Enantioselective Pt-Catalyzed Diboration of Unsaturated Hydrocarbons: A Versatile Tool for Synthesis

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Boston College
The Graduate School of Arts and Sciences
Department of Chemistry

ENANTIOSELECTIVE PLATINUM-CATALYZED DIBORATION OF
UNSATURATED HYDROCARBONS: A VERSATILE TOOL FOR SYNTHESIS

a dissertation

by

LAURA TARADAY KLIMAN

submitted in partial fulfillment of the requirements
for the degree of
Doctor of Philosophy

December 2011
ENANTIOSELECTIVE PLATINUM-CATALYZED DIBORATION OF UNSATURATED HYDROCARBONS: A VERSATILE TOOL FOR SYNTHESIS

by

LAURA TARADAY KLIMAN

Dissertation Advisor:
Professor James P. Morken

ABSTRACT: Platinum-catalyzed enantioselective diboration of various hydrocarbon starting materials to form stereodefined carbon-boron bonds is reported. The asymmetric Pt-catalyzed 1,4-diboration of trans-1,3-dienes provided 1,4-bis(boronate)esters in up to 98:2 er, representing the first enantioselective diene diboration. The enantioselective 1,2-diboration of cis-1,3-dienes and 4,4-disubstituted dienes afforded 1,2-bis(boronate)esters in up to 98:2 er. The intermediate allylboronates were utilized in aldehyde allylations to furnish polypropionate-like compounds and stereodefined carbon quaternary centers. The development of a Pt-catalyzed enantioselective diboration of terminal olefins is disclosed, giving the corresponding 1,2-diols in up to 97:3 er. Further optimization and expansion of the scope of this method is also discussed.
Dedicated to:

My grandmother, Bernice W. Kliman, for her unrelenting zest for life and learning.
I would first and foremost like to express my profound thanks to my advisor, Professor James P. Morken for his continuous guidance and support. His infectious passion for chemistry and dedication to his students created an extremely enjoyable environment in which to learn chemistry. He has helped to shape my career as a scientist in many ways, and for that I am especially grateful.

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I am extremely appreciative of Laura Brozek, Rob Ely, Chris Schuster, and Mike Ardolino for proofreading this dissertation.

To my entire family, I am forever indebted to you all for your continued support and encouragement throughout my life. I will never be able to fully convey the appreciation I have for my parents. Their unconditional love and support have helped make me the person I am today.
# TABLE OF CONTENTS

List of Abbreviations ........................................................................................................[ix

Chapter 1. Development, Scope, and Utility of the Enantioselective Platinum-Catalyzed 1,4-Diboration of \textit{trans}-1,3-Dienes ................................................................. 1

1.1. Introduction................................................................................................................. 1

1.2. Background.................................................................................................................. 5

1.3. Development of the Enantioselective Pt-Catalyzed 1,4-Diboration of \textit{trans}-1,3-Dienes ........................................................................................................ 13

1.4. Product Utility in the Enantioselective Pt-Catalyzed Diboration of \textit{trans}-1,3-Dienes .................................................................................................................... 34

1.5. Mechanistic Discussion for the Enantioselective Pt-Catalyzed Diboration of \textit{trans}-1,3-Dienes ........................................................................................................ 36

1.6. Conclusions .................................................................................................................. 39

1.7 Experimentals .............................................................................................................. 40

1.7.1 General Information ............................................................................................... 40

1.7.2. Preparation of Pt(dba)$_3$................................................................................... 42

1.7.3. Ligand Synthesis ................................................................................................. 43

1.7.3.1. BINOL-Derived Ligands ............................................................................... 43

1.7.3.2. Representative Procedure for the Synthesis of TADDOL-Derivatives ........ 43
1.7.3.3. TADDOL-Derived Phosphoramidite and Phosphite Ligand Synthesis .................................................................47
1.7.3.4. TADDOL-Derived Phosphonite Ligand Synthesis ..........47
1.7.3.5. Mixed TADDOL-Phosphonite Ligand Synthesis ..........50
1.7.3.6. Representative Procedure for (R,R)-TADDOL-Derived Phosphonites with Substituted Aryl Phosphines ...........53
1.7.4. Preparation of Acyclic 1,3-Dienes (Table 1.8) ...............57
1.7.5. Preparation of Cyclic 1,3-Diene Substrates (Table 1.9) ........60
1.7.6. Preparation of Chiral Diene 1.57 (Scheme 1.13) ...............62
1.7.7. Preparation of Internal 1,3-Diene 1.60 (Scheme 1.14) ........62
1.7.8. Representative Procedure for Diene Diboration/Oxidation .......63
1.7.9. Characterization and Proof of Stereochemistry .................64
1.7.10. Procedure for Butenolide Formation (Scheme 1.16) ...........92
1.7.11. Procedure for Diene Diboration/Allylation/Oxidation .........93

Chapter 2. Development, Scope, and Utility of the Enantioselective Pt-Catalyzed 1,2-Diboration of cis-1,3-Dienes: Application to Stereoselective Allylation .................102

2.1. Introduction .....................................................................................102
2.2. Background ....................................................................................106
2.3. Development of the Enantioselective Pt-Catalyzed 1,2-Diboration of cis-1,3-Dienes ...............................................................115
2.4. Development of the Tandem Enantioselective Pt-Catalyzed Diboration/Allylation of \textit{cis}-1,3-Dienes................................................................. 127

2.5 Conclusions.................................................................................. 133

2.6. Experimentals ............................................................................. 134

   2.6.1. General Information............................................................. 134

   2.6.2. Preparation of Pt(dba)$_3$.................................................... 136

   2.6.3. Preparation of Pt$_2$(dba)$_3$................................................ 137

   2.6.4. Preparation of Pt(nbe)$_3$.................................................... 138

   2.6.5. Ligand Synthesis................................................................. 139

   2.6.6. Preparation of \textit{cis}-1,3-Dienes.......................................... 150

   2.6.7. Representative Procedure for Diboration/Oxidation.......... 157

   2.6.8. Characterization and Proof of Stereochemistry (Table 2.4).... 158

   2.6.9. Representative Procedure for Diboration/Allylation/Oxidation ... 175

   2.6.10. Characterization and Proof of Stereochemistry (Table 2.6).... 176

Chapter 3. Development, Scope, and Utility of the Enantioselective Platinum-Catalyzed 1,2-Diboration of 4,4-Disubstituted Dienes: Application to Synthesis of Stereodefined Quaternary Centers......................................................... 199

   3.1. Introduction.............................................................................. 199

   3.2. Background............................................................................ 203

   3.3. Development of the Enantioselective Pt-Catalyzed 1,2-Diboration of 4,4-Disubstituted Dienes ......................................................... 212
3.4. Development of the Tandem Enantioselective Pt-Catalyzed Diboration/Allylation of 4,4-Disubstituted Dienes .................................................................220

3.5. Product Utility in the Enantioselective Pt-Catalyzed Diboration/Allylation of 4,4-Disubstituted Dienes .................................................................225

3.6. Conclusions .................................................................................................................227

3.7. Experiments ......................................................................................................................230
  3.7.1. General Information .................................................................................................230
  3.7.2. Preparation of Pt(dba)$_3$ ..........................................................................................232
  3.7.3. Ligand Synthesis .....................................................................................................233
  3.7.4. Preparation of 4,4-Disubstituted Dienes .................................................................235
  3.7.5. Representative Procedure for Diboration/Oxidation .................................................242
  3.7.6. Representative Procedure for Diboration/Allylation/Oxidation .........................255
  3.7.7. Characterization and Proof of Stereochemistry .........................................................256
  3.7.8. Procedure for Diboration/Allylation/Homologation/Oxidation .........................285
  3.7.9. Procedure for Diboration/Allylation/Protodeboronation .........................................288

Chapter 4. Development, Scope, and Utility of the Enantioselective Platinum-Catalyzed 1,2-Diboration of Terminal Alkenes .....................................................300

4.1. Introduction ....................................................................................................................300

4.2. Background ...................................................................................................................302
  4.2.1. Disilation of Alkenes ............................................................................................302
  4.2.2. Silaboration of Alkenes ..........................................................................................304
4.2.3. Diboration of Alkenes ................................................................. 305

4.2.4. Enantioselective Dihydroxylation of Alkenes .......................... 309

4.3. Development of the Enantioselective Pt-Catalyzed 1,2-Diboration of Terminal Alkenes ................................................................. 311

4.4. Synthetic Utility of the Pt-Catalyzed Enantioselective 1,2-Diboration of Terminal Alkenes ................................................................. 326

4.4.1. Decreased Catalyst Loading ....................................................... 326

4.4.2. Matteson Homologation ............................................................ 327

4.5. Further Optimization of the Pt-Catalyzed Enantioselective 1,2-Diboration of Terminal Alkenes ................................................................. 329

4.6. Progress Toward X-Ray Crystallographic Analysis of Platinum-Ligand Complexes and Kinetics Data ................................................................. 336

4.7. Conclusions .................................................................................. 343

4.8. Experimentals .............................................................................. 344

4.8.1. General Information ................................................................. 344

4.8.2. Preparation of Pt(dba)$_3$ ............................................................. 346

4.8.3. Preparation of Pt$_2$(dba)$_3$ ....................................................... 347

4.8.4. Ligand Synthesis ..................................................................... 348

4.8.5. Preparation of 1-Alkenes .......................................................... 349

4.8.6. Representative Procedure for Alkene Diboration/Oxidation ....... 352

4.8.7. Characterization and Proof of Stereochemistry ....................... 353
4.8.8. Procedure for Decreased Catalyst Loading.................................378
4.8.9. Procedure for Alkene Diboration/Homologation/Oxidation.........379
4.8.10. Procedure for Benchtop Diboration.................................................382
LG: leaving group
LRMS: low-resolution mass spectrometry
M: molar
NaHMDS: sodium bis(trimethylsilyl) amide
nbd: norbornadiene
NMO: N-methylmorpholino N-oxide
NMR: nuclear magnetic resonance
pin: pinacol
QUINAP: 1-(2-diphenylphosphino-1-naphthyl)isoquinoline
rt: room temperature
SFC: supercritical fluid chromatography
TADDOL: (4R,5R)-(−)-2,2-dimethyl-α, α, α ′, α ′-tetraphenyl-1,3-dioxolane-4,5-dimethanol
TBDPS: tert-butyldiphenylsilyl
TBS: tert-butyldimethylsilyl
Tf: trifluoromethanesulfonfyl
TFA: trifluoroacetyl
THF: tetrahydrofuran
TPAP: tetrapropylammonium perruthenate
Ts: p-toluenesulfonate
xylyl: 3,5-dimethylphenyl
y: yield

x
Chapter 1

Development, Scope, and Utility of the Enantioselective Platinum-Catalyzed 1,4-Diboration of trans-1,3-Dienes

1.1. Introduction

The field of organic chemistry has been transformed by the development of novel catalytic, enantioselective methods for the synthesis of complex molecules. Specifically, transition-metal catalyzed reactions have had a large impact on our ability to rapidly transform simple and inexpensive starting materials to a variety of highly functionalized compounds. In general, the establishment of new methods in asymmetric catalysis is carried out with a single transformation in mind. Thus, to access a large array of products, one would have to develop unique catalysts and reaction conditions for each transformation. In contrast, our research focuses on using enantioselective dimetallation, a reaction that gives a reactive intermediate which allows for the synthesis of a diverse range of functionalized products in a single step (Scheme 1.1).
Scheme 1.1. Dimetallation of Unsaturated Hydrocarbons to Access a Diverse Range of Products

A variety of dimetallation reactions have been reported in the literature, and these may employ disilanes, distannanes, silylboranes, silylgermanes, and borylstannanes as dimetallating reagents.\(^1\) Although these methods give access to a dimetallated intermediate, the known transformations of silicon, tin, and germanium bonds are restricted to protonation and oxidation, with a few examples of cross-coupling reactions. Additionally, these dimetallation reagents can be toxic and expensive. In order to use dimetallation as a useful synthetic tool, we considered that the intermediate must contain a carbon-metal bond that can be easily subjected to a broad array of functionalizations.

Utilizing diboron reagents in this type of reaction sequence not only expands the number of transformations available, but these reagents are also non-toxic and inexpensive. The power of catalytic, enantioselective diboration comes from the inherent reactivity of carbon-boron bonds. This reactivity is due to the empty p-orbital on the boron atom, which is prone to nucleophilic attack. If the nucleophile contains an attached leaving group, a stereoretentive 1,2-shift will occur to form a new carbon-nucleophile bond (Scheme 1.2). By this mechanism, organoboranes are known to participate in oxidation, amination, sulfination and phosphination, and a variety of homologation reactions. Organoboronates also participate in transmetallation and are therefore widely utilized in cross-coupling reactions.

**Scheme 1.2. Reactivity of Carbon-Boron Bonds**

\[
\begin{align*}
R_1B & \overset{\text{Nu-LG}}{\longrightarrow} R_2B \\
\text{Nu} & \rightarrow R_1B \overset{\text{LG}}{\longrightarrow} \text{Nu}B \overset{\text{LG}}{\longrightarrow} R_2
\end{align*}
\]

---

The first example of the addition of diboron reagents to unsaturated hydrocarbons was the diboration of alkynes, reported by Suzuki and Miyaura, followed by investigations from Marder and Smith. These influential studies provided the foundation for the development of novel diboration reactions; however, the diboration of alkynes does not provide optically active products. The development of methods that enable the synthesis of stereodefined carbon-boron bonds is therefore synthetically valuable. The Morken group has published several reports in the area of enantioselective diboration including the Rh-catalyzed diboration of alkenes with bis(catecholato)diboron (B$_2$(cat)$_2$) (Scheme 1.3, eq 1), and the Pd-catalyzed diboration of allenes with bis(pinacolato)diboron (B$_2$(pin)$_2$) (Scheme 1.3, eq 2). The expansion of enantioselective diboration to other unsaturated hydrocarbon starting materials would further advance the scope of this methodology. In this chapter, I will describe the development of the first enantioselective 1,4-diboration of trans-1,3-dienes.

---

1.2. Background

Although many studies have been carried out on dimetallations of alkynes, allenes, and alkenes, the use of 1,3-dienes as substrates in dimetallation reactions has received less attention. One of the first successful catalytic dimetallations of 1,3-dienes was described by Ito and Suginome.\(^\text{11}\) In the presence of both nickel and platinum catalysts, (dimethylphenylsilyl)pinacolborane \((\text{1.1})\) furnishes 1,4-silaboration products in high yields (Scheme 1.4). However, unsymmetrical diene substrates suffered from low levels of regioselectivity in the silaboration; and the use of chiral catalysts in the silaboration of prochiral dienes was not reported.

Scheme 1.4. Suginome and Ito Silaboration of 1,3-Dienes

Moberg accomplished the first enantioselective silaboration of 1,3-cyclohexadiene, which was catalyzed by Pt(acac)\(_2\) in the presence of chiral BINOL-derived phosphoramidite ligands to arrive at the 1,4-silaboration product in moderate yield and enantiopurity (Scheme 1.5).\(^\text{12}\) Although this was a significant advance in the field of dimetallation, the substrate scope was extremely limited and the reaction required 2.5 equivalents of diene relative to the silaboration reagent. Beyond the asymmetric silaboration of 1,3-cyclohexadiene reported by Moberg, there have been no examples of other enantioselective dimetallation reactions of dienes, highlighting a deficiency in the current methods for catalytic, enantioselective dimetallation.

Scheme 1.5. Enantioselective Pt-Catalyzed Silaboration of 1,3-Dienes

In the late 1990s, Miyaura and co-workers published the first example of the addition of diboron reagents across 1,3-dienes to provide a variety of allylboron compounds.\textsuperscript{13} Their studies showed that platinum(0) complexes were capable of catalyzing this transformation in the presence of bis(pinacolato)diboron (1.4), and that the regioselectivity of the reaction was highly dependent on the ligand. In the diboration of \textit{trans}-1,3-pentadiene, with 3 mol\% of Pt(PPh\textsubscript{3})\textsubscript{4}, the (Z)-1,4-bis(boronate)ester 1.5 was obtained in 84\% yield as the sole reaction product. However, in the absence of phosphine ligands, Miyaura found that 1,2-diboration of the terminal olefin was the predominant pathway and the 1,2-bis(boronate)ester 1.6 was provided in 92\% yield (Scheme 1.6).

**Scheme 1.6.** Non-Enantioselective Diboration of 1,3-Dienes

The mechanism proposed by Miyaura for the Pt-catalyzed diboration of 1,3-dienes is shown below (Scheme 1.7). The first step involves oxidative addition of the diboron compound to the Pt(0)-catalyst to arrive at the Pt-bis(boryl) species 1.7. After ligand dissociation, the diene coordinates to the metal in the S-cis conformation and inserts into one of the Pt-B bonds to give the π-allyl(boryl)platinum(II) species 1.8. Reductive elimination to the less substituted terminal carbon then provides the observed (Z)-1,4-bis(borinate)ester.
The reactivity of the platinum catalysts described above are promising for the development of an enantioselective diboration of 1,3-dienes; however, the products discussed in Miyaura’s report were obtained in racemic form and the use of chiral ligands to control selectivity had yet to be realized. As an alternative, the use of chiral diboron reagents was employed by Marder and Norman in the 1,4-diboration of 1,3-dienes to arrive at diastereomERICally enriched allyboron products. A variety of chiral diolate ligands were used in the diboration reaction, with the tartrate-derived diboron reagent 1.9 giving the best results. The Pt-catalyzed addition of 1.9 across trans-1,3-pentadiene proceeded with good conversion, however; the highest diastereoselectivity observed was only 60:40 for the 1,4-bis(boronate)ester product 1.10 (Scheme 1.8).

---

Scheme 1.8. Diastereoselective Diboration of 1,3-Dienes with Chiral Diborons

In 2003, the Morken group published another example of a 1,4-diboration of 1,3-dienes through the use of chiral diboron reagents. They utilized the reactivity of the intermediate allylboronate 1.12 (Scheme 1.9) in a tandem allylation reaction to access products with increased complexity. The diene diboration did not create any stereocenters, but the chiral tartrate element was able to effectively influence stereoselection in a subsequent allylboration reaction. When employing the commercially available bis(diethyl-L-tartrateglycolato)diboron (1.11) in the diboration/allylation sequence, the desired 1,3-diol was afforded in 72% yield, >19:1 dr, and 87:13 er (Scheme 1.9). Although the chiral allylboronate gave moderate enantioselectivity when coupled with cyclohexanecarboxaldehyde, other aldehyde substrates suffered from diminished levels of enantioselectivity (67:33-85:15 er). The use of chiral diboron reagents in the diboration of 1,3-dienes allowed access to synthetically interesting products with modest levels of stereoselectivity. A catalytic, enantioselective diboration of prochiral 1,3-dienes that does not utilize stoichiometric chiral reagents must be developed in order to take full advantage of the power of diene diboration.

Scheme 1.9. Catalytic Diene Diboration/Allylation with Chiral Diboronates

The Morken group reported the first catalytic, enantioselective diboration of 1,2-dienes in 2004 with the use of Pd(0) and TADDOL-derived phosphoramidite ligands to provide enantioenriched 1,2-bis(boronate)esters in up to 96:4 er. In a subsequent publication, the mechanism of the diboration reaction was determined from both laboratory experiments and DFT calculations, and the enantioselectivity was improved to provide 1,2-bis(boronate)esters in up to 99:1 er. The mechanism for the diboration of 1,2-dienes is illustrated below (Scheme 1.10), with rate-determining oxidation addition of $\text{B}_2(\text{pin})_2$ to Pd(0) to form the Pd-bis(boryl) species (1.13) as the first step. The Pd-bis(boryl) adduct then coordinates to the terminal olefin of the allene to arrive at 1.14, followed by migratory insertion of the terminal alkene into one of the palladium-boron bonds. This insertion step is believed to go through an unusual transition state (1.15) where the internal olefin of the 1,2-diene develops $\pi$-bonding character to the palladium simultaneously with carbon-boron bond formation, directly giving the $\eta^3$-allyl palladium...
complex 1.16. Reductive elimination from 1.16 delivers the observed 1,2-bis(borate) ester 1.17.

Scheme 1.10. Mechanism for Pd-Catalyzed Enantioselective Diboration of 1,2-Dienes

It was thought that the diboration of 1,3-dienes might proceed through an analogous mechanism to allene diboration, benefiting from the unique interaction between the adjacent olefin and the metal center during the insertion step (Scheme 1.11, structure 1.18). Therefore, it was of great interest to determine whether the catalysts used in the asymmetric diboration of 1,2-dienes would also catalyze the enantioselective diboration of 1,3-dienes to give 1,4-bis(borane)esters (1.19) with high levels of regio- and enantioselectivity.
1.3. Development of the Enantioselective Pt-Catalyzed 1,4-Diboration of *trans*-1,3-Dienes\textsuperscript{16}

Before I joined the project, fellow graduate student Heather Burks had surveyed some transition-metal catalysts for the diboration of commercially available *trans*-1,3-pentadiene with B\textsubscript{2}(pin)\textsubscript{2} (Table 1.1). Initial studies involved the use of the previously described palladium(0)-catalyst that was successful in the diboration of 1,2-dienes; however, it was found that Pd\textsubscript{2}(dba)\textsubscript{3} in conjunction with PCy\textsubscript{3} was not effective in catalyzing the diboration of 1,3-dienes. The chiral phosphoramidite ligand (\textit{R, R})-1.22 was also unsuccessful at providing the desired 1,4-bis(boronate)ester (1.20) under Pd(0)-catalysis. When employing 3 mol\% of Pt(PPh\textsubscript{3})\textsubscript{4} in the diboration reaction, the 1,4-diboration of *trans*-1,3-pentadiene was accomplished in 60\% yield. The effectiveness of Pt(0)-catalysis was not surprising based on the previous results published by Miyaura and co-workers on the racemic diene diboration.\textsuperscript{12} More excitingly, it was found that Pt(dba)\textsubscript{3} in the presence of an external phosphine ligand was a competent catalyst system for the 1,4-diboration of dienes. The use of PPh\textsubscript{3} as a ligand afforded the product in 40\% yield,

while employing the more electron-rich PCy$_3$ gave 66% yield of the diboration product, indicating the potential for success of chiral monodentate phosphine ligands in an enantioselective diboration of 1,3-dienes. When employing Pt(dba)$_3$ in the absence of a phosphine ligand, the sole product observed was the 1,2-bis(boronate)ester 1.21, which is produced from 1,2-diboration of the terminal olefin of the diene (entry 6). Therefore, the enantioselective 1,4-diboration of 1,3-dienes should not be affected by phosphine-free Pt-catalysis since the background reaction provides a different reaction product.

**Table 1.1. Transition-Metal Catalyst Survey for Diboration of trans-1,3-Pentadiene**

<table>
<thead>
<tr>
<th>entry</th>
<th>metal (x mol%)</th>
<th>ligand</th>
<th>% yield 1.20$^a$</th>
<th>% yield 1.21$^a$</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Pd$_2$(dba)$_3$ (5%)</td>
<td>PCy$_3$</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>2</td>
<td>Pd$_2$(dba)$_3$ (5%)</td>
<td>(R,R)-1.22</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>3</td>
<td>Pt(PPh$_3$)$_4$ (3%)</td>
<td>-</td>
<td>60</td>
<td>0</td>
</tr>
<tr>
<td>4</td>
<td>Pt(dba)$_3$ (6%)</td>
<td>PPh$_3$</td>
<td>40</td>
<td>0</td>
</tr>
<tr>
<td>5</td>
<td>Pt(dba)$_3$ (6%)</td>
<td>PCy$_3$</td>
<td>66</td>
<td>0</td>
</tr>
<tr>
<td>6</td>
<td>Pt(dba)$_3$ (6%)</td>
<td>-</td>
<td>0</td>
<td>58</td>
</tr>
</tbody>
</table>

$^a$ The isolated yield was determined by subjecting the intermediate 1,4-bis(boronate)ester 1.20 to an allylation with benzaldehyde, followed by oxidation.
It was at this point that I joined the project and began to investigate the optimal ligand for the enantioselective diene diboration. The first class of ligands surveyed in this reaction was BINOL-derived phosphoramidites (Table 1.2). Both diastereomers of Feringa’s α-methylbenzylamine phosphoramidite ligand\textsuperscript{17} were tested in the diboration of \textit{trans}-1,3-pentadiene (entries 1 and 2). Ligand \textbf{1.23} gave a 1:1 mixture of 1,4- and 1,2-diboration product, with 42\% yield of the desired 1,4-diboration product in only 68:32 er, representing the matched case. The opposite diastereomer \textbf{1.24} also gave a 1:1 mixture of regioisomers, with only 17\% yield of the 1,4-product in 62:38 er, representing the mismatched case. Without substitution at the α-position of the amine in the BINOL-derived ligand, no diboration product was formed (entries 3 and 4). The lack of diboration reaction with ligands \textbf{1.25} and \textbf{1.26} is potentially due to insertion of the Pt(0)-catalyst into one of the C-H bonds on the dimethylamine moiety, thereby shutting down the desired reaction pathway.\textsuperscript{18} The partially hydrogenated BINOL-derived ligand \textbf{1.27} was also surveyed in the diboration of \textit{trans}-1,3-pentadiene and provided a 3:1 ratio of regioisomers, and 27\% of the desired 1,4-product in 79:21 er. Due to the low yields and selectivites in diene diboration with BINOL-derived phosphoramidites, and the difficult synthesis and purification of BINOL-derived phosphonite ligands, TADDOL-derived ligand scaffolds became the focus for the development of the enantioselective diboration of \textit{trans}-1,3-dienes.

Table 1.2. BINOL-Derived Ligands in Pt-Catalyzed Diene Diboration

![Chemical structure]

<table>
<thead>
<tr>
<th>entry</th>
<th>ligand</th>
<th>(1,4):(1,2)</th>
<th>% yield</th>
<th>er</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td><img src="image1" alt="Structure 1.23" /></td>
<td>1:1</td>
<td>42</td>
<td>68:32</td>
</tr>
<tr>
<td>2</td>
<td><img src="image2" alt="Structure 1.24" /></td>
<td>1:1</td>
<td>17</td>
<td>62:38</td>
</tr>
<tr>
<td>3</td>
<td><img src="image3" alt="Structure 1.25" /></td>
<td>-</td>
<td>0</td>
<td>-</td>
</tr>
<tr>
<td>4</td>
<td><img src="image4" alt="Structure 1.26" /></td>
<td>-</td>
<td>0</td>
<td>-</td>
</tr>
<tr>
<td>5</td>
<td><img src="image5" alt="Structure 1.27" /></td>
<td>3:1</td>
<td>27</td>
<td>79:21</td>
</tr>
</tbody>
</table>

a The regioselectivity was determined from the crude $^1$H NMR of the 1,3-diol obtained by subjecting the intermediate 1,4-bis(boronate)ester 1.20 to an allylation with benzaldehyde, followed by oxidation. b The isolated yield was determined by analysis of the diboration/allylation/oxidation product. c The er was determined by chiral GC analysis of the diboration/allylation/oxidation product.
TADDOL ligands were first prepared by Seebach and coworkers in the early 1990s and are synthesized from commercially available tartaric acid. Their ease of preparation and high tunability make them optimal ligands for enantioselective catalysis. A variety of TADDOL-derived phosphorous ligands were initially surveyed to determine which class of ligand would provide the highest level of enantioselectivity in the 1,4-diboration of trans-1,3-pentadiene (Table 1.3). The TADDOL-derived phosphite \((R,R)-1.28\) provided trace amounts of product in the diboration reaction. The phosphoramidite ligand \((R,R)-1.29\) gave a 2.5:1 ratio of regioisomers and the desired 1,4-product was isolated in 30% yield with a 53:47 er. When employing the less frequently utilized phosphonite ligands \((R,R)-1.30\) and \((R,R)-1.31\), the diboration proceeded with improved regioselectivity favoring the 1,4-product 1.20. Ligand \((R,R)-1.30\) containing 3,5-di-tert-butyl substituted aryl rings on the TADDOL backbone provided the desired product in 40% isolated yield and 60:40 er. Decreasing the size of the substituents on the aryl rings with ligand \((R,R)-1.31\) improved the reactivity and enantioselectivity to afford the desired product in 58% yield with 80:20 er. From this ligand survey it was clear that TADDOL-derived phosphonites provided the best regio- and enantioselectivities in the Pt-catalyzed diene diboration reaction.

---

The influence of the substitution pattern on the aryl rings of the TADDOL backbone was then examined to improve selectivity in the diboration reaction (Table 1.4).

At this point, it had also been determined that toluene was a superior solvent to tetrahydrofuran in the diboration of trans-1,3-pentadiene, and all subsequent diboration reactions were carried out in toluene at 60 °C. Increasing the size of the 3- and 5-substituents on the TADDOL backbone from hydrogen (ligand \((R,R)-1.31\)) to methoxy (ligand \((R,R)-1.32\)) or methyl (ligand \((R,R)-1.32\)) showed similar levels of enantioselectivity, but the regioselectivity was increased to >20:1 in both cases, leading to improved isolated yield of the desired product (entries 2 and 3). However, when further
increasing the steric bulk of the aryl rings on the TADDOL backbone, the regioselectivity and enantioselectivity were dramatically diminished (entries 4-8). The results shown in entries 9 and 10 suggest that TADDOL-derived phosphonite ligands containing aryl rings with an electron-donating group in the para-position give the 1,4-diboration product with slightly decreased enantioselectivity and start to favor the 1,2-diboration pathway as compared with ligand \((R,R)-1.33\).

Table 1.4. TADDOL-Derived Phosphonite Ligands in Pt-Catalyzed Diene Diboration

<table>
<thead>
<tr>
<th>entry</th>
<th>ligand</th>
<th>Ar</th>
<th>((1,4):(1,2)^a)</th>
<th>% yield(^b)</th>
<th>er(^c)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>((R,R)-1.31)</td>
<td>Ph</td>
<td>4.3:1</td>
<td>75</td>
<td>85:15</td>
</tr>
<tr>
<td>2</td>
<td>((R,R)-1.32)</td>
<td>3,5-(MeO)(_2)Ph</td>
<td>&gt;20:1</td>
<td>97</td>
<td>84:16</td>
</tr>
<tr>
<td>3</td>
<td>((R,R)-1.33)</td>
<td>3,5-Me(_2)Ph</td>
<td>&gt;20:1</td>
<td>82</td>
<td>85:15</td>
</tr>
<tr>
<td>4</td>
<td>((R,R)-1.34)</td>
<td>3,5-Et(_2)Ph</td>
<td>16.7:1</td>
<td>69</td>
<td>76:24</td>
</tr>
<tr>
<td>5</td>
<td>((R,R)-1.35)</td>
<td>3,5-(t)-Bu(_2)Ph</td>
<td>3.4:1</td>
<td>53</td>
<td>66:34</td>
</tr>
<tr>
<td>6</td>
<td>((R,R)-1.36)</td>
<td>3-(i)-Pr-Ph</td>
<td>11:1</td>
<td>80</td>
<td>77:23</td>
</tr>
<tr>
<td>7</td>
<td>((R,R)-1.37)</td>
<td>1-naphthyl</td>
<td>2.6:1</td>
<td>39</td>
<td>78:22</td>
</tr>
<tr>
<td>8</td>
<td>((S,S)-1.38)</td>
<td>2-naphthyl</td>
<td>5:1</td>
<td>63</td>
<td>15:85</td>
</tr>
<tr>
<td>9</td>
<td>((R,R)-1.39)</td>
<td>3,5-Me(_2)-4-MeO-Ph</td>
<td>1:1.7</td>
<td>59</td>
<td>84:16</td>
</tr>
<tr>
<td>10</td>
<td>((R,R)-1.40)</td>
<td>3,5-F(_2)-4-MeO-Ph</td>
<td>1:1.1</td>
<td>22</td>
<td>83:17</td>
</tr>
</tbody>
</table>

\(^a\) The regioselectivity was determined from the crude \(^1\)H NMR of the 1,3-diol obtained by subjecting the intermediate 1,4-bis(boronate)ester \(1.20\) to an allylation with benzaldehyde, followed by oxidation. \(^b\) The isolated yield was determined by analysis of the diboration/allylation/oxidation product. \(^c\) The er was determined by chiral GC analysis of the diboration/allylation/oxidation product.
To further improve the enantioselectivity in the Pt-catalyzed diene diboration reaction, the use of mixed TADDOL ligands containing different functional groups on the TADDOL backbone was tested in the diboration of trans-1,3-pentadiene. When analyzing a 3D-structure of the ligand bound to platinum (vide infra), it was hypothesized that the pseudo-equatorial and pseudo-axial substituents on the TADDOL backbone would have different influences on the steric environment of the metal (Figure 1.1). Therefore, the use of mixed TADDOL ligands (i.e. R¹ ≠ R²) might enhance the steric biases surrounding the metal center and improve enantioselectivity.

**Figure 1.1.** Mixed TADDOL Ligand Bound to Platinum

![Mixed TADDOL Ligand Bound to Platinum](image)

Results with mixed TADDOL ligands in the enantioselective diboration of trans-1,3-pentadiene are shown in Table 1.5. Ligands *(R,R)*-1.42 and *(R,R)*-1.43 containing one alkyl and one aryl substituent showed excellent reactivity in the diboration reaction, providing 95% and 84% yield of the 1,4-diboration product respectively; however, the products were nearly racemic (entries 1 and 2). When employing mixed
TADDOL ligands with different aryl rings on the backbone, both the regioselectivity and enantioselectivity were diminished as compared with \((R,R)-1.33\) (entries 3 and 4).

Another tunable moiety of the TADDOL-derived phosphonite ligands that was explored for the diene diboration reaction was the aromatic group on phosphorous. Because phosphorous is directly attached to the metal center in the active catalyst, changes to the functional group on phosphorous should have a significant impact on the level of stereochemical induction in the diboration reaction. A variety of TADDOL-derived phosphonite ligands with modified aryl substitution on phosphorous were
synthesized and surveyed in the Pt-catalyzed diboration of trans-1,3-pentadiene (Table 1.6). Increasing the steric bulk of the aryl ring on phosphorous with ligands derived from the parent TADDOL (Ar¹=Ph) severely decreased the regio- and enantioselectivities (entry 1-4). Altering the electronic properties of the aryl substituent on phosphorous with ligand \((R,R)-1.51\) gave a 1:1 mixture of regioisomers and only 28% yield of the 1,4-diboration product in 82:18 er. When utilizing TADDOL-derived ligands with \(m\)-xylyl rings on the backbone, a similar trend was observed. If the steric bulk of \(Ar_2\) was too large, both the regio- and enantioselectivity were sharply diminished as compared with \((R,R)-1.33\). Ligand \((R,R)-1.52\), containing a \(m\)-xylyl ring on phosphorous, gave 49% yield of the 1,4-product in 92:8 er, but showed decreased regioselectivity.
Having surveyed a variety of TADDOL-derived ligands in the enantioselective Pt-catalyzed 1,4-diboration of trans-1,3-pentadiene it was determined that \((R,R)-1.33\) was the optimal ligand in the diboration reaction due to the high levels of regioselectivity and enantioselectivity obtained with this ligand (Table 1.6, entry 7). Although ligand \((R,R)-1.52\) showed improved levels of enantioselectivity compared with ligand \((R,R)-1.33\) (92:8 er versus 85:15 er), the difficult synthesis of \((R,R)-1.52\) and lower

### Table 1.6. Aryl-Phosphorous Derivatives of TADDOL-Derived Phosphonite Ligands in Pt-Catalyzed Diene Diboration

<table>
<thead>
<tr>
<th>entry</th>
<th>ligand</th>
<th>(\text{Ar}^1)</th>
<th>(\text{Ar}^2)</th>
<th>((1,4):(1,2)^a)</th>
<th>% yield(^b)</th>
<th>er(^c)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>((R,R)-1.46)</td>
<td>Ph</td>
<td>3,5-Me(_2)Ph</td>
<td>3.8:1</td>
<td>82</td>
<td>85:15</td>
</tr>
<tr>
<td>2</td>
<td>((R,R)-1.47)</td>
<td>Ph</td>
<td>3,5-(t)-Bu(_2)Ph</td>
<td>1.7:1</td>
<td>41</td>
<td>76:24</td>
</tr>
<tr>
<td>3</td>
<td>((R,R)-1.48)</td>
<td>Ph</td>
<td>2-MePh</td>
<td>1:1</td>
<td>44</td>
<td>58:42</td>
</tr>
<tr>
<td>4</td>
<td>((R,R)-1.49)</td>
<td>Ph</td>
<td>1-naphthyl</td>
<td>1:4.4</td>
<td>9</td>
<td>60:40</td>
</tr>
<tr>
<td>5</td>
<td>((R,R)-1.50)</td>
<td>Ph</td>
<td>2-naphthyl</td>
<td>&gt;20:1</td>
<td>73</td>
<td>81:19</td>
</tr>
<tr>
<td>6</td>
<td>((R,R)-1.51)</td>
<td>Ph</td>
<td>4-OMePh</td>
<td>1:1</td>
<td>28</td>
<td>82:18</td>
</tr>
<tr>
<td>7</td>
<td>((R,R)-1.33)</td>
<td>3,5-Me(_2)Ph</td>
<td>Ph</td>
<td>&gt;20:1</td>
<td>82</td>
<td>85:15</td>
</tr>
<tr>
<td>8</td>
<td>((R,R)-1.52)</td>
<td>3,5-Me(_2)Ph</td>
<td>3,5-Me(_2)Ph</td>
<td>5:1</td>
<td>49</td>
<td>92:8</td>
</tr>
<tr>
<td>9</td>
<td>((R,R)-1.53)</td>
<td>3,5-Me(_2)Ph</td>
<td>3,5-(t)-Bu(_2)Ph</td>
<td>1.2:1</td>
<td>32</td>
<td>60:40</td>
</tr>
<tr>
<td>10</td>
<td>((R,R)-1.54)</td>
<td>3,5-Me(_2)Ph</td>
<td>1-naphthyl</td>
<td>1.7:1</td>
<td>trace</td>
<td>-</td>
</tr>
</tbody>
</table>

\(^a\) The regioselectivity was determined from the crude \(^1\)H NMR of the 1,3-diol obtained by subjecting the intermediate 1,4-bis(boronate)ester \(1.20\) to an allylation with benzaldehyde, followed by oxidation. \(^b\) The isolated yield was determined by analysis of the diboration/allylation/oxidation product. \(^c\) The er was determined by chiral GC analysis of the diboration/allylation/oxidation product.
isolated yield and regioselectivity obtained led us to move forward with ligand \((R,R)-1.33\) in an expanded solvent survey in the diene diboration reaction. A number of polar and non-polar aprotic solvents were examined in the reaction as shown in Table 1.7. Other aromatic solvents, including benzene and (trifluoromethyl)benzene gave good yields of the desired 1,4-diboration product, but with decreased regio- and enantiomeric purity as compared to toluene (entries 1-3). Hexane, a non-aromatic, non-polar solvent provided the 1,4-product with the same level of enantiopurity as toluene; however, the regioselectivity and isolated yield were diminished (entry 4). Polar, non-aromatic solvents such as tert-butyl methyl ether, tetrahydrofuran and ethyl acetate gave lower yields as well as decreased regio- and enantioselectivities (entries 5-7). Employing halogenated solvents, such as dichloromethane, inhibited the diboration reaction, most likely due to insertion of the Pt(0)-catalyst into one of the C-Cl bonds. Toluene was therefore determined to be the optimal solvent for the Pt-catalyzed enantioselective 1,4-diboration of 1,3-dienes.
Table 1.7. Solvent Study with \((R,R)\)-xylylTADDOL-PPh \((R,R)\)-1.33 in Diene Diboration

\[
\begin{align*}
\text{Pt(dba)}_3 & \; (3 \text{ mol\%}) \\
(R,R)-1.33 & \; (6 \text{ mol\%}) \\
& \xrightarrow{\text{B}_2(\text{pin})_2, \text{ solvent}} \\
& 60 ^\circ \text{C, 14 h} \\
\end{align*}
\]

<table>
<thead>
<tr>
<th>entry</th>
<th>solvent</th>
<th>((1,4):(1,2)^a)</th>
<th>% yield$^b$</th>
<th>er$^c$</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>PhMe</td>
<td>&gt;20:1</td>
<td>75</td>
<td>85:15</td>
</tr>
<tr>
<td>2</td>
<td>PhH</td>
<td>12.3:1</td>
<td>69</td>
<td>83:17</td>
</tr>
<tr>
<td>3</td>
<td>PhCF$_3$</td>
<td>9.8:1</td>
<td>82</td>
<td>82:18</td>
</tr>
<tr>
<td>4</td>
<td>(n)-C$<em>6$H$</em>{14}$</td>
<td>6.2:1</td>
<td>68</td>
<td>85:15</td>
</tr>
<tr>
<td>5</td>
<td>(t)-BuOMe</td>
<td>6.2:1</td>
<td>62</td>
<td>83:17</td>
</tr>
<tr>
<td>6</td>
<td>THF</td>
<td>15:1</td>
<td>58</td>
<td>80:20</td>
</tr>
<tr>
<td>7</td>
<td>EtOAc</td>
<td>7.3:1</td>
<td>61</td>
<td>84:16</td>
</tr>
<tr>
<td>8</td>
<td>CH$_2$Cl$_2$</td>
<td>-</td>
<td>0</td>
<td>-</td>
</tr>
</tbody>
</table>

$^a$ The regioselectivity was determined from the crude $^1$H NMR of the 1,3-diol obtained by subjecting the intermediate 1,4-bis(boronate)ester 1.20 to an allylation with benzaldehyde, followed by oxidation. $^b$ The isolated yield was determined by analysis of the diboration/allylation/oxidation product. $^c$ The er was determined by chiral GC analysis of the diboration/allylation/oxidation product.

Until this point, analysis of the diboration reaction was carried out on syn-1,3-diol 1.55, which was obtained by subjecting the intermediate 1,4-bis(boronate)ester to an allylation with benzaldehyde followed by oxidation (Scheme 1.12). It was assumed that conservation of enantiomeric purity was high enough that the er for 1.55 reflected the er for 1.20. To simplify and further improve the utility of the diene diboration reaction, the direct oxidation of 1,4-bis(boronate)ester 1.20 with H$_2$O$_2$ and NaOH was examined and found to provide 1,4-diol 1.56 in equivalent yield and enantiomeric purity as 1,3-diol.
There are only two other examples of a direct 1,4-oxygenation of acyclic 1,3-dienes,\textsuperscript{20} and they are not subject to high levels of stereocontrol with chiral ligands. Furthermore, aside from the Lindlar reduction of 1,4-butyndiols, there are limited methods for the synthesis of (Z)-1,4-diols.\textsuperscript{21} Therefore, the synthesis of enantioenriched 1,4-diols via Pt-catalyzed 1,4-diboration of 1,3-dienes is of great synthetic value.

**Scheme 1.12.** Direct Oxidation of the 1,4-Bis(Boronate)Ester to the 1,4-Diol

\[
\text{Me} = \begin{array}{c}
\text{Me} \\
\text{Ph} \\
\text{Ph}
\end{array}
\]

With the optimal conditions for the enantioselective Pt-catalyzed diene diboration in hand, a variety of acyclic terminal 1,3-dienes were prepared and examined to determine substrate scope of the reaction (Table 1.8). Increasing the size of the alkyl chain on the 1,3-diene substrate from methyl to hexyl and homobenzyl improved the


enantioselectivity in the diboration reaction, providing the corresponding 1,4-diols in 83% yield, 92:8 er and 81% yield, 92:8 er respectively (entries 1 and 2). Further increasing the steric bulk adjacent to the diene with branched alkyl substitution resulted in higher levels of enantioselectivity giving the 1,4-diol products in 96:4 er (entries 3-5). However, this also led to decreased regioselectivity lowering the isolated yield of the 1,4-diboration product. The increased steric bulk next to C4 of the diene makes carbon-boron bond formation more difficult at that position, resulting in competing 1,2-diboration of the terminal olefin. Dienes bearing substitution at the 2- and 3-position were tolerated, but suffered from lower levels of enantioselectivity with \((R,R)-1.33\). Nevertheless, when the more sterically bulky ligand \((R,R)-1.35\) was employed, the enantioselectivity was improved, allowing access to trisubstituted \((Z)\)-allylic alcohols with synthetically useful levels of enantiopurity and complete alkene sterecontrol (entries 6 and 7). Protected allylic oxygenation was also tolerated in the reaction, with larger protecting groups giving higher levels of selectivity. However, these substrates proved to be less reactive in the diboration reaction and required either additional \(\text{B}_2(\text{pin})_2\) or heat to provide useful amounts of the desired product. 1,3-Dienes bearing conjugated aromatic substitution were also tested in the Pt-catalyzed diboration and these were converted to the corresponding 1,4-diols in up to 98:2 er. These substrates were more reactive than the aliphatic dienes, and the diboration reaction could be carried out at room temperature.
Table 1.8. Pt-Catalyzed Diene Diboration Substrate Scope: Acyclic Dienes

\[
\begin{align*}
\text{Pt(dba)}_3 \text{ (3 mol\%)} & \quad \text{ligand (6 mol\%)} \\
& \quad \text{B}_2\text{(pin)}_2, \text{ toluene, } 60 \, ^\circ\text{C, 12 h} \\
& \quad \text{then H}_2\text{O}_2, \text{ NaOH, rt, 3 h}
\end{align*}
\]

\[
\begin{array}{ccccccc}
\text{entry} & \text{diene} & \text{product} & \% \text{ yield}^a & \text{er}^b \\
1 & \text{C}_6\text{H}_{13} & \text{C}_6\text{H}_{13} & 83 & 92:8 \\
2 & \text{Ph} & \text{Ph} & 81 & 92:8 \\
3 & \text{Cy} & \text{Cy} & 83 & 96:4 \\
4 & \text{tBu} & \text{tBu} & 49 & 96:4 \\
5 & \text{BnO} & \text{BnO} & 48 & 96:4 \\
6 & \text{Me} & \text{Me} & 95^c & 81:19 \\
7 & \text{Me} & \text{Me} & 89^c & 73:27 \\
8 & \text{TBDPSO} & \text{TBDPSO} & 70 & 94:6^d \\
9 & \text{BnO} & \text{BnO} & 83 & 81:19^e \\
10 & \text{Ph} & \text{Ph} & 77 & 92:8^f \\
11 & \text{o-tolyl} & \text{o-tolyl} & 89 & 98:2^f \\
\end{array}
\]

\(\text{ligand:}\)

\[
\begin{array}{c}
\text{Me} \\
\text{O} \\
\text{P-Ph} \\
\text{Me} \\
\text{Me} \\
\text{Ar} \\
\text{Ar} \\
\text{Ar} \\
\text{Ar} \\
\end{array}
\]

\[
\begin{array}{c}
\text{(R,R)-1.33: } \text{Ar} = 3,5\text{-dimethylphenyl} \\
\text{(R,R)-1.35: } \text{Ar} = 3,5\text{-di-t-butylphenyl}
\end{array}
\]

\(\text{a Isolated yield of purified material. Value is an average of two experiments. b Determined by GC analysis of a derivitized product. c (S,S)-1.35 used as ligand. d Diboration run with 3.0 equiv B}_2\text{(pin)}_2. e Diboration run at 80 \, ^\circ\text{C. f Diboration run at room temperature.}\)
We next investigated the Pt-catalyzed diboration of cyclic dienes. The 1,4-dioxygenation of cyclic 1,3-dienes has been previously accomplished using a [4+2] cycloaddition of $^{1}\text{O}_2$ with cyclohexadiene derivatives; however, the use of a chiral catalyst in this reaction has yet to be achieved and substrate control is necessary to induce stereoselectivity. The only enantioselective method that accomplishes this transformation was a Pd-catalyzed dialkoxylation reaction described by Bäckvall and co-workers. Unfortunately, the chiral benzoquinone ligands used in their method did not surpass 77:23 er. Utilizing the optimal conditions for the enantioselective Pt-catalyzed diboration, we were pleased to see that cyclic 1,3-dienes reacted to form the diboration/oxidation products in good yield and with useful levels of enantiopurity (Table 1.9). This method represents the state of the art for 1,4-dioxygenation of cyclic 1,3-dienes. Cyclic 1,3-dienes bearing substitution at C2 gave the desired 1,4-diol in 83% yield and 94:6 er after oxidation of the 1,4-bis(boronate)ester intermediate (entry 1). Dienes containing substitution at C1 underwent 1,2-diboration of the less substituted alkene to provide the corresponding 1,2-diol in good yield and enantiopurity. Increasing the sterics of the C1 group from Me to Cy led to a decrease in enantioselectivity from 93:7 to 80:20 (entries 2 and 3). Interestingly, 1-methoxy-1,3-cyclohexadiene was tolerated in the diene diboration reaction; however, the product was obtained in only 51% yield and 73:27 er (entry 4). Treatment of the 1,2-diol obtained from the diboration/oxidation reaction with mild acid allows access to 4-hydroxycyclohexenone, a widely utilized intermediate for the

synthesis of biologically relevant compounds. Due to the wide array of TADDOL-derived ligands available, it is likely that a modified ligand structure would afford the product with higher levels of enantiomeric purity.

**Table 1.9. Pt-Catalyzed Diene Diboration Substrate Scope: Cyclic Dienes**

<table>
<thead>
<tr>
<th>entry</th>
<th>diene</th>
<th>product</th>
<th>% yield&lt;sup&gt;a&lt;/sup&gt;</th>
<th>er&lt;sup&gt;b&lt;/sup&gt;</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>n-Bu</td>
<td>n-Bu</td>
<td>83</td>
<td>94:6</td>
</tr>
<tr>
<td>2</td>
<td>Me</td>
<td>Me</td>
<td>68</td>
<td>93:7</td>
</tr>
<tr>
<td>3</td>
<td>Cy</td>
<td>Cy</td>
<td>65(15)&lt;sup&gt;c&lt;/sup&gt;</td>
<td>80:20</td>
</tr>
<tr>
<td>4</td>
<td>MeO</td>
<td>MeO</td>
<td>51</td>
<td>73:27</td>
</tr>
</tbody>
</table>

<sup>a</sup> Isolated yield of purified material. Value is an average of two experiments. <sup>b</sup> Determined by GC or SFC analysis of a derivatized product. <sup>c</sup> Yield in parentheses is of the 1,4-diboration product.
To further probe the capabilities of the catalyst system for the enantioselective
diboration of 1,3-dienes, preliminary experiments were conducted to determine if
stereocontrol in the diboration of chiral dienes would be dictated by the substrate or the
catalyst. Chiral diene 1.57 was synthesized as a single enantiomer\textsuperscript{24} and subjected to the
platinum-catalyzed diboration reaction with both enantiomers of ligand 1.33. When
(R,R)-1.33 was employed, 1,4-diol 1.58 was obtained in 84% yield with 2:1 dr,
representing the mismatched ligand/substrate combination (Scheme 1.13, eq 1). Ligand
(S,S)-1.33 provided 1,4-diol 1.59 in 80% yield with 5.4:1 dr, representing the matched
case (Scheme 1.13, eq. 2). The major diastereomer in both cases was determined by X-
ray crystallography. The differing and low levels of diastereoselectivity obtained with
each enantiomer of ligand showed a lack of catalyst control in the Pt-catalyzed diene
diboration reaction. It is interesting to note that the use of PCy\textsubscript{3} as the ligand in the
diboration of diene 1.57 resulted in only 42% yield of the desired 1,4-diol in a 1:1
mixutre of diastereomers (Scheme 1.13, eq. 3).

\textsuperscript{24} Evans, D. A.; Ennis, M. D.; Mathre, D. J. J. Am. Chem. Soc. 1982, 104, 1737.
Scheme 1.13. Catalyst Control vs Substrate Control in Pt-Catalyzed Diene Diboration

The 1,4-diboration of internal 1,3-dienes was also examined using the optimized catalyst system (Scheme 1.14). Excitingly, the diboration of diene 1.60 proceeded with complete regioselectivity, providing the corresponding 1,4-diol 1.61 in 68% yield, >20:1 dr and 70:30 er. The low level of stereochemical induction in the diboration of this substrate is not surprising due to the steric similarity of the substituents at the termini of the diene. Amongst prochiral internal 1,3-dienes, this is likely one of the most challenging substrates, and future optimization of ligand structure and reaction conditions are of great interest.
**Scheme 1.14.** Enantioselective Pt-Catalyzed Diboration of Internal 1,3-Dienes

In an attempt to improve the enantioselectivity of the Pt-catalyzed diboration of aliphatic 1,3-dienes, the use of the chiral diboron reagent $\text{B}_2[(+)-\text{pinanediolate}]_2$ was investigated in conjunction with the chiral ligand (Scheme 1.15). Unfortunately, no improvements were observed with either (R,R)-1.33 (eq. 1) or (S,S)-1.33 (eq. 2).

**Scheme 1.15.** Enantioselective Pt-Catalyzed Diene Diboration with Chiral Diboron

In an attempt to improve the enantioselectivity of the Pt-catalyzed diboration of aliphatic 1,3-dienes, the use of the chiral diboron reagent $\text{B}_2[(+)-\text{pinanediolate}]_2$ was investigated in conjunction with the chiral ligand (Scheme 1.15). Unfortunately, no improvements were observed with either (R,R)-1.33 (eq. 1) or (S,S)-1.33 (eq. 2).
1.4. Product Utility in the Enantioselective Pt-Catalyzed Diboration of 
trans-1,3-Dienes

After successfully developing the first enantioselective 1,4-diboration of 
trans-1,3-dienes, it was of great interest to determine the utility of the diboration products 
in the synthesis of complex molecules. In addition to the formation of 2-buten-1,4-diols, 
diene diboration can offer a novel approach to the synthesis of enantiomerically enriched 
butenolides from simple and inexpensive 1,3-dienes (Scheme 1.16). Butenolides (1.65) 
and their derived butyrolactones (1.66) are prevalent in a wide variety of natural products 
and biologically active compounds, but few methods exist for their preparation.25 
Following diboration and oxidation of 1,3-decadiene, the unpurified 1,4-diol is perfectly 
situated to undergo oxidative cyclization to the butenolide. Subsequent oxidation using 
TPAP and NMO afforded the cyclized butenolide 1.64 in 68% yield over two steps with 
no loss of enantiopurity.26

Scheme 1.16. Butenolide Formation from Diboration/Oxidation Products

It was also found that the α-chiral allylboronate functionality embedded in the 1,4-bis(boronate)ester products can also be utilized for stereoselective allylation of aldehydes to form syn-1,3-diols. As an example, after the diboration, benzaldehyde was added to the reaction mixture and the allylation was allowed to proceed at room temperature for 6 h. Upon oxidation of the remaining carbon-boron bond, the diboration/allylation/oxidation product 1.68 was obtained in 66% yield and 91:9 er showing complete conservation of enantiomeric purity from the allylboronate to the aldehyde (Scheme 1.17). It is noteworthy that the product was obtained as a single constitutional isomer and that only one of the two possible allylboronate moieties present in 1.67 reacted to give the observed product. The allylation likely proceeds through transition state 1.69, minimizing A(1,3) strain, and with carbon-carbon bond formation occurring at the least hindered carbon of intermediate 1.67.
**Scheme 1.17. Utility of Diene Diboration Products in Aldehyde Allylation**

**1.5. Mechanistic Discussion for the Enantioselective Pt-Catalyzed Diboration of trans-1,3-Dienes**

With the first enantioselective 1,4-diboration of trans-1,3-dienes in hand, it was of interest to learn about the mechanistic details of the reaction. Specific focus was placed on the origin of the 1,4-selectivity, and the preference for the cis-alkene. A variety of possible reaction mechanisms were considered, including a mechanism analogous to that of allene diboration as discussed in Section 1.2, in which Pt coordinates to the least sterically hindered alkene of the diene and insertion occurs to form the primary carbon-boron bond first (Scheme 1.18). This mechanism provides an internal Pt-π(allyl) complex that would appear to have little steric or electronic preference for either reductive elimination pathway and may provide the 1,4- or 1,2-diboration product. Given the high
levels of regioselectivity observed in the diene diboration reaction favoring the 1,4-diboration pathway using the Pt/TADDOL-derived catalyst system, we reasoned that an alternate mechanism was operative.

**Scheme 1.18.** Possible Mechanism for Pt-Catalyzed Diboration of *trans*-1,3-Dienes

There are a few examples in the literature of reactions of transition-metal complexes with 1,3-dienes, but the work reported by Hughes and Powell in the early 1970s on polymerization reactions of Pd-allyl complexes with 1,3-dienes was particularly informative (Scheme 1.19).27 They propose a reaction mechanism in which the least sterically hindered olefin of the diene coordinates to palladium and that carbon-carbon bond formation occurs at C4 of the diene, remote from the metal center, through an electrocyclic-like transition state, 1.71. The carbon-carbon bond formation between C3 of the Pd-allyl and C4 of the diene can only occur when the diene adopts the S-cis conformation, positioning the C4 carbon in close proximity to the Pd-allyl species.

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**Scheme 1.19.** Proposed Mechanism for Pd-Catalyzed Polymerization of Pd-Allyl Complexes with 1,3-Dienes.

A similar mechanism for the Pt-catalyzed diboration of trans-1,3-dienes would explain the high levels of 1,4-regioselectivity observed in the reaction, as well as the formation of the (Z)-alkene (Scheme 1.18). The first step of the mechanism is likely oxidative addition of the Pt(0)-L complex into B_2(pin)_2 to arrive at the Pt-bis(boryl) species 1.72. Coordination of the diene in the S-cis conformation then occurs, with the least sterically hindered olefin binding to Pt(II). Carbon-boron bond formation then takes place at C4 of the diene as shown in structure 1.73, forming the secondary C-B bond first and provides the least sterically hindered Pt-π(allyl) complex 1.74. Reductive elimination from 1.74 then affords the observed 1,4-bis(boronate)ester 1.75. The key feature of the mechanism is the adoption of the S-cis conformation by the diene, explaining the 1,4-regioselectivity and the presence of the (Z)-alkene in the diboration product.
1.6. Conclusions

The first enantioselective platinum-catalyzed 1,4-diboration of *trans*-1,3-dienes was developed to afford 1,4-bis(boronate)esters in high yields and enantioselectivities. The direct oxidation of the bis(boryl) intermediates was accomplished to access 1,4-diols, representing the most enantioselective route to these structures. In addition, the reactive allylboronate intermediate was used in aldehyde allylation with complete conservation of enantiomeric purity to provide enantiomerically enriched *syn*-1,3-diols from simple and inexpensive starting materials. Furthermore, the diboration/oxidation product was used to synthesize a butenolide functionality, offering a novel approach to a variety of complex natural products.
1.7. Experimentals

1.7.1. General Information. $^1$H NMR spectra were recorded on Varian Unity Inova 500 MHz and Varian Gemini 400 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, integration, multiplicity ($s$ = singlet, $d$ = doublet, $t$ = triplet, $q$ = quartet, br = broad, $m$ = multiplet), coupling constants (Hz) and assignment. $^{13}$C {$^1$H}NMR spectra were recorded on Varian Unity Inova 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). $^{31}$P {$^1$H}NMR (121 MHz) were recorded on a Varian Unity Inova 300 spectrometer. Chemical shifts are reported for $^{31}$P NMR spectra using phosphoric acid as an external standard. Infrared (IR) spectra were recorded on a Bruker $\alpha$-P Spectrometer. Frequencies are reported in wavenumbers (cm$^{-1}$) as follows: strong (s), broad (br), medium (m), and weak (w). High-resolution mass spectrometry (ESI) was performed at Boston College, Chestnut Hill, MA. Elemental analysis was measured by Robertson Microlit Laboratories, Madison, NJ.

Liquid chromatography was performed using forced flow (flash chromatography) on silica gel (SiO$_2$, 230 x 450 Mesh) purchased from Silicycle. Thin layer chromatography was performed on 25 $\mu$m silica gel glass backed plates from Silicycle. Visualization was performed using ultraviolet light (254 nm), phosphomolybdic acid (PMA), and potassium permanganate (KMnO$_4$).
Analytical chiral gas-liquid chromatography (GLC) was performed on a Hewlett-Packard 6890 Series chromatograph equipped with a split mode capillary injection system, a flame ionization detector, and a Supleco β-Dex 120 column with helium as the carrier gas. Analytical chiral supercritical fluid chromatography (SFC) was performed on a Berger Instruments Supercritical Chromatograph equipped with an Alcott auto sampler and a Knauer UV detector with methanol as the modifier. Analytical chiral high-performance liquid chromatography (HPLC) was performed on a Shimadzu SCL-10A liquid chromatograph equipped with a UV detector and a Daicel Chiracel-OD column.

All reactions were conducted in oven- or flame-dried glassware under an inert atmosphere of nitrogen or argon. Toluene, tetrahydrofuran, methylene chloride, and diethyl ether were purified using Pure Solv MD-4 solvent purification system, from Innovative Technology, Inc., by passing the solvent through two activated alumina columns after being purged with argon. Triethylamine was distilled from calcium hydride. Potassium tetrachloroplatinate(II) was purchased from Strem Chemicals, Inc. Bis(pinacolato)diboron was obtained from Allychem Co., Ltd. and recrystallized from pentanes prior to use. Dibenzylideneacetone was purchased from Oakwood Chemicals. 1-methyl-1,3-cyclohexadiene were purchased from ChemSampCo. trans-1,3-hexadiene and cis-1,3-pentadiene were purchased from TCI America. Tetrapropylammonium perruthenate was purchased from Strem Chemicals, Inc. All other reagents were purchased from Aldrich and used without further purification.
1.7.2. Preparation of Pt(dba)$_3$.

Tris(dibenzylideneacetone)platinum was prepared using the literature procedure\textsuperscript{1} with slight modification. To a three-neck 500 mL round-bottom flask equipped with a magnetic stir bar and reflux condenser was added dibenzylideneacetone (3.95 g, 16.8 mmol), tetrabutylammonium chloride (2.0 g, 7.2 mmol), and sodium acetate (3.55 g, 43.3 mmol). Methanol (210 mL) was added and the solution was warmed to 70 °C in an oil bath until the solids dissolved (5 minutes). In a separate 50 mL pear-shaped flask was added potassium tetrachloroplatinate (1.00 g, 2.41 mmol) and water (8 mL), and the mixture gently warmed until solids dissolved. The contents of the pear shaped flask were transferred to the three-neck flask and the reaction was allowed to stir at 70 °C for 3 hours. After 3 h, the reaction was cooled to ambient temperature, transferred to a one-neck 500 mL round-bottom flask and concentrated by rotary evaporation to half the volume. The reaction mixture was then filtered on a Büchner funnel and the remaining solids were washed with copious amounts of water and methanol until all yellow dibenzylideneacetone crystals were removed. The resulting solid residue was placed under high vacuum for 24 hours to remove residual methanol and water. This procedure furnished a dark brown solid (1.84 g, 85% yield) consistent with Pt(dba)$_3$. Anal Calc’d for C$_{51}$H$_{42}$O$_3$Pt: C, 68.22; H, 4.71. Found: C, 67.09; H, 4.49 (average of two experiments). Platinum analysis was performed by ICP Optical Emission Spectroscopy; calculated for Pt(dba)$_3$: 21.73% Pt; found 21.92% (average of two experiments).

1.7.3. Ligand Synthesis

1.7.3.1. BINOL-Derived Ligands. All BINOL-derived ligands were prepared following the literature procedures and spectral data were in accordance with the literature as follows: 1.23 and 1.24,2 1.25,3 1.26,4 1.27.5

1.7.3.2. Representative Procedure for the Synthesis of TADDOL-Derivatives. 3,5-DiethylphenylTADDOL was prepared according to the literature procedure6 with slight modification. To a flame dried 100 mL 2-neck round bottom flask equipped with magnetic stir bar and reflux condenser was added crushed magnesium turnings (401.0 mg, 16.50 mmol) under N2. The apparatus was flame-dried again, a single crystal of I2 was added and the reaction mixture was diluted with tetrahydrofuran (29 mL). To another flame dried 25 mL pear-shaped flask was added 1-bromo-3,5-diethylbenzene (3.91 g, 18.33 mmol) and tetrahydrofuran (12 mL). The solution of 1-bromo-3,5-diethylbenzene in tetrahydrofuran was slowly added to the magnesium mixture at room temperature via syringe. The reaction was allowed to reflux at 80 °C in an oil bath for 2 h, at which time the reaction was cooled to 0 °C, and a solution of (4R,5R)-2,2-dimethyl-1,3-dioxolane-4,5-dicarboxylic acid in tetrahydrofuran (4 mL) was added slowly via syringe.

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The reaction was allowed to reflux for 12 h, after which it was cooled to 0 °C and quenched with \( \text{NH}_4\text{Cl} \) (10 mL, sat. aq.). The organic and aqueous layers were separated and the aqueous layer was extracted with ethyl acetate (3 x 30 mL). The combined organics were dried over \( \text{Na}_2\text{SO}_4 \), filtered, and concentrated in vacuo. The crude material was purified by silica gel chromatography (1-50% ethyl acetate/hexanes) to afford the title compound as a yellow solid (2.23g, 88% yield).

