ASYMMETRIC HYDROGENATION OF UNFUNCTIONALIZED TRISUBSTITUTED AND TETRASUBSTITUTED OLEFINs

by

Malisa V. Troutman

B.S. Chemistry, Duke University, 1992

M. Phil. Organic Chemistry, Churchill College,
Cambridge University, 1993

Submitted to the Department of
Chemistry in Partial Fulfillment of the
Requirements for the Degree of

DOCTOR OF PHILOSOPHY
IN ORGANIC CHEMISTRY

at the
Massachusetts Institute of Technology
September 1998

© Massachusetts Institute of Technology, 1998
All rights reserved

Signature of Author

Department of Chemistry
July 15, 1998

Certified by

Stephen L. Buchwald
Thesis Supervisor

Accepted by

Dietmar Seyferth
Chairman, Departmental Committee on Graduate Studies
This doctoral thesis has been examined by a committee of the Department of Chemistry as follows:

Professor Timothy M. Swager

Chairman

Professor Stephen L. Buchwald

Thesis Supervisor

Professor Gregory C. Fu
ASYMMETRIC HYDROGENATION OF UNFUNCTIONALIZED TRISUBSTITUTED AND TETRASUBSTITUTED OLEFINS

by

Malisa V. Troutman

Submitted to the Department of Chemistry in partial fulfillment of the requirements for the degree of Doctor of Philosophy at the Massachusetts Institute of Technology

Abstract

A highly reactive chiral catalyst for the asymmetric hydrogenation of aryl trisubstituted olefins was generated by combining the complex (EBTHI)MMe₂ (EBTHI = ethylenebistetrahydroindenyl, M = Ti, Zr) with [PhMe₂NH]⁺[(BC₆F₅)₄]⁻ under a hydrogen atmosphere. A number of unfunctionalized trisubstituted olefins could be hydrogenated rapidly at room temperature under 80 psig H₂ with a wide range of ee's (7 - 97%). Reduction of some substrates under a deuterium atmosphere revealed that olefins which gave low ee's were being isomerized to 1,1-disubstituted olefins prior to reduction. In some cases, additional deuterium was introduced at nonolefinic carbon atoms, indicating that the metal complexes also catalyze directed C-H activation.

The zirconium-based catalyst was also applied to the first highly enantioselective hydrogenations of unfunctionalized tetrasubstituted olefins. Hydrogenations of 1,2-dimethyl-3,4-dihydronaphthalene proceeded with high enantioselectivity, but were accompanied by side reactions. At 80 - 2000 psig H₂, hydrogenations of a number of fully substituted unfunctionalized indenes proceeded cleanly to give mostly cis products with ee's of 78 - 99%; rates and enantioselectivities increased with increasing pressure. Again, deuteration experiments showed that isomerization processes may occur under the reaction conditions.

Thesis Supervisor: Professor Stephen L. Buchwald
Title: Camille Dreyfus Professor of Chemistry
Acknowledgments

My advisor, Steve Buchwald, gave me a challenging project which expanded my knowledge far beyond the strictly organic chemistry of my previous work. I am grateful for his support and advice over the last five years. The members of his laboratory possess truly impressive backgrounds in organic, organometallic, and inorganic chemistry. They also taught me much about creating a sanity-preserving environment. Special thanks to my awesome baymates Natasha Kablaoui and Shana Sturla, and the GMT crowd, past and present.

The text was proofread by Fred Hicks and Rob Singer; the experimental sections were proofread by Joseph Sadighi, Seble Wagaw, and Bryant Yang. Their comments are greatly appreciated.

God blessed me with terrific companionship at Park Street, Grace Chapel, the Church of the Advent, and in the GCF. These friends and many others outside the Institute will be long remembered. Far outside Massachusetts, my mother and brother were always there.

This work was supported by the National Science Foundation and the National Institutes of Health. As noted in the experimental sections, Boulder Scientific and Exxon provided valuable catalyst and cocatalyst.
# Table Of Contents

## Chapter 1

Asymmetric Hydrogenation of Unfunctionalized Trisubstituted Olefins with Cationic Titanocene and Zirconocene Catalysts

<table>
<thead>
<tr>
<th>Section</th>
<th>Page</th>
</tr>
</thead>
<tbody>
<tr>
<td>Introduction</td>
<td>7</td>
</tr>
<tr>
<td>Results and Discussion</td>
<td>22</td>
</tr>
<tr>
<td>Experimental Procedures</td>
<td>35</td>
</tr>
<tr>
<td>References</td>
<td>52</td>
</tr>
</tbody>
</table>

## Chapter 2

Asymmetric Hydrogenation of Unfunctionalized Tetrasubstituted Olefins with a Cationic Zirconocene Catalyst

<table>
<thead>
<tr>
<th>Section</th>
<th>Page</th>
</tr>
</thead>
<tbody>
<tr>
<td>Introduction</td>
<td>56</td>
</tr>
<tr>
<td>Results and Discussion</td>
<td>61</td>
</tr>
<tr>
<td>Experimental Procedures</td>
<td>76</td>
</tr>
<tr>
<td>References</td>
<td>97</td>
</tr>
</tbody>
</table>

Abbreviations

<table>
<thead>
<tr>
<th>Page</th>
</tr>
</thead>
<tbody>
<tr>
<td>99</td>
</tr>
</tbody>
</table>
Chapter 1

Asymmetric Hydrogenation of Unfunctionalized Trisubstituted Olefins with Cationic Titanocene and Zirconocene Catalysts
The asymmetric hydrogenation of olefins has long been recognized as a powerful method of generating optically pure compounds.\textsuperscript{1,2} As a reagent for reduction, hydrogen offers a number of advantages, such as low cost and a lack of byproducts. A variety of hydrogenation catalysts have been developed and tremendous efficiency has been achieved in the case of both asymmetric and nonasymmetric catalysis. Homogeneous organotransition metal complexes are especially useful when control of chemoselectivity and stereoselectivity are crucial.\textsuperscript{3} The ever-growing demand for useful methods for the direct synthesis of enantiomerically enriched chiral molecules has led to the development of a related family of metal complexes which are effective for highly enantioselective hydrogenation.

Most homogeneous enantioselective olefin reduction systems involve late transition metal-based complexes as catalysts and functionalized olefins as substrates. Chirality is often derived from bidentate phosphine ligands. Many of these catalysts are initially tested on acylaminoacrylic acids since the products are derivatives of chiral amino acids and high enantioselectivities have been attained. In addition, late transition metal catalysts have been used in the enantioselective reductions of allylic and homoallylic alcohols, $\alpha,\beta$-unsaturated esters and amides, and $\alpha$-aryl enamides (Scheme 1).\textsuperscript{4-8}

A variety of mechanisms can be proposed for catalytic hydrogenation systems based on known reactions of late transition metal complexes. In a few cases, rigorous kinetics studies of elementary reaction steps have led to the development of mechanistic schemes which are useful for predicting the catalyst's behavior under various conditions. The introduction of chiral ligands can significantly alter mechanistic considerations. Pioneering studies by
Scheme 1

\[
\begin{align*}
\text{DuPHOS} &= \begin{array}{c}
\text{R}^1 \text{R}^2 \text{R}^3 \text{R}^4 \\
\text{Me-BPE} &= \begin{array}{c}
\text{R}^1 \text{R}^2 \text{R}^3 \text{R}^4
\end{array}
\end{array}
\]

\[
\begin{align*}
\text{R} = &\text{OR, NHR} \\
\text{Me} &\text{COR}
\end{align*}
\]

\[
\begin{align*}
\text{COOH} \quad \text{[(COD)Rh(DuPHOS)]}^{+}[\text{SbF}_6]^- \\ \text{NHCOR} \quad 2 \text{ atm H}_2
\end{align*}
\]

\[
\begin{align*}
\text{COOH} \quad \text{[(COD)Rh(Me-BPE)]}^{+}[\text{SbF}_6]^- \\
\text{NHCOR} \quad \text{2 atm H}_2
\end{align*}
\]

\[
\begin{align*}
\text{Me} \quad \text{COR} \\
\text{R = OR, NHR}
\end{align*}
\]

\[
\begin{align*}
\text{CN} \\
\text{CoCl}_2, \text{NaBH}_4
\end{align*}
\]

94 - 99% ee

95 - 99.5% ee

95 - 99.6% ee

95 - 98% ee

92 - 99% ee
Halpern described reductions of ethyl (Z)-α-acetamidocinnamate by a cationic rhodium catalyst with bidentate ligands such as the achiral phosphine diphos and the chiral phosphine CHIRAPHOS (Scheme 2). The activity and selectivity demonstrated by [Rh(CHIRAPHOS)]⁺ is thought to depend on two significant discoveries:

(1) In the presence of olefin, [Rh(bisphosphine)(alkene)]⁺ is formed reversibly, and the amido oxygen atom is coordinated to the Rh atom. This complex can undergo oxidative addition with H₂.

(2) In the case of the chiral phosphine CHIRAPHOS, two diastereomeric olefin complexes are possible. The minor diastereomer is present in such a small amount that it cannot be observed at room temperature. However, this complex is much more reactive towards H₂ than the major (observed) diastereomer is. Thus, it is the minor complex which is responsible for producing the enantiomer observed.

The enantioselectivity observed for the overall reaction depends on the rate of the major complex's reaction with H₂ versus the rate of its conversion into the minor diastereomer through the dissociated [Rh(CHIRAPHOS)]⁺ complex. At higher H₂ pressures, the reaction of the major complex with H₂ becomes more predominant, and the ee is lowered. In contrast, higher temperature leads to a higher ee.
Scheme 2

(SS)-CHIRAPHOS

\[
\begin{align*}
\text{major diastereomer} & \quad \text{minor diastereomer} \\
\text{major product} & \quad \text{minor product}
\end{align*}
\]
Pressure and temperature were also found to have dramatic effects on the enantioselective hydrogenation of the allylic alcohol geraniol with Ru((S)-tol-BINAP).\textsuperscript{10} In addition to catalyzing the reduction, Ru((S)-tol-BINAP) catalyzes the isomerization of geraniol to γ-geraniol (Scheme 3). When the reduction was carried out under D\textsubscript{2} atmosphere, deuterium was found in the methyl group adjacent to the site of reduction. Other experiments showed that under a wide range of pressures at room temperature, γ-geraniol is reduced preferentially to the (S)-enantiomer of citronellol, while geraniol is reduced to the (R)-enantiomer. As in the [Rh(CHIRAPHOS)]\textsuperscript{+} system, the rates of hydrogenation versus isomerization of these substrates can be affected by changes in

\begin{scheme}
\begin{equation}
\begin{aligned}
\text{geraniol} & \xrightarrow{\text{Ru((S)-tol-BINAP)}} \text{H}_2 & \xrightarrow{\text{Ru((S)-tol-BINAP)}} \text{γ-geraniol} \\
\end{aligned}
\end{equation}
\end{scheme}
temperature and pressure. In fact, in separate experiments the Ru((S)-tol-BINAP) catalyst was shown to be capable of producing either (R) or (S)-citronellol from geraniol, depending on the temperature and pressure applied.

These experiments underscore the fact that overall ee is not necessarily a reflection of a chiral catalyst's inherent selectivity. A highly diastereoselective elementary step may be competing with other pathways whose prominence is subject to kinetic influences.

The substrates discussed above have heteroatoms located within one or

Scheme 4

\[ (+)-BDPCH = \]
\[ \text{[Rh}(1,5\text{-hexadiene})\text{Cl}]_2 \]
\[ (+)\text{-BDPCH} \]
\[ 50 \text{ atm H}_2, 50 \text{ °C} \]
\[ 14.4\% \text{ ee} \]
\[ 33.0\% \text{ ee} \]

\[ (+)\text{-bourgeanic acid} \]

\[ \text{Me} - \text{Me} - \text{OH} \]
\[ \text{H}_2 \]
\[ \text{Rh(NBD)(DIPHOS-4)}^+ \]
\[ \text{BF}_4^- \]
\[ 1:1 \text{ mixture} \]
two carbon atoms of the olefin itself. In general, chelation of these heteroatoms to the metal center is necessary for the reaction to proceed with high efficiency and stereoselectivity. When the heteroatoms are not present the desired products generally cannot be obtained with high ee's. Among the few published examples of attempted reductions of unfunctionalized olefins are those shown in Scheme 4. (E)-2-Phenyl-2-butene was hydrogenated by the rhodium complex of (+)-trans-BDPCH at 50 °C and 50 atm H₂ to 2-phenylbutane with only a 14% ee; α-ethylstyrene was hydrogenated to the same product with 33% ee. A bishomoallylic alcohol containing a stereogenic center was intended to be a precursor to (+)-bourgeanic acid; however, its reduction with chiral rhodium complexes gave a 1 : 1 ratio of products due to isomerization of the double bond.

The successful application of asymmetric hydrogenation methods to such olefins would considerably expand the range of potential target molecules. The chiral catalysts would have to be able to differentiate the re and si sides of the olefin without guidance from nearby heteroatoms. Several early transition metal-based catalysts and lanthanide-based catalysts have shown potential in related transformations. The precatalysts in Scheme 5 were converted into metal hydrides and applied to the asymmetric reduction of 1,1-disubstituted olefins. In the case of 2-phenyl-1-butene, high ee's could be obtained at low temperature.
Among the early metal complexes applied to asymmetric olefin hydrogenation reactions are the stereorigid *ansa*-metallocenes \((R,R,R)\) and \((S,S,S)-(EBTHI)\) \(\text{Ti}\)(Binol) (EBTHI = ethylenebistetrahydroindenylo, Binol = \(1,1'\)-binaphth-2,2'-diolate),\textsuperscript{17} which are obtained by resolving \((\pm)-(EBTHI)\)\(\text{TiCl}_2\) with \((R)\)- or \((S)\)-binaphthol (Scheme 6).\textsuperscript{17,18} These complexes can serve as precatalysts for the highly enantioselective hydrogenation of a number of double bond-containing substrates, including imines\textsuperscript{19,20} and enamines.\textsuperscript{21}
Scheme 6

\[(S, S)-(EBTHI)-MX_2\] \hspace{1cm} \[(R, R)-(EBTHI)-MX_2\]

\[
\begin{align*}
X_2 &= \text{Binol, Cl}_2, F_2 \\
\text{EBTHI} &= \text{ethylenebis tetrahydroindenyl} \\
\text{Binol} &= 1,1'-\text{binaphth-2,2'-dilalate}
\end{align*}
\]

Recently, these complexes were used to carry out the first highly enantioselective hydrogenations of unfunctionalized trisubstituted olefins (Table 1). Under argon atmosphere, the precatalysts shown above were placed under conditions known to reduce them to titanium(III) hydrides (n-BuLi, PhSiH3). At hydrogen pressures of 80 - 2400 psig at 65 °C these catalysts hydrogenated a number of olefins with high ee's; the conditions required varied with the substrate. \textit{Trans-}\(\alpha\)-methylstilbene (entry 1) was hydrogenated in 9 hours at 80 psig, but the reduction of 1-methyl-3,4-dihydronaphthalene (entry 6) required more forcing conditions (1800 psig, 184 hours), and the \(Z\) olefin \textit{cis-}\(\alpha\)-methylstilbene did not react appreciably even at high pressure. However, a mixture of \(E\) and \(Z\) isomers of 2-(4-methoxyphenyl)-2-butene (entry 3) was fully reduced to 2-(4-methoxyphenyl)butane; the product's ee suggests that the \(E\) and \(Z\) isomers are reduced stereoselectively to opposite enantiomers.
Table 1

\[
(S, S, S)-(EBTHI)Ti(Binol) \xrightarrow{\text{5 mol %}} (1) 10 \text{ mol % } n-\text{BuLi} \xrightarrow{(2) 12.5 \text{ mol % } \text{PhSiH}_3} \xrightarrow{(1) \text{ olefin}} (2) \text{H}_2 (2000 \text{ psig}) \xrightarrow{\text{65} \text{ °C}}
\]

<table>
<thead>
<tr>
<th>Entry</th>
<th>Olefin</th>
<th>Product</th>
<th>Time</th>
<th>ee</th>
<th>Yield</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>\begin{tikzpicture} \draw (0,0) -- (0.5,0) -- (0.5,0.5) -- (0,0.5) -- cycle; \end{tikzpicture}</td>
<td>\begin{tikzpicture} \draw (0,0) -- (0.5,0) -- (0.5,0.5) -- (0,0.5) -- cycle; \end{tikzpicture}</td>
<td>9 h</td>
<td>&gt;99%</td>
<td>94%</td>
</tr>
<tr>
<td>2</td>
<td>\begin{tikzpicture} \draw (0,0) -- (0.5,0) -- (0.5,0.5) -- (0,0.5) -- cycle; \end{tikzpicture}</td>
<td>\begin{tikzpicture} \draw (0,0) -- (0.5,0) -- (0.5,0.5) -- (0,0.5) -- cycle; \end{tikzpicture}</td>
<td>48 h</td>
<td>95%</td>
<td>79%</td>
</tr>
<tr>
<td>3</td>
<td>\begin{tikzpicture} \draw (0,0) -- (0.5,0) -- (0.5,0.5) -- (0,0.5) -- cycle; \end{tikzpicture}</td>
<td>\begin{tikzpicture} \draw (0,0) -- (0.5,0) -- (0.5,0.5) -- (0,0.5) -- cycle; \end{tikzpicture}</td>
<td>146 h</td>
<td>31%</td>
<td>80%</td>
</tr>
<tr>
<td>4</td>
<td>\begin{tikzpicture} \draw (0,0) -- (0.5,0) -- (0.5,0.5) -- (0,0.5) -- cycle; \end{tikzpicture}</td>
<td>\begin{tikzpicture} \draw (0,0) -- (0.5,0) -- (0.5,0.5) -- (0,0.5) -- cycle; \end{tikzpicture}</td>
<td>43 h</td>
<td>95%</td>
<td>75%</td>
</tr>
<tr>
<td>5</td>
<td>\begin{tikzpicture} \draw (0,0) -- (0.5,0) -- (0.5,0.5) -- (0,0.5) -- cycle; \end{tikzpicture}</td>
<td>\begin{tikzpicture} \draw (0,0) -- (0.5,0) -- (0.5,0.5) -- (0,0.5) -- cycle; \end{tikzpicture}</td>
<td>48 h</td>
<td>93%</td>
<td>80%</td>
</tr>
<tr>
<td>6</td>
<td>\begin{tikzpicture} \draw (0,0) -- (0.5,0) -- (0.5,0.5) -- (0,0.5) -- cycle; \end{tikzpicture}</td>
<td>\begin{tikzpicture} \draw (0,0) -- (0.5,0) -- (0.5,0.5) -- (0,0.5) -- cycle; \end{tikzpicture}</td>
<td>184 h</td>
<td>83%</td>
<td>70%</td>
</tr>
</tbody>
</table>

The catalyst was tolerant of aryl and alkyl ethers and tertiary amines. The methyl ether (entry 5) is derived from a trisubstituted allylic alcohol in which the hydroxy group is positioned at the disubstituted end of the double bond. Late transition metal-based systems are not known to reduce such substrates with high enantioselectivity. (Geraniol and nerol, which are reduced effectively by
Ru(BINAP), feature a hydroxy group at the monosubstituted end of the double bond.\textsuperscript{4)}

The mechanism of this reaction is thought to be analogous to that proposed for the hydrogenation of imines by the same catalyst.\textsuperscript{20} In this scenario, the titanium hydride inserts into the double bond with the Ti atom bonded to the carbon at the monosubstituted end of the double bond. This titanium-alkyl intermediate then undergoes hydrogenolysis via sigma-bond metathesis with H\textsubscript{2}, giving the product and regenerating the titanium hydride.

Scheme 7

The configuration of the products observed in the reduction of both imines and olefins is rationalized by the transition state model shown in Scheme 8.\textsuperscript{20} The olefin is expected to approach as depicted in order to maximize overlap of the metal and olefin orbitals.\textsuperscript{23} Because of its proximity to the Ti atom and the EBTHI ligand, substituent R'' is thought to be the most important factor in determining enantioselectivity; groups R and R' are further away and have less influence. The olefin will therefore react at the face which
minimizes interactions between substituent R'' and the tetrahydroindenyl moiety of the ligand.

