Strategic Applications of Pinacolato Allylboron Reagents: New Reactions in Enantioselective Allyl-Allyl Cross-Coupling and Allylboration to Form New Carbon-Heteroatom Bonds

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STRATEGIC APPLICATIONS OF PINACOLATO ALLYLBORON REAGENTS: NEW REACTIONS IN ENANTIOSELECTIVE ALLYL-ALLYL CROSS-COUPLING AND ALLYLBORATION TO FORM NEW CARBON-HETEROATOM BONDS

a dissertation

by

ROBERT E. KYNE, JR.

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ABSTRACT

ROBERT E. KYNE, JR.:

Strategic Applications of Pinacolato Allylboron Reagents: New Reactions in Enantioselective Allyl-Allyl Cross-Coupling and Allylboration to Form New Carbon Heteroatom Bonds

Under the direction of Professor James P. Morken

Detailed within this dissertation are three new reactions involving allylboron reagents. Chapter 1 describes the development of Pd-catalyzed allyl-allyl cross-coupling for the preparation of enantioenriched all-carbon quaternary stereogenic centers. This methodology represents a novel approach to a significant challenge for synthetic chemists. Subsequently, an allyl-allyl cross-coupling is described which generates functionally differentiated 1,5-dienes. Such structures allow for several chemoselective manipulations, which add a significant practical note to this cross-coupling methodology. Chapter 2 details the development of the allylboration of nitrosobenzene with *(Z)*-crotylboronate derivatives, which results in the formation of branched allylic alcohols. This methodology provides a regioselective complement to standard boron oxidation conditions.

ACKNOWLEDGEMENTS

While countless individuals have aided my journey through graduate school, I owe an incalculable debt of gratitude to my advisor, Professor Jim Morken. His extraordinary wealth of scientific knowledge, boundless curiosity, and kind and humble nature have been a source of limitless inspiration for me, and I am grateful for both his tutelage and encouragement. I also express sincere gratitude to my committee members; Professors T. Ross Kelly, Marc L. Snapper, and Kian L. Tan, for both their input into my education and cultivation of a highly intellectual and scholarly culture at Boston College. Additionally, I gratefully acknowledge Professor Timo V. Ovaska (Connecticut College) for his foundational instruction and inspiration, consistent support, and ongoing friendship.

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Finally, to my family and friends, I could not have done this without you. To my beautiful wife, Grace, who stuck by me through this adventure: I am thankful for your love and support, and look forward to joyously writing the next chapters of our lives together. I am grateful to my mother, Chris, Gabrielle, and the rest of my family for their boundless encouragement and support. Finally, thank you to my incredible friends Amanda Worthy, Dr. Dave Moebius, Dr. Sarah Poe, and Ethan Van Arnam.

to Grace

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LIST OF ABBREVIATIONS

Ac: acetyl

BARF: tetrakis[3,5-bis(trifluoromethyl)phenyl]borate

Bn: benzyl

Boc: *tert*-butoxycarbonyl

Boc_2O: di-*tert*-butyldicarbonate

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

cee: conserved enantiomeric excess

cod: cyclooctadiene

Cy: cyclohexyl

dba: dibenzylidene acetone

DCE: dichloroethane

DCM: dichloromethane

DFT: density functional theory

DMF: dimethylformamide

DMS: dimethylsulfide

dppbenzene: 1,2-bis(diphenylphosphino) benzene

dr: diastereomeric ratio

eq: equation

equiv: equivalent(s)

er: enantiomeric ratio

Et_2O: diethyl ether

EtOAc: ethyl acetate

GLC: gas liquid chromatography

h: hour(s)

HG-II: Hoveyda-Grubbs second generation catalyst

HPLC: high performance liquid chromatography

kcal: kilocalorie

L: ligand

LG: leaving group

M: metal

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

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

NMR: nuclear magnetic resonance

phen: 1,10-phenanthroline

phthal: phthalimide

pin: pinacol

QuinoxP*: 2,3-Bis(*tert*)-butylmethylphosphino)quinoxaline

SFC: supercritical fluid chromatography

terph: 3,5-diphenylbenzene

TBDPS: *tert*-butyldiphenylsilyl

TBS: *tert*-butyldimethylsilyl

THF: tetrahydrofuran

TMS: trimethylsilyl

TPAP: tetrapropylammonium perruthenate

y: yield

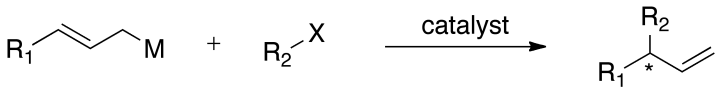
Chapter 1

Enantioselective Allyl-Allyl Cross-Coupling: Synthesis of All-Carbon Quaternary Centers and Functionally Differentiated Vicinal Olefins

I. Introduction

The catalytic cross-coupling of organometallic reagents and organic electrophiles has proven to be one of the most important developments in synthetic chemistry over the past half century. Notably, several of the pioneers in this field were recognized by the greater scientific community with the 2010 Nobel Prize in chemistry for their development of this technology.[1] While there has been rapid development in the area of catalytic cross-coupling since its inception, an area of only modest gains is the enantioselective coupling of prochiral allyl-metal reagents with organic electrophiles (Scheme 1.1).[2]

Scheme 1.1: **Enantioselective Cross-Coupling of Prochiral Allyl-Metals**

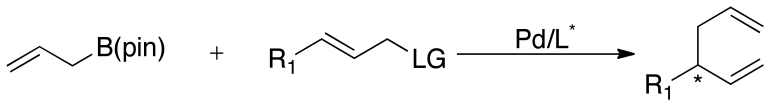


[1] Heck, R. F.; Negishi, E.-i.; Suzuki, A. *Angew. Chem., Int. Ed.* **2010**, *49*, 8300.

[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.

As recently as 2002, Nobel laureate Ei-ichi Negishi noted the numerous challenges that face the cross-coupling of allyl-metal reagents and allylic electrophiles, stating that they "...appear to be intrinsically prone to various side reactions..." and that developments up to that point were "...judged to be generally unsatisfactory...".[3] It was with this significant challenge in mind that our group initiated studies towards the development of a general cross-coupling method between an allylic electrophile and an allylboron nucleophile (Scheme 1.2).[4] The success of this program has offered a paradigm shift in reactivity and granted access to branched 1,5-dienes in high levels of enantioselectivity.

Scheme 1.2: General Enantioselective Allyl-Allyl Cross-Coupling



It was of interest to explore other problems that could potentially be addressed using this coupling technology. Of particular value would be the catalytic and enantioselective synthesis of all-carbon quaternary stereogenic centers, the preparation of which remains a significant challenge to the synthetic

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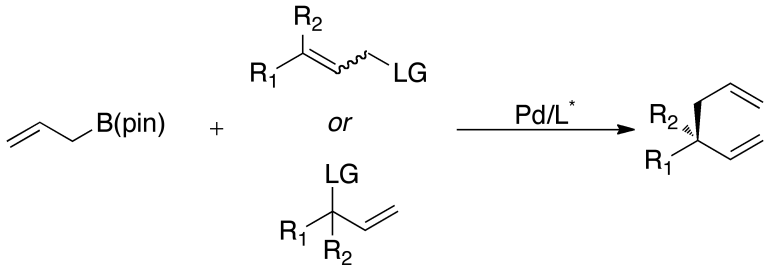
[3] Negishi, E.-i; Liao, B. In *Handbook of Organopalladium Chemistry for Organic Synthesis, Vol. 1;* Negishi, E.-i.; de Meijere, A., Eds.; Wiley-Interscience: West Lafayette, 2002, p. 591-596.

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

community.[5] This difficulty may stem largely from a reduced steric bias between enantiotopic faces of substrates and significant steric repulsion of carbon substituents. We postulated that these issues could be addressed through allyl-allyl cross-coupling between an allylboron nucleophile and an appropriately substituted allylic electrophile (Scheme 1.3).

Scheme 1.3: General Allyl-Allyl Cross-Coupling to Produce a 4° Center



A key issue associated with vicinal olefins is the chemoselectivity of further transformations. Specifically, selective functionalization of the 1,5-diene product is currently best controlled through exploitation of a steric bias within the substrates. Thus, we sought to develop a general method for differentiating the olefins by installing a synthetic handle on one of the coupling partners (Scheme 1.4). The results of this study, in addition to those of all-carbon quaternary center formation *via* allyl-allyl cross-coupling, are presented herein.

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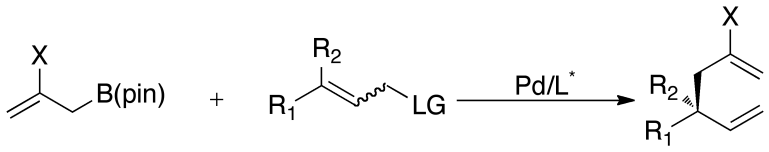
[5] (a) Das, J. P.; Marek, I. *Chem. Commun.* **2011**, *47*, 4593. (b) Cozi, P. G.; Hilgraf, R.; Zimmermann, N. *Eur. J. Org. Chem.* **2007**, 5969. (c) Trost, B. M.; Jian, C. *Synthesis* **2006**, 369. (d) Christoffers, J.; Baro, A. *Adv. Synth. Catal.* **2005**, *447*, 1473. (e) Douglas, C. J.; Overman, L. E. *Proc. Natl. Acad. Sci. U.S.A.* **2004**, *101*, 5363. (f) Corey, E. J.; Guzman-Perez, A. *Angew. Chem., Int. Ed.* **1998**, *37*, 338.

Scheme 1.4: General Preparation of Functionally Differentiated 1,5-Dienes

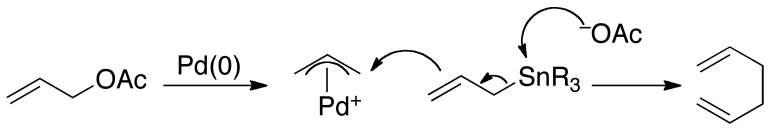


II. Background

A. Allyl-Allyl Cross-Coupling *via* an Outer-Sphere Mechanism

In his 1980 seminal publication on the topic, Professor Barry Trost disclosed the unsymmetrical allyl-allyl coupling of an allylstannane and an allyl acetate under palladium catalysis.[6] While the scope of this early work is limited, it does provide key mechanistic insight into the coupling reaction: a lack of allyl-carbon scrambling suggests an outer-sphere attack on the cationic Pd π-allyl intermediate (Scheme 1.5). In this case, it is suggested that the acetate counterion promotes an S_N2' attack on the π-allyl structure, resulting in the observed 1,5-diene product.

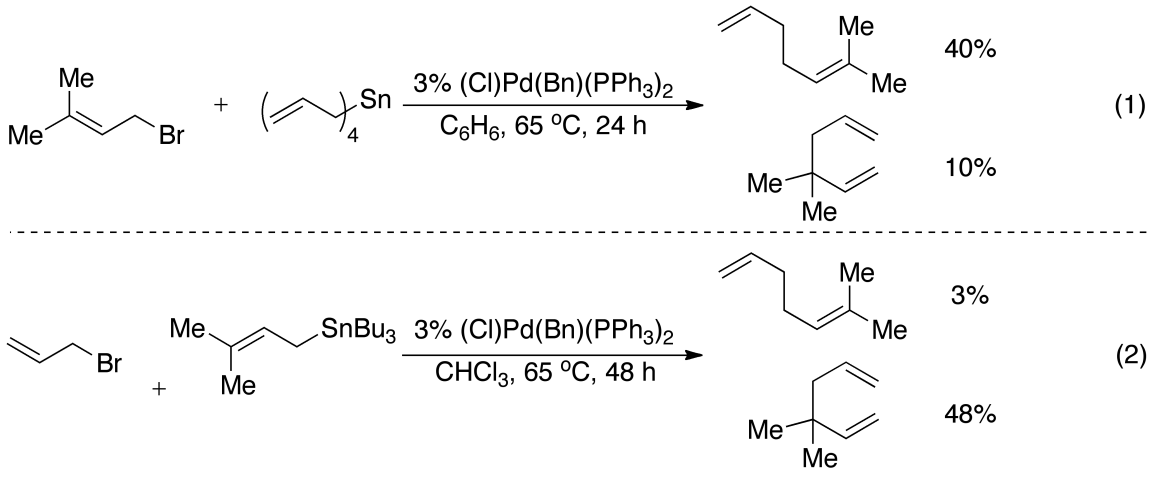
Scheme 1.5: Trost Allylstannane/Allyl Acetate Coupling



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

In a communication that was received by the publisher less than one month after the Trost disclosure, Professor J. K. Stille and Godschalx describe the Pd-catalyzed cross-coupling of allylstannes with allyl halide electrophiles.[7] Interestingly, Stille found that while allyl scrambling of the electrophilic component was observed (Scheme 1.6, eq. 1), the stannyl nucleophile reacts with near complete inversion, often resulting in the more sterically hindered product (Scheme 1.6, eq. 2). These results are consistent with those of Trost and are strongly suggestive of an outer-sphere allyl-allyl cross-coupling mechanism. While both of these studies are important and mechanistically interesting, it was not until 2009 when the outer-sphere coupling of two allylic components was rendered synthetically viable.

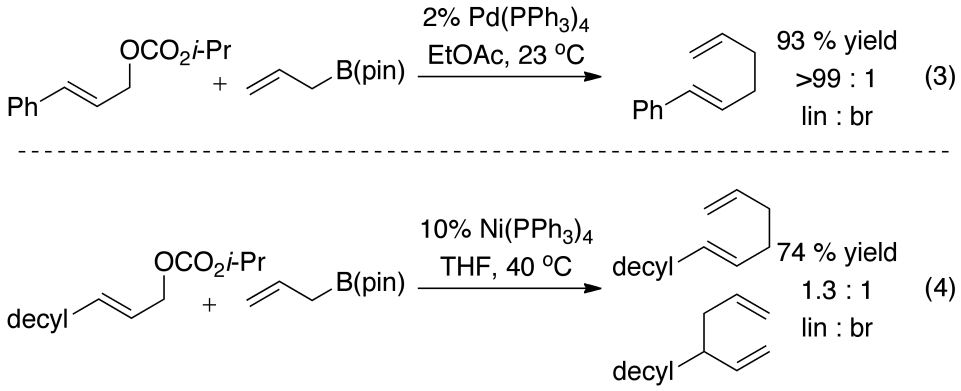
Scheme 1.6: Stille Allylstannane/Allyl Bromide Coupling



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

Concurrently with our group's development of the branch-selective allyl-allyl cross-coupling of allylboronates and allyl carbonates (*vida infra*), Professor Shū Kobayashi and co-workers presented their work on the unsymmetrical cross-coupling of allylboronic acid pinacol ester [allylB(pin)] and allylic carbonates to yield primarily linear 1,5-dienes.[8] They demonstrate that while both Ni(0) and Pd(0) are effective catalysts for this transformation, mixtures of branched and linear 1,5-dienes are often formed. Electron-rich aromatic substrates are particularly linear selective, resulting in products in up to >99 : 1 isomer ratio under Pd-catalysis (Scheme 1.7, eq. 3). Conversely, electron-poor aromatic and alkyl substrates suffer from lower regioselectivity. Even under Ni(0)-catalysis, which generally performs better than Pd(0) for challenging substrates, a 1.3 : 1.0 ratio of linear to branched isomers was isolated for the alkyl substrate shown (Scheme 1.7, eq. 4).

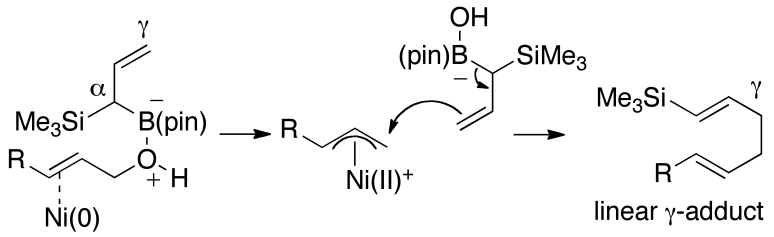
Scheme 1.7: Kobayashi Ni(0) vs. Pd(0) Allyl-Allyl Cross-Coupling



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

In their follow-up communication, Kobayashi *et al.* demonstrated the catalytic coupling of allylB(pin) and allylic *alcohols*, thus obviating the need to activate the oxygen as a leaving group.[9] Here, while both electron-rich and electron poor aromatic substrates give uniformly >99 : 1 linear to branched selectivity under Ni(0)-catalysis, alkyl substrates still suffer from more modest product ratios (4 : 1). Their proposed mechanism invokes activation of the alcohol by the boron of allylB(pin), facilitating formation of a cationic nickel π-allyl. The newly-formed four-coordinate boronate is thus activated for nucleophilic attack on the metal-allyl system. When an α-silyl allylboron derivative is used, exclusive formation of the γ-product is observed, which the authors cite as evidence of an outer-sphere mechanism (Scheme 1.8). Notably, however, Kobayashi does state that they cannot rule out a transmetallative inner-sphere reductive elimination mechanism.

Scheme 1.8: Kobayashi Allylboron/Allylic Alcohol Cross-Coupling

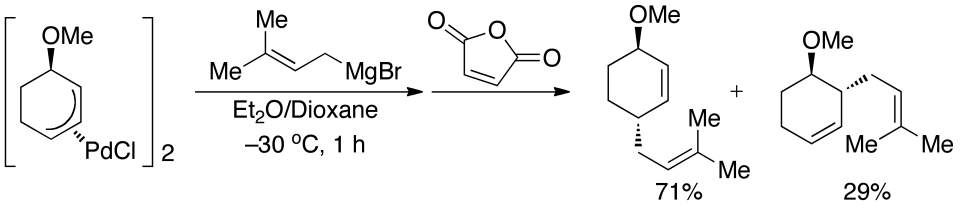


[9] Jiménez-Aquino, A.; Flegeau, E. F.; Schneider, U.; Kobayashi, S. *Chem. Commun.* **2011**, *47*, 9456.

B. Allyl-Allyl Cross-Coupling *via* an Inner-Sphere Mechanism

In Professor Schwartz's 1980 communication on inner-sphere allyl-allyl cross-coupling, he describes a process by which a stoichiometric Pd(II) complex is formed with unsymmetrical allylic ligands (Scheme 1.9).[10] Addition of maleic anhydride promotes reductive elimination, which affords the least sterically strained 1,5-diene as the major product of the reaction (typically linear). Key to the author's mechanistic insight was the observation that carbon-carbon bond formation occurs on the same face from which Pd added. An outer-sphere attack would result in net retention of the starting material stereochemistry. As Schwartz observed an inversion of the stereochemistry with respect to the substrate, an inner-sphere coupling is supported, despite a regioisomeric mixture of products.

Scheme 1.9: Schwartz's Inner-Sphere Allyl-Allyl Cross-Coupling

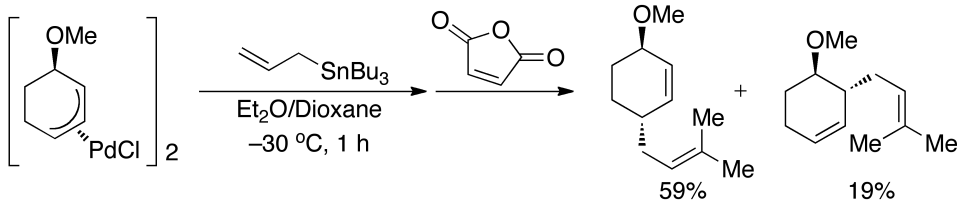


In two follow-up reports, Schwartz and Goliaszewski expand the scope of the nucleophilic coupling partner to include the allylstannane derivatives utilized

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

previously by Trost and Stille for their outer-sphere couplings.[11] Importantly, the Schwartz coupling with allyl tributylstannane maintains the same net inversion of stereochemistry as was observed with allyl Grignard reagents (Scheme 1.10). Thus, the Trost/Stille coupling and the Schwartz coupling offer complimentary reactivity profiles with similar reagents, affording access to either stereoisomeric product.

Scheme 1.10: Schwartz's Allyl-Allyl Cross-Coupling with Allylstannanes



Professors Peter Jolly[12] and Klaus Pörschke[13] made important contributions to the mechanistic understanding of these cross-couplings by forming and isolating a bis(allyl)Pd(II) species with a bidentate phosphine ligand at –30 °C. It was found that, upon slowly warming to room temperature, allyl-allyl cross-coupling proceeds to generate 1,5-hexadiene. Pörschke demonstrated that, under particularly rigorous conditions, one could actually isolate the

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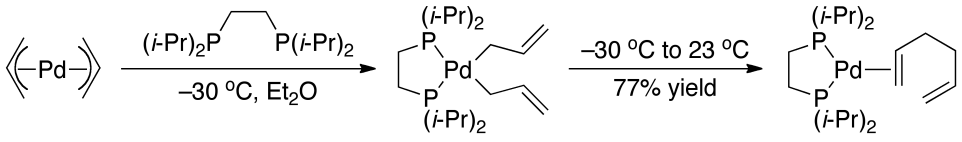
[11] (a) Goliaszewski, A.; Schwartz, J. *Tetrahedron* **1985**, *41*, 5789. (b) Goliaszewski, A.; Schwartz, J. *Organometallics* **1985**, *4*, 417.

[12] Jolly, P. W. *Angew. Chem., Int. Ed.* **1985**, *24*, 283.

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

resultant Pd(0) species with Pd bound to one of the product olefins (Scheme 1.11). One key feature that neither of these manuscripts touch upon is through which carbon the coupling event occurs, as this turns out to be an important detail in further allyl-allyl cross-coupling developments.

Scheme 1.11: Jolly/Pörschke Cross-Coupling



C. Experimental and DFT Studies of 3,3′ Reductive Elimination

While the studies discussed thus far have involved intermolecular processes, some very insightful theoretical work has been carried out by Professor Antonio Echavarren and co-workers on the intramolecular cross-coupling of allylstannanes and allyl acetates (Scheme 1.12). In their initial report, the smooth conversion of **1.01** to **1.02** is demonstrated under palladium catalysis with PPh_3 as the ligand.[14] It is notable that a mixture of olefin isomers on both the nucleophilic and electrophilic coupling partners is tolerated and results in a single product stereoisomer.

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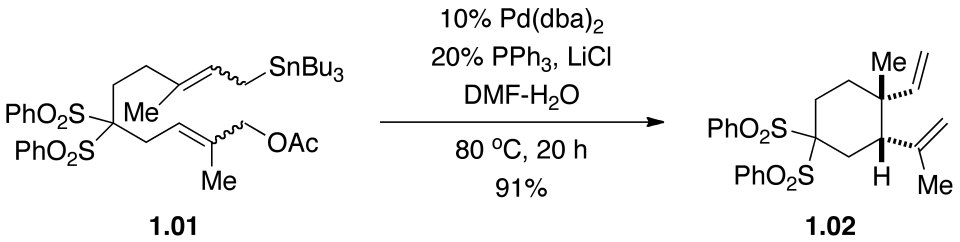
[14] Cuerva, J. M.; Gómez-Bengoa, E.; Méndez, M.; Echavarren, A. M. *J. Org. Chem.* **1997**, *62*, 7540.

Scheme 1.12: Echavarren's Intramolecular Allyl-Allyl Cross-Coupling



1.01 **1.02**

While no support for a 3,3′ reductive elimination pathway is offered in the initial report, a 2002 article by Echavarren that heavily features DFT studies was the most conclusive theoretical evidence to date for this novel metallo-Cope-type elimination mechanism (Figure 1.1).[15] Energy barriers were calculated for reductive elimination from a bis(η^3-allyl)Pd(II) complex (**1.03**), (η^1-allyl)(η^3-allyl)Pd(PH_3) (**1.04**), and bis(η^1-allyl)Pd(PH_3)$_2$ (**1.05**), and for **1.05**, barriers for 3,3′,1,3′, and 1,1′ reductive elimination were calculated. Interestingly, 3,3′ reductive elimination from **1.05** is favored by over 12 kcal/mol as compared to the other reductive elimination modes. In addition to being powerful support for their study, these calculations opened the door for other synthetic chemists to exploit this newly confirmed mode of reactivity.

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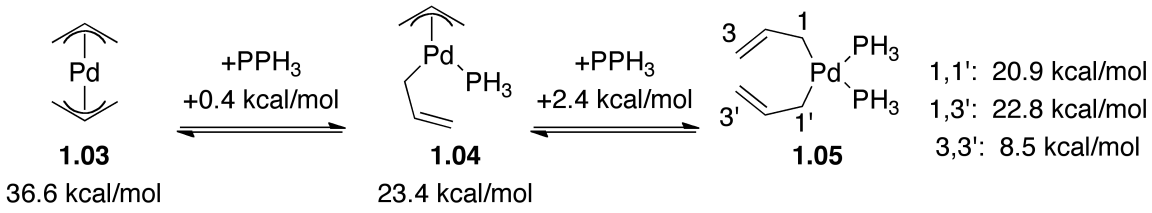
[15] Méndez, M.; Cuerva, J. M.; Gómez-Bengoa, E.; Cárdenas, D. J.; Echavarren, A. M. *Chem. Eur. J.* **2002**, *8*, 3620.

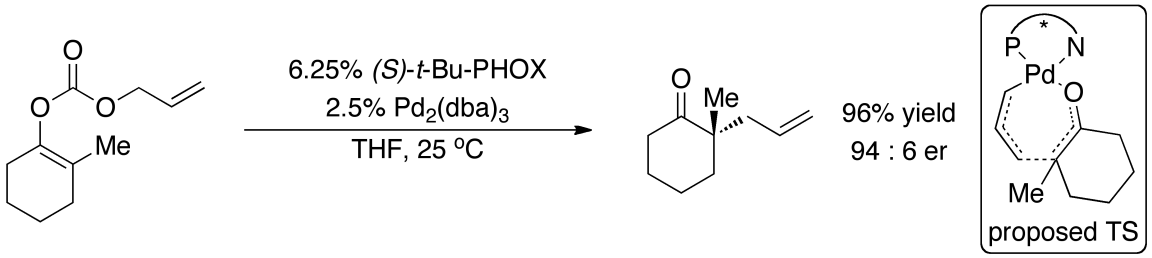
Figure 1.1: Energy Barriers for Various Reductive Eliminations



1.03 36.6 kcal/mol **1.04** 23.4 kcal/mol **1.05**

In an impressive demonstration of the synthetic value of the 3,3′ reductive elimination pathway, Professor Stoltz *et al.* describe an enantioselective Tsuji allylation that forms all-carbon quaternary centers from alpha substituted allylenol carbonates.[16] Their DFT calculations suggest 1,1′ reductive elimination to be about 41 kcal/mol less favorable in THF than the analogous 3,3′ elimination pathway. The authors are able to take advantage of this reaction construct to access α-keto all-carbon quaternary centers in up to 94 : 6 er (Scheme 1.13).

Scheme 1.13: Stoltz's Tsuji Allylation *via* 3,3′ Reductive Elimination



[16] 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.

Over the last several years the Morken group has taken advantage of an interesting variant of 3,3′ reductive elimination in the 1,4-conjugate allylation of dialkylidene ketones[17] and the 1,2-allylboration of dienals (Scheme 1.14).[18] Dialkylidene ketone **1.06** was treated with allylB(pin) and Ni(0), employing a TADDOL-derived phosphonite ligand to afford 1,4-allylated ketone **1.08** in high yield and enantioselectivity. DFT studies suggest that this reaction proceeds through a 3,3′ reductive elimination such as transition structure **1.07** (eq. 5). The reaction of dienal **1.09** proceeds through a similar reactivity mode to afford secondary alcohol **1.10** in high enantioselectivity and yield (eq. 6). These novel coupling reactions evolved into the general allyl-allyl cross-coupling method that is currently under development in our group's laboratories (*vide infra*).

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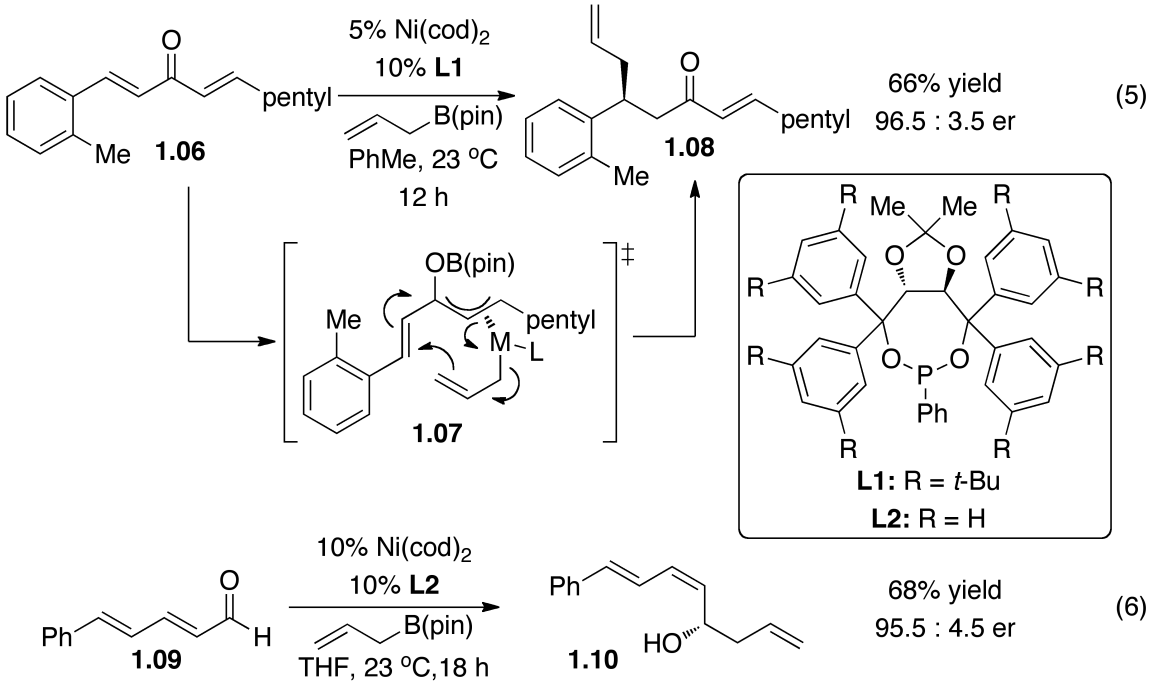
[17] (a) Sieber, J. D.; Liu, S.; Morken, J. P. *J. Am. Chem. Soc.* **2007**, *129*, 2214. (b) Sieber, J. D.; Morken, J. P. *J. Am. Chem. Soc.* **2008**, *130*, 4978. (c) Brozek, L. A.; Sieber, J. D.; Morken, J. P. *Org. Lett.* **2011**, *13*, 995.

[18] Zhang, P.; Morken, J. P. *J. Am. Chem. Soc.* **2009**, *131*, 12550.

Scheme 1.14: 1,4- and 1,2-Allylboration *via* 3,3′ Reductive Elimination



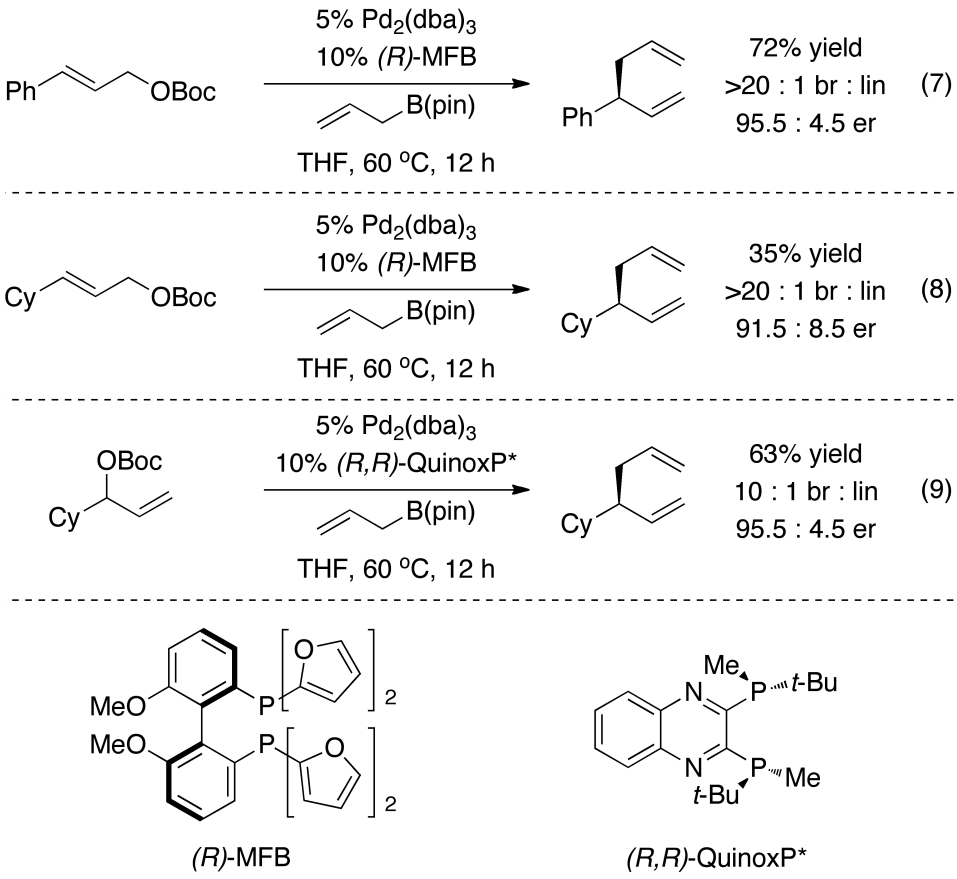
D. Branched and Enantioselective Inner-Sphere Allyl-Allyl Cross-Coupling

In 2010, the Morken group presented an approach for regiocontrol in allyl-allyl cross-coupling reactions. Using simple allylic carbonates and allylboron derivatives as the nucleophile, a Pd-catalyst system was devised to provide 1,5-dienes with a high preference for branched products in high levels of enantioselectivity.[4] Having gleaned insight from the group's experience with 3,3′ reductive elimination and the Echavarren DFT study,[19] it was postulated that a bidentate phosphine ligand with a small bite angle would have direct control over 3,3′ vs 1,1′ reductive elimination. Gratifyingly, it was found that *(R)*-MeO-furyl-

[19] see section **II.C** and references therein

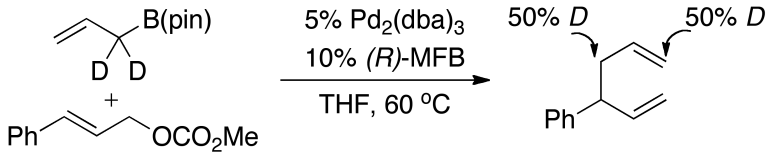
BIPHEP [*(R)*-MFB] had a profound effect on regioselectivity for the coupling of aryl substrates with allylB(pin) (Scheme 1.15, eq. 7). In the case of alkyl allylic carbonates, *(R,R)*-QuinoxP* was shown to give increased enantioselectivity versus *(R)*-MFB, though the corresponding branched allylic carbonate had to be employed to ameliorate the problem of low conversion (Scheme 1.15, eq. 8-9). In all, Morken and co-workers were able to demonstrate this operationally simple, branch-selective allyl-allyl cross-coupling on 14 substrates, with yields up to 91%, er's up to 97 : 3, and branched : linear ratios that were generally >20 : 1.

Scheme 1.15: Morken Group's Branch-Selective Allyl-Allyl Cross-Coupling



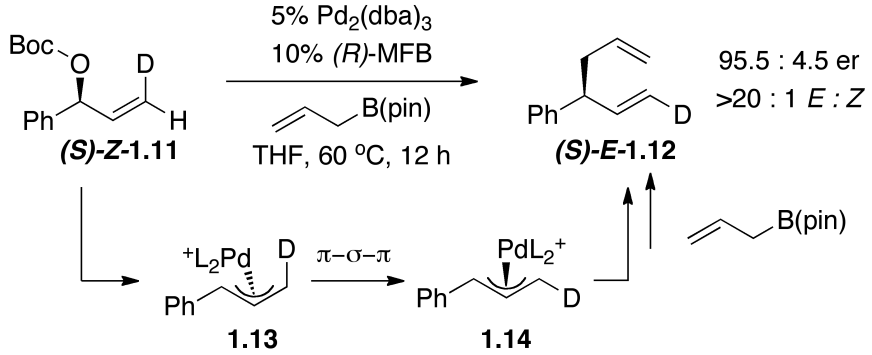
Additionally, Morken *et al.* described two key isotopic labeling experiments that lend support to an inner-sphere coupling mechanism. First, when deuterium labeled allylB(pin) was employed in the cross-coupling, complete scrambling of the deuterium atoms was observed. As a typical outer-sphere nucleophilic attack mechanism would likely proceed with inversion of the label, it seems plausible that allylB(pin) transmetallates with Pd, where the metal can scramble the label through π-σ-π isomerization of the allyl group (Scheme 1.16).

Scheme 1.16: Deuterium Labeling Support for AllylB(pin) Transmetallation



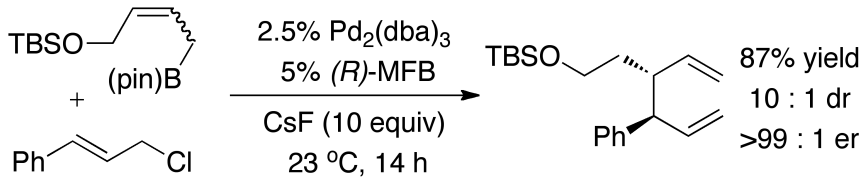
A second labeling study also implicates an inner-sphere reductive elimination pathway (Scheme 1.17). Enantioenriched ***(S)-Z*-1.11** was synthesized and reacted under the standard conditions, affording exclusively ***(S)-E*-1.12**. This result is consistent with an *anti* displacement of the carbonate (**1.13**), followed by π-σ-π isomerization to provide **1.14**, which then undergoes transmetallation and reductive elimination to afford the observed product. Diene **1.12** is only available through this pathway, thus supporting an inner-sphere reductive elimination. With the marked success of this new method, the Morken group sought to further explore and expand the scope of reactions that undergo an inner sphere 3,3′ reductive elimination.

Scheme 1.17: Deuterium Labeling Study Supporting an Inner-Sphere Path



A follow-up communication from the Morken group extolled the virtues of a cross-coupling between crotyl chloride derivatives and prochiral substituted allylboronic esters.[20] They found that under similar reaction conditions to the initial report, 1,5-dienes bearing adjacent stereocenters could be readily synthesized in an enantio- and diastereoselective fashion (Scheme 1.18). These products are of particular note as they represent branched Cope-type products that cannot otherwise be accessed by catalytic enantioselective methods.

Scheme 1.18: Diastereoselective Allyl-Allyl Cross-Coupling



One of the latest developments in 3,3′ reductive elimination is the synthesis of enantioenriched 1,5-enynes by a stereospecific Pd-catalyzed allyl-propargyl cross-coupling.[21] Mechanistically related to allyl-allyl cross-coupling, allyl-propargyl coupling undergoes a 3,3′ elimination from an (η^1-allyl)Pd(allenyl) species such as **1.15** (Scheme 1.19). Beginning with enantioenriched propargyl acetate **1.16**, a Pd-catalyzed cross-coupling with allylB(pin) occurs to deliver the 1,5-enyne (**1.17**) in >99 : 1 *cee*. While further reaction development is ongoing in

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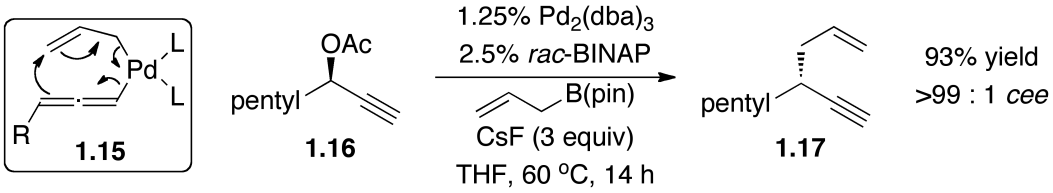
[20] Brozek, L. A.; Ardolino, M. J.; Morken, J. P. *J. Am. Chem. Soc.* **2011**, *133*, 16778.

[21] Ardolino, M. J.; Morken, J. P. *J. Am. Chem. Soc.* **2012**, *134*, *submitted*.

this field of catalysis, my contributions were first focused on the synthesis of all-carbon quaternary centers *via* allyl-allyl cross-coupling. Such a method, if successful, would add to a short list of all-carbon quaternary center-forming allylic substitution reactions.

Scheme 1.19: Allyl-Propargyl Coupling to Generate 1,5-Enynes



E. The Synthesis of All-Carbon Quaternary Centers *via* Allylic Substitution

Due to a confluence of steric factors, the catalytic enantioselective synthesis of all-carbon quaternary centers remains a significant challenge to synthetic chemists.[22] Several useful methods have been developed for generating quaternary centers, including Heck reactions,[23] enolate α-

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[22] (a) Das, J. P.; Marek, I. *Chem. Commun.* **2011**, *47*, 4593. (b) Cozzi, P. G.; Hilgraf, R.; Zimmermann, N. *Eur. J. Org. Chem.* **2007**, 5969. (c) Trost, B. M.; Jiang, C. *Synthesis* **2006**, 369. (d) Christoffers, J.; Baro, A. *Adv. Synth. Catal.* **2005**, *447*, 1473. (e) Douglas, C. J.; Overman, L. E. *Proc. Natl. Acad. Sci. U.S.A.* **2004**, *101*, 5363. (f) Corey, E. J.; Guzman-Perez, A. *Angew. Chem., Int. Ed.* **1998**, *37*, 388.

[23] (a) Overman, L. E. *Pure Appl. Chem.* **1994**, *66*, 1423. (b) Shibasaki, M.; Borden, C.; Kojima, A. *Tetrahedron* **1997**, *53*, 7371. (c) Shibasaki, M.; Erasmus, M. V.; Ohshima, T. *Adv. Synth. Catal.* **2004**, *346*, 1533.

arylations,[24] and enolate α-allylations.[25] Additionally, both conjugate addition[26] and allylic substitution[27] have provided significant means for accessing all-carbon quaternary stereogenic centers.

Copper-catalyzed allylic substitution has provided several key methods for the formation of quaternary centers from linear allylic phosphonates. While these methods are of significant value to the synthetic community, one key drawback is the need to synthesize isomerically pure allylic phosphonate substrates, as this has a direct impact on the configuration and optical purity of the isolated products.

In some of their early work on the subject, Professor Hoveyda and co-workers developed a peptide ligand for copper-catalyzed addition of alkyl zinc

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[24] Review: (a) Bellina, F.; Rossi, R. *Chem. Rev.* **2010**, *110*, 1082. Selected References: (b) Liao, X.; Weng, Z.; Hartwig, J. F. *J. Am. Chem. Soc.* **2008**, *130*, 195. (c) Chen, G.; Kwong, F. Y.; Chan, H. O.; Yu, W.; Chan, A. S. C. *Chem. Commun.* **2006**, 1413. (d) Hamada, T.; Chieffi, A.; Åhman, J.; Buchwald, S. L. *J. Am. Chem. Soc.* **2002**, *124*, 1261. (e) Spielvogel, D. J.; Buchwald, S. L. *J. Am. Chem. Soc.* **2002**, *124*, 3500. (f) Lee, S.; Hartwig, J. F. *J. Org. Chem.* **2001**, *66*, 3402. (g) Åhman, J.; Wolfe, J. P.; Troutman, M. V.; Palucki, M.; Buchwald, S. L. *J. Am. Chem. Soc.* **1998**, *120*, 1918.

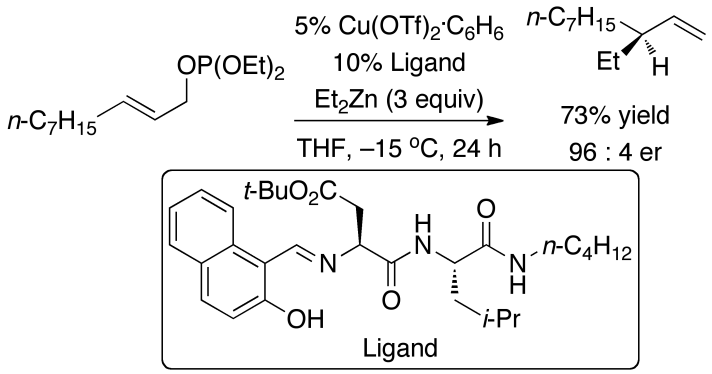
[25] Reviews: (a) Mohr, J. T.; Stoltz, B. M. *Chem.–Asian J.* **2007**, *2*, 1476. (b) Braun, M.; Meier, T. *Angew. Chem., Int. Ed.* **2006**, *45*, 6952. Selected References: (c) Mohr, J. T.; Behenna, D. C.; Harned, A. M.; Stoltz, B. M. *Angew. Chem., Int. Ed.* **2005**, *44*, 6924. (d) Trost, B. M.; Schroeder, G. M. *Chem.–Eur. J.* **2005**, *11*, 174. (e) Trost, B. M.; Xu, J. *J. Am. Chem. Soc.* **2005**, *127*, 2846. (f) Behenna, D. C.; Stoltz, B. M. *J. Am. Chem. Soc.* **2004**, *126*, 15044.; (g) You, S.; Hou, X.; Dai, L.; Zhu, X. *Org. Lett.* **2001**, *3*, 149. (h) Trost, B. M.; Schroeder, G. M. *J. Am. Chem. Soc.* **1999**, *121*, 6759.

[26] (a) Alexakis, A.; Bäckvall, J.-E.; Krause, N.; Pàmies, O.; Diéguez, M. *Chem. Rev.* **2008**, *108*, 2796. (b) Harutyunyan, S. R.; Hartog, T.; Geurts, K.; Minnaard, A. J.; Feringa, B. L. *Chem. Rev.* **2008**, *108*, 2824. (c) Gutanov, A. *Eur. J. Org. Chem.* **2008**, 4547. (d) Hawner, C.; Alexakis, A. *Chem. Commun.* **2010**, *46*, 7295.

[27] (a) Hoveyda, A. H.; Hird, A. W.; Kacprzynski, M. A.; *Chem. Commun.* **2004**, 1779. (b) Helmchen, G.; Ernst, M.; Paradies, G. *Pure Appl. Chem.* **2004**, *76*, 495. (c) Hartwig, J. F.; Stanley, L. M. *Acc. Chem. Res.* **2010**, *43*, 1461. (d) Bruneau, C.; Renaud, J. L.; Demerseman, B. *Pure Appl. Chem.* **2008**, *80*, 861. (e) Lu, Z.; Ma, S. *Angew. Chem., Int. Ed.* **2008**, *47*, 258.

reagents to trisubstituted allylic phosphonates (Scheme 1.20).[28] This tunable ligand scaffold proved amenable to providing high levels of enantioselection for a variety of alkyl and aryl allylic phosphonates. The scope of this methodology was somewhat limited by the availability of dialkyl zinc reagents.

Scheme 1.20: Cu-Catalyzed Allylic Substitution with a Peptide Ligand



From this work spawned an impressive series of communications spanning seven years in which Hoveyda *et al.* describe the addition of a variety of zinc or aluminum reagents to allylic phosphonates. While these methods continue to operate under the purview of Cu-catalysis, the peptide ligand was exchanged for NHC·Ag complexes. With this new generation of catalyst, Hoveyda and co-workers were able to successfully demonstrate the addition of

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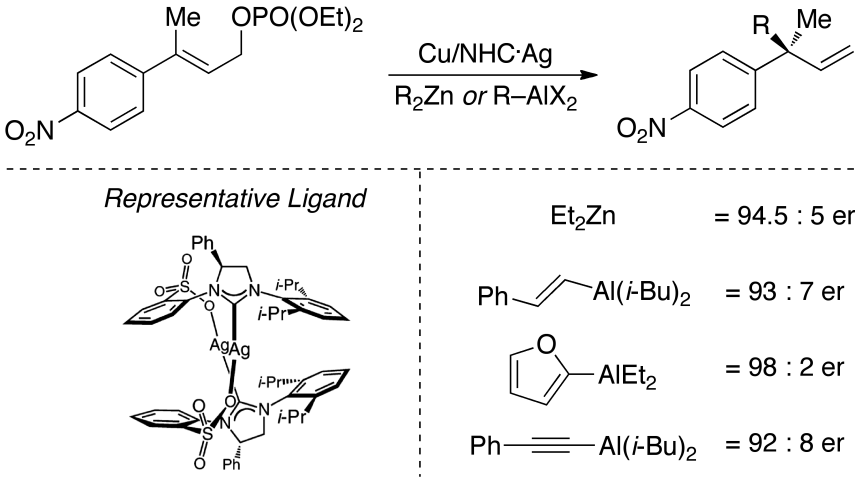
[28] (a) Luchaco-Cullis, C. A.; Mizutani, H.; Murphy, K. E.; Hoveyda, A. H. *Angew. Chem., Int. Ed.* **2001**, *40*, 1456. (b) Kacprzynski, M. A.; Hoveyda, A. H. *J. Am. Chem. Soc.* **2004**, *126*, 10676.

alkyl-,[29] vinyl-,[30] aryl-,[31] and alkynyl[32] metal reagents in high enantiomeric excesses and good yields (Scheme 1.21).

Scheme 1.21: Cu/NHC·Ag Cat. Allylic Substitution With Zn/Al Reagents



Most recently, Hoveyda and Jung have reported the synthesis of all-carbon quaternary stereogenic centers through the addition of allenylboronic acid pinacol ester [allenylB(pin)] to tertiary allylic phosphonates.[33] This methodology continues the successful trend of copper-catalyzed allylic substitution, this time employing a more simple chiral NHC-sulfoxide ligand. Scheme 1.22 shows a

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[29] Larsen, A. O.; Leu, W.; Oberhuber, C. N.; Campbell, J. E.; Hoveyda, A. H. *J. Am. Chem. Soc.* **2004**, *126*, 11130.

[30] Gao, F.; McGrath, K. P.; Lee, Y.; Hoveyda, A. H. *J. Am. Chem. Soc.* **2010**, *132*, 14315.

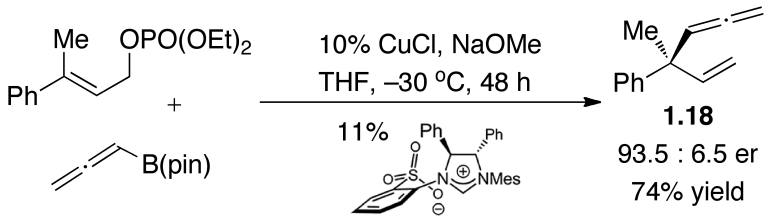
[31] Gao, F.; Lee, Y.; Mandai, K.; Hoveyda, A. H. *Angew. Chem., Int. Ed.* **2010**, *49*, 8370.

[32] Dabrowski, J. A.; Gao, F.; Hoveyda, A. H. *J. Am. Chem. Soc.* **2011**, *133*, 4778.

[33] Jung, B.; Hoveyda, A. H. *J. Am. Chem. Soc.* **2012**, *134*, 1490.

representative example of this chemistry, with allenyl all-carbon quaternary stereogenic center-bearing **1.18** being formed in 93.5 : 6.5 er and 74% yield.

Scheme 1.22: Cu-Catalyzed AllenylB(pin) Allylic Substitution



As demonstrated, Cu-catalyzed allylic substitution to generate quaternary stereogenic centers requires isomerically pure starting materials. This is also the case for several other transition metals including Ru, W, and Ir.[34] Quite contrarily, Pd and Mo participate in rapid π-σ-π isomeriztion, and thus for terminal allylic substrates, isomerically pure configurations are not a requirement *and* branched

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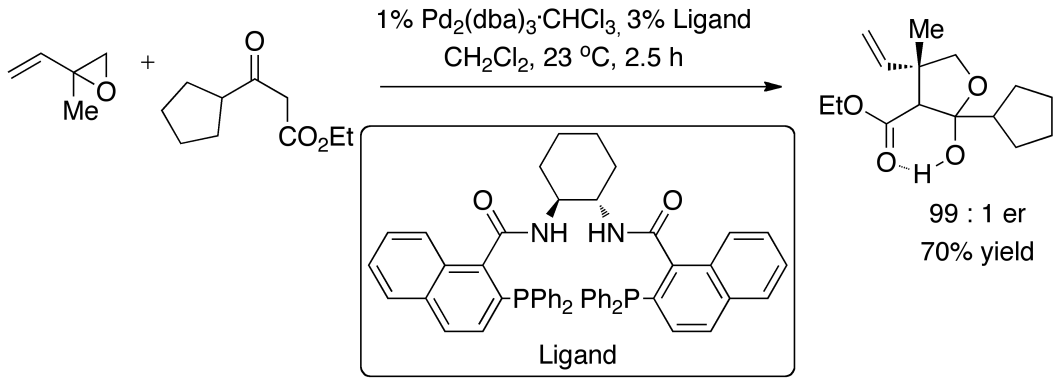
[34] Ir: (a) Takeuchi, R.; Shinga, N. *Org. Lett.* **1999**, *1*, 265. (b) Ohmura, T.; Hartwig, J. F. *J. Am. Chem. Soc.* **2002**, *124*, 15164. (c) Bartels, B.; García-Yebra, C.; Rominger, F.; Helmchen, G. *Eur. J. Inorg. Chem.* **2002**, 2569. (d) Polet, D.; Alexakis, A.; Tissot-Crouset, K.; Corminboeuf, C.; Ditrich, K. *Chem.–Eur. J.* **2006**, *12*, 3596. (e) Stanley, L. M.; Bai, C.; Ueda, M.; Hartwig, J. F. *J. Am. Chem. Soc.* **2010**, *132*, 8918. (f) Takeuchi, R.; Ue, N.; Tanabe, K.; Yamashita, K.; Shiga, N. *J. Am. Chem. Soc.* **2001**, *123*, 9525. Under appropriate conditions, π-σ-π isomerization with Ir can be rapid. See: (g) Bartels, B.; Helmchen, G. *Chem. Commun.* **1999**, 741. Ru: (h) Trost, B. M.; Fraisse, P. L.; Ball, Z. T. *Angew. Chem., Int. Ed. Engl.* **1995**, *34*, 462. (j) Prétôt, R.; Lloyd-Jones, G. C.; Pfaltz, A. *Pure Appl. Chem.* **1998**, *70*, 1035.

products can be favored.[35] With that reactivity profile in mind, several methodologies have been developed which exploit this rapid isomerization.

In 2001, Professor Trost and co-workers cleverly took advantage of palladium's inherent reactivity in a nucleophilic addition to vinylepoxides.[36] Pd(0) and a Trost ligand perform an S_N2' epoxide opening which, after isomerization, undergoes ligand directed nucleophilic attack of the malonate to deliver the observed optically enriched hemiacetal product (Scheme 1.23). While this is indeed an interesting and highly enantioselective exploitation of rapid π-σ-π isomerism, the utility of this reaction is fairly narrow.

Scheme 1.23: Trost Pd-Catalyzed Nucleophilic Vinylepoxide Opening

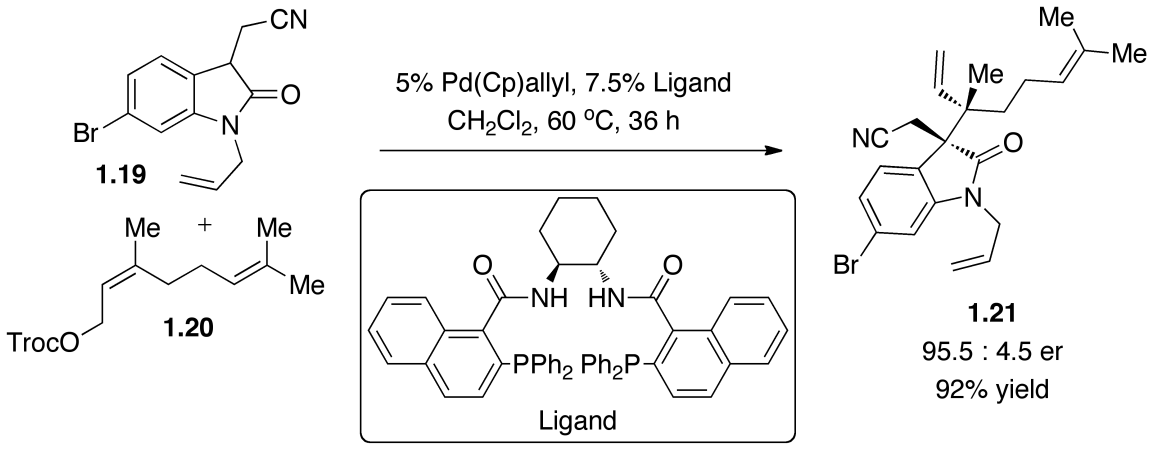


[35] Mo: (a) Trost, B. M.; Hachiya, I. *J. Am. Chem. Soc.* **1998**, *120*, 1104. (b) Malkov, A. V.; Gouriou, L.; Lloyd-Jones, G. C.; Starý, I.; Langer, V.; Spoor, P.; Vinader, V.; Kočovský, P. *Chem.–Eur. J.* **2006**, *12*, 6910. (c) Trost, B. M.; Zhang, Y. *Chem.–Eur. J.* **2010**, *16*, 296. Reviews for Pd: (d) Trost, B. M.; Van Vranken, D. L. *Chem. Rev.* **1996**, *96*, 395. (e) Pregosin, P. S.; Salzmann, R. *Coord. Chem. Rev.* **1996**, *155*, 35.

[36] Trost, B. M.; Jiang, C. *J. Am. Chem. Soc.* **2001**, *123*, 12907.

Most recently, Trost *et al.* disclosed their studies on the Pd-catalyzed prenylation of oxindoles in the context of natural product synthesis. The researchers were able to take advantage of π-σ-π isomerization to generate adjacent quaternary stereogenic centers in high enantioselectivity (Scheme 1.24).[37] This landmark transformation uses similar reaction conditions to the preceeding report, but in this case a nerol derived carbonate (**1.20**) is being coupled to oxindole derivative **1.19**. The resultant coupling delivers **1.21** in a remarkable 95.5 : 4.5 er and 91% yield, representing the first such vicinal quaternary stereogenic center-forming asymmetric allylic alkylation.

Scheme 1.24: Vicinal Quaternary Centers Through Trost Coupling



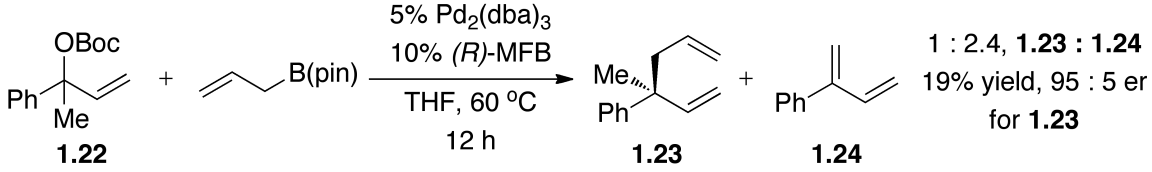
[37] Trost, B. M.; Malhotra, S.; Chan, W. H. *J. Am. Chem. Soc.* **2011**, *133*, 7328.

III. Reaction Development for the Synthesis of All-Carbon Quaternary Stereogenic Centers[38]

A. Initial Results and Optimization of Reaction Conditions

The development of an enantioselective allyl-allyl cross-coupling to generate enantioenriched all-carbon quaternary stereogenic centers was initiated by Dr. Ping Zhang with contributions from both myself and Hai Le. As a lead experiment, tertiary allylic carbonate **1.22** was synthesized and treated with allylB(pin) under the previously optimized conditions for branch-selective allyl-allyl cross-coupling (Scheme 1.25).[4] While 1,5-diene **1.23** was produced in 95 : 5 er and isolated in a 19% yield, the major product of this first experiment was 1,3-diene **1.24**, which was formed in a 2.4 : 1 ratio with desired product **1.23**.

Scheme 1.25: Initial Quaternary Center-Forming Allyl-Allyl Cross-Coupling



While generation of the quaternary stereogenic center was successful from a selectivity viewpoint, it was clear that a dominant side reaction would need to be suppressed for this to be a synthetically viable transformation. We

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

considered our likely reaction mechanism to determine the source of **1.24** (Figure 1.2). The formation of 1,3-dienes from tertiary allylic carbonates is well represented in the literature, having been shown to operate through β-hydride elimination from Pd π-allyl complexes.[39] Thus, after insertion of Pd(0) into **1.22** to form allylic structure **1.25**, isomerization to η^1-allyl **1.26** provides the opportunity for either general base elimination of Pd(II) by *tert*-butoxide or β-hydride elimination to form **1.24**. An additional elimination pathway is available after transmetallation with allyB(pin) from intermediate **1.27**. From this (bis)η^1-allyl intermediate, a metallo-ene hydride abstraction can occur by way of **1.28** to afford **1.24** and propene gas as a side product.[40]

With these plausible pathways in mind, an experiment was devised to test for β-elimination. In the absence of allylB(pin), carbonate **1.22** was subjected to the reaction conditions and the results were compelling. In 12 hours, full conversion of the tertiary carbonate to undersired 1,3-diene **1.24** was observed (Scheme 1.26). Informed by these results, we envisioned that acceleration of transmetallation of allylB(pin) would suppress the β-elimination pathway and increase the yield of desired 1,5-diene **1.23**.

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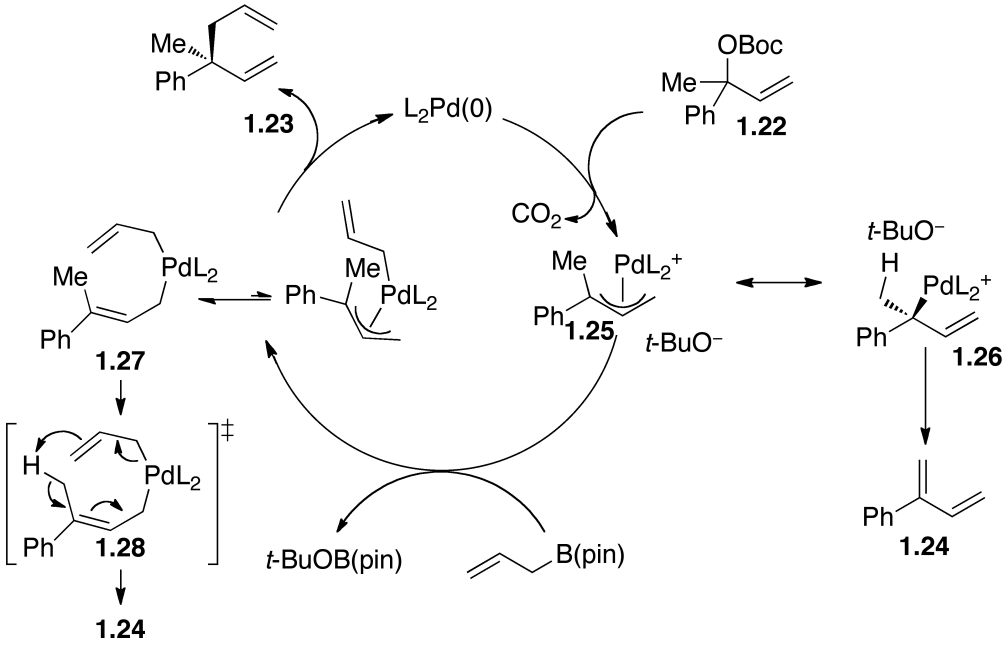
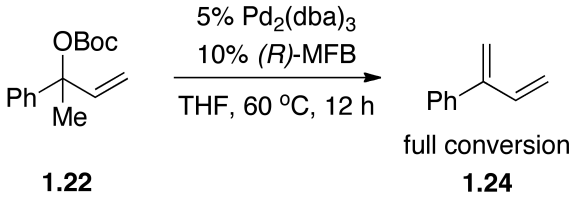
[39] For related examples, see: (a) Tsuji, J.; Yamakawa, T.; Kaito, M.; Mandai, T. *Tetrahedron Lett.* **1978**, *19*, 2075. (b) Trost, B. M.; Verhoeven, T. R.; Fortunak, J. M. *Tetrahedron Lett.* **1979**, *20*, 2301. (c) Takacs, J. M.; Lawson, E. C.; Clement, F. *J. Am. Chem. Soc.* **2007**, *119*, 5956.

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

Figure 1.2: Proposed Catalytic Cycle and Elimination Pathways



Scheme 1.26: Control Experiment in Support of β-Elimination



An initial screening of inorganic base additives was undertaken as they have been previously shown to accelerate transmetallation in Suzuki-Miyaura cross-coupling reactions. Specifically, Cs_2CO_3[41] and CsF[42] were screened in

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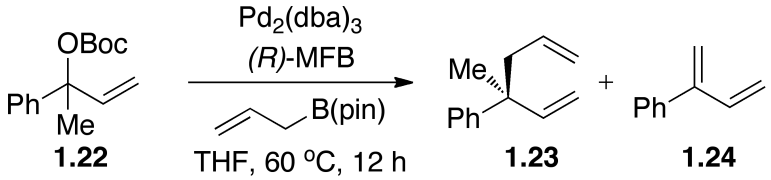
[41] Cs_2CO_3 in Pd-catalyzed cross-couplings: (a) Littke, A. F.; Fu, G. C. *Angew. Chem., Int. Ed.* **1998**, *37*, 3387. (b) Haddach, M.; McCarthy, J. R. *Tetrahedron Lett.* **1999**, *40*, 3109. (c) Johnson, C. R.; Braun, M. P. *J. Am. Chem. Soc.* **1993**, *115*, 11014. (d) Molander, G. A.; Ito, T. *Org. Lett.* **2001**, *3*, 393.

[42] Wright, S. W.; Hageman, D. L.; McClure, L. D. *J. Org. Chem.* **1994**, *59*, 6095.

various amounts, and in the case of CsF, the results were particularly promising. There is a clear trend between equivalents of CsF and the ratio of **1.23** : **1.24** (Table 1.1). Importantly, when 10 equivalents of CsF were employed, a 20 : 1 ratio of products was observed with a 95 : 5 enantiomer ratio (entry 5).

Table 1.1: Initial Optimization with Base Additives



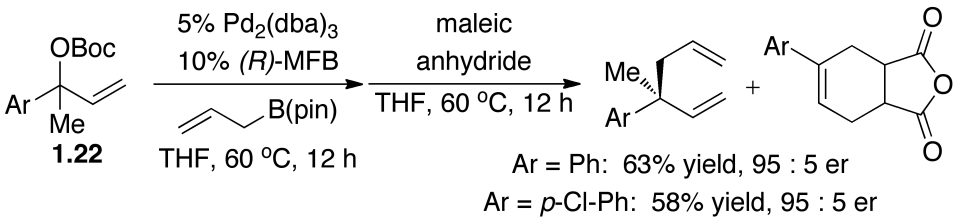
entry	conditions	**1.23** : **1.24**	er	yield (%)[a]
1	10% catalyst	1 : 1	96 : 4	38
2	10% cat./1.2 equiv Cs_2CO_3	2 : 1	96 : 4	90
3	5% cat./1.2 equiv CsF	5 : 1	96 : 4	79
4	4% cat./3 equiv CsF	9 : 1	95 : 5	82
5	4% cat./10 equiv CsF	20 : 1	95 : 5	77

[a] isolated yields of chromatographically inseparable mixture of products

While entry 5 represents a synthetically viable transformation, separation of the all-hydrocarbon product mixture chromatographically was an intractable problem. One solution to this obstacle was to add a dieneophile to the reaction mixture after 12 hours, resulting in a Diels-Alder reaction between **1.24** and the dieneophile. Provided the additive was a polar compound, the resulting adduct

would have appreciably different chromatographic properties than **1.23** and allow for facile separation of the by-product from the desired 1,5-diene. Maleic anhydride was selected as an ideal candidate for the Diels-Alder reaction and was employed as shown in Scheme 1.27. After allowing the crude reaction mixture to stir with maleic anhydride for two hours at 60 °C, the Diels-Alder adduct and 1,5-diene were readily separated by silica gel chromatography, affording the product in both good yield and er when the aryl group is either phenyl or 4-Cl-phenyl.

Scheme 1.27: Byproduct Removal by Diels-Alder Cycloaddition



Although sequestering the 1,3-diene byproduct was a viable solution, it does not solve the problem of 1,3-diene formation. Therefore it was of interest to devise a method that suppressed 1,3-diene formation to the point of being undetectable. A survey of the literature provided inspiration for screening water as an additive as it has been shown to accelerate transmetallation in Suzuki-Miyaura cross-couplings and may act analogously in our methodology . Recent computational and experimental evidence suggests that this acceleration comes

by way of a Pd(II)–OH type intermediate (**1.28**, Table 1.2). It is shown that the metal-bound oxygen can coordinate boron, facilitating transmetallation in an intramolecular fashion.[43] Thus, water was employed in varying ratios as a co-solvent with THF. When a 10 : 1 THF : water ratio in conjunction with 3 equivalents of CsF was employed, it led to a 50 : 1 ratio of **1.23** : **1.24**, suppressing 1,3-diene formation below levels detectable by ^{1}H NMR (Table 1.2, entry 5). It is clear from Table 1.2 that water and CsF work in tandem to provide the optimal reaction conditions (compare entries 1 and 5), though in what way is not clear at this time. It is possible that an intermediate structure such as **1.29** or **1.29a** is operative, forming a six-centered transition structure, the likes of which are ubiquitous in synthetic chemistry.

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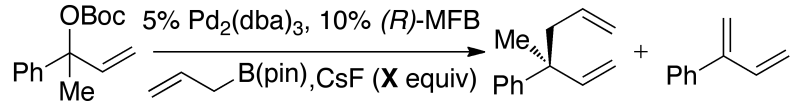
[43] (a) Amatore, C.; Jutand, A.; Le Duc, G. *Chem.–Eur. J.* **2011**, *17*, 2492. (b) Carrow, B. P.; Hartwig, J. F. *J. Am. Chem. Soc.* **2011**, *133*, 2116. (c) Suzaki, Y.; Osakada, K. *Organometallics* **2006**, *25*, 3251.

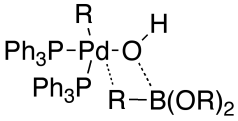
Table 1.2: Use of H_2O as a Co-Solvent in Allyl-Allyl Cross-Coupling



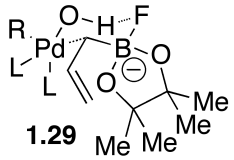
1.22 **1.23** **1.24**

entr	THF : H_2O	**X**	**1.23** : **1.24**	er	yield (%)[a]
y	10 : 1	none	20 : 1	96 : 4	90
1	10 : 1	1.2	25 : 1	96 : 4	86
2	20 : 1	1.2	20 : 1	96 : 4	84
3	5 : 1	1.2	33 : 1	96 : 4	84
4	10 : 1	3	50 : 1	96 : 4	90
5					

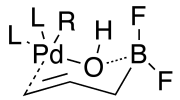
[a] isolated yields of chromatographically inseparable mixture of products



1.28



1.29



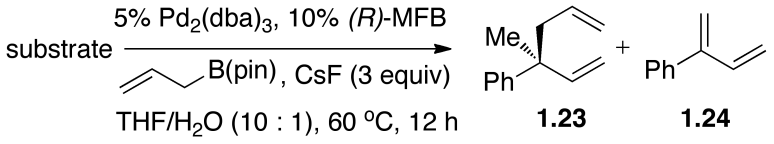
1.29a

B: Substrate Scope Development and Electrophile Geometry

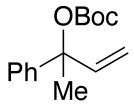
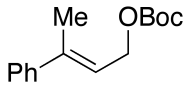
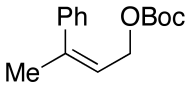
It was of interest to study the effect of substrate conformation on the reaction, as we observed partial isomerization to the linear isomer upon silica gel purification of several of our branched substrates. Thus, as shown in Table 1.3, both *E* and *Z* linear isomers of **1.33** and the branched allylic carbonate (**1.22**) gave the same high level of enantioselection. This stereoconvergent nature is one of the key factors that set Pd-catalyzed allyl-allyl cross-coupling apart from the work done in Cu-catalyzed allylic substitution.[44]

[44] see section **II.E** and references therein

Table 1.3: Electrophile Isomers and Their Cross-Couplings



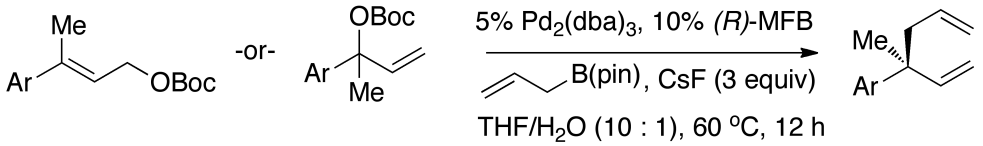
1.23 **1.24**

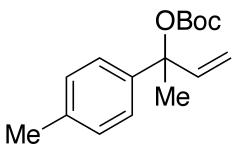
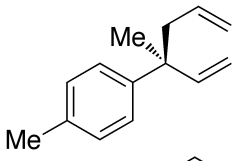
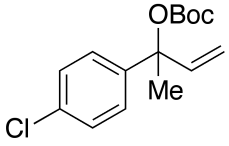
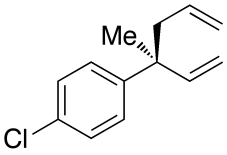
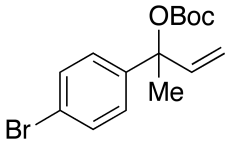
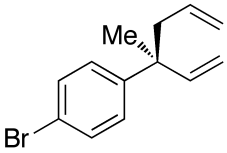
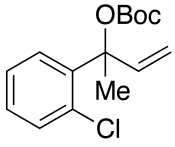
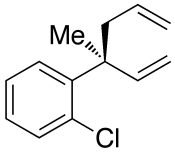
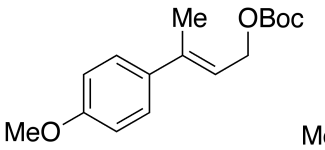
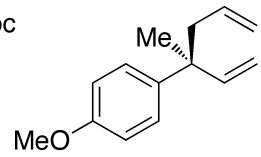
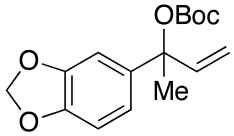
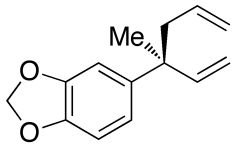
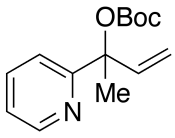
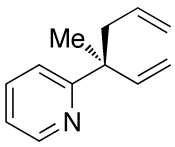
entry	substrate	**1.23** : **1.24**	er	yield (%)
1	 **1.22**	>20 : 1	96 : 4	90
2	 ***(E)*-1.33**	>20 : 1	96 : 4	86
3	 ***(Z)*-1.33**	11 : 1	96 : 4	80

Having established optimal conditions for the allyl-allyl cross-coupling, we first surveyed a series of aryl-methyl substrates in the reaction (Table 1.4). We found a reasonable substrate tolerance for the transformation. In addition to a *para*-tolyl substituted allylic carbonate, *para*-halogenation was also tolerated in both excellent enantioselectivity and yield (entries 1-3). Notably, insertion into the aryl-halide bond by Pd(0) was not competitive. Additionally, *ortho*-chloro substitution was well tolerated, albeit under somewhat forcing reaction conditions (entry 4). This product in particular appears well aligned for further synthetic manipulation. Electron-rich aromatic substrates (entries 5-6) gave highly enantioenriched products in good yield. Entry six is an illustrative example of using a mixture of branched and linear carbonates in the reaction, which cleanly converge to a single product. Finally, 2-pyridyl-containing entry 7 offers an

example of a heteroaromatic substrate successfully participating in this reaction. Interestingly, this substrate requires no water to minimize β-elimination. It is possible that the pyridyl nitrogen aides transmetallation by Lewis base activation of boron.

Table 1.4: Aryl-Methyl Substrates in Allyl-Allyl Cross-Coupling

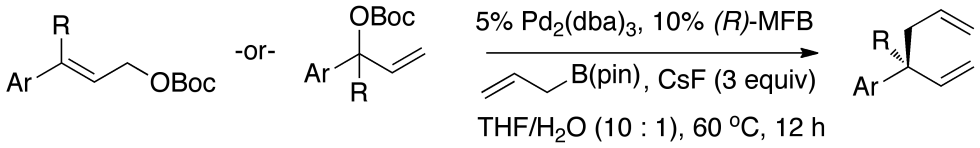


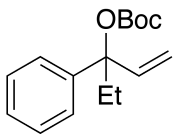
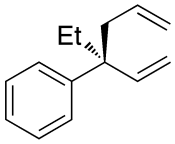
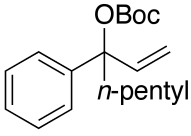
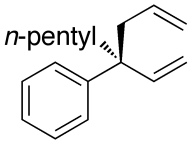
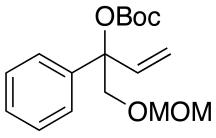
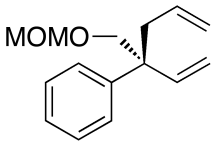
entry	substrate	product	1,5- : 1,3-diene	er	yield (%)[a]
1			17 : 1	96 : 4	76
2[b]			>20 : 1	95 : 5	70
3			20 : 1	95 : 5	90
4[c]			4 : 1	92 : 8	96
5[d]			12 : 1	94 : 6	83
6[b,d]			6 : 1	96 : 4	94
7[e]			>20 : 1	95 : 5	81

[a] Isolated yield of purified product mixture of 1,5- and 1,3-diene.
[b] Mixture of branched and linear substrate used.
[c] Reaction conditions: 10 equiv CsF, 3 equiv allylB(pin), 5 : 1 THF : H_2O.
[d] Reaction run at 80 °C. [e] Reaction run in THF with *no* H_2O.

In addition to aryl-methyl substrates, aryl-*n*-alkyl allylic carbonates are also good candidates for this coupling reaction (Table 1.5). Ethyl and *n*-pentyl substituents give high levels of enantioselection, though with increased levels of 1,3-diene formation (entries 1 and 2). Heteroatom substitution is also tolerated in the reaction as demonstrated by a MOM ether (entry 3). While this substrate suffers little from β-elimination, the product is delivered with a somewhat diminished level of enantioselectivity. In alignment with the 2-pyridyl substrate (Table 1.4, entry 7), entry 3 also does not require a mixed solvent system with water to suppress 1,3-diene formation.

