# Asymmetric Carbon-Carbon Bond Formation Via 3,3'-Reductive Elimination of Allyl Palladium Complexes

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# ASYMMETRIC CARBON-CARBON BOND FORMATION *VIA* 3,3′-REDUCTIVE ELIMINATION OF ALLYL PALLADIUM COMPLEXES

a dissertation

by

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ABSTRACT

LAURA A. BROZEK: Asymmetric Carbon-Carbon Bond Formation *via* 3,3′-Reductive Elimination of Allyl Palladium Complexes

(Under the direction of Professor James P. Morken)

This dissertation describes the development of two enantioselective methods of carbon-carbon bond formation. Chapter one discusses the development of an enantioselective Pd(0)-catalyzed conjugate addition of allylboronic acid pinacol ester to $\alpha,\beta$-unsaturated methylidene ketones. Utilizing the same rationale for regio- and enantiocontrol as in the related enantioselective conjugate allylation of arylidene ketones, this method addresses the gap in technology by expanding the scope of the reaction to include alkyl-substituted enones. Chapter two examines the coupling of allyl electrophiles and allyl metal reagents. With computational insight into the reaction mechanism, a catalyst system was designed to control regioselectivity and enantioselectivity. Isotope labeling studies were carried out to probe the mechanism of the transformation. The reaction also proves to be diastereoselective when a substituted allyl boron reagent is employed.

# ACKNOWLEDGMENTS

For my scientific education, I am indebted to many faculty members who have shaped my academic growth. In particular, I am grateful for the guidance I have received from Professor Jim Morken. His thoughtful insight into reaction development is always paired with an excitability and curiosity that has continually energized my research. I have constantly been inspired by and impressed with the other faculty members in the Boston College chemistry department. I have shared helpful chalkboard discussions with my committee members Professor Lawrence Scott and Professor Kian Tan, and I am grateful for their tutelage. I am thankful, also, for the quality of instruction I received as an undergraduate student at UC Berkeley. In particular, Professor Dean Toste and Dr. Ahamindra Jain were formative influences in my pursuit of organic chemistry research.

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Ac: acetyl

BINAP: 2,2′-bis(diphenylphosphino)-1,1′-binapthyl

BIPHEP: 2,2′-bis(diphenylphosphino)-6,6′-dimethoxy-1,1′-biphenyl

Bn: benzyl

Boc: *tert*-butoxycarbonyl

$Boc_2O$: di-*tert*-butyldicarbonate

$B_2(pin)_2$: bis(pinacolato) diboron

cod: cyclooctadiene

Cp: cyclopentadienyl

Cy: cyclohexyl

dba: dibenzylidene acetone

DCE: dichloroethane

DCM: dichloromethane

DFT: density functional theory

DIOP: 4,5-bis(diphenylphosphinomethyl)-2,2-dimethyl-1,3-dioxolane

DMF: dimethylformamide

DMS: dimethylsulfide

dppb: 1,4-bis(diphenylphosphino)butane

dppbenzene: 1,2-bis(diphenylphosphino) benzene

dppe: 1,2-bis(diphenylphosphino)ethane

dppf:1,1′-bis(diphenylphosphino)ferrocene

dppp: 1,3-bis(diphenylphosphino)propane

dr: diastereomeric ratio

DTBM: di-*tert*-butylmethyl

Duphos: 1,2-bis(phospholano)benzene

eq: equation

equiv: equivalent(s)

er: enantiomeric ratio

EtOAc: ethyl acetate

GLC: gas liquid chromatography

h: hour(s)

HG2: Hoveyda-Grubbs second generation catalyst

HPLC: high performance liquid chromatography

kcal: kilocalorie

L: ligand

LG: leaving group

M: metal

NMO: *N*-methylmorpholino *N*-oxide

NMR: nuclear magnetic resonance

phthal: phthalimide

pin: pinacol

List of Abbreviations

rt: room temperature

SegPhos: 5,5′-bis(diphenylphosphino)-
4,4′-bi-1,3-benzodioxole

SFC: supercritical fluid chromatography

TBDPS: *tert*-butyldiphenylsilyl

TBS: *tert*-butyldimethylsilyl

Tf: trifluoromethanesulfonyl

TFA: trifluoroacetyl

THF: tetrahydrofuran

TMS: trimethylsilyl

TPAP: tetrapropylammonium perruthenate

y: yield

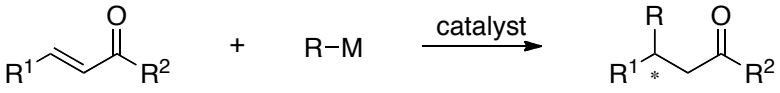
## Chapter 1

## The Palladium-Catalyzed Enantioselective Conjugate Allylation of α,β-Unsaturated Methylidene Ketones

### I. Introduction

The conjugate addition of organometallic reagents to α,β-unsaturated carbonyl compounds is a valuable transformation within organic synthesis. Such methods not only construct a carbon-carbon bond, but also have the capacity to establish a stereogenic center (Scheme 1.1).

**Scheme 1.1: General Catalyzed Conjugate Addition**




Due to the significant synthetic utility of such an asymmetric process, many research groups have studied the metal-catalyzed enantioselective 1,4-addition of organometallic reagents to α,β-unsaturated carbonyl electrophiles.[1,2] Conjugate

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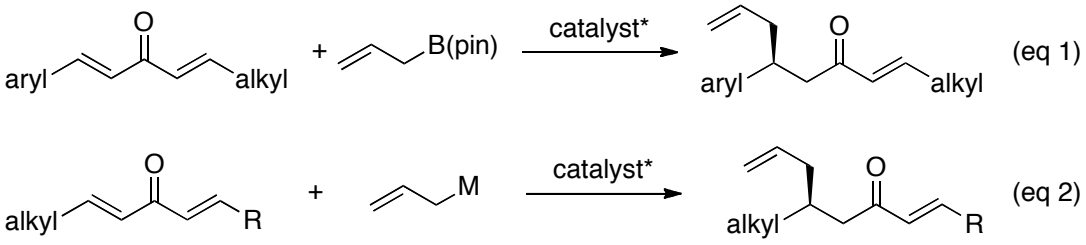
[1] (a) Tomioka, K.; Nagaoka, Y. In *Comprehensive Asymmetric Catalysis*; Jacobsen, E. N.; Pfaltz, A.; Yamamoto, H., Eds.; Springer-Verlag: Berlin, 1999; Vol. 3, p 1105. (b) Lopez, F.; Feringa, B. L. In *Asymmetric Synthesis - The Essentials*; Christmann, M.; Bräse, S., Eds.; Wiley-VCH: Weinheim, 2007, p 78. (c) Ji, J.-X.; Chan, A. S. C. In *Catalytic Asymmetric Synthesis*; Ojima, I., Ed.; Wiley: Hoboken, N. J., 2010; p 439.

[2] Reviews: (a) Rossiter, B. E.; Swingle, N. M. *Chem. Rev*. **1992**, *92*, 771. (b) Sibi, M. P.; Manyem, S. *Tetrahedron* **2000**, *56*, 8033. (c) Christoffers, J.; Koripelly, G.; Rosiak, A.; Rössle, M. *Synthesis* **2007**, 1279.

addition reactions utilizing vinyl, aryl, and alkyl-substituted organometal compounds are well developed. However, the use of allylmetal nucleophiles in enantioselective conjugate allylation reactions has proven to be particularly challenging,[3] and is limited to few examples.

In order to overcome this deficiency in synthetic methodolgy, the development of methods for asymmetric conjugate allylation is an area of study that deserves attention. These reactions are powerful tools for organic synthesis, owing largely to the malleability of the alkene functional group. Previous studies published by Morken and coworkers explored the transition metal-catalyzed enantioselective 1,4-addition of an allyl boron reagent to non-symmetric arylidene alkylidene ketones (Scheme 1.2, equation 1).[4] This method generates a homoallylic stereocenter in high yield and with excellent levels of enantioenrichment. Furthermore, the process proved to be chemoselective for allylation of the aryl-substituted enone.

**Scheme 1.2: Catalytic Asymmetric Conjugate Allylation**




[3] For a discussion of the challenges associated with allylcuprates, see: Nakamura, E.; Mori, S. *Angew. Chem. Int. Ed.* **2000**, *39*, 3750.

[4] (a) Sieber, J. D.; Liu, S.; Morken, J. P. *J. Am. Chem. Soc.* **2007**, *129*, 2214. (b) Sieber, J. D.; Morken, J. P. *J. Am. Chem. Soc.* **2008**, *130*, 4978.

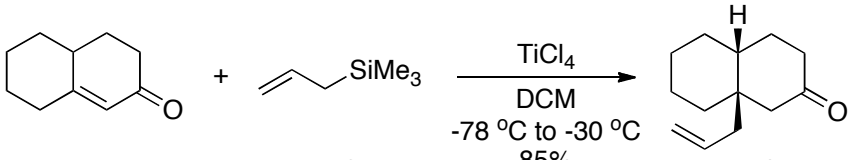
Though this transformation is valuable, it does not permit a reversal of chemoselectivity for addition at the alkylidene carbon. Therefore, the development of a catalytic, asymmetric reaction that would effect the chemoselective conjugate allylation of an alkyl-substituted enone was investigated (Scheme 1.2, equation 2). The results are presented herein.

## II. Background

### A. Non-Enantioselective 1,4-Allylation Reactions

A 1977 publication by Hosomi and Sakurai disclosed the earliest example of the 1,4-selective addition of allyltrimethylsilane **1.2** to cyclic and acyclic $\alpha,\beta$-unsaturated enones.[5] The reaction utilized a stoichiometric quantity of $TiCl_4$ as a Lewis acid to promote conjugate allylation, and was effective for the stereoselective installation of an angular allyl group into a fused cyclic enone (Scheme 1.3).

**Scheme 1.3: Ti-Mediated Allylsilane Conjugate Addition**

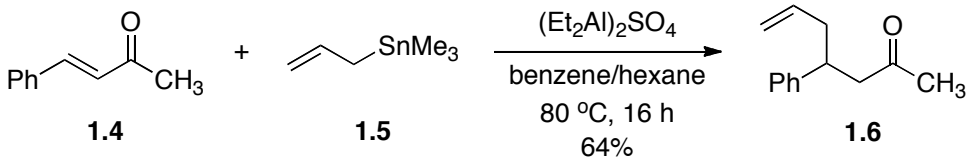



**1.1** **1.2** **1.3**

[5] Hosomi, A.; Sakurai, H. *J. Am. Chem. Soc.* **1977**, *99*, 1673.

Allyltrimethylstannane **1.5** has also been an effective conjugate allylation reagent. Though stoichiometric Lewis acid $(Et_2Al)_2SO_4$ promotes 1,2-addition of **1.5** to aldehydes, Sakurai and co-workers demonstrated that selective 1,4-allylation is observed with enone substrates (Scheme 1.4).[6]

**Scheme 1.4: Al-Mediated Allylstannane Conjugate Addition**




Although alkyl- and arylcuprates are typically reagents of choice to effect the selective 1,4-nucleophilic addition to an $\alpha,\beta$-unsaturated carbonyl compound, the selectivity of allylcuprates is less reliable.[7] In order to probe this selectivity issue, Lipshutz and coworkers undertook spectroscopic studies of several allylic copper reagents, and this study suggested their $\sigma$-bound nature.[8] With these data, the reactivity of such reagents could be attenuated to achieve a selective transformation. Lower order allyl copper reagents, compounds that are less reactive than a copper -*ate* complex, underwent efficient and selective 1,4-addition to enone substrates with stoichiometric chlorotrimethylsilane (TMS-Cl) as a Lewic acidic additive (Scheme 1.5). The TMS-Cl,

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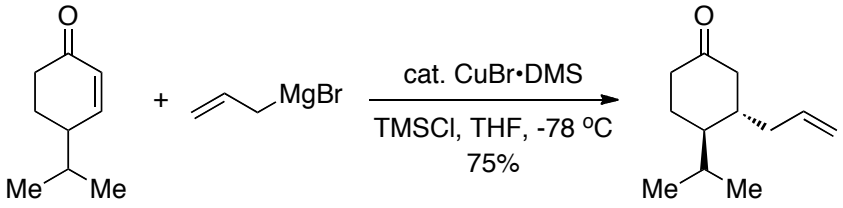
[6] Hosomi, A.; Iguchi, H.; Endo, M.; Sakurai, H. *Chem. Lett.* **1979**, *8*, 977.

[7] (a) House, H. O.; Fischer Jr., W. F. *J. Org. Chem.* **1969**, *34*, 3615. (b) Posner, G. H. *Org. React.* **1972**, *19*, 1.

[8] (a) Lipshutz, B. H.; Ellsworth, E. L.; Dimock, S. H.; Smith, R. A. J. *J. Am. Chem. Soc.* **1990**, *112*, 4404. (b) Lipshutz, B. H.; Hackmann, C. *J. Org. Chem.* **1994**, 7437.

which activates the enone to accelerate conjugate addition, is necessary for a selective process; in its absence, both reaction conversion and selectivity for 1,4-addition is low.

**Scheme 1.5: Allylcuprate Conjugate Addition**



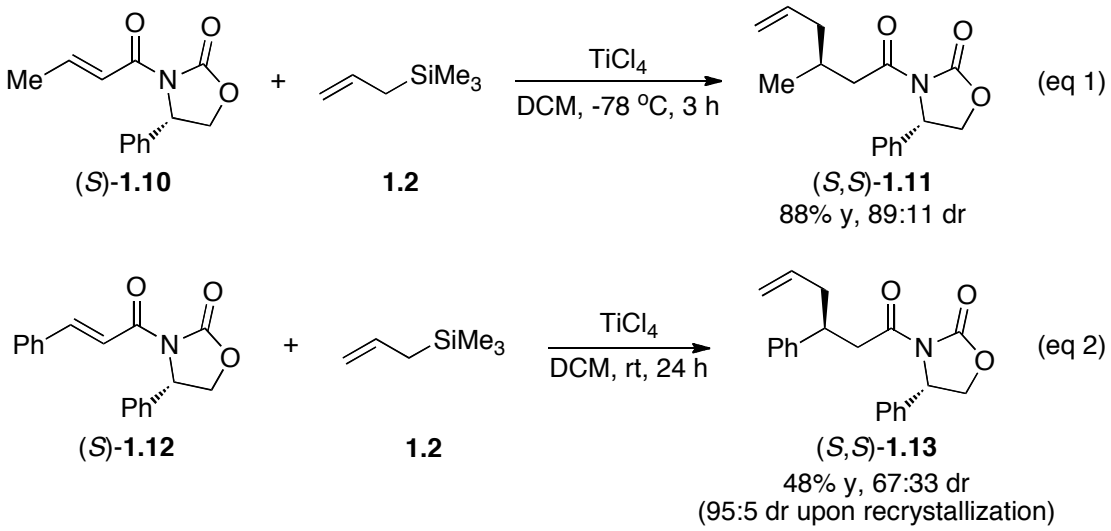

**1.7** **1.8** **1.9**

**B. Auxiliary-Controlled Conjugate Allylation Reactions**

Until recently, stereocontrol in 1,4-additions of allyl metal nucleophiles to $\alpha,\beta$-unsaturated carbonyl compounds was limited to the use of chiral auxiliaries. In particular, a number of research groups have employed the Evans oxazolidinone in conjugate allylation reactions. In 1992, Wu and coworkers demonstrated that alkyl- and aryl-substituted enantioenriched amides **1.10** and **1.12** undergo Hosomi-Sakurai conjugate allylation (Scheme 1.6).[9] The $TiCl_4$ Lewis acid serves to chelate both the enone oxygen and the carbonyl of the Evans auxiliary to enable a selective allylation. The arylidene substrate **1.12** reacts with lower diastereoselectivity (equation 2), but this may be improved upon recrystallization. Finally, the auxiliary may be cleaved with LiOH to furnish the enantioenriched carboxylic acid.

[9] Wu, M.-J.; Wu, C.-C.; Lee, P.-C. *Tetrahedron Lett.* **1992**, *33*, 2547.

**Scheme 1.6: Diastereoselective Hosomi-Sakurai Conjugate Addition**




The Williams group has also employed the Evans oxazolidinone as a chiral auxiliary for the asymmetric addition of both allylstannanes[10] and allyl copper reagents[11] to $\alpha,\beta$-unsaturated carbonyl electrophiles (Scheme 1.7). Reaction of the allyl copper reagent, formed *in situ* from the corresponding Grignard reagent **1.8** and copper (I) bromide, utilizes Lewis acid $BF_3 \cdot OEt_2$ to generate (*S*,*S*)-**1.11** (equation 1). The stereocontrol element in the reaction is a magnesium chelate structure, which restricts the conformation of the substrate in the allylation event. Notably, the use of allyltributylstannane **1.14** reverses the facial selectivity for the allylation, and the opposite diastereomer is obtained with the same chiral auxiliary (equation 2).

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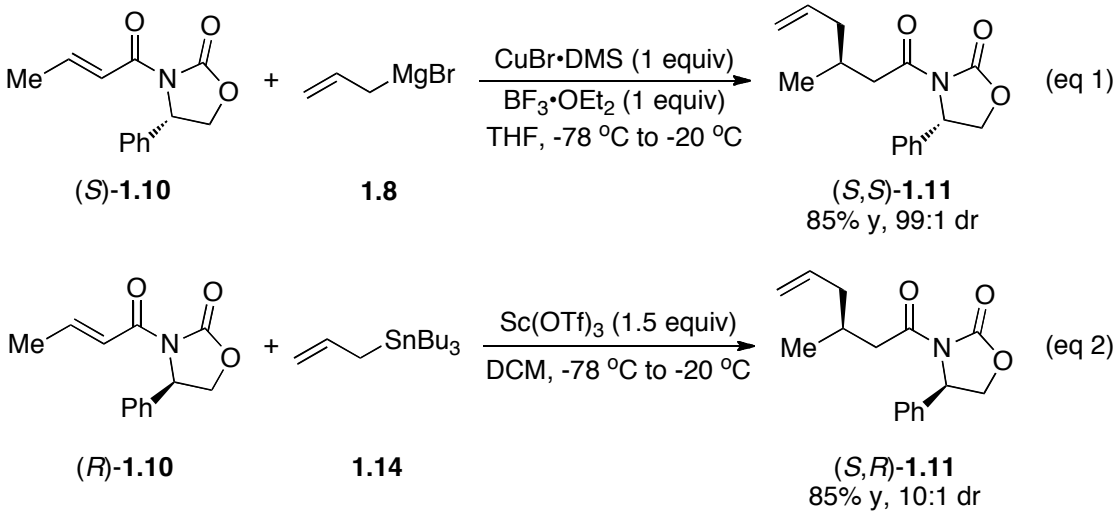
[10] Williams, D. R.; Mullins, R. J.; Miller, N. A. *Chem. Commun.* **2003**, 2220.

[11] Williams, D. R.; Kissel, W. S.; Li, J. J. *Tetrahedron Lett.* **1998**, *39*, 8593.

**Scheme 1.7: Diastereoselective Allyl Copper and Allylstannane Conjugate Additions**




### C. Catalytic Asymmetric Conjugate Allylation Reactions

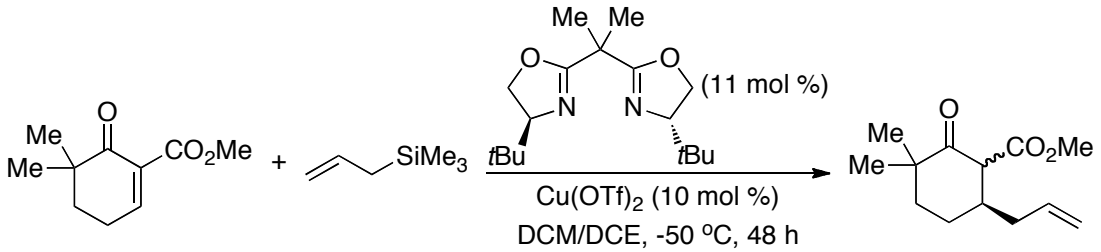
Though the use of a cleavable chiral auxiliary provides a clever route to the enantioenriched 1,4-allylation adduct, there are only a small number of asymmetric methods that achieve this transformation with stereocontrol by a catalyst. In fact, when this alkylidene conjugate allylation project was under development, there were only two catalytic asymmetric methods known in the literature.

In one of these methods, the Snapper group demonstrated the first example of an asymmetric, 1,4-selective Hosomi-Sakurai allylation reaction.[12] In the presence of a copper catalyst and an enantioenriched bis(oxazoline) ligand, the air- and moisture-tolerant allyltrimethylsilane **1.2** undergoes efficient conjugate allylation to cyclic unsaturated ketoesters in excellent yields and enantioselectivities (Scheme 1.8). The

[12] Shizuka, M.; Snapper, M. L. *Angew. Chem. Int. Ed.* **2008**, *47*, 5049.

method was effectively applied to sterically hindered substrates, as well as cyclic ketoesters of several ring sizes. Notably, the α-methyl ester may be readily decarboxylated to afford the enantioenriched β-substituted cyclic ketone.

**Scheme 1.8: Asymmetric Hosomi-Sakurai Conjugate Allylation**

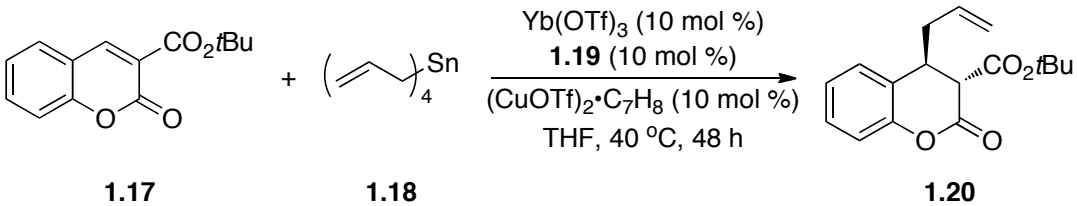



**1.15** **1.2** **1.16**
65% y, 99:1 er

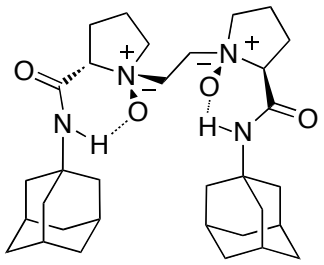
More recent work, published shortly after ours, examined the use of other allyl metal reagents in asymmetric catalytic 1,4-addition reactions. Feng and coworkers applied a dual-activation strategy to the conjugate addition of tetraallylstannane to coumarin derivatives (Scheme 1.9).[13] This reaction is promoted by a ytterbium Lewis acid and a chiral bis(amineoxide) ligand. In this transformation, the chiral bis(amineoxide)-Yb(III) complex is responsible for activating the coumarin while the allylstannane transmetallates to the copper co-catalyst to form the active nucleophile.

[13] Kuang, Y.; Liu, X.; Chang, L.; Wang, M.; Lin, L.; Feng, X. *Org. Lett.* **2011**, *13*, 3814.

**Scheme 1.9: Conjugate Allylation of Coumarins**




**1.17** **1.18** **1.20**
99% y, 96:4 er

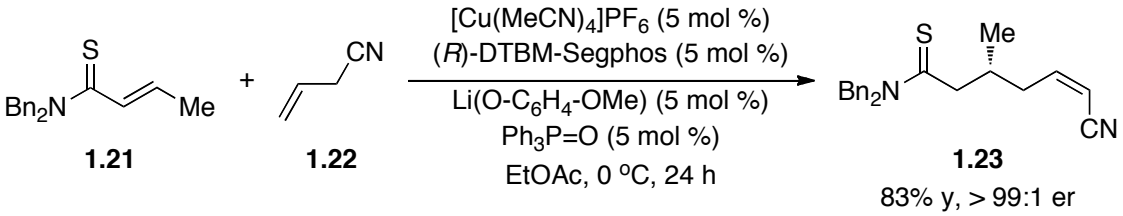



**1.19**

In an aligned study, Masakatsu Shibasaki and coworkers studied a Cu-catalyzed asymmetric conjugate addition of allyl cyanide to α,β-unsaturated thioamides under proton transfer conditions (Scheme 1.10).[14] The reaction operates under a system of soft Lewis acid/hard Brønsted base cooperative catalysis. An aryloxide Brønsted base facilitates the deprotonation of allyl cyanide. The chiral bidentate phosphine-copper complex, a soft Lewis acid, activates the soft Lewis basic allyl cyanide pronucleophile, while concomitantly activating the thioamide electrophile for conjugate allylation. Products are obtained with excellent yields and enantioselectivities. Notably, both β-aryl and alkyl substituted thioesters undergo the allylation reaction efficiently.

[14] Yanagida, Y.; Yazaki, R.; Kumagai, N.; Shibasaki, M. *Angew. Chem. Int. Ed.* **2011**, *50*, 7910.

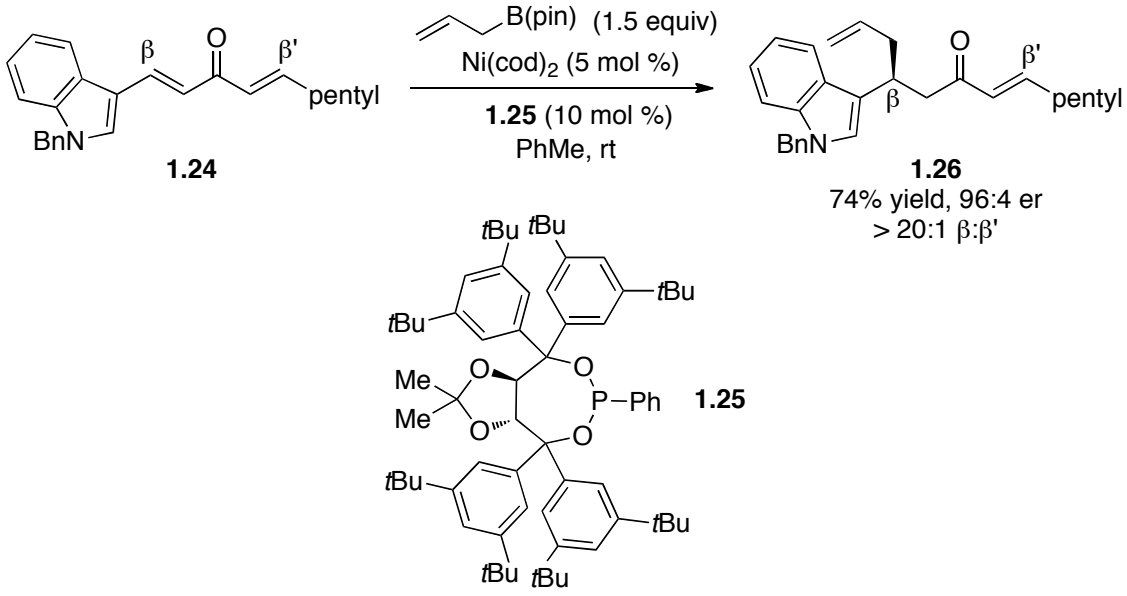
**Scheme 1.10: Conjugate Addition of Allyl Cyanide to Thioamides**




**D. Catalytic Asymmetric Conjugate Allylation With Allylboron Reagents *via* 3,3′-Reductive Elimination**

Prior to these examples, a significant advancement in allylation chemistry, and the earliest known example of catalytic, asymmetric 1,4-allyl addition, was developed in our laboratory.[4] These studies examined the asymmetric conjugate addition of allylboronic acid pinacol ester [allylB(pin)] to non-symmetric arylidene alkylidene ketones catalyzed by Ni(0) and a TADDOL-derived phosphonite ligand (TADDOL = *trans*-4,5-bis(diphenylhydroxymethyl)-2,2-dimethyldioxolane) (Scheme 1.11). This transformation not only affords products in high yields and enantioselectivities, but also exhibits chemoselectivity, generally favoring allyl addition to the benzylic site.

**Scheme 1.11: Catalytic Enantioselective Allylboron Conjugate Addition**




The regioselective outcome of the conjugate allylation reaction may be understood by examination of the reaction mechanism. The proposed catalytic cycle (Scheme 1.12) has been substantiated by experimental evidence as well as DFT calculations. In the first step, the Ni(0) catalyst **I** binds to the less hindered alkylidene enone (versus the arylidene enone), presumably due to its relative steric accessibility, to form **II**. Consistent with findings published by MacKenzie[15] and subsequent work from Ogoshi and Kurosawa,[16] the Lewis acidic allylB(pin) activates the enone carbonyl, which facilitates the oxidative addition of the metal catalyst to the enone, forming oxygenated

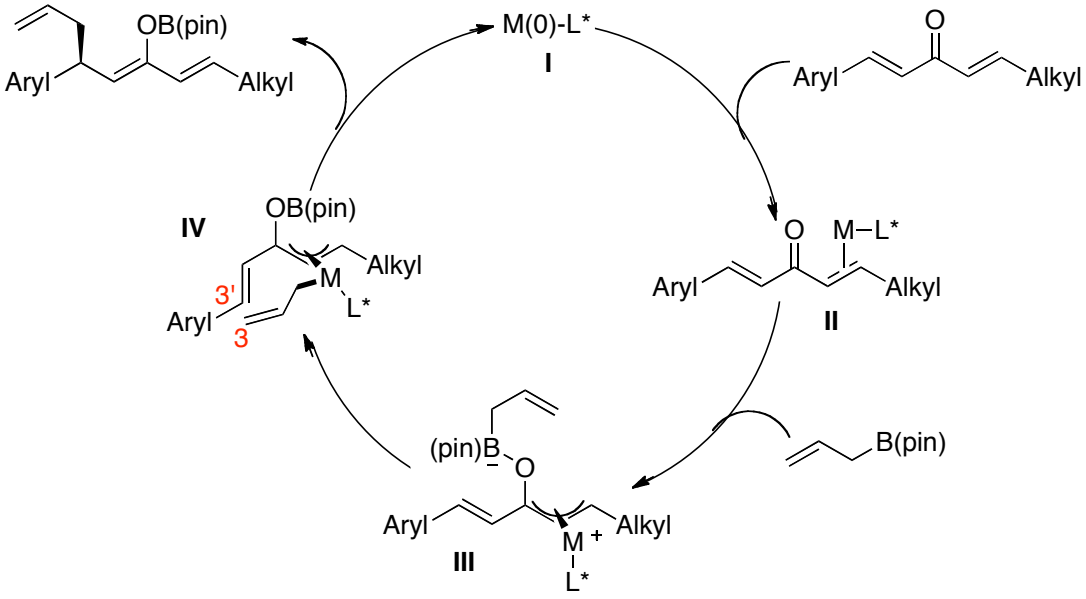
---

[15] For Ni(0) oxidative addition to α,β-unsaturated carbonyls, see: (a) Johnson, J. R.; Tully, P. S.; Mackenzie, P. B.; Sabat, M. *J. Am. Chem. Soc.* **1991**, *113*, 6172. (b) Grisso, B. A.; Johnson, J. R.; Mackenzie, P. B. *J. Am. Chem. Soc.* **1992**, *114*, 5160.

[16] For Pd(0) oxidative addition to α,β-unsaturated carbonyls, see: (a) Ogoshi, S.; Yoshida, T.; Nishida, T.; Morita, M.; Kurosawa, H. *J. Am. Chem. Soc.* **2001**, *123*, 1944. (b) Morita, M.; Inoue, K.; Ogoshi, S.; Kurosawa, H. *Organometallics* **2003**, *22*, 5468.

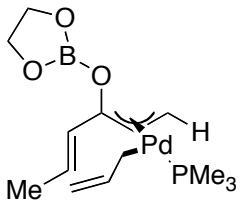
$\eta^3$-$\pi$-allyl complex **III**. Subsequent transmetallation of the allyl group from the boronate to Ni forms **IV**. This is followed by carbon-carbon bond formation by reductive coupling to furnish the boron enolate, which is protonated to the enone upon aqueous workup.

**Scheme 1.12: Catalytic Cycle of Conjugate Allylation**

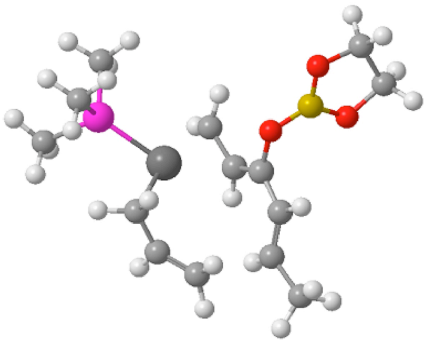



Importantly, these alkylidene arylidene enone substrates displayed enhanced reactivity in conjugate allylation in comparison to simple enones. Sieber and Morken posited that this was due to the energetics of the reductive elimination step. DFT calculations completed by Dr. Shubin Liu at University of North Carolina at Chapel Hill suggested that the carbon-carbon bond formation occurs between carbons 3 and 3′ of the allyl units (see **IV**). In fact, for simplified **1.27** (Figure 1.1), DFT calculations concluded that 3,3′-reductive elimination has a remarkably small activation barrier of 1.52 kcal/mol.

**Figure 1.1: Calculated Transition State Structure**




**1.27**



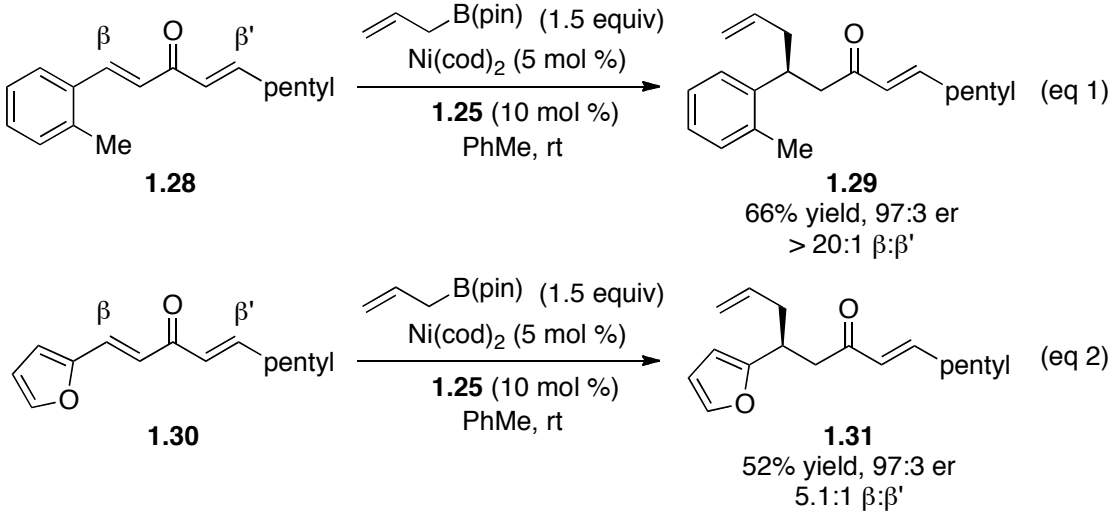
In this conjugate allylation, the alkylidene effectively serves as an activator for conjugate allylation to the arylidene enone. Though this process is very efficient for the generation of benzylic stereocenters, we wished to develop a method of complementary chemoselectivity for allyl boron addition at the alkylidene carbon. Utilizing our knowledge of reaction mechanism and reagent selectivity, we explored the catalytic asymmetric conjugate allylation of $\alpha,\beta$-unsaturated methylidene ketones.

## III. Development of a Pd-Catalyzed Enantioselective Conjugate Allylation of α,β-Unsaturated Methylidene Ketones[17]

### A. Reaction Development: Identification of an Optimal Catalyst System

Examination of the substrate scope in the conjugate allylation methodology developed by Sieber and Morken suggests that the steric size of the aryl group controls the chemoselectivity of the allylation reaction for the Ni(0)/TADDOL-derived phosphonite ligand system. For example, *ortho*-methyl substituted **1.28** gives a highly chemoselective transformation with allylation at the arylidene carbon (Scheme 1.13, equation 1). In contrast, 2-furyl substituted **1.30** affords only moderate chemoselection (equation 2).

**Scheme 1.13: Chemoselectivity in Conjugate Allylation**




**1.28**

**1.29**
66% yield, 97:3 er
> 20:1 β:β'

**1.30**

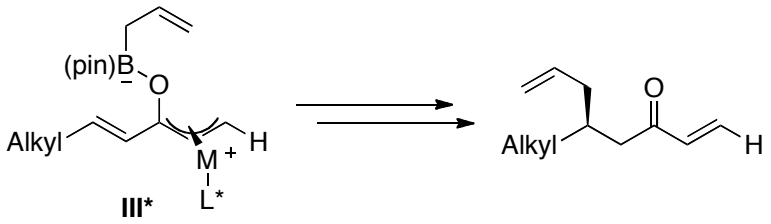
**1.31**
52% yield, 97:3 er
5.1:1 β:β'

[17] Brozek, L. A.; Sieber, J. D.; Morken, J. P. *Org. Lett.* **2011**, *13*, 995.

The diminished chemoselectivity for substrates with relatively small arenes is a result of comparable Ni π-allyl complex stabilities at the arylidene and alkylidene sites. Generally speaking, with a sterically demanding aryl group, the energy difference between the regioisomeric complexes strongly biases π-allyl complex formation to occur at the less hindered alkylidene site, resulting in regioselective allylation at the arylidene carbon.

Given the contrasteric nature of regioselectivity in the conjugate allylation reaction, it was reasoned that replacing an aryl group with a proton in the substrate (Scheme 1.14, **III***) would grant chemoselective access to the alkylidene allylation product (Scheme 1.14).

**Scheme 1.14: Modification of Conjugate Allylation Substrate**




At the time I joined the project, a Morken group graduate student, Joshua Sieber, had conducted preliminary investigations into the conjugate allylation of α,β-unsaturated methylidene ketone **1.32**.[18] He discovered that $Pd_2(dba)_3$ and TADDOL-derived phosphoramidites were a competent catalyst system for chemoselective asymmetric

[18] Sieber, J. D. *The Tandem Catalytic Asymmetric Allene Diboration/Imine Allylation and The Asymmetric Transition-Metal-Catalyzed Conjugate Allylation of Activated Enones.* Doctoral Dissertation, Boston College, Chestnut Hill, MA, 2008.

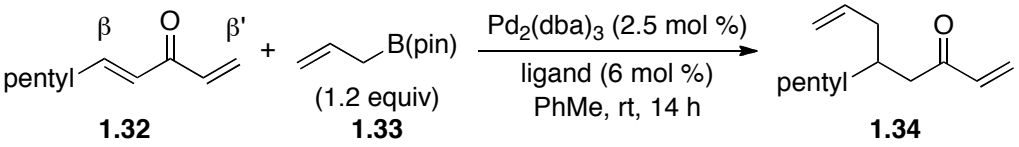
conjugate allylation. In particular, phosphoramidites with sterically demanding amino groups and 3,5-disubstitution on the aryl rings of the TADDOL backbone afforded the desired product in promising levels of enantioselectivity. In contrast, Ni(0) catalysts, which were successful in the related arylidene conjugate allylation methodology, are non-selective in conjunction with phosphoramidites; mixtures of regioisomeric products are obtained in racemic or near-racemic form.

Expanding upon his initial studies of ligand structure, I joined Josh Sieber in a survey of 3,5-di-*tert*-butylTADDOL-phosphoramidites in the allylation of **1.32** (Table 1.1). Increasing the size of the amino moiety on the phosphoramidite from dimethylamino (**1.35**, entry 1, see Figure 1.2 for ligand structures) to *N*,*N*-dibenzylamino (**1.36**, entry 2) dramatically improved the chemoselectivity, and, to a lesser extent, the enantioselectivity of the transformation. Cyclic piperidine **1.37** and azepane **1.38** amino groups (entries 3 and 5) provided moderate enantioselectivity. Notably, the allylation reaction was not regio- or enantioselective when using ligand **1.37** and $Ni(cod)_2$. However, particularly promising results occurred with added $\alpha$-substitution on cyclic amines.

The chiral 2-methyl piperidine moiety on ligand **1.39** afforded the desired product in enhanced chemo- and enantioselectivity (entry 5). This effect is specific to the diastereomer used: the mismatched ligand **1.40** (entry 6), with opposite configuration of the TADDOL backbone, performed with diminished enantioselectivity. It is noteworthy that a turnover in enantioselection is observed between these ligands, and is indicative that the configuration of the TADDOL backbone is the dominant stereochemical influence in the ligand. Though the enantioenriched 2-methylpyrrolidine-substituted phosphoramidite **1.41** performed with suboptimal enantioselection (entry 7), ligands with

prolinol-derived amino moieties showed promise in the conjugate allylation reaction (**1.42**, entry 8). We wished to probe reaction selectivity with this ligand scaffold, however, we were unsuccessful in our attempts to synthesize 3,5-di-*tert*-butylTADDOL-phosphoramidites with other protected prolinol derivatives, such as benzyl ether or *tert*-butyldimethyl silyl ether. Therefore, $Pd_2(dba)_3$ and ligand **1.39** were chosen as the optimal catalyst system for alkylidene conjugate allylation.

**Table 1.1: Chiral Ligand Survey**



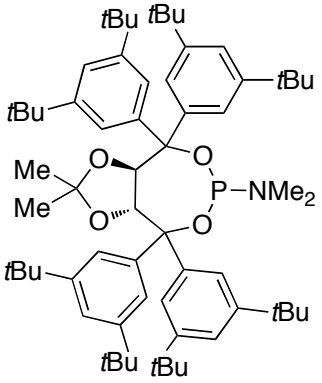

**1.32** **1.33** **1.34**

| entry | ligand[a] | β:β'[b] | yield (%)[c] | er[d] |
|---|---|---|---|---|
| 1 | **1.35** | 20:1 | 15 | 66:34 |
| 2 | **1.36** | > 50:1 | 14 | 75:25 |
| 3 | **1.37** | 35:1 | 10 | 75:25 |
| 4[e] | **1.37** | 1.5:1 | 44 | 50:50 |
| 5 | **1.38** | > 50:1 | 50 | 76:24 |
| **6** | **1.39** | **> 50:1** | **39** | **93:7** |
| 7 | **1.40** | > 50:1 | 47 | 28:72 |
| 8 | **1.41** | > 50:1 | 35 | 19:81 |
| 9 | **1.42** | > 50:1 | 11 | 14:86 |

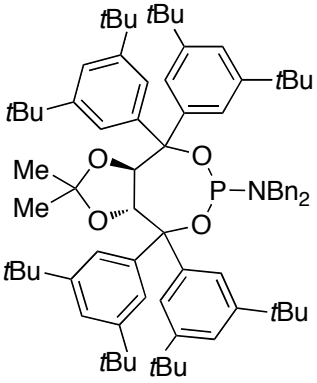
[a] See Figure 1.2 for ligand structures. [b] Value determined by GLC analysis of the unpurified reaction mixture. [c] Isolated yield after silica gel chromatography. Isolated as a mixture of constitutional isomers. [d] Determined by chiral GLC analysis. [e] Reaction with 5 mol % $Ni(cod)_2$ instead of Pd-catalyst.

Though the conjugate allylation reaction with ligand **1.39** afforded the desired product in excellent chemoselectivity and optical purity, the yield of the transformation was unsatisfactory. Analysis of the crude reaction mixture by $^{1}H$ NMR revealed resonances that we attributed to the boron enolate. Though the enolate was surprisingly resistant to protonation in aqueous workup, acidification of the aqueous layer with ammonium chloride or acetic acid afforded the reaction product in a superior yield of 59%.

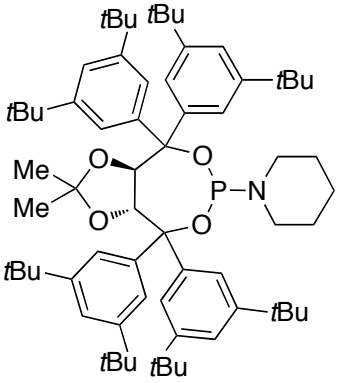
**Figure 1.2: 3,5-di-*t*BuPh-TADDOL-derived Chiral Phosphoramidites**



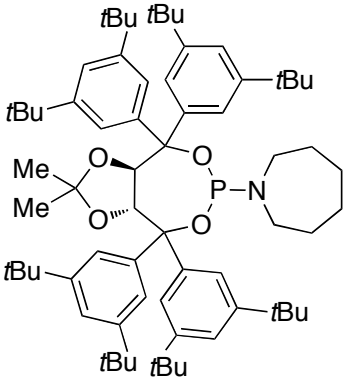
**1.35**



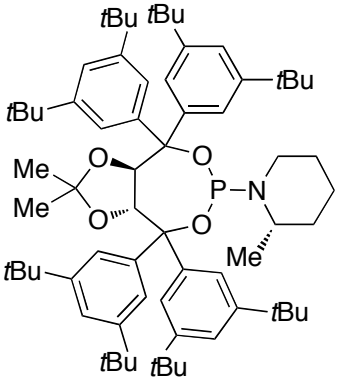
**1.36**



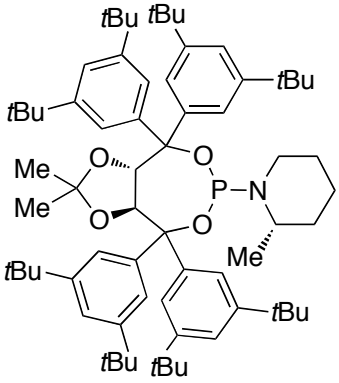
**1.37**



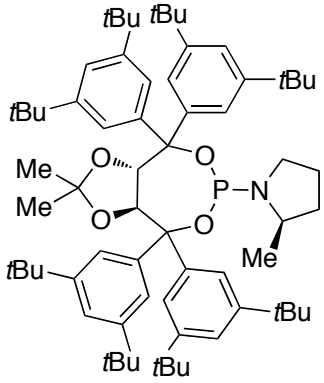
**1.38**



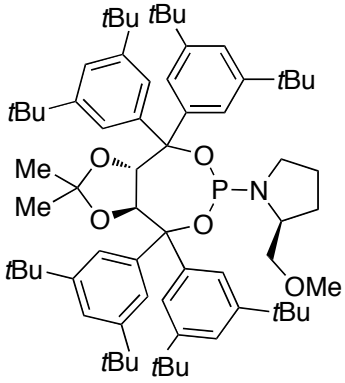
**1.39**



**1.40**



**1.41**

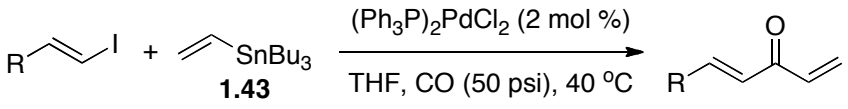


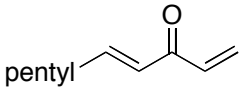
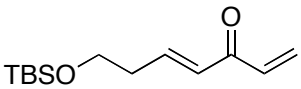
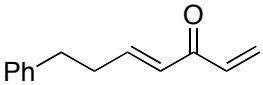
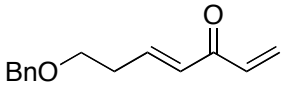
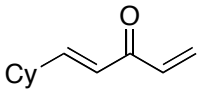
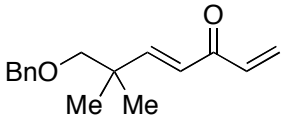
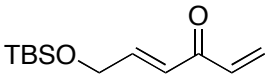
**1.42**

## B. Scope of Pd-Catalyzed Conjugate Allylation

Having developed optimal conditions for alkylidene conjugate allylation, we surveyed a variety of alkyl-substituted α,β-unsaturated methylidene ketones. These unsymmetric substrates were prepared in good yields using a carbonylative Stille coupling reaction.[19]

**Table 1.2: Carbonylative Stille Coupling**




| entry | product | yield (%) | entry | product | yield (%) |
|---|---|---|---|---|---|
| 1 |  **1.44** | 57 | 5 |  **1.48** | 69 |
| 2 |  **1.45** | 72 | 6 |  **1.49** | 56 |
| 3 |  **1.46** | 73 | 7 |  **1.50** | 71 |
| 4 |  **1.47** | 73 | | | |

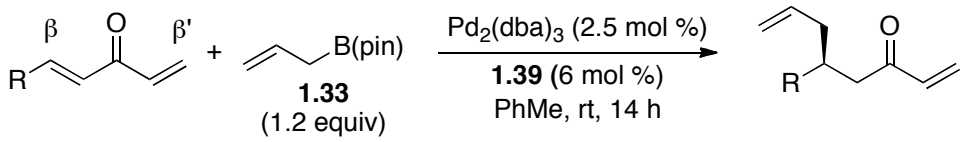
The scope of alkylidene conjugate allylation is given in Table 1.3. Utilizing the optimized experimental conditions, the simple *n*-pentyl-substituted methylidene enone

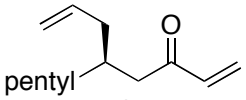
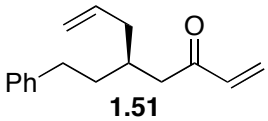
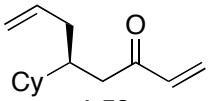
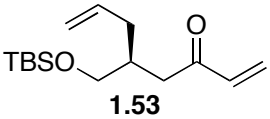
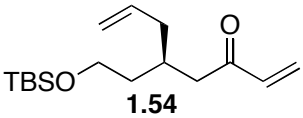
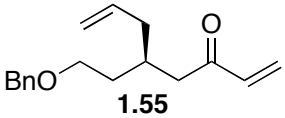
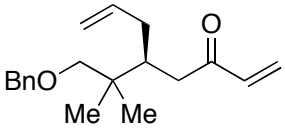
[19] Goure, W. F.; Wright, M. E.; Davis, P. D.; Labadie, S. S.; Stille, J. K. *J. Am. Chem. Soc.* **1984**, *106*, 6417.

undergoes efficient reaction with allylB(pin) (**1.33**) with a high level of stereocontrol and in good yield (entry 1). This reaction is the first example of a catalytic asymmetric conjugate allylation of an acyclic aliphatic enone.

Aliphatic substrates containing aromatic rings (entry 2) yield products in good levels of enantioselection, while branching adjacent to the enone enhances the enantioselectivity (entries 3 and 7). Both benzyl and silyl-protected oxygenated aliphatic substrates are tolerated in the reaction, albeit with diminished enantioselectivity (entries 4-6).

**Table 1.3: Substrate Scope in Asymmetric Conjugate Allylation**




| entry | substrate[a] | product | β:β'[b] | yield (%)[c] | er[d] |
|---|---|---|---|---|---|
| 1 | **1.44** |  **1.34** | > 100:1 | 59 | 93:7 |
| 2 | **1.45** |  **1.51** | > 100:1 | 79 | 94:6 |
| 3 | **1.46** |  **1.52** | > 100:1 | 57 | 95:5 |
| 4 | **1.47** |  **1.53** | > 100:1 | 91 | 91:9 |
| 5 | **1.48** |  **1.54** | > 100:1 | 53 | 92:8 |
| 6 | **1.49** |  **1.55** | > 100:1 | 53 | 91:9 |
| 7[e] | **1.50** |  **1.56** | > 100:1 | 81 | 96:4 |

[a] See Table 1.2 for substrate structures. [b] Determined by $^1$H or GLC analysis of the unpurified reaction mixture. [c] Isolated after silica gel chromatography. Value is an average of at least two experiments. [d] Enantiomeric ratio determined by chiral GLC, SFC, or HPLC analysis. [e] Experiment for 48 h and quenched with glacial acetic acid at 45 °C for 3 h.

Though the conjugate allylation method developed previously in our group provided an efficient route to allylation products of aromatic enones, we were curious to investigate aromatic substituted α,β-unsaturated methylidene enones. Attempts to synthesize the aromatic substrates by the carbonylative Stille cross-coupling were unsuccessful, providing the product in prohibitively low yield. Substrates **1.58** and **1.60** (Scheme 1.15, equations 1 and 2) were therefore generated by oxidation of the corresponding allylic alcohol. Dienone **1.62** (Scheme 1.15, equation 3) was synthesized by vinyl Grignard addition to an α,β-unsaturated Weinreb amide. Unfortunately, this transformation was plagued with byproduct **1.63**, the result of methoxymethylamine addition to the newly generated vinyl ketone.

**Scheme 1.15: Aromatic Enone Substrate Synthesis**

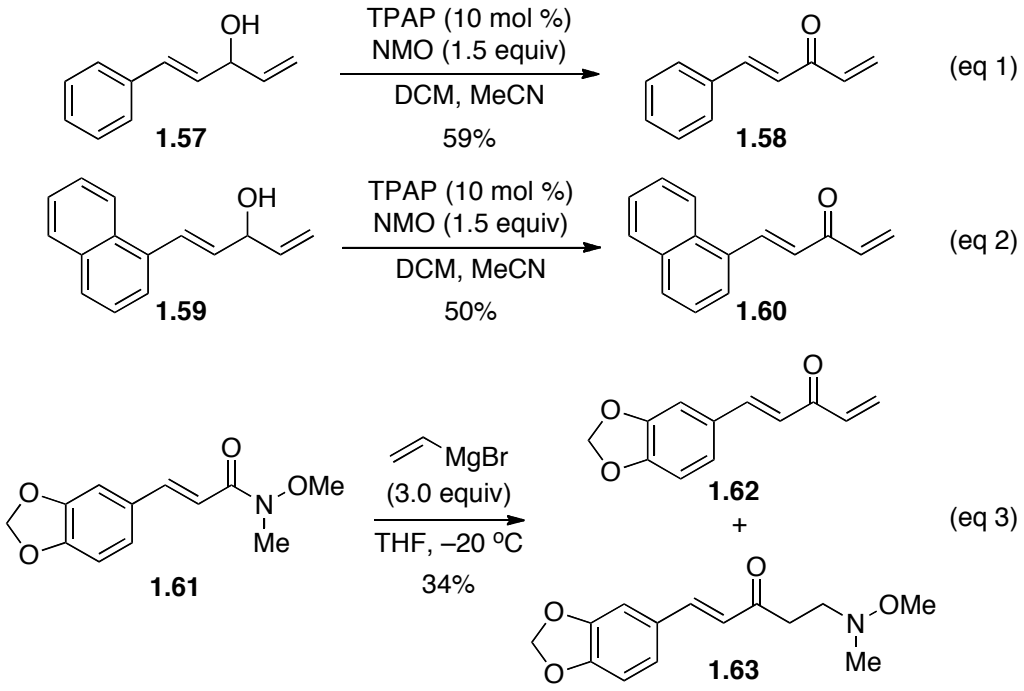
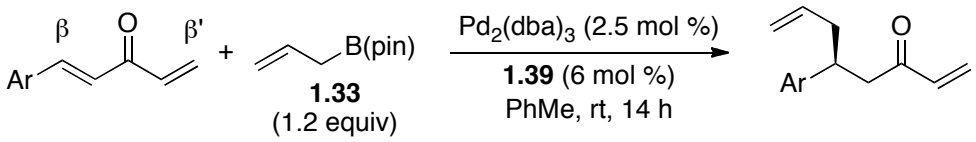
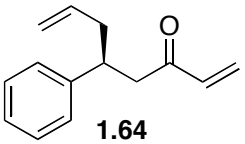
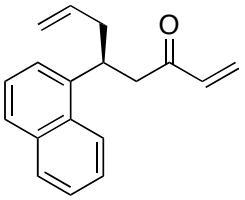
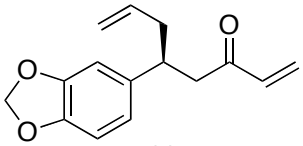


**Table 1.4: Aromatic Substrate Scope in Asymmetric Conjugate Allylation**




| entry | substrate[a] | product | β:β'[b] | yield (%)[c] | er[d] |
|---|---|---|---|---|---|
| 1 | **1.58** |  **1.64** | > 100:1 | 80 | 95:5 |
| 2 | **1.60** |  **1.65** | > 100:1 | 37 | 96:4 |
| 3 | **1.62** |  **1.66** | > 100:1 | 76 | 95:5 |

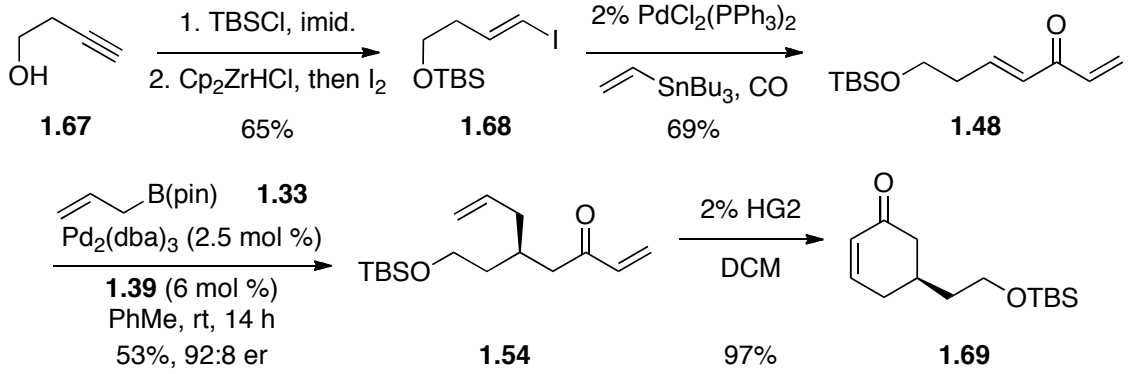
[a] See Scheme 1.14 for substrate structures. [b] Determined by $^1$H or GLC analysis of the unpurified reaction mixture. [c] Isolated after silica gel chromatography. Value is an average of at least two experiments. [d] Enantiomeric ratio determined by chiral GLC, SFC, or HPLC analysis.

As demonstrated in Table 1.4, aromatic enones, including those containing oxygenation, react with good yields and enantioselectivity, which indicates the generality of α,β-unsaturated methylidene substrates in the Pd-catalyzed asymmetric conjugate allylation method.

### C. Product Transformations and Other Related Reactions

The products of alkylidene conjugate allylation contain functional groups that are amenable to further transformation, marking their potential as valuable synthetic intermediates. To demonstrate product utility, we envisioned a short asymmetric synthesis of cyclohexenone **1.69**, which has previously been utilized as a critical intermediate in the total synthesis of stenine.[20]

**Scheme 1.16: Synthetic Application**




From 1-butyn-4-ol, silyl protection and reductive iodination with Schwartz's reagent[21] affords vinyl iodide **1.68** (Scheme 1.16). Carbonylative Stille cross coupling yields the conjugate allylation substrate **1.48** (see Table 1.2). Conjugate allylation, following conditions outlined in Table 1.3, furnishes the optically enriched allylation product **1.54**. Metathesis between the methylidene ketone and the newly installed allyl group with Hoveyda-Grubbs second generation catalyst[22] closes the ring and provides

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[20] Zhu, L.; Lauchli, R.; Loo, M.; Shea, K. J. *Org. Lett.* **2007**, *9*, 2269.

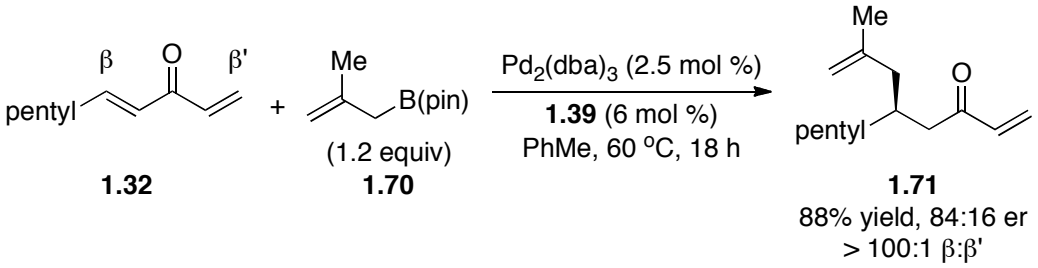
[21] Labinger, J. A.; Schwartz, J. *Angew. Chem. Int. Ed. Engl.* **1976**, *15*, 333.

[22] Garber, S. B.; Kingsbury, J. S.; Gray, B. L.; Hoveyda, A. H. *J. Am. Chem. Soc.* **2000**, *122*, 8168.

cyclohexenone **1.69**. This synthesis is completed in five steps and 23% overall yield, a favorable improvement over the previous eight step non-enantioselective synthesis.

In order to probe the effect of allylmetal reagent substitution on the reactivity and enantioselectivity in the conjugate allylation reaction, methallylboronic acid pinacol ester **1.70** was prepared.[23] Preliminary results utilizing the optimal catalyst system from the Pd-catalyzed asymmetric alkylidene conjugate allylation reaction supplied the desired product (Scheme 1.17). Methallyl substituted enone **1.71** was isolated in excellent yield and chemoselectivity, albeit with reduced optical activity. Still, this is an encouraging result, and may warrant further exploration in the future.

**Scheme 1.17: Pd-Catalyzed Asymmetric Conjugate Addition With Methallylboronic Acid Pinacol Ester**




**1.32** **1.70** **1.71**
88% yield, 84:16 er
> 100:1 β:β'

## IV. Conclusions

The previous limitation in the chemoselective conjugate allylation of non-symmetric arylidene alkylidene ketones has been overcome. Based on observations of chemoselectivity in related Ni-catalyzed conjugate allylation methodology, a new class of

[23] Zhang, P.; Roundtree, I. A.; Morken, J. P. *manuscript in preparation.*

α,β-unsaturated methylidene ketones has been rationally designed, allowing for asymmetric conjugate allylation of alkylidene ketones. The following insights have been gained from this study:

**1.** Allylboronic acid pinacol ester undergoes conjugate addition to α,β-unsaturated methylidene ketones with the use of a Pd(0) catalyst and a sterically demanding TADDOL-derived phosphoramidite ligand.

**2.** Attenuation of the substitution on the activating olefin of the substrate provides a handle for controlling the chemoselectivity.

**3.** Products of conjugate allylation hold promise as intermediates in organic synthesis.

**4.** Additional substitution on the allylmetal reagent is feasible, though improving the enantioselectivity of this reaction requires further study.

## V. Experimental Procedures

### A. General Information

$^{1}H$ NMR spectra were recorded on either a Varian Gemini-400 (400 MHz), a Varian Gemini-500 (500 MHz), a Varian Inova-500 (500 MHz), or a Varian Gemini-600 (600 MHz) spectrometer. Chemical shifts are reported in ppm with the solvent resonance as the internal standard ($CDCl_3$: 7.26 ppm). Data are reported as follows: chemical shift, integration, multiplicity (s = singlet, d = doublet, t = triplet, q = quartet, p = pentet, br = broad, m = multiplet, app = apparent), and coupling constants (Hz). $^{13}C$ NMR spectra were recorded on either a Varian Gemini-400 (100 MHz), a Varian Gemini-500 (125 MHz), or a Varian Gemini-600 (150 MHz) spectrometer with complete proton decoupling. Chemical shifts are reported in ppm with the solvent resonance as the internal standard ($CDCl_3$: 77.0 ppm). Infrared (IR) spectra were recorded on a Bruker alpha spectrophotometer, $\nu_{max}$ $cm^{-1}$. Bands are characterized as broad (br), strong (s), medium (m), and weak (w). High resolution mass spectrometry (ESI) was performed at the Mass Spectrometry Facility, Boston College.

Liquid Chromatography was performed using forced flow (flash chromatography) on silica gel ($SiO_2$, 230×450 Mesh) purchased from Silicycle. Thin Layer Chromatography was performed on 25 μm silica gel plates purchased from Silicycle. Visualization was performed using ultraviolet light (254 nm), potassium permanganate ($KMnO_4$) in water, or phosphomolybdic acid (PMA) in ethanol. Analytical chiral gas-liquid chromatography (GLC) was performed on a Hewlett-Packard 6890 Series chromatograph equipped with a split mode capillary injection system, a flame ionization

detector, and a Supelco β-Dex 120 column or a Supelco Chiraldex G-TA with helium as the carrier gas. Analytical chiral supercritical fluid chromatography (SFC) was performed on a Berger Instruments Supercritical Chromatograph equipped with an Alcott auto sampler and a Knauer UV detector with methanol as the modifier. Analytical high performance liquid chromatography (HPLC) was performed on an Agilent 1120 compact chromatograph equipped with gradient pump and variable wavelength detector. Carbonylation was performed in an Argonaut Technologies Endeavor® Catalyst Screening System using CO supplied by Airgas, Inc.

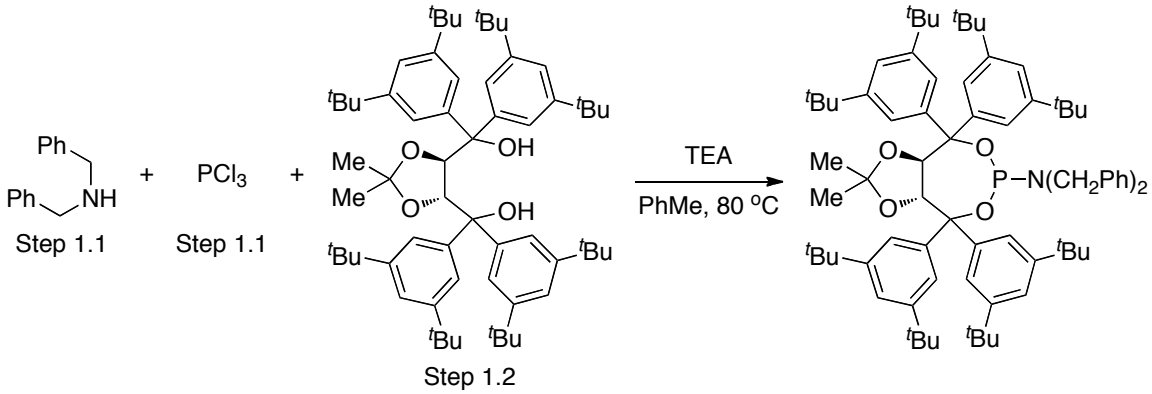
All reactions were conducted in oven- or flame-dried glassware under an inert atmosphere of nitrogen or argon. Tetrahydrofuran (THF), dichloromethane (DCM), and toluene (PhMe) were purified using a Pure Solv MD-4 solvent purification system from Innovative Technology Inc. by passing through two activated alumina columns after being purged with argon. Triethylamine was distilled from calcium hydride. Neutral alumina ($Al_2O_3$, 32-63 μm) was purchased from Sorbent Technologies. Tris(dibenzylideneacetone) dipalladium(0) ($Pd_2(dba)_3$), *trans*-dichlorobis(triphenylphosphine) palladium(II) ($(Ph_3P)_2PdCl_2$), and tetrapropylammonium perruthenate (TPAP) were purchased from Strem Chemicals, Inc. Tributylvinylstannane was purchased from Alfa Aesar. Allylboronic acid pinacol ester [allylB(pin)] was generously donated by Frontier Scientific, Inc. All other reagents were purchased from either Fisher or Aldrich and used without further purification.

