Asymmetric Catalysis of Carbon-Carbon Bond Forming Reactions: Use of a Sustainable Feedstock Ethylene

Dissertation

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By

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ABSTRACT

Nature has established numerous methods for synthesis of complex molecules utilizing simple and abundant resources such as the use of CO₂, H₂O and N₂ using sunlight as a source of energy. Even more impressive are the high chemo-, regio-, and stereoselectivities observed in these transformations with a wide variety of both prochiral and chiral substrates. However, methods for the enantioselective incorporation of feedstock materials such as CO, HCN, CO₂ or simple alkenes into prochiral molecules are limited and remain an important challenge in the field. The hydrovinylation reaction (HV), where ethylene is added across a carbon-carbon double bond, has been known for nearly fifty years, starting with the works of Hata, Alderson and Wilke. These pioneers established the catalytic addition of ethylene across alkenes using various metal catalysts at high pressure. During the past few years, through an approach that relied mostly on mechanistic insights and systematic examination of ligand effects, our group discovered a number of protocols for Ni(II)- and Co(II)-catalyzed enantioselective hydrovinylation (HV) reactions of vinylarenes, 1,3-dienes and strained olefins. This work has shown that asymmetric HV provides arguably the best solution to the classical “side chain stereochemistry problem” in organic synthesis. Since, applications of these reactions for stereoselective syntheses of several important classes of compounds have appeared. We also observed significant ligand effects on Ni(II)-catalyzed 1,6-diene cyclization reaction where hemilabile phosphine ligands catalyze five-membered carbocyclic ring formation, N-heterocyclic carbene ligands yield a six-membered ring carbocyclic ring as the major
product. While the Ni(II)-catalyzed hydrovinylation (HV) reaction is one of the most selective asymmetric catalyzed carbon-carbon bond forming reactions, its use has been limited to alkenes conjugated to an aromatic ring and strained alkenes. The major limitations of scope became apparent as we began to explore 1,3-dienes. In an effort to find solutions to the unsolved problems in asymmetric HV of 1,3-dienes, we recently found Co(II)-bisphosphine complexes show much improved regioselectivity with broader functional group compatibility in 1,3-dienes. By utilizing finely tuned catalysts derived from Co(II)-bisphosphine complexes and Me₃Al or methylaluminoxane (MAO) acyclic (E) and (Z)-1,3-dienes were found to undergo efficient hydrovinylation giving mostly 1,4-hydrovinylation products in an atmosphere of ethylene. Additionally, in the absence of ethylene, under otherwise identical conditions, this Co-catalyst promotes an unusual isomerization of (E) and (Z)-1,3-dienes almost exclusively to (Z)-isomer. In order to expand the hydrovinylation chemistry, we turned our attention to one of the mostly widely used intermediates on organic chemistry, viz., silyl enol ethers. Trialkylsilyl enol ethers are exceptionally versatile intermediates often used as enolate surrogates for the synthesis of carbonyl compounds. Yet there are no reports of broadly applicable, catalytic methods for the synthesis of chiral silyl enol ethers carrying latent functionalities useful for synthetic operations beyond the many possible reactions of the enol ether moiety itself. The work presented herein reports a general procedure for highly catalytic (substrate : catalyst ratio up to 1000:1) and enantioselective (96% to >99% major enantiomer) synthesis of silyl enol ethers bearing a vinyl group at a chiral carbon at the β-position. The reactions, run under ambient conditions, use trialkylsiloxoy-1,3-dienes and ethylene (1 atmosphere) as precursors, and readily available (bis-
phosphine)-cobalt(II) complexes as catalysts. Once we have established the HV reaction conditions of the siloxydienes, we turn our attention towards diastereoselective functionalization of the hydrovinylated products. Under optimized conditions, we are able to successfully utilize our 1,4-hydrovinylated products as reactive nucleophilic synthons for several electrophilic reactions keeping moderate to good diastereomeric ratios. The silyl enolates can be readily converted into novel enantiopure vinyl triflates, a class of highly versatile cross-coupling reagents, enabling the syntheses of other enantiomerically pure trisubstituted alkene intermediates not easily accessible by current methods.

During our Co(II)-catalyzed HV of racemic 4-isopropyl-1-vinylcycloalkene, we observed enantiopure [(S,S)-BDPP]CoCl$_2$ accelerates the reaction of both members of the racemic starting material, but does so in divergent pathways leading to enantiodivergent hydrovinylation reaction of 1,3-dienes. While the (R) enantiomer reacts with enantiopure catalyst [(S,S)-BDPP]CoCl$_2$ to place the vinyl group on equatorial position to make cis product with 95% ee, (S) enantiomer reacts with enantiopure catalyst [(S,S)-BDPP]CoCl$_2$ completely enantiodivergent pathway to put vinyl group on the thermodynamically unfavorable axial position to make trans product with 99% ee. The exceptionally high enantioselectivity in the formation of two diastereomeric products cis and trans from racemic substrate confirms enantiodivergent chemistry in our Co(II)-catalyzed HV on 1-vinylcycloalkenes. This divergent selectivity derives purely from rate differences associated with the diastereomeric transition states involving the catalyst and each of the substrate enantiomers.
This work is dedicated to Babuji and Maa
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This is probably the most important page in my thesis. My journey towards becoming a Ph.D chemist would have never been possible if several people mentioned here hadn’t walked this path with me.

Without a doubt, I would like to begin with Professor T. V. RajanBabu. My life at Ohio State would have been completely different if I did not join Professor RajanBabu’s research group. From the very first day I met with Prof. RajanBabu at IITBombay, India, he was always my mentor and he still is. The experience and knowledge I have gained with every interaction with him has had a tremendous impact on my professional and personal aspirations, and for this, I am forever grateful.

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This journey would have never been possible without the support and encouragement from my sister, my grandparents and the rest of my family. Finally, I would have never been able reach here today, without the unconditional love and support of my parents. 

_Maa and Babuji, this work is dedicated to you two._
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PUBLICATIONS


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Major Field: Chemistry
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<table>
<thead>
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<tr>
<td>α</td>
<td>alpha</td>
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<tr>
<td>[α]</td>
<td>specific rotation</td>
</tr>
<tr>
<td>Ac</td>
<td>acetyl</td>
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<tr>
<td>aq</td>
<td>aqueous</td>
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<tr>
<td>atm</td>
<td>atmospheres</td>
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<tr>
<td>β</td>
<td>beta</td>
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<td>BARF</td>
<td>tetrakis[(3,5-trifluoromethyl)phenyl]borate</td>
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<td>9-BBN</td>
<td>9-borobicyclo-[3.3.1]nonane</td>
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<td>cod</td>
<td>1,5-cyclooctadiene</td>
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<td>Term</td>
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<td>------</td>
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</tr>
<tr>
<td>CSP GC</td>
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</tr>
<tr>
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CHAPTER 1

INTRODUCTION

1.1. Introduction

Since the pioneering work of Winkler in 1828 on the addition of HCN to benzaldehyde, organic chemists have been interested in developing ingenious approaches for the creation of carbon-carbon bonds, as they are essential for the synthesis of small molecules in every field of daily life, from pharmaceuticals to agrichemicals, polymer materials to commodity chemicals. Although nature has evolved numerous methods for the construction of carbon-carbon bonds utilizing simple and abundant resources such as the use of CO$_2$, H$_2$O and sunlight for the production of carbohydrates, synthetic chemists have been slow to learn from Nature’s model. Many of the traditional carbon-carbon bond forming transformations involve complex starting materials, non-environment friendly chemicals and also generate significant amount of waste side-products (examples can be seen in Wittig reaction and Stille coupling). With increased demands to move towards environment friendly ‘green’ chemistry, use of neutral feedstock materials such as CO$_2$, CO and H$_2$ (syn gas) and ethylene shows enormous potential for the installation of new carbon-carbon bonds. If successful, this chemistry will result in very powerful synthetic methods to install new carbon-carbon bonds with sustainable, cheap, highly abundant feedstock materials with high levels of chemo-
regio- and stereoselectivity. In this chapter, we will try to summarize our contributions to the area of employment of sustainable feedstock ethylene for the construction of new carbon-carbon bonds. Since this dissertation will mainly focus on the cobalt catalyzed ethylene addition across a double bond, the reader is urged to consult various reviews for details of early history and development of this class of reactions.\textsuperscript{6-9} Along these lines, other pioneering work in this area also include the use of nickel,\textsuperscript{10} ruthenium,\textsuperscript{11} palladium\textsuperscript{12} catalysts. As this is not an extensive review of ethylene addition with all metal catalysts, we will keep our discussion limited only to cobalt catalyzed reactions. Apart from our group, there are several other groups who have also contributed significantly in this field of research.\textsuperscript{13,14,15} However, due to the nature of this chapter, we will only summarize the most significant work done in this field. We hope at the end of this chapter, we will be able to highlight the significance of this chemistry that will provide access to synthetic chemists ways to start from readily available starting materials for the synthesis of enantiopure value-added intermediates.

1.2. Hydrovinylation Reaction

Among the olefin dimerization reactions, homodimerization of propene with Ni(phosphine)(allyl)(X) catalyst provides one of the most efficient methods

\textbf{Scheme 1.1. Ni(II)-Catalyzed Reaction of Propylene: Dimersol Process}

\[ \begin{align*}
\text{Ni}^{2+} \text{YP} & \xrightarrow{\text{AlX}_{3}} \text{Ni}^{2+} \text{YP}^{[\text{YAlX}_{3}]} \\
\text{TON} > 625000 \text{ [propene]} \text{Ni}^{-1} \text{h}^{-1} \end{align*} \]
for new carbon-carbon bond formation (with an astonishingly high turnover frequency $>625000$ propylene$[\text{Ni}]^{-1}[\text{h}]^{-1}$)$^{16}$ (Scheme 1.1). This amazing result in homogeneous catalysis inspired us to think about the possibility of co-dimerizing ethylene with other alkenes (Hydrovinylation Reaction, Scheme 1.2) to catalytically access new carbon-carbon bonds with desired chemo-, regio- and stereoselectivity. The ability to form new carbon-carbon bonds while simultaneously setting new stereocenters from prochiral starting materials brings great value in fine chemical synthesis.

Scheme 1.2. Selective Hydrovinylation Reactions

\[
\text{R} + \text{H} \rightarrow \text{R}^* \quad \text{cat. [PNi-H]} + X^- \rightarrow \text{H}^+ \rightarrow \text{R}^* + \text{H}
\]

1.3. Early History of Hydrovinylation Reaction

The hydrovinylation reaction has been known for nearly fifty years, starting with the work of Hata,$^{11}$ Alderson$^{17}$ and Wilke.$^{18,19}$ These pioneers established the catalytic addition of ethylene across activated/unactivated alkenes using various metal catalysts at high pressures. Styrene has served as a prototypical substrate for hydrovinylation reaction across most methodologies and several metals such as palladium,$^{12}$ rhodium, ruthenium,$^{11,20}$ cobalt$^{21-24}$ and nickel,$^{10,25,26}$ have been tested with various ligands. However, in most cases, the reactions yielded mixture of products with extensive isomerization of primary products were observed (equation 1.1). Due to persistent
isomerization of the primary product, low conversion, poor selectivity and extreme reaction conditions (high pressure of ethylene), more recent work has focused on improving the reaction conditions to afford codimerization of ethylene with other alkenes under mild conditions in high yield and selectivity.

1.3.1. Notable Early Results on Hydrovinylation Reaction

The first report of hydrovinylation in the open literature came from Hata when he used Fe(acetylacetonate)$_3$ and triethylaluminum for codimerization of ethylene with 1,3-butadiene, 1,3-pentadiene and isoprene to get a mixture of adducts.$^{11}$ Approximately the same time, Alderson, Jenner and Lindsey at Dupont Central Research reported the use of hydrated rhodium and ruthenium chlorides to effect the dimerization of ethylene and various olefins at very high pressure of ethylene (1000 psi).$^{17}$ The first report of cobalt-catalyzed dimerization of ethylene was reported using (N$_2$)Co(H)(PPh$_3$)$_3$ complex at ambient temperature and pressure.$^{24}$ In 1972, Wilke and coworkers reported the first
example of asymmetric hydrovinylation exploiting [(allyl)NiCl]_2 with (-)-

dimethyl(methyl)phosphine as the ligand in 53% enantiomeric excess (equation 1.2).\cite{27,28}

The enantiomeric excess of this reaction was low by current standards, however this was
among of first reported examples of a metal catalyzed asymmetric carbon-carbon bond
forming reaction using sustainable feedstock ethylene. Under similar conditions, norbornene and norbornadiene yielded the corresponding 2-exo-vinylproducts in 65% ee
(at -70 °C) and 78% ee (at -65 °C), respectively (equation 1.3). In this context, it is worth
mentioning that Wilke also claimed in a patent high ee’s in asymmetric hydrovinylation
of variety of vinyl arenes using [η^3-(allyl)NiCl]_2/(R,R)-(L1)/Et_3Al_2Cl_3 (equation 1.4).
This catalyst system affords high enantioselectivities for asymmetric

\[
\text{ethylene (1 atm), [(allyl)NiCl]_2, L1, Et_3Al_2Cl_3, CCl_2Cl_2, -60 °C, 2.5 h, S/C = 1948; L1:Ni:Al = 1:1:3 (97% yield, 93% ee, R)}
\]

hydrovinylation of styrene (93% ee, R), 4-isobutylstyrene (85% ee, R), 4-chlorostyrene
(95% ee, R) and 2-methylstyrene (83% ee, R). More recently, Wilke has summarized
several years of work on allylmetal and metal hydride intermediates on this field in a
review article.\cite{29} Among the many carbon-carbon bond-forming reactions catalyzed by a
cationic metal hydrides, remarkable results on homodimerization of propene, [which also
forms the basis of the Dimersol technology]\cite{30} (Scheme 1.1)] give us deep insight and
motivation for further development of simpler and practical methods for asymmetric hydrovinylation reaction.

1.4. Early History of Cobalt Catalyzed Co-dimerization of Ethylene

With several initial papers describing the co-dimerization of ethylene and butadiene using a variety of catalysts, some of the more significant recent work involved simple ethylene polymerization with cobalt catalysts. First, Brookhart and co-workers\textsuperscript{31} utilized bis-(imido)pyridine ligands with cobalt (Scheme 1.3) upon activation with modified methylaluminoxane ([AlMeO]\textsubscript{n} dissolved in C\textsubscript{6}HF\textsubscript{5}, MMAO, Figure 1.1), for the synthesis of low-molecular weight polymers of ethylene, devoid of branching, unlike that of previous nickel or palladium catalysts. Gibson et. al., using similar ligands found that cobalt worked well in their system, albeit at a vastly lower rate compared to iron (II) or iron (III) catalysts.\textsuperscript{32}

Scheme 1.3. Cobalt Catalyzed Formation of Low-Molecular Weight Polyethylene
1.4.1. Notable Early Results on Cobalt Catalyzed Hydrovinylation Reactions

It was the work of Gerhard Hilt and co-workers that brought back cobalt catalyzed co-dimerization of alkenes and dienes after a significant period of inactivity, but with significant changes from the previous work.\textsuperscript{13,33-36} Hilt introduced a cobalt (I)-catalyzed co-dimerization of various terminal olefins with 2,3-dimethyl-1,3-butadiene (3), or isoprene that used tetra-N-butylammonium borohydride and zinc (II) iodide to reduce [dppe]CoBr\textsubscript{2} (equation 1.5). In his early findings, Hilt saw that conjugated olefins, like n-butylacrylate (4) gave the linear product 5 while unconjugated alkenes favor the branched product (like 7, equation 1.6). The yields were excellent, and the reaction conditions tolerated a wide variety of functional groups, including esters, ethers, and vinyl silanes. The Hilt methodology relies on the reduction of cobalt (II) to cobalt (I) and then follows a standard transition metal oxidative addition/reductive elimination pathway.
Hilt proposed a mechanism that starts with cobalt (I) first forming a five-membered cobaltocycle 9 with the diene through an oxidative [1+4] cyclization reaction. Coordination to the α-olefin to generate intermediate 10 followed by bond migration and insertion into the α-olefin gives a seven-membered cobaltocycle 11. A β-hydride elimination to get intermediate 12 followed by reductive elimination provides the product and regenerates the active cobalt catalyst (Scheme 1.4).

Subsequently, Hilt et al. disclosed their efforts using isoprene as a substrate in their co-dimerization reaction with the catalyst system consisting of CoBr₂(dppe) and Zn/ZnI₂ as mild reducing agent (equation. 1.7). Also, in this work they introduced boronic esters as a suitable substrate for the hydrovinylation reaction, giving a new functional handle for

Scheme 1.4. Proposed Catalytic Cycle for Cobalt (I)-Catalyzed Hydrovinylation
post-reaction modification (equation 1.8). It was demonstrated in later work that the boronic ester could be present on either the \( \alpha \)-olefin or diene and further employed in an allylboration reaction with aldehydes to generate a variety of alcohols (equation 1.8).^{37}

![Chemical Reaction Diagram]

Another early result on cobalt catalyzed hydrovinylation reaction that is worthy of mention is the work of Vogt and co-workers, who began their investigation of alternative metals like iron (II) and cobalt (II) for the styrene hydrovinylation. CoCl\(_2\)(dppe) in presence of diethylaluminum chloride (Et\(_2\)AlCl) provided an active catalyst for the hydrovinylation of styrene to result 3-phenyl-1-butene (2) in 93% conversion (equation 1.9).^{38,39} Most notably, even at 60 °C, their catalyst system did not isomerize the terminal double bond of the hydrovinylated product (18) to internal alkene, until the depletion of starting material. The combination of CoCl\(_2\)(ligand) system with suitable activator was further expanded to asymmetric version of this reaction. Unfortunately, under these conditions, several commercially available chiral ligands were not compatible with the
asymmetric hydrovinylation reaction of styrene. Except, bis(phosphine)amide ligand \( \text{L3} \) which gave 74% conversion of the desired product 3-phenyl-1-butene with an enantiomeric excess of 47\%.\(^{40}\) Commercially available ligands, \([+](2S,3S)-O\text{-isopropylidene}-2,3\text{-dihydroxy}-1,4\text{-bis(diphenylphosphino)butane}] \)(S,S-DIOP, see Figure 1.2) and ethane-1,2-diylbis[(2-methoxyphenyl)phenylphosphane] (DIPAMP, see Figure 1.2) were largely inactive for this reaction, with DIPAMP giving 30% conversion and 26% ee of the \((R)\) enantiomer. The use of Lewis-basic centers on the ligands \( \text{L2} \) or \( \text{L4} \) completely shut down the reaction, most likely due to over-coordination to cobalt, thus leaving no open sites for the catalytic reaction to occur. Vogt \textit{et. al.} also illustrated a modest improvement in the asymmetric hydrovinylation of styrene using a trialkyl amine scaffold-type bis(phosphino)amide ligand \( \text{L5} \) in their methodology, which led to 80% conversion and 50% ee of the \((S)\) enantiomer of 3-phenyl-1-butene.
1.5. A Brief History of Recent Efforts in Nickel-Catalyzed Asymmetric Hydrovinylation

Before we start a discussion of our efforts on cobalt catalyzed hydrovinylation methodology, a summary of previous nickel-catalyzed hydrovinylation results is presented to give a complete picture of this area (Figure 1.3). With several years of work, our group was able to optimize the hydrovinylation reactions with Ni(II)-salts with appropriate ligands and counter-anions. For brevity, we will attempt to give a quick overview of this area highlighting the best results in last 15 years.\(^6\)\(^9\) Even though it might seem, redundant to discuss the Ni(II)-catalyzed asymmetric hydrovinylation, it is really essential to get a broader picture to appreciate the efforts behind the development of Co(II)-catalytic system.

In our initial research in this area, we found that [(allyl)NiBr]\(_2\) in the presence of an appropriate phosphine ligand and weakly coordinating triflate anion is an extremely effective catalytic system for the hydrovinylation of vinylarenes under atmospheric pressure of ethylene.\(^{41}\) With this the then-new protocol, we were able to do hydrovinylation on a series of vinylarenes with excellent selectivity for branched product with high yields (equation 1.10). Although we were able to address the chemo- and regioselectivity issues on hydrovinylation reaction, several key questions still remained unanswered, especially with respect to asymmetric version of the hydrovinylation reaction. We started systematically examining the ligand effects, mostly relying on mechanistic insights, to discover a number of protocols for highly enantioselective hydrovinylation reactions of vinyl arenes, 1,3-dienes, and strained olefins. Figure 1.3,
summarizes our systemic investigations and progress on the Ni(II)-catalyzed hydrovinylation reaction.

During the optimization studies on Ni(II)-catalyzed hydrovinylation of vinyl arenes, we noticed that chelating, bidentate phosphine ligands resulted in complete inhibition of the hydrovinylation reaction. With the knowledge of this observation, we found that weakly coordinating counter anion that helped to open up (at the same time preserve) the coordination site at nickel, eventually helped the catalytic cycle for the hydrovinylation. Following up, monodentate phosphine ligands, bearing a hemilabile group\textsuperscript{42} with the appropriate bite angles proved to be an excellent ligand for the Ni-catalyzed hydrovinylation reaction (Figure 1.3, equation 1.11 and 1.12). The hemilabile ligand would not just only stabilize the catalytic Ni-intermediate via internal coordination but also undergo facile displacement by incoming alkenes during the appropriate stages of catalytic cycle.

The systematic investigation of ligands provided a major breakthrough when we observed that chiral phosphoramidites, previously introduced by Feringa and coworkers,\textsuperscript{43,44} showed excellent yield and enantioselectivities in the hydrovinylation reaction (Figure 1.3, equation 1.13).\textsuperscript{45-47} In 2006, we reported that the hydrovinylation of 1,1-disubstituted vinylarenes with phosphoramidite ligands can be used to generate all-carbon quaternary centers with excellent selectivity and enantiomeric excess (Figure 1.3, equation 1.14).\textsuperscript{48,49} Although the discussion thus far has mainly focused on new reaction development, applications of this chemistry for the generation of an alkyl bearing chiral center next to a cycloalkane or an aromatic ring have also been in our plans. Accordingly,
Figure 1.3. Development of Nickel Catalyzed Hydrovinylation

Initial Protocol 1998

Development of Ligands, Introducing the Concept of Hemilabile Ligands for HV 1998-2004

Development of New Ligands, Phosphoramidite Ligands for Asymmetric HV 2003-2014

Development of Substrate Scope, Generation of All Carbon Quaternary Center 2006-2014

Application to Natural Product Synthesis 2009-present

Our Initial Protocol on Vinyl arene Achtal version, JACS, 1998, 120, 459

Our First Trial on Hemilabile Ligands, JACS, 1999, 121, 9869

New Class of Hemilabile Phospholane Ligands, Org Lett., 2004, 6, 1515

Excellent Enantioselectivity with Phosphoramidite Ligands Org Lett., 2008, 10, 1657

Generation for All Carbon Quaternary Center JACS, 2006, 128, 5620


Pseudopterosins G-J JACS, 2011, 133, 5776

(+)-cis Tricentrin A JACS, 2012, 143, 5496
we were able to successfully synthesize nonsteroidal anti-inflammatory drugs (NSAID) Naproxen, Ibuprofen and Fenoprofen with very high yield and enantioselectivities (Figure 1.3, 19) with Ni-catalyzed hydrovinylation reaction. This result indeed demonstrated the power of this chemistry where 1 atm of highly abundant feedstock material, ethylene, can be employed for the generation asymmetric carbon-carbon bond with a catalyst turnover >7000 and nearly perfect selectivity towards only one product with an enantioselectivity more than 97%.

Having demonstrated the solution for this classical “side-chain stereochemistry” problem on the synthesis of NSAIDs, we became interested on the syntheses on complex natural products with installation of more than one stereo-center with the new methodology. Thus the totally stereoselective syntheses of the aglycones of pseudopterosins (PST A-F, G-J) (Figure 1.3, 20) starting from 2,3-dimethoxy-4-methylstyrene were accomplished. Using finely tuned phosphoramidite ligands, asymmetric hydrovinylation was used to install three of four chiral centers of this molecule with excellent enantioselectivities at every stage of the synthesis [early stage HV: er = >97:3, middle stage HV: dr = 92:8, late stage HV: dr = >99:1]. Subsequently the total syntheses of antibacterial trikentrins were completed which demonstrated the remarkable group compatibility of the methodology with unprotected indole nucleus (Figure 1.3, 21).

Though our initial research goal was to study a prototypical asymmetric carbon-carbon bond forming reaction involving ethylene and vinylarenes, we were also interested in an expansion of the scope of this reaction to include other substrates,
including 1,3-dienes. In the rest of our discussion, we will summarize the attempts to address this new challenge with the development of a new catalytic system involving cobalt.

1.6. Transition from Nickel to Cobalt-Catalyzed Asymmetric Hydrovinylation

The hydrovinylation of 1,3-dienes, using the well-established Ni-protocols, gave unsatisfactory results except for two substrates, 1,3-cyclohexadiene and 1-vinylcyclohexene (equation 1.15a and 1.15b).48,54

\[
\begin{align*}
\text{ethylene (1 atm)} & \quad [(\text{allylNiBr})_2, \text{PPh}_3, \text{NaBAr}_4, \text{CH}_2\text{Cl}_2] \\
\text{- 55 °C, 21 h} & \quad \text{94% conversion} \\
& \quad >99\% \text{ selectivity}
\end{align*}
\]

(1.15a)

\[
\begin{align*}
\text{ethylene (1 atm)} & \quad [(\text{allylNiBr})_2, \text{PPh}_3, \text{NaBAr}_4, \text{CH}_2\text{Cl}_2] \\
\text{- 55 °C, 16 h} & \quad \text{68% conversion} \\
& \quad >99\% \text{ selectivity}
\end{align*}
\]

(1.15b)

We also successfully employed custom-synthesized Feringa-type ligands in the 1,2 hydrovinylation of the 1-vinylcycloalkenes, including the installation of the C20 stereocenter on steroid 26 (Scheme 1.5, equation 1.16 and 1.17). With the correct choice of ligand, desired configuration (either S or R) at C20 stereocenter could be installed in excellent stereoselectivity; however, the method was troubled by a significant amount of 1,4-hydrovinylation (29 and 30), accounting for 15% to 35% of the mass balance in the reactions.54 More disappointingly, simple 1,3-dienes, a very important class of substrates, altogether failed the Ni(II)-catalyzed asymmetric hydrovinylation reaction, despite a significant and prolonged effort (Scheme 1.6). We believed if these formidable
challenges of regio- and stereoselectivity of the addition of ethylene to such 1,3-dienes can be solved, this reaction could give access to the synthetically useful 1,4-skipped dienes. These 1,4-skipped dienes with an alkyl bearing central chiral carbon could be further functionalized in to wide range of extremely valuable synthetic motifs.

**Scheme 1.5. Nickel Catalyzed Hydrovinylation of Steroid 26**

![Scheme 1.5. Nickel Catalyzed Hydrovinylation of Steroid 26]

**Scheme 1.6. Nickel Catalyzed Hydrovinylation of Unactivated 1,3-Dienes**

![Scheme 1.6. Nickel Catalyzed Hydrovinylation of Unactivated 1,3-Dienes]

1.7. Cobalt Catalyzed Hydrovinylation of 1,3-Dienes

We ascribed the poor selectivity in the Ni(II)-catalyzed HV of acyclic dienes to the inability of the metal to control the conformational flexibility of 1,3-dienes. Based on
several precedents on the literature, we envisioned that a putative \([\text{LCo(II)-H}]^+\) species\(^{55-57}\) may have control over the conformational flexibility of 1,3-dienes through the formation of an \(\eta^4\) coordination complex with the dienes. While Ni(II)-catalyzed hydrovinylation of vinylarenes was completely inhibited by chelating bis-phosphines, many experiments in the literature suggested that chelating ligands can be used in the cobalt- or iron-mediated reactions\(^{15}\) since these metals are capable of higher coordination numbers. Our explorations started with an examination of 1,\(n\)-bis-diphenylphosphinoalkane-complexes of cobalt(II) \(X_2\text{Co}[\text{(Ph}_2\text{P-(CH}_2\text{)_n-PPh}_2)]\) as catalysts in the presence of various additives in the reactions of ethylene with prototypical 1,3-dienes.

1.7.1. Optimization of a Protocol for Co-Catalyzed Hydrovinylation: Effect of Ligands

For the initial studies, \((E)-1,3\)-nonadiene \((32a)\) was chosen as a prototypical 1,3-diene substrate. After an initial series of experiments varying temperature, time, solvents and sequence of addition of various reagents, we settled on a general protocol that is outlined in equation 1.18.\(^{58,59}\) The reactivity of the substrate and the distribution of products are highly dependent on the bite angle of the ligand employed (Table 1.1). A Co-complex containing larger bite angle, 1,4-\(\text{bis}\)-diphenylphosphinobutane (dppb), was identified as the most reactive and selective ligand in this series which yielded the \((Z)-1,4\)-HV product \(33a\) in 96% isomeric purity in less than 0.5 h at 0 °C (Table 1.1, entry 4).
During our investigation, we also observed that higher temperature increased the geometric isomer of the branched product to yield \((E)-1,4\text{-HV}\) as the major product (Table 1.1, entry 1 and 2). Strikingly, smaller bite angle \(\beta = 72\) ligand\(^{60}\) bis-diphenylphosphinomethane (dppm), yielded 1,2-HV product \(35a\) as the major product with very little of the 1,4-\(Z\) adduct \(33a\) or the 1,4-linear adduct \(36a\). On the contrary, ligand with a large bite angle \(\beta = 122^\circ\), BISBI \((2,2'-(diphenylphospinomethyl)-1,1'-biphenyl)\), gave the 1,4-\(Z\)-adduct \(33a\) as the major \(65\%\) product, but with up to 34\% of the 1,2-adduct \(35a\). Finally monodentate phosphine cobalt complexes, \(\text{Cl}_2\text{Co(Ph}_3\text{P)}_2\), in the presence of \(\text{Me}_3\text{Al}\) gave mostly polymeric materials (Table 1.1, entry 7). Other popular classes of ligands, bis-oxazolines, chelating bis- amines and \(N\)-heterocyclic carbenes (Figure 1.4) for this reaction failed to yield any HV products in reactions of \((E)-1,3\)-nonadiene under conditions similar to what has been prescribed for the bis-phosrophines in equation 1.13.
Table 1.1. Hydrovinylation of 32a (R= C₅H₁₁) Catalyzed by Cl₂Co(P~P). Effect of Ligands and Temperature

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<td>dppe</td>
<td>85</td>
<td>10/3</td>
<td>0/6/&gt;99</td>
<td></td>
<td>73</td>
<td>15/0/0</td>
</tr>
<tr>
<td>3</td>
<td>dppp</td>
<td>91</td>
<td>10/5</td>
<td>–40/8/&gt;99</td>
<td></td>
<td>85</td>
<td>0/0/0</td>
</tr>
<tr>
<td>4</td>
<td>dppb</td>
<td>98</td>
<td>10/5</td>
<td>0/0,5/&gt;99</td>
<td></td>
<td>96</td>
<td>0/0/0</td>
</tr>
<tr>
<td>5</td>
<td>dppm</td>
<td>72</td>
<td>10/3</td>
<td>rt/2/&gt;99</td>
<td></td>
<td>3</td>
<td>30/67/0</td>
</tr>
<tr>
<td>6</td>
<td>BISBI</td>
<td>122</td>
<td>100/10</td>
<td>-12/6/100</td>
<td></td>
<td>65</td>
<td>0/34/0</td>
</tr>
<tr>
<td>7</td>
<td>2 Ph₃P</td>
<td>-</td>
<td>3/5</td>
<td>-10/12/-</td>
<td></td>
<td>0</td>
<td>0/0/0</td>
</tr>
</tbody>
</table>

See equation 1.18 for the scheme. Estimated by GC and NMR. The rest is starting material. Entries 3-5 in neat CH₂Cl₂.

Figure 1.4. Assorted Ligands Found Unsuitable for Co(II)-Catalyzed Hydrovinylation

1.7.2. Optimization of a Protocol for Co-Catalyzed Hydrovinylation: Effect of Promoters

After the initial ligand optimization, we turned our attention on scanning of commonly used promoters (hydrate reagents, alkylating agents, Lewis acids) for the hydrovinylation of standard diene (E)-1,3-nonadiene (32a). However, the reaction showed a remarkable selectivity only with trimethylaluminum and methylaluminoxane activator, all other trials on different class of activators failed to give significant conversion to desired hydrovinylated products. Based on our results on Table 1.2 (entries
trimethylaluminum and methylaluminoxane were chosen as standard activators for further studies of the hydrovinylation of 1,3-dienes.

Table 1.2. Effect of Promoters in the $X_2Co(P\sim P)$-Catalyzed Hydrovinylation of 1,3-Dienes

<table>
<thead>
<tr>
<th>Entry</th>
<th>P~P</th>
<th>Additive (mol%)</th>
<th>Temp (°C) Time (h)</th>
<th>Conversion [products]</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>dppp</td>
<td>no additive</td>
<td>rt (2)</td>
<td>0</td>
</tr>
<tr>
<td>2</td>
<td>dppp</td>
<td>$\text{Me}_2\text{B}$ (100)</td>
<td>rt (2)</td>
<td>0</td>
</tr>
<tr>
<td>3</td>
<td>dppp</td>
<td>$\text{Et}_2\text{B}$ (100)</td>
<td>rt (2)</td>
<td>0</td>
</tr>
<tr>
<td>4</td>
<td>dppp</td>
<td>$\text{Ph}_3\text{B}$ (100)</td>
<td>rt (2)</td>
<td>0</td>
</tr>
<tr>
<td>5</td>
<td>dppp</td>
<td>$\text{i-BuAH}$ (100)</td>
<td>rt (2)</td>
<td>0</td>
</tr>
<tr>
<td>6</td>
<td>dppp</td>
<td>LiEt$_3$BH (100)</td>
<td>rt (2)</td>
<td>0</td>
</tr>
<tr>
<td>7</td>
<td>dppb</td>
<td>Zn/ZnI$_2$ (5, 5)</td>
<td>rt, (16)</td>
<td>0</td>
</tr>
<tr>
<td>8</td>
<td>dppe</td>
<td>PhMgBr (400)</td>
<td>rt (7)</td>
<td>0</td>
</tr>
<tr>
<td>9</td>
<td>dppe</td>
<td>Mn (100)</td>
<td>rt (14)</td>
<td>0</td>
</tr>
<tr>
<td>10</td>
<td>dppe</td>
<td>lnI$_1$ (100)</td>
<td>-10 - rt (10)</td>
<td>0</td>
</tr>
<tr>
<td>11</td>
<td>dppe</td>
<td>$\text{Et}_2\text{AlOEt}$ (100)</td>
<td>rt (2)</td>
<td>0</td>
</tr>
<tr>
<td>12</td>
<td>dppm</td>
<td>$\text{MeMgBr, AgOTf}$ (100, 100)</td>
<td>0 - rt (4)</td>
<td>0</td>
</tr>
<tr>
<td>13</td>
<td>dppb</td>
<td>Et$_2$AlCl (50)</td>
<td>-10 (2)</td>
<td>0$^b$</td>
</tr>
<tr>
<td>14</td>
<td>dppb</td>
<td>EtAlCl$_3$ (50)</td>
<td>-10 (2)</td>
<td>0$^b$</td>
</tr>
<tr>
<td>15</td>
<td>dppp</td>
<td>Zn/ZnI$_2$ (20, 20)</td>
<td>0 - rt (5)</td>
<td>0</td>
</tr>
<tr>
<td>16</td>
<td>dppe</td>
<td>Zn/ZnI$_2$ (20, 20)</td>
<td>0 –rt (5)</td>
<td>72 [56% 1,4-Z (33a); 11% 1,4-Z-lin (36a)]$^c$</td>
</tr>
<tr>
<td>17</td>
<td>Br$_2$Co (dppb)</td>
<td>Zn/ZnI$_2$ (20, 20)</td>
<td>0 -rt (4)</td>
<td>0</td>
</tr>
<tr>
<td>18</td>
<td>Br$_2$Co (dppe)</td>
<td>Zn/ZnI$_2$ (20, 20)</td>
<td>0 -rt (4)</td>
<td>100 [85% 1,4-Z (33a); 15% 1,4-Z-lin (36a)]</td>
</tr>
<tr>
<td>19</td>
<td>Br$_2$Co (dppp)</td>
<td>Zn/ZnI$_2$ (20, 20)</td>
<td>0 –rt (4)</td>
<td>100 [79% 1,4-Z (33a); 21% 1,4-Z-lin (36a)]</td>
</tr>
<tr>
<td>20</td>
<td>Br$_2$Co (dppp)</td>
<td>Zn/ZnI$_2$ (20, 20)</td>
<td>0 –rt (4)</td>
<td>100 [79% 1,4-Z (33a); 21% 1,4-Z-lin (36a)]</td>
</tr>
</tbody>
</table>

$^a$ See eqn 1.18 for details. All using Cl$_2$Co(P~P) unless indicated otherwise. Entries 13-20 using (E)-C$_4$H$_7$-CH=CH-CH=CH$_2$. $^b$ No volatile products (polymers?). $^c$ 2% Each 2 other isomers. [Table adapted from Chem. Sci., 2015, 6, 3994-4008.]

1.7.3. Scope of Substrates on Co-Catalyzed Hydrovinylation of 1,3-Dienes

A series of linear 1,3-dienes were subjected to the hydrovinylation reaction using (dppb)CoCl$_2$ complex with trimethylaluminum as co-catalyst, resulting in excellent yields
and selectivities for the 1,4-Z adducts (Table 1.3). The general optimized procedure used for the reactions is shown in equation 1.19.