Scheme 8

Although the precatalyst (EBTHI)Ti(Binol) is air-stable, the air and moisture sensitivity of the active catalyst, the high pressures, and the long reaction times required for complete reduction make the system less appealing. One strategy for developing a more reactive system would be to increase the electrophilicity of the metal center. Highly electrophilic hydrogenation catalysts could potentially be generated from Cp₂MR⁺, which is thought to be the active species when Group 4 metallocenes are used as Ziegler-Natta olefin polymerization catalysts.²⁴-²⁷ This species is thought to be a formally cationic 14e⁻ complex. Neutral d¹ Cp₂TiR and d⁰ Cp₂MR₂ complexes do not participate in olefin insertion reactions, but the cationic d⁰ species Cp₂MR⁺
catalyzes the polymerization of ethylene and \(\alpha\)-olefins. More highly substituted olefins generally are not polymerized. The reaction of \(\text{rac-EBTHI}\)zirconium(IV)dichloride and MAO (methylaluminoxane) with \(\alpha\)-olefins gives highly isotactic polymers; the EBTHI ligand was originally developed for this stereoselective reaction.\(^{28}\)

![Scheme 9 Image]

The MAO cocatalyst has a complex structure, and polymerizations do not proceed efficiently unless a large excess is used. Therefore, a number of simpler, characterizable Group 4 metallocenes of the form \([\text{Cp}_2\text{MR}(\text{L})]^+[\text{X}]^-\) (\(\text{M} = \text{Ti}\) or \(\text{Zr}\); \(\text{R} = \text{alkyl}\); \(\text{L} = \text{coordinating solvent ligand}\); \(\text{X} = \text{monomeric anion}\)) have been synthesized in order to better understand polymerization mechanisms.\(^{24,25,29}\) Anions such as BF\(_4\)^- and OTf^- are unsuitable because of their propensity to react with the metal complex or bind covalently to the metal center.\(^{27}\) In fact, the cationic metal complex \([\text{Cp}^*\text{ZrMe}_2]\text{BPh}_4\) is so reactive that it forms covalent bonds with the phenyl ligands of \([\text{BPh}_4]^-\).\(^{30}\) Recently the anion \(\text{B(C}_6\text{F}_5)_4^-\) has been employed as a more weakly coordinating substitute.\(^{31,32}\) Reaction of \(\text{Cp}_2\text{MMe}_2\) compounds with \([\text{R}'_3\text{NH}]^+[\text{B(C}_6\text{F}_5)_4]\) in benzene or toluene affords \([\text{Cp}_2\text{MMe}]^+[\text{B(C}_6\text{F}_5)_4]^+\) complexes by protonolysis of an \(\text{R}\) group (an amine byproduct \(\text{NR}'_3\) is also formed).\(^{30}\) The triphenylcarbenium salt \([\text{Ph}_3\text{C}]^+[\text{B(C}_6\text{F}_5)_4]\) also generates this complex from \(\text{Cp}_2\text{MMe}_2\) in addition to the noncoordinating byproduct \(\text{CH}_3\text{CPh}_3\).\(^{33}\) A "cation-
like alkyl metallocene has been synthesized without side products from the reaction of Cp^*2ZrMe_2 with B(C_6F_5)_3; a crystal structure showed that this complex contains a bridging methyl group between the boron and zirconium atoms.\textsuperscript{34}

Scheme 10

\[ \text{Cp}_2MX_2 + \text{MeLi} \rightarrow \text{Cp}_2\text{MMe}_2 \]

\[ \text{Cp}_2\text{MMe}_2 + [R_3NH]^+[B(C_6F_5)_4]^- \rightarrow \text{Cp}_2\text{MMe}^+[B(C_6F_5)_4]^+ + \text{NR}_3 \]

\[ \text{Cp}_2\text{MMe}_2 + [R_3NH]^+[\text{Co(C}_2\text{B}_9\text{H}_11)_2]^+ \rightarrow \text{Cp}_2\text{MMe}^+[\text{Co(C}_2\text{B}_9\text{H}_11)_2]^+ + \text{NR}_3 \]

\[ \text{Cp}_2\text{MMe}_2 + [\text{Ph}_3\text{C}]^+[B(C_6F_5)_4]^+ \rightarrow \text{Cp}_2\text{MMe}^+[B(C_6F_5)_4]^+ + \text{Ph}_3\text{CMe} \]

\[ \text{Cp}^*2\text{ZrMe}_2 + \text{B(C}_6\text{F}_5)_3 \rightarrow \text{H}_2 \rightarrow (\text{C}_6\text{F}_5)_3\text{B}^- \]

These complexes can be converted into cationic metallocene hydrides by placing them under a hydrogen atmosphere as illustrated above. In fact, the (EBTHI)zirconocene(IV) hydride generated in this way has been applied to the asymmetric reduction of disubstituted olefins (Scheme 11). The catalyst system (\(R, R, R\))-(EBTHI)Zr(Binol) / MAO hydrogenated 2-phenyl-1-butene with an ee of 36\%,\textsuperscript{35} and the similar system (\(S, S\))-(EBTHI)ZrMe_2/[PhMe_2NH][Co(C_2B_9H_11)_2] hydrogenated the same substrate with an ee of 23\%.\textsuperscript{36} If the olefin were trisubstituted, the orientation of the double bond with respect to the catalyst would be expected to resemble the transition states shown in Scheme 8. The results obtained for the reduction of trisubstituted olefins with the
(EBTHI)titanocene(III) catalyst indicate that, in theory, high ee's are possible for these substrates.

Scheme 11

\[
\begin{align*}
\text{(R, R, R)-(EBTHI)Zr(Binol) (0.2 mol \%)} \\
\text{MAO (284 Al/Zr)} \\
\xrightarrow{20 \text{ atm H}_2} \\
\text{benzene} \\
\text{36\% ee}
\end{align*}
\]

\[
\begin{align*}
\text{(S, S)-(EBTHI)ZrMe}_2 \text{ (1 mol \%)} \\
\text{[PhMe}_2\text{NH}^+\text{[Co(C}_2\text{B}_9\text{H}_11)_2]^+ (1 \text{ mol \%)}} \\
\xrightarrow{100 \text{ atm H}_2} \\
\text{benzene} \\
\text{23\% ee}
\end{align*}
\]
Results and Discussion

In order to generate a cationic metalloocene catalyst for the reduction of trisubstituted olefins, \((S, S, S)-(EBTHI)Ti(Binol)\) was converted into \((S, S)-(EBTHI)TiMe_2\) by reaction with methyllithium.\textsuperscript{17} This complex was isolated and stored in a nitrogen-filled glovebox; its reaction with \(B(C_6F_5)_3\) followed by pressurization of the reaction vessel with \(H_2\) gave a catalyst which was highly active for the reduction of \textit{trans}-\(\alpha\)-methylstilbene. The product 1,2-diphenylpropane was obtained with an ee of 95\% in just 20 min at room temperature under 80 psig \(H_2\). In contrast, the Ti(III) hydride system had required 9 h at 65 °C and 2000 psig \(H_2\).\textsuperscript{22}

Scheme 12

Application of this catalyst system to other substrates was not as successful; during the hydrogenations of 2 and 3, significant amounts of byproducts were obtained (Scheme 13). A white solid identified as 1-ethyl-5-methoxy-3-(4-methoxyphenyl)-1,2,3-trimethylindane, a dimer of the starting material, was isolated from the hydrogenation products of 2. The \(^1H\) NMR of this material was similar to spectra of products obtained from acid-catalyzed dimerizations of 2-arylbutenes (and other precursors to 2-arylbutyl carbocations.)\textsuperscript{37-39} A naphthalene derivative was obtained in addition to the

\[\text{Scheme 12}\]

\[\begin{array}{c}
(S, S)-(EBTHI)TiMe_2 \\
B(C_6F_5)_3 \\
5 \text{ mol \%}
\end{array}\]

\[\text{toluene r. t.}\]

\[\begin{array}{c}
80 \text{ psig } H_2 \\
\rightarrow
\end{array}\]

\[\begin{array}{c}
\text{95\% ee} \\
\text{93\% yield}
\end{array}\]
expected tetrahydronaphthalene product from 3; ee's were also much lower than those expected based on the Ti(III) hydride system.²²

Scheme 13

(S, S)-(EBTHI)TiMe₂
B(C₆F₅)₃
5 mol %
80 psig H₂
toluene
r. t.

69% ee

89 : 8 : 3
61% total yield

26%

Control reactions of these substrates with polymerization cocatalysts such as B(C₆F₅)₃ and [CPh₃][B(C₆F₅)₄] alone revealed that these Lewis acids
can react directly with the olefins to give the byproducts observed (Scheme 14). For instance, the reaction of 2 with B(C₆F₅)₃ gave a mixture of dimers of 2. In the case of dihydronaphthalene 4, a disproportionation reaction occurred, and the products were recovered in a 1 : 1 ratio. The aromatization of 1,2-dihydronaphthalene by stoichiometric [CPh₃]+ has been described previously. In the present catalytic examples, the Lewis acids may trigger proton-catalyzed disproportionation. The reaction of complexes such as (EBTHI)TiMe₂ with B(C₆F₅)₃ is reversible, so the borane is available to react with olefins during the reduction process. Although the reaction of (EBTHI)TiMe₂ with [CPh₃][B(C₆F₅)₄] should be irreversible, unreacted traces of the Lewis acid may be sufficient to cause side reactions. Hydrogenations did not go to completion when a larger ratio of titanium precatalyst to [CPh₃][B(C₆F₅)₄] was used.

Scheme 14

Because the above cocatalysts were unsuitable, the non-Lewis acidic cocatalyst [PhMe₂NH][B(C₆F₅)₄] was allowed to react with (±)-(EBTHI)TiMe₂ in a manner similar to that described above (Table 2). For 2 and 3, conversion was low, although no side products were observed.
Table 2

(±)-(EBTHI)TiMe₂ + [PhMe₂NH]+[B(C₆F₅)₄]⁻  
5 mol %  
80 psig H₂  
toluene or benzene  
r. t.  
→ olefin

<table>
<thead>
<tr>
<th>Olefin</th>
<th>Product</th>
<th>Time</th>
<th>Result</th>
</tr>
</thead>
<tbody>
<tr>
<td><img src="image1" alt="image" /></td>
<td><img src="image2" alt="image" /></td>
<td>1 day</td>
<td>20% conversion</td>
</tr>
<tr>
<td><img src="image3" alt="image" /></td>
<td><img src="image4" alt="image" /></td>
<td>1 day</td>
<td>30% conversion</td>
</tr>
</tbody>
</table>

Zirconocene-based catalysts have been found to be more active than titanocenes in polymerization studies, but the activity and enantioselectivity of zirconium catalysts with the EBTHI ligand in trisubstituted olefin reduction has not been examined. Thus, (R, R)-(EBTHI)ZrMe₂ was synthesized in a manner similar to that described for the titanocene compound. This complex was allowed to react with [PhMe₂NH][B(C₆F₅)₄] in toluene or benzene for 20 minutes under argon, and hydrogen atmosphere was introduced, followed by the olefin.

A survey of various substrates showed that the zirconium system was indeed more reactive than the titanium-based system, since most of these reactions went to completion rapidly in an hour or less (Table 3). However, the zirconium catalyst was often much less selective. In some cases (2, 4, 5), the sense of enantioselection was actually reversed.
Table 3

\[
(R, R)'-(EBTHI)ZnMe_2 + [\text{PhMe}_2\text{NH}]^+\text{[B(C_6F_5)_4]}^- \xrightarrow{80 \text{ psig } H_2, \text{ r. t.}} \text{olefin}
\]
5 mol %

<table>
<thead>
<tr>
<th>Olefin</th>
<th>Product</th>
<th>Yield</th>
<th>ee</th>
<th>Solvent</th>
</tr>
</thead>
<tbody>
<tr>
<td><img src="image1.png" alt="image" /></td>
<td><img src="image2.png" alt="image" /></td>
<td>94%</td>
<td>97%</td>
<td>toluene</td>
</tr>
<tr>
<td><img src="image3.png" alt="image" /></td>
<td><img src="image4.png" alt="image" /></td>
<td>88%</td>
<td>20%</td>
<td>toluene</td>
</tr>
<tr>
<td><img src="image5.png" alt="image" /></td>
<td><img src="image6.png" alt="image" /></td>
<td>98%</td>
<td>7%</td>
<td>benzene</td>
</tr>
<tr>
<td><img src="image7.png" alt="image" /></td>
<td>(-) Isomer</td>
<td>76%</td>
<td>10%</td>
<td>benzene</td>
</tr>
<tr>
<td><img src="image8.png" alt="image" /></td>
<td><img src="image9.png" alt="image" /></td>
<td>93%</td>
<td>19%</td>
<td>toluene</td>
</tr>
<tr>
<td><img src="image10.png" alt="image" /></td>
<td><img src="image11.png" alt="image" /></td>
<td>89%</td>
<td>76%</td>
<td>toluene</td>
</tr>
</tbody>
</table>

The reduction of a number of olefins was carried out under deuterium atmosphere in order to assess the contribution of isomerization pathways to the overall ee (Table 4). Reaction of trans-\(\alpha\)-methylstilbene (1) under these
conditions and examination of the product by $^1$H NMR and $^2$H NMR showed that deuterium was only found at the carbon atoms which had been part of the olefin. However, the reduction products of olefins 2, 4, and 6 contained significant amounts of deuterium at the methyl groups adjacent to the aromatic rings. In addition, the amounts of deuterium found at the formerly olefinic carbons were lower than expected. In the case of 2, deuterium was also observed at the aromatic ring and the methoxy group. Evidently complexation of the catalyst with the oxygen atom directed C-H activation at these nearby

<table>
<thead>
<tr>
<th>Olefin</th>
<th>Product (% D incorporation)</th>
<th>Time</th>
<th>Result</th>
</tr>
</thead>
<tbody>
<tr>
<td><img src="image" alt="Structure 1" /> 1</td>
<td><img src="image" alt="Structure 2" /> 2</td>
<td>65 min</td>
<td>96% ee</td>
</tr>
<tr>
<td><img src="image" alt="Structure 3" /> 6</td>
<td><img src="image" alt="Structure 4" /> 4</td>
<td>120 min</td>
<td>2% ee</td>
</tr>
<tr>
<td><img src="image" alt="Structure 5" /> 4</td>
<td><img src="image" alt="Structure 6" /> 2</td>
<td>50 min</td>
<td>12% ee</td>
</tr>
<tr>
<td><img src="image" alt="Structure 7" /> 2</td>
<td><img src="image" alt="Structure 8" /> 2</td>
<td>75 min</td>
<td>12% ee</td>
</tr>
</tbody>
</table>
positions. Like hydrogenolysis, this transformation probably involves a four-center sigma bond metathesis. (The (EBTHI)Ti(III) hydride catalyst apparently reacts with the ortho-hydrogens of 2-phenylpyrrole in a similar fashion.)

Racemic 1-methyl-1,2,3,4-tetrahydronaphthalene was subjected to the deuteration conditions (Scheme 15). As in the olefin reduction, a trace of deuterium was found in the 4-position, but no deuterium was observed in the methyl group.

Scheme 15

\[
(R, R)-(EBTHI)ZrMe_2 [PhMe_2NH]_3[B(C_6F_5)_4] \quad 80 \text{ psig } D_2 \quad \text{toluene} \quad 2 \text{ h}
\]

Thus, deuterium incorporation at this position either takes place in the starting material, or, more likely, disubstituted olefin is being formed through isomerization of the starting material. This isomerization can only arise if the Zr-H bond inserts into the starting material such that the Zr atom is bonded to the more substituted end of the olefin (Scheme 16). It is possible that the resulting Zr-alkyl intermediate directly undergoes hydrogenolysis; however, it is not known which enantiomer of the product would be favored by such a process. Alternatively, β-hydride elimination to the disubstituted olefin can take place; based on the experiments shown in Scheme 11 in the introduction, such an olefin would be reduced with a low ee, favoring the enantiomer shown in Scheme 16 below. This explains the deuterium in the methyl groups and the reversal of selectivity observed for substrates 2, 4 and 5. The transition state
model in Scheme 8 of the introduction describes the reduction of trisubstituted olefins by a catalyst which inserts with the metal atom at the less substituted carbon atom, leading to product enriched in the other enantiomer.

Scheme 16

Corroborating evidence for the 2-aryl-1-butene intermediate was obtained by hydrogenation of 8, which gave (R) product with a similar ee to that seen for the hydrogenation of 2:

29
The apparent formation of a more hindered metal alkyl intermediate is not that surprising given that this catalyst is more electrophilic than the neutral titanocene(III) system discussed in the introduction. In this intermediate the metal atom is closer to the aromatic ring, which is likely stabilizing it through π-electron donation (Scheme 18). (A similar explanation was offered for the regioselectivity of aryl olefin hydrosilylation by lanthanocene hydrides.\textsuperscript{42}) In the case of \textit{trans-α}-methylstilbene, coordination of an aromatic ring together with the lower steric hindrance at the less substituted carbon apparently directs the regioselectivity, and the reaction follows the same course as that predicted for titanocene(III) reduction of this substrate.
The reversal in selectivity for the hydrogenation of 2 was only observed when the metal catalyst was a zirconium complex. The hydrogenation of 2 by the \((S, S, S)-(\text{EBTHI})\text{TiMe}_2 / \text{B(C}_6\text{F}_5)_3\) system (Scheme 13) favors the \((R)\)-enantiomer of the product, as does the \((S, S, S)-(\text{EBTHI})\text{Ti(Binol)} / \text{n-BuLi / PhSiH}_3\) system.\(^{22}\) This suggests that for the cationic titanium catalyst, the contribution to the ee from isomerization to a disubstituted olefin is diminished. The titanium catalyst may be less likely to give the more sterically crowded intermediate which provides entry into the isomerized olefin, since the \((\text{EBTHI})\text{Ti}\) complex is more compact than the \((\text{EBTHI})\text{Zr}\) complex. (A comparison of the crystal structures of \((\text{EBTHI})\text{TiCl}_2\) and \((\text{EBTHI})\text{ZrCl}_2\) revealed that the average distance between the cyclopentadienyl carbon atoms and the metal atom is 2.43 Å for Ti and 2.53 Å for Zr.\(^{17,43}\) In any case, it could be easier to attain high ee's using the titanium-based system. As previously noted, the \((\text{EBTHI})\text{TiMe}_2 / [\text{PhMe}_2\text{NH}][\text{B(C}_6\text{F}_5)_4]\) system was not stable enough to fully reduce 2. However, the deuteration of 2 by the zirconium system demonstrates that the metal center has a very high affinity for oxygen; complexation of Ti to the anisole oxygen may have a detrimental influence on activity. A derivative of 2 with a bulkier protecting group (TBDMS) was synthesized. Again, the products obtained from Ti- and Zr-based reductions were enriched in different enantiomers; the ee was low when the Zr complex was used as the catalyst and moderate when the Ti complex was used (Table 5). Both reductions proceeded rapidly to completion, and yields were high for both reactions. The ee's for the
The cationic titanocene hydrogenations of 2 and 9 were still lower than those expected based on the results from the (EBTHI)Ti(III) hydride catalyzed reduction of 2.\textsuperscript{22} It is possible that isomerization is playing a role even in these systems.