## B. Experimental Procedures

### 1. Preparation of Phosphoramidite Ligands

Phosphoramidite ligand **1.35** was prepared according to literature procedure.[24]

Preparation of [3,5-(*tert*-Bu)$_2$-TADDOL]PN(CH$_2$Ph)$_2$ (**1.36**):




To an oven-dried scintillation vial equipped with a magnetic stir bar in the dry-box was added triethylamine (35 mg, 0.25 mmol) and PhMe (2.5 mL). To this solution was added freshly distilled dibenzylamine (40 mg, 0.20 mmol), followed by phosphorus trichloride (28 mg, 0.20 mmol). The vial was capped with a teflon cone-lined cap and sealed with electrical tape. The vial was removed from the dry-box and heated to 80 °C with stirring 12 h. The reaction was cooled to ambient temperature, then a solution of 3,5-di-*tert*-butylphenylTADDOL (183 mg, 0.20 mmol) in PhMe (0.5 mL) was added in the dry-box. The vial that had contained the solution of the diol was rinsed with THF (0.5 mL), and this was added to the reaction vessel. The scintillation vial was capped and sealed and removed from the dry-box and allowed to stir at 80 °C for 7 h. The reaction was cooled to ambient temperature, and diethyl ether (5 mL) was added to the reaction mixture.

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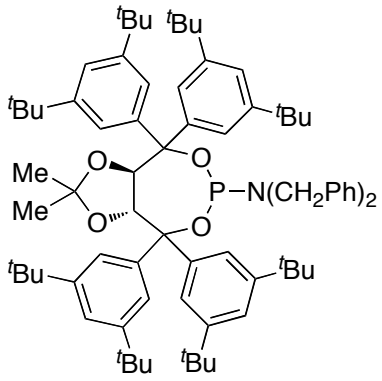
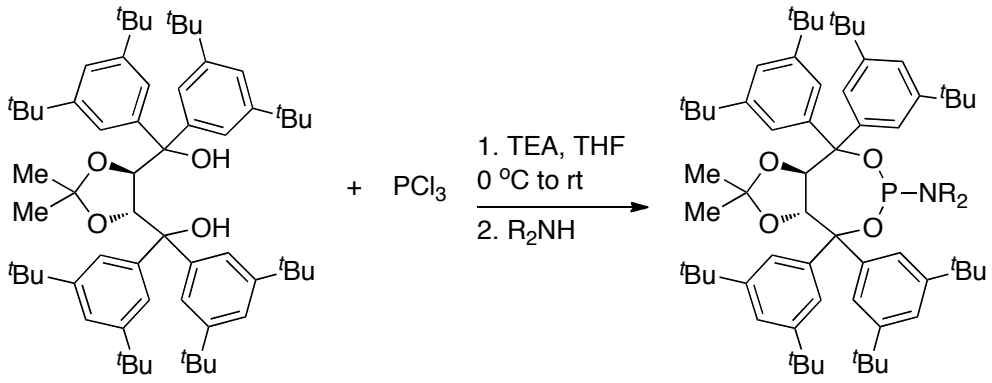
[24] Woodward, A. R.; Burks, H. E.; Chan, L. M.; Morken, J. P. *Org. Lett.*, **2005**, *7*, 5505.

Triethylamine hydrochloride salts precipitated out of the solution, and the reaction mixture was filtered over celite and washed with diethyl ether (3 x 10 mL); then the filtrate was concentrated *in vacuo*. The crude reaction mixture was purified on silica gel (55:1 hexanes:ethyl acetate) to afford 37 mg (16%) of a white solid. $R_f$ = 0.38 (55:1 hexanes:ethyl acetate, stain in PMA).

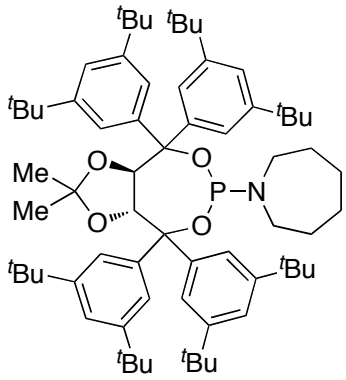



**[3,5-(*tert*-Bu)$_2$-TADDOL]PN(CH$_2$Ph)$_2$ (1.36).** $^1$H NMR (600 MHz, $CDCl_3$): $\delta$ 0.10 (3H, s), 1.12 (18H, s), 1.21 (18H, s), 1.23 (18H, s), 1.28 (18H, s), 1.47 (3H, s), 3.97 (2H, dd, *J* = 15.6 Hz, 10.8 Hz), 4.73 (1H, d, *J* = 9.0 Hz), 4.82 (2H, dd, *J* = 15.6 Hz, 7.8 Hz), 5.42 (1H, dd, *J* = 9.0 Hz, 2.4 Hz), 7.15 (1H, t, *J* = 1.8 Hz), 7.16-7.21 (3H, m), 7.21-7.22 (2H, m), 7.22-7.23 (3H, m), 7.23-7.25 (3H, m), 7.35-7.39 (6H, br m), 7.71 (2H, d, *J* = 1.8 Hz), 7.72 (2H, d, *J* = 1.8 Hz); $^{13}$C NMR (150 MHz, $CDCl_3$): $\delta$ 24.0, 28.0, 29.7, 30.3, 31.3, 31.4, 31.48, 31.50, 34.6, 34.8, 34.9, 35.0, 47.8, 47.9 , 81.9, 83.0, 83.1, 83.5, 83.6, 110.1, 119.9, 120.1, 120.2, 120.5, 121.6, 121.9, 123.7, 126.6, 128.2, 128.4, 138.71, 138.72, 140.6, 142.1, 146.2, 146.7, 148.5, 148.7, 148.9, 149.3, 149.8; $^{31}$P NMR (161 MHz, $CDCl_3$): $\delta$ 138.5. IR (neat): 2961 (s), 2904 (m), 2865 (m), 1598 (m), 1477 (w), 1455 (w), 1393 (w), 1249 (m), 1201 (m), 1059 (m), 946 (w), 880 (m), 864 (m), 787 (w), 710 (w) cm$^{-1}$. HRMS-(TOF MS ES+) for $C_{77}H_{107}NO_4P$ [M+H]: calculated: 1140.7938, found: 1140.7972. $[\alpha]^{20}_D$ = -42.7 (*c* = 0.22, $CHCl_3$).

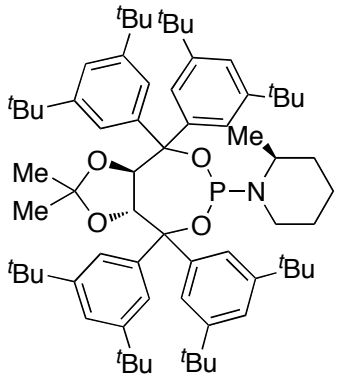
Phosphoramidite ligands **1.37**, **1.38**, **1.39**, **1.40**, **1.41**, and **1.42** were prepared according to the representative procedure for phosphoramidite synthesis, as follows. Characterization of **1.37** is in accordance with the literature.[4b]



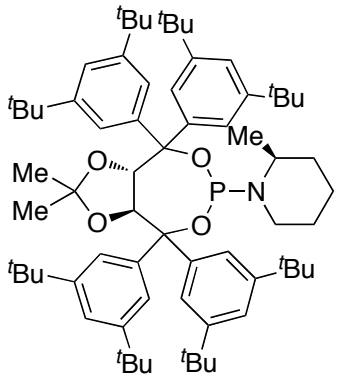

**Representative Procedure:** To a flame-dried 25 mL round-bottomed flask equipped with magnetic stir bar was added 3,5-di-*tert*-butylphenylTADDOL (400 mg, 0.44 mmol). The flask was flushed with $N_2$, then THF (6 mL) was added. The solution was cooled to 0 °C, then triethylamine (0.2 mL, 1.49 mmol), and phosphorus trichloride (0.05 mL, 0.52 mmol) were added, dropwise. The solution was warmed to rt for 45 min, then was cooled to 0 °C again, and (*S*)-(+)-2-methylpiperidine (0.1 mL, 0.87 mmol) was added. The solution was allowed to warm to rt and stir overnight. Diethyl ether (10 mL) was then added to the solution, and the triethylamine hydrochloride salts precipitated out of solution. The reaction mixture was filtered over celite and washed with diethyl ether (3 x 10 mL), then the filtrate was concentrated *in vacuo*. The crude reaction mixture was purified on silica gel (35:1 hexane:ethyl acetate) to afford a white solid (414 mg, 91% yield). $R_f$ = 0.30 (30:1 hexanes: ethyl acetate, stain in PMA).



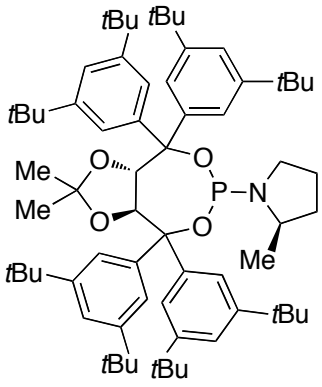
**[3,5-(*t*Butyl)$_2$-TADDOL]PNC$_6$H$_{12}$ (1.38).** The representative procedure was followed, employing azepane as amine nucleophile. $^1$H NMR (500 MHz, $CDCl_3$): $\delta$ 0.05 (3H, s), 1.24 (18H, s), 1.26 (18H, s), 1.28 (18H, s), 1.29 (18H, s), 1.49 (3H, s), 1.64-1.71 (4H, m), 1.72-1.84 (4H, m), 3.38-3.51 (4H, m), 4.66 (1H, d, $J$ = 9.0 Hz), 5.30 (1H, dd, $J$ = 9.0 Hz, 2.5 Hz), 7.12 (2H, d, $J$ = 1.5 Hz), 7.20 (1H, t, $J$ = 2.0 Hz), 7.21-7.23 (2H, m), 7.24 (1H, t, $J$ = 2.0 Hz), 7.39 (2H, br s), 7.63 (2H, d, $J$ = 1.5 Hz), 7.65 (2H, d, $J$ = 1.5 Hz); $^{13}$C NMR (125 MHz, $CDCl_3$): $\delta$ 23.8, 27.1, 28.0, 31.4, 31.6, 31.6 (d, $^3J_{CP}$ = 4.0 Hz), 34.8, 34.9, 35.0, 46.8 (d, $^2J_{CP}$ = 21.0 Hz), 80.7, 80.8, 82.4, 82.5, 83.6, 83.8, 83.89, 83.92, 109.6, 119.9, 120.0, 120.1, 120.6, 121.5, 122.0, 123.7, 141.2, 142.2, 146.3, 146.6, 148.6, 148.7, 149.1, 149.5. $^{31}$P NMR (202 MHz, $CDCl_3$): $\delta$ 141.5. IR (neat): 3084 (w), 2958 (s), 2907 (s), 2860 (m), 1599 (m), 1480 (m), 1451 (m), 1396 (m), 1362 (m), 1244 (m), 1198 (m) cm$^{-1}$. LRMS-(ESI+) for $C_{69}H_{104}NO_4P$ [M+H]: calculated: 1042.8, found: 1043.3. $[\alpha]^{20}_D$ = -37 ($c$ = 2.0, $CHCl_3$). The crude reaction mixture was purified on silica gel (55:1 hexanes:ethyl acetate) to afford 179 mg (88%) of a white solid. $R_f$ = 0.38 (55:1 hexanes:ethyl acetate, stain in PMA).



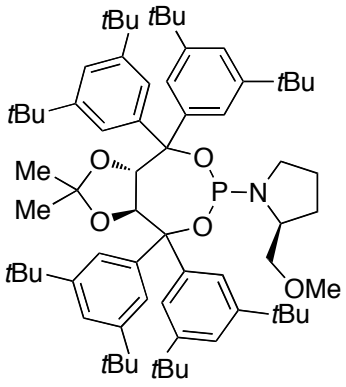
**[3,5-(*t*Butyl)$_2$-TADDOL]PNC$_6$H$_{12}$ (1.39).** The representative procedure was followed, employing (*S*)-(+)-2-methylpiperidine as amine nucleophile. $^1$H NMR (500 MHz, $CDCl_3$): $\delta$ 0.06 (3H, s), 1.25 (18H, s), 1.27 (18H, s), 1.30 (18H, s), 1.31 (18H, s), 1.51 (4H, br s), 1.58-1.74 (3H, m), 1.74-1.87 (2H, m), 3.34-3.46 (1H, m), 3.47-3.59 (1H, m), 4.03-4.17 (1H, m), 4.65 (1H, d, $J$ = 8.5 Hz), 5.28 (1H, dd, $J$ = 8.5 Hz, 2.5 Hz), 7.15 (2H, d, $J$ = 2.0 Hz), 7.19-7.24 (3H, m), 7.26 (1H, t, $J$ = 1.5 Hz), 7.36-7.48 (2H, m), 7.65 (2H, d, $J$ = 1.5 Hz), 7.67 (2H, d, $J$ = 2.0 Hz); $^{13}$C NMR (125 MHz, $CDCl_3$): $\delta$ 18.7 (d, $^2J_{CP}$ = 9.6 Hz), 20.8, 23.8, 27.6, 28.0, 31.4, 31.48, 31.49, 31.5, 32.7, 34.75, 34.76, 34.9, 35.0, 39.9 (d, $^2J_{CP}$ = 19.0 Hz), 47.6 (d, $^2J_{CP}$ = 20.0 Hz), 80.65, 80.59, 82.4, 82.5, 83.6, 83.7, 83.87, 83.90, 109.4, 119.8, 119.9, 120.1, 120.5, 121.6, 122.0, 123.7, 141.4, 142.3, 146.3, 146.6, 148.6, 148.7, 149.1, 149.5; $^{31}$P NMR (202 MHz, $CDCl_3$): $\delta$ 137.6. IR (neat): 3076 (w), 2962 (s), 2907 (s), 2861 (m), 1599 (m), 1472 (m), 1388 (m), 1362 (m), 1248 (m), 1206 (m), 1160 (m) cm$^{-1}$. LRMS-(ESI+) for $C_{69}H_{104}NO_4P$ [M+H]: calculated: 1042.8, found: 1043.3. $[\alpha]^{20}_D$ = -23 ($c$ = 2.3, $CHCl_3$). The crude reaction mixture was purified on silica gel (35:1 hexanes:ethyl acetate) to afford 414 mg (91%) of a white solid. $R_f$ = 0.30 (30:1 hexanes:ethyl acetate, stain in PMA).



**[3,5-(*t*Butyl)$_2$-TADDOL]PNC$_6$H$_{12}$ (1.40).** The representative procedure was followed, employing (*S*)-(+)-2-methylpiperidine as amine nucleophile and di-*tert*-butylphenylTADDOL derived from D-tartaric acid. $^1$H NMR (500 MHz, $CDCl_3$): $\delta$ 0.10 (3H, s), 1.30 (18H, s), 1.32 (18H, s), 1.34 (18H, s), 1.34 (18H, s), 1.52-1.65 (5H, m), 1.65-1.74 (2H, m), 1.74-1.87 (1H, m), 1.93-2.03 (1H, m), 3.33 (1H, app q, $J$ = 12.0 Hz), 3.51-3.62 (1H, m), 4.30-4.40 (1H, m), 4.65 (1H, d, $J$ = 8.5 Hz), 5.28 (1H, dd, $J$ = 8.5 Hz, 2.5 Hz), 7.20 (2H, d, $J$ = 2.0 Hz), 7.24-7.30 (4H, m), 7.50 (2H, br s), 7.69 (2H, d, $J$ = 1.5 Hz), 7.73 (2H, d, $J$ = 2.0 Hz); $^{13}$C NMR (125 MHz, $CDCl_3$): $\delta$ 18.1 (d, $^2J_{CP}$ = 5.1 Hz), 20.4, 23.8, 27.7, 28.1, 31.4, 31.5, 32.2, 34.77, 34.79, 34.9, 35.0, 40.0, (d, $^2J_{CP}$ = 27.0 Hz) 46.6 (d, $^2J_{CP}$ = 15.0 Hz), 80.46, 80.49, 82.1, 82.2, 83.9, 84.04, 84.09, 84.1, 109.5, 119.9, 120.1, 120.5, 121.5, 122.0, 123.7, 141.1, 142.3, 146.5, 146.6, 146.7, 148.7, 149.1, 149.4; $^{31}$P NMR (202 MHz, $CDCl_3$): $\delta$ 138.0. IR (neat): 3075 (w), 2962 (s), 2911 (s), 2865 (m), 1599 (m), 1480 (m), 1396 (m), 1379 (m), 1362 (s), 1252 (s), 1201 (m) cm$^{-1}$. LRMS-(ESI+) for $C_{69}H_{104}NO_4P$ [M+H]: calculated: 1042.8, found: 1043.4. $[\alpha]^{20}_D$ = +29 (*c* = 3.4, $CHCl_3$). The crude reaction mixture was purified on silica gel (30:1 hexanes:ethyl acetate) to afford 181 mg (80%) of a white solid. $R_f$ = 0.47 (30:1 hexanes:ethyl acetate, stain in PMA).

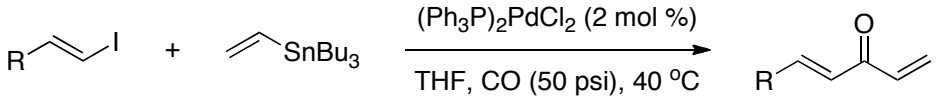



**[3,5-(*t*Butyl)$_2$-TADDOL]PNC$_5$H$_{10}$ (1.41).** The representative procedure was followed, employing (*R*)-2-(methyl)pyrrolidine as amine nucleophile and di-*tert*-butylphenylTADDOL derived from D-tartaric acid. $^1$H NMR (500 MHz, $CDCl_3$): δ 0.07 (3H, s), 1.23 (18H, s), 1.25 (18H, s), 1.27 (18H, s), 1.28 (21H, s), 1.46 (3H, s), 1.47-1.56 (1H, m), 1.80-1.88 (1H, m), 1.92 (1H, dddd, *J* = 12.0 Hz, 7.0 Hz), 1.99-2.07 (1H, m), 3.40-3.46 (1H, m), 3.68-3.74 (1H, m), 4.06 (1H, dq, *J* = 6.5 Hz, 6.5 Hz), 4.69 (1H, d, *J* = 8.5 Hz), 5.28 (1H, dd, *J* = 8.5 Hz, 3.0 Hz), 7.13 (2H, d, *J* = 2.0 Hz), 7.21 (4H, app tt, *J* = 11.5 Hz, 2.0 Hz), 7.36-7.41 (2H, m), 7.61 (4H, dd, *J* = 17.5 Hz, 2.0 Hz); $^{13}$C NMR (125 MHz, $CDCl_3$): δ 23.7 (d, $^2J_{CP}$ = 5.5 Hz), 23.9, 25.3, 25.4, 28.0, 31.43, 31.49, 31.50, 34.5, 34.6, 34.8, 34.9, 35.0, 44.6, (d, $^2J_{CP}$ = 12.5 Hz), 52.9 (d, $^2J_{CP}$ = 15.8 Hz), 80.9, 82.5, 82.6, 83.6, 83.76, 83.84, 109.7, 119.8, 120.0, 120.1, 120.6, 121.5, 122.0, 123.67, 123.69, 141.3, 142.3, 146.3, 146.6, 148.6, 148.7, 149.1, 149.5; $^{31}$P NMR (202 MHz, $CDCl_3$): δ 137.0. IR (neat): 2961 (s), 2905 (m), 2866 (m), 1598 (m), 1477 (m), 1459 (w), 1362 (m), 1249 (m), 1201 (m), 1166 (w), 1072 (w), 1037 (m), 900 (m), 880 (m), 864 (w), 786 (w), 761 (w) cm$^{-1}$. HRMS-(ESI+) for $C_{68}H_{103}NO_4P$ [M+H]: calculated: 1028.7625, found: 1028.7676. The crude reaction mixture was purified on silica gel (50:1 hexanes:ethyl acetate) to afford 168 mg (75%) of a white solid.

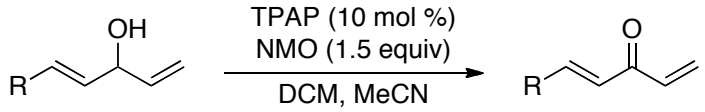



**[3,5-(*t*Butyl)$_2$-TADDOL]PNC$_6$H$_{12}$O (1.42).** The representative procedure was followed, employing (*S*)-(+)-2-(methoxymethyl)pyrrolidine as amine nucleophile and di-*tert*-butylphenylTADDOL derived from D-tartaric acid. $^1$H NMR (500 MHz, $CDCl_3$): $\delta$ 0.09 (3H, s), 1.24 (18H, s), 1.25 (18H, s), 1.28 (18H, s), 1.29 (18H, s), 1.43 (3H, s) 1.90-2.00 (4H, m), 3.20 (1H, t, $J$ = 9.0 Hz), 3.26 (3H, s), 3.37-3.43 (1H, m), 3.50 (1H, dd, $J$ = 9.0 Hz, 4.0 Hz), 3.74-3.80 (1H, m), 3.99-4.07 (1H, m), 4.73 (1H, d, $J$ = 8.5 Hz), 5.30 (1H, dd, $J$ = 8.5 Hz, 2.5 Hz), 7.20 (2H, d, $J$ = 1.5 Hz), 7.20-7.26 (4H, m), 7.34 (2H, br s), 7.59 (2H, d, $J$ = 1.5 Hz), 7.61 (2H, dd, $J$ = 2.0 Hz); $^{13}$C NMR (125 MHz, $CDCl_3$): $\delta$ 24.0, 25.0, 27.9, 29.5, 31.2, 31.3, 31.4, 31.50, 31.51, 34.7, 34.8, 34.88, 34.9, 44.7, (d, $^2J_{CP}$ = 9.6 Hz), 56.2 (d, $^2J_{CP}$ = 18.5 Hz), 58.8, 76.5, 81.3, 82.7, 82.8, 83.4, 83.5, 109.8, 119.9, 120.1, 120.2, 120.6, 121.5, 122.0, 123.67, 123.70, 124.7, 141.1, 142.1, 146.1, 146.5, 148.6, 148.8, 149.1, 149.6; $^{31}$P NMR (202 MHz, $CDCl_3$): $\delta$ 137.0. IR (neat): 3059 (w), 2977 (s), 2926 (s), 1615 (m), 1365 (m), 1276 (m), 1223 (m), 1188 (m), 1141 (m), 1071 (m), 911 (m), 863 (s), 815 (w), 726 (m) cm$^{-1}$. HRMS-(ESI+) for $C_{69}H_{105}NO_5P$ [M+H]: calculated: 1058.7725, found: 1058.7699. The crude reaction mixture was purified on silica gel (35:1 hexanes:ethyl acetate) to afford 115 mg (50%) of a white solid. $R_f$ = 0.55 (19:1 hexanes:ethyl acetate, stain in PMA).

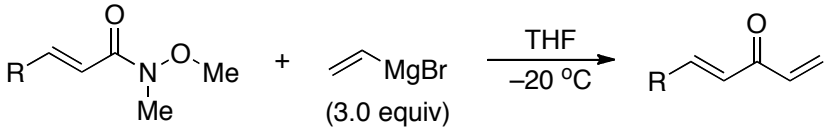
**2. Preparation of Unsaturated Methylidene Ketones**




**Representative Procedure A:**[19] An oven-dried glass reaction vial was placed into a well of the Argonaut Technologies Endeavor® and charged with *trans*-dichlorobis-(triphenylphosphine) palladium(II) (61 mg, 0.09 mmol) and THF (4.3 mL). To the resulting solution was added (*E*)-(2-iodovinyl)cyclohexane (1.020 g, 4.33 mmol), and tributylvinylstannane (1.5 mL, 5.20 mmol). The Endeavor was sealed and purged with CO. Stirring was started at 400 rpm and the Endeavor was heated to 40 °C and charged with 50 psi CO for 4 hours. The Endeavor was vented and cooled to ambient temperature. The vial was removed. The reaction mixture was diluted with 9:1 pentane:diethyl ether and filtered through neutral alumina. The solution was concentrated *in vacuo*, then diluted with diethyl ether (40 mL) and saturated aqueous KF solution (20 mL). The mixture was allowed to stir for 3 hours, then the organics were collected, dried over $Na_2SO_4$, filtered, and concentrated *in vacuo*. The crude reaction mixture was purified on silica gel (30:1 hexanes:ethyl acetate) to afford 518 mg (73%) of a light yellow oil. $R_f$ = 0.24 (30:1 hexanes:ethyl acetate, stain in $KMnO_4$).



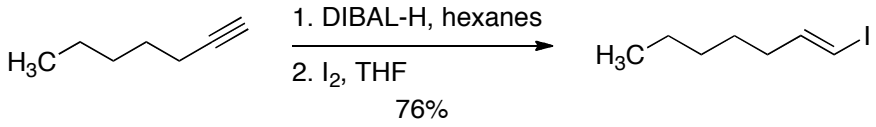

**Representative Procedure B:** Under $N_2$ atmosphere, a flame-dried round-bottomed flask with stir bar was charged with 4Å molecular sieves. A separate flame-dried flask was charged with (*E*)-1-phenylpenta-1,4-dien-3-ol (250 mg, 1.56 mmol), DCM (10 mL), and acetonitrile (1 mL). This solution was transferred to the first flask containing sieves by cannula. *N*-methylmorpholine-*N*-oxide (274 mg, 2.34 mmol) was added under $N_2$, and the resulting solution stirred 5 minutes. Tetrapropylammonium perruthenate (55 mg, 0.16 mmol) was then added, and the solution was allowed to stir overnight. The solution was filtered on silica and concentrated *in vacuo*. The crude reaction mixture was purified on silica gel (30:1 hexanes:ethyl acetate) to afford 145 mg (59%) of a yellow oil. $R_f$ = 0.20 (30:1 hexanes:ethyl acetate, stain in $KMnO_4$).

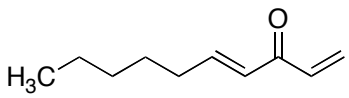



**Representative Procedure C:** To a flame-dried round-bottomed flask with stir bar was added (*E*)-3-(benzo[*d*][1,3]dioxol-5-yl)-*N*-methoxy-*N*-methylacrylamide (200 mg, 0.85 mmol). The flask was flushed with $N_2$ and THF (8 mL) was added. The resulting solution was cooled to –20 °C (ethylene glycol/dry ice) and vinylmagnesium bromide (2.55 mL, 1 M in THF) was added dropwise. The reaction was monitored by TLC and upon consumption of starting material at 1.5 hours, the reaction mixture was poured onto a pad of silica that had been slurry-packed in 1:1 hexane:ethyl acetate and flushed through the plug with 1:1 hexane:ethyl acetate in order to avoid the 1,4-addition of

methoxymethylamine into the resulting vinyl ketone product. The solution was then concentrated *in vacuo*, and the crude reaction mixture was purified on silica gel (10:3:1 toluene:hexanes:ethyl acetate) to afford 58 mg (34%) of a yellow solid. $R_f$ = 0.35 (10:3:1 toluene:hexanes:ethyl acetate, stain in $KMnO_4$).

***Preparation of (E)-deca-1,4-dien-3-one.*** From (*E*)-1-iodohept-1-ene, synthesized as shown below,[25] procedure A was followed.




**(*E*)-deca-1,4-dien-3-one (1.44).** $^1$H NMR (400 MHz, $CDCl_3$): $\delta$ 0.90 (3H, t, *J* = 6.8 Hz), 1.29-1.33 (4H, m), 1.47-1.51 (2H, m), 2.25 (2H, app qd, *J* = 6.8 Hz, 1.6 Hz), 5.81 (1H, dd, *J* = 10.4 Hz, 1.6 Hz), 6.28 (1H, dd, *J* = 17.6 Hz, 1.6 Hz), 6.36 (1H, app dt, *J* = 15.6 Hz, 1.6 Hz), 6.61 (1H, dd, *J* = 17.6 Hz, 10.4 Hz), 6.95 (1H, app dt, *J* = 15.6 Hz, 6.8 Hz); $^{13}$C NMR (100 MHz, $CDCl_3$): $\delta$ 13.9, 22.4, 27.7, 31.3, 32.6, 128.0, 128.0, 134.8, 148.9, 189.5; IR (neat): 2962 (s), 2932 (s), 2865 (m), 1662 (s), 1632 (s), 1611 (s), 1468 (w), 1396 (s), 1223 (s), 1105 (m), 978 (s) $cm^{-1}$. HRMS-(ESI+) for $C_{10}H_{17}O$ [M+H]: calculated: 153.1279, found: 153.1284. The crude reaction mixture was purified on silica gel (35:1 hexanes:ethyl acetate) to afford a light yellow oil (285 mg, 57% yield). $R_f$ = 0.20 (35:1 hexanes:ethyl acetate, stain in $KMnO_4$).

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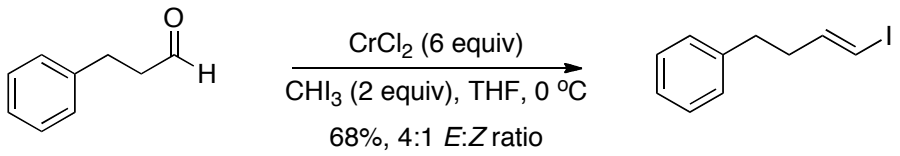
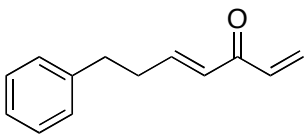
[25] Simpson, J. H.; Stille, J. K. *J. Am. Chem. Soc.* **1987**, *109*, 2138.

***Preparation of (E)-7-phenylhepta-1,4-dien-3-one.*** From (*E*)-(4-iodobut-3-en-1-yl)benzene, synthesized as shown below,[26] procedure A was followed.

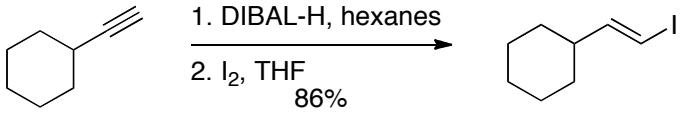


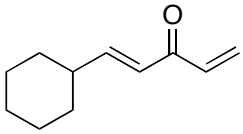




**(*E*)-7-phenylhepta-1,4-dien-3-one (1.45).** $^{1}$H NMR (500 MHz, $CDCl_3$): $\delta$ 2.56-2.61 (2H, m), 2.81 (2H, t, *J* = 7.5 Hz), 5.81 (1H, dd, *J* = 10.5 Hz, 1.0 Hz), 6.26 (1H, dd, *J* = 17.5 Hz, 1.0 Hz), 6.38 (1H, app dt, *J* = 15.5 Hz, 1.5 Hz), 6.58 (1H, dd, *J* = 17.5 Hz, 10.5 Hz), 6.97 (1H, app dt, *J* = 15.5 Hz, 7.5 Hz), 7.18-7.23 (3H, m), 7.28-7.31 (2H, m); $^{13}$C NMR (125 MHz, $CDCl_3$): $\delta$ 34.4, 34.4, 126.2, 128.3, 128.5, 128.5, 128.6, 134.9, 140.7, 147.6, 189.7; IR (neat): 2927 (br, w), 1665 (s), 1631 (s), 1610 (s), 1454 (w), 1403 (s), 1216 (m), 984 (s), 746 (w), 699 (s) cm$^{-1}$. HRMS-(ESI+) for $C_{13}H_{15}O_2$ [M+H]: calculated: 187.1123, found: 187.1118. The crude reaction mixture was purified on silica gel (25:1 hexanes: ethyl acetate) to afford a clear, colorless oil (251 mg, 72% yield, *E* isomer only). $R_f$ = 0.13 (35:1 hexanes:ethyl acetate, stain in $KMnO_4$).

[26] Takai, K.; Nitta, K.; Utimoto, K. *J. Am. Chem. Soc.* **1986**, *108*, 7408.

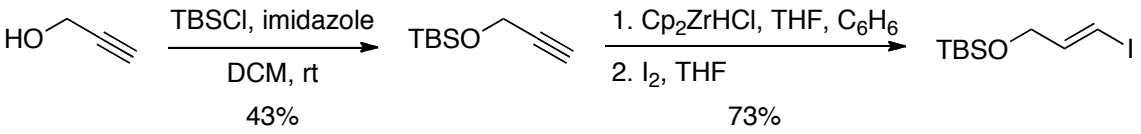
***Preparation of (E)-1-cyclohexylpenta-1,4-dien-3-one.*** From (*E*)-(2-iodovinyl)-cyclohexane, synthesized as shown below,[25] procedure A was followed.

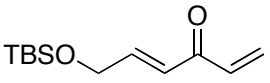



**(*E*)-1-cyclohexylpenta-1,4-dien-3-one (1.46).** $^{1}$H NMR (400 MHz, $CDCl_3$): $\delta$ 1.12-1.37 (5H, m), 1.66-1.71 (1H, m), 1.73-1.80 (4H, m), 2.13-2.22 (1H, m), 5.80 (1H, dd, *J* = 10.8 Hz, 1.6 Hz), 6.25-6.33 (2H, m), 6.62 (1H, dd, *J* = 17.2 Hz, 10.8 Hz), 6.88 (1H, dd, *J* = 16.0 Hz, 7.2 Hz); $^{13}$C NMR (125 MHz, $CDCl_3$): $\delta$ 25.7, 25.9, 31.7, 40.9, 125.7, 128.2, 134.9, 153.9, 190.2; IR (neat): 2925 (s), 2852 (m), 1665 (s), 1630 (m), 1612 (m), 1449 (w), 1403 (m), 1213 (m), 985 (m), 963 (m) cm$^{-1}$. HRMS-(ESI+) for $C_{11}H_{17}O$ [M+H]: calculated: 165.1279, found: 165.1281. The crude reaction mixture was purified on silica gel (30:1 hexanes:ethyl acetate) to afford a light yellow oil (518 mg, 73% yield). $R_f$ = 0.24 (30:1 hexanes:ethyl acetate, stain in $KMnO_4$).

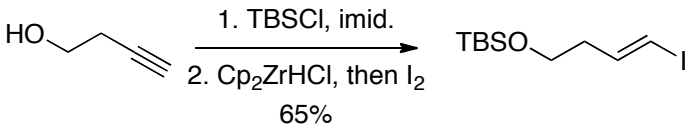
***Preparation of (E)-6-((tert-butyldimethylsilyl)oxy)hexa-1,4-dien-3-one.*** From (*E*)-*tert*-butyl((3-iodoallyl)oxy)dimethylsilane, synthesized as shown below,[21] procedure A was followed.

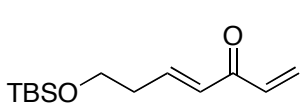



**(*E*)-6-((*tert*-butyldimethylsilyl)oxy)hexa-1,4-dien-3-one (1.47).** $^{1}$H NMR (500 MHz, $CDCl_3$): $\delta$ 0.09 (6H, s), 0.93 (9H, s), 4.39 (2H, dd, *J* = 3.5 Hz, 2.5 Hz), 5.84 (1H, dd, *J* = 11.0 Hz, 1.5 Hz), 6.29 (1H, dd, *J* = 17.5 Hz, 1.5 Hz), 6.59 (1H, dd, *J* = 17.5 Hz, 11.0 Hz), 6.68 (1H, app dt, *J* = 15.5 Hz, 2.5 Hz), 6.97 (1H, app dt, *J* = 15.5 Hz, 3.0 Hz); $^{13}$C NMR (125 MHz, $CDCl_3$): $\delta$ –5.4, 18.3, 25.8, 62.4, 125.3, 128.6, 135.4, 146.8, 189.6; IR (neat): 2930 (w), 2857 (w), 1669 (m), 1637 (w), 1255 (m), 1135 (s), 963 (m), 835 (s), 778 (m) cm$^{-1}$. HRMS-(ESI+) for $C_{12}H_{23}O_2Si$ [M +H]: calculated: 227.1467, found: 227.1465. The crude reaction mixture was purified on silica gel (35:1-25:1 hexanes:ethyl acetate) to afford a clear, colorless oil (265 mg, 73% yield). $R_f$ = 0.10 (35:1 hexanes:ethyl acetate, stain in $KMnO_4$).

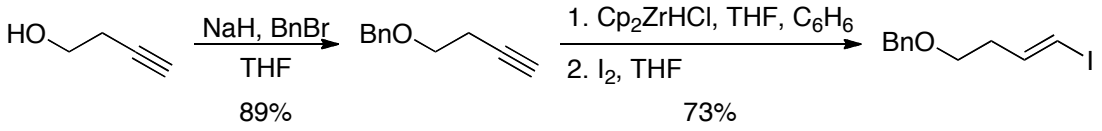
***Preparation of (E)-7-(tert-butyldimethylsilyloxy)hepta-1,4-diene-3-one.*** From (*E*)-*tert*-(butyl((4-iodobut-3-en-1-yl)oxy)dimethylsilane, synthesized as shown below,[21] procedure A was followed.

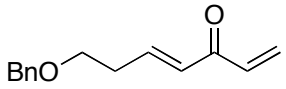



**(*E*)-7-(*tert*-butyldimethylsilyloxy)hepta-1,4-diene-3-one (1.48).** $^1$H NMR (400 MHz, $CDCl_3$): $\delta$ 0.05 (6H, s), 0.89 (9H, s), 2.47 (2H, qd, *J* = 6.4 Hz, 1.6 Hz), 3.75 (2H, t, *J* = 6.4 Hz), 5.82 (1H, dd, *J* = 10.4 Hz, 1.6 Hz), 6.28 (1H, dd, *J* = 17.6 Hz, 1.6 Hz), 6.41 (1H, dt, *J* = 16.0 Hz, 1.2 Hz), 6.61 (1H, dd, *J* = 17.6 Hz, 10.4 Hz), 6.94 (1H, dt, *J* = 16.0 Hz, 7.2 Hz); $^{13}$C NMR (125 MHz, $CDCl_3$): $\delta$ 18.3, 25.9, 36.2, 61.5, 101.3, 128.4, 129.7, 134.7, 145.6, 189.7; IR (neat): 2955 (w), 2930 (w), 2857 (w), 1669 (m), 1634 (w), 1613 (w), 1403 (w), 1255 (m), 1097 (s), 984 (m), 836 (s), 777 (s) cm$^{-1}$. HRMS-(ESI+) for $C_{13}H_{25}O_2Si$ [M+H]: calculated: 241.1624, found: 241.1617. The crude reaction mixture was purified on silica gel (35:1 hexanes:ethyl acetate) to afford a light yellow oil (317 mg, 69% yield). $R_f$ = 0.15 (35:1 hexanes:ethyl acetate, stain in $KMnO_4$).

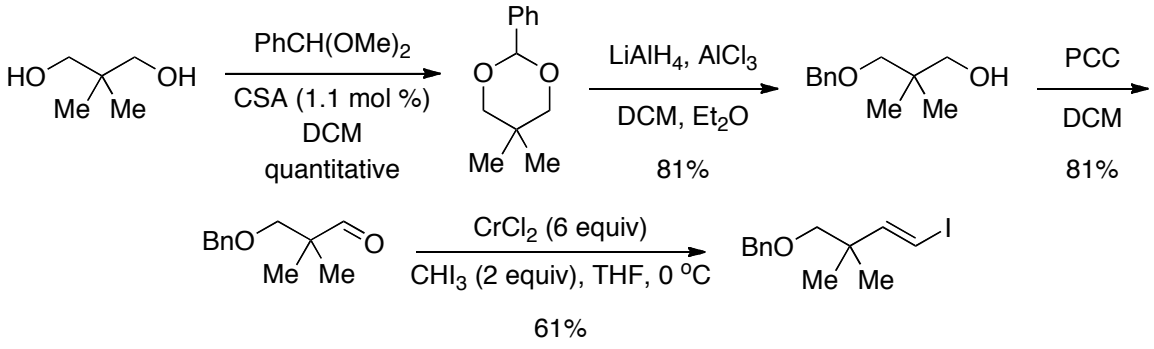
***Preparation of (E)-7-(benzyloxy)hepta-1,4-dien-3-one.*** From (*E*)-(((4-iodobut-3-en-1-yl)oxy)methyl)benzene, synthesized as shown below,[21] procedure A was followed.

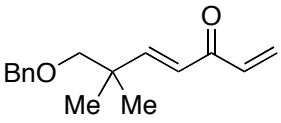



**(*E*)-7-(benzyloxy)hepta-1,4-dien-3-one (1.49).** $^{1}$H NMR (500 MHz, $CDCl_3$): $\delta$ 2.57 (2H, app qd, $J$ = 6.5 Hz, 1.5 Hz), 3.62 (2H, t, $J$ = 6.5 Hz), 4.53 (2H, s), 5.82 (1H, dd, $J$ = 10.5 Hz, 1.5 Hz), 6.28 (1H, dd, $J$ = 17.0 Hz, 1.5 Hz), 6.44 (1H, app dt, $J$ = 16.0 Hz, 1.5 Hz), 6.60 (1H, dd, $J$ = 17.0 Hz, 10.5 Hz), 6.96 (1H, app dt, $J$ = 16.0 Hz, 6.5 Hz), 7.28-7.37 (5H, m); $^{13}$C NMR (125 MHz, $CDCl_3$): $\delta$ 33.1, 68.3, 73.1, 127.7, 127.7, 128.4, 128.6, 129.5, 134.8, 138.0, 145.2, 189.6; IR (neat): 2858 (br, w), 1666 (s), 1632 (m), 1610 (m), 1403 (w), 1097 (s), 985 (m), 742 (m), 699 (m), 407 (m) cm$^{-1}$. HRMS-(ESI+) for $C_{14}H_{17}O_2$ [M+H]: calculated: 217.1229, found: 217.1224. The crude reaction mixture was purified on silica gel (25:1-15:1 hexanes:ethyl acetate) to afford a light yellow oil (216 mg, 56% yield). $R_f$ = 0.12 (15:1 hexanes:ethyl acetate, stain in $KMnO_4$).

***Preparation of (E)-7-(benzyloxy)-6,6-dimethylhepta-1,4-dien-3-one.*** From (*E*)-(((4-iodo-2,2-dimethylbut-3-en-1-yl)oxy)methyl)benzene, synthesized as shown below,[27] procedure A was followed.




**(*E*)-7-(benzyloxy)-6,6-dimethylhepta-1,4-dien-3-one (1.50).** $^1$H NMR (500 MHz, $CDCl_3$): $\delta$ 1.12 (6H, s), 3.29 (2H, s), 4.52 (2H, s), 5.81 (1H, dd, *J* = 10.5 Hz, 1.5 Hz), 6.28 (1H, dd, *J* = 17.5 Hz, 1.5 Hz), 6.33 (1H, d, *J* = 16.0 Hz), 6.63 (1H, dd, *J* = 17.5 Hz, 10.5 Hz), 6.97 (1H, d, *J* = 16.0 Hz), 7.28-7.36 (5H, m); $^{13}$C NMR (125 MHz, $CDCl_3$): $\delta$ 23.9, 38.5, 73.3, 78.2, 125.4, 127.4, 127.5, 128.3, 128.4, 134.9, 138.4, 155.3, 190.2; IR (neat): 2963 (w), 2867 (br, w), 1665 (s), 1630 (m), 1612 (m), 1404 (m), 1212 (w), 1104 (s), 987 (m), 738 (m), 698 (m) cm$^{-1}$. HRMS-(ESI+) for $C_{16}H_{21}O_2$ [M+H]: calculated: 245.1542, found: 245.1534. The crude reaction mixture was purified on silica gel (35:1-30:1 hexanes:ethyl acetate) to afford a clear, colorless oil (203 mg, 71% yield). $R_f$ = 0.14 (35:1 hexanes:ethyl acetate, stain in $KMnO_4$).

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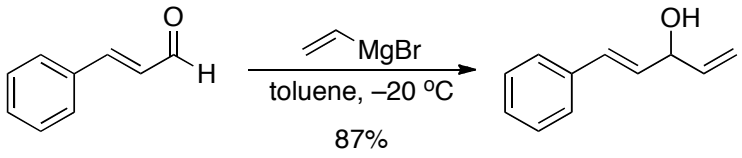
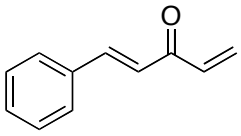
[27] Burks, H. E.; Kliman, L. T.; Morken, J. P. *J. Am. Chem. Soc.* **2009**, *131*, 9134.

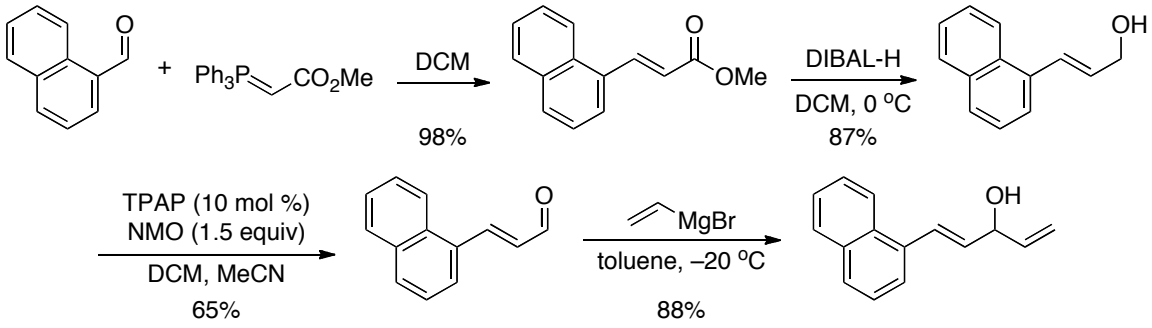
***Preparation of (E)-1-phenylpenta-1,4-dien-3-one.*** From (*E*)-1-phenylpenta-1,4-dien-3-ol, synthesized as shown below, procedure B was followed.

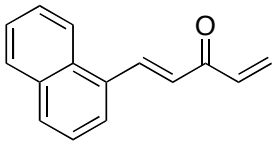



**(*E*)-1-phenylpenta-1,4-dien-3-one (1.58).** $^{1}$H NMR (500 MHz, $CDCl_3$): δ 5.89 (1H, dd, *J* = 10.5 Hz, 1.0 Hz), 6.39 (1H, dd, *J* = 17.5 Hz, 1.0 Hz), 6.72 (1H, dd, *J* = 17.5 Hz, 10.5 Hz), 7.02 (1H, d, *J* = 16.0 Hz), 7.40-7.42 (3H, m), 7.58-7.60 (2H, m), 7.68 (1H, d, *J* = 16.0 Hz); $^{13}$C NMR (125 MHz, $CDCl_3$): δ 124.1, 128.4, 128.6, 128.9, 130.6, 134.6, 135.4, 143.9, 189.5; IR (neat): 1656 (s), 1622 (s), 1594 (s), 1450 (w), 1402 (m), 1200 (m), 1104 (m), 988 (m), 688 (w) $cm^{-1}$. HRMS-(ESI+) for $C_{11}H_{11}O$ [M+H]: calculated: 159.0810, found: 159.0813. The crude reaction mixture was purified on silica gel (30:1 hexanes:ethyl acetate) to afford a yellow oil (145 mg, 59% yield). $R_f$ = 0.20 (30:1 hexanes:ethyl acetate, stain in $KMnO_4$).

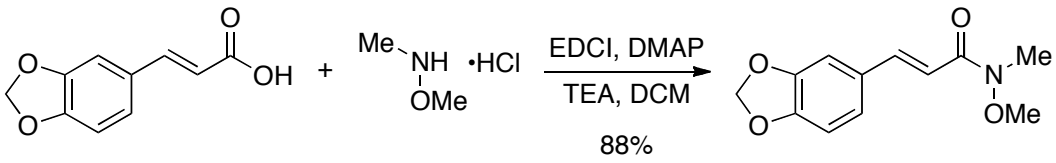
***Preparation of (E)-1-(naphthalen-1-yl)penta-1,4-dien-3-one.*** From (*E*)-1-(naphthalen-1-yl)penta-1,4-dien-3-ol, synthesized as shown below, procedure B was followed.

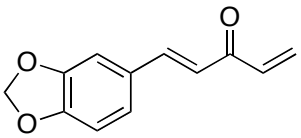



**(*E*)-1-(naphthalen-1-yl)penta-1,4-dien-3-one (1.60).** $^{1}$H NMR (400 MHz, $CDCl_3$): $\delta$ 5.95 (1H, dd, *J* = 10.8 Hz, 1.2 Hz), 6.44 (1H, dd, *J* = 17.6 Hz, 1.2 Hz), 6.77 (1H, dd, *J* = 17.6 Hz, 10.8 Hz), 7.12 (1H, d, *J* = 16.0 Hz), 7.49-7.62 (3H, m), 7.84 (1H, d, *J* = 7.2 Hz), 7.88-7.93 (2H, m), 8.23 (1H, d, *J* = 8.0 Hz), 8.55 (1H, dd, *J* = 16.0 Hz); $^{13}$C NMR (100 MHz, $CDCl_3$): $\delta$ 123.6, 125.3, 125.7, 126.5, 126.7, 127.2, 129.02, 129.03, 131.1, 131.9, 132.3, 133.9, 136.0, 141.1, 189.6; IR (neat): 3049 (w), 1655 (m), 1617 (m), 1592 (s), 1509 (w), 1402 (m), 1347 (m), 1202 (m), 1112 (m), 982 (m), 799 (m), 777 (s) $cm^{-1}$. HRMS-(ESI+) for $C_{15}H_{13}O$ [M+H]: calculated: 209.0966, found: 209.0970. The crude reaction mixture was purified on silica gel (20:1 hexanes:ethyl acetate) to afford a yellow oil (164 mg, 50% yield). $R_f$ = 0.27 (20:1 hexanes:ethyl acetate, stain in $KMnO_4$).

***Preparation of (E)-1-(benzo[d][1,3]dioxol-5-yl)penta-1,4-dien-3-one.*** From (*E*)-3-(benzo[*d*][1,3]dioxol-5-yl)-*N*-methoxy-*N*-methylacrylamide, synthesized as shown below, procedure C was followed.



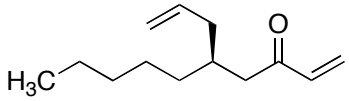




**(*E*)-1-(benzo[*d*][1,3]dioxol-5-yl)penta-1,4-dien-3-one (1.62).** $^{1}$H NMR (500 MHz, $CDCl_3$): $\delta$ 5.86 (1H, dd, *J* = 10.5 Hz, 1.0 Hz), 6.02 (2H, s), 6.36 (1H, dd, *J* = 17.5 Hz, 1.5 Hz), 6.69 (1H, dd, *J* = 17.5 Hz, 10.5 Hz), 6.84 (1H, s), 6.84 (1H, d, *J* = 16.0 Hz), 7.06-7.10 (2H, m), 7.60 (1H, d, *J* = 16.0 Hz); $^{13}$C NMR (125 MHz, $CDCl_3$): $\delta$ 101.6, 106.6, 108.7, 122.3, 125.1, 128.2, 129.1, 135.6, 143.8, 148.4, 150.0, 189.3; IR (neat): 1651 (m), 1585 (s), 1490 (s), 1448 (s), 1404 (m), 1359 (w), 1249 (s), 1206 (s), 1095 (m), 1037 (s), 985 (m), 930 (m), 854 (w), 813 (m) cm$^{-1}$. HRMS-(ESI+) for $C_{12}H_{11}O_3$ [M+H]: calculated: 203.0708, found: 203.0710. The crude reaction mixture was purified on silica gel (10:3:1 toluene:hexanes:ethyl acetate) to afford 58 mg (34%) of a yellow solid. $R_f$ = 0.35 (10:3:1 toluene:hexanes:ethyl acetate, stain in $KMnO_4$).

### 3. Representative Procedure for Conjugate Allylation

An oven-dried 2-dram vial equipped with a magnetic stir bar was charged with tris(dibenzylideneacetone) dipalladium(0) (3 mg, 0.003 mmol), **1.39** (8 mg, 0.008 mmol), and toluene (0.26 mL) in a dry-box under argon atmosphere. The vial was capped and stirred for five minutes, then (*E*)-6-((*tert*-butyldimethylsilyl)oxy)hexa-1,4-dien-3-one (30 mg, 0.132 mmol) was added, followed by allylboronic acid pinacol ester (27 mg, 0.159 mmol). The vial was sealed, removed from the dry-box, and allowed to stir at rt for 14 h. The reaction was quenched with saturated aqueous $NH_4Cl$ solution (0.5 mL) and extracted into dichloromethane (3 x 3 mL). The combined organics were dried with $MgSO_4$, filtered, and concentrated *in vacuo*. The crude reaction mixture was purified on silica gel (35:1 hexanes:ethyl acetate) to afford a clear, colorless oil (32.3 mg, 91% yield). $R_f$ = 0.31 (35:1 hexanes:ethyl acetate, stain in $KMnO_4$).

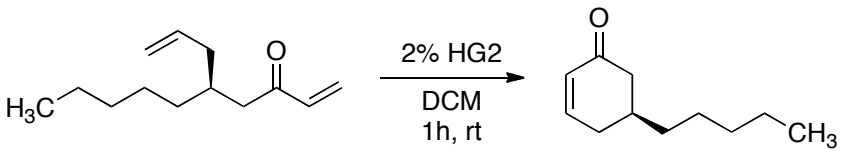
**4. Characterization and Analysis of Stereochemistry**



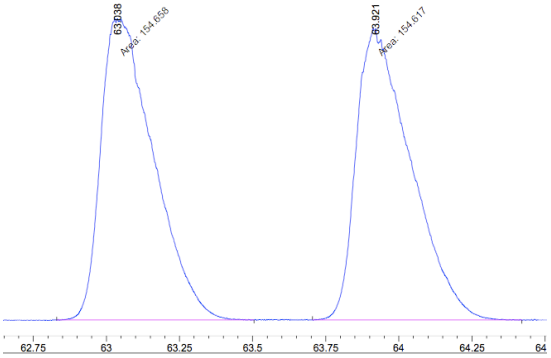
**(*S*)-5-allyldec-1-en-3-one (1.34).** The title compound was prepared *via* the representative procedure for conjugate allylation. $^{1}$H NMR (400 MHz, $CDCl_3$): $\delta$ 0.87 (3H, t, $J$ = 7.2 Hz), 1.20-1.31 (8H, m), 1.98-2.15 (3H, m), 2.45 (1H, dd, $J$ = 16.4 Hz, 6.4 Hz), 2.54 (1H, dd, $J$ = 16.4 Hz, 6.4 Hz), 4.98-5.02 (2H, m), 5.69-5.79 (1H, m), 5.79 (1H, dd, $J$ = 10.4 Hz, 0.8 Hz), 6.20 (1H, dd, $J$ = 17.6 Hz, 1.2 Hz), 6.35 (1H, ddd, $J$ = 17.6 Hz, 10.4 Hz, 0.8 Hz); $^{13}$C NMR (100 MHz, $CDCl_3$): $\delta$ 14.0, 22.6, 26.4, 32.0, 33.8, 33.8, 38.3, 44.0, 116.5, 127.6, 136.5, 136.9, 200.6; IR (neat): 3076 (w), 2958 (s), 2924 (s), 2848 (s), 1700 (s), 1683 (s), 1641 (m), 1611 (m), 1459 (m), 1396 (m), 1379 (m), 1299 (w), 1202 (w) cm$^{-1}$. HRMS-(ESI+) for $C_{13}H_{23}O$ [M+H]: calculated: 195.1749, found: 195.1836. The crude reaction mixture was purified on silica gel (35:1 hexanes:ethyl acetate) to afford a clear, colorless oil (31.0 mg, 59% yield). $R_f$ = 0.33 (35:1 hexanes:ethyl acetate, stain in $KMnO_4$).

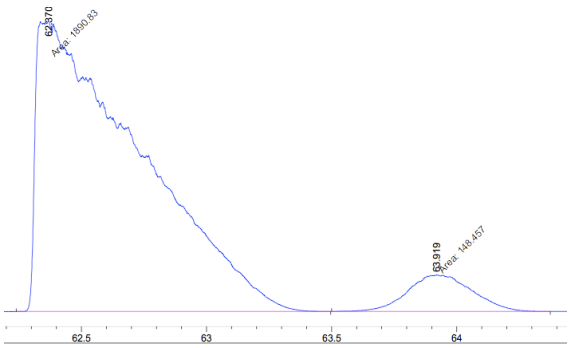
***Analysis of Stereochemistry:***

The title compound was treated with Hoveyda-Grubbs second generation catalyst to afford the ring closing metathesis product for GC analysis, as depicted below. The analogous racemic material was prepared *via* the same route, using $Ni(cod)_2$ and triphenylphosphine as the achiral catalyst system in the conjugate allylation reaction. The absolute stereochemistry was assigned by analogy (see page 54-55).




*Chiral GLC (CD-GTA, Supelco, 80 °C for 30 min, ramp 2 °C/min up to 120 °C, 20 psi) - analysis of metathesis product.*

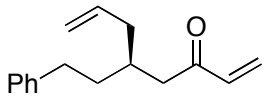



Racemic

Derived From Reaction Product

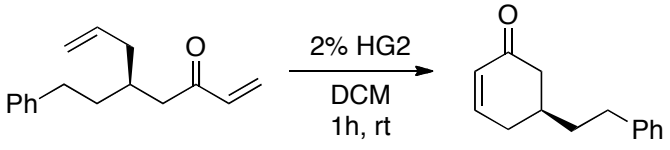
| Peak # | RetTime [min] | Type | Width [min] | Area [pA*s] | Height [pA] | Area % |
|---|---|---|---|---|---|---|
| 1 | 62.370 | MM | 0.4794 | 1890.82520 | 65.73421 | 92.72012 |
| 2 | 63.919 | MM | 0.2994 | 148.45734 | 8.26445 | 7.27988 |



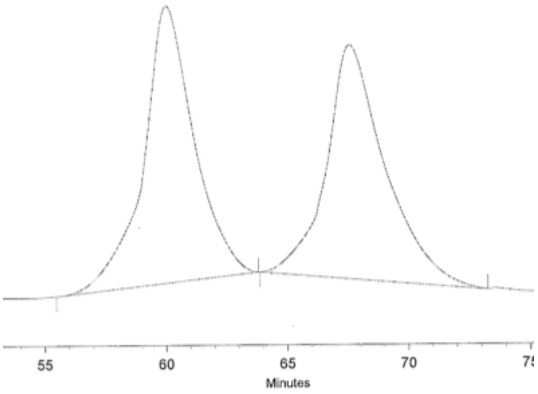
**(*S*)-5-phenethylocta-1,7-dien-3-one (1.51).** The title compound was prepared *via* the representative procedure for conjugate allylation. $^{1}$H NMR (500 MHz, $CDCl_3$): $\delta$ 1.60-1.68 (2H, m), 2.07-2.12 (1H, m), 2.15-2.21 (2H, m), 2.52 (1H, dd, *J* = 16.5 Hz, 6.5 Hz), 2.56-2.68 (3H, m), 5.02-5.06 (2H, m), 5.72-5.80 (1H, m), 5.79 (1H, dd, *J* = 10.5 Hz, 1.0 Hz), 6.20 (1H, dd, *J* = 17.5 Hz, 1.0 Hz), 6.34 (1H, dd, *J* = 17.5 Hz, 10.5 Hz), 7.16-7.19 (3H, m), 7.25-7.29 (2H, m); $^{13}$C NMR (125 MHz, $CDCl_3$): $\delta$ 33.2, 33.4, 35.7, 38.1, 43.8, 117.0, 125.7, 128.0, 128.3, 128.3, 136.1, 136.8, 142.3, 200.5; IR (neat): 2923 (br, m), 1680 (s), 1614 (w), 1454 (w), 1401 (m), 1076 (w), 992 (m), 914 (m), 747 (m), 699 (s) $cm^{-1}$. HRMS-(ESI+) for $C_{16}H_{21}O$ [M +H]: calculated: 229.1592, found: 229.1597. The crude reaction mixture was purified on silica gel (33:1 hexanes:ethyl acetate) to afford a clear, colorless oil (38.9 mg, 79% yield). $R_f$ = 0.23 (31:1 hexanes:ethyl acetate, stain in $KMnO_4$).

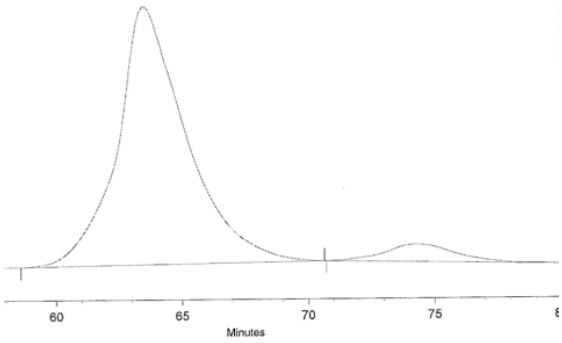
***Analysis of Stereochemistry:***

The title compound was treated with Hoveyda-Grubbs second generation catalyst to afford the ring closing metathesis product for HPLC analysis, as depicted below. The analogous racemic material was prepared *via* the same route, using $Ni(cod)_2$ and triphenylphosphine as the achiral catalyst system in the conjugate allylation reaction. The absolute stereochemistry was assigned by analogy.



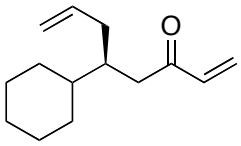
*Chiral HPLC (OD, Chiralcel, 1 mL/min, 0.8% isopropanol, 220 nm) - analysis of metathesis product.*




Racemic Derived From Reaction Product

| Time | Area | Area % | Height | Height % |
|---|---|---|---|---|
| 63.467 | 66011756 | 93.55 | 344336 | 93.60 |
| 74.233 | 4553520 | 6.45 | 23543 | 6.40 |

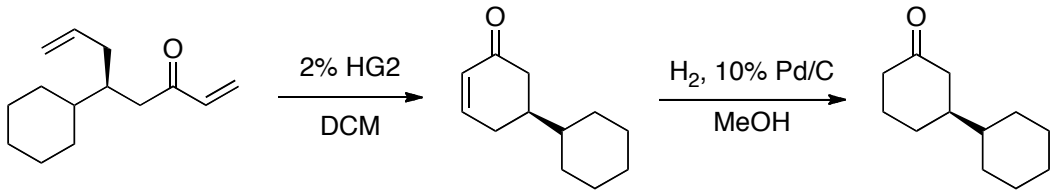


**(*S*)-5-cyclohexylocta-1,7-dien-3-one (1.52).** The title compound was prepared *via* the representative procedure for conjugate allylation, with the following modification: the reaction was quenched with 5 drops glacial acetic acid, then allowed to stir for 15 minutes at room temperature. After this time, saturated aqueous $NH_4Cl$ solution (0.5 mL) was added and the extraction protocol described in the general procedure was followed. $^1H$ NMR (400 MHz, $CDCl_3$): $\delta$ 0.94-1.05 (2H, m), 1.07-1.25 (3H, m), 1.29-1.37 (1H, m), 1.58-1.74 (5H, m), 1.90-2.02 (2H, m), 2.11-2.18 (1H, m), 2.45 (1H, dd, *J* = 16.4 Hz, 6.8 Hz), 2.54 (1H, dd, *J* = 16.4 Hz, 6.0 Hz), 4.96-5.01 (2H, m), 5.66-5.75 (1H, m), 5.78 (1H, dd, *J* = 10.4 Hz, 1.2 Hz), 6.20 (1H, dd, *J* = 17.6 Hz, 1.2 Hz), 6.35 (1H, dd, *J* = 17.6 Hz, 10.4 Hz); $^{13}C$ NMR (125 MHz, $CDCl_3$): $\delta$ 26.7, 29.6, 30.0, 35.8, 38.8, 40.3, 41.2, 116.3, 127.6, 136.8, 137.4, 201.1; IR (neat): 2924 (s), 2582 (m), 2358 (w), 1699 (m), 1682 (m), 1615 (w), 1448 (m), 1401 (m), 1082 (w), 993 (m), 960 (w), 912 (m) $cm^{-1}$. HRMS-(ESI+) for $C_{14}H_{23}O$ [M+H]: calculated: 207.1749, found: 207.1744. The crude reaction mixture was purified on silica gel (34:1 hexanes:ethyl acetate) to afford a clear, colorless oil (35.7 mg, 57% yield). $R_f$ = 0.39 (34:1 hexanes:ethyl acetate, stain in $KMnO_4$).

