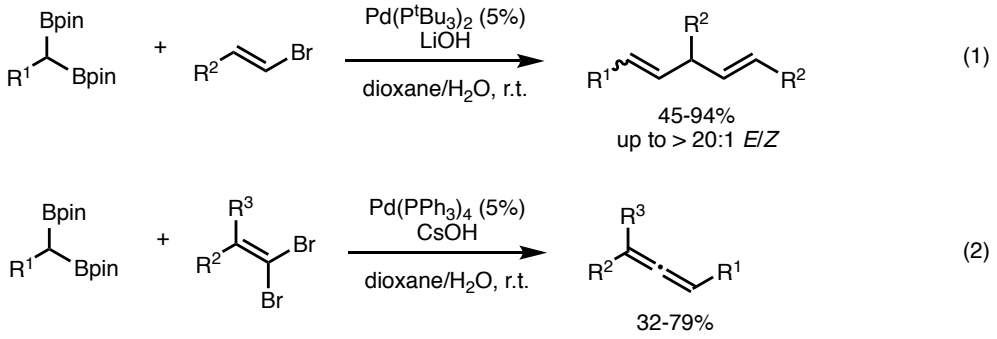


It was not until work was done by Wang and coworkers that the cross-coupling of geminal bis(boronates) with alkenyl electrophiles was realized. Employing palladium-phosphine complexes and alkenyl bromides effected the cross-couplings depicted in Scheme 1.12.[20] However, under these reaction conditions, the allylic boronate product was

[19] Sun, H. –Y.; Kubota, K.; Hall, D. G. *Chem. Eur. J.* **2015**, *21,* 19186-19194
[20] Li, H.; Zhang, Z.; Shanggaun, X.; Huang, S.; Chen, J.; Zhang, Y; Wang, J. *Angew. Chem. Int. Ed.* **2014**, *53*, 11921-11925

susceptible to additional cross-coupling to produce a diene (Scheme 1.12, eq. 1). Although asymmetric catalysis is precluded because the product is achiral, this method is a powerful route to skipped dienes. Employing alkenyl dibromides demonstrated an efficient synthesis of substituted allenes as well (Scheme 1.12, eq. 2).

Scheme 1.12 Cross-Coupling of Geminal Bis(Boronates) with Alkenyl Electrophiles

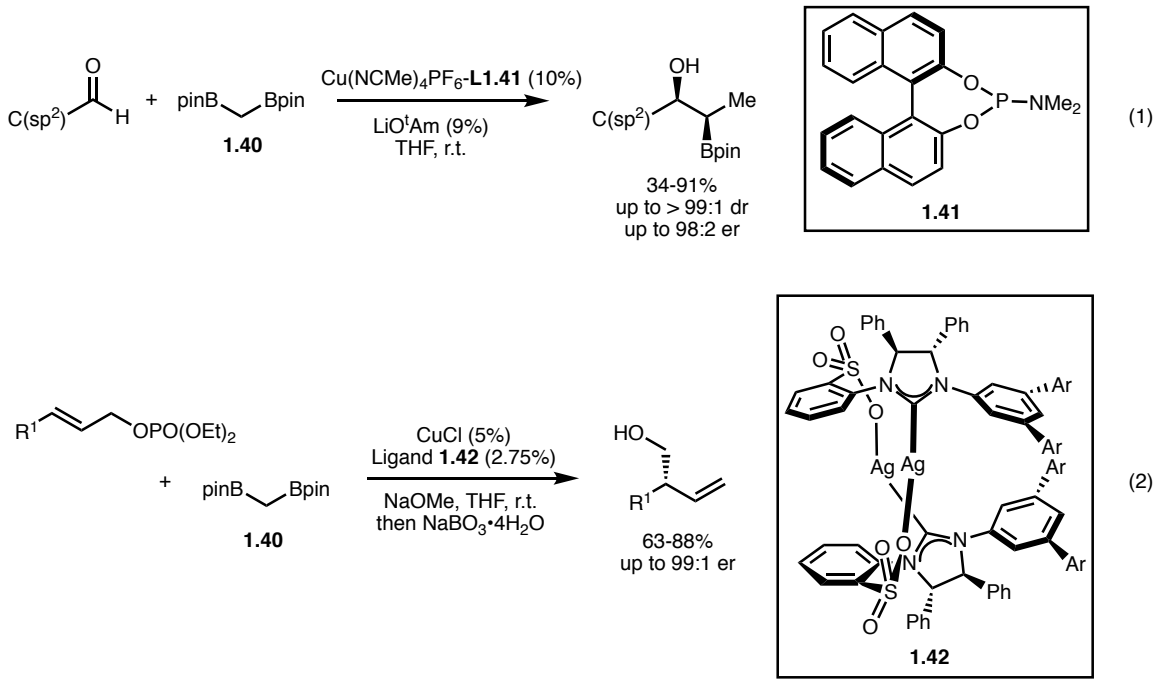


In addition to palladium-catalyzed cross-couplings, new developments have been made employing copper catalysis in reactions with geminal bis(boronates). These efforts were pioneered by the Meek and Hoveyda labs. Meek and coworkers have developed a copper-catalyst that effects a deborylative addition of bis(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)methane (**1.40**) to aldehydes. This reaction produces *syn* 1,2-hydroxyboronates in good yields with excellent diastereo- and enantioselectivity (Scheme 1.13, eq. 1).[21] The newly developed method was also extended to additions to α-ketoesters which furnished tertiary β-hydroxy boronates.[22] In addition to reactions with carbonyl compounds, Hoveyda and coworkers used copper-NHC catalysis to engage **1.40** in allylic substitution. This reaction produced α-hydroxy allylic stereocenters with excellent

[21] Joannou, M. V.; Moyer, B. S.; Meek, S. J. *J. Am. Chem. Soc.* **2015**, *137*, 6176-6179
[22] Murray, S. A.; Green, J. C.; Tailor, S. B.; Meek, S. J. *Angew. Chem. Int. Ed.* **2016**, *55*, 9065-9069

enantioselectivity (Scheme 1.13, eq. 2).[23] The copper-catalyzed allylic substitution was further extended for the synthesis of a natural product.

Scheme 1.13 Enantioselective Copper-Catalysis with Geminal Bis(Boronates)



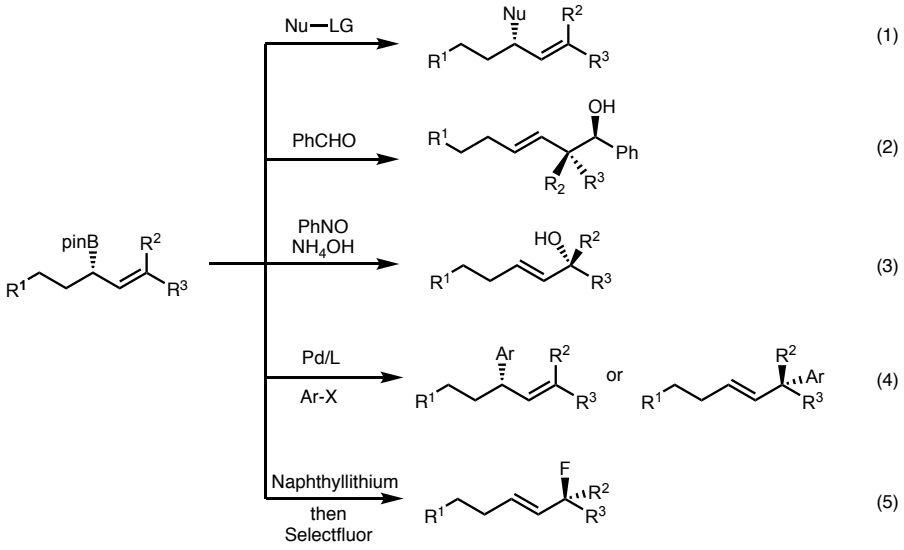
1.2.2 Catalytic, Enantioselective Synthesis of Allylic Boronates

The development of methods for the synthesis of nonracemic allylic boronates has received much recent attention in the field of synthetic organic chemistry.[24] This interest stems from the fact that, in addition to typical stereospecific transformations of organoboronates, allylic boronates have additional modes of reactivity. Allylic boronates can undergo a stereospecific functionalization with a variety of reagents to provide a broad range of reaction products (i.e. oxidation, amination, etc.) (Scheme, 1.14, eq. 1). In

[23] Shi, Y.; Hoveyda, A. H. *Angew. Chem. Int. Ed.* **2016**, *55*, 3455-3458
[24] Diner, C.; Szabo, K. J. *J. Am. Chem. Soc.* **2017**, *139,* 2-14

addition to direct functionalization, allylic boronates can undergo well-precedented allylation reactions with carbonyl compounds to produce two contiguous stereocenters (Scheme 1.14, eq. 2.). Related nitrosobenzene-mediated oxidation reaction with allylic transposition produces highly valuable tertiary allylic alcohols (Scheme 1.14, eq. 3).[25] Allylic boronates also have the propensity to undergo subsequent metal-catalyzed stereospecific cross-couplings, with either α- or γ- selectivity (Scheme 1.14, eq. 4).[26] Lastly, a newly developed method by Aggarwal and coworkers shows that activation of allylic boronates with a non-transferable aryl lithium can promote the stereospecific γ-selective electrophilic substitution with a wide variety of electrophiles (Scheme 1.14, eq. 5).[27]

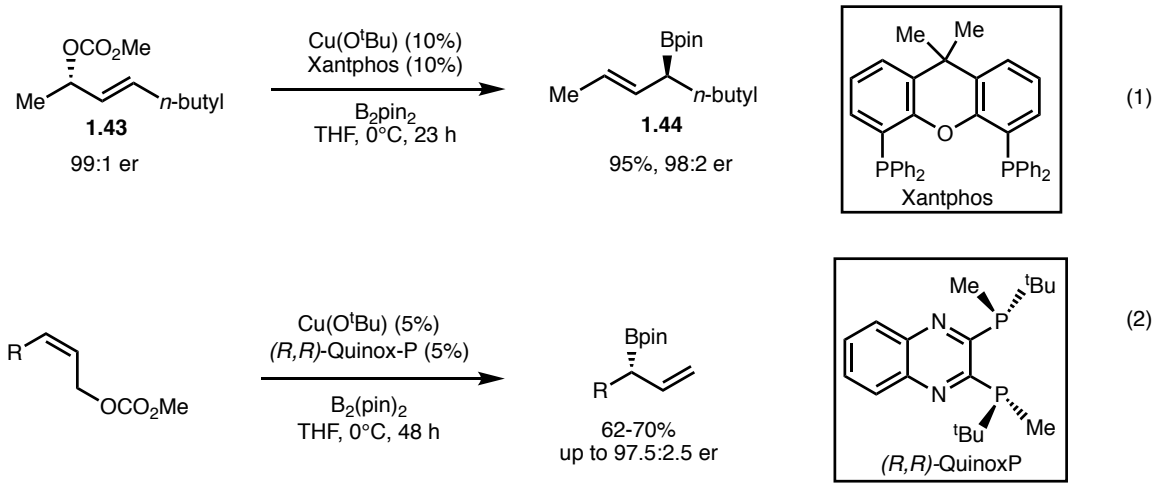
Scheme 1.14 Stereospecific Transformations of Nonracemic Allylic Boronates



[25] Kyne, R. E. Ryan, M. C.; Kliman, L. T.; Morken, J. P. *Org Lett.* **2010**, *12*, 3796-3799
[26] a) Chausset-Boissarie, L.; Ghozati, K.; LaBine, E.; Chen, J. L. – Y.; Aggarwal, V. K.; Crudden, C. M. *Chem. Eur. J.* **2013**, *19*, 17698-17701 b) Yang, Y.; Buchwald, S. L.; *J. Am. Chem. Soc.* **2013**, *135*, 10642-10645 c) Potter, B.; Edelstein, E. K.; Morken, J. P. *Org. Lett.* **2016**, *18*, 3286-3289
[27] Garcia-Ruiz, C; Chen, J. L. – Y.; Sandford, C.; Feeny, K; Lorenzo, P.; Berionni, G; Mayr, H; Aggarwal, V. K. *J. Am. Chem. Soc.* **2017**, *139*, 15324-15327

Pioneering studies done by Matteson and coworkers on the synthesis of nonracemic allylic boronates used chiral ligands on boron.[28] Work done by Sawamura, Ito and coworkers realized a catalytic synthesis of chiral allylic boronates. Employing a copper catalyst promoted a stereospecific borylation of nonracemic allylic carbonate **1.43** (Scheme 1.15, eq. 1).[29] The reaction was shown to be γ-selective and occurred with good yield and enantiospecificity. Sawamura and Ito expanded upon this work by using a chiral copper-QuinoxP catalyst to render the borylation of *(Z)*-allylic carbonates enantioselective.[30] This was the first example of this type of reaction, and it occurred with good yields and excellent enantioselectivity (Scheme 1.15, eq. 2).

Scheme 1.15 Synthesis of Nonracemic Organoboronates by Sawamura and Ito



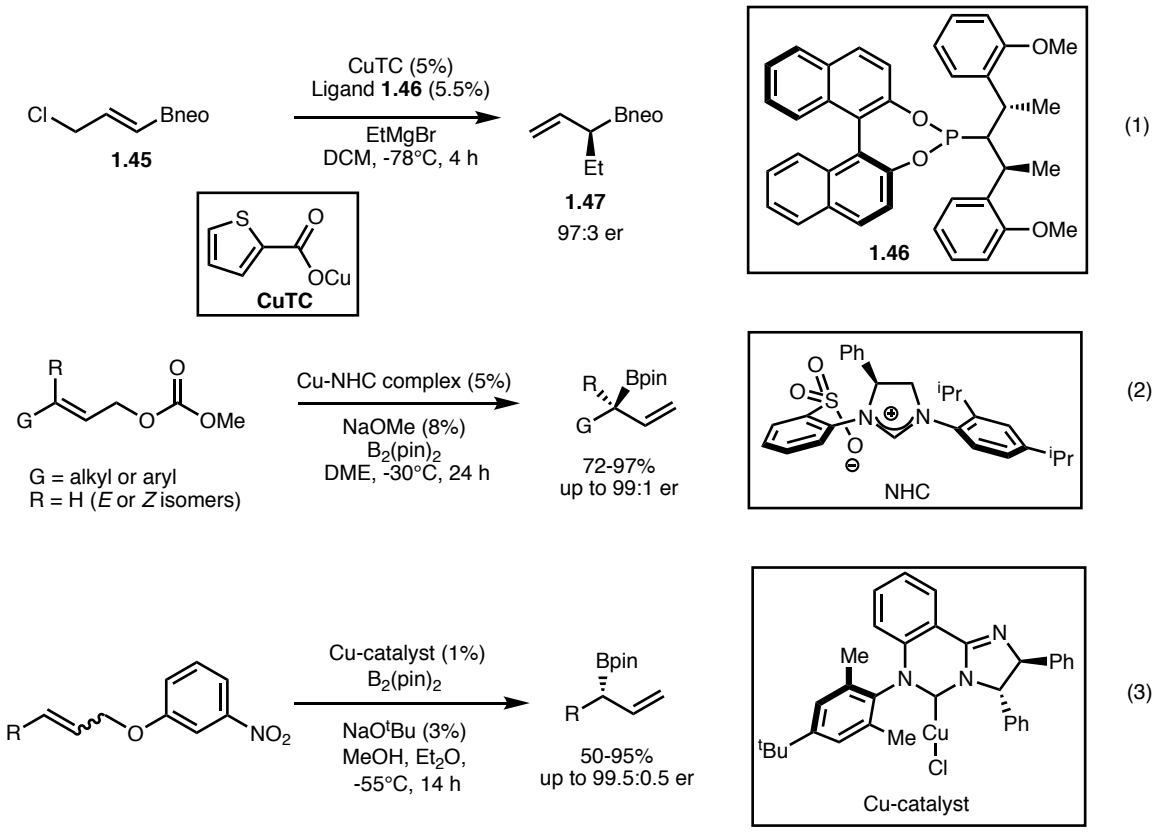
After this pioneering work on the catalytic synthesis of nonracemic allylic boronates through allylic substitution, Hall, Hoveyda and McQuade greatly expanded upon the strategy. Hall and coworkers showed that allylic chloride **1.45** could undergo substitution reactions with a copper-phosphoramidite complex with good

[28] Sadhu, K. M.; Hurst, G. D.; Kurosky, J. M.; Matteson, D. S.; *Organometallics* **1988**, *3*, 804-806
[29] Kawakami, C.; Ito, H.; Sawamura, M. *J. Am. Chem. Soc.* **2005**, *127*, 16034-16035
[30] Ito, S.; Sasaki, Y.; Matsuura, K.; Ito, H.; Sawamura, M. *J. Am. Chem. Soc.* **2007**, *129*, 14856-14857

enantioselectivity (Scheme 1.16, eq. 1).[31] A significant contribution to allylic substitution was done by Hoveyda and coworkers. Employing a Cu-NHC complex converted substituted allylic carbonates into tertiary allylic boronates in a stereoconvergent manner and with excellent enantioselectivity (Scheme 1.16, eq. 2).[32] This reaction was shown to be very broad and is a powerful method for the synthesis of nonracemic tertiary organoboronates. Lastly, McQuade and coworkers employed a Cu-NHC catalyst for a stereoconvergent synthesis of nonracemic allylic boronates from aryl allylic ether electrophiles (Scheme, 1.16, eq. 3).[33] The allylic substitution of aryl allylic ether electrophiles proceeded with good yields and excellent enantioselectivity.

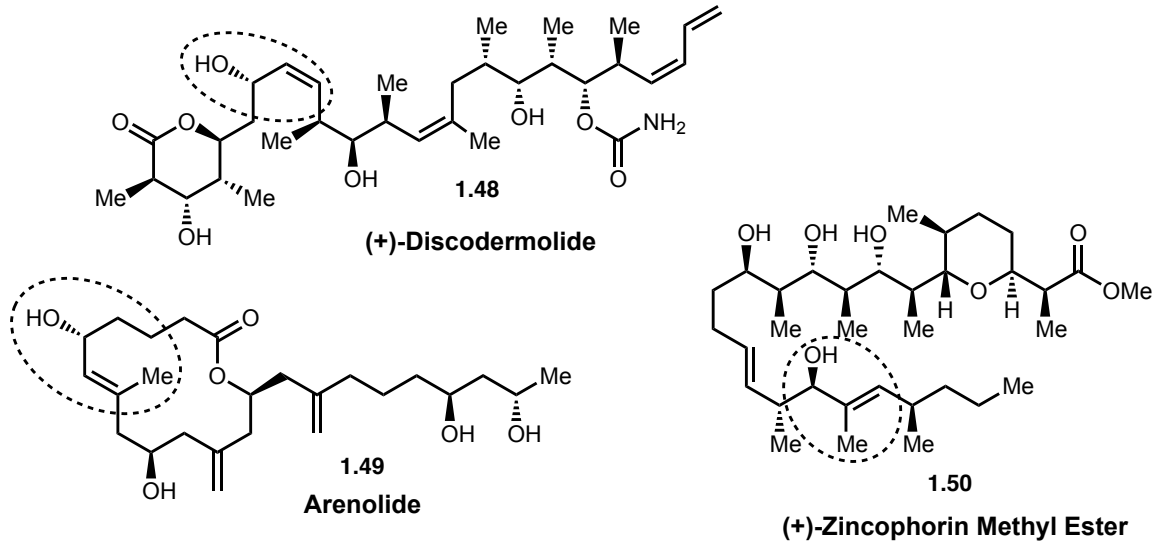
[31] Carosi, L. Hall, D. G. *Angew. Chem. Int. Ed.* **2007**, *46*, 5913-5915
[32] Guzman-Martinez, A.; Hoveyda, A. H. *J. Am. Chem. Soc.* **2010**, *132*, 10634-10637
[33] Park, J. K.; Lackey, H. H.; Ondrusek, B. A.; McQuade, D. T. *J. Am. Chem. Soc.* **2011**, *133*, 2410-2413

Scheme 1.16 Advances in the Synthesis of Nonracemic Allylic Boronates through Allylic Substitution



While all of these methods are efficient and selective for the synthesis of terminally substituted allylic boronates, the ability to synthesize more substituted allylic boronates in one catalytic step is highly desirable. Because many natural products contain more substituted allylic alcohol stereocenters (Figure 1.1), the ability to synthesize these types of allylic motifs in a catalytic fashion would be useful.

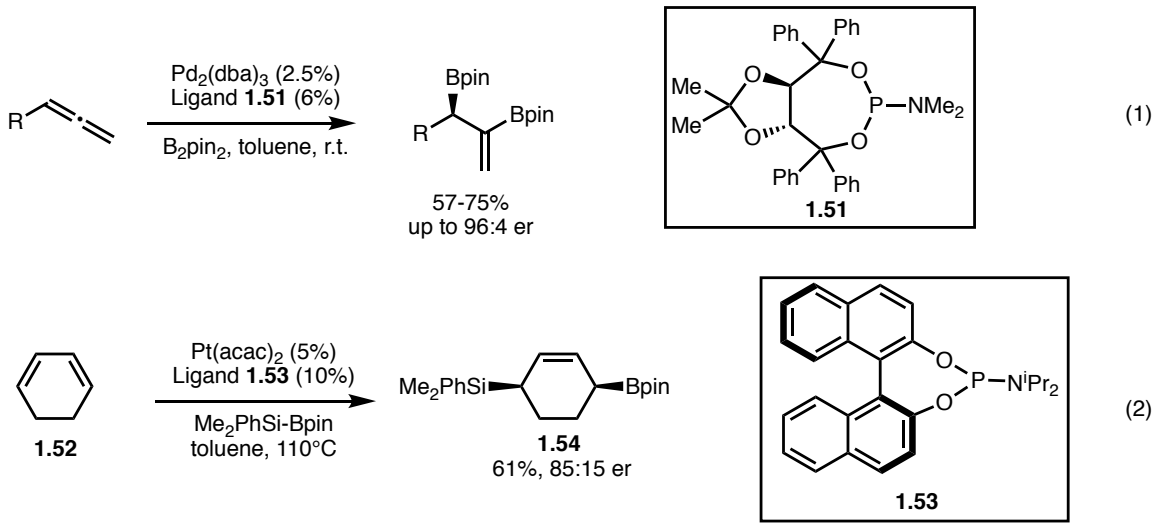
Figure 1.1 Natural Products Containing Substituted Allylic Alcohol Stereocenters



Early work in dimetallation reactions by Morken and Moberg began to address this area in catalysis. Morken and coworkers used a palladium-phosphoramidite catalyst to affect an enantioselective diboration of allenes (Scheme 1.17, eq. 1).[34] The allylic boronate products contain a useful alkenyl boron and were produced in high yields and enantioselectivity. These products exhibit versatile reactivity: they undergo stereospecific allylation of aldehydes and imines as well as diastereoselective hydroboration-cross-coupling sequences.[35] In addition to diboration, Moberg and coworkers developed an asymmetric silaboration of cyclohexadiene (**1.52**) that furnished cyclic nonracemic allylic boronate **1.54** with good enantioselectivity (Scheme 1.17, eq. 2).[36] It is worth noting that the scope of this reaction was limited to cyclohexadiene.

[34] a) Pelz, N. F.; Woodward, A. R.; Burks, H. E.; Sieber, J. D.; Morken, J. P. *J. Am. Chem. Soc.* **2004**, *126*, 16328-16239 b) Burks, H. E.; Liu, S.; Morken, J. P. *J. Am. Chem. Soc.* **2007**, *129*, 8766-8773
[35] a) Woodward, A. R.; Burks, H. E.; Chan, L. M.; Morken, J. P. *Org. Lett.* **2005**, *7*, 5505-5507 b) Seiber, J. D.; Morken. J. P. *J. Am. Chem. Soc.* **2006**, *128*, 74-75 c) Pelz, N. F.; Morken, J. P. *Org. Lett.* **2006**, *8*, 4557-4559
[36] Gerdin, M.; Moberg, C. *Adv. Synth. Catal.* **2005**, *347*, 749-753

Scheme 1.17 Catalytic Dimetallation Reactions for the Synthesis of Nonracemic Allylic Boronates

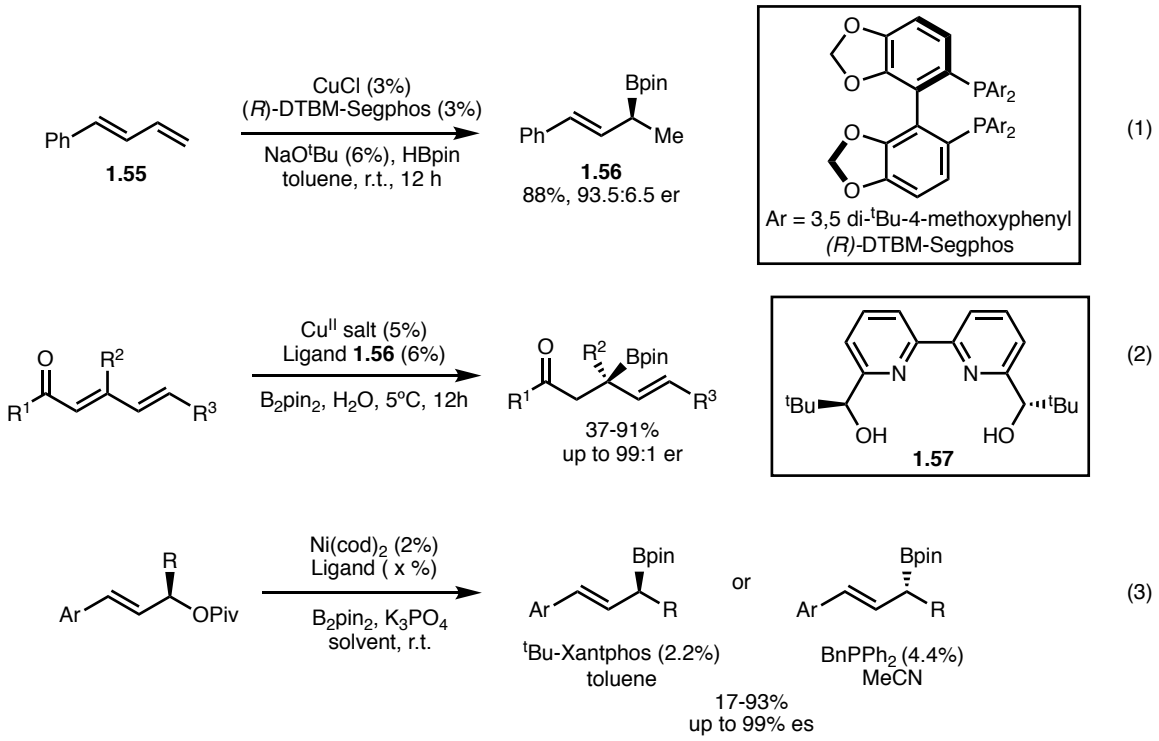


With regards to a general method for the synthesis of γ-substituted nonracemic allylic boronates through mono-borylation, the Yun group developed an asymmetric hydroboration using a copper-DTBM Segphos catalyst (Scheme 1.18, eq. 1).[37] One example of a diene hydroboration was demonstrated which produced nonracemic γ-aryl allylic boronate **1.56** in good yield and enantioselectivity. As a general route to γ-substituted allylic boronates, an elegant conjugate borylation of dienone and dienoesters was developed by Kobayashi and coworkers.[38] In water, a copper-diamine catalyst produced nonracemic allylic boronates in good yields and excellent enantioselectivity (Scheme 1.18, eq. 2). This work enabled the synthesis of tertiary nonracemic γ-substituted allylic boronates. More recently, Watson and coworkers employed a nickel catalyst to accomplish a stereodivergent borylation of nonracemic allylic carbonates (Scheme 1.18,

[37] Noh, D.; Yoon, S. K.; Won, J.; Lee, J. Y.; Yun, J. *Chem Asian. J.* **2011**, *6*, 1967-1969
[38] Kitanosono, T.; Xu, P.; Kobayashi, S. *Chem. Commun.* **2013**, *49,* 8184-8186

eq. 3).[39] Depending upon the ligand and solvent chosen affected both stereoretentive and stereoinvertive borylations with excellent enantiospecificities. Although similar to Sawamura's first report, this method demonstrates one of the most general approaches for the synthesis of nonracemic γ-aryl allylic boronates. Moreover, it occurs with readily available starting materials and is an efficient reaction with divergent stereochemical outcomes.

Scheme 1.18 Synthesis of γ-Substituted Nonracemic Allylic Boronates



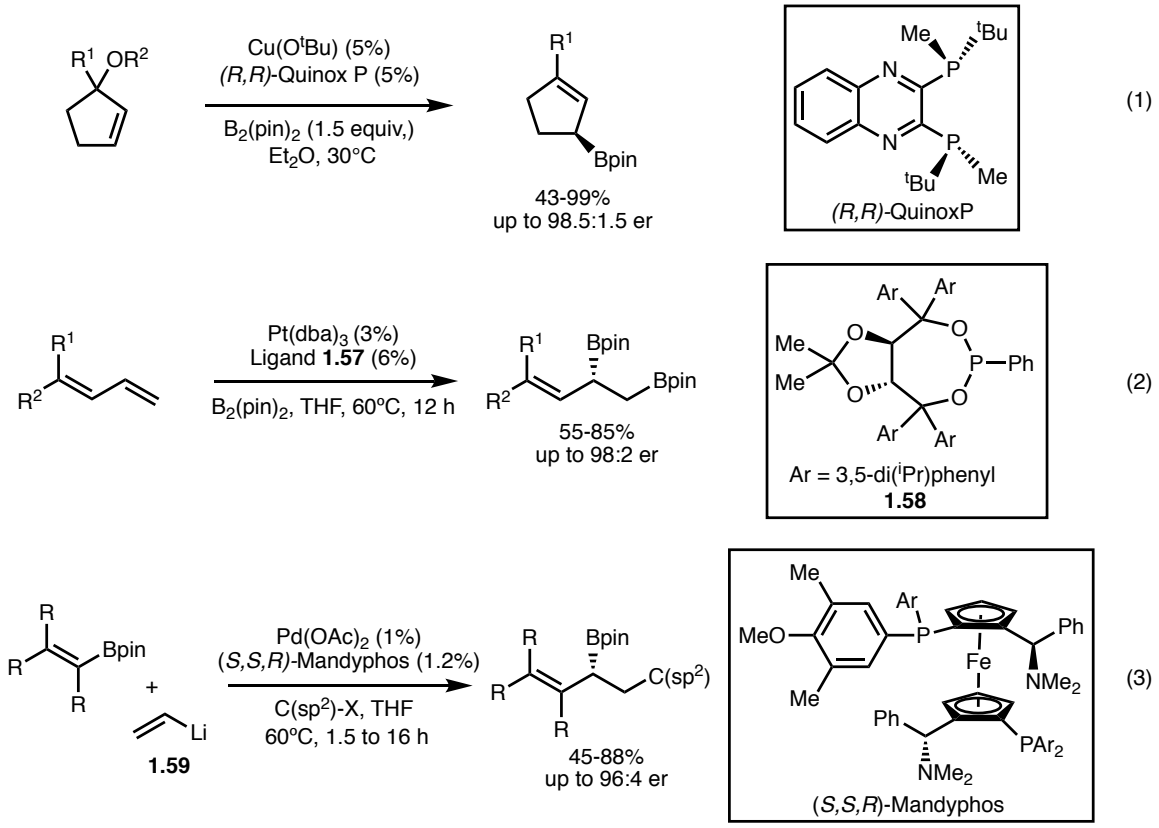
With regards to the synthesis of highly valuable nonracemic γ,γ-disubstituted allylic boronates, there a few catalytic methods developed. The first report was by Sawamura, Ito and coworkers on a copper-catalyzed enantioconvergent allylic borylation of cyclic ethers (Scheme 1.19, eq. 1).[40] An advantage of this method is that employing racemic allylic

[39] Zhou, Q.; Srinivas, H. D.; Zhang, S.; Watson, M. P. *J. Am. Chem. Soc.* **2016**, *138,* 11989-11995
[40] Kunii, S.; Sawamura, M.; Ito, H. *Nat. Chem.* **2010**, *2*, 972-976

ethers results in convergence to one product enantiomer with high stereoselectivity. However, the reaction is restricted to cyclic substrates. The synthesis of linear, nonracemic γ,γ-disubstituted allylic boronates was elusive until 2012. Morken and coworkers developed a platinum-catalyzed enantioselective 1,2-diboration of substituted 1,3-dienes (Scheme 1.19, eq. 2).[41] The diboration provided nonracemic allylic boronates with good yields and excellent enantioselectivity. The synthetic utility was demonstrated by the allylation of aldehydes and by tandem double allylation reactions to synthesize cyclic molecules that bear four contiguous stereocenters.[42] Lastly, an expansion of the conjunctive cross-coupling developed by Morken and coworkers[43] allowed for the synthesis of nonracemic γ,γ-disubstituted allylic boronates. Employing bis(alkenyl) boron "ate" complexes, the palladium-induced 1,2-migration of alkenyl groups provides nonracemic allylic boronate in good yields and enantioselectivity (Scheme 1.19, eq. 3).[44]

[41] Kliman, L. T.; Mlynarski, S. N.; Ferris, G. E.; Morken, J. P. *Angew. Chem. Int. Ed.* **2012**, *51*- 521-524
[42] Ferris, G. E.; Hong, K.; Roundtree, I. A.; Morken, J. P. *J. Am. Chem. Soc.* **2013**, *135*, 2501-2504
[43] Zhang, L.; Lovinger, G. L.; Edelstein, E. K.; Szymaniak, A. A.; Chierchia, M. P.; Morken, J. P. *Science* **2016**, *351*, 70-74
[44] Edelstein, E. K.; Namirembe, S.; Morken, J. P. *J. Am. Chem. Soc.* **2017**, *139*, 5027-5030

Scheme 1.19 Catalytic, Enantioselective Synthesis of γ,γ-Disubstituted Allylic Boronates



The catalytic synthesis of nonracemic allylic boronates has been elaborated. The immense synthetic utility of these reagents highlights the need for new methods to be developed. The next part of this chapter will explain the development of an enantioselective Suzuki-Miyaura cross-coupling for the synthesis of nonracemic γ,γ-disubstituted allylic boronates.

1.3 Development of an Enantiotopic-Group-Selective Suzuki-Miyaura Cross-Coupling of Geminal Bis(Boronates) with Alkenyl Electrophiles[45]

1.3.1 Synthesis of Geminal Bis(Boronates)

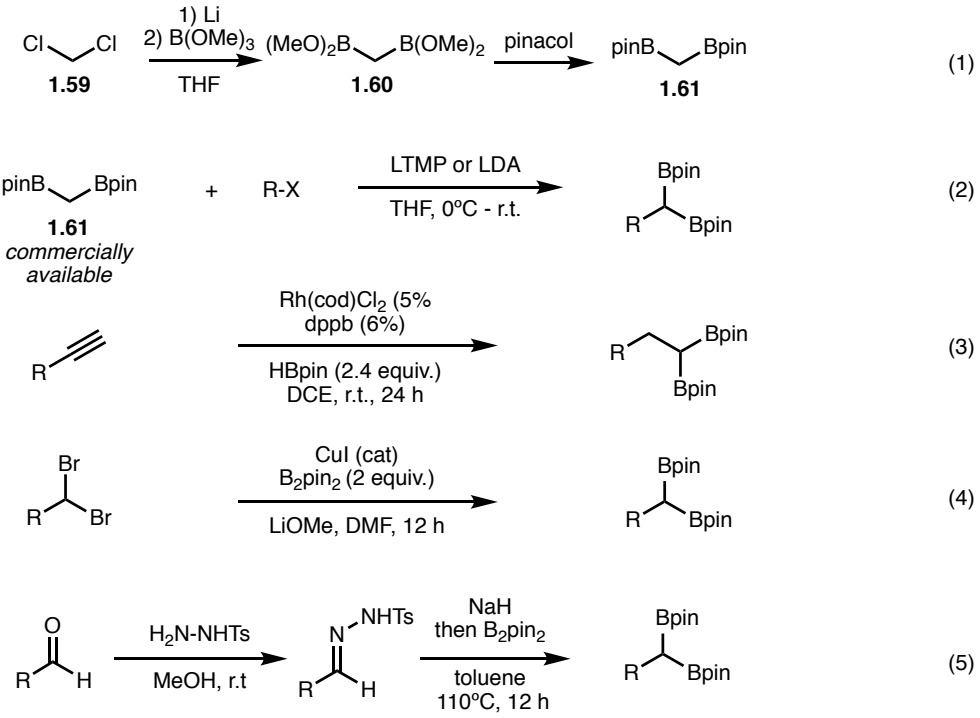
Geminal bis(boronates) are increasingly being incorporated in enantioselective, catalytic reactions. Consequently, the development of new catalytic methods for the synthesis of geminal bis(boronates) is highly desirable.[46] The first reported synthesis of geminal bis(boronates) by Matteson and coworkers, involves the double-lithiation of dichloromethane (Scheme 1.20, eq. 1). Subsequent addition to trimethyl borate and esterification with pinacol provides methylene bis(boronate) **1.61**.[47] The synthesis of substituted geminal bis(boronates) was realized by Matteson and coworkers through the deprotonation and alkylation of methylene bis(boronate) **1.61** (Scheme 1.20, eq. 2).[45b] A catalytic method for the synthesis of geminal bis(boronates) was elusive until the report by Endo, Shibata and coworkers in 2009. A rhodium catalyst and pinacolborane promoted the double hydroboration of alkynes (Scheme 1.20, eq. 3).[48] An advantage of this catalytic system using pinacolborane is the ideal atom-economy of the boron reagent. It will become apparent that newer catalytic methods generally use two equivalents of diboron reagents

[45] Potter, B.; Szymaniak, A. A.; Edelstein, E. K. *J. Am. Chem. Soc.* **2014**, *136*, 17918-17921
[46] For a review see: a) Shimizu, M.; Hiyama, T. *Proc. Jpn. Acad., Ser. B* **2008**, *84*, 75-85 b) Nallagona, R.; Padala, K.; Masarwa, A. *Org. Biomol. Chem.* **2018**, *16*, 1050-1064 c) Miralles, N.; Maza, R. J.: Fernandez, E. *Adv. Synth. Catal.* **2018**, *Early View*. DOI: 10.1002/adsc.201701390
[47] a) Castle, R. B.; Matteson, D. S. *J. Am. Chem. Soc.* **1968**, *90*, 2194 b) Moody, R. J.; Matteson, D. S. *Organometallics* **1982**, *1*, 20-28
[48] a) Shibata, T.; Endo, K. *Synlett* **2009**, *8,* 1331-1335 b) For the double hydroboration of alkynes with BCl_3 see: Soundararajan, R.; Matteson, D. S. *Organometallics* **1995**, *14*, 4157-4166

and thus suffer from inefficient boron-atom-economy. It is worth noting that for the double hydroboration of alkynes, newer methods with copper by Yun and coworkers, and cobalt by Huang and coworkers have been developed.[44] The cobalt-catalyzed hydroboration of alkenyl boronates has also been reported by Chirik and coworkers for the synthesis of geminal bis(boronates).[44] After the seminal catalytic report, the diborylation of dibromoalkanes was then developed independently by Ito and coworkers in addition to Steel, Marder, Liu and coworkers.[49] Employing different copper-catalysts and reaction conditions allowed for the synthesis of geminal bis(boronates) from readily available geminal dihaloalkanes (Scheme 1.20, eq. 4). It is worth noting that using modified conditions of the copper borylation, Morken and coworkers were able to scale the diborylation of dibromomethane.[15] Consequently, methylene bis(boronate) **1.61** is now commercially available. Lastly, Wang and coworkers developed a transition-metal free diborylation of *in situ* generated diazo compounds (Scheme 1.20, eq. 5).[50] The diazo diborylation allowed for the synthesis of geminal bis(boronates) in two simple steps from readily available aldehydes. It is worth noting that the diborylation of diazo compounds with a platinum-catalyst had been previously developed by Srebnik and coworkers.[51]

[49] a) Kubota, K.; Ito, H. *Org. Lett.* **2012**, *14*, 890-893 b) Steel, P. G.; Marder, T. B., Liu, L. *Angew. Chem. Int. Ed.* **2012**, *51,* 528-532
[50] Li, H.; Shangguan, X.; Zhang, Z; Huang, S.; Zhang, Y.; Wang, J. *Org. Lett.* **2014**, 16*,* 448-451
[51] Ali, H. A.; Goldberg, I.; Srebnik, M. *Organometallics* **2001**, *20,* 3962-3965

Scheme 1.20 Synthesis of Geminal Bis(Boronates)



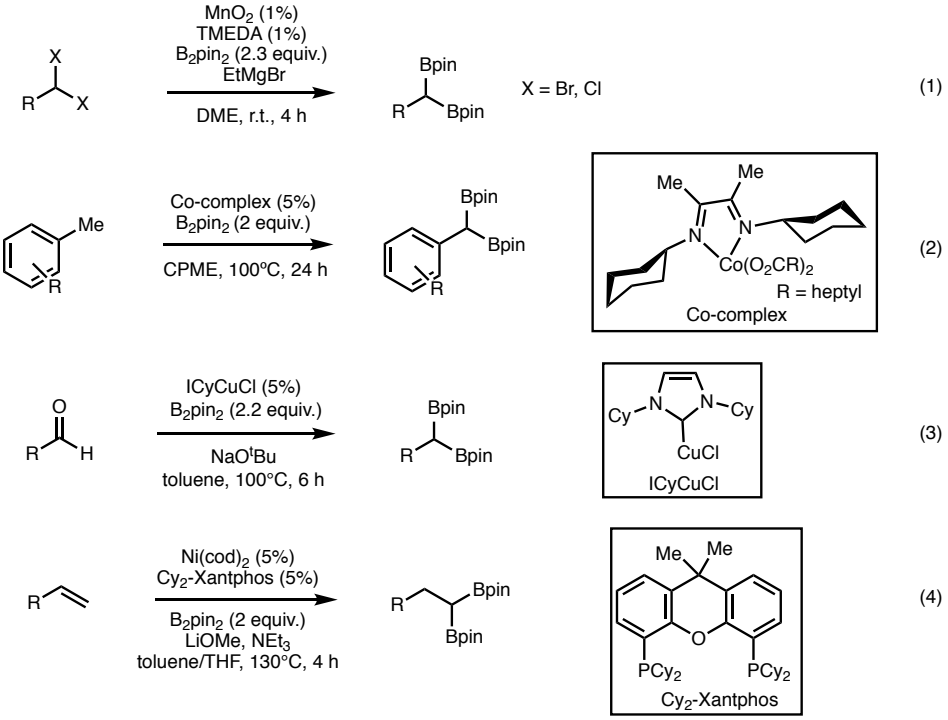
While the aforementioned reports represent efficient routes for the synthesis of geminal bis(boronates), newer methods are continuously being developed. The development of newer methods emphasizes the synthetic utility of geminal bis(boronates). As depicted in Scheme 1.21 (eq. 1), Cook and coworkers reported a diborylation of dibromo- or dichloroalkanes employing low-loadings of a manganese catalyst.[52] The manganese system demonstrates an expansion and improvement upon the aforementioned copper-catalyzed borylation of dibromoalkanes. Chirik and coworkers reported a benzylic C-H diborylation with a cobalt-bis(imine) catalyst for the synthesis of benzylic geminal bis(boronates) (Scheme 1.21, eq. 2).[53] The cobalt-catalyst represents an extension of Hartwig's iridium-catalyzed benzylic borylation employing an earth-abundant catalyst.[54]

[52] Atack, T. C.; Cook, S. P. *J. Am. Chem. Soc.* **2016**, 13*8,* 6139-6142
[53] a) Palmer, W. N.; Obligacion, J. V.; Pappas, I.; Chirik, P. J. *J. Am. Chem. Soc.* **2016**, 13*8,* 766-769 b) Palmer, W. N.; Zarate, C.; Chirik, P. J. *J. Am. Chem. Soc.* **2017**, 13*9,* 2589-2592
[54] Cho, S. W.; Hartwig, J. F. *Chem. Sci.* **2014**, *5*, 694-698

More recently, Lan, Liu and coworkers reported a copper-catalyzed direct diborylation of aldehydes through the intermediacy of an α-hydroxyboronate (Scheme 1.21, eq. 3).[55] The aldehyde diborylation is an improvement upon the diazo and dihaloalkane diborylations as it does not involve the intermediate formation of a hydrazone or dihaloalkane, respectively. Lastly, Fu and coworkers developed an efficient diborylation of alkenes with an earth-abundant nickel catalyst (Scheme 1.21, eq. 4).[56] The alkene diborylation highlights the ability synthesize geminal bis(boronates) from simple, feedstock chemicals. In addition to incorporating feedstock chemicals, the alkene diborylation might be viewed as an improvement upon the double hydroboration of alkynes. The continuous development of new, catalytic methods for the synthesis of geminal bis(boronates) underscores the importance of these reagents for synthetic organic chemistry.

[55]Wang, L.; Zhang, T.; Sun, W.; He, Z.; Xia, C.; Lan, Y.; Liu, C. *J. Am. Chem. Soc.* **2017**, *139*, 5257-5264
[56] Li, L.; Gong, T; Lu, X; Xiao, B.; Fu, Y. *Nature Communications* **2017**, *8*:345, 1

Scheme 1.21 New Methods for the Synthesis of Geminal Bis(Boronates)



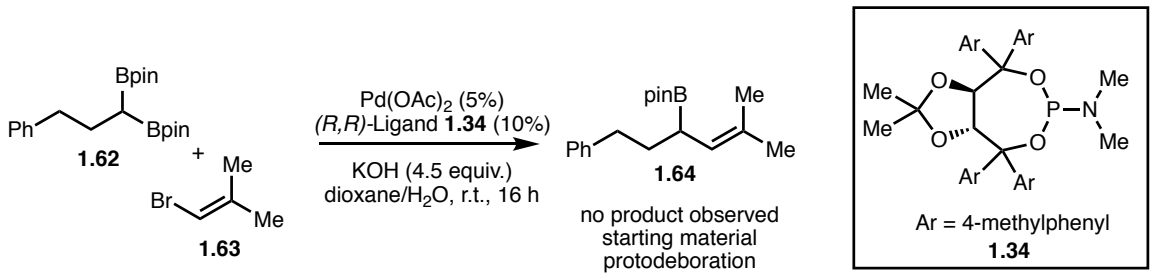
1.3.2 Reaction Discovery, Optimization, and Scope[45]

As described earlier, the cross-coupling of geminal bis(boronates) is an appealing approach for the development of an enantioselective Suzuki-Miyaura cross-coupling. The ability to expand an enantioselective cross-coupling to alkenyl electrophiles would provide nonracemic allylic boronates. The synthesis of nonracemic allylic boronates from readily prepared geminal bis(boronates) could be highly impactful.

To initiate studies on the cross-coupling of alkenyl electrophiles, 1-bromo-2-methyl propene (**1.63**) was incorporated in a catalytic cross-coupling of geminal bis(boronates) using the same conditions as with aryl electrophiles. As depicted in Scheme 1.22, the

reaction resulted in no formation of allylic boronate product **1.64**. Only recovered starting material or protodeboration of the starting material was observed.

Scheme 1.22 Initial Investigation of Reactivity for Geminal Bis(Boronate) Cross-Coupling with Alkenyl Electrophiles and Monodentate Ligands

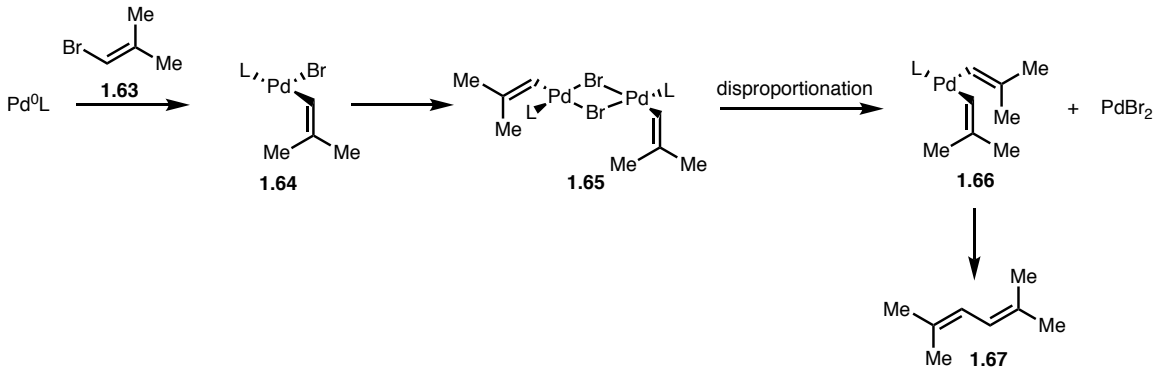


It was hypothesized that the lack of reaction might be due to employing a monodentate ligand resulting in an open coordination site on palladium. Combining an open coordination site with a less bulky alkenyl electrophile (c.f. an aryl electrophile) might allow for Lewis-basic adducts to coordinate to palladium and inhibit transmetallation. Lewis-basic adducts might include another equivalent of ligand, solvent, or pinacol from hydrolysis of the geminal bis(boronate).[57] In addition to Lewis-basic coordination, an open coordination site after oxidative addition with alkenyl electrophiles might allow for palladium disproportionation (Scheme 1.23).[58] The tendency of palladium disproportionation might be more facile with alkenyl electrophiles compared to aryl electrophiles due to the steric environment. After oxidation addition, an open coordination site might allow for **1.64** to dimerize and form adduct **1.65**. Subsequent disproportionation allows for the formation of bis(alkenyl) palladium species **1.66** and $PdBr_2$. Reductive

[57] Employing a deuterated pinacol derived geminal bis(boronate) in a competition experiment, it was shown in the aryl electrophile cross-coupling paper that the geminal bis(boronates) are readily hydrolyzed.
[58] Gushin, V. V.; Alper, H. *Organometallics* **1993**, *12*, 1890-1901

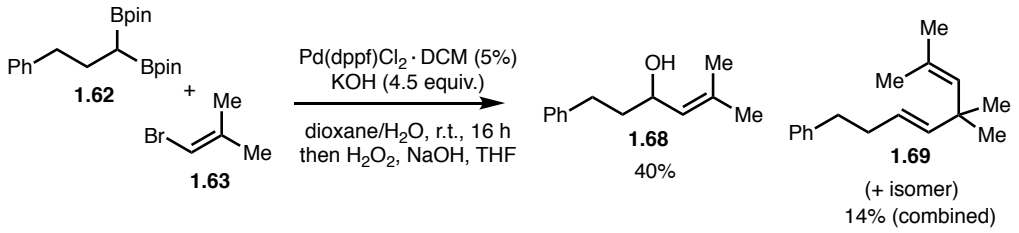
elimination then yields the alkenyl electrophile dimerization product **1.67** from the undesired reactivity.

Scheme 1.23 Disproportionation of Pd-II Oxidative Addition Adduct with Monodentate Ligands



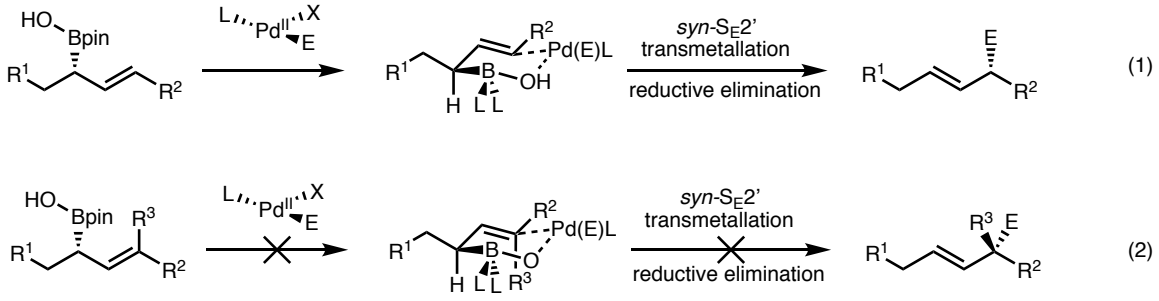
To address the hypothetical inhibition process, a bidentate ligand was employed with alkenyl electrophile **1.63**. A bidentate ligand would create a more hindered palladium (II) oxidative addition adduct without an open coordination site for binding an inhibitor. Upon conducting the reaction of **1.63** with palladium-1,1'-bis(diphenylphosphino)ferrocene, an appreciable amount of allylic alcohol **1.68** was observed after oxidation (Scheme 1.24). The production of the desired allylic alcohol supports the hypothesis for inhibition. However, diene product **1.69** (plus the α-coupling isomer) was also observed.

Scheme 1.24 Initial Investigation of Reactivity for Geminal Bis(Boronate) Cross-Coupling with Alkenyl Electrophiles



As described earlier, it has been shown that allylic boronates are highly reactive towards cross-coupling reactions.[26] This heightened reactivity arises upon activation of the organoboronate and binding to palladium, the intermediate can form a favorable six-membered transition state (Scheme 1.25, eq. 1). The formation of a six-membered transition state allows for delivery of a palladium to the γ-carbon by a *syn* S_E2' transmetallation. Subsequent reductive elimination then furnishes the γ-selective cross-coupling product. It was hypothesized that increasing the steric component of the alkenyl electrophile might be an approach to slow down the allylic boronate cross-coupling pathway (Scheme 1.25, eq. 2). Increasing the steric hindrance to an unfavorable six-membered transition state might suppress this pathway for the cross-coupling of the desired allylic boronate product.

Scheme 1.25 γ-Selective Cross-Coupling of Allylic Boronates

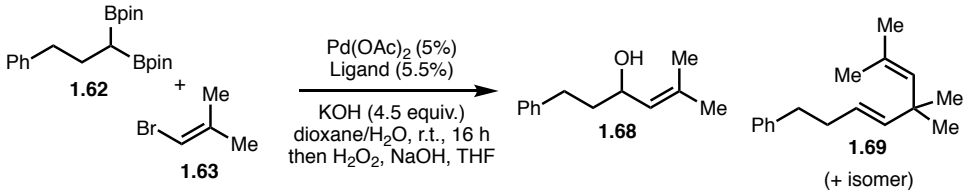


However, the presence of the diene product in Scheme 1.24 showed that even while using a relatively bulky alkenyl electrophile (c.f. *trans*-1-bromo-1-propene), over-coupling of the allylic boronate product is an issue. Consequently, a catalyst for the desired reaction needed to be developed that can not only suppress the product double-coupling pathway, but also render the cross-coupling enantioselective.

To address the issues of reactivity and enantioselectivity, a survey of chiral bidentate ligands was conducted. Employing bidentate ligands such as *(R,R)*-Me-BPE

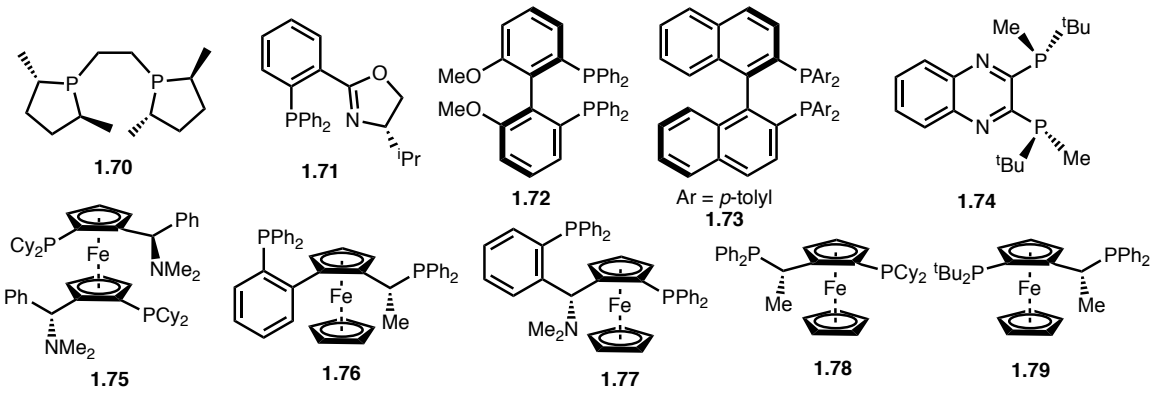
(**1.70**) and (*S*)-^{i}Pr-Phox (**1.71**) furnished no allylic alcohol product **1.68** in the cross-coupling reaction (Table 1.1, entries 1-2). It was not until *(R)*-MeO-Biphep (**1.72**) was used that product **1.65** was observed, although it was formed in moderate enantioselectivity (Table 1.1, entry 3). In addition to selectivity, ligand **1.72** suffered from low chemoselectivity as increased amount of diene products were observed. *(R)-p*-tol-BINAP (**1.73**) produced low levels of reactivity (Table 1.1, entry 4), while *(R,R)*-QuinoxP (**1.74**) produced low chemoselectivity in modest enantioselectivity (Table 1.1, entry 5). Surveying ferrocene-based chiral bidentate ligands, *(S,S,R)*-Mandyphos (**1.75**) gave a non-reactive catalyst (Table 1.1, entry 6). (*R,R*)-WalPhos (**1.76**) afforded good reactivity, although low chemoselectivity and very low enantioselectivity (Table 1.1, entry 7). (*R,R)*-TaniaPhos (**1.77**) produced low reactivity and moderate enantioselectivity (Table 1.1, entry 8). It was not until investigating the ferrocene-based Josiphos ligand class where promising results were observed. Employing Josiphos ligand **1.78** afforded good reactivity and chemoselectivity, with moderate enantioselectivity (Table 1.1, entry 9). Simply increasing the steric component of the ferrocenyl phosphine substituents from dicyclohexyl to di-*tert*-butyl (**1.79**) resulted in an increase in reactivity and chemoselectivity (Table 1.1, entries 9 vs. 10). In addition to good chemoselectivity, the enantioselectivity was also greatly increased to a 90:10 ratio (Table 1.1, entry 10).

Table 1.1 Initial Ligand Investigation of Chiral Bidentate Ligands



Entry	*Ligand*	*Yield **1.68** (%)*[a]	*Yield **1.69** (%)*[a]	*e.r.*[b]
1	**1.70**	< 5	< 5	n.d.
2	**1.71**	< 5	< 5	n.d.
3	**1.72**	10	30	27:73
4	**1.73**	< 10	< 5	n.d.
5	**1.74**	10	20	30:70
6	**1.75**	< 5	< 5	n.d.
7	**1.76**	22	22	52:48
8	**1.77**	10	< 5	72:28
9	**1.78**	47	13	65:35
10	**1.79**	60	< 5	10:90

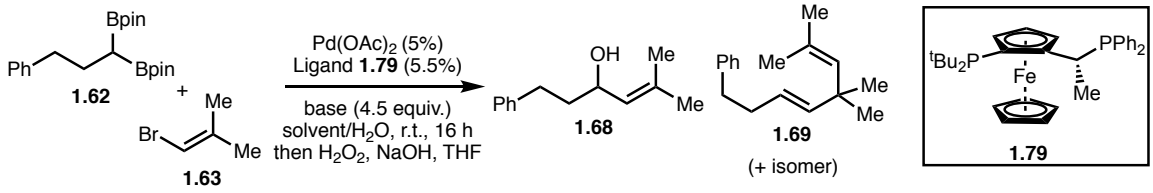
[a]Yield determined by ^{1}H-NMR with respect to 1,1,2,2-tetrachloroethane as an internal standard.
[b]Enantiomer ratios determined using chiral SFC analysis of the allylic alcohol **1.68**



Having found a relatively efficient and selective ligand (**1.79**) that is commercially available, an exhaustive survey of conditions was undertaken to further increase reactivity and enantioselectivity. As depicted in Table 1.2, the impact of the solvent and base was analyzed. Employing different ethereal solvents such as THF produced similar levels of reactivity and enantioselectivity as 1,4-dioxane (Table 1.2, entry 1 vs. 2). The less polar

ethereal solvent MTBE completely inhibited the reaction likely due to insolubility of the bis(boron) "ate" complex (Table 1.2, entry 3). Switching to more polar solvents like DMF and MeCN resulted in either lower reactivity or no reactivity (Table 1.2, entries 4-5). Changing the base to NaOH showed an increase in reactivity but slight decrease in enantioselectivity (Table 1.2, entry 6). Further analysis of the base with CsOH or LiOH produced lower reactivity but similar enantioselectivity as KOH (Table 1.2, entries 7-8).

Table 1.2 Solvent and Base Surveying for Cross-Coupling of Geminal Bis(Boronates) with Alkenyl Bromide and Ligand 1.79



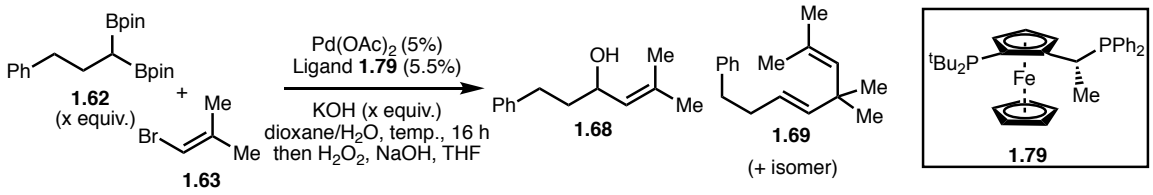
Entry	*Solvent*	*Base*	*Yield **1.68** (%)*[a]	*Yield **1.69** (%)*[a]	*e.r.*[b]
1	**1,4-dioxane**	**KOH**	60	< 5	91:9
2	**THF**	**KOH**	40	< 5	91:9
3	**MTBE**	**KOH**	< 5	< 5	n.d.
4	**DMF**	**KOH**	34	< 5	88:12
5	**MeCN**	**KOH**	< 5	< 5	n.d.
6	**1,4-dioxane**	**NaOH**	80	< 5	88:12
7	**1,4-dioxane**	**CsOH**	50	< 5	90:10
8	**1,4-dioxane**	**LiOH**	45	< 5	91:9

[a]Yield determined by ^{1}H-NMR with respect to 1,1,2,2-tetrachloroethane as an internal standard.
[b]Enantiomer ratios determined using chiral SFC analysis of the allylic alcohol **1.68**

With 1,4-dioxane as the solvent and KOH as the optimal base, further perturbations of the reaction conditions were conducted. As depicted in Table 1.3, adjusting the amount of geminal bis(boronate) produced similar results (Table 1.3, entries 1-4). Varying the amounts of base resulted in diminished reactivity and enantioselectivity (Table 1.3, entry 1 vs. entries 5-6). Lastly, decreasing the reaction temperatures resulted in an increase in

enantioselectivity with slightly diminished efficiency (Table 1.3, entry 1 vs. entries 7-9). At this point, it was considered that higher enantioselectivity at lower temperatures could be combined with a more efficient catalyst for an optimal reaction.

Table 1.3 Varying Substrate Equivalents and Temperature of the Cross-Coupling of Geminal Bis(Boronates) with Alkenyl Bromide and Ligand 1.79



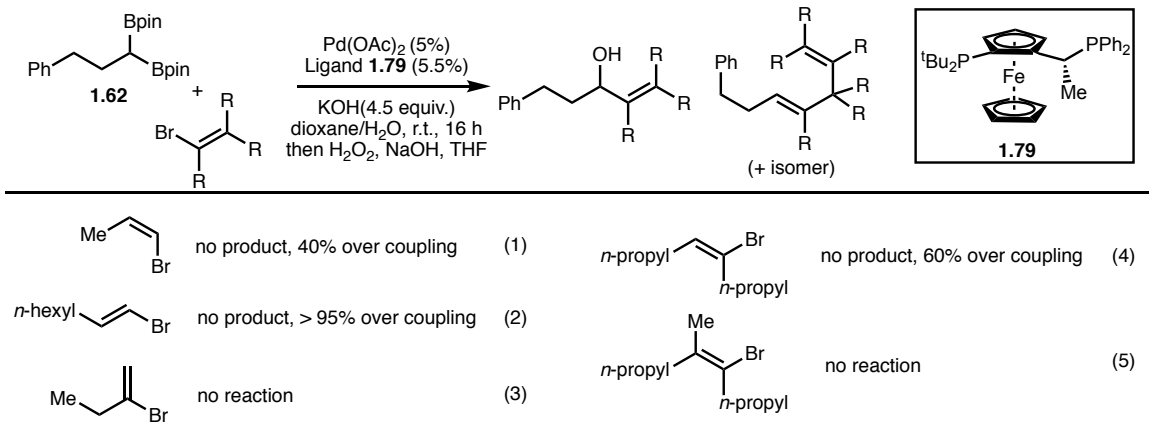
Entry	*Diboron Equiv.*	*Base Equiv.*	*Temperature (°C)*	*Yield **1.68** (%)*[a]	*Yield **1.69** (%)*[a]	*e.r.*[b]
1	**1**	**4.5**	**r.t.**	58	< 5	91:9
2	**1.1**	**4.5**	**r.t.**	45	< 5	91:9
3	**1.5**	**4.5**	**r.t.**	46	< 5	91:9
4	**2**	**4.5**	**r.t.**	58	< 5	91:9
5	**1**	**3**	**r.t.**	33	< 5	88:12
6	**1**	**9**	**r.t.**	42	< 5	88:12
7	**1**	**4.5**	**5**	43	< 5	94:6
8	**1**	**4.5**	**10**	49	< 5	93:7
9	**1**	**4.5**	**15**	62	< 5	92:8

[a]Yield determined by ^{1}H-NMR with respect to 1,1,2,2-tetrachloroethane as an internal standard.
[b]Enantiomer ratios determined using chiral SFC analysis of the allylic alcohol **1.68**

Before undertaking a ligand investigation, altering the alkenyl electrophiles with optimal ligand **1.79** was tested. As depicted in Scheme 1.26, either *cis*- or *trans*-substituted alkenyl bromides did not afford the desired product, but only the over-coupled products (Scheme 1.26, eq. 1-2). 1,1-Disubstituted alkenyl bromides were unreactive to the depicted reaction conditions (Scheme 1.26, eq. 3). More substituted alkenyl bromides (Scheme 1.26, eq. 4-5) either suffered from poor chemoselectivity or no reactivity. From the survey

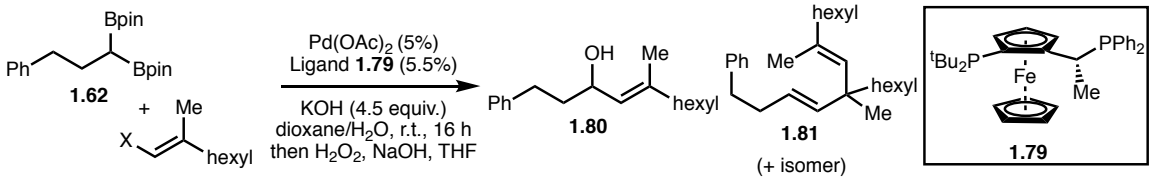
of electrophile substitution, it was decided that the original choice of electrophile was optimal.

Scheme 1.26 Analysis of Alkenyl Electrophiles for the Cross-Coupling of Geminal Bis(Boronates) with Alkenyl Bromide and Ligand 1.79



In addition to substitution, the nature of the electrophile was also investigated as depicted in Table 1.4. Compared to alkenyl bromides, alkenyl chlorides produced lower reactivity but comparable enantioselectivity (Table 1.4, entries 1 vs. 2). Alkenyl iodides reacted with much worse chemoselectivity and, surprisingly, enantioselectivity. Similar enantioselectivity for the alkenyl chloride and bromide suggests the convergence to a palladium (II) hydroxide intermediate for transmetallation. However, lower enantioselectivity for the alkenyl iodide substrate might be a result of competitive transmetallation of a palladium (II) iodide intermediate.

Table 1.4 Electrophile Survey for the Cross-Coupling of Geminal Bis(Boronates) with Alkenyl Bromide and Ligand 1.79



Entry	*X =*	*Yield **1.80** (%)*[a]	*Yield **1.81** (%)*[a]	*e.r.*[b]
1	**Br**	40	< 5%	88:12
2	**Cl**	23	< 5%	86:14
3	**I**	16	35	73:27

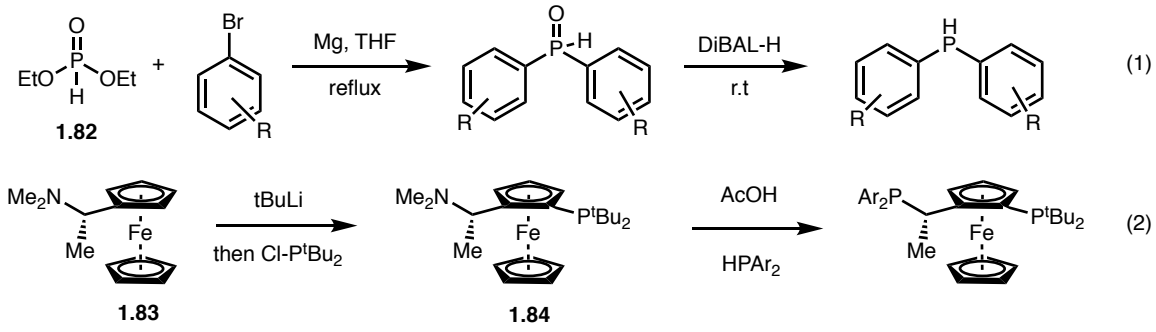
[a]Yield determined by ^{1}H-NMR with respect to 1,1,2,2-tetrachloroethane as an internal standard.
[b]Enantiomer ratios determined using chiral SFC analysis of the allylic alcohol **1.80**

While surveying reaction conditions revealed that lower temperature increases enantioselectivity, the reaction efficiency needed to be addressed. To address this, the effect of the ligand was investigated. As previously elaborated, the di-*tert*-butylphosphino substituent on the ferrocene was essential for chemoselectivity and enantioselectivity (Table 1.1, entry 9 vs. 10). Taking this into account, the effect of altering the electronic and steric properties of the diarylphosphino group were of interest. It is worth noting that ligands with dialkyl substituents (i.e -P^{t}Bu$_2$, -PCy$_2$) produced inferior results as compared to the diphenylphosphino substituent. To begin ligand synthesis, efficient routes developed by Busacca, Senanayake and coworkers were utilized for the synthesis of secondary phosphines (Scheme 1.27, eq. 1).[59] Simple Grignard additions to diethyl phosphite (**1.82**), followed by DiBAL-H reduction afforded secondary aryl phosphines with good yields. With phosphine in hand, the subsequent synthesis employed commercially available Ugi's

[59] Busacca, C. A.; Senanayake, C. H. *et al. Org. Lett.* **2005**, *7*, 4277-4280

amine (**1.83**), or readily prepared and resolved through chiral recrystallization.[60] Directed lithiation of Ugi's amine and trapping with chlorodi-*tert*-butylphosphine produced amino-phosphinoferrocene **1.84** on large scale (Scheme 1.27, eq. 2).[61] Treatment with acetic acid and the external secondary phosphine resulted in substitution of the phosphine for the desired Josiphos ligand.

Scheme 1.27 Synthesis of Secondary Phosphines and Josiphos Ligands

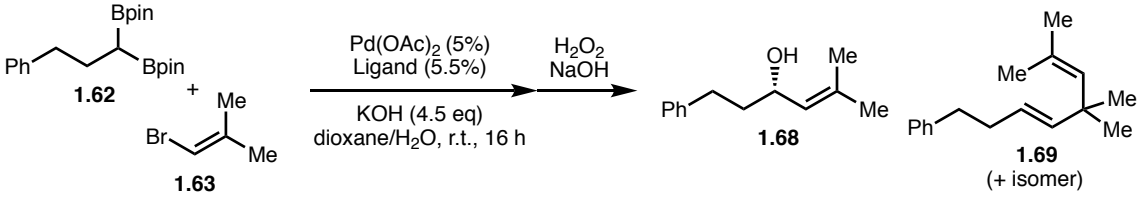


With an efficient procedure for the synthesis of Josiphos ligands adapted, a variety of ligands were subjected to the standard reaction conditions. Increasing the steric bulk of the phosphine at different positions of the benzene ring resulted in a less chemoselective and enantioselective reactions (Table 1.5, entries 1-4). Even increasing the steric bulk at the remote *para* position (**1.85**) resulted in a large reduction in efficiency and enantioselectivity (Table 1.5, entry 2). The same trend was observed with steric bulk at the *ortho* and *meta* positions (Table 1.5, entries 3-4). From the observed sensitivity of the reaction to the steric environment of the benzene ring, it was hypothesized a smaller phosphine aryl substituent might be more efficient. Ligand **1.88** was synthesized incorporating a 2-furylphosphino substituent and employed in the reaction. Supporting the hypothesis that incorporating a smaller aryl substituent, the reaction was more efficient but

[60] Gokel, G. W.; Ugi, I. K. *J. Chem. Ed.* **1972**, *49*, 294-296
[61] Mejia, E.; Aardoom, R.; Togni, A. *Eur. J. Inorg. Chem.* **2012**, *31*, 5021-5032

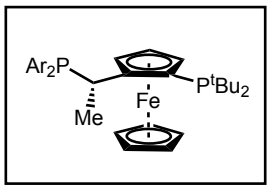
less selective than diphenylphosphino (Table 1.5, entries 1 vs. 5). With the steric effect investigated, the electronic properties of the diarylphosphino group were modified. More electron-rich *p*-methoxyphenyl ligand **1.89** suffered from very poor efficiency and a slight decrease in enantioselectivity (Table 1.5, entry 6). The lower reactivity might be a consequence of a more electron rich palladium slowing down the proposed transmetallation. Altering the ligand to include inductively-withdrawing substituents (*p*-fluorophenyl substituted ligands **1.90**, **1.91**) reestablished efficiency and enantioselectivity. (Table 1.5, entries 7-8). Ligand **1.91** was extremely efficient but slightly less selective, potentially due to small changes in the *meta* substitution steric parameters (Table 1.5, entries 4 vs. 8). It was hypothesized that a less sterically demanding but electron-withdrawing diarylphosphino ligand would be optimal for the reaction. To test these two features, *p*-trifluoromethylphenyl ligand **1.92** was synthesized and analyzed in the reaction conditions. Ligand **1.92** afforded the desired product in excellent efficiency and maintained high enantioselectivity (Table 1.5, entry 9).

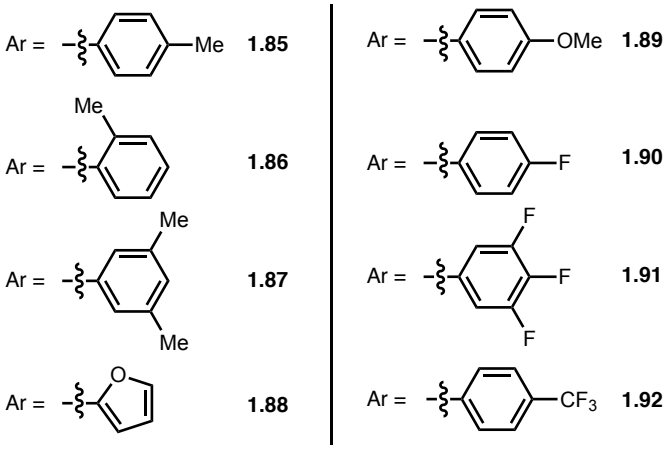
Table 1.5 Ligand Investigation for the Cross-Coupling of Geminal Bis(Boronates) with Alkenyl Bromide



Entry	*Ligand*	*Yield **1.68** (%)*[a]	*Yield **1.69** (%)*[a]	*e.r.*[b]
1	**1.79**	60	< 5	90:10
2	**1.85**	22	< 5	82:18
3	**1.86**	14	< 5	63:37
4	**1.87**	29	22	52:48
5	**1.88**	85	< 5	76:24
6	**1.89**	16	10	85:15
7	**1.90**	44	< 5	90:10
8	**1.91**	97	< 5	85:15
9	**1.92**	95	< 5	91:9

[a]Yield determined by ^{1}H-NMR with respect to 1,1,2,2-tetrachloroethane as an internal standard.
[b]Enantiomer ratios determined using chiral SFC analysis of the allylic alcohol **1.68**

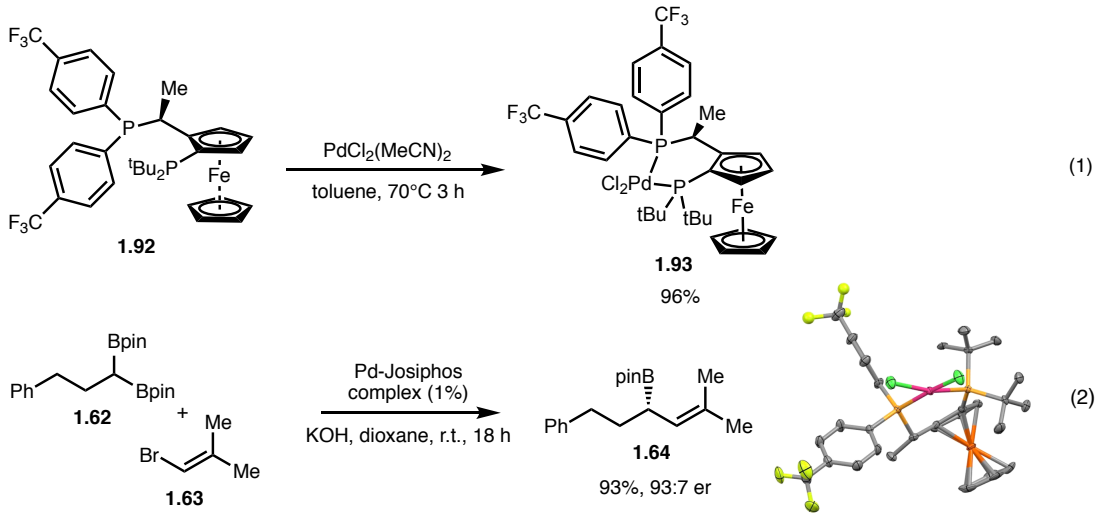




Having discovered a ligand capable of high reactivity and enantioselectivity, a brief reanalysis of conditions was conducted. However, no increase in enantioselectivity was observed at lower temperatures or by varying the reaction conditions. To maximize the efficiency of the reaction set-up, a palladium dichloride-Josiphos complex was synthesized

(Scheme 1.28, eq. 1). Using Josiphos·$PdCl_2$ complex in the reaction allowed the reaction to be run with 1% catalyst loading without the aid of a glove-box (Scheme 1.28, eq. 2). The Josiphos·$PdCl_2$ complex at reduced loadings provided a slight boost in enantioselectivity with excellent efficiency

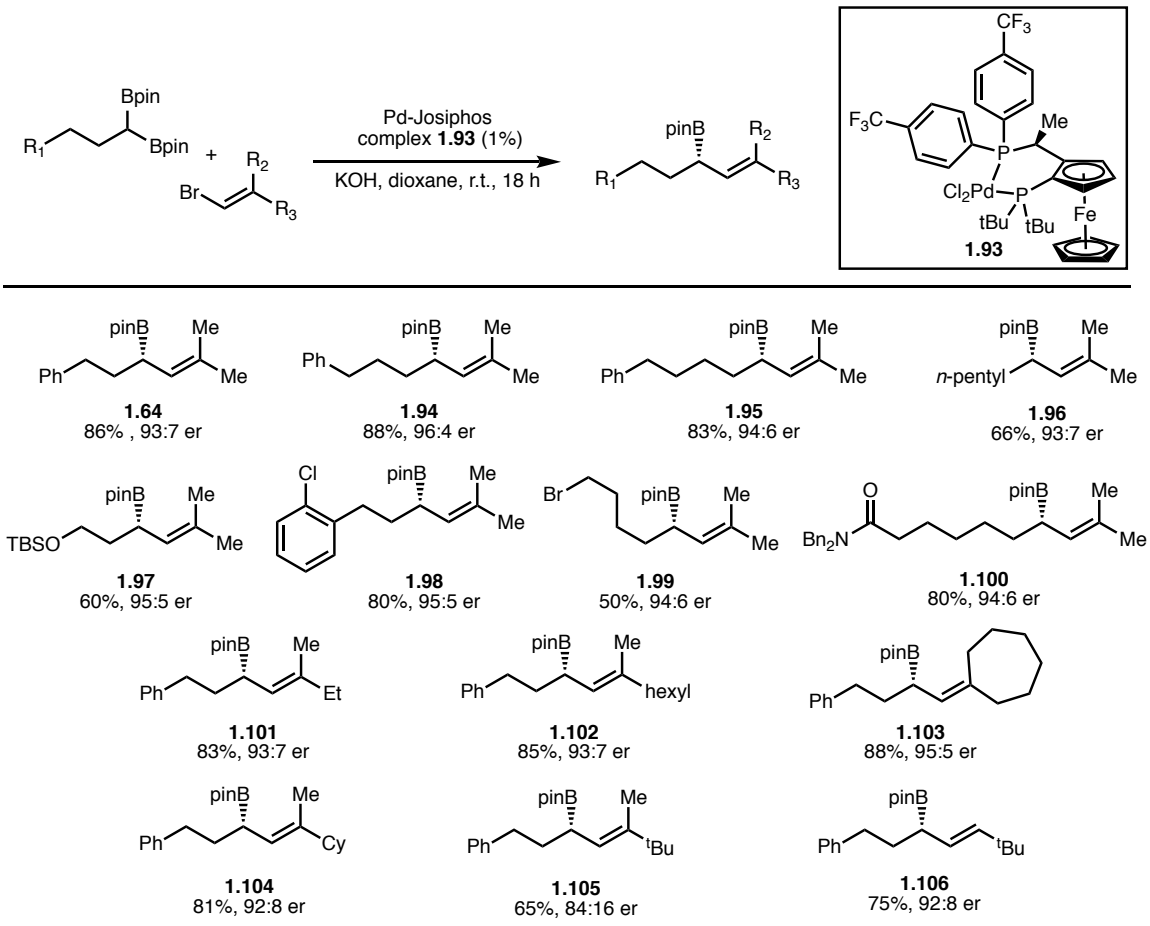
Scheme 1.28 Synthesis of Josiphos·$PdCl_2$ Complex and Incorporation into the Cross-Coupling of Geminal Bis(Boronates) with Alkenyl Bromide



Having developed an efficient and enantioselective catalyst for the cross-coupling of geminal bis(boronates) with alkenyl bromides, the generality of the reaction was explored. Substrates with a variety of alkyl substituents on the geminal bis(boronate) substrate (**1.64**, **1.94**, **1.95**, **1.96**) reacted in good yields and high enantioselectivity. A variety of functional groups such as protected alcohols (**1.97**), aryl chlorides (**1.98**), alkyl bromides (**1.99**) and amides (**1.100**) were tolerated under the reaction conditions. In regards to the scope of the alkenyl electrophile, a variety of unsymmetrical β,β-disubstituted alkenyl bromides (**1.101**, **1.102**) reacted with similar efficiency and selectivity in the reaction. Cyclic alkenyl bromides (**1.103**) also produced excellent results.

Increasing the steric bulk of the unsymmetrical β,β-disubstituted alkenyl bromides (**1.104**, **1.105**) resulted in slightly diminished enantioselectivity. Employing *trans*-disubstituted alkenyl bromides (**1.106**) required a bulky *tert*-butyl group to suppress over-coupling of the allylic boronate product. The cross-coupling proceeded in good efficiency and enantioselectivity.

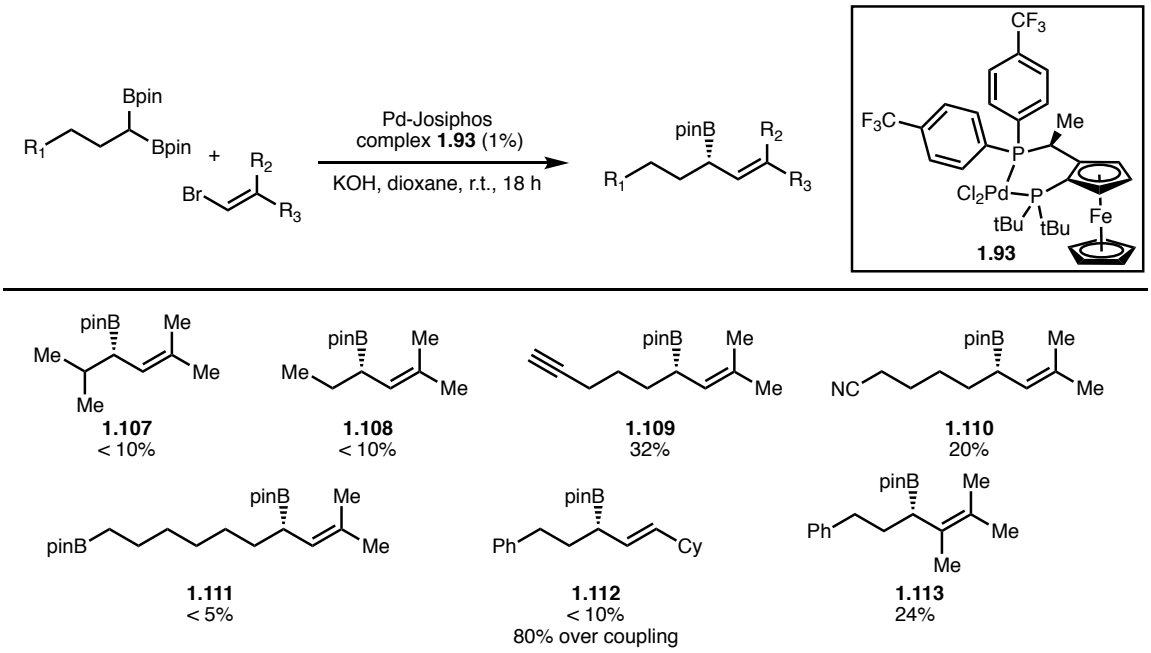
Table 1.6 Substrate Scope for the Enantiotopic-Group Selective Cross-Coupling of Geminal Bis(Boronates) with Alkenyl Electrophiles



1.5 equiv. diboron reagent, 4.5 equiv. KOH. Yields reported are isolated yields that are the average of two experiments. Enantiomer ratios are the average of two experiments and determined using chiral SFC analylsis of oxidized allylic alcohol, or the alcohol as a result of benzaldehyde allylation. (See experimental section)

In regards to challenging substrates for the cross-coupling, β-branching of the geminal bis(boronate) (**1.107**) resulted in sluggish reactivity (Table 1.7). Short-chained alkyl groups (**1.108**) also suffered from poor reactivity. The low reactivity might be due to insolubility of the bis(boron) "ate" complexes as the reaction forms a gel. Subsequent studies conducted in our laboratory[24c] found that increasing the catalyst loading could overcome the reactivity problem of substrates **1.107** and **1.108**. Any types of coordinating π-bonds (**1.109**, **1.110**) resulted in diminished, efficiency potentially due to binding of palladium and inhibiting catalysis. Distal alkyl boronates (**1.111**) also resulted in inhibition of catalysis. As alluded to, having a less bulky *trans*-disubstituted alkenyl bromide (**1.112**) resulted in predominant over coupling of the allylic boronate. Lastly, under these optimized reaction conditions, more substituted alkenyl bromides (**1.113**) did result in product formation but with low efficiency.

Table 1.7 Challenging Substrates for the Enantiotopic-Group Selective Cross-Coupling of Geminal Bis(Boronates) with Alkenyl Electrophiles



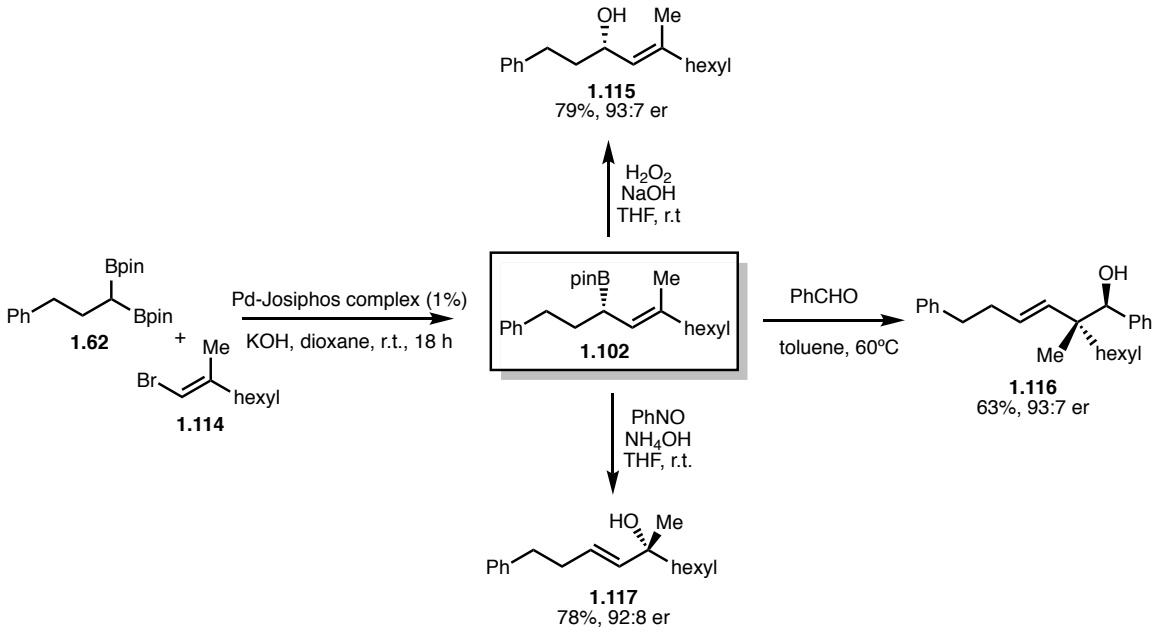
Yield determined by ^{1}H-NMR with respect to 1,1,2,2-tetrachloroethane as an internal standard.

1.3.3 Synthetic Utility and Mechanistic Considerations[45]

After exploring the scope of the palladium-catalyzed cross-coupling of geminal bis(boronates) with alkenyl electrophiles, the synthetic utility of the allylic boronate products was investigated. As depicted in Scheme 1.29, oxidation of the allylic boronate in a one-pot process afforded nonracemic γ,γ-disubstituted allylic alcohol **1.115** in good yield and enantioselectivity. Treatment of the nonracemic allylic boronate product with benzaldehyde and heating promoted a stereospecific allylation reaction to afford **1.116** with complete stereospecificity. The synthetic utility of nonracemic γ,γ-disubstituted allylic boronates was highlighted as the allylation reaction produced two contiguous

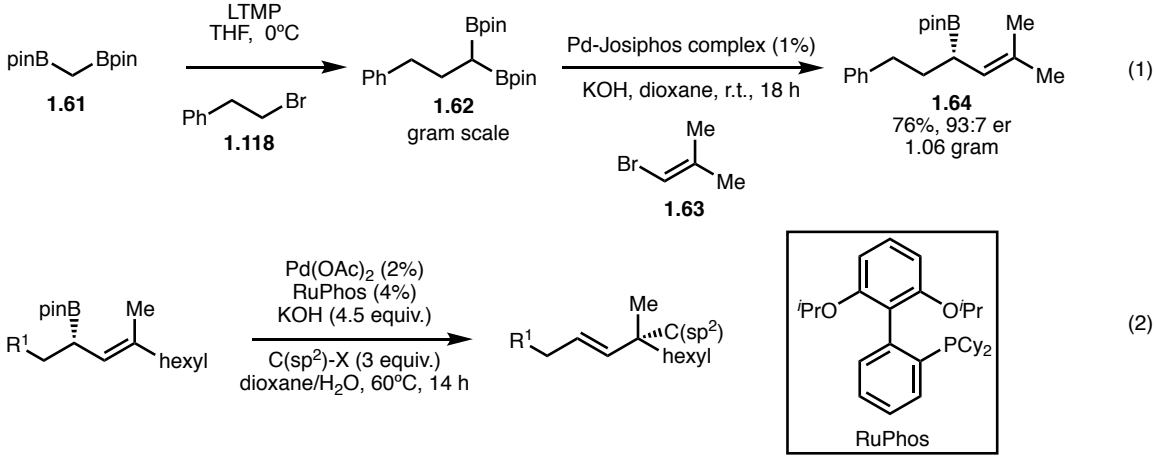
stereocenters. Lastly, nitrosobenzene-mediated oxidation[25] with allylic transposition afforded highly valuable nonracemic tertiary allylic alcohol **1.117** with good enantiospecificity.

Scheme 1.29 Transformations of Nonracemic Allylic Boronate Products



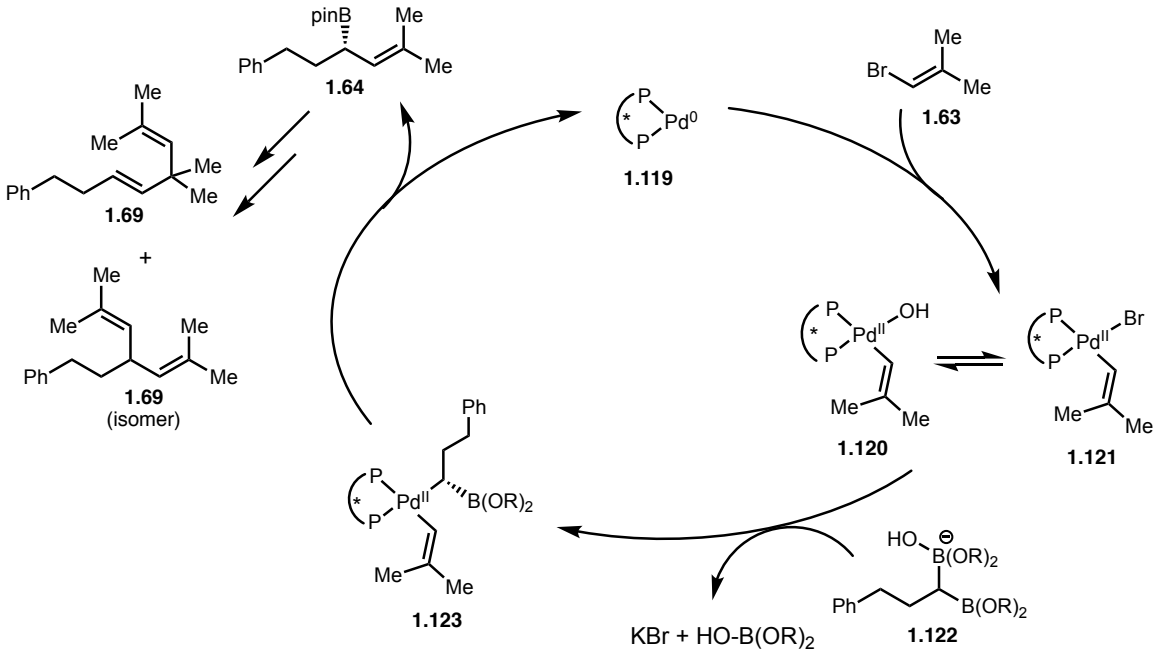
To further expand the synthetic utility of the cross-coupling, a large-scale preparation of geminal bis(boronate) **1.62** was performed. A subsequent gram-scale cross-coupling without the aid of a glove-box afforded nonracemic allylic boronate **1.64** with good yield and enantioselectivity (Scheme 1.30, eq. 1). The gram scale reaction produced similar efficiency and enantioselectivity to the smaller-scale reaction conducted. Subsequent work done by Morken and coworkers involved the cross-coupling of the nonracemic allylic boronate products with a wide-variety of aryl and alkenyl electrophiles (Scheme 1.30, eq. 2).[24c] The cross-coupling efficiently synthesized all carbon quaternary stereocenters with good yields and enantiospecificities.

Scheme 1.30 Synthetic Utility of Cross-Coupling and Sequential Allylic Boronate Cross-Coupling



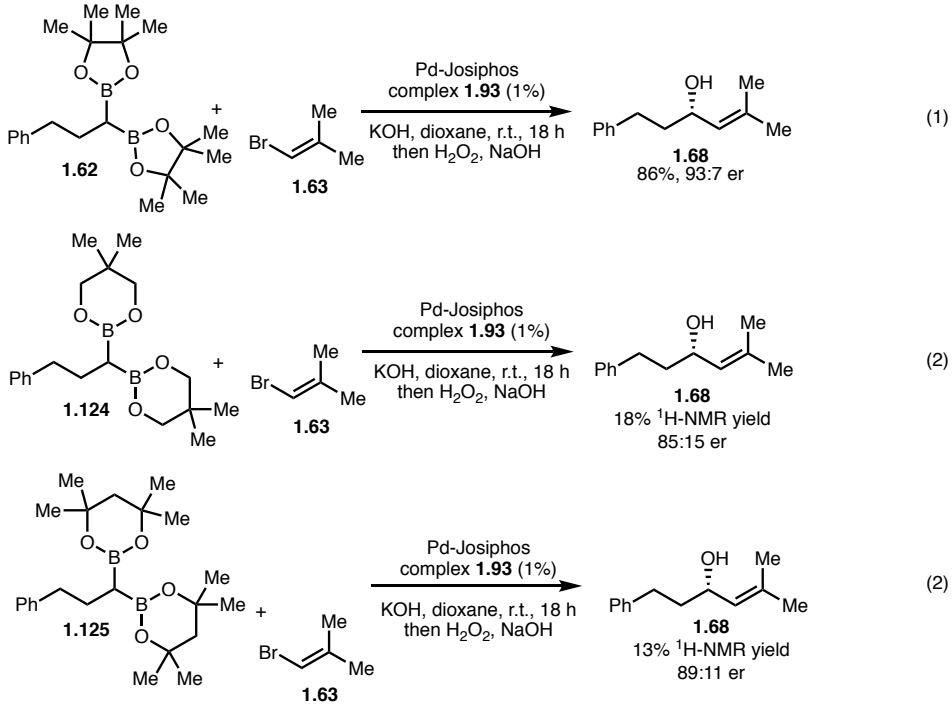
With the synthetic utility of the nonracemic allylic boronate products demonstrated, the mechanism of the cross-coupling was studied. The catalytic cycle is proposed to begin with phosphine ligated palladium (0) (**1.119**) oxidative addition with the alkenyl bromide (**1.63,** Figure 2). Oxidative addition forms palladium (II) halide complex (**1.121**), which under basic aqueous conditions is in equilibrium with a palladium (II) hydroxide species (**1.120**). Activation of geminal bis(boronate) to the bis(boron) "ate" complex promotes the enantiodetermining transmetallation to palladium (II) intermediate **1.123**. Subsequent reductive elimination furnishes the desired nonracemic allylic boronate product **1.64**. Further undesired cross-coupling of the allylic boronate results in the formation of diene products **1.69**.

Figure 1.2 Proposed Mechanism for the Cross-Coupling of Geminal Bis(Boronates) with Alkenyl Bromide



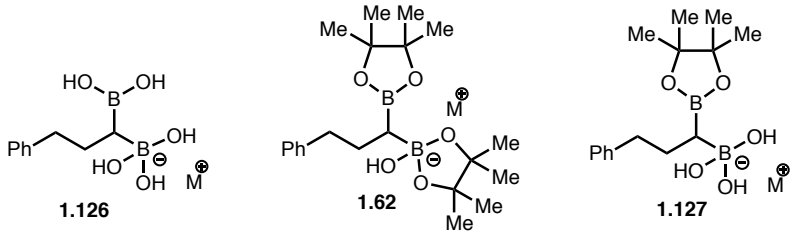
Since the geminal bis(boron) "ate" complex is involved in the enantiodetermining transmetallation, the nature of this complex was of interest. To explore the nature the bis(boron) "ate" complex, two geminal bis(boronates) with differing diol ligands on boron were synthesized. Employing neopentyl glycol-derived substrate (**1.124**) and 2,4-dimethylpentanediol-derived substrate (**1.125**) in the cross-coupling with alkenyl bromide **1.63** produced sluggish reactivity and lower enantioselectivity (Scheme 1.31, eqs. 1-3).

Scheme 1.31 Boron Ligand Experiments to Identify Active Species for Transmetallation



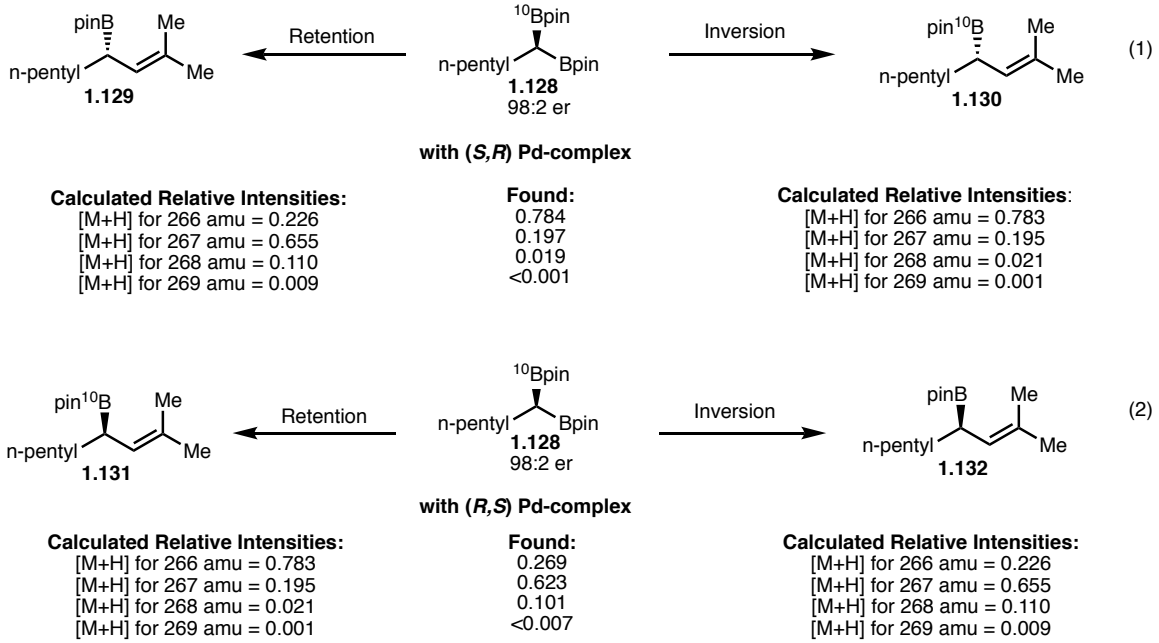
The lower observed enantioselectivity in Scheme 1.31 (eqs. 2-3) suggest that the different geminal bis(boronate) substrates do not converge to the same active species for transmetallation. Consequently, the activated bis(boronic) acid intermediate **1.126** does not appear to provide the observed enantioselectivity (Figure 1.3). The lower yields for substrates **1.124** and **1.125** could be a result of facile hydrolysis to the inactive geminal bis(boronic) acid. However, distinguishing between activated intermediates **1.62** and **1.127** (Figure 1.3) with the data from the geminal bis(boronate) diol studies is challenging. While it has been shown that the geminal bis(boronates) readily hydrolyze in basic aqueous conditions, species **1.62** and **1.127** are likely in equilibrium. From this equilibrium, the geminal bis(boronic) ester **1.62** could be the active species for transmetallation.

Figure 1.3 Active Species of Geminal Bis(Boronate) for Transmetallation



After investigating the active species for transmetallation, the nature of transmetallation was of interest. To probe whether the transmetallation was stereoretentive or stereoinvertive, the synthesis of a ^{10}B and ^{11}B labeled geminal bis(boronate) **1.128** was conducted. The ^{10}B-^{11}B labeled geminal bis(boronate) was then subjected to the standard reaction conditions to probe the stereochemistry of transmetallation. Employing the (*S,R*)-Josiphos·$PdCl_2$ complex, if the reaction occurred with retention of configuration the ^{11}B enriched product **1.129** would be observed. Conversely, if the reaction occurred through inversion the ^{10}B enriched product **1.130** would be observed (Scheme 1.29, eq. 1). Analysis of the reaction product by mass spectrometry analysis found the values to match very closely to the calculated relative intensities for the stereoinvertive transmetallation product **1.130**. The same analysis was done employing the opposite enantiomer of catalyst, the (*R*,*S*)-Josiphos·$PdCl_2$ complex. Again, the data was consistent for the stereoinvertive transmetallation product **1.132** (Scheme 1.32, eq. 2).

Scheme 1.32 Stereochemistry of Transmetallation Mechanistic Experiment



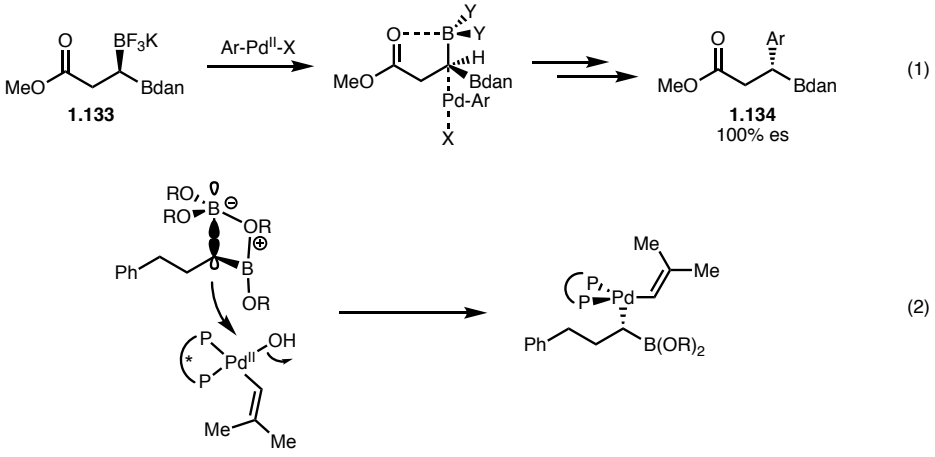
Reaction run using standard conditions: 1% Pd-Josiphos complex, 1.5 equiv. diboron, 4.5 equiv. KOH, dioxane/H_2O, r.t., 18 h

The cross-coupling of a geminal bis(boronate) occurring by a stereoinvertive pathway has been previously reported by Hall and coworkers. However, a stereoinvertive transmetallation required a β-ester group to assist by coordination to boron (Scheme 1.33, eq. 1).[62] The carbonyl coordination to boron in a stereoinvertive transmetallation has also been reported by Suginome for the cross-coupling of α-aminoboronates and Molander for the cross-coupling of a β-amido organoboronates.[63] However, these examples entail the cross-coupling on nonracemic mono-organoboronates. While coordination of the adjacent boron might be present in the cross-coupling of geminal bis(boronates), it would require the formation of a four-membered ring through binding of the pinacol oxygen to the

[62] Lee, J. C. H.; McDonald, R.; Hall, D. G. *Nat. Chem.* **2011**, *3*, 894-899
[63] a) Awano. T.; Ohmura, T.; Suginome, M. *J. Am. Chem. Soc.* **2010**, *132*, 13191-13193 b) Sandrock, D. L.; Jean-Gerard, L.; Chen, C. – Y.; Dreher, S. D.; Molander, G. A. *J. Am. Chem. Soc.* **2010**, *132*, 17108-17110

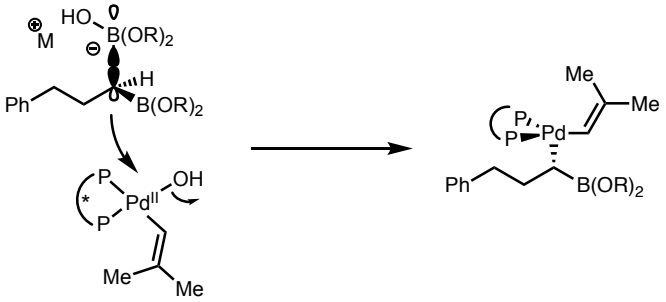
adjacent boron (Scheme 1.33, eq. 2). The formation of a four-membered ring seems energetically less favorable than the five-membered ring formation proposed by Hall and coworkers.

Scheme 1.33 Stereoinvertive Transmetallation of Unsymmetrical Nonracemic Geminal Bis(Boronates)



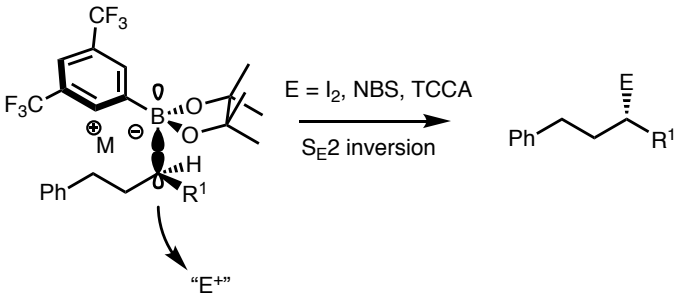
With the knowledge that the transmetallation goes through a stereoinvertive pathway two specific mechanisms appear reasonable. One pathway could be an outer-sphere, stereoinvertive transmetallation without coordination to palladium through a S_E2-type substitution (Scheme 1.34). An outer-sphere mechanism might be consistent with the observation that a more electron deficient ligand (i.e. *p*-trifluoromethylphenylphosphino) provides higher reactivity. A more electron deficient ligand would make palladium more electrophilic and facilitate a S_E2-type substitution. Employing a more electron-rich ligand (i.e. *p*-methoxyphenyl) did result it much lower reactivity potentially supporting the hypothesis that increased electrophilicity leads to higher reactivity.

Scheme 1.34 Outer-sphere, Stereoinvertive Transmetallation



An S_E2-type substitution is also supported by work done by Aggarwal and coworkers.[64] Activation of an organoboronate with a non-transferable electron deficient aryllithium affords an activated boron "ate" complex that reacts by a stereoinvertive S_E2 substitution with a wide variety of electrophiles (Scheme 1.35).

Scheme 1.35 Boron "Ate" Complexes as Nucleophiles in Organic Synthesis

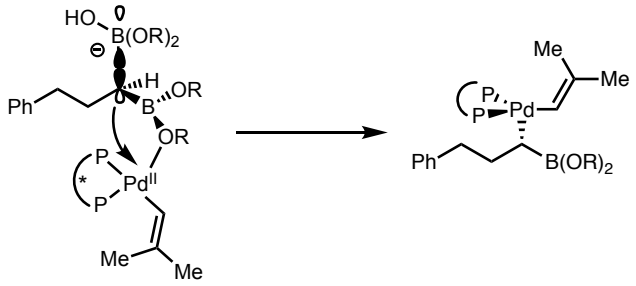


In addition to an outer-sphere transmetallation, neighboring group participation by the adjacent organoboronate of the geminal bis(boronate) must be considered. Coordination to the adjacent organoboronate by the palladium (II) oxidative addition adduct would lead to an inner-sphere, stereoinvertive transmetallation (Scheme 1.36). A more electron deficient palladium would assist in the coordination of the neighboring oxygen to palladium. In-depth kinetic analysis is required to determine the rate-

[64] Larouche-Gauthier, R.; Elford, T. G.; Aggarwal, V. K. *J. Am. Chem. Soc.* **2011**, *133*, 16794-16797

determining step of the reaction, which might shed light on the mechanism of transmetallation.

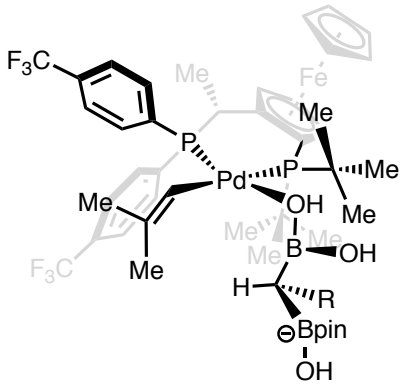
Scheme 1.36 Inner-sphere, Stereoinvertive Transmetallation



With the potential mechanisms for the stereoinvertive transmetallation elaborated, it was of interest to understand the stereochemical outcome. A stereochemical model is proposed based off the Josiphos-$PdCl_2$ crystal structure for the enantiodetermining transmetallation step (Figure 1.4). From the crystal structure, the di-*tert*-butylphosphino group has a large steric effect with one *tert*-butyl group almost protruding above the palladium center. The other *tert*-butyl group essentially blocks the bottom, back quadrant relative to the palladium center. After oxidative addition, the alkenyl substituent might be directed towards the diarylphosphino group. This would avoid a steric penalty of having the alkenyl group interact with the bulky di-*tert*-butylphosphino group. Having previously described multiple mechanisms for transmetallation, it is assumed an inner-sphere transmetallation is operating. This mode of transmetallation has the advantage that the neighboring boron moiety is assisting in bringing the two molecules together to promote a stereoinvertive transmetallation. Additionally, it is assumed the species for transmetallation is a mono-boronic acid, mono-boronic ester geminal bis(boronate). This species would have the advantage of a smaller steric environment close to the di-*tert*-butylphosphino group. The configuration of the geminal bis(boronate) is such that the C-

B bond of the boron "ate" complex is aligned with the palladium center. Additionally, the R substituent might be directed away to avoid a steric penalty with the alkenyl group on palladium. Taking into account this configuration of the geminal bis(boronate) is consistent with the stereochemical outcome for a stereoinvertive transmetallation.

Figure 1.4 Stereochemical Model for the Cross-Coupling of Geminal Bis(Boronates) with Alkenyl Electrophiles



1.4 Conclusion

An enantioselective Suzuki-Miyaura cross-coupling of geminal bis(boronates) with alkenyl electrophiles has been presented. This method highlights an addition to the increasing utility of the geminal bis(boronates) in asymmetric catalysis. This method also contributes a powerful method for the synthesis of nonracemic allylic boronates, more specifically challenging γ,γ-disubstituted allylic boronates. The reaction was able to efficiently synthesize highly valuable nonracemic allylic boronates with high enantioselectivity. The nonracemic allylic boronate products have been shown to be versatile in synthetic organic chemistry. Mechanistic investigations into the reaction have shown that the reaction occurs through a stereoinvertive transmetallation

Future efforts to further expand the substrate scope to include a variety of alkenyl electrophile substitution patterns is of interest. In addition to alkenyl electrophiles, the incorporation of alkyl electrophiles in the cross-coupling would represent a powerful addition to the utility of geminal bis(boronates) in transition-metal catalysis.

1.5 Experimental

1.5.1 General Information

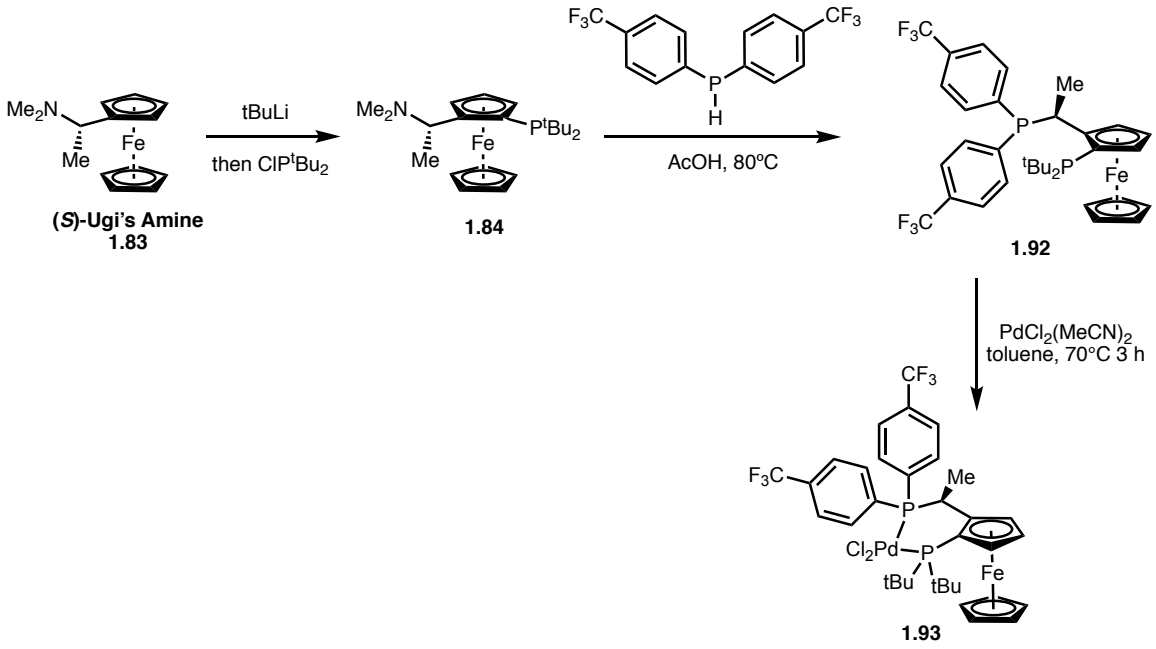
^{1}H NMR spectra were recorded on either a Varian Gemini-500 (500 MHz), Varian Inova-500 (500 MHz), or Varian Gemini-600 (600 MHz) spectrometer. Chemical shifts are reported in ppm with the solvent resonance as the internal standard ($CHCl_3$: 7.26 ppm). Data are reported as follows: chemical shift, integration, multiplicity (s = singlet, d = doublet, t = triplet, q = quartet, p = pentet, m = multiplet), and coupling constants (Hz). ^{13}C NMR spectra were recorded on either a Varian Gemini-500 (125 MHz), or Varian Gemini-600 (150 MHz) spectrometer with complete proton decoupling. Chemical shifts are reported in ppm with the solvent resonance as the internal standard ($CDCl_3$: 77.16 ppm). ^{31}P NMR spectra were recorded on a Varian Gemini-500 (202 MHz), or Varian Gemini-600 (240 MHz) spectrometer. 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. ^{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

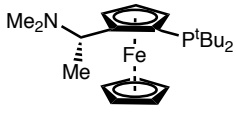
Research Autopol IV Polarimeter. High-resolution mass spectrometry (ESI+) was performed at the Mass Spectrometry Facility, Boston College, Chestnut Hill, MA.

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) and ceric ammonium molybdate (CAM) in ethanol. 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.

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 (CH_2Cl_2), 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. Hexane was purified using a Glass Contour solvent purification system custom manufactured by SG Waters, LLC (Nashua, NH). Bis(pinacolato)diboron was generously donated by Allychem Co., Ltd. and used without further purification. Chemicals were purchased from Sigma Aldrich, Alfa Aeser, Acros Organics, Fisher Scientific, Oakwood Chemical, Combi-Blocks, TCI America, Matrix Scientic and used without further purification.

1.5.2 Ligand Synthesis and Characterization

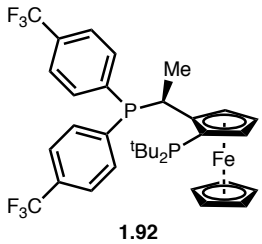




1.84

Dimethyl{(*S*)-1-[(*R*)-2-(di-*tert*-butylphosphanyl)ferrocenyl]ethyl}amine (1.84) Prepared according to a literature precedent with slight modification.[60] To a 100-mL round-bottom flask equipped with a magnetic stir bar and reflux condenser was added (*S*)-Ugi's amine[59] (1.32 g, 5.12 mmol). The amine was azeotroped with benzene (3 x 100 μL) and placed under N_2. Et_2O (33 mL) was added and the reaction was cooled to -78°C. *t*BuLi (3.60 mL, 6.14 mmol, 1.7M in pentanes) was cautiously added dropwise. The reaction was stirred at -78°C for 30 minutes and then warmed to room temperature for 1 hour. The reaction was re-cooled to -78°C and di-*tert*-butylchlorophosphine (1.07 mL, 5.60 mmol) was added as a solution in Et_2O (1 mL) *via* syringe. The reaction stirred at -78°C for 5 minutes before warming to room temperature. After stirring for 18 hours, the reaction was quenched with a saturated solution of Na_2CO_3 (10 mL). The reaction was poured into a

separatory funnel with Et_2O (30 mL). The layers were separated and the organic layer was successively washed with H_2O (20 mL) and brine (20 mL). The organic layer was dried over $Na_2SO_{4(s)}$, filtered and concentrated *in vacuo*. The crude material was purified by silica gel chromatography (5% ethyl acetate/hexanes to 30% ethyl acetate/hexanes) to afford the title compound as a red solid (1.36 g, 66% yield), which was stored in an Ar-filled drybox. R_f = 0.05 in 50% ethyl acetate/hexanes on TLC. ^{1}H NMR (500 MHz, $CDCl_3$) δ 4.54 (s, 1H), 4.38 (t, *J* = 2.0 Hz, 1H), 4.26 (s, 1H), 4.16 (s, 5H), 3.60 (dq, *J* = 10.0, 6.0 Hz, 1H), 2.19 (s, 6H), 1.50 (d, *J* = 12.0 Hz, 9H), 1.46 (d, *J* = 7.0 Hz, 3H), 0.92 (d, *J* = 11.5 Hz). ^{13}C NMR (150 MHz, $CDCl_3$) δ 101.60 (d, *J* = 25.5 Hz), 77.21, 72.25 (d, *J* = 5.7 Hz), 70.09, 68.39 (d, *J* = 4.5 Hz), 68.20, 56.75 (d, *J* = 12.7 Hz), 41.91, 33.26 (d, *J* = 20.8 Hz), 31.84 (d, *J* = 18.5 Hz), 30.87 (d, *J* = 15.1 Hz), 30.39 (d, *J* = 13.9 Hz), 16.85. ^{31}P NMR (202 MHz, $CDCl_3$) δ 14.21. IR (neat) ν_{max} 3097 (w), 2970 (m), 2940 (m), 2888 (m), 2857 (s), 2813 (m), 2769 (m), 1473 (m), 1455 (s), 1384 (w), 1359 (s), 1262 (w), 1240 (w), 1194 (w), 1176 (w), 1154 (s), 1109 (s), 1089 (s), 1061 (m), 1041 (s), 1002 (s), 929 (s), 817 (s) cm^{-1}. HRMS (ESI+) calc. for $C_{22}H_{37}FeNP$ $[M+H]^+$ 402.2013, found 402.2008. $[\alpha]^{20}_D$: +260.2 (c = 0.722, $CHCl_3$, *l* = 50 mm). Melting point: 47-51 °C.

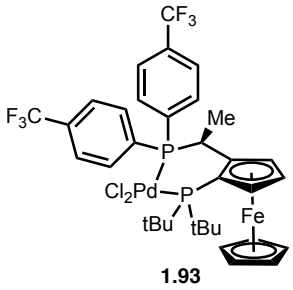


1.92

(*S*)-1-[(*R*)-2-(Di*tert*butylphosphanyl)ferrocenyl]ethyldi[4-(trifluoromethyl)phenyl]phosphine (1.92). Prepared according to a literature precedent with slight modification.[2] In an Ar-filled drybox, an oven-dried 2-dram vial with magnetic stir bar was charged with **1.84** (330 mg, 0.82 mmol). The vial was sealed with a rubber septum and removed from the glove box. Freshly degassed (*via* constant bubbling with N_2 for one hour

prior to use) glacial AcOH (500 μL) was added under an atmosphere of N_2. The reaction was stirred and bis(4-trifluoromethlphenyl)phosphine (278 mg, 0.86 mmol) was added in a solution of glacial AcOH (500 μL) *via* syringe. The reaction was heated to 80°C for 18 hours. The reaction was cooled to room temperature and the solvent removed *in vacuo*. The mixture was diluted with CH_2Cl_2 (30 mL) and poured into a separatory funnel containing a saturated solution of Na_2CO_3 (15 mL). The layers were separated and the organic layer was successively washed with H_2O (20 mL) and brine (20 mL). The organic layer was dried over $Na_2SO_{4(s)}$, filtered and concentrated *in vacuo*. The crude material was purified by silica gel chromatography (hexanes to 3% ethyl acetate/hexanes) to afford the title compound as a red solid (306.2 mg, 55% yield, 95% purity), which was stored in an Ar-filled drybox. R_f = 0.5 in 10% ethyl acetate/hexanes on TLC. ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.58-7.46 (m, 8H), 4.34 (m, 2H), 4.18 (s, 5H), 4.10 (s, minor conformer), 4.00 (s, 1H), 3.91 (s, minor conformer), 3.62 (m, 1H), 1.53 (d, *J* = 12.0 Hz, 9H), 1.44 (t, *J* = 7.8 Hz, 3H), 1.04 (d, *J* = 10.8 Hz, 9H). ^{13}C NMR (150 MHz, $CDCl_3$) δ 143.50 (d, *J* = 22.0 Hz), 141.06 (d, *J* = 23.2 Hz), 136.07 (d, *J* = 20.8 Hz), 132.25 (d, *J* = 15.1 Hz), 131.52 (q, *J* = 32.4 Hz), 129.85 (q, *J* = 32.4 Hz), 125.03 (m), 124.85 (m), 98.87 (dd, *J* = 27.7, 18.4 Hz), 77.87 (dd, *J* = 36.9, 3.5 Hz), 72.67 (d, *J* = 5.9 Hz), 70.31, 68.85 (dd, *J* = 11.6, 4.7 Hz), 68.49, 33.46 (d, *J* = 20.8 Hz), 32.15 (d, *J* = 19.6 Hz), 31.03 (dd, *J* = 13.9, 2.4 Hz), 30.70 (d, *J* = 13.9 Hz), 29.38 (dd, *J* = 17.3, 12.7 Hz), 20.34 (dd, *J* = 4.7 Hz). ^{31}P NMR (242 MHz, $CDCl_3$) δ 13.13 (d, *J* = 17.5 Hz), -0.32 (d, *J* = 16.3 Hz). ^{19}F NMR (470 MHz, $CDCl_3$) δ -62.76, -62.82. IR (neat) ν_{max} 3092 (w), 2971 (w), 2942 (w), 2891 (w), 2861 (w), 1606 (m), 1395 (m), 1321 (s), 1164 (m), 1125 (s), 1107 (m), 1059 (s), 1015 (m), 908 (w), 826 (s), 733 (m), 699 (m) cm^{-1}. HRMS (ESI+) calc. for $C_{34}H_{39}F_6FeP_2$ $[M+H]^+$ 679.1781, found

679.1779. $[\alpha]^{20}_D$: +75.4 (c = 0.740, $CHCl_3$, *l* = 50 mm). Melting point: 156-163 ^oC (decomposition).



1.93

1.93·$PdCl_2$. In an Ar-filled glove box, an oven-dried 100-mL round bottom flask with magnetic stir bar was charged with $(ACN)_2PdCl_2$ (290 mg, 1.12 mmol) and **1.92** (758 mg, 1.12 mmol). The flask was removed from the drybox. Toluene (60 mL) was added and the reaction was heated to 70^{o}C for 3 hours under N_2. The reaction was cooled to room temperature and the solvent removed *in vacuo*. CH_2Cl_2 (10 mL) was added and the solution was filtered through a plug of Celite. The solvent was removed *in vacuo* and the solid washed with Et_2O (3 x 4 mL). The red solid was dried under vacuum for 12 hours to afford the title compound as a red solid (921 mg, 96% yield), which was stored under air in a dessicator. ^{1}H NMR (600 MHz, $CDCl_3$) δ 8.26 (t, *J* = 9.0 Hz, 2H), 7.79 (dd, *J* = 11.4, 7.8 Hz, 2H), 7.67 (d, *J* = 7.2 Hz, 2H), 7.60 (d, *J* = 6.6 Hz, 2H), 4.99 (s, 1H), 4.73 (m, 2H), 4.23 (s, 5H), 3.61 (dq, *J* = 14.4, 7.2 Hz, 1H), 2.10 (d, *J* = 15.6 Hz, 9H), 1.39 (dd, *J* = 13.8, 7.2 Hz, 3H), 1.10 (d, *J* = 14.4 Hz, 9H). ^{31}P NMR (242 MHz, $CDCl_3$) δ 53.75 (d, *J* = 4.6 Hz), 43.91 (d, *J* = 4.6 Hz). ^{19}F NMR (470 MHz, $CDCl_3$) δ -63.04, -63.37. IR (neat) ν_{max} 3080 (w), 2960 (w), 2898 (w), 2870 (w) 1608 (w), 1458 (w), 1396 (m), 1321 (s), 1281 (w), 1168 (m), 1128 (s), 1061 (s), 1015 (m), 909 (m), 830 (m), 729 (m) cm^{-1}. HRMS (ESI+) calc. for $C_{34}H_{38}ClF_6FeP_2Pd$ $[M\text{-}Cl]^+$ 819.0426, found 819.0432. $[\alpha]^{20}_D$: -401.3 (c = 1.03, $CHCl_3$, *l* = 50 mm). Melting point: 204-219 ^{o}C (decomposition)**.**

1.5.3 Full Ligand Optimization

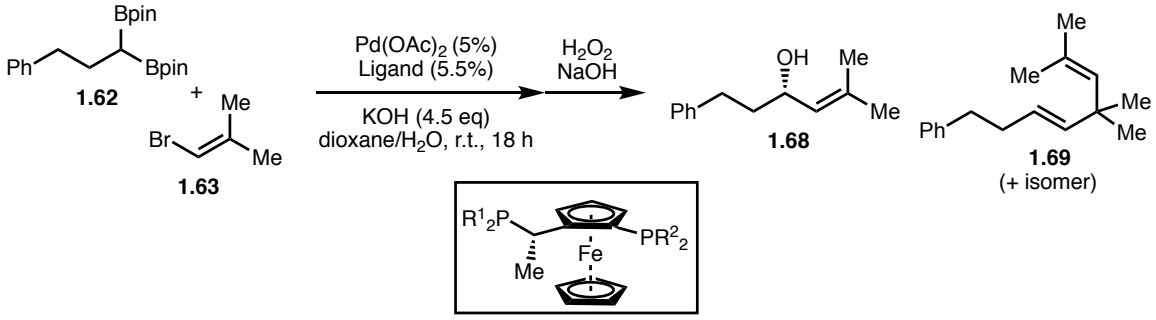
JosiPhos ligands were either purchased according to the general information or prepared according to the procedures above (**1.5.2**).

Method A. An oven-dried 2-dram vial with magnetic stir bar was charged with (*S,R*)-JosiPhos (0.0055 mmol) and geminal bis(boronate) **1.62** (74.0 mg, 0.20 mmol) in an Ar-filled drybox. The vial was sealed with rubber septum and removed from the drybox. $Pd(OAc)_2$ in dioxane (500 μL, 0.005 mmol, 0.01M) was added *via* syringe and the reaction stirred at room temperature under N_2 for 1 hour. Then 1-bromo-2-methylprop-1-ene (10.2 μL, 0.10 mmol) and 8M $KOH_{(aq)}$[65] (56 μL, 0.45 mmol) were added sequentially *via* syringe. The reaction was stirred under an atmosphere of N_2 at room temperature for 18 hours. The reaction was diluted with Et_2O (2 mL) and filtered through a plug of Celite with additional Et_2O (5 mL). The filtrate was concentrated *in vacuo*. 1,1,2,2-Tetrachloroethane was added as an internal standard (~10 mg) and yield was determined by ^{1}H-NMR analysis. THF (3 mL) was added to a scintillation vial containing the crude filtrate and equipped with a stir bar. The vial was sealed with a septum and an exit needle inserted. The reaction was cooled to 0^{o}C, and H_2O_2 (500 μL, 30 wt% in H_2O) and 3M NaOH (500 μL) were added sequentially *via* syringe. The reaction was warmed to room temperature and stirred for no less than 3 hours. The reaction was re-cooled to 0^{o}C and quenched with a saturated solution of $Na_2S_2O_3$ (200 μL). The reaction was warmed to room temperature, diluted with Et_2O (3 mL), and then filtered through a plug of silica gel with additional Et_2O (5 mL). The solvent was removed *in vacuo* and the crude mixture was purified by silica gel chromatography

[65] $KOH_{(aq.)}$ was sparged with N_2 for 30 min at room temperature before use.

(10% ethyl acetate/hexanes) to afford secondary allylic alcohol **1.68.** The enantiomeric excess was determined by chiral SFC analysis (for full characterization see below).

Table 1.8 Extensive Ligand Optimization



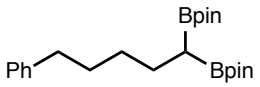
Entry	*R_1*	*R_2*	*Yield 1.68 (%)[a]*	*Yield 1.69 (%)[a]*	*er[b]*
1	3,5-xylyl	Ph	22	27	57:43
2	Cy	Ph	21	13	54:46
3	Cy	3,5-di(Me)-4-OMe-phenyl	14	20	64:36
4	Cy	Cy	40	5	68:32
5	*t*Bu	Cy	50	<2	69:31
6	Ph	Cy	50	15	65:35
7	Ph	*i*Pr	40	<2	78:22
8	Ph	1-Adamantyl	24	<2	62:38
9	Ph	*t*Bu	60	<2	91:9
10	2-Me-phenyl	*t*Bu	14	<2	63:37
11	4-F-phenyl	*t*Bu	44	<5	90:10
12	4-OMe-phenyl	*t*Bu	16	10	85:15
13	3,5-di(OMe)phenyl	*t*Bu	45	<2	79:21
14	4-Me-phenyl	*t*Bu	22	<5	82:18
15	3-Me-phenyl	*t*Bu	48	10	83:17
16	3,5-xylyl	*t*Bu	29	22	52:48
17	2-furyl	*t*Bu	85	<5	76:24
18	2-naphthyl	*t*Bu	27	10	70:30
19	Benzo[b]phosphindole	*t*Bu	20	23	55:45
20	*t*Bu	*t*Bu	25	<2	57:43
21	Cy	*t*Bu	<10	<2	n.d.
22	4-CF_3-phenyl	*t*Bu	95	<2	91:9
23	2-CF_3-phenyl	*t*Bu	89	<2	75:25
24	3,4,5-tri(F)phenyl	*t*Bu	97	<2	85:15

[a]Yield was determined by ^{1}H-NMR in comparison to 1,1,2,2-tetrachloroethane as an internal standard. [c]Enantiomer ratio determined by chiral SFC analysis of corresponding alcohol.

1.5.4 Synthesis and Characterization of Geminal Bis(Boronates)

Geminal bis(boronates) were prepared according to literature procedures.[15,16]

Method B. Prepared according to a literature precedent with slight modification.[47b] In an Ar-filled drybox, an oven-dried 50-mL round bottom flask with magnetic stir bar was charged with lithium 2,2,6,6-tetramethylpiperidide (440 mg, 3.0 mmol). The flask was sealed with a rubber septum, removed from the drybox. THF (10 mL) was added and the reaction was cooled to 0 °C. A solution of bis(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)methane (804 mg, 3.0 mmol) in THF (5 mL) was added *via* syringe and the mixture was allowed to stir at 0 °C for 5 minutes. Then a solution of the corresponding alkyl bromide (3.3 mmol) in THF (5 mL) was added. The reaction mixture was allowed to warm to room temperature and stir for 2 hours. The reaction was diluted with Et_2O (10 mL) and filtered through Celite with Et_2O (10 mL). The solvent was removed *in vacuo* and the crude mixture was purified by silica gel chromatography.

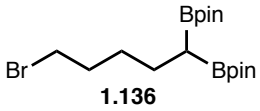


1.135

2,2'-(4-Phenylpentane-1,1-diyl)bis(4,4,5,5-tetramethyl-1,3,2-dioxaborolane) (1.135) Prepared according to *Method B* with (4-bromobutyl)benzene[66] as the electrophile. The crude mixture was purified by silica gel chromatography (5% ethyl acetate/hexanes, stain in CAM) to afford the title compound as a white solid (43%). R_f = 0.5 in 10% ethyl acetate/hexanes on TLC. ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.27-7.21 (m, 2H), 7.18-7.12 (m, 3H), 2.59 (t, *J* = 7.0 Hz, 2H), 1.59 (m, 4H), 1.32 (m, 2H), 1.22 (s, 12H), 1.20 (s, 12H), 0.72 (t, *J* = 7.5 Hz, 1H). ^{13}C NMR (125 MHz,

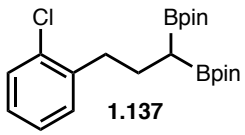
[66] Hardouin, C.; Kelso, M. J.; Romero, F. A.; Rayl, T. J.; Leung, D.; Hwang, I.; Cravatt, B. F.; Boger, D. L. *J. Med. Chem*., **2007**, *50*, 3359-3368

$CDCl_3$) δ 1.43.13, 128.59, 128.27, 125.56, 83.03, 35.94, 32.26, 31.50, 25.70, 24.96, 24.66. ^{11}B NMR (160 MHz, $CDCl_3$) δ 33.85. IR (neat) ν_{max} 3085 (w), 3061 (w), 3026 (w), 2976 (s), 2928 (m), 2856 (m), 1584 (w), 1454 (m), 1354 (s), 1308 (s), 1265 (s), 1214 (m), 1137 (s), 969 (s), 849 (s), 745 (m), 698 (s) cm^{-1}. HRMS (ESI+) calc. for $C_{23}H_{39}B_2O_4$ $[M+H]^+$ 401.3034, found 401.3014. Melting point: 41-42 °C.



1.136

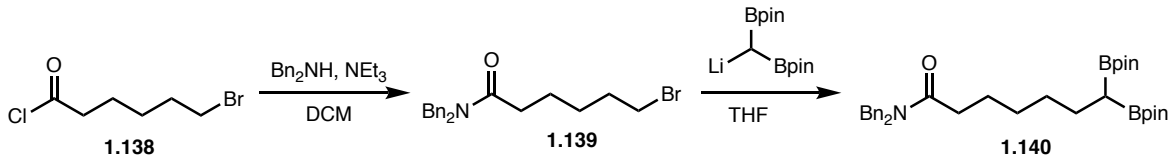
2,2'-(5-Bromopentane-1,1-diyl)bis(4,4,5,5-tetramethyl-1,3,2 dioxaborolane) (1.136) Prepared according to *Method B* with 1,4-dibromobutane as the electrophile. The crude mixture was purified by silica gel chromatography (5% ethyl acetate/hexanes, stain in CAM) to afford the title compound as a white solid (52%). R_f = 0.5 in 10% ethyl acetate/hexanes on TLC. ^1H NMR (500 MHz, $CDCl_3$) δ 3.39 (t, *J* = 7.0 Hz, 2H), 1.84 (p, *J* = 7.0 Hz, 2H), 1.57 (q, *J* = 8.0 Hz, 2H), 1.42 (m, 2H), 1.23 (s, 12H), 1.22 (s, 12H), 0.72 (t, *J* = 8.0 Hz, 1H). ^{13}C NMR (125 MHz, $CDCl_3$) δ 83.13, 34.21, 33.03, 31.08, 25.01, 24.99, 24.66. ^{11}B NMR (160 MHz, $CDCl_3$) δ 33.81. IR (neat) ν_{max} 2976 (s), 2930 (m), 2861 (w), 1459 (w), 1354 (s), 1306 (s), 1245 (s), 1213 (m), 1164 (s), 1004 (w), 968 (s), 905 (w), 849 (s), 734 (w) cm^{-1}. HRMS (ESI+) calc. for $C_{17}H_{37}B_2BrNO_4$ $[M+NH_4]^+$ 420.2092, found 402.2100. Melting point: 48-50 °C.

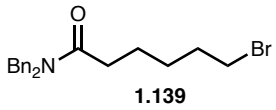


1.137

2,2'-(3-(2-Chlorophenyl)propane-1,1-diyl)bis(4,4,5,5-tetramethyl-1,3,2-dioxaborolane) (1.137) Prepared according to *Method A* with 2-chlorophenethylbromide as the electrophile. The crude mixture was purified by silica gel chromatography (10% ethyl acetate/hexanes, stain in CAM) to afford the title compound as a white solid (75%). R_f = 0.3 in 10% ethyl acetate/hexanes on TLC.

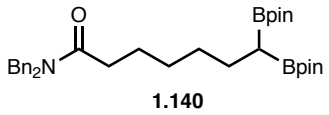
^{1}H NMR (500 MHz, $CDCl_3$) δ 7.29 (dd, *J* = 7.5, 1.5 Hz, 1H), 7.22 (dd, *J* = 8.0, 2.0 Hz, 1H), 7.14 (dt, *J* = 7.0, 1.5 Hz, 1H), 7.08 (dt, *J* = 8.0, 2.0 Hz, 1H), 2.73-2.79 (m, 2H), 1.87 – 1.82 (m, 2H), 1.24 (s, 12H), 1.23 (s, 12H), 0.83 (t, *J* = 8.0 Hz, 1H). ^{13}C NMR (125 MHz, $CDCl_3$) δ 140.54, 134.01, 130.71, 129.35, 127.07, 126.64, 83.15, 36.18, 26.25, 25.05, 24.65. ^{11}B NMR (160 MHz, $CDCl_3$) δ 33.82. IR (neat) ν_{max} 2977 (w), 2929 (w), 2865 (w), 1474 (w), 1356 (m), 1310 (s), 1258 (m), 1215 (s), 1137 (s), 1105 (w), 970 (m), 846 (m), 755 (m), 679 (w) cm^{-1}. HRMS (ESI+) calc. for $C_{21}H_{34}B_2ClO_4$ $[M+H]^+$ 407.2332, found 407.2340. Melting point: 87-90 ^{o}C.





***N,N*-Dibenzyl-6-bromohexanamide (1.139)** To an oven-dried, 100-mL round-bottom flask equipped with a magnetic stir bar under an atmosphere of N_2, was added CH_2Cl_2 (18 mL), triethylamine (1.2 mL, 8.4 mmol) and dibenzylamine (1.6 mL, 8.4 mmol) *via* syringe. The reaction was stirred and cooled to 0^{o}C. 6-Bromohexanoyl chloride (1.1 mL, 7.0 mmol) was added dropwise *via* syringe over a period of 10 minutes. The reaction was warmed to room temperature and stirred for 4 hours under N_2. The reaction was quenched by addition of H_2O (4 mL) and poured into a separatory funnel containing 3M NaOH (15 mL). The layers were separated and the aqueous layer was extracted with CH_2Cl_2 (2 x 15 mL). The organic layers were combined, dried over $Na_2SO_{4(s)}$, filtered, and concentrated *in vacuo*. The crude mixture was purified by silica gel

chromatography (25% ethyl acetate/hexanes, stain in CAM) to afford the title compound as a yellow oil (2.3g, 88%). R_f = 0.2 in 20% ethyl acetate/hexanes on TLC.

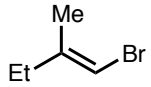


1.140

***N,N*-Dibenzyl-7,7-bis(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)heptanamide (1.140)** Prepared according to *Method B* with *N,N*-dibenzyl-6-bromohexanamide as the electrophile. The crude mixture was purified by silica gel chromatography (25% ethyl acetate/hexanes, stain in CAM) to afford the title compound as a yellow oil (55%). R_f = 0.2 in 20% ethyl acetate/hexanes on TLC. ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.39-7.24 (m, 8H), 7.20 (d, *J* = 7.5 Hz, 2H), 7.14 (d, *J* = 7.0 Hz, 2H), 4.59 (s, 2H), 4.43 (s, 2H), 2.39 (t, *J* = 8.0 Hz, 2H), 1.70 (p, *J* = 7.5 Hz, 2H), 1.53 (q, *J* = 7.0 Hz, 2H), 1.35-1.22 (m, 4H), 1.21 (s, 6H), 1.20 (s, 6H), 0.69 (t, *J* = 7.5 Hz, 1H). ^{13}C NMR (125 MHz, $CDCl_3$) δ 173.87, 137.68, 136.77, 129.00, 128.64, 128.35, 127.63, 127.37, 126.49, 82.95, 49.99, 48.06, 33.47, 32.40, 29.63, 25.66, 25.57, 24.94, 24.60. ^{11}B NMR (160 MHz, $CDCl_3$) δ 33.71. IR (neat) ν_{max} 3029 (w), 2978 (m), 2929 (w), 2858 (w), 1641 (m), 1452 (m), 1358 (m), 1311 (s), 1267 (m), 1213 (m), 1137 (s), 969 (m), 908 (s), 849 (m), 726 (s), 698 (m) cm^{-1}. HRMS (ESI+) calc. for $C_{33}H_{50}B_2NO_5$ $[M+H]^+$ 562.3875, found 562.3861.

1.5.5 Synthesis and Characterization of Alkenyl Bromides

Method C. Prepared according to a literature precedent with slight modification.[67] In an Ar-filled drybox, an oven-dried 100-mL round bottom flask was charged with Cp_2ZrCl_2 (640 mg, 2.2 mmol). The flask was removed from the drybox and CH_2Cl_2 (15 mL) was added followed cautiously by trimethylaluminium (2.9 mL, 30 mmol) *via* syringe. The reaction was cooled to -23°C and water (270 μL, 15 mmol) was added dropwise with vigorous stirring. After stirring for 10 minutes, the corresponding alkyne (10 mmol) was added in a solution of CH_2Cl_2 (5 mL). The reaction was stirred for an additional 10 minutes at -23°C before adding NBS (5.3 g, 30 mmol) as a solid. The reaction was allowed to warm to room temperature and stirred under N_2 for 12 hours. The reaction was cooled to 0°C and carefully quenched with a saturated solution of K_2CO_3 (3 mL). After stirring for 10 minutes, excess $Na_2SO_{4(s)}$ was added. The mixture was filtered through a short pad of silica and concentrated *in vacuo*. The crude mixture was purified by silica gel chromatography.

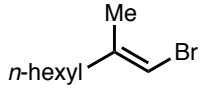


1.141

(*E*)-1-Bromo-2-methylbut-1-ene (1.141) Prepared according to a literature precedent with slight modification.[67] In an Ar-filled drybox, to an oven-dried 2-neck 100-mL round bottom flask equipped with a magnetic stirbar was charged with Cp_2ZrCl_2 (643 mg, 2.2 mmol). The flask was sealed with rubber septa and removed from the drybox. Under a constant pressure of N_2, one septum was replaced a Dewar condenser. CH_2Cl_2 (15 mL) was added to the reaction vessel followed cautiously by trimethylaluminium (2.88 mL, 30 mmol) *via* syringe. The reaction was cooled to -23°C and water (270 μL, 15 mmol) was added dropwise with vigorous stirring. After stirring for

[67] Lim, S.; Wipf, P. *Angew. Chem. Int. Ed. Engl.* **1993**, *32*, 1068-1071

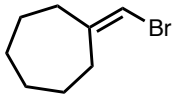
10 minutes, the Dewar condenser was cooled to -78 °C and butyne (0.9 mL, 10 mmol) was added dropwise *via* the condenser. The reaction was stirred for an additional 10 minutes at -23°C before adding NBS (5.3 g, 30 mmol) as a solid. The reaction was allowed to warm to room temperature and stirred under N_2 for 12 hours. The reaction was cooled to 0°C and carefully quenched with a saturated solution of K_2CO_3 (3 mL). After stirring for 10 minutes, excess $Na_2SO_{4(s)}$ was added. The mixture was filtered through a short pad of silica and concentrated *in vacuo*. The crude mixture was purified on silica gel (pentane, stain in CAM) to afford a clear, colorless oil (44% yield). R_f = 0.9 in pentanes on TLC. The spectral data matched those reported in the literature.[68]



1.142

(*E*)-1-Bromo-2-methyloct-1-ene (1.142) Prepared according to *Method C*. The crude reaction mixture was purified by silica gel chromatography (pentanes, stain in CAM) to afford a clear, colorless oil (64% yield). R_f = 0.9 in pentanes on TLC. ^{1}H NMR (500 MHz, $CDCl_3$) δ 5.88 (s, 1H), 2.09 (t, *J* = 7.5 Hz, 2H), 1.78 (s, 3H), 1.42 (p, *J* = 7.0 Hz, 2H), 1.36-1.21 (m, 6H), 0.89 (t, *J* = 7.5 Hz, 3H). ^{13}C NMR (125 MHz, $CDCl_3$) δ 142.18, 100.98, 38.48, 31.77, 28.89, 27.62, 22.72, 19.16, 14.20. IR (neat) ν_{max} 3070 (w), 2955 (m), 2926 (s), 2856 (m), 1632 (w), 1458 (m), 1377 (m), 1283 (m), 1160 (m), 771 (m), 712 (s) cm^{-1}. HRMS (ESI+) calc. for $C_9H_{18}Br$ $[M+H]^+$ 205.0592, found 205.0595.

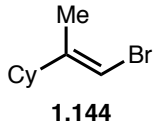
[68] Normant, J. F.; Chuit, C.; Cahiez, G.; Villiera, J. *Synthesis*, **1974**, 803-805



1.143

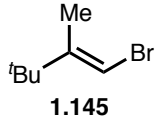
(Bromomethylene)cycloheptane (1.143) Prepared according to a literature precedent with slight modification.[69] A 50-mL round-bottom flask equipped with a magnetic stir bar was charged with (bromomethyl)triphenylphosphonium bromide[70] (1.13 g, 2.60 mmol). The flask was purged with N_2 for 5 minutes and THF (7 mL) was added. The reaction was cooled to -78°C and a solution of KO*t*Bu (292 mg, 2.60 mmol) in THF (3 mL) was added dropwise. The reaction was stirred at -78°C for 5 minutes before warming to room temperature over 30 minutes. Cycloheptanone (236 μL, 2.00 mmol) was added neat and the reaction was stirred under N_2 at room temperature for 16 hours. The reaction was diluted with Et_2O (10 mL) and quenched with H_2O (10 mL). The mixture was added to a separatory funnel and the layers separated. The aqueous layer was then extracted with Et_2O (3 x 10 mL). The organic layers were combined, dried over $Na_2SO_{4(s)}$, filtered, and concentrated *in vacuo*. The crude mixture was purified by silica gel chromatography (pentanes, stain in CAM) to afford a clear, colorless oil (64% yield). R_f = 0.9 in pentanes on TLC. ^{1}H NMR (500 MHz, $CDCl_3$) δ 5.92 (s, 1H), 2.37 (t, J = 6.0 Hz, 2H), 2.31 (t, J = 6.0 Hz, 2H), 1.69-1.47 (m, 8H). ^{13}C NMR (125 MHz, $CDCl_3$) δ 147.47, 101.14, 36.50, 33.40, 30.11, 29.31, 28.85, 26.18. IR (neat) ν_{max} 3070 (w), 2921 (s), 2850 (m), 1614 (w), 1441 (m), 1291 (m), 1159 (w), 763 (s), 729 (m), 682 (m) cm^{-1}. HRMS (ESI+) calc. for $C_8H_{14}Br$ $[M+H]^+$ 189.0279, found 189.0273.