The reaction conditions appeared to be compatible with a series of simple alkyl chain containing 1,3-dienes (Table 1.3, entries 1-7) along with functionalized diene possessing benzyl ether (Table 1.3, entry 15, 32i). The ester bearing substrate 32h (Table 1.3, entries 12-14) showed uniquely different reactivity as neither the commonly used dppp complex (Table 1.3, entry 12) nor the dppb complex (Table 1.3, entry 13) was able to affect the hydrovinylation of this substrate. However, cobalt complex with a narrow bite-angle bis-phosphine ligand, dppm gave an excellent yield of the product 33h (Table 1.3, entry 14). 1,3-Dienes with fully conjugated aromatic ring showed remarkable electronic effect in the hydrovinylation reaction and yielded exclusively a 1,2-(E)-adduct, 35g (Table 1.3, entry 10, Figure 1.5). Likewise (E)-2-methyl-1-phenyl-1,3-butadiene (32l) gave only a 1,2-HV product (35l, Figure 1.5) with both the dppm and dppp complexes (Table 1.3, entries 18 and 19). 3-Substituted 1,3-butadienes, β-myrcene (32m) and isoprene (2-methyl-1,3-butadiene, 32n) gave very high yields of 1,4-linear adducts 36m and 36n (Figure 1.5) in which the hydrogen adds to the less substituted double bond (Table 1.3, entries 20 - 22).
Table 1.3. Scope of Substrates in the Co-Catalyzed Hydrovinylation of Linear 1,3-Dienes

<table>
<thead>
<tr>
<th>Entry</th>
<th>Diene (32)</th>
<th>R in 32 equation 1.14</th>
<th>Cl2Co(P–P) (P–P), mol%</th>
<th>Conditions</th>
<th>Yield(%)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td></td>
<td>Al/Co</td>
<td>temp (°C)/time (h)</td>
<td></td>
</tr>
<tr>
<td>1</td>
<td>C5H11 (32a)</td>
<td>dppb (10)</td>
<td>5</td>
<td>0/0.5</td>
<td>&gt;95</td>
</tr>
<tr>
<td>2</td>
<td>C5H11 (32b)</td>
<td>dppb (5)</td>
<td>3</td>
<td>-10/6 b</td>
<td>&gt;95</td>
</tr>
<tr>
<td>3</td>
<td>C7H15 (32c)</td>
<td>dppb (5)</td>
<td>3</td>
<td>-10/6 b</td>
<td>&gt;95</td>
</tr>
<tr>
<td>4</td>
<td>C8H17 (32d) (E:Z 54:46)</td>
<td>dppb (5)</td>
<td>3</td>
<td>-10/6 b</td>
<td>&gt;95</td>
</tr>
<tr>
<td>5</td>
<td>cyclohexyl (32e) (E:Z 54:45)</td>
<td>dppb (10)</td>
<td>20</td>
<td>-10/8 c</td>
<td>82</td>
</tr>
<tr>
<td>6</td>
<td>CH3 (32f)</td>
<td>dppb (10)</td>
<td>20</td>
<td>-10/6 b</td>
<td>&gt;95</td>
</tr>
<tr>
<td>7</td>
<td>Ph (32g)</td>
<td>dppb (10)</td>
<td>3</td>
<td>-20/0</td>
<td>&gt;99 (86)</td>
</tr>
<tr>
<td>8</td>
<td>Ph (32g)</td>
<td>dppb (10)</td>
<td>3</td>
<td>-10/6 b</td>
<td>&gt;99 (87)</td>
</tr>
<tr>
<td>9</td>
<td>CH2CO2Et (32h)</td>
<td>dppm (10)</td>
<td>3</td>
<td>-20/7</td>
<td>0</td>
</tr>
<tr>
<td>10</td>
<td>Ph (32g)</td>
<td>dppb (10)</td>
<td>20</td>
<td>-10/8 c</td>
<td>0</td>
</tr>
<tr>
<td>11</td>
<td>CH3CH2OBn (32i)</td>
<td>dppb (10)</td>
<td>20</td>
<td>-15/14 c</td>
<td>&gt;97 &lt;2</td>
</tr>
<tr>
<td>12</td>
<td>CH3CH2Ph (32j) (E:Z 53:47)</td>
<td>dppb (10)</td>
<td>20</td>
<td>-10/8 c</td>
<td>84</td>
</tr>
<tr>
<td>13</td>
<td>CH2CO2Et (32h)</td>
<td>dppb (10)</td>
<td>20</td>
<td>-10/8 c</td>
<td>84</td>
</tr>
<tr>
<td>14</td>
<td>CH2CO2Et (32h)</td>
<td>dppb (10)</td>
<td>20</td>
<td>-10/8 c</td>
<td>84</td>
</tr>
<tr>
<td>15</td>
<td>CH2CO2Et (32h)</td>
<td>dppb (10)</td>
<td>20</td>
<td>-10/8 c</td>
<td>84</td>
</tr>
<tr>
<td>16</td>
<td>CH2CO2Et (32h)</td>
<td>dppb (10)</td>
<td>20</td>
<td>-10/8 c</td>
<td>84</td>
</tr>
<tr>
<td>17</td>
<td>CH2CO2Et (32h)</td>
<td>dppb (10)</td>
<td>20</td>
<td>-10/8 c</td>
<td>84</td>
</tr>
<tr>
<td>18</td>
<td>Other Dienes</td>
<td>dppb (10)</td>
<td>20</td>
<td>-10/8 c</td>
<td>84</td>
</tr>
<tr>
<td>19</td>
<td>4-Me2N-C6H4 (32k)</td>
<td>dppb (10)</td>
<td>20</td>
<td>-10/8 c</td>
<td>84</td>
</tr>
<tr>
<td>20</td>
<td>β-myrcene (32l)</td>
<td>dppb (10)</td>
<td>20</td>
<td>-10/8 c</td>
<td>84</td>
</tr>
<tr>
<td>21</td>
<td>isoprene (32m)</td>
<td>dppb (10)</td>
<td>20</td>
<td>-10/8 c</td>
<td>84</td>
</tr>
<tr>
<td>22</td>
<td>isoprene (32m)</td>
<td>dppb (10)</td>
<td>20</td>
<td>-10/8 c</td>
<td>84</td>
</tr>
</tbody>
</table>

a See equation 1.19 for procedure. b Solvent CH2Cl2:tolune 4:1. c MAO as ‘Al-Me’ source. d 1,2-linear product 35g (99%). e 1,2-linear product 35l, 97%. f Product 35l 62%. g Co:Al 1:3 (Z)-2-Methyl-6-(3-propenyl)octa-2,6-diene (36m). See Figure 1.5 for structures of 35g, 35l, 36g, 36k, 36m and 36n. [Table adapted from Chem. Sci., 2015, 6, 3994-4008.]
1.7.4. Co(II)-Catalyzed Asymmetric Hydrovinylation of 1,3-Dienes

With our optimized hydrovinylation conditions, we turned our attention to asymmetric variants of these reactions. Several commercially available chiral bisphosphines ligands (structures are shown in Figure 1.6) were attempted in the asymmetric hydrovinylation reactions of prototypical diene 32. The distribution of products and the enantioselectivities of the chiral products obtained are listed in Table 1.4. Chelating chiral ligands with comparable bite angles corresponding to their achiral version, showed almost similar reactivities in the hydrovinylation reaction. In general, bis-diarylphosphino-ligands with comparable bite angles to dppe, dppp and dppb are the most reactive (Table 1.4, entries 1-3 and 7-9, 17, 18; ligands L11, L12, L13, L17, L18, L19, L27, L28) ligands for asymmetric version of this reaction. Predictably, narrow bite-angles, (S,S)-chiraphos (L11) and (R)-prophos (L12) gave the 1,2-HV product 35a as the major product, along with minor amounts of 33a, the 1,4-(Z)-adduct (Table 1.4, entries 1 and 2). The enantioselectivities for these products are low, with the ee for 33a almost always higher than that of the any other adducts in these reactions. Other phosphine ligands with 2-carbon chains in the backbone, L13 and L14, give 33a as the major product with very low enantioselectivities (Table 1.4, entries 3 and 4). Two chiral analogs of dpmm, miniphos L15 and trichickenfootphos L16 were synthesized (Table 1.4,
entries 5 and 6), however both of these chiral ligands are found to be ineffective for the hydrovinylation reaction. Following up the achiral reaction with (dppp)CoCl₂ and (dppb)CoCl₂, structurally analogous [(S,S)-BDPP]CoCl₂ and [(S,S)-DIOP]CoCl₂ complex gave the best yields (99%) and enantioselectivities (97% and 95%) with 0.05 equivalents of the catalyst for the hydrovinylation of 1,3-nonadiene (Table 1.4, entries 7 and 8). A constrained analog of dppb, L₁₉, derived from proline

Table 1.4. Enantioselective HV of (E)-nona-1,3-diene. Effect of Chiral Ligands

<table>
<thead>
<tr>
<th>Entry</th>
<th>Ligand</th>
<th>Conversion</th>
<th>Products (%ratio %ee)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>L₁₁</td>
<td>99</td>
<td>33a 41/78(S) 55/16</td>
</tr>
<tr>
<td>2</td>
<td>L₁₂</td>
<td>99</td>
<td>34a 18/44 62/1</td>
</tr>
<tr>
<td>3</td>
<td>L₁₃</td>
<td>99</td>
<td>35a 90/8   0</td>
</tr>
<tr>
<td>4</td>
<td>L₁₄</td>
<td>66</td>
<td>36a 54/1   0</td>
</tr>
<tr>
<td>5</td>
<td>L₁₅</td>
<td>40</td>
<td>7/-       31/8</td>
</tr>
<tr>
<td>6</td>
<td>L₁₆</td>
<td>0</td>
<td>-/-       -/-</td>
</tr>
<tr>
<td>7</td>
<td>L₁₇</td>
<td>99</td>
<td>79/10    59/12</td>
</tr>
<tr>
<td>8</td>
<td>L₁₈</td>
<td>99</td>
<td>86/64(S) 2/-</td>
</tr>
<tr>
<td>9</td>
<td>L₁₉</td>
<td>99</td>
<td>86/64(S) 2/-</td>
</tr>
<tr>
<td>10</td>
<td>L₂₀</td>
<td>0</td>
<td>-/-       -/-</td>
</tr>
<tr>
<td>11</td>
<td>L₂₁</td>
<td>0</td>
<td>-/-       -/-</td>
</tr>
<tr>
<td>12</td>
<td>L₂₂</td>
<td>88</td>
<td>66/8      0</td>
</tr>
<tr>
<td>13</td>
<td>L₂₃</td>
<td>95</td>
<td>63/14    0</td>
</tr>
<tr>
<td>14</td>
<td>L₂₄</td>
<td>80</td>
<td>39/95(S) 0</td>
</tr>
<tr>
<td>15</td>
<td>L₂₅</td>
<td>-6</td>
<td>6/-       0</td>
</tr>
<tr>
<td>16</td>
<td>L₂₆</td>
<td>99</td>
<td>28/20    59/12</td>
</tr>
<tr>
<td>17</td>
<td>L₂₇</td>
<td>87</td>
<td>79/10    0</td>
</tr>
<tr>
<td>18</td>
<td>L₂₈</td>
<td>95</td>
<td>95/87(S) 0</td>
</tr>
<tr>
<td>19</td>
<td>L₂₉</td>
<td>0</td>
<td>-/-       -/-</td>
</tr>
<tr>
<td>20</td>
<td>L₃₀</td>
<td>0</td>
<td>-/-       -/-</td>
</tr>
</tbody>
</table>

a See equation 1.19 for typical procedure (R = C₅H₁₁). b Determined by CSP GC. c See Figure 1.6 for structures of ligands. d At -45 °C /8 h. e Rest starting material. [Table adapted from Chem. Sci., 2015, 6, 3994-4008.]

also gives 33a as the major product, albeit in relatively low ee (Table 1.4, entry 9). Biaryl ligands (Table 1.4, entries 10, 11 and 15) are typically unreactive to the hydrovinylation reaction, except (R)-MeO-Biphe (L₁₂) and (S)-Segphos (L₁₃), where
some conversion to our desired product were observed with very low ee’s (Table 1.4, entries 12 and 13). Both electron rich and poor ligands were attempted for the hydrovinylation reaction. Electron-rich phospholanes L24 showed high ee (95%) for the formation of the 1,4-Z-HV product 33a, even though it gave up to 40% of the linear achiral product 36a (Table 1.4, entry 14). Ferrocene derived ligand Josiphos-1 (L27) showed 79% of desired 1,4-Z-HV product 33a with only 10% ee. On the contrary, electron withdrawing ligand analog Josiphos-2, L28 [a ligand with diphenylphosphino-substituent, to one with a more electron-withdrawing di-(bis-1,3-CF3-phenylphosphino)-ligand] gave an excellent conversion to desired 1,4-Z-HV product giving up to 87% ee, with <4 % of the linear adduct 36a as a contaminant (Table 1.4, entry 18). Among other ferrocene derived ligands only Walphos (L26) showed any kind of reactivity in our system. Noticeably, Walphos (L26) is the only ligand among the many we tested gave the (E)-1,4 and (E)-1,2- adducts 34a and 35a as the major products, both in only modest selectivities (Table 1.4, entry 16). All other trials with various chiral backbones in the ligand structure are not competent for this hydrovinylation reaction under the standard conditions (L29 and L30, Table 1.4, entries 19 and 20).
Figure 1.6. Ligands for Co(II)-Catalyzed Asymmetric Hydrovinylation of 1,3-Dienes
1.7.5. Scope of Substrates in the Asymmetric Hydrovinylation of 1,3-Dienes

A close examination of the results presented in Table 1.4 suggests that BDPP (L17), DIOP (L18) and Josiphos 2 (L28) have the best potential for the asymmetric hydrovinylation of (E)-1,3-dienes. A variety of simple and functionalized 1,3-dienes were tested with these chiral cobalt complexes and the results are documented in Table 1.5. Simple, linear (E)-1,3-dienes gave excellent yield and enantioselectivities with BDPP (L17), DIOP (L18) ligands (Table 1.5. entries 1-9). In a mixture of (Z)- and (E)-terminal 1,3-dienes, (E)-isomer reacts significantly faster than the (Z)-isomer, leaving behind almost exclusively (Z)-1,3-dienes at the end of reaction (will be discussed later in chapter 4). During our ligand study, we also noted that complexes of Josiphos 2 (L28) are much more active as compared to BDPP (L17) and DIOP (L18), even though the ee’s are slightly lower on the desired (Z)-1,4-HV product 33a.

1.7.6. Mechanistic Considerations

Based on several observations in the literature23,32,55,61 and analogy to our own previous work on the mechanism of Ni-catalyzed hydrovinylation of vinylarenes,62 we propose a mechanism for this reaction which is shown in Scheme 1.7. In this mechanism we hypothesize that a cationic cobalt hydride VII is the active catalyst61 in the reaction. This species could be formed by metathesis of the Al-Me/Co-Cl bonds and migratory insertion of an alkene into Co-Me bond, followed by β-hydride elimination (panel A).

The putative catalyst VII upon coordination of a diene would form VIII (panel B). We believe this η⁴-complex (VIII) is responsible for the high selectivity of the reaction. The
conformation of the coordinated diene to the s-cis arrangement imposes the selectivity in
the hydrovinylation product, a possibility that does not exist in any corresponding Ni(II)-
species. Addition of the Co-H via an η^4-diene complex VIII would produce a syn-anti-
(allyl)Co-species IX which would undergo coupling with ethylene to give XI. β-hydride
elimination from XI regenerates the catalyst giving major product as 1,4-Z
hydrovinylation product.

Table 1.5. Co-Catalyzed Asymmetric HydroVinylation of Linear 1,3-Diene ^a

<table>
<thead>
<tr>
<th>Entry</th>
<th>Diene (32) R in 32 equation 1,14</th>
<th>(P–P) in Cl₂Co(P–P)</th>
<th>Al/Co</th>
<th>Conditions temp (°C)/time (h)</th>
<th>Yield (%)</th>
<th>33 (e)ee ^b</th>
<th>36 (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>C₂H₆ (32a-E)</td>
<td>L₁₈ (R,R)-DIOP</td>
<td>3</td>
<td>-45 /6</td>
<td>&gt;95</td>
<td>95.0(S)</td>
<td></td>
</tr>
<tr>
<td>2</td>
<td></td>
<td>L₁₇ (S,S)-BDPP</td>
<td>3</td>
<td>-45/6</td>
<td>97.1</td>
<td>97.1(R)</td>
<td></td>
</tr>
<tr>
<td>3</td>
<td></td>
<td>L₂₄ Tangphos</td>
<td>3</td>
<td>-10/8</td>
<td>39</td>
<td>95.0(S)</td>
<td>40</td>
</tr>
<tr>
<td>4</td>
<td></td>
<td>L₂₈ Josiphos 2⁺</td>
<td>3</td>
<td>-20/14</td>
<td>&gt;95</td>
<td>87.0(S)</td>
<td>&lt;4</td>
</tr>
<tr>
<td>5</td>
<td>C₆H₁₃ (32b-E)</td>
<td>L₁₈ (R,R)-DIOP</td>
<td>3</td>
<td>-45 /6</td>
<td>&gt;95</td>
<td>95.3(S)</td>
<td></td>
</tr>
<tr>
<td>6</td>
<td></td>
<td>L₂₈ Josiphos 2⁺</td>
<td>3</td>
<td>-20/14</td>
<td>&gt;98</td>
<td>95.4(S)</td>
<td></td>
</tr>
<tr>
<td>7</td>
<td>C₆H₁₇ (32c-E)</td>
<td>L₁₈ (R,R)-DIOP</td>
<td>3</td>
<td>-45 /6</td>
<td>95</td>
<td>96.1(S)</td>
<td>&lt;3</td>
</tr>
<tr>
<td>8</td>
<td></td>
<td>L₂₈ Josiphos 2⁺</td>
<td>3</td>
<td>-20/14</td>
<td>88</td>
<td>86.0(S)</td>
<td>&lt;3</td>
</tr>
<tr>
<td>9</td>
<td>C₆H₁₇ (32d-E)</td>
<td>L₁₈ (S,S)-DIOP</td>
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<td>53</td>
<td>74.0(R)</td>
<td>5</td>
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<tr>
<td>10</td>
<td>cyclohexyl (32e)</td>
<td>L₁₈ (S,S)-DIOP</td>
<td>3</td>
<td>-10/8</td>
<td>49</td>
<td>84.0(R)</td>
<td>5</td>
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<tr>
<td>11</td>
<td>CH₃ (32f-E)</td>
<td>L₁₈ (R,R)-DIOP</td>
<td>3</td>
<td>-45 /6</td>
<td>&gt;95^j</td>
<td>90.1(S)</td>
<td></td>
</tr>
<tr>
<td>12</td>
<td>Ph (32g-E)</td>
<td>L₁₈ (S,S)-DIOP</td>
<td>3</td>
<td>0/5</td>
<td>46</td>
<td>-^g</td>
<td>55</td>
</tr>
<tr>
<td>13</td>
<td>CH₂CO₂Et (32h-E)</td>
<td>L₁₇ (S,S)-BDPP</td>
<td>10</td>
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<td>84</td>
<td>92(R)</td>
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<tr>
<td>14</td>
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<td>3</td>
<td>10/8</td>
<td>0</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>15</td>
<td></td>
<td>L₁₈ (R,R)-DIOP</td>
<td>3</td>
<td>-20 /6</td>
<td>40^i</td>
<td>99.0(S)</td>
<td>0</td>
</tr>
<tr>
<td>16</td>
<td></td>
<td>L₁₈ (S,S)-DIOP</td>
<td>3</td>
<td>-10/6</td>
<td>99</td>
<td>94.0(R)</td>
<td>6</td>
</tr>
<tr>
<td>17</td>
<td>CH₂CH₂OBn (32i-E)</td>
<td>L₁₇ (S,S)-BDPP</td>
<td>3</td>
<td>-10 /9</td>
<td>&gt;99</td>
<td>92.0(R)</td>
<td>0</td>
</tr>
<tr>
<td>18</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

^a See equation 1.18 for procedure. ^b Determined by CSP GC. Configurations are tentative and are based on
the known product of HV of 1-methylbuta-1,3-diene. ^c 1 mol% Co. ^d Reaction stopped after most of the
(E)-isomer was converted, recovered starting material (E:Z = 1:17). ^e Reaction stopped after most of the
(E)-isomer is converted, recovered starting material (E:Z = 1:49). ^f Estimated by GC, volatile products. ^g
1,2–Adduct. ^h 5 mol%, i rest starting material. j Using MAO.
[Table adapted from Chem. Sci., 2015, 6, 3994-4008.]
There are several key features we noted during our experimental observations on hydrovinylation of 1,3-dienes.

1. Cobalt complexes of chelating bis-phosphine ligands with narrow bite angles such as dppm give predominantly the 1,2-adduct whereas fully conjugated aromatic dienes preferentially forms 1,4-linear adduct, 36. We hypothesized that along with our major
catalytic cycle, with smaller bite angle ligands, ethylene addition takes space at C₂ of X. XV will form, which after β-hydride elimination of VII would lead to the 1,2-HV product 35. In the fully conjugated aromatic diene system, hydride addition takes place at C₄ of VIII to give XII, which upon addition of ethylene at C₁ would lead to the 1,4-linear adduct, 36.

2. We also noticed that low temperature reaction predominantly made (Z) configuration of the internal double bond of the hydrovinylated product, however increase in temperature gave a mixture of (E) and (Z) isomers. We proposed that the initially formed adduct IX (syn-anti) is configurationally stable at low temperature and this would account for the Z-geometry seen in the major product 33. However, at higher temperature, the syn-anti isomer of IX undergoes isomerization to the more stable IX (syn-syn), that resulted in to more the 1,4-adduct 34 with an E-configuration of the double bond.

3. Further support for the intermediacy of the η⁴-complex also comes from the enhanced reactivity of the E-isomer in a mixture of (Z)- and (E)-terminal 1,3-dienes (more to follow in next section 1.8) For steric reasons, the formation of the η⁴-complex should be significantly favored for the (E)-isomer of the diene, which can adapt an s-cis conformation much more easily as compared to the corresponding (Z)-diene.

1.8. Chemoselectivity in Catalyzed Reactions of (Z)- and (E)-1,3-Dienes with [1,n-Bisphosphine]CoCl₂/Me₃Al. Hydrovinylation and Isomerization

During these studies of Co-catalyzed asymmetric hydrovinylation we noticed significant rate differences in the reactions of (E)- and (Z)-1,3-dienes. With the
Cl₂Co(DIOP) complex, the (E)-isomers react significantly faster, leaving behind essentially unreacted (Z)-isomer near the end of the reaction (Table 1.5, entries 10, 11). In the case of substrate 32e (entry 11, E:Z = 47:53), the unreacted starting material left behind at the end of the HV reaction (-10 °C, 8 h) using the complex Cl₂Co(DIOP) is essentially pure (Z)-isomer (E:Z = 1:49) (equation 1.20a). It is also important to note that throughout the hydrovinylation reaction with the mixture of (E)- and (Z)-1,3-dienes, we have never observed any isomerization of the (Z)-(32e) into the thermodynamically favored (E)-isomer. Question raised whether in the absence of ethylene, under proper conditions, kinetic control might prevail in the (E)-(Z)-isomerization of 32e, and if so, using ligand effects could one make the (Z)-isomer? These expectations have indeed been borne out and we are able to successfully promote an unusual isomerization of the (E)/(Z)-

mixture of 32e almost exclusively to the Z-isomer (equation 1.20b). The isomerization of the dienes is highly dependant on the ligand and temperature of the reaction. Details on the reaction conditions, substrate scope and mechanism of this isomerization reaction will be discussed on chapter 3.
1.9. Ni(II) vs Co(II)-Hydrovinylation of 1,3-Dienes

In short, a new cobalt-catalyzed hydrovinylation system was developed as a complement to the established nickel-catalyzed 1,2-hydrovinylation, which does not work in simple 1,3-dienes capable of existing as s-cis/s-trans isomers. This new reaction of 1,3-dienes yields exclusively 1,4-hydrovinylated product (Figure 1.7). The substrate scope was considerably expanded from simple 1,3-diene to functionalized linear dienes including those containing ester, trisubstituted double bond and ether, moieties with excellent yields and enantioselectivities. The success in the cobalt-catalyzed hydrovinylation of simple acyclic dienes prompted us to investigate yet another set of substrates that gave a mixture of 1,2- and 1,4-adducts, viz., 1-vinylcycloalkenes (Scheme 1.5, equation 1.16 and 1.17).
1.10. Co (II)-Catalyzed Hydrovinylation of 1-Vinylcycloalkenes

Hydrovinylation of racemic-4-tert-butyl-1-vinylcycloalkene revealed that, in sharp contrast to Ni(II)-catalyzed reaction, the (dppp)CoCl₂/trimethylaluminum combination catalyst gave almost exclusively 1,4-adducts as a mixture of cis (39a) and trans (39b) isomers [4.8 : 1] (Scheme 1.8, 37 to 39a and 39b). We also identified that methylaluminoxane could serve as an effective replacement of the hydrocarbon solutions of Me₃Al as co-catalyst for the hydrovinylation reaction of 1-vinylcycloalkenes.

Scheme 1.8. 1,2- vs 1,4-Hydrovinylation of 4-tert-Butyl-1-vinylcyclohexene

1.10.1. Substrate Scope of Co(II)-Catalyzed Hydrovinylation of 1-Vinylcycloalkenes

With the newly developed catalytic system of cobalt complexes combined with methylaluminoxane co-catalyst, a broad range of substrates was examined. The scope of the reaction is illustrated with the examples shown in Table 1.6. Under standard condition, the hydrovinylation is highly chemoselective for the enantiopure substrate 40, which was prepared from commercially available (-)-perillaldehyde via a Wittig reaction, gives two products cis-41a (2R,4S) and trans-41b (2S,4S) with a ration of 4:1. Conformationally flexible 1-vinylcycloalkenes (44a-c) gave predominantly 1,4-hydrovinylated products with >95% isolated yields. Substrates 44d, 44e, 44f, which gave
exclusively 1,2-hydrovinylated product under the Ni(II)-catalyst,\textsuperscript{48} gave quantitative yields of 1,4-hydrovinylated product under standard Co(II)-hydrovinylation conditions.

1.10.2. Co(II)-Catalyzed Asymmetric Hydrovinylation of 1-Vinylcycloalkenes

After the initial results on achiral hydrovinylation of 1-Vinylcycloalkenes, further exploration on asymmetric version was attempted. Based on our previous results, on 1,3-dienes, the chelating bis-phosphine ligands (S,S)-BDPP [(2S,4S)-bis-(diphenylphosphino)pentane], (R,R)-BDPP, (S,S)-DIOP [(+)-(2S,3S)-O-isopropylidene-2,3-dihydroxy-1,4-bis(diphenylphosphino)butane], (R,R)-DIOP, and (S,S)-ChiraPhos [(2S,3S)-(−)-bis(diphenylphosphino)butane] were chosen as the chiral ligands to be screened for asymmetric cobalt (II) catalyzed hydrovinylation reaction. The reaction conditions were essentially the same as those that were established for the non-asymmetric reactions described earlier in this dissertation (Table 1.6). Most satisfyingly, we observed [(S,S)-BDPP]CoCl\(_2\)/MAO catalytic system gave the best regio- and enantioselectivities (>98%) for the hydrovinylation of a series of 1-vinylcycloalkenes and the corresponding benzannulated derivatives and the results are shown in Table 1.7.

![Reaction scheme](image)
Table 1.6. Hydrovinylation Results of Various 1-Vinylcycloalkenes$^a$

<table>
<thead>
<tr>
<th>Entry</th>
<th>Diene</th>
<th>Product</th>
<th>Conv. (%)</th>
<th>Regiosel. $^b$</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>(\text{Bu} )</td>
<td>[37]</td>
<td>&gt;99</td>
<td>98:2</td>
</tr>
<tr>
<td></td>
<td></td>
<td>(\text{Bu} )</td>
<td>[39a (cis): 39b (trans)= 81:17]</td>
<td>&gt;99</td>
</tr>
<tr>
<td>2</td>
<td>40</td>
<td>[41a (cis): 41b (trans)= 4:1]</td>
<td>&gt;99</td>
<td>&gt;99</td>
</tr>
<tr>
<td>3</td>
<td>42</td>
<td>[43a (cis): 43b (trans)= 1:9]</td>
<td>93$^c$</td>
<td>96:4</td>
</tr>
<tr>
<td>4</td>
<td>44a</td>
<td>45a + 46a</td>
<td>&gt;99</td>
<td>80:20</td>
</tr>
<tr>
<td>5</td>
<td>44b</td>
<td>45b + 46b</td>
<td>&gt;99</td>
<td>98:2</td>
</tr>
<tr>
<td>6</td>
<td>44c</td>
<td>45c</td>
<td>&gt;99</td>
<td>&gt;99</td>
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<td>7</td>
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<td>8</td>
<td>44e</td>
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<td>&gt;99</td>
<td>&gt;99</td>
</tr>
<tr>
<td>9</td>
<td>44f</td>
<td>45f</td>
<td>~97</td>
<td>&gt;99</td>
</tr>
</tbody>
</table>

$^a$ See scheme 1.8 for procedure. $^b$ 1,4-HV vs 1,2-HV, estimated from NMR and GC. $^c$ Rest (E)-isomer. $^d$ 46a and 46b are 1,2-HV products. [Table adapted from J. Am. Chem. Soc. 2012, 134, 6556-6559.]
Table 1.7. Asymmetric Hydrovinylation of Various 1-Vinylcycloalkenes\(^a\)

<table>
<thead>
<tr>
<th>Entry</th>
<th>Diene</th>
<th>Conv. (%)</th>
<th>1,4-HV:(1,2\text{-HV})</th>
<th>Product (% ee(^c))</th>
<th>(configuration)(^d)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td><img src="LaTeX" alt="44a" /></td>
<td>&gt;99</td>
<td>85:14</td>
<td>45a [&gt;99 (S)(^f)]</td>
<td></td>
</tr>
<tr>
<td>2</td>
<td><img src="LaTeX" alt="44b" /></td>
<td>&gt;95</td>
<td>96:4</td>
<td>45b [&gt;99 (S)(^f)]</td>
<td></td>
</tr>
<tr>
<td>3</td>
<td><img src="LaTeX" alt="44c" /></td>
<td>&gt;99</td>
<td>&gt;99</td>
<td>45c [&gt;99 (S)]</td>
<td></td>
</tr>
<tr>
<td>4</td>
<td><img src="LaTeX" alt="44d" /></td>
<td>&gt;99</td>
<td>&gt;99:&lt;1</td>
<td>45d [&gt;99 (S)]</td>
<td></td>
</tr>
<tr>
<td>5</td>
<td><img src="LaTeX" alt="44e" /></td>
<td>&gt;99</td>
<td>&gt;99</td>
<td>45e [&gt;99 (S)]</td>
<td></td>
</tr>
<tr>
<td>6</td>
<td><img src="LaTeX" alt="44f" /></td>
<td>~97</td>
<td>&gt;99</td>
<td>45f [&gt;99 (S)]</td>
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<tr>
<td>7</td>
<td><img src="LaTeX" alt="37" /></td>
<td>&gt;99</td>
<td>87:13</td>
<td>39a (cis), 39b (trans) [&gt;99(^e,f) (2S, 4R)]</td>
<td></td>
</tr>
</tbody>
</table>

\(^a\) See equation 1.21 for procedure. \(^b\) 1,4-HV and 1,2-HV were estimated from NMR and GC. \(^c\) Major product, determined by chiral stationary phase GC. \(^d\) Assigned by the analogy to products 45b and 45e, whose configurations were confirmed by comparison to known derivatives. \(^e\) ee for the 1,2-HV product: <5\% 39a : 39b = 1.4 : 1.0; ee for both the diastereomers are >99\%, configuration of 39a is (2S, 4R), configuration of 39b is presumed to be (2S, 4S). [Table adapted from J. Am. Chem. Soc. 2012, 134, 6556-6559.]

Reactions of two prototypical dienes, 1-vinylcyclohexene and 1-vinylcycloheptene, showing the optimized conditions, and the possible side reactions, are shown in equation 1.21. The hydrovinylated products 45a and 45b are obtained essentially as single enantiomers, whereas the 1,2-HV products 46a and 46b are formed in much lower ee’s.
1.11. Co(II)-Catalyzed Hydrovinylation of Chiral 1-Vinylcycloalkenes and Stereodivergent Reactions

Asymmetric hydrovinylation on 4-tert-butyl-1-vinylcyclohexene (37) with standard [(S,S)-BDPP]CoCl$_2$/methylaluminoxane condition gave 1,4-hydrovinylation (~vs 1,2-hydrovinylation 3.2 : 1) product with excellent enantioselectivities of both cis (39a, 2S,4R, 98% ee) and trans (39b, 2S,4S, 98% ee) isomers (equation 1.22)$^{69}$ The exceptionally high enantioselectivity in the formation of both diastereomeric products (39a and 39b) from the racemic substrate 37 clearly revealed that the individual isomers of the racemate 37 reacted with a very divergent pathway to form highly enantioselective diastereomeric products. This is a classic example of enantiodivergent parallel kinetic resolution where starting from a racemic compound, each enantiomer reacts to give completely different set of diastereomers upon reaction with an enantiopure catalyst. A series of racemic 4-substituted-1-vinylcycloalkenes were examined under these hydrovinylation condition and details of these studies will be further discussed on chapter 5.

![Chemical reaction diagram](image-url)
1.12. Expansion of the Scope of Co-Catalyzed Asymmetric Hydrovinylation. Synthesis of Chiral Enolates and Their Application

Since our initial result on Ni-catalyzed ethylene addition across the double bond of styrene on 1998, hydrovinylation chemistry has advanced well beyond what we envisioned. Substrate scope in hydrovinylation chemistry has been expanded from vinylarenes to simple, unactivated, linear 1,3-dienes and 1-vinylcycloalkenes with excellent chemo-, regio-, and enantioselectivity. As our understanding and control over the chemistry have progressed, we questioned ourselves to expand the chemistry with broader functional group compatibility and hence increased synthetic utility. Inspired by the original work on hydrovinylation of linear 1,3-dienes and the successful development of its asymmetric version, we propose to study substrates that upon hydrovinylation would give highly versatile nucleophilic synthons, which could be subjected to a myriad of electrophilic reactions for the synthesis of diverse building blocks. 1,3-siloxydienes have been found to be an excellent substrate for this chemistry. Upon hydrovinylation, 1,3-siloxydienes will give access to enantiopure trialkylsilyl enol ethers which are exceptionally versatile intermediates often used as enolate surrogates for the synthesis of carbonyl compounds (Scheme 1.9). Additionally, there are no reports of broadly applicable, catalytic methods for the synthesis of chiral silyl enol ethers carrying latent functionalities useful for synthetic operations beyond the many possible reactions of the enol ether moiety itself. Development of highly efficient and enantioselective protocols for the synthesis of functionalized silyl enol ethers would considerably expand the utility of these venerable intermediates.
Our studies started with an examination of the hydrovinylation of a prototypical trimethylsiloxy-1,3-diene, 47a, under conditions described in equation 1.18. Among the cobalt complexes, (dppp)CoCl₂, gave an exceptionally clean reaction to yield the product (E)-48a in quantitative yield with methylaluminoxane as an activator.

More satisfyingly, under the optimized conditions, asymmetric hydrovinylation of this substrate (47a) using the cobalt (II)-DIOP-complex, gave excellent yields and enantiomeric excess for the expected hydrovinylated product (equation 1.23). All the additional details of this reaction along with the substrate scope and ligand study will be further discussed on chapter 4.

1.12.1. Applications of Asymmetric Hydrovinylation of Siloxydienes

Since silyl enolates are among the most useful carbon nucleophiles, the enantiopure β-vinyl silyl enolates formed from the asymmetric hydrovinylation reaction provide a
direct route to many different types of α, β-di-functionalized carbonyl compounds.\textsuperscript{72-74} The simplest of these reactions, acid-mediated hydrolysis, gives potentially valuable β-vinyl ketones (equation 1.24a). Under optimized conditions, the silyl enolates were further derivatized for a variety of carbon-heteroatom and carbon-carbon bond-forming reactions keeping moderate to good diastereomeric ratios (equation 1.24b). Details on derivatization results with the synthetic utility of these products will be discussed on chapter 4.

\begin{equation}
\begin{array}{c}
R_3SiO & \text{electrophiles} & (E^+)\\
1,2\text{-vicinal chiral centers}
\end{array}
\end{equation}

1.12.2. Synthesis and Application of the Enantiopure Vinyl Triflates

These enantiopure silyl enolates (48) obtained from the cobalt catalyzed hydrovinylation reaction was further transformed into vinyl triflates which considerably expand the scope and utility of this chemistry.\textsuperscript{75,76} Not unexpectedly, these vinyl triflates undergo prototypical cross-coupling reactions catalyzed by Pd(0) catalyst with complete retention of configuration at the double bond and preservation of the vinyl-bearing stereogenic center (Figure 1.8). Examples of these reactions will be thoroughly discussed in chapter 4.
1.13. Conclusions and Future Prospects

Through an approach that relies mostly on mechanistic insights and systematic examination of metal complexes, we have discovered a number of new reactions for the addition of ethylene, across a series of very important class of commonly available prochiral precursors, e.g. 1,3-dienes, 1-vinylcycloalkenes and vinylarenes using cobalt (Figure 1.9). Additionally, compared to our Ni-protocol on hydrovinylation reaction, bis-phosphine cobalt complexes provide complete control on the regioselectivity towards selective 1,4-addition in the hydrovinylation reaction of 1,3-dienes and 1-vinylcycloalkenes. These results did set up the foundation for our future studies on a broader class of substrates, silyl enol ethers. Hydrovinylation on silyl enol ethers will considerably expand the scope and versatility of hydrovinylation methodology. A broad overview of our previous work on cobalt catalyzed hydrovinylation reaction prior to this dissertation work has been depicted in Figure 1.9. Further expansion of cobalt catalyzed hydrovinylation chemistry on functionalized dienes (silyl enol ethers and enol acetates) and applications of the various intermediates prepared during the hydrovinylation reaction will be discussed in the following chapters of this dissertation.
Figure 1.9. Progress and Development of Co(II)-Catalyzed Hydrovinylation

Initial Challenge 2009-10
- Co(II)-catalyzed hydrovinylation
- Initial protocol
- Development of new substrates, 1-vinyl cycloalkenes
- Complementary selectivity compared to Ni-HV 2010

Initial Protocol 2010-2015
- Ethylene (1 atm)
- CL2Co(S,S)-DIOP (0.05 equiv.)
- Me3Al (Al:Co = 3-20)

Development of New Substrates, 1-Vinyl cycloalkenes, Complementary Selectivity compared to Ni-HV 2010
- 1-Vinylcycloalkenes show 1,4-HV with Co(II) catalyst, JACS, 2012, 134, 6556.

Low Enantioselectivity for Vinylarenes 2012-present
- 4-Substituted-1-vinylcycloalkenes also show enantiodivergent parallel kinetic resolutions on Co(II)-catalyzed asymmetric hydrovinylation

Broader Application, Co-HV on Silycycloenes and its application 2012-present
- Future Goals: Broader Application in the Synthesis of Medicinally Active Drug Candidates Mechanistic Investigations

Future Results on Co(II)-asymmetric HV, JACS, 2010, 132, 3295.
With Broader Substrate Scope and Ligand study Chem. Sci. 2015, 6, 3994.
1.14. References


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(36) Hilt, G.; Roesner, S. Synthesis 2011, 662-668.
CHAPTER 2

Triarylphosphines Ligands with Hemilabile Alkoxy Groups: Ligands for Nickel(II)-Catalyzed Olefin Dimerization Reactions. Hydrovinylation of Vinylarenes, 1,3-Dienes, and Cycloisomerization of 1,6-Dienes


2.1. Introduction

Our attempts to find new protocols for the Ni(II)-catalyzed asymmetric hydrovinylation (HV)\(^1\) of activated alkenes such as vinylarenes,\(^2\) 1,3-dienes,\(^3\) and bicyclo[2.2.1]-heptenes\(^4\) have resulted in the identification of several different types of ligands that are capable of effecting this remarkable transformation with very high efficiency and selectivity (Scheme 2.1). These include 2’-alkoxy-1-diarylphosphino-1,1’-binaphthyl derivatives (L1),\(^2a\) \(^5\) 1-aryl-2,5-dialkylphospholanes (L2),\(^2b\), \(^2c\) phosphoramidites derived from 1,1’-biaryl-2,2’-dihydroxy compounds (L3),\(^2d\), \(^2e\), \(^6\) and, diarylphosphinites (L4).\(^7\)
During these investigations we concentrated most of our efforts on the development of asymmetric variants of these reactions, and, thus on enantio-pure ligands. For the synthesis of racemic mixtures of the products, we often resorted to the original protocol that was developed for the HV of vinylarenes, which involved the use of a combination of [(allyl)NiBr]_2, Ph_3P and AgOTf (equation 2.1),^2a or, in some cases, the use of the more expensive 1:1 mixture of the enantiopure ligands with a Ni(II) precursor. While these have been reliable procedures and served our purpose well, occasionally we faced difficulties with the former protocol (equation 2.1) due to the sensitivity of the reaction to temperature, especially in the case of reactions of vinylarenes. Unless the temperature is rigorously maintained (– 50 °C to – 56 °C) in this moderately exothermic reaction, in

**Scheme 2.1. Selected Examples of Asymmetric Hydrovinylation of Alkenes**

**Figure 2.1. Assorted Ligands for Asymmetric Hydrovinylation of Alkenes**
addition to the expected product 2, varying amounts of an isomerization product, 3 and a dimer, 4 are formed as impurities. We wondered whether we could design a simple, yet more robust phosphine ligand based on our recognition of the role of an appropriately placed hemilabile ligating atom in this reaction. Accordingly, we prepared a series of 2-alkoxyaryl and 2-(alkoxyalkyl)aryl-diphenylphosphines (equation 2.2, L5, L6, L7) in which the hemilabile oxygen atom is placed on β-, γ or δ- carbon in relation to the chelating phosphine. This subtle variation in the ligand has a dramatic effect on the efficiency and selectivity of several HV reactions. Such ligand effects extend to a mechanistically related cycloisomerization of 1,6-dienes. Here we document the results of these studies.