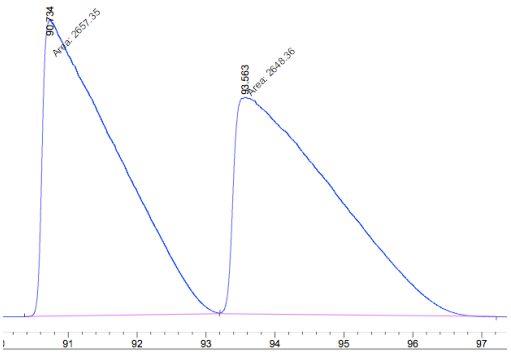
***Proof of Stereochemistry:***

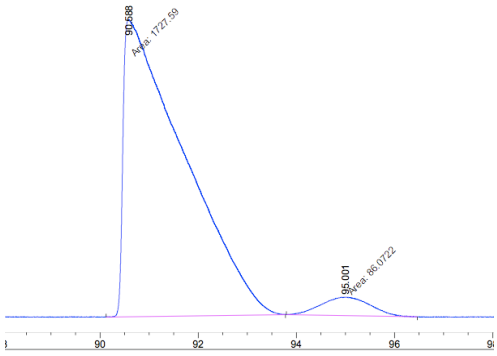
The title compound was treated with Hoveyda-Grubbs second generation catalyst to afford the ring closing metathesis product for GC analysis, as depicted below. The analogous racemic material was prepared *via* the same route, using $Ni(cod)_2$ and triphenylphosphine as the achiral catalyst system in the conjugate allylation reaction. Absolute stereochemistry was determined first by hydrogenation of the metathesis

product (below), then comparison of its optical rotation ($[\alpha]^{20}_D$ = -14.566 (*c* = 0.81, $CHCl_3$)) with the rotation of authentic (*R*)-3-cyclohexylcyclohexanone ($[\alpha]^{22}_D$ = +11.9 (*c* = 1.05, $CHCl_3$)) as previously reported in the literature,[28] and the stereochemistry was assigned to be the opposite configuration.




*Chiral GLC (β-dex, Supelco, 130 °C, 20 psi) - analysis of the metathesis product.*



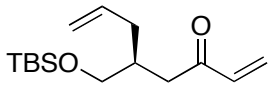




Racemic

Derived from Reaction Product

| Peak # | RetTime [min] | Type | Width [min] | Area [pA*s] | Height [pA] | Area % |
|---|---|---|---|---|---|---|
| 1 | 90.588 | MM | 1.4299 | 1727.58643 | 20.13632 | 95.25422 |
| 2 | 95.001 | MM | 1.1440 | 86.07224 | 1.25395 | 4.74578 |

[28] Tuttle, J. B.; Ouellet, S. G.; MacMillan, D. W. C. *J. Am. Chem. Soc.* **2006**, *128*, 12662.

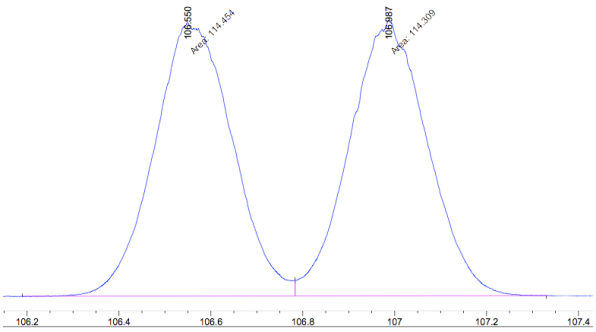



**(*S*)-5-((*tert*-butyldimethylsilyloxy)methyl)octa-1,7-dien-3-one (1.53).** The title compound was prepared *via* the representative procedure for conjugate allylation. $^{1}$H NMR (400 MHz, $CDCl_3$): $\delta$ 0.01 (3H, s), 0.02 (3H, s), 0.88 (9H, s), 1.99-2.07 (1H, m), 2.13-2.24 (2H, m), 2.46 (1H, dd, *J* = 16.4 Hz, 6.4 Hz), 2.71 (1H, dd, *J* = 16.4 Hz, 6.4 Hz), 3.48 (1H, dd, *J* = 10.0 Hz, 5.2 Hz), 3.54 (1H, dd, *J* = 10.0 Hz, 5.2 Hz), 4.95-5.04 (2H, m), 5.70-5.80 (1H, m), 5.80 (1H, dd, *J* = 10.4 Hz, 1.2 Hz), 6.21 (1H, dd, *J* = 17.6 Hz, 1.2 Hz), 6.35 (1H, dd, *J* = 17.6 Hz, 10.4 Hz); $^{13}$C NMR (125 MHz, $CDCl_3$): $\delta$ –5.5, 18.2, 25.9, 35.6, 36.6, 40.6, 64.6, 116.6, 127.8, 136.5, 137.0, 200.6; IR (neat): 2955 (m), 2929 (m), 2857 (m), 1684 (w), 1401 (w), 1254 (m), 1097 (m), 836 (s), 777 (m) cm$^{-1}$. HRMS-(ESI+) for $C_{15}H_{29}O_2Si$ [M+H]: calculated: 269.1937, found: 269.1929. The crude reaction mixture was purified on silica gel (35:1 hexanes:ethyl acetate) to afford a clear, colorless oil (32.2 mg, 91% yield). $R_f$ = 0.31 (35:1 hexanes:ethyl acetate, stain in $KMnO_4$).

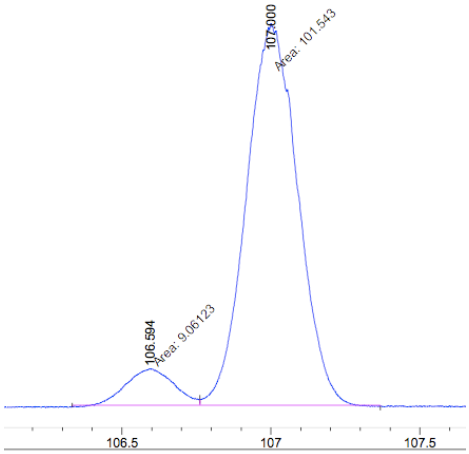
***Analysis of Stereochemistry:***

Enantioselectivity was determined by GC analysis of the title compound as compared to racemic material, prepared using $Ni(cod)_2$ and triphenylphosphine as the achiral catalyst system in the conjugate allylation reaction. Absolute stereochemistry was assigned by analogy.

*Chiral GLC (CD-GTA, Supelco, 65 °C for 40 min, ramp 0.8 °C/min up to 120 °C, 20 psi) - analysis of the title compound.*

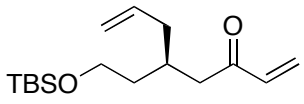



Racemic




Reaction Product

| Peak # | RetTime [min] | Type | Width [min] | Area [pA*s] | Height [pA] | Area % |
|---|---|---|---|---|---|---|
| 1 | 106.594 | MF | 0.1866 | 9.06123 | 8.09493e-1 | 8.19251 |
| 2 | 107.000 | FM | 0.1994 | 101.54268 | 8.48935 | 91.80749 |

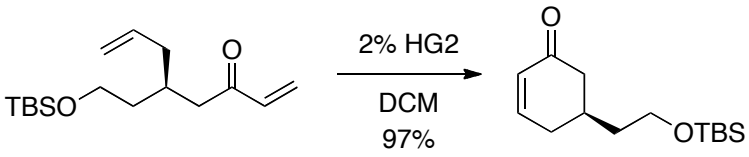



**(*R*)-5-(2-(*tert*-butyldimethylsilyloxy)ethyl)octa-1,7-dien-3-one (1.54).** The title compound was prepared *via* the representative procedure for conjugate allylation. $^{1}$H NMR (500 MHz, $CDCl_3$): $\delta$ 0.03 (6H, s), 0.88 (9H, s), 1.46-1.52 (1H, m), 1.54-1.60 (1H, m), 2.03-2.07 (1H, m), 2.12-2.15 (1H, m), 2.22 (1H, p, *J* = 6.5 Hz), 2.56 (2H, d, *J* = 7.0 Hz), 3.65 (2H, dd, *J* = 6.5 Hz, 3.5 Hz), 4.99-5.03 (2H, m), 5.70-5.78 (1H, m), 5.79 (1H, dd, *J* = 10.5 Hz, 1.0 Hz), 6.20 (1H, dd, *J* = 17.5 Hz, 1.0 Hz), 6.34 (1H, dd, *J* = 17.5 Hz, 10.5 Hz); $^{13}$C NMR (125 MHz, $CDCl_3$): $\delta$ –5.3, 18.3, 25.9, 30.9, 36.6, 38.4, 43.9, 61.2, 116.9, 127.9, 136.3, 136.8, 200.6; IR (neat): 2928.5 (w), 2856.8 (w), 1682.4 (w), 1400.0 (w), 1253.5 (m), 1095.1 (s), 993.4 (w), 959.0 (w), 912.9 (w), 834.3 (s), 774.6 (s) $cm^{-1}$. HRMS-(ESI+) for $C_{16}H_{31}O_2Si$ [M+H]: calculated: 283.2093, found: 283.2087. The crude reaction mixture was purified on silica gel (40:1 hexanes:ethyl acetate) to afford a clear, colorless oil (25.7 mg, 53% yield). $R_f$ = 0.35 (35:1 hexanes:ethyl acetate, stain in $KMnO_4$).

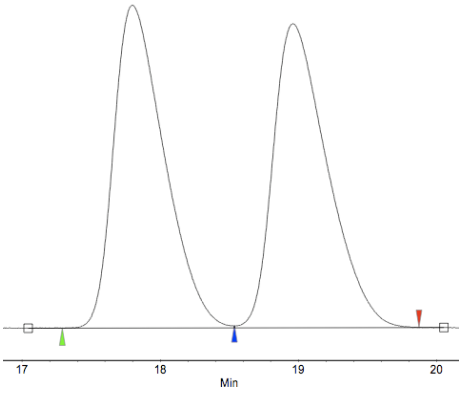
***Proof of Stereochemistry:***

The title compound was treated with Hoveyda-Grubbs second generation catalyst to afford the ring closing metathesis product for SFC analysis, as depicted below. The analogous racemic material was prepared *via* the same route, using $Ni(cod)_2$ and triphenylphosphine as the achiral catalyst system in the conjugate allylation reaction. In order to determine absolute stereochemistry, the metathesis product was subjected to deprotection of the silyl ether, followed by 1,4-hydrogenation of the enone to afford **1.72**, as shown below. The optical rotation of **1.72**, derived from the conjugate allylation product ($[\alpha]^{20}_D$ = -9.349 (*c* = 0.385, $CHCl_3$)) was compared to the rotation of

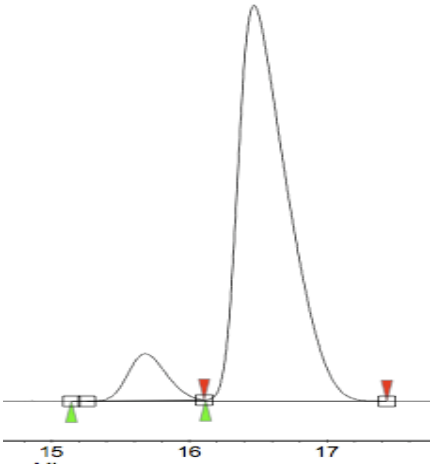
authentic (*S*)-3-(2-hydroxyethyl)cyclohexanone ($[\alpha]^{20}_D$ = +14.0 (*c* = 0.08, $CHCl_3$) as previously reported in the literature,[29] and the stereochemistry was assigned to be the opposite configuration.




*Chiral SFC (OD-H, Chiralpak, 220nm, 1.0 mL/min, 0.4% MeOH, 150 bar, 50 °C) - analysis of the metathesis product.*

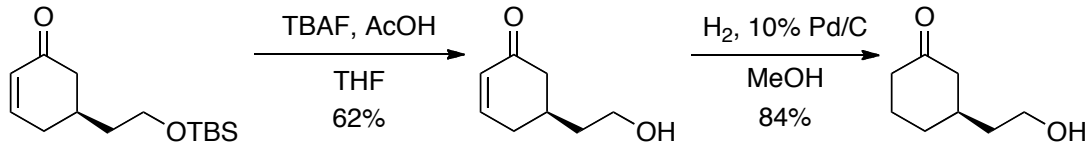



Racemic



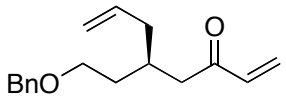

Derived from Reaction Product

| Index | Name | Start | Time | End | RT Offset | Quantity | Height | Area | Area |
|---|---|---|---|---|---|---|---|---|---|
| | | [Min] | [Min] | [Min] | [Min] | [% Area] | [µV] | [µV.Min] | [%] |
| 2 | UNKNOWN | 15.14 | 15.68 | 16.11 | 0.00 | 8.49 | 590.1 | 191.7 | 8.492 |
| 1 | UNKNOWN | 16.12 | 16.47 | 17.44 | 0.00 | 91.51 | 4992.3 | 2065.5 | 91.508 |




**1.72**

[29] Jiricek, J.; Blechert, S. *J. Am. Chem. Soc.* **2004**, *126*, 3534.

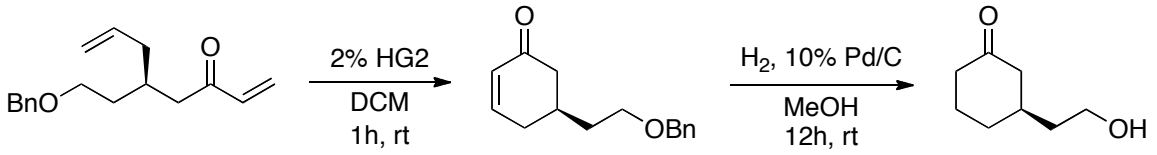



**(*R*)-5-(2-(benzyloxy)ethyl)octa-1,7-dien-3-one (1.55).** The title compound was prepared *via* the representative procedure for conjugate allylation. $^{1}$H NMR (400 MHz, $CDCl_3$): δ 1.56-1.72 (2H, m), 2.02-2.15 (2H, m), 2.26 (1H, app p, *J* = 1.6 Hz), 2.55 (2H, d, *J* = 6.8 Hz), 3.51 (2H, app dt, *J* = 6.4 Hz, 2.4 Hz), 4.47 (2H, s), 4.98-5.04 (2H, m), 5.68-5.76 (1H, m), 5.77 (1H, dd, *J* = 10.4 Hz, 1.2 Hz), 6.17 (1H, dd, *J* = 17.6 Hz, 1.2 Hz), 6.32 (1H, dd, *J* = 17.6 Hz, 10.4 Hz), 7.27-7.34 (5H, m); $^{13}$C NMR (125 MHz, $CDCl_3$): δ 31.1, 33.6, 38.5, 43.8, 68.3, 72.8, 117.0, 127.5, 127.6, 127.9, 128.3, 136.2, 136.8, 138.4, 200.5; IR (neat): 2923 (s), 2855 (s), 1698 (s), 1680 (s), 1614 (m), 1454 (m), 1401 (m), 1365 (m), 1206 (w), 1100 (s), 1028 (w), 993 (m), 962 (m), 914 (m), 736 (s), 698 (s) $cm^{-1}$. HRMS-(ESI+) for $C_{17}H_{23}O_2$ [M+H]: calculated: 259.1698, found: 259.1702. The crude reaction mixture was purified on silica gel (24:1 toluene:diethyl ether) to afford a clear, colorless oil (26.0 mg, 53% yield). $R_f$ = 0.28 (21:1 toluene:diethyl ether, stain in PMA).

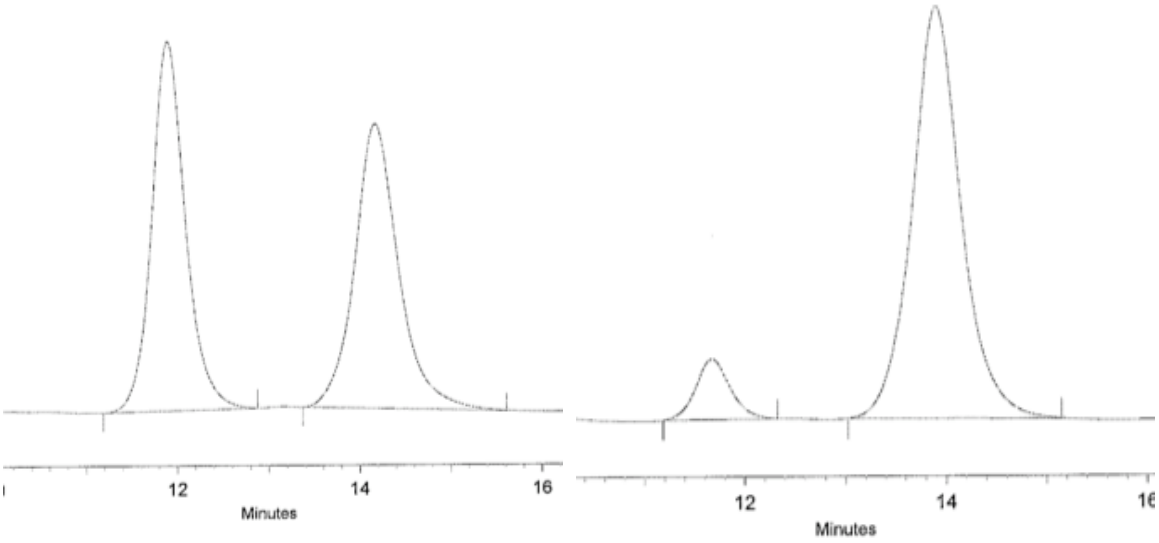
***Proof of Stereochemistry:***

Enantioselectivity was determined by HPLC analysis of the title compound as compared to racemic material, prepared using $Ni(cod)_2$ and triphenylphosphine as the achiral catalyst system in the conjugate allylation reaction. In order to determine the absolute stereochemistry, the reaction product was treated with Hoveyda-Grubbs second generation catalyst followed by catalytic hydrogenation, as shown below. The optical rotation of the compound derived from the allylation reaction product ($[\alpha]^{20}_D$ = -9.914 (*c* = 0.355, $CHCl_3$)) was compared to the rotation of authentic (*S*)-3-(2-

hydroxyethyl)cyclohexanone ($[\alpha]^{20}_D$ = +14.0 (*c* = 0.08, $CHCl_3$) as previously reported in the literature,[29] and the stereochemistry was assigned to be the opposite configuration.

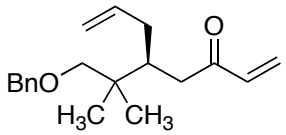



*Chiral HPLC (OD, Chiralcel, 1 mL/min, 1.0% isopropanol, 220 nm) - analysis of title compound.*




Racemic Reaction Product

| Time | Area | Area % | Height | Height % |
|---|---|---|---|---|
| 11.667 | 3124720 | 9.41 | 130298 | 12.82 |
| 13.883 | 30081289 | 90.59 | 885967 | 87.18 |



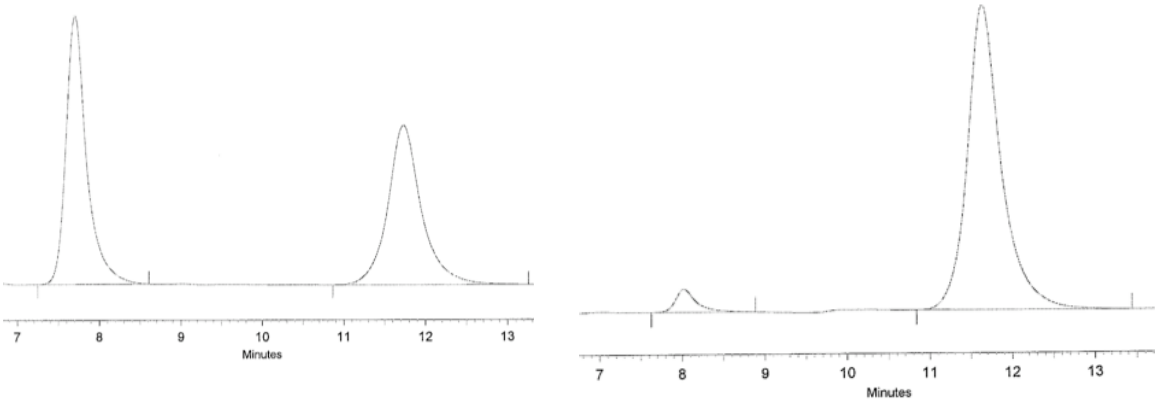

**(*S*)-5-(1-benzyloxy)-2-methylpropan-2-yl)octa-1,7-dien-3-one (1.56).** The title compound was prepared *via* the representative procedure for conjugate allylation, with the following modifications: The conjugate allylation was allowed to stir at room temperature for 48 h, rather than 14 h. Additionally, for reaction work-up, the reaction was diluted with $CHCl_3$ (0.5 mL), then quenched with glacial acetic acid (0.2 mL) and allowed to stir at 45 °C for 3 h. After this time, saturated aqueous $NH_4Cl$ solution (0.5 mL) was added and the extraction protocol described in the general procedure was followed. $^1H$ NMR (500 MHz, $CDCl_3$): $\delta$ 0.89 (3H, s), 0.92 (3H, s), 1.75-1.82 (1H, m), 2.30-2.36 (2H, m), 2.39 (1H, dd, *J* = 17.0 Hz, 6.0 Hz), 2.71 (1H, dd, *J* = 17.0 Hz, 5.0 Hz), 3.18 (2H, dd, *J* = 14.5 Hz, 9.0 Hz), 4.43 (2H, s), 4.91-4.98 (2H, m), 5.65-5.73 (1H, m), 5.69 (1H, dd, *J* = 10.5 Hz, 1.0 Hz), 6.15 (1H, dd, *J* = 17.5 Hz, 1.0 Hz), 6.32 (1H, dd, *J* = 17.5 Hz, 10.5 Hz), 7.26-7.35 (5H, m); $^{13}C$ NMR (125 MHz, $CDCl_3$): $\delta$ 22.6, 23.3, 35.4, 37.4, 39.1, 40.8, 73.0, 78.1, 116.1, 127.1, 127.3, 127.4, 128.2, 136.6, 138.3, 138.7, 200.6; IR (neat): 2959 (m), 2926 (m), 2855 (m), 1683 (s), 1616 (w), 1454 (m), 1399 (m), 1365 (m), 1098 (s), 993 (m), 911 (m), 736 (m), 698 (m) $cm^{-1}$. HRMS-(ESI+) for $C_{19}H_{27}O_2$ [M+H]: calculated: 287.2011, found: 287.2007. The crude reaction mixture was purified on silica gel (35:1 hexanes:ethyl acetate) to afford a clear, colorless oil (28.2 mg, 81% yield). $R_f$ = 0.21 (35:1 hexanes:ethyl acetate, stain in $KMnO_4$).

***Analysis of Stereochemistry:***

Enantioselectivity was determined by HPLC analysis of the title compound as compared to racemic material, prepared using $Pd_2(dba)_3$ and a 1:1 mixture of **1.39** and

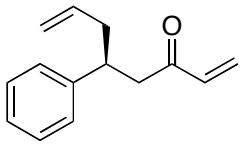
***ent*-1.39** as the racemic catalyst system in the conjugate allylation reaction. Absolute stereochemistry was determined by analogy.

*Chiral HPLC (OD, Chiralcel, 1 mL/min, 1% isopropanol, 220nm) - analysis of title compound.*




Racemic Reaction Product

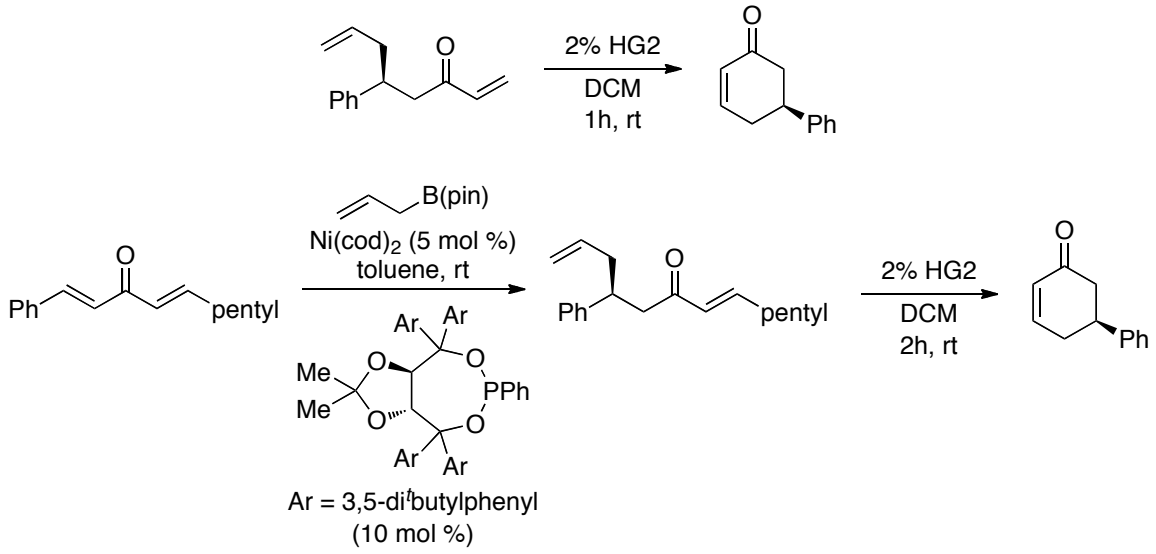
| Time | Area | Area % | Height | Height % |
|---|---|---|---|---|
| 8.017 | 269914 | 4.50 | 15175 | 7.08 |
| 11.650 | 5725910 | 95.50 | 199241 | 92.92 |



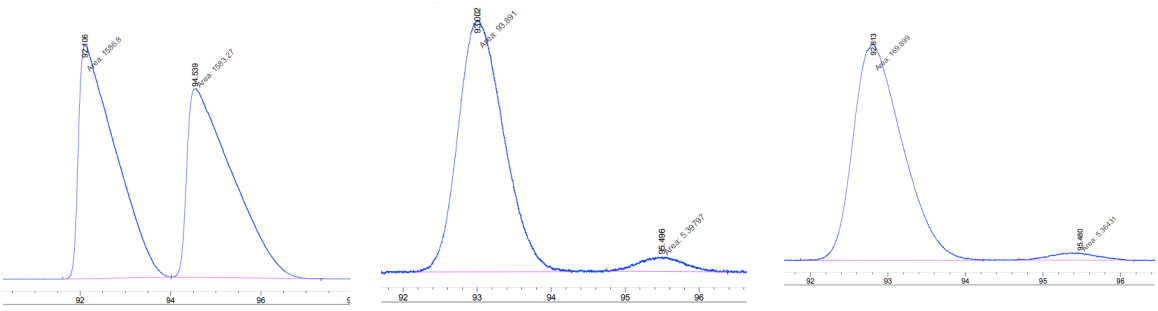
**(*S*)-5-phenylocta-1,7-dien-3-one (1.64).** The title compound was prepared *via* the representative procedure for conjugate allylation $^{1}$H NMR (500 MHz, $CDCl_3$): $\delta$ 2.40 (2H, app t, $J$ = 7.0 Hz), 2.90 (2H, app dq, $J$ = 16.0 Hz, 6.5 Hz), 3.33 (1H, p, $J$ = 7.0 Hz), 4.95-5.01 (2H, m), 5.65 (1H, app ddt, $J$ = 17.0 Hz, 10.0 Hz, 7.0 Hz), 5.76 (1H, dt, $J$ = 10.5 Hz, 0.5 Hz), 6.15 (1H, dt, $J$ = 17.5 Hz, 0.5 Hz), 6.28 (1H, ddd, $J$ = 17.5 Hz, 10.5 Hz, 0.5 Hz), 7.17-7.20 (3H, m), 7.27-7.30 (2H, m); $^{13}$C NMR (125 MHz, $CDCl_3$): $\delta$ 40.6, 40.7, 45.6, 116.8, 126.4, 127.5, 128.1, 128.4, 136.1, 136.7, 144.1, 199.4; IR (neat): 2923 (br, w), 1680 (s), 1614 (w), 1401 (m), 1076 (w), 1032 (m), 915 (m), 761 (m), 700 (s) $cm^{-1}$. HRMS-(ESI+) for $C_{14}H_{17}O$ [M+H]: calculated: 201.1279, found: 201.1277. The crude reaction mixture was purified on silica gel (35:1 hexanes:ethyl acetate) to afford a light yellow oil (35.7 mg, 80% yield). $R_f$ = 0.21 (35:1 hexanes:ethyl acetate, stain in $KMnO_4$).

***Proof of Stereochemistry:***

The title compound was treated with Hoveyda-Grubbs second generation catalyst to afford the ring closing metathesis product for GC analysis, as depicted below. The analogous racemic material was prepared *via* the same route, using $Ni(cod)_2$ and triphenylphosphine as the achiral catalyst system in the conjugate allylation reaction. Absolute stereochemistry was determined by comparison of the GC trace of the metathesis product to authentic (*S*)-5-phenylcyclohex-2-enone, prepared as shown below.[4b]

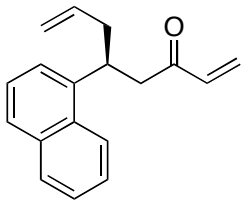



*Chiral GLC (β-dex, Supelco, 130 °C, 25 psi) - analysis of the metathesis product.*



Racemic Derived from Reaction Product From Authentic Product

| Peak # | RetTime [min] | Type | Width [min] | Area [pA*s] | Height [pA] | Area % |
|---|---|---|---|---|---|---|
| 1 | 93.002 | MM | 0.7148 | 93.89096 | 2.18914 | 94.56337 |
| 2 | 95.496 | MM | 0.6915 | 5.39797 | 1.30109e-1 | 5.43663 |

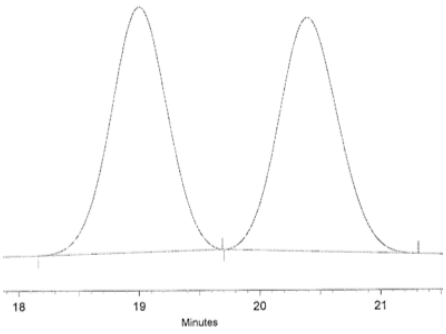


**(*S*)-5-(naphthalen-1-yl)octa-1,7-dien-3-one (1.65).** The title compound was prepared *via* the representative procedure for conjugate allylation. $^{1}$H NMR (500 MHz, $CDCl_3$): $\delta$ 2.50-2.61 (2H, m), 3.00 (1H, dd, *J* = 17.0 Hz, 5.5 Hz), 3.09 (1H, dd, *J* = 17.0 Hz, 8.0 Hz), 4.32 (1H, app p, *J* = 7.0 Hz), 4.93-4.96 (1H, m), 5.03 (1H, app dq, *J* = 17.0 Hz, 1.5 Hz), 5.68 (1H, app ddt, *J* = 17.0 Hz, 10.5 Hz, 7.0 Hz), 5.77 (1H, dd, *J* = 10.5 Hz, 1.0 Hz), 6.18 (1H, dd, *J* = 17.5 Hz, 1.0 Hz), 6.32 (1H, dd, *J* = 17.5 Hz, 10.5 Hz), 7.36 (1H, dd, *J* = 7.0 Hz, 1.0 Hz), 7.43 (1H, app t, *J* = 7.5), 7.48 (1H, app td, *J* = 6.5 Hz, 1.0 Hz), 7.54 (1H, app td, *J* = 7.0 Hz, 1.5 Hz), 7.72 (1H, d, *J* = 8.0 Hz), 7.85 (1H, dd, *J* = 8.0 Hz), 8.20 (1H, d, *J* = 8.5 Hz); $^{13}$C NMR (125 MHz, $CDCl_3$): $\delta$ 39.9, 45.3, 116.9, 123.2, 125.3, 125.5, 126.0, 126.9, 128.0, 128.9, 131.6, 134.0, 136.1, 136.7, 140.2, 199.3; IR (neat): 2957 (m), 2921 (s), 2851 (m), 1681 (m), 1614 (w), 1464 (w), 1398 (m), 992 (w), 965 (w), 915 (w), 797 (m), 778 (s) cm$^{-1}$. HRMS-(ESI+) for $C_{18}H_{19}O$ [M+H]: calculated: 251.1436, found: 251.1424. The crude reaction mixture was purified on silica gel (30:1 hexanes:ethyl acetate) to afford a light yellow oil (22.2 mg, 37% yield). $R_f$ = 0.23 (30:1 hexanes:ethyl acetate, stain in $KMnO_4$).

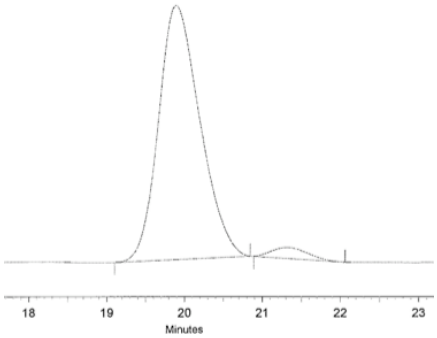
***Analysis of Stereochemistry:***

Enantioselectivity was determined by HPLC analysis of the title compound as compared to racemic material, prepared using $Ni(cod)_2$ and triphenylphosphine as the achiral catalyst system in the conjugate allylation reaction. Absolute stereochemistry was assigned by analogy.

*Chiral HPLC (OD-R, Chiralcel, 1.5 mL/min, 0.6% isopropanol, 220nm) - analysis of title compound.*

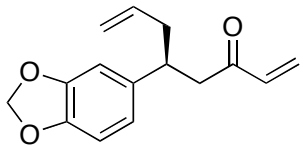



Racemic




Reaction Product

| Time | Area | Area % | Height | Height % |
|---|---|---|---|---|
| 19.883 | 14745341 | 96.41 | 398643 | 95.89 |
| 21.317 | 549196 | 3.59 | 17102 | 4.11 |

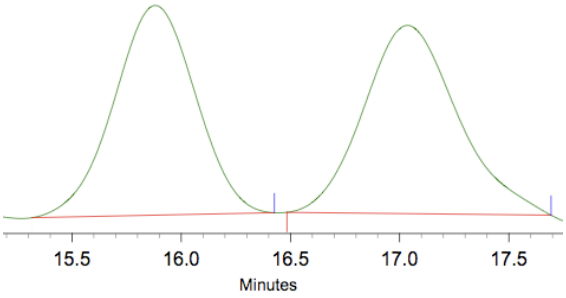


**(*S*)-5-(benzo[*d*][1,3]dioxol-5-yl)octa-1,7-dien-3-one (1.66).** The title compound was prepared *via* the representative procedure for conjugate allylation. $^{1}$H NMR (500 MHz, $CDCl_3$): $\delta$ 2.34 (2H, app dt, $J$ = 7.0 Hz, 1.5 Hz), 2.84 (2H, app dq, $J$ = 16.5 Hz, 6.5 Hz), 3.25 (1H, app p, $J$ = 7.0 Hz), 4.95-5.01 (2H, m), 5.65 (1H, app ddt, $J$ = 17.0 Hz, 10.0 Hz, 7.0 Hz), 5.76 (1H, dd, $J$ = 10.5 Hz, 1.5 Hz), 5.92 (2H, s), 6.15 (1H, dd, $J$ = 17.5 Hz, 1.0 Hz), 6.28 (1H, dd, $J$ = 18.0 Hz, 10.5 Hz), 6.64 (1H, dd, $J$ = 8.0 Hz, 1.5 Hz), 6.69 (1H, d, $J$ = 1.5), 6.71 (1H, d, $J$ = 8.0 Hz); $^{13}$C NMR (125 MHz, $CDCl_3$): $\delta$ 40.6, 40.8, 45.8, 100.8, 107.7, 108.1, 116.8, 120.6, 128.1, 136.1, 136.7, 138.0, 145.9, 147.6, 199.4; IR (neat): 2919 (m), 2851 (w), 1711 (m), 1611 (w), 1503 (m), 1489 (s), 1441 (m), 1245 (s), 1098 (w), 1039 (m), 935 (w), 811 (w) $cm^{-1}$. HRMS-(ESI+) for $C_{15}H_{17}O_3$ [M+H]: calculated: 245.1178, found: 245.1174. The crude reaction mixture was purified on silica gel (24:1 hexanes:ethyl acetate) to afford a light yellow oil (34.9 mg, 76% yield) that could not be separated from dibenzylideneacetone (38.2 mg, mass of product mixture). $R_f$ = 0.24 (24:1 hexanes:ethyl acetate, stain in $KMnO_4$).

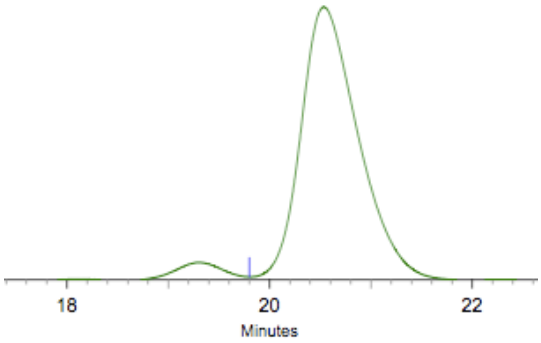
***Analysis of Stereochemistry:***

Enantioselectivity was determined by HPLC analysis of the title compound as compared to racemic material, prepared using $Ni(cod)_2$ and triphenylphosphine as the achiral catalyst system in the conjugate allylation reaction. Absolute stereochemistry was assigned by analogy.

*Chiral HPLC (OD-R, Chiralcel, 1.0 mL/min, 0.5% isopropanol, 220nm) - analysis of title compound.*



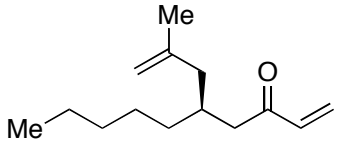

Racemic




Reaction Product

| Retention Time | Area | Area % | Height | Height % |
|---|---|---|---|---|
| 19.303 | 25462821 | 5.20 | 758410 | 6.05 |
| 20.533 | 463864021 | 94.80 | 11771477 | 93.95 |

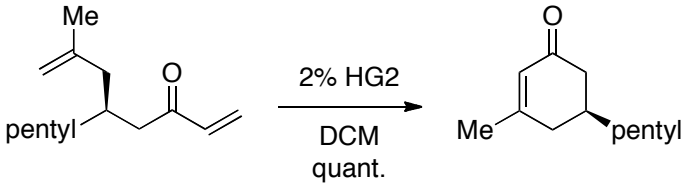
**5. Experimental and Characterization Data for Related Tranformations**



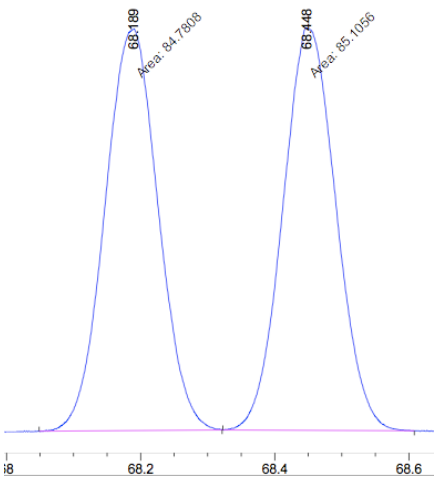

**(*S*)-5-(2-methylallyl)dec-1-en-3-one (1.71).** The title compound was prepared *via* the representative procedure for conjugate allylation with the following modifications: 2-methylallyl boronic acid pinacol ester was used. $^1$H NMR (500 MHz, $CDCl_3$): $\delta$ 0.87 (3H, t, $J$ = 7.5 Hz), 1.22-1.29 (8H, m), 1.70 (3H, s), 1.89 (1H, dd, 13.5 Hz, 8.5 Hz), 2.07 (1H, dd, 13.5 Hz, 7.0 Hz), 2.14-2.19 (1H, m), 2.44 (1H, dd, $J$ = 16.0 Hz, 7.5 Hz), 2.52 (1H, dd, $J$ = 16.0 Hz, 6.0 Hz), 4.66 (1H, dd, $J$ = 1.5 Hz, 1.0 Hz), 4.75 (1H, dd, $J$ = 2.0 Hz, 1.5 Hz), 5.78 (1H, dd, $J$ = 10.5 Hz, 1.0 Hz), 6.19 (1H, dd, $J$ = 17.5 Hz, 1.0 Hz), 6.35 (1H, dd, $J$ = 17.5 Hz, 10.5 Hz). The crude reaction mixture was purified on silica gel (50:1 hexanes:ethyl acetate) to afford a clear oil (29.5 mg, 88% yield). $R_f$ = 0.19 (50:1 hexanes:ethyl acetate, stain in $KMnO_4$).

***Analysis of Stereochemistry:***

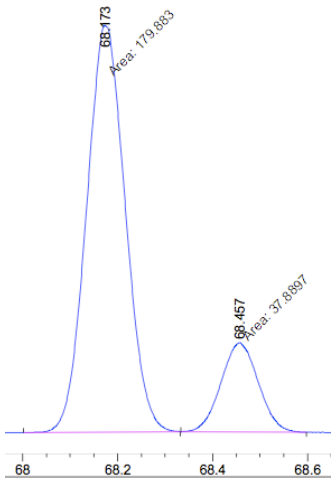
The title compound was treated with Hoveyda-Grubbs second generation catalyst to afford the ring closing metathesis product for GC analysis, as depicted below. The analogous racemic material was prepared *via* the same route, using $Pd_2(dba)_3$ and a 1:1 mixture of **(*R,R*)-1.35** and **(*S,S*)-1.35** as the racemic catalyst system in the conjugate allylation reaction. The absolute stereochemistry was assigned by analogy.



*Chiral GLC (β-dex, Supelco, 80 °C, 30 min, then 2°/min to 160 °C, 10 min, 25 psi) - analysis of the metathesis product.*




racemic




Derived from Reaction Product

| Peak # | RetTime [min] | Type | Width [min] | Area [pA*s] | Height [pA] | Area % |
|---|---|---|---|---|---|---|
| 1 | 68.173 | MM | 0.0945 | 179.88330 | 31.73661 | 82.60128 |
| 2 | 68.457 | MM | 0.0907 | 37.88972 | 6.96296 | 17.39872 |

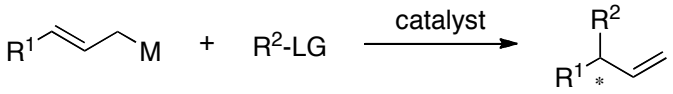
## Chapter 2

# Enantioselective Allyl-Allyl Cross-Coupling *via* 3,3′-Reductive Elimination of Allyl Metal Complexes

## I. Introduction

The catalytic cross-coupling of organometallic reagents with organic electrophiles is a powerful tool in the assembly of complex organic molecules. Such transformations allow facile carbon-carbon bond formation, and may also afford the construction of a stereogenic center.[1] Though such cross-couplings are well documented, few studies have documented the enantioselective cross-coupling of prochiral allyl metal reagents with organic electrophiles. These hold particular significance due to the malleability of the olefinic functional group (Scheme 2.1).[2]

**Scheme 2.1: General Enantioselective Allyl Metal Cross-Coupling**

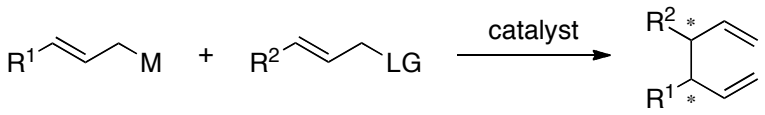



[1] *Metal-Catalyzed Cross-Coupling Reactions*; de Meijere, A.; Diederich, F., Eds.; Wiley-VCH: New York, 2004.

[2] (a) Yamamoto, Y.; Takada, S.; Miyaura, N. *Chem. Lett.* **2006**, *35*, 1368. (b) Yamamoto, Y.; Takada, S.; Miyaura, N.; Iyama, T.; Tachikawa, H. *Organometallics* **2009**, *28*, 152.

An important yet under-developed subsection of this chemistry is the asymmetric cross-coupling of allylic electrophiles and allyl metal reagents. With the use of prochiral coupling partners, this carbon-carbon bond-forming method is capable of generating products bearing two stereogenic centers as well as vicinal alkenes, a common motif in natural products (Scheme 2.2). The exploration of this reaction has been impeded by a number of challenges, including tendency toward undesired homocoupling, as well as difficulties in controlling enantio- and regioselectivity with respect to each coupling partner.[3] Furthermore, transition metal π-allyl complexes with alkyl substitution are known to undergo β-hydride elimination to form 1,3-dienes under mild conditions.[4]

**Scheme 2.2: General Enantioselective Allyl-Allyl Cross-Coupling**




Seeking to overcome the challenges associated with this transformation, we have developed an asymmetric cross-coupling of prochiral allyl electrophiles with allyl metal reagents. The chiral catalyst system provides a handle for regiocontrol in the allyl-allyl cross-coupling reaction, generating products in high levels of selectivity. By employing substituted allyl metal reagents, we have also established a diastereoselective transformation. The development of these methods, as well as detailed studies into the reaction mechanism, are presented herein.

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[3] Negishi, E.-i.; Liao, B. In *Handbook of Organopalladium Chemistry for Organic Synthesis, Vol. 1*; Negishi, E.-i.; de Meijere, A., Eds.; Wiley-Interscience: West Lafayette, 2002; p 591.

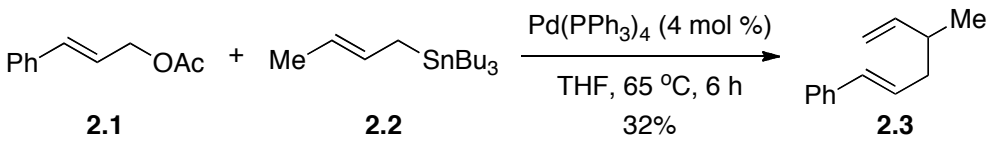
[4] Keinen, E.; Kumar, S.; Dangur, V.; Vaya, J. *J. Am. Chem. Soc.* **1994**, *116*, 11151.

## II. Background

### A. Allyl-Allyl Coupling Reactions and Mechanistic Proposals For An Outer Sphere Reaction Pathway

In 1980, Trost and coworkers reported the first example of a catalytic coupling of an allyl electrophile and an allyl metal.[5] In this seminal publication, cinnamyl acetate **2.1** was reacted with crotyltri(*n*-butyl)stannane **2.2** under Pd(0)-catalysis to provide a single regioisomer of the cross-coupling product **2.3** in modest yield (Scheme 2.3).

**Scheme 2.3: Trost Allylstannane Cross-Coupling**



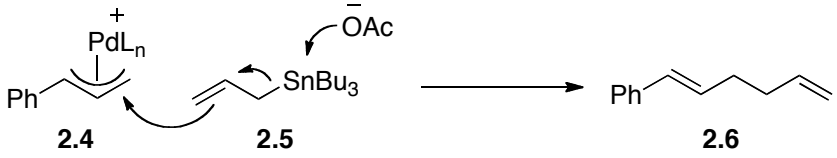

**2.1** **2.2** **2.3**

Trost refutes the possibility of a transmetallation-reductive elimination sequence for coupling with the allyl stannane based on the isolation of product **2.3** in which only allylic transposition is observed. He suggests that a scrambling of the crotyl group would occur if it were to transmetallate onto the Pd-catalyst, leading to a mixture of regioisomeric products. Furthermore, when utilizing tetra(*n*-butyl)stannane, no cross-coupling is observed, indicating the inherent difficulty for transmetallation of alkyl stannanes. In light of these observations, Trost proposes an outer sphere mechanism for this transformation (Scheme 2.4); that is, through an $S_E2'$ pathway, the crotyl stannane directly attacks the $\eta^3$-cinnamyl ligand on the Pd intermediate, forming the

[5] Trost, B. M.; Keinan, E. *Tetrahedron Lett.* **1980**, *21*, 2595.

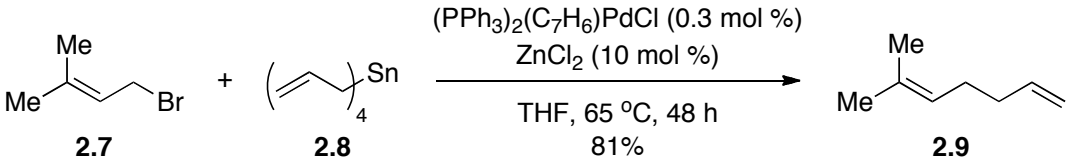
cross-coupling product **2.6**. Though this method tolerates substitution at both the β- and γ-sites of the allylic stannane, the scope of allyl acetates is limited to those containing substitution that precludes β-hydride elimination.

**Scheme 2.4: Outer Sphere Allyl-Allyl Coupling Mechanism**




At the same time, Stille and coworkers disclosed an allyl-allyl cross-coupling reaction between alkyl-substituted allylic bromides and tetraallylstannane **2.8** catalyzed by Pd and Zn (Scheme 2.5).[6] The Stille group noted carbon-carbon bond formation at the least sterically hindered site of the allyl electrophile, the scope of which is not limited by the presence of β-hydrogens. Like Trost, Stille proposes an outer sphere mechanism for nucleophilic attack based on observed allylic transposition of the tin reagent.

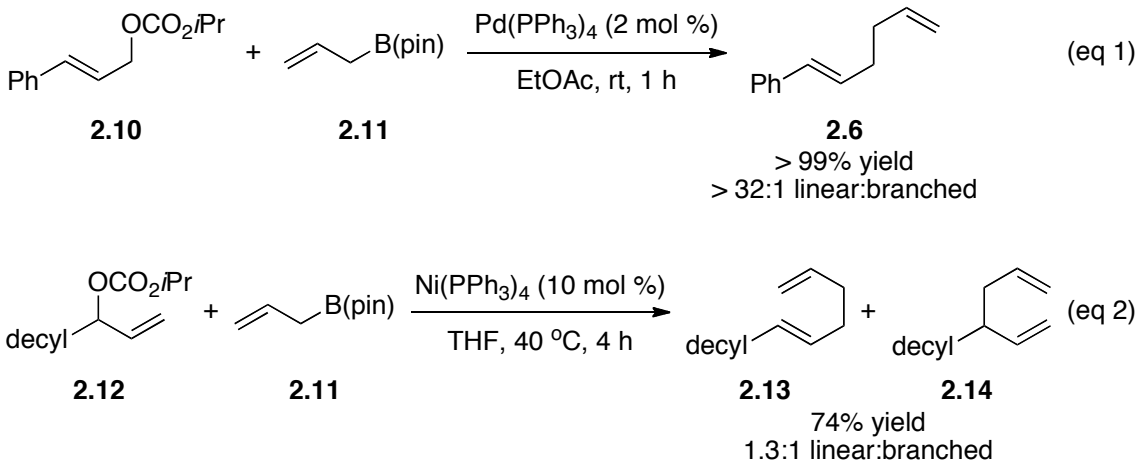
**Scheme 2.5: Stille Allylstannane Cross-Coupling**




[6] Godschalx, J.; Stille, J. K. *Tetrahedron Lett.* **1980**, *21*, 2599.

In 2009, concurrent with the development of our own allyl-allyl coupling method, the Kobayashi group explored a catalytic intermolecular non-symmetrical $sp^3$-$sp^3$ allyl-allyl cross-coupling reaction.[7] Utilizing allylboronic acid pinacol ester [allylB(pin)] (**2.11**), an allyl carbonate electrophile is converted to the 1,5-diene coupling product under Pd(0)- or Ni(0)-catalysis (Scheme 2.6). Aryl-substituted carbonates favor the linear achiral coupling product **2.6** under Pd(0)-catalysis (equation 1); however, the alkyl-substituted carbonates suffer from β-hydride elimination under the same conditions. To suppress formation of the 1,3-diene product, $Ni(PPh_3)_4$ may be employed, although the linear to branched product ratio suffers (equation 2). Notably, the linear and branched isomers of the carbonate starting material react analogously.

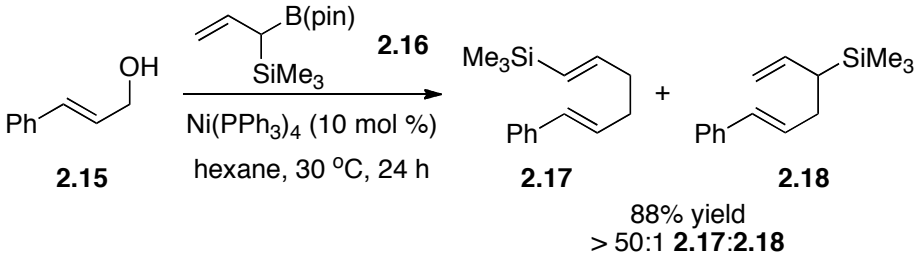
**Scheme 2.6: Kobayashi Allyl-Allyl Cross-Coupling Method**




[7] Flegeau, E. F.; Schneider, U.; Kobayashi, S. *Chem. Eur. J.* **2009**, *15*, 12247.

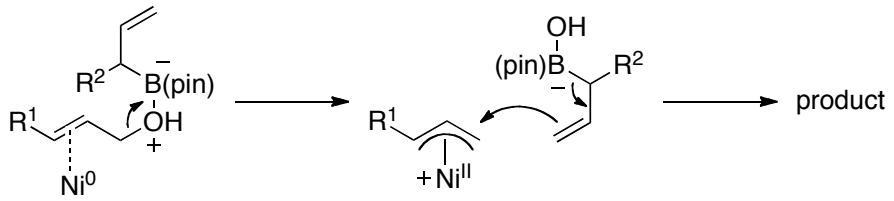
Following their initial report, the Kobayashi group recently extended this method to include allyl alcohols as the electrophilic cross-coupling partner.[8] Branched and linear allyl alcohols participate in allyl-allyl cross-coupling with allylB(pin) (**2.11**) under Ni(0)-catalysis, favoring the linear coupling product in excellent regioselectivity. Included in their communication is one example of coupling with an $\alpha$-substituted allylboron reagent **2.16** (Scheme 2.7). Based on the regiochemical outcome of this reaction, the authors propose a mechanism that accounts for activation of the allylic alcohol as well as the excellent selectivity for the linear product (Scheme 2.8). Mediated by Lewis acid activation of the allylic alcohol with the allylboron reagent, the Ni(0)-catalyst undergoes oxidative addition to form an $\eta^3$-$\pi$-allyl complex. Similar to the mechanisms described by Trost and Stille, the borate nucleophile directly attacks the allyl ligand on Ni in an outer sphere process. Still, even with this proposed mechanism, the Kobayashi group concedes that a transmetallative pathway *via* a bis($\eta^1$-allyl)nickel intermediate is plausible.

**Scheme 2.7: Allyl Alcohol Cross-Coupling**




[8] Jiménez-Aquino, A.; Flegeau, E. F.; Schneider, U.; Kobayashi, S. *Chem. Commun.* **2011**, *47*, 9456.

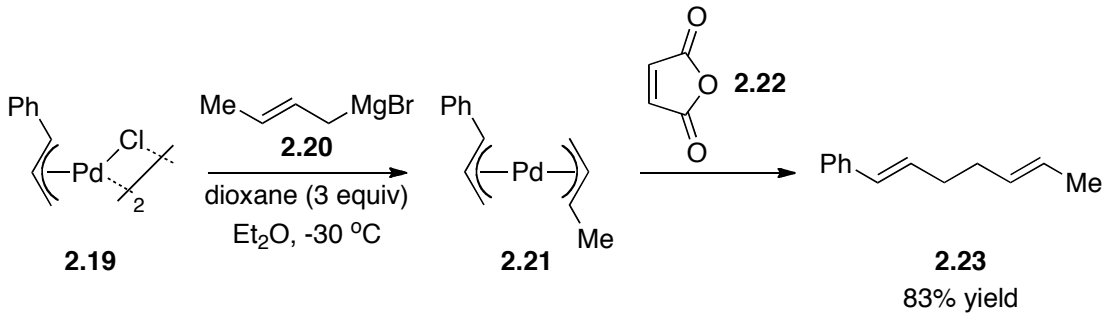
**Scheme 2.8: Alcohol Activation and Outer Sphere Allyl-Allyl Coupling**




**B. Allyl-Allyl Coupling *Via* An Inner Sphere Reaction Mechanism**

The possibility of a transmetallation-reductive elimination pathway for the cross-coupling of two allyl fragments was first put forth by Goliaszewski and Schwartz in 1984.[9] The authors prepared unsymmetrically substituted (allyl)(allyl′)palladium(II) complexes by treatment of an allylic palladium chloride with an allylic Grignard reagent (Scheme 2.9). Dioxane was used as an additive to suppress allylic ligand metathesis by forming adducts with the magnesium salts, enabling a selective transformation. Next, π-acid ligation with maleic anhydride (**2.22**) induced reductive elimination to form 1,5-diene products. Notably, in the absence of **2.22**, no coupling products were observed.

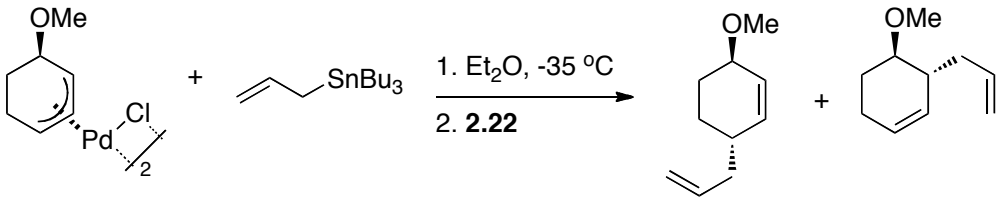
**Scheme 2.9: Grignard Addition to Form (allyl)(allyl′)palladium(II) Intermediate**




[9] Goliaszewski, A.; Schwartz, J. *J. Am. Chem. Soc.* **1984**, *106*, 5028.

Organostannanes are widely known to be reactive in the transfer of an organic group to a Pd(II) intermediate. Furthermore, unlike Grignard reagents, organostannanes are compatible with a wide array of functional groups. Schwartz and coworkers extended their previous method by employing allylic stannanes in their study of unsymmetrically substituted (allyl)(allyl′)Pd(II) complexes, and made several key observations about the reactivity of these systems.[10] First, unlike magnesium halide residues, organotin halides are soluble under the reaction conditions. This enables ligand metathesis between the Sn and Pd species, leading to the formation of small amounts of homocoupling products. Second, *trans*-configured allylPd **2.24** reacts with overall retention of stereochemistry (Scheme 2.10), which substantiates the theorized transmetallation-reductive elimination mechanistic pathway. Favoring the inner sphere reaction mechanism, Schwartz proposes that, indeed, a bis(allylic)Pd intermediate is generated in the Trost method. However, in the absence of **2.22** or another π-acid, this reversibly formed bis(allylic)Pd intermediate is unable to undergo reductive elimination, and instead products of direct attack are observed.

**Scheme 2.10: Retention of Configuration to Substantiate Mechanism**



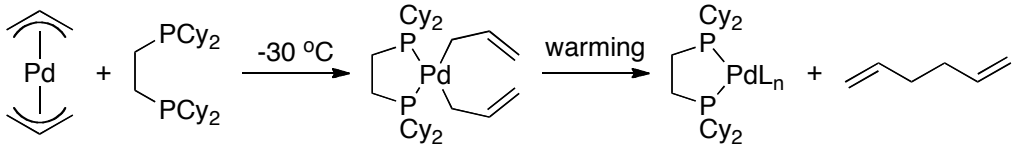

**2.24** **2.5** **2.25** **2.26**

78% yield, 3:1 **2.25**:**2.26**

[10] (a) Goliaszewski, A.; Schwartz, J. *Tetrahedron* **1985**, *41*, 5779. For a catalytic method starting from allylic bromides, see (b) Goliaszewski, A.; Schwartz, J. *Organometallics* **1985**, *4*, 417.

Further experimental evidence points to the plausibility of an inner sphere reaction pathway for allyl-allyl coupling. In a study detailing the structure and reactivity of allyl Pd complexes, Jolly observed a ligand-induced reductive coupling of two allyl groups (Scheme 2.11).[11] Treatment of bis($\eta^3$-allyl)Pd complex **2.27** with a bidentate phosphine ligand (**2.28**) yields bis($\eta^1$-allyl)Pd complex **2.29**, which, at temperatures under -30 °C, is stable toward isolation and characterization.[12] Upon warming, the complex reductively eliminates, generating hexadiene **2.31** and Pd(0) complex **2.30**.

**Scheme 2.11: Reductive Elimination from Bis($\eta^1$)allylPd Complexes**




**2.27** **2.28** **2.29** **2.30** **2.31**

### C. DFT Calculations and the 3,3′-Reductive Elimination Mechanism

Unsymmetric bis(allyl)Pd complexes, intermediates in the Pd-catalyzed reaction of allyl chlorides and allyl stannanes, have demonstrated amphiphilic behavior in organic synthesis.[13] In particular, these intermediates are effective reagents for the 1,2-allylation of aldehydes and imines.[14] However, Yamamoto and coworkers demonstrated that,

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[11] Jolly, P. W. *Angew. Chem.* **1985**, *97*, 279; *Angew. Chem. Int. Ed. Engl.* **1985**, *24*, 283.

[12] Krause, J.; Bonrath, W.; Pörschke, K. R. *Organometallics* **1992**, *11*, 1158.

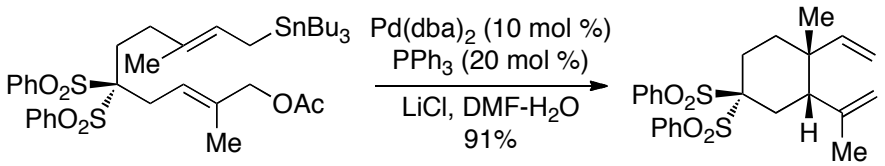
[13] Szabó, K. J. *Chem. Eur. J.* **2000**, *6*, 4413.

[14] (a) Nakamura, H.; Iwama, H.; Yamamoto, Y. *J. Am. Chem. Soc.* **1996**, *118*, 6641. (b) Nakamura, H.; Nakamura, K.; Yamamoto, Y. *J. Am. Chem. Soc.* **1998**, *120*, 4242. (c) Nakamura, H.; Aoyagi, K.; Shim, J.-G.; Yamamoto, Y. *J. Am. Chem. Soc.* **2001**, *123*, 372. (d) Nakamura, H.; Iwama, H.; Yamamoto, Y. *Chem. Commun.* **1996**, 1459.

even in the presence of aldehydes, addition of a phosphine ligand controls the chemoselectivity, and only the product of Stille allyl-allyl cross-coupling is observed.[15]

This Pd-catalyzed coupling of two allyl fragments was employed by Echavarren and coworkers in the synthesis of (±)-10-*epi*-elemol.[16] En route to the natural product, intramolecular cross-coupling of the acetate and stannane units in **2.32** yielded **2.33** as a single isomer (Scheme 2.12). Echavarren suggests the intermediacy of an unsymmetric (allyl)(allyl′)Pd complex but does not speculate about the details of the reductive elimination event.

**Scheme 2.12: Intramolecular Allyl-Allyl Coupling**




**2.32** **2.33**

In a subsequent publication, Echavarren and coworkers utilized DFT calculations to study the intermediates involved in the C-C bond forming event during allyl-allyl coupling.[17] The activation energy barriers toward reductive elimination were studied for model complexes **2.27**, **2.34**, and **2.35** (Figure 2.1). Of the possibly isomeric

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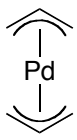
[15] Nakamura, H.; Bao, M.; Yamamoto, Y. *Angew. Chem. Int. Ed.* **2001**, *40*, 3208.

[16] Cuerva, J. M.; Gómez-Bengoa, E.; Méndez, M.; Echavarren, A. M. *J. Org. Chem.* **1997**, *62*, 7540.

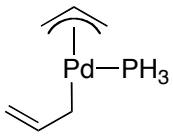
[17] Méndez, M.; Cuerva, J. M.; Gómez-Bengoa, E.; Cárdenas, D. J.; Echavarren, A. M. *Chem. Eur. J.* **2002**, *8*, 3620. Calculations performed using the B3LYP density functional with the 6-31G* basis set.

intermediates, those complexes with $\eta^3$-bound allyl ligands (**2.27** and **2.34**) exhibit high energy barriers for reductive elimination. Phosphine-association to achieve **2.34** and **2.35** is calculated to be a slightly endothermic process. In the presence of phosphino-donor ligands, however, the lowest activation barrier corresponds to the bis($\eta^1$-allyl)Pd complex **2.35**, though the ground state of this structure is somewhat higher in energy than the other two complexes. From **2.35**, there exist three possible mechanisms for reductive elimination, depending upon which carbon atoms participate in C-C bond formation (C1-C1′, C1-C3′, or C3-C3′). Reductive coupling between C3 and C3′ (depicted in Figure 2.1) is overwhelmingly preferred for reductive elimination. More recently, DFT calculations have also examined the reductive coupling of *cis*-[Pd($\eta^1$-allyl)$_2$(PMe$_3$)(L)] complexes with L = $\pi$-acid, olefin, or phosphine ligands.[18] 3,3′-reductive elimination was likened to a metallopericyclic reaction, and was the favored reaction pathway across all examples.

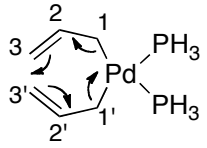
**Figure 2.1: Calculated Reductive Elimination Barriers for Bis(allyl)Pd-Complexes**




**2.27**
$E_a$ = 36.6 kcal/mol




**2.34**
$E_a$ = 23.4 kcal/mol



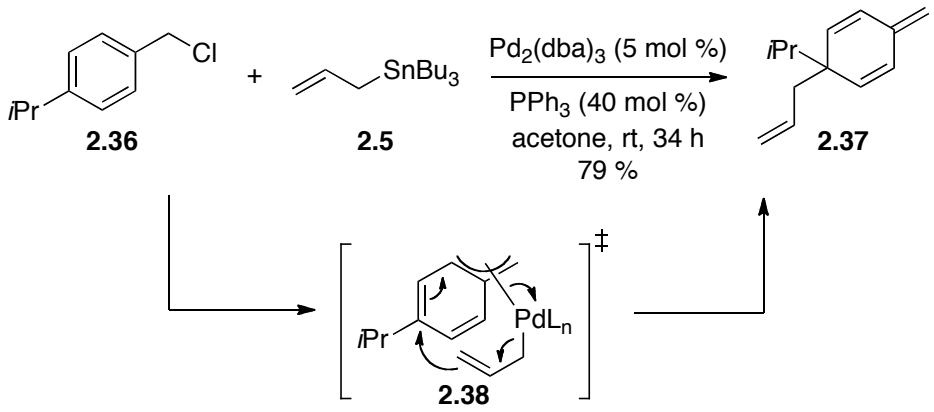

**2.35**
$E_a$(3,3') = 8.5 kcal/mol
$E_a$(1,3') = 22.8 kcal/mol
$E_a$(1,1') = 20.9 kcal/mol

[18] Pérez-Rodríguez, M.; Braga, A. A. C.; de Lera, A. R.; Maseras, F.; Álvarez, R.; Espinet, P. *Organometallics* **2010**, *29*, 4983.