[69] Harrowven, D. C.; Pascoe, D. D.; Guy, I. L. *Angew. Chem. Int. Ed.* **2007**, *46*, 425-425
[70] Vassilikogiannakis, G.; Hatzimarinaki, M.; Orfanopoulos, M. *J. Org. Chem*. **2000**, *65*, 8180-8187



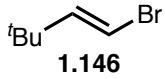
1.144

(*E*)-(1-Bromoprop-1-en-2-yl)cyclohexane (1.144). Prepared according to *Method C*. The crude reaction mixture was purified by silica gel chromatography (pentanes, stain in CAM) to afford a clear, colorless oil (47% yield). R_f = 0.9 in pentanes on TLC. ^{1}H NMR (500 MHz, $CDCl_3$) δ 5.92 (s, 1H), 2.02 (m, 1H), 1.8-1.65 (m, 7H), 1.33-1.09 (m, 6H). ^{13}C NMR (125 MHz, $CDCl_3$) δ 146.92, 101.12, 47.07, 31.71, 26.60, 26.27, 17.75. IR (neat) ν_{max} 3069 (w), 2924 (s), 2852 (s), 1624 (m), 1447 (s), 1377 (m), 1306 (m), 1280 (m), 1165 (m), 1033 (m), 898 (m), 773 (s), 712 (s) cm^{-1}. HRMS (ESI+) calc. for $C_9H_{16}Br$ $[M+H]^+$ 203.0435, found 203.0435.



1.145

(*E*)-1-Bromo-2,3,3-trimethylbut-1-ene (1.145) Prepared according to *Method C*. The crude reaction mixture was purified by silica gel chromatography (pentanes, stain in CAM) to afford a clear, colorless oil (25% yield). R_f = 0.9 in pentanes on TLC. The spectral data matched those reported in the literature.[71]



1.146

(*E*)-1-Bromo-3,3-dimethylbut-1-ene (1.146) Prepared according to a literature precedent with slight modification.[72] To an oven-dried 25 mL round-bottom flask equipped with a magnetic stir bar under N_2 was added 3,3-dimethylbut-1-yne (370 μL, 3.0 mmol). DIBAL-H (3.3 mL, 3.3 mmol, 1.0 M in hexanes) was added *via* syringe and the reaction was stirred for 15 minutes at room temperature before heating to 50^{o}C for 5 hours. The reaction was cooled to room temperature and Et_2O (2 mL) was added. The reaction was further cooled to -78^{o}C and NBS (640 mg, 3.6 mmol) was added as a solid. Upon warming to room temperature, the reaction was stirred for 16 hours. To quench,

[71] Lipshutz, B.H.; Butler, T.; Lower, A. *J. Am. Chem. Soc*. **2006**, *128*, 15396-15398
[72] Hanessian, S.; Tehim, A.; Chen, P. *J. Org. Chem*. **1993**, *58*, 7768-7781

the reaction was poured into a mixture of 6M HCl (10 mL), pentanes (20 mL), and ice. The layers were separated in a separatory funnel, and the aqueous layer was extracted with pentanes (3 x 20 mL). The organic layers were combined and washed successively with 1M NaOH (10 mL) and a saturated solution of $Na_2S_2O_3$ (10 mL). The organic layer was dried over $Na_2SO_{4(s)}$, filtered, and concentrated *in vacuo*. The crude mixture was purified by silica gel chromatography (pentanes, stain in $KMnO_4$) to afford a clear, colorless oil (160 mg, 33% yield). R_f = 0.9 in pentanes on TLC. ^{1}H NMR (500 MHz, $CDCl_3$) δ 6.22 (d, J = 14.0 Hz, 1H), 5.98 (d, J = 13.5 Hz, 1H), 1.04 (s, 9H). ^{13}C NMR (125 MHz, $CDCl_3$) δ 148.64, 102.02, 35.83, 29.133. IR (neat) ν_{max} 3085 (w), 2961 (m), 2932 (w), 2905 (w), 2868 (w), 1614 (w), 1463 (w), 1364 (m), 1263 (m), 945 (m), 906 (s), 774 (m) cm^{-1}. HRMS (ESI+) calc. for $C_6H_{12}Br$ $[M+H]^+$ 163.0122, found 163.0125.

1.5.6 Procedures for Enantiotopic-Group-Selective Suzuki Coupling

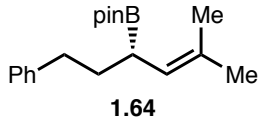
Method D. A 2-dram vial with magnetic stir bar was charged with **1.90·PdCl$_2$** (0.9 mg, 0.0010 mmol) and 1,1-diborylalkane (0.15 mmol). The vial was sealed with rubber septum, and purged with N_2 for 10 minutes. Dioxane (250 μL) was added and the reaction stirred for 5 minutes. Then a solution of vinyl bromide in dioxane (250 μL, 0.10 mmol, 0.4M) and 8M $KOH_{(aq)}$[65] (56 μL, 0.45 mmol) were added sequentially *via* syringe. The reaction was stirred under an atmosphere of N_2 at room temperature for 18 hours. The reaction was diluted with Et_2O (2 mL) and filtered through a plug of Celite with additional Et_2O (5 mL). The filtrate was concentrated *in vacuo* and purified by silica gel

chromatography to afford the desired compound. The enantiomeric ratio was determined for the alcohol obtained from subjecting the purified allyl boronate product to either hydrogen peroxide oxidation (*Method E*) or benzaldehyde allylation (*Method F*).

Method E, *oxidation to secondary allylic alcohol*. THF (3 mL) was added to the purified allylic boronate in a scintillation vial equipped with a stir bar. The vial was sealed with a septum and an exit needle inserted. The reaction was cooled to 0^{o}C, and H_2O_2 (500 μL, 30 wt% in H_2O) and 3M NaOH (500 μL) were added sequentially *via* syringe. The reaction was warmed to room temperature and stirred for no less than 3 hours. The reaction was re-cooled to 0^{o}C and quenched with a saturated solution of $Na_2S_2O_3$ (200 μL). The reaction was warmed to room temperature, diluted with Et_2O (3 mL), and then filtered through a plug of silica gel with additional Et_2O (5 mL). The solvent was removed *in vacuo* and the crude mixture was purified by silica gel chromatography to afford the corresponding secondary allylic alcohol.

Method F, *allylboration with benzaldehyde*. Toluene (500 μL) was added to the purified allylic boronate in a 2-dram vial equipped with a stir bar under N_2. The reaction was stirred and benzaldehyde (50 μL, 0.5 mmol) was added. The reaction was heated to 60^{o}C for 24 hours under N_2. Upon cooling to room temperature, the reaction was diluted with Et_2O (3 mL) and filtered through a short pad of Celite with additional Et_2O (5 mL). The solvent was removed *in vacuo* and the crude mixture was purified by silica gel chromatography to afford the corresponding secondary homoallylic alcohol.

1.5.7 Characterization of Reaction Products and Analysis of Stereochemistry



1.64

(*S*)-4,4,5,5-Tetramethyl-2-(5-methyl-1-phenylhex-4-en-3-yl)-1,3,2-dioxaborolane (1.64). The reaction was performed according to the *Representative Procedure (Method D).* The crude mixture was purified by silica gel chromatography (20% CH_2Cl_2/hexanes, stain in CAM) to afford a clear, colorless oil (27.9mg, 93% yield). R_f = 0.6 in 50% CH_2Cl_2/hexanes on TLC. ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.27-7.24 (m, 2H), 7.17-7.13 (m, 3H), 5.09 (d, *J* = 9.5 Hz, 1H), 2.64 (ddd, *J* = 13.5, 10.5, 5.5 Hz, 1H), 2.53 (ddd, *J* = 13.0, 10.5, 6.0 Hz, 1H), 1.99 (q, *J* = 8.5 Hz, 1H), 1.83 (ddt, *J* = 13.0, 10.0, 6.0 Hz, 1H), 1.72 (s, 3H), 1.67 (m, 1H), 1.59 (s, 3H), 1.23 (s, 6H), 1.22 (s, 6H). ^{13}C NMR (125 MHz, $CDCl_3$) δ 143.06, 131.31, 128.63, 128.32, 125.65, 125.06, 83.09, 35.64, 33.71, 24.92, 24.69, 18.4. ^{11}B NMR (160 MHz, $CDCl_3$) δ 33.06. IR (neat) ν_{max} 3084 (w), 3062 (w), 3026 (m), 2976 (s), 2924 (s), 2856 (m), 1603 (s), 1495 (m), 1453 (m), 1369 (s), 1315 (s), 1269 (m), 1214 (m), 1141 (s), 1105 (m), 967 (s), 838 (m), 698 (s) cm^{-1}. HRMS (ESI+) calc. for $C_{19}H_{30}BO_2$ $[M+H]^+$ 301.2339, found 301.2335. $[\alpha]^{20}_D$: +1.73 (c = 0.925, $CHCl_3$, *l* =50 mm).

Gram Scale Procedure

A 50-mL round bottom flask with magnetic stir bar was charged with **1.93·$PdCl_2$** (42.8 mg, 0.050 mmol) and geminal bis(boronate) **1.62** (2.79 g, 7.5 mmol). The flask was sealed with rubber septum, and purged with N_2 for 20 minutes. Dioxane (25 mL) was added and the reaction stirred for 5 minutes. 1-Bromo-2-methylprop-1-ene (512 μL, 5.0 mmol)[73] and 8M $KOH_{(aq)}$[65] (2.80 mL, 22.5 mmol) were added sequentially *via* syringe. The reaction was stirred under an atmosphere of N_2 at room temperature for 18 hours. The reaction was diluted with Et_2O (15 mL) and poured into a separatory funnel with Et_2O (10 mL). The layers were separated and the aqueous layer was extracted with Et_2O (2 x 20 mL). The organic layers were combined, dried over $Na_2SO_{4(s)}$, filtered, and concentrated *in vacuo*. The crude material was purified by silica gel chromatography (20% CH_2Cl_2/hexanes, stain in CAM) to afford the title compound as a yellow oil (1.06 g, 71% yield) which co-eluted with protodeboration of the starting material (380 mg). The spectral data matched those above.

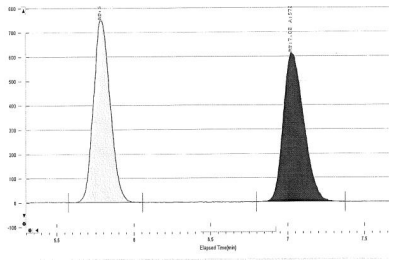
Analysis of Stereochemistry:

The enantiomeric ratio was determined by chiral SFC analysis of the corresponding secondary allylic alcohol. The racemic alcohol was prepared analogously with racemic **1.79** and the corresponding geminal bis(boronate) according to *Method A*.

Chiral SFC (OD-H, Chiraldex, 3 mL/min, 7% ^{i}PrOH, 100 bar, 35 ^{o}C)-analysis of the reaction product.

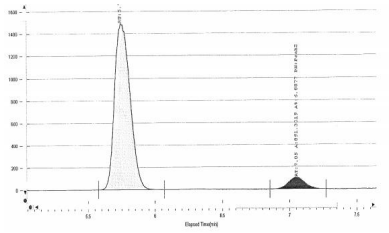
[73] 1-Bromo-2-methylprop-1-ene was sparged with N_2 for 30 min at room temperature before use.

Racemic

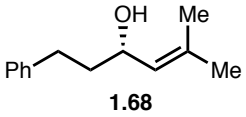


Peak Info					
Peak No	% Area	Area	RT (min)	Height (mV)	K'
1	49.442	5595.4807	5.78	748.4358	0.0068
2	50.558	5721.7898	7.02	613.2783	0.0082
Total:	100	11317.2705			

Reaction product



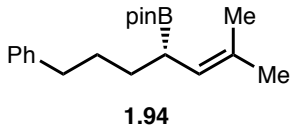
Peak Info					
Peak No	% Area	Area	RT (min)	Height (mV)	K'
1	93.1123	12049.1209	5.74	1495.2346	0.0057
2	6.8877	891.3019	7.05	104.2689	0.007
Total:	100	12940.4228			



1.68

(*S*)-5-Methyl-1-phenylhex-4-en-3-ol (1.68). The reaction was performed according to the *Representative Procedure (Method E)*. The crude mixture was purified by silica gel chromatography (8% ethyl acetate/pentanes, stain in CAM) to afford a clear, colorless oil. R_f = 0.4 in 7/2/1 hexanes/CH_2Cl_2/ethyl acetate on TLC. ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.29-7.26 (m, 2H), 7.20-7.17 (m, 3H), 5.22 (d, *J* = 9.0 Hz, 1H), 4.37 (q, *J* = 9.0 Hz), 1H), 2.67 (m, 2H), 1.92 (ddt, *J* = 13.5, 9.5, 6.5 Hz, 1H), 1.76 (ddt, *J* = 13.0, 10.0, 6.0 Hz, 1H), 1.74 (s, 3H), 1.66 (s, 3H), 1.34 (s, 1H). ^{13}C NMR (125 MHz, $CDCl_3$) δ 142.21, 135.75, 128.53, 128.47, 128.06, 125.89, 68.31, 39.30, 31.95, 25.94, 18.41. IR (neat) ν_{max} 3359 (br), 3061 (w), 3026 (w), 2968 (w), 2926 (s), 2856 (m),

1495 (m), 1453 (s), 1376 (m), 1042 (s), 1006 (m), 746 (m), 698 (s) cm^{-1}. HRMS (ESI+) calc. for $C_{13}H_{17}$ $[M+H-H_2O]^+$ 173.1330, found 173.1338. $[\alpha]^{20}_D$: -36.1 (c = 0.400, $CHCl_3$, *l* =50 mm). The absolute stereochemistry was assigned by comparing the optical rotation with a reported value in the literature for (*S*)-**1.68**, $[\alpha]^{20}_D$: -28.3 (c = 0.05, $CDCl_3$, 90:10 er).[74]



1.94

(*S*)-4,4,5,5-Tetramethyl-2-(2-methyl-7-phenylhept-2-en-4-yl)-1,3,2-dioxaborolane (1.94) The reaction was performed according to the *Representative Procedure (Method D).* The crude mixture was purified by silica gel chromatography (20% CH_2Cl_2/hexanes, stain in CAM) to afford a clear, colorless oil (26.4 mg, 84% yield). R_f = 0.7 in 50% CH_2Cl_2/hexanes on TLC. ^{1}H-NMR (500 MHz, $CDCl_3$) δ 7.24-7.27 (m, 2H), 7.14-7.17 (m, 3H), 5.03 (d, *J* = 9.5 Hz, 1H), 2.54-2.63 (m, 2H), 1.97 (q, *J* = 8.0 Hz, 1H), 1.69 (s, 3H), 1.52-1.66 (m, 6H), 1.39-1.45 (m, 1H), 1.22 (s, 6H), 1.21 (s, 6H). ^{13}C-NMR (125 MHz, $CDCl_3$) δ 143.06, 130.87, 128.53, 128.33, 125.64, 125.33, 83.04, 36.21, 31.48, 31.20, 26.01, 24.89, 24.69, 18.32. ^{11}B-NMR (160 MHz, $CDCl_3$) δ 33.03. IR (neat) ν_{max} 3026 (m), 2977 (s), 2926 (s), 2855 (s), 1603 (w) 1496 (m), 1453 (m) 1370 (s), 1317 (s), 1272 (m), 1214 (m), 1143 (s), 1106 (m), 968 (m), 886 (m), 835 (m), 747 (m), 698 (s). HRMS (ESI) calc. for $C_{20}H_{32}B_1O_2$ $[M+H]^+$ 315.2495, found 315.2490. $[\alpha]^{20}_D$: +8.67 (c = 0.870, $CHCl_3$, *l* = 50 mm).

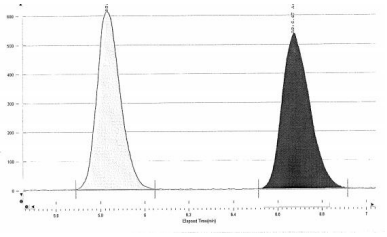
[74] Lurain, A. E.; Maestri, A.; Kelly, A. R.; Carroll, P. J.; Walsh, P. J. *J. Am. Chem. Soc*. **2004**, *126*, 13608-13609

Analysis of Stereochemistry:

The enantiomeric ratio was determined by chiral SFC analysis of the corresponding secondary allylic alcohol. The racemic alcohol was prepared analogously with racemic **1.79** and the corresponding geminal bis(boronate) according to *Method A*.

Chiral SFC (OD-H, Chiraldex, 3 mL/min, 7% ^{i}PrOH, 100 bar, 35 ^{o}C)-analysis of the reaction product.

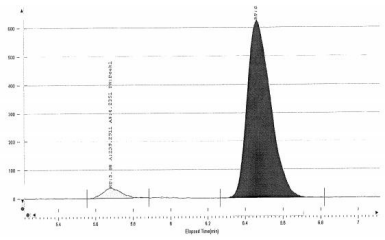
Racemic



Peak Info

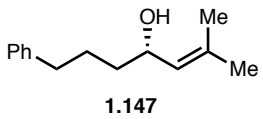
Peak No	% Area	Area	RT (min)	Height (mV)	K'
1	49.5817	4510.7816	5.83	611.7988	0.0069
2	50.4183	4586.8921	6.67	534.2568	0.0079
Total:	100	9097.6737			

Reaction product



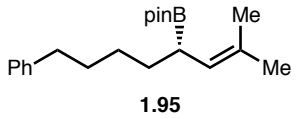
Peak Info

Peak No	% Area	Area	RT (min)	Height (mV)	K'
1	4.2351	239.2911	5.68	35.3769	0.0066
2	95.7649	5410.8592	6.46	624.9614	0.0076
Total:	100	5650.1503			



1.147

(*S*)-2-Methyl-7-phenylhept-2-en-4-ol (1.147). The reaction was performed according to the *Representative Procedure (Method E).* The crude mixture was purified by silica gel chromatography (20% ethyl acetate/hexanes, stain in CAM) to afford a clear, colorless oil. R_f = 0.5 in 20% ethyl acetate/hexanes on TLC. ^{1}H-NMR (500 MHz, $CDCl_3$) δ 7.26-7.29 (m, 2H), 7.16-7.19 (m, 3H), 5.16 (d, *J* = 8.5 Hz, 1H), 4.36 (m, 1H), 2.63 (t, *J* = 7.0 Hz, 2H), 1.72 (s, 3H), 1.59-1.69 (m, 6H), 1.44-1.51 (m, 1H), 1.26 (d, *J* = 3.0 Hz, 1H). ^{13}C-NMR (125 MHz, $CDCl_3$) δ 142.58, 135.41, 128.56, 128.42, 128.24, 125.85, 68.72, 37.43, 36.03, 27.43, 25.92, 18.39. IR (neat) ν_{max} 3358 (br), 3063 (w), 3026 (m), 2923 (s), 2855 (s), 1673 (m), 1584 (m), 1553 (m), 1496 (s), 1452 (s), 1375 (s), 1056 (s), 985 (s), 747 (s), 698 (s). HRMS (ESI) calc. for $C_{14}H_{19}$ [M+H-H_2O]$^+$ 187.1486, found 187.1480. $[\alpha]^{20}_D$: -6.53 (c = 0.575, $CHCl_3$, *l* = 50 mm).



1.95

(*S*)-4,4,5,5-Tetramethyl-2-(2-methyl-8-phenyloct-2-en-4-yl)-1,3,2-dioxaborolane (1.95) The reaction was performed according to the *Representative Procedure (Method D).* The crude mixture was purified by silica gel chromatography (20% CH_2Cl_2/hexanes, stain in CAM) to afford a clear, colorless oil (26.3mg, 80%). R_f = 0.8 in 50% CH_2Cl_2/hexanes on TLC. ^{1}H-NMR (500 MHz, $CDCl_3$) δ 7.24-7.27 (m, 2H), 7.14-7.17 (m, 3H), 5.03 (d, *J* = 9.0 Hz, 1H), 2.54-2.63 (m, 2H), 1.91-1.95 (q, *J* = 8.0 Hz, 1H), 1.69 (s, 3H), 1.51-1.63 (m, 5H), 1.25-1.44 (m, 4H), 1.21 (s, 6H), 1.19 (s, 6H). ^{13}C-NMR (125 MHz, $CDCl_3$) δ 143.06, 130.76, 128.56, 128.31, 125.63, 125.50, 83.00, 36.05, 31.68, 31.64, 29.01, 25.99, 24.85, 24.67, 18.29. ^{11}B-NMR (160 MHz, $CDCl_3$) δ 33.01. IR (neat) ν_{max} 3026 (w), 2976 (s), 2925 (s), 2855 (s), 1604 (w), 1453 (m), 1370 (s), 1316 (s), 1266 (m), 1214 (m), 1143 (s), 1107 (m), 967 (m), 838 (m) 746 (m),

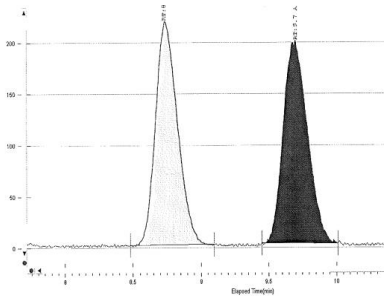
698 (s). HRMS (ESI) calc. for $C_{21}H_{34}B_1O_2$ $[M+H]^+$ 329.2651, found 329.2664. $[\alpha]^{20}_D$: +10.7 (c = 0.680, $CHCl_3$, *l* = 50 mm).

Analysis of Stereochemistry:

The enantiomeric ratio was determined by chiral SFC analysis of the corresponding secondary allylic alcohol. The racemic alcohol was prepared analogously with racemic **1.79** and the corresponding geminal bis(boronate) according to *Method A*.

Chiral SFC (OD-H, Chiraldex, 3 mL/min, 5% ^{i}PrOH, 100 bar, 35 ^{o}C)-analysis of the reaction product.

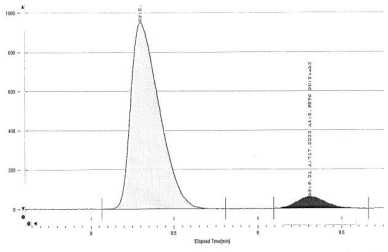
Racemic



Peak Info

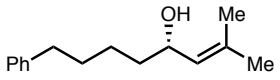
Peak No	% Area	Area	RT (min)	Height (mV)	K'
1	49.7522	2430.8773	8.73	217.4886	0.0126
2	50.2478	2455.0913	9.7	196.8144	0.014
Total:	100	4885.9686			

Reaction product



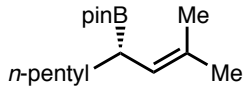
Peak Info

Peak No	% Area	Area	RT (min)	Height (mV)	K'
1	94.0104	11257.0005	8.3	949.3018	0.0093
2	5.9896	717.2033	9.31	60.5243	0.0104
Total:	100	11974.2038			



1.148

(*S*)-2-Methyl-8-phenyloct-2-en-4-ol (1.148) The reaction was performed according to the *Representative Procedure (Method E)*. The crude mixture was purified by silica gel chromatography (20% ethyl acetate/hexanes, stain in CAM) to afford a clear, colorless oil. R_f = 0.5 in 20% ethyl acetate/hexanes on TLC. ^{1}H-NMR (500 MHz, $CDCl_3$) δ 7.26-7.29 (m, 2H), 7.17-7.19 (m, 3H), 5.16 (d, *J* = 8.5 Hz, 1H), 4.31-4.36 (m, 1H), 2.60-2.63 (t, *J* = 8.5 Hz, 2H), 1.72 (s, 3H), 1.59-1.68 (m, 6H), 1.31-1.50 (m, 3H), 1.28 (d, *J* = 3.5 Hz, 1H). ^{13}C-NMR (125 MHz, $CDCl_3$) δ 142.81, 135.31, 128.54, 128.40, 128.35, 125.78, 68.80, 37.68, 36.10, 31.65, 25.92, 25.33, 18.37. IR (neat) ν_{max} 3344 (br), 3063 (w), 3026 (m), 2927 (s), 2855 (s), 1673 (m), 1603 (m), 1495 (m), 1452 (s), 1375 (m), 1051 (s), 999 (s), 840 (m), 745 (s), 697 (s), 510 (m). HRMS (ESI) calc. for $C_{12}H_{21}$ $[M+H-H_2O]^+$ 201.1643, found 201.1653. $[\alpha]^{20}_D$: -10.1 (c = 0.440, $CHCl_3$, *l* = 50 mm).



1.96

(*S*)-4,4,5,5-Tetramethyl-2-(2-methylnon-2-en-4-yl)-1,3,2-dioxaborolane (1.96) The reaction was performed according to the *Representative Procedure (Method D)*. The crude mixture was purified by silica gel chromatography (10% CH_2Cl_2/hexanes, stain in CAM) to afford a clear, colorless oil (17.6 mg, 66% yield). R_f = 0.7 in 50% CH_2Cl_2/hexanes on TLC. ^{1}H NMR (500 MHz, $CDCl_3$) δ 5.03 (d, *J* = 9.5 Hz, 1H), 1.92 (q, *J* = 7.5 Hz, 1H), 1.69 (s, 3H), 1.59 (s, 3H), 1.49 (m, 1H), 1.36-1.28 (m, 19H), 0.86 (t, *J* = 6.5 Hz, 3H). ^{13}C NMR (125 MHz, $CDCl_3$) δ 130.60, 125.68, 82.97, 32.11, 31.77, 29.06, 25.99, 24.88, 24.69, 22.76, 18.29, 14.21. ^{11}B NMR (160 MHz, $CDCl_3$) δ 33.01. IR (neat) ν_{max} 2976 (w), 2960 (w), 2923 (m), 2855 (w), 1458 (w), 1369 (m), 1314 (s), 1269 (w), 1215 (w), 1142 (s), 967 (m), 881 (w), 836 (m), 672 (w) cm^{-1}.

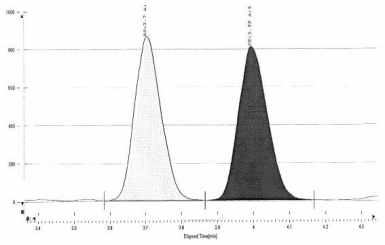
HRMS (ESI+) calc. for $C_{16}H_{32}BO_2$ $[M+H]^+$ 267.2495, found 267.2492. $[\alpha]^{20}_D$: +14.7 (c = 0.875, $CHCl_3$, *l* =50 mm).

Analysis of Stereochemistry:

The enantiomeric ratio was determined by chiral SFC analysis of the corresponding secondary homoallylic alcohol. The racemic alcohol was prepared analogously with racemic **1.79** and the corresponding geminal bis(boronate) according to *Methods A* and *F*.

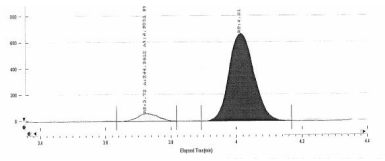
Chiral SFC (OD-H, Chiraldex, 3 mL/min, 7% ^{i}PrOH, 100 bar, 35 ^{o}C)-analysis of the reaction product.

Racemic

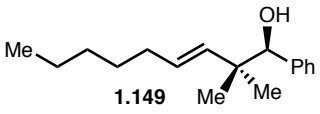


Peak Info					
Peak No	% Area	Area	RT (min)	Height (mV)	K'
1	49.3209	4404.786	3.7	861.5076	0.006
2	50.6791	4526.0804	3.99	809.8917	0.0064
Total:	100	8930.8664			

Reaction product

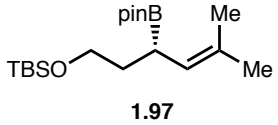


Peak Info					
Peak No	% Area	Area	RT (min)	Height (mV)	K'
1	6.9031	264.3612	3.72	60.1114	0.0046
2	93.0969	3565.2192	4.01	669.7593	0.0049
Total:	100	3829.5804			



1.149

(*R*,*E*)-2,2-Dimethyl-1-phenylnon-3-en-1-ol (1.149) The reaction was performed according to the *Representative Procedure (Method F).* The crude mixture was purified by silica gel chromatography (20% CH_2Cl_2/pentanes, stain in CAM) to afford a colorless oil. R_f = 0.1 in 20% CH_2Cl_2/pentanes on TLC. ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.31-7.23 (m, 5H), 5.49-5.46 (m, 2H), 4.38 (d, *J* = 2.5 Hz, 1H), 2.08-2.02 (m, 3H), 1.41-1.24 (m, 6H), 0.99 (s, 3H), 0.93 (s, 3H), 0.90 (t, *J* = 7.5 Hz, 3H). ^{13}C NMR (125 MHz, $CDCl_3$) δ 141.01, 136.61, 130.56, 127.99, 127.54, 127.41, 80.95, 41.63, 33.00, 31.58, 29.41, 25.29, 22.68, 21.74, 14.21. IR (neat) ν_{max} 3460 (br), 3063 (w), 3028 (w), 2957 (s), 2925 (s), 2855 (m), 1453 (m), 1380 (w), 1186 (w), 1041 (m), 979 (m), 740 (m), 701 (s) cm^{-1}. HRMS (ESI+) calc. for $C_{17}H_{25}$ $[M+H-H_2O]^+$ 229.1956, found 229.1958. $[\alpha]^{20}_D$: +39.7 (c = 0.375, $CHCl_3$, *l* =50 mm).



1.97

(*S*)-*tert*-Butyldimethyl((5-methyl-3-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)hex-4-en-1-yl)oxy)silane (1.97) The reaction was performed according to the *Representative Procedure (Method D).* The crude mixture was purified by silica gel chromatography (40% CH_2Cl_2/hexanes, stain in CAM) to afford a clear, colorless oil (22.0 mg, 62% yield). R_f = 0.5 in 50% CH_2Cl_2/hexanes on TLC. ^{1}H NMR (500 MHz, $CDCl_3$) δ 5.01 (d, *J* = 9.5 Hz, 1H), 3.56 (m, 2H), 2.03 (q, *J* = 8.5 Hz, 1H), 1.75 (tt, *J* = 13.5, 7.0 Hz, 1H), 1.68 (s, 3H), 1.62-1.50 (m, 4H), 1.22 (s, 6H), 1.21 (s, 6H), 0.88 (s, 9H), 0.03 (s, 6H). ^{13}C NMR (125 MHz, $CDCl_3$) δ 131.29, 124.79, 83.05, 62.75, 34.63, 26.15, 25.96, 24.87, 24.68, 18.53, 18.31, -5.11, -5.13. ^{11}B NMR (160 MHz, $CDCl_3$) δ 32.95. IR (neat) ν_{max} 2976 (w), 2956 (m), 2928 (s), 2857 (s), 1471 (m), 1360 (s), 1315 (s), 1252 (s), 1143 (s), 1093 (s), 1005 (m), 935 (m), 833 (s), 773 (s), 664 (m) cm^{-1}. HRMS

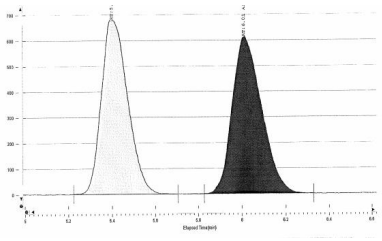
(ESI+) calc. for $C_{19}H_{40}BO_3Si$ $[M+H]^+$ 355.2839, found 355.2843. $[\alpha]^{20}_D$: +21.6 (c = 1.05, $CHCl_3$, *l* =50 mm).

Analysis of Stereochemistry:

The enantiomeric ratio was determined by chiral SFC analysis of the corresponding secondary homoallylic alcohol. The racemic alcohol was prepared analogously with racemic **1.79** and the corresponding geminal bis(boronate) according to *Methods A* and *F*.

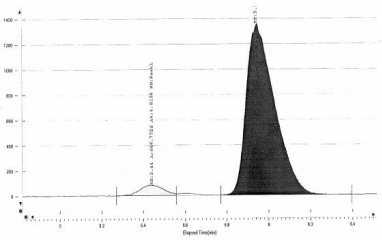
Chiral SFC (OD-H, Chiraldex, 3 mL/min, 5% ^{i}PrOH, 100 bar, 35 ^{o}C)-analysis of the reaction product.

Racemic

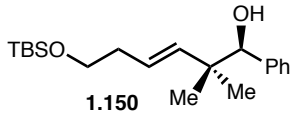


Peak Info					
Peak No	% Area	Area	RT (min)	Height (mV)	K'
1	49.8617	5691.7632	5.4	678.3895	0.006
2	50.1383	5723.3385	6.01	611.5664	0.0067
Total:	100	11415.1017			

Reaction product

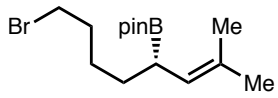


Peak Info					
Peak No	% Area	Area	RT (min)	Height (mV)	K'
1	4.8138	646.7726	5.44	82.5489	0.0058
2	95.1862	12788.9862	5.94	1352.7745	0.0063
Total:	100	13435.7588			



1.150

(*R*,*E*)-6-((*tert*-Butyldimethylsilyl)oxy)-2,2-dimethyl-1-phenylhex-3-en-1-ol (1.150) The reaction was performed according to the *Representative Procedure (Method F).* The crude mixture was purified by silica gel chromatography (3% ethyl acetate/hexanes, stain in CAM) to afford a clear, colorless oil. R_f = 0.3 in 5% ethyl acetate/hexanes on TLC. ^{1}H NMR (500 MHz, $CDCl_3$) 7.33-7.23 (m, 5H), 5.54 (d, *J* = 16.5 Hz, 1H), 5.48 (dt, *J* = 16.0, 7.0 Hz, 1H), 4.37 (d, *J* = 3.0 Hz, 1H), 3.65 (t, *J* = 7.0 Hz, 2H), 2.29 (q, *J* = 6.5 Hz, 2H), 2.12 (d, *J* = 3.0 Hz, 1H), 1.00 (s, 3H), 0.93 (s, 3H), 0.90 (s, 9H), 0.06 (s, 6H). ^{13}C NMR (125 MHz, $CDCl_3$) δ 140.96, 138.90, 128.00, 127.55, 127.43, 126.85, 80.81, 63.15, 41.80, 36.64, 26.14, 25.17, 21.55, 18.55, -5.09. IR (neat) ν_{max} 3446 (br), 3086 (w), 3028 (m), 2955 (s), 2928 (s), 2857 (s), 1493 (m), 1384 (m), 1360 (m), 1254 (s), 1187 (m), 1097 (s), 1044 (m), 834 (s), 775 (s), 702 (m) cm^{-1}. HRMS (ESI+) calc. for $C_{20}H_{33}OSi$ $[M+H-H_2O]^+$ 317.2301, found 317.2317. $[\alpha]^{20}_D$: +40.0 (c = 0.470, $CHCl_3$, *l* =50 mm).



1.99

(*S*)-2-(8-Bromo-2-methyloct-2-en-4-yl)-4,4,5,5-tetramethyl-1,3,2-dioxaborolane (1.99) The reaction was performed according to the *Representative Procedure (Method D).* The crude mixture was purified by silica gel chromatography (20% CH_2Cl_2/hexanes, stain in CAM) to afford a clear, colorless oil (17.2 mg, 52% yield). R_f = 0.7 in 50% CH_2Cl_2/hexanes on TLC. ^{1}H NMR (500 MHz, $CDCl_3$) δ 5.01 (d, *J* = 9.5 Hz, 1H), 3.39 (t, *J* = 6.5 Hz, 2H), 1.93 (q, *J* = 7.5 Hz, 1H), 1.84 (p, *J* = 6.5 Hz, 2H), 1.69 (s, 3H), 1.60 (s, 3H), 1.58-1.33 (m, 4H), 1.23 (s, 6H), 1.22 (s, 6H). ^{13}C NMR (125 MHz, $CDCl_3$) δ 131.00, 124.89, 82.95, 33.94, 32.92, 30.66, 27.73, 25.83, 24.73, 24.53, 18.16. ^{11}B NMR (160 MHz, $CDCl_3$) δ 32.93. IR (neat) ν_{max} 2977 (s), 2927 (s), 2856

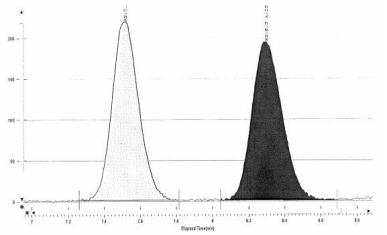
(m), 1447 (w), 1370 (s), 1318 (s), 1272 (m), 1213 (w), 1144 (s), 1106 (w), 968 (m), 837 (m), 684 (w) cm^{-1}. HRMS (ESI+) calc. for $C_{15}H_{29}BBrO_2$ $[M+H]^+$ 331.1444, found 331.1437. $[\alpha]^{20}_D$: +15.5 (c = 0.580, $CHCl_3$, *l* =50 mm).

Analysis of Stereochemistry:

The enantiomeric ratio was determined by chiral SFC analysis of the corresponding secondary homoallylic alcohol. The racemic alcohol was prepared analogously with racemic **1.79** and the corresponding geminal bis(boronate) according to *Methods A* and *F*.

Chiral SFC (OD-H, Chiraldex, 3 mL/min, 7% ^{i}PrOH, 100 bar, 35 ^{o}C)-analysis of the reaction product.

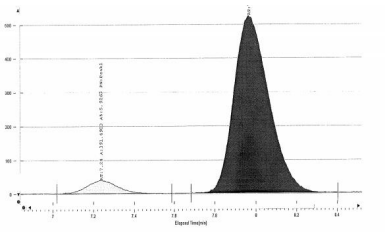
Racemic



Peak Info

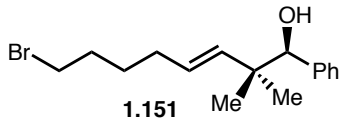
Peak No	% Area	Area	RT (min)	Height (mV)	K'
1	49.8344	2250.631	7.52	218.3679	0.0068
2	50.1656	2265.5901	8.3	194.2613	0.0075
Total:	100	4516.2211			

Reaction product



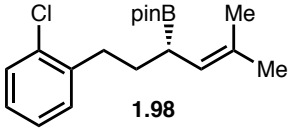
Peak Info

Peak No	% Area	Area	RT (min)	Height (mV)	K'
1	5.9263	391.4903	7.24	38.8167	0.0068
2	94.0737	6214.4968	7.97	523.5658	0.0075
Total:	100	6605.9871			



1.151

(*R,E*)-8-Bromo-2,2-dimethyl-1-phenyloct-3-en-1-ol (1.151) The reaction was performed according to the *Representative Procedure (Method F).* The crude mixture was purified by silica gel chromatography (3% ethyl acetate/hexanes, stain in CAM) to afford a clear, colorless oil. R_f = 0.2 in 5% ethyl acetate/hexanes on TLC. ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.33-7.24 (m, 5H), 5.52 (d, *J* = 15.5 Hz, 1H), 5.42 (dt, *J* = 16.0, 7.0 Hz, 1H), 4.40 (d, *J* = 2.0 Hz, 1H), 3.41 (t, *J* = 7.0 Hz, 2H), 2.09 (q, *J* = 6.5 Hz, 2H), 1.98 (d, *J* = 3.0 Hz, 1H), 1.86 (p, *J* = 7.0 Hz, 2H), 1.56-1.48 (m, 2H), 1.00 (s, 3H), 0.94 (s, 3H). ^{13}C NMR (125 MHz, $CDCl_3$) δ 141.08, 137.47, 129.16, 127.95, 127.60, 127.50, 81.10, 41.62, 33.87, 32.38, 32.08, 28.17, 25.12, 22.04. IR (neat) ν_{max} 3455 (br), 3085 (w), 3062 (w), 3028 (w), 2960 (s), 2928 (s), 2856 (m), 1729 (w), 1585 (w), 1492 (w), 1452 (s), 1362 (m), 1249 (m), 1186 (m), 1082 (w), 1040 (s), 1003 (m), 978 (s), 740 (s), 702 (s) cm^{-1}. HRMS (ESI+) calc. for $C_{16}H_{22}Br$ $[M+H-H_2O]^+$ 293.0905, found 293.0905. $[\alpha]^{20}_D$: +32.4 (c = 0.200, $CHCl_3$, *l* =50 mm).



1.98

(*S*)-2-(1-(2-Chlorophenyl)-5-methylhex-4-en-3-yl)-4,4,5,5-tetramethyl-1,3,2-dioxaborolane (1.98) The reaction was performed according to the *Representative Procedure (Method C).* The crude mixture was purified by silica gel chromatography (30% DCM/hexanes, stain in CAM) to afford a clear, colorless oil (28.3 mg, 85% yield). R_f = 0.3 in 50% DCM/hexanes on TLC. ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.30 (d, *J* = 8.0 Hz, 1H), 7.19 (dd, *J* = 7.0, 1.5 Hz, 1H), 7.15 (t, *J* = 7.5, 1H), 7.09 (dt, *J* = 7.0, 2.0 Hz, 1H), 5.11 (dd, *J* = 9.5, 1.5 Hz, 1H), 2.77 (ddd, *J* = 14.0, 11.0, 5.5 Hz, 1H), 2.64 (ddd, *J* = 13.5, 11.0, 5.5 Hz, 1H), 2.02 (q, *J* = 8.5 Hz, 1H), 1.83 (ddt, *J* = 12.0, 10.0, 5.5 Hz, 1H), 1.73 (s, 3H), 1.71–1.60 (m, 4H), 1.24 (s, 6H), 1.23 (s, 2H). ^{13}C

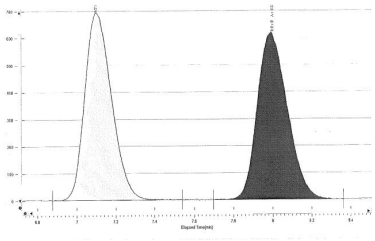
NMR (125 MHz, $CDCl_3$) δ 140.57, 134.06, 131.49, 130.57, 129.47, 127.14, 126.73, 124.92, 83.15, 33.30, 31.74, 26.02, 24.93, 24.71, 18.38. ^{11}B NMR (160 MHz, $CDCl_3$) δ 32.97. IR (neat) ν_{max} 3066 (w), 2976 (m), 2925 (m), 2858 (m), 1572 (w), 1474 (m), 1443 (m), 1370 (s), 1341 (s), 1317 (s), 1268 (m), 1244 (m), 1215 (m), 1165 (m), 1141 (s), 1102 (m), 1053 (m), 986 (w), 876 (w), 855 (w), 838 (w), 750 (s), 679 (m) cm^{-1}. HRMS (ESI+) calc. for $C_{19}H_{29}BClO_2$ $[M+H]^+$ 335.1949, found 335.1945. $[\alpha]^{20}_D$: +2.70 c = 1.130, $CHCl_3$, *l* =50 mm).

Analysis of Stereochemistry:

The enantiomeric ratio was determined by chiral SFC analysis of the corresponding secondary allylic alcohol. The racemic alcohol was prepared analogously with racemic **1.79** and the corresponding geminal bis(boronate) according to *Method A.*

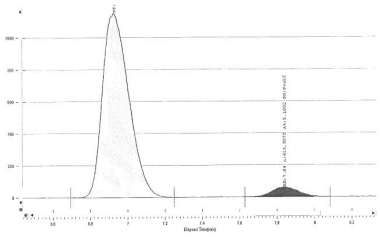
Chiral SFC (OD-H, Chiraldex, 3 mL/min, 7% ^{i}PrOH, 100 bar, 35 ^{o}C)-analysis of the reaction product.

Racemic



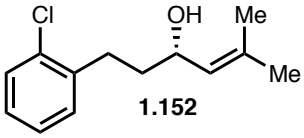
Peak Info					
Peak No	% Area	Area	RT (min)	Height (mV)	K'
1	49.9825	6589.0133	7.1	690.7413	0.0075
2	50.0175	6593.6248	8	617.5016	0.0084
Total:	100	13182.6381			

Reaction product



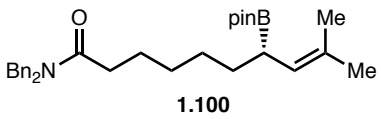
Peak Info

Peak No	% Area	Area	RT (min)	Height (mV)	K'
1	94.8198	11255.4809	6.93	1152.1104	0.0071
2	5.1802	614.9075	7.84	61.8495	0.008
Total:	100	11870.3884			



1.152

(*S*)-1-(2-Chlorophenyl)-5-methylhex-4-en-3-ol (1.152) The reaction was performed according to the *Representative Procedure (Method D).* The crude mixture was purified by silica gel chromatography (20% ethyl acetate/hexanes, stain in CAM) to afford a clear, colorless oil. R_f = 0.3 in 7/2/1 hexanes/CH_2Cl_2/ethyl acetate on TLC. ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.33 (dd, *J* = 7.0, 1.0 Hz, 1H), 7.23 (dd, *J* = 7.0, 1.5 Hz, 1H), 7.18 (dt, *J* = 7.0, 1.0 Hz, 1H), 7.13 (dt, *J* = 8.0, 2.0 Hz, 1H), 5.23 (dt, *J* = 9.0, 1.5 Hz, 1H), 4.42 (dtd, J = 10.2, 6.6, 3.6 Hz, 1H), 2.85-2.71 (m, 2H), 2.00 (t, J = 7.2 Hz, 2H), 1.91 (ddt, J = 12.6, 9.6, 6.0 Hz, 1H), 1.76 (ddt, J = 11.4, 9.6, 5.4 Hz, 1H), 1.66 (s, 3H), 1.41 (p, J = 7.2 Hz, 2H), 1.37 (d, J = 7.8 Hz, 1H), 1.32-1.24 (m, 6H), 0.88 (t, J = 7.2 Hz, 3H). ^{13}C NMR (125 MHz, $CDCl_3$) δ 139.81, 135.86, 134.09, 130.45, 129.60, 127.93, 127.40, 126.88, 68.41, 37.55, 29.83, 25.92, 18.41 IR (neat) ν_{max} 3347 (br), 3066 (w), 3014 (w), 2967 (m), 2928 (m), 2863 (w), 1675 (w), 1571 (w), 1474 (m), 1443 (m), 1376 (w), 1051 (s), 1035 (m), 1003 (w), 9112 (w), 844 (w), 823 (w), 750 (s), 681 (w) cm^{-1}. HRMS (ESI+) calc. for $C_{13}H_{16}Cl$ $[M+H-H_2O]^+$ 207.0941, found 207.0938. $[\alpha]^{20}_D$: -34.8 (c = 0.680, $CHCl_3$, *l* =50 mm).



1.100

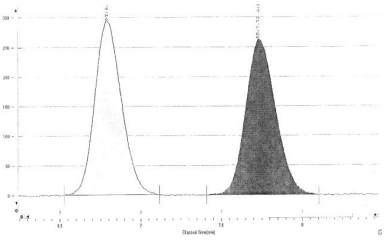
(*S*)-*N*,*N*-Dibenzyl-9-methyl-7-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)dec-8-enamide (1.100) The reaction was performed according to the *Representative Procedure (Method D).* The crude reaction mixture was purified by column chromatography on SiO_2 (10% ethyl acetate in hexanes, stain in CAM) to afford an inseparable mixture of the title compound and protodeboration of the geminal bis(boronate) **1.140**. The mixture was oxidized according to the *Representative Procedure (Method E)* to **1.153** as follows.

Analysis of Stereochemistry:

The enantiomeric ratio was determined by chiral SFC analysis of the corresponding secondary allylic alcohol. The racemic alcohol was prepared analogously with racemic **1.79** and the corresponding geminal bis(boronate) according to *Method A.*

Chiral SFC (AD-H, Chiraldex, 3 mL/min, 20% MeOH, 100 bar, 35 ^{o}C)-analysis of the reaction product.

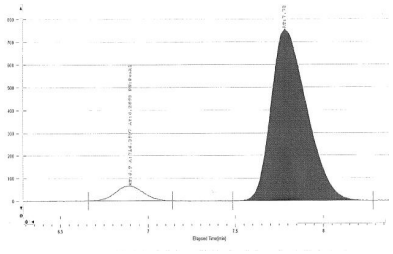
Racemic



Peak Info

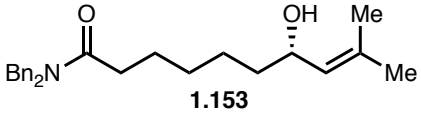
Peak No	% Area	Area	RT (min)	Height (mV)	K'
1	49.8147	3381.5262	6.79	294.5873	0.0112
2	50.1853	3406.6783	7.73	262.9152	0.0127
Total:	100	6788.2045			

Reaction product



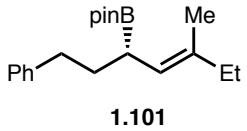
Peak Info

Peak No	% Area	Area	RT (min)	Height (mV)	K'
1	6.2895	716.3997	6.9	65.375	0.0085
2	93.7105	10673.9495	7.78	756.9625	0.0096
Total:	100	11390.3492			



1.153

(*S*)-*N*,*N*-Dibenzyl-7-hydroxy-9-methyldec-8-enamide (1.153). The reaction was performed according to the *Representative Procedure (Method E)*. The crude reaction mixture was purified by column chromatography on SiO_2 (25% ethyl acetate in hexanes, stain in CAM) to afford a clear, colorless oil. R_f = 0.29 in 40% ethyl acetate/hexanes on TLC. ^{1}H-NMR (500 MHz, $CDCl_3$) δ 7.35-7.38 (t, *J* = 6.5 Hz, 2H), 7.28-7.32 (m, 4H), 7.21 (d, *J* = 7.0 Hz, 2H), 7.15 (d, *J* = 7.0 Hz, 2H), 5.14 (d, *J* = 9.0 Hz, 1H), 4.60 (s, 2H), 4.44 (s, 2H), 4.31 (q, *J* = 6.5 Hz, 1H), 2.41 (t, *J* = 7.5 Hz, 2H), 1.70-1.75 (m, 1H) 1.72 (s, 3H), 1.67 (s, (3H), 1.60-1.54 (m, 1H), 1.26-1.43 (m, 7H). ^{13}C-NMR (125 MHz, $CDCl_3$) δ 173.76, 137.70, 136.80, 135.26, 129.08, 128.73, 128.44, 128.33, 127.72, 127.50, 126.51, 68.78, 50.04, 48.24, 37.71, 33.31, 29.53, 25.92, 25.53, 25.41, 18.39. IR (neat) ν_{max} 3422 (br), 3062 (w), 3029 (w), 2926 (s), 2855 (m), 2363 (w), 2341 (w), 1637 (s), 1494 (m), 1451 (s), 1361 (m), 1301 (w), 1215 (m), 1077 (m), 1011 (m), 954 (w), 732 (m), 699 (s). HRMS (ESI) calc. for $C_{25}H_{33}NO$ $[M+H-H_2O]^+$ 362.2484, found 362.2472. $[\alpha]^{20}_D$: -11.4 (c = 0.280, $CHCl_3$, *l* = 50 mm).



1.101

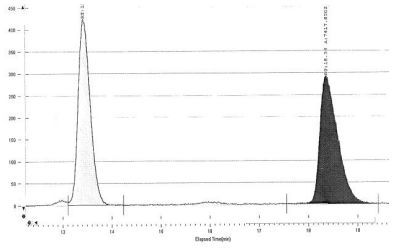
(*S*)-4,4,5,5-Tetramethyl-2-(5-methyl-1-phenylhex-4-en-3-yl)-1,3,2-dioxaborolane (1.101) The reaction was performed according to the *Representative Procedure (Method D).* The crude mixture was purified by silica gel chromatography (30% CH_2Cl_2/hexanes, stain in CAM) to afford a clear, colorless oil (25.2 mg, 80% yield). R_f = 0.6 in 50% CH_2Cl_2/hexanes on TLC. ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.29-7.23 (m, 2H), 7.20-7.13 (m, 3H), 5.08 (d, *J* = 10.0 Hz, 1H), 2.65 (ddd, *J* = 13.5, 10.0, 5.0 Hz, 1H), 2.54 (ddd, *J* = 14.0, 10.5, 6.0 Hz, 1H), 2.06-1.96 (m, 3H), 1.85 (ddt, *J* = 13.5, 10.5, 6.5 Hz, 1H), 1.69 (ddt, *J* = 13.5, 8.5, 5.0 Hz, 1H), 1.60 (s, 3H), 1.23 (s, 6H), 1.22 (s, 6H), 1.00 (t, *J* = 7.5 Hz, 3H). ^{13}C NMR (125 MHz, $CDCl_3$) δ 143.06, 137.01, 128.64, 128.32, 125.64, 123.72, 83.04, 35.64, 33.65, 32.79, 24.88, 24.65, 16.48, 13.34. ^{11}B NMR (160 MHz, $CDCl_3$) δ 32.92. IR (neat) ν_{max} 3084 (w), 3063 (w), 3026 (w), 2975 (s), 2926 (s), 2855 (m), 1739 (w), 1604 (w), 1496 (w), 1455 (m), 1370 (s), 1317 (s), 1270 (m), 1192 (m), 1143 (s), 1108 (m), 1072 (w), 967 (m), 876 (w), 847 (m), 748 (m), 699 (s) cm^{-1}. HRMS (ESI+) calc. for $C_{20}H_{32}BO_2$ $[M+H]^+$ 315.2495, found 315.2499. $[\alpha]^{20}_D$: +3.21 (c = 0.650, $CHCl_3$, *l* =50 mm).

Analysis of Stereochemistry:

The enantiomeric ratio was determined by chiral SFC analysis of the corresponding secondary allylic alcohol. The racemic alcohol was prepared analogously with racemic **1.79** and the vinyl bromide **1.141** according to *Method A*.

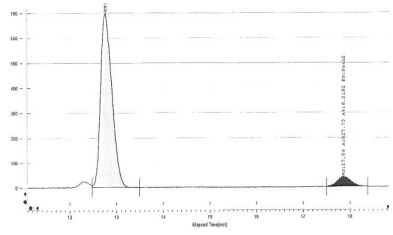
Chiral SFC (OD-H, Chiraldex, 3 mL/min, 3% ^{i}PrOH, 100 bar, 35 ^{o}C)-analysis of the reaction product.

Racemic

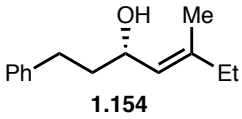


Peak Info					
Peak No	% Area	Area	RT (min)	Height (mV)	K'
1	49.5242	7277.9925	13.42	423.4229	0.0183
2	50.4758	7417.8502	18.36	291.7892	0.0251
Total:	100	14695.8427			

Reaction product



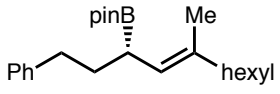
Peak Info					
Peak No	% Area	Area	RT (min)	Height (mV)	K'
1	93.4818	11871.0159	12.76	702.5557	0.0172
2	6.5182	827.73	17.86	40.9241	0.024
Total:	100	12698.7459			



1.154

(*S*,*E*)-5-Methyl-1-phenylhept-4-en-3-ol (1.154) The reaction was performed according to the *Representative Procedure (Method E).* The crude mixture was purified by silica gel chromatography (20% ethyl acetate/hexanes, stain in CAM) to afford a clear, colorless oil. R_f = 0.3 in 7/2/1 hexanes/CH_2Cl_2/ethyl acetate on TLC. ^{1}H NMR (500 MHz, $CDCl_3$) 7.30-7.25 (m, 2H), 7.22-7.16 (m, 3H), 5.21 (dd, *J* = 8.5, 1.0 Hz, 1H), 4.40 (dq, *J* = 9.5, 3.0 Hz, 1H), 2.74-2.61 (m, 2H), 2.03 (q, *J* = 7.5 Hz, 2H), 1.93 (ddt, *J* = 13.0, 9.5, 6.5 Hz, 1H), 1.77 (ddt, *J* = 12.5, 10.0, 6.0 Hz, 1H), 1.66 (s, 3H), 1.33 (d, *J* = 3.0 Hz, 1H), 1.02 (t, *J* = 7.5 Hz, 3H). ^{13}C NMR (125 MHz, $CDCl_3$) δ 142.23, 141.05, 128.53, 128.47, 126.40, 125.89, 68.25, 39.36, 32.39, 31.98, 16.72, 12.62.

IR (neat) ν_{max} 3258 (br), 3024 (w), 3000 (w), 2948 (m), 2926 (m), 2880 (w), 2834 (w), 1608 (m), 1510 (s), 1445 (m), 1341 (w), 1301 (m), 1243 (s), 1176 (m), 1023 (m), 1002 (m), 833 (m), 820 (m), 701 (m) cm^{-1}. HRMS (ESI+) calc. for $C_{14}H_{19}$ $[M+H-H_2O]^+$ 187.1487, found 187.1487. $[\alpha]^{20}_D$: -23.8 (c = 0.375, $CHCl_3$, *l* =50 mm).



1.102

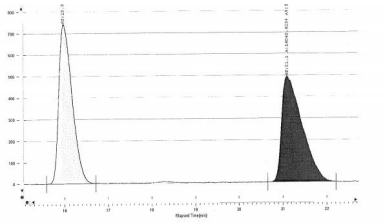
(*S,E*)-4,4,5,5-Tetramethyl-2-(5-methyl-1-phenylundec-4-en-3-yl)-1,3,2-dioxaborolane (1.102) The reaction was performed according to the *Representative Procedure (Method D).* The crude mixture was purified by silica gel chromatography (20% CH_2Cl_2/hexanes, stain in CAM) to afford a clear, colorless oil (32.2 mg, 87% yield). R_f = 0.6 in 50% CH_2Cl_2/hexanes on TLC. ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.28-7.22 (m, 2H), 7.18-7.13 (m, 3H), 5.07 (d, *J* = 9.5 Hz, 1H), 2.65 (ddd, *J* = 13.0, 10.0, 5.0 Hz, 1H), 2.52 (ddd, *J* = 13.5, 10.5, 6.0 Hz, 1H), 2.00 (m, 3H), 1.84 (ddt, *J* = 13.0, 10.0, 6.5 Hz, 1H), 1.68 (ddt, *J* = 14.5, 10.5, 5.5 Hz, 1H), 1.57 (s, 3H), 1.41-1.19 (m, 20H), 0.88 (t, *J* = 6.5 Hz, 3H). ^{13}C NMR (125 MHz, $CDCl_3$) δ 143.09, 135.29, 128.65, 128.32, 125.64, 125.00, 83.05, 40.00, 35.67, 33.68, 31.99, 28.96, 28.22, 24.90, 24.69, 22.85, 16.48, 14.29. ^{11}B NMR (160 MHz, $CDCl_3$) δ 33.08. IR (neat) ν_{max} 3085 (w), 3062 (w), 3026 (w), 2976 (m), 2957 (m), 2925 (s), 2856 (s), 1604 (w), 1496 (w), 1479 (m), 1370 (s), 1317 (s), 1269 (m), 1214 (m), 1143 (s), 1108 (m), 968 (m), 847 (m), 747 (m), 699 (s) cm^{-1}. HRMS (ESI+) calc. for $C_{24}H_{40}BO_2$ $[M+H]^+$ 371.3121, found 371.3124. $[\alpha]^{20}_D$: +6.60 (c = 1.39, $CHCl_3$, *l* =50 mm).

Analysis of Stereochemistry:

The enantiomeric ratio was determined by chiral SFC analysis of the corresponding secondary allylic alcohol. The racemic alcohol was prepared analogously with racemic **1.79** and the vinyl bromide **1.142** according to *Method A*.

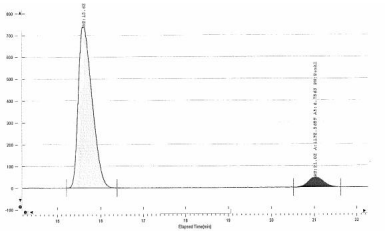
Chiral SFC (OD-H, Chiraldex, 3 mL/min, 4% ^{i}PrOH, 100 bar, 35 ^{o}C)-analysis of the reaction product.

Racemic

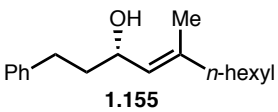


Peak Info					
Peak No	% Area	Area	RT (min)	Height (mV)	K'
1	49.6515	15818.3629	15.97	743.0835	0.0211
2	50.3485	16040.4234	21.1	492.201	0.0279
Total:	100	31858.7863			

Reaction Product



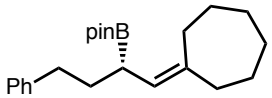
Peak Info					
Peak No	% Area	Area	RT (min)	Height (mV)	K'
1	93.2137	16380.625	15.62	739.3971	0.0203
2	6.7863	1192.5689	21.02	46.7032	0.0273
Total:	100	17573.1939			



1.155

(*S*,*E*)-5-Methyl-1-phenylundec-4-en-3-ol (1.155) The reaction was performed according to the *Representative Procedure (Method E)* without the need to first purify the allylic boronate by silica gel chromatography. The crude oxidation mixture was purified by silica gel chromatography (20% ethyl

acetate/hexanes, stain in CAM) to afford a clear, colorless oil (21.3 mg, 82% yield). R_f = 0.4 in 7/2/1 hexanes/CH_2Cl_2/ethyl acetate on TLC. ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.31-7.25 (m, 2H), 7.24-7.15 (m, 3H), 5.22 (d, *J* = 8.5 Hz, 1H), 4.39 (q, *J* = 7.0 Hz, 1H), 2.67 (m, 2H), 2.00 (t, *J* = 7.5 Hz, 2H), 1.93 (ddt, *J* = 13.5, 9.5, 6.5 Hz, 1H), 1.76 (ddt, *J* = 13.5, 10.0, 6.5 Hz, 1H), 1.64 (s, 3H), 1.45-1.24 (m, 9H), 0.89 (t, *J* = 5.5 Hz, 3H). ^{13}C NMR (125 MHz, $CDCl_3$) δ 142.24, 139.62, 128.53, 128.47, 127.59, 125.89, 68.26, 39.73, 39.37, 31.98, 31.88, 29.09, 27.84, 22.78, 16.71, 14.24. IR (neat) ν_{max} 3432 (br), 3084 (w), 3062 (w), 3026 (w), 2954 (m), 2925 (s), 2856 (s), 1667 (w), 1603 (w), 1495 (m), 1454 (s), 1379 (m), 1300 (w), 1272 (w), 1052 (m), 1030 (m), 1006 (m), 914 (w), 746 (m), 724 (m), 698 (s) cm^{-1}. HRMS (ESI+) calc. for $C_{18}H_{27}$ $[M+H-H_2O]^+$ 243.2113, found 243.2122. $[\alpha]^{20}_D$: -18.4 (c = 0.540, $CHCl_3$, *l* =50 mm).



1.103

(*S*)-2-(1-Cycloheptylidene-4-phenylbutan-2-yl)-4,4,5,5-tetramethyl-1,3,2-dioxaborolane (1.103) The reaction was performed according to the *Representative Procedure (Method D).* The crude mixture was purified by silica gel chromatography (30% CH_2Cl_2/hexanes, stain in CAM) to afford a clear, colorless oil (31.2 mg, 88% yield). R_f = 0.7 in 50% CH_2Cl_2/hexanes on TLC. ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.28-7.23 (m, 2H), 7.19-7.13 (m, 3H), 5.10 (d, *J* = 10 Hz), 1H), 2.67 (ddd, *J* = 13.5, 10.5, 5.5 Hz, 1H), 2.54 (ddd, *J* = 14.0, 11.0, 6.5 Hz, 1H), 2.22 (m, 4H), 1.99 (q, *J* = 9.0 Hz, 1H), 1.84 (ddt, *J* = 12.5, 10.0, 6.0 Hz, 1H), 1.69 (ddt, *J* = 14.0, 10.0, 5.5 Hz, 1H), 1.62-1.47 (m, 8H), 1.24 (s, 6H), 1.23 (s, 6H). ^{13}C NMR (125 MHz, $CDCl_3$) δ 143.05, 140.95, 128.64, 128.31, 125.64, 125.52, 83.04, 38.06, 35.73, 33.63, 30.65, 30.04, 30.03, 29.32, 27.13, 24.91, 24.69. ^{11}B NMR (160 MHz, $CDCl_3$) δ 33.85. IR (neat) ν_{max}

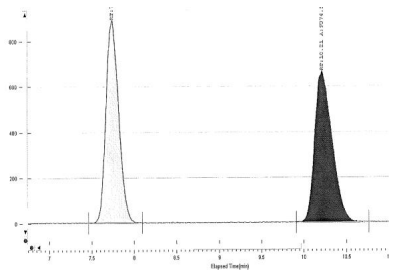
3084 (w), 3062 (w), 3026 (w), 2976 (m), 2921 (s), 2852 (m), 1603 (w), 1496 (w), 1454 (m), 1355 (s), 1316 (s), 1270 (m), 1214 (w), 1142 (s), 1106 (m), 967 (m), 852 (m), 837 (m), 748 (m), 699 (s) cm^{-1}. HRMS (ESI+) calc. for $C_{23}H_{36}BO_2$ $[M+H]^+$ 355.2808, found 355. 2805. $[\alpha]^{20}_D$: +15.3 (c = 1.28, $CHCl_3$, *l* =50 mm).

Analysis of Stereochemistry:

The enantiomeric ratio was determined by chiral SFC analysis of the corresponding secondary allylic alcohol. The racemic alcohol was prepared analogously with racemic **1.79** and the vinyl bromide **1.143** according to *Method A*.

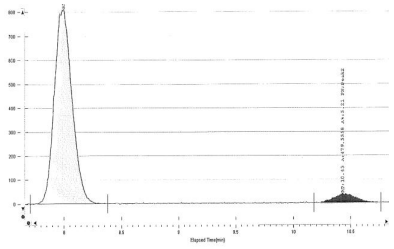
Chiral SFC (OD-H, Chiraldex, 3 mL/min, 10% ^{i}PrOH, 100 bar, 35 ^{o}C)-analysis of the reaction product.

Racemic

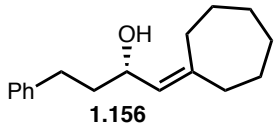


Peak Info					
Peak No	% Area	Area	RT (min)	Height (mV)	K'
1	49.7253	9272.1324	7.74	887.7173	0.0094
2	50.2747	9374.5651	10.21	662.7859	0.0123
Total:	100	18646.6975			

Reaction product

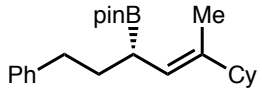


Peak Info					
Peak No	% Area	Area	RT (min)	Height (mV)	K'
1	94.79	8725.0498	8	811.7093	0.0098
2	5.21	479.5558	10.43	37.6452	0.0128
Total:	100	9204.6056			



1.156

(*S*)-1-Cycloheptylidene-4-phenylbutan-2-ol (1.156) The reaction was performed according to the *Representative Procedure (Method E)*. The crude mixture was purified by silica gel chromatography (20% ethyl acetate/hexanes, stain in CAM) to afford a clear, colorless oil. R_f = 0.4 in 7/2/1 hexanes/CH_2Cl_2/ethyl acetate on TLC. ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.30- 7.15 (m, 5H), 5.23 (d, *J* = 8.5 Hz, 1H), 4.39 (q, *J* = 7.0 Hz, 1H), 2.69 (m, 4H), 2.32-2.2 (m, 4H), 1.92 (ddt, *J* = 13.0, 10.0, 6.5 Hz, 1H), 1.76 (ddt, *J* = 13.5, 10.0, 6.0 Hz), 1.66-1.48 (m, 8H), 1.37 (s, 1H). ^{13}C NMR (125 MHz, $CDCl_3$) δ 145.28, 142.26, 128.52, 128.46, 128.20, 125.88, 67.90, 39.37, 37.97, 32.04, 30.32, 29.73, 29.13, 29.09, 27.48. IR (neat) ν_{max} 3420 (br), 3085 (w), 3061 (w), 3026 (w), 2920 (s), 2851 (s), 2676 (w), 1726 (w), 1655 (w), 1495 (m), 1453 (s), 1276 (w), 1179 (w), 1043 (s), 1030 (m), 996 (m), 914 (w), 746 (s), 698 (s) cm^{-1}. HRMS (ESI+) calc. for $C_{17}H_{23}$ $[M+H-H_2O]^+$ 227.1800, found 227.1801. $[\alpha]^{20}_D$: -34.6 (c = 0.635, $CHCl_3$, *l* =50 mm).



1.104

(*S,E*)-2-(5-Cyclohexyl-1-phenylhex-4-en-3-yl)-4,4,5,5-tetramethyl-1,3,2-dioxaborolane (1.104) The reaction was performed according to the *Representative Procedure (Method D)*. The crude mixture was purified by silica gel chromatography (30% CH_2Cl_2/hexanes, stain in CAM) to afford a clear, colorless oil (30.2 mg, 82% yield). R_f = 0.6 in 50% CH_2Cl_2/hexanes on TLC. ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.28-7.22 (m, 2H), 7.18-7.12 (m, 3H), 5.06 (d, *J* = 9.0 Hz, 1H), 2.64 (ddd, *J* = 14.5, 10.5, 5.5 Hz, 1H), 2.52 (ddd, *J* = 13.5, 10.5, 6.5 Hz, 1H), 1.99 (q, *J* = 9.0 Hz, 1H), 1.90-1.78 (m, 2H), 1.77-1.60 (m, 6H), 1.56 (s, 3H), 1.35-1.06 (m, 17H). ^{13}C NMR (125 MHz, $CDCl_3$) δ 143.07, 140.57, 128.67, 128.31, 125.64, 123.11, 82.99, 47.79,

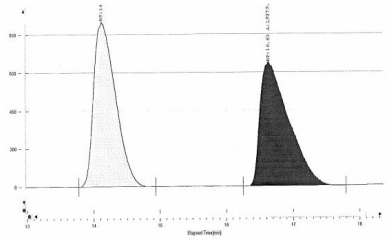
35.64, 33.58, 32.34, 32.30, 26.96, 26.58, 24.86, 24.61, 14.94. ^{11}B NMR (160 MHz, $CDCl_3$) δ 32.78. IR (neat) ν_{max} 3084 (w), 3062 (w), 3026 (w), 2977 (m), 2924 (s), 2852 (s), 1603 (w), 1496 (w), 1480 (m), 1370 (s), 1317 (s), 1270 (m), 1215 (w), 1143 (s), 987 (m), 844 (m), 748 (m), 699 (s) cm^{-1}. HRMS (ESI+) calc. for $C_{24}H_{38}BO_2$ $[M+H]^+$ 369.2965, found 369.2965. $[\alpha]^{20}_D$: +10.1 (c = 0.955, $CHCl_3$, *l* =50 mm).

Analysis of Stereochemistry:

The enantiomeric ratio was determined by chiral SFC analysis of the corresponding secondary allylic alcohol. The racemic alcohol was prepared analogously with racemic **1.96** and the vinyl bromide **1.144** according to *Method A*.

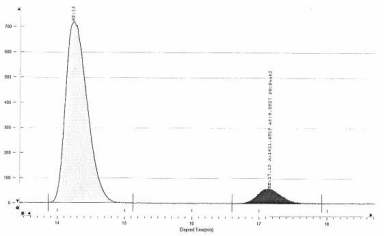
Chiral SFC (OD-H, Chiraldex, 3 mL/min, 6% ^{i}PrOH, 100 bar, 35 ^{o}C)-analysis of the reaction product.

Racemic



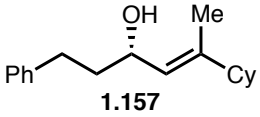
Peak Info					
Peak No	% Area	Area	RT (min)	Height (mV)	K'
1	50.33	19636.7296	14.12	870.4627	0.0175
2	49.67	19379.2032	16.63	651.6902	0.0206
Total:	100	39015.9328			

Reaction product



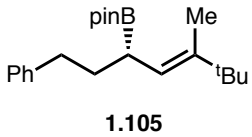
Peak Info

Peak No	% Area	Area	RT (min)	Height (mV)	K'
1	91.9193	16058.2004	14.22	719.351	0.0164
2	8.0807	1411.6929	17.15	59.3303	0.0198
Total:	100	17469.8933			



1.157

(*S*,*E*)-5-Cyclohexyl-1-phenylhex-4-en-3-ol (1.157) The reaction was performed according to the *Representative Procedure (Method E)*. The crude mixture was purified by silica gel chromatography (20% ethyl acetate/hexanes, stain in CAM) to afford a clear, colorless oil. R_f = 0.6 in 20% ethyl acetate/hexanes on TLC. ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.30-7.24 (m, 2H), 7.21-7.15 (m, 3H), 5.21 (d, *J* = 8.0 Hz, 1H), 4.39 (q, *J* = 7.0 Hz, 1H), 2.66 (m, 2H), 1.93 (ddt, *J* = 13.0, 9.5, 6.5 Hz, 1H), 1.85 (m, 1H), 1.81-1.64 (m, 6H), 1.62 (s, 3H), 1.36-1.09 (m, 6H). ^{13}C NMR (125 MHz, $CDCl_3$) δ 144.53, 142.26, 128.54, 128.47, 125.89, 125.88, 68.18, 47.37, 39.38, 31.99, 31.97, 26.80, 26.47, 15.19. IR (neat) ν_{max} 3329 (br), 3084 (w), 3062 (w), 3026 (w), 2924 (s), 2852 (s), 1662 (w), 1603 (w), 1495 (w), 1382 (m), 1265 (w), 1189 (w), 1052 (m), 1030 (m), 1006 (m), 746 (m), 698 (s) cm^{-1}. HRMS (ESI+) calc. for $C_{18}H_{25}$ [M+H-H_2O]$^+$ 241.1956, found 241.1951. $[\alpha]^{20}_D$: -13.8 (c = 0.600, $CHCl_3$, *l* =50 mm).



1.105

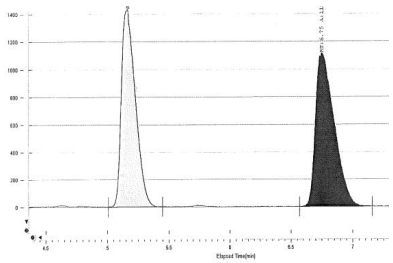
(*S,E*)-4,4,5,5-Tetramethyl-2-(5,6,6-trimethyl-1-phenylhept-4-en-3-yl)-1,3,2-dioxaborolane (1.105) The reaction was performed according to the *Representative Procedure (Method D).* The crude mixture was purified by silica gel chromatography (30% CH_2Cl_2/hexanes, stain in CAM) to afford a clear, yellow oil (23.5 mg, 69% yield). R_f = 0.6 in 50% CH_2Cl_2/hexanes on TLC. ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.27-7.21 (m, 2H), 7.17-7.12 (m, 3H), 5.11 (d, *J* = 9.0 Hz, 1H), 2.63 (ddd, *J* = 15.0, 10.0, 5.5 Hz, 1H), 2.53 (ddd, *J* = 13.0, 6.5, 3.0 Hz, 1H), 1.99 (q, *J* = 8.5 Hz, 1H), 1.85 (ddt, *J* = 13.5, 10.0, 7.0 Hz 1H) 1.71 (dtd, *J* = 13.5, 9.5, 5.5 Hz, 1H), 1.59 (s, 3H), 1.21 (s, 6H), 1.20 (s, 6H). ^{13}C NMR (125 MHz, $CDCl_3$) δ 143.03, 128.65, 128.31, 125.64, 121.72, 82.95, 36.33, 35.71, 33.57, 29.38, 24.80, 24.58, 13.50. ^{11}B NMR (128 MHz, $CDCl_3$) δ 32.76. IR (neat) ν_{max} 3085 (w), 3062 (w), 3026 (w), 2966 (s), 2930 (s), 2861 (m), 1735 (w), 1604 (w), 1495 (w), 1478 (m), 1455 (m), 1357 (s), 1315 (s), 1263 (m), 1214 (m), 1199 (m), 1143 (s), 1106 (m), 967 (m), 847 (m), 748 (m), 698 (s) cm^{-1}. HRMS (ESI+) calc. for $C_{22}H_{36}BO_2$ $[M+H]^+$ 343.2808, found 343.2806. $[\alpha]^{20}_D$: +14.2 (c = 1.175, $CHCl_3$, *l* =50 mm).

Analysis of Stereochemistry:

The enantiomeric ratio was determined by chiral SFC analysis of the corresponding secondary allylic alcohol. The racemic alcohol was prepared analogously with racemic **1.79** and the vinyl bromide **1.145** according to *Method A*.

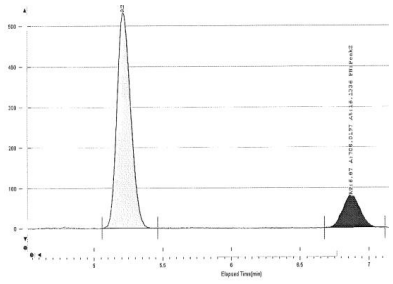
Chiral SFC (OD-H, Chiraldex, 3 mL/min, 7% ^{i}PrOH, 100 bar, 35 ^{o}C)-analysis of the reaction product.

Racemic

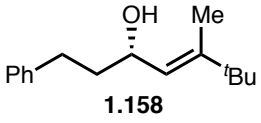


Peak Info					
Peak No	% Area	Area	RT (min)	Height (mV)	K'
1	48.9057	11332.7807	5.17	1434.773	0.0049
2	51.0943	11839.9449	6.75	1113.5943	0.0065
Total:	100	23172.7256			

Reaction product



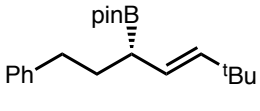
Peak Info					
Peak No	% Area	Area	RT (min)	Height (mV)	K'
1	83.8664	3680.4547	5.21	531.1999	0.0064
2	16.1336	708.0197	6.87	79.3984	0.0085
Total:	100	4388.4744			



1.158

(*S,E*)-5,6,6-Trimethyl-1-phenylhept-4-en-3-ol (1.158). The reaction was performed according to the *Representative Procedure (Method E)*. The crude mixture was purified by silica gel chromatography (20% ethyl acetate/hexanes, stain in CAM) to afford a clear, colorless oil. R_f = 0.4 in 7/2/1 hexanes/CH_2Cl_2/ethyl acetate on TLC. ^{1}H NMR (500 MHz, $CDCl_3$) 7.30-7.24 (m, 2H), 7.22-7.15 (m, 3H), 5.27 (dd, *J* = 8.5, 1.0 Hz, 1H), 4.40 (q, *J* = 7.0 Hz, 1H), 2.74-2.60 (m, 2H), 1.94 (ddt, *J* = 13.0, 9.5, 7.0 Hz, 1H), 1.77 (ddt, *J* = 13.5, 10.0, 6.0 Hz, 1H), 1.65 (s, 3H), 1.05 (s, 9H) . ^{13}C NMR (125 MHz, $CDCl_3$) δ 147.00, 142.27, 128.54, 128.49, 125.90,

124.74, 68.62, 39.44, 36.28, 32.02, 29.10, 13.30. IR (neat) ν_{max} 3402 (br), 3085 (w), 3062 (w), 3026 (w), 2954 (s), 2867 (m), 1654 (w), 1603 (w), 1495 (m), 1478 (m), 1454 (m), 1377 (m), 1360 (m), 1259 (w), 1052 (m), 1071 (s), 1005 (m), 914 (w), 841 (w), 746 (m), 698 (s) cm^{-1}. HRMS (ESI+) calc. for $C_{16}H_{23}$ $[M+H-H_2O]^+$ 215.1800, found 215.1807. $[\alpha]^{20}_D$: -22.5 (c = 0.485, $CHCl_3$, *l* =50 mm).



1.106

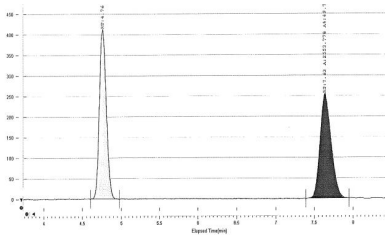
(*S*,*E*)-2-(6,6-Dimethyl-1-phenylhept-4-en-3-yl)-4,4,5,5-tetramethyl-1,3,2-dioxaborolane (1.106). The reaction was performed according to the *Representative Procedure (Method D)*. The crude mixture was purified by silica gel chromatography (30% CH_2Cl_2/hexanes, stain in CAM) to afford a white solid (24.6 mg, 75% yield). R_f = 0.6 in 7:2:1 hexanes/CH_2Cl_2/ethyl acetate on TLC. ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.28-7.23 (m, 2H) 7.19 – 7.13 (m, 3H), 5.47 (dd, *J* = 15.5, 1.0 Hz, 1H), 5.26 (dd, *J* = 15.5, 8.5 Hz, 1H), 2.63 (ddd, *J* = 14.0, 9.5, 5.5 Hz, 1H) 2.55 (ddd, *J* = 13.5, 10.0, 5.5 Hz, 1H), 1.88-1.75 (m, 2H), 1.70 (ddt, *J* = 12.0, 6.0, 4.5 Hz, 1H) 1.24 (s, 6H), 1.23 (s, 6H), 0.99 (s, 9H) . ^{13}C NMR (126 HMz, $CDCl_3$) δ 143.06, 141.70, 128.66, 128.34, 125.67, 124.94, 83.15, 35.52, 33.15, 33.09, 30.07, 24.88, 24.66. ^{11}B NMR (160 MHz, $CDCl_3$) δ 33.01. IR (neat) ν_{max} 3085 (w), 3063 (w), 3026 (w), 2976 (s), 2957 (s), 2930 (s), 2862 (m), 1604 (w), 1496 (w), 1456 (m), 1360 (s), 1320 (s), 1266 (m), 1214 (m), 1143 (s), 1108 (w), 970 (s), 854 (m), 747 (m), 699 (s) cm^{-1}. HRMS (ESI+) calc. for $C_{21}H_{34}BO_2$ $[M+H]^+$ 329.2652, found 329.2661. $[\alpha]^{20}_D$: +10.6 (c = 0.665, $CHCl_3$, *l* =50 mm). Melting point: 48-51 ^oC.

Analysis of Stereochemistry:

The enantiomeric ratio was determined by chiral SFC analysis of the corresponding secondary allylic alcohol. The racemic alcohol was prepared analogously with racemic **1.79** and the vinyl bromide **1.146** according to *Method A*.

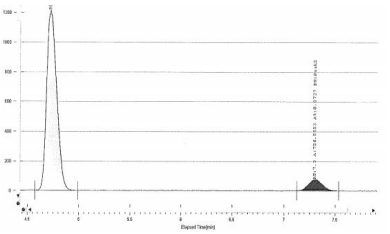
Chiral SFC (OD-H, Chiraldex, 3 mL/min, 7% ^{i}PrOH, 100 bar, 35 ^{o}C)-analysis of the reaction product.

Racemic

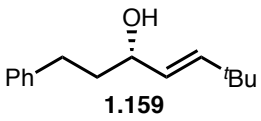


Peak Info					
Peak No	% Area	Area	RT (min)	Height (mV)	K'
1	50.2435	2578.7738	4.76	411.9121	0.0064
2	49.7565	2553.778	7.63	254.0157	0.0103
Total:	100	5132.5518			

Reaction product



Peak Info					
Peak No	% Area	Area	RT (min)	Height (mV)	K'
1	91.9263	8272.3213	4.72	1211.6924	0.0044
2	8.0737	726.5453	7.3	76.2806	0.0068
Total:	100	8998.8666			

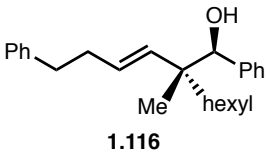


1.159

(*S*,*E*)-6,6-Dimethyl-1-phenylhept-4-en-3-ol (1.159) The reaction was performed according to the *Representative Procedure (Method E)*. The crude mixture was purified by silica gel chromatography (20% ethyl

acetate/hexanes, stain in CAM) to afford a clear, colorless oil. R_f = 0.5 in 7/2/1 hexanes/CH_2Cl_2/ethyl acetate on TLC. ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.30-7.24 (m, 2H), 7.22-7.16 (m, 3H), 5.67 (d, *J* = 15.5 Hz, 1H), 5.39 (dd, *J* = 15.5, 7.0 Hz, 1H), 4.10-4.04 (m, 1H), 2.75-2.62 (m, 2H), 1.93-1.76 (m, 2H), 1.45 (d, *J* = 3.0 Hz, 1H), 1.02 (s, 9H). ^{13}C NMR (125 MHz, $CDCl_3$) δ 143.56, 142.19, 128.60, 128.50, 127.64, 125.92, 72.83, 39.07, 32.95, 31.99, 29.67. IR (neat) ν_{max} 3356 (br), 3085 (w), 3062 (w), 3026 (w), 2956 (s), 2863 (s), 1661 (w), 1603 (w), 1496 (m), 1455 (m), 1390 (w), 1362 (m), 1267 (w), 1202 (w), 1100 (w), 1031 (m), 973 (s), 911 (m), 746 (s), 698 (s) cm^{-1}. HRMS (ESI+) calc. for $C_{15}H_{21}$ $[M+H-H_2O]^+$ 201.1643, found 201.1632. $[\alpha]^{20}_D$: -7.94 (c = 0.500, $CHCl_3$, *l* =50 mm)

1.5.8 Transformations of Allylic Boronate Products



1.116

(1*R*,2*R*)-2-Methyl-1-phenyl-2-((*E*)-4-phenylbut-1-en-1-yl)octan-1-ol (1.116). After performing the enantiotopic-group-selective cross-coupling (*Method D*), the crude mixture containing **1.102** was diluted with Et_2O (3 mL) and filtered through Celite with additional Et_2O (5 mL). The solvent was removed *in vacuo* and the crude residue transferred to a 2-dram vial with Et_2O. The solvent was again removed under vacuum, and the vial equipped with a magnetic stir bar. After purging with N_2, toluene (500 μL) was added. The reaction was stirred and benzaldehyde (50 μL, 0.5 mmol) was added. The reaction was heated to 60^{o}C for 24 hours under N_2. Upon cooling to room temperature, the reaction was diluted with Et_2O (3 mL) and filtered through a short pad of Celite with additional Et_2O (5 mL). To simplify purification, the residue was further oxidized according to *Method E* and the title

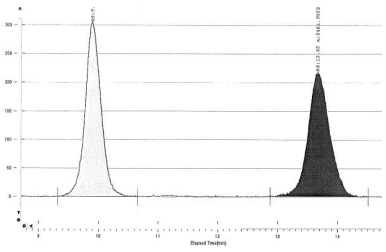
compound was obtained by silica gel chromatography (30% CH_2Cl_2/hexanes) as a clear, colorless oil (28.0 mg, 80% yield). R_f = 0.4 in 50% CH_2Cl_2/hexanes on TLC. ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.30-7.63 (m, 10H), 5.47 (dt, *J* = 15.5, 6.5 Hz, 1H), 5.34 (d, *J* = 16.0 Hz, 1H), 4.29 (s, 1H), 2.74 (t, *J* = 7.5 Hz, 2H), 2.44 (q, *J* = 7.0 Hz, 2H), 1.88 (s, 1H), 1.36-1.04 (m, 10H), 0.87 (t, *J* = 7.0 Hz, 3H), 0.83 (s, 3H). ^{13}C NMR (125 MHz, $CDCl_3$) δ 141.84, 140.73, 136.74, 130.86, 128.62, 128.51, 128.22, 127.49, 127.36, 126.06, 80.32, 45.24, 38.07, 36.06, 34.89, 32.03, 30.24, 24.15, 22.82, 17.28, 14.22. IR (neat) ν_{max} 3453 (br), 3085 (w), 3062 (w), 3027 (w), 2954 (m), 2927 (s), 2856 (m), 1495 (w), 1453 (m), 1377 (w), 1037 (m), 981 (m), 745 (s), 699 (s) cm^{-1}. HRMS (ESI+) calc. for $C_{25}H_{33}$ $[M+H-H_2O]^+$ 333.2582, found 333.2576. $[\alpha]^{20}_D$: +34.1 (c = 1.19, $CHCl_3$, *l* =50 mm).

Analysis of Stereochemistry:

The enantiomeric ratio was determined by chiral SFC analysis. The racemic alcohol was prepared analogously with racemic **1.79.**

Chiral SFC (OJ-H, Chiraldex, 3 mL/min, 7% ^{i}PrOH, 100 bar, 35 ^{o}C)-analysis of the reaction product.

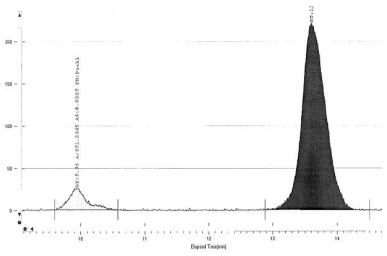
Racemic



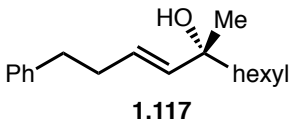
Peak Info

Peak No	% Area	Area	RT (min)	Height (mV)	K'
1	50.3986	5570.0836	9.89	305.0753	0.0125
2	49.6014	5481.9853	13.65	218.2576	0.0173
Total:	100	11052.0689			

Reaction product



Peak Info					
Peak No	% Area	Area	RT (min)	Height (mV)	K'
1	8.0339	491.2665	9.94	25.9686	0.0123
2	91.9661	5623.661	13.6	221.7518	0.0168
Total:	100	6114.9275			



1.117

(*R,E*)-5-methyl-1-phenylundec-3-en-5-ol (1.117)[25] After performing the enantiotopic-group-selective cross-coupling (*Method D*), the crude mixture containing **1.102** was diluted with Et_2O (3 mL) and filtered through Celite with additional Et_2O (5 mL). The solvent was removed in vacuo and the crude residue transferred to a 2-dram vial with Et_2O. The solvent was again removed under vacuum, and the vial equipped with a magnetic stir bar. After purging with N_2, THF (1 mL) was added and the reaction was cooled to 0^oC. Nitrobenzene (32.1 mg, 0.30 mmol) was added as a solution in THF (1 mL) via syringe. The reaction was warmed to room temperature and stirred under N_2 for one hour. The reaction was re-cooled to 0^oC and 3M $NH_4OH_{(aq)}$ (500 μL, 1.6 mmol) was added. The reaction was warmed to room temperature and stirred under N_2 for 16 hours. To quench, the reaction was diluted with Et_2O (3 mL) and filtered through a plug of silica with additional Et_2O (5 mL). The solvent was removed under vacuum. To simplify purification, the crude residue was further oxidized according to *Method E*, and the title compound was obtained by silica gel chromatography (20%

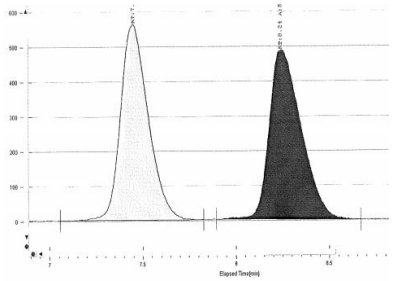
CH_2Cl_2/hexanes to 40% CH_2Cl_2/hexanes) as a clear, yellow oil (16.4 mg). R_f = 0.3 in 50% CH_2Cl_2/hexanes on TLC. ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.29-7.25 (m, 2H), 7.20-7.15 (m, 3H), 5.63 (dtd, *J* = 15.5, 6.5, 2.0 Hz, 1H), 5.51 (dd, *J* = 15.5, 1.5 Hz, 1H), 2.70 (t, *J* = 8.0 Hz, 2H), 2.36 (ddd, *J* = 15.5, 8.0, 1.0 Hz, 2H), 1.46 (m, 2H), 1.32-1.20 (m, 12H), 0.89 (t, *J* = 6.0 Hz, 3H). ^{13}C NMR (125 MHz, $CDCl_3$) δ 141.96, 137.96, 128.62, 128.39, 126.96, 125.92, 72.92, 43.00, 36.00, 34.19, 31.96, 29.88, 28.08, 24.10, 22.78, 14.22. IR (neat) ν_{max} 3470 (br), 3026 (w), 2956 (m), 2928 (s), 2856 (m), 1454 (m), 1375 (w), 971 (m), 746 (m), 698 (s) cm^{-1}. HRMS (ESI+) calc. for $C_{18}H_{27}$ $[M+H-H_2O]^+$ 243.2113, found 243.2102. $[\alpha]^{20}_D$: -0.704 (c = 0.690, $CHCl_3$, *l* =50 mm).

Analysis of Stereochemistry:

The enantiomeric ratio was determined by chiral SFC analysis. The racemic alcohol was prepared analogously with racemic **1.79.**

Chiral SFC (OD-H, Chiraldex, 3 mL/min, 5% ^{i}PrOH, 100 bar, 35 ^{o}C)-analysis of the reaction product.

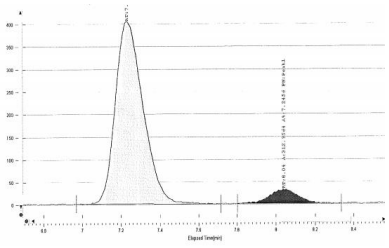
Racemic



Peak Info

Peak No	% Area	Area	RT (min)	Height (mV)	K'
1	50.013	5821.7491	7.45	564.4994	0.0084
2	49.987	5818.7191	8.24	486.3836	0.0093
Total:	100	11640.4682			

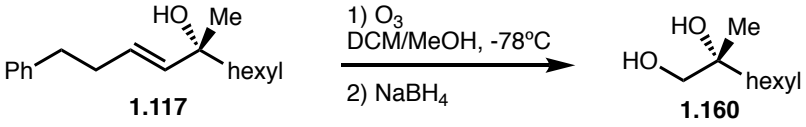
Reaction product

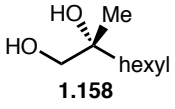


Peak Info					
Peak No	% Area	Area	RT (min)	Height (mV)	K'
1	92.7544	4006.2951	7.23	404.4908	0.01
2	7.2456	312.9564	8.04	31.4308	0.0111
Total:	100	4319.2515			

1.5.9 Structure Proof of Product 1.117

The absolute structure of **1.117** was determined by ozonolysis/reduction to the corresponding diol **1.160**, and subsequent comparison with the Sharpless Asymmetric Dihydroxylation[75] product of 2-methyloct-1-ene, which is known to afford the (*R)* isomer utilizing AD-Mix-β.[76] Racemic **1.160** was prepared according to a literature procedure.[77]





(*R*)-2-Methyloctane-1,2-diol (1.160) A 4-dram vial was charged with **1.115** (55 mg, 0.21 mmol), CH_2Cl_2 (2 mL), and MeOH (2 mL). The reaction was stirred and cooled to -78°C. A stream of O_3 was bubbled into the reaction for approximately 3 minutes as the color changed from bright yellow to red/brown. $NaBH_4$ (76

[75] Sharpless, K. B.; Amberg, W.; Bennani, Y. L.; Crispino, G. A.; Hartung, J.; Jeong, K.; Kwong, H.; Morikawa, K.; Wang, Z.; Xu, D.; Zhang, X. *J. Org. Chem.* **1992**, *57*, 2768.
[76] Arasaki, H.; Iwata, M.; Nishimura, D.; Itoh, A.; Masaki, Y. *Synlett* **2004**, *3*, 546.
[77] Albert, B. J.; Sivaramakrihnan, A.;Naka, T.; Czaicki, N.L.; Koide, K. *J. Am. Chem. Soc*. **2007**, *129*, 2648.

mg, 2.0 mmol) was added as a solid. The reaction stirred at -78°C for 5 minutes before warming to room temperature and further stirring for 12 hours. H_2O (2 mL) was added and the reaction was poured into a separatory funnel with ethyl acetate (10 mL). The layers were separated and the aqueous layer was extracted with ethyl acetate (4 x 10 mL). The organic layers were combined, dried over $Na_2SO_{4(s)}$, filtered and concentrated *in vacuo*. The crude material was purified by silica gel chromatography (20% ethyl acetate/hexanes to 30% ethyl acetate/hexanes) to afford the title compound as a clear, colorless oil (11.7 mg, 38% yield). R_f = 0.3 in 50% ethyl acetate/hexanes on TLC. The spectral data matched those reported in the literature.[78]

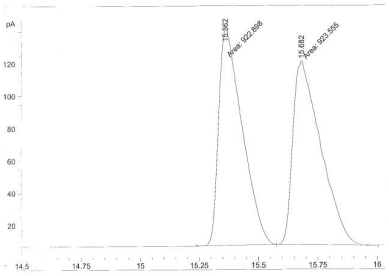
Analysis of Stereochemistry:

The enantiomer ratio was determined by chiral GC analysis of the corresponding acetonide which was prepared as follows: The diol was combined with dimethoxypropane (1 mL) and a single crystal of *p*-TsOH, and heated to 60°C for 20 minutes. The reaction was cooled to room temperature, filtered through a pad of silica gel with diethyl ether (5 mL), and concentrated *in vacuo* to afford pure acetonide.

Chiral GC (β-Dex 120, Supelco, 100°C for 5 minutes, then ramp 1.0°C/min, 20 psi)-analysis of the reaction product.

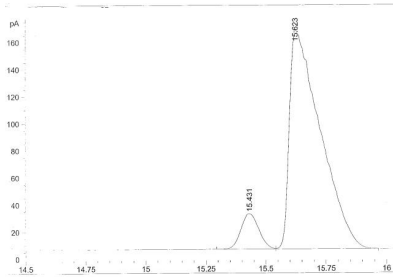
[78] Park, J.; Pedersen, S. F. *Tetrahedron*, **1992**, *48*, 2069.

Racemic



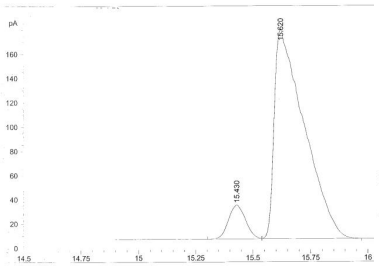
Peak #	RetTime [min]	Type	Width [min]	Area [pA*s]	Height [pA]	Area %
1	15.362	MM	0.1151	922.89752	133.61723	49.98220
2	15.682	MM	0.1352	923.55469	113.86636	50.01780

(R)-Isomer from AD-Mix-β



Peak #	RetTime [min]	Type	Width [min]	Area [pA*s]	Height [pA]	Area %
1	15.431	BV	0.0632	136.16568	25.97442	8.67880
2	15.623	VB	0.1052	1432.77991	162.38312	91.32120

Reaction Product Diol 1.158



Peak #	RetTime [min]	Type	Width [min]	Area [pA*s]	Height [pA]	Area %
1	15.430	BV	0.0635	143.93559	28.23802	8.48570
2	15.620	VB	0.1056	1552.27844	173.48526	91.51430

1.5.10 Cross-Coupling of (*S*)-^{10}B-1.128

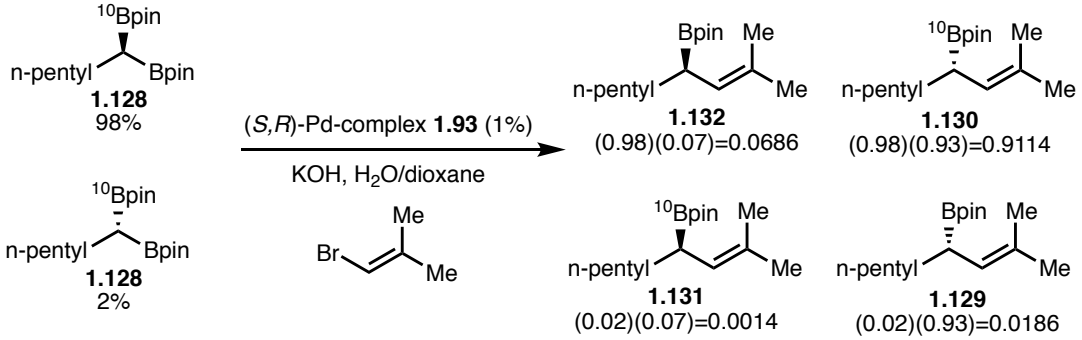
(*S*)-^{10}B-1.128 was prepared according to a literature procedure.[16]

1. Using (S,R)-Complex and assuming inversion during coupling:

note: bis(boronate) starting material (**(*S*)-^{10}B-1.128**) = 98:2 er

cross-coupling reaction selectivity = 93:7 er

natural abundance of boron is ^{10}B:^{11}B = 19.9:80.1



^{10}B = (0.199)(0.0686) + 0.9114 + 0.0014 + (0.199)(0.0186) = **0.930**

^{11}B = (0.801)(0.0686) + (0.801)(0.0186) = **0.070**

Relative [M+H] distributions for ^{10}B:

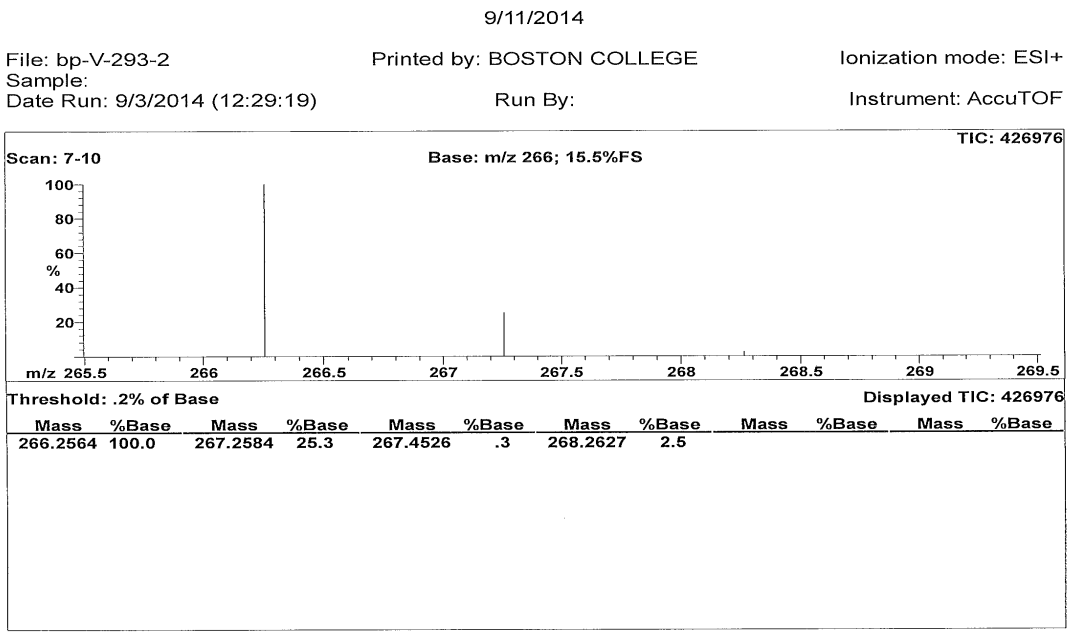
$^{12}C_{16}H_{32}{}^{10}BO_2$ [M+H]:	266.3	*0.842*
$^{12}C_{15}{}^{13}CH_{32}{}^{10}BO_2$ [M+H]:	267.3	*0.146*
$^{12}C_{14}{}^{13}C_2H_{32}{}^{10}BO_2$ [M+H]:	268.3	*0.012*

Relative [M+H] distributions for ^{11}B:

$^{12}C_{16}H_{32}{}^{11}BO_2$ [M+H]:	267.3	*0.842*
$^{12}C_{15}{}^{13}CH_{32}{}^{11}BO_2$ [M+H]:	268.3	*0.146*
$^{12}C_{14}{}^{13}C_2H_{32}{}^{11}BO_2$ [M+H]:	269.3	*0.012*

Calculated Relative Intensities:
[M+H] for 266 amu = (**0.930**)(*0.842)* = 0.783
[M+H] for 267 amu = (**0.930**)(*0.146*) + (**0.070**)(*0.842*) = 0.195
[M+H] for 268 amu = (**0.930**)(*0.012) +* (**0.070**)(*0.146*) = 0.021
[M+H] for 269 amu = (**0.070**)(*0.012)* = 0.001

Found:
0.783
0.195
0.021
<0.01



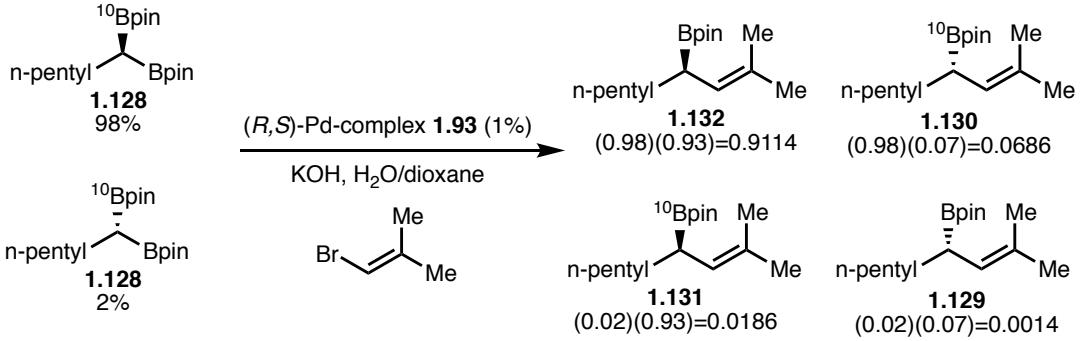
Spectrum 1: Mass Spectrum corresponding to the cross-coupling of **(*S*)-^{10}B-1.128** with **(*S,R*)-1.93·PdCl$_2$**

2. Using (R,S)-Complex assuming inversion during coupling:

note: bis(boronate) starting material (**(*S*)-^{10}B-1.128**) = 98:2 er

cross-coupling reaction selectivity = 93:7 er

natural abundance of boron is ^{10}B:^{11}B = 19.9:80.1



^{10}B = (0.199)(0.9114) + 0.0686 + 0.0186 + (0.199)(0.0014) = **0.269**

^{11}B = (0.801)(0.9144) + (0.801)(0.0014) = **0.731**

Relative [M+H] distributions for ^{10}B:

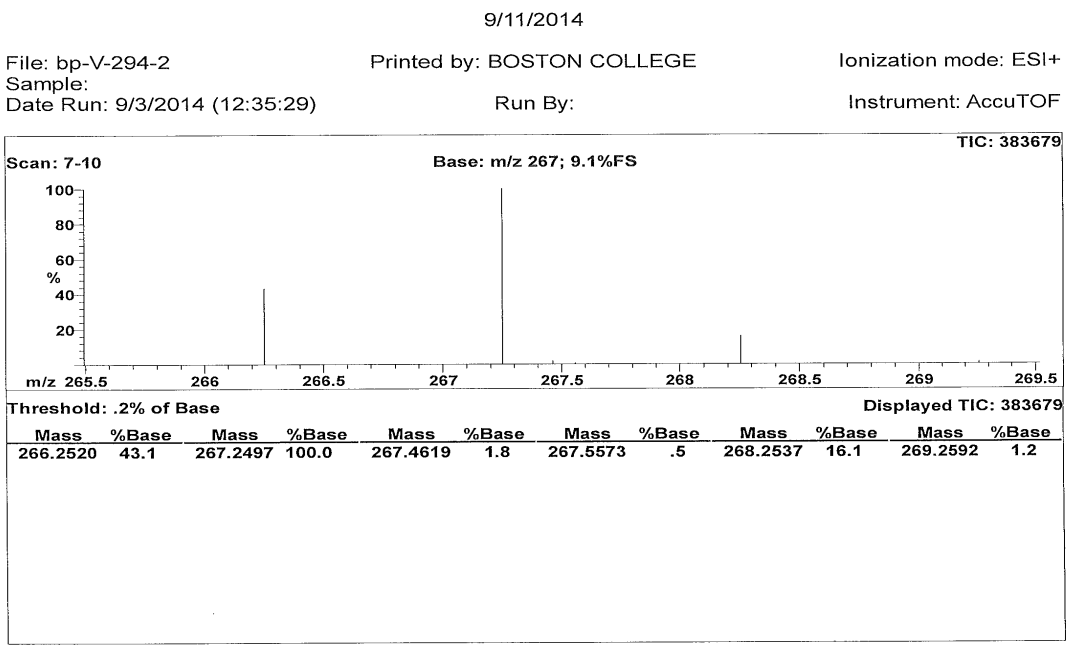
$^{12}C_{16}H_{32}{}^{10}BO_2$ [M+H]:	266.3	*0.842*
$^{12}C_{15}{}^{13}CH_{32}{}^{10}BO_2$ [M+H]:	267.3	*0.146*
$^{12}C_{14}{}^{13}C_2H_{32}{}^{10}BO_2$ [M+H]:	268.3	*0.012*

Relative [M+H] distributions for ^{11}B:

$^{12}C_{16}H_{32}{}^{11}BO_2$ [M+H]:	267.3	*0.842*
$^{12}C_{15}{}^{13}CH_{32}{}^{11}BO_2$ [M+H]:	268.3	*0.146*
$^{12}C_{14}{}^{13}C_2H_{32}{}^{11}BO_2$ [M+H]:	269.3	*0.012*

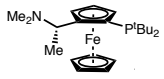
Calculated Relative Intensities:
[M+H] for 266 amu = (**0.269**)(*0.842*) = 0.226
[M+H] for 267 amu = (**0.269**)(*0.146*) + (**0.731**)(*0.842*) = 0.655
[M+H] for 268 amu = (**0.269**)(*0.012*) + (**0.731**)(*0.146*) = 0.110
[M+H] for 269 amu = (**0.731**)(*0.012*) = 0.009

Found:
0.269
0.623
0.101
0.007



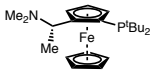
Spectrum 2: Mass Spectrum corresponding to the cross-coupling of **(*S*)-^{10}B-1.128** with **(*R*,*S*)- 1.93·PdCl$_2$**

1.5.11 Compound Spectra


Me2N
PtBu2
Me
Fe

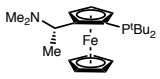
1.84

10
9
8
7
6
5
4
3
2
1
0 ppm

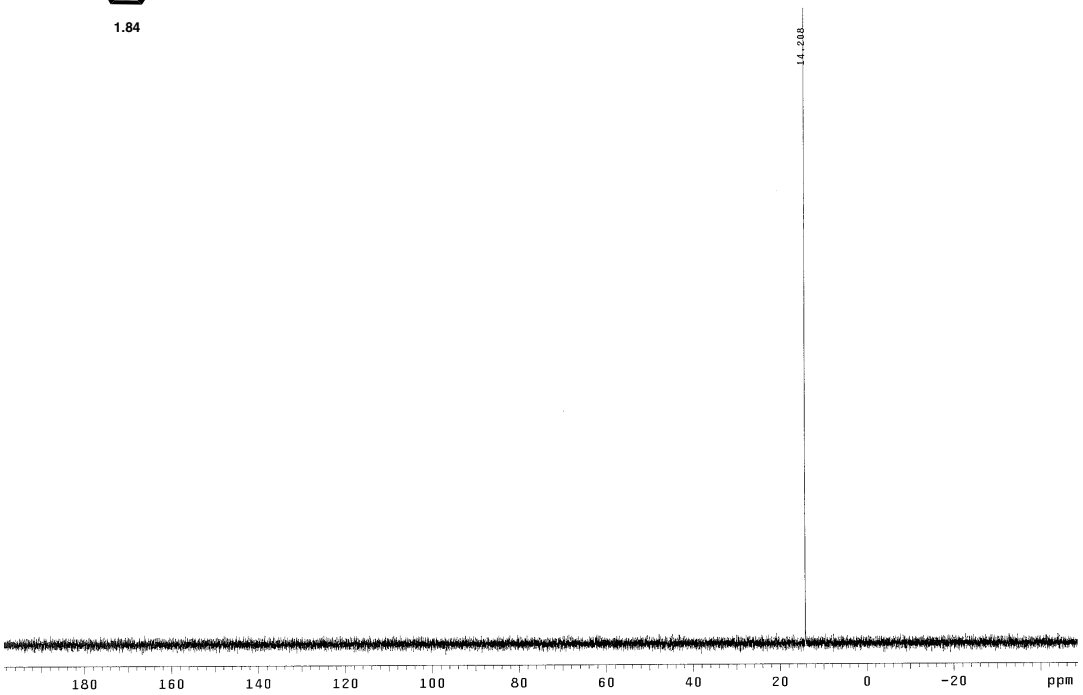

Me2N
PtBu2
Me
Fe

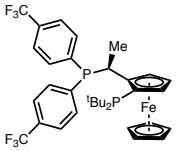
1.84

220
200
180
160
140
120
100
80
60
40
20
0 ppm


Me2N
PtBu2
Me
Fe

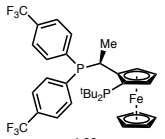
1.84


14.208
180
160
140
120
100
80
60
40
20
0
-20
ppm


F3C
Me
P
tBu2P
Fe
F3C

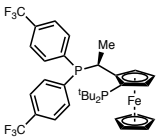
1.92

10
9
8
7
6
5
4
3
2
1
0 ppm

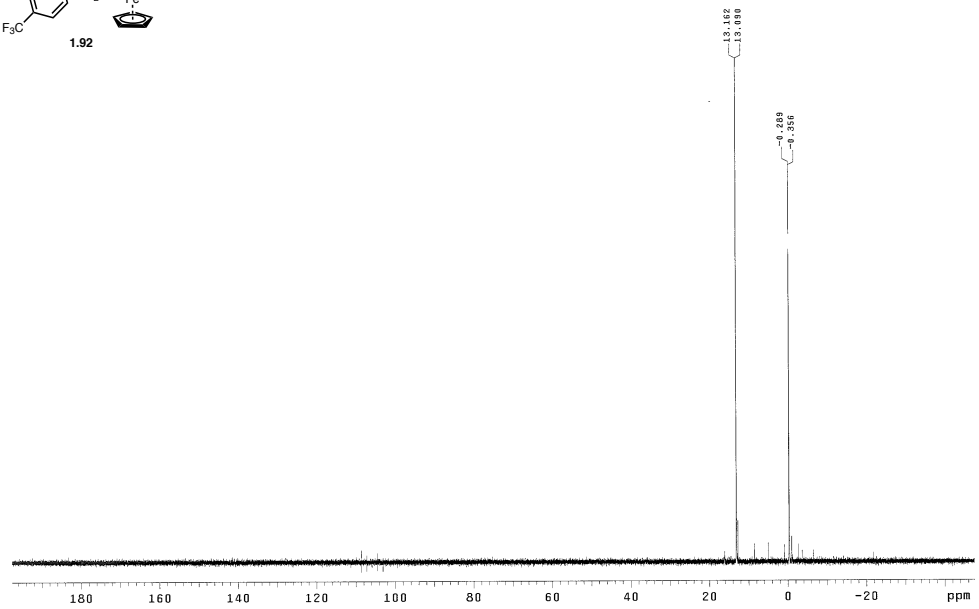

F3C
Me
P
tBu2P
Fe
F3C

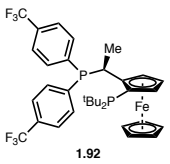
1.92

220
200
180
160
140
120
100
80
60
40
20
0
ppm


F3C
Me
P
tBu2P
Fe
F3C

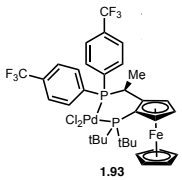
1.92


13.162
13.090
-0.289
-0.356
180
160
140
120
100
80
60
40
20
0
-20
ppm


F3C
Me
P
tBu2P
Fe
F3C

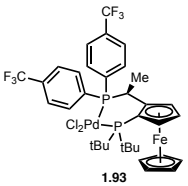
1.92

-62.761
-62.817
20
0
-20
-40
-60
-80
-100
-120
-140
-160
-180
ppm


CF3
F3C
Me
P
Cl2Pd
P
tBu
tBu
Fe

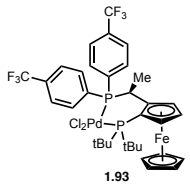
1.93

10
9
8
7
6
5
4
3
2
1
0 ppm


CF3
F3C
Me
P
Cl2Pd
P
tBu
tBu
Fe

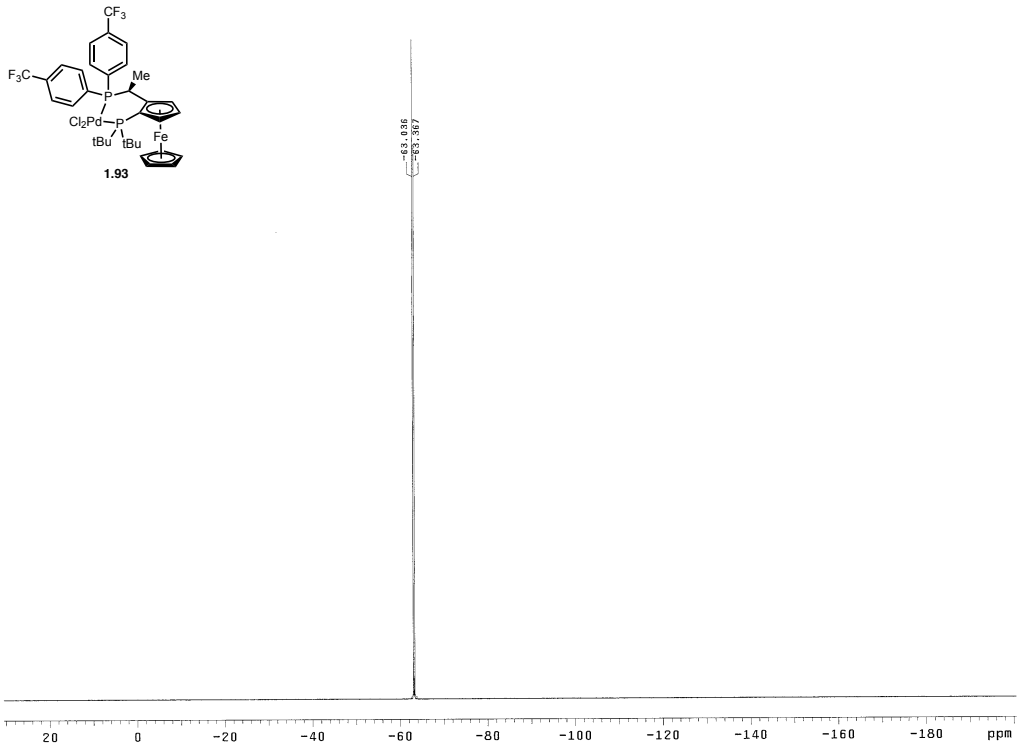
1.93

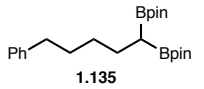
220
200
180
160
140
120
100
80
60
40
20
0
ppm


CF3
F3C
Me
P
Cl2Pd
P
tBu
tBu
Fe

1.93

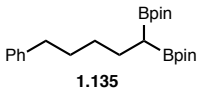
53.760
53.741
43.924
43.905
90
80
70
60
50
40
30
20
10
ppm


CF3
F3C
Me
P
Cl2Pd
P
tBu
tBu
Fe
1.93
-63.036
-63.967
20
0
-20
-40
-60
-80
-100
-120
-140
-160
-180
ppm