2.2. Ligand Effects on Hydrovinylation of Vinylarenes

Our initial investigations of styrene and 4-methylstyrene as a prototypical substrates using the previously disclosed catalyst system [(allyl)NiBr]_2/Ph_3P/AgOTf showed the extreme sensitivity of the reaction to temperature changes (equation 2.1). While at –78 °C (6 h) there is very low conversion of styrene, at room temperature, extensive isomerization of the initially formed product 2 to a mixture of 2-arylbutenes (3) and a styrene dimer (4) are observed. Varying amounts of these side products are observed at intermediate temperatures, and the reaction was eventually optimized for a series of vinylarenes where these products were found to be virtually absent around –55 °C. We turned our attention to the ligands L5, L6 and L7, each carrying a hemilabile oxygen with the hope of finding a HV protocol under ambient conditions, without the complications of isomerization of the double bond or the dimerization reaction. These
aryldiphenylphosphino-ligands were readily synthesized from the corresponding bromoaryl derivatives by Li exchange followed by treatment with Ph₂PCL at low temperature (equation 2.2).

\[ \text{(2.2)} \]

Ligands L₅, L₆ and L₇ were examined in the hydrovinylation of a number of vinylarenes including 4-methylstyrene, using a procedure shown in equation 2.3. The illustrative results are shown in Table 2.1. As seen from the entries 1-3, the activities of the putative [(allyl)NiL][BARF] complexes as catalysts for the hydrovinylation reaction are dramatically different depending on L. The o-benzyloxyphenyldiphenylphosphine (L₅) is the most active ligand, even more active than the [(allyl)Ni(Ph₃P)][OTf], used in the original protocol (equation 2.1). This catalyst with L₅ not only effects the hydrovinylation of 4-methylstyrene at -55 °C, but it also promotes further isomerization.
of the primary product 7b at this low temperature (entry 1a) giving up to 33% of a conjugated product 8b as a mixture of trans- and cis-isomers in a ratio of 2.0:1.2. At room temperature (entry 1b) an exceptionally clean reaction ensues giving a mixture of the isomerized products cis-8 and trans-8 with none of the primary product 7b. We also noticed a very significant salt effect in these reactions. While AgOTf, with a coordinating counter ion, is ineffective in conjunction with a hemilabile ligand (entry 1c), AgSbF$_6$ with a more dissociating anion is a suitable replacement for NaBARF (entry 1d).

In sharp contrast to L5, the (o-benzylxoy methyl)phenyldiphenylphosphine (L6) promotes only a sluggish reaction at – 55 °C, requiring a prolonged period (~ 11 h) at rt for complete conversion of the starting material (entry 2). Most gratifyingly, unlike many other ligand systems we have examined, there is no sign of isomerization of the primary product, 7, to 8 even at room temperature. Dimerization of the vinylarenes was also observed.

Ligand L7, with an ethano-bridge between the oxygen and the aryl moiety, behaves like L6, except that the corresponding Ni(II) complex is much less reactive (entries 3a and 3b). However the selectivity for the primary product 7 is equally impressive (98%, entry 3b).
Table 2.1. Effect of Ligands on Ni(II)-Catalyzed Hydrovinylation of 4-Methylstyrene$^a$

<table>
<thead>
<tr>
<th>Entry</th>
<th>Ligand</th>
<th>Temp. °C</th>
<th>Time (h)</th>
<th>Conv.</th>
<th>Product, yield(%)</th>
<th>Selectivity (% of 7)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1a</td>
<td></td>
<td>-55</td>
<td>2</td>
<td>&gt;99</td>
<td>67</td>
<td>33</td>
</tr>
<tr>
<td>1b</td>
<td></td>
<td>rt</td>
<td>20</td>
<td>&gt;99</td>
<td>0</td>
<td>&gt;99</td>
</tr>
<tr>
<td>1c</td>
<td></td>
<td>-55</td>
<td>2</td>
<td>&lt;4$^{bc}$</td>
<td>&lt;4</td>
<td>-</td>
</tr>
<tr>
<td>1d</td>
<td></td>
<td>-55</td>
<td>2</td>
<td>&gt;99$^d$</td>
<td>70</td>
<td>29</td>
</tr>
<tr>
<td>2</td>
<td>L6</td>
<td>23 °C</td>
<td>11</td>
<td>&gt;99</td>
<td>&gt;99</td>
<td>0</td>
</tr>
<tr>
<td>3</td>
<td>L7</td>
<td>-55 °C</td>
<td>16 h</td>
<td>0</td>
<td>0</td>
<td>--</td>
</tr>
<tr>
<td></td>
<td></td>
<td>23 °C</td>
<td>2.5</td>
<td>48</td>
<td>48</td>
<td>0</td>
</tr>
</tbody>
</table>

$^a$ see equation 2.3 for procedure, results from Aibin Zhang (The Ohio State University, 2014) $^b$ using AgOTf. $^c$ rest starting material. $^d$ using AgSbF$_6$

The modified procedure (equation 2.3) for hydrovinylation using ligand L6 was applied to several vinylarenes and the results are shown in Table 2.2. As expected, most vinylarenes react with ethylene (1 atm) at room temperature to give nearly quantitative yields of the HV products (3-aryl-1-butenes, 7). Electronically deactivated vinylarenes (entries 3, 4, 8, Table 2.2) and those with Lewis basic substituents (entries 5, 9 and 11) react slower compared to electron-rich ones. Activated substrates such as 2- and 3-vinylfurans undergo very fast reactions (< 2 h at rt) to give >99% yield of the expected products (entries 6 and 7). Substrates that need prolonged reaction times (e. g., 4-bromostyrene, 4-methoxystyrene and 2-vinylnaphthalene do undergo competitive isomerization of the primary product to give varying amounts of the 2-arylbutenes (8). Most notably, even in these cases the yields of the primary products are quite acceptable.
Table 2.2. Use of 2-Benzylxoxymethylphenylidiphenylphosphine (L6) for rt HV of Vinylarenes

<table>
<thead>
<tr>
<th>Entry</th>
<th>Vinylarenes (6)</th>
<th>Cat. (equiv.)</th>
<th>Time (h)</th>
<th>Yield (%)</th>
<th>Regiosel. (% of 7)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>styrene (6a)</td>
<td>0.007</td>
<td>15</td>
<td>&gt;99</td>
<td>&gt;99</td>
</tr>
<tr>
<td>2</td>
<td>4-Me-styrene (6b)</td>
<td>0.007</td>
<td>11</td>
<td>&gt;99</td>
<td>&gt;98</td>
</tr>
<tr>
<td>3</td>
<td>3-F-4-Ph-styrene (6c)</td>
<td>0.014</td>
<td>20</td>
<td>89(a)</td>
<td>&gt;99</td>
</tr>
<tr>
<td>4</td>
<td>3-PhC(O)-styrene (6d)</td>
<td>0.014</td>
<td>20</td>
<td>83(c)</td>
<td>&gt;99</td>
</tr>
<tr>
<td>5</td>
<td>2-vinyl-6-OMe-naphthalene (6e)</td>
<td>0.014</td>
<td>64</td>
<td>&gt;99</td>
<td>&gt;99</td>
</tr>
<tr>
<td>6</td>
<td>2-vinylfuran (6f)</td>
<td>0.007</td>
<td>2</td>
<td>&gt;99</td>
<td>&gt;99</td>
</tr>
<tr>
<td>7</td>
<td>3-vinylfuran (6g)</td>
<td>0.007</td>
<td>2</td>
<td>&gt;99</td>
<td>&gt;99</td>
</tr>
<tr>
<td>8</td>
<td>4-Br-styrene (6h)</td>
<td>0.014</td>
<td>48</td>
<td>89(c)</td>
<td>&gt;99</td>
</tr>
<tr>
<td>9</td>
<td>4-OMe-styrene (6i)</td>
<td>0.007</td>
<td>72</td>
<td>&gt;99</td>
<td>87(d)</td>
</tr>
<tr>
<td>10</td>
<td>2-vinylfluorene (6j)</td>
<td>0.014</td>
<td>19</td>
<td>&gt;99</td>
<td>74(d)</td>
</tr>
<tr>
<td>11</td>
<td>2,3-(OMe)-4-Me-styrene (6k)</td>
<td>0.014</td>
<td>44</td>
<td>80(d)</td>
<td>&gt;99</td>
</tr>
</tbody>
</table>

\(a\) see equation 2.3 for procedure, results from Aibin Zhang (The Ohio State University, 2014) \(b\) by NMR, GC. \(c\) rest starting material. \(d\) rest isomerized product.

Finally, the enhanced reactivity of the ligand L5 has one significant application where the isomerization is not a competitive process. This is in the room temperature-HV of 1-alkylstyrenes, which generate an all-carbon quaternary center.\(^{10}\) The dramatic difference in the reactivities of the three ligands is shown in equation 2.4. The less reactive complexes of ligands L6 and L7 gave very low conversions. Under otherwise identical
conditions, the electron-deficient vinylarenes 10c gave a lower yield. The ligand L5 facilitates the conversion of 1-methylene tetraline (11) to the corresponding adduct 12 (equation 2.5). A minor side product in the reaction has been identified as the isomerized product 13.

2.3. Ligand Effects on Hydrovinylation of 1,3-Dienes

Nickel(II)-catalyzed HV of 1,3-cyclooctadiene is one of the first metal-catalyzed asymmetric reactions ever reported\(^\text{11}\) even though the useful levels of selectivities were achieved only recently.\(^\text{1a}\) Alternate procedures using Ru(II)\(^\text{12}\) and Co(II) complexes\(^\text{13}\) as catalysts have recently appeared. In connection with our own work in the Ni(II)-catalyzed asymmetric HV of selected 1,3-dienes using phospholane and phosphoramidite complexes of Ni(II), we have briefly reported on the use of ligand L5 for the synthesis of authentic racemic products.\(^\text{3a}\) A comparison of the efficacy of this ligand with that of L6 and L7 in the Ni(II)-catalyzed HV of a prototypical 1,3-diene, 4-‘Bu-1-vinylecyclohexene (14), is shown in equation 2.6. As compared to the vinylarenes, 1,3-dienes are much less reactive, yet the regioselectivity in the formation of the 1,2-HV product (15) from racemic 14 is excellent. The most useful ligand for this transformation
is \textbf{L5}, which gives a quantitative yield of the product(s) as a 2:1 mixture of diastereomers.\textsuperscript{9} In sharp contrast, the catalysts from ligands \textbf{L6} and \textbf{L7}, even after prolonged periods at room temperature, left significant amounts of unreacted starting material. These ligand effects are further confirmed by the hydrovinylation of two other prototypical 1,3-dienes, 1,3-cyclohexadiene (16) and the benzopyran derivative (18) (equation 2.7 and 2.8).\textsuperscript{9} Other results (Table 2.3, entries 1-6) are included here for the sake of completion.\textsuperscript{3a,b} Entries in column 5 of Table 2.3 confirm the utility of \textbf{L5} as an excellent ligand for the 1,2-hydrovinylation of a broad class of 1,3-dienes. Only 1-vinylcyclohexene 20 and estrone-derived diene 30 gave a mixture of 1,2- and 1,4-hydrovinylation products.

\textbf{2.4. Ligand Effects on Cycloisomerization of 1,6-Dienes}

Soon after the discovery of the original HV protocol (equation 2.1) we reported\textsuperscript{14} that these conditions can be modified to effect cycloisomerization of 1,6-dienes to methylenecyclopentanes, examples of which are shown in equation 2.9 and equation 2.10.\textsuperscript{15} Both [(allyl)NiBr]\textsubscript{2} and a related palladium source, [(allyl)PdCl]\textsubscript{2}, were used as precursors in otherwise identical conditions. The Pd(II)-catalyzed reaction appear to be more compatible with broader set of substrates, even though isomerization of the primary
Table 2.3. Ligand Effects in Hydrovinylation of 1,3-Dienes<sup>a</sup>

<table>
<thead>
<tr>
<th>Entry</th>
<th>Substrate</th>
<th>Major product</th>
<th>[(allyl)Ni&lt;sub&gt;L5&lt;/sub&gt;]&lt;sup&gt;+&lt;/sup&gt; cat (mol%)/ (°C)/ t (h)</th>
<th>Yield/ regiosel.</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>20</td>
<td>21</td>
<td>1.4/-40/23</td>
<td>&gt;99/68&lt;sup&gt;b&lt;/sup&gt;</td>
</tr>
<tr>
<td>2</td>
<td>22a,b</td>
<td>23a,b</td>
<td>1.4/-43/21</td>
<td>&gt;99/98</td>
</tr>
<tr>
<td>3</td>
<td>24</td>
<td>25</td>
<td>1.4/-23/21</td>
<td>&gt;99/94</td>
</tr>
<tr>
<td>4</td>
<td>26</td>
<td>27</td>
<td>2.8/25/43</td>
<td>&gt;99/96</td>
</tr>
<tr>
<td>5</td>
<td>28</td>
<td>29</td>
<td>2.5/0/4</td>
<td>&gt;99/99&lt;sup&gt;c&lt;/sup&gt;</td>
</tr>
<tr>
<td>6</td>
<td>30</td>
<td>31</td>
<td>2.0/rt/14 h</td>
<td>63&lt;sup&gt;d&lt;/sup&gt;/66&lt;sup&gt;e&lt;/sup&gt;</td>
</tr>
</tbody>
</table>

<sup>a</sup> See equation 2.6 for procedure, major product: 1,2-HV. Data from ref 3a (entries 1-4), ref 14 (entry 5) and ref 3b (entry 6). rest of the results from Aibin Zhang (The Ohio State University, 2014)  
<sup>b</sup> rest 1,4-addition product (1,2:1,4 = 2.9:1.0). 
<sup>c</sup> diastereoselectivity C<sub>3</sub> (S<R = 59:41). 
<sup>d</sup> diastereoselectivity C<sub>20</sub>(S): C<sub>20</sub>(R) = 1.0:2.5. 
<sup>e</sup> rest 1,4-HV with C<sub>16</sub>-vinyl.

product (e.g., 33a to 35a, equation 2.9) can be a serious problem in these reactions. Occasionally regioselectivity (e.g., formation of a methylenecyclohexane, 34e, in equation 2.10b) can also be different from the Ni(II)-catalyzed reactions. Since formally this cyclization reaction can be described as an intramolecular version of the hydrovinylation (strictly a hydroalkenylation) reaction, we decided to examine a
modified procedure using the hemilabile ligands L5-L7 for this reaction. The results are shown in equation 2.11.

![Equation 2.11](image)

The ligands L5, L6 and L7 were tested in the Ni(II)-catalyzed cyclization reactions using essentially the same procedure used for the intermolecular reactions (equation 2.11). Most strikingly, the ligands L6 and L7 were found to be totally ineffective in the cyclization, whereas L5 gave excellent yields for the cyclization of the prototypical substrates 32a-e. In a glovebox a solution of ligand L5 and [(allyl)NiBr]2 was transferred...
into the vial containing NaBARF. The resulting solution allowed to stand for 1.5 h. The catalyst solution prepared above was transferred to the reaction vessel via cannula, followed by 1.0 mL rinsing of the source vial. The system was cooled to 0 °C in an ice bath and diallyl malonate (32a, 34 mg, 0.16 mmol) was added to the reaction mixture via a micro litre syringe. The reaction mixture was allowed to stir at rt for 5 h. The reaction was exposed to air and diluted with pentane to quench the reaction. The crude cyclized product that was then eluted through a plug of silica with pentane to remove any nickel salts was concentrated. The products were analyzed by gas chromatography, and, subsequently purified by column chromatography to determine the yield of the reaction. The prototypical substrates (32a-e) shown under equation 2.11, gave the methylenecyclopentane (33a-e), along with traces of a methylenecyclohexane (34a-e), resulting from a different regioselectivity (35 vs 36 in Scheme 2.2) the insertion of the putative [LNi-H]⁺ that is assumed to initiate the cyclization reaction (Scheme 2.2). Under these conditions only small amounts (<5%) of isomerized products were detected by GC. The reaction works equally well for the formation of nitrogen-containing heterocyclic compounds from the corresponding 1,6-dienes. Judicious choice of the

**Scheme 2.2. Possible Control of Regioselectivity in the Cationic Metal Hydride Mediated Cyclization of 1,6-Dienes**
protecting group on nitrogen is crucial for the success of the reaction. While an arylsufonyl protecting group (e.g., 32d, 32e) is perfectly compatible with the reaction, leading to excellent yields of the cyclization product, Lewis basic centers present in the benzylamine 32f or the benzamide 32g totally inhibits the cyclization reaction.

*Preparation of Authentic Methylene cyclohexane Products (34) and the Effect of N-Heterocyclic Carbenes (NHC) Ligands.* Various anecdotal observations on the effect of phosphine ligands of differing steric demands in the Ni(II) and Pd(II)-catalyzed cyclization reactions of 1,6-dienes suggest that it might be possible to control the regioselectivity of the initial metal-hydride addition (Scheme 2.2), and, hence the product distribution [in equation 2.11: methylenecyclopentane (33) vs methylenecyclohexane (34)] by ligand tuning. Such a possibility was further bolstered by the uncommon regioselectivity observed by Ho in the tail-to-tail heterodimerization of styrene with a 1-alkenes.\(^{17}\) In this reaction, whose mechanism is similar to that of the diene cyclization, the larger size of an NHC carbene ligand has been invoked to rationalize the selectivity. Thus we decided to examine a series of the NHC carbenes with varying steric demands\(^ {18}\) as ligands for the cyclization under our new protocol (equation 2.12) and results are shown in Table 2.4.

\[
\begin{align*}
\text{Ni(COD)}_2/\text{COD/CH}_2\text{Cl}_2 \quad (\text{allyl})\text{bromide, add NHC} \\
\text{NaBARF followed by } 32 \\
(0.2 \text{ equiv. cat, rt, 5 h}) \\
\begin{cases}
Z_{32} + Z_{34} & \text{[33]} \\
Z_{35} & \text{(no trace)}
\end{cases}
\end{align*}
\]

\[(2.12)\]

\[
\begin{array}{|c|c|c|c|c|}
\hline
\text{Ligands: } & \text{L8} & \text{L9} & \text{L10} & \text{L11} \\
\hline
\text{R} \quad \text{mesityl} & \text{i-propyl} & \text{adamantyl} & \text{t-butyl} \\
\hline
\%V_{26}^a & 26 & 29 & 37 & 37 \\
\hline
\end{array}
\]

\(^a\) proportional to size of the ligand, see: ref. 18
Table 2.4. Cyclization of 1,6-Dienes using (allyl)Ni(NHC)BARF

<table>
<thead>
<tr>
<th>Entry</th>
<th>Substrate</th>
<th>Ligand L8 (IMes)</th>
<th>Ligand L9 (IPr)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>33 (%)</td>
<td>34 (%)</td>
</tr>
<tr>
<td>1</td>
<td>32a</td>
<td>3</td>
<td>92&lt;sup&gt;b&lt;/sup&gt;</td>
</tr>
<tr>
<td>2</td>
<td>32b</td>
<td>6</td>
<td>82</td>
</tr>
<tr>
<td>3</td>
<td>32c</td>
<td>71&lt;sup&gt;b&lt;/sup&gt;</td>
<td>29</td>
</tr>
<tr>
<td>4</td>
<td>32d</td>
<td>65</td>
<td>29&lt;sup&gt;f&lt;/sup&gt;</td>
</tr>
<tr>
<td>5</td>
<td>32e</td>
<td>65</td>
<td>35</td>
</tr>
<tr>
<td>6</td>
<td>32f, 32g</td>
<td>0</td>
<td>0</td>
</tr>
</tbody>
</table>

<sup>a</sup> see equation 2.12 for procedure. <sup>b</sup> de = 48:22.

The carbene complexes were prepared in situ starting from Ni(COD)<sub>2</sub>, allyl bromide and the NHC ligand<sup>19,20</sup> followed by addition of NaBARF (equation 2.12). As documented in entries 1-5, Table 2.4, smaller NHC ligands L8 and L9 are competent ligands to effect the cyclization, whereas larger ligands L10 and L11 gave no products. Substrates 32a and 32b, where Thorpe-Ingold effect is operative, gave excellent yields of the methylenecyclohexane derivative 34, with the cyclopentane derivative 33 as a side-product (entries 1 and 2, columns 4 and 6). The larger of the two ligands, L9 gave almost exclusively the cyclohexane derivative 34 (entries 1 and 2, column 6). Other substrates 32c-32e gave varying proportions of the two cyclic products, in each case giving more of the six-membered product with the larger NHC ligand L9.

2.5. Mechanistic Proposal

The absence of isomerization of the primary products in reactions catalyzed by \{(allyl)Ni(L6) [BARF]\} (equation 2.3) as compared to (allyl)Ni(Ph<sub>3</sub>P)(OTf) (equation 2.1) is striking, and, maybe rationalized by a mechanism (Scheme 2.3) which derives considerable support from our computational study of this reaction.<sup>21</sup> In this mechanism, the pre-catalyst 37 reacts with ethylene to give the insertion product 38, which undergoes
a β-hydride transfer to the vinylarene via 40 to give 41 (vis-à-vis a β-hydride elimination to give a discrete [LNi-H]+ intermediate 39), presumed to be the catalyst resting state. We found that the intermediate 39, most likely responsible for the isomerization reactions, is very high in energy on the reaction coordinate diagram. Once 41 is generated, it undergoes further coupling with ethylene to give 43, which transfers a β-hydride to a vinylarene to give the product 45, in that process regenerating the catalyst 41. As before a β-hydride elimination to 39 has prohibitively high energy of activation. The stability and reactivity of the putative intermediates 37 and 41 for different ligands L5-L7 may explain the considerable differences between these ligands.

Scheme 2.3. A Mechanistic Proposal to Explain the Absence of Isomerization with Hemilabile Ligand-Nickel Complexes

2.6. Conclusions

Substitution of one of the phenyl groups of Ph₃P with a 2-benzylxoy-, benzyloxymethyl- or benzylxyethyl-phenyl moiety results in a set of simple ligands L5,
L6 and L7, which exhibit strikingly different behavior in various Ni(II)-catalyzed olefin dimerization reactions. Complexes of ligands L5 and L6 are most active for hydrovinylation (HV) of vinylarenes, with the former leading to extensive isomerization of the primary 3-aryl-1-butenes into 2-aryl-2-butenes even at low temperature. *Ligand L6 is the most optimal, leading to up to quantitative yields of HV products at ambient temperature with no trace of isomerization.* In sharp contrast, hydrovinylation of a variety of 1,3-dienes is best catalyzed by Ni(II)-complexes of L5. Ligands L6 and L7 are much less effective in the HV of dienes. Ni(II)-Catalyzed cycloisomerization of 1,6-dienes into methylenecyclopentanes, a reaction mechanistically related to the other hydrovinylation reactions, is also uniquely effect by Ni(II)-complexes of L5. In an attempt to prepare authentic samples of the methylenecyclohexane products, Ni(II)-complexes of NHC-ligands were examined. In sharp contrast to the phosphines, which give the methylenecyclopentanes, these larger size rings are the major products in the NHC-mediated reactions.

### 2.7. Experimental Procedures

**General Methods** Reactions requiring air-sensitive manipulations were conducted under an inert atmosphere of nitrogen by using Schlenk techniques or a Vacuum Atmospheres glovebox. Dichloromethane was distilled from calcium hydride under nitrogen and stored over molecular sieves. Tetrahydrofuran was distilled under nitrogen from sodium/benzophenone ketyl. Catalyst precursors [(allyl)NiBr]₂ and NaBARF were prepared according to the literature.²c,f The [(allyl)NiBr]₂ was stored in a freezer in the drybox. Ethylene (99.5%) was purchased from Matheson Inc., and passed through a
column of Drierite® before use. Analytical TLC was performed on Silicycle precoated (0.25 mm) silica gel 60 F254 plates. Flash column chromatography was carried out on silica gel 40 (Scientific Adsorbents Incorporated, Microns Flash). Conversion of the products was determined by gas chromatographic analysis, which was performed on an Agilent HP-5 column (30 m length X 0.325 mm diameter) using helium or hydrogen as a carrier gas (25 psi). Absence of polymeric impurities was ascertained by NMR and, except for the volatile materials, the isolated yield of the products were not significantly different from the conversions.

Ligands L5, L6 and L7 were prepared according to literature procedures.3a Precursors for the NHC ligands, L8, L9, L10 and L11 were purchased as the corresponding imidazolium salts from Strem Chemicals.

All other precursors are described in the publications that deal with the synthesis of the HV products (see below). Spectroscopic and gas chromatographic data for the HV products (including separations on chiral stationary phase gas or liquid chromatography of chiral materials) are described the publications cited below.

**Preparation of Ligand L5.**3a A mixture of 2-bromophenol (1.73g, 10 mmol), benzyl bromide (1.20 mL, 1.71g, 10 mmol) and K$_2$CO$_3$ (2.2g, 16 mmol) in acetone (20 mL) was refluxed for 18 h under nitrogen. After removal of acetone, water was added and the mixture was extracted with ether. The organic layers were washed with water, dried and concentrated under vacuum. The resulting residue was purified by flash column chromatography on silica gel (eluting with hexanes/ethyl acetate = 100/1) to afford 2.08 g (79%) of 2-bromophenyl benzyl ether.
To the solution of 2-bromophenyl benzyl ether (789 mg, 3 mmol) in THF (5 mL) was added \( n\)-BuLi (1.9 mL, 1.6 M in hexanes, 3 mmol) at -78 °C under nitrogen. After the resulting solution was stirred at this temperature for 30 min, a solution of chlorodiphenylphosphine (696 mg, 3 mmol) in THF (5 mL) was added at -78 °C. Then the mixture was allowed to warm to room temperature and stirred for 1 h. Water was added to quench the reaction and the mixture was extracted with ether. The organic layers were combined, washed with brine, dried over MgSO\(_4\) and concentrated. The resulting residue was purified by column chromatography on silica gel (eluting with hexanes/ethyl acetate=100/1) to get 490 mg (45%) of L5. \(^1\)H NMR (500 MHz, CDCl\(_3\)): \( \delta \) 7.55-7.30 (m, 11 H), 7.30-7.20 (m, 3 H), 7.15-7.05 (m, 2 H), 7.00-6.90 (m, 2 H), 6.90-6.80 (m, 1 H), 5.10 (s, 2 H); \(^{13}\)C NMR (125.7 MHz, CDCl\(_3\)): \( \delta \) 159.97, 138.83, 136.68, 134.21, 133.59, 130.21, 128.75, 128.48, 128.31, 127.55, 126.93, 126.54, 121.28, 111.47, 70.03; \(^{31}\)P NMR (202.4 MHz, CDCl\(_3\)): \( \delta \) -15.53; HRMS (ESI): m/z 407.1193 ([M+Na+O]\(^+\), exact mass calcd for C\(_{25}\)H\(_{21}\)O\(_2\)PNa 407.1171).

**Preparation of Ligand L6.**\(^{3a}\) A solution of 2-bromobenzaldehyde (2.34 mL, 3.7g, 20 mmol) in THF (20 mL) was slowly added to a stirred slurry of NaBH\(_4\) (760 mg, 20 mmol) in THF (40 mL) at room temperature. After 20 h, the mixture was cooled in an ice-salt bath, and 1:1 concentrated HCl-water was added dropwise carefully until the resulting solution was acidic. The aqueous solution was saturated with NaCl and extracted with ether. The combined extracts were washed once with water, dried and concentrated. The crude product was used for the next step without further purification.

To the solution of the crude alcohol from the previous step in THF (20 mL) was added
KH (964 mg, 24 mmol) at 0 °C under nitrogen and the resulting mixture was stirred for 30 min at this temperature. Benzyl bromide (2.6 mL, 22 mmol) was added all at once via syringe. The mixture was stirred at 0 °C for 30 min and then allowed to warm to room temperature and stirred for 1 h. After the mixture was cooled to 0 °C, water was added to quench the reaction and the mixture was extracted with ether. The organic layers were washed with brine, dried and concentrated to give a yellow oil which was purified by column chromatography (eluting with hexanes/ethyl acetate=20/1) to afford 3.8 g (69% in two steps) of 1-bromo-2-benzyloxymethylbenzene.

To the solution of 1-bromo-2-benzyloxymethylbenzene (554 mg, 2 mmol) in THF (5 mL) was added n-BuLi (1.25 mL, 1.6 M in hexanes, 2 mmol) at -78 °C under nitrogen. After the resulting solution was stirred at this temperature for 30 min, a solution of chlorodiphenylphosphine (696 mg, 3 mmol) in THF (5 mL) was added at -78 °C. Then the mixture was allowed to warm to room temperature and stirred for 1 h. Water was added to quench the reaction and the mixture was extracted with ether. The organic layers were combined, washed with brine, dried over MgSO₄ and concentrated. The resulting yellow liquid was crystallized from methanol in the freezer to give 574 mg (75%) of L6. ¹H NMR (500 MHz, CDCl₃): δ 7.80-7.70 (m, 1 H), 7.50-7.25 (m, 17 H), 7.10-7.00 (m, 1 H), 4.94 (s, 2 H), 4.59 (s, 2 H); ¹³CNMR (125.7 MHz, CDCl₃): δ 142.80, 138.31, 136.71, 135.62, 133.95, 133.61, 129.06, 128.82, 128.72, 128.41, 128.22, 127.84, 127.79, 127.49, 72.47, 70.65; ³¹P NMR (202.4 MHz, CDCl₃): δ -15.63; HRMS (ESI): m/z 421.1310, ([M+Na+O]⁺, exact mass calcd for C₂₆H₂₃O₂PNa 421.1328).

Preparation of Ligand L7.²a To a solution of 2-bromophenethylalcohol (905 mg, 4.5
mmol) in THF (5 mL) was added KH (200 mg, 5 mol) in one portion at 0 °C under argon. The resulting suspension was stirred at 0 °C for 30 min and then benzyl bromide (0.54 mL, 4.5 mmol) was added dropwise at 0 °C. The mixture was allowed to warm to room temperature and stirred for 1 h. Water was added to quench the reaction and the mixture was extracted with ether and the organic layers were combined, washed with brine, dried and concentrated. The resulting residue was purified by column chromatography on silica gel (eluting with hexanes/ethyl acetate=20/1) to get 1.24 (95%) of 2-bromophenethyl benzyl ether.

To a solution of 2-bromophenethyl benzyl ether (1.24 g, 4.26 mmol) in THF (15 mL) was added n-BuLi (2.7 mL, 1.6 M in hexanes, 4.26 mmol) at -78 °C under argon. After the resulting solution was stirred at this temperature for 30 min, a solution of chlorodiphenylphosphine (988 mg, 4.26 mmol) in THF (5 mL) was added at -78 °C. Then the mixture was allowed to warm to room temperature and stirred for 1 h. Water was added to quench the reaction and the mixture was extracted with ether. The organic layers were combined, washed with brine, dried over MgSO₄ and concentrated. The resulting residue was purified by column chromatography on silica gel (eluting with hexanes/ethyl acetate=100/1) to get 1.09 (65%) of ligand L7. ¹H NMR (500 MHz, CDCl₃): δ 7.40-7.20 (m, 17 H), 7.13 (td, J = 8.09, 1.74 Hz, 1 H), 6.88 (dd, J = 7.50, 4.20 Hz, 1 H), 4.41 (s, 2 H), 3.61 (t, J = 7.29 Hz, 2 H), 3.22 (t, J = 7.29 Hz, 2 H); ¹³C NMR (125.7 MHz, CDCl₃): δ 143.50, 138.62, 136.96, 136.09, 134.07, 133.88, 130.14, 129.04, 128.75, 128.61, 128.38, 127.66, 127.50, 126.73, 72.82, 70.79, 34.80; ³¹P NMR (202.4 MHz, CDCl₃): δ -15.20; HRMS (ESI): m/z 435.1466 ([M+Na+O]⁺, exact mass calcd for C₂₇H₂₅O₂PNa 435.1484).
Cycloisomerization of 1,6-Dienes

The following starting materials are prepared using literature methods: 32a,22 32b,22 32c,23 32d,24 32e,24 32f,25 32g,26 Carbene precursor salts IMes.HCl, IPr.HCl, IAda.HCl, tBu.HCl are commercially available from Strem Chemicals.

Typical Procedure for 1,6-diene Cyclization Using [(allyl)NiBr] and L5 Catalyst (equation 2.11). In a glovebox, NaBARF (14.7 mg, 0.0167 mmol, 10 mol%), ligand L5 (6.15 mg, 0.0167 mmol, 10 mol%), and [(allyl)NiBr]2 (3.0 mg, 0.008 mmol, 5.0 mol%) were weighed into separate glass vials. The hemilabile ligand was dissolved in anhydrous DCM (1.0 mL) and transferred to the vial containing [(allyl)NiBr]2, followed by 1.0 mL rinsing of the source vial. The resulting yellow solution of ligand L5 and [(allyl)NiBr]2 was transferred to the vial containing NaBARF, followed by 1.0 mL rinsing of the source vial. The resulting orange-yellow solution was diluted with DCM (1.0 mL) and allowed to stand for 1.5 h.

Cyclization procedure: A 25 mL three-necked flask equipped with a rubber septum, flow-controlled nitrogen inlet, thermometer, and magnetic stirring bar was flame-dried and purged with nitrogen. The catalyst solution prepared above was transferred to the reaction vessel via cannula, followed by 1.0 mL rinsing of the source vial. The system was cooled to 0 °C in an ice bath and diallyl malonate (32a, 34 mg, 0.16 mmol) was added in to the reaction mixture by microliter syringe. The reaction mixture was allowed
to stir at rt for 5 h. The reaction was exposed to air and diluted with pentane to quench the reaction. The crude cyclized product that was then eluted through a plug of silica with pentane to remove any nickel salts was concentrated and further analyzed by NMR and GC.

**Typical Procedure for 1,6-diene Cyclization Starting with Allyl Bromide Ni(COD)$_2$ and ligand L5:** In a glovebox, Ni(COD)$_2$ (123 mg, 0.45 mmol) was dissolved in 1 mL 1,5-cyclooctadiene. Allyl bromide (54.4 mg, 0.45 mmol) was then added dropwise. The resulting slurry was then stirred for 5 minutes, rapidly resulting in the formation of a blood-red allylnickel(II) bromide dimer. 2 mL of toluene was added to dissolve all material. A solution of hemilabile ligand L5 (165 mg, 0.45 mmol) in 2 mL of toluene was then added and the mixture was stirred for 5 min. The solution was filtered over celite and concentrated under reduced pressure. The resulting orange solid was washed with 3 1 mL portions of cold hexanes and dried in vacuo to yield ca. 200 mg of product (95% yield).

**Cyclization procedure:** In a glovebox, NaBARF (8.3 mg, 0.0094 mmol, 10 mol%) and [allyl]Ni(L5)Br (4.5 mg, 0.0094 mmol, 10 mol%) were weighed into separate glass vials. The complex was dissolved in anhydrous DCM (1.0 mL). The resulting yellow solution of the complex was transferred to the vial containing NaBARF, followed by 1.0 mL rinsing of the source vial. The resulting orange-yellow solution was diluted with
DCM (1.0 mL) and allowed to stand for 1.5 h. A 25 mL three-necked flask equipped with a rubber septum, flow-controlled nitrogen inlet, thermometer, and magnetic stirring bar was flame-dried and purged with nitrogen. The catalyst solution prepared above was transferred to the reaction vessel via cannula, followed by 1.0 mL rinsing of the source vial. The system was cooled to 0 °C in an ice bath and diallyl malonate (32a, 10 mg, 0.047 mmol) was added to the reaction mixture by microlter syringe. The reaction mixture was allowed to stir at rt for 5 h. The reaction was exposed to air and diluted with pentane to quench the reaction. The crude cyclized product that was then eluted through a plug of silica with pentane to remove any nickel salts was concentrated and further analyzed by NMR and GC.

**Typical Procedure for the Preparation of Free Carbene from the Corresponding Carbene Salt.** In a glovebox, 1,3-bis(2,6-diisopropylphenyl)imidazolium chloride (425 mg, 1.0 mmol, 1 eq) and KOtBu (168.4 mg, 1.5 mmol, 1.5 eq) were suspended in 5 mL THF and stirred for 12 hours. THF was then removed under reduced pressure to yield a yellow-orange solid. To the solid was added 1 mL of toluene, which dissolved most of the material. The resulting material was treated with 10 mL hexanes to precipitate excess
KOtBu and unreacted starting material and the mixture was filtered through a glass fritted funnel. The precipitate was washed with 2 \( \text{1 mL} \) portions of hexanes. The filtrate was concentrated and dried under vacuum to yield the carbene \textbf{L9} as a solid (310 mg, 80\% yield).

**Typical Procedure for 1,6-Diene Cyclization Using Ni(COD)_2 and Free Carbene:** In a glovebox, Ni(COD)_2 (123 mg, 0.45 mmol) was dissolved in 1 \( \text{mL} \) 1,5-cyclooctadiene. Allyl bromide (54.4 mg, 0.45 mmol) was then added dropwise. The resulting slurry was then stirred for 5 minutes, rapidly resulting in the formation of a blood-red allylnickel(II) bromide dimer. Toluene (2 mL) was added to dissolve all material. A solution of free the free IPr carbene \textbf{L9} (175 mg, 0.45 mmol) in 2 \( \text{mL} \) of toluene was then added and the mixture was stirred for 5 min. The solution was filtered over celite and concentrated in vacuum. The resulting orange solid was washed with 3 \( \text{1 mL} \) portions of cold hexanes and dried under reduced pressure to yield ca. 210 mg of product (82\% yield).

**Cyclization Procedure:** In a glovebox, NaBARF (8.3 mg, 0.0094 mmol, 10 \text{ mol\%}) and [allyl]Ni(\textbf{L9})Br (5.3 mg, 0.0094 mmol, 10 \text{ mol\%}) were weighed into separate glass vials. The complex was dissolved in anhydrous DCM (1.0 mL). The resulting yellow solution of the complex was transferred to the vial containing NaBARF, followed by 1.0 mL rinsing of the source vial. The resulting orange-yellow solution was diluted with DCM (1.0 mL) and allowed to stand for 1.5 h. A 25 mL three-necked flask equipped with a rubber septum, flow-controlled nitrogen inlet, thermometer, and magnetic stirring bar was flame-dried and purged with nitrogen. The catalyst solution prepared above was transferred to the reaction vessel via cannula, followed by 1.0 mL rinsing of the source
vial. The system was cooled to 0 °C in an ice bath and diallyl malonate (32a, 10 mg, 0.047 mmol) was added in to the reaction mixture by microliter syringe. The reaction mixture was allowed to stir at rt for 5 h. The reaction was exposed to air and diluted with pentane to quench the reaction. The crude cyclized product that was then eluted through a plug of silica with pentane to remove any nickel salts was concentrated and further analyzed by NMR and GC.

![Chemical structure](image)

**1H NMR (CDCl₃, 400 MHz):**

15a δ 4.91 (q, J = 2.1 Hz, 1 H), 4.80 (q, J = 2.1 Hz, 1 H), 3.73 (s, 3 H), 3.72 (s, 3 H), 3.04-3.08 (m, 1 H), 2.92-2.97 (m, 1 H), 2.53-2.59 (m, 2 H), 1.72-1.80 (m, 1 H), 1.10 (d, J = 6.3 Hz, 3 H). **13C NMR (CDCl₃, 100 MHz):** δ 172.6, 172.5, 153.4, 105.8, 58.4, 53.0, 53.0, 42.5, 40.8, 37.5, 18.2. **GC (methyl silicone 120 °C):** Rₜ 6.76 min.

![Chemical structure](image)

**1H NMR (CDCl₃, 400 MHz):**

28 δ 4.73 (s, 2 H), 3.71 (s, 6 H), 3.72 (s, 3 H), 2.68 (s, 2 H), 2.10-2.13 (m, 2 H), 2.04-2.07 (m, 2 H), 1.63-1.69 (m, 2 H). **13C NMR (CDCl₃, 100 MHz):** δ 171.8, 144.3, 110.9, 57.0, 52.7, 39.9, 34.1, 31.8, 31.4, 24.4, 22.9. **GC (methyl silicone 120 °C):** Rₜ 7.69 min.