**D. Reactions Proceeding Through a 3,3′-Reductive Elimination Mechanism**

A 3,3′-reductive elimination mechanism has been observed in other reactions in which allyl-metal complexes are key intermediates. In one such example, under Pd-catalysis the coupling reaction of benzyl chlorides with allyltributylstannane generated an unexpected allylative dearomatization product **2.37** (Scheme 2.13).[19] This reaction proceeded under mild conditions, tolerated electron poor and electron rich arenes, and reacted with *p*-substituted benzyl chlorides to produce dearomatization products with a quaternary center. Through DFT calculations, it was proposed that reductive elimination occurs between the $\eta^1$-allyl terminus and the para position of the $\eta^3$-benzyl ligand (see **2.38**).[20]

**Scheme 2.13: Allylative Dearomatization *via* 3,3′-Reductive Elimination**




Morken and coworkers have published several asymmetric, catalytic strategies for allylation of unsaturated carbonyl compounds. Computational and experimental data

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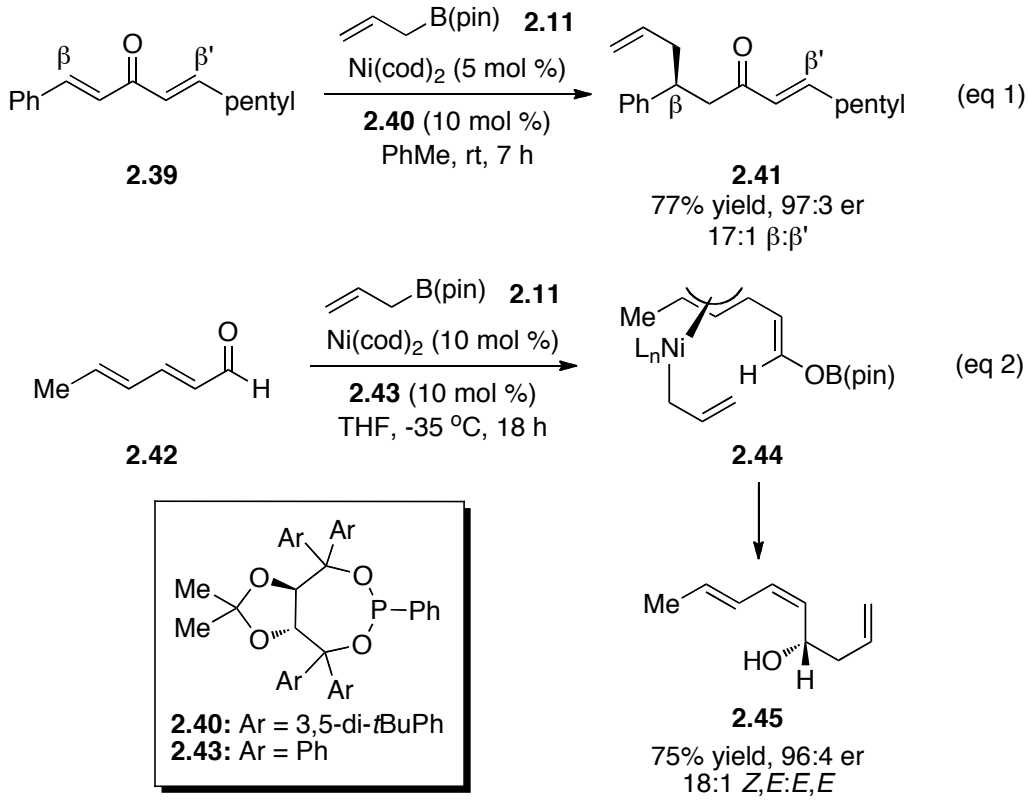
[19] Bao, M.; Nakamura, H.; Yamamoto, Y. *J. Am. Chem. Soc.* **2001**, *123*, 759.

[20] Ariafard, A.; Lin, Z. *J. Am. Chem. Soc.* **2006**, *128*, 13010.

have demonstrated that both the 1,4-allylation of dialkylidene ketones (Scheme 2.14, equation 1; see also Chapter 1)[21a-c] and 1,2-allylation of dienals (Scheme 2.14, equation 2)[21d] proceed through the intermediacy of allyl metal complexes such as **2.44** that undergo a 3,3′-reductive elimination mechanism.

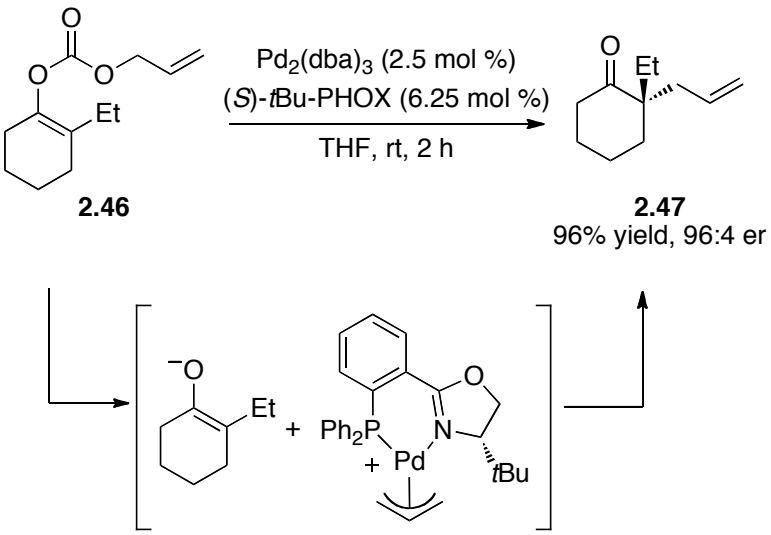
**Scheme 2.14: 1,4- and 1,2-Allylation *via* 3,3′-Reductive Elimination**




[21] (a) Sieber, J. D.; Liu, S.; Morken, J. P. *J. Am. Chem. Soc.* **2007**, *129*, 2214. (b) Sieber, J. D.; Morken, J. P. *J. Am. Chem. Soc.* **2008**, *130*, 4978. (c) Brozek, L. A.; Sieber, J. D.; Morken, J. P. *Org. Lett.* **2011**, *13*, 995.

In 2007, Stoltz and Goddard investigated the mechanism for the asymmetric Tsuji decarboxylative allylation reaction.[22] This allylation proceeds in high regio- and enantioselectivity from prochiral enol carbonates **2.46** to afford products with a quaternary α-stereocenter **2.47** (Scheme 2.15). DFT calculations provide strong evidence for an inner sphere 3,3′-reductive elimination pathway; similar to a seven-centered metallo-Claisen rearrangement, C-C bond formation occurs between the allyl terminus and the α-carbon of the O-bound enolate.

**Scheme 2.15: Inner Sphere Tsuji Decarboxylative Allylation**



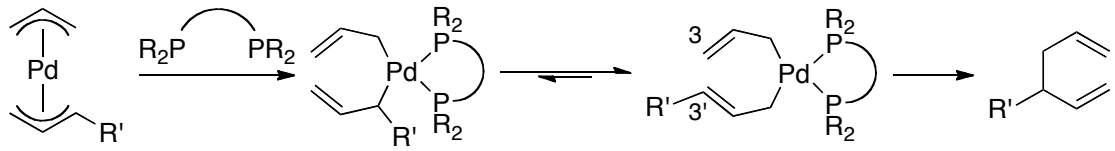

[22] Keith, J. A.; Behenna, D. C.; Mohr, J. T.; Ma, S.; Marinescu, S. C.; Oxgaard, J.; Stoltz, B. M.; Goddard, III, W. A. *J. Am. Chem. Soc.* **2007**, *129*, 11876.

## III. Development of a Regioselective Asymmetric Allyl-Allyl Cross-Coupling[23]

### A. Hypothesis for Catalyst-Controlled Reaction Regioselectivity

The value of a coupling reaction is attributable to not only the efficiency, but also the selectivity of the transformation. In the cross-coupling of a prochiral allylic electrophile and an unsubstituted allyl metal reagent, it is desirable to exert control over the enantioselectivity as well as the regioselectivity of the reaction. Based on calculated reductive elimination energy barriers from bis(allyl) metal complexes discussed in section II.C, we reasoned that selection of a bidentate ligand scaffold could allow access to the chiral branched allyl-allyl coupling product. Bidentate phosphine ligands, which occupy two coordination sites on palladium metal centers, would prompt each allyl group to adopt an $\eta^1$-binding mode (Scheme 2.16). We further hypothesized that an equilibrium process would enable isomerization of the allyl groups, favoring the least hindered complex **2.50** in which the substitution is directed away from the ligand scaffold. From complex **2.50**, 3,3′-reductive elimination produces the branched coupling product **2.51**. Furthermore, by employing a chiral ligand, influencing the asymmetry of the process was deemed feasible.

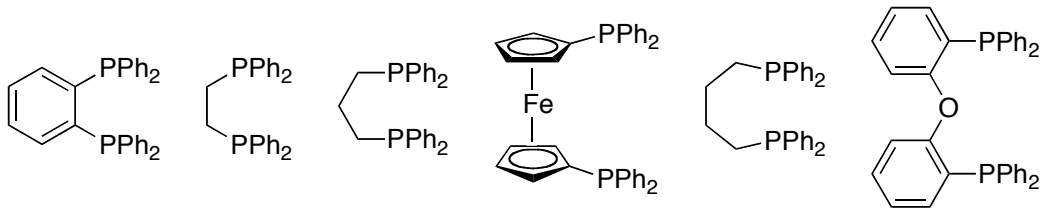
**Scheme 2.16: Hypothesis for Regiocontrol in Allyl-Allyl Coupling**




[23] Zhang, P. Z.; Brozek, L. A.; Morken, J. P. *J. Am. Chem. Soc.* **2010**, *132*, 10686.

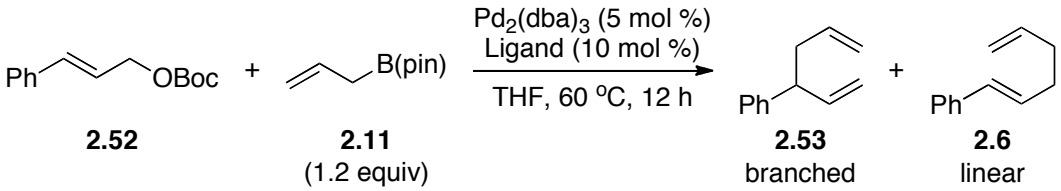
A variety of achiral bidentate phosphine ligands were surveyed in the Pd(0)-catalyzed allyl-allyl coupling of cinnamyl *tert*-butylcarbonate (**2.52**) and (allylB(pin) (**2.11**) (Table 2.1). While the monodentate ligand triphenylphosphine preferentially produced the linear 1,5-diene **2.6** (entry 1), bidentate ligands generally favored formation of branched 3,3′-reductive elimination product **2.53**. Furthermore, results show that the branched-to-linear product ratio is a function of the bite angle of the ligand.[24] Ligands with small bite angles such as dppbenzene and dppe (entries 2 and 3) favor the branched product in up to a 98:2 ratio, while ligands with larger bite angles, such as DPEphos, are much less selective (entry 7). This observation is compelling in its support of our regioselectivity hypothesis; as the P-Pd-P bond angle in intermediate **2.50** (Scheme 2.16) is compressed, carbons 1 and 1′ move farther away from one another, further favoring 3,3′-reductive elimination relative to the 1,1′-pathway that may be responsible for linear product formation.

**Figure 2.2: Achiral Bidentate Ligand Structures**




[24] van Leeuwen, P. W. N. M.; Kamer, P. C. J.; Reek, J. N. H.; Dierkes, P. *Chem. Rev.* **2000**, *100*, 2741.

**Table 2.1: Achiral Bidentate Ligand Survey**




**2.52** **2.11** (1.2 equiv) **2.53** branched **2.6** linear

| entry | ligand[a] | $\beta_n$ o [b] | yield (%)[c] | branched:linear[d] |
|---|---|---|---|---|
| 1 | $PPh_3$ | - | 68 | 1:>20 |
| 2 | **dppbenzene** | **83** | **70** | **97:3** |
| 3 | **dppe** | **85** | **77** | **98:2** |
| 4 | dppp | 91 | 80 | 97:3 |
| 5 | dppf | 96 | 43 | 94:6 |
| 6 | dppb | 98 | 77 | 38:62 |
| 7 | DPEphos | 102 | 58 | 72:28 |

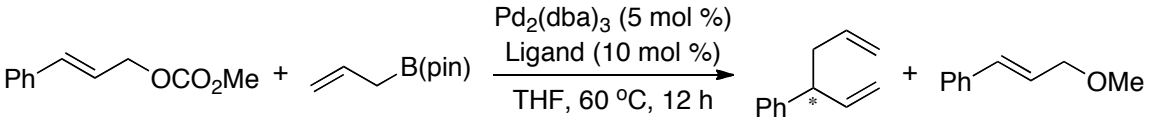
[a] See Figure 2.2 for ligand structures. [b] See footnote 24. [c] Isolated yield after silica gel chromatography. [d] Determined by GLC analysis.

### B. Reaction Development: Identification of an Optimal Chiral Catalyst System

With the understanding that regioselectivity correlates with ligand bite angle, we sought to identify a chiral bidentate phosphine ligand that would permit regiocontrol in an asymmetric allyl-allyl coupling reaction. Methyl carbonate **2.54** was treated with allylB(pin) (**2.11**) under Pd(0) catalysis, and the effect of the chiral ligand on reactivity, regioselectivity, and stereoselectivity was determined (Table 2.2). (*R*,*R*)-BINAP (**2.56**) (see Figure 2.3 for structure) and its tolyl analogue **2.57** afford the desired product **2.53** in good enantioselectivity but low yield (entries 1 and 2), due in part to the formation of the undesired methyl ether byproduct **2.55**. Tartaric acid-derived (*R*,*R*)-DIOP (**2.58**) provided a racemic product (entry 3). Ligands within the DuPhos family exhibited increasing enantioselectivity with increased size of the ligand; however, in the absence

of an additive to aid transmetallation, reaction conversion was poor (entries 4-7). Electron-rich bidentate ligands (*S*)-SegPhos **2.62** (entry 8) and (*R*)-MeO-furyl-BIPHEP **2.63** (entry 9) were highly enantioselective, but again, undesired methyl ether **2.55** restricted the yield.

**Table 2.2: Chiral Bidentate Ligand Survey - Methyl Carbonate**



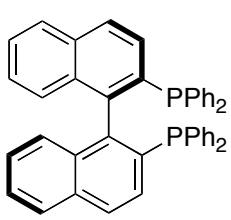

**2.54** **2.11** (1.2 equiv) **2.53** **2.55**

| entry | ligand[a] | **2.53** (% in crude)[b] | **2.55** (% in crude) | **2.53** yield (%)[c] | er[d] |
|---|---|---|---|---|---|
| 1 | **2.56** | 46 | 44 | 34 | 90:10 |
| 2 | **2.57** | 45 | 12 | 47 | 92:8 |
| 3 | **2.58** | 54 | 42 | 93 | 50:50 |
| 4 | **2.59** | 88 | 13 | 60 | 90:10 |
| 5 | **2.60** | 13 | 1 | 14 | 92:8 |
| 6 | **2.61** | 1 | 1 | NA | NA |
| 7[e] | **2.61** | 44 | 26 | 30 | 94:6 |
| 8 | **2.62** | 51 | 33 | 47 | 95:5 |
| 9 | **2.63** | 76 | 24 | 67 | 97:3 |

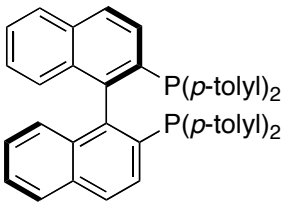
[a] See Figure 2.3 for ligand structures. [b] Percentage of products as determined by crude $^1$H NMR analysis. [c] Isolated yield after silica gel chromatography. [d] Determined by GLC analysis. [e] With 2 equiv NaOMe as additive.

Methyl ether byproduct **2.55** presumably arises from addition of methoxide, expelled from the carbonate, to the (allyl)Pd intermediate. We reasoned that byproduct formation might be suppressed by utilizing carbonates that release sterically encumbered or electron-deficient alkoxides upon oxidative addition of Pd(0) (Table 2.3).

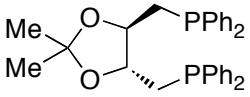
**Figure 2.3: Chiral Bidentate Ligand Structures**



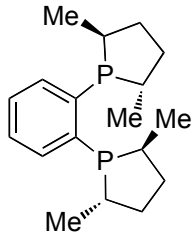

(*R*)-BINAP
**2.56**



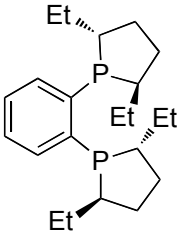

(*R*)-*p*-tolyl-BINAP
**2.57**



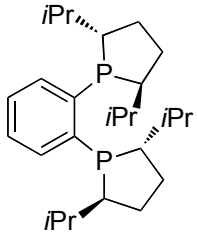

(*R*,*R*)-DIOP
**2.58**



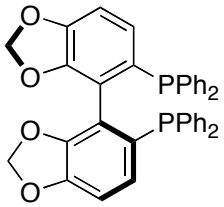

(*S*,*S*)-Me-Duphos
**2.59**



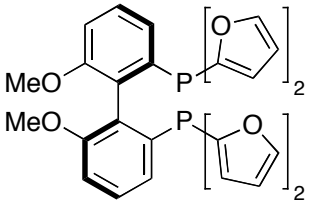

(*R*,*R*)-Et-Duphos
**2.60**




(*R*,*R*)-*i*Pr-Duphos
**2.61**



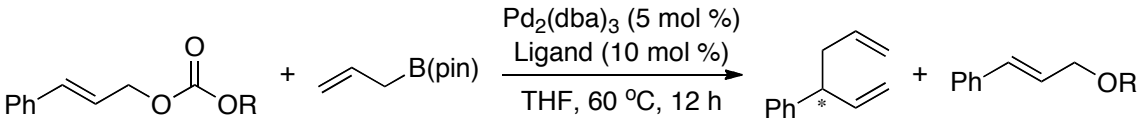

(*S*)-SegPhos
**2.62**




(*R*)-MeO(furyl)BIPHEP
**2.63**

With hindered isopropyl carbonate **2.10**, reaction conversion suffered with (*R*)-BINAP and (*S*,*S*)-Me-Duphos ligands (entries 1 and 2), although no ethereal byproducts were observed. Surprisingly, reaction of carbonate **2.65**, with less nucleophilic phenoxide as its leaving group, achieved complete conversion. However, significant quantities of ethereal byproducts formed; with (*S*)-SegPhos (entry 3), cinnamyl alcohol **2.15** was observed. In order to achieve high conversion and minimal product from alkoxide nucleophilic attack, *tert*-butyl carbonate **2.52** was examined in the allyl-allyl coupling with the most promising chiral bidentate ligands (Table 2.4). Though small amounts of *tert*-butyl cinnamyl ether (< 5%) were observed, MeO(furyl)BIPHEP (**2.63**) provided the desired product in improved yield and enantioselectivity (entry 6).

**Table 2.3: Chiral Bidentate Ligand Survey - *i*Pr- and Ph-Carbonate**

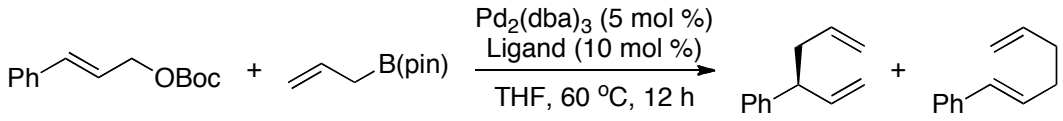



**2.11** (1.2 equiv) **2.53** **2.64**

| entry | R | ligand[a] | conversion (%)[b] | **2.64** (% in crude)[c] | **2.53** yield (%)[d] | er[e] |
|---|---|---|---|---|---|---|
| 1 | *i*Pr (**2.10**) | **2.56** | 60 | < 1 | 28 | 92:8 |
| 2 | *i*Pr (**2.10**) | **2.59** | 55 | < 1 | 37 | 92:8 |
| 3 | Ph (**2.65**) | **2.62** | > 99 | 16[f] | 29 | 95:5 |
| 4 | Ph (**2.65**) | **2.63** | > 99 | 45 | 24 | 97:3 |

[a] See Figure 2.3 for ligand structures. [b] Determined by crude $^1$H NMR analysis. [c] Percentage of byproduct as determined by crude $^1$H NMR analysis. [d] Isolated yield after silica gel chromatography. [e] Determined by GLC analysis. [f] 20% cinnamyl alcohol **2.15** present in crude $^1$H NMR.

**Table 2.4: Chiral Bidentate Ligand Survey - *t*Butyl Carbonate**



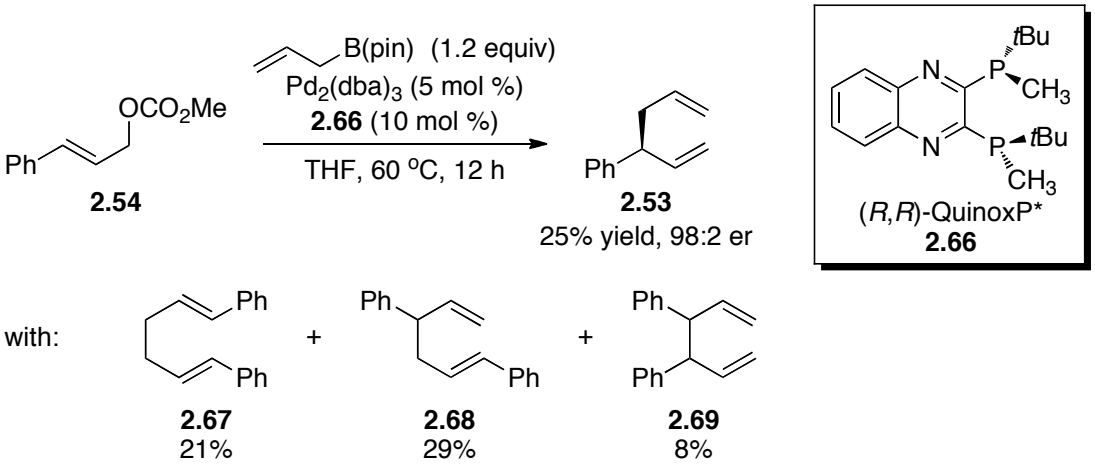

**2.52** **2.11** (1.2 equiv) **2.53** **2.6**

| entry | ligand[a] | branched:linear[b] | yield (%)[c] | er |
|---|---|---|---|---|
| 1 | **2.56** | > 20:1 | 50 | 92:8 |
| 2 | **2.59** | > 20:1 | 60 | 92:8 |
| 3 | **2.60** | > 20:1 | 39 | 94:6 |
| 4 | **2.61** | > 20:1 | 10 | 95:5 |
| 5 | **2.62** | > 20:1 | 48 | 96:4 |
| 6 | **2.63** | > 20:1 | 72 | 96:4 |

[a] See Figure 2.3 for ligand structures. [b] Determined by crude $^1$H NMR analysis. [c] Isolated yield after silica gel chromatography. [d] Determined by chiral GLC analysis.

In our ligand survey, the bidentate P-chiral ligand (*R*,*R*)-QuinoxP* (**2.66**)[25] performed well, but produced unexpected byproducts. This ligand furnished dimers of the cinnamyl carbonate starting material in addition to the desired coupling product (Scheme 2.17). Encouraged by the high levels of enantioselection afforded by ligand **2.66**, efforts were put forth to hinder dimer formation.

**Scheme 2.17: (*R*,*R*)-QuinoxP* as Ligand**




We reasoned that low yield of desired allyl-allyl coupling product **2.53** might be due to a slow transmetallation step, so, in hopes of activating allylB(pin), we studied the reaction with a number of basic additives ($Cs_2CO_3$, $K_3PO_4$, NaOH, ethanol, and triethylamine). Unfortunately, no additive provided a significant decrease in dimer formation. Similarly, attempting the reaction with increased equivalents of allylB(pin), $Pd(OAc)_2$ as catalyst, or carbonate **2.10** as starting material, yielded insufficient

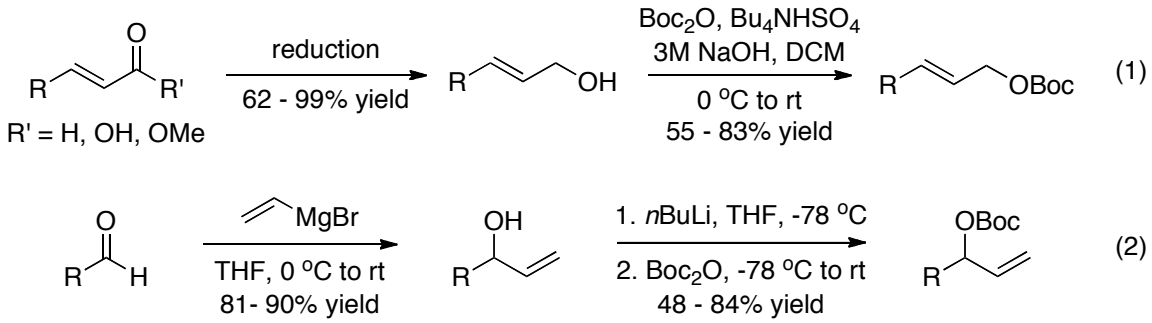
[25] Imamoto, T.; Sugita, K.; Yoshida, K. *J. Am. Chem. Soc.* **1995**, *127*, 11934.

quantities of **2.53**. Finally, a solvent screen was conducted (toluene, dioxane, acetonitrile, and ethyl acetate) in hopes of solublizing the borate complex for transmetallation. Again, however, yields for desired **2.53** did not surpass 40% due to cinnamyl dimer formation. Though the challenge of byproduct formation is unsolved, the high enantioselectivity of this ligand (up to 99:1 er) may make it worth revisiting for future classes of substrates that will be studied in allyl-allyl cross-coupling.

### C. Scope of Pd-Catalyzed Asymmetric Allyl-Allyl Coupling

Having selected (*R*)-MeO(furyl)BIPHEP (**2.63**) as the optimal ligand for the allyl-allyl cross-coupling reaction, we wished to survey a variety of allylic carbonate substrates and examine functional group tolerance. Linear and branched allylic carbonates were efficiently prepared from the corresponding allylic alcohols in a single step (Scheme 2.18).[26]

**Scheme 2.18: Preparation of Allylic Carbonates**

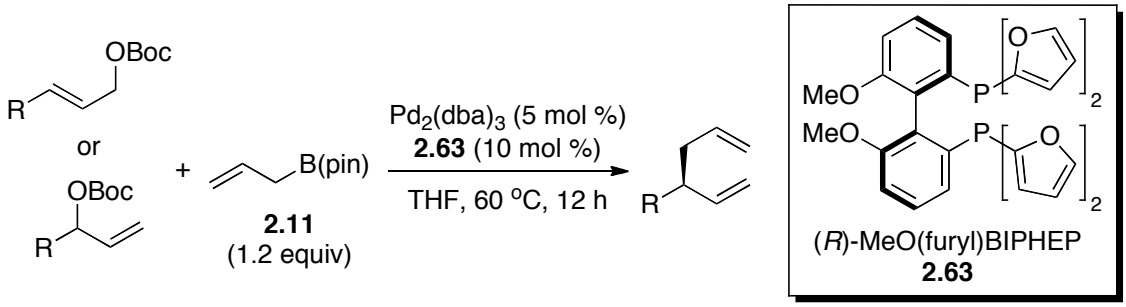


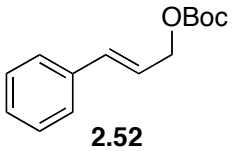
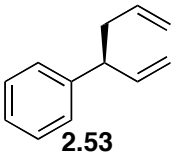
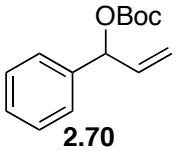
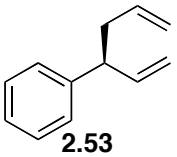
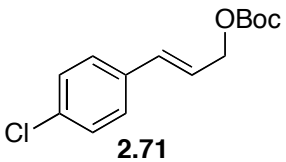
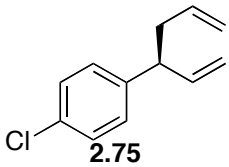
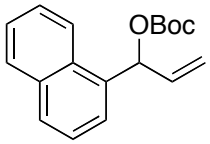
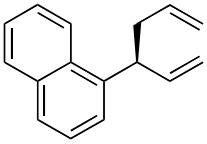
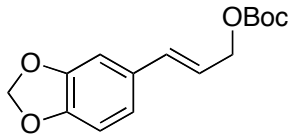
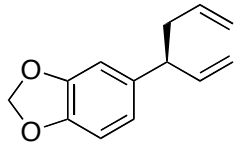
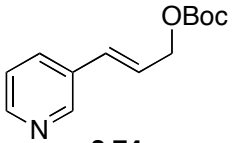
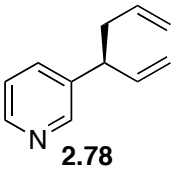

[26] Trost, B. M.; Fraisse, P. L.; Ball, Z. T. *Angew. Chem. Int. Ed.* **2002**, *41*, 1059.

The scope of allyl-allyl coupling with aryl-substituted substrates is given in Table 2.5. Both linear (**2.52**) and branched (**2.70**) isomers of the cinnamyl *tert*-butyl carbonate give analogous yields and enantioselectivity (entries 1 and 2), suggesting a common intermediate. Halogenated substrate **2.71** reacts with slightly lower yield, but in good enantio- and regioselection (entry 3). *Ortho*-substituted 1-naphthyl substrate **2.72** reacts with improved yield, suggesting that hindered allyl electrophiles may be well-tolerated. Heteroatoms are also permitted; both oxygenated (**2.73**) as well pyridyl substrates (**2.74**) react in good yields and enantioselectivities.

One limitation in the allyl-allyl coupling method, however, is that electron-poor substrates perform with diminished enantioselectivity. Both *para*-trifluoromethyl **2.79** and *para*-methyl ester **2.80** yield products with lower optical purity (Table 2.6), demonstrating that both resonance- and inductively-withdrawing groups are not yet well tolerated in this reaction.

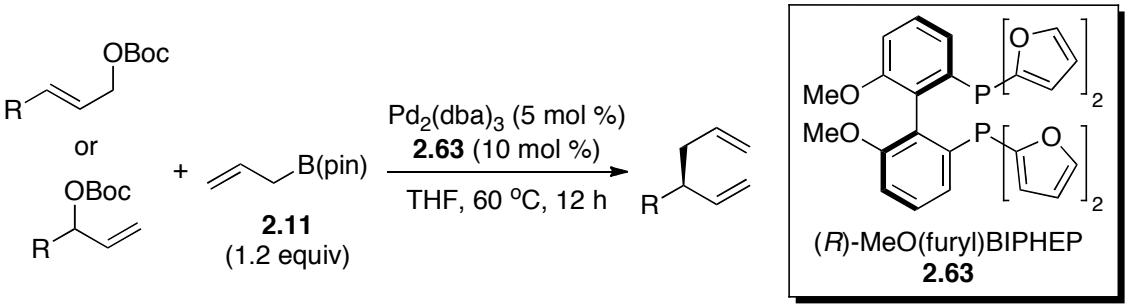
**Table 2.5: Asymmetric Allyl-Allyl Coupling: Aryl-Substituted Substrates**

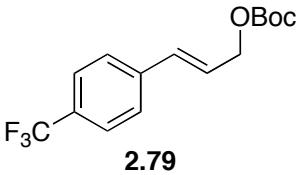
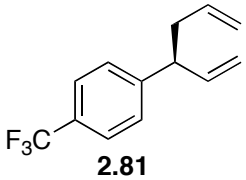
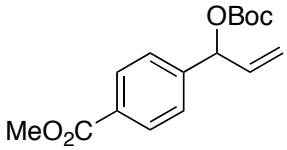
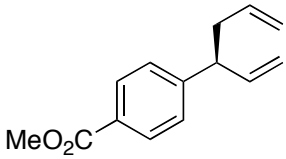



| entry | substrate | product | regioselectivity[a] | yield (%)[b] | er[c] |
|---|---|---|---|---|---|
| 1 |  **2.52** |  **2.53** | > 20:1 | 72 | 96:4 |
| 2 |  **2.70** |  **2.53** | > 20:1 | 75 | 96:4 |
| 3 |  **2.71** |  **2.75** | > 20:1 | 59 | 95:5 |
| 4 |  **2.72** |  **2.76** | > 20:1 | 87 | 95:5 |
| 5 |  **2.73** |  **2.77** | > 20:1 | 83 | 96:4 |
| 6 |  **2.74** |  **2.78** | > 20:1 | 52 | 95:5 |

[a] Determined by $^1$H NMR analysis of the unpurified reaction mixture. [b] Isolated after silica gel chromatography. Value is an average ot two experiments. [c] Enantiomeric ratio determined by chiral GLC, SFC, or HPLC analysis.

**Table 2.6: Asymmetric Allyl-Allyl Coupling: Electron Deficient Substrates**

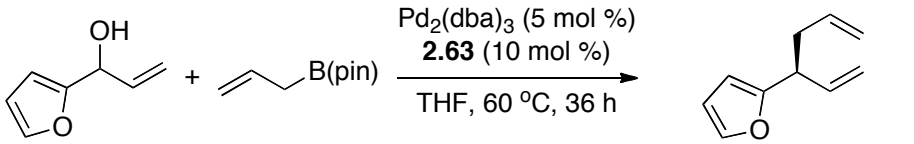



| entry | substrate | product | regioselectivity[a] | yield (%)[b] | er[c] |
|---|---|---|---|---|---|
| 1 |  **2.79** |  **2.81** | > 20:1 | 60 | 87:13 |
| 2 |  **2.80** |  **2.82** | > 20:1 | 48 | 63:37 |

[a] Determined by $^1$H NMR analysis of the unpurified reaction mixture. [b] Isolated after silica gel chromatography. Value is an average ot two experiments. [c] Enantiomeric ratio determined by chiral GLC analysis.

Intriguingly, certain unactivated allylic alcohols also participate as substrates in the allyl-allyl coupling reaction (Scheme 2.19). Using increased equivalents of allylB(pin) **2.11**, this feature is limited thus far to electron-rich substrates such as **2.83**, which *via* electron resonance, may aid in displacement of the allylic hydroxyl group and formation of the ($\eta^3$-$\pi$-allyl)Pd intermediate.

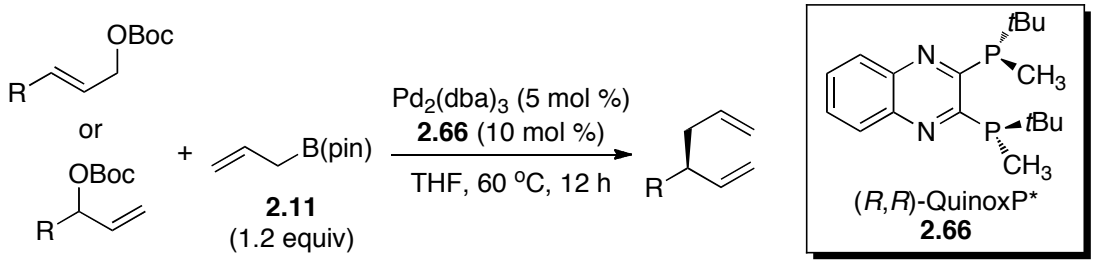
**Scheme 2.19: Coupling Reaction With Allylic Alcohol Substrate**

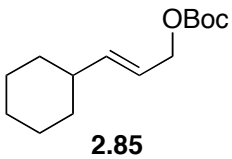
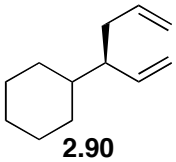
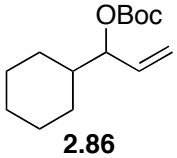
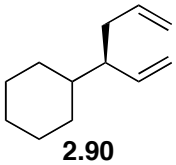
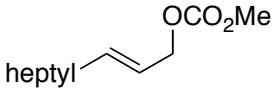
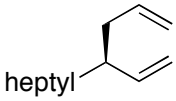
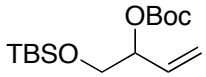
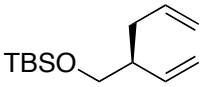
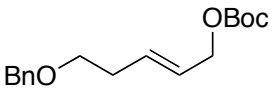
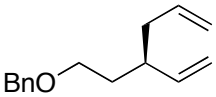



**2.83** **2.11** (2.0 equiv) **2.84** 64% yield, 94:6 er > 20:1 regioselectivity

Alkyl-substituted substrates also participate in the allyl-allyl coupling reaction (Table 2.7). When cyclohexyl-substituted carbonate **2.85** was subjected to the reaction conditions with (*R*)-MeO(furyl)BIPHEP **2.63**, enantioselectivity was inadequate, at 91:9 er. Encouraged by the high levels of enantioselection observed with (*R*,*R*)-QuinoxP* (**2.66**) as ligand with aryl carbonates, we examined it with alkyl-substituted substrates. Fortunately, ligand **2.66** proved well-suited for this reaction, providing the desired product **2.90** in excellent enantioselectivity. Importantly, dimerization of the starting material did not occur. Though reaction with linear cyclohexyl carbonate **2.85** was low-yielding (entry 1), the branched isomer **2.86** provided the product in sufficient yield (entry 2). Enantioselectivity decreases with *n*-alkyl substrate **2.87**. Substrates with allylic and homoallylic oxygenation (silyl ether **2.88** and benzyl ether **2.89**) react with excellent regioselectivity and good levels of enantioenrichment. Overall, the Pd(0)-catalyzed allyl-allyl coupling reaction proves to be a general method with tolerance for a wide variety of functional groups. Judicious choice of bidentate chiral ligand allows access to enantioenriched aryl- or alkyl-substituted 1,5-diene coupling products.

**Table 2.7: Asymmetric Allyl-Allyl Coupling: Alkyl-Substituted Substrates**



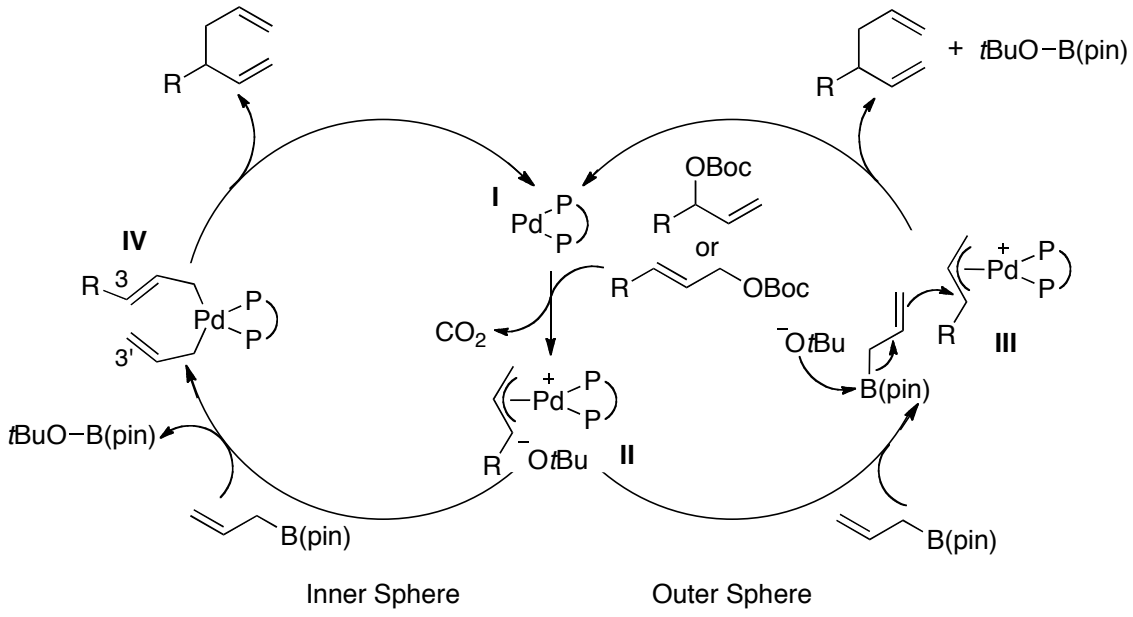

| entry | substrate | product | regioselectivity[a] | yield (%)[b] | er[c] |
|---|---|---|---|---|---|
| 1 |  **2.85** |  **2.90** | 3:1 | 9 | 97:3 |
| 2 |  **2.86** |  **2.90** | 10:1 | 63 | 96:4 |
| 3 |  **2.87** |  **2.91** | 11:1 | 80 | 92:8 |
| 4 |  **2.88** |  **2.92** | > 20:1 | 91 | 95:5 |
| 5 |  **2.89** |  **2.93** | > 20:1 | 85 | 93:7 |

[a] Determined by $^1$H NMR analysis of the unpurified reaction mixture. [b] Isolated after silica gel chromatography. Value is an average ot two experiments. [c] Enantiomeric ratio determined by chiral GLC, SFC, or HPLC analysis.

**D. Asymmetric Allyl-Allyl Coupling: Studies Into Reaction Mechanism**

As discussed in Sections II.C and II.D, there is significant evidence that a 3,3′-reductive elimination mechanism is operative in the coupling of two allyl fragments. However, early proposals by Trost[5] and Stille[6] suggest that such a coupling product may arise from external nucleophilic attack on an ($\eta^3$-$\pi$-allyl)Pd complex. We wished to examine each of these mechanistic possibilities in the context of the allyl-allyl coupling that we developed (Scheme 2.20). In the outer sphere process, the Pd(0) complex undergoes oxidative addition to the allyl carbonate to form ($\eta^3$-$\pi$-allyl)Pd(II) complex **II**. Next, allylB(pin) is activated by the alkoxide for nucleophilic backside displacement of the Pd(II) from the allyl unit (as in **III**) to form the branched 1,5-diene product.

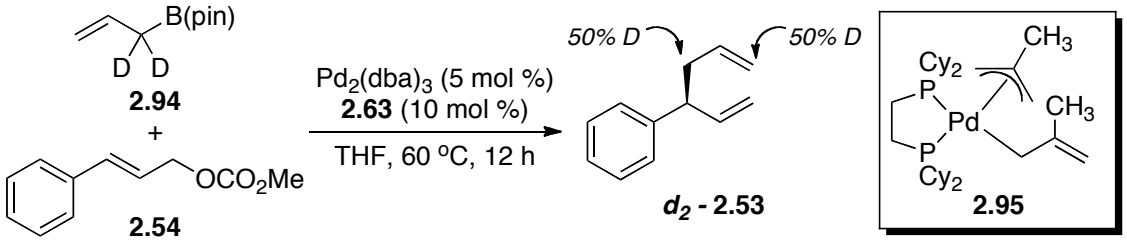
**Scheme 2.20: Inner Sphere and Outer Sphere Allyl-Allyl Coupling Mechanisms**



In the inner sphere mechanism, from **II**, alkoxide-activation of allylB(pin) facilitates transmetallation onto Pd(II) to form bis($\eta$1-allyl)Pd complex **IV**. Carbon-carbon bond formation occurs between carbons 3 and 3′ to form the branched 1,5-diene product. Because we hypothesized that 3,3′-reductive elimination in conjunction with a bidentate ligand-Pd(0) catalyst system provides a paradigm for regiocontrol in the coupling reaction, we undertook experiments to eliminate the possibility of an outer sphere reaction mechanism.

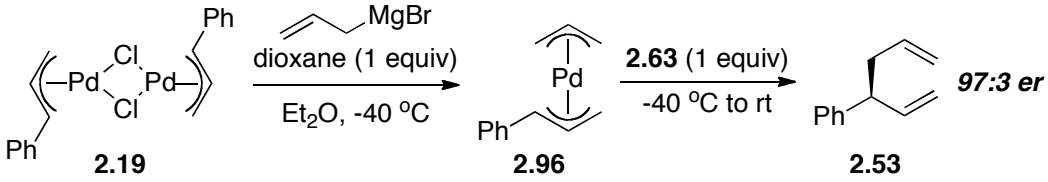
In our first experiment to determine which aforementioned mechanism operates in the catalytic enantioselective allyl-allyl coupling reaction, we employed deuterium-labeled allylB(pin) **2.94** as the allyl metal nucleophile in the allyl-allyl coupling reaction. In the presence of Pd(0) and MeO(furyl)BIPHEP **2.63**, the isotope label was evenly scrambled between the methylene carbon and the allyl terminus, while recovered **2.94** remained unscrambled (Scheme 2.21). In the outer sphere transformation, which Trost argues to proceed by an $S_E2'$ mechanism, allylic transposition would deliver a produce with deuterium exclusively at the allyl terminus. In an inner sphere reaction mechanism, it is conceivable that the isotope scrambling may take place by $\pi$-$\sigma$-$\pi$ isomerization after the transmetallation event. Though four-coordinate bis(allyl)Pd complexes typically adopt the bis($\eta^1$)-binding mode, this scrambling equilibrium may occur through the intermediacy of a five-coordinate Pd(II) complex similar to **2.95**, which has been observed by Jolly and coworkers.[11]

**Scheme 2.21: Allyl-Allyl Coupling Using Deuterium-Labeled AllylB(pin)**




We sought to further rule out coupling by an outer sphere reaction mechanism by studying the stoichiometric reductive couplings of bis(allyl)metal complexes carried out by Schwartz and coworkers. We outlined a synthesis of ($\eta^3$-allyl)($\eta^3$-cinnamyl)Pd (II) complex **2.96**, and reasoned that exposing such an intermediate to MeO(furyl)BIPHEP (**2.63**) would cause each allyl group to adopt the $\eta^1$-configuration. 3,3′-Reductive elimination from this complex, the same intermediate that exists after transmetallation in the inner sphere mechanism, should furnish the enantioenriched coupling product **2.53** in the same selectivity observed in the catalytic reaction (Scheme 2.22). In a compelling argument for an inner sphere coupling, the first time this reaction was attempted, the product was isolated in 97:3 er!

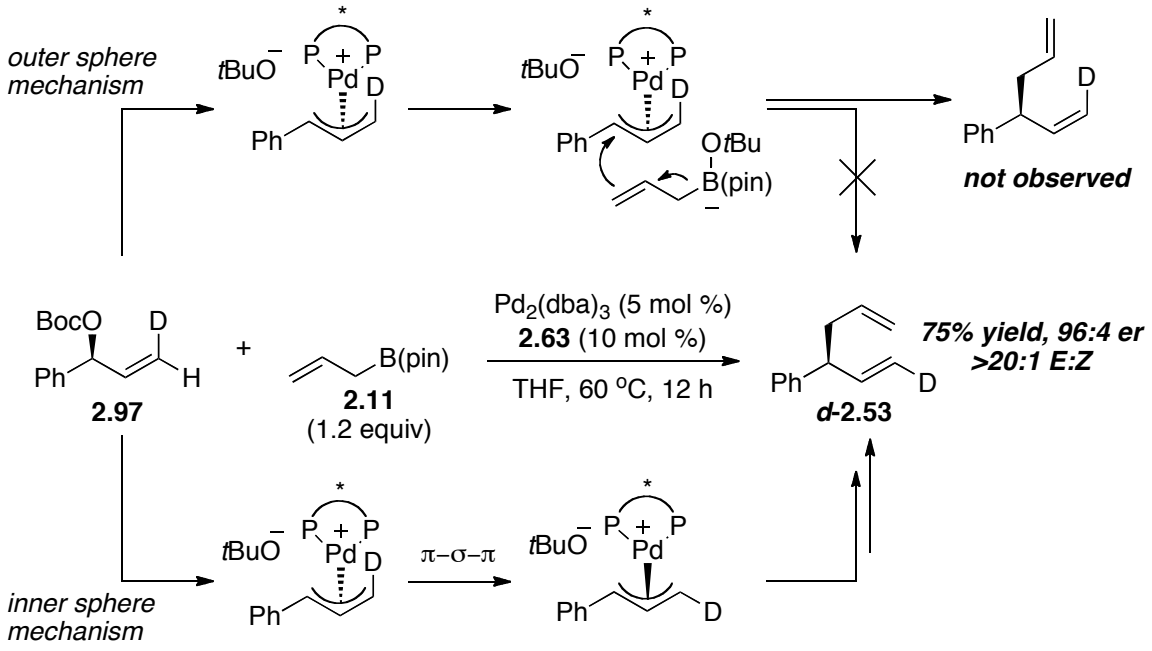
**Scheme 2.22: Stoichiometric Allyl-Allyl Coupling Reaction**



Unfortunately, however, this reaction suffered from a lack a reproducibility. To ameliorate this problem, a number of reaction temperatures were examined. The reductive elimination step, after the addition of **2.63** to **2.96**, was run at temperatures ranging from -30 °C to reflux; reductive elimination at reflux in THF afforded the product, but in 16% yield and in 93:7 er. Other allyl metal reagents were also examined for the generation of intermediate **2.96**, but neither allylB(pin) nor its trifluoroborate analog successfully transmetallated to Pd, and instead ligand metathesis to undesired hydrocarbon byproducts was observed. A variety of other bidentate ligands were investigated, but these also gave inconsistent results. (*R*,*R*)-QuinoxP* (**2.66**) produced the desired product in selectivities ranging from 91:9 to 88:12 er and yields never surpassing 11%.

With dubious results from the stoichiometric allyl-allyl coupling reaction, we designed another experiment that would allow us to distinguish between inner and outer sphere reaction pathways. Enantioenriched carbonate **2.97** was prepared with a deuterium isotope label in the *cis*-configuration. Reaction of **2.97** with allylB(pin), $Pd_2(dba)_3$, and MeO(furyl)BIPHEP (**2.63**) provided ***d*-2.53** as a single isomer in 96:4 er. Of significant mechanistic consequence, the deuterium isomerized to the *trans*-configuration (Scheme 2.23).

**Scheme 2.23: Asymmetric Coupling Reaction With a Deuterium-Labeled Carbonate**




In each possible reaction pathway, the Pd(0) catalyst must first displace the leaving group from the backside of the allylic carbonate.[27] It follows that in the outer sphere reaction pathway (top scheme), the borate would attack the phenyl-substituted allylic carbon in an $S_E2'$ fashion from the front face of the complex. This generates the correct enantiomer of product observed with chiral ligand **2.63**, however, this path does not result in isomerization of the olefin; the deuterium label remains in the *cis*-configuration. This product was not observed.

Because chiral ligand **2.63** is employed, we recognize that Pd must reductively eliminate from the front face of the complex in order to generate the observed

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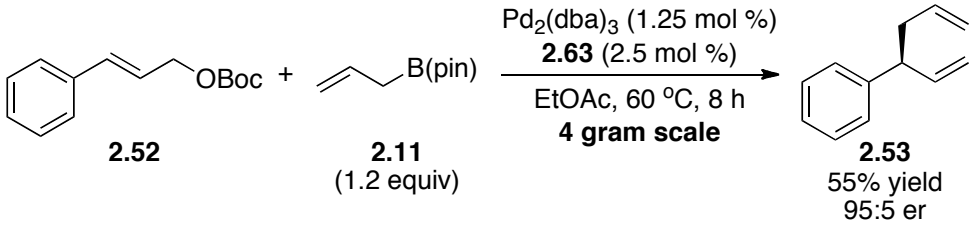
[27] (a) Hayashi, T.; Hagihara, T.; Konishi, M.; Kumada, M. *J. Am. Chem. Soc.* **1983**, *105*, 7767. (b) Trost, B. M.; Verhoeven, T. R. *J. Am. Chem. Soc.* **1980**, *102*, 4730.

enantiomer and diastereomer of product. In the inner sphere pathway, the Pd(II) complex undergoes π-σ-π isomerization, and through bond rotation the deuterium isomerizes to the *trans*-configuration. Transmetallation of the allylic borate may follow, then 3,3′-reductive elimination generates ***d*-2.53**, with a *trans*-isotope label. Similarly, π-σ-π isomerization may occur after the transmetallation event through the intermediacy of a five-coordinate palladium complex. The observed configuration of the product effectively rules out the existence of an outer sphere mechanism in the Pd(0)-catalyzed asymmetric allyl-allyl cross-coupling.

### E. Related Reactions and β-Substituted Allyl Boron Reagents

Curious about the practicality and scalability of the coupling reaction, we treated 4 grams of carbonate **2.52** with allylB(pin) under Pd(0)-catalysis (Scheme 2.24). The catalyst loading was lowered to 2.5% Pd(0) and 2.5% MeO(furyl)BIPHEP (**2.63**). Furthermore, tetrahydrofuran was exchanged for ethyl acetate, a more environmentally benign solvent. The reaction furnished the product in good enantioselectivity, though in lower yield.

**Scheme 2.24: Large-Scale Allyl-Allyl Coupling Reaction**




**2.52**

**2.11**
(1.2 equiv)

**2.53**
55% yield
95:5 er

Following the successful development of a Pd(0)-catalyzed allyl-allyl cross-coupling reaction, we wished to probe the effect of additional substitution on each coupling partner involved in the transformation. Carbonate **2.98**, with β-substitution, provided the coupling product in low yield and unsatisfactory enantioselectivity when applying the standard allyl-allyl coupling conditions (Scheme 2.25, equation 1). Increased equivalents of allylB(pin) and added triethylamine (3 equivalents each) provided a substantial boost in yield (60%; not shown), although the enantioselectivity was unaffected. Ethyl- and isopropyl-substituted DuPhos ligands failed to produce an active catalyst, although QuinoxP* (**2.66**), which had previously demonstrated significant enantioselection, provided **2.99** in excellent enantioenrichment and low yield (equation 2). Increasing equivalents of allylB(pin) and adding triethylamine provided the linear product **2.100** (equation 3), as did reaction with cesium fluoride additive. We surmise that the linear product is not directly produced in the coupling. Rather, potentially catalyzed by residual Pd(II) salts, a Cope rearrangement equilibrium process is initiated.[28] To our knowledge, this Pd(II)-catalyzed Cope process was observed with only β-methyl-substituted 1,5-diene **2.100**. This is consistent with a hypothesis put forth by Overman, which suggests that a successful Pd(II)-catalyzed Cope rearrangement requires that the 2 and 5 carbons of the 1,5-diene contain one hydrogen and one non-hydrogen substituent.[29]

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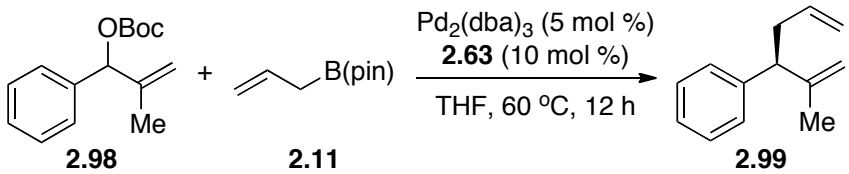
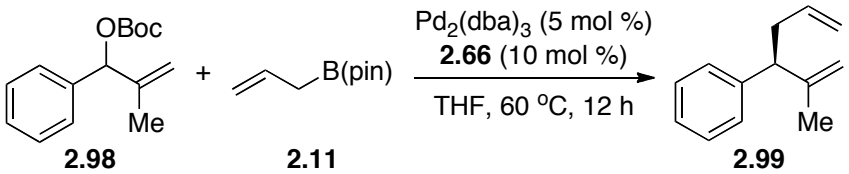
[28] Review: Hill, R. K. *Comp. Org. Syn.* **1991**, *5*, 785.

[29] Review: Overman, L. E. *Angew. Chem. Int. Ed. Engl.* **1984**, *23*, 579.

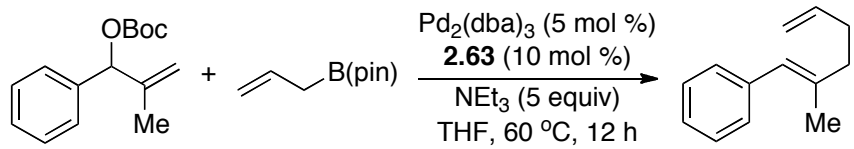
## 2.25: Cross-Coupling of β-Substituted Allyl Carbonates




**2.98** **2.11** (1.2 equiv) **2.99** 12% yield 67:33 er (eq 1)




**2.98** **2.11** (1.2 equiv) **2.99** 14% yield 97:3 er (eq 2)

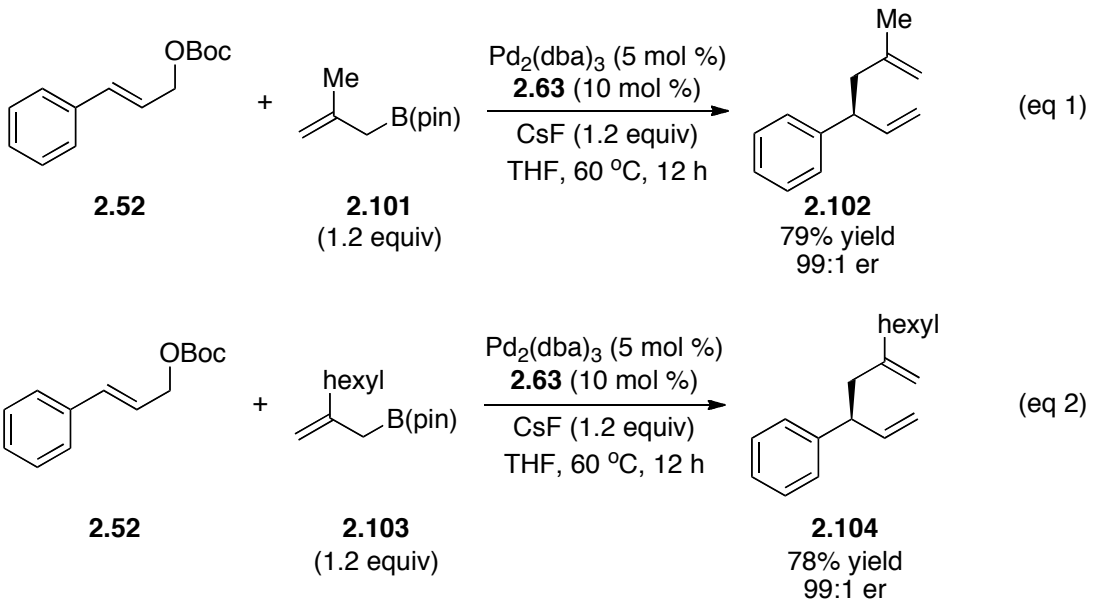



**2.98** **2.11** (5.0 equiv) **2.100** 64% yield (eq 3)

Substitution on the β-position of the allyl boron reagent, however, was very well tolerated in the coupling reaction. Both β-methyl **2.101** and β-alkyl **2.103** substituted reagents, prepared by Miyaura borylation of allylic acetates,[30] furnish the corresponding products **2.102** and **2.104** in good yield and unprecedented enantioselectivity (Scheme 2.26).

[30] Ishiyama, T.; Ahiko, T.-a.; Miyaura, N. *Tetrahedron Lett.* **1996**, *37*, 6889.

**Scheme 2.26: Cross-Coupling of β-Substituted Allyl Boron Reagents**



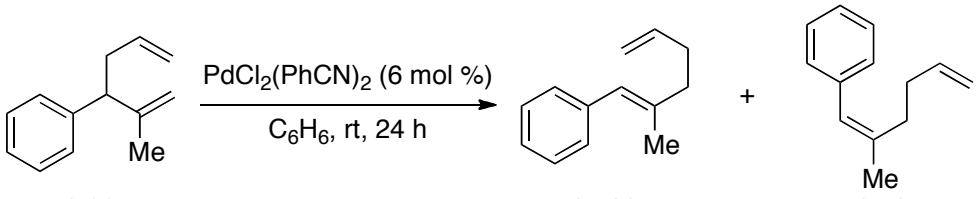

The success of β-substituted allyl boron reagents in the coupling led us to examine the efficiency and selectivity of γ-substituted allyl boron reagents. Specifically, we were curious about not only enantioselectivity and functional group tolerance in such transformations, but, unlike in the allyl-allyl coupling reaction with **2.11**, these substrates also posed questions of diastereoselectivity and regioselectivity in both the allyl electrophile and allyl metal components.

## IV. Development of an Asymmetric Diastereoselective Allyl-Allyl Cross-Coupling[31]

### A. Significance of the Development of a Route to 3,4-Disubstituted 1,5-Dienes

The Cope rearrangement is a [3,3]-sigmatropic rearrangement that provides access to compounds with vicinal alkenes, a commonly occurring structure in natural products. The thermodynamic variant of this reaction is well-studied, and many efforts have been put forth to develop a Pd(II)-catalyzed Cope rearrangement. For example, Overman and coworkers published the first example of a Cope rearrangement catalyzed by $PdCl_2$ (Scheme 2.27).[32] The reaction displays far greater reactivity and selectivity than the thermodynamic process: without a catalyst, the reaction occurs at 177 °C, the halflife of the reaction is 13 h, and the ratio of **2.100** to **2.105** is 3:1. Unfortunately, such reactions do not lend themselves well to asymmetric catalysis, because the rearrangement is reversible and thermodynamically favors the achiral linear 1,5-dienes.

**Scheme 2.27: Pd(II)-Catalyzed Cope Rearrangement**




**2.99** 87% **2.100** 93 : 7 **2.105**

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[31] Brozek, L. A.; Ardolino, M. J.; Morken, J. P. *J. Am. Chem. Soc.* **2011**, *133*, 16778.

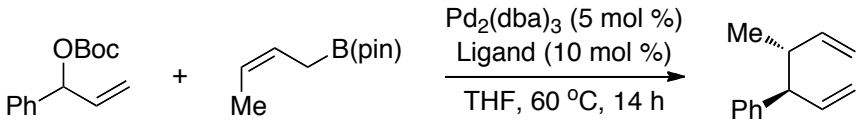
[32] Overman, L. E.; Knoll, F. M. *J. Am. Chem. Soc.* **1980**, *102*, 865.

With the successful results of Pd(0)-catalyzed asymmetric allyl-allyl cross-coupling, we envisioned an extension of the method to a diastereoselective coupling with γ-substituted allyl boron reagents. This method would provide complementary regioselectivity to the catalytic Cope rearrangement, and further, would permit ligand-based enantioselection.

**B. Reaction Optimization**

We began exploring the diastereoselective allyl-allyl cross-coupling transformation by examining the reaction of branched allylic carbonate **2.70** with *cis*-crotylboronic acid pinacol ester [*cis*-crotylB(pin)] (**2.106**) under Pd(0)-catalysis with a variety of bidentate chiral ligands (Table 2.8). Achiral bisphosphine dppbenzene is reactive, generating the product in a 3:1 ratio of diastereomers (entry 1). (*R*,*R*)-DIOP (**2.58**) unexpectedly gives linear isomer **2.3** in 36% yield (entry 2), but ligands in the Duphos series were successful in the reaction (entries 3-5), providing the product in up to 97:3 er. The highest enantioselection from the chiral ligand survey comes from (*R*)-MeO(furyl)BIPHEP (**2.63**) (entry 6), which is also the optimal ligand from asymmetric allyl-allyl coupling with allylB(pin) (**2.11**) as the metal nucleophile (Section III.B). Unfortunately, the reaction produces only 13% yield of the desired product; the rest of the material was diverted to the formation of ethereal byproducts, such as dicinnamylether and *tert*-butylcinnamyl ether, which amounted to 75% of the crude reaction mixture.

**Table 2.8: Chiral Ligand Screen in Diastereoselective Allyl-Allyl Coupling**



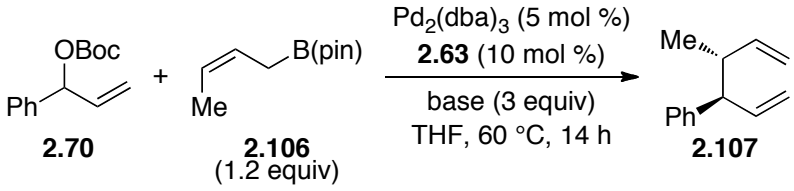

**2.70** **2.106** (1.2 equiv) **2.107**

| entry | ligand[a] | yield (%)[b] | dr[c] | er[d] |
|---|---|---|---|---|
| 1 | dppbenzene | 41 | 3:1 | - |
| 2 | (*R*,*R*)-DIOP **2.58** | > 5[e] | - | - |
| 3 | (*S*,*S*)-Me-Duphos **2.59** | 45 | 3:1 | 90:10 |
| 4 | (*R*,*R*)-Et-Duphos **2.60** | 49 | 3.5:1 | 93:7 |
| 5 | (*R*,*R*)-*i*Pr-Duphos **2.61** | 27 | 4.5:1 | 97:3 |
| 6 | (*R*)-MeO(furyl)BIPHEP **2.63** | 13 | 2.6:1 | 99:1 |

[a] See Figure 2.3 for ligand structures. [b] Isolated yield after silica gel chromatography [c] Determined by $^1$H NMR analysis. [d] Determined by GLC analysis. [e] Linear product **2.3** was isolated in 36% yield.