Bpin
Ph
Bpin

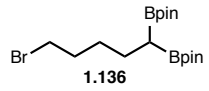
1.135

10
9
8
7
6
5
4
3
2
1
0 ppm


Bpin
Ph
Bpin

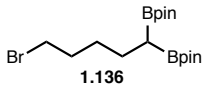
1.135

220
200
180
160
140
120
100
80
60
40
20
0 ppm


Bpin
Br
Bpin

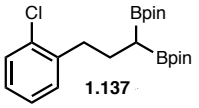
1.136

10
9
8
7
6
5
4
3
2
1
0 ppm


Bpin
Br
Bpin

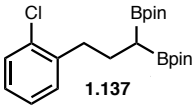
1.136

220
200
180
160
140
120
100
80
60
40
20
0 ppm


Cl
Bpin
Bpin

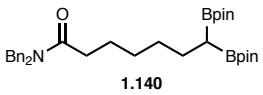
1.137

10
9
8
7
6
5
4
3
2
1
0 ppm


Cl
Bpin
Bpin

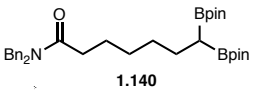
1.137

220
200
180
160
140
120
100
80
60
40
20
0 ppm


O
Bpin
Bn2N
Bpin

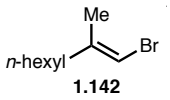
1.140

10
9
8
7
6
5
4
3
2
1
0 ppm


O
Bpin
Bn2N
Bpin

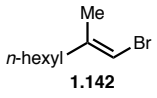
1.140

220
200
180
160
140
120
100
80
60
40
20
0 ppm


Me
n-hexyl
Br

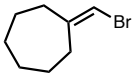
1.142

10
9
8
7
6
5
4
3
2
1
0 ppm

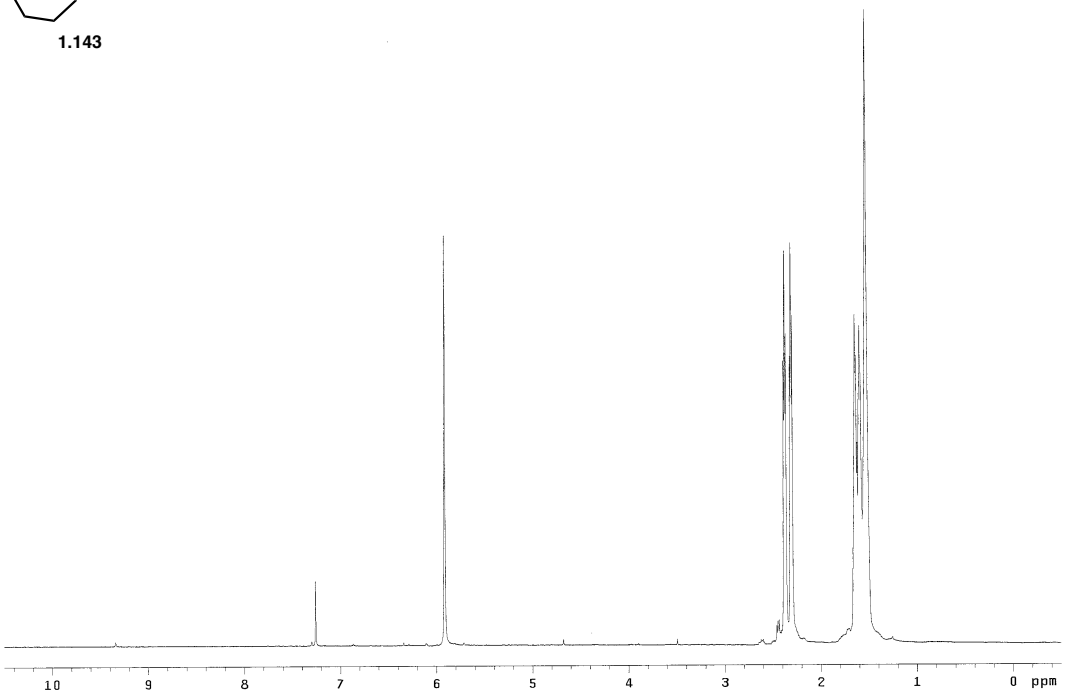

Me
n-hexyl
Br

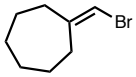
1.142

220
200
180
160
140
120
100
80
60
40
20
0 ppm


Br

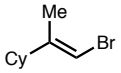
1.143


10
9
8
7
6
5
4
3
2
1
0 ppm

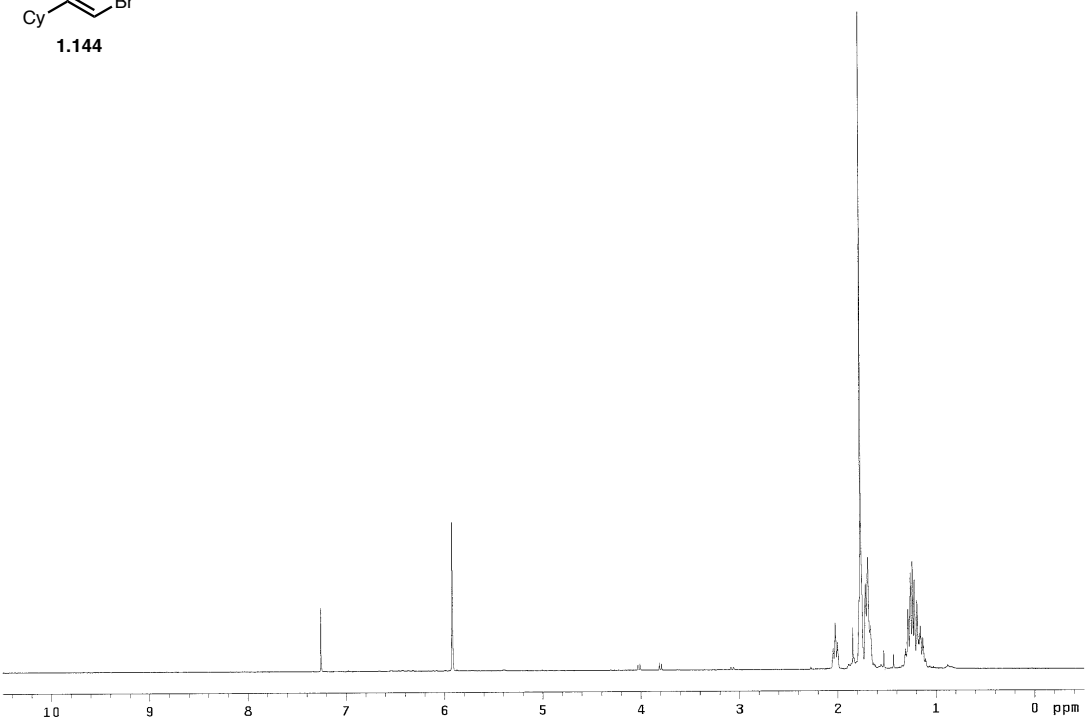

Br

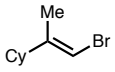
1.143

220
200
180
160
140
120
100
80
60
40
20
0 ppm

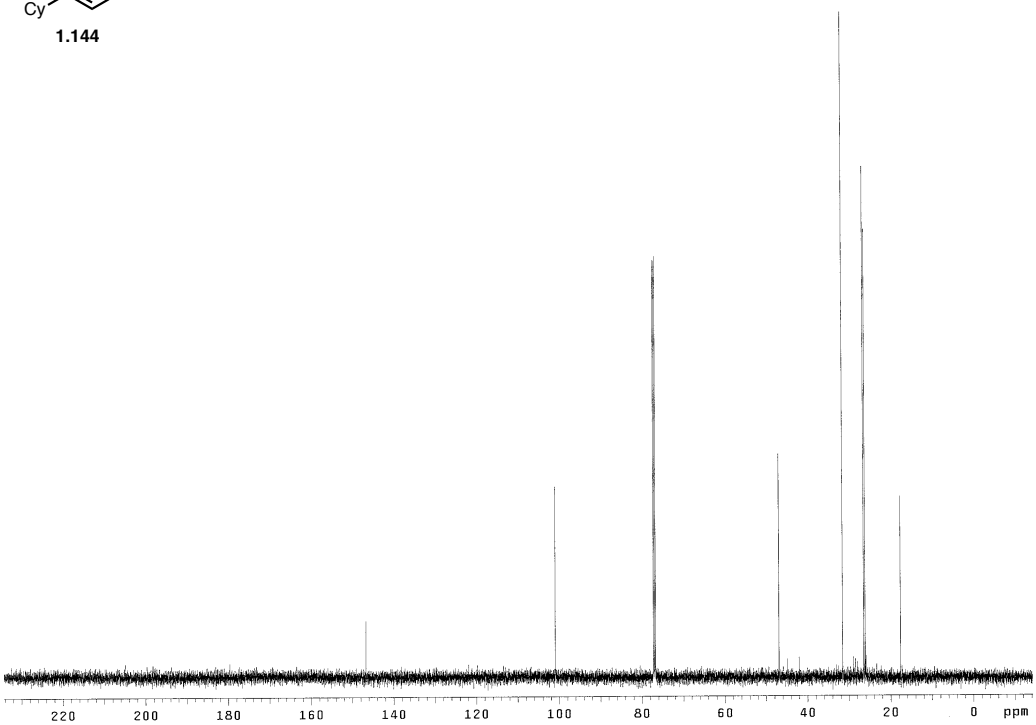

Me
Cy
Br

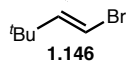
1.144


10
9
8
7
6
5
4
3
2
1
0 ppm


Me
Cy
Br

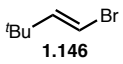
1.144


220
200
180
160
140
120
100
80
60
40
20
0 ppm


tBu
Br

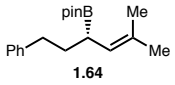
1.146

10
9
8
7
6
5
4
3
2
1
0 ppm


tBu
Br

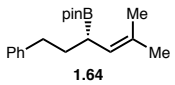
1.146

220
200
180
160
140
120
100
80
60
40
20
0 ppm


pinB
Me
Ph
Me

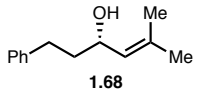
1.64

10
9
8
7
6
5
4
3
2
1
0
ppm


pinB
Me
Ph
Me

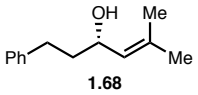
1.64

220
200
180
160
140
120
100
80
60
40
20
0
ppm


OH
Me
Ph
Me

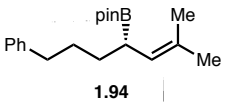
1.68

10
9
8
7
6
5
4
3
2
1
0 ppm


OH
Me
Ph
Me

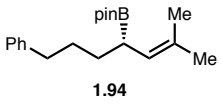
1.68

220
200
180
160
140
120
100
80
60
40
20
0 ppm


pinB
Me
Ph
Me

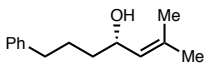
1.94

10
9
8
7
6
5
4
3
2
1
0 ppm

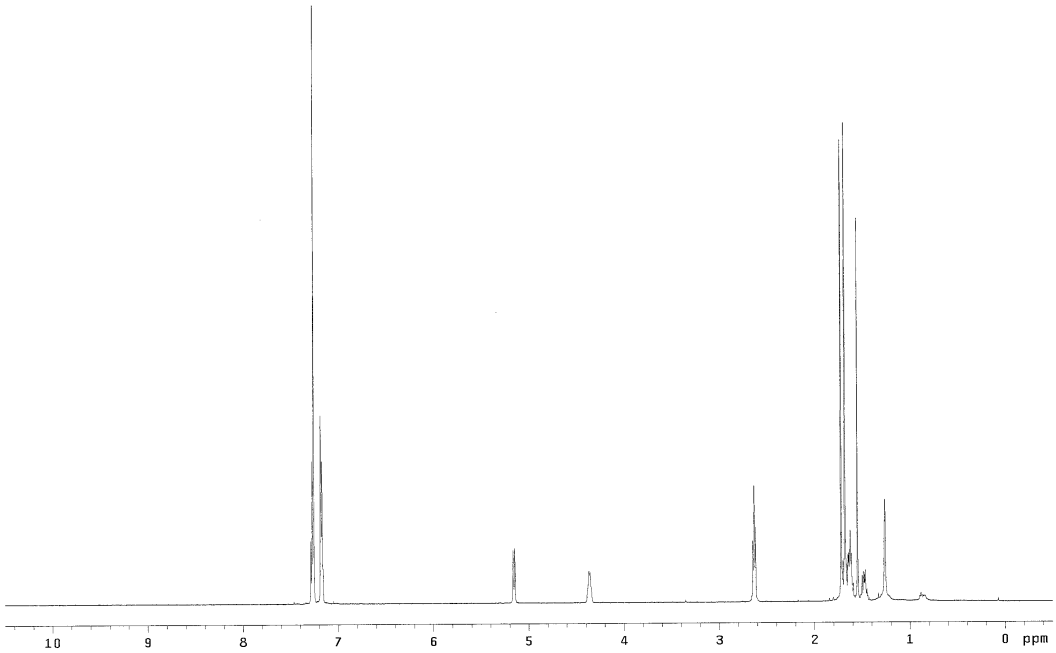

pinB
Me
Ph
Me

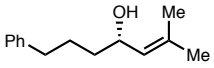
1.94

220
200
180
160
140
120
100
80
60
40
20
0 ppm

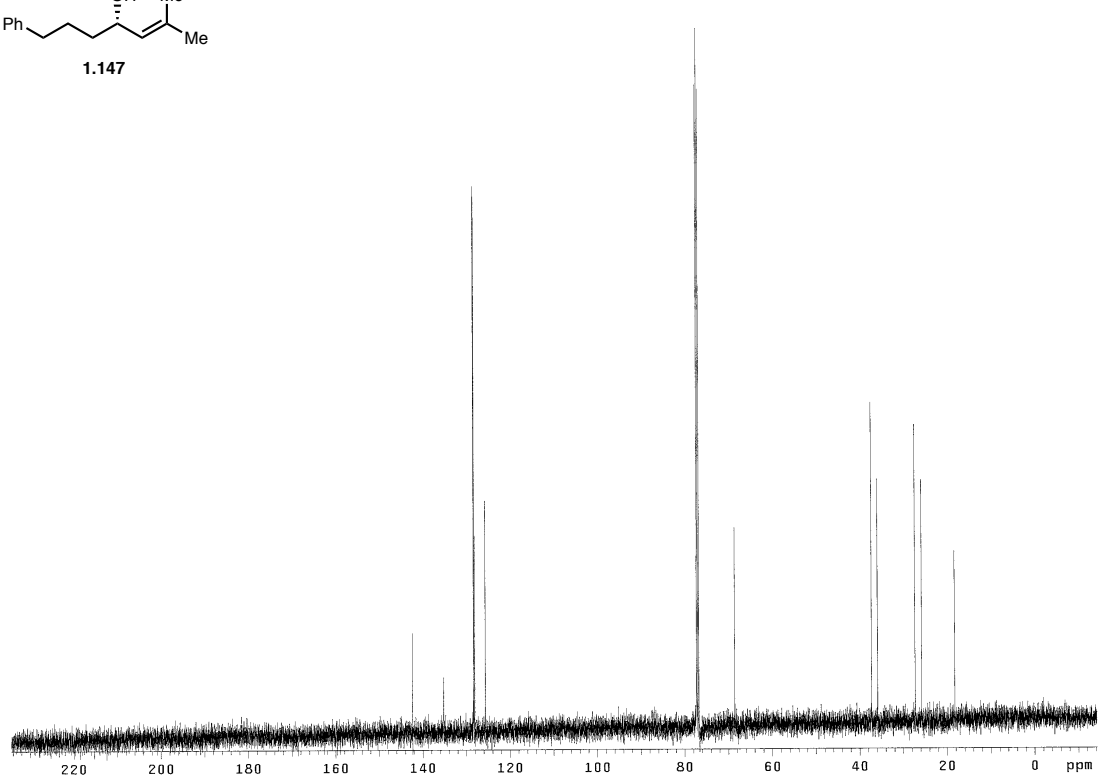

OH
Me
Ph
Me

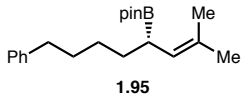
1.147


10
9
8
7
6
5
4
3
2
1
0 ppm


OH
Me
Ph
Me

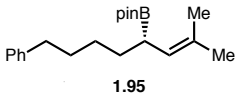
1.147


220
200
180
160
140
120
100
80
60
40
20
0 ppm


pinB
Me
Ph
Me

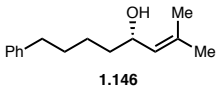
1.95

10
9
8
7
6
5
4
3
2
1
0 ppm


pinB
Me
Ph
Me

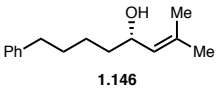
1.95

220
200
180
160
140
120
100
80
60
40
20
0 ppm


OH
Me
Ph
Me

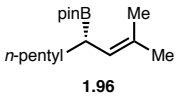
1.146

10
9
8
7
6
5
4
3
2
1
0
ppm


OH
Me
Ph
Me

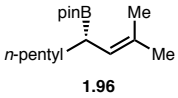
1.146

220
200
180
160
140
120
100
80
60
40
20
0
ppm


pinB
Me
n-pentyl
Me

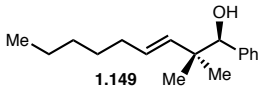
1.96

10
9
8
7
6
5
4
3
2
1
0 ppm

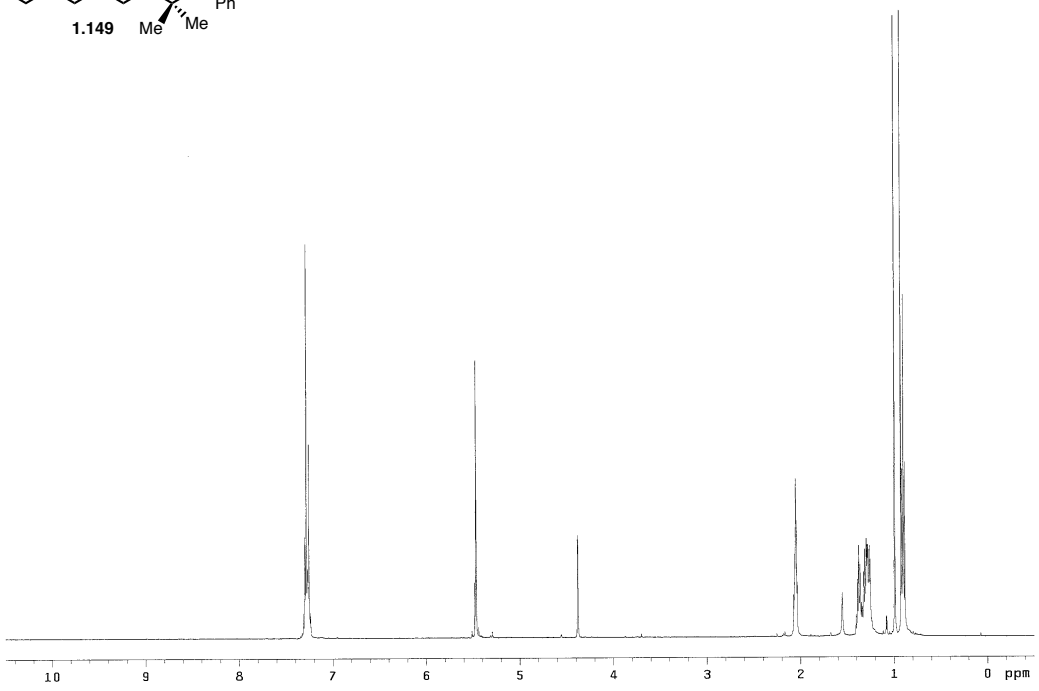

pinB
Me
n-pentyl
Me

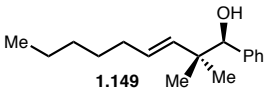
1.96

220
200
180
160
140
120
100
80
60
40
20
0 ppm

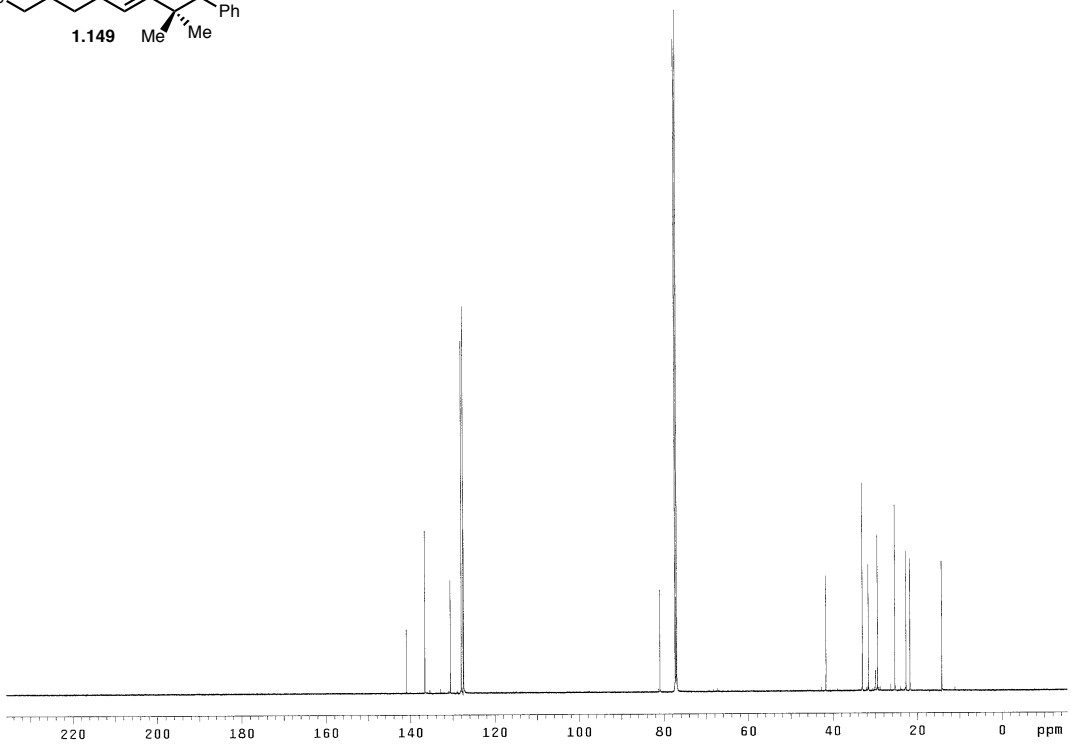

OH
Me
Ph
Me
Me

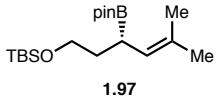
1.149


10
9
8
7
6
5
4
3
2
1
0 ppm


OH
Me
Ph
Me
Me

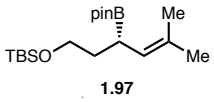
1.149


220
200
180
160
140
120
100
80
60
40
20
0 ppm


pinB
Me
TBSO
Me

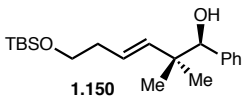
1.97

10
9
8
7
6
5
4
3
2
1
0
ppm


pinB
Me
TBSO
Me

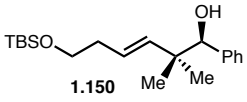
1.97

220
200
180
160
140
120
100
80
60
40
20
0
ppm

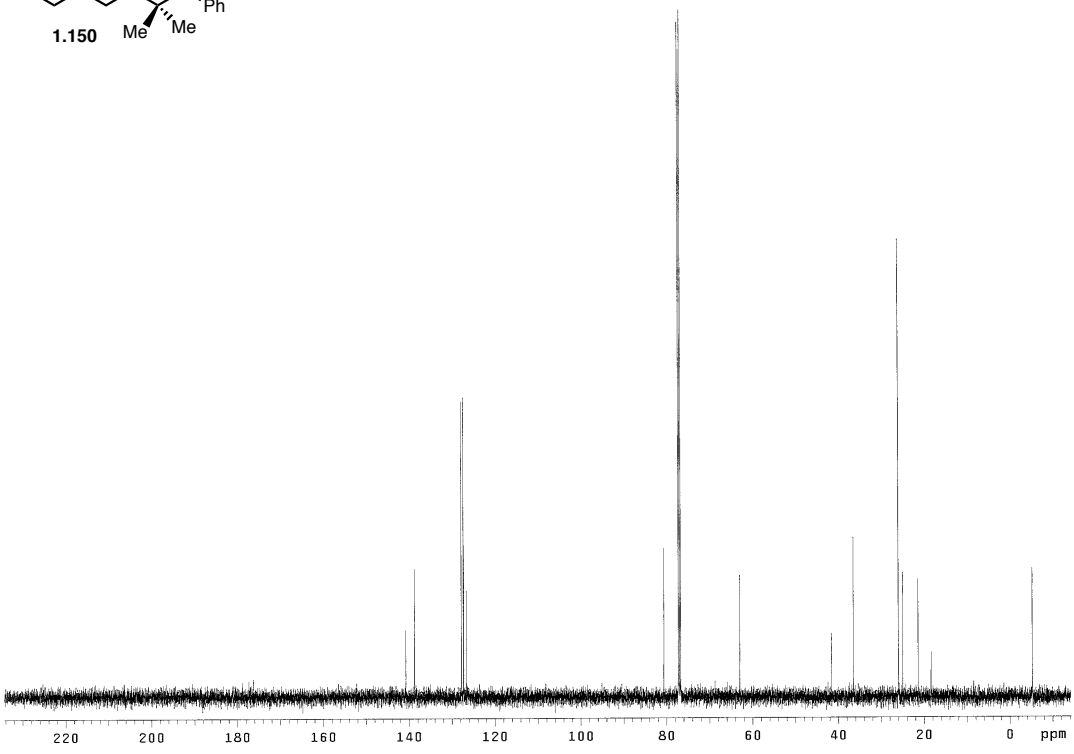

OH
TBSO
Ph
Me
Me

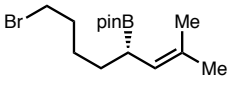
1.150

10
9
8
7
6
5
4
3
2
1
0
ppm

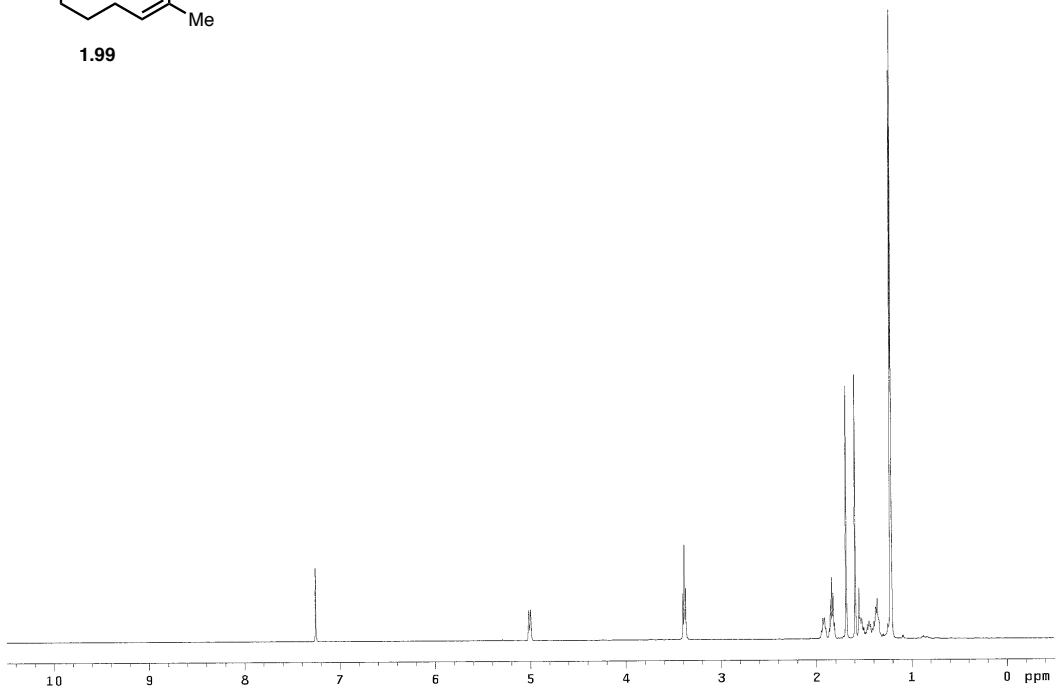

OH
TBSO
Ph
Me
Me

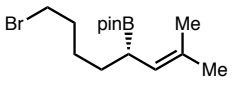
1.150


220
200
180
160
140
120
100
80
60
40
20
0
ppm

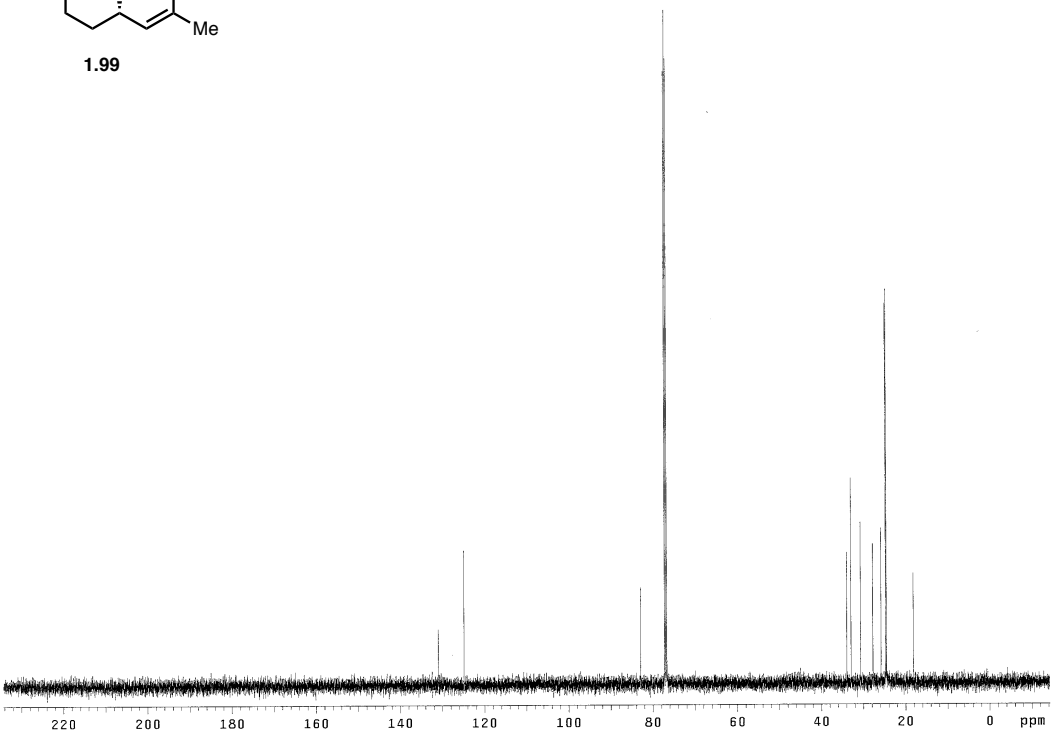

Br
pinB
Me
Me

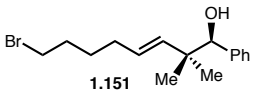
1.99


10
9
8
7
6
5
4
3
2
1
0 ppm

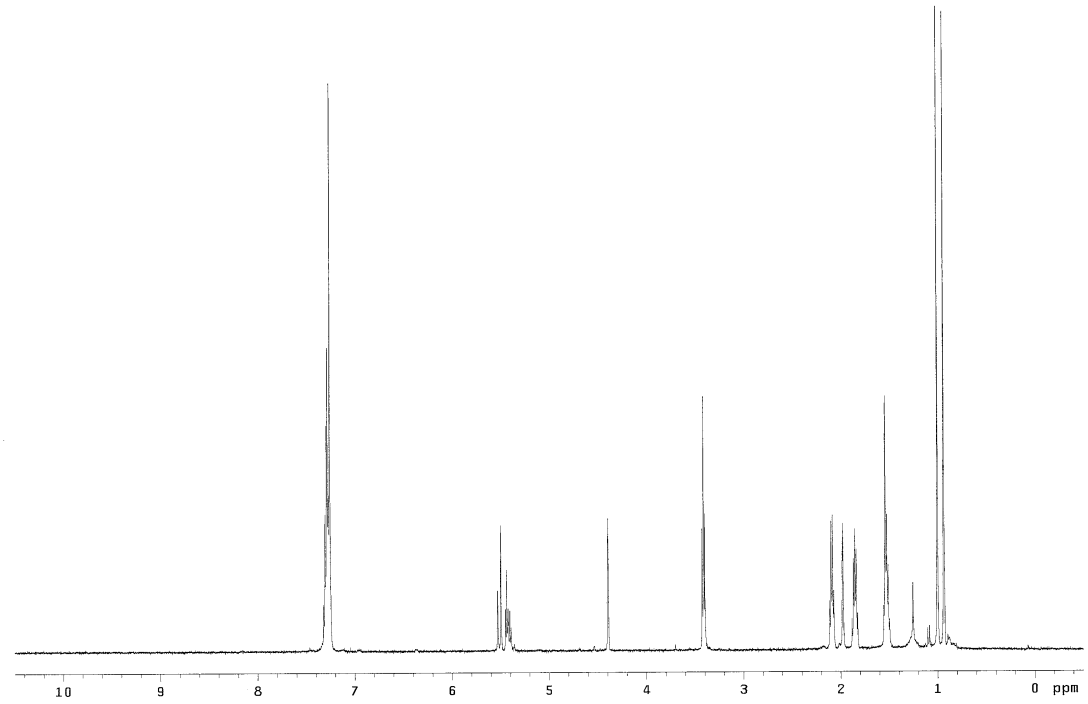

Br
pinB
Me
Me

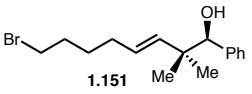
1.99


220
200
180
160
140
120
100
80
60
40
20
0 ppm

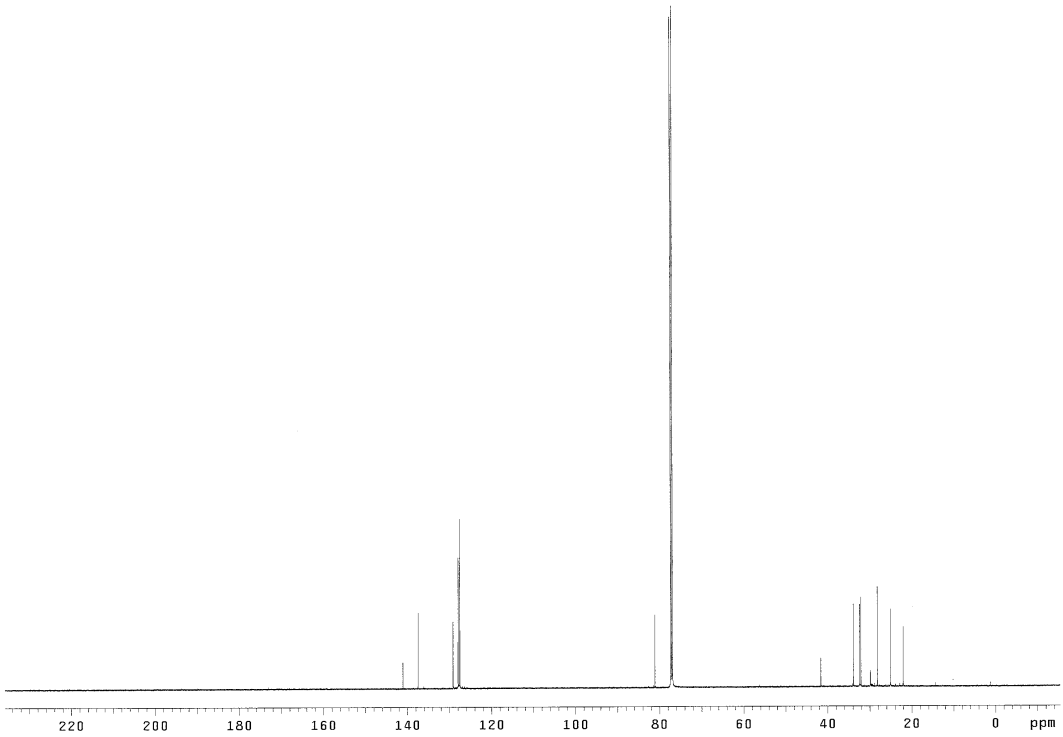

Br
OH
Ph
Me
Me

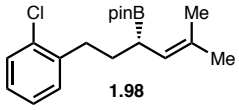
1.151


10
9
8
7
6
5
4
3
2
1
0 ppm


Br
OH
Ph
Me
Me

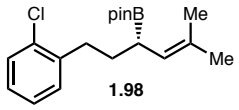
1.151


220
200
180
160
140
120
100
80
60
40
20
0 ppm

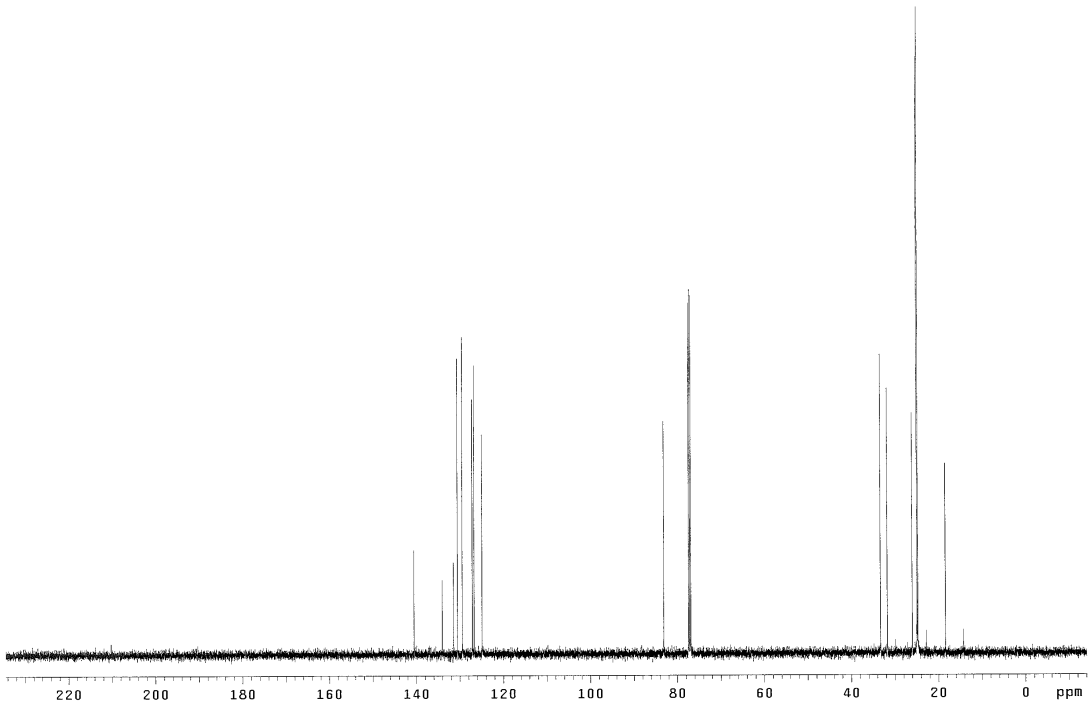

Cl
pinB
Me
Me

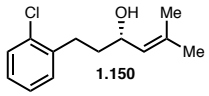
1.98

10
9
8
7
6
5
4
3
2
1
0 ppm

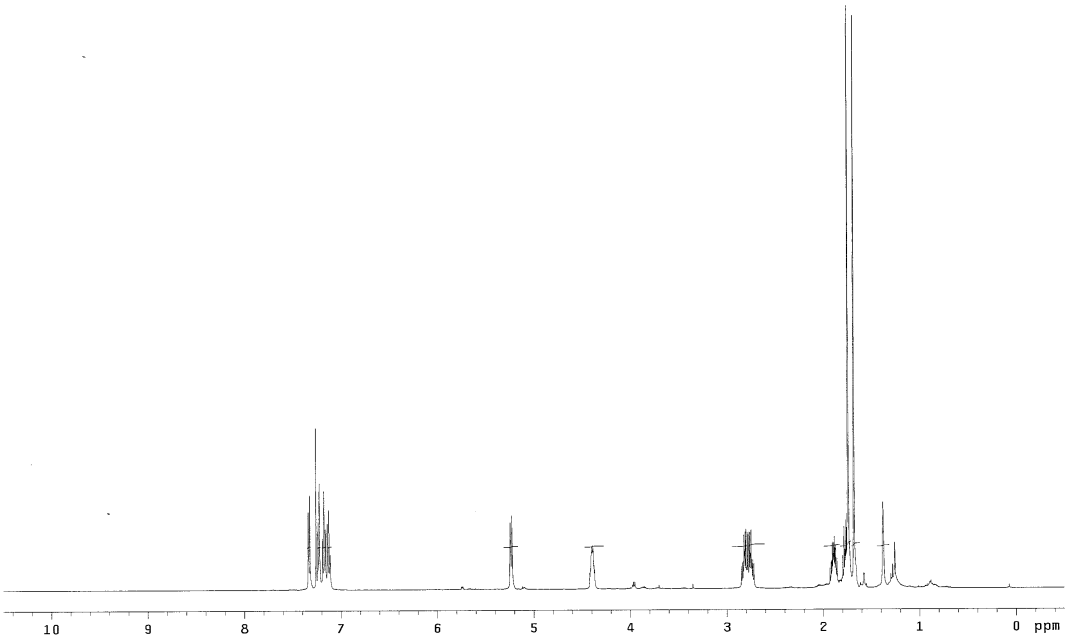

Cl
pinB
Me
Me

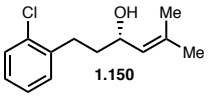
1.98


220
200
180
160
140
120
100
80
60
40
20
0 ppm

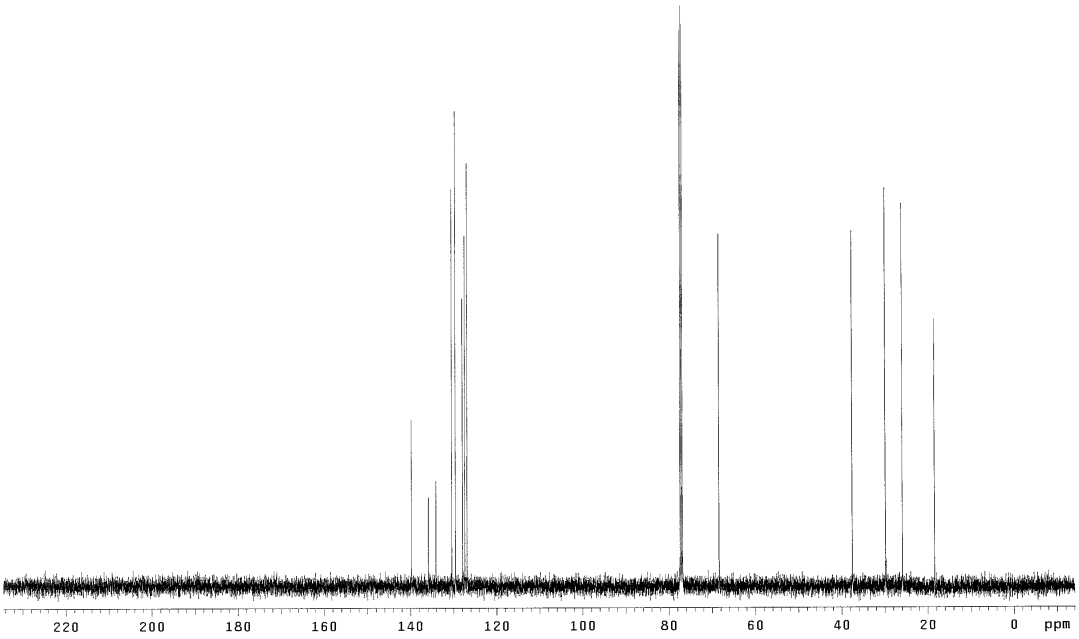

Cl
OH
Me
Me

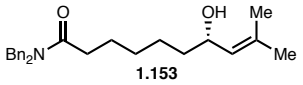
1.150


10
9
8
7
6
5
4
3
2
1
0
ppm

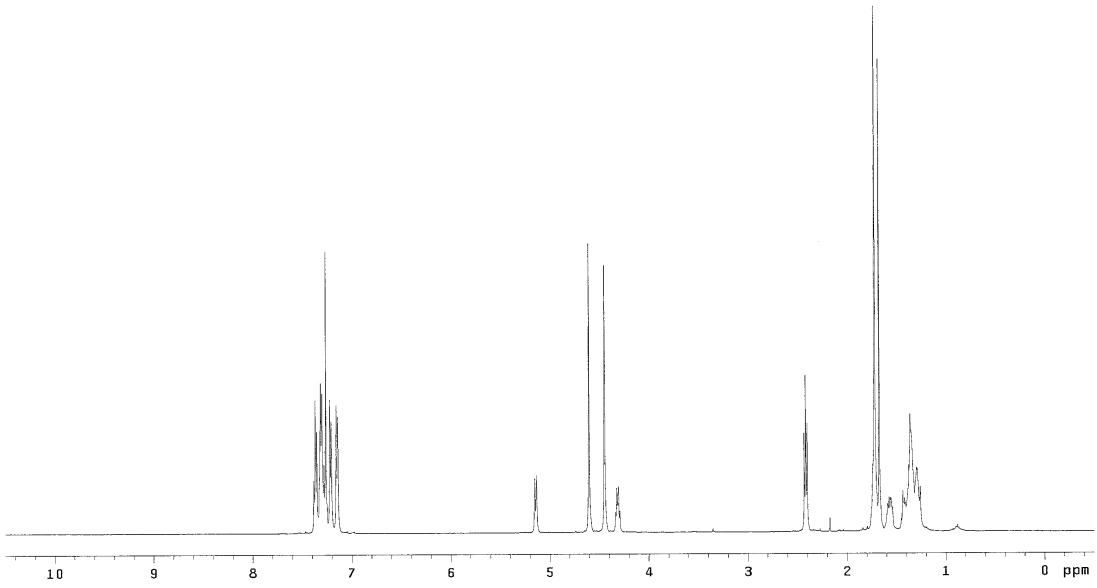

Cl
OH
Me
Me

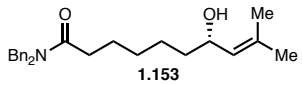
1.150


220
200
180
160
140
120
100
80
60
40
20
0
ppm

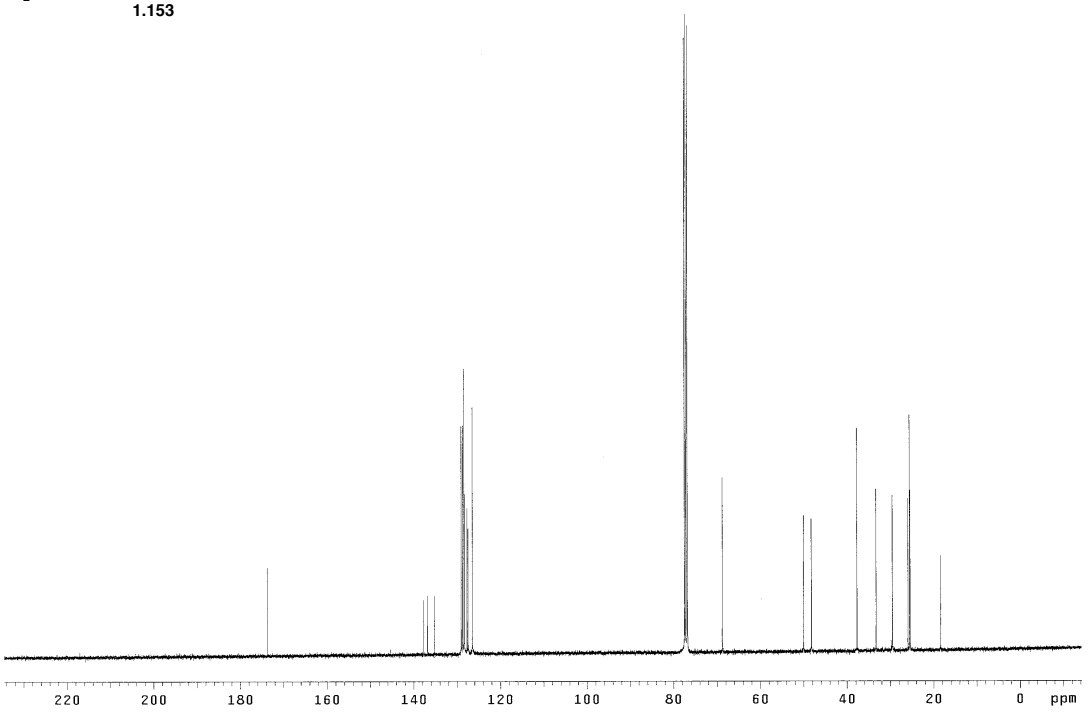

O
OH
Me
Bn2N
Me

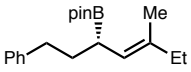
1.153


10
9
8
7
6
5
4
3
2
1
0 ppm


O
OH
Me
Bn2N
Me

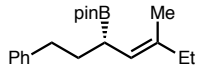
1.153


220
200
180
160
140
120
100
80
60
40
20
0 ppm

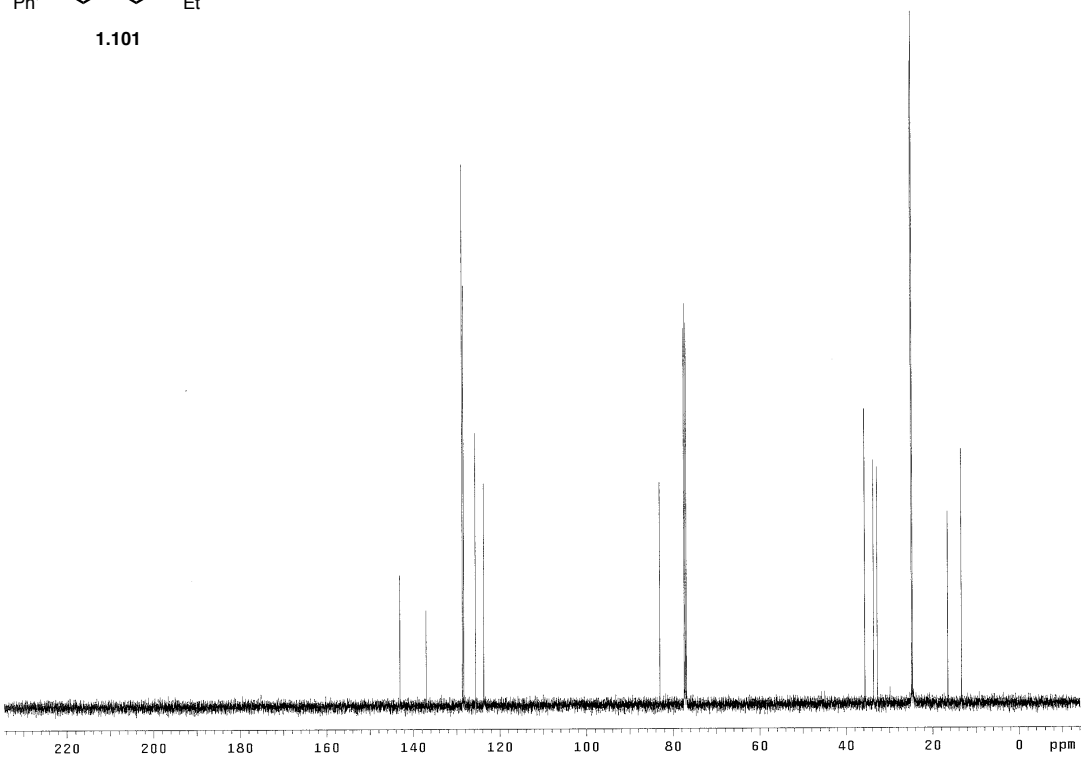

pinB
Me
Ph
Et

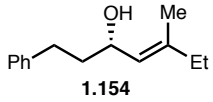
1.101

10
9
8
7
6
5
4
3
2
1
0 ppm


pinB
Me
Ph
Et

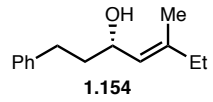
1.101


220
200
180
160
140
120
100
80
60
40
20
0 ppm


OH
Me
Ph
Et

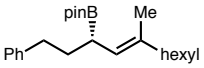
1.154

10
9
8
7
6
5
4
3
2
1
0 ppm


OH
Me
Ph
Et

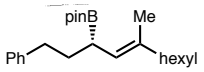
1.154

220
200
180
160
140
120
100
80
60
40
20
0 ppm

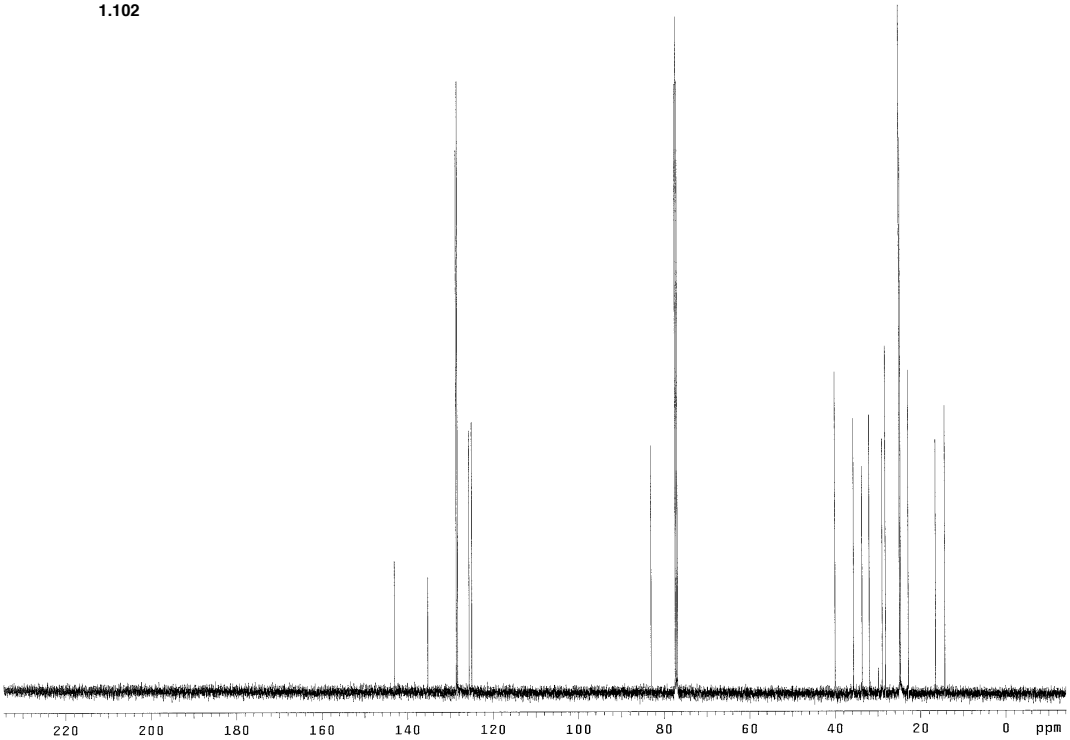

pinB
Me
Ph
hexyl

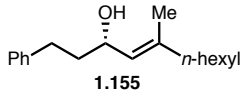
1.102

10
9
8
7
6
5
4
3
2
1
0
ppm

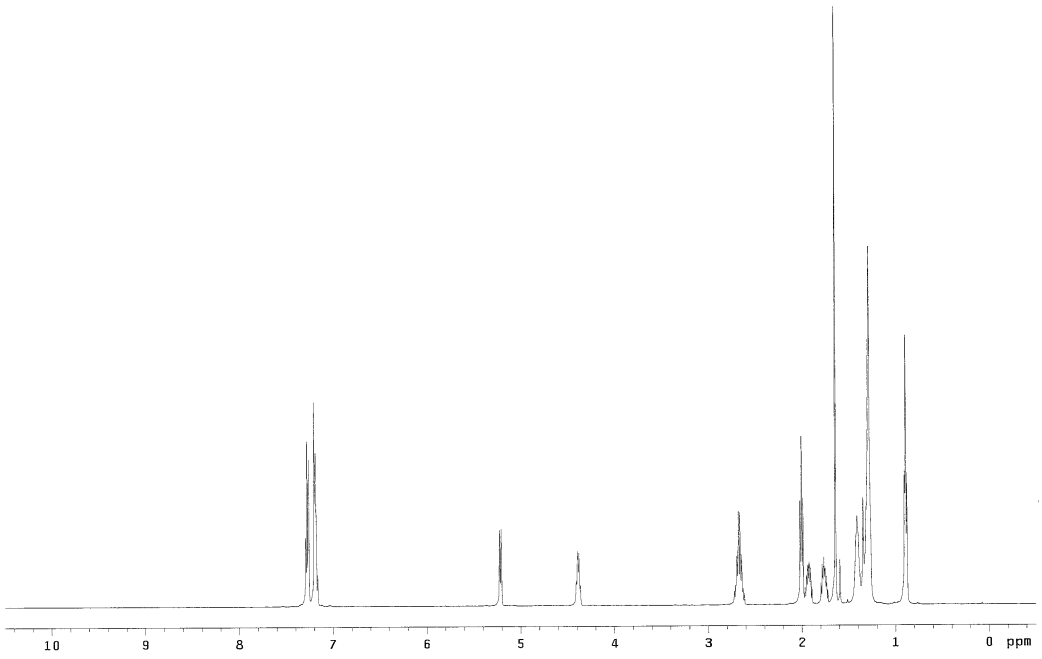

pinB
Me
Ph
hexyl

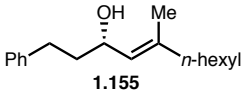
1.102


220
200
180
160
140
120
100
80
60
40
20
0
ppm

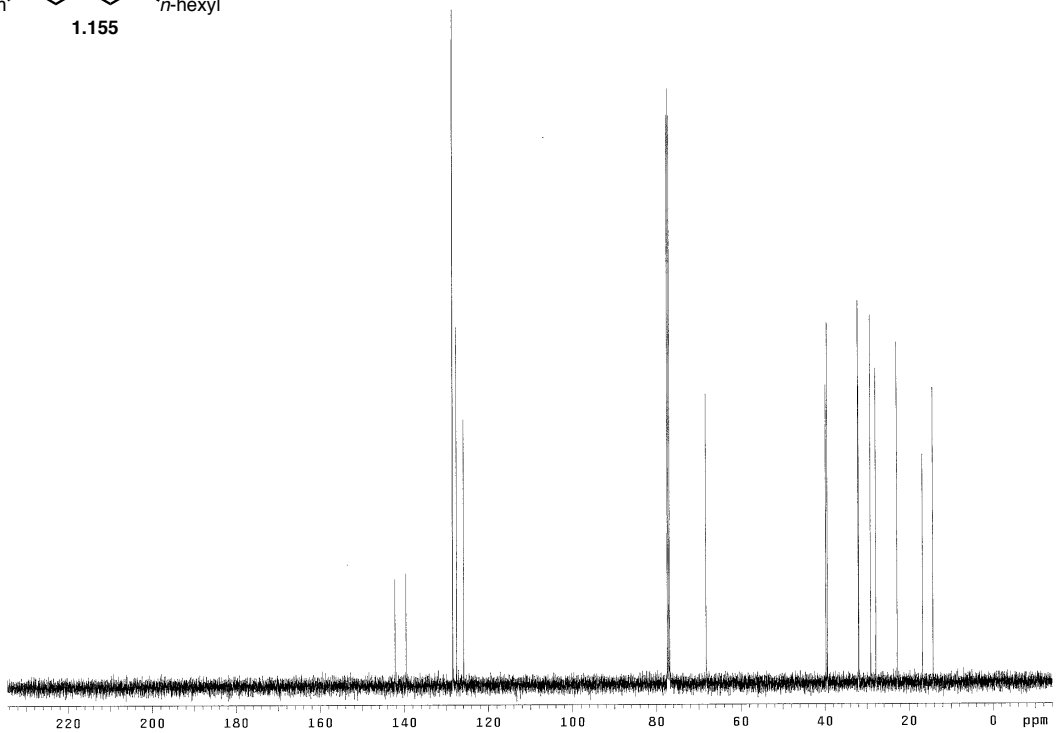

OH
Me
Ph
n-hexyl

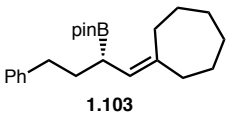
1.155


10
9
8
7
6
5
4
3
2
1
0 ppm


OH
Me
Ph
n-hexyl

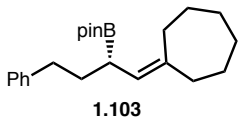
1.155


220
200
180
160
140
120
100
80
60
40
20
0 ppm

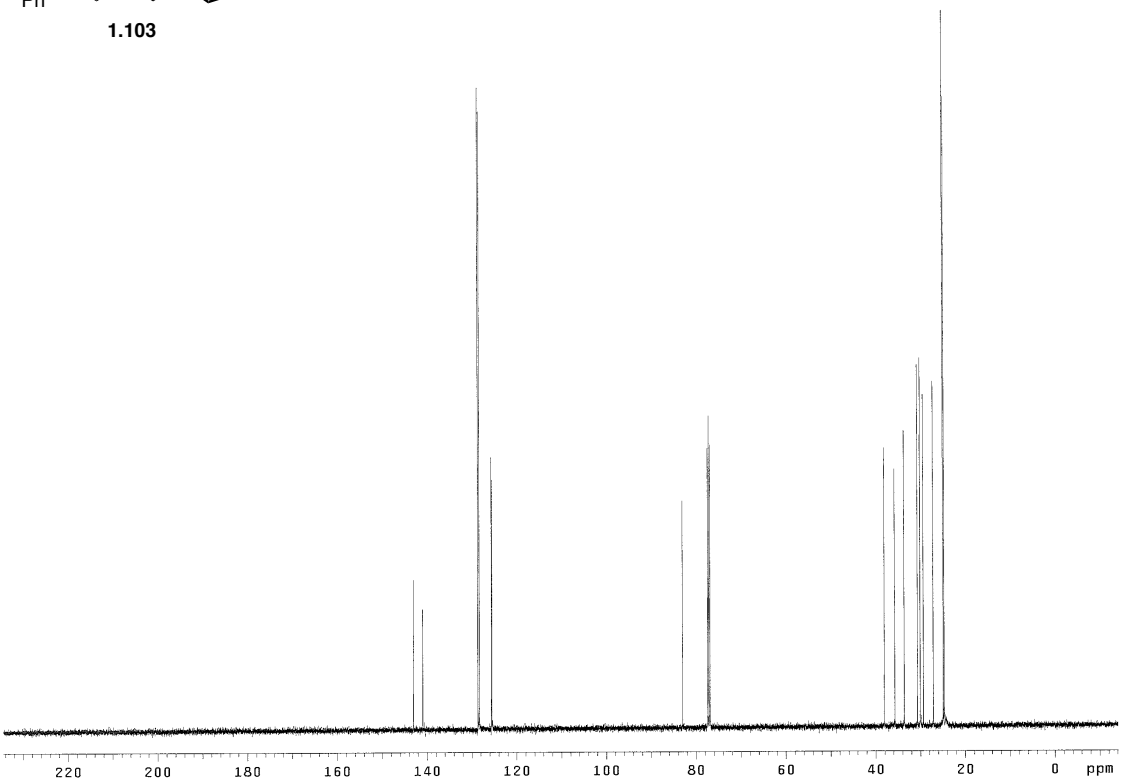

pinB
Ph

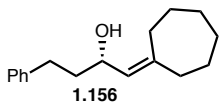
1.103

10
9
8
7
6
5
4
3
2
1
0 ppm

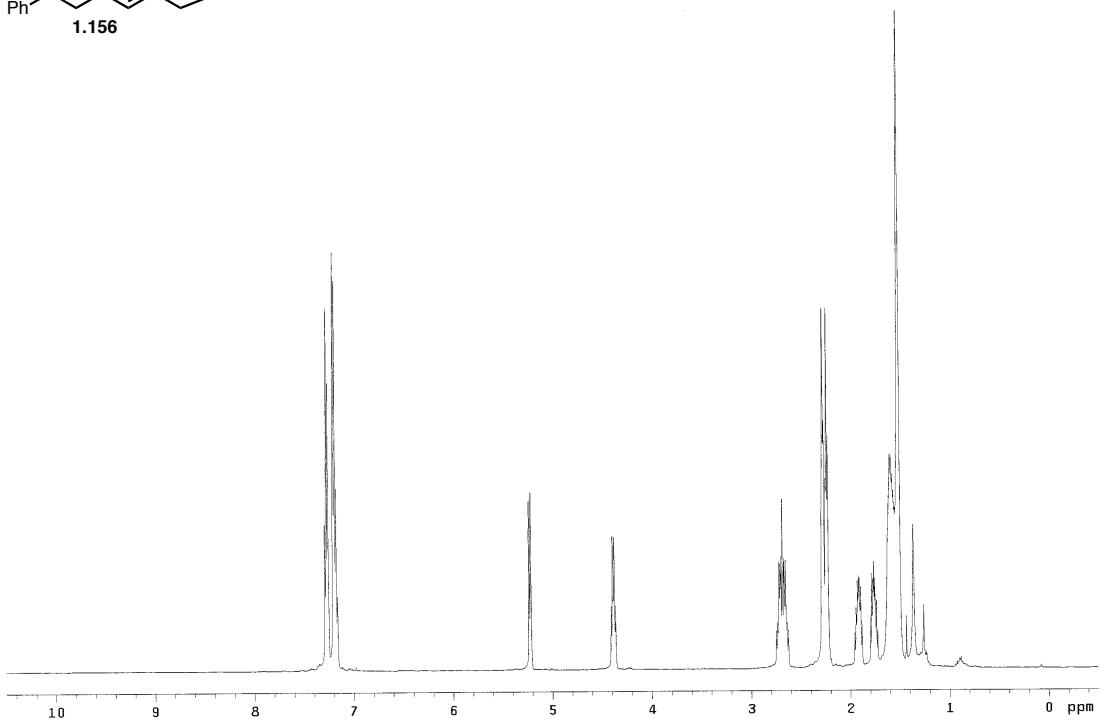

pinB
Ph

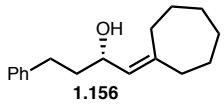
1.103


220
200
180
160
140
120
100
80
60
40
20
0 ppm


OH
Ph

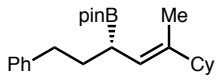
1.156


10
9
8
7
6
5
4
3
2
1
0
ppm

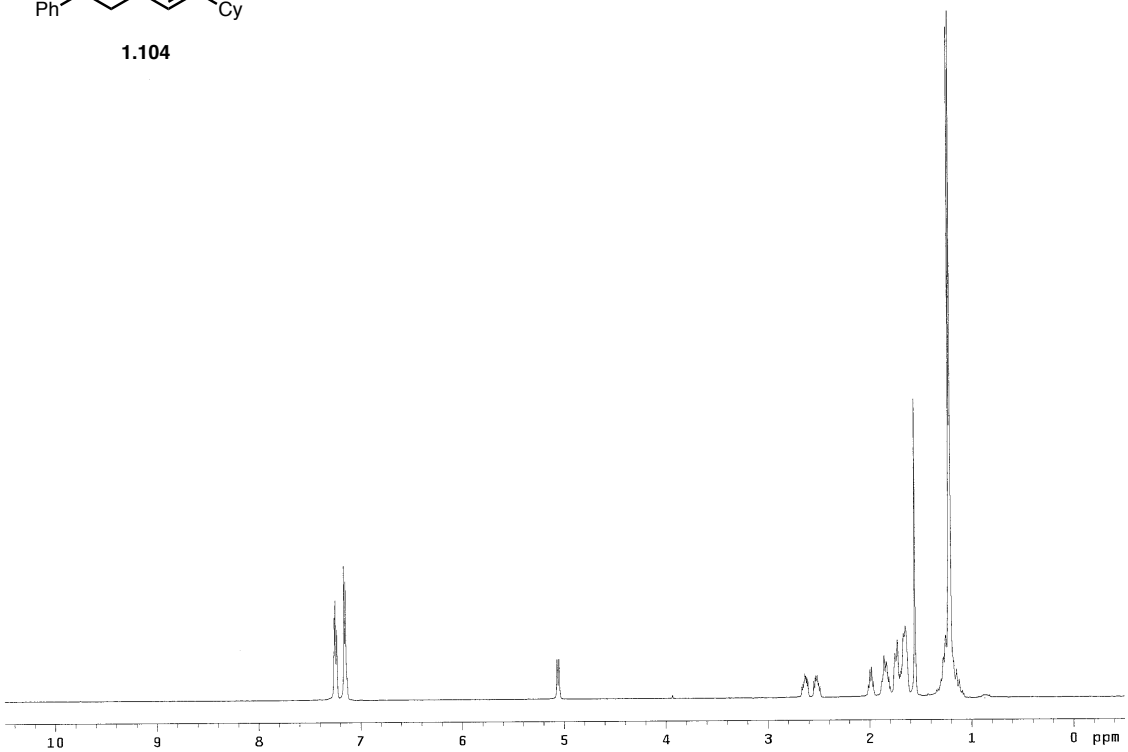

OH
Ph

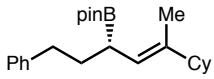
1.156

220
200
180
160
140
120
100
80
60
40
20
0
ppm

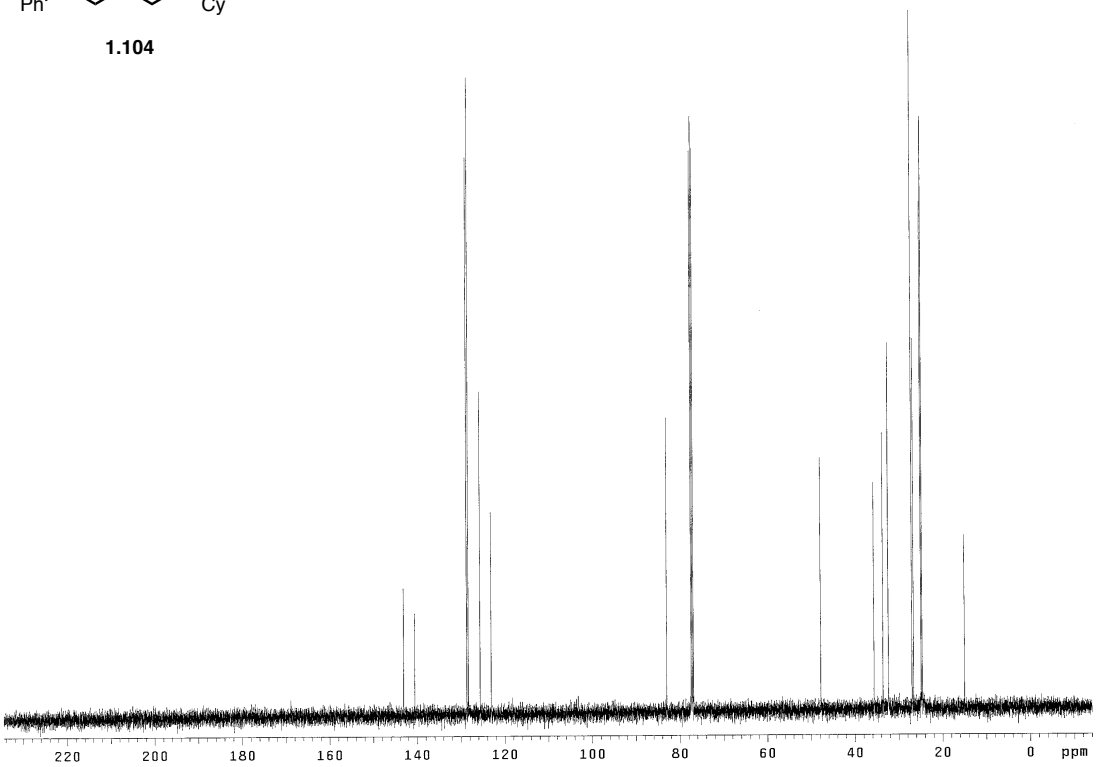

pinB
Me
Ph
Cy

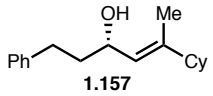
1.104


10
9
8
7
6
5
4
3
2
1
0 ppm


pinB
Me
Ph
Cy

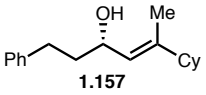
1.104


220
200
180
160
140
120
100
80
60
40
20
0 ppm

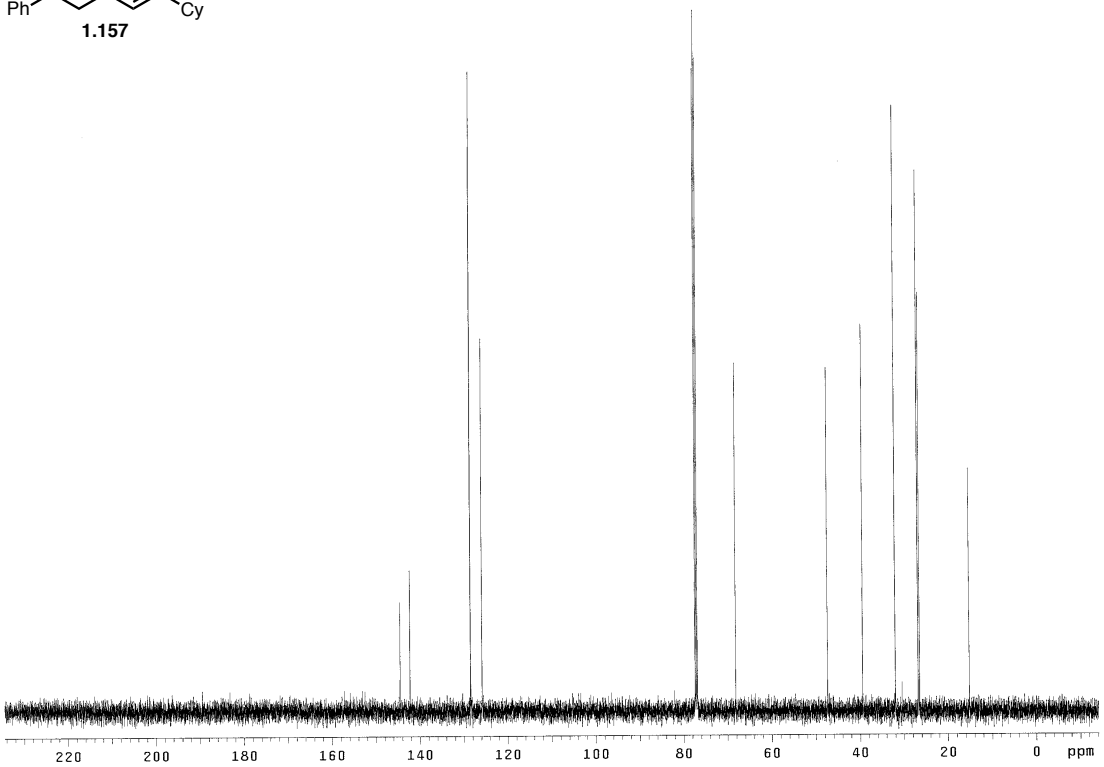

OH
Me
Ph
Cy

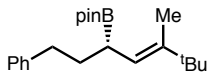
1.157

10
9
8
7
6
5
4
3
2
1
0 ppm

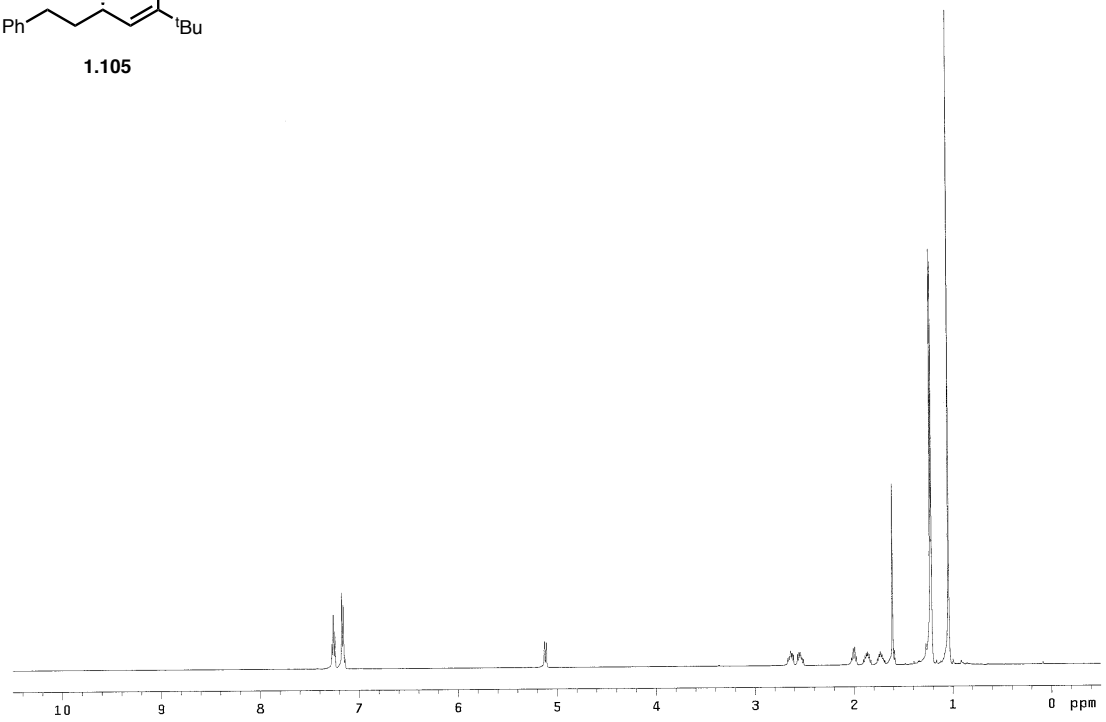

OH
Me
Ph
Cy

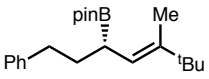
1.157


220
200
180
160
140
120
100
80
60
40
20
0 ppm


pinB
Me
Ph
tBu

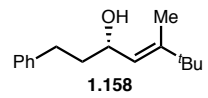
1.105


10
9
8
7
6
5
4
3
2
1
0 ppm


pinB
Me
Ph
tBu

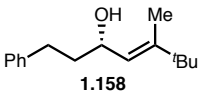
1.105

220
200
180
160
140
120
100
80
60
40
20
0 ppm

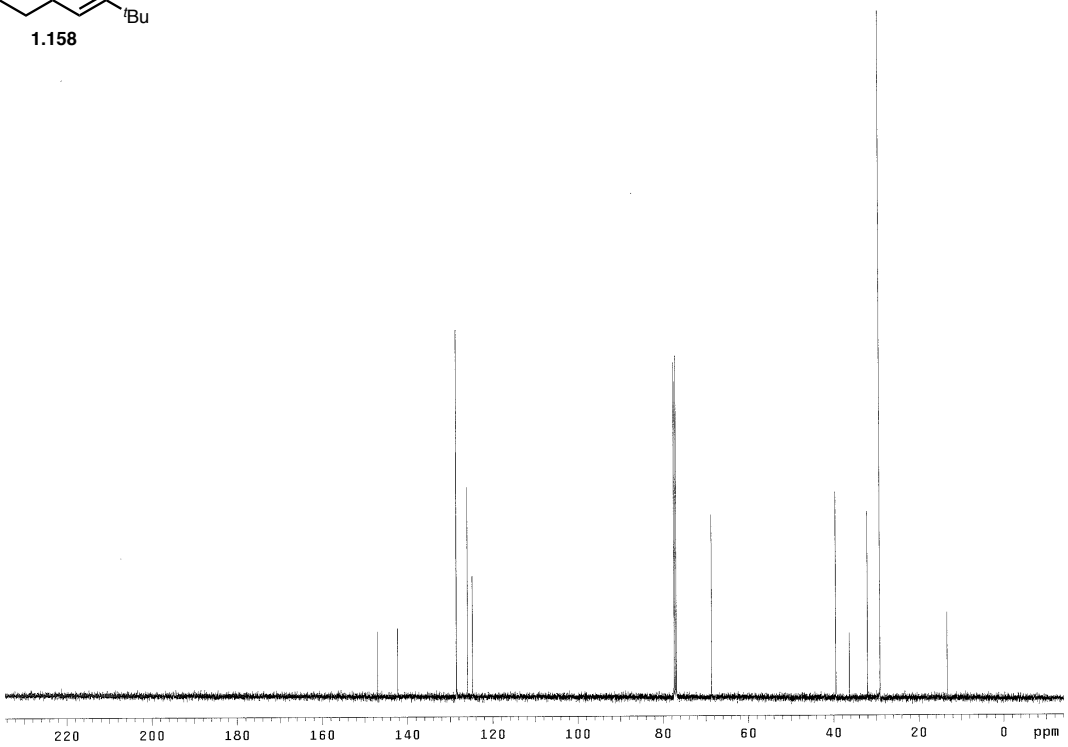

OH
Me
Ph
tBu

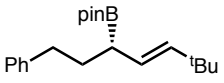
1.158

10
9
8
7
6
5
4
3
2
1
0 ppm


OH
Me
Ph
tBu

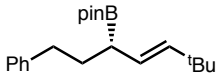
1.158


220
200
180
160
140
120
100
80
60
40
20
0 ppm

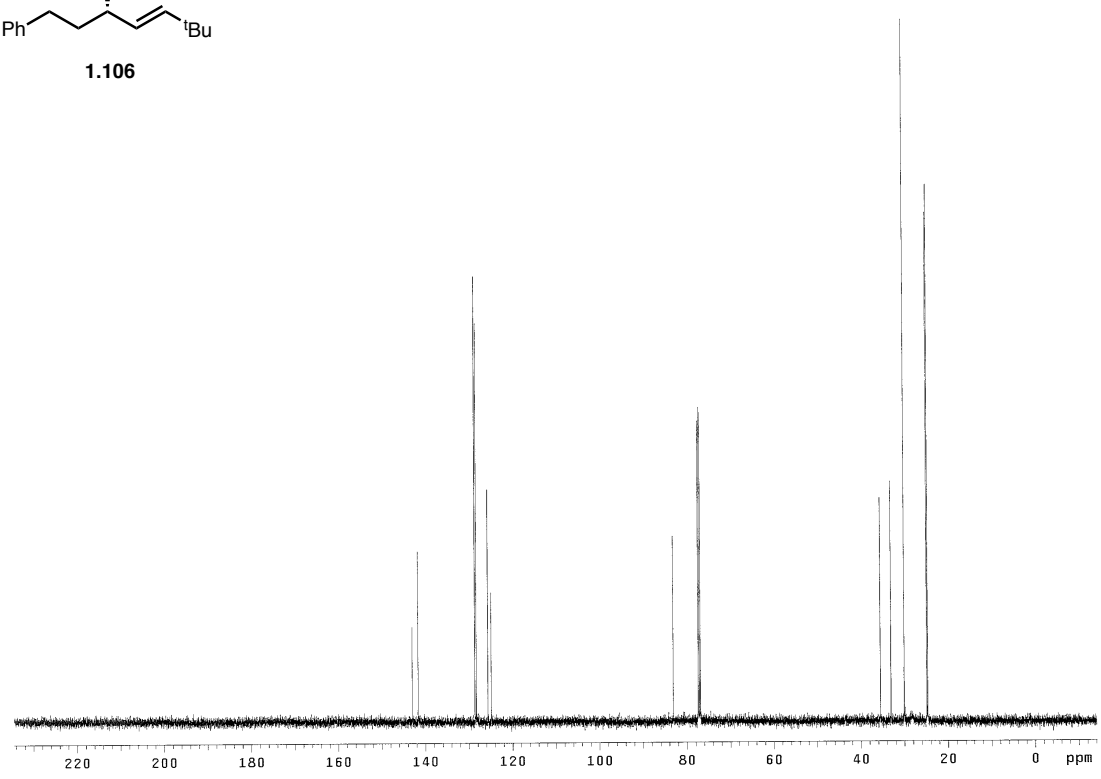

pinB
Ph
tBu

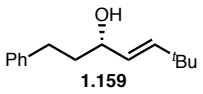
1.106

10
9
8
7
6
5
4
3
2
1
0 ppm


pinB
Ph
tBu

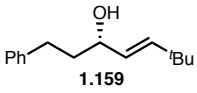
1.106


220
200
180
160
140
120
100
80
60
40
20
0 ppm

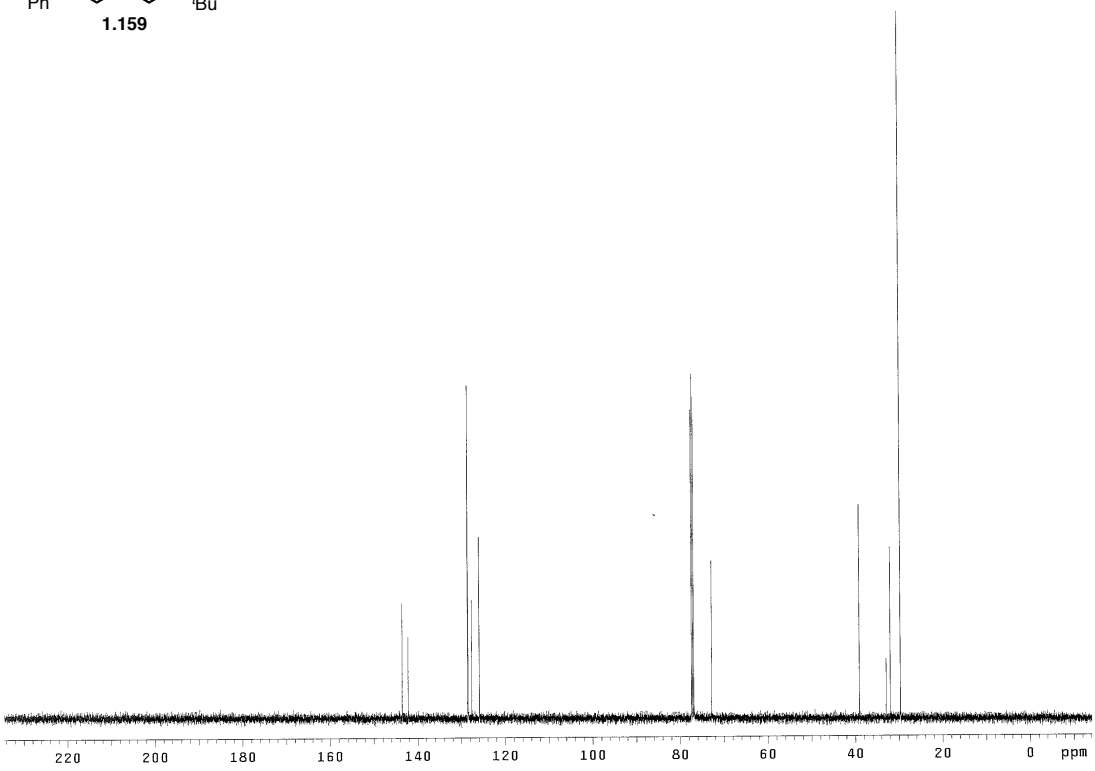

OH
Ph
tBu

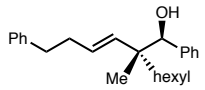
1.159

10
9
8
7
6
5
4
3
2
1
0 ppm


OH
Ph
tBu

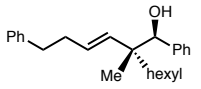
1.159


220
200
180
160
140
120
100
80
60
40
20
0 ppm


OH
Ph
Ph
Me
hexyl

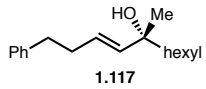
1.116

10
9
8
7
6
5
4
3
2
1
0
ppm


OH
Ph
Ph
Me
hexyl

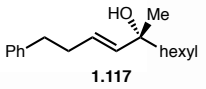
1.116

220
200
180
160
140
120
100
80
60
40
20
0
ppm


HO
Me
Ph
hexyl

1.117

10
9
8
7
6
5
4
3
2
1
0 ppm


HO
Me
Ph
hexyl

1.117

220
200
180
160
140
120
100
80
60
40
20
0 ppm

CHAPTER 2

Development of an Enantioselective Catalytic-Conjunctive Cross-Coupling Enabled by a Metal-Induced Metallate Rearrangement

2.1 Introduction

Transition-metal catalysis has become one of the major focuses for methods development in synthetic organic chemistry.[1] Transition-metal catalysis allows for the exploration of new bonds to be broken and formed. In the realm of transition-metal catalysis, palladium has received much attention in the discovery of new C-C bond forming reactions. Examples of these types of palladium-catalyzed reactions include the Heck reaction, Suzuki-Miyaura cross-coupling, Negishi cross-coupling, Hiyama cross-coupling amongst other reactions.[2] The utility of these reactions is highlighted by the 2010 Nobel Prize being awarded to Heck, Negishi and Suzuki for development of palladium catalyzed cross-coupling reactions.

---

[1] Bolm, M.; Bellar, M. *Transition Metals for Organic Synthesis: Building Blocks and Fine Chemicals. Second Revised and Enlarged Edition* **2004**, *Wiley-VCH*, 662 pp. (Vol. 1), 652 pp (Vol. 2) ISBN 3-52730613-7

[2] Johansson Seechurn, C. C. C.; Kitching, M. O.; Colacot, T. J.; Snieckus, V. *Angew. Chem. Int. Ed.* **2012**, *51*, 5062-5085

The Suzuki-Miyaura cross-coupling has become one of the most widely developed and utilized reactions in academia.[3] The pharmaceutical industry has employed the Suzuki-Miyaura cross-coupling even more so for the synthesis of biologically relevant molecules.[3] As a consequence, the Suzuki-Miyaura reaction has been extensively studied and the mechanism is becoming well understood. The ability to incorporate a new elementary step in the catalytic cycle for the Suzuki-Miyaura cross-coupling would represent a powerful advancement in the area of palladium catalysis. This chapter will describe the development of a palladium-catalyzed conjunctive-cross-coupling, which incorporates an alternative transmetallation step into the Suzuki-Miyaura cross-coupling.

2.2 Background

2.2.1 Suzuki-Miyaura Cross-Coupling and Alkenyl Boron "Ate" Complex 1,2 Metallate Rearrangements

The Suzuki-Miyaura cross-coupling has become one of the most widely used transition-metal catalyzed reactions and the mechanistic details have been extensively studied. Elegant work done by Soderquist[4], Hartwig[5], Amatore and Jutland,[6] Lloyd-Jones[7]

[3] a) Miyaura, N.; Suzuki, A. *Chem. Rev.* **1995**, *95*, 2457-2483 b) Yasuda, N.; King, A. O. *Topic Organomet. Chem.* **2004**, *6*, 205-245 c) Torborg, C.; Beller, M. *Adv. Synth. Catal.* **2009**, *351*, 3027-3043 d) Budaran, V. L.; Shuttleworth, P. S.; Clark, J. H.; Luque, R. *Current Organic Synthesis* **2010**, *7*, 614-627 e) Suzuki, A. *Angew. Chem. Int. Ed.* **2011**, *50*, 6723-6737 f) Navarro, O.; Maluenda, I. *Molecules* **2015**, *20*, 7528-7557

[4]Matos, K.; Soderquist, J. A. *J. Org. Chem.* **1998**, *63*, 461-470

[5]Carrow, B. P.; Hartwig, J. F. *J. Am. Chem. Soc.* **2011**, *133*, 2116-2119

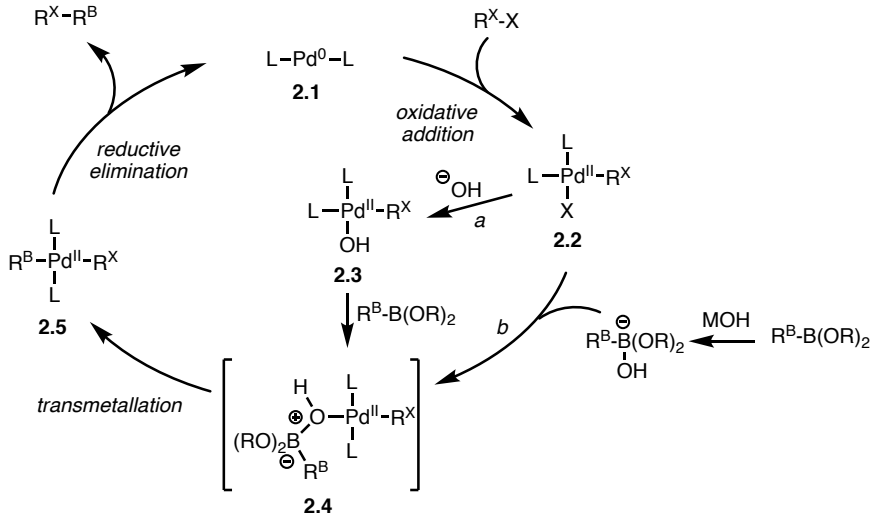
[6]Le Duc, G.; Amatore, C.; Jutland, A. *Chem. Eur. J.* **2012**, *18*, 6616-6625

[7]Lenox, A. J. J.; Lloyd-Jones, G. C. *Angew. Chem. Int. Ed.* **2013**, *52*-7362-7370

and Denmark[8] has shed light on the mechanism of the reaction. Most of the focus of these studies has been on the transmetallation step of the Suzuki-Miyaura cross-coupling. The transmetallation step is one of the fundamental steps of transition-metal cross-coupling catalytic cycles. Taking into account the mechanistic work, the general reaction mechanism for a Suzuki-Miyaura cross-coupling is depicted in Scheme 2.1. The catalytic cycle begins with oxidative addition of ligated palladium (0) (**2.1**) with the electrophile to form palladium (II)-halide adduct **2.2**. The next transmetallation step could occur by one of two pathways. One possibility (pathway "*a"*) proceeds through the formation of a palladium (II)-hydroxide intermediate (**2.3**) where addition to the organoboron reagent forms activated transmetallation intermediate **2.4**. Alternatively, external activation of the organoboronate (pathway "*b*") and addition to palladium (II)-halide intermediate **2.2** forms the activated transmetallation intermediate **2.4**. Subsequent transmetallation then forms palladium (II) intermediate **2.5**. Reductive elimination furnishes the desired product while reforming palladium (0) to restart the catalytic cycle. With the general mechanism of the Suzuki-Miyaura cross-coupling elaborated, the ability to introduce alternative steps into the catalytic cycle would represent a powerful addition to transition-metal catalysis.

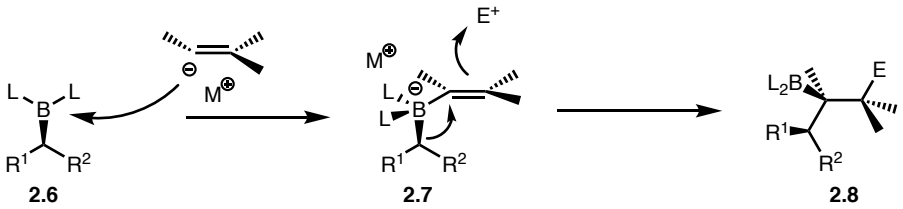
[8] a) Thomas, A. A.; Denmark, S. E. *Science* **2016**, *352*, 329-332 b) Thomas, A. A.; Wang, H.; Zahrt, A. F.; Denmark, S. E. *J. Am. Chem. Soc.* **2017**, *139*, 3805-3821

Scheme 2.1 General Mechanism of the Suzuki-Miyaura Cross-Coupling



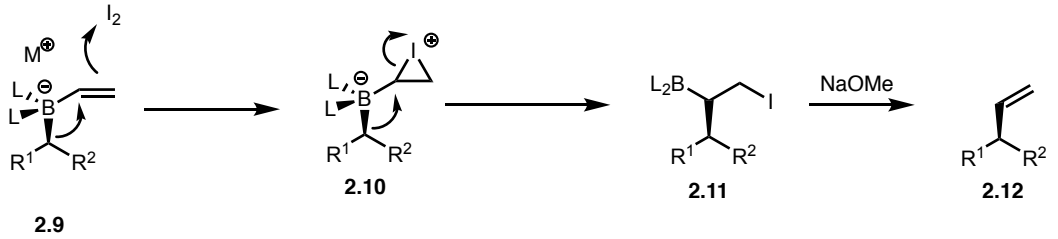
To probe the idea for new modes of catalysis, employing vinyl organoboron "ate" complexes was considered. Reactions of organoboronates with alkenyl nucleophiles generally form alkenyl organoboron "ate" complexes (**2.7**, Scheme 2.2). To induce a 1,2-metallate rearrangement of alkenyl organoboron "ate" complexes typically requires the use of a stoichiometric electrophilic activator of the π-system. After migration, a new C-C bond and new carbon-electrophile bond are formed (**2.8**). However, these adducts (**2.8**) are generally unstable and typically undergo elimination under the reaction conditions to reestablish unsaturation.

Scheme 2.2. **General Reactions of Alkenylboron "Ate" Complexes**



The Zweifel olefination is a widely-utilized reaction and illustrates the reactivity of alkenyl organoboron "ate" complexes (Scheme 2.3).[9] In this reaction, activation of the vinyl organoboron "ate" complex with iodine results in the formation of iodonium species **2.10**. The iodonium intermediate then undergoes a 1,2-migration to form a new carbon-carbon bond and new carbon-iodine bond (**2.11**). Subsequent treatment with sodium methoxide induces the elimination to form the net vinylation product **2.12**.

Scheme 2.3 Zweifel Olefination

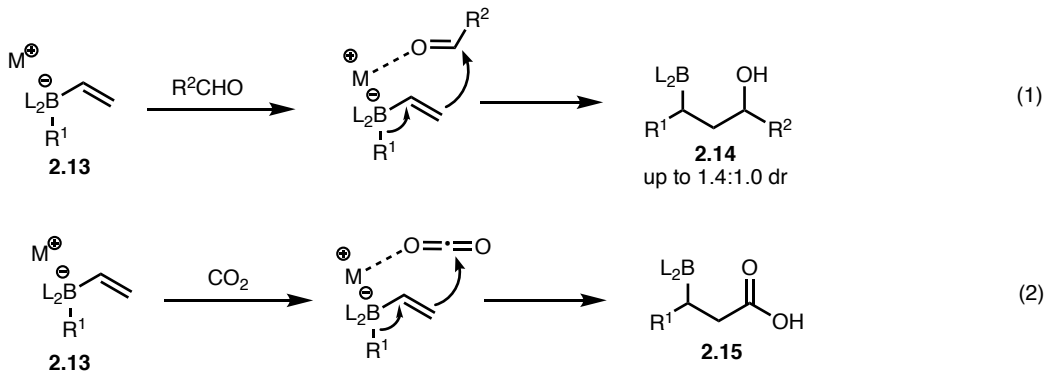


While the Zweifel olefination has been extensively developed,[10] alternative electrophilic activators that divert from the 1,2-migration-elimination reaction sequence are lacking. Work done by Utimoto and coworkers realized a new reaction of vinyl organoboron "ate" complexes avoiding elimination of the organoboron group.[11] The newly developed reaction showed that vinyl organoboron "ate" complexes can undergo a 1,2-migration and addition sequence to aldehydes (Scheme 2.4, eq. 1). The products of the reaction are synthetically useful γ-hydroxy organoboronates, a precursor to 1,3-diol motifs. However, under these reaction conditions employing organolithium or organomagnesium reagents, only low levels of diastereoselectivity were observed. Deng and coworkers were able to expand upon the vinyl organoboron "ate" complex reactivity to promote a 1,2-

[9] a) Jesthi, P. K.; Matteson, D. S. *J. Organomet. Chem.* **1976**, *110*, 25-37 b) Matteson, D. S. *Synthesis* **1975**, 147-159 c) Thomas, R. C.; Walker, J. A.; Evans, D. A. *Tetrahedron Lett.* **1976**, *17*, 1427-1430 d) Crawford, T. C.; Thomas, R. C.; Evans, D. A. *J. Org. Chem.* **1976**, *41*, 3947-3953
[10] Armstrong, R. J.; Aggarwal, V.K. *Synthesis* **2017**, *49*, 3323-3336
[11] Uchida, K.; Nozaki, H.; Utimoto, K. *Tetrahedron* **1977**, *33*, 1949-1952

migration and addition sequence to carbon dioxide to synthesize β-boryl carboxylic acids (Scheme 2.4, eq. 2).[12]

Scheme 2.4 Previous Work of Nucleophilic 1,2-Migrations of Vinylboron "Ate" Complexes

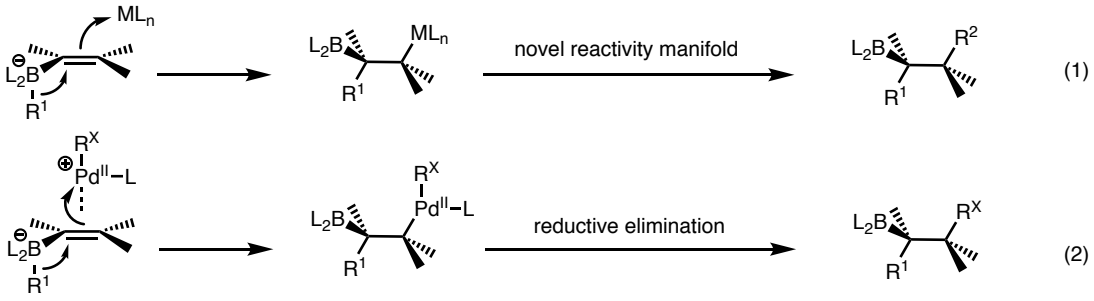


Based on the previous work with vinyl organoboron "ate" complexes, it was hypothesized that 1,2-metallate rearrangements might be incorporated into transition-metal catalysis. Instead of a stoichiometric activator, a transition-metal might activate the alkenyl organoboron "ate" complex for a 1,2-metallate rearrangement (Scheme 2.5, eq. 1). The newly formed carbon-metal bond could be further functionalized in the course of catalytic reactions. Choosing palladium to promote the 1,2-metallate rearrangement might allow for incorporation into Suzuki-Miyaura cross-coupling reactions. After oxidative addition, and dissociation of the counterion would generate a cationic palladium (II) complex. The newly formed cationic palladium (II) intermediate might then be a sufficient π-activator to induce a 1,2-metallate rearrangement (Scheme 2.5, eq. 2). Subsequent reductive elimination would furnish a new carbon-carbon bond. More importantly, incorporating a chiral catalyst to distinguish the enantiotopic faces of the vinyl organoboron "ate" complex

[12] Lu, D. –A.; Xu, W. –H.; Deng, M. –Z. *J. Chem. Soc., Chem. Commun*. **1985**, *0*, 1478-1479

could render the reaction enantioselective. The aforementioned catalytic process would result in the formation of two new carbon-carbon bonds and a boron-containing carbon stereocenter in one-step from simple starting materials.

Scheme 2.5 Transition-Metal Induced 1,2-Metallate Rearrangements



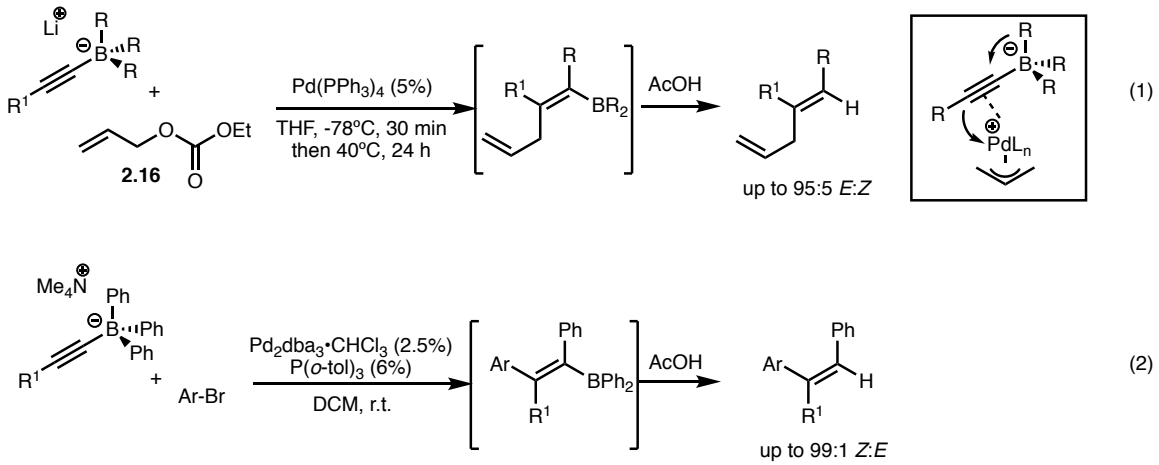
2.2.2 Previous Work on Metal-Induced 1,2-Rearrangements

The development of an enantioselective metal-induced 1,2-metallate rearrangement would represent a powerful addition to transition-metal catalysis. Consequently, there have been reports of alkynyl organoboron "ate" complexes undergoing similar modes of reactivity. Early work done by Deng and coworkers demonstrated that alkynyl trialkyl organoborane "ate" complexes undergo addition to palladium (II) π-allyl electrophiles. (Scheme 2.6, eq. 1).[13] While other interpretations of the mechanism are possible, the reaction might go through a palladium-induced 1,2-metallate rearrangement. As depicted in Scheme 2.6 (eq. 1), palladium (II) activation of the alkynyl organoborane "ate" complexes induces a 1,2-migration of the R group onto the alkyne. Murakami and coworkers expanded upon the reactivity of alkynyl organoboron "ate" complexes by

[13] Chen, Y.; Li, N. –S.; Deng, M. –Z. *Tetrahedron Lett.* **1990**, *31*, 2405-2406

employing a different palladium catalyst and allyl bromide electrophiles.[14] Murakami and coworkers also reported the cross-coupling of alkynyl triphenylborane "ate" complexes with a variety of aryl electrophiles (Scheme 2.6, eq. 2).[15] However, under the newly developed reaction conditions by Murakami the (*Z*)-isomer was observed to be the major product.

Scheme 2.6 Previous Work of Metal-Induced Metallate Rearrangements of Alkynyl Triorganoborane "Ate" Complexes

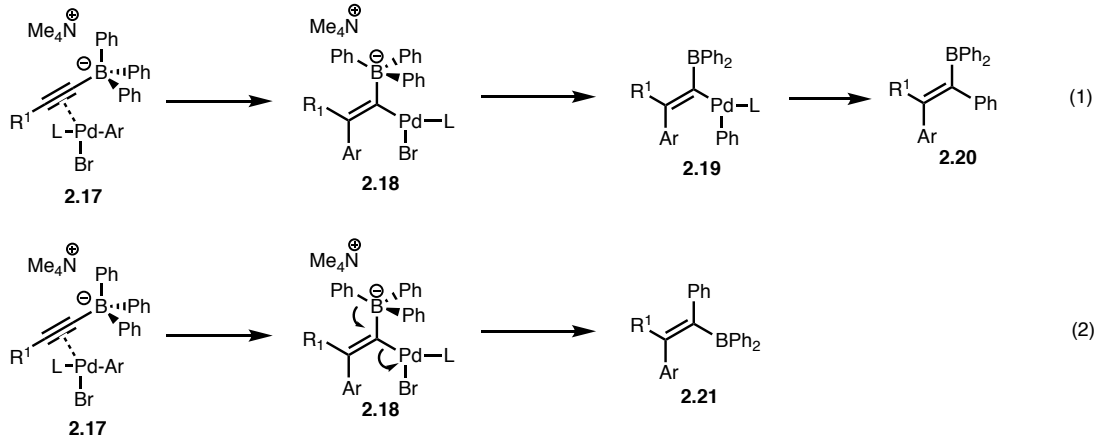


To explain the observed stereochemical outcome, Murakami and coworkers proposed an alternative mechanism to the metal-induced 1,2-metallate rearrangement depicted in Scheme 2.6, eq. 1. The formation of the (*Z*)-isomer was rationalized by coordination of palladium (II) to the alkynyl organoboron "ate" complex (**2.17**) and *syn* carbopalladation to form intermediate **2.18** (Scheme 2.7, eq. 1). Subsequent intramolecular transmetallation (**2.19**) and reductive elimination furnishes the major *(Z)*-isomer of product. The proposed intramolecular transmetallation was tentatively supported through

[14] Ishida, N.; Shinmoto, T.; Sawano, S.; Miura, T.; Murakami, M. *Bull. Chem. Soc. Jpn.* **2010**, *83*, 1380-1385
[15] Ishida, N.; Muira, T.; Murakami, M. *Chem. Commun.* **2007**, 4381-4383

a cross-over experiment (not pictured). However, under these reaction conditions the minor *(E)*-isomer of product was observed in statistically significant amounts. The (*E*)-isomer was proposed to arise by a *syn* carbopalladation (**2.18**), followed by reductive displacement of palladium by the organoboron "ate" complex (Scheme 2.7, eq. 2). Alternatively, the (*E*)-isomer might be produced by a palladium-induced 1,2-metallate rearrangement in analogy to the work by Deng and coworkers in Scheme 2.6, eq. 1. In the development of an enantioselective, palladium-induced 1,2-metallate rearrangement of vinyl organoboronate "ate" complexes, these possible mechanistic pathways have to be taken into consideration.

Scheme 2.7 Alternative Mechanisms for the Palladium Cross-Coupling of Alkynyl Triphenylborane "Ate" Complexes

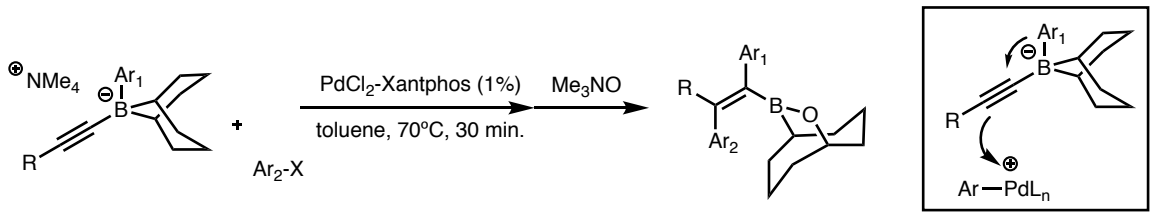


More recently, Murakami and coworkers and expanded upon the first report to include the cross-coupling of 9-BBN derived alkynyl organoborane "ate" complexes (Scheme 2.8, eq. 1).[16] For the observed major stereochemical outcome, Murakami invokes a *syn* carbopalladation-reductive displacement sequence in analogy to the previous report

[16] Ishida, N.; Shimamoto, Y.; Murakami, M. *Org. Lett.* **2009**, *11*, 5434-5437

(Scheme 2.7, eq. 2). An alternative mechanistic pathway consistent with the stereochemical outcome is a palladium-induced 1,2-metallate rearrangement (Scheme 2.8).

Scheme 2.8 Previous work on Palladium-Induced Metallate Rearrangements



2.3 Development of an Enantioselective Palladium-Induced Metallate Rearrangement of Vinylboron "Ate" Complexes[17]

2.3.1 Reaction Discovery, Optimization, and Scope[17]

To begin the investigation for an enantioselective palladium-induced metallate rearrangement of vinyl organoboron "ate" complexes, careful analysis of the reaction parameters was necessary. With regards to the aryl electrophile for the reaction, aryl triflates were chosen. The triflate anion is known to be non-coordinating and readily dissociates from palladium to form cationic palladium. Access to cationic palladium might be crucial due to the increased ability to bind the alkene of the vinyl organoboron "ate" complex and promote the desired 1,2-metallate rearrangement. The nature of the

[17] Zhang, L.; Lovinger, G. L.; Edelstein, E. K.; Szymaniak, A. A.; Chierchia, M. P. *Science* **2016**, *351*, 70-74

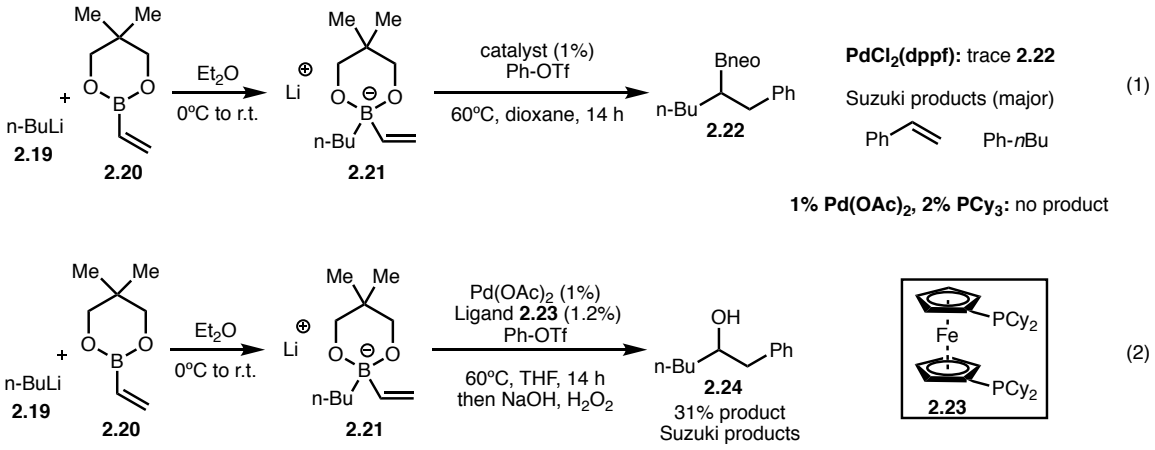
organoboronate was considered likely to have an impact upon the reactivity and practicality of the methodology. Organoboronic esters were chosen as they are generally air and moisture stable as well as configurationally stable. In addition to stability, nucleophilicity parameter studies done by Mayr and Aggarwal have shown that neopentyl diol-derived organoboron "ate" complexes are most nucleophilic. The increased nucleophilicity is proposed to be a consequence of the steric environment as compared to pinacol boronic esters.[18] Taking the nucleophilicity into account, vinyl boronic acid neopentyl ester was chosen to explore the reactivity of a metal-induced metallate rearrangement.

With regards to the ligand for palladium, it was hypothesized that bidentate phosphines have the highest potential to promote the desired palladium-induced 1,2-metallate rearrangement. A larger steric environment might help promote alkene binding over binding to the oxygen on the neopentyl diol boron ligand. Binding to the more sterically encumbered neopentyl oxygen might be a possible mechanism to promote undesired direct Suzuki-Miyaura cross-coupling. In addition to oxygen binding, a wide-bite-angle bidentate ligand might aid in facilitating reductive elimination over β-elimination. To investigate the proposed reactivity for a palladium-induced 1,2-metallate rearrangement of vinyl organoboron "ate" complexes, the reactions depicted in Scheme 2.9 were conducted. Employing monodentate tricyclohexylphosphine as the ligand resulted in no product formation under the depicted catalytic conditions (Scheme 2.9, eq. 1). A 1,1'-bis(diphenylphosphino)ferrocene palladium dichloride catalyst afforded trace organoboronate product **2.22** in addition to Suzuki-Miyaura products (Scheme 2.9, eq. 1). To explore other ferrocene-based bidentate phosphine ligands, the use of a palladium

[18] a) Berionni, G. Leonov, L. I.; Mayer, P.; Ofial, A. R.; Mayr, H.; *Angew. Chem. Int. Ed.* **2015**, *54*, 2780-2783 b) Feeney, K.; Berrionni, G.; Mayr, H.; Aggarwal, V. *Org. Lett.* **2015**, *17*, 2614-2617

acetate pre-catalyst was necessary. By employing ligand **2.23** and palladium acetate for catalyst formation, an appreciable amount of alcohol product **2.24** was isolated after oxidation. In addition to the desired product, Suzuki-Miyaura products (*n*-butyl benzene and styrene) were also observed. The observation of Suzuki-Miyaura products shows that the chiral catalyst needs to have the ability to chemoselectivity engage in alkene binding for the desired 1,2-metallate rearrangement. In addition to chemoselectivity, the catalyst must differentiate the enantiotopic faces of the vinyl organoboron "ate" complex.

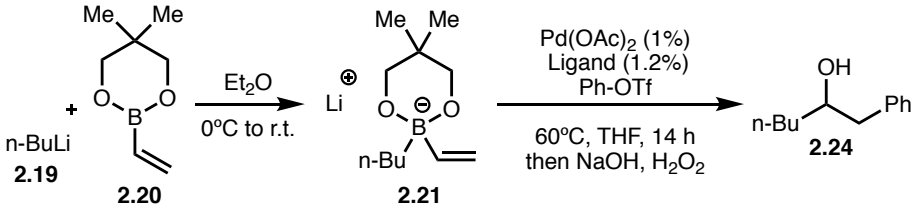
Scheme 2.9 Initial Investigations for the Discovery of a Palladium-Induced Metallate Rearrangement of Vinylboron "Ate" Complexes



To render the palladium-induced 1,2-metallate rearrangement enantioselective, a survey of chiral bidentate phosphine ligands was undertaken. Employing commonly used, small-bite-angle chiral bidentate ligands like *(S,S)*-QuinoxP (**2.25**) and (*S,S*)-Me-DuPhos (**2.26**) showed no reactivity in the desired palladium-induced 1,2-metallate rearrangement (Table 2.1, entries 1-2). Analyzing *(S)*-MeO-furyl BIPHEP (**2.27**) as the ligand afforded the desired product albeit in modest enantioselectivity (Table 2.1, entry 3). Since the initial discovery employed achiral ferrocene-based phosphine ligands, chiral variants of these ligands were of interest. Josiphos ligand **2.28** produced comparable yields to *(S)*-MeO-

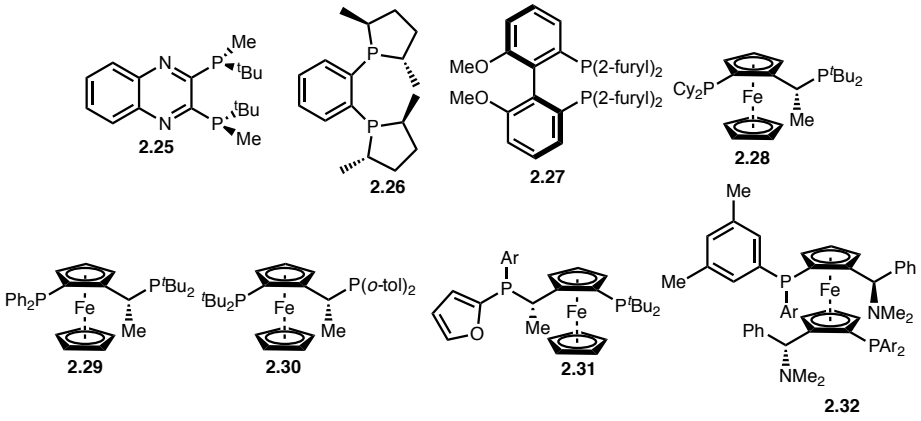
furyl BIPHEP and also an increase in enantioselectivity (Table 2.1, entries 3 vs. 4). With the increase in enantioselectivity, a survey of commercially available Josiphos ligands was carried out. Varying the electronics of the phosphino group on the ferrocene ring to diphenylphosphino (**2.29)** resulted in diminished yield and enantioselectivity (Table 2.1, entry 5). Maintaining an electron-rich phosphine group on the ferrocene while changing the electronic properties of the other phosphine group was analyzed with Josiphos ligand **2.30**. Varying the electronics of the other phosphine group gave excellent reactivity, however an almost racemic reaction occurred (Table 2.1, entry 6). Decreasing the size of the diarylphosphino substitution (**2.31**) resulted in lower reactivity and increased enantioselectivity (Table 2.1, entry 7). From these data, altering the dialkylphosphino substitutions in Josiphos ligand **2.28** were ineffective (Table 2.1, entry 4). An entirely different ferrocene-based bidentate phosphine class was of interest and the Mandyphos ligand class was analyzed. Mandyphos ligand **2.32** produced a very efficient reaction and proceeded with excellent enantioselectivity (Table 2.1, entry 8). From the substantial increase in enantioselectivity, the Mandyphos ligand class was further investigated.

Table 2.1 Initial Chiral Ligand Investigation for the Palladium-Induced Metallate Rearrangement of Vinylboron "Ate" Complexes



Entry	*Ligand*	*Yield **2.24** (%)*[a]	*e.r.*[b]
1	**2.25**	< 10	n.d.
2	**2.26**	< 5	n.d.
3	**2.27**	30	72:28
4	**2.28**	39	18:82
5	**2.29**	24	34:66
6	**2.30**	85	47:53
7	**2.31**	39	65:35
8	**2.32**	77	96:4

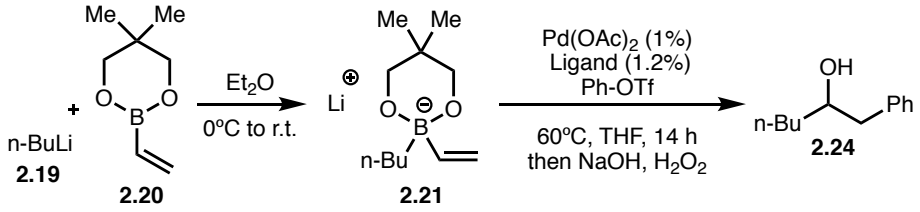
[a]Yield calculated by H-NMR with respect to 1,1,2,2-tetrachloroethane as an internal standard.
[b]Enantiomer ratios (er) determined using chiral SFC analysis of alcohol **2.24**.



Increasing the steric bulk of the diarylphosphino substituent to *o*-tolyl (**2.33**) resulted in a decrease in enantioselectivity (Table 2.2, entry 1 vs. 2). Decreasing the steric bulk of the diarylphosphino to diphenylphosphino (**2.34**) resulted in a significant decrease in efficiency and slight decrease in enantioselectivity (Table 2.2, entry 3). Varying the steric and electronic properties to dicyclohexylphopshino (**2.35**) resulted in a drastic

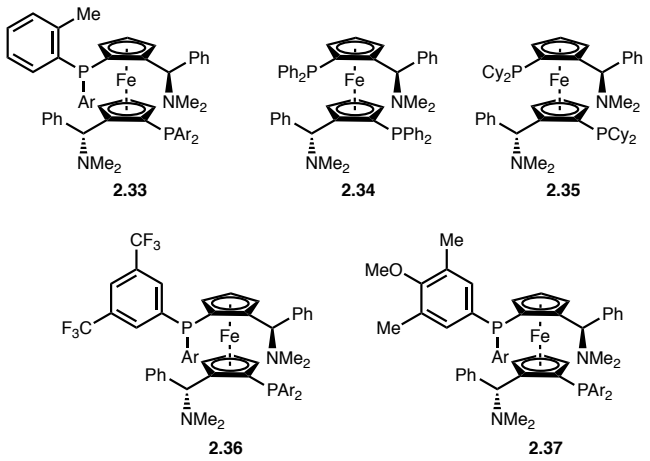
decrease in efficiency and enantioselectivity (Table 2.2, entry 4). An inductively-withdrawing diarylphosphino group with 3,5-ditrifluoromethylphenyl (**2.36**) resulted in complete inhibition of the reaction (Table 2.2, entry 5). Lastly, varying the electronic properties of optimal 3,5-*xylyl* (**2.32**) ligand to 4-methoxy-3,5-dimethylphenyl (**2.37**) resulted in higher enantioselectivity (Table 2.2, entry 6).

Table 2.2 Investigation into the Mandyphos Ligand Class for the Palladium-Induced Metallate Rearrangement of Vinylboron "Ate" Complexes



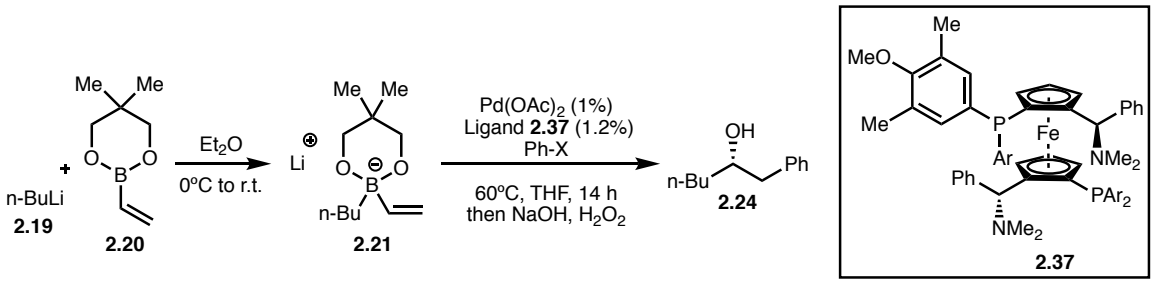
Entry	*Ligand*	*Yield **2.24** (%)*[a]	*e.r.*[b]
1	**2.32**	77	96:4
2	**2.33**	78	84:16
3	**2.34**	42	92:8
4	**2.35**	23	80:20
5	**2.36**	< 5	n.d.
6	**2.37**	77	98:2

[a]Yield calculated by H-NMR with respect to 1,1,2,2-tetrachloroethane as an internal standard.
[b]Enantiomer ratios (er) determined using chiral SFC analysis of alcohol **2.24**.



Having discovered an efficient and selective catalyst for the palladium-induced 1,2-metallate rearrangement, the reaction conditions were further investigated. It was of interest to analyze whether more widely available aryl halide electrophiles are competent in the reaction. Employing chlorobenzene in the reaction with optimal ligand **2.37** resulted in no conversion to the desired product (Table 2.3, entry 2). Bromobenzene and iodobenzene showed very low conversion but gave comparable enantioselectivity (Table 2.3, entries 3-4). Employing different sulfonate electrophiles such as phenyl mesylate or phenyl tosylate showed no conversion to the desired product (Table 2.3, entries 5-6). Interestingly, adding 1% lithium iodide to a reaction with phenyl triflate as the electrophile severely inhibited the reaction resulting in only 13% conversion (Table 2.1, entry 7). These data demonstrate that the initial choice to use aryl triflate electrophiles was crucial for high reactivity. Any incorporation of halide impurities (i.e. 1% LiI) shut down the reaction, presumably by binding to the cationic palladium intermediate. In addition to lithium iodide additives, aryl halide electrophiles are not effective in the reaction due to the generation of lithium halide co-products of the reaction.

Table 2.3 Investigation into Aryl Electrophiles for the Palladium-Induced Metallate Rearrangement of Vinylboron "Ate" Complexes



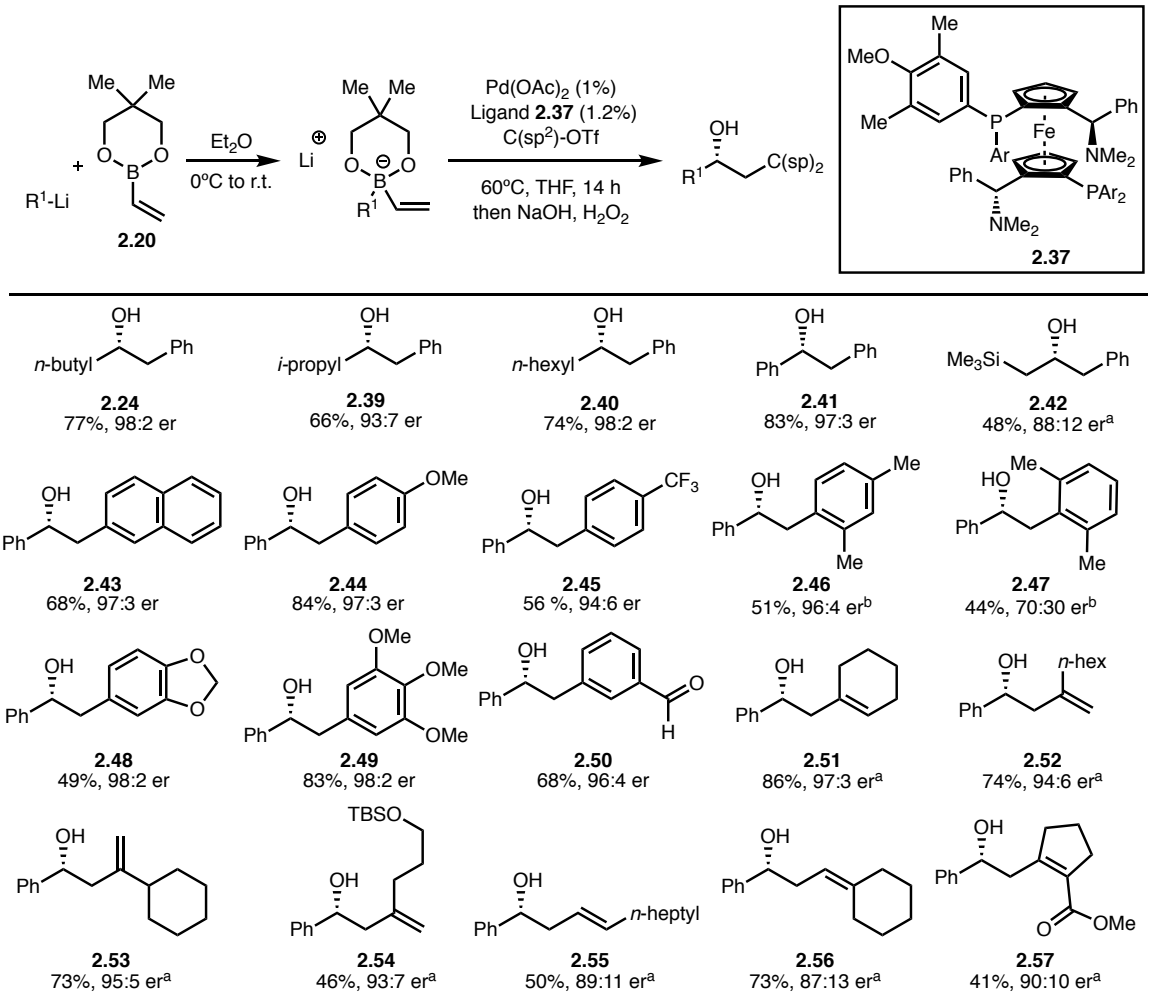
Entry	*X =*	*Yield **2.24** (%)*[a]	*e.r.*[b]
1	OTf	77	98:2
2	Cl	< 5	n.d.
3	Br	9	96:4
4	I	9	96:4
5	OTs	< 5	n.d.
6	OMs	< 5	n.d.
7[c]	OTf	13	98:2

[a]Yield calculated by H-NMR with respect to 1,1,2,2-tetrachloroethane as an internal standard.
[b]Enantiomer ratios (er) determined using chiral SFC analysis of alcohol **2.24**.
[c]1% LiI added into reaction

With the optimal reaction conditions and catalyst developed, the scope of the palladium-induced metallate rearrangement, termed "conjunctive cross-coupling" was explored. Commercially available organolithium reagents and vinyl boronic acid neopentyl ester (**2.20**) were employed to synthesize the vinyl organoboron "ate" complex for the reaction. In addition to phenyl (**2.41**) as the migrating group, a variety of alkyl migrating groups produced efficient reactions and excellent enantioselectivity (**2.38**, **2.39**, **2.40**). Trimethylsilyl methyllithium (**2.42**) required the use of vinyl boronic acid pinacol ester to achieve higher efficiency and as a result slightly lower levels of enantioinduction were observed. For aryl electrophiles and pinacol organoboronates, more efficient and less enantioselective reactions are typically observed for the palladium-catalyzed cross-

coupling of vinyl organoboron "ate" complexes. A variety of substituents on the aryl triflate (**2.43**, **2.48**) could be tolerated and the reactions occurred with high levels of efficiency and enantioselectivity. Varying the electronic properties of the electrophile to electron-rich (**2.44**, **2.49**) and electron-deficient (**2.45**) maintained excellent results. Increasing the steric encumbrance of the electrophile with 2-methylphenyl triflate (**2.46**) required higher temperatures for good reactivity. It was not until 2,6-dimethylphenyl triflate (**2.47**) was employed that lower enantioselectivity was observed. It is worth noting that an aryl electrophile containing reactive functional groups, such as an aldehyde (**2.50**), was tolerated. This can be rationalized by the fact that the organolithium is trapped by the organoboronate to form the "ate" complex before being exposed to the electrophile. Catalysis with the vinyl organoboron "ate" complex is then faster than any side reactions with the aldehyde. 1,1-Disubstituted alkenyl triflate reagents (**2.51**, **2.52**, **2.53**, **2.54**) were productive in the reaction with good yields and enantioselectivity. Employing vinyl boronic acid pinacol ester was shown to produce better reactivity and enantioselectivity with alkenyl electrophiles. Varying the substitution of the alkenyl triflate electrophiles (**2.55**, **2.56**) produced good yields and enantioselectivity and a α,β-unsaturated ester triflate (**2.57**) was tolerated.

Table 2.4 Substrate Scope of the Palladium-Induced Metallate Rearrangement of Vinylboron "Ate" Complexes

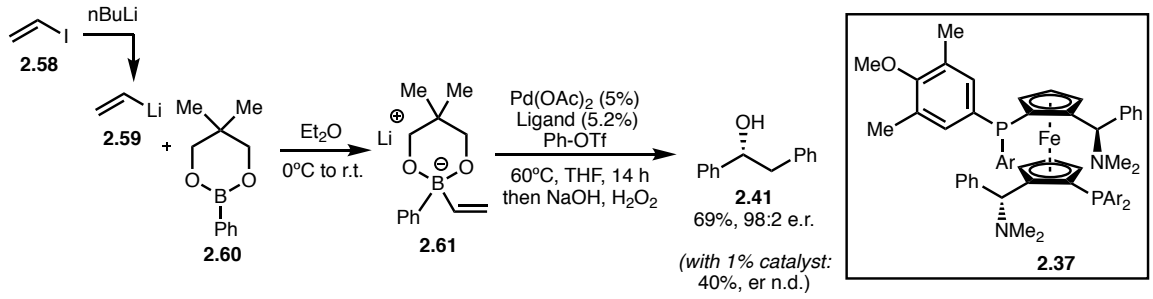


Isolated yields and enantiomer ratios are the average of two experiments. Enantiomer ratio determined on the alcohol product using chiral SFC analysis. [a]Vinyl boronic acid pinacol ester used in place of **2.20**. [b]Reaction carried out at 80°C

An appealing feature of the conjunctive cross-coupling is that the vinyl organoboron "ate" complex is formed in a convergent manner. It has been demonstrated that commercially available organolithium reagents and vinyl boronic esters produce an organoboron "ate" complex that engages in the reaction. An alternative method to produce the vinyl organoboron "ate" complex would entail using vinyllithium and an organoboronate. Employing this "ate" complex formation strategy would be a powerful

addition by allowing for broad expansion of the scope of migrating groups. However, to accomplish the alternative "ate" complex formation requires halide free vinyllithium due to halide inhibition of catalysis. Typical lithium-halogen exchange with vinyl halide reagents represents a problematic pathway for the preparation of vinyllithium as some lithium halide byproducts are generally produced. Employing vinyl iodide **2.58** and *n*-butyllithium to generate vinyllithium, the reaction suffered from a significant drop in efficiency with 1% catalyst loading (Scheme 2.10). Even increasing the catalyst loading five-fold resulted in only a moderate boost in efficiency while maintaining high enantioselectivity.

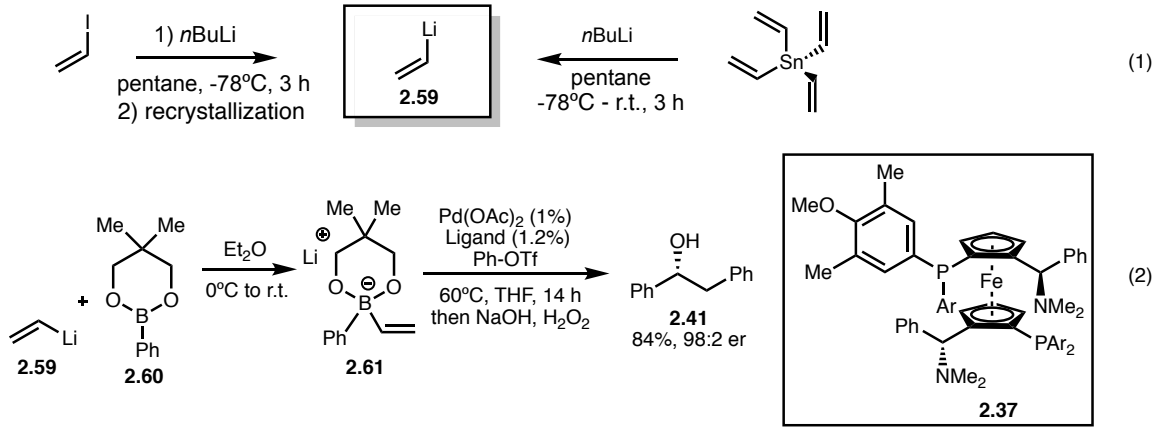
Scheme 2.10 Generation of Vinyllithium from Lithium-Halogen Exchange for the Palladium-Induced Metallate Rearrangement of Vinylboron "Ate" Complexes



With these data, it was concluded that higher purity vinyllithium would be necessary for the conjunctive cross-coupling to proceed at optimal efficiency. To address this issue, two methods to synthesize higher purity vinyllithium were adopted (Scheme 2.11, eq. 1). The first method involved lithium-halogen exchange between vinyl iodide and *n*-butyllithium followed by multiple pentane washes and low temperature recrystallization in diethyl ether. With higher purity vinyllithium obtained, the conjunctive cross-coupling was conducted under standard reaction conditions using 1% catalyst (Scheme 2.11, eq. 2). Higher efficiency was reestablished while maintaining excellent

enantioselectivity. A less labor-intensive method to produce halide free vinyllithium involves lithium-tin exchange with tetravinyltin (Scheme 2.11, eq. 1). This alternative method only requires pentane washes to obtain suitable quality vinyllithium for the standard reaction.

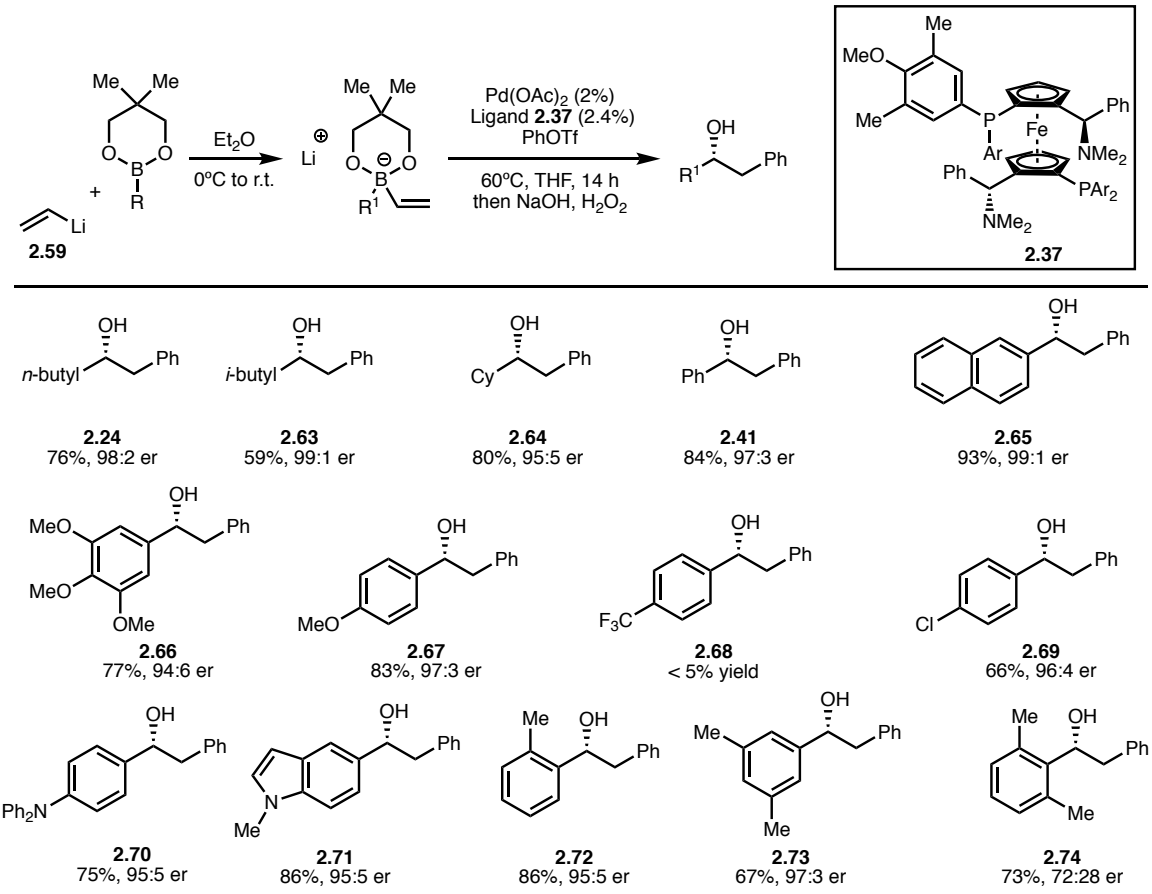
Scheme 2.11 Generation of Higher Purity Vinyllithium for the Palladium-Induced Metallate Rearrangement of Vinyl Organoboron "Ate" Complexes



With the preparation of higher quality vinyllithium established, the scope of the reaction was explored employing the alternative method for vinyl organoboron "ate" complex formation. A variety of alkyl migrating groups (**2.24**, **2.63**, **2.64)** provided the desired product with high efficiency and excellent enantioselectivity. Polyaromatic (**2.65)** and electron-rich aryl (**2.66**, **2.67**) migrating groups maintained excellent results. However, inductively-withdrawing migrating groups (**2.68**) resulted in no reaction product. The high reactivity of electron-donating migrating groups and absence in reactivity for electron-withdrawing migrating groups might support the build up of anionic charge on the migrating carbon. The *p*-trifluoromethylphenyl group was inductively withdrawing enough to stabilize the anionic character on the migrating carbon and shut down the 1,2-migration. Aryl chloride (**2.69**), heteroatom-substituted (**2.70**) and heterocyclic (**2.71**)

migrating groups provided excellent results. A variety of arene substitutions (**2.72**, **2.73**) maintained excellent efficiency and enantioselectivity. However, a 2,6-dimethylphenyl migrating group (**2.74**) contains too much steric encumbrance resulting in lower enantioselectivity.

Table 2.5 Scope of Migrating Groups in the Palladium-Induced Metallate Rearrangement of Vinylboron "Ate" Complexes

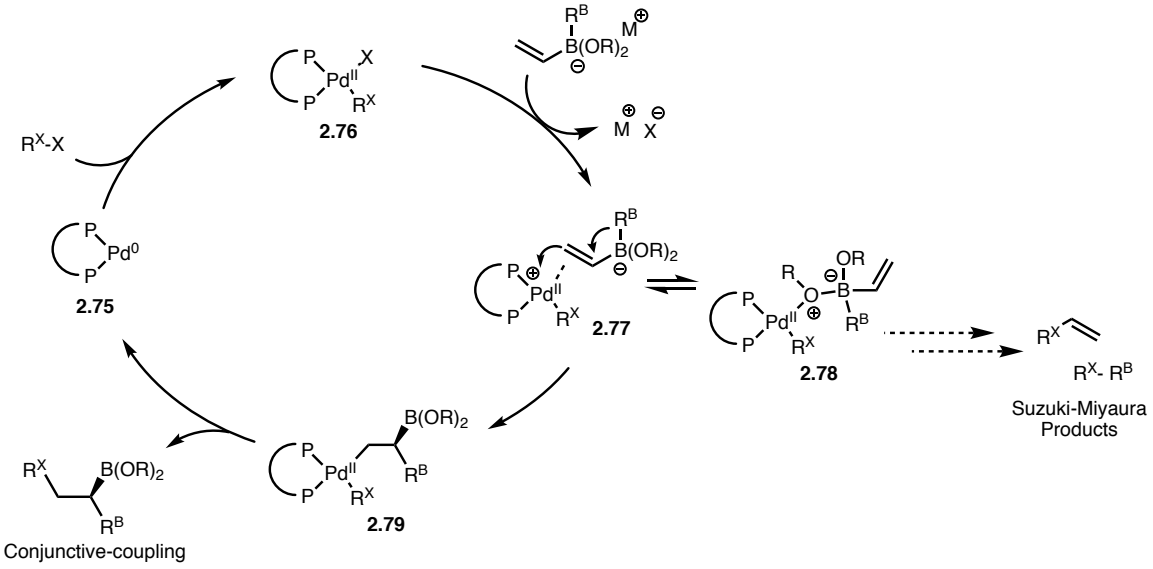


Isolated yields and enantiomer ratios are the average of two experiments. Enantiomer ratio determined on the alcohol product using chiral SFC analysis

2.3.2 Mechanism of Conjunctive Cross-Coupling[17]

The proposed catalytic cycle for the conjunctive cross-coupling begins with Mandyphos-ligated palladium (0) (**2.75**) undergoing oxidative addition with the electrophile to form palladium (II) intermediate **2.76**. Dissociation of the leaving group counterion forms the desired cationic palladium (II)-alkene complex (**2.77**). The alkene-bound complex might be in equilibrium with the oxygen-bound palladium complex **2.78**. The oxygen-bound complex might be an intermediate that leads to typical Suzuki-Miyaura cross-coupling products. From alkene-bound complex **2.77**, the desired 1,2-migration forms the carbon-bound palladium (II) intermediate **2.79**. Subsequent reductive elimination furnishes the desired conjunctive cross-coupling product and regenerates the palladium (0) catalyst to restart the catalytic cycle.

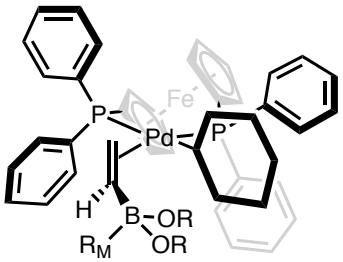
Figure 2.1 Proposed Mechanism of the Conjunctive cross-coupling



A stereochemical model for the enantioselective palladium-catalyzed conjunctive cross-coupling is proposed based off a similar $PdCl_2$-Mandyphos crystal structure obtained

by Hayashi and Ito (Figure 2.2).[19] The dimethylamino groups and aryl substituents have been removed, and the phenyl group on palladium altered for simplicity. The enantiodetermining step is thought to be the metallate rearrangement based off of kinetic studies done in our laboratory. It is proposed that palladium binds the alkene such to have the large four-coordinate boron group directed away from the diarylphosphino substituent. Upon a palladium induced 1,2-metallate rearrangement affords the desired product consistent with the stereochemical outcome observed.

Figure 2.2 Stereochemical Model for the Conjunctive Cross-Coupling



2.4 Conclusion

The development of an enantioselective, catalytic palladium-induced 1,2-metallate rearrangement involving vinyl organoboron "ate" complexes leads to conjunctive cross-coupling. This method represents a powerful new tool to synthesize nonracemic organoboronates by merging two nucleophiles and an electrophile under enantioselective, catalytic conditions. The conjunctive cross-coupling also illustrates a new alternative to the transmetallation step in asymmetric Suzuki-Miyaura cross-coupling reactions. This

[19] 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

method was shown to be very broad with regards to the scope of the reaction and applicable for the synthesis pharmaceutically relevant molecules.

The discovery of new catalytic steps in transition-metal catalysis allows for the potential to develop new reactions. The aforementioned metal-induced 1,2-metallate arrangement is powerful since it could be inserted into a wide-array of metal-catalyzed reactions. Further studies into new types of reactions and employing new metals for the 1,2-metallate rearrangement could have a profound impact on synthetic organic and organometallic chemistry.

2.5 Experimental

2.5.1 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 ($CDCl_3$: 7.24 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 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.

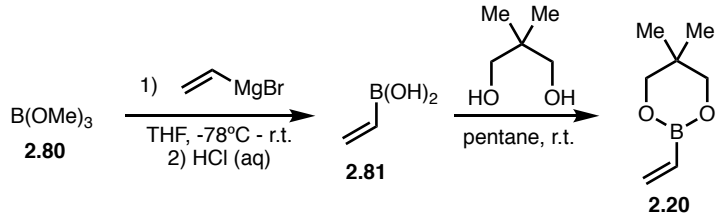
All reactions were conducted in oven- or flame-dried glassware under an inert atmosphere of nitrogen or argon. Tetrahydrofuran (THF), diethyl ether (Et_2O), dichloromethane (DCM) and toluene were purified using Pure Solv MD-4 solvent purification system, from Innovative Technology, Inc., by passing the solvent through two activated alumina columns after purging with argon. Palladium (II) acetate, (S_p,S_p)-**2.37**, 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

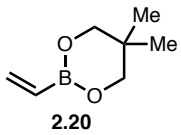
anhydride were purchased from Oakwood Chemicals and used without further purification. All other reagents were purchased from either Aldrich, Alfa Aesar or Acros and used without further purification.

2.5.2 Experimental Procedures

1. General Procedures for the Preparation of Boronic Esters

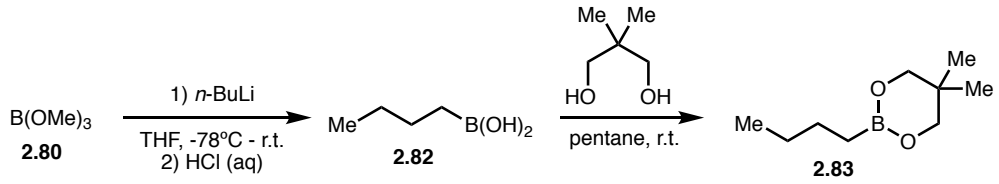
To an oven-dried round bottom flask with magnetic stir bar was added boronic acid (1.0 eq) and pentane. The suspension was cooled to 0℃ and 2,2-dimethyl-1,3-propanediol (neopentyl glycol) (1.05 eq) was added neat and the reaction solution was allowed to warm to room temperature and stirred at room temperature for 3 hours. If a water layer was observed it was removed and the resulting pentane solution was dried with over Na_2SO_4, filtered with Et_2O, and the solvent was removed under reduced pressure. The resulting residue was purified on silica gel (plug using CH_2Cl_2 as the eluent).

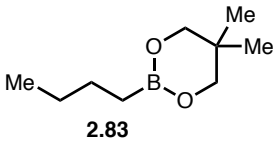




5,5-dimethyl-2-vinyl-1,3,2-dioxaborinane (2.20) To an oven-dried 250 mL round bottom flask with magnetic stir bar under N_2 was added trimethylborate (9.95 g, 95.80 mmol, 1.78 eq) and 50 ml of THF. The reaction flask was cooled to -78℃ and vinyl magnesium bromide (60 ml, 0.90M, 54 mmol, 1.0 eq) was added over 2 hours via syringe pump. After addition of vinyl magnesium bromide the reaction

solution was allowed to warm to room temperature and stir for 8 hours, after which 1M HCl *(aq)* (30 mL) was added followed by 25 mL of deionized water and the reaction solution was allowed to stir at room temperature for 2 hours. The reaction solution was extracted 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 over Na_2SO_4, filtered with Et_2O and the solvent was removed under reduced pressure. The resulting oil was subjected to general procedure for the preparation of boronic esters and the crude product was purified by vacuum distillation (under house vac) while heating to 83°C. The product was isolated as a clear colorless oil (5.81 g, 77 % yield). All spectral data was in accordance with the literature.[20]

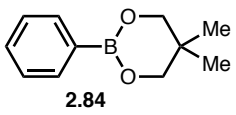




2-butyl-5,5-dimethyl-1,3,2-dioxaborinane (2.83). To an oven-dried 250 mL round bottom flask with magnetic stir bar under N_2 was added trimethylborate (11.21 g, 106.8 mmol, 1.78 eq) and 50 mL of THF. The reaction flask was cooled to -78℃ and *n*BuLi (23.72 mL, 2.53M, 60 mmol, 1.0 eq) was added over 2 hours via syringe pump. After addition of nBuLi the reaction solution was allowed to warm to room temperature and stirred at room temperature for 8 hours, after which 1M HCl *(aq)* (30 ml) was added and the reaction solution was allowed to stir at room temperature for 2 hours. The reaction solution was extracted with 4 x 20 mL of Et_2O and the combined organic layers were washed with brine, dried with sodium sulfate, filtered

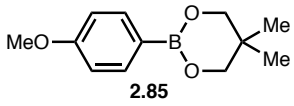
[20] Clark, D.A.; Wilson, R. J.; Kaminsky, L. *Org. Lett.* **2015**, *17*, 3126-3129

with Et_2O and the solvent was removed under reduced pressure. The resulting oil was subjected to the general procedure for preparation of boronic esters. The product was isolated as a clear colorless oil (5.26 g, 52% yield). All spectral data was in accordance with the literature.[21]



2.84

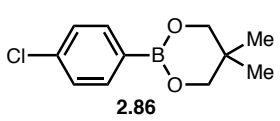
5,5-dimethyl-2-phenyl-1,3,2-dioxaborinane (2.84) Prepared according to the general procedure above with phenylboronic acid (0.268 g, 22.0 mmol), neopentyl glycol (2.41 g, 23.1 mmol), and pentane (60 mL). The resulting white solid (4.18 g, quantitative yield) was used without further purification. All spectral data was in accordance with the literature.[22] This compound is also commercially available [CAS: 5123-13-7].



2.85

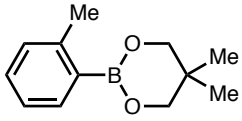
2-(4-methoxyphenyl)-5,5-dimethyl-1,3,2-dioxaborinane (2.85) Prepared according to the general procedure above with 4-methoxyphenylboronic acid (0.4559 g, 3.0 mmol), neopentyl glycol (0.328 g, 3.15 mmol) and pentane (9.0 mL). The crude residue was purified on a silica gel plug with CH_2Cl_2 to afford the product as a white solid (0.650 g, 98%). All spectral data was in accordance with the literature.[23]

[21] Vater, H. D.; Marsden, S. P.; Blakemore, P. R. *Org. Lett.* **2006**, *8*, 773-776
[22] Chatani, N. Remond, E.; Kita, Y.; Kinuta, H.; Tobisu, M. *J. Am. Chem. Soc.* **2012**, *134*, 115-118
[23] Percec, V.; Huang, C.; Rosen, B. M. *Org. Lett*. **2008**, *10*, 2597-2600



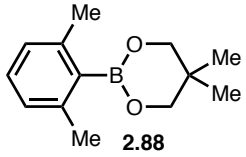
2.86

2-(4-chlorophenyl)-5,5-dimethyl-1,3,2-dioxaborinane (2.86) Prepared according to the general procedure above with 4-chlorophenylboronic acid (0.4691 g, 3.0 mmol), neopentyl glycol (0.328 g, 3.15 mmol), and pentane (9 mL). The crude residue was purified on a silica gel plug with CH_2Cl_2 to afford the product as a white solid (0.667 g, 99% yield). All spectral data was in accordance with the literature.[24]



2.87

5,5-dimethyl-2-(*o*-tolyl)-1,3,2-dioxaborinane (2.87) Prepared according to the general procedure above with *o*-tolylboronic acid (0.4079 g, 3.0 mmol), neopentyl glycol (0.328 g, 3.15 mmol), and pentane (9.0 mL). The crude residue was purified on a silica gel plug with CH_2Cl_2 to afford the product as a colorless oil (0.611 g, quantitative yield). All spectral data was in accordance with the literature.[25]

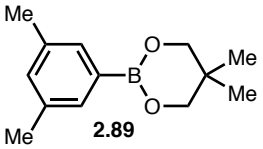


2.88

2-(2,6-dimethylphenyl)-5,5-dimethyl-1,3,2-dioxaborinane (2.86) Prepared according to the general procedure above with 2,6-dimethylphenylboronic acid (0.4499 g, 3.0 mmol), neopentyl glycol (0.328 g, 3.15 mmol), and pentane (9.0 mL). The crude residue was purified on silica gel plug with CH_2Cl_2 to afford the product as a 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,

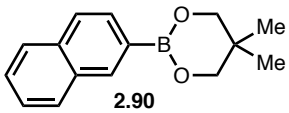
[24] Snieckus, V.; Zhao, Y. *Angew. Chem. Int. Ed.* **2014**, *356*, 1527-1532
[25] Iwasaw, N.; Takya, J.; Aoki, M.; Ukai, K. *J. Am. Chem. Soc.* **2006**, *128*, 8706-8707

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.



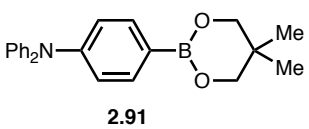
2.89

2-(3,5-dimethylphenyl)-5,5-dimethyl-1,3,2-dioxaborinane (2.89) Prepared according to the general procedure above with 3,5-dimethylphenylboronic acid (0.4499 g, 3.0 mmol), neopentyl glycol (0.328 g, 3.15 mmol), and pentane (9.0 mmol). The crude residue was purified with silica gel plug with CH_2Cl_2 to afford the product as a white solid (0.479 g, 73%). All spectral data was in accordance with the literature.[25]



2.90

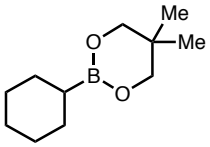
5,5-dimethyl-2-(naphthalen-2-yl)-1,3,2-dioxaborinane (2.90) Prepared according to the general procedure above with 2-napthylboronic acid (2.00 g, 11.6 mmol), neopentyl glycol (1.27 g, 12.18 mmol), and pentane (100.0 mL). The crude residue was purified on a silica gel plug with CH_2Cl_2 to afford the product as a white solid (2.79 g, quantitative yield). All spectral data was in accordance with the literature.[25]



2.91

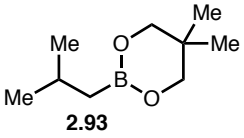
4-(5,5-dimethyl-1,3,2-dioxaborinan-2-yl)-N,N-diphenylaniline (2.91) Prepared according to the general procedure above with 4-(diphenylamino)phenylboronic acid (0.4935 g, 1.7 mmol, 1

equiv.), neopentyl glycol (0.187 g, 1.79 mmol, 1.05 equiv.), and pentane (10 mL). The crude residue was purified on a silica gel plug with CH_2Cl_2 to afford the product as a white solid (0.466 g, 77%). All spectral data was in accordance with the literature.[26]



2.92

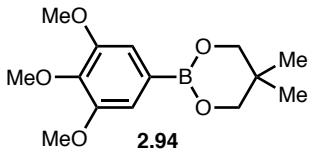
2-cyclohexyl-5,5-dimethyl-1,3,2-dioxaborinane (2.92) Prepared according to the general procedure above with cycylohexylboronic acid (1.98 g, 15.5 mmol), neopentyl glycol (1.70 g, 16.28 mmol), and pentane (100 mL). The crude residue was purified on a silica gel plug with CH_2Cl_2 to afford the product as a colorless oil (3.00 g, 99% yield). All spectral data was in accordance with the literature.[27]



2.93

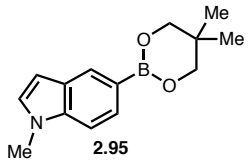
2-isobutyl-5,5-dimethyl-1,3,2-dioxaborinane (2.93) Prepared according to the general procedure above with (2-methylpropyl)boronic acid (0.3058 g, 3.0 mmol), neopentyl glycol (0.328 g, 3.15 mmol), and pentane (9.0 mL). The crude residue was purified on a silica gel plug with CH_2Cl_2 to afford the product as a colorless oil (0.398 g, 78% yield). All spectral data was in accordance with the literature.[28]

[26] Williams, J. A.; Goodall, W. *Chem. Commun.* **2001**, *23*, 2514-2515
[27] Bose, S. K.; Fucke, K.; Liu, L.; Steel, P. G.; Marder, T. B. *Angew. Chem. Int. Ed.* **2014**, *53*, 1799-1803
[28] Barsamian, A. L.; Wu, Z.; Blakemore, P. R. *Org. Biomol. Chem.* **2015**, *13*, 3781-3786



2.94

5,5-dimethyl-2-(3,4,5-trimethoxyphenyl)-1,3,2-dioxaborinane (2.94) Prepared according to the general procedure above with 3,4,5-trimethoxyphenylboronic acid (1.91 g, 9.0 mmol), neopentyl glycol (0.984 g, 9.45 mmol), and pentane (100.0 mL). The crude residue was purified on a silica gel plug with CH_2Cl_2 to afford the product as a 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.

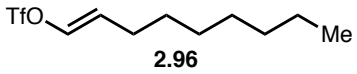


2.95

5-(5,5-dimethyl-1,3,2-dioxaborinan-2-yl)-1-methyl-1*H*-indole (2.95) Prepared according to the general procedure above with (1-methyl-1H-indol-5-yl)boronic acid (0.500 g, 2.772 mmol), neopentyl glycol (0.306 g, 2.910 mmol), and pentane (100.0 mL). The crude residue was purified on a silica gel plug with CH_2Cl_2 to afford the product as a white solid (0.4739 g, 70 % yield). 1H 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.

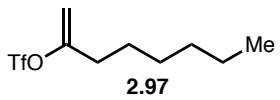
2. Procedures for Preparation of Alkenyl Trifluoromethanesulfonates



2.96

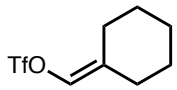
***(E)*-non-1-en-1-yl trifluoromethanesulfonate (2.96)** The title compound was prepared according to a literature precedence with slight modification.[29] In an Ar-filled glove box, CsF (5.01 g, 33.0 mmol, 3.0 equiv.) and N-Phenyl-bis(trifluoromethanesulfonimide) (7.86 g, 22.0 mmol, 2.0 equiv.) were 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[30] (95/5 mixture of E/Z isomers, 2.36 g, 11 mmol) in dimethoxyethane (30 mL) was added. After addition, the pressure vessel was quickly sealed with a screw cap. The solution was stirred vigorously at room temperature for 4 hours after which the pressure was released and the reaction mixture was diluted with pentane (100 mL), washed twice with water and once with brine, dried over Na_2SO_4, filtered and concentrated under reduced pressure. The crude oil was purified by silica gel chromatography (100% pentane) to afford the title compound as a clear colorless oil (1.51 g, 50% yield). All spectral data was in accordance with the literature.[31]

[29] McCammant, M. S.; Liao, L.; Sigman, M. S. *J. Am. Chem. Soc.* **2013**, *135*, 4167-4170
[30] Matsuzawa, S.; Horiguchi, Y.; Nakamura, E.; Kuwajima, I. *Tetrahedron* **1989**, *35*, 349-362
[31] Shirakawa, E.; Imazaki, Y.; Hayashi, T. *Chem. Commun.* **2009**, *34*, 5088-5090



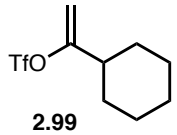
2.97

oct-1-en-2-yl trifluoromethanesulfonate (2.97) The title compound was prepared according to the procedure reported in the literature.[32] All spectral data was in accordance with the literature.



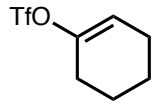
2.98

cyclohexylidenemethyl trifluoromethanesulfonate (2.98) The title compound was prepared according to the procedure reported in the literature.[33] All spectral data was in accordance with the literature.



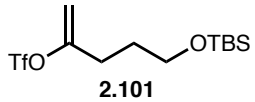
2.99

1-cyclohexylvinyl trifluoromethanesulfonate (2.99) The title compound was prepared according to the procedure reported in the literature.[34] All spectral data was in accordance with the literature.



2.100

cyclohex-1-en-1-yl trifluoromethanesulfonate (2.100) The title compound was prepared according to the procedure reported in the literature.[35] All spectral data was in accordance with the literature.

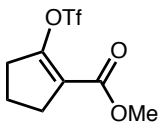


2.101

5-((*tert*-butyldimethylsilyl)oxy)pent-1-en-2-yl trifluoromethanesulfo-nate (2.101) Prepared following a published procedure with slight modifications.[33] 4-Pentyn-1-ol (1.44 mL, 15.5 mmol, 1.0 equiv.) was

[32] Takai, K.; Sakogawa, K.; Kataoka, Y.; Oshima, K.; Utimoto, K. *Org. Synth.* **1995**, *72*, 180
[33] Treptow, W.; Stang, P. J. *Synthesis* **1980**, 283-284
[34] Al-huniti, M. H.; Lepore, S. D. *Org. Lett.* **2014**, *16*, 4154-4157
[35] Lim, B. Y.; Jung, B. E.; Cho, C. G. *Org. Lett.* **2014**, *16*, 4492-4495

placed in a flame-dried round bottom flask and dissolved in dry pentane (15 mL). The solution was cooled to - 40℃ and triflic acid (2.5 mL, 27.8 mmol, 1.6 equiv.) was added dropwise with stirring. The mixture was stirred for 10 minutes at -40℃ and allowed to warm to room temperature over 30 minutes. The mixture was quenched with water (10 mL), extracted with diethyl ether and washed with saturated sodium bicarbonate solution and brine. The crude 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 a clear yellow oil (1.84 g, 7.8 mmol, 1 equiv.) was placed in a flame dried round bottom flask with imidazole (1.10 g, 16 mmol, 2 equiv.) and dissolved in CH_2Cl_2 (20 mL). The solution was flushed with N_2 and cooled to 0℃. *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 stirred at room temperature for 2 hours after which 1M HCl solution (5 mL) were added. The mixture was extracted with CH_2Cl_2 and washed with sodium bicarbonate solution and brine, dried over Na_2SO_4, filtered, and concentrated under reduced pressure. The crude mixture was purified by silica gel chromatography (1% ethyl acetate in hexane) to afford the title compound as a clear 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.

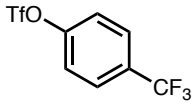


2.102

5-hydroxypent-1-en-2-yl trifluoromethanesulfonate (2.102) The title compound was prepared according to the procedure reported in the literature.[36] All spectral data was in accordance with the literature.

3. General Procedure for the Synthesis of Aryl Trifluoromethanesulfonates

Aryl Trifluoromethansulfonates were made according to literature procedure with slight modification.[37] To a solution of the corresponding phenol and pyridine in CH_2Cl_2 at 0℃, a solution of trifluoromethanesulfonic anhydride in CH_2Cl_2 was added dropwise. The mixture was then warmed to room temperature and allowed to stir for 1 hour. The mixture was diluted with Et_2O, quenched with 3M HCl *(aq)* and washed successively with $NaHCO_3$ *(aq, sat.)* and brine. The solution was dried over Na_2SO_4, filtered with Et_2O, and the solvent was removed under reduced pressure. The residue was purified on silica gel chromatography to afford aryl trifluoromethanesulfonates.

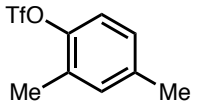


2.103

4-(trifluoromethyl)phenyl trifluoromethanesulfonate (2.103) Prepared according to the general procedure above with 4-trifluoromethylphenol (0.630 g, 3.8 mmol), trifluoromethanesulfonic anyhydride (0.774 mL, 4.6 mmol), pyridine (0.615 mL, 7.6 mmol), and CH_2Cl_2 (6.0 mL). The crude residue was purified on silica gel chromatography (10% ethyl acetate in hexanes) to afford the

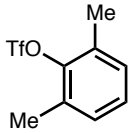
[36] Logan, A. W. J.; Parker, J. S.; Hallside, M. S.; Burton, J. W. *Org. Lett.* **2012**, *14*, 2940-2943
[37] Goosen, L. J.; Linder, C.; Rodriguez, N.; Lange, P. P. *Chem. Eur. J.* **2009**, *15*, 9336-9349

product as a colorless oil (1.180 g, 98% yield). All spectral data was in accordance with the literature.[38]



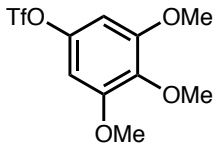
2.104

2,4-dimethylphenyl trifluoromethanesulfonate (2.104) Prepared according to the general procedure above with 2,4-dimethylphenol (0.906 mL, 7.5 mmol), trifluoromethanesulfonic anhydride (1.50 mL, 9.0 mmol), pyridine (1.2 mL, 15.0 mmol), and CH_2Cl_2 (13.0 mL). The crude residue was purified with silica gel chromatography (5% ethyl acetate in hexanes) to afford the product as a colorless oil (1.680 g, 88% yield). All spectral data was in accordance with the literature.[39]



2.105

2,6-dimethylphenyl trifluoromethanesulfonate (2.105) Prepared according to the general procedure above with 2,6-dimethylphenol (0.611 g, 5.0 mmol), trifluoromethanesulfonic anhydride (1.0 mL, 6.0 mmol), pyridine (0.809 mL, 10.0 mmol), and CH_2Cl_2 (8.0 mL). The crude residue was purified with silica gel chromatography (17% ethyl acetate in hexanes) to afford the product as a yellow oil (1.124 g, 88% yield). All spectral data was in accordance with the literature.[40]

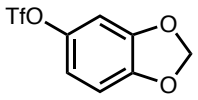


2.106

3,4,5-trimethoxyphenyl trifluoromethanesulfonate (2.106) Prepared according to the general procedure above with 3,4,5-trimethoxyphenol (0.921 g, 5.0 mmol), trifluoromethanesulfonic anhydride (1.0 mL, 6.0

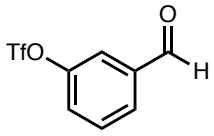
[38] Gill, D.; Hester, A. J.; Lloyd-Jones, G. C. *Org. Biomol. Chem.* **2004**, *2*, 2547-2548
[39] Radivoy, G. ; Alonso, F.; Yus, M. *Tetrahedron* **1999**, *55*, 14479-14490
[40] Mori, H.; Matsuo, T.; Yoshioka, Y.; Katsumura, S. *J. Org. Chem.* **2006**, *71*, 9004-9012

mmol), pyridine (0.809 mL, 10.0 mmol), and CH_2Cl_2 (8.0 mL). The crude residue was purified with silica gel chromatography (20% ethyl acetate in hexanes) to afford the product as an off white solid (1.552 g, 98% yield). All spectral data was in accordance with the literature.[41]



2.107

benzo[*d*][1,3]dioxol-5-yl trifluoromethanesulfonate (2.107) Prepared according to the general procedure above with sesamol (1.04 g, 7.5 mmol), trifluoromethansulfonic anhydride (1.5 mL, 9.0 mmol), pyridine (1.2 mL, 15.0 mmol), and CH_2Cl_2 (13.0 mL). The crude residue was purified with silica gel chromatography (5% ethyl acetate in hexanes) to afford the product as colorless oil (1.89 g, 94%). All spectral data as in accordance with the literature.[42]

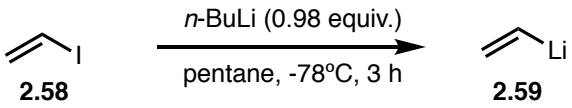


2.108

3-formylphenyl trifluoromethanesulfonate (S-27). Prepared according to the general procedure above with 3-hydroxybenzaldehyde (916 mg, 7.5 mmol), trifluoromethanesulfonic anhydride (1.5 mL, 9.0 mmol), pyridine (1.2 mL, 15.0 mmol), and CH_2Cl_2 (10 mL). The crude residue was purified by silica gel chromatography (10% ethyl acetate in hexanes) to afford the product as a colorless oil (1.47 g, 77% yield). All spectral data was in accordance with the literature.[37]

[41] Anderson, D.; MacMillan, D. W. *Org. Lett.* **2004**, *6*, 4569-4662
[42] Stille, J. K.; Echavarren, A. M. *J. Am. Chem. Soc.* **1987**, *109*, 5478-5486

4. Procedure for Preparation of Vinyllithium



2.58 **2.59**

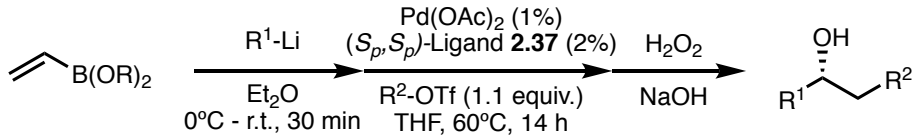
To an oven-dried 250 mL round bottom flask with magnetic stir bar in an Ar-filled glovebox was added vinyl iodide (12.1670 g, 76.6611 mmol, 1.00 eq) and pentane (35 ml). The reaction flask was sealed with a rubber septa, removed from the glovebox, cooled to -78℃ under argon, and maintained at this temperature while *n*BuLi (29.7 ml, 75.1410 mmol, 0.98 eq) was added via syringe pump over two hours. Vinyllithium formation was observed as a white suspension in the reaction flask within 2-3 minutes of initial *n*BuLi addition. Upon completion of slow addition, the reaction solution was allowed to stir for an additional hour at between -50 and -78℃. The vinyllithium suspension was transferred via 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 minutes and removal of pentane as described above. The solid vinyllithium was then dried for 15 minutes 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 via 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 (72.8280 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 cooling the solution to -45℃ over 1 h using a Cryocool and maintaining this temperature overnight (10 h) and then reducing the temperature to -78℃ for 6 hours 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.

5. Procedures for Conjunctive Cross-Coupling

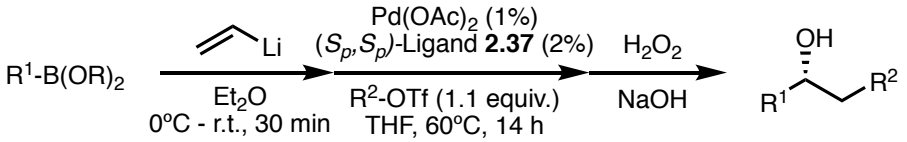
Method A:



To an oven-dried 2-dram vial equipped with a magnetic stir bar in an Ar-filled glovebox was added vinyl boronic ester (0.30 mmol, 1.00 equiv.) and diethyl ether (0.3 mL), sealed with a septum cap, and removed from the glovebox. The reaction vial was cooled to 0℃, and an alkyl/aryl lithium solution (0.30 mmol, 1.0 equiv.) was added at 0℃. The reaction vial was allowed to warm to room temperature and stirred for 30 minutes. Then, the solvent was carefully removed under reduced pressure, and the reaction vial was brought back into the glovebox. To a separate oven-dried 2-dram vial equipped with a magnetic stirbar in the glovebox was added $Pd(OAc)_2$ (0.003 mmol, 0.01 equiv.), (S_p, S_p)-**2.37** (0.0036 mmol, 0.012 equiv.), and THF (0.3 mL). The $Pd(OAc)_2$/(S_p, S_p)-**2.37** solution was allowed to stir for 20 minutes at room temperature. Then the $Pd(OAc)_2$/(S_p, S_p)-**2.37** solution was transferred into the reaction vial, followed by THF (0.9 mL), and aryl/vinyl triflate (0.33 mmol, 1.10 equiv.). The reaction vial was sealed with a polypropylene cap, taped, and brought out of the glovebox where it was allowed to stir at 60℃ for 14 hours. The resulting mixture was cooled to room temperature, filtered through a silica gel plug with diethyl ether, and concentrated under reduced pressure. The reaction mixture was diluted with THF (3 mL), cooled to 0℃, 3M NaOH (2 mL) was added, followed by 30% H_2O_2 (1.0 mL), dropwise. The reaction mixture was allowed to warm to room temperature, and was allowed to stir for 4 hours. The reaction mixture was cooled to 0℃ and saturated aq. $Na_2S_2O_3$ (3 mL) was added dropwise. The reaction mixture was allowed to warm to

room temperature and the aqueous layer was extracted with ethyl acetate (3 x 20 mL). The combined organic layers were dried over Na_2SO_4, filtered, and concentrated under reduced pressure, and subsequently purified via silica gel column chromatography to afford the desired products.

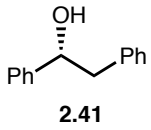
Method B:



To an oven-dried 2-dram vial equipped with a magnetic stir bar in an Ar-filled glovebox was added alkyl/aryl boronic ester (0.30 mmol, 1.0 equiv.) and diethyl ether (0.3 mL), sealed with a septum cap, and removed from the glovebox. The reaction vial was cooled to 0℃, and a vinyl lithium solution (0.30 mmol, 1.0 equiv.) was added at 0℃. The reaction vial was allowed to warm to room temperature and stirred for 30 minutes. Then, the solvent was carefully removed under reduced pressure, and the reaction 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)-**2.37** (0.0072 mmol, 0.024 equiv.), and THF (0.6 mL). The $Pd(OAc)_2$/(S_p, S_p)-**2.37** solution was allowed to stir for 20 minutes at room temperature. Then the $Pd(OAc)_2$/(S_p, S_p)-**2.37** solution was transferred into the reaction vial, followed by THF (0.6 mL), and aryl/vinyl triflate (0.33 mmol, 1.10 equiv.) was added. The reaction vial was sealed with a polypropylene cap, taped, and brought out of the glovebox where it was allowed to stir at 60℃ for 14 hours. The resulting mixture was cooled to room temperature, filtered through a silica gel plug with diethyl ether, concentrated under reduced pressure. The reaction

mixture was diluted with THF (3 mL), cooled to 0℃, 3M NaOH (2 mL) was added, followed by 30% H_2O_2 (1.0 mL), dropwise. The reaction mixture was allowed to warm to room temperature, and was allowed to stir for 4 hours. The reaction mixture was cooled to 0℃ and saturated aq. $Na_2S_2O_3$ (3 mL) was added dropwise. The reaction mixture was allowed to warm to room temperature and the aqueous layer was extracted with ethyl acetate (3 x 20 mL). The combined organic layers were dried over Na_2SO_4, filtered, and concentrated under reduced pressure, and subsequently purified via silica gel column chromatography to afford the desired products.

2.5.3 Characterization of Conjunctive-Cross-Coupling Products and Analysis of Stereochemistry



2.41

(R)*-1,2-diphenylethan-1-ol (2.41)** The reaction was performed according to the general procedure ***(Method A) with 5,5-dimethyl-2-vinyl-1,3,2-dioxaborinane (**2.20**) (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)-**2.37** (3.80 mg, 0.0036 mmol) in THF (1.2 mL, 0.25 M, 0.012 equiv.). The crude mixture was purified by silica gel chromatography (5% ethyl acetate in hexanes, stain in CAM) to afford a 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).

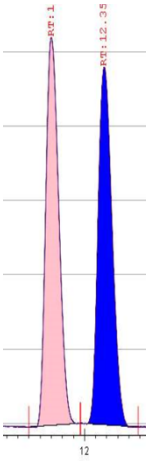
^{13}C NMR (150 MHz, $CDCl_3$) δ 143.95, 138.17, 129.66, 128.66, 128.56, 127.76, 126.77, 126.04, 75.49, 46.25. HRMS (DART) for $C_{14}H_{13}$ $[M+H-H_2O]^+$ calculated: 181.1017, found: 181.1021. $[\alpha]^{20}_D$: +11.787 (c = 0.635, $CHCl_3$, *l* =50 mm) (lit: $[\alpha]^{20}_D$ = +12.5 (c = 1.01, $CHCl_3$, 98:2 e.r.).[43]

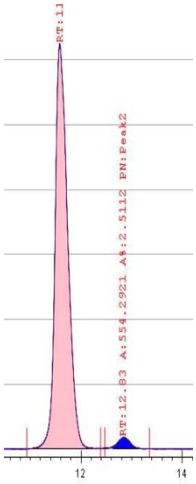
Analysis of Stereochemistry:

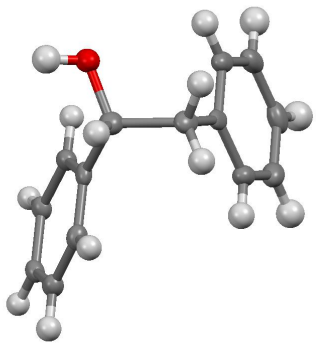
Racemic compound was prepared according to the general procedure (***Method A***) with vinyl boronic acid pinacol ester, and $Pd(OAc)_2$ (5 mol%) and 1,1′-Bis(dicyclohexyl-phosphino)ferrocene (6 mol%) as the catalyst. Absolute stereochemistry was determined by single crystal X-ray diffraction.

Chiral 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**



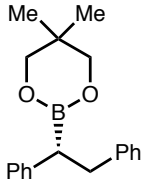




Peak No	% Area	Area	RT (min)
1	50.2599	8450.5728	11.4
2	49.7401	8363.1658	12.35
Total:	100	16813.7386	

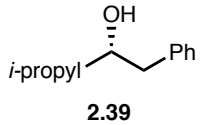
Peak No	% Area	Area	RT (min)
1	97.4888	21518.079	11.58
2	2.5112	554.2921	12.83
Total:	100	22072.3711	

[43] Guo, J.; Chen, J.; Lu, Z. *Chem. Commun.* **2015**, *51*, 5725-5727



2.109

(*R*)-2-(1,2-diphenylethyl)-5,5-dimethyl-1,3,2-dioxaborinane (2.109) The reaction was performed according to the general procedure ***(Method A)*** without oxidation step with 5,5-dimethyl-2-vinyl-1,3,2-dioxaborinane (**2.20**) (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)-**2.37** (3.80 mg, 0.0036 mmol) in THF (1.2 mL, 0.25 M, 0.012 equiv.). The crude mixture was purified by silica gel chromatography (30% CH_2Cl_2 in pentane, stain in CAM) to afford a colorless solid (67.0mg, 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).