![Chemical structure](image)

**1H NMR (CDCl₃, 400 MHz):**

29 δ 4.89-4.90 (m, 1 H), 4.78-4.79 (m, 1 H), 4.14-4.21 (m, 4 H), 3.01-3.06 (m, 1 H), 2.90-2.96 (m, 1 H), 2.51-2.57 (m, 2 H), 1.74-1.78 (m, 1 H), 1.21-1.25 (m, 6 H), 1.10 (d, J = 6.3 Hz, 3 H). **13C NMR (CDCl₃, 100 MHz):** δ 172.2, 172.1, 153.7, 105.6, 61.6, 58.5, 42.3, 40.7, 37.5, 18.2, 14.2. **GC (methyl silicone 120 °C):** Rₜ 11.59 min.
$^1$H NMR (CDCl$_3$, 400 MHz):$^{30}$ $\delta$ 4.74 (s, 2 H), 4.13-4.21 (m, 4 H), 2.67 (s, 2 H), 2.10-2.14 (m, 2 H), 2.04-2.06 (m, 2 H), 1.64-1.70 (m, 2 H) 1.24 (t, $J = 8.7$ Hz, 6 H). $^{13}$C NMR (CDCl$_3$, 100 MHz): $\delta$ 171.4, 144.5, 110.7, 61.4, 56.8, 39.8, 34.2, 31.3, 24.4, 14.3. GC (methyl silicone 120 °C): R$_t$ 13.76 min.

$^1$H NMR (CDCl$_3$, 400 MHz): $\delta$ 4.88-4.89 (m, 1 H, diastereomers), 4.79-4.80 (m, 1 H, diastereomers), 4.10-4.17 (m, 2 H, diastereomers), 2.84-2.91 (m, 0.27 H), 2.73-2.82 (m, 0.73 H), 2.57-2.69 (m, 2 H), 2.11-2.27 (m, 1 H), 1.64-1.71 (m, 1 H), 1.58-1.60 (m, 1 H), 1.24-1.27 (m, 3 H, diastereomers), 1.12 (d, $J = 6.6$ Hz, 3 H, one diastereomer), 1.065 (d, $J = 6.8$ Hz, 3 H, one diastereomer). $^{13}$C NMR (CDCl$_3$, 100 MHz): $\delta$ 176.2, 175.7, 156.0, 155.3, 105.0, 105.0, 60.6, 42.6, 42.0, 41.6, 39.2, 39.1, 38.2, 37.5, 36.5, 36.4, 22.6, 19.6, 18.3, 14.5, 14.3, 13.7. GC (methyl silicone 90 °C): R$_t$ 7.099 mins & 7.395 min.

$^1$H NMR (CDCl$_3$, 400 MHz):$^{31}$ $\delta$ 4.68 (s, 2 H), 4.10-4.16 (s, 2 H), 2.47-2.51 (m, 1 H), 2.33-2.40 (m, 1 H), 2.17-2.29 (m, 2 H), 1.93-2.02 (m, 2 H), 1.82-1.89 (m, 1 H), 1.67-1.69 (m, 1 H), 1.54-1.60 (m, 1 H), 1.24-1.28 (m, 3 H). $^{13}$C NMR (CDCl$_3$, 100 MHz): $\delta$ 175.5, 147.2, 108.8, 60.5, 44.6, 43.6, 37.5, 34.6, 28.9, 26.8, 14.5. GC (methyl silicone 90 °C): R$_t$ 8.44 min.

$^1$H NMR (CDCl$_3$, 400 MHz):$^{30}$ $\delta$ 7.82-7.85 (m, 2 H), 7.59-7.63 (m, 1 H), 7.52-7.56 (m, 2 H), 4.90-4.92 (m, 1 H), 4.84-4.87 (m, 1 H), 3.94-3.99 (m, 1 H), 3.74-3.79 (m, 1 H), 3.58-3.62 (m, 1 H), 2.70-2.74 (m, 1 H), 2.64-2.68 (m, 1 H), 1.04 (d, $J = 6.5$ Hz, 3 H). $^{13}$C NMR (CDCl$_3$, 100MHz): $\delta$ 149.4, 136.3, 133.0, 129.3, 127.9, 106.3, 55.3, 52.3, 37.7, 16.3. GC (methyl silicone 180 °C): R$_t$ 9.131 min.
$^1$H NMR (CDCl$_3$, 400 MHz): $^{32}$ δ 7.78-7.84 (m, 2 H, 6 & 5 member ring), 7.49-7.62 (m, 2 H, 6 & 5 member ring), 4.90-4.92 (m, 1 H, 6 & 5 member ring), 4.84-4.87 (m, 1 H, 5 member ring), 4.81-4.82 (m, 1 H, 6 member ring), 3.94-3.99 (m, 1 H, 5 member ring), 3.74-3.79 (m, 1 H, 5 member ring), 3.58-3.62 (m, 1 H, 5 member ring), 3.54 (s, 2 H, 6 member ring), 3.10 (t, $J = 5.5$ Hz, 2 H, 6 member ring), 2.70-2.74 (m, 1 H), 2.64-2.68 (m, 1 H), 2.09-2.12 (m, 2 H, 6 member ring), 1.66-1.72 (m, 2 H, 6 member ring), 1.04 (d, $J = 6.5$ Hz, 3 H, 5 member ring). $^{13}$C NMR (CDCl$_3$, 100 MHz): 6 member ring: δ 140.7, 136.6, 132.9, 129.2, 128.0, 112.0, 52.6, 46.6, 32.2, 25.9. GC (methyl silicone 180 °C): $R_t$ 9.131 mins (33d) and 9.978 mins (34d).

$^1$H NMR (CDCl$_3$, 400 MHz): $^{15}$δ 7.70-7.72 (m, 2 H), 7.32-7.34 (m, 2 H), 4.89-4.91 (m, 1 H), 4.84-4.86 (m, 1 H), 3.96-3.97 (m, 1 H), 3.72-3.76 (m, 1 H), 3.54-3.61 (m, 1 H), 2.66-2.72 (m, 2 H), 2.43 (s, 3 H), 1.04 (d, $J = 6.5$ Hz, 3 H). $^{13}$C NMR (CDCl$_3$, 100 MHz): δ 149.6, 143.8, 140.6, 133.2, 129.9, 128.0, 106.2, 55.3, 52.4, 37.7, 21.8, 16.3. GC (methyl silicone 180 °C): $R_t$ 13.350 mins

$^1$H NMR (CDCl$_3$, 400 MHz): $^{25}$ δ 7.68-7.72 (m, 2 H, 5 member ring), 7.65-7.68 (m, 2 H, 6 member ring), 7.32-7.33 (m, 2 H, 6 & 5 member ring), 4.89-4.91 (m, 1 H, 6 & 5 member ring), 4.84-4.86 (m, 1 H, 5 member ring), 4.81-4.82 (m, 1 H, 6 member ring), 3.93-3.97 (m, 1 H, 5 member ring), 3.72-3.76 (m, 1 H, 5 member ring), 3.56-3.60 (m, 1 H, 5 member ring), 3.51 (s, 2 H, 6 member ring), 3.08 (t, $J = 5.5$ Hz, 2 H, 6 member ring), 2.65-2.72 (m, 2 H, 5 member ring), 2.43 (s, 3 H, 6 & 5 member ring), 2.09-2.12 (m, 2 H, 6 member...
ring), 1.66-1.72 (m, 2 H, 6 member ring), 1.04 (d, J = 6.5 Hz, 3 H, 5 member ring). $^{13}$C NMR (CDCl$_3$, 100 MHz): 6 member ring: $\delta$ 143.7, 140.9, 133.5, 129.0, 128.0, 112.0, 52.6, 46.6, 32.2, 25.9, 21.7. GC (methyl silicone 180 °C): R$_t$ 13.35 min (33e) and 14.667 min (34e).

References describing spectroscopic and chromatographic data on compounds reported in this chapter:


10a, 10b, 10c, 12, 13: Zhang, A.; RajanBabu, T. V. J. Am. Chem. Soc. 2006, 128, 5620.


33a, 34a, 35a, 33e, 34e: Radetich, B.; RajanBabu, T. V. J. Am. Chem. Soc. 1998, 120, 8007.
2.7. References


(9) The ratios of products in this and other reactions reported in this paper are best determined by gas chromatography where baseline separations of isomers are observed. Since full characterization of all compounds reported in this paper have been documented before (see Supporting Information for citations) only gas chromatograms for the various experiments are included in the Supporting Information.


CHAPTER 3

Chemoselective Reactions of (E)-1,3-Dienes: Cobalt-Mediated Isomerization to (Z)-1,3-Dienes and Reactions with Ethylene


3.1. Backgrounds and Significance

Metal catalyzed alkene isomerization\(^1\)\(^2\) is a powerful chemical transformation since it can readily be transformed into a wide variety of other functionalities, as well as it is an alternate way of positioning an unsaturation from a pre-existing carbon-carbon double bond with control of the stereochemistry. Among the methods available for the formation of alkenes, relatively few allow the direct access of thermodynamically less-stable Z-isomer,\(^3\) even though in many biologically important compounds this configuration is important.\(^3\) In our recent studies on Co(II)-catalyzed asymmetric hydrovinylation (HV) of unactivated 1,3-dienes, we were mechanistically interested on the rate differences of E vs Z dienes and the possible pathways of E/Z isomerization to access the Z-selective olefins. We recently reported a new protocol for a highly enantioselective Co(II)-catalyzed
asymmetric hydrovinylation (HV) of unactivated 1,3-dienes that involve the use of a [bis-phosphine]CoCl₂ and Me₃Al (Scheme 3.1).⁴,⁵

In order to explain the improved selectivity in the Co-catalyzed reactions as compared to the corresponding Ni-catalyzed reactions⁶ (Scheme 3.1), we invoked⁴ an η⁴-cobalt-hydride complex 4 that restricts the conformations of the reactive intermediates in the former (Scheme 3.2). Complex 4 subsequently forms an allyl-cobalt intermediate 5, which undergoes ethylene insertion and β-hydride elimination to regenerate

**Scheme 3.1. Ni(II)- and Co(II)-Catalyzed Hydrovinylation of 1,3-Dienes**

the presumed [LCo-H]⁺ catalyst 3⁷ to complete the catalytic cycle. When an E/Z-mixture of a prototypical 1,3-diene was subjected to our standard HV conditions (except for the presence of ethylene), the terminal (Z)-1,3-diene was found to be totally unreactive. The attendant implication is that the (Z)-isomer is unreactive towards [LCoH]⁺ or the equivalent catalyst. Since such hydride species are also known to be capable of isomerization of alkenes, we wondered if conditions can be found to maximize the Z-isomer from an E/Z-mixture under kinetic conditions.⁸ The results of these studies are described in this chapter.
3.2. Hydrovinylation of (Z+E)-1,3-Dienes

The enantioselectivity in the asymmetric HV of a mixture of (E)-8 and (Z)-8 (Z:E = 53:47) using [(S,S)-DIOP]CoCl₂/Me₃Al (TMA) was found to depend on the conversion, with the (E)-isomer reacting at a significantly faster rate (equation 4.1, Table 3.1). At low conversions (entries 1-3, Table 3.1), only E-8 undergoes hydrovinylation giving a maximum of ~ 83% ee. As conversion increases, the proportion of Z-8 increases, leaving behind, at 23 h, essentially pure (Z)-8 (Z:E = 98:2, entry 5). A minor product (<5%), tentatively identified as a linear hydrovinylation product (10), is also formed at higher conversions. A similar behavior is observed with (S,S)-2,4-BDPP ligand except a notable decrease in enantioselectivity (from 85% ee at 21% conversion to 73% ee at 61% conversion, entries 6-10) results. These results are most readily rationalized if one assumes that the (Z)-isomer is a reluctant partner in the HV reaction, while the (E)-isomer undergoes a fast reaction giving the (S)-9 [with (S,S)-DIOP] as the major product. With the more reactive BDPP complex, at higher temperatures (-15 °C), upon complete conversion of the (E)-isomer, the (Z)-isomer undergoes the reaction, giving enantiomeric product, along with 10. The (DIOP)CoCl₂ complex shows much more discrimination in the reactions of the (Z)- and (E)-isomers of the starting diene, leaving behind almost all...
Scheme 3.2. A Working Hypothesis on the Mechanism of Co(II)-Catalyzed Hydrovinylation

of the (Z)-isomer unreacted (46%, Z:E = 98:2, entry 5) at the end of the reaction (entry 5, compared to 25% in entry 10 using 2,4-BDPP). The lower enantioselectivity at higher conversions using the BDPP ligand (entries 9 and 10) also suggests that the 1,4-HV of the (Z)-8 gives predominantly the opposite enantiomer. Implicit in these observations is also the striking absence of the isomerization of the (Z)-(8) into the thermodynamically favored (E)-isomer in the presence of the presumed Co(II)-hydride intermediates. Since (E)-8 appears to readily engage the [L.Co-H]+ in the facile hydrovinylation, in the absence of ethylene, under proper conditions, kinetic control might prevail in the (E)-(Z)-isomerization of 8, and if so, using ligand effects could one make the (Z)-isomer? These expectations have indeed been borne out and here we report the details of these investigations.
Before we describe our results, attention should be drawn to a related paper by Hilt et al., who documented a distinctly different protocol for the \( E/Z \) isomerization of 1,3-dienes.\(^8\) In this report (Scheme 3.3), a Co(I) complex prepared under reducing conditions from a tridentate pyridine-imine ligand (11), CoBr\(_2\), Zn and ZnI\(_2\) gave moderate yields of (Z)-1,3-dienes (14) from a 1:1 mixture of (Z)- and (E)-dienes (13). Behavior of the 1,3-diene was found to be highly dependent on the ligand, with a bis-phosphine-CoBr\(_2\) under identical conditions (i.e., with Zn/ZnI\(_2\)) giving modest yields of a product (15), arising via a 1,5-hydrogen migration. The difference between Hilt’s [bis-phosphine]Co(I)-chemistry and the [bis-phosphine] CoCl\(_2\)/Me\(_3\)Al-mediated reactions described in this paper is highlighted by the total absence of the 1,5-hydrogen migration, and the higher yields of \( E \) to \( Z \) isomerization products obtained.

### Table 3.1. Chemoselectivity in the Asymmetric HV of \((E)-\) and \((Z)-8\)

<table>
<thead>
<tr>
<th>Entry</th>
<th>Time (h)</th>
<th>( % (\text{9}) )</th>
<th>( \text{ee}% (\text{9}) )</th>
<th>( % (\text{8}) )</th>
<th>( \text{Z:E} (\text{8}) )</th>
<th>10</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>(S,S)-DIOP</td>
<td>(S,S)-BDPP(^d),</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>1</td>
<td>0.5</td>
<td>16</td>
<td>80</td>
<td>84</td>
<td>2.1:1.0</td>
<td>-</td>
</tr>
<tr>
<td>2</td>
<td>1.2</td>
<td>23</td>
<td>81</td>
<td>77</td>
<td>2.7:1.0</td>
<td>-</td>
</tr>
<tr>
<td>3</td>
<td>3</td>
<td>26</td>
<td>83</td>
<td>71</td>
<td>3.4:1.0</td>
<td>3</td>
</tr>
<tr>
<td>4</td>
<td>6</td>
<td>31</td>
<td>82</td>
<td>65</td>
<td>4.4:1.0</td>
<td>4</td>
</tr>
<tr>
<td>5</td>
<td>23</td>
<td>49</td>
<td>84</td>
<td>46</td>
<td>49:1</td>
<td>5</td>
</tr>
<tr>
<td>6</td>
<td>1</td>
<td>21</td>
<td>85</td>
<td>79</td>
<td>1.9:1.0</td>
<td>&lt;1</td>
</tr>
<tr>
<td>7</td>
<td>2</td>
<td>30</td>
<td>85</td>
<td>70</td>
<td>2.6:1.0</td>
<td>&lt;1</td>
</tr>
<tr>
<td>8</td>
<td>5.2</td>
<td>42</td>
<td>82</td>
<td>49</td>
<td>7.1:1.0</td>
<td>9</td>
</tr>
<tr>
<td>9</td>
<td>8</td>
<td>47</td>
<td>77</td>
<td>43</td>
<td>13.3:1.0</td>
<td>10</td>
</tr>
<tr>
<td>10</td>
<td>23</td>
<td>61</td>
<td>73</td>
<td>25</td>
<td>49:1</td>
<td>13</td>
</tr>
</tbody>
</table>

\(^a\) See equation 3.1 for procedure, results from Yam Timsina (The Ohio State University, 2014) \(^b\) Determined by GC. \(^c\) at \(-45 \degree \text{C}. \,(S)-\text{9} \) major. \(^d\) at \(-15 \degree \text{C}. \,(R)-\text{9} \) major.
Scheme 3.3. Co(I)-Catalyzed Isomerization Reactions

3.3. Isomerization of a Z/E-Mixture of a 1,3-Diene into the (Z)-Isomer

The initial scouting experiments were carried out on a mixture of (Z)- and (E)-8 using CoCl₂ complexes of chelating bis-diphenylphosphinoalkane ligands under conditions similar to the HV except for the presence of ethylene (equation 3.2). The composition of isomers and identification of the product(s) were determined by ¹H and ¹³C NMR spectroscopy and gas chromatography.⁹ The results are presented in Table 3.2.

Table 3.2. Isomerization of 1,3-Diene (Z/E)-8. Ligand Effects

<table>
<thead>
<tr>
<th>Entry</th>
<th>Starting mat. (Z):(E)-8</th>
<th>Ligand</th>
<th>Bite angle</th>
<th>Temp (°C)</th>
<th>Product (Z):(E)-8</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>33:67</td>
<td>[DPPM]</td>
<td>72</td>
<td>-15/14</td>
<td>37:63</td>
</tr>
<tr>
<td>2</td>
<td>33:67</td>
<td>[DPPE]</td>
<td>85</td>
<td>-10/14</td>
<td>74:26</td>
</tr>
<tr>
<td>3</td>
<td>33:67</td>
<td>[DPPP]</td>
<td>91</td>
<td>-16/22</td>
<td>82:18</td>
</tr>
<tr>
<td>4</td>
<td>33:67</td>
<td>[DPPP]¹</td>
<td>91</td>
<td>-4/16</td>
<td>33:67</td>
</tr>
<tr>
<td>5</td>
<td>33:67</td>
<td>[DPPB]</td>
<td>98</td>
<td>-15/14</td>
<td>&gt;99:&lt;1</td>
</tr>
<tr>
<td>6</td>
<td>33:67</td>
<td>[DPPpent]²</td>
<td>--</td>
<td>-15/14</td>
<td>&gt;99:&lt;1</td>
</tr>
<tr>
<td>7</td>
<td>33:67</td>
<td>(S,S)-DIOP</td>
<td>98</td>
<td>-10/12</td>
<td>100:0¹</td>
</tr>
</tbody>
</table>

¹ See equation 3.2 for procedure, results from Yam Timsina (The Ohio State University, 2014) ² Using CoBr₂. ³ bis-1,5-diphenylphosphino pentane. ⁴ Isomeric product not seen in GC or NMR.
As shown in the Table 3.2, the Z/E composition of the products is highly dependent on the ligand. A Co-complex containing ligand with a small bite-angle 1,1-bis-diphenylphosphinomethane (DPPM, bite angle $\beta = 72$) showed little tendency to effect the isomerization (entry 1), whereas complexes of large bite angle ligands, 1,4-bis-diphenylphosphinobutane (entry 5) 1,5-bis-diphenylphosphinopentane (entry 6) and DIOP (entry 7) gave quantitative conversion to the (Z)-isomer at low temperature. Bis-Diphenylphosphinopropane (DPPP, bite angle 91) gave up to 82% of the (Z)-isomer at -15 $^\circ$C (entry 3). The reaction is specific for the chloride complex; as shown in the entry 4, the corresponding bromide complex is ineffective for the isomerization reaction.

We have examined the isomerization of the mixtures of a number of 1,3-dienes under the optimized conditions (equation 3.2) and the most significant results are listed in Table 3.3. An expanded list of complexes and their effect on the isomerization of each of the dienes is included in the Supporting Information. As can be seen in entries 1-9, the isomerization reaction is broadly applicable giving excellent yields of the (Z)-isomers of most dienes. As inferred from the scouting studies (Table 3.2), ligands with relatively large bite angles, DPPB and DPPPent were found to be the most generally applicable for this reaction. For substrates where the diene is conjugated to an aromatic moiety (entries 5, 6 and 7), DPPPent is the ligand of choice, giving excellent conversion to the expected (Z)-isomer. DPPB leads to slightly lower selectivities. The isomerization reaction gives satisfactory results even in substrates that contain Lewis basic centers (entries 6 and 7). A preparative scale experiment (3 mmol) using 16 as the starting material gave 91% isolated yield of the expected product.
Table 3.3. Co(II)-Catalyzed Isomerization of (Z)- and (E)-1,3-Dienes

<table>
<thead>
<tr>
<th>Entry</th>
<th>(E+Z)-1,3-diene</th>
<th>Z:E</th>
<th>L in [L]CoCl₂</th>
<th>Temp (°C) time (h)</th>
<th>Yield (%)</th>
<th>Z:E⁵</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td><img src="#" alt="8" /></td>
<td>33:67</td>
<td>DPPM</td>
<td>-15/14</td>
<td>&gt;90⁵</td>
<td>37:63⁶</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>DPPB</td>
<td>-15/14</td>
<td>&gt;90⁵</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>DPPPent</td>
<td>-15/14</td>
<td>&gt;90⁵</td>
<td>&gt;99:&lt;1</td>
</tr>
<tr>
<td>2</td>
<td><img src="#" alt="16" /></td>
<td>46:54</td>
<td>DPPM</td>
<td>-18/14</td>
<td>&gt;90⁵</td>
<td>50:50⁶</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>DPPB</td>
<td>-10/12</td>
<td>&gt;90⁵</td>
<td>&gt;99:&lt;1</td>
</tr>
<tr>
<td>3</td>
<td><img src="#" alt="17" /></td>
<td>47:53</td>
<td>DPPB</td>
<td>-15/14</td>
<td>92</td>
<td>97:3</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>DPPPent</td>
<td>-15/14</td>
<td>&gt;95</td>
<td>97:3</td>
</tr>
<tr>
<td>4</td>
<td><img src="#" alt="18" /></td>
<td>51:49</td>
<td>DPPM</td>
<td>0/24</td>
<td>95</td>
<td>57:43⁶</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>DPPB</td>
<td>0/24</td>
<td>97</td>
<td>97:3</td>
</tr>
<tr>
<td>5</td>
<td><img src="#" alt="19" /></td>
<td>60:40</td>
<td>DPPB</td>
<td>-12/13</td>
<td>&gt;99</td>
<td>80:20⁶</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>DPPPent</td>
<td>-12/13</td>
<td>&gt;99</td>
<td>&gt;99:&lt;1</td>
</tr>
<tr>
<td>6</td>
<td><img src="#" alt="20" /></td>
<td>67:33</td>
<td>DPPB</td>
<td>-12/14</td>
<td>&gt;99</td>
<td>72:28⁶</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>DPPPent</td>
<td>-12/14</td>
<td>&gt;99</td>
<td>&gt;99:&lt;1</td>
</tr>
<tr>
<td>7</td>
<td><img src="#" alt="21" /></td>
<td>66:34</td>
<td>DPPB</td>
<td>0/24</td>
<td>&gt;90</td>
<td>93:7⁶</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>DPPPent</td>
<td>0/24</td>
<td>&gt;90</td>
<td>93:7⁶</td>
</tr>
<tr>
<td>8</td>
<td><img src="#" alt="22" /></td>
<td>53:47</td>
<td>DPPB</td>
<td>0/24</td>
<td>&gt;95⁴</td>
<td>98:2</td>
</tr>
<tr>
<td>9</td>
<td><img src="#" alt="23" /></td>
<td>45:55</td>
<td>DPPB</td>
<td>-15/16</td>
<td>85⁵</td>
<td>&gt;99:&lt;1</td>
</tr>
</tbody>
</table>

See equation 3.2 for procedure. For an expanded list of ligand effects for each substrate, see experimental section. ⁵ Yield of volatile products were estimated from NMR and GC. ⁶ Rest (E)-isomer. ⁷ Product contains an unidentified impurity from the starting material.

The isomerization reaction appears to be limited to terminal 1,3-dienes as illustrated by the examples shown in equation 3.3 and 3.4. Substrates 24 and 25 failed to undergo the
reaction under a variety of conditions using the ligands discussed previously. The starting material was recovered virtually unchanged.

\[ \text{(see equation 4.3)} \]

\[ L = \text{DPPB, DPPPent} \]

3.4. A Plausible Mechanism of the Isomerization

The experiments listed in previous sections suggest that one reason for the poor reactivity/selectivity of the Z-substrates might be their reluctance to form an $\eta^4$-complex.\(^{11}\) A plausible explanation for the observed results, based on the assumption that the initial $[LCo-H]^+$ addition to the 1,3-diene is reversible, is shown in Scheme 3.4. An intramolecular hydride delivery via an $\eta^4$-complex 4E gives the *syn-anti*-Co(allyl)-complex 5as.\(^{13}\) This species could undergo the familiar $\pi$-$\sigma$-$\pi$ isomerization\(^{13}\) to give, among others, an *anti-anti* complex (5aa). Hydride elimination from this species would generate a diene complex 4Z, which for steric reasons, might dissociate to give the (Z)-diene. The (Z)-diene, once formed, will most likely exist in the (s)-*trans* conformation, precluding any further $\eta^4$-complexation with the Co(II)-catalyst.\(^{14}\)
Scheme 3.4. A Plausible Mechanism for the E to Z-Isomerization of a 1,3-Diene

3.5. Co(II)-Catalyzed Isomerization of Terminal Alkenes

While we were mostly involved on the isomerization of Z/E-Mixture of a 1,3-Diene into the (Z)-isomer, we also observed the isomerization of simple terminal alkenes to internal alkenes with our Co(II)-catalytic system. A prototypical example of this

Scheme 3.5. Co(II)-Catalyzed Isomerization of Terminal Alkene 26

>99% conversion by GC

E : Z = 78:22

87
transformation is shown in Scheme 3.5 and Table 3.4 lists the optimization results using various Co(II)-complexes. Unlike most other similar isomerization reactions that use Ni, Pd, Ir, Rh and Ru catalysts which provide mostly the E-isomer product,\(^1,2,8\) the configuration of the products in the Co(II)-catalyzed isomerizations depend on the ligand, activator and temperature of the reaction. Results on the isomerization of prototypical substrate 26 showed that MAO did not have any E vs Z selectivity on the product ratio.

### Table 3.4. Initial Optimization Results of Isomerization of Terminal Alkene 26\(^a\)

<table>
<thead>
<tr>
<th>Entry</th>
<th>Complex</th>
<th>Activator</th>
<th>Ethylene</th>
<th>temp (°C)</th>
<th>SM left (%)</th>
<th>Z:E</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>CoCl(_2)(DPPM)</td>
<td>MAO</td>
<td>✓</td>
<td>rt/15 h</td>
<td>-</td>
<td>22:78</td>
</tr>
<tr>
<td>2</td>
<td>CoCl(_2)(DPPE)</td>
<td>MAO</td>
<td>✓</td>
<td>rt/20 h</td>
<td>9</td>
<td>29:60</td>
</tr>
<tr>
<td>3</td>
<td>CoCl(_2)(DPPP)</td>
<td>MAO</td>
<td>✓</td>
<td>rt/20 h</td>
<td>3</td>
<td>33:62</td>
</tr>
<tr>
<td>4</td>
<td>CoCl(_2)(DPPB)</td>
<td>MAO</td>
<td>✓</td>
<td>rt/20 h</td>
<td>3</td>
<td>32:65</td>
</tr>
<tr>
<td>5</td>
<td>CoCl(_2)(DPPM)</td>
<td>MAO</td>
<td>✓</td>
<td>rt/18 h</td>
<td>-</td>
<td>22:78</td>
</tr>
<tr>
<td>6</td>
<td>CoCl(_2)(DPPM)</td>
<td>TMA</td>
<td>✓</td>
<td>0/12 h</td>
<td>57</td>
<td>18:25</td>
</tr>
<tr>
<td>7</td>
<td>CoCl(_2)(DPPM)</td>
<td>TMA</td>
<td>✓</td>
<td>0/15 h</td>
<td>67</td>
<td>14:19</td>
</tr>
<tr>
<td>8</td>
<td>CoCl(_2)(DPPB)</td>
<td>TMA</td>
<td>✓</td>
<td>0/12 h</td>
<td>66</td>
<td>28:6</td>
</tr>
<tr>
<td>9</td>
<td>CoCl(_2)(DPPB)</td>
<td>TMA</td>
<td>✓</td>
<td>0/15 h</td>
<td>62</td>
<td>29:8</td>
</tr>
<tr>
<td>10</td>
<td>CoCl(_2)(DPPF)</td>
<td>TMA</td>
<td>✓</td>
<td>5/18 h</td>
<td>44</td>
<td>43:13</td>
</tr>
<tr>
<td>11</td>
<td>CoCl(_2)(DPPF)</td>
<td>TMA</td>
<td>✓</td>
<td>0/22 h</td>
<td>18</td>
<td>38:44</td>
</tr>
<tr>
<td>12</td>
<td>CoCl(_2)(DPPF)</td>
<td>TMA</td>
<td>✓</td>
<td>0/15 h</td>
<td>41</td>
<td>22:37</td>
</tr>
<tr>
<td>13</td>
<td>CoCl(_2)(DPPF)</td>
<td>TMA</td>
<td>✓</td>
<td>0 - rt/12 h</td>
<td>27</td>
<td>34:38</td>
</tr>
<tr>
<td>14</td>
<td>CoCl(_2)(DPPPent)</td>
<td>TMA</td>
<td>✓</td>
<td>0/18 h</td>
<td>26</td>
<td>22:52</td>
</tr>
<tr>
<td>15</td>
<td>CoCl(_2)(S-BINAP)</td>
<td>TMA</td>
<td>✓</td>
<td>0/18 h</td>
<td>90</td>
<td>1:9</td>
</tr>
<tr>
<td>16</td>
<td>CoCl(_2)(DPEphos)</td>
<td>TMA</td>
<td>✓</td>
<td>5/18 h</td>
<td>78</td>
<td>7:14</td>
</tr>
</tbody>
</table>

\(^a\) all the reactions are done with 10 mol% loading of Co(II)-complexes  
\(^b\)TMA (trimethylaluminum) used 2 equiv. MAO (methylaluminoxane) used 5 equiv.  
\(^c\) 20 mol% loading was used

However, low temperature reaction with trimethylaluminum as an activator showed that smaller bite angle ligand (DPPM) preferentially isomerized to E olefin (Table 3.4, entry 6), whereas larger bite angle ligand (DPPB and DPPF) isomerized to Z olefin (Table 3.4, entry 9 and 10). However, all low temperature reactions suffer with poor conversion. Increasing the temperature accelerated the thermodynamic ratio and lost any E/Z
selectivity of the product. Experimentally the use of ethylene did not change the isomerization selectivity, although addition of ethylene made the reaction significantly faster. In attempt to make more selective alkene, reaction was tried with larger bite angle ligands like DPEphos, BISBI (β = 113 °), but the results were not encouraging. The scope of the reaction is shown on Table 3.5, which lists other terminal alkenes that undergo isomerization under the described conditions.

Table 3.5. Substrate Scope of Co(II)-Catalyzed Isomerization of Terminal Alkenes

<table>
<thead>
<tr>
<th>Entry</th>
<th>Alkene</th>
<th>Product</th>
<th>Ligand/activator /ethylene</th>
<th>Temp (° C)/ time (h)</th>
<th>SM left (%)</th>
<th>Z:E</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td><img src="entry1.png" alt="Image" /></td>
<td><img src="entry2.png" alt="Image" /></td>
<td>CoCl₂(DPPB)/TMA/ethylene</td>
<td>rt/12h</td>
<td>-</td>
<td>95% conv.</td>
</tr>
<tr>
<td>2</td>
<td><img src="entry3.png" alt="Image" /></td>
<td><img src="entry4.png" alt="Image" /></td>
<td>CoCl₂(DPPM)/TMA/ethylene</td>
<td>0/12h</td>
<td>43 (&gt;95% ee)</td>
<td>25:32</td>
</tr>
<tr>
<td>3</td>
<td><img src="entry5.png" alt="Image" /></td>
<td><img src="entry6.png" alt="Image" /></td>
<td>CoCl₂(DPPM)/MAO/ethylene</td>
<td>rt/15h</td>
<td>4</td>
<td>24:71</td>
</tr>
<tr>
<td>4</td>
<td><img src="entry7.png" alt="Image" /></td>
<td><img src="entry8.png" alt="Image" /></td>
<td>CoCl₂(DPPB)/MAO/ethylene</td>
<td>rt/15h</td>
<td>5</td>
<td>30:66</td>
</tr>
<tr>
<td>5</td>
<td><img src="entry9.png" alt="Image" /></td>
<td><img src="entry10.png" alt="Image" /></td>
<td>CoCl₂(DPPB)/TMA/ethylene</td>
<td>0/24h</td>
<td>-</td>
<td>66:33</td>
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<tr>
<td>6</td>
<td><img src="entry11.png" alt="Image" /></td>
<td><img src="entry12.png" alt="Image" /></td>
<td>CoCl₂(DPPM)/MAO/ethylene</td>
<td>rt/15h</td>
<td>16</td>
<td>14:61</td>
</tr>
<tr>
<td>7</td>
<td><img src="entry13.png" alt="Image" /></td>
<td><img src="entry14.png" alt="Image" /></td>
<td>CoCl₂(DPE)/MAO/ethylene</td>
<td>rt/20h</td>
<td>8</td>
<td>19:69</td>
</tr>
<tr>
<td>8</td>
<td><img src="entry15.png" alt="Image" /></td>
<td><img src="entry16.png" alt="Image" /></td>
<td>CoCl₂(DPP)/MAO/ethylene</td>
<td>rt/20h</td>
<td>9</td>
<td>16:63</td>
</tr>
<tr>
<td>9</td>
<td><img src="entry17.png" alt="Image" /></td>
<td><img src="entry18.png" alt="Image" /></td>
<td>CoCl₂(DPPB)/MAO/ethylene</td>
<td>rt/20h</td>
<td>11</td>
<td>15:73</td>
</tr>
<tr>
<td>10</td>
<td><img src="entry19.png" alt="Image" /></td>
<td><img src="entry20.png" alt="Image" /></td>
<td>CoCl₂(DPPM)/TMA/ethylene</td>
<td>0/12h</td>
<td>35</td>
<td>26:38</td>
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<tr>
<td>11</td>
<td><img src="entry21.png" alt="Image" /></td>
<td><img src="entry22.png" alt="Image" /></td>
<td>CoCl₂(DPPB)/TMA/ethylene</td>
<td>0/12h</td>
<td>49</td>
<td>42:9</td>
</tr>
<tr>
<td>12</td>
<td><img src="entry23.png" alt="Image" /></td>
<td><img src="entry24.png" alt="Image" /></td>
<td>CoCl₂(DPPB)/TMA/ethylene</td>
<td>0-rt/22h</td>
<td>5</td>
<td>48:4</td>
</tr>
</tbody>
</table>

*a* 10 mol% catalyst loading with 5 equiv. MAO or 2 equiv. of TMA  
*b* 3% hydrovinylation product was observed  
*c* left over starting alkene was racemic
3.6. Conclusions

In summary, attempts to effect asymmetric hydrovinylation of a mixture of (Z)- and (E)-1,3-dienes using (P~P)CoCl₂/Me₃Al reveal that there is a significant difference in the relative rates of ethylene incorporation, with the (E)-isomer reacting significantly faster. In the absence of ethylene, under otherwise identical conditions, this Co-catalyst promote an unusual isomerization of an (E)/(Z)-mixture of 1,3-dienes almost exclusively to the Z-isomer. This result is strikingly different from the related reaction mediated by the reagent combination [(P~P)CoBr₂/Zn/ZnI₂), where a product of 1,5- hydrogen shift is the major.⁸d,1⁵ A mechanism that involves an intramolecular hydride addition via an η⁴-complex and subsequent π-σ-π- isomerization of the intermediate Co(allyl) species, is proposed for this reaction.

3.7. Experimental Section

**General Methods** Reactions requiring air-sensitive manipulations were conducted under an inert atmosphere of nitrogen by using Schlenk techniques or a Vacuum Atmospheres glovebox. Dichloromethane was distilled from calcium hydride under nitrogen and stored over molecular sieves. Ethylene (99.5%) was purchased from Matheson Inc., and passed through a column of Drierite® before use. Analytical TLC was performed on silicycle precoated (0.25 mm) silica gel 60 F254 plates. Flash column chromatography was carried out on silica gel 40 (Scientific Adsorbents Incorporated, Microns Flash). Absence of polymeric impurities was ascertained by NMR of the crude materials. Except for the volatile materials, the isolated yield of the products was not significantly different from the conversions. The percentage compositions were determined by uncalibrated
analysis of the areas. This is possible since the response of volatile isomeric hydrocarbons are essentially same in flame ionization detection as determined by comparison of GC-derived compositions with that obtained from $^1$H NMR in several cases. Gas chromatographic analyses were performed on an Agilent 7820A using a HP-1 Methylsilicone column (30 m x 0.250 mm, 0.25 mm film thickness) and an FID detector. Enantiomeric excesses of chiral compounds were determined by chiral stationary phase gas chromatographic (CSP GC) analyses, which were performed on a Hewlett-Packard 5890 with Cyclodex-B capillary GC column (60 m x 0.25 mm, 0.25 µm film thickness) or on an Agilent 7820A using a Cyclosil-B capillary GC column (25 m x 0.25 mm, 0.25 µm film thickness) using hydrogen as a carrier gas. The columns containing Chiral Stationary Phase (CSP) materials were also used for analysis of some of the geometric isomers because they gave better separation. These are indicated under appropriate chromatograms. Where ever appropriate, %$\text{ee}$’s were determined from chromatograms where base-line separation of the enantiomers was achieved for an authentic racemic mixture. Limits of detection of the minor enantiomer were established by analyzing mixtures of both enantiomers of known compositions. Optical rotations were recorded at the sodium D line in solvents indicated using filtered (45 m nylon filter).

**Synthesis of (Z+E)-1,3-Dienes**

**Typical Procedure for the Synthesis of (Z+E)-1,3-Dienes:** A 250 mL 3-necked flask equipped with a magnetic stirring bar, stoppers, and a nitrogen inlet was flame-dried and purged with nitrogen. The flask was charged with allyltriphenylphosphonium bromide (4.8 g, 12.48 mmol, 1.5 equiv.) and anhydrous THF (32.0 mL). 2.5 M $n$-BuLi (4.0 mL, 10
9.98 mmol, 1.2 equiv.) was added dropwise via syringe and the reaction mixture was allowed to stir at 0 °C for 1 h. A solution of corresponding aldehyde (8.32 mmol) dissolved in anhydrous THF was added and the reaction mixture was allowed to stir at ambient temperature for 3-5 h until all the starting material aldehyde was disappeared in TLC. The reaction mixture was diluted with pentane, filtered over Celite® and the filtrate was concentrated and purified via flash column chromatography (pentane-ether, 20:1) to yield the 1,3 diene as a mixture of $E$- and $Z$-isomers. The products were identified by NMR spectroscopy and analyzed by GC.

References Describing Spectroscopic Data on Starting Materials Reported in this Chapter


(Z+E)-1-Benzylbuta-1,3-diene (18):$^{17}$ $^1$H NMR (CDCl$_3$, 400MHz): $\delta$ 7.28-7.33 (m, 4 H, $E$ & $Z$ isomer), 7.19-7.24 (m, 6 H, $E$ and $Z$ isomer), 6.74- 6.84 (m, 1 H, $Z$ isomer), 6.31-6.40 (m, 1 H, $E$ isomer), 6.09-6.18 (m, 2H, $E$ & $Z$ isomer), 5.83-5.90 (m, 1 H, $E$ isomer), 5.61-5.67 (m, 1 H, $Z$ isomer), 5.27-5.32 (m, 1 H, $Z$ isomer), 5.13-5.21 (m, 2 H, $E$ and $Z$ mixture), 5.01-5.03 (m, 1 H, $E$ isomer), 3.56 (d, $J = 7.7$ Hz, 2 H, $Z$ isomer),
3.44 (d, \( J = 6.9 \) Hz, 2 H, \( E \) isomer). It is important to use \( n \)-BuLi as a base for ylide generation. Use of KO\( ^t \)Bu gives the conjugated product.