**3,5-DimethylphenylTADDOL.** Prepared according to the representative procedure. Spectral data are in accordance with the literature.\(^7\)

![3,5-DimethylphenylTADDOL](image)

**3,5-DiethylphenylTADDOL.** \(^1\)H NMR (400 MHz, CDCl\(_3\)): \( \delta \) 0.94 (6H, s), 1.13 (12H, t, \( J = 7.6 \) Hz), 1.22 (12H, t, \( J = 7.6 \) Hz), 2.54 (8H, q, \( J = 15.2 \) Hz, 7.6 Hz), 2.61 (8H, q, \( J = 14.8 \) Hz, 7.2 Hz), 3.78 (2H, s), 4.67 (2H, s), 6.91 (2H, s), 6.96 (2H, s), 7.00 (4H, s), 7.20 (4H, s); \(^{13}\)C NMR (CDCl\(_3\)): \( \delta \) 15.51, 15.94, 27.04, 28.94, 29.08, 76.68, 77.00, 77.32, 78.29, 81.00, 109.2, 124.6, 125.8, 126.1, 126.5, 142.6, 142.7, 143.6, 145.9. IR (neat): 3299 (br w), 2962 (s), 2930 (w).

(m), 1599 (w), 1457 (m), 1238 (w), 1063 (m) 871 (s), 746 (m) cm$^{-1}$. $[\alpha]_D^{20} = +8.555$ ($c = 0.522$, CHCl$_3$, $l = 50$ mm).

**3,5-Di-tert-butylphenylTADDOL.** Prepared according to the representative procedure. Spectral data are in accordance with the literature.$^8$

![3,5-Di-tert-butylphenylTADDOL](image)

**3,5-DimethoxyphenylTADDOL.** Prepared according to the representative procedure. Spectral data are in accordance with the literature.$^9$

![3,5-DimethoxyphenylTADDOL](image)

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3-iso-PropylphenylTADDOL. Prepared according to the representative procedure. \(^1\)H NMR (300 MHz, CDCl\(_3\)): \(\delta\) 0.95 (6H, s), 1.11 (12H, dd, \(J = 7.2, 2.4\) Hz), 1.22 (12H, d, \(J = 6.9\) Hz), 2.73-2.825 (2H, m), 2.831-2.93 (2H, m), 3.69 (2H, s), 4.64 (2H, s), 7.07-7.32 (12H, m), 7.29-7.37 (4H, m).

1-NaphthylTADDOL. Prepared according to the representative procedure. Spectral data are in accordance with the literature.\(^7\)

2-NaphthylTADDOL. Prepared according to the representative procedure. Spectral data are in accordance with the literature.\(^7\)

3,5-Dimethyl-4-methoxyphenylTADDOL. Prepared according to the representative procedure. \(^1\)H NMR (300 MHz, CDCl\(_3\)): \(\delta\) 1.03 (6H, s), 2.17 (12H, s), 2.27 (12H, s), 3.65 (6H, s), 3.74 (6H, s), 3.97 (2H, s), 4.41 (2H, s), 6.92 (4H, s), 7.16 (4H, s).
3,5-Difluoro-4-methoxyphenylTADDOL. Prepared according to the representative procedure. $^1$H NMR (400 MHz, CDCl$_3$): δ 1.19 (6H, s), 3.96 (6H, s), 3.98 (2H, s), 4.02 (6H, s), 4.26 (2H, s), 6.85 (4H, d, $J = 9.6$ Hz), 7.05 (4H, d, $J = 9.6$ Hz).

1.7.3.3. TADDOL-Derived Phosphoramidite and Phosphite Ligand Synthesis. All phosphoramidite ligands were prepared following the literature procedures and spectral data are in accordance with the literature as follows: (R,R)-1.22,$^{10}$ (R,R)-1.28,$^{11}$ (R,R)-1.30.$^{12}$

1.7.3.4. TADDOL-Derived Phosphonite Ligand Synthesis. All phosphonite ligands were prepared following the representative procedure below, and spectral data are in accordance with the literature as follows: (R,R)-1.31,$^{13}$ (R,R)-1.33 and (R,R)-1.35,$^{14}$ (R,R)-1.37 and (R,R)-1.38.$^{15}$

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Representative Procedure for the Preparation of TADDOL-Derived Phosphonites.

To a flame dried 100 mL round bottom flask equipped with magnetic star bar was added 3,5-diethylphenylTADDOL (2.23 g, 3.23 mmol) and tetrahydrofuran (32.3 mL, 0.1 M) under N₂. Triethylamine (1.53 mL, 10.97 mmol) was added via syringe and the reaction mixture was brought to 0 °C in an ice bath. Dichlorophenylphosphine (0.48 mL, 3.55 mmol) was added dropwise via syringe at 0 C, the reaction was brought to room temperature and was allowed to stir for 2 h. The reaction was diluted with Et₂O, filtered through celite and concentrated in vacuo. The crude material was purified by silica gel chromatography (5% ethyl acetate/hexanes) to afford the title compound as a white solid (2.31 g, 90% yield).

\((R,R)\)-3,5-DiethylphenylTADDOLPPh (1.34). \(^1\)H NMR (400 MHz, CDCl₃): \(\delta\) 0.18 (3H, s), 1.20 (24H, m), 1.55 (3H, s), 2.60 (16H, m), 4.89 (1H, d, \(J = 8.4\) Hz), 5.65 (1H, dd, \(J = 8.4\) Hz, 4.8 Hz), 6.87 (1H, s), 6.93 (2H, s), 6.96 (1H, s), 7.07 (2H, s), 7.16 (2H, s), 7.30 (2H, s), 7.47 (3H, s), 7.55 (2H, s), 7.86 (2H, s); \(^{13}\)C NMR (CDCl₃): \(\delta\) 15.42, 15.53, 15.73, 15.92, 24.64, 27.95, 28.94, 29.12, 82.53, 82.77, 83.01, 83.52, 83.59, 84.29, 110.9, 124.5, 124.6, 125.9, 126.3, 126.4, 126.5, 126.6, 128.1, 128.2, 129.7, 130.0, 130.3, 141.5, 141.6, 142.6, 142.9, 143.3, 143.5, 146.3, 146.9. \(^{31}\)P NMR (162 MHz, CDCl₃): \(\delta\) 156.7. IR (neat): 2962 (s), 2931 (m), 2872 (w), 1599 (w), 1458 (m), 1160 (m), 1069 (m), 875 (s), 806 (m) cm⁻¹. \([\alpha]_D^{20} = -59.634 (c = 0.660, \text{CHCl}_3, l = 50\text{ mm}).\)
(R,R)-3,5-DimethoxyphenylTADDOLPPh (1.32). Prepared according to the representative procedure. $^1$H NMR (300 MHz, CDCl$_3$): $\delta$ 0.34 (3H, s), 1.55 (3H, s), 3.67 (6H, s), 3.71 (18H, s), 4.72 (1H, d, $J = 8.7$ Hz), 5.54 (1H, dd, $J = 8.4$, 4.5 Hz), 6.27-6.35 (4H, m), 6.66-6.77 (6H, m), 7.00 (2H, d, $J = 1.5$ Hz), 7.46-7.48 (3H, m), 7.82-7.87 (2H, m); $^{31}$P NMR (121 MHz, CDCl$_3$): $\delta$ 157.5.

(R,R)-3-*i*so-propylphenylTADDOLPPh (1.36). Prepared according to the representative procedure. $^1$H NMR (300 MHz, CDCl$_3$): $\delta$ 0.14 (3H, s), 1.09-1.25 (24H, m), 1.53 (3H, s), 2.77-2.91 (4H, m), 4.81 (1H, d, $J = 8.4$ Hz), 5.59 (1H, dd, $J = 8.7$, 4.8 Hz), 7.01-7.21 (9H, m), 7.31-7.55 (10H, m), 7.83-7.87 (2H, m); $^{31}$P NMR (121 MHz, CDCl$_3$): $\delta$ 156.9.

(R,R)-3,5-dimethyl-4-methoxyphenylTADDOLPPh (1.39). Prepared according to the representative procedure. $^1$H NMR (300 MHz, CDCl$_3$): $\delta$ 0.20 (3H, s), 1.54 (3H, s), 2.205 (6H, s), 2.212 (6H, s), 2.22 (6H, s), 2.25 (6H, s), 3.61 (3H, s), 3.66 (3H, s), 3.67 (3H, s), 3.72 (3H, s), 4.68 (1H, d, $J = 8.7$ Hz), 5.46 (1H, dd, $J = 8.4$, 4.5 Hz), 6.69 (2H, s), 7.04 (2H, s), 7.18 (2H,
$7.47$-$7.49$ (5H, m), $7.78$-$7.83$ (2H, m); $^{31}$P NMR (121 MHz, CDCl$_3$): $\delta$ 155.7.

**(R,R)-3,5-difluoro-4-methoxyphenylTADDOLPPh (1.40).** Prepared according to the representative procedure. $^1$H NMR (300 MHz, CDCl$_3$): $\delta$ 0.43 (3H, s), 1.62 (3H, s), 3.93 (3H, s), 3.96 (3H, s), 3.98 (3H, s), 4.02 (3H, s), 4.41 (1H, d, $J$ = 8.7 Hz), 5.27 (1H, dd, $J$ = 8.7, 4.8 Hz), 6.94 (4H, dd, $J$ = 9.6, 7.5 Hz), 7.08 (2H, d, $J$ = 9.3 Hz), 7.34 (2H, d, $J$ = 9.9 Hz), 7.57-7.59 (3H, m), 7.76-7.81 (2H, m); $^{31}$P NMR (121 MHz, CDCl$_3$): $\delta$ 159.9.

### 1.7.3.5. Mixed TADDOL Phosphonite Ligand Synthesis

Mixed TADDOL-derived ligands were prepared from the dimethyl tartrate acetonide according to the scheme below. The Weinreb amide was prepared following the literature procedure and spectral data are in accordance with the literature.$^{16}$

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Preparation of (1R,1'R)-1,1'-((4R,5R)-2,2-dimethyl-1,3-dioxolane-4,5-diyl)bis(1-phenylethanol).

The following procedure was adapted from the literature.\textsuperscript{17} To a flame-dried round-bottomed flask with a magnetic stir bar was added the diamide (500 mg, 1.81 mmol) and tetrahydrofuran (23 mL). The reaction mixture was cooled to $-78 \, ^\circ C$ (dry ice/acetone) and a solution of phenylmagnesium bromide (8.1 mL, 0.67 M in THF, 5.43 mmol) was added dropwise \textit{via} cannula. The reaction mixture was allowed to stir at $-78 \, ^\circ C$ for 2 h, and was then warmed to room temperature and allowed to stir for another 1.5 h. The reaction was cooled to 0 °C and quenched with NH$_4$Cl (10 mL, sat. aq.). The aqueous layer was separated and washed with ethyl acetate (3 x 20 mL). The combined organic layers were dried over Na$_2$SO$_4$, filtered, and concentrated by rotary evaporation. The crude product was purified by column chromatography on SiO$_2$ (5% ethyl acetate/hexanes) to afford the diketone as a clear, colorless oil (476.7 mg, 85% yield), which was used in the next reaction. To a flame-dried round-bottom flask with a magnetic stir bar was added methylmagnesium bromide (1.8 mL, 0.90 M in 3:1 toluene:THF, 1.61 mmol). The solution was cooled to 0 °C and a 0 °C solution of the diketone (100 mg, 0.125 M in THF, 0.32 mmol) was added slowly under nitrogen atmosphere \textit{via} cannula. The reaction mixture was allowed to stir at 0 °C for 4 h and was then carefully quenched with NH$_4$Cl (10 mL, sat. aq.). The reaction mixture was diluted with water (10 mL) and the layers were separated. The aqueous layer was washed with ethyl acetate (3 x 10 mL) and the

\textsuperscript{17} Prasad, K. R.; Chandrakumar, A. \textit{Synthesis} \textbf{2006}, \textit{13}, 2159.
combined organics were dried over Na$_2$SO$_4$, filtered, and concentrated by rotary evaporation. The crude product was purified by column chromatography on SiO$_2$ (10-20% ethyl acetate/hexanes) to afford the diol as a white solid (96.0 mg, 87% yield).

$(1R,1'R)-1,1'-(4R,5R)-2,2$-dimethyl-1,3-dioxolane-4,5-diyl)bis(1-phenylethanol). $^1$H NMR (300 MHz, CDCl$_3$): $\delta$ 1.29 (6H, s), 1.44 (6H, s), 2.93 (2H, s), 4.18 (2H, s), 7.15-7.27 (6H, m), 7.34-7.38 (4H, m).

$(3aR,4R,8R,8aR)-2,2$-dimethyl-4,6,8-triphenyltetrahydro-[1,3]dioxolo[4,5-e][1,3,2]dioxaphosphepine (1.42). Prepared according to the representative procedure in Section 1.6.4.4. $^1$H NMR (400 MHz, CDCl$_3$): $\delta$ 0.59 (3H, s), 1.01 (3H, s), 4.74 (1H, dd, $J$ = 9.2, 6.0 Hz), 5.08-5.13 (1H, m), 5.56 (1H, dd, $J$ = 12.4, 6.0 Hz), 5.64 (1H, d, $J$ = 6.8 Hz), 7.27-7.41 (11H, m), 7.42-7.52 (8H, m), 7.67 (3H, d, $J$ = 8.4 Hz), 7.76-7.81 (3H, m); $^{31}$P NMR (162 MHz, CDCl$_3$): $\delta$ 163.8. LRMS-(ESI+) for C$_{25}$H$_{26}$O$_4$P [M+H]: calculated: 421.15, found: 421.06.

$(3aR,4R,8R,8aR)-2,2,4,8$-tetramethyl-4,6,8-triphenyltetrahydro-[1,3]dioxolo[4,5-e][1,3,2]dioxaphosphepine (1.43). Prepared according to the
representative procedure in Section 1.6.4.4. \(^1\)H NMR (400 MHz, CDCl\(_3\)): \(\delta\) 0.33 (3H, s), 1.43 (3H, s), 1.72 (3H, s), 1.85 (3H, s), 4.31 (1H, d, \(J = 8.8\) Hz), 4.64 (1H, dd, \(J = 8.8, 4.4\) Hz), 7.25-7.39 (8H, m), 7.46-7.53 (2H, m), 7.61-7.66 (2H, m), 7.80-7.89 (3H, m); \(^{31}\)P NMR (162 MHz, CDCl\(_3\)): \(\delta\) 153.9. LRMS-(ESI+) for C\(_{27}\)H\(_{30}\)O\(_4\)P [M+H]: calculated: 449.18, found: 449.08.

1.7.3.6. Representative Procedure for (R,R)-TADDOL-Derived Phosphonites with Substituted Aryl Phosphines.

The following representative procedure was adapted from a previously reported procedure by Rieger.\(^{18}\) In the glove-box, bis(diethylamino)phosphorous chloride (500.0 mg, 2.37 mmol) was added to an oven-dried round-bottomed flask with a magnetic stir bar. The flask was sealed, brought to the bench, and charged with diethyl ether (4.5 mL) under a N\(_2\) atmosphere. The reaction mixture was cooled to \(-78\) °C and (3,5-di-tert-butylphenyl)magnesium bromide (5.0 mL, 0.52 M in Et\(_2\)O, 2.6 mmol) was added dropwise as a solution in Et\(_2\)O . The reaction was then allowed to warm to rt and stir for

14 h. The reaction mixture was cooled to 0 °C and HCl (7.1 mL, 2.0 M in Et₂O, 14.24 mmol) was added dropwise as a solution in Et₂O. The reaction was allowed to stir at 0 °C for 2 h, and was then cannula filtered to a separate flame-dried round-bottomed flask. The solvent was removed in vacuo and the crude oil was used immediately in the next reaction. Synthesis of the TADDOL-derived phosphonite ligand was performed according to the representative procedure described above (Section 1.6.4.4).

\[(3aR,8aR)-6-(3,5-dimethylphenyl)-2,2-dimethyl-4,4,8,8-
\text{tetraphenyltetrahydro-[1,3]dioxolo[4,5-e][1,3,2]}\]
\text{dioxaphosphepine (1.46).} Spectral data are in accordance with the literature.\(^\text{19}\)

\[(3aR,8aR)-2,2-dimethyl-4,8,8-tetraphenyl-6-(o-tolyl)
\text{tetrahydro-[1,3]dioxolo[4,5-e][1,3,2]}\]
\text{dioxaphosphepine (1.48).} Spectral data are in accordance with the literature.\(^\text{20}\)

(3aR,8aR)-2,2-dimethyl-6-(naphthalen-1-yl)-4,4,8,8-tetraphenyltetrahydro-[1,3]dioxolo[4,5-e][1,3,2]dioxaphosphepine (1.49). Prepared according to the representative procedure in Section 1.6.4.4. $^1$H NMR (300 MHz, CDCl$_3$): δ 0.21 (3H, s), 1.56 (3H, s), 4.84 (1H, d, $J = 8.7$ Hz), 5.79 (1H, dd, $J = 8.7, 4.8$ Hz), 7.12-7.23 (5H, m), 7.25-7.38 (8H, m), 7.40-7.50 (5H, m), 7.55-7.58 (2H, m), 7.62-7.67 (1H, m), 7.84-7.88 (3H, m), 7.98 (1H, d, $J = 8.1$ Hz), 8.21 (1H, dd, $J = 9.0, 4.5$ Hz), 8.39 (1H, t, $J = 6.3$ Hz); $^{31}$P NMR (121 MHz, CDCl$_3$): δ 156.0.

(3aR,8aR)-6-(4-methoxyphenyl)-2,2-dimethyl-4,4,8,8-tetraphenyltetrahydro-[1,3]dioxolo[4,5-e][1,3,2]dioxaphosphepine (1.51). Spectral data are in accordance with the literature.$^{21}$

(3aR,8aR)-4,4,6,8,8-pentakis(3,5-dimethylphenyl)-2,2-dimethyltetrahydro-[1,3]dioxolo[4,5-e][1,3,2]dioxaphosphepine (1.52). Spectral data are in accordance with the literature.$^{22}$

(3aR,8aR)-6-(3,5-di-tert-butylphenyl)-4,4,8,8-tetrakis(3,5-dimethylphenyl)-2,2-dimethyltetrahydro-[1,3]dioxolo[4,5-e][1,3,2]dioxaphosphepine (1.53). Prepared according to the representative procedure in Section 1.6.4.4. $^1$H NMR (300 MHz, CDCl$_3$): $\delta$ 0.20 (3H, s), 1.37 (6H, s), 1.38 (12H, s), 1.56 (3H, s), 2.22-2.30 (24H, m), 4.73 (1H, d, $J = 8.7$ Hz), 5.51 (1H, dd, $J = 8.7$, 4.8 Hz), 6.77 (1H, s), 6.84 (2H, s), 6.87 (1H, s), 6.92 (2H, s), 7.07 (2H, s), 7.14 (2H, s), 7.17 (1H, s), 7.35 (1H, d, $J = 2.1$ Hz), 7.46 (1H, s), 7.55 (1H, t, $J = 1.8$ Hz), 7.78 (1H, dd, $J = 8.4$ Hz, 1.8 Hz); $^{31}$P NMR (121 MHz, CDCl$_3$): $\delta$ 157.0.

(3aR,8aR)-4,4,8,8-tetrakis(3,5-dimethylphenyl)-2,2-dimethyl-6-(naphthalen-1-yl)tetrahydro-[1,3]dioxolo[4,5-e][1,3,2]dioxaphosphepine (1.54). Prepared according to the representative procedure in Section 1.6.4.4. $^1$H NMR (300 MHz, CDCl$_3$): $\delta$ 0.22 (3H, s), 1.60 (3H, s), 2.22 (6H, s), 2.24 (11H, s), 2.30 (7H, s), 4.83 (1H, d, $J = 8.1$ Hz), 5.71 (1H, dd, $J = 8.4$, 4.5 Hz), 6.78 (1H, s), 6.83 (1H, s), 6.86 (1H, s), 6.29 (1H, s), 7.03 (2H, s), 7.09 (2H, s), 7.14 (2H, s), 7.37-7.53 (4H, m), 7.62 (1H, t, $J = 7.5$ Hz), 7.87 (1H, d, $J = 8.4$ Hz), 7.97 (1H, d, $J = 8.1$ Hz), 8.31-8.40 (2H, m); $^{31}$P NMR (121 MHz, CDCl$_3$): $\delta$ 155.8.
1.7.4. Preparation of Acyclic 1,3-Dienes (Table 1.8).

A. 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: \textit{trans}-1-phenyl-1,3-butadiene (Table 1.8, entry 10),\textsuperscript{23} \textit{trans}-1-cyclohexyl-1,3-butadiene (Table 1.8, entry 3),\textsuperscript{24} \textit{trans}-1,3-decadiene (Table 1.8, entry 1) and \textit{trans}-6-phenyl-1,3-hexadiene (Table 1.8, entry 2).\textsuperscript{25} Spectral data are in accordance with the literature references.

B. Preparation of (E)-\textit{tert}-butyl(penta-2,4-dienyloxy)diphenylsilane.

\[
\text{\begin{align*}
\text{Ph}_3\text{P}-\text{C} &= \text{O} \\
\text{H} &\quad \text{DCM, rt} \\
&\quad \text{87\%} \\
\end{align*}}
\]

\[
\text{\begin{align*}
\text{MeO} &\quad \text{2) DIBAL-H} \\
&\quad \text{DCM, 0}\degree\text{C} \\
&\quad \text{95\%} \\
\text{MeO} &\quad \text{3) TBDPS-Cl} \\
&\quad \text{Et}_3\text{N, DCM} \\
&\quad \text{imidazole} \\
&\quad \text{84\%}
\end{align*}}
\]

\[
\text{(E)-\textit{tert}-butyl(penta-2,4-dienyloxy)diphenylsilane (Table 1.8, entry 8).} \text{\textsuperscript{1H} NMR (400 MHz, CDCl}_3\text{) \(\delta 1.05\text{ (9H, s) 4.23 (2H, d,} \\
J = 5.2\text{ Hz), 5.05 (1H, d, } J = 10.4\text{ Hz), 5.17 (1H, d, } J = 16.8\text{ Hz), 5.77 (1H, dt, } J = 14.4\text{ Hz, 4.8 Hz,} \\
\text{2H, m), 7.34-7.43 (6H, m), 7.65-7.68 (4H, m); } \text{\textsuperscript{13}C\text{ NMR (100} \\
\text{MHz, CDCl}_3\text{): \(\delta 136.6, 135.5, 133.6, 132.8, 130.3, 129.6, 127.6, 116.5, 64.0, 26.9, 19.3;}
\]


IR (neat): 2930.6 (w), 2856.9 (w), 1427.6 (m), 1111.1 (s), 1003.8 (m), 822.8 (w), 739.3 (w), 701.0 (s), 504.3 (m); HRMS-(ESI+) for C$_{21}$H$_{27}$O$_{1}$Si$_{1}$ [M+H]: calculated: 323.1831, found: 323.1835.

C. Preparation of (E)-((2,2-dimethylhexa-3,5-dienyloxy)methyl)benzene.

\[
\begin{array}{c}
\text{HO-} & \text{PhO} \\
\text{Me} & \text{Me} \\
\end{array} 
\quad \rightarrow \quad 
\begin{array}{c}
\text{BnO-} & \text{PhO} \\
\text{Me} & \text{Me} \\
\end{array}
\]

1) PhCH(OMe)$_2$

CSA, DCM, rt, 2h, 99%

2) LAH, AlCl$_3$

DCM:Et$_2$O (1:1)

-10 to 50°C, 83%

\[
\begin{array}{c}
\text{BnO-} & \text{Me} \\
\text{Me} & \text{Me} \\
\end{array} 
\quad \rightarrow \quad 
\begin{array}{c}
\text{BnO-} & \text{Me} \\
\text{Me} & \text{Me} \\
\end{array}
\]

PH$_3$P

O

OMe

1) DIBAL-H, DCM,

0°C, 92%

2) TPAP, NMO, DCM

4 Å MS, rt, 75%

\[
\begin{array}{c}
\text{BnO-} & \text{Me} \\
\text{Me} & \text{Me} \\
\end{array} 
\quad \rightarrow \quad 
\begin{array}{c}
\text{BnO-} & \text{Me} \\
\text{Me} & \text{Me} \\
\end{array}
\]

81%

(\text{E})-(2,2-dimethylhexa-3,5-dienyloxy)methyl)benzene

(Table 1.8, entry 5). $^1$H NMR (400 MHz, CDCl$_3$) δ 0.98 (6H, s), 3.12 (2H, s), 4.44 (2H, s), 4.91 (1H, dd, $J = 10.2$ Hz, 1.8 Hz), 5.04 (1H, dd, $J = 17.0$ Hz, 1.8 Hz), 5.68 (1H, d, $J = 16.0$ Hz), 5.97 (1H, dd, $J = 15.6$ Hz, 10.4 Hz), 6.24 (1H, dt, $J = 16.8$ Hz, 8.6 Hz), 7.14-7.27 (5H, m); $^{13}$C NMR (100 MHz, CDCl$_3$): δ 142.3, 138.7, 137.6, 128.2, 127.9, 127.3, 115.2, 79.2, 73.3, 37.6, 24.6; IR (neat): 2959.9 (w), 2859.1 (w), 1496.3 (w), 1377.4 (w), 1096.0 (s), 1004.1 (s), 951.6 (w), 898.1 (m), 734.3 (s), 696.6 (s); HRMS-(ESI+) for C$_{15}$H$_{21}$O$_{1}$ [M+H]: calculated: 217.1592, found: 217.1604.
D. Preparation of (E)-2-methyldeca-1,3-diene. To a flame-dried two-neck flask with a magnetic stir bar equipped with a reflux condenser was added CsF (2.14 g, 14.11 mmol, 2.4 equiv). The apparatus was flame-dried again, brought into the dry box, and trans-1-octen-1-yl boronic acid (1.00 g, 6.41 mmol, 1.1 equiv) was added, followed by Pd(PPh₃)₄ (203.8 mg, 0.18 mmol, 0.03 equiv) and 2-bromopropene (520 L, 5.88 mmol, 1.0 equiv). The reaction mixture was removed from the dry box, benzene (32 mL) was added under nitrogen, and the reaction was heated to 70 °C for 17 h. After being cooled to room temperature, the reaction was quenched with the addition of deionized water (15 mL) and the layers were separated. The organic layer was extracted with ethyl acetate (3 x 20 mL), and the combined organics were dried over Na₂SO₄, filtered, and concentrated in vacuo. The crude material was purified by silica gel chromatography (100% hexanes) to afford the title compound as a clear, colorless liquid (741 mg, 83%).

(E)-2-methyldeca-1,3-diene (Table 1.8, entry 6). ᵃH NMR (400 MHz, CDCl₃): δ 0.87 (3H, t, J = 7.0 Hz), 1.23-1.40 (8H, m), 1.81 (3H, s), 2.08 (2H, q, J = 6.8 Hz), 4.84 (2H, s), 5.64 (1H, dt, J = 15.6 Hz, 6.8 Hz), 6.12 (1H, d, J = 15.6 Hz); ᵃ³C NMR (100 MHz, CDCl₃): δ 142.2, 132.7, 131.0, 114.0, 32.8, 31.8, 29.5, 29.0, 22.7, 18.7, 14.1; IR (neat): 2923.9 (s), 2855.2 (m), 1609.2 (w), 1455.9 (m), 1377.3 (w), 963.2 (s), 880.2 (s), 724.2 (w) cm⁻¹; HRMS-(ESI⁺) for C₁₁H₂₁ [M+H]: calculated: 153.1643, found: 153.1644.
E. Preparation of (E)-1-(buta-1,3-dienyl)-2-methylbenzene.

(E)-1-(buta-1,3-dienyl)-2-methylbenzene (Table 1.8, entry 11). The reaction was performed according to the general procedure with potassium tert-butoxide (1.99 g, 17.77 mmol), methyltriphenylphosphonium bromide (6.56 g, 18.37 mmol), 2-methyl-trans-cinnamaldehyde (866.1 mg, 5.92 mmol), and THF (24 mL) to give the title compound as a clear, colorless liquid (549 mg, 64%). R<sub>f</sub> = 0.56 (100% hexanes, stain in KMnO<sub>4</sub>). ¹H NMR (400 MHz, CDCl<sub>3</sub>): δ 2.34 (3H, s), 5.16 (1H, dd, J = 10 Hz, 1.6 Hz), 5.32 (1H, dd, J = 16.8 Hz, 1.2 Hz), 6.53 (1H, dt, J = 16.8 Hz, 9.6 Hz), 6.68 (1H, dd, J = 15.2 Hz, 10.0 Hz), 6.77 (1H, d, J = 15.6 Hz), 7.12-7.17 (3H, m), 7.48 (1H, d, J = 6.4 Hz); ¹³C NMR (100 MHz, CDCl<sub>3</sub>): δ 137.4, 135.9, 135.5, 130.7, 130.4, 130.3, 127.4, 126.0, 125.1, 117.4, 19.8; IR(neat): 2968.8 (w), 1598.9 (w), 1482.9 (w), 1459.7 (w), 1000.7 (s), 947.2 (m), 897.6 (m), 750.3 (s), 718.3 (m); HRMS-(ESI+) for C<sub>11</sub>H<sub>13</sub> [M+H]: calculated: 145.1017, found: 145.1019.

1.7.5. Preparation of Cyclic 1,3-Diene Substrates (Table 1.9).

1-Methyl-1,3-cyclohexadiene was purchased from ChemSampCo and used without further purification. 1-Methoxy-1,3-cyclohexadiene was purchased from Aldrich and distilled before use.
**A. Preparation of 2-butylcyclohexa-1,3-diene (Table 1.9, entry 1).** The title compound was synthesized from the requisite triflate as shown below. The spectral data was in accordance with the literature.\(^{26}\)

![Chemical reaction diagram]

\[\text{LDA, -78 °C, THF} \quad \text{OTf} \quad \text{BuMgBr, CuI, THF, -20 °C} \]

\[\text{42%} \quad \text{58%} \]

**B. Preparation of [1,1'-bi(cyclohexane)]-1,3-diene (Table 1.9, entry 3).** The title compound was prepared according to the scheme below from modified literature procedures.\(^{27}\)

![Chemical reaction diagram]

\[\text{CyMgCl, CeCl}_3 \cdot 7\text{H}_2\text{O, THF, 0 °C} \quad \text{NO}_2 \quad \text{Et}_3\text{N, DCM} \quad 0 °\text{C to rt} \]

\[\text{89%} \quad \text{49%} \]

**[1,1'-bi(cyclohexane)]-1,3-diene (Table 1.9, entry 3).** \(^1\)H NMR (400 MHz, CDCl\(_3\)): \(\delta 0.82-0.88\) (2H, m), 1.08-1.32 (5H, m), 1.36-1.43 (1H, m), 1.59-1.77 (4H, m), 1.81-1.88 (1H, m), 2.03-2.12 (2H, m), 5.61 (1H, d, \(J = 5.2\) Hz), 5.63-5.67 (1H, m), 5.86-5.67 (1H, m).

---


1.7.6. Preparation of Chiral Diene 1.57 (Scheme 1.13).

(R,E)-(2-methylhexa-3,5-dien-1-yl)benzene (1.57). ¹H NMR (400 MHz, CDCl₃): δ 0.98 (3H, d, J = 6.8 Hz), 2.44-2.53 (2H, m), 2.66-2.72 (1H, m), 4.94 (1H, dd, J = 10.0, 1.6 Hz), 5.07 (1H, dd, J = 16.8, 1.2 Hz), 5.67 (1H, dd, J = 15.6, 6.8 Hz), 5.98 (1H, dd, J = 15.6, 10.4 Hz), 6.28 (1H, ddd, J = 17.6, 10.8, 10.8 Hz), 7.11-7.18 (3H, m), 7.24-7.27 (2H, m).

1.7.7. Preparation of Internal 1,3-Diene 1.60 (Scheme 1.14).

The title compound was prepared following the literature procedure and spectral data are in accordance with the literature.²⁸

---

1.7.8. Representative Procedure for Diene Diboration/Oxidation.

In the dry box, an oven-dried 6-dram vial with magnetic stir bar was charged with Pt(dba)$_3$ (6.0 mg, 6.7 $\mu$mol), ($R,R$)-xylylTADDOLPPh (1.33) (9 mg, 13.2 $\mu$mol), and toluene (2.20 mL, 0.1 M). After stirring in the dry box for 1 h, B$_2$(pin)$_2$ (58.6 mg, 32.1 $\mu$mol) was added to the mixture followed by ($E$)-1-cyclohexyl-1,3-butadiene (30.0 mg, 22.0 $\mu$mol). The vial was sealed with a polypropylene cap, removed from the dry box, and stirred at 60 °C for 12 h. The reaction mixture was cooled to 0 °C (ice/water) and charged with tetrahydrofuran (3 mL), 3 M sodium hydroxide (2 mL), and 30% hydrogen peroxide (1 mL). The reaction was gradually warmed to room temperature and allowed to stir for 4 h at which time the vial was cooled to 0 °C (ice/water) and saturated aqueous sodium thiosulfate was added dropwise over 5 min. The reaction mixture was diluted ethyl acetate and the aqueous and organic layers were separated. The aqueous layer was washed with ethyl acetate (3 x 15 mL) and the combined organics were washed with brine. The organic layer was dried over Na$_2$SO$_4$, filtered, and the volatiles were removed by rotary evaporation. The crude reaction mixture was purified on silica gel (30-50% ethyl acetate/hexanes) to afford a clear, colorless oil (31.0 mg, 80% yield).
1.7.9. Characterization and Proof of Stereochemistry

(R,Z)-dec-2-ene-1,4-diol (Table 1.8, entry 1). $^1$H NMR (400 MHz, CDCl$_3$): $\delta$ 0.87 (3H, t, $J = 6.8$ Hz), 1.22-1.28 (8H, br s), 1.30-1.46 (1H, m), 1.56-1.60 (1H, m), 4.09 (1H, dd, $J = 12.9$ Hz, 5.6 Hz), 4.30 (1H, dd, $J = 13.2$ Hz, 7.6 Hz), 4.42 (1H, q, $J = 7.0$ Hz), 5.54 (1H, dd, $J = 11.2$ Hz, 8.4 Hz), 5.70 (1H, ddd, $J = 11.2$ Hz, 7.6 Hz, 5.6 Hz); $^{13}$C NMR (100 MHz, CDCl$_3$): $\delta$ 14.2, 22.7, 25.4, 29.3, 31.9, 37.5, 58.7, 67.9, 130.3, 135.5; IR (neat): 3314 (br s), 2955 (s), 2855 (s), 1459 (m), 1378 (m), 1018 (s) cm$^{-1}$. HRMS-(ESI+) for C$_{10}$H$_{20}$O$_2$Na [M+Na]: calculated: 195.1361, found: 195.1372. $[\alpha]_D = +11.02$ (c = 0.42, CHCl$_3$, l = 50 mm). The crude reaction mixture was purified on silica gel (50% ethyl acetate/hexanes) to afford a clear, colorless oil (31.0 mg, 83% yield). $R_f = 0.16$ (50% ethyl acetate/hexanes, stain in PMA).

Proof of Stereochemistry:

The title compound was subjected to ozonolysis and reduction as described below. To a 25-mL round-bottomed flask with magnetic stir bar was added (R,Z)-dec-2-1,4-diol (11 mg, 64.6 µmol) and dichloromethane (1.6 mL). The flask was cooled to -78 °C (dry ice/isopropanol) and treated with ozone until a pale blue color was observed. To the cooled solution was added methanol (1.6 mL) and sodium borohydride (24 mg, 37.8 mmol). The reaction mixture was gradually warmed to room temperature and allowed to
stir for 2 h, at which time volatiles were removed by rotary evaporation. The solid residue was dissolved in ethyl acetate and water and the aqueous and organic layers were separated. The aqueous layer was washed with ethyl acetate (3 x 10 mL) and the combined organic extracts were washed with brine, dried over Na₂SO₄, filtered, and concentrated in vacuo. The resultant oil was purified by column chromatography on silica gel with (50% ethyl acetate/hexanes) to afford a clear oil in 79% yield (9.3 mg). The resulting 1,2-diol was treated with 2,2-dimethoxypropane and catalytic \( p \)-toluenesulfonic acid (below). The resulting ketal was compared to the racemic ketal of octane-1,2-diol prepared from dihydroxylation of octene with osmium tetroxide and 4-methylmorpholine \( N \)-oxide. The authentic sample was prepared from the Sharpless asymmetric dihydroxylation of 1-octene utilizing AD-mix \( \alpha \).

![Chemical Reaction Diagram](image-url)
Chiral GLC (β-dex, Supelco, 100 °C) – analysis of the acetonide of octane-1,2-diol.

\((R,Z)\)-6-Phenylhex-2-ene-1,4-diol (Table 1.8, entry 2).

\(^1\text{H}\) NMR (400 MHz, CDCl\(_3\)): \(\delta\) 1.59 (1H, br s), 1.75-2.01 (1H, br s), 1.79 (1H, m), 1.95 (1H, m), 2.69 (2H, m), 4.13 (1H, dd, \(J = 13.2\) Hz, 6 Hz), 4.25 (1H, ddd, \(J = 13.2\) Hz, 7.2 Hz, 1.6 Hz), 4.45 (1H, q, \(J = 7.0\) Hz), 5.62 (1H, ddt, \(J = 11.2\) Hz, 8.0 Hz, 1.6 Hz), 5.75 (1H, ddd, \(J = 11.2\) Hz, 7.2 Hz, 6 Hz), 7.17-7.21 (2H, m), 7.26-7.30 (3H, m); \(^{13}\text{C}\) NMR (100 MHz, CDCl\(_3\)): \(\delta\) 31.8, 39.0, 58.9, 67.4, 126.0, 128.4, 128.5, 130.6, 135.1, 141.6; IR (neat): 3312 (br s), 3024 (m), 2925 (m), 2859 (m), 1453 (m), 1012 (s), 696 (s) cm\(^{-1}\); HRMS-(ESI\(^+\)) for C\(_{12}\)H\(_{16}\)O\(_2\)Na [M
+Na]: calculated: 215.1048, found: 215.1039; $[\alpha]_D = +35.56$ (c = 1.03, CHCl$_3$, l = 50 mm). The crude reaction mixture was purified on silica gel (50% ethyl acetate/hexanes) to afford a clear, colorless oil (95 mg, 78% yield). R$_f$ = 0.25 (50% ethyl acetate, stain in PMA).

**Proof of Stereochemistry:**

The title compound was treated with ozone in the procedure described for (R,Z)-dec-2-ene-1,4-diol. The resulting 1,2-diol was treated with 2,2-dimethoxypropane and catalytic p-toluenesulfonic acid. The resulting ketal was compared to the racemic ketal of 4-phenyl-butane-1,2-diol prepared from dihydroxylation of 4-phenyl-1-butene with osmium tetraoxide and 4-methylmorpholine N-oxide.

Chiral SFC (OD-H, 1.5% MeOH, 4 mL/min, 50 °C, 150 psi) – analysis of the diol of 4-phenyl-butane-1,2-diol.
(S,Z)-5-(tert-butyldiphenylsilyloxy)pent-2-ene-1,4-diol (Table 1.8, entry 8). The reaction was performed according to the representative procedure with Pt(dba)$_3$ (6.4 mg, 7.1 µmol), (R,R)-xylylTADDOLPPh (1.33) (9.6 mg, 13.9 µmol), (E)-((2,2-dimethylhexa-3,5-dienyloxy)methyl)benzene (75 mg, 0.23 mmol), B$_2$(pin)$_2$ (177.1 mg, 0.70 mmol) in toluene (2.3 mL) for 12 h at 60 °C, followed by oxidation, to afford an inseparable 1:4 mixture of the 1,2- and 1,4-dihydroxylations products. To facilitate purification, the crude reaction mixture was dissolved in THF:Et$_2$O:H$_2$O (1:1:1) and NaIO$_4$ (4 equiv) was added at room temperature (oxidative cleavage of both the 1,2-diboration product and pinacol). The reaction mixture was stirred for 2 h, after which time it was diluted with ethyl acetate, and the layers were separated. The aqueous layer was extracted with ethyl acetate (3 x 10 mL). The combined organics were dried over Na$_2$SO$_4$, filtered, and concentrated in vacuo. The crude material was purified by column chromatography on SiO$_2$ to afford the title compound as a clear, colorless oil (58.0 mg, 70% yield) $R_f = 0.38$ (30-50% ethyl acetate/hexane, stain in PMA). $^1$H NMR (400 MHz, CDCl$_3$): $\delta$ 1.06 (9H, s), 2.29 (1H, br s), 2.92 (1H, br s), 3.53-3.62 (2H, m), 4.02 (1H, ddd, $J = 13.4$ Hz, 6.0 Hz, 1.2 Hz), 4.16 (1H, ddd, $J = 13.6$ Hz, 7.2 Hz, 1.2 Hz), 4.49-4.53 (1H, m), 5.43-5.53 (1H, m), 5.76 (1H, dddd, $J = 8.4$ Hz, 7.2 Hz, 6.0 Hz, 1.6 Hz), 7.36-7.45 (6H, m), 7.63-7.68 (4H, m); $^{13}$C NMR (100 MHz, CDCl$_3$): $\delta$ 19.2, 26.8, 26.9 (1,2-diol), 58.0 (1,2-diol), 58.8, 66.2 (1,2-diol), 67.4, 68.7, 70.1 (1,2-diol), 127.5 (1,2-diol), 127.65 (1,2-diol), 127.73 (1,2-diol), 127.8, 129.7 (1,2-diol), 129.8 (1,2-diol), 129.90, 129.92, 130.1, 130.8 (1,2-diol), 132.3 (1,2-diol), 132.6,
132.8 (1,2-diol), 132.9 (1,2-diol), 133.5 (1,2-diol), 135.5, 135.8, 135.9; IR (neat): 3353.5 (br s), 2892.6 (w), 2857.5 (w), 1471.8 (m), 1111.0 (s), 1047.2 (m), 739.8 (m), 701.4 (s), 504.9 (m) cm\(^{-1}\); HRMS-(ESI+) for C\(_{21}\)H\(_{29}\)O\(_3\)Si [M+H]: calculated: 357.1886, found: 357.1891; \([\alpha]_D = -4.5\) (c = 1.33, CHCl\(_3\), l =10 mm).

**Analysis of Stereochemistry:**

The absolute stereochemistry was assigned by analogy.

*Chiral HPLC (Chiracel-OD, 1.5 mL/min, 2% IPA, 220 nm) – analysis of the title compound*

**Graphs:**
- Racemic
- Reaction product
- Coinjection of pdt + racemic
(R,Z)-1-Cyclohexylbut-2-ene-1,4-diol (Table 1.8, entry 3).  

$^1$H NMR (400 MHz, CDCl$_3$): $\delta$ 0.89-1.01 (2H, m), 1.10-1.25 (3H, m), 1.34-1.41 (1H, m), 1.65-1.90 (5H, m), 2.38 (2H, br s), 4.06-4.15 (1H, m), 4.06-4.15 (1H, m), 4.29 (1H, ddd, $J = 12.8$ Hz, 7.6 Hz, 1.6 Hz), 5.55 (1H, ddt, $J = 11.2$ Hz, 8.4 Hz, 1.6 Hz), 5.77 (1H, m); $^{13}$C NMR (100 MHz, CDCl$_3$): $\delta$ 26.1, 26.2, 26.6, 28.7, 28.8, 43.9, 58.8, 72.2, 130.9, 133.9; IR (neat): 3325 (br s), 2923 (s), 2851 (s), 2300 (w), 1449 (m), 1015 (s) cm$^{-1}$; HRMS-(ESI$^+$) for C$_{10}$H$_{18}$O$_2$Na [M+Na]: calculated: 193.1204, found: 193.1199; $[\alpha]_D = +18.01$ (c = 0.98, CHCl$_3$, $l = 50$ mm). The crude reaction mixture was purified on silica gel (50% ethyl acetate/hexanes) to afford a clear, colorless oil (31.0 mg, 80% yield). $R_f = 0.17$ (50% ethyl acetate, stain in PMA).

Proof of stereochemistry:

The title compound was treated with ozone in the procedure described for (R,Z)-dec-2-ene-1,4-diol. The resulting 1,2-diol was treated with 2,2-dimethoxypropane and catalytic $p$-toluenesulfonic acid. The resulting ketal was compared to the racemic ketal of 1-cyclohexylethane-1,2-diol prepared from treatment of vinyl cyclohexane with osmium tetraoxide and 4-methylmorpholine $N$-oxide. The authentic sample was prepared from the Sharpless asymmetric dihydroxylation of vinyl cyclohexane utilizing AD-mix $\alpha$. 

70
Chiral GLC (β-dex, Supelco, 130 °C) – analysis of the acetonide of 1-cyclohexylethane-1,2-diol.

racemic reaction product authentic coinjection of reaction product + racemic
The reaction was performed according to the representative procedure with Pt(dba)$_3$ (5.1 mg, 5.7 µmol), (R,R)-xylylTADDOLPPh (1.33) (7.6 mg, 11.1 µmol), (E)-((2,2-dimethylhexa-3,5-dienyloxy)methyl)benzene (40 mg, 0.18 mmol), B$_2$(pin)$_2$ (49.3 mg, 0.19 mmol) in toluene (1.8 mL) for 12 h at 60 °C, followed by oxidation, to afford an inseparable 1:1 mixture of the 1,2- and 1,4-dihydroxylation products. To facilitate purification, the crude reaction mixture was dissolved in THF:Et$_2$O:H$_2$O (1:1:1) and NaIO$_4$ (4 equiv) was added at room temperature (oxidative cleavage of both the 1,2-diboration product and pinacol). The reaction mixture was stirred for 2 h, after which time it was diluted with ethyl acetate, and the layers were separated. The aqueous layer was extracted with ethyl acetate (3 x 10 mL). The combined organics were dried over Na$_2$SO$_4$, filtered, and concentrated in vacuo. The crude material was purified by column chromatography on SiO$_2$ to afford the title compound as a clear, colorless oil (22.2 mg, 48% yield) R$_f$ = 0.31 (30-50% ethyl acetate/hexane, stain in PMA); $^1$H NMR (500 MHz, CDCl$_3$): δ 0.89 (3H, s), 0.93 (3H, s), 3.32 (1H, d, J = 9.0 Hz), 3.39 (1H, d, J = 9.0 Hz), 3.57 (1H, br s), 4.11 (1H, dd, J = 13.0 Hz, 6.0 Hz), 4.29 (1H, ddd, J = 13.0 Hz, 7.5 Hz, 1.5 Hz), 4.32 (1H, d, J = 8.5 Hz), 4.51 (2H, m.), 5.56-5.60 (1H, m), 5.79-5.84 (1H, m), 7.29-7.37 (5H, m); $^{13}$C NMR (125 MHz, CDCl$_3$): δ 19.9, 22.3, 38.6, 58.9, 73.8, 74.6, 79.5, 127.7, 128.0, 128.6, 131.3, 137.7; IR (neat): 3376 (s), 2960 (s), 2924 (s), 2854 (s), 1453 (s), 1361 (s), 1281 (s), 1091 (s), 1074
(s), 1001 (m) cm⁻¹; HRMS-(ESI+) for C₁₅H₂₃O₃ [M+H]: calculated: 251.1647, found: 251.1658. \([\alpha]_D = -22.8\) (c = 0.75, CHCl₃, \(l = 10\) mm).

**Analysis of Stereochemistry:**

The absolute stereochemistry was assigned by analogy.

*Chiral SFC (AD-H, 2% MeOH, 4 mL/min, 50 °C, 150 psi, 254 nm) – analysis of the title compound.*
(S,Z)-2-methyldec-2-ene-1,4-diol (Table 1.8, entry 6). The reaction was performed according to the representative procedure with Pt(dba)$_3$ (8.0 mg, 8.9 µmol), (R,R)-3,5-^t_Bu$_2$PhTADDOLPPh (1.35) (12.1 mg, 17.6 µmol), (E)-2-methyldeca-1,3-diene (44.7 mg, 0.29 mmol), B$_2$(pin)$_2$ (78.3 mg, 0.31 mmol) in toluene (3.0 mL) for 12 h at 60 °C, followed by oxidation, to afford the title compound as a clear, colorless oil (52.2 mg, 95% yield). R$_f$ = 0.22 (50% ethyl acetate/hexane, stain in PMA); $^1$H NMR (400 MHz, CDCl$_3$): δ 0.85 (3H, t, $J$ = 6.6 Hz), 1.18-1.32 (8H, m), 1.36-1.42 (1H, m), 1.52-1.58 (1H, m), 1.79 (3H, s), 2.88 (2H, br s), 3.88 (1H, d, $J$ = 12.0 Hz), 4.28 (1H, d, $J$ = 12.4 Hz), 4.36 (1H, q, $J$ = 6.8 Hz), 5.29 (1H, d, $J$ = 8.4 Hz); $^{13}$C NMR (100 MHz, CDCl$_3$): δ 138.1, 131.1, 67.7, 61.7, 37.6, 31.8, 29.2, 25.4, 22.6, 21.8, 14.0; IR(neat): 3333.1 (br), 2955.6 (m), 2927.0 (s), 2856.9 (m), 1455.2 (w), 1377.3 (w), 1005.1 (s), 950.5 (w) cm$^{-1}$; HRMS-(ESI$^+$) for C$_{11}$H$_{21}$O$_1$ [M-H$_2$O+H]: calculated: 169.1592, found: 169.1560; $[\alpha]_D$ = -4.36 (c = 1.34, CHCl$_3$, $l$ = 50 mm).

Proof of Stereochemistry:

The title compound was treated with ozone in the procedure described for (R,Z)-dec-2-ene-1,4-diol. The resulting 1,2-diol was treated with 2,2-dimethoxypropane and catalytic p-toluenesulfonic acid. The resulting ketal was compared to the racemic ketal of octane-1,2-diol prepared from dihydroxylation of octene with osmium tetraoxide and 4-
methylmorpholine N-oxide. The authentic sample was prepared from the Sharpless asymmetric dihydroxylation of octene utilizing AD-mix α.

*Chiral GLC (β-dex, Supelco, 100 °C, 20 psi) – analysis of the acetonide of octane-1,2-diol.*

![Chiral GLC graphs](image)

- racemic
- reaction product
- authentic
(S,Z)-1-Phenylbut-2-ene-1,4-diol (Table 1.8, entry 10). The reaction was performed according to the representative procedure; however, the diboration was run at room temperature. $^1$H NMR (500 MHz, CDCl$_3$): δ 1.8-2.0 (1H, br s), 2.3-3.5 (1H, br s), 4.23 (1H, dd, $J = 13.2$ Hz, 4.3 Hz), 4.43 (1H, dd, $J = 13$ Hz, 5.5 Hz), 5.57 (1H, d, $J = 7.0$ Hz), 5.79-5.81 (1H, m), 5.79-5.81 (1H, m), 7.29 (1H, tt, $J = 6.8$ Hz, 2.0 Hz), 7.34-7.40 (4H, m); $^{13}$C NMR (125 MHz, CDCl$_3$): δ 59.0, 70.3, 126.1, 127.9, 128.8, 130.2, 134.6, 143.2; IR (neat): 3319 (br s), 3026 (m), 2923 (m), 2854 (m), 1450 (m), 1016 (s), 968 (s), 845 (s), 696 (s) cm$^{-1}$; HRMS-(ESI$^+$) for C$_{10}$H$_{12}$O$_2$Na [M+Na]: calculated: 187.0735, found: 187.0741; $[\alpha]_D = +123.29$ (c = 0.99, CHCl$_3$, $l = 50$ mm). The crude reaction mixture was purified on silica gel (50% ethyl acetate/hexanes) to afford a white solid (83 mg, 83% yield). $R_f = 0.16$ (50% ethyl acetate, stain in PMA).

**Proof of Stereochemistry:**

The 1,4-dihydroxylation product (S,Z)-1-phenylbut-2-ene-1,4-diol was treated with ozone in the procedure described for (R,Z)-dec-2-ene-1,4-diol. The resulting 1,2-diol was treated with 2,2-dimethoxypropane and catalytic $p$-toluenesulfonic acid. The resulting ketal was compared to the racemic ketal of 1-phenyl-ethane-1,2-diol prepared from the dihydroxylation of styrene with osmium tetroxide and 4-methylmorpholine $N$-oxide. The authentic sample was prepared from the Sharpless asymmetric dihydroxylation of styrene utilizing AD-mix $\alpha$. 

76
Chiral GLC (β-dex, Supelco, 140 °C, 20 psi) – analysis of the acetonide of 1-phenylethane-1,2-diol.

racemic reaction product authentic coinjection of reaction product + racemic
(S,Z)-1-o-tolylbut-2-ene-1,4-diol (Table 1.8, entry 11). The reaction was performed according to the representative procedure with Pt(dba)$_3$ (14.2 mg, 15.8 µmol), (R,R)-xylylTADDOLPPh (1.33) (21.4 mg, 31.2 µmol), (E)-1-(buta-1,3-dienyl)-2-methylbenzene (75.0 mg, 0.52 mmol), B$_2$(pin)$_2$ (138.7 mg, 0.55 mmol) in toluene (5.2 mL) for 12 h at room temperature, followed by oxidation, to afford the title compound as a clear, colorless oil (82.4 mg, 89% yield). $R_f = 0.17$ (50% ethyl acetate/hexane, stain in PMA); $^1$H NMR (400 MHz, CDCl$_3$): $\delta$ 1.24 (2H, br s), 2.34 (3H, s), 4.25 (1H, dd, $J = 12.8$ Hz, 5.2 Hz), 4.41 (1H, dd, $J = 12.8$ Hz, 6.0 Hz), 5.74-5.82 (2H, m), 7.12-7.22 (3H, m), 7.49 (1H, d, $J = 7.2$ Hz); $^{13}$C NMR (100 MHz, CDCl$_3$): 140.9, 134.9, 133.8, 130.5, 130.3, 127.6, 126.3, 125.6, 67.3, 58.7, 19.2; IR (neat): 3317.5 (br), 3021.4 (w), 2924.1 (w), 2940.6 (m), 1211.6 (w), 1016.3 (s), 940.7 (w), 753.7 (m) cm$^{-1}$; HRMS-(ESI+) for C$_{11}$H$_{13}$O$_1$ [M-H$_2$O+H]: calculated: 161.0966, found: 161.0962; $[\alpha]_D = +16.30$ (c = 0.43, CHCl$_3$, l = 10 mm).

Proof of Stereochemistry:

The title compound was treated with ozone in the procedure described for (R,Z)-dec-2-ene-1,4-diol. The resulting 1,2-diol was treated with 2,2-dimethoxypropane and catalytic $p$-toluenesulfonic acid. The resulting ketal was compared to the racemic ketal of 1-ortho-tolylethane-1,2-diol prepared from treatment of 2-methylstyrene with osmium tetroxide and 4-methylmorpholine $N$-oxide. The authentic sample was prepared from the Sharpless asymmetric dihydroxylation of 2-methylstyrene utilizing AD-mix $\beta$. 
Chiral SFC (AD-H, 4% MeOH, 3 mL/min, 50 °C, 150 psi, 220 nm)-analysis of 1-ortho-tolylethane-1,2-diol.

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racemic          reaction product          authentic          coinjection of reaction product + racemic
(1R,4S)-2-butylocyclohex-2-ene-1,4-diol (Table 1.9, entry 1). The reaction was performed according to the representative procedure with Pt(dba)$_3$ (4.0 mg, 4.5 µmol), (R,R)-xylylTADDOLPPh (1.33) (6.0 mg, 8.8 µmol), 2-butylocyclohexa-1,3-diene (20 mg, 0.147 mmol), B$_2$(pin)$_2$ (39.1 mg, 0.154 mmol) in toluene (1.5 mL) for 12 h at 60 °C, followed by oxidation, to afford the title compound as a clear, colorless oil (20.8 mg, 83% yield). R$_f$ = 0.20 (50% ethyl acetate/hexane, stain in PMA); $^1$H NMR (400 MHz, CDCl$_3$): $\delta$ 0.89 (3H, t, $J = 7.0$ Hz), 1.21-1.47 (3H, m), 1.61-1.85 (5H, m), 2.01-2.20 (2H, m), 3.99 (1H, s), 4.13 (1H, s), 5.53 (1H, s); $^{13}$C NMR (100 MHz, CDCl$_3$): $\delta$ 141.7, 127.4, 66.66, 66.62, 33.3, 29.9, 29.2, 27.9, 22.6, 14.0; IR (neat): 3301.0 (br), 2928.4 (s), 2858.7 (m), 1457.1 (w), 1276.5 (w), 1049.2 (m), 1027.7 (w), 979.8 (m), 957.4 (w) cm$^{-1}$; HRMS-(ESI+) for C$_{10}$H$_{17}$O$_1$ [M-H$_2$O +H]: calculated: 153.1279, found: 153.1279; $[\alpha]_D = +29.02$ (c = 0.90, CHCl$_3$, l = 50 mm).

Proof of Stereochemistry:

The authentic compound was synthesized as shown below. Treatment of hexanal with aqueous formaldehyde and dimethylamine hydrochloride provided aldehyde S$_2$. Brown allylation$^{30}$ followed by TBS-protection furnished the protected allylic alcohol S$_3$. Hydroboration with dicyclohexylborane$^{31}$ gave primary alcohol S$_4$, which was then

oxidized with TPAP/NMO\textsuperscript{32} followed by addition of vinylmagnesium bromide to afford diene S6. Ring-closing metathesis, using Hoveyda-Grubbs 2\textsuperscript{nd} generation catalyst,\textsuperscript{33} followed by TBAF deprotection provided the desired 1,4-diol in 4\% overall yield.

Chiral GLC (β-dex, Supelco, 140 °C, 20 psi) – analysis of the bis(acylated) 1,4-diol.

\begin{figure}[h]
\centering
\includegraphics[width=\textwidth]{diagram.png}
\caption{Synthesis of desired product.}
\end{figure}


(1S,2R) -4-methylcyclohex-3-ene-1,2-diol (Table 1.9, entry 2). The reaction was performed according to the representative procedure with Pt(dba)$_3$ (20.3 mg, 22.6 µmol), (S,S)-xylyltADDOLPPh (ent-1.33) (30.6 mg, 44.6 µmol), 1-methylcyclohexa-1,3-diene (70 mg, 0.74 mmol), B$_2$(pin)$_2$ (198.3 mg, 0.78 mmol) in toluene (7.4 mL) for 12 h at 60 °C, followed by oxidation, to afford the title compound as a white solid (79.1 mg, 83% yield of inseparable mixture of 1,2- and 1,4-product). $R_f = 0.12$ (50% ethyl acetate/hexane, stain in PMA); mp 76-82 °C; $^1$H NMR (400 MHz, CDCl$_3$): $\delta$ 1.61-1.82 (7H, m), 2.81 (2H, br s), 3.88 (1H, br s), 4.09 (1H, br s), 5.52 (1H, br s); $^{13}$C NMR (100 MHz, CDCl$_3$): $\delta$ 138.6, 128.1, 68.0, 66.3, 29.0, 27.8, 20.3; IR (neat): 3312.5 (br), 2940.3 (m), 2865.1 (w), 1443.2 (m), 1280.1 (w), 1039.7 (s), 980.4 (m), 950.2 (s) cm$^{-1}$; HRMS-(ESI+) for C$_7$H$_{11}$O$_1$ [M-H$_2$O+H]: calculated: 111.0810, found: 111.0815; $[\alpha]_D$ = -15.62 (c = 0.32, CHCl$_3$, $l = 10$ mm).

Proof of Stereochemistry:

The title compound was subjected to allylic oxidation with DDQ as shown below. The specific rotation of the enone was compared to the known value in the literature. $[\alpha]_D = +142.5$ (c = 1.08, CHCl$_3$).
Chiral GLC (β-dex, Supelco, 90 °C for 5 min, ramp 2 °C/min to 160 °C, 20 psi) – analysis of the bis(acylated) 1,2-diol.
\((3R,4S)\)-[1,1'-bi(cyclohexan)]-1-ene-3,4-diol (Table 1.9, entry 3).

The reaction was performed according to the representative procedure with \(\text{Pt(dba})_3\) (3.4 mg, 3.8 µmol), \((R,R)\)-xylyltADDOLPPh \(1.33\) (5.1 mg, 7.4 µmol), [1,1'-bi(cyclohexane)]-1,3-diene (20 mg, 0.123 mmol), \(\text{B}_2(\text{pin})_2\) (32.9 mg, 0.130 mmol) in toluene (1.2 mL) for 12 h at 60 °C, followed by oxidation, to afford the title compound as a clear, colorless oil (15.7 mg, 65% yield). \(R_f = 0.23\) (50% ethyl acetate/hexane, stain in PMA); \(^1\text{H NMR (400 MHz, CDCl}_3\):} \(\delta 1.04-1.16\) (3H, m), 1.22-1.27 (2H, m), 1.62-1.81 (8H, m), 1.93-2.01 (1H, m). 2.06-2.13 (1H, m), 2.24 (2H, br s), 3.68-3.72 (1H, m), 4.05-4.11 (1H, m), 5.42 (1H, ddd, \(J = 4.0, 1.2, 1.2\) Hz).

**Analysis of Stereochemistry:**

The enantioselectivity was determined by preparing the bis(acylated) 1,2-diol using acetic anhydride. The analogous racemic material was prepared using \(\text{PCy}_3\) as the achiral ligand in the diboration reaction. The absolute stereochemistry was assigned by analogy.
Chiral GC (β-Dex, 160 °C, 20 psi, s/r = 35:1) – analysis of the bis(acylated) 1,2-diol.

racemic diboration product
The reaction was performed according to the representative procedure with Pt(dba)$_3$ (12.4 mg, 13.8 µmol), ($R,R$)-xylylTADDOLPh (1.33) (18.6 mg, 27.2 µmol), 1-methoxycyclohexa-1,3-diene (50 mg, 0.454 mmol), B$_2$(pin)$_2$ (230.5 mg, 0.908 mmol) in toluene (4.5 mL) for 12 h at 60 °C, followed by oxidation, to afford the title compound as a colorless oil (33.4 mg, 51% yield). R$_f$ = 0.12 (50% ethyl acetate/hexane, stain in PMA); $^1$H NMR (300 MHz, CDCl$_3$): δ 1.71-1.89 (2H, m), 2.08-2.22 (2H, m), 3.52 (3H, s), 3.72 (1H, ddd, $J$ = 10.2, 3.9, 3.9 Hz), 4.22 (1H, dd, $J$ = 4.5, 4.5 Hz), 4.73 (1H, d, $J$ = 5.1 Hz).

Analysis of Stereochemistry:

The enantioselectivity was determined by treating the title compound with $p$-TsOH to form ($S$)-4-hydroxycyclohex-2-enone as shown below. The analogous racemic material was prepared using PCy$_3$ as the achiral ligand in the diboration reaction. The absolute stereochemistry was assigned by analogy.
Chiral SFC (AD-H, 2.0% MeOH, 3 mL/min, 50 °C, 150 psi) – analysis of (S)-4-hydroxycyclohex-2-enone.

racemic

diboration product
(4R,5R,Z)-5-methyl-6-phenylhex-2-ene-1,4-diol (1.58). The reaction was performed according to the representative procedure with Pt(dba)$_3$ (6.3 mg, 7.0 µmol), (R,R)-xylylTADDOLPPh (1.33) (9.5 mg, 13.9 µmol), (R,E)-(2-methylhexa-3,5-dien-1-yl)benzene (40 mg, 0.232 mmol), B$_2$(pin)$_2$ (61.9 mg, 0.244 mmol) in toluene (2.3 mL) for 12 h at 60 °C, followed by oxidation, to afford the title compound as a white solid (40.2 mg, 84% yield). R$_f$ = 0.27 (50% ethyl acetate/hexane, stain in PMA); $^1$H NMR (400 MHz, CDCl$_3$): δ 0.80 (3H, d, $J$ = 6.8 Hz), 1.60 (2H, br s), 1.82-1.87 (1H, m), 2.30-2.38 (1H, m), 2.91 (1H, dd, $J$ = 13.2, 4.8 Hz), 4.12 (1H, dd, $J$ = 12.8, 6.0 Hz), 4.21-4.31 (2H, m), 5.61-5.66 (1H, m), 5.75-5.83 (1H, m), 7.14-7.19 (3H, m), 7.26-7.28 (2H, m).

X-Ray Crystal Structure:
(4S,5R,Z)-5-methyl-6-phenylhex-2-ene-1,4-diol (1.59). The reaction was performed according to the representative procedure with Pt(dba)$_3$ (6.3 mg, 7.0 µmol), (S,S)-xylylTADDOLPh (ent-1.33) (9.5 mg, 13.9 µmol), (R,E)-(2-methylhexa-3,5-dien-1-yl)benzene (40 mg, 0.232 mmol), B$_2$(pin)$_2$ (61.9 mg, 0.244 mmol) in toluene (2.3 mL) for 12 h at 60 °C, followed by oxidation, to afford the title compound as a white solid (40.2 mg, 84% yield). R$_f$ = 0.26 (50% ethyl acetate/hexane, stain in PMA); $^1$H NMR (400 MHz, CDCl$_3$): δ 0.89 (3H, d, $J$ = 6.8 Hz), 1.77 (2H, br s), 1.83-1.89 (1H, m), 2.34 (1H, dd, $J$ = 13.2, 8.8 Hz), 2.83 (1H, dd, 13.2, 6.0 Hz), 4.11 (1H, dd, $J$ = 12.8, 5.6 Hz), 4.23 (1H, ddd, $J$ = 13.2, 7.2, 1.2 Hz), 4.30-4.32 (1H, m), 5.63-5.67 (1H, m), 5.73-5.79 (1H, m), 7.14-7.19 (3H, m), 7.23-7.28 (2H, m).