2.39

(R)*-3-methyl-1-phenylbutan-2-ol (2.39)** The reaction was performed according to the general procedure **(*Method A) with 5,5-dimethyl-2-vinyl-1,3,2-dioxaborinane (**2.20**) (42.0 mg, 0.30 mmol), isopropyllithium (0.441 mL, 0.68M in pentane, 0.30 mmol), phenyltrifluoromethanesulfonate (74.60 mg, 0.33 mmol), palladium (II) acetate (0.670 mg, 0.003 mmol), (S_p, S_p)-**2.37** (3.80 mg, 0.0036 mmol) in THF (1.2 mL, 0.25 M). The crude mixture was purified by silica gel chromatography (30%

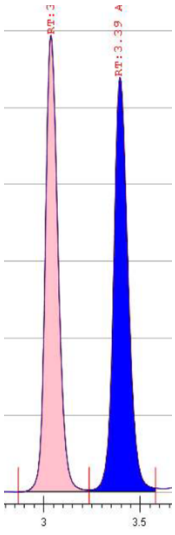
CH_2Cl_2 in hexanes) to afford a yellow oil. (32.5 mg, 66% yield). ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.30 (2H, t, *J* = 7.2 Hz), 7.21-7.24 (3H, m), 3.57-3.59 (1H, m), 2.84 (1H, dd, *J* = 13.8, 3.0 Hz), 2.32 (1H, dd, *J* = 13.2, 9.0 Hz,), 1.77-1.72 (1H, m), 1.42 (1H, d, *J* = 3.6 Hz), 0.99 (3H, s), 0.98 (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).

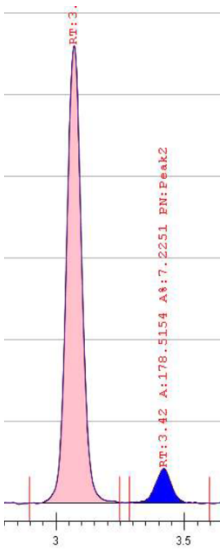
Analysis of Stereochemistry

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 2.41, 2.24, and 2.40).

Chiral 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.

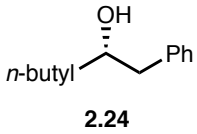
Racemic Material **Standard Conditions**





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

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



2.24

(S)*-1-phenylhexan-2-ol (2.24)** The reaction was performed according to the general procedure ***(Method A) with 5,5-dimethyl-2-vinyl-1,3,2-dioxaborinane (**2.20**) (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)-**2.37** (3.80 mg, 0.0036 mmol, 0.012 equiv.) in THF (1.2 mL, 0.25 M). The crude mixture was purified by silica gel chromatography (50% CH_2Cl_2 in pentane, stain in CAM) to afford a 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,

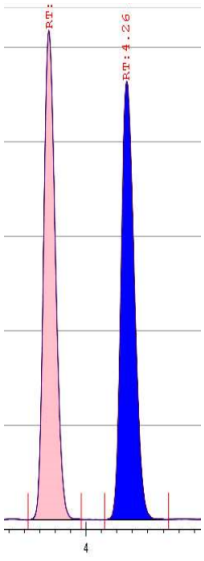
22.85, 14.21. HRMS (DART) for $C_{12}H_{17}$ $[M+H-H_2O]^+$ calculated: 161.1330, found: 161.1335. $[\alpha]^{20}_D$: +14.786 (c = 0.510, $CHCl_3$, *l* =50 mm). (lit: $[\alpha]^{28}_D$: +6.3, c = 1.0, $CHCl_3$, 68:32 e.r.).[44]

Analysis of Stereochemistry:

Racemic compound was prepared according to the general procedure (***Method A***) with vinyl boronic acid pinacol ester, 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.[43]

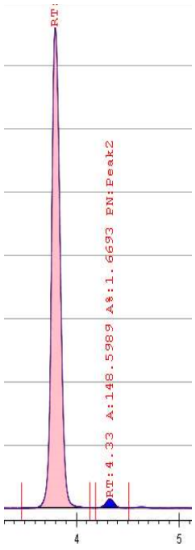
Chiral SFC (Chiracel OD-H, 5% IPA, 3 mL/min, 100 bar, 35 °C, 210-270 nm) – analysis of (R)-1,2-diphenylethan-1-ol

Racemic Material



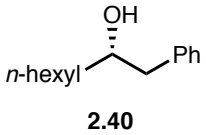
Peak No	% Area	Area	RT (min)
1	49.8946	5442.8203	3.76
2	50.1054	5465.8191	4.26
Total:	100	10908.6394	

Standard Conditions



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

[44] Ema, T.; Ura, N; Yoshii, M.; Korenaga, T.; Sakai, T. *Tetrahedron* **2009**, *65*, 9583-9591



2.40

(S)*-1-phenyloctan-2-ol (2.40)** The reaction was performed according to the general procedure ***(Method A) with 5,5-dimethyl-2-vinyl-1,3,2-dioxaborinane (**2.20**) (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)-**2.37** (3.80 mg, 0.0036 mmol, 0.012 equiv.) in THF (1.2 mL, 0.25 M). The crude mixture was purified by silica gel chromatography (50% CH_2Cl_2 in pentane, stain in CAM) to afford a 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 e.r.). All spectral data was in accordance with the literature.[45]

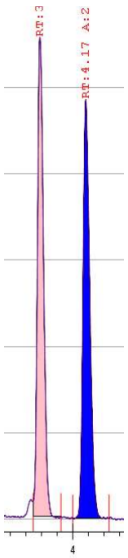
Analysis of Stereochemistry:

Racemic compound was prepared according to the literature.[44] Absolute stereochemistry was determined by comparison to the literature.[44]

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

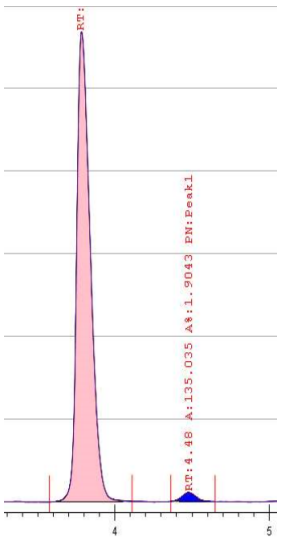
[45] Mlynarski, S. N.; Schuster, C. H.; Morken. J. P *Nature* **2014**, *505*, 386-390

Racemic Material

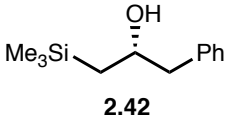


Peak No	% Area	Area	RT (min)
1	50.7244	2991.7195	3.58
2	49.2756	2906.2689	4.17
Total:	100	5897.9884	

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	



2.42

(R)*-1-phenyl-3-(trimethylsilyl)propan-2-ol (2.42)** The reaction was performed according to the general procedure ***(Method A) with vinyl boronic 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)-**2.37** (3.80 mg, 0.0036 mmol, 0.012 equiv.) in THF (1.2 mL, 0.25 M). The crude mixture was purified by silica gel chromatography (5% ethyl acetate in pentane, stain in CAM) to afford a 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,

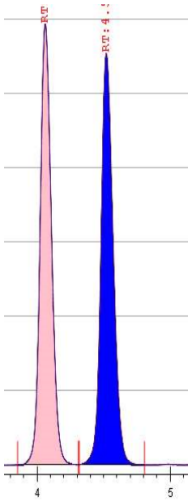
129.56, 128.73, 126.63, 71.08, 47.70, 25.99, -0.57. IR (neat) ν_{max} 3582.1 (br), 3441.2 (br) 3062.7 (w), 3028.2 (w), 2951.4 (w), 2917.7 (w), 1495.6 (w), 1454.0 (w), 1247.0 (s), 1076.0 (m), 1056.2 (m), 1018.7 (m), 854.8 (s), 837.4 (s), 743.8 (s), 698.5 (s) cm^{-1}. HRMS (DART) for $C_{12}H_{24}NOSi$ $[M+NH_4]^+$ calculated: 226.1627, found 226.1622. $[\alpha]^{20}_D$: +3.850 (c = 1.135, $CHCl_3$, *l* =50 mm).

Analysis of Stereochemistry:

Racemic compound was prepared according to the general procedure (*Method A*) with vinyl boronic acid pinacol ester, 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 2.41, 2.24, and 2.40).

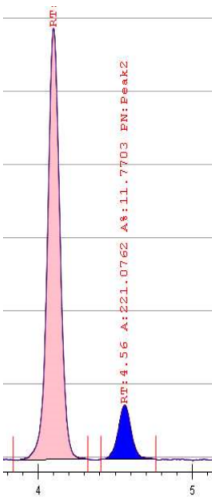
Chiral SFC (Chiracel OD-H, 2% IPA, 3 mL/min, 100 bar, 35 °C, 210-270 nm) – analysis of (R)-1-phenyl-3-(trimethylsilyl)propan-2-ol.

Racemic Material

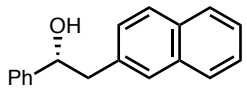


Peak No	% Area	Area	RT (min)
1	49.9308	3484.2905	4.06
2	50.0692	3493.9499	4.52
Total:	100	6978.2404	

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	



2.43

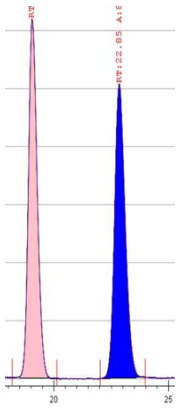
(R)*-2-(naphthalen-2-yl)-1-phenylethan-1-ol (2.43)** The reaction was performed according to the general procedure ***(Method A) with 5,5-dimethyl-2-vinyl-1,3,2-dioxaborinane (**2.20**) (42.0 mg, 0.30 mmol, 1.00 equiv.), phenyl lithium (0.167 mL, 1.9M in dibutyl ether, 0.30 mmol, 1.00 equiv.), 2-naphthyltrifluoromethanesulfonate (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)-**2.37** (3.8 mg, 0.0036 mmol, 0.012 equiv.) in THF (1.2 mL, 0.25 M). The crude mixture was purified by silica gel chromatography (50% CH_2Cl_2 in pentane, stain in CAM) to afford a 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).

Analysis of Stereochemistry:

Racemic compound was prepared according to the general procedure (*Method A*) with vinyl boronic acid pinacol ester, 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 2.41, 2.24, and 2.40).

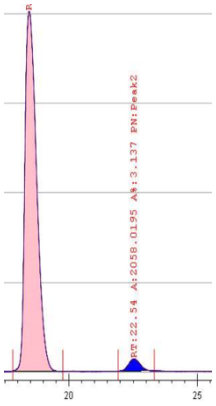
Chiral SFC (Chiracel OD-H, 10% IPA, 3 mL/min, 100 bar, 35 °C, 210-270 nm) – analysis of (R)-2-(naphthalen-2-yl)-1-phenylethan-1-ol.

Racemic Material

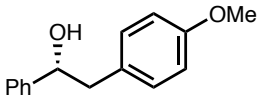


Peak No	% Area	Area	RT (min)
1	50.215	8280.1194	19.03
2	49.785	8209.2224	22.85
Total:	100	16489.3418	

Standard Conditions



Peak No	% Area	Area	RT (min)
1	96.863	63545.7182	18.44
2	3.137	2058.0195	22.54
Total:	100	65603.7377	



2.44

(R)*-2-(4-methoxyphenyl)-1-phenylethan-1-ol (2.44)** The reaction was performed according to the general procedure (Method A***) with 5,5-dimethyl-2-vinyl-1,3,2-dioxaborinane (**2.20**) (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)-**2.37** (3.8 mg, 0.0036 mmol, 0.012 equiv.) in THF (1.2 mL, 0.25 M). The crude mixture was purified by silica gel column chromatography (10% ethyl acetate in hexanes) to afford a 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),

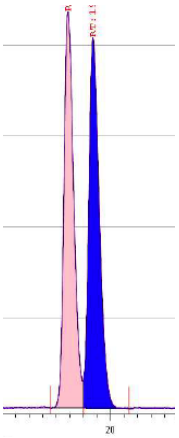
2.98 (1H, dd, J = 13.8, 4.8 Hz), 2.91 (1H, dd, J= 14.4, 9.0 Hz), 1.97 (1H, s); ^{13}C NMR (150 MHz, $CDCl_3$) δ 158.6, 144.0, 130.6, 130.1, 128.6, 127.7, 126.0, 114.1, 75.6, 55.4, 45.3; IR (neat) ν_{max} 3407.9 (br), 2999.5 (m), 2834.9 (m), 1611.0 (m), 1583.6 (w), 1510.0 (s), 1453.3 (m), 1242.4 (s), 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).

Analysis of Stereochemistry:

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 2.41, 2.24, and 2.40).

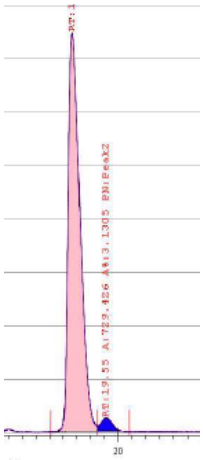
Chiral SFC (Chiracel OD-H, 5% IPA, 3 mL/min, 100 bar, 35 °C, 210-270 nm) – analysis of (R)-2-(4-methoxyphenyl)-1-phenylethan-1-ol

Racemic Material

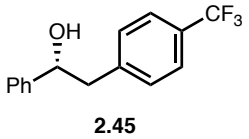


Peak No	% Area	Area	RT (min)
1	49.8369	5531.1911	18.43
2	50.1631	5567.3946	19.35
Total:	100	11098.5857	

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	



2.45

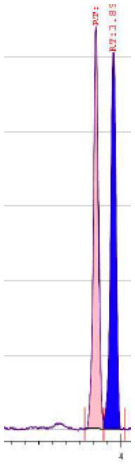
(R)*-1-phenyl-2-(4-(trifluoromethyl)phenyl)ethan-1-ol (2.45)** The reaction was performed according to the general procedure (Method A***) with 5,5-dimethyl-2-vinyl-1,3,2-dioxaborinane (**2.20**) (42.0 mg, 0.30 mmol, 1.00 equiv.), phenyl lithium (0.167 mL, 1.9M in dibutyl ether, 0.30 mmol, 1.00 equiv.), 4-(trifluoromethyl)phenyl trifluoromethanesulfonate (**2.103**) (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)-**2.37** (3.8 mg, 0.0036 mmol, 0.012 equiv.) in THF (1.2 mL, 0.25 M). The crude mixture was purified by silica gel column chromatography (5% ethyl acetate in hexanes) to afford a 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).

Analysis of Stereochemistry:

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 2.41, 2.24, and 2.40).

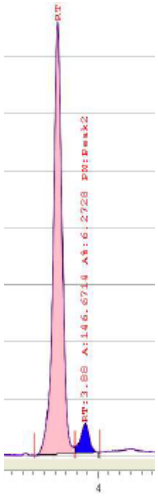
Chiral SFC (Chiracel OD-H, 5% IPA, 3 mL/min, 100 bar, 35 °C, 210-270 nm) – analysis of (R)-1-phenyl-2-(4-(trifluoromethyl)phenyl)ethan-1-ol

Racemic Material

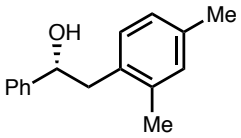


Peak No	% Area	Area	RT (min)
1	50.473	557.993	3.64
2	49.527	547.5345	3.89
Total:	100	1105.5275	

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	



2.46

(R)*-2-(2,4-dimethylphenyl)-1-phenylethan-1-ol (2.46)** 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 (**2.20**) (42.0 mg, 0.30 mmol), phenyllithium (0.167 mL, 1.9M in dibutyl ether, 0.30 mmol), 2,4-dimethylphenyl trifluoromethanesulfonate (**2.104**) (83.90 mg, 0.33 mmol), palladium (II) acetate (0.670 mg, 0.003 mmol), (S_p, S_p)-**2.37** (3.80 mg, 0.0036 mmol) in THF (1.2 mL, 0.25 M). The crude mixture was purified by silica gel chromatography (40% CH_2Cl_2 in hexanes) to afford a clear 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,

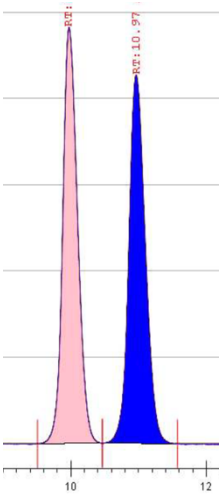
4.2 Hz), 2.94 (1H, dd, *J* = 13.8, 9.0 Hz), 2.29 (3H, s), 2.26 (3H, s), 1.92 (1H, d, *J* = 2.4 Hz); ^{13}C NMR (150 MHz, $CDCl_3$) δ 144.4, 136.8, 136.5, 133.3, 131.5, 130.4, 128.6, 127.7, 126.9, 125.9, 74.6, 43.2, 21.1, 19.7 IR (neat) ν_{max} 3418 (br), 3027 (w), 3004 (w), 2921 (m), 2856 (w), 1493 (w), 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).

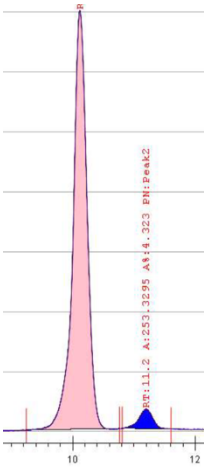
Analysis of Stereochemistry

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 2.41, 2.24, and 2.40).

Chiral 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.

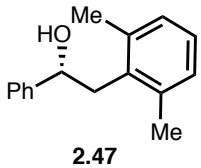
Racemic Material **Standard Conditions**





Peak No	% Area	Area	RT (min)
1	50.3811	7320.6585	9.97
2	49.6189	7209.9062	10.97
Total:	100	14530.5647	

Peak No	% Area	Area	RT (min)
1	95.677	5606.6891	10.12
2	4.323	253.3295	11.2
Total:	100	5860.0186	



2.47

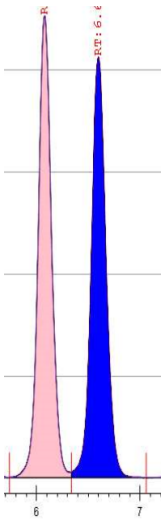
(R)*-2-(2,6-dimethylphenyl)-1-phenylethan-1-ol (2.47)** The reaction was performed according to the general procedure ***(Method A) with 5,5-dimethyl-2-vinyl-1,3,2-dioxaborinane (**2.20**) (42.0 mg, 0.30 mmol, 1.00 equiv.), phenyllithium (0.167 mL, 1.9M in dibutyl ether, 0.30 mmol, 1.00 equiv.), 2,6-dimethylphenyl trifluoromethanesulfonate (**2.105**) (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)-**2.37** (3.80 mg, 0.0036 mmol, 0.012 equiv.) in THF (1.2 mL, 0.25 M). The crude mixture was purified by silica gel chromatography (30% CH_2Cl_2 in pentane, stain in CAM) to afford a 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).

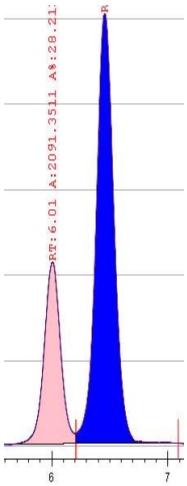
Analysis of Stereochemistry:

Racemic compound was prepared according to the general procedure (***Method A***) with vinyl boronic acid pinacol ester, 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 2.41, 2.24, and 2.40).

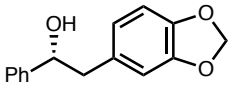
Chiral SFC (Chiracel OD-H, 8% IPA, 3 mL/min, 150 bar, 35 °C, 210-270 nm) – analysis of (R)-2-(2,6-dimethylphenyl)-1-phenylethan-1-ol.

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	



2.48

(R)*-2-(benzo[*d*][1,3]dioxol-5-yl)-1-phenylethan-1-ol (2.48)** The reaction was performed according to the general procedure ***(Method A) with 5,5-dimethyl-2-vinyl-1,3,2-dioxaborinane (**2.20**) (42.0 mg, 0.30 mmol), phenyllithium (0.167 mL, 1.9M in dibutyl ether, 0.30 mmol), benzo[d][1,3]dioxol-5-yl trifluoromethanesulfonate (**2.107**) (88.50 mg, 0.33 mmol), palladium (II) acetate (0.67 mg, 0.003 mmol), (S_p, S_p)-**2.37** (3.8 mg, 0.0036 mmol) in THF (1.2 mL, 0.25 M). The crude mixture was purified by silica gel chromatography (5% EtOAc in hexanes) to afford a 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)

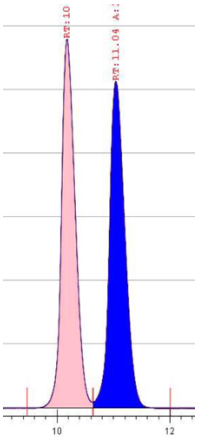
ν_{max} 3411 (br), 3062 (w), 3028 (w), 2919 (m), 1607 (w), 1501 (s), 1440 (s), 1243 (s), 1187 (m), 1187 (m), 1036 (s), 928 (s), 699 (s), 537 (m) cm^{-1}; HRMS-(DART): for $C_{15}H_{13}O_2$ $[M+H-H_2O]^+$: calculated: 225.0915, found: 225.0916. $[\alpha]^{20}_D$ = + 1.35 (c = 1.025, $CHCl_3$, *l* = 50 mm).

Analysis of Stereochemistry

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 2.41, 2.24, and 2.40).

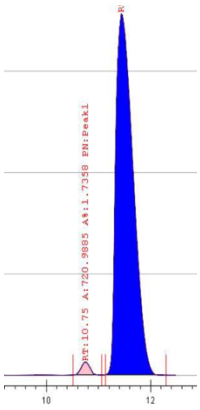
Chiral SFC (Chiracel OJ-H, 8% IPA, 3 mL/min, 100 bar, 35°C, 210-270 nm) – analysis of (R)-2-(benzo[d][1,3]dioxol-5-yl)-1-phenylethan-1-ol.

Racemic Material

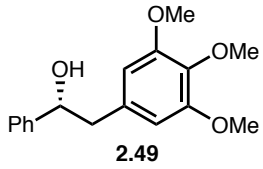


Peak No	% Area	Area	RT (min)
1	50.088	19597.5824	10.18
2	49.912	19528.6842	11.04
Total:	100	39126.2666	

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	



2.49

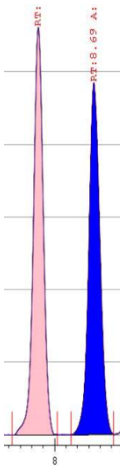
***(R)*-1-phenyl-2-(3,4,5-trimethoxyphenyl)ethan-1-ol (2.49)** The reaction was performed according to the general procedure *(**Method A**)* with 5,5-dimethyl-2-vinyl-1,3,2-dioxaborinane (**2.20**) (42.0 mg, 0.30 mmol, 1.00 equiv.), phenyl lithium (0.167 mL, 1.9M in dibutyl ether, 0.30 mmol, 1.00 equiv.), 3,4,5-trimethoxyphenyl trifluoromethanesulfonate (**2.106**). (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)-**2.37** (3.80 mg, 0.0036 mmol, 0.012 equiv.) in THF (1.2 mL, 0.25 M). The crude mixture was purified by silica gel chromatography (15-20% ethyl acetate in pentane, stain in CAM) to afford a 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).

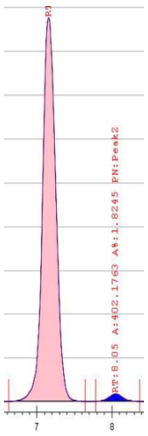
Analysis of Stereochemistry:

Racemic compound was prepared according to the general procedure (***Method A***) with vinyl boronic acid pinacol ester, 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 2.41, 2.24, and 2.40).

Chiral 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.

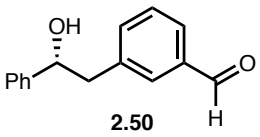
Racemic Material **Standard Conditions**





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	



2.50

(*R*)-3-(2-hydroxy-2-phenylethyl)benzaldehyde (2.50) 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.(**2.108**) (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)-**2.37** (3.80 mg, 0.0036 mmol, 0.012 equiv.) in THF (1.2 mL, 0.25 M). The crude mixture was purified by silica gel chromatography (20% EtOAc in Hexanes) to afford a clear 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:

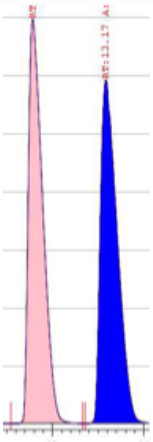
$C_{15}H_{18}N_1O_1$ $[M+NH_4]^+$: calculated: 244.1339, found: 244.1338. $[\alpha]_D^{20}$: +3.63 (c = 0.84, $CHCl_3$, *l* =50 mm).

Analysis of Stereochemistry:

Racemic compound was prepared according to the general procedure (***Method A***) with vinyl boronic acid pinacol ester, 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 2.41, 2.24, and 2.40).

Chiral 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.

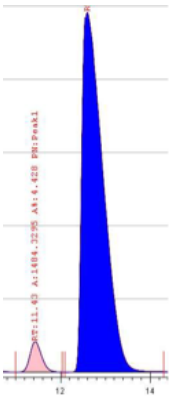
Racemic Material



Peak Info

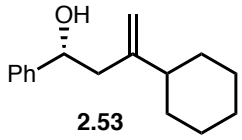
Peak No	% Area	Area	RT (min)
1	49.9128	15091.73	11.57
2	50.0872	15144.4606	13.17
Total:	100	30236.1906	

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	



2.53

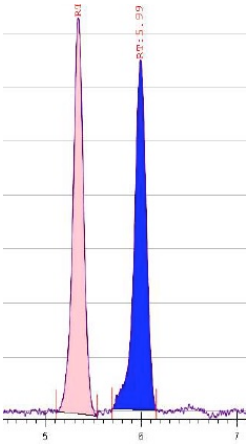
(R)*-3-cyclohexyl-1-phenylbut-3-en-1-ol (2.53)** The reaction was performed according to the general procedure (Method A***) with 4,4,5,5-tetramethyl-2-vinyl-1,3,2-dioxaborolane (46.2 mg, 0.30 mmol, 1.00 equiv.), phenyl lithium (0.167 mL, 1.9M in dibutyl ether, 0.30 mmol, 1.00 equiv.), 1-cyclohexylvinyl trifluoromethanesulfonate (**2.99**) (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)-**2.37** (3.8 mg, 0.0036 mmol, 0.012 equiv.) in THF (1.2 mL, 0.25 M). The crude mixture was purified by silica gel column chromatography (5% ethyl acetate in hexane) to afford a 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).

Analysis of Stereochemistry:

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 2.41, 2.24, and 2.40).

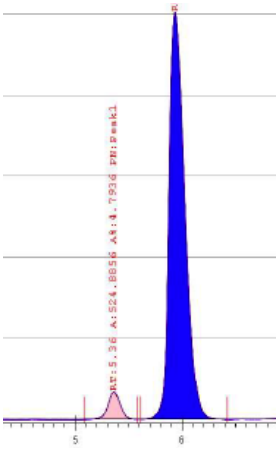
Chiral SFC (Chiracel OD-H, 5% IPA, 3 mL/min, 100 bar, 35 °C, 210-270 nm) – analysis of (R)-3-cyclohexyl-1-phenylbut-3-en-1-ol

Racemic Material

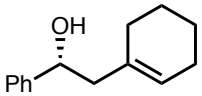


Peak No	% Area	Area	RT (min)
1	50.0769	284.402	5.34
2	49.9231	283.5282	5.99
Total:	100	567.9302	

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	



2.51

(R)*-2-(cyclohex-1-en-1-yl)-1-phenylethan-1-ol (2.51)** 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 (**2.100**) (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)-**2.37** (3.80 mg, 0.0036 mmol, 0.012 equiv.) in THF (1.2 mL, 0.25 M). The crude mixture was purified by silica gel chromatography (30% CH_2Cl_2 in pentane) to afford a clear 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,

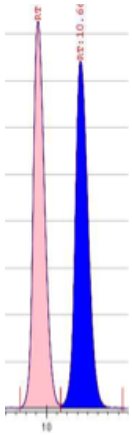
22.4. IR (neat) ν_{max} 3406.1 (br), 3028.27 (m), 2922.0 (s), 2922.5 (s), 2855.4 (s), 2833.9 (s), 1493.2 (s) 1451.1 (m), 1050.2 (m), 1006.6 (s), 753.4 (m), 699.0 (s), 547.2 (s) cm^{-1}. HRMS-(DART) for: $C_{14}H_{17}$ $[M+H-H_2O]^+$: calculated: 185.1330, found: 185.1329. $[\alpha]_D^{20}$: +72.35 (c = 0.74, $CHCl_3$, *l* =50 mm).

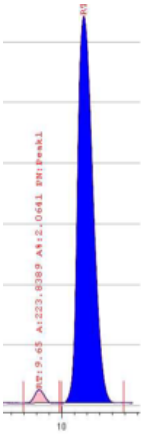
Analysis of Stereochemistry:

Racemic compound was prepared according to the general procedure (***Method A***) 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 2.41, 2.24, and 2.40).

Chiral 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.

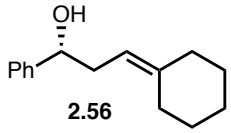
Racemic Material **Standard Conditions**





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	



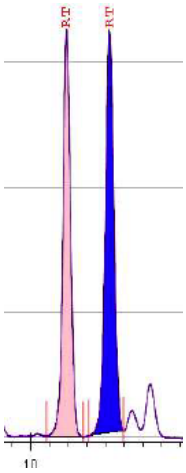
(R)*-3-cyclohexylidene-1-phenylpropan-1-ol (2.56)** The reaction was performed according to the general procedure (Method A***) with 4,4,5,5-tetramethyl-2-vinyl-1,3,2-dioxaborolane (46.2 mg, 0.30 mmol, 1.00 equiv.), phenyl lithium (0.167 mL, 1.9M in dibutyl ether, 0.30 mmol, 1.00 equiv.), cyclohexylidenemethyl trifluoromethanesulfonate (**2.98**) (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)-**2.37** (3.8 mg, 0.0036 mmol, 0.012 equiv.) in THF (1.2 mL, 0.25 M). The crude mixture was purified by silica gel column chromatography (3 % ethyl acetate in hexane) to afford a 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).

Analysis of Stereochemistry:

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 2.41, 2.24, and 2.40).

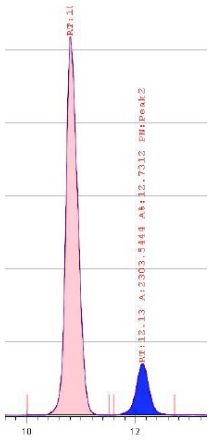
Chiral SFC (Chiracel OD-H, 5% IPA, 3 mL/min, 100 bar, 35 °C, 210-270 nm) – analysis of (R)-3-cyclohexylidene-1-phenylpropan-1-ol

Racemic Material

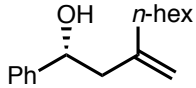


Peak No	% Area	Area	RT (min)
1	47.2345	4658.0381	10.96
2	52.7655	5203.4843	12.11
Total:	100	9861.5224	

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	



2.52

(R)*-3-methylene-1-phenylnonan-1-ol (2.52)** 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 (**2.97**) (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)-**2.37** (3.80 mg, 0.0036 mmol, 0.012 equiv.) in THF (1.2 mL, 0.25 M). The crude mixture was purified by silica gel chromatography (30% CH_2Cl_2 in pentane) to afford a clear 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,

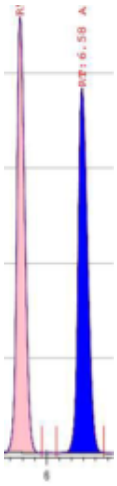
m), 0.90 (3H, t, J = 6.6). ^{13}C NMR (125 MHz, $CDCl_3$) δ 146.7, 144.24, 128.5, 127.6, 125.9, 125.9, 112.9, 71.7, 46.9, 35.9, 31.9, 30.5, 29.2, 29.2, 27.8, 22.8, 14.2. IR (neat) ν_{max} 3383.7 (w), 2955.3 (s), 2924.0 (s), 2854.0 (s), 1493.7 (s), 1454.3 (m), 1041.5 (m), 968.8 (s), 755.9 (s), 699.1 (s) cm^{-1}. HRMS-(DART) for: $C_{16}H_{23}$ $[M+H-H_2O]^+$: calculated: 215.1800, found: 215.1801. $[\alpha]_D^{20}$: +36.69 (c = 1.23, $CHCl_3$, l =50 mm).

Analysis of Stereochemistry:

Racemic compound was prepared according to the general procedure (***Method A***) 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 2.41, 2.24, and 2.40).

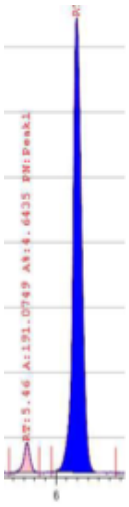
Chiral SFC (Chiracel OD-H, 5% IPA, 3 mL/min, 100 bar, 35 °C, 210-270 nm) – analysis of (R)-3-methylene-1-phenylnonan-1-ol.

Racemic Material

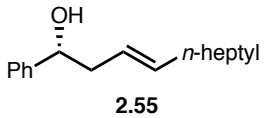


Peak Info			
Peak No	% Area	Area	RT (min)
1	50.4307	4230.6695	5.56
2	49.5693	4158.4116	6.58
Total:	100	8389.0811	

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	



2.55

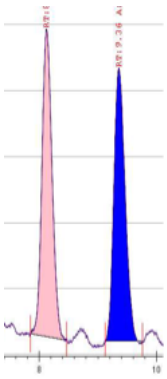
(R,E)*-1-phenylundec-3-en-1-ol (2.55)** The reaction was performed according to the general procedure (Method A***) with 4,4,5,5-tetramethyl-2-vinyl-1,3,2-dioxaborolane (46.2 mg, 0.30 mmol, 1.00 equiv.) phenyl lithium (0.167 mL, 1.9M in dibutyl ether, 0.30 mmol, 1.00 equiv.), (E)-non-1-en-1-yl trifluoromethanesulfonate (**2.96**) (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)-**2.37** (3.80 mg, 0.0036 mmol, 0.012 equiv.) in THF (1.2 mL, 0.25 M). The crude mixture was purified by silica gel chromatography (30% CH_2Cl_2 in pentane) to afford a clear 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).

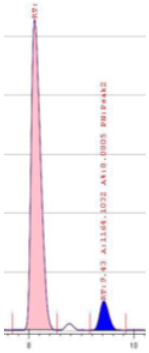
Analysis of Stereochemistry:

Racemic compound was prepared according to the general procedure (***Method A***) 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 2.41, 2.24, and 2.40).

Chiral 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.

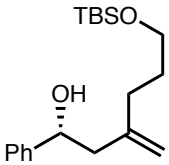
Racemic Material **Standard Conditions**





Peak Info			
Peak No	% Area	Area	RT (min)
1	50.3629	557.0803	8.12
2	49.6371	549.0516	9.36
Total:	100	1106.1319	

Peak Info			
Peak No	% Area	Area	RT (min)
1	91.9195	13242.1375	8.11
2	8.0805	1164.1032	9.43
Total:	100	14406.2407	



2.54

(R)*-6-(*tert*-butyldimethylsilyloxy)-3-methylene-1-phenylhexan-1-ol (2.54)** 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 (**2.101**) (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)-**2.37** (3.80 mg, 0.0036 mmol, 0.012 equiv.) in THF (1.2 mL, 0.25 M). The crude mixture was purified by silica gel chromatography (3% ethyl acetate in hexanes) to afford a 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),

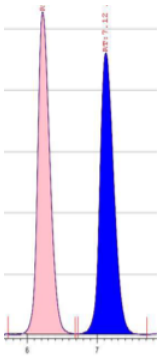
1644.4 (s), 1492.5 (m), 1454.1 (s), 1254.3 (s), 1101.3 (s), 835.4 (s), 775.2 (s), 699.2 (s) cm^{-1}.HRMS-(DART) for: $C_{19}H_{31}O_1Si_1$ $[M+H-H_2O]^+$: calculated: 303.2144, found: 303.2154. $[\alpha]_D^{20}$: +22.00 (c = 0.26, $CHCl_3$, *l* =50 mm).

Analysis of Stereochemistry:

Racemic compound was prepared according to the general procedure (***Method A***) 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 2.41, 2.24, and 2.40).

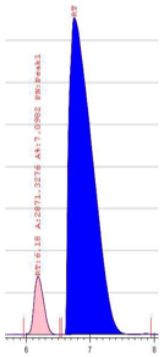
Chiral SFC (Chiracel OD-H, 5% IPA, 3 mL/min, 100 bar, 35 °C, 210-270 nm) – analysis of 6-((tert-butyldimethylsilyl)oxy)-3-methylene-1-phenylhexan-1-ol.

Racemic Material

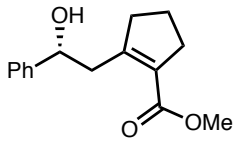


Peak Info			
Peak No	% Area	Area	RT (min)
1	50.0691	3171.9339	6.22
2	49.9309	3163.182	7.12
Total:	100	6335.1159	

Standard Conditions



Peak Info			
Peak No	% Area	Area	RT (min)
1	7.0982	2871.3276	6.18
2	92.9018	37580.4402	6.75
Total:	100	40451.7678	



2.57

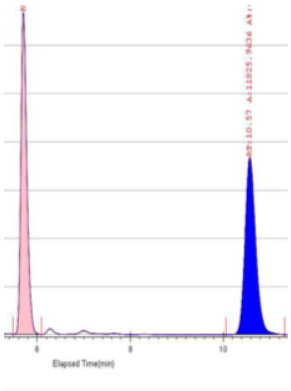
(*R*)-methyl 2-(2-hydroxy-2-phenylethyl)cyclopent-1-enecarboxylate (2.57) The reaction was performed according to the general procedure (***Method A***) with 4,4,5,5-tetramethyl-2-vinyl-1,3,2-dioxaborolane (46.2 mg, 0.30 mmol, 1.00 equiv.) phenyl lithium (0.167 mL, 1.9M in dibutyl ether, 0.30 mmol, 1.00 equiv.), 5-hydroxypent-1-en-2-yl trifluoromethanesulfonate (**2.102**) (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)-**2.37** (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 hours. A phosphate buffer solution was used instead of 3M NaOH solution. The crude mixture was purified by silica gel chromatography (40% CH_2Cl_2 in Hexanes) to afford a clear 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. $[\alpha]_D^{20}$: +73.65 (c = 0.68, $CHCl_3$, l =50 mm).

Analysis of Stereochemistry:

Racemic compound was prepared according to the general procedure (***Method A***) 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 2.41, 2.24, and 2.40).

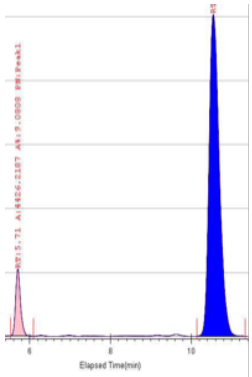
Chiral SFC (Chiracel OD-H, 5% IPA, 3 mL/min, 100 bar, 35 °C, 210-270 nm) – Methyl (R)-2-(2-hydroxy-2-phenylethyl)cyclopent-1-ene-1-carboxylate.

Racemic Material

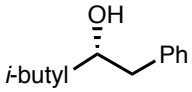


Peak Info			
Peak No	% Area	Area	RT (min)
1	50.236	11938.1215	5.7
2	49.764	11825.9636	10.57
Total:	100	23764.0851	

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	



2.63

***(S)*-4-methyl-1-phenylpentan-2-ol (2.63)** The reaction was performed according to the general procedure **(*Method B*)** with 2-isobutyl-5,5-dimethyl-1,3,2-dioxaborinane (**2.202**) (51.0 mg, 0.30 mmol), vinylllithium (0.211 mL, 1.42M in diethyl ether, 0.30 mmol), phenyltrifluoromethanesulfonate (74.60 mg, 0.33 mmol), palladium (II) acetate (1.34 mg, 0.006 mmol), (S_p, S_p)-**2.37** (7.60 mg, 0.0072 mmol) in THF (1.2 mL, 0.25 M). The crude mixture was purified by silica gel chromatography (40% CH_2Cl_2 in hexanes) to afford a clear 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

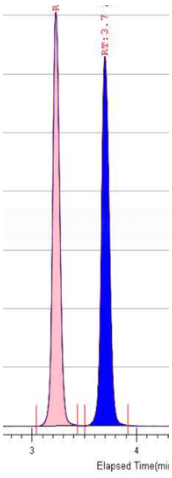
(br), 3027 (w), 2953 (m), 2921 (m), 2868 (w), 2362 (w), 1512 (w), 1466 (m), 1346 (w), 1136 (w), 1078 (m), 1019 (m), 743 (s), 697 (s), 603 (w) cm^{-1}; HRMS-(DART) for $C_{12}H_{17}$ $[M+H-H_2O]^+$: calculated: 161.1330, found: 161.1337. $[\alpha]^{20}_D = +4.736$ (c = 0.285, $CHCl_3$, *l* = 50 mm).

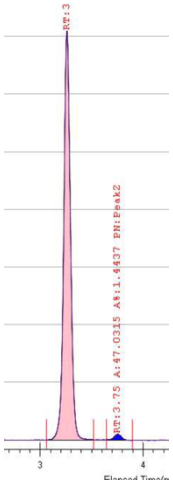
Analysis of Stereochemistry

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 2.41, 2.24, and 2.40).

Chiral 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.

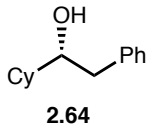
Racemic Material **Standard Conditions**





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	



2.64

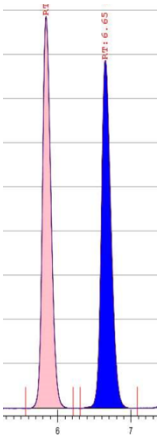
(R)*-1-cyclohexyl-2-phenylethan-1-ol (2.64)** The reaction was performed according to the general procedure (Method B***) with 2-cyclohexyl-5,5-dimethyl-1,3,2-dioxaborinane (2.201) (58.8 mg, 0.30 mmol, 1.00 equiv.), vinyl lithium (0.210 mL, 1.42 M in Et_2O, 0.30 mmol, 1.00 equiv.), phenyltrifluoromethanesulfonate (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)-**2.37** (7.60 mg, 0.0072 mmol,0.024 equiv.) in THF (1.20 mL, 0.25 M). The crude mixture was purified by silica gel chromatography (5% ethyl acetate in hexanes, stain in CAM) to afford a 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).

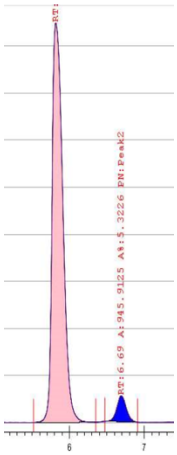
Analysis of Stereochemistry:

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 2.41, 2.24, and 2.40).

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

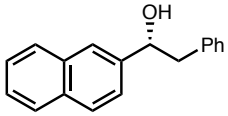
Racemic Material **Standard Conditions**





Peak No	% Area	Area	RT (min)
1	49.9353	7108.9938	5.84
2	50.0647	7127.4132	6.65
Total:	100	14236.407	

Peak No	% Area	Area	RT (min)
1	94.6774	16825.8605	5.81
2	5.3226	945.9125	6.69
Total:	100	17771.773	



2.65

(R)*-1-(naphthalen-2-yl)-2-phenylethan-1-ol (2.65)** The reaction was performed according to the general procedure (Method B***) with 5,5-dimethyl-2-(naphthalen-2-yl)-1,3,2-dioxaborinane (**2.90**) (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)-**2.37** (7.60 mg, 0.0072 mmol,0.024 equiv.) in THF (1.20 mL, 0.25 M). The crude mixture was purified by silica gel chromatography (15% ethyl acetate in hexanes, stain in CAM) to afford a 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),

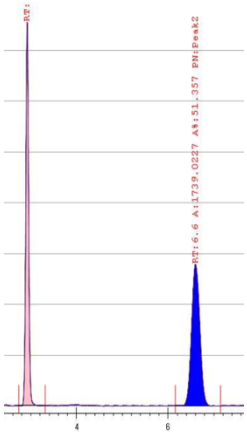
3025.9 (w), 2914.8 (w), 1601.1 (w), 1494.2 (w). 1360.6 (w), 1077.5 (w), 1043.3 (m), 893.2 (m), 818.4 (s), 743.5 (s), 727.6 (s), 698.7 (s), 481.6 (s) cm^{-1}. HRMS (DART) for $C_{18}H_{15}$ $[M+H-H_2O]^+$ calculated: 231.1174, found: 231.1170. $[\alpha]^{20}_D$: -2.515 (c = 1.340, $CHCl_3$, *l* =50 mm).

Analysis of Stereochemistry:

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 2.41, 2.24, and 2.40).

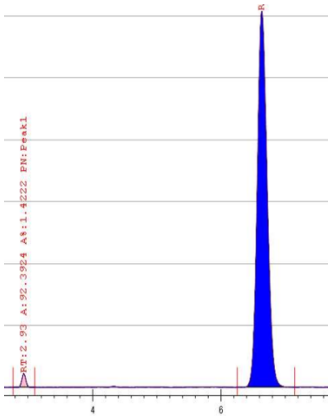
Chiral SFC (Chiracel ODR-H, 15% MeOH, 3 mL/min, 100 bar, 35 °C, 210-270 nm) – analysis (R)-1-(naphthalen-2-yl)-2-phenylethan-1-ol.

Racemic Material

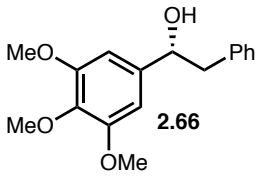


Peak No	% Area	Area	RT (min)
1	48.643	1647.1222	2.92
2	51.357	1739.0227	6.6
Total:	100	3386.1449	

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	



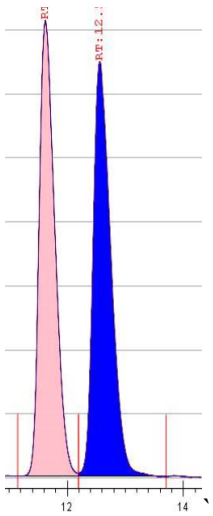
(R)*-2-phenyl-1-(3,4,5-trimethoxyphenyl)ethan-1-ol (2.66)** The reaction was performed according to the general procedure ***(Method B) with 2-(3,4,5-trimethoxyphenyl)-5,5-dimethyl-1,3,2-dioxaborinane (**2.94**) (84.0 mg, 0.30 mmol, 1.00 equiv.), vinyl lithium (0.210 mL, 1.42 M in Et_2O, 0.30 mmol, 1.00 equiv.), phenyltrifluoromethanesulfonate (74.60 mg, 0.33 mmol, 1.10 equiv.), palladium (II) acetate (1.30 mg, 0.0060 mmol, 0.020 equiv.), 2.37 (7.60 mg, 0.0072 mmol, 0.024 equiv.) in THF (1.20 mL, 0.25 M). The crude mixture was purified by silica gel chromatography (10% ethyl acetate in hexanes, stain in CAM) to afford a 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).

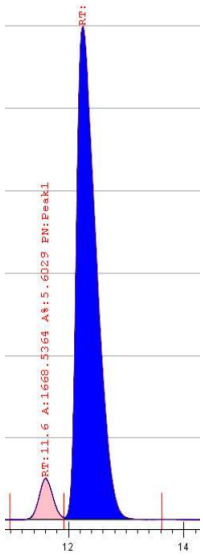
Analysis of Stereochemistry:

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 2.41, 2.24, and 2.40).

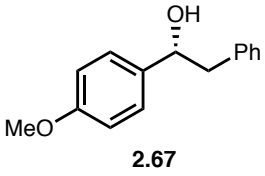
Chiral SFC (Chiracel ODR-H, 6% MeOH, 3 mL/min, 100 bar, 35 °C, 210-270 nm) – analysis of (R)-2-phenyl-1-(3,4,5-trimethoxyphenyl)ethan-1-ol.

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	



2.67

(R)*-1-(4-methoxyphenyl)-2-phenylethan-1-ol (2.67)** The reaction was performed according to the general procedure ***(Method B) with 2-(4-methoxyphenyl)-5,5-dimethyl-1,3,2-dioxaborinane (**2.85**) (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)-**2.37** (7.60 mg, 0.0072 mmol, 0.024 equiv.) in THF (1.20 mL, 0.25 M). The crude mixture was purified by silica gel chromatography (40% CH_2Cl_2 in pentane, stain in CAM) to afford a 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),

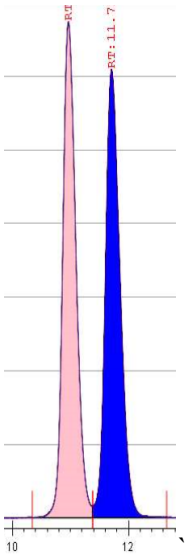
2918.0 (w), 2835.9 (w), 1611.4 (m), 1512.2 (s), 1454.2 (w), 1302.3 (w), 1246.0 (s), 1157.1 (m), 1032.9 (m). 831.9 (m), 699.4 (m) cm^{-1}. HRMS (DART) for $C_{15}H_{15}O$ $[M+H-H_2O]^+$ calculated: 211.1123, found: 211.1123. $[\alpha]^{20}_D$: -2.0386 (c = 1.275, $CHCl_3$, *l* =50 mm).

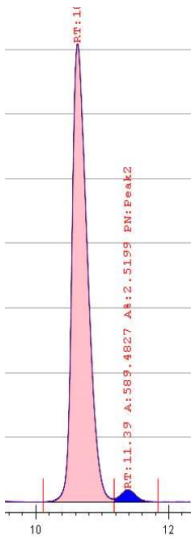
Analysis of Stereochemistry:

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 2.41, 2.24, and 2.40).

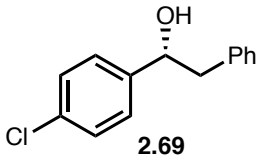
Chiral SFC (Chiracel OD-H, 8% IPA, 3 mL/min, 100 bar, 35 °C, 210-270 nm) – analysis of (R)-1-(4-methoxyphenyl)-2-phenylethan-1-ol.

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	



2.69

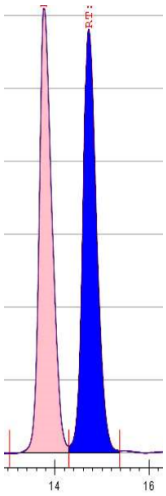
***(R)*-1-(4-chlorophenyl)-2-phenylethan-1-ol (2.69)** The reaction was performed according to the general procedure *(**Method B**)* with 2-(4-chlorophenyl)-5,5-dimethyl-1,3,2-dioxaborinane (**2.86**) (67.30 mg, 0.30 mmol, 1.00 equiv.), vinyl lithium (0.176 mL, 1.72 M in Et_2O, 0.30 mmol, 1.00 equiv.), 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)-**2.37** (7.60 mg, 0.0072 mmol, 0.024 equiv.) in THF (1.20 mL, 0.25 M). The crude mixture was purified by silica gel chromatography (30% CH_2Cl_2 in pentane, stain in CAM) to afford a clear 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).

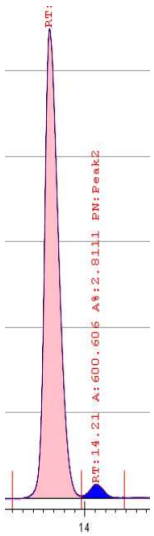
Analysis of Stereochemistry:

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 2.41, 2.24, and 2.40).

Chiral 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.

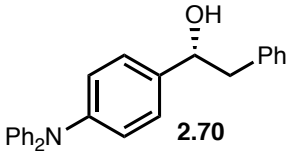
Racemic Material **Standard Conditions**





Peak No	% Area	Area	RT (min)
1	49.0709	11621.9899	13.76
2	50.9291	12062.0942	14.72
Total:	100	23684.0841	

Peak No	% Area	Area	RT (min)
1	97.1889	20764.8334	13.31
2	2.8111	600.606	14.21
Total:	100	21365.4394	



***(R)*-1-(4-(diphenylamino)phenyl)-2-phenylethan-1-ol (2.70)**

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 (**2.91**) (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)-**2.37** (7.60 mg, 0.0072 mmol, 0.024 equiv.) in THF (1.20 mL, 0.25 M). The crude mixture was purified by silica gel chromatography (40% CH_2Cl_2 in hexanes) to afford a 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,

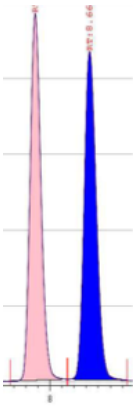
46.1. IR (neat) ν_{max} 3383.1 (br), 3061.3 (m), 2922.1 (w), 2854.4(w), 1589.0 (s), 1508.9 (s), 1314.1 (m), 1277.3 (s), 752.2 (s), 696.0 (s) cm^{-1}. HRMS-(DART) for: $C_{26}H_{22N}N_1$ [M+H-H_2O]$^+$: calculated: 348.1752, found: 348.1763. $[\alpha]_D^{20}$: -7.79 (c =0 .43, $CHCl_3$, *l* =50 mm).

Analysis of Stereochemistry:

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 2.41, 2.24, and 2.40).

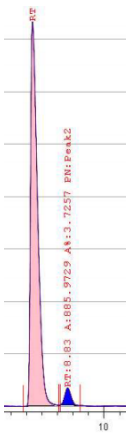
Chiral SFC (Chiracel OD-H, 5% IPA, 3 mL/min, 100 bar, 35 °C, 210-270 nm) – analysis of (R)-1-(4-(diphenylamino)phenyl)-2-phenylethan-1-ol.

Racemic Material

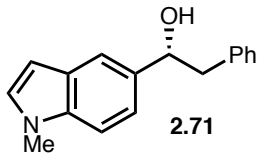


Peak Info			
Peak No	% Area	Area	RT (min)
1	50.0189	6007.4743	7.75
2	49.9811	6002.9239	8.66
Total:	100	12010.3982	

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	



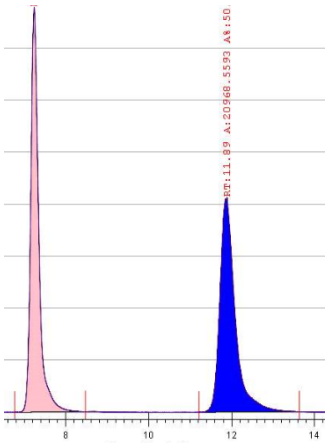
(R)*-1-(1-methyl-1H-indol-5-yl)-2-phenylethanol (2.71)** The reaction was performed according to the general procedure (Method B***) with 5-(5,5-dimethyl-1,3,2-dioxaborinan-2-yl)-1-methyl-1*H*-indole (**2.95**) (75.20 mg, 0.30 mmol, 1.00 equiv.), vinyl lithium (0.210 mL, 1.42 M in Et_2O, 0.30 mmol, 1.00 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)-**2.37** (7.60 mg, 0.0072 mmol, 0.024 equiv.) in THF (1.20 mL, 0.25 M). The crude mixture was purified by silica gel chromatography (15% ethyl acetate in hexanes, stain in CAM) to afford a white solid (64.8 mg, 86% yield). 1H 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).

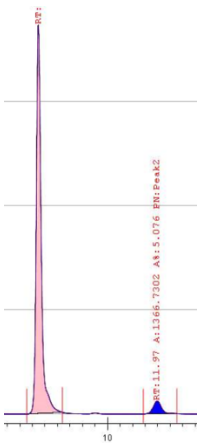
Analysis of Stereochemistry:

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 2.41, 2.24, and 2.40).

Chiral 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.

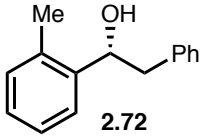
Racemic Material **Standard Conditions**





Peak No	% Area	Area	RT (min)
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	94.924	25558.6592	7.23
2	5.076	1366.7302	11.97
Total:	100	26925.3894	



2.72

(R)*-2-phenyl-1-(o-tolyl)ethan-1-ol (2.72)** The reaction was performed according to the general procedure ***(Method B) with 5,5-dimethyl-2-(o-tolyl)-1,3,2-dioxaborinane (**2.87**). (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)-**2.37** (7.60 mg, 0.0072 mmol, 0.012 equiv.) in THF (1.20 mL, 0.25 M). The crude mixture was purified by silica gel chromatography (2% ethyl acetate in pentane, stain in CAM) to afford a 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,

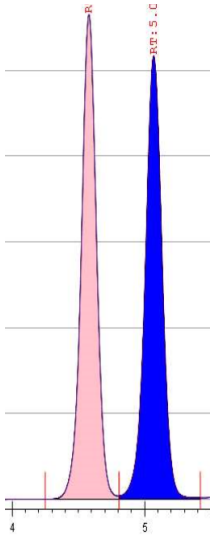
134.49, 130.41, 129.58, 128.66, 127.43, 126.74, 126.48, 125.37, 71.85, 45.15, 19.12. IR (neat) ν_{max} 3384.9 (br), 3061.3 (w), 2920.4 (w), 2859.95 (w), 1603.1 (w), 1494.1 (m), 1454.0 (m), 1076.0 (m), 1038.8 (m), 755.1 (s). 738.2 (m), 698.4 (s) cm^{-1}. HRMS (DART) for $C_{15}H_{15}$ $[M+H-H_2O]^+$ calculated: 195.1174, found: 195.1181. $[\alpha]^{20}_D$: +30.812 (c = 1.760, $CHCl_3$, *l* =50 mm).

Analysis of Stereochemistry:

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 2.41, 2.24, and 2.40).

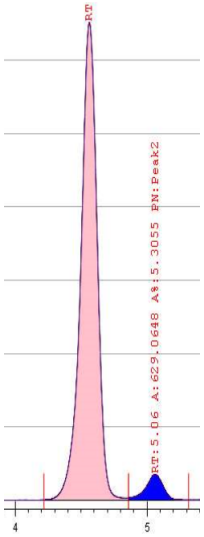
Chiral SFC (Chiracel OJ-H, 10% IPA, 3 mL/min, 100 bar, 35 °C, 210-270 nm) – analysis (R)-2-phenyl-1-(o-tolyl)ethan-1-ol.

Racemic Material

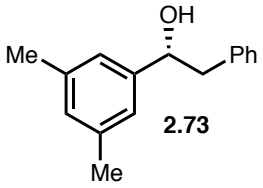


Peak No	% Area	Area	RT (min)
1	49.4517	8989.9843	4.58
2	50.5483	9189.3254	5.07
Total:	100	18179.3097	

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	



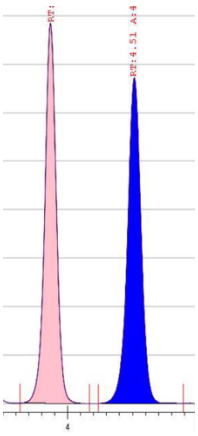
***(R)*-1-(3,5-dimethylphenyl)-2-phenylethan-1-ol (2.73)** The reaction was performed according to the general procedure **(*Method B*)** with 2-(3,5-dimethylphenyl)-5,5-dimethyl-1,3,2-dioxaborinane (65.4 mg, 0.30 mmol) (**2.89**), vinylllithium (0.211 mL, 1.42M in diethyl ether, 0.30 mmol), phenyltrifluoromethanesulfonate (74.60 mg, 0.33 mmol), palladium (II) acetate (1.34 mg, 0.006 mmol), (S_p, S_p)-**2.37** (7.60 mg, 0.0072 mmol) in THF (1.2 mL, 0.25 M). The crude mixture was purified by silica gel chromatography (40% CH_2Cl_2 in hexanes) to afford a clear 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).

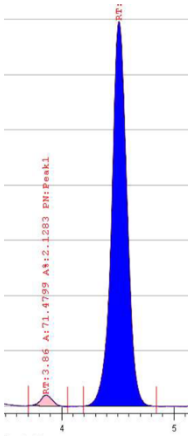
Analysis of Stereochemistry

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 2.41, 2.24, and 2.40).

Chiral 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.

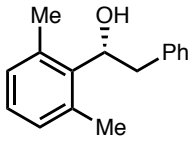
Racemic Material **Standard Conditions**





Peak No	% Area	Area	RT (min)
1	49.8529	4861.1049	3.87
2	50.1471	4889.7919	4.51
Total:	100	9750.8968	

Peak No	% Area	Area	RT (min)
1	2.1283	71.4799	3.86
2	97.8717	3287.0332	4.51
Total:	100	3358.5131	



2.74

(R)*-1-(2,6-dimethylphenyl)-2-phenylethan-1-ol (2.74)** The reaction was performed according to the general procedure (Method B***) with 2-(2,6-dimethylphenyl)-5,5-dimethyl-1,3,2-dioxaborinane (**2.88**) (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)-**2.37** (7.60 mg, 0.0072 mmol,0.024 equiv.) in THF (1.20 mL, 0.25 M). The crude mixture was purified by silica gel chromatography (40% CH_2Cl_2 in pentane, stain in CAM) to afford a 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,

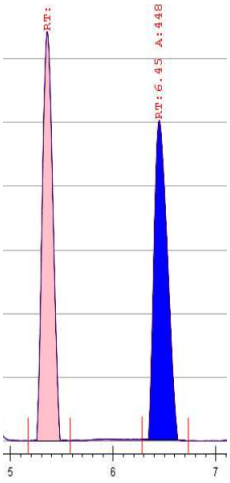
127.30, 126.66, 72.00, 42.33, 20.96. IR (neat) ν_{max} 3549.2 (br), 3429.9 (br), 3062.1 (w), 3025.8 (w), 2925.0 (w), 2864.5 (w), 1601.8 (w), 1495.1 (m), 1468.0 (m), 1453.1 (w), 1045.3 (m) 769.9 (s), 752.6 (s), 700.0 (s) cm^{-1}. HRMS (DART) for $C_{16}H_{17}$ $[M+H-H_2O]^+$ calculated: 209.1330, found: 209.1323. $[\alpha]^{20}_D$: -6.573 (c = 1.660, $CHCl_3$, *l* =50 mm).

Analysis of Stereochemistry:

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 2.41, 2.24, and 2.40).

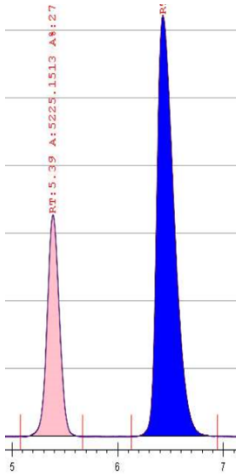
Chiral SFC (Chiracel OJ-H, 10% IPA, 3 mL/min, 100 bar, 35 °C, 210-270 nm) – analysis (R)-1-(2,6-dimethylphenyl)-2-phenylethan-1-ol.

Racemic Material



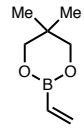
Peak No	% Area	Area	RT (min)
1	50.288	4540.9221	5.36
2	49.712	4488.9112	6.45
Total:	100	9029.8333	

Standard Conditions

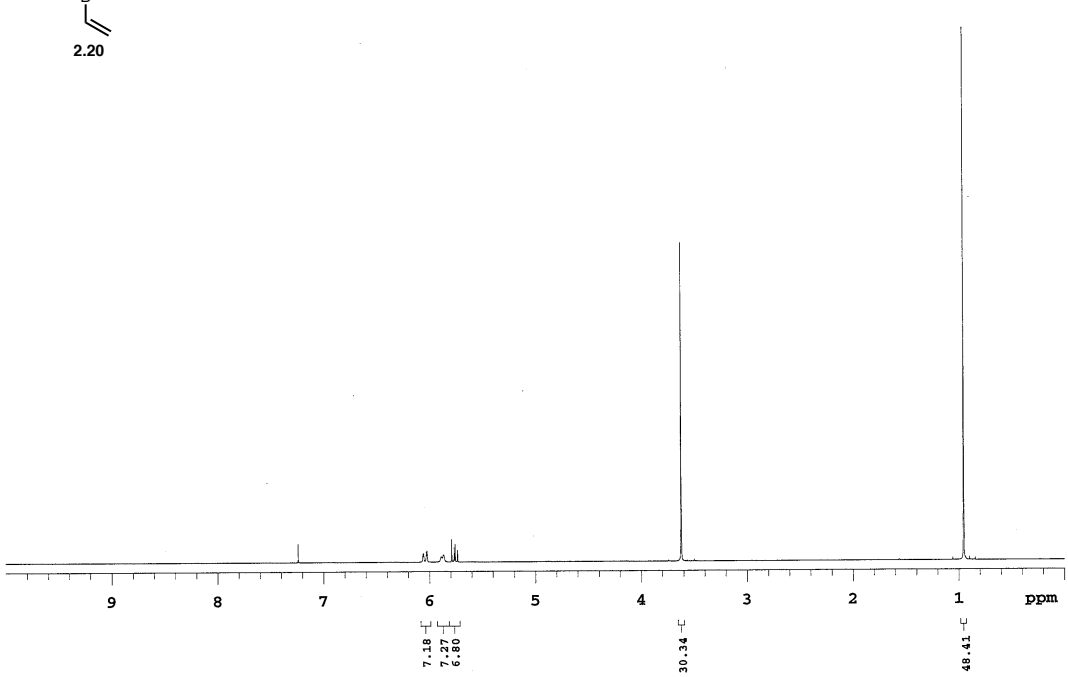


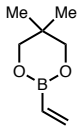
Peak No	% Area	Area	RT (min)
1	27.1761	5225.1513	5.39
2	72.8239	14001.8745	6.43
Total:	100	19227.0258	

2.5.4 Compound Spectra

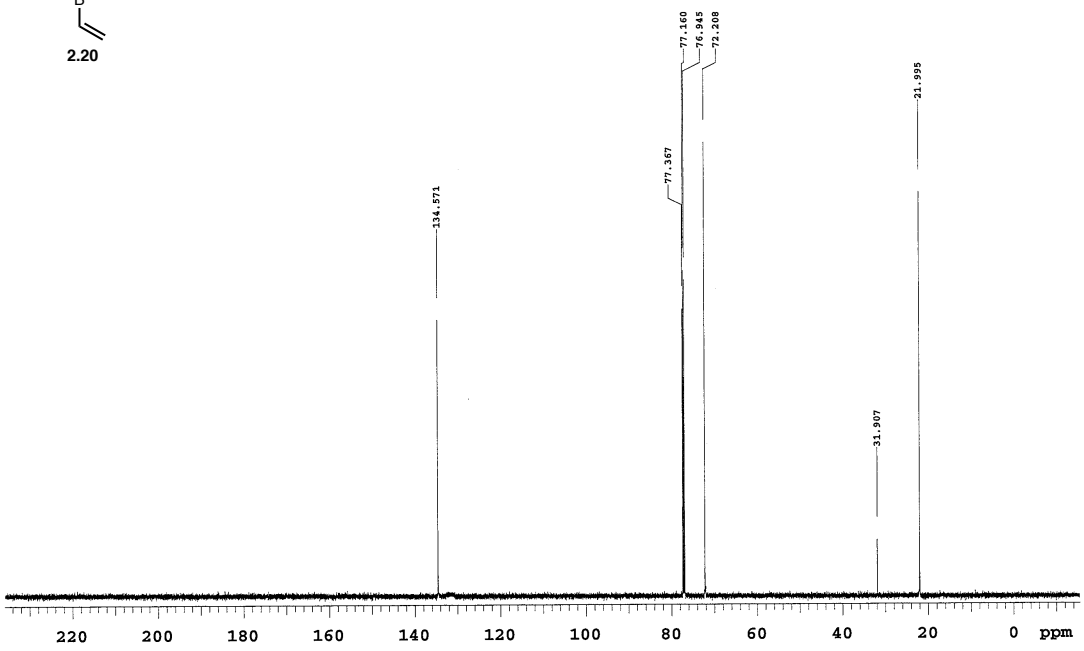

Me
Me
O
B
O

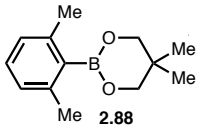
2.20


9
8
7
6
5
4
3
2
1
ppm
7.18
7.27
6.80
30.34
48.41

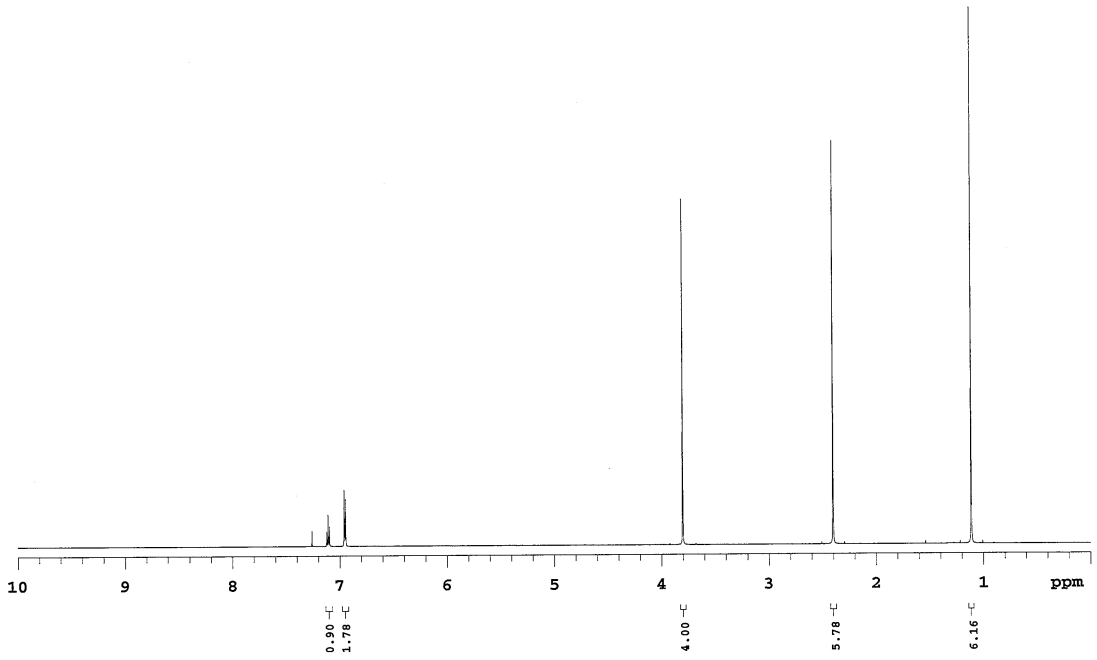

Me
Me
O
B
O

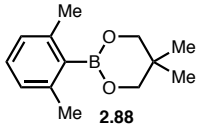
2.20


134.571
77.367
77.160
76.945
72.208
31.907
21.995
220
200
180
160
140
120
100
80
60
40
20
0
ppm

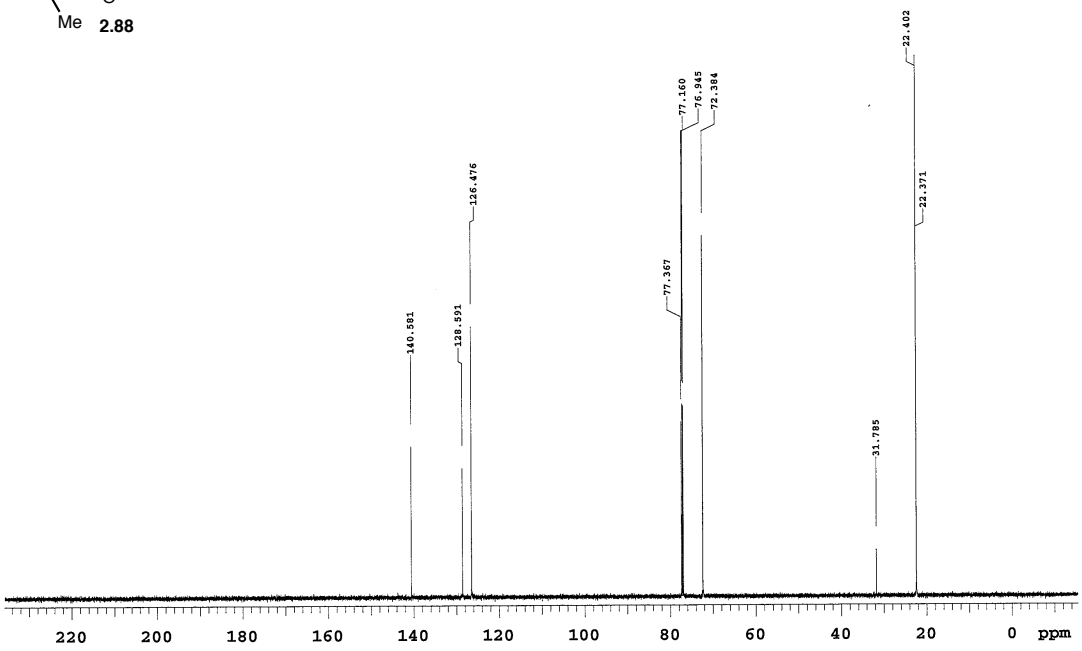

Me
O
B
O
Me
Me
Me

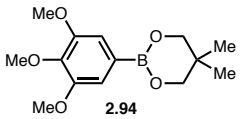
2.88


10
9
8
7
6
5
4
3
2
1
ppm
0.90
1.78
4.00
5.78
6.16

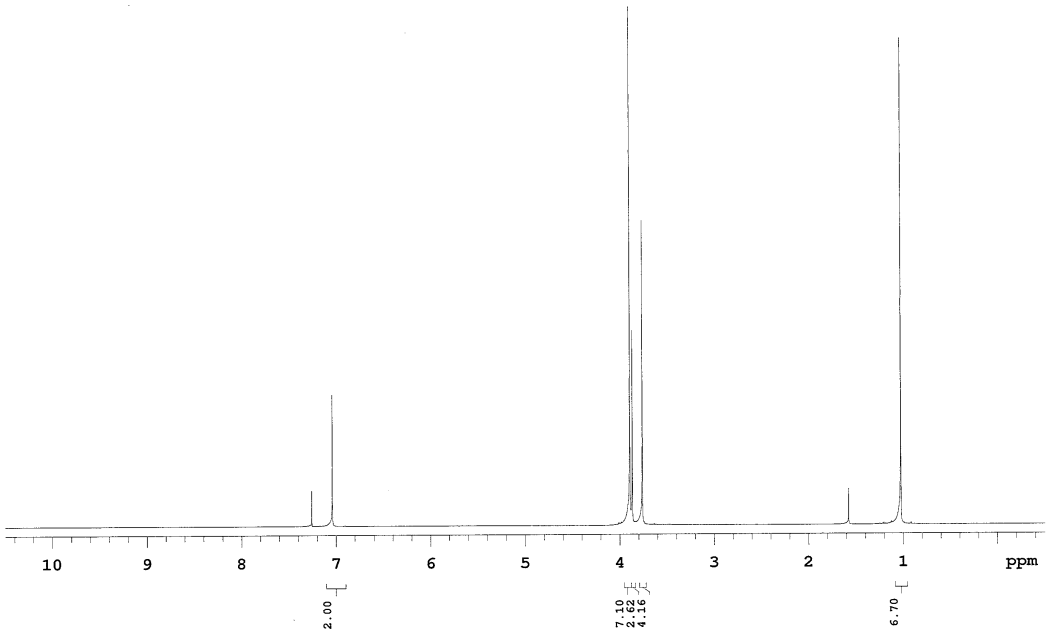

Me
O
B
O
Me
Me
Me

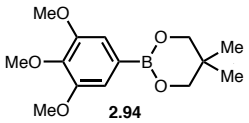
2.88


140.581
128.591
126.476
77.367
77.160
76.945
72.384
31.785
22.402
22.371
220
200
180
160
140
120
100
80
60
40
20
0
ppm

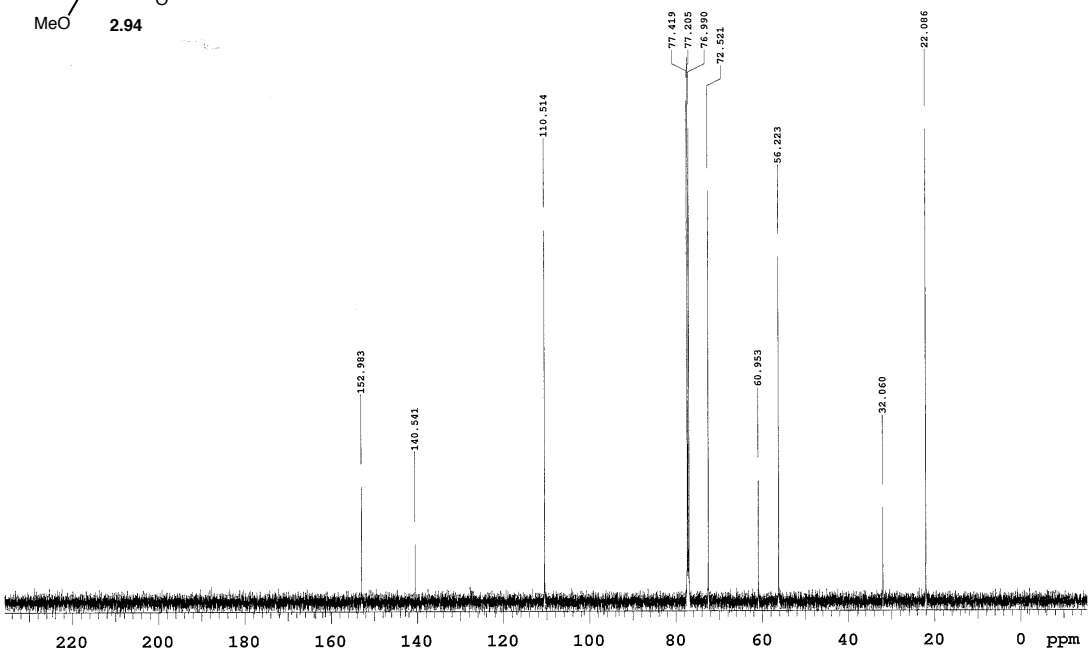

MeO
MeO
MeO
B
O
O
Me
Me

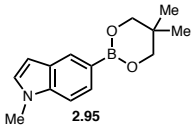
2.94


10
9
8
7
6
5
4
3
2
1
ppm
2.00
7.10
2.62
4.16
6.70

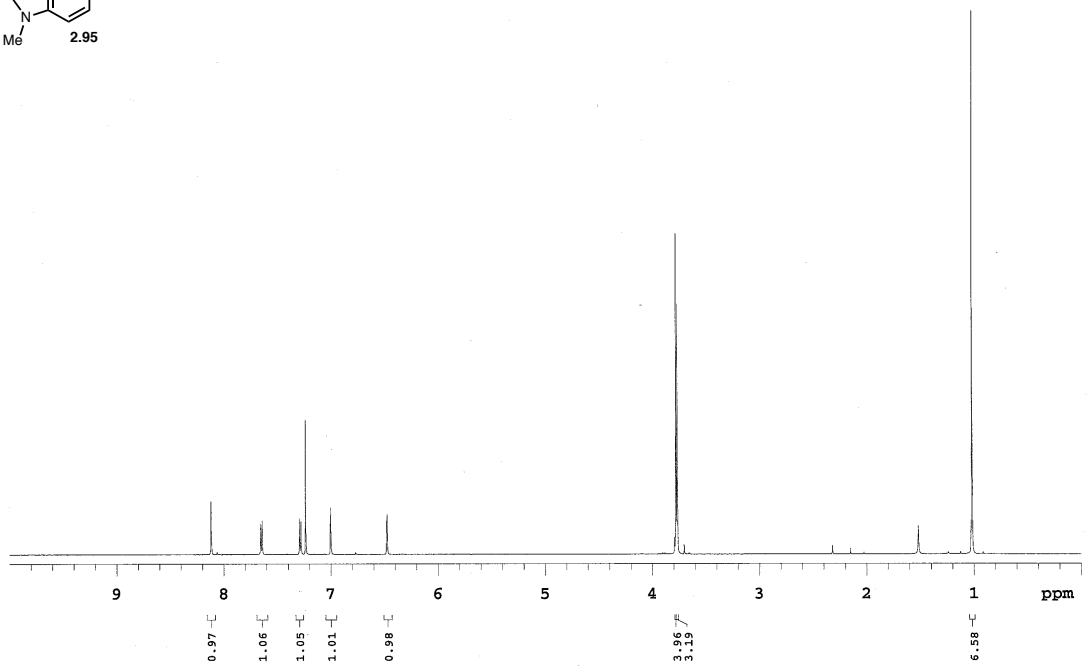

MeO
MeO
MeO
B
O
O
Me
Me

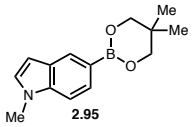
2.94


152.983
140.541
110.514
77.419
77.205
76.990
72.521
60.953
56.223
32.060
22.086
220
200
180
160
140
120
100
80
60
40
20
0
ppm

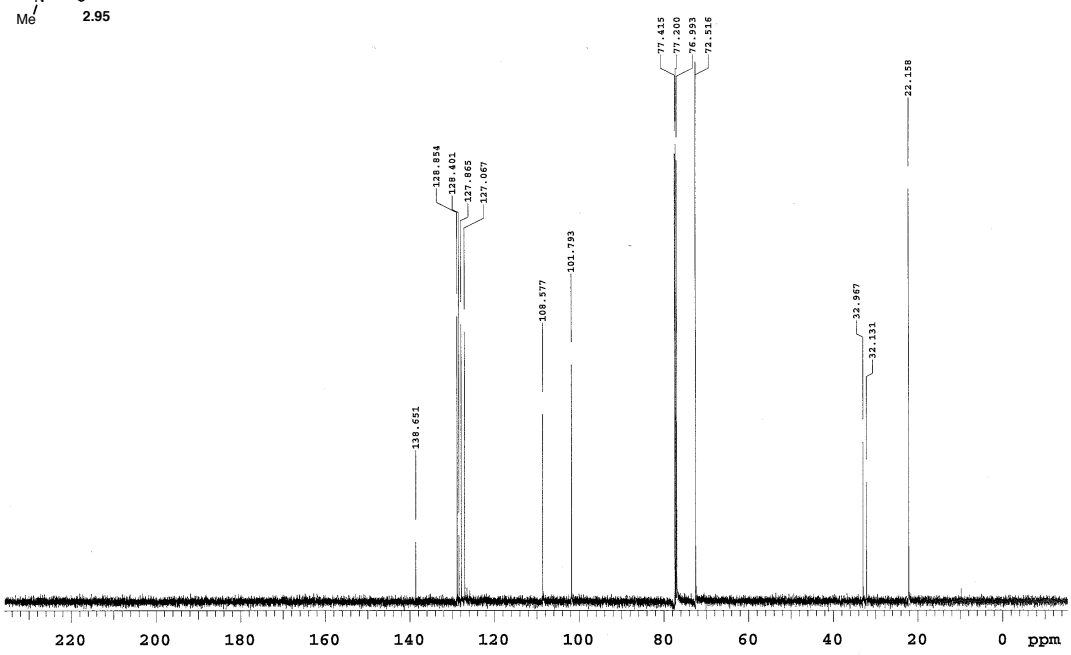

Me
Me
O
B
O
N
Me

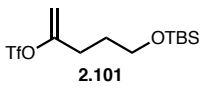
2.95


9
8
7
6
5
4
3
2
1
ppm
0.97
1.06
1.05
1.01
0.98
3.96
3.19
6.58

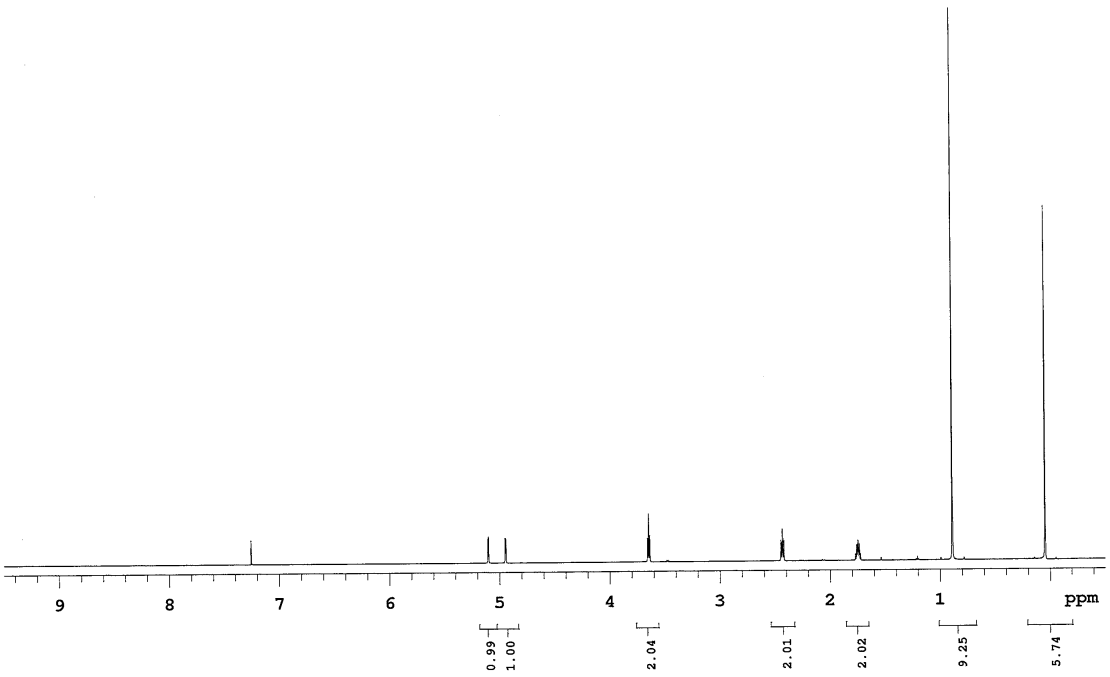

Me
Me
O
B
O
N
Me

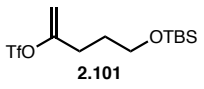
2.95


77.415
77.200
76.993
72.516
128.854
128.401
127.865
127.067
101.793
108.577
138.651
32.967
32.131
22.158
220
200
180
160
140
120
100
80
60
40
20
0
ppm

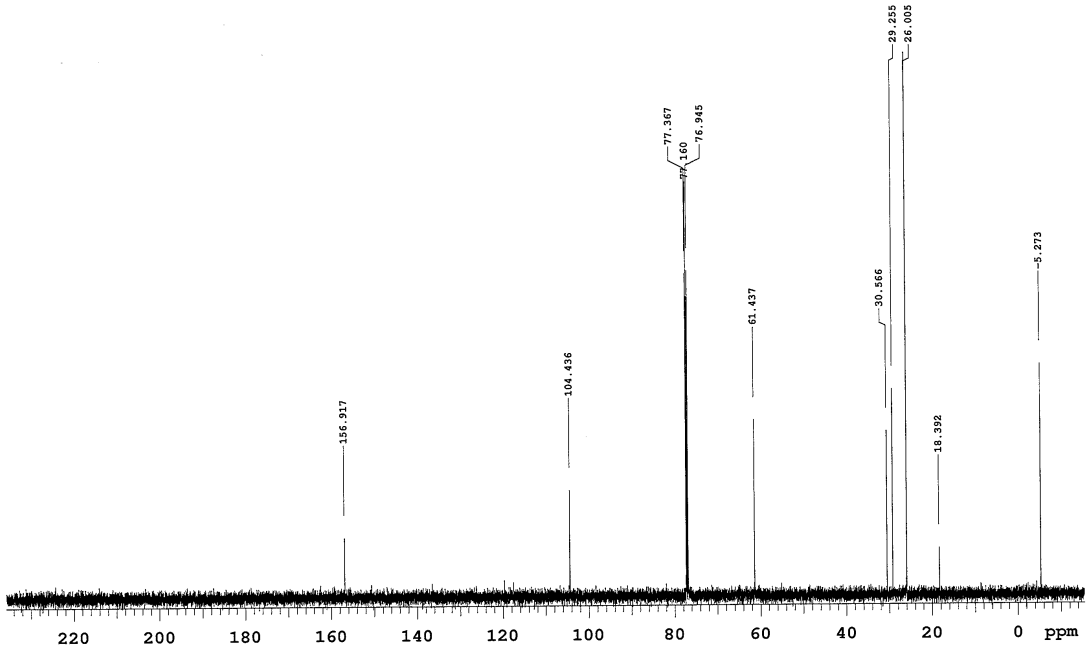

TfO
OTBS

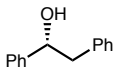
2.101


9
8
7
6
5
4
3
2
1
ppm
0.99
1.00
2.04
2.01
2.02
9.25
5.74

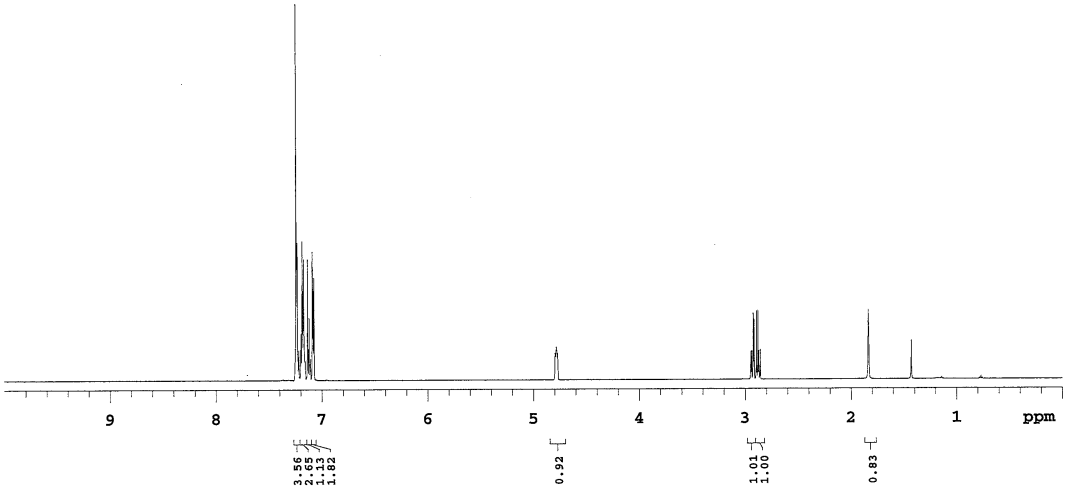

TfO
OTBS

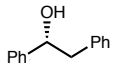
2.101


156.917
104.436
77.367
77.160
76.945
61.437
30.566
29.255
26.005
18.392
-5.273
220
200
180
160
140
120
100
80
60
40
20
0
ppm

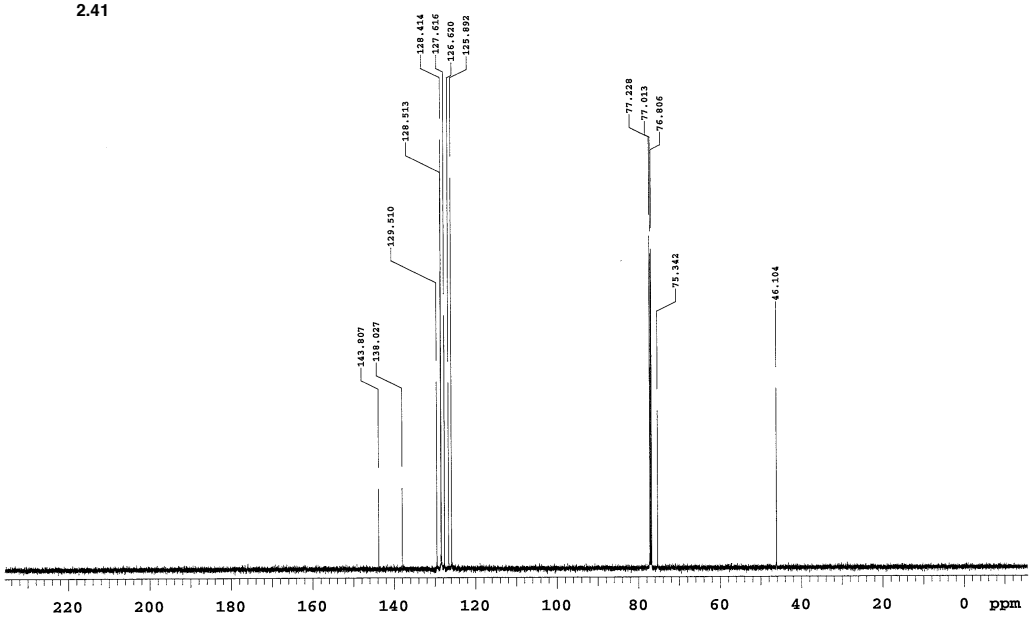

OH
Ph
Ph

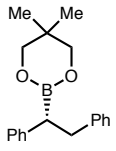
2.41


9
8
7
6
5
4
3
2
1
ppm
3.56
2.65
2.13
1.82
0.92
1.01
1.00
0.83

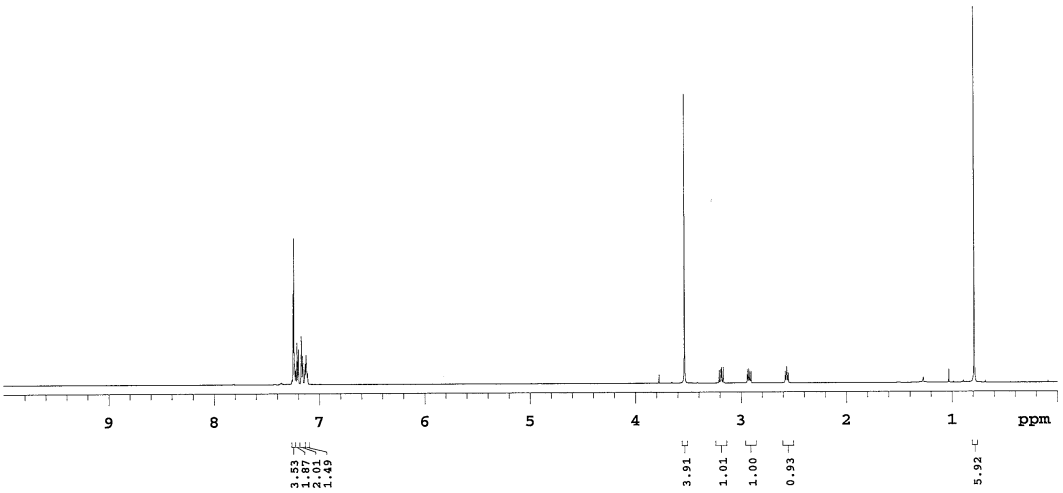

OH
Ph
Ph

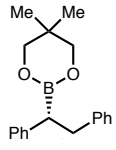
2.41


128.414
127.616
126.620
125.892
128.513
129.510
143.807
139.027
77.228
77.013
76.806
75.342
46.104
220
200
180
160
140
120
100
80
60
40
20
0
ppm

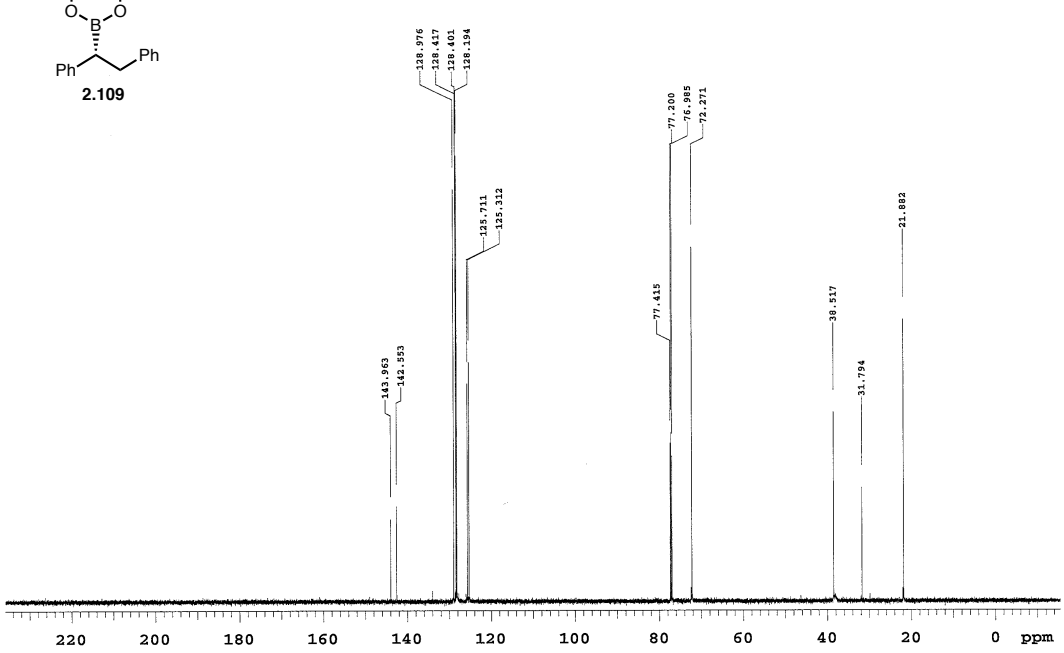

Me
Me
O
B
O
Ph
Ph

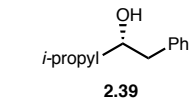
2.109


9
8
7
6
5
4
3
2
1
ppm
3.53
1.87
2.01
1.49
3.91
1.01
1.00
0.93
5.92

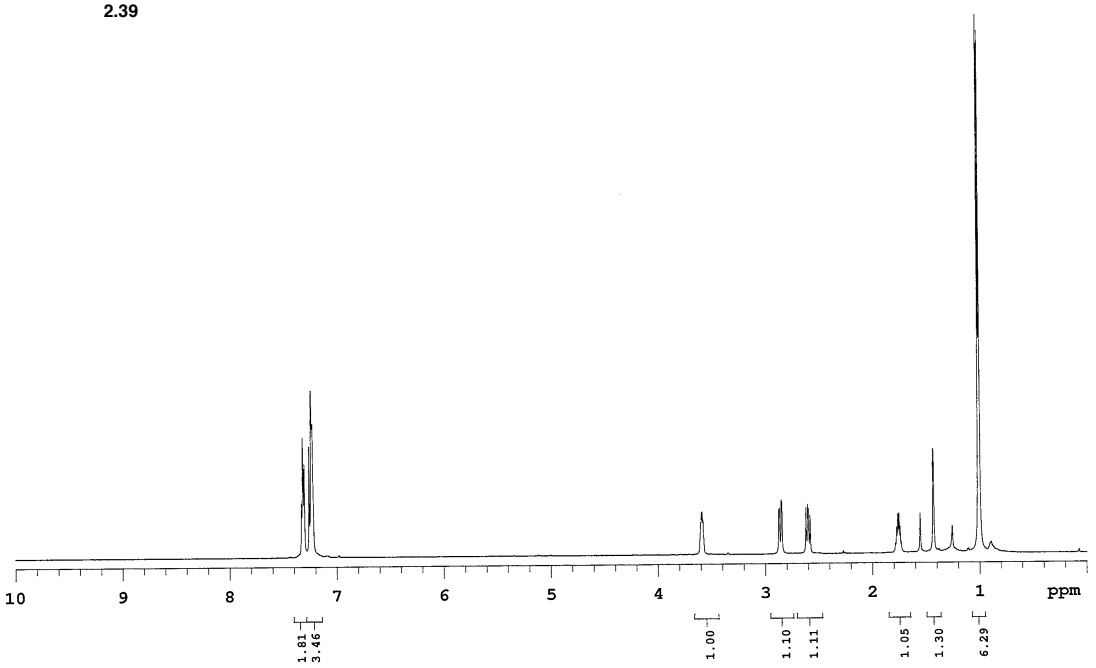

Me
Me
O
B
O
Ph
Ph

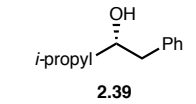
2.109


128.976
128.417
128.401
128.194
125.711
125.312
77.200
76.985
77.415
72.271
143.963
142.553
38.517
31.794
21.882
220
200
180
160
140
120
100
80
60
40
20
0
ppm

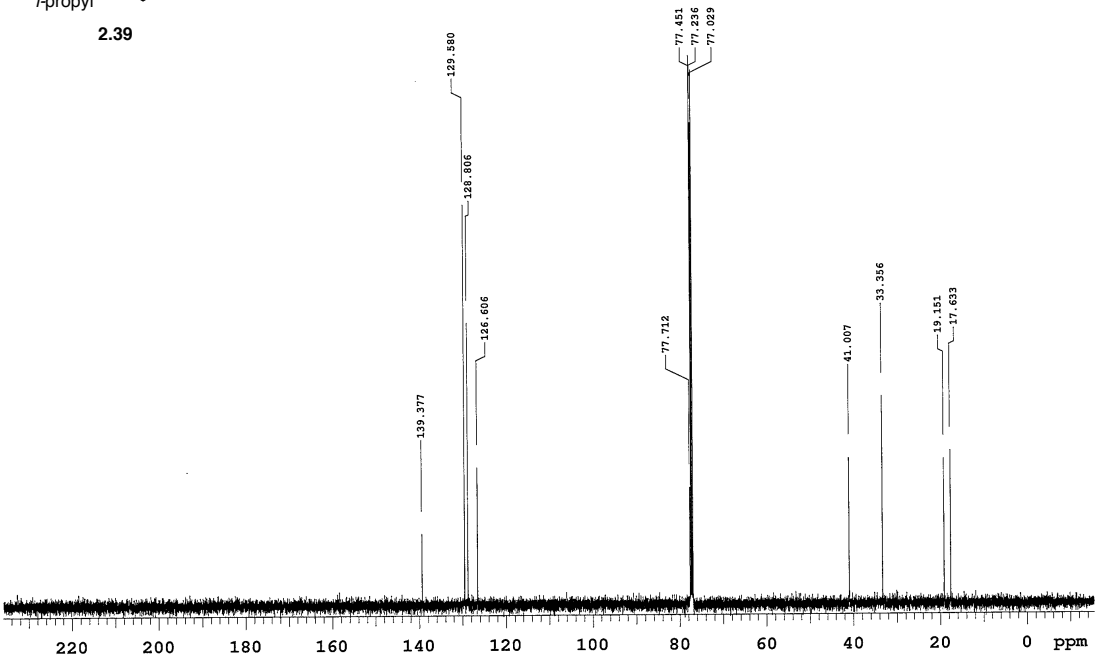

OH
i-propyl
Ph

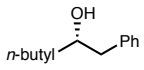
2.39


10
9
8
7
6
5
4
3
2
1
ppm
1.81
3.46
1.00
1.10
1.11
1.05
1.30
6.29

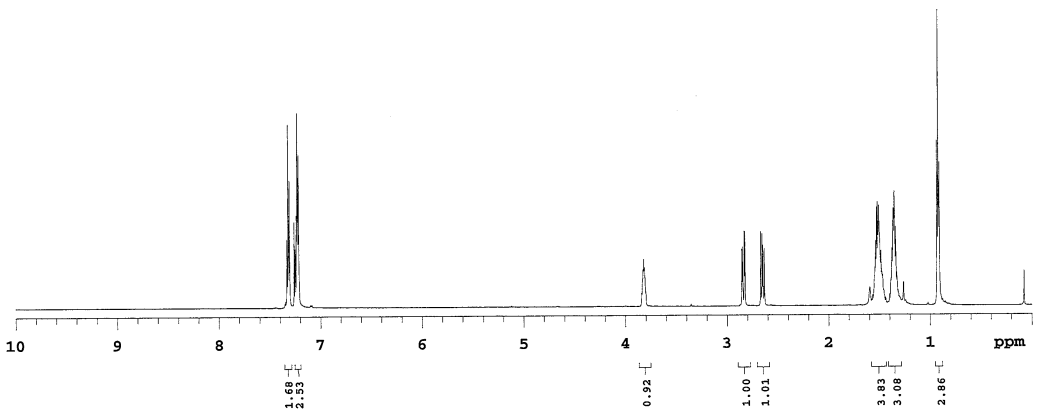

OH
i-propyl
Ph

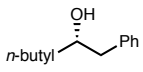
2.39


139.377
129.580
128.806
126.606
77.712
77.451
77.236
77.029
41.007
33.356
19.151
17.633
220
200
180
160
140
120
100
80
60
40
20
0
ppm

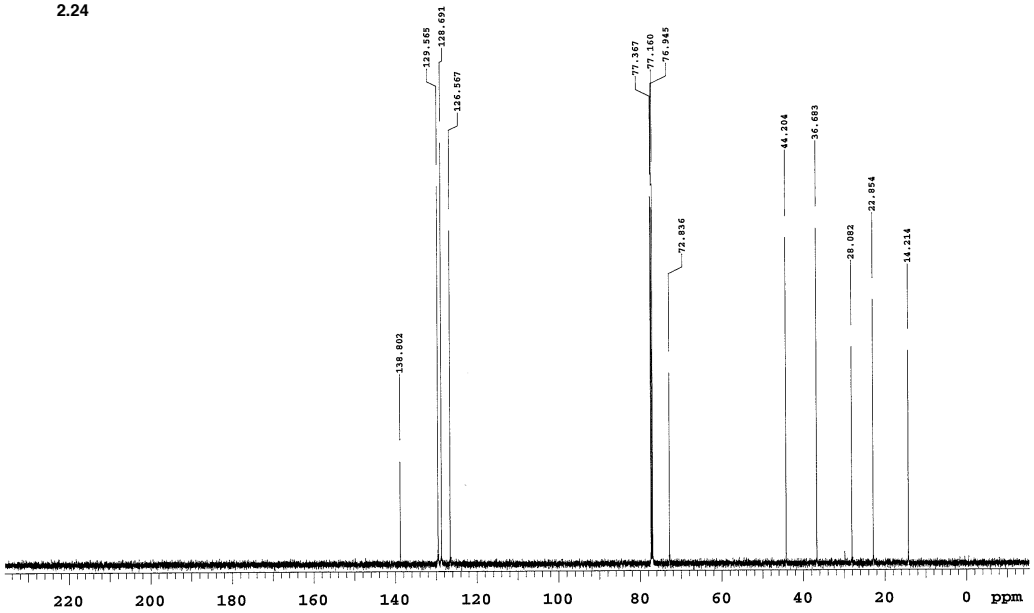

OH
n-butyl
Ph

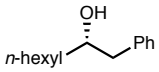
2.24


10
9
8
7
6
5
4
3
2
1
ppm
1.68
2.53
0.92
1.00
1.01
3.83
3.08
2.86

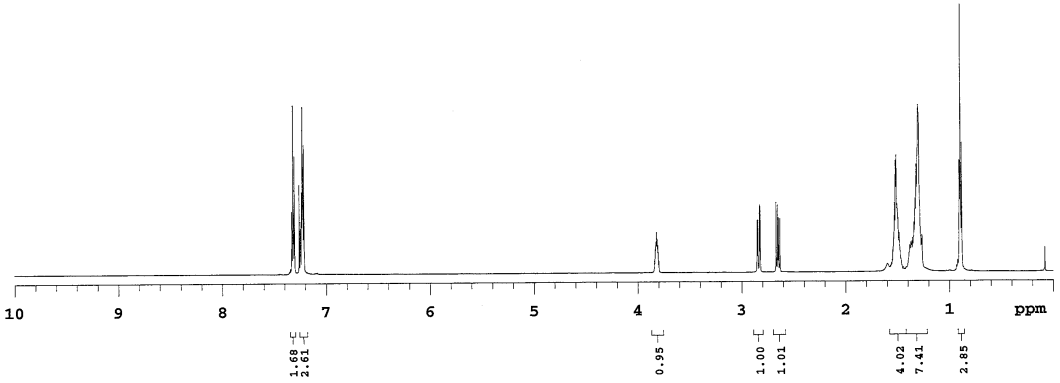

OH
n-butyl
Ph

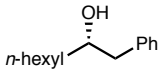
2.24


139.565
128.691
126.567
77.367
77.160
76.945
72.836
44.204
36.683
28.082
22.854
14.214
138.802
220
200
180
160
140
120
100
80
60
40
20
0
ppm

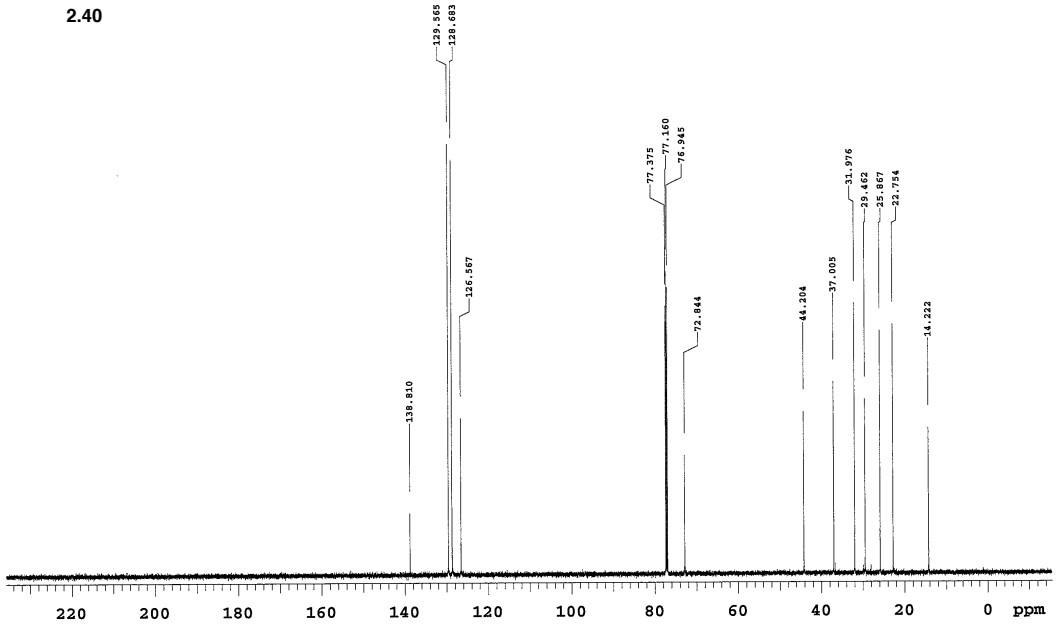

OH
n-hexyl
Ph

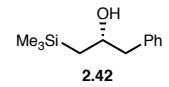
2.40


10
9
8
7
6
5
4
3
2
1
ppm
1.68
2.61
0.95
1.00
1.01
4.02
7.41
2.85


OH
n-hexyl
Ph

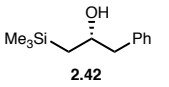
2.40


139.565
128.683
126.567
138.810
77.375
77.160
76.945
72.844
44.204
37.005
31.976
29.462
25.867
22.754
14.222
220
200
180
160
140
120
100
80
60
40
20
0
ppm

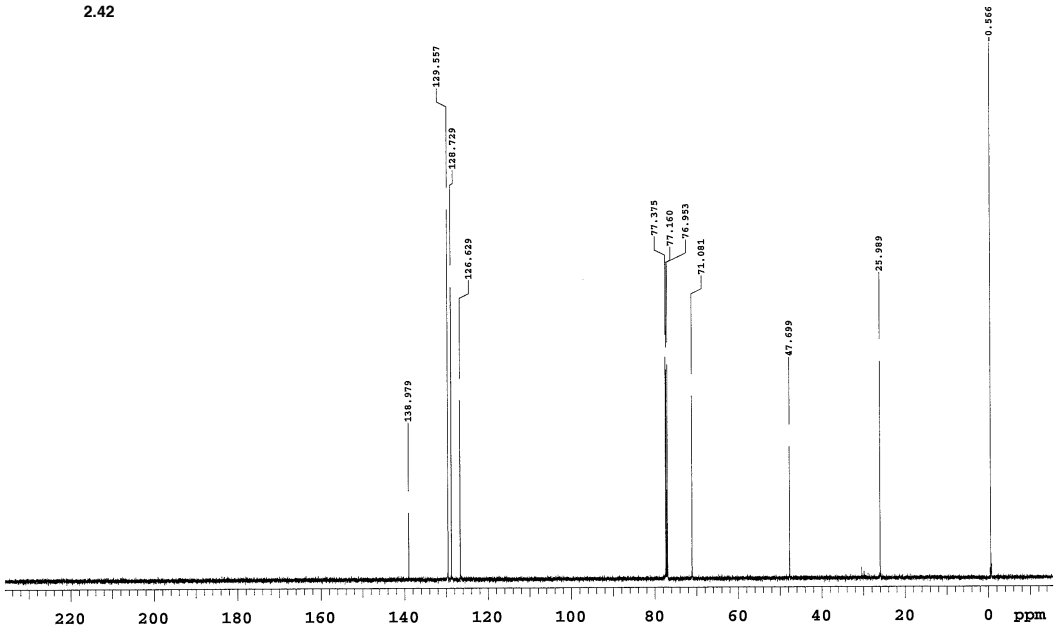

OH
Me3Si
Ph

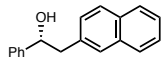
2.42

10
9
8
7
6
5
4
3
2
1
ppm
1.66
2.54
0.91
1.00
1.00
0.91
2.05
8.20

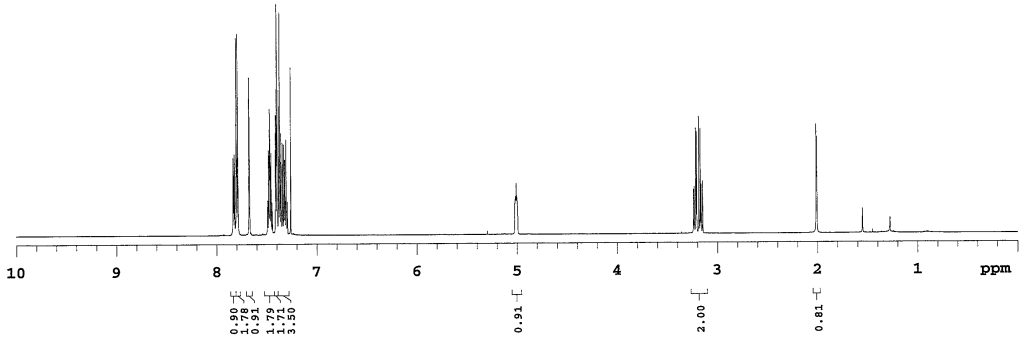

OH
Me3Si
Ph

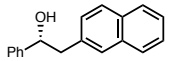
2.42


139.557
138.979
128.729
126.629
77.375
77.160
76.953
71.081
47.699
25.989
0.566
220
200
180
160
140
120
100
80
60
40
20
0
ppm

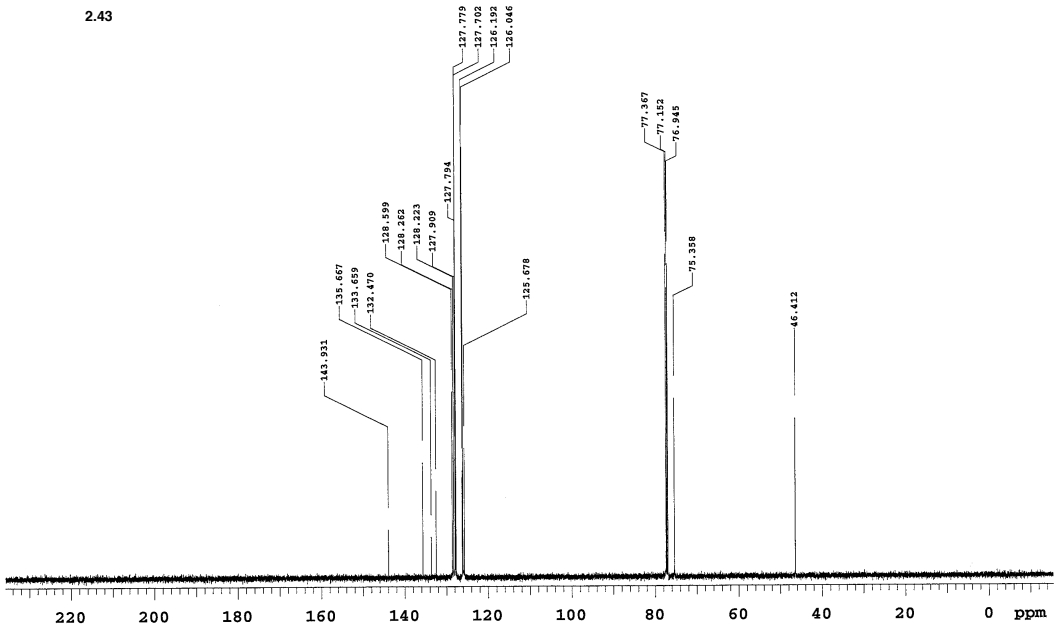

OH
Ph

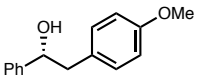
2.43


10
9
8
7
6
5
4
3
2
1
ppm
0.90
1.78
0.91
1.79
1.71
3.50
0.91
2.00
0.81

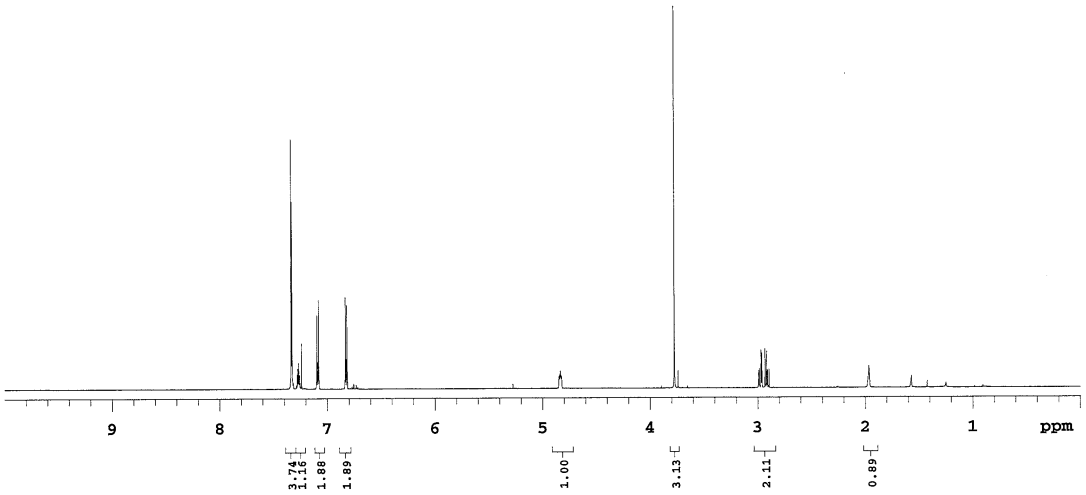

OH
Ph

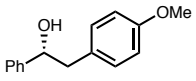
2.43


127.779
127.702
126.192
126.046
128.599
128.262
128.223
127.909
127.794
135.667
133.659
132.470
125.678
143.931
77.367
77.152
76.945
75.358
46.412
220
200
180
160
140
120
100
80
60
40
20
0
ppm

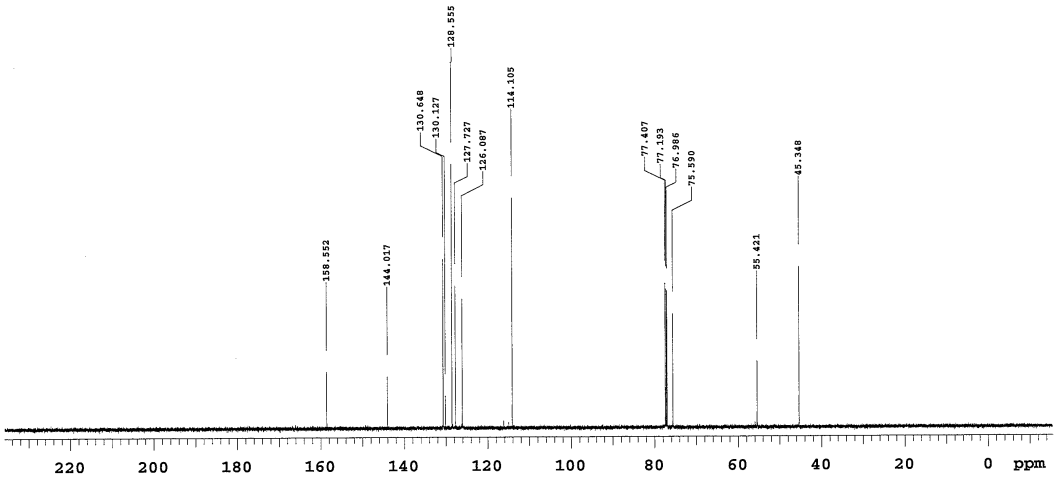

OH
OMe
Ph

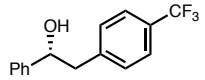
2.44


9
8
7
6
5
4
3
2
1
ppm
3.74
1.16
1.88
1.89
1.00
3.13
2.11
0.89

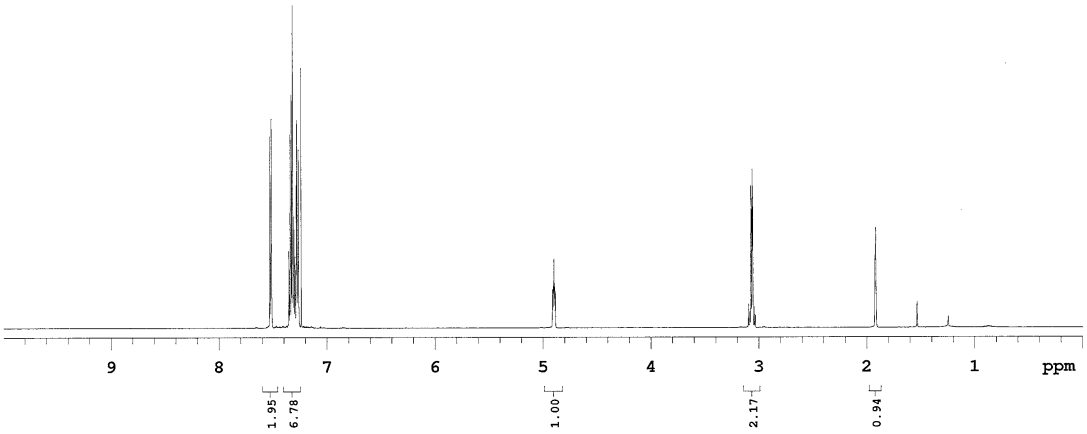

OH
OMe
Ph

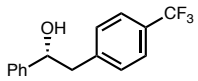
2.44


158.552
144.017
130.648
130.127
138.555
127.727
126.087
114.105
77.407
77.193
76.986
75.590
55.421
45.348
220
200
180
160
140
120
100
80
60
40
20
0
ppm

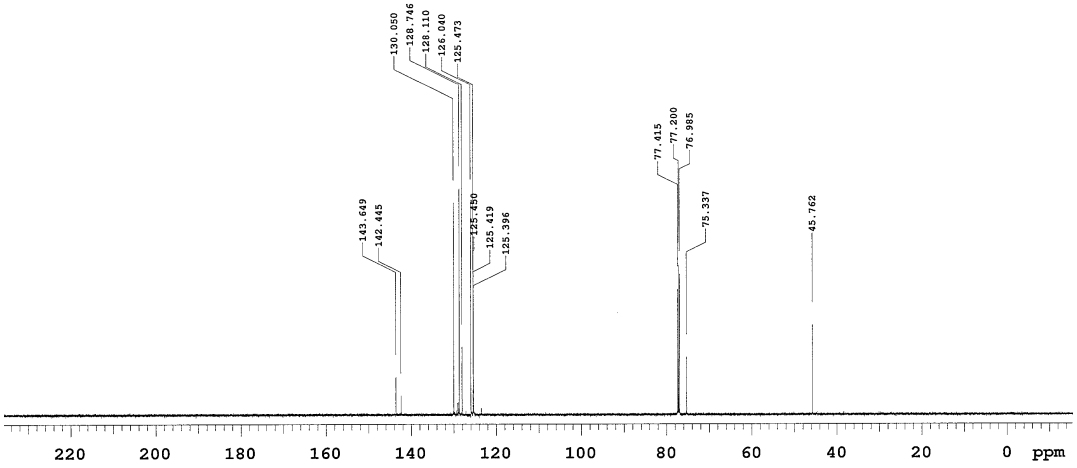

OH
Ph
CF3

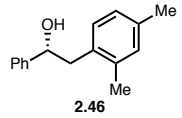
2.45


9
8
7
6
5
4
3
2
1
ppm
1.95
6.78
1.00
2.17
0.94

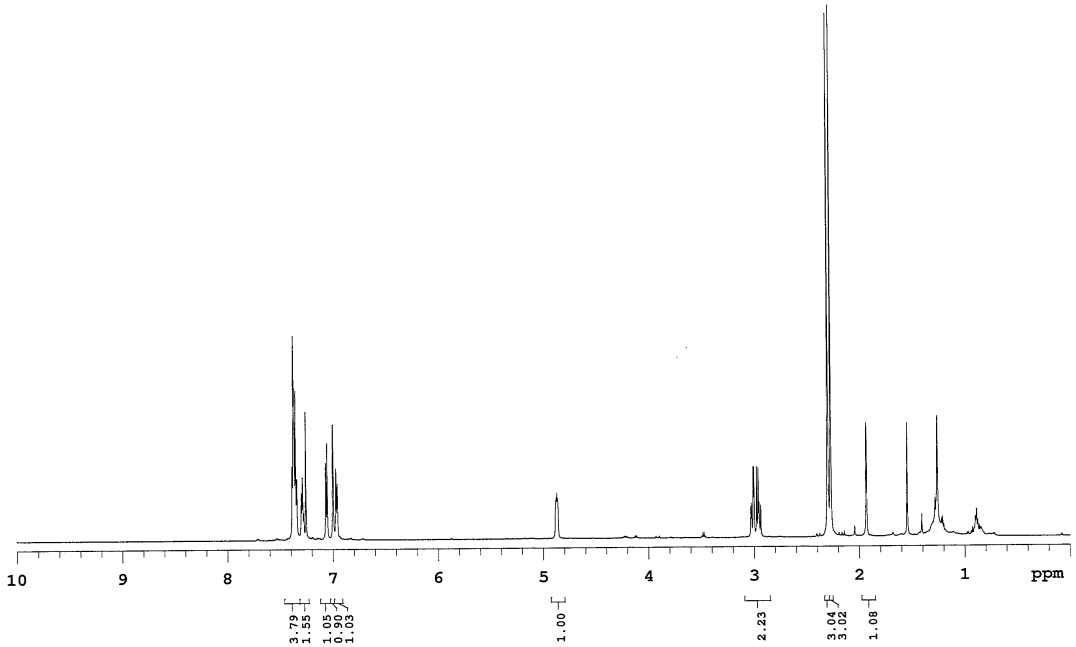

OH
Ph
CF3

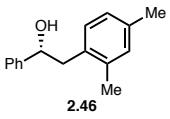
2.45


130.050
128.746
128.110
126.040
125.473
143.649
142.445
125.450
125.419
125.396
77.415
77.200
76.985
75.337
45.762
220
200
180
160
140
120
100
80
60
40
20
0
ppm

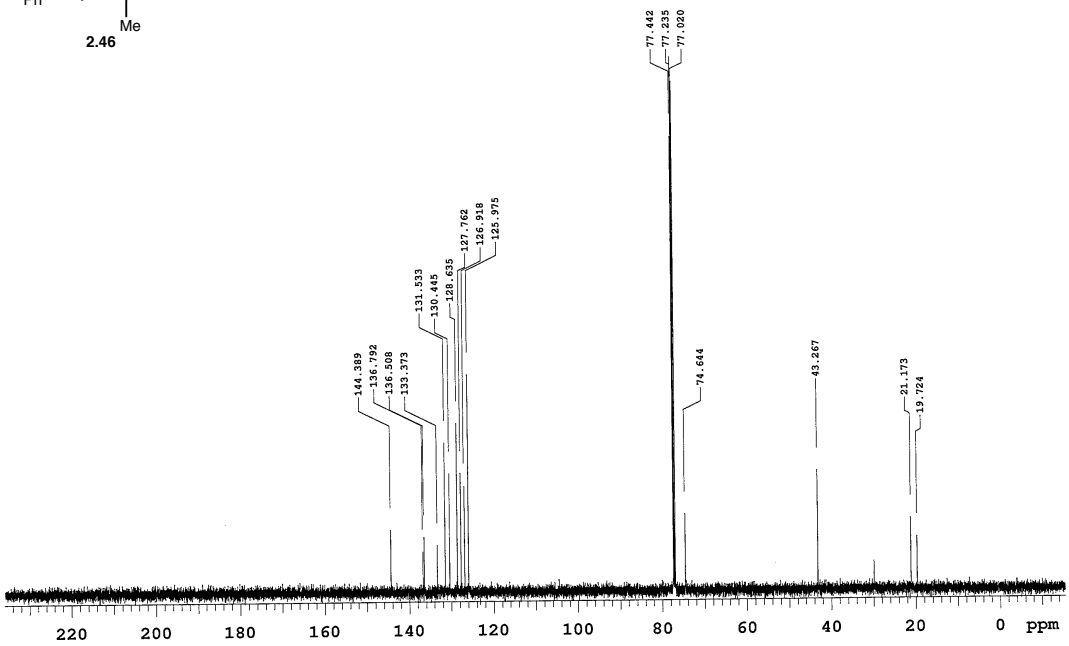

OH
Ph
Me
Me

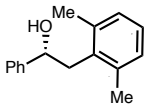
2.46


10
9
8
7
6
5
4
3
2
1
ppm
3.79
1.55
1.05
0.90
1.03
1.00
2.23
3.04
3.02
1.08

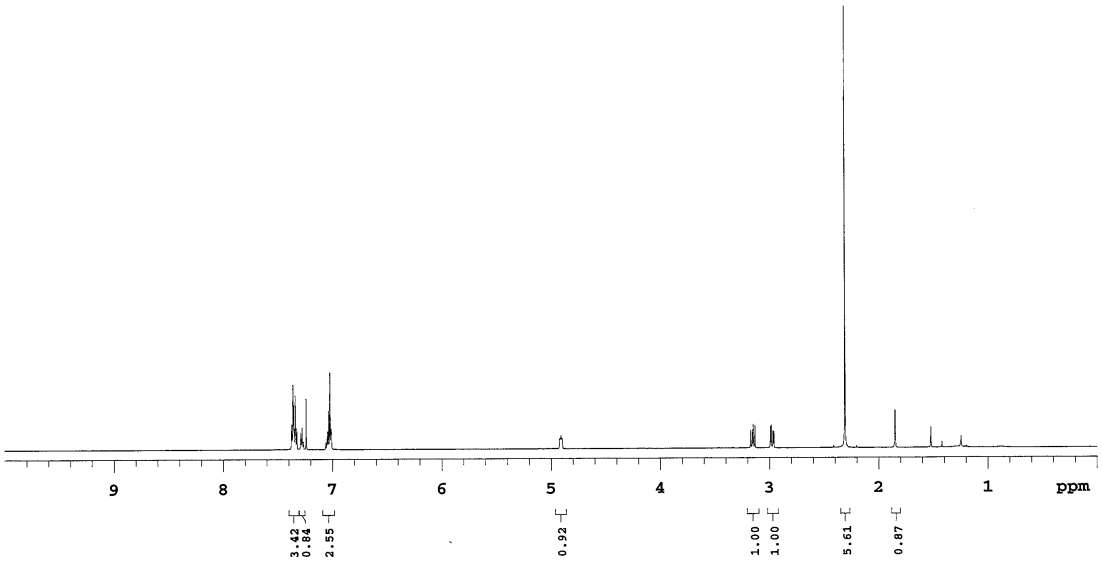

OH
Ph
Me
Me

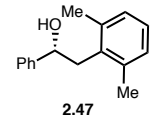
2.46


77.442
77.235
77.020
144.389
136.792
136.508
133.373
131.533
130.445
128.635
127.762
126.918
125.975
74.644
43.267
21.173
19.724
220
200
180
160
140
120
100
80
60
40
20
0
ppm


Me
HO
Ph
Me

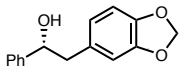
2.47


9
8
7
6
5
4
3
2
1
ppm
3.42
0.84
2.55
0.92
1.00
1.00
5.61
0.87

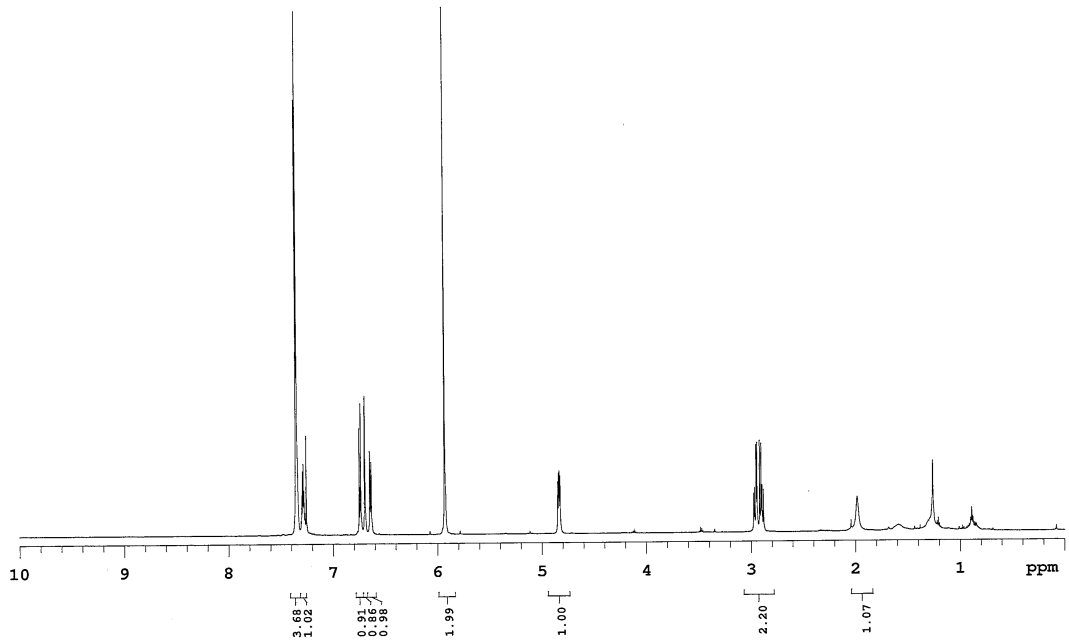

Me
HO
Ph
Me

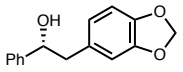
2.47

144.636
137.584
135.069
128.576
128.530
127.702
126.636
125.701
77.375
77.160
76.945
74.186
39.957
20.546
220
200
180
160
140
120
100
80
60
40
20
0
ppm

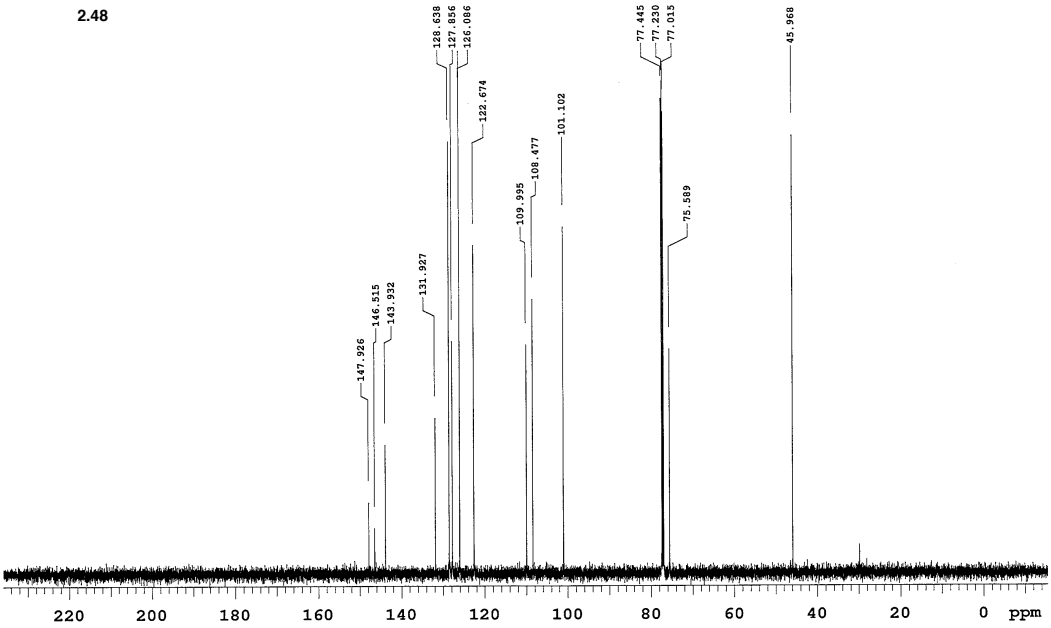

OH
Ph
O
O

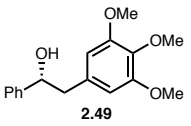
2.48


10
9
8
7
6
5
4
3
2
1
ppm
3.68
1.02
0.91
0.86
0.98
1.99
1.00
2.20
1.07

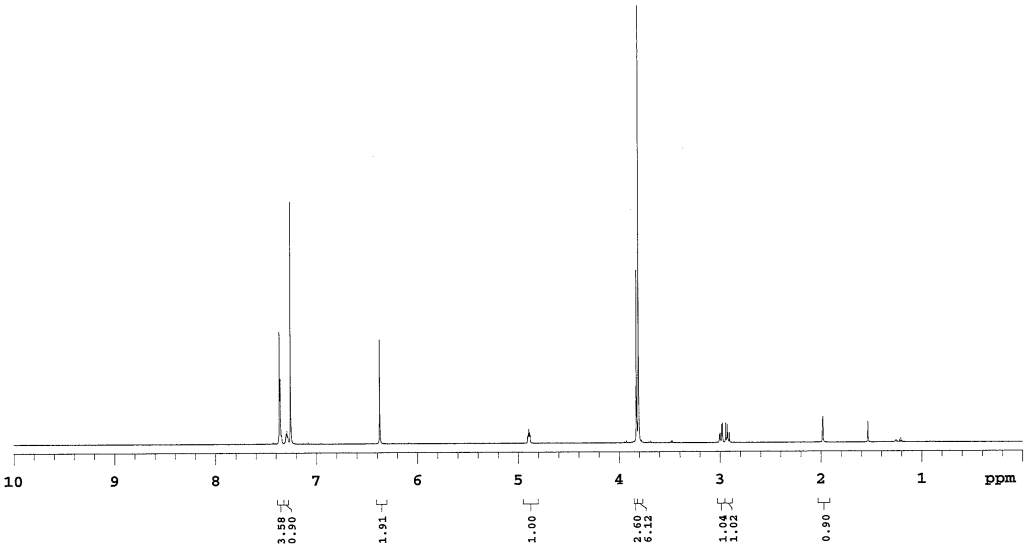

OH
Ph
O
O

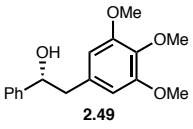
2.48


147.926
146.515
143.932
131.927
128.638
127.856
126.086
122.674
109.995
108.477
101.102
77.445
77.230
77.015
75.589
45.968
220
200
180
160
140
120
100
80
60
40
20
0
ppm

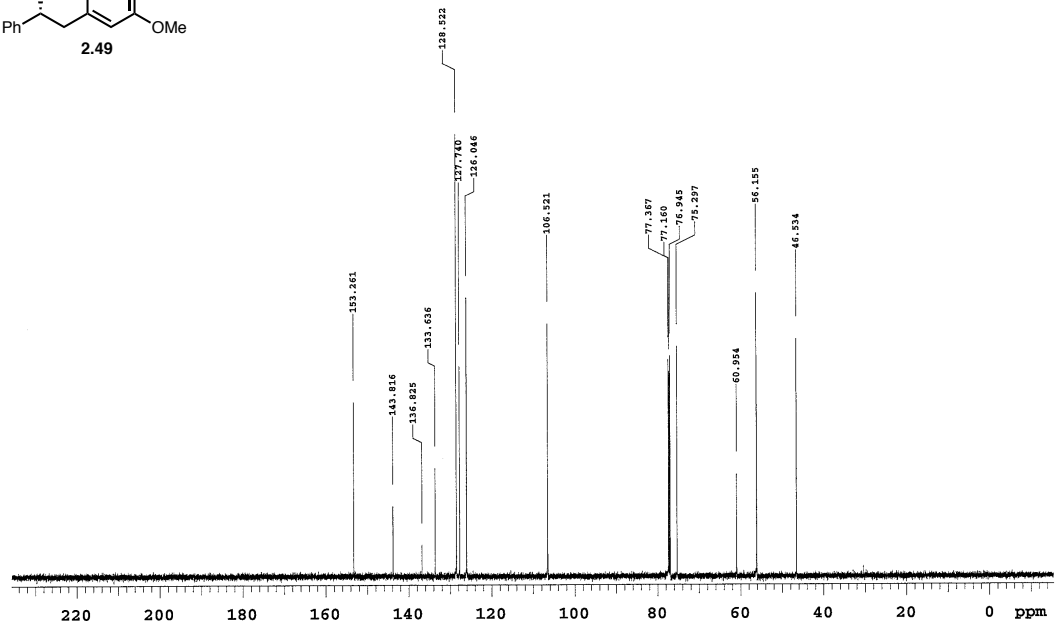

OMe
OMe
OH
Ph
OMe

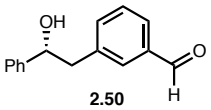
2.49


10
9
8
7
6
5
4
3
2
1
ppm
3.58
0.90
1.91
1.00
2.60
6.12
1.04
1.02
0.90

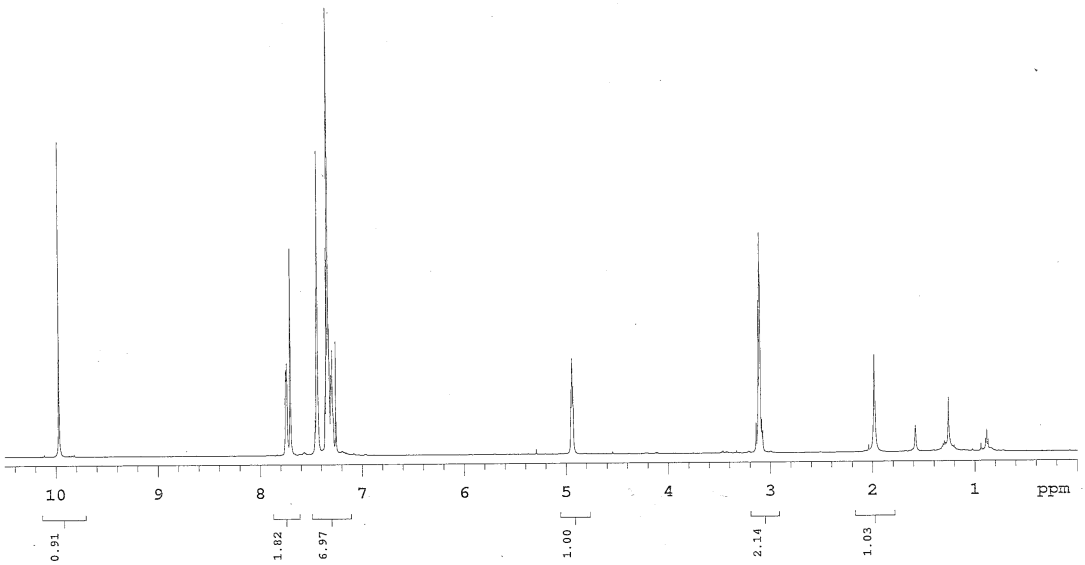

OMe
OMe
OH
Ph
OMe

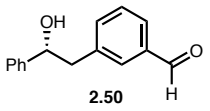
2.49


128.522
127.740
126.046
106.521
77.367
77.160
76.945
75.297
56.155
46.534
60.954
153.261
143.616
136.825
133.636
220
200
180
160
140
120
100
80
60
40
20
0
ppm

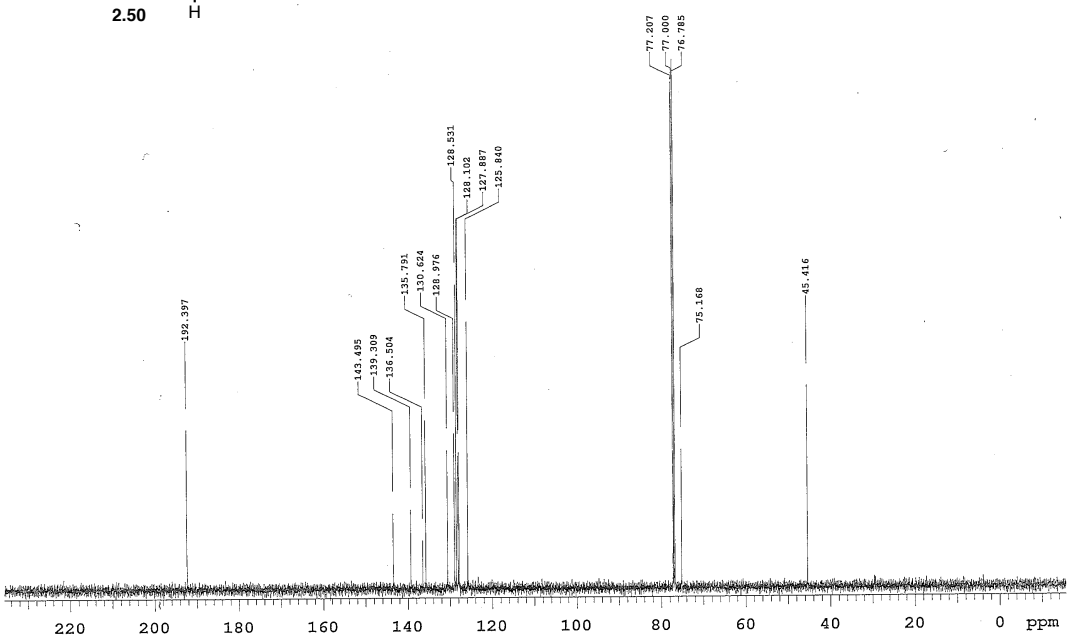

OH
Ph
O
H

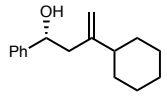
2.50


10
9
8
7
6
5
4
3
2
1
ppm
0.91
1.82
6.97
1.00
2.14
1.03

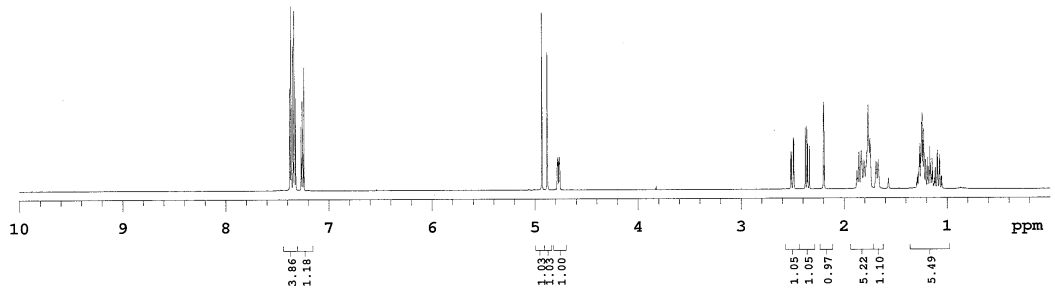

OH
Ph
O
H

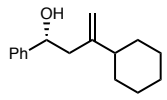
2.50


192.397
143.495
139.309
136.504
135.791
130.624
128.976
128.531
128.102
127.887
125.840
77.207
77.000
76.785
75.168
45.416
220
200
180
160
140
120
100
80
60
40
20
0
ppm