In fact, for dihydronaphthalene 4, the Ti- and Zr-catalyzed reductions favored the same enantiomer with similar ee's. The Ti catalyst was noticeably less active and demonstrated a tendency to aromatize the starting material. This substrate required long reaction times under conditions of titanocene(III) hydride-catalyzed reduction.\textsuperscript{22} The predicted, less sterically hindered alkyl intermediate may not be so easily formed from this Z olefin; isomerization may be the dominant mechanistic pathway for both metals.
Table 6

\[(R, R)-(EBTHI)MMe_2 + [PhMe_2NH]^+B(C_6F_5)_4^- \xrightarrow{80 \text{ psig } H_2 \text{ toluene r. t.}} \text{olefin} \]

<table>
<thead>
<tr>
<th>Olefin</th>
<th>Metal</th>
<th>Product(s)</th>
<th>Yield</th>
<th>ee</th>
</tr>
</thead>
<tbody>
<tr>
<td><img src="attachment1" alt="image" /></td>
<td>Me</td>
<td>Zr</td>
<td><img src="attachment2" alt="image" /></td>
<td><img src="attachment3" alt="image" /></td>
</tr>
<tr>
<td><img src="attachment4" alt="image" /></td>
<td>Me</td>
<td>Ti</td>
<td><img src="attachment5" alt="image" /> + s.m.</td>
<td><img src="attachment6" alt="image" /></td>
</tr>
</tbody>
</table>
Conclusion

The catalyst systems (EBTHI)TiMe₂ / [PhMe₂NH][B(C₆F₅)₄] and (EBTHI)ZrMe₂ / [PhMe₂NH][B(C₆F₅)₄] were shown to be highly reactive for the reduction of aryl trisubstituted olefins under hydrogen atmosphere. In fact, some of the reduction products obtained by using these systems showed evidence for directed C-H activation. Although good ee's were obtained for some substrates, in some cases aryl substitution at the double bond led to a loss of regioselectivity and undesired isomerization reactions. The degree to which this unexpected process occurred depended upon the catalyst; when the titanium-based catalyst was used, the isomerization pathway was less prevalent. This suggests that the unwanted formation of the more hindered metal alkyl intermediate is sensitive to steric factors, since Ti is smaller than Zr. The olefins in this study all had methyl and aryl substitution on one end of the double bond; it is possible that reactions of more hindered aryl olefins would proceed with high regioselectivity. Of course, replacing the aryl group with an alkyl group would also remove the coordinating π electrons which cause a reversal in regioselectivity in the first place. However, separation of the reduction products from these substrates on chiral columns could be difficult. This problem could be mitigated by the presence of polar functionality elsewhere in the molecule. It has been demonstrated that catalysts similar to those used here can polymerize α-olefins containing heteroatoms with bulky protecting groups.⁴⁴ If the functional group compatibility of these catalysts was explored more thoroughly, other classes of olefins could be examined as hydrogenation substrates, leading to a better understanding of the catalysts' potential in asymmetric reduction.
Experimental Procedures

General Considerations. All manipulations involving air-sensitive materials were conducted in a Vacuum Atmospheres glovebox under an atmosphere of nitrogen or using standard Schlenk techniques under argon. Unless stated otherwise, all reactions were conducted in flasks sealed with a rubber septum under a positive pressure of argon. (Caution: Reactions under high pressure should be carried out behind an appropriate safety shield.) THF was distilled under argon from sodium/ benzophenone ketyl. Toluene was distilled under nitrogen from molten sodium. Anhydrous benzene, diisopropylamine, pentane, hexanes, DMSO, and CH$_2$Cl$_2$ were obtained from Aldrich and used without further purification. TMSCl was distilled under argon from CaH$_2$. rac-(EB)ZrCl$_2$ was a gift from Boulder Scientific. [CPh$_3$][B(C$_6$F$_5$)$_4$] was obtained from Austin Chemical Company. [PhMe$_2$NH][B(C$_6$F$_5$)$_4$] and B(C$_6$F$_5$)$_3$ were gifts from Exxon. 1-Methyl-3,4-dihydronaphthalene and 6-methoxy-1-methyl-3,4-dihydronaphthalene were synthesized as described in reference 22. Resolved (EBTHI)Ti(Binol) and (EBTHI)Zr(Binol) were synthesized as described in references 18 and 45, respectively. All other reagents were available from commercial sources and were used without further purification, unless otherwise noted.

Flash chromatography was performed on E. M. Science Kieselgel 60 (230-400 mesh) unless otherwise noted. Yields refer to isolated yields of compounds of greater than 95% purity as estimated by capillary GC and $^1$H NMR analysis, and in the cases of unknown compounds, by elemental analysis. Yields indicated in this section refer to a single experiment, while those reported in the tables are an average of two or more runs, so the numbers may differ slightly. All compounds were characterized by $^1$H NMR, $^{13}$C NMR, and IR.
spectroscopy. Previously unreported compounds were also characterized by elemental analysis (E & R Analytical Laboratory, Inc.). Nuclear magnetic resonance (NMR) spectra were recorded on a Varian XL-300, a Varian VXR-500, or a Varian Unity 300. Splitting patterns are designated as follows: s, singlet; d, doublet; dd, doublet of doublets; t, triplet; td, triplet of doublets; q, quartet; qd, quartet of doublets; m, multiplet. All $^1$H NMR spectra are reported in δ units, parts per million (ppm) downfield from tetramethylsilane. All $^{13}$C NMR and $^2$H NMR spectra are reported in ppm relative to deuterochloroform (77 ppm and 7.24 ppm, respectively.) Infrared (IR) spectra were recorded on an ASi Applied Systems ReactIR 1000 (solids were measured neat on a DiComp probe.) Gas chromatography (GC) analyses were performed on a Hewlett-Packard 5890 or 6890 gas chromatograph with an FID detector using a 25 m x 0.20 mm capillary column with cross-linked SE-30 as a stationary phase. Chiral GC analyses were performed on a Hewlett-Packard 5890 gas chromatograph using a Chiraldex B-PH or Chiraldex G-TA column (20 m x 0.25 mm). Chiral HPLC analyses were performed on a Hewlett-Packard 1100 system with an HP 1100 Diode Array Detector using a Chiracel OJ column or Chiracel OD column (25 cm x 0.46 cm). Racemic compounds analogous to the enantiomerically enriched compounds described below were prepared by reduction of the olefin substrates under hydrogen atmosphere catalyzed by Pd/C. The HPLC or GC retention times of the racemic products matched those of the enantiomerically enriched products.

$(R, R)$-(EBTHI)TiMe$_2$: This complex was synthesized using a modification of the literature procedure.$^{17}$ A suspension of $(R, R, R)$-(EBTHI)Ti(Binol) (579 mg, 0.971 mmol) in diethyl ether (40 mL) was cooled to -78 °C in a Schlenk flask under argon. A solution of methyllithium in diethyl ether (1.4 M, 3.5 mL, 4.9
mmol) was added via syringe. The reaction mixture was allowed to warm to room temperature and was stirred for 2 h. The diethyl ether was removed in vacuo on a Schlenk line. Pentane (20 mL) was added, and the resulting mixture was stirred briefly and filtered under argon atmosphere. This procedure was repeated twice (10 mL pentane each time). The combined pentane filtrates were concentrated in vacuo on a Schlenk line to a volume of ca. 5 - 10 mL. The solution was cooled to -70 °C and briefly stirred; yellow crystals appeared. After 10 - 15 min, cooling was discontinued and the pentane was transferred via cannula from the crystals. The crystals were dried on a Schlenk line under vacuum and isolated in a nitrogen-filled glovebox (136 mg, 41%). ^1H NMR (300 MHz, C₆D₆): 6 6.57 (d, J = 3.0 Hz, 2 H); 5.78 (d, J = 3.0 Hz, 2 H); 3.07 - 2.83 (m, 4 H); 2.24 - 2.14 (m, 6 H); 1.71 - 1.37 (m, 10 H); 0.02 (s, 6 H). (S, S)-(EBTHI)TiMe₂ was synthesized by the same procedure from (S, S, S)-(EBTHI)Ti(Binol).

(R, R)-(EBTHI)ZrMe₂: This complex was synthesized using a modification of the literature procedure. A solution of methyllithium-lithium bromide complex in diethyl ether (1.5 M, 2.7 mL, 4.0 mmol) was added via syringe to a solution of (R, R, R)-(EBTHI)Zr(Binol) (1.13 g, 1.77 mmol) in benzene (20 mL) under argon, giving rise to a white suspension. (Note: The methyllithium-lithium bromide solution was stored at all times in a nitrogen-filled glovebox.) The flask was wrapped in foil to protect from light, and the reaction mixture was stirred for 1 h. The benzene was removed in vacuo on a Schlenk line, leaving an off-white solid. Hexanes (15 mL) were added and the solid was broken up with a spatula under a stream of argon. The mixture was stirred for 70 min and filtered under argon atmosphere. This procedure was repeated twice (10 mL hexanes, 15 min stirring each time). The combined filtrates were concentrated in vacuo on a
Schlenk line to afford a white solid. This material was transferred to a nitrogen-filled glovebox and dissolved in minimal pentane (5 mL). The solution was cooled to -20 °C and allowed to stand overnight, during which time crystals formed. Decantation of the pentane afforded \((R, R)\)-(EBTHI)ZrMe\(_2\) as white crystals (522 mg, 76%). \(^1\)H NMR (300 MHz, CDCl\(_3\)):\(^3\) \(^6\) 6.16 (d, \(J = 2.4 \text{ Hz}, 2 \text{ H})\); 5.12 (d, \(J = 3.0 \text{ Hz}, 2 \text{ H})\); 2.89 - 2.80 (m, 2 H); 2.69 - 2.60 (m, 2 H); 2.36 (s, 4 H); 2.31 - 2.22 (m, 2 H); 2.02 - 1.92 (m, 2 H); 1.78 - 1.54 (m, 6 H); 1.46 - 1.40 (m, 2 H); -0.10 (s, 6 H).

\((E)-2-(4-methoxy)-2\text{-butene}\) \((2)\): A solution of \(p\)-methoxyacetophenone (4.00 g, 26.6 mmol) in THF (40 mL) was added dropwise to a solution of ethyl magnesium bromide in diethyl ether (2.7 M, 20 mL, 54 mmol) under argon at 0 °C. The reaction mixture was allowed to warm to room temperature and was stirred overnight. A saturated aqueous solution of NH\(_4\)Cl was added dropwise until the mixture was neutralized, followed by diethyl ether and water. The aqueous phase was separated and extracted with diethyl ether (2x). The combined organic phases were washed with saturated aqueous NaCl solution and dried over MgSO\(_4\). The solution was concentrated to a yellow oil (4.94 g), which was partially purified by flash chromatography (10% EtOAc/hexanes \(\rightarrow\) 25% EtOAc/hexanes). The resulting material (3.69 g) was dissolved in acetonitrile (60 mL), and DMSO (30 μL, 0.42 mmol) was added. The solution was heated to 50 °C, and TMSCl (50 μL, 0.39 mmol) was added. The reaction mixture was stirred for 20 min, and concentrated \textit{in vacuo} at room temperature. Purification by flash column chromatography (100% hexanes \(\rightarrow\) 10% CH\(_2\)Cl\(_2\)/hexanes) afforded 2 as a colorless oil (1.43 g, 33%) as well as a mixture of 2 and other isomers (1.20 g, 28%). \(^1\)H NMR (300 MHz, CDCl\(_3\)): \(^6\) δ
7.33 - 7.28 (m, 2 H); 6.87 - 6.82 (m, 2 H); 5.81 - 5.74 (m, 1 H); 3.30 (s, 3 H); 2.00 (s, 3 H); 1.78 (d, J = 6.9 Hz, 3 H).

(E)-2-(4-(tert-butyldimethylsilyloxy)phenyl)-2-butene (5): By a procedure similar to that above, 4-(tert-butyldimethylsilyloxy)acetophenone was converted to 5, a colorless oil (41%). $^1$H NMR (300 MHz, CDCl$_3$): δ 7.23 (d, J = 8.8 Hz, 2 H); 6.76 (d, J = 8.8 Hz, 2 H); 5.77 (q, J = 6.6 Hz, 1 H); 1.99 (s, 3 H); 1.77 (d, J = 6.6 Hz, 3 H); 0.98 (s, 9 H); 0.18 (s, 6 H). $^{13}$C NMR (75 MHz, CDCl$_3$): δ 154.2, 137.1, 134.9, 126.3, 120.7, 119.5, 25.9, 18.4, 15.6, 14.3, -4.2. IR (neat): 2957, 2895, 2860, 1606, 1509, 1471 cm$^{-1}$. Anal. calcd for C$_{17}$H$_{28}$OSi: C, 73.22; H, 9.98. Found: C, 73.31; H, 10.11.

(E)-2-(4-fluorophenyl)-2-butene (6): A solution of n-BuLi in hexane (1.6 M, 15 mL, 24 mmol) was added to a suspension of ethyltriphenylphosphonium iodide (10.0 g, 24.0 mmol) in THF (70 mL) under argon at 0 °C, and the reaction mixture was stirred for 30 min. After addition of 4'-fluoroacetophenone (1.8 mL, 14.8 mmol), the reaction was allowed to warm to room temperature and heated to reflux for 17 h. The reaction mixture was allowed to cool to room temperature, and solutions of 4 : 1 hexanes : diethyl ether and 1 : 1 methanol : water were added. The aqueous phase was separated and extracted with 4 : 1 hexanes : ether. The combined organic phases were washed with 1 : 1 methanol : water, water, and saturated aqueous NaCl solution. The organic phases were then dried over MgSO$_4$, filtered, and concentrated in vacuo. Two successive purifications by flash column chromatography (hexanes) afforded 6 (779 mg, 35%) and the corresponding (Z) isomer (142 mg, 6%). For the (E) isomer (6): $^1$H NMR (300 MHz, CDCl$_3$): δ 7.34 - 7.27 (m, 2 H); 7.01 - 6.94 (m, 2 H); 5.79 (qd, J = 1.5 Hz, J = 6.9 Hz, 1 H); 2.00 (t, J = 0.9 Hz, 3 H); 1.78 (dd, J =
0.9 Hz, J = 6.9 Hz, 3 H). $^{13}$C NMR (125 MHz, CDCl$_3$): δ 162.6, 160.7, 140.1(2), 134.5, 127.0, 126.9, 122.3, 114.9, 114.7, 15.6, 14.3. IR (neat): 2988, 2922, 2860, 1888, 1602, 1505, 1444 cm$^{-1}$. Anal. calcd for C$_{10}$H$_{11}$F: C, 79.97; H, 7.38. Found: C, 79.93; H, 7.33. For the (Z) isomer: $^1$H NMR (300 MHz, CDCl$_3$): δ 7.18 - 7.12 (m, 2 H); 7.05 - 6.98 (m, 2 H); 5.56 (qd, J = 1.4 Hz, J = 6.9 Hz, 1 H); 2.00 - 1.99 (m, 3 H); 1.59 - 1.53 (m, 3 H). A nuclear Overhauser enhancement study was undertaken to determine the relative configuration of the two isomers. For the (E) isomer, irradiation of the C-1 methyl hydrogens at δ 2.00 gave a 0% enhancement at the vinyl hydrogen. For the (Z) isomer, irradiation of the C-1 methyl hydrogens at δ 2.00 gave a 3% enhancement at the vinyl hydrogen, while irradiation of the C-4 methyl hydrogens at δ 1.57 gave no enhancement at the C-1 methyl hydrogens. Based on these observations, the configurations of the isomers were assigned as shown:

- **2-methyl-3,4-dihydronaphthalene (7):** A solution of diisopropylamine (6.8 mL, 48.5 mmol) in THF (70 mL) under argon was cooled to -78 ºC. A solution of n-BuLi in hexane (1.6 M, 30 mL, 48 mmol) was added slowly via syringe, and the mixture was allowed to warm to room temperature. After 30 min, the flask was again cooled to -78 ºC and a solution of 1-tetralone (6.5 mL, 48.9 mmol) in THF (30 mL) was added. The reaction mixture was stirred for 1 h, and methyl iodide (13 mL, 209 mmol) was added. The reaction mixture was
stirred at -78 °C for 1 h and allowed to warm to room temperature over a period of 1 h. Diethyl ether and 1 N HCl solution were added, and the aqueous phase was separated and extracted with diethyl ether. The combined organic phases were washed with water, saturated aqueous NaHCO₃ solution, and saturated aqueous NaCl solution, and were then dried over MgSO₄, filtered, and concentrated in vacuo. Two successive purifications by flash column chromatography (5% EtOAc/hexanes) afforded 2-methyl-1-tetralone as a colorless oil (4.42 g, 58%). ¹H NMR (300 MHz, CDCl₃): δ 8.04 (d, J = 7.9 Hz, 1 H); 7.46 (t, J = 6.6 Hz, 1 H); 7.32 - 7.22 (m, 2 H); 3.05 - 2.94 (m, 2 H); 2.63 - 2.56 (m, 1 H); 2.25 - 2.16 (m, 1H); 1.96 - 1.82 (m, 1H); 1.28 (d, J = 6.7 Hz, 3 H).

2-Methyl-1-tetralone (1.49 g, 9.30 mmol) was dissolved in THF (60 mL) and MeOH (30 mL). Sodium borohydride (579 mg, 15.3 mmol) was added in portions. The reaction mixture was stirred for 6 h, and 1 N HCl solution was added slowly to neutralize the mixture, followed by diethyl ether. The aqueous phase was separated and extracted with diethyl ether. The combined organic phases were washed with saturated aqueous NaCl solution, dried over MgSO₄, filtered, and concentrated in vacuo. Diethyl ether (50 mL) and 4 N HCl (20 mL) were added to the crude product. The mixture was stirred for 5.5 h, but GC analysis showed that the reaction was proceeding slowly. The organic layer was separated and washed with saturated aqueous NaCl solution and dried over MgSO₄. The solution was concentrated in vacuo and the crude oil was dissolved in toluene (50 mL). p-Toluenesulfonic acid (20 mg) was added, and the mixture was refluxed for 1.5 h and then allowed to cool to room temperature. Diethyl ether and saturated aqueous NaHCO₃ solution were added. The organic phase was separated and washed with saturated aqueous NaCl solution, dried over MgSO₄, filtered, and concentrated in vacuo. Purification by flash column chromatography (hexanes) afforded 7 as a colorless oil (1.07 g,
80%). $^1$H NMR (300 MHz, CDCl$_3$): δ 7.24 - 7.04 (m, 3 H); 6.94 (d, $J = 7.2$ Hz, 1 H); 6.21 (s, 1 H); 2.81 (t, $J = 8.1$ Hz, 2 H); 2.23 (t, $J = 8.1$ Hz, 2 H); 1.90 (s, 3 H).

2-(4-methoxyphenyl)-1-butene (8):$^{51}$ A suspension of methyltriphenylphosphonium bromide (6.55 g, 18.3 mmol) in THF (40 mL) under argon was cooled to 0 °C. A solution of n-BuLi in hexane (1.6 M, 11.4 mL, 18.2 mmol) was added, and the reaction mixture was stirred for 1 h. Upon addition of 4'-methoxyacetophenone (3.2 mL, 18.3 mmol), the reaction mixture was allowed to warm to room temperature and was then heated to reflux for 19 h. The reaction was allowed to cool to room temperature, and solutions of 4 : 1 hexanes : diethyl ether and 1 : 1 methanol : water were added. The aqueous phase was separated and extracted with 4 : 1 hexanes : ether. The combined organic phases were washed with 1 : 1 methanol : water, water, and saturated aqueous NaCl solution, and then dried over MgSO$_4$, filtered, and concentrated in vacuo. Purification by flash column chromatography (hexanes → 5% CH$_2$Cl$_2$/hexanes) afforded 8 as a colorless oil (1.31 g, 44%). $^1$H NMR (300 MHz, CDCl$_3$): δ 7.38 - 7.33 (m, 2 H); 6.88 - 6.83 (m, 2 H); 5.20 (s, 1 H); 4.97 (q, $J = 1.5$ Hz, 1 H); 3.80 (s, 3 H); 2.52 - 2.45 (m, 2 H); 1.10 (t, $J = 7.4$ Hz, 3 H). Anal. calcd for C$_{11}$H$_{14}$O: C, 81.44; H, 8.70. Found: C, 81.23; H, 8.63.

**General Procedure A for the asymmetric reduction of olefins at 80 psig H$_2$ with (S, S)-(EBTHI)TiMe$_2$/B(C$_6$F$_5$)$_3$:** In a nitrogen-filled glovebox, a dry Fischer-Porter bottle containing a stir bar was charged with (S, S)-(EBTHI)TiMe$_2$ (0.05 equiv) and B(C$_6$F$_5$)$_3$ (0.05 equiv). The bottle was sealed, removed from the glovebox, evacuated and backfilled with argon. Toluene was added and the reaction mixture was stirred for 2 - 3 min. The bottle was pressurized to 80 psig H$_2$ and vented to 10 psig (3x) and then
repressurized to 80 psig H₂. A solution of the olefin (1 equiv) in toluene was added via pressure syringe. The reaction was stirred at room temperature for the time specified; the bottle was then carefully vented and opened to the air. The reaction mixture was transferred directly onto a silica gel column and the product was purified by flash column chromatography (toluene) followed by Kugelrohr distillation.