\(^{13}\)C NMR (CDCl\(_3\), 100MHz): \( \delta \) 140.6, 140.3, 137.1, 133.7, 132.3, 132.1, 130.8, 130.2, 128.8, 128.7, 128.6, 128.6, 126.3, 126.3, 118.2, 115.9, 39.1, 34.1


\((Z+E)-1\)-(2-Furyl)-1,3-butadiene (21):\(^{18}\)H NMR (CDCl\(_3\), 400MHz): \( \delta \) 7.43 (d, \( J = 1.6 \) Hz, 1 H, \( Z \) isomer), 7.31-7.38 (m, 2 H, \( E \) and \( Z \) isomers), 6.70 (dd, \( J = 15.6 \) Hz, 10.8 Hz, 1 H, \( E \) isomer), 6.41-6.49 (m, 1 H, \( E \) isomer), 6.40 (dd, \( J = 3.3 \) Hz, 1.8 Hz, 1 H, \( Z \) isomer), 6.34-6.39 (m, 2 H, \( E \) isomer), 6.32 (d, \( J = 3.3 \) Hz, 1 H, \( Z \) isomer), 6.09-6.10 (m, 1 H, \( Z \) isomer), 5.36 (dd, \( J = 17 \) Hz, 1.9 Hz, 1 H, \( Z \) isomer), 5.31-5.35 (m, 1 H, \( E \) isomer), 5.25-5.28 (m, 1 H, \( Z \) isomer), 5.16 (d, \( J = 10 \) Hz, 1 H, \( E \) isomer).

\(^{13}\)C NMR (CDCl\(_3\), 100MHz): \( \delta \) 153.7, 153.2, 142.6, 142.4, 136.9, 134.5, 128.4, 127.9, 120.6, 119.9, 117.9, 117.2, 111.8, 111.5, 110.8, 108.7.

CSP GC (cyclosil B, 80 °C): \( R_T \) 11.672 min (Z), 12.879 min (E). Z:E = 66:34.
(Z+E)-1-(4′-Butyl-1′-cyclohexyl)-1,3-butadiene (22): 1-(4′-butyl-1′-cyclohexyl)-1,3-butadiene was synthesized from the corresponding aldehyde equatorial conformer of 4-tert-butylcyclohexanecarboxaldehyde.

\[
\text{H NMR (CDCl}_3, 400 \text{ MHz}: \delta 6.65 (\text{dddd}, J = 1 \text{ Hz, 10 Hz, 11 Hz and 16.8 Hz, 1 H, Z isomer}), 6.26-6.35 (m, 1 H, E isomer), 5.99-6.05 (m, 1 H, E isomer), 5.88-5.94 (m, 1 H, Z isomer), 5.65 (dd, } J = 15.3 \text{ Hz, 6.8 Hz, 1 H, E isomer), 5.25-5.29 (m, 1 H, Z isomer), 5.14-5.21 (m, 1 H, Z isomer), 5.04-5.12 (m, 2 H, E and Z isomer), 4.94-4.97 (m, 1 H, E isomer), 2.35-2.38 (m, 1 H, Z isomer), 1.90-1.92 (m, 1 H, E isomer), 1.72-1.83 (m, 8 H, E and Z isomer), 1.50-1.59 (m, 1 H, E isomer), 0.95-1.23 (m, 9 H, E and Z isomer), 0.85 (s, 9 H, E isomer), 0.84 (s, 9 H, Z isomer).
\]

\[
\text{C NMR (CDCl}_3, 100 \text{ MHz}: \delta 141.3, 139.0, 137.6, 132.6, 128.4, 127.4, 116.6, 114.7, 47.7, 47.5, 40.9, 37.1, 33.7, 33.2, 32.4, 32.0, 27.6, 27.5, 27.4, 27.1, 26.9.
\]

\[
\text{GC (methyl silicone, 100 °C): R}_t 15.677 \text{ min (Z isomer), 17.185 min (impurity), 17.653 min (E isomer). Z:E = 53:47.}
\]

Chemoselective Asymmetric Hydrovinylations

Asymmetric Hydrovinylation of a Mixture of (Z)- and (E)-8 Using [(S,S)-DIOP]CoCl₂ and [(S,S)-BDPP]CoCl₂


Asymmetric Hydrovinylation of a Mixture of (Z)- and (E)-16 Using [(S,S)-DIOP]CoCl₂ and [(S,S)-BDPP]CoCl₂

Asymmetric Hydrovinylation of a Mixture of (Z)- and (E)-16 Using [(S,S)-DIOP]CoCl₂ and [(S,S)-BDPP]CoCl₂

![Image of reaction scheme]


Synthesis of Authentic (R/S)-9. Hydrovinylation of (E/Z)-1-cyclohexyl-1,3-diene (Z) and (E)-8 using [DPPB]CoCl₂

![Image of reaction scheme]


Procedure of Isomerization of 1,3-Dienes

Typical Procedure for Co(II)-Catalyzed Isomerization using Trimethylaluminum as Co-catalyst at 0 °C: To a flame-dried three-necked round-bottom flask equipped with a flow-control gas inlet, a rubber septa, and a magnetic stir-bar, [dppb]CoCl₂ catalyst
(0.003g, 10 mol%) was added while inside a glove box filled with nitrogen. The flask was removed from the glovebox with the flow-control inlet closed, placed on a vacuum line, and the stopcock opened to vacuum to remove the nitrogen, and subsequently purged with argon. Distilled, dried dichloromethane (1.0 mL) was added at room temperature to make a 0.01 M solution with respect to the cobalt catalyst. Trimethylaluminum solution (0.014 mL solution, 2 M in toluene), was added dropwise via a syringe (10 eq with respect to catalyst) and the solution color changed from deep blue to red-brown with white fume-clouds over the solution. The solution was stirred under argon for 5 min to allow for the fumes to dissipate and the vessel was cooled down to 0°C. After stirring under argon for five minutes, dried 1,3-diene (0.010g, 0.05 mmol) was added in one portion via syringe to the catalyst and stirred for 16-18 hours at 0°C. To quench the reaction, the flow-control inlet opened to air, the reaction solution was diluted with 5 mL pentane and 0.1 mL methanol was introduced into the flask and stirred for 5 minutes. The reaction solution was passed through a silica plug followed by washing with pentane (3 x 10 mL), careful removal of solvent in vacuo (no use of hot water bath!) yielded crude colorless oil that was pure enough to use for characterization further.

**References Describing Spectroscopic Data on Isomerized Product (with reaction conditions) Reported in this Chapter**

L)CoCl₂-Catalyzed Isomerization of 18

The reaction was done under the typical conditions described above. The results with different ligands are tabulated below. GC and NMR spectra are attached.

<table>
<thead>
<tr>
<th>Entry</th>
<th>Complex</th>
<th>Product (Z:E)</th>
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</thead>
<tbody>
<tr>
<td>1</td>
<td>CoCl₂(DPPM)</td>
<td>57:42</td>
</tr>
<tr>
<td>2</td>
<td>CoCl₂(DPPB)</td>
<td>97:3</td>
</tr>
<tr>
<td>3</td>
<td>CoCl₂(DPPPent)</td>
<td>95:5</td>
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</table>

1-Benzylbuta-1,3-diene (Z-18): 1H NMR (CDCl₃, 400 MHz): δ 7.26-7.31 (m, 2 H), 7.19-7.21 (m, 3 H), 6.11-6.17 (m, 1 H), 5.59-5.66 (m, 1 H), 5.28 (d, J = 16.8 Hz, 1 H), 5.18 (d, J = 10.2 Hz, 1 H), 3.55 (d, J = 7.7 Hz, 2 H).

¹³C NMR (CDCl₃, 100MHz): δ 140.4, 131.9, 130.6, 130.0, 128.5, 128.4, 126.1, 118.0, 33.9.

GC (cyclosil B 100 °C): Rₜ 20.197 min (E), 22.326 min (Z) ; Z:E = 97:3.

(L)CoCl₂-Catalyzed Isomerization of 21

The reaction was done under the typical conditions described above. The results with different ligands are tabulated below. GC and NMR spectra are attached.
### Table

<table>
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<th>Entry</th>
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<tr>
<td>1</td>
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<td>14% impurity from starting material</td>
</tr>
<tr>
<td>2</td>
<td>CoCl₂(DPPB)</td>
<td>93:7</td>
<td>14% impurity from starting material</td>
</tr>
<tr>
<td>3</td>
<td>CoCl₂(DPPPent)</td>
<td>93:7</td>
<td></td>
</tr>
<tr>
<td>4</td>
<td>CoCl₂(DPPF)</td>
<td>93:7</td>
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</tr>
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</table>

### 1-(2-furyl)-1,3-butadiene (Z-21): \(^1\)H NMR (CDCl₃, 400MHz): \(\delta\) 7.43 (d, \(J = 1.6\) Hz, 1 H), 7.34-7.38 (m, 1 H, minor, \(E\) isomer), 7.28-7.32 (m, 1 H, minor, \(E\) isomer), 6.40 (dd, \(J = 3.3\) Hz, 1.8 Hz, 1 H), 6.32 (d, \(J = 3.3\) Hz, 1 H), 6.09-6.10 (m, 1 H), 5.36 (dd, \(J = 17\) Hz, 1.9 Hz, 1 H), 5.25-5.28 (m, 1 H).

\(^{13}\)C NMR (CDCl₃, 100MHz): \(\delta\) 153.5, 142.4, 134.3, 127.7, 119.7, 116.9, 111.2, 110.6, 34.1.

GC (cyclosil B 80 °C): \(R_T\) 11.672 min (Z), 12.879 min (E). \(Z:E = 93:7\).

### (L)CoCl₂-Catalyzed Isomerization of 22

![Diagram of isomerization reaction]

The reaction was done under the typical conditions described above. The results with different ligands are tabulated below. GC and NMR spectra are attached.

### Table

<table>
<thead>
<tr>
<th>Entry</th>
<th>Complex</th>
<th>Product (Z:E)</th>
<th>Comments</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>CoCl₂(DPPM)</td>
<td>53:38</td>
<td>14% impurity from starting material</td>
</tr>
<tr>
<td>2</td>
<td>CoCl₂(DPPB)</td>
<td>&gt;99:&lt;1</td>
<td>14% impurity from starting material</td>
</tr>
</tbody>
</table>

### 1-(4'-butyl-1'-cyclohexyl)-1,3-butadiene (Z-22): \(^1\)H NMR (CDCl₃, 400MHz): \(\delta\) 6.65 (dddd, \(J = 1\) Hz, 10 Hz, 11 Hz & 16.8 Hz, 1 H), 5.88-5.98 (m, 1 H), 5.25-5.30 (m, 1 H), 5.14-5.21 (m, 1 H), 5.05-5.10 (m, 1 H), 2.32-2.40 (m, 1 H), 1.72-1.79 (m, 5 H), 1.02-1.10
(m, 4 H), 0.84 (s, 9 H, Z isomer).

$^{13}$C NMR (CDCl$_3$, 100MHz): $\delta$ 139.0, 132.6, 127.4, 116.6, 47.5, 37.1, 33.7, 32.4, 32.0, 29.7, 27.6, 27.5, 27.4, 26.9.

GC (methyl silicone 100 °C): $R_t$ 15.677 min (Z isomer), 17.653 min (E isomer). $Z:E = >99:<1$. The product contains the impurity carried over from the starting material ($R_T = 17.185$ min.).

**Synthesis of 4-tert-Butyl-1-vinylcyclohexene Derivative (24)**

A 250 mL three-necked round-bottom equipped with a magnetic stir bar, flow control gas inlet, and septa was flame-dried and purged with argon. The flask was charged with 7.8 mmol of trimethylsilyl acetylene, 13 mL dry, distilled THF and chilled to 0 °C. To the chilled solution, 3.1 mL of a 2.5 M solution of $n$-butyllithium in hexanes was added dropwise and stirred for 30 min. A solution of 6.5 mmol cycloketone was added neat to the lithium (trimethylsilyl)acetylene solution dropwise at 0 °C and then warmed to 25 °C for 2 h. The reaction was quenched with NH$_4$Cl, extracted with (3 x 20 mL) ether; the combined organic layers were dried with MgSO$_4$, filtered to remove the solid, and the solvent removed in vacuo to give a white solid, which was immediately carried forward. The solid was dissolved in 50 mL of a 1:1 9 M H$_2$SO$_4$ (aq) : MeOH solution and refluxed for three hours. After cooling to room temperature, the solution was extracted with (3 x
25 mL) ether, the combined organic extracts washed successively with saturated NaHCO₃ (aq), distilled water, and then dried with MgSO₄, filtered to remove the solid, and the solvent removed in vacuo to give a clear oil which was immediately carried forward for the next Wittig reaction. Crude ¹H NMR (CDCl₃, 400 MHz): δ 6.89-6.91 (m, 1 H), 2.51-2.57 (m, 1 H), 2.30-2.33 (m, 1 H), 2.27 (s, 3 H), 1.95-2.06 (m, 2 H), 1.88-1.94 (m, 1 H), 1.22-1.31 (m, 1 H), 1.02-1.12 (m, 1 H), 0.89 (s, 9 H); ¹³C NMR (CDCl₃, 100 MHz): δ 199.2, 141.4, 139.7, 43.4, 32.1, 27.9, 27.1, 25.3, 24.5, 23.4.

A 50 mL three-necked round-bottom flask equipped with a magnetic stir bar, flow control gas inlet, and septa was flame dried and purged with argon. 1.2 g (3.2 mmol) ethyltriphenyl-phosphonium bromide was added to the flask under a strong stream of argon, 5 mL dry, distilled THF was added to make a slurry, and the mixture chilled to 0 °C. To the slurry, 1.3 mL (3.2 mmol) of a 2.5 M n-butyllithium solution in hexanes was added over a period of 10 min, and then the ice bath removed to allow the salt to completely dissolve. The enone (0.5 g, 2.8 mmol) was dissolved in 5 mL dry, distilled THF and added dropwise to the ylide, and stirred for 2 hours at ambient room temperature. The solution was poured into 50 mL pentanes and the solids filtered off through celite. The solvent was carefully removed in vacuo due to volatility of the product and the residue purified by flash column chromatography to give 0.43 g (5% ether : pentane, Rf= 0.66, 80% yield, Z:E = 68:32 (GC). ¹H NMR (CDCl₃, 400 MHz): δ 5.78-5.80 (m, 1 H, E isomer), 5.57 (q, J = 6.8 Hz, 1 H, E isomer), 5.40-5.42 (m, 1 H, Z isomer, E:Z = 1:2), 5.14 (qq, J = 6.8 Hz, 1.5 Hz, 1 H, Z isomer, E:Z = 1:2), 2.33-2.38 (m, 1 H), 2.04-2.20 (m, 9 H, E and Z mixture), 1.82-192 (m, 6 H, E and Z mixture), 1.77 (b, 3 H), 1.72-1.77 (m, 6 H), 1.59 (dq, J = 6.8 Hz, 1.5 Hz, 3 H, Z isomer), 1.14-1.32 (m, 6 H, E
and Z mixture), 0.88 (s, 9 H, Z isomer), 0.87 (s, 9 H, E isomer); $^{13}$C NMR (CDCl$_3$, 100 MHz): δ 139.2, 137.7, 137.6, 135.9, 123.9, 122.5, 119.1, 118.4, 44.1, 44.0, 32.3, 32.2, 29.2, 27.5, 27.3, 27.2, 26.8, 24.4, 24.3, 23.4, 14.7, 14.0, 13.3. GC (methyl silicone 130 °C): R$_T$ 4.98 min, (Z); 8.64 min (E). Z:E = 68:32.

**(L)CoCl$_2$-Catalyzed Isomerization of 24**

The reaction was done under the typical conditions described above. Analysis of the product by GC and NMR showed no reaction under these conditions.

![Diagram of (L)CoCl$_2$-Catalyzed Isomerization of 24](image)

**Synthesis of Terminal Alkenes**

![Diagram of Synthesis of Terminal Alkenes](image)

**Synthesis of 1-(Pent-3-enyloxy)-4-methoxybenzene (26):** To a stirred solution of 4-methoxyphenol (1 g, 8.06 mmol), 4-penten-1-ol (0.90 g, 10.48 mmol), and triphenylphosphine (2.75 g, 10.48 mmol) in anhydrous THF (20 mL) was added diisopropylazodicarboxylate (2.12 g, 10.48 mmol) slowly at 0 °C. After the reaction was stirred overnight at rt, the mixture was diluted with EtOAc (20 mL) and water (20 mL) and separated. The crude compound was extracted with EtOAc (3 x 20 mL), and the combined organic layers were dried over Na$_2$SO$_4$. The resulting product was purified by
chromatography to afford 1.5 g (93%) of 26. 1H NMR (CDCl3, 400MHz): δ 6.83-6.84 (m, 4 H), 5.80 -5.91 (m, 1 H), 5.03-5.09 (m, 1 H), 4.98-5.01 (m, 1 H), 3.92 (t, J = 8 Hz, 2 H), 3.77 (s, 3 H), 2.20-2.26 (m, 2 H), 1.86 (tt, J = 8 Hz, 1.2 Hz, 2 H). 13C NMR (CDCl3, 100MHz): δ 153.7, 153.2, 137.9, 115.5, 115.1, 114.6, 67.9, 55.8, 30.1, 28.6. GC (methyl silicone 130 °C): Rₜ 10.88 mins.

1-Methylene-2,3-dihydro-1H-indene (28): 1-Methylene-2,3-dihydro-1H-indene was synthesized using known literature method of wittig reaction of triphenylmethylphosphonium bromide on commercially available 1-indanone. GC (methyl silicone 80 °C): Rₜ 10.211 mins.

(4R)-4,8-Dimethyl-1,7-nonadiene (30): (4R)-4,8-Dimethyl-1, 7-nonadiene was synthesized using known literature method of wittig reaction of triphenylmethylphosphonium bromide on commercially available (R)-(+) -citronellal. GC (methyl silicone 80 °C): Rₜ 5.327 mins.

Synthesis of 6-tert-Butyldimethylsiloxy)hex-1-ene (34): To a solution of 0.581 g (5.81 mmol) of 5-hexene-1-ol in 5 mL of DMF at 0 °C under nitrogen was added 1.19 g (17.4 mmol) of imidazole and 1.31 g (8.72 mmol) of tert-butyldimethylsilyl chloride. The mixture was stirred at rt for 2 days and subsequently quenched with 10 mL of water. The aqueous layer was extracted with ether (3 X 10 mL). The combined organic layers were washed with 2 N aqueous NaOH solution and then brine and dried over MgSO4 before
concentration in vacuo. The residue was purified by flash chromatography on silica gel, eluting with hexane/ethyl acetate (98:2), to afford the silyl ether (34) as a clear oil (1.19 g, 96%). 1H NMR (CDCl₃, 400MHz): δ 5.73-5.90 (m, 1 H), 4.91-5.06 (m, 2 H), 3.62 (t, J = 6.4 Hz, 2 H), 2.03-2.12 (m, 2 H), 1.38-1.60 (m, 4 H), 0.90 (s, 9 H), 0.05 (s, 6 H). GC (methyl silicone 90 °C): Rₜ 8.47 mins.

**Procedure of Isomerization of Terminal Alkenes**

For terminal alkenes, similar procedure for isomerization of 1,3-dienes was followed.

![1-methoxy-4-(pent-3-en-1-yloxy)benzene(27)](image)

Based on ¹H NMR and GC, the product 27 conversion and E/Z ratio were estimated as 99% and 3.5:1.0 respectively. 1H NMR (CDCl₃, 400MHz): δ 6.81-6.89 (m, 4 H), 5.45-5.65 (m, 1 H, E & Z mixture), 3.92 (t, J = 7 Hz, 2 H), 3.915 (t, J = 6.8 Hz, 2 H), 3.77 (s, 3 H, E & Z mixture), 2.50-2.55 (m, 2 H, Z isomer), 2.42-2.47 (m, 2 H, E isomer), 1.65-1.69 (m, 3 H, E & Z mixture). ¹³C NMR (CDCl₃, 100MHz): δ 153.8, 153.2, 127.6, 126.9, 126.5, 125.8, 115.6, 114.6, 68.6, 68.1, 55.8, 32.7, 27.3, 18.0, 12.9. GC (methyl silicone 130 °C): Rₜ 11.7 mins (E), 12.3 mins (Z).

![3-methyl-1H-indene (29)](image)

The products were identified by comparison of gas chromatogram and spectral properties of the sample from the previous literature. ¹H NMR (CDCl₃, 400MHz): δ 7.45-7.47 (m, 1 H), 7.30-7.37 (m, 2 H), 7.19-
7.23 (m, 1 H), 6.21-6.22 (m, 1 H), 3.32-3.33 (m, 2 H), 2.18-2.20 (m, 3 H). $^{13}$C NMR (CDCl$_3$, 100MHz): $\delta$ 146.1, 144.3, 140.0, 128.7, 126.0, 124.4, 123.6, 118.8, 37.6, 13.0.


(R)-4,8-Dimethylnon-2-ene (31)$^{25}$: The products were identified by comparison of gas chromatogram and spectral properties of the sample from the previous literature. $^1$H NMR (CDCl$_3$, 400MHz): $\delta$ 5.34-5.43 (m, 2 H, $E$ & $Z$ mixture), 5.28 (ddq, $J = 1$ Hz, 7.4 Hz & 15.3 Hz, 1 H, $E$ isomer), 5.07-5.18 (m, 3 H, $E$ & $Z$ isomer), 2.39-2.51 (m, 1 H, $Z$ isomer), 2.02-2.11 (m, 1 H, $E$ isomer), 1.91-2.02 (m, 2 H, $E$ & $Z$ isomer), 1.68-1.69 (m, 6 H, $E$ & $Z$ mixture), 1.64-1.66 (m, 3 H, $E$ isomer), 1.61-1.62 (m, 3 H, $Z$ isomer), 1.59 (b, 6 H, $E$ & $Z$ mixture), 1.26-1.32 (m, 4 H, $E$ & $Z$ mixture), 0.95 (d, $J = 6.7$ Hz, 3 H, $E$ isomer), 0.93 (d, $J = 6.7$ Hz, 3 H, $Z$ isomer). $^{13}$C NMR (CDCl$_3$, 100MHz): $\delta$ 137.5, 137.2, 131.1, 128.4, 126.9, 124.9, 122.9, 122.4, 37.7, 37.3, 36.3, 30.9, 29.7, 26.0, 25.8, 25.7, 21.1, 20.8, 17.9, 17.7, 17.6. GC (cyclosil B 80 °C): R$_t$ 12.033 mins ($Z$), 12.245 mins ($E$).

Tridec-2-ene (33)$^{26}$: The products were identified by comparison of gas chromatogram and spectral properties of the sample from the previous literature. $^1$H NMR (CDCl$_3$, 400MHz): $\delta$ 5.33-5.48 (m, 2 H, $E$ & $Z$ mixture), 1.94-2.05 (m, 2 H, $E$ & $Z$ mixture), 1.59-1.65 (m, 3 H, $E$ & $Z$ mixture), 1.26-1.34 (m, 16 H, $E$ & $Z$ mixture), 0.88 (t, $J = 6.7$ Hz, 3 H). $^{13}$C NMR (CDCl$_3$, 100MHz): $\delta$ 131.7, 130.9, 124.5, 123.6, 32.6, 31.9, 29.7, 29.64, 29.57, 29.54, 29.4, 29.3, 29.2, 26.8, 22.7, 22.3, 17.9, 14.1,
14.0, 12.7  GC (methyl silicone 100 °C): Rₜ 10.185 mins (1-Tridecene 17), 10.780 mins (E), 11.391 mins (Z).

\[ \text{tert-butyl(hex-4-en-1-yloxy)dimethylsilane (35):} \] The products \((E)\) and \((Z)-12\) (95%, 1:1) were identified by comparison of gas chromatogram and spectral properties of the sample from the previous literature.
3.8. References


(9) Precise proportion of isomeric compounds were determined by gas chromatography and NMR. See Supporting Information for details including chromatograms of products from various reactions.

(10) At higher temperatures (-10 °C, 1 atm ethylene) (DPPB)CoCl₂/MAO converts both (Z) and (E)-8 to racemic 9 in quantitative yield.

(11) We have carried out Co-catalyzed asymmetric HV of E/Z-mixtures of 16 and 17 and observed results similar to what is documented in Table 3.1 for E/Z-8.


(14) We have carried out high-level DFT calculations (Gaussian 09, geometries optimized with the 6-31G* basis set in conjunction with the B3LYP) on two of the molecules (8) and (16). Not surprisingly, the E-isomer is the more stable one (Kₑₑ/ₑₚ = 3924 and 24.8 respectively, 298 K) and both isomers exist almost exclusively in the s-trans form. The Z-isomer, once generated, will also exist exclusively in the s-trans conformation (Kₛₛₛₛ/ₛₙₛ = 1998 and 612 respectively), preventing a stable η₄-coordination to Co(II).

(16) We have also observed up to 69% conversion of a (Z/E)-mixture (46:54) of 16 to a product of 1,5-H-shift (15, R = C₇H₁₄) by using (DPPE)CoBr₂ (20 mol%)/Zn/ZnI₂ (40 mol%) for 72 h.


CHAPTER 4

Asymmetric Catalysis with Ethylene for the Synthesis of Functionalized Chiral Enolates


4.1. Introduction

Development of efficient and enantioselective routes to chemical intermediates that have proven utility for the preparation of varied classes of organic compounds is among the most impactful areas of research in modern organic synthesis.\(^1\)\(^-\)\(^3\) Successful outcome of such research, especially when it involves highly catalytic reactions that combine readily available precursors and feedstock carbon sources, can have profound impact on the synthesis and manufacture of fine chemicals. Trialkylsilyl enolates (Figure 4.1, a, M = R\(_3\)Si)\(^4\)\(^-\)\(^6\) are among the most widely used nucleophilic reagents in organic synthesis because of the ease of their preparation and the facile reactions they undergo with a broad range of electrophiles to form highly functionalized carbonyl compounds.\(^6\)\(^-\)\(^7\) Often these reactions exhibit exquisite reagent- and catalyst-dependent selectivity at every level –
Figure 4.1. Regio- and Stereoselective Synthesis of Functionalized Silyl Enolates via Catalytic Asymmetric Reactions

a Alpha-functionalization of carbonyl compounds via silyl enolates

\[ \text{R}^1 \text{R}^2 \text{O} \rightarrow \text{R}^1 \text{R}^2 \text{E} \]

- C-C or C-heteroatom bond formation
- reagent/catalyst dependent selectivity

b Diastereoselective metal-catalyzed organo-zirconium addition followed by silylation

\[ \text{Cp}_2\text{Cl}\text{Zr} \rightarrow \text{R} (1.2 \text{ equiv.}) \]

2. MeLi (2.6 equiv., –78°C to rt)

\[ \text{Me}_3\text{SiCl} (3.6 \text{ equiv.}), \text{Et}_3\text{N} (12 \text{ equiv.) urea-H}_2\text{O}_2 (10 \text{ equiv.)}, 48 \text{ h} \]

yield: 82-98%

ee: 93-96%

5a

5b

E:Z 1:2.8

ee: 69%

c Au(I)-catalyzed intramolecular cyclization of a siloxydienyne

6 (76%, 95% ee)

d Cobalt(II)-catalyzed asymmetric hydrovinylation of a siloxydiene (this work)

Figure 4.1. a. Alpha-functionalization of carbonyl compounds via silyl enolates. b. Silyl enolates generated by asymmetric-catalyzed conjugate addition of a vinyl-zirconium reagent followed by a difficult silylation protocol. c. Gold(I)-catalyzed cycloaddition of a siloxydienyne gives a functionalized, albeit, highly specialized, silyl enolate. d. This work: Cobalt(II)-catalyzed asymmetric hydrovinylation of a siloxy-1,3-dienes gives silyl enolates with a vinyl-bearing b-chiral center in high yield and selectivity. These compounds can be converted into the corresponding triflates in high yield.
chemo-, regio-, and stereoselectivity – in the bond-forming processes. These include reactions with alkylating agents,\textsuperscript{8} carbonyl compounds,\textsuperscript{9-12} oxidizing agents,\textsuperscript{13} heteroatom transfer agents,\textsuperscript{14,15} aromatic nitro-compounds,\textsuperscript{16} allylic carbonates,\textsuperscript{17} and even unactivated $\pi$-basic moieties such as alkynes.\textsuperscript{18-20} Development of highly catalytic asymmetric protocols for the synthesis of functionalized silyl enolates would considerably expand the scope and utility of these venerable intermediates. The closest precedent for a catalytic reaction that results in the regio- and stereoselective synthesis of a silyl enol ether involves a Rh(L*)-catalyzed diastereoselective conjugate addition of vinylzirconium reagent to an $\alpha,\beta$-unsaturated ketone followed by a very inefficient \textit{in situ} silylation of the resulting weakly reactive Zr-enolate using several equivalents of trimethylsilyl chloride, triethyl amine and large excess of urea (Figure 4.1, b).\textsuperscript{21} Other reported example of the formation of a silyl enolate product (6) through an asymmetric-catalyzed reaction involves a gold-catalyzed intramolecular cyclization of a siloxy-1,3-dien-7-yne (Figure 4.1, c).\textsuperscript{20} Highly specialized silyl enolate products are also formed, but never isolated, in asymmetric metal-catalyzed hetero-Diels-Alder reactions of siloxy-1,3-dienes such as the Danishefsky diene.\textsuperscript{22-25} Ding and coworkers have discovered highly efficient catalysts for solvent-free enantioselective hetero-Diels-Alder reaction with Danishefsky diene and benzaldehyde, however they were never able to isolate the enantiopure silyl enol ether end of their reaction.\textsuperscript{24} Catalytic asymmetric aza-Diels-Alder reaction of Danishefsky diene and $\alpha$-imino esters has been also reported with hydrolyzed ketone as the major product.\textsuperscript{25}

In our quest to Co-catalyzed asymmetric hydrovinylation reaction of functionalized dienes, we found a general procedure for a highly catalytic, chemo-, regio- and
enantioselective synthesis of silyl enolates that carry a vinyl-bearing chiral center at the β-position (Figure 4.1, d). The reactions, which proceed under ambient conditions (room temperature, 1 atmosphere ethylene), couple 1,3-siloxydienes and ethylene, a sustainable feedstock carbon source. Further, they use as little as 0.001 – 0.05 equivalents of readily available cobalt complexes and give products in high yield (>90%) and exceptionally high enantioselectivity (92-99 %ee). The silyl enolates can be readily converted into novel enantiopure vinyl triflates, which are also highly valued intermediates for a variety of cross-coupling reactions.

4.2. Hydrovinylation of Trialkylsiloxy-1,3-Dienes

Our studies started with an examination of the hydrovinylation of a prototypical trimethylsiloxy-1,3-diene, 8a, under conditions described in Figure 4.2, panel a. In early optimization studies using various cobalt (II)-complexes of 1,n-bis-diphenylphosphinoalkane ligands and various promoters, we recognized that trimethylaluminum, a Lewis acidic alkylating agent which we had successfully used previously, gave unacceptable yields of the expected hydrovinylation products (9a). Alternate procedures using Zn/ZnI2 in place of the aluminum reagents also gave unsatisfactory results (Figure 4.2, panel b). The major product in these reactions arises from simple decomposition of the silyl enolate to regenerate the ketone 7 from which the siloxy1,3-diene was initially prepared. On the other hand, a relatively weaker alkylating
Figure 4.2. Ligand Optimization, Starting Material Preparation and Reactivity

Differences on Siloxydienes

**a** Optimization of ligands for hydrovinylolation of 2-siloxy-1,3-dienes

![Chemical diagram]

<table>
<thead>
<tr>
<th>Entry</th>
<th>-SiR₃ in 8</th>
<th>P-Pᵇ</th>
<th>Conv. (%)</th>
<th>9 (%)</th>
<th>10 (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Me₃Si (8a)</td>
<td>dppm</td>
<td>97</td>
<td>81</td>
<td>8</td>
</tr>
<tr>
<td>2</td>
<td>Me₃Si (8a)</td>
<td>dppe</td>
<td>96</td>
<td>91</td>
<td>0</td>
</tr>
<tr>
<td>3</td>
<td>Me₃Si (8a)</td>
<td>dppp</td>
<td>100</td>
<td>&gt;99</td>
<td>0</td>
</tr>
<tr>
<td>4</td>
<td>Me₃Si (8a)</td>
<td>dppb</td>
<td>83</td>
<td>-</td>
<td>9</td>
</tr>
<tr>
<td>5</td>
<td>Et₃Si (8b)</td>
<td>dppp</td>
<td>&gt;99</td>
<td>&gt;95</td>
<td>0</td>
</tr>
<tr>
<td>6</td>
<td>t-BuMe₂Si (8c)</td>
<td>dppp</td>
<td>&gt;99</td>
<td>&gt;95</td>
<td>0</td>
</tr>
</tbody>
</table>

ᵃ See figure 4.2, panel a for reaction scheme. ᵇ P-P 1,n-bis-phosphine. ᶜ conversion, established by gas chromatography.

d Best ligand: dppp 8a, 8b or 8c: >99% 9; 0% 10

**b** Optimization of hydrovinylolation of 2-siloxy-1,3-dienes under reducing conditions Zn/ZnI₂

![Chemical diagram]

<table>
<thead>
<tr>
<th>Entry</th>
<th>-SiR₃ in 8</th>
<th>P-Pᵇ</th>
<th>Time (h)</th>
<th>Conv. (%)</th>
<th>9 (%)</th>
<th>10 (%)</th>
<th>11a (%)</th>
<th>7 (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Me₃Si (8a)</td>
<td>dppp</td>
<td>2</td>
<td>100</td>
<td>86</td>
<td>0</td>
<td>7%</td>
<td>7%</td>
</tr>
<tr>
<td>2</td>
<td>Me₃Si (8a)</td>
<td>dppp</td>
<td>2</td>
<td>&gt;99</td>
<td>82</td>
<td>0</td>
<td>0</td>
<td>18</td>
</tr>
<tr>
<td>3</td>
<td>Me₃Si (8a)</td>
<td>dppb</td>
<td>2</td>
<td>47ᵇ</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>47</td>
</tr>
<tr>
<td>4</td>
<td>Me₃Si (8a)</td>
<td>dppb</td>
<td>15</td>
<td>&gt;97</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>&gt;97</td>
</tr>
</tbody>
</table>

ᵃ P-P 1,n-bis-phosphine ᵇ conversion, established by gas chromatography. ᵈ 53% unreacted starting material

(Figure 4.2. Continued)
Figure 4.2. Ligand Optimization, Starting Material Preparation and Reactivity
Differences on Siloxydienes (Continued)

c Synthesis of 1-(1-siloxy-1-vinyl)cyclo-1-alkenes

\[
\begin{align*}
\text{cyclohexanone} & \quad 1. \text{MeOH, conc. H}_2\text{SO}_4 \\
\text{cycloheptanone} & \quad 2. \text{MeOH, conc. H}_2\text{SO}_4 \\
\text{cyclooctanone} &
\end{align*}
\]

\[
\begin{align*}
\text{O} & \quad 1. \text{O} \quad \text{TMS} \\
\text{MeOH} & \quad \text{n-BuLi/THF} \\
\text{LDA/THF} & \quad \text{R}_3\text{SiCl} \\
\text{OSiR}_3 &
\end{align*}
\]

\[
\begin{align*}
\text{8l} & \quad n = 1 \\
\text{8m} & \quad n = 2 \\
\text{8p} & \quad n = 3
\end{align*}
\]

d Dramatic effect of the trialkysiloxy-substituent on reactivity

\[
\begin{align*}
\text{Cl}_2\text{Co}[(S,S)-\text{BDPP}](0.001 \text{ equiv.}) & \quad \text{MAO (4 equiv.), CH}_2\text{Cl}_2, \text{rt, 36 h}
\end{align*}
\]

\[
\begin{align*}
\text{8m} & \quad Z = \text{OTMS}, >90\% \text{ y.}, >96\% \text{ ee} \\
\text{8q} & \quad Z = \text{H}, <1\% \text{ reaction}
\end{align*}
\]

Figure 4.2. a. Hydrovinylolation reaction optimization with achiral bis-phosphine ligands on 2-Silox-1,3-dienes. b. Hydrovinylation reaction optimization with achiral bis-phosphine ligands on 2-Silox-1,3-dienes under reducing conditions. c. 1-(1-Trialkysiloxyvinyl)-1-cycloalkenes are readily prepared by Meyer-Schuster rearrangement of alkynyl tertiary alcohols followed by enolate formation and silylation. d. A 2-trialkysiloxy substituent in 8m increases the reactivity compared to the unsubstituted diene 8q.

agent, methylaluminoxane (MAO), which is an easily handled solid reagent that is often used in alkene polymerizations using late transition metal complexes,\textsuperscript{31} gave excellent yields of the addition products. In all cases, the major product was identified as the branched 1,4-adduct, \((E)-9\), where the configuration of the double bond has been established by nOe (nuclear Overhauser effect) studies.\textsuperscript{32} A minor side-product that is observed in some of the reactions is the linear 1,4-adduct \(10a\). Among the cobalt complexes, \(\text{Cl}_2\text{Co}(\text{dppp})\) gave an exceptionally clean reaction to yield the product \((E)-9a\) in quantitative yield (Figure 4.2, panel a). Likewise, the corresponding triethyilsilyl and \(t\)-butyldimethysilylxylo dienes, 8b and 8c, also gave the respective adducts (9b and 9c) in excellent yields and exquisite \(E\)-selectivity.\textsuperscript{32} The siloxydiene are significantly more
reactive compared to the corresponding unsubstituted dienes. For example, with 0.001 equiv. catalyst, there is practically no reaction under otherwise identical conditions for comparable substrates without the siloxy substituent (Figure 4.2, panel d).

The hydrovinylation reaction has a broad scope as illustrated by the examples 8a-8p in Table 4.1. Under the optimized conditions [1 atmosphere ethylene, Cl₂Co(dppp) (0.05 equiv.), MAO (2 equiv.), CH₂Cl₂], the reactions of 4-alkyl-2-trimethylsiloxo dienes 8a-8p proceed at room temperature giving excellent yields of the hydrovinylation products. The structures of all products have been rigorously established by spectroscopic techniques. In all cases except 8k, the hydrovinylation favors the branched product in which the hydrogen is attached to the terminal, unsubstituted carbon, C₁, and the vinyl group to the C₄ of the original diene. Methyl substitution at C₁ (compare 8h and 8i) results in a reversal of this outcome with the exclusive formation of 9i from the 8i.