Table 1.5: Aryl-*n*-Alkyl Substrates in Allyl-Allyl Cross-Coupling

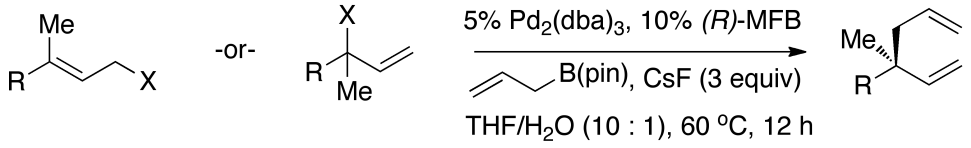


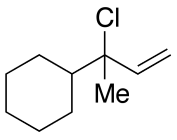
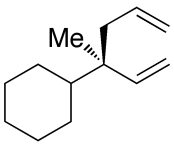
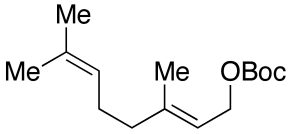
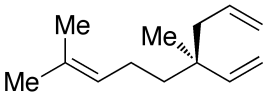
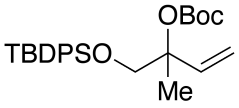
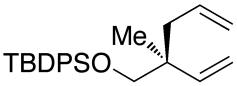
entry	substrate	product	1,5- : 1,3-diene	er	yield (%)[a]
1[b]			6 : 1	94 : 6	97
2[b]			6 : 1	95 : 5	58
3[c]			>20 : 1	90 : 10	78

[a] Isolated yield of purified product mixture of 1,5- and 1,3-diene.
[b] Reaction run at 80 °C. [c] Reaction run in THF with *no* H_2O.

With the success of aryl-alkyl substrates, it was of interest to explore the possibility of utilizing (bis)alkyl substrates in allyl-allyl cross coupling. These substrates offer a significant challenge in that there is greater opportunity for 1,3-diene formation due to the increased abundance of hydrogens β to Pd. It was found that a cyclohexyl-methyl bearing allylic chloride (Table 1.6, entry 1) gave high enantioselectivity, with a reasonable 8 : 1 ratio of product to 1,3-diene. Notably, however, if the steric bias between the two substituents is diminished, as in the case of entries 2 and 3, enantioselectivity suffers greatly.

Table 1.6: (Bis)Alkyl Substrates in Allyl-Allyl Cross-Coupling



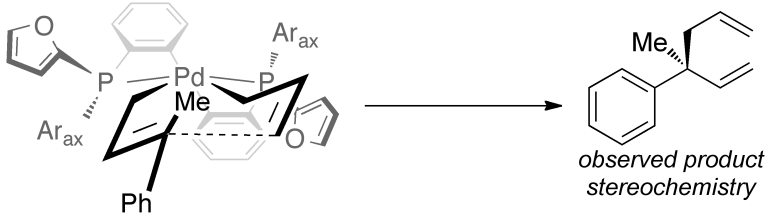
entry	substrate	product	1,5- : 1,3-diene	er	yield (%)[a]
1[b,c,d]			8 : 1	97 : 3	48
2[e]			4 : 1	76 : 24	96
3[c]			>10 : 1	67 : 33	>90[f]

[a] Isolated yield of purified product mixture of 1,5- and 1,3-diene. [b] Run for 36 h.
[c] Reaction run in THF with *no* H_2O. [d] mixture of branched and linear isomers used.
[e] Conditions: 3 equiv allylB(pin), 10 equiv CsF, 5 : 1 THF : H_2O.
[f] Yield not repeated, unpublished data.

C. Model for Observed Stereochemistry

A crystal structure of $PdCl_2$ complexed with *(R)*-MFB obtained by our group[20] allowed a model for the observed stereochemical outcome to be developed (Figure 1.3). With two η^1-bound allyl ligands on Pd (**1.34**), minimization of A[1,3] interactions between either phenyl or methyl and Pd will favor the indicated structure in the transition state. While phenyl and methyl have similar *A*-values (2.8 and 1.74 kcal/mol, respectively), the phenyl group's rotational isomerism effectively shields C–C bond formation at the 3 and 3′ carbons when phenyl is inside of the transition state structure. Thus, when bond formation occurs with methyl preferentially directed towards the metal center, **1.22** will be formed. This model is consistent with the observation that when there is little steric bias between the two substituents on the electrophile (see Table 1.6, entry 2), enantioselectivity suffers and explains why substrate olefin geometry does not effect the reaction outcome.

Figure 1.3: Proposed Stereochemical Model



1.34 **1.22**

D. Product Manipulations and Application to Synthesis

Having developed an effective technology for generating quaternary stereogenic centers, we sought to demonstrate the utility of the vicinal olefins in synthesis. To that end, we have initiated studies aimed at the total synthesis of alkaloid natural product (+)-buphanisine (Scheme 1.28). While (+)-buphanisine is known to inhibit ascorbic acid biosynthesis,[45] and several racemic syntheses exist in the literature,[46] no enantioselective total synthesis has been reported. It was envisioned that the target structure would be available from cyclohexenone derivative **A** by way of a key diastereoselective aza-Michael addition, which has been demonstrated on a related structure.[47] Intermediate **A** could be generated from the ozonlysis and subsequent aldol condensation of cyclopentenone **B**. Structure **B** is the direct product of a cationic Pd-catalyzed cyclization of 1,5-diene **C**, which is the expected product of our allyl-allyl cross-coupling methodology. Bicyclic precursor **D** should be readily available from inexpensive starting reagents.

To test the feasibility of the transformation of **C** to **A**, 1,5-diene **1.23** was subjected to the cyclization conditions developed by Professor Ross

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[45] Evidente, A.; Cicala, M. R.; Randazzo, G.; Riccio, R.; Calabrese, G.; Liso, R.; Arrigoni, O. *Phytochemistry* **1983**, *22*, 2193.

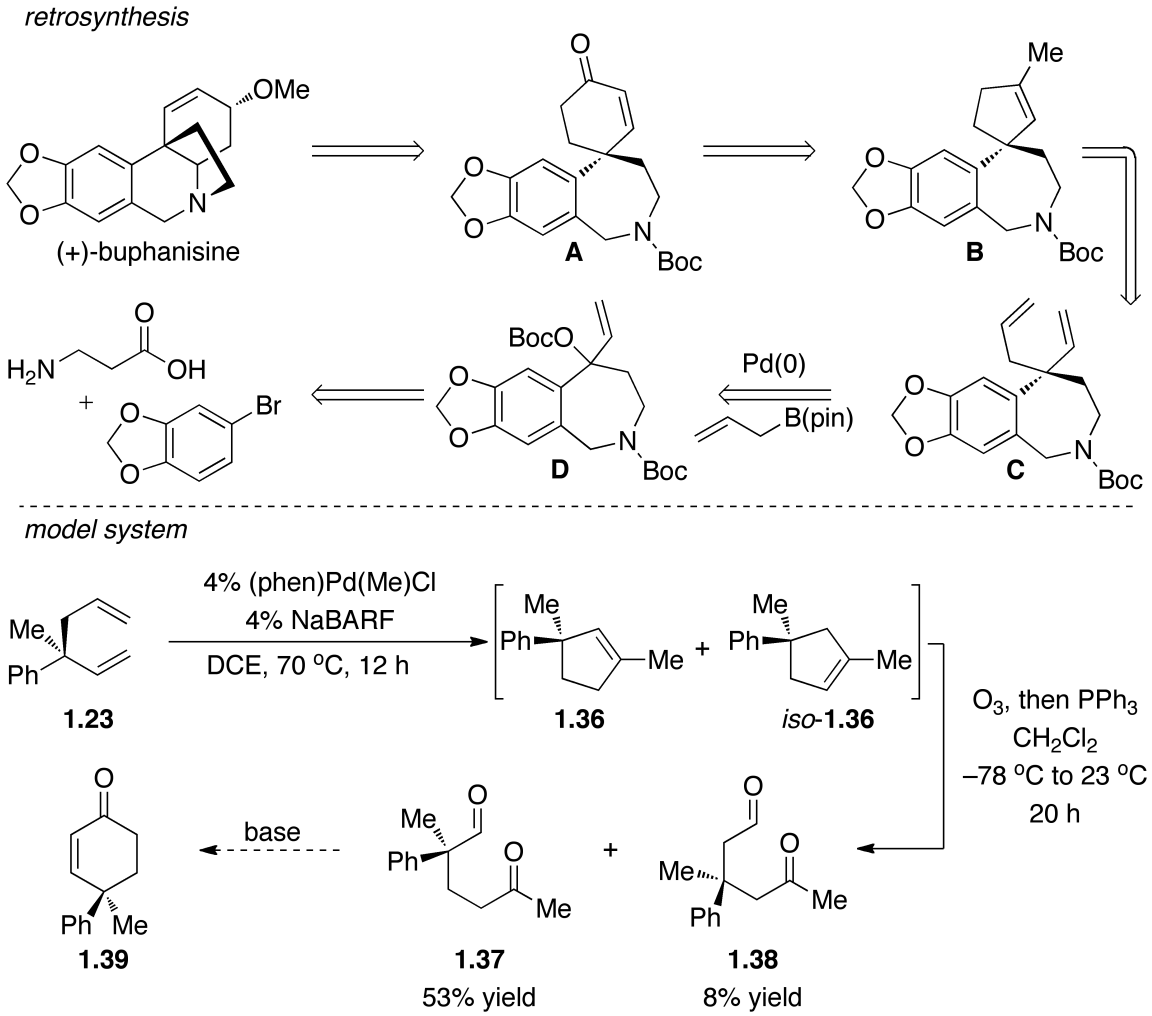
[46] (a) Martin, S. F.; Campbell, C. L. *Tetrahedron Lett.* **1987**, *28*, 503. (b) Martin, S. F.; Campbell, C. L. *J. Org. Chem.* **1988**, *53*, 3184.

[47] Sánchez, I. H.; López, F. J.; Soria, J. J.; Larraza, M. I.; Flores, H. J. *J. Am. Chem. Soc.* **1983**, *105*, 7640.

Widenhoefer and co-workers as a general strategy for cyclizing vicinal olefins.[48] A mixture of cyclized products **1.36** and *iso*-**1.36** was observed by ^{1}H NMR analysis, which was directly ozonized followed by treatment with PPh_3 to reveal a 10 : 1 mixture of ketoaldehydes **1.37** and **1.38** in a 6.25 : 1 isomer ratio, which also represents the ratio of cyclized products **1.36** and *iso*-**1.36**. An aldol condensation of **1.37** would provide **1.39**, which maps onto the cyclohexenone core of advanced retrosynthetic intermediate **A**. Intermediate **1.36** may be favored over *iso*-**1.36** due to the inability of the *in situ* generated Pd–H to reinsert into the endocyclic olefin when it is situated adjacent to the quaternary center. Driven by the success of this model system, studies toward the total synthesis of (+)-buphanisine are ongoing in our laboratories.

[48] Kisanga, P.; Goj, L. A.; Widenhoefer, R. A. *J. Org. Chem.* **2001**, *66*, 635.

Scheme: 1.28: Synthetic Studies Towards (+)-Buphanisine



Additionally, it was important to investigate the chemoselective functionalization of the 1,5-dienes. In particular, we sought to exploit the potential steric bias between the cross-coupling product olefins. It was postulated that reactions involving large organometallic species would benefit most from the subtle steric influences within these coupling products. We were pleased to find that several useful reactions demonstrated complete selectivity

between the vicinal olefins (Scheme 1.29). We first investigated cross metathesis with allyl methylcarbonate. While the reaction catalyzed with HG-II did provide up to 22% yield of the desired product, the primary species isolated was the allyl carbonate dimer. Further investigations revealed that cross-metathesis with ethyl acrylate utilizing HG-II gave an 81% yield of α,β-unsaturated ester **1.40** (eq. 10).[49] Similarly, a Heck coupling under Jeffery conditions afforded *trans* styrenyl derivative **1.41** in 69% yield (eq. 11).[50] Finally, using chemistry developed by our group, we demonstrated Pt-catalyzed alkene diboration utilizing a TADDOL phosphonite ligand which gave, after oxidation, 56% yield of expected diol **1.42** in 9 : 1 dr (eq. 12).[51] Notably, in the absence of a chiral ligand, the derived diol was isolated in a 1 : 1 dr with diminished chemoselectivity between the olefins.

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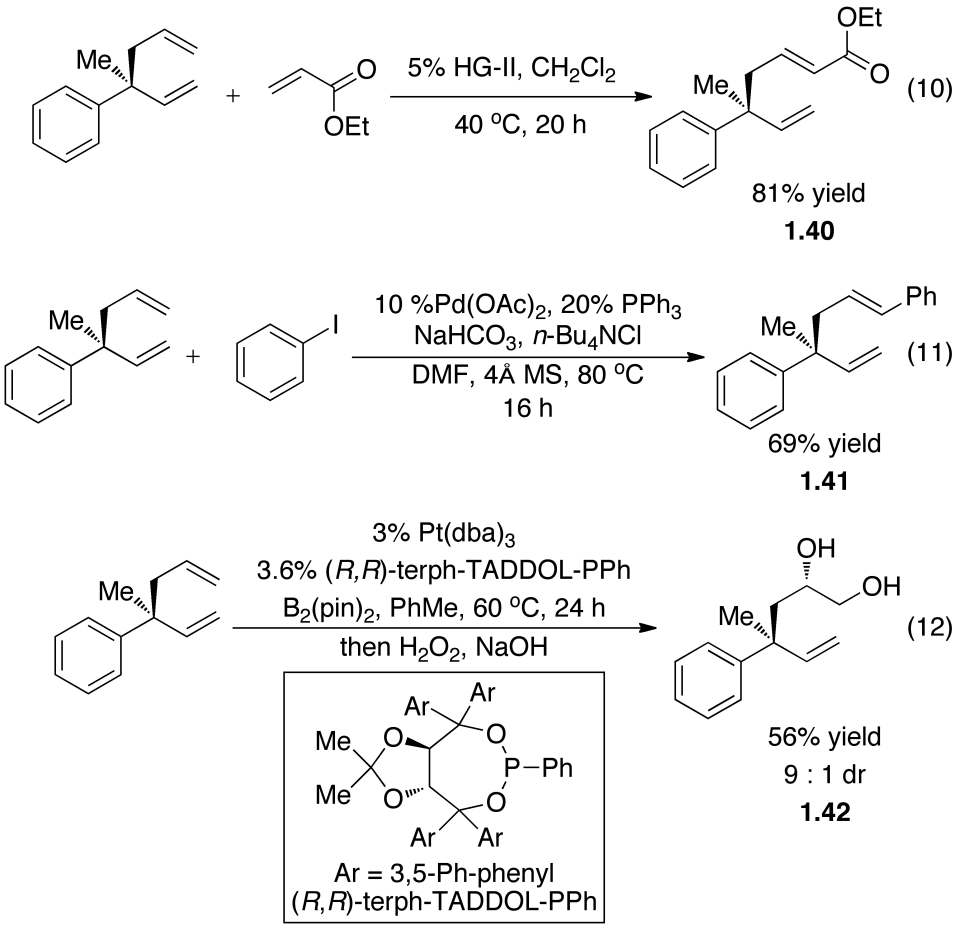
[49] (a) BouzBouz, S.; Simmons, R.; Cossy, J. *Org. Lett.* **2004**, *6*, 3465. (b) Garber, S. B.; Kingsbury, J. S.; Gray, B. L.; Hoveyda, A. H. *J. Am. Chem. Soc.* **2000**, *122*, 8168. (c) Blackwell, H. E.; O'Leary, D. J.; Chatterjee, A. K.; Washenfelder, R. A.; Bussman, D. A.; Grubbs, R. H. *J. Am. Chem. Soc.* **2000**, *122*, 58.

[50] (a) Jeffery, T. *Tetrahedron Lett.* **1985**, *26*, 2667. (b) Jeffery, T. *Tetrahedron* **1996**, *52*, 10113. Review of the Heck reaction: (c) Beletskaya, I. P.; Cheprakov, A. V. *Chem. Rev.* **2000**, *100*, 3009.

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

Scheme 1.29: Chemoselective Functionalization of 1,5-Dienes



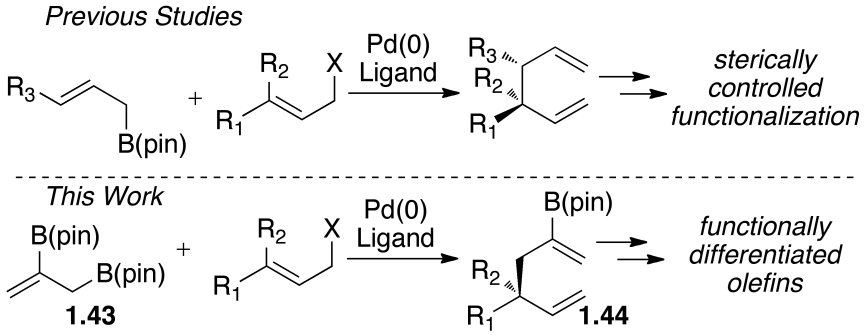
IV. Reaction Development for Allyl-Allyl Cross-Coupling to Generate Functionally Differentiated 1,5-Dienes[52]

A. Initial Results and Optimization of Reaction Conditions

Despite the success of our enantio- and branch-selective allyl-allyl cross-coupling methodology, considerable challenges remain. Specifically, and as described in the previous section, chemoselective functionalization of the product olefins is currently best controlled by steric influences. It was therefore of interest to develop an allyl-allyl cross-coupling methodology that resulted in functionally differentiated olefins, where subsequent manipulations would be less bound to steric constraints. In studies initiated by Dr. Laura A. Brozek and aided by Hai Le, we produced the enantioselective coupling of an allylic electrophile with 1,2-diboron reagent **1.43** (Scheme 1.30). This advance provides access to readily manipulated 1,5-diene frameworks (**1.44**), which should have a significant impact on the utility of allyl-allyl cross-coupling in the purview of enantioselective synthesis.

[52] Kyne, R. E.; Brozek, L. A.; Le, H.; Morken, J. P. manuscript in preparation.

Scheme 1.30: Allyl-Allyl Coupling Methodologies



Diboron **1.43** is an attractive candidate for this new coupling reaction as it provides 1,5-diene **1.44** bearing a vinylboronic ester. Such functional groups can be readily oxidized, cross-coupled,[53] or homologated,[54] in addition to a variety of other transformations (*vida infra*). Allylboron **1.43** (Scheme 1.31) is synthesized through a Pt(0)-catalyzed 1,2-diboration of allene gas with $B_2(pin)_2$.[55] We found that this diboration could be run on >14 g scale. The product is readily purified by Kügelrohr distillation and stored for months at –20 ºC with no detectable decomposition, making it an ideal nucleophile for reaction development.

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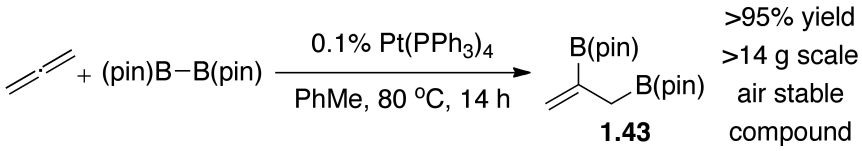
[53] (a) Suzuki, A.; Miyaura, N.; Abiko, S.; Itoh, M.; Brown, H. C.; Sinclair, J. A.; Midland, M. M. *J. Am. Chem. Soc.* **1973**, *95*, 3080. (b) Leung, T.; Zweifel, G. *J. Am. Chem. Soc.* **1974**, *96*, 5620. (c) Yamada, K.; Miyaura, N; Itoh, M.; Suzuki, A. *Synthesis* **1977**, 679. (d) Hara, S.;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

[54] 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.

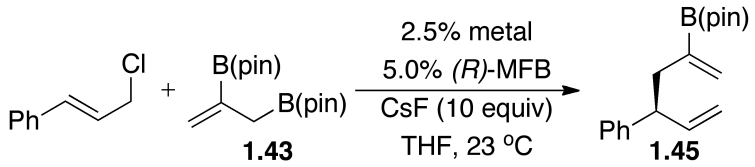
[55] Ishiyama, T.; Kitano, T.; Miyaura, N. *Tetrahedron Lett.* **1998**, *39*, 2357.

Scheme 1.31: Multi-Gram-Scale Preparation of 1,2-Diboron Reagent



A 99 : 1 er was obtained when diboron **1.43** was subjected to standard allyl-allyl cross-coupling conditions utilizing $Pd_2(dba)_3$ as the metal source. Unfortunately, the reaction suffered from significant byproduct formation and low isolated yield (Table 1.7, entry 1). It was quickly determined that Pd(II) sources suppressed ethereal byproduct formation while not impacting the high levels of enantioselectivity (entries 2 and 3). In fact, when $(\eta^3\text{-allylPdCl})_2$ was employed as the Pd source, byproduct formation was negligible, allowing for a 77% isolated yield and a 99 : 1 er of 1,5-diene **1.45** (entry 3).

Table 1.7: Optimization of Reaction Conditions

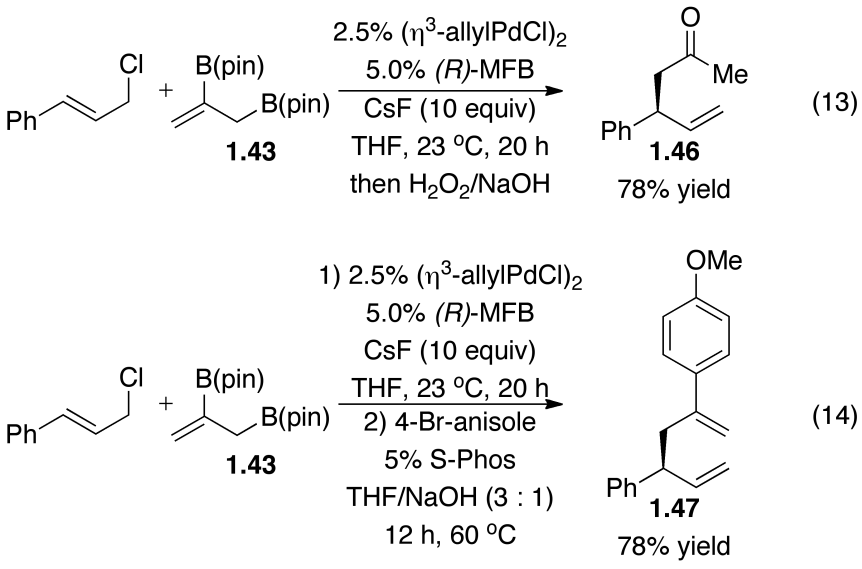


entry	metal	yield **1.45** (%)	**1.45** : ethers	er
1	$Pd_2(dba)_3$	38	2 : 1	99 : 1
2	$(\eta^3\text{-cinnamylPdCl})_2$	66	8.25 : 1	99 : 1
3	$(\eta^3\text{-allylPdCl})_2$	77	>20 : 1	99 : 1

B. Manipulation of 1,5-Hexadiene Framework

Having established an efficient and selective transformation in entry 3 (Table 1.7), we sought to probe the utility of these products with a pair of single-flask reactions (Scheme 1.32). First, allyl-allyl cross-coupling was immediately followed by an oxidative work-up, affording β-vinyl ketone **1.46** in 78% yield. Compound **1.46** represents an important class of compounds that has recently received attention in the literature (eq. 13).[33] Additionally, allyl-allyl cross-coupling was partnered with a Suzuki-Miyaura cross-coupling (eq. 14). In this case, additional palladium catalyst was not required; the palladium employed for the allyl-allyl coupling is also serviceable for the Suzuki-Miyaura reaction and delivers styrene derivative **1.47** in 78% yield.

Scheme 1.32: Single-Flask Operations Involving 1.45



Additional functionalizations were then pursued to further demonstrate the synthetic utility of the borylated allyl-allyl coupling products (Scheme 1.33). Copper-mediated halogenation of **1.45** delivered vinyl halides **1.48** and **1.49** in 85 and 80% yield, respectively (eq. 15-16).[56] Additionally, we were keenly interested in being able to selectively react the monosubstituted olefin while leaving the vinylboron intact. To this end, it was found that cross-metathesis with ethyl acrylate was completely chemoselective, affording α,β-unsaturated ester **1.50** in 63% yield as a single olefin isomer (eq. 17).[57] Thus, by altering the nucleophilic coupling partner, we are able to chemoselectively react with either olefin of our 1,5-diene, providing a practical solution to a significant problem in allyl-allyl cross-coupling. Pleased with these developments, we sought to investigate the breadth of the substrate tolerance for this transformation.

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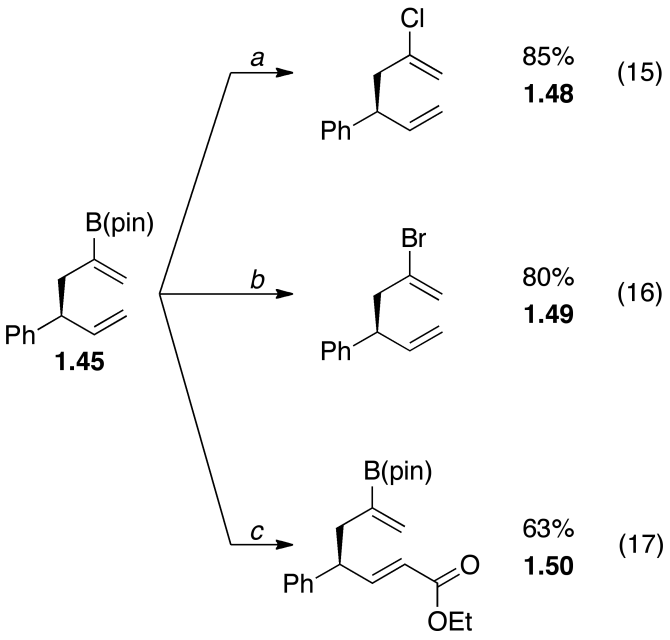
[56] Murphy, J. M.; Liao, X.; Hartwig, J. F. *J. Am. Chem. Soc.* **2007**, *129*, 15434.

[57] Cross-metathesis of a 1,1-disubstituted vinyl boron is quite slow, see: Morrill, C.; Funk, T. W.; Grubbs, R. H. *Tetrahedron Lett.* **2004**, *45*, 7733.

Scheme 1.33: Selective Transformations of 1.45



85% **1.48** (15)

80% **1.49** (16)

63% **1.50** (17)

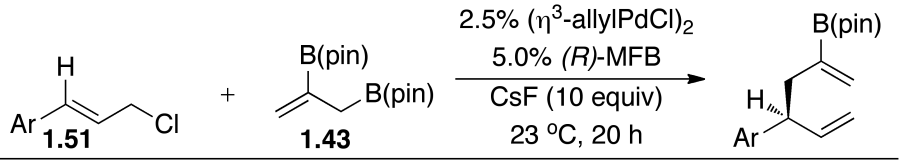
Conditions: *a*: $CuCl_2$ (3 equiv), MeOH/H_2O (1 : 1), 80 °C, 12 h. *b*: $CuBr_2$ (3 equiv), MeOH/H_2O (1 : 1), 90 °C, 12 h. *c*: 5% HG-II, ethyl acrylate (3 equiv), 40 °C, 20 h.

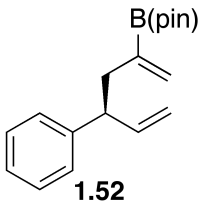
C. Substrate Scope Development

This allyl-allyl cross-coupling was found to process a range of aryl substrates (Table 1.8). Several electron-rich aromatic substrates (**1.51**) participated very well in the reaction (**1.52-1.54**, **1.56**), giving enantioselectivities up to 99 : 1 er. Thiophene-containing **1.55** demonstrates that sulfur-containing heterocycles, prevalent structures in medicinally relevant targets, are competent

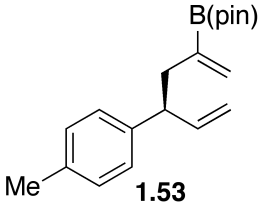
electrophiles in this coupling reaction, giving 98 : 2 er.[58] As observed previously, aryl-halide bonds do not interfere with the reaction, with product **1.57** formed in 99 : 1 er.

Table 1.8: Simple Aryl Substrate Allyl-Allyl Cross-Coupling

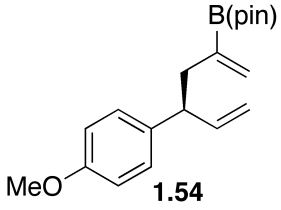




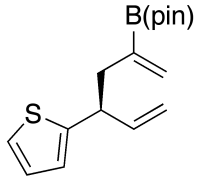
1.52
77% yield
99 : 1 er



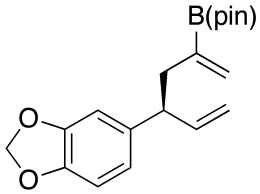
1.53
67% yield
99 : 1 er



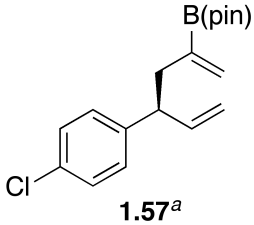
1.54
79% yield
99 : 1 er



1.55
79% yield
98 : 2 er



1.56
72% yield
96 : 4 er



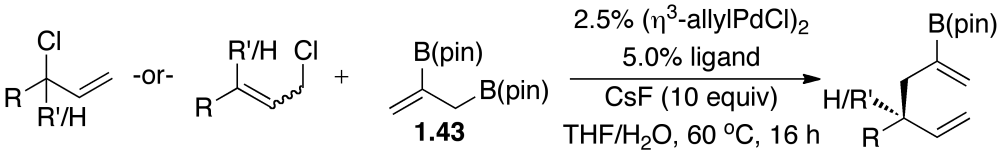
1.57[a]
78% yield
99 : 1 er

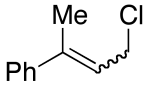
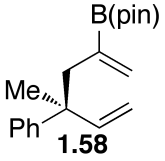
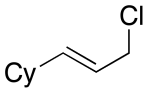
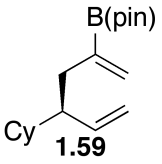
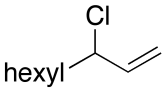
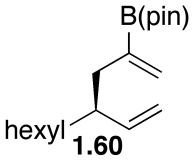
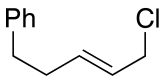
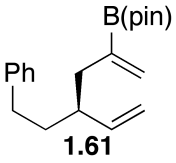
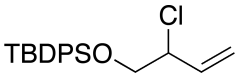
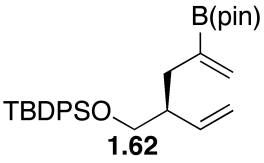
[a] 10% catalyst loading.

[58] See for example: (a) Wu, C.; Decker, E. R.; Blok, N.; Bui, H.; You, T. J.; Wang, J.; Bourgoyne, A. R.; Knowles, V.; Berens, K. L.; Holland, G. W.; Brock, T. A.; Dixon, R. A. F. *J. Med. Chem.* **2004**, *47*, 1969. (b) Guo, H. F.; Shao, H. Y.; Yang, Z. Y.; Xue, S. T.; Li, X.; Liu, Z. Y.; He. X. B.; Jian, J. D.; Zhang, Y. Q.; Si, S. Y.; Li, Z. R. *J. Med. Chem.* **2010**, *53*, 1819. (c) Rogers, E.; Araki, H.; Batory, L. A.; McInnis, C. E.; Njardarson, J. T. *J. Am. Chem. Soc.* **2007**, *129*, 2768. (d) Qin, Z.; Kasrati, I.; Chandrasena, R. E. P.; Liu, H.; Yao, P.; Petukhov, P. A.; Bolton, J. L.; Thatcher, G. R. J. *J. Med. Chem.* **2007**, *50*, 2682. (e) Guinchard, X.; Denis, J. N. *J. Org. Chem.* **2008**, *73*, 2028.

Several substrates illustrate the ability to convert isomeric mixtures to enantioenriched products (Table 1.9). Product **1.58**, containing an all-carbon quaternary stereogenic center was synthesized in 97 : 3 er and a 75% yield. Several alkyl substrates (**1.59**-**1.62**) were competent participants in the present methodology. Cyclohexyl-bearing **1.59** was prepared smoothly under the conditions developed for the aryl coupling. Less hindered *n*-alkyl substrates **1.60**-**1.62** suffered from competitive β-elimination which resulted in undesired 1,3-diene byproducts. However, consistent with previous observations, the combined influence of *(R,R)*-QuinoxP* [4] and a mixed THF/H_2O solvent system[38] ameliorated the situation and allowed access to good yields and enantioselectivities.

Table 1.9: Allyl-Allyl Cross-Coupling with Isomeric Mixtures of Substrates



entry	substrate	product	ligand	yield (%)	er
1[a]	 0 : 1 br : lin 3.2 : 1 *E : Z*	 **1.58**	*(R)*-MFB	75	97 : 3
2[b]	 1 : 4 br : lin >20 : 1 *E : Z*	 **1.59**	*(R)*-MFB	66	96 : 4
3[c]	 5 : 1 br : lin >20 : 1 *E : Z*	 **1.60**	*(R,R)*-QuinoxP*	72	>95 : 5
4[c]	 1 : 5 br : lin >20 : 1 *E : Z*	 **1.61**	*(R,R)*-QuinoxP*	72	92 : 8
5[c,d]	 2 : 1 br : lin 1 : >20 *E : Z*	 **1.62**	*(R,R)*-QuinoxP*	54	94 : 6

[a] reaction run in 20 : 1 THF:H_2O for 20 h. [b] reaction run at 23 °C in anhydrous THF. [c] reaction run in 20 : 1 THF:H_2O. [d] Cs_2CO_3 used as base

It is interesting to note that the present methodology resulted in improved enantioselectivities when compared to allyl-allyl coupling with simple allylB(pin) (Scheme 1.34).[4] Equations 18 and 20 show that, with simple cinnamyl derived

substrates, the enantioselectivity improves to 99 : 1 er from 95.5 : 4.5 er. More surprising still is the improved selectivity when *p*-CF_3-containing substrates are compared. In equation 21, **1.65** is prepared in a 96 : 4 er, which is appreciably higher than the 87 : 13 er observed when allylB(pin) is employed as the nucleophile (eq. 19). The increased selectivity in the coupling of **1.43** with electron-withdrawing substrates is an important advance from the original methodology, where low enantioselectivities may be attributed to a rapid reductive elimination in the case of electron withdrawing substrates, resulting in incomplete isomerization of the electrophile.[59] It is possible, as shown in Figure 1.4, that the additional vinylB(pin) group causes a developing diaxial interaction to occur. This could slow down reductive elimination, allowing for complete isomerization of the Pd-bound allyl group, thus resulting in higher enantioselectivity. It may also simply be the case that the enhanced interaction between pinacol and the adjacent axial furyl group more significantly disfavors the competing chair structure.

[59] Hartwig, J. F. *Inorg. Chem.* **2007**, *46*, 1936.

Scheme 1.34: Improved Enantioselectivities vs. AllylB(pin)

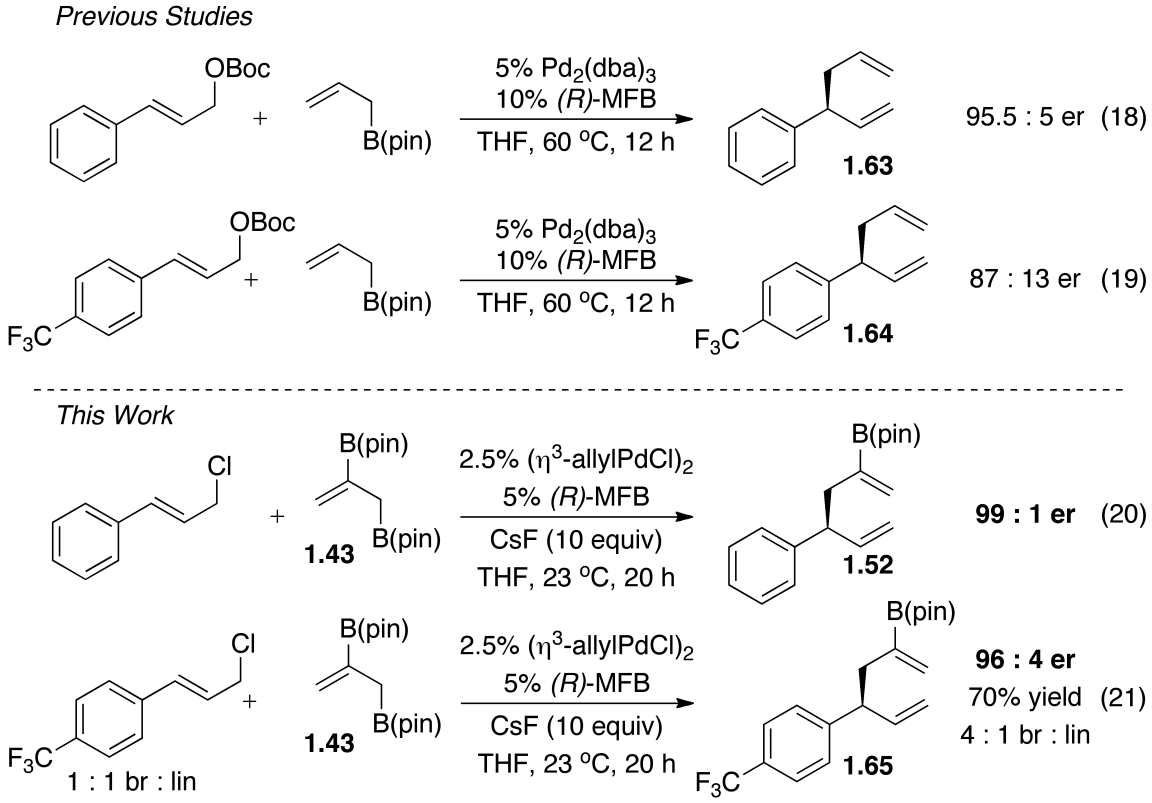
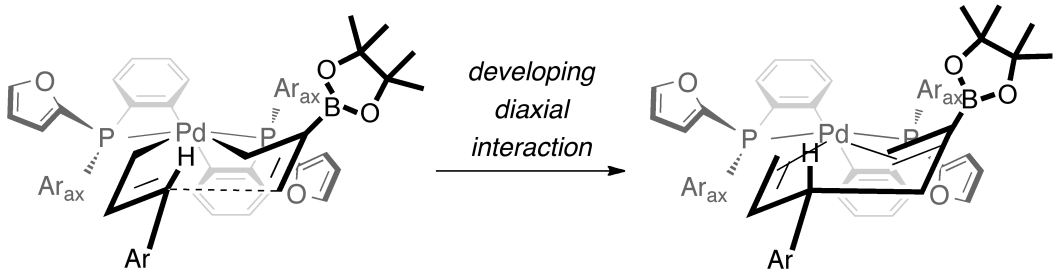


Figure 1.4: Developing Diaxial Strain



V. Conclusions

A novel method for the catalytic and enantioselective synthesis of all-carbon quaternary centers has been presented. Through Pd-catalyzed allyl-allyl cross-coupling, a broad substrate tolerance has been demonstrated in the synthesis of quaternary stereogenic centers, adding a valuable method to the synthetic chemists' repertoire. Notably, mixtures of branched and linear substrates converge to one enantioenriched product through π-σ-π isomerization, adding a significant practical note to this chemistry. Additionally, an allyl-allyl cross-coupling reaction has been developed to address the issue of chemoselective manipulation of 1,5-dienes by functionally differentiating the alkenes. The vicinal olefin-containing products, often generated in excellent levels of enantioselectivity, have been shown to readily undergo selective reactions. Notably, either olefin can be targeted for further alterations, broadening the synthetic utility of these compounds.

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 reference ($CDCl_3$: 7.26 ppm). Data are reported as follows: chemical shift, integration, multiplicity (s = singlet, d = doublet, t = triplet, q = quartet, m = multiplet), coupling constants (Hz) (some reported to the nearest 0.5 Hz). ^{13}C NMR spectra were recorded on either a Varian Gemini-400 (100 MHz), a Varian Gemini-500 (125 MHz) or a Varian Inova-500 (125 MHz) spectrometer with complete proton decoupling. Chemical shifts are reported in ppm with the solvent resonance as the reference ($CDCl_3$: 77.0 ppm). Infrared (IR) spectra were recorded on a Bruker alpha spectrophotometer, ν_{max} cm^{-1}. Bands are characterized as broad (br), strong (s), medium (m), and weak (w). High-resolution mass spectra (ESI) were obtained at the Mass Spectrometry Facility, Boston College.

Liquid Chromatography was performed using 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) or potassium permanganate ($KMnO_4$) in water. Analytical chiral gas-liquid chromatography (GC) 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 an Agilent Technologies 6850 equipped with a split mode capillary injection system, a flame ionization detector, and a Supelco Chiraldex G-TA or 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. X-Ray crystallography was performed on a Bruker Kappa Apex Duo fully automated single crystal diffractometer, duo wavelength system with high brightness copper source, and anomalous dispersion was used.

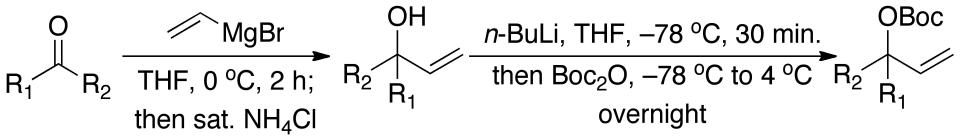
All reactions were conducted in oven- or flame-dried glassware under an atmosphere of nitrogen or argon. Tetrahydrofuran (THF) was purified using a Pure Solv MD-4 solvent purification system from Innovative Technology Inc. (*R*)-(+)-2,2'-bis(di-2-furanylphosphino)-6,6'-dimethoxy-1,1'-biphenyl [(*R*)-MeO-Fur-BIPHEP] was purchased from Strem Chemicals, Inc. or Aldrich, or generously donated by Solvias. (*R,R*)-(–)-2,3-Bis(*t*-butylmethylphosphino)quinoxaline [(*R,R*)-QuinoxP*] was purchased from Strem Chemicals. Allylboronic acid pinacol ester [allylB(pin)] was generously donated by Frontier Scientific, Inc. MethallylB(pin)

was synthesized as described in the literature.[4] $B_2(pin)_2$ was generously donated by AllyChem. Co., Inc. Allene gas was purchased from ChemSampCo. All other reagents were purchased from either Fisher or Aldrich and used without further purification.

A note about NMR spectra: Due to the boron quadrupole, carbons directly attached to this element are often not detected in ^{13}C spectra. See Wrackmeyer, B. *Prog. In NMR Spectroscopy*, **1979**, *12*, 227. In some cases, the ^{2}J and ^{3}J $^{11}B/^{1}H$ coupling makes determination of some $^{1}H/^{1}H$ coupling constants difficult.

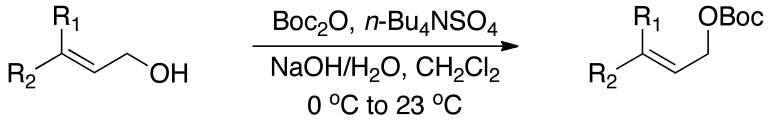
B. Experimental Procedures

1. Preparation and Charaterization of Allylic Carbonates



Representative Procedure A:[4] To a flame-dried round-bottom flask equipped with a stir bar was added 1.0 M vinylmagnesium bromide in THF (15.0 mL, 15 mmol) and THF (10 mL). The solution was cooled to 0 °C and acetophenone (1.20 g, 10.0 mmol) in THF (10 mL) was added dropwise *via* cannula. The reaction was allowed to stir at 0 °C for 2 hours. The reaction was then quenched with sat. NH_4Cl (aq.), and extracted into diethyl ether three times. The combined organics were washed with brine, dried over Na_2SO_4, filtered, and then

concentrated *in vacuo*. The unpurified reaction mixture was purified on silica gel (15:1 hexanes/EtOAc) to afford 1.20 g (81% yield) of 2-phenylbut-3-en-2-ol as a light yellow oil. R_f = 0.26 (3:1 hexanes/EtOAc, stain in $KMnO_4$). To a separate flame-dried round-bottom flask equipped with stir bar was added 2-phenylbut-3-en-2-ol (1.20 g, 8.10 mmol) and THF (16.0 mL). The solution was cooled to –78 °C (dry ice/acetone) followed by dropwise addition of *n*-butyllithium (3.55 mL, 8.51 mmol) in hexane (2.40 M). The reaction was allowed to stir for 30 minutes at –78 °C, after which Boc_2O (2.29 g, 10.5 mmol) in THF (5.0 mL) was added dropwise *via* cannula. The reaction was allowed to warm to 4 °C in a cold room and stir overnight. The reaction was diluted with diethyl ether and water. The organic layer was separated and the aqueous layer was extracted into diethyl ether three times. The combined organics were washed with brine, dried over Na_2SO_4, filtered, and then concentrated *in vacuo*. The unpurified reaction mixture was purified on silica gel (neutralized with 5% TEA, eluted with 100:1 hexanes/EtOAc) to afford 1.65 g (82% yield) of *tert*-butyl (2-phenylbut-3-en-2-yl) carbonate as a light yellow oil. R_f = 0.39 (8:1 hexanes/EtOAc, stain in $KMnO_4$).



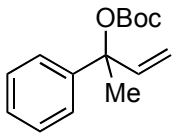
Representative Procedure B:[1] To a round-bottom flask equipped with a stir bar was added geraniol (1.54 g, 10.0 mmol) and methylene chloride (5 mL). The

resulting solution was charged with Boc_2O (2.60 g, 12.0 mmol) and Bu_4NHSO_4 (68.0 mg, 0.2 mmol). The solution was cooled to 0 °C and aqueous NaOH (5.4 mL, 30% solution in H_2O) was added dropwise. The solution was allowed to stir overnight at room temperature. The reaction mixture was diluted with diethyl ether and water, and then extracted into diethyl ether three times. The combined organics were washed with 1M HCl, water, brine, dried over Na_2SO_4, filtered, and then concentrated *in vacuo*. The unpurified reaction mixture was purified on silica gel (50:1 hexanes/EtOAc) to afford 1.85 g (73% yield) of (*E*)-*tert*-butyl (3,7-dimethylocta-2,6-dien-1-yl) carbonate as a light yellow oil. R_f = 0.55 (8:1 hexanes/EtOAc, stain in $KMnO_4$).

***Preparation of (E)-tert-butyl (3,7-dimethylocta-2,6-dien-1-yl) carbonate* (Table 1.6, entry 2).** From commercially available geraniol, procedure B was followed. Spectral data is in accordance with literature.[60]

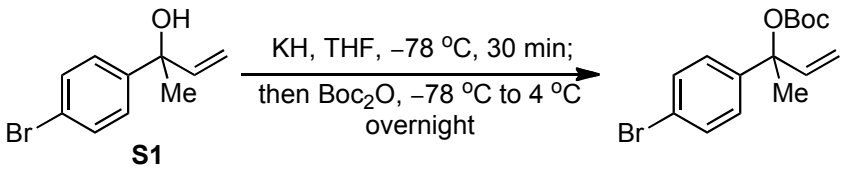
Preparation of tert-butyl (2-phenylbut-3-en-2-yl) carbonate. From commercially available acetophenone, procedure A was followed.

[60] Snyder, S. A.; Treitler, D. S. *Angew. Chem. Int. Ed.* **2009**, *48*, 7899.



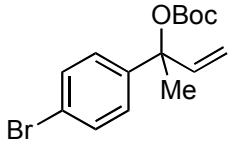
***tert*-butyl (2-phenylbut-3-en-2-yl) carbonate (1.22; Table 1.3, entry 1)**. ^{1}H NMR (500 MHz, $CDCl_3$): δ 1.41 (9H, s, C(C**H**$_3$)$_3$), 1.87 (3H, s, OCC**H**$_3$), 5.27 (1H, dd, *J* = 10.5, 0.5 Hz, CH=C**H**$_{cis}$H$_{trans}$), 5.28 (1H, dd, *J* = 17.5, 0.5 Hz, CH=CH$_{cis}$**H**$_{trans}$), 6.34 (1H, dd, *J* = 17.5, 10.5 Hz, C**H**=CH$_2$), 7.24-7.27 (1H, m, Ar-**H**), 7.32-7.35 (2H, m, Ar-**H**), 7.37-7.40 (2H, m, Ar-**H**); ^{13}C NMR (100 MHz, $CDCl_3$): δ 25.8, 27.8, 81.8, 83.8, 115.1, 125.1, 127.2, 128.2, 141.0, 143.7, 151.5; IR (neat): 2980.4 (w), 2943.7 (w), 1743.1 (s), 1448.4 (w), 1368.7 (m), 1276.6 (s), 1254.2 (s), 1150.0 (s), 1070.5 (m), 792.9 (m), 699.1 (m) cm^{-1}; HRMS (ESI+) for $C_{10}H_{11}$ [M–OBoc]: calculated: 131.0681, found: 131.0859; The unpurified reaction mixture was purified on silica gel (neutralized with 5% TEA, flashed with 100:1 hexanes/EtOAc) to afford 1.65 g (82% yield) of a light yellow oil. R_f = 0.39 (8:1 hexanes/EtOAc, stain in $KMnO_4$).

Preparation of 2-(4-bromophenyl)but-3-en-2-yl tert-butyl carbonate. From commercially available 4'-bromoacetophenone, procedure A was followed for the synthesis of allylic alcohol (**S-1**), which was converted to the carbonate as shown below.



S1

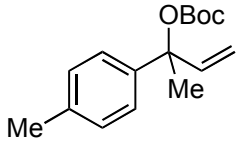
Procedure: A flame-dried round-bottom flask was charged with KH (562.0 mg, 30 wt % in mineral oil, 4.2 mmol) and purged with N_2 three times. Dry hexane (5 mL) was added and the flask was gently swirled. Once the KH settled on the bottom of the flask, hexane was removed *via* cannula. This process was repeated twice, then THF (4.0 mL) was added to create a suspension. The suspension was transferred *via* cannula to another flame-dried round-bottom flask containing a solution of allylic alcohol (**S1**) (852.0 mg, 4.0 mmol) in THF (3.0 mL) at –78 °C. The reaction was allowed to stir for 30 minutes at this temperature, followed by addition of Boc_2O (1.13 g, 5.2 mmol) in THF (1.0 mL) *via* cannula. The reaction was allowed to warm to 4 °C in a cold room and stir overnight. The reaction was diluted with diethyl ether and water. The organic layer was separated and the aqueous layer was extracted into diethyl ether three times. The combined organics were washed with brine, dried over Na_2SO_4, filtered, and concentrated *in vacuo*. The unpurified reaction mixture was purified on silica gel (neutralized with 5% TEA, eluted with 100:1 hexanes/EtOAc) to afford 1.10 g (84% yield) of a light yellow oil. R_f = 0.50 (8:1 hexanes/EtOAc, stain in $KMnO_4$).



2-(4-bromophenyl)but-3-en-2-yl *tert*-butyl carbonate. (Table 1.4, entry 3). ^{1}H NMR (500 MHz, $CDCl_3$): δ 1.42 (9H, s, C(C**H**$_3$)$_3$), 1.84 (3H, s, OCC**H**$_3$), 5.26-5.29 (2H, m, CH=C**H**$_2$), 6.30 (1H, dd, *J* = 17.0, 11.0 Hz, C**H**=CH_2), 7.26 (2H, ddd, *J* = 8.5, 2.5, 2.0 Hz, Ar-

H), 7.46 (2H, ddd, *J* = 8.5, 2.5, 2.0 Hz, Ar-**H**); ^{13}C NMR (125 MHz, $CDCl_3$): δ 25.6, 27.7, 82.0, 83.2, 115.5, 121.3, 126.9, 131.3, 140.5, 142.9, 151.4; IR (neat): 2980.5 (w), 2935.2 (w), 1742.2 (s), 1488.1 (w), 1368.4 (m), 1280.2 (s), 1253.7 (s), 1153.1 (s), 1113.6 (m), 1090.9 (s), 1077.2 (s), 1008.2 (s), 926.3 (m), 820.9 (s), 720.2 (m) cm^{-1}; HRMS (ESI+) for $C_{10}H_{10}Br$ [M–OBoc]: calculated: 208.9966, found: 208.9975.

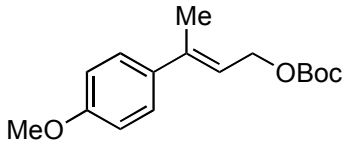
Preparation of tert-butyl (2-(p-tolyl)but-3-en-2-yl) carbonate. From commercially available 4'-methylacetophenone, procedure A was followed.



***tert*-butyl (2-(*p*-tolyl)but-3-en-2-yl) carbonate (Table 1.4, entry 1)**. ^{1}H NMR (500 MHz, $CDCl_3$): δ 1.43 (9H, s, C(C**H$_3$**)$_3$), 1.87 (3H, s, OCC**H$_3$**), 2.34 (3H, s, Ar-C**H$_3$**), 5.26 (1H, d, *J* = 11.0 Hz, CH=C**H**$_{cis}$H$_{trans}$), 5.28 (1H, d, *J* = 17.5 Hz, CH=CH$_{cis}$**H**$_{trans}$), 6.35 (1H, ddd, *J* = 17.5, 11.0, 0.5 Hz, C**H**=CH$_2$), 7.16 (2H, d, *J* = 8.0 Hz, Ar-**H**), 7.28 (2H, d, *J* = 8.0 Hz, Ar-**H**); ^{13}C NMR (125 MHz, $CDCl_3$): δ 21.0, 25.7, 27.7, 81.6, 83.7, 114.8, 124.9, 128.9, 136.8, 140.7, 141.1, 151.5; IR (neat): 2979.9 (w), 2933.0 (w), 1743.0 (s), 1513.2 (w), 1455.9 (w), 1368.0 (m), 1274.9 (s), 1252.7 (s), 1122.0 (s), 1093.4 (s), 1073.1 (m), 850.6 (m), 791.2 (m), 533.4 (w) cm^{-1}; HRMS (ESI+) for $C_{11}H_{13}$ [M–OBoc]: calculated: 145.1017, found: 145.1023; The unpurified reaction mixture was purified on silica gel (neutralized with 5% TEA,

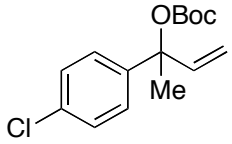
eluted with 100:1 hexanes:EtOAc) to afford 1.91 g (89% yield) of a light yellow oil. R_f = 0.49 (8:1 hexanes:EtOAc, stain in $KMnO_4$).

Preparation of (E)-tert-butyl (3-(4-methoxyphenyl)but-2-en-1-yl) carbonate. From commercially available 4'-methoxyacetophenone, procedure A was followed. *tert*-Butyl (2-(4-methoxyphenyl)but-3-en-2-yl) carbonate was originally formed, which was isomerized to the corresponding linear isomer upon silica gel chromatography.



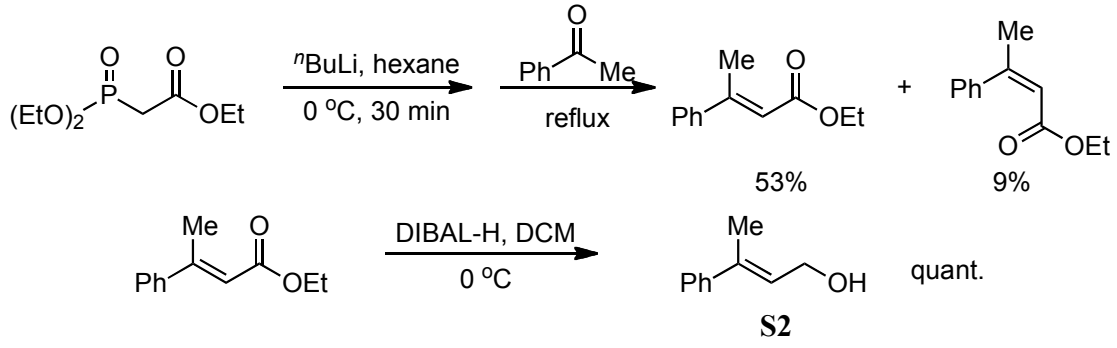
(*E*)-*tert*-butyl (3-(4-methoxyphenyl)but-2-en-1-yl) carbonate (Table 1.4, entry 5). ^{1}H NMR (500 MHz, $CDCl_3$): δ 1.50 (9H, s, C(C**H**$_3$)$_3$), 2.10 (3H, s, C**H**$_3$C=CH), 3.81 (3H, s, OC**H**$_3$), 4.77 (2H, d, *J* = 7.0 Hz, C**H**$_2$OBoc), 5.85-5.88 (1H, m, ArMeC=C**H**), 6.84-6.87 (2H, m, Ar-**H**), 7.33-7.36 (2H, m, Ar-**H**); ^{13}C NMR (125 MHz, $CDCl_3$): δ 16.2, 27.8, 55.2, 64.0, 82.0, 113.6, 119.4, 126.9, 134.9, 139.9, 153.6, 159.1; IR (neat): 2979.5 (w), 2934.4 (w), 2836.9 (w), 1734.7 (s), 1645.2 (m), 1711.7 (s), 1458.7 (w), 1368.4 (m), 1271.6 (s), 1243.5 (s), 1155.3 (s), 1083.4 (m), 825.1 (m), 792.6 (m) cm^{-1}; HRMS (ESI+) for $C_{11}H_{13}O$ [M–OBoc]: calculated: 161.0966, found: 161.0969; The unpurified reaction mixture was purified on silica gel (neutralized with 5% TEA, eluted with 100:1 hexanes/EtOAc) to afford 873 mg (75% yield) of a light yellow oil. R_f = 0.42 (8:1 hexanes/EtOAc, stain in $KMnO_4$).

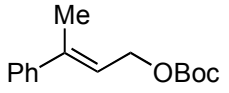
Preparation of tert-butyl-(2-(4-chlorophenyl)but-3-en-2-yl)carbonate. From commercially available 4'-chloroacetophenone, procedure A was followed.



***tert*-butyl-(2-(4-chlorophenyl)but-3-en-2-yl)carbonate (Table 1.4, entry 2):** ^{1}H NMR (500 MHz, $CDCl_3$): δ 1.42 (9H, s, C(C**H**$_3$)$_3$), 1.85 (3H, s, CC**H**$_3$), 5.25-5.29 (2H, m, CH=C**H**$_2$), 6.30 (1H, dd, *J* = 17.4, 10.8 Hz, CC**H**=CH$_2$), 7.29-7.31 (4H, m, Ar-**H**); ^{13}C NMR (125 MHz, $CDCl_3$): δ 25.7, 27.8, 82.0, 83.2, 115.5, 126.6, 128.4, 133.1, 140.6, 142.3, 151.4; IR (neat): 2981.0 (w), 2004.2 (w), 1745.7 (s), 1492.0 (w), 1369.5 (m) 1284.6 (s), 1158.2 (s), 1013.2 (s), 827.7 (w), 421.7 (w) cm^{-1}; HRMS (ESI+) for $C_{10}H_{10}Cl$ [M–OBoc]: calculated: 165.0471, found: 165.0464. The unpurified material was used for the subsequent coupling reaction without further purification.

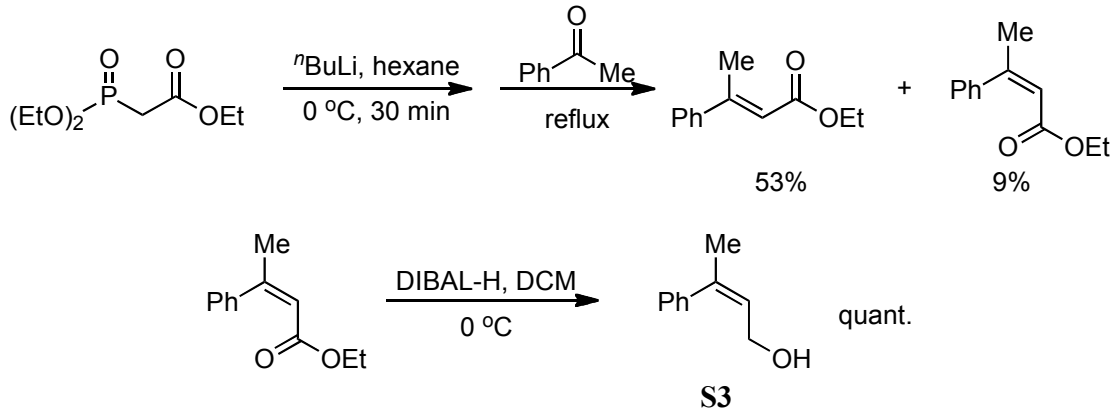
Preparation of (E)-tert-butyl (3-phenylbut-2-en-1-yl) carbonate. From allylic alcohol **S2**, synthesized as shown below, procedure B was followed.

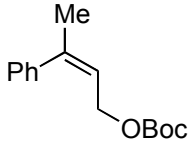




(*E*)-*tert*-butyl (3-phenylbut-2-en-1-yl) carbonate (Table 1.3, entry 2). ^{1}H NMR (500 MHz, $CDCl_3$): δ 1.51 (9H, s, C(C**H**$_3$)$_3$), 2.31 (3H, d, *J* = 1.0 Hz, C**H**$_3$C=CH), 4.80 (2H, d, *J* = 7.0 Hz, C=CHC**H**$_2$OBoc), 5.93 (1H, tq, *J* = 7.0, 1.0 Hz, C=C**H**CH$_2$), 7.26-7.29 (1H, m, Ar-**H**), 7.32-7.35 (2H, m, Ar-**H**), 7.40-7.42 (2H, m, Ar-**H**); ^{13}C NMR (125 MHz, $CDCl_3$): δ 16.2, 27.7, 68.9, 82.0, 121.0, 125.8, 127.5, 128.2, 140.4, 142.5, 153.5; IR (neat): 2979.7 (w), 2939.9 (w), 1735.6 (s), 1445.2 (w), 1390.0 (m), 1333.2 (s), 1270.8 (s), 1156.6 (s), 1086.1 (m), 927.4 (w), 860.3 (m), 751.3 (m), 695.0 (m) cm^{-1}; HRMS (ESI+) for $C_{10}H_{11}$ [M–OBoc]: calculated: 131.0861, found: 131.0866; The unpurified reaction mixture was purified on silica gel (50:1 hexanes/EtOAc) to afford 2.20 g (79% yield) of a light yellow oil. R_f = 0.71 (3:1 hexanes/EtOAc, stain in $KMnO_4$).

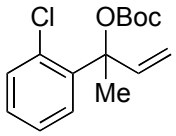
Preparation of (Z)-tert-butyl (3-phenylbut-2-en-1-yl) carbonate. From allylic alcohol **S3**, synthesized as shown below, procedure B was followed.





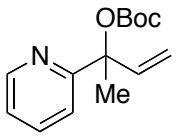
(*Z*)-*tert*-butyl (3-phenylbut-2-en-1-yl) carbonate (Table 1.3, entry 3). ^{1}H NMR (500 MHz, $CDCl_3$): δ 1.47 (9H, s, C(C**H$_3$**)$_3$), 2.09-2.10 (3H, m, C**H$_3$**C=CH), 4.50 (2H, dd, *J* = 7.0, 1.0 Hz, C=CHC**H$_2$**OBoc), 5.67-5.70 (1H, m, C=C**H**CH$_2$), 7.17-7.19 (1H, m, Ar-**H**), 7.26-7.29 (2H, m, Ar-**H**), 7.32-7.36 (2H, m, Ar-**H**); ^{13}C NMR (125 MHz, $CDCl_3$): δ 25.4, 27.8, 64.7, 81.9, 120.9, 127.4, 127.7, 128.2, 140.3, 142.8, 153.5; IR (neat): 2978.5 (w), 2932.6 (w), 1736.8 (s), 1493.7 (w), 1444.1 (w), 1368.6 (m), 1273.4 (s), 1251.6 (s), 1159.1 (s), 1092.4 (m), 860.3 (m), 793.3 (m), 701.6 (m) cm^{-1}; HRMS (ESI+) for $C_{10}H_{11}$ [M–OBoc]: calculated: 131.0861, found: 131.0864; The unpurified reaction mixture was purified on silica gel (50:1 hexanes/EtOAc) to afford 398 mg (89% yield) of a light yellow oil. R_f = 0.51 (8:1 hexanes/EtOAc, stain in $KMnO_4$).

Preparation of tert-butyl-(2-(chlorophenyl)but-3-en-2-yl)carbonate. From commercially available 2'-chloroacetophenone, procedure A was followed.



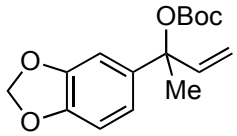
***tert*-butyl-(2-(chlorophenyl)but-3-en-2-yl)carbonate (Table 1.4, entry 4):** ^{1}H NMR (500 MHz, $CDCl_3$): δ 1.43 (9H, s, C(C**H$_3$**)$_3$), 1.95 (3H, s, CC**H$_3$**), 5.23 (1H, d, *J* = 17.6 Hz, CCH=CH$_{cis}$**H$_{trans}$**), 5.28 (1H, d, *J* = 10.9 Hz, CCH=C**H$_{cis}$**H$_{trans}$), 6.49 (1H, dd, *J* = 17.6, 10.9 Hz, CC**H**=CH$_2$), 7.20-7.28 (m, 2H, Ar-**H**), 7.35-7.37 (m, 1H, Ar-**H**), 7.47-7.49 (m, 1H, Ar-**H**); ^{13}C NMR (125 MHz, $CDCl_3$): δ 24.8, 27.7, 81.9, 83.2, 115.4, 126.6, 127.8, 128.6, 131.6, 131.7, 139.9, 140.2, 151.4; IR (neat): 2981.4 (w), 2934.2 (w), 1741.4 (s), 1473.1 (w), 1369.2 (m), 1285.8 (s), 1256.3 (m), 1157.2 (s), 1134.2 (m), 1102.3 (m), 1038.8 (m), 926.9 (w), 791.6 (w), 755.5 (w) cm^{-1}; HRMS (ESI+) for $C_{15}H_{23}ClNO_3$ [M+NH_4^+]: calculated: 300.1367, found: 300.1371. The unpurified reaction mixture was purified on silica gel (hexanes to 32:1 hexanes/ EtOAc) to afford a clear, colorless oil (1.40 g, 67% yield). R_f = 0.18 (32:1 hexanes/EtOAc, stain in $KMnO_4$).

Preparation of tert-butyl-(2-pyridin-2-yl)but-3-en-2-yl)carbonate. From commercially available 2-acetylpyridine, procedure A was followed.



***tert*-butyl-(2-pyridin-2-yl)but-3-en-2-yl)carbonate (Table 1.4, entry 7):** ^{1}H NMR (500 MHz, $CDCl_3$): δ 1.39 (9H, s, C(C**H$_3$**)$_3$), 1.87 (3H, s, CC**H$_3$**), 5.25 (1H, dd, *J* = 10.9, 0.7 Hz, CCH=C**H**$_{cis}$H$_{trans}$), 5.31 (1H, dd, *J* = 17.6, 0.7 Hz, CCH=CH$_{cis}$**H**$_{trans}$), 6.44 (1H, dd, *J* = 17.6, 10.9 Hz, CC**H**=CH$_2$), 7.12-7.15 (1H, m, Ar-**H**), 7.37-7.39 (1H, m, Ar-**H**), 7.62-7.65 (1H, m, Ar-**H**), 8.54-8.55 (1H, m, Ar-**H**); ^{13}C NMR (125 MHz, $CDCl_3$): δ 25.0, 27.6, 81.9, 84.0, 115.0, 119.5, 122.0, 136.4, 140.1, 148.6, 151.5, 162.1; IR (neat): 2980.9 (w), 2936.2 (w), 1742.8 (s), 1588.8 (w), 1368.3 (m), 1278.0 (s), 1255.0 (s), 1156.7 (s), 1106.6 (s), 853.6 (m), 748.7 (m), 684.1 (m), 403.3 (w) cm^{-1}; HRMS (ESI+) for $C_{14}H_{20}NO_3$ [M+H]: calculated: 250.1443, found: 250.1440. The unpurified reaction mixture was purified on silica gel (9:1 hexanes/EtOAc) to afford a clear, pale-yellow oil (126 mg, 52% yield). R_f = 0.22 (9:1 hexanes/EtOAc, stain in $KMnO_4$).

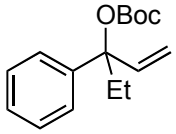
Preparation of 2-(benzo[d][1,3]dioxol-5-yl)but-3-en-2-yl-tert-butyl-carbonate. From commercially available 3',4'-(methylenedioxy)acetophenone, procedure A was followed.



2-(benzo[*d*][1,3]dioxol-5-yl)but-3-en-2-yl-*tert*-butyl-carbonate (Table 1.4, entry 6): ^{1}H NMR (500 MHz, $CDCl_3$): δ 1.42 (9H, s, C(C**H$_3$**)$_3$), 1.84 (3H, s, CC**H$_3$**), 5.25 (1H, dd, *J* = 10.8, 0.7 Hz, CCH=C**H**$_{cis}$H$_{trans}$), 5.27 (1H dd, *J* = 17.4, 0.7 Hz, CCH=CH$_{cis}$**H**$_{trans}$),

5.95 (2H, s, OC**H**$_2$O), 6.30 (1H, dd, *J* = 17.4, 10.8 Hz, CC**H**=CH$_2$), 6.76 (1H, d, *J* = 8.1 Hz, Ar-**H**), 6.85-6.89 (2H, m, Ar-**H**); ^{13}C NMR (125 MHz, $CDCl_3$): δ 25.7, 27.7, 81.7, 83.5, 101.0, 106.1, 107.8, 114.9, 118.4, 137.7, 141.0, 146.6, 147.6, 151.4; IR (neat): 2980.7 (w), 2932.1 (w), 1742.3 (s), 1486.7 (s), 1435.7 (m), 1393.9 (m), 1277.2 (s), 1241.5 (s), 1156.5 (s), 1094.5 (s), 1037.6 (s), 909.5 (m), 810.7 (m), 729.7 (s) cm^{-1}; HRMS (ESI+) for $C_{16}H_{21}O_5$ [M+H]: calculated: 293.1389, found: 293.1375. The unpurified reaction mixture was purified on silica gel (9:1 hexanes/EtOAc) to afford a clear, pale-yellow oil (244 mg, 23% yield). R_f = 0.12 (19:1 hexanes/EtOAc, stain in $KMnO_4$).

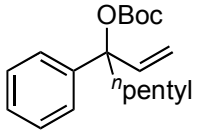
Preparation of tert-butyl (3-phenylpent-1-en-3-yl) carbonate. From commercially available propiophenone, procedure A was followed.



***tert*-butyl (3-phenylpent-1-en-3-yl) carbonate (Table 1.5, entry 1)**. ^{1}H NMR (500 MHz, $CDCl_3$): δ 0.82 (3H, t, *J* = 7.5 Hz, $CH_2C\mathbf{H_3}$), 1.42 (9H, s, $C(C\mathbf{H_3})_3$), 2.27 (1H, dq, *J* = 14.0, 7.5 Hz, $C\mathbf{H_a}H_bCH_3$), 2.33 (1H, dq, *J* = 14.0, 7.5 Hz, $CH_a\mathbf{H_b}CH_3$), 5.29 (1H, dd, *J* = 11.0, 1.0 Hz, CH=C$\mathbf{H_{\textit{cis}}}H_{\textit{trans}}$), 5.32 (1H, dd, *J* = 17.5, 1.0 Hz, CH=$CH_{\textit{cis}}\mathbf{H_{\textit{trans}}}$), 6.22 (1H, dd, *J* = 17.5, 11.0 Hz, C**H**=CH$_2$), 7.23-7.26 (1H, m, Ar-**H**), 7.31-7.38 (4H, m, Ar-**H**); ^{13}C NMR (125 MHz, $CDCl_3$): δ 7.7, 27.7, 30.9, 81.5, 85.9, 115.1, 125.5, 127.0, 128.0, 140.0, 142.6, 151.4; IR (neat): 3060.8 (w), 2978.5 (m), 2973.4 (w), 2881.6 (w), 1742.5 (s), 1640.1 (w), 1493.9 (w), 1448.3 (m), 1368.2 (m), 1269.4 (s), 1271.1

(s), 1152.7 (s), 1117.0 (m), 866.4 (s), 697.7 (s) cm^{-1}; HRMS (ESI+) for $C_{11}H_{13}$ [M –OBoc]: calculated: 145.1017, found: 145.1021; The unpurified reaction mixture was purified on silica gel (neutralized with 5% TEA, eluted with 100:1 hexanes/ EtOAc) to afford 2.97 g (87% yield) of a light yellow oil. R_f = 0.46 (8:1 hexanes/ EtOAc, stain in $KMnO_4$).

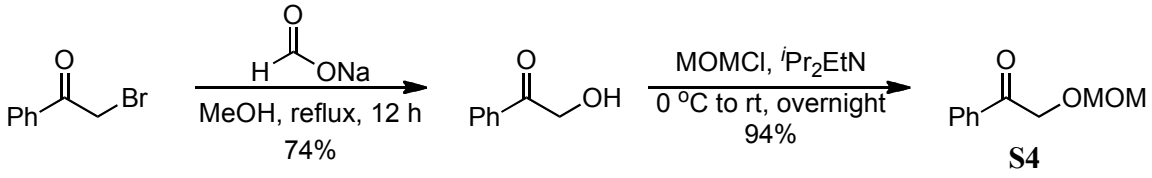
Preparation of tert-butyl (3-phenyloct-1-en-3-yl) carbonate. From commercially available hexanophenone, procedure A was followed.



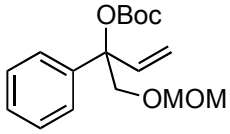
***tert*-butyl (3-phenyloct-1-en-3-yl) carbonate (Table 1.5, entry 2)**. ^{1}H NMR (500 MHz, $CDCl_3$): δ 0.84 (3H, t, *J* = 7.0 Hz, CH_2CH_3), 1.14-1.30 (6H, m, $(CH_2)_3CH_3$), 1.42 (9H, s, $C(CH_3)_3$), 2.19-2.30 (2H, m, $CH_2(CH_2)_3CH_3$), 5.27 (1H, dd, *J* = 11.0, 1.0 Hz, $CH=CH_{cis}H_{trans}$), 5.30 (1H, dd, *J* = 17.5, 1.0 Hz, $CH=CH_{cis}H_{trans}$), 6.23 (1H, ddd, *J* = 17.5, 11.0, 0.5 Hz, $CH=CH_2$), 7.23-7.26 (1H, m, Ar-**H**), 7.31-7.38 (4H, m, Ar-**H**); ^{13}C NMR (125 MHz, $CDCl_3$): δ 14.0, 22.4, 22.9, 27.8, 31.9, 37.9, 81.6, 85.7, 114.9, 125.4, 127.0, 128.1, 140.4, 142.9, 151.4; IR (neat): 2957.2 (w), 2931.4 (w), 2870.6 (w), 1743.9 (s), 1448.4 (w), 1368.1 (m), 1271.1 (s), 1153.0 (s), 1123.9 (s), 910.9 (m), 790.2 (m), 697.8 (s) cm^{-1}; HRMS (ESI+) for $C_{14}H_{19}$ [M–OBoc]: calculated: 187.1487, found: 187.1484; The unpurified reaction mixture was purified on silica gel (neutralized with 5% TEA, eluted with 100:1 hexanes/EtOAc)

to afford 4.11 g (89% yield) of a light yellow oil. R_f = 0.56 (8:1 hexanes/EtOAc, stain in $KMnO_4$).

Preparation of tert-butyl (1-(methoxymethoxy)-2-phenylbut-3-en-2-yl) carbonate. From ketone **S4**, synthesized as shown below, procedure A was followed.



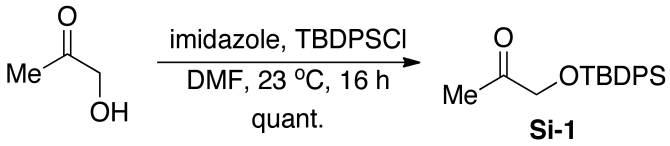
S4



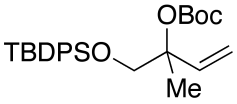
***tert*-butyl (1-(methoxymethoxy)-2-phenylbut-3-en-2-yl) carbonate (Table 1.5, entry 3)**. ^{1}H NMR (500 MHz, $CDCl_3$): δ 1.42 (9H, s, C(C**H$_3$**)$_3$), 3.21 (3H, s, OC**H$_3$**), 4.13 (1H, d, *J* = 10.0 Hz, CC**H$_a$**H$_b$O), 4.17 (1H, d, *J* = 10.0 Hz, CCH$_a$**H$_b$**O), 4.56 (1H, d, *J* = 6.5 Hz, OC**H$_a$**H$_b$O), 4.59 (1H, d, *J* = 6.5 Hz, OCH$_a$**H$_b$**O), 5.36 (1H, dd, *J* = 17.5, 0.5 Hz, CH=CH$_{cis}$**H$_{trans}$**), 5.40 (1H, dd, *J* = 11.0, 0.5 Hz, CH=C**H$_{cis}$**H$_{trans}$), 6.38 (1H, dd, *J* = 17.5, 11.0, Hz, C**H**=CH$_2$), 7.26-7.29 (1H, m, Ar-**H**), 7.33-7.36 (4H, m, Ar-**H**); ^{13}C NMR (125 MHz, $CDCl_3$): δ 27.7, 55.3, 71.4, 82.0, 84.2, 96.5, 116.9, 125.7, 127.5, 128.1, 137.7, 140.4, 151.3; IR (neat): 2979.7 (w), 2933.7 (w), 2886.8 (w), 2823.9 (w), 1743.8 (s), 1495.0 (w), 1449.2 (w), 1393.9 (m), 1270.9 (s), 1252.2 (s), 1147.8 (s), 1038.5 (s), 918.8 (m), 857.5 (m), 719.7 (s) cm^{-1}; HRMS (ESI+) for $C_{12}H_{15}O_2$ [M–OBoc]: calculated: 191.1072, found: 191.1073; The unpurified

reaction mixture was purified on silica gel (neutralized with 5% TEA, eluted with 15:1 hexanes/EtOAc) to afford 2.35 g (80% yield) of a light yellow oil. R_f = 0.30 (8:1 hexanes/EtOAc, stain in $KMnO_4$).