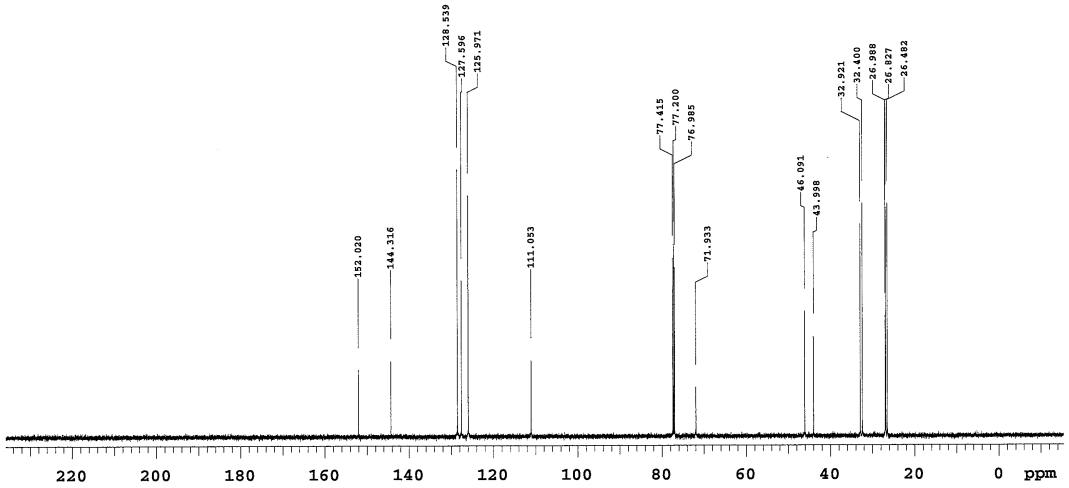

OH
Ph

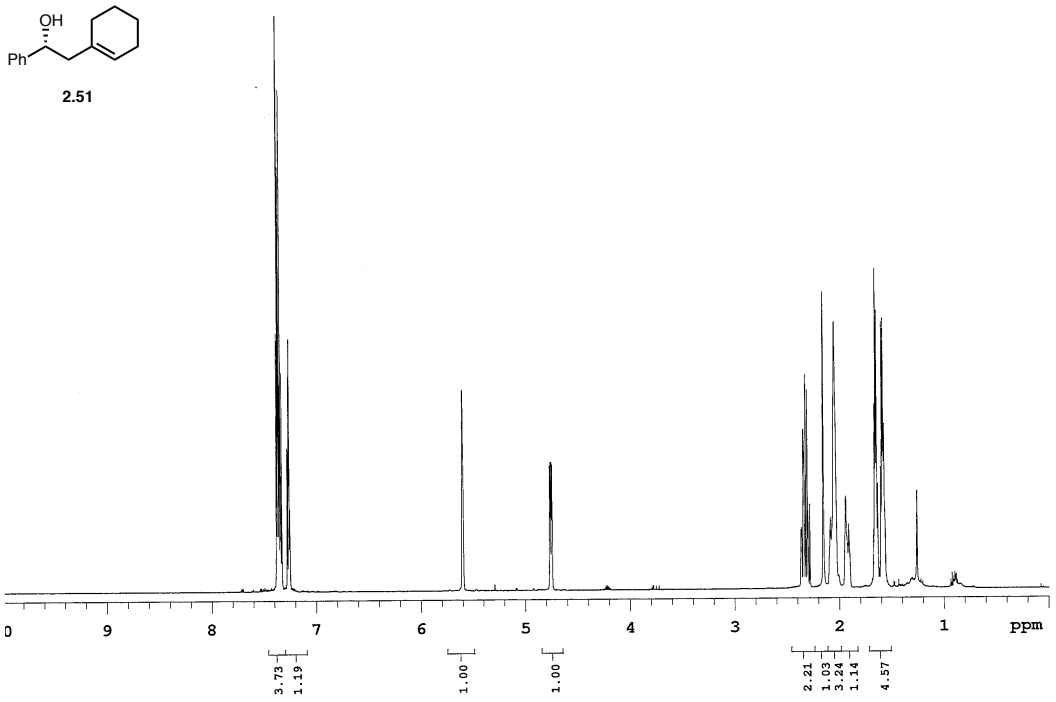
2.53

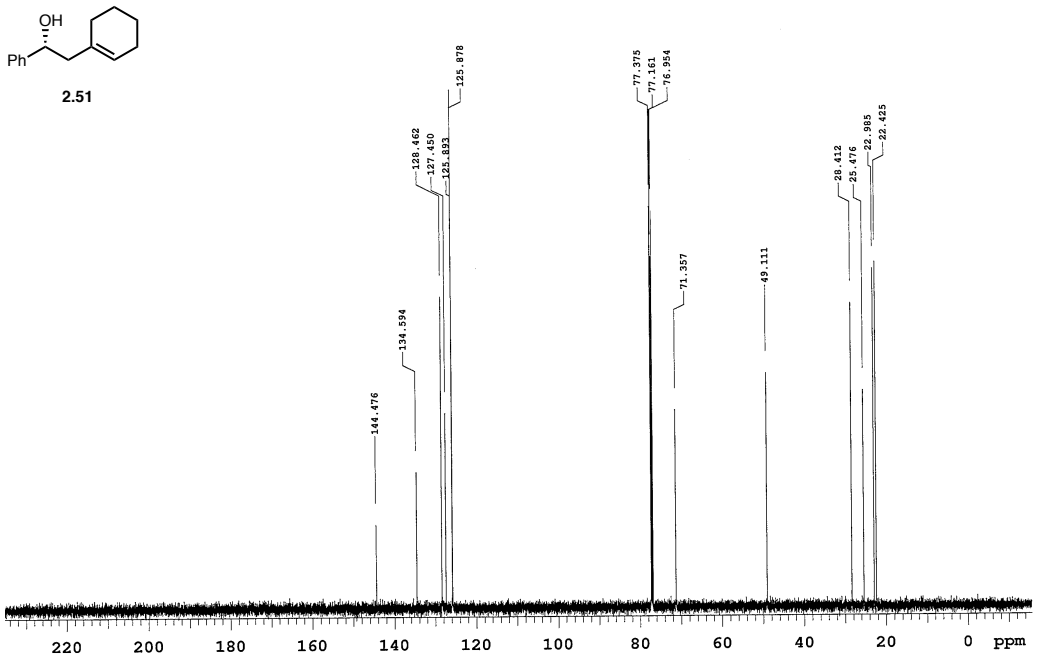

10
9
8
7
6
5
4
3
2
1
ppm
3.86
1.18
1.03
1.01
1.00
1.05
1.05
0.97
5.22
1.10
5.49

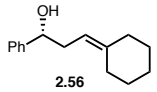

OH
Ph

2.53

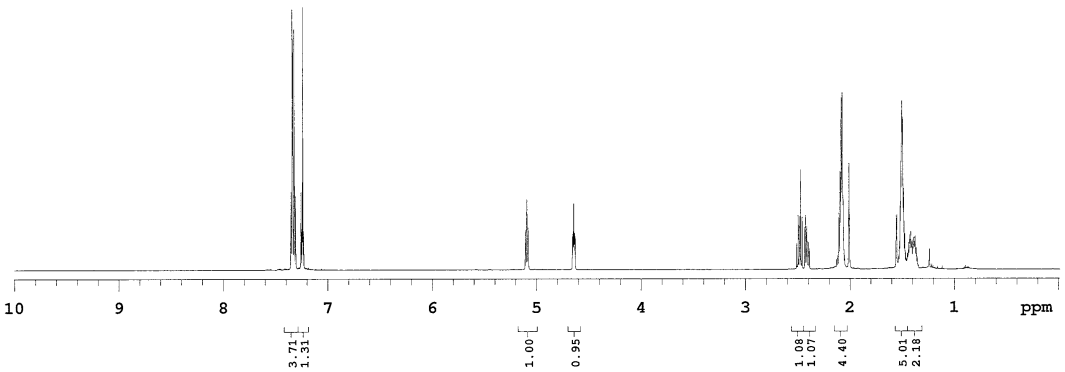

128.539
127.596
125.971
152.020
144.316
111.053
77.415
77.200
76.985
71.933
46.091
43.998
32.921
32.400
26.988
26.827
26.482
220
200
180
160
140
120
100
80
60
40
20
0
ppm

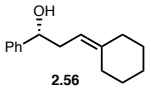

OH
Ph
2.51
0
9
8
7
6
5
4
3
2
1
ppm
3.73
1.19
1.00
1.00
2.21
1.03
3.24
1.14
4.57


OH
Ph
2.51
144.476
134.594
128.462
127.450
125.893
125.878
77.375
77.161
76.954
71.357
49.111
29.412
25.476
22.985
22.425
220
200
180
160
140
120
100
80
60
40
20
0
ppm

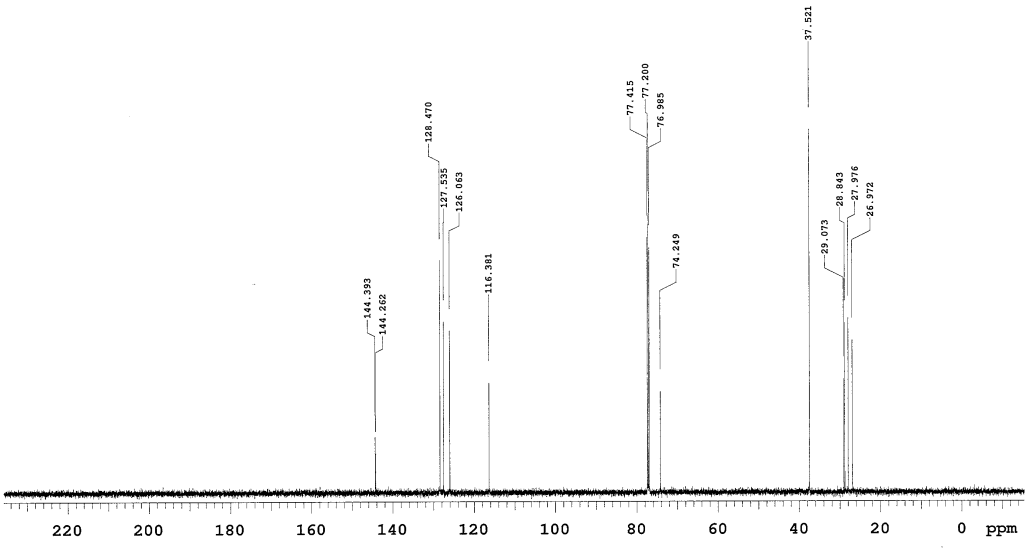

OH
Ph

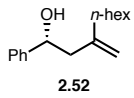
2.56


10
9
8
7
6
5
4
3
2
1
ppm
3.71
1.31
1.00
0.95
1.08
1.07
4.40
5.01
2.18


OH
Ph

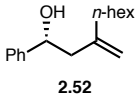
2.56


144.393
144.262
128.470
127.535
126.063
116.381
77.415
77.200
76.985
74.249
37.521
29.073
28.843
27.376
26.372
220
200
180
160
140
120
100
80
60
40
20
0
ppm


OH
n-hex
Ph

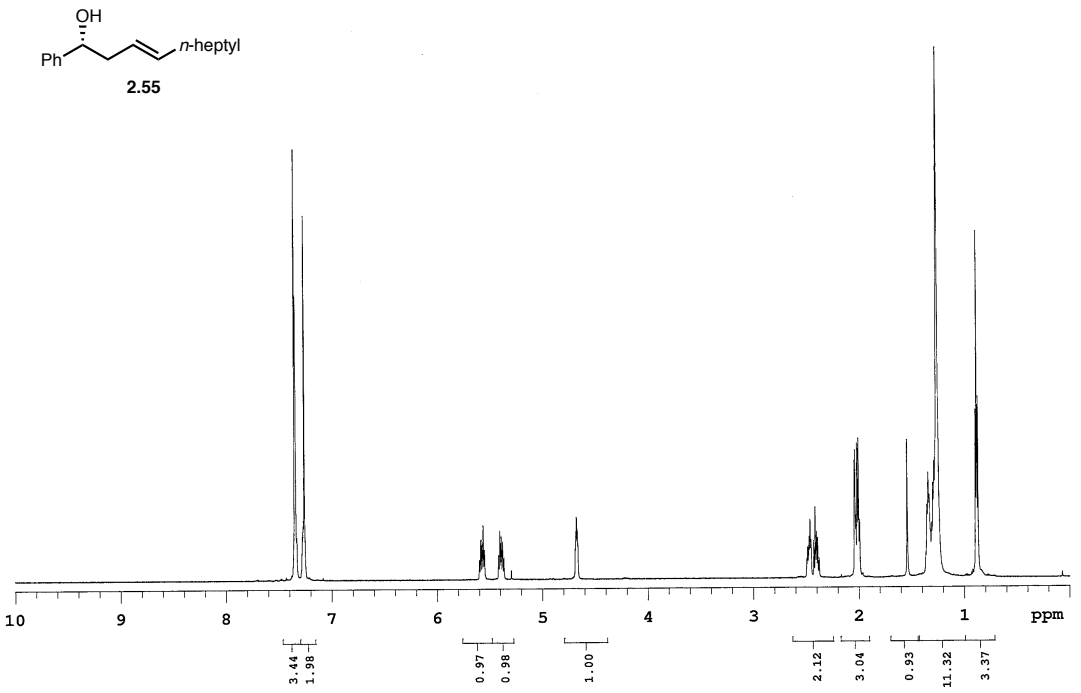
2.52

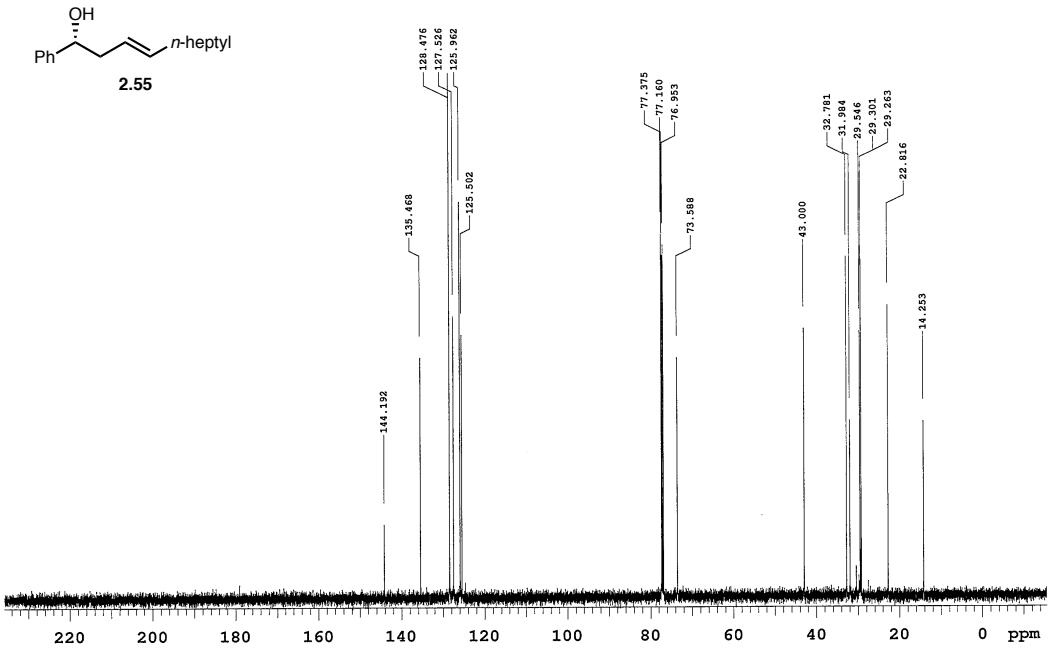
10
9
8
7
6
5
4
3
2
1
ppm
3.65
1.11
2.10
1.00
1.07
1.04
0.94
2.10
2.53
6.56
3.01

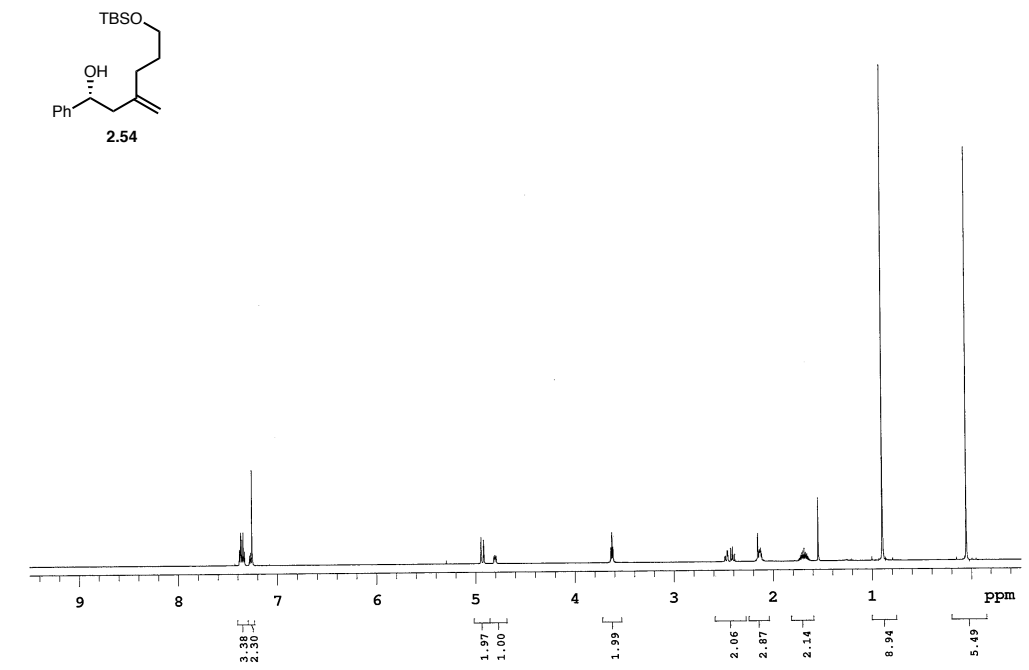

OH
n-hex
Ph

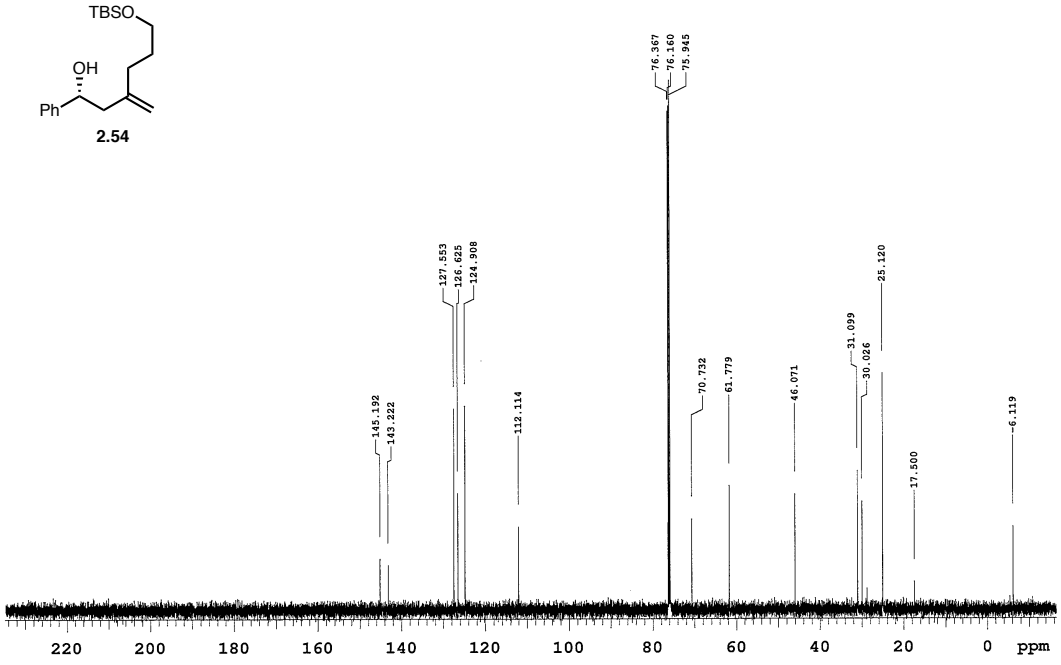
2.52

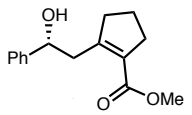
146.698
144.253
128.515
127.579
125.901
112.891
77.375
77.160
76.953
71.679
46.918
35.917
31.861
29.155
27.791
22.754
14.222
220
200
180
160
140
120
100
80
60
40
20
0
ppm


OH
Ph
n-heptyl
2.55
10
9
8
7
6
5
4
3
2
1
ppm
3.44
1.98
0.97
0.98
1.00
2.12
3.04
0.93
11.32
3.37

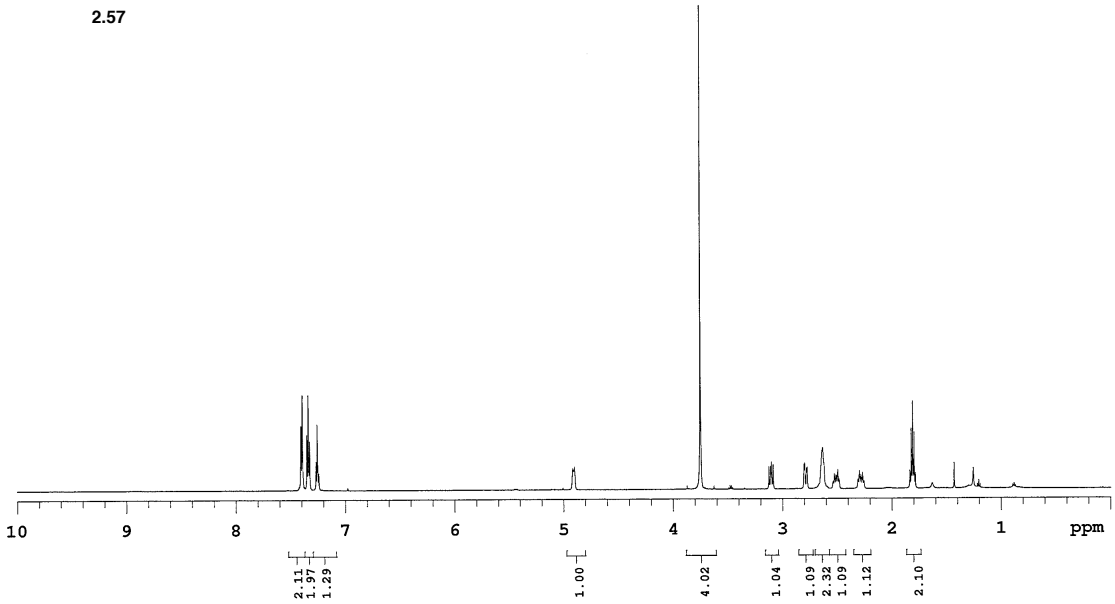

OH
Ph
n-heptyl
2.55
128.476
127.526
125.962
125.502
135.468
144.192
77.375
77.160
76.953
73.588
43.000
32.781
31.984
29.546
29.301
29.263
22.816
14.253
220
200
180
160
140
120
100
80
60
40
20
0
ppm

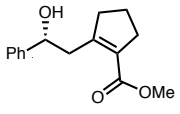

TBSO
OH
Ph
2.54
9
8
7
6
5
4
3
2
1
ppm
3.38
2.30
1.97
1.00
1.99
2.06
2.87
2.14
8.94
5.49


TBSO
OH
Ph
2.54
76.367
76.160
75.945
127.553
126.625
124.908
145.192
143.222
112.114
70.732
61.779
46.071
31.099
30.026
25.120
17.500
-6.119
220
200
180
160
140
120
100
80
60
40
20
0
ppm

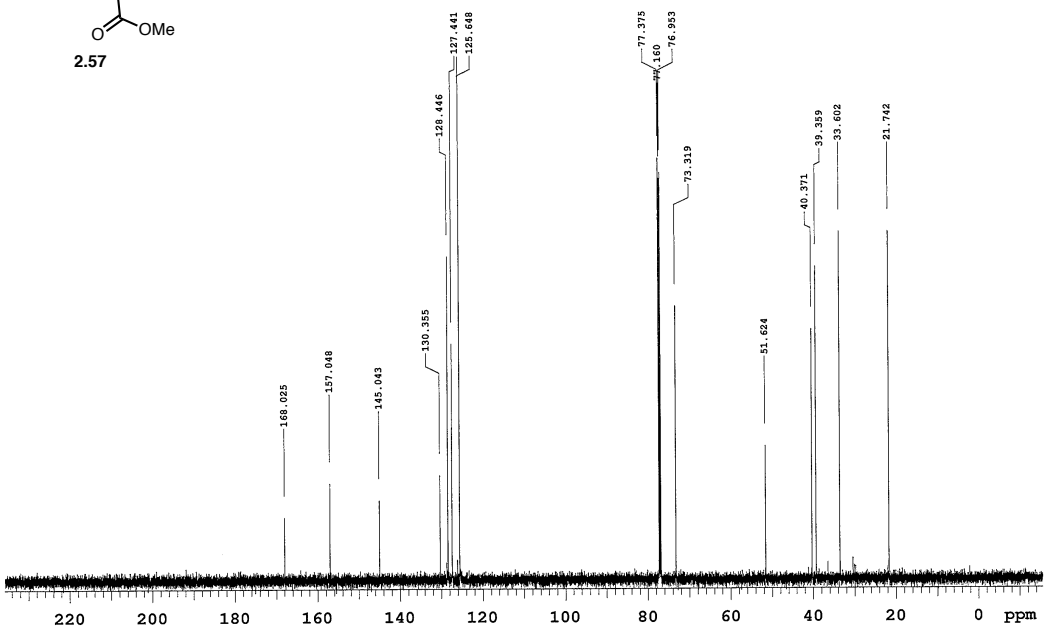

OH
Ph
O
OMe

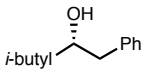
2.57


10
9
8
7
6
5
4
3
2
1
ppm
2.11
1.97
1.29
1.00
4.02
1.04
1.08
2.32
1.09
1.12
2.10

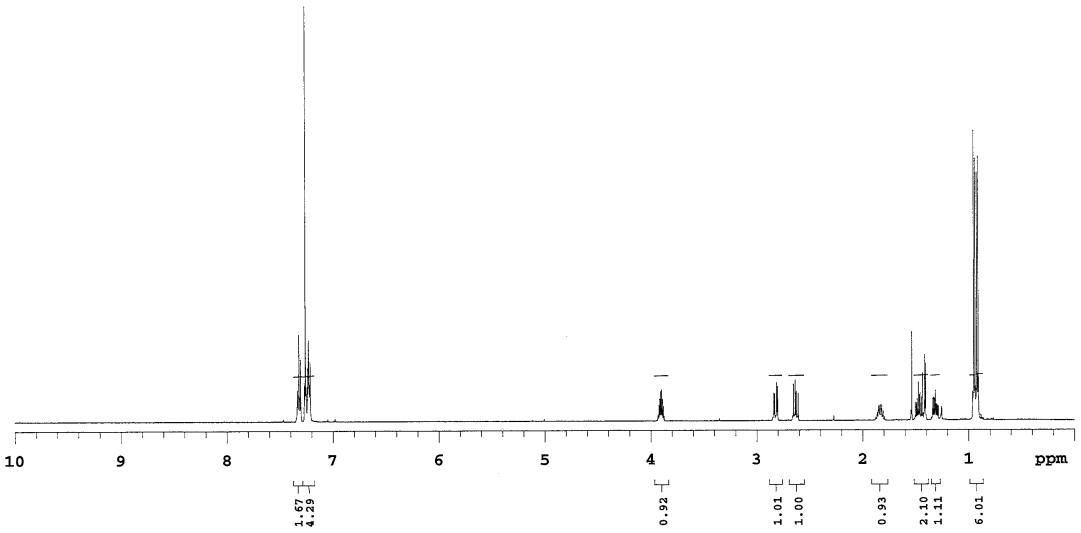

OH
Ph
O
OMe

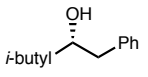
2.57


168.025
157.048
145.043
130.355
128.446
127.441
125.648
77.375
77.160
76.953
73.319
51.624
40.371
39.359
33.602
21.742
220
200
180
160
140
120
100
80
60
40
20
0
ppm

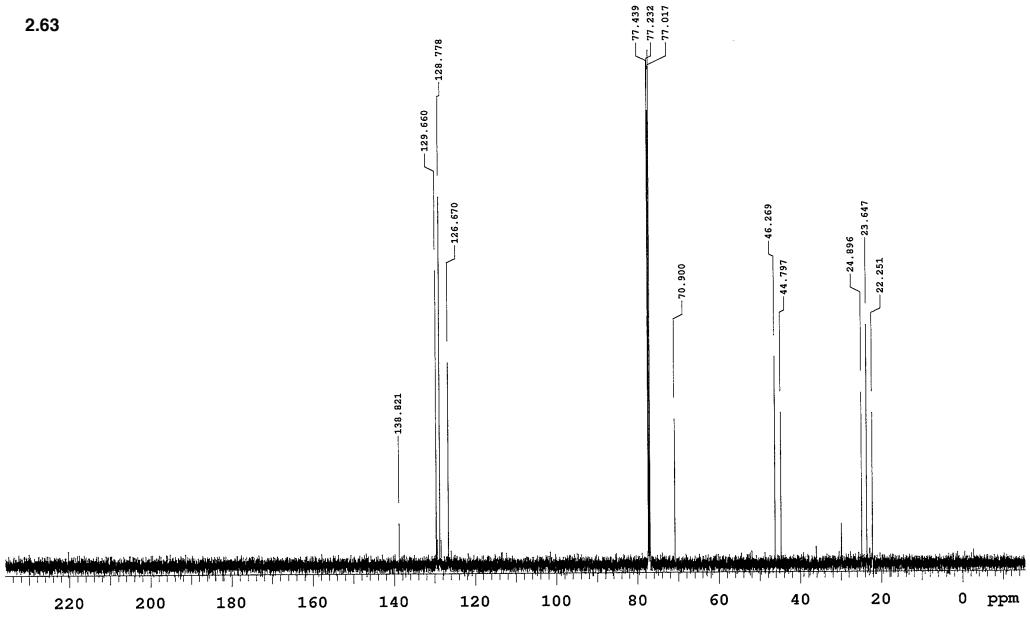

OH
i-butyl
Ph

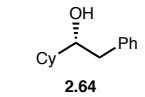
2.63


10
9
8
7
6
5
4
3
2
1
ppm
1.67
4.29
0.92
1.01
1.00
0.93
2.10
1.11
6.01

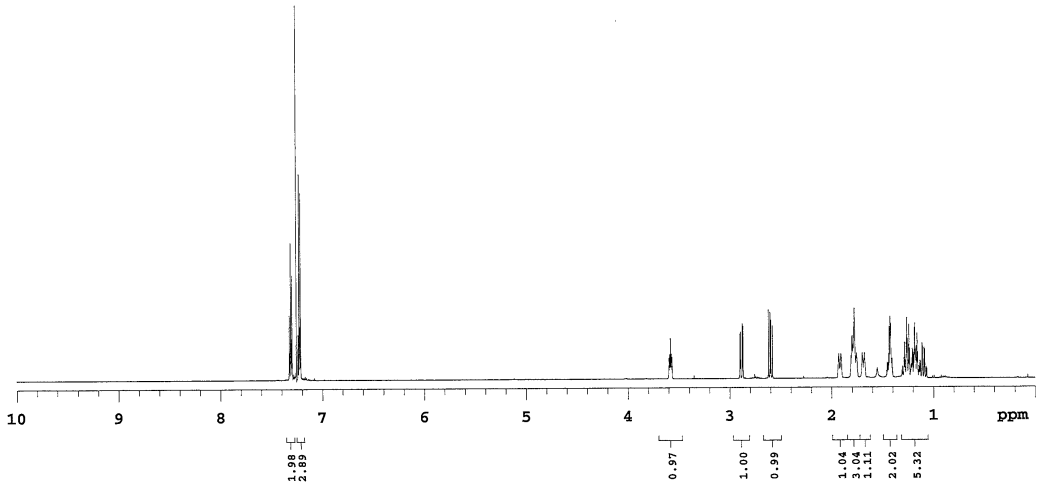

OH
i-butyl
Ph

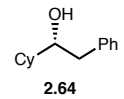
2.63


138.821
129.660
128.778
126.670
77.439
77.232
77.017
70.900
46.269
44.797
24.896
23.647
22.251
220
200
180
160
140
120
100
80
60
40
20
0
ppm

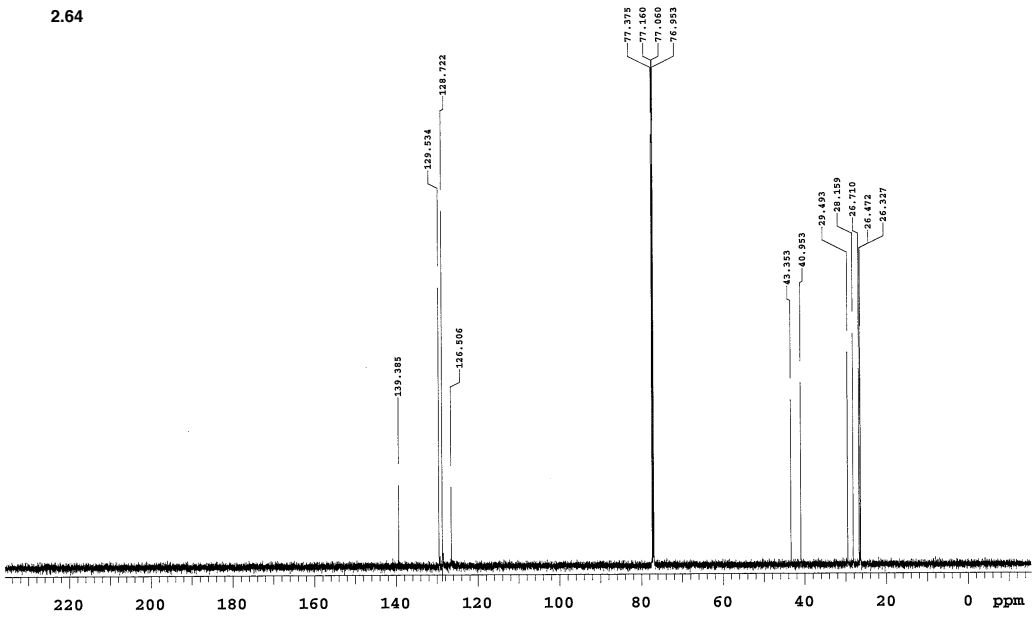

OH
Cy
Ph

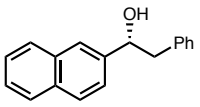
2.64


10
9
8
7
6
5
4
3
2
1
ppm
1.98
2.89
0.97
1.00
0.99
1.04
3.04
1.11
2.02
5.32

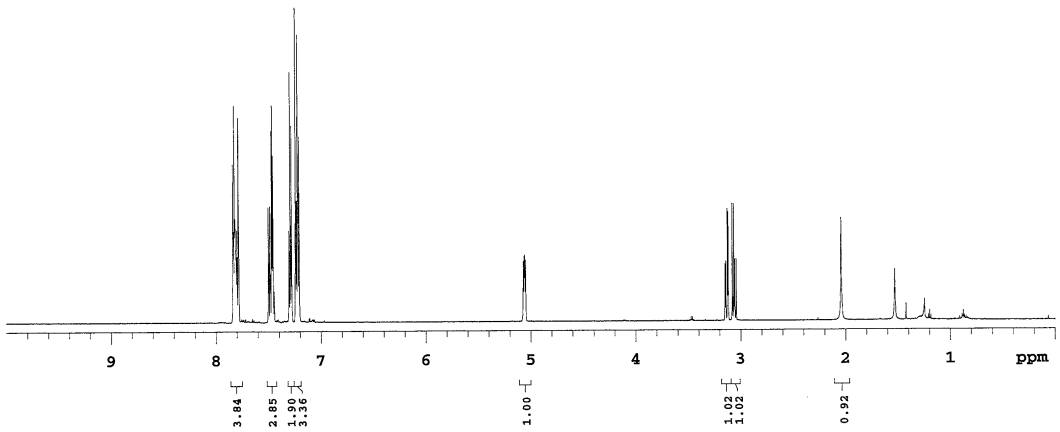

OH
Cy
Ph

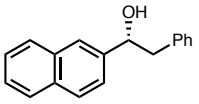
2.64


77.375
77.160
77.060
76.953
128.722
129.534
139.385
126.506
43.353
40.953
28.493
28.159
26.710
26.472
26.327
220
200
180
160
140
120
100
80
60
40
20
0
ppm

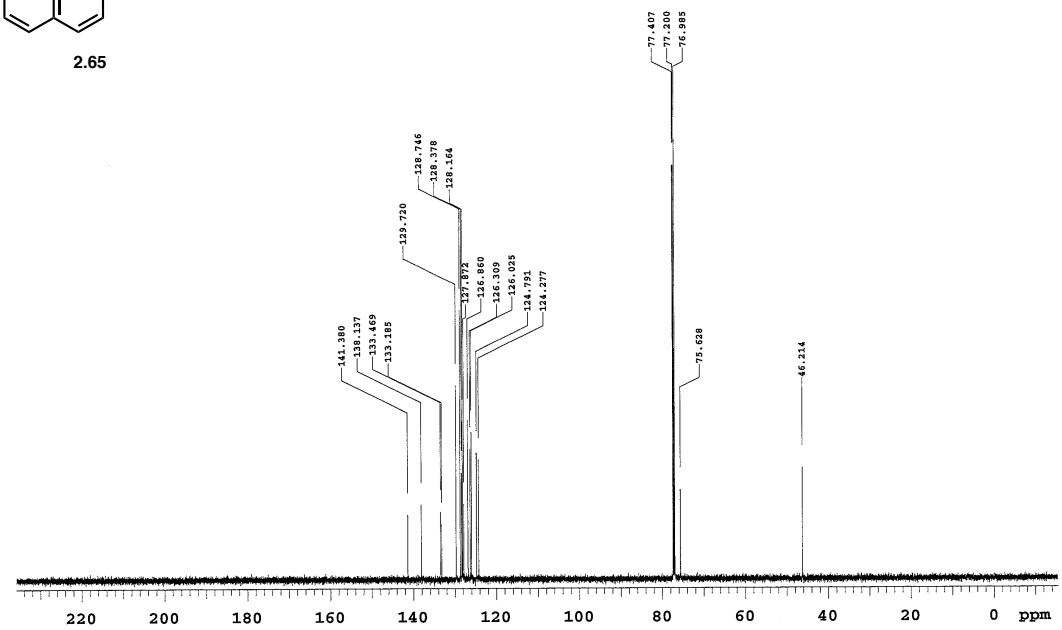

OH
Ph

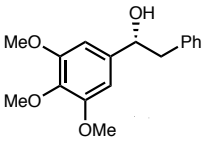
2.65


9
8
7
6
5
4
3
2
1
ppm
3.84
2.85
1.90
3.36
1.00
1.02
1.02
0.92

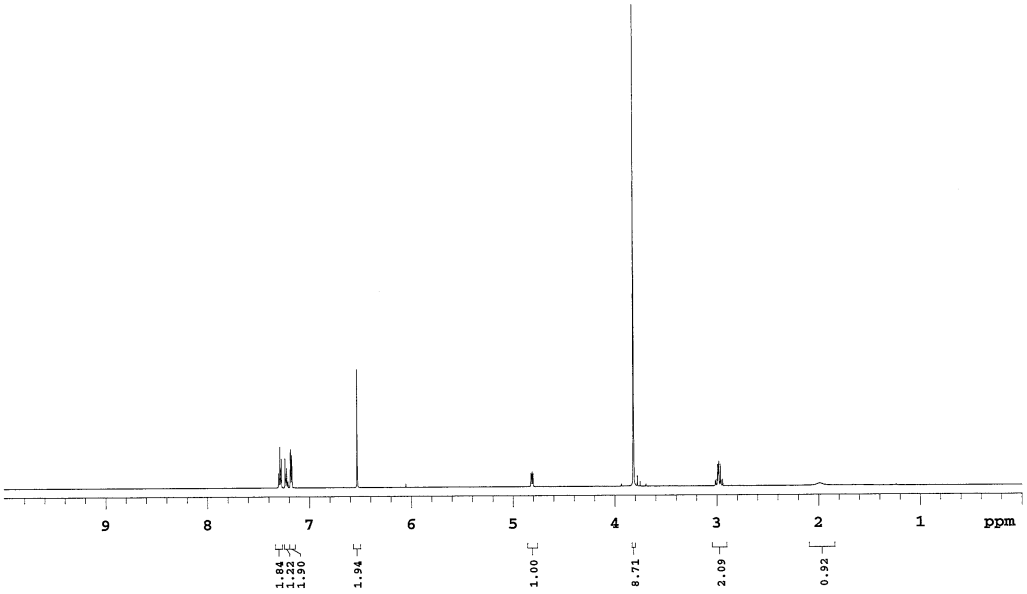

OH
Ph

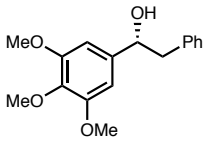
2.65


77.407
77.200
76.985
128.746
128.370
128.164
129.720
127.872
126.860
126.309
126.025
124.791
124.277
141.380
138.137
133.469
133.185
75.628
46.214
220
200
180
160
140
120
100
80
60
40
20
0
ppm

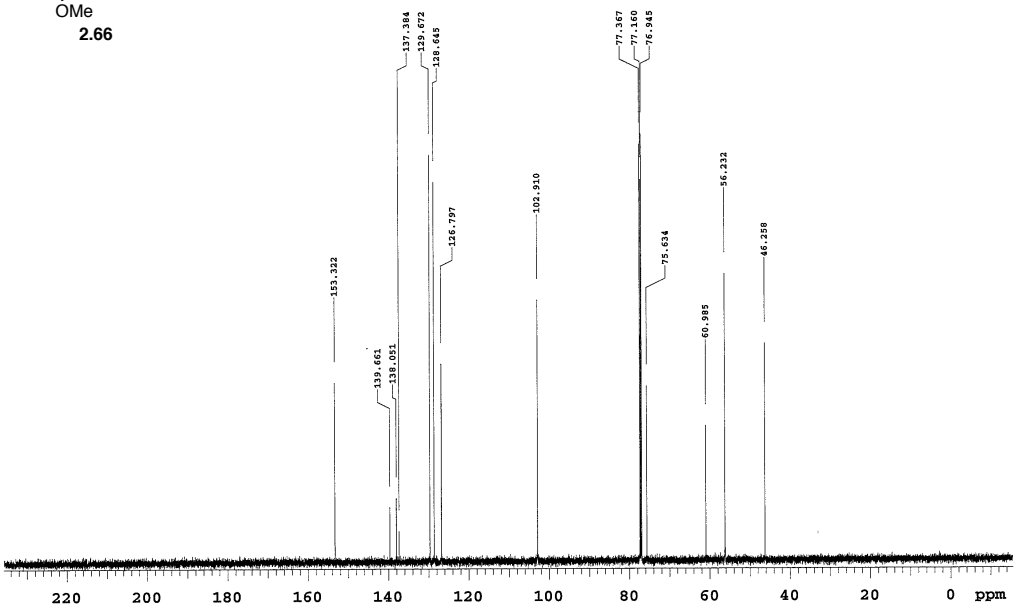

OH
MeO
Ph
MeO
OMe

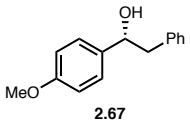
2.66


9
8
7
6
5
4
3
2
1
ppm
1.84
1.22
1.90
1.94
1.00
8.71
2.09
0.92

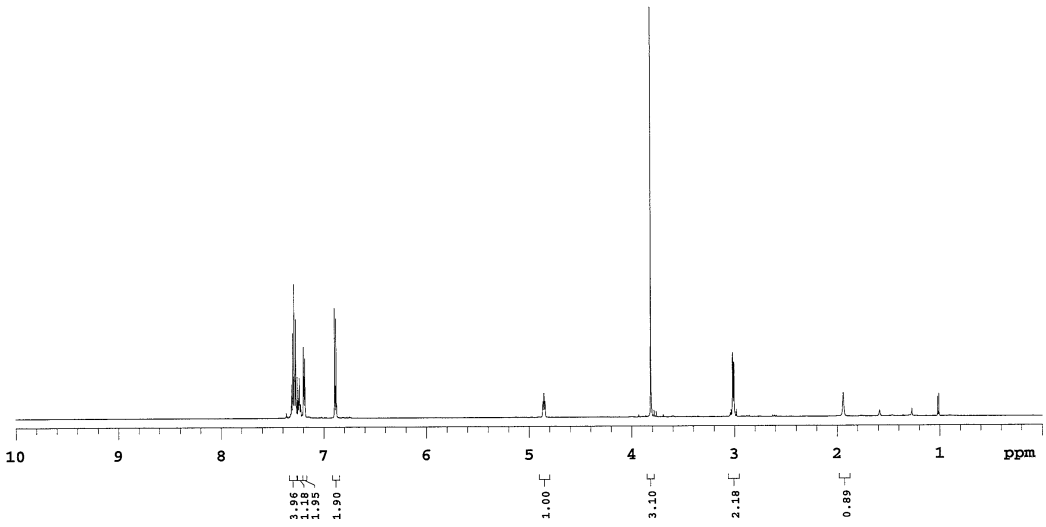

OH
MeO
Ph
MeO
OMe

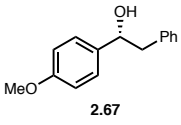
2.66


153.322
139.661
138.051
137.384
129.672
128.645
126.797
102.910
77.367
77.160
76.945
75.634
60.985
56.232
46.258
220
200
180
160
140
120
100
80
60
40
20
0
ppm

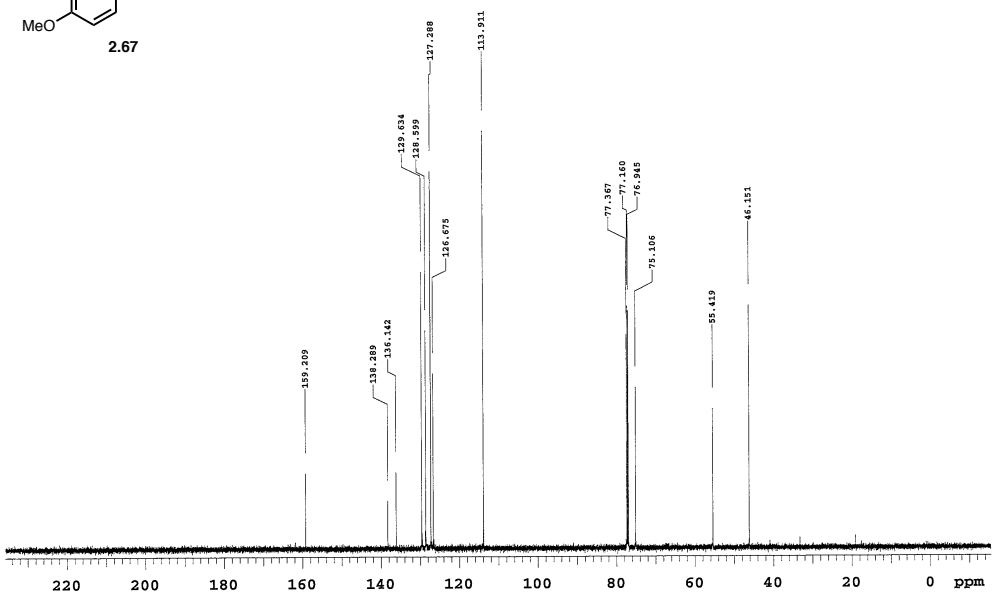

OH
Ph
MeO

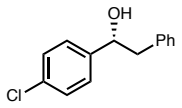
2.67


10
9
8
7
6
5
4
3
2
1
ppm
3.96
1.18
1.95
1.90
1.00
3.10
2.18
0.89

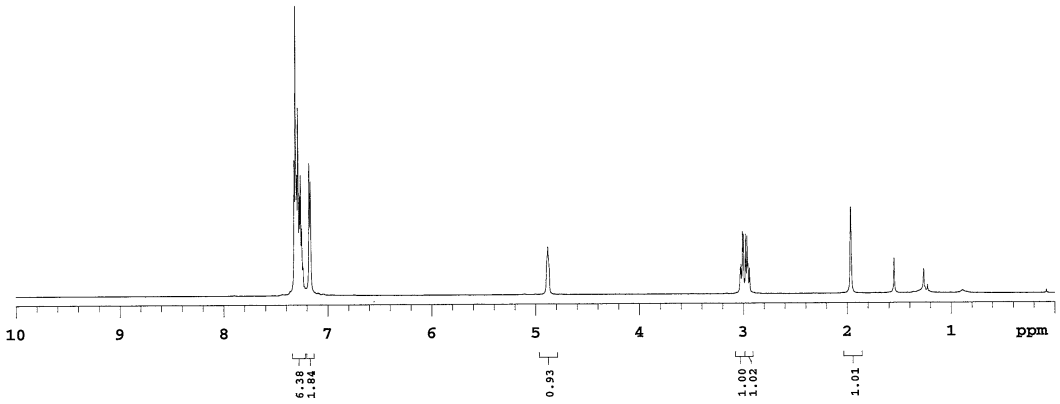

OH
Ph
MeO

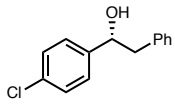
2.67


159.209
138.289
136.142
129.034
128.599
127.288
126.675
113.911
77.367
77.160
76.945
75.106
55.419
46.151
220
200
180
160
140
120
100
80
60
40
20
0
ppm

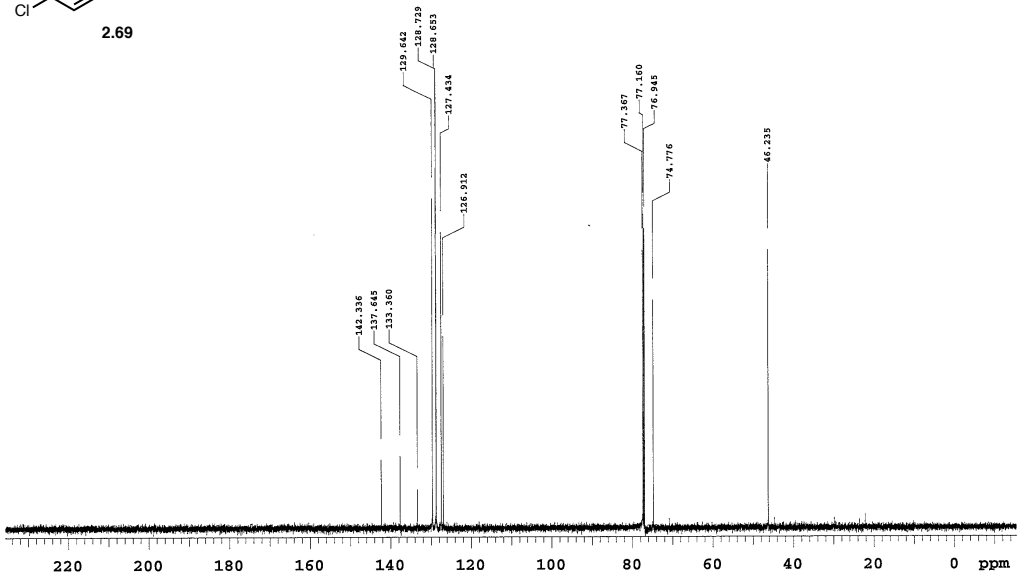

OH
Ph
Cl

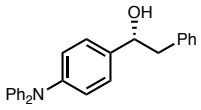
2.69


10
9
8
7
6
5
4
3
2
1
ppm
6.38
1.84
0.93
1.00
1.02
1.01

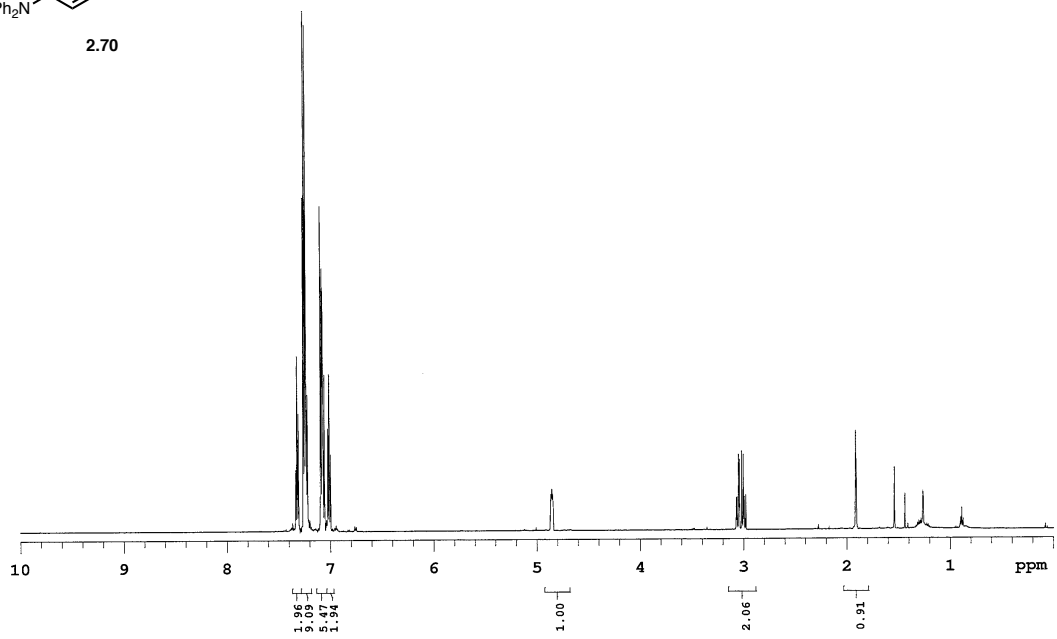

OH
Ph
Cl

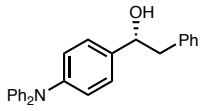
2.69


142.336
137.645
133.360
129.642
128.729
128.653
127.434
126.912
77.367
77.160
76.945
74.776
46.235
220
200
180
160
140
120
100
80
60
40
20
0
ppm

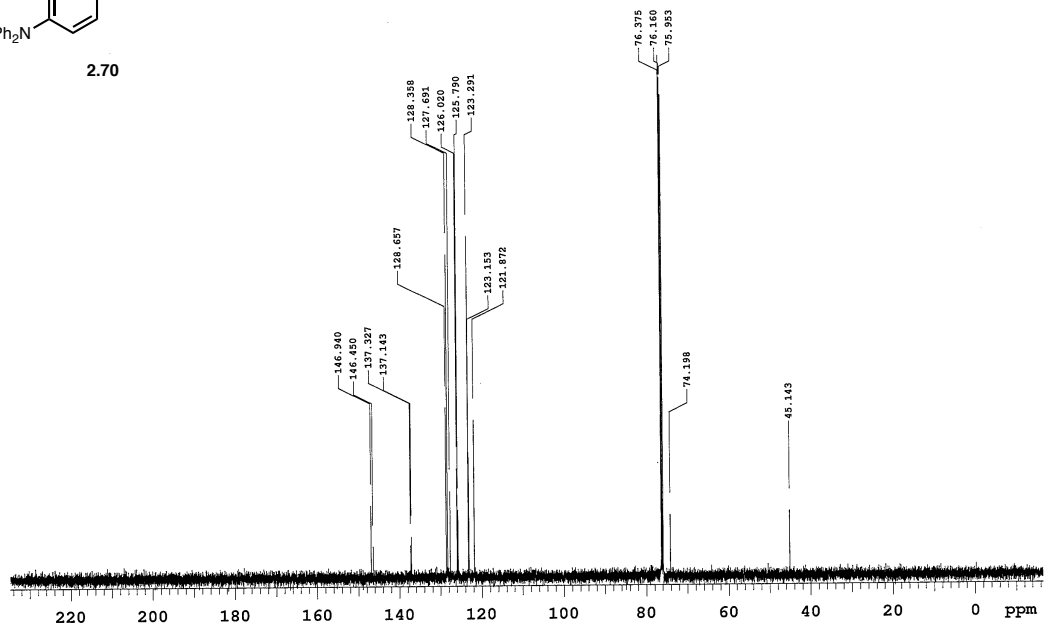

OH
Ph
Ph2N

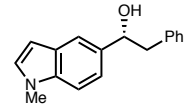
2.70


10
9
8
7
6
5
4
3
2
1
ppm
1.96
9.09
5.47
1.94
1.00
2.06
0.91

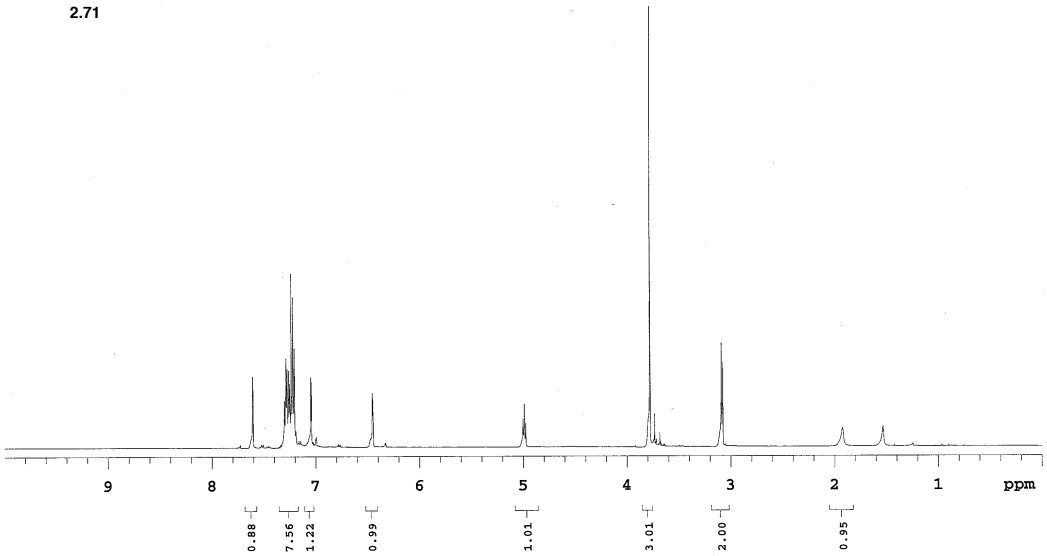

OH
Ph
Ph2N

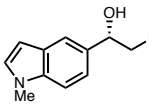
2.70


146.940
146.450
137.327
137.143
128.657
128.358
127.691
126.020
125.790
123.291
123.153
121.872
76.375
76.160
75.953
74.198
45.143
220
200
180
160
140
120
100
80
60
40
20
0
ppm

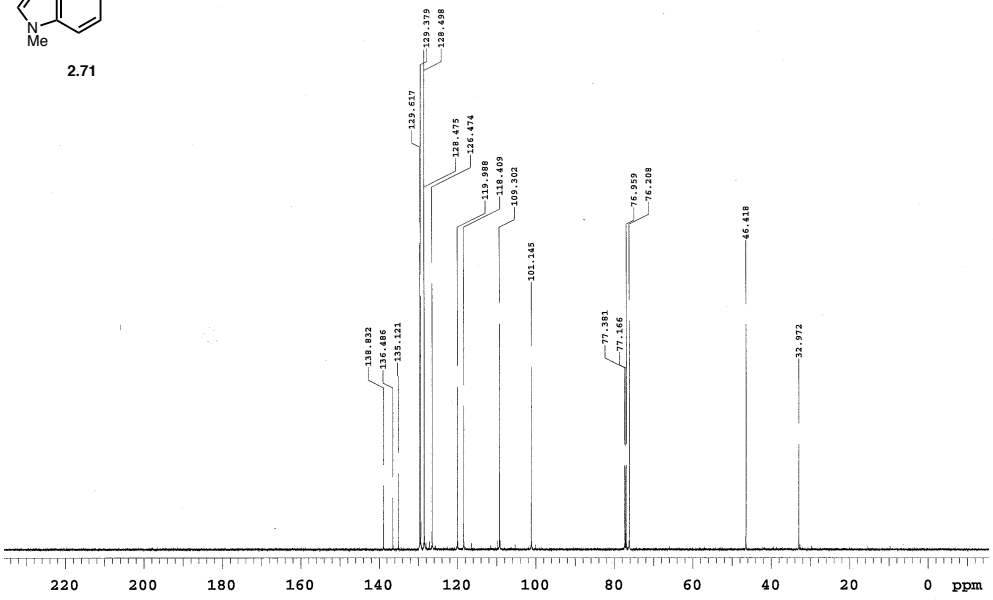

OH
Ph
N
Me

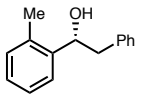
2.71


9
8
7
6
5
4
3
2
1
ppm
0.88
7.56
1.22
0.99
1.01
3.01
2.00
0.95

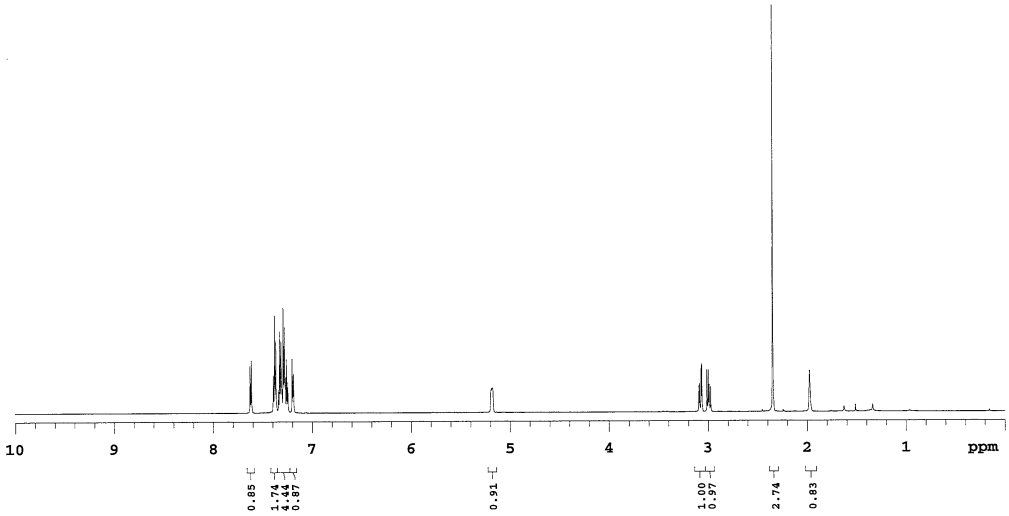

OH
Ph
N
Me

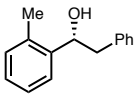
2.71


138.832
136.486
135.121
129.617
129.379
128.498
128.475
126.474
119.988
118.499
109.302
101.145
77.381
77.166
76.959
76.208
46.418
32.972
220
200
180
160
140
120
100
80
60
40
20
0
ppm

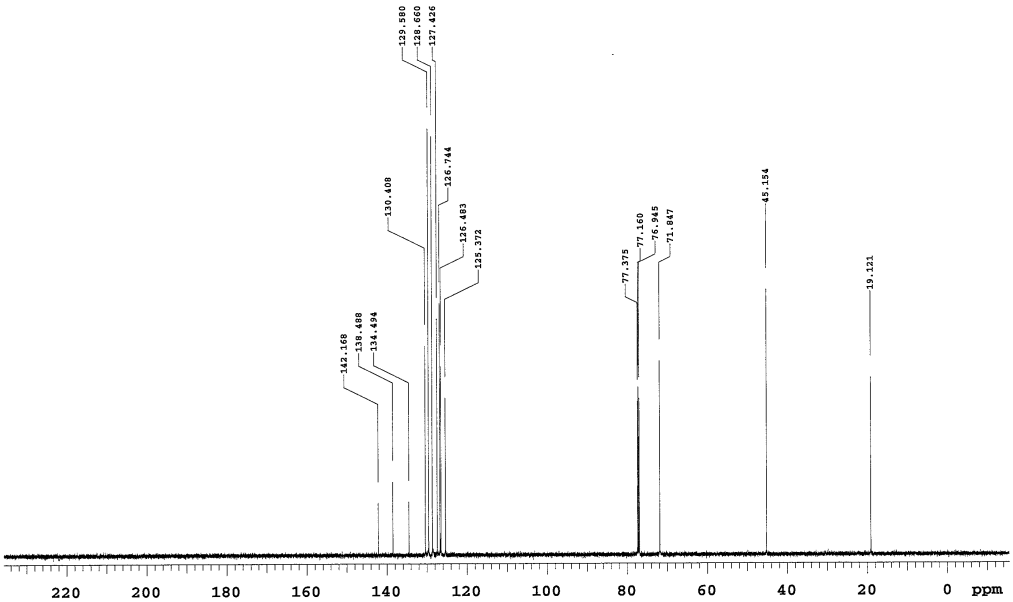

Me
OH
Ph

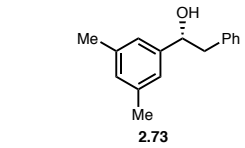
2.72


10
9
8
7
6
5
4
3
2
1
ppm
0.85
1.74
4.44
0.87
0.91
1.00
0.97
2.74
0.83

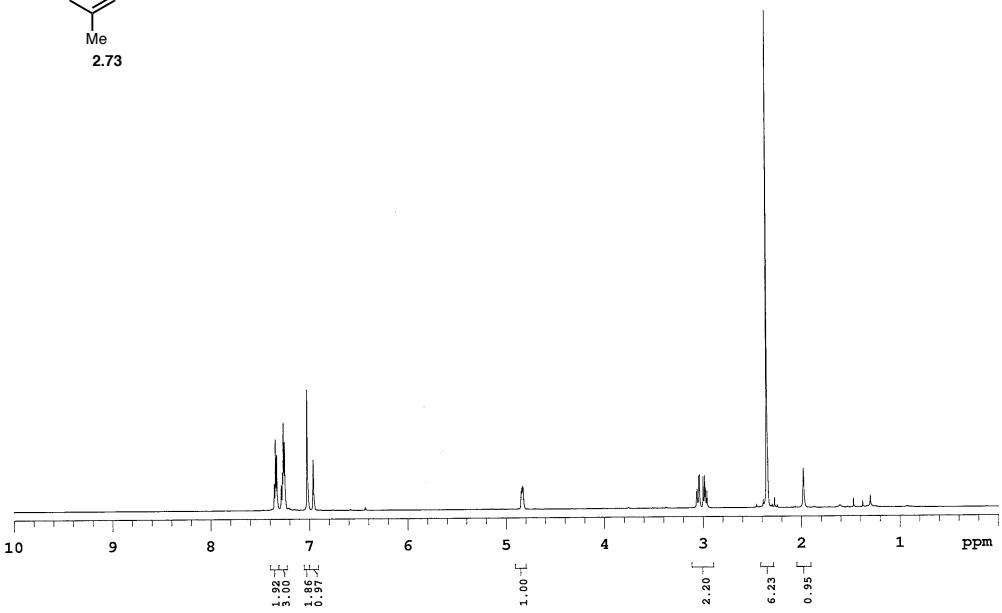

Me
OH
Ph

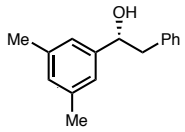
2.72


142.168
138.488
134.494
130.408
129.580
128.660
127.426
126.744
126.483
125.372
77.375
77.160
76.945
71.847
45.154
19.121
220
200
180
160
140
120
100
80
60
40
20
0
ppm


OH
Me
Ph
Me

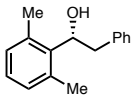
2.73


10
9
8
7
6
5
4
3
2
1
ppm
1.92
3.00
1.86
0.97
1.00
2.20
6.23
0.95

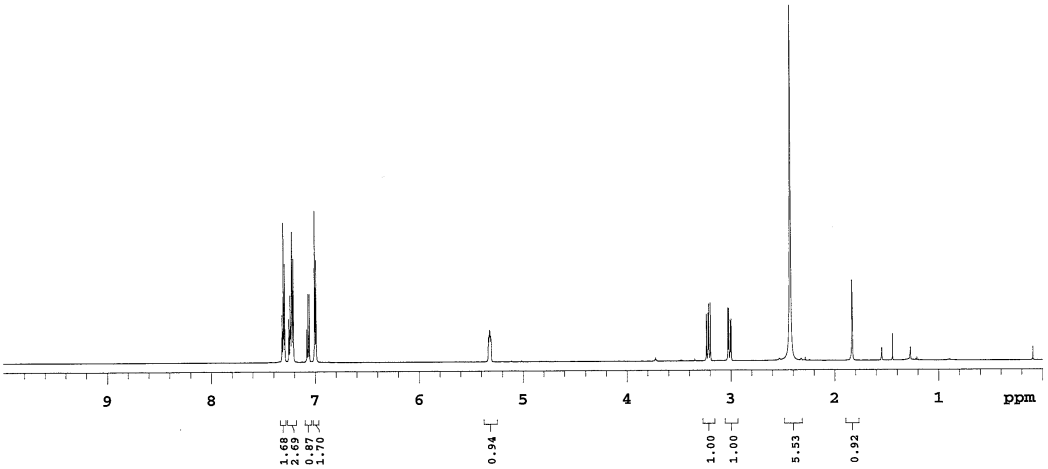

OH
Me
Ph
Me

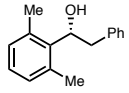
2.73

144.052
138.571
138.165
129.686
129.410
128.690
126.765
123.852
77.450
77.235
77.028
75.549
46.280
21.526
220
200
180
160
140
120
100
80
60
40
20
0
ppm

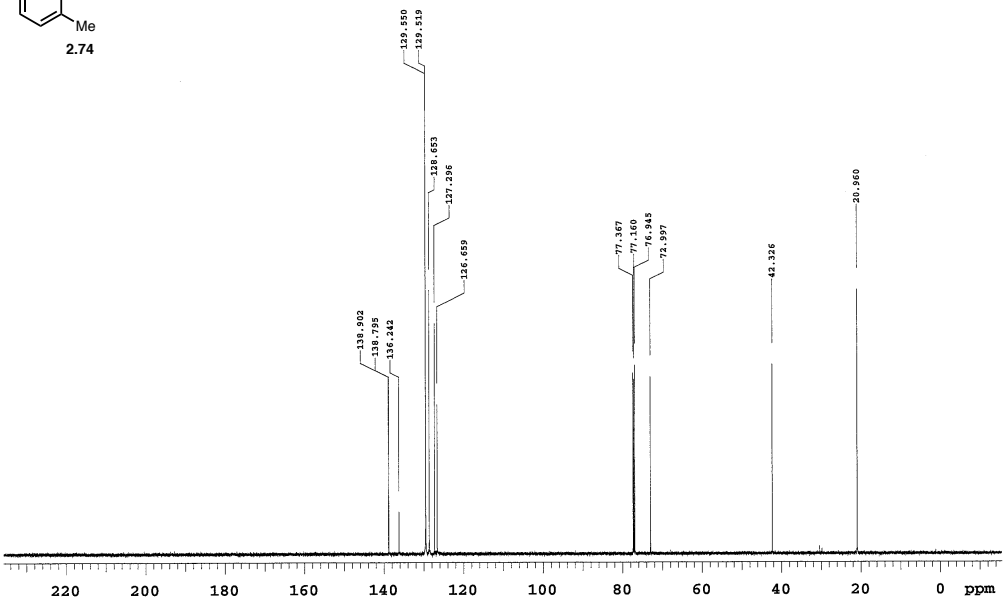

Me
OH
Ph
Me

2.74


9
8
7
6
5
4
3
2
1
ppm
1.68
2.69
0.87
1.70
0.94
1.00
1.00
5.53
0.92


Me
OH
Ph
Me

2.74


139.550
139.519
128.653
127.296
126.659
138.902
138.795
136.242
77.367
77.160
76.945
72.997
42.326
20.960
220
200
180
160
140
120
100
80
60
40
20
0
ppm

CHAPTER 3

Development of a Platinum-Catalyzed Hydrosilylation of Alkenyl Boronates for the Synthesis of Nonracemic Geminal Silylboronates

3.1 Introduction

The hydrosilylation of olefins and alkynes has become a widely developed and utilized reaction in organic chemistry. The increase in hydrosilylation methods development is because the hydrosilylation of carbon-carbon multiple bonds is considered as one of the most efficient methods to synthesize organosilicon compounds.[1] The increased utility has become apparent in organic chemistry methodology development[2], but also extensively employed in the industrial setting. Consequently, olefin hydrosilylation is considered the most important reaction in the silicone industry.[1] The hydrosilylation of olefins has been developed for the synthesis of valuable structures such as silicone polymers, oils, and resins in addition to organofunctional silanes and siloxanes.[1]

[1] Stein, J.; Gao, Y.; Colborn, R. E.; Hutchins, G.; Lewis, L. N. *Platinum Metals Rev.* **1997**, *41*, 66-75 b) Stohrer, J. Troegel, D. *Coord. Chem. Rev.* **2011**, *255*, 1440-1459

[2] a) Nakajima, Y.; Shimada, S. *RSC Adv.* **2015**, *5*, 20603-20616 b) Marciniec, B. *Comprehensive Handbook on Hydrosilylation, 1st Edition* **1992**, Pergamon: Oxford, UK., ISBN 9780080402727

The industrial synthesis of organosilanes generally focuses on the synthesis of linear, achiral silanes. The hydrosilylation of olefins for the synthesis of branched, nonracemic organosilanes might have high impact ramifications for the organosilane industry. Access to nonracemic, branched organosilanes might allow for the synthesis of organosilane polymers and resins with different chemical and physical properties.

The development of methods for the synthesis of branched, nonracemic organosilanes can also be useful for the synthesis of pharmaceutically relevant molecules. Organosilanes have the ability to undergo a wide-array of transformations, a few examples being the Hiyama cross-coupling[3] and the Tamao-Fleming oxidation.[4] Nonracemic, allylic organosilanes are extremely useful reagents for stereospecific transformations to generate more complex stereomotifs. Examples include stereospecific cross-couplings, allylation reactions of carbonyl compounds, and annulation reactions.[5]

To access organosilanes, metal-catalyzed enantioselective hydrosilylations of α-olefins and styrenes have received much attention with new methods continuously being developed. The hydrosilylation of more functionalized olefins would allow for the synthesis of new classes of nonracemic organosilane products. This chapter will discuss the development of an enantioselective platinum-catalyzed hydrosilylation of alkenyl boronates to synthesize nonracemic geminal silylboronates.

[3] Nakao, Y.; Hiyama, T. *Chem. Soc. Rev.* **2011**, *40*, 4893-4901
[4] a) Ishida, N.; Tanaka, T. Kumada, M.; Tamao, K. *Organometallics* **1983**, *2*, 1694-1696 b) Henning, R.; Plaut, H.; Flemming, I. *J. Chem. Soc., Chem. Commun.* **1984**, 29-31
[5] Masse, C. E.; Panek, J. S. *Chem. Rev.* **1995**, *95*, 1293-1316

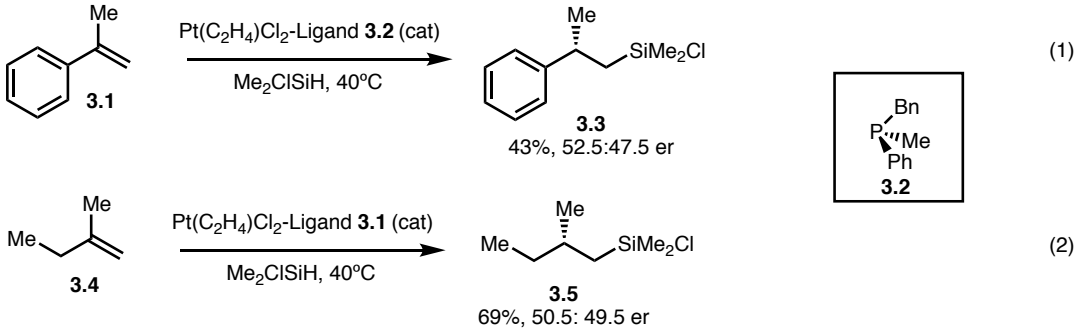
3.2 Background

3.2.1 Asymmetric Metal-Catalyzed Hydrosilylations of Olefins

As previously mentioned, the hydrosilylation of olefins has received much attention within the realm of synthetic organic chemistry methodology development.[2] However, much of the focus recently has been on the development of new, earth-abundant catalysts for the synthesis of linear, achiral organosilanes.[6] The focus on earth-abundant catalysts is because almost all industrial olefin hydrosilylations use platinum-based catalysts.[1] The need for earth-abundant catalysts arises because the silicone industry accounts for most of the worlds platinum consumption.[1] In spite of the industrial use of platinum catalysts, very few methodologies for enantioselective, platinum-catalyzed olefin hydrosilylation exist. Pioneering work done by Kumada and coworkers in 1971 describe the first enantioselective platinum-catalyzed hydrosilylation of olefins.[7] Employing a platinum-complex with chiral phosphine ligand **3.2**, α-methylstyrene underwent a hydrosilylation with chlorodimethylsilane to synthesize nonracemic chlorosilane **3.3** (Scheme 3.1, eq. 1). Under these conditions the reaction proceeded with low enantioselectivity. In addition to α-methylstyrene, 2-methylbut-1-ene (**3.4**) underwent the hydrosilylation to furnish chlorosilane **3.5** with very low enantioselectivity (Scheme 3.1, eq. 2).

[6] Du, X.; Huang, Z. *ACS Catal.* **2017**, *7*, 1227-1243
[7] Yamamoto, K.; Hayashi, T.; Kumada, M. *J. Am. Chem. Soc.* **1971**, *93*, 5301-5302

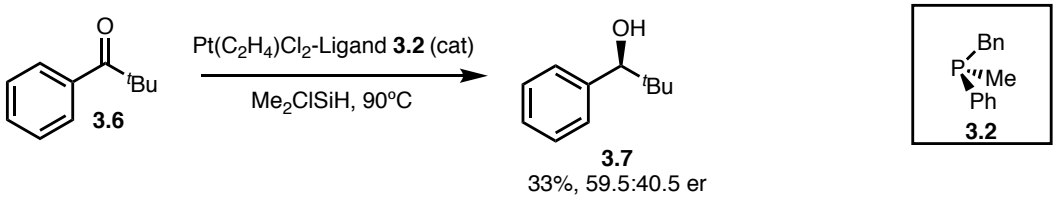
Scheme 3.1 First Platinum-Catalyzed Hydrosilylation of Olefins



Regardless of enantioselectivity, Kumada's report represented the first enantioselective hydrosilylation of olefins employing platinum catalysis. Kumada and coworkers further investigated the reaction by using different chiral phosphine ligands, however, the reactions still suffered from low enantioselectivity.[8] To this date, the reaction by Kumada and coworkers still remains the only example of an enantioselective platinum-catalyzed olefin hydrosilylation.

It is worth noting that as an enantioselective platinum-catalyzed hydrosilylation, Kumada and workers also extended the catalyst system for the hydrosilylation of ketones.[9] Employing aryl ketone **3.6** and the same catalytic conditions as the olefin hydrosilylation resulted in nonracemic benzylic alcohol **3.7** (Scheme 3.2). In this case, the product was furnished with slightly higher enantioselectivity than the olefin hydrosilylation.

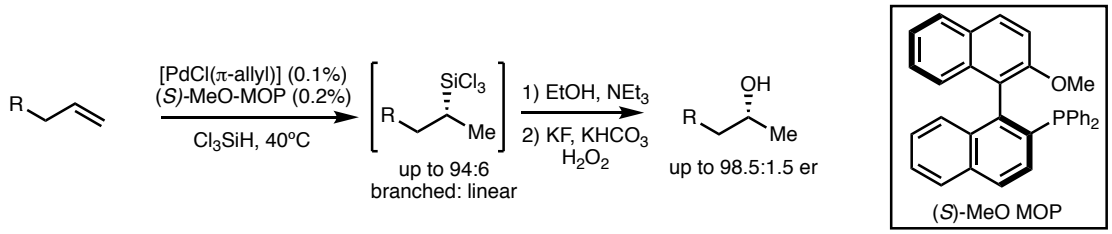
Scheme 3.2 Platinum-Catalyzed Enantioselective Hydrosilylation of Ketones



[8] Yamamoto, K.; Hayashi, T.; Zembayashi, M.; Kumada, M. *J. Organomet. Chem.* **1976**, *118*, 161-181
[9] a) Yamamoto, K.; Hayashi, T.; Kumada, M. *J. Organomet. Chem.* **1972**, *46*, C65−C67 b) Yamamoto, K.; Hayashi, T.; Kumada, M. *J. Organomet. Chem.* **1976**, *112*, 253-262

The development of catalytic, enantioselective methods for olefin hydrosilylation did not see immediate success after the seminal report by Kumada and coworkers. It was not until 1991 when Hayashi and coworkers developed a new catalytic system for the enantioselective hydrosilylation of olefins.[10] Applying a newly developed chiral monodentate ligand, (*S*)-MeO-MOP, to palladium catalysis realized a branched-selective, enantioselective hydrosilylation of α-olefins (Scheme 3.3). Upon formation of the nonracemic trichlorosilane, ethanolysis and oxidation generated nonracemic alcohols and allowed for the determination of the enantiomer ratio.

Scheme 3.3 Palladium-Catalyzed Enantioselective Hydrosilylation of Olefins

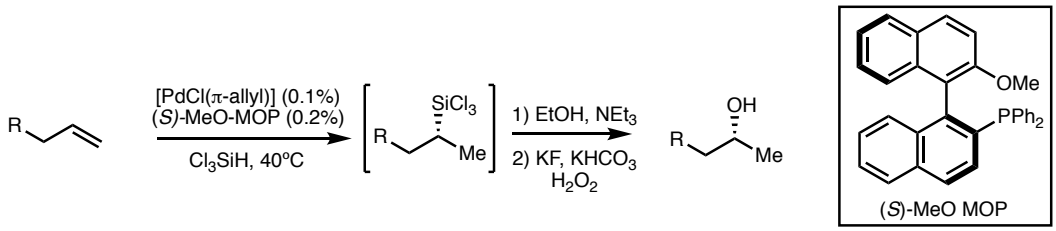


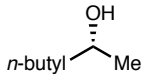
While this example represented the first example of an enantioselective palladium-catalyzed hydrosilylation of α-olefins, the substrate scope was relatively limited. However, this prcoess signifies an important advancement in enantioselective palladium catalysis. As depicted in Table 3.1, various *n*-alkyl substituted olefins (**3.8**, **3.9**, **3.10**) reacted with good chemoselectivities and excellent enantioselectivity. Varying the substitution to phenethyl (**3.11**) maintained high enantioselectivity with slightly diminished chemoselectivity. More sterically encumbered vinylcyclohexane (**3.12**) resulted in significantly diminished chemoselectivity with excellent enantioselectivity. Following this highly impactful development, a large number of new palladium-based catalysts have been

[10] Uozumi, Y.; Hayashi, T. *J. Am. Chem. Soc.* **1991**, *113*, 9887-9888

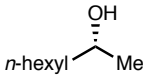
developed for the enantioselective hydrosilylation of olefins.[11] In addition to palladium, numerous methods employing rhodium catalysis have also been developed.[12]

Table 3.1 Substrate Scope for the First Palladium-Catalyzed Enantioselective Hydrosilylation of Olefins

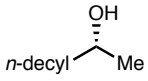




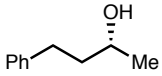
3.8
89:11
linear:branched
70%, 97:3 er



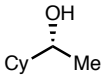
3.9
93:7
linear:branched
71%, 97.5:2.5 er



3.10
94:6
linear:branched
75%, 97.5:2.5 er



3.11
81:19
linear:branched
68%, 98.5:1.5 er

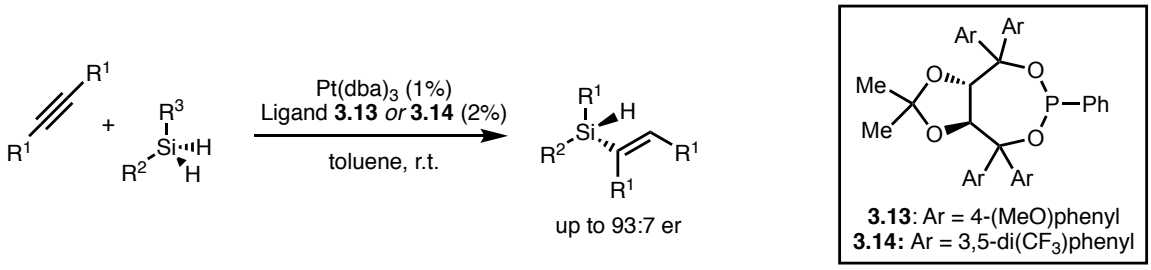


3.12
66:34
linear:branched
45%, 98:2 er

New methods are still being developed for enantioselective hydrosilylations of carbon-carbon multiple bonds. Although not an olefin hydrosilylation, it is worth noting that Tomooka and coworkers demonstrated a platinum-catalyzed enantioselective hydrosilylation of alkynes.[13] Employing a platinum-phosphonite catalyst, an enantioselective-at-silicon hydrosilylation of symmetrical alkynes was realized (Scheme 3.4). While only a few examples provided good enantioselectivity, this methodology still encompasses one of the few enantioselective, platinum-catalyzed hydrosilylations.

[11] a) Illa, H.; Bell, H. P.; Tietze, L. F. *Chem. Rev.* **2004**, *104*, 3453-3516 b) Rudd, M.; Gibson, S. E. *Adv. Synth. Catal.* **2007**, *349*, 781-791
[12] Naito, T.; Yoneda, T.; Ito, J. – I.; Nishiyama, H. *Synlett* **2012**, *23*, 2957-2960 and references within
[13] Igawa, K.; Yoshihiro, D.; Ichikawa, N.; Kokan, N.; Tomooka, K. *Angew. Chem. Int. Ed.* **2012**, *51*, 12745-12748

Scheme 3.4 Platinum-Catalyzed Hydrosilylation of Alkynes

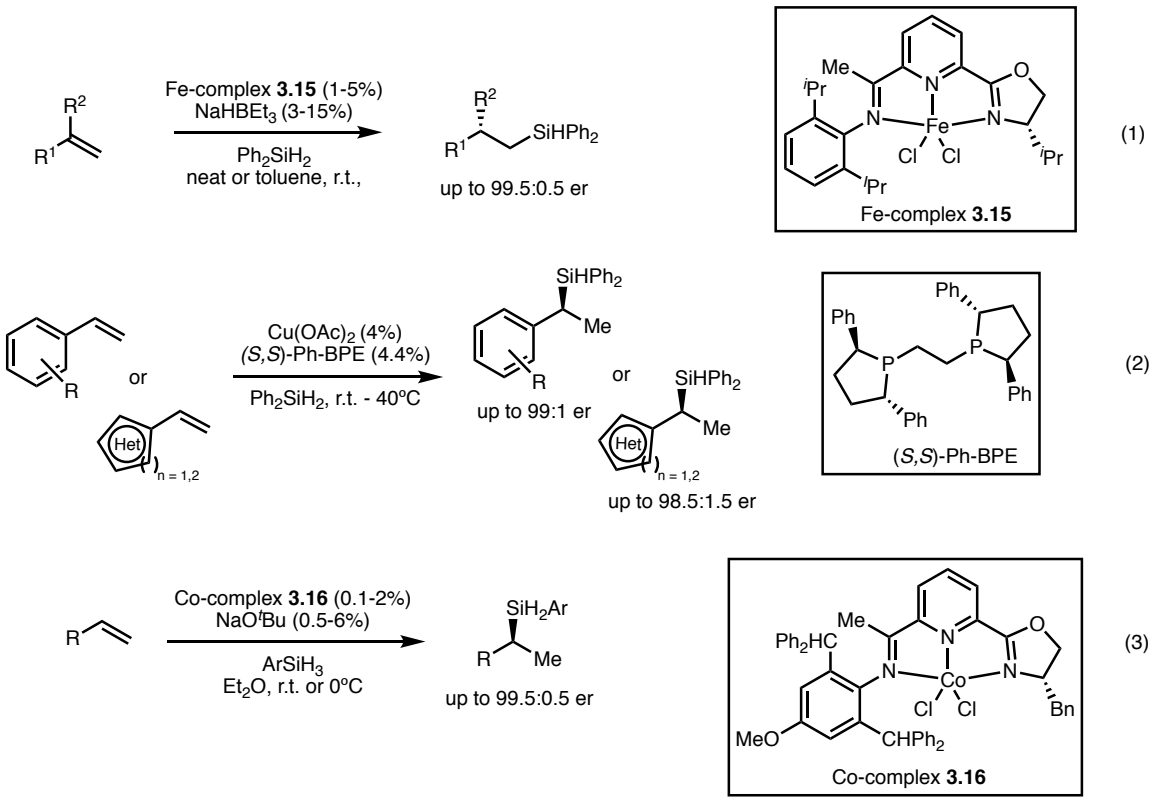


As mentioned above, much effort in the area of hydrosilylation chemistry has focused on the use of earth-abundant catalysts for the synthesis of linear, achiral organosilanes. This focus is also applicable for enantioselective hydrosilylations to synthesize branched, nonracemic organosilanes. Lu and coworkers recently reported a highly efficient iron-catalyzed enantioselective hydrosilylation of 1,1-disubstituted alkenes with excellent efficiency and enantioselectivity (Scheme 3.5, eq. 1).[14] The scope of the reaction was shown to be quite broad, producing high enantioselectivity when one of the R groups was an aromatic group. When both R groups were alkyl, the enantioselectivity was diminished. This method represents a powerful addition to enantioselective hydrosilylations and a significant expansion of the first report by Kumada for the platinum-catalyzed hydrosilylation of 1,1-disubstituted olefins. More recently, Buchwald and coworkers reported a copper-catalyzed enantioselective hydrosilylation of styrenes and heteroaromatic styrenes with excellent enantioselectivity (Scheme 3.5, eq. 2).[15] This method employs a readily available commercial catalyst and represents the first enantioselective hydrosilylation with copper catalysis. The newly developed copper system is a significant addition to the field of asymmetric hydrosilylations and an

[14] Chen, J.; Cheng, B.; Cao, M.; Lu, Z. *Angew. Chem. Int. Ed.* **2015**, *54*, 4661-4664
[15] Gribble Jr., M. W.; Pirnot, M. T.; Bandar, J. S.; Liu, R. Y.; Buchwald, S. L. *J. Am. Chem. Soc.* **2017**, *139*, 2191-2195

alternative to palladium catalysis. Lastly, Lu and coworkers expanded upon the iron-complex system by using a similar ligand scaffold with cobalt as the metal. The newly developed catalyst allowed for the enantioselective hydrosilylation of α-olefins (Scheme 3.5, eq. 3).[16] The reaction produced excellent enantioselectivity with styrenes, and maintained good enantioselectivity even with aliphatic α-olefins. The examples by Lu, in addition to the previously mentioned catalyst systems, represent impactful earth-abundant metal-catalyzed enantioselective hydrosilylations.

Scheme 3.5 Recent Earth-Abundant Metal-Catalyzed Enantioselective Olefin Hydrosilylations



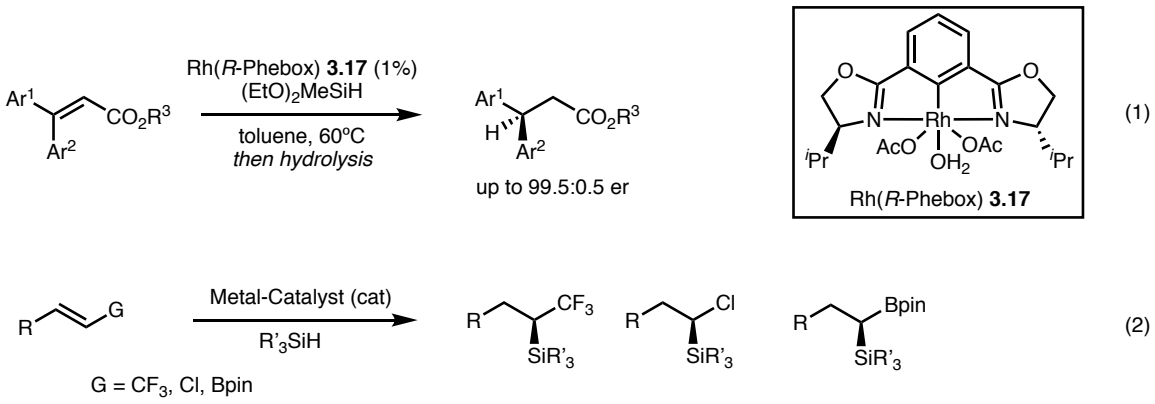
[16] Cheng, B.; Lu, P.; Zhang, H.; Cheng, X.; Lu, Z. *J. Am. Chem. Soc.* **2017**, *139*, 9439-9442

The enantioselective hydrosilylation of simple olefins has extensively been developed with a wide variety of metal catalysts. However, the metal-catalyzed enantioselective hydrosilylation of functionalized olefins remains underdeveloped. The enantioselective hydrosilylation of more functionalized olefins could represent a significant advance in the field of hydrosilylations. The chiral product is an organosilane, that is a useful functional group handle for further manipulation. One example that could be considered to fall under this category is the metal-catalyzed enantioselective conjugate reduction of α,β-unsaturated esters. Recently, Nishiyama and coworkers reported the rhodium-catalyzed enantioselective conjugate reduction of α,β-unsaturated esters with organosilanes (Scheme 3.6, eq. 1).[17] Nishiyama's report represents an enantioselective hydrosilylation of functionalized olefins to synthesize tertiary stereocenters. However, during the mechanism, tautomerization to the more stable oxygen-bound rhodium enolate occurs. After subsequent hydrolysis, the organosilane moiety is removed from the reaction product. The development of an enantioselective hydrosilylation of functionalized olefins where a nonracemic organosilane is retained in the reaction product might represent an impactful methodology (Scheme 3.6, eq. 2). An enantioselective hydrosilylation of alkenyl trifluoromethane substrates might incorporate a pharmaceutically-relevant trifluoromethyl bioisostere and maintain a silicon-containing carbon stereocenter. Enantioselective alkenyl chloride hydrosilylations might furnish nonracemic α-chlorosilanes for further manipulation of both functional groups. The potential to incorporate an organoboronate moiety into an enantioselective hydrosilylation might also be immensely advantageous.

[17] Itoh, K.; Tsuruta, A.; Ito, J. – I.; Yamamoto, Y.; Nishiyama, H. *J. Org. Chem.* **2012**, *77*, 10914-10919 and references within

The ability to functionalize the organoboronate and organosilicon groups in a divergent manner might represent a streamlined route to synthesize functionalized stereocenters.

Scheme 3.6 Enantioselective Hydrosilylation of Functionalized Olefins



3.2.2 Synthesis and Utility of Geminal Bis(Metallate) Reagents

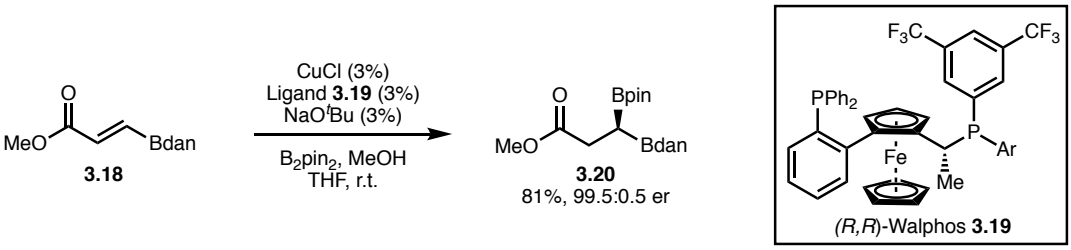
The development of an enantioselective hydrosilylation of alkenyl boronates might represent an impactful synthesis of nonracemic geminal silylboronates. The product of the reaction would fall into a class of compounds called geminal bis(metallate) reagents. The enantioselective synthesis of these types of reagents has received much attention recently, and the utility of these reagents in the preparation of complex stereomotifs explored.

The synthesis of racemic geminal bis(metallate) reagents involving zinc, chromium and copper has been extensively studied over the past twenty to thirty years.[18] However, a significant contribution would be the catalytic synthesis of chemically and configurationally stable nonracemic geminal bis(metallate) reagents. To explore this

[18] Marek, I.; Normant, J. – F. *Chem. Rev.* **1996**, *96*, 3241−3268

reagent class, the synthesis of symmetrical, achiral geminal bis(boronates) was studied with numerous methods developed.[19] It was not until 2011 when Hall and coworkers developed a synthesis of unsymmetrical, nonracemic geminal bis(boronates).[20] A copper-Walphos catalyst promoted the enantioselective conjugate-borylation of boryl-substituted α,β-unsaturated ester **3.18**. The copper-catalyst system afforded nonracemic geminal bis(boronate) **3.20** with good yield and excellent enantioselectivity.

Scheme 3.7 First Report for the Catalytic Synthesis of Nonracemic Geminal Bis(Boronates)



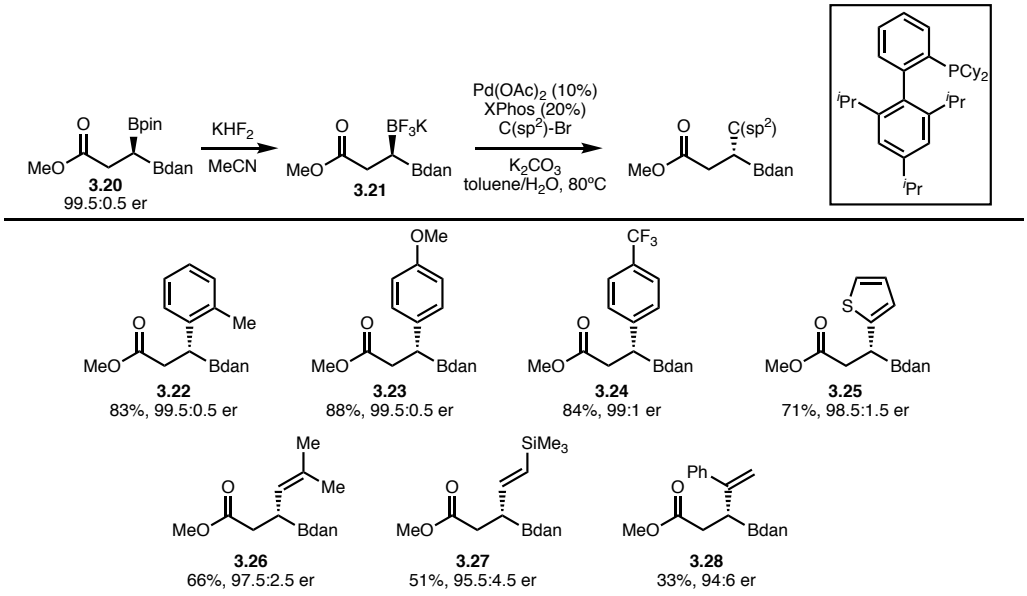
The method by Hall and coworkers represents the first enantioselective synthesis of nonracemic geminal bis(boronates) and the functionalization of these products was effectively demonstrated. As depicted in Table 3.2, conversion of **3.20** into the trifluoroborate salt allowed for a palladium-catalyzed cross-coupling with aryl and alkenyl bromide electrophiles. Conversion of the pinacol boronic ester into the trifluoroborate salt was essential as pinacol boronic ester **3.20** underwent the cross-coupling with complete loss of stereoselectivity. The cross-coupling tolerated sterically encumbered aryl electrophiles (**3.22**), electronically differentiated aryl electrophiles (**3.23**, **3.24**), and heterocyclic electrophiles (**3.25**) with good yields and excellent enantiospecificities.

[19] a) Shimizu, M.; Hiyama, T. *Proc. Jpn. Acad., Ser. B* **2008**, *84*, 75-85 b) Nallagona, R.; Padala, K.; Masarwa, A. *Org. Biomol. Chem.* **2018**, *16*, 1050-1064 c) Miralles, N.; Maza, R. J.: Fernandez, E. *Adv. Synth. Catal.* **2018**, *Early View*. DOI: 10.1002/adsc.201701390

[20] Lee, J. C. H.; McDonald, R.; Hall, D. G. *Nat. Chem.* **2011**, *3*, 894-899

Alkenyl bromides of a variety of substitution patterns (**3.26**, **3.27**) produced similar results. It is worth noting that α-bromostyrene (**3.28**) resulted in a less-efficient and enantiospecific cross-coupling.

Table 3.2 Stereoinvertive Cross-Coupling of Nonracemic Geminal Bis(Boronates) with Aryl and Alkenyl Halides

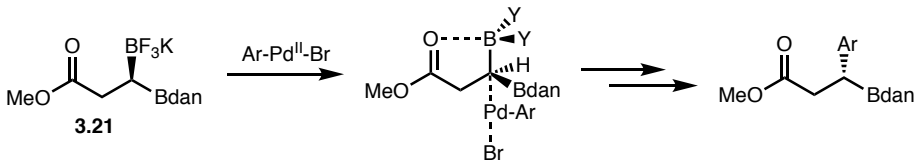


The synthetic utility was further demonstrated by conversion of product **3.26** into the pinacol boronic ester which allowed for an allylation of benzaldehyde with excellent enantiospecificity (not pictured). Mechanistically intriguing, the stereochemical outcome of the cross-coupling was determined to result in a stereoinvertive cross-coupling. Hall and coworkers rationalized this outcome based on precedent by Suginome and Molander for the cross-coupling of β-boryl carbonyl compounds.[21] The neighboring carbonyl is proposed to bind to a potential boronic acid intermediate, which facilitates a stereoinvertive transmetallation (Scheme 3.8). The seminal report by Hall and coworkers represents a

[21] a) Awano. T.; Ohmura, T.; Suginome, M. *J. Am. Chem. Soc.* **2010**, *132*, 13191-13193 b) Sandrock, D. L.; Jean-Gerard, L.; Chen, C. – Y.; Dreher, S. D.; Molander, G. A. *J. Am. Chem. Soc.* **2010**, *132*, 17108-17110

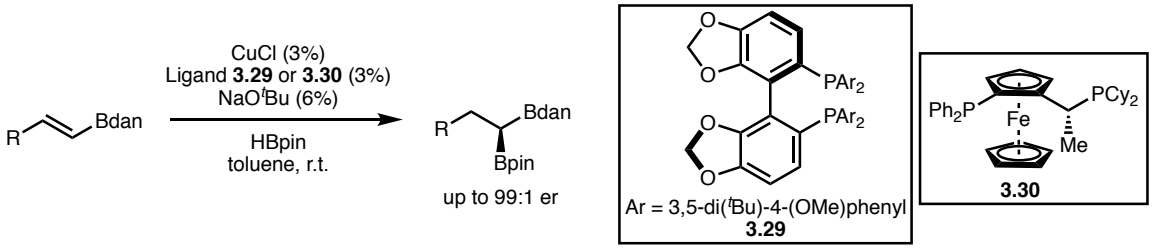
highly impactful addition to the synthesis of stable, isolable nonracemic geminal bis(metallates).

Scheme 3.8 Proposal for a Stereoinvertive Transmetallation



In 2013, Yun and coworkers reported an alternative strategy for the synthesis of nonracemic geminal bis(boronates).[22] The approach employed similar conditions to the previously developed enantioselective hydroboration of β-substituted styrenes.[23] Switching to alkenyl diaminonaphthalene boronates (Bdan) realized the enantioselective hydroboration for the synthesis of nonracemic geminal bis(boronates) (Scheme 3.9). The reaction proceeded with complete regiocontrol producing excellent yields and enantioselectivity. Conducting the reaction with either styrenyl or alkyl substituted alkenyl boronates provide products with high enantioselectivity.

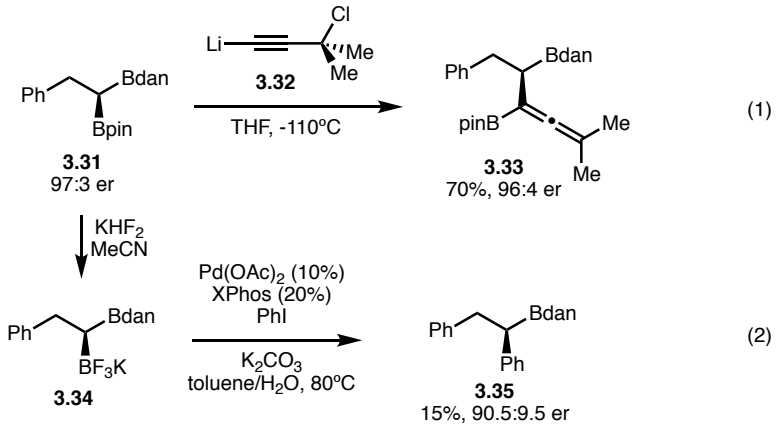
Scheme 3.9 Copper-Catalyzed Hydroboration of Alkenyl Diaminonaphthalene Boronates



[22] Feng, X.; Jeon, H.; Yun, J. *Angew. Chem. Int. Ed.* **2013**, *52*, 3989-3992
[23] Noh, D.; Yoon, S. K.; Won, J.; Lee, J. Y.; Yun, J. *Chem. Asian. J.* **2011**, *6*, 1967-1969

With regards to the synthetic utility of these products, Yun and coworkers carried out the selective homologation of geminal bis(boronate) **3.31** with lithiated propargyl chloride **3.32**. Stereoretentive 1,2-migration onto the alkyne and elimination of the chloride afforded the allenyl bis(boronate) **3.33**. (Scheme 3.10, eq. 1). Product **3.33** represents a versatile vicinal bis(boronate) with electronically differentiated organoboronates for further functionalization. In addition to homologation, conversion of the pinacol boronic ester into the trifluoroborate salt **3.34** allowed for a palladium-catalyzed cross-coupling with iodobenzene. Using similar conditions to the cross-coupling reported by Hall and coworkers produced benzylic organoboronate **3.35** in low yield. The reaction also suffered from a small erosion of stereochemistry, but unlike Hall's occurred by a stereoretentive transmetallation. The observed stereochemical outcome highlights and reinforces the proposal by Hall and coworkers that the carbonyl coordination is essential for a stereoinvertive transmetallation (Scheme 3.8). The carbonyl coordination might also assist in increasing the reactivity of the cross-coupling.

Scheme 3.10 Functionalization of Nonracemic Geminal Bis(Boronates)

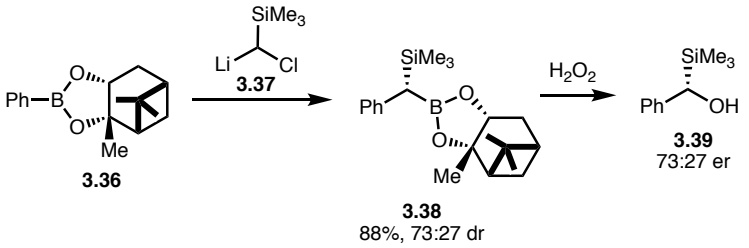


While unsymmetrical, nonracemic geminal bis(boronates) have been shown to be useful towards further functionalization, to this date, the work done by Hall and Yun are the only reported methods for the synthesis of these reagents. Further studies on the divergent functionalization of the two electronically differentiated organoboronate groups could have a profound impact towards the synthesis of complex stereomotifs.

An alternative approach to the divergent reactivity of differentiated geminal bis(boronates) could be realized by instead using two different metal groups. For this to be feasible, both metal groups would require the capacity to undergo subsequent transformations similarly to organoboronates. Within the realm of configurationally stable and isolable geminal bis(metallates), geminal silylboronates could represent an easily accessible alternative. The first synthesis of a nonracemic, isolable geminal silylboronate was reported in 1983 by Matteson and coworkers.[24] Employing (+)-pinane-diol derived organoboronate **3.36** and chlorosilyllithium **3.37**, the homologation occured with a 73:27 diastereomer ratio (Scheme 3.11). Analysis of the reaction stereoselectivity was carried out by oxidation to the nonracemic silyl alcohol **3.39** and comparison to a known compound. It is worth noting that Soderquist and coworkers reported the asymmetric hydroboration of alkenylsilanes with (+)-diisopinocampheylborane with similar diastereoselectivities. However, the product had to be oxidized to the corresponding silyl alcohol to be isolated.[25]

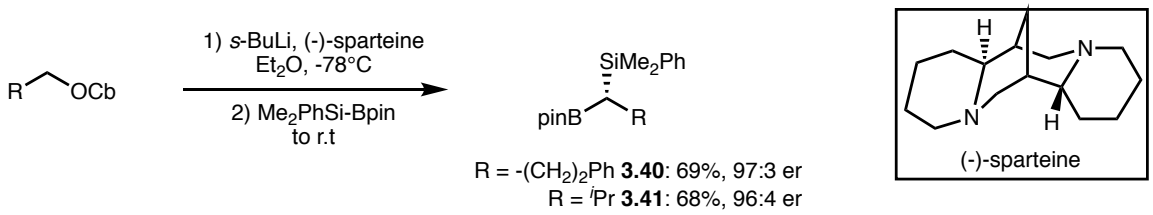
[24] Tsai, D. J. S.; Matteson, D. S. *Organometallics* **1983**, *2*, 236-241
[25] Lee, S. – J. H.; Soderquist, J. A. *Tetrahedron* **1988**, *44*, 4033-4042

Scheme 3.11 First Reported Synthesis of Nonracemic Geminal Silylboronates



A general method for the synthesis of nonracemic, isolable geminal silylboronates was elusive until work done by Aggarwal and coworkers in 2011.[26] Although stoichiometric (-)-sparteine is required to induce selectivity, the silylboration of lithiated carbamates was capable of synthesizing nonracemic geminal silylboronates with excellent enantioselectivity (Scheme 3.12).

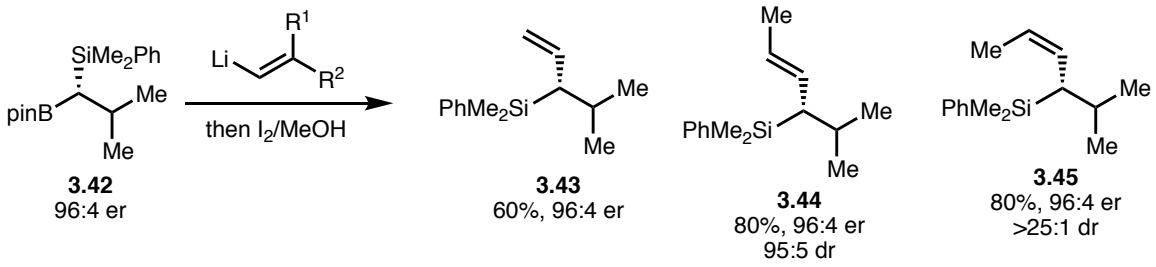
Scheme 3.12 Synthesis of Nonracemic Geminal Silylboronates by an Enantioselective Lithiation of Carbamates



The synthetic utility was demonstrated through Zweifel olefinations with a variety of stereochemically-defined organolithium reagents. These reactions produced highly valuable nonracemic allylic silanes of differing alkene substitution patterns (Scheme 3.13).

[26] Binanzer, M.; de Ceglie, M. C.; Gallanti, M.; Glasspoole, B. W.; Kendrick, S. J. F.; Sonawane, R. P.; Vazquez-Romero, A.; Webster, M. P.; Aggarwal, V. K. *Org. Lett.* **2011**, *13*, 1490-1493

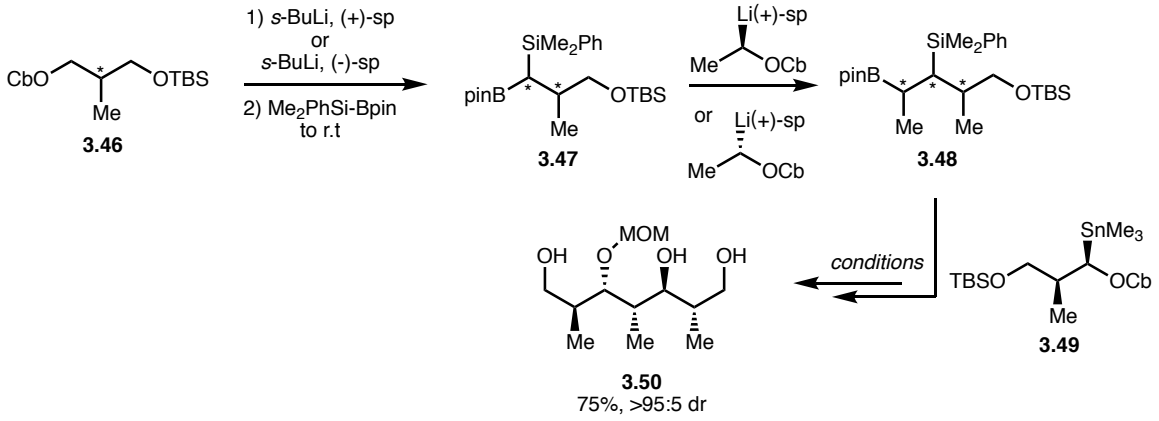
Scheme 3.13 Zweifel Olefinations of Geminal Silylboronates



More recently, Aggarwal and coworkers expanded upon on the first report with subsequent lithiation-borylation reactions of nonracemic geminal silylboronates for the synthesis of stereotriads and stereopentads.[27] Carbamate **3.46** was readily prepared from commercially available Roche ester. Next, enantioselective lithiation and silylboration furnished **3.47** with two contiguous stereocenters (Scheme 3.14). Further homologation of **3.47** with either enantiomer of lithiated carbamate produced stereotriad **3.48**. The organoboronate and organosilane groups might be perceived as masked hydroxyl groups, and all eight stereoisomers of stereotriad **3.48** were synthesized impressively with excellent diastereoselectivity. Merging **3.48** with reagent **3.49** generated a stereopentad motif, and subsequent oxidations arrived at tetrol **3.50** with excellent diastereoselectivity.

[27] Millan, A.; Grigol Martinez, P. D.; Aggarwal, V. K. *Chem. Eur. J.* **2017**, *24*, 730-735

Scheme 3.14 Lithiation-Borylation Strategy for the Synthesis of Nonracemic Silylboronates and Stereopentads

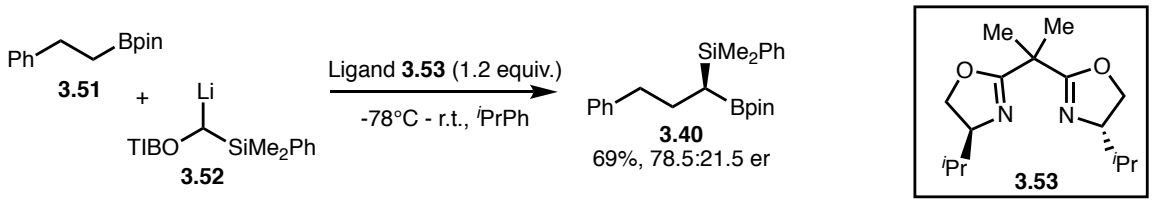


Alternative organoboronate functionalizations might be applied for the incorporation of heteroatoms, alkenes or carbon groups into the synthesized stereomotifs.[28] The method developed by Aggarwal and coworkers represents an efficient, although non-catalytic, synthesis of nonracemic geminal silylboronates. The synthetic utility was elegantly demonstrated through the synthesis of complex stereomotifs.

Based on the work done by Aggarwal, Blakemore and coworkers recently developed a different system for the enantioselective synthesis of geminal silylboronates.[29] When employing organoboronate **3.51**, BOX-ligand **3.53** promoted the silylboration of lithiated benzoates. However, this reaction only afforded product **3.40** in moderate enantioselectivity (Scheme 3.15).

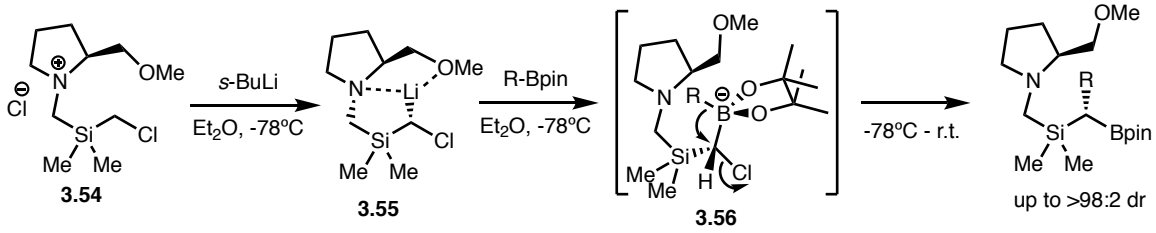
[28] Sandford, C.; Aggarwal, V. K. *Chem. Commun.* **2017**, *53*, 5481-5494
[29] Barsamian, A. L.; Wu, Z.; Blakemore, P. R. *Org. Biomol. Chem.* **2015**, *13*, 3781-3786.

Scheme 3.15 BOX-Ligand Enabled Enantioselective Lithiation and Synthesis of Nonracemic Geminal Silylboronates



Lastly, within the area of enantioselective lithiation, Aggarwal and coworkers more recently developed a new alternative to using (-)-sparteine.[30] Employing a proline-derived directing group embedded in chloromethylsilyl precursor **3.54**, affected an enantioselective lithiation to produce diastereomeric lithium complex **3.55** (Scheme 3.16). Treatment of this complex with an external organoboronate produces activated complex **3.56**. Subsequent 1,2-migration furnished the desired nonracemic geminal silylboronate with excellent diastereoselectivity. The newly developed method represents a powerful addition to enantioselective lithiation by employing a readily available directing group from an inexpensive chiral pool. This approach also avoids using increasingly scarce sparteine as the chiral auxiliary.[31]

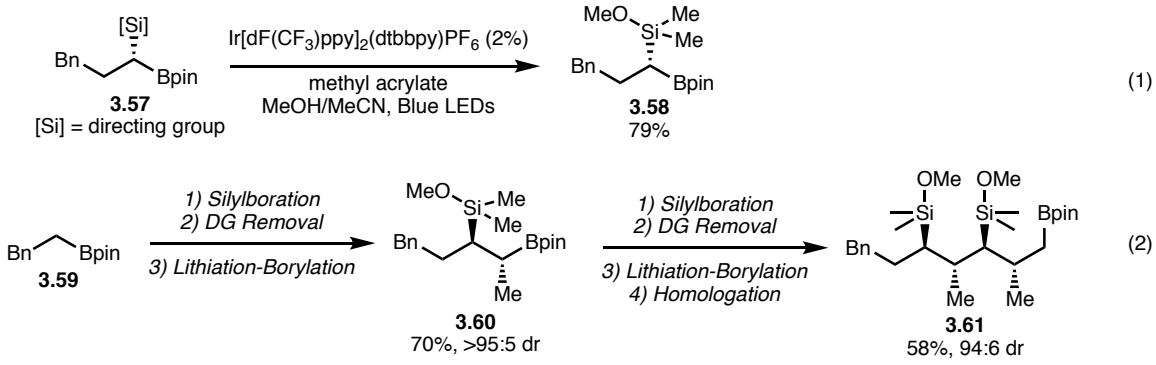
Scheme 3.16 Proline-Derived Directing Group for Enantioselective Lithiation



[30] Bootwicha, T.; Feilner, J. M.; Myers, E. L.; Aggarwal, V. K. *Nat. Chem.* **2017**, *9*, 896-902
[31] Ritter, S. K. *C&EN* **2017**, *95*, 18-20

Another appealing feature to this method is the ease with which the directing group can be removed under mild photoredox conditions. Removal of the directing group afforded the stable and diversifiable methoxy silane group as displayed in **3.58** (Scheme 3.17, eq. 1). The synthetic utility was expanded through iterative silylborations and lithiation-borylation procedures to form compounds with contiguous stereocenters (Scheme 3.17, eq. 2). Silylboration of **3.59**, followed by directing group removal and enantioselective lithiation-borylation provided **3.60** with excellent diastereoselectivity. Performing an analogous sequence, followed by a Matteson homologation, provided stereotetrad **3.61** with good yield and excellent diastereoselectivity. A one-pot *m*-CPBA oxidation of the organosilane and organoboronate groups afforded the triol (not pictured). The described iterative procedure was conducted to synthesize a variety of compounds of differing relative stereochemical configurations.

Scheme 3.17 Utility of Proline-Derived Directed Enantioselective Lithiation and Silylboration

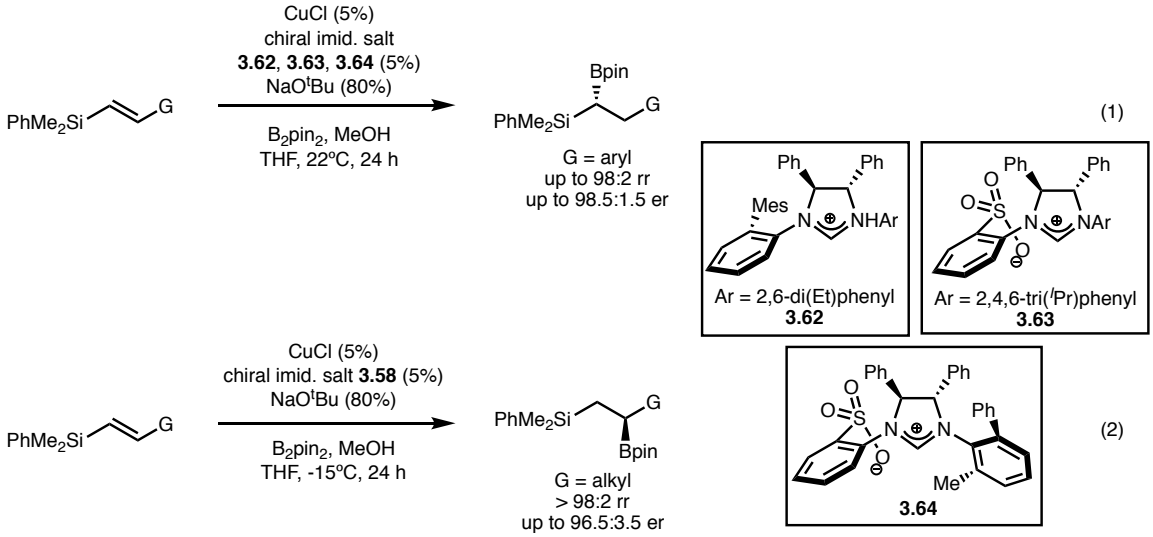


The work done by Aggarwal and coworkers provides a highly stereoselective synthesis of nonracemic geminal silylboronates utilizing sparteine or a proline-derived directing group in a stoichiometric fashion. However, the development of methods to

synthesize nonracemic geminal silylboronates in a catalytic fashion is highly desirable. The development of a catalytic system for the synthesis of nonracemic geminal silylboronates was elusive until 2013. Hoveyda and coworkers developed an elegant copper-catalyzed borylation of alkenylsilanes.[32] A copper-NHC ligand complex (**3.62**, **3.63**, or **3.64**) successfully promoted the hydroboration of alkenylsilanes with excellent enantioselectivity to produce geminal silylboronates (Scheme 3.18, eq. 1). For the observed regioselective outcome, the alkenylsilane required aryl substitution to facilitate aryl stabilization of the organocopper intermediate. The aryl stabilization was shown to work synchronously with the ligand scaffold to affect the regiochemical outcome. With alkyl-substituted alkenylsilanes, the regioisomeric outcome observed resulted in the synthesis of vicinal silylboronates with excellent enantioselectivity (Scheme 3.18, eq. 2). The regiochemical outcome was rationalized through silicon stabilization of the organocopper intermediate in addition to ligand effects.

[32] Meng, F.; Jang, H.; Hoveyda, A. H. *Chem. Eur. J.* **2013**, *19*, 3204-3214

Scheme 3.18 First Report of a Catalytic, Enantioselective Synthesis of Nonracemic Geminal Silylboronates

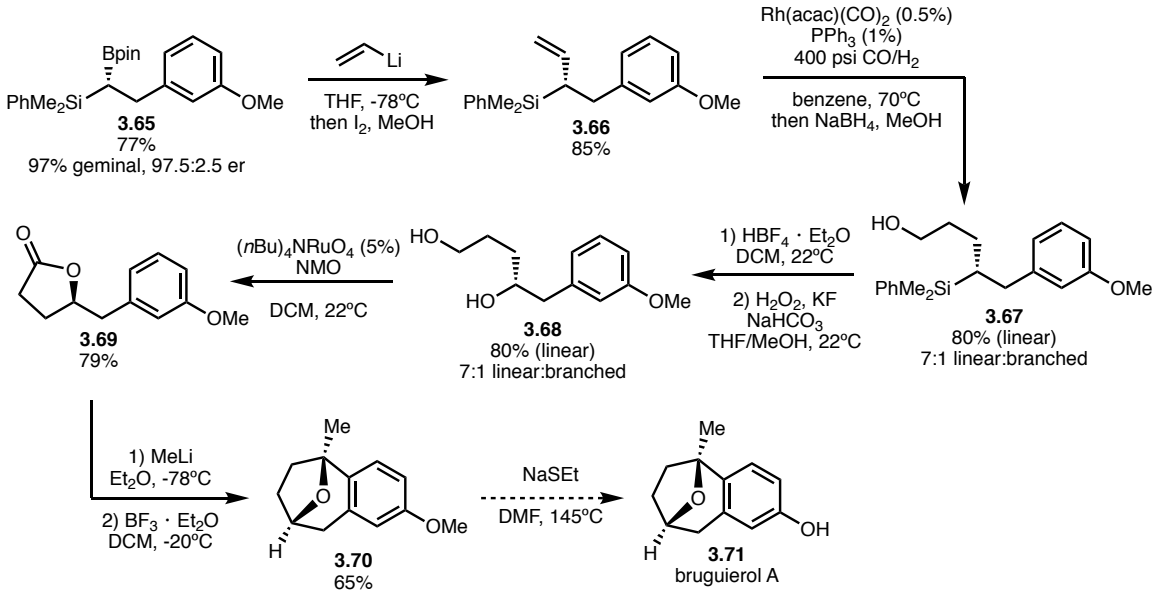


To demonstrate the utility of geminal silylboronates, Hoveyda and coworkers carried out the formal synthesis of natural product bruguierol A (Scheme 3.19). From a readily available aryl acetylene, protosilylation provided the requisite alkenylsilane (not pictured). The aforementioned enantioselective copper-catalyzed hydroboration afforded nonracemic geminal silylboronate **3.65** in excellent regio- and enantioselectivity. Subsequent Zweifel olefination provided allyl silane **3.66**, and a linear selective hydroformylation-reduction sequence arrived at alcohol **3.67** with good yields. Oxidation of the organosilicon group (**3.68**) and oxidative lactonization provided nonracemic lactone **3.69** in good yield. Methyllithium carbonyl addition and subsequent Lewis-acid mediated cyclization afforded tricylic **3.70** in good overall yield. The last step to the natural product **3.71** had previously been reported.[33] The seminal report by Hoveyda and coworkers for the

[33] Hu, B; Xing, S.; Ren, J.; Wang, Z. *Tetrahedron* **2010**, *66*, 5671-5674

catalytic synthesis of nonracemic geminal silylboronates was shown to be efficient and impactful for application towards the synthesis of natural products.

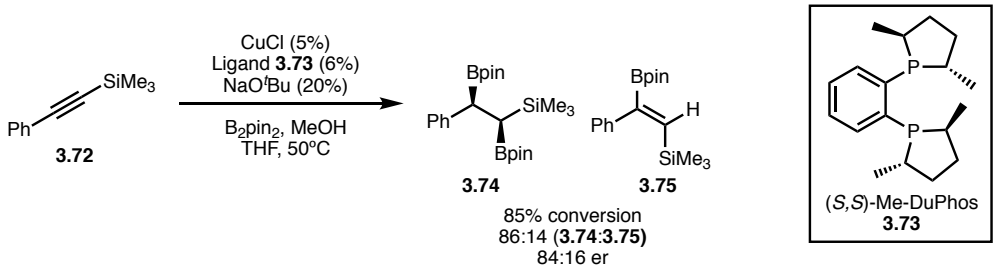
Scheme 3.19 Synthetic Utility of Geminal Silylboronates by the Synthesis of Natural Product Bruguierol A



It is worth noting that Yun and coworkers reported an isolated example of nonracemic geminal silylboronate synthesis by the diborylation of silyl-protected aryl acetylenes.[34] For this method, trimethylsilyl protected phenylacetylene reacted under the influence of a copper-DuPhos catalyst to produce nonracemic geminal silylboronate **3.74** with good enantioselectivity (Scheme 3.20). However, under these reaction conditions, unreacted intermediate **3.75** was also observed. The report by Yun and coworkers only included one enantioselective example and even for the racemic diborylation, the scope was limited to aryl acetylenes.

[34] Jung, H. – Y.; Yun, J. *Org. Lett.* **2012**, *14*, 2606-2609

Scheme 3.20 Enantioselective Diborylation of Silyl-Protected Aryl Acetylenes

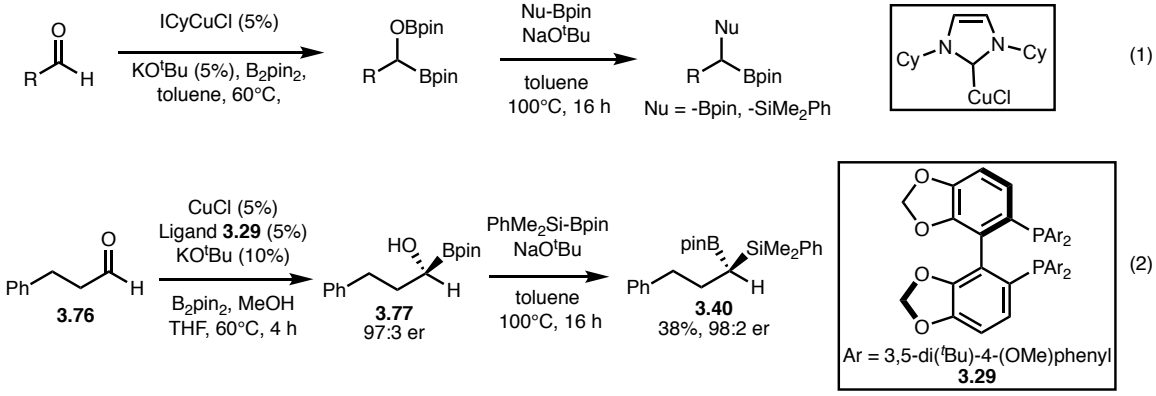


The copper-catalyzed hydroboration method developed by Hoveyda and coworkers was shown to be limited to styrenyl silanes, and the copper-catalyzed diborylation by Yun and coworkers limited to aryl acetylenes. Taking this into account, a general method for the catalytic synthesis of nonracemic geminal silylboronates bearing any substitution is still desirable. Recently, Lan, Liu and coworkers reported the copper-NHC complex catalyzed diborylation of aldehydes to synthesize α-hydroxy organoboronate intermediates (Scheme 3.21, eq. 1).[35] Subsequent treatment of the α-hydroxy organoboronate with another equivalent of diboron reagent or silylboron reagent promotes a deoxygenative borylation/silylation to synthesize geminal bis(boronates) or geminal silylboronates respectively. The method was expanded to include one example of an enantioselective diborylation of hydrocinnamaldehyde **3.76** with a copper-DTBM Segphos catalyst (Scheme 3.21, eq. 2). The diborylation synthesized nonracemic α-hydroxy organoboronate **3.77** with excellent enantioselectivity; subsequent silylation produced nonracemic geminal silylboronate **3.40**. While the deoxygenative silylation generated nonracemic geminal silylboronate **3.40** with excellent enantioselectivity, the reaction suffered from low

[35] Wang, L.; Zhang, T.; Sun, W.; He, Z.; Xia, C.; Lan, Y.; Liu, C. *J. Am. Chem. Soc.* **2017**, *139*, 5257-5264

efficiency. In addition to low efficiency, it also required the use of 2.5 equivalents of a B-B and B-Si bonded reagent, the latter being quite expensive. x

Scheme 3.21 Synthesis of Nonracemic Geminal Silylboronates via Deoxygenative Silylation of α-Hydroxy Organoboronates



The current technology for the synthesis of nonracemic geminal silylboronates has been shown to be highly enantioselective, however, limitations still exist. The development of a general catalytic method for the synthesis of geminal silylboronates containing a variety of substitutions could represent an impactful contribution towards the synthesis and utility of these reagents. Furthermore, employing inexpensive reagents and readily available starting materials is highly desirable.

3.2.3 Synthetic Utility of Organosilanes and Geminal Silylboronates

Silicon has received much attention in synthetic organic chemistry throughout the years.[36] The utility of silicon has been demonstrated extensively through its use as protecting groups for alcohols and alkynes, in the context of silyl enol ethers for Mukaiyama Aldol reactions, as Lewis-acids for carbonyl additions amongst a plethora of other applications. A variety of transformations have been developed transform organosilanes into useful functional groups in organic chemistry. One such example is the widely-developed Peterson olefination for the synthesis of stereochemically defined alkenes.[37] Adapting organosilane transformations to geminal silylboronates could greatly expand upon the synthetic utility of these reagents for the synthesis of biologically relevant molecules. In addition to target synthesis, adapting organosilane reactions to geminal silylboronates might uncover new modes of reactivity.

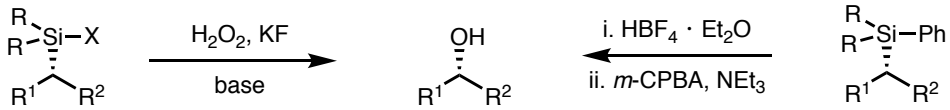
While organosilanes have the ability to undergo 1,2-metallate rearrangements similar to organoboronates, silicon suffers from the inability to be as easily activated by nucleophiles. The reluctance towards activation results in lower reactivity in 1,2-migrations. Developing new methods to functionalize organosilanes through 1,2-metallate rearrangements might represent powerful additions to synthetic organic chemistry and immensely expand the utility of organosilane reagents. Nonetheless, one of the widely developed and applied transformations of organosilanes is the Tamao-Fleming oxidation.[4]

---

[36] Barbero, A.; Walter, D.; Fleming, I. *Chem. Rev.* **1997**, *97*, 2063-2192.
[37] a) Peterson, D. J.; *J. Org. Chem.* **1968**, *33*, 780-784 b) Ager, D. J. *Synthesis* **1999**, *5*, 384-398 c) van Staden, L. F.; Gravestock, D.; Ager, D. J. *Chem. Soc. Rev.* **2002**, *31*, 195-200

Tamao and coworkers reported that treating haloorganosilanes with hydrogen peroxide and fluoride promotes the stereorententive oxidation of the organosilane (Scheme 3.22). Independently, Fleming and coworkers reported a two-pot sequence employing phenyl-substituted organosilanes. Fluorination of the phenyl group *in situ* produces an organofluorosilane and subsequent treatment with a peroxide promotes the oxidation of the organosilane group.

Scheme 3.22 Tamao-Fleming Oxidation of Organosilanes



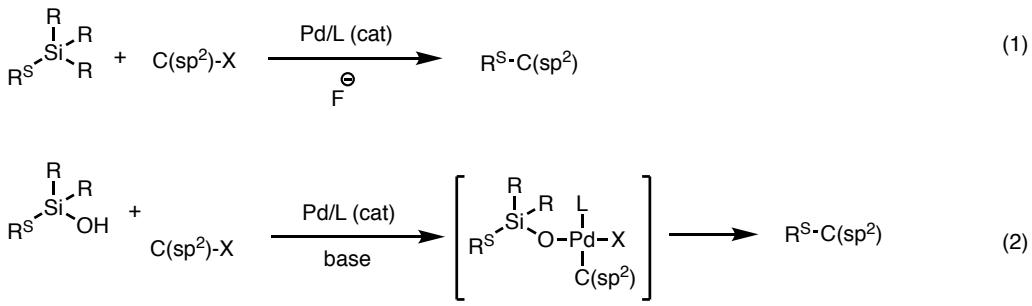
The two methods complement each other for the oxidation of organosilane groups bearing different substituents. In regards to nonracemic organosilanes, numerous applications of the Tamao-Fleming oxidation for the synthesis of nonracemic alcohols have been reported. Alkenylsilane oxidation allows for the use of alkenylsilanes as masked ketones.[38] In addition to the procedures developed by Tamao and Fleming, numerous variants of these reaction conditions have been developed and allow oxidations of organosilanes bearing specific functional groups.

Another widely developed transformation of organosilanes, and a fundamental organometallic reaction, is the Hiyama cross-coupling (Scheme 3.23, eq. 1).[39] Addition to the organosilane with a sufficient fluoride source will form an activated organosilicate complex that engages in transmetallation. Subsequent reductive elimination furnishes the desired cross-coupling product (Scheme 3.23, eq. 1). The Hiyama cross-coupling has been

[38] Kumada, M.; Tamao, K. *Tet. Lett.* **1984**, *25*, 321-324
[39] a) Yoshida, J.; Tamao, K.; Yamamoto, H.; Kakui, T.; Uchida, T.; Kumada, M. *Organometallics* **1982**, *1*, 542-549 b) Hatanaka, Y.; Hiyama, T. *J. Org. Chem.* **1988**, *53*, 918-920 c) Nakao, Y.; Hiyama, T. *Chem. Soc. Rev.* **2011**, *40*, 4893-4901

shown to be versatile by avoiding organometallics such as organomagnesium or organolithium reagents, and utilizes readily available organosilane starting materials. Denmark and coworkers greatly expanded upon the Hiyama cross-coupling by developing a fluoride free cross-coupling of organosilanes (Scheme 3.23, eq. 2).[40] Denmark and coworkers employed organosilanols whereby treatment with base forms organosilanoates. The organosilanoates are then competent to undergo transmetallation under mild conditions to promote the desired cross-coupling.

Scheme 3.23 Transition-Metal Catalyzed Cross-Coupling of Organosilanes: Hiyama-Denmark Cross-Coupling

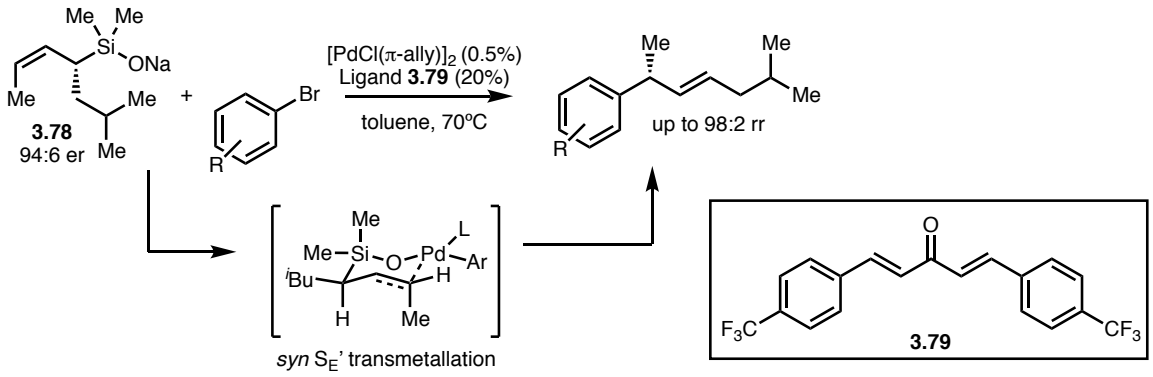


The development of organosilanoate cross-couplings has immensely increased the utility of cross-coupling reactions with organosilanes, most notably for the pharmaceutical industry to avoid the use of fluoride. Denmark and coworkers showcased organosilanoates for the stereospecific cross-coupling of nonracemic allylic organosilanoates (Scheme 3.24).[41] Employing a palladium-dibenzylideneacetone derived catalyst, promoted a γ-selective *syn* transmetallation with a variety of aryl electrophiles to generate nonracemic tertiary allylic stereocenters. The observed high regioselectivity was rationalized by a six-membered transition state depicted in Scheme 3.24. The allylic cross-coupling by

[40] Regens, C. S.; Denmark, S. E. *Acc. Chem. Res.* **2008**, *41*, 1486-1499
[41] Werner, N. S.; Denmark, S. E.; *J. Am. Chem. Soc.* **2010**, *132*, 3612-3620

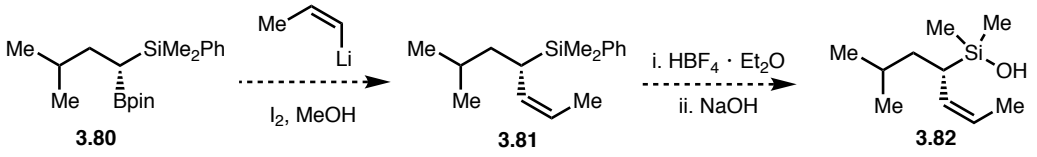
Denmark represents a powerful utilization of nonracemic allylic organosilanes, and adds to other widely developed reactions.[5]

Scheme 3.24 Stereospecific Cross-Coupling of Nonracemic Allylic Silanoates



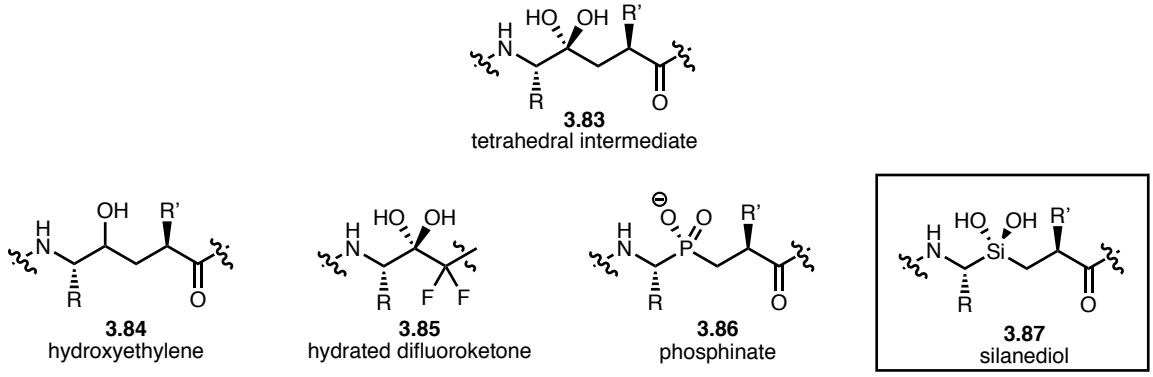
In the report by Denmark, the synthesis of nonracemic allylic organosilanoate **3.78** required nine synthetic steps, including an enzymatic resolution. Nonracemic geminal silylboronates might provide a streamlined route to **3.78** for the elegant allylic cross-coupling developed by Denmark, amongst other uses of nonracemic allylic organosilanes. From nonracemic geminal silylboronate **3.80**, using the conditions developed by Aggarwal for the Zweifel olefination might produce nonracemic allylic organosilane **3.81** with the indicated olefin geometry (Scheme 3.25). Subsequent removal of the phenyl group from silicon and hydrolysis might provide the nonracemic allylic organosilanol **3.82**. If a one-step, catalytic route to **3.80** could be developed, the cross-coupling precursor **3.82** would be produced in a streamlined four synthetic steps without the need of an enzymatic resolution.

Scheme 3.25 Proposed Streamlined Synthesis of Nonracemic Allylic Silanol



In addition to synthetic organic chemistry, organosilanes have been incorporated into drug targets in the pharmaceutical industry. Silicon has been widely used as a bioisostere to carbon due to the similar covalent bonding and geometry. The similar bonding and geometry can be exploited to increase the lipophilicity of drugs by incorporating silicon instead of carbon.[42] In addition to the advantage of increased lipophilicity, Skrydstrup and coworkers have done extensive studies on silanediol motifs as bioisosteres for the tetrahedral intermediate involved in enzymatic hydrolysis (Scheme 3.26).[43] Hydroxyethylene (**3.84**), hydrated difluoroketone (**3.85**), phosphinate (**3.86**) and silanediol motifs (**3.87**) are commonly explored tetrahedral intermediates in the pharmaceutical industry. Silanediol motifs have received considerable attention, most notably in the development of peptide mimics.

Scheme 3.26 Common Tetrahedral Intermediates as Bioisosteres



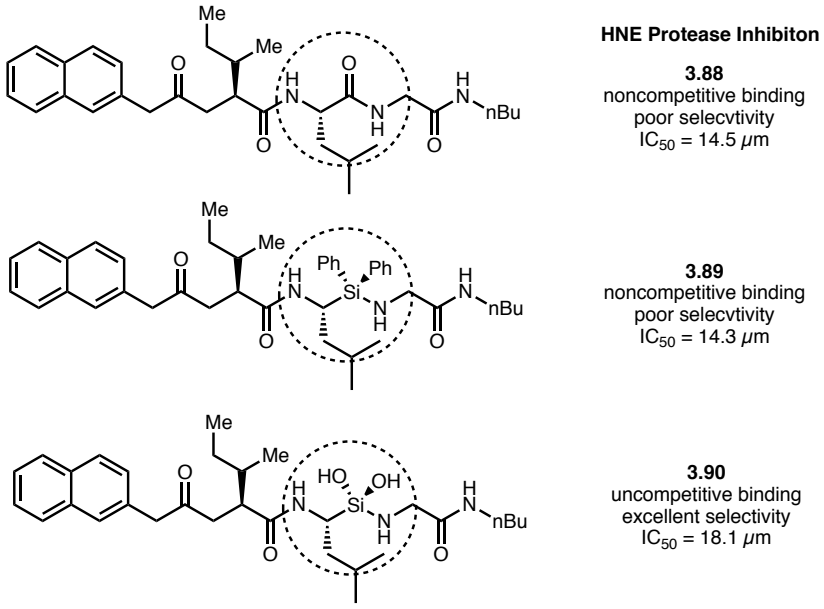
Silanediols as peptide mimics is highlighted by inhibition studies of a HNE protease, an important protein for peptide degradation, studied by Skrydstrup and

[42] a) Mills, J. S.; Showell, G. A. *Expert Opin. Invest. Drugs* **2004**, *13*, 1149-1157 b) Reḿond, E.; Martin, C.; Martinez, J.; Cavelier, F. *Chem. Rev.* **2016**, *116*, 11654-11684 c) Ramesh, R.; Reddy, D. S. *J. Med. Chem.* **2017**, *ASAP* DOI:10.1021/acs.jmedchem.7b00718

[43] a) Nielsen, L.; Skrydstrup, T. *J. Am. Chem. Soc.* **2008**, *130*, 13145-13151 b) Hernandez, D.; Lindsay, K. B.; Nielsen, L.; Mittag, T.; Bjerglund, K. Friis, S.; Mose, R.; Skrydstrup, T. *J. Org. Chem.* **2010**, *75*, 3283-3293

coworkers (Scheme 3.27).[44] Peptide **3.88** underwent noncompetitive binding of the protease with high potency, but suffered from poor selectivity. The same results were observed with the diphenylsilane motif **3.89**. However, switching to the silanediol motif **3.90** changed the mode of inhibition entirely to uncompetitive binding. The change in the mode of protein inhibition produced excellent selectivity while maintaining similar potency. The study by Skrydstrup reinforces the increasing use of silicon in the pharmaceutical industry for the synthesis of carbon bioisosteres, silanediol motifs as well α-silyl amino acids.

Scheme 3.27 Inhibition Studies of HNE Protease by Silanediol Motifs

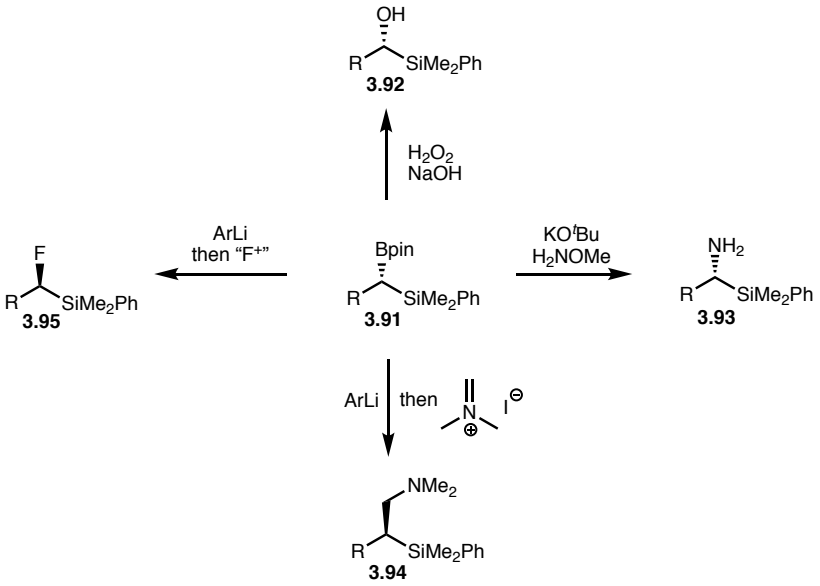


The incorporation of nonracemic organosilanes into pharmaceutically relevant molecules expands the potential for nonracemic geminal silylboronates to have a profound impact not only in synthetic organic chemistry but in drug development. These nonracemic geminal silylboronates have the potential to undergo a wide array of the known

[44] Min, G. K.; Hernandez, D.; Skrydstrup T. *Acc. Chem. Res.* **2013**, *46*, 457-470

organoboronate functionalizations[28] to then incorporate functionalized silicon-containing carbon stereocenters into products (Scheme 3.28). To highlight a few of many potential examples, oxidation might produce the nonracemic silyl alcohols (**3.92**) and amination might afford silyl amines (**3.93**). The amination of geminal silylboronates might provide a streamlined synthesis of the nonracemic silyl amine derivative that Skrydstrup and coworkers employed for the aforementioned studies. Activation of the geminal silylboronate by employing conditions developed by Aggarwal and coworkers and nucleophilic addition to Eschenmosher salt might generate nonracemic β-amino organosilanes (**3.94**). In addition to Eschenmosher salt, nucleophilic addition to electrophilic fluorinating reagents could allow access to fluorinated nonracemic organosilanes (**3.95**) combining two widely used bioisosteres. Nonracemic geminal silylboronates have potential reactivity to be widely explored and developed for the synthesis of pharmaceutically relevant molecules.