Dienes with bulkier substituents (R) at the C₄ position (8f, R = t-Bu and 8g, R = i-Pr) take up to 20 h to give moderate yields of the products. An enantiopure siloxydiene derived from (-)-citronellal, 8j, undergoes the reaction giving excellent yield of the expected product as a mixture of 1:1 diastereomers with an achiral Cl₂Co(dppp) complex (entry and 8g, R = i-Pr) take up to 20 h to give moderate yields of the products. An enantiopure siloxydiene derived from (-)-citronellal, 8j, undergoes the reaction giving excellent yield of the and 8g, R = i-Pr) take up to 20 h to give moderate yields of the products. An enantiopure siloxydiene derived from (-)-citronellal, 8j, undergoes the reaction giving excellent yield of the expected product as a mixture of 1:1 diastereomers with an achiral Cl₂Co(dppp) complex (entry 8). But as shown in Figure 4.3, panel a and b, a chiral
Table 4.1. Scope of Hydrovinylation of 2-Siloxo-1,3-Dienes

<table>
<thead>
<tr>
<th>Entry</th>
<th>Substrate (8)</th>
<th>Product (9)</th>
<th>Time (h)</th>
<th>Yield (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>8a R = C₄H₉</td>
<td>9a R = C₄H₉</td>
<td>0.25</td>
<td>&gt;99⁺,⁻</td>
</tr>
<tr>
<td>2</td>
<td>8d R = C₆H₁₃</td>
<td>9d R = C₆H₁₃</td>
<td>0.50</td>
<td>93</td>
</tr>
<tr>
<td>3</td>
<td>8e R = cyclohexyl</td>
<td>9e R = cyclohexyl</td>
<td>0.25</td>
<td>95</td>
</tr>
<tr>
<td>4</td>
<td>8f R = i-Pr</td>
<td>9f R = i-Pr</td>
<td>20</td>
<td>76</td>
</tr>
<tr>
<td>5</td>
<td>8g R = i-Pr</td>
<td>9g R = i-Pr</td>
<td>20</td>
<td>91</td>
</tr>
<tr>
<td>6</td>
<td>8h</td>
<td>9h (4:1)</td>
<td>0.25</td>
<td>90</td>
</tr>
<tr>
<td>7</td>
<td>8i</td>
<td>9i</td>
<td>3</td>
<td>79⁺</td>
</tr>
<tr>
<td>8</td>
<td>8j</td>
<td>9j (1:1)</td>
<td>0.25</td>
<td>91</td>
</tr>
<tr>
<td>9</td>
<td>8k Ph</td>
<td>10k Ph</td>
<td>0.50</td>
<td>80⁺,⁻</td>
</tr>
<tr>
<td>10</td>
<td>8l</td>
<td>9l</td>
<td>0.25</td>
<td>90</td>
</tr>
<tr>
<td>11</td>
<td>8m R₃ = Me₃</td>
<td>9m R₃ = Me₃</td>
<td>0.25</td>
<td>91</td>
</tr>
<tr>
<td>12</td>
<td>8n R₃ = Et₃</td>
<td>9n R₃ = Et₃</td>
<td>0.25</td>
<td>90</td>
</tr>
<tr>
<td>13</td>
<td>8o R₃ = t-Bu(Me)₂</td>
<td>9o R₃ = t-Bu(Me)₂</td>
<td>0.25</td>
<td>75</td>
</tr>
</tbody>
</table>

+a See figure 4.2, panel a for reaction scheme.  
⁺ No other products detected by GC.  
⁻ After hydrolysis to ketone.  
⁺⁺ Only a 1,4-linear product 10k is formed.  
⁻⁻ geometry of silyl enol ether was confirmed by nOE studies.
cobalt complex derived from the chiral ligand DIOP imparts exquisite reagent control in the generation of the new chiral center at C₄ (more later). A diene with a phenyl substituent in the C4-position (8k) does not give any of the expected product. Instead a linear 1,4-adduct, (Z)-6-phenyl-1,4-hexadiene (10k), is formed in 80% yield (entry 9). Entries 10-14 show a class of substrates where one of the double bonds of diene is embedded in a cycloalkane, which allows for the regio- and stereoselective preparation of 1,2-dialkylated cycloalkanes, a ubiquitous structural motif in the chemistry of many natural products. The substrates for these reactions are readily prepared from the corresponding cycloalkanones in two steps using the Meyer-Schuster rearrangement as a key step, as shown in Figure 4.2, panel c. The siloxydienes 8l–8p, derived from C₆–C₈ cycloalkanones, lead to exclusive formation of the branched 1,4-hydrovinylation products (9l-9p) with the vinyl group attached to a ring carbon. No trace of the alternate achiral linear 1,4-adduct was observed in any of the reactions. As shown in entries 12 and 13, the triethylsiloxy- and t-butyldimethylsiloxy- (8n and 8o) derivatives engage in the reaction just as well as the trimethylsilyloxy-derivative (8m) giving comparable yields of the expected products. The t-butyldimethylsiloxy-adduct, 9o, is hydrolytically stable and is readily purified by column chromatography on silica gel.

4.3. Asymmetric Hydrovinylation of Trialkylsiloxy-1,3-Dienes

As alluded to earlier, enantiopure silyl enol ethers with additional functionalizable moieties are potentially valuable, yet rare, intermediates in organic chemistry and we turned our attention to the asymmetric version of the hydrovinylation of siloxydienes as possible precursors for such compounds. Asymmetric hydrovinylations of prototypical
siloxydienes 8a-c were attempted using various Co(II)-complexes of several commercially available chiral bisphosphines in the presence of MAO as a promoter. Based on the initial observations, 2,3-O-isopropylidene-2,3-dihydroxy-1,4-\textit{bis}\-(diphenylphosphino)butane (DIOP) and 2,3 \textit{bis}\-(diphenylphosphino)pentane (BDPP) were chosen for further study under conditions shown in Table 4.2. As is the case with the structurally analogous complex (dppp)CoCl$_2$, the asymmetric catalytic reaction of 8a using the [(\textit{S},\textit{S})-BDPP]CoCl$_2$ complex is exceptionally facile, and proceeds to completion in less than 30 minutes at room temperature (entry 3) with 0.05 equivalents of the catalyst. The configuration of the product was established by converting the ketone (11a) from the adduct 9a to a saturated derivative 12 using Wilkinson’s catalyst [RhCl(PPh$_3$)$_3$(cat)/CH$_2$Cl$_2$/ 25 °C/ 16 h)] and comparing the specific rotation ([\(\alpha\)]$_{23}^D$) in chloroform with that of an authentic sample.$^{32}$

The reaction is typically complete in less than 3 hours with 1 mol% catalyst (entry 4). In a preparative scale reaction (5 g) using 0.01 equivalents of the catalyst, 90% yield of the product was isolated in 1 hour with no loss of enantioselectivity [entry 2 under Cl$_2$Co(S,S)-(DIOP)]. While both triethylsiloxydiene 8b and t-butyldimethylsiloxydiene 8c gave excellent yields of the expected products under identical conditions (entries 6 and 7), the observed enantioselectivity in the product in each case is significantly lower as compared to the reaction of the trimethylsilyl derivative 8a. To our delight we find that the Cl$_2$Co[(\textit{S},\textit{S})-DIOP] complex gave excellent yields (>90%) and enantioselectivities (95-99\% ee) for all three siloxydienes (Table 4.2, Column 8).
Table 4.2. Optimization of Enantioselectivity in the Hydrovinylation of 8a-8c

<table>
<thead>
<tr>
<th>Entry</th>
<th>Substrate</th>
<th>Cl₂Co(S,S)-BDPP</th>
<th>Cl₂Co(S,S)-DIOP</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>Cat (equiv.)</td>
<td>Time (h)</td>
</tr>
<tr>
<td>1</td>
<td></td>
<td>0.05</td>
<td>3</td>
</tr>
<tr>
<td>2</td>
<td></td>
<td>0.10</td>
<td>0.16</td>
</tr>
<tr>
<td>3</td>
<td></td>
<td>0.05</td>
<td>0.5</td>
</tr>
<tr>
<td>4</td>
<td></td>
<td>0.01</td>
<td>3</td>
</tr>
<tr>
<td>5</td>
<td></td>
<td>0.002</td>
<td>3.5</td>
</tr>
<tr>
<td>6</td>
<td>R₃SiO</td>
<td>0.05</td>
<td>1</td>
</tr>
<tr>
<td>7</td>
<td>R₃SiO</td>
<td>0.05</td>
<td>1</td>
</tr>
</tbody>
</table>

a Determined by chiral stationary phase gas chromatography (CSP GC). b (S,S)-BDPP gives the (S) enantiomer and (S,S)-DIOP gives the (R)-enantiomer. c Reaction on 5 mmol scale (~ 5.0 g) with 0.01 equiv. catalyst gave 90% yield and 98% ee. d Enantiomeric excess determined by CSP GC after hydrolysis to the ketone 11a.

Further scope of the enantioselective transformation was explored using the siloxydiynes previously listed in Table 4.1 and the results are shown in Table 4.3. Since the cobalt(II)-BDPP-complex gave acceptable yields and enantioselectivities for most of the substrates, our studies were largely limited to this catalyst. However, substrates 8a and 8d, gave relatively lower selectivities (entries 1 and 5) with this complex. Gratifyingly, asymmetric hydrovinylation (HV) of these substrates using the cobalt (II)-DIOP-complex, gave excellent yields and 98% ee for the expected products (Table 4.3, entries 2 and 6). The sterically demanding 4-<t-butyl-2-trimethylsiloxy-1,3-buta</t>diene (8f) failed to react even under more forcing conditions. The corresponding i-propyl-derivative 8g reacts sluggishly (20 h, 0.05 equiv. of catalyst), yet giving very high ee for
the expected product, 9g (entry 9). The product 9h, from the substrate siloxydiene 8h, formed in 94% ee (entry 10), is an important chiral fragment, potentially useful for the synthesis of polyketides. For example, a related enolate has been used in an approach to important antifungal agent Callystatin A.34

The siloxydienes derived from cyclic ketones 8l-8p (see Table 4.2 for structures) are also excellent substrates for the asymmetric hydrovinylation, giving excellent yields of the expected product in very high enantioselectivities (entries 11-16). A preparative scale run on 2.5 mmol scale of the substrate 8m uses only 0.01 equivalent of the catalyst (2 h, rt) to >90% yield of the product in 96% ee (entry 12). Indeed this reaction can be run

Table 4.3. Asymmetric hydrovinylation of siloxy-1,3-dienes

<table>
<thead>
<tr>
<th>Entry</th>
<th>Substrate</th>
<th>Catalyst (mol%)</th>
<th>Time</th>
<th>Product</th>
<th>Yield (%)</th>
<th>ee (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>8a</td>
<td>5 mol%, 30 min</td>
<td></td>
<td>(S)-9a</td>
<td>&gt;95</td>
<td>84</td>
</tr>
<tr>
<td>2</td>
<td>8a</td>
<td>5 mol%, 10 min</td>
<td>d</td>
<td>(R)-9a</td>
<td>95</td>
<td>98</td>
</tr>
<tr>
<td>3</td>
<td>8b</td>
<td>5 mol%, 10 min  a</td>
<td></td>
<td>(R)-9b</td>
<td>&gt;90</td>
<td>&gt;95</td>
</tr>
<tr>
<td>4</td>
<td>8c</td>
<td>5 mol%, 10 min  d</td>
<td></td>
<td>(R)-9c</td>
<td>&gt;90</td>
<td>95</td>
</tr>
<tr>
<td>5</td>
<td>8d</td>
<td>5 mol%, 30 min</td>
<td></td>
<td>(S)-9d</td>
<td>&gt;95</td>
<td>&gt;80</td>
</tr>
<tr>
<td>6</td>
<td>8d</td>
<td>5 mol%, 10 min  d</td>
<td></td>
<td>(R)-9d</td>
<td>96</td>
<td>97</td>
</tr>
<tr>
<td>7</td>
<td>8e</td>
<td>5 mol%, 30 min</td>
<td></td>
<td>(S)-9e</td>
<td>93</td>
<td>97</td>
</tr>
<tr>
<td>8</td>
<td>8f</td>
<td>20 mol%, 24 h</td>
<td></td>
<td>(S)-9f</td>
<td>0</td>
<td>--</td>
</tr>
<tr>
<td>9</td>
<td>8g</td>
<td>5 mol%, 20 h</td>
<td></td>
<td>(S)-9g</td>
<td>88</td>
<td>&gt;95</td>
</tr>
<tr>
<td>10</td>
<td>8h</td>
<td>5 mol%, 15 min</td>
<td></td>
<td>(S)-9h</td>
<td>&gt;90       d</td>
<td>94</td>
</tr>
<tr>
<td>11</td>
<td>8i</td>
<td>5 mol%, 30 min</td>
<td></td>
<td>(R)-9i</td>
<td>90</td>
<td>&gt;92</td>
</tr>
<tr>
<td>12</td>
<td>8m</td>
<td>1 mol%, 2 h</td>
<td></td>
<td>(R)-9m</td>
<td>&gt;90</td>
<td>96</td>
</tr>
<tr>
<td>13</td>
<td>8n</td>
<td>0.1 mol%, 36 h</td>
<td></td>
<td>(R)-9n</td>
<td>&gt;90</td>
<td>93</td>
</tr>
<tr>
<td>14</td>
<td>8o</td>
<td>5 mol%, 15 min</td>
<td></td>
<td>(R)-9o</td>
<td>78</td>
<td>87</td>
</tr>
<tr>
<td>15</td>
<td>8p</td>
<td>5 mol%, 20 h</td>
<td></td>
<td>(R)-9p</td>
<td>68</td>
<td>99</td>
</tr>
</tbody>
</table>

a Using Cl₂Co(S,S)-BDPP except entries 2, 3, 4 and 6, which use the (S,S)-DIOP complex. b See Table 4.1 for structures of siloxydienes and the corresponding products. c Determined by CSP GC. d Using Cl₂Co(S,S)-DIOP. e 10h (9%) also formed. For this substrate (S,S)-DIOP complex gave 70% ee. f Isolated by column chromatography. g Configurations 9i was confirmed by comparison of specific rotation ([α]D) of a derivative with that of an authentic sample. Configurations of 9m – 9p were assigned by analogy to that of 9i.
with as little as 0.001 equivalent (substrate:catalyst 1000:1, 2.5 mmol scale) of the catalyst (entry 13). The product from the t-butyldimethylsiloxydiene 8o is hydrolytically stable and can be purified by column chromatography on silica gel.

We find that the hydrovinylation of silyl enol ethers is several orders of magnitude faster compared to the corresponding unsubstituted dienes. An example of this increased reactivity is shown in Figure 4.2, panel d. While the siloxy diene 8m undergoes the asymmetric HV reaction at room temperature with 0.001 equiv. catalyst in 36 h, the corresponding unsubstituted diene 8q gives very little product under identical conditions. However, use of 0.05 equiv catalyst (6 h, rt) fully converts 8q to the expected product in >99% yield and 99% ee.

4.3.1. Reagent control on hydrovinylation of enantiopure and racemic 1,3-siloxydiene 8j:

Since the enantiopure siloxydiene (S)-8j showed no inherent selectivity in the formation of the newly created chiral center in the HV reaction with the achiral catalyst Cl2Co(dppp) (Table 4.1, entry 8, diastereomeric ratio 1:1, also see Figure 4.3, panel a), we examined the reaction of this substrate with Cl2Co(S,S)-DIOP. As shown in panel a, Figure 4.3, the enantiomeric complexes (R,R)- and (S,S)-Cl2Co(DIOP) exert excellent reagent control in the hydrovinylation reaction, and the adducts are formed in diastereomeric ratios of 96:4 and 3:97 in the respective cases. Having recognized the high catalyst selectivity over the substrate, we focused our study on the other enantiomer of the siloxydiene, (R)-8j. Under standard optimized achiral hydrovinylation (DPPP) condition, (R)-8j yields two products (4S,6R)-9j and (4R,6R)-9j with no inherent
Figure 4.3. Reagent Control in Asymmetric Hydroyvinylation of a Chiral 1,3-Diene

Reagent control in the asymmetric HV of a chiral 1,3-diene

(a) 
(S)-8j → CoCl₂[0.05 equiv. L] MAO (2 equiv.) DCM, rt, 15 min
L = (dppp) C₆:R:S 49:51
L = (R,R)-DIOP (4S,6S)-9j C₆: S (dr = 96:4)
L = (S,S)-DIOP (4R,6S)-9j C₆: R (dr = 97:3)

(b) 
(R)-8j → CoCl₂[0.05 equiv. L] MAO (2 equiv.) DCM, rt, 15 min
L = (dppp) C₆: R:S 50:50
L = (R,R)-DIOP (4S,6R)-9j C₆: S (dr = 85:11)
L = (S,S)-DIOP (4R,6R)-9j C₆: R (dr = 74:12)

(c) 
(rac)-8j → CoCl₂[0.05 equiv. L] MAO (2 equiv.) DCM, rt, 15 min
L = (dppp) 4 diastereomers (94% yield)
L = (R,R)-DIOP (4S,6S)-9j : (4S,6R)-9j = 48:52
L = (S,S)-DIOP (4R,6R)-9j : (4R,6S)-9j = 50:50

Figure 4.3. a. A chiral 1,3-diene, (S)-8j, shows no inherent selectivity in reactions with achiral catalysts, but excellent reagent control is observed in the asymmetric catalyzed reaction b. Chiral 1,3-diene, (R)-8j shows exquisite reagent control on the product in the asymmetric catalyzed reaction c. Racemic 1,3-diene, (rac)-8j shows no conventional kinetic resolution in the asymmetric hydroyvinylation reaction. Whereas the reaction is completely enantiospecific in the formation of products (4S,6R)-9j and (4R,6R)-9j with respect to chiral catalyst, where (S,S)-Cl₂Co(DIOP) favors primarily (4R,6R)-9j (Figure 4.3, panel b) as the major diastereomer and (R,R)-Cl₂Co(DIOP) produces (4S,6R)-9j as the major product under optimized condition (Figure 5.3, panel b). The high specificity of the products was further confirmed by rigorous NMR and gas chromatogram studies. This exquisite selectivity on the product confirms the absolute control of (DIOP)CoCl₂ catalyst on our hydroyvinylation reaction, which exclusively introduces the vinyl group with fixed
configuration on the C-C bond forming step on hydrovinylation of 1,3-siloxydienes, and most significantly, without considering the substrate chirality.

With the help of $^1$H, $^{13}$C NMR and gas chromatogram spectra of all possible four diastereomers of the hydrovinylation of (S)-8j and (R)-8j were identified and characterized (Figure 4.3, panel a and b). (S,S)-Cl$_2$Co(DIOP) exclusively introduces (R)-stereochemistry in the vinyl addition whereas (R,R)-Cl$_2$Co(DIOP) assigned the (S)-stereochemistry across the linear 1,3-siloxydiene hydrovinylation. Even though asymmetric hydrovinylation on enantiopure 1,3-siloxydienes shows exquisite catalyst-selectivity for the C-C bond-forming step (addition of vinyl group across the diene), from more practical point of view, we were really interested on the catalyst selectivity on racemic 1,3-siloxydienes. From our last discussion on hydrovinylation of enantiopure 1,3-siloxydienes (Figure 4.3, panel a and b), we could expect a similar stereodivergent reaction on racemic 1,3-diene (rac)-8j, and do not necessarily involve a kinetic resolution. Under standard optimized achiral hydrovinylation (DPPP) condition, (rac)-8j yields all four diastereomers, (4S,6R)-9j, (4R,6R)-9j, (4R,6S)-9j, (4S,6S)-9j, with no inherent selectivity (Figure 4.3, panel c). It is important to note that there is almost no diasteromeric preference on the product distribution at the end of achiral hydrovinylation on rac-8j. However, chiral catalyst (S,S)-Cl$_2$Co(DIOP) identifies very specifically individual enantiomers of the racemic starting material to form only two diastereomeric products (4R,6R)-9j and (4R,6S)-9j with very high enantioselectivities of both diastereomers. This can be explained by absolute selectivity possessed by the chiral catalyst (S,S)-Cl$_2$Co(DIOP), which completely overrides the substrate control and proceeds by the stereoselective addition of vinyl group across the 1,3-siloxydiene of both
the enantiomers of rac-8j. Overriding any substrate control, (S,S)-Cl₂Co(DIOP) exclusively introduces (R)-stereochemistry in the vinyl addition of both enantiomers of rac-8j. The reaction commenced with the selective introduction of (S)-stereochemistry in the vinyl addition of both enantiomers of rac-8j with (R,R)-Cl₂Co(DIOP) (Figure 4.3, panel c). The overall result distinctly recognized the complete control of catalyst on the vinyl addition of hydrovinylation reaction in excellent yields and enantioenrichment. It is also noticeable that we never observed any conventional kinetic resolution in our system, both enantiomers of our substrate reacts with our chiral catalyst at almost similar rate to form the diastereomeric products in high yields and enantiomeric enrichment.

4.4. Hydrovinylation of 2-Acetoxy-1,3-Dienes

During our studies on hydrovinylation of Trialkylsilyloxy-1,3-dienes, we wondered whether Co(II)-hydrovinylation conditions could be applied for the hydrovinylation of 2-acetoxy-1,3-dienes. To our delight, under optimized reaction conditions [1 atmosphere ethylene, Cl₂Co(dppp) (0.05 equiv.), MAO (2 equiv.), CH₂Cl₂], the reactions of 2-acetoxydienes 8q-8v (equation 4.1, Table 4.4) proceed at room temperature giving excellent yields of the hydrovinylation products. Once again, alkylating agent MAO plays a very important role in our catalytic system, as neither trimethylaluminum or Zn/ZnI₂ gives satisfactory hydrovinylation results. Configuration of the double bond has been established by nOe (nuclear Overhauser effect) studies. The hydrovinylation reaction on 2-acetoxydienes has broad scope on as illustrated by the examples 8q-8v (Table 4.4). The reactions show complete conversion to 1,4-hydrovinylation products with in 3 h with moderate to good yields (82-91%). Most importantly, unlike our
siloxycarbene hydrovinylation products, all acetoxydiene hydrovinylation products 8q-8v are hydrolytically stable and readily purified by column chromatography on silica gel.

![Chemical reaction diagram]

Table 4.4. Scope of Hydrovinylation of 2-Acetoxy-1,3-Dienes

<table>
<thead>
<tr>
<th>Entry</th>
<th>Substrate (8)</th>
<th>Product (9)</th>
<th>Time (h)</th>
<th>Yield (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>8q R = C₄H₉</td>
<td>9q R = C₄H₉</td>
<td>3</td>
<td>85⁺</td>
</tr>
<tr>
<td>2</td>
<td>8r R = C₆H₁₃</td>
<td>9r R = C₆H₁₃</td>
<td>3</td>
<td>89</td>
</tr>
<tr>
<td>3</td>
<td>8s R = cyclohexyl</td>
<td>9s R = cyclohexyl</td>
<td>3</td>
<td>82</td>
</tr>
<tr>
<td>4ᵇ</td>
<td>8t R = i-Pr</td>
<td>9t R = i-Pr</td>
<td>3</td>
<td>80</td>
</tr>
<tr>
<td>5</td>
<td></td>
<td>8u</td>
<td>3</td>
<td>81</td>
</tr>
<tr>
<td>6</td>
<td>8v</td>
<td>9v</td>
<td>3</td>
<td>91</td>
</tr>
</tbody>
</table>

* See equation 4.1 for reaction scheme. ⁺ Needs 0.1 equiv. catalyst loading. ³ E geometry of enol acetate was confirmed by nOEs.

4.5. Asymmetric Hydrovinylation of 2-Acetoxy-1,3-Dienes

Enantiopure enol acetates with an additional β-vinyl group are highly useful synthetic intermediates for further design, and development of many biologically active natural products. Based on our previous results on asymmetric hydrovinylation on Trialkysilyloxy-1,3-dienes, Co(II)-complexes of 2,3-O-isopropylidene-2,3-dihydroxy-
1,4-*bis*-(diphenylphosphino)butane (DIOP) and 2,3 *bis*-(diphenylphosphino)pentane (BDPP) ligands were chosen for further studies on asymmetric hydrovinylation of prototypical acetoxydienes 8q-v under conditions shown in Table 4.5. The reactions are relatively slower than Trialkylsilyloxy-1,3-diene hydrovinylation, proceeds to completion within 6-12 h with 0.05 equiv. of catalyst loading. Satisfyingly, we find that the Cl₂Co[(S,S)-DIOP] complex gave high yields (86-90%) and enantioselectivities (99 %ee) for simple linear acetoxydienes (9q-r, Table 5.5). Both cyclohexyl and i-Pr tethered acetoxydienes gave (9s-t, Table 5.5) high yields and enantioselectivities of the expected products with Cl₂Co[(S,S)-BDPP] complex. The acetoxydienes derived from cyclic ketones are also excellent substrates (8u-v, Table 5.5) for asymmetric hydrovinylation with Cl₂Co[(S,S)-BDPP] complex. Most satisfyingly, we never observed any decomposition of enolacetates to hydrolyzed ketones with our chiral catalyst in presence of methylaluminoxane as an activator.

**Table 4.5. Asymmetric Hydrovinylation of 2-Acetoxy-1,3-dienes**

<table>
<thead>
<tr>
<th>Entry</th>
<th>Substrate</th>
<th>Catalyst (mol%)</th>
<th>Time</th>
<th>Product</th>
<th>Yield (%)</th>
<th>ee (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>8q</td>
<td>5 mol%, 6 h</td>
<td></td>
<td>(R)-9q</td>
<td>86</td>
<td>99</td>
</tr>
<tr>
<td>2</td>
<td>8r</td>
<td>5 mol%, 6 h</td>
<td></td>
<td>(R)-9r</td>
<td>90</td>
<td>&gt;92</td>
</tr>
<tr>
<td>3</td>
<td>8s</td>
<td>5 mol%, 6 h</td>
<td></td>
<td>(S)-9s</td>
<td>84</td>
<td>96</td>
</tr>
<tr>
<td>4</td>
<td>8t</td>
<td>10 mol%, 12 h</td>
<td></td>
<td>(S)-9t</td>
<td>83</td>
<td>95</td>
</tr>
<tr>
<td>5</td>
<td>8u</td>
<td>5 mol%, 3 h</td>
<td></td>
<td>9u</td>
<td>90</td>
<td>93</td>
</tr>
<tr>
<td>6</td>
<td>8v</td>
<td>5 mol%, 3 h</td>
<td></td>
<td>9v</td>
<td>90</td>
<td>98</td>
</tr>
</tbody>
</table>

* Using Cl₂Co(S,S)-BDPP except entries 1 and 2, which use the (S,S)-DIOP complex.  

We also investigated making our 1,4-skipped enol acetates directly from the hydrovinylated 1,4-skipped silyoxydienes. We were able to make lithium enolate of our
hydrovinylated product 9a using MeLi in THF, which could be further trapped by acetic anhydride to make the desired 1,4-skipped enol acetates 9q (equation 4.2a). We did not observe any erosion of enantioselectivity of our products during these conversions.

4.6. Reactions of Functionalized Silyl Enolates

Since silyl enolates are among the most useful carbon nucleophiles, the enantiopure β-vinyl silyl enolates formed from the asymmetric HV reactions provide a direct route to many different types of α,β-di-functionalized carbonyl compounds. Some typical reactions of these versatile intermediates are shown in Figure 4.4. The simplest of these reactions, acid-mediated hydrolysis, gives potentially valuable β-vinyl ketones (Figure 4.4, a). Except the highly restricted examples of α-allylation of a ketone enolate,\textsuperscript{17, 35-38} and catalytic asymmetric conjugate alkenylation of conjugate enones using alkenyl zirconium,\textsuperscript{39a} alkenyl boronate\textsuperscript{39b,c} and alkenyl aluminum reagents,\textsuperscript{39d,e} there are very few reports known for the general, preparatively useful catalytic enantioselective synthesis of such β-vinyl compounds, especially in the acyclic series.\textsuperscript{38} The lone example of vinylation reported in the literature,\textsuperscript{39f} involving a Rh-catalyzed addition of a vinyl trifluoroboronate to (E)-benzylideneacetone, proceeds with low enantioselectivity (42% ee). Examples of β-vinyl ketones that are readily synthesized from the hydrovinylation products are also shown in Figure 4.4, b. While acrylic hydrovinyalted siloxydienes were
hydrolyzed with 2(N) HCl solution to synthesize these novel β-vinyl ketones, cyclic siloxydienes yields best diastereoselectivities in the products when hydrolyzed in presence of Lewis acids (BF$_3$.OEt$_2$) at very low temperatures (-78 °C). Details of experimental procedure along with various optimization conditions are listed in experimental section. We expect these novels, nearly enantiopure intermediates to have many synthetic applications including annulation reactions.

The absolute configuration of 11a was determined by conversion into the known saturated derivative 12a (Figure 4.4, a) and comparison of specific rotation and retention behavior in chiral stationary phase gas chromatography. Likewise, configuration of trans-1-acetyl-2-vinyl-cyclohexanone (11l-trans), which was prepared by base-catalyzed isomerization of 11l-cis, was ascertained by its conversion into a saturated derivative, (1R,2R)-1-acetyl-2-ethylcyclohexane. While there exists enantioselective methods for the synthesis of the trans-compounds such as 11l-trans, no such method is currently available for synthesis of the corresponding cis-compounds 11l-cis, 11m or 11n. Also simple reduction of vinyl group in these compounds will give access to the saturated derviates, (1R,2R)-1-acetyl-2-ethylcycloalkanes in both cis and trans configurations. Our hydrovinylation route will provide access to synthesize both cis and trans- β-vinyl and β-ethyl ketones in the same methodology sequence.

Products of other prototypical reactions of the silyl enolate 9a and 9m are shown in Figure 4.4, panel c. The resident chiral center in the silyl enolate controls the diastereoselectivity in the formation of the new bond to varying degrees. While the
Figure 4.4. Reactions of Functionalized Silyl Enolates *

**a** Hydrovinylation Route to Acyclic $\beta$-Vinylketones

1. base, $R_2SiCl$
2. asymmetric HV
3. $R_2SiO$ using [(S,S)-DIOP]CoCl$_2$

$R = C_6H$_

$\text{Reaction}$ $\rightarrow$ $2M$ HCl

**b** $\beta$-Vinyl Ketones Prepared via Asymmetric Hydrovinylation

(yield of hydrolysis, % ee shown in brackets)

11d (80, 90) 11e (76, 96) 11f (90, 94) 11g (80, 0, $d_r = 99:1$) 11h (80, $R$ = 98.2) 11i-(cis (67, 91) 11i-trans (67, 92) 11j (68, >95) 11m (68, >95) 11n (78, >99)

**c** Typical Electrophilic Reactions of the Silyl Enol Ether 9a and 9m

13 (>99%, $d_r$=1:1) 14 (56% yield, $d_r$=2.2:1.0)

Figure 4.4. Reactions of $\beta$-vinyl silylenolates. **a**, $\beta$-Vinyl silyl enolates and the hydrolysis products (panel **b**) are potentially valuable chiral synths that have not been synthesized previously via catalytic asymmetric reactions. The hydrolysis products 11l-11n, are formed as a mixture of cis- and trans isomers, with the former predominating. Both isomers are produced in $>91\%$ ee. Base-catalyzed equilibration of the mixture gives the trans-product (e.g., 11i-trans) as the major one. **c**. The silyl enolates can be used for a variety of carbon-heteroatoms and carbon-carbon bond-forming reactions as illustrated by the halogenation (13), oxidation (14), alkylation (15), Mukaiyama-Michael reaction (16-18), aldol (19, 20), $\alpha$-nitroarylation (21). Mukaiyama-Michael reactions of 9m give compounds with all carbon quaternary centers (24 and 25). * Compound 13 and 22b were synthesized by Jordan Page (The Ohio State University). Compound 14, 22a, and 23 were synthesized by Kendra Dewese (The Ohio State University).
CuBr$_2$-mediated $\alpha$-bromination (13, 22b) and methyl rhenium trioxide-mediated $\alpha$-hydroxylation (14, 22a) proceed with only low diastereoselectivity, products of several TiCl$_4$-mediated reactions such as Mukaiyama-Reetz alkylation with $t$-butyl chloride (15) and the Mukaiyama-Michael reactions (16, 17, 18) are formed with synthetically useful selectivity. The addition of 9a to (E)-3-octene-2-one is especially striking in that formation of only 2 out of the 4 products (18) with diastereoselectivities 13 : 1. Aldol reaction of silyl enolate 9a with benzaldehyde and cyclohexanecarboxaldehyde gave access to $\beta$-hydroxy carbonyl compounds (19a and 19b) with good yields and moderate selectivities. The addition of 9a to phenyltosyl imine is also exciting in that formation of only 2 out of the 4 products with high diastereoselectivity (20, dr 7 : 1). Finally, fluoride mediated $\alpha$-nitroarylation of the enolate with 4-bromo-nitrobenzene$^{16}$ gives the adduct(s) 21 in a diastereomeric ratio of 2:1. Reactions of the silyl enolate 9m give similar products 22 – 25. Note that the products of Mukaiyama-Michael addition and fluoride mediated $\alpha$-alkylation reaction, compounds 23 and 24 have an all-carbon quaternary center. Applications of the highly functionalized carbonyl compounds such as 23 and 24 for the synthesis of spirocyclic or fused (hydrazulene) ring systems can be envisaged. In cases where the diastereomeric products can be separated by column chromatography, this approach provides an exceptionally short synthesis of highly functionalized enantiopure ketones from readily available 2-siloxy-1,3-dienes.$^{32}$

In the Mukaiyama reaction, the Zimmerman-Traxler and Evans’ models are not satisfactory for predicting diastereoselectivity. Several open (non-chelated) transition states have been considered as useful methods. Noyori reported syn selectivity for the reaction of a mixture of (E) and (Z)-silyl enol ether with benzaldehyde (Figure 4.5, panel
a), independent of enolate geometry. This result was predicted with an open transition state model. The (E)-silyl enol ether in our hydrovinylated product 9a will possibly react with benzaldehyde or cyclohexanecarboxaldehyde in similar way. The open transition state model (shown in Figure 4.5, panel b) predicts the syn diastereomers as the major product after the aldol reaction. Similar model can be used to predict the diastereoselection for Mannich reaction where only two diastereomers were observed at the end of reaction (Figure 4.5, panel c). However, with the help of this open transition state model, it is really difficult to predict the reason behind the diastereoselection on Michael reaction (Figure 4.5, panel d). In the proton NMR of product 17, major diasteromer shows a doublet of a doublet of a doublet at 2.46 with coupling constant 8.2 Hz, 8.2 Hz and 5.0 Hz. Based upon the chemical shift, we predicted this proton to be H1 at erythro diastereomer which has two vicinal hydrogen coupling with dihedral angle 0° and one vicinal hydrogen coupling with dihedral angle 120°. With our tentative proton coupling constant values, we assigned erythro as our major diastereomer in Michael addition reaction.
Figure 4.5. Diastereoselection of Aldol, Mannich and Michael Reaction

a  Noyori Open Transition Model: Both E and Z Enolate Give Syn Diastereoselectivity as the Major Product

b  Possible Diastereoselection for Aldol Reaction with Enatiopure Silyl Enol Ether

c  Possible Diastereoselection for Mannich Reaction with Enatiopure Silyl Enol Ether

d  Possible Diastereoselection for Michael Reaction with Enatiopure Silyl Enol Ether

Figure 4.5. a. Noyori open transition model. b. Possible diastereoselection for the Aldol reaction using open transition state model. c. Possible diastereoselection for the Mannich reaction using open transition state model. d. Possible diastereoselection for the Michael reaction using open transition state model.
4.7. Generation of Enolates: Synthesis and Applications of the Enantiopure Vinyl Triflates

Conversion of enantiopure silyl enolates to suitable precursors for cross-coupling would considerably expand the scope and utility of this chemistry. For this we turned to vinyl triflates which could be formed from lithium enolates\(^4\) and subsequent trapping by \(\text{PhN} \cdot \text{Tf}\)\(_2\) (Figure 4.6, a).\(^{42}\) Configuration of the double bond has been established by nOe (nuclear Overhauser effect) studies. Not unexpectedly, the vinyl triflates undergo prototypical cross-coupling reactions catalyzed by Pd(0). Examples of Kumada, Stille and Suzuki coupling (32-34) of the prototypical vinyl triflate 25 are shown in Figure 4.6, a. The conversions of the silyl enolates to the vinyl triflates and their subsequent cross coupling reactions proceed with complete retention of configuration at the double bond and preservation of the vinyl-bearing stereogenic center. The reactivity difference between the mono-substituted and the stereo-defined trisubstituted double bonds in the 1,4-skipped diene products should make these enantiopure intermediates valuable components for further synthesis. Following the example of the conversion of 9a into 25, various vinyl triflates (26-31) were prepared in good yields (Figure 4.6, b).
Figure 4.6. Synthesis and Applications of the Enantiopure Vinyl Triflates

**a** Enantiopure enol triflates and their reactions

1. MeLi /ether, THF, 0 °C
2. NITl, -78 °C, 6 h

9a \([R-(\_)]\) (>99% ee)

1. EtMgBr /ether, \(\text{Cl}_2\text{Ni(dppp)}_2\)
2. Toluene, Sn\((n-\text{Bu})_3\)

25 \([(R-(\_)]\) (80%, 99% ee)

Kumada Coupling

Elliott

Suzuki Coupling

26 (75%, 99% ee)

27 (72%, 96% ee)

28 (74%, 95% ee)

29 (70%, >95% ee)

30 (70%, 94% ee)

31a \((\text{dr 37:1 } @ C_\alpha)\) (71%, 99% ee) from (S,S-DIOP)

31b \((\text{dr 23:1 } @ C_\alpha)\) (75%, 99% ee) from (R,R-DIOP)

32 (62%, 96% ee)

33a (61%, 96% ee)

33b (67%, 96% ee)

33c (64%, 94% ee)

34 (67%, 99% ee)

**b** Enol triflates prepared via asymmetric hydrovinylation of siloxydienes

**a, b.** Enantiopure triflates readily synthesized from the silyl enolates undergo various cross-coupling reactions. Tf: trifluoromethylsulfonyl.
Selective reduction of the vinyl group of our hydrovinylated product would expand substrate utility. Selective reduction in such substrates would test these reactions in two important ways: will the hydrovinylated products be compatible with prototypical hydrogenation conditions? And more importantly, will we be able to selectively reduce the vinyl group retaining the enantioselectivity of the hydrovinylated product? We choose standard hydrovinylated substrates \( R\)-9a and \( R\)-9m and as the model substrates to conduct the hydrogenation reaction. In early optimization studies we recognized that Wilkinson catalyst (0.1 equiv.), Pearlman catalyst (0.1 equiv.) and Crabtree catalyst (0.1 equiv.), which have been routinely used for hydrogenation reactions, gave us unsatisfactory results with our siloxy substrates. Under high pressure of \( H_2 \), in Fischer-porter tube (35 psi of \( H_2 \)), we always observed decomposition of the –OTMS functional group with formation of the saturated ketone \( 9a \) to \( 12a \), Figure 4.7, panel a and b) at the end of the reaction. Additionally, under mild hydrogenation condition, we always observed incomplete conversion to our desired product (Figure 4.7, panel a and b). On the other hand, relatively weak reducing agent, methyldiethoxysilane, in presence of Co(II)-bisimiopyridine complexes gave excellent yields to selectively reduced products (Figure 4.7, panel a and b). To our delight, in all cases, (except for the trifaltes, product 38, Figure 4.7, panel c), Co(II)-bisimiopyridine complex \([\text{CoCl}_2(\text{Pr-PDI})]\) selectively reduces the vinyl group retaining the original enantioselectivity from the hydrovinylation reaction. The hydrovinylated product 9m, originally derived from cycloheptanone is also compatible with our mild reducing condition, selectively reducing the \( \beta \)-vinyl group with high yield and preserving the chirality in the product. Most excitingly, among all
Figure 4.7. Selective Reduction of Vinyl Group of Hydrovinylated Products

a. Selective reduction of hydrovinylated product using Co(II)-Pr-PDI complex

b. Selective reduction of hydrovinylated product 9m using Co(II)-Pr-PDI complex

Yields are reported in parenthesis with enantiomeric excess: a Due to the volatility of these compounds in presence of toluene, all the yields were reported as GC yields, b product 37 did not resolve in chiral GC or HPLC, original hydrovinylated substrate has 95% ee even with 0.2 equiv. catalyst loading, we observed only 6% conv. with chiral starting material, rest is unreacted starting material.

Figure 4.7. a. Unsatisfactory results for the selective hydrogenation of hydrovinylated product 9a with normal hydrogenation conditions, on the other side Co(II)-bisimiopyridine complexes shows excellent conversion for selective reduction of β-vinyl groups b. Unsatisfactory results for the selective hydrogenation of hydrovinylated product 9m with normal hydrogenation conditions, on the other side Co(II)-bisimiopyridine complexes shows excellent conversion for selective reduction of β-vinyl groups c. Substrate scope for selective reduction of vinyl groups with Co(II)-bisimiopyridine complexes.

** Co(II)-bisimiopyridine catalyzed hydrosilylation and reduction reactions were initially optimized by Balaram Raya (The Ohio State University).
substrates (Figure 4.7, panel c), we have never observed any erosion of enantiomeric excess of the starting materials after the reduction. Selective reduction of vinyl groups without affecting the functionality of these chiral enolates considerably expands the scope of this chemistry. Detailed study on different bisiminopyridine ligands for hydrogenation methods and expansion of substrate scope are ongoing.