X-Ray Crystal Structure:
(2S,5R,Z)-undec-3-ene-2,5-diol (1.61). The reaction was performed according to the representative procedure with Pt(dba)$_3$ (7.2 mg, 6.6 µmol), (R,R)-diethylphenylTADDOLPh (1.34) (12.6 mg, 15.8 µmol), (2E, 4E)-undeca-2,4-diene (40 mg, 262.7 µmol), B$_2$(pin)$_2$ (198.3 mg, 275.8 µmol) in THF (2.6 mL) for 12 h at 60 °C, followed by oxidation, to afford the title compound as a clear, colorless oil (29.1 mg, 68% yield). R$_f$ = 0.15 (50% ethyl acetate/hexane, stain in PMA). Spectral data are in accordance with the literature.$^{34}$

Proof of Stereochemistry:

The title compound was treated with ozone in the procedure described for (R,Z)-dec-2-ene-1,4-diol. The resulting octane-1,2-diol was treated with 2,2-dimethoxypropane and catalytic p-toluenesulfonic acid. The resulting ketal was compared to the racemic ketal of octane-1,2-diol prepared from dihydroxylation of octene with osmium tetraoxide and 4-methylmorpholine N-oxide. The authentic sample was prepared from the Sharpless asymmetric dihydroxylation of octene utilizing AD-mix α.

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Chiral GLC (β-dex, Supelco, 100 °C, 20 psi) – analysis of the acetonide of octane-1,2-diol.
1.7.10. Procedure for Butenolide Formation (Scheme 1.16).

Oxidation of the 1,4-hydroxylated product was performed according to the literature procedure. To a flame-dried flask was added a solution of (R,Z)-dec-2-ene-1,4-diol (50 mg, 0.29 mmol) in DCM:MeCN (3.0 mL, 9:1), followed by 4-methylmorpholine N-oxide (102.0 mg, 0.87 mmol) under N\textsubscript{2} atmosphere. The reaction mixture was stirred at room temperature for 10 min, after which time tetrapropylammonium perruthenate (5.1 mg, 14.5 µmol) was added. The reaction was allowed to stir for 5 h, and was then diluted with CH\textsubscript{2}Cl\textsubscript{2} (5 mL), filtered over a pad of silica, and was washed with CH\textsubscript{2}Cl\textsubscript{2}. The volatiles were removed by rotary evaporation and the crude product was purified by column chromatography on SiO\textsubscript{2} (10-20% ethyl acetate/hexanes) to afford the desired product as a clear, colorless oil (33.2 mg, 68% yield).

(R)-5-hexylfuran-2(5H)-one (1.62). \textsuperscript{1}H NMR (400 MHz, CDCl\textsubscript{3}): \(\delta\) 0.86 (3H, t, \(J = 7.0\) Hz), 1.22-1.45 (8H, m), 1.58-1.78 (2H, m), 4.98-5.02 (1H, m), 6.07 (1H, dd, \(J = 5.6\) Hz, 2.0 Hz), 7.42 (1H, dd, \(J = 6.0\) Hz, 1.6 Hz); \textsuperscript{13}C NMR (100 MHz, CDCl\textsubscript{3}): \(\delta\) 156.4, 121.6, 83.6, 33.4, 31.7, 29.9, 29.1, 25.1, 22.7, 14.2; IR (neat): 2924.6 (m), 2856.88 (w), 1746.4 (s), 1464.8 (w), 1160.3 (m), 1099.4 (m), 815.8 (s); HRMS-(ESI+) for C\textsubscript{10}H\textsubscript{17}O\textsubscript{2} [M+H]: calculated: 169.1229, found: 169.1231.

Chiral GLC (β-dex, Supelco, 100 °C for 5 min, ramp 3 °C/min to 160 °C, 20 psi).

1.7.11. Procedure for Diene Diboration/Allylation/Oxidation (Scheme 1.17).

In the dry box, an oven-dried 6-dram vial with magnetic stir bar was charged with Pt(dba)$_3$ (15.8 mg, 17.6 µmol), (R,R)-xylylTADDOLPPh (L1) (23.7 mg, 34 µmol), and toluene (5.8 mL, 0.1 M). After stirring for 1 h, B$_2$(pin)$_2$ (154.1 mg, 0.606 mmol) was added to the mixture followed by (E)-1,3-decadiene (80 mg, 0.578 mmol). The vial was sealed with a polypropylene cap, removed from the dry box, and stirred at 60 °C for 12 h. The reaction mixture was cooled to ambient temperature and charged with freshly washed (10% sodium carbonate followed by sodium sulfite) and distilled benzaldehyde (65 µL, 0.606 mmol). The reaction was allowed to stir at room temperature for 6 h at which time the reaction mixture was cooled to 0 °C (ice/water) and charged with tetrahydrofuran (3.0 mL), 3 M sodium hydroxide (2.0 mL), and 30% hydrogen peroxide.
(1.0 mL). The reaction was gradually warmed to room temperature and allowed to stir for 12 h at which time the vial was cooled to 0 °C (ice/water). Saturated aqueous sodium thiosulfate was added dropwise over 5 min, the reaction mixture was diluted with ethyl acetate and the aqueous and organic layers were separated. The aqueous layer was rinsed with ethyl acetate (3 x 15 mL), and the combined organic were washed with brine. The organic layer was dried over Na$_2$SO$_4$, filtered, and volatiles were removed by rotary evaporation. The crude reaction mixture was purified on silica gel (50% ethyl acetate/hexanes) to afford a clear, colorless oil (99.6 mg, 66% yield).

(1S,2S)-2-((E)-oct-1-enyl)-1-phenylpropane-1,3-diol (1.66). $^1$H (500 MHz, CDCl$_3$): $\delta$ 0.86 (3H, t, $J = 7.5$ Hz), 1.09-1.26 (8H, m), 1.86-1.91 (2H, m), 2.46 (1H, br s), 2.59-2.63 (1H, m), 3.73 (1H, dd, $J = 10.5$ Hz, 4.5 Hz), 3.82 (1H, dd, $J = 11.0$ Hz, 7.3 Hz), 4.73 (1H, d, $J = 8$ Hz), 5.15 (1H, dtt, $J = 15.5$ Hz, 8.5 Hz, 1.5 Hz), 5.38 (1H, dt, $J = 15.5$ Hz, 7.0 Hz), 7.24-7.36 (5H, m); $^{13}$C NMR (125 MHz, CDCl$_3$): $\delta$ 14.2, 22.7, 28.7, 29.2, 31.8, 32.7, 51.6, 65.5, 78.2, 126.5, 126.8, 127.8, 128.4, 135.1, 142.9; IR (neat): 3334 (br s), 2954 (s), 2923 (s), 2853 (s), 1453 (s), 1377 (w), 1015 (s), 967 (s), 758 (s), 698 (s) cm$^{-1}$; HRMS-(ESI+) for C$_{17}$H$_{26}$O$_2$Na [M+Na]: calculated 285.1831, observed: 285.1841. The crude reaction mixture was purified on silica gel (50% ethyl acetate/hexanes) to afford a clear, colorless oil (99.6 mg, 66% yield). $R_f = 0.62$ (50% ethyl acetate, stain in PMA).
Chiral GLC (β-dex, Supelco, 160 °C) – analysis of the acetonide of (1S,2S)-2-(E)-oct-1-enyl)-1-phenylpropane-1,3-diol.

Proof of Stereochemistry:

To a flame-dried 10 mL round-bottomed flask with magnetic stir bar was added 1,3-diol (52.8 mg, 0.201 mmol) and dichloromethane (2.51 mL, 0.08 M) under nitrogen. The reaction mixture was cooled to -40 °C (dry ice with ethylene glycol) and charged with freshly distilled diisopropylethylamine (77 μL, 0.4426 mmol), followed by
methanesulfonyl chloride (16 µL, 0.201 mmol). The reaction mixture was allowed to warm to -10 °C over 3 h and was then quenced with 1 M K₂CO₃ (20 mL) and allowed to stir at rt for 20 min. The reaction mixture was transferred to a separatory funnel and the aqueous and organic layers separated. The aqueous layer was washed three times with dichloromethane. The organic extracts were combined, dried (Na₂SO₄), and filtered over cotton. Volatiles were removed by rotary evaporation. The unpurified material was carried onto the next step. Procedure was adapted from the literature.₃⁶

![Chemical structure](image)

To a 10 mL flame-dried round-bottomed flask with magnetic stir bar was added the unpurified mesylate and tetrahydrofuran (338 µL). The flask was cooled to 0 °C and charged with anhydrous methanol (26 µL, 7.1 M, distilled over calcium hydride) and 2.0 M lithium borohydride in THF (331 mL, 0.663 mmol) over a 10 min period. The reaction was allowed to stir for 4 h at 0 °C, at which time 1 M NaOH (10 mL) was added over 15 min. Ethyl acetate was then added to the reaction mixture. The aqueous and organic layers were separated, and the aqueous layer was washed three times with ethyl acetate. The organic layers were combined, washed with brine, dried (Na₂SO₄), filtered, and concentrated by rotary evaporation. The unpurified material was purified by silica gel

chromatography with 5% ethyl acetate/hexanes as the eluant to afford 18.9 mg of a clear oil (40% yield). Procedure was adapted from the literature.³

(1S,2R,E)-2-methyl-1-phenyldec-3-en-1-ol. ¹H (500 MHz, CDCl₃): δ 0.87 (3H, t, J = 7 Hz), 0.97 (3H, d, J = 6.5 Hz), 1.22-1.30 (8H, m), 1.94-1.98 (2H, m), 2.51-2.54 (1H, m), 4.58 (1H, t, J = 4.8 Hz), 5.30 (1H, ddt, J = 15.5 Hz, 7.5 Hz, 1.5 Hz), 5.44 (1H, m), 7.23-7.34 (5H, m); ¹³C NMR (125 MHz, CDCl₃): δ 14.2, 14.9, 22.7, 28.9, 29.5, 31.8, 32.7, 43.8, 77.6, 126.6, 127.3, 128.0, 131.5, 132.3, 142.7; IR (neat): 3387 (m), 3028 (s), 2957 (s), 2871 (s), 1453 (s), 1018 (m), 967 (s), 700 (s) cm⁻¹; HRMS-(ESI+) for C₁₇H₂₅[M-H₂O+H]: calculated: 229.1956, found: 229.1960. The crude reaction mixture was purified on silica gel (50% ethyl acetate/hexanes) to afford a clear oil (18.9 mg, 40% yield). Rᵥ = 0.57 (50% ethyl acetate, stain in PMA). [α]₀ = -7.24 (c = 1.10, CHCl₃). Optical rotation is in accordance with the literature.³⁷

Chapter 2

Development, Scope, and Utility of the Enantioselective Platinum-Catalyzed 1,2-Diboration of cis-1,3-Dienes: Application to Stereoselective Allylation

2.1. Introduction

Polyketides are a valuable class of natural products that not only possess a diverse range of biological activities and pharmacological properties, but often contain interesting chemical structures as well. Studies by Newman and Cragg suggest that roughly 20% of top-selling small molecule therapeutics are polyketides\(^1\) and that compounds containing polyketide functionality are five times more likely to possess useful biological activity compared to other families of natural products.\(^2\) Some of the most well known polyketide natural products are shown in Figure 2.1, including erythromycin, epothilones A-F, discodermolide, and ixabepilone. Erythromycin has been widely utilized as a potent antibiotic for the past 60 years and is still a common target for organic chemists.\(^3\) The epothilones have received substantial attention throughout the organic chemistry community for their efficacious anti-tumor activity and several are in


early clinical trials for the treatment of lung, breast, and prostate cancer. The most potent natural microtubule-stabilizing agent known to date, discodermolide, shows activity against a variety of cancer cell lines with IC\textsubscript{50} values ranging from 3-80 nm. In 2004, Novartis undertook the daunting task of synthesizing 60 g of (+)-discodermolide for Phase I clinical trials. Their synthesis included 39 chemical steps with 17 purifications, and took 20 months to complete. Unfortunately, clinical trials with discodermolide have been terminated due to undesired lung toxicities.

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5 For a review on the total syntheses of discodermolide see: Smith III, A. B.; Freeze, B. S. *Tetrahedron*, 2008, 64, 261.


Figure 2.1. Important Polyketide Natural Products

All of the natural products shown in Figure 2.1 contain at least one propionate unit, and it is likely that this functionality plays a significant role in the beneficial pharmacological properties found in this class of compounds. Therefore, methods that allow rapid construction of valuable polyketide structures have been heavily studied. Among the strategies to prepare polyketides, the stereoselective addition of crotylmethyl reagents (2.1) to prochiral carbonyl compounds ranks as one of the leading ways to generate polypropionate substructures. One disadvantage to the majority of crotylation reactions is that they deliver products bearing a terminal olefin (2.2). Additional synthetic

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manipulations are therefore required to obtain further functionality at the alkene site (Scheme 2.1, structure 2.3).

**Scheme 2.1.** General Carbonyl Crotaylmetallation Strategy Delivers Terminal Alkene

A solution to this problem has been the use of the vinylogous aldol reaction to generate homoallylic alcohols with useful substitution at the olefin position (Scheme 2.2). However, the majority of these methods are *anti*-selective and the development of a general and efficient *syn*-selective version has not been reported. It is clear that a catalytic enantioselective process that provides access to highly functionalized *syn*-polypropionate structures from simple starting materials, and does not rely on the use of stoichiometric chiral auxiliaries, is particularly desirable.

**Scheme 2.2.** General Vinylogous Aldol Reaction Delivers Propionate Products with Functionalized Alkene

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2.2. Background

The first examples of catalytic enantioselective crotylation of aldehydes were reported by Yamamoto in 1991 through the use of chiral acyloxy boranes (CAB) as Lewis-acid catalysts (Scheme 2.3). The CAB catalyst 2.7 is especially effective for the addition of substituted allylic silanes to aromatic aldehydes. With 20 mol% of 2.7, the β,γ-disubstituted allylic silane 2.6 undergoes addition to benzaldehyde to give the syn-homoallylic alcohol 2.8 in 74% yield, 97:3 dr and 98:2 er. It is noteworthy that high syn-selectivities are observed regardless of the stereochemical purity of the starting silane. Aliphatic aldehydes can also be used, providing homoallylic alcohol 2.9 with high syn-selectivity, but in low yield.

Scheme 2.3. Yamamoto’s CAB-Catalyzed syn-Selective Crotylsilation Reaction

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The use of chiral Lewis bases as promoters for asymmetric crotylation of carbonyl compounds was pioneered by Denmark and co-workers in 1994.\textsuperscript{11} They first discovered the ability of stoichiometric amounts of chiral phosphoramides to promote the addition of allylsilanes to benzaldehyde in good yield and diastereoselectivity; however, the homoallylic alcohol products were obtained with modest enantiopurities (80:20 er). In 2001, they developed a catalytic variant of this reaction utilizing bisphosphoramidate 2.\textsuperscript{11}, which catalyzed the addition of \((Z)\)-crotylsilane 2.\textsuperscript{10} to benzaldehyde to provide homoallylic alcohol 2.\textsuperscript{12} in 89% yield, 99:1 dr and 97:3 er (Scheme 2.4).\textsuperscript{9b} The use of \(\alpha,\beta\)-unsaturated aldehydes was also successfully demonstrated, but crotylsilation of aliphatic aldehydes was not reported. Additionally, 5 equivalents of \(i\)-Pr\textsubscript{2}NEt were required to assist in catalyst turnover.\textsuperscript{12}

\textbf{Scheme 2.4.} Denmark’s Lewis-base Promoted \textit{syn-}Selective Crotylsilation Reaction

\begin{center}
\begin{figure}
\centering
\includegraphics[scale=0.5]{Scheme2.4.png}
\end{figure}
\end{center}

Dennis Hall has also significantly contributed to the area of catalytic carbonyl allylation, taking advantage of allyl- and crotlylboron reagents. In a recent study from his laboratory,\textsuperscript{13} they reported a novel class of C\textsubscript{2}-symmetric chiral diols in combination with SnCl\textsubscript{4} exploiting Yamamoto’s Lewis-acid assisted Brønsted acidity (LBA) catalysis.\textsuperscript{14} This dual acid manifold was efficient at catalyzing the crotlylboration of aliphatic aldehydes to provide the corresponding syn-homoallylic alcohol propionate units in good yields and enantiopurities (Scheme 2.5). The use of aromatic aldehydes in the crotlylboration reaction was not discussed. In a later publication, Hall and co-workers further improved the enantioselectivity of their catalyst system to achieve up to 98:2 er.\textsuperscript{15} However, it was only applied to the anti-selective crotlylboration of aldehydes, further supporting the need for a general catalytic enantioselective method to arrive at syn-propionate structures.

\textit{Scheme 2.5.} Hall’s Vivol/Sn-Catalyzed \textit{syn}-Selective Crotlylboration of Aldehydes

\begin{align*}
\text{Me} &\quad \text{B(pin)} \quad 2.13 \quad + \quad \text{TBDPSO} \quad 2.14 \quad \text{O} \\
&\quad \overset{\text{Na}_2\text{CO}_3 \text{ (0.2 equiv)}}{\text{SnCl}_4 \text{ (10 mol\%)} } \quad \text{toluene, -78 °C, 16 h} \\
&\quad \rightarrow \quad \text{TBDPSO} \quad \overset{\text{Me}}{\text{OH}} \quad 2.16 \\
&\quad \text{75\% yield, 90:10 er}
\end{align*}

Another powerful example of an aldehyde crotylboration that provides stereodefined homoallylic alcohols was reported by Aggarwal and co-workers.\textsuperscript{16} They take advantage of Hoppe’s sparteine-complexed lithiated carbamates\textsuperscript{17} in the homologation of (Z)-vinylboronic esters (2.18) to generate enantiopure α-chiral crotylboronates. Subsequent addition of an aldehyde provides the syn-homoallylic alcohols with excellent levels of diastereomeric and enantiomeric purity, albeit in moderate yields (Scheme 2.6). The use of 4 equivalents of MgBr\textsubscript{2}\textperiodcentered Et\textsubscript{2}O as a Lewis acid was required to promote both the 1,2-rearrangement in the homologation step and the addition of the intermediate crotylboronic ester to the aldehyde. Furthermore, this method relies on superstoichiometric amounts of (−)-sparteine as a chiral modifier, and access to the unnatural opposite enantiomer is challenging.

\textit{Scheme 2.6.} Aggarwal’s Lithiation-Borylation-Allylation Reaction to Access Stereodefined \textit{syn}-Homoallylic Alcohols

\begin{align*}
1) \text{s-BuLi (1.4 equiv),} \\
\text{(−)-sparteine (1.4 equiv)} \\
\text{Et\textsubscript{2}O, -78 °C, 5 h} \\
2) \quad \text{(1.5 equiv), -78 °C to rt, 30 min} \\
\text{Me} \\
\text{2.18} \\
3) \text{MgBr\textsubscript{2}-OEt\textsubscript{2} (4 equiv), rt, 30 min} \\
4) \text{CyCHO (2 equiv), rt, 15 min} \\
5) \text{H\textsubscript{2}O\textsubscript{2}, NaOH, 0 °C to rt} \\
\text{2.19: R = Ph(CH\textsubscript{2})\textsubscript{2}, 59\% yield} \\
\text{99:1 dr, 99:1 er} \\
\text{2.20: R = Me, 46\% yield,} \\
\text{99:1 dr, 99:1 er}
\end{align*}


All of the above described crotylmetallation methods furnish homoallylic alcohol products with unfunctionalized olefins. If further substitution at the alkene site is desired, additional synthetic manipulations are required. To address this limitation, there have been several new methods developed for the synthesis of homoallylic alcohols containing a functionalized alkene. One strategy developed by Krische involves the Ru-catalyzed reductive coupling of 2-silyl-butadiene (2.21) with aldehydes or primary alcohols through a hydrogen transfer/crotylmetallation process. The overall transformation provides carbonyl crotylation products in good yields and with high levels of syn-diastereoselectivity and enantioselectivity without the generation of stoichiometric byproducts (Scheme 2.7). Furthermore, the propionate products contain a vinylsilane instead of an unfunctionalized alkene, making additional synthetic transformations possible. It was reasoned that the silyl group in 2.21 enforced the generation of pseudo-(Z)-α-crotylruthenium isomers to favor the formation of syn-crotylation products. In the absence of this functional group, the hydrohydroxyalkylation of 1,3-butadiene provides crotylation products with prohibitively low levels of diastereoselectivity.

**Scheme 2.7.** Krische’s syn-Hydrohydroxyalkylation of 2-Silyl-Butadiene

Another method that provides crotlyation products bearing a functionalized alkene was reported by Panek and co-workers in 2010.\textsuperscript{19} They demonstrate the use of enantioenriched crotysilanes \textit{2.23} and \textit{2.25} in the crotylation of benzaldehyde to arrive at \textit{syn}-vinylogous aldol products \textit{2.24} and \textit{2.26} in good yields and with conservation of enantiomeric purity (Scheme 2.8). However, the substrate scope is limited and the diastereoselectivities are low in some cases. Additionally, crotysilanes \textit{2.23} and \textit{2.25} are synthesized in low yields by enantioselective Rh(II)- or Cu(I)-catalyzed Si-H insertion to an \textit{α}-diazovinylacetate. The crotylation reagents cannot be used directly in aldehyde allylation reactions and must be purified and recrystallized in order to obtain useful levels of enantiomeric purity.

\textit{Scheme 2.8.} Panek’s \textit{syn}-Selective Crotysilation to Access Vinylogous Aldol Products

\begin{equation}
\text{Me}_2\text{SiPh}_3\text{C}O\text{Me}\underset{\text{SiPh}_3}{\longrightarrow}\text{PhCHO, TMSOMe}\quad\text{TMSOTf, -60 °C}\quad\text{OMe}\text{Ph}_2\text{C}O\text{Me}\\text{eq. 1}
\end{equation}

\begin{equation}
\text{Me}_2\text{SiMe}_2\text{Ph}\text{C}O\text{Me}\underset{\text{SiMe}_2\text{Ph}}{\longrightarrow}\text{PhCHO, TMSOBn}\quad\text{TMSOTf, -78 °C}\quad\text{OBn}\text{Me}_2\text{C}O\text{Me}\\text{eq. 2}
\end{equation}

\textit{eq. 1
79\% yield, 6.3:1 dr, 98:2 er

\textit{eq. 2
51\% yield, 11:1 dr, 98:2 er

Similar to Aggarwal’s method described in Scheme 2.6, Artissan also utilized Hoppe’s enantioselective deprotonation strategy to access functionalized crotyl titanium reagents that can be used to deliver stereodefined polypropionate-like structures that contain a synthetic handle on the alkene (Scheme 2.9).\(^{20}\) They reported the deprotonation of crotylcarbamate 2.27 in the presence of \(n\text{-BuLi}\) and (−)-sparteine followed by transmetalation to arrive at \((R,E)\)-allyltitanate 2.28. Subsequent addition of propionaldehyde led to the formation of \((Z)\)-\(\text{anti}\)\)-homoallylic alcohol 2.29 in 80% yield, 99:1 dr, and 96:4 er. They successfully demonstrated the utility of the vinylcarbamate in alkyne formation and Ni-catalyzed cross-coupling reactions. Ardisson has applied this powerful method to the total synthesis of a variety of natural products including tylonolide\(^{18a}\) and discodermolide,\(^{18b}\) however, the method is restricted to the formation of the \(\text{anti}\)\)-diastereomer of product due to the stereochemical instability of \(\text{cis}\)\)-crotyllithium reagents.

**Scheme 2.9.** Ardisson’s \(\text{anti}\)-Selective Crotyltitanation

A more recent advance in the synthesis of functionalized allylmetal reagents was reported by Roush and co-workers.\textsuperscript{21} Their method involved the hydroboration of allenylstannane 2.30 with Brown’s chiral $d^{lpc}$ borane, which afforded the dimetallated allylboron 2.31 upon a diastereoselective 1,3-boratropic shift (Scheme 2.10). Addition of an aldehyde to this intermediate provided enantioenriched homoallylic alcohols (2.32) in good yields for a variety of aldehyde substrates. The products obtained in this method contain a vinylstannane that could be utilized in Stille cross-coupling reactions\textsuperscript{22} for further C-C bond formation at the olefin unit. However, this work did not allow access to propionate-derived compounds due to lack of substitution on the allene starting material.

\textit{Scheme 2.10.} Roush’s Enantioselective Synthesis of ($E$)-$\delta$-Stannyl Homoallylic Alcohols

![Scheme 2.10](image)

To expand the utility of this allylboration methodology, Roush later developed the enantioconvergent hydroboration of racemic allenes to arrive at ($E$)-$\delta$-stannyl-$anti$-homoallylic alcohols in good yields and high levels of enantiomeric purity (Scheme


2.11). Hydroboration of racemic allenylstannane 2.33 with (4Ipc)₂BH converted both allene enantiomers into the same nonracemic intermediate which, upon addition of benzaldehyde, underwent stereocontrolled crotylboration to provide the enantiomerically enriched anti-homoallylic alcohol 2.35 in an excellent 67% yield, 15:1 dr, and 95:5 er.

When utilizing the Et-substituted allene 2.34, the hydroboration/crotylation product was obtained in 61% yield and 98:2 er, but the diastereoselectivity decreased to 6:1. The syn-crotylboration product cannot be produced in high yield or enantiopurity because the dimetallated intermediate is formed under kinetic control in favor of the (E)-crotylboron. The broad applicability of this method is further restricted by the use of stoichiometric Sn reagents on account of their high toxicity.

**Scheme 2.11.** Roush’s Enantioselective Synthesis of (E)-δ-Stannyl-anti-Homoallylic Alcohols

By incorporating a synthetic handle at the alkene site, Ardisson and Roush developed useful solutions to the limitations faced by many crotylmetallation reactions.

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However, both methods rely on superstoichiometric amounts of a chiral modifier. In the protocol reported by Roush, the use of Brown’s (\(d\)-Ipc)\(_2\)BH generates 2.8 equivalents of a secondary alcohol byproduct, isopinocampheol, which frequently complicates isolation of the desired crotylboration product, also a secondary alcohol.\(^{24}\) This feature has prevented implementation of this technology at the process level. It is clear that the need exists for a general method that provides syn-polyketide substructures through a process that has the following characteristics: diastereo- and enantiocontrol is achieved through the use of a chiral catalyst; starting materials are inexpensive and non-toxic; isolation of reactive intermediates is not required so that only a single purification is necessary; and the product contains an additional synthetic handle for chain-extending polyketide synthesis.

2.3. Development of the Enantioselective Pt-Catalyzed 1,2-Diboration of cis-1,3-Dienes\(^{25}\)

As discussed in Chapter 1, Section 1.4, the proposed mechanism for the Pt-catalyzed 1,4-diboration of trans-1,3-dienes involves coordination of the diene to the Pt-bis(boryl) complex followed by carbon-boron bond formation at C4 of the diene, remote from the metal center (Scheme 2.12, structure 2.37). Subsequent reductive elimination at the less sterically hindered terminal carbon provides (Z)-1,4-bis(boronate)ester 2.38. We propose that the regioselectivity in this reaction is highly dependent on the conformation


of the 1,3-diene during the insertion step. The trans-1,3-dienes used in the 1,4-diboration reaction are able to adopt the S-cis conformation that is necessary for this type of insertion mechanism.

**Scheme 2.12.** Proposed Insertion Mechanism for Pt-Catalyzed 1,4-Diboration of trans-1,3-Dienes

In an effort to further probe the operative mechanism for diene diboration, we considered the diboration of a diene that highly disfavored the S-cis conformer. Utilizing cis-1,3-pentadiene should force the diene to adopt the S-trans conformation due to the A\(^{1,3}\) strain present in the S-cis conformation (Scheme 2.13). This might prohibit the 1,4-diboration pathway and encourage a 1,2-insertion mechanism (2.40) to provide 1,2-bis (boronate)ester 2.41. The direct oxidation of this intermediate should provide (Z)-allylic alcohol 2.42. The products of the 1,2-diboration/oxidation of cis-1,3-dienes are chemically interesting in their own regard, but the synthetic utility of the reactive α-chiral...
(Z)-crotylboronate embedded in the bis(boronate)ester intermediate (2.41) is far more valuable.

**Scheme 2.13.** Proposed Insertion Mechanism for Pt-Catalyzed 1,2-Diboration of *cis*-1,3-Dienes

According to the influential studies by Hoffmann,26 these features should allow for highly stereoselective carbonyl crotylation reactions. After diboration and subsequent aldehyde addition, the crotylboration would likely proceed through a closed, 6-membered ring transition state as depicted in 2.43 in which the CH₂B(pin) occupies the equatorial position to avoid an A(1,3) interaction with the *cis* substituent (Scheme 2.14). This reaction should provide a *syn*-crotylboration product containing a *trans*-alkene (2.44). Most importantly, a unique feature of a crotylboration using 2.41 is that the product would contain an additional carbon-boron bond that could be used for subsequent

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synthetic manipulations, addressing the previous limitations described in Section 2.2. The development of a tandem Pt-catalyzed enantioselective diboration/allylation sequence would provide a simple and general solution to the synthesis of syn-polypropionate subunits bearing a functional group handle for chain-extending reactions.

Scheme 2.14. Pt-Catalyzed Diboration to Access α-Chiral Allylboronates for the Synthesis of Enantioenriched Polypropionate Units

In order to achieve the above-described goal, we first needed to develop the catalytic enantioselective 1,2-diboration of cis-1,3-dienes and determine if a catalyst system similar to that used in the 1,4-diboration of trans-1,3-dienes would render this process highly regio- and stereoselective. To that end, commercially available cis-1,3-pentadiene was used as a test substrate in the Pt-catalyzed diboration reaction with a variety of phosphine ligands (Table 2.1). In the presence of 3 mol% Pt(dba)₃ and 6 mol% PCy₃, the 1,2-diboration/oxidation product 2.42 was generated in 14% yield, with a 1.2:1 regioselectivity favoring the 1,2-diboration product (entry 2). Utilizing the chiral 3,5-
xylyl-TADDOL-derived phosphonite ligand (R,R)-2.46, which served as the optimal ligand for the Pt-catalyzed 1,4-diboration of trans-1,3-dienes, we were pleased to see that 1,2-diol 2.42 could be obtained in 50% yield with a 5.3:1 ratio of regioisomers; however, the enantiomeric ratio was only 90:10 (entry 5). Increasing the size of the substituent attached to aryl ring of the TADDOL backbone with ligand (R,R)-2.47 led to an increase in the enantioselectivity of the diboration reaction, providing 1,2-diol 2.42 in 52% yield and 94:6 er (entry 6). No additional improvements in selectivity were observed when performing the diboration in toluene or at room temperature (entries 7 and 8). Further increasing the size of the substituents on the aryl rings of the TADDOL backbone to i-propyl or t-butyl led to a decrease in both reactivity and enantioselectivity (entrie 9 and 10). The diboration of cis-1,3-pentadiene with ligand (R,R)-2.49 favored the 1,4-product 2.39 over the desired 1,2-product giving a 1:2.6 ratio of regioisomers. It was reasoned that a ligand which contained meta-substituents with steric bulk in between that of ethyl and i-propyl would further improve the enantioselectivity of the diboration reaction. Ligand (R,R)-2.50, containing 3,5-di-i-butyl groups, was prepared and examined in the Pt-catalyzed diboration of cis-1,3-pentadiene. Excitingly, this modified TADDOL-ligand afforded the desired 1,2-diol 2.42 in 69% yield, 4.8:1 regioselectivity, and 95:5 er (entry 11).
Table 2.1. Ligand Survey for Pt-Catalyzed 1,2-Diboration of cis-1,3-Dienes

<table>
<thead>
<tr>
<th>entry</th>
<th>ligand</th>
<th>Ar</th>
<th>1,2:1,4&lt;sup&gt;a&lt;/sup&gt; % yield 2.42</th>
<th>er</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>none</td>
<td>-</td>
<td>0</td>
<td>-</td>
</tr>
<tr>
<td>2</td>
<td>PCy&lt;sub&gt;3&lt;/sub&gt;</td>
<td>-</td>
<td>1.2:1</td>
<td>14</td>
</tr>
<tr>
<td>3</td>
<td>PBn&lt;sub&gt;3&lt;/sub&gt;</td>
<td>-</td>
<td>0</td>
<td>-</td>
</tr>
<tr>
<td>4&lt;sup&gt;b&lt;/sup&gt;</td>
<td>(R,R)-2.45</td>
<td>Ph</td>
<td>ND</td>
<td>&lt;10</td>
</tr>
<tr>
<td>5</td>
<td>(R,R)-2.46</td>
<td>3,5-dimethylphenyl</td>
<td>5.3:1</td>
<td>50</td>
</tr>
<tr>
<td>6</td>
<td>(R,R)-2.47</td>
<td>3,5-diethylphenyl</td>
<td>4.0:1</td>
<td>52</td>
</tr>
<tr>
<td>7&lt;sup&gt;b&lt;/sup&gt;</td>
<td>(R,R)-2.47</td>
<td>3,5-diethylphenyl</td>
<td>ND</td>
<td>47</td>
</tr>
<tr>
<td>8&lt;sup&gt;c&lt;/sup&gt;</td>
<td>(R,R)-2.47</td>
<td>3,5-diethylphenyl</td>
<td>ND</td>
<td>14</td>
</tr>
<tr>
<td>9</td>
<td>(R,R)-2.48</td>
<td>3,5-di-i-propylphenyl</td>
<td>3.8:1</td>
<td>22</td>
</tr>
<tr>
<td>10</td>
<td>(R,R)-2.49</td>
<td>3,5-di-t-butylphenyl</td>
<td>1:2.6</td>
<td>12</td>
</tr>
<tr>
<td>11</td>
<td>(R,R)-2.50</td>
<td>3,5-di-i-butylphenyl</td>
<td>4.8:1</td>
<td>69</td>
</tr>
</tbody>
</table>

<sup>a</sup> ND = not determined <sup>b</sup> diboration run in toluene <sup>c</sup> diboration run at room temperature

In addition to TADDOL-derived phosphonite ligands, the chiral monodentate phosphine ligand (R,R)-t-Bu-OxaPHOS 2.51, developed by fellow graduate student Chris Schuster, was tested in the Pt-catalyzed 1,2-diboration reaction (Scheme 2.15).<sup>27</sup> Although this novel ligand was competent in the reaction, the desired 1,2-diol was furnished in only 28% yield and 83:17 er. The initial results obtained with the (R,R)-t-Bu-OxaPHOS ligand are promising, highlighting the potential for improved ligand structures.

Scheme 2.15. Pt-Catalyzed Diboration of cis-1,3-Pentadiene with OxaPHOS Ligand

The nature of the Pt(0) source was also surveyed in the 1,2-diboration of cis-1,3-pentadiene (Table 2.2). In the presence of \((R,R)-2.47\), Pt(dba)\(_3\), Pt\(_2\)(dba)\(_3\), and Pt(nbe)\(_3\) all provided comparable levels of enantioselection. Pt(nbe)\(_3\) afforded the desired 1,2-diol in the highest relative yield and ratio of regioisomers (entry 3); however, Pt(dba)\(_3\) was selected as the optimal platinum pre-catalyst due to the ease of its synthesis compared to Pt\(_2\)(dba)\(_3\) and Pt(nbe)\(_3\).

Table 2.2. Survey of Pt(0)-Source in the 1,2-Diboration of cis-1,3-Pentadiene

<table>
<thead>
<tr>
<th>entry</th>
<th>Pt(0) (x mol%)</th>
<th>1,2:1,4</th>
<th>% yield</th>
<th>er</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Pt(dba)(_3) (3 mol%)</td>
<td>4.0:1</td>
<td>52</td>
<td>94:6</td>
</tr>
<tr>
<td>2</td>
<td>Pt(_2)(dba)(_3) (2.5 mol%)</td>
<td>4.8:1</td>
<td>56</td>
<td>94:6</td>
</tr>
<tr>
<td>3</td>
<td>Pt(nbe)(_3) (5 mol%)</td>
<td>5.9:1</td>
<td>65</td>
<td>93:7</td>
</tr>
</tbody>
</table>
Once the platinum pre-catalyst was selected, it was of interest to determine the optimal metal:ligand ratio, as well as the ideal catalyst loading. To that end, a small range of cis-1,3-diene substrates was tested in the Pt-catalyzed 1,2-diboration with varying reaction conditions (Table 2.3). Utilizing the nonyl substituted cis-1,3-diene, it was found that the chiral phosphonite ligand (R,R)-2.47 was more reactive and regioselective compared to the achiral phosphine ligand PCy3, providing the corresponding 1,2-diol in 85% yield, 6:1 regioselectivity and 95:5 er (entries 1 and 2). Altering the metal:ligand ratio from 1:2 (entry 2) to 1:1.2 (entry 3), the nonyl substituted 1,2-diol was obtained with the same level of enantiopurity, but both the regioselectivity and isolated yield diminished. A similar, but more extreme trend was also observed with the cyclohexyl substituted cis-1,3-diene substrate (entries 4 and 5), proving that a metal:ligand ratio of 1:2 gave the best results in the diboration reaction. The Pt-catalyzed diboration was then tested with a lower catalyst loading while maintaining a metal:ligand ratio of 1:2. With 0.6 mol% Pt(dba)3 and 1.2 mol% (R,R)-2.47 and an increased [substrate], the nonyl-substituted 1,2-diol product was provided in 39% yield, 3.1:1 regioselectivity and 96:4 er (entry 6). Similarly, the diboration/oxidation product of cis-1,3-pentadiene was generated with comparable enantiomeric purity, but in only 15% isolated yield (entry 7).
Table 2.3. Examination of Metal:Ligand Ratio and Catalyst Loading in 1,2-Diboration

![Reaction Scheme]

<table>
<thead>
<tr>
<th>entry</th>
<th>R</th>
<th>Pt(dba)₃ (x mol%)</th>
<th>ligand (y mol%)</th>
<th>1,2:1,4</th>
<th>% yield</th>
<th>er</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>nonyl</td>
<td>3 mol%</td>
<td>PCy₃ (6 mol%)</td>
<td>3.5:1</td>
<td>57</td>
<td>-</td>
</tr>
<tr>
<td>2</td>
<td>nonyl</td>
<td>3 mol%</td>
<td>(R,R)-2.47 (6 mol%)</td>
<td>6:1</td>
<td>85</td>
<td>95:5</td>
</tr>
<tr>
<td>3</td>
<td>nonyl</td>
<td>3 mol%</td>
<td>(R,R)-2.47 (3.6 mol%)</td>
<td>4:1</td>
<td>74</td>
<td>95:5</td>
</tr>
<tr>
<td>4</td>
<td>Cy</td>
<td>3 mol%</td>
<td>(R,R)-2.47 (6 mol%)</td>
<td>4:1</td>
<td>77</td>
<td>97:3</td>
</tr>
<tr>
<td>5</td>
<td>Cy</td>
<td>3 mol%</td>
<td>(R,R)-2.47 (3.6 mol%)</td>
<td>2.3:1</td>
<td>63</td>
<td>96:4</td>
</tr>
<tr>
<td>6ᵃ</td>
<td>nonyl</td>
<td>0.6 mol%</td>
<td>(R,R)-2.47 (1.2 mol%)</td>
<td>3.1:1</td>
<td>39(43)b</td>
<td>96:4</td>
</tr>
<tr>
<td>7ᵃ</td>
<td>Me</td>
<td>0.6 mol%</td>
<td>(R,R)-2.47 (1.2 mol%)</td>
<td>NDc</td>
<td>15</td>
<td>93:7</td>
</tr>
</tbody>
</table>

- **a** Diboration run with [substrate] = 0.5 M
- **b** Value in parentheses is % conversion
- **c** ND = not determined

The inspiration for the selective 1,2-diboration of cis-1,3-dienes was based upon the notion that in order for 1,4-diboration to occur, the diene substrate must adopt the S-cis conformation, and that cis-1,3-dienes largely favor the S-trans conformation. Even in the case of 1,3-butadiene there is a 4 kcal/mol difference in energy between the S-cis and S-trans conformers. The addition of 1,3-allylic strain present in cis-1,3-pentadiene likely contributes approximately 4 kcal/mol of additional strain energy. However, in the Pt-catalyzed diboration of cis-1,3-pentadiene, minor amounts of the 1,4-diboration/oxidation

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product 2.39 were consistently produced. The formation of this product could be explained by one of two arguments: 1) the diene isomerizes under the reaction conditions to form trans-1,3-pentadiene, which then undergoes the expected 1,4-diboration to afford 2.39; or 2) small amounts of the S-cis conformation are accessed under the reaction conditions, allowing 1,4-diboration to occur. To test which of these two possibilities was more likely, the 1,4-diol was isolated and the enantiomeric purity was analyzed. If diene isomerization was operative, it would be expected that the same level of enantioselection would occur for the 1,4-diboration of cis-1,3-pentadiene as for the 1,4-diboration of trans-1,3-pentadiene. However, as shown in Scheme 2.15, the 1,4-diol obtained from the diboration of cis-1,3-pentadiene was produced in 16% yield and only 61:39 er. In contrast, the Pt-catalyzed diboration of trans-1,3-pentadiene with (R,R)-2.47 furnished 1,4-diol 2.39 in 69% yield and 76:24 er (Chapter 1, Table 1.4). Therefore, it is unlikely that diene isomerization occurs under the reaction conditions. Due to the elevated temperature of the diboration reaction, it is more likely that some of the S-cis conformation is present, and the 1,4-diboration can take place, albeit in a less enantioselective fashion. Interestingly, the same major enantiomer of product is obtained for both the 1,4-diboration of trans-1,3-pentadiene and cis-1,3-pentadiene.
Scheme 2.16. Analysis of 1,4-Product Obtained from Diboration of cis-1,3-Pentadiene

With the optimized conditions in hand for the enantioselective Pt-catalyzed 1,2-diboration of 1,3-dienes, a variety of cis-1,3-diene substrates were prepared and examined in the diboration reaction (Table 2.4). It is important to note that although ligand (R,R)-2.50 provided the highest levels of enantioselection in the diboration of cis-1,3-pentadiene, ligand (R,R)-2.47 gave excellent levels of enantioselectivity for other diene substrates. Therefore, due to the difficulty of synthesizing (R,R)-2.50, ligand (R,R)-2.47 was utilized as the optimal ligand for all other diene substrates. Increasing the length of the alkyl chain from Me to pentyl or nonyl led to an increase in enantioselectivity (entries 2 and 3). Substrates bearing both α- and β-branching were tolerated in the diboration reaction, providing their corresponding 1,2-diol products in 97:3 er and 96:4 er respectively (entries 4 and 5). Interestingly, the i-butyl substituted diene performed with excellent levels of regioselectivity, favoring the 1,2-diboration product (14:1). Entry 7 illustrates that the presence of silyl protected ethers is allowed in the diboration reaction albeit with lower regioselectivity, furnishing the corresponding 1,2-diol in 56% yield and 95:5 er. The cis-1,3-diene substrate that included a non-conjugated aromatic ring proceeded well in the diboration reaction, affording the
diboration/oxidation product in 62% yield and 95:5 er (entry 6). However, substrates containing a conjugated aromatic ring suffered from low levels of enantioselectivity (entry 8). The decreased amount of stereocontrol observed for this reaction is most likely due to the planarity of the substrate, making facial selectivity challenging for the chiral catalyst system.

**Table 2.4.** Substrate Scope for the Pt-Catalyzed 1,2-Diboration of *cis*-1,3-Dienes

<table>
<thead>
<tr>
<th>entry</th>
<th>diene</th>
<th>product</th>
<th>1,2 : 1,4&lt;sup&gt;a&lt;/sup&gt; % yield&lt;sup&gt;b&lt;/sup&gt;</th>
<th>er&lt;sup&gt;c&lt;/sup&gt;</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Me</td>
<td>Me OH</td>
<td>4:1&lt;sup&gt;d&lt;/sup&gt;</td>
<td>93:7</td>
</tr>
<tr>
<td></td>
<td></td>
<td>5:1&lt;sup&gt;d&lt;/sup&gt;</td>
<td>52</td>
<td></td>
</tr>
<tr>
<td>2</td>
<td>pentyl</td>
<td>nonyl OH</td>
<td>4:1</td>
<td>95:5</td>
</tr>
<tr>
<td>3</td>
<td>nonyl</td>
<td>pentyl OH</td>
<td>6:1</td>
<td>96:4</td>
</tr>
<tr>
<td>4</td>
<td>i-Bu</td>
<td>i-Bu OH</td>
<td>14:1</td>
<td>96:4</td>
</tr>
<tr>
<td>5</td>
<td>Cy</td>
<td>Cy OH</td>
<td>4:1</td>
<td>97:3</td>
</tr>
<tr>
<td>6</td>
<td>Ph</td>
<td>Ph OH</td>
<td>4:1</td>
<td>95:5</td>
</tr>
<tr>
<td>7</td>
<td>TBDPSO</td>
<td>TBDPSO OH</td>
<td>3:1</td>
<td>95:5</td>
</tr>
<tr>
<td>8</td>
<td>Ph</td>
<td>Ph OH</td>
<td>3:1</td>
<td>81:19</td>
</tr>
</tbody>
</table>

<sup>a</sup> Regioselectivity determined from the crude <sup>1</sup>H NMR  
<sup>b</sup> Isolated yield of the 1,2-diol  
<sup>c</sup> Enantioselectivity determined by GC analysis of a derivative employing a chiral stationary phase  
<sup>d</sup> Ligand *(R,R)-2.47* used in the diboration reaction
2.4. Development of the Tandem Enantioselective Pt-Catalyzed Diboration/Allylation of cis-1,3-Dienes

Having successfully developed the first catalytic enantioselective 1,2-diboration of cis-1,3-dienes to access enantioenriched (Z)-1,2-bis(boronate)esters, it was of great interest to determine if the α-chiral allylboronate would be competent and selective in a tandem diboration/allylation sequence. Initial investigations involved the catalytic diboration of cis-1,3-pentadiene using Pt(dba)$_3$ and PCy$_3$ followed by an allylation to benzaldehyde (Scheme 2.17) The diboration was performed in THF and upon completion, the solvent was removed in vacuo and dichloromethane was added to the reaction mixture, followed by benzaldehyde. The reaction mixture was heated to 40 °C for 8 h and the reaction was then oxidized with alkaline H$_2$O$_2$. The desired diboration/allylation/oxidation product 2.53 was obtained in 48% yield with an excellent level of diastereomeric purity; however, 31% yield of an undesired side product was also isolated from the reaction mixture. The side product was identified as 1,4-diol 2.54, which arises from subsequent allylation of the initial product 2.52 to a second equivalent of aldehyde. Interestingly, the bis(allylation) product 2.54 appeared to be a single diastereomer, although, the relative stereochemistry of the two additional stereocenters was not determined.
Scheme 2.17. Initial Results for Tandem Diboration/Allylation Sequence

In order to improve the isolated yield of the desired mono(allylation) product 2.53, a systematic survey of reaction conditions was carried out (Table 2.5). Not surprisingly, increasing the reaction time of the allylation from 8 h to 40 h cleanly afforded the bis(allylation) product 2.54 in 71% yield (entry 2). Decreasing the temperature of the allylation reaction in combination with lowering the reaction concentration provided 40% yield of the desired syn-1,5-diol, but significant amounts of the bis(allylation) product were still produced (entry 3). Running the allylation reaction at 4 °C successfully stopped the formation of the bis(allylation) product, but the mono (allylation) only went to 46% conversion and the desired syn-1,5-diol 2.53 was obtained in 37% yield (entry 4). When the diboration reaction was carried out on a scale that delivered two or three-fold excess of the 1,2-bis(boronate)ester relative to benzaldehyde the production of the undesired bis(allylation) product was prevented while furnishing useful yields of the desired mono(allylation) product (entries 5 and 6). It was also reasoned that utilizing a less electrophilic aldehyde would diminish the amount of 2.54 formed in the reaction. In that regard, isobutyraldehyde was tested in the tandem
diboration/allylation sequence. When the allylation was carried out at room temperature, the 1,2-diol 2.42 was the only product isolated from the reaction, suggesting that the less reactive aldehyde did slow down the second allylation. Heating the allylation of isobutyraldehyde to 40 °C for 24 h provided 48% yield of the desired syn-1,5-diol, with minor amounts of the bis(allylation) product. From these experiments, it was clear that the optimum conditions for the diboration/allylation/oxidation sequence required at least 2.0 equivalents of the 1,2-bis(boronate)ester relative to the aldehyde.

Table 2.5. Optimization of Tandem Diboration/Allylation of cis-1,3-Pentadiene

<table>
<thead>
<tr>
<th>entry (x equiv)</th>
<th>R</th>
<th>temp (°C)</th>
<th>time</th>
<th>conc</th>
<th>%yield 2.53</th>
<th>%yield 2.54</th>
<th>%yield 2.42</th>
</tr>
</thead>
<tbody>
<tr>
<td>1&lt;sup&gt;b&lt;/sup&gt;</td>
<td>1.0</td>
<td>Ph</td>
<td>40</td>
<td>8 h</td>
<td>0.5 M</td>
<td>48</td>
<td>31</td>
</tr>
<tr>
<td>2</td>
<td>1.0</td>
<td>Ph</td>
<td>40</td>
<td>24 h</td>
<td>0.5 M</td>
<td>0</td>
<td>71</td>
</tr>
<tr>
<td>3</td>
<td>1.0</td>
<td>Ph</td>
<td>25</td>
<td>40 h</td>
<td>0.1 M</td>
<td>40</td>
<td>42</td>
</tr>
<tr>
<td>4</td>
<td>1.0</td>
<td>Ph</td>
<td>4</td>
<td>12 h</td>
<td>0.1 M</td>
<td>37(46)&lt;sup&gt;c&lt;/sup&gt;</td>
<td>0</td>
</tr>
<tr>
<td>5</td>
<td>2.0</td>
<td>Ph</td>
<td>25</td>
<td>12 h</td>
<td>0.25 M</td>
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<td>0</td>
</tr>
<tr>
<td>6</td>
<td>3.0</td>
<td>Ph</td>
<td>25</td>
<td>12 h</td>
<td>0.1 M</td>
<td>63(79)&lt;sup&gt;c&lt;/sup&gt;</td>
<td>0</td>
</tr>
<tr>
<td>7</td>
<td>1.0</td>
<td>i-Pr</td>
<td>25</td>
<td>11 h</td>
<td>0.1 M</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>8</td>
<td>1.0</td>
<td>i-Pr</td>
<td>40</td>
<td>24 h</td>
<td>0.1 M</td>
<td>48</td>
<td>12</td>
</tr>
</tbody>
</table>

<sup>a</sup> Isolated yield based on aldehyde.  <sup>b</sup> The bis(allylation) product 2.54 appeared to be a single diastereomer.  <sup>c</sup> Isolated 18% yield of the 1,4-diboration/allylation/oxidation product.  <sup>d</sup> Value in parentheses is the % conversion in the allylation.
With the optimal conditions for the tandem enantioselective diboration/allylation/oxidation in hand, a variety of aldehyde substrates were examined in the reaction sequence with cis-1,3-pentadiene (Table 2.6). As was expected, the (Z)-crotylboronate intermediate delivered the syn-propionate products with >20:1 diastereoselectivity in all cases, and the product alkene was consistently found to be in the trans configuration. Both linear and α-branched aliphatic aldehydes participated in the reaction sequence, with excellent conservation of enantiomeric purity from the crotylboronate to the aldehyde (entries 2, 5, and 6). Aromatic and α,β-unsaturated aldehydes were also tolerated in the reaction and furnished their corresponding syn-1,5-diols in 64-71% yield and up to 95:5 er. Additionally, aldehydes containing α-oxygenation engaged in the allylation reaction to provide highly functionalized syn-polyketide subunits in excellent yield and stereoisomeric purity. In all cases, the reactive allylboronate did not require isolation, and the tandem reaction sequence was performed in a single flask.
Table 2.6. Tandem Diboration/Allylation/Oxidation Sequence to Access syn-1,5-Diols

![Chemical structure and reaction scheme]

Even though the majority of polyketide targets contain propionate subunits, it would be synthetically valuable to be able to access a more diverse range of products through the same methodology by simply using different starting materials. In that

131
regard, cis-1,3-dienes containing varying substituents were examined in the tandem diboration/allylation/oxidation sequence with propionaldehyde (Scheme 2.18). With the i-butyl substituted cis-1,3-diene, the desired 1,5-diol 2.55 was obtained in 68% yield, >20:1 diastereoselectivity, and 96:4 er in a single flask reaction (eq. 1). The nonyl substituted cis-1,3-diene also performed well in the tandem reaction sequence to afford 2.56 in 70% yield, >20:1 dr, and 97:3 er (eq. 2).

Scheme 2.18. Tandem Diboration/Allylation/Oxidation of Substituted cis-1,3-Dienes
2.5. Conclusions

The first enantioselective 1,2-diboration of cis-1,3-dienes was developed using Pt-catalysis to afford 1,2-bis(boronate)esters in excellent yields and enantioselectivities. The bis(boronate)ester intermediates were directly oxidized to access enantioenriched (Z)-1,2-diols across a wide range of diene substrates. The turnover in regioselectivity for the Pt-catalyzed diboration of cis-1,3-dienes versus trans-1,3-dienes provides evidence for the necessity of accessing the S-cis conformation in order for the 1,4-diboration pathway to operate. The product regioselectivity can be controlled by simply manipulating the olefin diastereomer in the starting diene. The reactive (Z)-crotylboronate intermediate formed from the 1,2-diboration of cis-1,3-dienes was successfully utilized in a tandem diboration/allylation/oxidation sequence to provide enantiomerically enriched syn-polypropionate products in high yields and diastereoselectivities. The conservation of enantiopurity in this process was found to be nearly perfect for a variety of aldehyde substrates. This methodology represents a simple and cost-effective approach to the synthesis of syn-polyketide substructures starting from readily available dienes without the need to purify reactive intermediates, and provides products that contain an allylboronic ester that can be used for a variety of further synthetic transformations.
2.6. Experimentals

2.6.1. General Information. $^1$H NMR spectra were recorded on either a Varian Gemini-400 (400 MHz), a Varian Gemini-500 (500 MHz), a Varian Inova-500 (500 MHz), or a Varian Gemini-600 (600 MHz) spectrometer. Chemical shifts are reported in ppm with the solvent resonance as the internal standard (CDCl$_3$: 7.24 ppm). Data are reported as follows: chemical shift, integration, multiplicity (s = singlet, d = doublet, t = triplet, q = quartet, p = pentet, br = broad, m = multiplet, app = apparent), and coupling constants (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 Gemini-600 (150 MHz) spectrometer with complete proton decoupling. Chemical shifts are reported in ppm with the solvent resonance as the internal standard (CDCl$_3$: 77.0 ppm). Infrared (IR) spectra were recorded on a Bruker alpha spectrophotometer, $\nu_{\text{max}}$ cm$^{-1}$. Bands are characterized as broad (br), strong (s), medium (m), and weak (w). High resolution mass spectrometry (ESI) was performed at the Mass Spectrometry Facility, Boston College.

Liquid Chromatography was performed using forced flow (flash chromatography) on silica gel (SiO$_2$, 230×450 Mesh) purchased from Silicycle. Thin Layer Chromatography was performed on 25 µm silica gel plates purchased from Silicycle. Visualization was performed using ultraviolet light (254 nm), potassium permanganate (KMnO$_4$) in water, or phosphomolybdic acid (PMA) in ethanol. Analytical chiral gas-liquid chromatography (GLC) was performed on a Hewlett-Packard 6890 Series chromatograph equipped with a split mode capillary injection system, a flame ionization
detector, and a Supelco β-Dex 120 column with helium as the carrier gas. Analytical chiral supercritical fluid chromatography (SFC) was performed on a TharSFC Method Station II equipped with Waters 2998 Photodiode Array Detector.

All reactions were conducted in oven- or flame-dried glassware under an inert atmosphere of nitrogen or argon. Tetrahydrofuran, dichloromethane, acetonitrile, and diethyl ether were purified using Pure Solv MD-4 solvent purification system, from Innovative Technology, Inc., by passing the solvent through two activated alumina columns after being purged with argon. Triethylamine was distilled from calcium hydride. Potassium tetrachloroplatinate(II) was purchased from Acros Organics. Dibenzylideneacetone was purchased from Oakwood Chemicals. Tetrabutylammonium chloride was purchased from Fluka. Sodium acetate was purchased from Fisher Scientific. Norbornene was purchased from Aldrich and was sublimed prior to use. Bis (pinacolato)diboron was generously donated by Allychem Co., Ltd. and was recrystallized from pentane prior to use. Dichlorophenylphosphine, tris (dibenzylidenacetone) dipalladium (0), and tri-t-butylphosphine, were purchased from Strem Chemicals, Inc. and used without further purification. (Z)-penta-1,3-diene was purchased from ChemSampCo and was used without purification. 1,3,5-Tribromobenzene was purchased from Alfa Aesar. Benzaldehyde, hydrocinnamaldehyde, cinnamaldehyde, nonenal, propionaldehyde, iso-butyraldehyde, and benzyloxyacetaldehyde were purchased from Aldrich and distilled prior to use. All other reagents were purchased from Aldrich and used without further purification.
2.6.2. Preparation of Pt(dba)$_3$.

Tris(dibenzylideneacetone)platinum was prepared using the literature procedure$^1$ with slight modification. To a three-neck 500 mL round-bottom flask equipped with a magnetic stir bar and reflux condenser was added dibenzylideneacetone (3.95 g, 16.80 mmol), tetrabutylammonium chloride (2.00 g, 7.20 mmol), and sodium acetate (3.55 g, 43.30 mmol). Methanol (210.0 mL) was added and the solution was warmed to 70 °C in an oil bath until the solids dissolved (5 minutes). In a separate 50 mL pear-shaped flask was added potassium tetrachloroplatinate (1.00 g, 2.41 mmol) and water (8.0 mL), and the mixture gently warmed until solids dissolved. The contents of the pear shaped flask were transferred to the three-neck flask and the reaction was allowed to stir at 70 °C for 3 h. After 3 h, the reaction was cooled to ambient temperature, transferred to a one-neck 500 mL round-bottom flask and concentrated by rotary evaporation to half the volume. The reaction mixture was then filtered on a Büchner funnel and the remaining solids were washed with copious amounts of water and methanol until all yellow dibenzylideneacetone crystals were removed. The resulting solid residue was placed under high vacuum for 24 hours to remove residual methanol and water. This procedure furnished a dark brown solid (1.84 g, 85%) consistent with Pt(dba)$_3$. Anal Calc’d for C$_{51}$H$_{42}$O$_3$Pt: C, 68.22; H, 4.71. Found: C, 67.09; H, 4.49 (average of two experiments). Platinum analysis was performed by ICP Optical Emission Spectroscopy; calculated for Pt(dba)$_3$: 21.73% Pt; found 21.92% (average of two experiments).

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2.6.3. *Preparation of Pt\(_2(dba)_3\).*

Tris(dibenzylideneacetone)diplatinum was prepared using the literature procedure.\(^1\) To a two-neck 25 mL round-bottom flask equipped with a magnetic stir bar and reflux condenser was added dibenzylideneacetone (1.98 g, 8.43 mmol), tetrabutylammonium chloride (1.00 g, 3.61 mmol), and sodium acetate (1.78 g, 21.80 mmol). Methanol (102.0 mL) was added and the solution was warmed to 70 °C in an oil bath until the solids dissolved (5 minutes). In a separate 50 mL pear-shaped flask was added potassium tetrachloroplatinate (500.0 mg, 1.20 mmol) and water (6.3 mL), and the mixture gently warmed until solids dissolved. The contents of the pear shaped flask were transferred to the three-neck flask and the reaction was allowed to stir at 70 °C for 3 hours. After 3 h, the reaction was cooled to ambient temperature, transferred to a one-neck 500 mL round-bottom flask and concentrated by rotary evaporation to half the volume. The reaction mixture was then filtered on a Büchner funnel and the remaining solids were washed with copious amounts of water and methanol until all yellow dibenzylideneacetone crystals were removed. The solid product was then dissolved in hot tetrahydrofuran (100 mL) and filtered. The filtrate volume was reduced to 10 mL using rotary evaporation and then methanol (12 mL) was slowly added. After cooling the solution to -25 °C in the freezer for 1 h the crystallized product was isolated by filtration, washed with methanol (40 mL) and dried under vacuum to provide a black crystalline solid (348.9 mg, 53%). Anal Calc’d for C\(_{51}H_{42}O_3Pt_2\): C, 56.04; H, 3.87. Found: C, 56.40; H, 3.73 (average of two experiments). Platinum analysis was performed by ICP Optical
Emission Spectroscopy; calculated for Pt$_2$(dba)$_3$: 35.70% Pt; found 33.72% (average of two experiments).

2.6.4. Preparation of Pt(nbe)$_3$\(^{2}\)

A flame-dried 100 mL 3-neck round-bottomed flask equipped with magnetic stir bar and addition funnel was charged with finely powdered PtCl$_2$(COD)$^3$ (3.50 g, 9.35 mmol) and freshly sublimed norbornene (7.0 g, 74.30 mmol) under N$_2$. Diethyl ether (10.7 mL, 0.88 M) was added, and the reaction was cooled to -30 °C (dry ice/ethanol/ethylene glycol). The addition funnel was charged with a freshly prepared solution of cyclooctatetraene dilithium (46.3 mL, 0.20 M), which was then added dropwise to the reaction while maintaining an internal temperature of -30 °C. The light brown reaction mixture was allowed to warm to room temperature and the solvent was removed \textit{in vacuo}. The remaining residue was dried for an additional hour before being brought into the glove box where the solid was scraped and washed with dry and degassed hexane (3 x 100 mL). The extract was filtered through a plug of alumina and the filtrate was evaporated \textit{in vacuo} to produce an off-white solid which was used without further purification (1.67 g, 52%). Anal Calc’d for C$_{21}$H$_{30}$Pt: C, 52.82; H, 6.33. Found: C, 52.84; H, 6.29.


2.6.5. Ligand Synthesis.

The following TADDOL-derived phosphonite ligands were prepared using the literature procedure and spectral data are in accordance with the literature as follows: 

(R,R)-2.45, (R,R)-2.46 and (R,R)-2.49.

Preparation of 1,1′-(5-bromo-1,3-phenylene)bis(2-methylpropan-1-ol). To a flame-dried 1 L round-bottomed flask equipped with magnetic stir bar was added 1,3,5-tribromobenzene (4.00 g, 12.71 mmol) and diethyl ether (500.0 mL) under N₂. The reaction was cooled to -78 °C and tert-butyllithium (33.2 mL, 1.7 M solution in pentane) was added dropwise via syringe. After stirring at -78 °C for 2 h, iso-butyraldehyde (4.6 mL, 50.82 mmol) was added and the reaction was allowed to warm to 0 °C before being quenched with saturated aqueous ammonium chloride (20 mL). The organic and aqueous layers were separated and the aqueous layer was washed with

diethyl ether (3 x 50 mL). The combined organic layers were washed with brine (50 mL),
dried over Na₂SO₄, filtered, and concentrated by rotary evaporation. The crude reaction
mixture was purified by column chromatography on silica gel (100% dichloromethane,
then 100% ethyl acetate) to afford a brown solid (3.64 g, 95%).

1,1'-(5-bromo-1,3-phenylene)bis(2-methylpropan-1-ol).

\[
\begin{align*}
\text{Me} & \quad \text{OH} \\
\text{Br} & \quad \text{Me} \\
\text{Me} & \quad \text{Me}
\end{align*}
\]

\(^1\)H NMR (500 MHz, CDCl₃): \(\delta \) 0.80 (6H, d, \( J = 7.0 \) Hz), 0.94
(6H, d, \( J = 6.5 \) Hz), 1.86 (2H, d, \( J = 2.5 \) Hz), 1.91 (2H, m),
4.36 (2H, dd, \( J = 6.5 \) Hz, 2.5 Hz), 7.14 (1H, ddd, \( J = 5.5 \) Hz, 5.5 Hz 1.5 Hz), 7.35 (2H,
dd, \( J = 2.5 \) Hz, 1.5 Hz); \(^13\)C NMR (100 MHz, CDCl₃): \(\delta \) 18.05, 19.15, 19.17, 35.55,
79.41, 122.49, 123.65, 123.71, 128.72, 128.74, 145.93, 145.96; IR (neat): 3364.1 (m),
2960.1 (s), 2872.8 (m), 1572.7 (w), 1467.5 (m), 1156.8 (w), 1033.1 (s), 710.8 (m) cm\(^{-1}\);
HRMS-(ESI+) for C\(_{14}\)H\(_{25}\)BrNO\(_2\) [M+NH\(_4\)]: calculated: 318.1068, found: 318.1057.

Preparation of 1-bromo-3,5-bis(2-methylprop-1-en-1-yl)benzene.