Preparation of tert-butyl (1-((tert-butyldiphenylsilyl)oxy)-2-methylbut-3-en-2-yl) carbonate. From ketone **Si-1**, synthesized as shown below, procedure A was followed.



Si-1

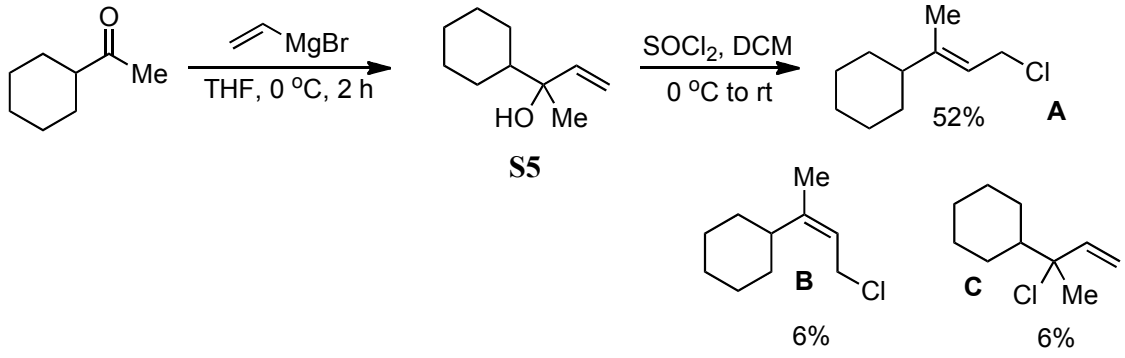


***tert*-butyl (1-((*tert*-butyldiphenylsilyl)oxy)-2-methylbut-3-en-2-yl) carbonate (Table 1.6, entry 3).** ^{1}H NMR (500 MHz, $CDCl_3$): δ 1.04 (9H, s), 1.44 (9H, s), 1.59 (3H, s), 3.68 (1H, d, *J* = 10.5 Hz), 3.84 (1H, d, *J* = 10.5 Hz), 5.19 (1H, dd, *J* = 11.0, 1.0 Hz), 5.21 (1H, dd, *J* = 17.5, 1.0 Hz), 6.03 (1H, dd, *J* = 17.5, 11.0 Hz), 7.33-7.40 (6H, m), 7.63-7.66 (4H, m); ^{13}C NMR (125 MHz, $CDCl_3$): δ 19.4, 20.9, 26.8, 27.9, 68.4, 81.5, 83.2, 115.2, 127.6, 129.7, 133.4, 135.7, 139.3, 151.8 ; IR (neat): 3072 (w), 2931 (w), 2858 (w), 1737 (s), 1472 (w), 1368 (w), 1274 (m), 1255 (m), 1165 (m), 1104 (s), 819 (m), 701 (s), 613 (m), 504 (s), 488 (m) cm^{-1}; HRMS (ESI+) for $C_{26}H_{40}O_4NSi$ [M+NH_4^+]: calculated: 458.2727, found: 458.2731; The unpurified

reaction mixture was purified on silica gel (3%EtOAc/hexanes) to afford 579 mg (83% yield) of a light yellow oil. R_f = 0.38 (3% EtOAc/hexanes, stain in $KMnO_4$).

2. Preparation and Characterization of Allylic Chlorides

Preparation of (4-chlorobut-2-en-2-yl)cyclohexane and (2-chlorobut-3-en-2-yl)cyclohexane **(Table 1.6, entry 1)** . From commercially available 1-cyclohexylethanone, procedure A was followed to synthesize allylic alcohol **S5**, which was converted the chlorides as shown below.



Procedure:[61] To a flame-dried round-bottom flask under a N_2 atomosphere was added $SOCl_2$ (1.45 mL, 20.0 mmol) and CH_2Cl_2 (8 mL) at room temperature. The resulting solution was cooled to 0 °C, and 2-cyclohexylbut-3-en-2-ol (**S5**, 308 mg, 2.0 mmol) was added dropwise. The solution was stirred at 0 °C for 0.5 h, then allowed to warm to room temperature and stir for an additional 1.5 h. The

[61] Penjišević, J.; Šukalović, V.; Andrić, D.; Kostić-Rajačić, S.; Šoškić, V.; and Roglić, G. *Arch. Pharm. Chem. Life Sci.* **2007**, *340*, 456.

solution was then cooled to 0 °C and ice-cold DI water was added to quench excess $SOCl_2$. The mixture was extracted with diethyl ether three times. The combined organics were dried over $MgSO_4$, filtered, and concentrated *in vacuo* to afford 220 mg (64% yield) of a light brown oil. The unpurified reaction mixture were used without further purification. ^{1}H NMR (500MHz, $CDCl_3$): δ 1.20-1.35 (m), 1.61 (s), 1.68-1.71 (m), 1.74-1.78 (m), 1.79-1.81(m), 4.11 (**A** & **B**, 2H, d, *J* = 8.0 Hz, CHC**H$_2$**), 5.13 (**C**, 1H, d, *J* = 10.8 Hz, CCH=C**H*$_{cis}$**H$_{trans}$), 5.26 (**C**, 1H, d, *J* = 17.3 Hz, CCH=CH$_{cis}$**H*$_{trans}$***), 5.34-5.41 (**B**, m, 1H, C=C**H**), 5.40-5.45 (**A**, m, C=C**H**), 6.01 (**C**, dd, *J* = 17.2, 10.7 Hz, CC**H**=CH$_2$); ^{13}C NMR (100 MHz, $CDCl_3$): δ 14.4, 19.8, 26.0, 26.2, 26.5, 30.9, 31.5, 41.3, 47.1, 118.4, 147.9; HRMS (ESI+) for $C_{10}H_{17}$ [M–Cl]: calculated: 137.1330, found: 137.1331.

3. Representative Procedures for Allyl-Allyl Cross-Coupling:

Representative Procedure for $Pd_2(dba)_3$ Catalyzed Coupling (without water)

An oven-dried 2-dram vial equipped with a magnetic stir bar was charged with tris(dibenzylideneacetone) dipalladium(0) (3.6 mg, 0.004 mmol), (*R*)-(+)-2,2'-bis(di-2-furanylphosphino)-6,6'-dimethoxy-1,1'-biphenyl (4.2 mg, 0.008 mmol), and THF (1.0 mL) in a dry-box under an argon atmosphere. The vial was capped and stirred for 5 minutes, then *tert*-butyl (2-phenylbut-3-en-2-yl) carbonate (49.6 mg, 0.20 mmol) was added, followed by allylboronic acid pinacol ester (40.4 mg,

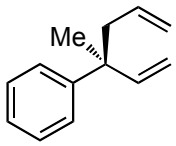
0.24 mmol) and cesium fluoride (91.1 mg, 0.60 mmol). The vial was sealed, removed from the dry-box, and allowed to stir at 60 °C for 12 hours. The vial was then cooled to ambient temperature, diluted with diethyl ether, filtered through a plug of silica gel and concentrated *in vacuo*. Analysis of the unpurified reaction mixture using ^{1}H NMR was used to determine the ratio of product to elimination product. Silica gel chromatography (pentane) afforded 27.4 mg (82% yield) of a colorless oil, with 7.3:1 allyl-allyl coupling product to elimination product.

Representative Procedure for $Pd_2(dba)_3$ Catalyzed Coupling (with water)

An oven-dried 2-dram vial equipped with a magnetic stir bar was charged with tris(dibenzylideneacetone) dipalladium(0) (3.6 mg, 0.004 mmol), (*R*)-(+)-2,2'-bis(di-2-furanylphosphino)-6,6'-dimethoxy-1,1'-biphenyl (4.2 mg, 0.008 mmol), and 1.0 mL of THF in a dry-box under an argon atmosphere. The vial was capped and stirred for 5 minutes, then *tert*-butyl (2-phenylbut-3-en-2-yl) carbonate (49.6 mg, 0.20mmol) was added, followed by allylboronic acid pinacol ester (40.4 mg, 0.24 mmol) and cesium fluoride (91.1 mg, 0.60 mol). The vial was sealed with a septum, removed from the dry-box, and then deoxygenated water (0.1 mL) was added by syringe under N_2 atomosphere. The septum was quickly replaced with a cap, and the vial was sealed again and allowed to stir at 60 °C for 12 hours. The reaction was then cooled to ambient temperature, diluted with

diethyl ether, filtered through a plug of $MgSO_4$ (top) and silica gel (bottom) and concentrated *in vacuo*. Analysis of the unpurified reaction mixture using ^1H NMR was used to determine the ratio of product to elimination ratio. Silica gel chromatography (pentane) afforded 31.0 mg (90% yield) of a colorless oil of the allyl-allyl coupling product, with less than 5% elimination product.

C. Characterization and Analysis of Stereochemistry



(*S*)-(3-methylhexa-1,5-dien-3-yl)benzene (1.23, Table 1.3, entry 1). ^1H NMR (500 MHz, $CDCl_3$): δ 1.38 (3H, s, C**H$_3$**), 2.52 (1H, dd, *J* = 14.0, 7.0 Hz, C**H$_a$**H$_b$CH=CH$_2$), 2.57 (1H, dd, *J* = 14.0, 7.0 Hz, CH$_a$**H$_b$**CH=CH$_2$), 4.98-5.14 (4H, m, CCH=C**H$_2$** & CH$_2$CH=C**H$_2$**), 5.62 (1H, dddd, *J* = 17.0, 10.0, 7.0, 7.0 Hz, CH$_2$C**H**=CH$_2$), 6.06 (1H, dd, *J* = 17.0, 11.0 Hz, CC**H**=CH$_2$), 7.18-7.22 (1H, m, Ar-**H**), 7.30-7.35 (4H, m, Ar**H**); ^{13}C NMR (125 MHz, $CDCl_3$): δ 24.9, 44.0, 45.5, 112.0, 117.2, 125.9, 126.6, 128.1, 135.1, 146.5, 147.0; IR (neat): 3080.8 (w), 3023.5 (w), 3004.7 (w), 2974.9 (w), 2921.5 (w), 1637.6 (w), 1599.9 (w), 1493.1 (w), 1444.5 (w), 1411.6 (w), 1371.5 (w), 1074.6 (w), 1028.9 (w), 995.7 (w), 911.0 (s), 764.2 (s), 697.3 (s) cm^{-1}; HRMS (ESI+) for $C_{13}H_{17}$ [M +H]: calculated: 173.1330, found: 173.1337; $[\alpha]^{20}_D$ = –4.46 (*c* = 1.54, $CHCl_3$).[62] The unpurified reaction mixture was purified on silica gel (pentane) to afford a

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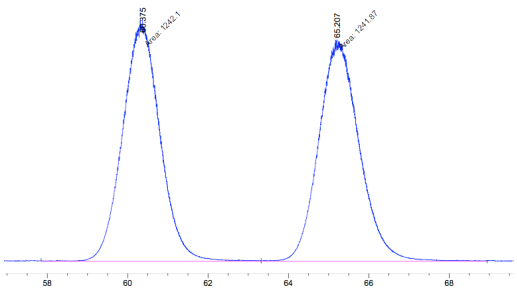
[62] Sonawane, R. P.; Jheengut, V.; Rabalakos, C.; Larouche-Gauthier, R.; Scott, H. K.; Aggarwal, V. K. *Angew. Chem. Int. Ed.* **2011**, *50*, 3760.

clear, colorless oil (31.0 mg, 90% yield), with less than 5% elimination product. R_f = 0.75 (8:1 hexane/EtOAc, stain in $KMnO_4$).

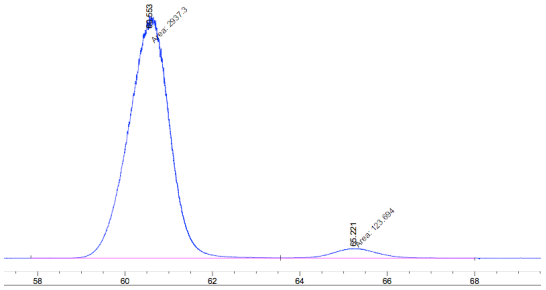
Proof of Stereochemistry:

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 assigned by analogy to **S6**. Spectral data and optical rotation are in accordance with literature.[64]

Chiral GC (CD-GTA, Supelco, 60 ˚C, 25 psi) - analysis of title compound

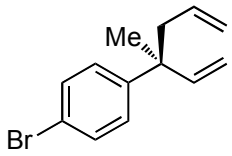


racemic



reaction product

Peak #	RetTime [min]	Type	Width [min]	Area [pA*s]	Height [pA]	Area %
1	60.553	MF	1.0818	2937.30469	45.25162	95.95903
2	65.221	FM	1.1593	123.69395	1.77827	4.04097

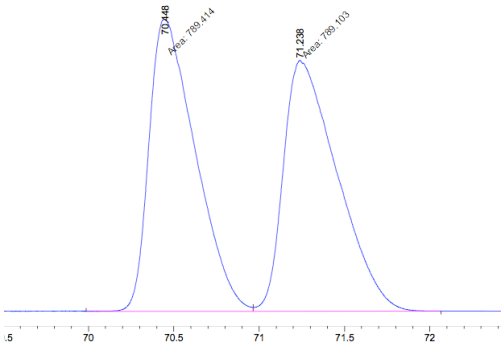


(*S*)-1-bromo-4-(3-methylhexa-1,5-dien-3-yl)benzene (Table 1.4, entry 3). ^{1}H NMR (500 MHz, $CDCl_3$): δ 1.34 (3H, s, C**H$_3$**), 2.48 (1H, dd, *J* = 13.5, 7.5 Hz, C**H$_a$**H$_b$CH=CH$_2$), 2.52 (1H, dd, *J* = 13.5, 7.5 Hz, CH$_a$**H$_b$**CH=CH$_2$), 4.99-5.06 (3H, m, CCH=CH$_{cis}$**H$_{trans}$** & CH$_2$CH=C**H$_2$**), 5.14 (1H, dd, *J* = 10.5, 1.0 Hz, CCH=C**H$_{cis}$**H$_{trans}$), 5.57 (1H, dddd, *J* = 17.0, 10.0, 7.5, 7.5 Hz, CH$_2$C**H**=CH$_2$), 6.00 (1H, dd, *J* = 17.5, 10.5 Hz, CC**H**=CH$_2$), 7.18-7.21 (2H, m, Ar-**H**), 7.40-7.43 (2H, m, Ar-**H**); ^{13}C NMR (125 MHz, $CDCl_3$): δ 24.9, 43.9, 45.4, 112.5, 117.6, 119.8, 128.6, 131.1, 134.6, 145.9, 146.0; IR (neat): 3097.2 (w), 3004.2 (w), 2974.9 (w), 2919.3 (w), 2849.9 (w), 1637.9 (w), 1489.7 (m), 1412.9 (w), 1106.4 (m), 1007.5 (s), 912.5 (s), 818.9 (s), 729.3 (m), 533.8 (m) cm^{-1}; HRMS (ESI+) for $C_{13}H_{16}Br$ [M+H]: calculated: 251.0435, found: 251.0430; $[\alpha]^{20}_D$ = –5.363 (*c* = 2.51, $CHCl_3$). The unpurified reaction mixture was purified on silica gel (pentane) to afford a clear, colorless oil (44.7 mg, 90% yield), with 20:1 allyl-allyl coupling product to elimination product. R_f = 0.72 (8:1 hexanes/EtOAc, stain in $KMnO_4$).

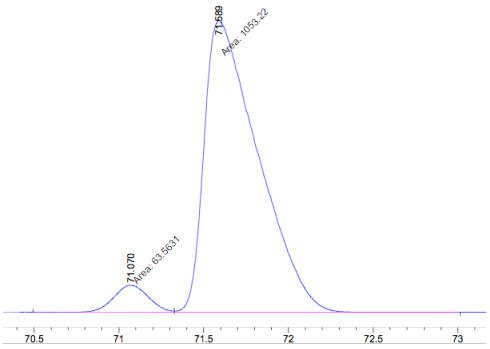
Proof of Stereochemistry:

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 assigned by analogy to **S6**.

Chiral GC (β-dex, Supelco, 100 ˚C 10 min, ramp 0.5 deg/min to 180 ˚C, 25 psi) - analysis of title compound

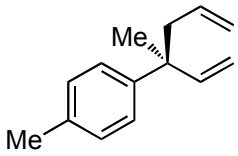


racemic



reaction product

Peak #	RetTime [min]	Type	Width [min]	Area [pA*s]	Height [pA]	Area %
1	71.070	MF	0.2384	63.56308	4.44339	5.69163
2	71.589	FM	0.3674	1053.21863	47.77425	94.30837



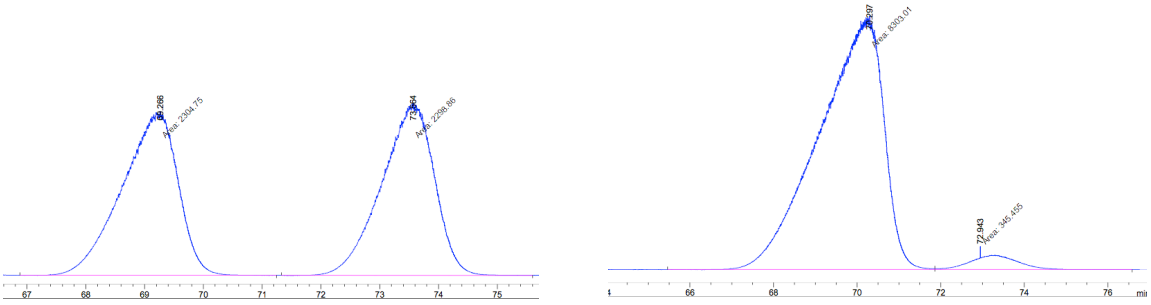
(*S*)-1-methyl-4-(3-methylhexa-1,5-dien-3-yl)benzene (Table 1.4, entry 1). ^{1}H NMR (500 MHz, $CDCl_3$): δ 1.35 (3H, s, C**H**$_3$CCH=CH$_2$), 2.33 (3H, s, ArC**H**$_3$), 2.50 (1H, dddd, *J* = 14.0, 7.0, 1.5, 1.5 Hz, C**H**$_a$H$_b$CH=CH$_2$), 2.55 (1H, dddd, *J* = 14.0, 7.0, 1.5, 1.5 Hz, CH$_a$**H**$_b$CH=CH$_2$), 4.97-5.06 (3H, m, CCH=CH$_{cis}$**H**$_{trans}$ & CH$_2$CH=C**H**$_2$), 5.11 (1H, dd, *J* = 10.5, 1.0 Hz, CCH=C**H**$_{cis}$H$_{trans}$), 5.61 (1H, dddd, *J* = 17.0, 10.0, 7.0, 7.0 Hz, CH$_2$C**H**=CH$_2$), 6.03 (1H, dd, *J* = 17.0, 10.5 Hz, CC**H**=CH$_2$), 7.11-7.13 (2H, m, Ar-**H**), 7.21-7.23 (2H, m, Ar-**H**); ^{13}C NMR (125 MHz, $CDCl_3$): δ 20.9, 24.9, 43.7, 45.5, 111.8, 117.1, 126.5, 128.8, 135.2, 135.3, 144.0, 146.7; IR (neat): 3078.6 (w), 3003.5 (w), 2974.6 (w), 2921.4 (w), 1638.1 (s), 1512.9 (m), 1454.7 (w),

1412.8 (w), 1370.5 (w), 996.0 (m), 910.9 (s), 814.1 (s), 728.6 (m) cm^{-1}; HRMS (ESI+) for $C_{14}H_{19}$ [M+H]: calculated: 187.1487, found: 187.1477; $[\alpha]^{20}_D$ = –2.877 (*c* = 1.83, $CHCl_3$). The unpurified reaction mixture was purified on silica gel (pentane) to afford a clear, colorless oil (27.9 mg, 76% yield), with 17:1 allyl-allyl coupling product to elimination product. R_f = 0.63 (8:1 hexanes/EtOAc, stain in $KMnO_4$).

Proof of Stereochemistry:

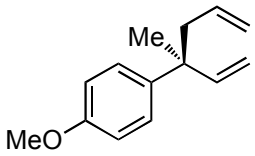
Enantioselectivity was determined by comparison of the title compound with racemic material prepared using 1,2-bis(diphenylphosphino)benzene as the achiral ligand in the allyl-allyl coupling reaction. Absolute stereochemistry was assigned by analogy to **S6**.

Chiral GC (CD-GTA, Supelco, 70 ˚C, 25 psi) - analysis of title compound



racemic reaction product

Peak #	RetTime [min]	Type	Width [min]	Area [pA*s]	Height [pA]	Area %
1	70.297	MF	1.7618	8303.00879	78.54633	96.00559
2	72.943	FM	0.7885	345.45468	7.30192	3.99441

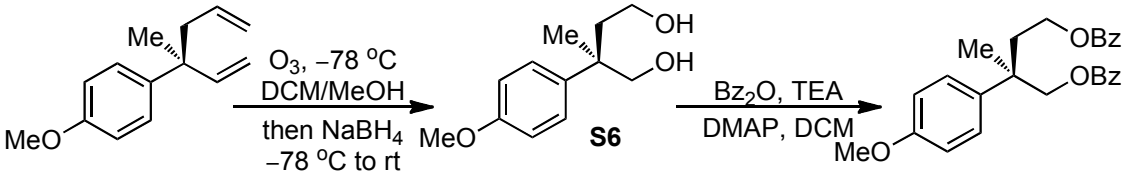


(*S*)-1-methoxy-4-(3-methylhexa-1,5-dien-3-yl)benzene (S6, Table 1.4, entry 5). ^{1}H NMR (500 MHz, $CDCl_3$): δ 1.34 (3H, s, C**H$_3$**), 2.48 (1H, dd, *J* = 14.0, 7.0 Hz, C**H$_a$**H$_b$CH=CH$_2$), 2.53 (1H, dd, *J* = 14.0, 7.0 Hz, CH$_a$**H$_b$**CH=CH$_2$), 3.79 (3H, s, OC**H$_3$**), 4.97-5.10 (4H, m, CCH=C**H$_2$** & CH$_2$CH=C**H$_2$**), 5.60 (1H, dddd, *J* = 17.0, 10.0, 7.0, 7.0 Hz, CH$_2$C**H**=CH$_2$), 6.02 (1H, dd, *J* = 17.5, 11.0 Hz, CC**H**=CH$_2$), 6.83-6.86 (2H, m, Ar-**H**), 7.22-7.25 (2H, m, Ar-**H**); ^{13}C NMR (125 MHz, $CDCl_3$): δ 25.0, 43.4, 45.6, 55.2, 111.7, 113.4, 117.1, 127.6, 135.2, 139.0, 146.8, 157.6; IR (neat): 3072.7 (w), 3000.7 (w), 2973.7 (w), 2933.0 (w), 2834.5 (w), 1637.1 (w), 1510.3 (s), 1296.3 (m), 1246.3 (s), 1181.1 (s), 1035.5 (s), 996.3 (m), 910.4 (s), 826.6 (s) cm^{-1}; HRMS (ESI+) for $C_{14}H_{19}O$ [M+H]: calculated: 203.1436, found: 203.1443; $[\alpha]^{20}_D$ = –6.027 (*c* = 1.14, $CHCl_3$). The unpurified reaction mixture was purified on silica gel (50:1 pentane/Et_2O) to afford a clear, colorless oil (42.0 mg, 83% yield), with 12:1 allyl-allyl coupling product to elimination product. R_f = 0.56 (8:1 hexanes/ EtOAc, stain in $KMnO_4$).

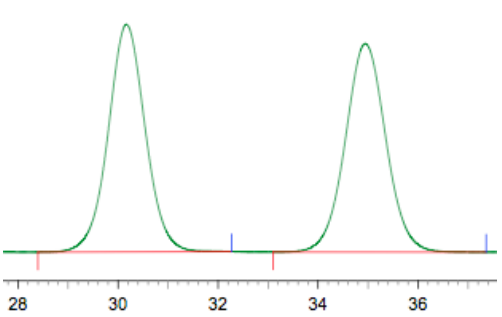
Proof of Stereochemistry:

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 the achiral ligand in the allyl-allyl coupling reaction. Absolute stereochemistry was

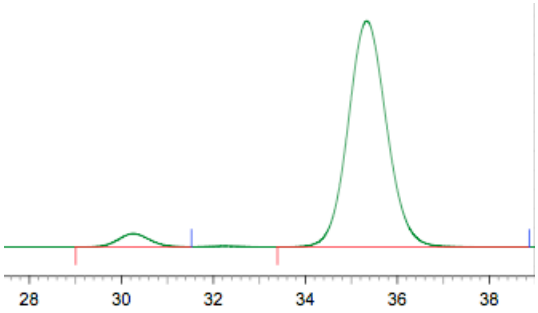
determined by X-ray crystallographic analysis (anomalous dispersion) of the diol (**S6**).



Chiral HPLC (AD-H, Chirapak, 1 mL/min, 2% isopropanol, 220 nm) – analysis of 2-(4-methoxyphenyl)-2-methylbutane-1,4-diyl dibenzoate

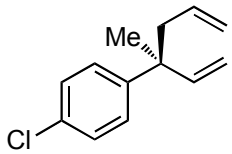


racemic



reaction product

Retention Time	Area	Area %	Height	Height %
30.257	55422548	4.61	1151133	5.53
35.337	1146702137	95.39	19674468	94.47
Totals	1202124685	100.00	20825601	100.00

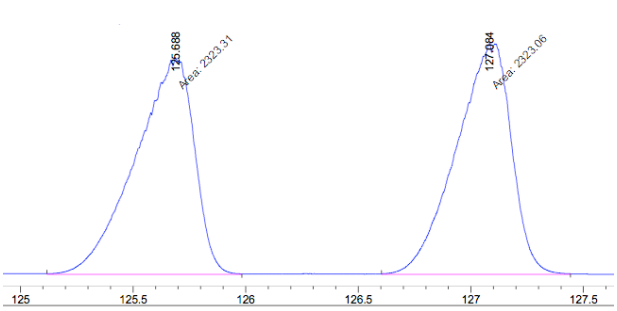


(*S*)-4-chloro-4-(3-methylhexa-1,5-dien-3-yl)benzene (Table 1.4, entry 2). ^{1}H NMR (500 MHz, $CDCl_3$): δ 1.35 (3H, s, CC**H$_3$**), 2.48 (1H, dd, *J* = 13.9, 7.2 Hz, C**H$_a$**H$_b$C=CH$_2$), 2.53 (1H, dd, *J* = 13.9, 7.2 Hz, CH$_a$**H$_b$**C=CH$_2$), 4.99-5.06 (3H, m, CCH=CH$_{cis}$**H$_{trans}$** & CH$_2$CH=C**H$_2$**), 5.13 (1H, d, *J* = 10.8 Hz, CCH=C**H$_{cis}$**), 5.57 (1H, dddd, *J* = 16.8, 9.8, 7.2, 7.2 Hz, CH$_2$C**H**=CH$_2$), 6.00 (1H, dd, *J* = 17.6, 10.8 Hz, CC**H**=CH$_2$), 7.24-7.28 (4H, m, Ar-**H**); ^{13}C NMR (125 MHz, $CDCl_3$): δ 24.9, 43.8, 45.5, 112.4, 117.6, 128.1, 128.2, 131.7, 134.6, 145.5, 146.0; IR (neat): 3081.2 (w), 2924.1 (s), 2867.5 (m), 1638.9 (w), 1493.3 (s), 1461.0 (w), 1399.5 (w), 1372.0 (w), 1097.1 (m), 1012.8 (s), 995.8 (m), 915.6 (s), 825.2 (s), 748.7 (w), 536.6 (w) cm^{-1}; HRMS (ESI+) for $C_{13}H_{16}Cl$ [M+H]: calculated: 207.0941, found: 207.0940; $[\alpha]^{20}_D$ = –2.087 (*c* = 0.40, $CHCl_3$). The unpurified material was purified on silica gel (pentane) to afford a clear, colorless oil (50.8 mg, 70% yield), with less than 5% elimination product. R_f = 0.70 (pentane, stain in $KMnO_4$).

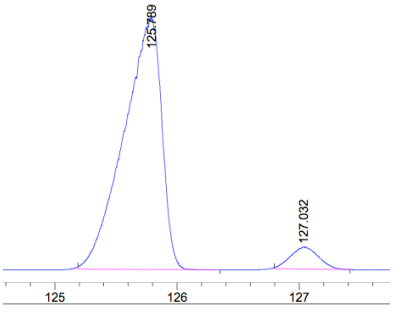
Proof of Stereochemistry:

Enantioselectivity was determined by comparison of the title compound with racemic material prepared using 1,2-bis(diphenylphosphino)benzene as achiral ligand in the allyl-allyl coupling reaction. Absolute stereochemistry was assigned by analogy to **S6**.

Chiral GC (CD-GTA, Supelco, 60 °C, 80 min, 1.0 deg/min to 120 °C, 25 psi)-analysis of title compound

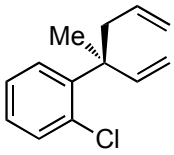


racemic



reaction product

Peak #	RetTime [min]	Type	Width [min]	Area [pA*s]	Height [pA]	Area %
1	125.789	BB	0.2567	3800.16162	177.55411	93.86945
2	127.032	BB	0.1903	248.18599	15.54616	6.13055



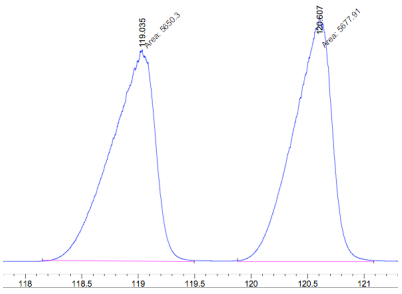
(*S*)-1-chloro-2-(3-methylhexa-1,5-dien-3-yl)benzene (Table 1.4, entry 4). ^{1}H NMR (500 MHz, $CDCl_3$): δ 1.49 (3H, s, CC**H$_3$**), 2.63 (1H, dd, *J* = 13.9, 7.2 Hz, C**H$_a$**H$_b$CH=CH$_2$), 3.02 (1H, dd, *J* = 13.9, 7.2 Hz, CH$_a$**H$_b$**CH=CH$_2$), 4.93-4.96 (m, 2H, CCH=CH$_{cis}$**H$_{trans}$** & CH$_2$CH=C**H$_{cis}$**H$_{trans}$), 5.03 (1H, m, CH$_2$CH=CH$_{cis}$**H$_{trans}$**), 5.10 (1H, dd, *J* = 10.7, 1.0 Hz, CCH=C**H$_{cis}$**H$_{trans}$), 5.52 (1H, dddd, *J* = 17.0, 10.3, 7.2, 7.2 Hz, CH$_2$C**H**=CH$_2$), 6.20 (1H, dd, *J* = 17.6, 10.7 Hz, CC**H**=CH$_2$), 7.14-7.17 (1H, m, Ar-**H**), 7.19-7.22 (1H, m, Ar-**H**), 7.33-7.35 (1H, m, Ar-**H**), 7.36-7.38 (1H, m, Ar-**H**); ^{13}C NMR (125 MHz, $CDCl_3$): δ 25.7, 42.9, 45.0, 112.3, 117.3, 126.4, 127.6, 129.2, 131.7, 133.8, 134.8, 143.2, 145.7; IR (neat): 3077.2 (w), 3003.9 (w), 2975.9 (w),

2921.8 (w), 1638.5 (w), 1468.2 (m), 1430.2 (m), 1411.7 (m), 1037.9 (m), 993.6 (m), 913.6 (s), 860.0 (m), 757.0 (m) cm^{-1}; HRMS (ESI+) for $C_{13}H_{16}Cl$ [M+H]: calculated: 207.0941, found: 207.0940. $[\alpha]^{20}_D = -25.936$ (*c* = 0.97, $CHCl_3$). The unpurified reaction mixture was purified on silica gel (pentane) to afford a clear, colorless oil (38.3 mg, 97% yield), with 4:1 allyl-allyl coupling product to elimination product. $R_f = 0.58$ (pentane, stain in $KMnO_4$).

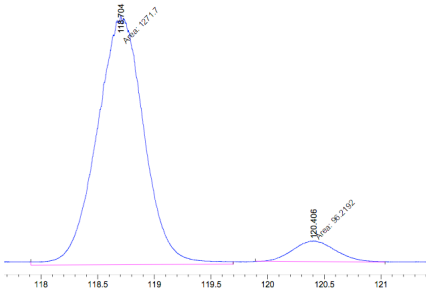
Proof of Stereochemistry:

Enantioselectivity was determined by comparison of the title compound with racemic material prepared using 1,2-bis(diphenylphosphino)benzene as achiral ligand in the allyl-allyl coupling reaction. Absolute stereochemistry was assigned by analogy to **S6**.

Chiral GC (CD-GTA, Supelco, 60 °C, 80 min, 1.0 deg/min to 120 °C, 25 psi)-analysis of the title compound

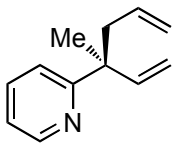


racemic



reaction product

Peak #	RetTime [min]	Type	Width [min]	Area [pA*s]	Height [pA]	Area %
1	118.704	MM	0.4831	1271.70264	43.87696	92.96603
2	120.406	MM	0.4385	96.21922	3.65722	7.03397



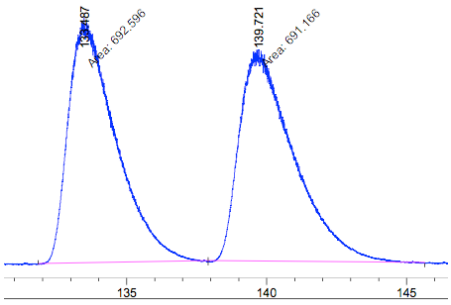
(*S*)-2-(3-methylhexa-1,5-dien-3-yl)pyridine (Table 1.4, entry 7). ^{1}H NMR (500 MHz, $CDCl_3$): δ 1.42 (3H, s, CC**H$_3$**), 2.61 (1H, dddd, *J* = 13.9, 7.0, 1.3, 1.3 Hz, C**H$_a$**H$_b$CH=CH$_2$), 2.70 (1H, dddd, *J* = 13.9, 7.5, 1.3, 1.3 Hz, CH$_a$**H$_b$**CH=CH$_2$), 4.97 (1H, dddd, *J* = 9.6, 2.2, 1.3, 1.3 Hz, CH$_2$CH=C**H$_{cis}$**H$_{trans}$), 5.01 (1H, dddd, *J* = 17.0, 2.2, 1.3, 1.3 Hz, CH$_2$CH=CH$_{cis}$**H$_{trans}$**), 5.09 (1H, dd, *J* = 17.5, 1.2 Hz, CCH=CH$_{cis}$**H$_{trans}$**), 5.16 (1H, dd, *J* = 10.8, 1.2 Hz, CCH=C**H$_{cis}$**H$_{trans}$), 5.62 (1H, dddd, *J* = 17.0, 9.6, 7.5, 7.0 Hz, CH$_2$C**H**=CH$_2$), 6.19 (1H, dd, *J* = 17.5, 10.8 Hz, CC**H**=CH$_2$), 7.10 (1H, ddd, *J* = 5.9, 4.9, 1.2 Hz, Ar-**H**), 7.28 (1H, ddd, *J* = 8.1, 1.0, 1.0 Hz, Ar-**H**), 7.60 (1H, ddd, *J* = 8.0, 7.3, 1.9 Hz, Ar-**H**), 8.59 (1H, dq, *J* = 4.7, 1.0 Hz, Ar-**H**); ^{13}C NMR (125 MHz, $CDCl_3$): δ 23.5, 45.0, 46.7, 112.6, 117.3, 121.0, 121.1, 135.1, 136.1, 145.5,

148.8, 165.9; IR (neat): 3079.3 (w), 3004.4 (m), 2975.2 (m), 2926.7 (w), 1638.1 (m), 1587.5 (s), 1569.7 (m), 1468.5 (m), 1430.0 (m), 1047.1 (m), 913.4 (s), 788.4 (m), 747.1 (s), 402.7 (w) cm^{-1}; HRMS (ESI+) for $C_{12}H_{16}N$ [M+H]: calculated: 174.1283, found: 174.1291; $[\alpha]^{20}_D$ = +28.437 (*c* = 0.36, $CHCl_3$). The unpurified reaction mixture was purified on silica gel (19:1 pentane/Et_2O) to afford a clear, colorless oil (40.0 mg, 81% yield), with less than 5% elimination product. R_f = 0.26 (9:1 pentane/Et_2O, stain in $KMnO_4$).

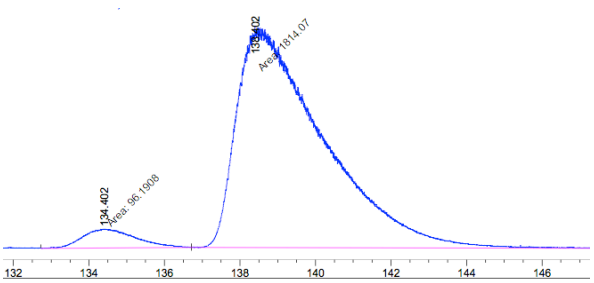
Proof of Stereochemistry:

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 assigned by analogy to **S6**.

Chiral GC (CD-GTA, Supelco, 55 °C, 25 psi)-analysis of title compound

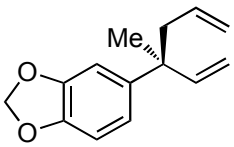


racemic



reaction product

Peak #	RetTime [min]	Type	Width [min]	Area [pA*s]	Height [pA]	Area %
1	134.402	MM	1.6146	96.19075	9.92949e-1	5.03547
2	138.402	MM	2.6311	1814.07385	11.49119	94.96453



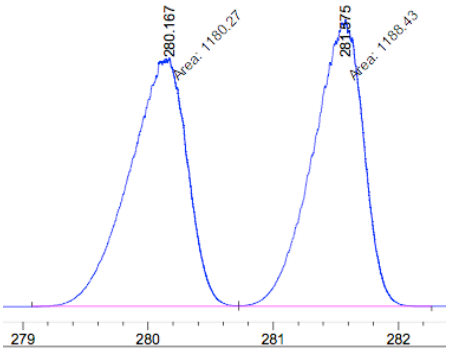
(*S*)-5-(3-methylhexa-1,5-dien-3-yl)benzo[*d*][1,3]dioxole (Table 1.4, entry 6). ^{1}H NMR (500 MHz, $CDCl_3$): δ 1.32 (3H, s, CC**H$_3$**), 2.46 (1H, dd, *J* = 13.8, 7.1 Hz, C**H$_a$**H$_b$CH=CH$_2$), 2.51 (1H, dd, *J* = 13.8, 7.1 Hz, CH$_a$**H$_b$**CH=CH$_2$), 4.98-5.03 (2H, m, CH$_2$CH=C**H$_2$**), 5.04 (1H, dd, *J* = 17.4, 1.1 Hz, CCH=CH$_{cis}$**H$_{trans}$**), 5.10 (1H, dd, *J* = 10.8, 1.1 Hz, CCH=C**H$_{cis}$**H$_{trans}$), 5.60 (1H, dddd, 17.4, 10.3, 7.1, 7.1 Hz, CH$_2$C**H**=CH$_2$), 5.93 (2H, s, OC**H$_2$**O), 6.00 (1H, dd, *J* = 17.4, 10.8 Hz, CC**H**=CH$_2$), 6.73-6.78 (2H, m, Ar-**H**), 6.82-6.84 (1H, m, Ar-**H**); ^{13}C NMR (125 MHz, $CDCl_3$): δ 25.2, 43.9, 45.6, 100.8, 107.6, 107.7, 111.9, 117.3, 119.5, 135.0, 141.1, 145.5, 146.6, 147.5; IR (neat): 3077.7 (w), 2971.8 (w), 2922.9 (w), 2775.6 (w), 1637.9 (w), 1503.8 (m), 1485.1 (s), 1431.9 (m), 1232.4 (s), 1039.7 (s), 938.4 (m), 912.5 (s), 808.5 (m),

554.3 (w) cm^{-1}; HRMS (ESI+) for $C_{14}H_{17}O_2$ [M+H]: calculated: 217.1229, found: 217.1224; $[\alpha]^{20}_D = -1.600$ (*c* = 0.69, $CHCl_3$). The unpurified reaction mixture was purified on silica gel (pentane) to afford a clear, colorless oil (39.4 mg, 94% yield), with 6:1 allyl-allyl coupling product to elimination product. R_f = 0.39 (pentane, stain in $KMnO_4$).

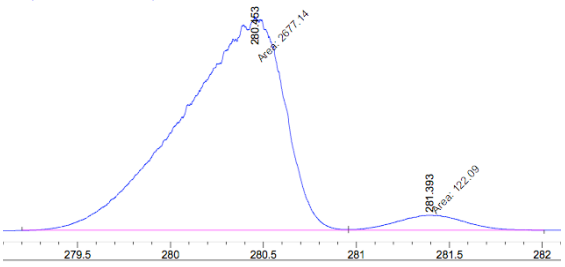
Proof of Stereochemistry:

Enantioselectivity was determined by comparison of the title compound with racemic material prepared using 1,2-bis(diphenylphosphino)benzene as achiral ligand in the allyl-allyl coupling reaction. Absolute stereochemistry was assigned by analogy to entry **S6**.

Chiral GLC (CD-GTA, Supelco, 55 °C, 25 psi)-analysis of title compound

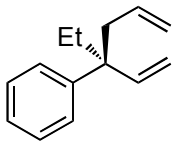


racemic



reaction product

Peak #	RetTime [min]	Type	Width [min]	Area [pA*s]	Height [pA]	Area %
1	280.453	MM	0.6316	2677.13745	70.64734	95.63845
2	281.393	MM	0.4152	122.08971	4.90134	4.36155

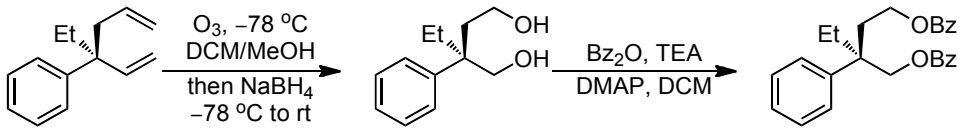


(*S*)-(3-ethylhexa-1,5-dien-3-yl)benzene (Table 1.5, entry 1). ^{1}H NMR (500 MHz, $CDCl_3$): δ 0.75 (3H, t, J = 7.5 Hz, C**H$_3$**), 1.78 (1H, dq, J = 13.5, 7.5 Hz, C**H$_a$**H$_b$CH$_3$), 1.84 (1H, dq, J = 13.5, 7.5 Hz, CH$_a$**H$_b$**CH$_3$), 2.55 (2H, d, J = 7.0 Hz, C**H$_2$**CH=CH$_2$), 4.98 (1H, dddd, J = 10.5, 2.5, 1.5, 1.0 Hz, CH$_2$CH=C**H$_{cis}$**H$_{trans}$), 5.02 (1H, dddd, J = 17.0, 2.0, 1.5, 1.0 Hz, CH$_2$CH=CH$_{cis}$**H$_{trans}$**), 5.10 (1H, dd, J = 17.5, 1.0 Hz, CCH=CH$_{cis}$**H$_{trans}$**), 5.22 (1H, dd, J = 11.0, 1.5 Hz, CCH=C**H$_{cis}$**H$_{trans}$), 5.59 (1H, ddt, J = 17.5, 10.0, 7.0 Hz, CH$_2$C**H**=CH$_2$), 5.94 (1H, dd, J = 17.5, 11.0 Hz, CC**H**=CH$_2$), 7.18-7.21 (1H, m, Ar-**H**), 7.29-7.33 (4H, m, Ar-**H**); ^{13}C NMR (125 MHz, $CDCl_3$): δ 8.3, 29.4, 41.2, 47.6, 113.0, 116.9, 125.8, 127.4, 127.9, 135.0, 145.2, 145.5; IR (neat): 3081.4 (w), 3023.4 (w), 3003.9 (w), 2969.5 (w), 2928.9 (w), 2878.8 (w), 1637.3 (w), 1599.2 (w), 1493.5 (w), 1445.0 (m), 1032.3 (m), 910.7 (s), 782.1 (m), 720.2 (s) cm^{-1}; HRMS (ESI+) for $C_{14}H_{19}$ [M+H]: calculated: 187.1487, found: 187.1486; $[\alpha]^{20}_D$ = –18.262 (c = 0.87, $CHCl_3$). The unpurified reaction mixture was purified on silica gel (pentane) to afford a clear, colorless oil (34.9 mg, 97% yield), with 6:1 allyl-allyl coupling product to elimination product. R_f = 0.80 (8:1 hexanes/EtOAc, stain in $KMnO_4$).

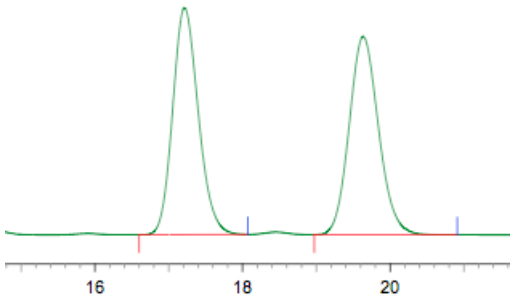
Proof of Stereochemistry:

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

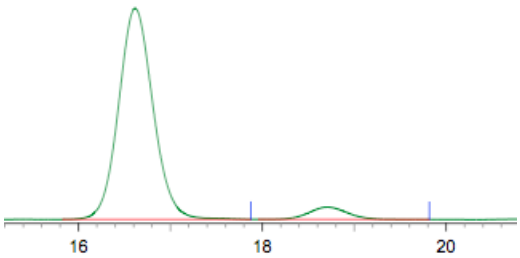
prepared *via* the same route using 1,2-bis(diphenylphosphino)benzene as the achiral ligand in the allyl-allyl coupling reaction. Absolute stereochemistry was assigned by analogy to entry **S6**.



Chiral HPLC (AD-H, Chiralpak, 1 mL/min, 2% isopropanol, 220 nm) – analysis of 2-ethyl-2-phenylbutane-1,4-diyl dibenzoate

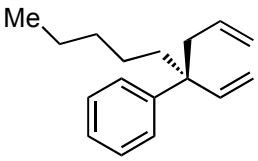


racemic



reaction product

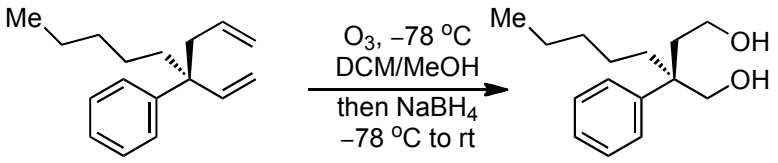
Retention Time	Area	Area %	Height	Height %
16.617	52915233	93.90	2028796	94.50
18.707	3435601	6.10	118052	5.50
Totals	56350834	100.00	2146848	100.00



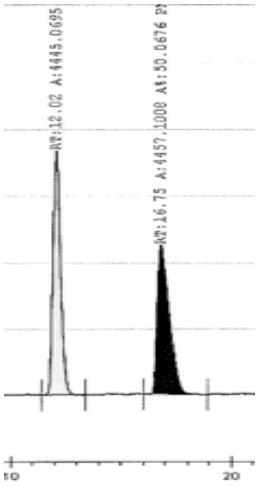
(*S*)-(4-vinylnon-1-en-4-yl)benzene (Table 1.5, entry 2). ^{1}H NMR (500 MHz, $CDCl_3$): δ 0.83 (3H, t, *J* = 7.0 Hz, C**H$_3$**), 1.05-1.29 (6H, m, (C**H$_2$**)$_3$CH$_3$), 1.67-1.79 (2H, m, C**H$_2$**(CH$_2$)$_3$CH$_3$), 2.55 (2H, d, *J* = 7.5 Hz, C**H$_2$**CH=CH$_2$), 4.96-5.02 (2H, m, CH$_2$CH=C**H$_2$**), 5.08 (1H, dd, *J* = 17.0, 1.0 Hz, CCH=CH$_{cis}$**H$_{trans}$**), 5.19 (1H, dd, *J* = 10.5, 1.0 Hz, CCH=C**H$_{cis}$**H$_{trans}$), 5.58 (1H, ddt, *J* = 17.0, 10.0, 7.0 Hz, CH$_2$C**H**=CH$_2$), 5.94 (1H, dd, *J* = 17.0, 10.5 Hz, CC**H**=CH$_2$), 7.16-7.20 (1H, m, Ar-**H**), 7.28-7.32 (4H, m, Ar-**H**); ^{13}C NMR (125 MHz, $CDCl_3$): δ 14.1, 22.5, 23.4, 32.5, 37.1, 41.9, 47.3, 112.7, 116.9, 125.8, 127.3, 127.9, 135.1, 145.5, 145.8; IR (neat): 3081.1 (w), 3004.0 (w), 2930.7 (m), 2860.5 (w), 1637.5 (w), 1493.8 (w), 1445.3 (m), 1378.1 (w), 1073.2 (m), 910.6 (s), 697.8 (s) cm^{-1}; HRMS (ESI+) for $C_{17}H_{25}$ [M+H]: calculated: 229.1956, found: 229.1954; $[\alpha]^{20}_D$ = –5.292 (*c* = 1.69, $CHCl_3$). The unpurified reaction mixture was purified on silica gel (pentane) to afford a clear, colorless oil (34.6 mg, 78% yield), with 6:1 allyl-allyl coupling product to elimination product. R_f = 0.86 (8:1 hexanes/EtOAc, stain in $KMnO_4$).

Proof of Stereochemistry:

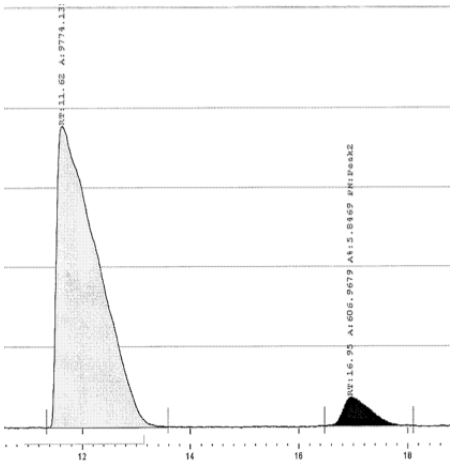
The title compound was subjected to ozonolysis and reduction, as depicted below. The resulting diol was analyzed by chiral SFC. The analogous racemic material was prepared *via* the same route using 1,2-bis(diphenylphosphino)benzene as the achiral ligand in the allyl-allyl coupling reaction. Absolute stereochemistry was assigned by analogy to entry **S6**.



Chiral SFC (AS-H, Chiralpak, 3 mL/min, 3% methanol, 220 nm) – analysis of 2-pentyl-2-phenylbutane-1,4-diol



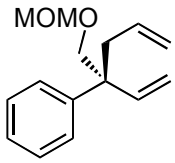
racemic



reaction product

Peak Name	Number	Concentration	Area %	Area	Area Sum
Peak1	1	0	94.1531	9774.1352	
Peak2	2	0	5.8469	606.9679	10381.1031

RT (min)	St. (min)	End (min)	Height
11.62	11.3404	13.5842	189.5781
16.95	16.4748	18.0968	17.9589

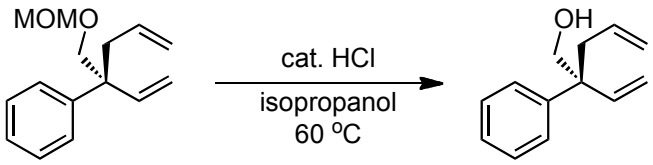


(*R*)-(3-((methoxymethoxy)methyl)hexa-1,5-dien-3-yl)benzene (Table 1.5, entry 3). ^{1}H NMR (500 MHz, $CDCl_3$): δ 2.67 (2H, d, *J* = 7.0 Hz, C**H**$_2$CH=CH$_2$), 3.25 (3H, s, OC**H**$_3$), 3.78 (1H, d, *J* = 9.0 Hz,

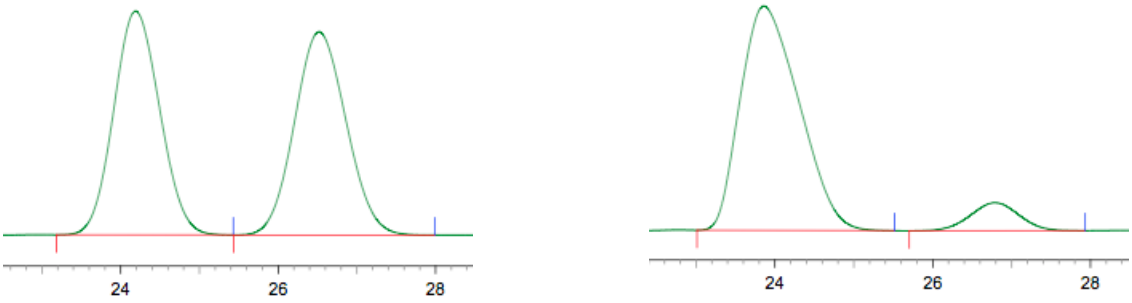
CC**H**$_a$H$_b$O), 3.84 (1H, d, *J* = 9.0 Hz, CCH$_a$**H**$_b$O), 4.56 (1H, d, *J* = 6.5 Hz, OC**H**$_a$H$_b$O), 4.59 (1H, d, *J* = 6.5 Hz, OCH$_a$**H**$_b$O), 5.01 (1H, dddd, *J* = 10.0, 2.0, 1.5, 1.0 Hz, CH$_2$CH=C**H**$_{cis}$H$_{trans}$), 5.06 (1H, dddd, *J* = 17.0, 2.0, 1.5, 1.0 Hz, CH$_2$CH=CH$_{cis}$**H**$_{trans}$), 5.12 (1H, dd, *J* = 17.0, 1.0 Hz, CCH=CH$_{cis}$**H**$_{trans}$), 5.26 (1H, dd, *J* = 11.0, 1.0 Hz, CCH=C**H**$_{cis}$H$_{trans}$), 5.64 (1H, ddt, *J* = 17.0, 10.0, 7.0 Hz, CH$_2$C**H**=CH$_2$), 6.04 (1H, dd, *J* = 17.0, 11.0 Hz, CC**H**=CH$_2$), 7.19-7.23 (1H, m, Ar-**H**), 7.30-7.36 (4H, m, Ar-**H**); ^{13}C NMR (125 MHz, $CDCl_3$): δ 40.3, 48.2, 55.3, 72.5, 96.7, 114.2, 117.7, 126.3, 127.4, 128.0, 134.4, 142.8, 143.4; IR (neat): 3170.5 (w), 3081.9 (w), 2978.5 (m), 2925.9 (w), 2822.2 (w), 1638.2 (w), 1600.1 (w), 1495.3 (w), 1466.8 (w), 1290.2 (w), 1215.8 (m), 1150.9 (m), 1110.5 (s), 998.5 (s), 748.5 (m) cm^{-1}; HRMS (ESI+) for $C_{15}H_{21}O_2$ [M+H]: calculated: 233.1542, found: 233.1551; $[\alpha]^{20}_D$ = +0.850 (*c* = 1.94, $CHCl_3$). The unpurified reaction mixture was purified on silica gel (100:1 pentane/Et_2O) to afford a clear, colorless oil (26.9 mg, 58% yield), with less than 5% elimination product. R_f = 0.51 (8:1 hexanes/EtOAc, stain in $KMnO_4$).

Proof of Stereochemistry:

The title compound was subjected to acid catalyzed MOM deprotection, as depicted below. The resulting alcohol was subjected to HPLC analysis. 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. Absolute stereochemistry was assigned by analogy to **S6**.

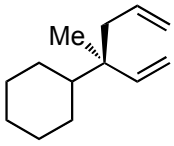


Chiral HPLC (OD-R, Chiracel, 0.5 mL/min, 2% isopropanol, 220 nm) – analysis of 2-phenyl-2-vinylpent-4-en-1-ol



racemic reaction product

Retention Time	Area	Area %	Height	Height %
23.860	822324844	90.57	15924827	88.91
26.790	85579539	9.43	1987248	11.09
Totals	907904383	100.00	17912075	100.00



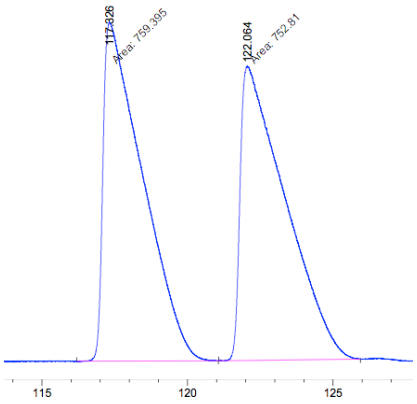
(*S*)-(3-methylhexa-1,5-dien-3-yl)cyclohexane (Table 1.6, entry 1). ^{1}H NMR (500 MHz, $CDCl_3$): δ 0.87-0.98 (m), 1.20-1.29 (m), 1.62-1.76 (m), 2.10 (2H, d, *J* = 7.0 Hz, CC**H$_2$**CH), 4.88 (1H, dd, *J* = 17.6, 1.5 Hz, CCH=C**H$_a$**H$_b$), 4.96-5.02 (3H, m, CCH=CH$_a$**H$_b$** & CH$_2$CHC=C**H$_2$**), 5.70-5.79 (1H, m, CH$_2$C**H**=CH$_2$), 5.75 (1H, dd, *J* = 17.6, 8.7 Hz, CC**H**=CH$_2$); ^{13}C NMR (100 MHz, $CDCl_3$): δ 19.2, 26.8, 27.1, 27.7, 42.2, 43.3, 45.8, 112.1, 116.5, 135.7, 146.1; IR (neat): 2924.6 (s), 2852.8 (m), 1638.3 (w), 1448.9 (m), 1374.2

(w), 1002.7 (w), 909.9 (m); HMRS (ESI+) for $C_{13}H_{22}$ [M+H]: calculated: 179.1805, found: 179.1800; $[\alpha]^{20}_D$ = +6.858 (*c* = 0.96, $CHCl_3$). The unpurified reaction mixture was purified on silica gel (pentane) to afford a colorless oil (23.3 mg, 45% yield), with 7:1 allyl-allyl coupling product to elimination product. R_f = 0.83 (pentane, stain in $KMnO_4$).

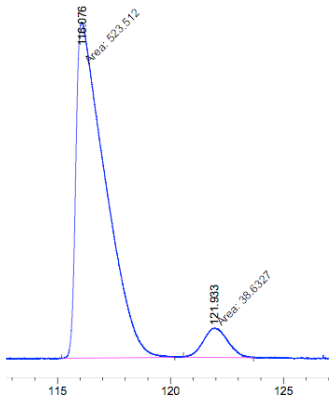
Proof of Stereochemistry:

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.

Chiral GC (CD-GTA, Supelco, 70 °C, 20 psi)-analysis of the title compound



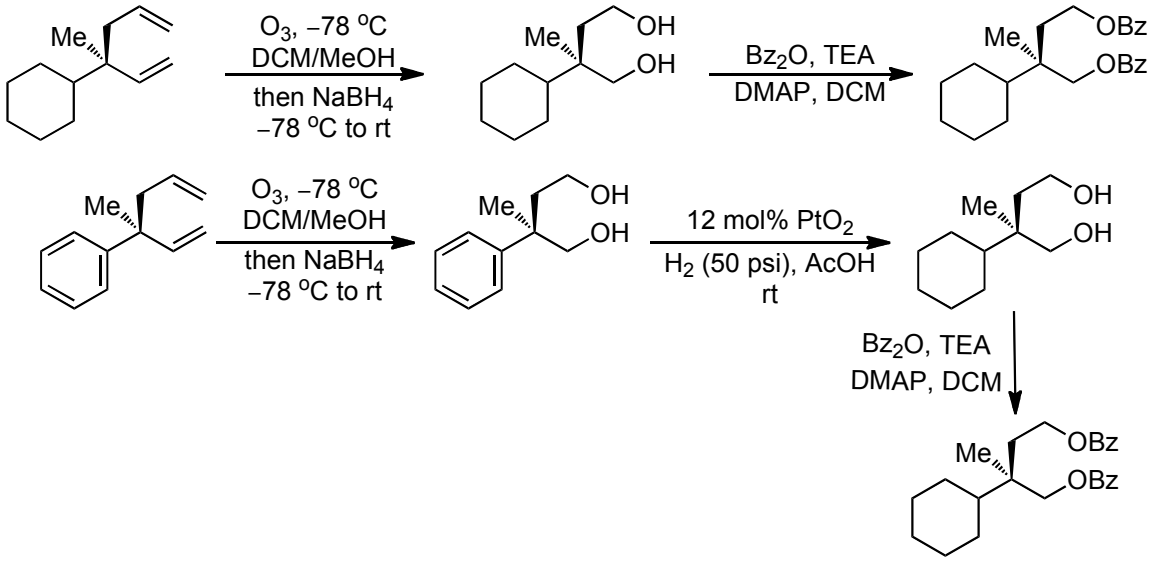
racemic



reaction product

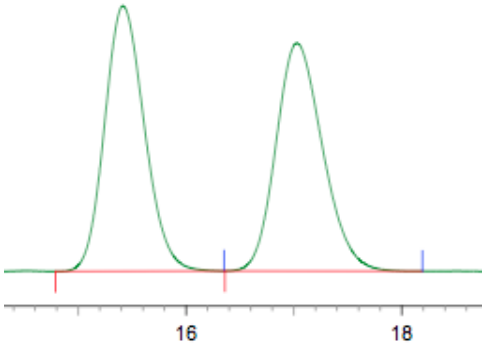
Peak #	RetTime [min]	Type	Width [min]	Area [pA*s]	Height [pA]	Area %
1	116.076	MM	1.4937	523.51239	5.84140	93.12763
2	121.933	MM	1.2522	38.63267	5.14192e-1	6.87237

Absolute stereochemistry was determined by converting the allyl-allyl coupling product to a dibenzoate by ozonolysis/reduction and dibenzoate protection of the corresponding diol, as shown below. *Via* chiral HPLC, the resulting dibenzoate was compared to the one derived from (*S*)-(3-methylhexa-1,5-dien-3-yl)benzene from ozonolysis/reduction, hydrogenation and dibenzoate protection of the resulting diol, as depicted below.[63]

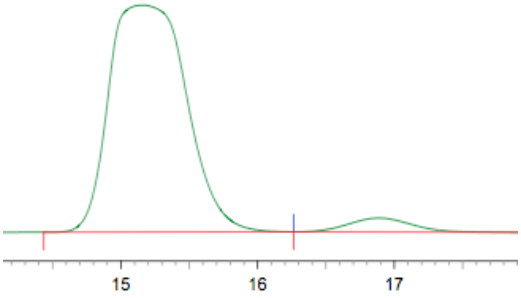


[63] For hydrogenation procedure, see: Hill, R. K.; Cullison, D. A. *J. Am. Chem. Soc.* **1973**, *95*, 1229.

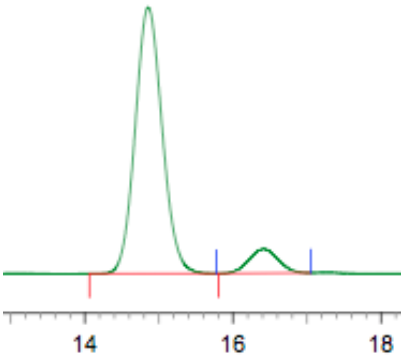
Chiral HPLC (AD-H, Chirapak, 0.5 mL/min, 2% isopropanol, 220 nm) – analysis of 2-cyclohexyl-2-methylbutane-1,4-diyl dibenzoate



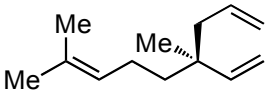
racemic



derived from (*S*)-(3-methylhexa-1,5-dien-3-yl)benzene



derived from reaction product

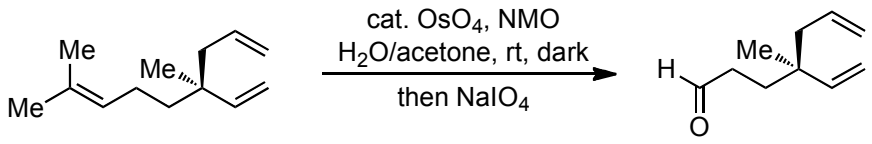


(*S*)-4,8-dimethyl-4-vinylnona-1,7-diene (Table 1.6, entry 2). ^{1}H NMR (500 MHz, $CDCl_3$): δ 0.97 (3H, s, CH_2=CHCC**H$_3$**), 1.26-1.34 (2H, m, C=CHCH$_2$C**H$_2$**), 1.58 (3H, s, (C**H$_3$**)$_a$(CH_3)$_b$C=CH), 1.67 (3H, s, (CH_3)$_a$(C**H$_3$**)$_b$C=CH), 1.88 (2H, ddd, *J* = 8.5, 8.0, 8.0 Hz, C=CHC**H$_2$**CH$_2$), 2.03-2.19 (2H, m, C**H$_2$**CH=CH$_2$), 4.91 (1H, dd, *J* = 18.0, 1.5 Hz, CCH=CH$_{cis}$**H$_{trans}$**), 4.98-5.03 (3H, m, CH$_2$CH=C**H$_2$** &

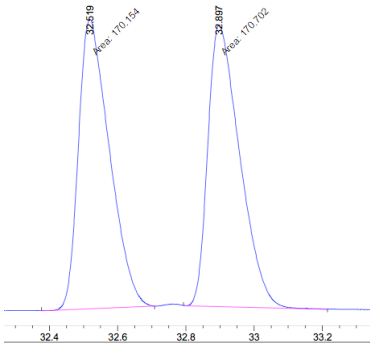
CCH=C**H**$_{cis}$H$_{trans}$), 5.07-5.10 (1H, m, $(CH_3)_2C$=C**H**), 5.71-5.80 (2H, m, CH_2C**H**=CH_2 & CC**H**=CH_2); ^{13}C NMR (125 MHz, $CDCl_3$): δ 17.6, 22.7, 22.8, 25.7, 39.5, 40.4, 45.2, 111.7, 116.8, 124.9, 131.1, 135.3, 146.7; IR (neat): 3078.7 (w), 2966.6 (m), 2915.3 (m), 2855.5 (w), 1638.9 (w), 1439.9 (w), 1413.4 (w), 1374.8 (w), 996.4 (m), 910.4 (s), 832.7 (w) cm^{-1}; HRMS (ESI+) for $C_{13}H_{23}$ [M+H]: calculated: 179.1800, found: 179.1795; $[\alpha]^{20}_D$ = +7.449 (*c* = 0.97, $CHCl_3$). The unpurified reaction mixture was purified on silica gel (pentane) to afford a clear, colorless oil (32.6 mg, 96% yield), with 4:1 allyl-allyl coupling product to elimination product. R_f = 0.81 (8:1 hexane/EtOAc, stain in $KMnO_4$).

Proof of Stereochemistry:

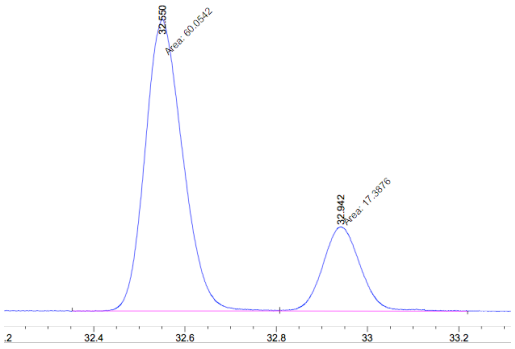
The title compound was subjected to dihydroxylation/cleavage, as depicted below. The resulting aldehyde was subjected to chiral GC analysis. The analogous racemic material was prepared *via* the same route using 1,2-bis(diphenylphosphino)benzene as achiral ligand in the allyl-allyl coupling reaction. Absolute stereochemistry was assigned by analogy to Table 1.6, entry 1.



Chiral GC (β-dex, Supelco, 60 ˚C, 10 min, ramp 2 deg/min to 160 ˚C, 25 psi) - analysis of 4-methyl-4-vinylhept-6-enal

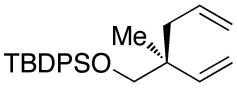


racemic



reaction product

Peak #	RetTime [min]	Type	Width [min]	Area [pA*s]	Height [pA]	Area %
1	32.550	MF	0.0952	60.05421	10.51814	77.54754
2	32.942	FM	0.0958	17.38759	3.02506	22.45246

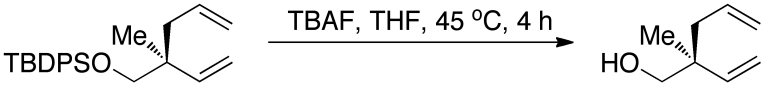


(*S*)-*tert*-butyl((2-methyl-2-vinylpent-4-en-1-yl)oxy)diphenylsilane (Table 1.6, entry 3). ^{1}H NMR (500 MHz, $CDCl_3$): δ 0.98 (3H, s), 1.05 (9H, s), 2.18 (1H, ddd, *J* = 13.7, 7.8, 1.0 Hz), 2.24 (1H, ddd, *J* = 13.7, 6.8, 1.0 Hz), 3.38 (1H, d, *J* = 9.7 Hz), 3.42 (1H, d, *J* = 9.7 Hz), 4.93-5.04 (2H, m), 5.67-5.76 (1H, m), 5.83 (1H, dd, *J* = 17.7, 10.8 Hz), 7.34-7.42 (6H, m), 7.63-7.65 (4H, m); ^{13}C NMR (125 MHz, $CDCl_3$): δ 19.4, 20.4, 26.9, 41.6, 42.2, 70.8, 112.9, 117.0, 127.6, 129.5, 133.8, 135.2, 135.7, 144.2; IR (neat): 2952 (s), 2919 (s), 2850 (s), 2015 (w), 1722 (w), 1463 (m), 1429 (w), 1272 (m), 1112 (m), 709 (m), 407 (m) cm^{-1}; HRMS (ESI+) for $C_{24}H_{33}OSi$ [M+H]: calculated: 365.2301, found: 365.2304; The unpurified reaction

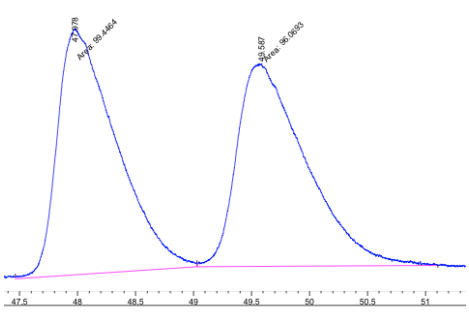
mixture was purified on silica gel (pentane) to afford a clear, colorless oil (27 mg, >90% yield). R_f = 0.37 (pentane, stain in $KMnO_4$).

Proof of Stereochemistry:

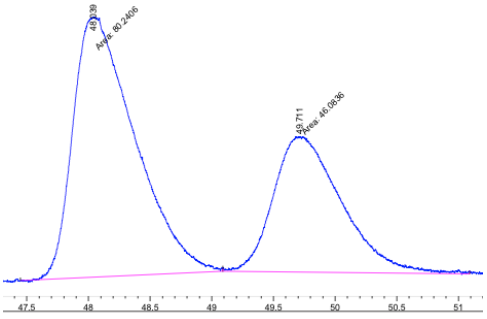
The title compound was subjected to TBAF deprotection, as depicted below. The resulting alcohol was subjected to chiral GC analysis. The analogous racemic material was prepared *via* the same route using 1,2-bis(diphenylphosphino)benzene as achiral ligand in the allyl-allyl coupling reaction. Absolute stereochemistry was assigned by analogy to Table 1.6, entry 1.



Chiral GC (β-dex, Supelco, 70 ˚C, 20 psi) - analysis of the alcohol



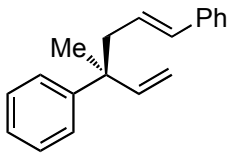
racemic



reaction product

Peak #	RetTime [min]	Type	Width [min]	Area [pA*s]	Height [pA]	Area %
1	48.039	MM	0.5799	80.24062	2.30626	63.51961
2	49.711	MM	0.6392	46.08356	1.20158	36.48039

D. Functionalization of the Allyl-Allyl Coupling Product (Scheme 1.29)



(*S*,*E*)-(4-methylhexa-1,5-diene-1,4-diyl)dibenzene (1.41):[64] To a flame-dried 2-dram vial equipped with a stir bar was added powdered molecular sieves (4 Å, 600 mg) and sodium bicarbonate (63.0 mg, 0.750 mmol). The vial was sealed with a septum and purged three times with N_2. DMF (1.5 mL) was then added by syringe, and the resulting suspension was allowed to stir at room temperature for 15 minutes. The septum was then removed, and triphenylphosphine (15.7 mg, 0.060 mmol) was added all at once to the reaction mixture. The septum was then replaced, and vial was charged with (*S*)-(3-methylhexa-1,5-dien-3-yl)benzene (51.6 mg, 0.300 mmol) and iodobenzene (97.9 mg, 0.480 mmol) *via* syringe. The vial was flushed with N_2 for 1 minute. The reaction was allowed to stir for another 15 minutes. The septum was removed again, and $Pd(OAc)_2$ (6.7 mg, 0.030 mmol) was quickly added all at once followed by immediate sealing with a screw cap. The reaction was heated in an oil bath to 80 °C and allowed to stir for 16 h. The red slurry was then cooled to room temperature and water and Et_2O were added. The organic layer was transferred out by a pipet and filtered through a plug of silica gel (bottom) and $MgSO_4$ (top), and the remaining aqueous layer was washed with more ether (3x) and the organics were filtered. The combined organics were

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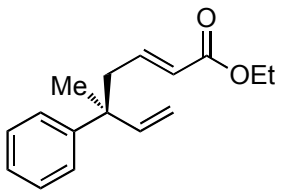
[64] Jeffery, T. *Tetrahedron* **1996**, *52*, 10113.

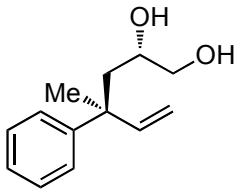
concentrated *in vacuo* and purified by silica gel chromatography (100:1 hexanes/ EtOAc) to yield a clear, colorless oil (51.8 mg, 70% yield). ^{1}H NMR (500 MHz, $CDCl_3$): δ 1.41 (3H, s, C**H$_3$**), 2.66 (1H, dd, *J* = 14.0, 7.0 Hz, C**H$_a$**H$_b$CH=CHPh), 2.70 (1H, dd, *J* = 14.0, 7.0 Hz, CH$_a$**H$_b$**CH=CHPh), 5.09 (1H, ddd, *J* = 18.0, 1.5, 1.0 Hz, CH=CH$_{cis}$**H$_{trans}$**), 5.15 (1H, dt, *J* = 10.5, 1.0 Hz, CH=C**H$_{cis}$**H$_{trans}$), 6.02 (1H, dddd, *J* = 15.5, 8.0, 7.5, 1.5 Hz, CH$_2$C**H**=CHPh), 6.10 (1H, ddd, *J* = 17.5, 11.0, 1.0 Hz, C**H**=CH$_2$), 6.27 (1H, dd, *J* = 15.5, 1.5 Hz, CH$_2$CH=C**H**Ph), 7.15-7.26 (6H, m, Ar-**H**), 7.30-7.37 (4H, m, Ar-**H**); ^{13}C NMR (125 MHz, $CDCl_3$): δ 25.1, 44.6, 44.7, 112.2, 125.95, 126.03, 126.6, 126.9, 127.0, 128.1, 128.4, 132.4, 137.7, 146.5, 147.0; IR (neat): 3082.3 (w), 3057.7 (w), 3025.6 (w), 2966.1 (w), 2927.0 (w), 1653.4 (s), 1598.6 (w), 1493.1 (m), 1444.7 (m), 1411.3 (w), 1371.7 (w), 965.2 (s), 908.2 (s), 733.9 (s), 696.5 (s) cm^{-1}; HRMS (ESI+) for $C_{19}H_{21}$ [M+H]: calculated: 249.1643, found: 249.1649. $[\alpha]^{20}_D$ = –45.342 (*c* = 2.10, $CHCl_3$).



(*S*,*E*)-ethyl 5-methyl-5-phenylhepta-2,6-dienoate (1.40):[65] To an oven-dried 2-dram screw-cap vial equipped with a stir bar was added (*S*)-(3-methylhexa-1,5-dien-3-yl)benzene (64.6 mg, 0.375 mmol), ethyl acrylate (0.12 mL, 1.125 mmol), Hoveyda-Grubbs 2nd Generation catalyst (11.9 mg, 0.019 mmol), and methylene chloride (1.5 mL). The vial was then purged for 15 seconds with

[65] BouzBouz, S.; Simmons, R.; Cossy, J. *Org. Lett.* **2004**, *6*, 3465.

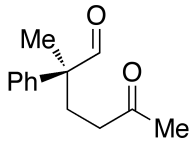
nitrogen, capped, and sealed with tape. The solution was heated to 40 °C and allowed to stir for 14 h. The solution was then cooled to room temperature and *tert*-butylvinylether (5 drops) was added to the reaction. The resulting solution was allowed to stir at room temperature for 30 minutes. The reaction was then concentrated under reduced pressure and purified by flash chromatography (silica gel, 3% Et_2O/pentane) to yield a clear, colorless oil (78.7 mg, 86% yield). ^{1}H NMR (500 MHz, $CDCl_3$): δ 1.26 (3H, t, J =7.1 Hz, $OCH_2C\mathbf{H_3}$), 1.39 (3H, s, $CC\mathbf{H_3}$), 2.66 (1H, ddd, J = 14.1, 7.6, 1.5 Hz, $C\mathbf{H_a}H_bCH{=}CHC$), 2.70 (1H, ddd, J = 14.1, 7.6, 1.5 Hz, $CH_a\mathbf{H_b}CH{=}CHC$), 4.15 (2H, q, J = 7.1 Hz, $OC\mathbf{H_2}CH_3$), 5.08 (1H, dd, J = 17.5, 1.2 Hz, $CCH{=}CH_{cis}\mathbf{H_{trans}}$), 5.17 (1H, dd, J = 10.8, 1.2 Hz, $CCH{=}C\mathbf{H_{cis}}H_{trans}$), 5.82 (1H, ddd, J = 15.7, 1.5, 1.5 Hz, $CH_2CH{=}C\mathbf{H}C$), 6.03 (1H, d, J = 17.5, 10.8 Hz, $CC\mathbf{H}{=}CH_2$), 6.78 (1H, ddd, J = 15.7, 7.6, 7.6 Hz, $CH_2C\mathbf{H}{=}CHC$), 7.19-7.23 (1H, m, Ar-**H**), 7.30-7.33 (4H, m, Ar-**H**); ^{13}C NMR (100 MHz, $CDCl_3$): δ 14.2, 25.2, 43.8, 44.2, 60.2, 112.8, 123.8, 126.2, 126.4, 128.3, 145.6, 146.2 (2C), 166.3; IR (neat): 3085.9 (w), 3057.6 (w), 2978.0 (w), 1719.6 (s), 1653.3 (m), 1494.4 (w), 1445.4 (w), 1412.4 (w), 1310.9 (m), 1264.6 (m), 1155.8 (w), 1096.4 (w), 983.2 (w), 766.4 (w), 700.5 (m) cm^{-1}; HRMS (ESI+) for $C_{16}H_{21}O_2$ [M+H]: calculated: 245.1542, found: 245.1552. $[\alpha]^{20}_D$ = –28.519 (c = 0.23, $CHCl_3$).