**General Procedure B for the asymmetric reduction of olefins at 80 psig H₂ with (R, R)-(EBTHI)ZrMe₂/[PhMe₂NH][B(C₆F₅)₄]:** In a nitrogen-filled glovebox, a dry Fischer-Porter bottle containing a stir bar was charged with (R, R)-(EBTHI)ZrMe₂ (0.05 equiv) and [PhMe₂NH][B(C₆F₅)₄] (0.05 equiv). The bottle was sealed, removed from the glovebox, evacuated and backfilled with argon. Solvent (benzene or toluene) was added and the mixture was stirred for 20 min. The bottle was pressurized to 80 psig H₂ and vented to 10 psig (3x) and then repressurized to 80 psig H₂. A solution of olefin (1 equiv) in solvent (benzene or toluene) was added via pressure syringe. The reaction was stirred at room temperature for the time specified; the bottle was then carefully vented and opened to the air. The reaction mixture was transferred directly onto a silica gel column and the product was purified by flash column chromatography (hexanes).

**General Procedure C for the asymmetric reduction of olefins at 80 psig D₂:** In a nitrogen-filled glovebox, a dry Fischer-Porter bottle containing a stir bar was charged with (R, R)-(EBTHI)ZrMe₂ (0.05 equiv) and [PhMe₂NH][B(C₆F₅)₄] (0.05 equiv). The bottle was sealed, removed from the glovebox, evacuated and backfilled with argon. Toluene (4 mL) was added and the mixture was stirred for 1 h. The bottle was pressurized to 80 psig D₂ and
vented to 10 psig (3x) and then repressurized to 80 psig D₂. A solution of olefin (1.74 mmol) in toluene (1.5 mL, 0.5 mL wash) was added via pressure syringe. The reaction was stirred at room temperature for the time specified; the bottle was then carefully vented and opened to the air. The reaction mixture was transferred directly onto a silica gel column and the product was purified by flash column chromatography (hexanes).

(R)-1,2-diphenylpropane: Following General Procedure A, trans-α-methylstilbene (1) (351 mg, 1.81 mmol) in toluene (6 mL) was converted to a colorless oil (332 mg, 93%) in 20 min. Chiral GC analysis (Chiraldex G-TA column) determined that the product had an ee of 95%. ¹H NMR (300 MHz, CDCl₃): δ 7.29 - 7.06 (m, 10 H); 3.03 - 2.90 (m, 2 H); 2.75 (dd, J = 7.3 Hz, J = 12.4 Hz, 1 H); 1.23 (d, J = 6.7 Hz, 3 H). [α]²⁵°C -81° (c 11.1, CHCl₃).

Reduction/dimerization of (E)-2-(4-methoxyphenyl)-2-butene (2): Following General Procedure A, 2 (324 mg, 2.00 mmol) in toluene (6 mL) was converted to a colorless oil in 20 h. Two successive Kugelrohr distillations afforded a colorless oil (200 mg) and a white solid (84 mg.) Analysis by ¹H NMR indicated that the oil consisted of a mixture of starting material (8%), (Z)-2-(4-methoxyphenyl)-2-butene (3%), and 2-(4-methoxyphenyl)-butane (89%). Chiral HPLC analysis (Chiralcel OD column) determined that the reduction product 2-(4-methoxyphenyl)-butane had an ee of 69%. For the oil: ¹H NMR (300 MHz, CDCl₃): δ 7.30 (d, J = 8.7 Hz); 7.12 - 7.07 (m); 6.86 - 6.81 (m); 3.81 (s); 3.80 (s); 3.78 (s); 2.54 (sextet, J = 7.1 Hz); 2.00 (s); 1.76 (dd, J = 1.2 Hz, J = 6.9 Hz); 1.56 (quintet, J = 7.2 Hz); 1.20 (d, J = 6.9 Hz); 0.81 (t, J = 7.4 Hz).

For the solid, 1-ethyl-5-methoxy-3-(4-methoxyphenyl)-1,2,3-trimethylindane (mp 80 - 82.4 °C): ¹H NMR (300 MHz, CDCl₃): δ 7.19 - 7.14 (m,
2 H); 7.04 (d, J = 8.1 Hz, 1 H); 6.85 - 6.78 (m, 3 H); 6.36 (d, J = 2.4 Hz); 3.80 (s, 3 H); 3.70 (s, 3 H); 2.32 (quartet, J = 7.4 Hz, 1 H); 1.70 - 1.59 (m, 2 H); 1.46 (s, 3 H); 1.13 (s, 3 H); 0.89 (d, J = 7.5 Hz, 3 H); 0.77 (t, J = 7.4 Hz, 3 H). \(^{13}\)C NMR (125 MHz, CDCl\(_3\)): \(\delta\) 158.8, 157.4, 153.2, 142.7, 142.3, 128.2, 123.7, 113.3, 113.1, 109.2, 55.3, 55.2, 53.2, 52.7, 47.6, 33.5, 25.8, 23.2, 9.4, 9.0. IR (neat): 2957, 2934, 1610, 1513, 1486, 1459 cm\(^{-1}\). Anal. calcd for C\(_{22}\)H\(_{28}\)O\(_2\): C, 81.44; H, 8.70. Found: C, 81.46; H, 8.73.

**Reduction/aromatization of 6-methoxy-1-methyl-3,4-dihyronaphthalene (3):** Following General Procedure A, 3 (378 mg, 2.17 mmol) in toluene (6 mL) was converted to a colorless oil (357 mg) in 14.5 h. Analysis by \(^{1}\)H NMR indicated that this oil consisted of a 2:1 mixture of 6-methoxy-1-methyl-1,2,3,4-tetrahyronaphthalene and 2-methoxy-5-methylnaphthalene. Chiral HPLC analysis (Chiralcel OD column) determined that the reduction product had an ee of 6%. \(^{1}\)H NMR (300 MHz, CDCl\(_3\)): \(\delta\) 7.90 (dd, \(J = 0.6\) Hz, \(J = 9.0\) Hz); 7.60 (d, \(J = 8.4\) Hz); 7.33 (dd, \(J = 7.0\) Hz, \(J = 8.2\) Hz); 7.19 - 7.10 (m); 6.70 (dd, \(J = 2.8\) Hz, \(J = 8.6\) Hz); 6.60 (d, \(J = 3.0\) Hz); 3.92 (s); 3.76 (s); 2.88 - 2.79 (m); 2.76 - 2.71 (m); 2.66 (s); 1.95 - 1.81 (m); 1.77 - 1.64 (m); 1.55 - 1.46 (m); 1.25 (d, \(J = 6.9\) Hz). The signals at 3.76, 2.88 - 2.71, and 1.95 - 1.25 ppm correspond to 6-methoxy-1-methyl-1,2,3,4-tetrahyronaphthalene,\(^{22}\) and the signal at 2.66 ppm corresponds to the naphthalene derivative.

**Disproportionation of 1-methyl-3,4-dihyronaphthalene (4):** A flame-dried Schlenk flask with a stir bar was charged with [CPh\(_3\)][B(C\(_6\)F\(_5\))\(_4\)] (40 mg, 0.043 mmol) in a nitrogen-filled glovebox. The flask was brought out, evacuated, and backfilled with argon. Benzene was added (2 mL) followed by
4 (157 mg, 1.09 mmol) and additional benzene (3 mL). The reaction mixture was stirred for 2 h, at which time it was loaded directly onto a silica gel column. Purification by flash column chromatography (hexanes) followed by Kugelrohr distillation afforded a colorless oil (136 mg), consisting of a 1:1 mixture of 1-methylnaphthalene and 1-methyl-1,2,3,4-tetrahydronaphthalene. $^1$H NMR (300 MHz, CDCl$_3$): δ 7.98 (d, 1 H); 7.82 (d, 1 H); 7.69 (d, 1 H); 7.54 - 7.43 (m, 2 H); 7.39 - 7.27 (m, 2 H); 7.22 - 7.16 (m, 1 H); 7.14 - 7.01 (m, 3 H); 2.95 - 2.84 (m, 1 H); 2.78 - 2.70 (m, 2 H); 2.68 (s, 3 H); 1.97 - 1.78 (m, 2 H); 1.77 - 1.64 (m, 1 H); 1.56 - 1.48 (m, 1 H); 1.27 (t, $J = 8.0$ Hz, 3 H). The peaks at 7.98, 7.82, 7.69, 7.54 - 7.43, 7.39 - 7.27, and 2.68 ppm correspond to 1-methylnaphthalene; $^5_2$ the remaining peaks correspond to 1-methyl-1,2,3,4-tetrahydronaphthalene.$^2_2$

**(S)-1,2-diphenylpropane:** Following General Procedure B, trans-α-methylstilbene (1) (194 mg, 1.00 mmol) in toluene (4 mL) was converted to a colorless oil (187 mg, 96%) in 1 h. Chiral HPLC analysis (Chiralcel OJ column) determined that the product had an ee of 98%. $^1$H NMR (300 MHz, CDCl$_3$)$^{2_2}$ δ 7.30 - 7.06 (m, 10 H); 3.03 - 2.91 (m, 2 H); 2.76 (dd, $J = 7.6$ Hz, $J = 12.8$ Hz, 1 H); 1.24 (d, $J = 6.6$ Hz, 3 H). [α]$^{25}$° $^1$C +87° (c 0.53, CHCl$_3$). Anal. calcd for C$_{15}$H$_{16}$: C, 91.78; H, 8.22. Found: C, 91.87; H, 8.38.

**(R)-2-(4-methoxyphenyl)butane:** Following General Procedure B, 2 (292 mg, 1.80 mmol) in toluene (6 mL) was converted to a colorless oil (234 mg, 79%) in 1 h. Chiral GC analysis (Chiralaldex G-TA column) determined that the product had an ee of 23%. $^1$H NMR (300 MHz, CDCl$_3$)$^{2_2}$ δ 7.11 - 7.07 (m, 2 H); 6.86 - 6.81 (m, 2 H); 3.78 (s, 3 H); 2.54 (sextet, $J = 7.0$ Hz, 1 H); 1.56 (quintet, $J = 7.4$ Hz, 2 H); 1.21 (d, $J = 6.9$ Hz, 3 H); 0.81 (t, $J = 7.4$ Hz, 3 H). [α]$^{25}$° -9.4°
(c 0.64, CHCl₃). Anal. calcd for C₁₁H₁₆O: C, 80.44; H, 9.82. Found: C, 80.34; H, 10.00.

(R)-2-(4-(tert-butyldimethylsilyloxy)phenyl)butane: Following General Procedure B, 5 (260 mg, 0.99 mmol) in benzene (4 mL) was converted to a colorless oil (256 mg, 98%) in 50 min. Chiral HPLC analysis (Chiracel OJ column) determined that the product had an ee of 7%. ¹H NMR (300 MHz, CDCl₃): δ 7.01 (d, J = 9.0 Hz, 2 H); 6.75 (d, J = 8.3 Hz, 2 H); 2.56 - 2.49 (m, 1 H); 1.54 (quintet, J = 7.3 Hz, 2 H); 1.20 (d, J = 7.2 Hz, 3 H); 0.98 (s, 9 H); 0.80 (t, J = 7.4 Hz, 3 H); 0.18 (s, 6 H). ¹³C NMR (75 MHz, CDCl₃): δ 153.4, 140.2, 127.6, 119.6, 41.0, 31.5, 25.9, 22.0, 18.4, 12.3, -4.2. IR (neat): 2960, 2932, 2858, 1831, 1608, 1511, 1472, 1462 cm⁻¹. [α]²⁵°C -1.8° (c 3.9, CHCl₃). Anal. calcd for C₁₆H₂₈OSi: C, 72.66; H, 10.67. Found: C, 72.45; H, 10.87.

2-(4-fluorophenyl)butane: Following General Procedure B, 6 (152 mg, 1.01 mmol) in benzene (4 mL) was converted to a colorless oil (113 mg, 73%) in 3.5 h. Chiral GC analysis (Chiraldex G-TA column) determined that the product had an ee of 13%. ¹H NMR (300 MHz, CDCl₃): δ 7.15 - 7.08 (m, 2 H); 7.00 - 6.92 (m, 2 H); 2.58 (sextet, J = 7.0 Hz, 1 H); 1.61 - 1.51 (m, 2 H); 1.21 (d, J = 7.2 Hz, 3 H); 0.80 (t, J = 7.5 Hz, 3 H). ¹³C NMR (125 MHz, CDCl₃): δ 162.1, 160.2, 143.2(2), 128.3, 128.2, 115.0, 114.8, 41.0, 31.3, 22.0, 12.1. IR (neat): 2964, 2930, 2876, 1884, 1606, 1509, 1459 cm⁻¹. [α]²⁵°C -3.3° (c 2.4, CHCl₃). Anal. calcd for C₁₀H₁₃F: C, 78.91; H, 8.61. Found: C, 78.80; H, 8.53.

(S)-1-methyl-1,2,3,4-tetrahydronaphthalene: Following General Procedure B, 4 (267 mg, 1.85 mmol) in toluene (6 mL) was converted to a colorless oil (252 mg, 93%) in 50 min. Chiral GC analysis (Chiraldex G-TA
column) determined that the product had an ee of 19%. $^1$H NMR (300 MHz, CDCl$_3$): $^2$2 $\delta$ 7.22 - 7.18 (m, 1 H); 7.15 - 7.03 (m, 3 H); 2.94 - 2.87 (m, 1 H); 2.82 - 2.70 (m, 2 H); 1.97 - 1.80 (m, 2 H); 1.79 - 1.66 (m, 1 H); 1.58 - 1.48 (m, 1 H); 1.29 (d, $J$ = 6.9 Hz, 3 H). [$\alpha$]$^{25}$$^o$C +3.7° (c 0.81, dioxane).

**(S)-2-methyl-1,2,3,4-tetrahydronaphthalene:** Following General Procedure B, 7 (250 mg, 1.73 mmol) in toluene (6 mL) was converted to a colorless oil (226 mg, 90%) in 50 min. Chiral GC analysis (Chiralaldex G-TA column) determined that the product had an ee of 76%. $^1$H NMR (300 MHz, CDCl$_3$): $\delta$ 7.10 - 7.03 (m, 4 H); 2.83 - 2.78 (m, 3 H); 2.39 (dd, $J$ = 10.6 Hz, $J$ = 16.4 Hz, 1 H); 1.90 - 1.81 (m, 2 H); 1.45 - 1.34 (m, 1 H); 1.06 (d, $J$ = 6.6 Hz, 3 H). $^{13}$C NMR (125 MHz, CDCl$_3$): $\delta$ 136.9, 136.6, 129.0, 128.8, 125.3(2), 38.1, 31.5, 29.3, 22.0. IR (neat): 3061, 3016, 2918, 2849, 1581, 1494, 1454, 1434 cm$^{-1}$. [$\alpha$]$^{25}$$^o$C -81° (c 0.16, dioxane).

**Reduction of trans-$\alpha$-methylstilbene (1) under D$_2$ atmosphere:** Following General Procedure C, trans-$\alpha$-methylstilbene (1) (185 mg, 0.95 mmol) was converted to a colorless oil (174 mg) in 65 min. Chiral HPLC analysis (Chiracel OJ column) determined that the product had an ee of 96%. $^1$H NMR (300 MHz, CDCl$_3$): $\delta$ 7.31 - 7.03 (m, 10 H); 3.02 - 2.90 (m, 0.34 H); 2.73 (s, 1 H); 1.23 - 1.20 (m, 3 H). $^2$H NMR (46 MHz, CHCl$_3$): $\delta$ 2.97.

**Reduction of (E)-2-((4-fluorophenyl)-2-butene (6) under D$_2$ atmosphere:** In a nitrogen-filled glovebox, a dry Fischer-Porter bottle containing a stir bar was charged with ($R$, $R$)-(EBTHI)ZrMe$_2$ (19 mg, 0.049 mmol) and [PhMe$_2$NH][B(C$_6$F$_5$)$_4$] (41 mg, 0.051 mmol). The bottle was sealed, removed from the glovebox, evacuated and backfilled with argon. Benzene (3
mL) was added and the mixture was stirred for 20 min. The bottle was pressurized to 80 psig D2 and vented to 10 psig (2x) and then repressurized to 80 psig D2. A solution of 6 (153 mg, 1.02 mmol) in benzene (0.5 mL, 0.5 mL wash) was added via pressure syringe. The reaction was stirred at room temperature for 2 h, at which time the bottle was carefully vented and opened to the air. The reaction mixture was transferred directly onto a silica gel column, and flash chromatography (hexanes) afforded a colorless oil (97 mg). Chiral GC analysis (Chiraldex G-TA column) determined that the product had an ee of 2%. 1H NMR (300 MHz, CDCl3): δ 7.15 - 7.08 (m, 2 H); 7.00 - 6.92 (m, 2 H); 2.59 - 2.53 (m, 0.50 H); 1.61 - 1.51 (m, 1.09 H); 1.22 - 1.17 (m, 2.62 H); 0.81 - 0.78 (m, 3 H). 2H NMR (46 MHz, CHCl3): δ 2.55, 1.52, 1.19.

Reduction of 1-methyl-3,4-dihyronaphthalene (4) under D2 atmosphere: Following General Procedure C, 4 (260 mg, 1.80 mmol) was converted to a colorless oil (245 mg) in 50 min. Chiral GC analysis (Chiraldex G-TA column) determined that the product had an ee of 12%. 1H NMR (300 MHz, CDCl3): δ 7.22 - 7.01 (m, 4 H); 2.95 - 2.83 (m, 0.43 H); 2.82 - 2.66 (m, 2 H); 1.98 - 1.80 (m, 1.58 H); 1.80 - 1.65 (m, 1 H); 1.59 - 1.47 (m, 1 H); 1.32 - 1.22 (m, 1.67 H). 2H NMR (46 MHz, CHCl3): δ 2.89, 1.92, 1.26.

Reduction of (E)-2-(4-methoxyphenyl)-2-butene (2) under D2 atmosphere: Following General Procedure C, 2 (281 mg, 1.73 mmol) was converted to a colorless oil (279 mg) in 1.25 h. Chiral GC analysis (Chiraldex G-TA column) determined that the product had an ee of 12%. 1H NMR (300 MHz, CDCl3): δ 7.09 (s, 2 H); 6.85 - 6.82 (m, 0.08 H); 3.79 - 3.75 (m, 1.85 H); 2.59 - 2.49 (m, 0.40 H); 1.61 - 1.49 (m, 1.12 H); 1.22 - 1.18 (m, 2.72 H); 0.83 - 0.79 (m, 3 H). 2H NMR (46 MHz, CHCl3): δ 6.86, 3.79, 3.76, 2.52, 1.53, 1.20.
Deuteration of (±)-1-methyl-1,2,3,4-tetrahydronaphthalene: Following General Procedure C, (±)-1-methyl-1,2,3,4-tetrahydronaphthalene (146 mg, 0.998 mmol) was converted to a colorless oil (116 mg) in 2 h. $^1$H NMR (300 MHz, CDCl$_3$): δ 7.21 - 7.03 (m, 4 H); 2.94 - 2.87 (m, 1 H); 2.78 - 2.73 (m, 1.90 H); 1.97 - 1.80 (m, 2 H); 1.80 - 1.66 (m, 1 H); 1.58 - 1.48 (m, 1 H); 1.29 (t, J = 6.9 Hz, 3 H). $^2$H NMR (46 MHz, CHCl$_3$): δ 2.89, 2.74.

Reduction of 2-(4-methoxyphenyl)-1-butene (8): Following General Procedure B, 8 (287 mg, 1.77 mmol) in toluene (6 mL) was converted to a colorless oil (240 mg, 83%) in 15 min. Chiral GC analysis (Chiralpak G-TA column) determined that the product, (R)-2-(4-methoxyphenyl)butane, had an ee of 29%. $^1$H NMR (300 MHz, CDCl$_3$): δ 7.12 - 7.07 (m, 2 H); 6.86 - 6.81 (m, 2 H); 3.78 (s, 3 H); 2.54 (sextet, J = 7.0 Hz, 1 H); 1.56 (quintet, J = 7.3 Hz, 2 H); 1.21 (d, J = 6.9 Hz, 3 H); 0.81 (t, J = 7.2 Hz, 3 H). [α]$^{25}$°C = -8.1° (c 2.1, CHCl$_3$).