4.9. Conclusion

We describe a new method for the synthesis of enantiopure silyl enolates with a vinyl-group bearing β-stereogenic center in a highly catalytic reaction between siloxy-1,3-dienes and ethylene. The precursor siloxydienes are readily synthesized from α, β-unsaturated or cyclic ketones, and the catalysts are derived from commercially available ligands and an earth abundant metal (cobalt). The products undergo several useful reactions with electrophiles including hydrolysis, halogenation, alkylation, aldol and conjugate addition reactions. The enantiopure silyl enolates can be converted into vinyl triflates, which undergo typical cross-coupling reactions giving versatile intermediates, which are otherwise difficult to obtain by conventional methods. Further expansion of this chemistry to structural analogs of siloxy-1,3-dienes and applications of the various intermediates prepared during this study for the synthesis of medicinally relevant targets are the subjects of ongoing investigations.

4.10. Experimental Procedures

**General methods** Air-sensitive reactions were conducted under an inert atmosphere of argon using Schlenk techniques or a Vacuum Atmospheres glovebox. Solvents were distilled from the appropriate drying agents under nitrogen. Ethylene (99.5%) was
purchased from Matheson, Inc., and passed through Drierite® and potassium hydroxide before use. Analytical TLC was performed on Siliccycle pre-coated (0.25 mm) silical gel 60 F254 plates. Flash column chromatography was carried out on silica gel 40 (Sorbtech Chemicals), Gas chromatographic analysis was conducted on an Agilent 7820A using hydrogen as the carrier gas, equipped with a methyl silicone column (30 m X 0.32 mm, 0.25 µm film thickness). Enantiomeric excess of chiral compounds were determined by chiral stationary phase gas chromatographic (CSP GC) analysis, which were performed on an Agilent 7820A using hydrogen as the carrier gas, equipped with a Cyclosil-B (30 m X 0.25 mm, 0.25 µm film thickness), capillary GC columns purchased from Agilent. Each GC was equipped with FID detectors and integrators or a computer. Optical rotations were recorded on a Rudolph 21CFR 11 polarimeter at the sodium D line in chloroform or dichloromethane on solutions filtered through a 45 micron nylon filter.

**Synthesis of Cobalt Complexes:** Literature methods were used for the preparation of complexes (dppm)CoCl₂ and (dppp)CoCl₂. For (dppb)CoCl₂, [(R,R)-DIOP]CoCl₂, [(S,S)-DIOP]CoCl₂, [(S,S)BDPP]CoCl₂, and [(R,R)BDPP]CoCl₂, a procedure modified from RajanBabu and co-workers was used: Anhydrous CoCl₂ (50.5 mg, 0.390 mmol) was added to a previously flame-dried 50-mL round two-necked bottom flask fitted with a flow control gas inlet and magnetic stir-bar loaded in a glove box under nitrogen. The nitrogen atmosphere was removed and the flask purged with dry argon. Freshly distilled, degassed THF (5 mL) was added, and upon stirring at room temperature for 15 min, a clear deep blue solution formed. A solution of (S,S)-BDPP (181 mg, 0.410 mmol) in freshly distilled, degassed ether (5 mL) was added dropwise to yield a blue turbid solution. After stirring at room temperature for 15 h, 20 mL freshly distilled, degassed
hexane was added in one portion to yield a blue precipitate. The resulting precipitate was filtered on a sintered glass fret under argon atmosphere, and washed with diethyl ether and hexane (1:1) mixture (3 X 5 mL) to remove any unreacted (S,S)-BDPP, resulting in quantitative yield of a light blue solid, which was used with no further purification.

**Typical Procedure for Synthesis of Methylaluminoxane (MAO):**³¹,⁴⁵ A 250–mL, three-necked, round-bottomed flask equipped with a rubber septum, a Teflon-taped flow-controlled argon inlet, a reflux condenser, and a magnetic stirring bar is flame-dried and purged with argon. Under argon from a Schlenk line, the flask is then charged with aluminum sulfate hydrate (5.25 g, 8.3 mmol) and anhydrous toluene (18 mL). (Note 2) The flask is then cooled to −10 °C in a ice/salt bath, at which time trimethylaluminum (2M in toluene) (28 mL, 55.5 mmol) is added via syringe with stirring. The cold bath is removed and the reaction mixture is allowed to warm to 0 °C gradually (ca. 15 min), then to ambient temperature over another 15 min. The reaction mixture is stirred at ambient temperature for another 6 h and then the reaction mixture is placed over a silicone oil bath and gradually heated to 65 °C for next 8 h. After the heating period, the mixture is slowly brought to ambient room temperature. A Schlenk filter (12” column fitted with male ground joints and a microporous fret in the center) and a 250 mL single-necked round bottom is flame dried and quickly attached to the 250 mL three-necked reaction flask. The solution was filtered to remove the aluminum salt with positive pressure of argon and the filtrate in 250 mL single necked flask is put under vacuum pump (<0.1 mm of Hg) attached with a liquid nitrogen trap to remove all the toluene. The solid is then dried under vacuum for 12 h and cooled to ambient temperature to afford 1.3 g (40%) of the Methylaluminoxane (MAO) as a free-flowing, fine, white crystals. Typically, the salt is
stored at freezer (-8 °C) in a glove-box. COMMERCIAL AVAILABLE MAO DOES NOT HAVE THE SAME REACTIVITY OF OUR IN-HOUSE PREPARATION.

**General Procedure to Synthesize α,β- Unsaturated Ketones:** A 100 mL single-necked round-bottom equipped with a magnetic stir bar was charged with 11 mL acetone, 15 mL 2.5 M NaOH (aq) and cooled to 0 °C. To the mixture was added 12.6 mL (9.95 g, 138 mmol) isobutyraldehyde (or the corresponding aldehyde) dropwise over 1 h and the mixture was stirred at room temperature for 1 h. The reaction was quenched with 10 mL 6M HCl (aq) and the organic phase removed *in vacuo*. The resulting aqueous phase was extracted with (3 x 50 mL) diethyl ether, the combined organic extracts dried with MgSO₄, filtered to remove the solid, and the solvent removed *in vacuo* to give the crude product, which was immediately carried forward to the dehydration step. A 250 mL single-necked round-bottom flask equipped with a magnetic stir bar and a Dean-Stark trap was charged with the aldol product in 100 mL benzene and 0.150 g (0.871 mmol) *para*-toluenesulfonic acid. The mixture was refluxed for four hours, collecting ~10 mL water and then cooled to room temperature. The benzene was washed with 20 mL NaHCO₃ (aq), and the aqueous layer was extracted with (3 x 30 mL) ether. The combined organic layer was dried with MgSO₄, filtered to remove the solid, and the solvent removed *in vacuo* to give the crude product which was purified by column chromatography to get the product as a clear oil 9.75 g (63% yield). Careful column chromatography had been done to separate E/Z isomers.

**Cyclohexyl-trans-3-buten-2-one (ketone precursor for 8e):**

\[
\text{Cyclohexyl-trans-3-buten-2-one} (\text{ketone precursor for 8e})\text{.}^6 \]  

\[
\text{H NMR (400 MHz, CDCl}_3\text{) } \delta \text{ 6.72 (dd, 1H, } J = 16.1 \text{ Hz, } 6.8 \text{ Hz), 6.01 (dd, 1H, } J
\]
\begin{align*}
\text{= 16.1 Hz, 1.4 Hz), 2.23 (s, 3H), 2.07-2.16 (m, 1H), 1.74-1.78 (m, 4H), 1.62-1.71 (m, 1H), 1.27-1.35 (m, 1H), 1.07-1.23 (m, 3H).}
\end{align*}

5,5-Dimethyl-trans-3-hexen-2-one (ketone precursor for 8f):\(^{46}\) \(^1\)H NMR (400 MHz, CDCl\(_3\)) \(\delta\) 6.78 (d, 1H, \(J = 16\) Hz), 6.00 (d, 1H, \(J = 16\) Hz), 2.25 (s, 3H), 1.09 (s, 9H).

5-Methyl-trans-3-hexen-2-one (ketone precursor for 8g):\(^{47}\) \(^1\)H NMR (400 MHz, CDCl\(_3\)) \(\delta\) 6.77 (dd, 1H, \(J = 6.8\) Hz, 16 Hz), 6.03 (dd, 1H, \(J = 1.2\) Hz, 16 Hz), 2.48 (m, 1H, \(J = 5.2\) Hz), 2.26 (s, 3H), 1.09 (d, 6H, \(J = 6.8\) Hz).

(S,E)-6,10-Dimethylundeca-3,9-dien-2-one (ketone precursor for 8j):\(^{48}\) \(^1\)H NMR (400 MHz, CDCl\(_3\)) \(\delta\) 6.77 (dt, 1H, \(J = 15.9\) Hz, 7.4 Hz), 6.07 (dt, 1H, \(J = 15.9\) Hz, 7.4 Hz), 6.06 (dt, 1H, \(J = 15.9\) Hz, 1.4 Hz), 5.05-5.10 (m, 1H), 2.24 (s, 3H), 2.20-2.24 (m, 1H), 1.90-2.10 (m, 3H), 1.68 (d, 3H, \(J = 1.1\) Hz), 1.62-1.65 (m, 1H), 1.60 (s, 3H), 1.30-1.38 (m, 1H), 1.14-1.23 (m, 1H), 0.91 (d, 3H, \(J = 66.7\) Hz).

Benzyldienacetone (ketone precursor for 8k):\(^{46}\) \(^1\)H NMR (400 MHz, CDCl\(_3\)) \(\delta\) 7.49-7.55 (m, 3H), 7.39-7.41 (m, 3H), 6.72 (d, 1H, \(J = 16.1\) Hz), 2.37 (s, 3H).

General Procedure to Synthesize 1-Acetylcycloalkenes: A 250 mL three-necked round-bottom equipped with a magnetic stir bar, flow control gas inlet, and septa was flame-dried and purged with argon. The flask was charged with 55 mmol of trimethylsilyl acetylene, 100 mL dry, distilled THF and chilled to 0 °C. To the chilled
solution, 22 mL of a 2.5 M solution of n-butyllithium in hexanes was added dropwise and stirred for 30 min. A solution of 50 mmol cycloketone was added neat to the lithium (trimethylsilyl)acetylene solution dropwise at 0 °C and then warmed to 25 °C for 2 h. The reaction was quenched with NH₄Cl, extracted with (3 x 50 mL) ether; the combined organic layers were dried with MgSO₄, filtered to remove the solid, and the solvent removed in vacuo to give a white solid, which was immediately carried forward. The solid was dissolved in 100 mL of a 1:1 9 M H₂SO₄ (aq) : MeOH solution and refluxed for three hours. After cooling to room temperature, the solution was extracted with (3 x 100 mL) ether, the combined organic extracts washed successively with saturated NaHCO₃ (aq), distilled water, and then dried with MgSO₄, filtered to remove the solid, and the solvent removed in vacuo to give a clear oil. The crude product was purified by flash chromatography using silica gel and (5:95) ether: hexane to give the product as a clear oil.

**1-Acetylcyclohexene (ketone precursor for 8l):**⁴⁹ ¹H NMR (400 MHz, CDCl₃) δ 6.85 (t, 1H, J = 3.2 Hz), 2.22 (s, 3H), 2.20 (dd, 4H, J = 2 Hz, 3.2 Hz), 1.56 (q, J = 2.4 Hz).

**1-Acetylcycloheptene (ketone precursor for 8m):**⁴⁹ ¹H NMR (400 MHz, CDCl₃) δ 7.01 (t, 1H, J = 6.8 Hz), 2.42 (d, 2H, J = 5.2 Hz), 2.28 (t, 2H, J = 6.4 Hz), 2.27 (s, 3H), 1.69 (quintet, 2H, J = 6 Hz), 1.49 (quintet, 2H, J = 2.8 Hz), 1.38 (quintet, 2H, J = 5.6 Hz).

**1-Acetylcyclooctene (ketone precursor for 8p):**⁴⁹ ¹H NMR (400 MHz,
CDCl$_3$) $\delta$ 6.86 (t, 1H, $J = 8.4$ Hz), 2.43 (d, 2H, $J = 6$ Hz), 2.32 (t, 2H, $J = 6.4$ Hz), 2.29 (s, 3H), 1.53 – 1.64 (m, 2H), 1.44 – 1.59 (m, 6H).

**General Procedure for the Synthesis of the Siloxydienes:** A 100 mL three-necked round-bottom flask equipped with a magnetic stir bar, a gas inlet, and septa was flame-dried and purged with argon. The flask was charged with 4.20 mL (3.04 g, 30.0 mmol) diisopropylamine and 60 mL dry, distilled THF. The mixture was chilled to $-78$ °C and 12 mL of $n$-butyllithium (2.5 M solution in hexanes) was added slowly. The mixture stirred for 30 min., and then 25 mmol of the respective ketone was added neat dropwise and allowed to stir for 2 h. To the enolate mixture, 3.80 mL (3.26 g, 30.0 mmol) distilled trimethylsilyl chloride was added rapidly, the cooling bath was removed, and the mixture allowed to warm to room temperature and stir for $\sim 10$ h (small aliquots has been taken out, quenched by saturated solution of NH$_4$Cl, organic phase has been injected in GC to monitor the reaction). The reaction was quenched with a saturated solution of NH$_4$Cl (aq) and extracted with (3 x 30 mL) ether. The combined organic layer was dried with MgSO$_4$, filtered to remove the solid, and the solvent removed *in vacuo* to give the crude product that was purified by bulb-to-bulb distillation to get the product as a clear oil. The purity of these compounds were ascertained by gas chromatography.

![OTMS]

**2-Trimethylsilyloxy-1,3-octadiene (8a):** Prepared from commercially available *trans*-3-octen-2-one (yield 70%). $^1$H NMR (500 MHz, CDCl$_3$) $\delta$ 5.91 (dd, 1H, $J = 8.5$ Hz, 17 Hz), 5.84 (d, 1H, $J = 17$ Hz), 4.19 (s, 2H), 2.08 (q, 1H, $J = 8.5$ Hz), 1.29-1.40 (m, 4H), 0.89 (t, 3H, $J = 9$ Hz), 0.21 (s, 9H).

$^{13}$C NMR (125 MHz, CDCl$_3$) $\delta$ 155.0, 131.8, 127.6, 93.9, 67.9, 25.6, 22.2, 13.8, -0.02.
GC (cyclosil B, 50 °C): $R_t$ 195.88 min

HRMS (ESI-MS): m/z 199.1522 ([M + Na]); exact mass calculated for $C_{11}H_{22}OSiNa$ 199.1519.

2-Triethylsilyloxy-1,3-octadiene (8b): Prepared from trans-3-octen-2-one and chlorotriethylsilane (yield 65%). $^1$H NMR (400 MHz, CDCl$_3$) $\delta$ 5.97-6.04 (m, 1H), 5.87 (dt, 1H, $J = 15$ Hz, 1.3 Hz), 4.19-4.21 (m, 2H), 2.09 (q, 1H, $J = 6.9$ Hz), 1.28-1.43 (m, 4H), 0.99 (t, 9H, $J = 7.7$ Hz), 0.89 (t, 3H, $J = 7.2$ Hz), 0.72 (q, 6H, $J = 8$ Hz).

$^{13}$C NMR (100 MHz, CDCl$_3$) $\delta$ 155.2, 131.8, 127.6, 93.4, 31.7, 31.3, 22.3, 13.9, 6.7, 4.9

GC (cyclosil B, 140 °C): $R_t$ 10.76 min

HRMS (ESI-MS): m/z 241.1980 ([M + H]); exact mass calculated for $C_{14}H_{29}OSi$ 241.1982.

2-tert-Butyldimethylsilyloxy-1,3-octadiene (8c): Prepared from trans-3-octen-2-one (98%) and tert-butyldimethylsilylchloride (yield 66%). $^1$H NMR (400 MHz, CDCl$_3$) $\delta$ 5.96-6.04 (m, 1H), 5.87 (dt, 1H, $J = 15.2$ Hz, 1.2 Hz), 4.19-4.20 (m, 2H), 2.09 (q, 1H, $J = 6.7$ Hz), 1.28-1.42 (m, 4H), 0.97 (s, 9H), 0.9 (t, 3H, $J = 7.1$ Hz), 0.17 (s, 6H).

$^{13}$C NMR (100 MHz, CDCl$_3$) $\delta$ 155.2, 131.9, 127.7, 93.8, 31.8, 31.4, 25.8, 22.3, 18.3, 13.9, -4.7

GC (cyclosil B, 140 °C): $R_t$ 7.32 min
HRMS (ESI-MS): m/z 241.1979 ([M + H]); exact mass calculated for C\textsubscript{14}H\textsubscript{29}OSi 241.1982.

2-Trimethylsilyloxy-1,3-decadiene (8d): Prepared from commercially available trans-3-decen-2-one (yield 74%). \textsuperscript{1}H NMR (400 MHz, CDCl\textsubscript{3}) \(\delta\) 5.95 (dt, 1H, \(J = 6.7\) Hz, 15.2 Hz), 5.87 (dt, 1H, \(J = 15.2\) Hz, 1 Hz), 4.22 (s, 2H), 2.09 (q, 1H, \(J = 6.9\) Hz), 1.23-1.43 (m, 6H), 0.88 (t, 3H, \(J = 6.8\) Hz), 0.22 (s, 9H).

\textsuperscript{13}C NMR (100 MHz, CDCl\textsubscript{3}) \(\delta\) 155.0, 132.0, 127.6, 94.1, 32.1, 31.7, 29.1, 28.9, 22.6, 14.1, 0.0.

GC (cyclosil B, 70 °C): \(R_t\) 265.94 min

HRMS (ESI-MS): m/z 227.1738 ([M + Na]); exact mass calculated for C\textsubscript{13}H\textsubscript{26}O\textsubscript{3}SiNa 227.1737.

4-Cyclohexyl-2-trimethylsilyloxy-1,3(E)-hexadiene (8e): (Yield 71%). \textsuperscript{1}H NMR (400 MHz, CDCl\textsubscript{3}) \(\delta\) 5.81-5.93 (m, 2H), 4.23 (d, 2H, \(J = 3.3\) Hz), 1.97-2.05 (m, 1H), 1.71-1.75 (m, 4H), 1.62-1.68 (m, 1H), 1.06-1.33 (m, 5H), 0.22 (s, 9H).

\textsuperscript{13}C NMR (100 MHz, CDCl\textsubscript{3}) \(\delta\) 155.2, 137.5, 125.1, 94.4, 40.2, 32.7, 26.2, 26.0, 0.0

GC (cyclosil B, 90 °C): \(R_t\) 156 min

HRMS (ESI-MS): m/z 247.0391 ([M + Na]); exact mass calculated for C\textsubscript{13}H\textsubscript{26}O\textsubscript{3}SiNa 247.0389.
5,5-Dimethyl-2-trimethylsilyloxy-1,3(E)-hexadiene (8f): (Yield 45%).

\[
\text{\textsuperscript{1}H NMR} \quad (400 \text{ MHz, CDCl}_3) \delta 5.96 \text{ (ab quartet, 1H, } J = 15.6 \text{ Hz),} \\
5.79 \text{ (d, 1H, } J = 15.6 \text{ Hz),} \quad 4.25 \text{ (d, 2H, } J = 7.7 \text{ Hz),} \quad 1.04 \text{ (s, 9H),} \quad 0.23 \text{ (s, 9H).}
\]

\text{\textsuperscript{13}C NMR} (100 MHz, CDCl\textsubscript{3}) \delta 155.3, 142.4, 122.6, 94.5, 32.7, 29.5, 0.05.

GC (cyclosil B, 80 \textdegree C): \text{R,} 14.55 \text{ min}

HRMS (ESI-MS): m/z 221.1335 ([M + Na]); exact mass calculated for C\textsubscript{11}H\textsubscript{22}OSiNa
221.1332.

5-Methyl-2-trimethylsilyloxy-1,3(E)-hexadiene (8g): (Yield 49%) \text{\textsuperscript{1}H NMR} (400 MHz, CDCl\textsubscript{3}) \delta 5.94 \text{ (AB quartet, 1H, } J = 6.4 \text{ Hz),} \\
5.84 \text{ (d, 1H, } J = 15.6 \text{ Hz),} \quad 4.25 \text{ (d, 1H, } J = 4.4 \text{ Hz),} \quad 2.42 \text{ (octet, 1H, } J = 6.4 \text{ Hz),} \quad 1.03 \text{ (d, 6H, } J = 6.8 \text{ Hz),} \quad 0.24 \text{ (s, 9H).} \quad \text{\textsuperscript{1}H NMR shows a 10:1 ratio of E and Z compounds based upon integration of the isopropyl doublets.}

\text{\textsuperscript{13}C NMR} (100 MHz, CDCl\textsubscript{3}) \delta 155.1, 138.7, 124.8, 94.3, 30.6, 22.2, 0.00.

GC (cyclodex B, 75 \textdegree C): \text{R,} 71.07 \text{ min}

GC-MS (methyl silicone): m/z ([M+] 184.35; exact mass calculated for C\textsubscript{10}H\textsubscript{20}OSi
184.13.

(Z)-Trimethyl(penta-1,3-dien-3-yl)oxy)silane (8h): Prepared from commercially available pent-1-en-3-one (yield 82%) by literature
procedure.\textsuperscript{50} \( Z:E = 94:6 \). \(^1\)H NMR (400 MHz, CDCl\(_3\)) \( \delta \) 6.17 (dd, 1H, \( J = 17 \text{ Hz}, 10.6 \text{ Hz} \)), 5.22-5.27 (m, 1H), 4.92-4.95 (m, 1H), 4.88 (q, 1H, \( J = 7 \text{ Hz} \)), 1.65 (d, 3H, \( J = 7 \text{ Hz} \)), 0.22 (s, 9H).

\(^{13}\)C NMR (100 MHz, CDCl\(_3\)) \( \delta \) 136.3, 135.4, 111.3, 110.1, 30.8, 1.8.

GC (cyclosil B, 50 °C): \( R_t \) 15.86 min (\( E \)) and 18.07 min (\( Z \)).

GC-MS (methyl silicone): \( m/z \) ([M\(^+\)]) 156.33; exact mass calculated for \( \text{C}_8\text{H}_{16}\text{OSi} \) 156.10.

NOESY NMR confirms (\( E \))-\textbf{8h} due to observed nOe between the TMS group and hydrogens at C5.

\( (((2Z,4E)\text{-Hexa-2,4-dien-3-yl})\text{oxy})\text{trimethylsilane} \) (\textbf{8i}): Prepared from commercially available (\( E \))-hex-4-en-3-one and chlorotrimethylsilane (yield 68\%). (C2 \( Z:E = 85:15 \)). \(^1\)H NMR (600 MHz, CDCl\(_3\)) \( \delta \) 6.23 (minor \( E \), dq, 1H, \( J = 15 \text{ Hz}, 1.6 \text{ Hz} \)), 5.90-5.96 (minor \( E \), m, 1H), 5.86 (major \( Z \), dq, 1H, \( J = 15.2 \text{ Hz}, 1.6 \text{ Hz} \)), 5.68-5.74 (major \( Z \), m, 1H), 4.74-4.77 (minor \( E \), m, 1H), 4.73 (major \( Z \), q, 1H, \( J = 7 \text{ Hz} \)), 1.80 (minor \( E \), d, 1H, \( J = 6.8 \text{ Hz} \)), 1.74 (major \( Z \), d, 1H, \( J = 6.8 \text{ Hz} \)), 1.65 (minor \( E \), d, 1H, \( J = 7.3 \text{ Hz} \)), 1.74 (major \( Z \), d, 1H, \( J = 7.0 \text{ Hz} \)), 0.20 (major \( Z \), s, 9H), 0.18 (minor \( E \), s, 9H).

\(^{13}\)C NMR (150 MHz, CDCl\(_3\)) \( \delta \) 149.4, 129.9, 123.1, 107.1, 17.6, 11.5, 0.6. Minor C2 \( E \) isomer: 147.9, 125.8, 123.9, 104.5, 17.9, 11.3, 0.2.

GC (cyclosil B, 60 °C): \( R_t \) 20.52 min (\( E \)) and 22.19 min (\( Z \)).
GC-MS (*methyl silicone*): m/z ([M+] 170.22; exact mass calculated for C₉H₁₈OSi 170.11.

NOESY NMR confirms (*E*)-8i due to observed nOe between TMS group and hydrogens at C5.

\[(S,E)-((6,10\text{-dimethylundeca}-1,3,9\text{-trien}-2\text{-yl})oxy)\text{trimethylsilane (8j)}: \text{(Yield 71%)}\]

\[1^H \text{NMR (400 MHz, CDCl}_3\text{)} \delta 5.84-5.96 (m, 2H), 5.07-5.12 (m, 1H), 4.23 (s, 2H), 2.11 (td, 1H, \text{ } J = 14 Hz, 5.9 Hz), 1.90-2.04 (m, 3H), 1.68 (d, 3H, \text{ } J = 1 Hz), 1.60 (s, 3H), 1.49-1.56 (m, 1H), 1.30-1.40 (m, 1H), 1.11-1.20 (m, 1H), 0.88 (d, 3H, \text{ } J = 6.6 Hz), 0.22 (s, 9H).

\[13^C \text{NMR (100 MHz, CDCl}_3\text{)} \delta 154.9, 131.1, 130.5, 128.8, 124.8, 94.3, 39.5, 36.7, 32.8, 25.7, 25.6, 19.5, 17.6, 2.9, 0.05.

GC (cyclosil B, 130 °C): Rₜ 30.58 min.

HRMS (ESI-MS): m/z 289.1916 ([M + Na]); exact mass calculated for C₁₆H₃₀OSiNa 289.1920.

\[4\text{-Phenyl-2-trimethylsilyloxy-1,(E)-butadiene (8k): (Yield 59%)} \]

\[1^H \text{NMR (500 MHz, CDCl}_3\text{)} \delta 7.54 (d, 2H, \text{ } J = 7.5 Hz), 7.43 (t, 2H, \text{ } J = 7.5 Hz), 7.36 (t, 1H, \text{ } J = 7.5 Hz), 7.00 (d, 1H, \text{ } J = 15.5 Hz), 6.72 (d, 1H, \text{ } J = 16 Hz), 4.59 (d, 2H, \text{ } J = 15 Hz), 0.44 (s, 9H).

\[13^C \text{NMR (100 MHz, CDCl}_3\text{)} \delta 155.2, 136.9, 129.4, 128.7, 127.8, 126.9, 126.5, 97.0, 0.23.

GC (cyclosil B, 110 °C): Rₜ 76.49 min
HRMS (ESI-MS): m/z 241.1022 ([M + Na]); exact mass calculated for C_{13}H_{18}OSiNa 241.1029.

**1-Vinyl(1-trimethylsilyloxy)-1-cyclohexene (8l):** (Yield 63%) \(^1\)H NMR

(500 MHz, CDCl\(_3\)) \(\delta\) 6.17 (bs, 1H), 4.33 (s, 1H), 4.17 (s, 1H), 2.11 (m, 4m), 1.64 (q, 2H, \(J = 5.5\) Hz), 1.55 (q, 2H, \(J = 5.5\) Hz), 0.20 (s, 9H).

\(^{13}\)C NMR (125 MHz, CDCl\(_3\)) \(\delta\) 156.6, 133.1, 125.3, 89.7, 25.4, 24.9, 22.7, 22.2, 0.02.

GC (cyclosil B, 100 °C): R\(_t\) 22.49 min

HRMS (ESI-MS): m/z 219.1184 ([M + Na]); exact mass calculated for C_{11}H_{20}OSiNa 219.1176.

**1-Vinyl(1-trimethylsilyloxy)-1-cycloheptene (8m):** (Yield 71%) \(^1\)H NMR

(500 MHz, CDCl\(_3\)) \(\delta\) 6.31 (t, 1H, \(J = 7\) Hz), 4.46 (s, 1H), 4.22 (s, 1H), 2.30 (d, 2H, \(J = 5.5\) Hz), 2.10 (q, 2H, \(J = 7\) Hz), 1.72 – 1.75 (m, 2H), 1.45 – 1.51 (m, 2H), 0.20 (s, 9H).

\(^{13}\)C NMR (125 MHz, CDCl\(_3\)) \(\delta\) 157.2, 140.7, 129.9, 90.7, 32.3, 28.7, 28.1, 26.4, 26.3, 0.00.

GC (cyclosil B, 110 °C): R\(_t\) 21.99 min

HRMS (ESI-MS): m/z 233.1340 ([M + Na]); exact mass calculated for C_{12}H_{22}OSiNa 233.1332.
1-Vinyl(1-triethylsilyloxy)-1-cycloheptene (8n): Prepared from ketone precursor for 8m and chlorotriethylsilane (Yield 77%) \(^1\)H NMR (400 MHz, CDCl\(_3\)) \(\delta\) 6.38 (t, 1H, \(J = 7\) Hz), 4.4 (d, 1H, \(J = 0.8\) Hz), 4.23 (s, 1H), 2.31-2.34 (m, 2H), 2.19-2.24 (m, 2H), 1.73-1.77 (m, 2H), 1.47-1.53 (m, 4H), 0.99 (t, 9H, \(J = 7.7\) Hz), 0.71 (q, 6H, \(J = 7.8\) Hz).

\(^{13}\)C NMR (100 MHz, CDCl\(_3\)) \(\delta\) 157.5, 140.8, 129.8, 90.2, 32.4, 28.7, 28.1, 26.5, 26.4, 6.8, 4.9.

GC (cyclosil B, 140 °C): \(R_t\) 25.79 min

HRMS (ESI-MS): m/z 275.1809 ([M + Na]); exact mass calculated for C\(_{15}\)H\(_{28}\)OSiNa 275.1802.

1-Vinyl(1-tert-butyldimethylsilyloxy)-1-cycloheptene (8o): Prepared from ketone precursor for 8m and tert-butyldimethylsilylchloride (Yield 75%) \(^1\)H NMR (400 MHz, CDCl\(_3\)) \(\delta\) 6.36 (t, 1H, \(J = 7\) Hz), 4.45 (d, 1H, \(J = 0.8\) Hz), 4.22 (s, 1H), 2.31-2.33 (m, 2H), 2.19-2.23 (m, 2H), 1.74-1.77 (m, 2H), 1.47-1.54 (m, 4H), 0.96 (t, 9H), 0.16 (s, 6H).

\(^{13}\)C NMR (100 MHz, CDCl\(_3\)) \(\delta\) 157.7, 140.9, 129.9, 90.6, 32.4, 28.8, 28.1, 26.5, 26.4, 25.9, 18.3, -4.6.

GC (cyclosil B, 140 °C): \(R_t\) 16.82 min

HRMS (ESI-MS): m/z 275.1798 ([M + Na]); exact mass calculated for C\(_{15}\)H\(_{28}\)OSiNa 275.1802.
1-Vinyl(1-trimethylsilyloxy)-1-cyclooctene (8p): (Yield 72%) $^1$H NMR (500 MHz, CDCl$_3$) $\delta$ 6.15 (t, 1H, $J$ = 8.5 Hz), 4.46 (s, 1H), 4.25 (s, 1H), 2.36 (d, 2H, $J$ = 6.5 Hz), 2.16–2.20 (m, 2H), 1.43–1.57 (m, 8H), 0.19 (s, 9H).

$^{13}$C NMR (125 MHz, CDCl$_3$) $\delta$ 156.0, 136.5, 128.2, 91.3, 30.2, 29.1, 27.13, 27.10, 26.0, 25.2, 0.07.

GC (cyclosil B, 110 $^\circ$C): $R_t$ 31.01 min

HRMS (ESI-MS): m/z 247.1491 ([M + Na]); exact mass calculated for C$_{13}$H$_{24}$OSiNa 247.1489.

(E)-octa-1,3-dien-2-yl acetate (8q): Prepared from trans-3-octen-2-one (98%) and acetic anhydride. $^1$H NMR (400 MHz, CDCl$_3$) $\delta$ 5.95 (dt, 1H, $J$ = 15.6 Hz, 1.4 Hz), 5.75 (dt, 1H, $J$ = 15.6 Hz, 6.9 Hz), 4.882-4.884 (m, 1H), 4.76-4.77 (m, 1H), 2.22 (s, 3H), 2.08-2.13 (m, 2H), 1.27-1.41 (m, 4H), 0.89 (t, 3H, $J$ = 7.2 Hz).

$^{13}$C NMR (100 MHz, CDCl$_3$) $\delta$ 168.8, 151.9, 132.9, 123.9, 103.4, 31.9, 31.0, 22.2, 20.8, 13.9.

GC (cyclosil B, 100$^\circ$C): $R_t$ 21.014 mins

HRMS (ESI-MS): m/z 191.1060 ([M + Na]); exact mass calculated for C$_{10}$H$_{16}$O$_2$Na 191.1043.

(E)-deca-1,3-dien-2-yl acetate (8r): Prepared from trans-dec-3-en-2-one (98%) and acetic anhydride. $^1$H NMR (400 MHz, CDCl$_3$)
δ 5.95 (dt, 1H, J = 15.6 Hz, 1.3 Hz), 5.75 (dt, 1H, J = 15.6 Hz, 6.9 Hz), 4.88 (b, 1H), 4.76-4.77 (m, 1H), 2.22 (s, 3H), 2.07-2.12 (m, 2H), 1.35-1.43 (m, 2H), 1.27-1.36 (m, 6H), 0.88 (t, 3H, J = 6.7 Hz).

$^{13}$C NMR (100 MHz, CDCl$_3$) δ 168.7, 152.0, 132.9, 123.9, 103.3, 32.2, 31.6, 28.8, 22.6, 20.8, 14.0.

GC (cyclosil B, 130°C): R$_t$ 16.019 mins

HRMS (ESI-MS): m/z 219.1351 ([M + Na]); exact mass calculated for C$_{12}$H$_{20}$O$_2$Na 219.1331.

(E)-4-cyclohexylbuta-1,3-dien-2-yl acetate (8s): Prepared from ketone precursor of 8e and acetic anhydride. $^1$H NMR (400 MHz, CDCl$_3$) δ 5.91 (dd, 1H, J = 14.5 Hz, 1.2 Hz), 5.70 (dd, 1H, J = 15.7 Hz, 6.7 Hz), 4.89 (d, 1H, J = 1.0 Hz), 4.77 (d, 1H, J = 1.2 Hz), 2.22 (s, 3H), 1.97-2.05 (m, 1H), 1.68-1.77 (m, 4H), 1.63-1.68 (m, 1H), 1.04-1.31 (m, 5H).

$^{13}$C NMR (100 MHz, CDCl$_3$) δ 168.7, 152.2, 138.2, 121.6, 103.5, 40.2, 32.5, 26.1, 25.9, 20.8.

GC (cyclosil B, 130°C): R$_t$ 27.383 mins

HRMS (ESI-MS): m/z 217.1197 ([M + Na]); exact mass calculated for C$_{12}$H$_{18}$O$_2$Na 217.1199.

(E)-5-methylhexa-1,3-dien-2-yl acetate (8t): Prepared from ketone precursor of 8g and acetic anhydride. $^1$H NMR (400 MHz, CDCl$_3$) δ 5.91
(dd, 1H, J = 15.7 Hz, 1.2 Hz), 5.73 (dd, 1H, J = 15.7 Hz, 6.6 Hz), 4.90 (d, 1H, J = 1.0 Hz), 4.77 (d, 1H, J = 1.2 Hz), 2.32-2.40 (m, 1H), 2.22 (s, 3H).

$^{13}$C NMR (100 MHz, CDCl$_3$) $\delta$ 168.8, 152.0, 139.3, 121.3, 103.6, 30.7, 21.9, 21.4, 20.8.

GC (cyclosil B, 100 °C): R$_t$ 8.327 min

HRMS (ESI-MS): m/z 177.0885 ([M + Na]); exact mass calculated for C$_9$H$_{14}$O$_2$Na 177.0886.

OAc

1-(cyclohex-1-en-1-yl)vinyl acetate (8u): $^1$H NMR (400 MHz, CDCl$_3$) $\delta$

5.91 (t, 1H, J = 4.1 Hz), 4.96 (d, 1H, J = 1.0 Hz), 4.70 (d, 1H, J = 0.8 Hz), 2.21 (s, 3H), 2.15-2.19 (m, 2H), 2.11-2.14 (m, 2H), 1.64-1.72 (m, 2H), 1.55-1.63 (m, 2H).

$^{13}$C NMR (100 MHz, CDCl$_3$) $\delta$ 169.1, 153.8, 130.3, 125.8, 99.9, 25.3, 24.7, 22.3, 21.8, 20.8.

GC (cyclosil B, 100 °C): R$_t$ 38.676 mins

HRMS (ESI-MS): m/z 189.0879 ([M + Na]); exact mass calculated for C$_{10}$H$_{14}$O$_2$Na 189.0886.

OAc

1-(cyclohept-1-en-1-yl)vinyl acetate (8v): $^1$H NMR (400 MHz, CDCl$_3$) $\delta$

6.09 (t, 1H, J = 6.9 Hz), 5.05 (d, 1H, J = 1.9 Hz), 4.73 (d, 1H, J = 1.9 Hz), 2.35-2.37 (m, 2H), 2.21-2.24 (m, 2H), 2.19 (s, 3H), 1.73-1.79 (m, 2H), 1.46-1.57 (m, 4H).
Typical Procedure for Co(II)-Catalyzed Hydrovinylation Using Methylaluminoxane as Co-catalyst. Co(dppp)Cl₂ Catalyzed Hydrovinylation of 2-Trimethylsilyloxy-1,3-octadiene: To a flame-dried three-necked round-bottom flask equipped with a flow-control gas inlet, a rubber septum, and a magnetic stir-bar, [dppp]CoCl₂ catalyst (0.013 g, 0.024 mmol, 0.05 equivalents) and methylaluminoxane (0.055 g, 0.95 mmol, 2.0 equivalents with respect to the substrate, assuming a standard weight of 58.08 g/mol) were added while inside a glove box filled with nitrogen. The flask was removed from the glovebox with the flow-control inlet closed, placed on a vacuum line, and the stopcock opened to vacuum to remove the nitrogen, and subsequently purged with argon (Cobalt catalyst is sensitive under nitrogen in solution, all our hydrovinylation reactions have been performed under argon atmosphere). Distilled, dried dichloromethane (2.0 mL) was added at room temperature to make a 0.01 M solution with respect to the cobalt catalyst, and upon addition of dichloromethane, the solution turned dark red, indicating the formation of the organo-cobalt species. The flow control valve was closed to argon and an ethylene line was added through the septum. Two 25 mL volumes of gas were removed with a syringe while a stream of ethylene entered the flask, and then the flow of ethylene was reduced to
prevent solvent evaporation. After stirring under ethylene for five minutes, dried 2-
trimethylsilyloxy-1,3-octadiene (0.10 g, 0.475 mmol) was added in 0.5 mL dry, distilled
dichloromethane in one portion via syringe to the catalyst and the mixture was stirred at
room temperature (23 – 25 °C). Upon completion (reaction aliquot has been taken out
after every 15 min and injected in achiral methylsilicone column GC to monitor the
reaction), the flow-control stopcock was opened to air, and the solution was carefully
quenched at room temperature with 0.1 mL of MeOH. The solution was diluted with 5
mL pentanes and filtered through a plug of celite on a fretted funnel, washing with (4 x 5
mL) portions of pentanes. The solvent was removed in vacuo to give the product as a
clear oil (>99% conversion by GC, 91% isolated yield). The resulting oil was clean
enough for characterization.

\[
\text{OTMS} \quad \text{Typical Procedure for Asymmetric Co(II)-Catalyzed}
\]

\[
\text{Hydrovinylation Using Methylaluminoxane as Co-catalyst.}
\]

\[
\text{Co[(S,S)-BDPP)]Cl}_2 \quad \text{Catalyzed Hydrovinylation of 2-Trimethylsilyloxy-1,3-}
\]

\[
\text{octadiene: To a flame-dried three-necked round-bottom flask equipped with a flow-}
\]

\[
\text{control gas inlet, a rubber septum, and a magnetic stir-bar, (S,S-BDPP)CoCl}_2 \text{ catalyst}
\]

\[
(0.014 \text{ g, 0.024 mmol, 0.05 equivalents}) \text{ and methylaluminoxane (0.055 g, 0.95 mmol,}
\]

\[
2.0 \text{ equivalents with respect to the substrate, assuming a standard weight of 58.08 g/mol)
\]

\[
\text{were added while inside a glove box filled with nitrogen. The flask was removed from}
\]

\[
\text{the glovebox with the flow-control inlet closed, placed on a vacuum line, and the}
\]

\[
\text{stopcock opened to vacuum to remove the nitrogen, and subsequently purged with argon.}
\]

\[
\text{Distilled, dried dichloromethane (2.0 mL) was added at room temperature to make a 0.01}
\]

\[
\text{M solution with respect to the cobalt catalyst, and upon addition of dichloromethane, the}
\]
solution turned dark red, indicating the formation of the organo-cobalt species. The flow control valve was closed to argon and an ethylene line was added through the septum. Two 25 mL volumes of gas were removed with a syringe while a stream of ethylene entered the flask, and then the flow of ethylene was reduced to prevent solvent evaporation. After stirring under ethylene for five minutes, dried 2-trimethylsilyloxy-1,3-octadiene (0.10 g, 0.475 mmol) was added in 0.5 mL dry, distilled dichloromethane in one portion via syringe to the catalyst and the mixture was stirred at room temperature (23 – 25 °C). Upon completion (reaction aliquot has been taken out after every half an hour and injected in achiral methylsilicone column GC to monitor the reaction), the flow-control stopcock was opened to air, and the solution was carefully quenched at room temperature with 0.1 mL of MeOH. The solution was diluted with 5 mL pentanes and filtered through a plug of celite on a fretted funnel, washing with (4 x 5 mL) portions of pentanes. The solvent was removed \textit{in vacuo} to give the product as clear oil (>99% conversion by GC, 90% isolated yield). The resulting oil was clean enough for characterization.