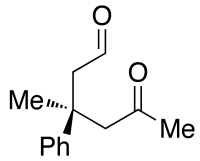
(4*S*)-4-methyl-4-phenylhex-5-ene-1,2-diol (1.42):[66] In the dry-box an oven-dried 20 mL scintillation vial equipped with a magnetic stir bar was charged with $Pt(dba)_3$ (8.1 mg, 0.009 mmol), 3,5-(*R*,*R*)-diphenylTADDOLPPh (12.3 mg, 0.010 mmol), $B_2(pin)_2$ (77.0 mg, 0.304 mmol) and THF (2.9 mL, 0.1 M). The vial was sealed with a polypropylene cap and removed from the dry-box. The solution was allowed to stir at 80 °C for 30 minutes, at which time the reaction was cooled to room temperature and brought back into the dry-box. (*S*)-(3-methylhexa-1,5-dien-3-yl)benzene (50.0 mg, 0.290 mmol) was then added to the reaction mixture. The vial was again sealed and removed from the dry-box. The reaction was heated to 60 °C and allowed to stir for 24 h. The reaction was then cooled to 0 °C (ice-water bath) and charged with 3 M NaOH (2 mL) and 30% H_2O_2 (w/w) (1 mL). The resulting mixture was allowed to stir for 4 h while slowly warming to room temperature. The mixture was again cooled to 0 °C (ice-water bath) and quenched with saturated aqueous $Na_2S_2O_3$ (5 mL), added drop-wise *via* syringe. The mixture was diluted with water (10 mL) and extracted with EtOAc (3 x 25 mL). The combined organic layers were dried over $MgSO_4$, filtered, concentrated *in vacuo*, and purified by flash chromatography (silica gel, 1:1 pentane/EtOAc) to afford a clear, pale yellow oil (57.9 mg, 56% yield of title compound), with 1:1.3 desired product to pinacol. R_f = 0.28 (2:3 hexanes/EtOAc, stain in $KMnO_4$). ^1H NMR (500 MHz, $CDCl_3$): δ 1.48 (s, 3H, C**H**$_3$), 1.91 (2H, d, J = 5.4 Hz, C**H**$_2$CHOH),

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

2.24-2.72 (2H, m, 2(O**H**)), 3.31 (1H, dd, *J* = 11.1, 7.8 Hz, C**H**$_a$H$_b$OH), 3.39 (1H, dd, *J* = 11.1, 3.2 Hz, CH$_a$**H**$_b$OH), 3.66-3.70 (1H, m, CH$_2$C**H**OH), 5.10 (1H, d, *J* = 17.6 Hz, CH=CH$_{cis}$**H**$_{trans}$), 5.14 (1H, d, *J* = 10.9 Hz, CH=C**H**$_{cis}$H$_{trans}$), 6.14 (1H, dd, *J* = 17.6, 10.9 Hz, C**H**=CH$_2$), 7.18-7.21 (1H, m, Ar-**H**), 7.29-7.35 (4H, m, Ar-**H**); ^{13}C NMR (125 MHz, $CDCl_3$): δ 24.8, 43.5, 44.2, 67.3, 69.6, 112.1, 126.2, 126.5, 128.3, 146.7, 147.1; IR (neat): 3364.9 (br, s), 3058.0 (w), 2973.9 (w), 2931.9 (w), 1634.4 (w), 1599.6 (w), 1444.7 (m), 1373.0 (m), 1154.3 (m), 1096.5 (m), 1061.5 (s), 1001.7 (m), 912.8 (s), 764.2 (s), 698.9 (s) cm^{-1}; HRMS (ESI+) for $C_{13}H_{19}O_2$ [M+H]: calculated: 207.1385, found: 207.1395. $[\alpha]^{20}_D$ = +35.227 (*c* = 0.52, $CHCl_3$).



1.37

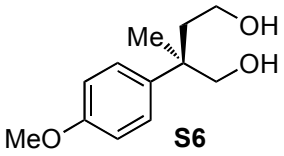


1.38

(*S*)-2-methyl-5-oxo-2-phenylhexanal and (*S*)-3-methyl-5-oxo-3-phenylhexanal (1.37 and 1.38): A flame-dried 3-neck 25 mL round-bottom flask equipped with a stir bar and condenser was successively charged with (phen)Pd(Me)Cl (1.5 mg, 0.0044 mmol), NaBARF (3.9 mg, 0.0044 mmol), (*S*)-(3-methylhexa-1,5-dien-3-yl)benzene (19 mg, 0.11 mmol), and DCE (2.2 mL). The resulting was solution was heated to 70 °C and allowed to stir for 12 h. The reaction was then allowed to cool to room temperature, diluted with pentane (10 mL), and passed through a short plug of silica gel eluting with pentane. The solution was concentrated under reduced pressure and diluted with CH_2Cl_2 (5.5 mL). The resulting solution

was cooled to –78 °C and sparged with O_3 until the solution appeared faint blue. The solution was then sparged with N_2 until it appeared clear and colorless, at which point PPh_3 (144 mg, 0.55 mmol) was added all at once. The reaction was allowed to slowly warm to room temperature while stirring for 12 h. The solution was concentrated *in vacuo* and purified by flash chromatography (silica gel, 20% EtOAc/hexanes) to afford a clear, pale yellow oil (13.6 mg, 61% yield of title compounds, 6.25 : 1, **1.37** : **1.38**). R_f = 0.25 (20% EtOAc/hexanes, stain in $KMnO_4$). ^1H NMR (500 MHz, $CDCl_3$): δ 9.65 (1H, s, **1.37**), 9.50 (1H, s, **1.38**), 7.42-7.19 (10H, m, **1.37**+**1.38**), 2.35-2.15 (8H, m, **1.37**+**1.38**), 2.06 (3H, s, **1.38**), 1.92 (3H, s, **1.37**), 1.52 (3H, s, **1.37**), 1.45 (3H, s, **1.38**).

E. X-RAY CRYSTALLOGRAPHIC DATA FOR S6



S6

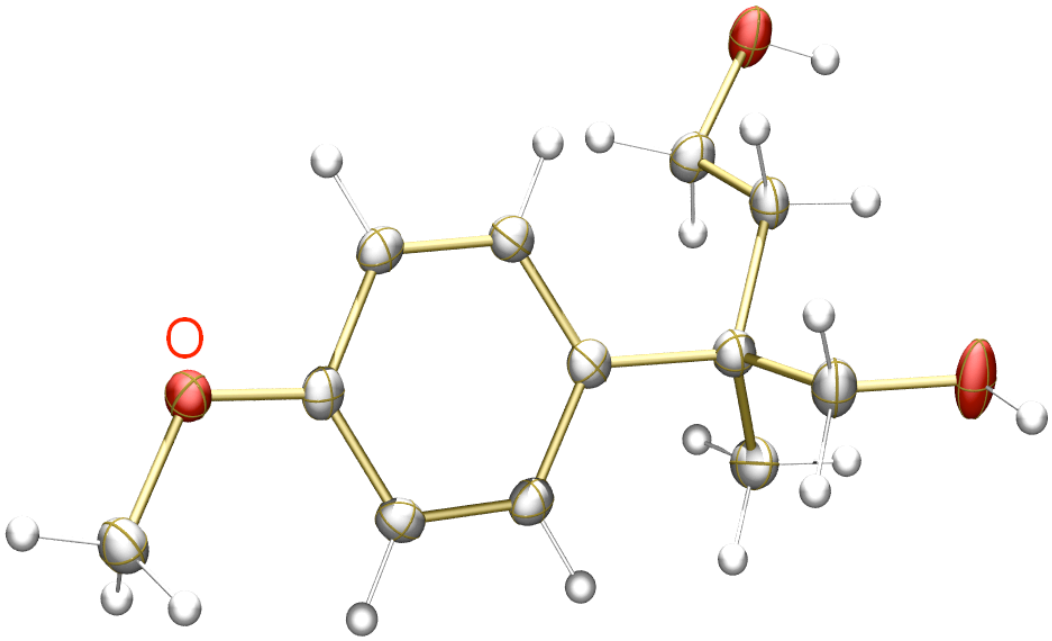


Table 1. Crystal data and structure refinement for C12H18O3.

Identification code	C12H18O3
Empirical formula	C12 H18 O3
Formula weight	210.26
Temperature	100(2) K
Wavelength	1.54178 ≈
Crystal system	Monoclinic

Space group	P 21	
Unit cell dimensions	a = 5.8880(2) ≈	α= 90∞.
	b = 7.5873(3) ≈	β= 101.821(2)∞.
	c = 12.5089(5) ≈	γ = 90∞.
Volume	546.97(4) ≈^{3}	
Z	2	
Density (calculated)	1.277 Mg/m^3	
Absorption coefficient	0.732 mm^{-1}	
F(000)	228	
Crystal size	0.10 x 0.06 x 0.02 mm^3	
Theta range for data collection	3.61 to 68.16∞.	
Index ranges	-7<=h<=6, -9<=k<=8, -15<=l<=15	
Reflections collected	7510	
Independent reflections	1859 [R(int) = 0.0281]	
Completeness to theta = 68.16∞	98.1 %	
Absorption correction	Semi-empirical from equivalents	
Max. and min. transmission	0.9855 and 0.9304	
Refinement method	Full-matrix least-squares on F^2	
Data / restraints / parameters	1859 / 3 / 142	
Goodness-of-fit on F^2	1.032	
Final R indices [I>2sigma(I)]	R1 = 0.0316, wR2 = 0.0828	

R indices (all data)	R1 = 0.0325, wR2 = 0.0838
Absolute structure parameter	0.05(19)
Extinction coefficient	na
Largest diff. peak and hole	0.216 and -0.158 e.≈$^{-3}$

Table 2. Atomic coordinates (x 10^4) and equivalent isotropic displacement parameters (≈^{2}x 10^3) for C12H18O3. U(eq) is defined as one third of the trace of the orthogonalized U^{ij} tensor.

	x	y	z	U(eq)
O(1)	5875(2)	4852(1)	-1273(1)	22(1)
O(2)	14611(2)	1066(2)	3945(1)	28(1)
O(3)	13718(3)	7591(2)	4063(1)	35(1)
C(1)	7003(3)	4947(2)	-206(1)	18(1)
C(2)	9102(3)	4038(2)	63(1)	19(1)
C(3)	10404(3)	4103(2)	1116(1)	19(1)
C(4)	9658(3)	5045(2)	1945(1)	19(1)
C(5)	7537(3)	5908(2)	1655(1)	20(1)
C(6)	6206(3)	5870(2)	601(1)	19(1)

C(7)	3712(3)	5764(2)	-1573(1)	25(1)
C(8)	11174(3)	5300(2)	3089(1)	21(1)
C(9)	9724(3)	5231(3)	3982(1)	27(1)
C(10)	13205(3)	3989(2)	3359(1)	21(1)
C(11)	12571(3)	2069(2)	3496(1)	23(1)
C(12)	12204(3)	7156(2)	3056(1)	25(1)

Table 3. Bond lengths [≈] and angles [∞] for C12H18O3.

O(1)-C(1)	1.3659(18)
O(1)-C(7)	1.430(2)
O(2)-C(11)	1.436(2)
O(2)-H(2O)	0.851(16)
O(3)-C(12)	1.425(2)
O(3)-H(3O)	0.839(17)
C(1)-C(6)	1.387(2)
C(1)-C(2)	1.395(2)
C(2)-C(3)	1.383(2)
C(2)-H(2B)	0.9500
C(3)-C(4)	1.401(2)

C(3)-H(3B)	0.9500
C(4)-C(5)	1.391(2)
C(4)-C(8)	1.536(2)
C(5)-C(6)	1.389(2)
C(5)-H(5A)	0.9500
C(6)-H(6A)	0.9500
C(7)-H(7A)	0.9800
C(7)-H(7B)	0.9800
C(7)-H(7C)	0.9800
C(8)-C(12)	1.538(2)
C(8)-C(10)	1.539(2)
C(8)-C(9)	1.540(2)
C(9)-H(9A)	0.9800
C(9)-H(9B)	0.9800
C(9)-H(9C)	0.9800
C(10)-C(11)	1.522(2)
C(10)-H(10A)	0.9900
C(10)-H(10B)	0.9900
C(11)-H(11A)	0.9900
C(11)-H(11B)	0.9900
C(12)-H(12A)	0.9900
C(12)-H(12B)	0.9900

C(1)-O(1)-C(7)	117.36(12)
C(11)-O(2)-H(2O)	107.1(16)
C(12)-O(3)-H(3O)	110.6(17)
O(1)-C(1)-C(6)	124.63(14)
O(1)-C(1)-C(2)	116.05(13)
C(6)-C(1)-C(2)	119.32(14)
C(3)-C(2)-C(1)	120.19(14)
C(3)-C(2)-H(2B)	119.9
C(1)-C(2)-H(2B)	119.9
C(2)-C(3)-C(4)	121.77(14)
C(2)-C(3)-H(3B)	119.1
C(4)-C(3)-H(3B)	119.1
C(5)-C(4)-C(3)	116.60(14)
C(5)-C(4)-C(8)	120.21(14)
C(3)-C(4)-C(8)	122.88(14)
C(6)-C(5)-C(4)	122.65(14)
C(6)-C(5)-H(5A)	118.7
C(4)-C(5)-H(5A)	118.7
C(1)-C(6)-C(5)	119.45(14)
C(1)-C(6)-H(6A)	120.3
C(5)-C(6)-H(6A)	120.3

O(1)-C(7)-H(7A)	109.5
O(1)-C(7)-H(7B)	109.5
H(7A)-C(7)-H(7B)	109.5
O(1)-C(7)-H(7C)	109.5
H(7A)-C(7)-H(7C)	109.5
H(7B)-C(7)-H(7C)	109.5
C(4)-C(8)-C(12)	104.31(13)
C(4)-C(8)-C(10)	113.60(13)
C(12)-C(8)-C(10)	107.78(13)
C(4)-C(8)-C(9)	111.65(13)
C(12)-C(8)-C(9)	109.33(14)
C(10)-C(8)-C(9)	109.90(13)
C(8)-C(9)-H(9A)	109.5
C(8)-C(9)-H(9B)	109.5
H(9A)-C(9)-H(9B)	109.5
C(8)-C(9)-H(9C)	109.5
H(9A)-C(9)-H(9C)	109.5
H(9B)-C(9)-H(9C)	109.5
C(11)-C(10)-C(8)	116.45(14)
C(11)-C(10)-H(10A)	108.2
C(8)-C(10)-H(10A)	108.2
C(11)-C(10)-H(10B)	108.2

C(8)-C(10)-H(10B)	108.2
H(10A)-C(10)-H(10B)	107.3
O(2)-C(11)-C(10)	110.24(14)
O(2)-C(11)-H(11A)	109.6
C(10)-C(11)-H(11A)	109.6
O(2)-C(11)-H(11B)	109.6
C(10)-C(11)-H(11B)	109.6
H(11A)-C(11)-H(11B)	108.1
O(3)-C(12)-C(8)	111.52(13)
O(3)-C(12)-H(12A)	109.3
C(8)-C(12)-H(12A)	109.3
O(3)-C(12)-H(12B)	109.3
C(8)-C(12)-H(12B)	109.3
H(12A)-C(12)-H(12B)	108.0

Symmetry transformations used to generate equivalent atoms:

Table 4. Anisotropic displacement parameters ($\approx^{2}$x 10^{3}) for C12H18O3. The anisotropicdisplacement factor exponent takes the form: $-2\pi^{2}[\ h^{2}\ a^{*2}U^{11} + ... + 2\ h\ k\ a^{*}\ b^{*}\ U^{12}\ ]$

	U^{11}	U^{22}	U^{33}	U^{23}	U^{13}	U^{12}
O(1)	23(1)	21(1)	20(1)	0(1)	1(1)	2(1)
O(2)	40(1)	17(1)	24(1)	-1(1)	-6(1)	4(1)
O(3)	49(1)	13(1)	32(1)	1(1)	-15(1)	-4(1)
C(1)	22(1)	12(1)	20(1)	1(1)	2(1)	-3(1)
C(2)	22(1)	14(1)	22(1)	-1(1)	6(1)	-1(1)
C(3)	19(1)	15(1)	24(1)	1(1)	4(1)	0(1)
C(4)	20(1)	14(1)	22(1)	2(1)	4(1)	-2(1)
C(5)	22(1)	16(1)	23(1)	-2(1)	6(1)	-2(1)
C(6)	19(1)	14(1)	25(1)	3(1)	4(1)	2(1)
C(7)	23(1)	24(1)	26(1)	2(1)	1(1)	2(1)
C(8)	21(1)	18(1)	21(1)	-1(1)	2(1)	1(1)
C(9)	27(1)	31(1)	21(1)	-1(1)	3(1)	3(1)
C(10)	22(1)	20(1)	19(1)	0(1)	-1(1)	-1(1)
C(11)	29(1)	16(1)	24(1)	0(1)	3(1)	2(1)
C(12)	28(1)	17(1)	25(1)	1(1)	-4(1)	0(1)

Table 5. Hydrogen coordinates (x 10^4) and isotropic displacement parameters ($\approx^2$x 10 ^{3})for C12H18O3.

	x	y	z	U(eq)
H(2O)	15150(40)	1480(30)	4579(14)	43
H(3O)	14020(40)	8670(20)	4090(20)	52
H(2B)	9638	3373	-479	23
H(3B)	11842	3494	1282	23
H(5A)	6976	6549	2200	24
H(6A)	4762	6472	434	23
H(7A)	3081	5595	-2354	37
H(7B)	3956	7025	-1420	37
H(7C)	2616	5298	-1150	37
H(9A)	8439	6072	3808	40
H(9B)	10707	5536	4689	40
H(9C)	9103	4039	4019	40
H(10A)	14099	4054	2770	25
H(10B)	14246	4379	4043	25
H(11A)	11452	1993	3986	28
H(11B)	11822	1574	2777	28

H(12A)	13071	7218	2458	30
H(12B)	10928	8029	2901	30

Table 6. Torsion angles [∞] for C12H18O3.

C(7)-O(1)-C(1)-C(6)	-0.4(2)
C(7)-O(1)-C(1)-C(2)	179.72(14)
O(1)-C(1)-C(2)-C(3)	177.96(13)
C(6)-C(1)-C(2)-C(3)	-1.9(2)
C(1)-C(2)-C(3)-C(4)	1.1(2)
C(2)-C(3)-C(4)-C(5)	0.1(2)
C(2)-C(3)-C(4)-C(8)	-173.51(15)
C(3)-C(4)-C(5)-C(6)	-0.6(2)
C(8)-C(4)-C(5)-C(6)	173.28(15)
O(1)-C(1)-C(6)-C(5)	-178.35(15)
C(2)-C(1)-C(6)-C(5)	1.5(2)
C(4)-C(5)-C(6)-C(1)	-0.3(2)
C(5)-C(4)-C(8)-C(12)	-74.41(18)
C(3)-C(4)-C(8)-C(12)	99.03(17)
C(5)-C(4)-C(8)-C(10)	168.51(14)

C(3)-C(4)-C(8)-C(10)	-18.1(2)
C(5)-C(4)-C(8)-C(9)	43.6(2)
C(3)-C(4)-C(8)-C(9)	-143.01(16)
C(4)-C(8)-C(10)-C(11)	-68.29(18)
C(12)-C(8)-C(10)-C(11)	176.66(14)
C(9)-C(8)-C(10)-C(11)	57.60(19)
C(8)-C(10)-C(11)-O(2)	-168.99(12)
C(4)-C(8)-C(12)-O(3)	-178.69(14)
C(10)-C(8)-C(12)-O(3)	-57.66(17)
C(9)-C(8)-C(12)-O(3)	61.77(18)

Symmetry transformations used to generate equivalent atoms:

Table 7. Hydrogen bonds for C12H18O3 [≈ and ∞].

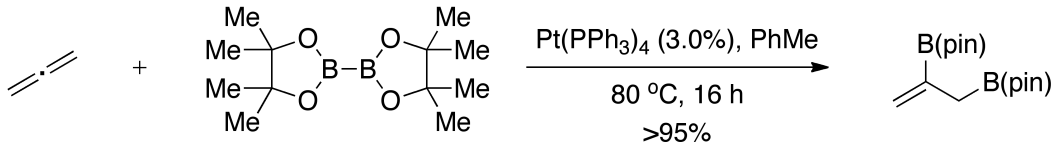
D-H...A	d(D-H)	d(H...A)	d(D...A)	<(DHA)
O(2)-H(2O)...O(3)#1	0.851(16)	1.891(17)	2.7404(17)	175(2)
O(3)-H(3O)...O(2)#2	0.839(17)	1.865(18)	2.6989(18)	172(2)

Symmetry transformations used to generate equivalent atoms:

#1 -x+3,y-1/2,-z+1 #2 x,y+1,z

VII. Experimental Procedures for Allyl-Allyl Coupling with 1.43

A. Preparation of Diboron Reagent 1.43



Preparation of 2,2'-(prop-2-ene-1,2-diyl)bis(4,4,5,5-tetramethyl-1,3,2-dioxaborolane): [67] In the dry-box, a flame-dried 15 mL pressure vessel equipped with a stir bar was charged with $B_2(pin)_2$ (813 mg, 3.2 mmol), $Pt(PPh_3)_4$ (119 mg, 0.096 mmol), and PhMe (6.4 mL). The vessel was then sealed with a septum, removed from the dry-box, placed under an atmosphere of N_2, and vigorously sparged with allene gas for 90 seconds. The septum was then rapidly exchanged for a screw cap, and the reaction was heated to 80 °C for 16 h. At this time, the reaction was cooled to room temperature and concentrated under reduced pressure. The crude reaction mixture was purified by Kügelrohr distillation (0.5 torr, 135 °C) to afford a clear, colorless oil (1.01 g, >95% yield). R_f = 0.56 (10:1 pentane:diethyl ether, stain in PMA). ^{1}H NMR (500 MHz, $CDCl_3$): δ 5.69 (1H, d, br, *J* = 3.5 Hz), 5.55 (1H, d, br, *J* = 3.5 Hz), 1.79 (2H, s, br), 1.24 (12H, s), 1.21 (12H, s); ^{13}C NMR (125 MHz, $CDCl_3$): δ 128.4, 83.4 (2C), 83.1 (2C), 25.0, 24.8 (4C), 24.7 (4C); IR (neat): 3062 (s), 2979 (w), 1615 (w), 1423 (m), 1344 (s), 1309 (s), 1142 (s), 1006 (w), 969 (w), 864 (w), 848 (w), 709 (w)

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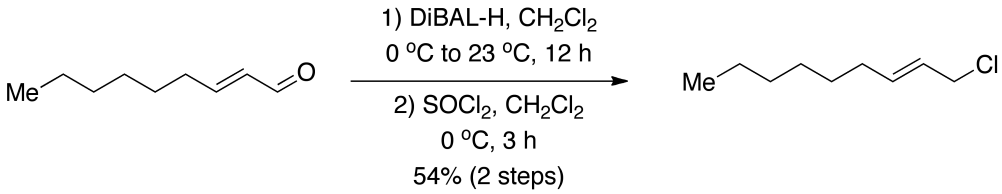
[67] Ishiyama, T.; Kitano, T.; Miyaura, N. *Tetrahedron Lett.* **1998**, *39*, 2357.

cm^{-1}; HRMS-(ESI+) for $C_{15}H_{29}O_4B_2$ [M+H]: calculated: 295.2252, found: 295.2258.

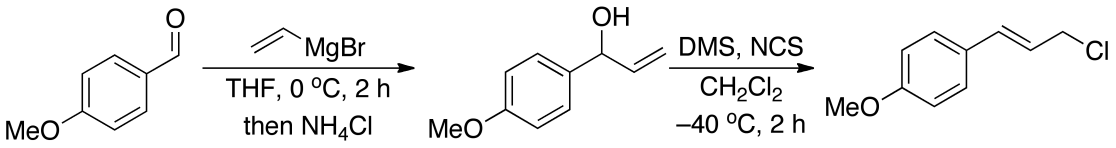
B. Preparation and Characterization of Allylic Chlorides

(*E*)-1-(3-chloroprop-1-en-1-yl)-4-methylbenzene (Table 1.8, substrate for **1.53**), (*E*)-1-chloro-4-(3-chloroprop-1-en-1-yl)benzene (Table 1.8, entry 4), (*E*)-(5-chloropent-3-en-1-yl)benzene (Table 1.9, entry 4), and (*Z*)-*tert*-butyl((4-chlorobut-2-en-1-yl)oxy)diphenylsilane (Table 1.9, entry 5) were prepared as described in the literature and isolated as a mixture of branched and linear isomers. All spectroscopic data was in accordance with the reported values.[20] (*E*)-(4-chlorobut-2-en-2-yl)benzene (Table 1.9, entry 1) was prepared by the procedure of Kara *et al*, with all spectral data in accordance with the literature.[68]



[68] Kishali, N.; Polat, M. F.; Altundas, R.; Kara, Y. *Helv. Chem. Acta* **2008**, *1*, 67.

(*E*)-1-chloronon-2-ene (Table 1.9, entry 3) was synthesized by the two-step procedure shown above (see ref. 20) from *trans*-2-nonenal and isolated as a mixture of isomers, with all spectral data in accordance with the literature.[69]



General Procedure C: To a flame-dried round-bottom flask equipped with a stir bar was added 1.0 M vinylmagnesium bromide in THF (17.0 mL, 12.0 mmol) and THF (10 mL). The solution was cooled to 0 °C and 4-methoxybenzaldehyde (1.22 mL, 10.0 mmol) in THF (10 mL) was added dropwise *via* cannula. The reaction was allowed to stir at 0 °C for 2 hours. The reaction was then quenched with sat. NH_4Cl (aq.), and extracted into diethyl ether three times. The combined organics were washed with brine, dried over Na_2SO_4, filtered, and then concentrated *in vacuo*. The reaction mixture was purified on silica gel (20% EtOAc/hexanes) to afford 1.29 g (78% yield) of 1-(4-methoxyphenyl)prop-2-en-1-ol as a light yellow oil. R_f = 0.20 (20% EtOAc/hexanes, stain in $KMnO_4$). To a separate flame-dried 10 mL round-bottom flask equipped with a stir bar was added *N*-chlorosuccinimide (86.8 mg, 0.65 mmol) and CH_2Cl_2 (2.0 mL) under an atmosphere of nitrogen. The solution was then cooled to –40 °C and DMS (59.2

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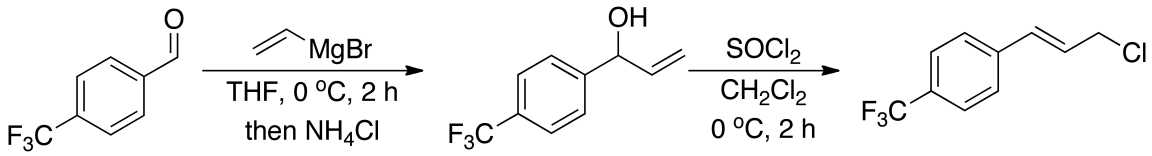
[69] Kumar, P.; Naidu, S. V. *J. Org. Chem.* **2005**, *70*, 4207. For branched isomer, see : Boughdady, N. M.; Chynoweth, K. R.; Hewitt, D. G. *Aust. J. Chem.* **1987**, *40*, 767.

μL, 0.8 mmol) was added dropwise *via* syringe. The reaction was allowed to stir for one hour, at which point 1-(4-methoxyphenyl)prop-2-en-1-ol (82.0 mg, 0.5 mmol) in CH_2Cl_2 (1.0 mL) was added dropwise *via* syringe. The resulting solution was then warmed to 0 ºC and allowed to stir for 1 h. At this time the reaction was diluted with brine (5 mL), extracted with CH_2Cl_2 (3 x 5 mL), and concentrated under reduced pressure. The crude oil was then redissolved in hexanes : H_2O (6 : 1), the layers seperated, and the aqueous layer further extracted with hexanes (3 x 10 mL). The combined organics were concentrated under reduced pressure to afford 88.4 mg (88% yield) of a white solid that was used without further purification.

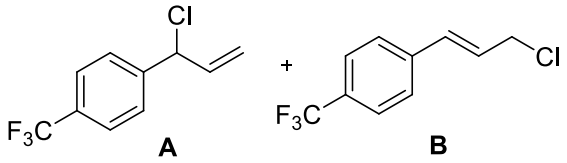
Preparation of (E)-1-(3-chloroprop-1-en-1-yl)-4-methoxybenzene (Table 1.8, substrate for 1.54): From commerically available 4-methoxybenzaldehyde, General Procedure C was followed. All spectra data is in accordance with the literature. [20]

Preparation of (E)-5-(3-chloroprop-1-en-1-yl)benzo[d][1,3]dioxole (Table 1.8, substrate for 1.56): From commerically available benzo[*d*][1,3]dioxole-5-carboxaldehyde General Procedure C was followed. All spectral data is in accordance with the literature. [20]

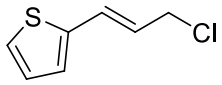


General Procedure D: To a flame-dried round-bottom flask equipped with a stir bar was added 1.0 M vinylmagnesium bromide in THF (17.2 mL, 12.0 mmol) and THF (10 mL). The solution was cooled to 0 °C and 4-(trifluoromethyl)benzaldehyde (1.37 mL, 10.0 mmol) in THF (10 mL) was added dropwise *via* cannula. The reaction was allowed to stir at 0 °C for 2 hours. The reaction was then quenched with sat. NH_4Cl (aq.), and extracted into diethyl ether three times. The combined organics were washed with brine, dried over Na_2SO_4, filtered, and concentrated *in vacuo*. The unpurified reaction mixture was purified on silica gel (15% EtOAc/hexanes) to afford 1.55 g (77% yield) of 1-(4-(trifluoromethyl)phenyl)prop-2-en-1-ol as a light yellow oil. R_f = 0.28 (15% EtOAc/hexanes, stain in $KMnO_4$). To a separate flame-dried round-bottom flask equipped with a stir bar was added 1-(4-(trifluoromethyl)phenyl)prop-2-en-1-ol (404 mg, 2.0 mmol) and THF (8.0 mL) under an atmosphere of nitrogen. The resulting solution was cooled to 0 °C and thionyl chloride (1.45 mL, 20.0 mmol) was added dropwise *via* syringe. The resulting solution was allowed to stir for 2 h, at which time the reaction was transferred to a separatory funnel containing ice cold brine (20 mL) and extracted with ice cold CH_2Cl_2 (3 x 20 mL). The combined

organics were concentrated under reduced pressure to afford 405 mg (92% yield) of a pale yellow oil which was used without further purification.



1-(1-chloroallyl)-4-(trifluoromethyl)benzene & **(*E*)-1-(3-chloroprop-1-enyl)-4-(trifluoromethyl)benzene (Scheme 1.35, eq. 21)**: ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.63-7.48 (**A** & **B**, 8H, m), 6.69 (**B**, 1H, d, *J* = 15.5 Hz) 6.41 (**B**, 1H, dt, *J* = 15.5, 7.0 Hz), 6.15 (**A**, 1H, ddd, *J* = 17.0, 10.0, 7.0 Hz), 5.48 (**A**, 1H, d, *J* = 7.0 Hz), 5.34 (**A**, 1H, d, *J* = 10.0 Hz), 5.30 (**A**, 1H, d, *J* = 17.0 Hz), 4.25 (**B**, 2H, d, *J* = 7.0 Hz); ^{13}C NMR (125 MHz, $CDCl_3$): δ 143.8, 139.4, 139.3, 137.0, 132.5, 130.7, 130.4, 130.2, 129.9, 127.8, 127.6, 127.1, 126.9, 125.7, 125.7, 125.6, 125.1, 124.9, 117.8, 62.2, 44.7; IR (neat): 2923 (w), 1616 (m), 1325 (s), 1251 (s), 1166 (s), 1124 (m), 1017 (s), 966 (m) cm^{-1}; HRMS (ESI+) for $C_{12}H_{13}Cl$ [M+H]: calculated 221.0267, found: 221.1116. The crude material was used without further purification (405 mg, 92% yield).



***(E)*-2-(3-chloroprop-1-enyl)thiophene (Table 1.8, 1.55):** From thiophene-2-carboxaldehyde, General Procedure D was followed. ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.21 (1H, d, *J* = 5.0 Hz), 7.01-6.97 (2H, m), 6.81 (1H, d, *J* = 15.0 Hz), 6.18 (1H, dt, *J* = 15.0, 7.5 Hz), 4.20 (2H, d, *J* = 7.0 Hz); ^{13}C NMR (125 MHz, $CDCl_3$): δ 140.7, 127.4, 127.3,

126.8, 125.2, 124.2, 45.2; IR (neat): 2923 (m), 1642 (m), 1437 (m), 1293 (m), 952 (s), 809 (m), 698 (s), 623 (m) cm^{-1}; HRMS (ESI+) for C_7H_8ClS [M+H]: calculated 159.0034, found: 159.0035. The crude material was used without further purification (153.5 mg, 97% yield).

(E)-(3-chloroprop-1-en-1-yl)cyclohexane (Table 1.9, entry 2): From commerically available cyclohexane carboxaldehyde General Procedure D was followed. All spectral data is in accordance with the literature.[70]

C. General Procedures for Allyl-Allyl Coupling with 1.43

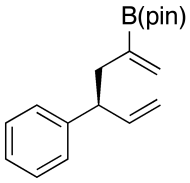
General Procedure E: In the dry-box, an oven-dried 1 dram vial equipped with a stir bar was charged with $(\eta^3\text{-allylPdCl})_2$ (1.4 mg, 0.0038 mmol), *(R)*-MFB (3.8 mg, 0.0075 mmol), and THF (0.75 mL). The resulting solution was allowed to stir at room temperature for 5 min. At this time, the vial was sequentially charged with cinnamyl chloride (22.8 mg, 0.15 mmol), **1.43** (53 mg, 0.18 mmol), and CsF (228 mg, 1.5 mmol). The vial was capped and sealed, removed from the dry-box, and allowed to stir at room temperature for 20 h. The slurry was then diluted with Et_2O, passed through a short plug of silica gel eluting with Et_2O, and concentrated under reduced pressure. The crude material was purified by silica gel chromatography (2% Et_2O/pentane) to afford (*S*)-4,4,5,5-tetramethyl-2-(4-

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

phenylhexa-1,5-dien-2-yl)-1,3,2-dioxaborolane as a clear, colorless oil (33 mg, 77% yield).

General Procedure F: In the dry-box, an oven-dried 1 dram vial equipped with a stir bar was charged with $(\eta^3\text{-allylPdCl})_2$ (2.5 mg, 0.0069 mmol), *(R,R)*-QuinoxP* (4.7 mg, 0.014 mmol), and THF (1.33 mL, 0.2 M). The vial was capped and allowed to stir for five minutes at room temperature. The vial was opened and sequentially charged with (*E*)-(5-chloropent-3-en-1-yl)benzene (50 mg, 0.277 mmol), **1.43** (94.7 mg, 0.332 mmol), and CsF (421 mg, 0.014 mmol). The vial was then capped with a rubber septum, sealed with electrical tape, removed from the dry-box, and placed under a positive pressure of nitrogen. Sparged DI water (0.07 mL) was then added *via* syringe, and the rubber septum was rapidly exchanged for a polypropylene cap. The vial was sealed with electrical tape, heated to 60 ºC, and allowed to stir for 16 h. The reaction was then cooled to room temperature, diluted with 6 drops of DI water, and passed through a pipette layered with 4 : 1 Na_2SO_4 : SiO_2. The crude product was concentrated under reduced pressure. The crude material was purified on silica gel (5% EtOAc/ hexanes) to afford (*S*)-4,4,5,5-tetramethyl-2-(4-phenethylhexa-1,5-dien-2-yl)-1,3,2-dioxaborolane as a clear, colorless oil (65 mg, 75% yield). R_f = 0.33 (5% EtOAc/hexanes, stain in $KMnO_4$).

D. Characterization and Analysis of Stereochemistry

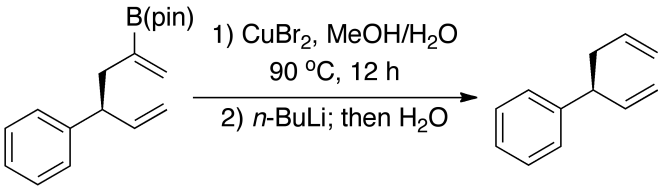


(*S*)-4,4,5,5-tetramethyl-2-(4-phenylhexa-1,5-dien-2-yl)-1,3,2-dioxaborolane (Table 1.8, 1.52): From commercially available cinnamyl chloride (22.9 mg, 0.15 mmol), representative procedure E was followed. ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.26-7.23 (2H, m), 7.20-7.15 (3H, m), 5.97 (1H, ddd, *J* = 17.0, 10.5, 7.5 Hz), 5.78 (1H, d, br, *J* = 3.5 Hz), 5.53 (1H, d, br, *J* = 3.0 Hz), 5.01 (1H, d, *J* = 10.5 Hz), 4.98 (1H, d, *J* = 17.0 Hz), 3.53 (1H, dd, *J* = 15.0, 7.5 Hz), 2.58 (2H, m), 1.24 (12H, s); ^{13}C NMR (125 MHz, $CDCl_3$): δ 147.3, 144.2, 141.9, 131.2, 128.2, 128.1, 127.8, 125.9, 114.2, 83.3 (2H), 49.8, 41.3, 24.8 (4H); IR (neat): 2978 (m), 1616 (w), 1421 (m), 1368 (s), 1309 (s), 1141 (s) cm^{-1}; HRMS (ESI+) for $C_{18}H_{26}BO_2$ [M +H]: calculated 285.1948, found: 285.2020; $[\alpha]^{20}_D$ = 5.998 (*c* = 1.525, $CHCl_3$). The crude material was purified on silica gel (2% Et_2O/pentane) to afford a clear, colorless oil (33 mg, 77% yield). R_f = 0.31 (2% Et_2O/pentane, stain in $KMnO_4$).

Proof of Stereochemistry:

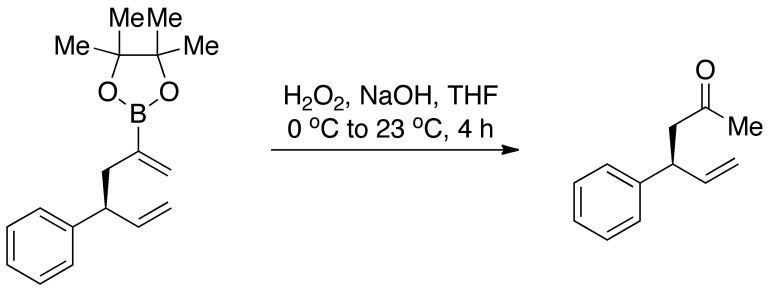
The title compound was oxidized with H_2O_2/NaOH to afford the corresponding ketone for GLC analysis, as depicted below. The analogous racemic material was prepared *via* the same route, using 1,2-bis(diphenylphosphino)benzene as the achiral ligand in the allyl-allyl coupling reaction. The absolute stereochemistry was assigned by converting the title

compound to the corresponding diene as shown below. By optical rotation, the 1,5-diene was compared to the identical compound prepared by allyl-allyl coupling with allylB(pin) as the nucleophile.[4]

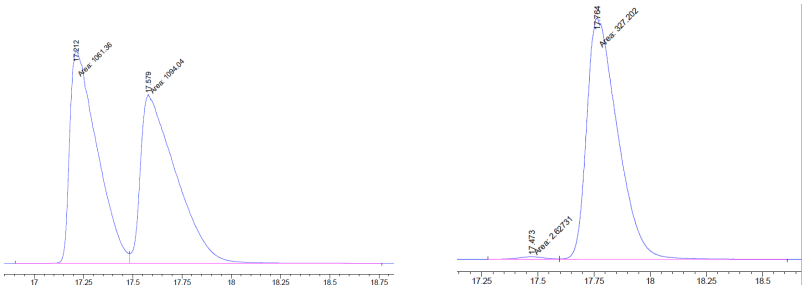


From reference 4: $[\alpha]^{D}_{20}$ = +12.237 (*c* = 0.440, $CHCl_3$)

Derived from reaction: $[\alpha]^{D}_{20}$ = +14.997 (*c* = 0.403, $CHCl_3$)

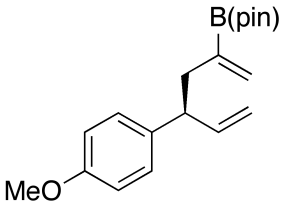


Chiral GLC (CD-BDM, Supelco, 110 °C, 25 psi)-analysis of corresponding ketone.



racemic reaction product

Peak #	RetTime [min]	Type	Width [min]	Area [pA*s]	Height [pA]	Area %
1	17.473	MF	0.1269	2.62731	3.44980e-1	0.79657
2	17.764	FM	0.1591	327.20193	34.27280	99.20343

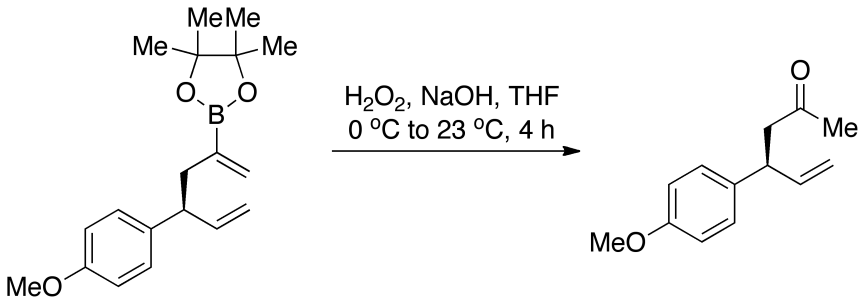


(*S*)-2-(4-(4-methoxyphenyl)hexa-1,5-dien-2-yl)-4,4,5,5-tetramethyl-1,3,2-dioxaborolane (Table 1.8, 1.54): From (*E*)-1-(3-chloroprop-1-en-1-yl)-4-methoxybenzene (27.4 mg, 0.15 mmol), representative procedure E was followed. ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.11 (2H, d, *J* = 8.5 Hz), 6.82 (2H, d, *J* = 8.5 Hz), 5.94 (1H, ddd, *J* = 17.0, 10.5, 7.5 Hz), 5.78 (1H, d, br, *J* = 3.5 Hz), 5.52 (1H, d, br, *J* = 3.0 Hz), 4.99 (1H, d, *J* = 10.5 Hz), 4.95 (1H, d, *J* = 17.0 Hz), 3.78 (3H, s), 3.48 (1H, dt, *J* = 15.0, 8.0 Hz), 2.57 (1H, dd, *J* = 14.0, 8.0 Hz), 2.52 (1H, dd, *J* = 14.0, 8.0 Hz), 1.23 (12H, s); ^{13}C NMR (125 MHz, $CDCl_3$): δ 157.9, 142.4, 136.4, 131.1, 128.8 (2C), 113.9, 113.7 (2C), 83.3 (2C), 55.2, 48.9, 41.4, 24.8 (4C); IR (neat): 2977 (m), 2932 (m), 1611 (m), 1510 (s), 1368 (s), 1247 (s), 1141 (s), 1037 (m), 861 (w) cm^{-1}; HRMS (ESI+) for $C_{19}H_{28}BO_3$ [M+H]: calculated 315.2055, found: 315.2072; $[\alpha]^{20}_D$ = 1.470 (*c* = 0.408, $CHCl_3$). The crude material was purified on silica gel (3% Et_2O/pentane) to afford a clear, colorless oil (36 mg, 79% yield). R_f = 0.20 (3% Et_2O/pentane, stain in $KMnO_4$).

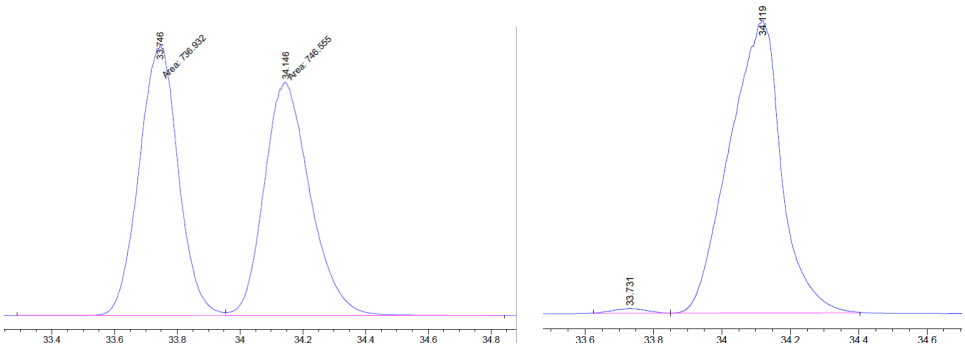
Analysis of Stereochemistry:

The title compound was oxidized with H_2O_2/NaOH to afford the corresponding ketone for GLC 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

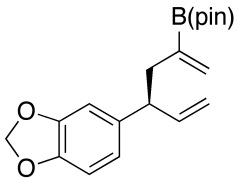
reaction. The absolute stereochemistry was assigned by analogy to **1.52** (p. 128)



Chiral GLC (CD-BDM, Supelco, 120 °C, 20 min, 25 psi)-analysis of corresponding ketone



Peak #	RetTime [min]	Type	Width [min]	Area [pA*s]	Height [pA]	Area %
1	33.731	MF	0.1313	39.36300	4.99698	1.24246
2	34.120	FM	0.1775	3128.79346	293.76785	98.75754

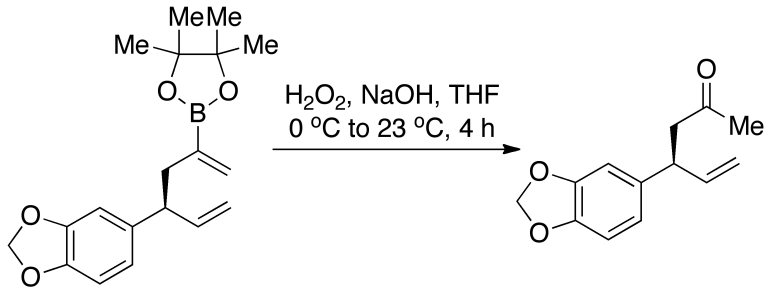


(*S*)-2-(4-(benzo[d][1,3]dioxol-5-yl)hexa-1,5-dien-2-yl)-4,4,5,5-tetramethyl-1,3,2-dioxaborolane (Table 1.8, 1.56): From (*E*)-5-(3-chloroprop-1-en-1-yl)benzo[*d*]

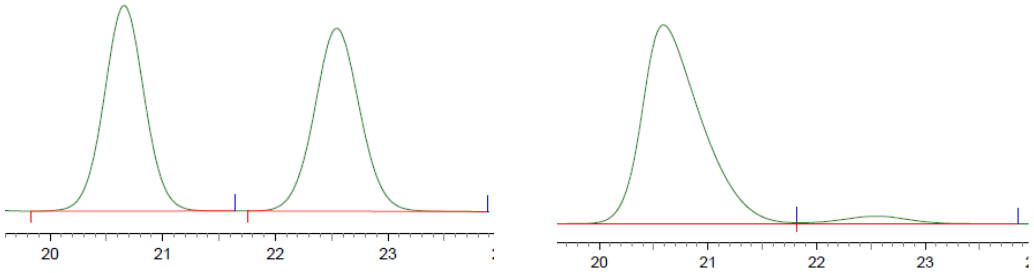
[1,3]dioxole (30.1 mg, 0.15 mmol), general procedure E was used. ^{1}H NMR (500 MHz, $CDCl_3$): δ 6.72-6.69 (2H, m), 6.63 (1H, d, *J* = 8.0 Hz), 5.90 (2H, s), 5.95-5.86 (1H, m), 5.78 (1H, d, br, *J* = 3.5 Hz), 5.53 (1H, d, br, *J* = 3.0 Hz), 4.99 (1H, d, *J* = 10.5 Hz), 4.97 (1H, d, *J* = 14.0 Hz), 3.46 (1H, dt, *J* = 15.0, 7.5 Hz), 2.54 (1H, dd, *J* = 13.5, 7.5 Hz), 2.48 (1H, dd, *J* = 13.5, 7.5 Hz), 1.24 (12H, s); ^{13}C NMR (125 MHz, $CDCl_3$): δ 147.5, 145.7, 142.1, 138.2, 131.2, 120.8, 114.0, 108.2, 108.0, 100.7, 83.3 (2C), 49.4, 41.4, 24.8 (4C); IR (neat): 2977 (m), 1611 (w), 1486 (s), 1440 (s), 1367 (s), 1308 (s), 1141 (s), 1039 (s), 938 (m), 862 (m), 737 (m) cm^{-1}; HRMS (ESI+) for $C_{19}H_{26}BO_4$ [M+H]: calculated 329.1846, found: 329.1919; $[\alpha]^{20}_D$ = 1.823 (*c* = 2.167, $CHCl_3$). The crude material was purified on silica gel (3% Et_2O/pentane) to afford a clear, colorless oil (37 mg, 72% yield). R_f = 0.21 (3% Et_2O/pentane, stain in $KMnO_4$).

Analysis of Stereochemistry:

The title compound was oxidized with H_2O_2/NaOH to afford the corresponding ketone for GLC 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 **1.52** (p. 128).

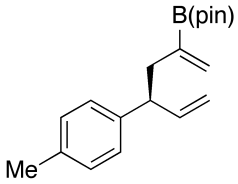


Chiral HPLC (OD-R, Chiracel, 1 mL/min, 0.5% iPA/hexane)-analysis of the corresponding ketone



racemic reaction product

Retention Time	Area	Area %	Height	Height %
20.590	444803996	95.90	11686105	96.35
22.550	19004236	4.10	442123	3.65

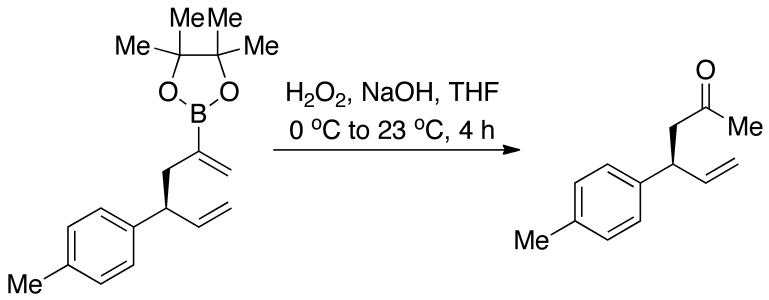


(*S*)-4,4,5,5-tetramethyl-2-(4-p-tolylhexa-1,5-dien-2-yl)-1,3,2-dioxaborolane (Table 1.8, 1.53): From (*E*)-1-(3-chloroprop-1-en-1-yl)-4-methylbenzene (24.9 mg, 0.15 mmol), general procedure E was used. ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.08 (4H, s), 5.94 (1H, ddd, *J* = 17.0, 10.5, 7.5 Hz), 5.77 (1H, d, br, *J* = 3.5 Hz), 5.53 (1H, d, br, *J* = 3.5 Hz), 4.98 (1H, d, *J* = 10.5 Hz), 4.97 (1H, d, *J* = 17.0 Hz),

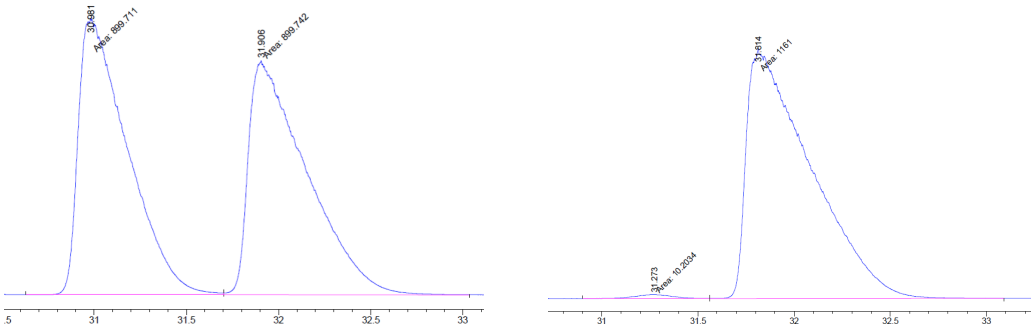
3.48 (1H, dt, J = 15.5, 7.5 Hz), 2.59-2.51 (2H, m), 2.29 (3H, s), 1.24 (12H, s); ^{13}C NMR (125 MHz, $CDCl_3$): δ 142.2, 141.2, 135.4, 131.0, 128.9 (2C), 127.7 (2C), 114.0, 83.3 (2C), 49.4, 41.4, 24.8 (4C), 20.9; IR (neat): 2977 (m), 1512 (w), 1368 (s), 1308 (s), 1141 (s), 861 (w), 736 (w) cm^{-1}; HRMS (ESI+) for $C_{19}H_{28}BO_2$ [M+H]: calculated 299.2275, found: 299.2193; $[\alpha]^{20}_D$ = 15.028 (c = 1.350, $CHCl_3$). The crude material was purified on silica gel (1% Et_2O/pentane) to afford a clear, colorless oil (32 mg, 66% yield). R_f = 0.28 (1% Et_2O/pentane, stain in $KMnO_4$).

Analysis of Stereochemistry:

The title compound was oxidized with H_2O_2/NaOH to afford the corresponding ketone for GLC 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 **1.52** (p. 128).

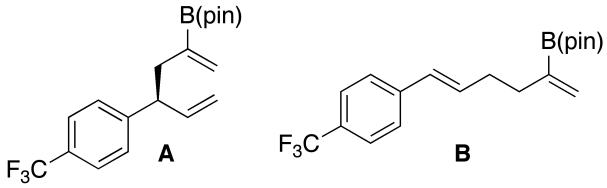


Chiral GLC (CD-BDM, Supelco, 110 °C, 50 min, 25 psi) -analysis of corresponding ketone



racemic reaction product

Peak #	RetTime [min]	Type	Width [min]	Area [pA*s]	Height [pA]	Area %
1	31.273	MF	0.2202	10.20343	7.72156e-1	0.87119
2	31.814	FM	0.3840	1161.00378	50.39377	99.12881



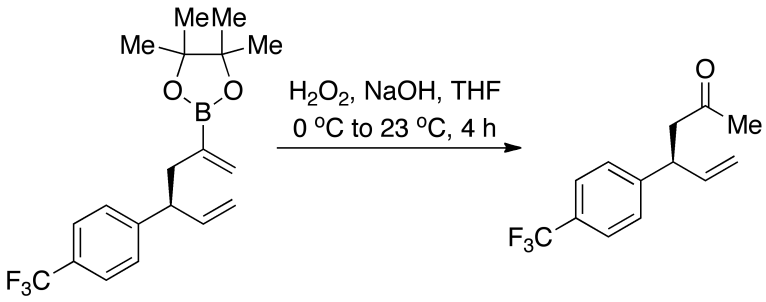
(*S*)-4,4,5,5-tetramethyl-2-(4-(4-(trifluoromethyl)phenyl)hexa-1,5-dien-2-yl)-1,3,2-dioxaborolane & **(E)-4,4,5,5-tetramethyl-2-(6-(4-(trifluoromethyl)phenyl)hexa-1,5-dien-2-yl)-1,3,2-dioxaborolane (Scheme**

1.35, 1.65): General Procedure E was used. ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.53 (4H, **A** & **B**, d, *J* = 8.5 Hz), 7.42 (2H, **A** & **B**, d, *J* = 8.5 Hz), 7.29 (2H, **A** & **B**, d, *J* = 13.0 Hz), 6.42-6.31 (**B**, 2H, m), 5.95 (**A**, 1H, ddd, *J* = 17.0, 10.5, 7.5 Hz), 5.83 (**B**, 1H, d, br, *J* = 3.0 Hz), 5.80 (**A**, 1H, d, br, *J* = 3.5 Hz), 5.66 (**B**, d, br, *J* = 3.0 Hz), 5.54 (**A**, 1H, d, br, *J* = 3.0 Hz), 5.05 (**A**, 1H, d, *J* = 10.5 Hz), 4.99 (**A**, 1H, d, *J* = 17.0 Hz), 3.60 (**A**, 1H, dt, *J* = 15.0, 7.5 Hz), 2.60 (**A**, 1H, dd, *J* = 13.0, 7.5 Hz), 2.39-2.33 (**B**, 4H, m), 2.55 (**A**, 1H, dd, *J* = 13.0, 7.5 Hz), 1.26 (**A**, 12H, s), 1.12 (**B**, 12H, s); ^{13}C NMR (125 MHz, $CDCl_3$): δ 148.22, 148.2, 141.1, 133.7, 131.7, 129.8, 128.7, 128.5, 128.3, 128.2, 126.0, 125.7, 125.4, 125.3, 125.2, 125.14, 125.1, 114.9, 83.4, 49.7, 41.1, 34.9, 32.8, 24.7, 24.6, 10.5; IR (neat): 2979 (m), 1616 (w), 1420 (m), 1369 (m), 1325 (s), 1164 (m), 1124 (s), 1068 (s), 861 (w) cm^{-1}; HRMS (ESI+) for $C_{19}H_{25}BF_3O_2$ [M+H]: calculated 353.1989, found: 353.1903; $[\alpha]^{20}_D$ = –2.541 (*c* = 1.275, $CHCl_3$). The crude material was purified on silica gel (2% Et_2O/pentane) to afford a clear, colorless oil (34 mg, 64% yield). R_f = 0.26 (2% Et_2O/pentane, stain in $KMnO_4$).

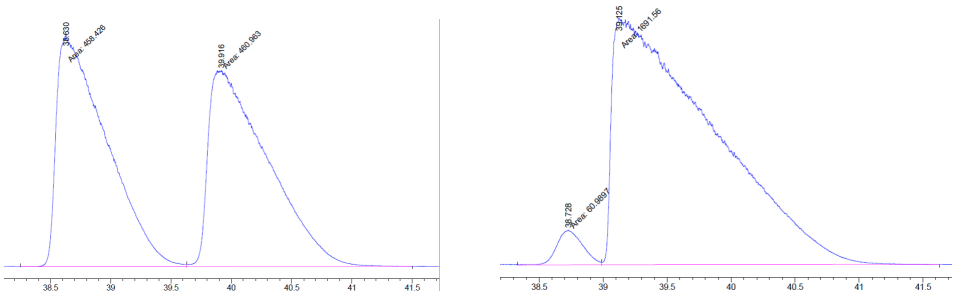
Analysis of Stereochemistry:

The title compound was oxidized with H_2O_2/NaOH to afford the corresponding ketone for GLC 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 **1.52** (p. 128).

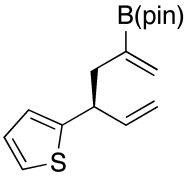


Chiral GLC (CD-BDM, Supelco, 100 °C, 25 psi)-analysis of corresponding ketone



racemic reaction product

Peak #	RetTime [min]	Type	Width [min]	Area [pA*s]	Height [pA]	Area %
1	38.728	MF	0.2334	60.98970	4.35550	3.48005
2	39.125	FM	0.9116	1691.56177	30.92603	96.51995

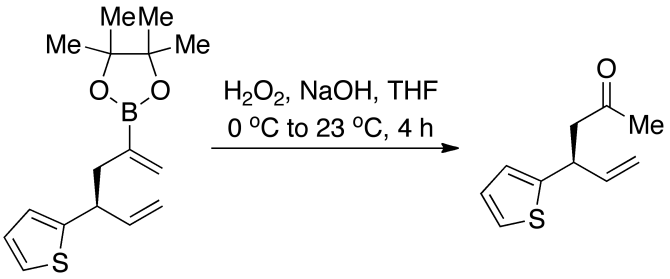


(*S*)4,4,5,5-tetramethyl-2-(4-(thiophen-2-yl)hexa-1,5-dien-2-yl)-1,3,2-dioxaborolane (Table 1.8, 1.55): From (*E*)-2-(3-chloroprop-1-en-1-yl)thiophene (21.1 mg, 0.15 mmol), general procedure E was used. ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.14 (1H,

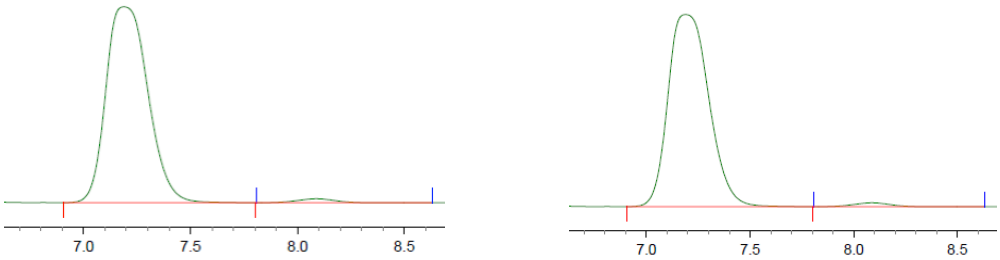
dd, *J* = 5.0, 1.0 Hz), 6.93 (1H, dd, *J* = 5.0, 3.5 Hz), 6.82-6.81 (1H, m), 5.94 (1H, ddd, *J* = 17.5, 9.5, 8.0 Hz), 5.83 (1H, d, br, *J* = 3.0 Hz), 5.59 (1H, d, br, *J* = 3.0 Hz), 5.06-5.02 (2H, m), 3.86 (1H, dd, *J* = 16.0, 8.0 Hz), 2.69 (1H, dd, *J* = 13.0, 7.5 Hz), 2.60 (1H, dd, *J* = 13.0, 7.5 Hz), 1.26 (12H, s); ^{13}C NMR (125 MHz, $CDCl_3$): δ 148.2, 141.4, 131.6, 126.5, 123.4, 123.1, 114.8, 83.4 (2C), 44.9, 42.4, 24.8 (4C); IR (neat): 2927 (s), 1617 (w), 1423 (m), 1388 (s), 1309 (s), 1142 (s), 829 (m), 735 (m) cm^{-1}; HRMS (ESI+) for $C_{16}H_{24}BO_2S$ [M+H]: calculated 291.1512, found: 291.1580; $[\alpha]^{20}_D$ = 29.239 (*c* = 1.108, $CHCl_3$). The crude material was purified on silica gel (1% Et_2O/pentane) to afford a clear, colorless oil (31 mg, 79% yield). R_f = 0.26 (3% Et_2O/pentane, stain in $KMnO_4$).

Analysis of Stereochemistry:

The title compound was oxidized with H_2O_2/NaOH to afford the corresponding ketone for GLC 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 **1.52** (p. 128).

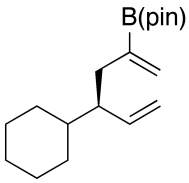


Chiral HPLC (OD-R, Chiracel, 1% i-PA/hexane, 1 mL/min, 220 nm)-analysis of corresponding ketone



racemic reaction product

Retention Time	Area	Area %	Height	Height %
7.190	928560242	98.22	67907201	98.04
8.087	16809644	1.78	1359094	1.96

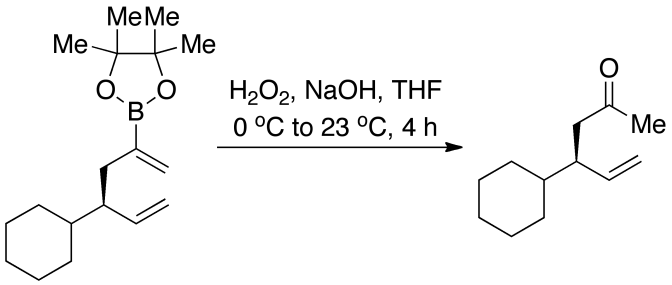


(*S*)-2-(4-cyclohexylhexa-1,5-dien-2-yl)-4,4,5,5-tetramethyl-1,3,2-dioxaborolane (Table 1.9, 1.59): From an isomeric mixture of (*E*)-(3-chloroprop-1-en-1-yl)cyclohexane (29 mg, 0.15 mmol), representative procedure E was followed. ^{1}H NMR (500 MHz, $CDCl_3$): δ 5.58-5.51 (2H, m), 5.77 (1H, d, br, J = 3.5 Hz), 4.93 (1H, dd, J = 10.5, 2.0 Hz), 4.85-4.81 (1H, m), 2.34 (1H, dd, J = 13.0, 5.0 Hz), 2.09 (1H, dd, J = 12.5, 9.5 Hz), 2.02 (1H, dddd (app dtd), J = 14.0, 9.5, 5.0, 5.0

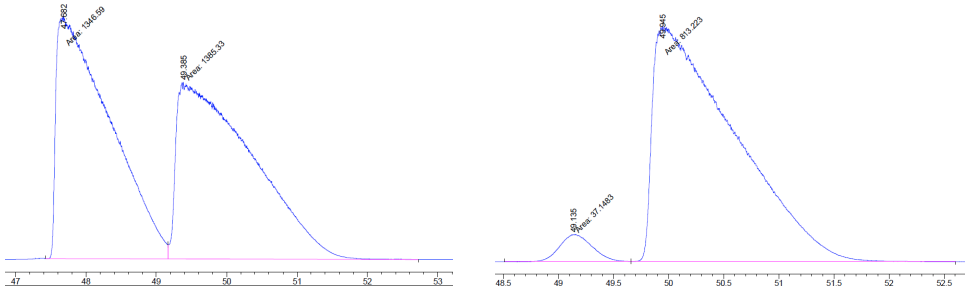
Hz), 1.71-1.60 (6H, m), 1.25 (12H, s), 1.24-1.01 (5H, m); ^{13}C NMR (125 MHz, $CDCl_3$): δ 141.1, 129.9, 114.9, 83.2 (2C), 50.1, 41.4, 37.9, 31.3, 29.1, 26.8, 26.7, 26.6, 24.7 (4C); IR (neat): 2922 (s), 1637 (w), 1447 (m), 1368 (s), 1344 (s), 1142 (s), 939 (m), 890 (m), 864 (m) cm^{-1}; HRMS (ESI+) for $C_{18}H_{32}BO_2$ [M+H]: calculated 291.2417, found: 291.2509; $[\alpha]^{20}_D$ = –2.004 (*c* = 2.180, $CHCl_3$). The crude material was purified on silica gel (2% Et_2O/pentane) to afford a clear, colorless oil (35 mg, 66% yield). R_f = 0.23 (2% Et_2O/pentane, stain in $KMnO_4$).

Analysis of Stereochemistry:

The title compound was oxidized with H_2O_2/NaOH to afford the corresponding ketone for GLC 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 **1.52** (p. 128).



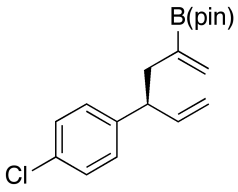
Chiral GLC (CD-BDM, Supelco, 90 °C, 25 psi) analysis of corresponding ketone



racemic

reaction product

Peak #	RetTime [min]	Type	Width [min]	Area [pA*s]	Height [pA]	Area %
1	49.135	MF	0.3398	37.14832	1.82202	4.36848
2	49.945	FM	0.8543	813.22266	15.86481	95.63152

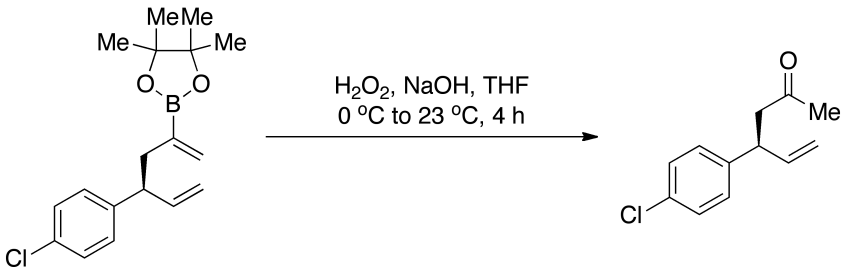


***(S)*-2-(4-(4-chlorophenyl)hexa-1,5-dien-2-yl)-4,4,5,5-tetramethyl-1,3,2-dioxaborolane (Table 1.8, 1.57).** The title compound was prepared *via* General Procedure E for allyl-allyl coupling on a 0.267 mmol scale with (*E*)-1-chloro-4-(3-chloroprop-1-en-1-yl)benzene and a 10% catalyst loading. ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.26-7.22 (2H, m), 7.12-7.09 (2H, m), 5.93 (1H, ddd, *J* = 17.5, 10.5, 7.5 Hz), 5.78 (1H, d, br, *J* = 3.5 Hz), 5.52 (1H, d, br, *J* = 3.5 Hz), 5.01 (1H, ddd (app

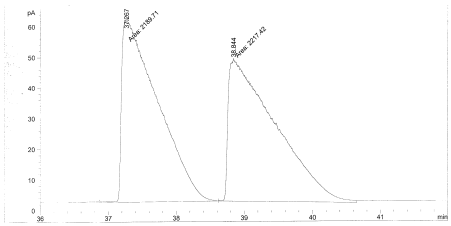
dt), *J* = 10.5, 1.5, 1.5 Hz), 4.97 (1H, ddd (app dt), *J* = 17.5, 1.5, 1.5 Hz), 3.51 (1H, ddd (app q), *J* = 7.5, 7.5, 7.5 Hz), 2.57 (1H, dd, *J* = 13.5, 7.5 Hz), 2.51 (1H, dd, *J* = 13.5, 7.5 Hz), 1.23 (12H, s); ^{13}C NMR (125 MHz, $CDCl_3$): δ 142.6, 141.6, 131.7, 131.5, 129.3 (2C), 128.4 (2C), 114.6, 83.4 (2C), 49.1, 41.3, 24.8 (4C); IR (neat): 2978 (m), 1637 (w), 1491 (m), 1424 (m), 1389 (s), 1310 (s), 1213 (m), 1141 (s), 1092 (m), 915 (w), 861 (w), 828 (w) cm^{-1}; HRMS-(ESI+) for $C_{18}H_{25}O_2BCl$ [M+H]: calculated: 319.1636, found: 319.1643. $[\alpha]^{20}_D$ = –1.739 (c = 0.575, $CHCl_3$). The crude reaction mixture was purified on silica gel (5% EtOAc/ hexanes) to afford a clear, colorless oil (66 mg, 78% yield). R_f = 0.24 (5% EtOAc/ hexanes, stain in $KMnO_4$).

Analysis of Stereochemistry:

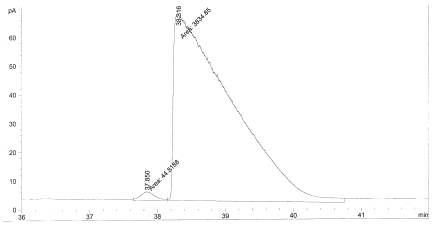
The title compound was oxidized with H_2O_2/NaOH to afford the corresponding ketone for GLC analysis, as depicted below. The analogous racemic material was prepared *via* the same route, using 1,2-bis(diphenylphosphino)benzene as the achiral ligand in the allyl-allyl coupling reaction. The absolute stereochemistry was assigned by analogy to **1.52** (p. 128).



Chrial GLC (CD-BDM, Supelco, 120 °C, 20 psi)-analysis of ketone

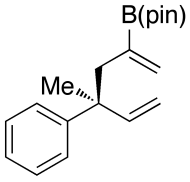


racemic



reaction product

Peak #	RetTime [min]	Type	Width [min]	Area [pA*s]	Height [pA]	Area %
1	37.850	MM	0.2512	44.81876	2.97332	1.15522
2	38.316	MM	0.9887	3834.84570	64.64339	98.84478

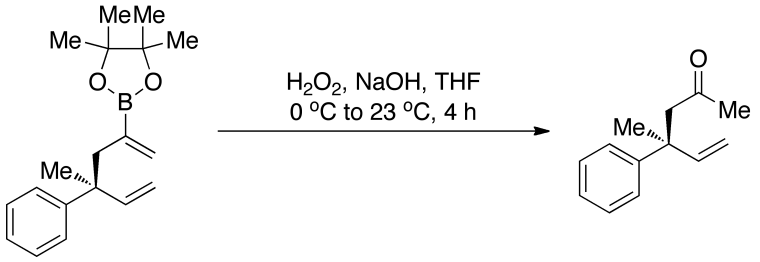


(*S*)-4,4,5,5-tetramethyl-2-(4-methyl-4-phenylhexa-1,5-dien-2-yl)-1,3,2-dioxaborolane (Table 1.9, 1.58). The title compound was prepared *via* General Procedure E for allyl-allyl coupling on a 0.300 mmol scale with (*E*)-(4-chlorobut-2-en-2-yl)benzene, at 60 °C and with a THF/H_2O (20 : 1) mixed solvent system. ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.35-7.27 (2H, m), 7.27-7.25 (2H, m), 7.15 (1H, app tt, *J* = 6.9, 1.5 Hz), 6.10 (1H, dd, *J* = 17.5, 11.0 Hz), 5.82 (1H, d, br, *J* = 3.5 Hz), 5.40 (1H, d, br, *J* = 3.5 Hz), 5.06 (1H, dd, *J* = 11.0, 1.5 Hz), 5.01 (1H, dd, *J* = 17.5, 1.5 Hz), 2.68 (1H,

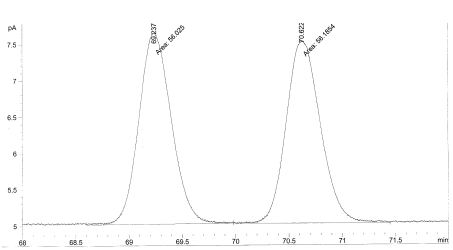
d, *J* = 12.0 Hz), 2.59 (1H, d, *J* = 12.0 Hz), 1.30 (3H, s), 1.18 (12H, s); ^{13}C NMR (125 MHz, $CDCl_3$): δ 147.8, 146.6, 12.8, 127.9 (2C), 126.8 (2C), 125.7, 112.2, 83.3 (2C), 45.5, 44.8, 24.9 (2C), 24.6 (2C), 24.0; IR (neat): 3059 (m), 2977 (w), 1635 (w), 1613 (w), 1444 (m), 1424 (m), 1367 (s), 1307 (s), 1193 (m), 1142 (s), 977 (w), 948 (w), 865 (w), 768 (m), 723 (s) cm^{-1}; HRMS-(ESI+) for $C_{19}H_{28}O_2B$ [M +H]: calculated: 299.2182, found: 299.2170. $[\alpha]^{20}_D$ = 4.316 (c = 0.630, $CHCl_3$). The crude reaction mixture was purified on silica gel (2% EtOAc/hexanes) to afford a clear, colorless oil (40 mg, 44% yield). R_f = 0.11 (2% EtOAc/hexanes, stain in $KMnO_4$).

Analysis of Stereochemistry

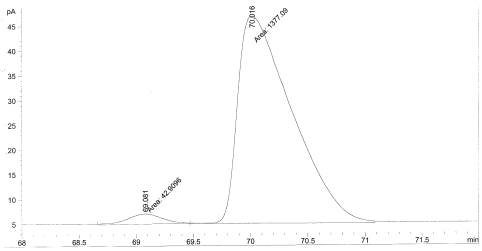
The title compound was oxidized with H_2O_2/NaOH to afford the corresponding ketone for GLC analysis, as depicted below. The analogous racemic material was prepared *via* the same route, using 1,2-bis(diphenylphosphino)benzene as the achiral ligand in the allyl-allyl coupling reaction. The absolute stereochemistry was assigned by analogy to **1.52** (p. 128).