To a flame-dried 250 mL 3-neck round-bottomed flask equipped with magnetic
stir bar and reflux condenser was added 1,1'-(5-bromo-1,3-phenylene)bis(2-
methylpropan-1-ol) (3.64 g, 12.08 mmol) and 4-TsOH•H₂O (1.62 g, 8.55 mmol). The
reaction apparatus was purged with N\(_2\) and toluene (120.0 mL) was added. The reaction
mixture was brought to reflux and stirred for 36 h. After completion, the reaction was
cooled to room temperature and diluted with ethyl acetate (60 mL). The organics were
washed with saturated aqueous sodium bicarbonate (3 x 50 mL), dried over Na₂SO₄,
filtered, and concentrated by rotary evaporation. The crude reaction mixture was purified by column chromatography on silica gel (100% hexanes) to afford a colorless oil (2.36 g, 74%).

**1-bromo-3,5-bis(2-methylprop-1-en-1-yl)benzene.**  \(^\text{1}^\text{H}
\text{NMR (500 MHz, CDCl}_3\text{): } \delta 1.83 (6\text{H, d, } J = 1.0 \text{ Hz}), 1.86 (6\text{H, d, } J = 1.5 \text{ Hz}), 6.16 (2\text{H, br s}), 6.96 (1\text{H, s}), 7.15 (2\text{H, d, } J = 1.0 \text{ Hz}); \text{13C NMR (100 MHz, CDCl}_3\text{): } \delta 19.66, 27.03, 122.00, 124.19, 128.07, 129.14, 137.06, 140.49; \text{IR (neat): } 2969.6 (\text{m}), 2911.6 (\text{m}), 1655.8 (\text{w}), 1589.1 (\text{m}), 1555.2 (\text{s}), 1444.5 (\text{m}), 873.7 (\text{s}) \text{ cm}^{-1}; \text{HRMS-(ESI+) for C}_{14}\text{H}_{18}\text{Br }[\text{M+H}]: \text{calculated: 265.0592, found: 265.0603.}

**Preparation of 1-bromo-3,5-di-iso-butylbenzene.** \(^7\)

To a flame-dried 250 mL round-bottomed flask equipped with magnetic stir bar was added 1-bromo-3,5-bis(2-methylprop-1-en-1-yl)benzene (2.36 g, 8.89 mmol) and dichloromethane (88.0 mL) under N\(_2\). The reaction was cooled to -78 °C and HBF\(_4\)•OEt\(_2\) (4.7 mL, 34.70 mmol) was added. After stirring at -78 °C for 3 h, triethylsilane (11.1 mL, 69.40 mmol) was added and the reaction was allowed to stir overnight while slowly warming to room temperature. Saturated aqueous sodium bicarbonate (50 mL) was added and the organic and aqueous layers were separated. The aqueous layer was washed with ethyl acetate (3 x 25 mL). The combined organics were washed with brine (25 mL),

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dried over Na$_2$SO$_4$, filtered and concentrated by rotary evaporation. The crude material was purified by column chromatography on silica gel (100% hexanes) to afford a colorless oil (2.32 g, 97%).

![1-bromo-3,5-di-iso-butylbenzene](image)

1-bromo-3,5-di-iso-butylbenzene. $^1$H NMR (500 MHz, CDCl$_3$): $\delta$ 0.87 (12H, d, $J = 7.0$ Hz), 1.82 (2H, m), 2.39 (4H, d, $J = 7.5$ Hz), 6.18 (1H, d, $J = 1.5$ Hz), 7.09 (2H, d, $J = 1.5$ Hz); $^{13}$C NMR (100 MHz, CDCl$_3$): $\delta$ 22.52, 30.39, 45.25, 122.09, 129.01, 129.54, 143.80; IR (neat): 2954.0 (s), 2923.5 (m), 1601.7 (w), 1568.5 (s), 1440.9 (m), 1167.4 (w), 865.4 (m), 700.1 (m) cm$^{-1}$; HRMS-(ESI+) for C$_{14}$H$_{22}$Br [M+H]: calculated 269.0905, found: 269.0899.

Preparation of 3,5-di-iso-butylphenylTADDOL.

3,5-Di-iso-butylphenylTADDOL was prepared according to the literature procedure with slight modification. To a flame-dried 100 mL 2-neck round-bottomed flask equipped with magnetic stir bar and reflux condenser was added crushed magnesium turnings (439.0 mg, 18.05 mmol) under N$_2$. The apparatus was flame-dried again, a single crystal of I$_2$ was added and the reaction mixture was diluted with tetrahydrofuran (29.0 mL). To another flame dried 25 mL pear-shaped flask was added 1-bromo-3,5-di-iso-butylbenzene (4.37 g, 16.25 mmol) and tetrahydrofuran (12.0 mL). The solution of 1-bromo-3,5-diethylbenzene in tetrahydrofuran was slowly added to the
magnesium mixture at room temperature via syringe. The reaction was heated to reflux at 80 °C in an oil bath for 3 h, at which time the reaction was cooled to 0 °C, and a solution of (4R,5R)-dimethyl 2,2-dimethyl-1,3-dioxolane-4,5-dicarboxylate (788.0 mg, 3.61 mmol) in tetrahydrofuran (4.0 mL) was added slowly via syringe. The reaction was allowed to reflux for 12 h, after which it was cooled to 0 °C and quenched with saturated aqueous NH₄Cl (10 mL). The organic and aqueous layers were separated and the aqueous layer was washed with ethyl acetate (3 x 30 mL). The combined organics were dried over Na₂SO₄, filtered, and concentrated in vacuo. The crude material was purified by column chromatography on silica gel (1-5% ethyl acetate/hexanes) to afford the title compound as a yellow solid (1.79 g, 55%).

3,5-Di-iso-butylphenylTADDOL. ¹H NMR (500 MHz, CDCl₃): δ 0.77 (24H, d, J = 6.5 Hz), 0.84 (24H, dd, J = 6.5 Hz, 3.5 Hz), 1.68 (4H, m), 1.81 (4H, m), 2.32 (8H, d, J = 7.0 Hz), 2.40 (8H, d, J = 7.0 Hz), 3.52 (2H, s), 4.68 (2H, s), 6.74 (2H, s), 6.81 (2H, s), 6.89 (4H, d, J = 1.5 Hz), 7.10 (4H, s); ¹³C NMR (100 MHz, CDCl₃): δ 22.24, 22.29, 22.34, 22.42, 27.00, 30.14, 30.33, 31.32, 45.41, 45.52, 77.32, 78.10, 81.28, 109.14, 125.81, 126.89, 128.70, 129.07, 139.97, 140.69, 142.60, 145.52, 148.20; IR (neat): 3320.1 (w), 2953.2 (s), 2923.4 (m), 2867.7 (m), 1601.1 (w), 1464.5 (m), 1166.8 (w), 881.7 (w) cm⁻¹; HRMS-(TOF MS ES⁺) for C₆₃H₉₄O₄Na [M+Na]: calculated:937.7050, found: 937.7065.
Preparation of (R,R)-3,5-di-iso-butylphenylTADDOLPPh (2.50).

To a flame-dried 50 mL round-bottomed flask equipped with magnetic star bar was added 3,5-di-iso-butylphenylTADDOL (1.79 g, 1.95 mmol) and tetrahydrofuran (19.5 mL) under N₂. Triethylamine (0.9 mL, 6.60 mmol) was added via syringe and the reaction mixture was cooled to 0 °C in an ice bath. Dichlorophenylphosphine (0.3 mL, 2.14 mmol) was added dropwise via syringe at 0 °C, the reaction was brought to room temperature and was allowed to stir for 2 h. The reaction was diluted with Et₂O (20 mL) under N₂, quickly filtered through celite and concentrated in vacuo. The crude material was purified by column chromatography on silica gel (5% ethyl acetate/hexanes) to afford the title compound as a white solid (1.85 g, 93%).

(R,R)-3,5-di-iso-butylphenylTADDOLPPh (2.50). ¹H NMR (400 MHz, CDCl₃): δ 0.06 (3H, s), 0.70 (24H, t, J = 6.8 Hz), 0.74 (24H, d, J = 6.0 Hz), 1.37 (3H, s), 1.58-1.71 (8H, m), 2.25 (8H, d, J = 6.8 Hz), 2.290 (8H, d, J = 7.2 Hz), 4.76 (1H, d, J = 8.8 Hz), 5.50 (1H, dd, J = 8.4 Hz, 4.4 Hz), 6.58 (1H, s), 6.63 (2H, s), 6.71 (1H, s), 6.83 (2H, s), 6.92 (1H, s), 7.01 (2H, s), 7.14 (1H, s), 7.34 (5H, br s), 7.69 (2H, br s); ¹³C NMR (100 MHz, CDCl₃): δ 22.20, 22.24, 22.25, 22.36, 22.42, 24.79, 27.76, 30.16, 30.17, 30.23, 30.55, 45.38, 45.50, 45.64, 77.20, 82.41, 82.45, 82.49, 82.72, 83.36, 83.44, 84.18, 84.23, 110.79, 125.82, 125.89, 127.17, 127.20, 127.75, 128.08, 128.14, 128.80, 128.89, 128.91, 129.03, 129.95, 130.19, 130.32; ³¹P NMR (202 MHz, CDCl₃): δ 156.11; IR
Preparation of 3,5-di-iso-propylphenylTADDOL.

3,5-Di-iso-propylphenylTADDOL was prepared according to the procedure described above for 3,5-di-iso-butylphenylTADDOL using 1-bromo-3,5-di-iso-propylbenzene, which was prepared according to the literature procedure from 2,6-diisopropylaniline as shown below.\(^8\)

3,5-di-iso-propylphenylTADDOL. \(^1^H\) NMR (500 MHz, CDCl\(_3\)): \(\delta\) 0.84 (6H, s), 1.06 (24H, dd, \(J = 7.5\) Hz, 7.0 Hz), 1.16 (24H, dd, \(J = 7.0\) Hz, 1.5 Hz), 2.72 (4H, dddd, \(J = 7.0\) Hz, 7.0 Hz, 7.0 Hz, 7.0 Hz), 2.81 (4H, dddd, \(J = 7.0\) Hz, 7.0 Hz, 7.0 Hz, 7.0 Hz), 3.63 (2H, s), 4.61 (2H, s), 6.86 (2H, s), 6.92 (2H, s), 6.95 (4H, d, \(J = 1.5\) Hz), 7.16 (4H, d, \(J = 1.7\) Hz); \(^1^3^C\) NMR (125 MHz, CDCl\(_3\)): \(\delta\) 23.87, 23.96, 24.00, 24.39, 26.95, 30.32, 34.16, 34.33, 78.50, 81.23, 108.9, 123.2, 123.4, 123.5, 124.5, 142.5, 145.8,

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147.3, 148.0; IR (neat): 3235.4 (w), 2967.2 (s), 2868.4 (m), 1599.3 (m), 1463.7 (m), 1073.2 (m), 872.4 (s), 739.8 (s), 709.6 (m) cm\(^{-1}\); HRMS (+MALDI) for C\(_{55}\)H\(_{78}\)O\(_4\)Na [M +Na]: calculated 825.5792, found: 825.5770. \([\alpha]\)\(_D\)\(^{25}\) = +19.88 (c = 0.97, CHCl\(_3\), l = 50 mm).

**Preparation of (R,R)-3,5-di-iso-propylphenylTADDOLPPh (2.48).**

To a flame dried 50 mL round bottom flask equipped with magnetic star bar was added 3,5-di-iso-propylphenylTADDOL (1.09 g, 1.36 mmol) and tetrahydrofuran (13.6 mL, 0.1 M) under N\(_2\). Triethylamine (0.65 mL, 4.64 mmol) was added via syringe and the reaction mixture was brought to 0 °C in an ice bath. Dichlorophenylphosphine (0.20 mL, 1.50 mmol) was added dropwise via syringe at 0 °C. The reaction was brought to room temperature and was allowed to stir for 2 h. The reaction was diluted with Et\(_2\)O (20 mL), filtered through celite and concentrated in vacuo. The crude material was purified by column chromatography on silica gel (3% ethyl acetate/hexanes, with 1% Et\(_3\)N to prevent hydrolysis) to afford the title compound as a white solid (1.03 g, 83%).

(R,R)-3,5-di-iso-propylphenylTADDOLPPh (2.48). \(^1\)H NMR (500 MHz, CDCl\(_3\)): \(\delta\) 0.11 (3H, s), 1.10-1.25 (48H, m), 1.51 (3H, s), 2.78-2.84 (8H, m), 4.91 (1H, d, \(J = 8.5\) Hz), 5.58 (1H, dd, \(J = 8.5\) Hz, 4.0 Hz), 6.83 (1H, s), 6.91 (2H, s), 6.94 (1H, s), 6.98 (2H, d, \(J = 2.0\) Hz), 7.18 (2H, br s), 7.34 (2H, s), 7.44-7.47 (3H, m), 7.51 (2H, s),
7.86-7.90 (2H, m); $^{13}$C NMR (125 MHz, CDCl$_3$): δ 23.86, 23.90, 23.98, 24.12, 24.19, 27.99, 34.03, 34.12, 34.16, 34.43, 82.76, 82.83, 83.22, 83.39, 83.84, 83.89, 84.31, 84.34, 110.4, 123.1, 123.3, 123.4, 123.5, 123.6, 124.7, 124.8, 125.1, 128.1, 128.2, 129.9, 130.1, 130.4, 141.4, 141.7, 142.1, 142.2, 146.2, 146.3, 146.8, 147.1, 147.3, 147.8, 147.9; $^{31}$P NMR (202 MHz, CDCl$_3$): δ 155.41; IR (neat): 2957.6 (s), 2868.3 (w), 1598.6 (w), 1464.9 (m), 1162.7 (w), 1027.6 (m), 877.8 (s), 799.7 (m), 735.3 (s), 693.3 (m) cm$^{-1}$. [α]$_D^{25}$ = -50.40 (c = 0.34, CHCl$_3$, l = 50 mm).

**Preparation of (R,R)-3,5-diethylphenylTADDOL.**

3,5-DiethylphenylTADDOL was prepared according to the literature procedure with slight modification. To a flame dried 100 mL 2-neck round-bottom flask equipped with magnetic stir bar and reflux condenser was added crushed magnesium turnings (401.0 mg, 16.50 mmol) under N$_2$. The apparatus was flame-dried again, a single crystal of I$_2$ was added and the reaction mixture was diluted with tetrahydrofuran (29 mL). To another flame dried 25 mL pear-shaped flask was added 1-bromo-3,5-diethylbenzene (3.91 g, 18.33 mmol) and tetrahydrofuran (12 mL). The solution of 1-bromo-3,5-diethylbenzene in tetrahydrofuran was slowly added to the magnesium mixture at room temperature via syringe. The reaction was allowed to reflux at 80 °C in an oil bath for 2 h, at which time the reaction was cooled to 0 °C, and a solution of (4R,5R)-2,2-dimethyl-1,3-dioxolane-4,5-dicarboxylic acid in tetrahydrofuran (4 mL) was added slowly via syringe. The reaction was allowed to reflux for 12 h, after which it was cooled
to 0 °C and quenched with NH₄Cl (10 mL, sat. aq.). The organic and aqueous layers were separated and the aqueous layer was extracted with ethyl acetate (3 x 30 mL). The combined organics were dried over Na₂SO₄, filtered, and concentrated in vacuo. The crude material was purified by silica gel chromatography (1-50% ethyl acetate/hexanes) to afford the title compound as a yellow solid (2.23g, 88% yield).

**3,5-DiethylphenylTADDOL.** ¹H NMR (400 MHz, CDCl₃): δ 0.94 (6H, s), 1.13 (12H, t, J = 7.6 Hz), 1.22 (12H, t, J = 7.6 Hz), 2.54 (8H, q, J = 15.2 Hz, 7.6 Hz), 2.61 (8H, q, J = 14.8 Hz, 7.2 Hz), 3.78 (2H, s), 4.67 (2H, s), 6.91 (2H, q, 6.96 (2H, s), 7.00 (4H, s), 7.20 (4H, s); ¹³C NMR (CDCl₃): δ 15.51, 15.94, 27.04, 28.94, 29.08, 76.68, 77.00, 77.32, 78.29, 81.00, 109.2, 124.6, 125.8, 126.1, 126.5, 142.6, 142.7, 143.6, 145.9. IR (neat): 3299 (br w), 2962 (s), 2930 (m), 1599 (w), 1457 (m), 1238 (w), 1063 (m) 871 (s), 746 (m) cm⁻¹. [α]D²⁰ = +8.555 (c = 0.522, CHCl₃, l = 50 mm).

**Preparation of (R,R)-3,5-diethylphenylTADDOLPPh (2.47).**

To a flame dried 100 mL round bottom flask equipped with magnetic star bar was added 3,5-diethylphenylTADDOL (2.23 g, 3.23 mmol) and tetrahydrofuran (32.3 mL, 0.1 M) under N₂. Triethylamine (1.53 mL, 10.97 mmol) was added via syringe and the reaction mixture was brought to 0 °C in an ice bath. Dichlorophenylphosphine (0.48 mL,
3.55 mmol) was added dropwise via syringe at 0 °C, the reaction was brought to room
temperature and was allowed to stir for 2 h. The reaction was diluted with Et₂O, filtered
through celite and concentrated in vacuo. The crude material was purified by silica gel
chromatography (5% ethyl acetate/hexanes) to afford the title compound as a white solid
(2.31 g, 90% yield).

(R,R)-3,5-DiethylphenylTADDOLPh (2.47). ¹H NMR (400
MHz, CDCl₃): δ 0.18 (3H, s), 1.20 (24H, m), 1.55 (3H, s), 2.60
(16H, m), 4.89 (1H, d, J = 8.4 Hz), 5.65 (1H, q, J = 8.4 Hz, 4.8
Hz), 6.87 (1H, s), 6.93 (2H, s), 6.96 (1H, s), 7.07 (2H, s), 7.16
(2H, s), 7.30 (2H, s), 7.47 (3H, s), 7.55 (2H, s), 7.86 (2H, s); ¹³C
NMR (CDCl₃): δ 15.42, 15.53, 15.73, 15.92, 24.64, 27.95, 28.94,
29.12, 82.53, 82.77, 83.01, 83.52, 83.59, 84.29, 110.9, 124.5, 124.6, 125.9, 126.3, 126.4,
126.5, 126.6, 128.1, 128.2, 129.7, 130.0, 130.3, 141.5, 141.6, 142.6, 142.9, 143.3, 143.5,
146.3, 146.9. ³¹P NMR (162 MHz, CDCl₃): δ 156.7. IR (neat): 2962 (s), 2931 (m), 2872
(w), 1599 (w), 1458 (m), 1160 (m), 1069 (m), 875 (s), 806 (m) cm⁻¹. [α]D⁰ = -59.634 (c =
0.660, CHCl₃, l = 50 mm).
2.6.6. Preparation of cis-1,3-Dienes.

A. Representative Procedure for cis-Selective Wittig Olefination.⁹

To a flame-dried 2-neck round-bottomed flask equipped with a reflux condenser was added triphenylphosphine (16.68 g, 63.61 mmol) under N₂, followed by acetonitrile (42.4 mL). 1-Bromohexane (7.00 g, 42.41 mmol) was then added via syringe and the reaction mixture was heated to 90 °C in an oil bath for 24 h. The reaction mixture was then cooled to room temperature and the solvent was removed by rotary evaporation to give the phosphonium salt as a white solid (17.83 g, 98%). To a flame-dried round bottomed flask was added potassium bis(trimethylsilyl)amide (3.27 g, 16.38 mmol) and the phosphonium salt (7.00 g, 16.38 mmol) in the glove box. The flask was sealed and brought to the bench. THF (227.0 mL) was added via syringe under N₂ and the solution was cooled to -78 °C (dry ice/acetone). The reaction mixture was allowed to stir at -78 °C for 1 h. To a second flame-dried round-bottomed flask was added acrolein (1.64 mL, 24.57 mmol) and THF (100.0 mL). The acrolein solution was cooled to -78 °C and was then slowly transferred via cannula to the ylide solution. The reaction mixture was stirred at -78 °C for 1 h, and then at room temperature for 1 h. The solvent was then removed by rotary evaporation to 1/4 of the original volume. The crude mixture was diluted with pentane (150 mL) and washed with H₂O (3 x 100 mL). The layers were separated and the

combined organics were dried with Na$_2$SO$_4$, filtered, and carefully concentrated (due to product volatility). The crude product was purified by column chromatography on silica gel (100% pentane, $R_f = 0.83$, stain in KMnO$_4$) to provide a clear, colorless liquid (1.69 g, 83%).

(Z)-nona-1,3-diene (Table 2.4, entry 2). $^1$H NMR (500 MHz, CDCl$_3$): $\delta$ 0.88 (3H, t, $J = 6.0$ Hz), 1.26-1.34 (4H, m), 1.38 (2H, dddd, $J = 7.5$ Hz, 7.5 Hz, 7.5 Hz, 7.5 Hz), 2.17 (2H, dt, $J = 8.0$ Hz, 8.0 Hz), 5.07 (1H, d, $J = 10.0$ Hz), 5.17 (1H, d, $J = 16.5$ Hz), 5.45 (1H, dt, $J = 10.5$ Hz, 7.5 Hz), 5.98 (1H, dd, $J = 11.0$ Hz, 11.0 Hz), 6.63 (1H, ddd, $J = 17.0$ Hz, 11.0 Hz, 11.0 Hz); $^{13}$C NMR (125 MHz, CDCl$_3$): $\delta$ 14.0, 22.5, 27.7, 29.3, 31.4, 116.6, 129.1, 132.3, 133.0; IR (neat): 2954.3 (m), 2925.4 (s), 2858.6 (m), 1465.3 (m), 1363.3 (w), 1076.4 (w), 967.4 (s), 726.5 (w) cm$^{-1}$; HRMS-(ESI+) for C$_9$H$_{17}$ [M+H]: calculated: 125.1330, found: 125.1331.

(Z)-trideca-1,3-diene (Table 2.4, entry 3). The title compound was prepared according to the representative procedure with the following modifications: The phosphonium salt was made using 1-bromodecane as the electrophile, and benzene as the solvent. The phosphonium salt was a viscous oil, and was used without purification. The olefination reaction was performed without modification to
provide a clear, colorless liquid (1.15 g, 54%, \( R_f = 0.70 \) in 100% hexanes, stain in \( \text{KMnO}_4 \)). \(^1\)H NMR (500 MHz, CDCl\(_3\)): \( \delta \) 0.86 (3H, t, \( J = 7.0 \) Hz), 1.24-1.31 (10H, m), 1.36 (2H, dddd, \( J = 6.5 \) Hz, 6.5 Hz, 6.5 Hz, 6.5 Hz), 2.16 (2H, dtd, \( J = 7.5 \) Hz, 7.5 Hz, 1.5 Hz), 5.06 (1H, d, \( J = 10.0 \) Hz), 5.15 (1H, d, \( J = 17.0 \) Hz), 5.44 (1H, dt, \( J = 10.5 \) Hz, 8.0 Hz), 5.98 (1H, dd, \( J = 11.0 \) Hz, 11.0 Hz), 6.62 (1H, ddd, \( J = 17.0 \) Hz, 11.0 Hz, 11.0 Hz); \(^{13}\)C NMR (125 MHz, CDCl\(_3\)): \( \delta \) 14.1, 22.7, 27.7, 29.25, 29.33, 29.5, 29.58, 29.62, 31.9, 116.6, 129.1, 132.3, 133.1; IR (neat): 2955.6 (w), 2922.4 (s), 2853.4 (m), 1464.8 (w), 1434.4 (w), 1377.3 (w), 995.4 (m), 900.3 (s), 783.9 (w), 721.5 (w), 653.6 (w) cm\(^{-1}\); HRMS-(ESI+) for C\(_{13}\)H\(_{25}\) [M+H]: calculated: 181.1956, found: 181.1948.

\( (Z) \)-6-methylhepta-1,3-diene (Table 2.4, entry 4). The title compound was prepared according to the representative procedure with the following modifications: The phosphonium salt was purchased from Aldrich. The olefination reaction was performed without modification to provide a clear, colorless liquid (1.45 g, 55%, \( R_f = 0.82 \) in 100% pentane, stain in \( \text{KMnO}_4 \)). \(^1\)H NMR (500 MHz, CDCl\(_3\)): \( \delta \) 0.89 (6H, d, \( J = 7.0 \) Hz), 1.64 (1H, m), 2.06 (2H, dd, \( J = 7.5 \) Hz, 7.5 Hz), 5.06, (1H, d, \( J = 10.0 \) Hz), 5.16 (1H, d, \( J = 17.0 \) Hz), 5.46 (1H, dt, \( J = 10.5 \) Hz, 8.0 Hz), 6.03 (1H, dd, \( J = 11.0 \) Hz, 11.0 Hz), 6.62 (1H, ddd, \( J = 17.0 \) Hz, 11.5 Hz, 11.5 Hz); \(^{13}\)C NMR (125 MHz, CDCl\(_3\)): \( \delta \) 22.3, 28.7, 36.8, 116.7, 129.9, 131.8, 132.5; IR (neat): 2955.5 (s), 2925.8 (s), 2869.9 (m), 1696.9 (w), 1466.7 (m),
1367.4 (m), 1150.3 (w), 1078.3 (w), 969.6 (s) cm\(^{-1}\); HRMS-(ESI+) for C\(_8\)H\(_{15}\) [M+H]: calculated: 111.1174, found: 111.1174.

**(Z)-buta-1,3-dien-1-ylcyclohexane (Table 2.4, entry 5).** The title compound was prepared according to the representative procedure with the following modifications: The phosphonium salt made using (bromomethyl)cyclohexane as the electrophile and acetonitrile as the solvent. The phosphonium salt was isolated as a white solid (8.26 g, 71%). The olefination reaction was performed without modification to provide a clear, colorless liquid (1.06 g, 83%, R\(_f\) = 0.58 in 100% hexanes, stain in KMnO\(_4\)). \(^1\)H NMR (500 MHz, CDCl\(_3\)): \(\delta\) 1.03-1.12 (2H, m), 1.13-1.20 (1H, m), 1.23-1.33 (3H, m), 1.51-1.73 (4H, m), 2.40-2.46 (1H, m), 5.05 (1H, d, \(J = 10.5\) Hz), 5.16 (1H, d, \(J = 16.5\) Hz), 5.29 (1H, dd, \(J = 10.0\) Hz, 10.0 Hz), 5.88 (1H, dd, \(J = 10.5\) Hz, 10.5 Hz), 6.64 (1H, ddd, \(J = 17.0\) Hz, 10.5 Hz, 10.5 Hz); \(^13\)C NMR (125 MHz, CDCl\(_3\)): \(\delta\) 25.8, 26.0, 33.2, 36.8, 116.6, 127.2, 132.6, 138.9; IR (neat): 2922.2 (s), 2851.0 (m), 1697.0 (w), 1448.8 (w), 1361.0 (w), 970.6 (w), 890.2 (w) cm\(^{-1}\); HRMS-(ESI+) for C\(_{10}\)H\(_{17}\) [M+H]: calculated: 137.1330, found: 137.1330.

**(Z)-hexa-3,5-dien-1-ylbenzene (Table 2.4, entry 6).** The title compound was prepared according to the representative procedure with the following modifications: The phosphonium salt was made using (3-bromopropyl)benzene as the electrophile, and acetonitrile as the solvent. The
phosphonium salt was a white solid, and was used without purification. The olefination reaction was performed without modification to provide a clear, colorless liquid (930.0 mg, 53%, $R_f = 0.50$ in 100% hexanes, stain in KMnO$_4$). $^1$H NMR (500 MHz, CDCl$_3$): $\delta$ 2.51 (2H, ddd, $J = 7.5$ Hz, 7.5 Hz, 7.5 Hz), 2.70 (2H, t, $J = 7.5$ Hz), 5.08 (1H, d, $J = 10.0$ Hz), 5.18 (1H, d, $J = 17.0$ Hz), 5.49 (1H, dt, $J = 10.5$ Hz, 7.5 Hz), 6.01 (1H, dd, $J = 11.0$ Hz, 11.0 Hz), 6.60 (1H, ddd, $J = 16.5$ Hz, 10.5 Hz, 10.5 Hz), 7.17-1.20 (3H, m), 7.30 (2H, t, $J = 8.0$ Hz); $^{13}$C NMR (100 MHz, CDCl$_3$): $\delta$ 29.6, 35.8, 117.2, 125.9, 128.3, 128.4, 129.7, 131.6, 132.1, 141.7; IR (neat): 2923.9 (w), 1495.5 (m), 1453.8 (m), 969.3 (s), 745.9 (m), 698.4 (s) cm$^{-1}$; HRMS-(ESI$^+$) for C$_{12}$H$_{15}$ [M+H]: calculated: 159.1174, found: 159.1179.

(Z)-tert-butyl(hexa-3,5-dien-1-yloxy)diphenylsilane (Table 2.4, entry 7). The title compound was prepared according to the representative procedure with the following modifications: 3-bromopropan-1-ol was protected as the silyl ether and used as the electrophile to make the phosphonium salt with acetonitrile as the solvent. The phosphonium salt was an off-white solid, and was used without purification. The olefination reaction was performed without modification to provide a clear, colorless liquid (953 mg, 61%, $R_f = 0.40$ in 100% hexanes, stain in KMnO$_4$). $^1$H NMR (500 MHz, CDCl$_3$): $\delta$ 1.03 (9H, s), 2.43 (2H, ddd, $J = 8.0$ Hz, 8.0 Hz, 8.0 Hz), 3.68 (2H, t, $J = 7.0$ Hz), 5.06 (1H, d, $J = 10.0$ Hz), 5.16 (1H, d, $J = 16.5$ Hz), 5.46 (1H, dt, $J = 10.5$ Hz, 8.0 Hz), 6.04 (1H, dd, $J = 11.0$ Hz, 11.0 Hz), 6.52
(1H, ddd, $J = 17.0$ Hz, 10.0 Hz, 10.0 Hz), 7.34-7.41 (6H, m), 7.65 (2H, d, $J = 1.5$ Hz), 7.66 (2H, d, $J = 1.5$ Hz); $^{13}$C NMR (100 MHz, CDCl$_3$): $\delta$ 19.2, 26.8, 31.3, 63.4, 117.2, 127.60, 128.6, 129.6, 130.9, 132.3, 133.9, 135.6; IR (neat): 2857.4 (w), 1427.5 (w), 1107.6 (m), 822.9 (w), 700.7 (s), 505.3 (m) cm$^{-1}$; HRMS-(ESI+) for C$_{22}$H$_{29}$OSi [M+H]: calculated 337.1987, found: 337.1975.

B. Preparation of (Z)-buta-1,3-dien-1-ylbenzene (Table 2.4, entry 8).

The borylation of phenylacetylene was performed following the literature procedure without modification. The resulting alkynyl pinacolboronate was subjected to hydroboration/protodeboronation according to the literature procedure. The resulting (Z)-alkenyl pinacolboronate was then subjected to a Suzuki cross-coupling with vinyl bromide as follows: To a flame-dried, round-bottomed flask equipped with magnetic stir bar was added Pd$_2$(dba)$_3$ (99.0 mg, 0.11 mmol) and P(‘Bu)$_3$ (87.9 mg, 0.44 mmol) in the glove box. The flask was sealed and brought to the bench. (Z)-4,4,5,5-tetramethyl-2-styryl-1,3,2-dioxaborolane (1.0 g, 2.47 mmol) was added as a solution in THF (10.0 mL) via syringe under N$_2$. The reaction mixture was then charged with THF (62.0 mL), and

aqueous potassium hydroxide (4.3 mL, 13.04 mmol). The flask was cooled to 0 °C and vinyl bromide (13.0 mL of 1.0 M solution in THF, 13.0 mmol) was added dropwise via syringe. The reaction was allowed to slowly warm to room temperature while stirring overnight. Saturated ammonium chloride (20 mL) was added to the reaction and the aqueous and organic layers were separated. The aqueous layer was washed with ethyl acetate (3 x 30 mL). The combined organics were dried over Na₂SO₄, filtered, and concentrated in vacuo. The crude material was purified by column chromatography on silica gel (100% hexanes, Rᵣ = 0.57, visualize by UV) to provide a clear, colorless liquid (270 mg, 48%).

(Z)-buta-1,3-dien-1-ylbenzene (Table 2.4, entry 8). ¹H NMR (500 MHz, CDCl₃): δ 5.22 (1H, d, J = 10.5 Hz), 5.36 (1H, d, J = 17.0 Hz), 6.26 (1H, dd, J = 11.5 Hz, 11.5 Hz), 6.46 (1H, d, J = 11.5 Hz), 6.88 (1H, ddd, J = 17.0 Hz, 11.0 Hz, 11.0 Hz), 7.22-7.25 (1H, m), 7.31-7.36 (4H, m); ¹³C NMR (100 MHz, CDCl₃): δ 119.6, 127.0, 128.4, 129.0, 130.4, 130.8, 133.2, 137.4; IR (neat): 29.186 (w), 1629.6 (m), 1450.1 (m), 968.1 (s), 694.3 (s), 638.9 (s) cm⁻¹; HRMS-(ESI+) for C₁₀H₁₁ [M +H]: calculated 131.0861, found: 131.0865. 156
2.6.7. **Representative Procedure for Diboration/Oxidation (Table 2.4)**

To an oven-dried 6-dram vial with magnetic stir bar in the glove box was added Pt (dba)$_3$ (8.7 mg, 10.0 µmol), (R,R)-3,5-diethylphenyl-TADDOLPh (2.47) (15.4 mg, 19.3 µmol), B$_2$(pin)$_2$ (85.9 mg, 338.1 µmol) and tetrahydrofuran (3.2 mL, [substrate] = 0.1 M). The vial was sealed with a polypropylene cap, removed from the glove box, and heated to 80 °C in an oil bath for 20 min. The vial was cooled to room temperature, returned to the glove box and charged with (Z)-nona-1,3-diene (40.0 mg, 322.0 µmol). The vial was sealed, removed from the glove box, and stirred at 60 °C for 12 h. The reaction mixture was cooled to 0 °C (ice/water) and charged with 3 M sodium hydroxide (2 mL), and 30% hydrogen peroxide (1 mL). The reaction was gradually warmed to room temperature and allowed to stir for 4 h at which time the vial was cooled to 0 °C (ice/water) and saturated aqueous sodium thiosulfate (2 mL) was added dropwise over 5 min. The reaction mixture was diluted with ethyl acetate (5 mL) and the aqueous and organic layers were separated. The aqueous layer was washed with ethyl acetate (3 x 15 mL). The combined organic layers were dried over Na$_2$SO$_4$, filtered, and concentrated by rotary evaporation. The crude reaction mixture was purified by column chromatography on silica gel (30-60% ethyl acetate/hexanes) to afford a clear, colorless oil (35.7 mg, 70%).
2.6.8. Characterization and Proof of Stereochemistry (Table 2.4)

(S,Z)-pent-3-ene-1,2-diol (Table 2.4, entry 1). The diboration was performed according to the representative procedure with (Z)-penta-1,3-diene (40.0 mg, 587.2 µmol), Pt(dba)$_3$ (15.8 mg, 17.6 µmol), (R,R)-3,5-di-iso-butylphenylTADDOLPPh (2.50) (35.9 mg, 35.2 µmol), and B$_2$(pin)$_2$ (156.5 mg, 616.4 µmol) in tetrahydrofuran (5.8 mL, 0.1 M). The crude reaction mixture was purified by column chromatography on silica gel (40-75% ethyl acetate/hexanes, R$_f$ = 0.11 in 50% ethyl acetate/hexanes, stain in PMA) to afford a clear, colorless oil (41.3 mg, 69%). $^1$H NMR (500 MHz, CDCl$_3$): δ 1.68 (3H, dd, $J$ = 6.5 Hz, 1.5 Hz), 2.46 (2H, br s), 3.47 (1H, dd, $J$ = 11.0 Hz, 8.0 Hz), 3.56 (1H, dd, $J$ = 11.5 Hz, 3.5 Hz), 4.56 (1H, ddd, $J$ = 8.5 Hz, 8.5 Hz, 3.5 Hz), 5.36 (1H, ddd, $J$ = 10.5 Hz, 8.5 Hz, 1.0 Hz), 5.65 (1H, dqq, $J$ = 10.5 Hz, 7.0 Hz, 1.0 Hz); $^{13}$C NMR (100 MHz, CDCl$_3$): δ 13.5, 66.2, 68.3, 128.7, 128.8; IR (neat): 3333.5 (s), 2921.0 (m), 1441.3 (m), 1067.3 (s), 1024.6 (s), 718.1 (m) cm$^{-1}$; HRMS-(ESI+) for C$_5$H$_{14}$NO$_2$ [M+NH$_4$]: calculated: 120.1024, found: 120.1021. $[$$\alpha$]$_{25}^D$ = +24.91 ($c$ = 0.58, CHCl$_3$, $l$ = 50 mm).

**Proof of Stereochemistry:**

The enantioselectivity was determined by treating the resulting 1,2-diol with acetic anhydride and triethylamine to afford the bis(acetate) for GLC analysis as shown
below. The analogous racemic material was prepared using PCy$_3$ as the achiral ligand in the diboration reaction.

\[
\text{MeOH} \quad \text{Ac$_2$O, Et$_3$N, DMAP, DCM} \quad \text{rt, 5 min} \quad \text{MeOAc}
\]

**Chiral GLC (β-Dex 120, Supelco, 60 °C for 5 min, ramp 2 °C/min to 130 °C, 20 psi, s/r = 35:1) - analysis of (Z)-pent-3-ene-1,2-diyldiacetate.**

The absolute configuration was determined by treating the resulting 1,2-diol with 2,2-dimethoxypropane and catalytic p-toluenesulfonic acid. The acetonide was then subjected to ozonolysis/reduction, followed by acylation of the primary alcohol (below). The authentic material was prepared by acylation of (S)-isopropyldeneglycerol, which was purchased from Aldrich.
Chiral GLC (β-Dex 120, Supelco, 60 °C for 5 min, ramp 3 °C/min to 120 °C, 20 psi, s/r = 35:1) - analysis of (2,2-dimethyl-1,3-dioxolan-4-yl)methyl acetate

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(S,Z)-non-3-ene-1,2-diol (Table 2.4, entry 2). The diboration was performed according to the representative procedure with (Z)-nona-1,3-diene (40.0 mg, 322.0 µmol), Pt(dba)$_3$ (8.7 mg, 10.0 µmol), (R,R)-3,5-diethylphenylTADDOLPh (2.47) (15.4 mg, 19.3 µmol), and B$_2$(pin)$_2$ (85.9 mg, 338.1 µmol) in tetrahydrofuran (3.2 mL, 0.1 M). The crude reaction mixture was purified by column chromatography on silica gel (30-60% ethyl acetate/hexanes, $R_f = 0.18$ in 50% ethyl acetate/hexanes, stain in PMA) to afford a clear, colorless oil (35.7 mg, 70%). $^1$H NMR (600 MHz, CDCl$_3$): $\delta$ 0.87 (3H, t, $J = 7.2$ Hz), 1.24-1.31 (4H, m), 1.32-1.38 (2H, m), 1.52 (2H, br s), 2.03-2.13 (2H, m), 3.48 (1H, dd, $J = 11.4$ Hz, 7.8 Hz), 3.57 (1H, dd, $J = 11.4$ Hz, 3.6 Hz), 4.54 (1H, dddd, $J = 11.4$ Hz, 7.8 Hz, 3.6 Hz, 1.0 Hz), 5.35 (1H, dd, $J = 10.2$ Hz, 10.2 Hz), 5.58 (1H, dddd, $J = 10.8$ Hz, 7.2 Hz, 7.2 Hz); $^{13}$C NMR (125 MHz, CDCl$_3$): $\delta$ 14.0, 22.5, 27.9, 29.3, 31.4, 66.4, 68.6, 127.8, 135.0; IR (neat): 3479.53 (br w), 2955.8 (s), 2928.7 (s), 2858.7 (m), 2361.9 (w), 1734.0 (s), 1458.3 (m), 1376.6 (m), 1230.2 (s), 1176.0 (s), 1121.3 (s), 1093.4 (s), 1041.3 (s) cm$^{-1}$; HRMS-(ESI+) for C$_9$H$_{22}$N$_1$O$_2$ [M+NH$_4$]: calculated: 176.1651, found: 176.1644. $[\alpha]_{D}^{25} = +12.37$ ($c = 0.91$, CHCl$_3$, $l = 50$ mm).

Proof of Stereochemistry:

The enantioselectivity was determined by treating the resulting 1,2-dienenantioselectivity was determined by treating the resulting 1,2-diol with 2,2-dimethoxypropane and catalytic $p$-toluenesulfonic acid. The acetonide was then subjected
to ozonolysis/reduction, followed by acylation of the primary alcohol. The authentic material was prepared by acylation of (S)-isopropylidenglycerol, which was purchased from Aldrich.

*Chiral GLC (β-Dex 120, Supelco, 60 °C for 5 min, ramp 3 °C/min to 120 °C, 20 psi, s/r = 35:1) - analysis of (2,2-dimethyl-1,3-dioxolan-4-yl)methyl acetate.*

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racemic derived from reaction product authentic
The diboration was performed according to the representative procedure with (Z)-trideca-1,3-diene (40.0 mg, 221.8 µmol), Pt(dba)$_3$ (6.1 mg, 5.5 µmol), (R,R)-3,5-diethylphenylTADDOLPh (2.47) (10.6 mg, 13.3 µmol), and B$_2$(pin)$_2$ (59.1 mg, 232.9 µmol) in tetrahydrofuran (2.2 mL, 0.1 M). The crude reaction mixture was purified by column chromatography on silica gel (30-50% ethyl acetate/hexanes, R$_f$ = 0.25 in 50% ethyl acetate/hexanes, stain in PMA) to afford a clear, colorless oil (40.4 mg, 85%). $^1$H NMR (500 MHz, CDCl$_3$): δ 0.86 (3H, t, $J$ = 6.5 Hz), 1.24-1.30 (12H, m), 1.31-1.38 (2H, m), 1.89 (2H, br s), 2.04-2.14 (2H, m), 3.48 (1H, dd, $J$ = 11.0 Hz, 8.0 Hz), 3.56 (1H, dd, $J$ = 11.0 Hz, 3.5 Hz), 4.54 (1H, ddd, $J$ = 7.5 Hz, 7.5 Hz, 7.5 Hz, 3.0 Hz), 5.34 (1H, dd, $J$ = 7.5 Hz, 7.5 Hz), 5.58 (1H, ddd, $J$ = 12.0 Hz, 7.5 Hz, 7.5 Hz); $^{13}$C NMR (125 MHz, CDCl$_3$): δ 14.1, 22.7, 28.0, 29.26, 29.30, 29.47, 29.53, 29.6, 31.9, 66.4, 68.6, 127.8, 135.0; IR (neat): 3363.4 (br m), 2955.2 (m), 2922.9 (s), 2858.8 (m), 1464.6 (w), 1376.8 (m), 1180.4 (m), 1154.8 (m), 1112.1 (w), 1075.2 (m), 1025.8 (m), 950.7 (m), 884.2 (m) cm$^{-1}$; HRMS-(ESI$^+$) for C$_{13}$H$_{30}$N$_1$O$_2$ [M+NH$_4$]: calculated: 232.2277, found: 232.2271. [α]$^{25}_D$ = +4.70 (c = 0.51, CHCl$_3$, l = 50 mm).

**Proof of Stereochemistry.**

The enantioselectivity was determined by treating the resulting 1,2-diol with 2,2-dimethoxypropane and catalytic p-toluenesulfonic acid. The acetonide was then subjected to ozonolysis/reduction, followed by acylation of the primary alcohol. The authentic
material was prepared by acylation of (S)-isopropylidenglycerol, which was purchased from Aldrich.

Chiral GLC ($\beta$-Dex 120, Supelco, 60 °C for 5 min, ramp 3 °C/min to 120 °C, 20 psi, s/r = 35:1) - analysis of (2,2-dimethyl-1,3-dioxolan-4-yl)methyl acetate.

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(S,Z)-6-methylhept-3-ene-1,2-diol (Table 2.4, entry 4). The diboration was performed according to the representative procedure with (Z)-6-methylhepta-1,3-diene (50.0 mg, 453.7 µmol), Pt(dba)$_3$ (12.2 mg, 13.6 µmol), (R,R)-3,5-diethylphenylTADDOLPh (2.47) (17.4 mg, 21.8 µmol), and B$_2$(pin)$_2$ (120.9 mg, 476.4 µmol) in tetrahydrofuran (4.5 mL, 0.1 M). The crude reaction mixture was purified by column chromatography on silica gel (30-70% ethyl acetate/hexanes, R$_f$ = 0.22 in 50% ethyl acetate/hexanes, stain in PMA) to afford a clear, colorless oil (61.5 mg, 94%). $^1$H NMR (500 MHz, CDCl$_3$): $\delta$ 0.88 (3H, d, $J$ = 5.0 Hz), 0.89 (3H, d, $J$ = 4.5 Hz), 1.23 (2H, br s), 1.62 (1H, m), 1.93-2.04 (2H, m), 3.47 (1H, dd, $J$ = 10.5 Hz, 8.5 Hz), 3.56 (1H, dd, $J$ = 11.0 Hz, 3.5 Hz), 4.52 (1H, ddd, $J$ = 8.5 Hz, 8.5 Hz, 3.5 Hz), 5.39 (1H, dd, $J$ = 11.0 Hz, 9.0 Hz), 5.59 (1H, ddd, 10.5 Hz, 7.5 Hz, 7.5 Hz); $^{13}$C NMR (125 MHz, CDCl$_3$): $\delta$ 22.2, 22.3, 28.5, 66.3, 68.6, 128.5, 133.5; IR (neat): 3346.2 (br m), 2954.7 (s), 2924.1 (s), 2869.4 (m), 1717.4 (w), 1464.3 (m), 1383.8 (m), 1367.0 (m), 1075.0 (s), 1026.9 (m) 869.8 (w) cm$^{-1}$; HRMS-(ESI$^+$) for C$_8$H$_{20}$N$_1$O$_2$ [M+NH$_4$]: calculated: 162.1494, found: 162.1497. [α]$^\text{D}_{25}$ = +9.42 ($c$ = 0.53, CHCl$_3$, $l$ = 50 mm).

**Proof of Stereochemistry.**

The enantioselectivity was determined by treating the resulting 1,2-diol with 2,2-dimethoxypropane and catalytic $p$-toluenesulfonic acid. The acetonide was then subjected to ozonolysis/reduction, followed by acylation of the primary alcohol. The authentic
material was prepared by acylation of (S)-isopropylideneglycerol, which was purchased from Aldrich.

Chiral GLC (β-Dex 120, Supelco, 60 °C for 5 min, ramp 3 °C/min to 120 °C, 20 psi, s/r = 35:1) - analysis of (2,2-dimethyl-1,3-dioxolan-4-yl)methyl acetate.

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racemic derived from reaction product authentic
(S,Z)-4-cyclohexylbut-3-ene-1,2-diol (Table 2.4, entry 5). The diboration was performed according to the representative procedure with (Z)-buta-1,3-dien-1-ylcyclohexane (50.0 mg, 367.0 µmol), Pt(dba)$_3$ (10.0 mg, 9.2 µmol), (R,R)-3,5-diethylphenylTADDOLPh (2.47) (17.6 mg, 22.0 µmol), and B$_2$(pin)$_2$ (97.9 mg, 385.4 µmol) in tetrahydrofuran (3.7 mL, 0.1 M). The crude reaction mixture was purified by column chromatography on silica gel (30-50% ethyl acetate/hexanes, $R_f = 0.22$ in 50% ethyl acetate/hexanes, stain in PMA) to afford a clear, colorless oil (48.1 mg, 77%). $^1$H NMR (500 MHz, CDCl$_3$): $\delta$ 1.03-1.18 (3H, m), 1.22-1.31 (3H, m), 1.62-1.72 (4H, m), 1.9 (2H, br s), 2.25-2.33 (1H, m), 3.48 (1H, dd, $J = 11.0$ Hz, 8.0 Hz), 3.55 (1H, dd, $J = 11.0$ Hz, 4.0 Hz), 4.55 (1H, ddd, $J = 8.5$ Hz, 8.0 Hz, 4.0 Hz), 5.24 (1H, dd, $J = 11.0$ Hz, 9.0 Hz), 5.43 (1H, dd, $J = 10.5$ Hz, 10.5 Hz); $^{13}$C NMR (125 MHz, CDCl$_3$): $\delta$ 25.66, 25.74, 25.8, 33.3, 33.5, 37.1, 66.7, 68.8, 125.8, 140.8; IR (neat): 3361.9 (br m), 2921.2 (s), 2849.7 (m), 1447.5 (m), 1373.0 (w), 1324.5 (w), 1146.9 (w), 1069.1 (m), 1025.5 (m), 947.9 (w), 889.6 (w), 744.7 (w) cm$^{-1}$; HRMS-(ESI+) for C$_{10}$H$_{22}$N$_1$O$_2$ [M+NH$_4$]: calculated: 188.1651, found: 188.1643. $[\alpha]^{25}_D = +9.50$ (c = 0.52, CHCl$_3$, l = 50 mm).

Proof of Stereochemistry.

The enantioselectivity was determined by treating the resulting 1,2-diol with 2,2-dimethoxypropane and catalytic p-toluenesulfonic acid. The acetonide was then subjected to ozonolysis/reduction, followed by acylation of the primary alcohol. The authentic
material was prepared by acylation of (S)-isopropylideneglycerol, which was purchased from Aldrich.

Chiral GLC (β-Dex 120, Supelco, 60 °C for 5 min, ramp 3 °C/min to 120 °C, 20 psi, s/r = 35:1) - analysis of (2,2-dimethyl-1,3-dioxolan-4-yl)methyl acetate.

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(S,Z)-6-phenylhex-3-ene-1,2-diol (Table 2.4, entry 6). The diboration was performed according to the representative procedure with (Z)-hexa-3,5-dien-1-ylbenzene (30 mg, 189.5 µmol), Pt(dba)$_3$ (5.1 mg, 5.7 µmol), (R,R)-3,5-diethylphenylTADDOLPh (2.47) (9.1 mg, 11.3 µmol), and B$_2$(pin)$_2$ (50.5 mg, 199.1 µmol) in tetrahydrofuran (1.9 mL, 0.1 M). The crude reaction mixture was purified on silica gel (40-60% ethyl acetate/hexanes, R$_f$ = 0.21 in 50% ethyl acetate/hexanes, stain in PMA) to afford a clear colorless oil (22.6 mg, 62% yield). $^1$H NMR (400 MHz, CDCl$_3$): $\delta$ 2.34-2.51 (2H, m), 2.65 (1H, ddd, $J = 13.6$ Hz, 7.2 Hz, 7.2 Hz), 2.72 (1H, ddd, $J = 14.0$ Hz, 7.2 Hz, 7.2 Hz), 3.43 (2H, d, $J = 6.0$ Hz), 4.31 (1H, m), 5.35 (1H, dd, $J = 9.2$ Hz, 9.2 Hz), 5.60 (1H, ddd, $J = 10.8$ Hz, 8.0 Hz, 8.0 Hz), 7.15-7.20 (3H, m), 7.26-7.30 (2H, m); $^{13}$C NMR (100 MHz, CDCl$_3$): $\delta$ 29.85, 35.56, 66.09, 68.28, 126.12, 128.35, 128.70, 128.92, 133.11, 141.33; IR (neat): 3361.9 (m), 2923.4 (m), 2855.5 (w), 1453.6 (m), 1074.3 (s), 1028.3 (m), 738.6 (m), 698.7 (s) cm$^{-1}$; HRMS-(ESI+) for C$_{12}$H$_{20}$NO$_2$ [M+NH$_4^+$]: calculated: 210.1494, found: 210.1496. $[\alpha]_D^{25} = +6.20$ (c = 0.69, CHCl$_3$, l = 50 mm).

Proof of Stereochemistry.

The enantioselectivity was determined by treating the resulting 1,2-diol with 2,2-dimethoxypropane and catalytic p-toluenesulfonic acid. The acetonide was then subjected to ozonolysis/reduction, followed by acylation of the primary alcohol. The authentic
material was prepared by acylation of (S)-isopropylideneglycerol, which was purchased from Aldrich.

*Chiral GLC (β-Dex 120, Supelco, 60 °C for 5 min, ramp 3 °C/min to 120 °C, 20 psi, s/r = 35:1) - analysis of (2,2-dimethyl-1,3-dioxolan-4-yl)methyl acetate.*

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(S,Z)-6-((tert-butyldiphenylsilyl)oxy)hex-3-ene-1,2-diol (Table 2.4, entry 7). The diboration was performed according to the representative procedure with ((Z)-tert-buty(hexa-3,5-dien-1-yloxy) diphenylsilane (60.0 mg, 178.3 µmol), Pt(dba)$_3$ (4.8 mg, 5.3 µmol), (R,R)-3,5-diethylphenylTADDOLPPh (2.47) (8.5 mg, 10.7 µmol), and B$_2$(pin)$_2$ (47.5 mg, 187.2 µmol) in tetrahydrofuran (1.8 mL, 0.1 M). The crude reaction mixture was purified by column chromatography on silica gel (20-50% ethyl acetate/hexanes, $R_f = 0.44$ in 50% ethyl acetate/hexanes, stain in PMA) to afford a clear colorless oil that was inseparable from the 1,4-diol and pinacol (58.3 mg, 6.1:1.6:1 product:1,4-diol:pinacol = 56%). $^1$H NMR (500 MHz, CDCl$_3$): 1,2-diol: $\delta$ 1.03 (9H, s), 1.96 (1H, br s), 2.32 (1H, ddd, $J = 13.0$ Hz, 6.0 Hz, 6.0 Hz), 2.36 (1H, br s), 2.44 (1H, ddd, $J = 14.5$ Hz, 7.0 Hz, 7.0 Hz), 3.46 (1H, dd, $J = 11.0$ Hz, 7.5 Hz), 3.55 (1H, d, $J = 9.5$ Hz), 3.62-3.69 (2H, m), 4.45 (1H, m), 5.53 (1H, dd, $J = 10.5$ Hz, 8.0 Hz), 5.62 (1H, ddd, $J = 10.5$ Hz, 8.0 Hz, 8.0 Hz), 7.36-7.43 (6H, m), 7.63-7.66 (4H, m); 1,4-diol: $\delta$ 1.04 (9H, s), 1.56 (2H, br s), 1.65 (1H, dddd, $J = 13.5$ Hz, 4.0 Hz, 4.0 Hz, 4.0 Hz), 1.86 (1H, dddd, $J = 19.0$ Hz, 8.5 Hz, 8.5 Hz, 5.0 Hz), 3.83 (1H, ddd, $J = 10.5$ Hz, 4.0 Hz, 4.0 Hz), 3.86 (1H, ddd, $J = 10.5$ Hz, 5.0 Hz, 5.0 Hz), 4.17 (1H, dd, $J = 13.0$ Hz, 5.5 Hz), 4.27 (1H, dd, $J = 13.0$ Hz, 6.5 Hz), 4.76 (1H, ddd, $J = 8.0$ Hz, 8.0 Hz, 4.0 Hz), 5.57 (1H, m), 5.73 (1H, ddd, $J = 11.5$ Hz, 6.0 Hz, 6.0 Hz), 7.36-7.43 (6H, m), 7.63-7.66 (4H, m); $^{13}$C NMR (100 MHz, CDCl$_3$): mixture of diols $\delta$ 9.0, 19.2, 26.8, 29.7, 31.3, 38.7, 58.9, 62.7, 63.2, 66.2, 67.9, 68.3, 127.7, 127.8, 129.7, 129.90, 129.92, 130.4, 130.4, 131.0, 133.4, 134.4, 135.56, 135.59; IR (neat):
3354.6 (m), 2928.9 (m), 1471.6 (w), 1427.4 (m), 1108.6 (s), 700.9 (s), 504.6 (s) cm⁻¹; HRMS-(ESI+) for C₂₂H₃₀O₃Si [M+H]: calculated: 371.2042, found: 371.2059. [α]²⁵_D = +10.18 (c = 0.45, CHCl₃, l = 50 mm).

**Proof of Stereochemistry.**

The enantioselectivity was determined by treating the resulting 1,2-diol with 2,2-dimethoxypropane and catalytic p-toluenesulfonic acid. The acetonide was then subjected to ozonolysis/reduction, followed by acylation of the primary alcohol. The authentic material was prepared by acylation of (S)-isopropylideneglycerol, which was purchased from Aldrich.

*Chiral GLC (β-Dex 120, Supelco, 60 °C for 5 min, ramp 3 °C/min to 120 °C, 20 psi, s/r = 35:1) - analysis of (2,2-dimethyl-1,3-dioxolan-4-yl)methyl acetate.*

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racemic | derived from reaction product | authentic
(S,Z)-4-phenylbut-3-ene-1,2-diol (Table 2.4, entry 8). The diboration was performed according to the representative procedure with (Z)-buta-1,3-dien-1-ylbenzene (30 mg, 230.4 µmol), Pt(dba)$_3$ (6.2 mg, 6.9 µmol), (R,R)-3,5-diethylphenylTADDOLPh (2.47) (11.0 mg, 13.8 µmol), and B$_2$(pin)$_2$ (61.4 mg, 241.9 µmol) in tetrahydrofuran (2.3 mL, 0.1 M). The crude reaction mixture was purified by column chromatography on silica gel (40-60% ethyl acetate/hexanes, R$_f$ = 0.24 in 50% ethyl acetate/hexanes, stain in PMA) to afford a white solid (20.8 mg, 55%). $^1$H NMR (500 MHz, CDCl$_3$): δ 2.25 (2H, br s), 3.54 (1H, dd, $J$ = 10.5 Hz, 8.0 Hz), 3.67 (1H, d, $J$ = 9.5 Hz), 4.63 (1H, ddd, $J$ = 8.5 Hz, 8.0 Hz, 3.0 Hz), 5.59 (1H, dd, $J$ = 11.5 Hz, 9.5 Hz), 6.60 (1H, d, $J$ = 11.5 Hz), 7.20-7.23 (3H, m), 7.27-7.30 (2H, m); $^{13}$C NMR (150 MHz, CDCl$_3$): δ 66.2, 68.7, 127.6, 128.3, 128.7, 129.7, 133.4, 136.2; IR (neat): 3350.7 (s), 2925.7 (w), 1493.4 (w), 1071.1 (s), 1020.4 (m), 699.4 (s) cm$^{-1}$; HRMS-(ESI+) for C$_{10}$H$_{16}$NO$_2$ [M+NH$_4$]: calculated: 182.1181, found: 182.1173. $\left[ \alpha \right]^{25}_{D} = +9.12$ (c = 0.49, CHCl$_3$, l = 50 mm).

**Proof of Stereochemistry.**

The enantioselectivity was determined by treating the resulting 1,2-diol with 2,2-dimethoxypropane and catalytic $p$-toluenesulfonic acid. The acetonide was then subjected to ozonolysis/reduction, followed by acylation of the primary alcohol. The authentic material was prepared by acylation of (S)-isopropylideneglycerol, which was purchased from Aldrich.
Chiral GLC (β-Dex 120, Supelco, 60 °C for 5 min, ramp 3 °C/min to 120 °C, 20 psi, s/r = 35:1) - analysis of (2,2-dimethyl-1,3-dioxolan-4-yl)methyl acetate.

- racemic
- derived from reaction product
- authentic

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2.6.9. Representative Procedure for Diboration/Allylation/Oxidation (Table 2.6).

To an oven-dried 6-dram vial with magnetic stir bar in the glove box was added Pt(dba)$_3$ (12.7 mg, 14.1 µmol), (R,R)-3,5-di-i-butylphenyl-TADDOLPPh (2.50) (28.8 mg, 28.3 µmol), B$_2$(pin)$_2$ (119.7 mg, 471.2 µmol) and tetrahydrofuran (4.7 mL, [substrate] = 0.1 M). The vial was sealed with a polypropylene cap, removed from the glove box, and heated to 80 °C in an oil bath for 20 min. The vial was cooled to room temperature, returned to the glove box and charged with (Z)-penta-1,3-diene (32.0 mg, 471.2 µmol). The vial was sealed, removed from the glove box, and stirred at 60 °C for 12 h. The reaction mixture was then cooled to ambient temperature and the solvent was removed in vacuo. The vial was sealed, returned to the glove box and charged with dichloromethane (1.0 mL) and freshly distilled benzaldehyde (25.0 mg, 235.6 µmol). The reaction was brought to the bench and allowed to stir at room temperature for 12 h at which time the reaction mixture was cooled to 0 °C (ice/water) and charged with tetrahydrofuran (2.0 mL), 3 M sodium hydroxide solution (2 mL), and 30 wt % hydrogen peroxide (1 mL). The reaction was gradually warmed to room temperature and allowed to stir for 12 h at which time the vial was cooled to 0 °C (ice/water). Saturated aqueous sodium thiosulfate (2 mL) was carefully added dropwise. The reaction mixture was diluted with ethyl acetate (5 mL) and the aqueous and organic layers were separated. The aqueous layer was rinsed with ethyl acetate (3 x 15 mL), and the combined organics were dried over Na$_2$SO$_4$, filtered, and volatiles were removed in vacuo. The crude reaction mixture was purified by
column chromatography on silica gel (30-60% ethyl acetate/hexanes, \( R_f = 0.23 \) in 50% ethyl acetate/hexanes, stain in PMA) to afford a clear, colorless oil (32.6 mg, 72%).

2.6.10. **Characterization and Proof of Stereochemistry (Table 2.6).**

(4\( R \),5\( S \),E)-4-methyl-5-phenylpent-2-ene-1,5-diol (Table 2.6, entry 1). \(^1\)H NMR (600 MHz, CDCl\(_3\)): \( \delta \) 1.01 (3H, d, \( J = 6.6 \) Hz), 1.23 (2H, br s), 2.56-2.60 (1H, m), 4.05 (2H, d, \( J = 3.6 \) Hz), 4.60 (1H, d, \( J = 5.4 \) Hz), 5.61-5.62 (2H, m), 7.26-7.30 (3H, m), 7.31-7.33 (2H, m); \(^13\)C NMR (150 MHz, CDCl\(_3\)): \( \delta \) 14.5, 43.4, 63.6, 77.6, 126.5, 127.5, 128.1, 130.1, 134.3, 142.6; IR (neat): 3355.9 (br m), 2967.3 (w), 2929.1 (w), 2873.0 (w), 1719.7 (w), 1452.3 (m), 1370.6 (w), 1259.5 (w), 1055.1 (w), 973.2 (s), 755.1 (m), 700.9 (s) cm\(^{-1}\); HRMS-(ESI+) for C\(_{12}\)H\(_{20}\)NO\(_2\) [M+NH\(_4\)]: calculated: 210.1494, found: 210.1492. \([\alpha]^{25}_D = -14.00\) (c = 0.90, CHCl\(_3\), l = 50 mm).

**Proof of Stereochemistry:**

The enantioselectivity was determined by subjecting the 1,5-diol to ozonolysis/reduction, followed by acetonide protection (as shown below) for GLC analysis. The analogous racemic material was prepared using PCy\(_3\) as the achiral ligand in the diboration reaction. The major diastereomer was determined by measuring the coupling
constant of the carbinol hydrogen in the six-membered ring ketal below by $^1$H NMR: $J = 4.0$ Hz, proving *syn* stereochemistry.

Chiral GLC ($\beta$-Dex 120, Supelco, 90 °C for 5 min, ramp 2 °C/min to 150 °C, 20 psi, $s/r = 35:1$) - analysis of 2,2,5-trimethyl-4-phenyl-1,3-dioxane.
The absolute stereochemistry was determined by subjecting the 1,5-diol to ozonolysis/reduction. The specific rotation of the resulting 1,3-diol ([α]$^{24}_D = -57.20$ (c = 0.16, CHCl$_3$, l = 50 mm)) was compared to literature values ([α]$^{24}_D = -51.60$ (c = 0.15, CHCl$_3$)).$^{12}$

\[ [\alpha]^{24}_D = -57.2 \ (c=0.16, \text{CHCl}_3) \]

The olefin geometry of the 1,5-diol was determined to be *trans* by measuring the coupling constants of the vinylic hydrogens from the $^1$H NMR taken in benzene: $^1$H NMR (500 MHz, C$_6$D$_6$): δ 0.97 (3H, d, $J = 6.5$ Hz), 2.42 (1H, ddq, $J = 13.0$ Hz, 13.0 Hz, 7.0 Hz), 3.79 (2H, dd, $J = 5.5$ Hz, 1.0 Hz), 4.38 (1H, d, $J = 5.5$ Hz), 5.44 (1H, ddd, $J = 16.0$ Hz, 5.5 Hz, 5.5 Hz), 5.54 (1H, dd, $J = 15.5$ Hz, 7.5 Hz), 7.06-7.10 (1H, m), 7.18-7.23 (3H, m).