The formation of ethereal byproducts was suggestive of a slow transmetallation step; that is, after oxidative addition, the expelled alkoxide might attack the Pd(π-allyl) intermediate species, outcompeting transmetallation of the allylic boron to Pd. We reasoned that addition of a base might activate boron by adding to its empty *p*-orbital, thus facilitating transmetallation. A focused screen of organic and inorganic bases revealed that the addition of base sped the rate of transmetallation relative to the rate of ether formation, and fewer ether byproducts were observed in the crude reaction mixture (Table 2.9). Cesium fluoride was identified as the most effective base in the coupling reaction (entry 3).

**Table 2.9: Base Survey to Aid Transmetallation**



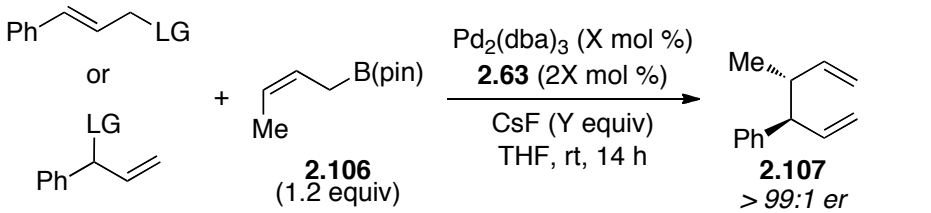

**2.70** **2.106** (1.2 equiv) **2.107**

| entry | base | yield (%)[a] | dr[b] | er[c] |
|---|---|---|---|---|
| 1 | $Et_3N$ | 34 | 4.5:1 | 99:1 |
| 2 | $Cs_2CO_3$ | 25 | 4.0:1 | > 99:1 |
| 3 | CsF | 61 | 4.2:1 | > 99:1 |

[a] Isolated yield after silica gel chromatography. [b] Determined by $^1H$ NMR analysis. [c] Determined by GLC analysis.

Following the improvement of the transmetallation step of the reaction mechanism, further studies were conducted to examine both the influence of catalyst loading and electrophile. When run at room temperature, diastereoselectivity was improved to 6:1 (Table 2.10, entry 1). While neither acetates nor trifluoroacetates provided significant improvements in reaction yield (entries 2 and 3), linear cinnamyl chloride allowed significant reduction in catalyst loading, and with 10 equivalents of CsF, the yield dramatically improved, furnishing the desired enantioenriched 1,5-diene in 90% yield.

**Table 2.10: Further Reaction Optimization**



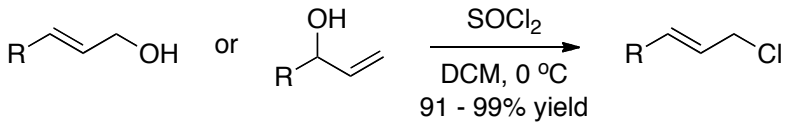

| entry | LG | X (% cat. loading) | Y (CsF equiv) | dr[a] | yield (%)[b] |
|---|---|---|---|---|---|
| 1 | OBoc | 5 | 3 | 6:1 | 50 |
| 2 | OAc | 5 | 3 | 6:1 | 26 |
| 3 | OTFA | 5 | 3 | 5:1 | 61 |
| 4 | Cl | 1.25 | 3 | 6:1 | 72 |
| 5 | Cl | 1.25 | 10 | 6:1 | 90 |

[a] Determined by $^1$H NMR analysis. [b] Isolated after silica gel chromatography.

### C. Scope of the Pd-Catalyzed Asymmetric Diastereoselective Allyl-Allyl Coupling

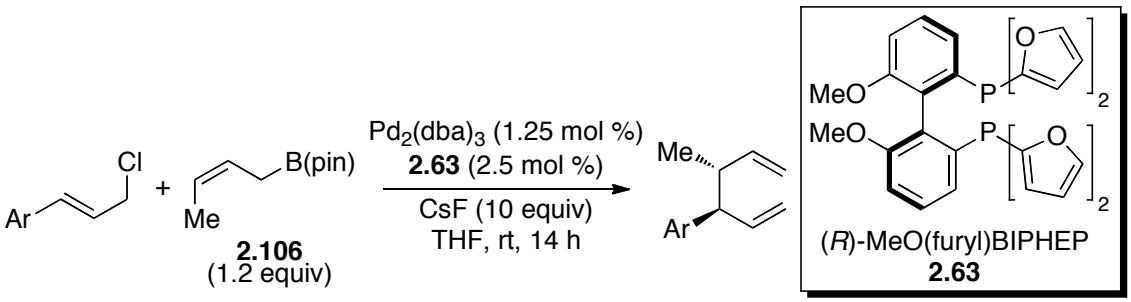
Substituted allylic chlorides were prepared by treatment of either the linear or branched isomer of the corresponding allylic alcohol with thionyl chloride (Scheme 2.28). Conveniently, most substrates do not require purification after an aqueous wash of the reaction mixture.

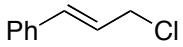
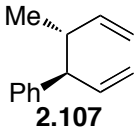
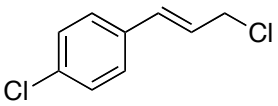
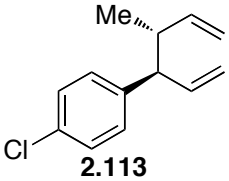
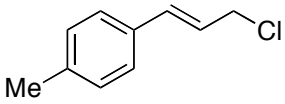
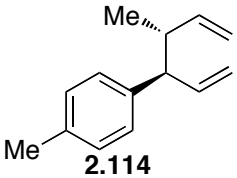
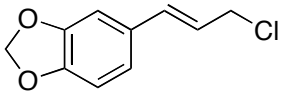
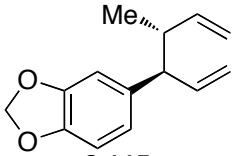
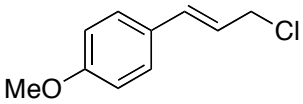
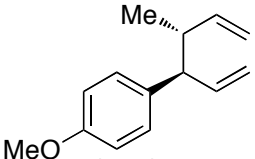
**Scheme 2.28: Preparation of Allylic Chloride Substrates**




The optimized conditions for diastereoselective allyl-allyl coupling were applied to a host of aryl-substituted allylic chlorides with *cis*-crotylB(pin) (**2.10**) (Table 2.11). Unsubstituted **2.107**, as well as halide- (**2.113**) and alkyl- (**2.114**) substituted aryl derivatives were well-tolerated at the *para*-position, giving the desired products in excellent enantioselectivity and yield. Electron-rich alkoxy-substituted substrates **2.111** and **2.112** furnished the corresponding products in good yield and er, but with slightly diminished diastereoselectivity, likely due to the increased reaction temperatures.

**Table 2.11: Substrate Scope of Aryl-Substituted Allylic Chlorides**

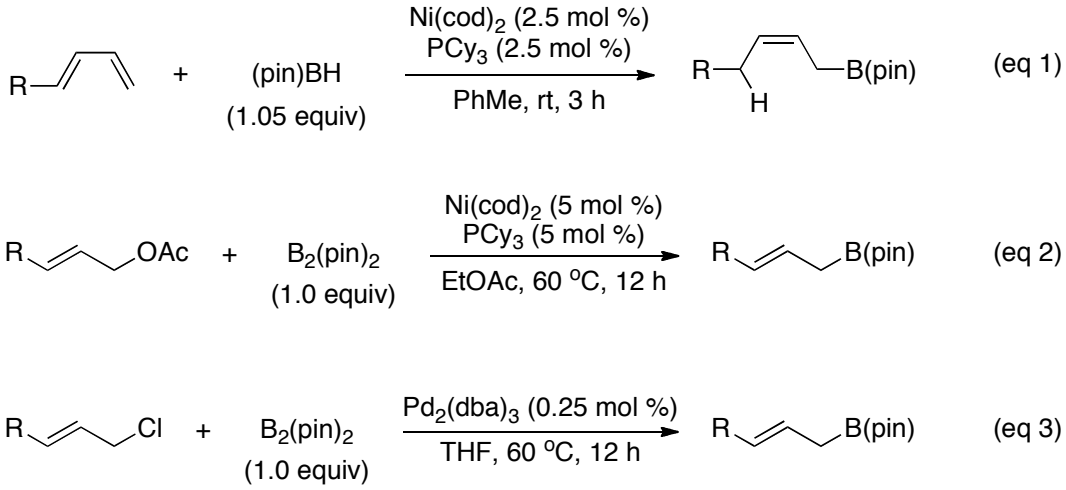



| entry | substrate | product | yield (%)[a] | dr[b] | er[c] |
|---|---|---|---|---|---|
| 1 |  **2.108** |  **2.107** | 90 | 6:1 | > 99:1 |
| 2 |  **2.109** |  **2.113** | 96 | 5:1 | > 99:1 |
| 3 |  **2.110** |  **2.114** | 93 | 6:1 | > 99:1 |
| 4[d] |  **2.111** |  **2.115** | 84 | 5:1 | 99:1 |
| 5[d] |  **2.112** |  **2.116** | 84 | 4:1 | 96:4 |

[a] Isolated after silica gel chromatography. Yield refers to the isolated yield of the diastereomeric mixture. Value is an average of at least two experiments. [b] Determined by analysis of $^1$H NMR. [c] Determined by chiral GLC analysis. [d] Reaction run at 60 °C.

To demonstrate that the diastereoselective allyl-allyl coupling is not limited to *cis*-crotylB(pin) (**2.106**), a selection of substituted allyl boron reagents were prepared. Both the *cis* and *trans* isomers of the coupling reagents were synthesized using methods developed in the Morken group. The *cis* isomer of the allyl boron reagents was generated from the Ni(0)-catalyzed 1,4-hydroboration of 1,3-dienes (Scheme 2.29, equation 1).[33] The *trans* isomer of the allyl boron reagents was produced by a Ni(0)- or Pd(0)-catalyzed borylation of an allylic electrophile (equations 2 and 3).[34]

**Scheme 2.29: Synthesis of Allyl Boron Reagents**

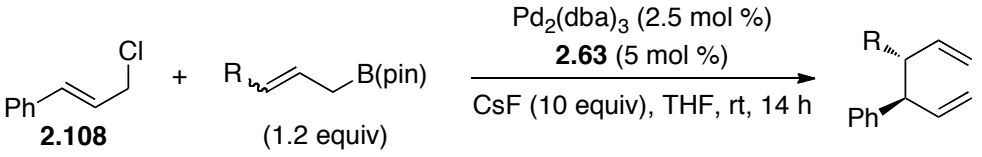


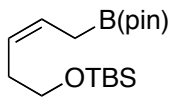
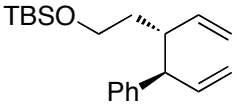
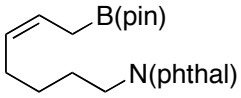
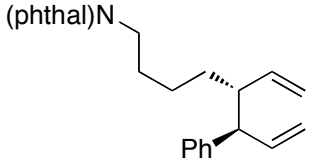
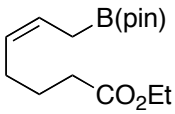
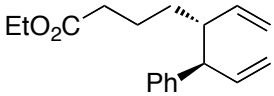
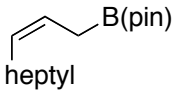
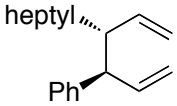
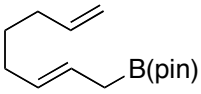
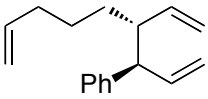
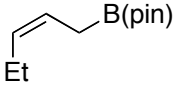
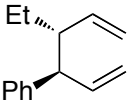
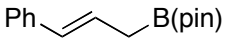
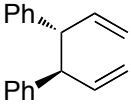

[33] (a) Ely, R. J.; Morken, J. P. *J. Am. Chem. Soc.* **2010**, *132*, 2534. (b) Ely, R. J.; Morken, J. P. *Org. Synth.* **2011**, *88*, 342.

[34] Zhang, P. Z.; Roundtree, I. A.; Morken, J. P. *Manuscript in preparation.*

Substituted allyl boron reagents were allowed to react with cinnamyl chloride **2.108** under the optimized coupling conditions (Table 2.12). Compared to *cis*-crotylB(pin) (**2.106**), more elaborate substitution on the allylboron coupling partner required higher catalyst loadings in order to achieve full conversion. Even so, the coupling reaction was amenable to a wide array of functional groups on the allyl boron reagent. Reagents containing complex heteroatom substitution, such as silyl ether **2.117**, phthalimide **2.118**, or ethyl ester **2.119** reacted with excellent levels of stereoselectivity (entries 1-3), and also provide a handle for further functionalization of the reaction product. Both aromatic and aliphatic substituted-allyl borons are effective reagents. One coupling partner that proved to be more challenging contained an appended alkene (**2.121**, entry 5), and furnished the product with diminished enantioselectivity (92:8 er). This alkene has the ability to bind to the metal center of the catalyst, and this may alter the substrate conformation during the reaction, possibly accounting for diminished reaction enantioselectivity.

**Table 2.12: Substrate Scope of Substituted Allyl Boron Reagents**

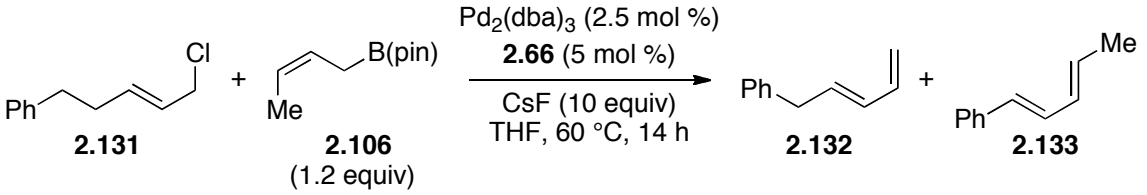



| entry | allyl boron | product | yield[a] | dr[b] | er[c] |
|---|---|---|---|---|---|
| 1 |  **2.117** |  **2.124** | 87 | 10:1 | > 99:1 |
| 2 |  **2.118** |  **2.125** | 76 | 5:1 | > 99:1 |
| 3 |  **2.119** |  **2.126** | 77 | 10:1 | > 99:1 |
| 4 |  **2.120** |  **2.127** | 71 | 7:1 | > 99:1 |
| 5 |  **2.121** |  **2.128** | 54 | 7:1 | 92:8 |
| 6 |  **2.122** |  **2.129** | 81 | 10:1 | > 99:1 |
| 7 |  **2.123** |  **2.130** | 80[d] | 14:1 | 97:3 |

[a] Yield refers to the isolated yield of the diastereomeric mixture after silica gel chromatography, and is an average of at least two experiments. [b] Determined by $^1$H NMR analysis. [c] Determined by GLC, HPLC, or SFC analysis. [d] Reaction with 1.25 mol % $Pd_2dba_3$ and 2.5 mol % **2.63** at 60 °C. Isolated material contains 40% of regioisomeric products.

Reaction of *cis*-crotylB(pin) (**2.106**) and aliphatic allylic chlorides proceeds with (*R*,*R*)-QuinoxP* (**2.66**), the optimal ligand for allyl-allyl coupling of aliphatic substrates as discussed in section III.B. Initially, however, β-hydride elimination from the intermediate Pd-π-allyl species appears to occur, and 1,3-dienes derived from the allyl chloride starting material are generated (Scheme 2.30).

**Scheme 2.30: 1,3-Diene Formation From Aliphatic Allyl Chlorides**




Previously, when exploring the allyl-allyl coupling reaction of allylic carbonates en route to quaternary stereocenters, Morken and coworkers discovered that the addition of water as reaction cosolvent suppressed the observed elimination products[35] presumably by accelerating the transmetallation step.[36] Applying this finding to the current diastereoselective allyl-allyl coupling precluded elimination and enabled us to access 1,5-dienes with 3,4-dialkyl substitution (Table 2.13). Hydrocinnamyl and *n*-heptyl allylic chlorides **2.134** and **2.135** furnished the product in high enantiomeric purity. Further, silyl ether **2.136** is a competent coupling partner, generating the enantioenriched homoallylic silyl ether.

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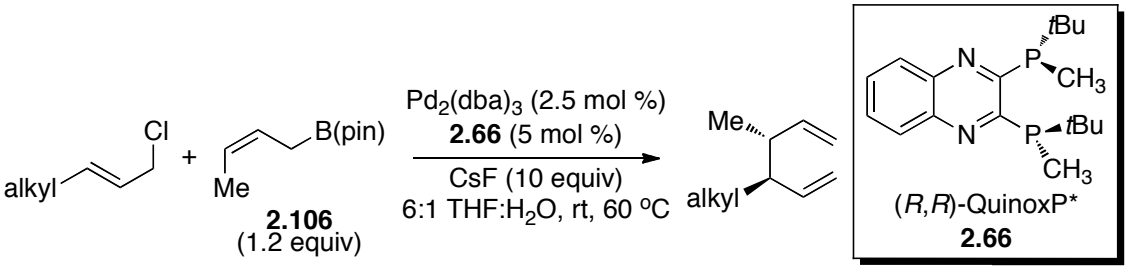
[35] Zhang, P.; Le, H.; Kyne, R. E.; Morken, J. P. *J. Am. Chem. Soc.* **2011**, *133*, 9716.

[36] Carrow, B. P.; Hartwig, J. F. *J. Am. Chem. Soc.* **2011**, *133*, 9716.

**Table 2.13: Substrate Scope of Alkyl-Substituted Allylic Chlorides**




| entry | substrate | product | yield (%)[a] | dr[b] | er[c] |
|---|---|---|---|---|---|
| 1 | Ph, Cl<br>**2.134** | Me, Ph<br>**2.137** | 64 | 7:1 | 96:4 |
| 2 | heptyl, Cl<br>**2.135** | Me, heptyl<br>**2.138** | 67 | 7:1 | 95:5 |
| 3[d] | TBDPSO, Cl<br>**2.136** | Me, TBDPSO<br>**2.139** | 51 | 6:1 | 97:3 |

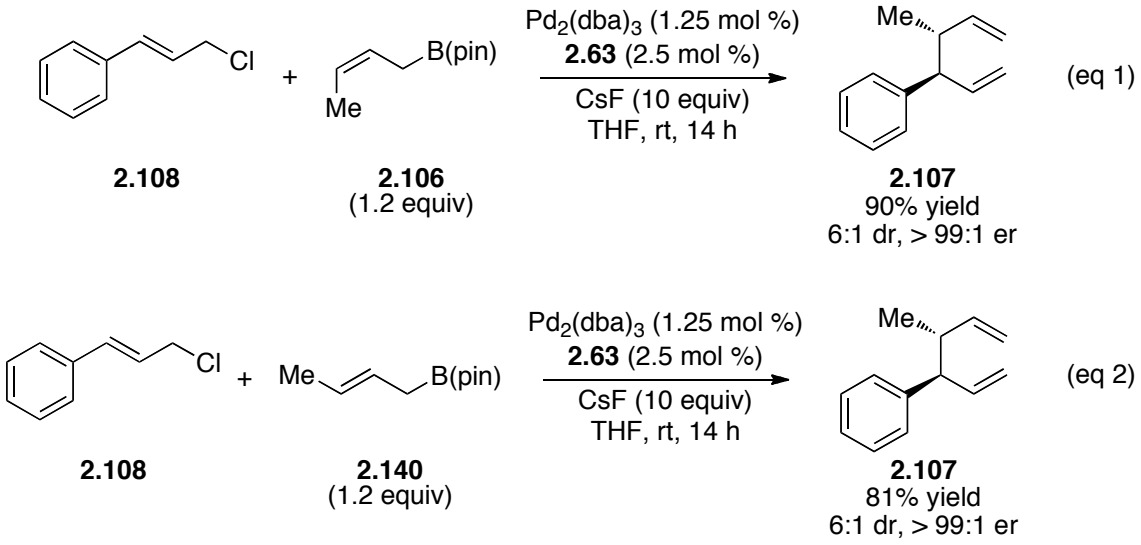
[a] Yield refers to the isolated yield of the diastereomeric mixture after silica gel chromatography, and is an average of at least two experiments. [b] Determined by $^1$H NMR analysis. [c] Determined by GLC, HPLC, or SFC analysis. [d] Reaction run in THF instead of 6:1 THF:$H_2O$ mixture.

## D. Comments on Reaction Mechanism and a Model for Stereocontrol in Diastereoselective Allyl-Allyl Coupling

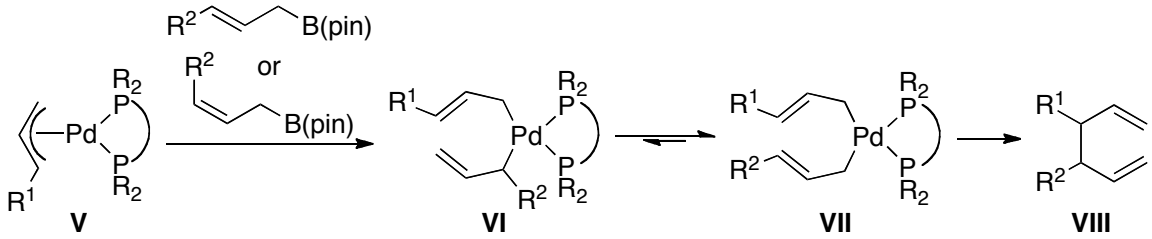
As demonstrated in Table 2.12, both *cis* and *trans* isomers of allyl boron reagents participate in the diastereoselective allyl-allyl coupling reaction. Curious to compare the reactivity and selectivity of these reagents, the *cis* and *trans* isomers of crotylB(pin) were reacted with cinnamyl chloride under Pd(0) catalysis (Scheme 2.31). The stereoselectivity in each is identical, and the yields are very similar. The convergent

stereochemical outcome indicates that, similar to the electrophile coupling partner, somewhere along the reaction pathway, the allyl group derived from the boron reagent has an opportunity to isomerize (Scheme 2.32).

**Scheme 2.31: Reactivity of the *cis* and *trans* Isomers of CrotylB(pin)**




**Scheme 2.32: Isomerization Pathway**

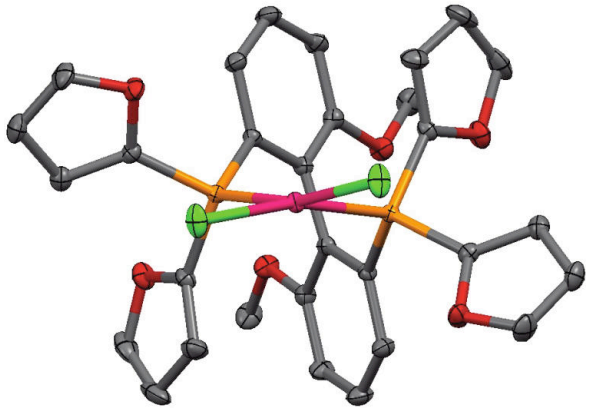



Transmetallation of the substituted allyl boron reagent to ($\eta^3$-$\pi$-allyl)Pd complex **V** proceeds by an $S_E2'$ mechanism to afford intermediate **VI** (Scheme 2.32) This complex

suffers from a disfavored steric interaction between the ligand and the substituent $R^2$. Therefore, complex **VI** undergoes isomerization to give favored complex **VII**, and subsequent 3,3′-reductive elimination produces the observed regioisomer of product **VIII**.

In order to understand the stereoinduction in the reaction, graduate student Michael Ardolino complexed (*R*)-MeO(furyl)BIPHEP **2.63** to $PdCl_2$ and obtained a crystal structure (Figure 2.4). The structure indicates that the ligand-metal complex is a seven-membered cyclic structure. The furyl substituents on phosphorus adopt psuedoaxial and psuedoequatorial positions, which have a significant effect on the placement of the chlorine ligands, which cant slightly above and below the square plane of the catalyst.

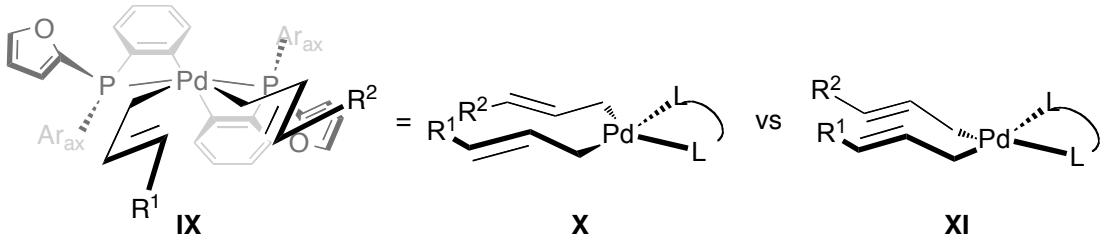
**Figure 2.4: Crystal Structure of $PdCl_2$ and (*R*)-MeO(furyl)BIPHEP**



By mapping allyl ligands onto the crystal structure shown in Figure 2.4, we may predict both reaction enantioselectivity and diastereoselectivity. In Figure 2.5, Substituents $R^1$ and $R^2$ occupy the open quadrants of the complex in order to minimize

interaction with pseudoequatorial furan rings (**IX**). Furthermore, the allyl ligands are placed in a pseudo-chair conformation, with $R^1$ and $R^2$ in the psuedoequatorial position (**X**). The minor diastereomer may be derived from either the pseudo-boat configuration (**XI**) or a substituent adopting a pseudoaxial position. In their computational studies into the mechanism for 3,3′-reductive elimination, Echavarren and coworkers calculated that the activation barrier for 3,3′-reductive elimination from the psuedo-chair conformation is lower than that from the psuedo-boat (8.5 kcal/mol vs 11.1 kcal/mol, respectively),[17] supporting our hypothesized transition state structure.

**Figure 2.5: Stereochemical Model**

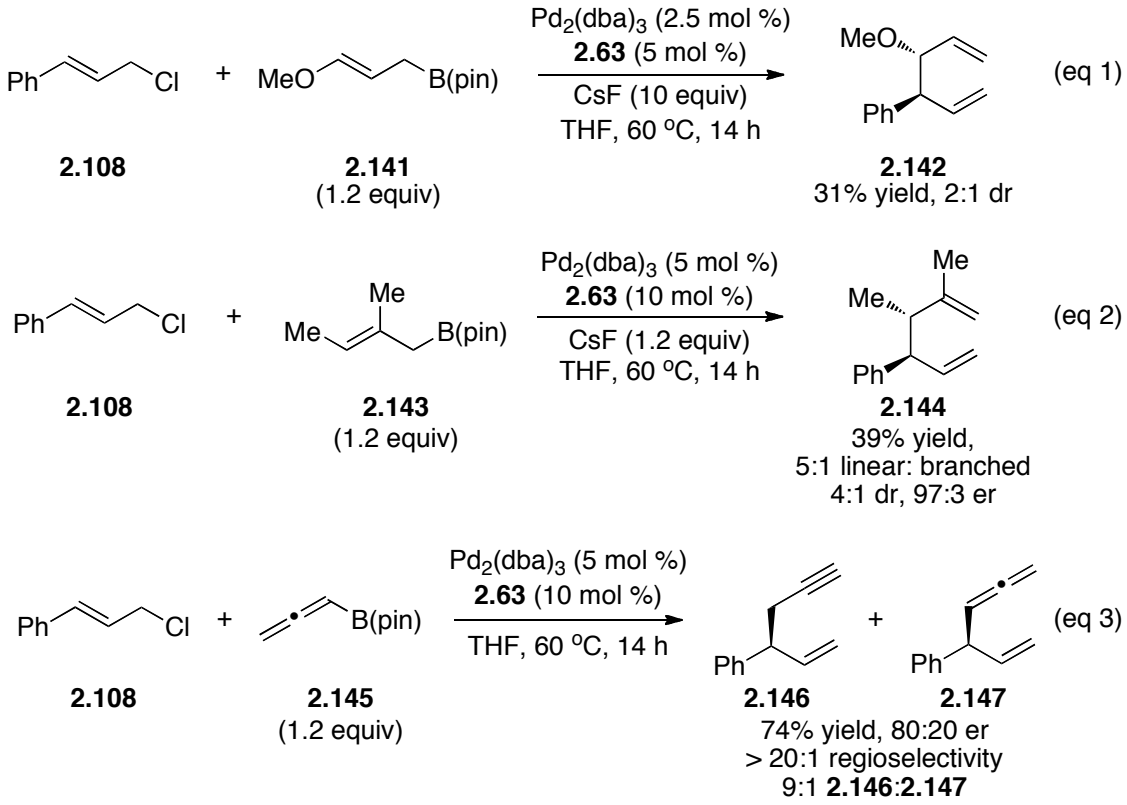



## E. Related Reactions

In order to expand the scope of the coupling reaction, several other nucleophilic allyl boron reagents were surveyed. Heteroatom-substituted allyl boron **2.141** reacted to form allylic ether **2.142** as a 2:1 diastereomeric mixture (Scheme 2.33, equation 1). This reaction generates vicinal alkenes with an oxygenated stereocenter, a structural motif that is prevalent in bioactive compounds and natural products. Due the observed low reactivity and selectivity, the success of such a process will require further development.

The reaction of β,γ-dimethylallylB(pin) (**2.143**) with cinnamyl chloride produced the desired product in excellent stereoselectivity, albeit in poor yield due to the prominent formation of the linear regioisomer (equation 2). Isoelectronic nucleophile allenylB(pin) (**2.145**) gives homopropargylation product **2.146** in good yield and moderate enantioselectivity (equation 3). Current studies in the Morken group are examining the cross-coupling of allyl and alkynyl units.

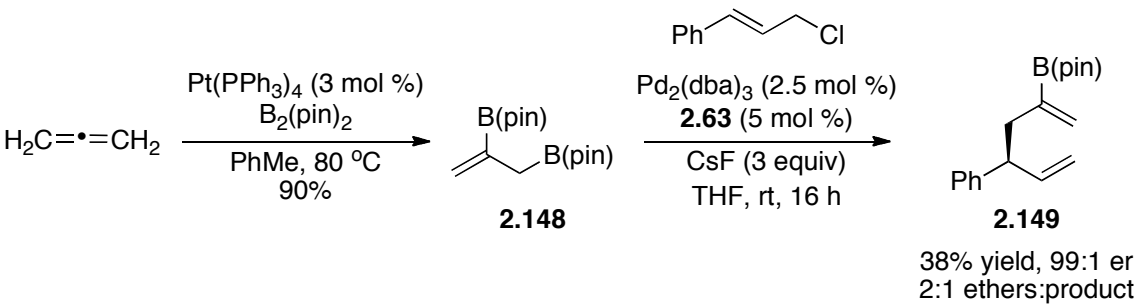
**Scheme 2.33: Reactions with Other Allyl Boron Reagents**




With the success of β-substituted allyl boron reagents, we wondered if 1,2-diborons such as **2.148** would participate in the allyl-allyl coupling reaction (Scheme

2.34). Products of such an allyl-allyl coupling (**2.149**) would contain a synthetically valuable vinylic carbon-boron bond, which lends itself readily to further manipulation in transformations such as oxidation, Suzuki coupling,[37] and Matteson homologation.[38] Reagent **2.148**, the product of Pt(0)-catalyzed diboration of allene,[39] reacts with cinnamyl chloride to produce the desired product in excellent enantioselectivity. Unfortunately, the reaction suffers from a low yield, which may be attributed to both low conversion as well as prominent formation of ethereal byproducts (see Section II.B). To optimize this reaction, a number of electrophiles were surveyed. Additionally, added equivalents of the allyl metal were utilized, but none of these modifications precluded ether formation or effectively raised reaction conversion.

**Scheme 2.34: Stereoselective Vinylboron-Generating Allyl-Allyl Cross-Coupling**



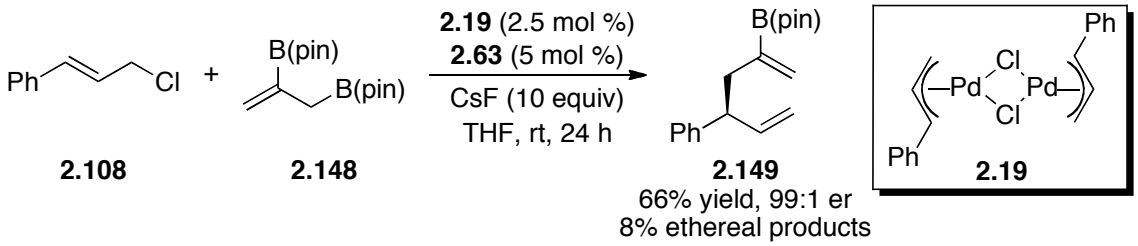

[37] (a) Suzuki, A.; Miyaura, N.; Abiko, S.; Itoh, M.; Brown, H. C.; Sinclair, J. A.; Midland, M. M. *J. Am. Chem. Soc.* **1973**, *95*, 3080. (b) Leung, T.; Zweifel, G. *J. Am. Chem. Soc.* **1974**, *96*, 5620. (c) Yamada, K.; Miyaura, N.; Itoh, M.; Suzuki, A. *Synthesis* **1977**, 679. (d) Hara, S.; Dojo, H.; Kato, T.; Suzuki, A. *Chem. Lett.* **1983**, 1125.

[38] (a) Sadhu, K. M.; Matteson, D. S. *Organometallics* **1985**, *4*, 1687. (b) Chen, A.; Ren, L.; Crudden, C. M. *J. Org. Chem.* **1999**, *64*, 9704. (c) Aggarwal, et al. *Chemical Record* **2009**, *9*, 24.

[39] Ishiyama, T.; Kitano, T.; Miyaura, N. *Tetrahedron Lett.* **1998**, *39*, 2357.

Finally, several Pd-catalysts were surveyed in the transformation. Remarkably, Pd(II) catalyst **2.19** enabled the reaction to proceed to full conversion with minimal ether formation. Currently, the Morken group is examining the application of these coupling conditions to aryl- and aliphatic-substituted allylic chlorides. After expansion of the substrate scope, future studies will be directed toward the manipulation of products such as **2.149**.

**Scheme 2.35: Identification of Optimal Pd(II)-Catalyst**




**2.108** **2.148** **2.149**
66% yield, 99:1 er
8% ethereal products

**2.19**

## V. Conclusions

A catalytic asymmetric method for the cross-coupling of prochiral allylic electrophiles with allyl metal nucleophiles has been developed. Based on computational studies of bis(allyl)metal complexes, a catalyst system was designed to allow for regioselectivity in the reductive coupling reaction. The following insights have been gained from these studies:

1. Aryl- and aliphatic-substituted allylic carbonates undergo efficient regioselective and enantioselective coupling with allylB(pin) under Pd(0) catalysis with a chiral bidentate ligand.
2. The ligand-preferred bite angle of the bidentate bis(phosphine) ligand affects the regiochemical outcome of the reaction: the branched to linear product ratio increases with decreasing bite angle.
3. Through isotope-labeling studies, we conclude that the allyl-allyl coupling proceeds through an inner sphere 3,3′-reductive elimination mechanism.
4. Substitution on the β-position of the allyl boron reagent is well tolerated in the coupling reaction.
5. Substitution on the γ-position of the allyl boron reagent leads to a diastereoselective coupling. This reaction proceeds with aryl- and aliphatic-substituted allylic chlorides and displays excellent functional group tolerance.
6. Products of allyl-allyl coupling are conducive to further functionalization, indicating their synthetic potential.
7. A variety of isoelectronic boron reagents were examined in the reaction; though the development of such reactions shows promise, further optimization is required.

## VI. Experimental Procedures

### A. General Information

$^{1}H$ NMR spectra were recorded on either a Varian Gemini-400 (400 MHz), a Varian Gemini-500 (500 MHz), or a Varian Inova-500 (500 MHz) spectrometer. Chemical shifts are reported in ppm with the solvent resonance as the internal standard ($CDCl_3$: 7.26 ppm). Data are reported as follows: chemical shift, integration, multiplicity (s = singlet, d = doublet, t = triplet, q = quartet, p = pentet, br = broad, m = multiplet, app = apparent), and coupling constants (Hz). $^{13}C$ NMR spectra were recorded on either a Varian Gemini-400 (100 MHz) or a Varian Gemini-500 (125 MHz) spectrometer with complete proton decoupling. Chemical shifts are reported in ppm with the solvent resonance as the internal standard ($CDCl_3$: 77.0 ppm). Infrared (IR) spectra were recorded on a Bruker alpha spectrophotometer, $\nu_{max}$ $cm^{-1}$. Bands are characterized as broad (br), strong (s), medium (m), and weak (w). High resolution mass spectrometry (ESI) was performed at the Mass Spectrometry Facility, Boston College.

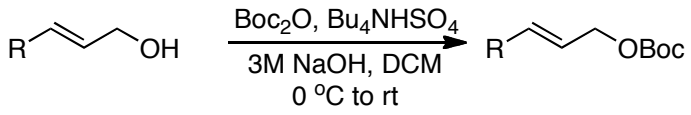
Liquid Chromatography was performed using forced flow (flash chromatography) on silica gel ($SiO_2$, 230×450 Mesh) purchased from Silicycle. Thin Layer Chromatography was performed on 25 μm silica gel plates purchased from Silicycle. Visualization was performed using ultraviolet light (254 nm), potassium permanganate ($KMnO_4$) in water, ceric ammonium molybdate (CAM) in water, or phosphomolybdic acid (PMA) in ethanol. Analytical chiral gas-liquid chromatography (GLC) was performed on a Hewlett-Packard 6890 Series chromatograph equipped with a split mode capillary injection system, a flame ionization detector, and a Supelco β-Dex 120 column, a

Supelco Chiraldex G-TA column, or a Supelco Asta Chiraldex B-DM with helium as the carrier gas. Analytical chiral supercritical fluid chromatography (SFC) was performed on a Thar SFC equipped with a Waters 2998 photodiode array detector and an analytical-2-prep column oven with methanol as the modifier. Analytical high performance liquid chromatography (HPLC) was performed on an Agilent 1120 compact chromatograph equipped with gradient pump and variable wavelength detector. Optical rotations were measured on a Rudolph Analytical Research Autopol IV Polarimeter.

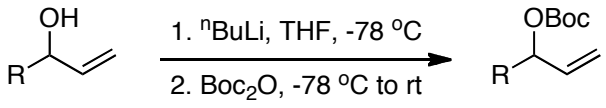
All reactions were conducted in oven- or flame-dried glassware under an inert atmosphere of nitrogen or argon. Tetrahydrofuran (THF), dichloromethane (DCM), and toluene (PhMe) were purified using a Pure Solv MD-4 solvent purification system from Innovative Technology Inc. by passing through two activated alumina columns after being purged with argon. Ethyl acetate and triethylamine were distilled from calcium hydride. Neutral alumina ($Al_2O_3$, 32-63 μm) was purchased from Sorbent Technologies. Bis(1,5-cyclooctadiene)nickel(0) [$Ni(cod)_2$], tris(dibenzylideneacetone) dipalladium(0) [$Pd_2(dba)_3$], tricyclohexylphosphine ($PCy_3$), (*R*)-(+)- and (*S*)-(-)-2,2′-bis(di-2-furanylphosphino)-6,6′-dimethoxy-1,1′-biphenyl [(*R*)- and (*S*)-MeO(furyl)BIPHEP], (*R*,*R*)-(-)-2,3-Bis(*t*-butylmethylphosphino)quinoxaline [(*R*,*R*)-QuinoxP*], and 1,2-bis(diphenylphosphino)benzene as well as all other achiral bisphosphine ligands were purchased from Strem Chemicals, Inc. Allylboronic acid pinacol ester [allylB(pin)] was generously donated by Fronteir Scientific, Inc. Pinacolborane (pinBH) was generously donated by BASF. *Trans*-1,3-pentadiene was purchased from ChemSampCo. Bis(pinacolato) diboron [$B_2(pin)_2$] was generously donated by Allychem. All other reagents were purchased from either Fisher or Aldrich and used without further purification.

## B. Experimental Procedures

### 1. Preparation of Carbonate Substrates

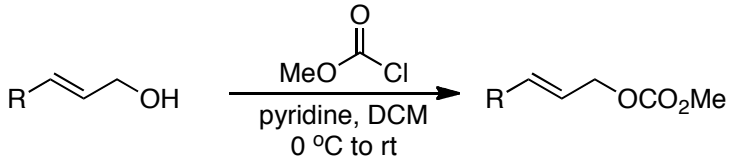



**Representative Procedure A:**[26] A round-bottomed flask with stir bar was charged with *p*-trifluoromethylcinnamyl alcohol (480 mg, 2.37 mmol) and methylene chloride (2 mL). To the resulting solution was added $Boc_2O$ (570 mg, 2.61 mmol) and $Bu_4NHSO_4$ (16.0 mg, 0.047 mmol) at room temperature. The solution was cooled to 0 °C and aqueous NaOH (1.2 mL, 30% solution) was added dropwise. The solution was allowed to stir overnight. The reaction mixture was diluted with diethyl ether and water, and was then extracted into diethyl ether three times. The combined organics were washed with 1M HCl, water, then brine, and dried over $MgSO_4$, filtered, then concentrated *in vacuo*. The crude reaction mixture was purified on silica gel (22:1 hexanes: ethyl acetate) to afford 512 mg (72%) of a white solid. $R_f$ = 0.28 (22:1 hexanes: ethyl acetate, stain in $KMnO_4$).




**Representative Procedure B:**[26] To a flame-dried round-bottomed flask with stir bar was added 1-(naphthalen-1-yl)prop-2-en-1-ol (530 mg, 2.88 mmol) and THF (7 mL). The solution was cooled to -78 °C (dry ice/acetone) and 1.18 mL (2.88 mmol) of a 2.45 M solution of butyllithium in hexane was added, dropwise. The solution was stirred for 30

minutes at -78 °C, $Boc_2O$ (629 mg, 2.88 mmol) in 4 mL THF was added. The reaction was allowed to warm to room temperature, stirring overnight. The reaction mixture was diluted with 10 mL of diethyl ether and 7 mL of water, and the mixture was stirred 15 minutes. The organic layer was separated and the aqueous layer was extracted into diethyl ether three times. Combined organics were washed with brine then dried over $MgSO_4$, filtered, then concentrated *in vacuo*. The crude reaction mixture was purified on silica gel (24:1 hexanes: ethyl acetate) to afford 691 mg (84%) of a clear, colorless oil. $R_f$ = 0.38 (20:1 hexanes: ethyl acetate, stain in $KMnO_4$).




**Representative Procedure C:**[40] A flame-dried round-bottomed flask with stir bar was charged with (*E*)-dec-2-en-1-ol (1.56 g, 10.0 mmol), methylene chloride (20 mL) and pyridine (1.19 g, 15.0 mmol). The resulting solution was cooled to 0 °C (ice-water) and then methyl chloroformate (570 mg, 2.61 mmol) was added dropwise. The reaction was allowed to stir at this temperature for an hour and then warm up to room temperature for another 12 hours. At this time, water was added, and the organic layer was washed with methylene chloride three times. The combined organic layers were then washed with saturated $CuSO_4$, followed by saturated $NH_4Cl$ and dried over $Na_2SO_4$, filtered, then concentrated. The crude reaction mixture was

[40] Gnamm, C.; Frank, G.; Miller, N.; Stork, T.; Brödner, K.; Helmchen, G. *Synthesis* **2008**, *20*, 3331.

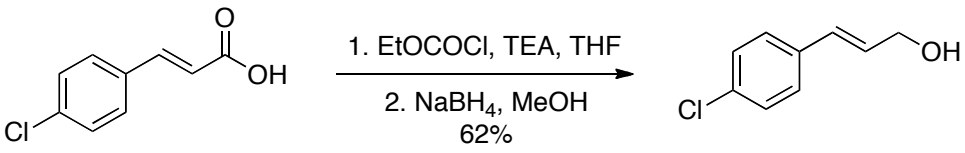
purified on silica gel (50:1 hexanes: ethyl acetate) to afford 2.10 g (99%) of a light yellow oil. $R_f$ = 0.45 (8:1 hexanes: ethyl acetate, stain in $KMnO_4$).

***Preparation of tert-butyl cinnamyl carbonate* (2.52).** From commercially available cinnamyl alcohol, procedure A was followed. Spectral data is in accordance with literature.[41]

***Preparation of cinnamyl methyl carbonate* (2.54).** From commercially available cinnamyl alcohol, procedure C was followed. Spectral data is in accordance with literature.[41]

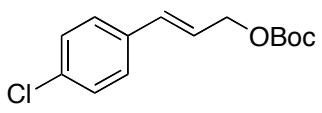
***Preparation of tert-butyl (1-phenylallyl) carbonate* (2.70).** From commercially available 1-phenylprop-2-en-ol, procedure B was followed. Spectral data is in accordance with literature.[41]

***Preparation of (E)-tert-butyl (3-(4-chlorophenyl)allyl) carbonate.*** From the corresponding allylic alcohol, synthesized as shown below,[42] procedure A was followed.



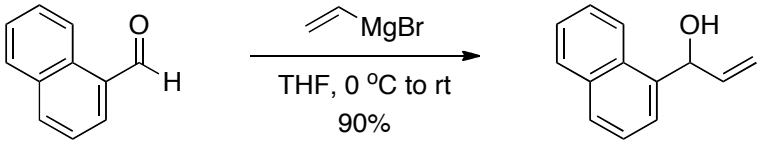

[41] Su, Y.; Jiao, N. *Org. Lett.* **2009**, *11*, 2980.

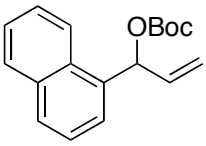
[42] Penjšević, J.; Šukalović, V.; Andrić, D.; Kostić-Rajačić, S.; Šoškic, V.; Roglić, G. *Arch. Pharm. Chem. Life. Sci.* **2007**, *340*, 456.




**(*E*)-*tert*-butyl (3-(4-chlorophenyl)allyl) carbonate (2.71)**. $^{1}$H NMR (500 MHz, $CDCl_3$): δ 1.50 (9H, s), 4.71 (2H, dd, *J* = 6.5 Hz, 1.5 Hz), 6.27 (1H, dt, *J* = 16.0 Hz, 6.5 Hz), 6.62 (1H, d, *J* = 16.0 Hz), 7.28-7.32 (4H, m); $^{13}$C NMR (125 Hz, $CDCl_3$): δ 27.8, 67.2, 82.3, 123.7, 127.8, 128.8, 133.0, 133.8, 134.7, 153.3; IR (neat): 2981 (w), 1739 (s), 1492 (w), 1370 (m), 1253 (s), 1158 (s), 1117 (m), 1090 (m), 968 (w), 847 (m), 792 (w) $cm^{-1}$; HRMS (ESI+) for $C_9H_8Cl$ [M-OBoc]: calculated: 151.0309, found: 151.0317; The crude reaction mixture was purified on silica gel (20:1 hexanes: ethyl acetate) to afford a clear, colorless oil (83%). $R_f$ = 0.30 (20:1 hexanes: ethyl acetate, stain in $KMnO_4$).

***Preparation of tert-butyl (1-(napthalen-1-yl)allyl) carbonate***. From the corresponding allylic alcohol, synthesized as shown below, procedure B was followed.

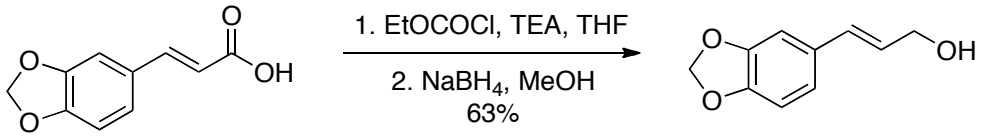


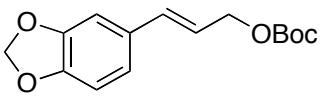




***tert*-butyl (1-(napthalen-1-yl)allyl) carbonate (2.72)**. $^{1}$H NMR (500 MHz, $CDCl_3$): δ 1.48 (9H, s), 5.30 (1H, app dt, *J* = 10.5 Hz, 1.5 Hz), 5.35 (1H, app dt, *J* = 17.0 Hz, 1.5 Hz), 6.21 (1H, ddd, *J* = 17.0 Hz, 10.5 Hz, 5.5 Hz), 6.78 (1H, d, *J* = 5.5 Hz), 7.46-7.56 (3H, m), 7.62 (1H, d, *J* = 7.0 Hz), 7.83 (1H, d, *J* = 8.0 Hz), 7.87 (1H, dd, *J* = 7.5 Hz, 1.5 Hz), 8.12 (1H, d, *J* = 8.5 Hz); $^{13}$C NMR (125 Hz, $CDCl_3$): δ 27.8, 76.3, 82.4, 117.5, 123.6, 125.1, 125.3, 125.7, 126.3, 128.8, 128.9, 130.6, 133.8, 134.4, 135.8, 152.9; IR (neat): 2980 (w), 1736 (s), 1369 (w),

1271 (s), 1250 (s), 1155 (s), 1101 (m), 1083 (m), 965 (m), 930 (m), 883 (m), 846 (m), 775 (s), 435 (w) $cm^{-1}$; HRMS (TOF MS ES+) for $C_{18}H_{20}O_3Na$ [M+Na]: calculated: 307.1310, found: 307.1314; The crude reaction mixture was purified on silica gel (25:1 hexanes: ethyl acetate) to afford a clear, colorless oil (84%). $R_f$ = 0.38 (20:1 hexanes: ethyl acetate, stain in $KMnO_4$).

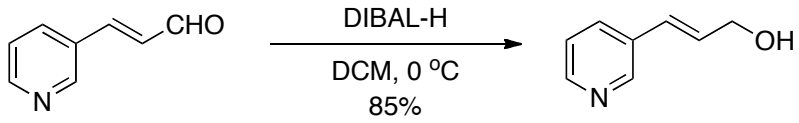
***Preparation of (E)-3-(benzo[d][1,3]dioxol-5-yl)allyl tert-butyl carbonate.*** From the corresponding allylic alcohol, synthesized as shown below,[42] procedure A was followed.

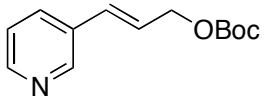



**(*E*)-3-(benzo[*d*][1,3]dioxol-5-yl)allyl *tert*-butyl carbonate (2.73)**. $^1H$ NMR (500 MHz, $CDCl_3$): δ 1.50 (9H, s), 4.68 (2H, dd, *J* = 6.5 Hz, 1.5 Hz), 5.96 (2H, s), 6.12 (1H, dt, *J* = 15.5 Hz, 6.5 Hz), 6.57 (1H, d, *J* = 15.5 Hz), 6.75 (1H, d, *J* = 8.0 Hz), 6.82 (1H, dd, *J* = 8.0 Hz, 1.5 Hz), 6.92 (1H, d, *J* = 1.5 Hz); $^{13}C$ NMR (100 Hz, $CDCl_3$): δ 27.8, 67.5, 82.2, 101.1, 105.8, 108.3, 121.0, 121.5, 130.6, 134.3, 147.6, 148.0, 153.3; IR (neat): 2979 (w), 1735 (s), 1490 (m), 1445 (m), 1369 (m), 1272 (s), 1246 (s), 1156 (s), 1124 (w), 1036 (s), 963 (m), 926 (m), 855 (s), 792 (m), 612 (w), 418 (w) $cm^{-1}$; HRMS (ESI+) for $C_{10}H_9O_2$ [M-OBoc]: calculated: 161.0597, found: 161.0604; The crude reaction mixture was purified on silica gel (20:1 hexanes: ethyl acetate) to afford a colorless oil (66%). $R_f$ = 0.12 (20:1 hexanes: ethyl acetate, stain in $KMnO_4$).

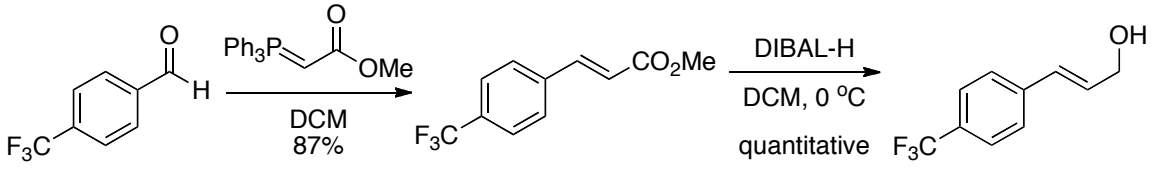
***Preparation of (E)-tert-butyl (3-(pyridin-3-yl)allyl) carbonate.*** From the corresponding allylic alcohol, synthesized as shown below, procedure A was followed.

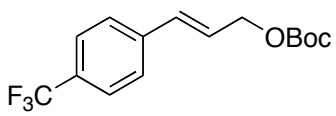



**(*E*)-*tert*-butyl (3-(pyridin-3-yl)allyl) carbonate (2.74)**. $^{1}$H NMR (400 MHz, $CDCl_3$): $\delta$ 1.44 (9H, s), 4.73 (2H, dd, *J* = 6.4 Hz, 1.2 Hz), 6.36 (1H, dt, *J* = 16.0 Hz, 6.0 Hz), 6.65 (1H, d, *J* = 16.0 Hz), 7.23-7.26 (1H, m), 7.69 (1H, app dt, *J* = 8.0 Hz, 1.6 Hz), 8.48 (1H, dd, *J* = 4.8 Hz, 1.6 Hz), 8.60 (1H, s) ; $^{13}$C NMR (100 Hz, $CDCl_3$): $\delta$ 27.8, 66.9, 82.5, 123.4, 125.4, 130.4, 131.8, 133.0, 148.5, 149.1, 153.2; IR (neat): 1736 (s), 1369 (m), 1252 (s), 1157 (s), 1115 (m), 968 (m), 862 (m), 792 (m), 707 (m) $cm^{-1}$; HRMS (ESI+) for $C_{13}H_{18}NO_3$ [M+H]: calculated: 236.1287, found: 236.1290; The crude reaction mixture was purified on silica gel (4:1 hexanes: ethyl acetate with 2% triethylamine) to afford a clear, colorless oil (55%). $R_f$ = 0.12 (4:1 hexanes: ethyl acetate with 2% triethylamine, visualize by UV).

***Preparation of (E)-tert-butyl(3-(4-(trifluoromethyl)phenyl)allyl) carbonate.*** From the corresponding allylic alcohol, synthesized as shown below, procedure A was followed.

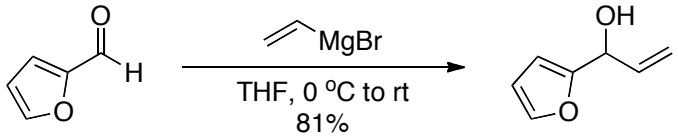





**(*E*)-*tert*-butyl(3-(4-(trifluoromethyl)phenyl)allyl) carbonate (2.79)**. $^{1}$H NMR (400 MHz, $CDCl_3$): δ 1.51 (9H, s), 4.74 (2H, dd, *J* = 6.4 Hz, 1.6 Hz), 6.38 (1H, dt, *J* = 16.0 Hz, 6.0 Hz), 6.70 (1H, d, *J* = 16.0 Hz), 7.48 (2H, d, *J* = 8.4 Hz), 7.58 (2H, d, *J* = 8.0 Hz); $^{13}$C NMR (100 Hz, $CDCl_3$): δ 27.8, 66.9, 82.5, 125.6 (q, *J* = 3.7 Hz) 125.7, 126.8, 129.7, 130.0, 132.5, 139.7, 153.3; IR (neat): 2982 (w), 1738, (s), 1616 (w), 1370 (w), 1324 (s), 1272 (s), 1252, (s), 1157 (s), 1118 (s), 1066 (s), 969 (m), 953 (m), 931 (w), 853 (m), 792 (m), 756 (w), 598 (w) $cm^{-1}$; HRMS (ESI+) for $C_{10}H_8F_3$ [M-OBoc]: calculated: 185.0573, found: 185.0579; The crude reaction mixture was purified on silica gel (22:1 hexanes: ethyl acetate) to afford a white solid (72%). $R_f$ = 0.28 (22:1 hexanes: ethyl acetate, stain in $KMnO_4$).

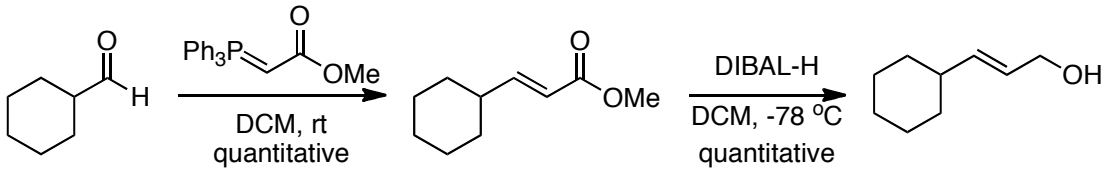
***Preparation of methyl-(4-(1-((tert-butoxycarbonyl)oxy)allyl)benzoate.*** From the corresponding allylic alcohol, synthesized as shown below, procedure B was followed.

***Preparation of 1-(furan-2-yl)prop-2-en-1-ol.*** **(2.83).** The allylic alcohol was synthesized as shown below. Spectral data is in accordance with the literature.[43]

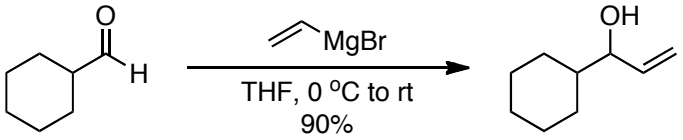


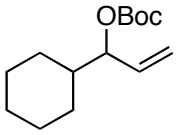

[43] Krauss, J.; Unterreitmeier, D. *Arch. Pharm. Chem. Life. Sci.* **2005**, *338*, 44.

***Preparation of (E)-tert-butyl (3-cyclohexylallyl) carbonate.*** **(2.85).** From the corresponding allylic alcohol, synthesized as shown below, procedure A was followed. Spectral data is in accordance with the literature.[44]




***Preparation of tert-butyl (1-cyclohexylallyl) carbonate****.* From the corresponding allylic alcohol, synthesized as shown below, procedure B was followed.



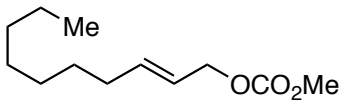




***tert*-butyl (1-cyclohexylallyl) carbonate (2.86)**. $^{1}$H NMR (400 MHz, $CDCl_3$): δ 0.88-1.30 (6H, m), 1.46 (9H, m), 1.46-1.80 (5H, m), 4.67 (1H, app t, *J* = 7.2 Hz), 5.19 (1H, dt, *J* = 10.4 Hz, 1.2 Hz), 5.22 (1H, dt, *J* = 17.2 Hz, 1.2 Hz), 5.75 (1H, ddd, *J* = 17.2 Hz, 10.4 Hz, 7.2 Hz); $^{13}$C NMR (100 Hz, $CDCl_3$): δ 25.8, 25.9, 26.3, 27.8, 28.4, 28.5, 41.5, 81.6, 82.2, 117.7, 135.0, 153.2; IR (neat): 2981 (w), 2927 (m), 2854 (w), 1737 (s), 1451 (w), 1368 (w), 1273 (s), 1251 (s), 1161 (s), 958 (m), 855 (m), 792 (m) $cm^{-1}$; HRMS (ESI+) for $C_9H_{15}$ [M-OBoc]: calculated: 123.1174, found: 123.1169; The crude reaction mixture was purified on silica gel (50:1

[44] Weix, D.J.; Markovi, D.; Ueda, M.; Hartwig, J. F. *Org. Lett.* **2009**, *11*, 2944.

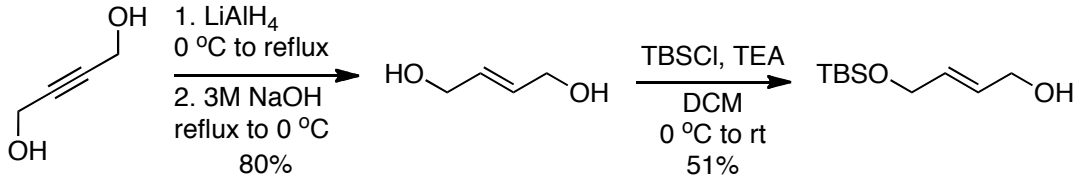
hexanes: ethyl acetate) to afford a clear, light yellow oil (48%). $R_f$ = 0.52 (8:1 hexanes: ethyl acetate, stain in $KMnO_4$).

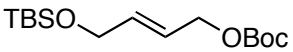
***Preparation of (E)-dec-2-enyl methyl carbonate.*** From commercially available *trans*-2-decen-1-ol, procedure C was followed.




**(*E*)-dec-2-enyl methyl carbonate (2.87)**. $^1$H NMR (400 MHz, $CDCl_3$): δ 0.86 (3H, t, *J* = 6.8 Hz), 1.25-1.39 (10H, m), 2.03 (2H, q, *J* =7.2 Hz), 3.75 (3H, s), 4.54 (2H, dd, *J* = 6.8 Hz, 0.8 Hz), 5.55 (1H, dtt, *J* = 15.6 Hz, 6.4 Hz, 1.2 Hz), 5.79 (1H, dt, *J* = 15.6 Hz, 7.8 Hz); $^{13}$C NMR (100 Hz, $CDCl_3$): δ 14.0, 22.6, 28.7, 29.02, 29.04, 31.7, 32.2, 54.5, 68.6, 123.1, 137.5, 155.6; IR (neat): 2956 (w), 2925 (m), 2855 (w), 1747 (s), 1442 (m), 1380 (w), 1253 (s), 943 (s), 792 (m) $cm^{-1}$; HRMS (ESI+) for $C_{10}H_{19}$ [M-$OCO_2Me$]: calculated: 137.1487, found: 139.1484; The crude reaction mixture was purified on silica gel (50:1 hexanes: ethyl acetate) to afford a clear, light yellow oil (99%). $R_f$ = 0.45 (8:1 hexanes: ethyl acetate, stain in $KMnO_4$).

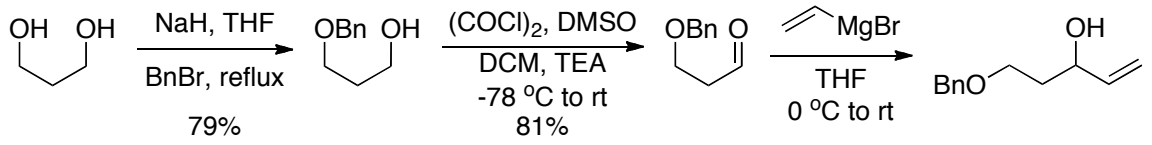
***Preparation of (E)-tert-butyl 4-(tert-butyldimethylsilyloxyl)but-2-enyl carbonate.*** From the corresponding allylic alcohol, synthesized as shown below, procedure A was followed.

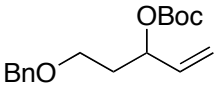



**(*E*)-*tert*-butyl 4-(*tert*-butyldimethylsilyloxyl)but-2-enyl carbonate (2.88)**. $^{1}$H NMR (400 MHz, $CDCl_3$): δ 0.03 (6H), 0.87 (9H, s), 1.45 (9H, s), 4.14-4.16 (2H, m), 4.52 (2H, d, *J* = 4.8 Hz), 5.75-5.87 (2H, m); $^{13}$C NMR (100 Hz, $CDCl_3$): δ -5.4, 18.3, 25.8, 27.7, 62.7, 66.8, 81.9, 123.2, 134.4, 153.3; IR (neat): 2955 (w), 2931 (w), 2886 (w), 2857 (w), 1740 (s), 1462 (w), 1392 (w), 1369 (m), 1274 (s), 1162 (s), 1107 (s), 1050 (m), 834 (s), 775 (s) $cm^{-1}$; HRMS (ESI+) for $C_{10}H_{21}OSi$ [M-OBoc]: calculated: 185.1362, found: 185.1363; The crude reaction mixture was purified on silica gel (35:1 hexanes: ethyl acetate) to afford a clear, light yellow oil (83%). $R_f$ = 0.41 (8:1 hexanes: ethyl acetate, stain in $KMnO_4$).

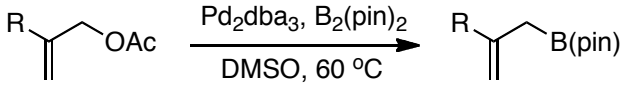
***Preparation of 5-(benzyloxy)pent-1-en-3-yl tert-butyl carbonate***. From the corresponding allylic alcohol, synthesized as shown below, procedure B was followed.



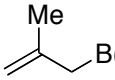

**5-(benzyloxy)pent-1-en-3-yl *tert*-butyl carbonate (2.89)**. $^{1}$H NMR (400 MHz, $CDCl_3$): $\delta$ 1.48 (9H, s), 1.86-1.94 (1H, m), 1.98-2.07 (1H, m), 3.49-3.58 (2H, m), 4.49 (2H, d, *J* = 0.8 Hz), 5.18-5.24 (1H, m), 5.19 (1H, app dt, *J* = 10.4 Hz, 1.2 Hz), 5.29 (1H, app dt, *J* = 17.2 Hz, 1.2 Hz), 5.81 (1H, ddd, *J* = 17.2 Hz, 10.4 Hz, 6.8 Hz), 7.26-7.35 (5H, m); $^{13}$C NMR (100 Hz, $CDCl_3$): $\delta$ 27.8, 34.5, 66.1, 73.1, 75.2, 82.0, 117.2, 127.6, 127.7, 128.4, 136.1, 138.3, 152.8; IR (neat): 2980 (w), 2931 (w), 2863 (w), 1739, (s), 1455 (w), 1368 (m), 1274 (s), 1254, (s), 1161 (s), 1101 (s), 990 (w), 931 (m), 854 (m), 792 (w), 738 (m), 698 (m) $cm^{-1}$; HRMS (ESI+) for $C_{17}H_{24}O_4$ [M+H]: calculated: 293.1753, found: 293.1751; The crude reaction mixture was purified on silica gel (100:1 hexanes: ethyl acetate) to afford a clear, colorless oil (59%). $R_f$ = 0.48 (8:1 hexanes: ethyl acetate, stain in $KMnO_4$).