Chrial GLC (CD-BDM, Supelco, 60 ˚C for 20 min, then 2.5 deg/min to 100 ˚C 20 psi)-analysis of ketone

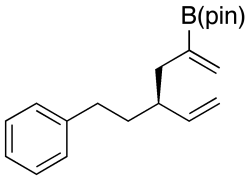


racemic



reaction product

Peak #	RetTime [min]	Type	Width [min]	Area [pA*s]	Height [pA]	Area %
1	69.081	MM	0.3505	42.90964	2.04024	3.02181
2	70.016	MM	0.5481	1377.08679	41.87139	96.97819

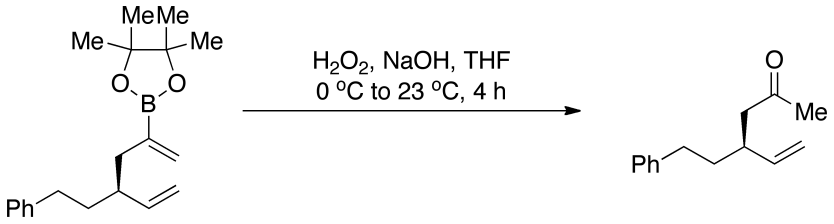


(*S*)-4,4,5,5-tetramethyl-2-(4-phenethylhexa-1,5-dien-2-yl)-1,3,2-dioxaborolane (Table 1.9, 1.61): The title compound was synthesized *via* General Procedure F for the allyl-allyl coupling with 0.277 mmol of (*E*)-(5-chloropent-3-en-1-yl)benzene. ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.26-7.22 (2H, m), 7.18-7.12 (3H, m), 5.79 (1H, d, br, *J* = 3.5 Hz), 5.58 (1H, ddd, *J* = 17.0, 10.0, 8.0 Hz), 5.54 (1H, d, br, *J* = 3.5 Hz), 4.99 (1H, dd, *J* = 10.0, 2.0 Hz), 4.94 (1H, ddd, *J* = 17.0,

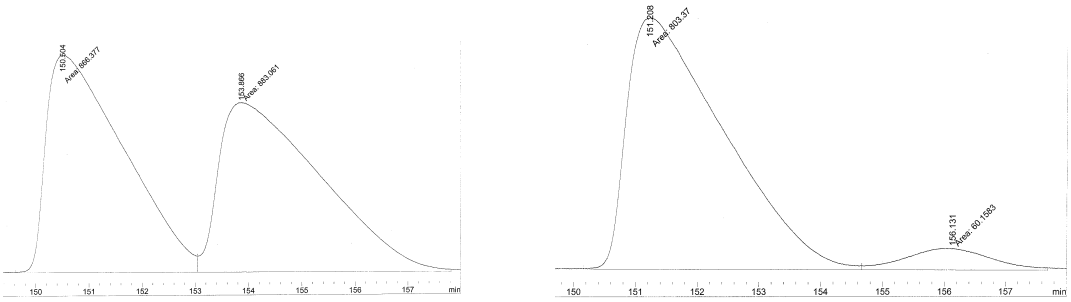
2.0, 1.0 Hz), 2.66 (1H, ddd, *J* = 14.0, 10.0, 5.0 Hz), 2.50 (1H, ddd, *J* = 14.0, 10.0, 6.5 Hz), 2.27-2.21 (2H, m), 2.20-2.13 (1H, m), 1.77-1.70 (1H, m), 1.53-1.46 (1H, m), 1.21 (12H, s); ^{13}C NMR (125 MHz, $CDCl_3$): δ 142.9, 142.7, 130.5, 128.4 (2C), 128.2 (2C), 125.5, 114.7, 83.3 (2C), 43.6, 41.3, 36.2, 33.5, 24.7 (4C); IR (neat): 3063 (m), 2978 (m), 2927 (m), 2858 (w), 1638 (w), 1615 (w), 1496 (m), 1369 (s), 1309 (s), 1189 (s), 970 (w), 942 (w), 911 (m), 863 (m), 828 (m), 699 (m), 671 (m) cm^{-1}; HRMS-(ESI+) for $C_{20}H_{30}O_2B$ [M+H]: calculated: 313.2339, found: 313.2349. $[\alpha]^{20}_D$ = 1.760 (c = 1.500, $CHCl_3$). The crude material was purified on silica gel (5% EtOAc/hexanes) to afford a clear, colorless oil (65 mg, 75% yield). R_f = 0.33 (5% EtOAc/hexanes, stain in $KMnO_4$).

Analysis of Stereochemistry

The title compound was oxidized with H_2O_2/NaOH to afford the corresponding ketone for GLC 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 **1.52** (p. 128).

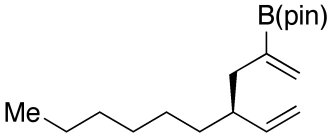


Chrial GLC (CD-BDM, Supelco, 60 ˚C for 20 min, then 2.5 deg/min to 100 ˚C, 20 psi)-analysis of ketone



racemic reaction product

Peak #	RetTime [min]	Type	Width [min]	Area [pA*s]	Height [pA]	Area %
1	151.208	MF	1.8223	803.37030	7.34767	93.03344
2	156.131	FM	1.5859	60.15827	6.32221e-1	6.96656

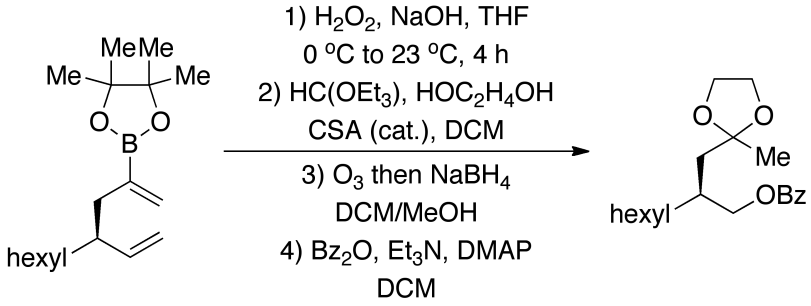


(*S*)-4,4,5,5-tetramethyl-2-(4-vinyldec-1-en-2-yl)-1,3,2-dioxaborolane (Table 1.9, 1.60): The title compound was synthesized *via* General Procedure F for the allyl-allyl coupling with 0.311 mmol of (*E*)-1-chloronon-2-ene. ^{1}H NMR (500 MHz, $CDCl_3$): δ 5.77 (1H, d, br, *J* = 3.5 Hz), 5.55-5.48 (2H, m), 4.89 (1H, dd, *J* = 10.5, 2.0 Hz), 4.86 (1H, ddd, *J* = 17.0, 2.0, 1.0 Hz), 2.22-2.07 (3H, m), 1.41-1.11 (22H, m), 0.85 (3H, t, *J* = 7.0 Hz); ^{13}C NMR (125 MHz, $CDCl_3$): δ 143.3,

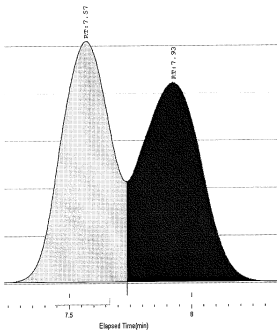
130.3, 114.0, 83.3 (2C), 44.1, 41.2, 34.5, 31.9, 29.4, 27.1, 24.7 (4C), 22.7, 14.1; IR (neat): 3066 (w), 2978 (s), 2926 (s), 2856 (m), 1640 (w), 1616 (w), 1421 (m), 1369 (s), 1308 (s), 1144 (s), 971 (m), 941 (m), 864 (m), 828 (m) cm^{-1}; HRMS-(ESI+) for $C_{18}H_{34}O_2B$ [M+H]: calculated: 293.2652, found: 293.2644. $[\alpha]^{20}_D$ = –4.148 (c = 2.150, $CHCl_3$). The crude material was purified on silica gel (5% EtOAc/hexanes) to afford a clear, colorless oil (67 mg, 73% yield). R_f = 0.60 (5% EtOAc/hexanes, stain in $KMnO_4$).

Analysis of Stereochemistry

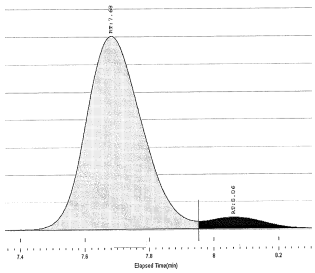
The title compound was converted to a benzoate for SFC analysis as depicted below. The analogous racemic material was prepared *via* the same route, using 1,2-bis(diphenylphosphino)benzene as the achiral ligand in the allyl-allyl coupling reaction. The absolute stereochemistry was assigned by analogy to compound **1.52** (p. 128).



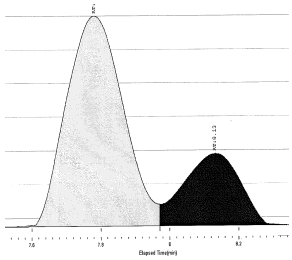
Chrial SFC (OJ-H, Chiralcel, 1.5 mL/min, no modifier, 220 nm)-analysis of benzoate



racemic

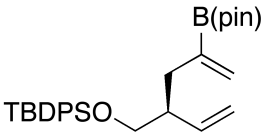


reaction product



product + racemic

Peak Name	Number	Concentration	Area %	Area	Area Sum
Peak1	1	0	94.434	8386.9334	
Peak2	2	0	5.566	494.3331	8881.2666

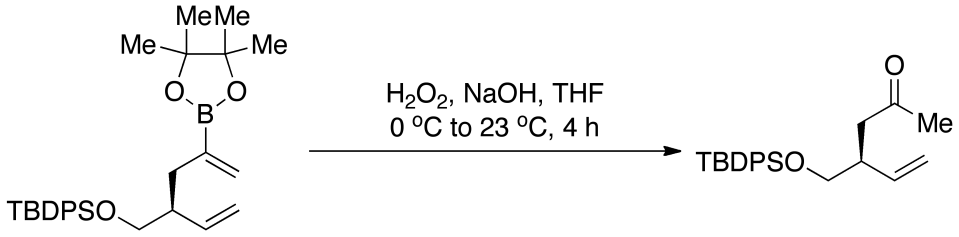


(*S*)-*tert*-butyldiphenyl((4-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)-2-vinylpent-4-en-1-yl)oxy)silane (Table 1.9, 1.62): The title compound was synthesized *via* General Procedure F for the allyl-allyl coupling with 0.261 mmol of (*Z*)-*tert*-butyl((4-chlorobut-2-en-1-yl)oxy)diphenylsilane and Cs_2CO_3 as the base. ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.67-7.64 (4H, m), 7.42-7.24 (6H, m), 5.79 (1H, d, br, J = 3.5 Hz), 5.66 (1H, ddd, J = 17.0, 10.0, 8.0 Hz), 5.55 (1H, d, br, 3.5 Hz), 4.98 (1H, dd, J = 11.0, 1.5 Hz), 4.96 (1H, ddd, J = 17.0, 2.0, 1.0 Hz), 3.61-3.55 (2H, m), 2.49-2.45 (2H, m), 2.11 (1H, ddd (app dt), J = 10.5, 10.5, 10.5 Hz), 1.22 (12H, s), 1.04 (9H, s); ^{13}C NMR (125 MHz, $CDCl_3$): δ 140.1, 135.7 (4C), 134.1,

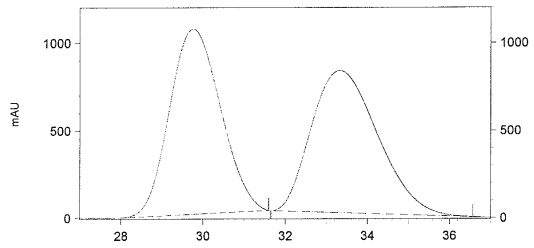
134.0, 130.7, 129.5, 129.4, 127.5 (4C), 115.5, 83.3 (2C), 66.9, 46.5, 36.9, 26.9, 24.7 (4C), 19.4 (3C); IR (neat): 3071 (w), 2977 (m), 2858 (m), 1640 (w), 1472 (s), 1388 (s), 1309 (s), 1213 (w), 1143 (s), 1110 (s), 913 (w), 823 (w), 800 (w), 739 (m), 702 (s), 614 (w), 505 (m) cm^{-1}; HRMS-(ESI+) for $C_{29}H_{41}O_3BSi$ [M+H]: calculated: 477.2996, found: 477.3004. $[\alpha]^{20}_D = 3.729$ (c = 0.665, $CHCl_3$). The crude material was purified on silica gel (5% EtOAc/hexanes) to afford a clear, colorless oil (68 mg, 55% yield). $R_f = 0.25$ (5% EtOAc/hexanes, stain in $KMnO_4$).

Analysis of Stereochemistry

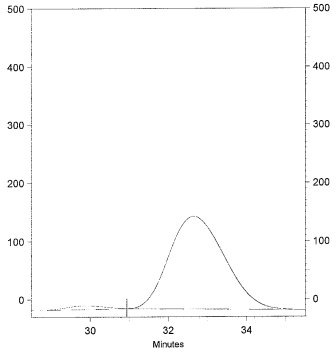
The title compound was oxidized with H_2O_2/NaOH to afford the corresponding ketone for GLC analysis, as depicted below. The analogous racemic material was prepared *via* the same route, using 1,2-bis(diphenylphosphino)benzene as the achiral ligand in the allyl-allyl coupling reaction. The absolute stereochemistry was assigned by analogy to **1.52** (p. 128).



Chrial HPLC (AS-H, Chiralcel, 0.2 mL/min, 0.2% isopropanol, 220 nm)-analysis of ketone



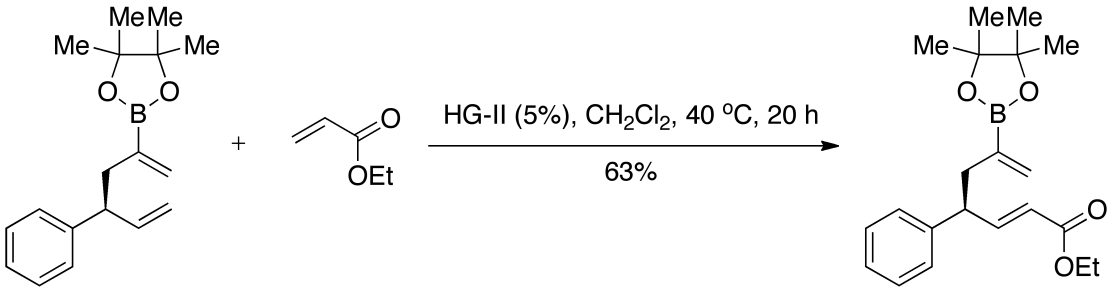
racemic

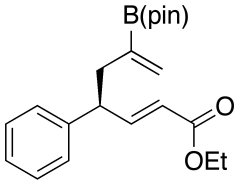


reaction product

Retention Time	Area	Area %	Height	Height %
29.883	7172651	2.65	107482	3.86
32.647	263486670	97.35	2674436	96.14

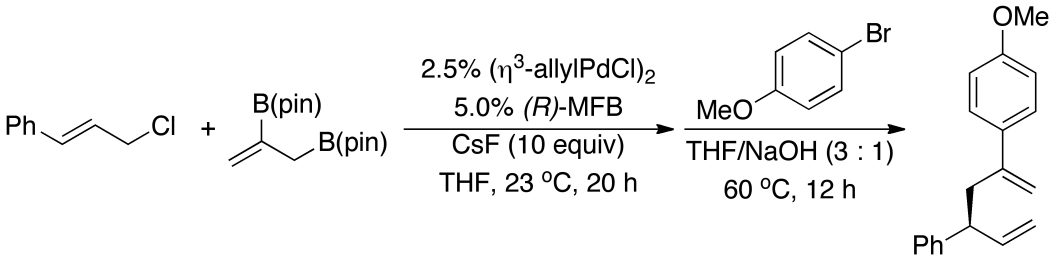
E. Procedures and Characterizations for Derivatives of 1.52

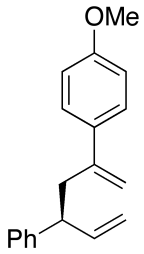




(*S*,*E*)-ethyl 4-phenyl-6-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)hepta-2,6-dienoate (Scheme 1.34, 1.50): In the dry-box, an oven-dried 1.0 dram vial equipped with a stir bar was charged with (*S*)-4,4,5,5-tetramethyl-2-(4-phenylhexa-1,5-dien-2-yl)-1,3,2-dioxaborolane (50 mg, 0.176 mmol), HG-II (5.6 mg, 0.009 mmol), ethyl acrylate (0.06 mL, 0.528 mmol), and CH_2Cl_2 (0.9 mL, 0.2 M). The vial was then capped and sealed with tape, removed from the dry-box, and allowed to stir at 40 ºC for 20 h. The reaction was then cooled to room temperature and 5 drops of *tert*-butylvinyl ether was added by pipette. The vial was capped and the reaction was allowed to stir at room temperature for 30 minutes. The reaction mixture was then then passed through a 6 cm plug of silica gel (10% ether/pentane) and concentrated under reduced pressure. The crude product was purified on silica gel (3% EtOAc/hexanes) to afford a clear, colorless oil (40 mg, 64% yield). R_f = 0.24 (10% EtOAc/hexanes, stain in $KMnO_4$). ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.29-7.24 (2H, m), 7.24-7.14 (3H, m), 7.07 (1H, dd, *J* = 15.5, 7.5 Hz), 5.79 (1H, d, br, *J* = 3.5 Hz), 5.72 (1H, dd, *J* = 15.5, 1.5 Hz), 5.52 (1H, d, br, *J* = 3.5 Hz), 4.13 (2H, q, *J* = 7.0 Hz), 3.68 (1H, dd, *J* = 15.5, 8.0 Hz), 2.65 (1H, dd, *J* = 13.5, 8.0 Hz), 2.58 (1H, dd, *J* = 13.5, 7.5 Hz), 1.26-1.22 (15H, m); ^{13}C NMR (125 MHz, $CDCl_3$): δ 166.6, 151.6, 142.1, 132.1, 128.5 (2C), 128.0 (2C), 126.6, 120.9, 83.4 (2C), 60.1, 48.3, 40.8, 24.8, 24.7 (4C), 14.2; IR (neat): 3028 (m), 2979 (w), 1719 (s), 1650 (w), 1425 (m), 1369 (s), 1310 (s), 1271 (m), 1169 (s), 1139 (s), 1096

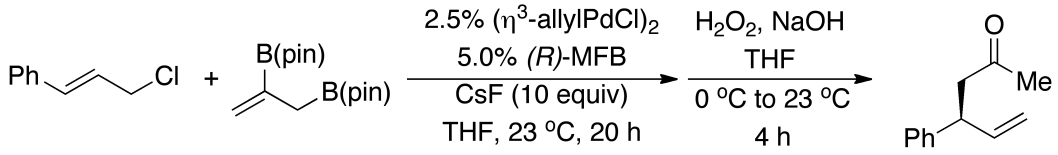
(w), 1044 (w), 862 (w), 761 (m) cm^{-1}; HRMS-(ESI+) for $C_{21}H_{30}O_4B$ [M+H]: calculated: 357.2237, found: 357.2238. $[\alpha]^{20}_D = 2.470$ (*c* = 4.000, $CHCl_3$).





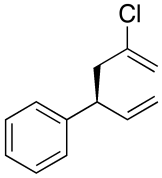
(*S*)-1-methoxy-4-(4-phenylhexa-1,5-dien-2-yl)benzene (Scheme 1.33, eq. 14, 1.47): With cinnamyl chloride (21.8 mg, 0.15 mmol), General Procedure E was followed for allyl-allyl cross coupling. After allowing to stir for 20 h at room temperature, the vial was brought back into the dry-box, where it was charged with 4-bromoanisole (33.7 mg, 0.18 mmol) and *S*-Phos (3.1 mg, 0.0075 mmol). The vial was capped with a rubber septum, removed from the dry-box, put under an atmosphere of nitrogen, and charged with 3M NaOH (0.3 mL). The rubber septum was then rapidly exchanged for a polypropylene cap. The vial was subsequently sealed with electrical tape, heated to 60 °C, and allowed to stir for 12 h. The reaction was allowed to cool to room temperature, diluted with water (5 mL) and extracted with Et_2O (3 x 10 mL). The combined organics were dried over $MgSO_4$, filtered, and concentrated under reduced pressure. The crude material was purified on silica gel (2% Et_2O/pentane) to afford a clear, colorless oil (33 mg, 82% yield). R_f

= 0.25 (2% Et_2O/pentane, stain in $KMnO_4$). ^1H NMR (500 MHz, $CDCl_3$): δ 7.30-7.28 (4H, m), 7.25-7.19 (1H, m), 7.18-7.12 (2H, m), 6.88-6.86 (2H, m), 5.98 (1H, ddd, *J* = 17.5, 10.5, 7.5 Hz), 5.14 (1H, d, br, *J* = 1.5 Hz), 5.01 (1H, d, *J* = 10.5 Hz), 4.93 (1H, d, *J* = 17.5 Hz), 4.86 (1H, m), 3.83 (3H, s), 3.40 (1H, dt, *J* = 14.5, 7.5 Hz), 2.93-2.85 (2H, m); ^{13}C NMR (125 MHz, $CDCl_3$): δ 159.0, 145.5, 143.9, 141.4, 133.5, 128.3 (2C), 127.7 (2C), 127.5 (2C), 126.2, 114.4, 113.7 (2C), 113.2, 55.3, 47.7, 41.8; IR (neat): 2935 (w), 1624 (m), 1511 (s), 1247 (s), 1179 (s), 1034 (m), 835 (m), 700 (m) cm^{-1}; HRMS (ESI+) for $C_{19}H_{21}O$ [M+H]: calculated 265.1592, found: 265.1601; $[\alpha]^{20}_D$ = –22.900 (*c* = 1.742, $CHCl_3$).



(*S*)-4-phenylhex-5-en-2-one (Scheme 1.33, 1.46): From cinnamyl chloride (21.8 mg, 0.15 mmol), General Procedure E was followed for allyl-allyl cross coupling. After allowing to stir for 20 h at room temperature, the vial was cooled to 0 °C and sequentially charged with THF (2 mL), 3M NaOH (2 mL), and 30%/wt H_2O_2. The resulting biphasic mixture was allowed to stir vigorously while warming to room temperature over 4 h. The reaction was then cooled to 0 °C and quenched with $Na_2S_2O_3$ (4 mL). The crude mixture was diluted with water (10 mL) and extracted with Et_2O (3 x 20 mL). The combined organics were dried

over $MgSO_4$, filtered, and concentrated under reduced pressure. The crude material was purified on silica gel (10% Et_2O/pentane) to afford a clear, colorless oil (20.6 mg mg, 82% yield). R_f = 0.34 (10% Et_2O/pentane, stain in $KMnO_4$). Spectral data is in accordance with the literature.[71] $[\alpha]^{20}_D$ = –5.625 (*c* = 1.070, $CHCl_3$).



(*S*)-(5-chlorohexa-1,5-dien-3-yl)benzene (Scheme 1.34, 1.48): The title compound was synthesized by the procedure of Hartwig *et al*. for the halogenation of vinyl boronic esters.[72] In a 20 mL scintillation vial, (*S*)-4,4,5,5-tetramethyl-2-(4-phenylhexa-1,5-dien-2-yl)-1,3,2-dioxaborolane (28.4 mg, 0.1 mmol) was dissolved in MeOH/H_2O (1 : 1, 2.5 mL total volume). The biphasic mixture was charged with $CuCl_2{\cdot}2H_2O$ (51.1 mg, 0.3 mmol), the vial was sealed, and the reaction was allowed to stir at 90 ºC for 12 h. After cooling to room temperature, the reaction mixture was diluted with water (5 mL) and extracted with Et_2O (3 x 10 mL). The combined organics were dried over $MgSO_4$, filtered, and concentrated under reduced pressure. The crude material was purified on silica gel (2% Et_2O/pentane) to afford a clear, colorless oil (17.3 mg, 85% yield). R_f = 0.45 (2% Et_2O/pentane, stain in $KMnO_4$). ^1H NMR (500 MHz, $CDCl_3$): δ 7.33-7.30 (2H, m), 7.24-7.20 (3H, m), 6.00 (1H, ddd, *J* = 17.0, 10.0, 7.5 Hz), 5.11-4.99 (4H, m), 3.74 (1H, dt, *J*

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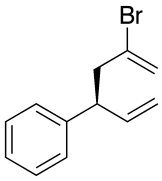
[71] Chen, J.; Peng, Q.; Lei, B.; Hou, X.; Wu, Y. *J. Am. Chem. Soc.* **2011**, *133*, 14180.

[72] Murphy, J. M.; Liao, X.; Hartwig, J. F. *J. Am. Chem. Soc.* **2007**, *129*, 15434.

= 15.0, 7.5 Hz), 2.74 (1H, dd, *J* = 14.5, 7.5 Hz), 2.70 (1H, dd, *J* = 14.5, 6.5 Hz); ^{13}C NMR (125 MHz, $CDCl_3$): δ 137.3, 135.1, 134.9, 123.2 (2C), 122.4 (2C), 121.2, 109.1, 108.8, 41.6, 39.9; IR (neat): 2924 (s), 2853 (m), 1635 (s), 1453 (m), 1207 (w), 963 (m), 917 (s), 881 (s), 699 (s), 676 (w) cm^{-1}; HRMS (ESI+) for $C_{12}H_{14}Cl$ [M+H]: calculated 193.0706, found: 193.0791 $[\alpha]^{20}_D$ = 4.109 (*c* = 0.308 , $CHCl_3$).



(*S*)-(5-bromohexa-1,5-dien-3-yl)benzene (Scheme 1.34, 1.49): The title compound was synthesized by the procedure of Hartwig *et al*. for the halogenation of vinyl boronic esters.[76] In a 20 mL scintillation vial, (*S*)-4,4,5,5-tetramethyl-2-(4-phenylhexa-1,5-dien-2-yl)-1,3,2-dioxaborolane (28.4 mg, 0.1 mmol) was dissolved in MeOH/H_2O (1 : 1, 2.5 mL total volume). The biphasic mixture was charged with $CuBr_2$ (67 mg, 0.3 mmol), sealed, and the reaction was allowed to stir at 90 ºC for 12 h. After cooling to room temperature, the reaction mixture was diluted with water (5 mL) and extracted with Et_2O (3 x 10 mL). The combined organics were dried over $MgSO_4$, filtered, and concentrated under reduced pressure. The crude material was purified on silica gel (2% Et_2O/pentane) to afford a clear, colorless oil (20.1 mg, 80% yield). R_f = 0.45 (2% Et_2O/pentane, stain in $KMnO_4$). ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.33-7.30 (2H, m), 7.24-7.20 (3H, m), 5.97 (1H, ddd, *J* = 17.5, 10.5, 7.0 Hz), 5.43 (1H, s), 5.36 (1H, s), 5.11-5.06 (2H, m), 3.75 (1H, dt, *J* = 14.5, 7.5 Hz), 2.85 (1H, dd, *J* = 14.5, 7.5 Hz), 2.78 (1H, dd, *J* = 13.5, 7.5 Hz); ^{13}C

NMR (125 MHz, $CDCl_3$): δ 137.2, 134.8, 126.7, 123.2 (2C), 122.4 (2C), 121.3, 113.3, 109.9, 42.2, 41.9; IR (neat): 3028 (m), 1630 (m), 1453 (w), 1202 (w), 1030 (w), 917 (s), 887 (s), 754 (s), 698 (s) cm^{-1}; HRMS (ESI+) for $C_{12}H_{14}Br$ [M+H]: calculated 238.0201, found: 239.0293 $[\alpha]^{20}_D = 9.74$ (*c* = 0.354 , $CHCl_3$).

Chapter 2

Allylation of Nitrosobenzene with Pinacol Allylboronates: A Regioselective Complement to Peroxide Oxidation

I. Introduction

Owing to their significant role in modern organic synthesis, the preparation of allylboron reagents has been heavily studied by an ever-growing number of groups spanning several decades.[73] Over the last eight years, the Morken group has developed a program devoted to the synthesis of allylboron reagents. Recent advances in catalytic hydroboration of dienes[74] and borylation of allylic electrophiles[75] have allowed for the rapid synthesis of valuable allylboron nucleophiles. Additionally, the Morken group has demonstrated the diboration of

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[73] For a recent review, see: Lachance, H.; Hall, D. G. In *Organic Reactions*; Denmark, S. E., Ed.; Wiley: New York, 2009; Vol. 73.

[74] (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. (c) Zaidlewicz, M.; Meller, J. *Tetrahedron Lett.* **1997**, *38*, 7279. (d) Satoh, M.; Nomoto, Y.; Miyaura, N.; Suzuki, A. *Tetrahedron Lett.* **1989**, *30*, 3789. (e) Matsumoto, Y.; Hayashi, T. *Tetrahedron Lett.* **1991**, *32*, 3387. (f) Wu, J. Y.; Moreau, B.; Ritter, T. *J. Am. Chem. Soc.* **2009**, *131*, 12915.

[75](a) Zhang, P.; Roundtree, I. A.; Morken, J. P. *Org. Lett.* **2012**, *14*, 1416. (b) Ishiyama, T.; Ahio, T.; Miyaura, N. *Tetrahedron Lett.* **1996**, *37*, 6889. (c) Dutheuil, G.; Selander, N.; Szabó, K. J.; Aggarwal, V. K. *Synthesis* **2008**, *14*, 2293. (d) Murata, M.; Watanabe, S.; Masuda, Y. *Tetrahedron Lett.* **2000**, *41*, 5877.

allenes[76] and 1,3-dienes[77] under transition metal catalysis, both of which afford versatile enantioenriched allylboron frameworks.

Allylboration has most commonly been applied a broad range of carbonyl[78] and imine[79] allylations which have evolved into powerful methods for the preparation of homoallylic alcohols and amines. Despite the success in these areas, the scope of other reactions available to allylboron reagents is somewhat limited. Several well-developed reactions include oxidation to generate allylic alcohols,[80] enantioselective cross-coupling,[81] enantioselective

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[76] (a) Pelz, N. F.; Woodward, A. R.; Burks, H. E.; Sieber, J. D.; Morken, J. P. *J. Am. Chem. Soc.* **2004**, *126*, 16328. (b) Burks, H. E.; Liu, S.; Morken, J. P. *J. Am. Chem. Soc.* **2007**, *129*, 8766. See also: (c) Ishiyama, T.; Kitano, T.; Miyaura, N. *Tetrahedron Lett.* **1998**, *39*, 2357. (d) Yang, F. Y.; Cheng, C. H. *J. Am. Chem. Soc.* **2001**, *123*, 761.

[77] (a) Kliman, L. T.; Mlynarski, S. M.; Ferris, G. E.; Morken, J. P. *Angew. Chem., Int. Ed.* **2012**, *51*, 521. (b) Schuster, C. H.; Li, B.; Morken, J. P. *Angew. Chem., Int. Ed.* **2011**, *50*, 7906. (c) Hong, K.; Morken, J. P. *J. Org. Chem.* **2011**, *76*, 9102. (d) Ely, R. J.; Morken, J. P. *Org. Lett.* **2010**, *12*, 4348. (e) Burks, H. E.; Kliman, L. T.; Morken, J. P. *J. Am. Chem. Soc.* **2009**, *131*, 9134. (f) Morgan, J. B.; Morken, J. P. *Org. Lett.* **2003**, *5*, 2573. See also: (g) Ishiyama, T.; Yamamoto, M; Miyaura, N. *Chem. Commun.* **1996**, 2073. (h) Ishiyama, T.; Yamamoto, M.; Miyaura, N. *Chem. Commun*. **1997**, 689. (i) Clegg, W.; Thorsten, J.; Marder, T. B.; Norman, N. C.; Orpen, A. G. Peakman, T. M.; Quayle, M. J.; Rice, C. R.; Scott, A. J. *J. Chem. Soc., Dalton Trans.* **1998**, 1431.

[78] See reference 17. For a review on carbonyl allylboration, see: Hall, D. G. *Pure Appl. Chem.* **2008**, *80*, 913.

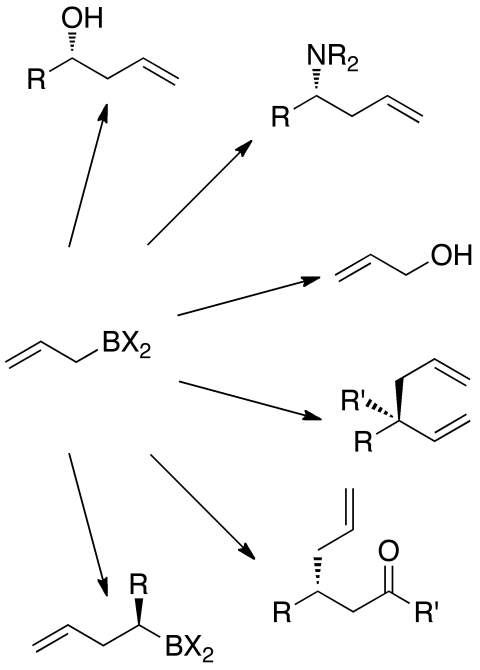
[79] (a) Sugiura, M.; Hirano, K.; Kobayashi, S. *Org. Synth.* **2006**, *83*, 170. (b) Sieber, J. D.; Morken, J. P. *J. Am. Chem. Soc.* **2006**, *128*, 74. (c) Elford, T. G.; Hall, D. G. *Tetrahedron Lett.* **2008**, *49*, 6995.

[80] For a review, see: Brown, H. C.; Snyder, C.; Rao, B. C. S.; Zweifel, G. *Tetrahedron* **1986**, *42*, 5505.

[81] See references: 4, 9, 10, 20, 21, 38, 50. Selected examples: (a) Nilsson, K.; Hallberg, A. *Acta Chem. Scand. B* **1987**, *41*, 569. (b) Kalinin, V. N.; Denisov, F. S.; Bubnov, Y. N. *Mendeleev Commun.* **1996**, 206. (c) Kotha, S.; Behera, M.; Shah, V. R. *Synlett* **2005**, *12*, 1877. (d) Yamamoto, Y.; Takada, S.; Miyaura, N. *Chem. Lett.* **2006**, *35*, 704. (e) Kotha, S.; Shah, V. R.; Mandal, K. *Adv. Synth. Catal.* **2007**, *349*, 1159. (f) Kotha, S.; Shah, V. R. *Eur. J. Org. Chem.* **2008**, *6*, 1054. (g) Gerbino, D. C.; Mandolesi, S. D.; Schmalz, H.; Podestá, J. C. *Eur. J. Org. Chem.* **2009**, *23*, 3964.

conjugate allylation,[82] and homologation reactions which generate homoallylboronates (Scheme 2.1).[83] It was thus of significant interest for our group to explore and diversify the reactivity profile of allylboron reagents.

Scheme 2.1: Existing Transformations for Allylboron Reagents



Specifically, we were interested in the direct allylative formation of a new carbon-heteroatom bond (Scheme 2.2). One could envision allylboration to be employed in the formation of allylic amines, allylic alcohols, allylic halides, or

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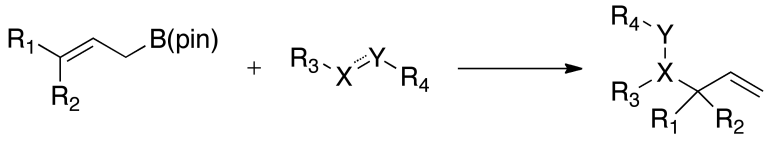
[82] See references 16a-c.

[83] For a review, see: Thomas, S. P.; French, R. M.; Jheengut, V.; Aggarwal, V. K. *The Chemical Record* **2009**, *9*, 24. Selected examples: (a) Hoffmann, R. W.; Stiasny, H. C. *Tetrahedron Lett.* **1995**, *36*, 4595. (b) Matteson, D. S.; Majumdar, D. *J. Am. Chem. Soc.* **1980**, *102*, 7588. (c) Matteson, D. S.; Majumdar, D. *J. Organomet. Chem.* **1980**, *184*, C41. (d) Stymiest, J. L.; Bagutski, V.; French, R. M.; Aggarwal, V. K. *Tetrahedron* **2009**, *65*, 9956.

allylic carboxylates by treatment of an allylboron with an appropriately substituted electrophile. To that end, a variety of electrophilic candidates were selected to be screened for reactivity in an allylboration reaction utilizing allylboronic acid pinacol ester derivatives. The development of the allylboration of nitrosobenzene to form allylic alcohols is presented herein.

Scheme 2.2: General Allylboration to Generate Carbon-Heteroatom Bonds



II. Background

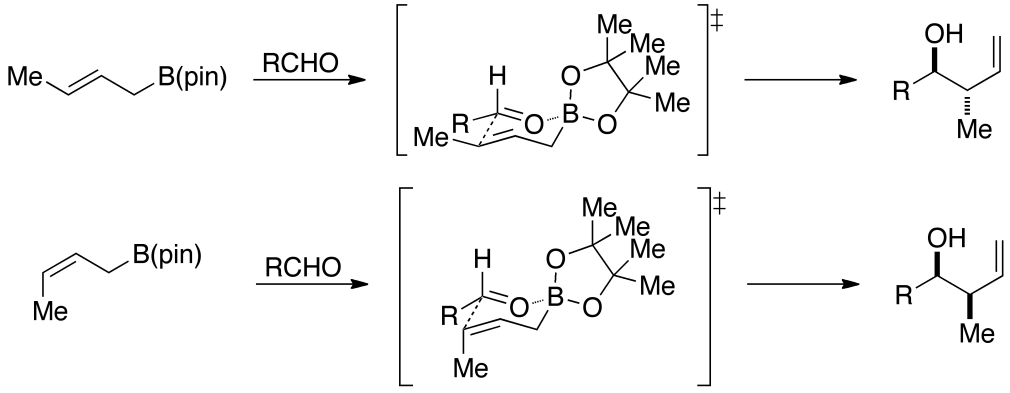
A. Allylboration of Aldehydes

The allylboration of aldehydes has undergone extensive development since its discovery by Mikhailov and Bubnov in 1964.[84] It was an observation by Professor Reinhard Hoffman and Hans-Joachim Zeiss 15 years later that brought this methodology to the forefront of synthetic chemistry. They found that the crotylboration of aldehydes was a highly diastereoelective reaction, exhibiting selectivities consistent with a six-membered chair-like transition state (Figure

[84] Mikhailov, B. M.; Bubnov, Y. N. *Izv. Akad. Nauk SSSR, Ser. Khim.* **1964**, 1874.

2.1).[85] A recent comprehensive account of these developments by Professor Dennis Hall and Hugo Lachance extols the power of this mechanism in the diastereo- and enantioselective synthesis of homoallylic alcohols.[73] While there is an exceedingly broad body of work on the subject, there are two types of enantioselective aldehyde allylboration reactions that deserve specific attention: namely, the use of chiral boron derivatives as well as chiral Brønsted acid-catalyzed enantioselective additions to aldehydes.

Figure 2.1: Hoffman's Chair-Like Crotylboration of Aldehydes



Professor William Roush developed diisopropyl tartrate-derived allyl- and crotylboron derivatives that have been used with great success in enantioselective additions to aldehydes (Scheme 2.3).[86] Allylboration of

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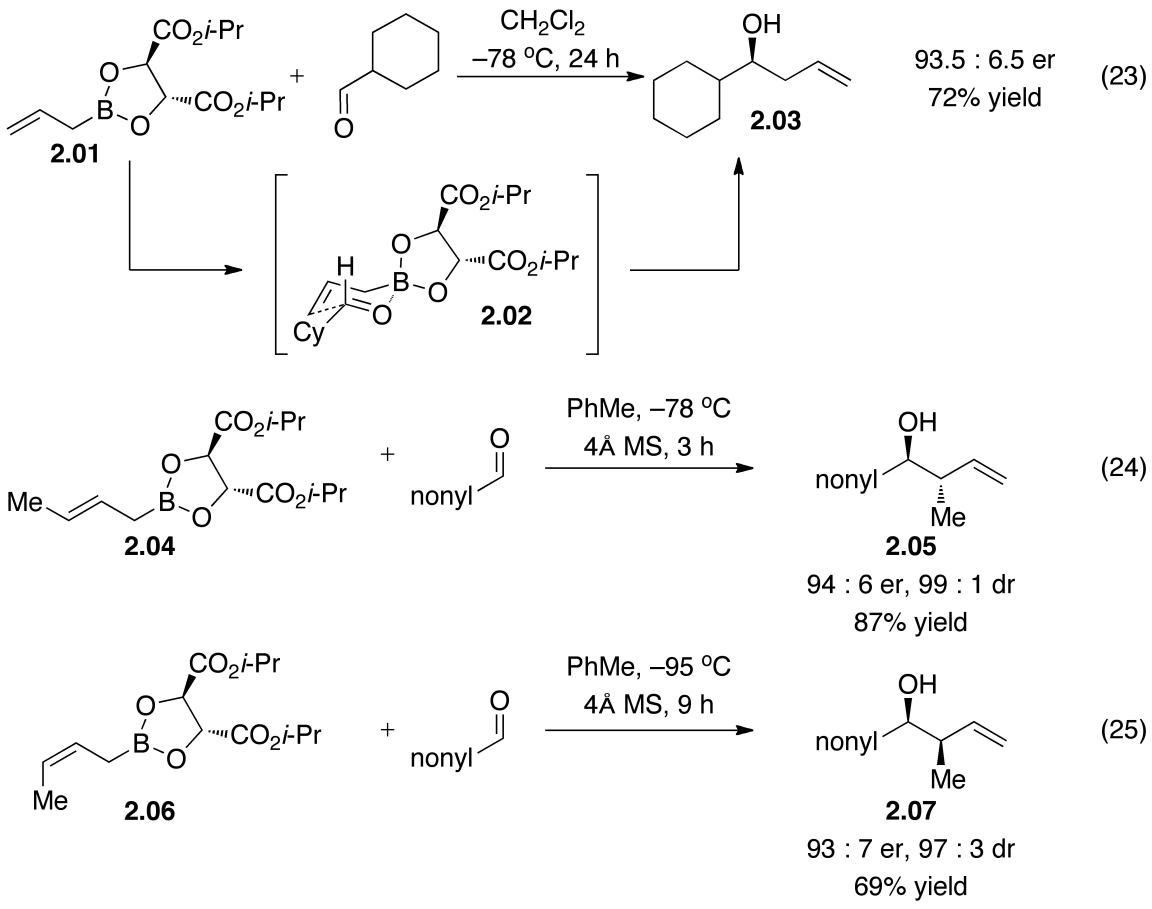
[85] (a) Hoffman, R. W.; Zeiss, H.-J. *Angew. Chem., Int. Ed. Engl.* **1979**, *18*, 306. (b) Hoffman, R. W.; Zeiss, H.-J. *J. Org. Chem.* **1981**, *46*, 1309.

[86] (a) Roush, W. R.; Walts, A. E.; Hoong, L. K. *J. Am. Chem. Soc.* **1985**, *107*, 8186. (b) Roush, W. R.; Ando, K.; Powers, D. B.; Palkowitz, A. D.; Halterman, R. L. *J. Am. Chem. Soc.* **1990**, *112*, 6339.

cyclohexane carboxaldehyde with **2.01** (eq. 23) yields secondary alcohol **2.03** in 93.5 : 6.5 er and good yield. This reaction has been shown to proceed through transition state **2.02**, which produces the observed major enantiomer. Upon addition to decanal, *(E)*-crotyl derivative **2.04** (eq. 24) resulted in the formation of *anti* diastereomer **2.05** in 94 : 6 er, while *(Z)*-**2.06** delivers *syn* **2.07** in 93 : 7 er and good yield (eq. 25).

Scheme 2.3: Roush's Enantioselective Allylboration



Despite the high diastereoselectivity of Roush's allylboronic esters, enantiomer ratios are typically modest. Thus, Professor H. C. Brown's bis(isopinocampheyl) allyl- and crotylboranes remain the standard bearer in the field of chiral boron allylation chemistry.[87] Using *(E)*- or *(Z)*-crotyl boranes with either (+)- or (–)-α-pinene and acetaldehyde, the four possible stereoisomers of 3-methyl-4-penten-2-ol can be realiably synthesized in up to 98 : 2 er and >99 : 1 dr (Scheme 2.4). These impressive results are tempered somewhat by the fact that alkylboranes are oxidatively unstable and must be rigorously kept air and water free. Despite these factors, the low cost and ease of synthesizing these reagents compared to other highly selective chiral auxiliaries has kept Brown's methodology at the forefront of allylation technology.[88]

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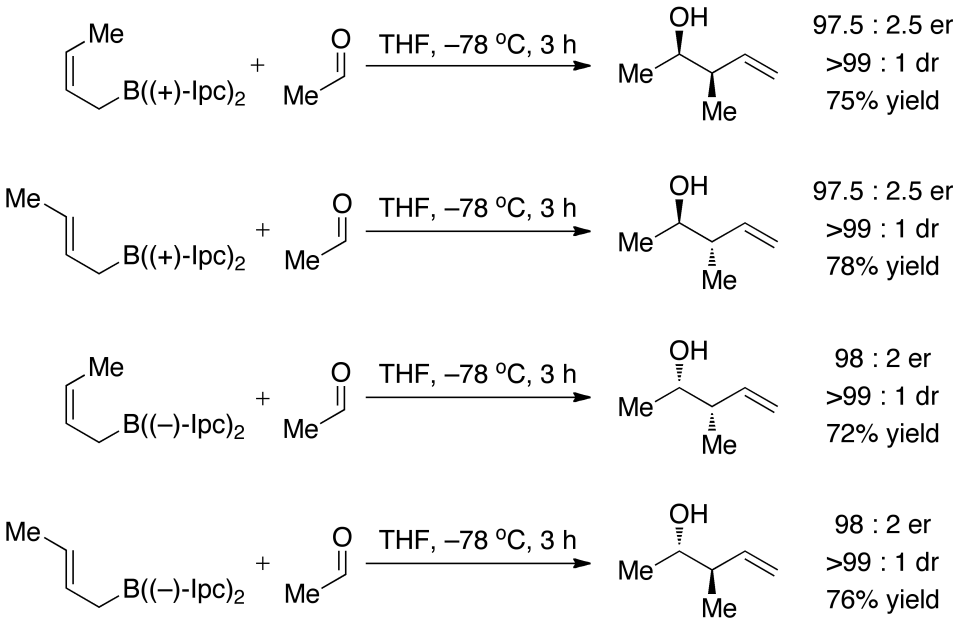
[87] (a) Brown, H. C.; Bhat, K. S. *J. Am. Chem. Soc.* **1986**, *108*, 293. (b) Brown, H. C.; Jadhav, P. K. *J. Am. Chem. Soc.* **1983**, *105*, 2092. (c) Brown, H. C.; Bhat, K. S. *J. Am. Chem. Soc.* **1986**, *108*, 5919.

[88] (a) Short, R. P.; Masamune, S. *J. Am. Chem. Soc.* **1989**, *111*, 1892. (b) Garcia, J.; Kim, B. M.; Masamune, S *J. Org. Chem.* **1987**, *52*, 4831. (c) Burgos, C. H.; Canales, E.; Matos, K.; Soderquist, J. A. *J. Am. Chem. Soc.* **2005**, *127*, 11572.

Scheme 2.4: H. C. Brown's (Ipc)-Crotylation



Recently, efforts from the synthetic community have focused on chiral Brønsted acid catalysis for enantioselective allylboration reactions. Notably, Professor Dennis Hall and Vivek Rauniyar have developed an impressive Sn/ chiral diol catalyst system that allows for the addition of allylboronic esters to aldehydes in a highly enantioselective fashion (**2.08**, Scheme 2.5).[89] This Lewis acid assisted Brønsted acid catalysis, a concept pioneered by Professor Yamamoto,[90] likely proceeds through a hydrogen bond between one of the acidic protons of the diol and a Lewis basic oxygen of the boronic ester. This

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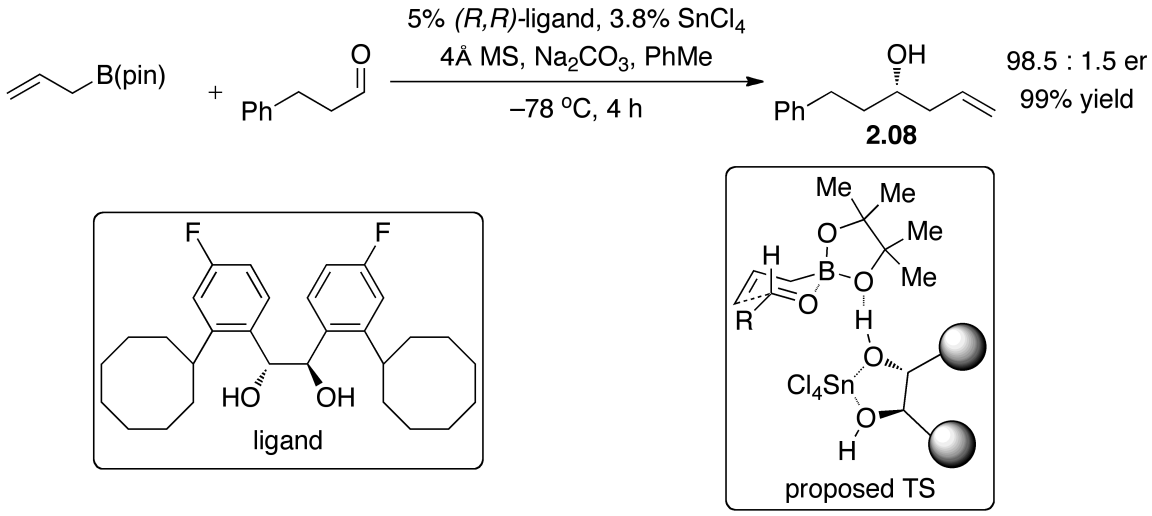
[89] (a) Rauniyar, V.; Hall, D. G. *J. Org. Chem.* **2009**, *74*, 4236. (b) Rauniyar, V.; Huimin, Z.; Hall, D. G. *J. Am. Chem. Soc.* **2008**, *130*, 8481. (c) Rauniyar, V.; Hall, D. G. *Angew. Chem., Int. Ed.* **2006**, *45*, 2426.

[90] For a review, see: Yamamoto, H.; Futatsugi, K. *Angew. Chem., Int. Ed.* **2005**, *44*, 1924.

coordination generates a chiral environment and thus may promote an enantioselective allylboration.

Scheme 2.5: Hall's Brønsted Acid Promoted Enantioselective Allylboration



The most recent development in chiral Brønsted acid catalysis of the allylboration of aldehydes was disclosed by Professor Jon Antilla and Pankaj Jain.[91] Their work has centered on the use of BINOL-derived phosphoric acid derivatives of the type developed by Akiyama and Terada.[92] Antilla found that sterically encumbered variants of these acids could catalytically promote the addition of allyl- and crotylboronic esters to an aldehyde to prepare homoallylic alcohols in both excellent enantioselectivities and yields (Scheme 2.6). Similar to

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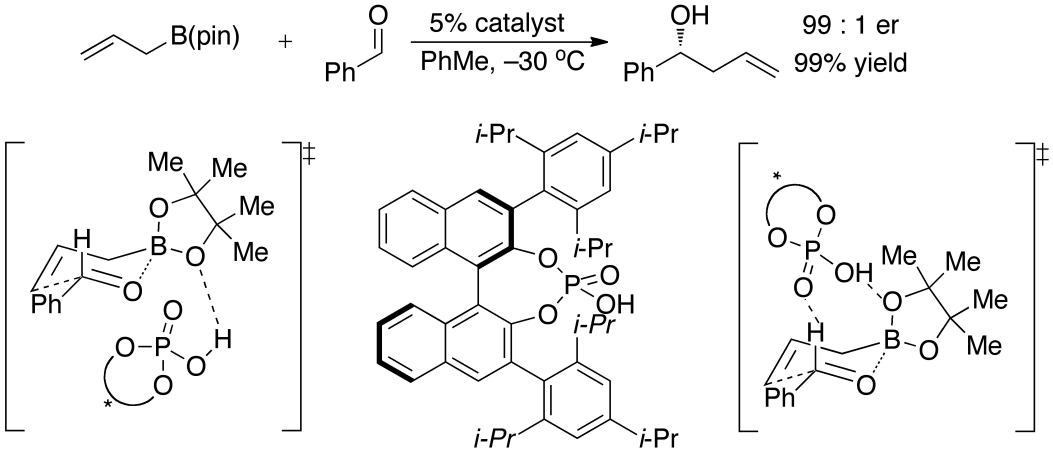
[91] Jain, P.; Antilla, J. C. *J. Am. Chem. Soc.* **2010**, *132*, 11884.

[92] For reviews, see: (a) Akiyama, T. *Chem. Rev.* **2007**, *107*, 5744. (b) Doyle, A. G.; Jacobsen, E. N. *Chem. Rev.* **2007**, *107*, 5173. (c) Terada, M. *Chem. Commun.* **2008**, 4097.

Hall's work, Antilla invokes a hydrogen bond between an oxygen of pinacol and the acidic proton of the Brønsted acid organocatalyst to generate a chiral scaffold. Subsequent to Antilla's studies, Professor Jonathan Goodman and co-workers published a computational study in which they show evidence for an alternate transition state.[93] Under their proposal, the phosphoric acid component of the ligand acts as both a hydrogen bond donor and acceptor, linking the allylboron and the aldehyde, and thus rigidifying the transition state.

Scheme 2.6: Antilla's Chiral Brønsted Acid-Catalyzed Allylboration



[93] Grayson, M. N.; Pellegrinet, S. C.; Goodman, J. M. *J. Am. Chem. Soc.* **2012**, *134*, 2716.

B. Catalytic Enantioselective Allylboration of Ketones

The enantioselective allylboration of ketones has presented a great challenge to synthetic chemists due to the difficulty in differentiating between the enantiotopic faces of a ketone relative to an aldehyde.[94] While Professor John Soderquist has developed an innovative 9-BBN derived chiral auxiliary for the allylboration of ketones,[95] key advances in catalytic enantioselective allylboration of these challenging substrates have been disclosed by Professors Shibasaki and Schaus.

Shibasaki and co-workers produced the first catalytic enantioselective allylboration of ketones in 2004.[96] The authors showed that in the presence of a Cu(II)/*(R,R)-i*-Pr-DuPHOS catalyst and a lanthanide Lewis acid co-catalyst which serves to activate the ketone, allyB(pin) adds to several aryl and alkyl acetophenone derivatives in excellent yield and moderate to good enantioselectivity (Scheme 2.7). A main drawback is that a significant steric bias between the two ketone substituents (i.e., *t*-Bu vs. Me) is required for synthetically useful levels of enantioselectivity.

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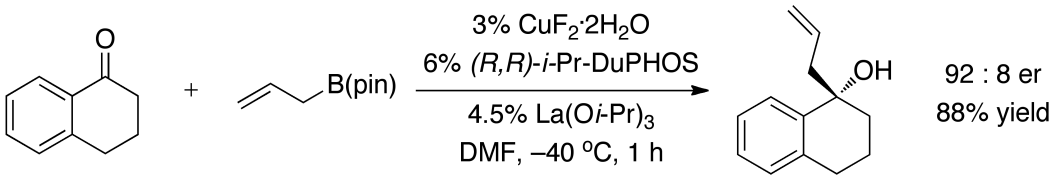
[94] TsOH readily promotes racemic allylboration of ketones: Matsuoka, H.; Kondo, K. *Tetrahedron Lett.* **2009**, *50*, 2320.

[95] Canales, E.; Prasad, K. G.; Soderquist, J. A. *J. Am. Chem. Soc.* **2005**, *127*, 11572.

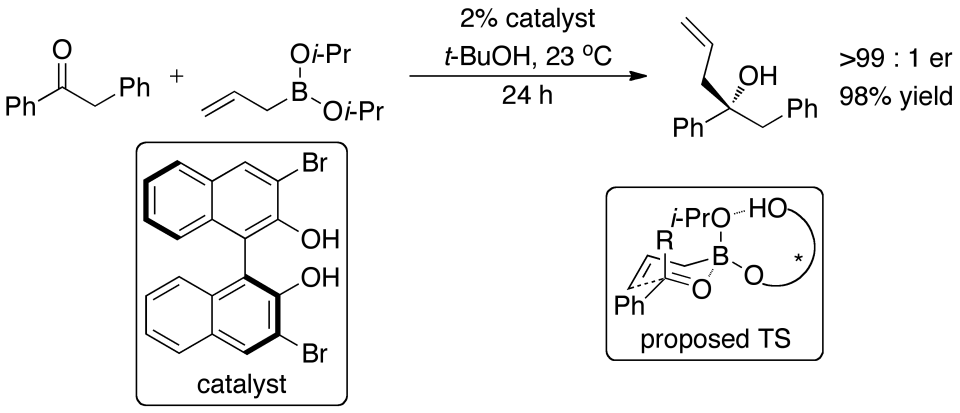
[96] Wada, R.; Oisaki, K.; Kanai, M.; Shibasaki, M. *J. Am. Chem. Soc.* **2004**, *126*, 8910.

Scheme 2.7: Shibasaki's Enantioselective Allylboration of Ketones



Schaus *et al.* have provided what stands as the most efficient and selective allylboration of ketones to date.[97] This operationally simple methodology utilizes a BINOL derivative and a diisopropoxy derived allylboronic ester as the nucleophile to allylate a broad range aryl and alkyl ketones in excellent enantioselectivities (Scheme 2.8). They suggest that the chiral diol displaces one ligand on boron and hydrogen bonds to the other ligated oxygen, thus acting as an exchangeable chiral auxiliary.

Scheme 2.8: Schaus' Optimized Allylboration of Ketones

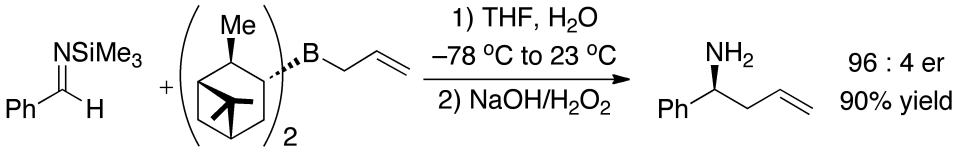


[97] (a) Lou, S.; Moquist, P. N.; Schaus, S. E. *J. Am. Chem. Soc.* **2006**, *128*, 12660. (b) Barnett, D. S.; Moquist, P. N.; Schaus, S. E. *Angew. Chem., Int. Ed.* **2009**, *48*, 8682.

C. Catalytic Enantioselective Allylboration of Imines

The racemic addition of allylboronic esters to imines is a well-established method for generating homallylic amines.[98] The development of a general allylboration of imines to an extent follows a similar track to the evolution of the allylboration of aldehydes. Furthermore, Professor H. C. Brown and co-workers demonstrated the addition of the *B*-allyldiisopinocampheylborane reagent to silyl imines and found it to be an effective chiral auxiliary for the generation of enantioenriched silyl homoallylic amines (Scheme 2.9).[99] While this method offers an operationally simple means for accessing these structural motifs, a catalytic enantioselective method was still desirable.

Scheme 2.9: Brown Allylboration of Imines



In 2006, the Morken group took advantage of its recently developed enantioselective diboration of prochiral allenes to address this need.[100] Pd-catalyzed diboration of a monosubstituted allene gives 2,3-(bis)boryl intermediate

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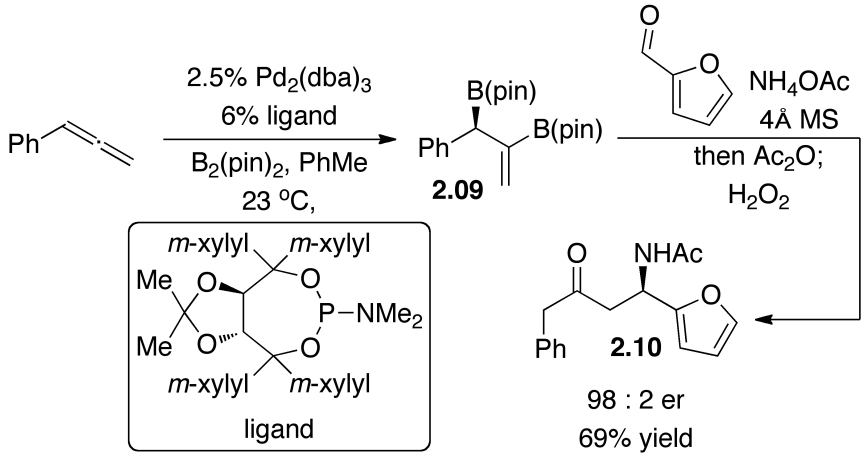
[98] For example, see: (a) Sugiura, M.; Hirano, K.; Kobayashi, S. *Org. Synth.* **2006**, *170*, 691. (b) Elford, T. G.; Hall, D. G. *Tetrahedron Lett.* **2008**, *49*, 6995.

[99] Chen, G.-M.; Ramachandran, P. V.; Brown, H. C. *Angew. Chem., Int. Ed.* **1999**, *38*, 825.

[100] Sieber, J. D.; Morken, J. P. *J. Am. Chem. Soc.* **2006**, *128*, 74.

2.09. This was then treated with an *in situ* generated imine followed by acylation and oxidative work-up to afford β-amidoketone **2.10** with excellent enantioselectivity and good yield over the one-pot three-step sequence (Scheme 2.10). While this rapid build-up of molecular complexity is admirable, it relies on the generation of an enantioenriched allylboron, rather than an enantioselective allylboron addition to an imine involving a chiral catalyst system.

Scheme 2.10: Morken Diboration/Imine Allylboration Sequence

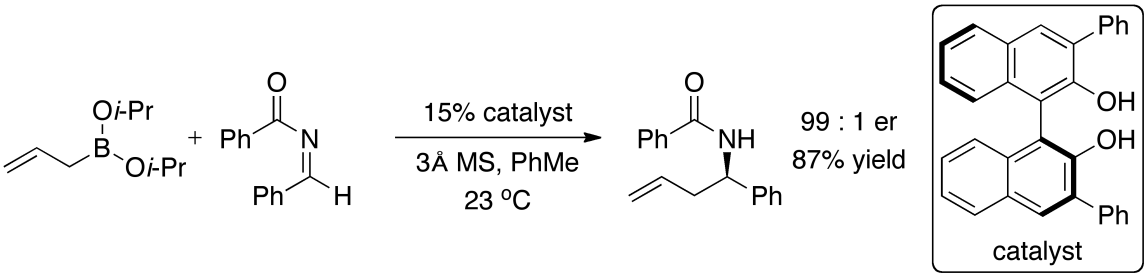


Professor Schaus *et al.* subsequently demonstrated a powerful method in which the addition of allylboronic esters to imines proceeds under enantioselective organocatalysis in an analagous method to that discussed previously for the allylboration of ketones (Scheme 2.11).[101] Again, a BINOL-derived catalyst provides efficient access to allylborated products, delivering the

[101] See section **II.B** and: Lou, S.; Moquist, P. N.; Schaus, S. E. *J. Am. Chem. Soc.* **2007**, *129*, 15398.

homoallylic acylamines in selectivities ≥95 : 5 er. As before, it is suggested that the chiral diol displaces one of the ligands on boron, generating a chiral environment for the allylboration reaction. While this protocol effectively generates homoallylic amines with a broad substrate tolerance, the state of the art in this field of allylboration was recently presented by Professors Hoveyda and Snapper.

Scheme 2.11: Schaus' Catalytic Enantioselective Imine Allylboration



In their 2011 communication, Vieira and co-authors demonstrated a versatile NHC–Cu-catalyzed allylboration of aldimines.[102] This operationally simple procedure proceeds by transmetallation between allylB(pin) and Cu, which generates a chiral allyl nucleophile *in situ*. Upon coordination of the aldimine, enantioselective allylation to generate optically enriched homoallylic amines proceeds smoothly. The authors show a broad substrate tolerance for this reaction for both aryl and aliphatic substrtates, with enantiomer ratios up to 98.5 : 1.5 (Scheme 2.12).

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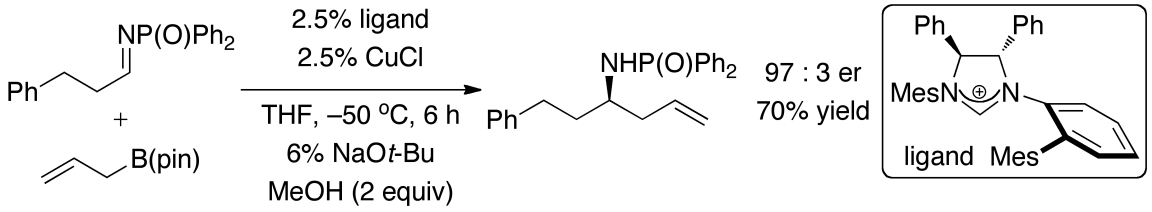
[102] Vieira, E. M.; Snapper, M. L.; Hoveyda, A. H. *J. Am. Chem. Soc.* **2011**, *133*, 3332.

Scheme 2.12: Hoveyda & Snapper's Allylboration of Aldimines



D. Allylborations Which Generate New Carbon–Heteroatom Bonds

As discussed in the preceding sections, allylboration reactions that form new C–C bonds *via* attack on a polarized π-system where carbon is the electrophilic center have been well-developed. A useful yet underdeveloped analogue of this chemistry would be the nucleophilic addition to an isoelectronic π-system in which the electrophilic center was a heteroatom (i.e., N or O). This would deliver products such as allylic alcohol or ether derivatives for oxygen electrophiles and allylic amine derivatives in the case of a nitrogen-centered electrophile.

Surprisingly, few examples of allylborations with these types of electrophiles exist. In fact, the two examples in the literature are both from Professor Yuri Bubnov. In a 2002 disclosure on the allylboration of nitrosobenzene (PhNO), Bubnov and co-workers showed that highly reactive triallylborane reacts with PhNO with low levels of *O*- vs. *N*-selectivity, even at –70 °C (Scheme 2.13).[103] The authors note that this lack of site selectivity is

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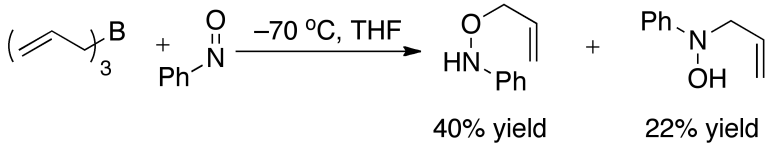
[103] Bubnov, Y. N.; Pershin, D. G.; Karionova, A. L.; Gurskii, M. E. *Mendeleev Commun.* **2002**, *12*, 202.

unprecedented in the allylboration of polarized π-systems, which generally exhibit high selectivities.

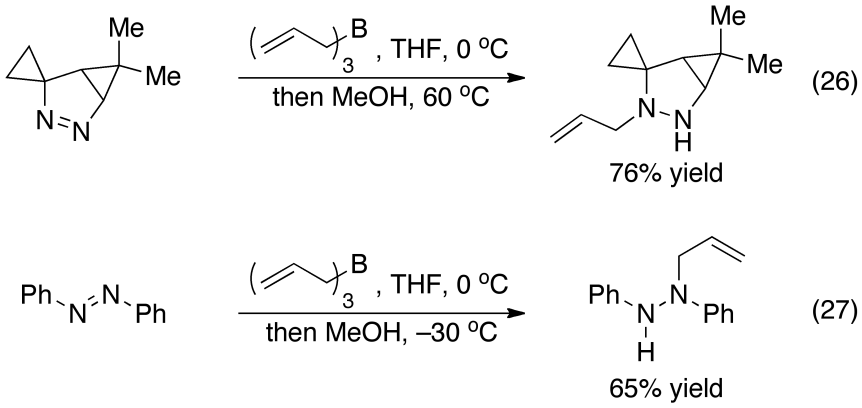
Scheme 2.13: Bubnov's Allylboration of PhNO with Triallylborane



More recently, Bubnov and co-workers demonstrated the first allylboration of N=N double bonds by describing the addition of triallylborane across azobenzene and pyrazolines to generate allyl-1,2-diphenylhydrazine and *N*-allylpyrazolidines, respectively (Scheme 2.14, eqs. 26 and 27).[104] With these two examples, the authors show that an allylboron can nucleophilically add to either *cis* or *trans* N=N π-systems, resulting in good yields of the expected products, though with a somewhat limited substrate tolerance.

[104] Klimenko, I. P.; Medvedev, A. F.; Korolev, V. A.; Kolomnikova, G. D.; Tomilov, Y. V.; Bubnov, Y. N. *J. Organomet. Chem.* **2009**, *694*, 2106.

Scheme 2.14: Bubnov's Allylboration of N=N π-Systems



E. PhNO as an Electrophile: *N*-Selective Aldol Reactions

While Bubnov has shown[103] PhNO to not be a site selective electrophile for allylboration chemistry, several groups have shown exquisite *N*- vs. *O*-selectivity for aldol reactions. Site- and enantioselective aldol additions were pioneered by Professor Hisashi Yamamoto in 2005[105] using cyclic enamines and a TADDOL derivative as a Brønsted acid catalyst. The authors showed that the resultant hydroxylamine could be prepared in up to 95.5 : 4.5 er and good yield (Scheme 2.15). While the scope of this study is limited, it is notable that under the reported conditions, aldol addition is completely chemoselective, affording only C–N bond formation. The authors postulate that an intramolecular hydrogen bond in the TADDOL catalyst generates a rigid, cyclic Brønsted acid catalyst, which may then in turn coordinate the oxygen of PhNO and create a chiral environment in which the addition can occur.

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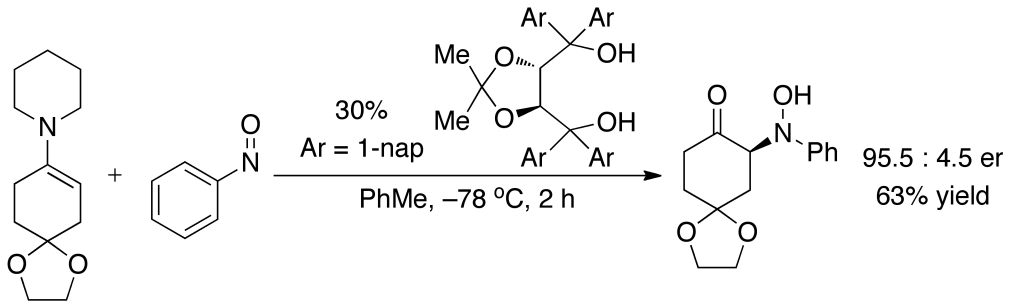
[105] Momiyama, N.; Yamamoto, H. *J. Am. Chem. Soc.* **2005**, *127*, 1080.

Scheme 2.15: TADDOL-Catalyzed *N*-Selective Aldol Addition to PhNO



While other groups have achieved modest enantioselectivities for *N*-selective PhNO additions,[106] Professor Xiaoming Feng and co-workers recently described a highly enantioselective addition of oxindoles to PhNO.[107] The researchers sought to use their expertise in rare-earth metal catalyst systems to develop a Sc(III)/*N,N′*-dioxide complex to catalyze *N*-selective addition to PhNO.[108] As shown in Scheme 2.16, when oxindole **2.11** is treated with $Sc(OTf)_3$, a (bis)-*N*-oxide catalyst, and PhNO at 30 °C, the reaction is completely *N*-selective providing **2.12** in 97.5 : 2.5 er. The authors demonstrate this methodology with a variety of substituted oxindoles while utilizing a wide variety of nitrosobenzene derivatives as the electrophilic partners. Their proposed transition state structure, **2.13**, represents a *Re*-face attack from the oxindole.

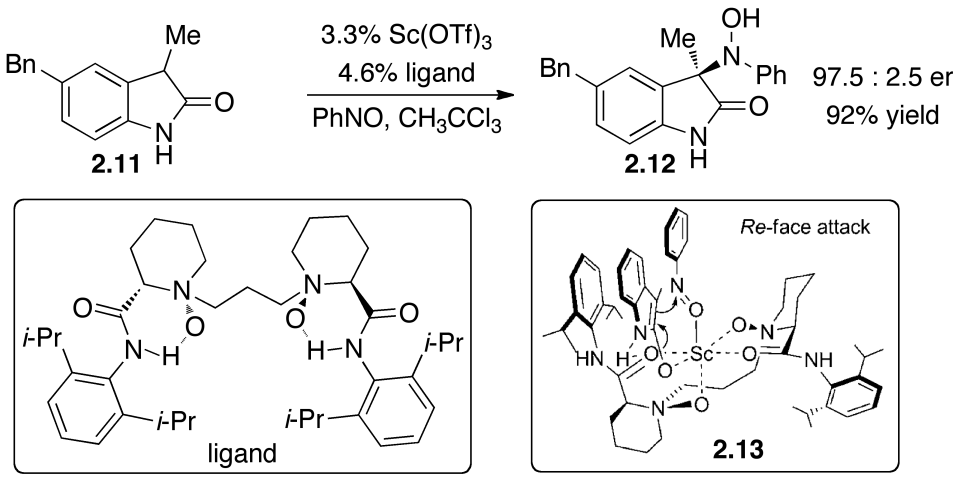
---

[106] For example, see: Zhang, T.; Cheng, L.; Liu, L.; Wang, D.; Chen, Y. *Tetrahedron: Asymmetry* **2010**, *21*, 2800.

[107] Shen, K.; Liu, X.; Wang, G.; Lin, L.; Feng, X. *Angew. Chem., Int. Ed.* **2011**, *50*, 4684.

[108] For select examples, see: (a) Yu, Z. P.; Liu, X. H.; Dong, Z. H.; Xie, M. S.; Feng, X. M. *Angew. Chem., Int. Ed.* **2008**, *47*, 1308. (b) Liu, Y. L.; Shang, D. J.; Zhou, X.; Liu, X. H.; Feng, X. M. *Chem. Eur. J.* **2009**, *15*, 2055. (c) Li, W.; Wang, J.; Hu, X. L.; Shen, K.; Wang, W. T.; Chu, Y. Y.; Lin, L. L.; Liuh, X. H.; Feng, X. M. *J. Am. Chem. Soc.* **2010**, *132*, 8532.

Scheme 2.16: Feng's *N*-Selective Oxindole Addition to PhNO

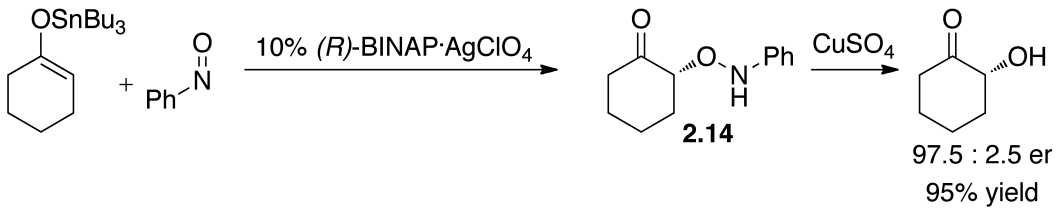


F. PhNO as an Electrophile: *O*-Selective Aldol Reactions

Earlier work by Professor Yamamoto's group was focused on developing a metal enolate addition to the oxygen of PhNO.[109] As shown in Scheme 2.17, Yamamoto *et al.* found a reasonable measure of success using tin enolates in an enantioselective aldol-type addition with a Ag/BINAP catalyst. The isolable aminoxy intermediate **2.14** was shown to be readily cleaved to the free alcohol with $CuSO_4$ resulting in an enantioselective α-hydroxylation of ketones.

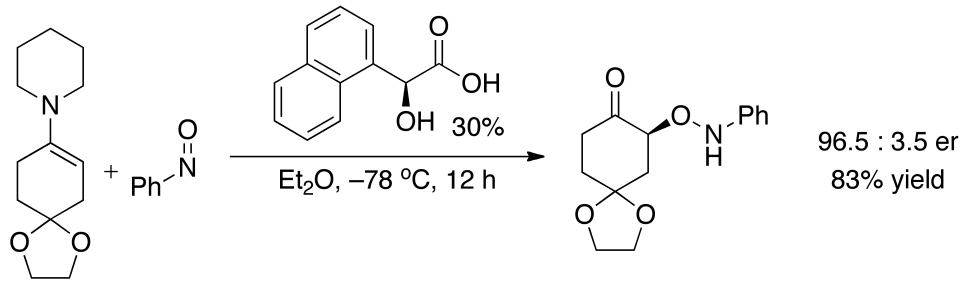
[109] Momiyama, N.; Yamamoto, H. *J. Am. Chem. Soc.* **2003**, *125*, 6038.

Scheme 2.17: Yamamoto's First *O*-Selective Aldol Addition to PhNO



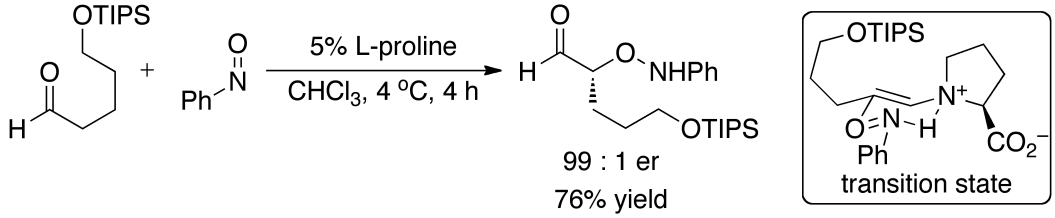
Subsequent to this initial report, Yamamoto and co-workers discovered a metal-free Brønsted acid catalyst that promotes *O*-selective enamine additions to PhNO.[105] While *N*-addition was promoted by TADDOL derivatives, enamine additions to oxygen were best catalyzed by aryl glycolic acid derivatives. 1-naphthyl glycolic acid facilitated the synthesis of several aminoxy derivatives in modest to good levels of enantioselectivity (Scheme 2.18). While TADDOL derivatives may coordinate the electrophile through hydrogen bonding to generate a chiral environment, glycolic acid derivatives may protonate the basic nitrogen of the electrophile. This would result in the formation of a chiral ion pair and activate the oxygen of PhNO for addition, possibly accounting for the turnover in *N*- vs. *O*-selectivity.

Scheme 2.18: Yamamoto's Glycolic Acid Catalyzed *O*-Selective Aldol Addition



While Yamamoto examined ketones and their derived enamines as nucleophiles for additions to PhNO, Professor David MacMillan and co-workers developed an operationally simple α-oxyamination of aldehydes catalyzed by L-proline.[110] The authors propose that the addition proceeds through a 6-membered ring transition state featuring a hydrogen bond between the nitrogen of PhNO and the protonated nitrogen of proline. This highly organized transition state likely accounts for the high levels of enantioselectivity observed in this methodology (Scheme 2.19).

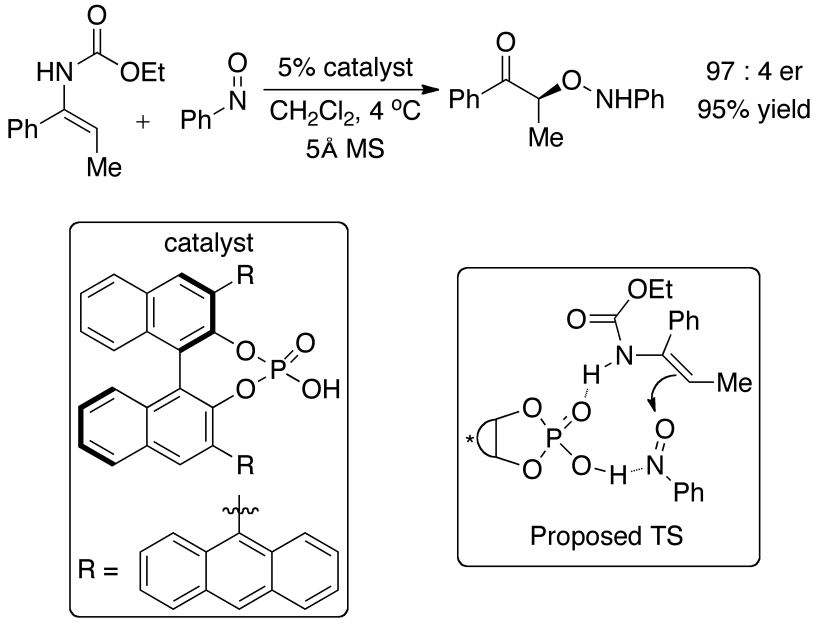
Scheme 2.19: MacMillan's Organocatalytic α-Oxidation of Aldehydes



[110] (a) Brown, S. P.; Brochu, M. P.; Sinz, C. J.; MacMillan, D. W. C. *J. Am. Chem. Soc.* **2003**, *125*, 10808. For an updated account, see (b) Simmons, B.; Walji, A. M.; MacMillan, D. W. C. *Angew. Chem., Int. Ed.* **2009**, *48*, 4349.