(4R,5R,E)-4-methyl-7-phenylhept-2-ene-1,5-diol (Table 2.6, entry 2). The diboration/allylation was performed according to the representative procedure with (Z)-penta-1,3-diene (40.6 mg, 596.2 µmol), Pt(dba)$_3$ (16.1 mg, 17.9 µmol), (R,R)-3,5-di-i-butylphenylTADDOLPPh (2.50) (36.5 mg, 35.8 µmol), B$_2$(pin)$_2$ (151.9 mg, 596.2 µmol) in tetrahydrofuran (6.0 mL, 0.1 M), freshly distilled hydrocinnamaldehyde (40.0 mg, 298.1 µmol) and dichloromethane (1.2 mL). The crude reaction mixture was purified by column chromatography on silica gel (30-50% ethyl acetate/hexanes, $R_f$ = 0.19 in 50% ethyl acetate/hexanes, stain in PMA) to afford a clear, colorless oil (45.9 mg, 70%). $^1$H NMR (600 MHz, CDCl$_3$): $\delta$ 1.02 (3H, d, $J$ = 6.6 Hz), 1.64-1.70 (1H, m), 1.76-1.82 (1H, m), 2.30 (1H, dd, $J$ = 12.0 Hz, 6.6 Hz), 2.63 (1H, ddd, $J$ = 13.8 Hz, 9.6 Hz, 6.6 Hz), 2.83 (1H, ddd, $J$ = 13.8 Hz, 9.6 Hz, 4.8 Hz), 3.50 (1H, ddd, $J$ = 9.0 Hz, 5.4 Hz, 3.0 Hz), 4.11 (2H, d, $J$ = 5.4 Hz), 5.61-5.71 (2H, m), 7.15-7.19 (3H, m), 7.23-7.29 (2H, m); $^{13}$C NMR (150 MHz, CDCl$_3$): $\delta$ 14.7, 32.5, 35.9, 42.4, 63.6, 74.3, 125.9, 128.41, 128.44, 130.0, 134.5, 142.1; IR (neat): 3350.7 (br m), 3024.3 (w), 2920.9 (m), 2855.7 (w), 1718.7 (w), 1495.8 (w), 1453.3 (m), 1377.1 (w), 1315.7 (w), 1259.9 (w), 1066.4 (s), 1028.2 (s), 973.4 (m), 920.0 (w), 870.4 (w), 746.6 (m), 699.8 (s) cm$^{-1}$; HRMS-(ESI+) for C$_{14}$H$_{24}$NO$_2$ [M +NH$_4$]: calculated: 238.1807, found: 238.1801. $\left[\alpha\right]_{D}^{25} = +26.52$ (c = 0.98, CHCl$_3$, l = 50 mm).
**Analysis of Stereochemistry:**

The enantioselectivity was determined by subjecting the 1,5-diol to ozonolysis/reduction, followed by acetonide protection. The analogous racemic material was prepared using PCy$_3$ as the achiral ligand in the diboration reaction. The major diastereomer was determined by measuring the coupling constant of the carbinol hydrogen in the six-membered ring ketal below by $^1$H NMR: $J = 3.5$ Hz, proving syn stereochemistry. The absolute stereochemistry was assigned by analogy.

*Chiral GLC (β-Dex 120, Supelco, 90 °C for 5 min, ramp 3 °C/min to 180 °C, 20 psi, s/r = 35:1) - analysis of 2,2,5-trimethyl-4-phenethyl-1,3-dioxane.*

![Chiral GLC Peaks](image)

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(2E,4R,5R,6E)-4-methyl-7-phenylhepta-2,6-diene-1,5-diol (Table 2.6, entry 3). The diboration/allylation was performed according to the representative procedure with (Z)-penta-1,3-diene (31.0 mg, 454.0 µmol), Pt(dba)$_3$ (12.2 mg, 13.6 µmol), (R,R)-3,5-di-i-butylphenylTADDOLPPh (2.50) (27.8 mg, 27.2 µmol), B$_2$(pin)$_2$ (115.3 mg, 454.0 µmol) in tetrahydrofuran (4.5 mL, 0.1 M), freshly distilled cinnamaldehyde (30 mg, 227.0 µmol), and dichloromethane (0.9 mL). The crude reaction mixture was purified by column chromatography on silica gel (30-50% ethyl acetate/hexanes, R$_f$ = 0.16 in 50% ethyl acetate/hexanes, stain in PMA) to afford a white solid (32.7 mg, 66%). $^1$H NMR (600 MHz, CDCl$_3$): $\delta$ 1.07 (3H, d, $J = 6.6$ Hz), 1.22 (2H, br s), 2.46-2.51 (1H, m), 4.12 (2H, d, $J = 4.2$ Hz), 4.20 (1H, dd, $J = 5.4$ Hz, 5.4 Hz), 5.69-5.76 (2H, m), 6.20 (1H, dd, $J = 15.6$ Hz, 6.6 Hz), 6.57 (1H, d, $J = 15.6$ Hz), 7.21-7.23 (1H, m), 7.29-7.33 (2H, m), 7.35-7.38 (2H, m); $^{13}$C NMR (150 MHz, CDCl$_3$): $\delta$ 15.2, 42.5, 63.6, 76.0, 126.5, 127.7, 128.6, 129.8, 130.6, 131.4, 133.7, 136.7; IR (neat): 3362.1 (br m), 2957.9 (w), 2924.8 (m), 2869.3 (w), 2854.6 (w), 1715.4 (w), 1494.7 (w), 1450.5 (m), 1377.4 (w), 1070.1 (w), 968.8 (s), 750.0 (m), 695.1 (m); HRMS-(ESI+) for C$_{14}$H$_{22}$NO$_2$ [M+NH$_4$]: calculated: 236.1651, found: 236.1653. $[\alpha]^{25}_D$ = -17.40 (c = 0.70, CHCl$_3$, $l$ = 50 mm).

**Analysis of Stereochemistry:**

The enantioselectivity was determined by SFC analysis of the reaction product. The analogous racemic material was prepared using PCy$_3$ as the achiral ligand in the
diboration reaction. The absolute stereochemistry was assigned by analogy. The olefin geometry of the 1,5-diol was determined to be trans by measuring the coupling constants of the vinylic hydrogens from the $^1$H NMR taken in benzene: $^1$H NMR (500 MHz, C$_6$D$_6$):

$\delta$ 1.01 (3H, d, $J = 9.0$ Hz), 2.29 (1H, ddd, $J = 8.5$ Hz, 8.5 Hz, 8.5 Hz), 3.83 (2H, d, $J = 7.0$ Hz), 3.97 (1H, ddd, $J = 8.0$ Hz, 2.0 Hz, 2.0 Hz), 5.53 (1H, ddd, $J = 20.0$ Hz, 5.5 Hz, 5.5 Hz), 5.63 (1H, dd, $J = 19.5$ Hz, 9.0 Hz), 6.13 (1H, dd, $J = 20.0$ Hz, 7.0 Hz), 6.51 (1H, d, $J = 20.0$ Hz), 7.03-7.09 (1H, m), 7.11-7.13 (2H, m), 7.26-7.28 (2H, m).

Chiral SFC (AD-H, Chiraldex, 5 mL/min, 5% MeOH, 100 bar, 35 °C) - analysis of reaction product.

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racemic

reaction product

coinjection of diboration product + racemic
(2E,4R,5R,6E)-4-methyltrideca-2,6-diene-1,5-diol (Table 2.6, entry 4). The diboration/allylation was performed according to the representative procedure with (Z)-1,3-pentadiene (30.0 mg, 440.4 µmol), Pt(dba)$_3$ (11.8 mg, 13.2 µmol), (R,R)-3,5-di-i-butylphenylTADDOLPh (2.50) (27.0 mg, 26.4 µmol), B$_2$(pin)$_2$ (117.4 mg, 462.4 µmol) in tetrahydrofuran (4.4 mL, 0.1 M), freshly distilled nonenal (31.0 mg, 220.2 µmol) and dichloromethane (0.9 mL). The crude reaction mixture was purified by column chromatography on silica gel (25-40% ethyl acetate/hexanes, $R_f = 0.37$ in 50% ethyl acetate/hexanes, stain in PMA) to afford a clear, colorless oil (32.7 mg, 66%). $^1$H NMR (500 MHz, CDCl$_3$): $\delta$ 0.86 (3H, t, $J$ = 6.5 Hz), 0.99 (3H, d, $J$ = 7.0 Hz), 1.23-1.34 (6H, m), 1.47 (2H, br s), 2.02 (2H, ddd, $J$ = 14.0 Hz, 7.0 Hz, 7.0 Hz), 2.36 (1H, m), 3.95 (1H, br s), 4.11 (2H, br s), 5.42 (1H, dd, $J$ = 15.5 Hz, 7.0 Hz), 5.60-5.72 (3H, m); $^{13}$C NMR (100 MHz, CDCl$_3$): $\delta$ 14.3, 15.5, 22.8, 29.0, 29.4, 31.9, 32.5, 42.5, 64.0, 76.5, 130.3, 130.4, 133.7, 134.3; IR (neat): 3355.2 (m), 2924.7 (s), 2854.7 (m), 1456.9 (w), 1003.2 (m), 968.9 (s) cm$^{-1}$; HRMS-(ESI+) for C$_{14}$H$_{30}$NO$_2$ [M +NH$_4$]: calculated: 244.2276, found: 244.2271. [$\alpha$]$^2$$_D$ = +12.73 (c = 0.54, CHCl$_3$, $l$ = 50 mm).

**Analysis of Stereochemistry:**

The enantioselectivity was determined by treating the 1,5-diol with benzoic anhydride and Et$_3$N to make the mono(benzoate) for SFC analysis. The analogous
racemic material was prepared using PCy$_3$ as the achiral ligand in the diboration reaction.

The absolute stereochemistry was assigned by analogy.

*Chiral SFC (AD-H, Chiraldex, 3 mL/min, 3% MeOH, 100 bar, 35 °C) - analysis of the mono(benzoate) of the reaction product.*
(4R,5R,E)-4-methylhept-2-ene-1,5-diol (Table 2.6, entry 5).

The diboration/allylation was performed according to the representative procedure with (Z)-penta-1,3-diène (58.6 mg, 860.8 µmol), Pt(dba)₃ (23.2 mg, 25.8 µmol), (R,R)-3,5-di-i-butylphenylTADDOLPPh (2.50) mg, 51.6 µmol), B₂(pin)₂ (218.6 mg, 860.8 µmol) in tetrahydrofuran (2.9 mL, 0.3 M), freshly distilled propionaldehyde (25.0 mg, 430.4 µmol), and dichloromethane (1.7 mL). The crude reaction mixture was purified by column chromatography on silica gel (30-50% ethyl acetate/hexanes, Rf = 0.15 in 50% ethyl acetate/hexanes, stain in PMA) to afford a clear, colorless oil (45.3 mg, 73%). ¹H NMR (500 MHz, CDCl₃): δ 0.94 (3H, t, J = 7.0 Hz), 1.00 (3H, d, J = 7.0 Hz), 1.32-1.41 (1H, m), 1.48-1.56 (1H, m), 1.69 (2H, br s), 2.25-2.31 (1H, m), 3.39 (1H, dddd, J = 4.5 Hz, 4.5 Hz 4.5 Hz, 4.5 Hz), 4.10 (2H, d; J = 4.5 Hz), 5.62-5.71 (2H, m); ¹³C NMR (125 MHz, CDCl₃): δ 10.4, 14.3, 26.9, 41.7, 63.6, 76.4, 129.6, 135.1; IR (neat): 3333.4 (br m), 2962.8 (w), 2931.0 (w), 2874.7 (w), 1457.3 (w), 1376.1 (w), 1081.6 (w), 1022.8 (w), 1003.9 (m), 971.9 (s), 704.7 (w) cm⁻¹; HRMS-(ESI+) for C₈H₂₀NO₂ [M+NH₄⁺]: calculated: 162.1494, found: 162.1499. [α]²⁵D = +26.74 (c = 0.50, CHCl₃, l = 50 mm).

**Analysis of Stereochemistry:**

The enantioselectivity was determined by subjecting the 1,5-diol to ozonolysis/reduction, followed by acetonide protection. The analogous racemic material was
prepared using PCy₃ as the achiral ligand in the diboration reaction. The absolute stereochemistry was assigned by analogy.

*Chiral GLC* (β-Dex 120, Supelco, 70 °C for 5 min, ramp 3 °C/min to 120 °C, 20 psi, s/r = 35:1) - analysis of 4-ethyl-2,2,5-trimethyl-1,3-dioxane.

![Chiral GLC peaks](image)

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racemic derived from reaction product
(4R,5R,E)-4,6-dimethylhept-2-ene-1,5-diol (Table 2.6, entry 6). The diboration/allylation was performed according to the representative procedure with (Z)-1,3-pentadiene (56.6 mg, 830.8 µmol), Pt(dba)$_3$ (22.4 mg, 24.9 µmol), (R,R)-3,5-di-i-butylphenylTADDOLPPh (2.50) (50.9 mg, 49.8 µmol), B$_2$(pin)$_2$ (221.5 mg, 872.4 µmol) in tetrahydrofuran (8.3 mL, 0.1 M), freshly distilled isobutyraldehyde (30.0 mg, 415.4 µmol) and dichloromethane (1.6 mL). The crude reaction mixture was purified by column chromatography on silica gel (25-40% ethyl acetate/hexanes, $R_f$ = 0.28 in 50% ethyl acetate/hexanes, stain in PMA) to afford a clear, colorless oil (40.8 mg, 62%). $^1$H NMR (500 MHz, CDCl$_3$): $\delta$ 0.90 (6H, dd, $J = 8.5$ Hz, 6.5 Hz), 1.02 (3H, d, $J = 8.0$ Hz), 1.39 (2H, br s), 1.73 (1H, m), 2.36 (1H, m), 3.15 (1H, dd, $J = 7.0$ Hz, 7.0 Hz), 4.10 (2H, d, $J = 5.5$ Hz), 5.62-5.71 (2H, m); $^{13}$C NMR (100 MHz, CDCl$_3$): $\delta$ 14.1, 17.0, 19.7, 30.6, 39.3, 63.7, 79.8, 129.1, 135.8; IR (neat): 3330.8 (m), 2959.2 (m), 2924.8 (s), 1459.0 (m), 1085.5 (m), 970.6 (s) cm$^{-1}$; HRMS-(ESI$^+$) for C$_9$H$_{22}$NO$_2$ [M+NH$_4$]: calculated: 176.1650, found: 176.1649. [$\alpha$]$^{25}_D$ = +10.54 ($c = 0.57$, CHCl$_3$, $l$ = 50 mm).

**Analysis of Stereochemistry:**

The enantioselectivity was determined by subjecting the 1,5-diol to ozonolysis/reduction, followed by acetonide protection. The analogous racemic material was prepared using PCy$_3$ as the achiral ligand in the diboration reaction. The absolute stereochemistry was assigned by analogy.
Chiral GLC (β-Dex 120, Supelco, 70 °C for 5 min, ramp 3 °C/min to 140 °C, 20 psi, s/r = 35:1) - analysis of 4-isopropyl-2,2,5-trimethyl-1,3-dioxane.

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(4R,5S,E)-6-(benzyloxy)-4-methylhex-2-ene-1,5-diol (Table 2.6, entry 7). The diboration/allylation was performed according to the representative procedure with (Z)-1,3-pentadiene (30.0 mg, 440.4 µmol), Pt(dba)$_3$ (11.8 mg, 13.2 µmol), (R,R)-3,5-di-i-butylphenylTADDOLPPh (2.50) (27.0 mg, 26.4 µmol), B$_2$(pin)$_2$ (117.4 mg, 462.4 µmol) in tetrahydrofuran (4.4 mL, 0.1 M), freshly distilled benzyloxyacetaldehyde (33.0 mg, 220.2 µmol) and dichloromethane (0.9 mL). The crude reaction mixture was purified by column chromatography on silica gel (35-50% ethyl acetate/hexanes, $R_f$ = 0.19 in 50% ethyl acetate/hexanes, stain in PMA) to afford a clear, colorless oil (37.5 mg, 72%). $^1$H NMR (500 MHz, CDCl$_3$): $\delta$ 1.06 (3H, d, $J$ = 7.0 Hz), 1.23 (2H, br s), 2.34 (1H, m), 3.37 (1H, dd, $J$ = 9.5 Hz, 7.5 Hz), 3.52 (1H, dd, $J$ = 9.5 Hz, 3.0 Hz), 3.63 (1H, ddd, $J$ = 8.0 Hz, 8.0 Hz, 3.5 Hz), 4.07 (2H, d, $J$ = 4.5 Hz), 4.50 (1H, d, $J$ = 11.5 Hz), 4.54 (1H, d $J$ = 11.5 Hz), 5.64-5.66 (2H, m), 7.26-7.36 (5H, m); $^{13}$C NMR (100 MHz, CDCl$_3$): $\delta$ 15.9, 39.6, 63.6, 72.6, 73.4, 73.6, 127.6, 127.8, 128.5, 129.7, 134.1, 137.9; IR (neat): 3380.3 (s), 2924.6 (s), 2858.7 (s), 1719.1 (w), 1453.9 (m), 1078.9 (s), 974.3 (s), 698.6 (m) cm$^{-1}$; HRMS-(ESI+) for C$_{14}$H$_{24}$NO$_2$ [M+NH$_4$]: calculated: 254.1756, found: 254.11755. [$\alpha$]$^{25}_{D}$ = +13.59 (c = 0.48, CHCl$_3$, l = 50 mm).
**Analysis of Stereochemistry:**

The enantioselectivity was determined SFC analysis of the reaction product. The analogous racemic material was prepared using PCy₃ as the achiral ligand in the diboration reaction. The absolute stereochemistry was assigned by analogy.

*Chiral SFC (AD-H, ChiralDEX, 100 bar, 5 mL/min, 4% MeOH, 35 °C)- analysis of reaction product.*
(4R,5R,E)-4-isobutylhept-2-ene-1,5-diol (2.55). The diboration/allylation was performed according to the representative procedure with (Z)-6-methylhepta-1,3-diene (75.9 mg, 688.7 µmol), Pt(dba)$_3$ (18.6 mg, 20.7 µmol), (R,R)-3,5-diethylphenylTADDOLPPh (2.47) (32.9 mg, 41.3 µmol), B$_2$(pin)$_2$ (174.9 mg, 688.7 µmol) in tetrahydrofuran (2.3 mL, 0.3 M), distilled propionaldehyde (20.0 mg, 344.3 µmol), and dichloromethane (1.4 mL), followed by oxidation to afford an inseparable 1:1 mixture of the 1,2-diol and diboration/allylation product. To facilitate purification, the crude reaction mixture was dissolved in THF:Et$_2$O:H$_2$O (1:1:1) and NaIO$_4$ (4 equiv) was added at room temperature (oxidative cleavage of both the 1,2-diboration product and pinacol). The reaction mixture was stirred for 2h, after which time it was diluted with ethyl acetate, and the layers were separated. The aqueous layer was extracted with ethyl acetate (3 x 10 mL). The combined organics were dried over Na$_2$SO$_4$, filtered, and concentrated in vacuo. The crude material was purified by column chromatography on silica gel (20-40% ethyl acetate/hexanes, R$_f$ = 0.23 in 50% ethyl acetate/hexanes, stain in PMA) to afford the title compound as a clear, colorless oil (46.3 mg, 72%). $^1$H NMR (600 MHz, CDCl$_3$): δ 0.81 (3H, d, $J$ = 6.6 Hz), 0.87 (3H, d, $J$ = 6.6 Hz), 0.94 (3H, t, $J$ = 7.2 Hz), 1.19-1.25 (2H, m), 1.26-1.33 (1H, m), 1.50-1.57 (2H, m), 1.73 (2H, br s), 2.22 (1H, dddd, $J$ = 9.6 Hz, 9.6 Hz, 5.4 Hz, 5.4 Hz), 3.36 (1H, ddd, $J$ = 8.4 Hz, 4.8 Hz, 3.0 Hz), 4.10 (2H, d, $J$ = 5.4 Hz), 5.47 (1H, dd, $J$ = 15.6 Hz, 9.6 Hz), 5.67 (1H, ddd, $J$ = 15.6 Hz, 6.0 Hz, 6.0 Hz); $^{13}$C NMR (150 MHz, CDCl$_3$): δ 10.5, 21.4, 23.9, 25.3, 26.5, 39.2, 46.5, 63.5, 76.5, 131.3, 133.2; IR (neat):
3351.3 (br m), 2954.7 (m), 2927.4 (m), 2869.3 (w), 1464.6 (w), 1382.8 (w), 1367.0 (w), 1074.2 (m), 1021.7 (m), 972.6 (s), 869.9 (w), 828.3 (w) cm\(^{-1}\); HRMS-(ESI\(^+\)) for C\(_{11}\)H\(_{26}\)NO\(_2\) [M+NH\(_4\)]: calculated: 204.1964, found: 204.1970. \([\alpha]\)\(^{25}\)\(_D\) = -21.07 (c = 0.58, CHCl\(_3\), l = 50 mm).

**Analysis of Stereochemistry:**

The enantioselectivity was determined by subjecting the 1,5-diol to ozonolysis/reduction, followed by acetonide protection. The analogous racemic material was prepared using PCy\(_3\) as the achiral ligand in the diboration reaction. The absolute stereochemistry was assigned by analogy.

*Chiral GLC (\(\beta\)-Dex 120, Supelco, 70 °C for 5 min, ramp 2 °C/min to 150 °C, 20 psi, s/r = 35:1) - analysis of 4-ethyl-5-isobutyl-2,2-dimethyl-1,3-dioxane.*

![Chiral GLC Peaks](image)

<table>
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The diboration/allylation was performed according to the representative procedure with (Z)-trideca-1,3-diene (124.2 mg, 688.7 µmol), Pt(dba)$_3$ (18.6 mg, 20.7 µmol), (R,R)-3,5-diethylphenyl-TADDOL-PhP$_2$ (32.9 mg, 41.3 µmol), B$_2$(pin)$_2$ (174.9 mg, 688.7 µmol) in tetrahydrofuran (2.3 mL, 0.3 M), distilled propionaldehyde (20.0 mg, 344.3 µmol), and dichloromethane (1.4 mL), followed by oxidation to afford an inseparable 1:1 mixture of the 1,2-diol and diboration/allylation product. To facilitate purification, the crude reaction mixture was dissolved in THF:Et$_2$O:H$_2$O (1:1:1) and NaIO$_4$ (4 equiv) was added at room temperature (oxidative cleavage of both the 1,2-diboration product and pinacol). The reaction mixture was stirred for 2h, after which time it was diluted with ethyl acetate, and the layers were separated. The aqueous layer was extracted with ethyl acetate (3 x 10 mL). The combined organics were dried over Na$_2$SO$_4$, filtered, and concentrated in vacuo. The crude material was purified by column chromatography on silica gel (20-35% ethyl acetate/hexanes, R$_f$ = 0.33 in 50% ethyl acetate/hexanes, stain in PMA) to afford a clear, colorless oil (61.7 mg, 70%). $^1$H NMR (500 MHz, CDCl$_3$): δ 0.86 (3H, t, $J$ = 6.5 Hz), 0.94 (3H, t, $J$ = 7.5 Hz), 1.22-1.33 (14H, m), 1.48-1.62 (2H, m), 2.07-2.13 (1H, m), 3.38 (1H, ddd, $J$ = 9.0 Hz, 5.5 Hz, 3.0 Hz), 4.12 (2H, dd, 6.0 Hz, 1.5 Hz), 5.47 (1H, dd, $J$ = 15.5 Hz, 9.5 Hz), 5.67 (1H, ddd, $J$ = 15.5 Hz, 6.0 Hz, 6.0 Hz); $^{13}$C NMR (150 MHz, CDCl$_3$): δ 10.4, 14.1, 22.7, 26.8, 27.4, 29.3, 29.59, 29.62, 29.7, 30.1, 31.9, 48.9, 63.6, 76.1, 131.4, 133.2; IR (neat): 3355.5 (br m), 2955.8 (w), 2922.5 (s),
2853.5 (m), 1463.3 (w), 1377.5 (w), 1078.2 (w), 1019.5 (w), 973.0 (m), 721.2 (w) cm⁻¹;
HRMS-(ESI+) for C₁₆H₃₆NO₂ [M+NH₄⁺]: calculated: 274.2746, found: 274.2751. [α]²⁵_D = -10.42 (c = 0.84, CHCl₃, l = 50 mm).

**Analysis of Stereochemistry:**

The enantioselectivity was determined by subjecting the 1,5-diol to ozonolysis/reduction. The resulting 1,3-diol was treated with benzoic anhydride and Et₃N to make the mono(benzoate) for SFC analysis. The analogous racemic material was prepared using PCy₃ as the achiral ligand in the diboration reaction. The absolute stereochemistry was assigned by analogy.

*Chiral SFC* (AD-H, ChiralDEX, 5 mL/min, 5% MeOH, 100 bar, 35 °C) - analysis of 2-(1-hydroxypropyl)undecyl benzoate.
Chapter 3

Development, Scope, and Utility of the Enantioselective Platinum-Catalyzed 1,2-Diboration of 4,4-Disubstituted Dienes: Application to Synthesis of Stereodefined Quaternary Centers

3.1. Introduction

The stereoselective formation of all-carbon quaternary stereocenters (3.1) is one of the most challenging tasks in organic chemistry. Most of the methods that accomplish this transformation have been developed within the last ten years, showing the continued interest in this field of research. Initial strategies involved chiral auxiliaries directly linked to the molecule of interest, whereas more recent strategies entailed advances in enantioselective catalysis. The most commonly utilized methods include allylic substitution, alkylation of tertiary carbons, cycloaddition, nucleophilic allylation, conjugate addition, and rearrangements (Scheme 3.1).
Scheme 3.1. General Strategies to Access Enantiopure Quaternary Carbon Stereocenters

The significant challenges associated with the construction of quaternary carbon stereocenters have also made the total synthesis of important natural products that contain quaternary carbons difficult. Because inversion of undesired configurations of quaternary centers is difficult, the stereoselectivities of reactions to form them often determine the total efficiency of the natural product syntheses. Scheme 3.2 highlights some recent natural products that were prepared by stereoselective formation of all-carbon quaternary centers using the general methods depicted above.¹

Scheme 3.2. Natural Products and Therapeutics Containing Quaternary Stereocenters

Typically, when alkylation or acylation of enolate equivalents is utilized as a strategy to access quaternary carbons, the stereoinduction at the newly formed quaternary carbon is achieved based on the influence of preexisting stereocenters. However, in the total synthesis of (−)-flustramine B reported by MacMillan, the catalytic asymmetric alkylation of an achiral enolate with chiral electrophiles was successfully employed.\(^2\) Mulzer\(^3\) and Ogasawara\(^4\) independently used conjugate addition of a vinyl cuprate to an α,β-unsaturated enone in their syntheses of morphine, although the adjacent chiral

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environments controlled the stereochemical outcome. The sterically hindered nature of quaternary centers make rearrangement reactions an attractive strategy for their construction. In Danishefsky’s total synthesis of gelsemine, two [3,3]-sigmatropic rearrangements were utilized to control to stereochemistry of the quaternary carbon centers.\(^5\) Alternately, cycloadditions, including the Diels-Alder and Pauson-Khand reactions, have shown significant applications in the synthesis of polycyclic natural products. Norzoanthamine, a marine polyketide natural product, was first synthesized in 2004 by Miyashita using an intramolecular Diels-Alder reaction to form two out of three quaternary carbon stereocenters.\(^6\) In Denmark’s synthesis of the serotonin antagonist LY426965, the catalytic enantioselective addition of a 3,3-disubstituted allylsilane to benzaldehyde represented the key step in constructing the all-carbon quaternary stereocenter.\(^7\)

Despite these recent advances in the area of stereoselective formation of quaternary carbons, significant challenges still remain, particularly in the construction of quaternary centers in acyclic systems. New catalytic enantioselective methods that allow for their rapid generation would have a large impact on the synthetic community.


3.2. Background

The enantioselective addition of allylmetal reagents to carbonyl compounds is well established as a powerful and general method for stereoselective carbon-carbon bond formation. This method has been widely applied in organic synthesis, especially in the total synthesis of polypropionate-derived natural products and biologically active compounds. However, few applications of this reaction to the formation of stereogenic quaternary centers have been developed.\(^8\) The limitations of this method reside in the difficulty of synthesizing geometrically pure 3,3-disubstituted allylmetal reagents and controlling the asymmetric induction with either internal chiral auxiliaries or external chiral catalysts.

Hoffmann pioneered much of the work on conservation of stereochemistry from chiral allylboronates to aldehydes,\(^9\) and was the first to prepare enantiomerically enriched homoallylic alcohols bearing an \(\alpha\)-quaternary stereocenter from 3,3-disubstituted allylboronates (3.4) (Scheme 3.3, eq. 1).\(^10\) The synthesis of allylboronates 3.4 was accomplished using Matteson’s procedure\(^11\) from \(\alpha\)-chloroethylboronates 3.2 and vinyllithium 3.3. The methyl group in the \(\alpha\)-position played a vital role in the conservation of enantiopurity in the allylboration of acetaldehyde, producing homoallylic alcohols 3.5 and 3.6 in good yields and high levels of diastereo- and enantiomeric purity. When employing auxiliary-induced stereoselection alone with tartrate ester derived

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allylboronate 3.7, the corresponding homoallylic alcohols 3.8 and 3.9 were obtained with high diastereoselectivity (≥ 98:2) but only moderate levels of enantioselectivity (Scheme 3.3, eq. 2).  

**Scheme 3.3.** First Examples of Allylaboration to Access Enantiomerically Enriched Quaternary Stereocenters

![Scheme 3.3](image)

To improve the efficiency for the generation of 3,3-disubstituted allylboronates, Hall developed a two-step, one-pot procedure to make tetrasubstituted 2-alkoxycarbonyl allylboronates 3.10 by carbocupration\(^\text{13}\) of readily available alkynoate esters followed by

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an electrophilic trap with halomethylboronates (Scheme 3.4). Because the vinylcuprate intermediate is configurationally unstable above –30 °C, the alkylation reaction necessitates the presence of 9 equivalents of HMPA in order to achieve useful $E/Z$ ratios. With these conditions, the tetrasubstituted allylboronates were prepared in moderate to good yield and with excellent levels of diastereoselectivity. When reacted with various aldehydes, allylboronates 3.10 formed the initial allylation products 3.11, which then cyclized to produce $\gamma$-lactones 3.12. Although the products were obtained in up to 89% yield and 20:1 dr, the reaction required 14 days at room temperature.

Scheme 3.4. Hall’s Synthesis of Tetrasubstituted Allylboronates to Access $\gamma$-Lactones

In 2004, Hall extended this methodology to the synthesis of enantiomerically enriched $\gamma$-lactones using chiral 3,3-dimethyl allylboronates 3.13 containing a carboxyester based auxiliary (Scheme 3.5). For these substrates, lactonization of

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homoallylic alcohols with large aryl-menthol auxiliaries necessitated the addition of a mild acid. Although the reaction proceeded to afford 3.14, the product was inseparable from the auxiliary and enantiomeric ratios greater than 91:9 were not achieved with this single auxiliary approach.

**Scheme 3.5.** Hall’s Enantioselective Allylboration: Single Auxiliary Approach

In order to improve the level of stereoinduction in the allylboration reaction, Hall and co-workers next examined the use of a dual auxiliary approach (Scheme 3.6). Corey’s 8-phenylmenthol and Villiéras’ boronic ester auxiliary\(^\text{16}\) were chosen based on their previous effectiveness in reactions of 2-carboxyester allylboronates. Upon the addition of the dual auxiliary substituted allylboronate 3.16 to various aldehydes, followed by acid-catalyzed cyclization, γ-lactones 3.17 were produced in 40-80% yield and 97:3-99:1 er. Although high selectivities were obtained, the method required the difficult synthesis of a 2-carboxyester allylboronate containing two chiral auxiliaries,

long reaction times, and surprisingly, this method was never applied to the preparation of enantiomerically enriched quaternary stereocenters.

**Scheme 3.6.** Hall’s Enantioselective Allylboration: Dual Auxiliary Approach

Denmark and co-workers reported the first example of a catalytic enantioselective method to synthesize homoallylic alcohols bearing adjacent quaternary stereocenters. This strategy uses 3,3-disubstituted allylic trichlorosilanes in the presence of 2,2’-bispyrrolidine-based bisphosphoramide catalyst 3.19 (Scheme 3.7). When employing the unsymmetrical allyltrichlorosilane derived from geraniol (3.18) in the addition to benzaldehyde, the Lewis-base catalyzed reaction operates through a closed transition state to deliver homoallylic alcohol 3.20 in 83% yield, 99:1 a anti:syn ratio, and 97:3 er (eq. 1). Utilizing the allyltrichlorosilane derived from nerol (3.21), containing the opposite olefin geometry, the corresponding homoallylic alcohol was afforded in 78% yield, a 98:2 syn:anti ratio, and 99:1 er. At the time, this represented the most powerful

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method to access stereodefined quaternary carbon centers from 3,3-disubstituted allylmetal reagents.

Scheme 3.7. Denmark’s Catalytic Enantioselective Allylsilation to Access Quaternary Stereocenters

In 2002, Denmark applied this methodology to the synthesis of serotonin antagonist LY426965. Preclinical studies indicated that LY426965 was a selective, full 5-HT1A antagonist that may have therapeutic use for smoking cessation and depression.

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disorders. Denmark’s synthesis involved the allylsilation of benzaldehyde with allylsilane 3.23 in the presence of 10 mol% of bisphosphoramide catalyst 3.19 to afford homoallylic alcohol 3.24 in 64% yield, 99:1 dr, and 97:3 er.

**Scheme 3.8.** Application of Denmark’s Allylsilation to the Synthesis of LY426965

Although successful, a more direct synthesis would have incorporated the allylation of cyclohexanecarboxaldehyde instead of benzaldehyde, which required a further chemoselective reduction. Unfortunately, the reaction does not tolerate aliphatic aldehydes. Instead of undergoing allylation, they are immediately consumed by the pathway depicted in Scheme 3.9 to form an α-chloro silyl ether 3.28, which is unreactive toward allylating reagents.

**Scheme 3.9.** Side Product Formation in Denmark’s Allylsilation of Aliphatic Aldehydes
All of the previously described methods to access stereodefined quaternary centers require several chemical steps for the preparation of the desired 3,3-disubstituted allylmetal species. Improving upon this strategy, Marek reported the use of allylzinc species in the allylation of aldehydes to synthesize enantiomerically enriched homoallylic alcohols in a single-pot reaction (Scheme 3.10). Allylzinc species were previously unknown for their use in enantioselective preparation of quaternary stereocenters due to the metallotropic equilibrium that rapidly equilibrates E- and Z-isomers of the allylmetal species. Starting with alkynyl sulfoxides 3.29, Marek demonstrated the power of the sulfoxide to increase the stability of the allylic organozinc species in its α-position through an intramolecular chelation (3.30). The enantioenriched sulfoxide also acts as a chiral auxiliary and a regiocontrol element in the initial carbocupration reaction. The in situ generated allylzinc species successfully reacted with aromatic aldehydes in high levels of diastereoselectivity to produce homoallylic alcohols 3.31 in good yields. When preparing homoallylic alcohols containing an adjacent tertiary center instead of a quaternary center (R² = H), the products were produced with diminished levels of diastereoselection. Additionally, reactions of aliphatic aldehydes were difficult to control in this reaction, limiting the overall scope of the methodology.

**Scheme 3.10.** Marek’s Multicomponent Carbometallation/Homologation/Allylation to Access Quaternary Stereocenters

Although significant advancements have been made in the field of stereoselective formation of quaternary centers through carbonyl allylation, several limitations still exist. Denmark’s methodology represents the first and only catalytic enantioselective allylmetallation of aromatic aldehydes to prepare enantiomerically enriched quaternary stereocenters. Other examples take advantage of one or more chiral auxiliaries to achieve synthetically useful levels of stereochemical induction. Furthermore, the use of aliphatic aldehydes remains a challenge in a variety of allylation reactions. Most importantly, all of the allylmetallations that generate quaternary carbons reported to date furnish homoallylic alcohol products with a terminal alkene, and multistep manipulations are necessary for further functionalization at the alkene site. It is clear that the field of organic chemistry is in need of the development of a general, catalytic enantioselective method for the construction of 3,3-disubstituted α-chiral allylmetal reagents **3.32** (Scheme 3.11). Their use in the addition to aromatic and aliphatic aldehydes to prepare
homoallylic alcohols bearing quaternary stereocenters and a synthetic handle would be a significant contribution to current allylmetallation strategies.

**Scheme 3.11.** Ideal Preparation of 3,3-Disubstituted Allylmetal Reagents to Access Enantioenriched Quaternary Carbon Centers

3.3. Development of the Enantioselective Pt-Catalyzed 1,2-Diboration of 4,4-Disubstituted Dienes

The strategy applied to the Pt-catalyzed 1,2-selective diboration of cis-1,3-dienes (Chapter 2) should also operate for the diboration of 4,4-disubstituted dienes. As depicted in Scheme 3.12, the presence of the R\textsuperscript{1} substituent on the diene causes a highly strained A\textsuperscript{1,3} interaction when in the S-cis conformation and forces the diene to adopt the S-trans conformation. As in the diboration of cis-1,3-dienes, this should slow 1,4-diboration, allowing 1,2-diboration of the terminal alkene to become the predominant reaction pathway (3.34) to form the 1,2-bis(boronate)ester 3.35. Direct oxidation of this intermediate would afford trisubstituted allylic alcohol 3.36.

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Scheme 3.12. Proposed Insertion Mechanism for the Pt-Catalyzed 1,2-Diboration of 4,4-Disubstituted Dienes

We envisioned that the inherent reactivity of the 3,3-disubstituted allylboronate 3.35 would allow for efficient addition to carbonyl electrophiles through a closed 6-membered ring transition state, placing the CH$_2$B(pin) in the equatorial position (Scheme 3.13, 3.37). The polypropionate-like products of this tandem 1,2-diboration/allylboration sequence would contain an enantiomerically enriched homoallylic alcohol with an $\alpha$-quaternary stereocenter and a trans alkene. The most unique feature of this overall transformation is the formation of an additional carbon-boron bond, providing a convenient synthetic handle for further chain-extending reactions (3.38).
Scheme 3.13. Pt-Catalyzed Diboration to Access α-Chiral 3,3-Disubstituted Allylboronates for the Synthesis of Enantioenriched Quaternary Centers

The foundation of a tandem diboration/allylation sequence to form stereodefined quaternary carbon centers lies in the development of an efficient catalytic enantioselective 1,2-diboration of 4,4-disubstituted dienes to form the crucial 3,3-disubstituted allylboron intermediate $3.35$. Initial studies focused on the optimization of the Pt-catalyzed 1,2-diboration reaction using the symmetric 4,4-disubstituted diene $3.39$ (Table 3.1). When employing 3 mol% of Pt(dba)$_3$ in the presence of 6 mol% of the achiral Lewis-basic phosphine ligand PCy$_3$, the diboration achieved 81% conversion, and the desired 1,2-diol $3.40$ was obtained in 64% yield upon subsequent oxidation (entry 1). Based on the success of TADDOL-derived phosphonite ligands in both the 1,4-diboration of trans-1,3-dienes and the 1,2-diboration of cis-1,3-dienes, ligand $(R,R)$-$3.41$ was examined in the diboration of $3.39$. Excitingly, the 1,2-diol $3.40$ was produced in 75% yield and 90:10 er (entry 2). Altering the steric environment of the ligand led to a clear trend with respect to enantioselectivity. Increasing the size of the 3- and 5-substituents on
the aryl rings of the TADDOL backbone from Me to Et, i-Pr, and t-Bu resulted in improved levels of enantioselection providing 3.40 in up to 97:3 er (entries 3-6). Further increasing the steric bulk of the chiral ligand by modifying the diol protecting group also caused an increase in the enantioselectivity; however, the reactivity suffered. The Pt-catalyzed diboration of 3.39 using ligand \((R,R)-3.46\), which contained the diethyl ketal, provided the desired 1,2-diol in 98:2 er, but only proceeded with 65% conversion (entry 8). In an attempt to increase conversion using ligands \((R,R)-3.45\) and \((R,R)-3.46\), 2 equivalents of \(\text{B}_2(\text{pin})_2\) were used in the diboration reaction, but no significant improvements were observed (entries 7 and 9). The 1,2-diol could be obtained in 99:1 er with ligand \((R,R)-3.47\) containing the di-i-propyl ketal, but the reaction only progressed to 50% conversion, which afforded 46% yield of the desired product (entry 10). It is noteworthy that in all cases none of the regioisomeric 1,4-diboration product was observed under the reaction conditions. The chiral ligand survey revealed that \((R,R)-3.44\) was the optimal ligand for the enantioselective Pt-catalyzed diboration of 4,4-disubstituted dienes, providing 3.40 in 78% yield and 97:3 er.
Table 3.1. Ligand Survey for Pt-Catalyzed 1,2-Diboration of 4,4-Disubstituted Dienes

<table>
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<tr>
<th>entry</th>
<th>ligand</th>
<th>R</th>
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<th>% conv</th>
<th>% yield</th>
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<tbody>
<tr>
<td>1</td>
<td>PCy₃</td>
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<td>-</td>
<td>81</td>
<td>64</td>
<td>-</td>
</tr>
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<td>(R,R)-3.41</td>
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<td>3,5-dimethylphenyl</td>
<td>78</td>
<td>75</td>
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<td>3</td>
<td>(R,R)-3.42</td>
<td>Me</td>
<td>3,5-diethylphenyl</td>
<td>93</td>
<td>78</td>
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<td>4</td>
<td>(R,R)-3.43</td>
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<td>90</td>
<td>85</td>
<td>93:7</td>
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<td>46</td>
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ᵃ 2.0 equiv of B₂(pin)$_₂$ were used in the diboration reaction

Although the diboration with symmetric diene 3.39 was a useful proof of concept, it was also important to demonstrate the viability of a catalytic enantioselective diboration of unsymmetrical 4,4-disubstituted diene substrates that would ultimately allow access to enantiomerically enriched all-carbon quaternary stereocenters. In this regard, the diboration of geraniol-derived diene 3.48 with various phosphorus-based ligands was examined (Table 3.2). Surprisingly, utilizing PCy₃ in the diboration reaction resulted in only 19% conversion and 12% isolated yield of the desired 1,2-diol 3.49. Numerous achiral phosphine ligands were surveyed in the diboration of 3.48; however,
none of them provided useful yields of the diboration/oxidation product. To our delight, the chiral TADDOL-derived phosphonite ligands \((R,R)-3.44\) and \((R,R)-3.45\) were very effective in the diboration reaction and proceeded with 95% and 83% conversion respectively and both furnished 1,2-diol 3.49 in 98:2 er (entries 8 and 9).

**Table 3.2.** Ligand Survey for Pt-Catalyzed 1,2-Diboration of Unsymmetrical 4,4-Disubstituted Dienes

<table>
<thead>
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<th>entry</th>
<th>ligand</th>
<th>% conv</th>
<th>% yield</th>
<th>er</th>
</tr>
</thead>
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<td>1</td>
<td>PCy3</td>
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<td>12</td>
<td>-</td>
</tr>
<tr>
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<td>none</td>
<td>0</td>
<td>0</td>
<td>-</td>
</tr>
<tr>
<td>3</td>
<td>PPh3</td>
<td>0</td>
<td>0</td>
<td>-</td>
</tr>
<tr>
<td>4</td>
<td>P(NMe2)3</td>
<td>0</td>
<td>0</td>
<td>-</td>
</tr>
<tr>
<td>5</td>
<td>P(OEt)3</td>
<td>0</td>
<td>0</td>
<td>-</td>
</tr>
<tr>
<td>6</td>
<td>PPh2(o-tolyl)</td>
<td>trace</td>
<td>0</td>
<td>-</td>
</tr>
<tr>
<td>7</td>
<td>((R,R)-3.44)</td>
<td>95</td>
<td>86</td>
<td>98:2</td>
</tr>
<tr>
<td>8</td>
<td>((R,R)-3.45)</td>
<td>83</td>
<td>77</td>
<td>98:2</td>
</tr>
</tbody>
</table>

Once the most effective chiral ligand was selected, it was of interest to determine the optimal metal:ligand ratio for the Pt-catalyzed diboration reaction. In the Pt-catalyzed diboration of *cis*-1,3-dienes, the metal:ligand ratio had a subtle impact on the
regioselectivity of the diboration reaction; with a larger excess of ligand relative to Pt (dba)$_3$, less of the undesired 1,4-diboration product was produced. Decreasing the amount of ligand led to a slight increase in the amount of 1,4-diboration product. Fortunately, the regioselectivity for the Pt-catalyzed diboration of 4,4-disubstituted dienes was unaffected by a decreased metal:ligand ratio. Employing 3 mol% of Pt(dba)$_3$ in the presence of 3.6 mol% ($R,R$)-3.44 led to an efficient and 1,2-selective diboration of 3.39 to generate the desired 1,2-diol 3.40 in 78% yield and 97:3 er (Scheme 3.14).

**Scheme 3.14.** Optimization of Metal:Ligand Ratio for Pt-Catalyzed 1,2-Diboration of 4,4-Disubstituted Dienes

With the optimal conditions for the enantioselective Pt-catalyzed diboration of 4,4-disubstituted dienes in hand, the extent of the substrate scope was investigated by preparing and examining a variety of symmetric and unsymmetric 4,4-disubstituted diene substrates (Table 3.3). Both straight-chain and branched aliphatic substitution on the diene was tolerated in the reaction to provide the desired 1,2-diol products in 67-87% yield and consistently excellent levels of enantioselection. Allylic silyl ethers were also
maintained under the reaction conditions and side products caused by allylic borylation chemistry were not observed. Notably, the geometry of the internal olefin of the diene did not affect the reactivity or enantioselectivity of the diboration reaction. The 4,4-disubstituted dienes derived from both geraniol and nerol proceeded efficiently to provide the corresponding 1,2-diols in 82-86% yield and 98:2 er (entries 4 and 5). Additionally, the presence of a remote trisubstituted alkene did not negatively affect the reaction and it remained intact under the reaction conditions. As illustrated by entry 7, substrates bearing basic nitrogen functionality were not tolerated under the reaction conditions, and none of the desired diboration product was observed. This might be due to the ability of nitrogen to interact negatively with the Pt-catalyst and shut down the reaction. In all cases, the regioselectivity for the diboration reaction was >20:1 in favor of the 1,2-diboration product.
Table 3.3. Substrate Scope for Enantioselective Pt-Catalyzed 1,2-Diboration of 4,4-Disubstituted Dienes

<table>
<thead>
<tr>
<th>entry</th>
<th>diene</th>
<th>product</th>
<th>% yield$^a$</th>
<th>er$^b$</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Me hexyl</td>
<td>hexyl OH OH</td>
<td>67</td>
<td>97:3</td>
</tr>
<tr>
<td>2</td>
<td>Me</td>
<td>Me OH OH</td>
<td>84</td>
<td>98:2</td>
</tr>
<tr>
<td>3</td>
<td>TBDPSO</td>
<td>TBDPSO OH OH</td>
<td>87</td>
<td>98:2</td>
</tr>
<tr>
<td>4</td>
<td>Me</td>
<td>Me OH OH</td>
<td>82</td>
<td>98:2</td>
</tr>
<tr>
<td>5</td>
<td>Me</td>
<td>Me OH OH</td>
<td>86</td>
<td>98:2</td>
</tr>
<tr>
<td>6</td>
<td>Me</td>
<td>Me OH OH</td>
<td>78</td>
<td>97:3</td>
</tr>
<tr>
<td>7</td>
<td>BocN</td>
<td>BocN OH OH</td>
<td>0</td>
<td>-</td>
</tr>
</tbody>
</table>

$^a$ Isolated yield of purified material. Value is an average of two experiments. 
$^b$ Determined by chiral GLC or SFC analysis.
3.4. Development of the Tandem Enantioselective Pt-Catalyzed Diboration/Allylation of 4,4-Disubstituted Dienes

Having successfully developed the first catalytic enantioselective 1,2-diboration of 4,4-disubstituted dienes to access enantioenriched 1,2-bis(boronate)esters, it was of great interest to determine if the 3,3-disubstituted α-chiral allylboronate intermediate would be selective in a tandem diboration/allylation sequence to form quaternary carbons. Investigation of this reaction sequence began with the addition of benzaldehyde to the crude reaction mixture of the diboration of symmetrical diene 3.39. When both the diboration and allylation reactions were performed in tetrahydrofuran, the desired 1,5-diol 3.50 was isolated in only 35% yield after 40 h at room temperature (entry 1). The inefficient allylation in THF was most likely due to the competitive coordination of the solvent to the allylboron intermediate. By simply removing the THF and adding dichloromethane as a non-coordinating solvent for the allylation reaction, the desired product 3.50 was obtained in 73% yield after 14 h at room temperature (entry 2). Heating the allylation reaction to 40 °C provided a slight improvement in yield (entry 3). It was also important to learn whether the allylation proceeded with high conservation of enantiomeric purity from the α-chiral allylboronate to the aldehyde. We were pleased to see that employing chiral TADDOL-derived phosphonite ligands in the tandem sequence resulted in excellent levels of enantioselectivity for the diboration/allylation/oxidation product 3.50 (entries 4-7). Lastly, it should be noted that by increasing the concentration of the allylation reaction, the reaction time was successfully decreased, and the 1,5-diol
could still be isolated in good yields. It is interesting to note that none of the bis-allylation product was observed with 4,4-disubstituted diene substrates, presumably due to the increased steric congestion adjacent to the nucleophilic carbon of the remaining allylboronate.

Table 3.4. Optimization of Tandem Diboration/Allylation/Oxidation of Symmetrical 4,4-Disubstituted Diene 3.39

<table>
<thead>
<tr>
<th>entry</th>
<th>ligand</th>
<th>solvent (M)</th>
<th>temp</th>
<th>time</th>
<th>% yield</th>
<th>er</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>PCy₃</td>
<td>THF (0.1 M)</td>
<td>rt</td>
<td>40 h</td>
<td>35</td>
<td>-</td>
</tr>
<tr>
<td>2</td>
<td>PCy₃</td>
<td>DCM (0.5 M)</td>
<td>rt</td>
<td>14 h</td>
<td>73</td>
<td>-</td>
</tr>
<tr>
<td>3</td>
<td>PCy₃</td>
<td>DCM (0.5 M)</td>
<td>40 °C</td>
<td>24 h</td>
<td>79</td>
<td>-</td>
</tr>
<tr>
<td>4</td>
<td>(R,R)-3.42</td>
<td>DCM (0.1 M)</td>
<td>rt</td>
<td>40 h</td>
<td>78</td>
<td>94:6</td>
</tr>
<tr>
<td>5</td>
<td>(R,R)-3.42</td>
<td>DCM (0.5 M)</td>
<td>40 °C</td>
<td>22 h</td>
<td>77</td>
<td>94:6</td>
</tr>
<tr>
<td>6</td>
<td>(R,R)-3.44</td>
<td>DCM (0.5 M)</td>
<td>40 °C</td>
<td>14 h</td>
<td>62</td>
<td>97:3</td>
</tr>
<tr>
<td>7</td>
<td>(R,R)-3.45</td>
<td>DCM (0.5 M)</td>
<td>40 °C</td>
<td>8 h</td>
<td>60</td>
<td>97:3</td>
</tr>
</tbody>
</table>

* Value in parentheses represents the [substrate] for the allylation reaction

The tandem diboration/allylation/oxidation sequence was also investigated with the unsymmetric geraniol-derived 4,4-disubstituted diene. Unfortunately, using allylation conditions optimized for the symmetric diene substrate 3.39 led to incomplete conversion
with respect to the allylation reaction. Further manipulation of reaction conditions showed that the conversion could be improved by heating the allylation to 60 °C in toluene and using 4.0 equivalents of aldehyde with respect to the 1,2-bis(boronate)ester. Although these conditions provided synthetically useful yields of the desired diboration/allylation/oxidation product, they were not ideal for the application of this method to synthesis. Without the possibility of over allylation with this class of diene substrates, it was found that useful yields could be obtained by using equimolar amounts of the 1,2-bis(boronate)ester and aldehyde, by increasing the concentration of the allylation reaction to 1.0 M, and by extending the reaction time. This also eliminated the need to exchange solvents between the diboration and allylation reactions, as the diboration is successfully carried out in toluene with equivalent yields and enantioselectivities.

A variety of aldehyde substrates were examined in the tandem diboration/allylation sequence with geraniol-derived diene 3.48 (Table 3.5). Uniformly high levels of diastereoselection and enantioselection were observed in the overall reaction to afford 1,5-diols containing quaternary carbon stereocenters. Straight-chain aliphatic substitution on the aldehyde was well tolerated, and the product derived from hydrocinnamaldehyde was obtained in 69% yield and a 97:3 er. Employing isobutyraldehyde under the optimized allylation conditions resulted in low isolated yields of the corresponding 1,5-diol likely due to increased steric hinderance. The yield was improved to 58% by using 3.0 equivalents of the aldehyde. Aromatic and α,β-unsaturated aldehydes also reacted efficiently providing their corresponding 1,5-diol products in 75-87% yield and 96:4-98:2
er. Notably, aldehydes bearing α-oxygenation were also tolerated in the reaction to afford highly functionalized propionate units from very simple starting materials in a single flask reaction.

Table 3.5. Tandem Diboration/Allylation/Oxidation Sequence to Access Enantioenriched Quaternary Carbon Stereocenters

<table>
<thead>
<tr>
<th>R</th>
<th>Product</th>
<th>Yield</th>
<th>dr</th>
<th>er</th>
</tr>
</thead>
<tbody>
<tr>
<td>Me</td>
<td>3.48</td>
<td>58%</td>
<td>&gt;20:1</td>
<td>97:3</td>
</tr>
<tr>
<td>Me</td>
<td>3.51</td>
<td>69%</td>
<td>&gt;20:1</td>
<td>97:3</td>
</tr>
<tr>
<td>Me</td>
<td>3.49</td>
<td>74%</td>
<td>&gt;20:1</td>
<td>97:3</td>
</tr>
<tr>
<td>Me</td>
<td>3.50</td>
<td>87%</td>
<td>&gt;20:1</td>
<td>98:2</td>
</tr>
<tr>
<td>Me</td>
<td>3.51</td>
<td>75%</td>
<td>&gt;20:1</td>
<td>97:3</td>
</tr>
<tr>
<td>Me</td>
<td>3.52</td>
<td>80%</td>
<td>&gt;20:1</td>
<td>96:4</td>
</tr>
</tbody>
</table>

* Experiment employed 3.0 equivalents of i-PrCHO
Due to the stereochemical predictability of allylboration reactions, we next sought to prepare both diastereomers of the diboration/allylation/oxidation products by simply employing opposite diastereomers of the starting 4,4-disubstituted diene (3.52). As illustrated in Table 3.6, the diene substrate derived from geraniol, which contains an (E)-alkene, produced the desired 1,5-diol products 3.53 in good yield and stereoselectivity with both benzaldehyde and propionaldehyde (entries 1 and 2). The diene substrate derived from nerol, bearing a (Z)-alkene, reacted with equal levels of enantiocontrol to allow access to the opposite diastereomer of product.

Table 3.6. Easy Access to Opposite Diastereomers of the Diboration/Allylation/Oxidation Product

<table>
<thead>
<tr>
<th>entry</th>
<th>R¹</th>
<th>R²</th>
<th>R³</th>
<th>% yield</th>
<th>dr</th>
<th>er</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Me</td>
<td>Me</td>
<td>Ph</td>
<td>87</td>
<td>&gt;20:1</td>
<td>97:3</td>
</tr>
<tr>
<td>2</td>
<td>Me</td>
<td>Me</td>
<td>Et</td>
<td>67</td>
<td>&gt;20:1</td>
<td>95:5</td>
</tr>
<tr>
<td>3</td>
<td>Me</td>
<td>Me</td>
<td>Ph</td>
<td>85</td>
<td>9:1</td>
<td>96:4</td>
</tr>
<tr>
<td>4</td>
<td>Me</td>
<td>Me</td>
<td>Et</td>
<td>67</td>
<td>&gt;20:1</td>
<td>96:4</td>
</tr>
</tbody>
</table>
3.5. Product Utility in the Enantioselective Pt-Catalyzed Diboration/Allylation of 4,4-Disubstituted Dienes

An attractive feature of the 1,2-diboration/allylation of 4,4-disubstituted dienes is that the direct product of the allylboration reaction (3.54) contains a remaining carbon-boron bond that can be used for further synthetic manipulations. The versatility of this remaining functional group was demonstrated by subjecting intermediate 3.54 to Matteson homologation conditions to install an additional methylene unit. Following oxidation, the overall 4-step, single-flask reaction sequence delivered the 1,6-diol 3.55 in 58% yield.

Scheme 3.15. Tandem Diboration/Allylation/Homologation/Oxidation of Symmetrical 4,4-Disubstituted Dienes

Applying the same strategy to the 3,3-disubstituted allylborationate obtained from the Pt-catalyzed 1,2-diboration of unsymmetric diene 3.48, 1,6-diols 3.57 and 3.59 were furnished in excellent yields and diastereoselectivities (Scheme 3.16). As demonstrated in

eq. 2, the enantiomeric purity of the diboration/allylation/homologation/oxidation product was unaltered during the homologation step, and 3.59 was determined to have a 97:3 er.

**Scheme 3.16.** Tandem Diboration/Allylation/Homologation/Oxidation of Unsymmetrical 4,4-Disubstituted Dienes

Due to the wide variety of transformations available to carbon-boron bonds, the synthetic utility of the boronate ester intermediate was further demonstrated by subjecting the crude diboration/allylation reaction mixture to protodeboronation conditions similar to those reported by Aggarwal (Scheme 3.17).\(^{22}\) Interestingly, the reaction did not proceed with direct protodeboronation at the \(\alpha\)-carbon. Instead, the reaction predominately occurred by an \(S_{E2}\) pathway to deliver the bishomoallylic alcohol product

3.61, bearing the terminal alkene, in 74% yield, 97:3 er and 5:1 regioisomeric ratio of alkene isomers.

**Scheme 3.17.** Tandem Pt-Catalyzed 1,2-Diboration/Allylation/Protodeboronation

3.6. Conclusions

The first enantioselective 1,2-diboration of 4,4-disubstituted dienes was developed. Using Pt-catalysts in the presence of TADDOL-derived phosphonite ligands, α-chiral 3,3-disubstituted allylboronates were obtained in high yields and excellent levels of enantiomeric purity. Direct oxidation of the diboration products furnished the corresponding 1,2-diols for a variety of diene substrates. More importantly, the inherent reactivity of the 3,3-disubstituted allylboronate intermediate was utilized in a tandem diboration/allylation sequence to access enantioenriched homoallylic alcohols containing an α-quaternary carbon stereocenter. The tandem reaction sequence proved to be highly selective across a range of aldehyde electrophiles, addressing the limitations of previously developed methods discussed in section 3.2. It was found that both
diastereomers of the homoallylic alcohol products could be generated by simply employing the 4,4-disubstituted diene with the opposite olefin configuration. Furthermore, the products of the diboration/allylation of 4,4-disubstituted dienes contain an additional carbon-boron bond, which provides a synthetic handle for chain-extending reactions. The utility of the compounds generated from this synthetic strategy was demonstrated by subjecting the diboration/allylation intermediate to either a Matteson homologation or protodeboronation, providing highly functionalized polypropionate-like substructures in a single flask reaction. This overall transformation represents the first catalytic enantioselective method to construct α-chiral 3,3-disubstituted allylmetal reagents that start from simple and inexpensive starting materials and provide access to enantioenriched all-carbon quaternary stereocenters.
3.7. Experimentals

3.7.1. General Information. $^1$H NMR spectra were recorded on either a Varian Gemini-400 (400 MHz), a Varian Gemini-500 (500 MHz), a Varian Inova-500 (500 MHz), or a Varian Gemini-600 (600 MHz) spectrometer. Chemical shifts are reported in ppm with the solvent resonance as the internal standard (CDCl$_3$: 7.24 ppm). Data are reported as follows: chemical shift, integration, multiplicity (s = singlet, d = doublet, t = triplet, q = quartet, p = pentet, br = broad, m = multiplet, app = apparent), and coupling constants (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 Gemini-600 (150 MHz) spectrometer with complete proton decoupling. Chemical shifts are reported in ppm with the solvent resonance as the internal standard (CDCl$_3$: 77.0 ppm). Infrared (IR) spectra were recorded on a Bruker alpha spectrophotometer, $\nu_{\text{max}}$ cm$^{-1}$. Bands are characterized as broad (br), strong (s), medium (m), and weak (w). High resolution mass spectrometry (ESI) was performed at the Mass Spectrometry Facility, Boston College.

Liquid Chromatography was performed using forced flow (flash chromatography) on silica gel (SiO$_2$, 230×450 Mesh) purchased from Silicycle. Thin Layer Chromatography was performed on 25 μm silica gel plates purchased from Silicycle. Visualization was performed using ultraviolet light (254 nm), potassium permanganate (KMnO$_4$) in water, or phosphomolybdic acid (PMA) in ethanol. Analytical chiral gas-liquid chromatography (GLC) was performed on a Hewlett-Packard 6890 Series chromatograph equipped with a split mode capillary injection system, a flame ionization
detector, and a Supelco \( \beta \)-Dex 120 column with helium as the carrier gas. Analytical chiral supercritical fluid chromatography (SFC) was performed on a TharSFC Method Station II equipped with Waters 2998 Photodiode Array Detector.

All reactions were conducted in oven- or flame-dried glassware under an inert atmosphere of nitrogen or argon. Tetrahydrofuran, dichloromethane, acetonitrile, and diethyl ether were purified using Pure Solv MD-4 solvent purification system, from Innovative Technology, Inc., by passing the solvent through two activated alumina columns after being purged with argon. Triethylamine was distilled from calcium hydride. Potassium tetrachloroplatinate(II) was purchased from Acros Organics. Dibenzylideneacetone was purchased from Oakwood Chemicals. Tetrabutylammonium chloride was purchased from Fluka. Sodium acetate was purchased from Fisher Scientific. Norbornene was purchased from Aldrich and was sublimed prior to use. Bis (pinacolato)diboron was generously donated by Allychem Co., Ltd. and was recrystallized from pentane prior to use. Dichlorophenylphosphine, tris (dibenzylidenacetone) dipalladium (0), and tri-\( t \)-butylphosphine, were purchased from Strem Chemicals, Inc. and used without further purification. (Z)-penta-1,3-diene was purchased from ChemSampCo and was used without purification. 1,3,5-Tribromobenzene was purchased from Alfa Aesar. Benzaldehyde, hydrocinnamaldehyde, cinnamaldehyde, nonenal, propionaldehyde, \( \text{iso} \)-butyraldehyde, and benzyloxyacetaldehyde were purchased from Aldrich and distilled prior to use. All other reagents were purchased from Aldrich and used without further purification.
3.7.2. Preparation of Pt(dba)$_3$.

Tris(dibenzylideneacetone)platinum was prepared using the literature procedure$^1$ with slight modification. To a three-neck 500 mL round-bottom flask equipped with a magnetic stir bar and reflux condenser was added dibenzylideneacetone (3.95 g, 16.80 mmol), tetrabutylammonium chloride (2.00 g, 7.20 mmol), and sodium acetate (3.55 g, 43.30 mmol). Methanol (210.0 mL) was added and the solution was warmed to 70 °C in an oil bath until the solids dissolved (5 minutes). In a separate 50 mL pear-shaped flask was added potassium tetrachloroplatinate (1.00 g, 2.41 mmol) and water (8.0 mL), and the mixture gently warmed until solids dissolved. The contents of the pear shaped flask were transferred to the three-neck flask and the reaction was allowed to stir at 70 °C for 3 h. After 3 h, the reaction was cooled to ambient temperature, transferred to a one-neck 500 mL round-bottom flask and concentrated by rotary evaporation to half the volume. The reaction mixture was then filtered on a Büchner funnel and the remaining solids were washed with copious amounts of water and methanol until all yellow dibenzylideneacetone crystals were removed. The resulting solid residue was placed under high vacuum for 24 hours to remove residual methanol and water. This procedure furnished a dark brown solid (1.84 g, 85%) consistent with Pt(dba)$_3$. Anal Calc’d for C$_{51}$H$_{42}$O$_3$Pt: C, 68.22; H, 4.71. Found: C, 67.09; H, 4.49 (average of two experiments). Platinum analysis was performed by ICP Optical Emission Spectroscopy; calculated for Pt(dba)$_3$: 21.73% Pt; found 21.92% (average of two experiments).

3.7.3. Ligand Synthesis.

The following ligands were prepared using the literature procedures or as previously described and spectral data are in accordance with the literature: \((R,R)-3.41\)^2 \((R,R)-3.42\) (refer to Chapter 2, Section 2.6.5), \((R,R)-3.43\)^3 \((R,R)-3.45\)^2

**Preparation of 3,5-di-iso-propylphenylTADDOL.**

\[
\text{Me} \quad \text{NH}_2 \quad \text{Me} \quad \text{Bu}_4\text{NBr}_3 \quad \text{DCM} \quad \text{Me} \quad \text{NH}_2 \quad \text{Me} \quad \text{NaNO}_2, \text{H}_3\text{PO}_4, 2\text{M HCl} \quad 4^\circ\text{C to rt} \quad \text{Me} \quad \text{Br} \quad \text{Br}
\]

3,5-Di-iso-propylphenylTADDOL was prepared according to the procedure described above for 3,5-di-iso-butylphenylTADDOL using 1-bromo-3,5-di-iso-propylbenzene, which was prepared according to the literature procedure from 2,6-diisopropylaniline as shown below."
7.16 (4H, d, J = 1.7 Hz); $^{13}$C NMR (125 MHz, CDCl$_3$): δ 23.87, 23.96, 24.00, 24.39, 26.95, 30.32, 34.16, 34.33, 78.50, 81.23, 108.9, 123.2, 123.4, 123.5, 124.5, 142.5, 145.8, 147.3, 148.0; IR (neat): 3235.4 (w), 2967.2 (s), 2868.4 (m), 1599.3 (m), 1463.7 (m), 1073.2 (m), 872.4 (s), 739.8 (s), 709.6 (m) cm$^{-1}$; HRMS-(+MALDI) for C$_{55}$H$_{78}$O$_4$Na [M +Na]: calculated 825.5792, found: 825.5770. [α]$_D^{25}$ = +19.88 (c = 0.97, CHCl$_3$, l = 50 mm).