## 2. Preparation of β-Substituted Allyl Boron Reagents




**Representative Procedure:** [45] A flame dried round-bottomed flask with stir bar was charged with tris(dibenzylideneacetone) dipalladium(0) (69.0 mg, 0.075 mmol) and $B_2(pin)_2$ (1.70 g, 6.60 mmol) in a dry-box under an argon atmosphere. The flask was sealed with a septum, and removed from the dry-box. Under an atmosphere of nitrogen, freshly distilled DMSO (18 mL) was added by syringe, followed by methallyl acetate (342 mg, 3.00 mmol). The reaction mixture was then heated to 60 °C in an oil bath for 12 hours. The reaction was diluted with diethyl ether and brine, and the aqueous layer was washed with diethyl ether three times. The combined organic layers were dried over $Na_2SO_4$, filtered, and concentrated. The crude reaction mixture was purified on silica gel (30:1 pentane: diethyl ether) to afford 338 mg (62%) of a clear, colorless oil. $R_f$ = 0.35 (8:1 hexanes: ethyl acetate, stain in $KMnO_4$).

***Preparation of 4,4,5,5-tetramethyl-2-(2-methallyl)-1,3,2-dioxaborolane.*** From commercially available methallyl acetate, the representative procedure was followed.

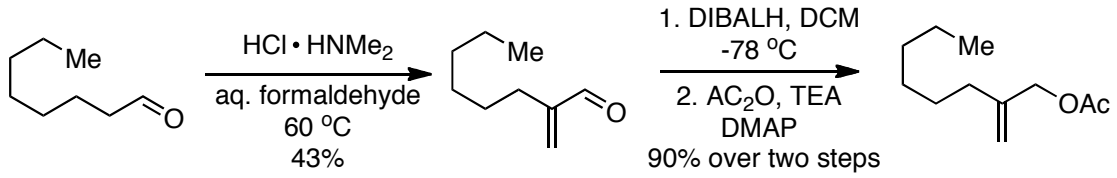


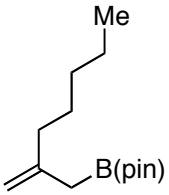

**4,4,5,5-tetramethyl-2-(2-methallyl)-1,3,2-dioxaborolane (2.101).** $^1$H NMR (500 MHz, $CDCl_3$): δ 1.25 (12H, s), 1.73 (2H, s), 1.77 (3H, m), 4.66 (1H, m), 4.68 (1H, m); $^{13}$C NMR (125 Hz, $CDCl_3$): δ 24.5, 24.6, 24.7,

[45] Ishiyama, T.; Ahiko, T.; Miyaura, N. *Tetrahedron Lett.* **1996**, *37*, 6889.

83.3, 110.2, 142.9; IR (neat): 3414 (br), 2979 (m), 2929 (w), 1648, (w), 1475 (m), 1455 (m), 1372 (s), 1326 (s), 1272 (m), 1144, (s), 982 (m), 881 (m), 850 (s) $cm^{-1}$; HRMS (ESI +) for $C_{10}H_{20}BO_2$ [M+H]: calculated: 183.1556, found: 183.1558; The crude reaction mixture was purified on silica gel (50:1 pentane: ether) to afford 336 mg of a clear, colorless oil (62% yield). $R_f$ = 0.35 (30:1 pentane: ether, stain in $KMnO_4$).

***Preparation of 4,4,5,5-tetramethyl-2-(2-methyleneoctyl)-1,3,2-dioxaborolane.*** From 2-methyeneoctyl acetate, synthesized as shown below, the representative procedure was followed.



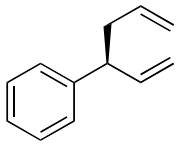




**4,4,5,5-tetramethyl-2-(2-methyleneoctyl)-1,3,2-dioxaborolane (2.103)**. $^1$H NMR (400 MHz, $CDCl_3$): δ 1.23 (3H, t, *J* = 8.4 Hz), 1.24 (12H, s), 1.24-1.31 (6H, m), 1.40-1.55 (2H, m), 1.71 (2H, s), 2.04 (2H, t, *J* = 7.6 Hz), 4.69 (1H, m), 4.70 (1H, m); $^{13}$C NMR (100 Hz, $CDCl_3$): δ 14.1, 22.6, 24.7, 27.6, 29.1, 31.8, 38.1, 83.2, 109.1, 146.8; IR (neat): 3073 (w), 2979 (m), 2957 (m), 2928 (s), 2858 (m), 1744 (w), 1641 (w), 1467 (w), 1379 (m), 1325 (s), 1273 (w), 1144 (s), 878 (m), 848 (m) $cm^{-1}$; HRMS (ESI+) for $C_{15}H_{30}BO_2$ [M+H]: calculated: 253.2339, found: 253.2341; The crude reaction mixture was purified on silica gel (100:1 pentane: diethyl ether) to afford a clear, colorless oil (11%). $R_f$ = 0.44 (8:1 hexanes: ethyl acetate, stain in $KMnO_4$).

### 3. Representative Procedure for Pd-Catalyzed Allyl-Allyl Cross-Coupling

An oven-dried 2-dram vial equipped with a magnetic stir bar was charged with tris(dibenzylideneacetone) dipalladium(0) (4.6 mg, 0.005 mmol), (*R*)-(+)-2,2'-bis(di-2-furanylphosphino)-6,6'-dimethoxy-1,1'-biphenyl (5.4 mg, 0.010 mmol), and 0.20 mL of THF in a dry-box under an argon atmosphere. The vial was capped and stirred for 5 minutes, then *tert*-butyl cinnamyl carbonate (23.4 mg, 0.100mmol) was added, followed by allylboronic acid pinacol ester (20.1 mg, 0.120 mmol). The vial was sealed, removed from the dry-box, and allowed to stir at 60 °C for 12 hours. After this time period, the reaction vial was cooled to ambient temperature, diluted with diethyl ether, filtered through a plug of silica gel and concentrated *in vacuo*. Analysis of the unpurified reaction mixture using $^1$H NMR was used to determine the branched to linear product ratio. Silica gel chromatography (pentane) afforded 11.4 mg (72%) of a colorless oil of the allyl-allyl coupling product as a mixture of isomers.

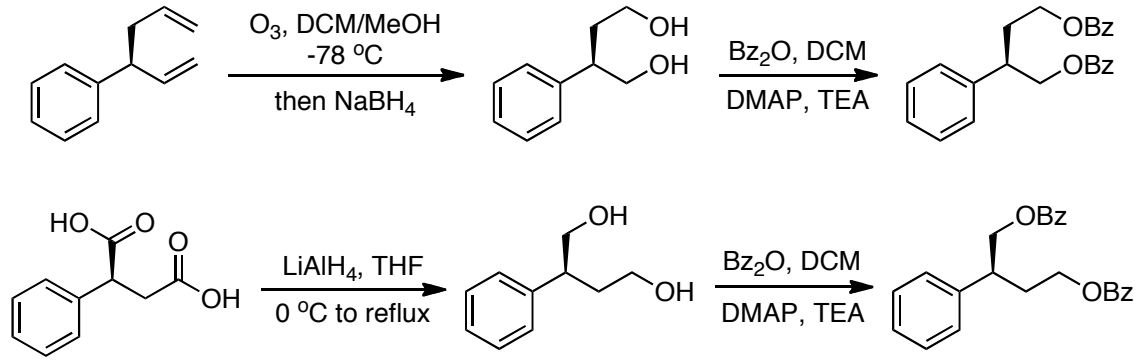
**4. Characterization of Products from Pd-Catalyzed Allyl-Allyl Cross-Coupling**



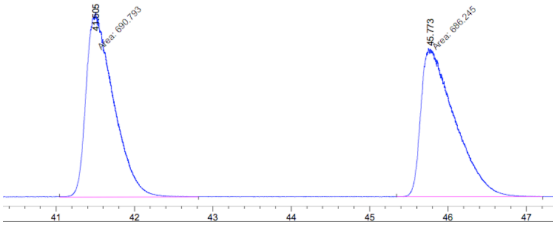
**(*S*)-hexa-1,5-dien-3-ylbenzene (2.53).** $^{1}$H NMR (500 MHz, $CDCl_3$): δ 2.47-2.51 (2H, m), 3.36 (1H, app q, *J* = 7.5 Hz), 4.96-5.07 (4H, m), 5.73 (1H, ddt, *J* = 17.0 Hz, 10.0 Hz, 7.5 Hz), 5.98 (1H, ddd, *J* = 17.0 Hz, 10.0 Hz, 7.5 Hz), 7.19-7.22 (3H, m), 7.29-7.32 (2H, m); $^{13}$C NMR (100 MHz, $CDCl_3$): δ 39.7, 49.6, 114.4, 116.1, 126.3, 127.7, 128.4, 136.6, 141.6, 143.7; IR (neat): 3078 (w), 3028 (w), 3004 (w), 2978 (w), 2924 (w), 1631 (s), 1601 (w), 1492 (s), 1452 (s), 1415 (w), 1073 (w), 991 (m), 910 (s), 753 (m), 698 (s) $cm^{-1}$; HRMS (ESI+) for $C_{12}H_{15}$ [M+H]: calculated: 159.1174, found: 159.1176; $[\alpha]^{20}_{D}$ = +12.237 (*c* = 0.44, $CHCl_3$). The crude reaction mixture was purified on silica gel (pentane) to afford a clear, colorless oil (11.4 mg, 72% yield). $R_f$ = 0.38 (pentane, stain in $KMnO_4$).

***Proof of Stereochemistry:***

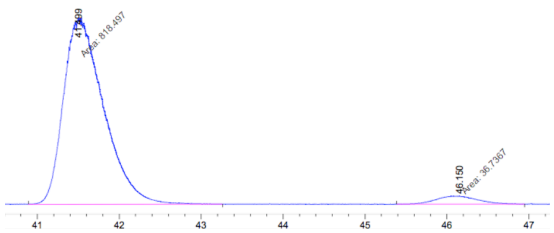
Enantioselectivity was determined by comparison of the title compound with racemic material prepared using 1,2-bis(diphenylphosphino)benzene as the achiral ligand in the allyl-allyl coupling reaction. Absolute stereochemistry was determined by converting the allyl-allyl coupling product to a dibenzoate by ozonolysis/reduction and benzoate protection of the corresponding diol, as shown below. *Via* chiral HPLC, the resulting dibenzoate was compared to authentic (*S*)-2-phenylbutane-1,4-diyl dibenzoate, which was derived from commercially available (*S*)-2-phenylsuccinic acid.




*Chiral GLC (CD-GTA, Supelco, 60 °C, 25 psi) - analysis of title compound*



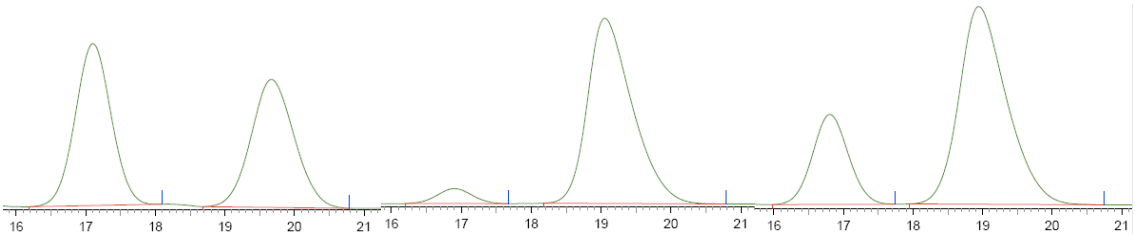
racemic



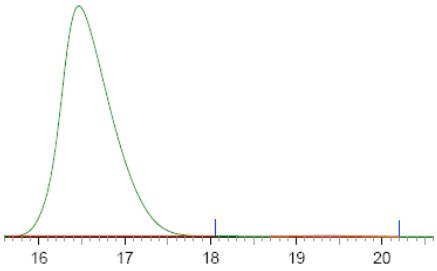
reaction product

| Peak # | RetTime [min] | Type | Width [min] | Area [pA*s] | Height [pA] | Area % |
|---|---|---|---|---|---|---|
| 1 | 41.499 | MM | 0.5666 | 818.49750 | 24.07773 | 95.70448 |
| 2 | 46.150 | MM | 0.5839 | 36.73672 | 1.04862 | 4.29552 |

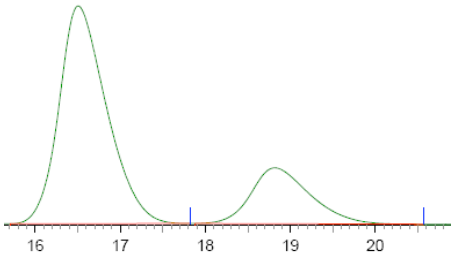
*Chiral HPLC (OD-R, Chiralcel, 1 mL/min, 1% isopropanol, 254 nm) – analysis of 2-phenylbutane-1,4-diyl dibenzoate.*



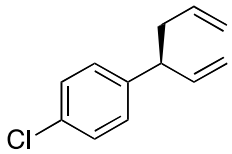

racemic derived from reaction product derivative + racemic coninjection




(*S*)-2-phenylbutane-1,4-diyl dibenzoate




(*S*)-2-phenylbutane-1,4-diyl dibenzoate + racemic

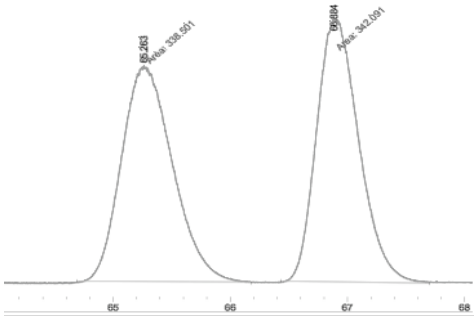


**(*S*)-1-chloro-4-(hexa-1,5-dien-3-yl)benzene (2.75)**. $^{1}$H NMR (500 MHz, $CDCl_3$): $\delta$ 2.46 (2H, app dtd, *J* = 21.5 Hz, 14.0 Hz, 7.5 Hz), 3.34 (1H, app q, *J* = 7.5 Hz), 4.96-5.08 (4H, m), 5.69 (1H, app ddt, *J* = 17.0 Hz, 10.0 Hz, 7.0 Hz), 5.94 (1H, ddd, *J* = 17.5, 10.5, 7.5 Hz), 7.12 (2H, app dt, *J* = 8.5 Hz, 2.5 Hz), 7.27 (2H, app dt, *J* = 9.0 Hz, 2.5 Hz); $^{13}$C NMR (125 Hz, $CDCl_3$): $\delta$ 39.6, 48.9, 114.8, 116.5, 128.5, 129.1, 132.0, 136.2, 141.1, 142.1; IR (neat): 3078.8 (w), 2978 (w), 2926 (w, br), 1640 (w), 1491 (s), 1407 (w), 1092 (s), 1014 (m), 922 (m), 914 (s), 827 (m), 524 (w) $cm^{-1}$; HRMS (ESI+) for $C_{12}H_{14}Cl$ [M+H]: calculated: 193.0784, found: 193.0793; $[\alpha]^{20}_{D}$ = +24.816 (*c* = 0.64, $CHCl_3$). The crude reaction mixture was purified on silica gel (pentane) to afford a clear, colorless oil (17.9 mg, 59% yield). $R_f$ = 0.6 (pentane, stain in $KMnO_4$).

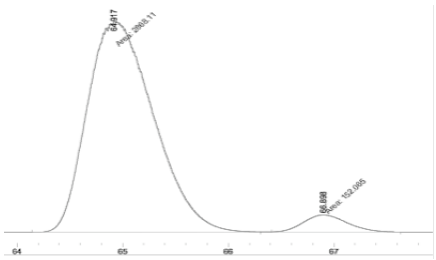
***Proof of Stereochemistry:***

Enantioselectivity was determined by comparison of the title compound with racemic material prepared using 1,2-bis(diphenylphosphino)benzene as the achiral ligand in the allyl-allyl coupling. The absolute stereochemistry was assigned by analogy.

*Chiral GLC (CD-GTA, Supelco, 80 °C for 60 min, ramp 3 °C/min to 120 °C, 25 psi) – analysis of the title compound.*

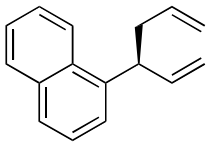


Racemic



Reaction Product

| Peak # | RetTime [min] | Type | Width [min] | Area [pA*s] | Height [pA] | Area % |
|---|---|---|---|---|---|---|
| 1 | 64.917 | MM | 0.7236 | 2868.11475 | 66.06399 | 94.96504 |
| 2 | 66.898 | MM | 0.4733 | 152.06499 | 5.35460 | 5.03496 |

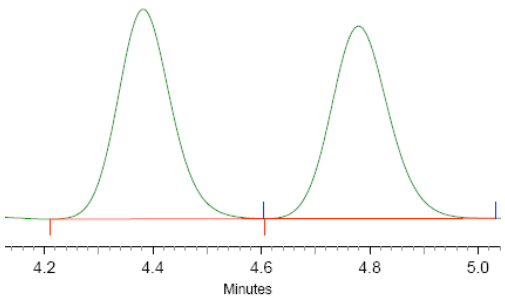


**(*S*)-1-(hexa-1,5-dien-3-yl)naphthalene (2.76).** $^{1}$H NMR (500 MHz, $CDCl_3$): $\delta$ 2.66-2.69 (2H, m), 4.23 (1H, app q, *J* = 7.0 Hz), 4.99-5.14 (4H, m), 5.83 (1H, app ddt, *J* = 17.0 Hz, 10.0 Hz, 7.0 Hz), 6.12 (1H, ddd, *J* = 17.0, 10.5, 7.0 Hz), 7.40 (1H, d, *J* = 7.0 Hz), 7.44-7.54 (3H, m), 7.74 (1H, d, *J* = 8.0 Hz), 7.87 (1H, dd, *J* = 7.0 Hz, 0.5 Hz), 8.12 (1H, d, *J* = 8.0 Hz); $^{13}$C NMR (100 Hz, $CDCl_3$): $\delta$ 39.3, 43.9, 115.0, 116.2, 123.4, 124.2, 125.4, 125.5, 125.8, 126.9, 128.9, 131.6, 134.0, 136.8, 139.7, 141.1; IR (neat): 3090 (w), 1638 (w), 992 (w), 912 (m), 796 (w), 776 (s) $cm^{-1}$; HRMS (ESI+) for $C_{16}H_{17}$ [M+H]: calculated: 209.1330, found: 209.1334; $[\alpha]^{20}_{D}$ = +26.602 (*c* = 0.89, $CHCl_3$). The crude reaction mixture was purified on silica gel (pentane) to afford a clear, colorless oil (27.1 mg, 87% yield). $R_f$ = 0.29 (pentane, stain in $KMnO_4$).

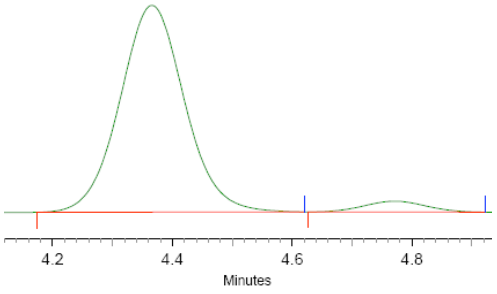
***Proof of Stereochemistry:***

Enantioselectivity was determined by comparison of the title compound with racemic material prepared using 1,2-bis(diphenylphosphino)benzene as the achiral ligand in the allyl-allyl coupling. The absolute stereochemistry was assigned by analogy.

*Chiral HPLC (OD-R, Chiraldex, 1 mL/min, 1% isopropanol in hexanes, 254 nm) – analysis of the title compound.*

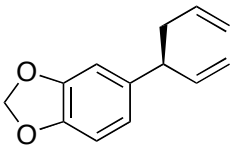



Racemic




Reaction Product

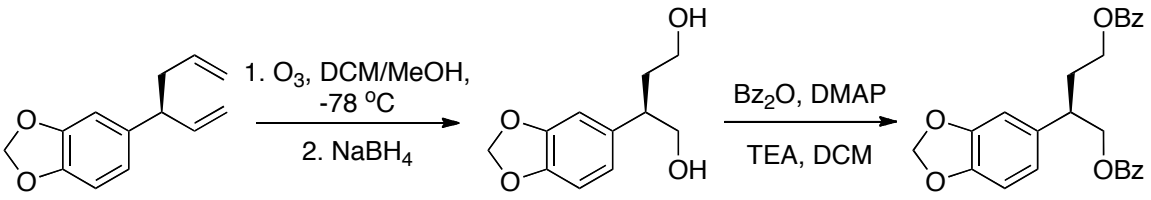
| Retention Time | Area | Area % | Height | Height % |
|---|---|---|---|---|
| 4.367 | 188084170 | 95.24 | 24956068 | 95.03 |
| 4.770 | 9408939 | 4.76 | 1303835 | 4.97 |



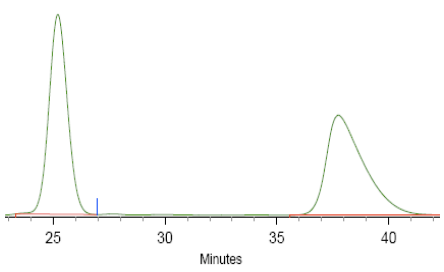
**(*S*)-5-(hexa-1,5-dien-3-yl)benzo[*d*][1,3]dioxole (2.77)**. $^{1}$H NMR (400 MHz, $CDCl_3$): δ 2.38-2.50 (2H, m), 3.28 (1H, app q, *J* = 7.6 Hz), 4.95-5.06 (4H, m), 5.71 (1H, app ddt, *J* = 16.8 Hz, 12.5 Hz, 6.8 Hz), 5.93 (2H, s), 5.93 (1H, ddd, *J* = 17.6 Hz, 10.4 Hz, 7.6 Hz), 6.64 (1H, dd, *J* = 8.0 Hz, 1.6 Hz), 6.69 (1H, d, *J* = 1.6 Hz), 6.74 (1H, d, *J* = 8.0 Hz); $^{13}$C NMR (125 Hz, $CDCl_3$): δ 39.8, 49.3, 100.8, 108.0, 108.1, 114.2, 116.1, 120.6, 136.5, 137.7, 141.6, 145.9, 147.6; IR (neat): 2895 (w, br), 1639 (w), 1503 (s), 1487 (s), 1440 (m), 1245 (s), 1040 (s), 914 (s), 810 (w) $cm^{-1}$; HRMS (ESI+) for $C_{13}H_{15}O_2$ [M+H]: calculated: 203.1072, found: 203.1079; $[\alpha]^{20}_D$ = +22.830 (*c* = 0.69, $CHCl_3$). The crude reaction mixture was purified on silica gel (80:1 pentane:diethyl ether) to afford a clear, colorless oil (23.4 mg, 83% yield). $R_f$ = 0.32 (60:1 pentane:diethyl ether, stain in $KMnO_4$).

***Proof of Stereochemistry:***

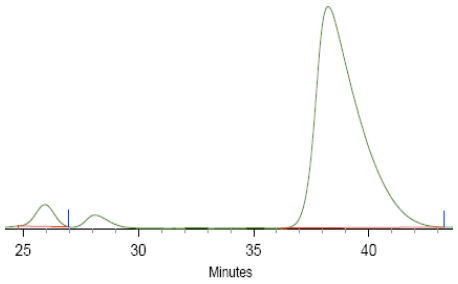
The title compound was subjected to ozonolysis and reduction. The resulting diol was protected with benzoic anhydride to afford the dibenzoate ester for HPLC analysis, as depicted below. The analogous racemic material was prepared via the same route using 1,2-bis(diphenylphosphino)benzene as achiral ligand in the allyl-allyl coupling reaction. The absolute stereochemistry was assigned by analogy.



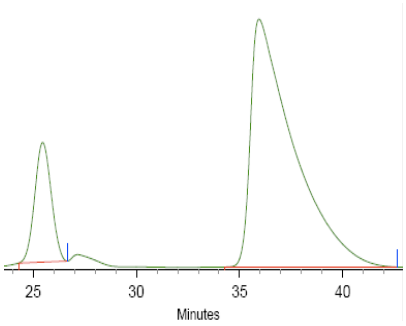
*Chiral HPLC (OD-R, Chiraldex, 1 mL/min, 3% isopropanol in hexanes, 220 nm) – analysis of the dibenzoate ester.*




Racemic

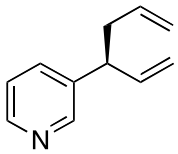



Derived from Reaction Product




Reaction Product + Racemic

| Retention Time | Area | Area % | Height | Height % |
|---|---|---|---|---|
| 25.947 | 9404811 | 4.10 | 166554 | 8.98 |
| 38.227 | 220148832 | 95.90 | 1687816 | 91.02 |

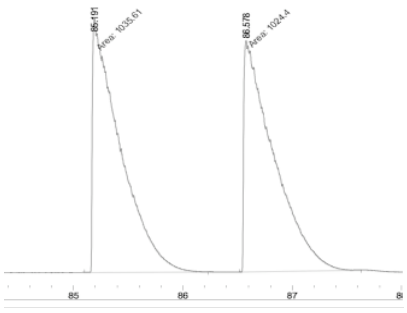


**(*S*)-3-(hexa-1,5-dien-3-yl)pyridine (2.78)**. $^{1}$H NMR (500 MHz, $CDCl_3$): δ 2.44-2.57 (2H, m), 3.40 (1H, app q, *J* = 7.0 Hz), 4.98-5.01 (2H, m), 5.05 (1H, app dt, *J* = 17.0 Hz, 1.0 Hz), 5.11 (1H, app dt, *J* = 10.5 Hz, 1.0 Hz), 5.70 (1H, app ddt, *J* = 17.5 Hz, 10.5 Hz, 7.0 Hz), 5.97 (1H, ddd, *J* = 17.0 Hz, 10.5 Hz, 7.0 Hz), 7.23 (2H, m), 7.50 (1H, app dt, *J* = 8.0 Hz, 2.0 Hz), 8.46 (1H, s); $^{13}$C NMR (125 Hz, $CDCl_3$): δ 39.5, 46.9, 115.4, 116.9, 123.3, 135.1, 135.7, 138.8, 140.4, 147.8, 149.7; IR (neat): 3078.9 (w), 2925.5 (w), 1640.0 (w), 1574.5 (w), 1478.3 (w), 1423.6 (m), 1025.2 (w), 993.1 (m), 914.9 (s), 810.6 (w), 715.7 (s), 401.4 (w) $cm^{-1}$; HRMS (ESI+) for $C_{11}H_{14}N$ [M+H]: calculated: 160.1126, found: 160.1119; $[\alpha]^{20}_{D}$ = +21.938 (*c* = 0.550, $CHCl_3$). The crude reaction mixture was purified on silica gel pretreated with 2% triethylamine in column eluent (3:1 pentane:diethyl ether) to afford a clear, light yellow oil (12.5 mg, 52% yield). $R_f$ = 0.17 (3:1 pentane:diethyl ether, visualize by UV).

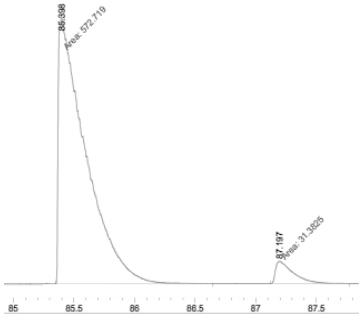
***Proof of Stereochemistry:***

Enantioselectivity was determined by comparison of the title compound with racemic material prepared using 1,2-bis(diphenylphosphino)benzene as the achiral ligand in the allyl-allyl coupling. The absolute stereochemistry was assigned by analogy.

*Chiral GLC (CD-GTA, Supelco, 60 °C for 60 min, ramp 2 °C/min to 100 °C, 25 psi) – analysis of the title compound.*

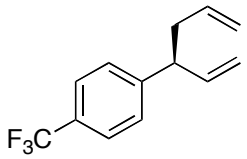



Racemic




Reaction Product

| Peak # | RetTime [min] | Type | Width [min] | Area [pA*s] | Height [pA] | Area % |
|---|---|---|---|---|---|---|
| 1 | 85.398 | MM | 0.2594 | 572.71948 | 36.80141 | 94.80510 |
| 2 | 87.197 | MM | 0.1692 | 31.38249 | 3.09128 | 5.19490 |

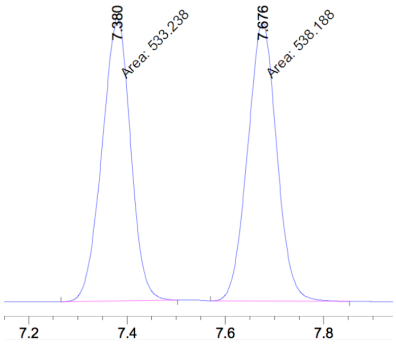


**(*S*)-1-(hexa-1,5-dien-3-yl)-4-(trifluoromethyl)benzene (2.81)**. $^{1}$H NMR (500 MHz, $CDCl_3$): δ 2.44-2.56 (2H, m), 3.43 (1H, app q, *J* = 7.5 Hz), 4.97-5.11 (4H, m), 5.69 (1H, dddd, *J* = 17.0 Hz, 10.0 Hz, 7.0 Hz, 7.0 Hz), 5.96 (1H, ddd, *J* = 17.5, 10.5, 7.0 Hz), 7.30 (2H, dd, *J* = 8.0 Hz, 0.5 Hz), 7.56 (2H, d, *J* = 8.0 Hz); $^{13}$C NMR (125 Hz, $CDCl_3$): δ 39.5, 49.4, 115.3, 116.7, 125.4 (q, *J* = 3.75 Hz), 128.1, 135.9, 140.6, 147.7; IR (neat): 2922 (s), 2851 (m), 2166 (m), 2036.7 (m), 2020 (m), 2005 (m), 1961 (w), 1326 (w), 485 (w), 453 (m), 438 (m), 422 (m) $cm^{-1}$; HRMS (ESI+) for $C_{12}H_{14}Cl$ [M+H]: calculated: 227.1048, found: 227.1047; $[\alpha]^{20}_{D}$ = +16.478 (*c* = 0.985, $CHCl_3$). The crude reaction mixture was purified on silica gel (pentane) to afford a clear, colorless oil (20.3 mg, 60% yield). $R_f$ = 0.63 (pentane, stain in $KMnO_4$).

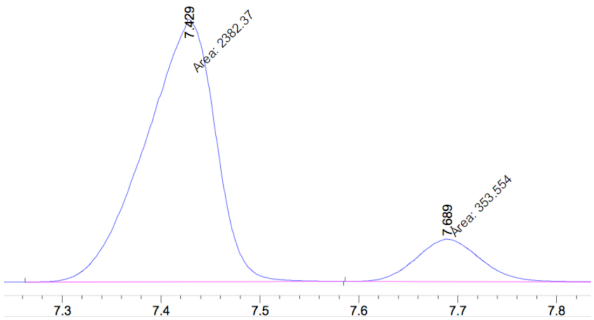
***Proof of Stereochemistry:***

Enantioselectivity was determined by comparison of the title compound with racemic material prepared using 1,2-bis(diphenylphosphino)benzene as the achiral ligand in the allyl-allyl coupling. The absolute stereochemistry was assigned by analogy.

*Chiral GLC (CD-GTA, Supelco, 100 °C, 25 psi) – analysis of the title compound.*

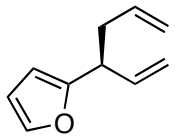



Racemic




Reaction Product

| Peak # | RetTime [min] | Type | Width [min] | Area [pA*s] | Height [pA] | Area % |
|---|---|---|---|---|---|---|
| 1 | 7.429 | MM | 0.0821 | 2382.36694 | 483.47037 | 87.07733 |
| 2 | 7.689 | MM | 0.0752 | 353.55417 | 78.31371 | 12.92267 |

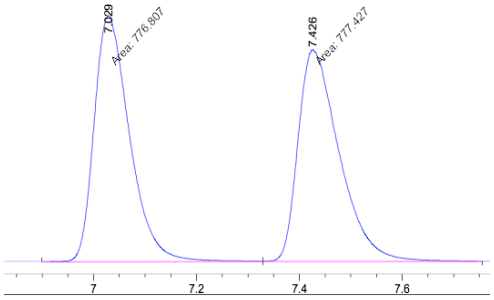


**(*S*)-2-(hexa-1,5-dien-3-yl)furan (2.84)**. $^{1}$H NMR (500 MHz, $CDCl_3$): δ 2.43 (1H, ddd, *J* = 14.0 Hz, 7.5 Hz, 7.0 Hz), 2.56 (1H, app dtt, *J* = 14.0 Hz, 7.0 Hz, 7.0 Hz, 1.5 Hz), 3.47 (1H, app q, *J* = 7.5 Hz), 5.00-5.12 (4H, m), 5.75 (1H, app ddt, *J* = 17.0 Hz, 10.0 Hz, 7.0 Hz), 5.87 (1H, ddd, *J* = 17.0 Hz, 10.5 Hz, 8.0 Hz), 6.04 (1H, dt, *J* = 3.0 Hz, 1.0 Hz), 6.30 (1H, dd, *J* = 3.0 Hz, 2.0 Hz), 7.34 (1H, dd, *J* = 2.0 Hz, 1.0 Hz); $^{13}$C NMR (125 Hz, $CDCl_3$): δ 37.7, 43.2, 105.1, 110.0, 115.7, 116.5, 132.9, 138.5, 141.2, 156.7; IR (neat): 2922.3 (s), 2851.9 (m), 1793.3 (w), 1727.3 (w), 1641.2 (w), 1462.8 (w), 1377.4 (w), 1274.1 (w), 1125.0 (w), 1077.4 (w), 823.4 (w) $cm^{-1}$; HRMS (ESI+) for $C_{10}H_{13}O$ [M+H]: calculated: 149.0966, found: 149.0968; $[\alpha]^{20}_D$ = +32.168 (*c* = 0.53, $CHCl_3$). The crude reaction mixture was purified on silica gel (pentane) to afford a clear, light yellow oil (9.5 mg, 64% yield). $R_f$ = 0.56 (8:1 hexanes: ethyl acetate, stain in $KMnO_4$).

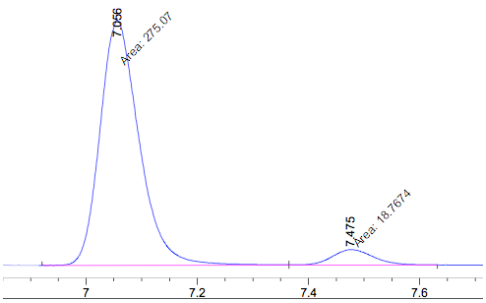
***Proof of Stereochemistry:***

Enantioselectivity was determined by comparison of the title compound with racemic material prepared using 1,2-bis(diphenylphosphino)benzene as the achiral ligand in the allyl-allyl coupling. The absolute stereochemistry was assigned by analogy.

*Chiral GLC (CD-GTA, Supelco, 70 °C, 25 psi) – analysis of the title compound.*

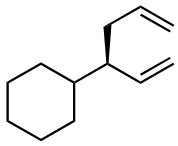



Racemic




Reaction Product

| Peak # | RetTime [min] | Type | Width [min] | Area [pA*s] | Height [pA] | Area % |
|---|---|---|---|---|---|---|
| 1 | 7.056 | MF | 0.0811 | 275.07043 | 56.54135 | 93.61302 |
| 2 | 7.475 | FM | 0.0875 | 18.76736 | 3.57612 | 6.38698 |



**(*S*)-hexa-1,5-dien-3-ylcyclohexane (2.90).** $^{1}$H NMR (500 Hz, $CDCl_3$): δ 0.87-1.30 (6H, m), 1.61-1.73 (5H, m), 1.89 (1H, m), 2.03-2.09 (1H, m), 2.19-2.24 (1H, m), 4.89-5.01 (4H, m), 5.59 (1H, ddd, *J* = 19.5 Hz, 10.5 Hz, 9.5 Hz), 5.74 (1H, app ddt, *J* = 17.2 Hz, 10.4 Hz, 6.8 Hz); $^{13}$C NMR (100 Hz, $CDCl_3$): δ 26.60, 26.63, 26.7, 29.4, 31.1, 36.4, 41.0, 49.8, 115.0, 115.2, 137.8, 140.9 ppm; IR (neat): 3075 (w), 2977 (w), 2921 (s), 2851 (s), 1640 (s), 1448 (m), 1419 (w), 994 (m), 908 (s), 705 (w) $cm^{-1}$; HRMS (ESI+) for $C_{12}H_{21}$ [M+H]: calculated: 165.1643, found: 165.1650; $[\alpha]^{20}_{D}$ = -4.322 (*c* = 0.62, $CHCl_3$). The crude reaction mixture was purified on silica gel (pentane) to afford a clear, colorless oil (10.3 mg, 63% yield of title compound). Mixture of branched to linear compounds: 10:1. $R_f$ = 0.85 (8:1 hexane: ethyl acetate, stain in $KMnO_4$).

***Proof of Stereochemistry:***

Enantioselectivity was determined by comparison of the title compound with authentic racemic material prepared using 1,2-bis(diphenylphosphino)benzene as the achiral ligand in the allyl-allyl coupling reaction. Absolute stereochemistry was determined by converting the allyl-allyl coupling product to a dibenzoate, by ozonolysis/ reduction and benzoate protection of the corresponding diol, as shown below. *Via* chiral HPLC the resulting dibenzoate was compared to (*R*)-2-cyclohexylbutane-1,4-diyl dibenzoate, which was prepared by diboration/homologation/oxidation of vinylcyclohexane, followed by dibenzoate protection as shown below.[46]

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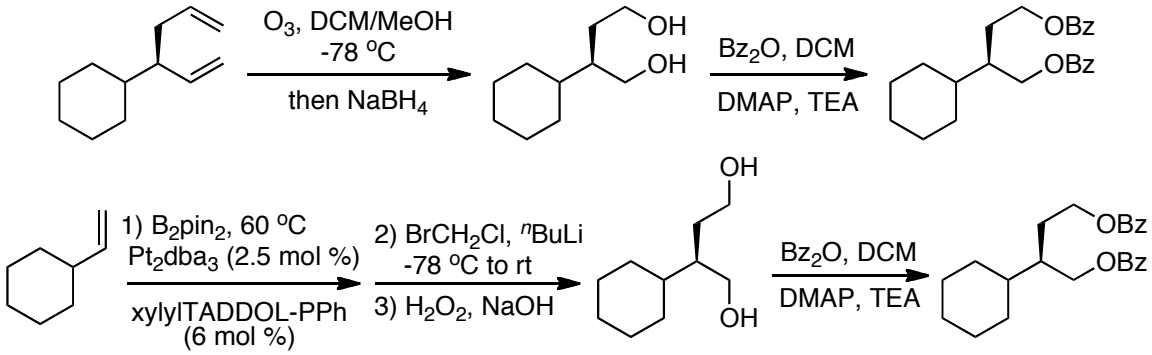
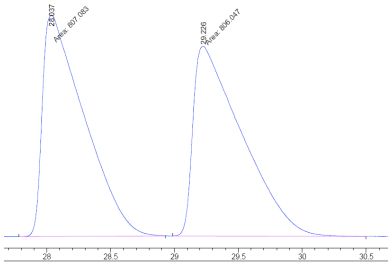
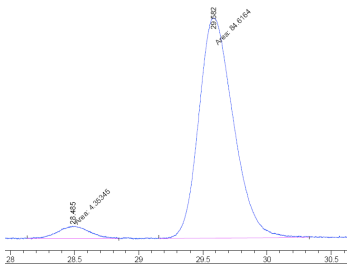
[46] Kliman, L. T.; Mlynarski, S. N.; Morken, J. P.; *J. Am. Chem. Soc.*, **2009**, *131*, 13210.




*Chiral GLC (β-dex, Supelco, 80 °C, 25 psi) - analysis of title compound*



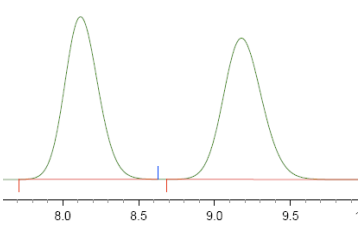
Racemic



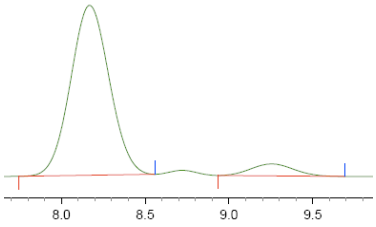
Reaction Product

| Peak # | RetTime [min] | Type | Width [min] | Area [pA*s] | Height [pA] | Area % |
|---|---|---|---|---|---|---|
| 1 | 28.486 | MM | 0.2998 | 4.78294 | 2.65896e-1 | 5.32266 |
| 2 | 29.580 | MM | 0.3141 | 85.07700 | 4.51380 | 94.67734 |

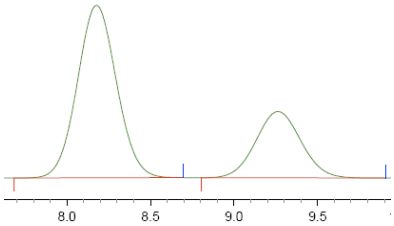
*Chiral HPLC (OD-R, Chiralcel, 1 mL/min, 1% isopropanol, 220 nm) – analysis of 2-cyclohexylbutane-1,4-diyl dibenzoate*



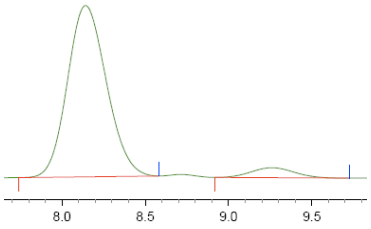

Racemic



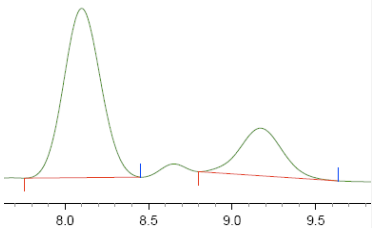

Derived from Reaction Product



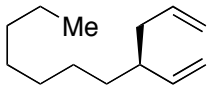

Derivative + Racemic




(*R*)-2-cyclohexylbutane-1,4-diyl dibenzoate



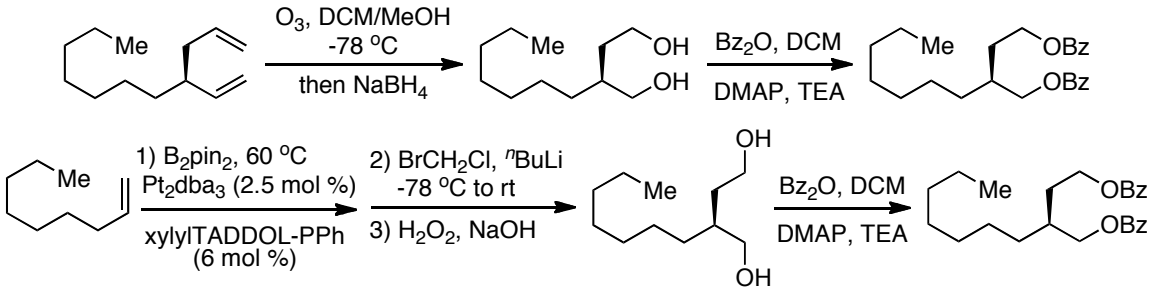

(*R*)-2-cyclohexylbutane-1,4-diyl dibenzoate + Racemic



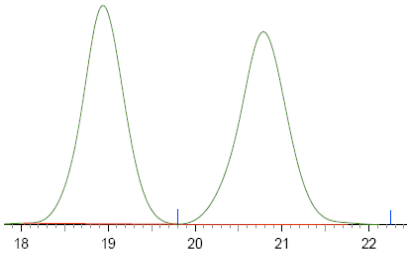

**(*S*)-4-vinylundec-1-ene (2.91).** $^{1}$H NMR (400 Hz, $CDCl_3$): δ 0.88 (3H, t, *J* = 6.8 Hz), 1.22-1.38 (12H, m), 2.01-2.14 (3H, m), 4.92-5.02 (4H, m), 5.58 (1H, ddd, *J* = 16.8 Hz, 10.4 Hz, 8.0 Hz), 5.76 (1H, app ddt, *J* = 17.2 Hz, 10.4 Hz, 6.8 Hz); $^{13}$C NMR (100 Hz, $CDCl_3$): δ 14.1, 22.7, 27.1, 29.3, 29.7, 31.9, 34.2, 39.5, 43.7, 114.1, 115.5, 137.2, 142.8; IR (neat): 3077 (w), 2957 (m), 2923 (s), 2854 (m), 1641 (s), 1465 (s), 1419 (w), 1378 (w), 993 (m), 909 (s) $cm^{-1}$; HRMS (ESI+) for $C_{13}H_{25}$ [M+H]: calculated: 181.1956, found: 181.1958; $[\alpha]^{20}_{D}$ = -2.828 (*c* = 0.76, $CHCl_3$). The crude reaction mixture was purified on silica gel (pentane) to afford a clear, colorless oil (14.4 mg, 80% yield of title compound). Mixture of branched to linear compounds: 11:1. $R_f$ = 0.86 (8:1 hexane: ethyl acetate).

***Proof of Stereochemistry:***

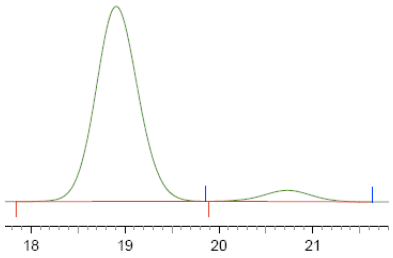
Enantioselectivity was determined by converting the allyl-allyl coupling product to a dibenzoate by ozonolysis/reduction and benzoate protection of the corresponding diol as shown below. *Via* chiral HPLC the resulting dibenzoate was compared to racemic material prepared using 1,2-bis(diphenylphosphino)benzene as the achiral ligand in the allyl-allyl coupling reaction. Absolute stereochemistry was determined by comparing the dibenzoate to authentic (*S*)-2-heptylbutane-1,4-diyl dibenzoate which was prepared by diboration/homologation/oxidation of 1-nonene, followed by dibenzoate protection as shown below.[46]



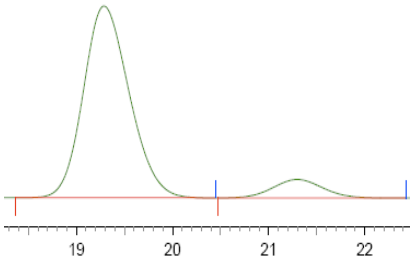

*Chiral HPLC (OD-R, Chiralcel, 0.5 mL/min, 1% isopropanol, 220 nm) – analysis of 2-heptylbutane-1,4-diyl dibenzoate*



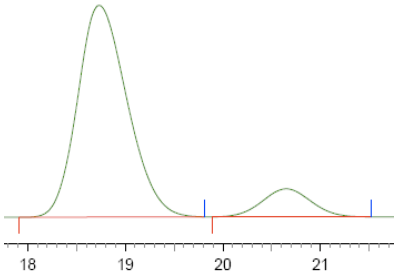

Racemic




(*S*)-2-heptylbutane-1,4-diyl dibenzoate

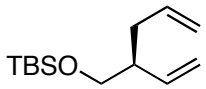



Derived from Reaction Product




Derivative + Racemic

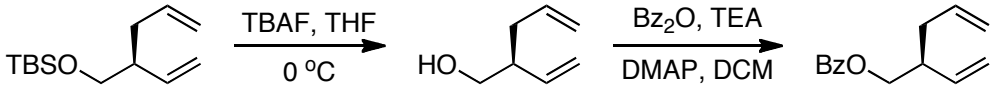
| Retention Time | Area | Area % | Height | Height % |
|---|---|---|---|---|
| 19.287 | 1013746288 | 90.51 | 30414501 | 91.21 |
| 21.297 | 106334887 | 9.49 | 2931252 | 8.79 |



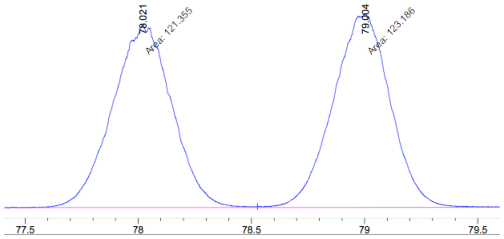

**(*S*)-*tert*-butyldimethyl((2-vinylpent-4-en-1-yl)oxy)silane (2.92).** $^{1}$H NMR (500 MHz, $CDCl_3$): δ 0.04 (6H, s), 0.89 (9H, s), 2.04-2.09 (1H, m), 2.24-2.33 (2H, m), 3.50-3.57 (2H, m), 4.98-5.06 (4H, m), 5.65-5.70 (1H, m), 5.78 (1H, app ddt, *J* = 17.0 Hz, 10.5 Hz, 7.0 Hz); $^{13}$C NMR (125 Hz, $CDCl_3$): δ -5.4, -5.4, 18.3, 25.9, 35.3, 46.0, 65.9, 115.4, 115.8, 136.9, 139.7; IR (neat): 3077.8 (w), 2955.7 (m), 2928.7 (m), 2857.2 (m), 1730.7 (m), 1641.3, (w), 1470.9 (m), 1253.4 (s), 1097.4 (s), 992.6, (m), 1097.4 (s), 912.0 (s), 834.1 (s), 773.7 (s) $cm^{-1}$; HRMS (ESI+) for $C_{13}H_{27}OSi$ [M+H]: calculated: 227.1831, found: 227.1831; $[\alpha]^{20}_{D}$ = +6.254 (*c* = 1.227, $CHCl_3$). The crude reaction mixture was purified on silica gel (pentane, then 50:1 pentane: ether) to afford a clear, colorless oil (20.6 mg, 91% yield). $R_f$ = 0.76 (8:1 hexanes: ethyl acetate, stain in $KMnO_4$).

***Proof of Stereochemistry:***

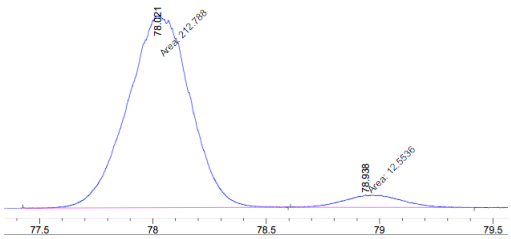
Enantioselectivity was determined by converting the allyl-allyl coupling product to a benzoate by deprotection of TBS group and benzoate protection of the corresponding alcohol as shown below. *Via* chiral GLC the resulting benzoate was compared to racemic material prepared using 1,2-bis(diphenylphosphino)benzene as the achiral ligand in the allyl-allyl coupling reaction. The absolute stereochemistry was assigned by analogy.



*Chiral GLC (CD-GTA, Supelco, 100 °C, 60 min, then 1 °C/min to 130 °C, 25 psi) – analysis of benzoate.*

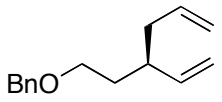



Racemic




Derived from reaction product

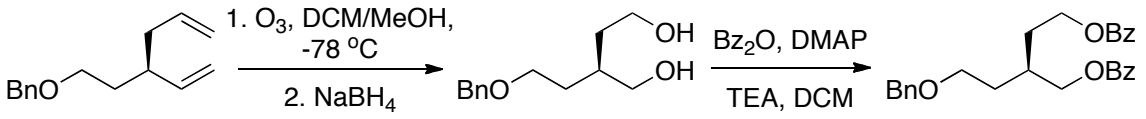
| Peak # | RetTime [min] | Type | Width [min] | Area [pA*s] | Height [pA] | Area % |
|---|---|---|---|---|---|---|
| 1 | 78.021 | MM | 0.3222 | 212.78847 | 11.00840 | 94.42910 |
| 2 | 78.938 | MM | 0.3000 | 12.55359 | 6.97340e-1 | 5.57090 |



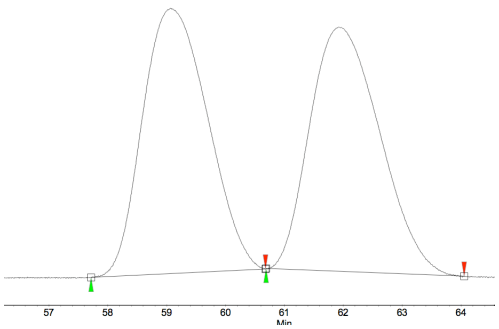
**(*R*)-(((3-vinylhex-5-en-1-yl)oxy)methyl)benzene (2.93)**. $^{1}$H NMR (400 MHz, $CDCl_3$): δ 1.49-1.57 (1H, m), 1.75-1.83 (1H, m), 2.05-2.19 (2H, m), 2.28 (1H, app dtd, *J* = 13.6 Hz, 8.4 Hz, 5.2 Hz), 3.42-3.53 (2H, m), 4.49 (2H, d, *J* = 2.0 Hz), 4.94-5.04 (4H, m), 5.59 (1H, ddd, *J* = 17.2 Hz, 10.4 Hz, 8.8 Hz), 5.76 (1H, app dtt, *J* = 20.8 Hz, 12.0 Hz, 5.6 Hz), 7.25-7.34 (5H, m); $^{13}$C NMR (100 Hz, $CDCl_3$): δ 34.0, 39.5, 40.4, 68.3, 72.9, 114.8, 115.9, 127.5, 127.6, 128.3, 136.7, 138.6, 141.9; IR (neat): 3074.5 (w), 2926.0 (m), 2856.6 (m), 1640.7, (m), 1495.9 (w), 1453.9 (m), 1419.2 (w), 1363.5, (m), 1204.2 (w), 1101.6 (s), 1028.0 (w), 994.4 (m), 912.1 (s), 735.0 (s), 697.1 (s) $cm^{-1}$; HRMS (ESI+) for $C_{15}H_{21}O$ [M+H]: calculated: 217.1592, found: 217.1590; $[\alpha]^{20}_D$ = -11.355 (*c* = 1.18, $CHCl_3$). The crude reaction mixture was purified on silica gel (100:1 hexanes: ethyl acetate) to afford a clear, colorless oil (24.3 mg, 75% yield of title compound) as a mixture of coupling product and diene (90:10). $R_f$ = 0.35 (100:1 hexanes: ethyl acetate, stain in $KMnO_4$).

***Proof of Stereochemistry:***

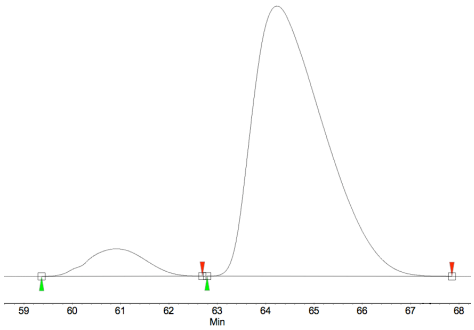
The title compound was subjected to ozonolysis and reduction. The resulting diol was protected with benzoic anhydride to afford the dibenzoate ester for HPLC analysis, as depicted below. The analogous racemic material was prepared via the same route using 1,2-bis(diphenylphosphino)benzene as achiral ligand in the allyl-allyl coupling reaction. The absolute stereochemistry was assigned by analogy.



*Chiral SFC (AD-H, Chiralpak, 220nm, 1 mL/min, 1% MeOH, ramped 0.1% per minute to 5% MeOH, 150 bar, 50 °C) – analysis of the dibenzoate ester.*

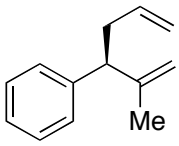



Racemic



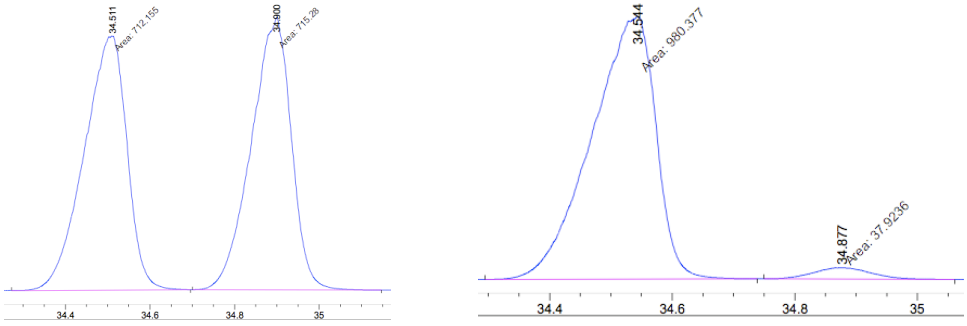

Reaction Product

| Index | Name | Start | Time | End | RT Offset | Quantity | Height | Area | Area |
|---|---|---|---|---|---|---|---|---|---|
| | | [Min] | [Min] | [Min] | [Min] | [% Area] | [µV] | [µV.Min] | [%] |
| 1 | UNKNOWN | 59.36 | 60.90 | 62.69 | 0.00 | 7.64 | 493.9 | 682.7 | 7.636 |
| 2 | UNKNOWN | 62.79 | 64.23 | 67.85 | 0.00 | 92.36 | 4850.2 | 8258.5 | 92.364 |
| | | | | | | | | | |
| Total | | | | | | 100.00 | 5344.2 | 8941.3 | 100.000 |




**(*S*)-(2-methylhexa-1,5-dien-3-yl)benzene (2.99).** $^1$H NMR (500 MHz, $CDCl_3$): δ 1.59 (3H, s), 2.47-2.55 (1H, m), 2.57-2.65 (1H, m), 3.30 (1H, t, *J* = 9.5 Hz), 4.87 (1H, t, *J* = 2.0 Hz), 4.93-5.04 (3H, m), 5.72 (1H, ddd, *J* = 17.0 Hz, 12.0 Hz, 8.5 Hz), 7.18-7.22 (3H, m), 7.28-7.31 (2H, m). Further spectral data is in accordance with the literature.[47]

*Chiral GLC (CD-GTA, Supelco, 60 °C, 20 min, then 2°/min to 120 °C, 30 min, 25 psi) – analysis of the title compound.*

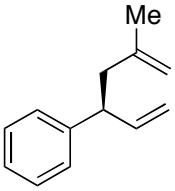



Racemic Reaction Product

| Peak # | RetTime [min] | Type | Width [min] | Area [pA*s] | Height [pA] | Area % |
|---|---|---|---|---|---|---|
| 1 | 34.544 | MM | 0.1215 | 980.37744 | 134.51584 | 96.27580 |
| 2 | 34.877 | MM | 0.1088 | 37.92358 | 5.81113 | 3.72420 |

Spectral data for linear isomer **2.100** is in accordance with the literature.[32]

[47] Molander, G. A.; Dowdy, E. D. *J. Org. Chem.* **1998**, *63*, 3386.

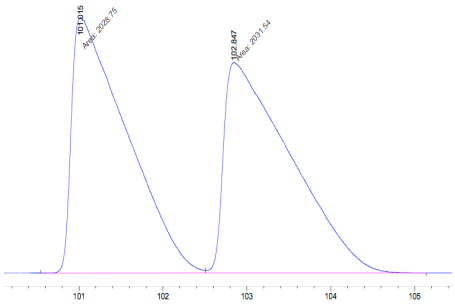



**(*S*)-(5-methylhexa-hexa-1,5-dien-3-ylbenzene (2.102).** $^{1}$H NMR (500 MHz, $CDCl_3$): $\delta$ 1.70 (3H, s), 2.45 (2H, app dtd, *J* = 14.0 Hz, 14.0 Hz, 8.0 Hz), 3.51 (1H, app q, *J* = 7.5 Hz), 4.64 (1H, m), 4.72 (1H, m), 4.98-5.04 (2H, m), 5.97 (1H, ddd, *J* = 17.0 Hz, 10.0 Hz, 7.0 Hz), 7.18-7.21 (3H, m), 7.26-7.32 (2H, m); $^{13}$C NMR (125 MHz, $CDCl_3$): $\delta$ 22.4, 44.0, 47.8, 112.3, 114.1, 126.2, 127.7, 128.4, 141.8, 143.4, 144.0; IR (neat): 3076 (w), 3028 (w), 2970 (w), 1638 (w), 1601 (w), 1494 (w), 1452 (w), 1415 (m), 1374 (w), 991 (m), 912 (s), 888 (s), 752 (s) cm$^{-1}$; HRMS (ESI+) for $C_{13}H_{17}$ [M+H]: calculated: 173.1330, found: 173.1330; $[\alpha]^{20}_{D}$ = +27.681 (*c* = 0.987, $CHCl_3$). The crude reaction mixture was purified on silica gel (pentane) to afford a clear, colorless oil (13.6 mg, 79% yield). $R_f$ = 0.48 (18:1 hexane: ethyl acetate, stain in $KMnO_4$).

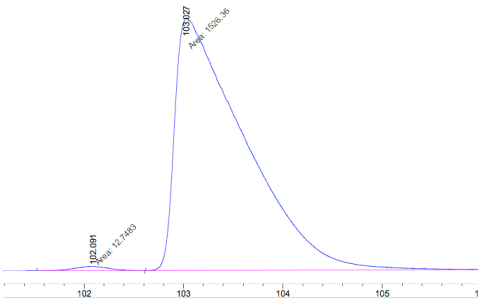
***Proof of Stereochemistry:***

Enantioselectivity was determined by comparison of the title compound with racemic material prepared using 1,2-bis(diphenylphosphino)benzene as the achiral ligand in the allyl-allyl coupling. The absolute stereochemistry was assigned by analogy.

*Chiral GLC (β-dex, Supelco, 80 °C, 25 psi) - analysis of title compound*

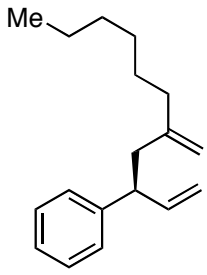



Racemic




Reaction Product

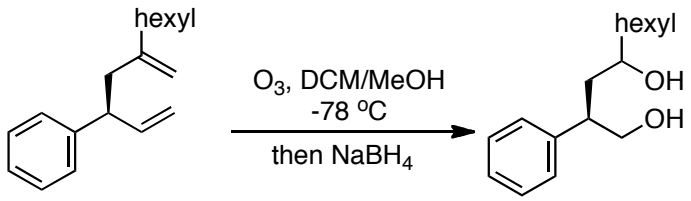
| Peak # | RetTime [min] | Type | Width [min] | Area [pA*s] | Height [pA] | Area % |
|---|---|---|---|---|---|---|
| 1 | 102.091 | MM | 0.3999 | 12.74831 | 5.31307e-1 | 0.82829 |
| 2 | 103.027 | MM | 0.8084 | 1526.36267 | 31.46725 | 99.17171 |



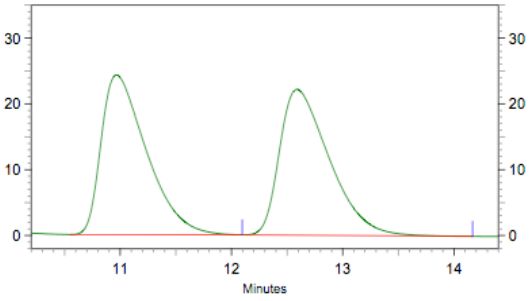

**(*S*)-(5-methyleneundec-1-en-3-yl)benzene (2.104)**. $^{1}$H NMR (400 MHz, $CDCl_3$): $\delta$ 0.89 (3H, t, *J* = 7.2 Hz), 1.24-1.44 (8H, m), 1.97 (2H, t, *J* = 7.6 Hz), 2.44 (2H, d, *J* = 7.6 Hz), 3.49 (1H, app q, *J* = 7.6 Hz), 4.67 (1H, s), 4.73 (1H, s), 4.99 (1H, dt, *J* = 17.6 Hz, 1.2 Hz), 5.02 (1H, dt, *J* = 10.4 Hz, 1.2 Hz), 5.97 (1H, ddd, *J* = 17.6 Hz, 10.4 Hz, 7.2 Hz), 7.17-7.21 (3H, m), 7.28-7.31 (2H, m); $^{13}$C NMR (100 Hz, $CDCl_3$): $\delta$ 13.0, 14.4, 27.9, 29.4, 32.1, 36.3, 42.4, 48.1, 111.4, 114.5, 126.5, 128.0, 128.7, 142.2, 144.5, 147.7; IR (neat): 3670 (w), 3028 (w), 2956 (m), 2927 (s), 2856 (m), 1643 (w), 1493 (w), 1453 (m), 1378 (w), 1074 (w), 991 (w), 912 (m), 891 (m), 753 (m), 673 (s) $cm^{-1}$; HRMS (ESI+) for $C_{18}H_{27}$ [M+H]: calculated: 243.2113, found: 243.2105; $[\alpha]^{20}_{D}$ = +24.191 (*c* = 0.75, $CHCl_3$). The crude reaction mixture was purified on silica gel (pentane) to afford a clear, colorless oil (18.9 mg, 78% yield). $R_f$ = 0.68 (8:1 hexanes: ethyl acetate, stain in $KMnO_4$).

***Proof of Stereochemistry:***

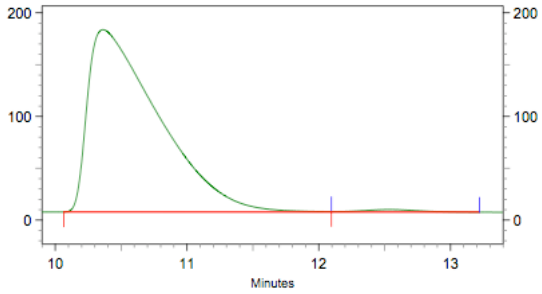
Enantioselectivity was determined by converting the allyl-allyl coupling product to a diol by ozonolysis/reduction. *Via* chiral HPLC the resulting diol was compared to racemic material prepared using 1,2-bis(diphenylphosphino)benzene as the achiral ligand in the allyl-allyl coupling reaction. The absolute stereochemistry was assigned by analogy.