Finally, Professor Guofu Zhong and co-workers recently disclosed their account of the development of a bifunctional Brønsted acid catalyst for the enantioselective addition to the oxygen of nitrosobenzene.[111] Their optimized conditions utilize enecarbamates as the nucleophile and a BINOL-derived phosphoric acid derivative for the organocatalyst (Scheme 2.20). Under these conditions, addition to PhNO generally proceeds smoothly, exhibiting high enantioselectivities and a tolerance for variously substituted ArNO derivatives.

Scheme 2.20: Zhong's Brønsted Acid Catalyzed *O*-Addition to PhNO



[111] Lu, M.; Lu, Y.; Zhu, D.; Zeng, X.; Li, X.; Zhong, G. *Angew. Chem., Int. Ed.* **2010**, *49*, 8588.

III. Reaction Development for the Allylboration of Nitrosobenzene with Allylboronic Acid Pinacol Ester Derivatives[112]

A. Initial Results and Optimization of Reaction Conditions

While Bubnov and co-workers successfully demonstrated that highly reactive triallylborane participated in allylboration with PhNO, significant questions remained. First, it was unclear whether more stable and less reactive allylboronic esters would be competent reagents for allylboration of PhNO. Secondly, despite being isoelectronic with benzaldehyde, Bubnov observed minimal site selectivity (*N* vs. *O*) in their allylboration. It was of interest to determine if use of an allylboronic ester would ameliorate this problem. Finally, it was not apparent whether such a transformation would proceed by allylic transposition or by a 1,2-migration, as is observed in a number of reactions involving organoboranes.[113] With these questions in mind we proceeded with our studies utilizing *(Z)*-allylboronic ester derivatives for nucleophilic additions to PhNO. With the Morken group's recent development of convenient methods for accessing allylB(pin) derivatives, I, with co-workers Michael Ryan and Dr. Laura Kliman, explored the allylboration of nitrosobenzene. A selective allylboration

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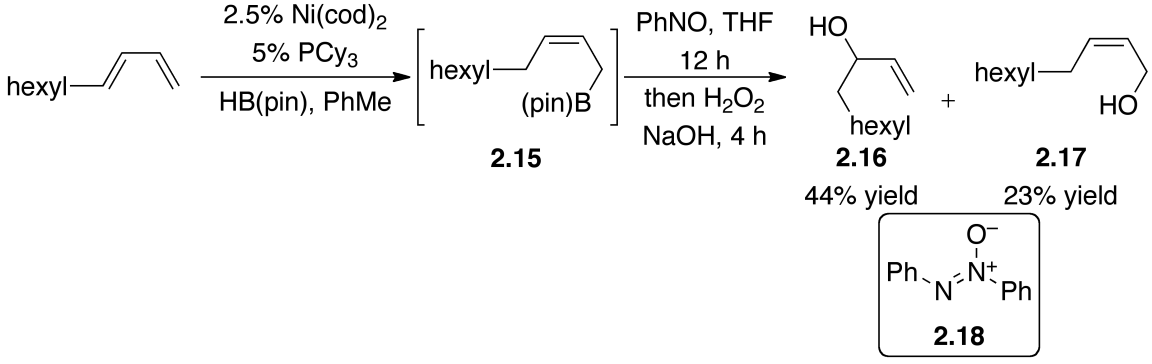
[112] Kyne, R. E.; Ryan, M. C.; Kliman, L. T.; Morken, J. P. *Org. Lett.* **2010**, *12*, 3796.

[113] (a) Hoffmann, R. W.; Stiasay, H. C. *Tetrahedron Lett.* **1995**, *36*, 4595. (b) Matteson, D. S.; Majumdar, D. *J. Am. Chem. Soc.* **1980**, *102*, 7588. (c) Matteson, D. S.; Majumdar, D. *J. Organomet. Chem.* **1980**, *184*, C41.

reaction would provide convenient access to either allylic alcohols or allylic amine derivatives.

We initiated our studies by treating readily available *trans*-1,3-decadiene-derived allylboronic ester **2.15**[74a] with 1.05 equivalents of nitrosobenzene followed by oxidative work-up in a single-flask operation. A 2 : 1 mixture of allylic alcohols **2.16** and **2.17** was obtained from the reaction. Importantly, there was no detectable *N*-allylation product or any N–O bound compounds present in the product mixture (Scheme 2.21). While this regioisomeric mixture of alcohols was intriguing, it was not immediately clear how or why a mixture was obtained.

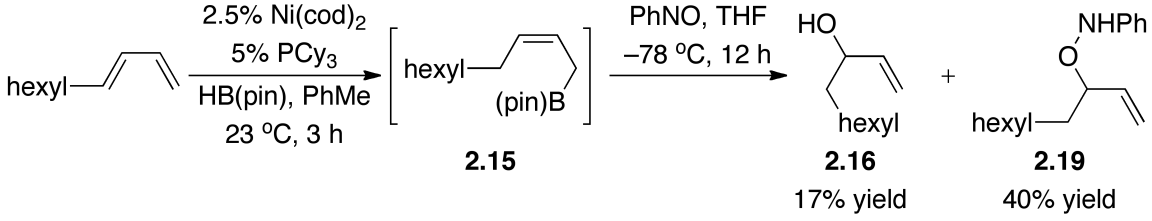
Scheme 2.21: Allylboration of PhNO-Initial Observation



While the formation of **2.17** could possibly be attributed to direct H_2O_2 oxidation of **2.15**, internal alcohol **2.16** may be the product of *O*-allylation. To validate this hypothesis, we attempted to run the reaction in such a way that an aminoxy bond would survive the reaction intact (Scheme 2.22). We found that

slow addition of PhNO at –78 °C afforded, after non-oxidative work-up, a mixture of alcohol **2.16** and allylic aminoxy species **2.19** in 17 and 40% yield, respectively. As observed previously, no *N*-allylated products were isolated, and several questions posed at the outset of this project were answered. First, this reaction appears to proceed with complete allylic transposition, resulting in internally oxygenated allylic products. Furthermore, the nucleophilic attack is highly regioselective, preferring attack at the oxygen of PhNO. Surprisingly, even in the absence of basic and oxidative work-up conditions, free alcohol **2.16** was isolated from the reaction mixture, implicating a N–O self-cleavage mechanism. We then sought to understand the mechanism of O–N bond cleavage with the aim of generating the free internal allylic alcohol as the sole product of the reaction.

Scheme 2.22: Control Experiment to Isolate 2.19

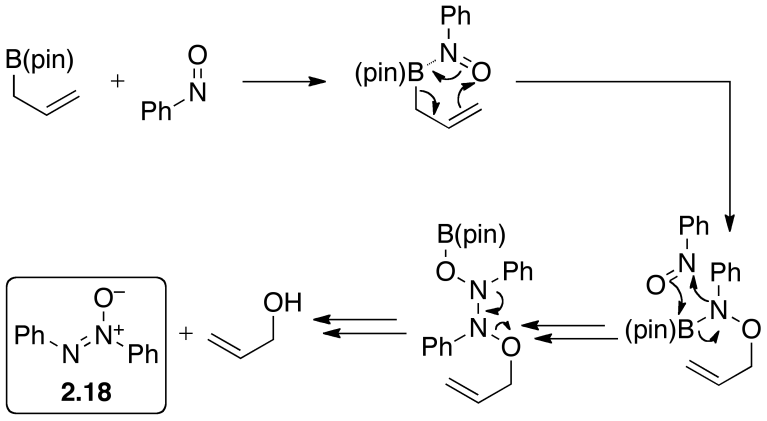


A key insight into the cleavage mechanism was gleaned from the presence of species **2.18** in Scheme 2.21,[114] which was minimally present in the

[114] **2.18** confirmed by ^{1}H NMR and mass spectrometry.

experiment shown in Scheme 2.22. A probable mechanism for the formation of **2.18** is shown in Scheme 2.23. Key to this pathway is that two equivalents of PhNO are required to generate a free alcohol. This mechanism suggests that zwitterionic **2.18** may be the result of nucleophilic attack from the aminoxy intermediate. This may account for terminal allylic alcohol **2.17**, derived from unreacted **2.15**, being present in Scheme 2.21. Of note, this cleavage mechanism is consistent with that of Barbas and co-workers.[115] Furthermore, when octylB(pin) is treated with PhNO, <5% oxidation is observed, further supporting this mechanistic hypothesis involving allylic transposition.

Scheme 2.23: Proposed Cleavage Mechanism



With these observations and mechanistic possibilities in mind, we postulated that additional equivalents of PhNO would drive the reaction to

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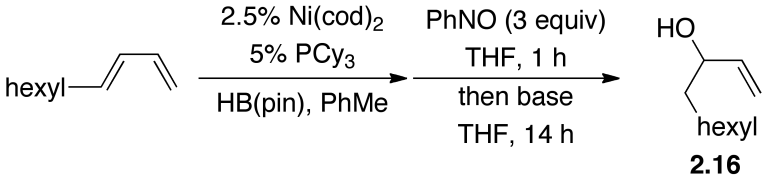
[115] (a) Ramachary, D. B.; Barbas, C. F., III. *Org. Lett.* **2005**, *7*, 1577. See also: (b) Becker, A. R.; Sternson, L. A. *J. Org. Chem.* **1980**, *45*, 1708.

completion (Table 2.1). As shown in entry 1, three equivalents of PhNO in an otherwise unchanged reaction resulted in a 69% yield of the desired internal alcohol as the exclusive product of allylboration. With the need for oxidative conditions seemingly obviated, NaOH was employed in the absence of hydrogen peroxide and delivered a comparable yield of desired alcohol **2.16** (entry 2). Importantly, in the absence of basic additives, only 37% yield of **2.16** was obtained (entry 3). Thus, several other Brønsted bases were screened (entries 4-7). NH_4OH was determined to be the optimal base to promote N–O bond cleavage, facilitating formation of **2.16** in 67% yield with complete chemo- and regioselectivity.

Table 2.1: Optimization of PhNO Allylboration



2.16

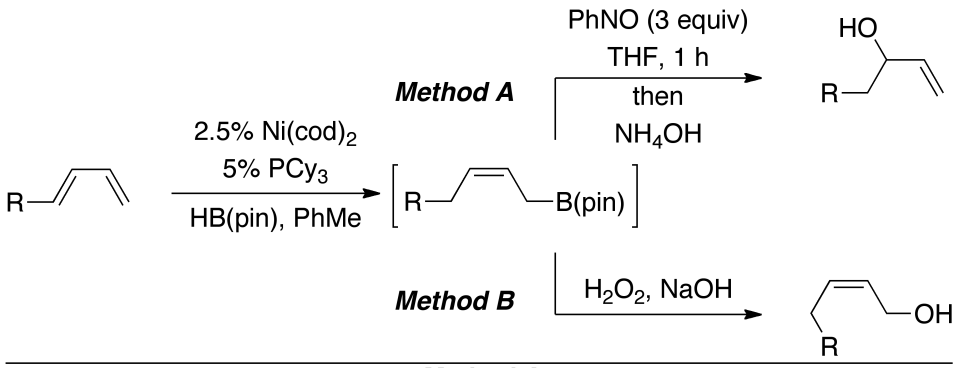
entry	base	yield **2.16** (%)[a]
1	$NaOH/H_2O_2$	69
2	NaOH	61
3	none	37
4	CsOH	55
5	LiOH	62
6	KOH	59
7	NH_4OH	67

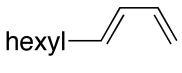
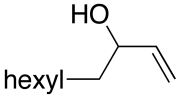
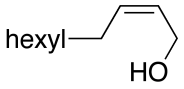
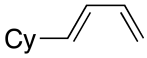
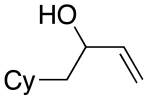
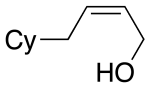
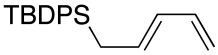
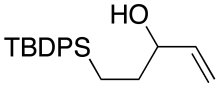
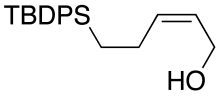
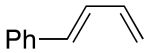
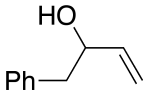
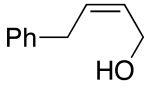
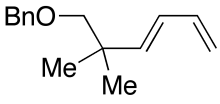
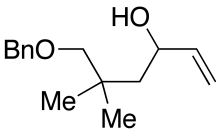
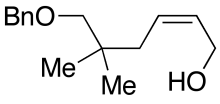
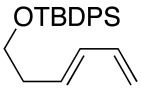
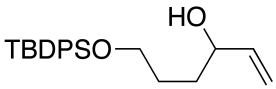
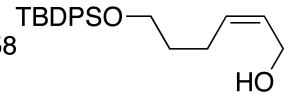
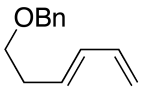
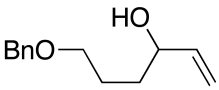
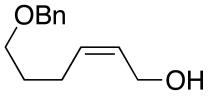
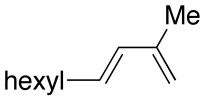
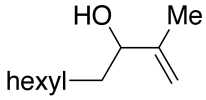
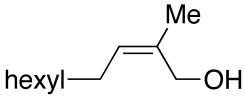
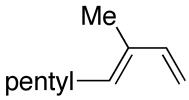
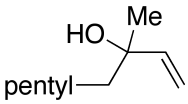
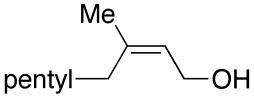
[a] Isolated yield of purified product

B. Substrate Scope Development

With a general procedure in hand, we investigated the substrate tolerance for this transformation by comparing regiocomplementary tandem hydroboration/PhNO allylation (Method A) and standard hydroboration/H_2O_2 oxidation (Method B)[74a] strategies (Table 2.2). Protected oxygen functionality (entries 2 and 5–7) is tolerated in the reaction, giving modest yields of product *via* Method A. Substrates with branching at the diene terminus (entries 2 and 5) participate, though a quaternary center further suppresses the yield of internal allylic alcohol formation (entry 5). Interestingly, while the reaction with a 2,4-disubstituted diene gives an low yield of desired product (entry 8), a 3,4-disubstituted diene (entry 9) is tolerated, providing a good yield of the corresponding tertiary alcohol. As demonstrated, Method B uniformly gives high yields of the terminal *(Z)*-allylic alcohol, thus implicating the PhNO allylation step in the diminished yields observed in Method A.

Table 2.2: Substrate Scope for Diene Hydroboration/Oxidation



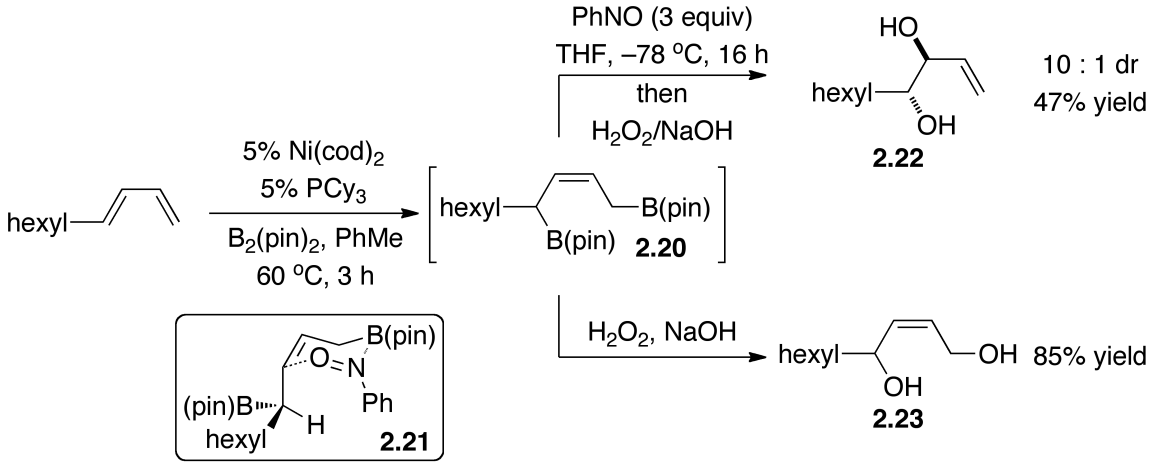
entry	diene	Method A product/yield (%)[a]		Method B product/yield (%)[a]	
1			66		85
2			62		81
3			57		56
4			64		91
5			44		89
6			58		95
7			63		93
8			33		93
9			58		81

[a] Isolated yield of purified product. Value is an average of two experiments.

C. Application to a Diastereoselective Transformation

It was postulated that use of an allylboronic ester containing an embedded stereocenter may render PhNO allylboration diastereoselective. A selective reaction could be achieved through exploitation of competing steric influences within the postulated 6-membered ring transition state that is consistent with allylic transpostion. To test this theory (Scheme 2.24), Ni(0)-catalyzed diboration of 1,3-decadiene was used to synthesize 1,4-(bis)boryl compound **2.20**.[63d] When treated *in situ* with H_2O_2/NaOH, the expected 1,4-(bis)allylic alcohol **2.23** was isolated in 85% yield. However, when **2.20** was treated with PhNO at room temperature in a single-flask operation, followed by oxidative work-up, internal *anti*-1,2-diol **2.22** was isolated in 2.6 : 1 dr (data not shown). Upon lowering the reaction temperature of the allylation step to –78 ºC, the derived diol was isolated in 10 : 1 dr and 47% yield. This reaction outcome is consistent with chair-like transition structure **2.21**. Nitrosobenzene presumably coordinates the least hindered allylboron with the small hydrogen directed into the center of the chair to minimize penalizing A[1,3] interactions. Additionally, the uncoordinated electron rich C–B bond is oriented with the π-system in such a manner that it may enhance the π-nucleophilicity of the alkene, thus accelerating the reaction from conformer **2.23**.

Scheme 2.24: Application of PhNO to a Diastereoselective Transformation

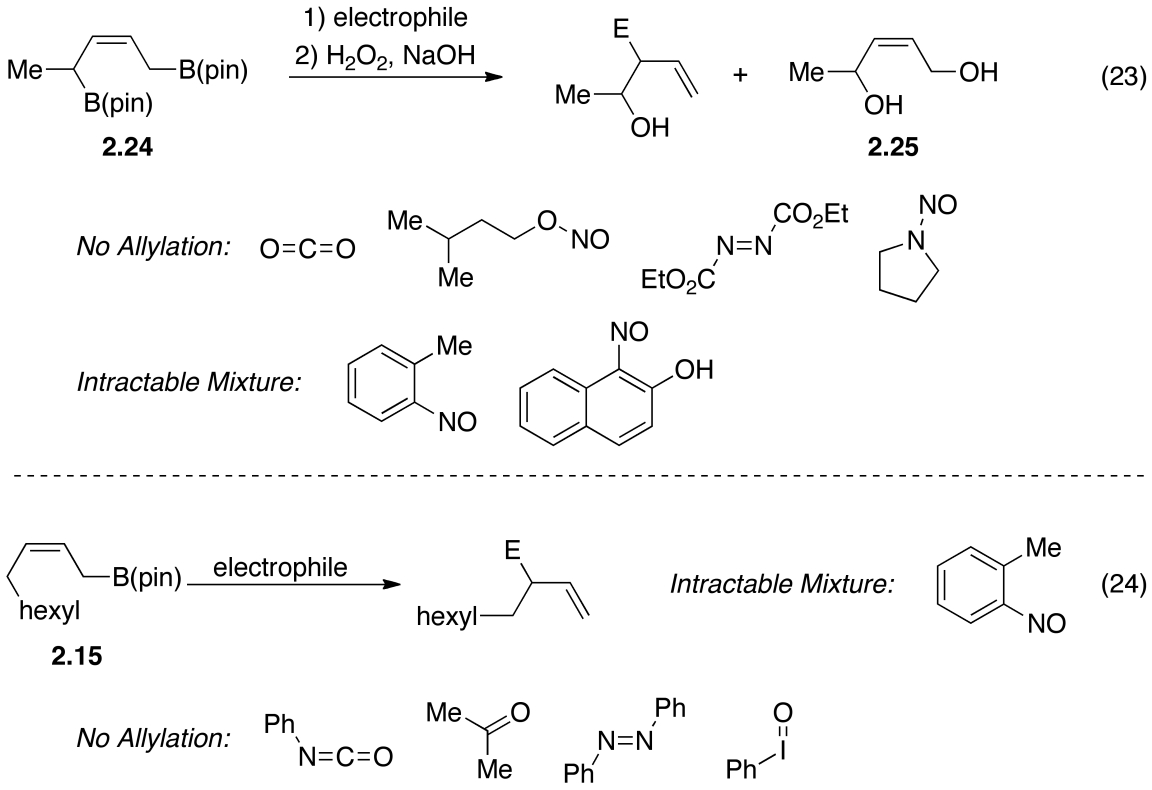


D. Allylboration Reactions With Alternative Electrophiles

While PhNO has been successfully employed in allylboration, it was of significant interest to attempt to broaden the scope of electrophiles available for allylboration chemistry. To that end, we studied a variety of potential electrophiles as summarized in Scheme 2.25. (Bis)boryl **2.24** was treated with a series of electrophiles which was followed by an oxidative work-up (eq. 23). When treated with dry ice, isopentyl nitrite, DEAD, and 1-nitrosopyrrolidine, only 1,4-diol **2.25**, derived from direct oxidation of **2.24**, was observed. Additionally, when **2.24** was treated with either 2-nitrosotoluene or 1-nitroso-2-naphthol, an intractable mixture of products was formed, though some allylation was evident from ^{1}H NMR analysis of the crude reaction mixtures. Similarly, when allylboron derivative **2.15** was treated with 2-nitrosotoluene, a complex mixture of products was obtained (eq. 24). Furthermore, when **2.15** was treated with

phenylisocyananate, acetone, azobenzene, or iodosobenzene, only starting materials were recovered. The results in equations 23 and 24 indicate that some mode of catalysis may be required to facilitate the direct allylboration of these electrophiles.

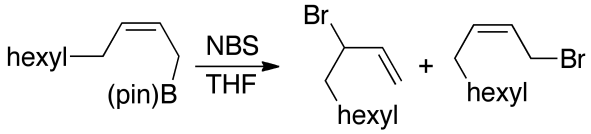
Scheme 2.25: Attempted Allylboration of Various Electrophiles



One additional electrophile, however, did allow for the isolation of a clean mixture of products (Scheme 2.26). When **2.15** was treated with NBS at 0 ºC, a 1 : 1 ratio of **2.26** and **2.27** was isolated from the reaction in a 43% combined yield. Regioisomer **2.26** is the product of allylboration, potentially through a

closed transition state. Allylbromide **2.27**, however, appears to be the product of a 1,2-migration, potentially in the fashion of standard boron oxidation with H_2O_2. In an attempt to favor a single regioisomer of product, NBS addition was executed at –78 °C, and the reaction was allowed to warm slowly to room temperature overnight. While the yield was similar to the first example at 45%, the product ratio shifted slightly in favor of branched allylic bromide **2.26** in a 2 : 1 ratio with **2.27**.

Scheme 2.26: Allylboration of NBS



2.15 **2.26** **2.27**

entry	temp (°C)	**2.26** : **2.27**	yield (%)
1	0 to 23	1 : 1	43
2	–78 to 23	2 : 1	45

IV. Conclusions

A new formal oxidation of allylboronic esters has been presented that offers a complementary method to standard allylboronic ester oxidation conditions. Nitrosobenzene has been employed as the stoichiometric oxidant and has, for the first time, been shown to be a regioselective electrophile in an allylboration reaction. Notably, this transformation proceeds smoothly with allylic transposition. Superstoichiometric PhNO in conjunction with a Brønsted base conspire to generate the free internal allylic alcohol. This methodology has been extended to the diastereoselective oxidation of a 1,4-(bis)boryl compound,

delivering an internal *anti*-1,2-diol in modest yield and good diastereoselectivity, highlighting the potential utility of this unique transformation.

V. Experimental Procedures

A. General Information

^{1}H NMR spectra were recorded on Varian Unity INOVA 500 MHz, Varian Gemini 400 MHz, and Varian VNMRS 500 MHz spectrometers. Chemical shifts are reported in ppm with the solvent resonance as the internal standard ($CDCl_3$: 7.24 ppm). Data are reported as follows: chemical shift, multiplicity (s = singlet, d = doublet, t = triplet, q = quartet, m = multiplet, br = broad, app = apparent), integration, coupling constants (Hz), and assignment. $^{13}C\{^{1}H\}$NMR spectra were recorded on Varian VNMRS 500 MHz (125 MHz) and Varian Gemini 400 MHz (100 MHz) spectrometers. Chemical shifts are reported in ppm with the solvent resonance as the internal standard ($CDCl_3$: 77.00 ppm). Infrared (IR) spectra were recorded on a Bruker α-P Spectrometer. Frequencies are reported in wavenumbers (cm^{-1}) as follows: strong (s), broad (br), medium (m), and weak (w). High-resolution mass spectrometry (ESI) was performed at Boston College, Chestnut Hill, MA.

Liquid chromatography was performed using flash chromatography on silica gel (SiO_2, 230 x 450 Mesh) purchased from Silicycle. Thin layer chromatography was performed on 25 μM silica gel glass-backed plates from Silicycle. Visualization was performed using ultraviolet light (254 nm), phosphomolybdic acid (PMA), potassium permanganate ($KMnO_4$), and ceric ammonium molybdate (CAM).

All reactions were conducted in oven- or flame-dried glassware under an atmosphere of nitrogen or argon. Toluene and tetrahydrofuran were purified using a Pure Solv MD-4 solvent purification system, from Innovative Technology, Inc., by passing the solvent through two activated alumina columns after being sparged with argon. Bis(1,5-cyclooctadiene)nickel(0) ($Ni(cod)_2$) and trichclohexylphosphine (PCy_3) were purchased from Strem Chemicals, Inc. 4,4,5,5-tetramethyl-1,3,2-dioxaborolane (HB(pin)) and nitrosobenzene (PhNO) were purchased from Aldrich and used without further purification. Bis(pinacolato)diboron ($B_2(pin)_2$) was obtained from AllyChem Co., Ltd., and recrystallized from pentane. All other reagents were purchased from Aldrich or Fisher and used without further purification.

B. Experimental Procedures

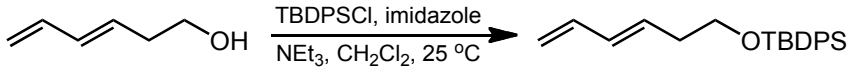
1. *Preparation and Characterization of Dienes*

The following dienes were prepared by Wittig olefination of the commercially available α,β-unsaturated aldehydes with methyltriphenylphosphonium bromide and potassium *tert*-butoxide in

tetrahydrofuran: *trans*-1,3-decadiene[116] (Table 2.2, entry 1) and *trans*-1-phenyl-1,3-butadiene[117] (Table 2.2, entry 4).

The following dienes were prepared by the literature procedure: (*E*)-2-methyldeca-1,3-diene[65e] (Table 2.2, entry 8), (*E*)-*tert*-butyl(penta-2,4-dienyloxy)diphenylsilane[60a] (Table 2.2, entry 3), (*E*)-3-methylnona-1,3-diene[4] (Table 2.2, entry 9), (*E*)-((2,2-dimethylhexa-3,5-dienyloxy)methyl)benzene[4] (Table 2.2, entry 5), and *trans*-1-cyclohexyl-1,3-butadiene[118] (Table 2.2, entry 2).

2. Preparation of (E)-tert-butyl(hexa-3,5-dien-1-yloxy)diphenylsilane (Table 2.2, entry 6). The title compound was synthesized as shown below from the known alcohol.[119]



***(E)-tert*-butyl(hexa-3,5-dien-1-yloxy)diphenylsilane (Table 2.2, entry 6)** To a flame-dried 50 mL round-bottom flask equipped with a stir bar was added imidazole (1.82 g, 26.7 mmol) and methylene chloride (18 mL, 0.5 M). The flask was then charged with (*E*)-hexa-3,5-dien-1-ol (874 mg, 8.9 mmol) followed by dropwise addition *via* syringe of TBDPSCl (7.34 g, 26.7 mmol). The resulting

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[116] Meyers, A. I.; Ford, M. E. *J. Org. Chem.* **1976**, *41*, 1735.

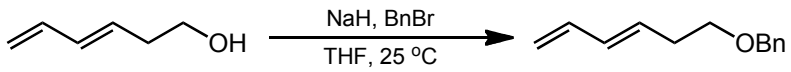
[117] Yeh, K. L.; Liu, B.; Lo, C. Y.; Huang, H. L.; Liu, R. S. *J. Am. Chem. Soc.* **2002**, *124*, 6510.

[118] Habrant, D.; Stengel, B.; Meunier, S.; Mioskowski, C. *Chem. Eur. J.* **2007**, *13*, 5433.

[119] Miller, C. A.; Batey, R. A. *Org. Lett.* **2004**, *6*, 699.

solution was allowed to stir for five minutes. Triethylamine (3.72 mL, 26.7 mmol) was then added dropwise *via* syringe. The resulting solution was allowed to stir for 15 hours. The reaction mixture was then diluted with CH_2Cl_2 (20 mL) and washed with brine (50 mL). The aqueous layer was extracted with CH_2Cl_2 (3 x 100 mL), dried over Na_2SO_4, filtered, and concentrated under reduced pressure. ^{1}H NMR (500 MHz, $CDCl_3$): δ 1.03 (s, 9H, C(C**H$_3$**)$_3$), 2.33 (dt, 2H, *J* = 7.4, 6.6 Hz, CH=CHC**H$_2$**), 3.69 (t, 2H, *J* = 6.6 Hz, SiOC**H$_2$**), 4.95 (dd, 1H, *J* = 10.2, 1.7 Hz, CH=C**H$_c$**H$_t$), 5.08 (dd, 1H, *J* = 17.1, 1.7 Hz, CH=C**H$_t$**H$_c$), 5.68 (ddd, 1H, *J* = 15.3, 7.5, 7.1 Hz, SiO(CH$_2$)$_2$C**H**), 6.03-6.08 (m, 1H, CH$_2$=CHC**H**), 6.28 (app dt, 1H, *J* = 17.1, 10.2 Hz, CH$_2$=C**H**), 7.34-7.42 (m, 4H, Ar-**H**), 7.63-7.66 (m, 6H, Ar-**H**) ppm; ^{13}C NMR (100 MHz, $CDCl_3$): δ 19.2, 26.8, 35.9, 63.5, 115.2, 127.6, 129.6, 131.6, 132.8, 133.9, 135.6, 137.2 ppm; IR (neat): 505 (s), 613 (s), 701 (w), 731 (s), 823 (s), 1003 (s), 1109 (s), 1428 (m), 1472 (m), 2858 (m), 2931 (m), 3071 (w); HRMS-(ESI+) for $C_{22}H_{29}OSi$ [M+H]: calculated: 337.1988, found 337.1995. The crude material was purified on silica gel (0.5% Et_2O/pentane) to afford a clear, colorless oil (2.56 g, 86% yield). R_f = 0.24 (0.5% Et_2O/pentane, stain in PMA).

C. Preparation of (E)-((hexa-3,5-dien-1-yloxy)methyl)benzene (Table 2.2, entry 7). The title compound was synthesized as shown below from the known alcohol.[5]



(*E*)-((hexa-3,5-dien-1-yloxy)methyl)benzene (Table 2.2, entry 7) A flame-dried 50 mL round-bottom flask equipped with a stir bar was brought into the dry-box and charged with sodium hydride (142 mg, 5.91 mmol). The flask was sealed with a rubber septum, removed from the box, and placed under an atmosphere of nitrogen. A separate flame-dried 25 mL round-bottom flask was charged with (*E*)-hexa-3,5-dien-1-ol (527 mg, 5.37 mmol) and THF (18 mL, 0.30 M). The resulting solution was taken up in a syringe and added drop-wise to the reaction flask (containing NaH). The resulting slurry was allowed to stir for 10 minutes. Benzyl bromide (703 μL, 5.91 mmol) was added *via* syringe to the reaction flask. The resulting slurry was allowed to stir for 68 hours at ambient temperature. The reaction was quenched with water (15 mL). The aqueous layer was extracted with EtOAc (3 x 50 mL) and the combined organic layers were dried over sodium sulfate followed by filtration and concentration under reduced pressure. ^{1}H NMR (500 MHz, $CDCl_3$): δ 2.40 (dt, 2H, J = 6.8, 5.7 Hz, $BnOCH_2C\mathbf{H_2}$), 3.51 (t, 2H, J = 6.6 Hz, $BnOC\mathbf{H_2}$), 4.51 (s, 2H, Ar-$C\mathbf{H_2}$), 4.98 (d, 1H, J = 10.0 Hz, CH=$C\mathbf{H_c}H_t$), 5.10 (d, 1H, J = 16.6 Hz, CH=$C\mathbf{H_t}H_c$), 5.71 (ddd, 1H, J = 15.4, 7.6, 7.1 Hz,

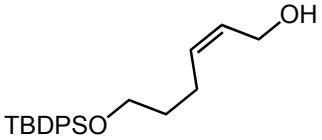
$CH_2C\mathbf{H}$=CH), 6.08-6.14 (m, 1H, CH_2=CHC**H**), 6.30 (app dt, 1H, *J* = 16.6, 10.2 Hz, C**H**=CH_2), 7.25-7.29 (m, 1H, Ar-**H**), 7.31-7.35 (m, 4H, Ar-**H**) ppm; ^{13}C NMR (100 MHz, $CDCl_3$): δ 33.0, 69.6, 72.9, 115.5, 127.6, 127.7, 128.4, 131.2, 132.7, 137.0, 138.4 ppm; IR (neat): 697 (s), 735 (s), 900 (s), 952 (m), 1004 (s), 1103 (s), 1206 (w), 1361 (m), 1479 (m), 1603 (w), 2789 (s), 3031 (w); HRMS-(ESI+) for $C_{13}H_{17}O$ [M+H]: calculated: 189.1279, found 189.1272. The crude material was purified on silica gel (0-5% EtOAc/hexanes) to afford the product as a clear, yellow oil (841 mg, 83% yield). R_f = 0.68 (10% EtOAc/hexanes, stain in PMA).

2. *Representative Procedure for Diene Hydroboration/Oxidation.*[60a]

In the dry-box, an oven-dried 20 mL scintillation vial equipped with a stir bar was charged successively with $Ni(cod)_2$ (2.5 mg, 0.009 mmol), PCy_3 (2.5 mg, 0.009 mmol), toluene (1.45 mL, 0.25 M), HB(pin) (69.4 mg, 0.54 mmol), and (*E*)- *tert*-butyl(hexa-4,5-dien-1-yloxy)diphenylsilane (121 mg, 0.36 mmol). The vial was sealed with a polypropylene cap, removed from the box, and allowed to stir at ambient temperature for 3 h. The reaction was then cooled to 0 °C (ice/water), diluted with THF (3 mL), and charged with 3 M NaOH (2 mL) and H_2O_2 (1 mL). The resulting mixture was allowed to stir for 12 h while slowly warming to room temperature. The mixture was then cooled to 0 °C (ice/water) and the reaction quenched by drop-wise addition of saturated aqueous sodium thiosulfate (2 mL). The reaction mixture was then diluted with brine (10 mL) and extracted with

CH_2Cl_2 (3 x 20 mL). The combined organic layers were dried over Na_2SO_4, filtered, and concentrated under reduced pressure. The crude reaction mixture was purified on silica gel (10% EtOAc/Hexanes) to afford a clear, colorless oil (121 mg, 95% yield). R_f = 0.16 (10% EtOAc/hexanes, stain in PMA).

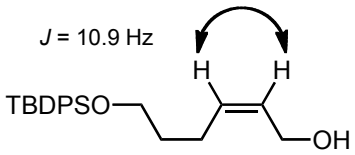
C. ***Full Characterization of Hydroboration/Oxidation Products.***

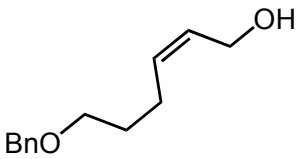


(*Z*)-6-((*tert*-butyldiphenylsilyl)oxy)hex-2-en-1-ol (Table 2.2, entry 6).[120] ^{1}H NMR (500 MHz, $CDCl_3$): δ 1.03 (s, 9H, C(C**H$_3$**)$_3$), 1.57 (tt, 2H, *J* = 7.6, 6.1 Hz, SiOCH$_2$C**H$_2$**), 2.18 (dt, 2H, *J* = 7.5, 6.9 Hz, SiO(CH$_2$)$_2$C**H$_2$**), 3.65 (t, 2H, *J* = 6.1 Hz, SiOC**H$_2$**), 4.16 (app t, 2H, *J* = 5.9 Hz, C**H$_2$**OH), 5.49 (dtt, 1H, *J* = 10.9, 7.8, 1.2 Hz, C**H**=CHCH$_2$OH), 5.62 (dtt, 1H, *J* = 10.9, 6.8, 1.5 Hz, CH=C**H**CH$_2$OH), 7.34-7.43 (m, 6H, Ar-**H**), 7.63-7.65 (m, 4H, Ar-**H**) ppm; ^{13}C NMR (100 MHz, $CDCl_3$): δ 19.2, 23.6, 26.8, 32.2, 58.4, 63.0, 127.6, 129.0, 129.6, 132.3, 133.8, 135.5 ppm; IR (neat): 505 (s), 613 (m), 702 (s), 739 (m), 823 (m), 1110 (s), 1389 (w), 1428 (m), 1472 (w), 2858 (m), 2931 (m), 3334 (m, b); HRMS-(ESI+) for $C_{22}H_{29}OSi$ [M+H–H_2O]: calculated: 337.1988, found 337.1982.

[120] Narco, K.; Baltas, M.; Gorrichon, L. *Tetrahedron* **1999**, *55*, 14013.

Proof of Stereochemistry: (*Z*)-alkene stereochemistry determined by coupling constants as shown below.



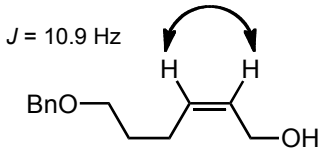


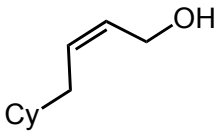
(*Z*)-6-(benzyloxy)hex-2-en-1-ol (Table 2.2, entry 7).[121] The reaction was performed with the general procedure. ^{1}H NMR (500 MHz, $CDCl_3$): δ 1.68 (tt, 2H, *J* = 7.4, 6.3 Hz, $BnOCH_2C\mathbf{H_2}$), 2.19 (dt, 2H, *J* = 8.4, 6.3 Hz, $BnO(CH_2)_2C\mathbf{H_2}$), 3.47 (t, 2H, *J* = 6.3 Hz, $BnOC\mathbf{H_2}$), 4.15 (d, br, 2H, *J* = 6.6 Hz, $C\mathbf{H_2}OH$), 4.48 (s, 2H, $ArC\mathbf{H_2}$), 5.51 (dtt, 1H, *J* = 10.9, 7.6, 1.3 Hz, $C\mathbf{H}$=$CHCH_2OH$), 5.64 (dtt, 1H, *J* = 10.9, 6.9, 1.4 Hz, CH=$C\mathbf{H}CH_2OH$), 7.25-7.28 (m, 2H, Ar-**H**), 7.29-7.35 (m, 3H, Ar-**H**) ppm; ^{13}C NMR (100 MHz, $CDCl_3$): δ 23.8, 29.2, 58.2, 69.1, 72.8, 127.5, 127.6, 128.3, 129.2, 132.0, 138.3 ppm; IR (neat): 698 (s), 736 (s), 1042 (s), 1100 (s), 1206 (w), 1364 (m), 1454 (m), 1496 (w), 2857 (s), 2927 (s), 3064 (w), 3375 (s, br); HRMS-(ESI+) for $C_{13}H_{17}O$ [M+H–H_2O]: calculated: 189.1279, found 189.1279. The crude reaction mixture was purified on silica gel (12.5% EtOAc/hexanes) to afford

[121] Schoemaker, J. M.; Luglag, V. R.; Borhan, B. *J. Am. Chem. Soc.* **2004**, *126*, 13600.

a clear, colorless oil (69 mg, 93% yield). R_f = 0.05 (10% EtOAc/hexanes, stain in PMA).

Proof of Stereochemistry: (*Z*)-alkene stereochemistry determined by coupling constants as shown below.





(*Z*)-4-cyclohexylbut-2-en-1-ol (Table 2.2, entry 2) (Compound S-5).[122] The reaction was performed with the general procedure. ^{1}H NMR (500 MHz, $CDCl_3$): δ 0.83-0.91 (m, 2H, Cy-**H**), 1.07-1.31 (m, 4H, Cy-**H**), 1.55 (s, 1H, O**H**), 1.60-1.69 (m, 5H, Cy-**H**), 1.95 (app t, 2H, *J* = 6.5 Hz, Cy-C**H$_2$**), 4.16 (s, br, 2H, C**H$_2$**OH), 5.54 (dtt, 1H, *J* = 11.0, 7.5, 1.3 Hz, $CyCH_2C$**H**=CH), 5.62 (dtt, 1H, *J* = 11.0, 6.8, 1.5 Hz, $CyCH_2CH$=C**H**) ppm; ^{13}C NMR (125 MHz, $CDCl_3$): δ 26.3, 26.5, 33.1, 35.1, 38.0, 58.6, 129.0, 131.7 ppm; IR (neat): 669 (w), 1016 (s), 1448 (s), 2851 (s), 2921 (s), 3014 (w), 3317 (s, br); HRMS-(ESI+) for $C_{10}H_{17}$ [M+H–H_2O]: calculated: 137.1330, found 137.1328. The crude reaction mixture was purified on silica gel (33% Et_2O/pentane) to afford a clear oil (46 mg, 81% yield). R_f = 0.15 (17% Et_2O/ pentane, stain in PMA).

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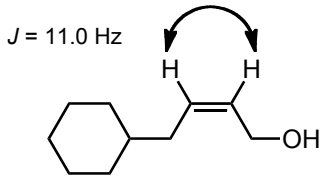
[122] Krysan, D.; Haight, A.; Menzia, J.; Welch, N. *Tetrahedron* **1994**, *50*(21), 6163.

Proof of Stereochemistry: (*Z*)-alkene stereochemistry determined by coupling constants as shown below.

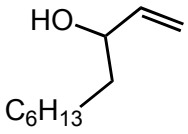


D. *General Procedure for Diene Hydroboration/Allylation.*

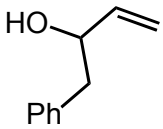
In the dry-box, and oven-dried 20 mL scintillation vial equipped with a stir bar was charged successively with $Ni(cod)_2$ (2.5 mg, 0.009 mmol), PCy_3 (2.5 mg, 0.009 mmol), toluene (1.45 mL, 0.25 M), HB(pin) (69.4 mg, 0.54 mmol), and *trans*-1,3-decadiene (50 mg, 0.36 mmol). The vial was sealed with a polypropylene cap, removed from the box, and allowed to stir at room temperature for 3 h. The reaction was then cooled to 0 °C (ice/water) and charged with PhNO (119 mg, 1.11 mmol) and THF (2 mL). The resulting solution was allowed to warm to ambient temperature while stirring for 1 h. The solution was then cooled to 0 °C (ice/water) and charged with 3 M NH_4OH (2 mL). The resulting mixture was allowed to stir for 14 h while warming to room temperature. The reaction mixture was then diluted with brine (10 mL) and extracted with CH_2Cl_2 (3 x 20 mL). The combined organic layers were dried over Na_2SO_4, filtered, and concentrated under reduced pressure. The crude reaction mixture was purified on silica gel

(10% Et_2O/pentane) to afford a clear, yellow oil (37 mg, 66% yield). R_f = 0.14 (10% Et_2O/pentane, stain in PMA).

E. ***Full Characterization of Hydroboration/PhNO Allylation Products.***



dec-1-en-3-ol (Table 2.2, entry 1, 2.16).[123] ^{1}H NMR (400 MHz, $CDCl_3$): δ 0.85 (t, 3H, *J* = 6.5 Hz, C**H$_3$**), 1.26-1.57 (m, 12H, (C**H$_2$**)$_6$), 4.05-4.08 (m, 1H, C**H**OH), 5.07 (dd, 1H, *J* = 10.4, 1.2 Hz, CH=C**H$_c$**H$_t$), 5.19 (dd, 1H, *J* = 17.2, 1.4 Hz, CH=C**H$_t$**H$_c$), 5.84 (ddd, 1H, *J* = 17.2, 10.4, 6.3 Hz, C**H**=CH$_2$) ppm; ^{13}C NMR (100 MHz, $CDCl_3$): δ 14.1, 22.6, 25.3, 29.2, 29.5, 31.8, 37.0, 73.3, 114.5, 141.3 ppm; IR (neat): 919 (s), 989 (s), 1465 (s), 2855 (s), 2925 (s), 2956 (m), 3354 (s, br); HRMS-(ESI+) for $C_{10}H_{19}$ [M+H–H_2O]: calculated: 139.1487, found 139.1486.



1-phenylbut-3-en-2-ol (Table 2.2, entry 4).[124] The reaction was performed with the general procedure. ^{1}H NMR (500 MHz, $CDCl_3$): δ 1.58 (d, 1H, *J* = 3.9 Hz, O**H**), 2.74 (dd, 1H, *J* = 13.7, 8.0 Hz, ArC**H$_2$**), 2.87 (dd, 1H, *J* = 13.5, 5.1 Hz, ArC**H$_2$**), 4.33-4.35 (m, 1H, C**H**OH), 5.12 (app dt, 1H, *J* = 10.9, 0.9 Hz, CH=C**H$_c$**H$_t$), 5.24 (app dt, 1H, *J* = 17.7, 1.2 Hz, CH=C**H$_t$**H$_c$), 5.92 (ddd, 1H, *J* = 17.7, 10.9, 5.8 Hz, C**H**=CH$_2$), 7.21-7.24 (m, 3H,

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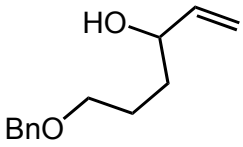
[123] de Frémont, P.; Marion, N.; Nolan, S. P. *J. Orgmet. Chem.* **2009**, *694*, 551.

[124] Ruano, J. L. G.; Marcos, V.; Alemán, J. *Angew. Chem. Int. Ed.* **2009**, *48*, 3155.

Ar-**H**), 7.29-7.32 (m, 2H, Ar-**H**) ppm; ^{13}C NMR (125 MHz, $CDCl_3$): δ 43.8, 73.6, 114.9, 126.5, 128.4, 129.5, 137.7, 140.1 ppm; IR (neat): 698 (s), 745 (s), 922 (s), 991 (s), 1030 (s), 1077 (m), 1117 (m), 1454 (m), 1496 (m), 2852 (w), 2921 (m, br), 3028 (w), 3375 (s, br); HRMS-(ESI+) for $C_{10}H_{11}$ [M+H–H_2O]: calculated: 131.0861, found 131.0858. The crude reaction mixture was purified on silica gel (15% Et_2O/pentane) to afford the title compound as a clear oil (36 mg, 64% yield). R_f = 0.08 (10% Et_2O/pentane, stain in CAM).



6-(benzyloxy)hex-1-en-3-ol (Table 2.2, entry 7).[125] The reaction was performed with the general procedure. ^{1}H NMR (500 MHz, $CDCl_3$): δ 1.56-1.74 (m, 4H, C(OH)(C**H$_2$)$_2$**), 2.30 (s, br, 1H, O**H**), 3.50 (t, 2H, *J* = 5.9 Hz, BnOC**H$_2$**), 4.10-4.12 (m, 1H, C**H**OH), 4.50 (s, 2H, PhC**H**$_2$), 5.08 (dt, 1H, *J* = 10.4, 1.5 Hz, CH=C**H$_c$**H$_t$), 5.21 (dt, 1H, *J* = 17.3, 1.4 Hz, CH=CH$_c$**H$_t$**), 5.85 (ddd, 1H, *J* = 17.3, 10.4, 6.1 Hz, C**H**=CH$_2$), 7.24-7.36 (m, 5H, Ar-**H**) ppm; ^{13}C NMR (100 MHz, $CDCl_3$): δ 25.7, 34.2, 70.3, 72.7, 73.0, 114.4, 127.6, 127.7, 128.4, 138.2, 141.1 ppm; IR (neat): 612 (w), 698 (s), 737 (s), 921 (s) 991 (s) 1099 (s), 1204 (w), 1276 (w, b), 1454 (m), 1496 (m), 2855 (s), 2924 (s), 3030 (w), 3065 (w), 3407 (s, br); HRMS-(ESI+) for $C_{13}H_{19}O_2$ [M+H]: calculated: 207.1385, found 207.1390. The crude reaction mixture was purified on silica gel (25% Et_2O/pentane) to afford a clear oil (47 mg, 63% yield). R_f = 0.12 (25% Et_2O/pentane, stain in PMA).

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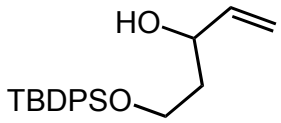
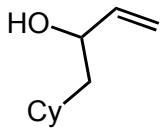
[125] Iyengar, R.; Schildknegt, K.; Morton, M.; Aubé, J. *J. Org. Chem.* **2005**, *70*, 10645.



5-((*tert*-butyldiphenylsilyl)oxy)pent-1-en-3-ol (Table 2.2, entry 3).[126] The reaction was performed with the general procedure. ^{1}H NMR (500 MHz, $CDCl_3$): δ 1.04 (s, 9H, C(C**H$_3$**)$_3$), 1.75-1.79 (m, 2H, CH(OH)C**H$_2$**), 3.17 (d, 1H, *J* = 2.7 Hz, O**H**), 3.79-3.89 (m, 2H, C**H$_2$**OSi), 4.42 (s, 1H, C**H**(OH)), 5.11 (dd, 1H, *J* = 10.4, 1.2 Hz, CH=C**H$_c$**H$_t$), 5.29 (dd, 1H, *J* = 17.4, 1.2 Hz, CH=CH$_c$**H$_t$**), 5.87 (ddd, 1H, *J* = 17.4, 10.4, 5.4 Hz, C**H**=CH$_2$), 7.37-7.44 (m, 6H, Ar-**H**), 7.66 (d, 4H, *J* = 7.9 Hz, Ar-**H**) ppm; ^{13}C NMR (100 MHz, $CDCl_3$): δ 19.0, 26.8, 38.4, 62.6, 72.1, 114.2, 127.7 (2C), 129.8 (2C), 133.0, 133.0, 135.5 (2C), 140.6 ppm; IR (neat): 487 (s), 502 (s), 613 (s), 699 (s), 736 (s), 822 (m), 921 (m), 996 (m), 1078 (s), 1106 (s), 1427 (m), 1472 (w), 2856 (w), 2929 (w), 3071 (w), 3415 (s, br); HRMS-(ESI+) for $C_{21}H_{29}O_2Si$ [M+H]: calculated: 341.1937, found 341.1923. The crude reaction mixture was purified on silica gel (10% Et_2O/pentane) to afford a clear oil (70 mg, 57% yield). R_f = 0.28 (10% Et_2O/pentane, stain in $KMnO_4$).



1-cyclohexylbut-3-en-2-ol (Table 2.2, entry 2).[127] The reaction was performed with the general procedure. ^{1}H NMR (400 MHz, $CDCl_3$): δ 0.87-0.96 (m, 4H, Cy-**H**), 1.12-1.78 (m, 10H, Cy-**H**, CyC**H$_2$**CH(O**H**)), 4.19 (s, b, 1H, **CH**OH), 5.07 (dd, 1H, *J* = 10.5, 1.2 Hz, CH=C**H$_c$**H$_t$), 5.20 (dd, 1H, *J* = 17.2, 1.2 Hz, CH=H$_c$**H$_t$**), 5.85 (ddd, 1H, *J* = 17.2,

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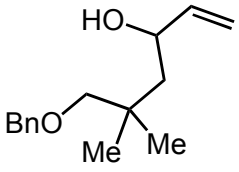
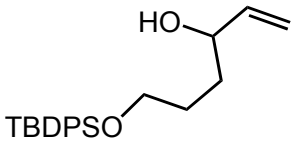
[126] Singh, O. V.; Han, H. *Org. Lett.* **2007**, *9*, 4801.

[127] Herold, P.; Duthaler, R.; Rihs, G.; Angst, C. *J. Org. Chem.* **1989**, *54*, 1178.

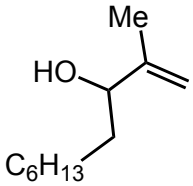
10.5, 6.3 Hz, C**H**=CH_2) ppm; ^{13}C NMR (100 MHz, $CDCl_3$): δ 26.2, 26.3, 26.5, 33.1, 33.8, 33.9, 44.9, 70.8, 114.2, 141.8 ppm; IR (neat): 919 (m), 990 (m), 1448 (m), 2851 (s), 2921 (s), 3353 (s, br); HRMS-(ESI+) for $C_{10}H_{17}$ [M+H–H_2O]: calculated: 137.1330, found 137.1337. The crude reaction mixture was purified on silica gel (10% Et_2O/pentane) to afford a clear oil (34 mg, 62% yield). R_f = 0.09 (10% Et_2O/pentane, stain in PMA).



6-(benzyloxy)-5,5-dimethylhex-1-en-3-ol (Table 2.2, entry 5). The reaction was performed with the general procedure. ^{1}H NMR (500 MHz, $CDCl_3$): δ 0.91 (s, 3H, C**H$_3$**), 1.01 (s, 3H, C**H$_3$**), 1.46-1.56 (m, 2H, C**H$_2$**COH), 3.24 (d, 1H, *J* = 9.1 Hz, C**H$_a$**H_bOBn), 3.27 (d, 1H, *J* = 9.1 Hz, CH_a**H$_b$**OBn), 4.05 (d, 1H, *J* = 2.5 Hz, O**H**), 4.20-4.23 (m, 1H, C**H**OH), 4.50 (d, 1H, *J* = 11.8 Hz, OC**H$_a$**H_bPh), 4.55 (d, 1H, *J* = 11.8 Hz, OCH_a**H$_b$**Ph), 5.01 (dt, 1H, *J* = 10.5, 1.5 Hz, C(OH)CH=**H$_c$**H_t), 5.21 (dt, 1H, *J* = 17.1, 1.6 Hz, C(OH)CH=H_c**H$_t$**), 5.83 (ddd, 1H, *J* = 17.1, 10.5, 5.6 Hz, C(OH)C**H**=CH_2), 7.26-7.35 (m, 5H, Ar-**H**) ppm; ^{13}C NMR (125 MHz, $CDCl_3$): δ 23.9, 28.0, 34.4, 48.9, 69.3, 73.6, 79.5, 113.2, 127.7, 127.8, 128.5, 137.5, 142.1 ppm; IR (neat): 610 (s), 697 (s), 734 (s), 916 (s), 989 (s), 1074 (s), 1092 (s), 1363 (m), 1474 (m), 2867 (m), 2925 (m), 2956 (m), 3413 (s, br); HRMS-(ESI+) for $C_{15}H_{22}O_2$ [M+H]: calculated: 235.1698, found 235.1694. The crude reaction mixture was purified on silica gel (17% Et_2O/pentane) to afford a clear oil (39 mg, 44% yield). R_f = 0.29 (17% Et_2O/pentane, stain in CAM).



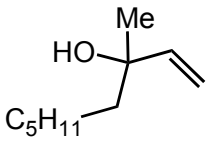
6-((*tert*-butyldiphenylsilyl)oxy)hex-1-en-3-ol (Table 2.2, entry 6). The reaction was performed with the general procedure. ^{1}H NMR (500 MHz, $CDCl_3$): δ 1.03 (s, 9H, SiC(C**H$_3$**)$_3$), 1.59-1.69 (m, 4H, C(OH)(C**H$_2$**)$_2$), 2.13 (d, 1H, *J* = 4.1 Hz, O**H**), 3.67-3.69 (m, 2H, C**H$_2$**OSi), 4.09-4.16 (m, 1H, C**H**OH), 5.09 (dt, 1H, *J* = 10.3, 1.4 Hz, CH=**H$_c$**H$_t$), 5.21 (dt, 1H, *J* = 17.3, 1.5 Hz, CH=CH$_c$**H$_t$**), 5.85 (ddd, 1H, *J* = 17.3, 10.3, 5.8 Hz, C**H**=CH$_2$), 7.35-7.48 (m, 6H, Ar-**H**), 7.63-7.66 (m, 4H, Ar-**H**) ppm; ^{13}C NMR (125 MHz, $CDCl_3$): δ 19.2, 26.8, 28.4, 33.9, 64.0, 72.8, 114.5, 127.6 (2C), 129.6 (2C), 133.7 (2C), 135.6 (2C), 141.2 ppm; IR (neat): 505 (s), 614 (m), 702 (s), 740 (m), 797 (m), 823 (m), 923 (w), 993 (m), 1109 (s), 1390 (w), 1427 (m), 1472 (w), 2857 (m, br), 2930 (m, br), 3050 (w), 3071 (w), 3380 (s, br); HRMS-(ESI+) for $C_{22}H_{30}O_2Si$ [M+H]: calculated: 355.2093, found 355.2086. The crude reaction mixture was purified on silica gel (17% Et_2O/pentane) to afford a clear oil (74 mg, 58% yield). R_f = 0.11 (17% Et_2O/pentane, stain in PMA).



2-methyldec-1-en-2-ol (Table 2.2, entry 8).[128] The reaction was performed with the general procedure. ^{1}H NMR (500 MHz, $CDCl_3$): δ 0.86 (t, 3H, 6.8 Hz, $(CH_2)_5$C**H$_3$**), 1.24-1.30 (m, 10H, CH_3(C**H$_2$**)$_5$), 1.41 (d, 1H, 3.6 Hz, O**H**), 1.50-1.53 (m, 2H, C**H$_2$**CH(OH)), 1.70 (s, 3H, CH_2=C(OH)(C**H$_3$**)), 4.02-4.05 (m, 1H, C**H**OH), 4.81

[128] Matsuo, J.; Kozai, T.; Nishikawa, O.; Hattori, Y.; Ishibashi, H. *J. Org. Chem.* **2008**, *73*, 6902.

(dq, 1H, *J* = 1.5, 1.5 Hz, C**H**$_2$=C), 4.91-4.92 (m, 1H, C**H**$_2$=C) ppm; ^{13}C NMR (125 MHz, $CDCl_3$): δ 14.1, 17.5, 22.6, 25.6, 29.2, 29.5, 31.8, 35.0, 76.0, 110.9, 147.7 ppm; IR (neat): 561 (w), 897 (s), 991 (m), 1025 (m), 1123 (w), 1376 (m), 1457 (m), 1651 (w), 2855 (s), 2924 (s), 3352 (s, br); HRMS-(ESI+) for $C_{11}H_{21}$ [M+H–H_2O]: calculated: 153.1643, found 153.1648. The crude reaction mixture was purified on silica gel with no applied pressure (8% EtOAc/hexanes) to afford a clear oil (13 mg, 22% yield). R_f = 0.12 (8% EtOAc/hexanes, stain in PMA).



3-methyl-non-1-en-3-ol (Table 2.2, entry 9).[129] The reaction was performed with the general procedure. ^{1}H NMR (500 MHz, $CDCl_3$): δ 0.85 (t, 3H, *J* = 6.6 Hz, C**H$_3$**$(CH_2)_4$), 1.24-1.30 (m, 12H, $CH_3(CH_2)_4$, O**H**, CH_2=CHC(C**H$_3$**)(OH)), 1.40-1.51 (m, 2H, CH_2=CHC(CH_3)(OH)C**H$_2$**), 5.02 (dd, 1H, *J* = 10.8, 0.6 Hz, CH=C**H$_c$**H$_t$), 5.17 (dd, 1H, *J* = 17.4, 0.6 Hz, CH=CH$_c$**H$_t$**), 5.89 (dd, 1H, *J* = 17.4, 10.8 Hz, C**H**=CH_2) ppm; ^{13}C NMR (125 MHz, $CDCl_3$): δ 14.0, 22.6, 23.8, 27.6, 29.7, 31.8, 42.4, 73.3, 111.4, 145.3 ppm; IR (neat): 724 (w), 919 (s), 995 (m), 1099 (m), 1306 (m), 1459 (m), 2858 (s), 2930 (s), 2957 (s), 3384 (s, br); HRMS-(ESI+) for $C_{10}H_{19}$ [M+H–H_2O]: calculated: 139.1487, found 139.1487. The crude reaction mixture was purified on silica gel (8% Et_2O/pentane) to afford a clear oil (33 mg, 58% yield). R_f = 0.12 (8% EtOAc/hexanes, stain in PMA).

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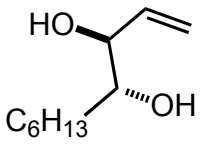
[129] Matsubara, S.; Okazoe, T.; Oshima, K.; Takai, K. *Chem. Bull. Soc. Jpn.* **1985**, *58*, 844.

F. ***Diboration/Allylation/Oxidation of trans-1,3-decadine (Scheme 2.24).***



***anti*-dec-1-ene-3,4-diol (2.22).**[130] In the dry-box, an oven-dried 20 mL scintillation vial equipped with a stir bar was charged successively with $Ni(cod)_2$ (9.0 mg, 0.03 mmol), PCy_3 (9.0 mg, 0.03 mmol), toluene (2.4 mL, 0.25 M), $B_2(pin)_2$ (229 mg, 0.9 mmol), and *trans*-1,3-decadiene (83 mg, 0.6 mmol). The vial was sealed with a polypropylene cap, removed from the box, and allowed to stir at 60 °C for 3 h. The polypropylene cap was exchanged for a rubber septum, the reaction was cooled to –78 °C (CO_2/acetone), and a solution of PhNO (193 mg, 1.80 mmol) in THF (4.86 mL, 0.37 M) was added to the reaction drop-wise over 40 minutes. The resulting solution was allowed to stir for 14 h while slowly warming to room temperature. The solution was then cooled to 0 °C (ice/water) and charged with 3 M NaOH (2.8 mL) and 30%/wt H_2O_2 (1.6 mL). The resulting mixture was allowed to stir for 4 h while warming to room temperature. The mixture was then cooled to 0 °C (ice/water) and quenched by dropwise addition of saturated aqueous sodium thiosulfate (2 mL). The reaction mixture was diluted with brine (10 mL) and extracted with CH_2Cl_2 (3 x 20 mL). The combined organic layers were dried over Na_2SO_4, filtered, and concentrated under reduced pressure. The

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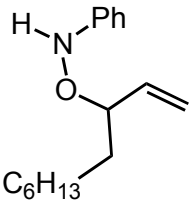
[130] Stereochemical assignment based on comparison to the spectral data of the known *trans*-diol: Lombardo, M.; Morganti, S.; Trombini, C. *J. Org. Chem.* **2003**, *68*, 997.

crude reaction mixture was purified on silica gel (50% EtOAc/hexanes) to afford a clear, colorless oil (49 mg, 47% yield). ^{1}H NMR (500 MHz, $CDCl_3$): δ 0.86 (t, 3H, J = 6.9 Hz, $(CH_2)_5C\mathbf{H_3}$), 1.23-1.55 (m, 12 H, $(C\mathbf{H_2})_5CH_3$, $(O\mathbf{H})_2$) 3.68 (ddd, 1H, J = 8.3, 3.9, 3.9 Hz, $(CH_2)_5C\mathbf{H}OH$), 4.08-4.10 (m, 1H, CH_2=CHC**H**OH), 5.26 (d, 1H, J = 10.5 Hz CH=$\mathbf{H_c}H_t$), 5.32 (dt, 1H J = 17.4, 1.5 Hz, CH=$CH_c\mathbf{H_t}$), 5.91 (ddd, 1H, J = 17.4, 10.5, 6.6 Hz, C**H**=CH_2); ^{13}C NMR (100 MHz, $CDCl_3$): δ 14.0, 22.6, 25.8, 29.3, 31.7, 32.1, 74.1, 75.9, 117.6, 136.0 ppm; IR (neat): 924 (s), 993 (s), 1031 (m), 1056 (m), 1317 (w), 1428 (w), 1459 (m), 2856 (s), 2926 (s), 2955 (m), 3375 (s, br); HRMS-(ESI+) for $C_{10}H_{19}O$ [M+H–H_2O]: calculated: 155.1435, found 155.1436. The crude reaction mixture was purified on silica gel (50% EtOAc/ hexanes) to afford a clear oil (29 mg, 47% yield). R_f = 0.21 (50% EtOAc/hexanes, stain in CAM).

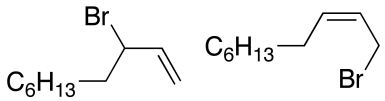
G. ***Preparation and Full Characterization of Hydroxylamine (Scheme 2.22).***



***O*-(dec-1-en-3-yl)-*N*-phenylhydroxylamine (2.19).** In the dry-box, an oven-dried 20 mL scintillation vial equipped with a stir bar was charged with $Ni(cod)_2$ (2.5 mg, 0.009 mmol), PCy_3 (2.5 mg, 0.009 mmol), HB(pin) (69 mg, 0.539 mmol), toluene (1.45 mL, 0.25 M), and *trans*-1,3-decadiene (50 mg, 0.361 mmol). The vial was sealed with a polypropylene cap, taped, and removed from the box. The reaction was allowed to stir at ambient temperature for 2 h. The polypropylene cap was then

exchanged for a rubber septum and the vial was placed under an atmosphere of nitrogen. The vial was cooled to –78 °C in a cryocool. Nitrosobenzene (41 mg, 0.379 mmol) was then dissolved in THF (3 mL), taken up in a syringe, and added dropwise to the reaction mixture at a rate of 0.6 mL/min. The resulting solution was allowed to stir at –78 °C for 13 h. The reaction was diluted with brine (20 mL) and extracted with CH_2Cl_2 (3 x 75 mL). The combined organic layers were dried over magnesium sulfate, filtered, and concentrated under reduced pressure. ^{1}H NMR (500 MHz, $CDCl_3$): δ 0.88 (t, 3H, 6.9 Hz, $(CH_2)_5C\mathbf{H_3}$), 1.22-1.47 (m, 10H, $(C\mathbf{H_2})_5CH_3$), 1.51-1.58 (m, 1H, $CH_3(CH_2)_5C\mathbf{H}_2$), 1.72-1.79 (m, 1H, $CH_3(CH_2)_5C\mathbf{H}_2$), 4.15 (dt, 1H, *J* = 7.8, 6.6 Hz, CH_2=CHC**H**(O)), 5.26 (dd, 1H, *J* = 18.3, 1.7 Hz, CH=$\mathbf{H_t}H_c$), 5.27 (dd, 1H, *J* = 10.5, 1.7 Hz, CH=$\mathbf{H_c}H_t$), 5.82 (ddd, 1H, *J* = 18.3, 10.5, 8.1 Hz, C**H**=CH_2), 6.86 (s, br, 1H, N**H**), 6.91-6.94 (m, 3H, Ar-**H**), 7.22-7.26 (m, 2H, Ar-**H**) ppm; ^{13}C NMR (125 MHz, $CDCl_3$): δ 14.1, 22.6, 25.4, 29.2, 29.6, 31.8, 33.6, 84.8, 114.5, 118.4, 121.8, 128.9, 138.1, 148.5 ppm; IR (neat): 488 (s), 691 (s), 731 (s), 762 (s), 863 (m), 891 (m), 925 (m), 962 (m), 1467 (m), 1494 (s), 1602 (s), 2855 (m), 2952 (s), 3283 (w); HRMS-(ESI+) for $C_{16}H_{26}NO$ [M+H]: calculated: 248.2014, found 248.2009. The crude reaction mixture was purified on silica gel (1% Et_2O/pentane) to afford the product as a clear, yellow oil (39 mg, 43% yield). R_f = 0.17 (1% Et_2O/pentane, stain in PMA).

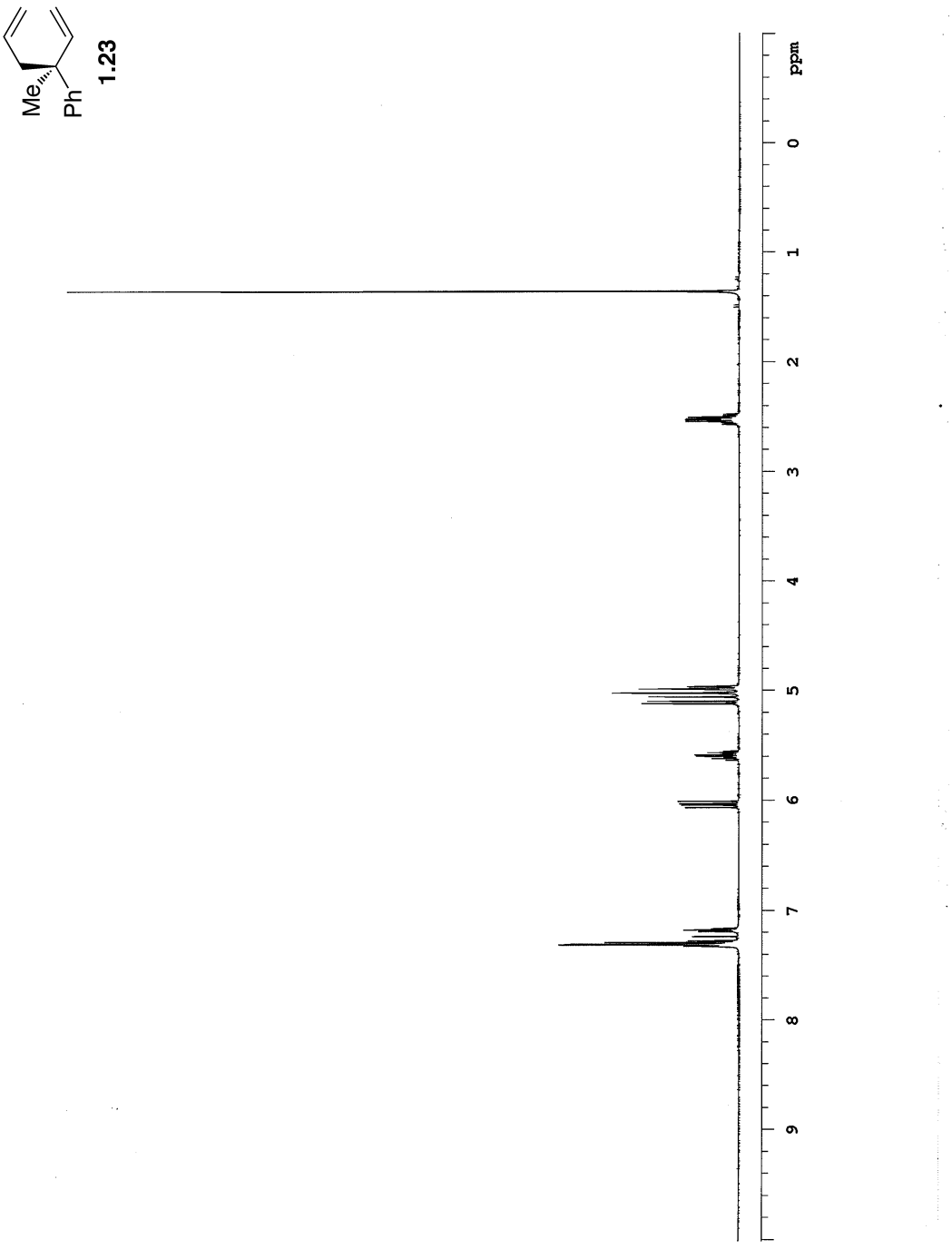
H. *Allylboration of N-Bromosuccinimide*



2.26 **2.27**

Preparation of 3-bromodec-1-ene (2.26) and (*Z*)-1-bromodec-2-ene (2.27). In the dry-box, an oven-dried 20 mL scintillation vial equipped with a stir bar was charged successively with $Ni(cod)_2$ (2.5 mg, 0.009 mmol), PCy_3 (2.5 mg, 0.009 mmol), toluene (1.45 mL, 0.25 M), HB(pin) (69.4 mg, 0.54 mmol), and *trans*-1,3-decadiene (50 mg, 0.36 mmol). The vial was sealed with a polypropylene cap, removed from the box, and allowed to stir at room temperature for 2 h. The reaction was then cooled to –78 °C (dry ice/acetone) and charged with *N*-Bromosuccinimide (96 mg, 0.54 mmol) in THF (3 mL). The reaction was allowed to slowly warm to room temperature and stir for 17 h. The solution was then diluted with water (10 mL) and extracted with Et_2O (3 x 20 mL). The combined organics were dried over $MgSO_4$, filtered, and concentrated under reduced pressure. ^1H NMR (300 MHz, $CDCl_3$): Please note that the spectrum also contains PhMe. δ 0.80-1.00 (6H, m, **2.26**, **2.27**), 1.15-1.55 (20H, m, **2.26**, **2.27**), 1.75-2.19 (4H, m, **2.26**, **2.27**), 3.94 (2H, d, J = 6.0 Hz, **2.27**), 4.47 (1H, ddd, J = 15.0, 6.0, 6.0 Hz, **2.26**), 5.04 (1H, d, J = 9.0 Hz, **2.26**), 5.20 (1H, d, J = 15 Hz, **2.26**), 5.59-5.81 (1H, m, **2.27**), 5.98 (1H, ddd, J = 15.0, 9.0, 9.0 Hz, **2.26**) ppm. The crude reaction mixture was purified on silica gel (100% pentane) to afford the product as a clear, pale yellow oil (35.4 mg, 45% yield). R_f = 0.67 (pentane, stain in CAM).