Scheme 3.28 Synthetic Utility of Nonracemic Geminal Silylboronates



3.3 Development of an Enantioselective Hydrosilylation of Alkenyl Boronates for the Synthesis of Nonracemic Geminal Silylboronates[45]

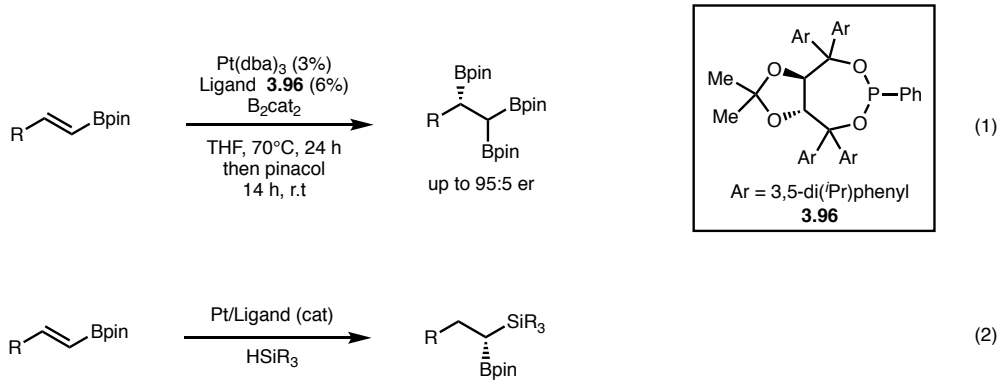
3.3.1 Reaction Discovery, Optimization, and Scope[45]

The development of a new method for the enantioselective hydrosilylation of functionalized olefins might represent a significant addition to synthetic organic chemistry. More specifically, a regio- and enantioselective hydrosilylation of alkenyl boronates for the synthesis of nonracemic geminal silylboronates could be powerful based on the aforementioned synthetic utility. Based on precedent from Morken and coworkers on the enantioselective diboration of alkenyl boronates[46], the hydrosilylation of alkenyl boronates was explored. In the diboration report, a platinum-phosphonite catalyst effectively promoted the enantioselective diboration[47] of alkenyl boronates with bis(catecholato)diboron (Scheme 3.29, eq. 1); subsequent boron ester exchange with pinacol, afforded nonracemic tris(organoboronates) with excellent enantioselectivity. It was hypothesized that by simply replacing the diboron reagent with an organosilane could allow for an enantioselective hydrosilylation for the synthesis of nonracemic geminal silylboronates (Scheme 3.29, eq. 2). Realization of this hypothesis, assuming well precedented "hydride-first" insertion[48], would rely on the formation of a stabilized α-boryl-

[45] Szymaniak, A. A.; Zhang, C.; Coombs, J. R.; Morken, J. P. *ACS Catal.* **2018**, *8*, 2897-2901
[46] Coombs, J. R.; Zhang, L.; Morken, J. P. *J. Am. Chem. Soc.* **2014**, *136*, 16140-16143
[47] Coombs, J. R.; Haeffner, F.; Kliman, L. T.; Morken, J. P. *J. Am. Chem. Soc.* **2013**, *135*, 11222-11231
[48] a) Chalk, A. J.; Harrod, J. F. *J. Am. Chem. Soc.* **1965**, *87*, 16-21 b) Chalk, A. J.; Harrod, J. F. *J. Am. Chem. Soc.* **1965**, *87*, 1133-1133 c) Taylor, R. B.; Roy, A. K. *J. Am. Chem. Soc.* **2002**, *124*, 9510-9524 d) Taige, M. A.; Ahrens, S.; Strassner, T. *J. Organomet. Chem.* **2011,** *696*, 2918-2927 e) Meister, T. K.; Riener, K.; Gigler, P.; Stohrer, J.; Herrmann, W. A.; Kuhn, F. E. *ACS Catal.* **2016**, *6,* 1274-1284

organoplatinum intermediate. As described in Chapter 1 of this dissertation, the formation of α-boryl organometallic species and α-boryl anions benefit from stabilization by the adjacent boron group. For the insertion into an alkenyl organoboronate, this stabilization might dictate regioselectivity to form an α-boryl organoplatinum species and afford a geminal silylboronate.

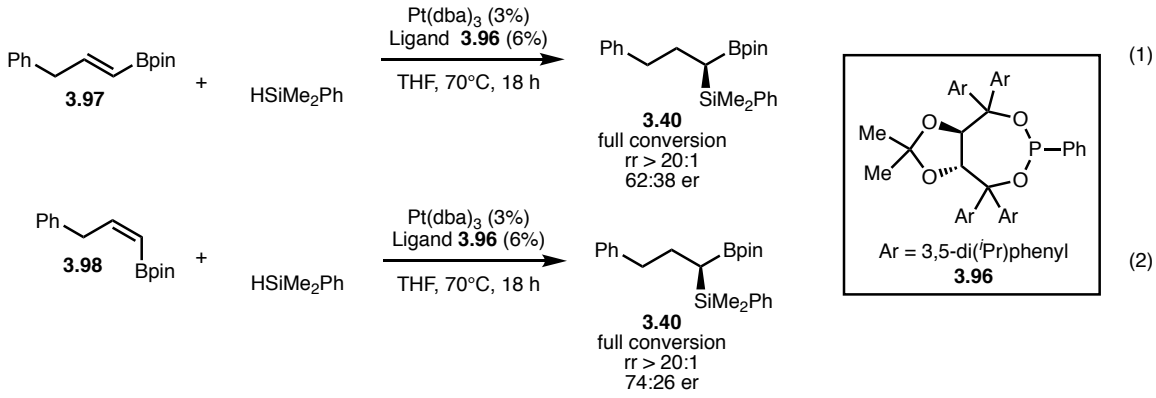
Scheme 3.29 Inspiration for the Development of an Enantioselective Hydrosilylation of Alkenyl Boronates



To probe this hypothesis, the experiments in Scheme 3.30 were conducted employing similar conditions to the enantioselective diboration of alkenyl boronates. With dimethylphenylsilane used as the organosilane source, the platinum-catalyzed hydrosilylation furnished geminal silylboronate **3.40** with full conversion and complete regiocontrol (Scheme 3.30, eq. 1). The initial hydrosilylation of (*E*)-alkenyl boronate **3.97** produced geminal silylboronate **3.40** with modest enantioinduction. Under the same reaction conditions, (*Z*)-alkenyl boronate **3.98** provided similar reactivity, but with a slight boost in enantioselectivity. (Scheme 3.30, eq. 2). Surprisingly, the two olefin isomers of starting material resulted in the same enantiomer of product. The observed stereoconvergence to one enantiomer suggests that the catalyst is not sensitive to the

orientation of the pinacol boronate group. Instead, the catalyst reacts with the same face of the olefin with the benzyl substituent aligned similarly for both isomers of substrate.[49a]

Scheme 3.30 Initial Discovery of a Platinum-Catalyzed Enantioselective Hydrosilylation of Alkenyl Boronates



Even though the (*Z*)-alkenyl boronate gave higher enantioselectivity, the synthesis of these boronates starting materials is less developed than for the *E* isomer.[49b] There have been a plethora of methods developed for the synthesis of (*E*)-alkenyl boronates through alkyne hydroborations, borylation reactions, a boron-Wittig reaction amongst other methods.[50] Taking this into account, it was highly desirable to optimize the reaction conditions for reaction of the readily prepared (*E*)-alkenyl boronates

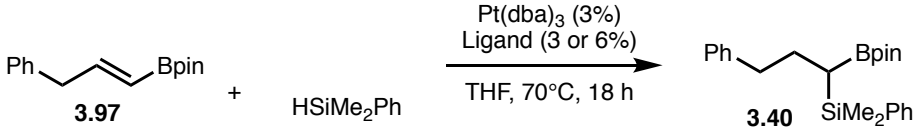
The process of optimizing the platinum-catalyzed hydrosilylation of *(E)*-alkenyl boronates began through first investigating general classes of chiral ligands for the reaction (Table 3.3). Employing commonly used chiral monodentate ligand (*S)*-MonoPhos (**3.99**)

[49] a) Park, J. K.; Lackey, H. H.; Ondrusek, B. A.; McQuade, D. T. *J. Am. Chem. Soc.* **2011**, *133,* 2410-2413 b) Obligacion, J. V.; Neely, J. M.; Yazdani, A. N.; Pappas, I. Chirik, P. J. *J. Am. Chem. Soc.* **2015**, *137*, 5855-5858 and references within

[50] For recent reviews: a) Barbeyron, R.; Benedetti, E.; Cossy, J.; Vasseur, J. –J.; Arseniyadis, S.; Smietana, M. *Tetrahedron* **2014**, *70*, 8431-8452 b) Yoshida, H. *ACS Catal.* **2016**, *6*, 1799-1811. For recent publications and references within: a) Ang, N. W. J.; Buettner, C. S.; Docherty, S.; Bismuto, A.; Carney, J. R.; Docherty, J. H.; Cowley, M. J.; Thomas, S. P. *Synthesis* **2018**, *50*, 803-808 b) Murray, S. A.; Luc, E. C. M.; Meek, S. J. *Org. Lett.* **2018**, *20*, 469-472 c) Coombs, J. R.; Zhang, L.; Morken, J. P. *Org. Lett.* **2015**, *17*, 1708-1711

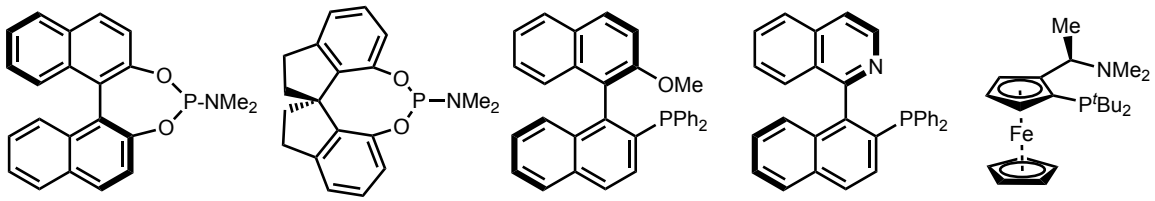
afforded geminal silylboronate product **3.40** although the reaction was racemic (Table 3.3, entry 2). Monodentate ligand (*R*)-SiPhos (**3.100**) resulted in no product formation (Table 3.3, entry 3). Hemilabile bidentate ligands were of interest as these types of ligands have been employed in palladium-catalyzed olefin hydrosilylations.[11] Analyzing the ligand used by Hayashi for the palladium-catalyzed hydrosilylation, *(R)*-OMe-MOP (**3.101**), resulted in trace product formation (Table 3.3, entry 4). (*R*)-Quinap (**3.102**) also resulted in no product formation (Table 3.3, entry 5). Lastly, using hemilabile bidentate ligand PPFA (**3.103**) resulted in substantial product formation, although once again product **3.40** was racemic (Table 3.3, entry 6). With these data, the TADDOL-derived ligand class was chosen for further ligand optimization.

Table 3.3 Initial Investigation into Chiral Ligands for the Platinum-Catalyzed Enantioselective Hydrosilylation of Alkenyl Boronates



Entry	*Ligand*	*Yield **3.40** (%)*[a]	*e.r.*[b]
1	**3.96**	> 95	62:38
2	**3.99**	50	50:50
3	**3.100**	< 5	n.d.
4	**3.101**	< 10	n.d.
5	**3.102**	< 5	n.d.
6	**3.103**	42	50:50

[a]Yield determined by ^{1}H-NMR with respect to 1,1,2,2-tetrachloroethane as an internal standard.
[b]Enantiomer ratio determined on the oxidized silyl alcohol using chiral SFC analysis.

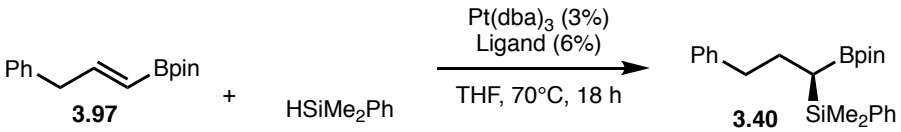


The first analysis of the TADDOL-derived ligand backbone focused on the aryl substituents of the phosphonite ligands. Decreasing the steric bulk of the TADDOL-derived phosphonite aryl substituents from 3,5-di(*i*-propyl)phenyl (**3.96**) to phenyl (**3.104**) substitution resulted in an increase in enantioselectivity (Table 3.4, entry 1 vs. 2). Further tuning the aryl substituent to a 3,5-xylyl (**3.105**) group resulted in a further increase in enantioselectivity (Table 3.4, entry 3). With the aryl substitutions of ligands **3.104** and **3.105**, the electronic properties of the phosphorus atom in these ligands was analyzed by employing phosphoramidite ligands in the reaction. Phenyl-substituted pyrrolidine-derived phosphoramidite (**3.106**) resulted in a significant increase in enantioselectivity as compared to the phosphonite analog (Table 3.4, entry 4 vs. 2). A similar trend was observed with the 3,5-xylyl substituted phosphoramidite (**3.107**) resulting in higher enantioselectivity (Table 3.4, entry 5 vs. 3). Ligand **3.107** also achieved the highest enantioselectivity yet at a 89:11 ratio. The increased enantioselectivity with phosphoramidite ligands might be due to better ability to donate to a platinum (II) oxidative addition adduct. BINOL-derived phosphoramidite ligands have been suggested to be slightly weaker donors than tricyclohexylphosphine.[51] Having a better donating ligand might result in a stronger, shorter Pt-P bond thus creating a more rigid chiral environment. The TADDOL-derived phosphoramidite ligand class was then further analyzed by varying the substitution on the nitrogen group. Replacing the pyrrolidine substituent with a dimethylamino group phosphoramidite (**3.108**) resulted in similar efficiency and enantioselectivity (Table 3.4, entry 6 vs. 5). However, extending the steric bulk to diethylamino (**3.109**) resulted in a significant decrease in both reactivity and

[51] Filipuzzi, S.; Pregosin, P. S.; Albinati, A.; Rizzato, S. *Organometallics* **2006**, *25*, 5955-5964

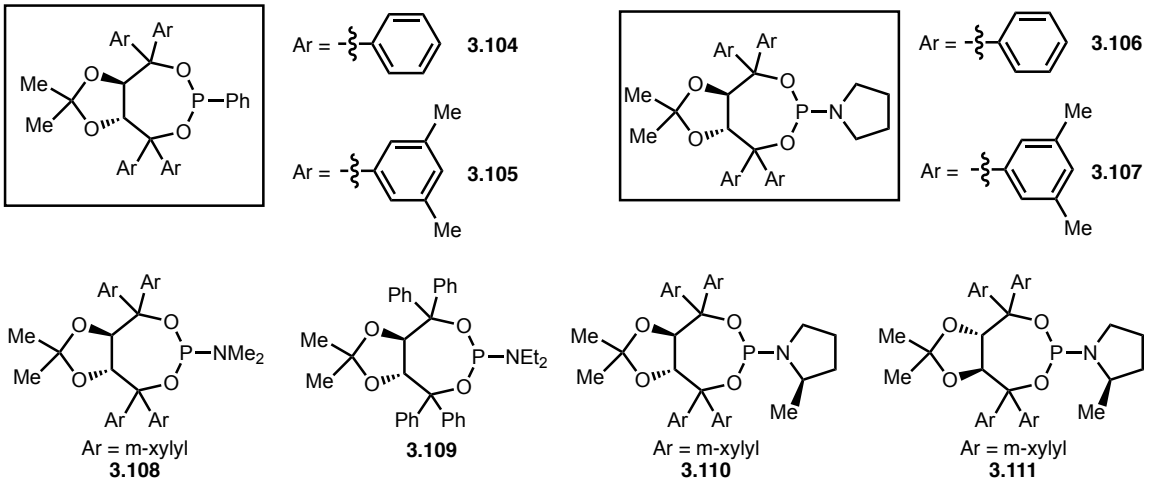
enantioselectivity (Table 3.4, entry 7). Lastly, incorporation of stereogenicity on the nitrogen substituent was studied. Proline-derived ligand **3.110** resulted in similar enantioselectivity as the parent pyrrolidine substitution (Table 3.4, entry 8). The opposite relative configuration of the two stereochemical elements was analyzed with ligand **3.111**. Probing the opposite configuration resulted in a substantial match-mismatch case with the other stereocenter on the ligand and resulted in a significantly lower enantioselectivity (Table 3.4, entry 9).

Table 3.4 Investigation of TADDOL-Derived Ligands for the Platinum-Catalyzed Enantioselective Hydrosilylation of Alkenyl Boronates



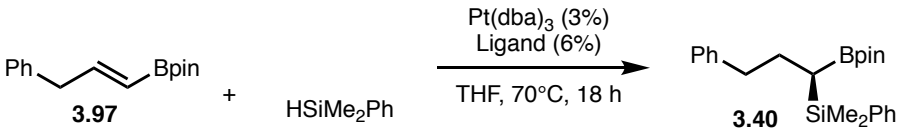
Entry	*Ligand*	*Yield **3.40** (%)*[a]	*e.r.*[b]
1	**3.96**	> 95	62:38
2	**3.104**	> 95	76:24
3	**3.105**	> 95	85:15
4	**3.106**	70	86:14
5	**3.107**	> 95	89:11
6	**3.108**	80	88:12
7	**3.109**	40	58:42
8	**3.110**	60	90:10
9	**3.111**	70	30:70

[a]Yield determined by ^{1}H-NMR with respect to 1,1,2,2-tetrachloroethane as an internal standard.
[b]Enantiomer ratio determined on the oxidized silyl alcohol using chiral SFC analysis.



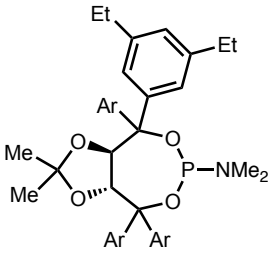
Knowing that the TADDOL-derived phosphoramidite ligands were more selective than the phosphonite analogs in the platinum-catalyzed hydrosilylation of alkenyl boronates, the aryl substituents were further investigated. Employing -3,5-di(ethyl)phenyl substituted phosphoramidite (**3.112**) showed that subtle increases in the steric component from 3,5-xylyl substitution results in a substantial decrease in enantioselectivity (Table 3.5, entry 3 vs 2). It is worth noting that for this ligand investigation, pyrrolidine and dimethylamino derived phosphoramidite ligands did not result in statistically significant changes in enantioselectivity (see Table 3.4). The dimethylamino phosphoramidite ligands used in this analysis were employed since the ligands were previously synthesized in our laboratory. Further increasing the steric encumbrance of the aryl substituents to 3,5-di(*i*-propyl)phenyl (**3.113**) and 3,5-di(*t*-butyl)phenyl (**3.114**) resulted in increasingly diminished enantioselectivity (Table 3.5, entries 4-5). Relocating the steric bulk to the *para* position of the arene with *p*-tolyl ligand (**3.115**) resulted in a similar outcome as with the parent phenyl-substituted phosphoramidite (Table 3.5, entry 6 vs. 1).

Table 3.5 Investigation of the Aryl Substituents of the TADDOL-Derived Phosphoramidite Ligands

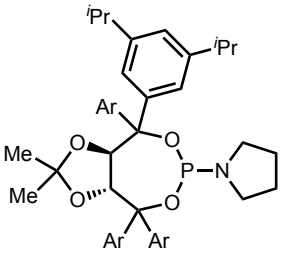


Entry	*Ligand*	*Yield **3.40** (%)*[a]	*e.r.*[b]
1	**3.106**	70	86:14
2	**3.107**	> 95	89:11
3	**3.112**	> 95	78:22
4	**3.113**	> 95	72:28
5	**3.114**	> 95	64:36
6	**3.115**	90	84:16

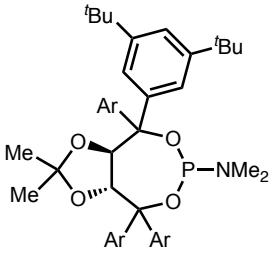
[a]Yield determined by ^{1}H-NMR with respect to 1,1,2,2-tetrachloroethane as an internal standard.
[b]Enantiomer ratio determined on the oxidized silyl alcohol using chiral SFC analysis.



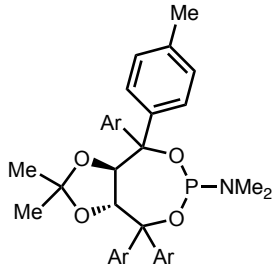
3.112



3.113



3.114



3.115

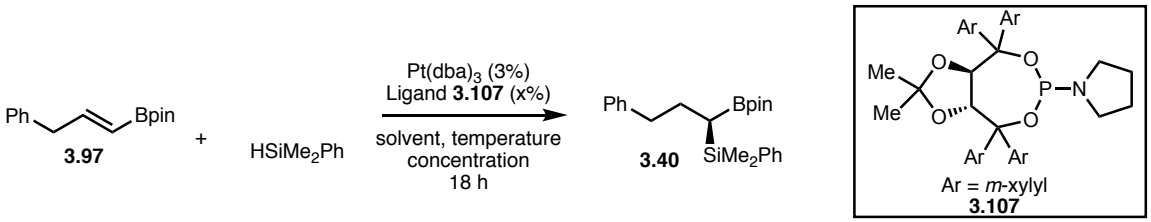
To achieve higher enantioselectivity from ligand development, further manipulation of the steric bulk at the *meta* positions of the arene, but with similar steric parameters as *xylyl* substitution was necessary. However, before undertaking further ligand design, a more in depth analysis of the reaction conditions was conducted.

In an effort to increase the enantioselectivity, changing the reaction temperature was first investigated. Decreasing the temperature of the platinum-catalyzed hydrosilylation with ligand **3.107** to 50°C did not result in an increase in enantioselectivity (Table 3.6, entry 2). Further decreasing the temperature to room temperature did produce

a boost in enantioselectivity but the yield of **3.40** was very low (Table 3.6, entry 3). Decreasing the amount of ligand improved the efficiency when the reaction was conducted at room temperature; but with a slight decrease in enantioselectivity (Table 3.6, entry 4). At room temperature with 6% ligand, the excess ligand equivalent might coordinate to platinum after oxidative addition. At elevated temperature, the ligand might readily coordinate and dissociate in equilibrium, allowing for olefin binding. However, at room temperature with excess ligand this equilibrium favors the doubly ligated platinum intermediate resulting in inhibition of catalysis. Tentatively supporting ligand inhibition, increasing the amount of ligand (1:4) at room temperature resulted in no product formation (Table 3.6, entry 5). With 6% ligand loading, increasing the concentration also improved the efficiency at room temperature while maintaining similar enantioselectivity (Table 3.6, entry 6 vs. 3). Increased reaction concentration might promote precipitation of free ligand, thus slowing down catalyst inhibition. Maintaining six-percent ligand loading, further analysis of the reaction conditions was conducted by using different solvents. The less polar solvent, methyl *tert*-butyl ether, produced higher efficiency and similar enantioselectivity at room temperature (Table 3.6, entry 7). The higher reactivity might be a result of heightened ligand insolubility in a less polar ethereal solvent. Diethyl ether was more efficient but slightly less selective than tetrahydrofuran (Table 3.6, entry 8). Different ethereal solvents such as 1,4-dioxane produced sluggish reaction efficiency (Table 3.6, entry 9). More polar solvent *N*,*N*-dimethylformamide produced both lower yield and enantioselectivity (Table 3.6, entry 10). 1,4-Dioxane and DMF might coordinate to platinum intermediates and slow down catalysis. With methyl *tert*-butyl ether being most efficient and enantioselective at room temperature, the temperature was further

decreased to 4°C. However, at this temperature the reaction yield suffered significantly and actually produced lower enantioselectivity (Table 3.6, entry 11). Trying to improve the reaction at 4°C by lowering the ligand-loading in methyl *tert*-butyl ether, resulted in much lower enantioselectivity (Table 3.6, entry 12). The worse reactivity at 4°C might be a result of decreased ligand solubility and dissociation from platinum allowing for a background reaction to occur. From investigation of the reaction conditions, methyl *tert*-butyl ether as the solvent and 6% ligand loading with 3% platinum complex were chosen as optimal for the hydrosilylation.

Table 3.6 Investigation of the Reaction Conditions with Ligand 3.107

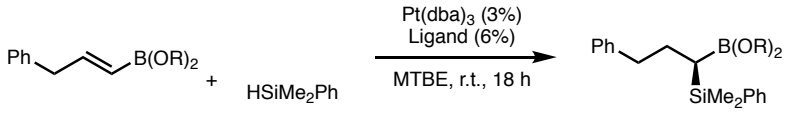


Entry	*Temp. (°C)*	*Solvent*	*Concentration (Molar)*	*Ligand %*	*Yield **3.40** (%)*[a]	*e.r.*[b]
1	70	THF	0.2	6	> 95	89:11
2	50	THF	0.2	6	> 95	88:12
3	r.t.	THF	0.2	6	14	93:7
4	r.t.	THF	0.2	3.2	71	91:9
5	r.t.	THF	0.2	12	< 5	n.d.
6	r.t.	THF	0.67	6	73	91:9
7	r.t.	MTBE	0.67	6	90	91:9
8	r.t.	Et_2O	0.67	6	89	89:11
9	r.t.	1,4-dioxane	0.67	6	40	89:11
10	r.t.	DMF	0.67	6	57	84:16
11	4	MTBE	0.67	6	24	87:13
12	4	MTBE	0.67	3.2	45	72:28

[a]Yield determined by ^{1}H-NMR with respect to 1,1,2,2-tetrachloroethane as an internal standard.
[b]Enantiomer ratio determined on the oxidized silyl alcohol using chiral SFC analysis.

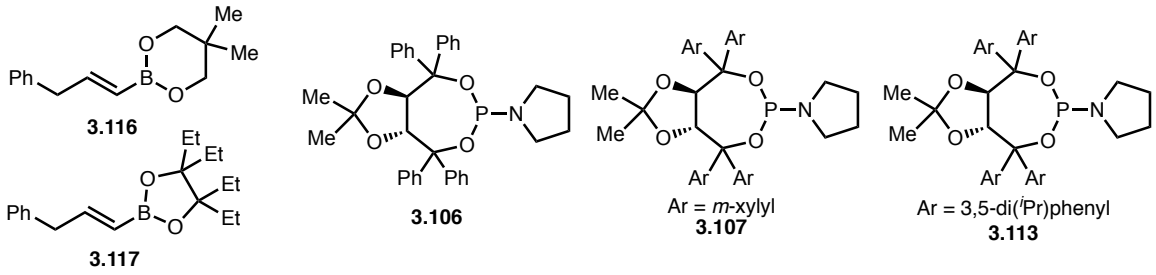
Further analysis of the reaction conditions was conducted by employing different diol ligands on the alkenyl boronate with a variety of phosphoramidite ligands. With phenyl substituted phosphoramidite ligand **3.106**, reaction of neopentyl boronic ester **3.116** occured in low reaction yield and significantly diminished enantioselectivity (Table 3.7, entry 1). Optimal 3,5-xylyl ligand **3.107** reestablished higher enantioselectivity but the reaction efficiency still suffered (Table 3.7, entry 2). The result with ligand **3.107** produced comparable enantioselectivity to the pinacol boronic ester derived starting materials (Table 3.4, entry 5). Similarly to the pinacol boronic ester substrate, increasing the steric bulk to the 3,5-di(*i*-propyl)phenyl ligand (**3.113**) with substrate **3.116** resulted in a decrease in enantioselectivity (Table 3.7, entry 3). A derivative of pinacol, 3,4-diethyl-hexanediol, was synthesized (**3.117**) and subjected to the optimal reaction conditions. However, substrate **3.117** suffered from lower reactivity and enantioselectivity (Table 3.7, entry 4). Consequently, varying the organoboronate starting material generally resulted in lower reactivity and in most cases worse enantioselectivity.

Table 3.7 Investigation of the Nature of the Alkenyl Boronate for the Platinum-Catalyzed Enantioselective Hydrosilylation



Entry	*Ligand*	*Substrate*	*Yield (%)*[a]	*e.r.*[b]
1	**3.106**	**3.116**	36	60:40
2	**3.107**	**3.116**	37	88:12
3	**3.113**	**3.116**	26	80:20
4	**3.107**	**3.117**	63	81:19

[a]Yield determined by ^{1}H-NMR with respect to 1,1,2,2-tetrachloroethane as an internal standard.
[b]Enantiomer ratio determined on the oxidized silyl alcohol using chiral SFC analysis.

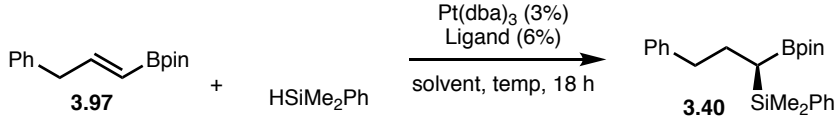


After further investigating the reaction conditions and nature of the alkenyl boronate for the platinum-catalyzed enantioselective hydrosilylation, a final ligand investigation was conducted. Pyrrolidine derived phosphoramidite ligands were chosen due to ease of synthesis and the inexpensive nature of the starting material. For the aryl groups of the TADDOL-derived ligands, it is hypothesized that σ-donating or withdrawing groups do not have a major impact on ligand electronics because the aryl substituents are three bonds removed from the phosphorus atom. However, the electronic nature of the arene ring could have an impact on conformational biases of the ligand structure through π-π type interactions. The 3,5-xylyl substituted phosphoramidite ligand was shown to be most optimal with the phenyl derivative being slightly less selective. Taking this into account, ligands with electronically different but sterically similar 3,5-substitutions were synthesized.

To probe the arene electronics, 3,5-di(fluoro)phenyl ligand (**3.118**) was synthesized and subjected to the optimal platinum-catalyzed hydrosilylation reaction conditions (methyl *tert*-butyl ether, room temperature). However, use of electronically differentiated ligand **3.118** resulted in no increase in enantioselectivity observed (Table 3.8, entry 1 vs. 2). The electronics were then adjusted, with the electronic donating aryl ether ligand 3,5-di(methoxy)phenyl ligand **3.119** being used. Employing the same reaction conditions

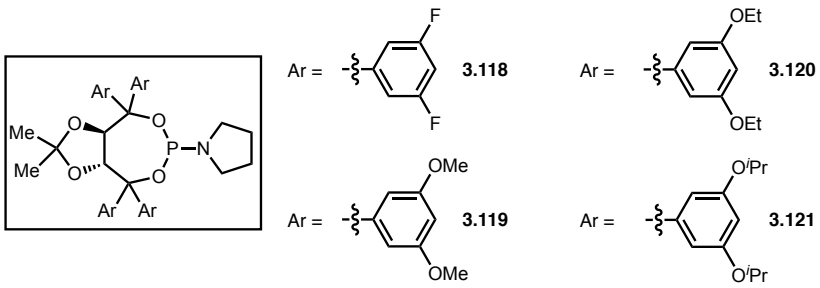
resulted in a slightly lower enantioselectivity compared to the 3,5-xylyl substitution (Table 3.8, entry 3). Extending the steric bulk was accomplished through the synthesis of 3,5-di(ethoxy)phenyl ligand **3.120**. Reaction conditions of tetrahydrofuran as the solvent at 70°C were chosen for ligand **3.120** since there were a greater number of ligands investigated with these conditions to draw comparison (Tables 3.4 and 3.5). Under these reaction conditions, ligand **3.120** provided good efficiency with a slight boost in enantioselectivity compared to the optimal ligand (Table 3.8, entry 5 vs. 4). Further increasing the sterics of the aryl ether substituent to 3,5-di(isopropoxy)phenyl (**3.121**) resulted in a slight decrease in enantioselectivity (Table 3.8, entry 6). With ligand **3.120** having achieved higher enantioselectivity, it was subjected to the optimal reaction conditions. At room temperature in methyl *tert*-butyl ether the platinum-catalyzed hydrosilylation produced higher enantioselectivity (Table 3.8, entry 7).

Table 3.8 Ligand Investigation for the Platinum-Catalyzed Enantioselective Hydrosilylation of Alkenyl Boronates



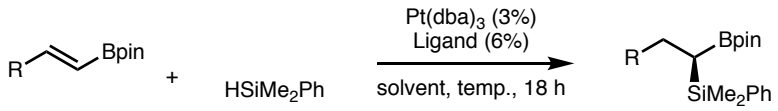
Entry	*Ligand*	*Solvent*	*Temp. (°C)*	*Yield **3.40** (%)*[a]	*e.r.*[b]
1	**3.107**	MTBE	r.t.	90	91:9
2	**3.118**	MTBE	r.t.	61	83:17
3	**3.119**	MTBE	r.t.	88	87:13
4	**3.107**	THF	70	> 95	89:11
5	**3.120**	THF	70	87	8:92[c]
6	**3.121**	THF	70	80	90:10
7	**3.120**	MTBE	r.t.	89	6:94[c]

[a]Yield determined by ^{1}H-NMR with respect to 1,1,2,2-tetrachloroethane as an internal standard.
[b]Enantiomer ratio determined on the oxidized silyl alcohol using chiral SFC analysis.
[c]*ent*-Ligand **3.120** used for the reaction



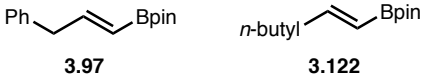
With a newly optimal ligand for the platinum-catalyzed enantioselective hydrosilylation of alkenyl boronate **3.97**, the reaction solvents were further investigated. Tetrahydrofuran, toluene and cyclohexane produced similar efficiencies and enantioselectivity as methyl *tert*-butyl ether (Table 3.9, entries 1-4). Only the chlorinated solvent 1,2-dichloroethane suffered with regards to both reactivity and enantioselectivity (Table 3.9, entry 5). It was then of interest for the alkenyl boronate to contain simple *n*-alkyl groups as these substrates would allow for greater generality of the reaction. Employing *n*-butyl substituted alkenyl boronate **3.122** with cyclohexane as the solvent and ligand **3.120** produced good yield and enantioselectivity (Table 3.9, entry 6). However, 3,5-di(isopropoxy)phenyl ligand (**3.121**) resulted in higher enantioselectivity for substrate **3.122** (Table 3.9, entry 7). Ligand **3.121** was then tested with a variety of solvents for *n*-butyl substrate **3.122.** Methyl *tert*-butyl ether, tetrahydrofuran and toluene all produced good reactivity and excellent enantioselectivity (Table 3.9, entries 8-10).

Table 3.9 Solvent Analysis with Optimal Ligands for the Platinum-Catalyzed Enantioselective Hydrosilylation of Alkenyl Boronates



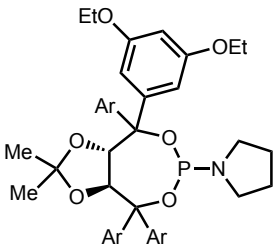
Entry	*Ligand*	*Substrate*	*Solvent*	*Yield (%)*[a]	*e.r.*[b]
1	**3.120**	**3.97**	MTBE	89	6:94[c]
2	**3.120**	**3.97**	THF	93	6:94[c]
3	**3.120**	**3.97**	toluene	94	7:93[c]
4	**3.120**	**3.97**	cyclohexane	99	6:94[c]
5	**3.120**	**3.97**	DCE	64	9:91[c]
6	**3.120**	**3.122**	cyclohexane	72	7:93[c]
7	**3.121**	**3.122**	cyclohexane	73	95:5
8	**3.121**	**3.122**	MTBE	99	95:5
9	**3.121**	**3.122**	THF	88	95:5
10	**3.121**	**3.122**	toluene	78	95:5

[a]Yield determined by ^{1}H-NMR with respect to 1,1,2,2-tetrachloroethane as an internal standard.
[b]Enantiomer ratio determined on the oxidized silyl alcohol using chiral SFC analysis.
[c]*ent*-Ligand **3.120** used for the reaction

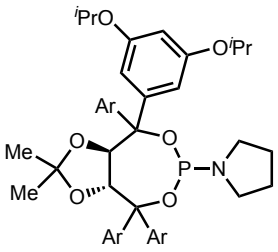


3.97

3.122



3.120



3.121

The results with substrates **3.97** and **3.122** show that the platinum-catalyzed enantioselective hydrosilylation is not sensitive to solvent choice. Solvent insensitivity is an appealing feature of the reaction and allows for potential telescoped reaction sequences that require specific solvents. Careful analysis of the data for both substrates showed that methyl *tert*-butyl ether was overall slightly more efficient for the reaction. More importantly, methyl *tert*-butyl ether was most efficient with *n*-butyl substrate **3.122** to

explore the generality of the reaction. Methyl *tert*-butyl ether also is an industrially friendly solvent as a safer choice for employing ethereal solvents.[52] Taking these features into account, methyl *tert*-butyl ether was chosen to explore the substrate scope of the enantioselective platinum-catalyzed hydrosilylation of alkenyl boronates.

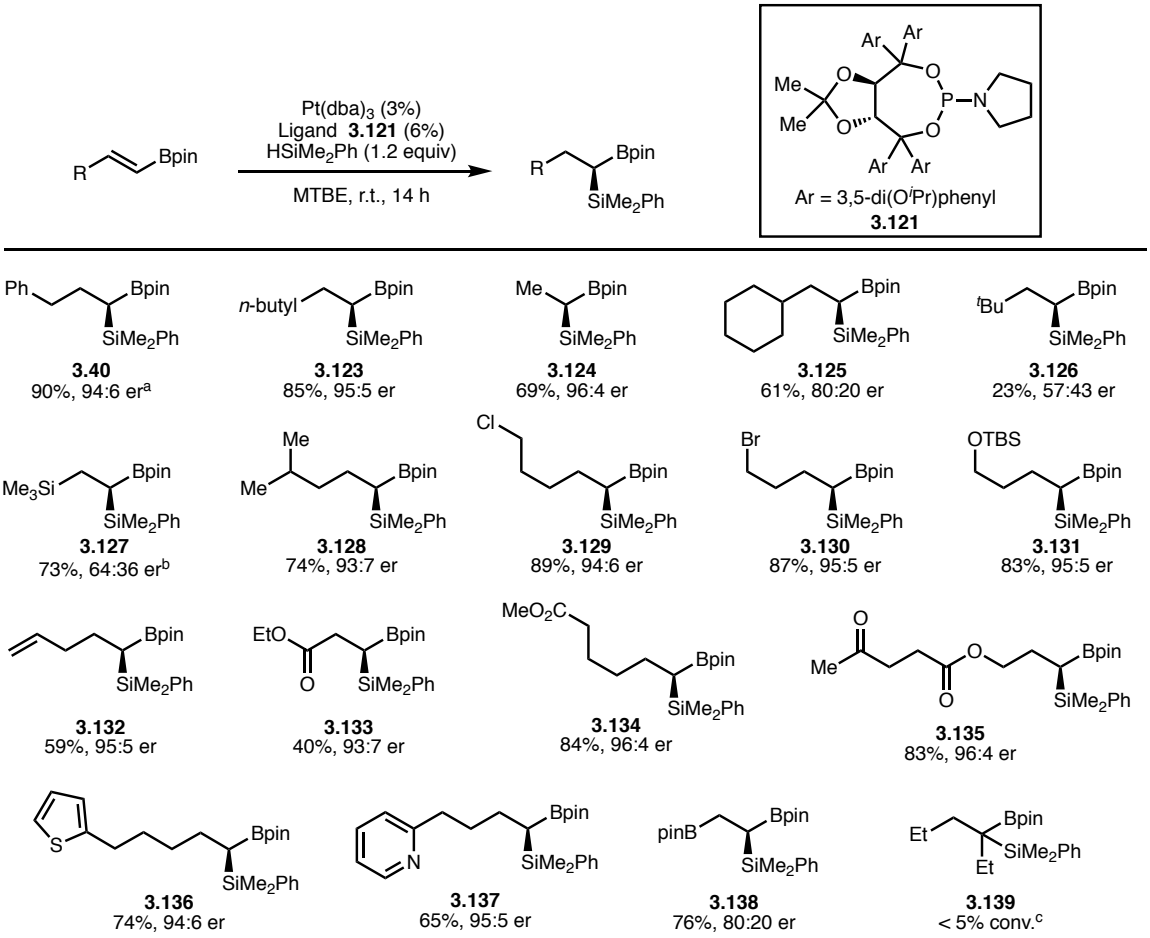
To explore the generality of the reaction, a variety of alkenyl boronates bearing different functionalities were synthesized. The reaction was carried out by pre-complexing tris(dibenzylideneacetone)platinum (0) and ligand **3.121** at 80°C for 15 minutes and subsequent cooling to room temperature. The reaction vial was then charged with the organosilane and alkenyl boronate for a room temperature reaction for 14 hours. It is worth noting that addition of the organosilane after the catalyst pre-complexation is essential. Addition of the organosilane during the catalyst pre-complexation resulted in lower reaction efficiency potentially due to catalyst dimerization after oxidative addition.

With the optimal conditions and reaction sequence developed, the scope of the reaction was explored as depicted in Table 3.10. The reaction tolerated both benzyl (**3.40**) and *n*-butyl (**3.123**) substituted alkenyl boronates with excellent reactivity and high enantioselectivity. Interestingly, simple vinyl boronic acid pinacol ester (**3.124**) engages in the reaction efficiently and with excellent enantioselectivity. Product **3.124** highlights a potentially synthetically useful methyl-substituted nonracemic geminal silylboronate. Addition of steric bulk to the alkenyl boronate (**3.125**, **3.126**) results in much lower reactivity and enantioselectivity. Even though the silicon group could also stabilize the platinum-carbon bond, trimethylsilyl substituted alkenyl boronate (**3.127**) maintains high chemoselectivity. Although from the increased steric encumbrance, product **3.127** suffers

[52] a) Henderson, R. K. *et al*. *Green. Chem*. **2011**, *13*, 854-862 b) Clark, J. H. *et al. Sustain Chem Process*, **2016**, *4*:7, 1-24

from lower enantioselectivity. Adjusting the steric bulk slightly further from the alkenyl boronate (**3.128**) reestablishes high reactivity and enantioselectivity. A variety of functional groups such as alkyl halides (**3.129**, **3.130**) and protected alcohols (**3.131**) are tolerated in the reaction with excellent yields and enantioselectivity. Interestingly, terminal olefins (**3.132**) can be incorporated into the substrate with excellent results and only trace terminal olefin hydrosilylation occurs. The observed chemoselectivity might be a result of the alkenyl boronate being a more polarized olefin and conjugating group. This polarization might make the alkenyl organoboronate more reactive towards hydrosilylation. β-Boryl ester substrates (**3.133**) can react with high enantioselectivity although with diminished yields a result of the regioisomeric insertion. Different ester substrates (**3.134**) and ketones (**3.135**) attached to the alkenyl boronates are tolerated with excellent reactivity and enantioselectivity. No carbonyl reduction is observed which is common with platinum/organosilane catalysis. Heterocycle containing substrates (**3.136, 3.137**) are also capable of undergoing the hydrosilylation with good reactivity and enantioselectivity. An interesting substrate, *trans*-1,2-diborylethylene engages in the reaction efficiently to synthesize 1,2-diboryl organosilane **3.138**. With the optimal catalyst system for mono-alkenyl boronates, the reaction to form **3.138** suffers from slightly diminished enantioselectivity. Lastly, at both room temperature and elevated temperatures, more substituted alkenyl boronates (**3.139**) fail to react under these conditions.

Table 3.10 Substrate Scope for the Platinum-Catalyzed Enantioselective Hydrosilylation of Alkenyl Boronates

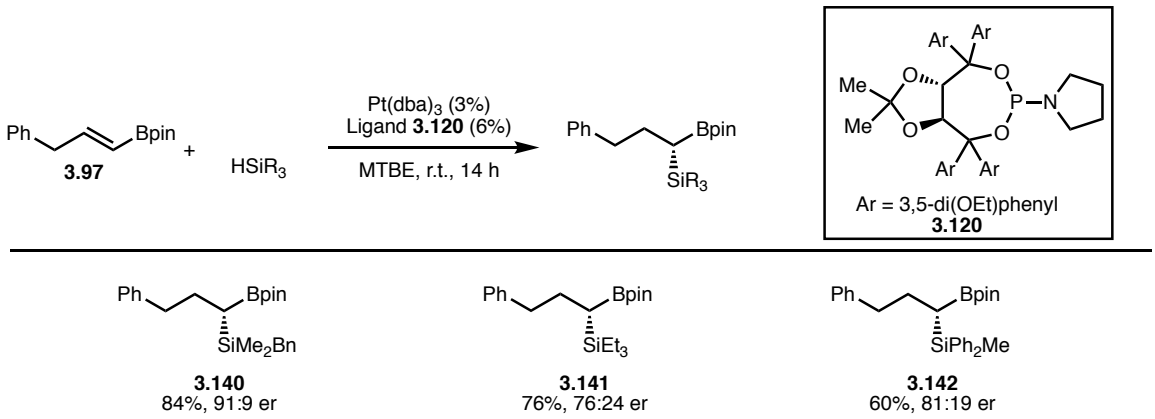


Isolated yields and enantiomer ratios are the average of two experiments. Enantiomer ratio determined using chiral SFC analysis on either directly the geminal silylboronate or the oxidized silyl alcohol. [a]Ligand **3.120** used for the reaction. [b]Reaction conducted at 70°C. [c]Reaction run at room temperature and 70°C.

With the scope of the reaction with alkenyl boronates explored, the nature of the organosilane reagent was then considered. Employing substrate **3.97** and optimal ligand **3.120**, benzyldimethylsilane (**3.140**) underwent the platinum-catalyzed hydrosilylation with good efficiency and comparable enantioselectivity as with dimethylphenylsilane. Benzyldimethylsilane reagents have been shown to be useful for Hiyama-cross couplings as the benzyl group is mildly hydrolyzed *in situ* to organofluorosilanes for

transmetallation.[53] More specifically, olefination of the organoboron moiety in **3.140** and mild hydrolysis of the benzylsilane group could allow for a more efficient synthesis of nonracemic allylic silanols for cross-coupling (Scheme 3.25).[41] With triethylsilane (**3.141**) enantioselectivity suffered in the reaction with ligand **3.120**. Methyldiphenylsilane (**3.142**) underwent the reaction with only moderately lower enantioselectivity than dimethylphenylsilane. The synthetic utility of methyldiphenylsilane could be displayed by a one-pot hydrosilylation and amination of the organoboronate to synthesize a silylamine. Hydrolysis of the diphenylsilane moiety would then produce an α-amino silanediol in three steps. These α-amino silanediols have been previously elaborated to be common bioisosteres in the pharmaceutical industry (Scheme 3.26).

Table 3.11 Scope of Organosilanes for the Platinum-Catalyzed Enantioselective Hydrosilylation of Alkenyl Boronates

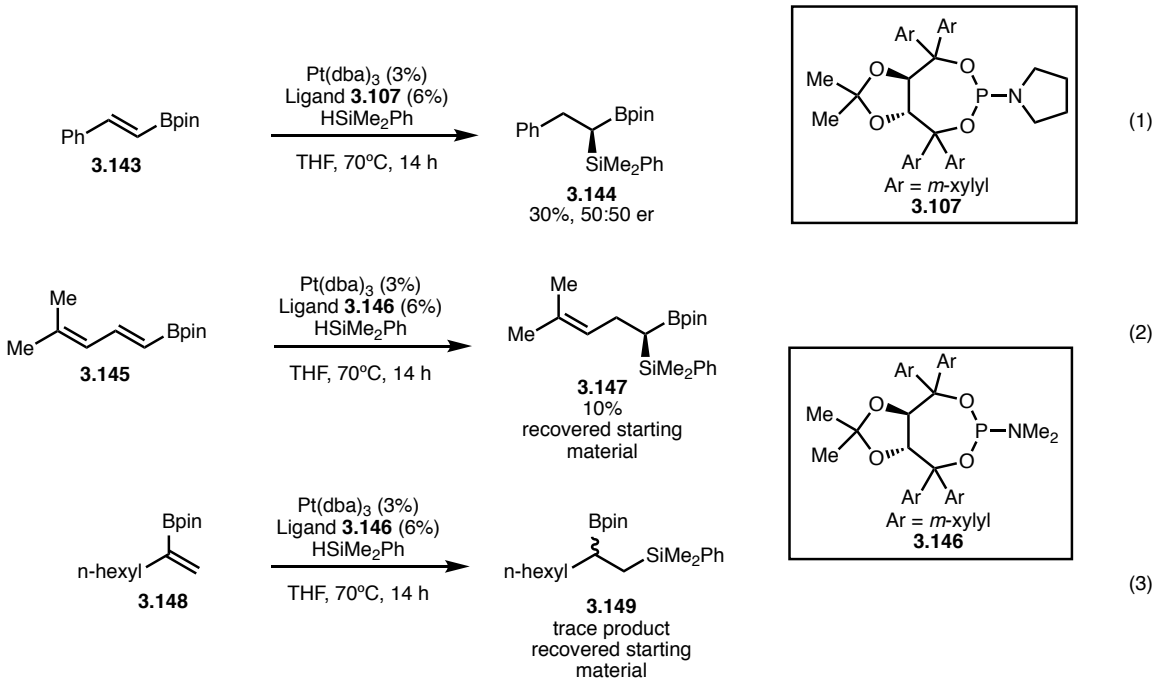


Isolated yields and enantiomer ratios are the average of two experiments. Enantiomer ratio determined using chiral SFC analysis on the oxidized silyl alcohol.

[53] For the utility of $BnMe_2Si$- group in cross-coupling, see: a) Machacek, M. R.; Ball, Z. T.; Trost, B. M. *Org. Lett.* **2003**, *5*, 1895-1898. b) Tymonko, S. A.; Denmark, S. E. *J. Am. Chem. Soc.* **2005**, *127*, 8004-8005. c) Nakao, Y.; Hiyama, T. *Chem. Soc. Rev.* **2011**, *40*, 4893-4901

While *trans*-1,2-disubtituted alkenyl boronates were shown to work well under these catalytic hydrosilylation conditions, it was of interest to explore other types of alkenyl boronates. Styrenyl organoboronate **3.143** underwent the platinum-catalyzed hydrosilylation with modest reactivity (Scheme 3.12, eq.1). Surprisingly, the reaction product was found to be racemic. The racemic outcome could be due the styrenyl substrate being a competent ligand for platinum, promoting dissociation of the chiral phosphine ligand. Additionally, the styrenyl subsrate might go through an alternative insertion into the Pt-Si bond, resulting in a non-selective reaction. The reactivity of styrenyl organoboronate **3.143** highslights that the platinum-catalyzed synthesis of nonracemic geminal silylboronates is a complementary approach to the copper catalysis developed by Hoveyda and coworkers. The copper catalysis was capable of producing geminal silylboronates when employing styrenyl substrates. Dienyl organoboronate **3.145** underwent the hydrosilylation reaction with severely diminished reactivity (Scheme 3.12, eq. 2). The diminished reactivity could be the result of insertion into the platinum-hydride to form a stabilized π-allyl platinum intermediate which might inhibit catalysis. Lastly, 1,1-disubstituted alkenyl boronate **3.148** also suffered from poor reactivity for the hydrosilylation (Scheme 3.12, eq. 3).

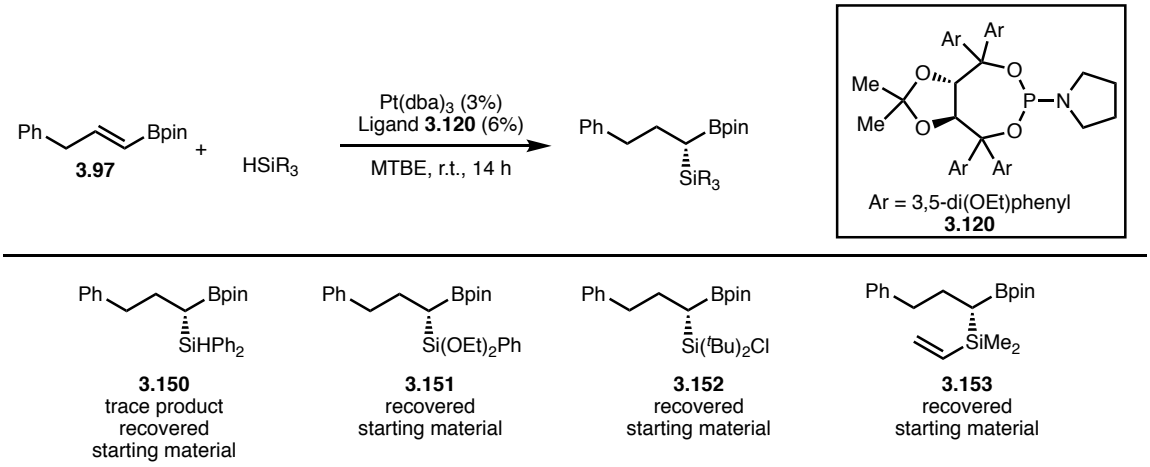
Table 3.12 Challenging Substrates for the Platinum-Catalyzed Enantioselective Hydrosilylation of Alkenyl Boronates



To further explore the utility of the platinum-catalyzed hydrosilylation of alkenyl boronates, it was of interest to expand the scope of the organosilane moiety. As alluded to earlier, the scope of organosilanes presented allow for the silicon moiety to be further transformed. However, the incorporation of chlorosilanes or alkoxysilanes into the reaction could be powerful as the silicon could be readily derivatized. Employing substrate **3.97** and optimal ligand **3.120**, the scope of different silanes was investigated. Diphenylsilane (**3.150**) only resulted in trace formation of the geminal silylboronate under these conditions. The low reactivity could be from potential competitive insertion into the product silicon-hydrogen bond, which may result in catalyst deactivation. Diethoxyphenylsilane (**3.151**) and chloro(di-*tert*-butyl)silane (**3.152**) resulted in no product formation under the depicted catalytic conditions. Both of these silane starting materials could suffer from competitive insertion into the silicon-oxygen and silicon-chlorine bonds

respectively, and inhibition of catalysis. Lastly, dimethylvinylsilane (**3.153**) also suffered from no product formation. While these silanes would have further increased the impact of the enantioselective hydrosilylation of alkenyl boronates through direct product functionalization, the organosilanes competent in the reaction allow for the further functionalization of the silicon moiety. With the scope of the platinum-catalyzed hydrosilylation of alkenyl boronates demonstrated, the synthetic utility of this process was investigated.

Table 3.13 Further Investigation to the Scope of Silanes for the Platinum-Catalyzed Enantioselective Hydrosilylation of Alkenyl Boronates



3.3.2 Synthetic Utility and Mechanistic Considerations[45]

As mentioned before, the synthesis of nonracemic geminal silylboronates is highly desirable for the application of these products towards the synthesis of functionalized stereocenters. The organoboronate moiety of the geminal silylboronate has the potential to undergo a wide variety of the transformations developed for organoboron reagents. Additionally, silicon's decreased reactivity in 1,2-metallate rearrangements can be taken advantage of for divergent functionalizations of the metal groups. Taking the reactivity differences into account, functionalizations of nonracemic geminal silylboronate **3.40** were undertaken. Oxidation of the organoboronate to silyl alcohol **3.154** proceeded with good yield and stereospecificity (Scheme 3.31). These silyl alcohol products have been shown to be useful chiral auxillaries for diastereoselective oxocarbenium ion allylation reactions.[54] Amination of the organoboronate moiety to silylamine **3.155** proceeded efficiently with good yield and enantiospecificity.[55] Silylamine products have received much attention in the pharmaceutical industry as described earlier. In addition to heteroatom incorporation, a modified procedure for the Matteson homologation afforded the nonracemic vicinal silylboronate **3.156** with good yield.[56] The effect of sodium triflate additives has been demonstrated to aid in organoboron "ate" complex formation through binding to the oxygen of the boron ligand and increasing the Lewis acidity of the organoboronate.[56b]

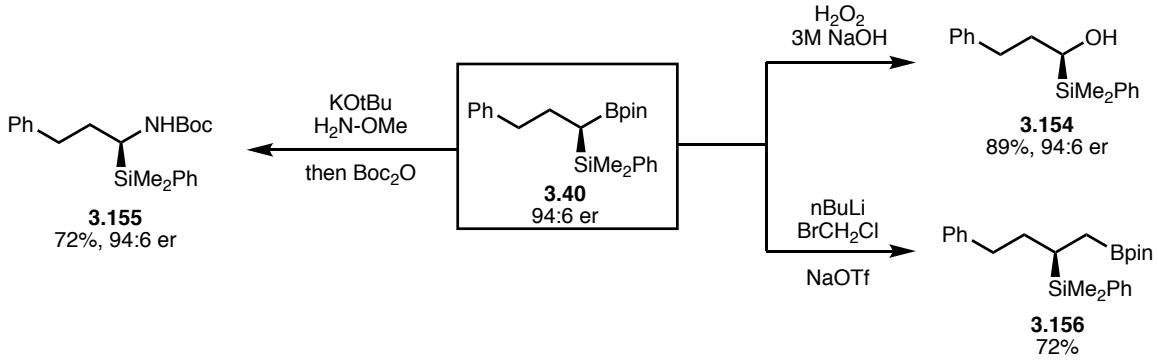
---

[54] Cossrow, J.; Rychnovsky, S. D. *Org. Lett.* **2002**, *4*, 147-150

[55] This is a modification of the following reference and its details will be reported separately: Mlynarski, S. N.; Karns, A. S.; Morken, J. P. *J. Am. Chem. Soc.* **2012**, *134*, 16449-16451

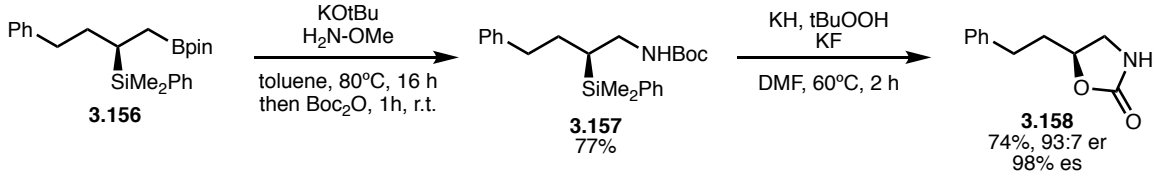
[56] (a) Mah, R. W. H.; Matteson, D. S. *J. Am. Chem. Soc.* **1963**, *85*, 2599-2603 (b) For effect of sodium triflate: Lovinger, G. J.; Aparece, M. D.; Morken, J. P. *J. Am. Chem. Soc.* **2017**, *139*, 3153-3160

Scheme 3.31 Functionalizations of Nonracemic Geminal Silylboronates



With the vicinal silylboronate, the divergent functionalizations of the organoboronate and organosilane groups was explored. Amination of the vicinal silylboronate **3.156** afforded the vicinal silylamine **3.157** with good yield after *Boc* protection of the nitrogen group. Subsequently, an anhydrous Tamao-Fleming oxidation[57] and cyclization on the *Boc* group afforded the oxazolidinone **3.158** with good yield and enantiospecificity. The aforementioned procedure could represent an efficient method for the preparation of nonracemic oxazolidinones that have differing substitution compared to the typical amino-acid derived oxazolidinones used as chiral auxillaries.

Scheme 3.32 Functionalization of the Organoboronate and Organosilane Groups

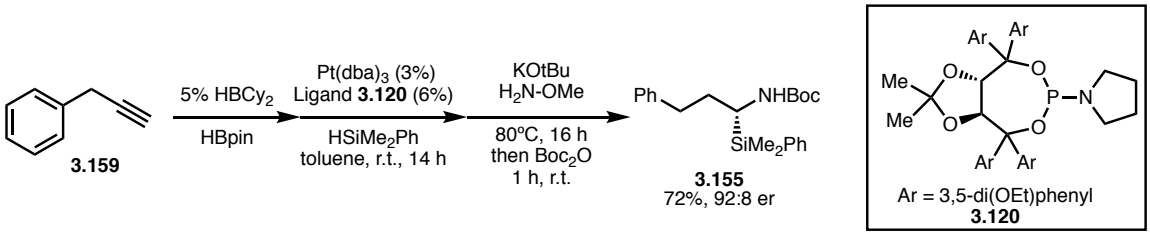


To further explore the utility of the platinum-catalyzed enantioselective hydrosilylation, it was of interest to explore a one-pot hydroboration-hydrosilylation procedure. To probe this, the reaction depicted in Scheme 3.33 was conducted. Starting

[57]) a) Smitrovich, J. H.; Woerpel, K. A. *J. Org. Chem.* **1996**, *61,* 6044-6046. b) Walleser, P.; Bruckner, R. *Eur. J. Org. Chem.* **2014**, *15*, 3210-3224

from commercially available 3-phenyl-1-propyne (**3.159**), a neat dicyclohexylborane catalyzed alkyne hydroboration[58] furnished the requisite alkenyl boronate. Next, the enantioselective platinum-catalyzed hydrosilylation was conducted in toluene and the one-pot procedure further extended to include amination of the organoboronate. Silylamine **3.155** was obtained in excellent yield and enantioselectivity. The one-pot procedure highlights the insensitivity of the hydrosilylation reaction to borane impurities and the ability to use different solvents in the reaction to accommodate for subsequent transformations.

Scheme 3.33 One-Pot Telescoped Synthesis of Silylamine

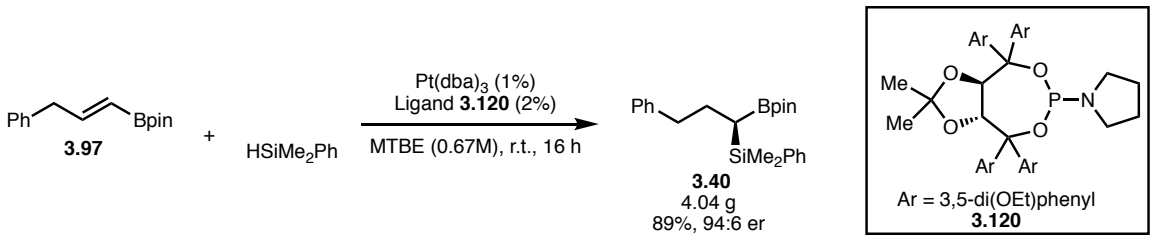


To broaden the applicability and utility of the reaction, it was of interest to conduct a large-scale, enantioselective hydrosilylation without the aid of a glove-box. To demonstrate this, the platinum pre-catalyst and ligand were weighed in the open air. The flask was then purged with nitrogen, the solvent introduced and the platinum catalyst stirred for fifteen minutes at 80°C. Subsequent cooling to room temperature and addition of the starting materials allowed for a reaction at room temperature for 16 hours. As depicted in Scheme 3.34, the reaction proceeded with excellent reactivity and enantioselectivity and delivered 4.04 grams of material without the aid of a glove-box. The large-scale reaction provided almost identical results to the small-scale reaction conducted

[58] Shirakawa, K.; Arase, A.; Hoshi, M. *Synthesis,* **2004**, *11*, 1814-1820

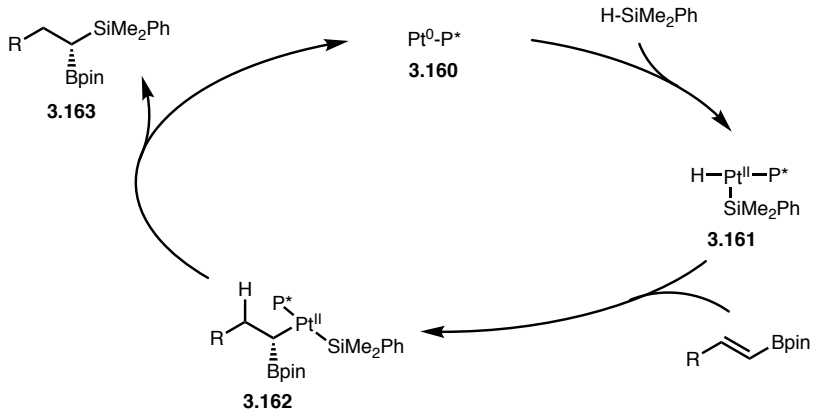
in the glove-box. It is worth noting that the catalyst-loading was reduced to 1% and the solvent volume reduced while maintaining high reactivity and enantioselectivity. These two features attest to the ability of this reaction to be conducted potentially on larger scales.

Scheme 3.34 Large-Scale, Glove-Box Free Platinum-Catalyzed Hydrosilylation



With the synthetic utility of the platinum-catalyzed hydrosilylation of alkenyl boronates for the synthesis of nonracemic geminal silylboronates demonstrated, the mechanism of the reaction was studied. It is proposed that the catalytic cycle begins with oxidative addition of the phosphine-ligated platinum (0) complex **3.160** with the organosilane to form platinum (II) complex **3.161** (Figure 3.1). Subsequently, enantiodetermining binding of the alkenyl boronate to platinum (II) complex **3.161** occurs. Assuming well-precedented "hydride first" olefin insertion[48] then forms the α-boryl stabilized organoplatinum (II) intermediate **3.162**. Reductive elimination furnishes the nonracemic geminal silylboronate **3.163** and regenerates platinum (0) complex **3.160** to restart the catalytic cycle.

Figure 3.1 Proposed Mechanism for the Platinum-Catalyzed Hydrosilylation of Alkenyl Boronates

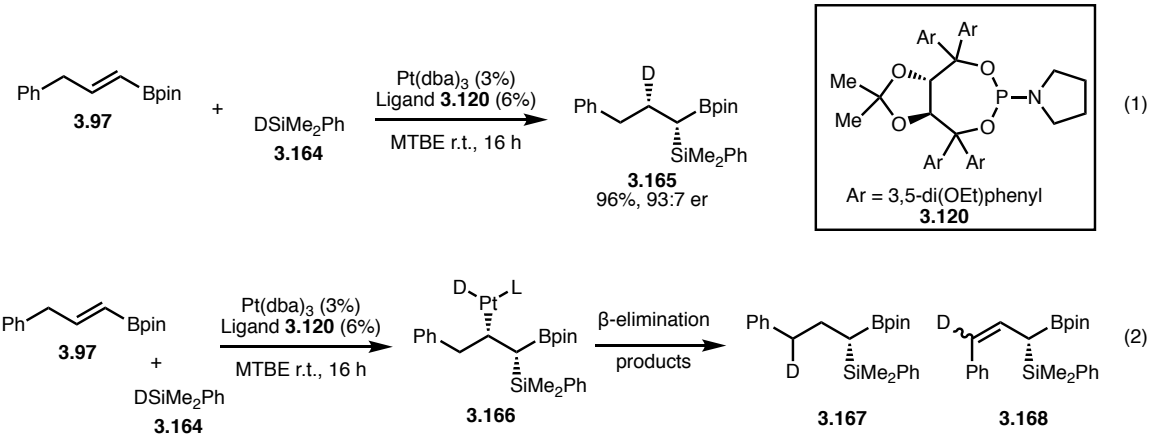


With alkenyl boronates being new substrates for the enantioselective hydrosilylation of olefins, it was of interest to study the alkenyl boronate insertion into the platinum-hydride. To probe this, deuterodimethylphenylsilane (**3.164**) was synthesized from the corresponding chlorodimethylphenylsilane and lithium aluminum deuteride.[59] Deuterodimethylphenylsilane was then used in the standard reaction conditions to reveal the deuterium incorporation and relative stereochemistry of the reaction product (Scheme 3.35, eq. 1). Analysis of the geminal silylboronate **3.165** by ^{1}H-NMR and ^{2}H-NMR showed that the reaction produced one diastereomer of **3.165** with no deuterium scrambling. While olefin insertion into a Pt-Si bond has been demonstrated, the reaction employed a bis(silyl)platinum complex and styrene at elevated temperatures (120°C) producing low yields.[60] In contrast, extensive studies recently by Roy[48c], Strassner[48d], and Kuhn[48e] in addition to theoretical studies by Sakaki[61] provide strong evidence for olefin insertion into the Pt-H bond in platinum-catalyzed hydrosilylations. In line with the 2,1-insertion into a

[59] Takale, B. S.; Tao, S. M.; Yu, X. Q.; Feng, X. J.; Jin, T.; Bao, M.; Yamamoto, Y. *Org. Lett.* **2014**, *16*, 2558-2561
[60] Yamashita, H.; Goto, M.; Tanaka, M. *Organometallics* **1997**, *16*, 4696-4704
[61] Mizoe, N.; Sugimoto, M.; Sakaki, S. *Organometallics* **1998**, *17*, 2510-2523

Pt-D observed by Kuhn[48e], if the hydrosilylation of alkenyl boronate **3.97** proceeded through a Pt-Si insertion, deuterium scrambling and olefin migration might be observed in some quantity as a consequence of β-elimination (Scheme 3.35, eq. 2). Intermediate **3.166** also has a heightened propensity to undergo β-elimination due to the benzylic C-H bonds forming a conjugated system. Taking into account the previous mechanistic work and no β-elimination products observed suggest olefin insertion into the Pt-H bond. Consequently, the deuterosilylation experiment supports the hypothesis that platinum-catalyzed enantioselective hydrosilylation of alkenyl boronates proceeds by insertion into the platinum-hydride to form a stabilized α-boryl organoplatinum (II) intermediate. The insertion also occurs by a *syn* addition as the relative configuration of the reaction product was confirmed by the synthesis of an authentic racemic sample.

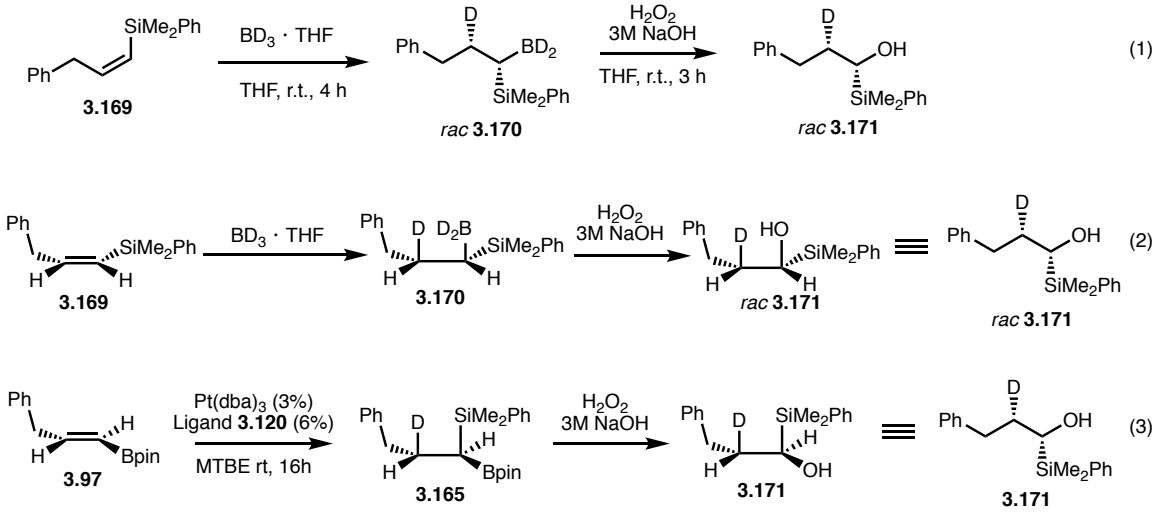
Scheme 3.35 Deuterosilylation Experiment for the Platinum-Catalyzed Hydrosilylation of Alkenyl Boronates



The authentic deuterosilylation product was synthesized by the deuteroboration of (*Z)*-alkenylsilane **3.169** which afforded deuteroorganoborane **3.170** (Scheme 3.36, eq. 1). Subsequent oxidation of the organoborane intermediate furnishes racemic deuterated silyl alcohol **3.171**. Analysis of this reaction shows that the deuteroboration of (*Z)*-alkenylsilane

3.169 produced the racemic *syn* deuterated silyl alcohol **3.171** (Scheme 3.6, eq. 2). Analysis of the platinum-catalyzed hydrosilylation from a *syn* insertion of the (*E*)-alkenyl boronate into the platinum-hydride furnished geminal silylboronate intermediate **3.165** (Scheme 3.36, eq. 3). After oxidation, the nonracemic *syn* silyl alcohol **3.171** was formed. Analysis of these two reaction products by ^{1}H-NMR showed that both reactions produced the same diastereomer. The ^{1}H-NMR data supports the hypothesis that the platinum-catalyzed hydrosilylation of alkenyl boronates undergoes a *syn* insertion likely to form an α-boryl stabilized organoplatinum (II) intermediate.

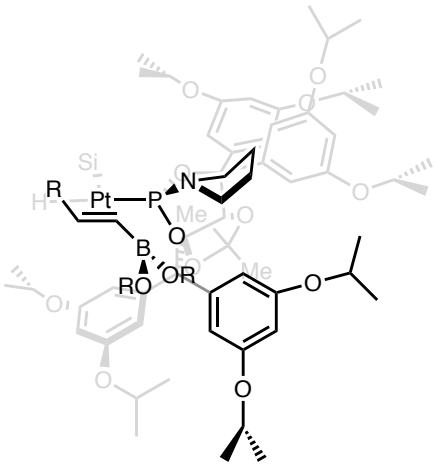
Scheme 3.36 Preparation of Authentic Deuterosilylation Product and Reaction Analysis



Having gained insight on the mechanism of the platinum-catalyzed hydrosilylation, it was of interest to understand the stereochemical outcome. A tentative model for enantioselectivity is proposed based upon the crystal structure of a platinum-TADDOL phosphonite complex used in the diboration of alkenes (Figure 3.2).[47] The model is proposed assuming olefin insertion in the platinum-hydride previously elaborated. It is thought that the critical steric component for enantioselectivity is directing the R group

away from the aryl and pyrrolidine groups. For the (*E*)-alkenyl boronate, the boronate group is situated between the aryl and pyrrolidine groups. As described previously in this chapter (Scheme 3.30), the two isomers of alkenyl boronate afford the same enantiomer of product. Consequently, the positioning of the boronate is not a critical feature for high enantioselectivity. The alignment of the insertion into the platinum-hydride proposed in Figure 3.2 is consistent with the observed stereochemical outcome.

Figure 3.2 Stereochemical Model for the Enantioselective Platinum-Catalyzed Hydrosilylation of Alkenyl Boronates



3.4 Conclusion

The development of a platinum-catalyzed enantioselective hydrosilylation of alkenyl boronates has been presented. This methodology was shown to be effective for the synthesis of a wide array of nonracemic geminal silylboronates from readily available starting materials. The hydrosilylation was shown to be applicable towards the telescoped synthesis of pharmaceutically relevant nonracemic silylamine products. The synthetic

utility was also showcased by divergent functionalization of the geminal dimetallic reagent. The scalability of the reaction was demonstrated by a large-scale enantioselective hydrosilylation without the aid of a glove-box.

The hydrosilylation of olefins is a well-studied and widely-developed process for applications in the silane industry. The development of enantioselective methods for the hydrosilylation of olefins has also been demonstrated for utility in natural product synthesis. The enantioselective hydrosilylation of alkenyl boronates presented provides a new alternative for the hydrosilylation of functionalized olefins. Further studies on the hydrosilylation of differentially substituted alkenyl boronates is highly desired as the divergent functionalization has been showcased. The development of enantioselective hydrosilylations of unexplored functionalized olefins could also have a profound impact on synthetic organic chemistry and add to a widely-developed area of chemistry.

3.5 Experimental

3.5.1 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 ($CDCl_3$: 7.24 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 ($CDCl_3$: 77.2 ppm). ^{11}B NMR spectra were recorded on a Varian Gemini-500 (128 MHz) or Varian Gemini-600 (160 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 aluminum backed plates from Silicycle. Small-scale silica gel columns performed using large-volume pipet (Fisher Catalog # 22-378893). Visualization was performed using ultraviolet light (254 nm), ceric ammonium molybdate (CAM) in ethanol or phosphomolybdic acid, cerium(IV) sulfate in ethanol with sulfuric acid (Seebach), and potassium permanganate in 10% sodium hydroxide.

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.

All reactions were conducted in oven- or flame-dried glassware under an inert atmosphere of nitrogen or argon unless stated otherwise. 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

was purchased from Strem Chemicals, Inc. and used without further purification. Reagents were purchased from Aldrich, Alfa Aesar, Acros, Oakwood, Strem, Combi-Blocks, TCI America and used without further purification.

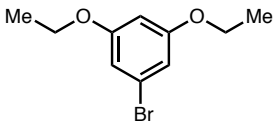
3.5.2 Experimental Procedures

1. Procedure for Preparation of $Pt(dba)_3$

$Pt(dba)_3$ was prepared according to a literature procedure with a slight modification. Sodium acetate (2.11 g, 25.7 mmol, 18.0 equiv), tetrabutylammonium chloride (1.19 g, 4.29 mmol, 3.00 equiv.) and *trans*, *trans*-dibenzylideneacetone (2.35 g, 10.01 mmol, 7.00 equiv.) were added to a 250 mL two-neck round bottom flask equipped with a stir bar and condenser. The solids were dissolved in methanol (65 mL) and heated to 70°C until full dissolution. In a separate vial, potassium tetrachloroplatinate (593 mg, 1.43 mmol, 1.00 equiv.) was dissolved in water (4.0 mL), heated gently with a heat gun for full dissolution and charged into the reaction flask. The reaction was heated to 70°C for 3 hours. After allowing to cool to room temperature, the reaction was concentrated to approximately half the volume. The solids were then filtered using a fritted funnel and washed with copious amounts of methanol (about 750 mL) and water (50 mL), until no yellow benzylideneacetone was observed. The resulting solid was placed on high-vacuum for 24 hours to remove all methanol and water, to afford a dark brown solid. (572 mg, 45%). All spectral data was in accordance with the literature.[47,62]

[62] Lewis, L. N.; Krafft, T. A.; Huffman, J. C. *Inorg. Chem.* **1992**, *31*, 3555-3557

2. Procedures for Preparation of TADDOL-Ligands



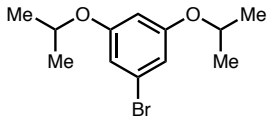
3.172

1-bromo-3,5-diethoxybenzene (3.172) To a flame-dried 250 mL round bottom flask equipped with a stir bar was added 1-bromo-3,5-dimethoxybenzene (2.17 g, 10.0 mmol, 1.00 equiv.), the flask purged with N_2 and then DCM (10 mL) was added. The reaction flask was cooled to 0°C and boron tribromide (5.51 g, 22.0 mmol, 2.20 equiv.) was added. The reaction was warmed to room temperature and allowed to stir overnight. The reaction was then cooled to -78°C, quenched with methanol and concentrated under reduced pressure. The crude mixture was redissolved in ethyl acetate, washed with water, dried over sodium sulfate, filtered and concentrated under reduced pressure. The crude product 1,3-dihydroxybromobenzene was used in the subsequent step without further purification.

To a 250 mL round bottom flask equipped with a stir bar was added 5-bromoresorcinol (1.89 g, 10.0 mmol, 1.00 equiv.), potassium carbonate, (5.53 g, 40.0 mmol, 4.0 equiv.) and DMF (40 mL). Iodoethane (6.24 g, 40.0 mmol, 4.0 equiv.) was then added and the reaction heated to 60°C for 18 hours. The reaction was cooled, diluted in ethyl acetate, washed with water, dried over sodium sulfate, filtered and concentrated under reduced pressure. The crude mixture was purified by silica gel chromatography (5% ethyl acetate in pentane) to afford a clear, yellow oil. (2.45 g, 82%)

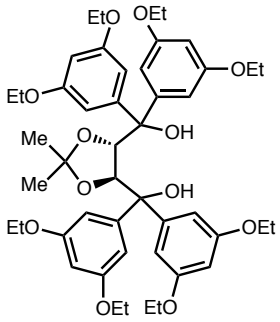
^{1}H NMR (600 MHz, $CDCl_3$): δ 6.64 (s, 2H), 6.36 (s, 1H), 3.98 (q, J = 7.0 Hz, 4H), 1.39 (t, J = 7.0 Hz, 6H). **^{13}C NMR** (151 MHz, $CDCl_3$): δ 160.67, 122.98, 110.40, 100.77, 63.91, 14.83. **IR** (neat): ν_{max} 2980 (w), 2932 (w), 2881 (w), 1595 (m), 1573 (s), 1479 (m), 1439

(m), 1277 (s), 1048 (s), 816 (m), 676(m) cm^{-1}. **HRMS** (DART) for $C_{10}H_{13}BrO_2$ $[M+H]^+$: calculated: 245.0177, found: 245.0188.



3.173

1-bromo-3,5-diispropoxybenzene (3.173) The compound was prepared as above but using 2-iodopropane in place of iodoethane. The crude mixture was purified by silica gel chromatography (2-3% ethyl acetate in pentane) to afford a clear yellow oil. (10.9 g, 99%) All spectra was in accordance with the literature.[63]



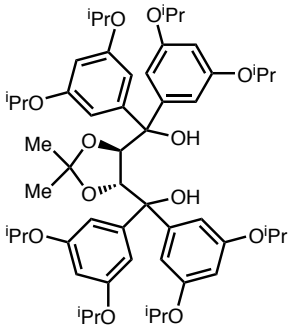
3.174

(4*S*,5*S*)-2,2-dimethyl-1,3-dioxolane-4,5-diyl)bis(bis(3,5 diethoxyphenyl)methanol) (3.174) (*R,R*)-3,5-Di-ethoxyphenylTADDOL was prepared according to the literature procedure with a slight modification.[64] (*S,S)*-3,5-Di-ethoxyphenylTADDOL was prepared in a likewise manner. To a flame-dried 100 mL two-neck round bottom flask equipped with a stir bar was added magnesium turnings (263 mg, 10.83 mmol, 5.4 equiv.), sealed, and then flame-dried again. Under N_2, a crystal of iodine in THF was added followed by 1-bromo-3,5-diethoxybromobenzene (2.21 g, 9.00 mmol, 4.5 equiv.) in THF (15 mL). The reaction flask was gently heated with a heat-gun to initiate and then heated to 80°C for 3 hours. The reaction was cooled to 0°C, dimethyl (4R,5R)-2,2-dimethyl-1,3-dioxolane-4,5-dicarboxylate (436 mg, 2 mmol, 1.00 equiv.) in THF (5 mL) was added and allowed to heat

[63] Cavanagh, C. W.; Aukland, M. H.; Hennessy, A.; Procter, D. J. *Chem. Commun.* **2015**, *51*, 9272-9275
[64] Sun, C.; Potter, B.; Morken, J. P. *J. Am. Chem. Soc.* **2014**, *136*, 6534-6537

at 80°C overnight. The reaction was cooled to room temperature and quenched with a saturated ammonium chloride solution. The aqueous layer was extracted with ethyl acetate, dried over sodium sulfate, filtered and concentrated under reduced pressure. The crude extract was purified by silica gel chromatography (15-25% ethyl acetate in pentane) to afford the title compound as a white solid. (927 mg, 56%)

^{1}H NMR (600 MHz, $CDCl_3$) δ 6.71 (s, 4H), 6.51 (s, 4H), 6.36 (s, 2H), 6.28 (s, 2H), 4.57 (s, 2H), 3.92-4.00 (m, 8H), 3.85-3.91 (m, 8H), 3.83 (s, 2H), 1.31-1.39 (m, 24H), 1.13 (s, 6H). **^{13}C NMR** (151 MHz, $CDCl_3$): δ 159.74, 159.32, 147.84, 145.22, 109.47, 107.56, 106.66, 100.55, 100.33, 81.67, 78.33, 63.63, 63.52, 27.55, 15.03, 14.94. **IR** (neat): ν_{max} 3304 (br), 2978 (s), 2931 (w), 2987 (w), 1591 (s), 1439 (s), 1389 (m), 1341 (w), 1164 (s), 1113 (m), 889 (w), 741 (s) cm^{-1}. **HRMS** (ESI) for $C_{47}H_{61}O_{11}$ $[M+H-H_2O]^+$: calculated: 801.4213, found: 801.4213. **$[\alpha]^{20}_D$**: +16.89 (c = 1.26, $CHCl_3$, *l* = 50 mm).

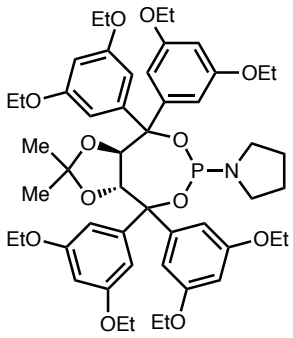


3.175

((4*R*,5*R*)-2,2-dimethyl-1,3-dioxolane-4,5-diyl)bis(bis(3,5-diisopropoxyphenyl)methanol) (3.175) (*R,R*)-3,5-Di-isopropoxyphenylTADDOL was prepared in accordance to the procedure above. The crude mixture was purified by silica gel chromatography (5-10% ethyl acetate in hexane) to afford a white solid. (3 g, 61%)

^{1}H NMR (600 MHz, $CDCl_3$) δ 6.69 (d, *J* = 2.2 Hz, 4H), 6.52 (d, *J* = 2.2 Hz, 4H), 6.36 (t, *J* = 2.2 Hz, 2H), 6.28 (t, *J* = 2.2 Hz, 2H). 4.61 (s, 2H), 4.45-4.51 (m, 4H), 4.36-4.41 (m, 4H), 3.69 (s, 2H), 1.23-1.31 (m, 48H), 1.05 (s, 6H). **^{13}C NMR** (151 MHz, $CDCl_3$): δ 158.70, 158.21, 148.14, 145.07, 109.69, 109.34, 107.90, 103.57, 103.06, 81.63, 78.35,

70.08, 69.92, 27.34, 22.43, 22.22, 22.18, 22.12. **IR** (neat): ν_{max} 3312 (br), 2975 (m), 2931 (w), 1591 (s), 1439 (m), 1371 (m), 1331 (m), 1244 (w), 1182 (m), 1113 (s), 963 (s), 840 (w) cm^{-1}. **HRMS** (ESI) for $C_{55}H_{77}O_{11}$ $[M+H-H_2O]^+$: calculated: 913.5461, found: 913.5460. **$[\alpha]^{20}_D$**: -10.86 (c = 1.18, $CHCl_3$, *l* = 50 mm).

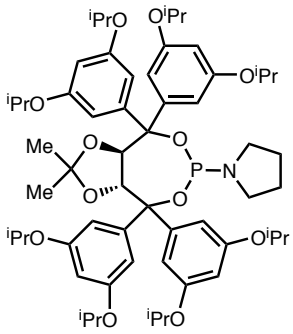


3.120

1-((3a*R*,8a*R*)-4,4,8,8-tetrakis(3,5-diethoxyphenyl)-2,2-dimethyltetrahydro-[1,3]dioxolo[4,5-*e*][1,3,2]dioxaphosphepin-6-yl)pyrrolidine (3.120) *(R,R)*-diethoxyTADDOLphoshporamidite was prepared according to a literature procedure.[64] *(S,S)*-diethoxyTADDOLphoshporamidite was prepared in a likewise manner. To a 100 mL round bottom flask equipped with a stir bar was added (*R,R)*-diethoxyTADDOL (927 mg, 1.13 mmol, 1.00 equiv.) and purged with N_2 three times. The solid was dissolved in THF (10 mL), cooled to 0°C and charged with triethylamine (0.536 mL, 3.85 mmol, 3.40 equiv.) and phosphorus trichloride (0.099 mL, 1.13 mmol, 1.00 equiv.). The solution was stirred for three hours at room temperature, cooled to 0°C and pyrrolidine (0.940 mL, 11.31 mmol, 10.0 equiv.) was added. The reaction was allowed to stir at room temperature overnight. The reaction mixture was filtered over a pad of celite with ether and concentrated under reduced pressure. The crude mixture was purified by silica gel chromatography (1-15% ethyl acetate in pentane, with 1% triethylamine) and further recrystallized with 1% ethyl acetate in pentane to afford a white solid. (666 mg, 64%)

^{1}H NMR (600 MHz, $CDCl_3$): δ 6.92 (d, *J* = 2.2 Hz, 2H), 6.75 (d, *J* = 2.2 Hz, 2H), 6.64 (s, 4H), 6.28-6.33 (m, 4H), 5.15 (dd, *J* = 8.5, 3.3 Hz, 1H), 4.72 (d, *J* = 8.5 Hz, 1H), 4.02 – 3.83

(m, 16H), 3.37-3.40 (m, 2H), 3.30 – 3.20 (m, 2H), 1.89 – 1.72 (m, 4H), 1.43 – 1.30 (m, 27H), 0.40 (s, 3H). **^{13}C NMR** (151 MHz, $CDCl_3$): δ 159.80, 159.37, 159.34, 159.02, 149.32, 148.83, 144.16, 111.56, 108.57, 108.10, 108.07, 106.51, 106.43, 100.93, 100.24, 100.06, 99.92, 83.09, 83.07, 82.61, 82.47, 81.73, 81.45, 81.40, 63.62, 63.54, 63.50, 63.45, 45.16, 45.06, 27.91, 26.31, 26.28, 25.69, 15.03, 15.01. **^{31}P NMR** (243 MHz, $CDCl_3$): δ 134.20. **IR** (neat): ν_{max} 2978 (w), 2933 (w), 2877 (w), 1590 (s), 1443 (m), 1390 (m), 1371 (w), 1039 (s), 995 (s), 884(m) cm^{-1}. **HRMS** (ESI) for $C_{51}H_{69}NO_{12}P$ $[M+H]^+$: calculated: 918.4557, found: 918.4554. **$[\alpha]^{20}_D$**: -81.50 (c = 1.07, $CHCl_3$, *l* = 50 mm).



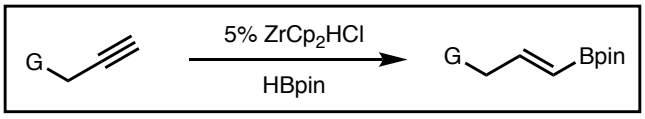
3.121

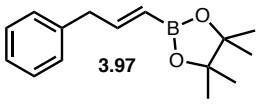
1-((3a*R*,8a*R*)-4,4,8,8-tetrakis(3,5-diisopropoxyphenyl)-2,2-dimethyltetrahydro-[1,3]dioxolo[4,5-*e*][1,3,2]dioxaphosphepin-6-yl)pyrrolidine (3.121) *(R,R)*-3,5-diisopropxyTADDOLphosphoramidite was prepared in accordance to the procedure above (1.00 mmol), to afford a white solid. (550 mg, 53%)

^{1}H NMR (600 MHz, $CDCl_3$): δ 6.89 (s, 2H), 6.73 (s, 2H), 6.60-6.61 (m, 4H), 6.27-6.32 (m, 4H), 5.20 (dd, *J* = 8.5, 3.0 Hz, 1H), 4.72 (d, 1H), 4.38-4.47 (m, 8H), 3.35-3.38 (m, 2H), 3.22-3.27 (m, 2H), 1.77-1.82 (m, 4H), 1.32 (s, 3H), 1.24-1.30 (m, 48H), 0.39 (s, 3H). **^{13}C NMR** (151 MHz, $CDCl_3$): δ 158.78, 158.32, 158.26, 157.96, 149.29, 148.70, 144.41, 144.16, 111.40, 109.63, 109.38, 107.61, 107.51, 104.29, 103.04, 102.88, 102.62, 83.07, 83.04, 82.68, 82.55, 81.57, 81.52, 70.07, 69.91, 69.85, 69.78, 45.12, 45.02, 27.78, 26.28, 26.25, 25.41, 22.43, 22.38, 22.36, 22.31, 22.20, 22.16, 22.12. **^{31}P NMR** (243 MHz, $CDCl_3$): δ 133.73. **IR** (neat): ν_{max} 2975, (m), 2932 (w), 2872 (w), 1590 (s), 1439 (s), 1382

(m), 1347 (m), 1289 (w), 1251 (w), 1182 (s), 1151 (s), 1114 (s), 1026 (m), 10006 (m), 845 (m) 786 (s) cm^{-1}. **HRMS** (ESI) for $C_{59}H_{85}NO_{12}P$ $[M+H]^+$: calculated: 1030.5806, found: 1030.5805. $[\alpha]^{20}_D$: -69.53 (c = 1.04, $CHCl_3$, *l* = 50 mm).

3. Procedures for Preparation of Alkenyl Boronates



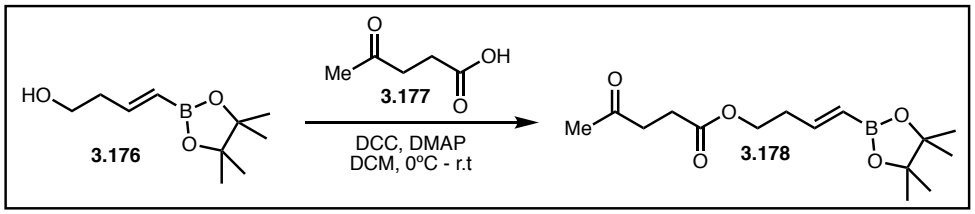


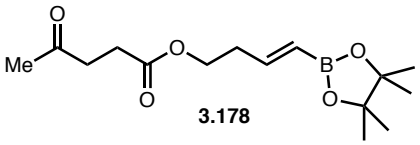
(*E*)-4,4,5,5-tetramethyl-2-(3-phenylprop-1-en-1-yl)-1,3,2-dioxaborolane (3.97) In a glove-box, to an oven-dried round bottom flask equipped with a stir bar, Schwartz's reagent (129 mg, 0.5 mmol, 0.05 equiv.), pinacolborane (1.45 mL, 10 mmol, 1.00 equiv) and 3-phenyl-1-propyne (1.49 mL, 12 mmol, 1.20 equiv) were added. The round bottom flask was sealed, and heated to 60°C under N_2 for 12 hours. The reaction was allowed to cool, diluted with Et_2O, passed through a pad of silica gel and concentrated under reduced pressure. The crude mixture was purified by silica gel chromatography (3-5% ethyl acetate in hexanes) to afford the title compound as a clear oil (1.55g, 65%) All spectral data was in accordance with the literature.[65]

[65] Kiesewetter, E. T.; O'Brien, R. V.; Yu, E. C.; Meek, S. J.; Schrock, R. R.; Hoveyda, A. H. *J. Am. Chem. Soc.* **2013**, *135*, 6026-6029

Starting material alkenyl boronates for **3.123**[66], **3.125**[50c], **3.126**[50c], **3.127**[67], **3.128**[68], **3.129**[46], **3.130**[68], **3.131**[68] were prepared according to the procedure above, and the spectra are in accordance with the literature.

Compound **3.124** utilized commercially available vinyl boronic acid pinacol ester.

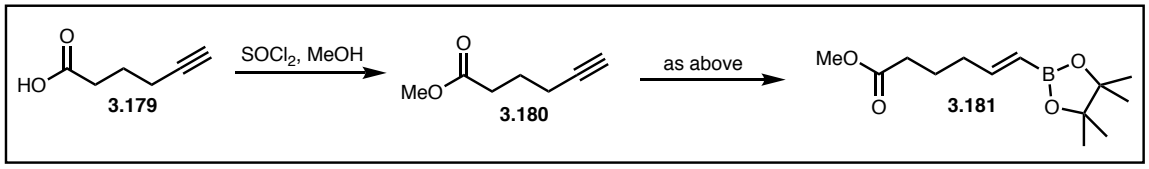


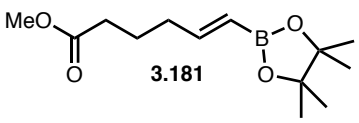


(*E*)-4-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)but-3-en-1-yl 4-oxopentanoate (3.178) In an oven-dried 250 mL round-bottom flask containing the alcohol (E)-4-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)but-3-en-1-ol[69] (1.19g, 6.00 mmol, 1.00 equv) and 4-oxopentanoic acid (1.05g, 9.00 mmol, 1.5 equiv) was added DCM (30 mL). The flask was cooled to 0°C and DMAP (146.6 mg, 1.20 mmol, 0.20 equiv) and *N,N'*-dicyclohexylcarbodiimide (2.48 g, 12.0 mmol, 2.00 equiv) were added sequentially, and the flask was allowed to warm to room temperature and stirred overnight. The mixture was cooled to 4°C in a freezer for two hours, and the resulting solid was vacuum filtered and washed with cold hexanes (10 mL). The filtrate was collected and purified by silica gel chromatography (20 – 33% ethyl acetate in hexanes) to afford a white solid. (1.27g 71%)

[66] Edelstein, E. K.; Namirembe, S.; Morken, J. P. *J. Am. Chem. Soc.* **2017**, *139,* 5027-5030
[67] Lawson, J. R.; Wilkins, L. C.; Melen, R. L. *Chem. Eur. J.* **2017**, *23*, 10997-11000
[68] Kageyuki, I.; Takaki, K.; Yoshida, H. *Org. Lett.* **2014**, *16*, 3512-3515
[69] Hydrozironcation of 3-butyn-1-ol done in an analogous fashion: Shen. X.; Nguyen, T. T.; Koh, M. J.; Xu, D.; Speed, A. W. H.; Schrock, R. R.; Hoveyda, A. H. *Nature*, **2017**, *541*, 380-385

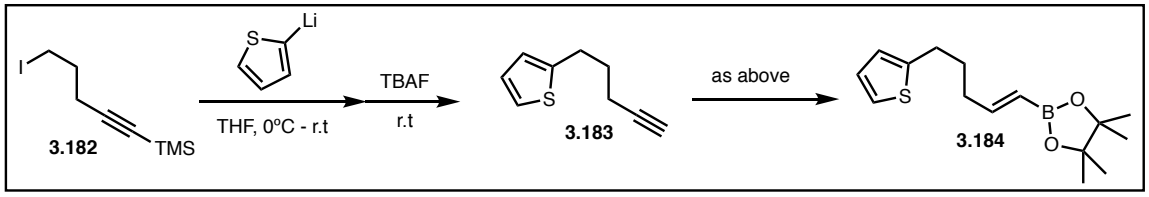
^{1}H NMR (600 MHz, $CDCl_3$): δ 6.54 (dt, *J* = 18.0, 6.4 Hz, 1H), 5.50 (d, 1H), 4.13 (t, *J* = 6.7 Hz, 2H), 2.72 (t, *J* = 6.6 Hz, 2H), 2.55 (t, *J* = 6.6 Hz, 2H), 2.44-2.48 (m, 2H), 2.16 (s, 3H), 1.25 (s, 12H). **^{13}C NMR** (151 MHz, $CDCl_3$): δ 206.64, 172.72, 148.96, 83.30, 63.24, 38.04, 34.87, 29.96, 28.07, 24.87. **^{11}B NMR**: (192 MHz, $CDCl_3$): δ 29.64. I**R** (neat): ν_{max} 2978 (w), 2973 (w), 1735 (m), 1719 (m), 1640 (m), 1579 (w), 1390 (s), 1358 (s), 1143 (s), 849(w) cm^{-1}. **HRMS** (ESI) for $C_{15}H_{26}BO_5$ $[M+H]^+$: calculated: 297.1873, found: 297.1874.

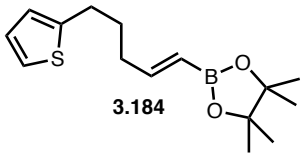




methyl (*E*)-6-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)hex-5-enoate (3.181) The commercially available carboxylic acid was esterified according to a literature procedure[70], and the boronic ester was synthesized by the hydrozirconation procedure above from the alkyne. All spectra data is in accordance to the literature.[71]

[70] Mlynarski, S. N.; Schuster, C. H.; Morken, J. P. *Nature*, **2014**, *505*, 386-390
[71] Jang, H.; Zhugralin, A. R.; Lee, Y.; Hoveyda, A. H. *J. Am. Chem. Soc.* **2011**, *133*, 7859-7871

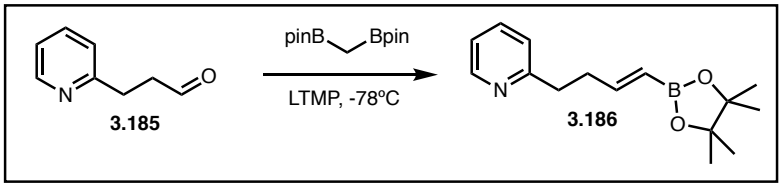


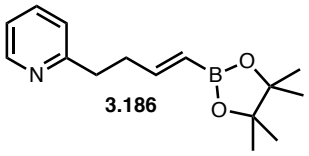


(*E*)-4,4,5,5-tetramethyl-2-(5-(thiophen-2-yl)pent-1-en-1-yl)-1,3,2-dioxaborolane (3.184) The alkyne was synthesized from the procedure above, starting from the iodo-alkyne[72] adapted from a literature procedure. The resulting alkyne was then subjected to the hydrozirconation procedure above and the crude mixture was purified by silica gel chromatography (1% ethyl acetate in hexanes) to afford a colorless oil. (209.4 mg, 68%)

^{1}H NMR (600 MHz, $CDCl_3$): δ 7.10 (dd, *J* = 5.2, 1.2 Hz, 1H), 6.90 (dd, *J* = 5.1, 3.4 Hz, 1H), 6.75-6.81 (m, 1H), 6.63 (dt, *J* = 17.9, 6.4 Hz, 1H), 5.47 (d, 1H), 2.83 (t, *J* = 7.7 Hz, 2H), 2.23 (q, *J* = 7.1 Hz, 2H), 1.79-1.84 (m, 2H), 1.27 (s, 12H). **^{13}C NMR** (151 MHz, $CDCl_3$): δ 153.38, 145.18, 126.67, 124.14, 122.90, 83.08, 35.04, 30.13, 29.33, 24.80. **^{11}B NMR**: (192 MHz, $CDCl_3$): δ 29.64. **IR** (neat): ν_{max} 2977 (w), 2930 (w), 2857 (w), 1638 (m), 1397 (s), 1319 (s), 1144 (w), 849 (m), 692 (m) cm^{-1}. **HRMS** (DART) for $C_{15}H_{24}BO_2S$ $[M+H]^+$: calculated: 279.1590, found: 279.1585.

[72] McCabe, J. M.; Brummond, K. M. *Tetrahedron,* **2006**, *62,* 10541-10554

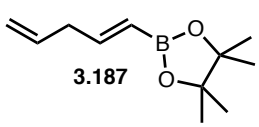




(*E*)-2-(4-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)but-3-en-1-yl)pyridine (3.186) This compound was synthesized according to a literature procedure.[50c] The aldehyde was synthesized using a literature procedure from the corresponding commercially available alcohol.[73] The crude mixture was purified by silica gel chromatography (20 – 30% ethyl acetate in hexanes) to afford a clear oil. (345 mg, 26%)

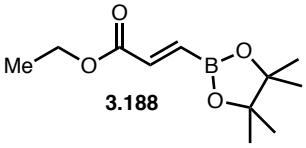
^{1}H NMR (600 MHz, $CDCl_3$) δ 8.50 (d, *J* = 5.0 Hz, 1H), 7.54-7.57 (m, 1H), 7.12 (d, *J* = 7.8 Hz, 1H), 7.07-7.09 (m, 1H), 6.69 (dt, *J* = 18.0, 6.3 Hz, 1H), 5.49 (d, *J* = 18.0 Hz, 1H), 2.89 (t, *J* = 9.3 Hz, 2H), 2.63 – 2.52 (m, 2H), 1.25 (s, 12H). **^{13}C NMR** (151 MHz, $CDCl_3$): δ 161.45, 153.24, 149.44, 136.477, 122.96, 121.26, 83.24, 37.04, 35.76, 24.94. **^{11}B NMR**: (160 MHz, $CDCl_3$) δ 26.07. **IR** (neat): ν_{max} 2978 (w), 2931 (w), 1637 (m), 1360 (s), 1318 (s), 1270 (s), 1164 (w), 970 (w), 749 (s) cm^{-1}. **HRMS** (DART) for $C_{15}H_{23}BO_2N$ $[M+H]^+$: calculated: 260.1822, found: 260.1835.

[73] Hoover, J. M.; Ryland, B. L.; Stahl, S. S. *J. Am. Chem. Soc.* **2013**, *135*, 2357-2367

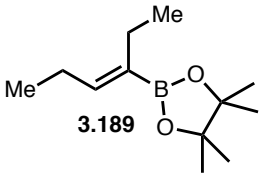


(*E*)-4,4,5,5-tetramethyl-2-(penta-1,4-dien-1-yl)-1,3,2-dioxaborolane (3.187) This compound was synthesized according to the procedure above from the commercially available alkyne, and the crude reaction mixture was purified by silica gel chromatography (5% ethyl acetate in hexanes) to afford a colorless oil. (853.3 mg, 88%)

^{1}H NMR (600 MHz, $CDCl_3$): δ 6.64 (dt, *J* = 17.9, 6.1 Hz, 1H), 5.79-5.86 (m, 1H), 5.48 (d, *J* = 18.0 Hz, 1H), 5.02-5.07 (m, 2H), 2.90 (t, *J* = 6.4 Hz, 2H), 1.26 (s, 12H). **^{13}C NMR** (151 MHz, $CDCl_3$): δ 151.78, 135.60, 116.39, 83.32, 40.06, 25.02. **^{11}B NMR**: (192 MHz, $CDCl_3$): δ 29.64. **IR** (neat): ν_{max} 2080 (w), 2978 (w), 2931 (w), 2895 (w), 1633 (m), 1358 (s), 1319 (s), 1143 (s), 996 (m), 848(m) cm^{-1}. **HRMS** (DART) for $C_{11}H_{20}BO_2$ $[M+H]^+$: calculated: 195.1556, found: 195.1547.



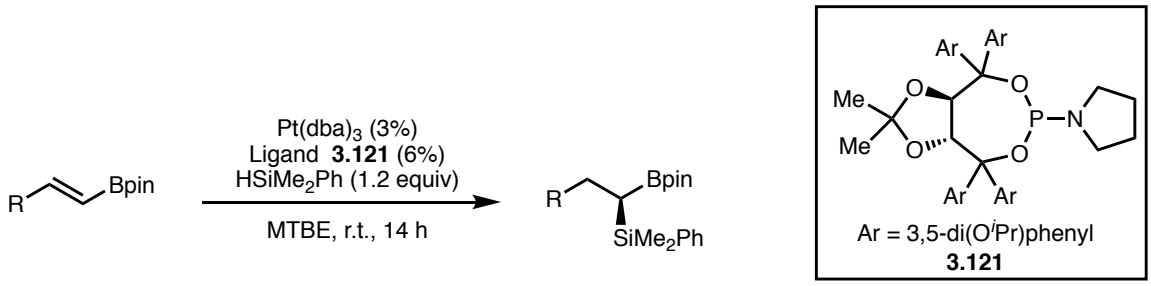
ethyl (*E*)-3-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)acrylate (3.188) This substrate was prepared according to a literature procedure, and all spectra matched the literature.[74]



(*Z*)-2-(hex-3-en-3-yl)-4,4,5,5-tetramethyl-1,3,2-dioxaborolane (3.189) This substrate was prepared according to a literature procedure, and all spectra matched the literature.[75]

[74] Lee, J.-E.; Kwon, J.; Yun, J. *Chem. Commun.* **2008**, *0*, 733-734
[75] Bismuto, A.; Thomas, S. P.; Cowley, M. J. *Angew. Chem. Int. Ed.* **2016**, *55*, 15356-15359

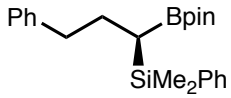
3.5.3 Procedures for the Hydrosilylation of Alkenyl Boronates, Determination of Absolute Stereochemistry, and Characterization of Reaction Products



Method A: Procedure for Hydrosilylation of Alkenyl Boronates

In a glove box, $Pt(dba)_3$ (5.4 mg, 0.006 mmol, 0.03 equiv.) and (*R,R)*-3,5-diethoxyTADDOLphoshoramidite (11.0 mg, 0.012 mmol, 0.06 equiv.) were added to an oven-dried two-dram vial equipped with a stir bar, dissolved in *tert*-butyl methyl ether (0.60 mL) and sealed with a teflon screw cap. A solution of (*E*)-4,4,5,5-tetramethyl-2-(3-phenylprop-1-en-1-yl)-1,3,2-dioxaborolane was prepared (61.3 mg in 0.50 mL, add 0.40 mL for 48.8 mg, 0.20 mmol, 1.00 equiv.) in a one-dram vial. Outside the glove box, the metal-ligand solution was heated to 80°C for 10 minutes, and allowed to cool to room temperature. Under N_2, the platinum-ligand complex was charged with (*E*)-4,4,5,5-tetramethyl-2-(3-phenylprop-1-en-1-yl)-1,3,2-dioxaborolane solution (0.40 mL) and dimethylphenylsilane (0.038 mL, 0.24 mmol, 1.20 equiv.), sealed with a septa and tape, and allowed to stir at room temperature for 14 hours. The reaction mixture was diluted with ether, filtered through a silica gel pipette plug and concentrated under reduce pressure.

The crude mixture was purified by silica gel chromatography (large volume pipet, 20% dichloromethane in hexanes) to afford a clear oil. (69.2 mg, 91%)



3.40

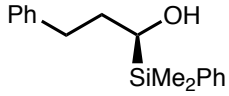
(*R*)-dimethyl(phenyl)(3-phenyl-1-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)propyl)silane (3.40) **^{1}H NMR** (600 MHz, $CDCl_3$) δ 7.47-7.48 (m, 2H), 7.27-7.34 (m, 3H), 7.23 (t, *J* = 7.6 Hz, 2H), 7.07-7.17 (m, 3H), 2.63-2.73 (m, 1H), 2.39-2.50 (m, 1H), 1.92 – 1.82 (m, 1H), 1.57-1.67 (m, 1H), 1.22 (s, 6H), 1.18 (s, 6H), 0.70 (d, *J* = 12.4 Hz, 1H), 0.30 (s, 3H), 0.29 (s, 3H). **^{13}C NMR** (151 MHz, $CDCl_3$): δ 142.81, 139.04, 134.04, 128.98, 128.74, 129.38, 127.79, 125.78, 83.02, 39.65, 28.25, 25.41, 24.49, -2.06, -3.13. **^{11}B NMR**: (160 MHz, $CDCl_3$) δ 34.83. **IR** (neat): ν_{max} 3067 (w), 2976 (m), 2927 (m), 1479 (w), 1378 (s), 1370 (s), 1307 (s), 1143 (s), 966 (w), 814 (s), 698 (s) cm^{-1}. **HRMS** (DART) for $C_{23}H_{37}BO_2SiN$ $[M+H]^+$: calculated: 398.2687, found: 398.267. **$[\alpha]^{20}_D$**: +21.39 (c = 1.05, $CHCl_3$, *l* = 50 mm).

Determination of Absolute Stereochemistry

Absolute stereochemistry was determined by comparison of the organoboronate optical rotation with the literature.[26] (Measured: $[\alpha]^{20}_D$: +21.39 (c = 1.05, $CHCl_3$, *l* = 50 mm), Literature $[\alpha]^{20}_D$: +24.0 (c = 1.00, $CHCl_3$), 97:3 er for (*R*)-dimethyl(phenyl)(3-phenyl-1-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)propyl)silane. The absolute stereochemistry was assigned to be (*R*)-dimethyl(phenyl)(3-phenyl-1-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)propyl)silane.

Method B: Procedure for the Oxidation of Geminal Silylboronates

SFC analysis was performed on the oxidized silylboronate. In a scintillation vial equipped with a stir bar and containing *(R)*-dimethyl(phenyl)(3-phenyl-1-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)propyl)silane was added THF (3 mL). The reaction vial was cooled to 0°C, charged with 3M sodium hydroxide (0.5 mL) and 29-32% hydrogen peroxide (0.50 mL) and allowed to stir at room temperature for 3 hours. The vial was then cooled to 0°C, and quenched with sodium thiosulfate (0.25 mL). The reaction solution was diluted with diethyl ether, and both organic and aqueous phase was passed through a silica gel large volume pipet to remove the aqueous layer. The organic extract was concentrated under reduced pressure, and the crude reaction mixture purified by silica gel chromatography (large volume pipet, 10% ethyl acetate in hexanes) to afford a clear oil. (24.0 mg, 89%)



3.154

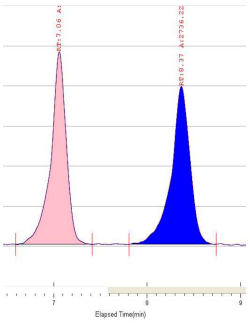
(*S*)-1-(dimethyl(phenyl)silyl)-3-phenylpropan-1-ol (3.154)

^{1}H NMR (600 MHz, $CDCl_3$) δ 7.55 (d, *J* = 8.4 Hz, 2H), 7.34-7.43 (m, 3H), 7.24-7.31 (m, 2H), 7.15-7.21 (m, 3H), 3.54 (t, *J* = 7.0 Hz, 1H), 2.85-2.96 (m, 1H), 2.58-2.68 (m, 1H), 1.77-1.92 (m, 2H), 1.08 (br s, 1H), 0.35 (s, 6H), 0.34 (s, 6H). **^{13}C NMR** (151 MHz, $CDCl_3$): δ 142.34, 136.66, 134.35, 129.62, 128.72, 128.60, 128.17, 126.01, 65.09, 35.44, 33.47, -5.23, -5.49. **IR** (neat): 3578 (br), 3066 (w), 2954 (m), 2851 (m), 1453 (m), 1427 (m), 1257 (s), 1112 (s), 829 (s), 698 (s) cm^{-1}. **HRMS** (DART) for $C_{17}H_{26}OSiN$ $[M+NH_4]^+$: calculated: 288.1784, found: 288.1792. **$[\alpha]^{20}_D$**: +5.36 (c = 1.20, $CHCl_3$, *l* = 50 mm).

Analysis of Stereochemistry:

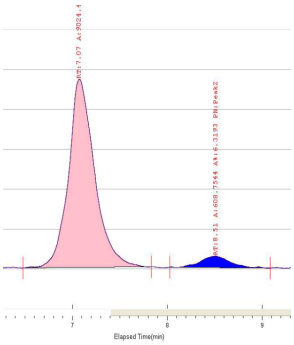
Racemic compound was prepared according to the hydrosilylation procedure (Method A) described using racemic ligand. Racemic ligand **3.107** was prepared by adding equal amounts of both enantiomers into a vial, dissolved in acetonitrile and then concentrated under reduced pressure. The solid was then placed on high vacuum to obtain a well dispersed mixture of ligand enantiomers.

Chiral SFC (Chiracel OJ-H, 10% IPA, 3 mL/min, 100 bar, 35 °C, 210-270 nm) – analysis of (S)-1-(dimethyl(phenyl)silyl)-3-phenylpropan-1-ol.



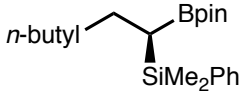
Peak Info			
Peak No	% Area	Area	RT (min)
1	50.334	2773.0263	7.06
2	49.666	2736.2213	8.37
Total:	100	5509.2476	

RACEMIC



Peak Info			
Peak No	% Area	Area	RT (min)
1	93.6807	9024.4975	7.07
2	6.3193	608.7544	8.51
Total:	100	9633.2519	

NONRACEMIC



3.123

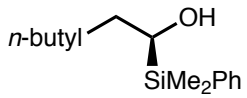
(*R*)-dimethyl(phenyl)(1-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)hexyl)silane (3.123) Reaction carried out using *(R,R)*-3,5-diisopropoxyTADDOLphosphoramidite (12.4 mg, 0.012 mmol, 0.06 equiv.) according to the procedure above (Method A). The crude reaction was purified by silica gel

chromatography (large volume pipet, 5-20% dichloromethane in hexanes) to afford a clear oil. (59.5 mg, 86%)

^{1}H NMR (600 MHz, $CDCl_3$) δ 7.49-7.57 (m, 2H), 7.29-7.36 (m, 3H), 1.49-1.60 (m, 1H), 1.28-1.37(m, 2H), 1.17-1.27 (m, 11H), 1.16 (s, 6H), 0.84 (t, J = 6.8 Hz, 3H), 0.64 (dd, J = 11.9, 2.7 Hz, 1H), 0.31 (s, 3H), 0.30 (s, 3H). **^{13}C NMR** (151 MHz, $CDCl_3$): δ 139.38, 134.05, 128.92, 127.76, 82.89, 33.12, 31.82, 25.99, 25.30, 24.89, 22.76, 14.25, -2.13, -3.06. **^{11}B NMR**: (160 MHz, $CDCl_3$) δ 34.42. **IR** (neat): 3069 (w), 3049 (w), 2923, (m), 2855 (w), 1480 (w), 1378 (m), 1348 (s), 1304 (s), 1143 (s), 956 (w), 832 (s), 698 (s) cm^{-1}. **HRMS** (DART) for $C_{20}H_{39}BO_2SiN$ $[M+NH_4]^+$: calculated: 364.2843, found: 364.2855. **$[\alpha]^{20}_D$**: +13.11 (c = 1.19, $CHCl_3$, l = 50 mm).

Analysis of Stereochemistry:

SFC analysis was performed on the oxidized silylboronate obtained according to procedure above (Method B) and purified by silica gel chromatography (large volume pipet, 10% ethyl acetate in hexanes) to afford a clear oil. Racemic product was synthesized according to the procedure above (Compound 3.154).



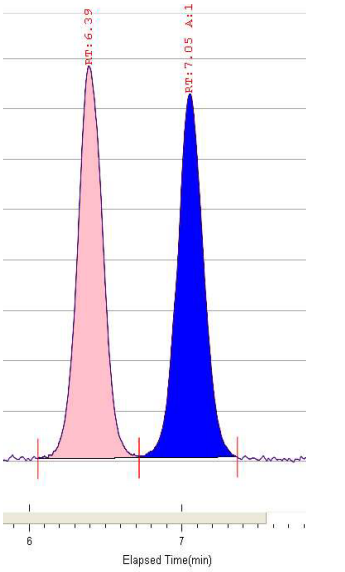
3.190

(*S*)-1-(dimethyl(phenyl)silyl)hexan-1-ol (3.190)

^{1}H NMR (600 MHz, $CDCl_3$) δ 7.52-7.62 (m, 2H), 7.31-7.42 (m, 3H), 3.51 (t, J = 7.1 Hz, 1H), 1.48-1.59 (m, 2H), 1.18-1.35 (m, 6H), 1.07 (br s, 1H), 0.87 (t, J = 7.0, 3H), 0.35 (s, 3H), 0.34 (s, 3H). **^{13}C NMR** (151 MHz, $CDCl_3$): δ 137.02, 134.33, 129.49, 128.09, 65.71, 33.58, 31.91, 26.71, 22.83, 14.26, -5.14, -5.44. **IR** (neat): 3441 (br), 3069 (w), 3051 (w), 3011 (m), 2956 (m), 2855 (w), 1427 (w), 1248 (s), 1112 (s), 916 (w),

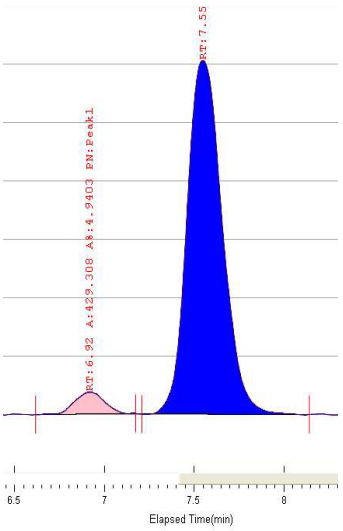
831 (s), 754 (s), 733 (s), 699 (s) cm^{-1}. **HRMS** (DART) for $C_{14}H_{28}OSiN$ $[M+NH_4]^+$: calculated: 254.194, found 254.1929. $[\alpha]^{20}_D$: +2.34 (c = 1.26, $CHCl_3$, *l* = 50 mm).

Chiral SFC (Chiracel OD-H, 2% IPA, 3 mL/min, 100 bar, 35 °C, 210-270 nm) – analysis of (S)-1-(dimethyl(phenyl)silyl)hexan-1-ol.



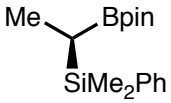
Peak Info			
Peak No	% Area	Area	RT (min)
1	51.1049	1804.0108	6.39
2	48.8951	1726.0053	7.05
Total:	100	3530.0161	

RACEMIC



Peak Info			
Peak No	Area	% Area	RT (min)
1	429.308	4.9403	6.92
2	8260.5239	95.0597	7.55
Total:	8689.8319	100	

NONRACEMIC



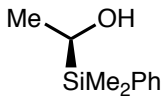
3.124

(*R*)-dimethyl(phenyl)(1-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)ethyl)silane (3.124) Reaction carried out using *(R,R)*-3,5-diisopropoxyTADDOLphosphoramidite (12.4 mg, 0.012 mmol, 0.06 equiv.) according to the procedure above (Method A). The crude reaction was purified by silica gel chromatography (large volume pipet, 15% dichloromethane in hexanes) to afford a clear oil. (40.6 mg, 70%)

^{1}H NMR (600 MHz, $CDCl_3$) δ 7.50-7.59 (m, 2H), 7.29-7.38 (m, 3H), 1.20 (s, 6H), 1.18 (s, 6H), 1.02 (d, *J* = 7.3 Hz, 3H), 0.61 (q, *J* = 7.2 Hz, 1H), 0.33 (s, 6H). **^{13}C NMR** (126 MHz, $CDCl_3$): δ 139.15, 134.07, 128.93, 127.75, 82.88, 25.20, 24.98, 9.53, -2.34, -3.56. **^{11}B NMR**: (160 MHz, $CDCl_3$) δ 34.58. **IR** (neat): 3069 (w), 3048 (w), 2976 (m), 2933 (m), 2873 (w), 1465 (w), 1305 (m), 1278 (s), 1248 (s), 1144 (s), 1111 (m), 971 (m), 814 (s) 699 (s) cm^{-1}. **HRMS** (DART) for $C_{16}H_{31}BO_2SiN$ $[M+NH_4]^+$: calculated: 308.2217, found: 308.2225. **$[\alpha]^{20}_D$**: +10.39 (c = 1.02, $CHCl_3$, *l* = 50 mm).

Analysis of Stereochemistry:

SFC analysis was performed on the oxidized silylboronate obtained according to procedure above (Method B) and purified by silica gel chromatography (large volume pipet, 10% ethyl acetate in hexanes) to afford a clear oil. Racemic product was synthesized according to the procedure above (Compound 3.154).

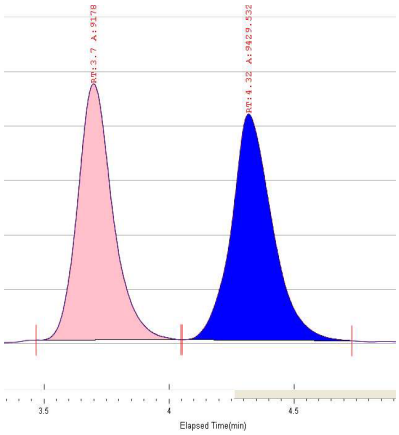


3.191

***(S)*-1-(dimethyl(phenyl)silyl)ethan-1-ol (3.191)**

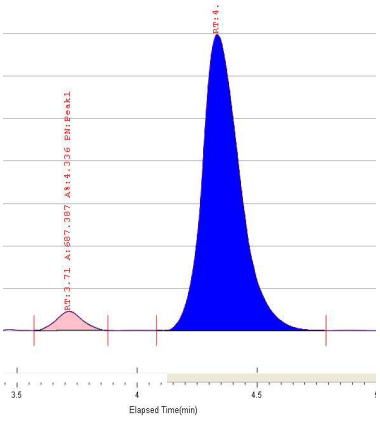
^{1}H NMR (600 MHz, $CDCl_3$) δ 7.53-7.60 (m, 2H), 7.34-7.43 (m, 3H), 3.69 (q, *J* = 7.5 Hz, 1H), 1.29 (d, *J* = 7.5 Hz, 3H), 1.03 (br s, 1H), 0.34 (s, 3H), 0.33 (s, 3H). **^{13}C NMR** (126 MHz, $CDCl_3$): δ 136.69, 134.33, 129.57, 128.13, 61.37, 19.68, -5.50, -5.90. **IR** (neat): 3387 (br), 3069 (w), 3052 (w), 2957 (m), 2925 (w), 2859 (w), 1457 (w), 1248 (w), 1215 (w), 1114 (w), 832 (s), 812 (s), 774 (s), 700 (s), 600 (w) cm^{-1}. **HRMS** (DART) for $C_{10}H_{17}OSi$ $[M+H]^+$: calculated: 181.1049, found 181.014. **$[\alpha]^{20}_D$**: -12.73 (c = 0.83, $CHCl_3$, *l* = 50 mm).

Chiral SFC (Chiracel OJ-H, 5% IPA, 3 mL/min, 100 bar, 35 °C, 210-270 nm) – analysis of (S)-1-(dimethyl(phenyl)silyl)ethan-1-ol.



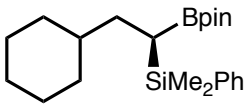
Peak Info			
Peak No	% Area	Area	RT (min)
1	49.3256	9178.558	3.7
2	50.6744	9429.5328	4.32
Total:	100	18608.0908	

RACEMIC



Peak Info			
Peak No	% Area	Area	RT (min)
1	4.336	687.387	3.71
2	95.664	15165.5789	4.33
Total:	100	15852.9659	

NONRACEMIC



3.125

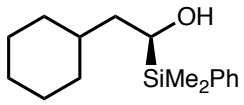
(*R*)-(2-cyclohexyl-1-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2 yl)ethyl)dimethyl(phenyl)silane (3.125) Reaction carried out using *(R,R)*-3,5-diethoxyTADDOLphosphoramidite (11 mg, 0.012 mmol, 0.06 equiv.) according to the procedure above (Method A). The crude reaction was purified by silica gel chromatography (large volume pipet, 5-20% dichloromethane in hexanes) to afford a clear oil. (45.4 mg, 61%)

^{1}H NMR (600 MHz, $CDCl_3$): δ 7.50-7.59 (m, 2H), 7.27-7.36 (m, 3H), 1.74 (d, *J* = 13.1 Hz, 1H), 1.58-1.71 (m, 4H), 1.49-1.57 (m, 1H), 1.06-1.24 (m, 17H), 0.79-0.88 (m, 1H), 0.73-0.79 (m, 1H), 0.66-0.73 (m, 1H), 0.31 (d, *J* = 3.2 Hz, 6H). **^{13}C NMR** (151 MHz, $CDCl_3$): δ 139.34, 134.06, 128.92, 127.76, 82.91, 40.55, 34.03, 33.36, 32.44, 26.94, 26.69, 26.61, 25.23, 24.99, -2.14, -3.06. **^{11}B NMR** (192 MHz, $CDCl_3$): δ 34.00. **IR** (neat): ν_{max} 3069 (w), 3050 (w), 2977 (w), 2920(m), 1448 (w), 1370 (m), 1307 (s), 1143 (s), 1112(m),

815 (s), 699 (s) cm^{-1}. **HRMS** (DART) for $C_{22}H_{41}BO_2SiN$ $[M+NH_4]^+$: calculated: 390.3000, found: 390.2997. $[\alpha]^{20}_D$: +11.45 (c = 1.02, $CHCl_3$, *l* = 50 mm).

Analysis of Stereochemistry:

SFC analysis was performed on the oxidized silylboronate obtained according to procedure above (Method B) and purified by silica gel chromatography (large volume pipet, 10% ethyl acetate in hexanes) to afford a clear oil. Racemic product was synthesized according to the procedure above (Compound 3.154).

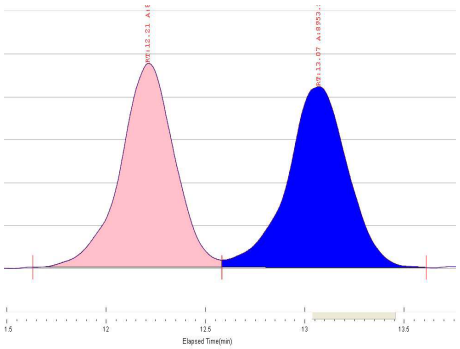


3.192

(*S*)-2-cyclohexyl-1-(dimethyl(phenyl)silyl)ethan-1-ol (3.192)

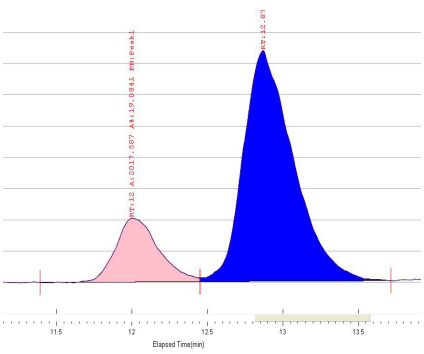
^{1}H NMR (600 MHz, $CDCl_3$): δ 7.53-7.60 (m, 2H), 7.32-7.43 (m, 3H), 3.68 (d, *J* = 9.9 Hz, 1H), 1.77-1.89 (m, 1H), 1.58-1.74 (m, 4H), 1.45-1.57 (m, 2H), 1.07-1.34 (m, 4H), 0.92-1.01 (m, 2H), 0.68-0.82 (m, 1H), 0.34 (s, 3H), 0.33 (s, 3H). **^{13}C NMR** (151 MHz, $CDCl_3$): δ 136.98, 134.34, 129.49, 128.09, 62.39, 41.07, 34.83, 34.09, 32.17, 26.89, 26.69, 26.39, -5.28, -5.57. **IR** (neat): 3450 (w), 3068 (w), 3048(w), 2920(s), 2849 (m), 1448 (w), 1247 (m), 1113 (m), 839 (m), 813 (s), 699 (s) cm^{-1}. **HRMS** (DART) for $C_{16}H_{30}OSiN$ $[M+NH_4]^+$: calculated: 280.2097, found: 280.2095. $[\alpha]^{20}_D$: +9.13 (c =1.02, $CHCl_3$, *l* = 50 mm).

Chiral SFC (Chiracel AD-H, 5% IPA, 3 mL/min, 100 bar, 35 °C, 210-270 nm) – analysis of (S)-2-cyclohexyl-1-(dimethyl(phenyl)silyl)ethan-1-ol.



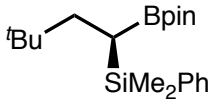
Peak Info			
Peak No	% Area	Area	RT (min)
1	50.1297	8999.7581	12.21
2	49.8703	8953.2041	13.07
Total:	100	17952.9622	

RACEMIC



Peak Info			
Peak No	% Area	Area	RT (min)
1	19.0841	2017.587	12
2	80.9159	8554.4895	12.87
Total:	100	10572.0765	

NONRACEMIC



3.126

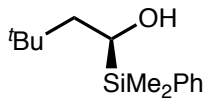
(*R*)-(3,3-dimethyl-1-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)butyl)dimethyl(phenyl)silane (3.126) Reaction carried out using *(R,R)*-3,5-diisopropoxyTADDOLphosphoramidite (12.4 mg, 0.012 mmol, 0.06 equiv.) according to the procedure above (Method A). The crude reaction was purified by silica gel chromatography (large volume pipet, 5-10% dichloromethane in hexanes) to afford a clear oil. (16.2 mg, 23%)

^{1}H NMR (600 MHz, $CDCl_3$): δ 7.50-7.59 (m, 2H), 7.29-7.36 (m, 3H), 1.58 (dd, *J* = 13.4, 11.2 Hz, 1H), 1.23 (d, *J* = 13.4 Hz, 1H), 1.18 (s, 6H), 1.15 (s, 6H), 0.77 (s, 9H), 0.63 (d, *J* = 11.1 Hz, 1H), 0.31 (d, *J* = 2.7 Hz, 6H). **^{13}C NMR** (151 MHz, $CDCl_3$): δ 138.93, 133.94, 128.73, 127.49, 82.74, 77.22, 77.01, 76.80, 39.56, 31.97, 28.96, 25.12, 24.94, -2.44, -3.41. **^{11}B NMR** (192 MHz, $CDCl_3$): δ 34.00. **IR** (neat): ν_{max} 3022 (w), 2977 (w), 2956 (w), 2866(w), 1476 (w), 1350 (s), 1297 (s), 1247 (m), 1144(s), 835 (s), 816 (s) cm^{-1}. **HRMS**

(DART) for $C_{20}H_{39}BO_2SiN$ $[M+NH_4]^+$: calculated: 364.2843, found: 364.2846. **$[\alpha]^{20}_D$**: -0.51 (c = 1.01, $CHCl_3$, *l* = 50 mm).

Analysis of Stereochemistry:

SFC analysis was performed on the oxidized silylboronate obtained according to procedure above (Method B) and purified by silica gel chromatography (large volume pipet, 10% ethyl acetate in hexanes) to afford a clear oil. Racemic product was synthesized according to the procedure above (Compound 3.154).

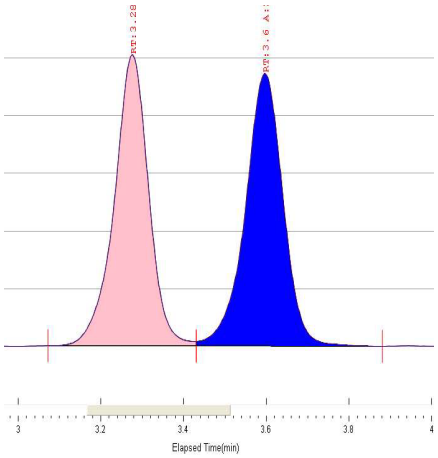


3.193

(*S*)-1-(dimethyl(phenyl)silyl)-3,3-dimethylbutan-1-ol (3.193)

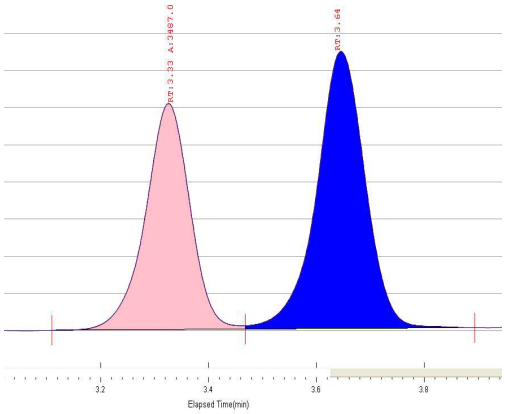
^{1}H NMR (600 MHz, $CDCl_3$): δ 7.52-7.62 (m, 2H), 7.33-7.42 (m, 3H), 3.70-3.79 (m, 1H), 1.39-1.48 (m, 2H), 0.92 (s, 9H), 0.32 (s, 3H), 0.31 (s, 3H). **^{13}C NMR** (151 MHz, $CDCl_3$): δ 136.72, 134.18, 129.33, 127.92, 62.80, 46.83, 31.43, 29.97, -5.60, -5.87. **IR** (neat): 3591 (w), 3483 (w), 3069(w), 2953(m), 2902 (w), 2868 (w), 1467 (w), 1427 (w), 1364 (w), 1248 (s), 1113 (m), 788 (s), 699 (s) cm^{-1}. **HRMS** (DART) for $C_{14}H_{28}OSiN$ $[M+NH_4]^+$: calculated: 254.194, found 254.1943. **$[\alpha]^{20}_D$**: +0.97 (c =0.41, $CHCl_3$, *l* = 50 mm).

Chiral SFC (Chiracel AD-H, 5% IPA, 3 mL/min, 100 bar, 35 °C, 210-270 nm) – analysis of (S)-1-(dimethyl(phenyl)silyl)-3,3-dimethylbutan-1-ol.



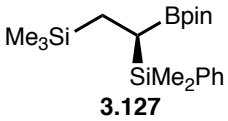
Peak Info			
Peak No	% Area	Area	RT (min)
1	49.3444	2905.0673	3.28
2	50.6556	2982.2637	3.6
Total:	100	5887.331	

RACEMIC



Peak Info			
Peak No	% Area	Area	RT (min)
1	42.8999	3487.0962	3.33
2	57.1001	4641.3511	3.64
Total:	100	8128.4473	

NONRACEMIC



3.127

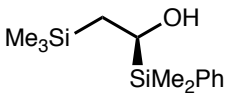
(*R*)-(2-(dimethyl(phenyl)silyl)-2-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)ethyl)trimethylsilane (3.127) Reaction carried out using *(R,R)*-3,5-diisopropoxyTADDOLphosphoramidite (12.4 mg, 0.012 mmol, 0.06 equiv.) according to the procedure above at 70°C (Method A). The crude reaction was purified by silica gel chromatography (large volume pipet, 5-15% dichloromethane in hexanes) to afford a clear oil. (52.9 mg, 73%)

^{1}H NMR (500 MHz, $CDCl_3$): δ 7.49-7.58 (m, 2H), 7.27-7.36 (m, 3H), 1.20 (s, 6H), 1.18 (s, 6H), 0.77-0.81 (m, 1H), 0.59 (d, J = 11.6 Hz, 1H), 0.44 (d, J = 14.6 Hz, 1H), 0.32 (d, J = 5.9, 6H), -0.09 (d, J = 1.6 Hz, 9H). **^{13}C NMR** (126 MHz, $CDCl_3$): δ 139.20, 134.16, 128.94, 127.73, 83.03, 25.52, 25.23, 10.95, -1.65, -2.13, -3.65. **^{11}B NMR** (192 MHz, $CDCl_3$): δ 34.10. **IR** (neat): ν_{max} 3069 (w), 3023 (w), 2977 (w), 2900(w), 1426 (w), 1341 (s), 1246 (s), 1143 (s), 990(w), 832 (s), 699 (s) cm^{-1}. **HRMS** (DART) for $C_{19}H_{39}BO_2Si_2N$

$[M+NH_4]^+$: calculated: 380.2612, found: 380.2621. $[\alpha]^{20}_D$: -5.03 (c = 1.03, $CHCl_3$, *l* = 50 mm).

Analysis of Stereochemistry:

SFC analysis was performed on the oxidized silylboronate obtained according to procedure above (Method B) and purified by silica gel chromatography (large volume pipet, 10% ethyl acetate in hexanes) to afford a clear oil. Racemic product was synthesized according to the procedure above (Compound 3.154).

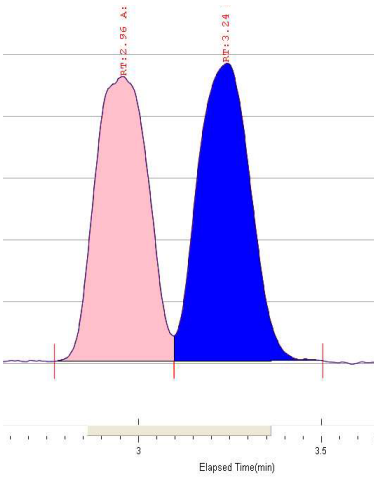


3.194

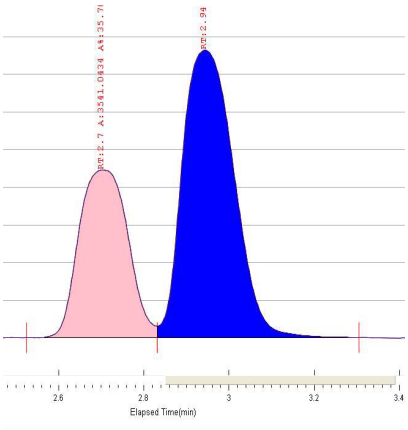
(*S*)-1-(dimethyl(phenyl)silyl)-2-(trimethylsilyl)ethan-1-ol (3.194)

^{1}H NMR (600 MHz, $CDCl_3$): δ 7.54-7.58 (m, 2H), 7.33-7.44 (m, 3H), 3.72 (ddd, *J* = 12.8, 5.8, 2.8 Hz, 1H), 0.63-0.96 (m, 3H), 0.33 (s, 3H), 0.32 (s, 3H), 0.04 (s, 9H). **^{13}C NMR** (151 MHz, $CDCl_3$): δ 136.94, 134.40, 129.51, 128.11, 63.06, 20.96, -0.50, -5.46, -5.95. **IR** (neat): 3594(w), 3473(w), 3069 (w), 3022(w), 2953(w), 2897 (w), 1427 (w), 1246 (s), 1113 (m), 943 (w), 831 (s), 700 (s) cm^{-1}. **HRMS** (DART) for $C_{13}H_{25}Si_2O$ $[M+NH_4]^+$: calculated: 253.1444, found 253.1440. $[\alpha]^{20}_D$: -1.26 (c =1.66, $CHCl_3$, *l* = 50 mm).

Chiral SFC (Chiracel ODR-H, 0% IPA, 3 mL/min, 100 bar, 35 °C, 210-270 nm) – analysis of (S)-1-(dimethyl(phenyl)silyl)-2-(trimethylsilyl)ethan-1-ol.

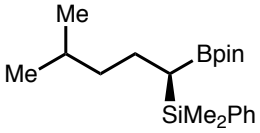


Peak Info			
Peak No	% Area	Area	RT (min)
1	49.2179	2323.3805	2.96
2	50.7821	2397.2225	3.24
Total:	100	4720.603	



Peak Info			
Peak No	% Area	Area	RT (min)
1	35.7038	3541.0434	2.7
2	64.2962	6376.7884	2.94
Total:	100	9917.8318	

RACEMIC **NONRACEMIC**



3.128

(*R*)-dimethyl(4-methyl-1-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)pentyl)(phenyl)silane (3.128) Reaction carried out using *(R,R)*-3,5-diisopropoxyTADDOLphosphoramidite (12.4 mg, 0.012 mmol, 0.06 equiv.) according to the procedure above (Method A). The crude reaction was purified by silica gel chromatography (large volume pipet, 10-20% dichloromethane in hexanes) to afford a clear oil. (55.4 mg, 80%)

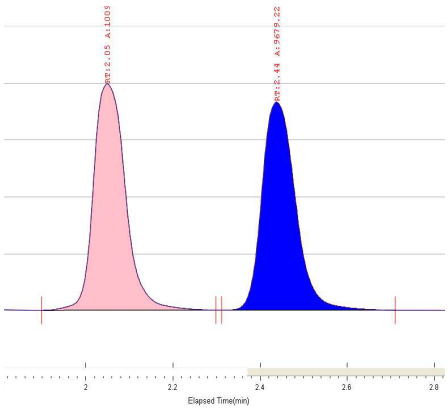
^{1}H NMR (600 MHz, $CDCl_3$) δ 7.70-7.53 (m, 2H), 7.29-7.36 (m, 3H), 1.42-1.60 (m, 2H), 1.29-1.40 (m, 2H), 1.20 (s, 6H), 1.10-1.18 (m, 7H), 0.75-0.84 (m, 6H), 0.59 (dd, *J* = 11.8, 3.3 Hz, 1H), 0.32 (s, 3H), 0.31 (s, 3H). **^{13}C NMR** (151 MHz, $CDCl_3$): δ 139.40, 134.05, 128.92, 127.76, 82.89, 42.85, 27.84, 25.34, 24.85, 23.78, 23.17, 22.42, -2.14, -3.02. **^{11}B NMR**: (160 MHz, $CDCl_3$) δ 34.61. **IR** (neat): 3069 (w), 3049 (w), 2976 (m), 2954 (m),

2687 (w), 1480 (w), 1378 (w), 1348 (s), 1304 (s), 1248 (m), 1143 (s), 1112 (m), 814 (s), 699 (s) cm^{-1}. **HRMS** (DART) for $C_{20}H_{39}BO_2SiN$ $[M+NH_4]^+$: calculated: 364.2843, found: 364.285. $[\alpha]^{20}_D$: +12.16 (c = 1.11, $CHCl_3$, *l* = 50 mm).

Analysis of Stereochemistry:

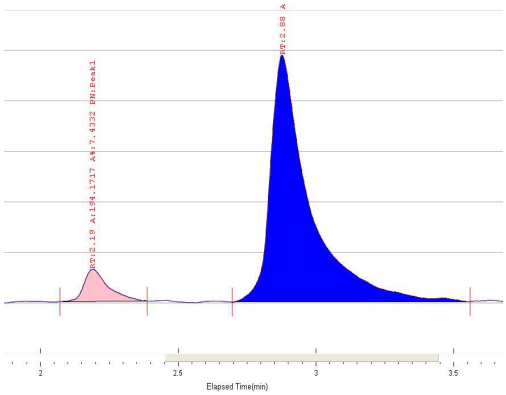
SFC analysis was performed directly on the silylboronate product. Racemic product was synthesized according to the procedure above (Compound 3.154).

Chiral SFC (Chiracel AD-H, 1% IPA, 3 mL/min, 100 bar, 35 °C, 210-270 nm) – analysis of (R)-dimethyl(4-methyl-1-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)pentyl)(phenyl)silane.



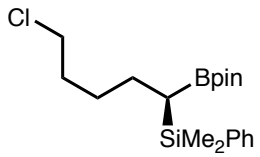
Peak Info			
Peak No	% Area	Area	RT (min)
1	51.0414	10091.0079	2.05
2	48.9586	9679.229	2.44
Total:	100	19770.2369	

RACEMIC



Peak Info			
Peak No	% Area	Area	RT (min)
1	7.4332	194.1717	2.19
2	92.5668	2418.0517	2.88
Total:	100	2612.2234	

NONRACEMIC



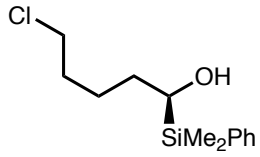
3.129

(*R*)-(5-chloro-1-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)pentyl)dimethyl(phenyl)silane (3.129) Reaction carried out using *(R,R)*-3,5-diisopropoxyTADDOLphosphoramidite (12.4 mg, 0.012 mmol, 0.06 equiv.) according to the procedure above (Method A). The crude reaction was purified by silica gel chromatography (large volume pipet, 20% dichloromethane in hexanes) to afford a clear oil. (61.7 mg, 84%)

^{1}H NMR (600 MHz, $CDCl_3$) δ 7.49-7.57 (m, 2H), 7.31-7.38 (m, 3H), 3.45 (t, *J* = 6.8 Hz, 2H), 1.63-1.78 (m, 2H), 1.43-1.63 (m, 2H), 1.25-1.40 (m, 2H), 1.21 (s, 6H), 1.17 (s, 6H), 0.64 (dd, *J* = 11.9, 2.8 Hz, 1H), 0.33 (s, 3H), 0.32 (s, 3H). **^{13}C NMR** (151 MHz, $CDCl_3$): δ 139.04, 133.99, 129.02, 127.81, 83.02, 45.26, 32.62, 30.55, 25.36, 25.32, 24.89, -2.12, -3.19. **^{11}B NMR**: (160 MHz, $CDCl_3$) δ 34.58. **IR** (neat): 3068 (w), 2976 (m), 2956 (m), 2857 (w), 1445 (w), 1350 (s), 1305 (s), 1143 (s), 1112 (m), 967 (w), 816 (s), 699 (m) cm^{-1}. **HRMS** (DART) for $C_{19}H_{32}BClO_2SiN$ $[M+NH_4]^+$: calculated: 384.2297, found: 384.2315. **$[\alpha]^{20}_D$**: +35.85 (c = 1.03, $CHCl_3$, *l* = 50 mm).

Analysis of Stereochemistry:

SFC analysis was performed on the oxidized silylboronate obtained according to procedure above (Method B) and purified by silica gel chromatography (large volume pipet, 10% ethyl acetate in hexanes) to afford a clear oil. Racemic product was synthesized according to the procedure above (Compound 3.154).



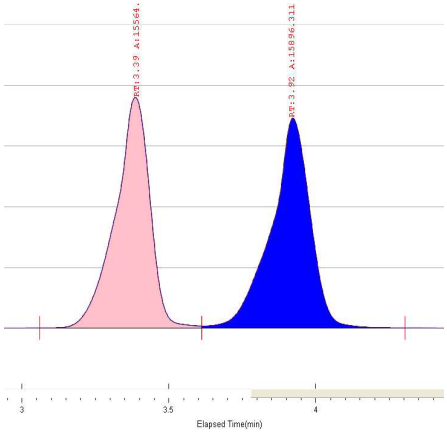
3.195

(*S*)-5-chloro-1-(dimethyl(phenyl)silyl)pentan-1-ol (3.195)

^{1}H NMR (600 MHz, $CDCl_3$) δ 7.52-7.59 (m, 2H), 7.33-7.43 (m, 3H), 3.46-3.56 (m, 3H), 1.65-1.87 (3H), 1.54 (q, *J* = 7.6 Hz, 2H), 1.39-

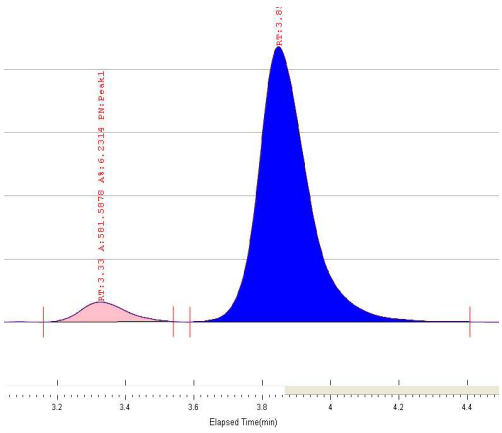
1.49 (m, 1H), 1.06 (br s, 1H), 0.35 (s, 3H), 0.34 (s, 3H). **^{13}C NMR** (151 MHz, $CDCl_3$): δ 136.65, 134.31, 129.63, 128.18, 65.44, 45.19, 32.82, 32.64, 24.46, -5.22, -5.49. **IR** (neat): 3426 (br), 3086 (w), 3069 (w), 2954 (m), 2861 (w), 1145 (m), 1407 (w), 1248 (s), 1112 (s), 933 (w), 833 (s), 777 (s), 700 (s) cm^{-1}. **HRMS** (DART) for $C_{13}H_{25}ClOSiN$ $[M+NH_4]^+$: calculated: 274.1394, found 274.1398. **$[\alpha]^{20}_D$**: +4.09 (c = 1.29, $CHCl_3$, *l* = 50 mm).

Chiral SFC (Chiracel OJ-H, 10% IPA, 3 mL/min, 100 bar, 35 °C, 210-270 nm) – analysis of (S)-5-chloro-1-(dimethyl(phenyl)silyl)pentan-1-ol.



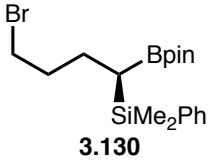
Peak Info			
Peak No	**% Area**	**Area**	**RT (min)**
1	49.4728	15564.5611	3.39
2	50.5272	15896.3116	3.92
Total:	100	31460.8727	

RACEMIC



Peak Info			
Peak No	**% Area**	**Area**	**RT (min)**
1	6.2314	581.5878	3.33
2	93.7686	8751.6431	3.85
Total:	100	9333.2309	

NONRACEMIC



3.130

(*R*)-(4-bromo-1-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)butyl)dimethyl(phenyl)silane (3.130) Reaction carried out using *(R,R)*-3,5-diisopropoxyTADDOLphosphoramidite (12.4 mg, 0.012 mmol, 0.06 equiv.) according to the procedure above (Method A). The crude reaction was purified by silica gel chromatography (large volume pipet, 20% dichloromethane in

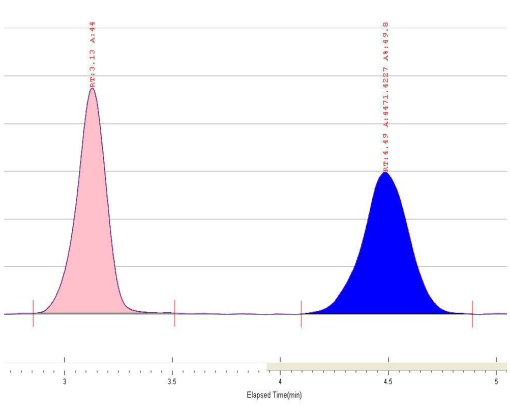
hexanes) to afford a clear oil. (69.1 mg, 87%)

^{1}H NMR (600 MHz, $CDCl_3$): δ 7.56 – 7.48 (m, 2H), 7.30-7.38 (m, 3H), 3.27-3.36 (m, 2H), 1.86-1.98 (m, 1H), 1.71-1.81 (m, 1H), 1.59-1.68 (m, 1H), 1.41-1.51 (m, 1H), 1.20 (s, 6H), 1.17 (s, 6H), 0.64 (dd, *J* = 12.0, 3.4 Hz, 1H), 0.34 (s, 3H), 0.33 (s, 3H). **^{13}C NMR** (151 MHz, $CDCl_3$): δ 138.76, 134.00, 129.09, 127.84, 83.11, 36.21, 33.54, 25.33, 24.89, 24.79, -2.17, -3.17. **^{11}B NMR** (192 MHz, $CDCl_3$): δ 34.20. **IR** (neat): ν_{max} 3069 (w), 3048 (w), 2977 (w), 2932 (w), 1480 (w), 1351 (s), 1254 (s), 1144 (s), 1112(w), 835 (m), 817 (m) cm^{-1}. **HRMS** (DART) for $C_{18}H_{34}BBrO_2SiN$ $[M+NH_4]^+$: calculated: 414.1635, found: 414.1650. **$[\alpha]^{20}_D$**: +20.98 (c = 1.05, $CHCl_3$, *l* = 50 mm).