*Chiral HPLC (AS-H, Chiralpak, 220nm, 1 mL/min, 2% isopropanol) – analysis of the diol.*




Racemic

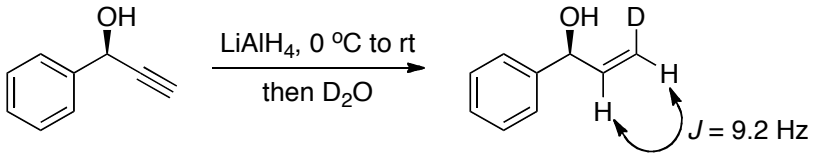


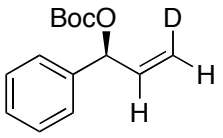

Derived from Reaction Product

| Retention Time | Area | Area % | Height | Height % |
|---|---|---|---|---|
| 10.363 | 110295188 | 98.88 | 2952849 | 98.61 |
| 12.533 | 1246973 | 1.12 | 41595 | 1.39 |

**5. Deuterium-Labeling Study (Section III.D)**

***Preparation of (S)-(-)-tert-butyl cis-3-[²H1]-1-phenylprop-2-enyl carbonate.*** From the deuterated allylic alcohol,[48] synthesized from commercially available (*S*)-1-phenylprop-2-yn-1-ol, >95% *ee*, procedure B was followed.

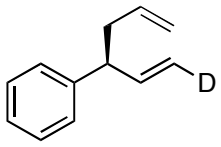


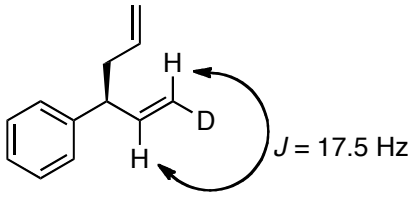

**(*S*)-(-)-*tert*-butyl cis-3-[²H1]-1-phenylprop-2-enyl carbonate (2.97)**. $^1$H NMR (400 MHz, $CDCl_3$): δ 1.47 (9H, s), 5.24 (1H, app dt, *J* = 9.2 Hz, 4.0 Hz), 6.01-6.04 (2H, m), 7.26-7.38 (5H, m); $^{13}$C NMR (100 Hz, $CDCl_3$): δ 27.8, 71.2, 82.3, 116.9 [t, $^1J$(C, $^2$H) = 23.8 Hz], 127.0, 128.2, 128.5, 136.1, 138.7, 152.7; IR (neat): 2981 (w), 2933 (w), 1739 (s), 1495 (w), 1394 (m), 1312 (s), 1274 (s), 1253 (s), 1086 (m), 967 (w), 895 (m), 699 (m) cm$^{-1}$; HRMS (ESI+) for $C_9H_8D$ [M-OBoc]: calculated: 118.0767, found: 118.0768; $[\alpha]^{20}_D$ = -29.776 (*c* = 0.97, $CHCl_3$). The crude reaction mixture was purified on silica gel (50:1 hexanes: ethyl acetate) to afford a clear, light yellow oil (93%). $R_f$ = 0.56 (8:1 hexanes: ethyl acetate, stain in $KMnO_4$).

[48] Kang, M. J.; Jang, J. S.; Lee, S. G. *Tetrahedron Lett.* **1995**, *36*, 8829.

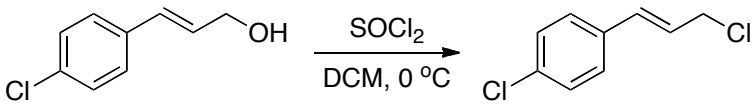
**Allyl-allyl coupling of deuterium-labeled starting material utilizing allylboronic acid pinacol ester:** The representative procedure for allyl-allyl coupling was applied.




**(*S*)-*trans*-1-[$^2$H1]-hexa-1,5-dien-ylbenzene (*d*-2.53)**. $^1$H NMR (500 MHz, $CDCl_3$): $\delta$ 2.49 (2H, m), 3.36 (1H, app q, $J$ = 7.0 Hz), 4.96-5.04 (3H, m), 5.73 (1H, ddt, $J$ = 17.5 Hz, 10.0 Hz, 7.0 Hz), 5.98 (1H, dd, $J$ = 17.5 Hz, 7.5 Hz), 7.19-7.32 (3H, m), 7.29-7.38 (2H, m); $^{13}$C NMR (100 Hz, $CDCl_3$): $\delta$ 39.7, 49.6, 114.1 [t, $^1J$(C, $^2$H) = 23.8 Hz], 116.1, 126.3, 127.7, 128.4, 136.6, 141.4, 143.7; IR (neat): 3077 (w), 3028 (w), 3003 (w), 2925 (w, br), 2857 (w, br), 1640 (w), 1600 (w), 1452 (w), 1416 (w), 979 (m), 912 (s), 747 (m) cm$^{-1}$; HRMS (ESI+) for $C_{12}H_{14}D$ [M+H]: calculated: 160.1237, found: 160.1233; $[\alpha]^{20}_D$ = +18.858 ($c$ = 0.88, $CHCl_3$). The crude reaction mixture was purified on silica gel (pentane) to afford a clear, colorless oil (11.7 mg, 77% yield). $R_f$ = 0.79 (8:1 hexanes: ethyl acetate, stain in $KMnO_4$).

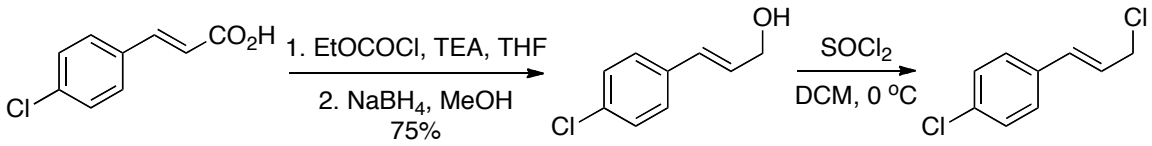


**6. Preparation of Substituted Allylic Chlorides**



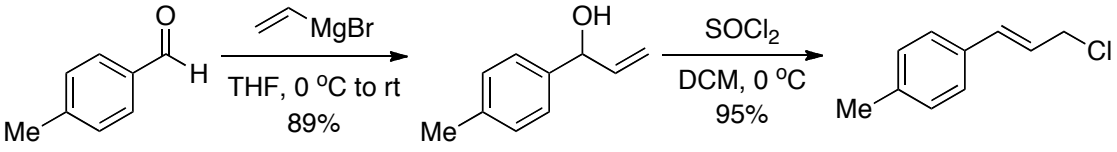

**Representative Procedure:** An oven-dried round-bottomed flask equipped with a magnetic stir bar was charged with dichloromethane (6.0 mL) and 1-(4-chlorophenyl)prop-2-en-1-ol (228 mg, 1.39 mmol) under nitrogen atmosphere. The solution was cooled to 0 °C and thionyl chloride (1.65 g, 13.88 mmol) was added dropwise. The solution was stirred at 0 °C for 2 h, then warmed to rt for 1 h. The reaction was quenched with ice water, extracted into dichloromethane (3 x 20 mL). The combined organics were dried over sodium sulfate, filtered, and concentrated *in vacuo* to afford a clear, colorless oil (155 mg, 99% yield) that was used without further purification.

***Preparation of (E)-1-chloro-4-(3-chloroprop-1-en-1-yl)benzene* (2.109).** From (*E*)-3-(4-chlorophenyl)prop-2-en-1-ol, synthesized as shown below,[42] the representative procedure was followed to afford a clear, colorless oil (155 mg, 99% yield). Spectral data is in accordance with the literature.[49]

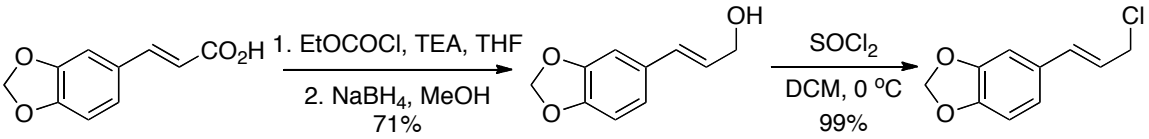


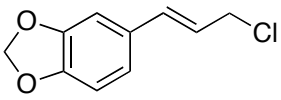

[49] Lölsberg, W.; Ye, S.; Schmalz, H. G. *Adv. Synth. Catal.* **2010**, *352*, 2023.

***Preparation of (E)-1-(3-chloroprop-1-en-1-yl)-4-methylbenzene* (2.110).** From 1-(*p*-tolyl)prop-2-en-1-ol, synthesized as shown below, the representative procedure was followed, with the following modification: After reaction work-up, the crude reaction mixture was dissolved in dichloromethane and stirred over activated charcoal, then filtered through celite and concentrated *in vacuo* to afford a clear, colorless oil (428 mg, 95% yield). Spectral data is in accordance with the literature.[49]




***Preparation of (E)-5-(3-chloroprop-1-en-1-yl)benzo[d][1,3]dioxole.*** From (*E*)-3-(benzo[d][1,2]dioxol-5-yl)prop-2-en-1-ol, synthesized as shown below, the representative procedure was followed.

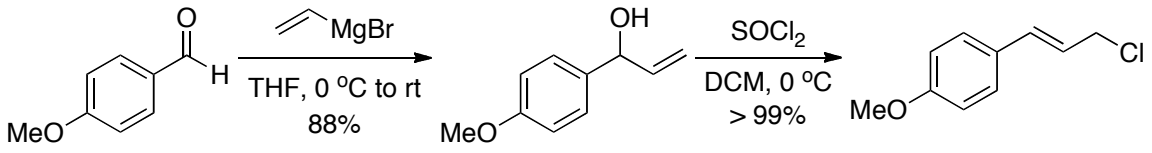


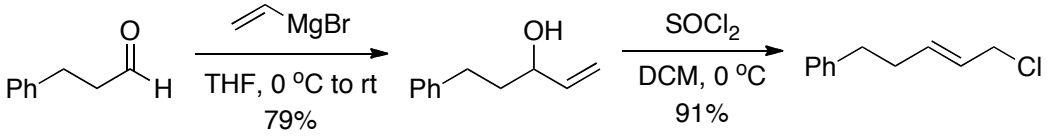

**(*E*)-5-(3-chloroprop-1-en-1-yl)benzo[*d*][1,3]dioxole (2.111).** $^{1}$H NMR (500 MHz, $CDCl_3$): $\delta$ 4.22 (2H, dd, $J$ = 7.5 Hz, 1.0 Hz), 5.96 (2H, s), 6.15 (1H, dt, $J$ = 15.5 Hz, 7.5 Hz), 6.56 (1H, d, $J$ = 15.5 Hz), 6.76 (1H, d, $J$ = 8.0 Hz), 6.82 (1H, dd, $J$ = 8.5 Hz, 2.0 Hz), 6.93 (1H, d, $J$ = 1.5 Hz); $^{13}$C NMR (125 MHz, $CDCl_3$): $\delta$ 45.6, 101.2, 105.9, 108.3, 121.7, 123.1, 130.3, 133.9, 147.8, 148.1; IR (neat): 1500 (m), 1490 (m), 1447 (m), 1246 (s), 1194 (m), 1100

(m), 1037 (s), 966 (m), 929 (m), 862 (w), 798 (s), 780 (w), 670 (m), 600 (m) $cm^{-1}$; HRMS-(ESI+) for $C_{10}H_{10}ClO_2$ [M+H]: calculated: 197.0369, found: 197.0374. Upon drying the crude reaction mixture with sodium sulfate, filtration of the solution, and concentration of the mixture *in vacuo*, a viscous yellow oil was obtained (163 mg, 99% yield), and was used in the allyl-allyl coupling reaction without further purification.

***Preparation of (E)-1-(3-chloroprop-1-en-1-yl)-4-methoxybenzene* (2.112).** From 1-(4-methoxyphenyl)prop-2-en-1-ol, synthesized as shown below, the representative procedure was followed to afford a clear, colorless oil (265 mg, quantitative yield). Spectral data is in accordance with the literature.[49]

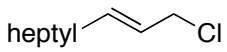



***Preparation of (E)-(5-chloropent-1-en-1-yl)benzene* (2.134).** From 5-phenylpent-1-en-3-ol, synthesized as shown below, the representative procedure was followed, with the following modification: The crude reaction mixture was purified on neutral alumina (pentane) to afford a clear, colorless oil (406 mg, 91% yield). Spectral data is in accordance with the literature.[50]



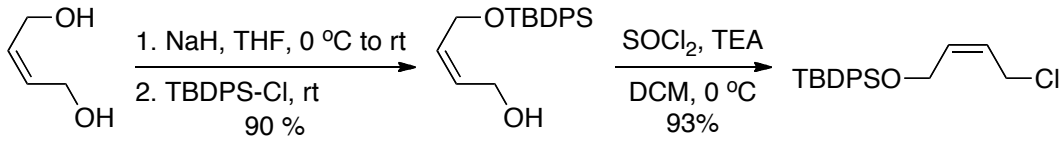

[50] Fuchter, M. J.; Levy, J.-N. *Org. Lett.* **2008**, *10*, 4919.

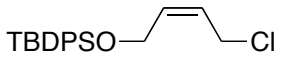
***Preparation of (E)-1-chlorodec-2-ene.*** From commercially available (*E*)-dec-2-en-1-ol, the representative procedure was followed.




**(*E*)-1-chlorodec-2-ene (2.135).** $^{1}$H NMR (500 MHz, $CDCl_3$): $\delta$ 0.88 (3H, t, *J* = 7.0 Hz), 1.26-1.31 (8H, m), 1.39 (2H, app t, *J* = 7.0 Hz), 2.09-2.13 (2H, m), 4.10 (2H, dd, *J* = 6.5 Hz, 3.0 Hz), 5.63 (2H, m); $^{13}$C NMR (125 MHz, $CDCl_3$): $\delta$ 14.1, 22.6, 27.1, 29.1, 29.2, 29.3, 31.8, 39.6, 125.1, 135.6; IR (neat): 3026 (w), 2957 (m), 2925 (s), 2885 (m), 1652 (w), 1459 (m), 1378 (w), 1250 (m), 757 (s), 724 (m), 676 (w) $cm^{-1}$. The crude reaction mixture was purified on neutral alumina (pentane) to afford a clear, colorless oil (419 mg, 89% yield). $R_f$ = 0.86 (pentane, stain in $KMnO_4$).

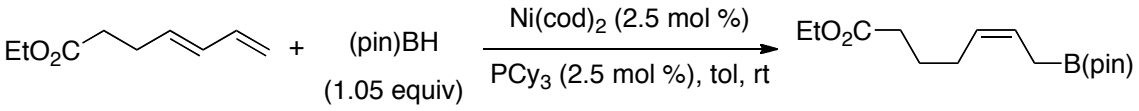
***Preparation of (Z)-tert-butyl((4-chlorobut-2-en-1-yl)oxy)diphenylsilane.*** From (*Z*)-4-((*tert*-butyldiphenylsilyl)oxy)but-2-en-1-ol, synthesized as shown below, the representative procedure was followed, with the following modification: An oven-dried round-bottomed flask equipped with a magnetic stir bar was charged with dichloromethane (20.0 mL), distilled triethylamine (0.47 mL, 3.52 mmol), and (*Z*)-4-((*tert*-butyldiphenylsilyl)oxy)but-2-en-1-ol (1.00 g, 3.06 mmol) under nitrogen atmosphere. The solution was cooled to 0 °C and thionyl chloride (0.24 mL, 3.37 mmol) was added dropwise. The solution was warmed to rt and stirred for 1 h. The reaction was quenched with ice water, then extracted into dichloromethane (3 x 20 mL). The mixture was dried over sodium sulfate, filtered, and concentrated *in vacuo*. The crude mixture was purified on a 1" pad of neutral alumina (20:1 pentane:diethyl ether) to afford a clear, colorless oil (978 mg, 93% yield).



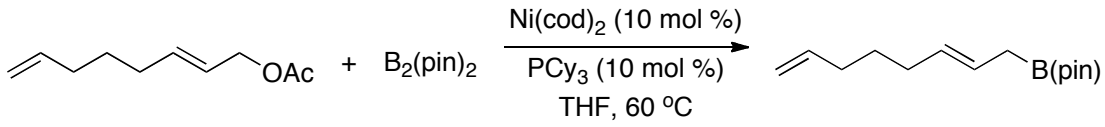




**(*Z*)-*tert*-butyl((4-chlorobut-2-en-1-yl)oxy)diphenylsilane (2.136).** $^{1}$H NMR (500 MHz, $CDCl_3$): $\delta$ 1.06 (9H, s), 3.96 (2H, dd, *J* = 7.0 Hz, 0.5 Hz), 4.30 (2H, dd, *J* = 6.0 Hz, 1.5 Hz), 5.65 (1H, dtt, *J* = 11.0 Hz, 8.0 Hz, 1.5 Hz), 5.78 (1H, dtt, *J* = 11.0 Hz, 6.0 Hz, 1.0 Hz), 7.39-7.46 (6H, m), 7.69 (4H, dd, *J* = 8.0 Hz, 1.5 Hz); $^{13}$C NMR (125 MHz, $CDCl_3$): $\delta$ 19.1, 26.7, 39.3, 59.9, 126.2, 127.7, 129.7, 133.28, 133.34, 135.5; IR (neat): 3071 (w), 2958 (m), 2931 (m), 2858 (m), 1472 (w), 1428 (m), 1391 (w), 1361 (w), 1256 (w), 1110 (s), 1072 (m), 998 (w), 941 (w), 823 (m), 740 (m), 701 (s), 613 (m), 505 (s), 490 (m) $cm^{-1}$; HRMS-(ESI+) for $C_{20}H_{26}ClOSi$ [M +H]: calculated: 345.1441, found: 345.1427. The crude reaction mixture was purified on neutral alumina (20:1 pentane:diethyl ether) to afford a clear, colorless oil (978 mg, 93% yield). $R_f$ = 0.73 (5:1 pentane:diethyl ether, stain in $KMnO_4$).

**7. Preparation of Substituted Allyl Boron Reagents**

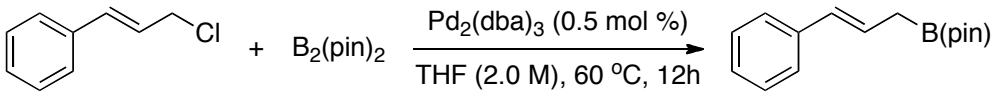



**Representative Procedure A:**[33] An oven-dried scintillation vial equipped with a magnetic stir bar was charged with bis(1,5-cyclooctadiene)nickel(0) (15 mg, 0.06 mmol), tricyclohexylphosphine (16 mg, 0.055 mmol), and toluene (4.4 mL) in a dry-box under argon atmosphere. The vial was capped and stirred for two minutes, then (*E*)-ethyl hepta-4,6-dienoate (340 mg, 2.205 mmol) was added, followed by pinacolborane (296 mg, 2.32 mmol). The vial was capped with a teflon cone-lined cap, sealed with electrical tape, removed from the dry-box, and allowed to stir at rt for 2 h. The reaction was concentrated *in vacuo*, and the crude reaction mixture was purified on silica gel (20:1 pentane:diethyl ether) to afford a clear, colorless oil (474 mg, 76% yield). $R_f$ = 0.38 (15:1 pentane:diethyl ether, stain in CAM).



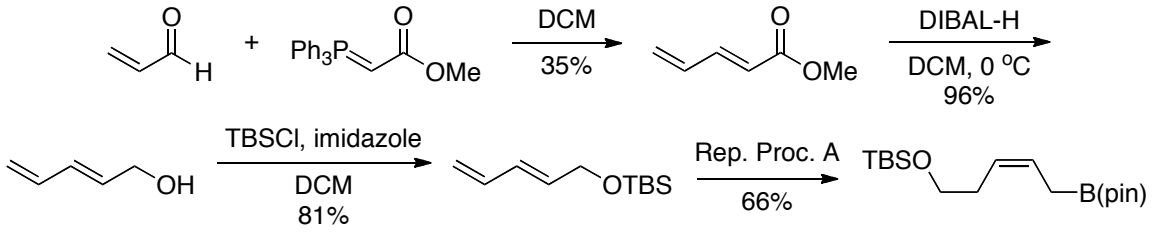

**Representative Procedure B:** An oven-dried scintillation vial equipped with a magnetic stir bar was charged with bis(1,5-cyclooctadiene)nickel(0) (82 mg, 0.30 mmol), tricyclohexylphosphine (83 mg, 0.30 mmol), and tetrahydrofuran (3.0 mL) in a dry box under argon atmosphere. The vial was capped and stirred for two minutes, then (*E*)-octa-2,7-dien-1-yl acetate (500 mg, 2.97 mmol) was added, followed by bis(pinacolato)diboron (754 mg, 2.97 mmol). The vial was capped with a teflon cone-

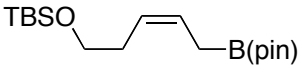
lined cap, sealed with electrical tape, removed from the dry-box, and was heated to 60 °C and allowed to stir for 36 h. At this time, the reaction was concentrated *in vacuo*. The crude reaction mixture was purified on silica gel (pentane, ramped gradually to 20:1 pentane:diethyl ether) to afford a clear, colorless oil (349 mg, 50% yield). $R_f$ = 0.43 (25:1 pentane:diethyl ether, stain in CAM).




**Representative Procedure C:** An oven-dried scintillation vial equipped with a magnetic stir bar was charged with $Pd_2(dba)_3$ (18 mg, 0.02 mmol), bis(pinacolato)diboron (1.02 g, 4.02 mmol), and tetrahydrofuran (2.0 mL) in a dry-box under argon atmosphere. The vial was capped and stirred for two minutes, then cinnamyl chloride (610 mg, 4.00 mmol) was added. The vial was capped with a teflon cone-lined cap, sealed with electrical tape, removed from the dry box, and was heated to 60 °C and allowed to stir for 12 h. At this time, the reaction was concentrated *in vacuo*. The crude reaction mixture was purified on silica gel (50:1 pentane:diethyl ether) to afford a clear, colorless oil (627 mg, 65% yield). $R_f$ = 0.44 (50:1 pentane:diethyl ether, stain in $KMnO_4$).

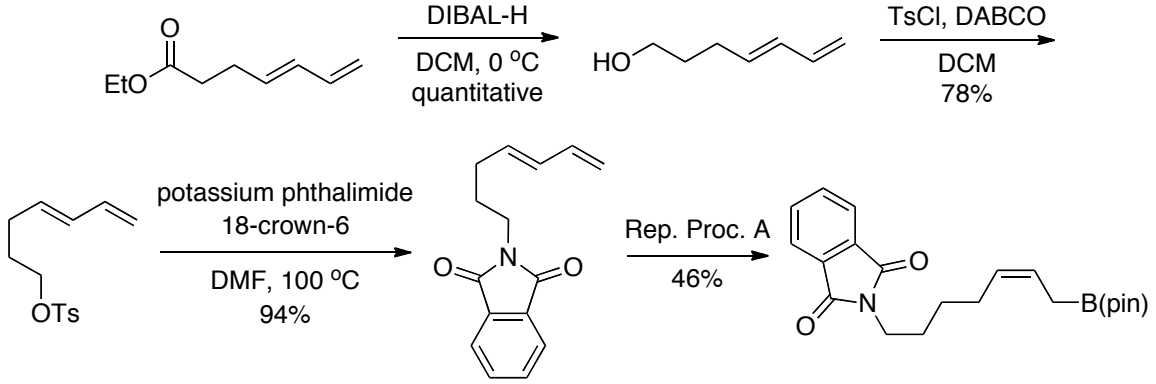
***Preparation of (Z)-tert-butyldimethyl((5-(4,4,5,5-tetramethyl-1,3,2-dioxaboronlan-2-yl)pent-3-en-1-yl)oxy)silane.*** From (*E*)-*tert*-butyldimethyl(penta-2,4-dien-1-yloxy)silane, synthesized as shown below, representative procedure A was followed.

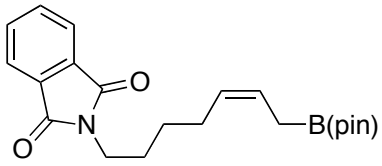



**(*Z*)-*tert*-butyldimethyl((5-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)pent-3-en-1-yl)oxy)silane (2.117).** $^{1}$H NMR (500 MHz, $CDCl_3$): $\delta$ 0.05 (6H, s), 0.89 (9H, s), 1.24 (12H, s), 1.69 (2H, d, $J$ = 8.0 Hz), 2.27 (2H, app qd, $J$ = 7.0 Hz, 1.5 Hz), 3.60 (2H, t, $J$ = 7.0 Hz), 5.39 (1H, dtt, $J$ = 10.5 Hz, 7.0 Hz, 1.5 Hz), 5.57 (1H, dtt, $J$ = 10.5 Hz, 8.0 Hz, 1.5 Hz); $^{13}$C NMR (125 MHz, $CDCl_3$): $\delta$ -5.24, 18.4, 24.8, 26.0, 31.0, 62.9, 83.2, 125.5, 126.1; IR (neat): 2978 (w), 2955 (w), 2929 (m), 2857 (m), 1718 (w), 1471 (w), 1379 (m), 1371 (m), 1326 (s), 1254 (m), 1215 (w), 1144 (s), 1097 (s), 1006 (w), 968 (w), 936 (w), 884 (w), 835 (s), 775 (s), 743 (w), 664 (w) cm$^{-1}$; HRMS-(ESI+) for $C_{17}H_{36}BO_3Si$ [M+H]: calculated: 327.2527, found: 327.2527. The crude reaction mixture was purified on silica gel (25:1 hexanes:ethyl acetate) to afford a clear, colorless oil (326 mg, 66% yield). $R_f$ = 0.24 (20:1 pentane:diethyl ether, stain in CAM).

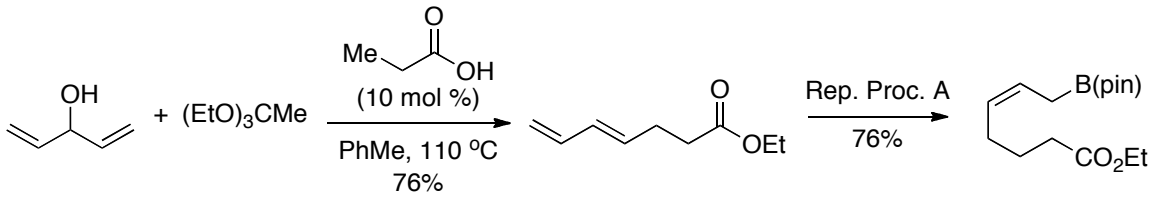
***Preparation of (Z)-2-(7-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)hept-5-en-1-yl)isoindoline-1,3-dione.*** From (*E*)-2-(hepta-4,6-dien-1-yl)isoindoline-1,3-dione,[33] synthesized as shown below, representative procedure A was followed.

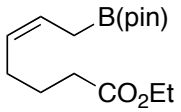



**(*Z*)-2-(7-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)hept-5-en-1-yl)isoindoline-1,3-dione (2.118).** $^{1}$H NMR (500 MHz, $CDCl_3$): $\delta$ 1.22 (12H, s), 1.37-1.43 (2H, m), 1.65 (2H, d, *J* = 7.0 Hz), 1.65-1.71 (2H, m), 2.06 (2H, app q, *J* = 7.5 Hz), 3.67 (2H, t, *J* = 7.5 Hz), 5.34 (1H, dtt, *J* = 10.5 Hz, 7.0 Hz, 1.5 Hz), 5.47 (1H, dtt, *J* = 10.5 Hz, 8.0 Hz, 1.5 Hz), 7.69 (2H, dd, *J* = 5.0 Hz, 3.0 Hz), 7.83 (2H, dd, *J* = 5.5 Hz, 3.0 Hz); $^{13}$C NMR (125 MHz, $CDCl_3$): $\delta$ 24.7, 26.5, 26.8, 28.2, 38.0, 83.2, 123.1, 124.7, 129.1, 132.2, 133.8, 168.4; IR (neat): 2977 (w), 2934 (w), 2862 (w), 1772 (w), 1712 (s), 1467 (w), 1437 (w), 1395 (m), 1370 (m), 1326 (m), 1144 (m), 1109 (w), 1040 (w), 847 (w), 720 (m), 530 (w) $cm^{-1}$; HRMS-(ESI+) for $C_{21}H_{29}BNO_4$ [M+H]: calculated: 370.2190, found: 370.2182. The crude reaction mixture was purified on silica gel (4:1 pentane:diethyl ether) to afford a clear, light yellow oil (71 mg, 46% yield). $R_f$ = 0.34 (3:1 pentane:diethyl ether, stain in CAM).

***Preparation of (Z)-ethyl 7-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)hept-5-enoate.*** From (*E*)-ethyl hepta-4,5-dienoate, synthesized as shown below,[51] representative procedure A was followed.




**(*Z*)-ethyl 7-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)hept-5-enoate (2.119).** $^{1}$H NMR (500 MHz, $CDCl_3$): $\delta$ 1.23 (12H, s), 1.24 (3H, t, *J* = 7.0 Hz), 1.65 (2H, d, *J* = 8.0 Hz), 1.68 (2H, app p, *J* = 7.5 Hz), 2.06 (2H, app q, *J* = 7.0 Hz), 2.29 (2H, t, *J* = 7.5 Hz), 4.11 (2H, q, *J* = 7.0 Hz), 5.35 (1H, dtt, *J* = 10.5 Hz, 7.0 Hz, 1.5 Hz), 5.53 (1H, dtt, *J* = 10.5 Hz, 8.0 Hz, 1.5 Hz); $^{13}$C NMR (125 MHz, $CDCl_3$): $\delta$ 14.2, 24.7, 24.8, 26.4, 33.8, 60.1, 83.2, 125.3, 128.5, 173.7; IR (neat): 2979 (m), 2934 (w), 1735 (s), 1448 (w), 1371 (m), 1326 (s), 1273 (w), 1241 (w), 1215 (w), 1165 (m), 1144 (s), 1110 (w), 1033 (w), 968 (w), 881 (w), 847 (m), 737 (w) $cm^{-1}$; HRMS-(ESI+) for $C_{15}H_{28}BO_4$ [M+H]: calculated: 283.2081, found: 283.2091. The crude reaction mixture was purified on silica gel (20:1 pentane:diethyl ether) to afford a clear, colorless oil (474 mg, 76% yield). $R_f$ = 0.38 (15:1 pentane:diethyl ether, stain in CAM).

***Preparation of (Z)-2-(dec-2-en-1-yl)-4,4,5,5-tetramethyl-1,3,2-dioxaborolane* (2.120).** This compound was prepared following literature procedure, and spectral data is in accordance with reported values.[33b]

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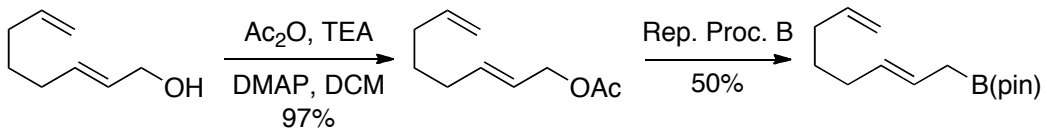
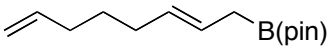
[51] Spino, C.; Crawford, J.; Bishop, J. *J. Org. Chem.* **1995**, *60*, 844.

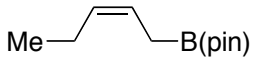
***Preparation of (E)-4,4,5,5-tetramethyl-2-(octa-2,7-dien-1-yl)-1,3,2-dioxaborolane.*** From (*E*)-octa-2,7,-dien-1-yl acetate, synthesized as shown below, representative procedure B was followed.




**(*E*)-4,4,5,5-tetramethyl-2-(octa-2,7-dien-1-yl)-1,3,2-dioxaborolane (2.121).** $^{1}$H NMR (500 MHz, $CDCl_3$): $\delta$ 1.24 (12H, s), 1.43 (2H, app p, *J* = 7.5 Hz), 1.64 (2H, d, *J* = 7.0 Hz), 1.97-2.06 (4H, m), 4.91-4.95 (1H, m), 4.99 (1H, app dq, *J* = 17.0 Hz, 2.0 Hz), 5.34-5.48 (2H, m), 5.80 (1H, app ddt, *J* = 17.0 Hz, 10.5 Hz, 6.5 Hz); $^{13}$C NMR (125 MHz, $CDCl_3$): $\delta$ 24.7, 28.8, 32.1, 33.2, 83.1, 114.3, 125.2, 130.5, 139.0; IR (neat): 2978 (m), 2927 (w), 2857 (w), 1640 (w), 1369 (m), 1323 (s), 1272 (w), 1214 (w), 1144 (s), 967 (m), 909 (w), 883 (w), 847 (w), 673 (w) $cm^{-1}$; HRMS-(ESI+) for $C_{14}H_{26}BO_2$ [M+H]: calculated: 237.2026, found: 237.2036. The crude reaction mixture was purified on silica gel (pentane, ramped gradually to 20:1 pentane:diethyl ether) to afford a clear, colorless oil (349 mg, 50% yield). $R_f$ = 0.43 (25:1 pentane:diethyl ether, stain in CAM).

***Preparation of (Z)-4,4,5,5-tetramethyl-2-(pent-2-en-1-yl)-1,3,2-dioxaborolane.*** From commercially available *trans*-1,3-pentadiene, representative procedure A was followed.




**(*Z*)-4,4,5,5-tetramethyl-2-(pent-2-en-1-yl)-1,3,2-dioxaborolane (2.122).** $^{1}$H NMR (500 MHz, $CDCl_3$): $\delta$ 0.96 (3H, t, $J$ = 7.5 Hz), 1.25 (12H, s), 1.67 (2H, d, $J$ = 8.0 Hz), 2.03 (2H, app pd, $J$ = 7.5 Hz, 1.0 Hz), 5.36-5.41 (1H, m), 5.43-5.49 (1H, m); $^{13}$C NMR (125 MHz, $CDCl_3$): $\delta$ 14.1, 20.3, 24.7, 83.2, 123.4, 131.6; IR (neat): 2977 (m), 2934 (w), 2875 (w), 1463 (w), 1371 (w), 1322 (s), 1273 (w), 1214 (w), 1165 (w), 1144 (s), 1112 (w), 966 (m), 887 (w), 848 (m), 738 (w), 672 (w) $cm^{-1}$; HRMS-(ESI+) for $C_{11}H_{22}BO_2$ [M+H]: calculated: 197.1713, found: 197.1718. The crude reaction mixture was purified on silica gel (1:1 pentane:dichloromethane) to afford a clear, colorless oil (711 mg, 83% yield). $R_f$ = 0.58 (1:1 pentane:dichloromethane, stain in CAM).

***Preparation of 2-cinnamyl-4,4,5,5-tetramethyl-1,3,2-dioxaborolane* (2.123).** From commercially available cinnamyl chloride, procedure C was followed. Spectral data is in accordance with reported values.[52]

***Preparation of (E)-2-(3-methoxyallyl)-4,4,5,5-tetramethyl-1,3,2-dioxaborolane* (2.141).** From commercially available acrolein dimethyl acetal, procedure B was followed. Spectral data is in accordance with reported values.[53]

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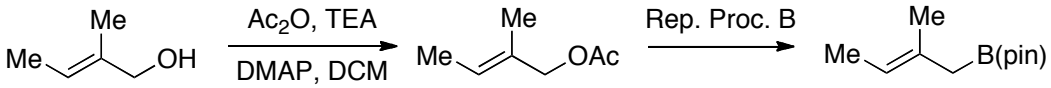
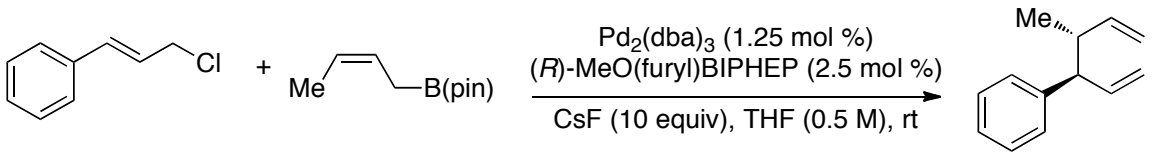
[52] Selander, N.; Paasch, J. R.; Szabó, K. J. *J. Am. Chem. Soc.* **2011**, *133*, 409.

[53] Brummond, K. M.; Lu, J. *Org. Lett.* **2001**, *3*, 1347.

***Preparation of (E)-4,4,5,5-tetramethyl-2-(2-methylbut-2-en-1-yl)-1,3,2-dioxaborolane*** **(2.143).** From (*E*)-2-methylbut-2-en-1-yl acetate, synthesized as shown below, procedure B was followed. Spectral data is in accordance with reported values.[54]




**8. Experimental Procedures for Diastereoselective Allyl-Allyl Coupling**




**Representative Procedure A:** An oven-dried two-dram vial equipped with magnetic stir bar was charged with $Pd_2(dba)_3$ (1.1 mg, 1.25 μmol), (*R*)-MeO(furyl)BIPHEP (1.4 mg, 2.50 μmol), and THF (0.2 mL) in a dry-box under argon atmosphere. The vial was capped and stirred for five minutes, then cinnamyl chloride (15.3 mg, 0.10 mmol) was added, followed by cesium fluoride (152.0 mg, 1.0 mmol), and *cis*-crotylboronic acid pinacol ester (21.8 mg, 0.12 mmol). The vial was sealed, removed from the dry-box, and allowed to stir at ambient temperature for 14 h. After this time, the reaction mixture was diluted with diethyl ether, filtered through a plug of silica gel and concentrated *in vacuo*. The crude reaction mixture was purified on silica gel (pentane) to afford a clear, colorless oil (15.6 mg, 90% yield). $R_f = 0.56$ (pentane, stain in PMA).

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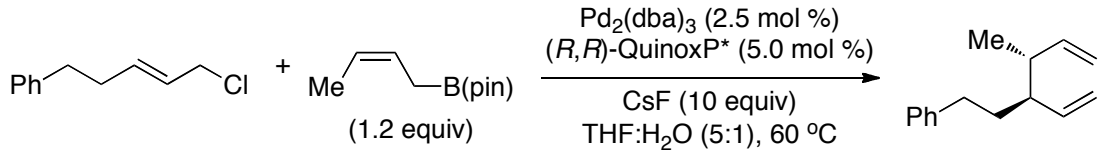
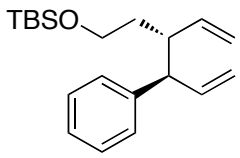
[54] Wu, J. Y.; Moreau, B.; Ritter, T. *J. Am. Chem. Soc.* **2009**, *131*, 1347.




**Representative Procedure B:** An oven-dried two-dram vial equipped with a magnetic stir bar was charged with $Pd_2(dba)_3$ (2.3 mg, 2.5 μmol), (*R*,*R*)-QuinoxP* (1.7 mg, 5.0 μmol), and THF (0.2 mL) in a dry-box under an argon atmosphere. The vial was capped and stirred for five minutes, then (*E*)-(5-chloropent-3-en-1-yl)benzene (18.0 mg, 0.1 mmol) was added, followed by cesium fluoride (152.0 mg, 1.0 mmol), and *cis*-crotylboronic acid pinacol ester (21.8 mg, 0.12 mmol). The vial was sealed with a rubber septum, removed from the dry box, and put under nitrogen atmosphere. Then 40 μL of deoxygenated water was added, the septum was replaced with a screw cap, and the reaction was heated to 60 °C and allowed to stir for 14 h. After this time, the reaction mixture was diluted with diethyl ether, filtered through a plug of silica gel and concentrated *in vacuo*. The crude reaction mixture was purified on silica gel (pentane) to afford a clear, colorless oil (12.9 mg, 64% yield). $R_f$ = 0.63 (pentane, stain in PMA).

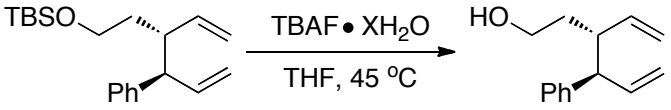
## 9. Characterization of Products from Diastereoselective Allyl-Allyl Coupling



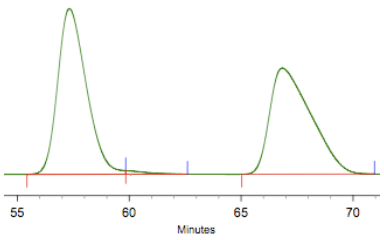

***tert*-butyldimethyl(((3*R*,4*R*)-4-phenyl-3-vinylhex-5-en-1-yl)oxy)silane (2.124).** The title compound was prepared *via* representative procedure A for allyl-allyl coupling, with the following modification: 2.5 mol % $Pd_2(dba)_3$ and 5.0 mol % (*R*)-MeO(furyl)BIPHEP were used. $^1$H NMR (500 MHz, $CDCl_3$): δ -0.04 (3H, s), -0.02 (3H, s), 0.86 (9H, s), 1.25-1.32 (1H, m), 1.53-1.60 (1H, m), 2.55 (1H, app dq, *J* = 10.0 Hz, 3.5 Hz), 3.19 (1H, app t, *J* = 8.5 Hz), 3.46-3.50 (1H, m), 3.57 (1H, ddd, *J* = 10.0 Hz, 7.5 Hz, 4.5 Hz), 4.94-4.95 (1H, m), 4.97-4.98 (1H, m), 5.02 (1H, app dq, *J* = 10.0 Hz, 1.0 Hz), 5.07 (1H, dd, *J* = 10.5 Hz, 2.0 Hz), 5.55 (1H, ddd, *J* = 17.5 Hz, 10.5 Hz, 9.5 Hz), 5.98 (1H, ddd, *J* = 17.5 Hz, 10.5 Hz, 9.0 Hz), 7.16-7.20 (3H, m), 7.29 (2H, app t, *J* = 7.0 Hz); $^{13}$C NMR (125 MHz, $CDCl_3$): δ -5.4, -5.3, 18.2, 25.9, 35.2, 45.3, 54.8, 60.8, 115.3, 116.2, 126.2, 128.2, 128.3, 140.4, 140.6, 143.1; IR (neat): 2954 (m), 2928 (m), 2894 (w), 2857 (m), 1472 (m), 1418 (w), 1388 (w), 1361 (w), 1255 (s), 1099 (s), 994 (w), 938 (w), 913 (m), 835 (s), 775 (s), 758 (w), 725 (w), 699 (m) $cm^{-1}$; HRMS-(ESI+) for $C_{20}H_{33}OSi$ [M +H]: calculated: 317.2301, found: 317.2296. $[\alpha]^{22}_D$ = -40.369 (*c* = 1.87, $CHCl_3$, from (*S*)-MeO(furyl)BIPHEP). The crude reaction mixture was purified on silica gel (100:1 pentane:diethyl ether) to afford a clear, colorless oil (41.3 mg, 87% yield). $R_f$ = 0.48 (50:1 pentane:diethyl ether, stain in PMA).

***Analysis of Stereochemistry:***

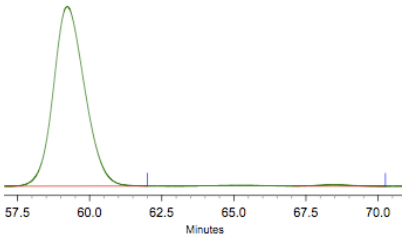
The title compound was subjected to TBAF-mediated deprotection of the silyl ether to afford the primary alcohol for HPLC analysis, as depicted below. The analogous racemic material was prepared *via* the same route, using 1,2-bis(diphenylphosphino)-benzene as the achiral ligand in the allyl-allyl coupling reaction. The absolute stereochemistry was assigned by analogy to compounds **2.107** and **2.130**.



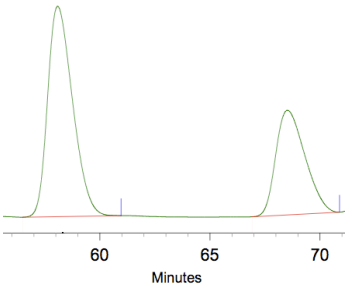

*Chiral HPLC (OJ-H, Chiralcel, 0.5 mL/min, 1.5% isopropanol, 220 nm) - analysis of primary alcohol.*




Racemic

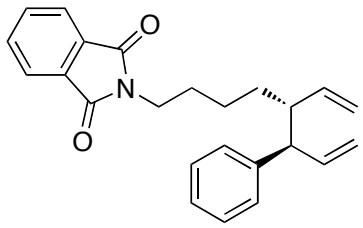



alcohol from ( *S*)-MeO(furyl)BIPHEP




alcohol from allyl-allyl coupling product
+ racemic co-injection

| Retention Time | Area | Area % | Height | Height % |
|---|---|---|---|---|
| 59.223 | 90773475 | 99.31 | 1198525 | 99.34 |
| 68.457 | 627879 | 0.69 | 8012 | 0.66 |



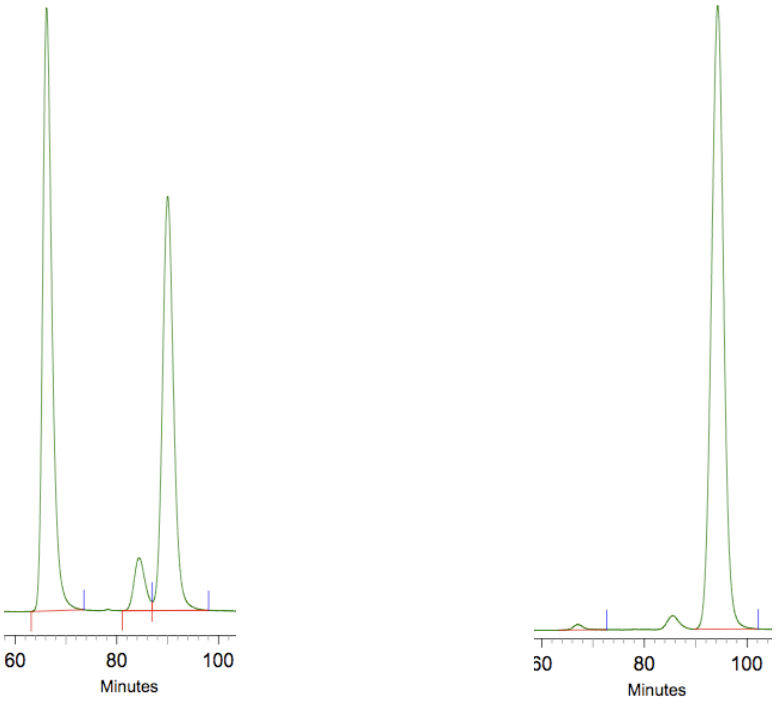
**2-((5*R*,6*R*)-6-phenyl-5-vinyloct-7-en-1-yl)isoindoline-1,3-dione (2.125).** The title compound was prepared *via* representative procedure A for allyl-allyl coupling, with the following modification: 2.5 mol % $Pd_2(dba)_3$ and 5.0 mol % (*R*)-MeO(furyl)BIPHEP were used. $^1$H NMR (500 MHz, $CDCl_3$): $\delta$ 1.10-1.24 (2H, m), 1.26-1.40 (2H, m), 1.45-1.53 (1H, m), 1.56-1.64 (1H, m), 2.33 (1H, app qd, *J* = 9.0 Hz, 3.5 Hz), 3.14 (1H, app t, *J* = 8.5 Hz), 3.58 (2H, t, *J* = 7.5 Hz), 4.90-4.92 (1H, m), 4.93-4.95 (1H, m), 5.00 (1H, app dq, *J* = 10.5 Hz, 1.0 Hz), 5.04 (1H, dd, *J* = 10.5 Hz, 1.5 Hz), 5.51 (1H, ddd, *J* = 17.0 Hz, 10.5 Hz, 9.5 Hz), 5.97 (1H, ddd, *J* = 17.0 Hz, 10.5 Hz, 8.5 Hz), 7.14-7.19 (3H, m), 7.25-7.29 (2H, m), 7.69 (2H, dd, *J* = 5.5 Hz, 3.0 Hz), 7.82 (2H, dd, *J* = 5.5 Hz, 3.0 Hz); $^{13}$C NMR (125 MHz, $CDCl_3$): $\delta$ 24.3, 28.3, 31.8, 37.9, 49.0, 55.0, 115.2, 116.2, 123.1, 126.2, 128.1, 128.4, 132.2, 133.8, 140.6, 143.3, 168.4; IR (neat): 2930 (m), 2860 (w), 1772 (m), 1712 (s), 1639 (w), 1467 (w), 1453 (w), 1437 (w), 1396 (s), 1369 (m), 1168 (w), 1048 (w), 995 (w), 914 (m), 761 (w), 720 (s), 702 (m), 530 (w) cm$^{-1}$; HRMS-(ESI+) for $C_{24}H_{26}NO_2$ [M+H]: calculated: 360.1964, found: 360.1960. $[\alpha]^{22}_D$ = +34.804 (*c* = 0.57, $CHCl_3$, from (*R*)-MeO(furyl)BIPHEP). The crude reaction mixture was purified on silica gel (20:1 to 15:1 pentane:diethyl ether) to afford a clear, colorless oil (32.5 mg, 76% yield). $R_f$ = 0.15 (16:1 pentane:diethyl ether, stain in PMA).

***Analysis of Stereochemistry:***

Enantioselectivity was determined by HPLC analysis of the title compound as compared to racemic material, prepared by mixing a 1:1 ratio of allyl-allyl coupling

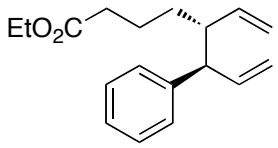
products derived from the (*R*) and (*S*) enantiomers of MeO(furyl)BIPHEP. Absolute stereochemistry was assigned by analogy to compounds **2.107** and **2.130**.

*Chiral HPLC (OJ-H, Chiralcel, 0.5 mL/min, 1.0% isopropanol, 220 nm) - analysis of title compound.*




racemic from (*S*)-MeO(furyl)BIPHEP

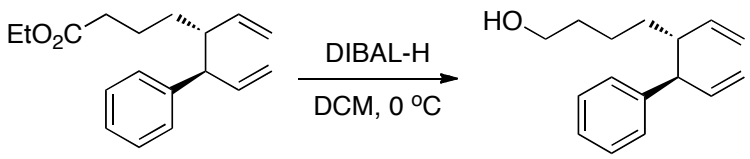
| Retention Time | Area | Area % |
|---|---|---|
| 67.033 | 6857466 | 0.75 |
| 94.290 | 908677585 | 99.25 |



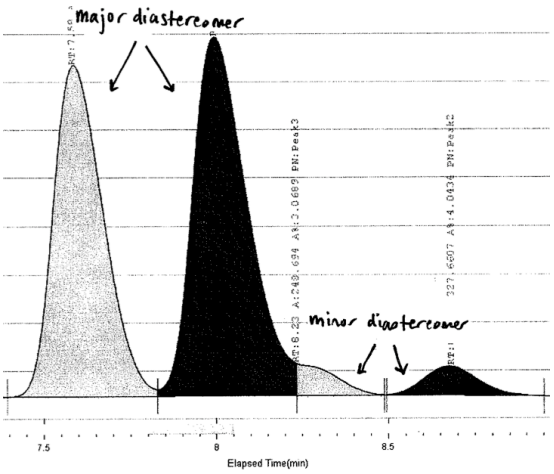
**(5*R*,6*R*)-ethyl 6-phenyl-5-vinyloct-7-enoate (2.126).** The title compound was prepared *via* representative procedure A for allyl-allyl coupling, with the following modification: 2.5 mol % $Pd_2(dba)_3$ and 5.0 mol % (*R*)-MeO(furyl)BIPHEP were used. $^1$H NMR (500 MHz, $CDCl_3$): $\delta$ 1.10-1.17 (1H, m), 1.20 (3H, app t, *J* = 7.0 Hz), 1.22-1.33 (1H, m), 1.42-1.48 (1H, m), 1.62-1.70 (1H, m), 2.11-2.23 (2H, m), 2.34 (1H, app qd, *J* = 9.0 Hz, 3.0 Hz), 3.16 (1H, app t, *J* = 8.5 Hz), 4.06 (2H, q, *J* = 7.5 Hz), 4.91-4.92 (1H, m), 4.95-4.96 (1H, m), 4.99-5.03 (1H, m), 5.09 (1H, dd, *J* = 10.0 Hz, 1.5 Hz), 5.54 (1H, ddd, *J* = 17.5 Hz, 10.5 Hz, 9.5 Hz), 5.97 (1H, ddd, *J* = 17.0 Hz, 10.0 Hz, 8.5 Hz), 7.15-7.21 (3H, m), 7.29 (2H, app t, *J* = 7.5 Hz); $^{13}$C NMR (125 MHz, $CDCl_3$): $\delta$ 14.2, 22.6, 31.8, 34.2, 49.1, 54.9, 60.1, 115.3, 116.4, 126.2, 128.1, 128.4, 140.4, 140.5, 143.2, 173.6; IR (neat): 3077 (w), 2978 (w), 2928 (w), 1733 (s), 1638 (w), 1373 (w), 1246 (w), 1164 (m), 1076 (w), 994 (w), 913 (m), 759 (w), 701 (s) cm$^{-1}$; HRMS-(ESI+) for $C_{18}H_{25}O_2$ [M+H]: calculated: 273.1854, found: 273.1844. $[\alpha]^{22}_D$ = -51.664 (*c* = 0.60, $CHCl_3$, from (*S*)-MeO(furyl)BIPHEP). The crude reaction mixture was purified on silica gel (40:1 pentane:diethyl ether) to afford a clear, colorless oil (31.5 mg, 77% yield). $R_f$ = 0.31 (40:1 pentane:diethyl ether, stain in PMA).

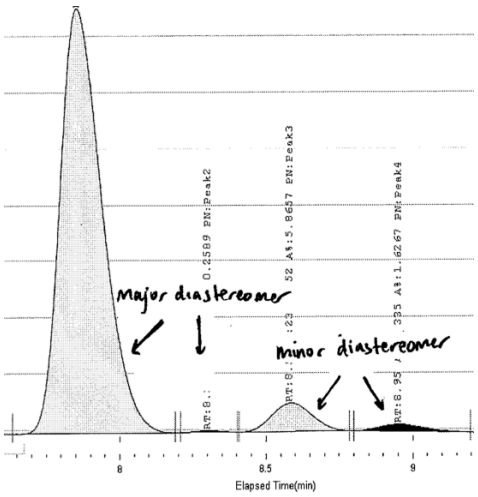
***Analysis of Stereochemistry:***

The title compound was subjected to DIBAL-H reduction to afford the primary alcohol for SFC analysis, as depicted below. The analogous racemic material was prepared *via* the same route, using 1,2-bis(diphenylphosphino)benzene as the achiral ligand in the allyl-allyl coupling reaction. The absolute stereochemistry was assigned by analogy to compounds **2.107** and **2.130**.




*Chiral SFC (AD-H, Chiralpak, 215 nm, 2.0 mL/min, 3.0% MeOH, 100 bar, 35 °C) - analysis of primary alcohol.*

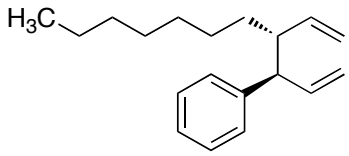



racemic

From ( *S*)-MeO(furyl)BIPHEP

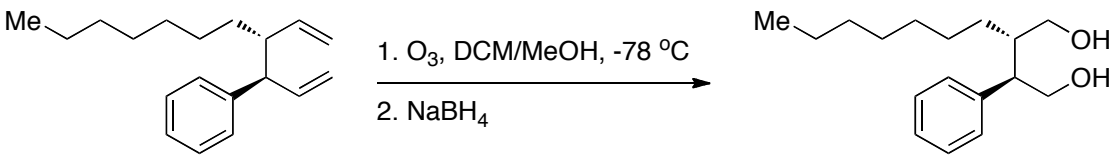
| Peak No | % Area | Area | RT (min) |
|---|---|---|---|
| 1 | 92.2487 | 3761.7756 | 7.85 |
| 2 | 0.2589 | 10.5558 | 8.3 |
| 3 | 5.8657 | 239.1952 | 8.58 |
| 4 | 1.6267 | 66.335 | 8.95 |



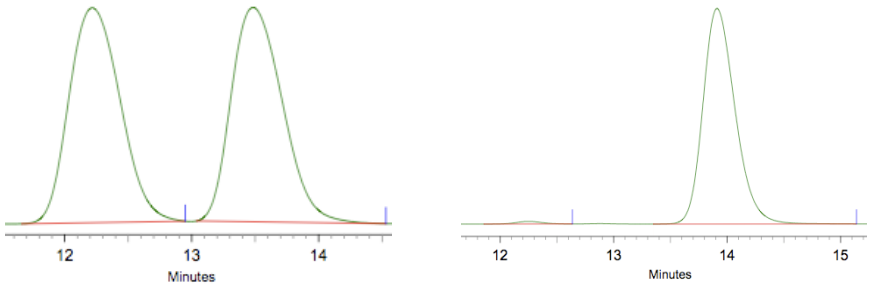
**((3*R*,4*R*)-4-vinylundec-1-en-3-yl)benzene (2.127).** The title compound was prepared *via* representative procedure A for allyl-allyl coupling, with the following modification: 2.5 mol % $Pd_2(dba)_3$ and 5.0 mol % (*R*)-MeO(furyl)BIPHEP were used. $^1$H NMR (500 MHz, $CDCl_3$): $\delta$ 0.86 (3H, t, *J* = 6.5 Hz), 1.07-1.28 (12H, m), 2.33 (1H, app dq, *J* = 9.0 Hz, 3.0 Hz), 3.17 (1H, app t, *J* = 8.5 Hz), 4.92-4.97 (2H, m), 5.01 (1H, ddd, *J* = 10.5 Hz, 2.0 Hz, 1.0 Hz), 5.06 (1H, dd, *J* = 10.5 Hz, 2.0 Hz), 5.55 (1H, ddd, *J* = 17.0 Hz, 10.0 Hz, 9.0 Hz), 5.99 (1H, ddd, *J* = 17.0 Hz, 10.5 Hz, 8.5 Hz), 7.16-7.28 (3H, m), 7.30 (2H, app t, *J* = 7.5 Hz); $^{13}$C NMR (125 MHz, $CDCl_3$): $\delta$ 14.1, 22.6, 27.0, 29.2, 29.4, 31.8, 32.3, 49.2, 55.0, 115.1, 115.8, 126.1, 128.1, 128.3, 140.7, 141.0, 143.5; IR (neat): 3077 (w), 2977 (m), 2928 (m), 1733 (s), 1638 (w), 1452 (w), 1419 (w), 1372 (w), 1246 (w), 1164 (m), 1115 (w), 1031 (w), 994 (w), 913 (m), 759 (w), 729 (w), 701 (s) cm$^{-1}$; HRMS-(ESI+) for $C_{19}H_{29}$ [M+H]: calculated: 257.2269, found: 257.2276. $[\alpha]^{22}_D$ = -52.976 (*c* = 0.87, $CHCl_3$, from (*S*)-MeO(furyl)BIPHEP). The crude reaction mixture was purified on silica gel (pentane) to afford a clear, colorless oil (27.3 mg, 71% yield). $R_f$ = 0.43 (pentane, stain in PMA).

***Analysis of Stereochemistry:***

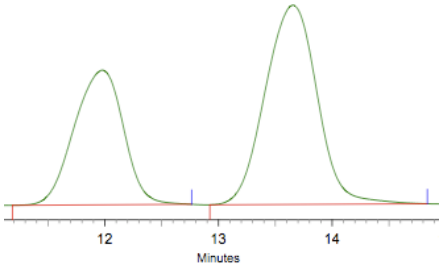
The title compound was subjected to ozonolysis and reduction to afford the 1,4-diol for HPLC analysis, as depicted below. The analogous racemic material was prepared *via* the same route, using 1,2-bis(diphenylphosphino)benzene as the achiral ligand in the allyl-allyl coupling reaction. The absolute stereochemistry was assigned by analogy to compounds **2.107** and **2.130**.




*Chiral HPLC (OJ-H, Chiralcel, 0.5 mL/min, 5.0% isopropanol, 217 nm) - analysis of 1,4-diol.*

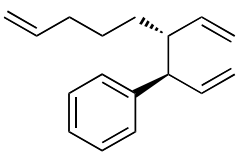



Racemic diol from (*S*)-MeO(furyl)BIPHEP




diol from allyl-allyl coupling product
+ racemic co-injection

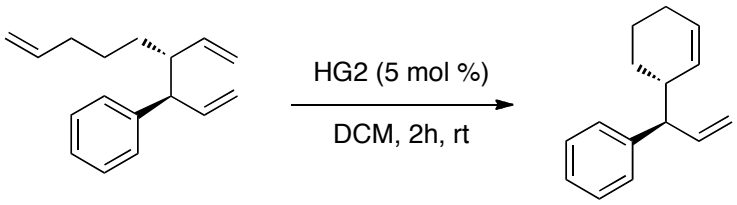
| Retention Time | Area | Area % | Height | Height % |
|---|---|---|---|---|
| 12.250 | 2095438 | 0.98 | 130102 | 1.20 |
| 13.910 | 211932281 | 99.02 | 10754123 | 98.80 |



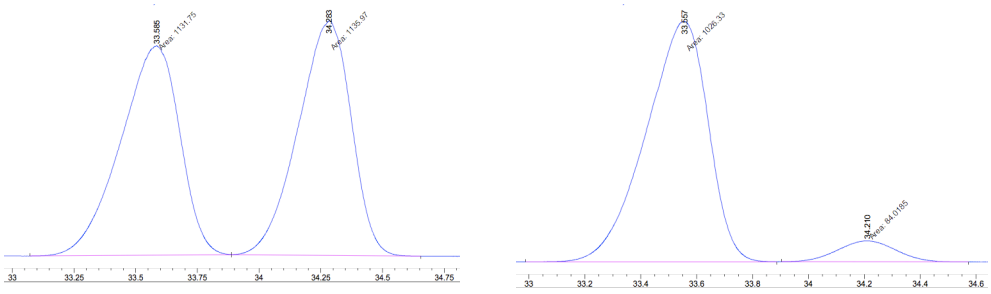
**((3*R*,4*R*)-4-vinylnona-1,8-dien-3-yl)benzene (2.128).** The title compound was prepared *via* representative procedure A for allyl-allyl coupling, with the following modification: 2.5 mol % $Pd_2(dba)_3$ and 5.0 mol % (*R*)-MeO(furyl)BIPHEP were used. $^1$H NMR (500 MHz, $CDCl_3$): δ 1.10-1.17 (1H, m), 1.19-1.33 (2H, m), 1.36-1.44 (1H, m), 1.86-1.92 (1H, m), 1.94-2.01 (1H, m), 2.34 (1H, app qd, *J* = 9.5 Hz, 3.5 Hz), 3.17 (1H, app t, *J* = 8.5 Hz), 4.88 (1H, app dp, *J* = 10.5 Hz, 1.0 Hz), 4.90-4.94 (3H, m), 5.02 (1H, dd, *J* = 10.0 Hz, 1.5 Hz), 5.07 (1H, dd, *J* = 10.0 Hz, 2.0 Hz), 5.55 (1H, ddd, *J* = 17.5 Hz, 10.5 Hz, 9.5 Hz), 5.72 (1H, app ddt, *J* = 17.0 Hz, 10.0 Hz, 6.5 Hz), 5.99 (1H, ddd, *J* = 17.0 Hz, 10.0 Hz, 8.5 Hz), 7.16-7.21 (3H, m), 7.30 (2H, app t, *J* = 7.5 Hz); $^{13}$C NMR (125 MHz, $CDCl_3$): δ 26.4, 31.9, 33.6, 49.1, 55.0, 114.2, 115.2, 116.0, 126.1, 128.1, 128.3, 138.9, 140.6, 140.8, 143.4; IR (neat): 3076 (w), 2976 (w), 2927 (m), 2856 (w), 1639 (m), 1494 (w), 1452 (w), 1417 (w), 993 (m), 966 (w), 911 (s), 759 (m), 700 (s) $cm^{-1}$; HRMS-(ESI+) for $C_{17}H_{23}$ [M +H]: calculated: 227.1800, found: 227.1809. $[\alpha]^{22}_D$ = -59.585 (*c* = 0.39, $CHCl_3$, from (*S*)-MeO(furyl)BIPHEP). The crude reaction mixture was purified on silica gel (pentane) to afford a clear, colorless oil (18.3 mg, 54% yield). $R_f$ = 0.39 (pentane, stain in PMA).

***Analysis of Stereochemistry:***

The title compound was treated with Hoveyda-Grubbs second generation catalyst to afford the ring closing metathesis product for GC analysis, as depicted below. The analogous racemic material was prepared *via* the same route, using 1,2-bis(diphenylphosphino)benzene as the achiral ligand in the allyl-allyl coupling reaction. The absolute stereochemistry was assigned by analogy to compounds **2.107** and **2.130**.