Appendix: Representative and Unpublished ^{1}H and ^{13}C NMR Spectra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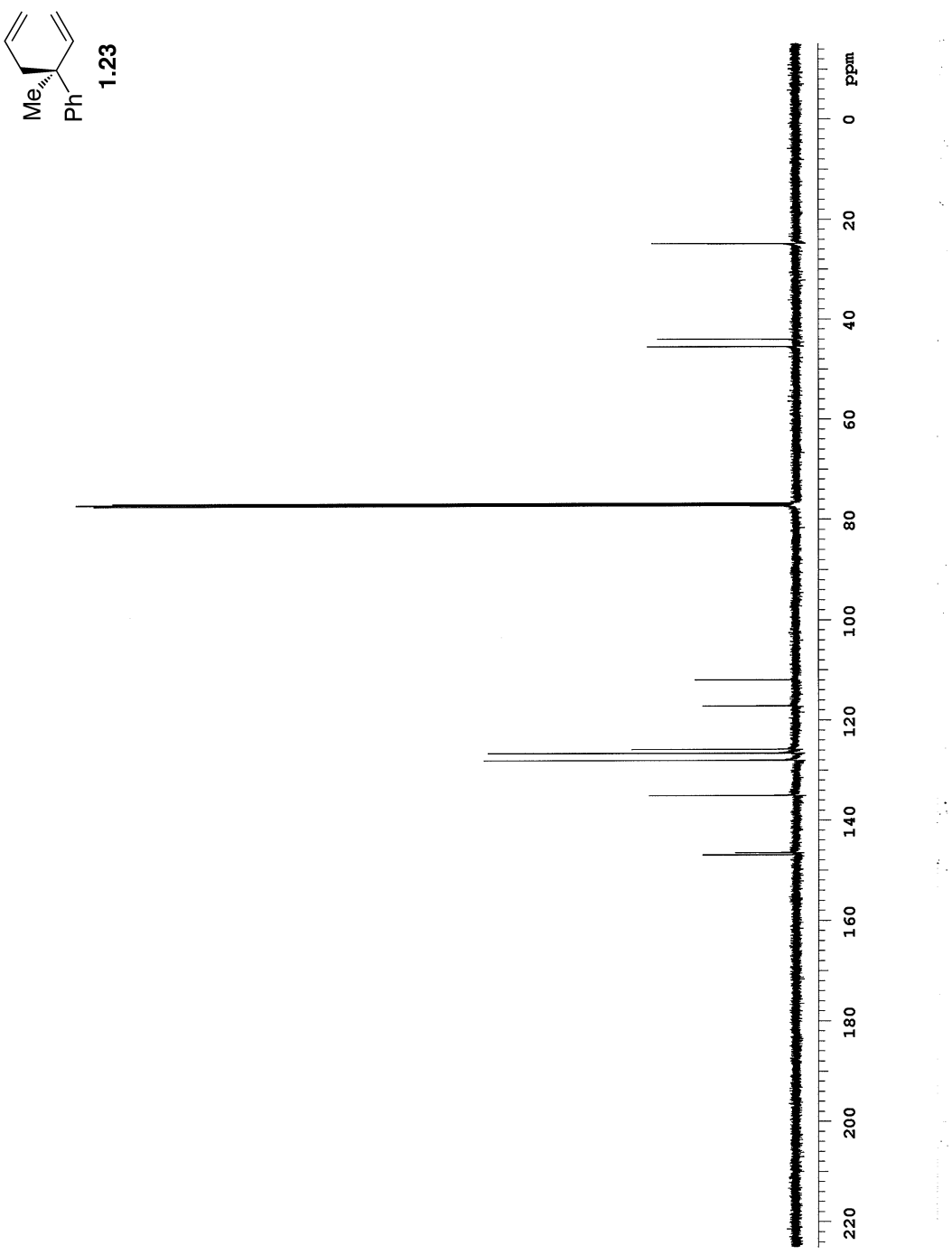
5
6
7
8
9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160
140
120
100
80
60
40
20
0
ppm

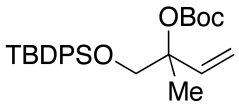
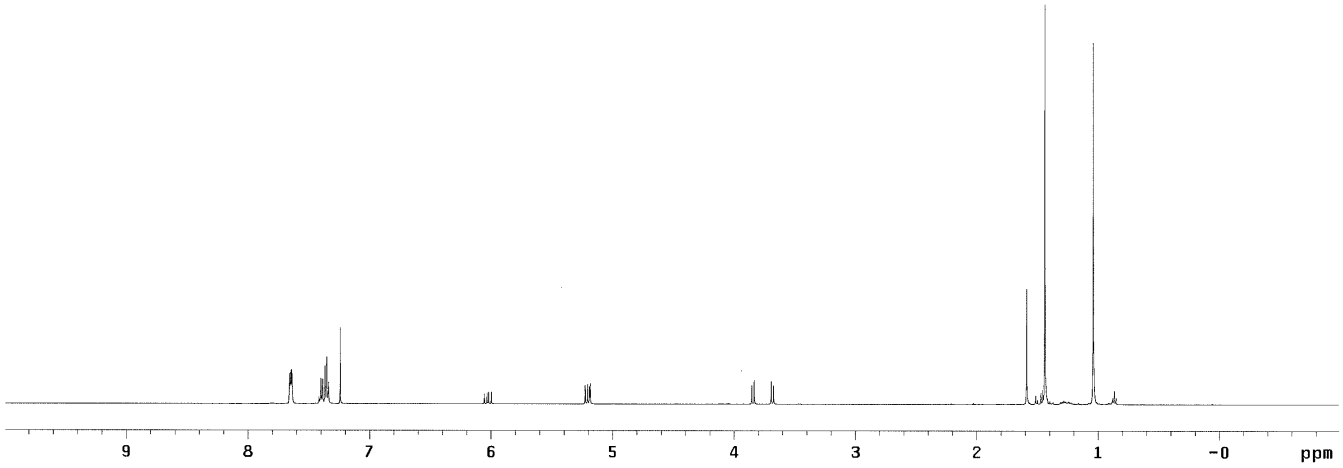


Table 1.6, entry 3



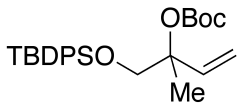
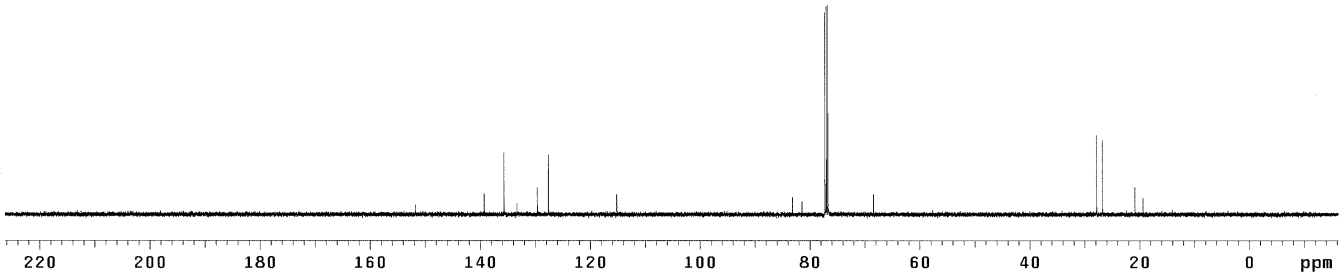


Table 1.6, entry 3



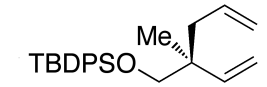
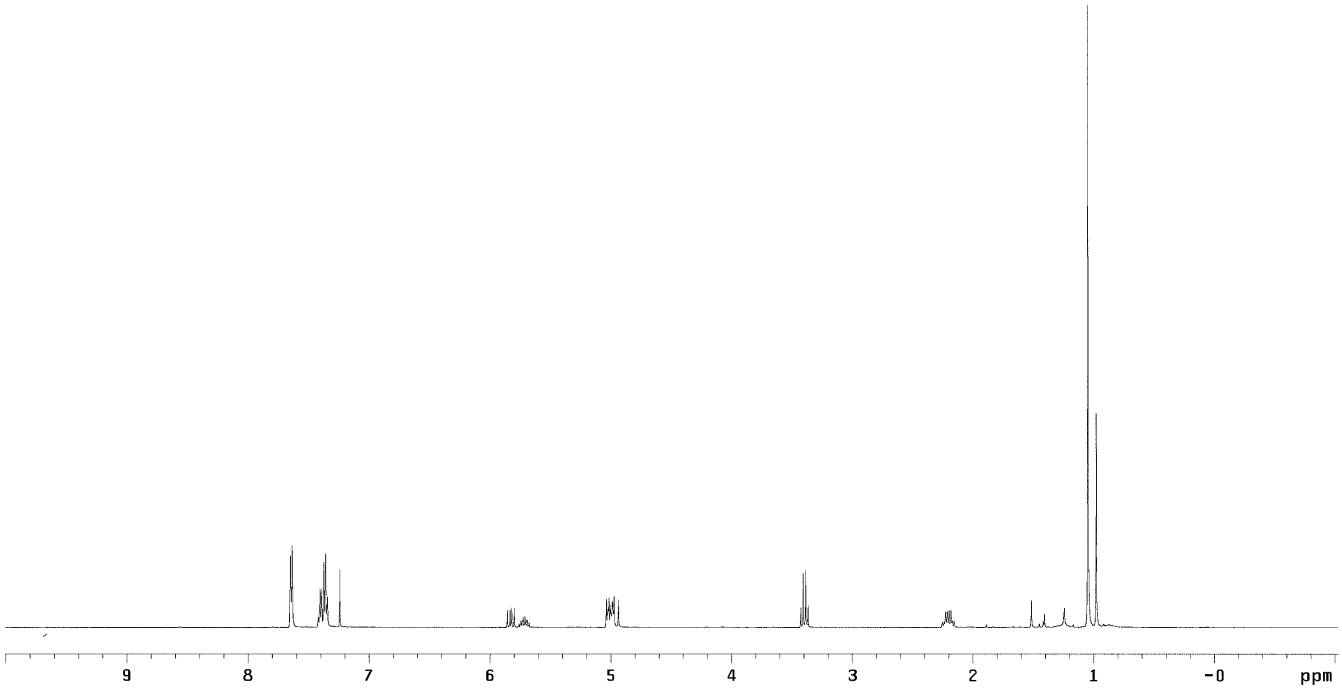
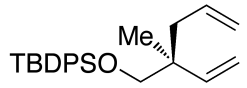


Table 1.6, entry 3





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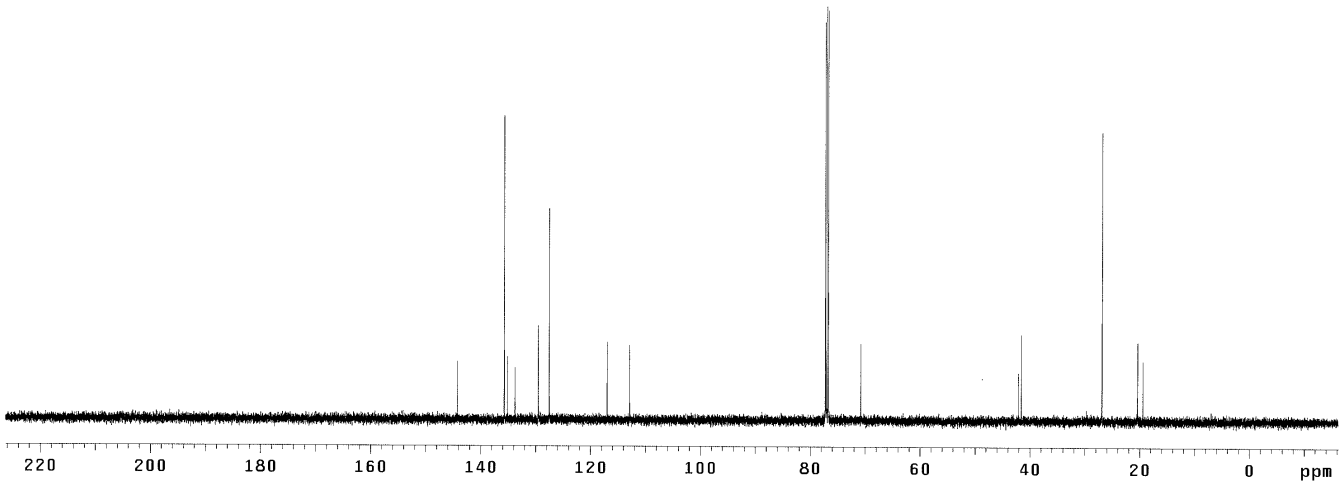

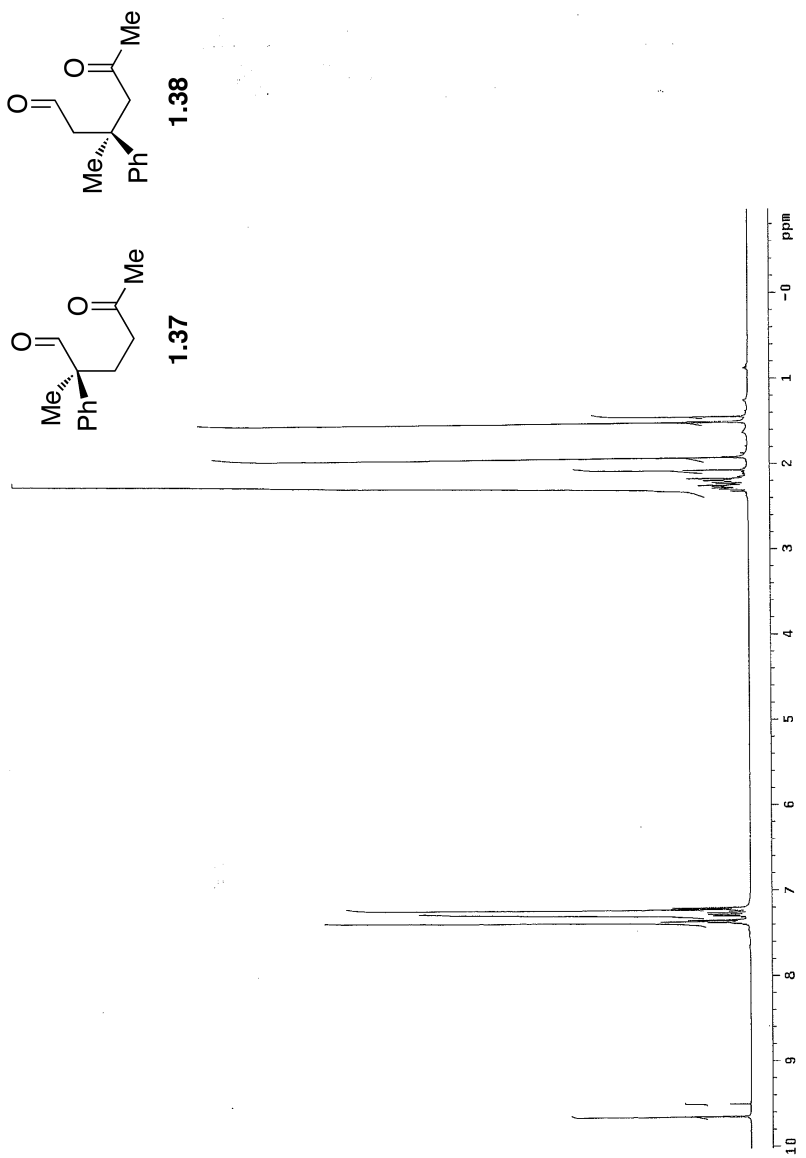
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Me
Ph
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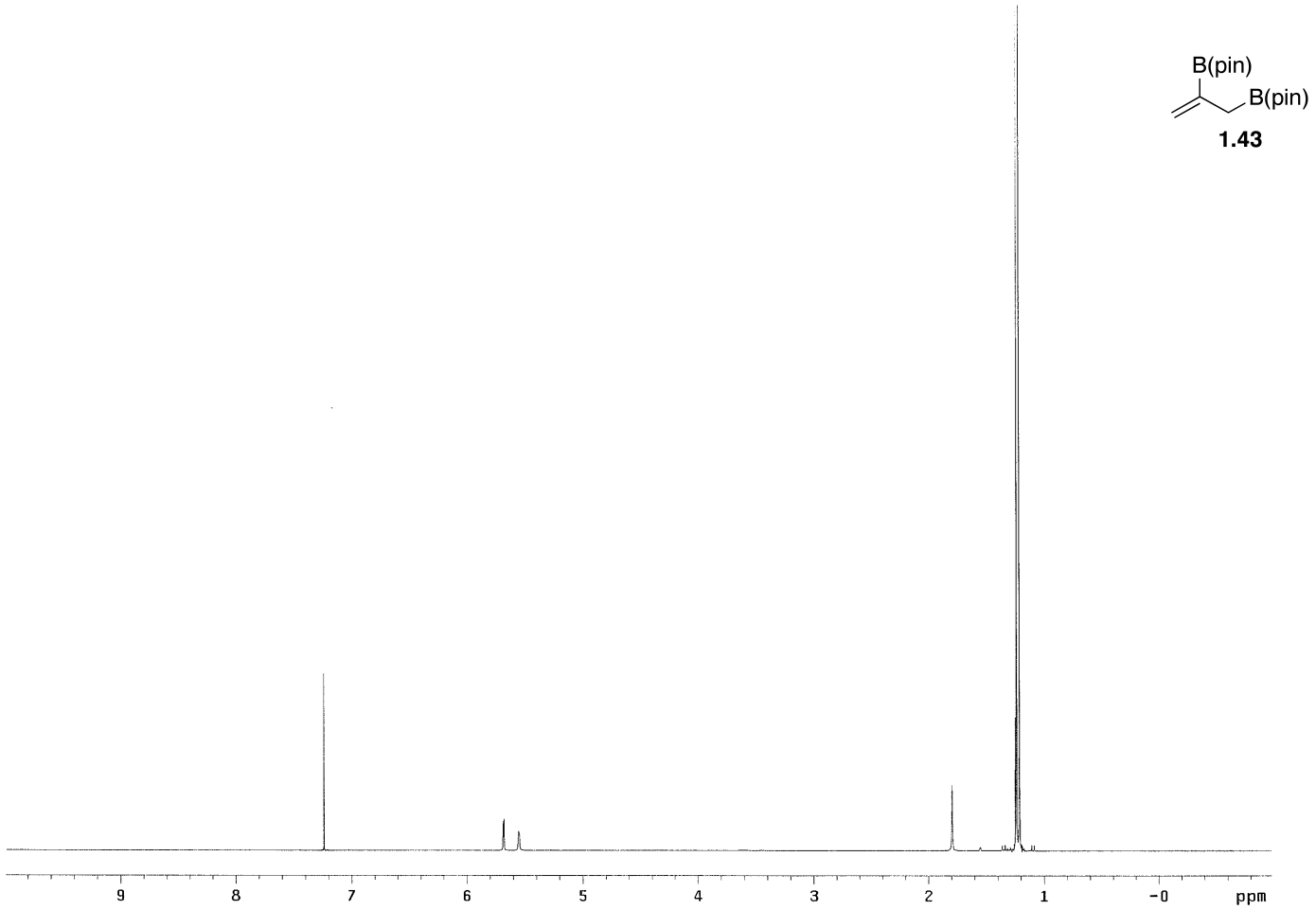
Me
Me
Ph
1.37
ppm
10
9
8
7
6
5
4
3
2
1
0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B(pin)
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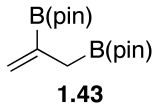
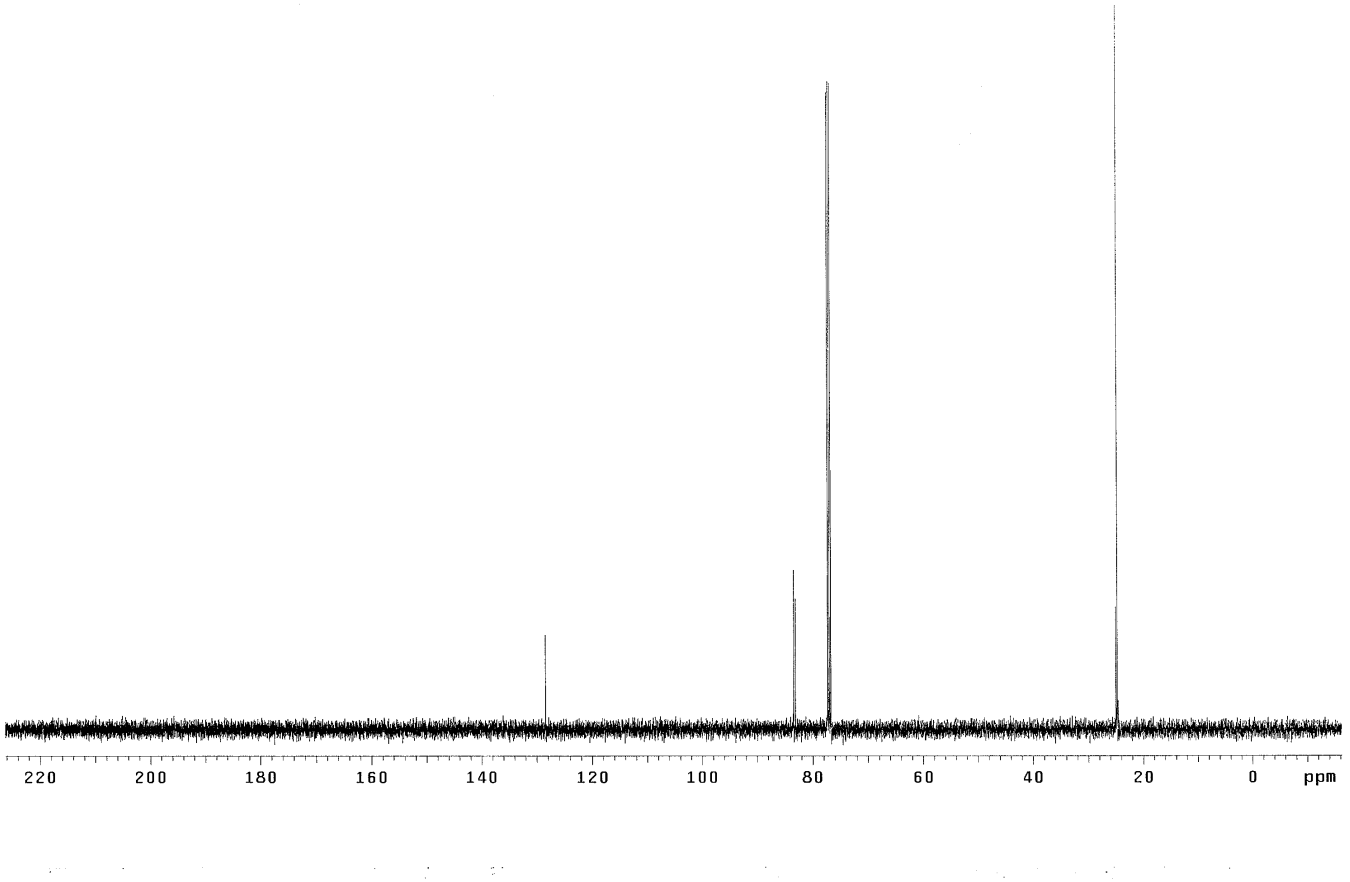
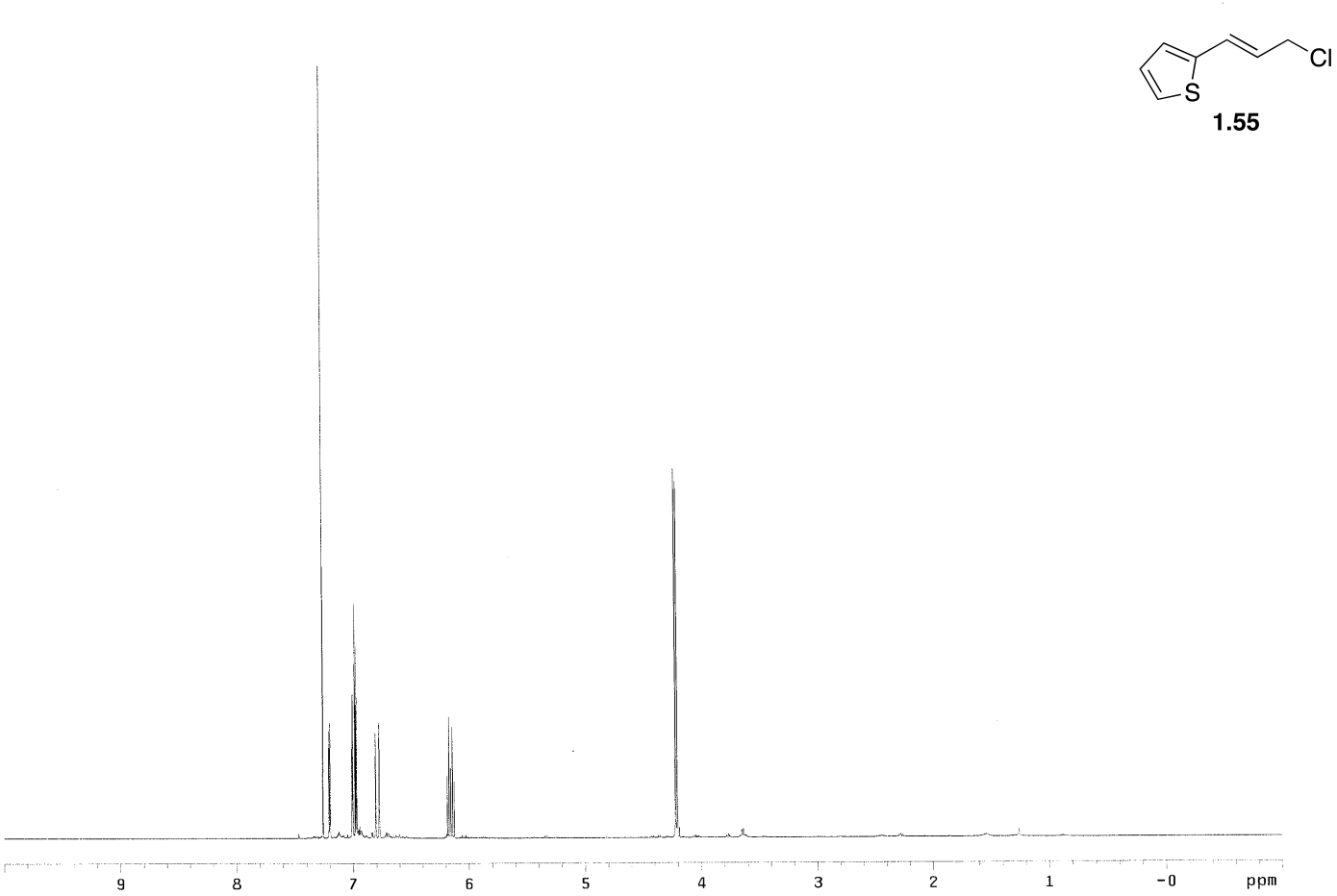
8
7
6
5
4
3
2
1
-0
ppm



1.43




Cl
S
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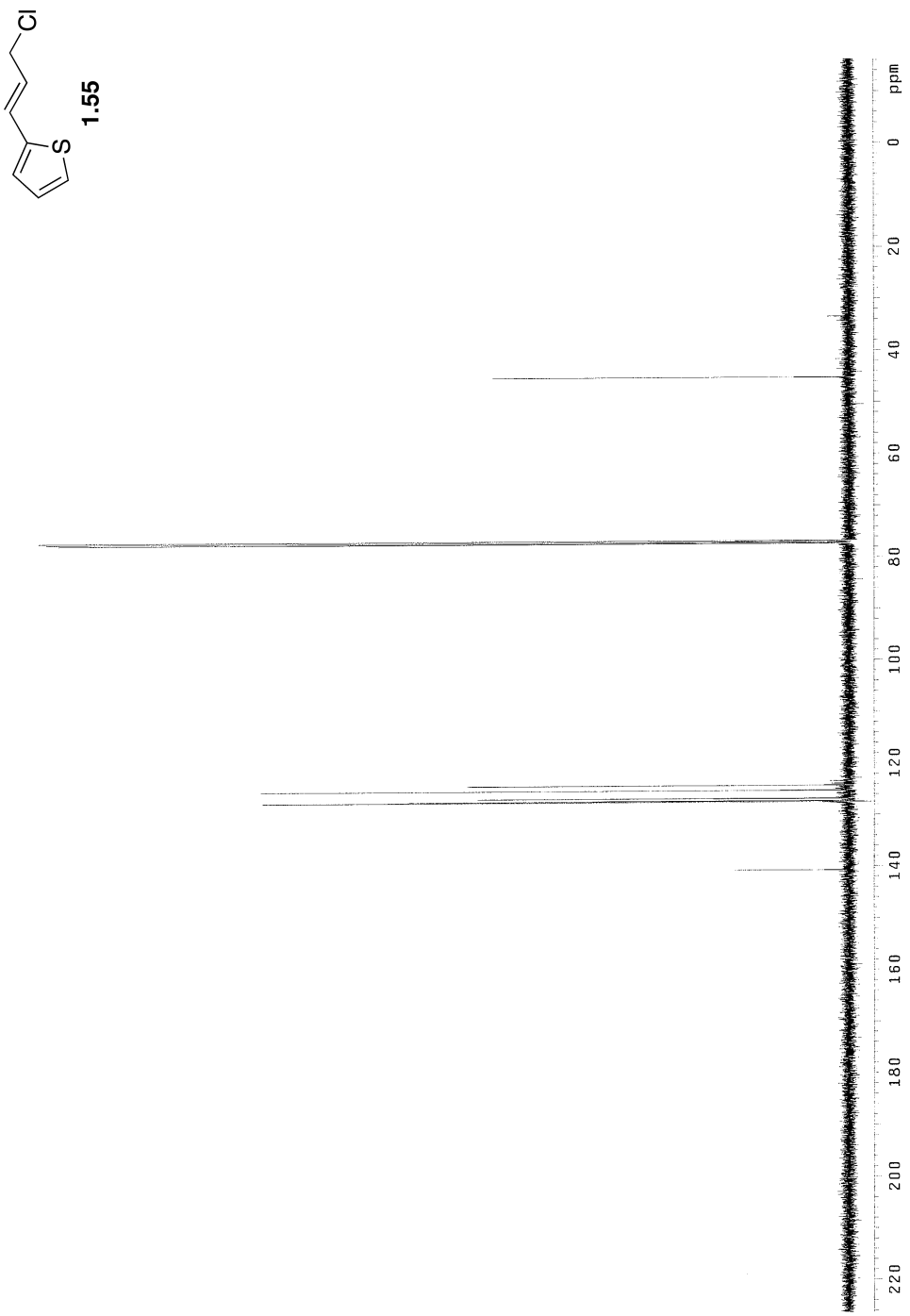
1
-0
ppm


Cl
S
1.55
ppm
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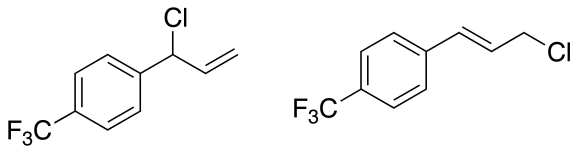
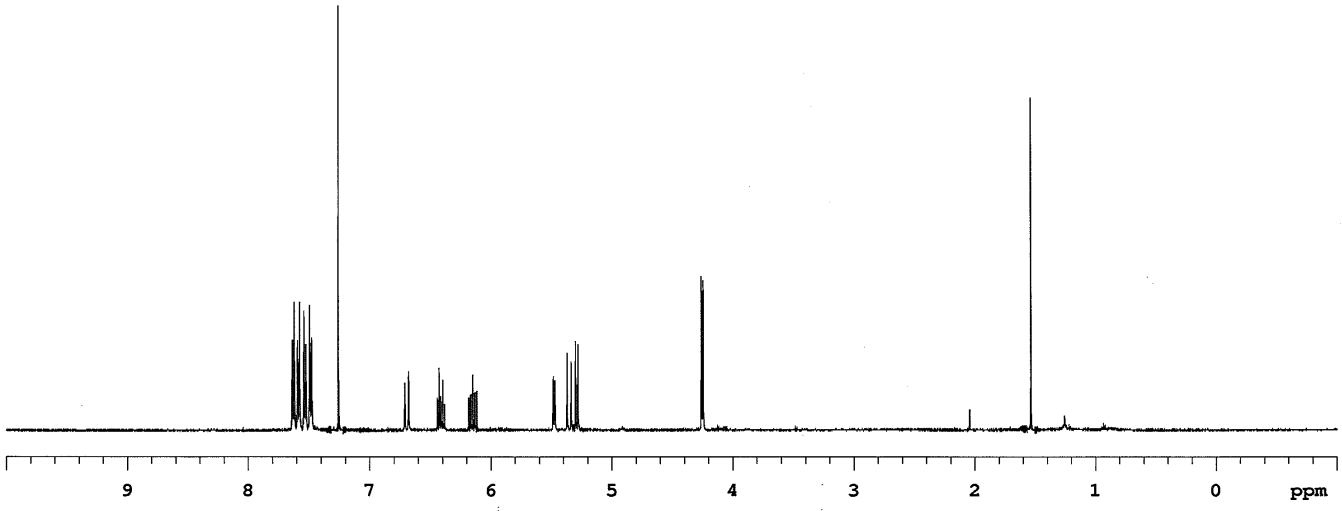
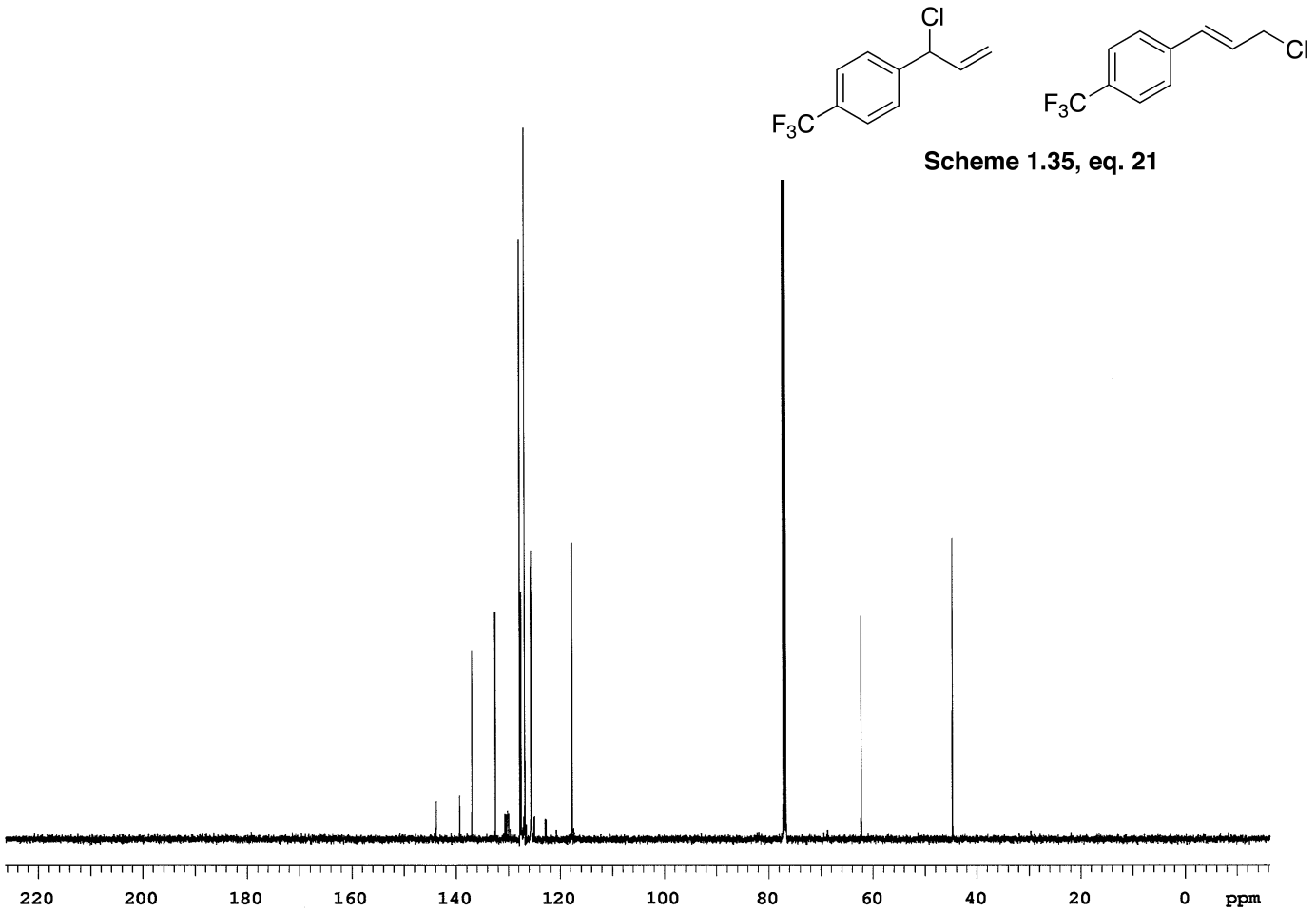
220

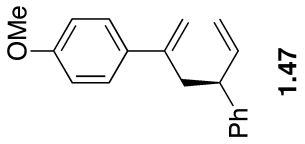


Scheme 1.35, eq. 21

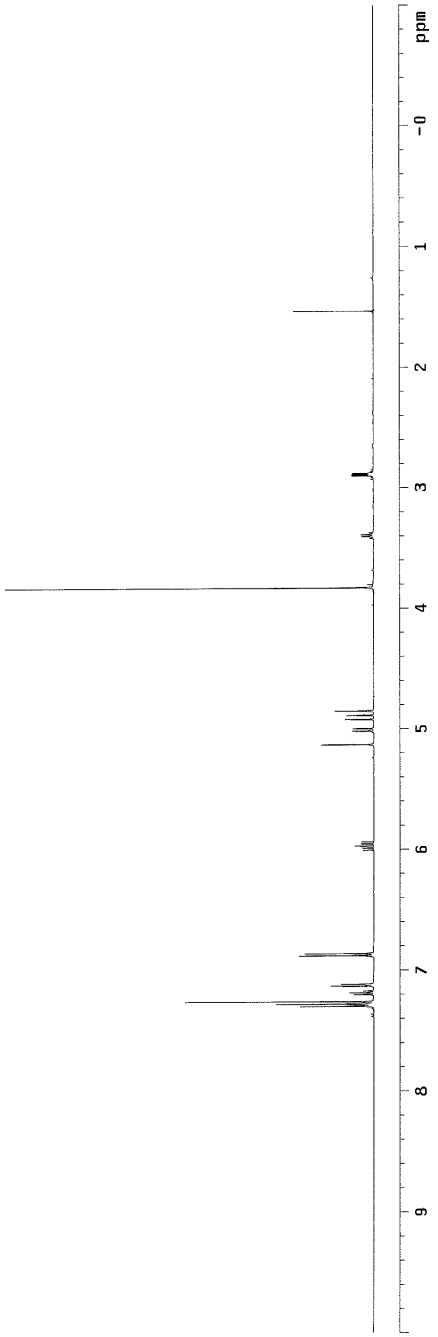


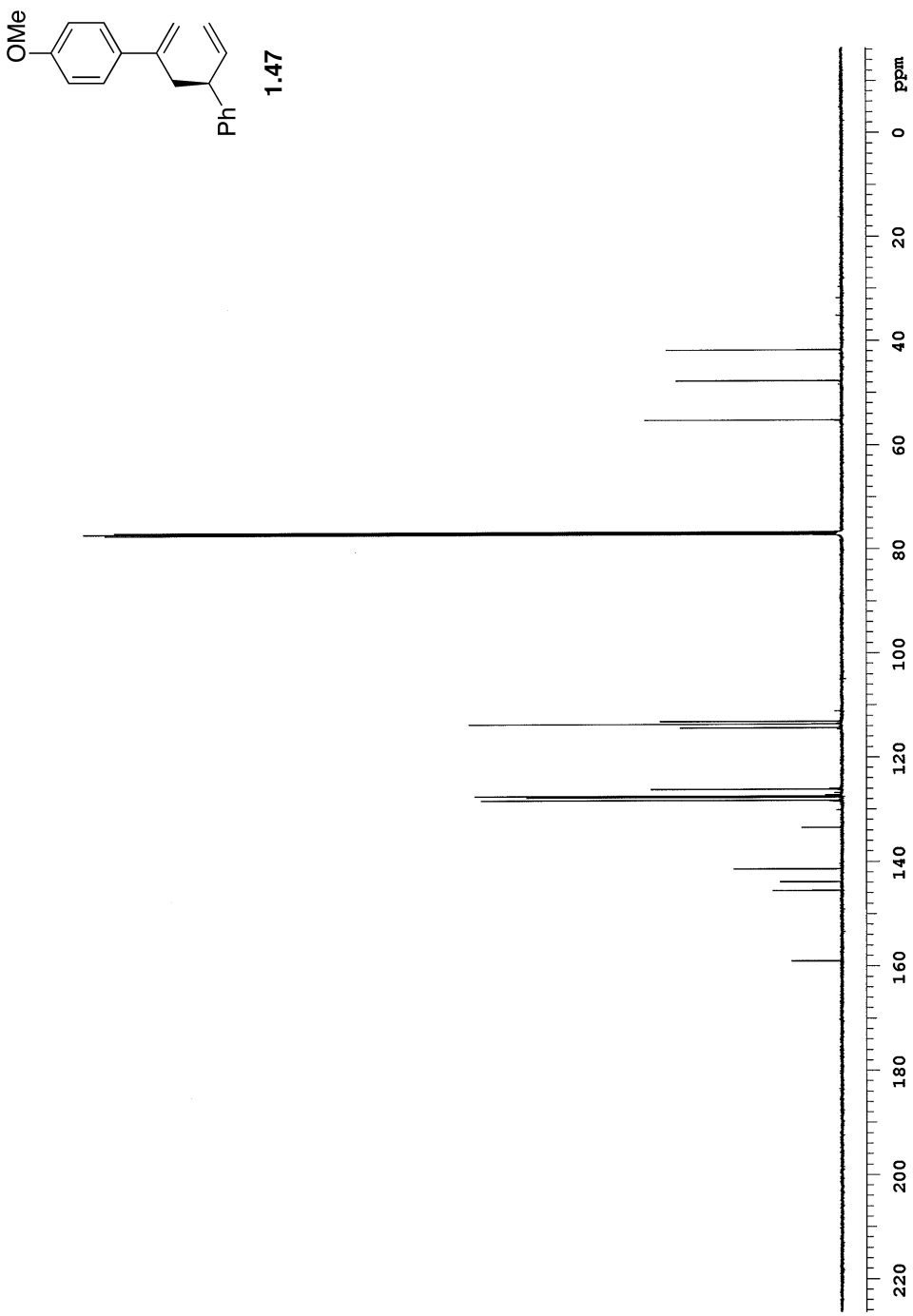


Scheme 1.35, eq. 21



1.47




OMe
Ph
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ppm
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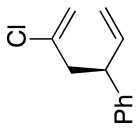
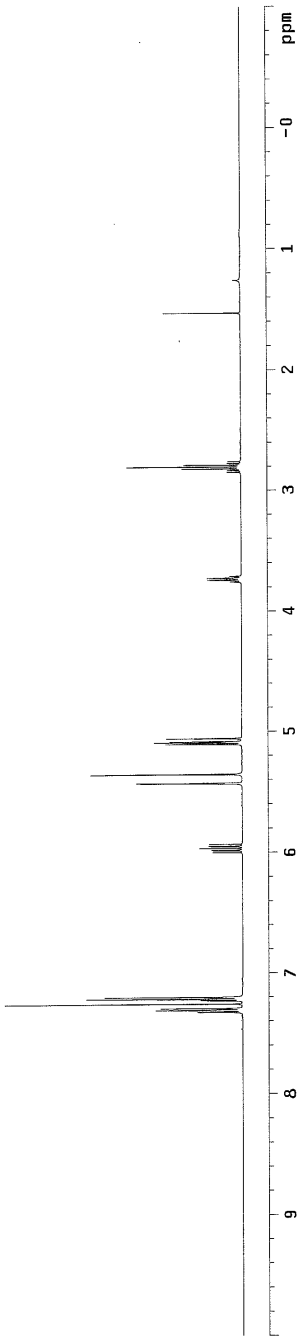
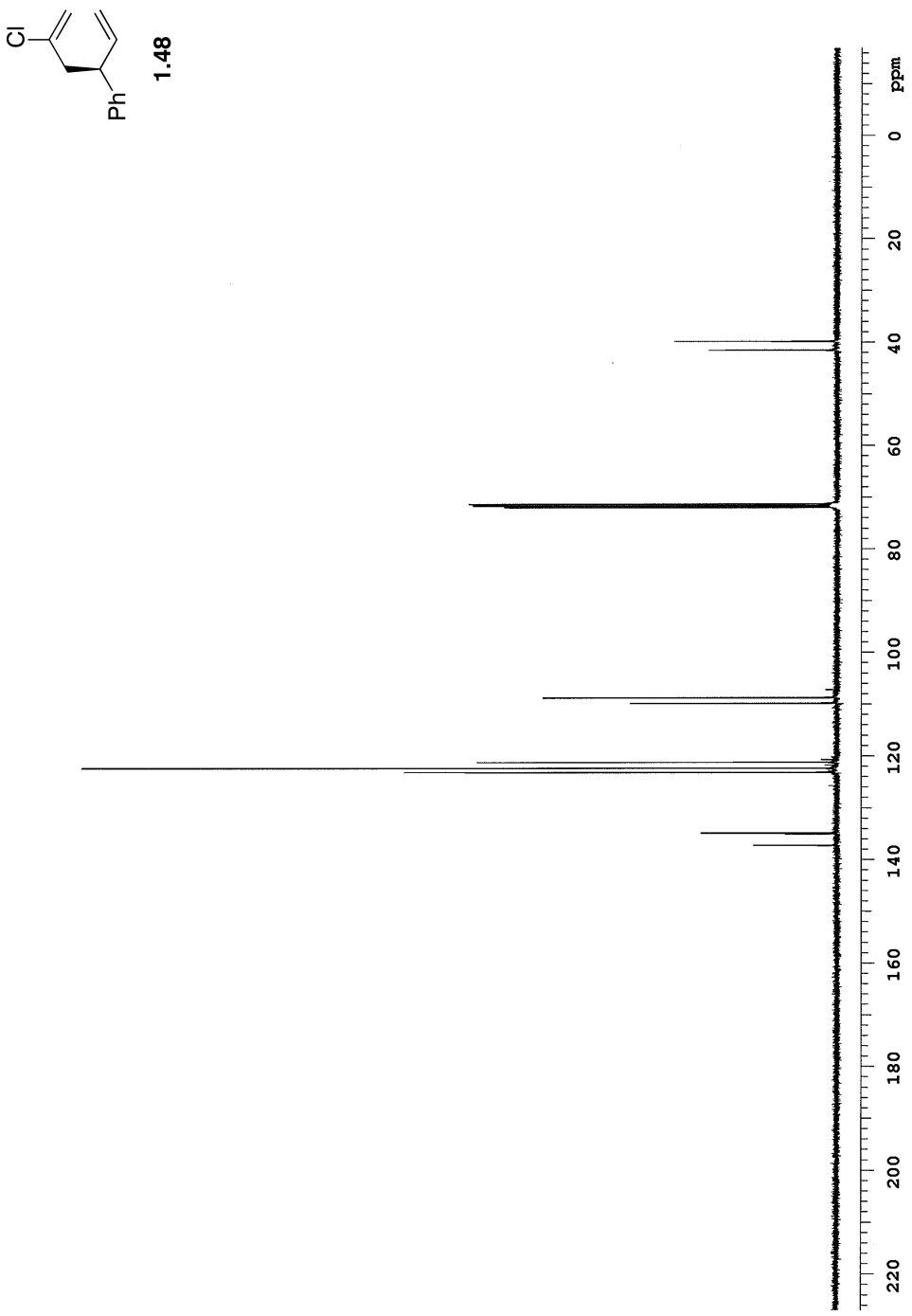
200
220



1.48




Cl
Ph
1.48
220
200
180
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120
100
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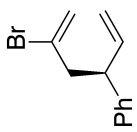
40
20
0
ppm



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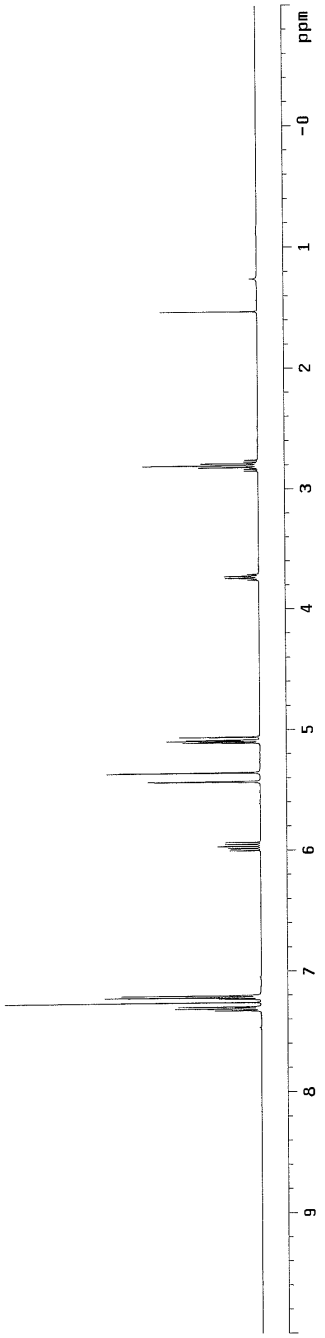

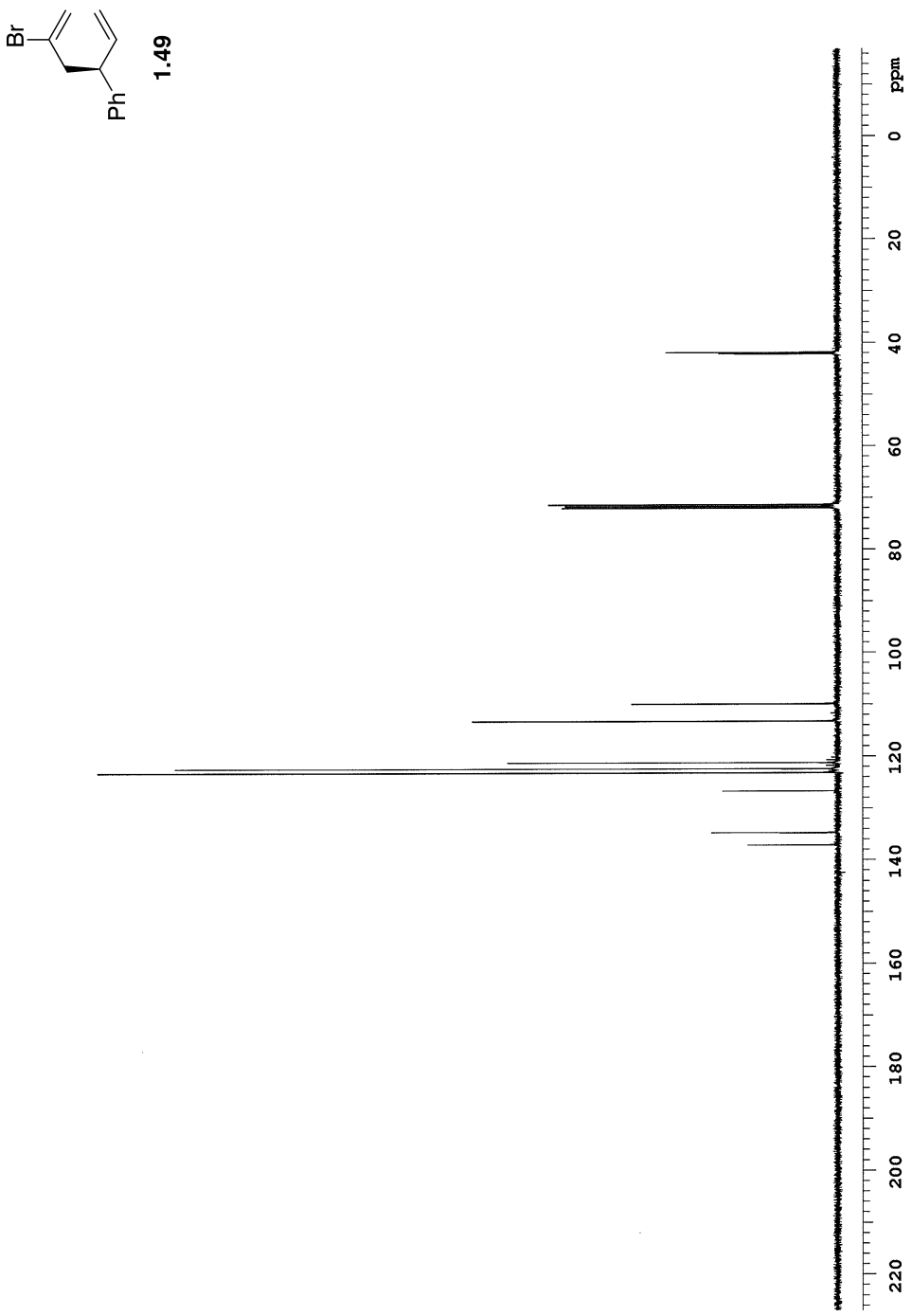
Br
Ph
1.49
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200
180
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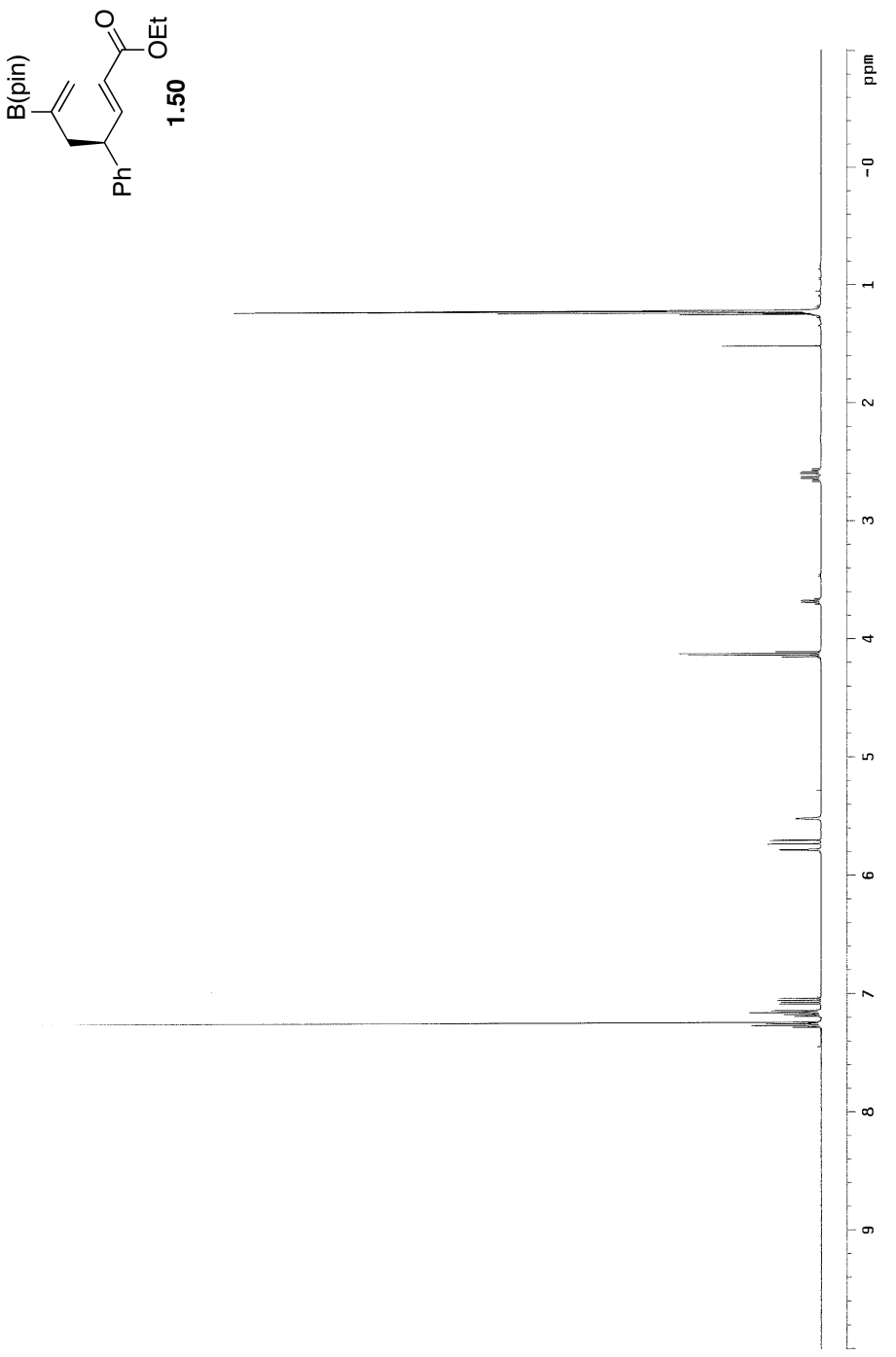
140
120
100
80
60
40
20
0
ppm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Ph
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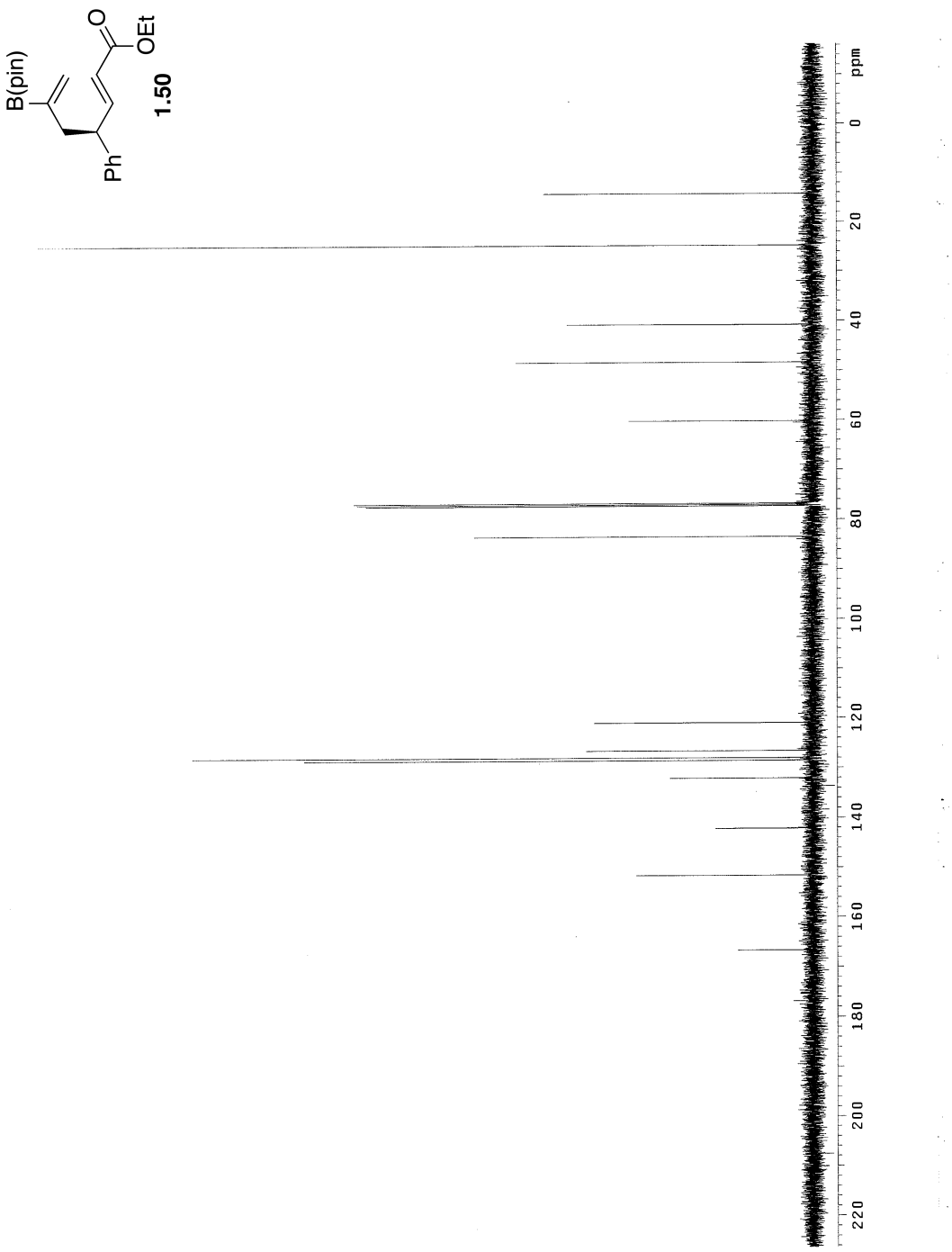
OEt
1.50
ppm
9
8
7
6
5
4
3
2
1
0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OEt
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ppm
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200
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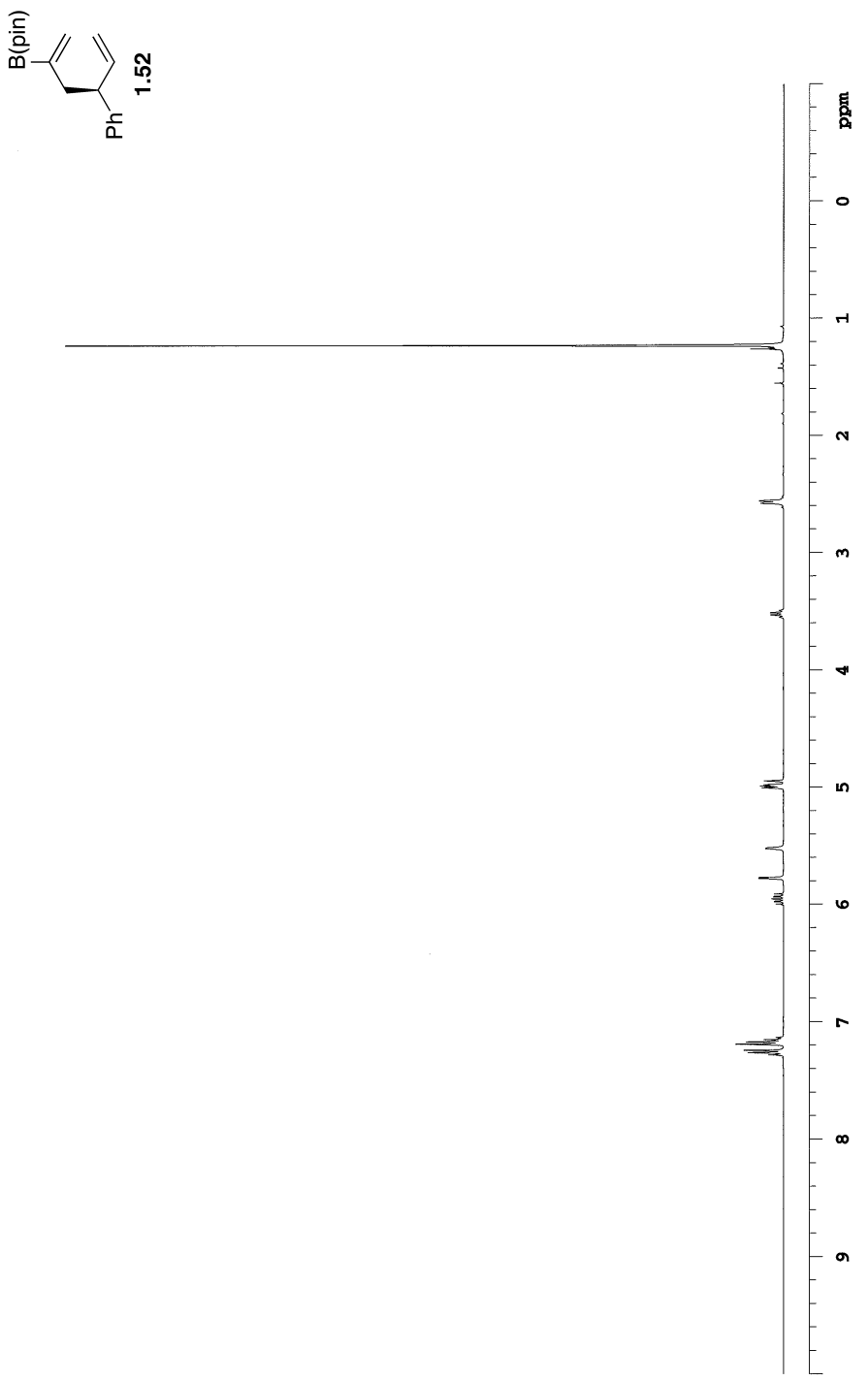
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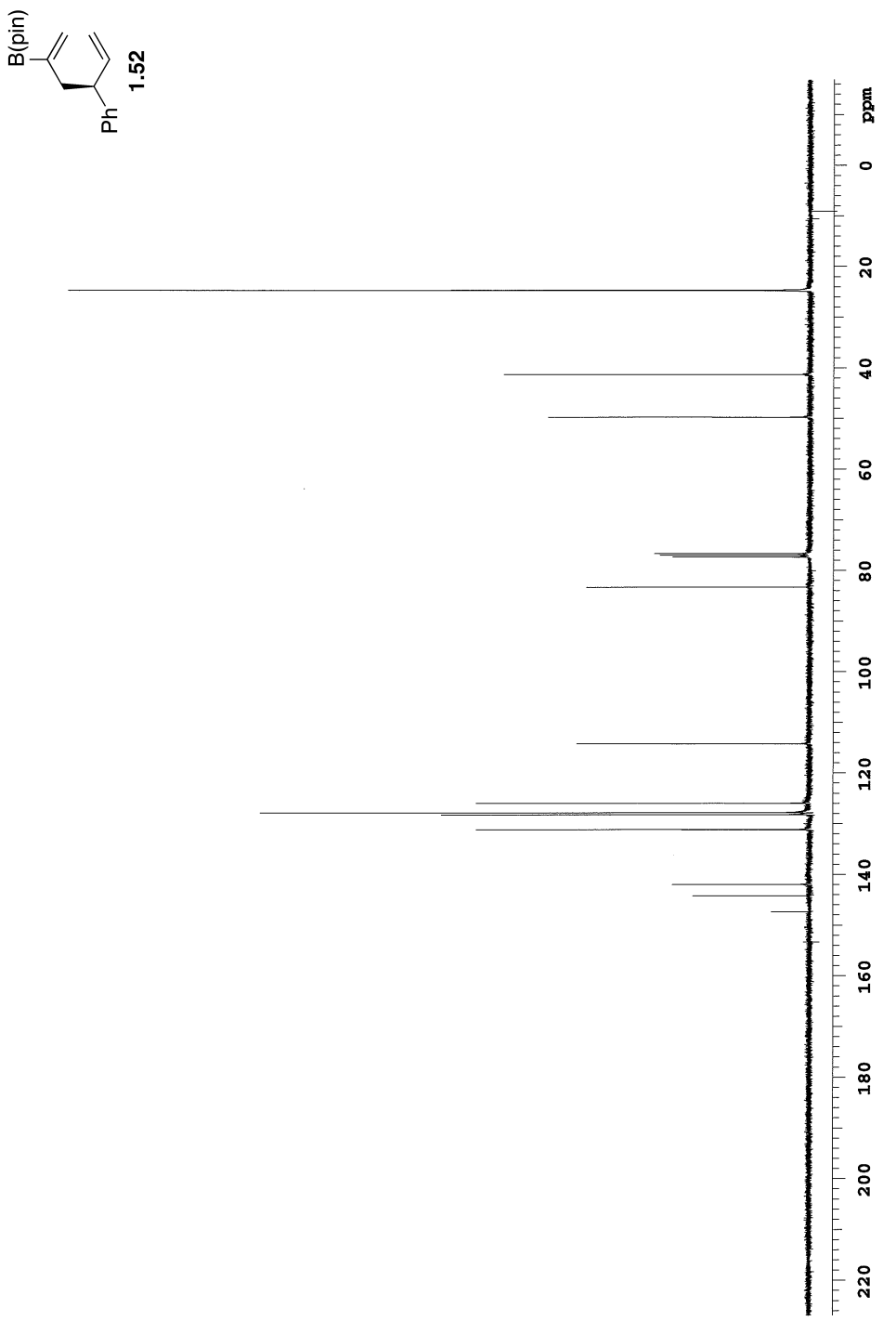
9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200
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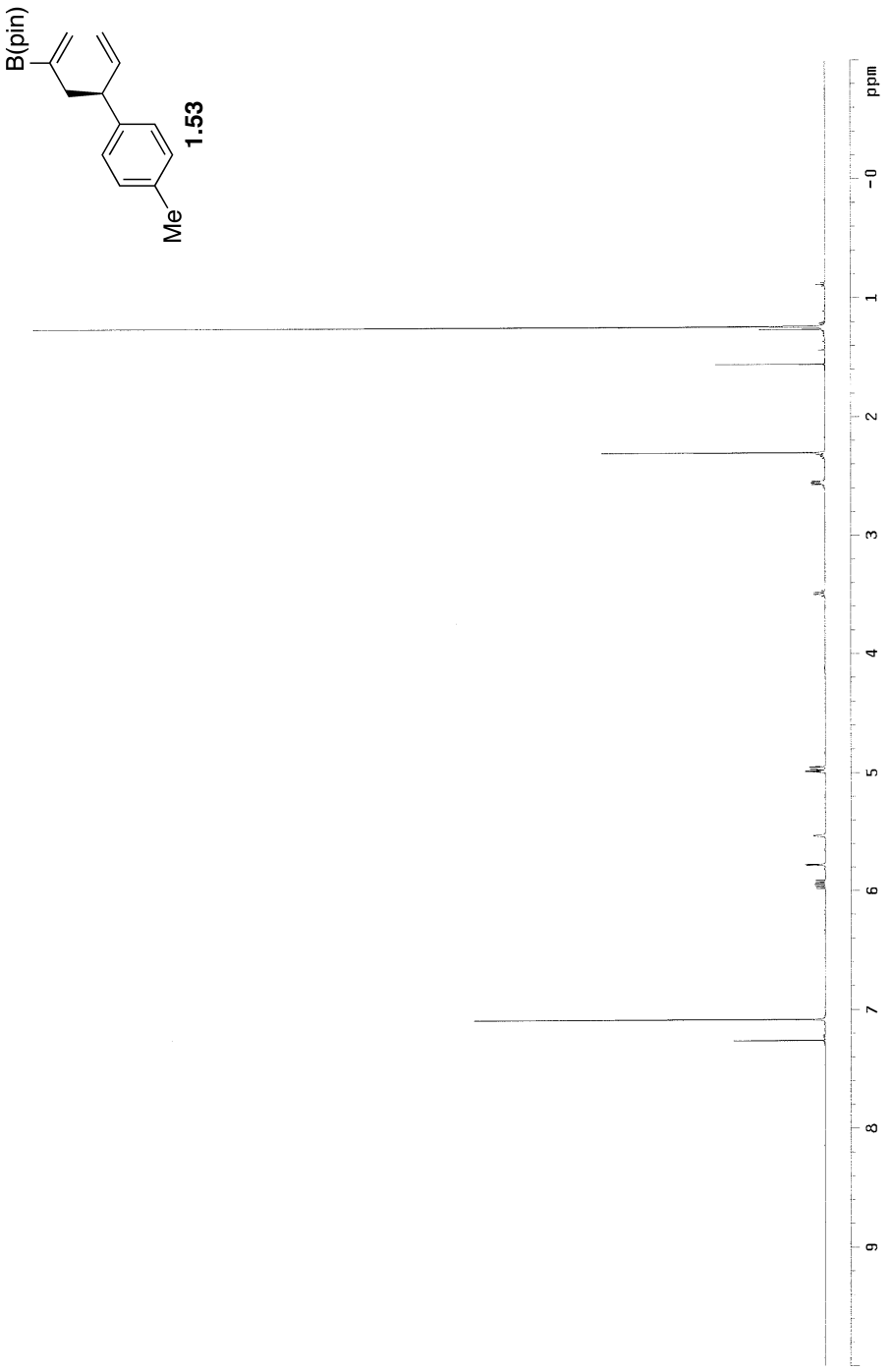
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Me
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ppm
-0
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2
3
4
5
6
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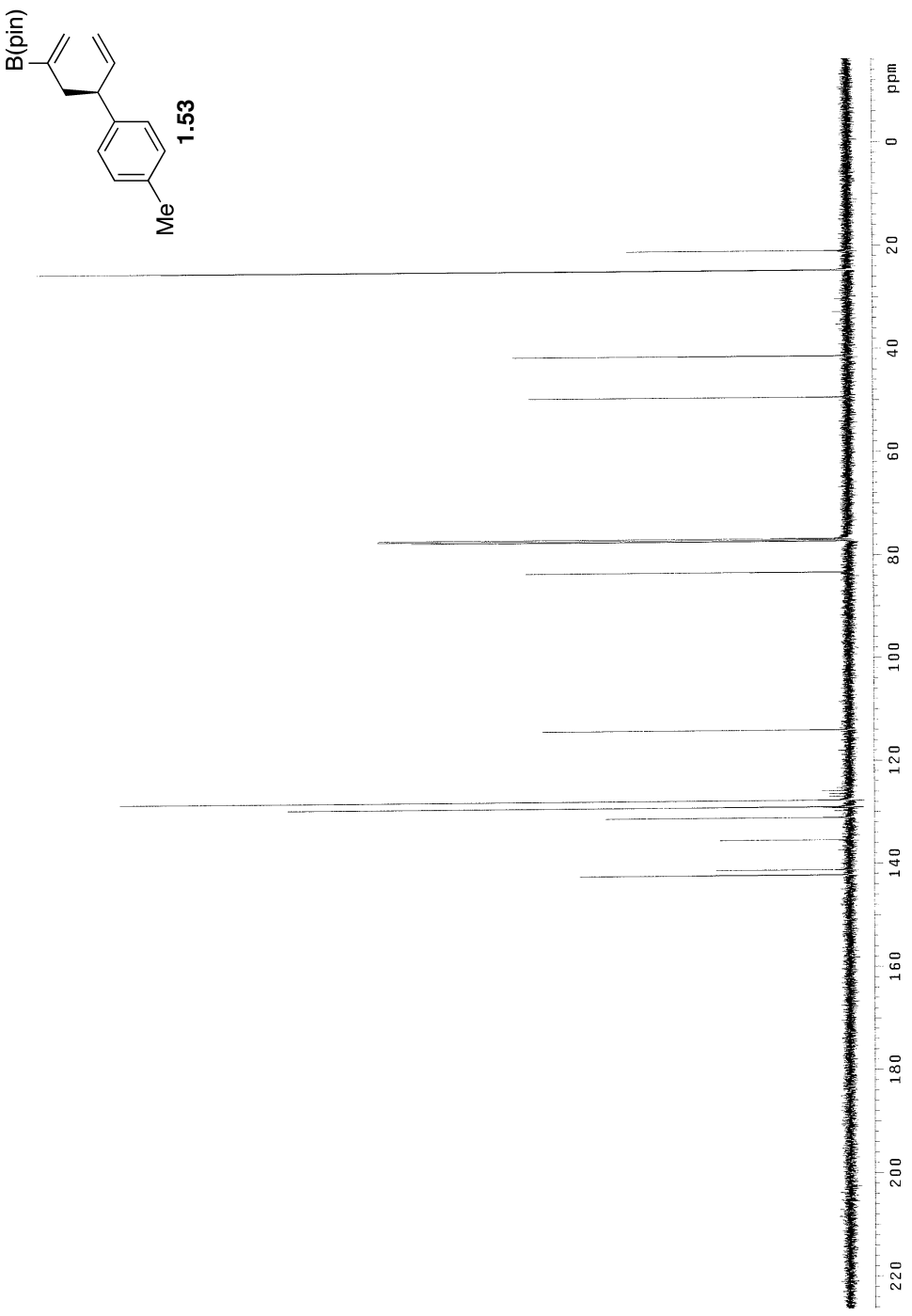
8
9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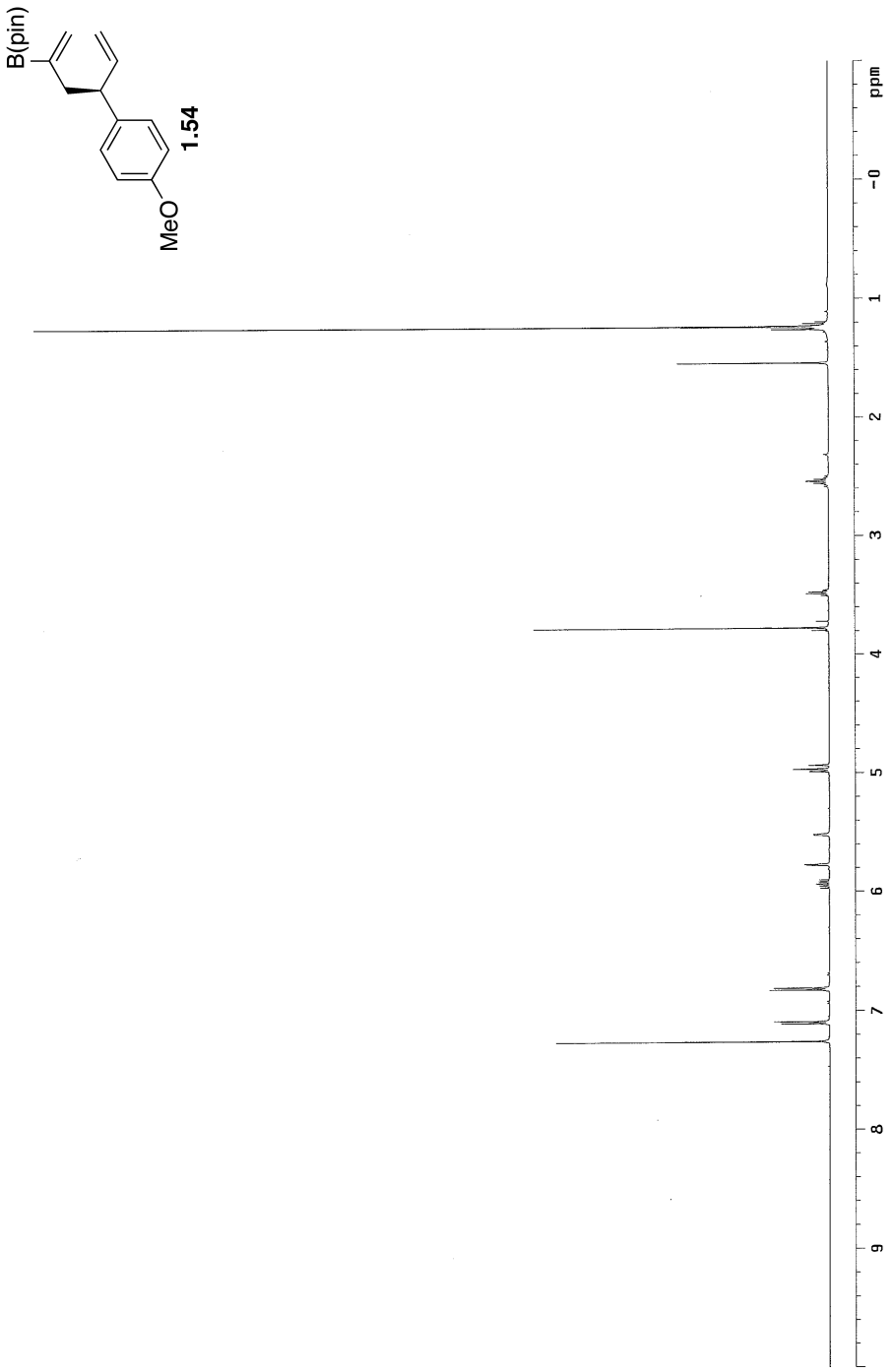
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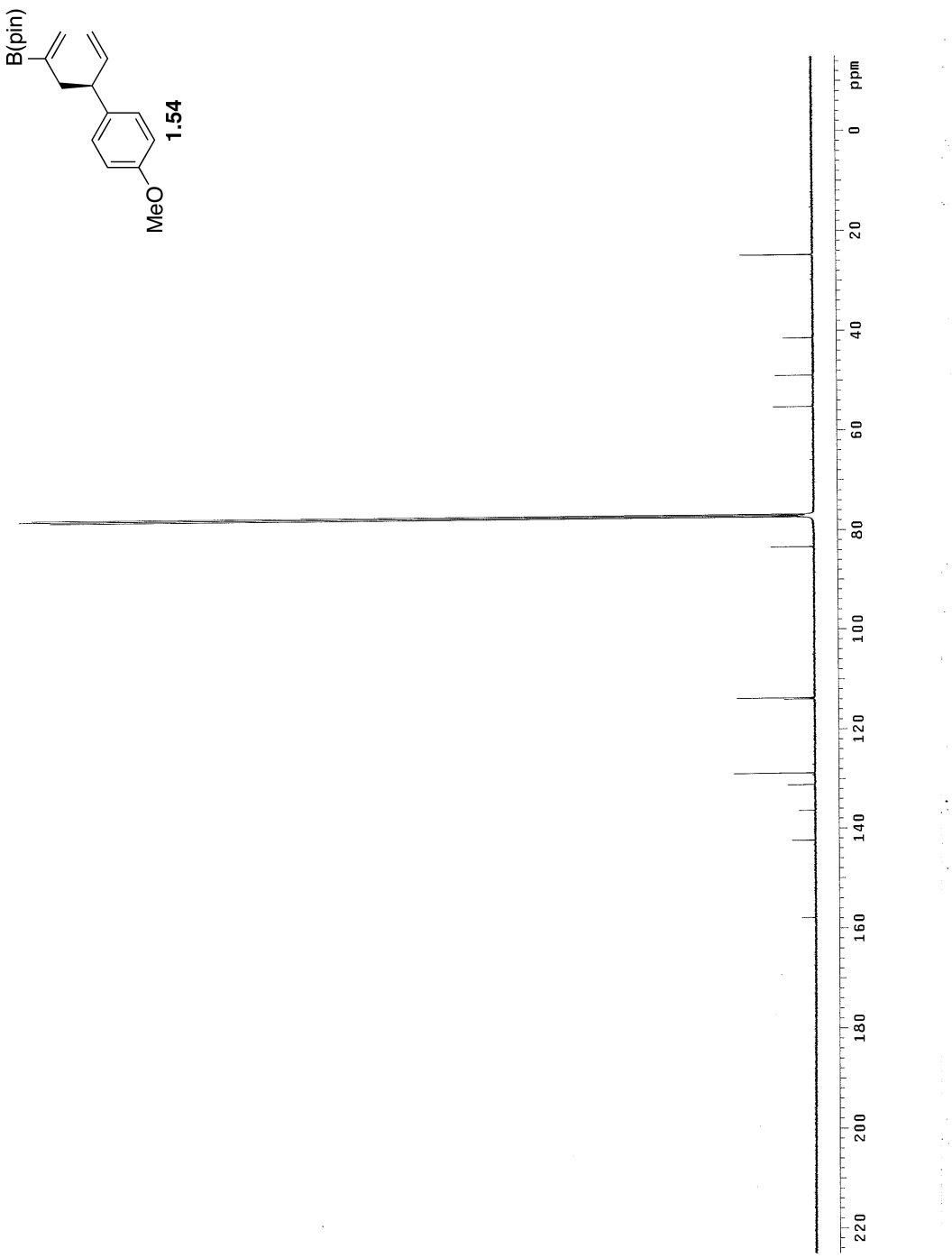
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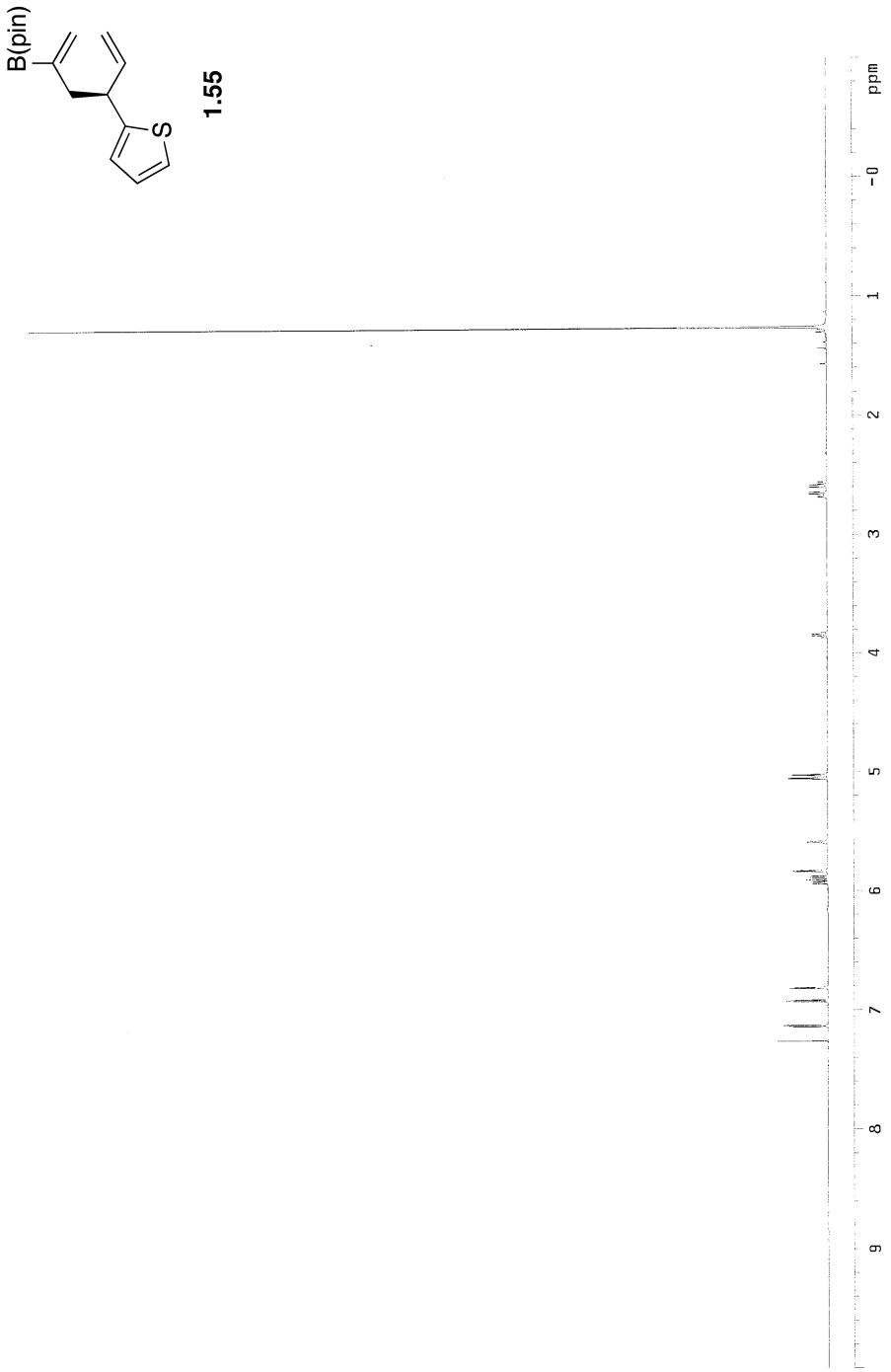
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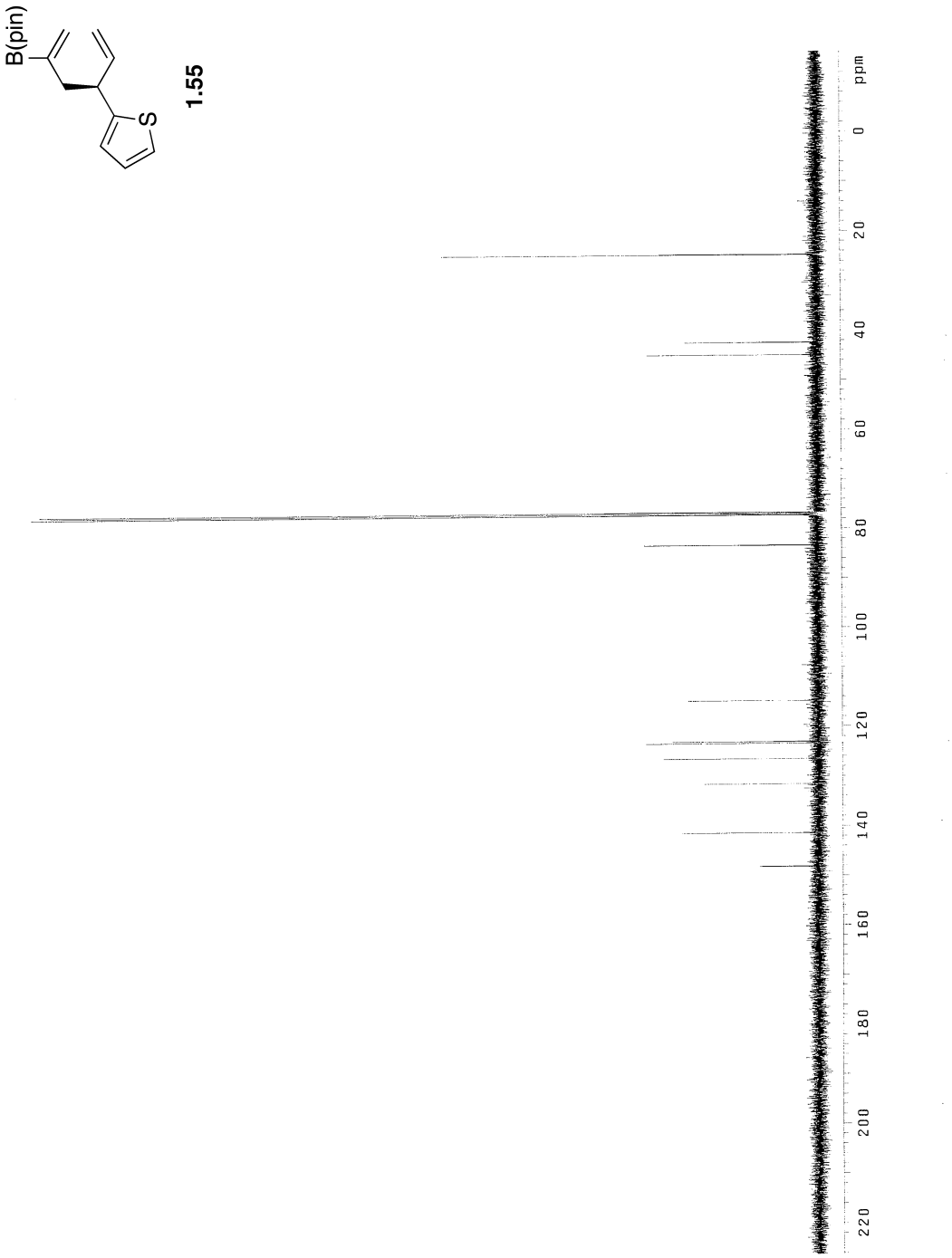
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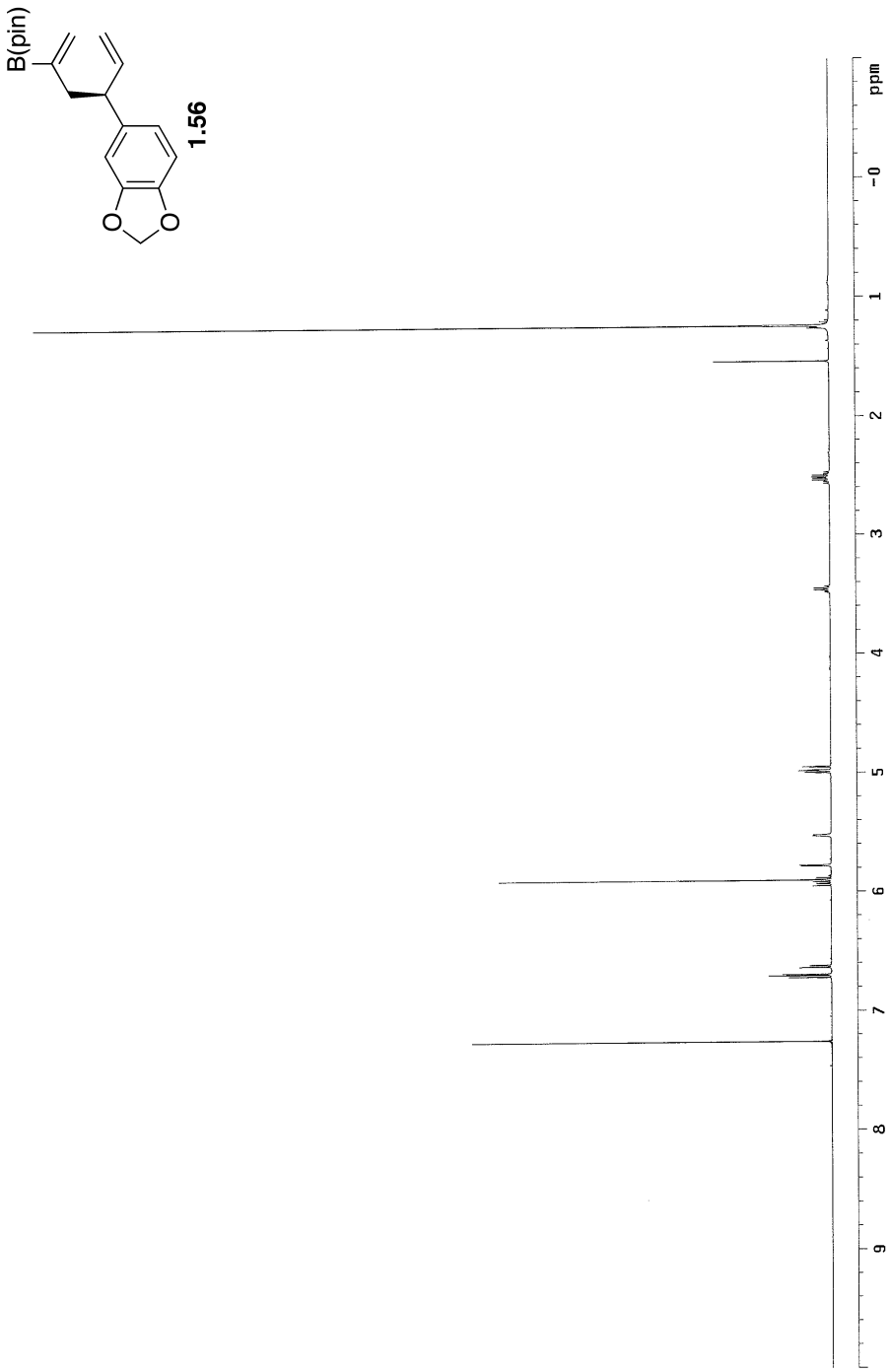
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O
ppm
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8
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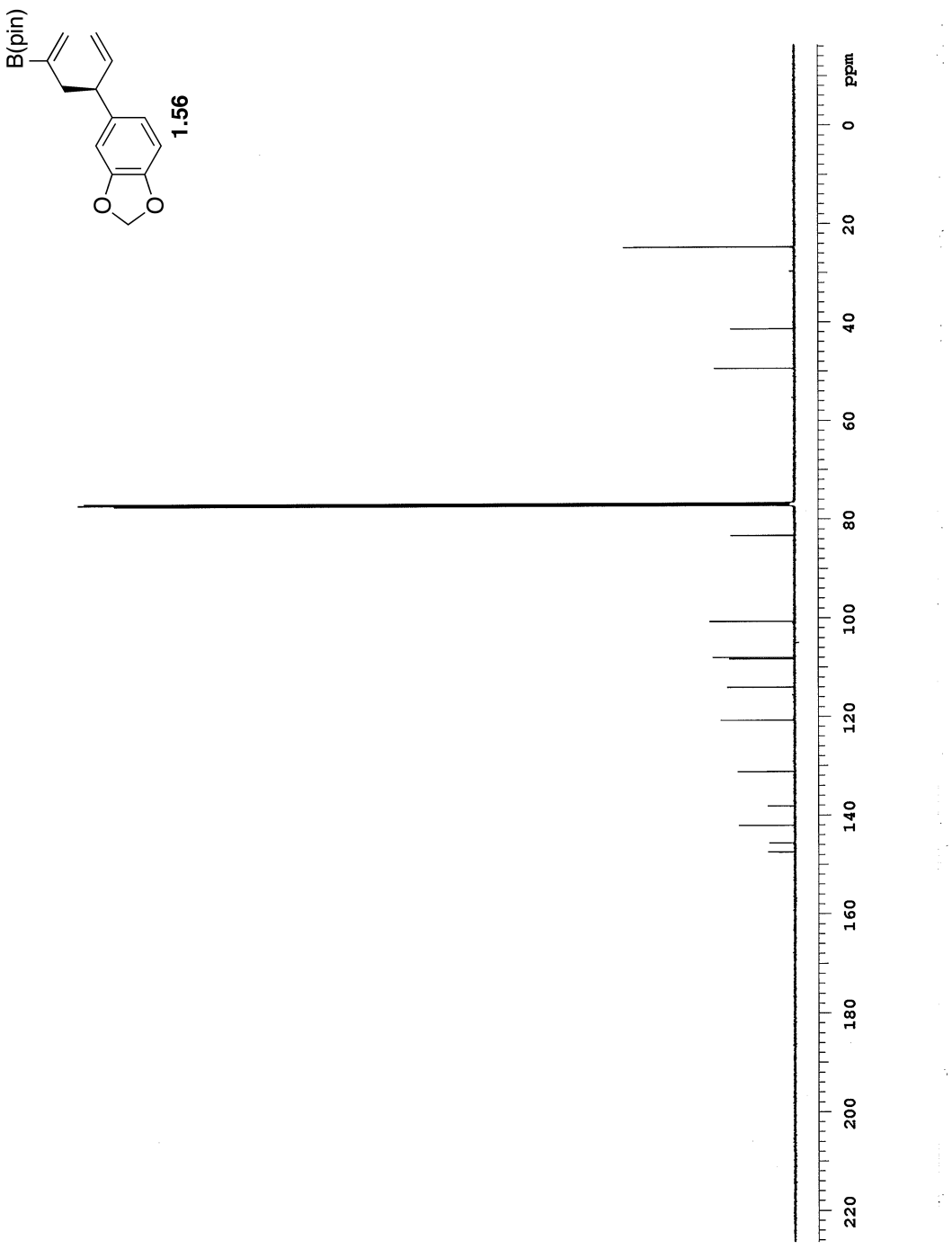
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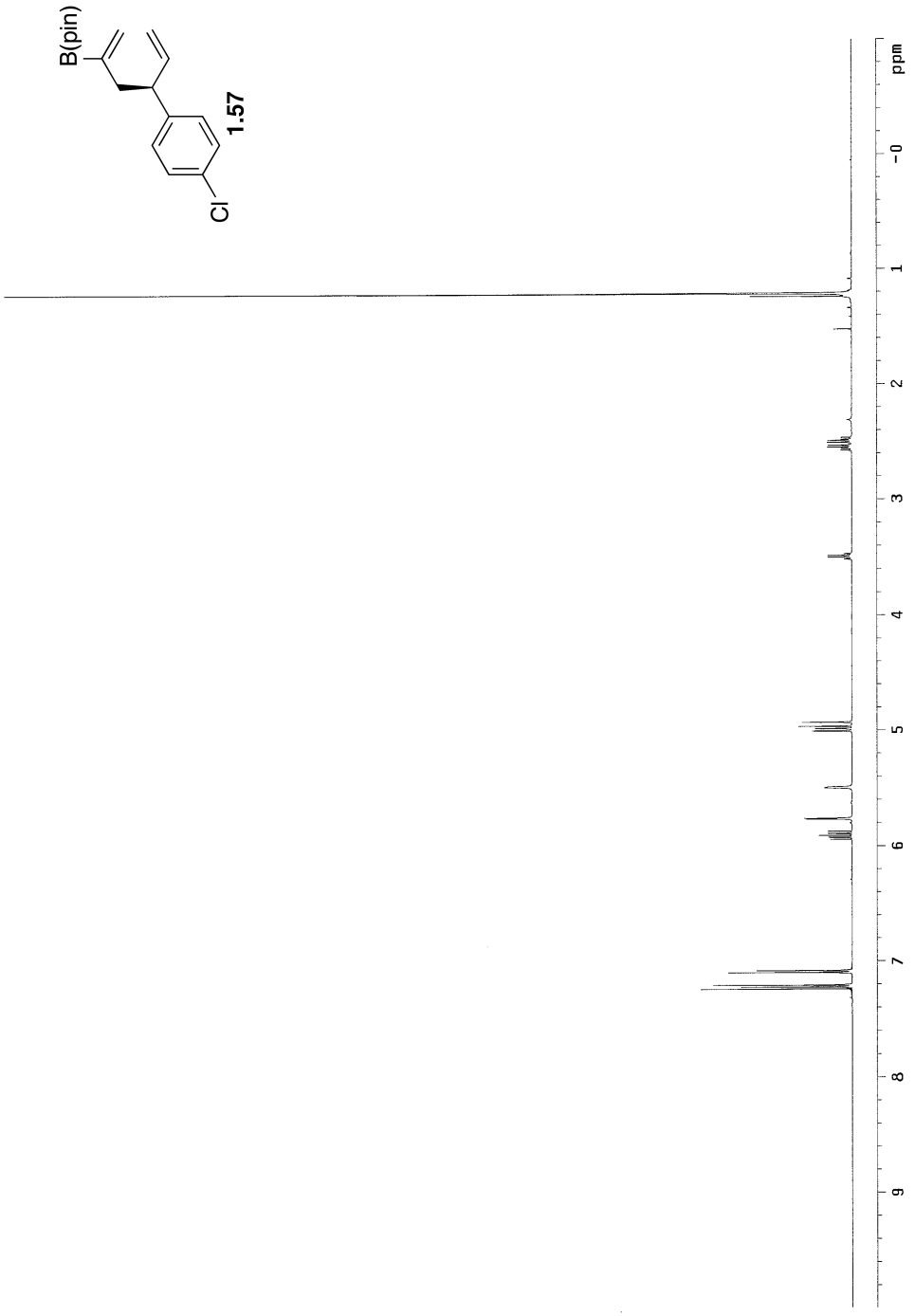
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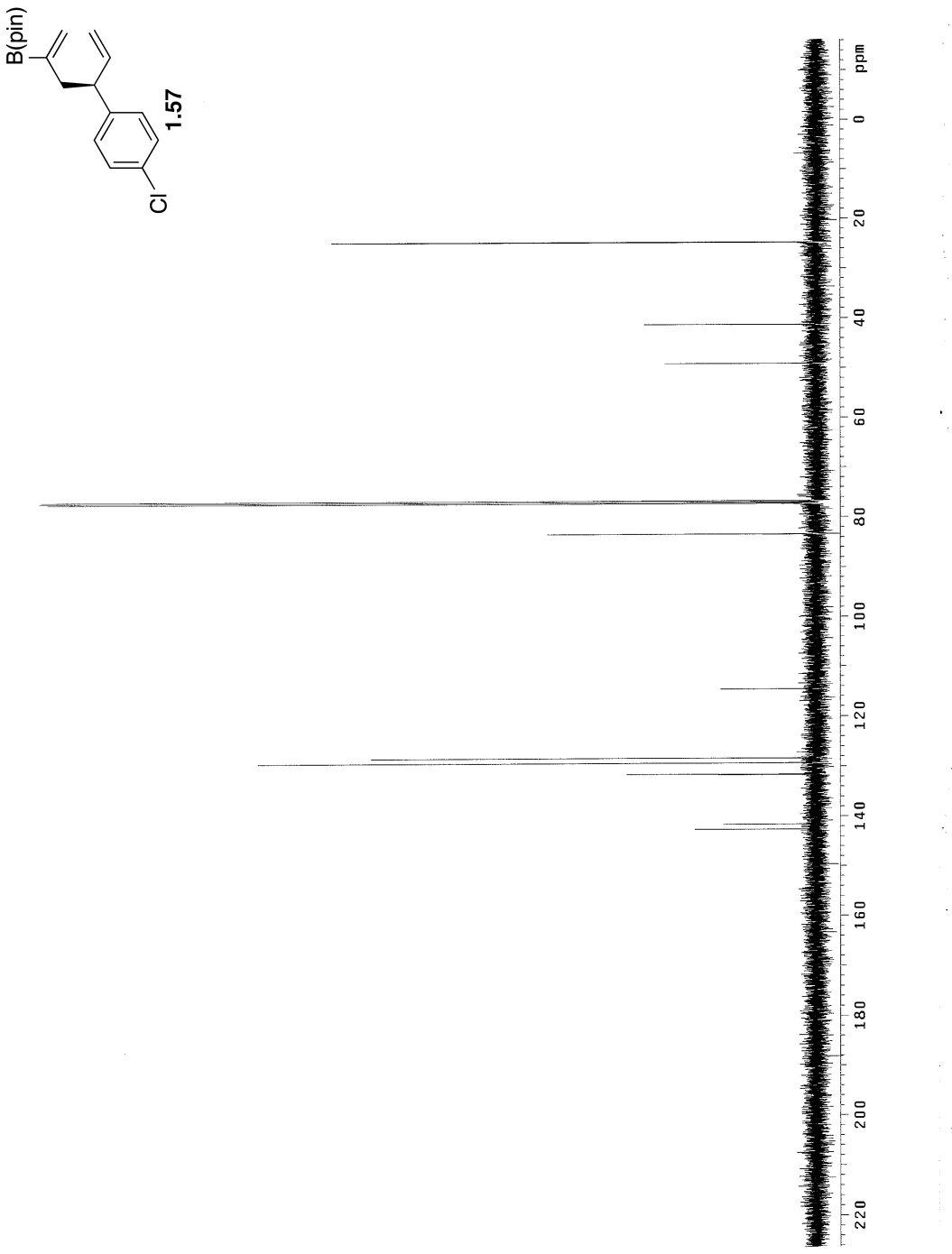
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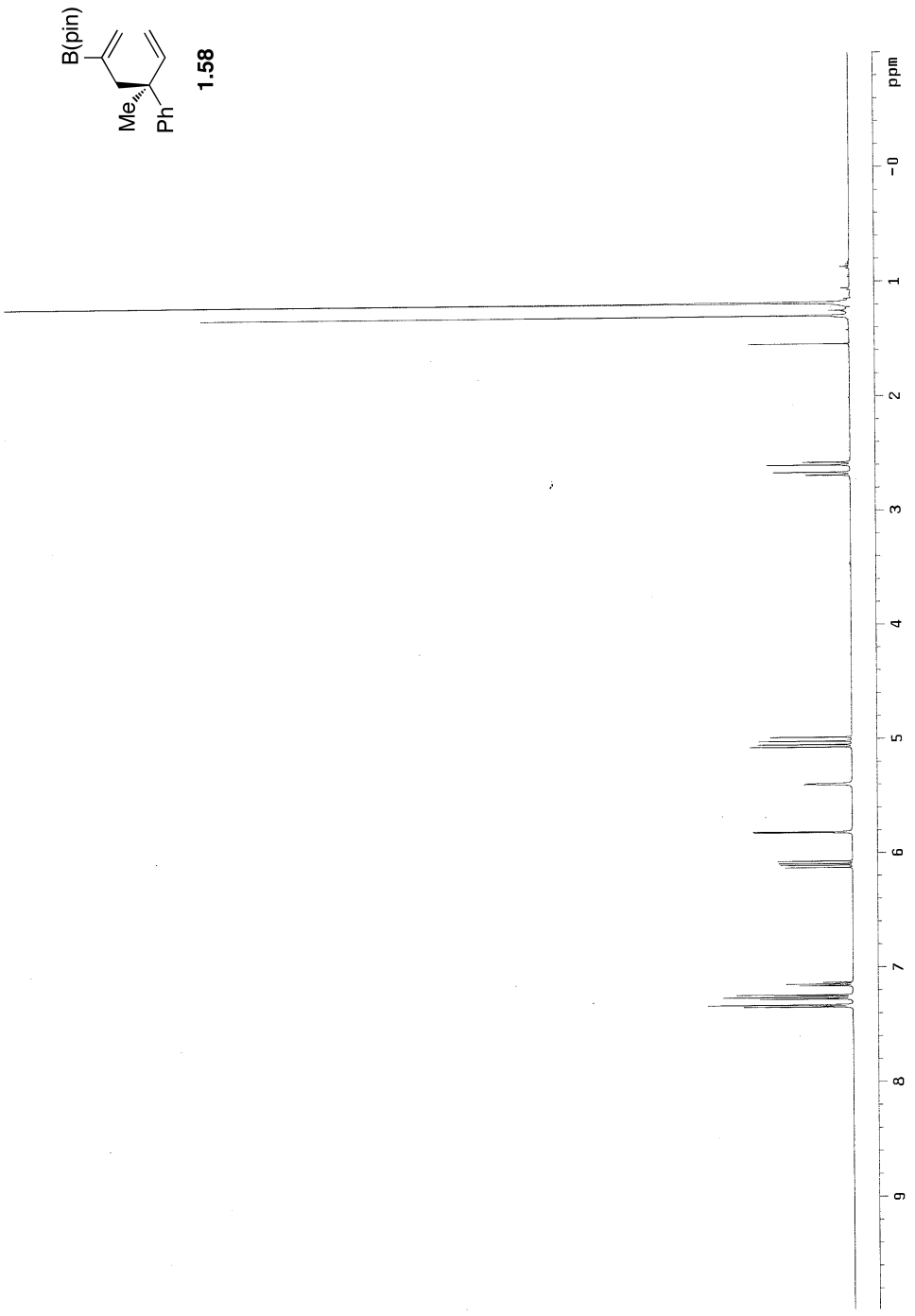
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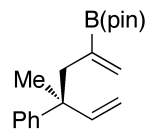