(S)-2-(4-(tert-butylidimethylsilyloxy)phenyl)butane: Following General Procedure B, (R, R)-(EBTHI)TiMe$_2$ (17 mg, 0.05 mmol) and [PhMe$_2$NH][B(C$_6$F$_5$)$_4$] (40 mg, 0.05 mmol) in benzene (4 mL) were used to convert 5 (258 mg, 0.98 mmol) to a colorless oil (248 mg, 96%) in 60 min. Chiral HPLC analysis (Chiracel OJ column) determined that the product had an ee of 61%. $^1$H NMR (300 MHz, CDCl$_3$): δ 7.01 (d, J = 9.0 Hz, 2 H); 6.75 (d, J = 8.9 Hz, 2 H); 2.53 - 2.48 (m, 1 H); 1.54 (quintet, J = 7.3 Hz, 2 H); 1.20 (d, J = 6.5 Hz, 3 H); 0.98 (s, 9 H); 0.79 (t, J = 7.4 Hz, 3 H); 0.18 (s, 6 H). [α]$^{25}$°C = +11° (c 3.0, CHCl$_3$).

The product (45 mg) was dissolved in a solution of TBAF in THF (1.0 M, 1 mL, 1 mmol), and the reaction mixture was stirred for 1.5 h. Diethyl ether and
water were added; the organic phase was separated, washed with saturated aqueous NaCl solution, dried over MgSO₄, filtered, and concentrated in vacuo. The crude oil was dissolved in benzene (1 mL), and a solution of 50% NaOH was added (1 mL), followed by Me₂SO₄ (1 mL) and tetrabutylammonium iodide (57 mg). The reaction mixture was stirred for 1 h, and workup proceeded as in the previous step. Flash chromatography (100% hexanes → 10% CH₂Cl₂/hexanes) afforded (S)-2-(4-methoxyphenyl)butane as a colorless oil (19 mg). Chiral GC analysis (Chiraldex G-TA column) determined an ee of 59%. ¹H NMR (500 MHz, CDCl₃): δ 7.09 (d, J = 8.8 Hz, 2 H); 6.83 (d, J = 8.5 Hz, 2 H); 3.78 (s, 3 H); 2.53 (sextet, J = 7.0 Hz, 1 H); 1.55 (quintet, J = 7.2 Hz, 2 H); 1.20 (d, J = 7.0 Hz, 3 H); 0.81 (t, J = 7.5 Hz, 3 H). [α]²⁵°C +16° (c 0.70, CHCl₃). The sign of rotation and the chiral GC analysis show that the product has the (S) configuration.²²

(S)-1-methyl-1,2,3,4-tetrahydronaphthalene (from titanium-catalyzed reduction of 1-methyl-3,4-dihydronaphthalene): Following General Procedure B, (R, R)-(EBTHI)TiMe₂ (30 mg, 0.088 mmol) and [PhMe₂NH][B(C₆F₅)₄] (71 mg, 0.089 mmol) in toluene (6 mL) were used to convert 4 (263 mg, 1.82 mmol) to a colorless oil in 20 min. ¹H NMR showed that the product consisted of a mixture of starting material (66%), 1-methyl-1,2,3,4-tetrahydronaphthalene (30%), and 1-methylnaphthalene (4%). Chiral GC analysis (Chiraldex G-TA column) determined that the reduction product had an ee of 17%.
References


Chapter 2

Asymmetric Hydrogenation of Unfunctionalized Tetrasubstituted Olefins with a Cationic Zirconocene Catalyst
Among double bond-containing substrates that are suitable as targets for asymmetric reduction, tetrasubstituted olefins are of particular interest because the products may contain two stereogenic centers. At the same time, tetrasubstituted olefins are generally the least reactive class of olefins in hydrogenation reactions; steric hindrance compromises their ability to bind to most transition metal complexes. However, Crabtree's catalyst \([\text{Ir}(\text{COD})(\text{PCy}_3)(\text{py})]^+\text{[PF}_6]^-\) is highly effective for the hydrogenation of tetrasubstituted olefins.\(^1\)

Attempts to develop asymmetric hydrogenation catalysts based on Crabtree's catalyst have not been very successful. The precatalyst \([\text{Ir}(\text{COD})(\text{bzn})(\text{nmdpp})]^+\text{[ClO}_4]^-\) (bzn = benzonitrile, nmdpp = \((-\)neomethylene)diphenylphosphine) hydrogenated the tetrasubstituted olefins below effectively at 20 °C and 1 atm \(\text{H}_2\); this catalyst was actually less active for the hydrogenation of trisubstituted analogs (Scheme 1). However, the ee's did not exceed 27\%.\(^2\)

Much higher selectivities for reduction of fully substituted acylaminoacrylic esters have been achieved by using cationic Rh catalysts. Some ligands which can be successfully used for the highly enantioselective reduction of monosubstituted enamides show lower activity and selectivity in the reductions of \(\beta,\beta\)-disubstituted substrates.\(^3,4\) It has recently been shown that these problems can be overcome through the use of bidentate phosphine ligands which have a more flexible backbone and more electron-rich substituents (Scheme 2). These characteristics make the complex more reactive towards the hindered olefins. For instance, the rhodium(I) complex of the fully alkyl-substituted phosphine Et-DuPHOS reduced the valine precursor
1 to the desired product with 74% ee. However, the ee obtained by using the less hindered Me-DuPHOS was 96.0% at 90 psi H₂, and the ee obtained by using the more flexible Me-BPE ligand was 98.2%. These catalysts were also applied to the hydrogenation of olefins with dissimilar substituents, often giving products with very high diastereomeric purity. The absolute configuration of the α-carbon was determined by the enantiomer of the catalyst chosen ((R, R) or (S, S)); the relative configuration of the β-carbon was determined by the olefin geometry (E or Z). Olefin 1 has also been hydrogenated with 93.0% ee by the rhodium complex of 2, another fully alkyl-substituted ligand which is stereogenic at phosphorous, and with 88% ee by the rhodium complex of BuTRAP.

The only general class of tetrasubstituted olefins outside of the acylaminoacrylic esters to be hydrogenated with high enantioselectivity are fully substituted aryl acrylic acids. At room temperature and 50 atm H₂, rhodium
Scheme 2

\[ \text{Me} \overset{\text{CO}_2\text{Me}}{\text{NHCOMe}} \quad [\text{Rh(P-P)}]^+ \quad \text{H}_2 \quad \text{Me} \overset{\text{CO}_2\text{Me}}{\text{NHCOMe}} \]

<table>
<thead>
<tr>
<th>Pressure</th>
<th>ee</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>74%</td>
</tr>
<tr>
<td></td>
<td>90 psi</td>
</tr>
<tr>
<td>Et-DuPHOS</td>
<td>Me-DuPHOS</td>
</tr>
<tr>
<td></td>
<td>96.0%</td>
</tr>
<tr>
<td></td>
<td>90 psi</td>
</tr>
<tr>
<td>Me-BPE</td>
<td></td>
</tr>
<tr>
<td></td>
<td>98.2%</td>
</tr>
<tr>
<td></td>
<td>90 psi</td>
</tr>
<tr>
<td>Me-BPE</td>
<td></td>
</tr>
<tr>
<td></td>
<td>88%</td>
</tr>
<tr>
<td></td>
<td>15 psi</td>
</tr>
<tr>
<td>BuTRAP</td>
<td></td>
</tr>
<tr>
<td></td>
<td>93.0%</td>
</tr>
<tr>
<td></td>
<td>90 psi</td>
</tr>
<tr>
<td>2</td>
<td></td>
</tr>
</tbody>
</table>

\[ \text{R} \overset{\text{CO}_2\text{Me}}{\text{NHCOMe}} \quad [(\text{COD})\text{Rh(Me-BPE)}]^+\text{OTf}^{-} \quad \text{R} \overset{\text{CO}_2\text{Me}}{\text{NHCOMe}} \]

90 psi \text{H}_2

80 - 99% ee
complexes of the ferrocenyl diphosphine 3 reduced olefins 4 to alkylcarboxylic acids with ee's of 92-98% (Scheme 3). Apparently, the terminal amino group of 3 interacts with the carboxylic acid group of the substrate, possibly forming an ammonium carboxylate. This feature appears to be responsible for the catalyst's effectiveness; the corresponding esters cannot be reduced with this catalyst, and complexes of ligands which lack a terminal amino group are much less active and selective. The cyclic olefins 5 and 6 could also be hydrogenated with good ee's; the reduction of 5 was completely cis-selective, while in the case of indene 6, a significant amount of trans product was obtained.  

Scheme 3

\[
\text{RhCl(NBD)} + \text{AgBF}_4 \quad 0.5 \text{ mol \%}
\]

\[
\begin{array}{c}
\text{R} = \text{Me, Et, Ph} \\
\text{Ar} = \text{Ph, 2-Naphthyl, 4-Cl-C}_6\text{H}_4, 4-\text{MeO-C}_6\text{H}_4
\end{array}
\]

R = Me, Et, Ph
Ar = Ph, 2-Naphthyl,
4-Cl-C\text{H}_4, 4-MeO-C\text{H}_4

92 - 98% ee

87% ee

77 : 23
The highly asymmetric reduction of unfunctionalized tetrasubstituted olefins has not been achieved. The early transition metal complexes described in Chapter 1 which have been successfully utilized in unfunctionalized olefin reduction have not been applied to tetrasubstituted substrates. As with the late transition metal complexes, steric hindrance is expected to be a problem.

As reported in Chapter 1, the highly electrophilic "catiionic" metalocene hydride system arising from hydrogenation of (EBTHI)-ZrMe$_2$/[PhMe$_2$NH][B(C$_6$F$_5$)$_4$] can reduce unfunctionalized trisubstituted olefins rapidly under mild conditions. Its reactivity towards olefins containing one more substituent is therefore expected to be good. In the absence of coordinating heteroatoms, it is difficult to predict the regioselectivity of addition to olefins with four alkyl substituents. As noted in Chapter 1, coordination of the metal atoms to aromatic rings can direct the insertion of the catalyst into nearby double bonds. Thus, reductions of aryl-substituted olefins may be expected to proceed with good regioselectivity. It cannot be predicted whether these reactions would proceed with high facial selectivity.
Results and Discussion

The relatively less hindered 2-methyl-3-aryl-2-butenes were examined in initial studies on the feasibility of reducing tetrasubstituted olefins using cationic zirconocene catalysts. \((R, R)-(EBTHI)\text{ZrMe}_2\) and \([\text{PhMe}_2\text{NH}^+][\text{B(C}_6\text{F}_5)_4]\) were allowed to react in benzene under argon, a hydrogen atmosphere was introduced, and the substrate was added. The hydrogenation of 1 proceeded only to about 60% conversion after 1 h, showing that these olefins are not reduced as rapidly as trisubstituted analogues (Chapter 1).

Table 1

\[
(R, R)-(EBTHI)\text{ZrMe}_2 + [\text{PhMe}_2\text{NH}]^+\text{[B(C}_6\text{F}_5)_4] \xrightarrow{\text{H}_2} \text{olefin}
\]

<table>
<thead>
<tr>
<th>Olefin</th>
<th>Pressure</th>
<th>Catalyst Loading</th>
<th>Yield</th>
<th>ee</th>
<th>Time</th>
</tr>
</thead>
<tbody>
<tr>
<td><img src="image1.png" alt="Image of 1" /></td>
<td>80 psig</td>
<td>8 mol %</td>
<td>79%</td>
<td>84%</td>
<td>16 h</td>
</tr>
<tr>
<td><img src="image2.png" alt="Image of 2" /></td>
<td>80 psig</td>
<td>5 mol %</td>
<td>95%</td>
<td>60%</td>
<td>17 h</td>
</tr>
</tbody>
</table>

A number of cyclic olefins were also examined; hydrogenation of these substrates creates two new stereogenic centers. Dihydronaphthalene 3 could not be fully reduced in one hour, but the reaction was complete when left overnight (Table 2). The expected cis isomer was obtained in a cis:trans ratio of
96:4 and had an ee of 92%. However, a significant amount of naphthalene byproduct was also obtained. The high ee observed for the product indicates that the naphthalene could not have been produced by a nonenantioselective catalytic disproportionation by the cocatalyst (as was proposed for the disproportionations observed in Chapter 1); the contribution from racemic product would lower the overall ee. In addition, a second byproduct (5,6-dimethyl-1,2,3,4-tetrahydronaphthalene) was formed. Under high pressure (2000 psig), the ee of the product was unchanged, and the only byproduct observed was 5,6-dimethyltetralin.

Table 2

\[(R, R)-(EBTHI)ZrMe_2 + [PhMe_2NH]^+[B(C_6F_5)_4]^{-}\] 
5 mol % 

<table>
<thead>
<tr>
<th>Olefin</th>
<th>Products</th>
<th>Pressure</th>
<th>Result</th>
<th>cis:trans</th>
</tr>
</thead>
<tbody>
<tr>
<td><img src="image1" alt="3" /></td>
<td>![image2] + ![image3]</td>
<td>80 psig</td>
<td>92% ee</td>
<td>96:4</td>
</tr>
<tr>
<td>(78% product 12% naphthalene 10% other tetralin)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><img src="image1" alt="3" /></td>
<td>![image2] + ![image3]</td>
<td>2000 psig</td>
<td>92% ee</td>
<td>&gt;99:1</td>
</tr>
<tr>
<td>(91% product 9% other tetralin)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

The aromatized product may originate from C-H activation of the benzylic 1-position of the dihydronaphthalene. This step would be promoted by complexation of the catalyst to the ring π-system. (Similar examples of directed
C-H activation by this catalyst are reported in Chapter 1.) β-Hydride elimination would give the naphthalene. Presumably, the naphthalene can then be hydrogenated at the less hindered ring, giving the 5,6-dimethyltetralin. Thus, the total amount of both byproducts represents the degree of aromatization.

Scheme 4

The catalyst was then applied to the reduction of 2,3-disubstituted-1H-indenes (Table 3). Indenes 4 and 5 could be reduced overnight to give products with high ee's and high cis:trans ratios. For substrates 6, 7, and 9, with phenyl substituents, high pressure was required, and the enantioselectivity was good to excellent. At low pressure, the sense of enantioselection for 9 was reversed.

When the reaction of 5 was carried out under D₂, \(^{1}\text{H} \) NMR and \(^{2}\text{H} \) NMR showed extensive deuterium incorporation into the 1-, 2-, and 3- positions of the indane; a small amount was also found in the methyl group (Scheme 5). No D was present in the butyl chain. Non-deuterated indane product was left unchanged by exposure to the catalyst under deuterium atmosphere.
Table 3

\[
(R, R)-\text{EBTHI} \text{ZrMe}_2 + [\text{PhMe}_2 \text{NH}]^+[\text{B(C}_6\text{F}_5)_4]^-
\xrightarrow{\text{H}_2, \text{benzene, r. t.}} \text{olefin}
\]

<table>
<thead>
<tr>
<th>Olefin</th>
<th>Pressure</th>
<th>Catalyst Loading</th>
<th>Yield/Conversion</th>
<th>ee</th>
<th>cis:trans</th>
<th>Time</th>
</tr>
</thead>
<tbody>
<tr>
<td><img src="image.png" alt="Image" /></td>
<td>80 psig 5 mol %</td>
<td>76%</td>
<td>86%</td>
<td>95:5</td>
<td>15 h</td>
<td></td>
</tr>
<tr>
<td><img src="image.png" alt="Image" /></td>
<td>80 psig 8 mol %</td>
<td>96%</td>
<td>92%</td>
<td>99:1</td>
<td>19 h</td>
<td></td>
</tr>
<tr>
<td><img src="image.png" alt="Image" /></td>
<td>80 psig 1000 psig 5 mol %</td>
<td>34% conv.</td>
<td>97%</td>
<td>98:2</td>
<td>12 h</td>
<td></td>
</tr>
<tr>
<td><img src="image.png" alt="Image" /></td>
<td>1500 psig 8 mol %</td>
<td>94%</td>
<td>98%</td>
<td>&gt;99:1</td>
<td>39 h</td>
<td></td>
</tr>
<tr>
<td><img src="image.png" alt="Image" /></td>
<td>80 psig 1000 psig 5 mol %</td>
<td>65% conv.</td>
<td>97%</td>
<td>97:3</td>
<td>21 h</td>
<td></td>
</tr>
<tr>
<td><img src="image.png" alt="Image" /></td>
<td>80 psig 1000 psig 5 mol %</td>
<td>57% conv.</td>
<td>5%</td>
<td>89:11</td>
<td>16 h</td>
<td></td>
</tr>
<tr>
<td><img src="image.png" alt="Image" /></td>
<td>80 psig 2000 psig 5 mol %</td>
<td>44% conv.</td>
<td>29% (+)</td>
<td>&gt;99:1</td>
<td>30 h</td>
<td></td>
</tr>
<tr>
<td><img src="image.png" alt="Image" /></td>
<td>94%</td>
<td>78% (−)</td>
<td>&gt;99:1</td>
<td>14 h</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
Scheme 5

\[(R, R)-(\text{EBTH})\text{ZrMe}_2 [\text{PhMe}_2\text{NH}]^+\text{[B(C}_5\text{F}_5)_4]^-.\]
\[\text{80 psig D}_2\]
\[\text{benzene}\]
\[\text{r. t.}\]
\[\rightarrow\]
\[\text{15 h}\]
\[\text{90% ee}\]
\[\text{90% ee}\]

The above experiments suggest that one of several isomerizations can occur before the Zr-alkyl intermediate undergoes hydrogenolysis (or deuterolysis.) As proposed in Chapter 1, the catalyst may react with the Zr center binding at the benzylic carbon atom so that the aryl ring can stabilize the metal center (Scheme 6). \(\beta\)-hydride elimination to a disubstituted olefin followed by rapid reduction would introduce deuterium into the methyl group.
However, the virtually complete deuterium incorporation into the 1H-position can arise a number of ways. If the catalyst reacts so that the zirconium resides at the 2-position rather than the 3-position of the indene, β-hydride elimination would produce one of two possible indene isomers, both of which could undergo insertion again (Scheme 7). Deuteration by this pathway would resemble the mechanism in Scheme 6 above.

In both of these schemes, the alternate olefin isomers already contain one stereogenic center. A loss of selectivity during hydrogenation of these intermediates would lead to a lower cis:trans ratio, but the selectivity must be high, since the observed ratios are high. (The products were identical to the products of Pd/C-catalyzed hydrogenation of the same indenes, which is expected to give cis indanes. In the case of 4, the cis product is reported in the
literature; in the case of 9, NOe studies on both cis and trans isomers provided corroborating evidence for the assignments.) If the trisubstituted olefin 10 is

Scheme 7

indeed an intermediate, as suggested in Scheme 7, hydrogenation would be expected to follow the models proposed in Chapter 1. Accordingly, the catalyst would insert with the Zr atom at the less-substituted (aryl-substituted) position as shown in Scheme 8, with the structures on the left favored over the structures on the right. It is not known which enantiomer of 10 would be produced in Scheme 7; however, the models in Scheme 8 suggest that hydrogenation of (S)-10 would favor trans product (which is not observed), while hydrogenation of (R)-10 would favor the cis product.
Scheme 8

Does this indicate that the final product has the \((R, R)\) configuration? A comparison of transition states representing insertions into the double bond of 5 is shown in Scheme 9. The possible isomerization pathways and the final products ((\(R, R\)) or \((S, S)\) indane) are depicted below. It is not clear which of the transition states are favored, since interactions between the ligand and either the Me or Bu groups could be taking place in any of them. Assignment of the product's absolute configuration will make further elucidation of the mechanism possible.
The experiments in Chapter 1 raise the possibility that the almost complete replacement of both hydrogens with deuterium at the 1H-position is occurring through an alternative mechanism. In these reactions, it was demonstrated that an aryl group or oxygen atom could direct C-H activation at adjacent carbon atoms. In Scheme 4 above, a benzylic Zr-alkyl intermediate was proposed for the aromatization of 3. Such an intermediate formed from an indene would result in a stabilized π-allyl structure (Scheme 10). Deuterolysis of this intermediate would introduce D into the 1- and possibly 3-ring positions.