Analysis of Stereochemistry:

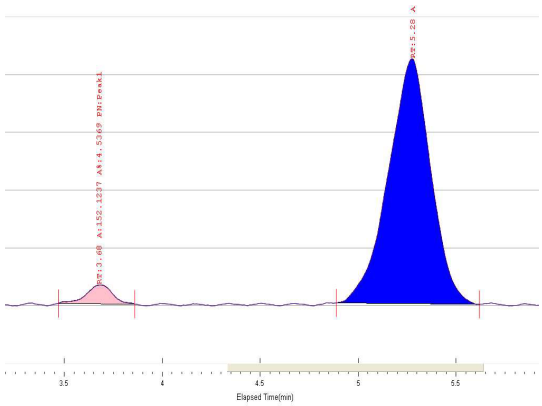
SFC analysis was performed directly on the silylboronate product. Racemic product was synthesized according to the procedure above (Compound 3.154).

Chiral SFC (Chiracel OJ-H, 1% IPA, 3 mL/min, 100 bar, 35 °C, 210-270 nm) – analysis of (R)-(4-bromo-1-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)butyl)dimethyl(phenyl)silane



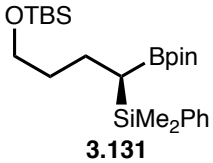
Peak Info			
Peak No	% Area	Area	RT (min)
1	50.1327	4495.2169	3.13
2	49.8673	4471.4227	4.49
Total:	100	8966.6396	

RACEMIC



Peak Info			
Peak No	% Area	Area	RT (min)
1	4.5369	152.1237	3.68
2	95.4631	3200.9023	5.28
Total:	100	3353.026	

NONRACEMIC



3.131

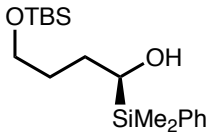
(R)-tert-butyl(4-(dimethyl(phenyl)silyl)-4-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)butoxy)dimethylsilane (3.131) Reaction carried out using *(R,R)*-3,5-diisopropoxyTADDOLphosphoramidite (12.4 mg, 0.012 mmol, 0.06 equiv.) according to the procedure above (Method A). The crude reaction was purified by silica gel chromatography (large volume pipet, 25-50% dichloromethane in hexanes) to afford a clear oil. (77.1 mg, 86%)

^{1}H NMR (600 MHz, $CDCl_3$) δ 7.48-7.57 (m, 2H), 7.30-7.36 (m, 3H), 3.47-3.58 (m, 2H), 1.56-1.65 (m, 1H), 1.46-1.56 (m, 1H), 1.34-1.45 (m, 2H), 1.20 (s, 6H), 1.16 (s, 6H), 0.86 (s, 9H), 0.63 (dd, *J* = 12.0, 3.0 Hz, 1H), 0.32 (d, *J* = 1.9 Hz, 6H), 0.00 (s, 6H). **^{13}C NMR** (151 MHz, $CDCl_3$): δ 139.17, 134.04, 128.95, 127.77, 82.93, 63.23, 36.50, 26.17, 25.31, 24.39, 22.28, 18.52, -2.15, -3.08, -5.02, -5.04. **^{11}B NMR**: (160 MHz, $CDCl_3$) δ 34.49. **IR** (neat): 3069 (w), 3052 (w), 2977 (w), 2953 (m), 2856 (w), 1470 (w), 1378 (s), 1249 (s),

1143 (s), 1099 (s), 969 (w), 823 (s), 773 (s), 663 (m) cm^{-1}. **HRMS** (DART) for $C_{24}H_{49}BO_3Si_2N$ $[M+NH_4]^+$: calculated: 466.3344, found: 466.3365. $[\alpha]^{20}_D$: +30.68 (c = 1.08, $CHCl_3$, *l* = 50 mm).

Analysis of Stereochemistry:

SFC analysis was performed on the oxidized silylboronate obtained according to procedure above (Method B) and purified by silica gel chromatography (large volume pipet, 10% ethyl acetate in hexanes) to afford a clear oil. Racemic product was synthesized according to the procedure above (Compound 3.154).

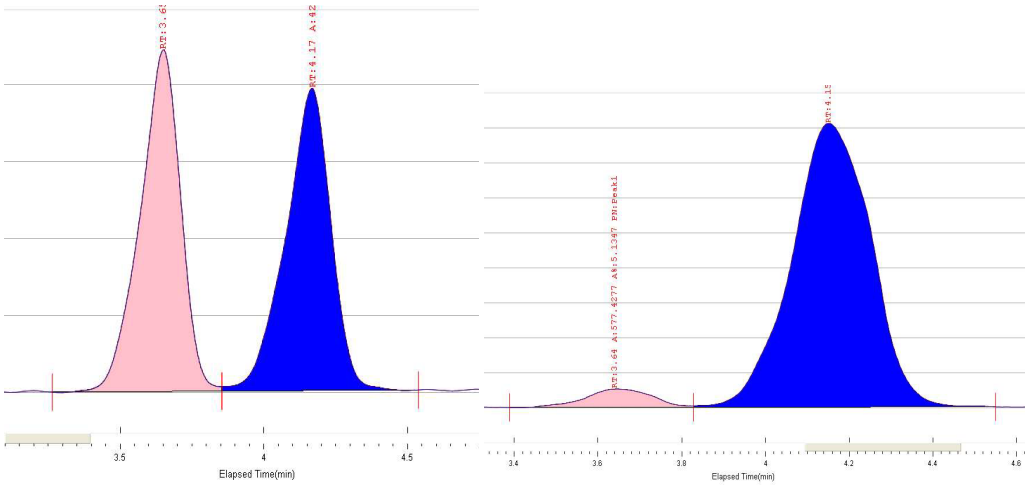


3.196

(*S*)-4-((*tert*-butyldimethylsilyl)oxy)-1-(dimethyl(phenyl)silyl)butan-1-ol (3.196)

^{1}H NMR (600 MHz, $CDCl_3$) δ 7.51-7.63 (m, 2H), 7.32-7.40 (m, 3H), 3.59-3.68 (m, 2H), 3.50 (dd, *J* = 11.3, 2.1 Hz, 1H), 2.19 (br s, 1H), 1.59-1.75 (m, 3H), 0.89 (s, 9H), 0.34 (s, 3H), 0.33 (s, 3H), 0.05 (d, *J* = 1.9 Hz, 6H). **^{13}C NMR** (151 MHz, $CDCl_3$): δ 137.32, 134.36, 129.39, 128.03, 65.07, 63.42, 30.77, 30.73, 26.13, 18.51, -5.15, -5.23, -5.29. **IR** (neat): 3427 (br), 3087 (w), 3020 (m), 2953 (m), 2867 (m), 1462 (w), 1360 (w), 1302 (s), 1098 (s), 1004 (w), 830 (s), 772 (s), 698 (s) cm^{-1}. **HRMS** (DART) for $C_{18}H_{35}O_2Si_2$ $[M+H]^+$: calculated: 339.2176, found 339.2187. $[\alpha]^{20}_D$: +1.55 (c = 1.18, $CHCl_3$, *l* = 50 mm).

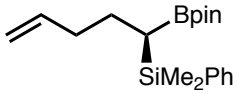
Chiral SFC (Chiracel OJ-H, 2% IPA, 3 mL/min, 100 bar, 35 °C, 210-270 nm) – analysis of (S)-4-((tert-butyldimethylsilyl)oxy)-1-(dimethyl(phenyl)silyl)butan-1-ol.



Peak Info			
Peak No	% Area	Area	RT (min)
1	50.3974	4358.336	3.65
2	49.6026	4289.5939	4.17
Total:	100	8647.9299	

Peak Info			
Peak No	% Area	Area	RT (min)
1	5.1347	577.4277	3.64
2	94.8653	10668.1874	4.15
Total:	100	11245.6151	

RACEMIC **NONRACEMIC**



3.132

(*R*)-dimethyl(phenyl)(1-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)pent-4-en-1-yl)silane (3.132) Reaction carried out using *(R,R)*-3,5-diisopropoxyTADDOLphosphoramidite (12.4 mg, 0.012 mmol, 0.06 equiv.) according to the procedure above (Method A). The crude reaction was purified by silica gel chromatography (large volume pipet, 2-15% dichloromethane in hexanes) to afford a clear oil. (39.0 mg, 59%)

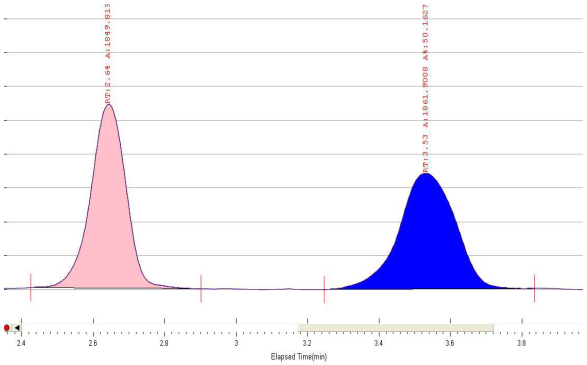
^{1}H NMR (600 MHz, $CDCl_3$): δ 7.50-7.56 (m, 2H), 7.27-7.34 (m, 3H), 5.70-5.81 (m, 1H), 4.82-5.03 (m, 2H), 2.05-2.19 (m, 1H), 1.89-2.01 (m, 1H), 1.61-1.71 (m, 1H), 1.36-1.46 (m, 1H), 1.20 (s, 6H), 1.16 (s, 6H), 0.68 (dd, J = 12.1, 3.2 Hz, 1H), 0.32 (d, J = 4.2 Hz, 6H). **^{13}C NMR** (151 MHz, $CDCl_3$): δ 139.13, 139.06, 134.05, 128.98, 127.79, 114.92, 82.98, 37.46, 25.54, 25.33, 24.96, -2.11, -3.09. **^{11}B NMR** (192 MHz, $CDCl_3$): δ 34.30. **IR** (neat):

ν_{max} 3070 (w), 3049 (w), 2972 (w), 2925(m), 1639 (w), 1350 (m), 1306 (m), 1143 (s), 1112(m), 848 (m), 699 (m) cm^{-1}. **HRMS** (DART) for $C_{19}H_{35}NO_2BSi$ $[M+NH_4]^+$: calculated: 348.2530, found: 348.2538. $\mathbf{[\alpha]^{20}_D}$: +14.97 (c = 1.08, $CHCl_3$, *l* = 50 mm).

Analysis of Stereochemistry:

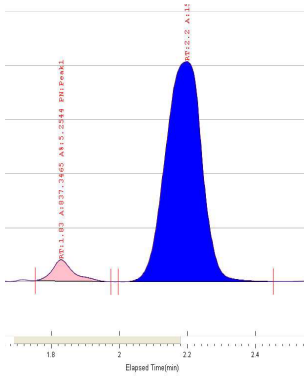
SFC analysis was performed directly on the silylboronate product. Racemic product was synthesized according to the procedure above (Compound 3.154).

Chiral SFC (Chiracel AD-H, 5% IPA, 3 mL/min, 100 bar, 35 °C, 210-270 nm) – analysis of (R)-dimethyl(phenyl)(1-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)pent-4-en-1-yl)silane.



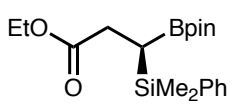
Peak Info			
Peak No	**% Area**	**Area**	**RT (min)**
1	49.8373	1849.8199	2.64
2	50.1627	1861.9008	3.53
Total:	100	3711.7207	

RACEMIC



Peak Info			
Peak No	**% Area**	**Area**	**RT (min)**
1	5.2544	837.3465	1.83
2	94.7456	15098.8179	2.2
Total:	100	15936.1644	

NONRACEMIC



3.133

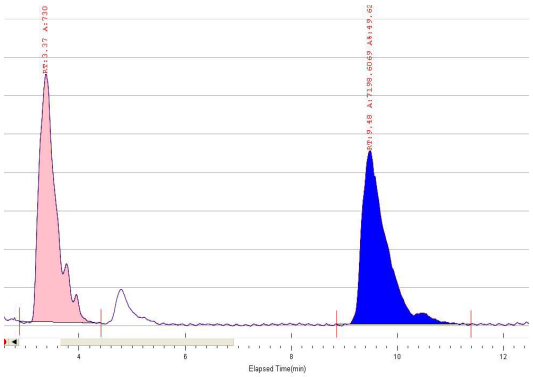
ethyl (*R*)-3-(dimethyl(phenyl)silyl)-3-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)propanoate (3.133) Reaction carried out using *(R,R)*-3,5-diisopropoxyTADDOLphosphoramidite (12.4 mg, 0.012 mmol, 0.06 equiv.) according to the procedure above at 70°C (Method A). The crude reaction was purified by silica gel chromatography (5% ethyl acetate in hexanes) to afford a clear oil. (29.1 mg, 40%)

^{1}H NMR (600 MHz, $CDCl_3$) δ 7.51 (dd, *J* = 6.4, 3.0 Hz, 2H), 7.27-7.38 (m, 3H), 3.94-4.14 (m, 2H), 2.49 (dd, *J* = 17.3, 12.8 Hz, 1H), 2.24 (dd, *J* = 17.3, 3.8 Hz, 1H), 1.19-1.25 (m, 9H), 1.16 (s, 6H), 1.00 (dd, *J* = 12.8, 3.8 Hz, 1H), 0.34 (d, *J* = 1.5 Hz, 6H). **^{13}C NMR** (151 MHz, $CDCl_3$): δ 175.00, 138.13, 134.01, 129.25, 127.95, 83.21, 60.53, 31.12, 25.22, 24.90, 14.47, -2.26, -3.54. **^{11}B NMR**: (160 MHz, $CDCl_3$) δ 30.36. **IR** (neat): 3070 (w), 3051 (w), 2977 (m), 2928 (m), 2852 (w), 1732 (s), 1427 (w), 1370 (s), 1337 (s), 1248 (s), 1139 (s), 1035 (m), 971 (m), 835 (s), 753 (s), 700 (s), 666 (s), cm^{-1}. **HRMS** (ESI) for $C_{19}H_{31}BO_4SiNa$ $[M+Na]^+$: calculated: 385.1995, found: 385.199493. **$[\alpha]^{20}_D$**: +16.59 (c = 1.16, $CHCl_3$, *l* = 50 mm).

Analysis of Stereochemistry:

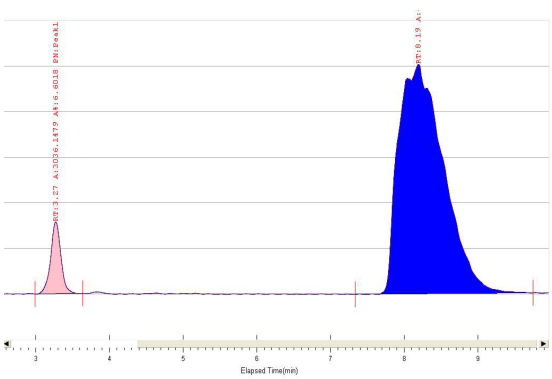
SFC analysis was performed directly on the silylboronate product. Racemic product was synthesized according to the procedure above (Compound 3.154).

Chiral SFC (Chiracel AD-H, 2% IPA, 3 mL/min, 100 bar, 35 °C, 210-270 nm) – analysis of ethyl (R)-3-(dimethyl(phenyl)silyl)-3-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)propanoate.



Peak Info			
Peak No	% Area	Area	RT (min)
1	50.3719	7306.5037	3.37
2	49.6281	7198.6069	9.48
Total:	100	14505.1106	

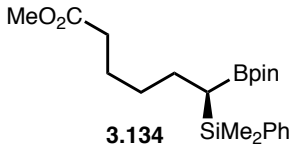
RACEMIC



Peak Info			
Peak No	% Area	Area	RT (min)
1	6.6018	3036.1479	3.27
2	93.3982	42953.5629	8.19
Total:	100	45989.7108	

NONRACEMIC

Note: the racemic trace contains the peak for the other regioisomer of hydrosilylation (ethyl 3-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)propanoate) that is difficult to isolate from the silylboronate.



3.134

methyl (*R*)-6-(dimethyl(phenyl)silyl)-6-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)hexanoate (3.134) Reaction carried out using *(R,R)*-3,5-diisopropoxyTADDOLphosphoramidite (12.4 mg, 0.012 mmol, 0.06 equiv.) according to the procedure above (Method A). The crude reaction was purified by silica gel chromatography (large volume pipet, 5% ethyl acetate in hexanes) to afford a clear oil. (65.6 mg, 84%)

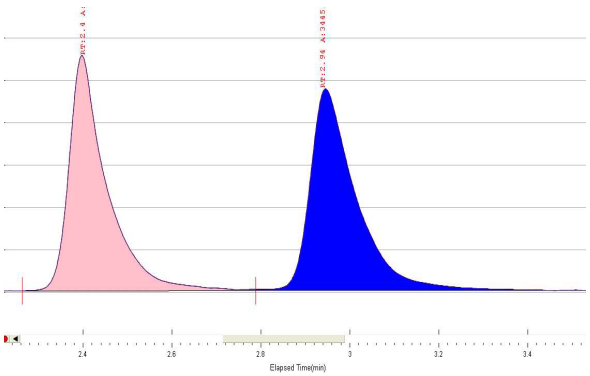
^{1}H NMR (600 MHz, $CDCl_3$): δ 7.45-7.58 (m, 2H), 7.37-7.34 (m, 3H), 3.63 (s, 3H), 2.19-2.26 (m, 2H), 1.50-1.61 (m, 3H), 1.27-1.41 (m, 2H), 1.21-1.27 (m, 1H), 1.20 (s, 6H), 1.17 (s, 6H) 0.62 (dd, *J* = 12.0, 2.9 Hz, 1H), 0.31 (s, 3H), 0.30 (s, 3H). **^{13}C NMR** (151 MHz, $CDCl_3$): δ 176.84, 141.56, 136.44, 131.42, 130.23, 85.39, 54.00, 36.66, 35.30, 28.10, 27.75,

27.41, 27.32, 0.30, -0.70. **^{11}B NMR** (192 MHz, $CDCl_3$): δ 34.20. **IR** (neat): ν_{max} 3068 (w), 3048 (w), 2976 (w), 2930 (w), 1739 (m), 1590 (w), 1370 (s), 1306 (m), 1143(s), 1112 (m), 846 (s) cm^{-1}. **HRMS** (ESI) for $C_{21}H_{35}BO_4SiNa$ $[M+Na]^+$: calculated: 413.2295, found: 413.2298. **$[\alpha]^{20}_D$**: +17.42 (c = 1.03, $CHCl_3$, *l* = 50 mm).

Analysis of Stereochemistry:

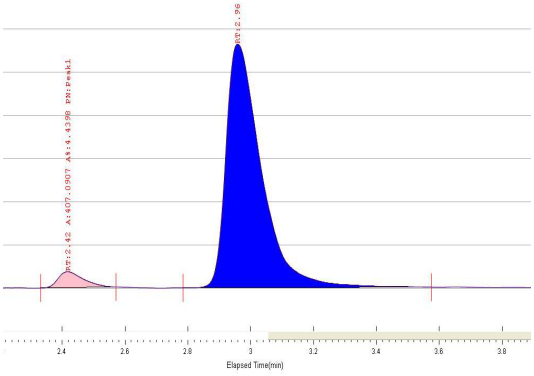
SFC analysis was performed directly on the silylboronate product. Racemic product was synthesized according to the procedure above (Compound 3.154).

Chiral SFC (Chiracel AD-H, 5% IPA, 3 mL/min, 100 bar, 35 °C, 210-270 nm) – analysis of methyl (R)-6-(dimethyl(phenyl)silyl)-6-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)hexanoate.



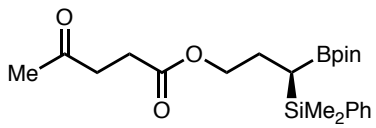
Peak Info			
Peak No	**% Area**	**Area**	**RT (min)**
1	48.8245	3287.0061	2.4
2	51.1755	3445.288	2.94
Total:	100	6732.2941	

RACEMIC



Peak Info			
Peak No	**% Area**	**Area**	**RT (min)**
1	4.4398	407.0907	2.42
2	95.5602	8762.0366	2.96
Total:	100	9169.1273	

NONRACEMIC



3.135

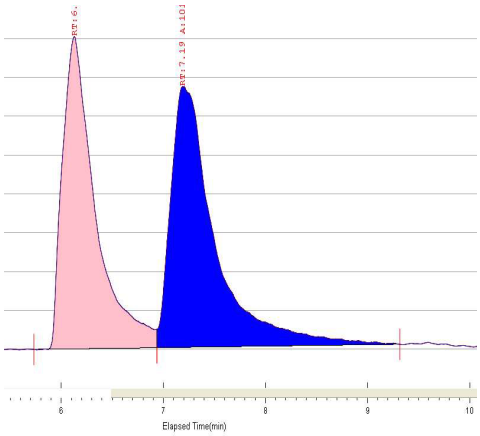
(*R*)-4-(dimethyl(phenyl)silyl)-4-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)butyl 4-oxopentanoate (3.135) Reaction carried out using *(R,R)*-3,5-diisopropoxyTADDOLphosphoramidite (12.4 mg, 0.012 mmol, 0.06 equiv.) according to the procedure above (Method A). The crude reaction was purified by silica gel chromatography (large volume pipet, 15%-20% ethyl acetate in hexanes) to afford a clear oil. (71.8 mg, 83%)

^{1}H NMR (600 MHz, $CDCl_3$): δ 7.45-7.58 (m, 2H), 7.30-7.39 (m, 3H), 3.93-4.02 (m, 2H), 2.68 (t, *J* = 6.7 Hz, 2H), 2.51 (t, *J* = 6.7 Hz, 2H), 2.16 (s, 3H), 1.64-1.73 (m, 1H), 1.43-1.61 (m, 1H), 1.45-1.53 (m, 1H), 1.36-1.41 (m, 1H), 1.20 (s, 6H), 1.17 (s, 6H), 0.62 (dd, *J* = 11.8, 3.3 Hz, 1H), 0.31 (s, 3H), 0.30 (s, 3H). **^{13}C NMR** (151 MHz, $CDCl_3$): δ 206.68, 172.75, 138.81, 133.89, 128.93, 127.71, 82.95, 64.63, 38.06, 31.84, 29.97, 28.10, 25.23, 24.80, 22.29, -2.22, -3.33**.** **^{11}B NMR** (192 MHz, $CDCl_3$): δ 34.10. **IR** (neat): ν_{max} 3069 (w), 3049 (w), 2976 (w), 2867 (w), 1734 (s), 1721 (s), 1351 (s), 1306 (m), 1143(s), 1112 (w), 836 (m) cm^{-1}. **HRMS** (ESI) for $C_{23}H_{37}BO_5SiNa$ $[M+Na]^+$: calculated: 455.2401, found: 455.2405. **$[\alpha]^{20}_D$**: +15.37 (c = 1.03, $CHCl_3$, *l* = 50 mm).

Analysis of Stereochemistry:

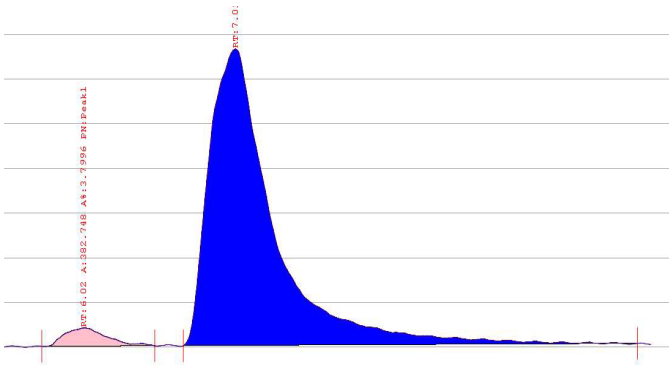
SFC analysis was performed directly on the silylboronate product. Racemic product was synthesized according to the procedure above (Compound 3.154).

Chiral SFC (Chiracel AD-H, 2% IPA, 3 mL/min, 100 bar, 35 °C, 210-270 nm) – analysis of (R)-4-(dimethyl(phenyl)silyl)-4-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)butyl 4-oxopentanoate.



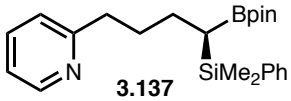
Peak Info			
Peak No	% Area	Area	RT (min)
1	47.038	9002.4221	6.13
2	52.962	10136.2126	7.19
Total:	100	19138.6347	

RACEMIC



Peak Info			
Peak No	% Area	Area	RT (min)
1	3.7996	382.748	6.02
2	96.2004	9690.6158	7.01
Total:	100	10073.3638	

NONRACEMIC



3.137

(*R*)-2-(4-(dimethyl(phenyl)silyl)-4-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)butyl)pyridine (3.137) Reaction carried out using *(R,R)*-3,5-diisopropoxyTADDOLphosphoramidite (12.4 mg, 0.012 mmol, 0.06 equiv.) according to the procedure above (Method A). The crude reaction was purified by silica gel chromatography (large volume pipet, 5-10% ethyl acetate in hexanes) to afford a clear oil. (48.9 mg, 62%)

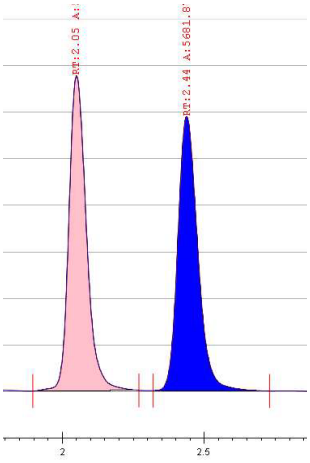
^{1}H NMR (600 MHz, $CDCl_3$) δ 8.47 (d, J = 4.8 Hz, 1H), 7.43-7.55 (m, 3H), 7.27-7.35 (m, 2H), 6.99-7.08 (m, 2H), 2.64-2.79 (m, 2H), 1.72-1.82 (m, 1H), 1.55-1.69 (m, 2H), 1.34-1.44 (m, 1H), 1.19 (s, 6H), 1.15 (s, 6H), 0.66-0.71 (m, 1H), 0.30 (s, 6H). **^{13}C NMR** (151 MHz, $CDCl_3$): δ 162.62, 149.31, 139.12, 136.32, 134.03, 128.91, 127.76, 122.73, 120.97, 82.93, 38.45, 33.42, 25.88, 25.35, 24.98, -2.09, -3.14. **^{11}B NMR**: (160 MHz, $CDCl_3$) δ 31.05. **IR** (neat): 3068 (w), 3045 (w), 2976 (m), 2925 (m), 2854 (w), 1589 (m), 1473 (w),

1459 (w), 1349 (s), 1304 (s), 1143 (s), 1111 (m), 967 (w), 815 (s), 699 (s) cm^{-1}. **HRMS** (DART) for $C_{23}H_{35}BO_2SiN$ $[M+H]^+$: calculated: 396.2534, found: 396.2551. **$[\alpha]^{20}_D$**: +15.92 (c = 1.17, $CHCl_3$, *l* = 50 mm).

Analysis of Stereochemistry:

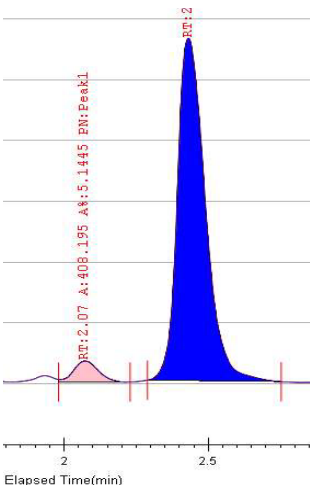
SFC analysis was performed directly on the silylboronate. Racemic product was synthesized according to the procedure above (Compound 3.154).

Chiral SFC (Chiracel AD-H, 15% IPA, 3 mL/min, 100 bar, 35 °C, 210-270 nm) – analysis of (R)-2-(4-(dimethyl(phenyl)silyl)-4-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)butyl)pyridine.



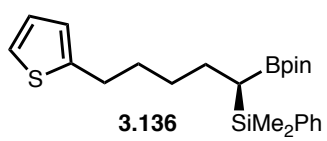
Peak Info			
Peak No	**% Area**	**Area**	**RT (min)**
1	50.4067	5775.0746	2.05
2	49.5933	5681.876	2.44
Total:	100	11456.9506	

RACEMIC



Peak Info			
Peak No	**% Area**	**Area**	**RT (min)**
1	5.1445	408.195	2.07
2	94.8555	7526.3499	2.43
Total:	100	7934.5449	

NONRACEMIC



3.136

(*R*)-dimethyl(phenyl)(1-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)-5-(thiophen-2-yl)pentyl)silane (3.136)

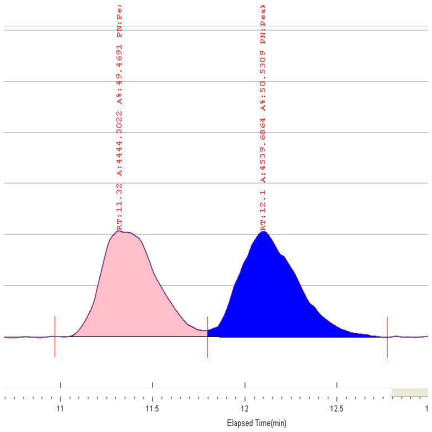
Reaction carried out using *(R,R)*-3,5-diisopropoxyTADDOLphosphoramidite (12.4 mg, 0.012 mmol, 0.06 equiv.) according to the procedure above (Method A). The crude reaction was purified by silica gel chromatography (large volume pipet, 5-15% dichloromethane in hexanes) to afford a clear oil. (59.3 mg, 74%)

^{1}H NMR (600 MHz, $CDCl_3$): δ 7.49-7.60 (m, 2H), 7.27-7.35 (m, 3H), 7.08 (dd, *J* = 5.1, 1.2 Hz, 1H), 6.89 (dd, *J* = 5.2, 3.4 Hz, 1H), 6.73 (d, *J* = 3.3 Hz, 1H), 2.75 (t, *J* = 7.6 Hz, 2H), 1.50-1.72 (m, 2H), 1.39-1.49 (m, 1H), 1.32-1.39 (m, 1H), 1.22-1.32 (m, 2H), 1.20 (s, 6H), 1.16 (s, 6H), 0.65 (dd, *J* = 12.0, 3.2 Hz, 1H), 0.34 (s, 3H), 0.33 (s, 3H). **^{13}C NMR** (151 MHz, $CDCl_3$): δ 145.94, 139.21, 134.02, 128.97, 127.79, 126.75, 124.08, 122.82, 82.93, 32.82, 31.71, 29.96, 25.75, 25.28, 24.89, -2.10, -3.14. **^{11}B NMR** (192 MHz, $CDCl_3$): δ 34.20. **IR** (neat): ν_{max} 3068 (w), 3021 (w), 2977 (w), 2928(w), 1440 (w), 1349 (s), 1247 (m), 1144 (s), 968(m), 835 (s), 697 (s) cm^{-1}. **HRMS** (DART) for $C_{23}H_{39}BO_2SSiN$ $[M+NH_4]^+$: calculated: 432.2564, found: 432.2577. **$[\alpha]^{20}_D$**: +14.13 (c = 1.04, $CHCl_3$, *l* = 50 mm).

Analysis of Stereochemistry:

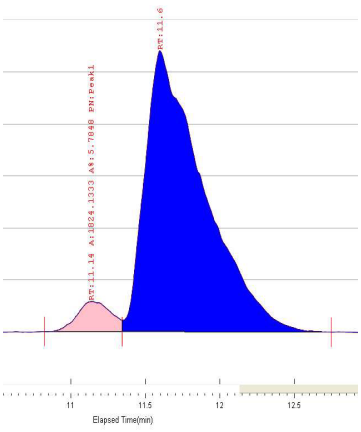
SFC analysis was performed directly on the silylboronate product. Racemic product was synthesized according to the procedure above (Compound 3.154).

Chiral SFC (Chiracel ODR-H, 1% IPA, 3 mL/min, 100 bar, 35 °C, 210-270 nm) – analysis of (R)-dimethyl(phenyl)(1-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)-5-(thiophen-2-yl)pentyl)silane.



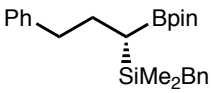
Peak Info			
Peak No	% Area	Area	RT (min)
1	49.4691	4444.3022	11.32
2	50.5309	4539.6864	12.1
Total:	100	8983.9886	

RACEMIC



Peak Info			
Peak No	% Area	Area	RT (min)
1	5.7848	1824.1333	11.14
2	94.2152	29708.8479	11.6
Total:	100	31532.9812	

NONRACEMIC



3.140

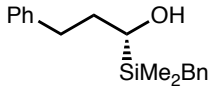
(*S*)-benzyldimethyl(3-phenyl-1-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)propyl)silane (3.140) Reaction carried out using *(S,S)*-3,5-diethoxyoxyTADDOLphosphoramidite (11.0 mg, 0.012 mmol, 0.06 equiv.) according to the procedure above (Method A). The crude reaction was purified by silica gel chromatography (large volume pipet, 15-30% dichloromethane in hexanes) to afford a clear oil. (62 mg, 79%)

^{1}H NMR (600 MHz, $CDCl_3$) δ 7.30 (t, *J* = 7.6 Hz, 2H), 7.17-7.24 (m, 5H), 7.07 (t, *J* = 7.4 Hz, 1H), 6.99 (d, *J* = 7.5 Hz, 2H), 2.69-2.82 (m, 1H), 2.43-2.56 (m, 1H), 2.09-2.21 (m, 2H), 1.87-1.99 (m, 1H), 1.66-1.76 (m, 1H), 1.30 (s, 6H), 1.29 (s, 6H), 0.53 (dd, *J* = 12.3, 2.9 H, 0.00 (d, *J* = 2.0 Hz, 1H)z, 6H). **^{13}C NMR** (151 MHz, $CDCl_3$): δ 142.91, 140.40, 128.75, 128.45, 128.38, 128.31, 125.85, 124.05, 83.04, 39.78, 28.32, 25.50, 25.32, 24.97, -3.19, -3.59. **^{11}B NMR**: (160 MHz, $CDCl_3$) δ 34.39. **IR** (neat): 3082 (w), 3060 (w), 2976

(m), 2925 (m), 1600 (w), 1493 (m), 1350 (s), 1305 (s), 1142 (s), 993 (w), 830 (s), 697 (s) cm^{-1}. **HRMS** (DART) for $C_{24}H_{39}BO_2SiN$ $[M+NH_4]^+$: calculated: 412.2843, found: 412.2844. $[\alpha]^{20}_D$: -17.42 (c = 1.03, $CHCl_3$, *l* = 50 mm).

Analysis of Stereochemistry:

SFC analysis was performed on the oxidized silylboronate obtained according to procedure above (Method B) and purified by silica gel chromatography (large volume pipet, 10% ethyl acetate in hexanes) to afford a clear oil. Racemic product was synthesized according to the procedure above (Compound 3.154).

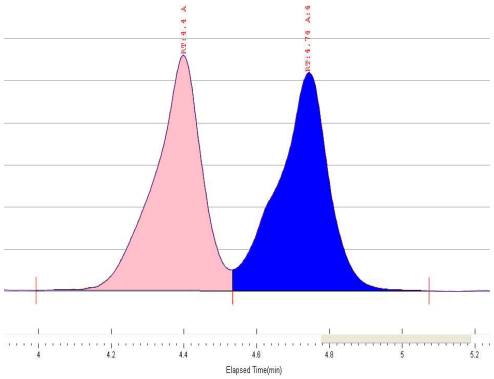


3.197

(*R*)-1-(benzyldimethylsilyl)-3-phenylpropan-1-ol (3.197)

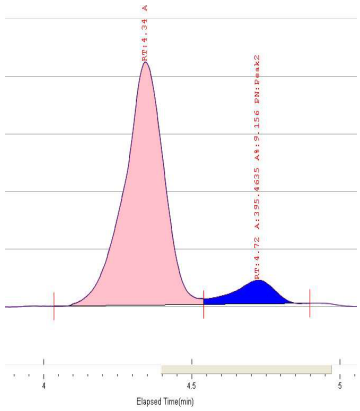
^{1}H NMR (600 MHz, $CDCl_3$) δ 7.27-7.34 (m, 2H), 7.17-7.24 (m, 5H), 7.09 (t, *J* = 7.4 Hz, 1H), 7.02 (d, *J* = 7.4 Hz, 2H), 3.40 (dd, *J* = 11.1, 3.0 Hz, 1H), 2.88-2.98 (m, 1H), 2.58-2.70 (m, 1H), 2.11-2.25 (m, 2H), 1.73-1.92 (m, 2H), 1.08 (br s, 1H), 0.04 (s, 3H), 0.01 (s, 3H). **^{13}C NMR** (151 MHz, $CDCl_3$): δ 142.30, 139.83, 128.70, 128.65, 128.56, 128.30, 126.07, 124.39, 64.52, 35.62, 33.49, 23.48, -5.44, -5.80. **IR** (neat): 3457 (br), 3081 (w), 3060 (w), 2999 (m), 2953 (m), 2922 (w), 1599 (m), 1493 (s), 1247 (s), 1056 (m), 798 (s), 698 (s) cm^{-1}. **HRMS** (DART) for $C_{18}H_{25}OSi$ $[M+H]^+$: calculated: 285.1675, found 285.1663. $[\alpha]^{20}_D$: -15.98 (c = 1.33, $CHCl_3$, *l* = 50 mm).

Chiral SFC (Chiracel OJ-H, 12% IPA, 3 mL/min, 100 bar, 35 °C, 210-270 nm) – analysis of (R)-1-(benzyldimethylsilyl)-3-phenylpropan-1-ol.



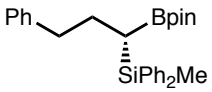
Peak Info			
Peak No	% Area	Area	RT (min)
1	50.2485	5035.3701	4.4
2	49.7515	4985.5582	4.74
Total:	100	10020.9283	

RACEMIC



Peak Info			
Peak No	% Area	Area	RT (min)
1	90.844	3923.7106	4.34
2	9.156	395.4635	4.72
Total:	100	4319.1741	

NONRACEMIC



3.142

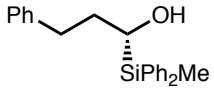
(*S*)-methyldiphenyl(3-phenyl-1-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)propyl)silane (3.142) Reaction carried out using *(S,S)*-3,5-diethoxyoxyTADDOLphosphoramidite (11.0 mg, 0.012 mmol, 0.06 equiv.) according to the procedure above (Method A). The crude reaction was purified by silica gel chromatography (large volume pipet, 20-33% dichloromethane in hexanes) to afford a clear oil. (71.7 mg, 81%)

^{1}H NMR (600 MHz, $CDCl_3$) δ 7.49-7.56 (m, 4H), 7.29-7.39 (m, 6H), 7.26 (t, J = 8.6 Hz, 2H), 7.16-7.20 (m, 1H), 7.12 (d, J = 7.6 Hz, 2H), 2.69-2.08 (m, 1H), 2.46-2.55 (m, 1H), 1.96-2.05 (m, 1H), 1.72-1.81 (m, 1H), 1.15 (s, 6H), 1.03-1.12 (m, 7H), 0.63 (s, 3H). **^{13}C NMR** (151 MHz, $CDCl_3$): δ 142.57, 137.16, 137.08, 135.03, 134.95, 129.20, 128.82, 128.40, 127.84, 127.77, 125.84, 83.08, 39.64, 28.52, 25.24, 24.81, -3.94. **^{11}B NMR**: (160 MHz, $CDCl_3$) δ 34.58. **IR** (neat): 3085 (w), 3068 (w), 3024 (w), 2926 (m), 2859 (m), 1480

(w), 1370 (m) 1351 (s), 1308 (s), 1143 (s), 1109 (m), 846 (m), 698 (s) cm^{-1}. **HRMS** (DART) for $C_{28}H_{39}BO_2SiN$ $[M+NH_4]^+$: calculated: 460.2843, found: 460.2851. $[\alpha]^{20}_D$: -10.24 (c = 1.02, $CHCl_3$, *l* = 50 mm).

Analysis of Stereochemistry:

SFC analysis was performed on the oxidized silylboronate obtained according to procedure above (Method B) and purified by silica gel chromatography (large volume pipet, 10% ethyl acetate in hexanes) to afford a clear oil. Racemic product was synthesized according to the procedure above (Compound 3.154).

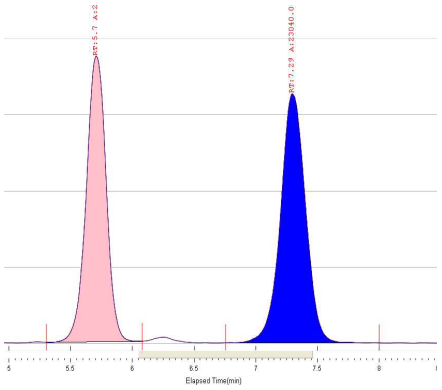


3.198

(*R*)-1-(methyldiphenylsilyl)-3-phenylpropan-1-ol (3.198)

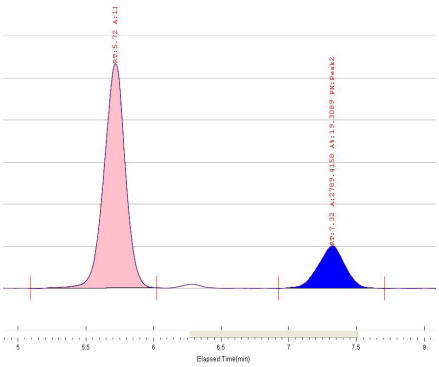
^{1}H NMR (600 MHz, $CDCl_3$) δ 7.61 (d, *J* = 6.8 Hz, 2H), 7.57 (d, *J* = 7.1 Hz, 2H), 7.32-7.45 (m, 6H), 7.25-7.31 (m, 2H), 7.13-7.22 (m, 3H), 3.88-3.98 (m, 1H), 2.89-3.00 (m, 1H), 2.60-2.73 (m, 1H), 1.88-1.99 (m, 2H), 1.20 (d, *J* = 5.1 Hz, 1H), 0.62 (s, 3H). **^{13}C NMR** (151 MHz, $CDCl_3$): δ 142.20, 135.29, 135.13, 134.97, 134.73, 129.86, 129.83, 128.76, 128.58, 128.24, 126.01, 64.09, 35.42, 33.45, -6.43. **IR** (neat): 3438 (br), 3067 (w), 3024 (w), 2924 (w), 2851 (w), 1495 (w), 1427 (m), 1251 (m), 1111 (s), 998 (m), 788 (m), 728 (m), 698 (s) cm^{-1}. **HRMS** (DART) for $C_{22}H_{28}OSiN$ $[M+NH_4]^+$: calculated: 350.194, found 350.1941. $[\alpha]^{20}_D$: -5.19 (c = 1.08, $CHCl_3$, *l* = 50 mm).

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



Peak Info			
Peak No	**% Area**	**Area**	**RT (min)**
1	47.6988	21012.5641	5.7
2	52.3012	23040.0429	7.29
Total:	100	44052.607	

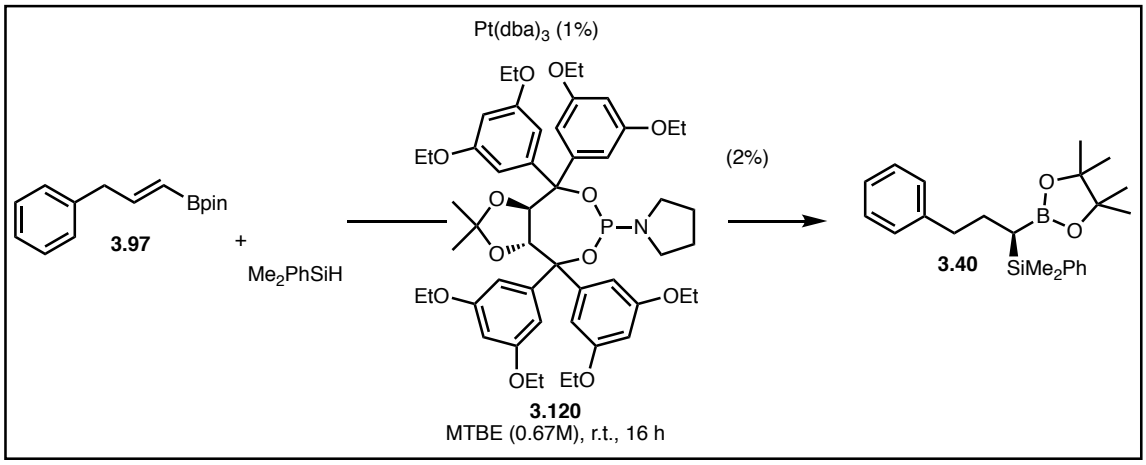
RACEMIC



Peak Info			
Peak No	**% Area**	**Area**	**RT (min)**
1	80.6911	11656.8696	5.72
2	19.3089	2789.4158	7.32
Total:	100	14446.2854	

NONRACEMIC

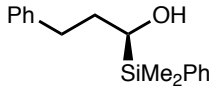
3.5.4 Procedure for Gram-Scale Hydrosilylation Outside of Glove-Box



A 100 mL two-neck round bottom flask equipped with a stir bar and condenser was flame-dried. $Pt(dba)_3$ (107 mg, 0.119 mmol, 0.01 equiv) and (*R,R)*-3,5-diethoxyTADDOLphoshoramidite (219 mg, 0.238 mmol, 0.02 equiv) were weighed out open to air, and transferred to the flame-dried round bottom flask. The round bottom flask was purged of air by vacuum and back-filled with nitrogen three times. Under nitrogen, MTBE (10 mL) was added and the reaction was allowed to reflux at 80°C for 10 minutes. The reaction flask was cooled to room temperature, and (*E*)-4,4,5,5-tetramethyl-2-(3-phenylprop-1-en-1-yl)-1,3,2-dioxaborolane (2.91g, 11.9 mmol, 1.00 quiv) was added as a solution of MTBE. (8 mL) Dimethylphenylsilane (2.19 mL, 14.3 mmol, 1.20 equiv) was then added and the reaction was allowed to stir at room temperature overnight for 16 hours. The reaction was then diluted with ether, filtered through a pad of silica and concentrated under reduced pressure. The crude mixture was then purified by silica gel chromatography (20-50% dichloromethane in hexanes) to afford a clear oil. (4.036g, 89%)

Analysis of Stereochemistry:

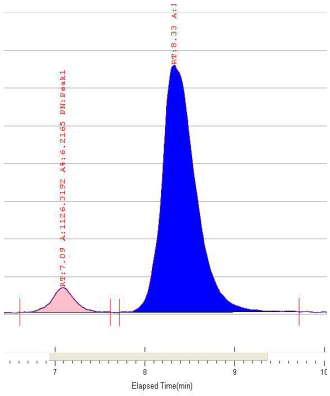
The enantioselectivity was determined by the oxidation of about 20 mg of purified silylboronate according to the procedure above (Method B), and purified by silica gel chromatography (large volume pipet, 10% ethyl acetate in hexanes) to afford a clear oil.



3.154

(*S*)-1-(dimethyl(phenyl)silyl)-3-phenylpropan-1-ol (3.154)

Chiral SFC (Chiracel OJ-H, 10% IPA, 3 mL/min, 100 bar, 35 °C, 210-270 nm) – analysis of (S)-1-(dimethyl(phenyl)silyl)-3-phenylpropan-1-ol.



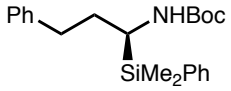
*See Compound **3.154** for racemic SFC trace.*

Peak Info			
Peak No	**% Area**	**Area**	**RT (min)**
1	6.2165	1126.3192	7.09
2	93.7835	16991.7778	8.33
Total:	100	18118.097	

NONRACEMIC

3.5.5 Transformations of Geminal Silylboronates

1. Amination



3.155

***tert-butyl-(S)*-(1-(dimethyl(phenyl)silyl)-3 phenylpropyl)carbamate (3.155)** In a glove box, potassium *tert*-butoxide (27 mg, 0.24 mmol, 1.50 equiv) was added to an oven dried two-dram vial equipped with a stir, dissolved in toluene (0.50 mL) and sealed with a teflon screw cap. Outside the glove box, a solution of methoxyamine (1.53 M in THF, 0.157 mL, 0.24 mmol, 1.50 equiv.) was added, followed by *(R)*-dimethyl(phenyl)(3-phenyl-1-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)propyl)silane (62.1 mg, 0.16 mmol, 1.00 equiv.) in a solution of toluene (0.5 mL). The reaction was sealed with tape, and heated to 80°C for 14 hours. The reaction was allowed to cool to room temperature, and di-*tert*-butyl dicarbonate (1.0 M in THF, 0.240 mL, 0.24 mmol, 1.50 equiv.) was added and allowed to stir at room temperature for 1.5 hours. The reaction mixture was diluted with diethyl ether, filtered through a celite pipet plug and concentrated under reduced pressure. The crude mixture was purified by silica gel chromatography (large volume pipet, 3% ethyl acetate in hexanes) to afford a clear solid. (41 mg, 72%)

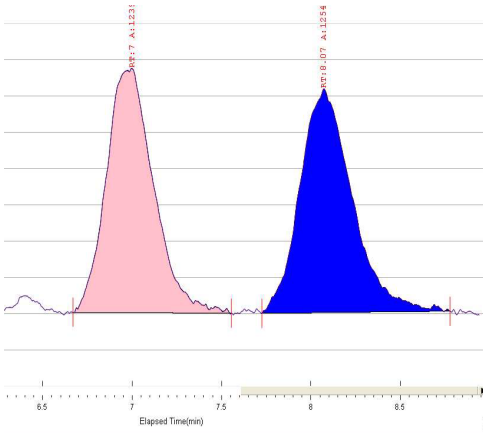
^{1}H NMR (600 MHz, $CDCl_3$) δ 7.47- 7.54 (m, 2H), 7.34-7.43 (m, 3H), 7.23-7.28 (m, 2H), 7.09-7.21 (m, 3H), 4.25 (d, *J* = 10.4 Hz, 1H), 3.37-3.48 (m, 1H), 2.69-2.82 (m, 1H), 2.50-2.62 (m, 1H), 1.74-1.88 (m, 1H), 1.51-1.60 (m, 1H), 1.45 (s, 9H), 0.35 (s, 3H), 0.33 (s, 3H). **^{13}C NMR** (126 MHz, $CDCl_3$): δ 156.42, 142.49, 136.38, 134.23, 129.59, 128.63, 128.50, 128.14, 125.90, 79.14, 40.74, 34.04, 34.00, 28.63, -4.43, -5.04. **IR** (neat): 3428 (br), 3066 (w), 3012 (w), 2927 (w), 2852 (w), 1692 (s), 1494 (s), 1453 (m), 1377 (m), 1215 (m), 1166 (s), 1014 (w), 829 (m), 749 (s), 698 (s) cm^{-1}. **HRMS** (DART) for $C_{22}H_{32}SiNO_2$

$[M+H]^+$: calculated: 370.2202, found 370.2216. $[\alpha]^{20}_D$: +0.63 (c = 1.08, $CHCl_3$, *l* = 50 mm).

Analysis of Stereochemistry:

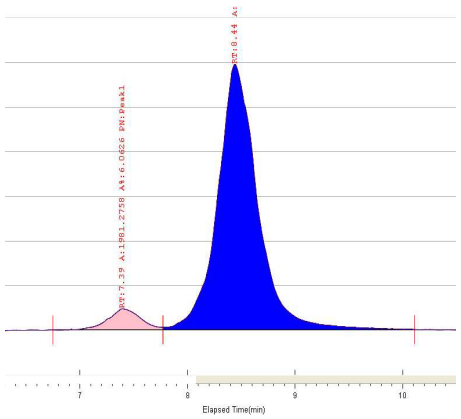
The enantioselectivity was determined directly on the silylamine.

Chiral SFC (Chiracel AD-H, 5% IPA, 3 mL/min, 100 bar, 35 °C, 210-270 nm) – analysis of tert-butyl (S)-(1-(dimethyl(phenyl)silyl)-3-phenylpropyl)carbamate.



Peak Info			
Peak No	**% Area**	**Area**	**RT (min)**
1	49.7078	1239.5315	7
2	50.2922	1254.1057	8.07
Total:	100	2493.6372	

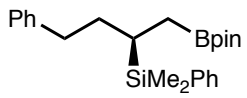
RACEMIC



Peak Info			
Peak No	**% Area**	**Area**	**RT (min)**
1	6.0626	1981.2758	7.39
2	93.9374	30698.9206	8.44
Total:	100	32680.1964	

NONRACEMIC

2. Homologation



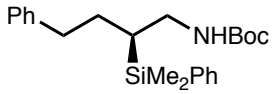
3.156

(*R*)-dimethyl(phenyl)(4-phenyl-1-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)butan-2-yl)silane (3.156) Starting material derived from procedure VI. In a glove box, sodium trifluoromethanesulfonate (516 mg, 3.00 mmol, 2.00 equiv.) was added to an oven dried 100 mL round bottom flask equipped with a stir bar. Outside the glove box under N_2, (*R*)-dimethyl(phenyl)(3-phenyl-1-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)propyl)silane (571 mg, 1.50 mmol, 1.00 equiv.) was added as a solution of THF (7.5 mL), followed by bromochloromethane (0.975 mL, 15.0 mmol, 10.0 equiv.). The reaction flask was cooled to -78°C and was charged with *n*-butyllithium (6.00 mL, 15.0 mmol, 10.0 equiv) dropwise using a syringe pump over 15 minutes. The reaction was kept at -78°C and stirred for 1 hour, and then allowed to warm to room temperature and stir for 14 hours. The reaction was cooled to 0°C, and quenched with a saturated ammonium chloride solution. The aqueous phase was extracted with diethyl ether and the combined extracts were washed with brine, dried over sodium sulfate, filtered and concentrated under reduced pressure. The crude reaction mixture was purified by silica gel chromatography (33% dichloromethane in hexanes) to afford a clear oil. (426 mg, 72%)

^{1}H NMR (500 MHz, $CDCl_3$) δ 7.50-7.55 (m, 2H), 7.31-7.37 (m, 3H), 7.21-7.27 (m, 2H), 7.13-7.18 (m, 1H), 7.07-7.12 (m, 2H), 2.66 (ddd, *J* = 13.3, 11.5, 5.1 Hz, 1H), 2.47 (ddd, *J* = 13.3, 11.4, 5.5 Hz, 1H), 1.72-1.83 (m, 1H), 1.49-1.61 (m, 1H), 1.25 (s, 6H), 1.24 (s, 6H), 1.01 (dd, *J* = 16.2, 5.6 Hz, 1H), 0.83 (dd, *J* = 16.2, 8.4 Hz, 1H), 0.30 (s, 3H), 0.29 (s, 3H). **^{13}C NMR** (126 MHz, $CDCl_3$): δ 143.39, 139.06, 134.29, 128.91, 128.55, 128.38, 127.82, 125.68, 83.21, 35.84, 35.11, 25.25, 25.02, 20.44, -3.73, -4.32. **^{11}B NMR**: (160 MHz,

$CDCl_3$) δ 34.26. **IR** (neat): 3085 (w), 3025 (w), 3002 (m), 2924 (w), 2856 (w), 1495 (w), 1453 (w), 1360 (s), 1320 (s), 1248 (m), 1215 (m), 1143 (s), 968 (m), 831 (s), 699 (s) cm^{-1}. **HRMS** (DART) for $C_{24}H_{39}BO_2SiN$ $[M+NH_4]^+$: calculated: 412.2843, found: 412.2846. $[\alpha]^{20}_D$: +3.48 (c = 1.03, $CHCl_3$, *l* = 50 mm).

3. Amination

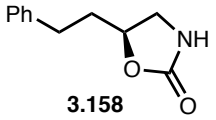


3.157

***tert*-butyl-(*S*)-(2-(dimethyl(phenyl)silyl)-4-phenylbutyl)carbamate (3.157)** This compound was synthesized in according to the procedure above (0.40 mmol) The crude mixture was purified by silica gel chromatography (large volume pipet, 5% ethyl acetate in hexane) to afford a clear oil. (117.5 mg, 77%)

^{1}H NMR (500 MHz, $CDCl_3$) δ 7.46-7.56 (m, 2H), 7.34-7.42 (m, 3H), 7.22-7.29 (m, 2H), 7.16-7.21 (m, 1H), 7.10 (d, *J* = 7.2 Hz, 2H), 4.29 (br s, 1H), 3.23-3.40 (m, 2H), 2.61-2.71 (m, 1H), 2.50-2.60 (m, 1H), 1.74-1.85 (m, 1H), 1.59-1.70 (m, 1H), 1.44 (s, 9H), 1.05-1.15 (m, 1H), 0.35 (s, 3H), 0.34 (s, 3H). **^{13}C NMR** (126 MHz, $CDCl_3$): δ 156.03, 142.51, 138.08, 133.98, 129.32, 128.56, 128.48, 128.12, 125.93, 79.09, 41.15, 35.44, 30.14, 28.61, 26.70, -3.93, -3.76. **IR** (neat): 3424 (br), 3067 (w), 3024 (w), 2975 (m), 2925 (w), 1700 (s), 1498 (s), 1365 (m), 1249 (s), 1168 (s), 1111 (m), 833 (m), 699 (s) cm^{-1}. **HRMS** (DART) for $C_{23}H_{34}O_2SiN$ $[M+NH_4]^+$: calculated: 384.2359, found 384.2359. $[\alpha]^{20}_D$: +4.61 (c = 1.12, $CHCl_3$, *l* = 50 mm).

4. Tamao-Fleming Oxidation



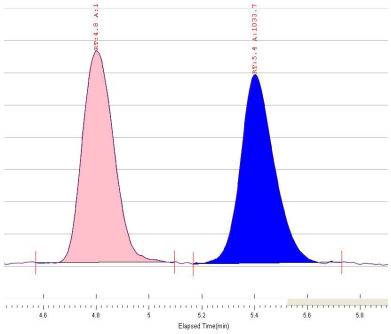
(*S*)-5-phenethyloxazolidin-2-one (3.158) This compound was synthesized according to a literature procedure. In a glove box, potassium hydride (138 mg, 3.41 mmol, 6.20 equiv.) was added to an oven dried 4-dram vial equipped with a stir bar and dissolved in DMF (1.5 mL). Outside the glove box under N_2, the vial was cooled to 0°C and charged with *tert*-butyl hydrogen peroxide (5.5M in nonane, 0.620 mL, 3.41 mmol, 6.20 equiv.) dropwise. After 10 minutes of stirring and complete evolution of hydrogen, potassium fluoride (64 mg, 1.10 mmol, 2.00 equiv) was added as a solid and *tert*-butyl (*R*)-(2-(dimethyl(phenyl)silyl)-4-phenylbutyl)carbamate (210 mg, 0.55 mmol, 1.00 equiv) was added as a solution of DMF (1.5 mL). The vial was resealed, purged with N_2 and heated to 60°C for 1.5 hours under N_2. The reaction was allowed to cool to room temperature, diluted with ethyl acetate, filtered through a celite pad and concentrated under reduced pressure. The resulting crude mixture was purified by silica gel chromatography (dichloromethane – 33% ethyl acetate in dichloromethane) to afford a white solid. (77.8 mg, 74%).

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.13-7.33 (m, 5H), 5.10 (br s, 1H), 4.53-4.68 (m, 1H), 3.63 (t, *J* = 8.4, 1H), 3.22 (t, *J* = 8.2 Hz, 1H), 2.78-2.90 (m, 1H), 2.65-2.78 (m, 1H), 2.06-2.20 (m, 1H), 1.85-1.99 (m, 1H). **^{13}C NMR** (126 MHz, $CDCl_3$): 160.28, 140.65, 128.76, 128.62, 126.44, 76.29, 46.08, 36.87, 31.20. **IR** (neat): 3277 (br), 3061 (w), 3026 (w), 2924 (m), 2856 (w), 1743 (s), 1491 (m), 1453 (m), 1377 (w), 1238 (s), 1079 (m), 746 (s), 699 (s) cm^{-1}. **HRMS** (DART) for $C_{11}H_{14}O_2N$ $[M+H]^+$: calculated: 192.1205, found 192.102. **$[\alpha]^{20}_D$**: -30.67 (c = 1.07, $CHCl_3$, *l* = 50 mm).

Analysis of Stereochemistry:

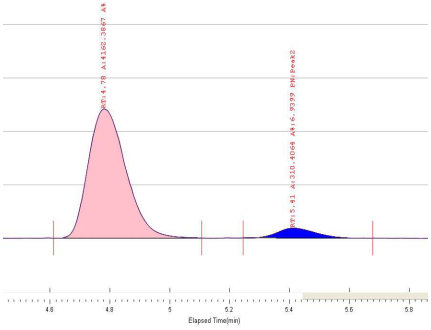
The stereospecificity was determined directly on the oxazolidinone.

Chiral SFC (Chiracel AS-H, 30% IPA, 3 mL/min, 100 bar, 35 °C, 210-270 nm) – analysis of (S)-5-phenethyloxazolidin-2-one.



Peak Info			
Peak No	**% Area**	**Area**	**RT (min)**
1	51.052	1078.1429	4.8
2	48.948	1033.7088	5.4
Total:	100	2111.8517	

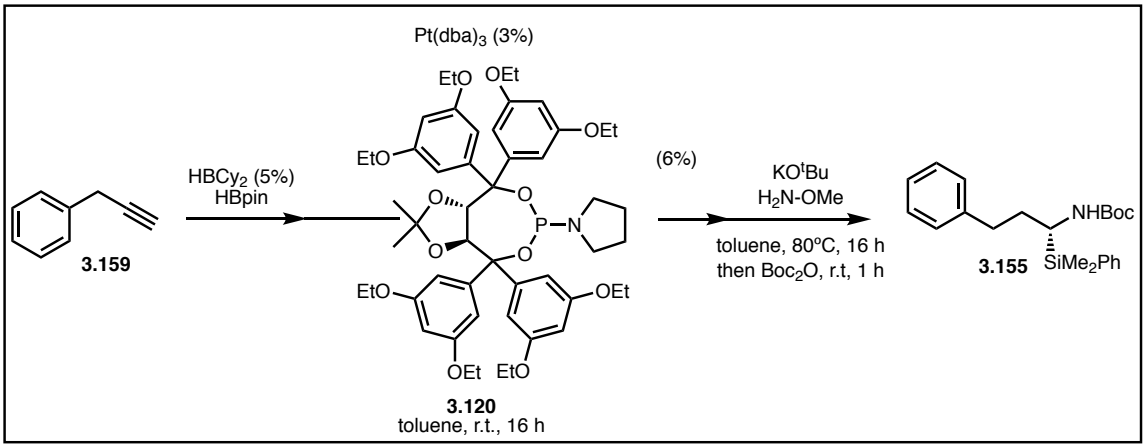
RACEMIC



Peak Info			
Peak No	**% Area**	**Area**	**RT (min)**
1	93.0601	4162.3867	4.78
2	6.9399	310.4064	5.41
Total:	100	4472.7931	

NONRACEMIC

3.5.6 Procedure for one-pot hydroboration-hydrosilylation-amination



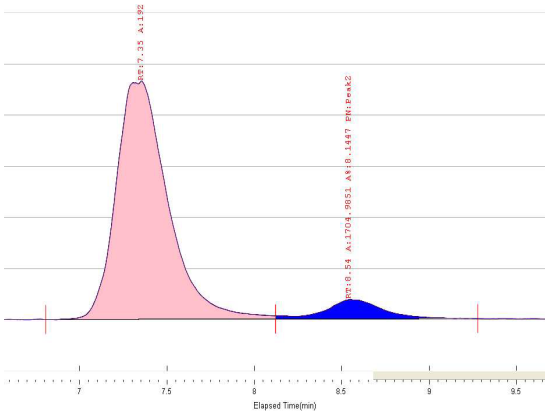
In a glove-box, an oven-dried 2 dram vial equipped with a stir bar was charged with 3-phenyl-1-propyne (11.6 mg, 0.10 mmol, 1.0 equiv), pinacolborane (13.4 mg, 0.105 mmol, 1.05 equiv) and dicyclohexylborane (0.89 mg, 0.05 mmol, 0.05 equiv), and sealed with a teflon septa cap. In a separate oven-dried 2 dram vial equipped with a stir bar, $Pt(dba)_3$ (2.7 mg, 0.03 mmol, 0.03 equiv), (*S,S)*-Di-ethoxyTADDOLphosphoramidite (5.5 mg, 0.06 mmol, 0.06 equiv) and toluene (0.20 mL) were added. In an oven-dried 1 dram vial, a stock solution of dimethylphenylsilane (32.8 mg, 0.24 mmol, 1.20 equiv.) in toluene (0.20 mL, add 0.10 mL) was prepared. Outside under nitrogen, the hydroboration was stirred for 2 hours at room temperature. During the hydroboration, the platinum-ligand solution was complexed for 20 minutes at 80°C, and then allowed to cool to room temperature. The hydroboration was then diluted in toluene (0.20 mL), and transferred under nitrogen to the platinum-ligand complex, rinsed with toluene (0.10 mL) and transferred. Dimethylphenylsilane solution (0.10 mL) was then added to the reaction mixture, the vial sealed and allowed to stir for 16 hours at room temperature.

The sealed reaction vial was then taken in the glove-box, and potassium *tert*-butoxide (16.8 mg, 0.15 mmol, 1.50 equiv) was added. Outside the glove-box under nitrogen, methoxyamine (0.075 mL, 2.0 M in THF, 0.15 mmol, 1.50 equiv) was added. The vial was then sealed, heated to 80°C for 16 hours. The reaction was allowed to cool to room temperature, and under nitrogen *Boc*-anhydride (0.15 mL, 0.15 mmol, 1.50 equiv) was added and stirred for 1 hour at room temperature. The reaction mixture was then filtered through a celite pipet plug with diethyl ether, and concentrated under reduced pressure. The crude reaction mixture was then purified by silica gel chromatography (large volume pipet, 5% ethyl acetate in hexanes) to afford a white solid. (26.7 mg, 72%)

Analysis of Stereochemistry:

The enantioselectivity was determined directly on the silylamine.

Chiral SFC (Chiracel AD-H, 5% IPA, 3 mL/min, 100 bar, 35 °C, 210-270 nm) – analysis of tert-butyl (S)-(1-(dimethyl(phenyl)silyl)-3-phenylpropyl)carbamate.

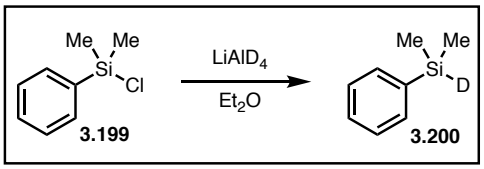


Peak Info			
Peak No	**% Area**	**Area**	**RT (min)**
1	91.8553	19228.739	7.35
2	8.1447	1704.9851	8.54
Total:	100	20933.7241	

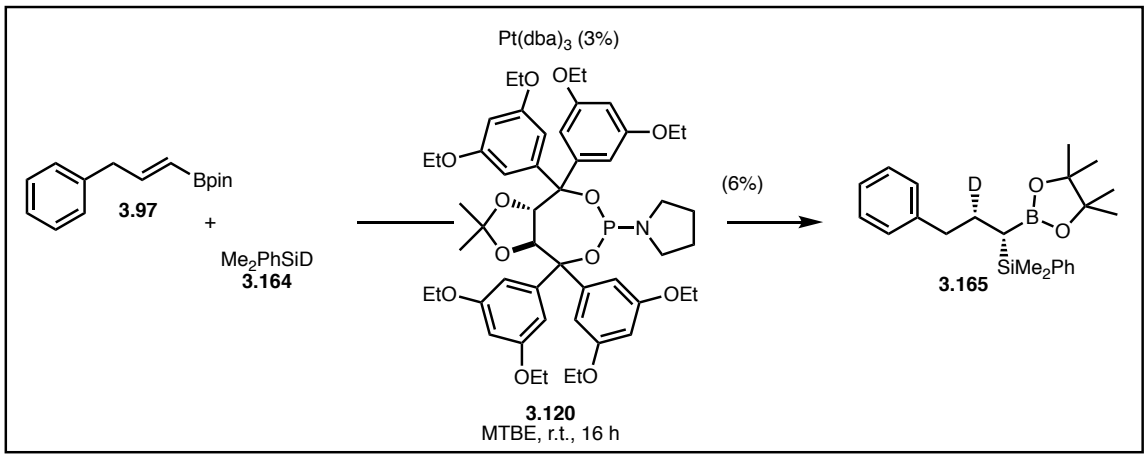
*See Compound **3.155** for racemic SFC trace.*

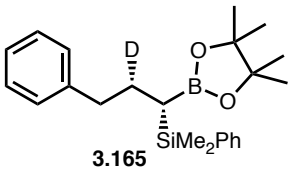
NONRACEMIC

3.5.7 Preparation of Deuterated Silane and Deuterosilylation Experiment



Dimethylphenyldeuterosilane was prepared according to a literature and the spectra were in accordance.[59]





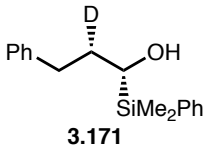
dimethyl(phenyl)((1S,2S)-3-phenyl-1-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)propyl-2-*d*)silane (3.165) Reaction carried out using *(S,S)*-3,5-diethoxyTADDOLphosphoramidite (5.5 mg, 0.06 mmol, 0.06 equiv.) according to the procedure above (Method A). The crude reaction was purified by silica gel chromatography (large volume pipet, 1% ethyl acetate in hexanes) to afford a clear oil. (36.6 mg, 96%)

^{1}H NMR (600 MHz, $CDCl_3$): δ 7.47-7.53 (m, 2H), 7.30-7.36 (m, 3H), 7.25 (t, *J* = 7.5 Hz, 2H), 7.14-7.18 (m, 1H), 7.12 (d, *J* = 7.5 Hz, 2H), 2.70 (dd, *J* = 13.4, 5.1 Hz, 1H), 2.46 (dd,

J = 13.4, 9.6 Hz, 1H), 1.88 (m, 1H), 1.22 (s, 6H), 1.20 (s, 6H), 0.71 (d, *J* = 12.0 Hz, 1H), 0.33 (s, 3H), 0.32 (s, 3H). **^{13}C NMR** (151 MHz, $CDCl_3$): δ 142.70, 138.95, 133.93, 128.88, 128.64, 128.28, 127.70, 125.68, 82.93, 39.48, 27.90, 27.77, 27.64, 25.32, 24.85, -2.14, -3.21. **^{2}H NMR** (77 MHz, $CDCl_3$): δ 1.64. **^{11}B NMR** (192 MHz, $CDCl_3$): δ 34.40. **IR** (neat): ν_{max} 3085 (w), 3067 (w), 2977 (w), 2926(w), 1602 (w), 1346 (s), 1306 (s), 1141 (s), 832 (m), 731 (m), 698 (s) cm^{-1}**.** **HRMS** (DART) for $C_{23}H_{36}DBO_2SiN$ $[M+NH_4]^+$: calculated: 399.2749, found: 399.2759. **$[\alpha]^{20}_D$**: -21.26 (c = 1.22, $CHCl_3$, *l* = 50 mm).

Analysis of Stereochemistry:

SFC analysis was performed on the oxidized silylboronate according to procedure above (Method B) and purified by silica gel chromatography (large volume pipet, 10% ethyl acetate in hexanes) to afford a clear oil.

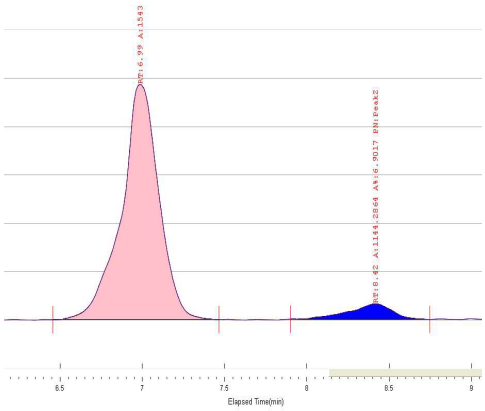


3.171

(1*R*,2*S*)-1-(dimethyl(phenyl)silyl)-3-phenylpropan-2-*d*-1-ol (3.171)

^{1}H NMR (600 MHz, $CDCl_3$): δ 7.52-7.63 (m, 2H), 7.34-7.45 (m, 3H), 7.24-7.32 (m, 2H), 7.12-7.24 (m, 3H), 3.54 (dd, *J* = 11.3, 4.4 Hz, 1H), 2.90 (dd, *J* = 13.7, 5.1 Hz, 1H), 2.62 (dd, *J* = 13.6, 9.3 Hz, 1H), 1.83 (m, 1H), 1.06 (d, *J* = 5.0 Hz, 1H), 0.35 (s, 3H), 0.34 (s, 3H). **^{13}C NMR** (126 MHz, $CDCl_3$): δ 142.09, 136.42, 134.11, 129.38, 128.48, 128.36, 127.94, 125.77, 64.83, 34.99, 34.84, 34.68, 33.16, -5.46, -5.71. **^{2}H NMR** (77 MHz, $CDCl_3$): δ 1.83. **IR** (neat): 3422 (w), 3067 (w), 3025(w), 2955(w), 2920 (w), 2362 (w), 1603 (w), 1454 (m), 1427 (m), 1248 (m), 1113 (m), 816(s), 735 (s) cm^{-1}. **HRMS** (DART) for $C_{17}H_{25}DOSiN$ $[M+NH_4]^+$: calculated: 289.1846, found: 289.1841. **$[\alpha]^{20}_D$**: -15.94 (c =0.63, $CHCl_3$, *l* = 50 mm

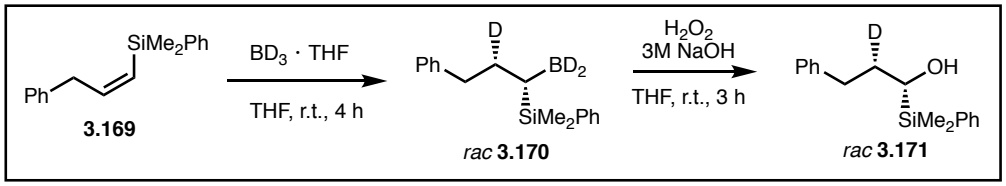
Chiral SFC (Chiracel OJ-H, 10% IPA, 3 mL/min, 100 bar, 35 °C, 210-270 nm) – analysis of (1R,2S)-1-(dimethyl(phenyl)silyl)-3-phenylpropan-2-d-1-ol.

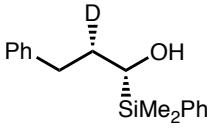


Peak Info			
Peak No	**% Area**	**Area**	**RT (min)**
1	93.0983	15435.5264	6.99
2	6.9017	1144.2864	8.42
Total:	100	16579.8128	

*See Compound **3.154** for racemic trace.*

NONRACEMIC





***rac* 3.171**

(*rac*)-1-(dimethyl(phenyl)silyl)-3-phenylpropan-2-*d*-1-ol (*rac* 3.171)

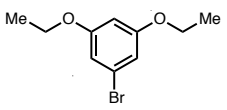
In a glove-box, (*Z*)-dimethyl(phenyl)(3-phenylprop-1-en-1-yl)silane[76] (50.4 mg, 0.20 mmol, 1.7 equiv.) was dissolved in THF (1.0 mL), charged with BD_3·THF (1.0 M in THF, 0.120 mL, 0.12 mmol, 1.0 equiv) and allowed to stir for 4 hours at room temperature. Outside the glove box under nitrogen, the reaction vial was cooled to 0°C, charged with 3M sodium hydroxide (0.5 mL) and 29-32% hydrogen peroxide (0.50 mL) and allowed to stir at room temperature for 3 hours. The vial was then cooled to 0°C, and

[76] Kubota, K.; Yamamoto, E.; Ito, H. *Adv. Synth. Catal.* **2013**, *355*, 3527-3531

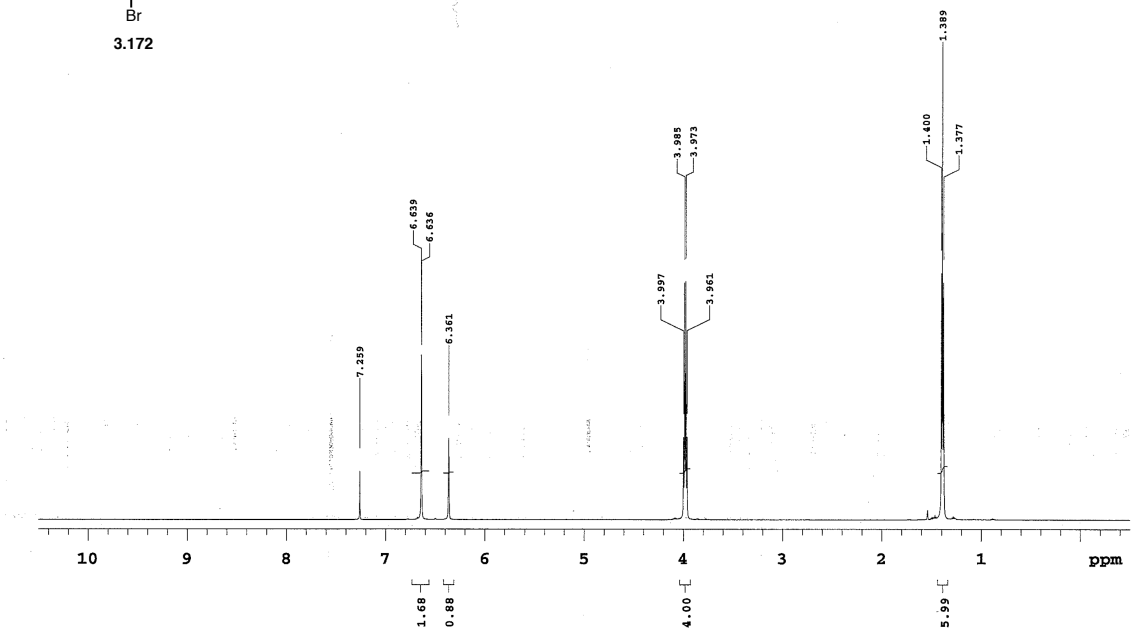
quenched with sodium thiosulfate (0.25 mL). The reaction solution was diluted with diethyl ether, and both organic and aqueous phase was passed through a silica gel large volume pipet to remove the aqueous layer. The organic extract was concentrated under reduced pressure, and the crude reaction mixture purified by silica gel chromatography (large volume pipet, 5% ethyl acetate in hexanes) to afford a clear oil. (47.1 mg, 85%)

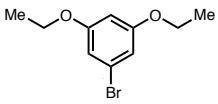
^{1}H NMR (600 MHz, $CDCl_3$): δ 7.55-7.61 (m, 2H), 7.38-7.44 (m, 3H), 7.27-7.32 (m, 2H), 7.18-7.23 (m, 3H), 3.54 (dd, *J* = 11.3, 5.1 Hz, 1H), 2.90 (dd, *J* = 13.7, 5.1 Hz, 1H), 2.62 (dd, *J* = 13.6, 9.3 Hz, 1H), 1.83 (m, 1H), 1.07 (d, *J* = 5.2 Hz, 1H), 0.35 (s, 3H), 0.34 (s, 3H) **^{13}C NMR** (126 MHz, $CDCl_3$): δ 142.33, 136.65, 134.35, 129.62, 128.72, 128.60, 128.17, 126.01, 65.04, 35.19, 35.06, 34.93, 33.38, -5.23, -5.49. **^{2}H NMR** (61 MHz, $CDCl_3$): δ 1.84. **IR** (neat): 3499 (br), 3085 (w), 3066 (m), 3025 (w), 2955 (w), 2855 (w), 1602 (w), 1495 (s), 1427 (s), 1248 (s), 1112 (s), 1013 (s), 777 (s), 698 (s) cm^{-1}. **HRMS** (DART) for $C_{17}H_{25}DOSiN$ $[M+NH_4]^+$: calculated: 289.1846, found: 289.1841.

3.5.8 Compound Spectra

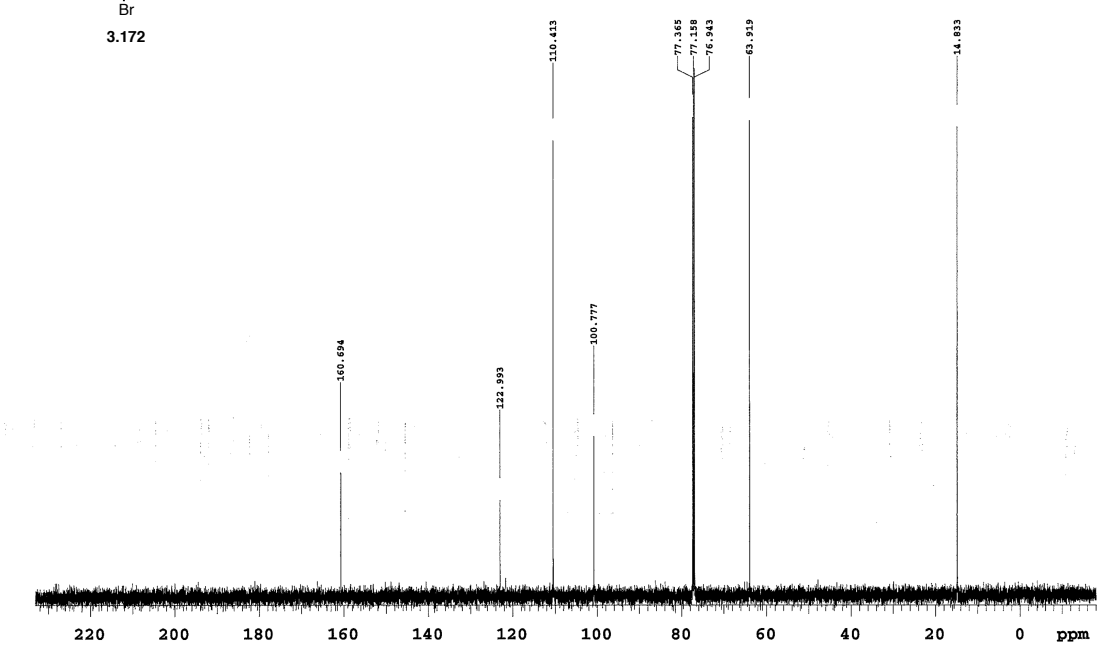

Me
O
O
Me
Br

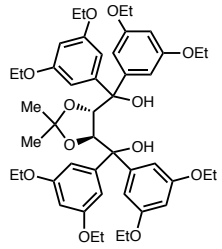
3.172


7.259
6.639
6.636
6.361
3.997
3.985
3.973
3.961
1.400
1.389
1.377
10
9
8
7
6
5
4
3
2
1
ppm
1.68
0.88
4.00
5.99


Me
O
O
Me
Br

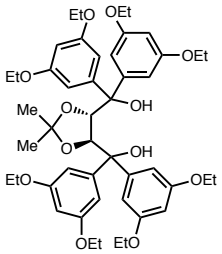
3.172


160.694
122.993
110.413
100.777
77.365
77.158
76.943
63.919
14.833
220
200
180
160
140
120
100
80
60
40
20
0
ppm

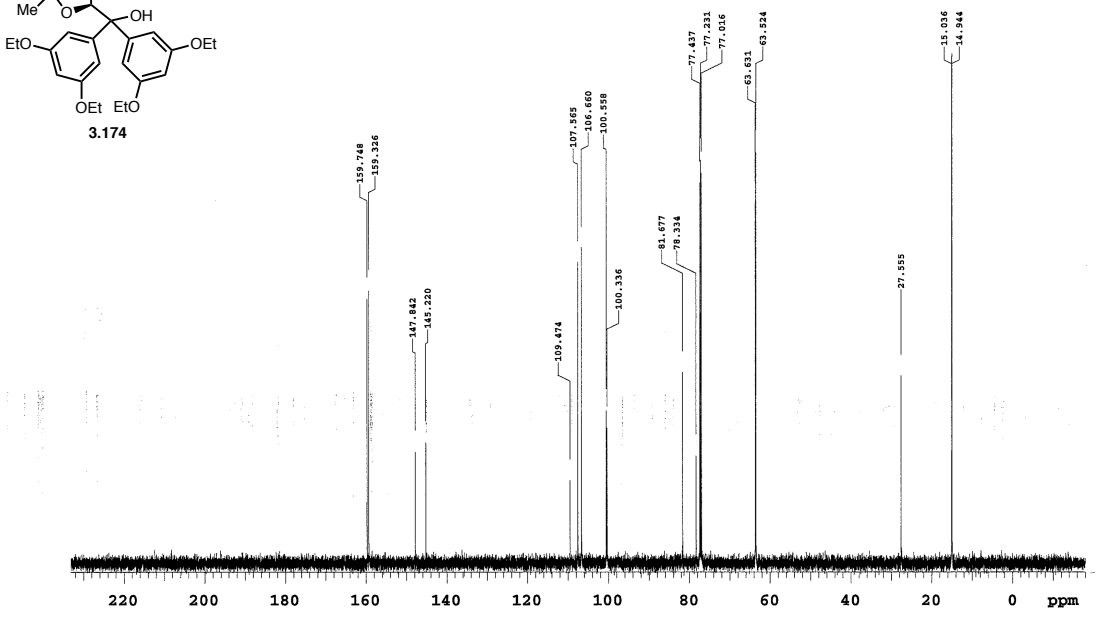

EtO
OEt
OEt
EtO
Me
O
OH
Me
O
OH
EtO
OEt
OEt
EtO

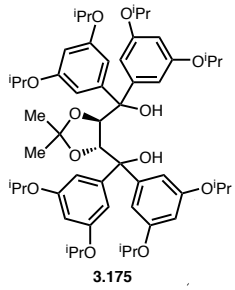
3.174

6.709
6.705
6.513
6.510
6.371
6.367
6.364
6.284
6.281
6.277
7.259
4.578
3.983
3.980
3.971
3.968
3.960
3.957
3.949
3.945
3.902
3.890
3.878
3.867
3.830
1.373
1.361
1.349
1.346
1.334
1.322
1.132
10
9
8
7
6
5
4
3
2
1
ppm
3.89
3.92
2.10
2.07
2.00
8.97
8.28
2.17
25.47
6.11


EtO
OEt
OEt
EtO
Me
O
OH
Me
O
OH
EtO
OEt
OEt
EtO

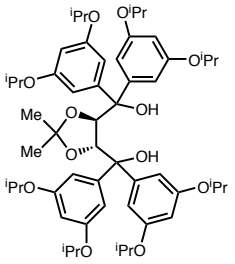
3.174


159.748
159.326
147.842
145.220
109.474
107.565
106.660
100.558
100.336
81.677
78.334
77.437
77.231
77.016
63.631
63.524
27.555
15.036
14.944
220
200
180
160
140
120
100
80
60
40
20
0
ppm

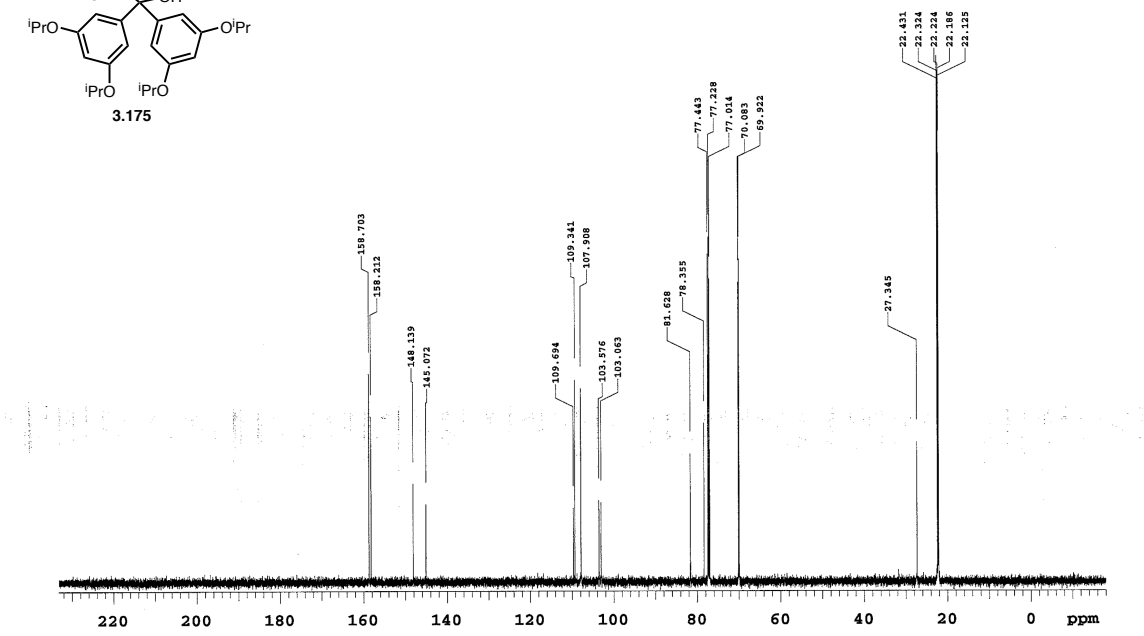

iPrO
OiPr
OiPr
iPrO
OH
Me
O
Me
O
OH
iPrO
OiPr
iPrO
iPrO

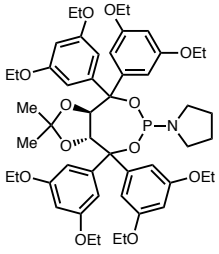
3.175

6.691
6.687
6.519
6.515
6.366
6.363
6.359
6.284
6.280
6.276
7.259
4.614
4.503
4.492
4.482
4.472
4.462
4.404
4.394
4.384
4.373
4.364
3.687
1.601
1.534
1.341
1.334
1.323
1.318
1.288
1.268
1.257
1.248
1.238
1.227
1.399
1.052
10
9
8
7
6
5
4
3
2
1
ppm
3.95
3.97
2.20
1.86
2.00
4.28
4.06
1.87
49.87
6.22

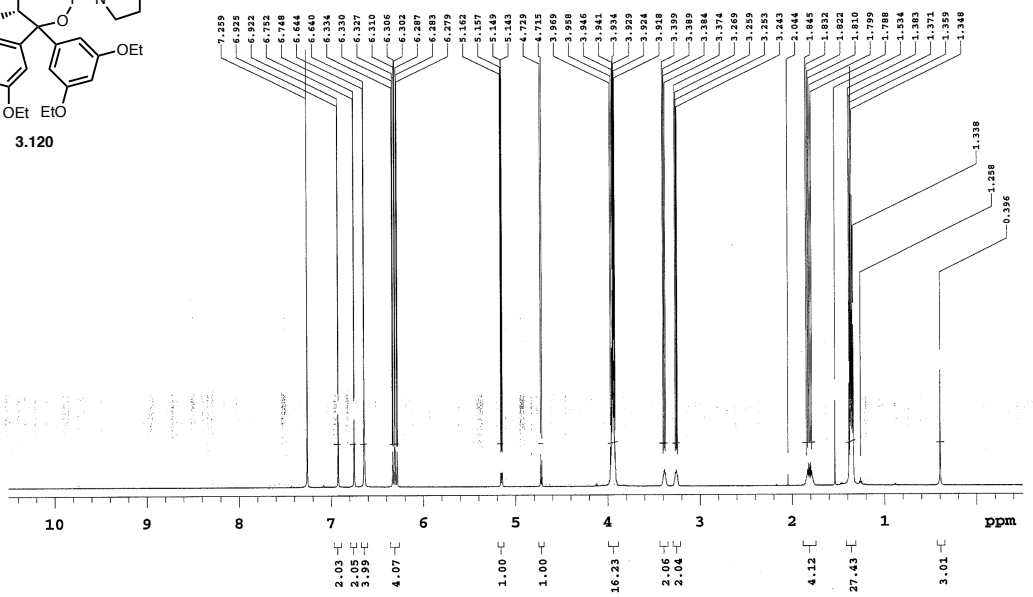

iPrO
OiPr
OiPr
iPrO
OH
Me
O
Me
O
OH
iPrO
OiPr
iPrO
iPrO

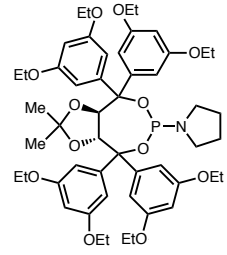
3.175


158.703
158.212
148.139
145.072
109.694
109.341
107.908
103.576
103.063
81.628
78.355
77.443
77.228
77.014
70.083
69.922
27.345
22.431
22.324
22.224
22.186
22.125
220
200
180
160
140
120
100
80
60
40
20
0
ppm

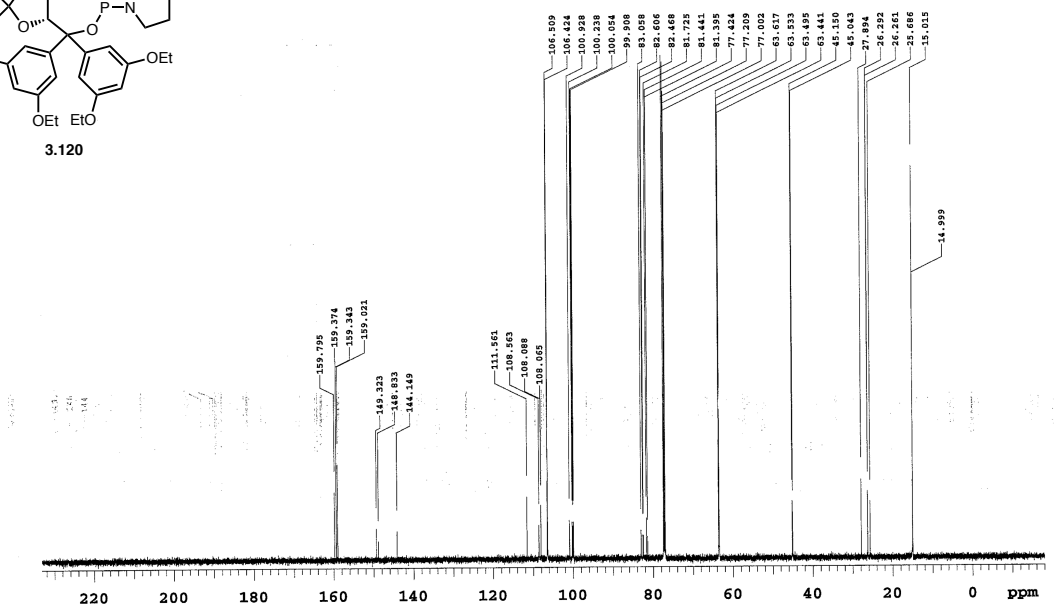


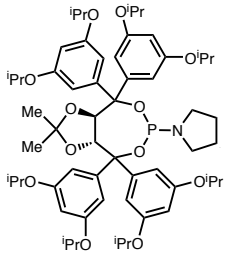
3.120


7.259
6.925
6.922
6.752
6.748
6.644
6.640
6.334
6.330
6.327
6.310
6.306
6.302
6.287
6.283
6.279
5.162
5.157
5.149
5.143
4.729
4.715
3.969
3.958
3.946
3.941
3.934
3.929
3.924
3.918
3.399
3.389
3.384
3.374
3.269
3.259
3.253
3.243
2.044
1.845
1.832
1.822
1.810
1.799
1.788
1.534
1.383
1.371
1.359
1.348
1.338
1.258
0.396
10
9
8
7
6
5
4
3
2
1
ppm
2.03
2.05
3.99
4.07
1.00
1.00
16.23
2.06
2.04
4.12
27.43
3.01

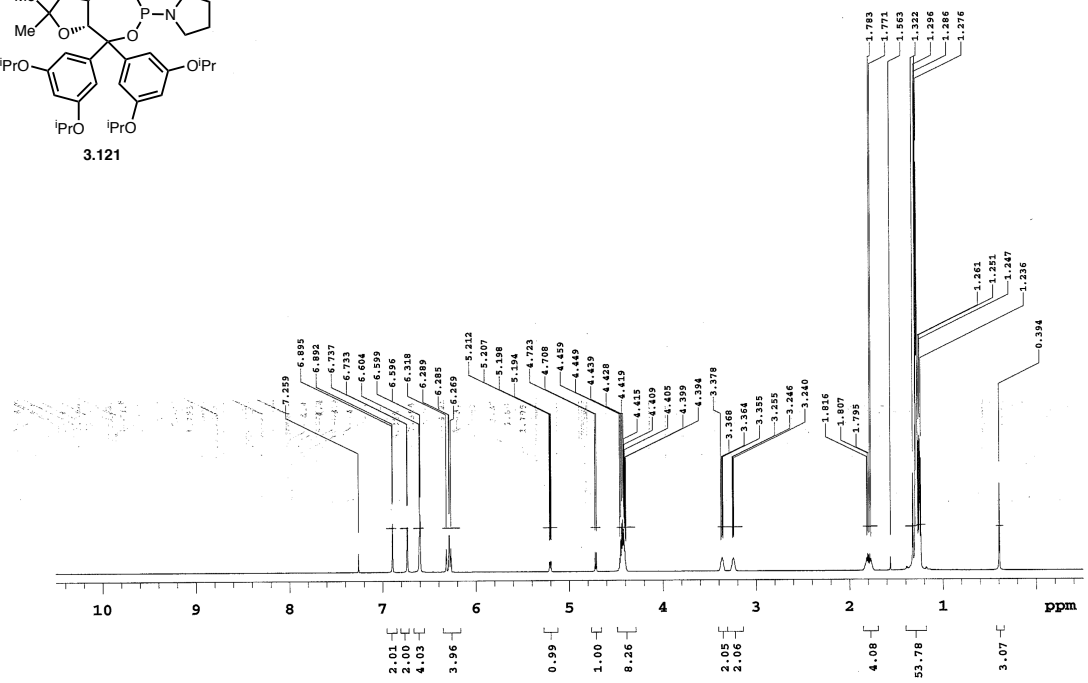


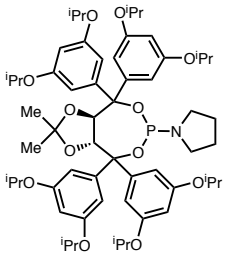
3.120


106.509
106.424
100.928
100.238
100.054
99.908
83.058
82.606
82.468
81.725
81.441
81.395
77.424
77.209
77.002
63.617
63.533
63.495
63.441
45.150
45.043
27.894
26.292
26.261
25.686
15.015
14.999
159.795
159.374
159.343
159.021
149.323
148.833
144.149
111.561
108.563
108.088
108.065
220
200
180
160
140
120
100
80
60
40
20
0
ppm

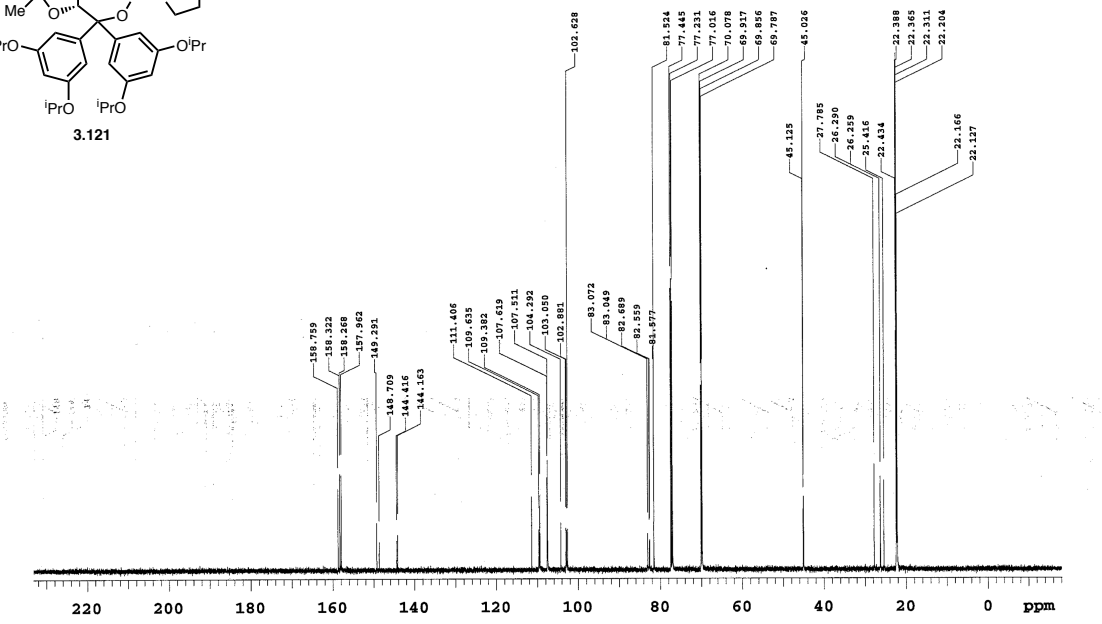


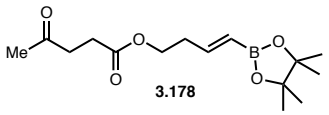
3.121


7.259
6.895
6.892
6.737
6.733
6.604
6.599
6.596
6.318
6.289
6.285
6.269
5.212
5.207
5.198
5.194
4.723
4.708
4.459
4.449
4.439
4.428
4.419
4.415
4.409
4.405
4.399
4.394
3.378
3.368
3.364
3.355
3.255
3.246
3.240
1.816
1.807
1.795
1.783
1.771
1.563
1.322
1.296
1.286
1.276
1.261
1.251
1.247
1.236
0.394
10
9
8
7
6
5
4
3
2
1
ppm
2.01
2.00
4.03
3.96
0.99
1.00
8.26
2.05
2.06
4.08
53.78
3.07



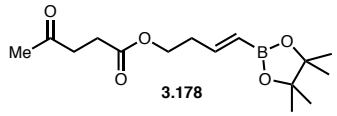
3.121


158.759
158.322
158.268
157.962
149.291
148.709
144.416
144.163
111.406
109.635
109.382
107.619
107.511
104.292
103.050
102.881
102.628
83.072
83.049
82.689
82.559
81.577
81.524
77.445
77.231
77.016
70.078
69.917
69.856
69.707
45.026
45.125
27.785
26.290
26.259
25.416
22.434
22.388
22.365
22.311
22.204
22.166
22.127
220
200
180
160
140
120
100
80
60
40
20
0
ppm


Me
O
O
O
B
O
O

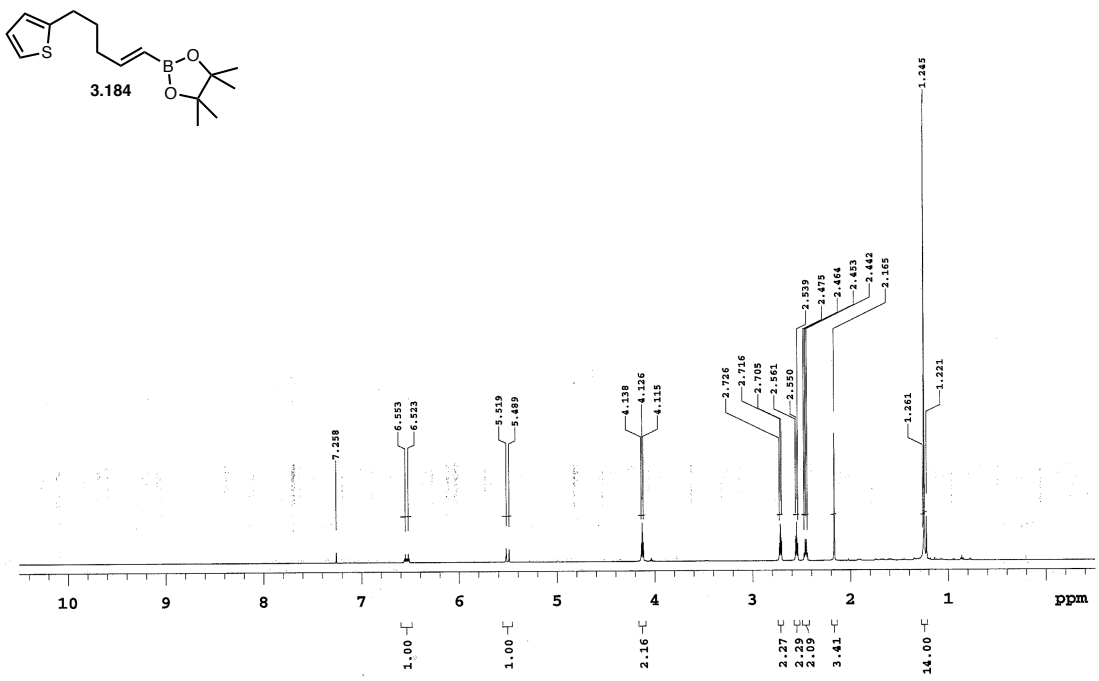
3.178

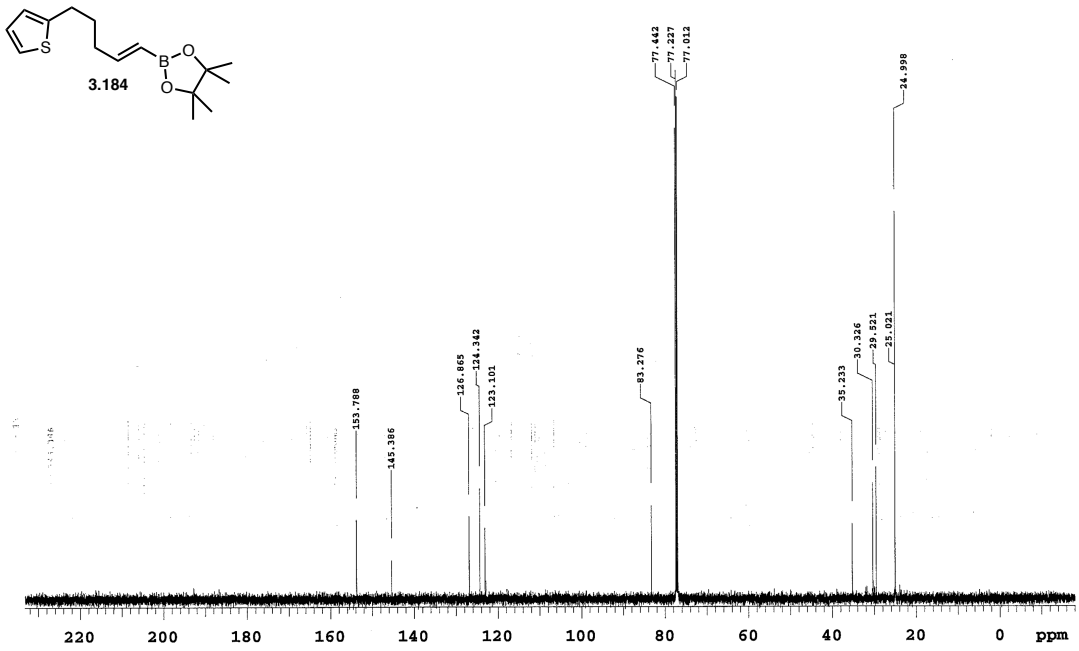
1.245
2.165
1.221
4.126
2.716
2.550
10
9
8
7
6
5
4
3
2
1
ppm
1.00
1.00
2.16
2.27
2.29
2.09
3.41
14.00

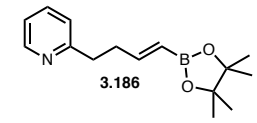

Me
O
O
O
B
O
O

3.178

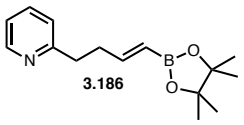
24.950
38.120
34.954
30.040
28.147
24.996
83.380
77.439
77.232
77.017
63.318
206.742
172.812
149.047
220
200
180
160
140
120
100
80
60
40
20
0
ppm

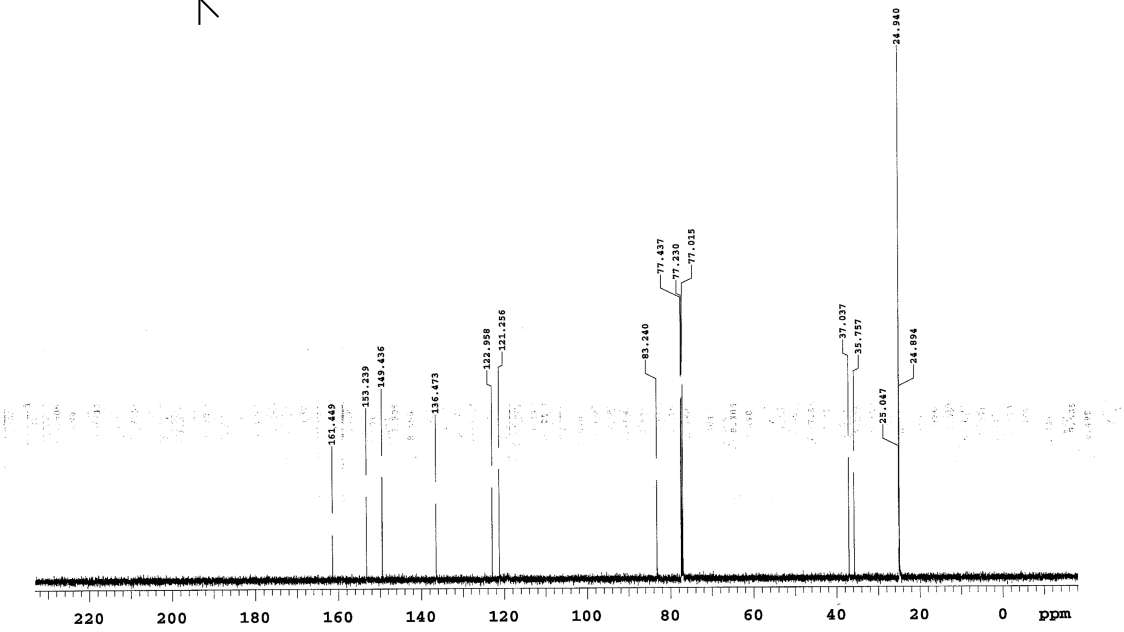

3.184
7.258
6.553
6.523
5.519
5.489
4.138
4.126
4.115
2.726
2.716
2.705
2.561
2.550
2.539
2.475
2.464
2.453
2.442
2.165
1.461
1.245
1.221
10
9
8
7
6
5
4
3
2
1
ppm
1.00
1.00
2.16
2.27
2.29
2.09
3.41
14.00

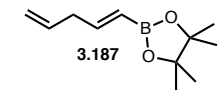

3.184
153.788
145.386
126.665
124.342
123.101
83.276
77.442
77.227
77.012
35.233
30.326
29.521
25.021
24.998
220
200
180
160
140
120
100
80
60
40
20
0
ppm


3.186

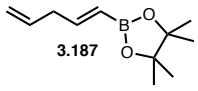
1.245
1.229
8.506
8.498
7.573
7.570
7.560
7.557
7.547
7.544
7.359
7.129
7.117
7.087
7.078
7.076
7.068
6.703
6.672
5.501
5.472
2.907
2.895
2.881
2.603
2.592
2.579
2.568
1.223
1.214
10
9
8
7
6
5
4
3
2
1
ppm
0.92
1.03
2.04
1.01
1.00
2.37
2.34
14.13


3.186

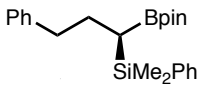

24.940
77.437
77.230
77.015
161.449
153.239
149.436
136.473
122.958
121.256
83.240
37.037
35.757
24.894
25.047
220
200
180
160
140
120
100
80
60
40
20
0
ppm


3.187

7.258
6.661
6.651
6.640
6.630
6.620
6.611
5.846
5.829
5.818
5.801
5.492
5.463
5.066
5.043
5.027
2.913
2.903
2.892
1.553
1.260
1.240
10
9
8
7
6
5
4
3
2
1
ppm
1.01
1.01
1.00
2.00
1.99
12.82

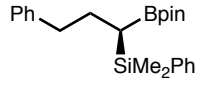

3.187

24.992
77.443
77.228
77.021
83.299
151.757
135.589
116.378
40.040
220
200
180
160
140
120
100
80
60
40
20
0
ppm

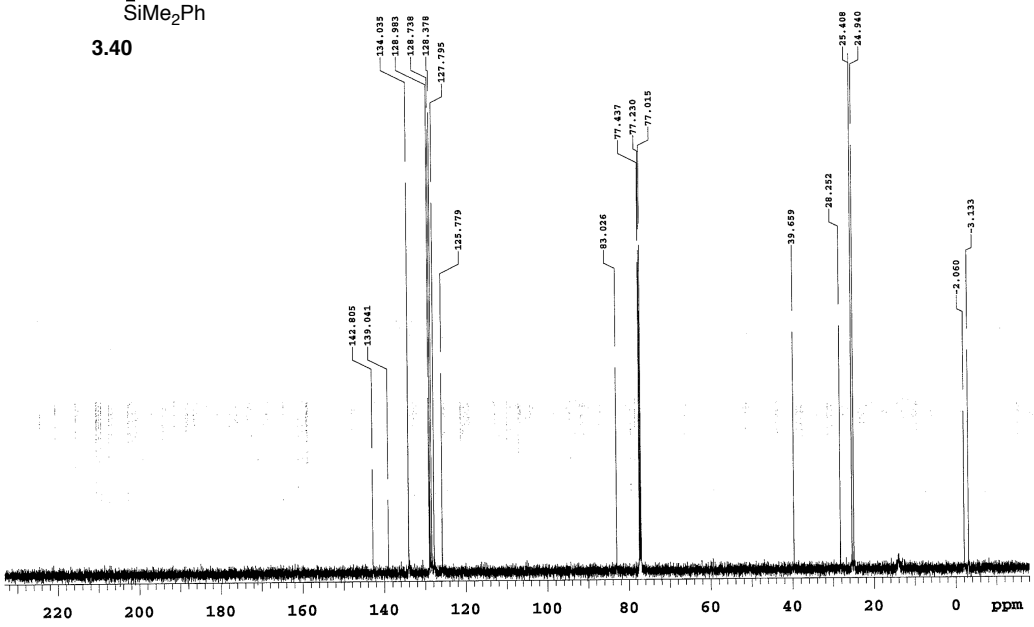

Ph
Bpin
SiMe2Ph

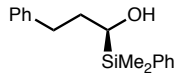
3.40

7.482
7.479
7.470
7.317
7.309
7.305
7.259
7.257
7.244
7.231
7.219
7.155
7.143
7.130
7.102
7.090
2.703
2.695
2.679
2.665
2.467
2.657
2.453
2.443
2.432
2.417
1.880
1.873
1.858
1.628
1.538
1.217
1.185
0.708
0.688
0.303
0.301
0.290
0.288
10
9
8
7
6
5
4
3
2
1
ppm
1.63
5.34
2.67
0.91
0.92
0.92
2.26
11.48
1.00
5.42


Ph
Bpin
SiMe2Ph

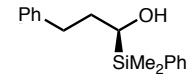
3.40


134.035
128.983
128.738
128.378
127.795
125.779
142.805
139.041
83.026
77.437
77.230
77.015
39.659
28.252
25.408
24.940
21.133
2.060
220
200
180
160
140
120
100
80
60
40
20
0
ppm


Ph
OH
SiMe2Ph

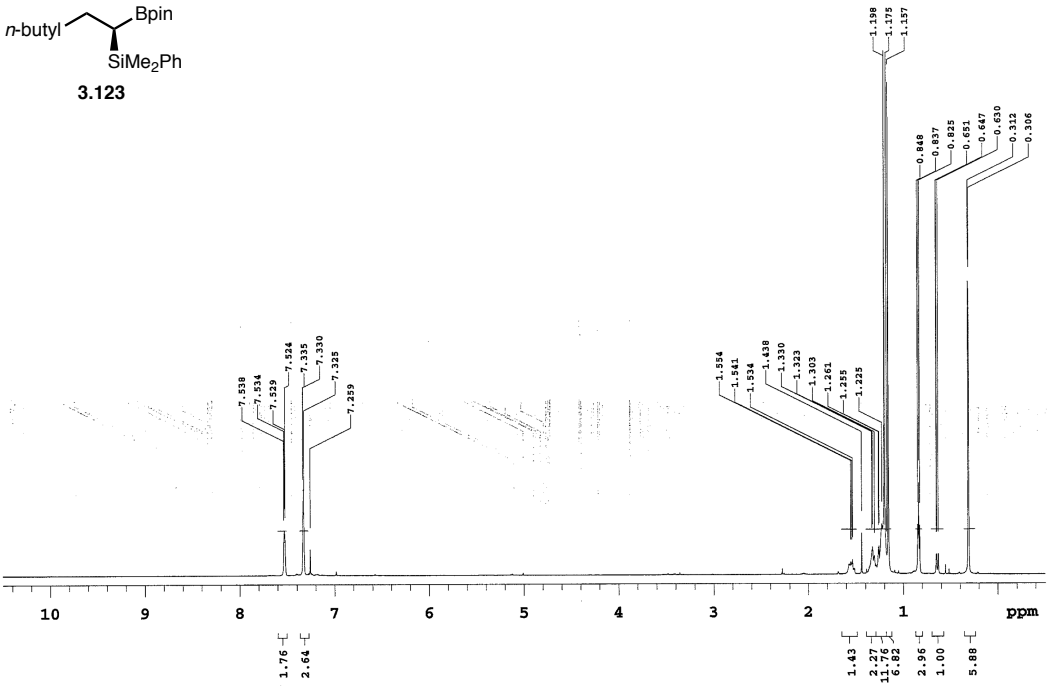
3.154

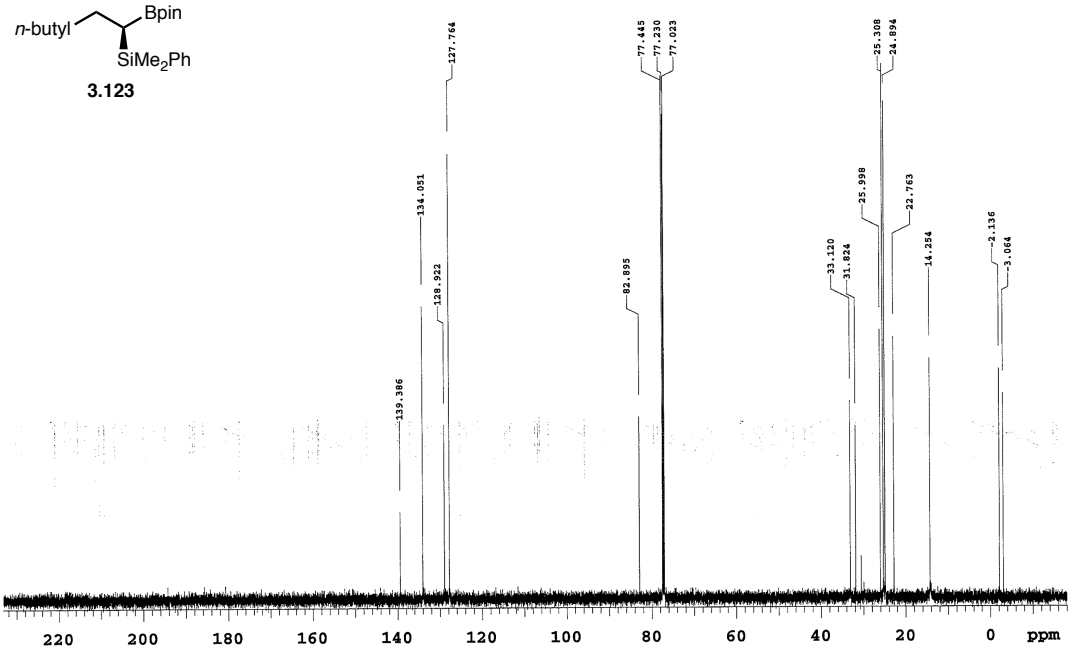
7.557
7.547
7.396
7.386
7.374
7.290
7.278
7.265
7.259
7.198
7.186
7.179
7.167
3.553
3.542
2.919
2.907
2.897
2.640
2.618
1.862
1.850
1.838
1.825
0.346
0.339
10
9
8
7
6
5
4
3
2
1
ppm
1.91
2.89
2.18
2.98
1.00
1.12
1.14
2.42
0.87
6.46

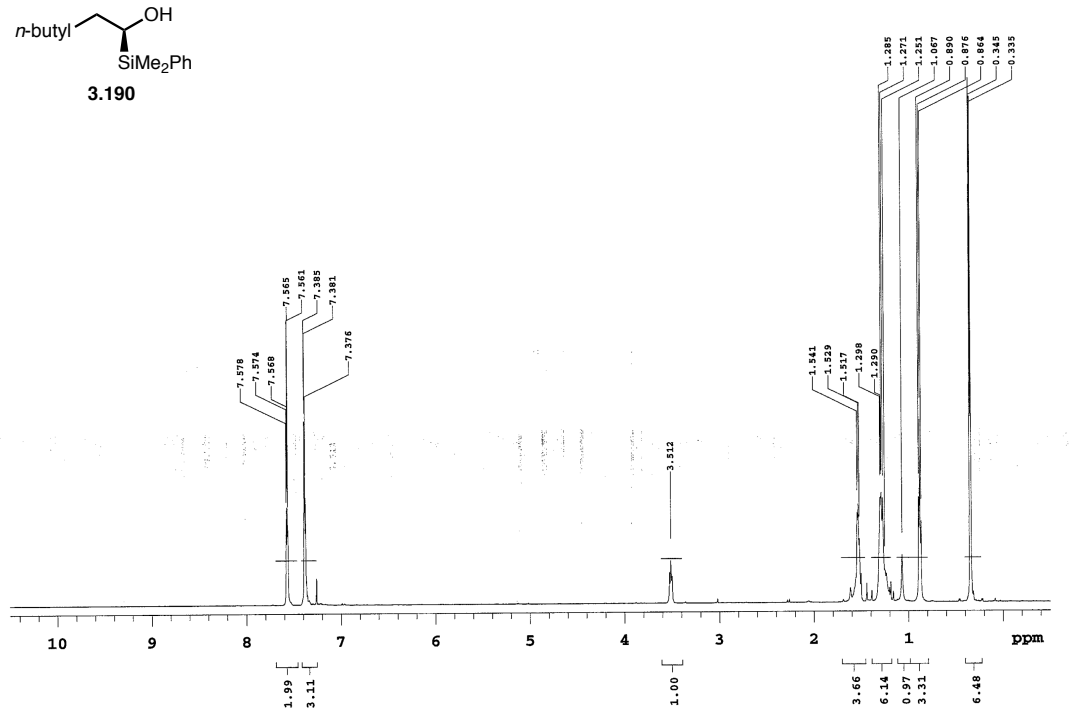

Ph
OH
SiMe2Ph

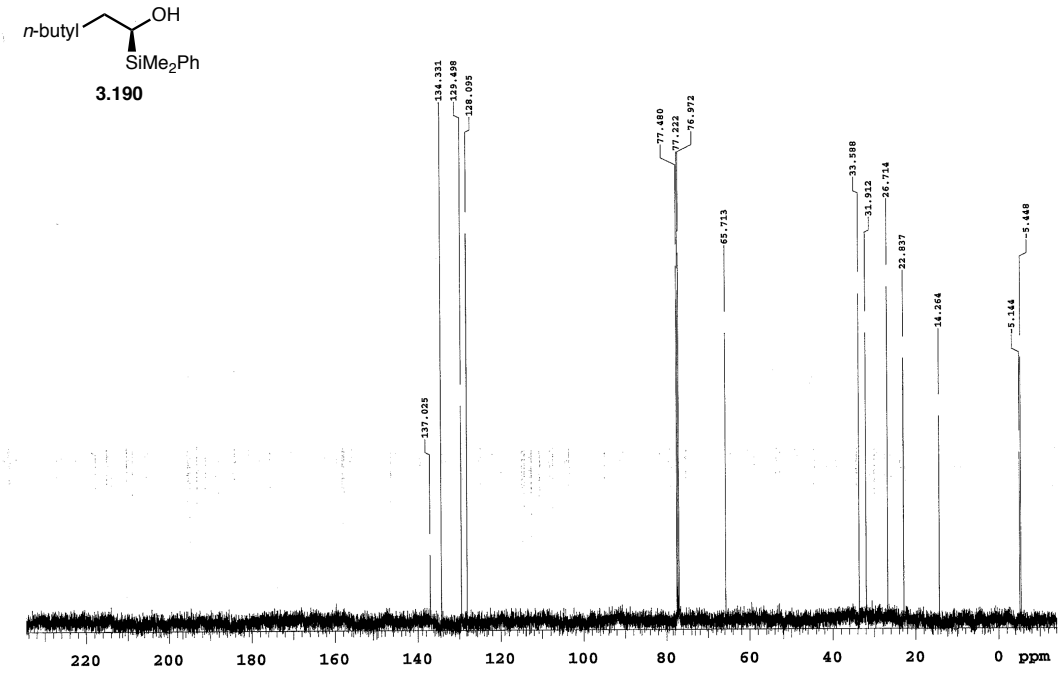
3.154

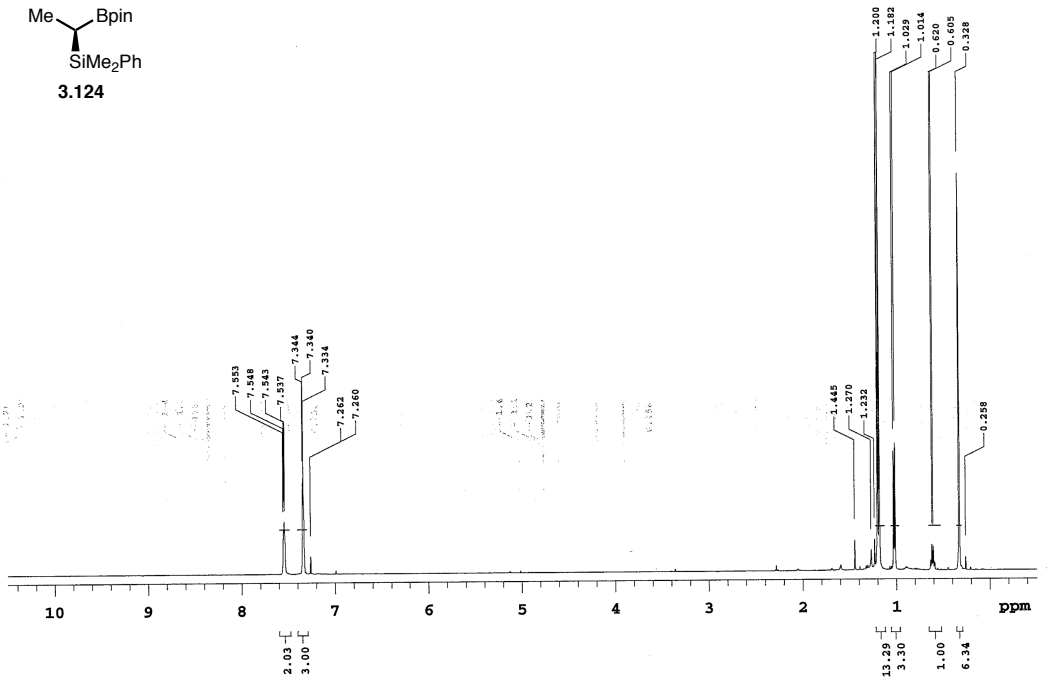
142.338
136.657
134.350
129.620
128.723
128.600
128.171
126.009
77.445
77.230
77.023
65.095
35.443
33.472
-5.226
-5.486
220
200
180
160
140
120
100
80
60
40
20
0
ppm

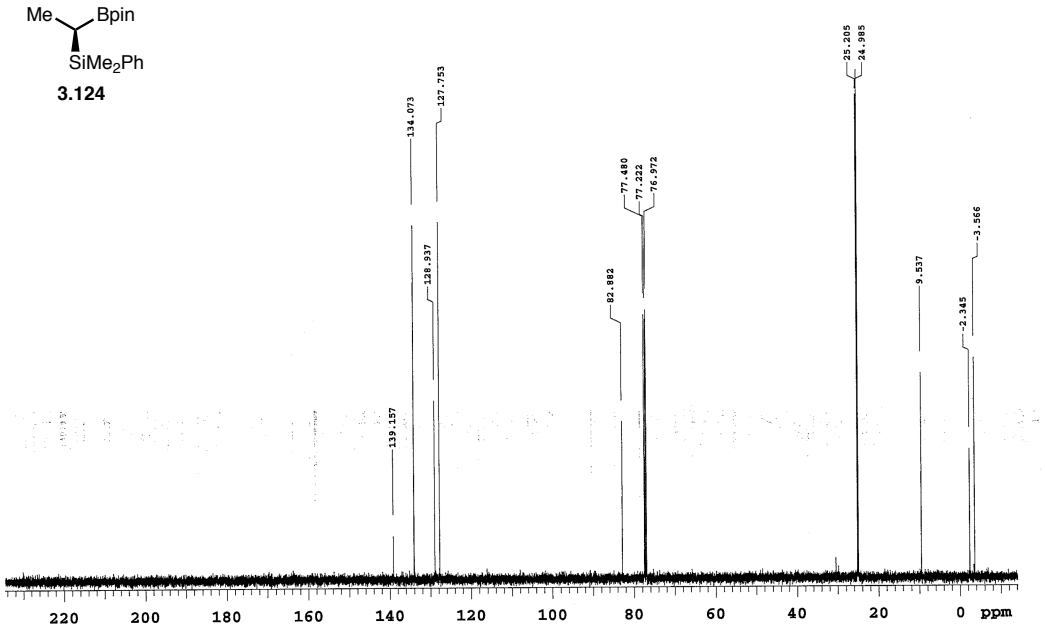

n-butyl
Bpin
SiMe2Ph
3.123
7.538
7.534
7.529
7.524
7.335
7.330
7.325
7.259
1.954
1.541
1.534
1.438
1.330
1.323
1.303
1.261
1.255
1.225
1.198
1.175
1.157
0.848
0.837
0.825
0.651
0.647
0.630
0.312
0.306
10
9
8
7
6
5
4
3
2
1
ppm
1.76
2.64
1.43
2.27
11.76
6.02
2.96
1.00
5.88

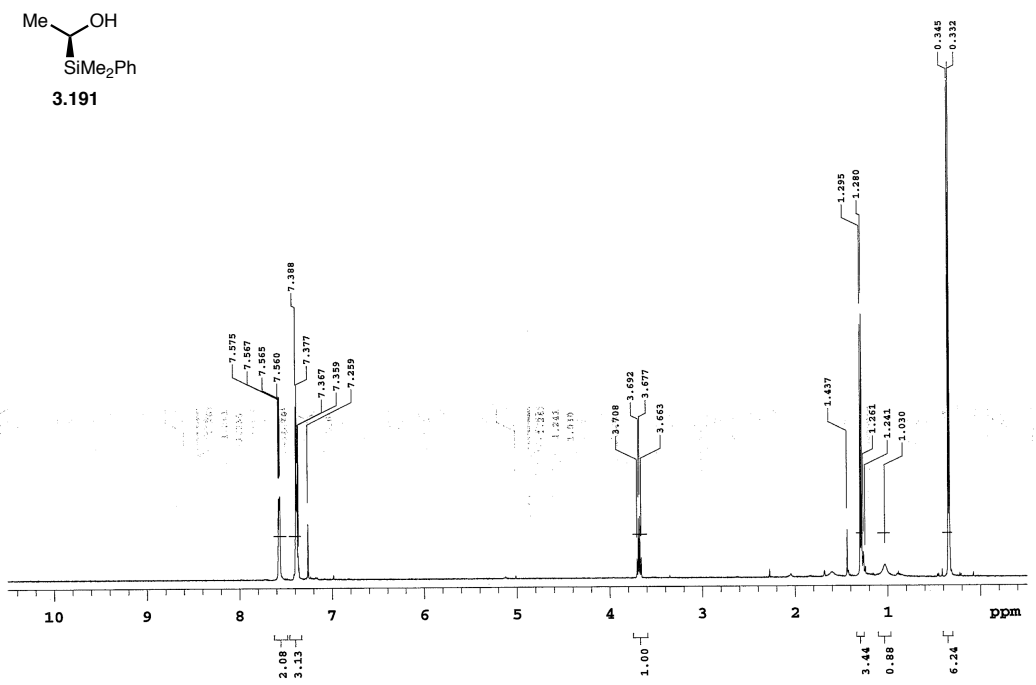

n-butyl
Bpin
SiMe2Ph
3.123
139.386
134.051
128.922
127.764
82.895
77.445
77.230
77.023
35.308
33.120
31.824
25.998
24.894
22.763
14.254
2.136
-3.064
220
200
180
160
140
120
100
80
60
40
20
0
ppm

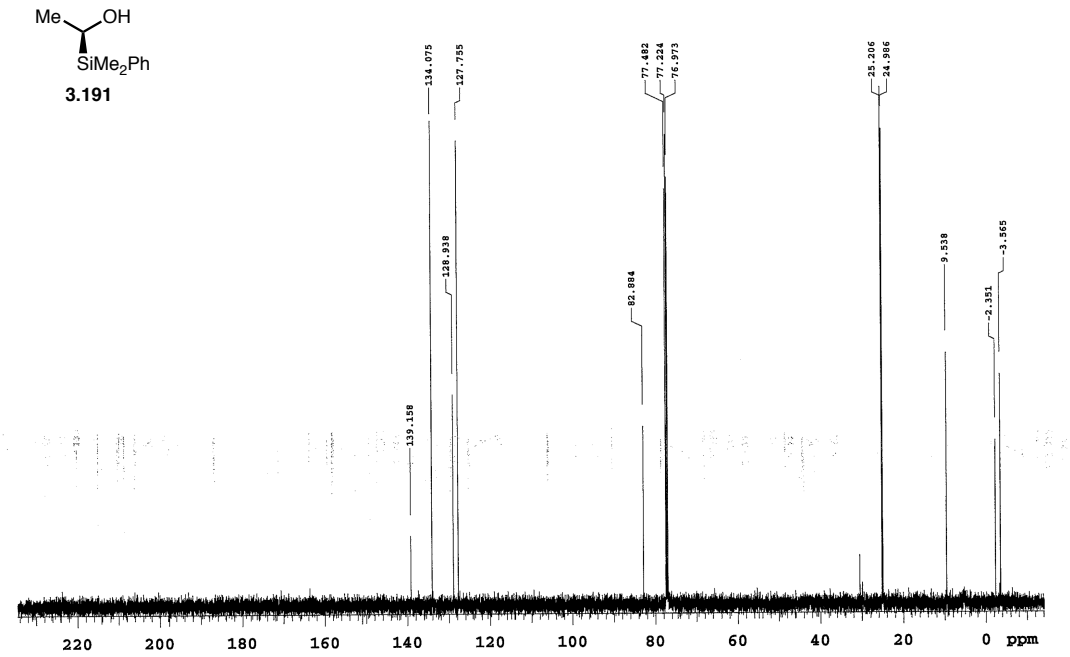

n-butyl
OH
SiMe2Ph
3.190
7.578
7.574
7.568
7.565
7.561
7.385
7.381
7.376
3.512
1.541
1.529
1.517
1.298
1.290
1.285
1.271
1.251
1.067
0.890
0.876
0.864
0.345
0.335
10
9
8
7
6
5
4
3
2
1
ppm
1.99
3.11
1.00
3.66
6.14
0.97
3.31
6.48

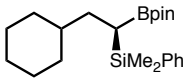

n-butyl
OH
SiMe2Ph
3.190
137.025
134.331
129.498
128.095
77.480
77.222
76.972
65.713
33.598
31.912
26.714
22.837
14.264
5.144
-5.448
220
200
180
160
140
120
100
80
60
40
20
0
ppm


Me
Bpin
SiMe2Ph
3.124
7.553
7.548
7.543
7.537
7.344
7.340
7.334
7.262
7.260
1.445
1.270
1.232
1.200
1.182
1.029
1.014
0.620
0.605
0.328
0.258
10
9
8
7
6
5
4
3
2
1
ppm
2.03
3.00
13.29
3.30
1.00
6.34

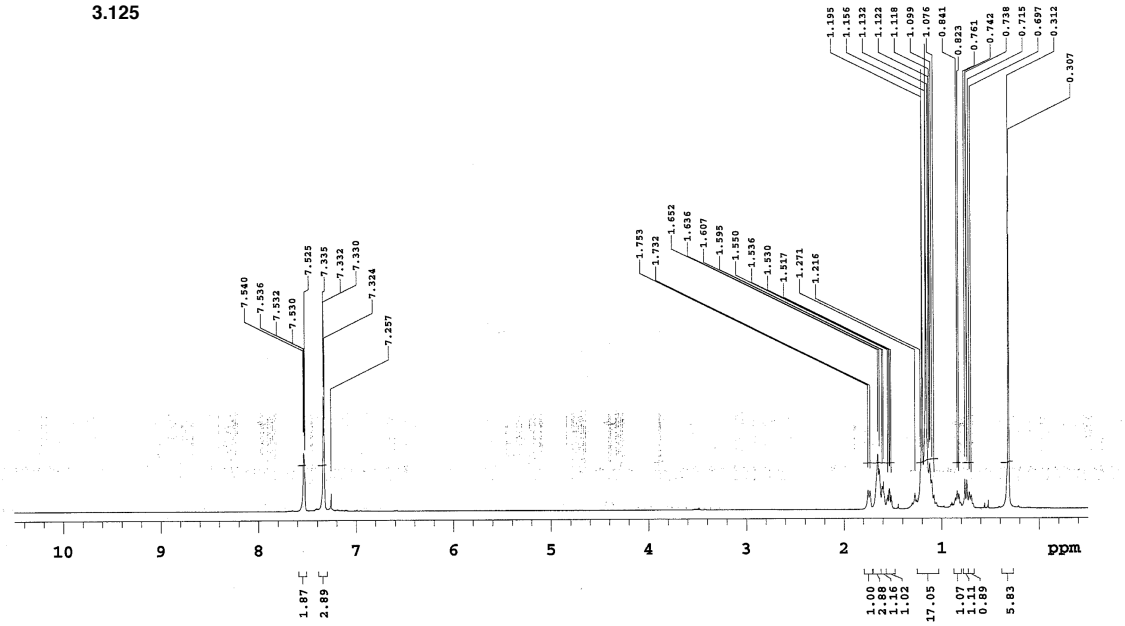

Me
Bpin
SiMe2Ph
3.124
139.157
134.073
128.937
127.753
82.882
77.480
77.222
76.972
25.205
24.985
9.537
-2.345
-3.566
220
200
180
160
140
120
100
80
60
40
20
0
ppm

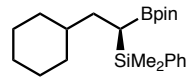

Me
OH
SiMe2Ph
3.191
7.575
7.567
7.565
7.560
7.388
7.377
7.367
7.359
7.259
3.708
3.692
3.677
3.663
1.437
1.395
1.280
1.261
1.241
1.030
0.345
0.332
10
9
8
7
6
5
4
3
2
1
ppm
2.08
3.13
1.00
3.44
0.88
6.24


Me
OH
SiMe2Ph
3.191
139.158
134.075
128.938
127.735
82.984
77.482
77.224
76.973
35.206
24.986
9.538
-2.351
-3.565
220
200
180
160
140
120
100
80
60
40
20
0
ppm

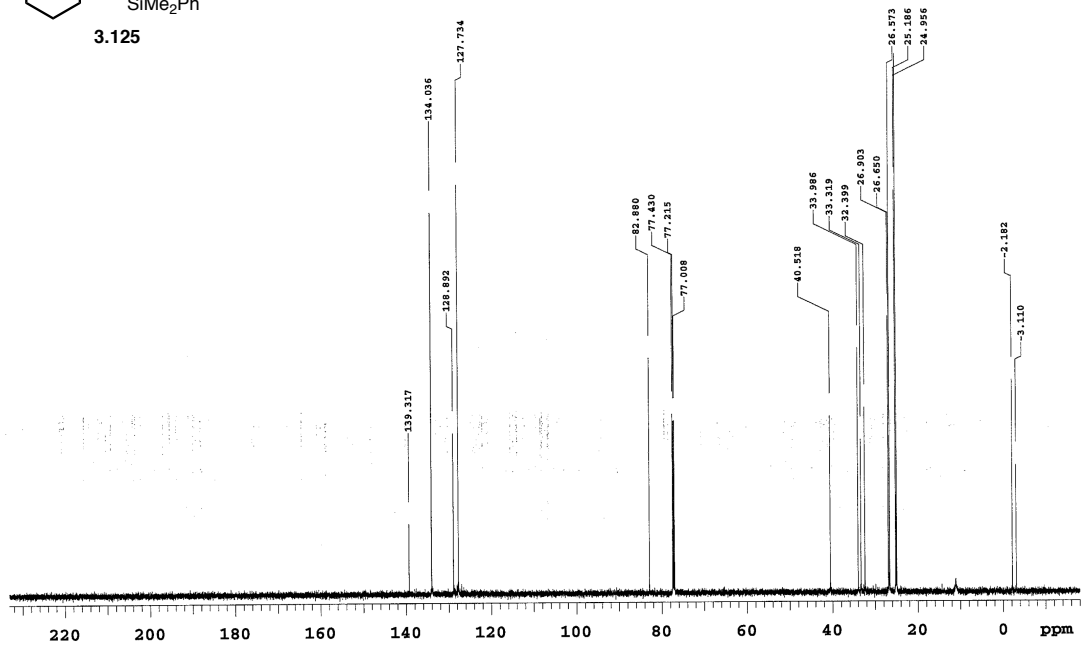

Bpin
SiMe2Ph

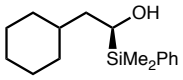
3.125


7.540
7.536
7.532
7.530
7.525
7.335
7.332
7.330
7.324
7.257
1.753
1.732
1.652
1.636
1.607
1.595
1.550
1.536
1.530
1.517
1.271
1.216
1.195
1.156
1.132
1.122
1.118
1.099
1.076
0.841
0.823
0.761
0.742
0.738
0.715
0.697
0.312
0.307
10
9
8
7
6
5
4
3
2
1
ppm
1.87
2.89
1.00
2.88
1.16
1.02
17.05
1.07
1.11
0.89
5.83

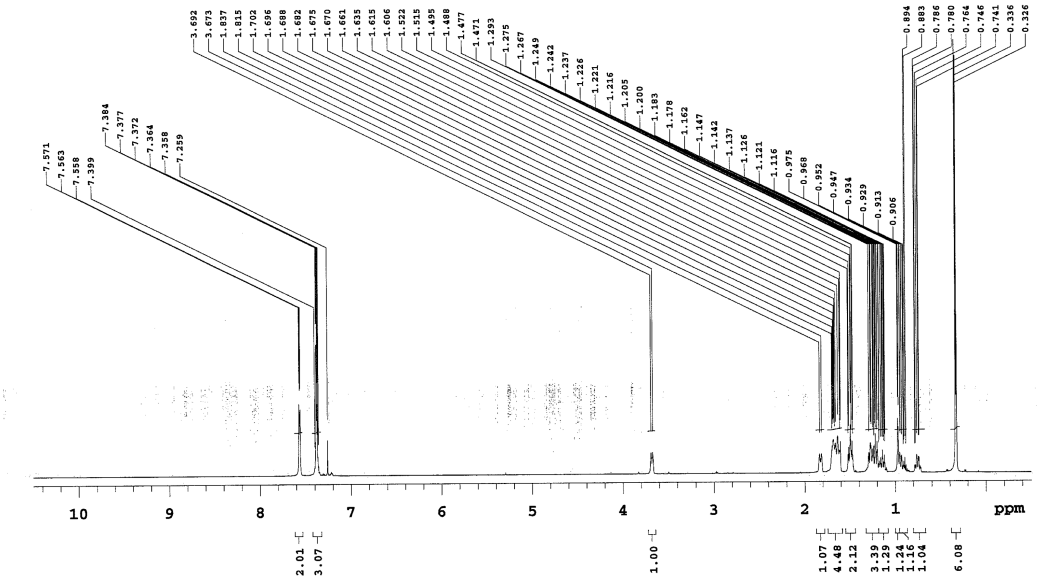

Bpin
SiMe2Ph

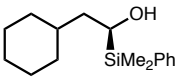
3.125


139.317
134.036
128.892
127.734
82.880
77.430
77.215
77.008
40.518
33.986
33.319
32.399
26.903
26.650
26.573
25.186
24.956
2.182
3.110
220
200
180
160
140
120
100
80
60
40
20
0
ppm

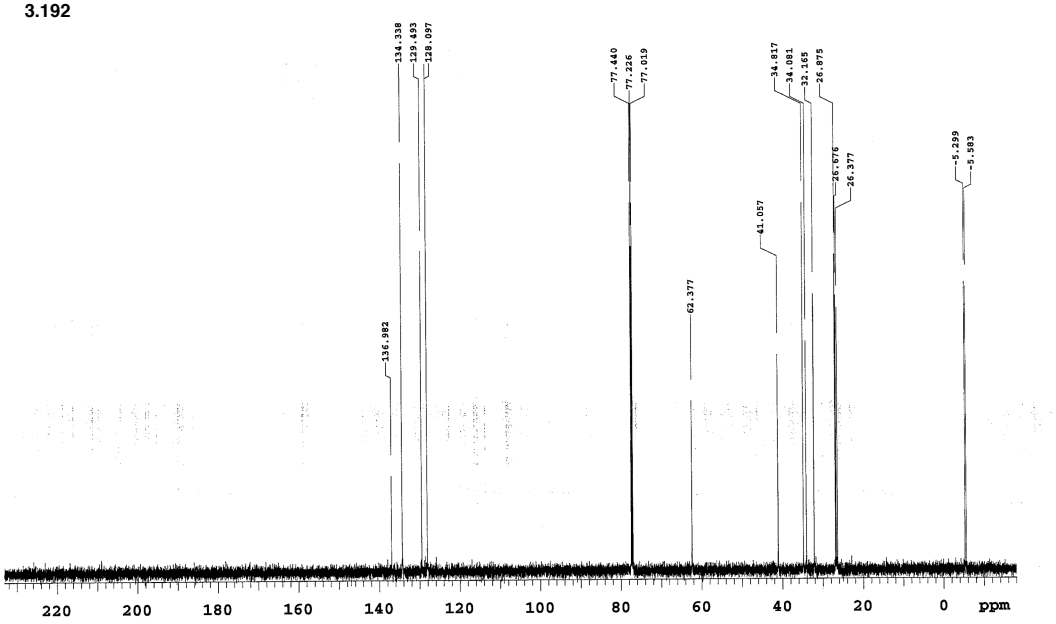

OH
SiMe2Ph

3.192


3.692
3.673
3.637
1.815
1.702
1.696
1.688
1.682
1.675
1.670
1.661
1.635
1.615
1.606
1.522
1.515
1.495
1.488
1.477
1.471
1.293
1.275
1.267
1.249
1.242
1.237
1.226
1.221
1.216
1.205
1.200
1.183
1.178
1.162
1.147
1.142
1.137
1.126
1.121
1.116
0.975
0.968
0.952
0.947
0.934
0.929
0.913
0.906
0.894
0.883
0.786
0.780
0.764
0.746
0.741
0.336
0.326
7.571
7.563
7.558
7.399
7.384
7.377
7.372
7.364
7.358
7.259
10
9
8
7
6
5
4
3
2
1
ppm
2.01
3.07
1.00
1.07
4.48
2.12
3.39
1.29
1.24
1.16
1.04
6.08

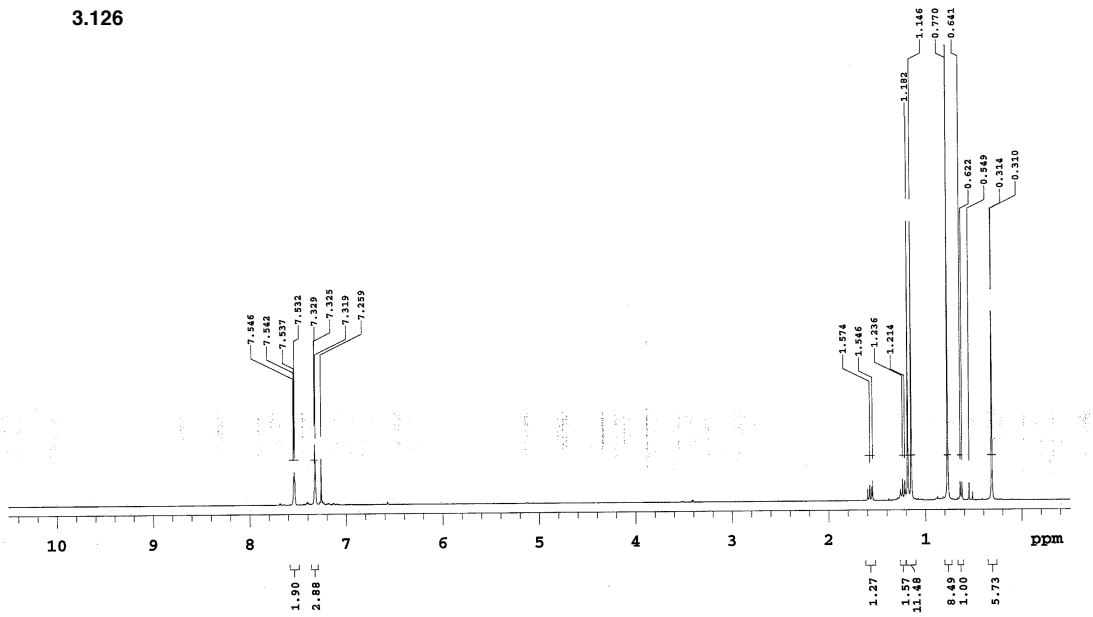

OH
SiMe2Ph

3.192


134.338
129.493
128.097
77.440
77.226
77.019
34.817
34.081
32.165
26.875
26.676
26.377
41.057
62.377
136.982
-5.399
-5.583
220
200
180
160
140
120
100
80
60
40
20
0
ppm