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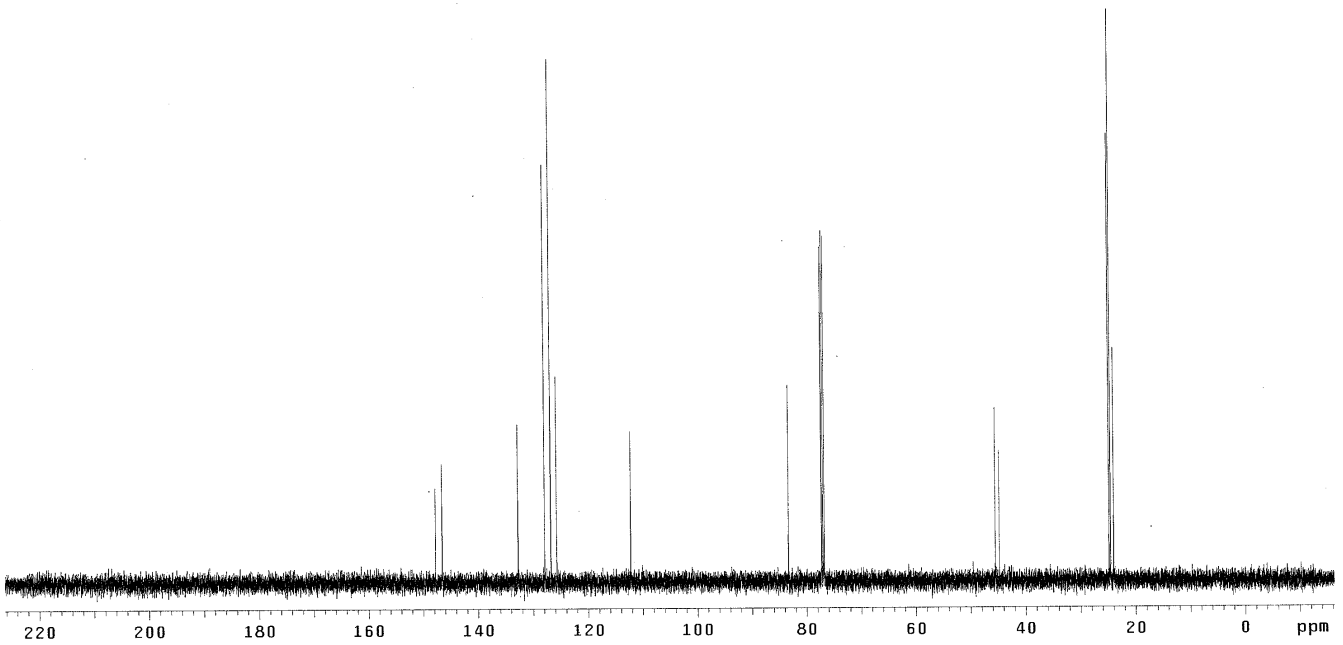

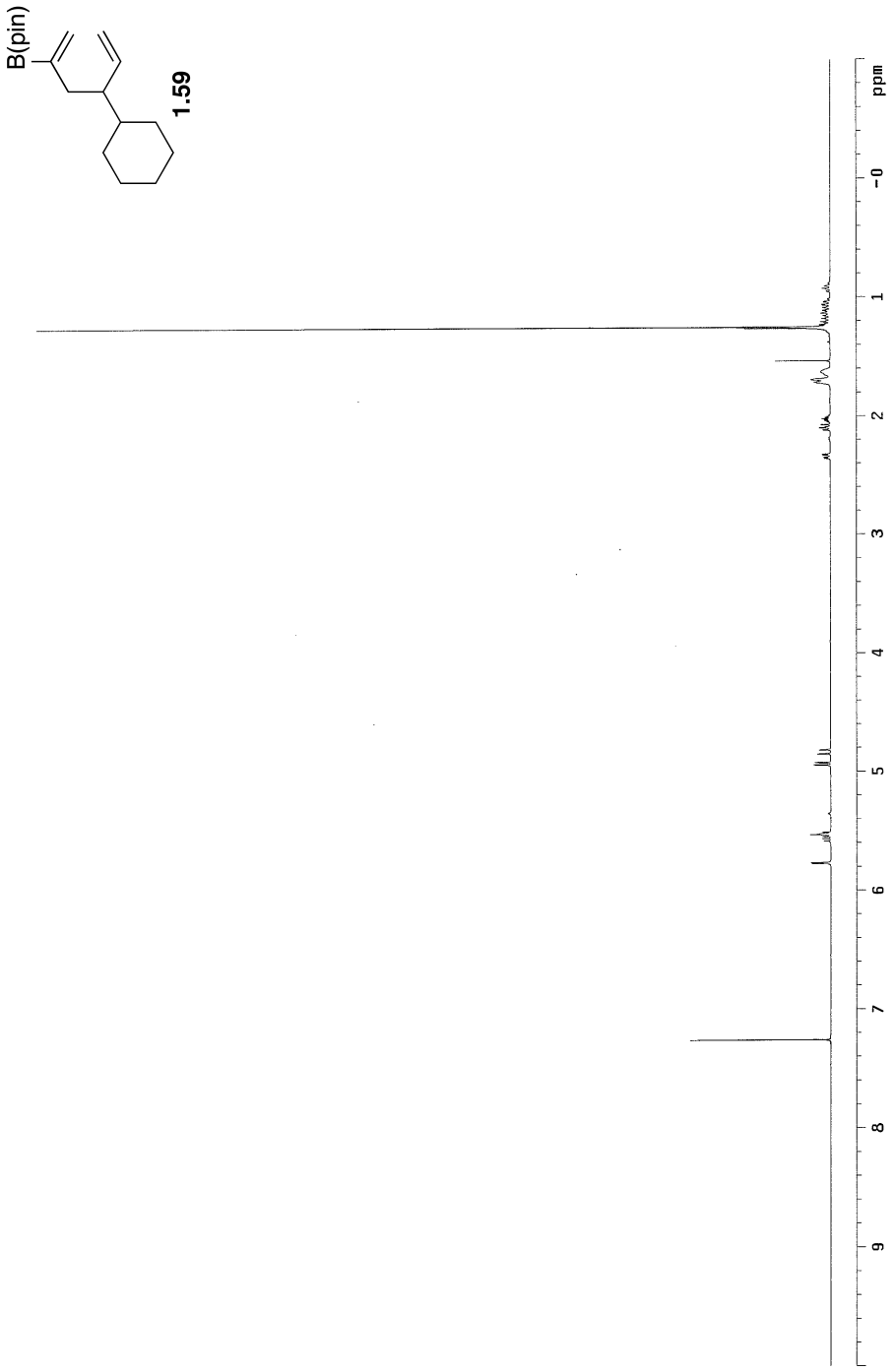
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6
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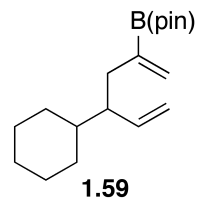
9



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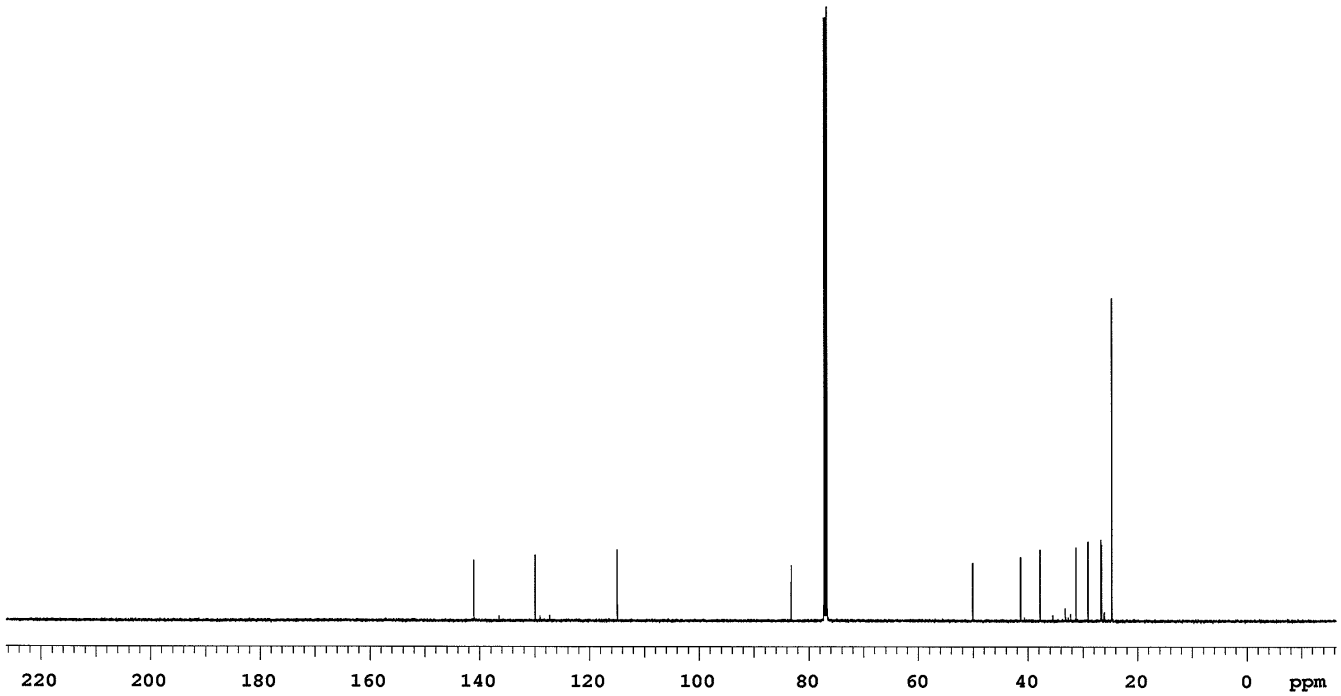

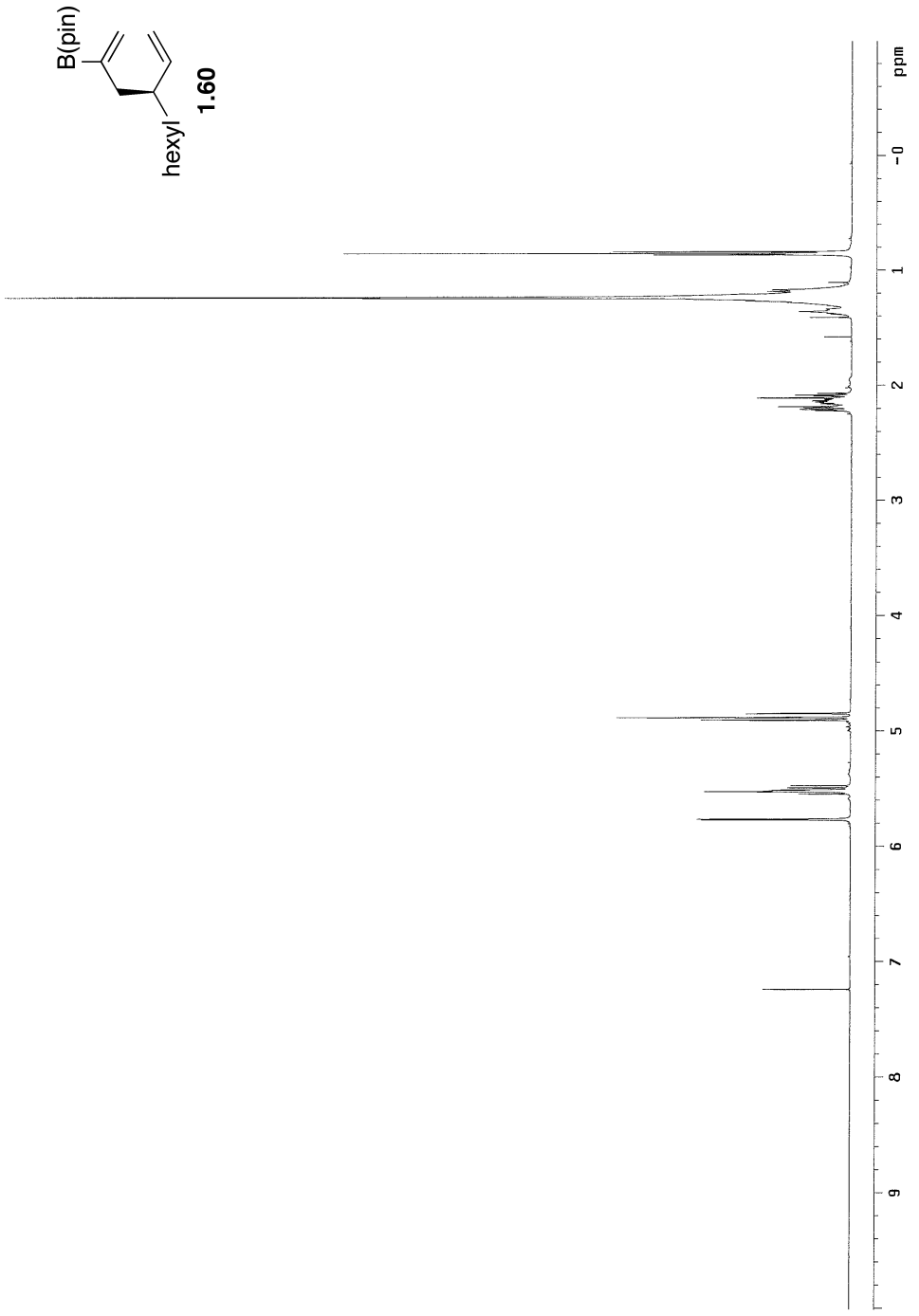
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ppm
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6
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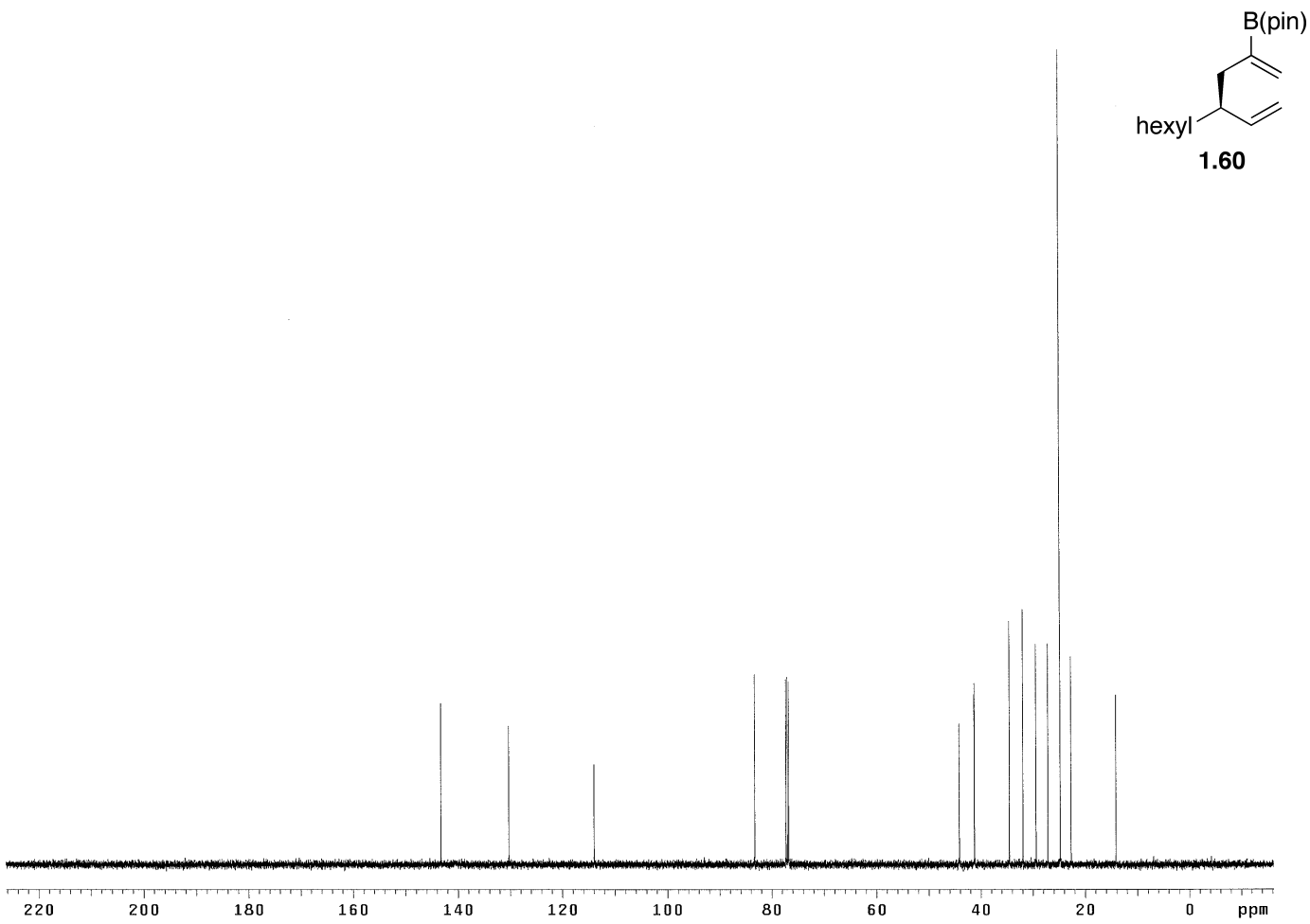
9



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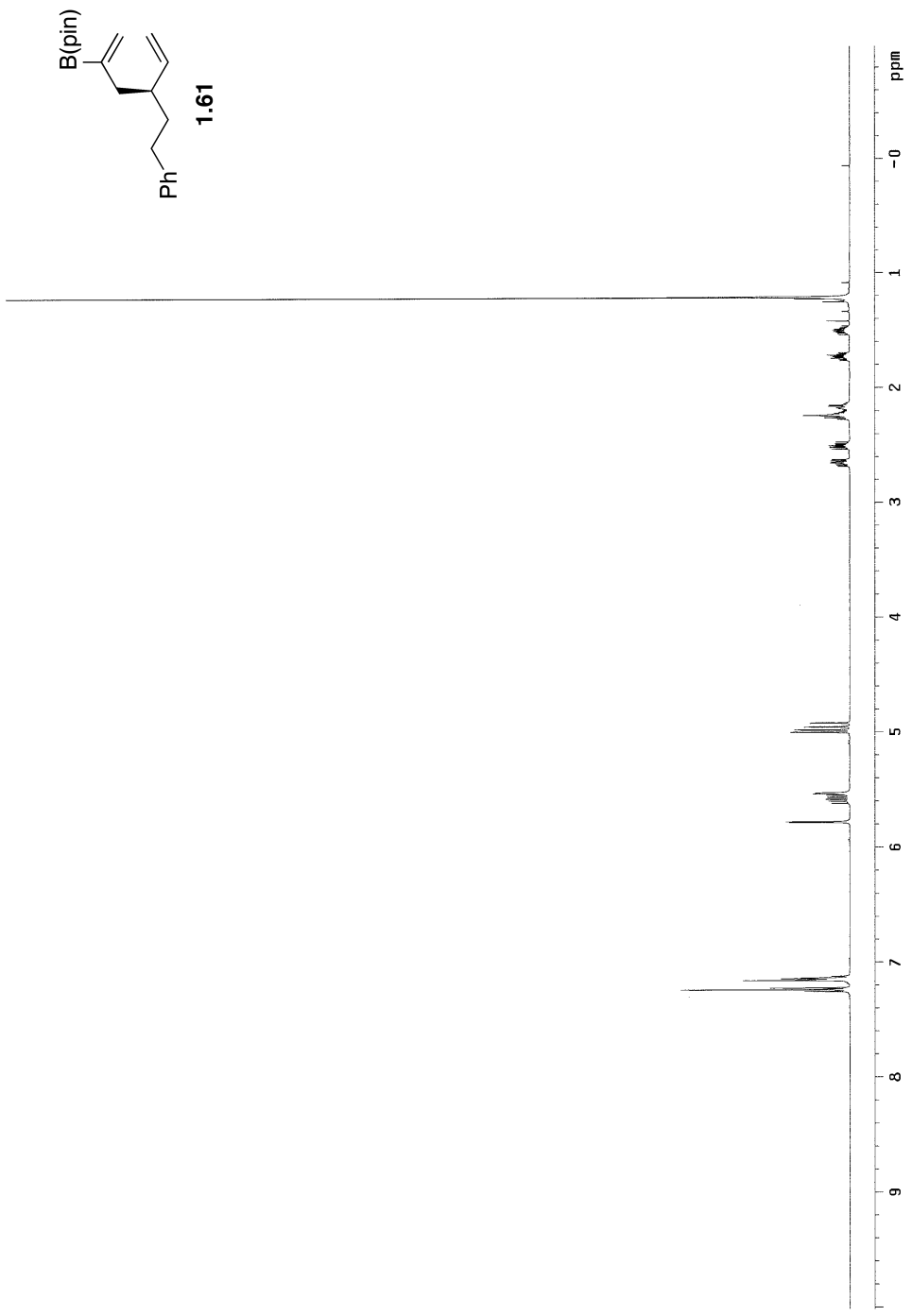
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Ph
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ppm
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2
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4
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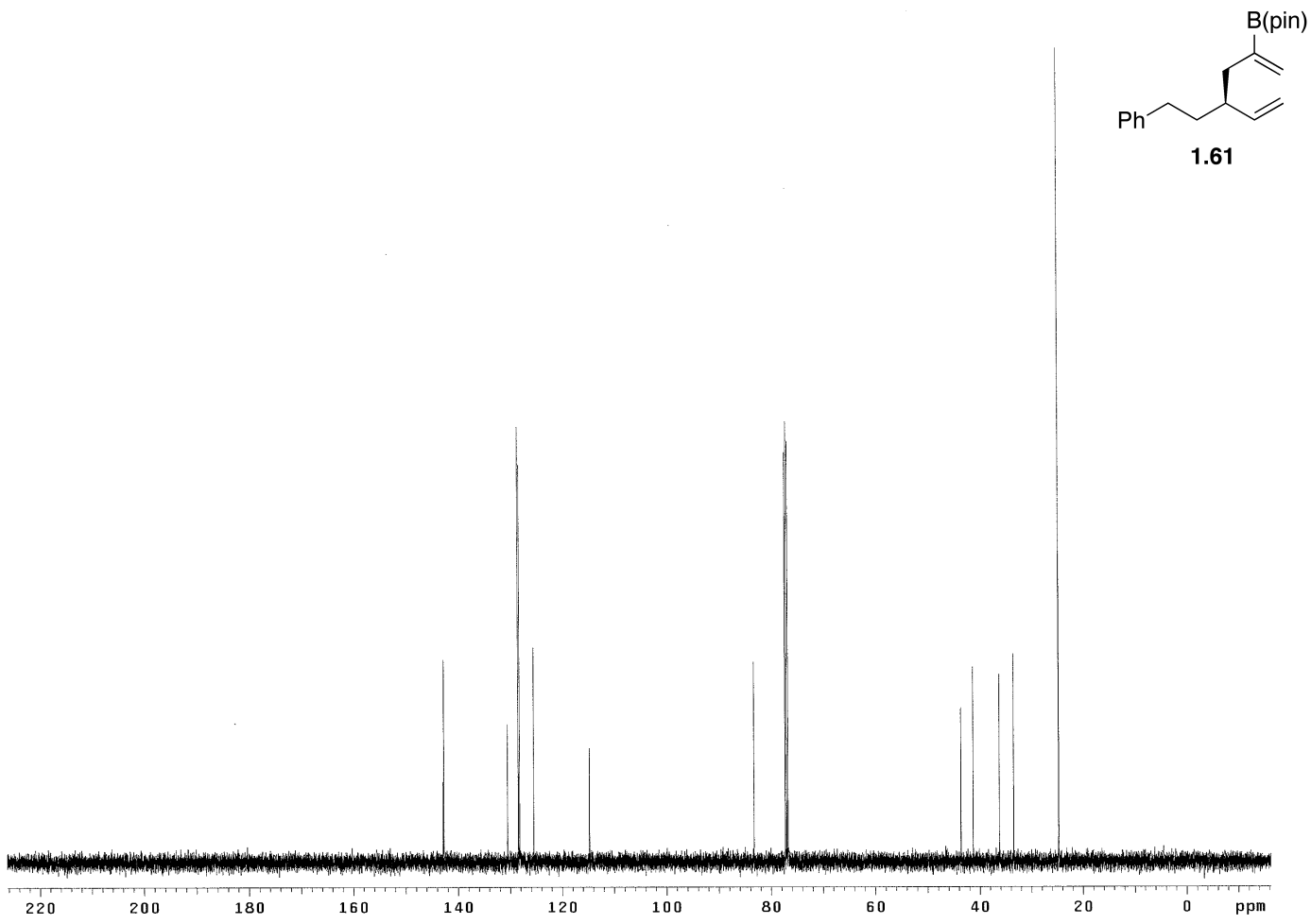
6
7
8
9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Ph
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200
180
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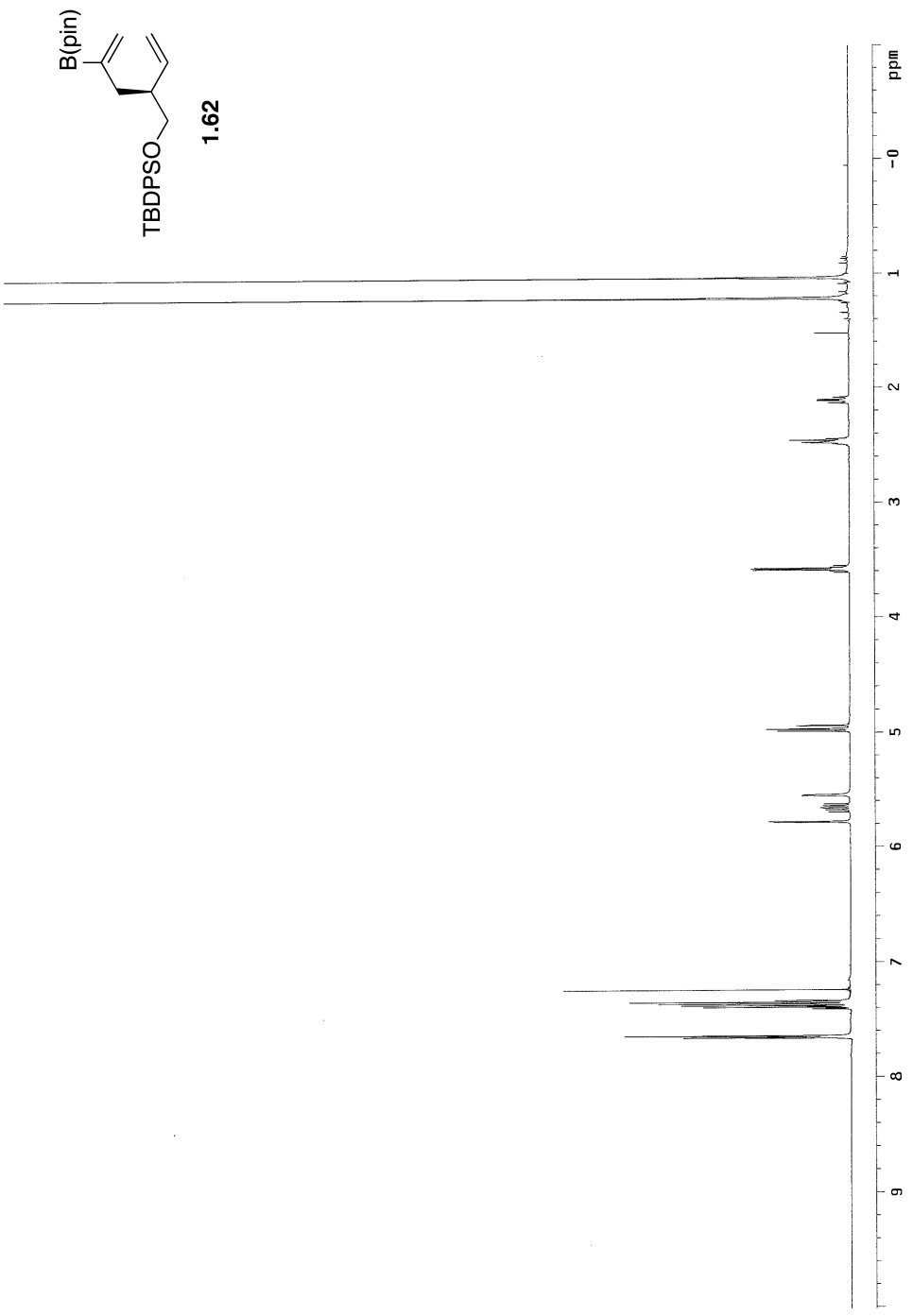
120
100
80
60
40
20
0
ppm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ppm
-0
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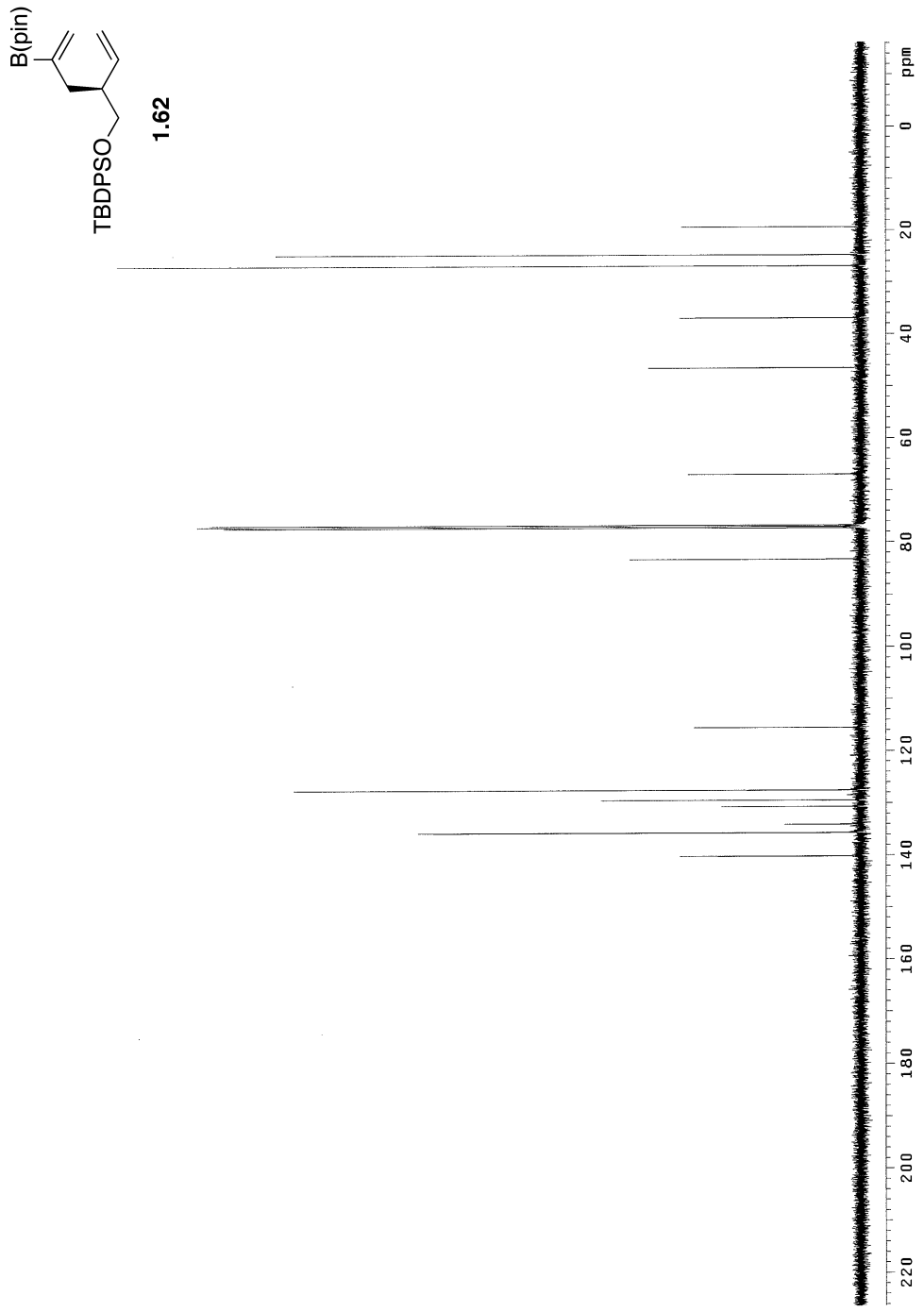
2
3
4
5
6
7
8
9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TBDPSO
1.62
ppm
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80
100
120
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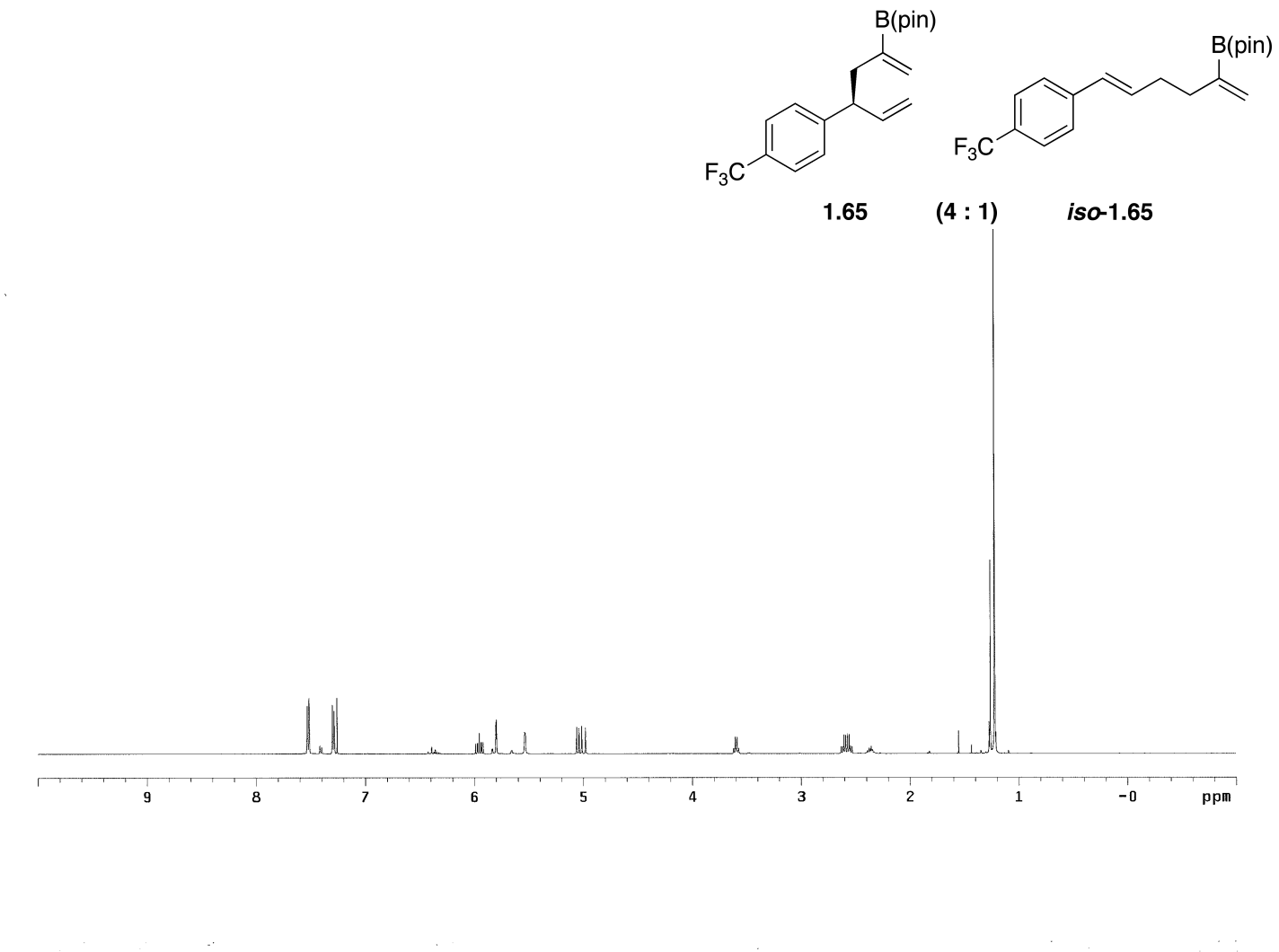
160
180
200
220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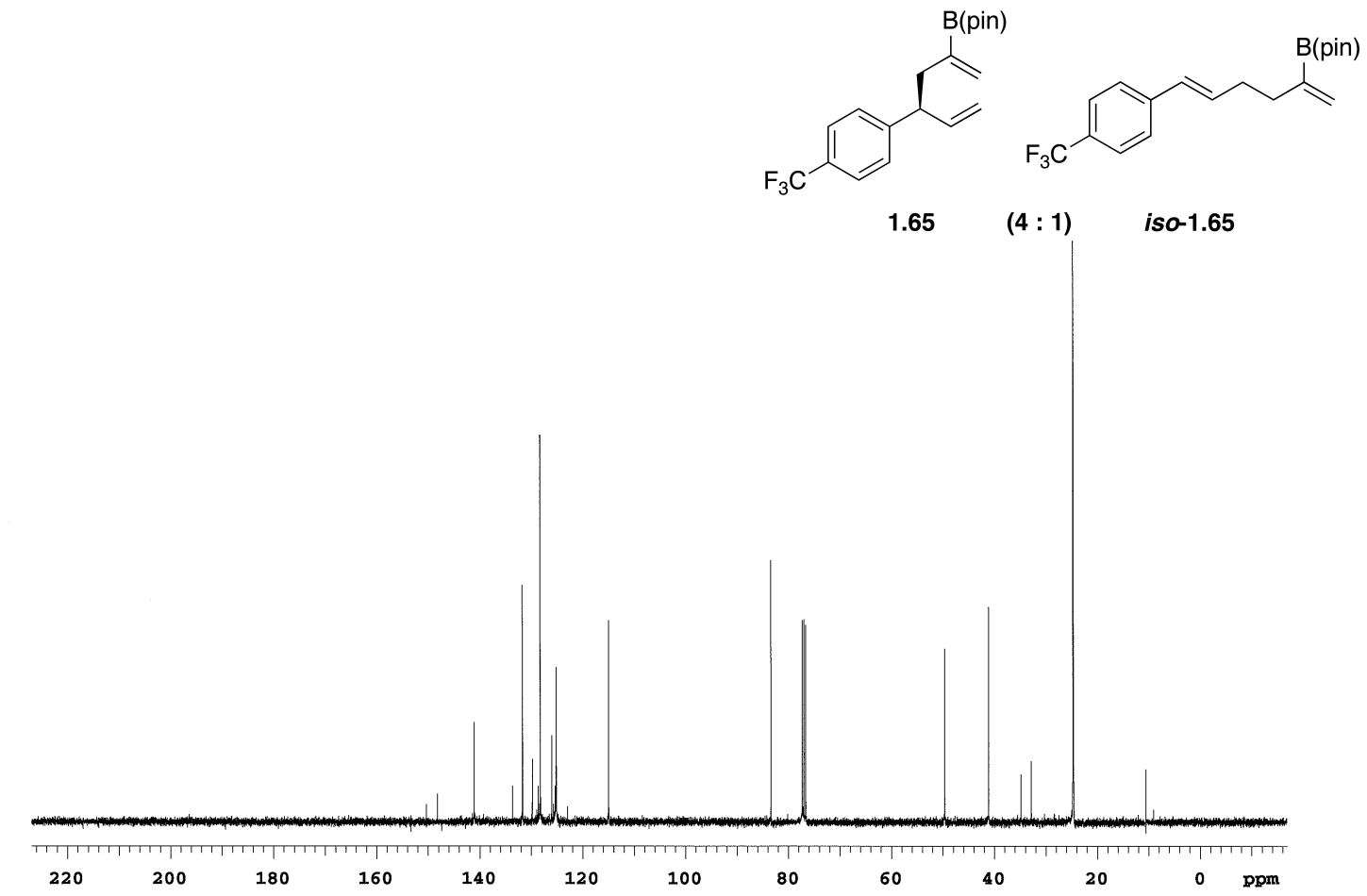
F3C
B(pin)
F3C
1.65
(4 : 1)
iso-1.65
9
8
7
6
5
4
3
2
1
-0
ppm


B(pin)
F3C
B(pin)
F3C
1.65
(4 : 1)
iso-1.65
220
200
180
160
140
120
100
80
60
40
20
0
ppm

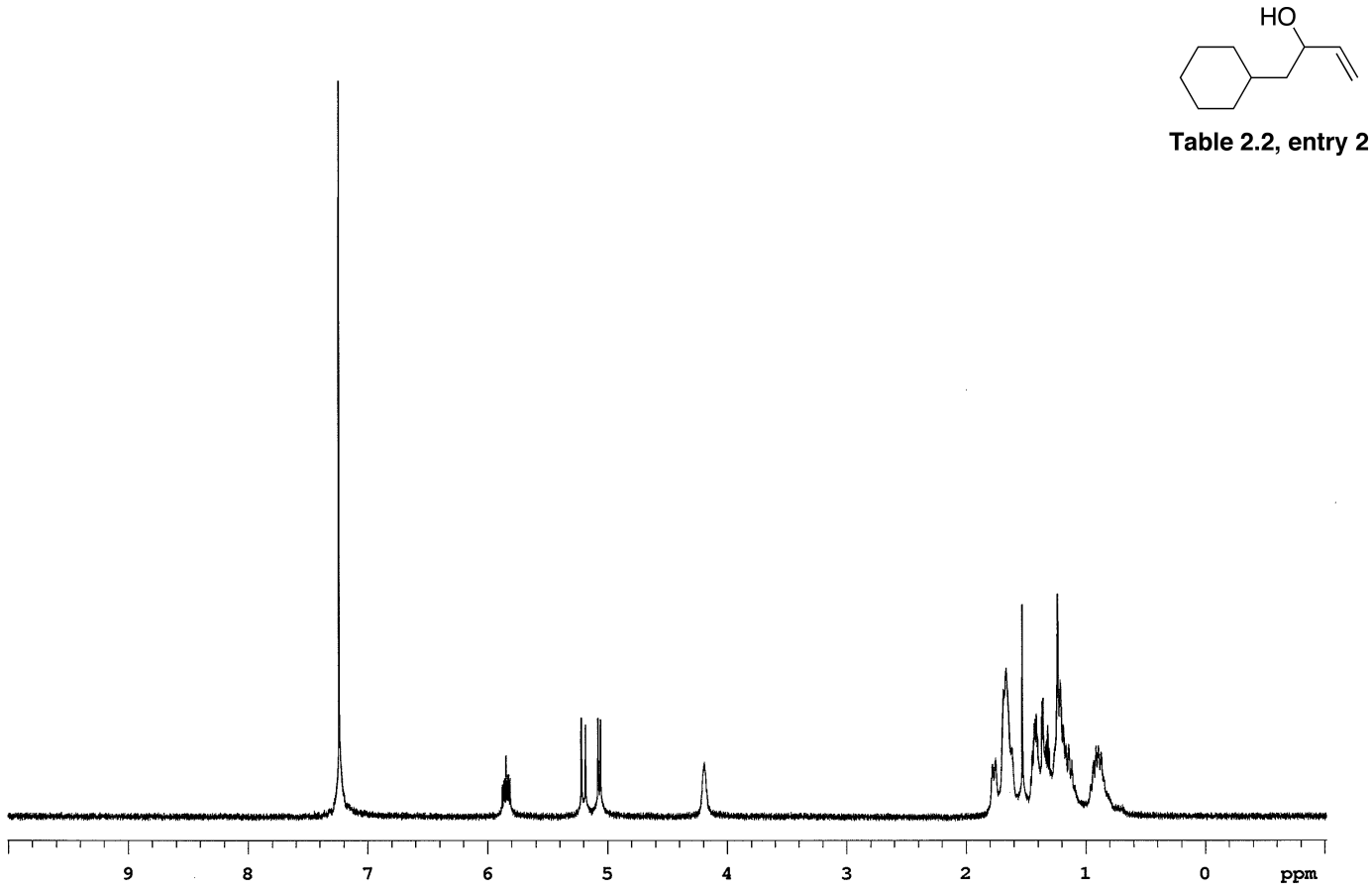


Table 2.2, entry 2

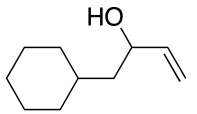
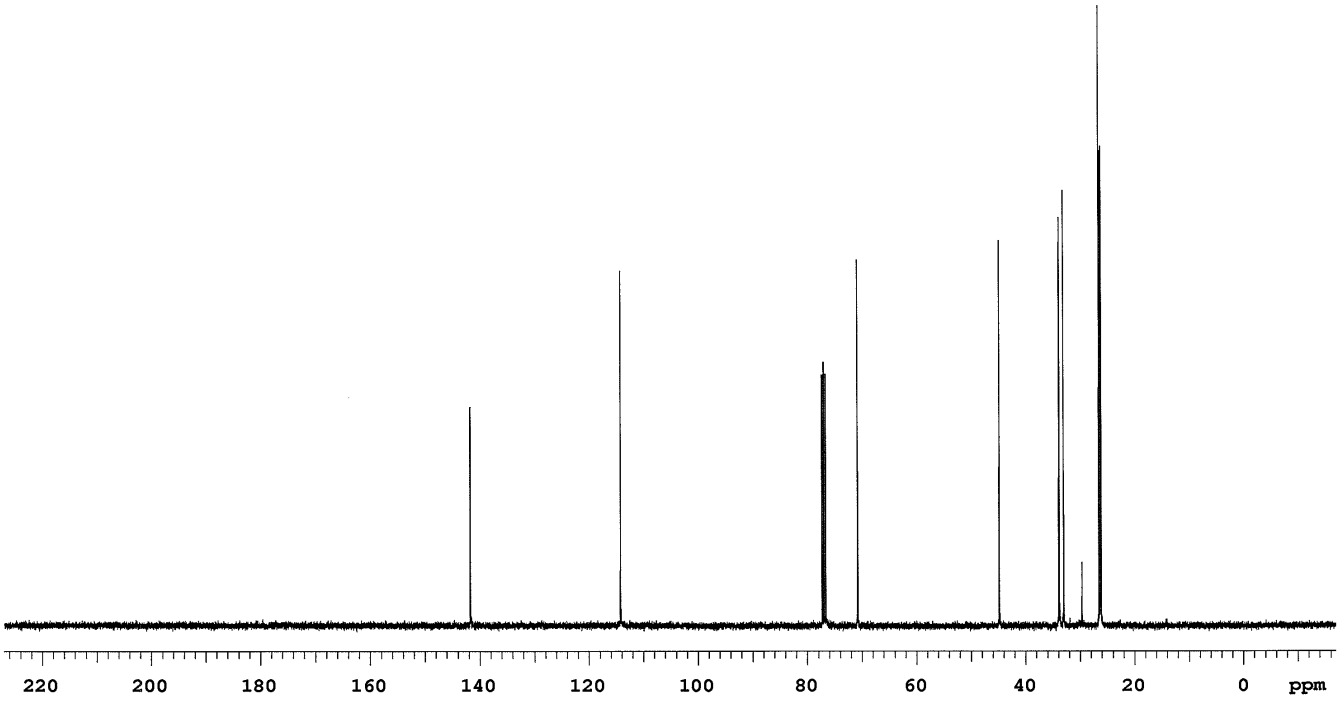
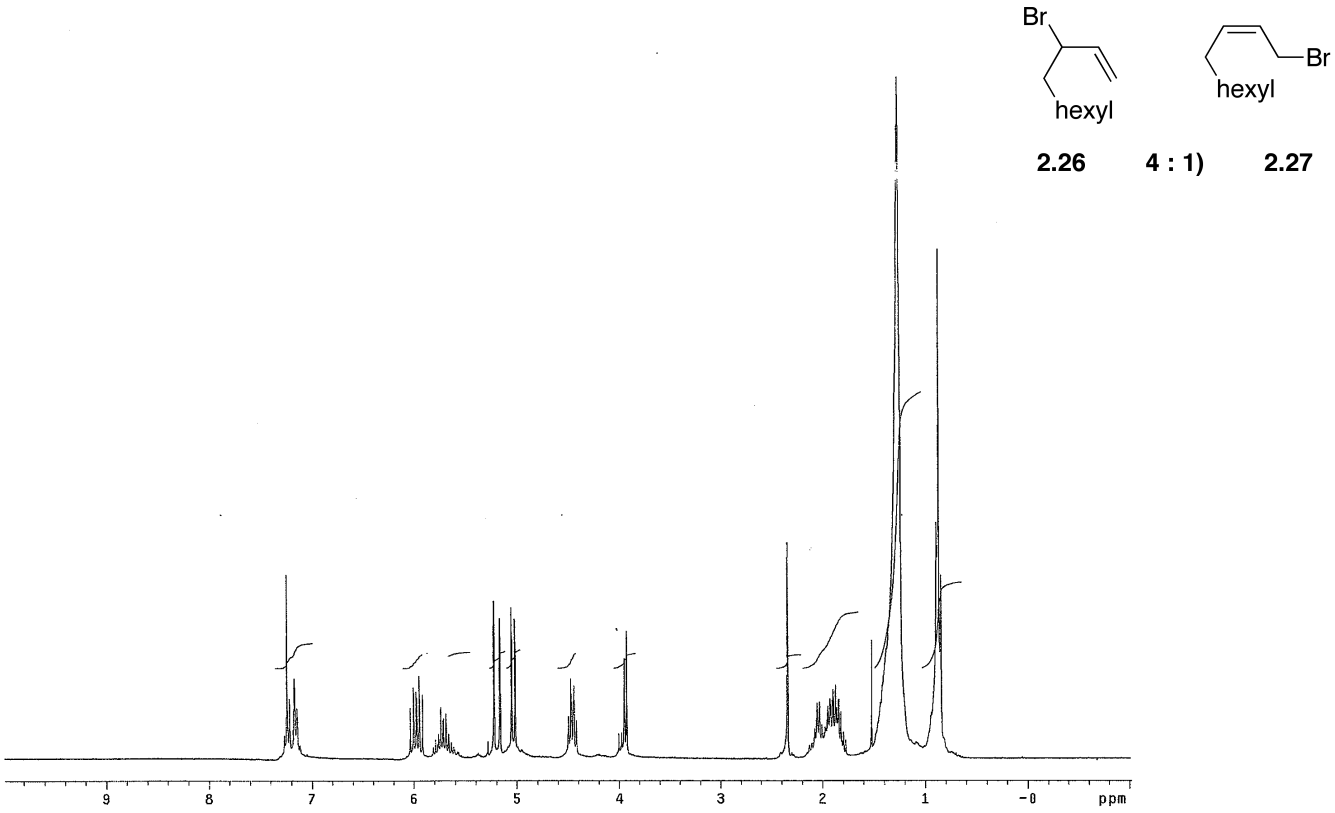


Table 2.2, entry 2




Br
hexyl
Br
hexyl
2.26
4 : 1)
2.27
9
8
7
6
5
4
3
2
1
-0
ppm