Scheme 10

Either of these reaction pathways should occur in the absence of hydrogen. Thus, (R, R)-(EBTHI)ZrMe₂ and [PhMe₂NH][B(C₆F₅)₄] were combined and stirred under argon and placed under deuterium atmosphere; the deuterium atmosphere was then removed and replaced with argon (Scheme 11). When olefin 5 was introduced into the mixture, the reaction turned brown; after 30 minutes only starting material was present except for a trace of product (<1%) as detected by GC. However, the starting material contained some deuterium at the 1-position of the indene ring. When D₂ was reintroduced, the pale yellow color instantly returned and the reaction
proceeded normally to give product which contained deuterium in the positions noted previously.

Scheme 11

\[
(R, R)-\text{EBTHI}Zr\text{Me}_2 \\
\text{[PhMe}_2\text{NH}]^+\text{[B(C}_6\text{F}_5)_4]^\text{-} \\
8 \text{ mol } \%
\] 

\[80 \text{ psig D}_2 \rightarrow \text{Ar} \rightarrow 5 \text{ min} \rightarrow \text{30 min} \rightarrow \text{23}\%\]

\% D incorporation:

\[89\% \text{ ee}\]

The reaction of 9 under D$_2$ was also examined in order to gain some insight into the reversal of selectivity observed at higher pressure (Scheme 12). Under 80 psig D$_2$ the reduction was allowed to proceed for one day, and both starting material and product were recovered. The starting material was virtually completely deuterated at the 1-position. The product was also almost fully deuterated at every position on the ring; deuteration at the methyl position was almost undetectable. However, the product was enriched in the (-) enantiomer (as shown by the order of elution on a chiral GC column), whereas hydrogenation of 9 at the same pressure gave indane which was enriched in the (+) enantiomer!
Scheme 12

\[
(R, R)-(EBTII)ZrMe_2 \quad [\text{PhMe}_2\text{NH}]^+\text{[B(C_6F_5)_4]}^- 
\begin{array}{c}
\text{80 psig D}_2 \\
\text{benzene} \\
\text{r. t.}
\end{array}
\rightarrow
\begin{array}{c}
\text{9} \\
\end{array}
\]

% D incorporation:

\[
\begin{array}{ccc}
\text{Ph} & \quad \text{Me} & \quad \text{Ph} \\
99\% & \quad + & \quad 95\%
\end{array}
\]

\[
\begin{array}{ccc}
\text{Ph} & \quad \text{Me} & \quad \text{Ph} \\
94\% & \quad \text{trace by } ^2\text{H NMR} & \quad 0\% \text{ by } ^1\text{H NMR} \\
98\% & \quad 90\%
\end{array}
\]

40% ee
41% conversion

<table>
<thead>
<tr>
<th>Pressure</th>
<th>Catalyst Loading</th>
<th>Yield</th>
<th>ee (isomer)</th>
<th>cis:trans</th>
</tr>
</thead>
<tbody>
<tr>
<td>80 psig H\textsubscript{2}</td>
<td>5 mol %</td>
<td>7% conv (1 h)</td>
<td>28% (+)</td>
<td>99:1</td>
</tr>
<tr>
<td></td>
<td></td>
<td>24% conv (4 h)</td>
<td>29% (+)</td>
<td>99:1</td>
</tr>
<tr>
<td></td>
<td></td>
<td>44% conv (30 h)</td>
<td>29% (+)</td>
<td>99:1</td>
</tr>
<tr>
<td>80 psig D\textsubscript{2}</td>
<td></td>
<td>41% conv (16 h)</td>
<td>40% (-)</td>
<td>99:1</td>
</tr>
<tr>
<td>2000 psig H\textsubscript{2}</td>
<td></td>
<td>94% yield</td>
<td>78% (-)</td>
<td>99:1</td>
</tr>
</tbody>
</table>

The dramatic influence of pressure on ee signals the presence of competing pathways with different stereochemical outcomes. As noted above, the high cis:trans ratio shows that the reversal in selectivity does not arise from hydrogenation of other olefin isomers (in contrast to the trisubstituted olefin hydrogenations described in Chapter 1.) Instead, the observed enantioselectivity probably depends on contributions from the various metal alkyl intermediates formed upon insertion of the metal-hydrogen bond into the starting material. These complexes may have differing rates of hydrogenolysis.
as well as differing rates of β-hydride elimination, both of which could be influenced by the pressure and identity of the reducing agent (H₂ or D₂). For instance, reduction that proceeds through an intermediate involving a metal alkyl with the Zr center at the 3-position (A) may give the (-) isomer preferentially, whereas reduction that proceeds with the metal center at the 2- or 1-position (B or C) may give the (+) isomer preferentially (Scheme 13: absolute configurations are assigned arbitrarily.) Intermediate A would be stabilized by two aromatic groups adjacent to the metal center. Reversible insertion / β-hydride elimination processes giving species A, B, and C would explain the incorporation of deuterium into all positions of the ring under D₂ atmosphere. The rate of hydrogenolysis of A versus the rate of its elimination to 9 (providing entry into pathways through B or C) would determine the ee and the enantiomer observed. At higher pressures, hydrogenolysis of A would be more predominant, giving the (-) enantiomer. The (-) product is also observed under 80 psig D₂, indicating that reaction through A is again predominant. Yet under the same pressure of H₂, pathways through B or C apparently become more important in this model, yielding (+) enantiomer as the product. This suggests that the kinetic isotope effect for β-hydride elimination of A to 9 (kH₂/kD₂) is larger than the kinetic isotope effect for hydrogenolysis of A (kH₁/kD₁). Thus, the rate of hydrogenolysis versus elimination would be greater under deuterium atmosphere than under hydrogen atmosphere, and under 80 psig large enough to overturn the selectivity. However, the scheme outlined below is just one of many which could be proposed to explain the data above.
Scheme 13

\[
\begin{align*}
\text{A} & \xrightarrow{\text{H}_2} \text{Ph} \quad \text{Ph} \\
\text{Zr(EBTHI)} & \text{Me} \quad \text{Me} \\
\text{B} & \xrightarrow{\text{H}_2} \text{Ph} \quad \text{Ph} \\
\text{Zr(EBTHI)} & \text{Me} \quad \text{Me} \\
\text{C} & \xrightarrow{(\text{EBTHI})Zr^+ \cdot \text{H}} \\
\text{H}_2 & \\
\text{D} & \\
\text{Ph} & \text{Ph} \\
\text{Me} & \text{Me} \\
\end{align*}
\]

\(-\) isomer? (absolute stereochemistry unknown)

\[
\begin{align*}
\text{H}_1 & \\
\text{H}_2 & \\
\text{D}_1 & \\
\text{D}_2 & \\
\end{align*}
\]

\[
k_{\text{H}_1}/k_{\text{D}_1} > k_{\text{H}_2}/k_{\text{D}_2}
\]
Conclusions

The highly electrophilic olefin reduction catalysts produced by combining $(R, R)$-(EBTHI)$\text{ZrMe}_2$ and [PhMe$_2$NH][B(C$_6$F$_5$)$_4$] under a hydrogen atmosphere are reactive enough to hydrogenate tetrasubstituted aryl olefins. For a series of fully substituted indenes containing either a methyl substituent or a phenyl substituent, ee's were good to very high; such results have not been previously attained for unfunctionalized tetrasubstituted olefins. The deuteration experiments provide evidence for a number of reaction pathways; it is possible that reaction at the 1$H$-position of the indene competes with insertion into the hindered double bond. The absolute configuration of the products remains to be established; it is not known whether all the indenes are reduced with the same sense of enantioselection. This information will be vital for gaining a greater understanding of the mechanism of this process.
Experimental Procedures

General Considerations. All manipulations involving air-sensitive materials were conducted in a Vacuum Atmospheres glovebox under an atmosphere of nitrogen or using standard Schlenk techniques under argon. Unless stated otherwise, all reactions were conducted in flasks sealed with a rubber septum under a positive pressure of argon. (Caution: Reactions under high pressure should be carried out behind an appropriate safety shield.) THF was distilled under argon from sodium/benzophenone ketyl. Toluene was distilled under argon from molten sodium. Anhydrous benzene, pentane, hexanes, and CH$_2$Cl$_2$ were obtained from Aldrich and used without further purification. rac-(EBI)ZrCl$_2$ was a gift from Boulder Scientific. [PhMe$_2$NH][B(C$_6$F$_5$)$_4$] was a gift from Exxon. Resolved (EBTHI)Zr(Binol) was synthesized as described in reference 11. All other reagents were available from commercial sources and were used without further purification, unless otherwise noted.

Flash chromatography was performed on E. M. Science Kieselgel 60 (230-400 mesh) unless otherwise noted. Yields refer to isolated yields of compounds of greater than 95% purity as estimated by capillary GC and $^1$H NMR analysis, and in the cases of unknown compounds, by elemental analysis. Yields indicated in this section refer to a single experiment, while those reported in the tables are an average of two or more runs, so the numbers may differ slightly. All compounds were characterized by $^1$H NMR, $^{13}$C NMR, and IR spectroscopy. Previously unreported compounds were also characterized by elemental analysis (E & R Analytical Laboratory, Inc.). Nuclear magnetic resonance (NMR) spectra were recorded on a Varian XL-300, a Varian VXR-500, or a Varian Unity 300. Splitting patterns are designated as follows: s,
singlet; d, doublet; dd, doublet of doublets; t, triplet; td, triplet of doublets; q,
quartet; qd, quartet of doublets; m, multiplet. All $^1$H NMR spectra are reported in
$\delta$ units, parts per million (ppm) downfield from tetramethylsilane. All $^{13}$C NMR
and $^2$H NMR spectra are reported in ppm relative to deuterochloroform (77 ppm
and 7.24 ppm, respectively.) Infrared (IR) spectra were recorded on an ASi
Applied Systems ReactIR 1000 (solids were measured neat on a DiComp
probe.) Gas chromatography (GC) analyses were performed on a Hewlett-
Packard 5890 or 6890 gas chromatograph with an FID detector using a 25 m x
0.20 mm capillary column with cross-linked SE-30 as a stationary phase. Chiral
GC analyses were performed on a Hewlett-Packard 5890 gas chromatograph
using a Chiraldex B-PH or Chiraladex G-TA column (20 m x 0.25 mm). Chiral
HPLC analyses were performed on a Hewlett-Packard 1100 system with an HP
1100 Diode Array Detector using a Chiracel OJ column (25 cm x 0.46 cm).
Racemic compounds analogous to the enantiomerically enriched compounds
described below were prepared by reduction of the olefin substrates under
hydrogen atmosphere catalyzed by Pd/C. The HPLC or GC retention times of
the racemic products matched those of the enantiomerically enriched products.

$(\textit{R, R})$-(EBTHI)ZrMe$_2$: This complex was synthesized using a modification of
the literature procedure.$^{12}$ A solution of methyllithium-lithium bromide complex
in diethyl ether (1.5 M, 2.7 mL, 4.0 mmol) was added via syringe to a solution of
$(\textit{R, R, R})$-(EBTHI)Zr(Binol) (1.13 g, 1.77 mmol) in benzene (20 mL) under argon,
giving rise to a white suspension. (Note: The methyllithium-lithium bromide
solution was stored at all times in a nitrogen-filled glovebox.) The flask was
wrapped in foil to protect from light, and the reaction mixture was stirred for 1 h.
The benzene was removed \textit{in vacuo} on a Schlenk line, leaving an off-white
solid. Hexanes (15 mL) were added and the solid was broken up with a spatula
under a stream of argon. The mixture was stirred for 70 min and filtered under argon atmosphere. This procedure was repeated twice (10 mL hexanes, 15 min stirring each time). The combined filtrates were concentrated in vacuo on a Schlenk line to a white solid. The flask was transferred to a nitrogen-filled glovebox and the solid was dissolved in minimal pentane (5 mL). The solution was cooled to -20 °C and allowed to stand overnight, during which time crystals formed. Decantation of the pentane afforded \((R, R)-(EBTHI)ZrMe_2\) as white crystals (522 mg, 76%). \(^1\)H NMR (300 MHz, CDCl\(_3\)):\(^{13}\) \(\delta\) 6.16 (d, \(J = 2.4\) Hz, 2 H); 5.12 (d, \(J = 3.0\) Hz, 2 H); 2.89 - 2.80 (m, 2 H); 2.69 - 2.60 (m, 2 H); 2.36 (s, 4 H); 2.31 - 2.22 (m, 2 H); 2.02 - 1.92 (m, 2 H); 1.78 - 1.54 (m, 6 H); 1.46 - 1.40 (m, 2 H); -0.10 (s, 6 H).

2-(4-fluorophenyl)-3-methyl-2-butene (1): A flame-dried Schlenk flask was charged with potassium tert-butoxide (2.26 g, 20.1 mmol) and a stir bar. DMSO (24 mL) was added, followed by isopropyltriphenylphosphonium iodide (8.66 g, 20.0 mmol). This mixture was added dropwise via cannula to a solution of 4'-fluoroacetophenone (705 mg, 5.10 mmol) in benzene (20 mL). The reaction was heated to reflux overnight. It was allowed to cool to room temperature, and pentane and water were added. The organic phase was separated and washed with water (2x) and saturated aqueous NaCl solution, dried over MgSO\(_4\), filtered, and concentrated in vacuo. Purification by flash column chromatography (hexanes) afforded 1 as a colorless oil (723 mg, 86%). \(^1\)H NMR (300 MHz, CDCl\(_3\)): \(\delta\) 7.09 - 6.95 (m, 4 H); 1.93 (s, 3 H); 1.80 (s, 3 H); 1.57 (s, 3 H). \(^{13}\)C NMR (125 MHz, CDCl\(_3\)): \(\delta\) 162.0, 160.1, 141.1(2), 129.9, 129.8, 129.0, 127.7, 114.8, 114.6, 22.0, 20.9, 20.5. IR (neat): 2988, 2915, 2860, 1600, 1509, 1449 cm\(^{-1}\). Anal. calcd for C\(_{11}\)H\(_{13}\)F: C, 80.45; H, 7.98. Found: C, 80.18; H, 8.10.
2-(4-(tert-butyldimethylsilyloxy)phenyl)-3-methyl-2-butene (2): A solution of 4-(tert-butyldimethylsilyloxy)acetophenone (2.52 g, 10.1 mmol) in diethyl ether (25 mL) was added dropwise via cannula to a solution of isopropyl magnesium chloride (2.0 M in diethyl ether, 16 mL, 32 mmol) under argon at 0 °C. The mixture was stirred at room temperature overnight. A saturated aqueous solution of NH₄Cl was added dropwise to quench the reaction, followed by diethyl ether and water. The aqueous phase was separated and extracted with diethyl ether. The combined organic phases were washed with saturated aqueous NaCl solution, dried over MgSO₄, filtered, and concentrated in vacuo. The resulting oil was dissolved in toluene (50 mL). p-Toluenesulfonic acid (20 mg) was added and the mixture was refluxed for 4 days. It was allowed to cool to room temperature, and diethyl ether and saturated aqueous NaHCO₃ solution were added. The organic phase was separated and washed with saturated aqueous NaCl solution, dried over MgSO₄, filtered, and concentrated in vacuo. Purification by flash column chromatography (hexanes) afforded 2 as a colorless oil (1.05 g, 38%). ¹H NMR (300 MHz, CDCl₃): δ 6.97 (d, J = 8.1 Hz, 2 H); 6.76 (d, J = 8.4 Hz, 2 H); 1.93 (s, 3 H); 1.78 (s, 3 H); 1.58 (s, 3 H); 0.98 (s, 9 H); 0.20 (s, 6 H). ¹³C NMR (75 MHz, CDCl₃): δ 153.5, 138.2, 129.6, 129.3, 126.8, 119.3, 25.7, 22.1, 20.8, 20.6, 18.2, -4.4. IR (neat): 2957, 2931, 2858, 1604, 1513, 1503, 1472, 1462 cm⁻¹. Anal. calcd for C₁₇H₂₈OSi: C, 73.85; H, 10.21. Found: C, 74.02; H, 10.28.

1,2-Dimethyl-3,4-dihydonaphthalene (3):¹⁵ A solution of 2-methyl-1-tetralone (3.98 g, 24.8 mmol) in THF (20 mL) was added dropwise via cannula to a solution of methylolithium-lithium bromide complex in diethyl ether (1.5 M, 25 mL, 38 mmol) under argon at 0 °C. The mixture was stirred at room temperature
for 2 h. A saturated aqueous solution of NH₄Cl was added dropwise to quench the reaction, followed by diethyl ether and water. The aqueous phase was separated and extracted with diethyl ether. The combined organic phases were washed with saturated aqueous NaCl solution, dried over MgSO₄, filtered, and concentrated *in vacuo*. The resulting oil was dissolved in benzene (30 mL). *p*-Toluenesulfonic acid (20 mg) was added and the mixture was refluxed for 20 h. The reaction mixture was allowed to cool to room temperature, and diethyl ether and saturated aqueous NaHCO₃ solution were added. The organic phase was separated and washed with saturated aqueous NaCl solution, dried over MgSO₄, filtered, and concentrated *in vacuo*. Purification by flash column chromatography (hexanes) afforded 3 as a light yellow oil (3.33 g, 85%). ¹H NMR (300 MHz, CDCl₃): δ 7.21 - 7.14 (m, 2 H); 7.08 - 7.06 (m, 2 H); 2.72 (t, *J* = 8.0 Hz, 2 H); 2.21 (t, *J* = 7.8 Hz, 2 H); 2.01 (s, 3 H); 1.90 (s, 3 H).

**2,3-Dimethyl-1H-indene (4):** A solution of 2-methyl-1-indanone (1.9 mL, 13.8 mmol) in THF (20 mL) was added dropwise via cannula to a solution of methyllithium-lithium bromide complex in diethyl ether (1.5 M, 14 mL, 21 mmol) under argon at 0 °C. The mixture was stirred at room temperature for 3.5 h. A saturated aqueous solution of NH₄Cl was added dropwise to quench the reaction, followed by diethyl ether and water. The aqueous phase was separated and extracted with diethyl ether. The combined organic phases were washed with saturated aqueous NaCl solution, dried over MgSO₄, filtered, and concentrated *in vacuo*. The resulting oil was dissolved in benzene (50 mL). *p*-Toluenesulfonic acid (20 mg) was added and the mixture was refluxed for 13.5 h. It was allowed to cool to room temperature, and diethyl ether and saturated aqueous NaHCO₃ solution were added. The organic phase was separated and washed with saturated aqueous NaCl solution, dried over MgSO₄, filtered, and
concentrated *in vacuo*. Purification by flash column chromatography (hexanes) afforded 4 as a light yellow oil (1.63 g, 82%). $^1$H NMR (300 MHz, CDCl$_3$):$^1$ $^1$H NMR (300 MHz, CDCl$_3$):$^1$ $^1$H NMR (300 MHz, CDCl$_3$):$^1$ 8 7.35 (td, $J = 0.9$ Hz, $J = 7.2$ Hz, 1 H); 7.28 - 7.19 (m, 2 H); 7.10 (td, $J = 1.5$ Hz, $J = 7.2$ Hz, 1 H); 3.24 (d, $J = 0.9$ Hz, 2 H); 2.05 (d, $J = 0.9$ Hz, 3 H); 2.02 (d, $J = 1.2$ Hz, 3 H). Anal. calcd for C$_{11}$H$_{12}$: C, 91.61; H, 8.39. Found: C, 91.53; H, 8.09.