**Preparation of (R,R)-3,5-di-iso-propylphenylTADDOLPPh (3.44).**

To a flame dried 50 mL round bottom flask equipped with magnetic star bar was added 3,5-di-iso-propylphenylTADDOL (1.09 g, 1.36 mmol) and tetrahydrofuran (13.6 mL, 0.1 M) under N$_2$. Triethylamine (0.65 mL, 4.64 mmol) was added via syringe and the reaction mixture was brought to 0 °C in an ice bath. Dichlorophenylphosphine (0.20 mL, 1.50 mmol) was added dropwise via syringe at 0 °C. The reaction was brought to room temperature and was allowed to stir for 2 h. The reaction was diluted with Et$_2$O (20 mL), filtered through celite and concentrated in vacuo. The crude material was purified by column chromatography on silica gel (3% ethyl acetate/hexanes, with 1% Et$_3$N to prevent hydrolysis) to afford the title compound as a white solid (1.03 g, 83%).

(R,R)-3,5-di-iso-propylphenylTADDOLPPh (3.44). $^1$H NMR (500 MHz, CDCl$_3$): δ 0.11 (3H, s), 1.10-1.25 (48H, m), 1.51 (3H, s), 2.78-2.84 (8H, m), 4.91 (1H, d, J = 8.5 Hz), 5.58 (1H, dd, J = 8.5 Hz, 4.0 Hz), 6.83 (1H, s), 6.91 (2H, s), 6.94 (1H, s), 6.98 (2H, d, J = 2.0 Hz).
Hz), 7.18 (2H, br s), 7.34 (2H, s), 7.44-7.47 (3H, m), 7.51 (2H, s), 7.86-7.90 (2H, m);

$^{13}$C NMR (125 MHz, CDCl$_3$): $\delta$ 23.86, 23.90, 23.98, 24.12, 24.19, 27.99, 34.03, 34.12,

34.16, 34.43, 82.76, 82.83, 83.22, 83.39, 83.84, 83.89, 84.31, 84.34. 110.4, 123.1, 123.3,

123.4, 123.5, 123.6, 124.7, 124.8, 125.1, 128.1, 128.2, 129.9, 130.1, 130.4, 141.4, 141.7,

142.1, 142.2, 146.2, 146.3, 146.8, 147.1, 147.3, 147.8, 147.9; $^{31}$P NMR (202 MHz, CDCl$_3$): $\delta$ 155.41; IR (neat): 2957.6 (s), 2868.3 (w), 1598.6 (w), 1464.9 (m), 1162.7 (w), 1027.6 (m), 877.8 (s), 799.7 (m), 735.3 (s), 693.3 (m) cm$^{-1}$. $[\alpha]_D^{25} = -50.40$ ($c = 0.34$, CHCl$_3$, l = 50 mm).

3.7.4. Preparation of 4,4-Disubstituted Dienes.

**Preparation of (E)-penta-2,4-dien-2-ylcyclohexane (Table 3.3, entry 2).**

The title compound was prepared as shown above from cyclohexylacetylene according to the literature procedure.$^5$ The Suzuki-Miyaura cross coupling was carried out according to the literature procedure$^6$ with slight modification as follows: To a flame-
dried 250 mL round-bottomed flask equipped with a stir bar in the glove box was added

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Pd$_2$(dba)$_3$ (173.0 mg, 189.0 µmol) and P('Bu)$_3$ (153.0 mg, 754.0 µmol). The reaction mixture was removed from the glove box and the vinylboronic acid pinacol ester (1.89 g, 7.54 mmol) was added under N$_2$ via syringe as a solution in THF (125 mL). Degassed aqueous KOH (3.0 M, 7.5 mL, 22.63 mmol) was then added to the reaction, followed by vinyl bromide (1.0 M in THF, 22.6 mL, 22.63 mmol). The reaction was allowed to stir at rt for 12 hours under N$_2$, at which time the reaction was quenched with saturated aqueous NH$_4$Cl (50 mL) and the layers were separated. The aqueous layer was washed with dichloromethane (3 x 100 mL) and the organic layers were combined, dried over MgSO$_4$, filtered, and concentrated in vacuo. The crude product was purified by column chromatography on SiO$_2$ (100% hexane, $R_f$ = 0.67, stain in CAM) to afford an inseparable heterogeneous mixture of a colorless oil and a white solid (913.5 mg, 30:1 product:homodimerized diene, 74%). The diene mixture can be further purified (to remove the homodimer) by Kugelrohr distillation under N$_2$ at 200 °C to afford the title compound as a clear, colorless oil (323.0 mg, 29%).

(E)-penta-2,4-dien-2-ylcyclohexane (Table 3.3, entry 2). $^1$H NMR (500 MHz, CDCl$_3$): $\delta$ 1.09-1.30 (5H, m), 1.64-1.70 (3H, m), 1.72 (3H, s), 1.72-1.77 (2H, m), 1.88 (1H, dddd, $J$ = 11.5 Hz, 11.5 Hz, 3.0 Hz, 3.0 Hz), 4.96 (1H, dd, $J$ = 10.0 Hz, 2.0 Hz), 5.08 (1H, dd, $J$ = 16.5 Hz, 2.0 Hz), 5.84 (1H, d, $J$ = 11.0 Hz), 6.59 (1H, dddd, $J$ = 16.5 Hz, 10.0 Hz, 10.0 Hz); $^{13}$C NMR (125 MHz, CDCl$_3$): $\delta$ 15.0, 26.3, 26.6, 31.6, 47.5, 114.5, 123.4, 133.6, 144.8; IR (neat): 3082.7 (w),
2924.1 (s), 2852.1 (s), 1646.7 (w), 1448.1 (m), 1019.4 (w), 985.1 (m), 890.3 (s), 657.8 (m) cm\(^{-1}\); HRMS-(ESI+) for C\(_{11}\)H\(_{19}\) [M+H]: calculated: 151.1487, found: 151.1482.

**Preparation of (E)-4-methyldeca-1,3-diene (Table 3.3, entry 1).**

The title compound was prepared as shown above from 1-octyne according to the literature procedure.\(^1\) The Suzuki-Miyaura cross coupling was carried out as described above for (E)-penta-2,4-dien-2-ylcyclohexane with slight modification as follows: To a flame-dried, round-bottomed flask equipped with a stir bar in the glove box was added Pd\(_2\)(dba)\(_3\) (132.0 mg, 144.2 µmol) and P(tBu)\(_3\) (117.0 mg, 578.3 µmol). The reaction mixture was removed from the glove box and the vinylboronic acid pinacol ester (1.45 g, 5.77 mmol) was added under N\(_2\) via syringe as a solution in THF (95 mL). Degassed aqueous KOH (3.0 M, 5.8 mL, 17.31 mmol) was then added to the reaction, followed by vinyl bromide (1.0 M in THF, 17.3 mL, 17.31 mmol). The reaction was allowed to stir at rt for 12 hours under N\(_2\), at which time the reaction was quenched with saturated aqueous NH\(_4\)Cl (50 mL) and the layers were separated. The aqueous layer was washed with dichloromethane (3 x 100 mL) and the organic layers were combined, dried over MgSO\(_4\), filtered, and concentrated *in vacuo*. The crude product was purified by column
chromatography on SiO$_2$ (100% hexane, $R_f = 0.69$, stain in PMA) to afford a clear, colorless oil as an inseparable mixture of the desired diene and homodimer product (716.0 mg, 24:1 product:homodimer, 76%). The diene mixture can be further purified (to remove the homodimer) by Kugelrohr distillation under N$_2$ at 225 °C to afford the title compound as a clear, colorless oil (235.0 mg, 27%).

**(E)-4-methyldeca-1,3-diene (Table 3.3, entry 1).** $^1$H NMR (400 MHz, CDCl$_3$): $\delta$ 0.86 (3H, t, $J = 6.0$ Hz); 1.23-1.30 (6H, m); 0.87 (3H, t, $J = 6.5$ Hz), 1.23-1.30 (6H, m), 1.37-1.43 (2H, m), 1.73 (3H, s), 2.02 (2H, t, $J = 7.0$ Hz), 4.95 (1H, dd, $J = 10.0$ Hz, 2.0 Hz), 5.06 (1H, dd, $J = 17.0$ Hz, 2.5 Hz), 5.83 (1H, dd, $J = 11.0$ Hz, 1.9 Hz), 6.56 (1H, ddd, $J = 17.0$ Hz, 11.0 Hz, 11.0 Hz); $^{13}$C NMR (125 MHz, CDCl$_3$): $\delta$ 14.1, 16.5, 22.6, 27.8, 29.0, 31.8, 39.8, 114.3, 125.3, 133.5, 140.0; IR (neat): 2956.8 (m), 2926.5 (s), 2885.9 (m), 1651.4 (w), 1457.5 (w), 1418.6 (w), 1379.2 (w), 986.0 (m), 896.0 (s), 657.1 (w); HRMS-(ESI+) for C$_{11}$H$_{21}$ [M+H]: calculated: 153.1643, found: 153.1646.

**Preparation of (E)-tert-butyl((2-methylpenta-2,4-dien-1-yl)oxy)diphenylsiline (Table 3.3, entry 3).**
(E)-tert-butyl((2-methylpenta-2,4-dien-1-yl)oxy)diphenylsilane (Table 3.3, entry 3). The title compound was prepared as shown above using standard procedures. The crude product was purified by column chromatography on SiO\(_2\) (2% ethyl acetate/hexanes, \(R_f = 0.37\), stain in KMnO\(_4\)) to afford a viscous, clear, colorless oil (715.0 mg, 71%, 20:1 \(E:Z\)). \(^1\)H NMR (500 MHz, CDCl\(_3\)): 1.06 (9H, s), 1.70 (3H, s), 4.09 (2H, d, \(J = 0.5\) Hz), 5.06 (1H, dd, \(J = 10.5\) Hz, 1.0 Hz), 5.17 (1H, dd, \(J = 17.0\) Hz, 1.5 Hz), 6.17 (1H, dd, \(J = 11.0\) Hz, 0.5 Hz), 6.61 (1H, ddd, \(J = 17.0\) Hz, 10.5 Hz, 10.5 Hz), 7.35-7.43 (6H, m), 7.66-7.68 (4H, m); \(^{13}\)C NMR (125 MHz, CDCl\(_3\)): \(\delta\) 13.9, 19.3, 26.8, 68.3, 116.2, 124.2, 127.6, 129.6, 132.8, 133.6, 135.5, 137.5; IR (neat): 2958.2 (w), 2930.5 (m), 2893.2 (w), 2856.3 (m), 1471.8 (w), 1462.0 (w), 1427.1 (m), 1380.4 (w), 1362.1 (w), 1297.9 (w), 1187.5 (w), 1148.4 (w), 1106.3 (s), 1028.8 (m), 989.9 (m), 939.8 (w), 900.1 (m), 823.0 (m), 739.0 (m), 699.9 (s), 659.1 (w), 615.8 (m), 597.5 (m), 573.5 (w), 503.1 (s), 488.1 (s), 431.0 (w) cm\(^{-1}\); HRMS-(ESI+) for C\(_{22}\)H\(_{29}\)OSi[M+H]: calculated: 337.1988, found: 337.1997.

**Preparation of (Z)-4,8-dimethylnona-1,3,7-triene (Table 3.3, entry 5).**
To a 50 mL round-bottomed flask equipped with a stir bar was added iodobenzene diacetate (2.30 g, 7.13 mmol) and TEMPO (101.3 mg, 0.65 mmol). Acetonitrile (6.5 mL) and pH 7 buffer (1.6 mL) were then added, and the reaction mixture was cooled to 0 °C in an ice bath. Nerol (1.00 g, 6.48 mmol) was added via syringe at 0 °C and the reaction was allowed to stir for 3 h (slowly warming to rt). The reaction was then quenched with saturated aqueous sodium thiosulfate (5 mL) and the layers were separated. The aqueous layer was washed with DCM (3 x 20 mL) and the combined organics were dried over Na$_2$SO$_4$, filtered, and concentrated in vacuo. The crude product was purified by column chromatography on SiO$_2$ (2-5% ethyl acetate/hexanes, R$_f$ = 0.45 in 5:1 hexanes:ethyl acetate, stain in PMA) to afford the aldehyde as a clear, colorless oil (987.4 mg, 100%).

To a flame-dried, round-bottomed flask in the glove box was added triphenylphosphonium bromide (2.76 g, 7.78 mmol) and potassium i-t-butoxide (873.4 mg, 7.78 mmol). The flask was sealed, brought to the bench, and charged with THF (20 mL) under N$_2$. The aldehyde (987.4 mg, 6.49 mmol) was then added as a solution in THF (6 mL). The reaction mixture was allowed to stir at rt for 30 min and was then diluted with Et$_2$O (30 mL). The solution was filtered over a pad of silica gel and the filtrate was concentrated in vacuo. The crude product was purified by column chromatography on SiO$_2$ (100% hexanes, R$_f$ = 0.60 in 5:1 hexanes:ethyl acetate, stain in PMA) to afford the title compound as a clear, colorless oil (821.3 mg, 84%). All spectral data were in accordance with the literature.

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**Preparation of (E)-4,8-dimethylnona-1,3,7-triene (Table 3.3, entry 4).**

The title compound was prepared from geraniol according to the procedure described above for (Z)-4,8-dimethylnona-1,3,7-triene. The crude product was purified by column chromatography on SiO\(_2\) (100% hexanes, R\(_f\) = 0.56 in 5:1 hexanes:ethyl acetate, stain in PMA) to afford the title compound as a clear, colorless oil (918.8 mg, 95%). All spectral data were in accordance with the literature. 

**Preparation of allylidene-cyclohexane.**

The title compound was prepared according to the literature procedure with slight modification.\(^8\) To a flame-dried, round-bottomed flask in the glove box was added the phosphonium salt (3.00 g, 15.22 mmol) and potassium \(t\)-butoxide (1.71 g, 15.22 mmol). The flask was sealed, brought to the bench, and THF (51 mL) was added via syringe under N\(_2\). The reaction mixture was cooled to 0 °C in an ice bath and charged with cyclohexanone (1.3 mL, 12.69 mmol, freshly distilled from MgSO\(_4\)). The flask was then fitted with a flame-dried reflux condenser and was heated to 70 °C in an oil bath for 14 h.

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The reaction mixture was then cooled to rt and diluted with diethyl ether (50 mL) and the layers were separated. The organic layer was washed with DI H$_2$O (2 x 25 mL) then dried over Na$_2$SO$_4$, filtered, and concentrated in vacuo. The crude product was purified by column chromatography on SiO$_2$ (100% hexanes) to give the title compound as a clear, colorless oil (1.36 g, 88%). All spectral data were in accordance with the literature.\(^9\)

3.7.5. Representative Procedure for Diboration/Oxidation (Table 3.3)

To an oven-dried 6-dram vial with magnetic stir bar in the glove box was added Pt(dba)$_3$ (8.9 mg, 9.9 \(\mu\)mol), \((R,R\)-3,5-di-iso-propylTADDOLPPh (3.44) (10.8 mg, 11.9 \(\mu\)mol), B$_2$(pin)$_2$ (88.0 mg, 346.5 \(\mu\)mol) and tetrahydrofuran (3.3 mL, [substrate] = 0.1 M). The vial was sealed with a polypropylene cap, removed from the glove box, and heated to 80 °C in an oil bath for 20 min. The vial was cooled to room temperature, returned to the glove box and charged with \((E\)-4-methyldeca-1,3-diene (50.0 mg, 328.3 \(\mu\)mol). The vial was sealed, removed from the glove box, and stirred at 60 °C for 12 h. The reaction mixture was cooled to 0 °C (ice/water) and charged with 3 M sodium hydroxide (2 mL), and 30% hydrogen peroxide (1 mL). The reaction was gradually warmed to room temperature and allowed to stir for 4 h at which time the vial was cooled to 0 °C (ice/water) and saturated aqueous sodium thiosulfate (2 mL) was added dropwise over 5 min. The reaction mixture was diluted with ethyl acetate (5 mL) and the aqueous and organic layers were separated. The aqueous layer was washed with ethyl acetate (3 x

15 mL). The combined organic layers were dried over Na$_2$SO$_4$, filtered, and concentrated by rotary evaporation. The crude reaction mixture was purified by column chromatography on silica gel (35-75% ethyl acetate/hexanes, R$_f$ = 0.18 in 50% ethyl acetate/hexane, stain in PMA) to afford a clear, colorless oil that was inseparable from pinacol (89.1 mg, 1:1.5 product:pinacol = 76%).

(S,E)-4-methyldec-3-ene-1,2-diol (Table 3.3, entry 1).

$^1$H NMR (500 MHz, CDCl$_3$): $\delta$ 0.85 (3H, t, $J$ = 7.0 Hz), 1.22-1.29 (6H, m), 1.33-1.39 (2H, m), 1.67 (3H, d, $J$ = 1.0 Hz), 1.97 (2H, t, $J$ = 7.0 Hz), 1.92 (2H, br s), 3.44 (1H, dd, $J$ = 11.0 Hz, 8.0 Hz), 3.53 (1H, dd, $J$ = 11.0 Hz, 3.5 Hz), 4.45 (1H, ddd, $J$ = 8.0 Hz, 8.0 Hz, 4.5 Hz), 5.11 (1H, dd, $J$ = 8.5 Hz, 1.5 Hz); $^{13}$C NMR (125 MHz, CDCl$_3$): $\delta$ 14.1, 16.7, 22.6, 27.6, 28.9, 31.7, 39.6, 66.4, 69.4, 122.6, 141.7; IR (neat): 3362.7 (br m), 2995.7 (m), 2926.3 (s), 2856.8 (m), 1458.0 (m), 1375.2 (m), 1075.2 (m), 1027.1 (m), 873.6 (w) cm$^{-1}$; HRMS-(ESI+) for C$_{11}$H$_{26}$NO$_2$ [M+NH$_4$]+: calculated: 204.1964, found: 204.1962. $[\alpha]_{D}^{20}$ = +8.27 ($c$ = 0.94, ethyl acetate, $l$ = 50 mm).

**Proof of Stereochemistry.**

The enantioselectivity was determined by treating the resulting 1,2-diol with 2,2-dimethoxypropane and catalytic $p$-toluenesulfonic acid. The acetonide was then subjected to ozonolysis/reduction, followed by acylation of the primary alcohol. The authentic
material was prepared by acylation of (S)-isopropylideneglycerol, which was purchased from Aldrich.

*Chiral GLC (β-Dex 120, Supelco, 60 °C for 5 min, ramp 3 °C/min to 120 °C, 20 psi, s/r = 35:1) - analysis of (2,2-dimethyl-1,3-dioxolan-4-yl)methyl acetate.*

![Chromatograms](image)

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(S,E)-4-cyclohexylpent-3-ene-1,2-diol (Table 3.3, entry 2). The diboration was performed according to the representative procedure with (E)-penta-2,4-dien-2-ylcyclohexane (50.0 mg, 332.7 µmol), Pt(dba)$_3$ (8.9 mg, 9.9 µmol), (R,R)-3,5-di-iso-propylTADDOLPh (3.44 mg) (10.8 mg, 12.0 µmol), and B$_2$(pin)$_2$ (88.7 mg, 349.3 µmol) in tetrahydrofuran (3.3 mL, 0.1 M). The crude reaction mixture was purified by column chromatography on silica gel (40-65% ethyl acetate/hexane, $R_f = 0.18$ in 50% ethyl acetate in hexane, stain in PMA) to afford a white solid (50.1 mg, 82%). $^1$H NMR (500 MHz, CDCl$_3$): $\delta$ 1.06-1.28 (6H, m), 1.64-.167 (2H, m), 1.66 (3H, s), 1.73 (2H, d, $J = 13.0$ Hz), 1.82 (1H, dddd, $J = 11.0$ Hz, 11.0 Hz, 2.5 Hz, 2.5 Hz), 2.16 (1H, br s), 2.26 (1H, br s), 3.43 (1H, dd, $J = 11.0$ Hz, 8.0 Hz), 3.53 (1H, dd, $J = 11.5$ Hz, 3.5 Hz), 4.46 (1H, dddd, $J = 8.5$ Hz, 8.5 Hz, 4.0 Hz), 5.11 (1H, d, $J = 8.5$ Hz); $^{13}$C NMR (125 MHz, CDCl$_3$): $\delta$ 15.1, 26.2, 26.55, 26.56, 31.67, 31.69, 47.2, 66.4, 69.4, 121.0, 146.4; IR (neat): 3405.5 (m), 3287.9 (br m), 2920.5 (s), 2848.2 (m), 1461.8 (w), 1444.6 (m), 1384.4 (w), 1343.4 (w), 1264.0 (w), 1214.3 (w), 1103.3 (m), 1079.1 (m), 1057.6 (m), 1026.7 (s), 978.2 (w), 990.7 (m), 876.4 (m), 827.2 (m), 704.5 (br m), 641.0 (m), 550.8 (m) cm$^{-1}$; HRMS-(ESI+) for C$_{11}$H$_{24}$NO$_2$ [M+NH$_4$]: calculated: 202.1807, found: 202.1813. [$\alpha$]$_{D}^{20}$ = +17.65 ($c = 2.12$, CHCl$_3$, $l = 50$ mm).

**Proof of Stereochemistry.**

The enantioselectivity was determined by treating the resulting 1,2-diol with 2,2-dimethoxypropane and catalytic $p$-toluenesulfonic acid. The acetonide was then subjected
to ozonolysis/reduction, followed by acylation of the primary alcohol. The authentic material was prepared by acylation of (S)-isopropylideneglycerol, which was purchased from Aldrich.

*Chiral GLC (β-Dex 120, Supelco, 60 °C for 5 min, ramp 3 °C/min to 120 °C, 20 psi, s/r = 35:1) - analysis of (2,2-dimethyl-1,3-dioxolan-4-yl)methyl acetate.*

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(S,E)-5-((tert-butyldiphenylsilyl)oxy)-4-methylpent-3-ene-1,2-diol (Table 3.3, entry 3). The diboration was performed according to the representative procedure with (E)-tert-butyl(2-methylpenta-2,4-dienyloxy)diphenylsilane (100.0 mg, 297.1 µmol), Pt(dba)$_3$ (8.0 mg, 8.9 µmol), (R,R)-3,5-di-iso-propylphenylTADDOLPPh (3.44) (9.7 mg, 10.7 µmol), and B$_2$(pin)$_2$ (79.0 mg, 311.1 µmol) in tetrahydrofuran (3.0 mL, 0.1 M). The crude reaction mixture was purified by column chromatography on silica gel (35-65% ethyl acetate/hexanes, $R_f = 0.20$ in 50% ethyl acetate/hexanes, stain in PMA) to afford a clear, colorless oil that was inseparable from pinacol (127.8 mg, 1:1 product:pinacol = 87%).

$^1$H NMR (500 MHz, CDCl$_3$): δ 1.04 (9H, s), 1.63 (3H, s), 1.92 (2H, br s), 3.46 (1H, dd, $J = 11.0$ Hz, 8.0 Hz), 3.53 (1H, dd, $J = 10.5$ Hz, 3.0 Hz), 4.04 (2H, s), 4.49 (1H, ddd, $J = 8.5$ Hz, 8.5 Hz, 4.0 Hz), 5.45 (1H, ddd, $J = 8.5$ Hz, 1.5 Hz, 1.5 Hz), 7.34-7.43 (6H, m), 7.62-7.66 (4H, m); $^{13}$C NMR (125 MHz, CDCl$_3$): δ 14.0, 19.2, 26.8, 66.3, 68.0, 69.1, 72.2, 127.6, 129.7, 133.5, 133.6, 135.52, 135.53, 139.5; IR (neat): 3361.5 (br m), 2929.9 (m), 2856.5 (m), 1471.8 (w), 1427.4 (m), 1389.4 (w), 1362.0 (w), 1109.3 (s), 1070.1 (s), 1028.0 (m), 823.9 (m), 740.0 (m), 700.9 (s), 614.9 (w), 503.9 (s), cm$^{-1}$. HRMS-(ESI+) for C$_{22}$H$_{34}$NO$_3$Si [M+NH$_4$]: calculated: 388.2299, found: 388.2303. [α]$_D^{20}$ = +13.72 (c = 2.85, CHCl$_3$, l = 50 mm).
Proof of Stereochemistry.

The enantioselectivity was determined by treating the resulting 1,2-diol with 2,2-dimethoxypropane and catalytic $p$-toluenesulfonic acid. The acetonide was then subjected to ozonolysis/reduction, followed by acylation of the primary alcohol. The authentic material was prepared by acylation of (S)-isopropylideneglycerol, which was purchased from Aldrich.

Chiral GLC (β-Dex 120, Supelco, 60 °C for 5 min, ramp 3 °C/min to 120 °C, 20 psi, s/r = 35:1) - analysis of (2,2-dimethyl-1,3-dioxolan-4-yl)methyl acetate.

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racemic derived from reaction product authentic
(S,E)-4,8-dimethylnona-3,7-diene-1,2-diol (Table 3.3, entry 4). The diboration was performed according to the representative procedure with (E)-4,8-dimethylnona-1,3,7-triene (75.0 mg, 499.1 µmol), Pt(dba)$_3$ (13.4 mg, 15.0 µmol), (R,R)-3,5-di-iso-propylphenylTADDOLPh (3.44) (16.3 mg, 18.0 µmol), and B$_2$(pin)$_2$ (133.1 mg, 524.1 µmol) in tetrahydrofuran (5.0 mL, 0.1 M). The crude reaction mixture was purified by column chromatography on silica gel (20-40% ethyl acetate/hexanes, R$_f$ = 0.13 in 50% ethyl acetate/hexanes, stain in PMA) to afford a clear, colorless oil that was inseparable from pinacol (80.4 mg, 9.7:1 product:pinacol = 82%). $^1$H NMR (500 MHz, CDCl$_3$): $\delta$ 1.58 (3H, s), 1.66 (3H, s), 1.69 (3H, s), 1.99-2.02 (2H, m), 2.06-2.10 (2H, m), 3.46 (1H, dd, $J$ = 11.0 Hz, 8.0 Hz), 3.53 (1H, dd, $J$ = 11.0 Hz, 4.0 Hz), 4.46 (1H, ddd, $J$ = 8.0 Hz, 8.0 Hz, 3.5 Hz), 5.05 (1H, t, $J$ = 6.0 Hz), 5.13 (1H, d, $J$ = 8.5 Hz); $^{13}$C NMR (125 MHz, CDCl$_3$): $\delta$ 16.8, 17.7, 25.6, 26.3, 39.5, 66.4, 69.4, 123.0, 123.7, 131.9, 141.3; IR (neat): 3349.0 (br m), 2967.7 (w), 2916.0 (m), 2857.6 (w), 1444.1 (w), 1377.9 (w), 1074.75 (m), 1021.0 (m) cm$^{-1}$; HRMS-(ESI$^+$) for C$_{11}$H$_{19}$O [M+H-H$_2$O]: calculated: 167.1436, found: 167.1442. $[\alpha]_D^{20}$ = +25.95 (c = 0.33, CHCl$_3$, $l$ = 50 mm).

**Analysis of Stereochemistry.**

The enantioselectivity was determined by treating the resulting 1,2-diol with 2,2-dimethoxypropane and catalytic $p$-toluenesulfonic acid to afford the acetonide for GLC analysis as shown below. The analogous racemic material was prepared by mixing
approximate equimolar amounts of the product made using \((R,R)-3,5\text{-di-iso-propylTADDOLPPh}\) and \((S,S)-3,5\text{-di-iso-propylTADDOLPPh}\) as the ligand in the diboration reaction. The absolute stereochemistry was assigned by analogy.

*Chiral GLC (\(\beta\)-Dex 120, Supelco, 90 °C for 5 min, ramp 2 °C/min to 160 °C, 20 psi, \(s/r = 35:1\)) - analysis of \((E)-4-(2,6\text{-dimethylhepta-1,5-dien-1-yl})\text{-2,2-dimethyl-1,3-dioxolane}\).*

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mixture of products from \((R,R)-3.44\) and \((S,S)-3.44\)
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derived from reaction product

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(S,Z)-4,8-dimethylnona-3,7-diene-1,2-diol (Table 3.3, entry 5). The diboration was performed according to the representative procedure with (Z)-4,8-dimethylnona-1,3,7-triene (30.0 mg, 199.7 µmol), Pt(dba)₃ (5.4 mg, 6.0 µmol), (R,R)-3,5-di-isopropylphenylTADDOLPh (3.44) (6.5 mg, 7.2 µmol), and B₂(pin)₂ (53.2 mg, 209.7 µmol) in tetrahydrofuran (2.0 mL, 0.1 M). The crude reaction mixture was purified by column chromatography on silica gel (20-50% ethyl acetate/hexanes, Rₑ = 0.24 in 50% ethyl acetate/hexanes, stain in PMA) to afford a clear, colorless oil that was inseparable from pinacol (40.7 mg, 2.2:1 product:pinacol = 86%). ¹H NMR (500 MHz, CDCl₃): δ 1.59 (3H, s), 1.67 (3H, s), 1.73 (3H, d, J = 1.0 Hz), 1.99 (2H, br s), 2.02-2.13 (4H, m), 3.45 (1H, dd, J = 11.5 Hz, 8.0 Hz), 3.54 (1H, dd, J = 11.5 Hz, 4.0 Hz), 4.42 (1H, ddd, J = 8.0 Hz, 8.0 Hz, 4.0 Hz), 5.06-5.10 (1H, m), 5.16 (1H, dd, J = 9.0 Hz, 1.5 Hz); ¹³C NMR (125 MHz, CDCl₃): δ 17.7, 23.4, 25.6, 26.5, 32.5, 66.6, 68.9, 123.7, 124.1, 132.6, 141.5; IR (neat): 3362.7 (br m), 2967.2 (m), 2917.8 (s), 2858.5 (m), 1668.5 (w), 1446.4 (m), 1376.4 (m), 1152.5 (w), 1075.0 (s), 1021.4 (s), 873.0 (m), 835.1 (m) cm⁻¹; HRMS-(ESI+) for C₁₁H₁₉O [M+H-H₂O]: calculated: 167.1436, found: 167.1442. [α]D²₀ = +13.25 (c = 2.10, CHCl₃, l = 50 mm).

Proof of Stereochemistry.

The enantioselectivity was determined by treating the resulting 1,2-diol with 2,2-dimethoxypropane and catalytic p-toluenesulfonic acid. The acetonide was then subjected
to ozonolysis/reduction, followed by acylation of the primary alcohol. The authentic material was prepared by acylation of \((S)\)-isopropylideneglycerol, which was purchased from Aldrich.

*Chiral GLC (β-Dex 120, Supelco, 60 °C for 5 min, ramp 3 °C/min to 120 °C, 20 psi, s/r = 35:1) - analysis of \((2,2\text{-dimethyl-1,3-dioxolan-4-yl})\text{methyl acetate.}\)

![Chiral GLC chromatograms](image)

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(S)-3-cyclohexylidenepropane-1,2-diol (Table 3.3, entry 6). The diboration was performed according to the representative procedure with allylidencyclohexane (50.0 mg, 409.1 µmol), Pt(dba)₃ (11.0 mg, 12.3 µmol), (R,R)-3,5-diethylphenylTADDOLPPh (3.44) (13.4 mg, 14.7 µmol), and B₂(pin)₂ (109.1 mg, 429.6 µmol) in tetrahydrofuran (4.0 mL, 0.1 M). The crude reaction mixture was purified by column chromatography on silica gel (30-60% ethyl acetate/hexanes, R_f = 0.18 in 50% ethyl acetate/hexanes, stain in PMA) to afford the title compound as a white solid (49.8 mg, 78%). ¹H NMR (500 MHz, CDCl₃): δ 1.44-1.57 (6H, m), 2.07 (2H, t, J = 6.0 Hz), 2.14-2.21 (2H, m), 2.27 (2H, br s), 3.44 (1H, dd, J = 11.0 Hz, 8.0 Hz), 3.52 (1H, dd, J = 11.0 Hz, 3.5 Hz), 4.48 (1H, ddd, J = 8.0 Hz, 8.0 Hz, 4.0 Hz), 5.06 (1H, d, J = 8.5 Hz); ¹³C NMR (125 MHz, CDCl₃): δ 26.5, 27.9, 28.4, 29.5, 37.0, 66.7, 68.6, 119.9, 145.7; IR (neat): 3379.4 (br m), 2925.8 (s), 2853.2 (m), 1447.4 (w), 1070.8 (w), 1025.2 (w) cm⁻¹; HRMS-(ESI⁺) for C₉H₁₅O [M+H-H₂O]: calculated: 139.1123, found: 139.1120. [α]D²⁰ = +9.46 (c = 1.51, CHCl₃, l = 50 mm).

**Analysis of Stereochemistry.**

The enantioselectivity was determined by treating the resulting 1,2-diol with 2,2-dimethoxypropane and catalytic p-toluenesulfonic acid to afford the acetonide for GLC analysis as shown below. The analogous racemic material was prepared using PCy₃ as the achiral ligand in the diboration reaction. The absolute stereochemistry be assigned by analogy.
Chiral GLC (β-Dex 120, Supelco, 90 °C for 5 min, ramp 3 °C/min to 160 °C, 20 psi, s/r = 35:1) - analysis of 4-(cyclohexyldenemethyl)-2,2-dimethyl-1,3-dioxolane.

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3.7.6. **Representative Procedure for Diboration/Allylation/Oxidation (Table 3.5).**

To an oven-dried 2-dram vial with magnetic stir bar in the glove box was added Pt (dba)$_3$ (13.4 mg, 15.0 µmol), (R,R)-3,5-di-iso-propylphenyl-TADDOLPPh (3.44) (16.4 mg, 18.0 µmol), B$_2$(pin)$_2$ (133.1 mg, 524.1 µmol) and toluene (0.5 mL, [substrate] = 1.0 M). The vial was sealed with a polypropylene cap, removed from the glove box, and heated to 80 °C in an oil bath for 20 min. The vial was cooled to room temperature, returned to the glove box and charged with (E)-4,8-dimethylnona-1,3,7-triene (75.0 mg, 499.1 µmol). The vial was sealed, removed from the glove box, and stirred at 60 °C for 12 h. The reaction mixture was then cooled to ambient temperature, returned to the glove box and charged with freshly distilled cinnamaldehyde (66.0 mg, 499.1 µmol). The reaction was brought to the bench and heated to 60 °C in an oil bath and was allowed to stir for 24 h. The reaction mixture was then cooled to 0 °C (ice/water) and charged with tetrahydrofuran (2.0 mL), 3 M sodium hydroxide solution (2 mL), and 30 wt % hydrogen peroxide (1 mL). The reaction was gradually warmed to room temperature and allowed to stir for 4 h, at which time the vial was cooled to 0 °C (ice/water) and saturated aqueous sodium thiosulfate (2 mL) was carefully added dropwise. The reaction mixture was diluted with ethyl acetate (5 mL) and the aqueous and organic layers were separated. The aqueous layer was rinsed with ethyl acetate (3 x 15 mL), and the combined organics were dried over Na$_2$SO$_4$, filtered, and volatiles were removed *in vacuo*. The crude reaction mixture was purified by column chromatography on silica gel (20-35% ethyl acetate/
hexanes, Rf = 0.32 in 50% ethyl acetate/hexanes, stain in PMA) to afford a clear, colorless oil (129.8 mg, 87%).

3.7.7. Characterization and Proof of Stereochemistry.

(S,E)-3-(1-(hydroxy(phenyl)methyl)cyclohexyl)prop-2-en-1-ol (3.50). The diboration was preformed according to the representative procedure with the following modifications: The diboration was carried out in tetrahydrofuran (2.5 mL) with allylidene cyclohexane (30.0 mg, 245.6 µmol), Pt(dba)_3 (6.7 mg, 7.4 µmol), (R,R)-3,5-di-iso-propylphenyl-TADDOLPPh (3.44) (13.4 mg, 14.7 µmol), and B_2(pin)_2 (65.5 mg, 257.9 µmol) for 8 h at 60 °C. The reaction mixture was then cooled to ambient temperature and the solvent was removed in vacuo. The vial was sealed, returned to the glove box and charged with dichloromethane (0.5 mL) and freshly distilled benzaldehyde (27.4 mg, 257.9 µmol). The allylation was allowed to stir at rt for 14 h, at which time the reaction was subjected to the standard oxidation conditions. The crude material was purified by column chromatography on silica gel (20-35% ethyl acetate/hexanes, Rf = 0.33 in 50% ethyl acetate/hexanes, stain in PMA) to afford the title compound as a clear, colorless oil (37.5 mg, 62%). ^1H NMR (600 MHz, CDCl_3): δ 1.05 (2H, m), 1.19-1.49 (8H, m), 1.82 (1H, s), 1.84 (1H, s), 4.12 (2H, d, J = 5.5 Hz), 4.29 (1H, s), 5.35 (1H, d, J = 16.5 Hz), 5.55 (1H, ddd, J = 16.5 Hz, 6.0 Hz, 6.0 Hz), 7.14-7.16 (2H, m), 7.17-7.24 (3H, m); ^13C NMR (125
MHz, CDCl$_3$): $\delta$ 22.0, 22.1, 26.2, 31.8, 33.1, 44.6, 64.0, 127.3, 127.4, 128.0, 131.5, 135.6, 140.8; IR (neat): 3364.6 (m), 2927.6 (s), 2853.5 (m), 1450.9 (m), 1156.5 (w), 1016.6 (m), 981.1 (m), 702.1 (s) cm$^{-1}$; HRMS-(ESI+) for C$_{16}$H$_{21}$O [M+H-H$_2$O]: calculated: 229.1592, found: 229.1600. $[\alpha]_D^{25} = -53.17$ (c = 0.40, CHCl$_3$, l = 50 mm).

**Analysis of Stereochemistry:**

The enantioselectivity was determined SFC analysis of the reaction product. The analogous racemic material was prepared using PCy$_3$ as the achiral ligand in the diboration reaction. The absolute stereochemistry was assigned by analogy.

**Chiral SFC** (AS-H, Chiraldex, 150 bar, 3 mL/min, 3% MeOH, 50 $^\circ$C) - analysis of reaction product.
(4S,5R,E)-4,6-dimethyl-4-(4-methylpent-3-en-1-yl)hept-2-ene-1,5-diol. The diboration/allylation was performed according to the representative procedure with the following modifications: (E)-4,8-dimethylnona-1,3,7-triene (75.0 mg, 499.1 µmol), Pt(dba)$_3$ (13.4 mg, 15.0 µmol), (R,R)-3,5-di-iso-propylphenylTADDOLPh (3.44) (16.4 mg, 18.0 µmol), B$_2$(pin)$_2$ (133.1 mg, 524.1 µmol) in toluene (0.50 mL, 1.0 M), and freshly distilled isobutyraldehyde (108.0 mg, 1.50 mmol). The crude material was purified by column chromatography on silica gel (20-35% ethyl acetate/hexanes, R$_f$ = 0.38 in 50% ethyl acetate/hexanes, stain in PMA) to afford the title compound as a clear, colorless oil (69.6 mg, 58%). $^1$H NMR (500 MHz, CDCl$_3$): δ 0.84 (3H, d, $J$ = 7.0 Hz), 0.96 (3H, d, $J$ = 7.0 Hz), 0.99 (3H, s), 1.35-1.44 (2H, m), 1.55 (3H, s), 1.64 (3H, s), 1.75-1.83 (1H, m), 1.85-1.94 (2H, m), 3.19 (1H, s), 4.12 (2H, d, $J$ = 5.5 Hz), 5.05 (1H, t, $J$ = 6.0 Hz), 5.58 (1H, ddd, $J$ = 16 Hz, 5.5 Hz, 5.5 Hz), 5.69 (1H, d, $J$ = 15.5 Hz); $^{13}$C NMR (125 MHz, CDCl$_3$): δ 16.6, 17.6, 18.8, 22.7, 23.5, 25.6, 28.6, 38.5, 44.4, 63.9, 81.4, 124.8, 128.3, 131.3, 138.5; IR (neat): 3375.5 (m), 2964.6 (s), 2871.8 (m), 1465.2 (m), 1378.4 (m), 1077.2 (w), 980.1 (s) cm$^{-1}$; HRMS-(ESI+) for C$_{15}$H$_{27}$O [M+H-H$_2$O]: calculated: 223.2062, found: 223.2070. [$\alpha$]$_D^{25}$ = -3.80 ($c$ = 1.21, CHCl$_3$, $l$ = 50 mm).

Analysis of Stereochemistry:

The enantioselectivity was determined by treating the 1,5-diol with benzoic anhydride and Et$_3$N to make the mono(benzoate) for SFC analysis. The analogous
racemic material was prepared by mixing approximate equimolar amounts of the
products made using (R,R)-3,5-di-iso-propylTADDOLPPh and (S,S)-3,5-di-iso-
propylTADDOLPPh as the ligands in the diboration reaction. The absolute
stereochemistry was assigned by analogy.

*Chiral SFC (AD-H, Chiraldex, 100 bar, 4 mL/min, 4% MeOH, 35 °C)- analysis of
(S,E)-4-((R)-1-hydroxy-2-methylpropyl)-4,8-dimethylnona-2,7-dien-1-yl benzoate.*

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**(4S,5R,E)**-4-methyl-4-(4-methylpent-3-en-1-yl)-7-phenylhept-2-ene-1,5-diol. The diboration/allylation was performed according to the representative procedure with **(E)**-4,8-dimethylnona-1,3,7-triene (70.0 mg, 465.9 µmol), Pt(dba)$_3$ (12.6 mg, 14.0 µmol), **(R,R)**-3,5-di-iso-propylphenylTADDOLPPh (L3) (15.2 mg, 16.7 µmol), B$_2$(pin)$_2$ (124.2 mg, 489.1 µmol) in toluene (0.45 mL, 1.0 M), and freshly distilled hydrocinnamaldehyde (62.5 mg, 465.9 µmol). The crude reaction mixture was purified on silica gel (30-60% ethyl acetate/hexanes) to afford an inseparable mixture of the product, pinacol, and 1,2-diol (152.6 mg). The mixture of diols was then dissolved in diethyl ether (3 mL), tetrahydrofuran (3 mL), and water (4 mL), and then cooled to 0 °C in an ice bath. NaIO$_4$ (521.8 mg, 2.44 mmol) was added and the reaction was allowed to warm to ambient temperature over 2h (oxidative cleavage of pinacol). The reaction mixture was quenched with saturated aqueous Na$_2$SO$_3$ (2 mL) and the layers were separated. The aqueous layer was extracted with ethyl acetate (3 x 10 mL). The combined organics were dried over Na$_2$SO$_4$, filtered, and concentrated in vacuo. The crude material was purified by column chromatography on silica gel (40-60% ethyl acetate/hexanes, $R_f$ = 0.33 in 50% ethyl acetate/hexanes, stain in PMA) to afford the title compound as a white solid (101.9 mg, 72%). $^1$H NMR (500 MHz, CDCl$_3$): δ 0.95 (3H, s), 1.21-1.38 (2H, m), 1.51-1.60 (1H, m), 1.54 (3H, s), 1.64 (3H, s), 1.74-1.81 (2H, m), 1.82-1.90 (1H, m) 1.96 (2H, br s), 2.58 (1H, ddd, $J$ = 14.0 Hz, 9.5 Hz, 7.0 Hz), 2.90 (1H, ddd, 14.0 Hz, 10.0 Hz, 5.0 Hz), 3.30 (1H, dd, $J$ = 10.5 Hz, 1.5 Hz), 4.12 (2H, d, $J$ = 4.0 Hz), 5.03 (1H, ddd, $J$
= 7.0 Hz, 7.0 Hz, 1.5 Hz), 5.57-5.65 (2H, m), 7.14-7.19 (3H, m), 7.22-7.27 (3H, m); \(^{13}\)C NMR (125 MHz, CDCl\(_3\)): \(\delta\) 17.4, 17.6, 22.7, 25.6, 32.9, 33.2, 37.6, 44.0, 63.7, 76.7, 124.6, 125.8, 128.3, 128.4, 131.4, 137.9, 142.3; IR (neat): 3328.2 (br m), 3025.6 (w), 2963.6 (m), 2923.9 (m), 2857.1 (m), 1603.3 (w), 1495.8 (w), 1453.4 (m), 1377.8 (m), 1304.2 (w), 1153.2 (w), 1081.9 (m), 1065.7 (m), 1043.0 (m), 1008.1 (m), 977.7 (s), 935.2 (m), 838.0 (w), 747.6 (m), 699.0 (s) cm\(^{-1}\); HRMS-(ESI+) for C\(_{20}\)H\(_{34}\)NO\(_2\) [M+NH\(_4\)]: calculated: 320.2590, found: 320.2598; \([\alpha]\)\(_D\)\(^{20}\) = +20.52 (\(c = 2.59, \text{CHCl}_3, l = 50\) mm).

**Proof of Stereochemistry:**

The olefin geometry of the 1,5-diol was determined to be trans by measuring the coupling constants of the vinylic hydrogens from the \(^1\)H NMR taken in pyridine: \(^1\)H NMR (500 MHz, C\(_5\)D\(_5\)N): \(\delta\) 1.19 (3H, s), 1.56 (3H, s), 1.67 (3H, s), 1.75 (2H, dd, \(J = 10.5\) Hz, 8.5 Hz), 1.88-1.96 (1H, m), 2.00-2.08 (2H, m), 2.09-2.18 (1H, m) 2.83 (1H, ddd, \(J = 13.5\) Hz, 10.0 Hz, 6.5 Hz), 3.24 (1H, ddd, \(J = 14.5\) Hz, 10.5 Hz, 4.5 Hz), 3.66 (1H, dd, \(J = 10.0\) Hz, 3.5 Hz), 4.49 (2H, d, \(J = 4.0\) Hz), 5.21 (1H, ddd, \(J = 7.0\) Hz, 7.0 Hz, 1.5 Hz), 5.93 (1H, ddd, \(J = 16.0\) Hz, 5.5 Hz, 5.5 Hz), 6.22 (1H, ddd, \(J = 16.0\) Hz, 1.5 Hz, 1.5 Hz), 7.22-7.25 (2H, m), 7.29-7.34 (3H, m).

The enantioselectivity was determined by SFC analysis of the reaction product. The analogous racemic material was prepared by mixing approximate equimolar amounts
of the products made using (R,R)-3,5-di-iso-propylTADDOLPPh and (S,S)-3,5-di-iso-propylTADDOLPPh as the ligands in the diboration reaction.

Chiral SFC (AD-H, Chiraldex, 100 bar, 4 mL/min, 4% MeOH, 35 °C) - analysis of the reaction product.

The absolute stereochemistry was determined using Mosher Ester analysis under the following procedure\textsuperscript{10}: To an oven-dried NMR tube with a septum under N\textsubscript{2} was added diol 32 (6.0 mg, 0.02 mmol) as a solution in C\textsubscript{6}D\textsubscript{6}:pyridine-d\textsubscript{5} (5:1, 0.6 mL). The (R)-MTPA-Cl (29 µL, 0.16 mmol) was added under N\textsubscript{2} via microsyringe and the reaction

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was heated to 60 °C in an oil bath and allowed to stir for 48 hours until full bis(acylation) was detected by \(^1\)H NMR. The reaction was cooled to ambient temperature and was quenched with \(N,N\)-dimethylethylene diamine (30 \(\mu\)L, 0.16 mmol). The mixture was diluted with Et\(_2\)O (10 mL) and washed with dilute HCl (1 x 10 mL) at 0°C, saturated aqueous sodium carbonate (1 x 10 mL) at 0°C, and brine (1 x 10 mL). The layers were separated and the organic layer was dried over MgSO\(_4\), filtered, and concentrated in vacuo. The resulting crude oil was then analyzed by \(^1\)H NMR to determine chemical shift data of the resulting (S)-Mosher ester. An analogous procedure was performed on diol 32 with (S)-MTPA-Cl to synthesize the (R)-Mosher Ester.

As described by Takeuchi\(^{10c}\), the most stable conformer of the Mosher Ester requires that the –CF\(_3\) and methine proton of the secondary alcohol be syn-coplanar. In this conformation, the phenyl substituent of the ester will impose an anisotropic,
magnetic shielding effect on protons above and below the plane of the phenyl ring. This shielding results in an upfield shift for the affected protons in the $^1$H NMR spectra. When the alcohol has been acylated with both enantiomers of the Mosher acid chloride (or carboxylic acid), then the relative chemical shifts in $^1$H NMR can be used to determine the absolute stereochemistry of the stereocenter in question. By convention, $\Delta \delta_{SR}$ ($\delta_S - \delta_R$) is positive for $R^1$ and negative for $R^2$. Upon Mosher Ester analysis, it was determined that the $(R,R)$-enantiomer of ligand produces the $(R)$-enantiomer of the corresponding secondary alcohol in the diboration/allylation/oxidation sequence of 1,1-disubstituted dienes. This conclusion is in accordance with the proven absolute stereochemistry of the 1,2-diboration/oxidation products, assuming the allylation proceeds in a closed-chair transition state as is typically observed for allyl(borurate) additions to aldehydes.
(4S,5S,E)-6-(benzyloxy)-4-methyl-4-(4-methylpent-3-en-1-yl)hex-2-ene-1,5-diol. The diboration/allylation was performed according to the representative procedure with (E)-4,8-dimethylnona-1,3,7-triene (75.0 mg, 499.1 µmol), Pt(dba)$_3$ (13.4 mg, 15.0 µmol), (R,R)-3,5-di-isopropylphenylTADDOLPPh (3.44) (16.4 mg, 18.0 µmol), B$_2$(pin)$_2$ (133.1 mg, 524.1 µmol) in toluene (0.50 mL, 1.0 M), and freshly distilled benzzyloxyacetaldehyde (75.0 mg, 499.1 µmol). The crude material was purified by column chromatography on silica gel (20-35% ethyl acetate/hexanes, $R_f = 0.19$ in 50% ethyl acetate/hexanes, stain in PMA) to afford the title compound as a clear, colorless oil (117.6 mg, 74%). $^1$H NMR (500 MHz, CDCl$_3$): δ 0.98 (3H, s), 1.33-1.46 (2H, m), 1.55 (3H, s), 1.64 (3H, s), 1.77-1.84 (1H, m), 1.87-1.94 (1H, m), 3.34 (1H, t, $J = 9.5$ Hz), 3.58 (1H, dd, $J = 9.5$ Hz, 2.5 Hz), 3.63 (1H, dd, $J = 9.0$ Hz, 2.5 Hz), 4.10 (2H, d, $J = 5.5$ Hz), 4.51 (2H, dd, $J = 17.0$ Hz, 12.0 Hz), 5.05 (1H, ddd, $J = 6.0$ Hz, 6.0 Hz, 1.5 Hz), 5.58 (1H, ddd, $J = 16.0$ Hz, 6.0 Hz, 6.0 Hz), 5.70 (1H, d, $J = 16.0$ Hz), 7.26-7.34 (5H, m); $^{13}$C NMR (125 MHz, CDCl$_3$): δ 17.6, 18.7, 22.4, 25.6, 37.6, 41.9, 63.9, 71.0, 73.3, 75.7, 124.6, 127.66, 127.74, 128.4, 131.3, 137.3, 137.9; IR (neat): 3412.8 (m), 2921.9 (s), 2859.4 (m), 1453.6 (m), 1092.4 (s), 982.7 (m), 736.4 (m), 698.1 (s) cm$^{-1}$; HRMS-(ESI+) for C$_{20}$H$_{34}$NO$_3$ [M+NH$_4^+$]: calculated: 336.2539, found: 336.2542. [α]$_D^{25}$ = +7.63 (c = 0.72, CHCl$_3$, l = 50 mm).
Analysis of Stereochemistry:

The enantioselectivity was determined by SFC analysis of the reaction product. The analogous racemic material was prepared by mixing approximate equimolar amounts of the products made using \((R,R)-3,5\text{-di-iso-propylTADDOLPPh}\) and \((S,S)-3,5\text{-di-iso-propylTADDOLPPh}\) as the ligands in the diboration reaction. The absolute stereochemistry was assigned by analogy.

*Chiral SFC (AD-H, ChiralDEX, 100 bar, 4 mL/min, 4\% MeOH, 35 °C) - analysis of the reaction product.*

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(2E,4S,5R,6E)-4-methyl-4-(4-methylpent-3-en-1-yl)-7-phenylhepta-2,6-diene-1,5-diol. The diboration/allylation was performed according to the representative procedure with (E)-4,8-dimethylnona-1,3,7-triene (75.0 mg, 499.1 µmol), Pt(dba)$_3$ (13.4 mg, 15.0 µmol), (R,R)-3,5-di-iso-propylphenylTADDOLPPh (3.44) (16.4 mg, 18.0 µmol), B$_2$(pin)$_2$ (133.1 mg, 524.1 µmol) in toluene (0.50 mL, 1.0 M), and freshly distilled cinnamaldehyde (66.0 mg, 499.1 µmol). The crude material was purified by column chromatography on silica gel (20-35% ethyl acetate/hexanes, R$_f$ = 0.32 in 50% ethyl acetate/hexanes, stain in PMA) to afford the title compound as a clear, colorless oil (129.8 mg, 87%). $^1$H NMR (500 MHz, CDCl$_3$): $\delta$ 1.02 (3H, s), 1.40 (2H, t, $J = 9.0$ Hz), 1.55 (3H, s), 1.64 (3H, s), 1.82-1.96 (2H, m), 3.99 (1H, dd, $J = 7.5$ Hz, 1.0 Hz), 4.18 (2H, d, $J = 4.5$ Hz), 5.05 (1H, t, $J = 7.0$ Hz), 5.66-5.74 (2H, m), 6.19 (1H, dd, $J = 16.0$ Hz, 7.5 Hz), 6.56 (1H, d, $J = 16.0$ Hz), 7.21-7.24 (1H, m), 7.30 (2H, ddd, $J = 7.0$ Hz, 7.0 Hz, 1.5 Hz), 7.36 (2H, dd, $J = 7.0$ Hz, 1.5 Hz); $^{13}$C NMR (125 MHz, CDCl$_3$): $\delta$ 17.6, 17.7, 22.7, 25.7, 37.8, 44.3, 63.8, 78.9, 124.6, 126.5, 127.7, 128.3, 128.6, 129.9, 131.4, 132.8, 136.7, 137.5; IR (neat): 3365.3 (m), 2923.9 (s), 2855.5 (m), 1448.9 (m), 1073.8 (m), 970.3 (s), 748.2 (m), 693.1 (m) cm$^{-1}$; HRMS-(ESI+) for C$_{20}$H$_{27}$O [M+H-H$_2$O]: calculated: 283.2062, found: 283.2055. [$\alpha$]$_D^{25}$ = +14.91 (c = 0.59, CHCl$_3$, $l$ = 50 mm).
Analysis of Stereochemistry:

The enantioselectivity was determined by HPLC analysis of the reaction product. The analogous racemic material was prepared by mixing approximate equimolar amounts of the products made using \((R,R)\)-3,5-di-\emph{iso}-propylTADDOLPPh and \((S,S)\)-3,5-di-\emph{iso}-propylTADDOLPPh as the ligands in the diboration reaction. The absolute stereochemistry was assigned by analogy.

\textit{Chiral HPLC (AD-H, Chiraldex, 1 mL/min, 5\% IPA, 254 nm) - analysis of the reaction product.}

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mixture of products from \((R,R)\)-3.44 and \((S,S)\)-3.44

reaction product from \((S,S)\)-3.44

reaction product spiked with “rac”
(2E,4S,5R,6E)-4-methyl-4-(4-methylpent-3-en-1-yl)trideca-2,6-diene-1,5-diol. The diboration/allylation was performed according to the representative procedure with (E)-4,8-dimethylnona-1,3,7-triene (70.0 mg, 465.9 µmol), Pt(dba)$_3$ (12.6 mg, 14.0 µmol), (R,R)-3,5-di-iso-propylphenylTADDOLPPh (3.44 mg, 16.7 µmol), B$_2$(pin)$_2$ (124.2 mg, 489.1 µmol) in toluene (0.45 mL, 1.0 M), and freshly distilled trans-2-nonenal (65.3 mg, 465.9 µmol). The crude material was purified by column chromatography on silica gel (30-60% ethyl acetate/hexanes, R$_f$ = 0.37 in 50% ethyl acetate/hexanes, stain in PMA) to afford the title compound as a clear, colorless oil (107.7 mg, 75%). $^1$H NMR (500 MHz, CDCl$_3$): $\delta$ 0.86 (3H, t, $J = 6.5$ Hz), 0.95 (3H, s), 1.22-1.38 (10H, m), 1.55 (3H, s), 1.58 (2H, br s), 1.64 (3H, d, $J = 1.0$ Hz), 1.77-1.93 (2H, m), 2.02 (2H, ddd, $J = 7.0$ Hz, 7.0 Hz, 7.0 Hz), 3.76 (1H, d, $J = 7.5$ Hz), 4.16 (2H, dd, $J = 3.0$ Hz, 1.5 Hz), 5.05 (1H, ddd, $J = 7.0$ Hz, 7.0 Hz, 1.5 Hz), 5.41 (1H, dddd, $J = 15.0$ Hz, 9.0 Hz, 1.5 Hz, 1.5 Hz), 5.61-5.69 (3H, m); $^{13}$C NMR (125 MHz, CDCl$_3$): $\delta$ 14.1, 17.5, 17.6, 22.58, 22.60, 25.6, 28.8, 29.1, 31.7, 32.4, 37.9, 43.7, 63.8, 79.1, 124.8, 128.5, 129.5, 131.2, 134.9, 137.9; IR (neat): 3348.7 (br w), 2959.4 (m), 2023.3 (m), 2854.5 (m), 1665.7 (w), 1455.3 (m), 1376.7 (m), 1302.5 (w), 1079.0 (m), 1004.8 (m), 970.9 (s) cm$^{-1}$; HRMS-(ESI+) for C$_{20}$H$_{35}$O [M+H–H$_2$O]: calculated: 291.2688, found: 291.2694; $[\alpha]_D^{20}$: -1.11 (c = 1.98, CHCl$_3$, l = 50 mm).
**Analysis of Stereochemistry:**

The enantioselectivity was determined by treating the 1,5-diol with benzoic anhydride and Et$_3$N to make the mono(benzoate) for HPLC analysis. The analogous racemic material was prepared by mixing approximate equimolar amounts of the products made using (R,R)-3,5-di-iso-propylTADDOLPPh and (S,S)-3,5-di-iso-propylTADDOLPPh as the ligands in the diboration reaction. The absolute stereochemistry was assigned by analogy.

*Chiral HPLC (AD-H, Chiraldex, 1 mL/min, 1% IPA, 220 nm) - analysis of (S,E)-4-((R)-1-hydroxypropyl)-4,8-dimethylnona-2,7-dien-1-yl benzoate.*

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(4S,5S,E)-5-(furan-2-yl)-4-methyl-4-(4-methylpent-3-en-1-yl) pent-2-ene-1,5-diol. The diboration/allylation was performed according to the representative procedure with (E)-4,8-dimethylnona-1,3,7-triene (70.0 mg, 465.9 µmol), Pt(dba)$_3$ (12.6 mg, 14.0 µmol), (R,R)-3,5-di-iso-propylphenylTADDOLPPh (3.44) (15.2 mg, 16.7 µmol), B$_2$(pin)$_2$ (124.2 mg, 489.1 µmol) in toluene (0.45 mL, 1.0 M), and freshly distilled 2-furfural (44.8 mg, 465.9 µmol). The crude material was purified by column chromatography on silica gel (30-60% ethyl acetate/hexanes, R$_f$ = 0.24 in 50% ethyl acetate/hexanes, stain in PMA) to afford the title compound as a clear, yellow oil (99.0 mg, 80%). $^1$H NMR (500 MHz, CDCl$_3$): $\delta$ 0.99 (3H, s), 1.23-1.31 (1H, m), 1.35-1.41 (1H, m), 1.54 (3H, s), 1.63 (3H, s), 1.85 (2H, ddd, $J$ = 17.5 Hz, 17.5 Hz, 9.0 Hz), 2.11 (1H, br s), 2.40 (1H, br s), 4.13 (2H, d, $J$ = 4.5 Hz), 4.45 (1H, s), 5.02 (1H, t, $J$ = 7.0 Hz), 5.63-5.71 (2H, m), 6.20 (1H, d, $J$ = 3.5 Hz), 6.31 (1H, dd, $J$ = 3.0 Hz, 1.5 Hz), 7.33 (1H, dd, $J$ = 1.0 Hz); $^{13}$C NMR (125 MHz, CDCl$_3$): $\delta$ 17.6, 17.7, 22.6, 25.6, 37.5, 44.5, 63.7, 74.4, 107.8, 110.1, 124.6, 129.7, 131.4, 137.2, 141.5, 154.5; IR (neat): 3356.4 (m br), 2967.3 (m), 2921.9 (m), 2856.6 (m), 1665.2 (w), 1502.2 (w), 1452.5 (m), 1377.0 (m), 1277.4 (w), 1223.4 (w), 1146.9 (m), 1077.5 (m), 1050.5 (m), 1007.1 (s), 976.4 (s), 946.9 (w), 932.8 (w), 902.7 (w), 884.4 (w), 838.7 (w), 808.4 (m), 731.9 (s) cm$^{-1}$; HRMS-(ESI +): for C$_{16}$H$_{28}$NO$_3$ [M+NH$_4$]: calculated: 282.2069, found: 282.2080; [a]$_{D}^{20}$ = +6.78 (c = 1.75, CHCl$_3$, l = 50 mm).
**Analysis of Stereochemistry:**

The olefin geometry of the 1,5-diol was determined to be \textit{trans} by measuring the coupling constants of the vinylic hydrogens from the $^1$H NMR taken in benzene: $^1$H NMR (500 MHz, C$_6$D$_6$): $\delta$ 1.04 (3H, s), 1.41-1.55 (2H, m), 1.53 (3H, d, $J = 1.0$ Hz), 1.64 (3H, d, $J = 1.0$ Hz), 1.96 (2H, ddd, $J = 15.0$ Hz, 15.0 Hz, 8.0 Hz), 2.43 (1H, br s), 3.93 (2H, d, $J = 5.0$ Hz), 4.42 (1H, s), 5.15 (1H, ddd, $J = 7.0$ Hz, 7.0 Hz, 1.5 Hz), 5.54 (1H, m), 5.68 (1H, dd, $J = 16.0$ Hz, 1.0 Hz), 6.07 (1H, dd, $J = 3.0$ Hz, 1.5 Hz), 6.15 (1H, d, $J = 3.0$ Hz), 7.04 (1H, dd, $J = 2.0$ Hz, 1.0 Hz).

The enantioselectivity was determined by SFC analysis of the reaction product. The analogous racemic material was prepared by mixing approximate equimolar amounts of the products made using (R,R)-3,5-di-\textit{iso}-propylTADDOLPPh and (S,S)-3,5-di-\textit{iso}-propylTADDOLPPh as the ligands in the diboration reaction. The absolute stereochemistry was assigned by analogy.
Chiral SFC (AD-H, Chiraldex, 100 bar, 4 mL/min, 4% MeOH, 35 °C)- analysis of reaction product.