*Chiral GLC (β-dex, Supelco, 135 °C, 20 psi) - analysis of the metathesis product.*

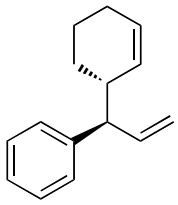


Racemic

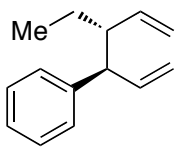


from (*S*)-MeO(furyl)BIPHEP

| Peak # | RetTime [min] | Type | Width [min] | Area [pA*s] | Height [pA] | Area % |
|---|---|---|---|---|---|---|
| 1 | 33.557 | MM | 0.2584 | 1026.32739 | 66.20870 | 92.43313 |
| 2 | 34.210 | MM | 0.2432 | 84.01846 | 5.75815 | 7.56687 |



**((*R*)-1-((*R*)-cyclohex-2-en-1-yl)allyl)benzene.** $^{1}$H NMR (500 MHz, $CDCl_3$): $\delta$ 1.09-1.16 (1H, m), 1.41-1.50 (2H, m), 1.66-1.70 (1H, m), 1.95-1.99 (2H, m), 2.42-2.47 (1H, m), 3.04 (1H, app t, $J$ = 9.0 Hz), 5.05-5.10 (2H, m), 5.73-5.80 (2H, m), 6.02 (1H, ddd, $J$ = 17.0 Hz, 10.0 Hz, 9.0 Hz), 7.17-7.21 (3H, m), 7.30 (2H, $J$ = 7.5 Hz); $^{13}$C NMR (125 MHz, $CDCl_3$): $\delta$ 21.6, 25.4, 27.7, 39.7, 56.2, 115.6, 126.1, 127.8, 128.1, 128.4, 129.5, 140.6, 143.7; IR (neat): 3025 (w), 2924 (s), 2857 (m), 1713 (w), 1492 (w), 1452 (w), 992 (w), 968 (w), 915 (m), 758 (w), 724 (m), 700 (s) $cm^{-1}$; HRMS-(ESI+) for $C_{15}H_{19}$ [M+H]: calculated: 199.1487, found: 199.1485. $[\alpha]^{22}_{D}$ = -12.409 ($c$ = 0.32, $CHCl_3$, from (*S*)-MeO(furyl)BIPHEP). The crude reaction mixture was purified on silica gel (pentane) to afford a clear, colorless oil (10.1 mg, 62% yield). $R_f$ = 0.50 (pentane, stain in $KMnO_4$).

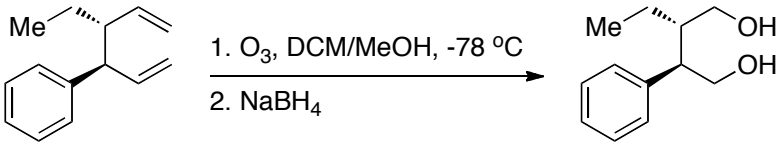



**((3*R*,4*R*)-4-ethylhexa-1,5-dien-3-yl)benzene (2.129).** The title compound was prepared *via* representative procedure A for allyl-allyl coupling, with the following modification: 2.5 mol % $Pd_2(dba)_3$ and 5.0 mol % (*R*)-MeO(furyl)BIPHEP were used. $^1$H NMR (500 MHz, $CDCl_3$): $\delta$ 0.79 (3H, td, *J* = 7.0 Hz, 1.0 Hz), 1.10 (1H, app ddt, *J* = 16.5 Hz, 14.0 Hz, 6.5 Hz), 1.35 (1H, app ddq, *J* = 7.5 Hz, 3.5 Hz, 1.0 Hz), 2.25 (1H, app dq, *J* = 9.0 Hz, 4.0 Hz), 3.19 (1H, app t, *J* = 8.5 Hz), 4.94 (1H, app dt, *J* = 13.0 Hz, 1.0 Hz), 4.97 (1H, app dt, *J* = 13.0 Hz, 1.0 Hz), 5.01 (1H, app dt, *J* = 10.5 Hz, 1.0 Hz), 5.08 (1H, dd, *J* = 10.0 Hz, 1.5 Hz), 5.50 (1H, dtd, *J* = 17.5 Hz, 010.0 Hz, 1.0 Hz), 6.00 (1H, dtd, *J* = 17.5 Hz, 9.5 Hz, 1.0 Hz), 7.17-7.21 (3H, m), 7.30 (2H, t, *J* = 7.5 Hz); $^{13}$C NMR (125 MHz, $CDCl_3$): $\delta$ 11.6, 25.2, 51.1, 54.8, 115.1, 116.0, 126.1, 128.1, 128.3, 140.7, 140.8, 143.5; IR (neat): 3078 (m), 3028 (w), 2974 (m), 2927 (w), 2886 (w), 1639 (m), 1601 (w), 1493 (m), 1453 (w), 1416 (w), 1372 (w), 1072 (w), 1030 (m), 992 (w), 911 (s), 758 (m), 722 (w), 670 (s), 527 (w) cm$^{-1}$; HRMS-(ESI+) for $C_{14}H_{19}$ [M+H]: calculated: 187.1487, found: 187.1487. $[\alpha]^{22}_D$ = +63.112 (*c* = 0.41, $CHCl_3$, from (*R*)-MeO(furyl)BIPHEP). The crude reaction mixture was purified on silica gel (pentane) to afford a clear, colorless oil (22.6 mg, 81% yield). $R_f$ = 0.49 (pentane, stain in PMA).

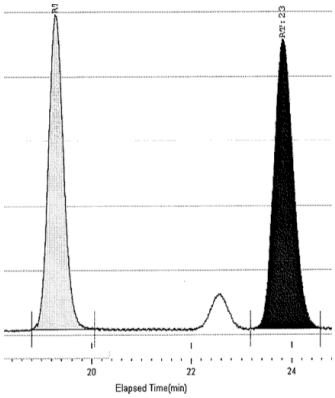
***Analysis of Stereochemistry:***

The title compound was subjected to ozonolysis and reduction to afford the 1,4-diol for SFC analysis, as depicted below. The analogous racemic material was prepared *via* the same route, using 1,2-bis(diphenylphosphino)benzene as the achiral ligand in the

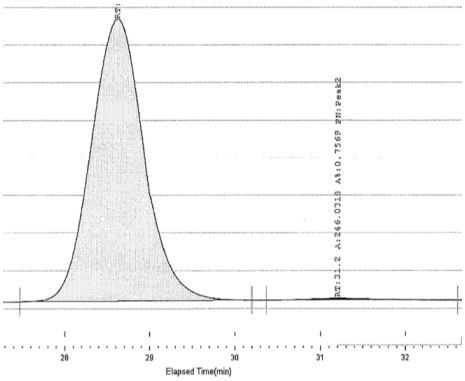
allyl-allyl coupling reaction. The absolute stereochemistry was assigned by analogy to compounds **2.107** and **2.130**.



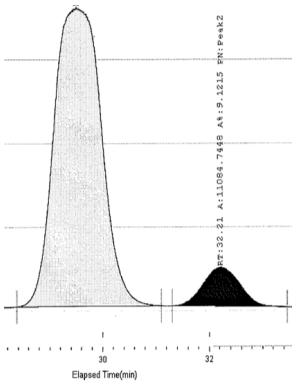

*Chiral SFC (AD-H, Chiralpak, total absorbance, 5.0 mL/min, 2.0% MeOH, 100 bar, 35 °C) - analysis of 1,4-diol.*




Racemic



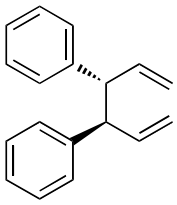

diol from ( *R*)-MeO(furyl)BIPHEP




diol from allyl-allyl coupling product
plus racemic co-injection

Peak Info

| Peak No | % Area | Area | RT (min) |
|---|---|---|---|
| 1 | 99.2431 | 32259.3864 | 28.61 |
| 2 | 0.7569 | 246.0318 | 31.2 |
| Total: | 100 | 32505.4182 | |



**(3*R*,4*R*)-hexa-1,5-diene-3,4-diyldibenzene (2.130).** The title compound was prepared *via* representative procedure A for allyl-allyl coupling, with the following modification: the reaction was run at 60 °C. $^{1}$H NMR (500 MHz, $CDCl_3$): $\delta$ 3.64 (2H, dd, *J* = 8.0 Hz, 2.0 Hz), 5.04 (2H, ddd, *J* = 17.0 Hz, 1.5 Hz, 0.5 Hz), 5.11 (2H, ddd, *J* = 10.5 Hz, 1.5 Hz, 0.5 Hz), 6.06-6.17 (2H, m), 7.02-7.37 (10H, m); $^{13}$C NMR (125 MHz, $CDCl_3$): $\delta$ 55.8, 115.8, 126.0, 128.1, 128.2, 140.5, 142.6; IR (neat): 3080 (w), 3062 (w), 3027 (m), 2922 (w), 1637 (w), 1600 (w), 1494 (m), 1452 (m), 1073 (w), 990 (w), 965 (w), 915 (m), 756 (m), 698 (s), 515 (w) $cm^{-1}$; HRMS-(ESI+) for $C_{18}H_{19}$ [M+H]: calculated: 235.1489, found: 235.1481. $[\alpha]^{22}_D$ = +54.233 (*c* = 0.55, $CHCl_3$, from (*R*)-MeO(furyl)BIPHEP). The crude reaction mixture was purified on silica gel (pentane) to afford a clear, colorless oil (18.8 mg, 80% yield). $R_f$ = 0.13 (pentane, stain in $KMnO_4$).

***Proof of Stereochemistry:***

The title compound was subjected to ozonolysis and reduction to afford the 1,4-diol for SFC analysis, as depicted below. The analogous racemic material was prepared *via* the same route, using 1,2-bis(diphenylphosphino)benzene as the achiral ligand in the allyl-allyl coupling reaction. In order to determine the absolute stereochemistry, the optical rotation of the 1,4-diol derived from the allyl-allyl coupling product ($[\alpha]^{20}_D$ = -42.144 (*c* = 0.335, $CHCl_3$, from (*R*)-MeO(furyl)BIPHEP)) was compared to the rotation of authentic (2*R*,3*R*)-2,3-diphenylbutane-1,4-diol ($[\alpha]^{25}_D$ = -48.2 (*c* = 0.249, $CHCl_3$)) as previously reported in the literature.[55]

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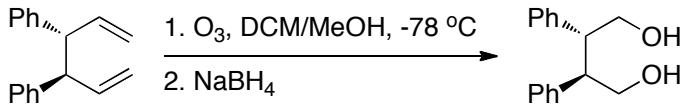
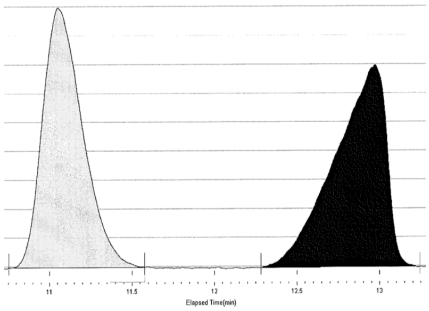
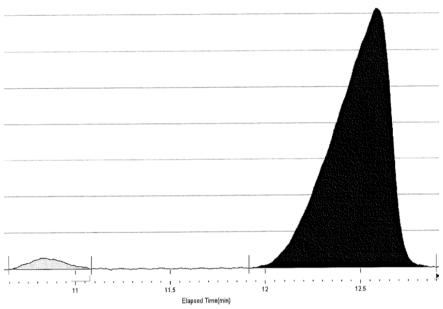
[55] Periasamy, M.; Ramani, G.; Muthukumaragopal, G. P. *Synthesis* **2009**, *10*, 1739.




*Chiral SFC (AD-H, Chiralpak, total absorbance, 5.0 mL/min, 5.0% MeOH, 100 bar, 35 °C) - analysis of 1,4-diol.*



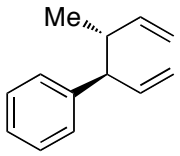
racemic



from ( *R*)-MeO(furyl)BIPHEP

| Peak Name | Number | Concentration | Area % |
|---|---|---|---|
| Peak1 | 1 | 0 | 2.6577 |
| Peak2 | 2 | 0 | 97.3423 |

| RT (min) | St. (min) | End (min) | Height |
|---|---|---|---|
| 10.84 | 10.6452 | 11.0803 | 6.0307 |
| 12.59 | 11.9138 | 12.8974 | 143.0457 |

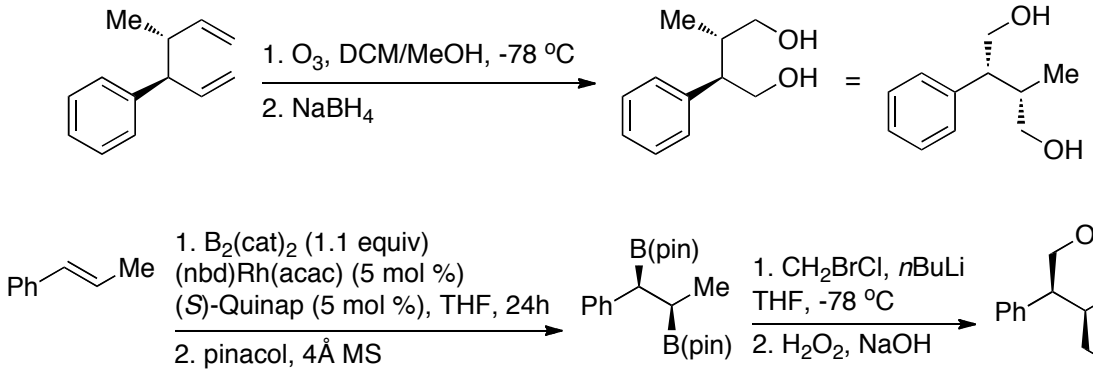



**((3*R*,4*R*)-4-methylhexa-1,5-dien-3-yl)benzene (2.107).** The title compound was prepared *via* representative procedure A for allyl-allyl coupling. $^{1}$H NMR (500 MHz, $CDCl_3$): $\delta$ 0.88 (3H, d, *J* = 6.5 Hz), 2.53 (1H, br app hextet, *J* = 8.0 Hz), 3.08 (1H, app t, *J* = 8.0 Hz), 4.97 (1H, ddd, *J* = 14.5 Hz, 2.0 Hz, 1.0 Hz), 4.99 (1H, ddd, *J* = 4.5 Hz, 1.5 Hz, 0.5 Hz), 5.02-5.04 (2H, m) 5.77 (1H, ddd, *J* = 16.5 Hz, 11.0 Hz, 8.0 Hz), 6.01 (1H, ddd, *J* = 17.0 Hz, 10.0 Hz, 8.5 Hz), 7.16-7.22 (3H, m), 7.30 (2H, app tt, *J* = 7.0 Hz, 1.5 Hz); $^{13}$C NMR (125 MHz, $CDCl_3$): $\delta$ 18.6, 42.8, 56.3, 114.0, 115.3, 126.2, 128.1, 128.3, 140.6, 142.5, 143.4; IR (neat): 3077 (w), 3028 (w), 2963 (m), 2931 (w), 2874 (w), 1639 (w), 1601 (w), 1494 (m), 1453 (w), 1418 (w), 1379 (w), 1073 (w), 1030 (w), 993 (m), 911 (s), 757 (w), 727 (m), 699 (s), 525 (w) $cm^{-1}$; HRMS-(ESI+) for $C_{13}H_{17}$ [M+H]: calculated: 173.1330, found: 173.1337. $[\alpha]^{22}_{D}$ = +35.997 (*c* = 0.36, $CHCl_3$, from (*R*)-MeO(furyl)BIPHEP). The crude reaction mixture was purified on silica gel (pentane) to afford a clear, colorless oil (15.6 mg, 90% yield). $R_f$ = 0.56 (pentane, stain in PMA).

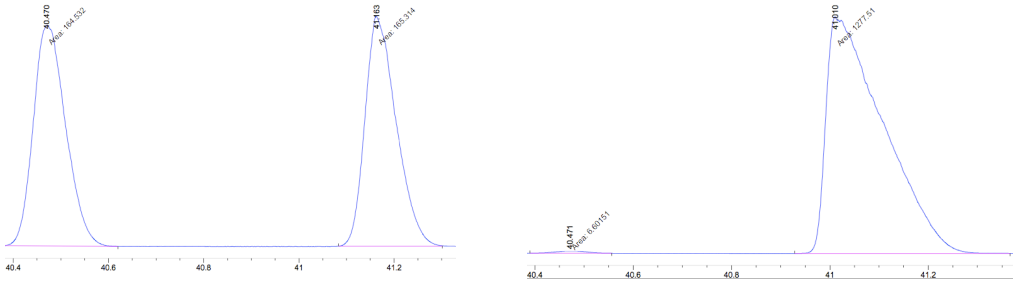
***Proof of Stereochemistry:***

Enantioselectivity was determined by GLC analysis of the title compound as compared to racemic material prepared by using 1,2-bis(diphenylphosphino)benzene as the achiral ligand in the allyl-allyl coupling reaction. Absolute stereochemistry was determined by subjecting the allyl-allyl coupling product to a ozonolysis and reduction to afford a 1,4-diol for HPLC analysis, as shown below. The resulting diol was compared to authentic (2*R*,3*S*)-2-methyl-3-phenylbutane-1,4-diol, prepared by diboration,

homologation, and oxidation of β -methylstyrene, as shown below, using chiral HPLC analysis.[56]




*Chiral GLC (CD-BDM, Supelco, 50 °C for 20 min, ramp 2.5 °C/min to 160 °C for 10 min, 20 psi) - analysis of title compound.*



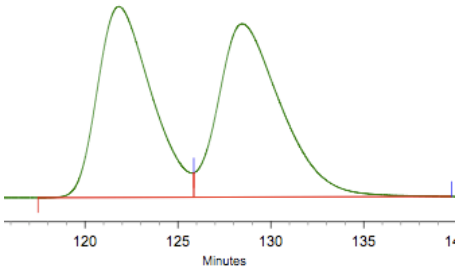
Racemic

from (*R*)-MeO(furyl)BIPHEP

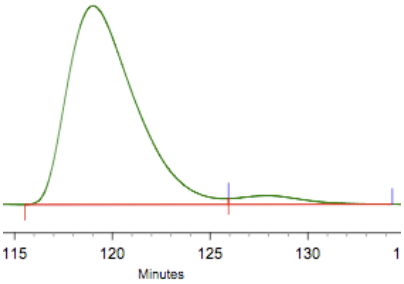
| Peak # | RetTime [min] | Type | Width [min] | Area [pA*s] | Height [pA] | Area % |
|---|---|---|---|---|---|---|
| 1 | 40.471 | MM | 0.0707 | 6.60151 | 1.55683 | 0.51409 |
| 2 | 41.010 | MM | 0.1345 | 1277.50818 | 158.34184 | 99.48591 |

[56] Morgan, J. B.; Miller, S. P.; Morken, J. P. *J. Am. Chem. Soc.* **2003**, *125*, 8702.

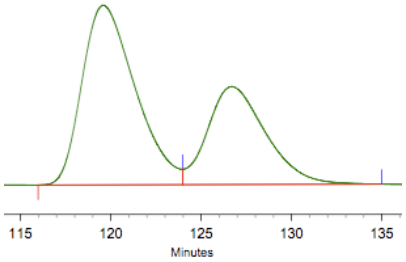
*Chiral HPLC (OD-R, Chiralcel, 0.25 mL/min, 3.0% isopropanol, 217 nm) - analysis of 1,4-diol.*



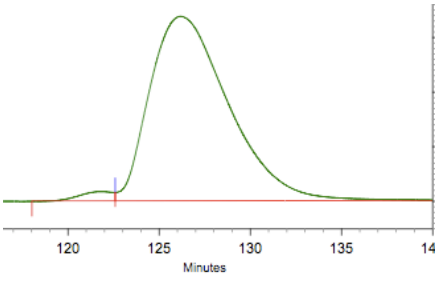

Racemic



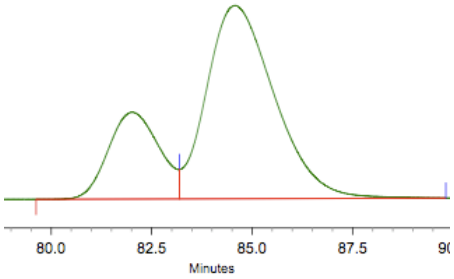

Diol from allyl-allyl coupling product; with (*R*)-MeO(furyl)BIPHEP



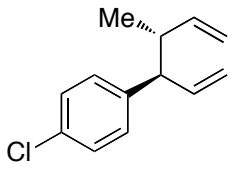

diol from allyl-allyl coupling product + racemic co-injection




diol from alkene diboration; with (*S*)-Quinap




diol from alkene diboration + racemic co-injection

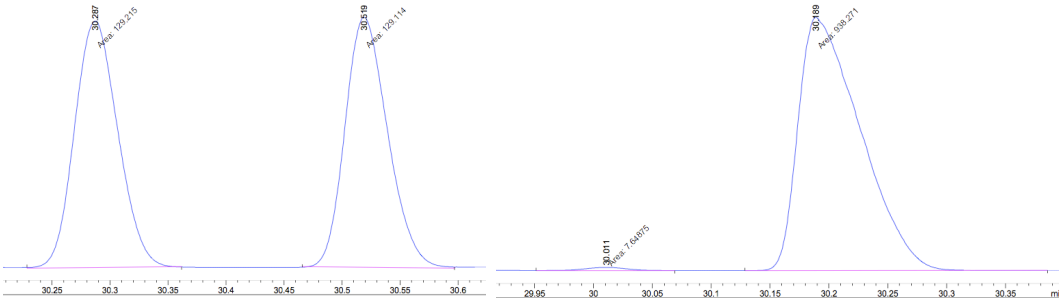



**1-chloro-4-((3*R*,4*R*)-4-methylhexa-1,5-dien-3-yl)benzene (2.113).** The title compound was prepared *via* representative procedure A for allyl-allyl coupling. $^{1}$H NMR (500 MHz, $CDCl_3$): $\delta$ 0.88 (3H, d, $J$ = 7.0 Hz), 2.49 (1H, br app hextet, $J$ = 7.5 Hz), 3.07 (1H, app t, $J$ = 8.0 Hz), 4.94-5.08 (4H, m), 5.74 (1H, ddd, $J$ = 17.0 Hz, 10.0 Hz, 7.5 Hz), 5.97 (1H, ddd, $J$ = 17.0 Hz, 10.0 Hz, 8.5 Hz), 7.09-7.12 (2H, m), 7.26-7.28 (2H, m); $^{13}$C NMR (125 MHz, $CDCl_3$): $\delta$ 18.5, 42.8, 55.5, 114.4, 115.8, 128.5, 129.5, 131.8, 140.0, 141.8, 142.0; IR (neat): 3079 (w), 2975 (w), 2926 (w), 1639 (m), 1491 (s), 1455 (w), 1406 (w), 1373 (s), 1299 (w), 1092 (s), 1015 (m), 992 (m), 913 (s), 817 (m), 726 (w), 680 (w), 625 (w), 562 (w), 524 (w) cm$^{-1}$; HRMS-(ESI+) for $C_{13}H_{16}Cl$ [M+H]: calculated: 207.0941, found: 207.0948. $[\alpha]^{22}_{D}$ = +97.733 ($c$ = 0.67, $CHCl_3$, from (*R*)-MeO(furyl)BIPHEP). The crude reaction mixture was purified on silica gel (pentane) to afford a clear, colorless oil (19.9 mg, 96% yield). $R_f$ = 0.76 (pentane, stain in PMA).

***Analysis of Stereochemistry:***

Enantioselectivity was determined by GLC analysis of the title compound as compared to racemic material, prepared by using 1,2-bis(diphenylphosphino)benzene as the achiral ligand in the allyl-allyl coupling reaction. The absolute stereochemistry was assigned by analogy to compounds **2.107** and **2.130**.

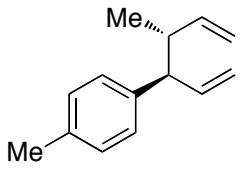
*Chiral GLC (CD-BDM, Supelco, 50 °C for 10 min, ramp 5 °C/min to 160 °C for 60 min, 20 psi) - analysis of title compound.*




Racemic

from (*R*)-MeO(furyl)BIPHEP

| Peak # | RetTime [min] | Type | Width [min] | Area [pA*s] | Height [pA] | Area % |
|---|---|---|---|---|---|---|
| 1 | 30.011 | MM | 0.0402 | 7.64875 | 3.17182 | 0.80860 |
| 2 | 30.189 | MM | 0.0611 | 938.27069 | 255.81476 | 99.19140 |

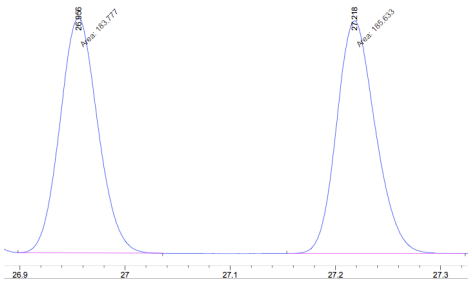



**1-methyl-4-((3*R*,4*R*)-4-methylhexa-1,5-dien-3-yl)benzene (2.114).** The title compound was prepared *via* representative procedure A for allyl-allyl coupling. $^{1}$H NMR (500 MHz, $CDCl_3$): $\delta$ 0.88 (3H, dd, *J* = 7.0 Hz, 1.0 Hz), 2.32 (3H, s), 2.51 (1H, br app hextet, *J* = 7.5 Hz), 3.07 (1H, app t, *J* = 8.0 Hz), 4.84-5.05 (4H, m), 5.77 (1H, dddd, *J* = 17.5 Hz, 10.5 Hz, 9.0 Hz, 1.0 Hz), 5.99 (1H, dddd, *J* = 17.0 Hz, 10.0 Hz, 9.0 Hz, 1.0 Hz), 7.04-7.12 (4H, m); $^{13}$C NMR (125 MHz, $CDCl_3$): $\delta$ 18.6, 21.0, 42.7, 55.9, 113.9, 115.1, 127.9, 129.0, 135.6, 140.3, 140.8, 142.7; IR (neat): 3077 (w), 2974 (m), 2961 (m), 2924 (w), 2868 (w), 1638 (m), 1513 (m), 1455 (w), 1416 (w), 1372 (w), 1110 (w), 992 (m), 911 (s), 810 (m), 722 (w), 528 (w) $cm^{-1}$; HRMS-(ESI+) for $C_{14}H_{19}$ [M+H]: calculated: 187.1487, found: 187.1479. $[\alpha]^{22}_{D}$ = +114.360 (*c* = 0.57, $CHCl_3$, from (*R*)-MeO(furyl)BIPHEP). The crude reaction mixture was purified on silica gel (pentane) to afford a clear, colorless oil (17.4 mg, 93% yield). $R_f$ = 0.60 (pentane, stain in PMA).

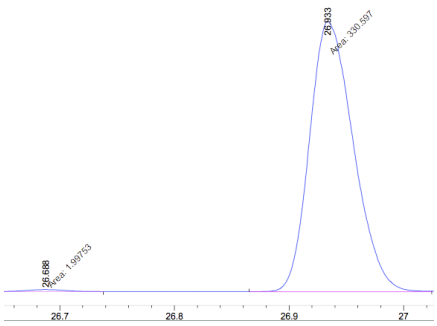
***Analysis of Stereochemistry:***

Enantioselectivity was determined by GLC analysis of the title compound as compared to racemic material, prepared by using 1,2-bis(diphenylphosphino)benzene as the achiral ligand in the allyl-allyl coupling reaction. The absolute stereochemistry was assigned by analogy to compounds **2.107** and **2.130**.

*Chiral GLC (CD-BDM, Supelco, 50 °C for 10 min, ramp 5 °C/min to 160 °C for 10 min, 20 psi) - analysis of title compound.*

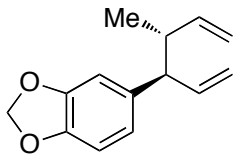



Racemic




from (*R*)-MeO(furyl)BIPHEP

| Peak # | RetTime [min] | Type | Width [min] | Area [pA*s] | Height [pA] | Area % |
|---|---|---|---|---|---|---|
| 1 | 26.688 | MM | 0.0379 | 1.99753 | 8.78039e-1 | 0.60059 |
| 2 | 26.933 | MF | 0.0442 | 330.59680 | 124.62852 | 99.39941 |

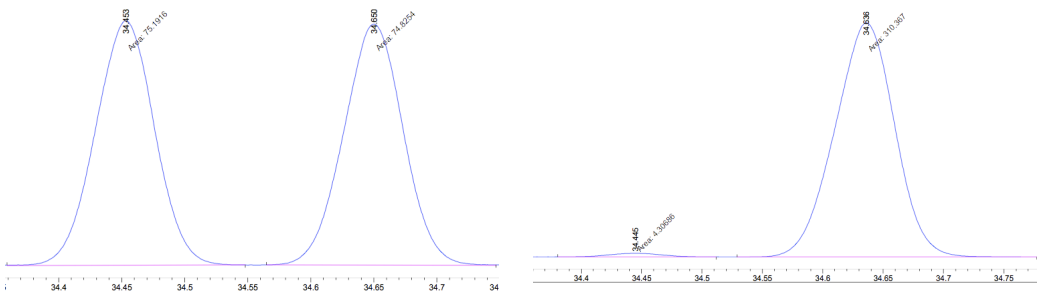


**5-((3*R*,4*R*)-4-methylhexa-1,5-dien-3-yl)benzo[*d*][1,3]dioxole (2.115).** The title compound was prepared *via* representative procedure A for allyl-allyl coupling, with the following modification: the reaction was run at 60 °C. $^{1}$H NMR (500 MHz, $CDCl_3$): δ 0.88 (3H, d, *J* = 6.5 Hz), 2.45 (1H, br app hextet, *J* = 7.5 Hz), 3.00 (1H, app t, *J* = 8.5 Hz), 4.94-5.05 (4H, m), 5.71-5.79 (1H, m), 5.91-5.98 (1H, m), 5.93 (2H, s), 6.62 (1H, ddd, *J* = 7.5 Hz, 1.5 Hz, 0.5 Hz), 6.68 (1H, d, *J* = 2.0 Hz), 6.74 (1H, d, *J* = 7.5 Hz); $^{13}$C NMR (125 MHz, $CDCl_3$): δ 18.5, 42.9, 55.9, 100.8, 108.0, 108.1, 108.3, 114.0, 115.2, 121.1, 131.3, 140.6, 142.5, 147.6; IR (neat): 3076 (w), 2974 (w), 2924 (w), 2891 (m), 1638 (w), 1504 (m), 1487 (s), 1441 (m), 1041 (s), 994 (w), 934 (m), 914 (m), 816 (w), 808 (m), 686 (w) $cm^{-1}$; HRMS-(ESI+) for $C_{14}H_{17}O_2$ [M+H]: calculated: 217.1229, found: 217.1239. $[\alpha]^{22}_D$ = +75.827 (*c* = 0.49, $CHCl_3$, from (*R*)-MeO(furyl)BIPHEP). The crude reaction mixture was purified on silica gel (50:1 pentane:diethyl ether) to afford a clear, colorless oil (18.2 mg, 84% yield). $R_f$ = 0.67 (50:1 pentane:diethyl ether, stain in PMA).

***Analysis of Stereochemistry:***

Enantioselectivity was determined by GLC analysis of the title compound as compared to racemic material, prepared by using 1,2-bis(diphenylphosphino)benzene as the achiral ligand in the allyl-allyl coupling reaction. The absolute stereochemistry was assigned by analogy to compounds **2.107** and **2.130**.

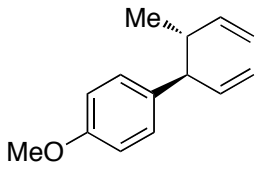
*Chiral GLC (CD-BDM, Supelco, 50 °C for 10 min, ramp 5 °C/min to 160 °C for 10 min, 20 psi) - analysis of title compound.*



racemic

from (*R*)-MeO(furyl)BIPHEP

| Peak # | RetTime [min] | Type | Width [min] | Area [pA*s] | Height [pA] | Area % |
|---|---|---|---|---|---|---|
| 1 | 34.445 | MM | 0.0513 | 4.30686 | 1.40058 | 1.36867 |
| 2 | 34.636 | MM | 0.0575 | 310.36737 | 89.95261 | 98.63133 |

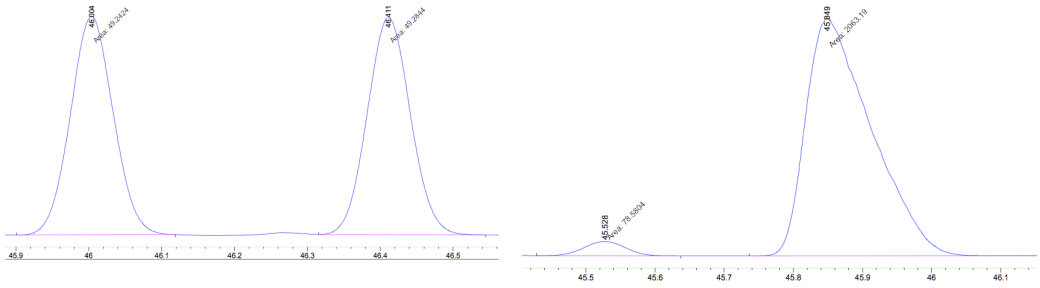



**1-methoxy-4-((3*R*,4*R*)-4-methylhexa-1,5-dien-3-yl)benzene (2.116).** The title compound was prepared *via* representative procedure A for allyl-allyl coupling, with the following modification: the reaction was run at 60 °C. $^{1}$H NMR (500 MHz, $CDCl_3$): δ 0.86 (3H, d, *J* = 6.5 Hz), 2.49 (1H, br app hextet, *J* = 7.0 Hz), 3.04 (1H, app t, *J* = 8.0 Hz), 3.79 (3H, s), 4.93-5.05 (4H, m), 5.31-5.78 (1H, m), 5.99 (1H, ddd, *J* = 10.5 Hz, 8.5 Hz, 2.0 Hz), 6.82-6.86 (2H, m), 7.06-7.13 (2H, m); $^{13}$C NMR (125 MHz, $CDCl_3$): δ 18.5, 42.9, 55.2, 55.3, 113.8, 113.9, 115.0, 115.1, 129.0, 135.4, 140.7, 140.9; IR (neat): 3076 (w), 2959 (w), 2932 (m), 2835 (w), 1638 (w), 1610 (m), 1583 (w), 1510 (s), 1464 (w), 1302 (w), 1245 (s), 1178 (m), 1107 (w), 1037 (m), 993 (m), 910 (s), 824 (m), 778 (w), 678 (w), 648 (w), 540 (w) $cm^{-1}$; HRMS-(ESI+) for $C_{14}H_{19}O$ [M+H]: calculated: 203.1436, found: 203.1441. $[\alpha]^{22}_D$ = +96.204 (*c* = 1.84, $CHCl_3$, from (*R*)-MeO(furyl)BIPHEP). The crude reaction mixture was purified on silica gel (50:1 pentane:diethyl ether) to afford a clear, colorless oil (17.1 mg, 84% yield). $R_f$ = 0.84 (50:1 pentane:diethyl ether, stain in PMA).

***Analysis of Stereochemistry:***

Enantioselectivity was determined by GLC analysis of the title compound as compared to racemic material, prepared by using 1,2-bis(diphenylphosphino)benzene as the achiral ligand in the allyl-allyl coupling reaction. The absolute stereochemistry was assigned by analogy to compounds **2.107** and **2.130**.

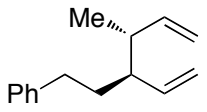
*Chiral GLC (CD-BDM, Supelco, 50 °C for 10 min, ramp 2.5 °C/min to 160 °C for 10 min, 20 psi) - analysis of title compound.*



Racemic

from (*R*)-MeO(furyl)BIPHEP

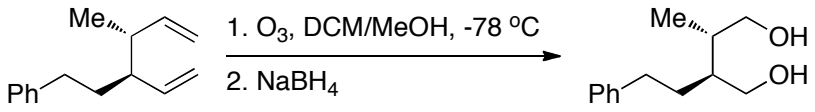
| Peak # | RetTime [min] | Type | Width [min] | Area [pA*s] | Height [pA] | Area % |
|---|---|---|---|---|---|---|
| 1 | 45.528 | MM | 0.0695 | 78.58038 | 18.84259 | 3.66894 |
| 2 | 45.849 | MM | 0.1095 | 2063.19287 | 313.92480 | 96.33106 |



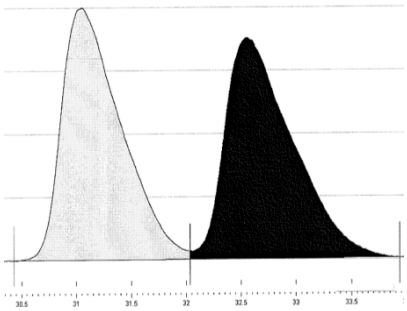

**((3*R*,4*R*)-4-methyl-3-vinylhex-5-en-1-yl)benzene (2.137).** The title compound was prepared *via* representative procedure B for allyl-allyl coupling. $^{1}$H NMR (500 MHz, $CDCl_3$): $\delta$ 0.98 (3H, d, *J* = 7.0 Hz), 1.54-1.62 (1H, m), 1.72 (1H, app dtd, *J* = 17.5 Hz, 6.5 Hz, 4.0 Hz), 1.99 (1H, app heptet, *J* = 5.0 Hz), 2.21-2.27 (1H, m), 2.49 (1H, ddd, *J* = 13.5 Hz, 10.5 Hz, 6.5 Hz), 2.65 (1H, ddd, *J* = 14.0 Hz, 10.5 Hz, 5.0 Hz), 4.94-5.03 (3H, m), 5.11 (1H, dd, *J* = 10.0 Hz, 2.0 Hz), 5.61 (1H, app dt, *J* = 17.5 Hz, 10.0 Hz), 5.72 (1H, ddd, *J* = 16.5 Hz, 11.0 Hz, 8.0 Hz), 7.15-7.18 (2H, m), 7.25-7.29 (3H, m); $^{13}$C NMR (125 MHz, $CDCl_3$): $\delta$ 17.7, 33.8, 34.0, 41.7, 49.0, 114.0, 116.2, 125.6, 128.2, 128.2, 128.4, 139.9, 141.6; IR (neat): 3075 (w), 3027 (w), 3000 (w), 2962 (m), 2925 (m), 2865 (m), 1639 (w), 1604 (w), 1496 (m), 1454 (m), 1422 (w), 1373 (w), 1030 (w), 996 (m), 912 (s), 748 (m), 698 (s) $cm^{-1}$; HRMS-(ESI+) for $C_{15}H_{21}$ [M+H]: calculated: 201.1643, found: 201.1645. $[\alpha]^{22}_{D}$ = +9.586 (*c* = 0.63, $CHCl_3$, from (*R*,*R*)-QuinoxP*). The crude reaction mixture was purified on silica gel (pentane) to afford a clear, colorless oil (12.9 mg, 64% yield). $R_f$ = 0.63 (pentane, stain in PMA).

***Analysis of Stereochemistry:***

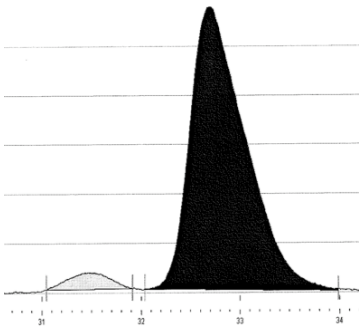
The title compound was subjected to ozonolysis and reduction to afford the 1,4-diol for SFC analysis, as depicted below. The analogous racemic material was prepared *via* the same route, using 1,2-bis(diphenylphosphino)benzene as the achiral ligand in the allyl-allyl coupling reaction. The absolute stereochemistry was assigned by analogy to compounds **2.107** and **2.130**.



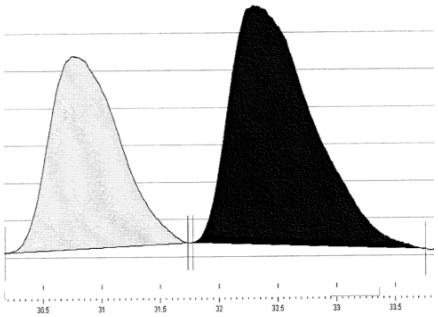

*Chiral SFC (OJ-H, Chiralpak, total absorbance, 3.0 mL/min, 2.0% MeOH, 100 bar, 35 °C) - analysis of 1,4-diol.*



racemic

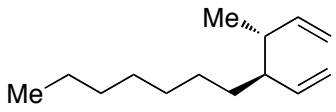


diol derived from allyl-allyl coupling product; from (*R*,*R*)-QuinoxP*



diol from allyl-allyl coupling product plus racemic co-injection

| Peak Name | Area % | Area | RT (min) |
|---|---|---|---|
| Peak1 | 4.2855 | 201.1763 | 31.46 |
| Peak2 | 95.7145 | 4493.226 | 32.7 |

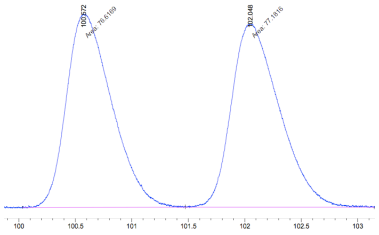



**(3*R*,4*R*)-3-methyl-4-vinylundec-1-ene (2.135).** The title compound was prepared *via* representative procedure B for allyl-allyl coupling. $^{1}$H NMR (500 MHz, $CDCl_3$): $\delta$ 0.88 (3H, t, *J* = 6.5 Hz), 0.97 (3H, dd, *J* = 6.5 Hz, 0.5 Hz), 1.19-1.39 (12H, m), 1.90 (1H, app heptet, *J* = 4.5 Hz), 2.20 (1H, app hextet, *J* = 7.0 Hz), 4.92-4.94 (1H, m), 4.95-4.97 (2H, m), 5.01 (1H, dd, *J* = 10.5 Hz, 2.0 Hz), 5.45 (1H, app dt, *J* = 17.0 Hz, 10.0 Hz), 5.73 (1H, dddd, *J* = 17.0 Hz, 10.5 Hz, 8.0 Hz, 0.5 Hz); $^{13}$C NMR (125 MHz, $CDCl_3$): $\delta$ 14.1, 17.7, 22.7, 27.5, 29.3, 29.7, 31.9, 32.0, 41.6, 49.5, 113.7, 115.4, 140.6, 141.9; IR (neat): 2958 (m), 2924 (s), 2854 (m), 1462 (w), 911 (w), 455 (w) $cm^{-1}$; HRMS-(ESI+) for $C_{14}H_{27}$ [M+H]: calculated: 195.2112, found: 195.2114. $[\alpha]^{22}_{D}$ = -3.140 (*c* = 0.45, $CHCl_3$, from (*R*,*R*)-QuinoxP*). The crude reaction mixture was purified on silica gel (pentane) to afford a clear, colorless oil (13.1 mg, 67% yield). $R_f$ = 0.95 (pentane, stain in PMA).

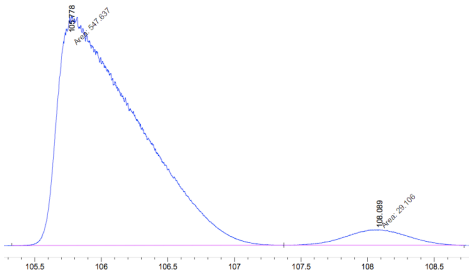
***Analysis of Stereochemistry:***

Enantioselectivity was determined by GLC analysis of the title compound as compared to racemic material, prepared by using 1,2-bis(diphenylphosphino)benzene as the achiral ligand in the allyl-allyl coupling reaction. The absolute stereochemistry was assigned by analogy to compounds **2.107** and **2.130**.

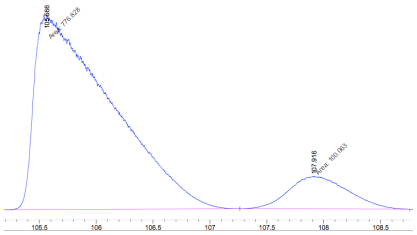
*Chiral GLC (CD-BDM, Supelco, 50 °C for 10 min, ramp 0.25 °C/min to 80 °C for 80 min, 20 psi) - analysis of title compound.*



racemic

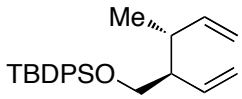


from (*R*,*R*)-QuinoxP*



allyl-allyl coupling product + racemic coinjection

| Peak # | RetTime [min] | Type | Width [min] | Area [pA*s] | Height [pA] | Area % |
|---|---|---|---|---|---|---|
| 1 | 105.778 | MM | 0.6886 | 547.63739 | 13.25515 | 94.95339 |
| 2 | 108.089 | MM | 0.5416 | 29.10597 | 8.95651e-1 | 5.04661 |

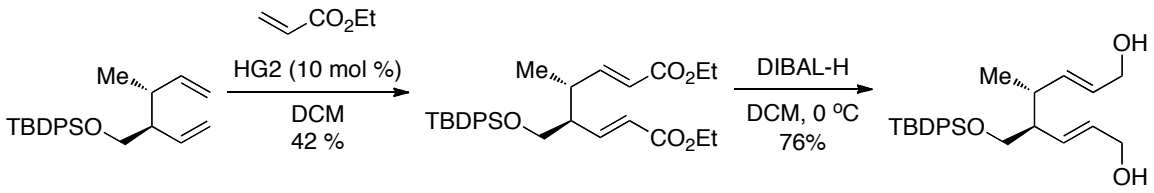



***tert*-butyl(((2*R*,3*R*)-3-methyl-2-vinylpent-4-en-1-yl)oxy)diphenylsilane (2.139).** The title compound was prepared *via* representative procedure A for allyl-allyl coupling, with the following modification: 2.5 mol % $Pd_2(dba)_3$ and 5.0 mol % (*R*,*R*)-QuinoxP* were used, and the reaction was run at 60°C. $^1$H NMR (500 MHz, $CDCl_3$): $\delta$ 0.99 (3H, d, *J* = 7.0 Hz), 1.06 (9H, s), 2.18-2.21 (1H, m), 2.58 (1H, app hextet, *J* = 5.0 Hz), 3.61 (1H, dd, *J* = 10.0 Hz, 6.0 Hz), 3.65 (1H, dd, *J* = 10.0 Hz, 7.0 Hz), 4.95-5.03 (3H, m), 5.06 (1H, dd, *J* = 10.5 Hz, 2.0 Hz), 5.61 (1H, ddd, *J* = 17.0 Hz, 10.0 Hz, 9.0 Hz), 5.70 (1H, ddd, *J* = 17.0 Hz, 10.5 Hz, 8.0 Hz), 7.33-7.45 (6H, m), 7.66-7.68 (4H, m); $^{13}$C NMR (125 MHz, $CDCl_3$): $\delta$ 18.0, 19.3, 26.0, 26.9, 27.3, 37.4, 51.8, 65.2, 114.3, 116.9, 127.2, 127.6, 127.9, 129.3, 129.5, 130.2, 134.4, 135.6, 137.2, 141.2; IR (neat): 3072 (w), 3050 (w), 2960 (m), 2931 (m), 2892 (w), 2858 (m), 1472 (w), 1428 (m), 1390 (w), 1361 (w), 1111 (s), 1027 (w), 998 (m), 915 (m), 822 (m), 739 (m), 701 (s), 613 (m), 505 (s), 487 (m) cm$^{-1}$; HRMS-(ESI+) for $C_{24}H_{33}OSi$ [M+H]: calculated: 365.2301, found: 365.2291. $[\alpha]^{22}_D$ = +9.905 (*c* = 1.07, $CHCl_3$, from (*R*,*R*)-QuinoxP*). The crude reaction mixture was purified on silica gel (pentane) to afford a clear, colorless oil (27.9 mg, 51% yield). $R_f$ = 0.64 (45:1 pentane:diethyl ether, stain in $KMnO_4$).

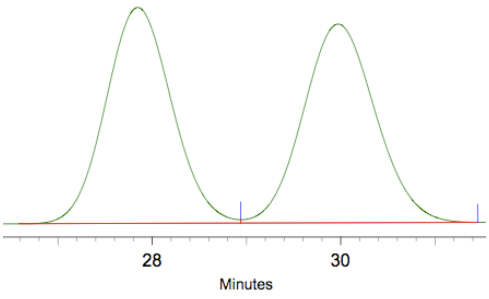
***Analysis of Stereochemistry:***

The title compound was subjected to cross metathesis and reduction to afford the diol for HPLC analysis, as depicted below. The analogous racemic material was prepared *via* the same route, using 1,2-bis(diphenylphosphino)benzene as the achiral

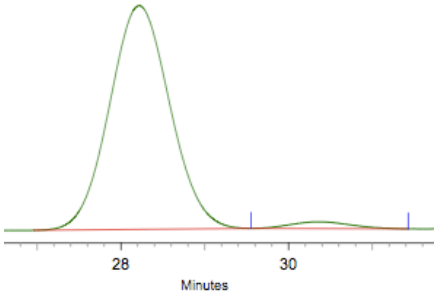
ligand in the allyl-allyl coupling reaction. The absolute stereochemistry was assigned by analogy to compounds **2.107** and **2.130**.




*Chiral HPLC (OD-H, Chiralcel, 2.5 mL/min, 0.5% isopropanol, 220 nm) - analysis of diol.*



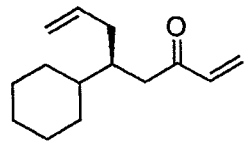

Racemic




diol derived from allyl-allyl coupling product; from (*R*,*R*)-QuinoxP*

| Retention Time | Area | Area % | Height | Height % |
|---|---|---|---|---|
| 28.217 | 47538691 | 97.09 | 946461 | 97.05 |
| 30.357 | 1422558 | 2.91 | 28731 | 2.95 |

## Appendix: Representative $^{1}H$ and $^{13}C$ Spectra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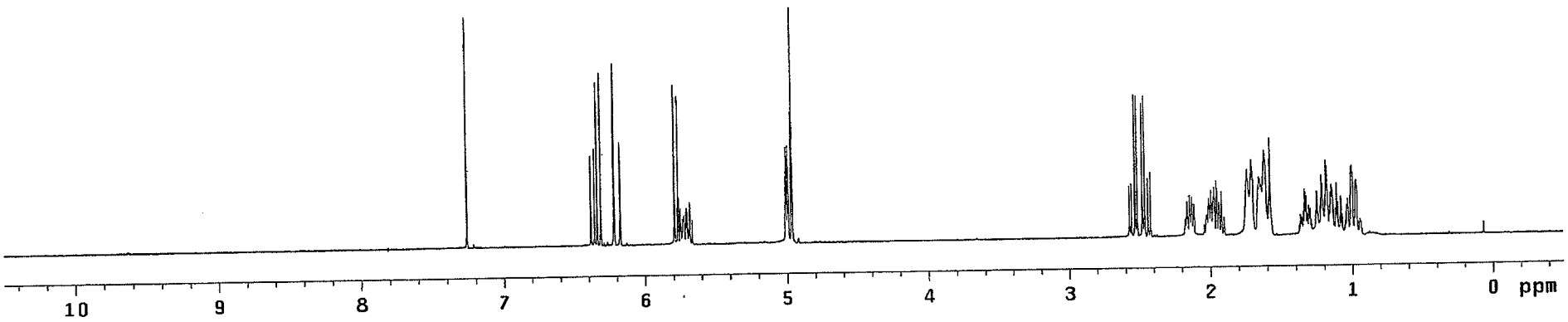
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8
7
6
5
4
3
2
1
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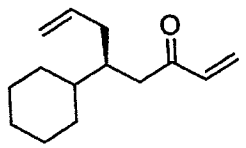
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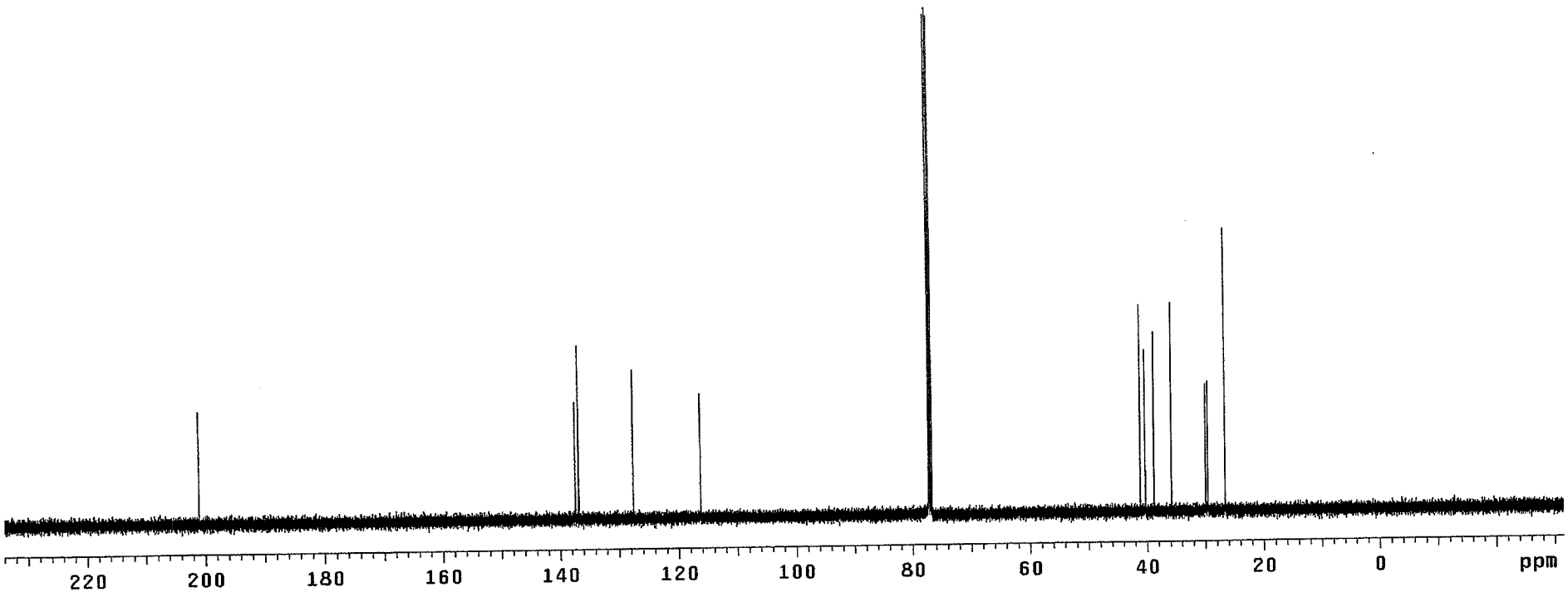
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20
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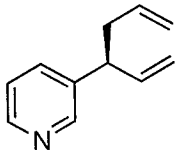
ppm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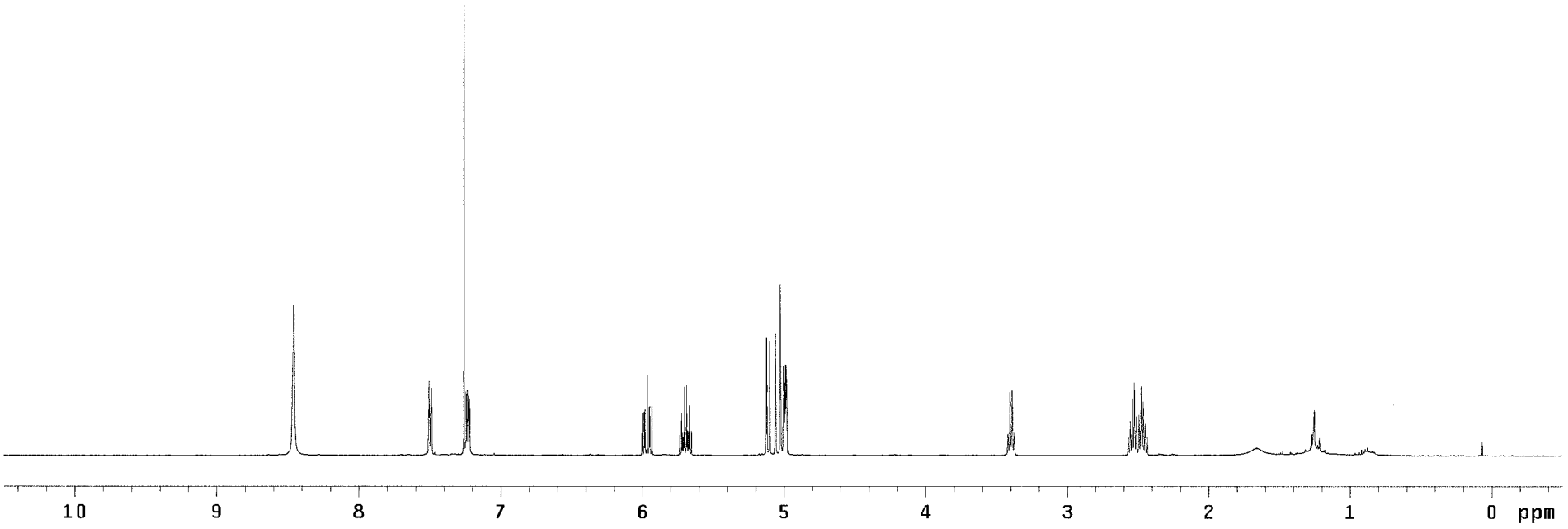
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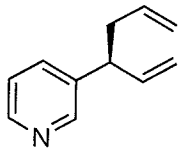
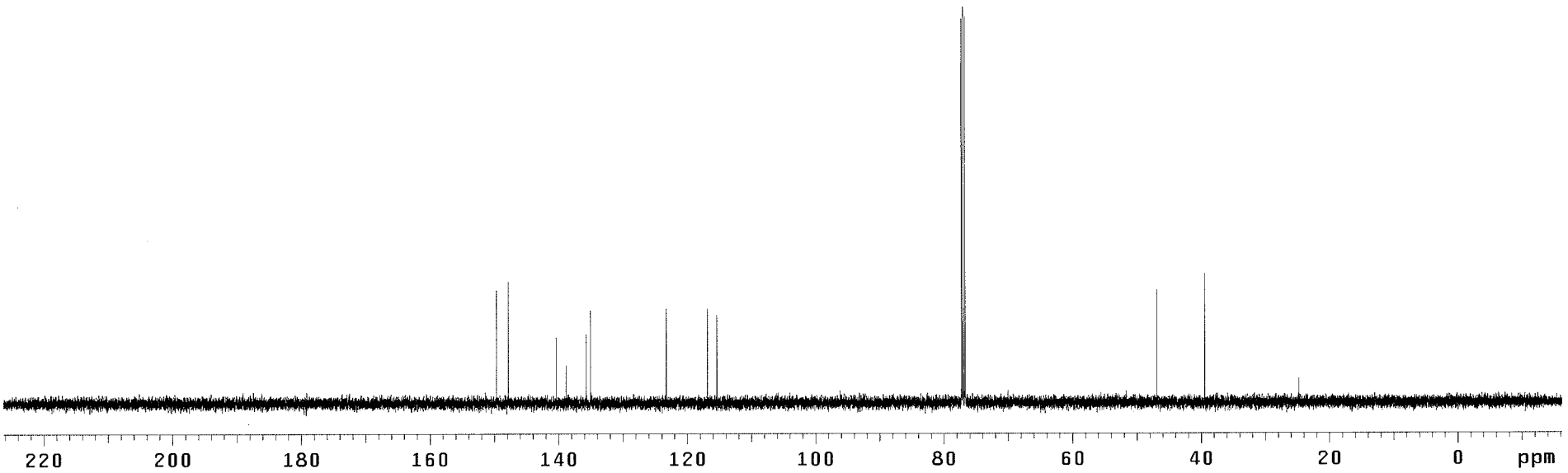

N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100
80
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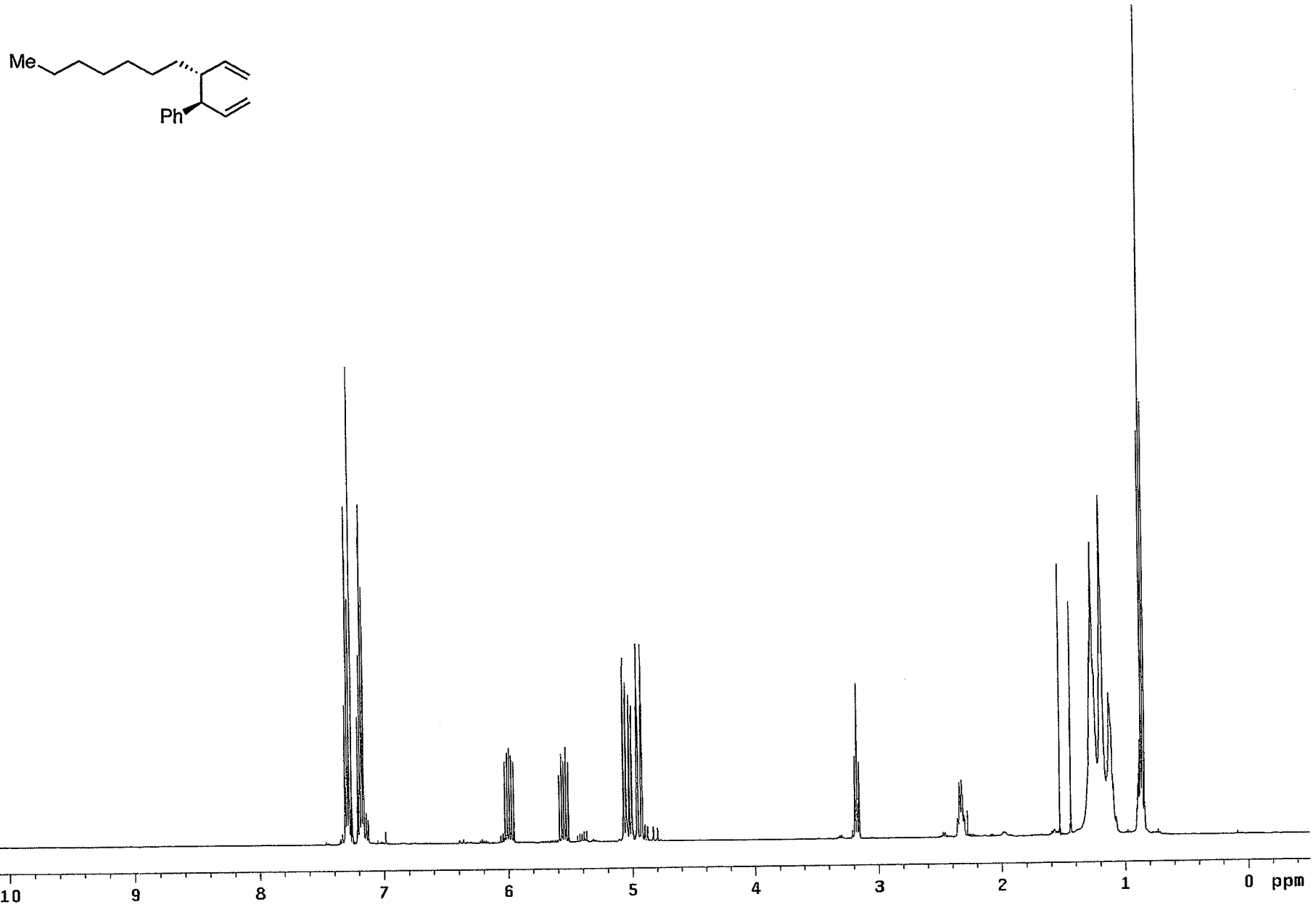
ppm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Ph
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5
4
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2
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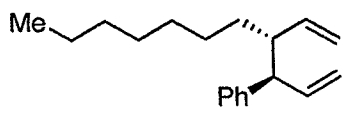
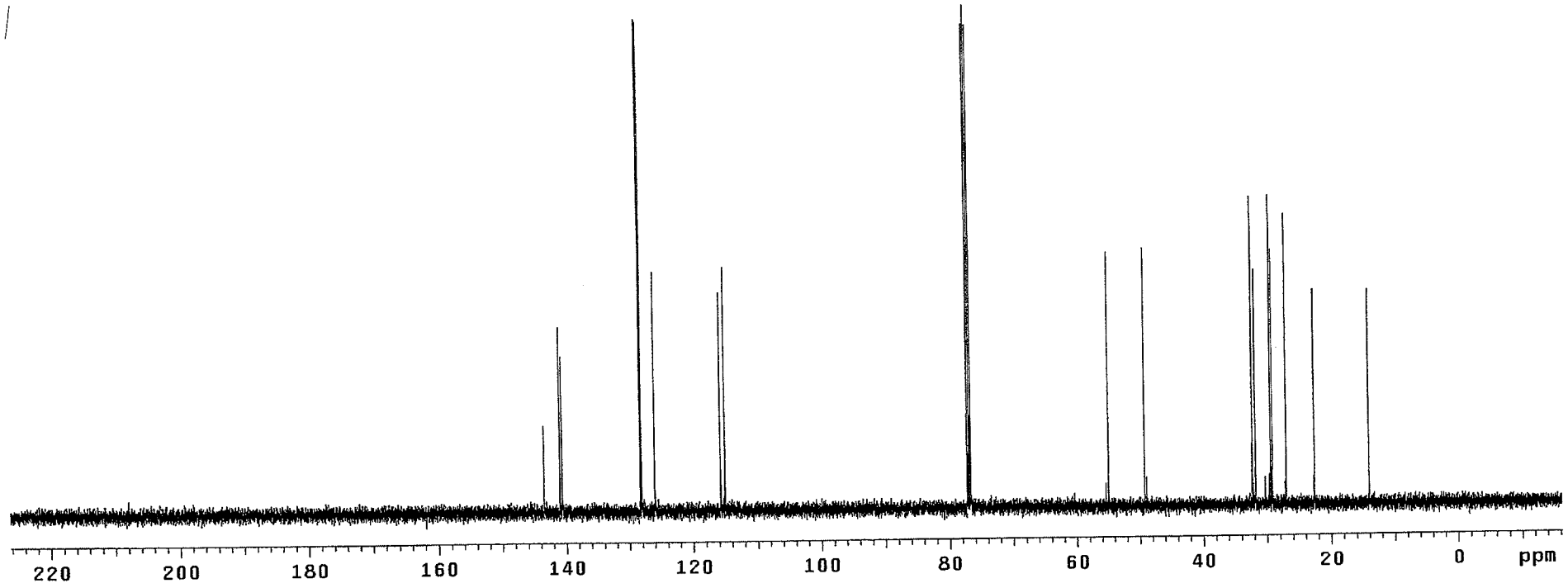
0
ppm


Me
Ph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ppm