2-Butyl-3-methyl-1H-indene (5):$^1$ Hexanophenone (4.2 mL, 23 mmol), hexamethylenetetramine (4.52 g, 32.2 mmol) and acetic anhydride (5 mL) were combined under argon, and the mixture was stirred at 80 °C overnight. The reaction mixture was allowed to cool to room temperature and was then poured into a mixture of 10% NaOH solution (50 mL) and CH$_2$Cl$_2$ (50 mL) with stirring. The organic layer was separated and washed with 1 N HCl solution. It was then concentrated *in vacuo* to an oil which was added dropwise by pipet to conc. H$_2$SO$_4$ solution (30 mL) with stirring. The next day the mixture was poured into 200 mL of crushed ice with stirring, and CH$_2$Cl$_2$ and water were added. The organic layer was separated, washed with saturated aqueous NaCl solution (3x), dried over MgSO$_4$, filtered, and concentrated *in vacuo*. Purification by flash column chromatography (30% EtOAc/hexanes) afforded 2-butyl-1-indanone as a yellow oil (2.49 g, 58%). $^1$H NMR (300 MHz, CDCl$_3$): $^1$H NMR (300 MHz, CDCl$_3$): $^1$H NMR (300 MHz, CDCl$_3$): 8 7.75 (d, $J = 7.5$ Hz, 1 H); 7.58 (td, $J = 1.2$ Hz, $J = 7.4$ Hz, 1 H); 7.46 (td, $J = 0.9$ Hz, $J = 7.6$ Hz, 1 H); 7.36 (td, $J = 0.9$ Hz, $J = 7.5$ Hz, 1 H); 3.33 (dd, $J = 8.0$ Hz, $J = 17.2$ Hz, 1 H); 2.82 (dd, $J = 3.8$ Hz, $J = 17.2$ Hz, 1 H); 2.69 - 2.62 (m, 1 H); 2.00 - 1.94 (m, 1 H); 1.50 - 1.34 (m, 5 H); 0.92 (t, $J = 7.2$ Hz, 3 H).

A solution of 2-butyl-1-indanone (2.49 g, 13.2 mmol) in THF (20 mL) was added dropwise via cannula to a solution of methyl lithium-lithium bromide complex in diethyl ether (1.5 M, 13 mL, 19.5 mmol) under argon at 0 °C. The
mixture was stirred at room temperature overnight. An saturated aqueous solution of NH₄Cl was added dropwise to quench the reaction, followed by diethyl ether and water. The aqueous phase was separated and extracted with diethyl ether. The combined organic phases were washed with saturated aqueous NaCl solution, dried over MgSO₄, filtered, and concentrated in vacuo. The crude oil was dissolved in toluene (50 mL). p-Toluenesulfonic acid (20 mg) was added and the mixture was refluxed for 2.5 h. At this time a crystal of I₂ was added, and the reaction was refluxed for an additional 2 h. It was allowed to cool to room temperature, and diethyl ether and saturated aqueous NaHCO₃ solution were added. The organic phase was separated and washed with saturated aqueous NaHCO₃ solution and saturated aqueous NaCl solution, dried over MgSO₄, filtered, and concentrated in vacuo. Purification by flash column chromatography (pentane) afforded 5 as a light yellow oil (1.93 g, 79%).

¹H NMR (300 MHz, CDCl₃): δ 7.37 (d, J = 7.5 Hz, 1 H); 7.29 - 7.21 (m, 2 H); 7.11 (td, J = 1.5 Hz, J = 7.1 Hz, 1 H); 3.27 (s, 2 H); 2.45 (t, J = 7.5 Hz, 2 H); 2.03 (s, 3 H); 1.56 - 1.46 (m, 2 H); 1.41 - 1.28 (m, 2 H); 0.92 (t, J = 7.4 Hz, 3H).

¹³C NMR (125 MHz, CDCl₃): δ 147.5, 142.8, 142.4, 132.3, 126.0, 123.6, 123.0, 118.0, 40.2, 31.9, 28.1, 22.6, 14.0, 10.2. IR (neat): 3066, 3042, 3018, 2930, 2856, 1629, 1606, 1466 cm⁻¹. Anal. calcd for C₁₄H₁₈: C, 90.26; H, 9.74. Found: C, 90.17; H, 9.74.

2-Phenyl-1-indanone:¹⁸ Thionyl chloride (2.6 mL, 35.6 mmol) was added via syringe to a suspension of 2,3-diphenylpropionic acid (4.93 g, 21.8 mmol) in benzene (6 mL) under argon. The reaction mixture was stirred at room temperature for 30 min, and then heated to reflux for 1.25 h. It was allowed to cool to room temperature, and solvent was removed by distillation at atmospheric pressure. Further distillation under vacuum (118 - 123 °C, 90
millitorr) afforded 2,3-diphenylpropionyl chloride: $^1$H NMR (300 MHz, CDCl$_3$): δ 7.37 - 7.32 (m, 3 H); 7.26 - 7.19 (m, 5 H); 7.09 - 7.07 (m, 2 H); 4.26 (t, $J = 7.5$ Hz, 1 H); 3.49 (dd, $J = 7.8$ Hz, $J = 14.1$ Hz, 1 H); 3.07 (dd, $J = 7.2$ Hz, $J = 13.8$ Hz, 1 H). The acid chloride was dissolved in benzene (20 mL), and the solution was added dropwise via cannula to a suspension of aluminum chloride (4.36 g, 32.7 mmol) in benzene (40 mL) under argon at 0 °C. The reaction mixture was stirred at room temperature for 1 h. Diethyl ether and 1 N HCl solution were added, and the aqueous phase was separated and extracted with diethyl ether. The organic phases were washed with saturated aqueous NaHCO$_3$ solution and saturated aqueous NaCl solution, dried over MgSO$_4$, filtered, and concentrated in vacuo to a yellow-white solid. Recrystallization (hexanes/CH$_2$Cl$_2$) afforded 2-phenyl-1-indanone as white crystals (3.46 g, 76%), mp 76 - 76.5 °C (lit 78 °C$^{18}$). $^1$H NMR (500 MHz, CDCl$_3$): δ 7.81 (d, $J = 7.5$ Hz, 1 H); 7.64 (td, $J = 1.0$ Hz, $J = 7.5$ Hz, 1 H); 7.53 (dd, $J = 1.0$ Hz, $J = 7.5$ Hz, 1 H); 7.42 (t, $J = 7.5$ Hz, 1 H); 7.33 - 7.30 (m, 2 H); 7.26 - 7.23 (m, 1 H); 7.19 - 7.18 (m, 2 H); 3.89 (dd, $J = 4.2$ Hz, $J = 8.8$ Hz, 1 H); 3.69 (dd, $J = 8.5$ Hz, $J = 17.5$ Hz, 1 H); 3.27 (dd, $J = 4.0$ Hz, $J = 17.5$ Hz, 1 H).

3-Methyl-2-phenyl-1H-indene (6): A solution of 2-phenyl-1-indanone (1.11 g, 5.33 mmol) in THF (20 mL) was added via cannula to a solution of methyllithium-lithium bromide complex in diethyl ether (1.5 M, 5.3 mL, 7.95 mmol) under argon at 0 °C. The mixture was stirred at room temperature for 1.5 h. A saturated aqueous solution of NH$_4$Cl was added dropwise to quench the reaction, followed by diethyl ether and water. The aqueous phase was separated and extracted with diethyl ether. The combined organic phases were washed with saturated aqueous NaCl solution, dried over MgSO$_4$, filtered, and concentrated in vacuo. The resulting oil was dissolved in toluene (50 mL).
Toluenesulfonic acid (20 mg) and a crystal of I$_2$ were added and the mixture was refluxed for 30 min. It was allowed to cool to room temperature, and diethyl ether and a saturated aqueous NaHCO$_3$ solution were added. The aqueous phase was separated and extracted with diethyl ether. The combined organic phases were washed with saturated aqueous NaHCO$_3$ solution and saturated aqueous NaCl solution, dried over MgSO$_4$, filtered, and concentrated in vacuo. Purification by flash column chromatography (hexanes) afforded an off-white solid (505 mg, 46%), mp 77 - 78.5 °C (lit 80 °C$^{19}$). $^1$H NMR (300 MHz, CDCl$_3$): δ 7.50 - 7.19 (m, 9 H); 3.74 (d, $J = 1.8$ Hz, 2 H); 2.31 (t, $J = 1.9$ Hz, 3 H). $^{13}$C NMR (125 MHz, CDCl$_3$): δ 147.4, 142.4, 140.3, 137.5, 134.7, 128.3, 128.2, 126.6, 126.4, 124.7, 123.3, 119.1, 40.9, 11.9. IR (neat): 3049, 3022, 2903, 1598, 1494, 1463, 1444 cm$^{-1}$. Anal. calcd for C$_{16}$H$_{14}$: C, 93.16; H, 6.84. Found: C, 93.34; H, 6.66.

3-Butyl-2-phenyl-1H-indene (7): A solution of 2-phenyl-1-indanone (2.30 g, 11.0 mmol) in diethyl ether (40 mL) was added via cannula to a solution of $n$-BuLi in hexane (1.6 M, 10.3 mL, 16.5 mmol) under argon at 0 °C. The mixture was stirred at room temperature for 1.5 h. A saturated aqueous solution of NH$_4$Cl was added dropwise to quench the reaction, followed by diethyl ether and water. The aqueous phase was separated and extracted with diethyl ether. The combined organic phases were washed with saturated aqueous NaCl solution, dried over MgSO$_4$, filtered, and concentrated in vacuo to an oil. The alcohol product was separated from the starting material by flash column chromatography (10% EtOAc/hexanes). The resulting oil was dissolved in toluene (50 mL). $p$-Toluenesulfonic acid (20 mg) and a crystal of I$_2$ were added and the mixture was refluxed for 2 h. The reaction mixture was allowed to cool to room temperature. Diethyl ether and saturated aqueous NaHCO$_3$ solution
were added, and the aqueous phase was separated and extracted with diethyl ether. The combined organic phases were washed with saturated aqueous NaHCO₃ solution and saturated aqueous NaCl solution, dried over MgSO₄, filtered, and concentrated in vacuo. Purification by two successive flash column chromatographies (hexanes) afforded 7 as a yellow oil (1.04 g, 38%). ¹H NMR (300 MHz, CDCl₃): δ 7.48 - 7.17 (m, 9 H); 3.72 (s, 2 H); 2.72 (t, J = 8.1 Hz, 2 H); 1.73 - 1.62 (m, 2 H); 1.44 (sextet, J = 7.3 Hz, 2 H); 0.94 (t, J = 7.4 Hz, 3 H). ¹³C NMR (75 MHz, CDCl₃): δ 146.7, 142.7, 140.3, 139.6, 137.7, 128.4, 128.1, 126.7, 126.3, 124.5, 123.4, 119.5, 41.4, 31.2, 26.0, 23.1, 13.9. IR (neat): 3052, 3020, 2955, 2928, 2859, 1604, 1492, 1466 cm⁻¹. Anal. calcd for C₁₉H₂₀: C, 91.88; H, 8.12. Found: C, 91.61; H, 8.39.

3-Ethyl-2-methyl-1H-indene (8):¹⁰ A solution of 2-methyl-1-indanone (1.95 g, 13.3 mmol) in THF (20 mL) was added via cannula to a solution of ethylmagnesium bromide in diethyl ether (3.0 M, 7 mL, 21 mmol) under argon at 0 °C. The mixture was stirred at room temperature for 5 h. A saturated aqueous solution of NH₄Cl was added dropwise to quench the reaction, followed by diethyl ether and water. The aqueous phase was separated and extracted with diethyl ether (2x). The combined organic phases were washed with water and saturated aqueous NaCl solution, dried over MgSO₄, filtered, and concentrated in vacuo. The resulting oil was dissolved in toluene (100 mL). p-Toluenesulfonic acid (10 mg) was added and the mixture was refluxed for 1 h. It was allowed to cool to room temperature, diethyl ether and saturated aqueous NaHCO₃ solution were added, and the aqueous phase was separated. The organic phase was washed with saturated aqueous NaCl solution, dried over MgSO₄, filtered, and concentrated in vacuo. Purification by flash column chromatography (hexanes) afforded 8 as a yellow oil (1.77 g, 84%). By ¹H
NMR, the product mixture was estimated to contain 3% 1-ethylidene-2-methylindane as determined by integration of a doublet at 1.83 ppm. $^1$H NMR (300 MHz, CDCl$_3$): $\delta$ 7.36 (dd, $J = 0.6$ Hz, $J = 7.2$ Hz, 1 H); 7.25 - 7.23 (m, 2 H); 7.12 - 7.07 (m, 1 H); 3.25 (s, 2 H); 2.52 (q, $J = 7.6$ Hz, 2 H); 2.06 (s, 3 H); 1.14 (t, $J = 7.6$ Hz, 3 H).

2-Methyl-3-phenyl-1H-indene (9):$^{21}$ A solution of 2-methyl-1-indanone (2.93 g, 20.0 mmol) in THF (30 mL) was added via cannula to a solution of phenyllithium in 70 : 30 cyclohexane : diethyl ether (1.8 M, 16.7 mL, 30.1 mmol) under argon at 0 °C. The mixture was stirred at room temperature for 0.5 h. A saturated aqueous solution of NH$_4$Cl was added dropwise to quench the reaction, followed by diethyl ether and water. The aqueous phase was separated and extracted with diethyl ether. The combined organic phases were washed with saturated aqueous NaCl solution, dried over MgSO$_4$, filtered, and concentrated in vacuo. A byproduct (biphenyl) was separated from the rest of the material by flash column chromatography (hexanes $\rightarrow$ CH$_2$Cl$_2$). The resulting oil was dissolved in toluene (50 mL). $\rho$-Toluenesulfonic acid (20 mg) and a crystal of I$_2$ were added and the mixture was refluxed for 45 min. It was allowed to cool to room temperature, and diethyl ether and saturated aqueous NaHCO$_3$ solution were added. The aqueous phase was separated and extracted with diethyl ether. The combined organic phases were washed with saturated aqueous NaHCO$_3$ solution and saturated aqueous NaCl solution, dried over MgSO$_4$, filtered, and concentrated in vacuo. Purification by flash column chromatography (100% hexanes $\rightarrow$ 10% CH$_2$Cl$_2$/hexanes) afforded 9 as a white solid (2.78 g, 67%), mp 58 - 60 °C (lit. 59.5 - 60.5 °C$^{22}$). $^1$H NMR (300 MHz, CDCl$_3$): $\delta$ 7.48 - 7.32 (m, 6 H); 7.23 - 7.12 (m, 3 H); 3.44 (s, 2 H); 2.14 (s, 3 H). Anal. calcd for C$_{16}$H$_{14}$: C, 93.16; H, 6.84. Found: C, 93.06; H, 6.94.
General Procedure A for the asymmetric reduction of olefins at 80 psig H₂: In a nitrogen-filled glovebox, a dry Fischer-Porter bottle containing a stir bar was charged with \((R, R)-(EBTHI)ZrMe₂\) (0.05 mmol) and
\([\text{Ph:Me}_2\text{NH}]\text{[B(C₆F₅)_4]}\) (0.05 mmol). The bottle was sealed, removed from the glovebox, evacuated and backfilled with argon. Benzene (3 mL) was added and the mixture was stirred for 20 min. The bottle was pressurized to 80 psig H₂ and vented to 10 psig (3x) and then repressurized to 80 psig H₂. A solution of olefin (1 mmol) in benzene (0.5 mL, 0.5 mL wash) was added via pressure syringe. The reaction mixture was stirred at room temperature for the time specified; the bottle was then carefully vented and opened to the air. The reaction mixture was transferred directly onto a silica gel column and the product was purified by flash column chromatography (hexanes).

General Procedure B for the asymmetric reduction of olefins at \(\geq 1000\) psig H₂: A flame-dried Schlenk flask was charged with olefin (1 mmol) and benzene (4 mL) under argon atmosphere. The flask was sealed and transferred to a nitrogen-filled glovebox containing a dry Parr reactor charged with \((R, R)-(EBTHI)ZrMe₂\) (0.05 mmol), \([\text{Ph:Me}_2\text{NH}]\text{[B(C₆F₅)_4]}\) (0.05 mmol), and a stir bar. The contents of the Schlenk were poured into the Parr reactor, and the reactor was sealed and removed from the glovebox. The reactor was pressurized to \(>1500\) psig H₂ and vented to 100 psig (2x) and repressurized to the desired pressure of H₂. The reaction mixture was stirred at room temperature for the time specified; the reactor was then carefully vented and opened to the air. The reaction mixture was transferred directly onto a silica gel column and the product was purified by flash column chromatography (hexanes).
2-(4-fluorophenyl)-3-methylbutane: Following General Procedure A, 1 (161 mg, 0.98 mmol) was converted to a colorless oil (124 mg, 76%) in 16 h. Chiral GC analysis (Chiraldex G-TA column) determined that the product had an ee of 85%. $^1$H NMR (300 MHz, CDCl$_3$): δ 7.12 - 7.06 (m, 2 H); 6.99 - 6.91 (m, 2 H); 2.41 (quintet, $J = 7.2$ Hz, 1 H); 1.77 - 1.66 (m, 1 H); 1.21 (d, $J = 7.2$ Hz, 3 H); 0.92 (d, $J = 6.9$ Hz, 3 H); 0.73 (d, $J = 6.9$ Hz, 3 H). $^{13}$C NMR (125 MHz, CDCl$_3$): δ 162.1, 160.2, 142.6(2), 128.9, 128.8, 114.8, 114.6, 48.1, 34.5, 21.0, 20.1, 18.9. IR (neat): 3041, 2967, 2873, 1604, 1504, 1460 cm$^{-1}$. $[\alpha]^{25}$°C +17° (c 3.3, CHCl$_3$). Anal. calcd for C$_{11}$H$_{15}$F: C, 79.48; H, 9.09. Found: C, 79.69; H, 9.09.

2-(4-(tert-butyldimethylsilyloxy)phenyl)-3-methylbutane: Following General Procedure A, 2 (273 mg, 0.987 mmol) was converted to a colorless oil (262 mg, 95%) in 17 h. Chiral GC analysis (Chiraldex B-PH column) of the derivative 2-(4-trifluoroacetyloxy)phenyl)-3-methylbutane determined that the product had an ee of 59%. $^1$H NMR (300 MHz, CDCl$_3$): δ 6.99 (d, $J = 8.5$ Hz, 2 H); 6.74 (d, $J = 8.3$ Hz, 2 H); 2.36 (quintet, $J = 7.1$ Hz, 1 H); 1.75 - 1.64 (m , 1 H); 1.19 (d, $J = 6.8$ Hz, 3 H); 0.97 (s, 9 H); 0.90 (d, $J = 6.8$ Hz, 3 H); 0.72 (d, $J = 6.7$ Hz, 3 H); 0.18 (s, 6 H). $^{13}$C NMR (75 MHz, CDCl$_3$): δ 153.4, 139.7, 128.3, 119.4, 45.9, 34.6, 25.7, 21.1, 20.2, 18.8, 18.2, -4.4. IR (neat): 2959, 2859, 1608, 1510, 1472, 1462 cm$^{-1}$. $[\alpha]^{25}$°C +11° (c 8.0, CHCl$_3$). Anal. calcd for C$_{17}$H$_{30}$OSi: C, 73.31; H, 10.86. Found: C, 73.44; H, 10.70.

Reduction of 3,4-dimethyl-1,2-dihydronaphthalene (3) at 80 psig: Following General Procedure A, 3 (165 mg, 1.01 mmol) was converted to a colorless oil (147 mg) in 19 h. Analysis by $^1$H NMR indicated that this oil
consisted of a mixture of the desired 1,2-dimethyl-1,2,3,4-dihydonaphthalene (78%), 1,2-dimethylnaphthalene (12%), and 5,6-dimethyl-1,2,3,4-tetrahydonaphthalene (10%). Chiral GC analysis (Chiraldex B-PH column) determined that the 1,2-dimethyl-1,2,3,4-tetrahydonaphthalene had an ee of 92%. $^1$H NMR (300 MHz, CCl$_4$): δ 7.91 (d, $J = 8.7$ Hz); 7.67 (d, $J = 8.4$ Hz); 7.49 (d, $J = 8.4$ Hz); 7.40 - 7.27 (m); 7.18 (d, $J = 8.4$ Hz); 6.99 - 6.91 (m); 6.74 (d, $J = 7.5$ Hz); 6.65 (d, $J = 7.5$ Hz); 2.82 - 2.74 (m); 2.68 (t, $J = 6.2$ Hz); 2.60 (t, $J = 6.6$ Hz); 2.57 (s); 2.47 (s); 2.20 (s); 2.06 (s); 2.01 - 1.90 (m); 1.83 - 1.59 (m); 1.10 (dd, $J = 0.9$ Hz, $J = 7.2$ Hz); 0.99 (dd, $J = 0.9$ Hz, $J = 6.9$ Hz). The doublets at 0.99 ppm and 1.10 ppm correspond to the cis isomer of 1,2-dimethyl-1,2,3,4-tetrahydonaphthalene, the singlets at 2.06 ppm and 2.20 ppm correspond to the methyl groups of 5,6-dimethyl-1,2,3,4-dihydonaphthalene, and the singlets at 2.47 ppm and 2.57 ppm correspond to the methyl groups of 1,2-dimethylnaphthalene.