![Graphs showing chromatograms](image)

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mixture of products from (R,R)-3.44 and (S,S)-3.44

derived from reaction product using (R,R)-3.44
reaction product spiked with “rac”
(4S,5S,E)-4-methyl-4-(4-methylpent-3-en-1-yl)-5-phenylpent-2-ene-1,5-diol (Table 3.6, entry 1). The diboration/allylation was performed according to the representative procedure with (E)-4,8-dimethylnona-1,3,7-triene (70.0 mg, 465.9 µmol), Pt(dba)_3 (12.6 mg, 14.0 µmol), (R,R)-3,5-di-iso-propylphenylTADDOLPPh (3.44) (15.2 mg, 16.7 µmol), B_2(pin)_2 (124.2 mg, 489.1 µmol) in toluene (0.45 mL, 1.0 M), and freshly distilled benzaldehyde (49.5 mg, 465.9 µmol). The crude reaction mixture was purified on silica gel (30-50% ethyl acetate/hexanes) to afford an inseparable mixture of the product and pinacol (160.2 mg). The mixture of diols was then dissolved in diethyl ether (3 mL), tetrahydrofuran (3 mL), and water (4 mL), and then cooled to 0 °C in an ice bath. NaIO_4 (521.8 mg, 2.44 mmol) was added and the reaction was allowed to warm to ambient temperature over 2h (oxidative cleavage of pinacol). The reaction mixture was quenched with saturated aqueous Na_2SO_3 (2 mL) and the layers were separated. The aqueous layer was extracted with ethyl acetate (3 x 10 mL). The combined organics were dried over Na_2SO_4, filtered, and concentrated in vacuo. The crude material was purified by column chromatography on silica gel (40-60% ethyl acetate/hexanes, R_f = 0.28 in 50% ethyl acetate/hexanes, stain in PMA) to afford the title compound as a clear, colorless oil (111.5 mg, 87%). ^1H NMR (500 MHz, CDCl_3): δ 1.22-1.30 (1H, m), 1.38-1.44 (1H, m), 1.53 (3H, s), 1.63 (3H, d, J = 1.0 Hz), 1.77-1.89 (2H, m), 4.15 (2H, m), 4.42 (1H, s), 5.02 (1H, ddd, J = 7.0 Hz, 7.0 Hz, 1.0 Hz), 5.61 (1H, ddd, J = 15.5 Hz, 5.0 Hz, 5.0 Hz), 5.72 (1H, dd, J = 16.0 Hz, 1.0 Hz), 7.22-7.30 (5H, m); ^13C NMR (125 MHz, CDCl_3): δ 17.0, 17.6,
22.8, 25.7, 37.8, 44.8, 63.8, 80.5, 124.6, 127.51, 127.53, 128.0, 130.0, 131.3, 137.6, 140.6; IR (neat): 3376.9 (br s), 3085.8 (w), 3061.3 (w), 3028.8 (w), 2968.5 (s), 2922.4 (s), 2856.9 (s), 1666.4 (w), 1493.3 (w), 1452.8 (s), 1377.4 (m), 1195.6 (w), 1082.4 (m), 1046.0 (m), 1011.6 (s), 979.7 (s), 903.5 (w), 839.6 (w), 702.9 (s) cm\(^{-1}\); HRMS-(ESI+) for C\(_{18}\)H\(_{30}\)NO\(_2\) [M+NH\(_4\)]: calculated: 292.2277, found: 292.2271; \([\alpha]\)\(_D\)\(^{20}\) = -25.07 (c = 3.00, CHCl\(_3\), l = 50 mm).

**Analysis of Stereochemistry:**

The enantioselectivity was determined by SFC analysis of the reaction product. The analogous racemic material was prepared by mixing approximate equimolar amounts of the products made using \((R,R)\)-3,5-di-\(iso\)-propylTADDOLPPh and \((S,S)\)-3,5-di-\(iso\)-propylTADDOLPPh as the ligands in the diboration reaction. The absolute stereochemistry was assigned by analogy.

*Chiral SFC (AD-H, Chiraldex, 100 bar, 4 mL/min, 4% MeOH, 35 °C)- analysis of reaction product.*
(4S,5R,E)-4-methyl-4-(4-methylpent-3-en-1-yl)hept-2-ene-1,5-diol (Table 3.6, entry 2). The diboration/allylation was performed according to the representative procedure with (E)-4,8-dimethylnona-1,3,7-triene (70.0 mg, 465.9 µmol), Pt(dba)$_3$ (12.6 mg, 14.0 µmol), (R,R)-3,5-di-iso-propylphenylTADDOLPh (3.44) (15.2 mg, 16.7 µmol), B$_2$(pin)$_2$ (124.2 mg, 489.1 µmol) in toluene (0.45 mL, 1.0 M), and freshly distilled propionaldehyde (27.0 mg, 465.9 µmol). The crude reaction mixture was purified on silica gel (30-60% ethyl acetate/hexanes) to afford an inseparable mixture of the product, pinacol, and 1,2-diol (129.4 mg). The mixture of diols was then dissolved in diethyl ether (3 mL), tetrahydrofuran (3 mL), and water (4 mL), and then cooled to 0 °C in an ice bath. NaIO$_4$ (521.8 mg, 2.44 mmol) was added and the reaction was allowed to warm to ambient temperature over 2h (oxidative cleavage of pinacol). The reaction mixture was quenched with saturated aqueous Na$_2$SO$_3$ (2 mL) and the layers were separated. The aqueous layer was extracted with ethyl acetate (3 x 10 mL). The combined organics were dried over Na$_2$SO$_4$, filtered, and concentrated in vacuo. The crude material was purified by column chromatography on silica gel (40-60% ethyl acetate/hexanes, R$_f$ = 0.24 in 50% ethyl acetate/hexanes, stain in PMA) to afford the title compound as a clear, colorless oil (70.7 mg, 67%). $^1$H NMR (500 MHz, CDCl$_3$): δ 0.94 (3H, s), 0.96 (3H, t, $J$ = 7.5 Hz), 1.16-1.26 (1H, m), 1.28-1.40 (2H, m), 1.51-1.59 (1H, m), 1.55 (3H, s), 1.64 (3H, d, 1.0 Hz), 1.75-1.83 (1H, m), 1.85-1.92 (1H, m), 2.03 (2H, br s), 3.17 (1H, dd, $J$ = 10.0 Hz, 1.5 Hz), 4.12 (2H, d, $J$ = 2.5 Hz), 5.05 (1H, ddd, $J$ = 7.0Hz, 7.0 Hz, 1.5 Hz).
Hz), 5.58-5.61 (2H, m); $^{13}$C NMR (125 MHz, CDCl$_3$): δ 11.5, 17.59 17.64, 22.7, 23.9, 25.6, 37.7, 44.0, 63.8, 79.3, 124.7, 129.2, 131.3, 138.1; IR (neat): 3340.5 (br m), 2964.8 (m), 2927.6 (m), 2874.3 (m), 1665.2 (w), 1454.9 (m), 1377.5 (m), 1313.7 (w), 1243.7 (w), 1100.1 (m), 1047.7 (w), 974.5 (s) cm$^{-1}$; HRMS-(ESI+) for C$_{14}$H$_{30}$NO$_2$ [M+NH$_4$]: calculated: 224.2277, found: 244.2274; $[^{\alpha}]$D$^{20}$ = +6.78 (c = 1.75, CHCl$_3$, l = 50 mm).

**Analysis of Stereochemistry:**

The olefin geometry of the 1,5-diol was determined to be trans by measuring the coupling constants of the vinylic hydrogens from the $^1$H NMR taken in d$_6$-benzene: $^1$H NMR (500 MHz, C$_6$D$_6$): δ 0.89 (3H, s), 1.00 (3H, t, $J = 7.5$ Hz), 1.19 (1H, dddd, $J = 14.5$ Hz, 10.5 Hz, 7.5 Hz, 7.5 Hz), 1.31-1.44 (3H, m), 1.56 (3H, s), 1.68 (3H, s), 1.87-2.02 (2H, m), 3.03 (1H, dd, $J = 10.5$ Hz, 2.0 Hz), 3.84 (2H, d, $J = 5.5$ Hz), 5.19 (1H, ddd, $J = 7.5$ Hz, 7.5 Hz, 1.0 Hz), 5.44 (1H, ddd, $J = 16.0$ Hz, 5.0 Hz, 5.0 Hz), 5.52 (1H, d, $J = 16.0$ Hz).

The enantioselectivity was determined by treating the 1,5-diol with benzoic anhydride and Et$_3$N to make the mono(benzoate) for HPLC analysis. The analogous racemic material was prepared by mixing approximate equimolar amounts of the products made using $(R,R)$-3,5-di-iso-propylTADDOLPPh and $(S,S)$-3,5-di-iso-propylTADDOLPPh as the ligands in the diboration reaction. The absolute stereochemistry was assigned by analogy.
Chiral HPLC (AD-H, Chiraldex, 1 mL/min, 1% IPA, 220 nm) - analysis of (S,E)-4-((R)-1-hydroxypropyl)-4,8-dimethylnona-2,7-dien-1-yl benzoate.

278

mixture of products from (R,R)-3.44 and (S,S)-3.44

derived from reaction product using (R,R)-3.44

reaction product spiked with "rac"

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(4R,5S,E)-4-methyl-4-(4-methylpent-3-en-1-yl)-5-phenylpent-2-ene-1,5-diol (Table 3.6, entry 3). The diboration/allylation was performed according to the representative procedure with (Z)-4,8-dimethylnona-1,3,7-triene (70.0 mg, 465.9 µmol), Pt(dba)$_3$ (12.6 mg, 14.0 µmol), (R,R)-3,5-di-iso-propylphenylTADDOLPPh (3.44) (15.2 mg, 16.7 µmol), B$_2$(pin)$_2$ (124.2 mg, 489.1 µmol) in toluene (0.45 mL, 1.0 M), and freshly distilled benzaldehyde (49.5 mg, 465.9 µmol). The crude reaction mixture was purified on silica gel (30-50% ethyl acetate/hexanes) to afford an inseparable mixture of the product and pinacol (171.9 mg). The mixture of diols was then dissolved in diethyl ether (3 mL), tetrahydrofuan (3 mL), and water (4 mL), and then cooled to 0 °C in an ice bath. NaIO$_4$ (521.8 mg, 2.44 mmol) was added and the reaction was allowed to warm to ambient temperature over 2h (oxidative cleavage of pinacol). The reaction mixture was quenched with saturated aqueous Na$_2$SO$_3$ (2 mL) and the layers were separated. The aqueous layer was washed with ethyl acetate (3 x 10 mL). The combined organics were dried over Na$_2$SO$_4$, filtered, and concentrated in vacuo. The crude material was purified by column chromatography on silica gel (40-60% ethyl acetate/hexanes, R$_f$ = 0.33 in 50% ethyl acetate/hexanes, stain in PMA) to afford the title compound as a clear, colorless oil as a mixture of diastereomers (108.0 mg, 85%, 9:1 dr). $^1$H NMR (500 MHz, CDCl$_3$): δ 1.06 (3H, s), 1.32-1.39 (2H, m), 1.53 (3H, s), 1.63 (3H, s), 1.76-1.92 (2H, m), 2.15 (1H, br s), 4.12 (2H, d, $J = 6.0$ Hz), 4.42 (1H, s), 5.00 (1H, ddd, $J = 7.0$ Hz, 7.0 Hz, 1.5 Hz), 5.55 (1H, ddd, $J = 15.5$ Hz, 5.5 Hz, 5.5 Hz), 5.66 (1H, dd, $J = 16.0$ Hz, 1.0 Hz), 7.22-7.30
(5H, m); $^{13}$C NMR (125 MHz, CDCl$_3$): $\delta$ 17.6, 19.5, 22.8, 25.7, 36.5, 44.2, 63.9, 81.1, 124.7, 127.4, 127.5, 127.8, 129.4, 131.2, 136.9, 141.2; IR (neat): 3364.0 (m br), 3029.5 (w), 2967.0 (m), 2925.7 (m), 2857.2 (m), 1493.3 (w), 1452.1 (m), 1376.7 (m), 1197.7 (w), 1080.0 (m), 1044.6 (m), 1011.7 (s), 980.0 (s), 745.3 (m), 703.1 (s); HRMS-(ESI+) for C$_{18}$H$_{30}$NO$_2$ [M+NH$_4$]: calculated: 292.2277, found: 292.2278; $[\alpha]_D^{20} = -24.17$ ($c = 3.81$, CHCl$_3$, $l = 50$ mm).

**Analysis of Stereochemistry:**

The enantioselectivity was determined by SFC analysis of the reaction product. The analogous racemic material was prepared by mixing approximate equimolar amounts of the product made using (R,R)-3,5-di-*iso-*propylTADDOLPPh and (S,S)-3,5-di-*iso-*propylTADDOLPPh as the ligand in the diboration reaction. The absolute stereochemistry was assigned by analogy.
Chiral SFC (AD-H, Chiraldex, 100 bar, 4 mL/min, 4% MeOH, 35 °C)- analysis of reaction product.

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<th>Height (nV)</th>
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(4R,5R,E)-4-methyl-4-(4-methylpent-3-en-1-yl)hept-2-ene-1,5-diol (Table 3.6, entry 4). The diboration/allylation was performed according to the representative procedure with (Z)-4,8-dimethylnona-1,3,7-triene (70.0 mg, 465.9 µmol), Pt(dba)$_3$ (12.6 mg, 14.0 µmol), (R,R)-3,5-di-iso-propylphenylTADDOLPPh (3.44) (15.2 mg, 16.7 µmol), B$_2$(pin)$_2$ (124.2 mg, 489.1 µmol) in toluene (0.45 mL, 1.0 M), and freshly distilled propionaldehyde (27.0 mg, 465.9 µmol). The crude reaction mixture was purified on silica gel (30-65% ethyl acetate/hexanes) to afford an inseparable mixture of the product, pinacol, and 1,2-diol (118.2 mg). The mixture of diols was then dissolved in diethyl ether (3 mL), tetrahydrofuran (3 mL), and water (4 mL), and then cooled to 0 °C in an ice bath. NaIO$_4$ (521.8 mg, 2.44 mmol) was added and the reaction was allowed to warm to ambient temperature over 2h (oxidative cleavage of pinacol). The reaction mixture was quenched with saturated aqueous Na$_2$SO$_3$ (2 mL) and the layers were separated. The aqueous layer was extracted with ethyl acetate (3 x 10 mL). The combined organics were dried over Na$_2$SO$_4$, filtered, and concentrated in vacuo. The crude material was purified by column chromatography on silica gel (40-60% ethyl acetate/hexanes, R$_f$ = 0.29 in 50% ethyl acetate/hexanes, stain in PMA) to afford the title compound as a clear, colorless oil (70.7 mg, 67%). $^1$H NMR (500 MHz, CDCl$_3$): δ 0.95 (3H, t, J = 7.5 Hz), 1.00 (3H, s), 1.20 (1H, dddd, J = 14.5 Hz, 10.5 Hz, 7.5 Hz, 7.5 Hz), 1.38 (2H, t, J = 8.5 Hz), 1.52-1.60 (2H, m), 1.56 (3H, s), 1.81-1.90 (2H, m), 3.17 (1H, d, J = 10.5 Hz), 4.12-4.13 (2H, m), 5.06 (1H, ddd, J = 7.0 Hz, 7.0 Hz, 1.0 Hz), 5.56-5.64 (2H, m); $^{13}$C
NMR (125 MHz, CDCl₃): δ 11.6, 17.6, 18.6, 22.6, 24.6, 25.7, 37.5, 43.9, 63.9, 80.0, 124.8, 128.8, 131.4, 137.6; IR (neat): 3353.8 (br m), 2965.9 (m), 2929.0 (m), 2874.7 (m), 1665.3 (w), 1455.1 (m), 1376.7 (m), 1312.9 (w), 1242.1 (w), 1102.2 (m), 1047.6 (w), 1010.9 (m), 975.5 (s), 940.5 (w) cm⁻¹; HRMS-(ESI+) for C₁₄H₃₀NO₂ [M+NH₄]: calculated: 244.2277, found: 244.2287. [α]D²⁰ = +22.17 (c = 1.52, CHCl₃, l = 50 mm).

**Analysis of Stereochemistry:**

The olefin geometry of the 1,5-diol was determined to be *trans* by measuring the coupling constants of the vinylic hydrogens from the ¹H NMR taken in benzene: ¹H NMR (500 MHz, C₆D₆): δ 0.94 (3H, t, J = 7.5 Hz), 0.96 (3H, s), 1.12 (1H, dddd, J = 15.0 Hz, 11.0 Hz, 7.5 Hz, 7.5 Hz), 1.39-1.47 (3H, m), 1.56 (3H, s), 1.68 (3H, s), 1.94-1.98 (2H, m), 3.03 (1H, dd, J = 10.5 Hz, 1.5 Hz), 8.84-8.90 (2H, m), 5.20 (1H, ddd, J = 7.0 Hz, 7.0 Hz, 1.0 Hz), 5.44 (1H, ddd, J = 16.0 Hz, 4.5 Hz, 4.5 Hz), 5.49 (1H, d, J = 16.5 Hz).

The enantioselectivity was determined by treating the 1,5-diol with benzoic anhydride and Et₃N to make the mono(benzoate) for HPLC analysis. The analogous racemic material was prepared by mixing approximate equimolar amounts of the products made using (R,R)-3,5-di-*iso*-propylTADDOLPPh and (S,S)-3,5-di-*iso*-propylTADDOLPPh as the ligands in the diboration reaction. The absolute stereochemistry was assigned by analogy.
Chiral HPLC (AD-H, Chiraldex, 1 mL/min, 1% IPA, 220 nm) - analysis of (R,E)-4-((R)-1-hydroxypropyl)-4,8-dimethylnona-2,7-dien-1-yl benzoate.

- Retention Time: 11.530, Area: 27547574, Area %: 4.29, Height: 1610403, Height %: 5.49
- Retention Time: 13.200, Area: 613910926, Area %: 95.71, Height: 27748826, Height %: 94.51
3.7.8. Procedure for Diboration/Allylation/Homologation/Oxidation (Scheme 3.16)

To an oven-dried 2-dram vial with magnetic stir bar in the glove box was added Pt(dba)$_3$ (13.4 mg, 15.0 µmol), (R,R)-3,5-di-iso-propylphenyl-TADDOLPPh (3.44) (16.3 mg, 18.0 µmol), B$_2$(pin)$_2$ (133.1 mg, 524.1 µmol) and toluene (0.5 mL, [substrate] = 1.0 M). The vial was sealed with a polypropylene cap, removed from the glove box, and heated to 80 °C in an oil bath for 20 min. The vial was cooled to room temperature, returned to the glove box and charged with (E)-4,8-dimethylnona-1,3,7-triene (75.0 mg, 499.1 µmol). The vial was sealed, removed from the glove box, and stirred at 60 °C for 12 h. The reaction mixture was then cooled to ambient temperature, returned to the glove box and charged with freshly distilled benzaldehyde (53.0 mg, 499.1 µmol). The reaction was heated to 60 °C in and oil bath and was allowed to stir for 24 h. The reaction mixture was then cooled to ambient temperature and the vial cap was exchanged for a septum. After the vial was purged with N$_2$, tetrahydrofuran (2.5 mL) was added via syringe, followed by bromochloromethane (84 µL, 1.25 mmol). The reaction mixture was then cooled to -78 °C (dry ice/acetone) and n-BuLi (0.50 mL, 1.25 mmol, 2.48 M in hexane) was added dropwise under N$_2$. The reaction was allowed to stir at 78 °C for 10 min, and was then allowed to warm to rt and stir for 7 h. The reaction mixture was then transferred to a scintillation vial using tetrahydrofuran (2 x 1 mL) to rinse the reaction vial. The reaction mixture was then cooled to 0 °C (ice/water) and charged with 3 M sodium hydroxide solution (2 mL) and 30 wt % hydrogen peroxide (1 mL). The reaction was
gradually warmed to room temperature and allowed to stir for 4 h, at which time the vial was cooled to 0 °C (ice/water) and saturated aqueous sodium thiosulfate (2 mL) was carefully added dropwise. The reaction mixture was diluted with ethyl acetate (5 mL) and the aqueous and organic layers were separated. The aqueous layer was rinsed with ethyl acetate (3 x 15 mL), and the combined organics were dried over Na$_2$SO$_4$, filtered, and volatiles were removed in vacuo. The crude reaction mixture was purified by column chromatography on silica gel (20-35% ethyl acetate/hexanes, $R_f = 0.32$ in 50% ethyl acetate/hexanes, stain in PMA) to afford a clear, colorless oil (119.5 mg, 83%).

**(1S,2S,E)-2-methyl-2-(4-methylpent-3-en-1-yl)-1-phenylhex-3-ene-1,6-diol (3.59).** $^1$H NMR (500 MHz, CDCl$_3$):

$\delta$ 0.88 (3H, s), 1.21-1.28 (1H, m), 1.38-1.43 (1H, m), 1.53 (3H, s), 1.64 (3H, s), 1.84 (2H, ddd, $J = 7.5$ Hz, 7.5 Hz, 7.5 Hz), 2.33 (2H, ddd, $J = 7.0$ Hz, 7.0 Hz, 7.0 Hz), 3.58-3.67 (2H, m), 4.37 (1H, s), 5.03 (1H, t, $J = 7.0$ Hz), 5.37 (1H, ddd, $J = 16.0$ Hz, 7.0 Hz, 7.0 Hz), 5.55 (1H, d, $J = 16.0$ Hz), 7.22-7.30 (5H, m); $^{13}$C NMR (125 MHz, CDCl$_3$): $\delta$ 17.0, 17.6, 22.9, 25.7, 36.2, 37.9, 45.3, 61.8, 80.3, 124.7, 127.1, 127.4, 127.5, 130.0, 131.2, 139.1, 140.7; IR (neat): 3378.7 (m), 2966.2 (m), 2925.7 (s), 2855.9 (m), 1452.6 (m), 1376.7 (w), 1046.3 (s), 982.3 (m), 745.6 (m), 702.6 (s) cm$^{-1}$; HRMS-(ESI+) for C$_{19}$H$_{32}$NO$_2$ [M+NH$_4$]: calculated: 306.2433, found: 306.2419. [$\alpha$]$_D^{25} = -55.77$ ($c = 0.34$, CHCl$_3$, $l = 50$ mm).
**Analysis of Stereochemistry:**

The enantioselectivity was determined by SFC analysis of the reaction product. The analogous racemic material was prepared by mixing approximate equimolar amounts of the products made using (R,R)-3,5-di-iso-propylTADDOLPPh and (S,S)-3,5-di-iso-propylTADDOLPPh as the ligands in the diboration reaction. The absolute stereochemistry was assigned by analogy.

*Chiral SFC (AD-H, Chiraldex, 100 bar, 5 mL/min, 5% MeOH, 35 °C)- analysis of reaction product.*
3.7.9. Procedure for Diboration/Allylation/Protodeboronation (Scheme 3.17).

To an oven-dried 2-dram vial with magnetic stir bar in the glove box was added Pt (dba)$_3$ (13.4 mg, 15.0 µmol), (R,R)-3,5-di-iso-propylphenyl-TADDOLPPh (3.44) (16.3 mg, 18.0 µmol), B$_2$(pin)$_2$ (133.1 mg, 524.1 µmol) and toluene (0.5 mL, [substrate] = 1.0 M). The vial was sealed with a polypropylene cap, removed from the glove box, and heated to 80 ºC in an oil bath for 20 min. The vial was cooled to room temperature, returned to the glove box and charged with (E)-4,8-dimethylnona-1,3,7-triene (75.0 mg, 499.1 µmol). The vial was sealed, removed from the glove box, and stirred at 60 ºC for 12 h. The reaction mixture was then cooled to ambient temperature, returned to the glove box and charged with freshly distilled hydrocinnamaldehyde (67.0 mg, 499.1 µmol). The reaction was heated to 60 ºC in and oil bath and was allowed to stir for 24 h. The reaction mixture was then cooled to ambient temperature, TBAF•nH$_2$O (521.9 mg, 2.00 mmol) was added and the vial was quickly sealed with a septum and purged with N$_2$. The reaction mixture was then transferred via syringe to a separate 25 mL flame-dried round-bottomed flask containing oven-dried 4 Å molecular sieves. The original vial was washed with toluene (2 x 1 mL), and the mixture was allowed to stir at rt for 10 min (to remove excess water from TBAF•nH$_2$O). The reaction mixture was then cannula transferred to an oven-dried scintillation vial fitted with a septum, and the flask was rinsed with toluene (2.5 mL, final [substrate] = 0.1 M). The reaction mixture was then heated to 60 ºC in an oil bath for 6 h, at which time it was cooled to rt and the volatiles were removed in vacuo and the residue was filtered over a silica plug (10% ethyl acetate/hexanes). The crude
material was then purified by column chromatography on silica gel (2-8% ethyl acetate/hexanes, \( R_f = 0.33 \) in 10% ethyl acetate/hexanes, stain in PMA) to afford a clear, colorless oil (105.8 mg, 74%, 5:1 terminal:internal alkene).

**\((\mathbf{3R,4S})-4\text{-allyl-4,8-dimethyl-1-phenylnon-7-en-3-ol} \ (3.61)\).**  
\(^1\)H NMR (500 MHz, CDCl\(_3\)): δ 0.84 (3H, s), 1.17-1.24 (2H, m), 1.32 (1H, ddd, \( J = 14.5 \) Hz, 14.5 Hz, 6.0 Hz) 1.51 (1H, br s), 1.57 (3H, s), 1.58-1.63 (1H, m), 1.65 (3H, s), 1.76-1.84 (1H, m), 1.86-1.94 (1H, m), 2.06 (1H, dd, \( J = 14.0 \) Hz, 7.0 Hz), 2.15 (1H, dd, \( J = 14.0 \) Hz, 8.0 Hz), 2.58 (1H, ddd, \( J = 16.0 \) Hz, 9.5 Hz, 6.5 Hz), 2.91 (1H, ddd, 14.5 Hz, 9.5 Hz, 4.0 Hz), 3.40 (1H, dd, \( J = 11.0 \) Hz), 5.01-5.09 (3H, m), 5.83 (1H, dddd, \( J = 17.0 \) Hz, 7.5 Hz, 7.5 Hz, 7.5 Hz), 7.15-7.20 (3H, m), 7.24-7.28 (2H, m); 13\(^C\) NMR (125 MHz, CDCl\(_3\)): δ 17.6, 20.3, 22.1, 25.7, 33.2, 33.4, 36.4, 40.3, 40.8, 76.7, 117.1, 124.8, 125.8, 128.4, 128.5, 131.3, 135.6, 142.4; IR (neat): 3444.9 (br w), 3063.0 (w), 3026.7 (w), 2924.6 (s), 2924.6 (s), 2859.0 (m), 1637.8 (w), 1602.7 (w), 1495.4 (w), 1454.2 (s), 1378.0 (m), 1076.7 (m), 1040.5 (m), 913.1 (m), 748.5 (m), 699.5 (s) cm\(^{-1}\); HRMS-(ESI+) for C\(_{20}\)H\(_{31}\)O [M+H]: calculated: 287.2375, found: 287.2377. [\(\alpha\)]\(_D\)\(^{25}\) = +40.54 (c = 0.69, CHCl\(_3\), \( l = 50 \) mm).
**Analysis of Stereochemistry:**

The enantioselectivity was determined by HPLC analysis of the reaction product. The analogous racemic material was prepared by mixing approximate equimolar amounts of the products made using \((R,R)-3,5\text{-di-iso-propylTADDOLPPh}\) and \((S,S)-3,5\text{-di-iso-propylTADDOLPPh}\) as the ligands in the diboration reaction. The absolute stereochemistry was assigned by analogy.

*Chiral HPLC (AD-H, Chiraldex, 1 mL/min, 0.5% IPA, 254 nm)- analysis of reaction product.*

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(3R,4S)-4,8-dimethyl-1-phenyl-4-((E)-prop-1-en-1-yl)non-7-en-3-ol. Purified by column chromatography on silica gel (2-8% ethyl acetate/hexanes, $R_f = 0.38$ in 10% ethyl acetate/hexanes, stain in PMA). $^1$H NMR (500 MHz, CDCl$_3$): δ 0.92 (3H, s), 1.20-1.27 (2H, m), 1.28-1.35 (1H, m), 1.53-1.61 (1H, m), 1.55 (3H, d, $J = 0.5$ Hz), 1.65 (3H, d, $J = 1.0$ Hz), 1.75-1.81 (1H, m), 1.82-1.88 (1H, m), 2.59 (1H, ddd, $J = 14.0$ Hz, 10.0 Hz, 7.0 Hz), 2.92 (1H, ddd, $J = 14.0$ Hz, 10.5 Hz, 5.0 Hz), 3.24 (1H, dd, $J = 10.5$ Hz, 1.5 Hz), 5.05 (1H, ddd, $J = 6.0$ Hz, 6.0 Hz, 1.5 Hz), 5.31 (1H, dq, $J = 15.5$ Hz, 1.5 Hz), 5.48 (1H, dq, $J = 15.5$ Hz, 6.0 Hz), 7.13-7.21 (3H, m), 7.24-7.28 (2H, m); $^{13}$C NMR (125 MHz, CDCl$_3$): δ 17.2, 17.6, 18.3, 22.8, 25.7, 32.8, 33.4, 37.8, 44.3, 76.6, 124.9, 125.7, 125.9, 128.3, 128.5, 131.3, 136.8, 142.6; HRMS-(ESI+) for C$_{20}$H$_{29}$ [M+H-H$_2$O]: calculated: 269.2269, found: 269.2260.
Chapter 4

Development, Scope, and Utility of the Enantioselective Platinum-Catalyzed 1,2-Diboration of Terminal Alkenes

4.1. Introduction

The development of novel catalytic, enantioselective transformations of simple and inexpensive unsaturated hydrocarbons to highly complex molecules has been a long standing goal in the organic chemistry community. Specifically, the stereoselective functionalization of prochiral terminal olefins remains an area of interest. One of the main drivers for the use of linear \( \alpha \)-olefins as starting materials for organic synthesis is their relative abundance and low cost of production. They are manufactured on multi-million ton scale worldwide by thermal cracking of natural gas and cost an average of $0.50/pound (Scheme 4.1).\(^1\) Ethylene alone is the feedstock for 30% of all petrochemicals. In 2000, 2.84 million metric tons of higher order linear \( \alpha \)-olefins were produced worldwide.

Scheme 4.1. Worldwide Annual Production of Linear α-Olefins in 2000 by Metric Ton

<table>
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<td>-</td>
</tr>
<tr>
<td>Worldwide</td>
<td>109 x 10^6</td>
<td>62 x 10^6</td>
<td>50 x 10^6</td>
</tr>
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</table>

It is because of their prevalence that organic chemists have developed a range of reactions to functionalize alkenes (Scheme 4.2). Methods to install oxygenation include hydration, oxymercuration, Wacker oxidation, and epoxidation. Polymerization reactions have also been widely utilized for the production of materials.

Scheme 4.2. Common Functionalizations of Terminal Alkenes
Less developed reactions of α-olefins include those in which chirality is installed in a stereoselective fashion. In some regards, controlling the level of enantiomeric induction is more challenging for α-olefins than for other more substituted substrates due to the lack of stereochemical information or bias inherent in a terminal alkene. In this chapter, I will present the enantioselective dimetallation of α-olefins. This reaction allows for tandem reaction sequences by creating two new carbon-metal bonds that could potentially be independently functionalized to afford highly complex molecules from simple and inexpensive starting materials (Scheme 4.3).

Scheme 4.3. Dimetallation of Terminal Alkenes to Access Highly Functionalized Products

4.2. Background

4.2.1. Disilation of Alkenes. The first catalytic dimetallation of an alkene was reported by Tanaka and co-workers in 1990 and involved the intermolecular disilation of norbornene with disilane 4.1 (Scheme 4.4).2 In the presence of 4 mol% Pt(PPh₃)₄, the disilated product, 4.2, was isolated in 26% yield. Unfortunately, competitive β-hydride

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elimination generated a significant amount of alkenyl silanes from many substrates, which resulted in diminished yields of the disilation products and limited substrate scope.

Scheme 4.4. Tanaka’s Catalytic Disilation of Alkenes

The intramolecular disilation of unactivated alkenes developed by Ito and Suginome\(^3\) utilized Pd(acac)\(_2\)-tert-alkyl isocyanide catalysts and was not complicated by undesired β-hydride elimination. The disilation reaction proved to be slow in the absence of the isocyanide ligand, which presented an opportunity for the development of an asymmetric variant. In one of the few examples of asymmetric catalysis using a chiral isocyanide ligand, Suginome and Ito reported the intramolecular disilation of 1,1-disubstituted alkene 4.3 to deliver disilane 4.5 in 59% yield and 89:19 er (Scheme 4.5).\(^4\) In conjunction with methods for the effective oxidation of carbon-silicon bonds, this development provides an interesting route to non-racemic polyol molecules.


**Scheme 4.5.** Catalytic Enantioselective Intramolecular Disilation of Alkenes Developed by Suginome and Ito

![Scheme 4.5](image)

**4.2.2. Silaboration of Alkenes.** In addition to disilation, Ito and co-workers also investigated the catalytic silaboration of unactivated alkenes. This transformation allows for the differential functionalization of each olefinic carbon. The intermolecular version of this reaction employed silaborane **4.6** and 2 mol% of Pt(ethylene)(PPh₃)₂ (Scheme 4.6). The desired racemic silaboration products **4.7** were generated in 46-74% yield for aromatic and aliphatic alkenes.

**Scheme 4.6.** Suginome and Ito’s Catalytic Silaboration of Unactivated Alkenes

![Scheme 4.6](image)

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More recently, the intramolecular variant of the Pt-catalyzed silaboration reaction was reported involving allylic silyl ether 4.8 (Scheme 4.7). While this process is not enantioselective, it is interesting that the diastereoselectivity of the reaction was highly dependent on the choice of phosphine ligand. Employing 5 mol% Pt(dba)$_2$ in the presence of 11 mol% PCy$_2$Ph, the anti-diastereomer of the silaboration product, 4.9, was obtained in 81% yield and 87:13 dr. The syn-diastereomer, 4.10, was generated in 84% yield and 93:7 dr by using P(O-2,4-$_t$Bu$_2$Ph)$_3$ as the ligand in the silaboration reaction.

**Scheme 4.7.** Diastereoselective Intramolecular Pt-Catalyzed Silaboration of Alkenes

4.2.3. **Diboration of Alkenes.** The use of diboron reagents in the dimetallation of unactivated alkene substrates has also received significant attention in the field of organic chemistry. With a Au-catalyst, Baker, Marder and Wescott published the first example of a catalytic diboration of terminal olefins (Scheme 4.8). Although the reaction required

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heating to 80 °C for 48 h, aryl-substituted alkenes reacted with 1.5 equiv B₂(cat)₂ to deliver the corresponding 1,2-bis(boronate)esters 4.12 with good conversion.

**Scheme 4.8.** First Catalytic Diboration of Terminal Alkenes by Baker, Marder, Westcott

Miyaura and Smith independently developed phosphine-free variants of a Pt-catalyzed diboration of α-olefins under mild conditions (Scheme 4.9). Miyaura utilized B₂(pin)₂ in the presence of 3 mol% Pt(dba)₂ to generate 1,2-bis(boronate)esters 4.15 in 76-86% yield for both alkyl and aryl substituted alkenes, however, the reaction required a large excess of the alkene starting material (eq. 1).

Smith and Iverson employed B₂(cat)₂, a more reactive diboron reagent, and 3 mol% Pt(COD)₂ to accomplish the catalytic diboration of terminal alkenes at room temperature to afford 1,2-diborylalkanes 4.16 in 84-95% yield (eq. 2). The mild conditions of their reactions proved tolerant of a variety of functional groups including esters and haloalkanes.

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306
By using chiral diboron reagents, Marder and Norman expanded on the Pt-catalyzed diboration of α-olefins discussed above (Scheme 4.10). Several diboron reagents derived from dimethyl-L-tartrate and other chiral diols were surveyed in the reaction, with 4.17 providing the highest diastereoselectivities. Although the reaction provided 1,2-bis(boronic)esters 4.18 in moderate to good yields, the diastereomeric purity did not exceed 80:20 dr. Furthermore, the reaction required 3 days at 4 °C to provide useful yields.

**Scheme 4.10.** Diastereoselective Diboration of Terminal Alkenes Through the Use of Chiral Diboron Reagents

In 2002, the Morken group began investigating the enantioselective diboration of alkenes with bis(catecholato)diboron 4.11. They found that Rh(I) salts in the presence of (S)-QUINAP were highly effective for the diboration of various alkene substrates to afford enantioenriched 1,2-diols upon subsequent oxidation of the carbon-boron bonds. While di- and trisubstituted alkenes reacted with extremely high levels of enantioselectivity, terminal alkenes suffered from low levels of stereocontrol in the absence of an adjacent quaternary substituted carbon (Scheme 4.11). Substrates lacking the necessary steric bulk next to the alkene site provided the corresponding 1,2-diols 4.19 in 66:34-88:12 er. The development of a general catalyst system for the enantioselective diboration of a broad range of aliphatic and aromatic α-olefins would greatly improve the synthetic utility of this method.

**Scheme 4.11.** First Catalytic Enantioselective Diboration of Alkenes

![Scheme 4.11. First Catalytic Enantioselective Diboration of Alkenes](image)

More recently, the Fernández group published the first transition-metal free diboration of unactivated alkenes (Scheme 4.12).\textsuperscript{12} In the presence of a Lewis base catalyst, a variety of diboron reagents (4.20) were successfully added across unactivated olefin substrates to generate 1,2-bis(boronate)esters 4.21 in 56-82% yield. This transformation represents very rare reactivity between a nucleophilic reagent and an electron-rich substrate.

\textit{Scheme 4.12}. Fernández Lewis Base Promoted Diboration of Alkenes

\[
\begin{align*}
\text{R} & \quad + \quad (\text{RO})_2\text{B-B(OR)}_2 \\
\text{MeOH, THF} & \quad \text{Cs}_2\text{CO}_3 \text{ or NaOtfBu (15 mol\%)} \\
70^\circ \text{C, 6 h} & \quad \text{B(OR)}_2 \\
\text{4.20} & \quad \text{B(OR)}_2 \\
\text{4.21} & \quad 56-82\% \text{ yield}
\end{align*}
\]

\textbf{4.2.4. Enantioselective Dihydroxylation of Alkenes.} While not a dimetallation reaction, another extremely powerful and widely utilized method to access enantioenriched 1,2-diols from alkene starting materials is the Sharpless asymmetric dihydroxylation reaction.\textsuperscript{13} This transformation utilizes catalytic osmium in the presence of dihydroquinidine-derived ligands. The most effective substrates for the dihydroxylation reaction are 1,1-disubstituted, \textit{trans}-1,2-disubstituted, and trisubstituted olefins. Because all of these substrates require similar reaction conditions and choice of


ligand, it was possible to create a premixed reaction system that contains all of the reactants, known as AD-mix, which is commercially available. However, when monosubstituted alkenes are subjected to the reaction conditions using the commercially available AD-mix, low levels of enantioselection are observed for substrates not containing a conjugated aryl ring (Scheme 4.13).

**Scheme 4.13.** Sharpless Asymmetric Dihydroxylation of Terminal Alkenes with (DHQD)$_2$-PHAL (AD-mix)

\[
R\equiv \overset{\text{OsO}_4}{\text{K}_2\text{CO}_3, \ K_3\text{Fe(CN)}_6} \overset{(\text{DHQD})_2\text{PHAL}}{\text{OH}} \overset{\text{OH}}{\text{R}} 4.19 \quad R= \text{aryl: 98:2-99:1 er} \\
R= \text{alkyl: 68:32-92:8 er}
\]

![Diagram of 1,4-bis(dihydroquinidinyl)phthalazine (DHQD)$_2$PHAL (AD-mix)](image)

Sharpless and co-workers continued to survey dihydroquinidine-phthalazine ligands to enhance the enantioselectivity for terminal alkene substrates and in 1996 reported an improved ligand structure derived from dihydroquinidine-anthraquinone (Scheme 4.14).\(^\text{14}\) This new class of ligands successfully improved the level of

enantioselection in the dihydroxylation of aliphatic α-olefins, delivering the 1,2-diols 4.19 in 86:14-96:4 er. However, the enantiomeric purity of the corresponding aromatic olefins was significantly diminished. This highlights the need for a simple and general solution to the catalytic enantioselective difunctionalization of terminal alkenes.

Scheme 4.14. Sharpless Asymmetric Dihydroxylation of Terminal Alkenes with (DHQD)$_2$-AQN

4.3. Development of the Enantioselective Pt-Catalyzed 1,2-Diboration of Terminal Alkenes$^{15}$

Based on the success of the Pt-catalyzed enantioselective 1,2-diboration of both cis-1,3-dienes and 4,4-disubstituted dienes (4.24) to deliver enantoenriched terminal 1,2-

diols 4.26 (Scheme 4.15, eq. 1), it can be reasoned that the internal olefin of the 1,3-diene is not necessary for catalytic 1,2-diboration to occur. If that is the case, then the possibility exists for a Pt-catalyzed enantioselective diboration of simple monosubstituted alkene substrates. This transformation would produce terminal 1,2-bis(boronate)esters 4.28, which could be directly oxidized to access enantiomerically enriched 1,2-diols 4.29 (eq. 2).

Scheme 4.15. Potential for Pt-Catalyzed Enantioselective Diboration of α-Olefins

During the development of the enantioselective Pt-catalyzed 1,4-diboration of trans-1,3-dienes (Chapter 1), studies revealed that some ligand structures delivered a regioisomeric mixture of 1,4- and 1,2-diboration products. Considering the original research conducted by Miyaura⁸ and Smith⁹ on phosphine-free Pt-catalyzed diboration of terminal alkenes, it was crucial to determine whether the 1,2-diboration product arose from a background reaction with Pt(dba)₃ without the phosphine ligand bound, or if the Pt-ligand complex was capable of catalyzing 1,2-diboration of the terminal olefin. In that
regard, analysis of the 1,2-diboration product arising from the Pt-catalyzed diboration of
*trans*-1,3-pentadiene was carried out (Table 4.1). In the absence of a phosphine ligand, the “base-free” Pt(dba)$_3$ provided 91% yield of the 1,2-diboration product $4.31$ after heating to 80 °C in tetrahydrofuran for 14 h (entry 1). Employing the chiral BINOL-derived phosphoramidite ligand $(R,R)$-$4.32$, the 1,4-bis(boronate)ester $4.30$ was furnished in 17% yield with a 62:38 er, and the 1,2-bis(boronate)ester $4.31$ was obtained in 13% yield with a nearly racemic 52:48 er (entry 2). Due to the extremely low enantiomeric purity of $4.31$ the results of this experiment did not confirm that the Pt-ligand complex was responsible for the production of the 1,2-diboration product. However, in the presence of the TADDOL-derived phosphoramidite ligand $(R,R)$-$4.33$, the diboration of *trans*-1,3-pentadiene afforded 77% yield of the 1,4-diboration product $4.30$ in 70:30 er, and 21% yield of the 1,2-diboration product $4.31$ in 63:37 er (entry 3). The non-racemic reaction product observed with $(R,R)$-$4.33$ proved that the Pt-ligand complex was indeed responsible for catalyzing the 1,2-diboration pathway. This highlighted the potential for a Pt-catalyzed asymmetric 1,2-diboration of simple $\alpha$-olefins in the presence of chiral TADDOL-derived phosphine ligands.
Table 4.1. Analysis of the 1,2-Diboration Product from Pt-Catalyzed Diboration of trans-1,3-Pentadiene

<table>
<thead>
<tr>
<th>entry</th>
<th>ligand</th>
<th>% yield 4.30&lt;sup&gt;a&lt;/sup&gt;</th>
<th>er 4.30&lt;sup&gt;b&lt;/sup&gt;</th>
<th>% yield 4.31&lt;sup&gt;a&lt;/sup&gt;</th>
<th>er 4.31&lt;sup&gt;b&lt;/sup&gt;</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>none</td>
<td>0</td>
<td>-</td>
<td>91</td>
<td>-</td>
</tr>
<tr>
<td>2</td>
<td>(R,R)-4.32</td>
<td>17</td>
<td>62:38</td>
<td>13</td>
<td>52:48</td>
</tr>
<tr>
<td>3</td>
<td>(R,R)-4.33</td>
<td>77</td>
<td>70:30</td>
<td>21</td>
<td>63:37</td>
</tr>
</tbody>
</table>

<sup>a</sup>The isolated yield was determined by analysis of the 1,3-diol obtained by subjecting the intermediate bis(borate)ester to an allylation with benzaldehyde, followed by oxidation. <sup>b</sup>The er was determined by chiral GC analysis of the diboration/allylation/oxidation product.

Initial investigations for an enantioselective 1,2-diboration of monosubstituted alkenes began with a survey of the transition-metal catalyst in the diboration of 1-octene (Table 4.2). In accordance with the findings of Miyaura and Smith, the use of Pt(dba)<sub>3</sub> in the absence of a basic phosphine ligand provided 80% yield of the desired 1,2-diol 4.34 (entry 1). However, with the addition of 6 mol% of the achiral Lewis basic phosphine...
ligand PCy₃, the diboration of 1-octene proceeded smoothly to deliver 89% yield of the corresponding 1,2-diol (entry 2). Excitingly, the use of 3 mol% Pt(dba)₃ with 6 mol% of the chiral TADDOL-derived phosphonite ligand (R,R)-4.35 provided 1,2-diol 4.34 in 81% yield and 92:8 er (entry 3). Using a different Pt(0)-precatalyst, Pt₂(dba)₃, with chiral ligand (R,R)-4.35 generated the desired 1,2-diboration product in a comparable 94% yield and 90:10 er. Both Ni(0)- and Pd(0)-catalysts proved to be ineffective in the diboration of 1-octene (entries 5 and 6).

**Table 4.2. Transition-Metal Catalyst Survey for the 1,2-Diboration of 1-Octene**

<table>
<thead>
<tr>
<th>entry</th>
<th>metal (x mol%)</th>
<th>ligand</th>
<th>% yield</th>
<th>er</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Pt(dba)₃ (3 mol%)</td>
<td>-</td>
<td>80</td>
<td>-</td>
</tr>
<tr>
<td>2</td>
<td>Pt(dba)₃ (3 mol%)</td>
<td>PCy₃</td>
<td>89</td>
<td>-</td>
</tr>
<tr>
<td>3</td>
<td>Pt(dba)₃ (3 mol%)</td>
<td>(R,R)-4.35</td>
<td>81</td>
<td>92:8</td>
</tr>
<tr>
<td>4</td>
<td>Pt₂(dba)₃ (2.5 mol%)</td>
<td>(R,R)-4.35</td>
<td>94</td>
<td>90:10</td>
</tr>
<tr>
<td>5</td>
<td>Ni(COD)₂ (5 mol%)</td>
<td>PCy₃</td>
<td>0</td>
<td>-</td>
</tr>
<tr>
<td>6</td>
<td>Pd₂(dba)₃ (2.5 mol%)</td>
<td>PCy₃</td>
<td>0</td>
<td>-</td>
</tr>
</tbody>
</table>

*Percent yield of the isolated 1,2-diol. Enantioselectivity determined by GC analysis of a derivative using a chiral stationary phase*

Once the most effective transition-metal catalyst was selected, a survey of the reaction temperature was performed (Table 4.3). Often, lowering the temperature of a
catalytic reaction results in an increase in the enantioselectivity; however, the opposite trend was observed in the case of Pt-catalyzed diboration of 1-octene. When the reaction was carried out at 4 °C, the desired diboration product was isolated in less than 10% yield and with a 72:28 er (entry 1). Increasing the temperature not only improved the reactivity, and therefore the isolated yield, but the enantioselectivity also increased significantly, with the best results occurring at 60 °C (entry 4). The diminished selectivities may be due to the phosphine-free Pt-catalyzed background reaction, which produces the racemic diboration product. Heating the diboration may increase the amount of Pt-phosphine ligand complex by increasing the rate of dissociation of the dba ligands, therefore improving the enantioselectivity.

Table 4.3. Temperature Survey for Pt-Catalyzed 1,2-Diboration of 1-Octene

<table>
<thead>
<tr>
<th>entry</th>
<th>temp (°C)</th>
<th>% yield\textsuperscript{a}</th>
<th>er\textsuperscript{b}</th>
</tr>
</thead>
<tbody>
<tr>
<td>1\textsuperscript{c}</td>
<td>4</td>
<td>&lt; 10</td>
<td>72:28</td>
</tr>
<tr>
<td>2\textsuperscript{c}</td>
<td>25</td>
<td>37</td>
<td>81:19</td>
</tr>
<tr>
<td>3\textsuperscript{c}</td>
<td>40</td>
<td>85</td>
<td>90:10</td>
</tr>
<tr>
<td>4</td>
<td>60</td>
<td>81</td>
<td>92:8</td>
</tr>
<tr>
<td>5</td>
<td>80</td>
<td>98</td>
<td>91:9</td>
</tr>
</tbody>
</table>

\textsuperscript{a} Percent yield of isolated product. \textsuperscript{b} Enantioselectivity determined by GC analysis of a derivative using a chiral stationary phase. \textsuperscript{c} 2.0 equivalents of B\textsubscript{2}(pin)\textsubscript{2} used in the reaction.
Until this point, all Pt-catalyzed alkene diboration reactions were performed by pre-complexing \( \text{Pt(dba)}_3 \) with the TADDOL-derived phosphonite ligand in toluene for 1 h at room temperature in the glove box, followed by addition of \( \text{B}_2(\text{pin})_2 \) and 1-octene, then heating to the desired temperature. Both \(^1\text{H}\) and \(^{31}\text{P}\) variable temperature NMR experiments were carried out in order to determine if complexation of the platinum catalyst with the chiral phosphine ligand was occurring under the typical reaction conditions. The NMR experiments revealed that the TADDOL-derived ligand did not complex to the Pt(0) pre-catalyst at room temperature as indicated by a lack of chemical shift perturbation on mixing. However, heating appeared to form a Pt-ligand complex. Furthermore, an interesting observation was made that the rate of pre-complexation was increased upon addition of the diboron reagent. This may be due to diboration, and therefore dissociation, of the dba ligands. Based on these experiments, it was reasoned that diminished levels of enantioselectivity may have resulted from the presence of uncomplexed platinum, and that the conditions for the pre-complexation required modification. These results may also explain the difference in enantiomeric purity of the 1,4- and 1,2-bis(boronate)esters obtained from the Pt-catalyzed diboration of \( \text{trans-1,3-pentadiene} \) in the absence of sufficient Pt-ligand complexation (Table 4.1).

A systematic survey of the pre-complexation conditions was performed for the diboration of 1-octene using ligand \((R,R)-4.35\) (Table 4.4). The results for the diboration with the initial procedure are shown in entry 1, providing 1,2-diol \(4.34\) in 81% yield and 92:8 er. Increasing the amount of ligand relative to \( \text{Pt(dba)}_3 \) should drive the
complexation of the chiral ligand to the metal. Indeed, employing 3 mol% Pt(dba)$_3$ and 10 mol% (R,R)-4.35, while maintaining the temperature of the pre-complexation afforded the diboration product in an improved 98% yield and 94:6 er (entry 2). It was reasoned that if the successful pre-complexation of the Pt and ligand was carried out at elevated temperatures, the diboration reaction could be performed at room temperature with the possibility of enhanced enantiocontrol. Unfortunately, this strategy proved to be ineffective, and resulted in diminished isolated yields of the desired 1,2-diol with no improvement in the enantioselectivity (entries 3 and 4). Executing both the pre-complexation and diboration reaction at 60 °C in toluene showed significantly improved results, furnishing 1,2-diol 4.34 in 95% yield and 93:7 er (entry 5). The addition of B$_2$(pin)$_2$ to the pre-complexation mixture further increased the reactivity and enantioselectivity, and 1,2-diol 4.34 was obtained in 99% yield and 94:6 er (entry 6). Utilizing THF as the solvent for the pre-complexation and the diboration reaction also showed improved results with respect to reactivity and enantioselectivity (entries 7 and 8). However, combining the increased ligand loading (10 mol%) with the heated pre-complexation nearly shut down the diboration reaction and the desired product was generated in only 9% yield (entry 9). Collectively, the data suggested that the enantioselectivity of Pt-catalyzed diboration of terminal alkenes was significantly affected by the presence of phosphine-free Pt catalysts, and that pre-complexation of the metal and ligand at elevated temperatures was required.
Table 4.4. Optimization of Pt-Ligand Pre-complexation for the Diboration of 1-Octene

With the optimal reaction conditions in hand, a survey of TADDOL-derived phosphonite ligands was carried out (Table 4.5). Having previously determined that ligand \((R,R)-4.35\), the optimal ligand for the diboration of \textit{trans}-1,3-dienes, provided the desired 1,2-diol \(4.34\) in good levels of enantiopurity, the steric environment of the aryl rings on the TADDOL-backbone was manipulated to further improve the enantioselectivity. Smaller substitution led to a decrease in the level of enantioselection as seen with ligands \((R,R)-4.36\) and \((R,R)-4.37\) (entries 1 and 2). Increasing the size of the 3- and 5-substituents on the aryl rings from methyl to ethyl led to a notable improvement in enantioselectivity, with ligand \((R,R)-4.38\) delivering 1,2-diol \(4.34\) in
84% yield and 96:4 er (entry 4). However, if the substituents on the aryl rings were too large, the enantioselectivity was diminished to 90:10 er (entry 5). The TADDOL-derived phosphonite ligand \((R,R)-4.40\) containing the formaldehyde-derived ketal generated the 1,2-diboration product \(4.34\) with severely diminished enantiomeric purity (entry 6).

**Table 4.5.** TADDOL-Derived Phosphonite Ligand Survey for the Pt-Catalyzed Diboration of 1-Octene

<table>
<thead>
<tr>
<th>entry</th>
<th>ligand</th>
<th>Ar</th>
<th>R</th>
<th>% yield(^a)</th>
<th>er(^b)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>((R,R)-4.36)</td>
<td>Ph</td>
<td>Me</td>
<td>24</td>
<td>80:20</td>
</tr>
<tr>
<td>2</td>
<td>((R,R)-4.37)</td>
<td>3,5-(OMe)(_2)Ph</td>
<td>Me</td>
<td>76</td>
<td>90:10</td>
</tr>
<tr>
<td>3</td>
<td>((R,R)-4.35)</td>
<td>3,5-Me(_2)Ph</td>
<td>Me</td>
<td>81</td>
<td>92:8</td>
</tr>
<tr>
<td>3(^c)</td>
<td>((R,R)-4.35)</td>
<td>3,5-Me(_2)Ph</td>
<td>Me</td>
<td>87</td>
<td>94:6</td>
</tr>
<tr>
<td>4(^c)</td>
<td>((R,R)-4.38)</td>
<td>3,5-Et(_2)Ph</td>
<td>Me</td>
<td>84</td>
<td>96:4</td>
</tr>
<tr>
<td>5</td>
<td>((R,R)-4.39)</td>
<td>3,5-tBu(_2)Ph</td>
<td>Me</td>
<td>74</td>
<td>90:10</td>
</tr>
<tr>
<td>6(^c)</td>
<td>((R,R)-4.40)</td>
<td>3,5-Me(_2)Ph</td>
<td>H</td>
<td>ND</td>
<td>82:18</td>
</tr>
</tbody>
</table>

\(^a\) Percent yield of isolated product. \(^b\) Enantioselectivity determined by GC analysis of a derivative using a chiral stationary phase. \(^c\) Diboration carried out in THF with heated pre-complexation procedure.

TADDOL-derived phosphoramidite ligands were also surveyed in the Pt-catalyzed diboration reaction (Table 4.6). A variety of substitution patterns on both the aryl rings of the TADDOL backbone and the amine moiety were examined in the
diboration of 1-octene, however, none of the ligands delivered the desired 1,2-diol 4.34 with synthetically useful levels of enantiomeric purity. It was clear that the most effective ligand for the enantioselective Pt-catalyzed diboration of monosubstituted alkenes was the 3,5-diethylphenyl substituted TADDOL-derived ligand $(R,R)$-4.38.

Table 4.6. TADDOL-Derived Phosphoramidite Ligand Survey for the Pt-Catalyzed Diboration of 1-Octene

<table>
<thead>
<tr>
<th>entry</th>
<th>ligand</th>
<th>Ar</th>
<th>R</th>
<th>% yield$^a$</th>
<th>er$^b$</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>$(R,R)$-4.41</td>
<td>Ph</td>
<td>NMe$_2$</td>
<td>68</td>
<td>84:16</td>
</tr>
<tr>
<td>2</td>
<td>$(R,R)$-4.42</td>
<td>Ph</td>
<td>NEt$_2$</td>
<td>35</td>
<td>70:30</td>
</tr>
<tr>
<td>3</td>
<td>$(R,R)$-4.43</td>
<td>Ph</td>
<td>$\text{N}$</td>
<td>66</td>
<td>83:17</td>
</tr>
<tr>
<td>4</td>
<td>$(R,R)$-4.44</td>
<td>Ph</td>
<td>$\text{N}$</td>
<td>35</td>
<td>85:15</td>
</tr>
<tr>
<td>5</td>
<td>$(R,R)$-4.45</td>
<td>3,5-Me$_2$Ph</td>
<td>NMe$_2$</td>
<td>77</td>
<td>90:10</td>
</tr>
<tr>
<td>6$^c$</td>
<td>$(R,R)$-4.45</td>
<td>3,5-Me$_2$Ph</td>
<td>NMe$_2$</td>
<td>78</td>
<td>92:8</td>
</tr>
<tr>
<td>7</td>
<td>$(R,R)$-4.46</td>
<td>3,5-Me$_2$Ph</td>
<td>$\text{N}$</td>
<td>76</td>
<td>91:9</td>
</tr>
<tr>
<td>8</td>
<td>$(R,R)$-4.47</td>
<td>3,5-Me$_2$Ph</td>
<td>$\text{N}$</td>
<td>40</td>
<td>88:12</td>
</tr>
<tr>
<td>9</td>
<td>$(R,R)$-4.48</td>
<td>3,5-Bu$_2$Ph</td>
<td>NMe$_2$</td>
<td>40</td>
<td>78:22</td>
</tr>
</tbody>
</table>

$^a$ Percent yield of isolated product. $^b$ Enantioselectivity determined by GC analysis of a derivative using a chiral stationart phase. $^c$ Diboration run in THF
The nature of the diboron reagent was also examined in the diboration of 1-octene by employing bis(catecholato)diboron 4.11 in place of bis(pinacolato)diboron (Scheme 4.16). Unfortunately, both the reactivity and enantioselectivity suffered and the diboration product was delivered in only 17% yield and 81:19 er.

Scheme 4.16. Bis(catecholato)diboron in the Pt-Catalyzed Diboration of 1-Octene

The scope of the enantioselective Pt-catalyzed diboration was then investigated by preparing and testing a variety of monosubstituted alkene substrates.(Table 4.7). In addition to 1-octene, other aliphatic α-olefins participated in the diboration reaction in a highly enantioselective fashion in the presence of ligand (R,R)-4.38. Notably, the selectivity of the reaction was unaffected by the nature of the alkyl substituent with n-alkyl (entries 1 and 3) and α-quaternary substituted carbons (entries 5 and 6) being
equally tolerated. Substrates bearing protected oxygen functionality proceeded cleanly in the diboration reaction with excellent levels of enantioselection (entries 9 and 10). Remarkably, monosubstituted alkenes containing allylic oxygenation did not suffer from competing π-allyl chemistry, which as been documented in related transition-metal-catalyzed reactions between diboron reagents and allylic ethers (entry 9).\textsuperscript{16} It is also worth noting that the Pt-catalyzed diboration of allylic ethers only occurred in the presence of the chiral phosphonite ligand $(R,R)$-4.38; in its absence or with PC$_3$ as the ligand, the corresponding 1,2-diol product was not detected. As demonstrated in entry 8, the Pt-catalyzed diboration of styrene proceeded efficiently to afford the desired diboration/oxidation product in good yield and with useful levels of enantiomeric purity, highlighting the generality of this method for both aliphatic and aromatic alkene substrates. Under the previous described Rh/QUINAP catalyst system, styrene reacted with prohibitively low levels of enantioselectivity (67:33 er).\textsuperscript{11}

\begin{thebibliography}{16}
\end{thebibliography}
Table 4.7. Substrate Scope for Enantioselective Pt-Catalyzed Diboration of α-Olefins

<table>
<thead>
<tr>
<th>entry</th>
<th>alkene</th>
<th>product</th>
<th>% yield&lt;sup&gt;a&lt;/sup&gt;</th>
<th>er&lt;sup&gt;b&lt;/sup&gt;</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>C&lt;sub&gt;6&lt;/sub&gt;H&lt;sub&gt;13&lt;/sub&gt;CH=CH&lt;sub&gt;2&lt;/sub&gt;</td>
<td>C&lt;sub&gt;6&lt;/sub&gt;H&lt;sub&gt;13&lt;/sub&gt;CH=CH&lt;sub&gt;2&lt;/sub&gt;CH(OH)OH</td>
<td>83</td>
<td>96:4</td>
</tr>
<tr>
<td>2</td>
<td>MeCH=CHMe</td>
<td>MeCH=CHMeCH(OH)OH</td>
<td>77</td>
<td>97:3</td>
</tr>
<tr>
<td>3</td>
<td>PhCH=CHPh</td>
<td>PhCH=CHPhCH(OH)OH</td>
<td>80</td>
<td>97:3</td>
</tr>
<tr>
<td>4</td>
<td></td>
<td></td>
<td>87</td>
<td>97:3</td>
</tr>
<tr>
<td>5</td>
<td>MeCH=CHMe</td>
<td>MeCH=CHMeCH(OH)OH</td>
<td>46</td>
<td>95:5</td>
</tr>
<tr>
<td>6</td>
<td>p-tolylCH=CHMe</td>
<td>p-tolylCH=CHMeCH(OH)OH</td>
<td>52</td>
<td>94:6</td>
</tr>
<tr>
<td>7</td>
<td>PhCH=CHPh</td>
<td>PhCH=CHPhCH(OH)OH</td>
<td>86</td>
<td>97:3</td>
</tr>
<tr>
<td>8</td>
<td>PhCH=CHPh</td>
<td>PhCH=CHPhCH(OH)OH</td>
<td>84</td>
<td>93:7</td>
</tr>
<tr>
<td>9</td>
<td>TBDPSOCH=CHTBDPSO</td>
<td>TBDPSOCH=CHTBDPSOCH(OH)OH</td>
<td>93</td>
<td>95:5&lt;sup&gt;c&lt;/sup&gt;</td>
</tr>
<tr>
<td>10</td>
<td>TBDPSOCH=CHTBDPSO</td>
<td>TBDPSOCH=CHTBDPSOCH(OH)OH</td>
<td>92</td>
<td>95:5</td>
</tr>
</tbody>
</table>

<sup>a</sup> Percent yield of isolated product, average of at least two experiments.  
<sup>b</sup> Enantioselectivity determined by GC analysis of a derivative using a chiral stationary phase.  
<sup>c</sup> Oxidation performed with H<sub>2</sub>O<sub>2</sub> in pH7 buffer. Racemization by silyl transfer occurs under basic conditions.
The Pt-catalyzed diboration of cyclic and acyclic internal olefins was also examined using ligand \((R,R)-4.38\) (Table 4.8). Unfortunately, non-conjugated internal alkenes proved to be unreactive in the diboration reaction. Both cis and trans disubstituted alkenes failed to provide detectable amounts of the corresponding diboration/oxidation products (entries 1 and 2). Almost all of the starting alkene was recovered when employing a non-volatile substrate (entry 2). Surprisingly, norbornene, which contains a strained internal olefin, did not generate the desired diboration product under the catalysis of either Pt(dba)\(_3\) or Pt(nbe)\(_3\) (entry 4). The terminal alkene substrate bearing an unprotected hydroxyl group did react, but was fully converted to an unknown product (entry 5).
Table 4.8. Unreactive Internal Alkene Substrates in Pt-Catalyzed Diboration

<table>
<thead>
<tr>
<th>entry</th>
<th>substrate</th>
<th>product</th>
<th>%yield</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Me</td>
<td>Me</td>
<td>no desired product</td>
</tr>
<tr>
<td>2</td>
<td>TBDPSO</td>
<td>TBDPSO</td>
<td>no desired product</td>
</tr>
<tr>
<td>3</td>
<td></td>
<td></td>
<td>no desired product</td>
</tr>
<tr>
<td>4</td>
<td></td>
<td></td>
<td>no desired product</td>
</tr>
<tr>
<td>5</td>
<td>HO</td>
<td>HO</td>
<td>no desired product</td>
</tr>
</tbody>
</table>

*Recovered >95% of the starting material. b Starting material converted to unknown product.*

4.4. Synthetic Utility of the Pt-Catalyzed Enantioselective 1,2-Diboration of Terminal Alkenes

4.4.1. Decreased Catalyst Loading. In order for a catalytic method to be synthetically useful on an industrial scale, the use of benign reaction solvents and extremely low catalysts loadings are required. In that regard, the Pt-catalyzed diboration of 1-octene was carried out in ethyl acetate with catalyst loadings of < 1 mol% (Table
4.9). Excitingly, the reactivity of the catalyst was maintained under these conditions and the desired 1,2-diol 4.34 was generated in 87% yield with only 0.6 mol% Pt(dba)₃ and 1.2 mol% \((R,R)-4.38\) (entry 1). However, the enantiomeric purity of the diboration product was slightly diminished in EtOAc relative to THF. Similar results were observed when further lowering the catalyst loading to 0.3 mol% Pt(dba)₃ and 0.6 mol% \((R,R)-4.38\) (entry 2).

**Table 4.9. Decreased Catalyst Loading for Pt-Catalyzed Enantioselective Diboration of 1-Octene**

<table>
<thead>
<tr>
<th>entry</th>
<th>x mol%</th>
<th>y mol%</th>
<th>% yield</th>
<th>er&lt;sup&gt;b&lt;/sup&gt;</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>0.6</td>
<td>1.2</td>
<td>87</td>
<td>94:6</td>
</tr>
<tr>
<td>2</td>
<td>0.3</td>
<td>0.6</td>
<td>83</td>
<td>92:8</td>
</tr>
</tbody>
</table>

<sup>a</sup> Percent yield is isolated product. <sup>b</sup> Enantioselectivity determined by GC analysis of a derivative using a chiral stationary phase.