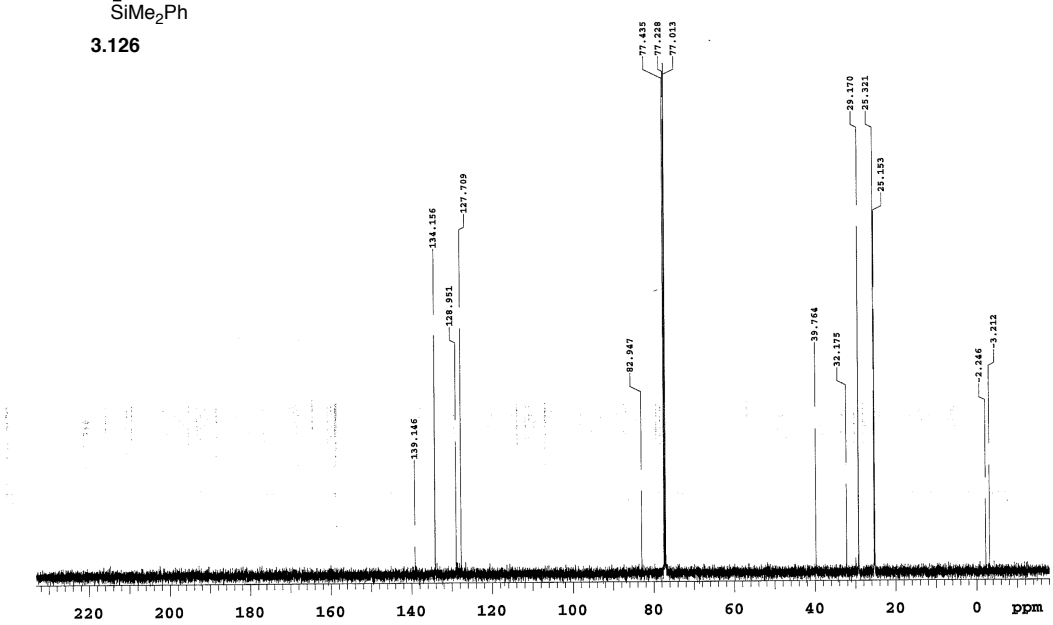

tBu
Bpin
SiMe2Ph

3.126


7.546
7.542
7.537
7.532
7.329
7.325
7.319
7.259
1.574
1.546
1.236
1.214
1.182
1.146
0.770
0.641
0.622
0.549
0.314
0.310
10
9
8
7
6
5
4
3
2
1
ppm
1.90
2.88
1.27
1.57
11.48
8.49
1.00
5.73

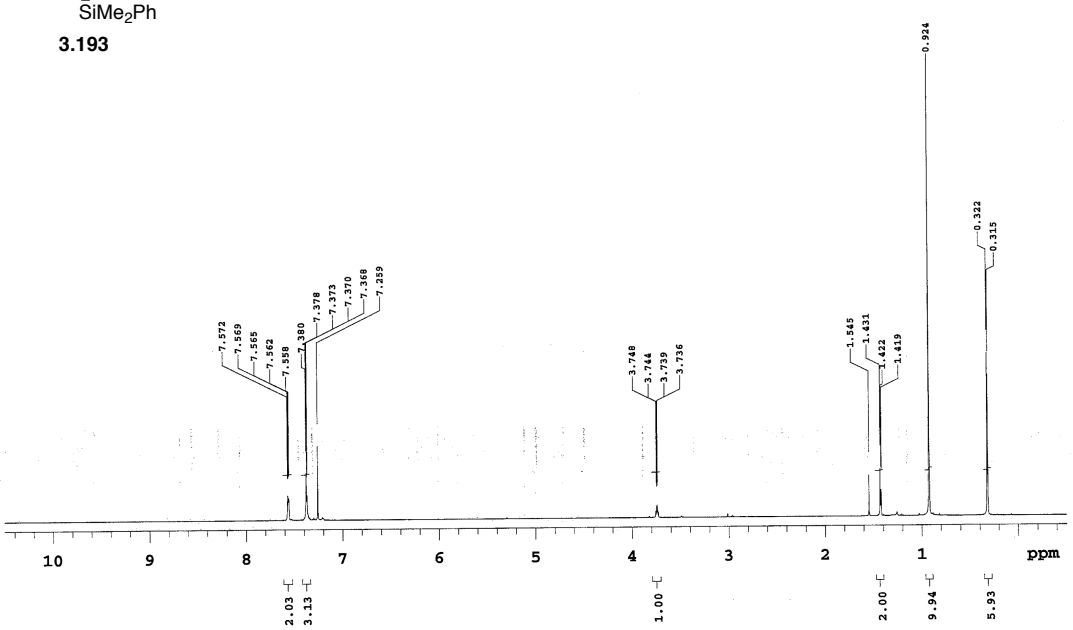

tBu
Bpin
SiMe2Ph

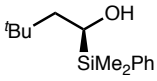
3.126


77.435
77.228
77.013
134.156
127.709
128.951
139.146
82.947
39.764
32.175
29.170
25.321
25.153
3.212
2.246
220
200
180
160
140
120
100
80
60
40
20
0
ppm

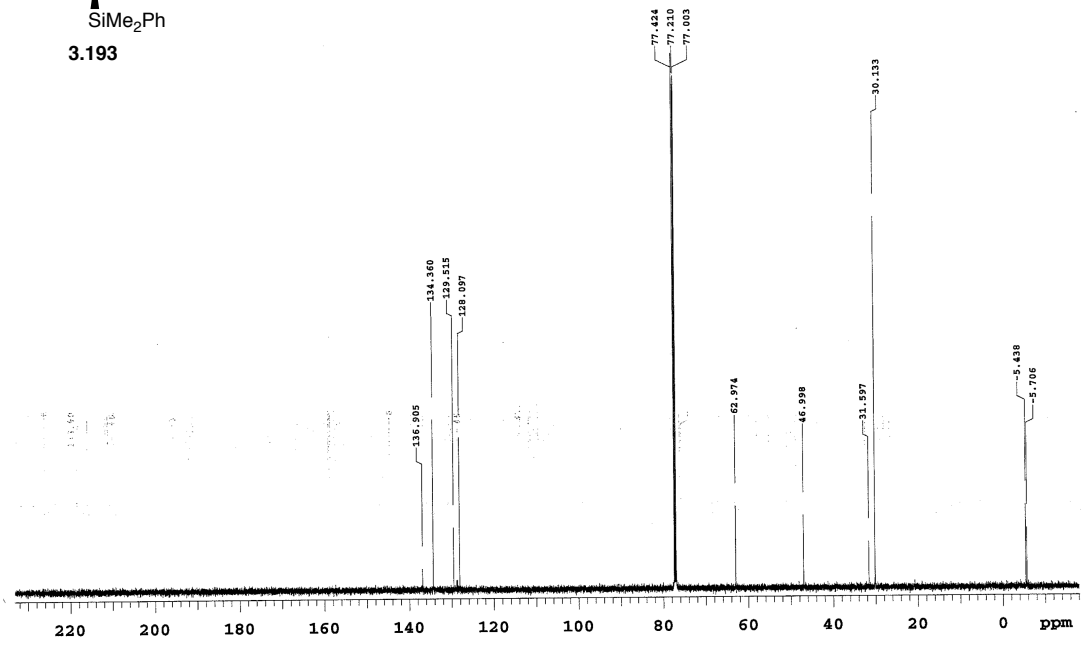

tBu
OH
SiMe2Ph

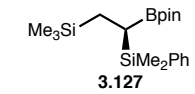
3.193


7.572
7.569
7.565
7.562
7.558
7.380
7.378
7.373
7.370
7.368
7.359
3.748
3.744
3.739
3.736
1.545
1.431
1.422
1.419
0.924
0.322
0.315
10
9
8
7
6
5
4
3
2
1
ppm
2.03
3.13
1.00
2.00
9.94
5.93

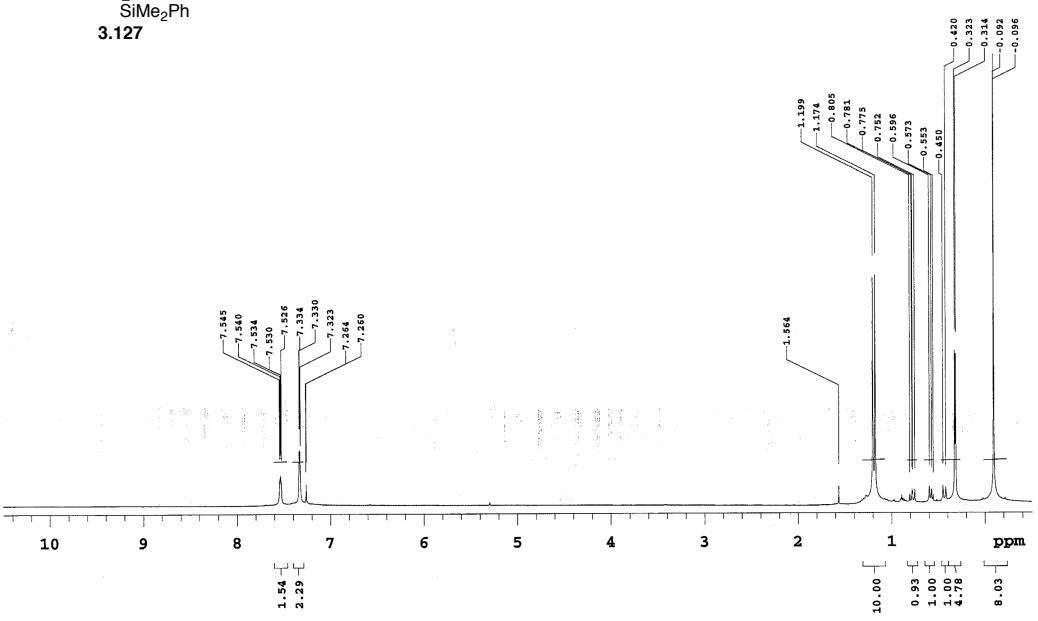

tBu
OH
SiMe2Ph

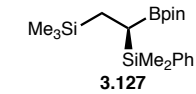
3.193


77.424
77.210
77.003
134.360
129.515
128.097
136.905
62.974
46.998
30.133
31.597
5.438
5.706
220
200
180
160
140
120
100
80
60
40
20
0
ppm

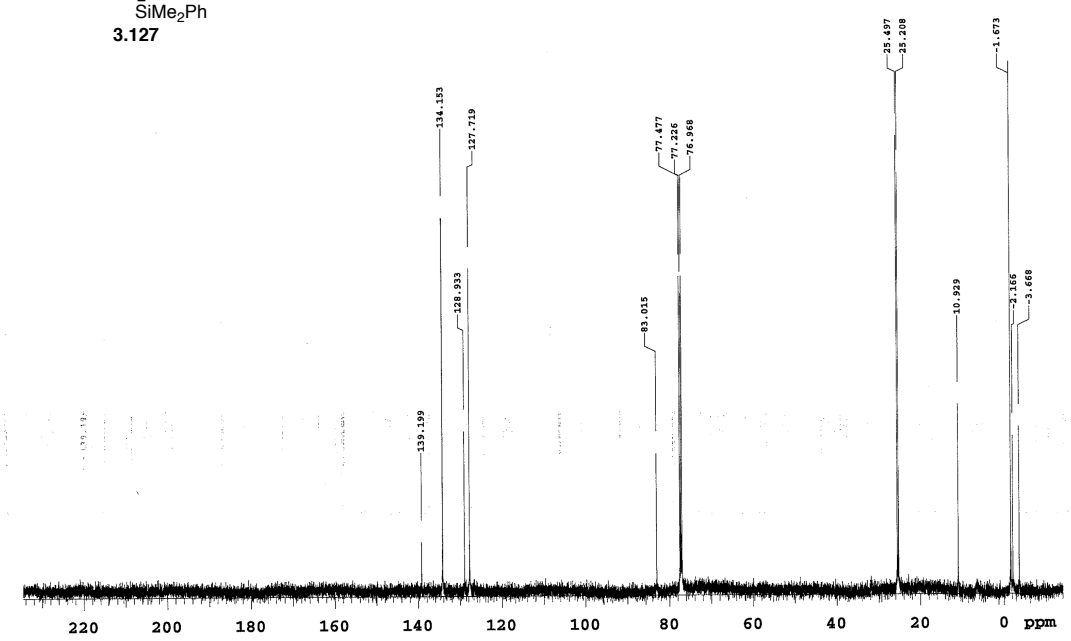

Me3Si
Bpin
SiMe2Ph

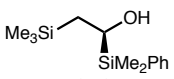
3.127


7.545
7.540
7.534
7.530
7.526
7.334
7.330
7.323
7.264
7.260
1.564
1.199
1.174
0.805
0.781
0.775
0.752
0.596
0.573
0.553
0.450
0.420
0.323
0.314
0.092
0.096
10
9
8
7
6
5
4
3
2
1
ppm
1.54
2.29
10.00
0.93
1.00
1.00
4.78
8.03

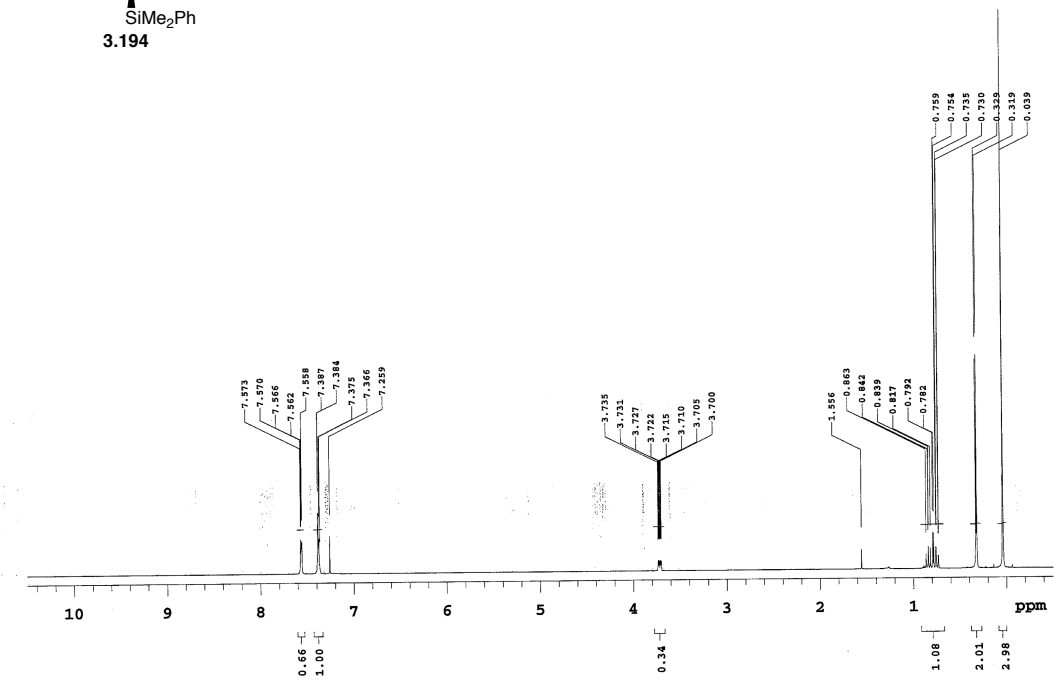

Me3Si
Bpin
SiMe2Ph

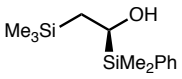
3.127


139.199
134.153
128.933
127.719
83.015
77.477
77.226
76.968
25.497
25.208
10.929
1.673
-3.166
-3.668
220
200
180
160
140
120
100
80
60
40
20
0
ppm

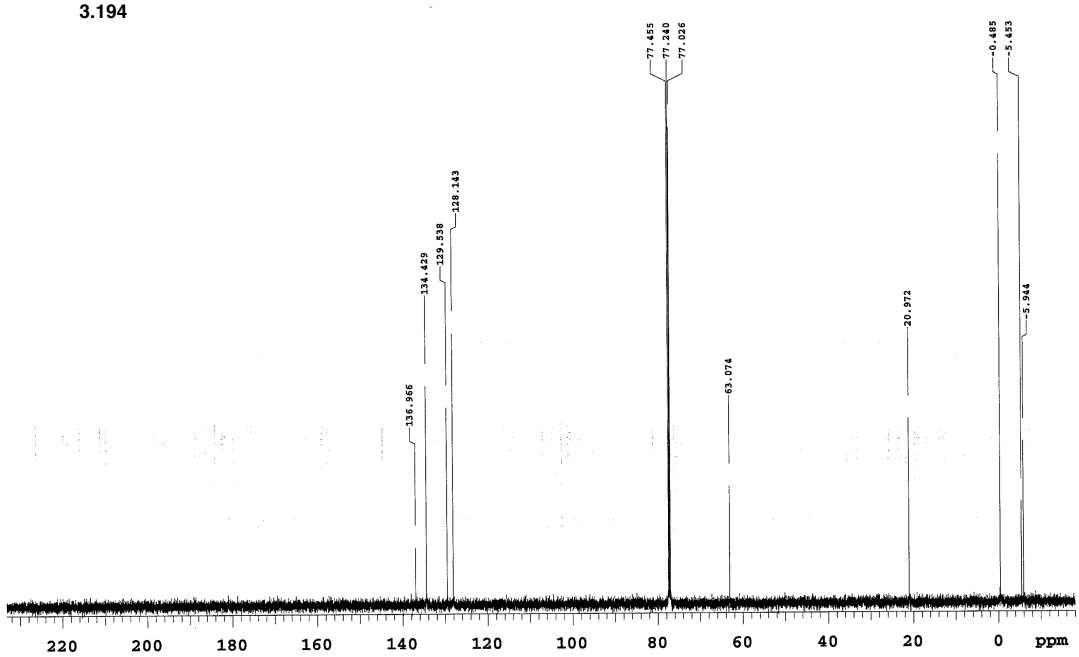

Me3Si
OH
SiMe2Ph

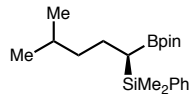
3.194


7.573
7.570
7.566
7.562
7.558
7.387
7.384
7.375
7.366
7.259
3.735
3.731
3.727
3.722
3.715
3.710
3.705
3.700
1.556
0.863
0.842
0.839
0.817
0.792
0.782
0.759
0.754
0.735
0.730
0.329
0.319
0.039
10
9
8
7
6
5
4
3
2
1
ppm
0.66
1.00
0.34
1.08
2.01
2.98

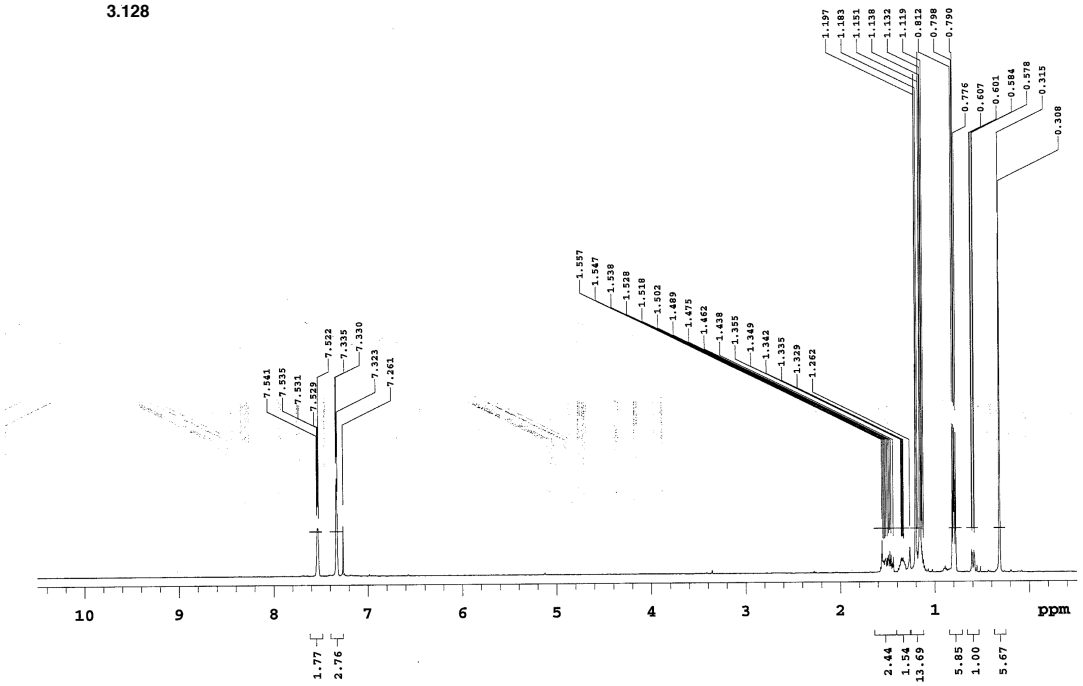

Me3Si
OH
SiMe2Ph

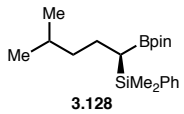
3.194


77.455
77.240
77.026
136.966
134.429
129.538
128.143
63.074
20.972
-0.485
-5.453
-5.944
220
200
180
160
140
120
100
80
60
40
20
0
ppm

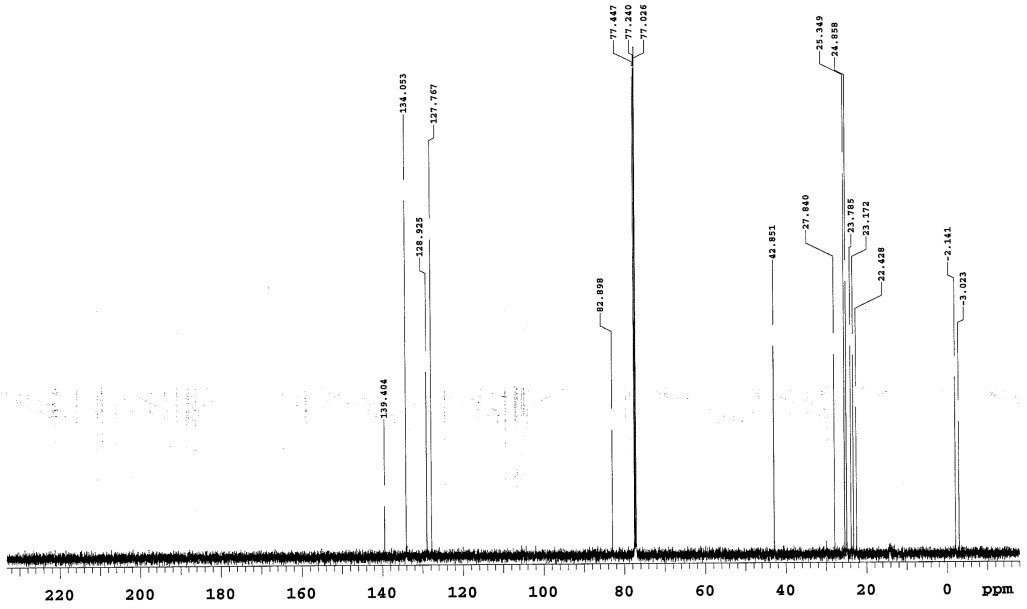

Me
Me
Bpin
SiMe2Ph

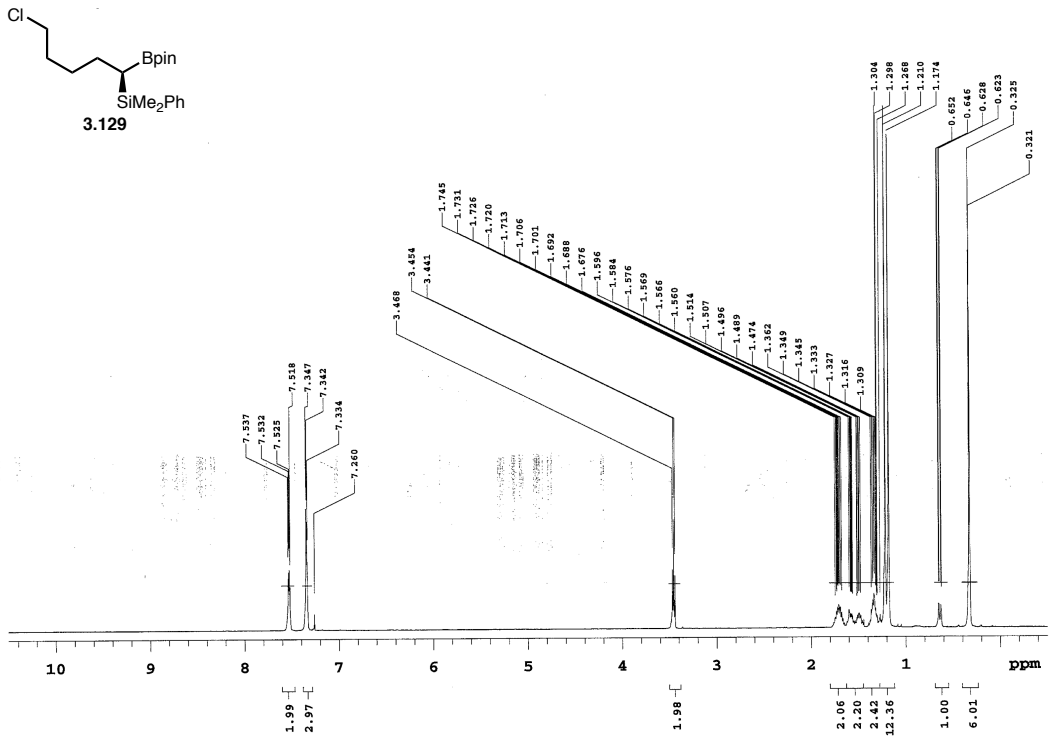
3.128

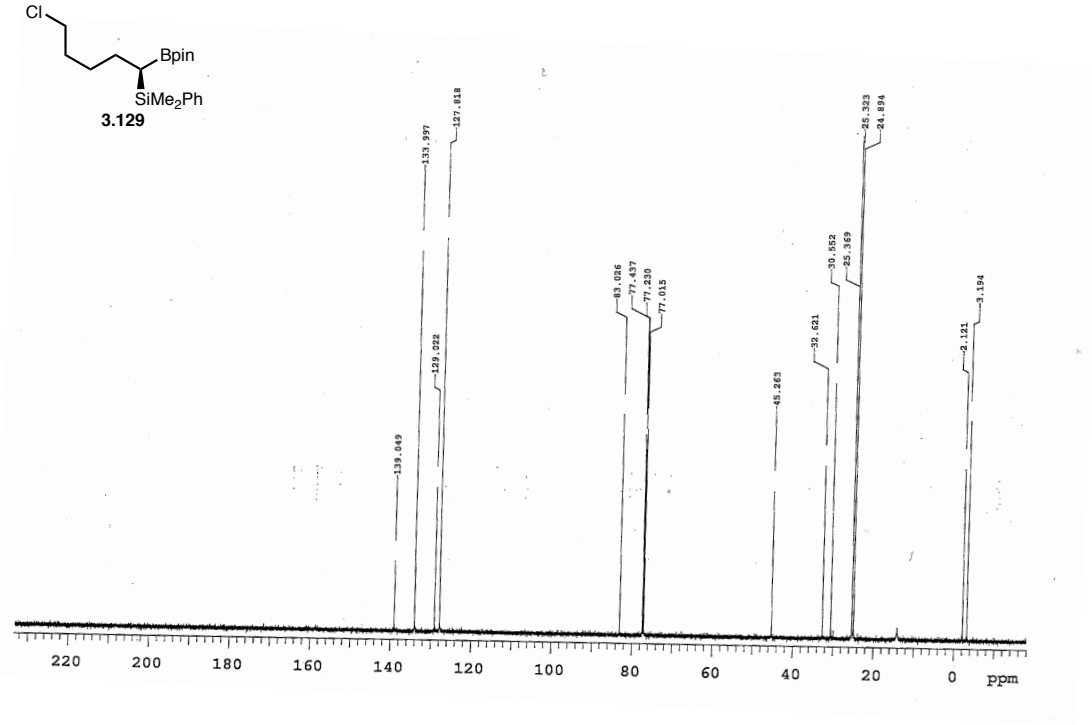

1.197
1.183
1.151
1.138
1.132
1.119
0.812
0.798
0.790
0.776
0.607
0.601
0.584
0.578
0.315
0.308
1.557
1.547
1.538
1.528
1.518
1.502
1.489
1.475
1.462
1.438
1.355
1.349
1.342
1.335
1.329
1.262
7.541
7.535
7.531
7.529
7.522
7.335
7.330
7.323
7.261
10
9
8
7
6
5
4
3
2
1
ppm
1.77
2.76
2.44
1.54
13.69
5.85
1.00
5.67

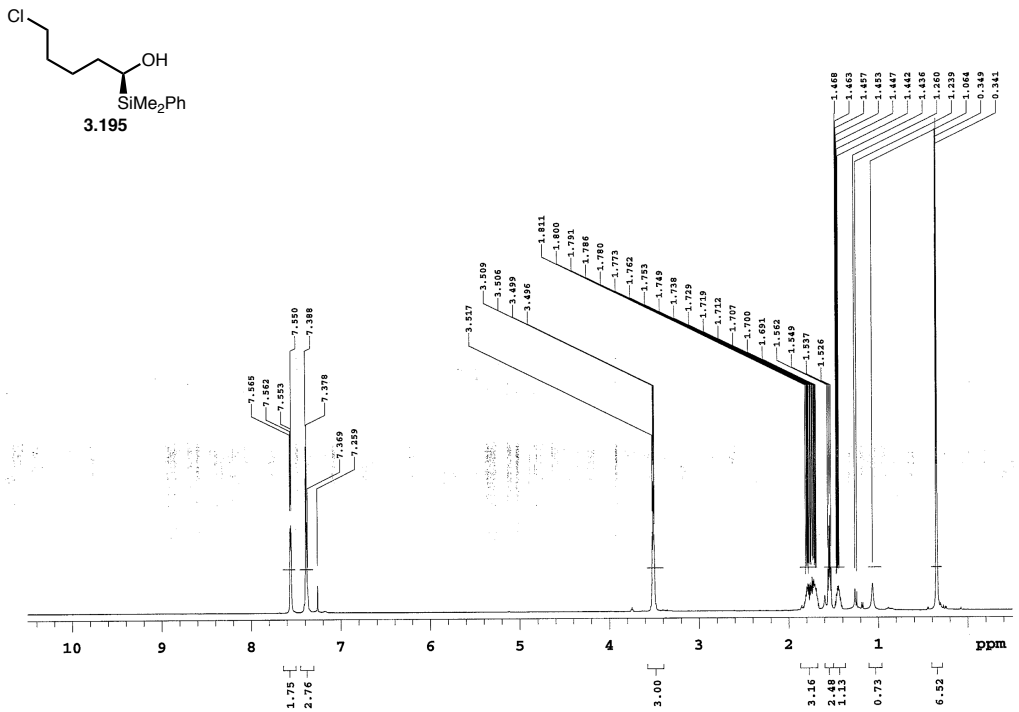

Me
Me
Bpin
SiMe2Ph

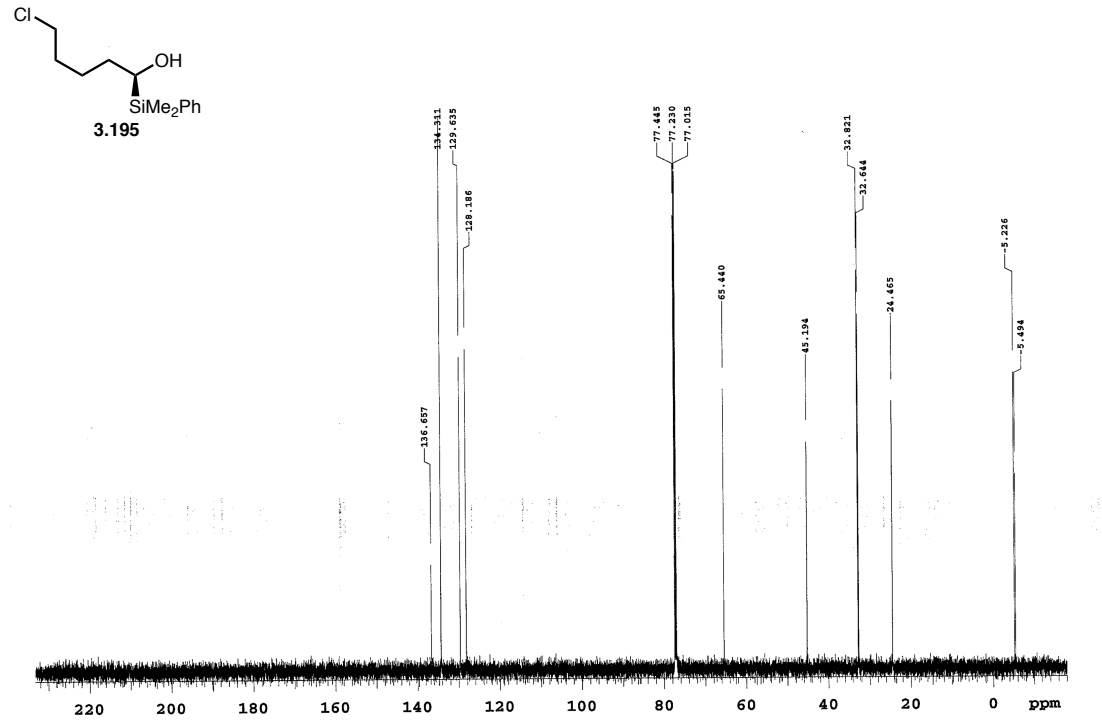
3.128

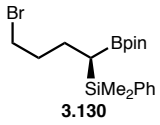

77.447
77.240
77.026
134.053
127.767
128.925
82.898
139.404
25.349
24.858
27.840
42.851
23.785
23.172
22.428
2.141
3.023
220
200
180
160
140
120
100
80
60
40
20
0
ppm


Cl
Bpin
SiMe2Ph
3.129
7.537
7.532
7.525
7.518
7.347
7.342
7.334
7.260
3.468
3.454
3.441
1.745
1.731
1.726
1.720
1.713
1.706
1.701
1.692
1.688
1.676
1.596
1.584
1.576
1.569
1.566
1.560
1.514
1.507
1.496
1.489
1.474
1.362
1.349
1.345
1.333
1.327
1.316
1.309
1.304
1.298
1.268
1.210
1.174
0.652
0.646
0.628
0.623
0.325
0.321
10
9
8
7
6
5
4
3
2
1
ppm
1.99
2.97
1.98
2.06
2.20
2.42
12.36
1.00
6.01

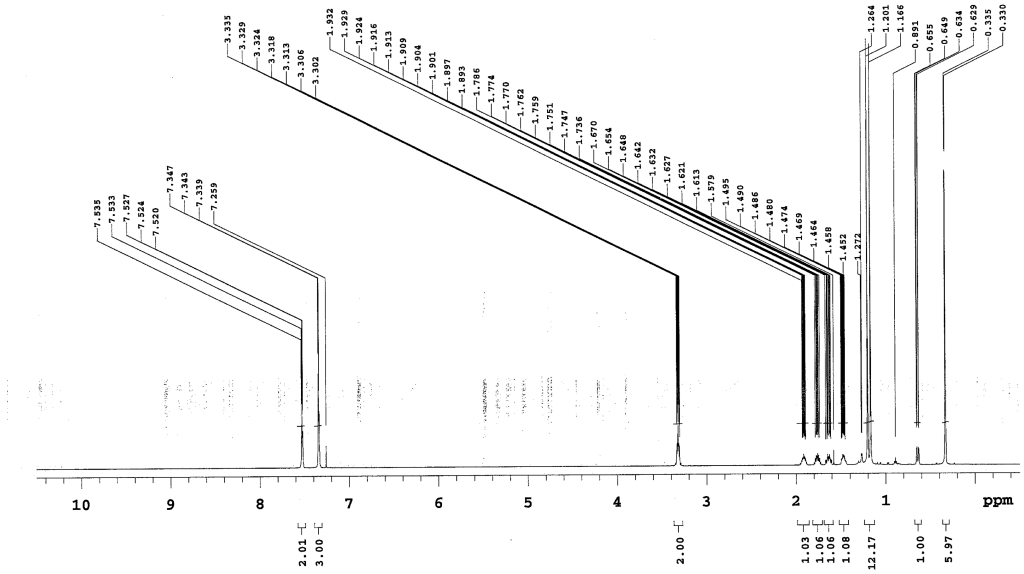

Cl
Bpin
SiMe2Ph
3.129
139.049
133.997
129.022
127.818
83.086
77.437
77.230
77.015
45.263
32.621
30.552
25.369
25.323
24.894
2.121
-3.194
220
200
180
160
140
120
100
80
60
40
20
0
ppm

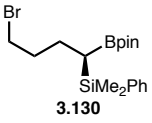

Cl
OH
SiMe2Ph
3.195
7.565
7.562
7.553
7.550
7.388
7.378
7.369
7.359
3.517
3.509
3.506
3.499
3.496
1.811
1.800
1.791
1.786
1.780
1.773
1.762
1.753
1.749
1.738
1.729
1.719
1.712
1.707
1.700
1.691
1.562
1.549
1.537
1.526
1.468
1.463
1.457
1.453
1.447
1.442
1.436
1.260
1.239
1.064
0.349
0.341
10
9
8
7
6
5
4
3
2
1
ppm
1.75
2.76
3.00
3.16
2.48
1.13
0.73
6.52


Cl
OH
SiMe2Ph
3.195
134.311
129.635
128.186
136.657
77.445
77.230
77.015
65.440
45.194
33.821
32.644
24.465
5.226
-5.494
220
200
180
160
140
120
100
80
60
40
20
0
ppm

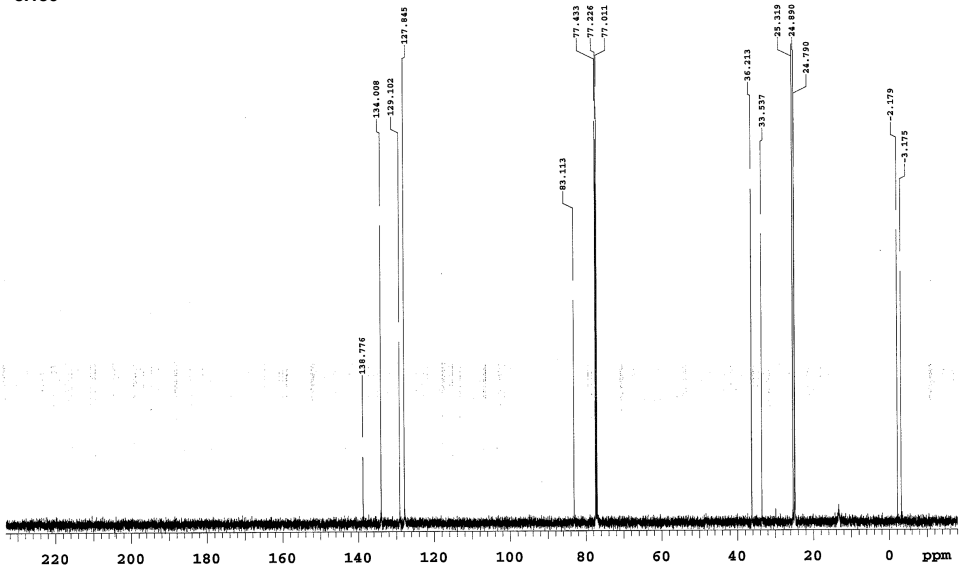

Br
Bpin
SiMe2Ph

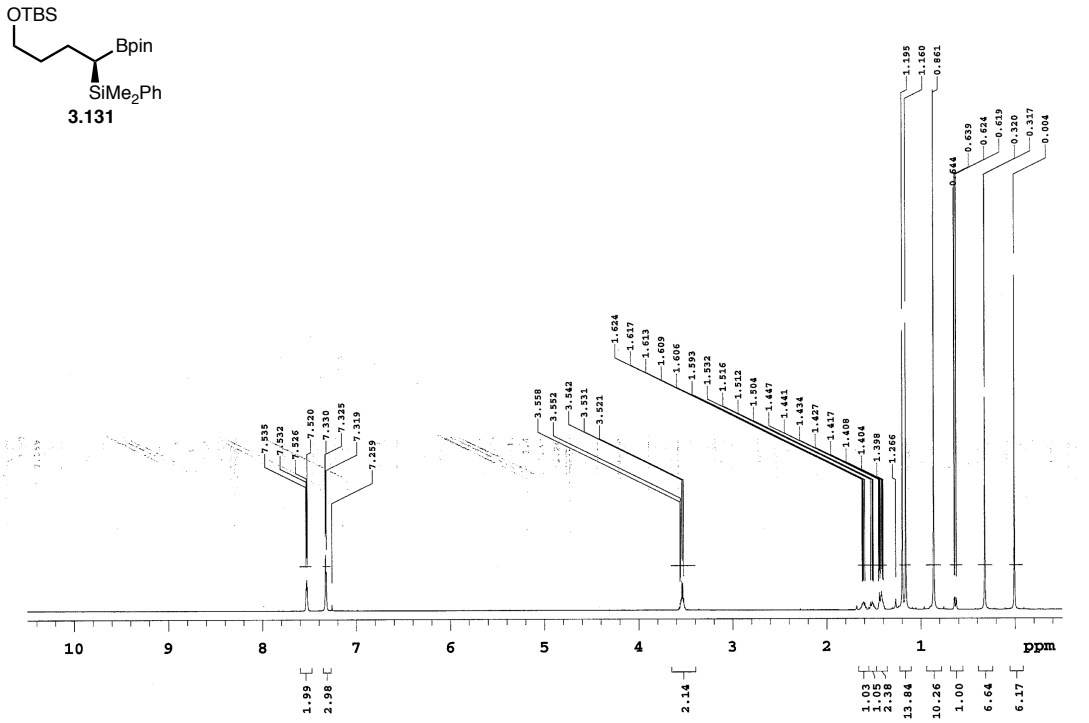
3.130

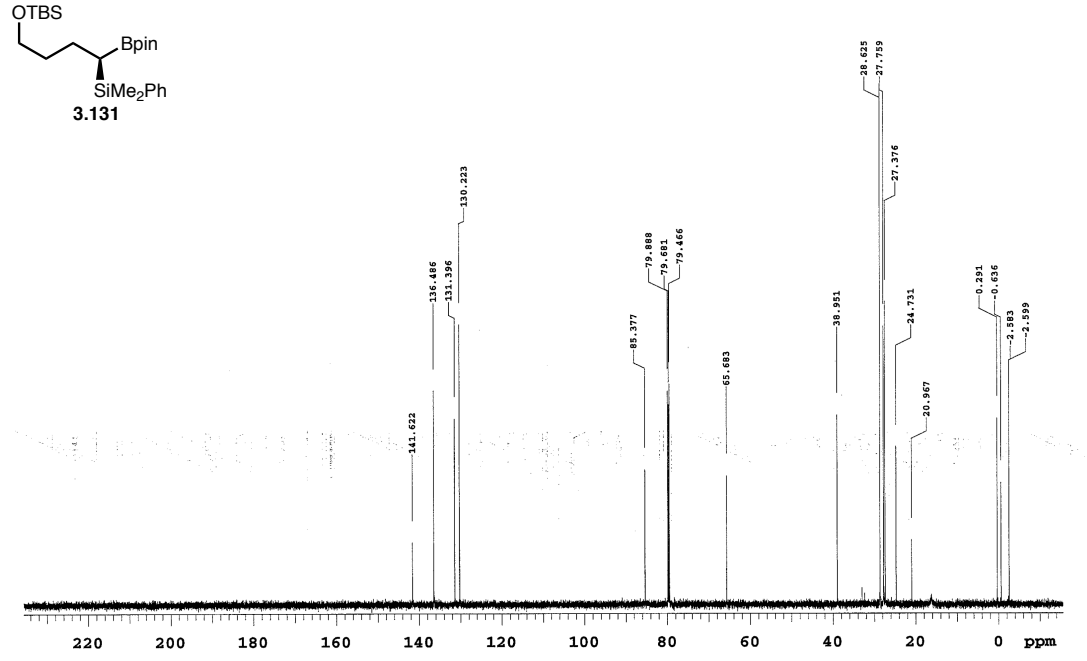

3.335
3.329
3.324
3.318
3.313
3.306
3.302
1.932
1.929
1.924
1.916
1.913
1.909
1.904
1.901
1.897
1.893
1.786
1.774
1.770
1.762
1.759
1.751
1.747
1.736
1.670
1.654
1.648
1.642
1.632
1.627
1.621
1.613
1.579
1.495
1.490
1.486
1.480
1.474
1.469
1.464
1.458
1.452
1.272
1.264
1.201
1.166
0.891
0.655
0.649
0.634
0.629
0.335
0.330
7.935
7.933
7.527
7.524
7.520
7.347
7.343
7.339
7.259
10
9
8
7
6
5
4
3
2
1
ppm
2.01
3.00
2.00
1.03
1.06
1.06
1.08
12.17
1.00
5.97

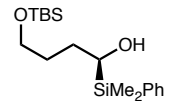

Br
Bpin
SiMe2Ph

3.130

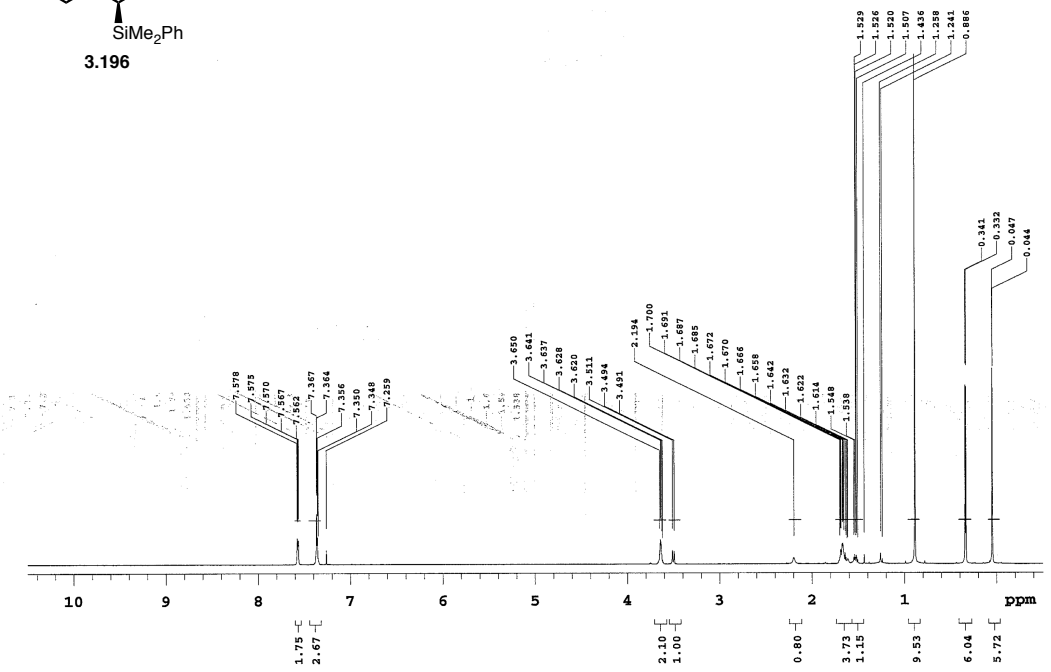

138.776
134.098
129.102
127.845
83.113
77.433
77.226
77.021
36.213
33.537
25.319
24.890
24.790
22.179
21.375
220
200
180
160
140
120
100
80
60
40
20
0
ppm

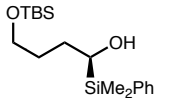

OTBS
Bpin
SiMe2Ph
3.131
7.538
7.532
7.526
7.520
7.330
7.325
7.319
7.259
3.558
3.552
3.542
3.531
3.521
1.624
1.617
1.613
1.609
1.606
1.593
1.532
1.516
1.512
1.504
1.447
1.441
1.434
1.427
1.417
1.408
1.404
1.398
1.266
1.195
1.160
0.861
0.644
0.639
0.624
0.619
0.320
0.317
0.004
10
9
8
7
6
5
4
3
2
1
ppm
1.99
2.98
2.14
1.03
1.05
2.38
13.84
10.26
1.00
6.64
6.17


OTBS
Bpin
SiMe2Ph
3.131
141.622
136.486
131.396
130.223
85.377
79.888
79.681
79.466
65.683
38.951
28.625
27.759
27.376
24.731
20.967
0.291
-0.636
-2.583
-2.599
220
200
180
160
140
120
100
80
60
40
20
0
ppm

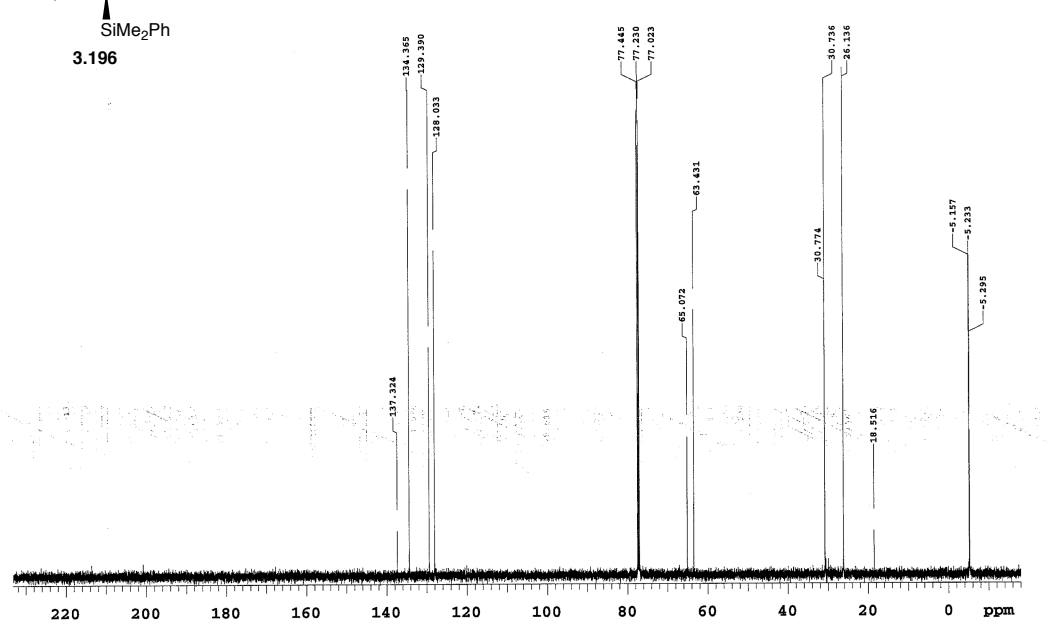

OTBS
OH
SiMe2Ph

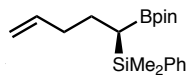
3.196


1.529
1.526
1.520
1.507
1.436
1.258
1.241
0.886
0.341
0.332
0.047
0.044
7.578
7.575
7.570
7.567
7.562
7.367
7.364
7.356
7.350
7.348
7.259
3.650
3.641
3.637
3.628
3.620
3.511
3.494
3.491
2.194
1.700
1.691
1.687
1.685
1.672
1.670
1.666
1.658
1.642
1.632
1.622
1.614
1.548
1.538
10
9
8
7
6
5
4
3
2
1
ppm
1.75
2.67
2.10
1.00
0.80
3.73
1.15
9.53
6.04
5.72

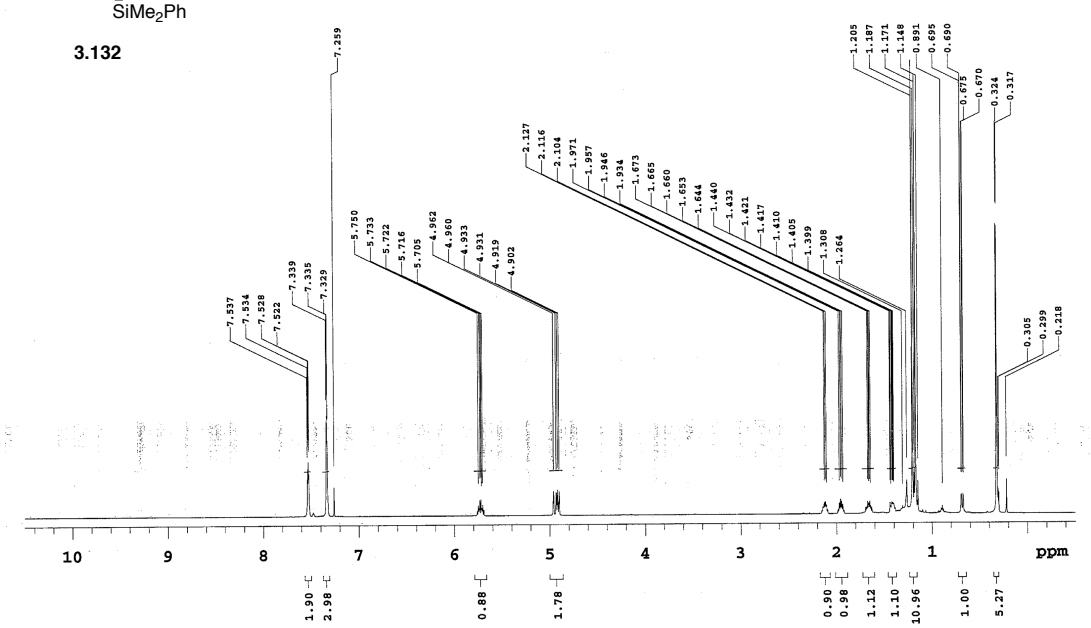

OTBS
OH
SiMe2Ph

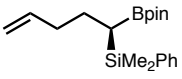
3.196


134.365
129.390
128.033
77.445
77.230
77.023
63.431
30.736
26.136
30.774
65.072
55.357
55.233
55.295
137.324
18.516
220
200
180
160
140
120
100
80
60
40
20
0
ppm

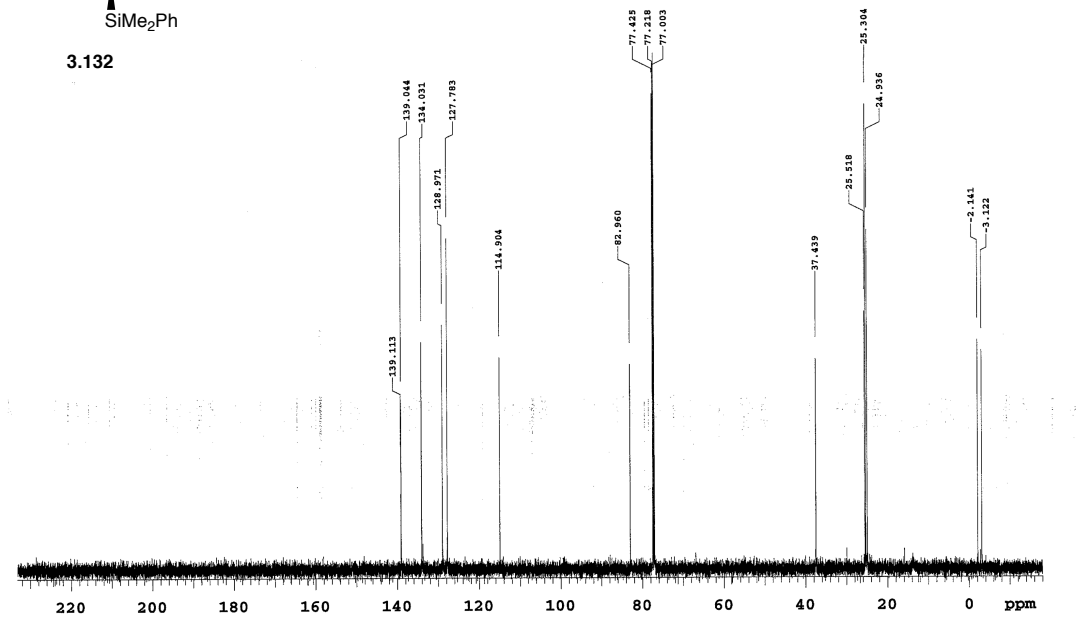

Bpin
SiMe2Ph

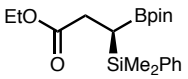
3.132


7.537
7.534
7.528
7.522
7.359
7.339
7.335
7.329
5.750
5.733
5.722
5.716
5.705
4.962
4.960
4.933
4.931
4.919
4.902
2.127
2.116
2.104
1.971
1.957
1.946
1.934
1.673
1.665
1.660
1.653
1.644
1.440
1.432
1.421
1.417
1.410
1.405
1.399
1.308
1.264
1.205
1.187
1.171
1.148
0.891
0.695
0.690
0.675
0.670
0.324
0.317
0.305
0.299
0.218
10
9
8
7
6
5
4
3
2
1
ppm
1.90
2.98
0.88
1.78
0.90
0.98
1.12
1.10
10.96
1.00
5.27

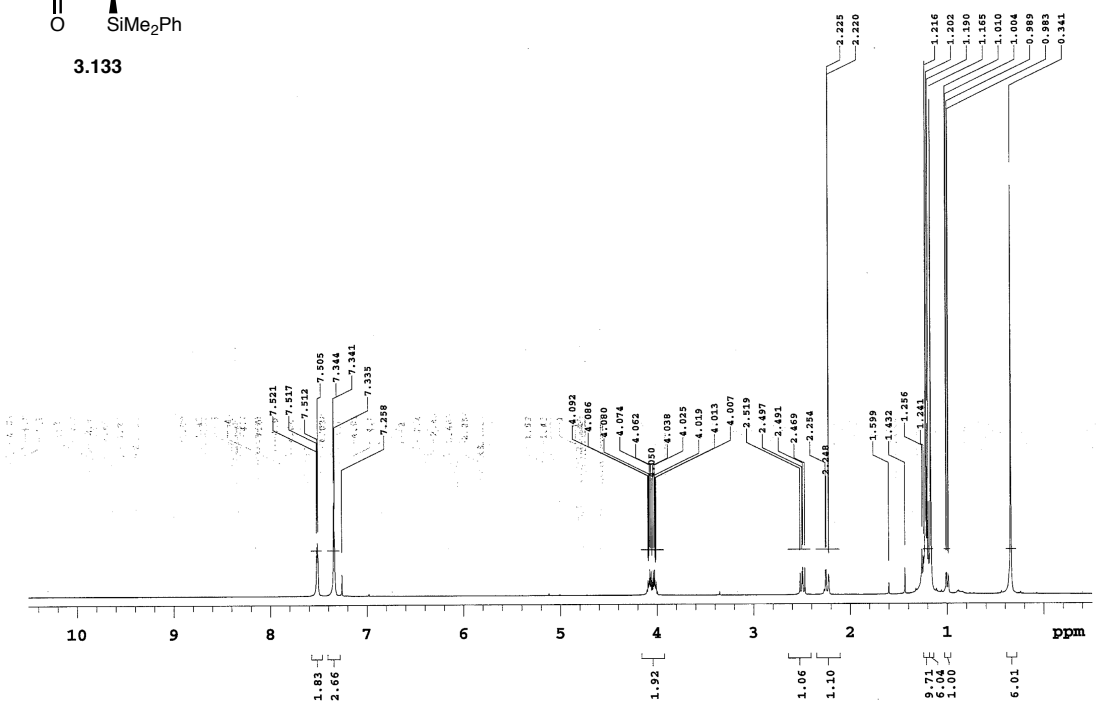

Bpin
SiMe2Ph

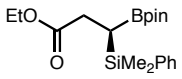
3.132


77.425
77.218
77.003
25.304
24.936
139.044
134.031
127.783
128.971
114.904
82.960
25.518
37.439
22.141
23.122
139.113
220
200
180
160
140
120
100
80
60
40
20
0
ppm

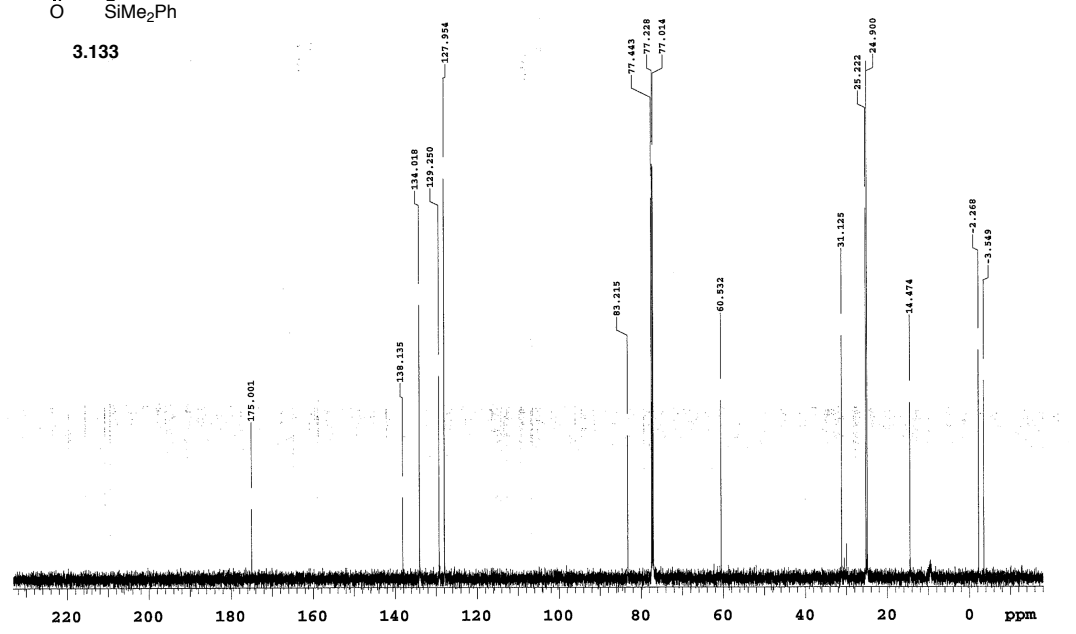

EtO
Bpin
O
SiMe2Ph

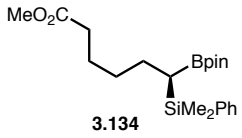
3.133


2.225
2.220
1.216
1.202
1.190
1.165
1.010
1.004
0.989
0.983
0.341
7.521
7.517
7.512
7.505
7.344
7.341
7.335
7.238
4.092
4.086
4.080
4.074
4.062
4.038
4.025
4.019
4.013
4.007
2.519
2.497
2.491
2.469
2.254
1.599
1.432
1.256
1.241
10
9
8
7
6
5
4
3
2
1
ppm
1.83
2.66
1.92
1.06
1.10
9.71
6.04
1.00
6.01

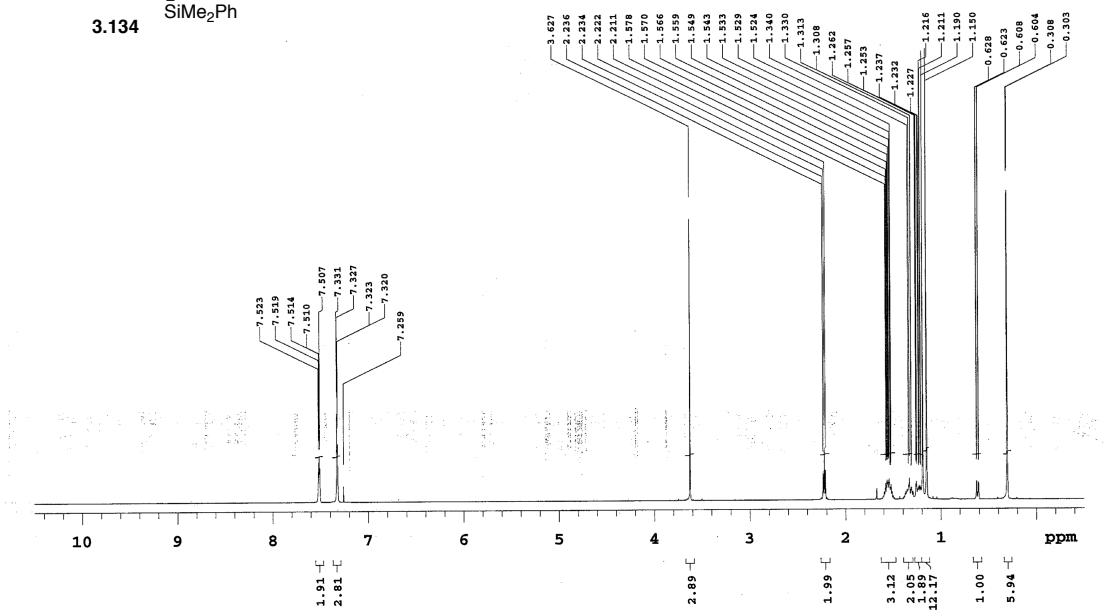

EtO
Bpin
O
SiMe2Ph

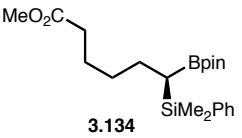
3.133


175.001
138.135
134.018
129.250
127.954
83.215
77.443
77.228
77.014
60.532
31.125
25.222
24.900
14.474
2.268
1.549
220
200
180
160
140
120
100
80
60
40
20
0
ppm

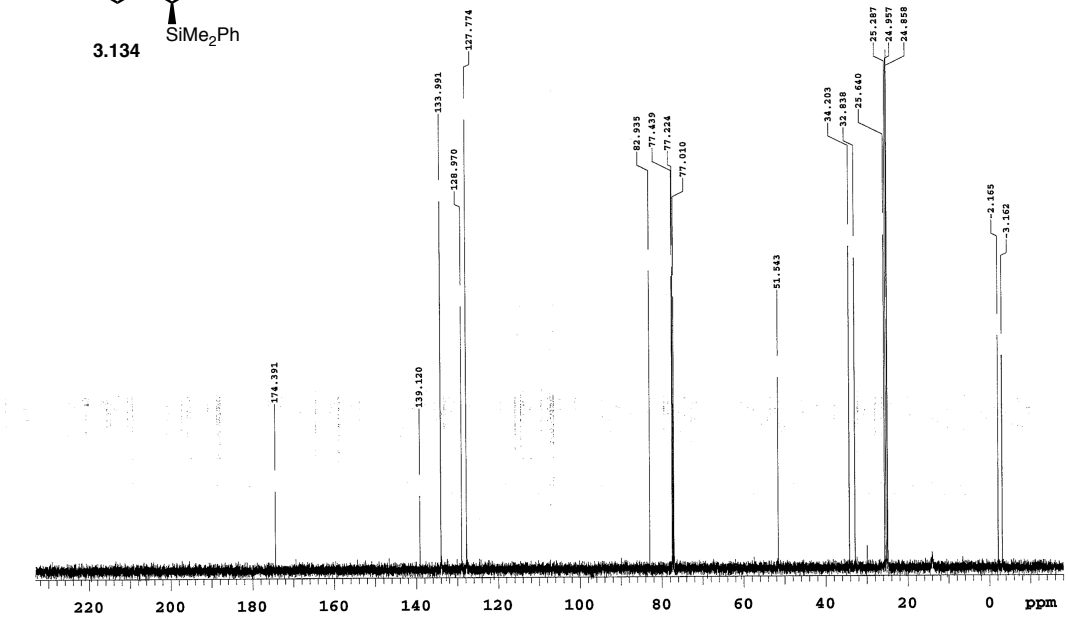

MeO2C
Bpin
SiMe2Ph

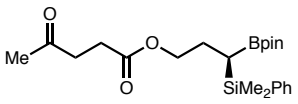
3.134


3.627
2.236
2.234
2.222
2.211
1.578
1.570
1.566
1.559
1.549
1.543
1.533
1.529
1.524
1.340
1.330
1.313
1.308
1.262
1.257
1.253
1.237
1.232
1.227
1.216
1.211
1.190
1.150
0.628
0.623
0.608
0.604
0.308
0.303
7.523
7.519
7.514
7.510
7.507
7.331
7.327
7.323
7.320
7.259
10
9
8
7
6
5
4
3
2
1
ppm
1.91
2.81
2.89
1.99
3.12
2.05
2.08
12.17
1.00
5.94

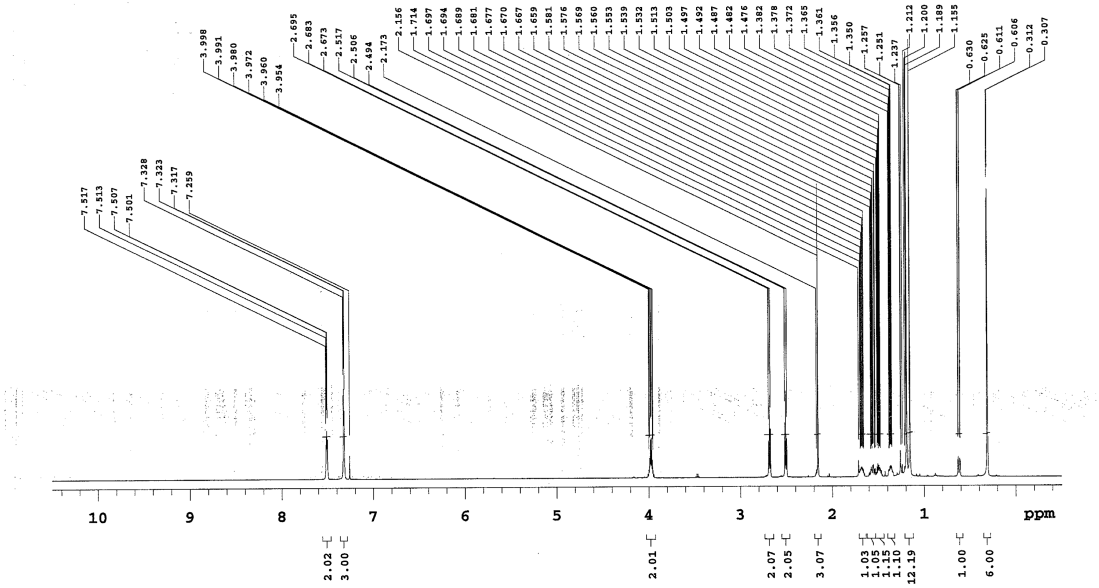

MeO2C
Bpin
SiMe2Ph

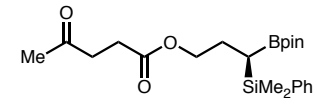
3.134


174.391
139.120
133.991
128.970
127.774
82.935
77.439
77.224
77.010
51.543
35.287
34.203
32.838
25.640
24.957
24.858
2.165
3.162
220
200
180
160
140
120
100
80
60
40
20
0
ppm

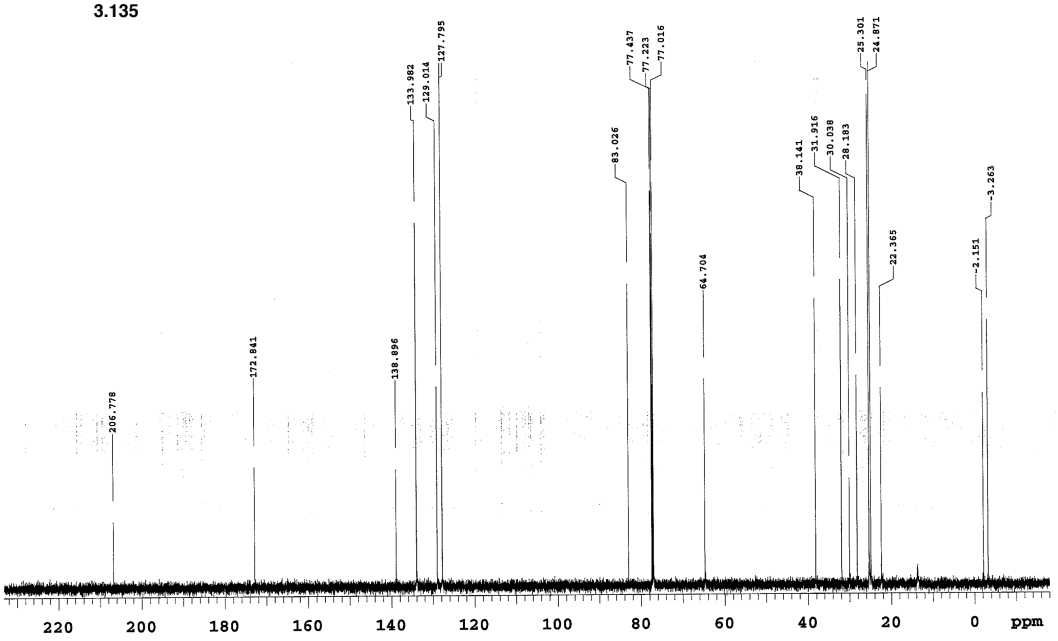

O
Me
O
O
Bpin
SiMe2Ph

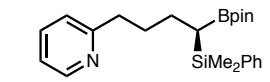
3.135


3.998
3.991
3.980
3.972
3.960
3.954
2.695
2.683
2.673
2.517
2.506
2.494
2.173
2.156
1.714
1.697
1.694
1.689
1.681
1.677
1.670
1.667
1.659
1.581
1.576
1.569
1.560
1.553
1.539
1.532
1.513
1.503
1.497
1.492
1.487
1.482
1.476
1.382
1.378
1.372
1.365
1.361
1.356
1.350
1.257
1.251
1.237
1.212
1.200
1.189
1.155
0.630
0.625
0.611
0.606
0.312
0.307
7.517
7.513
7.507
7.501
7.338
7.323
7.317
7.259
10
9
8
7
6
5
4
3
2
1
ppm
2.02
3.00
2.01
2.07
2.05
3.07
1.03
1.05
1.15
1.10
12.19
1.00
6.00


O
Me
O
O
Bpin
SiMe2Ph

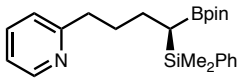
3.135


206.778
172.841
138.896
133.982
129.014
127.795
83.026
77.437
77.223
77.016
64.704
30.141
31.916
30.038
28.183
25.301
24.871
22.365
12.151
3.263
220
200
180
160
140
120
100
80
60
40
20
0
ppm

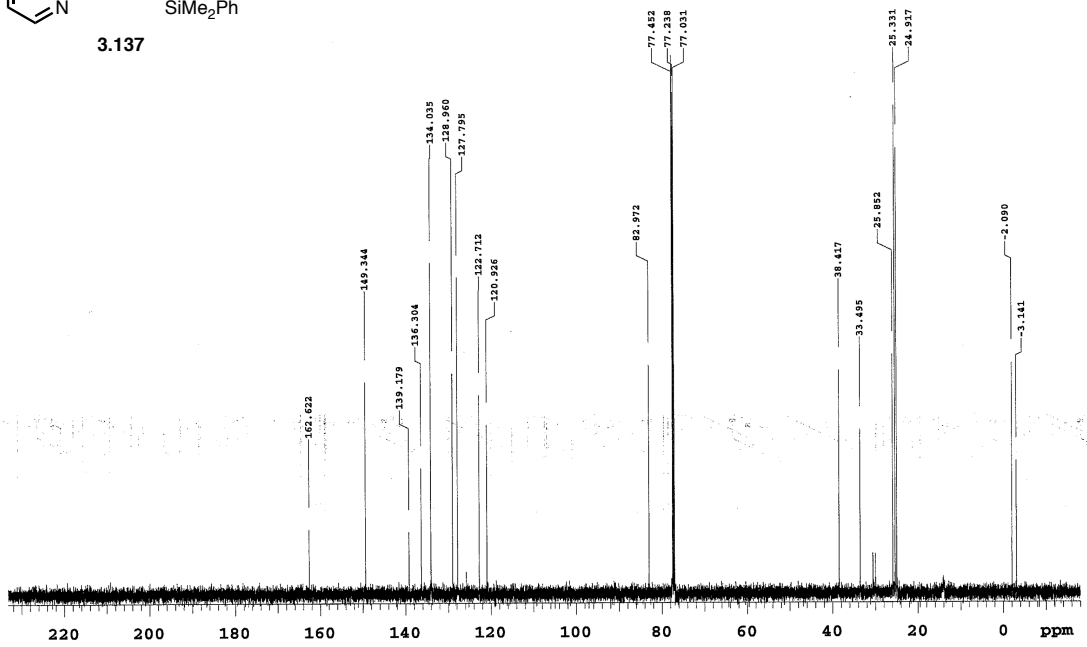

Bpin
N
SiMe2Ph

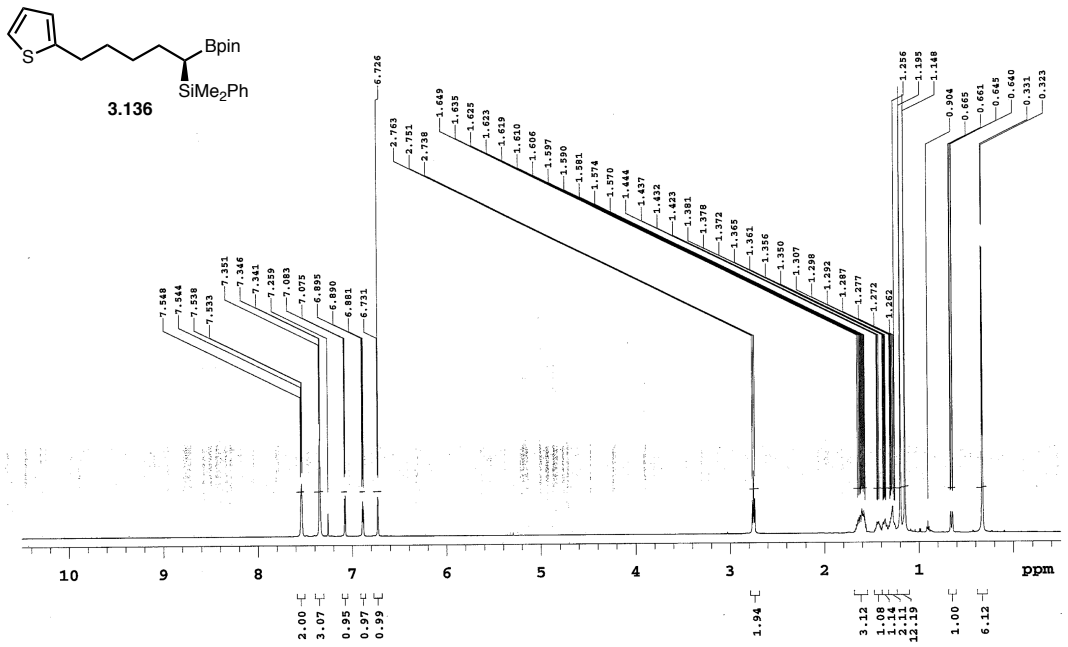
3.137

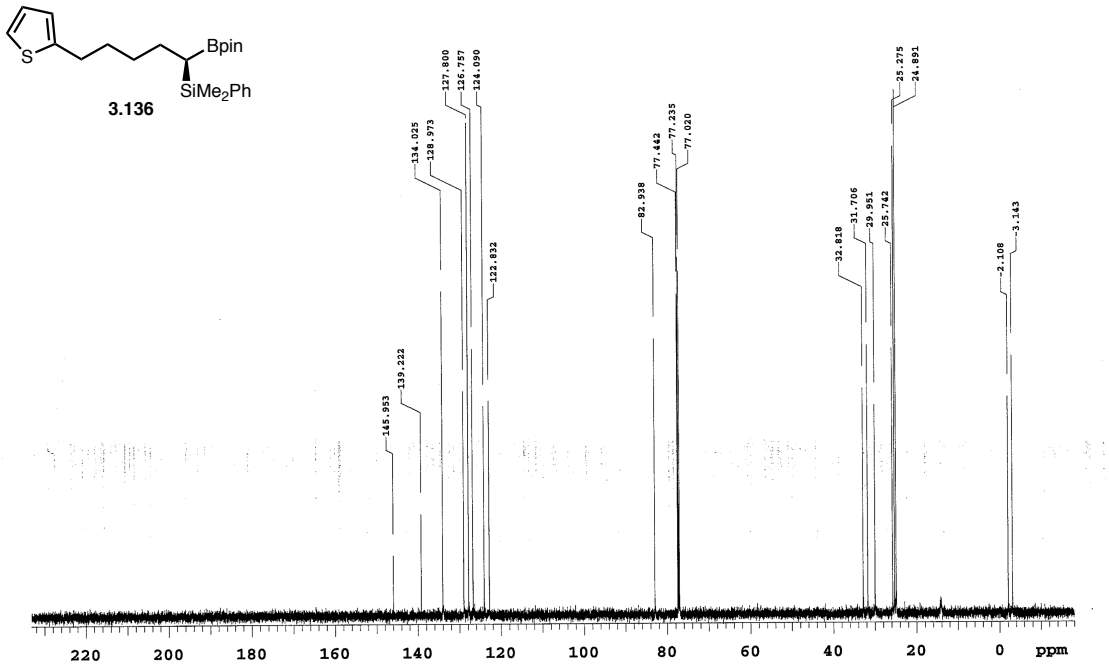
8.477
8.469
7.529
7.526
7.513
7.510
7.505
7.503
7.500
7.321
7.318
7.312
7.259
7.054
7.042
7.029
2.726
2.716
2.702
2.691
1.778
1.637
1.619
1.604
1.430
1.389
1.385
1.378
1.261
1.256
1.206
1.185
1.148
0.694
0.680
0.675
0.300
0.295
10
9
8
7
6
5
4
3
2
1
ppm
0.70
2.54
2.51
1.66
1.92
1.14
2.12
1.71
6.46
6.27
1.00
5.65

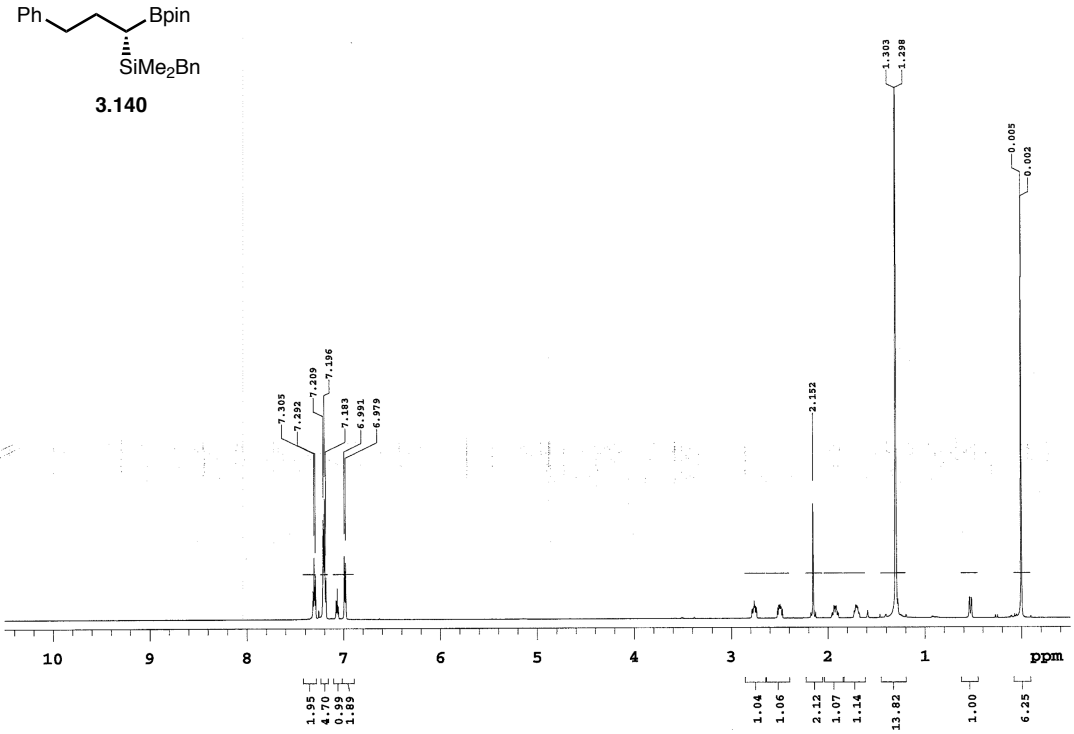

Bpin
N
SiMe2Ph

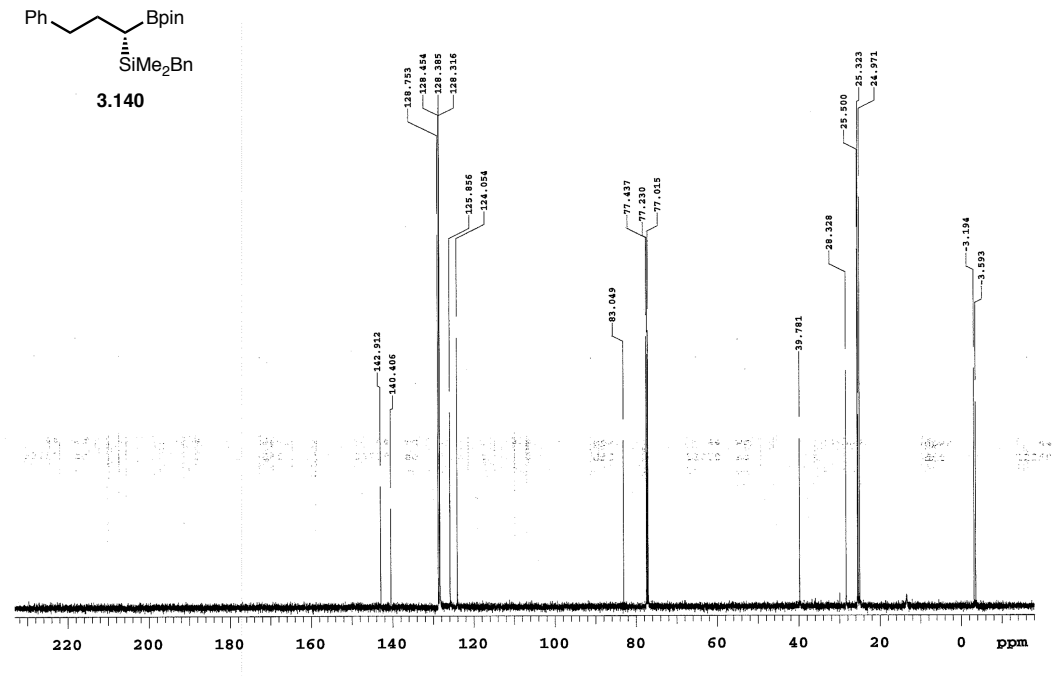
3.137

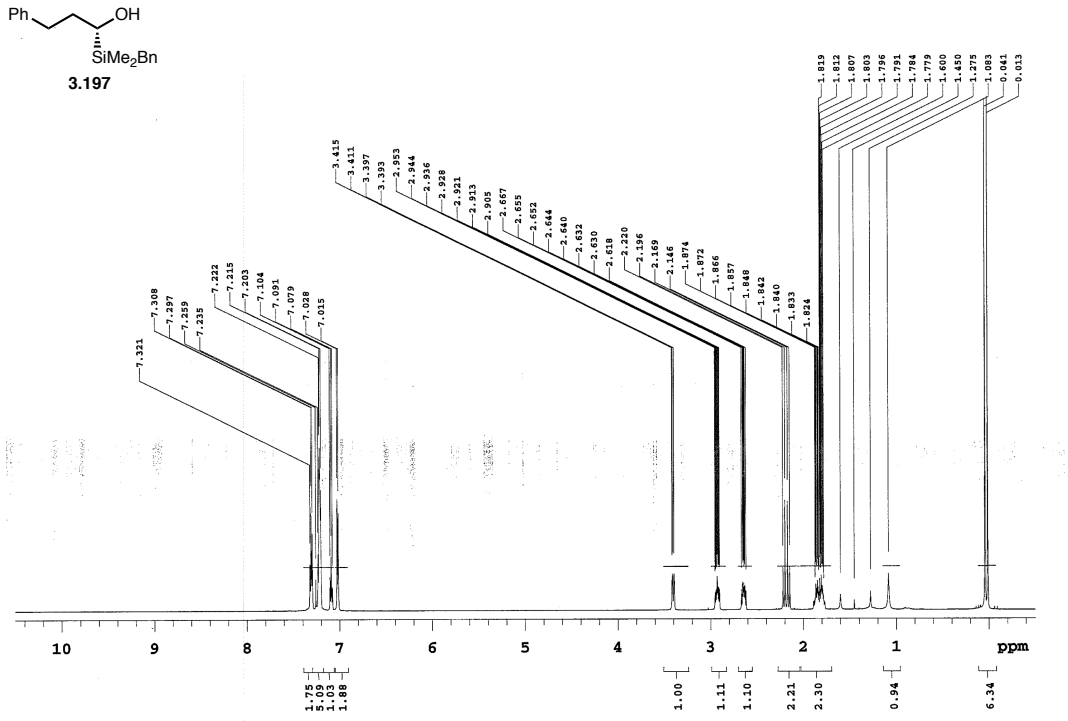

162.622
149.344
139.179
136.304
134.035
128.960
127.795
122.712
120.926
82.972
77.452
77.238
77.031
38.417
33.495
25.852
25.331
24.917
2.090
-3.141
220
200
180
160
140
120
100
80
60
40
20
0
ppm

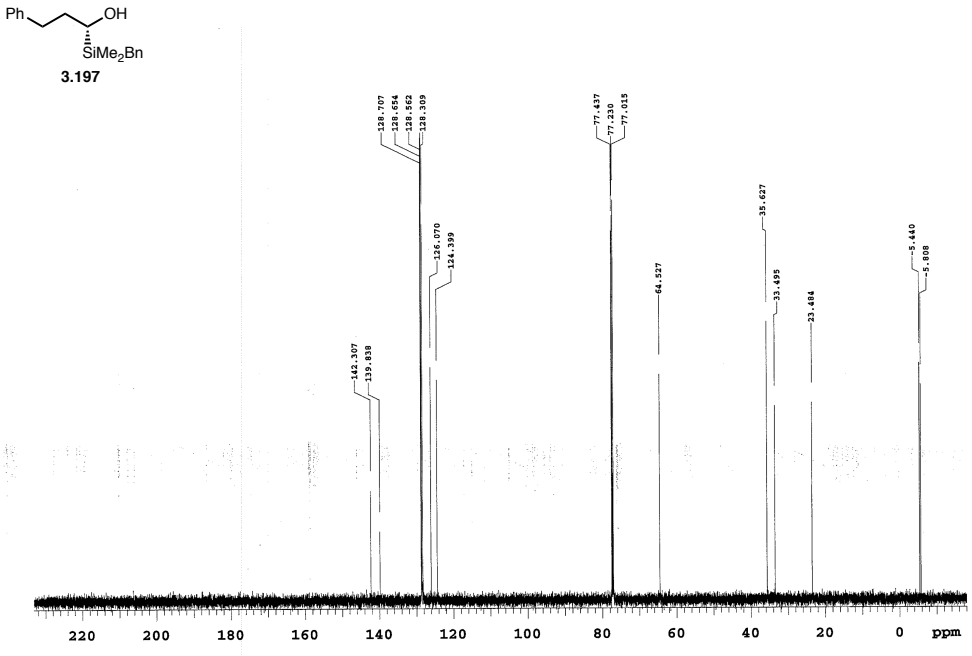

Bpin
SiMe2Ph
3.136
ppm

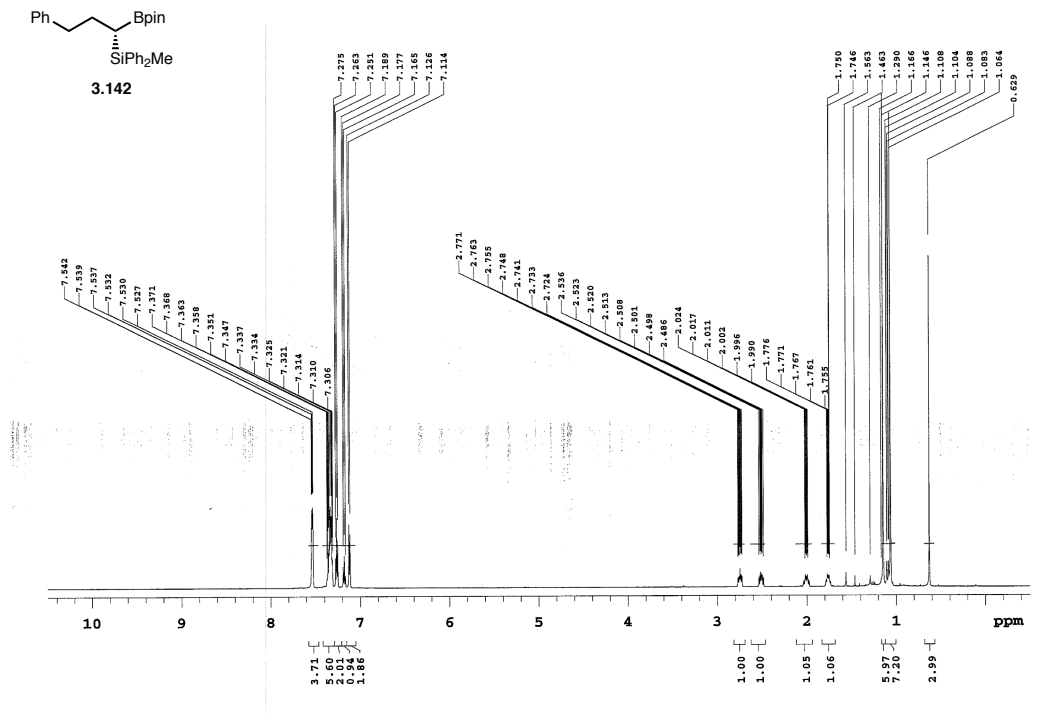

Bpin
SiMe2Ph
3.136
ppm

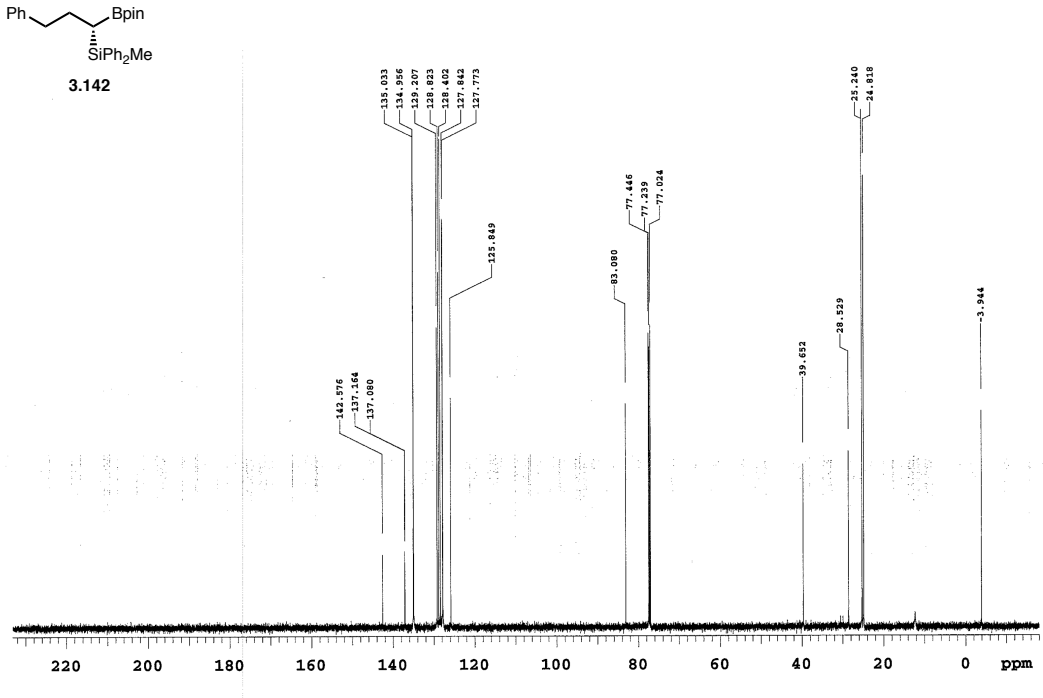

Ph
Bpin
SiMe2Bn
3.140
7.305
7.293
7.209
7.196
7.183
6.991
6.979
2.152
1.303
1.298
0.005
0.002
10
9
8
7
6
5
4
3
2
1
ppm
1.95
4.70
0.99
1.89
1.04
1.06
2.12
1.07
1.14
13.82
1.00
6.25

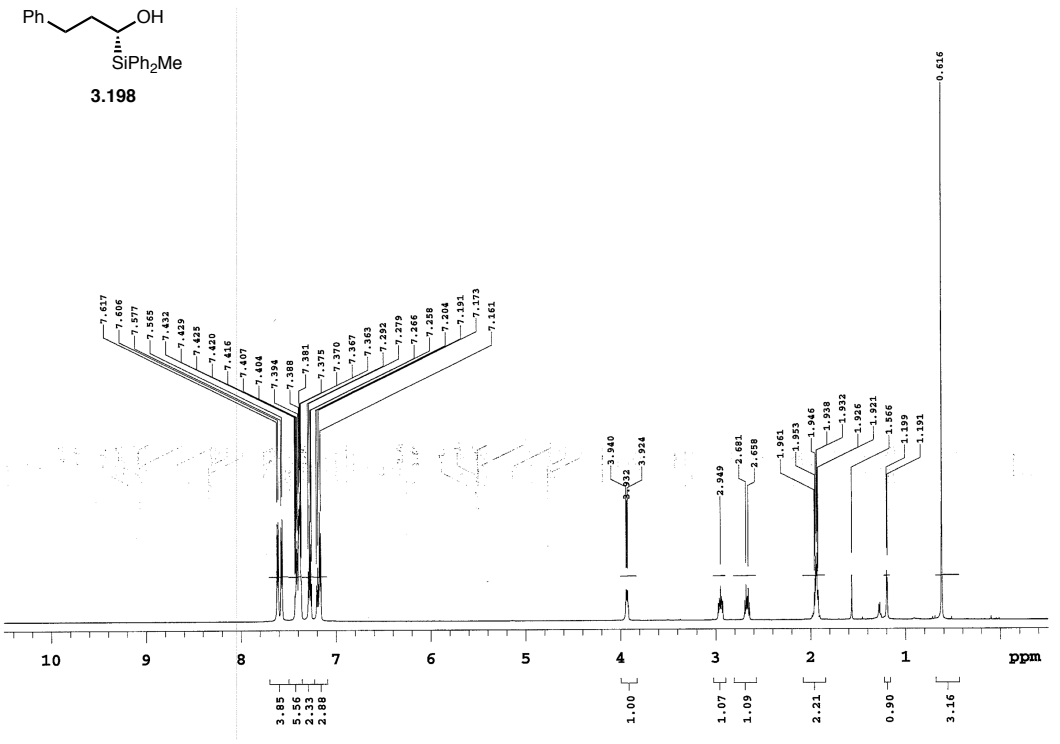

Ph
Bpin
SiMe2Bn
3.140
128.753
128.454
128.385
128.316
125.856
124.054
142.912
140.406
83.049
77.437
77.230
77.015
39.781
28.328
25.500
25.323
24.971
3.194
3.593
220
200
180
160
140
120
100
80
60
40
20
0
ppm

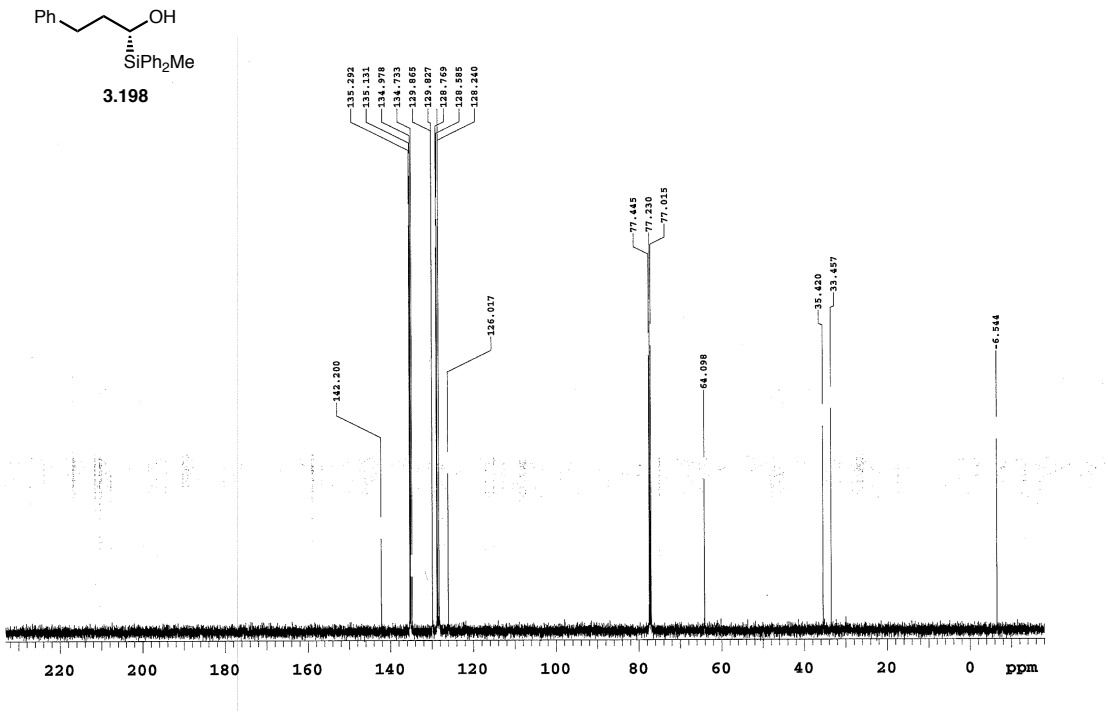

Ph
OH
SiMe2Bn
3.197
7.321
7.308
7.297
7.259
7.235
7.222
7.215
7.203
7.104
7.091
7.079
7.028
7.015
3.415
3.411
3.397
3.393
2.953
2.944
2.936
2.928
2.921
2.913
2.905
2.667
2.655
2.652
2.644
2.640
2.632
2.630
2.618
2.220
2.196
2.169
2.146
1.874
1.872
1.866
1.857
1.848
1.842
1.840
1.833
1.824
1.819
1.812
1.807
1.803
1.796
1.791
1.784
1.779
1.600
1.450
1.275
1.083
0.041
0.013
10
9
8
7
6
5
4
3
2
1
ppm
1.75
5.09
1.03
1.88
1.00
1.11
1.10
2.21
2.30
0.94
6.34

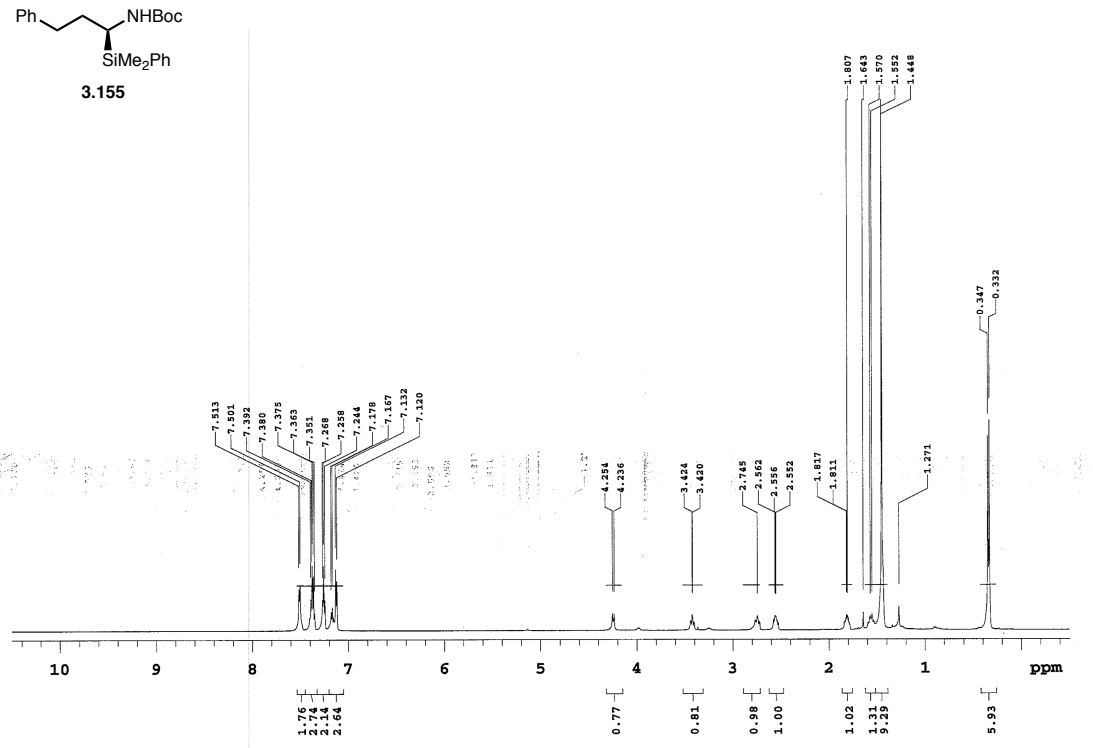

Ph
OH
SiMe2Bn
3.197
126.707
126.654
126.562
126.309
126.070
124.399
142.307
139.838
77.437
77.230
77.015
64.527
35.627
33.495
23.484
5.440
5.008
220
200
180
160
140
120
100
80
60
40
20
0
ppm

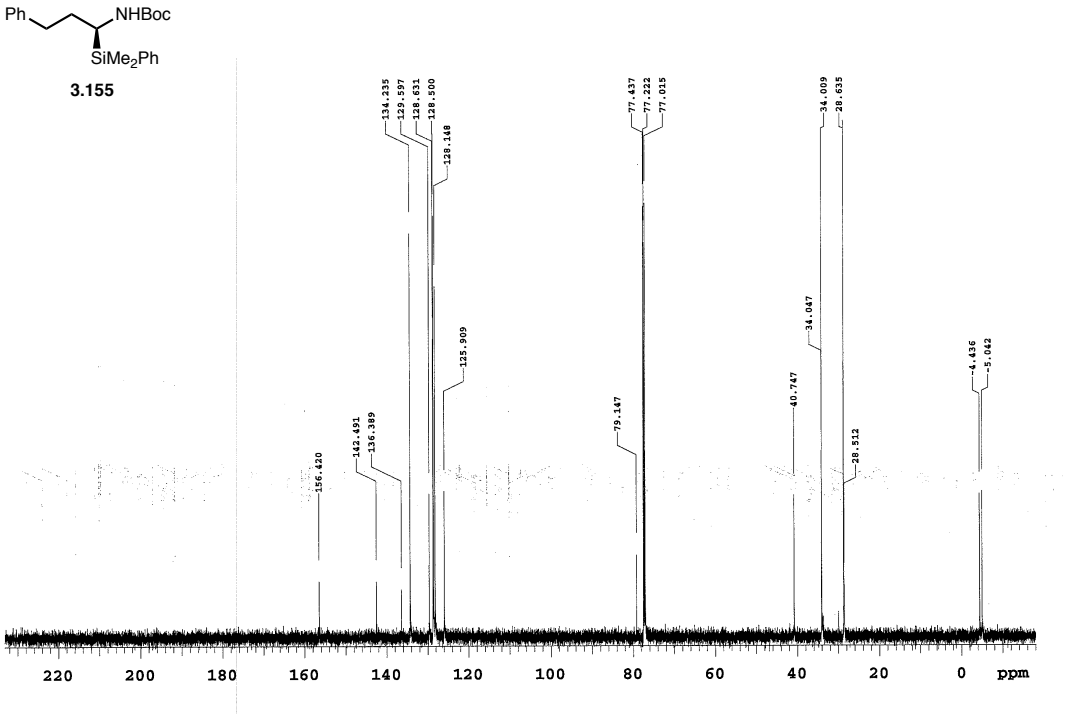

Ph
Bpin
SiPh2Me
3.142
7.542
7.539
7.537
7.532
7.530
7.527
7.371
7.368
7.363
7.358
7.351
7.347
7.337
7.334
7.325
7.321
7.314
7.310
7.306
7.275
7.263
7.251
7.189
7.177
7.165
7.126
7.114
2.771
2.763
2.755
2.748
2.741
2.733
2.724
2.536
2.523
2.520
2.513
2.508
2.501
2.498
2.486
2.024
2.017
2.011
2.002
1.996
1.990
1.776
1.771
1.767
1.761
1.755
1.750
1.746
1.563
1.463
1.290
1.166
1.146
1.108
1.104
1.088
1.083
1.064
0.629
10
9
8
7
6
5
4
3
2
1
ppm
3.71
5.60
2.01
2.94
1.86
1.00
1.00
1.05
1.06
5.97
7.20
2.99

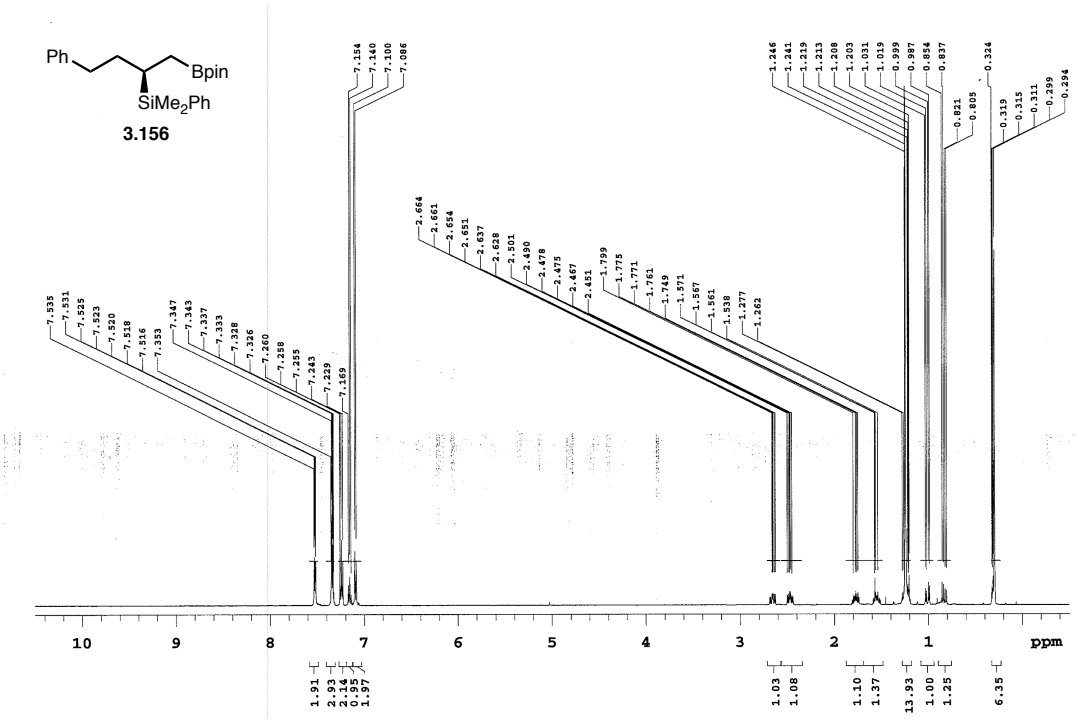

Ph
Bpin
SiPh2Me
3.142
135.033
134.956
129.207
128.823
128.402
127.842
127.773
125.849
83.080
77.446
77.239
77.024
142.976
137.164
137.080
39.652
28.529
25.240
24.818
3.944
220
200
180
160
140
120
100
80
60
40
20
0
ppm

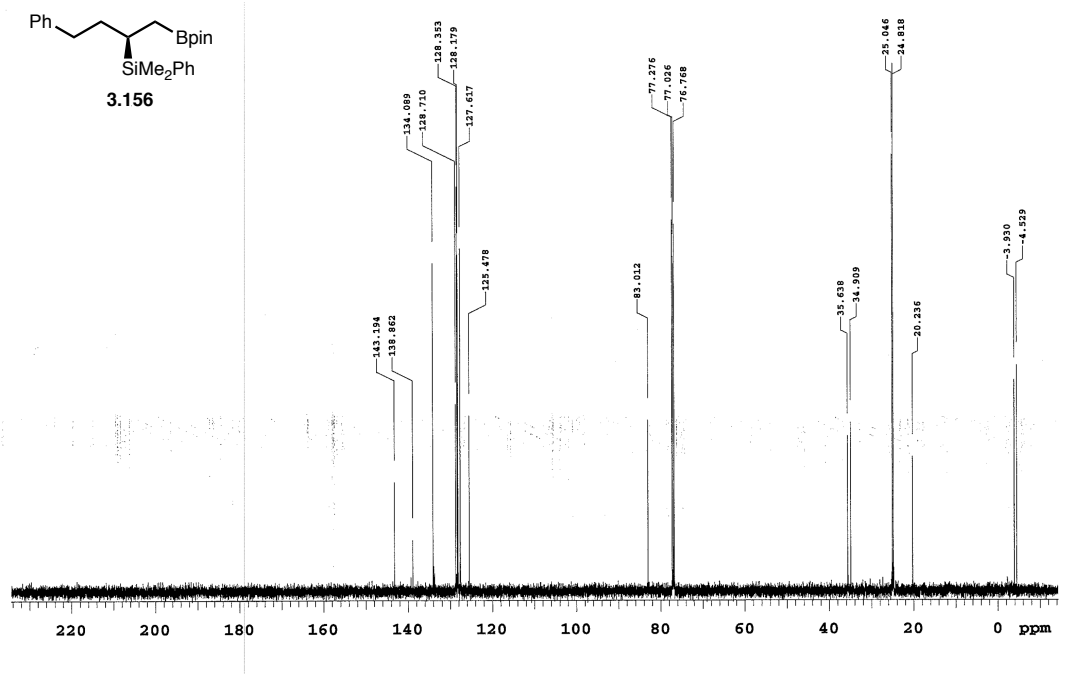

Ph
OH
SiPh2Me
3.198
7.617
7.606
7.577
7.565
7.432
7.429
7.425
7.420
7.416
7.407
7.404
7.394
7.388
7.381
7.375
7.370
7.367
7.363
7.292
7.279
7.266
7.258
7.204
7.191
7.173
7.161
3.940
3.932
3.924
2.949
2.681
2.659
1.961
1.953
1.946
1.938
1.932
1.926
1.921
1.566
1.199
1.191
0.616
10
9
8
7
6
5
4
3
2
1
ppm
3.85
5.56
2.33
2.88
1.00
1.07
1.09
2.21
0.90
3.16

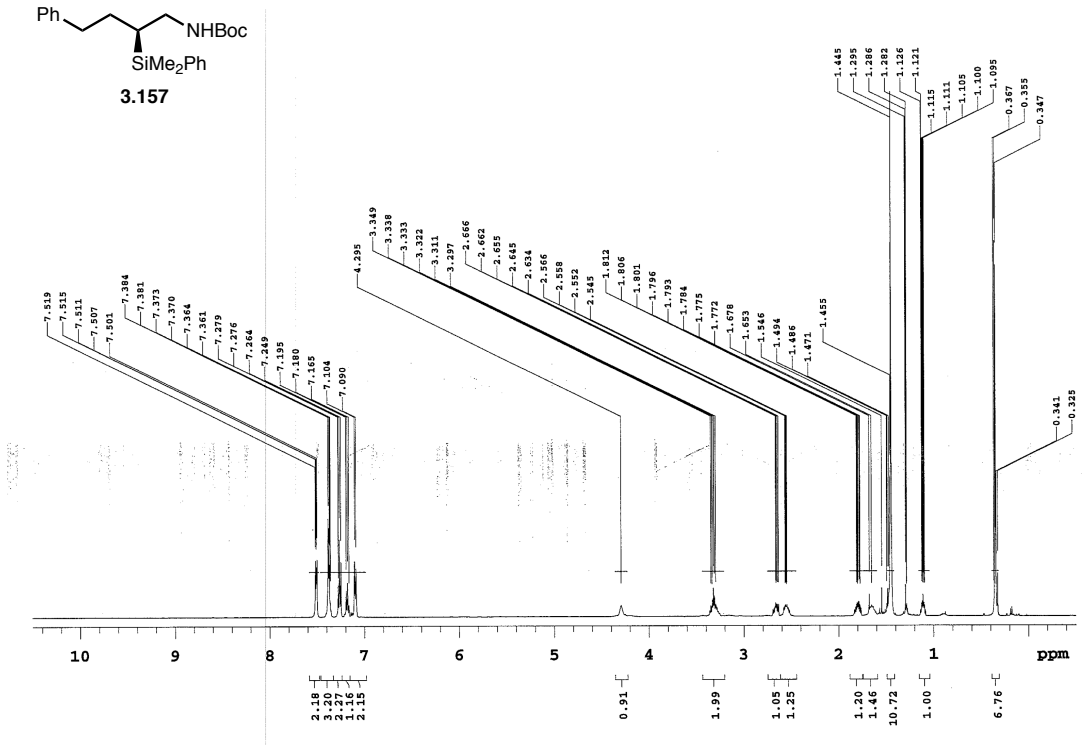

Ph
OH
SiPh2Me
3.198
135.292
135.131
134.978
134.733
130.865
129.827
128.769
128.585
128.240
77.445
77.230
77.015
126.017
142.200
64.098
35.420
33.457
16.544
220
200
180
160
140
120
100
80
60
40
20
0
ppm

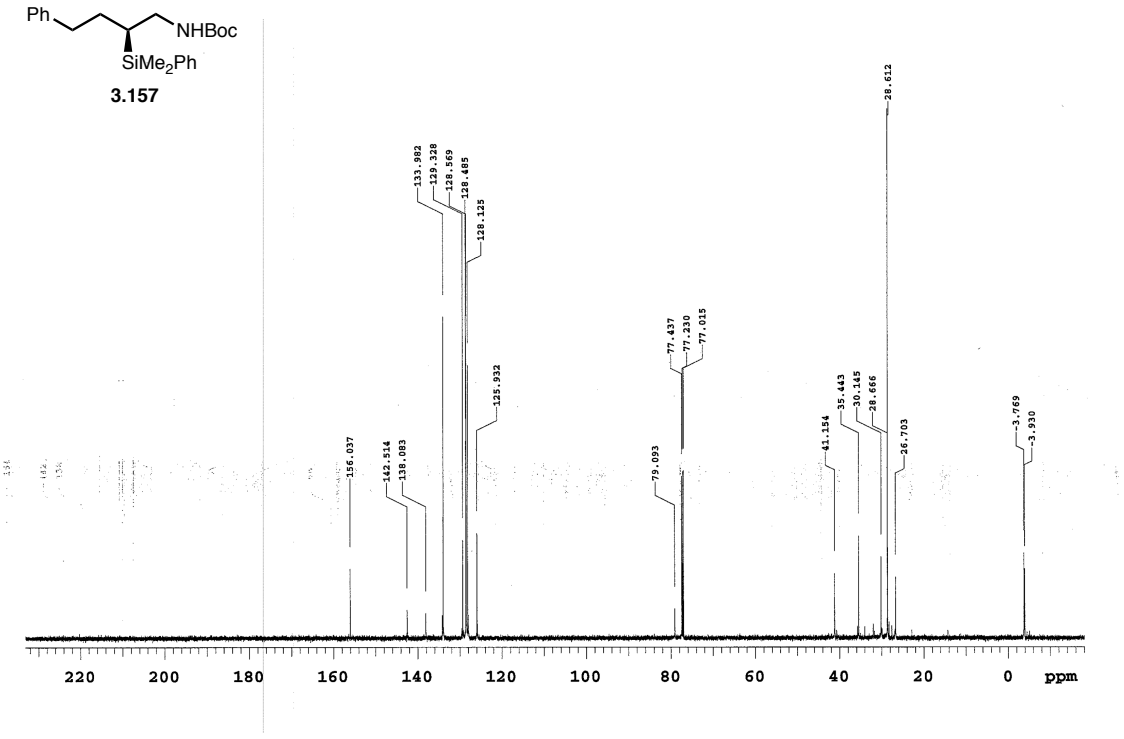

Ph
NHBoc
SiMe2Ph
3.155
7.513
7.501
7.392
7.380
7.375
7.363
7.351
7.268
7.258
7.244
7.178
7.167
7.132
7.120
4.254
4.236
3.424
3.420
2.745
2.962
2.556
2.552
1.817
1.811
1.807
1.643
1.570
1.552
1.448
1.271
0.347
0.332
10
9
8
7
6
5
4
3
2
1
ppm
1.76
2.74
2.14
2.64
0.77
0.81
0.98
1.00
1.02
1.31
9.29
5.93

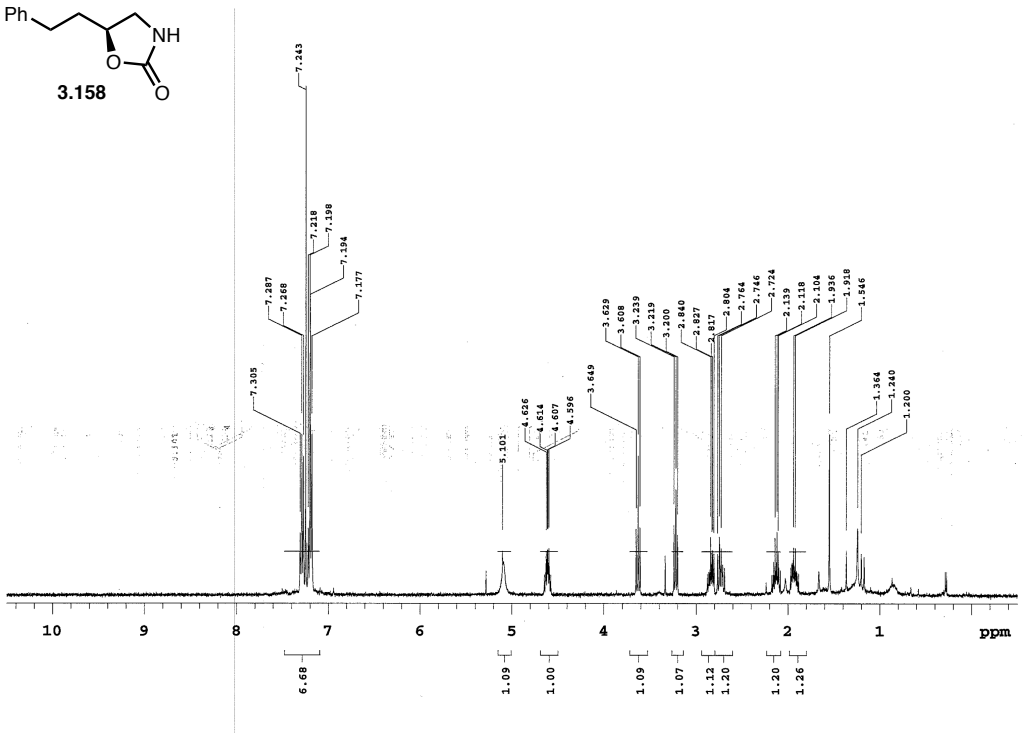

Ph
NHBoc
SiMe2Ph
3.155
134.335
129.597
128.631
128.500
128.148
125.909
156.420
142.491
136.389
77.437
77.222
77.015
79.147
34.009
28.635
34.047
40.747
28.512
4.436
-5.042
220
200
180
160
140
120
100
80
60
40
20
0
ppm

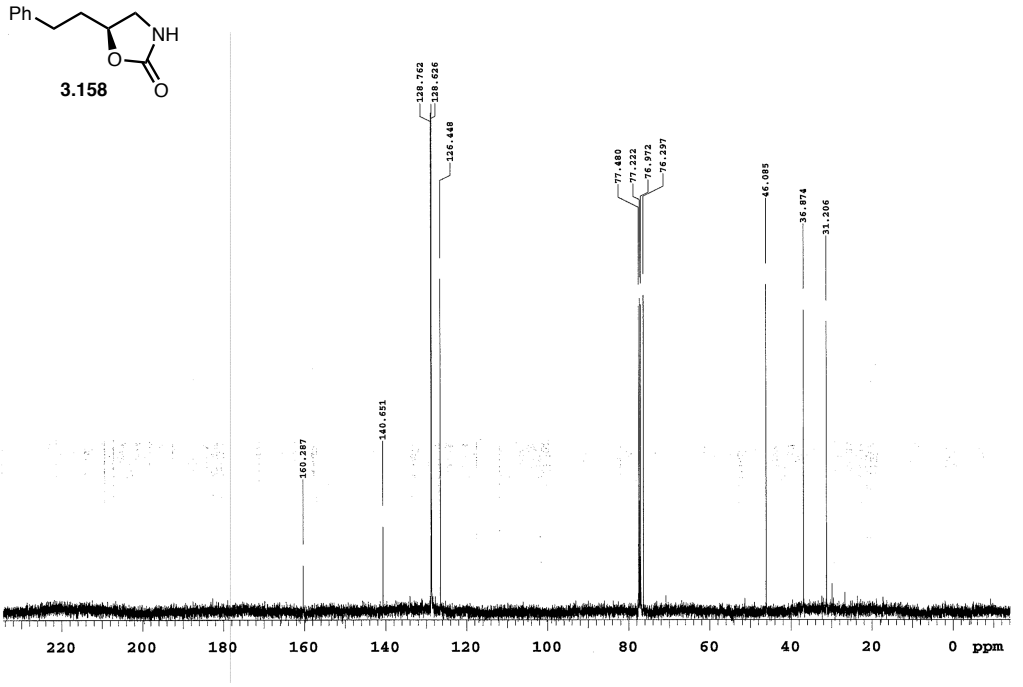

Ph
Bpin
SiMe2Ph
3.156
7.535
7.531
7.525
7.523
7.520
7.518
7.516
7.353
7.347
7.343
7.337
7.333
7.328
7.326
7.260
7.258
7.255
7.243
7.229
7.169
7.154
7.140
7.100
7.086
2.664
2.661
2.654
2.651
2.637
2.628
2.501
2.490
2.478
2.475
2.467
2.451
1.799
1.775
1.771
1.761
1.749
1.571
1.567
1.561
1.538
1.277
1.262
1.246
1.241
1.219
1.213
1.208
1.203
1.031
1.019
0.999
0.987
0.854
0.837
0.821
0.805
0.324
0.319
0.315
0.311
0.299
0.294
10
9
8
7
6
5
4
3
2
1
ppm
1.91
2.93
2.34
0.95
1.97
1.03
1.08
1.10
1.37
13.93
1.00
1.25
6.35

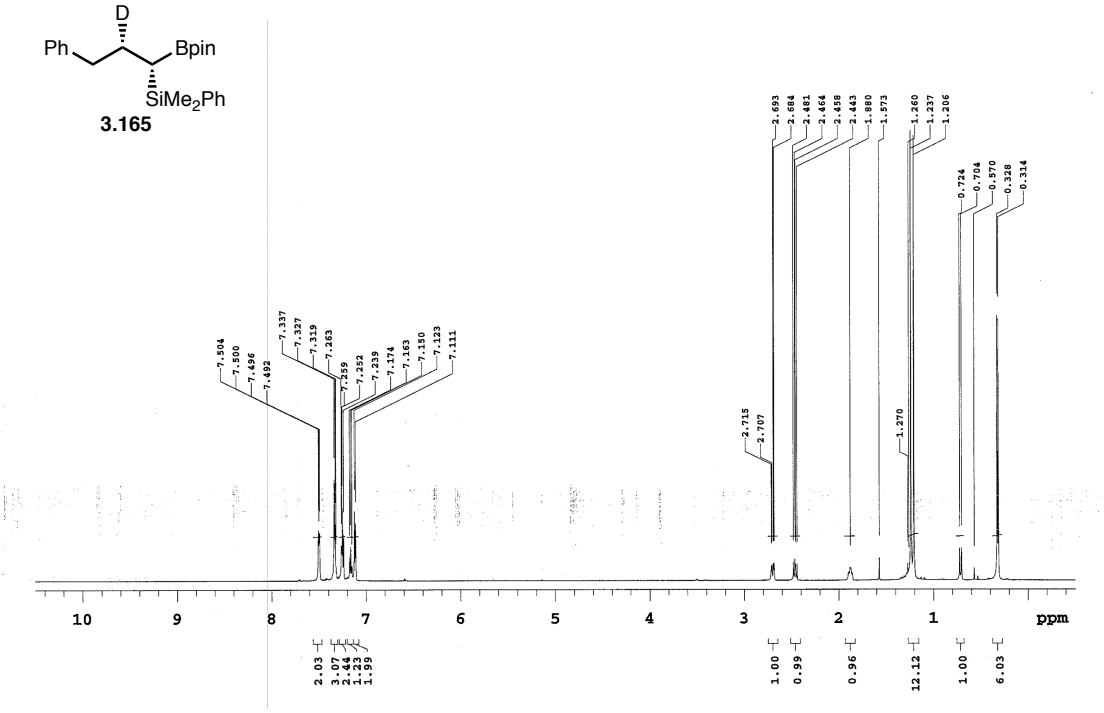

Ph
Bpin
SiMe2Ph
3.156
143.194
138.862
134.089
128.710
128.353
128.179
127.617
125.478
83.012
77.276
77.026
76.768
35.638
34.909
25.046
24.818
20.236
-3.930
-4.529
220
200
180
160
140
120
100
80
60
40
20
0
ppm

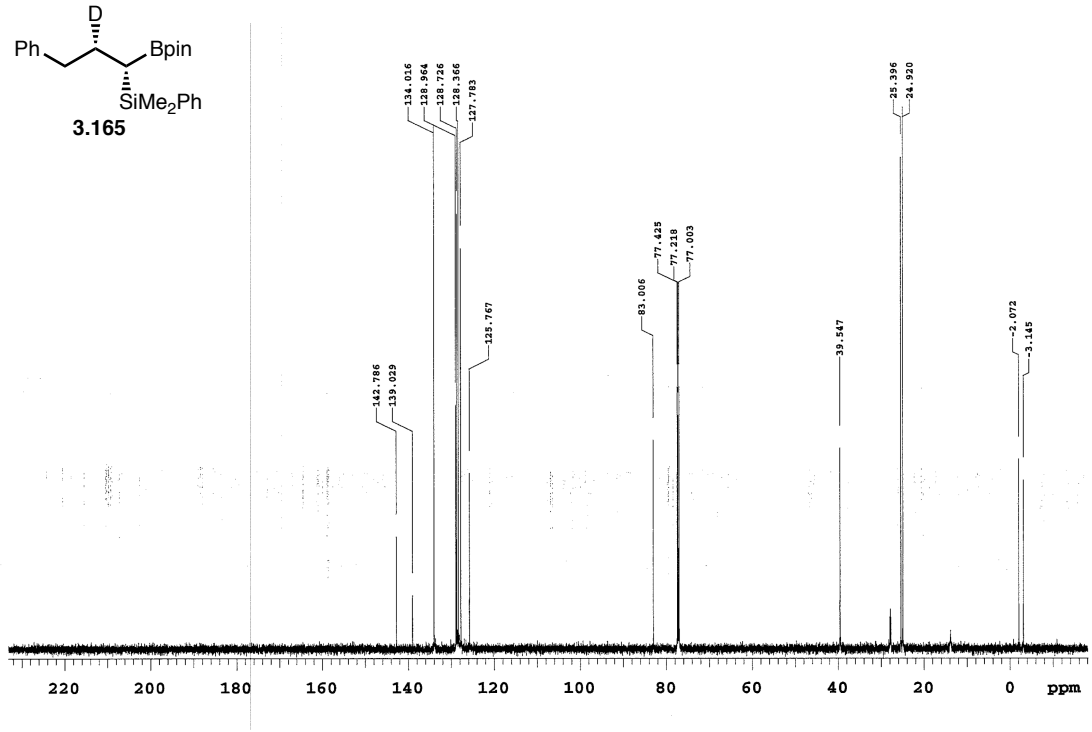

Ph
NHBoc
SiMe2Ph
3.157
7.519
7.515
7.511
7.507
7.501
7.384
7.381
7.373
7.370
7.364
7.361
7.279
7.276
7.264
7.249
7.195
7.180
7.165
7.104
7.090
4.295
3.349
3.338
3.333
3.322
3.311
3.297
2.666
2.662
2.655
2.645
2.634
2.566
2.558
2.552
2.545
1.812
1.806
1.801
1.796
1.793
1.784
1.775
1.772
1.678
1.653
1.546
1.494
1.486
1.471
1.455
1.445
1.295
1.286
1.282
1.126
1.121
1.115
1.111
1.105
1.100
1.095
0.367
0.355
0.347
0.341
0.325
10
9
8
7
6
5
4
3
2
1
ppm
2.18
2.20
2.27
1.16
2.15
0.91
1.99
1.05
1.25
1.20
1.46
10.72
1.00
6.76


Ph
NHBoc
SiMe2Ph
3.157
133.982
129.328
128.569
128.485
128.125
125.932
156.037
142.514
138.083
79.093
77.437
77.230
77.015
41.154
35.443
30.145
28.666
28.612
16.703
3.769
-3.930
220
200
180
160
140
120
100
80
60
40
20
0
ppm

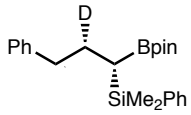

Ph
NH
O
O
3.158
7.305
7.287
7.268
7.243
7.218
7.198
7.194
7.177
5.101
4.626
4.614
4.607
4.596
3.649
3.629
3.608
3.239
3.219
3.200
2.840
2.827
2.817
2.804
2.764
2.746
2.724
2.139
2.118
2.104
1.936
1.918
1.546
1.364
1.240
1.200
10
9
8
7
6
5
4
3
2
1
ppm
6.68
1.09
1.00
1.09
1.07
1.12
1.20
1.20
1.26


Ph
NH
O
O
3.158
160.287
140.651
128.762
128.626
126.448
77.480
77.222
76.972
76.297
46.085
36.974
31.206
220
200
180
160
140
120
100
80
60
40
20
0
ppm

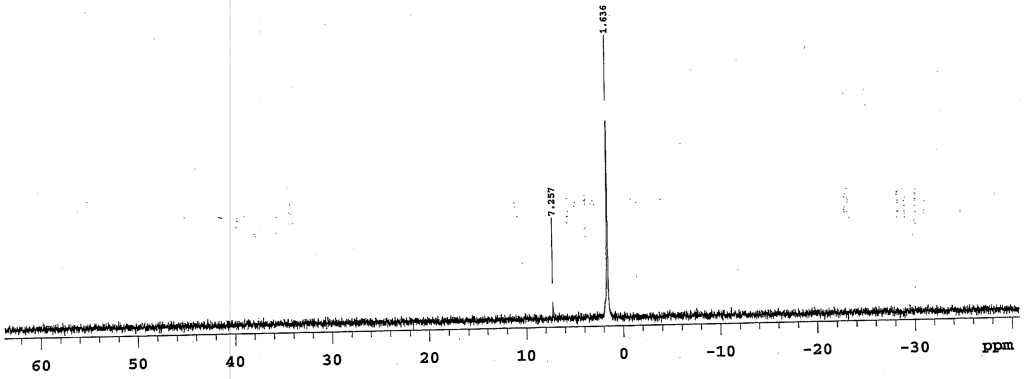

D
Ph
Bpin
SiMe2Ph
3.165
7.504
7.500
7.496
7.492
7.337
7.327
7.319
7.263
7.259
7.252
7.239
7.174
7.163
7.150
7.123
7.111
2.715
2.707
2.693
2.684
2.481
2.464
2.458
2.443
1.880
1.573
1.270
1.260
1.237
1.206
0.724
0.704
0.570
0.328
0.314
10
9
8
7
6
5
4
3
2
1
ppm
2.03
3.07
2.44
1.23
1.99
1.00
0.99
0.96
12.12
1.00
6.03

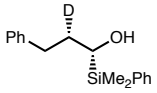

D
Ph
Bpin
SiMe2Ph
3.165
134.016
128.964
128.726
128.366
127.783
142.786
139.029
135.767
83.006
77.425
77.218
77.003
39.547
25.396
24.920
-2.072
-3.145
220
200
180
160
140
120
100
80
60
40
20
0
ppm

^{2}H-NMR

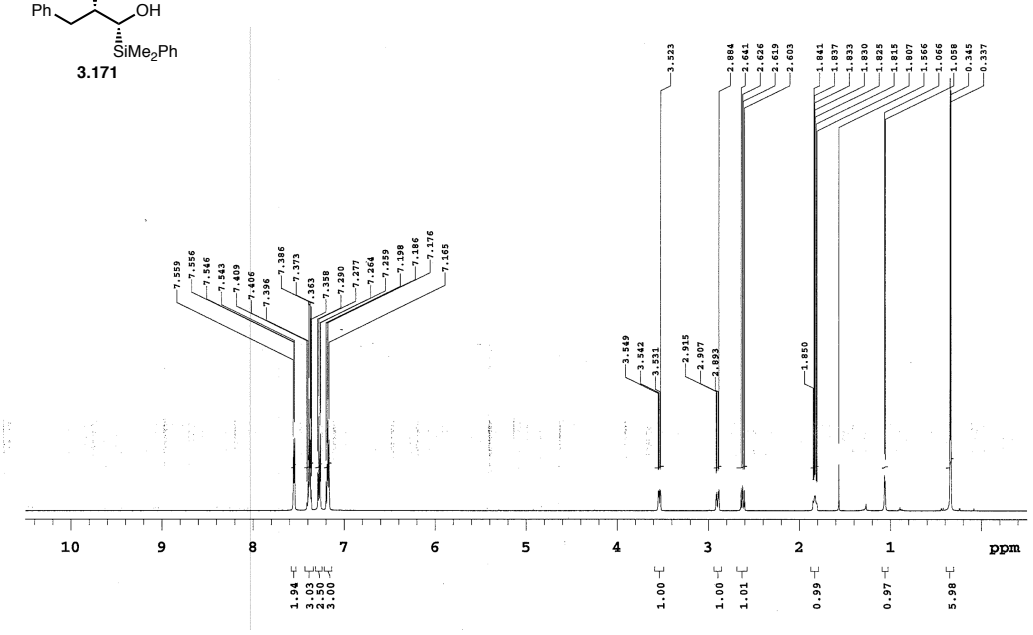


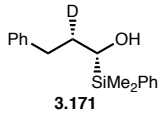
3.165





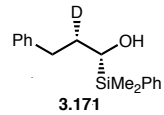
3.171



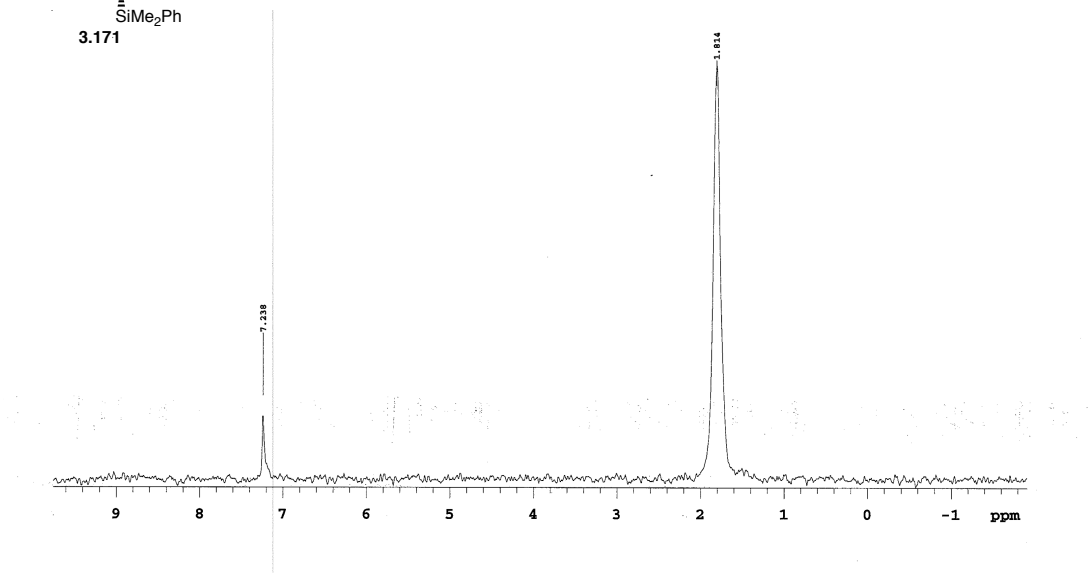


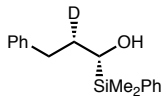
3.171

^{2}H-NMR

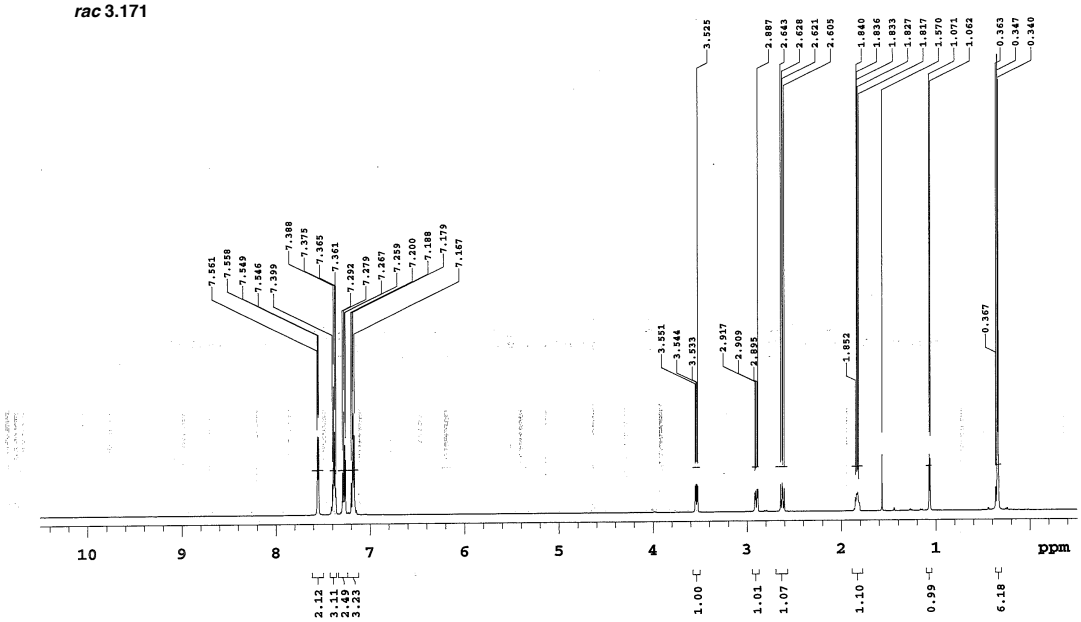


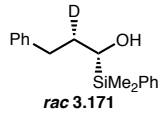
3.171



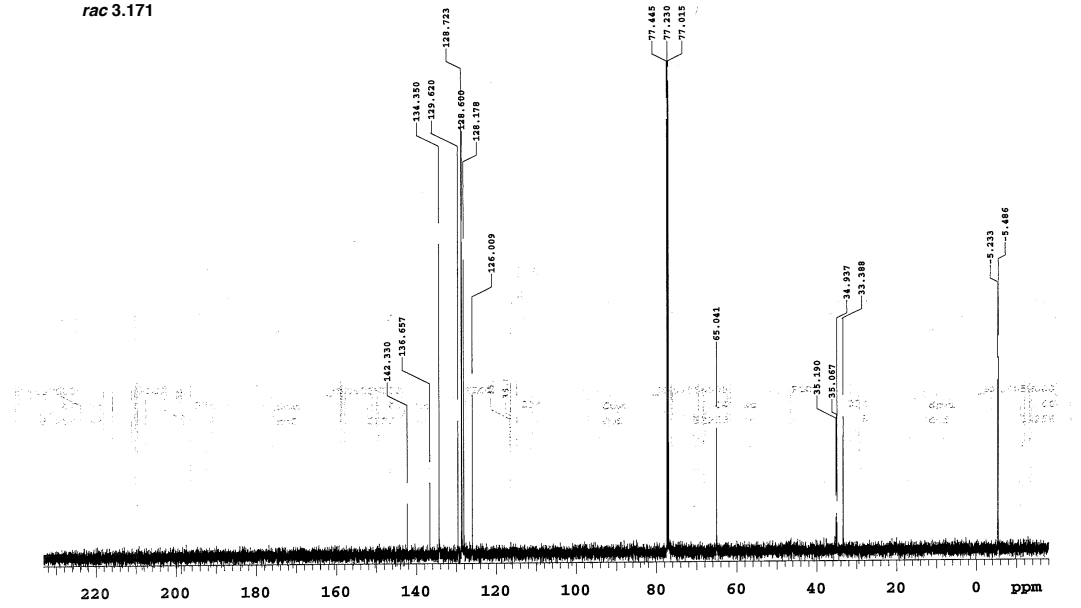


***rac* 3.171**

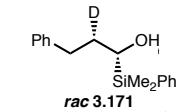




***rac* 3.171**

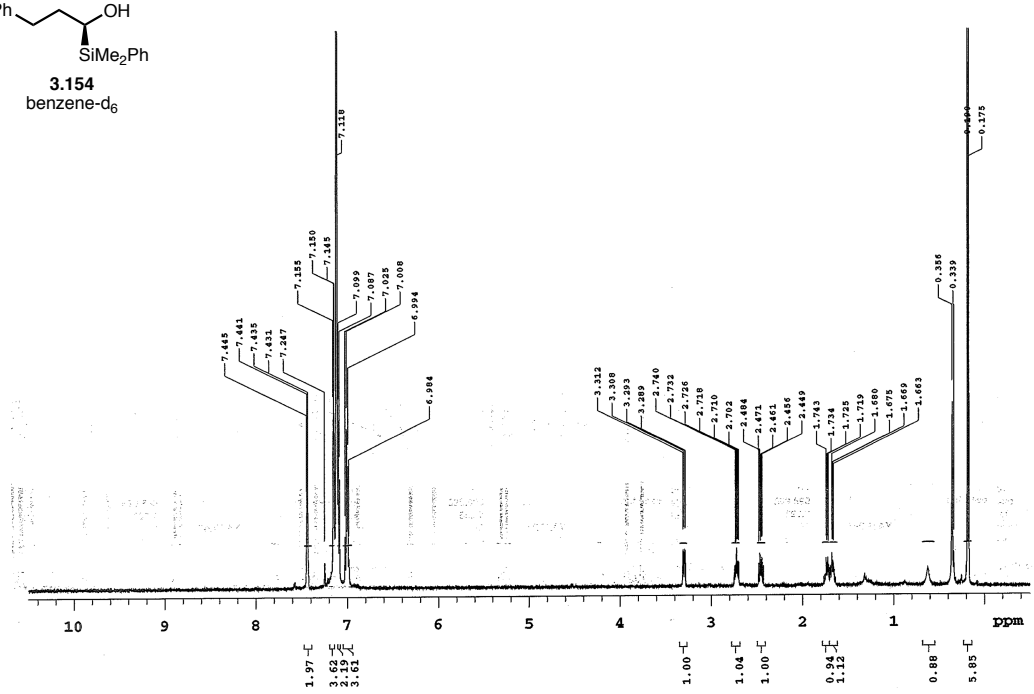


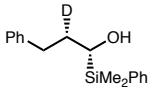
^{2}H-NMR



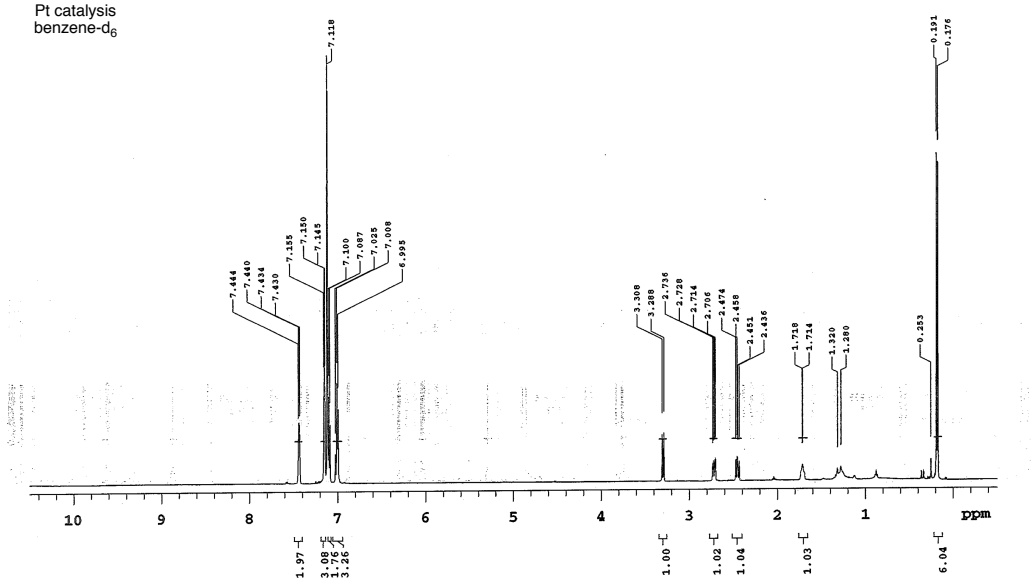
***rac* 3.171**

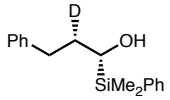
3.154
benzene-d_6





***ent* - 3.171**
Pt catalysis
benzene-d_6





***rac* 3.171**
BD_3 deuteroboration
benzene-d_6