Reduction of 3,4-dimethyl-1,2-dihydonaphthalene (3) at 2000 psig:
Following General Procedure A, 3 (154 mg, 0.97 mmol) was converted to a colorless oil (142 mg) in 13 h. Analysis by $^1$H NMR indicated that this oil consisted of a mixture of the desired 1,2-dimethyl-1,2,3,4-dihydonaphthalene (91%) and 5,6-dimethyl-1,2,3,4-tetrahydonaphthalene (9%). Chiral GC analysis (Chiraldex B-PH column) determined that the 1,2-dimethyl-1,2,3,4-tetrahydonaphthalene had an ee of 92%.

cis-1,2-dimethylindane: Following General Procedure A, 4 (146 mg, 1.01 mmol) was converted to a colorless oil (123 mg, 83%) in 15 h. Chiral GC analysis (Chiraldex B-PH column) determined that the product had an ee of 86%. $^1$H NMR (300 MHz, CDCl$_3$): δ 7.19 - 7.10 (m, 4 H); 3.14 (quintet, $J = 7.2$ Hz);
Hz, 1 H); 2.81 - 2.92 (m, 1 H); 2.61 - 2.51 (m, 2 H); 1.12 (d, J = 7.2 Hz, 3 H); 0.96 (d, J = 6.9 Hz, 3 H). [α]$_{D}^{25^\circ}$C $+$12° (c 0.51, CHCl$_3$). Anal. calcd for C$_{11}$H$_{14}$: C, 90.35; H, 9.65. Found: C, 90.56; H, 9.59.

cis-2-butyl-1-methylindane: Following General Procedure A, 5 (188 mg, 1.01 mmol) was converted to a colorless oil (182 mg, 96%) in 19 h. Chiral GC analysis (ChiralDEX B-PH column) determined that the product had an ee of 92%. $^1$H NMR (300 MHz, CDCl$_3$): δ 7.22 - 7.07 (m, 5 H); 3.14 (quintet, J = 7.1 Hz, 1 H); 2.88 (dd, J = 7.4 Hz, J = 15.2 Hz, 1 H); 2.60 (dd, J = 9.6 Hz, J = 15.3 Hz, 1 H); 2.43 - 2.32 (m, 1 H); 1.54 - 1.41 (m, 1 H); 1.40 - 1.28 (m, 5 H); 1.05 (d, J = 7.5 Hz, 3 H); 0.94 - 0.90 (m, 3 H). $^{13}$C NMR (125 MHz, CDCl$_3$): δ 149.8, 142.6, 126.1, 126.0, 124.4, 123.6, 43.6, 41.7, 36.7, 30.7, 29.8, 23.0, 15.4, 14.2. IR (neat): 3018, 2958, 2920, 2840, 1606, 1585, 1477, 1460 cm$^{-1}$. [α]$_{D}^{25^\circ}$C $+$8.4° (c 4.5, CHCl$_3$). Anal. calcd for C$_{14}$H$_{20}$: C, 89.29; H, 10.71. Found: C, 89.14; H, 10.66.

Reduction of 3-methyl-2-phenyl-1H-indene (6) at 80 psig: Following General Procedure A, 6 (205 mg, 0.99 mmol) was converted to a colorless oil (181 mg) in 12 h. Analysis by $^1$H NMR indicated that this oil consisted of 6 (66%) and cis-1-methyl-2-phenylindane (24%). Chiral GC analysis (ChiralDEX B-PH column) determined that the reduction product had an ee of 97%.

cis-1-methyl-2-phenylindane: Following General Procedure B at 1000 psig H$_2$, 6 (202 mg, 0.979 mmol) was converted to a colorless oil (181 mg, 89%) in 39 h. Chiral GC analysis (ChiralDEX B-PH column) determined that the product had an ee of 99%. $^1$H NMR (300 MHz, CDCl$_3$): δ 7.32 - 7.13 (m, 9 H); 3.75 (q, J = 7.8 Hz, 1 H); 3.50 (quintet, J = 7.4 Hz, 1 H); 3.32 - 3.16 (m, 2 H); 0.85 (d, J =
7.2 Hz, 3 H). $^{13}$C NMR (125 MHz, CDCl$_3$): δ 148.4, 142.6, 142.4, 128.2, 128.1, 126.5, 126.4, 126.1, 124.3, 123.7, 49.4, 43.7, 36.3, 16.1. IR (neat): 3062, 3023, 2958, 2925, 1602, 1586, 1492, 1476, 1453 cm$^{-1}$. [α]$^{25}$°C -184° (c 2.1, CHCl$_3$). Anal. calcd for C$_{16}$H$_{16}$: C, 92.26; H, 7.74. Found: C, 92.15; H, 7.79.

**Reduction of 3-butyl-2-phenyl-1H-indene (7) at 1000 psig:** Following General Procedure B at 1000 psig H$_2$, 7 (252 mg, 1.01 mmol) was converted to a colorless oil (244 mg) in 21 h. Analysis by $^1$H NMR indicated that this oil consisted of 7 (35%) and cis-1-butyl-2-phenylindane (65%).

The mixture could not be analyzed by HPLC since 7 had the same retention time as one of the product enantiomers. Thus, the oil (24 mg) was dissolved in CH$_2$Cl$_2$ and m-chloroperoxybenzoic acid (50 mg) was added. The mixture was stirred 1.5 h and was then concentrated in vacuo. Hexanes were added and the resulting suspension was purified by flash column chromatography (hexanes), affording pure cis-1-butyl-2-phenylindane (12 mg). Chiral HPLC analysis (Chiracel OJ column) determined that the product had an ee of 98%.

**cis-1-butyl-2-phenylindane:** Following General Procedure B at 1500 psig H$_2$, 7 (247 mg, 0.994 mmol) was converted to a colorless oil (235 mg, 94%) in 65 h. Chiral HPLC analysis (Chiracel OJ column) determined that the product had an ee of 98%. $^1$H NMR (500 MHz, CDCl$_3$): δ 7.29 - 7.16 (m, 9 H); 3.78 (q, J = 7.8 Hz, 1 H); 3.31 - 3.24 (m, 2 H); 3.15 (dd, J = 7.5 Hz, J = 15.5 Hz, 1 H); 1.30 - 1.24 (m, 2 H); 1.21 - 1.09 (m, 4 H); 0.75 (t, J = 7.2 Hz, 3 H). $^{13}$C NMR (125 MHz, CDCl$_3$): δ 147.3, 143.0, 142.2, 128.2, 128.1, 126.4, 126.1, 125.9, 124.5(2), 49.8, 49.1, 36.5, 29.7, 29.1, 22.7, 14.0. IR (neat): 3063, 3023, 2926, 2855.
1602, 1584, 1492, 1475, 1454 cm\(^{-1}\). [\(\alpha\)]\(^{25}\) \(^{\circ}\)C -150\(^{\circ}\) (c 2.7, CHCl\(_3\)). Anal. calcd for C\(_{16}\)H\(_{16}\): C, 91.14; H, 8.86. Found: C, 91.06; H, 8.94.

**Reduction of 3-ethyl-2-methyl-1H-indene (8) at 80 psig:** Following General Procedure A, 8 (162 mg, 1.02 mmol) was converted to a colorless oil (156 mg) in 16.5 h. Analysis by \(^1\)H NMR indicated that this oil consisted of 43% 8 (43%), cis-1-ethyl-2-methylindane (51%), and another product isomer (6%), presumably the trans product, as evidenced by a doublet of doublets at 3.08 ppm. Chiral GC analysis (Chiraldex G-TA column) determined that the cis product had an ee of 5%. \(^1\)H NMR (300 MHz, CDCl\(_3\)): \(\delta\) 7.36 (dd, \(J = 0.6\) Hz, \(J = 7.2\) Hz); 7.25 - 7.23 (m); 7.21 - 7.06 (m); 3.25 (s); 2.97 - 2.86 (m); 2.66 - 2.51 (m); 2.06 (s); 1.68 - 1.50 (m); 1.14 (t, \(J = 7.6\) Hz); 1.01 (t, \(J = 7.4\) Hz); 0.94 (d, \(J = 6.9\) Hz). The singlets at 3.25 and 2.06 ppm and the triplet at 1.14 ppm correspond to starting material; the signals at 2.90, 1.01, and 0.94 ppm correspond to cis product.

**Reduction of 3-ethyl-2-methyl-1H-indene (8) at 1000 psig:** Following General Procedure A, 8 (157 mg, 0.99 mmol) was converted to a colorless oil (124 mg) in 16 h. Analysis by \(^1\)H NMR indicated that this oil consisted of 8 (20%), cis-1-ethyl-2-methylindane (76%), and the trans isomer (4%). Chiral GC analysis (Chiraldex G-TA column) determined that the cis product had an ee of 40%.

**Reduction of 2-methyl-3-phenyl-1H-indene (9) at 80 psig:** Following General Procedure A, 9 (206 mg, 1.00 mmol) was converted to a colorless oil (151 mg) in 30 h. Analysis by \(^1\)H NMR indicated that this oil consisted of 9
(56%) and cis-2-methyl-1-phenylindane (44%). Chiral GC analysis (ChiralDex B-PH column) determined that the reduction product had an ee of 29%.

**cis-2-methyl-1-phenylindane:** Following General Procedure B at 2000 psig H₂, 9 (205 mg, 0.994 mmol) was converted to a colorless oil (194 mg, 94%) in 14 h. Chiral GC analysis (ChiralDex B-PH column) determined that the product had an ee of 78%. ¹H NMR (300 MHz, CDCl₃): δ 7.29 - 7.09 (m, 7 H); 7.00 - 6.97 (m, 2 H); 4.37 (d, J = 7.8 Hz, 1 H); 3.05 (dd, J = 7.2 Hz, J = 15.3 Hz, 1 H); 2.83 (septet, J = 7.2 Hz, 1 H); 2.67 (dd, J = 7.4 Hz, J = 15.1 Hz, 1 H); 0.70 (d, J = 6.9 Hz, 3 H). ¹³C NMR (125 MHz, CDCl₃): δ 146.2, 144.0, 141.5, 129.1, 128.0, 126.6, 126.4, 126.2, 125.4, 124.5, 55.2, 39.7, 39.5, 16.8. IR (neat): 3065, 3026, 2961, 2930, 2845, 1602, 1494, 1455 cm⁻¹. [α]²⁵° C -45° (c 2.5, CHCl₃).

Anal. calcd for C₁₆H₁₆: C, 92.26; H, 7.74. Found: C, 92.24; H, 7.84.

(±)-cis-2-Methyl-1-phenylindane (prepared by hydrogenation of 9 over Pd/C, 71 mg, 0.34 mmol) and potassium tert-butoxide (130 mg, 1.16 mmol) were dissolved in DMSO (3 mL) under argon. The mixture was heated to 80 °C and stirred for 30 min. The mixture was allowed to cool to room temperature, and hexanes and water were added. The organic phase was separated and washed with water and saturated aqueous NaCl solution, dried over MgSO₄, and concentrated *in vacuo*. Purification by flash chromatography afforded a colorless oil (26 mg). Analysis by ¹H NMR determined that this oil consisted of a mixture of *trans* (93%) and *cis* (7%) isomers of the starting material. For the *trans* isomer: ¹H NMR (300 MHz, CDCl₃): δ 7.36 - 7.08 (m, 7 H); 6.86 (d, J = 7.2 Hz, 2 H); 3.79 (d, J = 9.3 Hz, 1 H); 3.14 (dd, J = 7.5 Hz, J = 15.3 Hz, 1 H); 2.64 (dd, J = 9.4 Hz, J = 15.2 Hz, 1 H); 2.50 - 2.39 (m, 1 H); 1.18 (d, J = 6.6 Hz, 3 H). A nuclear Overhauser enhancement study was undertaken to determine the relative configuration of the two isomers. For the *cis* isomer, irradiation of
the C-2 methyl hydrogens at $\delta$ 0.70 gave a 3% enhancement at the C-1 phenyl ortho-hydrogens and a 1% enhancement at the C-1 hydrogen. For the trans isomer, irradiation of the C-2 methyl hydrogens at $\delta$ 1.18 gave a 0% enhancement at the C-1 phenyl ortho-hydrogens and a 4% enhancement at the C-1 hydrogen. Based on these observations, the relative configurations of the isomers were assigned as shown:

**Reduction of 2-Butyl-3-methyl-1H-indene (5) under D$_2$ atmosphere:**

In a nitrogen-filled glovebox, a dry Fischer-Porter bottle containing a stir bar was charged with $(R, R)$-(EBTHI)ZrMe$_2$ (31 mg, 0.080 mmol) and [PhMe$_2$NH][B(C$_6$F$_5$)$_4$] (65 mg, 0.081 mmol). The bottle was sealed, removed from the glovebox, evacuated and backfilled with argon. Benzene (3 mL) was added and the mixture was stirred for 20 min. The bottle was pressurized to 80 psig D$_2$ and vented to 10 psig (2x) and then repressurized to 80 psig D$_2$. A solution of 5 (185 mg, 0.993 mmol) in benzene (0.5 mL, 0.5 mL wash) was added via pressure syringe. The mixture was stirred at room temperature for 15 h; the bottle was then carefully vented and opened to the air. The reaction mixture was transferred directly onto a silica gel column and flash column chromatography (hexanes) afforded a colorless oil (176 mg). Chiral GC analysis (ChiralDEX B-PH column) determined an ee of 90%. $^1$H NMR (300 MHz, CDCl$_3$): $\delta$ 7.23 - 7.09 (m, 4 H); 3.13 (t, $J$ = 7.0 Hz, 0.13 H); 2.85 (s, 0.11 H); 2.58 (s, 0.03 H); 2.40 - 2.35 (m, 0.11 H); 1.52 - 1.45 (m, 1 H); 1.40 - 1.31 (m, 5
H); 1.06 - 1.02 (m, 2.73 H); 0.92 (t, J = 7.0 Hz, 3 H). $^2$H NMR (46 MHz, CHCl$_3$): δ 3.18, 2.89, 2.62, 2.40, 1.08.

**Reaction of 2-Butyl-3-methyl-1H-indene (5) under argon, then D$_2$ atmosphere:** In a nitrogen-filled glovebox, a dry Fischer-Porter bottle containing a stir bar was charged with ($R$, $R$)-(EBTHI)ZrMe$_2$ (31 mg, 0.080 mmol) and [HNMe$_2$Ph][B(C$_6$F$_5$)$_4$] (64 mg, 0.080 mmol). The bottle was sealed, removed from the glovebox, evacuated and backfilled with argon. Benzene (3 mL) was added and the mixture was stirred for 20 min. The bottle was pressurized to 80 psig D$_2$ and the mixture was stirred for 5 min. The bottle was then evacuated and repressurized with argon (2x). A solution of 5 (184 mg, 0.998 mmol) in benzene (0.5 mL, 0.5 mL wash) was added via pressure syringe, giving a brown mixture. The mixture was stirred at room temperature for 30 min, at which time an aliquot was removed. Analysis by $^1$H NMR indicated that this aliquot consisted of deuterated 5. $^1$H NMR (300 MHz, C$_6$D$_6$): δ 7.32 - 7.13 (m, 4 H); 3.03 (s, 1.54 H); 2.27 (t, J = 7.5 Hz, 1 H); 1.91 (s, 3 H); 1.40 - 1.30 (m, 2 H); 1.27 - 1.15 (m, 2 H); 0.86 (t, J = 7.2 Hz, 3 H). $^2$H NMR (46 MHz, CHCl$_3$): δ 3.00.

At 35 min the bottle was pressurized to 80 psig D$_2$ and vented to 10 psig (2x) and then repressurized to 80 psig D$_2$, causing the reaction mixture to become light yellow. It was stirred at room temperature for 15 h; the bottle was carefully vented and opened to the air. The reaction mixture was transferred directly onto a silica gel column, and flash column chromatography (hexanes) afforded a colorless oil (171 mg). Chiral GC analysis (Chiraldex B-PH column) determined an ee of 89%. $^1$H NMR (300 MHz, CDCl$_3$): δ 7.23 - 7.09 (m, 4 H); 3.13 (t, J = 7.0 Hz, 0.12 H); 2.85 (s, 0.09 H); 2.58 (s, 0.03 H); 2.40 - 2.35 (m, 0.09
H); 1.52 - 1.45 (m, 1 H); 1.40 - 1.31 (m, 5 H); 1.06 - 1.02 (m, 2.6 H); 0.92 (t, J = 7.0 Hz, 3 H). $^2$H NMR (46 MHz, CHCl$_3$): $\delta$ 3.14, 2.88, 2.59, 2.38, 1.05.

**Reduction of 2-Methyl-3-phenyl-1H-indene (9) under D$_2$ atmosphere:** In a nitrogen-filled glovebox, a dry Fischer-Porter bottle containing a stir bar was charged with $(R, R)$-(EBTHI)ZrMe$_2$ (19 mg, 0.049 mmol) and [PhMe$_2$NH][B(C$_6$F$_5$)$_4$] (40 mg, 0.050 mmol). The bottle was sealed, removed from the glovebox, evacuated and backfilled with argon. Benzene (3 mL) was added and the mixture was stirred for 20 min. The bottle was pressurized to 80 psig D$_2$ and vented to 10 psig (2x) and then repressurized to 80 psig D$_2$. A solution of 9 (205 mg, 0.994 mmol) in benzene (0.5 mL, 0.5 mL wash) was added via pressure syringe. The mixture was stirred at room temperature for 16 h; the bottle was then carefully vented and opened to the air. The reaction mixture was transferred directly onto a silica gel column and flash column chromatography (hexanes) afforded a colorless oil (199 mg). $^1$H NMR showed that the recovered product consisted of deuterated 9 (59%) and deuterated cis-2-methyl-1-phenylindane (41%). Chiral GC analysis (Chiraladex B-PH column) determined that the reduction product had an ee of 40%. $^1$H NMR (300 MHz, CDCl$_3$): $\delta$ 7.48 - 7.10 (m); 3.43 (s, 0.02 H); 2.13 (s, 3 H) (starting material); 7.48 - 7.10 (m); 7.00 - 6.97 (m, 2 H); 4.38 (s, 0.06 H); 3.02 (s, 0.05 H); 2.81 (s, 0.02 H); 2.65 (s, 0.10 H); 0.70 (s, 3 H) (product). $^2$H NMR (46 MHz, CHCl$_3$): $\delta$ 4.39, 3.45, 3.05, 2.83, 2.68.
References

**Abbreviations**

BINAP  
(diphenylphosphino)-1,1'-binaphthyl

tol-BINAP  
(di-p-tolylphosphino)-1,1'-binaphthyl

Binol  
1,1'-binaphth-2,2'-diolate

n-BuLi  
n-butyllithium

bzn  
benzonitrile

COD  
1,5-cyclooctadiene

Cp  
cyclopentadienyl

Cp*  
permethylcyclopentadienyl

Cy  
cyclohexyl

diphos  
1,2-bis(diphenylphosphino)ethane

DMSO  
dimethyl sulfoxide

EBI  
ethylenebisindenyl

EBTHI  
ethylenebis(tetrahydroindenyl)

ee  
enantiomeric excess

EtOAc  
ethyl acetate

FID  
flame ionization detector

GC  
gas chromatography

HPLC  
high performance liquid chromatography

IR  
infrared spectroscopy

MAO  
methylaluminoxane

NBD  
norbornadiene

NMR  
nuclear magnetic resonance

py  
pyridine

r. t.  
room temperature

TBAF  
tetrabutylammonium fluoride

TBDMS  
*tert*-butyldimethylsilyl

Tf  
triflate

THF  
tetrahydrofuran

TMSCl  
chlorotrimethylsilane