### 4.4.2. Matteson Homologation.

An important feature of diboration is that it offers the ability to access a diverse range of products from a single intermediate. In addition to the terminal 1,2-diols generated using Pt-catalyzed diboration of \(\alpha\)-olefins, this synthetic strategy provides a novel approach to access enantioenriched 1,4-diols utilizing the
Matteson homologation procedure.\textsuperscript{17} Subsequent to the Pt-catalyzed diboration of 1-octene, the reaction mixture was cooled to $-78 \, ^\circ\text{C}$ and subjected to 2 equivalents of LiCH$_2$Cl (Scheme 4.17). These conditions led to a single methylene insertion into each carbon-boron bond of 4.49 without the production of any bis-homologated products. Upon oxidative workup, the corresponding 1,4-diol 4.50 was afforded in 84% yield and 96:4 er. Importantly, the tandem diboration/homologation/oxidation could be carried out in a single reaction flask. This sequence represents the first and only method to directly synthesize enantioenriched 1,4-diols from terminal alkene substrates.

\textit{Scheme 4.17.} Pt-Catalyzed Alkene Diboration to Access Enantioenriched 1,4-Diols Through the Use of Matteson Homologation

\begin{center}
\begin{tikzpicture}
\node (a) at (0,0) {hexyl $\underbrace{\text{THF, 60 \, ^\circ\text{C, 12 h}}}$ Then H$_2$O$_2$, NaOH};
\node (b) at (2,0) {Pt(dba)$_3$ (3 mol\%) (\textit{R,R})-4.38 (6 mol\%) B$_2$(pin)$_2$ (1.05 equiv)};\node (c) at (4,0) {hexyl $\underbrace{\text{B(pin)}}$ \text{B(pin)}};\node (d) at (6,0) {2) CH$_2$BrCl n-BuLi, $-78 \, ^\circ\text{C}$};\node (e) at (8,0) {3) H$_2$O$_2$, NaOH};\node (f) at (10,0) {hexyl $\underbrace{\text{OH)}}$ \text{OH}};\node (g) at (0,-2) {4.49 96:4 er};\node (h) at (2,-2) {4.50 84\% yield, 96:4 er (single flask reaction)};\node (i) at (2.5,-4) {4.38 $\text{(R,R)}$ \text{Ar}};\node (j) at (3,-4) {4.38 $\text{Ar}$ \text{Ar} \text{Ar} \text{Ar} \text{Ar} \text{R} \text{R} \text{P-Ph}};\node (k) at (2,-5) {Ar = 3,5-diethylphenyl};\end{tikzpicture}
\end{center}

4.5. Further Optimization of the Pt-Catalyzed Enantioselective 1,2-Diboration of Terminal Alkenes

One potential disadvantage for the use of transition-metal catalysis in the development of enantioselective methods is that low oxidation state metals are often air sensitive and require the use of a glove-box with an inert atmosphere to avoid catalyst degradation. Industrial scale processes cannot accommodate such restrictions, and the development of methods that can be successfully carried out on the bench-top are therefore extremely valuable.

Pt(0) catalysts and phosphonite ligands are known to be air sensitive, especially in solution. However, Pt(dba)$_3$ and the TADDOL-derived phosphonite ligands that are used in Pt-catalyzed diboration are prepared on the bench-top without the need for rigorously deoxygenated or dried reagents. Therefore, it was reasoned that the enantioselective diboration could also be carried out on the bench-top and a variety of reaction conditions were examined (Table 4.10). Performing the entire reaction outside the glove-box in a scintillation vial exposed to air led to diminished yield and enantioselectivity, providing the desired 1,2-diol in 58% yield and 82:18 er (entry 2). Fortunately, both the reactivity and enantioselectivity were maintained when the diboration was carried out in either a Schlenk tube or a vial with a septum cap under nitrogen atmosphere (entries 3 and 4), proving that the glove box was not required to achieved synthetically useful levels of enantioinduction.
In collaboration with fellow graduate student Ryan Coombs, extensive additional optimization of the reaction conditions (ligand structure, substrate concentration, metal:ligand ratio, catalyst loading, and reaction time) was conducted and revealed improved conditions for “glove-box free” Pt-catalyzed diboration (Scheme 4.18). Using 1-tetradecene as a test substrate, it was determined that the catalyst loading could be dropped to 1 mol% Pt(dba)$_3$ and 1.2 mol% ligand (R,R)-4.51 to achieve excellent yields of 1,2-diol 4.52 in 97:3 er. Additionally, the reaction time was dramatically reduced to 2 h with a substrate concentration of 1.0 M in THF.

<table>
<thead>
<tr>
<th>entry</th>
<th>conditions</th>
<th>% yield$^a$</th>
<th>er$^b$</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>glove box</td>
<td>83</td>
<td>96:4</td>
</tr>
<tr>
<td>2</td>
<td>scintallation vial (exposed to air)</td>
<td>58</td>
<td>82:18</td>
</tr>
<tr>
<td>3</td>
<td>Schlenk tube (under N$_2$ atm)</td>
<td>74</td>
<td>95:5</td>
</tr>
<tr>
<td>4</td>
<td>vial with septum cap (under N$_2$ atm)</td>
<td>81</td>
<td>96:4</td>
</tr>
</tbody>
</table>

$^a$ Percent yield is isolated product. $^b$ Enantioselectivity determined by GC analysis of a derivative using a chiral stationary phase.

Table 4.10. Pt-Catalyzed Diboration of 1-Octene Outside the Glove Box
**Scheme 4.18.** Improved Reaction Conditions for the Enantioselective Pt-Catalyzed Diboration of 1-Tetradecene

Conducting GC analysis on the reaction progress of the Pt-catalyzed diboration of 1-tetradecene confirmed near complete conversion of the starting alkene to the desired 1,2-bis(boronate)ester product after 2 h at 60 °C (Figure 4.1).

**Figure 4.1.** Reaction Progress of Pt-Catalyzed Diboration of 1-Tetradecene by GC Analysis

Figure 4.1. Diboration carried out on the bench-top as follows: 1-tetradecene (2.55 mmol), B₂(pin)₂ (2.67 mmol), Pt(dba)₃ (25.5 µmol), (R,R)-4.51 (30.6 µmol) in THF (2.5 mL) at 60 °C, aliquots taken every 10 min. a) [1-Tetradecene] vs. time (disappearance of starting material). b) % conversion to 1,2-bis(boronate)ester product.
With the improved conditions for the enantioselective Pt-catalyzed alkene diboration selected, expansion of the substrate scope was next investigated (Table 4.11). A variety of aliphatic monosubstituted alkenes reacted with excellent levels of selectivity to furnish enantioenriched terminal 1,2-diols in good yields. It is noteworthy that substrates containing ester, amide and ketone functionality were tolerated in the diboration reaction (entries 3-5). Interestingly, 2-methyl-1,5-hexadiene reacted with excellent levels of chemoselectivity in favor of the terminal olefin to deliver the corresponding 1,2-diol in 83% yield and 97:3 er (entry 8). This represents the opposite sense of reactivity compared to the Sharpless asymmetric dihydroxylation, where dihydroxylation of the 1,1-disubstituted alkene is the major product (5:1 chemoselectivity, 42% combined yield, 87:13 er). Remarkably, the Pt-catalyzed diboration demonstrated impressive levels of catalyst control in the diboration of chiral alkene substrates. The alkene derived from (S)-citronellal was examined in the diboration reaction with both (R,R)-4.51 and (S,S)-4.51 as the chiral ligand, and each diastereomer of the diboration product was delivered in good yield and >20:1 dr (entries 9 and 10).
Table 4.11. Improved Enantioselective Pt-Catalyzed Diboration of Aliphatic α-Olefins

<table>
<thead>
<tr>
<th>entry</th>
<th>alkene</th>
<th>product</th>
<th>% yield (^a)</th>
<th>er (^b)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>hexyl</td>
<td>hexyl</td>
<td>81</td>
<td>96:4</td>
</tr>
<tr>
<td>2</td>
<td>dodecyl</td>
<td>dodecyl</td>
<td>79</td>
<td>96:4</td>
</tr>
<tr>
<td>3(^c)</td>
<td>MeO</td>
<td>MeO</td>
<td>74</td>
<td>96:4</td>
</tr>
<tr>
<td>4(^c)</td>
<td>Et(_2)N</td>
<td>Et(_2)N</td>
<td>76</td>
<td>96:4</td>
</tr>
<tr>
<td>5</td>
<td>Me</td>
<td>Me</td>
<td>53</td>
<td>94:6</td>
</tr>
<tr>
<td>6</td>
<td>Cy</td>
<td>Cy</td>
<td>81</td>
<td>96:4</td>
</tr>
<tr>
<td>7</td>
<td>TBDPSO</td>
<td>TBDPSO</td>
<td>91</td>
<td>95:5</td>
</tr>
<tr>
<td>8</td>
<td></td>
<td></td>
<td>83</td>
<td>97:3</td>
</tr>
<tr>
<td>9</td>
<td>Me</td>
<td>Me</td>
<td>80</td>
<td>&gt;20:1 dr</td>
</tr>
<tr>
<td>10(^d)</td>
<td>Me</td>
<td>Me</td>
<td>73</td>
<td>&gt;20:1 dr</td>
</tr>
<tr>
<td>11</td>
<td>Ph</td>
<td>Ph</td>
<td>85</td>
<td>97:3</td>
</tr>
<tr>
<td>12</td>
<td>Ph</td>
<td>Ph</td>
<td>78</td>
<td>96:4</td>
</tr>
<tr>
<td>13(^e)</td>
<td>Ph</td>
<td>Ph</td>
<td>83</td>
<td>94:6</td>
</tr>
</tbody>
</table>

\(^a\) Percent yield of isolated product, average of at least two experiments. \(^b\) Enantioselectivity determined by GC, HPLC or SFC analysis of a derivative using a chiral stationary phase. \(^c\) Oxidation performed with \(\text{H}_2\text{O}_2\) in pH 7 buffer. \(^d\) \((S,S)-4.51\) used as the ligand for the diboration reaction. \(^e\) Reaction run for 12 h.
The Pt-catalyzed diboration of aromatic alkenes was also investigated (Table 4.12). In general, aryl substituted olefins reacted with slightly lower levels of enantioselectivity as compared with aliphatic olefins. The steric environment of the phenyl ring adjacent to the olefin appeared to have a significant impact on the level of stereocontrol. The diboration 2-methylstyrene provided the corresponding diol is 79% yield and only 89:11 er (entry 2). Less encumbered aryl substituents, such as 2-methylstyrene and 4-methylstyrene gave comparable levels of enantioselectivity compared to the parent styrene substrate (entries 3 and 4). Electron-donating substituents on the aryl ring did not seem to affect the level of enantioselectivity, with meta- and para-methoxystyrene providing the corresponding 1,2-diols in 70% yield, 93:7 er and 72% yield, 95:5 er respectively (entries 5 and 6). Unfortunately, electron-withdrawing groups, such as trifluoromethyl had a negative effect on the enantioselectivity of the diboration reaction (entries 7 and 8). Notably, the Pt-catalyzed diboration of indene failed to produce any of the desired 1,2-diol, further illustrating the high levels of selectivity of the catalyst system for monosubstituted alkenes (entry 9).
Table 4.12. Improved Enantioselective Pt-Catalyzed Diboration of Aromatic α-Olefins

\[
\begin{align*}
\text{Pt(dba)}_3 \text{ (1.0 mol\%)} & \quad \text{(R,R)-4.51} \text{ (1.2 mol\%)} \\
\text{B}_2\text{(pin)}_2 \text{ (1.05 equiv)} & \quad \text{THF, 60 ºC, 12 h} \\
& \quad \text{then H}_2\text{O}_2, \text{ NaOH}
\end{align*}
\]

<table>
<thead>
<tr>
<th>entry</th>
<th>alkene</th>
<th>product</th>
<th>% yield&lt;sup&gt;a&lt;/sup&gt;</th>
<th>er&lt;sup&gt;b&lt;/sup&gt;</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Me</td>
<td>MeOH</td>
<td>83</td>
<td>94:6</td>
</tr>
<tr>
<td>2</td>
<td>Me</td>
<td>MeOH</td>
<td>79</td>
<td>89:11</td>
</tr>
<tr>
<td>3</td>
<td>MeO</td>
<td>MeOHOH</td>
<td>82</td>
<td>94:6</td>
</tr>
<tr>
<td>4</td>
<td>Me</td>
<td>MeOH</td>
<td>70</td>
<td>93:7</td>
</tr>
<tr>
<td>5</td>
<td>MeO</td>
<td>MeOHOH</td>
<td>70</td>
<td>92:8</td>
</tr>
<tr>
<td>6</td>
<td>MeO</td>
<td>MeOHOH</td>
<td>72</td>
<td>95:5</td>
</tr>
<tr>
<td>7</td>
<td>F&lt;sub&gt;3&lt;/sub&gt;C</td>
<td>F&lt;sub&gt;3&lt;/sub&gt;COH</td>
<td>61</td>
<td>90:10</td>
</tr>
<tr>
<td>8</td>
<td>F&lt;sub&gt;3&lt;/sub&gt;C</td>
<td>F&lt;sub&gt;3&lt;/sub&gt;COH</td>
<td>76</td>
<td>90:10</td>
</tr>
<tr>
<td>9</td>
<td></td>
<td></td>
<td>0</td>
<td></td>
</tr>
</tbody>
</table>

<sup>a</sup> Percent yield of isolated product, average of at least two experiments.  
<sup>b</sup> Enantioselectivity determined by GC, HPLC or SFC analysis of a derivative using a chiral stationary phase.

To learn more about the catalyst geometry and gain insight into a possible stereochemical model, it was of great interest to obtain crystallographic data of Pt-ligand complexes. In this regard, several Pt-TADDOL ligand complexes were synthesized and subjected to crystallization; however, only one complex was successfully analyzed by X-ray crystallography (Scheme 4.19). Treating the xylyl-TADDOL-derived phosphonite ligand \((R,R)\)-4.35 with platinum(II)-chloride provided complex 4.52 in quantitative yield after 24 h. X-ray analysis revealed the crystal structure shown in Figure 4.2, with two ligands bound to the Pt center in a trans configuration. Although it is hypothesized that the active catalyst in Pt-catalyzed diboration consists of a monoligated Pt-bis(boryl) complex, the crystal structure obtained confirms the influence of the aryl rings on the TADDOL-backbone on the steric environment around the Pt center.

Scheme 4.19. Preparation of a Pt(II)-Ligand Complex for X-Ray Analysis
Structural information regarding the active Pt-bis(boryl) complex would be paramount to the analysis of the reaction mechanism and stereochemical model. Preliminary experiments using stoichiometric amounts of Pt(nbe)$_3$ and ligand (R,R)-4.35 in the presence of both B$_2$(pin)$_2$ and B$_2$(cat)$_2$ provided promising results in the preparation of the desired Pt-bis(boryl) complexes (Scheme 4.20). Unfortunately, crystallization of these complexes was met with limited success. Interestingly, it was found by $^{31}$P NMR that oxidative addition of the Pt-(R,R)-4.35 complex into B$_2$(cat)$_2$ was faster than oxidative addition into B$_2$(pin)$_2$. 
Scheme 4.20. Preparation of Pt-bis(boryl) Complexes with B\(_2\)(pin)\(_2\) and B\(_2\)(cat)\(_2\)

With the limited crystallographic data obtained, it was difficult to determine a convincing stereochemical model; however, Scheme 4.21 represents our hypothesis based on experimental data and the crystal structure of complex 4.52. It is widely accepted that oxidative addition of Pt-ligand complexes delivers cis-bis(boryl) species. Given the size of the TADDOL-derived phosphonite ligands, it is unlikely that two ligands are coordinated to Pt in a cis configuration in the bis(boryl) complex. With a single ligand bound, the square planar Pt(II)-complex 4.55 has an open coordination site for the substrate to bind. We propose that coordination of the substrate is rapid and reversible, and that insertion of the substrate into the Pt-B bond is the stereochemical determining step. Given the steric bulk of the chiral TADDOL-derived ligand, the insertion likely
occurs when the substituent on the substrate is positioned away from the ligand (4.56). If the substituent is placed on the side adjacent to the large ligand, an unfavorable steric interaction may take place (4.57). The collective data from ligand surveys in the optimization of all the Pt-catalyzed diborations discussed in Chapters 1-4 suggest that the sterics of the ligand have the most significant impact on the level of enantioselectivity. Insertion from 4.56, would then form the internal C-B bond first and the less hindered, terminal C-Pt bond. Subsequent reductive elimination would deliver 1,2-bis(boronate) ester 4.58 as the major enantiomer with the C-B bond in the (S)-configuration, which is the observed enantiomer of product in the alkene diboration reaction. It is noteworthy that an analogous stereochemical model can be applied to the Pt-catalyzed diboration of 1,3-dienes as well to explain the major enantiomer obtained from the reaction.

Scheme 4.21. Proposed Stereochemical Model for Enantioselective Pt-Catalyzed Diboration
It is important to state that several uncontrollable variables exist in the
determination of a stereochemical model for enantioselective Pt-catalyzed diboration of
unsaturated hydrocarbons. First, the use of the crystal structure obtained from complex
4.52 does not closely represent the hypothesized active catalyst. With two TADDOL-
ligands bound to Pt(II) in the *trans* configuration, the ligands are likely positioned in a
much different fashion than they would be in a *cis*-configured Pt-bis(boryl) complex.
Second, the X-ray structure does not account for unhindered rotation about the Pt-P bond,
which would further change the orientation of the aryl groups on the TADDOL-
backbone. Furthermore, in the proposed stereochemical model, the formation of the
stereocenter occurs far removed from the chiral ligand. However, it is possible that the
stereocenters of the ligand position the aryl groups on the TADDOL-backbone in such a
way that there is a gearing effect of the pinacol groups on boron. This might thereby
affect the level of stereocontrol in the diboration reaction.

The determination of kinetic parameters for Pt-catalyzed diboration would also be
invaluable for further understanding the mechanistic details of the reaction. In that regard,
experiments were initiated to determine the heat of the reaction over time using
calorimetry in the diboration of 1-tetradecene. Having utilized multiple sources of Pt(0)
in the diboration of several unsaturated substrates, it was of interest to determine which
pre-catalyst was the most reactive. The diboration of 1-tetradecene was carried out in the
calorimeter employing ligand *(R,R)-4.51* in the presence of Pt(dba)₃, Pt₂(dba)₃, and Pt
(nbe)₃ (Figure 4.3). Based on the heat of the reaction curves, it is clear that all three Pt(0)-
sources are similar, but the diboration using Pt(dba)$_3$ is complete before the other Pt(0)-
sources. It would be interesting to also determine the difference in reaction rate using
different diboron sources, as well as the differences between aryl and alkyl substituted
substrates.

Figure 4.3. Comparison of Pt(0) Sources by Calorimetry in the Diboration of 1-
Tetradecene
Future kinetics experiments should involve the determination of the rate law and reaction order. The “different excess protocol” developed by Donna Blackmond\textsuperscript{18} would allow us to gain the insight into the kinetics of the reaction that we desire, while minimizing the number of experiments necessary to do so. Calorimetry is a typical method used to carry out reaction progress kinetic analysis; however, it is a global measurement and does not differentiate side reactions or other catalytic pathways from the desired reaction. The use of calorimetry for the kinetic analysis of the Pt-catalyzed alkene diboration reaction was complicated by the fact that \textasciitilde5\% of the hydroboration product is formed in addition to the diboration product. Additionally, it was determined that Pt(dba)\textsubscript{3} is capable of catalyzing the isomerization of 1-tetradecene to 2-tetradecence. Determination of the absolute kinetic data for the Pt-catalyzed diboration reaction is then further complicated because the heat of the side reactions is unknown. The combination of calorimetry with either GC analysis or ReactIR would allow for structural determination of the products being formed in the reaction. The power of such methods warrants further investigation into the kinetics of the Pt-catalyzed diboration of terminal alkenes and 1,3-dienes. The knowledge gained from future experiments would potentially allow for predictive ability in the diboration of other substrate classes and would greatly impact the utility of enantioselective diboration in general.

4.7. Conclusions.

The Pt-catalyzed enantioselective 1,2-diboration of monosubstituted alkenes was developed with the use of TADDOL-derived phosphonite ligands to generate 1,2-bis (boronate)esters. Subsequent oxidation afforded the corresponding terminal 1,2-diols in excellent yields and enantioselectivities for both aliphatic and aromatic substrates. The catalyst loading was successfully reduced to 0.6 mol% Pt(dba)$_3$ while maintaining useful reactivity and enantioselectivity. Pt-catalyzed alkene diboration offers a novel approach to access enantioenriched 1,4-diols from $\alpha$-olefins utilizing Matteson homologation of the intermediate 1,2-bis(boronate)ester. Progress toward preparation and crystal structure analysis of important Pt-complexes has been made, and efforts in that area are ongoing.
4.8. Experimentals.

4.8.1. General Information. $^1$H NMR spectra were recorded on Varian Unity Inova 500 MHz and Varian Gemini 400 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, integration, multiplicity ($s =$ singlet, $d =$ doublet, $t =$ triplet, $q =$ quartet, br = broad, $m =$ multiplet), coupling constants (Hz) and assignment. $^{13}$C{$^1$H}NMR spectra were recorded on Varian Unity Inova 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). $^{31}$P{$^1$H}NMR (162 MHz) were recorded on a Varian Unity Inova 400 spectrometer. Chemical shifts are reported for $^{31}$P NMR spectra using phosphoric acid as an external standard. Infrared (IR) spectra were recorded on a Bruker $\alpha$-P Spectrometer. Frequencies are reported in wavenumbers (cm$^{-1}$) as follows: strong (s), broad (br), medium (m), and weak (w). High-resolution mass spectrometry (ESI) was performed at Boston College, Chestnut Hill, MA. Elemental analysis was measured by Robertson Microlit Laboratories, Madison, NJ.

Liquid chromatography was performed using forced flow (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), and potassium permanganate (KMnO$_4$).
Analytical chiral gas-liquid chromatography (GLC) was performed on a Hewlett-Packard 6890 Series chromatograph equipped with a split mode capillary injection system, a flame ionization detector, and a Supelco β-Dex 120 column with helium as the carrier gas. Analytical chiral supercritical fluid chromatography (SFC) was performed on a Berger Instruments Supercritical Chromatograph equipped with an Alcott auto sampler and a Knauer UV detector with methanol as the modifier. Analytical chiral high-performance liquid chromatography (HPLC) was performed on a Shimadzu SCL-10A liquid chromatograph equipped with a UV detector and a Daicel Chiracel-OD column.

All reactions were conducted in oven- or flame-dried glassware under an inert atmosphere of nitrogen or argon. Tetrahydrofuran, dichloromethane, and diethyl ether were purified using Pure Solv MD-4 solvent purification system, from Innovative Technology, Inc., by passing the solvent through two activated alumina columns after being purged with argon. Ethyl acetate was distilled from calcium hydride and degassed. Triethylamine was distilled from calcium hydride. Potassium tetrachloroplatinate(II) was purchased from Acros Organics. Dibenzylideneacetone was purchased from Oakwood Chemicals. Tetrabutylammonium chloride was purchased from Fluka. Sodium acetate was purchased from Fisher Scientific. Bis(pinacolato)diboron was obtained from Allychem Co., Ltd. and recrystallized from pentane prior to use. Dichlorophenylphosphine was purchased from Strem Chemicals, Inc. and used without further purification. 1-octene, 4,4-dimethyl-1-pentene, 4-phenyl-1-butene, vinyl cyclohexane, 3,3-dimethyl-1-butene, allylbenzene, styrene, tert-butyldiphenylsilyl
chloride, imidazole, and bromochloromethane were purchased from Aldrich and used without further purification.

4.8.2. Preparation of Pt(dba)₃.

Tris(dibenzylideneacetone)platinum was prepared using the literature procedure with slight modification. To a three-neck 500 mL round-bottom flask equipped with a magnetic stir bar and reflux condenser was added dibenzylideneacetone (3.95 g, 16.80 mmol), tetrabutylammonium chloride (2.00 g, 7.20 mmol), and sodium acetate (3.55 g, 43.30 mmol). Methanol (210.0 mL) was added and the solution was warmed to 70 °C in an oil bath until the solids dissolved (5 minutes). In a separate 50 mL pear-shaped flask was added potassium tetrachloroplatinate (1.00 g, 2.41 mmol) and water (8.0 mL), and the mixture gently warmed until solids dissolved. The contents of the pear shaped flask were transferred to the three-neck flask and the reaction was allowed to stir at 70 °C for 3 h. After 3 h, the reaction was cooled to ambient temperature, transferred to a one-neck 500 mL round-bottom flask and concentrated by rotary evaporation to half the volume. The reaction mixture was then filtered on a Büchner funnel and the remaining solids were washed with copious amounts of water and methanol until all yellow dibenzylideneacetone crystals were removed. The resulting solid residue was placed under high vacuum for 24 hours to remove residual methanol and water. This procedure furnished a dark brown solid (1.84 g, 85%) consistent with Pt(dba)₃. Anal Calc’d for

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C₅₁H₄₂O₃Pt: C, 68.22; H, 4.71. Found: C, 67.09; H, 4.49 (average of two experiments).

Platinum analysis was performed by ICP Optical Emission Spectroscopy; calculated for Pt(dba)₃: 21.73% Pt; found 21.92% (average of two experiments).

4.8.3. Preparation of Pt₂(dba)₃

Tris(dibenzylideneacetone)diplatinum was prepared using the literature procedure.¹ To a two-neck 25 mL round-bottom flask equipped with a magnetic stir bar and reflux condenser was added dibenzylideneacetone (1.98 g, 8.43 mmol), tetrabutylammonium chloride (1.00 g, 3.61 mmol), and sodium acetate (1.78 g, 21.80 mmol). Methanol (102.0 mL) was added and the solution was warmed to 70 °C in an oil bath until the solids dissolved (5 minutes). In a separate 50 mL pear-shaped flask was added potassium tetrachloroplatinate (500.0 mg, 1.20 mmol) and water (6.3 mL), and the mixture gently warmed until solids dissolved. The contents of the pear shaped flask were transferred to the three-neck flask and the reaction was allowed to stir at 70 °C for 3 hours. After 3 h, the reaction was cooled to ambient temperature, transferred to a one-neck 500 mL round-bottom flask and concentrated by rotary evaporation to half the volume. The reaction mixture was then filtered on a Büchner funnel and the remaining solids were washed with copious amounts of water and methanol until all yellow dibenzylideneacetone crystals were removed. The solid product was then dissolved in hot tetrahydrofuran (100 mL) and filtered. The filtrate volume was reduced to 10 mL using rotary evaporation and then methanol (12 mL) was slowly added. After cooling the
solution to - 25 °C in the freezer for 1 h the crystallized product was isolated by filtration, washed with methanol (40 mL) and dried under vacuum to provide a black crystalline solid (348.9 mg, 53%). Anal Calc’d for C_{51}H_{42}O_{3}Pt_{2}: C, 56.04; H, 3.87. Found: C, 56.40; H, 3.73 (average of two experiments). Platinum analysis was performed by ICP Optical Emission Spectroscopy; calculated for Pt_{2}(dba)_{3}: 35.70% Pt; found 33.72% (average of two experiments).

4.8.4. Ligand Synthesis.

The following ligands were prepared using the literature procedures or as previously described and spectral data are in accordance with the literature: 4.32,^{2} (R,R)-4.33,^{3} (R,R)-4.35,^{4} (R,R)-4.36,^{5} (R,R)-4.37 (Chapter 1, Section 1.6.4.4), (R,R)-4.38 (Chapter 2, Section 2.6.5), (R,R)-4.39,^{4} (R,R)-4.40,^{6} (R,R)-4.41,^{7} (R,R)-4.42,^{4} (R,R)-4.44,^{7} (R,R)-4.48.^{8}

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4.8.5. Preparation of 1-Alkenes.

A. Preparation of allyloxy(tert-butyl)diphenylsilane (Table 4.7, entry 9). To a flame-dried, round bottom flask was added imidazole (3.52 g, 51.65 mmol). The flask was purged with nitrogen and charged with allyl alcohol (1.0 g, 17.23 mmol) and dichloromethane (34.4 mL). tert-Butyldiphenylsilyl chloride (13.4 mL, 51.65 mmol) and triethylamine (7.2 mL, 51.65 mmol) were added to the reaction mixture under nitrogen atmosphere and the reaction was allowed to stir at room temperature for 20 h. The reaction was then diluted with dichloromethane (30 mL) and washed with brine (15 mL). The layers were separated and the aqueous layer was extracted with dichloromethane (3 x 30 mL). The combined organics were dried over Na$_2$SO$_4$, filtered, and concentrated by rotary evaporation. The crude product was purified by column chromatography on SiO$_2$ (100% hexanes) to give the title compound as a clear, colorless liquid (4.39 g, 86% yield).

\begin{center}
\textbf{Allyloxy(tert-butyl)diphenylsilane (Table 4.7, entry 9).} $^1$H NMR (400 MHz, CDCl$_3$): $\delta$ 1.13 (9H, s), 4.26-4.28 (2H, m), 5.17 (1H, dd, $J = 10.8$ Hz, 2.0 Hz), 5.44 (1H, dd, $J = 16.8$ Hz, 2.8 Hz), 5.98 (1H, dddd, $J = 18.8$ Hz, 8.4 Hz, 4.0 Hz, 4.0 Hz), 7.40-7.49 (6H, m), 7.71-7.76 (4H, m); $^{13}$C NMR (100 MHz, CDCl$_3$): $\delta$ 19.3, 26.9, 64.6, 113.9, 127.6, 129.6, 133.6, 135.5, 136.9; IR (neat): 2931.3 (w), 2857.5 (m),
\end{center}
B. Preparation of (but-3-enyloxy)(tert-butyl)diphenylsilane. To a flame-dried, round bottom flask was added imidazole (2.83 g, 41.60 mmol). The flask was purged with nitrogen and charged with 3-buten-1-ol (1.0 g, 13.87 mmol) and dichloromethane (27.7 mL). tert-Butyldiphenylsilyl chloride (10.8 mL, 41.60 mmol) and triethylamine (5.8 mL, 41.60 mmol) were added to the reaction mixture under nitrogen atmosphere and the reaction was allowed to stir at room temperature for 20 h. The reaction was then diluted with dichloromethane (30 mL) and washed with brine (15 mL). The layers were separated and the aqueous layer was extracted with dichloromethane (3 x 30 mL). The combined organics were dried over Na$_2$SO$_4$, filtered, and concentrated by rotary evaporation. The crude product was purified by column chromatography on SiO$_2$ (100% hexanes) to give the title compound as a clear, colorless liquid (3.88 g, 90% yield).

(But-3-enyloxy)(tert-butyl)diphenylsilane. $^1$H NMR (400 MHz, CDCl$_3$): $\delta$ 1.19 (9H, s), 2.44 (2H, dd, $J = 13.2$ Hz, 6.4 Hz), 3.84 (2H, t, $J = 6.4$ Hz), 5.11-5.20 (2H, m), 5.95 (1H, dddd, $J = 16.8$ Hz, 10.0 Hz, 6.8 Hz, 6.8 Hz), 7.46-7.53 (6H, m), 7.80-7.82 (4H, m); $^{13}$C NMR (100 MHz, CDCl$_3$): $\delta$ 19.3, 26.9, 37.3, 63.5, 116.3, 127.6, 129.5, 133.9, 135.3, 135.5; IR (neat): 2930.5 (w), 2857.5 (w), 1427.4
(m), 1104.9 (s), 1087.7 (s), 910.6 (m), 822.4 (m), 736.3 (m), 698.8 (s) cm⁻¹; HRMS-(ESI⁺) for C₂₀H₂₇OSi [M+H]: calculated: 311.1831, found: 311.1834.

C. Preparation of (S)-4,8-dimethylnona-1,7-diene (Table 4.11, entry 9).

(S)-4,8-dimethylnona-1,7-diene (Table 4.11, entry 9). ¹H NMR (500 MHz, CDCl₃): δ 1.09-1.61 (1H, m), 1.29-1.36 (1H, m), 1.45-1.52 (1H, m), 1.58 (3H, s), 1.66 (3H, s), 1.83-1.90 (1H, m), 1.92-2.01 (2H, m), 2.03-2.08 (1H, m), 4.94-4.99 (2H, m), 5.06-5.09 (1H, m), 5.76 (1H, dddd, J = 17.5, 10.5, 7.5, 7.5 Hz); ¹³C NMR (125 MHz, CDCl₃): δ 17.7, 19.3, 25.6, 25.7, 32.4, 36.6, 41.3, 115.4, 124.8, 131.1, 137.7; IR (neat): 2955.0 (m), 2923.3 (s), 2853.8 (m), 1724.5 (w), 1458.7 (w), 1376.7 (w), 1272.0 (w) cm⁻¹; HRMS-(ESI⁺) for C₁₁H₂₁ [M+H]: calculated: 153.1643, found: 153.1639.

To an oven-dried 6-dram vial with magnetic stir bar in the dry box was added Pt(dba)$_3$ (18.3 mg, 20.4 µmol), (R,R)-3,5-diethylphenyl-TADDOLPPh (4.38) (32.0 mg, 40.1 µmol), B$_2$(pin)$_2$ (178.2 mg, 701.7 µmol) and tetrahydrofuran (6.7 mL, [substrate] = 0.1 M). The vial was sealed with a polypropylene cap, removed from the dry box, and heated to 80 °C in an oil bath for 30 min. The vial was cooled to room temperature, returned to the dry box and charged with 1-octene (75.0 mg, 668.8 µmol). The vial was sealed, removed from the dry box, and stirred at 60 °C for 12 h. The reaction mixture was cooled to 0 °C (ice/water) and charged with 3 M sodium hydroxide (2 mL), and 30% hydrogen peroxide (1 mL). The reaction was gradually warmed to room temperature and allowed to stir for 4 h at which time the vial was cooled to 0 °C (ice/water) and saturated aqueous sodium thiosulfate was added dropwise over 5 min. The reaction mixture was diluted with ethyl acetate and the aqueous and organic layers were separated. The aqueous layer was washed with ethyl acetate (3 x 15 mL). The combined organic layers were dried over Na$_2$SO$_4$, filtered, and concentrated by rotary evaporation. The crude reaction mixture was purified on silica gel (30-70% ethyl acetate/hexanes) to afford a clear, colorless oil (81.1 mg, 83% yield).
4.8.7. Characterization and Proof of Stereochemistry.

(S)-Octane-1,2-diol (Table 4.7, entry 1). The diboration was performed according to the representative procedure with 1-octene (75.0 mg, 668.8 µmol), Pt(dba)$_3$ (18.3 mg, 20.4 µmol), (R,R)-3,5-diethylphenylTADDOLPPh (4.38) (32.0 mg, 40.1 µmol), and B$_2$(pin)$_2$ (178.2 mg, 701.7 µmol) in tetrahydrofuran (6.7 mL, 0.1 M). The crude reaction mixture was purified on silica gel (30-70% ethyl acetate/hexanes, stain in KMnO$_4$) to afford a white solid (81.1 mg, 83% yield). Spectral data are in accordance with the literature. HRMS-(ESI+) for C$_8$H$_{19}$O$_2$ [M+H]: calculated: 147.1385, found: 147.1380. $[\alpha]_{D}^{20} = -1.538$ ($c = 0.784$, CHCl$_3$, $l = 50$ mm).

Proof of Stereochemistry:

The resulting 1,2-diol was treated with 2,2-dimethoxypropane and catalytic p-toluenesulfonic acid (below). The resulting ketal was compared to the racemic ketal of octane-1,2-diol prepared from dihydroxylation of 1-octene with osmium tetraoxide and 4-methylmorpholine N-oxide. The authentic (S)-isomer was prepared from the Sharpless asymmetric dihydroxylation of 1-octene utilizing AD-mix-$\alpha$.  

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Chiral GLC (β-dex, Supelco, 100 °C, 20 psi) – analysis of the acetonide of octane-1,2-diol
(S)-4,4-Dimethylpentane-1,2-diol (Table 4.7, entry 2). The diboration was performed according to the representative procedure with 4,4-dimethyl-1-pentene (75.0 mg, 763.8 µmol), Pt(dba)$_3$ (20.8 mg, 23.2 µmol), (R,R)-3,5-diethylphenylTADDOLPPh (3.48) (36.5 mg, 45.8 µmol), and B$_2$(pin)$_2$ (203.7 mg, 802.2 µmol) in tetrahydrofuran (7.6 ml, 0.1 M). The crude reaction mixture was purified on silica gel (30-70% ethyl acetate/hexanes, stain in KMnO$_4$) to afford a clear, colorless oil that could not be separated from pinacol (115.5 mg, 2:1 product:pinacol = 77% yield). Spectral data are in accordance with the literature.$^{11}$ HRMS-(ESI+) for C$_7$H$_{17}$O$_2$ [M+H]: calculated 133.1226, found: 133.1231.

**Proof of Stereochemistry:**

The resulting 1,2-diol was treated with benzoic anhydride, triethylamine and catalytic 4-(dimethylamino)pyridine (below). The resulting bis(benzoate) was compared to the racemic bis(benzoate) of 4,4-dimethylpentane-1,2-diol prepared from dihydroxylation of 4,4-dimethyl-1-pentene with osmium tetraoxide and 4-methylmorpholine N-oxide. The authentic (R)-isomer was prepared from the Sharpless asymmetric dihydroxylation of 4,4-dimethyl-1-pentene utilizing AD-mix-β.

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Chiral SFC (Chiracel OD-H, 0% MeOH, 3 mL/min, 150 bar, 50 °C, 220 nm) – analysis of the bis(benzoate) of 4,4-dimethylpentane-1,2-diol.

racemic  diboration product  authentic  coinjection of diboration product
(S)-4-Phenylbutane-1,2-diol (Table 4.7, entry 3). The diboration was performed according to the representative procedure with 4-phenyl-1-butene (75.0 mg, 571.6 µmol), Pt(dba)$_3$ (15.6 mg, 17.4 µmol), (R,R)-3,5-diethylphenylTADDOLPPh (3.48) (27.3 mg, 34.3 µmol), and B$_2$(pin)$_2$ (152.4 mg, 600.2 µmol) in tetrahydrofuran (5.72 mL, 0.1 M). The crude reaction mixture was purified on silica gel (30-70% ethyl acetate/hexanes, stain in KMnO$_4$) to afford a clear, colorless oil (81.7 mg, 86 % yield). Spectral data are in accordance with the literature.$^{12}$ HRMS-(ESI+) for C$_{10}$H$_{15}$O$_2$ [M+H]: calculated: 167.1072, found: 167.1077. $[^{13}]$D$^{20}$ = -16.240 (c = 1.143, CHCl$_3$, l = 50 mm).

Proof of stereochemistry:

The resulting 1,2-diol was treated with 2,2-dimethoxypropane and catalytic p-toluenesulfonic acid. The resulting ketal was compared to the racemic ketal of 4-phenylbutane-1,2-diol prepared from treatment of 4-phenyl-1-butene with osmium tetraoxide and 4-methylmorpholine N-oxide. The authentic (R)-isomer was prepared from the Sharpless asymmetric dihydroxylation of 4-phenyl-1-butene utilizing AD-mix-β.

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Chiral GLC (β-dex, Supelco, 100 °C, 20 psi) – analysis of the acetonide of 4-phenylbutane-1,2-diol.

racemic
diboration product
authentic
coinjection of diboration product + racemic
(S)-1-Cyclohexylethane-1,2-diol (Table 4.7, entry 4). The diboration was performed according to the representative procedure with vinyl cyclohexane (75.0 mg, 680.6 µmol), Pt(dba)$_3$ (18.6 mg, 20.7 µmol), (R,R)-3,5-diethylphenylTADDOLPPh (4.38) (32.5 mg, 40.8 µmol), and B$_2$(pin)$_2$ (181.5 mg, 714.6 µmol) in tetrahydrofuran (6.8 mL, 0.1 M). The crude reaction mixture was purified on silica gel (30-70% ethyl acetate/hexanes, stain in KMnO$_4$) to afford a clear, colorless oil (85.4 mg, 87% yield). Spectral data are in accordance with the literature.$^{13}$ HRMS-(ESI+) for C$_8$H$_{17}$O$_2$ [M+H]: calculated: 145.1229, found: 145.1222. $\left[\alpha\right]_{D}^{20} = +3.921$ (c = 0.510, CHCl$_3$, l = 50 mm).

**Proof of Stereochemistry:**

The resulting 1,2-diol was treated with 2,2-dimethoxypropane and catalytic p-toluenesulfonic acid. The resulting ketal was compared to the racemic ketal of 1-cyclohexylethane-1,2-diol prepared from treatment of vinyl cyclohexane with osmium tetraoxide and 4-methylmorpholine N-oxide. The authentic (R)-isomer was prepared from the Sharpless asymmetric dihydroxylation of vinyl cyclohexane utilizing AD-mix-β.

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Chiral GLC (Supelco β-dex, 130 °C, 20 psi) – analysis of the acetonide of 1-cyclohexylethane-1,2-diol.

racemic  
diboration product  
authentic
(S)-3,3-Dimethylbutane-1,2-diol (Table 4.7, entry 5). The diboration was performed according to the representative procedure with 3,3-dimethyl-1-butene (75.0 mg, 891.2 µmol), Pt(dba)$_3$ (24.4 mg, 27.1 µmol), (R,R)-3,5-diethylphenylTADDOLPPh (4.38) (42.6 mg, 53.5 µmol), and B$_2$(pin)$_2$ (237.6 mg, 935.8 µmol) in tetrahydrofuran (8.9 mL, 0.1 M). The crude reaction mixture was purified on silica gel (40-70% ether/pentane, stain in KMnO$_4$) to afford a clear, colorless oil that was inseparable from pinacol (193.7 mg, 1:3 product:pinacol = 46% yield). Spectral data are in accordance with the literature.$^{13}$ HRMS-(ESI+) for C$_6$H$_{15}$O$_2$ [M+H]: calculated: 119.1072, found: 119.1074.

**Proof of Stereochemistry:**

The title compound was compared to racemic 3,3-dimethylbutane-1,2-diol prepared from treatment of 3,3-dimethyl-1-butene with osmium tetraoxide and 4-methylmorpholine $N$-oxide. The absolute stereochemistry was assigned by analogy.
Chiral GLC (β-dex, Supelco, 90 °C, 20 psi) – analysis of 3,3-dimethylbutane-1,2-diol.

racemic

diboration product
(S)-3,3-Dimethyl-4-p-tolylbutane-1,2-diol (Table 4.7, entry 6). The diboration was performed according to the representative procedure with 3,3-dimethyl-4-(4-methylphenyl)-1-butene (75.0 mg, 430.3 µmol), Pt(dba)$_3$ (11.7 mg, 13.0 µmol), (R,R)-3,5-diethylphenylTADDOLPPh (4.38) (20.6 mg, 25.8 µmol) and B$_2$(pin)$_2$ (114.6 mg, 451.8 µmol) in tetrahydrofuran (4.3 mL, 0.1 M). The crude reaction mixture was purified on silica gel (30-70% ethyl acetate/hexanes) to afford a clear, colorless oil (46.6 mg, 52% yield). Spectral data are in accordance with the literature. HRMS-(ESI+) for C$_{13}$H$_{21}$O$_2$ [M+H]: calculated: 209.1542, found: 209.1545. $\alpha$$_{D}^{20}$ = -4.202 (c = 0.691, CHCl$_3$, l = 50 mm).

**Proof of Stereochemistry:**

The title compound was compared to the racemic 1,2-diol prepared from dihydroxylation of 3,3-dimethyl-4-(4-methylphenyl)-1-butene with osmium tetraoxide and 4-methylmorpholine N-oxide. The authentic (R)-isomer was prepared from the Sharpless asymmetric dihydroxylation of 3,3-dimethyl-4-(4-methylphenyl)-1-butene utilizing AD-mix-β.
Chiral SFC (Chiracel OD-H, 0.7% MeOH, 3 mL/min, 150 psi, 50 °C, 220 nm) – analysis of 3,3-dimethyl-4-p-tolylbutane-1,2-diol.

- racemic
- diboration product
- authentic
- coinjection of diboration product + racemic
(S)-3-Phenylpropane-1,2-diol (Table 4.7, entry 7). The diboration was performed according to the representative procedure with allylbenzene (75.0 mg, 634.6 µmol), Pt(dba)$_3$ (17.3 mg, 19.3 µmol), (R,R)-3,5-diethylphenylTADDOLPPh (4.38) (30.3 mg, 38.1 µmol), and B$_2$(pin)$_2$ (169.2 mg, 666.3 µmol) in tetrahydrofuran (6.3 mL, 0.1 M). The crude reaction mixture was purified on silica gel (30-70% ethyl acetate/hexanes, stain in KMnO$_4$) to afford a white solid (83.8 mg, 87% yield). $^1$H NMR (400 MHz, CDCl$_3$): δ 2.66-2.76 (2H, m), 2.83 (2H, br s), 3.44 (1H, dd, $J = 11.2$ Hz, 7.2 Hz), 3.61 (1H, dd, $J = 11.2$ Hz, 2.8 Hz), 3.85-3.90 (1H, m), 7.17-7.23 (3H, m), 7.26-7.30 (2H, m); $^{13}$C NMR (100 MHz, CDCl$_3$): δ 39.8, 65.9, 73.0, 126.5, 128.5, 129.3, 137.7; IR (neat): 3363.1 (br s), 2939.5 (w), 1495.8 (m), 1454.2 (m), 1089.7 (s), 1069.0 (s), 1030.6 (s), 745.3 (m), 699.6 (s) cm$^{-1}$; HRMS-(ESI+) for C$_8$H$_9$O$_1$ [M-H$_2$O+H]: calculated: 121.0653, found: 121.0657. $[\alpha]_D^{20} = -17.877$ (c = 0.576, CHCl$_3$, l = 50 mm).

Proof of Stereochemistry:

The title compound was compared to racemic 3-phenylpropane-1,2-diol prepared from treatment of allylbenzene with osmium tetraoxide and 4-methylmorpholine N-oxide. The authentic (R)-isomer was prepared from the Sharpless asymmetric dihydroxylation of allylbenzene utilizing AD-mix-β.
Chiral HPLC (Chiracel OD, 2.0% IPA, 1.5 mL/min, 220 nm)-analysis of 3-phenylpropane-1,2-diol.

racemic  
diboration product  
authentic
(S)-1-Phenylethane-1,2-diol (Table 4.7, entry 8). The diboration was performed according to the representative procedure with styrene (75.0 mg, 720.1 µmol), Pt(dba)$_3$ (19.7 mg, 21.9 µmol), (R,R)-3,5-diethylphenylTADDOLPh (3.48) (34.4 mg, 43.2 µmol), and B$_2$(pin)$_2$ (192.0 mg, 756.1 µmol) in tetrahydrofuran (7.2 mL, 0.1 M). The crude reaction mixture was purified on silica gel (30-70% ethyl acetate/hexanes, stain in KMnO$_4$) to afford a white solid (83.6 mg, 84% yield). Spectral data are in accordance with the literature.$^{13}$ HRMS-(ESI+) for C$_8$H$_9$O$_1$ [M-H$_2$O+H]: calculated: 121.0653, found: 121.0656. [$\alpha$]$_{D}^{20}$ = +53.883 ($c = 1.146$, CHCl$_3$, $l = 50$ mm).

Proof of Stereochemistry:

The title compound was treated with 2,2-dimethoxypropane and catalytic $p$-toluenesulfonic acid. The resulting ketal was compared to the racemic ketal of 1-phenylethane-1,2-diol prepared from treatment of styrene with osmium tetraoxide and 4-methylmorpholine $N$-oxide. The authentic (R)-isomer was prepared from the Sharpless asymmetric dihydroxylation of styrene utilizing AD-mix-β.
Chiral GLC (β-dex, Supelco, 140 °C, 20 psi) – analysis of the acetonide of 1-phenylethane-1,2-diol.

racemic  diboration product  authentic
(R)-3-(tert-Butyldiphenylsilyloxy)propane-1,2-diol (Table 4.7, entry 9). The diboration was performed according to the representative procedure with allyloxy(tert-butyl)diphenylsilane (75.0 mg, 250.3 µmol), Pt(dba)$_3$ (6.9 mg, 7.7 µmol), (R,R)-3,5-diethylphenylTADDOLPPh (4.38) (12.1 mg, 15.2 µmol), and B$_2$(pin)$_2$ (67.5 mg, 265.7 µmol) in tetrahydrofuran (2.5 mL, 0.1 M). The crude reaction mixture was purified on silica gel (20-30% ethyl acetate/hexanes) to afford a white solid (77.7 mg, 93% yield). R$_f$ = 0.39 (50% ethyl acetate/hexane, stain in KMnO$_4$); $^1$H NMR (400 MHz, CDCl$_3$): $\delta$ 1.05 (9H, s), 1.94 (1H, br s), 2.55 (1H, br s), 3.61-3.74 (4H, m), 3.76-3.82 (1H, m), 7.36-7.45 (6H, m), 7.62-7.65 (4H, m); $^{13}$C NMR (100 MHz, CDCl$_3$): $\delta$ 19.2, 26.9, 63.8, 65.2, 71.9, 127.8, 129.8, 132.8, 135.4; IR (neat): 3375.5 (br s), 2930.6 (m), 2857.8 (w), 1427.6 (m), 1111.7 (s), 823.7 (w), 740.3 (w), 701.6 (s) cm$^{-1}$; HRMS-(ESI+) for C$_{19}$H$_{30}$NO$_3$Si [M+NH$_4^+$]: calculated: 348.1995, found: 348.2000. $[^{\alpha}]$ $d^{20} = +1.836$ (c = 1.534, CHCl$_3$, l = 50 mm).

**Analysis of Stereochemistry:**

Absolute stereochemistry was assigned by analogy.
Chiral HPLC (Chiracel-OD, 2.0 % IPA, 1.5 mL/min, 220 nm) – analysis of the title compound.

racemic       diboration product

racemic       diboration product
(S)-4-(tert-Butyldiphenylsilyloxy)butane-1,2-diol (Table 4.7, entry 10). The diboration was performed according to the representative procedure with (but-3-enyloxy)(tert-butyl)diphenylsilane (100.0 mg, 322.1 µmol), Pt(db)₃ (8.8 mg, 9.8 µmol), (R,R)-3,5-diethylphenylTADDOLPPh (4.38) (15.4 mg, 19.3 µmol), and B₂(pin)₂ (85.9 mg, 338.2 µmol) in tetrahydrofuran (3.2 mL, 0.1 M). The crude reaction mixture was purified on silica gel (30-60% ethyl acetate/hexanes) to afford a clear, colorless oil that could not be separated from pinacol (137.1 mg, 1:1 product:pinacol = 92% yield). Rᵥ = 0.26 (50% ethyl acetate/hexane, stain in KMnO₄); ¹H NMR (400 MHz, CDCl₃): δ 1.03 (9H, s,), 1.59-1.66 (1H, m), 1.72-1.81 (1H, m), 3.50 (1H, dd, J = 11.2 Hz, 6.4 Hz), 3.62 (1H, dd, J = 11.2 Hz, 3.6 Hz), 3.85 (2H, t, J = 5.2 Hz), 3.97-4.01 (1H, m), 7.35-7.45 (6H, m), 7.64-7.66 (4H, m); ¹³C NMR (100 MHz, CDCl₃): δ 19.1, 24.9, 34.9, 62.5, 66.7, 71.6, 127.7, 129.8, 132.9, 135.5; IR (neat): 3380.8 (br s), 2930.1 (w), 2857.6 (w), 1427.6 (m), 1110.2 (s), 822.8 (w), 737.4 (m), 701.5 (s), 688.8 (m) cm⁻¹; HRMS-(ESI+) for C₂₀H₂₉O₃Si [M+H]: calculated: 345.1886, found: 345.1878. [α]₂₀D = +2.224 (c = 1.065, CHCl₃, l = 50 mm).

Proof of Stereochemistry:

The title compound was compared to racemic 4-(tert-butyldiphenylsilyloxy)butane-1,2-diol prepared from treatment of (but-3-enyloxy)(tert-butyl)diphenylsilane with osmium tetraoxide and 4-methylmorpholine N-oxide. The authentic (R)-isomer was
prepared from the Sharpless asymmetric dihydroxylation of (but-3-enyloxy)(tert-butyl) diphenylsilane utilizing AD-mix-β.

*Chiral HPLC (Chiracel-OD, 2.0% IPA, 1.5 mL/min, 220 nm) – analysis of the title compound.*

![Chromatograms](image-url)

- **racemic**
- **diboration product**
- **authentic**
(S)-5-methylhex-5-ene-1,2-diol (Table 4.11, entry 8). The diboration was performed according to the representative procedure with 2-methylhexa-1,5-diene (75.0 mg, 779.9 µmol), Pt(dba)$_3$ (7.0 mg, 7.8 µmol), (R,R)-3,5-di-iso-propylphenylTADDOLPh (4.51) (8.5 mg, 9.4 µmol), and B$_2$(pin)$_2$ (207.9 mg, 818.9 µmol) in tetrahydrofuran (0.8 mL, 1.0 M). The crude reaction mixture was purified on silica gel (30-50% ethyl acetate/hexanes) to afford a clear, colorless oil (84.3 mg, 83% yield). R$_f$ = 0.13 (50% ethyl acetate/hexane, stain in KMnO$_4$) $^1$H NMR (400 MHz, CDCl$_3$): δ 1.56-1.60 (2H, m), 1.72 (3H, s), 2.01 (2H, br s), 2.07 (1H, dddd, J = 7.5, 7.5, 7.5, 7.5 Hz), 2.17 (1H, dddd, J = 7.5, 7.5, 7.5, 7.5 Hz), 3.45 (1H, dd, J = 11.0, 8.0 Hz), 3.65 (1H, d, J = 11.0 Hz), 3.69-3.73 (1H, m), 4.70 (1H, s), 4.72 (1H, s); $^{13}$C NMR (125 MHz, CDCl$_3$): δ 22.3, 31.0, 33.8, 66.7, 72.0, 110.4, 145.4; IR (neat): 336.6 (s), 3074.1 (w), 2929.6 (s), 1447.6 (s), 1375.0 (m), 1333.5 (w), 1100.2 (m), 1053.3 (s), 886.0 (s) cm$^{-1}$; HRMS-(ESI+) for C$_7$H$_{15}$O$_2$ [M+H]: calculated: 131.1072, found: 131.1075.

Analysis of Stereochemistry:

The enantioselectivity was determined by treating the resulting 1,2-diol with 2,2-dimethoxypropane and catalytic p-toluenesulfonic acid. The analogous racemic material was prepared using PCy$_3$ as the achiral ligand in the diboration reaction. Absolute stereochemistry was assigned by analogy.
Chiral HPLC (Supelco β-Dex, 70 °C for 5 min, ramp 3 °C/min to 120 °C, 20 psi, s/r = 35:1) – analysis of the acetonide.

racemic

reaction product
The diboration was performed according to the representative procedure with \((S)-4,8\text{-dimethylnona-1,7-diene}\) (100.0 mg, 656.7 µmol), \(\text{Pt(dba)}_3\) (5.9 mg, 6.6 µmol), \((R,R)-3,5\text{-di-iso-propylphenylTADDOLPPh}\) (4.51) (7.2 mg, 7.9 µmol), and \(\text{B}_2\text{(pin)}_2\) (175.1 mg, 689.5 µmol) in tetrahydrofuran (1.3 mL, 0.5 M). The crude reaction mixture was purified on silica gel (20-40% ethyl acetate/hexanes) to afford a clear, colorless oil (97.7 mg, 80% yield). \(R_f = 0.32\) (50% ethyl acetate/hexane, stain in \(\text{KMnO}_4\)); \(^1\text{H}\) NMR (500 MHz, CDCl\(_3\)): \(\delta\) 0.92 (3H, d, \(J = 6.5\) Hz), 1.09-1.16 (1H, m), 1.28-1.42 (3H, m), 1.58 (3H, s), 1.66 (3H, s), 1.53-1.61 (1H, m), 1.88-2.02 (2H, m), 3.38 (1H, dd, \(J = 11.0, 8.0\) Hz), 3.62 (1H, dd, \(J = 11.0, 3.0\) Hz), 3.77-3.82 (1H, m), 5.05-5.08 (1H, m); \(^{13}\text{C}\) NMR (125 MHz, CDCl\(_3\)): \(\delta\) 20.1, 25.3, 25.7, 29.2, 29.4, 36.7, 40.5, 66.9, 70.5, 124.6, 135.3; IR (neat): 3363.4 (m), 2954.5 (m), 2924.6 (s), 2872.2 (m), 1457.4 (m), 1376.9 (s), 1145.0 (m), 1110.0 (m), 1063.3 (s), 1031.9 (m), 949.9 (w), 884.8 (w) cm\(^{-1}\).
(2R,4S)-4,8-dimethynon-7-ene-1,2-diol (Table 4.11, entry 10). The diboration was performed according to the representative procedure (S)-4,8-dimethylnona-1,7-diene (100.0 mg, 656.7 µmol), Pt(dbac)_3 (5.9 mg, 6.6 µmol), (S,S)-3,5-di-iso-propylphenylTADDOLPPh (4.51) (7.2 mg, 7.9 µmol), and B_2(pin)_2 (175.1 mg, 689.5 µmol) in tetrahydrofuran (1.3 mL, 0.5 M). The crude reaction mixture was purified on silica gel (20-40% ethyl acetate/hexanes) to afford a clear, colorless oil (88.8 mg, 73% yield). R_f = 0.36 (50% ethyl acetate/hexane, stain in KMnO_4); ^1H NMR (500 MHz, CDCl_3): δ 0.89 (3H, d, J = 7.0 Hz), 1.02-1.12 (1H, m), 1.14-1.23 (1H, m), 1.27-1.34 (1H, m), 1.42-1.48 (1H, m), 1.57 (3H, s), 1.59-1.68 (1H, m), 1.65 (3H, s), 1.90-2.02 (2H, m), 2.32 (2H, br s), 3.38 (1H, ddd, J = 11.0, 7.5, 1.0 Hz), 3.59 (1H, d, J = 11.0 Hz), 3.76-3.81 (1H, m), 5.05-5.08 (1H, m); ^13C NMR (100 MHz, CDCl_3): δ 17.6, 19.1, 25.4, 25.7, 28.7, 37.8, 40.2, 67.4, 70.1, 124.6, 131.3; IR (neat): 3363.1 (s), 2926.6 (s), 2872.6 (m), 1457.0 (m), 1377.0 (s), 1145.1 (m), 1065.3 (s), 1027.0 (m), 973.0 (m), 949.8 (m), 736.4 (m) cm^{-1}; HRMS-(ESI+) for C_{11}H_{23}O_2 [M+H]: calculated: 187.1698, found: 187.1693.
4.8.8. Procedure for Decreased Catalyst Loading (Table 4.9).

To an oven-dried 6-dram vial with magnetic stir bar in the dry box was added Pt (dba)$_3$ (14.6 mg, 16.3 µmol), (R,R)-3,5-diethylphenylTADDOLPh (4.38) (25.6 mg, 32.1 µmol), B$_2$(pin)$_2$ (712.8 mg, 2.81 mmol) and ethyl acetate (5.3 mL, 0.5 M). The vial was sealed with a polypropylene cap, removed from the dry box, and heated to 80 °C in an oil bath for 30 min. The vial was cooled to room temperature, returned to the dry box and charged with 1-octene (300.0 mg, 2.67 mmol). The vial was sealed, removed from the dry box, and stirred at 60 °C for 12 h. The reaction mixture was cooled to 0 °C (ice/water) and charged with 3 M sodium hydroxide (4 mL), and 30% hydrogen peroxide (2 mL). The reaction was gradually warmed to room temperature and allowed to stir for 4 h at which time the vial was cooled to 0 °C (ice/water) and saturated aqueous sodium thiosulfate was added dropwise over 5 min. The reaction mixture was diluted with ethyl acetate and the aqueous and organic layers were separated. The aqueous layer was washed with ethyl acetate (3 x 20 mL). The combined organic layers were dried over Na$_2$SO$_4$, filtered, and concentrated by rotary evaporation. The crude reaction mixture was purified on silica gel (30-70% ethyl acetate/hexanes) to afford a white solid (340.1 mg, 87% yield).
Chiral GLC ($\beta$-dex, Supelco, 100 °C, 20 psi) – analysis of the acetonide of octane-1,2-diol.

racemic
diboration product
authentic

To an oven-dried 6-dram vial with magnetic stir bar in the dry box was added Pt (dba)$_3$ (12.2 mg, 13.6 µmol), (R,R)-3,5-diethylphenylTADDOLPh (4.38) (21.3 mg, 26.7 µmol), B$_2$(pin)$_2$ (118.8 mg, 467.9 µmol) and tetrahydrofuran (4.5 mL, 0.1 M). The vial was sealed with a polypropylene cap, removed from the dry box, and heated to 80 °C in an oil bath for 30 min. The vial was cooled to room temperature, returned to the dry box and charged with 1-octene (50.0 mg, 445.6 µmol). The vial was sealed, removed from the dry box, and stirred at 60 °C for 12 h, after which the reaction was cooled to room temperature, fitted with a septum, and placed under nitrogen atmosphere. The crude reaction mixture was then charged with bromochloromethane (7 µL, 980.3 µmol) and cooled to −78 °C. n-BuLi (37 µL, 980.3 µmol) was added dropwise under nitrogen atmosphere and the reaction was allowed to stir at -78 °C for 10 min, at which time it was warmed to room temperature and stirred for 12 h. The reaction mixture was cooled to 0 °C (ice/water) and charged with 3 M sodium hydroxide (2 mL), and 30% hydrogen peroxide (1 mL). The reaction was gradually warmed to room temperature and allowed to stir for 4 h, at which time the vial was cooled to 0 °C (ice/water) and saturated aqueous sodium thiosulfate was added dropwise over 5 min. The reaction mixture was diluted with ethyl acetate and the aqueous and organic layers were separated. The aqueous layer was washed with ethyl acetate (3 x 20 mL) and the combined organic layers were dried over Na$_2$SO$_4$, filtered, and concentrated by rotary evaporation. The crude reaction
mixture was purified on silica gel (30-70% ethyl acetate/hexanes) to afford the desired 1,4-diol as a clear, colorless oil (64.6 mg, 83% yield).

\((S)\)-2-Hexylbutane-1,4-diol. \(^1\)H (400 MHz, CDCl\(_3\)): \(\delta\) 0.85 (3H, t, \(J = 6.8\) Hz), 1.19-1.35 (10H, m), 1.52-1.71 (3H, m), 2.97 (2H, br s), 3.45 (1H, dd, \(J = 10.8\) Hz, 6.8 Hz), 3.61-3.65 (2H, m), 3.73-3.78 (1H, m); \(^{13}\)C NMR (100 MHz, CDCl\(_3\)): \(\delta\) 14.1, 22.6, 27.0, 29.6, 31.7, 31.8, 35.8, 39.3, 61.2, 66.4; IR (neat): 3318.0 (br s), 2955.6 (m), 2925.0 (s), 2856.5 (m), 1466.2 (w), 1043.9 (w) cm\(^{-1}\); HRMS-(ESI+) for C\(_{10}\)H\(_{23}\)O\(_2\) [M+H]: calculated 175.1698, observed: 175.1693. \([\alpha]_D^{20} = -10.115 (c = 0.680, \text{CHCl}_3, l = 50\) mm).

**Proof of Stereochemistry**

The Matteson homologation reaction is known to proceed with retention of stereochemistry.\(^{14}\) The authentic (R)-isomer of the title compound was prepared using Evan’s alkylation,\(^{15}\) followed by ozonolysis and reduction as shown below.

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Chiral HPLC (Chiracel-OD, 1.0 mL/min, 0.5% IPA, 220 nm) – analysis of the bis (benzoate) of 2-hexylbutane-1,4-diol.

racemic diboration/homologation/oxidation pdt
4.8.10. Procedure for Benchtop Diboration (Scheme 4.18).

To an oven-dried vial with magnetic stir bar on the benchtop was added \(\text{Pt(dba)}_3\) (6.9 mg, 7.6 µmol), \((R,R)-3,5\text{-di-iso-propylphenylTADDOLPPh (4.51)}\) (8.3 mg, 9.2 µmol) and \(\text{B}_2\text{(pin)}_2\) (203.7 mg, 802.1 µmol). The vial was sealed with a septum cap and purged with \(\text{N}_2\). Tetrahydrofuran (0.8 mL, 1.0 M) was added \textit{via} syringe under \(\text{N}_2\) atmosphere. The nitrogen line was removed and the vial was heated to 80 °C in an oil bath for 20 min. The vial was cooled to room temperature and charged with 1-tetradecene (150.0 mg, 763.9 µmol). The reaction was then stirred at 60 °C in an oil bath for 3 h. The reaction mixture was cooled to 0 °C (ice/water) and charged with 3 M sodium hydroxide (4 mL), and 30% hydrogen peroxide (2 mL). The reaction was gradually warmed to room temperature and allowed to stir for 4 h at which time the vial was cooled to 0 °C (ice/water) and saturated aqueous sodium thiosulfate was added dropwise over 5 min. The reaction mixture was diluted with ethyl acetate and the aqueous and organic layers were separated. The aqueous layer was washed with ethyl acetate (3 x 20 mL). The combined organic layers were dried over \(\text{Na}_2\text{SO}_4\), filtered, and concentrated by rotary evaporation. The crude reaction mixture was purified on silica gel (30-70% ethyl acetate/hexanes) to afford a white solid (138.2 mg, 79% yield).