\textbf{Preparative Scale: Typical Procedure for Asymmetric Co(II)-Catalyzed Hydrovinylation Using Methylaluminoxane as Co-catalyst.} \((S,S)\text{-BDPP})\text{CoCl}_2\text{Catalyzed Hydrovinylation of 1-Vinyl(1-trimethylsilyloxy)-1-cycloheptene:}\) To a flame-dried three-necked round-bottom flask equipped with a flow-control gas inlet, a rubber septum, and a magnetic stir-bar, [(S,S)-BDPP]CoCl\textsubscript{2} catalyst (0.0016 g, 0.0028 mmol, 0.001 equivalents) and methylaluminoxane (0.275 g, 4.76 mmol, 2.0 equivalents with respect to the substrate, assuming a standard weight of 58.08 g/mol) were added while inside a glove box filled with nitrogen. The flask was removed
from the glovebox with the flow-control inlet closed, placed on a vacuum line, and the stopcock opened to vacuum to remove the nitrogen, and subsequently purged with argon. Distilled, dried dichloromethane (4.0 mL) was added at room temperature to make a 0.5 M solution with respect to the substrate, and upon addition of dichloromethane, the solution turned dark red, indicating the formation of the organo-cobalt species. The flow control valve was closed to argon and an ethylene line was added through the septum. Two 25 mL volumes of gas were removed with a syringe while a stream of ethylene entered the flask, and then the flow of ethylene was reduced to prevent solvent evaporation. After stirring under ethylene for five minutes, dried 1-Vinyl(1-trimethylsilyloxy)-1-cycloheptene (0.50 g, 2.38 mmol) was added in 0.5 mL dry, distilled dichloromethane in one portion via syringe to the catalyst and the mixture was stirred at room temperature (23 – 25 °C) for 36 h. Upon completion (reaction aliquot has been taken out after every 6h and injected in achiral methyilsilicone column GC to monitor the reaction), the flow-control stopcock was opened to air, and the solution was carefully quenched at room temperature with 2.0 mL of MeOH. The solution was diluted with 10 mL pentanes and filtered through a plug of celite on a fretted funnel, washing with (4 x 5 mL) portions of pentanes. The solvent was removed in vacuo to give the product as a clear oil (>99% conversion by GC, 93% isolated yield of the crude). The resulting oil was further purified by Kugelrohr distillation method (Yield after distillation 54%).

\[
\begin{align*}
\text{4-Vinyl-2-trimethylsilyloxy-2(E)-octene (9a): } & \ \text{\textsuperscript{1}H NMR (500 MHz, CDCl}\textsubscript{3}) \ \delta \ 5.68 \ (\text{ddd, } 1\text{H, } J = 4 \ \text{Hz, 6.5 Hz, 10 Hz}), \ 4.92 \ (\text{d, } 1\text{H, } J = 17 \ \text{Hz}), \ 4.87 \ (\text{d, } 1\text{H, } J = 10 \ \text{Hz}), \ 4.46 \ (\text{d, } 1\text{H, } J = 9.5 \ \text{Hz}), \ 2.67 \ (\text{quintet, } 1\text{H, } J = 7 \ \text{Hz}), \\
1.70 \ (\text{s, } 3\text{H}), \ 1.19 – 1.28 \ (\text{m, } 6\text{H}), \ 0.86 \ (\text{t, } 3\text{H, } J = 6.5 \ \text{Hz}), \ 0.18 \ (\text{s, } 9\text{H}).
\end{align*}
\]
$^{13}$C NMR (125 MHz, CDCl$_3$) δ 147.9, 142.6, 112.3, 111.3, 41.8, 35.7, 29.4, 22.7, 18.1, 14.0, 0.34.

GC (cyclosil B, 50 °C): R$_f$ from dppp: 252.13 min and 255.58 min; (S,S-BDPP)CoCl$_2$-derived product: 252.58 min (8%) and 255.60 min (92%); (S,S-DIOP)CoCl$_2$-derived product: 248.87 min (>99%).

HRMS (ESI-MS): m/z 227.1523 ([M+H]); exact mass calculated for C$_{13}$H$_{27}$OSi 227.1831.

$[\alpha]_D^{23}$ (c = 0.852, CHCl$_3$) + 7.22 [from (S,S-BDPP)]. $[\alpha]_D^{23}$ (c = 0.63, CHCl$_3$) − 5.6 [from (S,S-DIOP)]

NOESY NMR confirms (E)-9a due to observed nOe between α-enol hydrogen and TMS group and α-CH$_3$ with newly installed vinyl group.

Absolute stereochemistry has been determined by hydrolyzing enantiomERICALLY pure 9a to corresponding ketone 11a. Ketone 11a was further reduced to known literature compound 12a to confirm the absolute stereochemistry.$^{53}$ Hydrolysis procedure of 9a to synthesize 11a and hydrogenation procedure of 11a to 12a has been described later in hydrolysis procedure part. [(S,S)-BDPP]CoCl$_2$ introduces (S)-configuration at the stereogenic center, whereas [(S,S)-DIOP]CoCl$_2$ introduces (R)-configuration.

**4-Vinyl-2-triethylsilyloxy-2(E)-octene (9b):** $^1$H NMR (400 MHz, C$_6$D$_6$) δ 5.74 (ddd, 1H, J = 6.6 Hz, 10.3 Hz, 17.1 Hz), 5.06 (dt, 1H,
$J = 1.6 \text{ Hz}, 17.2 \text{ Hz}$), 4.97 (dt, 1H, $J = 1.3 \text{ Hz}, 10.2 \text{ Hz}$), 4.65 (dd, 1H, $J = 0.7 \text{ Hz}, 9.4 \text{ Hz}$), 2.68-2.76 (m, 1H), 1.74 (d, 3H, $J = 0.8 \text{ Hz}$), 1.17-1.45 (m, 6H), 1.01 (t, 9H, $J = 8 \text{ Hz}$), 0.84-0.89 (m, 3H), 0.68 (q, 6H, $J = 7.8 \text{ Hz}$).

$^1$H NMR (400 MHz, CDCl$_3$) δ 5.65-5.74 (m, 1H), 4.91-4.98 (m, 1H), 4.87-4.91 (m, 1H), 4.47 (dd, 0.5H, $J = 0.8 \text{ Hz}, 9.5 \text{ Hz}$), 4.23 (dd, 0.5H, $J = 0.8 \text{ Hz}, 9.3 \text{ Hz}$), 3.06-3.12 (m, 0.5H), 2.65-2.72 (m, 0.5H), 1.81 (d, 1.5H, $J = 0.8 \text{ Hz}$), 1.74 (d, 1.5H, $J = 0.9 \text{ Hz}$), 1.25-1.30 (m, 6H), 0.96-1.01 (m, 9H), 0.86-0.90 (m, 3H), 0.64-0.69 (m, 6H).

$^{13}$C NMR (100 MHz, C$_6$D$_6$) δ 149.4, 143.5, 113.1, 110.8, 42.9, 36.8, 30.5, 23.7, 18.9, 14.9, 7.6, 6.2.

$^{13}$C NMR (100 MHz, CDCl$_3$) δ 148.1, 146.5, 142.7, 112.2, 110.8, 110.5, 41.8, 39.6, 35.7, 35.2, 29.4, 22.8, 22.7, 22.6, 18.0, 14.1, 6.8, 6.7, 5.7, 5.1, 1.0

GC of compound 11a (ketone) (cyclosil B, 50 °C): R$_t$ from dpdp: 147.99 min and 150.60 min; from (S,S-BDPP): 150.64 min (20.6%) and 152.19 (79.4%); from (S,S-DIOP): 148.942 min (>95%).

HRMS (ESI-MS): $m/z$ 291.2240 ([M+Na]); exact mass calculated for C$_{16}$H$_{32}$OSiNa 291.2232.

$[\alpha]_D^{23} (c = 0.09, \text{CHCl}_3) +5.22$ [from (S,S-BDPP)]

4-Vinyl-2-dimethyl-t-butylsilyloxy-2(E)-octene (9c): Crude compound purified as corresponding ketone. $^1$H NMR (400 MHz, CDCl$_3$) δ 5.70 (ddd, 1H, $J = 6.7 \text{ Hz}, 10.3 \text{ Hz}, 17.2 \text{ Hz}$), 4.95 (ddd, 1H, $J = 1.5 \text{ Hz}, 1.8\text{Hz}$,
17 Hz), 4.89 (ddd, 1H, $J = 1.3$ Hz, 1.8 Hz, 10.2 Hz), 4.47 (dq, 1H, $J = 1$ Hz, 9.5 Hz),
2.65-2.72 (m, 1H), 1.72 (d, 3H, $J = 1.0$ Hz), 1.21-1.36 (m, 6H), 0.92-0.95 (m, 9H), 0.87-
0.90 (m, 3H), 0.13 (s, 6H).

$^{13}$C NMR (100 MHz, CDCl$_3$) $\delta$ 148.2, 142.6, 112.3, 111.1, 41.9, 35.7, 29.4, 25.7, 22.7,
18.1, 18.0, 14.1, -4.37, -4.40

GC of compound 11a (ketone) (cyclosil B, 50 °C): $R_t$ from dppp: 147.99 min and 150.60
min; from ($S$,$S$-BDPP): 151.32 min (21%) and 152.99 (79%); from ($S$,$S$-DIOP): 151.97
min (>95%).

HRMS (ESI-MS): $m/z$ 291.2237 ([M+Na]); exact mass calculated for C$_{16}$H$_{32}$O$_7$SiNa
291.2232.

[OTMS] 4-Vinyl-2-trimethylsilyloxy-2(E)-dece (9d): $^1$H NMR (400
MHz, CDCl$_3$) $\delta$ 5.70 (ddd, 1H, $J = 6.8$ Hz, 10.3 Hz, 17.1 Hz),
4.95 (dt, 1H, $J = 1.7$ Hz, 17.2 Hz), 4.89 (dt, 1H, $J = 1.4$ Hz, 10.2 Hz), 4.46 (dq, 1H, $J =$
1.3 Hz, 9.5 Hz), 2.66-2.73 (m, 1H), 1.72 (d, 3H, $J = 1.0$ Hz), 1.26-1.31 (m, 10H), 0.88 (t,
3H, $J = 6.7$ Hz), 0.19 (s, 9H).

$^{13}$C NMR (100 MHz, CDCl$_3$) $\delta$ 147.9, 142.6, 112.3, 111.3, 41.8, 36.0, 31.9, 29.3, 27.2,
22.6, 18.1, 14.1, 0.3

GC (cyclosil B, 70 °C): $R_t$ from dppp: 322.31 min and 326.53 min; from ($S$,$S$-BDPP):
322.97 min (10%) and 324.66 min (90%); from ($S$,$S$-DIOP): 320.48 min (>99%).
HRMS (ESI-MS): m/z 277.1949 ([M+Na]); exact mass calculated for C_{15}H_{30}OSiNa 227.1831.

[α]_D^{23} (c = 1.5, CHCl_3) – 3.0 [from (S,S-DIOP)]

4-Cyclohexyl-4-vinyl-2-trimethylsilyloxy-2(E)-butene (9e): ¹H NMR (400 MHz, CDCl_3) δ 5.64-5.73 (m, 1H), 4.93-4.95 (m, 1H), 4.89-4.92 (m, 1H), 4.58 (dd, 1H, J = 9.9 Hz, 0.9 Hz), 2.49-2.55 (m, 1H), 1.71 (d, 3H, J = 0.9 Hz), 1.61-1.66 (m, 1H), 1.05-1.11 (m, 7H), 0.84-1.01 (m, 3H), 0.19 (s, 9H).

¹³C NMR (100 MHz, CDCl_3) δ 148.0, 141.2, 113.2, 109.5, 48.2, 42.8, 31.1, 30.1, 26.6, 26.5, 26.49, 18.2, 0.4

GC (cyclosil-B, 90 °C): R_t from dppp: 117.85 min and 121.66 min; from (S,S-BDPP): 117.22 min (95.5%) and 216.14 min (1.5%).

HRMS (ESI-MS): m/z 275.1901 ([M+Na]); exact mass calculated for C_{15}H_{28}OSiNa 275.1911.

[α]_D^{23} (c = 1.1, CHCl_3) + 1.5 [from (S,S-BDPP)]

5,5-Dimethyl-4-vinyl-2-trimethylsilyloxy-2(E)-hexene (9f): ¹H NMR (400 MHz, CDCl_3) δ 5.76 (ddd, 1H, J = 15.5 Hz, 8.9 Hz, 7.9 Hz), 4.95-4.97 (m, 1H), 4.93 (ddd, 1H, J = 9.4 Hz, 2.1 Hz, 0.8 Hz), 4.67 (dq, 1H, J = 10.2 Hz, 0.9 Hz), 2.44-2.49 (m, 1H), 1.72 (d, 3H, J = 1.0 Hz), 0.86 (s, 9H), 0.19 (s, 9H).

¹³C NMR (100 MHz, CDCl_3) δ 148.1, 139.3, 114.3, 108.4, 52.9, 33.8, 27.6, 18.1, 0.40

GC (cyclosil-B, 50 °C): R_t from dppp: 20.86 min and 21.86 min.
HRMS (ESI-MS): \( m/z \ 249.1644 \) ([M+Na]); exact mass calculated for \( \text{C}_{13}\text{H}_{26}\text{OSiNa} \)
249.1645.

\[
\text{5-Methyl-4-vinyl-2-trimethylsilyloxy-2(}E\text{-hexene (9g):} \quad \text{\( ^1\text{H NMR} \)}
\]
(500 MHz, CDCl\( _3 \)) \( \delta \ 5.66-5.73 \) (m, 1H), 4.95 (d, 1H, \( J = 4 \)Hz), 4.93 (d, 1H, \( J = 12 \)Hz), 4.57 (d, 1H, \( J = 9.5 \)Hz), 2.49 – 2.53 (m, 1H), 1.72 (s, 3H), 1.57-1.64 (m, 1H), 0.83-0.91 (m, 6H), 0.21 (s, 9H).

\( ^{13}\text{C NMR} \) (125 MHz, CDCl\( _3 \)) \( \delta \ 148.3, 141.2, 113.5, 109.0, 48.8, 32.9, 20.5, 19.4, 18.2, 0.36.

GC (cyclosil-\( B, \) 50 \(^\circ \)C): \( R_t \) from dppp: 213.89 min and 218.71 min; from (\( S,S\)-BDPP): 217.13 min (99.48\%) and 216.14 min (0.52\%).

GS-MS (methyl silicone): \( m/z \ 212.30 \) ([M+]); exact mass calculated for 212.16.

\( [\alpha]_D^{23} \ (c = 17.7, \text{CHCl}_3) = + 10.35 \) [from (\( S,S\)-BDPP)]

\[
(E)-\text{Trimethyl(4-methylhexa-2,5-dien-3-yl)oxy)silane (9h):} \quad \text{\( ^1\text{H NMR} \)}
\]
(400 MHz, CDCl\( _3 \)) \( \delta \ 5.84 \) (ddd, 1H, \( J = 7 \) Hz, 10.2 Hz, 17.3 Hz), 5.03 (dt, 1H, \( J = 1.6 \) Hz, 17.3 Hz), 4.96 (ddd, 1H, \( J = 1.2 \) Hz, 1.8 Hz, 10.2 Hz), 4.55 (q, 1H, \( J = 6.8 \) Hz), 3.22-3.30 (m, 1H), 1.57 (d, 3H, \( J = 6.8 \) Hz), 1.09 (d, 3H, \( J = 6.9 \) Hz).

\( ^{13}\text{C NMR} \) (100 MHz, CDCl\( _3 \)) \( \delta \ 153.9, 141.0, 113.2, 99.4, 38.0, 17.3, 11.3, 0.4.

GC (cyclosil-\( B, \) 50 \(^\circ \)C): \( R_t \) from dppp: 22.95 min and 23.78 min (1,4-\( E \)) and 37.07 min (20\% -1,4-linear); from (\( S,S\)-BDPP): 23.20 min (3\%) and 23.99 min (88\%) (1,4-\( E \)) and 37.46 min (9\% 1,4-linear).
GC-MS (methyl silicone): m/z ([M+] 184.33; exact mass calculated for C_{10}H_{20}OSi 184.35.

[α]_D^{23} (c = 0.6, CHCl_3) + 32.7 [from (S,S-BDPP)]

(E)-trimethyl((5-methylhepta-3,6-dien-3-yl)oxy)silane (9i): Crude $^1$H NMR (600 MHz, CDCl_3) δ 5.76-5.80 (m, 1H), 4.97 (dt, 1H, $J = 1.7$ Hz, 17.2 Hz), 4.88 (dt, 1H, $J = 1.6$ Hz, 10.3 Hz), 4.43 (d, 1H, $J = 9.4$ Hz), 2.89-2.94 (m, 1H), 2.04-2.09 (m, 2H), 1.06 (d, 3H, $J = 6.9$ Hz), 1.02 (t, 3H, $J = 7.5$ Hz). Product was purified by hydrolysis of silylenolether to compound 11i

GC (cyclosil-B, 60 °C): R_t from dppp: 24.46 min (46%) and 24.76 min (46%) and minor impurities at 34.14 min (5%) and 45.41 (3%).

GC-MS (methyl silicone): m/z ([M+] 198.03; exact mass calculated for C_{11}H_{22}OSi 198.38.

[(4R,6S,E)-6,10-Dimethyl-4-vinylundeca-2,9-dien-2-yl)oxy]trimethylsilane [9j via (S,S-DIOP)CoCl_2-catalyzed reaction]: $^1$H NMR (400 MHz, CDCl_3) δ 5.70 (ddd, 1H, $J = 6.4$ Hz, 10.2 Hz, 16.8 Hz), 5.07-5.11 (m, 1H), 4.95 (dt, 1H, $J = 1.7$ Hz, 17.2 Hz), 4.88 (ddd, 1H, $J = 1.3$ Hz, 1.8 Hz, 10.2 Hz), 4.42 (dd, 1H, $J = 0.8$ Hz, 9.5 Hz), 2.78-2.86 (m, 1H), 1.91-2.02 (m, 2H), 1.73 (d, 3H, $J = 0.9$ Hz), 1.68 (d, 3H, $J = 1$ Hz), 1.60 (b, 3H), 1.44-1.52 (m, 1H), 1.12-1.37 (m, 4H), 0.85 (d, 3H, $J = 6.6$ Hz), 0.18 (s, 9H).

$^{13}$C NMR (100 MHz, CDCl_3) δ 148.1, 142.9, 131.0, 124.9, 112.0, 111.1, 43.3, 39.4, 37.7, 29.9, 25.7, 25.5, 19.2, 18.1, 17.6, 0.3.
GC (cyclosil B, 130 °C): R_t from dppp: 32.50 min and 33.19 min; from (S,S-DIOP): 32.52 min (95.5%) and 33.12 min (2.7%) (diastereomeric ratio 97:3).

HRMS (ESI-MS): m/z 317.2241 ([M+Na]); exact mass calculated for C_{18}H_{34}OSiNa 317.2232.

[α]_D^{23} (c = 1.65, CHCl_3) + 3.1 [from (S,S-DIOP)]

(((4S,6S,E)-6,10-Dimethyl-4-vinylundeca-2,9-dien-2-yl)oxy)trimethylsilane [9j- via (R,R-DIOP)CoCl_2-catalyzed reaction]: \(^1\)H NMR (600 MHz, CDCl_3) δ 5.54 (ddd, 1H, J = 8.8 Hz, 10.2 Hz, 17.1 Hz), 5.08-5.11 (m, 1H), 4.95 (dt, 1H, J = 1.7 Hz, 17.2 Hz), 4.89 (ddd, 1H, J = 1.2 Hz, 1.7 Hz, 10.2 Hz), 4.48 (dd, 1H, J = 0.7 Hz, 9.5 Hz), 2.78-2.83 (m, 1H), 1.88-2.03 (m, 2H), 1.73 (d, 3H, J = 0.8 Hz), 1.68 (d, 3H, J = 0.8 Hz), 1.60 (b, 3H), 1.45-1.50 (m, 1H), 1.28-1.38 (m, 4H), 0.89 (d, 3H, J = 6.6 Hz), 0.18 (s, 9H).

\(^{13}\)C NMR (100 MHz, CDCl_3) δ 147.7, 142.4, 130.9, 124.9, 112.3, 111.6, 43.6, 39.6, 36.7, 29.8, 25.7, 25.4, 19.9, 18.1, 17.6, 0.3.

GC (cyclosil B, 130 °C): R_t from dppp: 32.50 min and 33.19 min; from (R,R-DIOP): 32.46 min (4.1%) and 33.19 min (91.25%) (diastereomeric ratio 4:96).

HRMS (ESI-MS): m/z 317.2241 ([M+Na]); exact mass calculated for C_{18}H_{34}OSiNa 317.2232.

[α]_D^{23} (c = 0.52, CHCl_3) – 5.6 [from (R,R-DIOP)]
[(4R,6R,E)-6,10-Dimethyl-4-vinylundeca-2,9-dien-2-yl]oxy)trimethylsilane [9j via (S,S-DIOP)CoCl₂-catalyzed reaction]: ¹H NMR (400 MHz, CDCl₃) δ 5.65 (ddd, 1H, J = 6.7 Hz, 10.2 Hz, 17.2 Hz), 5.08-5.11 (m, 1H), 4.87-4.96 (m, 2H), 4.46-4.49 (m, 1H), 2.77-2.84 (m, 1H), 2.17-2.32 (m, 2H), 1.73 (b, 3H), 1.68 (b, 3H), 1.60 (b, 3H), 1.45-1.55 (m, 1H), 1.12-1.37 (m, 4H), 0.88-0.89 (m, 3H), 0.18 (s, 9H).

¹³C NMR (100 MHz, CDCl₃) δ 147.7, 142.5, 130.99, 124.95, 112.3, 111.6, 43.6, 39.6, 36.8, 29.8, 25.7, 25.4, 19.9, 18.1, 17.6, 0.3.

GC (cyclasil B, 130 ℃): Rₜ from dppp: 32.68 min and 33.29 min; from (S,S-DIOP): 32.47 min (12%) and 33.21 min (74%) (diastereomeric ratio 74:12).

HRMS (ESI-MS): m/z 317.2241 ([M+Na]); exact mass calculated for C₁₈H₃₄OSiNa 317.2232.

[(4S,6R,E)-6,10-Dimethyl-4-vinylundeca-2,9-dien-2-yl]oxy)trimethylsilane [9j via (R,R-DIOP)CoCl₂-catalyzed reaction]: ¹H NMR (600 MHz, CDCl₃) δ 5.70 (ddd, 1H, J = 6.3 Hz, 10.2 Hz, 16.9 Hz), 5.07-5.11 (m, 1H), 4.95 (dt, 1H, J = 1.7 Hz, 17.2 Hz), 4.87-4.90 (m, 1H), 4.42 (dd, 1H, J = 0.7 Hz, 9.5 Hz), 2.78-2.85 (m, 1H), 1.89-2.05 (m, 2H), 1.73 (d, 3H, J = 0.8 Hz), 1.68 (b, 3H), 1.60 (b, 3H), 1.45-1.55 (m, 1H), 1.25-1.37 (m, 4H), 0.85-0.86 (m, 3H), 0.18 (s, 9H).

¹³C NMR (100 MHz, CDCl₃) δ 148.0, 142.9, 131.0, 124.9, 112.0, 111.1, 43.3, 39.4, 37.7, 29.9, 25.7, 25.5, 19.2, 18.1, 17.6, 0.3.
GC (cyclosil B, 130 °C): R<sub>t</sub> from dppp: 32.68 min and 33.29 min; from (R,R-DIOP): 32.730 min (85%) and 33.207 min (11%) (diastereomeric ratio 85:11).

HRMS (ESI-MS): <i>m/z</i> 317.2241 ([M+Na]); exact mass calculated for C<sub>18</sub>H<sub>34</sub>O<sub>Si</sub>Na 317.2232.

1-Phenyl-3-trimethylsilyloxy-2,6-hexadiene (10k): <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>) δ 7.17-7.31 (m, 5H), 5.87 (ddt, 1H, J = 20 Hz, 10.1 Hz, 6.6 Hz), 5.12 (dq, 1H, J = 17 Hz, 1.6 Hz), 5.07 (dq, 1H, J = 10 Hz, 1.4 Hz), 4.87 (t, 1H, J = 7.8 Hz), 3.35 (d, 2H, J = 7.8 Hz), 2.93 (d, 2H, J = 6.6 Hz), 0.20 (s, 9H).

<sup>13</sup>C NMR (100 MHz, CDCl<sub>3</sub>) δ 150.5, 141.6, 134.6, 128.3, 128.1, 125.8, 116.2, 106.5, 36.3, 32.9, 0.4.

GC (cyclosil-B, 110 °C): R<sub>t</sub> from dppp: 70.04 min (1,4-linear).

HRMS (ESI-MS): <i>m/z</i> 269.1345 ([M+Na]); exact mass calculated for C<sub>15</sub>H<sub>22</sub>O<sub>Si</sub>Na 269.1332.

(E)-Trimethyl(1-(2-vinylcyclohexylidene)ethoxy)silane (9l): <sup>1</sup>H NMR (500 MHz, CDCl<sub>3</sub>) δ 5.80-5.87 (m, 1H), 4.98 (d, 1H, J = 10.5 Hz), 4.92 (d, 1H, J = 17.5 Hz), 3.14 (bs, 1H), 2.64 (dd, 1H, J = 3.5 Hz, 11.5 Hz), 1.78 (d, 1H, J = 1.5 Hz), 1.77 (s, 3H), 1.63 – 1.69 (m, 3H), 1.10 – 1.29 (m, 3H), 0.15 (s, 9H).

<sup>13</sup>C NMR (125 MHz, CDCl<sub>3</sub>) δ 141.3, 139.9, 117.9, 113.9, 39.9, 32.3, 26.8, 23.0, 21.7, 18.0, 0.59.
GC (cyclosil-B, 100 °C): R<sub>t</sub> from dppp: 28.16 min and 30.11 min; from (S,S-BDPP): 28.115 min (96%) and 30.671 min (4%).

HRMS (ESI-MS): m/z 247.1491 ([M+Na]); exact mass calculated for C<sub>13</sub>H<sub>24</sub>OSiNa 247.1489.

[α]<sub>D</sub><sup>23</sup> (c = 0.78, CHCl<sub>3</sub>) + 115.0 [from (S,S-BDPP)]

Absolute stereochemistry has been determined by hydrolyzing enantiomerically pure 9l to corresponding ketone 11l-cis. Ketone 11l-cis showed cis stereochemistry as the major diastereomer which has been transformed in to ketone 11l-trans by the known literature method<sup>51</sup> and confirmed the stereochemistry of the molecule.<sup>52-54</sup> Ketone 11l-trans was further reduced to known literature compound 12l-trans to confirm the absolute stereochemistry.<sup>52-54</sup> (S,S-BDPP)CoCl<sub>2</sub> introduces (R)-configuration at the stereogenic center in the cyclic series.

$$\text{(E)-Trimethyl(1-(2-vinylcycloheptylidene)ethoxy)silane (9m): } ^1\text{H NMR}$$

(400 MHz, CDCl<sub>3</sub>) δ 5.69 (ddd, 1H, J = 17 Hz, 10.5 Hz, 6 Hz), 4.88 (dt, 1H, J = 10 Hz, 2 Hz), 4.85 (quintet, 1H, J = 2 Hz), 2.99 (tq, 1H, J = 6 Hz, 1.4 Hz), 2.58 (dd, 1H, J = 13.4 Hz, 5.6 Hz), 1.86-1.93 (m, 1H), 1.76 (s, 3H), 1.67-1.75 (m, 2H), 1.49-1.58 (m, 2H), 1.29-1.40 (m, 1H), 1.28-1.15 (m, 3H), 0.19 (s, 9H).

$^{13}$C NMR (100 MHz, CDCl<sub>3</sub>) δ 142.8, 141.8, 120.5, 111.4, 44.7, 33.8, 31.3, 29.5, 26.4, 25.2, 18.2, 0.77.

GC (cyclosil-B, 110 °C): R<sub>t</sub> from dppp: 25.99 min and 26.35 min; from (S,S-BDPP): 26.01 min (97.8%) and 26.36 min (2.4%).
HRMS (ESI-MS): m/z 239.1454 ([M+H]); exact mass calculated for C_{14}H_{27}OSi 239.1651.

[α]_D^{23} (c = 0.309, CHCl_3) – 11.77. [from (S,S-BDPP)]

NOESY NMR confirms (E)-9m due to observed nOe between α-enol hydrogen and TMS group and α-CH_3 with newly installed vinyl group.

\[\text{(E)-triethyl(1-(2-vinylcycloheptylidene)ethoxy)silane (9n):} \]
\[\text{^1H NMR (400 MHz, CDCl}_3\text{)} \delta 5.69 (ddd, 1H, J = 16.8 Hz, 10.6 Hz, 6.3 Hz), 4.84-4.90 (m, 2H), 2.95-3.01 (m, 1H), 2.65 (dd, 1H, J = 13.3 Hz, 5.8 Hz), 1.86-1.93 (m, 1H), 1.78 (s, 3H), 1.68-1.75 (m, 2H), 1.50-1.57 (m, 3H), 1.12-1.40 (m, 3H), 0.99 (t, 9H, J = 7.9 Hz), 0.67 (q, 6H, J = 7.7 Hz).\]

\[\text{^13C NMR (100 MHz, CDCl}_3\text{)} \delta 142.9, 141.9, 119.8, 111.4, 44.9, 33.8, 31.4, 29.6, 26.4, 25.1, 18.2, 6.8, 5.79.\]

GC (cyclosil-B, 125 °C): R_t from dppp: 65.40 min and 66.55 min; from (S,S-BDPP): 65.77 min (96.6%) and 66.53 min (3.4%).

HRMS (ESI-MS): m/z 303.2221 ([M+Na]); exact mass calculated for C_{17}H_{32}OSiNa 303.2230.

[α]_D^{23} (c = 1.4, CHCl_3) + 2.4. [from (S,S-BDPP)]

\[\text{(E)-Triethyl(1-(2-vinylcycloheptylidene)ethoxy)silane (9o):} \]
\[\text{^1H NMR (400 MHz, CDCl}_3\text{)} \delta 5.70 (ddd, 1H, J = 16.7 Hz, 10.2 Hz, 6.2 Hz), 4.84-4.90 (m,} \]

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2H), 2.96-3.02 (m, 1H), 2.66 (dd, 1H, J = 13.6 Hz, 6.2 Hz), 1.85-1.93 (m, 1H), 1.77 (s, 3H), 1.68-1.75 (m, 2H), 1.15-1.40 (m, 6H), 0.95 (s, 9H), 0.14 (s, 3H) 0.13 (s, 3H).

$^{13}$C NMR (100 MHz, CDCl$_3$) $\delta$ 142.8, 141.9, 120.0, 111.3, 44.9, 33.8, 31.4, 29.8, 26.4, 25.96, 24.9, 22.3, 18.2, 14.0, -3.46, -3.80

GC (cyclosil-B, 125 °C): R, from dppp: 42.92 min and 44.13 min; from (S,S)-BDPP: 42.98 min (93.3%) and 44.14 min (6.7%).

HRMS (ESI-MS): m/z 303.2234 ([M+Na]); exact mass calculated for C$_{17}$H$_{32}$OSiNa 303.2230.

$[\alpha]_D^{23}$ (c = 1.5, CHCl$_3$) – 2.0. [from (S,S)-BDPP]

(E)-Trimethyl(1-(2-vinyleclocyloctyldene)ethoxy)silane (9p): $^1$H NMR (500 MHz, CDCl$_3$) $\delta$ 5.67 – 5.72 (m, 1H), 4.88 (d, 1H, $J = 12.5$ Hz), 4.85 (d, 1H, $J = 8$ Hz), 2.83 – 2.89 (m, 1H), 2.42 (dd, 2H, $J = 3$ Hz, 6 Hz), 1.87 – 1.91 (m, 2H), 1.81 (s, 3H), 1.45 – 1.74 (m, 8H), 0.21 (s, 9H).

$^{13}$C NMR (125 MHz, CDCl$_3$) $\delta$ 142.4, 141.9, 119.4, 111.4, 44.6, 28.6, 28.2, 27.9, 25.9, 25.6, 25.3, 18.1, 0.96.

GC (cyclosil-B, 110 °C): R, from dppp: 42.77 min and 43.56 min; from (S,S-BDPP): 64.74 min (99.74%) and 69.11 (0.26%).

HRMS (ESI-MS): m/z 253.1628 ([M+H]); exact mass calculated for C$_{15}$H$_{29}$OSi 253.1988.

$[\alpha]_D^{23}$ (c = 21.4, CHCl$_3$) – 3.91 [from (S,S-BDPP)]
(E)-4-vinylcyclohexenyl acetate (9q): \( ^1\)H NMR (400 MHz, CDCl\(_3\)) \( \delta \) 5.71 (ddd, 1H, \( J = 10.4 \) Hz, 10.4 Hz, 6.5 Hz), 5.03 (dt, 1H, \( J = 17 \) Hz, 1.6 Hz), 4.95-4.98 (m, 2H), 2.76-2.83 (m, 1H), 2.11 (s, 3H), 1.85 (d, 3H, \( J = 1.0 \) Hz), 1.24-1.39 (m, 6H), 0.87-0.91 (m, 3H).

\( ^{13}\)C NMR (100 MHz, CDCl\(_3\)) \( \delta \) 169.5, 145.7, 140.8, 119.9, 113.7, 41.2, 35.1, 29.9, 22.6, 21.0, 15.5, 14.0

GC (cyclosil B, 70°C): \( R_t \) from dppp: 110.634 mins and 112.667 mins; from (S,S-BDPP): 110.515 mins (other enantiomer not visible in GC).

HRMS (ESI-MS): \( m/z \) 219.1361 ([M+Na]); exact mass calculated for \( \text{C}_{12}\text{H}_{20}\text{O}_{2}\text{Na} \) 219.1356.

\([\alpha]_D^{23}\) (c = 0.4, CHCl\(_3\)) – 4.0. [from (S,S)-DIOP].

NOESY NMR confirms (E)-9q due to observed nOe between allyl-\( \text{CH}_3 \) with newly installed vinyl group.

(E)-4-vinyldec-2-en-2-yl acetate (9r): \( ^1\)H NMR (400 MHz, CDCl\(_3\)) \( \delta \) 5.70 (ddd, 1H, \( J = 17.0 \) Hz, 10.3 Hz, 6.5 Hz), 5.03 (dt, 1H, \( J = 17.2 \) Hz, 1.6 Hz), 4.94-4.98 (m, 2H), 2.76-2.86 (m, 1H), 2.11 (s, 3H), 1.85 (d, 3H, \( J = 1.0 \) Hz), 1.26-1.36 (m, 10H), 0.86-0.89 (m, 3H).

\( ^{13}\)C NMR (100 MHz, CDCl\(_3\)) \( \delta \) 169.5, 145.6, 140.8, 119.9, 113.7, 41.2, 35.4, 31.8, 29.3, 27.0, 22.6, 21.0, 15.5, 14.1.
GC (GTA column, 100 °C): enol acetate did not resolve in chiral GC, we hydrolyzed our enol acetate to the corresponding ketone under basic condition K$_2$CO$_3$/MeOH (rt, 12 h). Rt from dppp: 21.59 min and 22.00 min; from (S,S-DIOP): 21.75 min (3%) and 22.03 min (95%).

HRMS (ESI-MS): m/z 247.1662 ([M+Na]); exact mass calculated for C$_{14}$H$_{24}$O$_2$Na 247.1669.

$[\alpha]_D^{23}$ (c = 0.3, CHCl$_3$) – 5.3. [from (S,S)-DIOP]

(E)-4-cyclohexylhexa-2,5-dien-2-yl acetate (9s): $^1$H NMR (600 MHz, CDCl$_3$) δ 5.69 (ddd, 1H, $J = 16.8$ Hz, 10.6 Hz, 7.3 Hz), 5.04 (dd, 1H, $J = 10.2$ Hz, 0.9 Hz), 4.99-5.02 (m, 1H), 4.98 (d, 1H, $J = 1.1$ Hz), 2.59-2.63 (m, 1H), 2.10 (s, 3H), 1.84 (d, 3H, $J = 1.0$ Hz), 1.61-1.78 (m, 8H), 0.91-1.15 (m, 3H).

$^{13}$C NMR (150 MHz, CDCl$_3$) δ 169.5, 145.7, 139.5, 118.5, 114.6, 47.7, 42.4, 30.9, 30.1, 26.51, 26.45, 26.41, 21.0, 15.6.

GC (cyclosil B, 100 °C): enol acetate did not resolve in chiral GC, we hydrolyzed our enol acetate to the corresponding ketone under basic condition K$_2$CO$_3$/MeOH (rt, 12 h). Rt from dppp: 65.959 min and 68.568 min; from (S,S-BDPP): 65.959 min (98%) and 68.568 min (2%).

HRMS (ESI-MS): m/z 245.1499 ([M+Na]); exact mass calculated for C$_{14}$H$_{22}$O$_2$Na 245.1512.

$[\alpha]_D^{23}$ (c = 0.15, CHCl$_3$) + 10.0. [from (S,S)-BDPP]
(E)-4-isopropylhexa-2,5-dien-2-yl acetate (9t): $^1$H NMR (600 MHz, CDCl$_3$) $\delta$ 5.70 (ddd, 1H, $J = 17.2$ Hz, 10.3 Hz, 7.0 Hz), 4.99-5.05 (m, 3H), 2.58-2.62 (m, 1H), 2.10 (s, 3H), 1.84 (d, 3H, $J = 0.8$ Hz), 1.64 (septet, 1H, $J = 6.7$ Hz), 0.90 (d, 3H, $J = 6.8$ Hz), 0.88 (d, 3H, $J = 6.7$ Hz).

$^{13}$C NMR (150 MHz, CDCl$_3$) $\delta$ 169.5, 145.9, 139.5, 118.1, 114.8, 48.2, 32.6, 21.0, 20.3, 19.4, 15.6.

GC (cyclosil B, 50 °C): enol acetate did not resolve in chiral GC, we hydrolyzed our enol acetate to the corresponding ketone under basic condition K$_2$CO$_3$/MeOH (rt, 12 h). $R_t$ from dpp: 68.47 min and 69.63 min; from (S,S-BDPP): 70.720 min (>98%).

HRMS (ESI-MS): $m/z$ 205.1192 ([M+Na]); exact mass calculated for C$_{11}$H$_{18}$O$_2$Na 205.1199.

$[\alpha]_D^{23}$ (c = 0.25, CHCl$_3$) + 18.4. [from (S,S)-BDPP]

(E)-1-(2-vinylcyclohexylidene)ethyl acetate (9u): $^1$H NMR (600 MHz, CDCl$_3$) $\delta$ 5.83 (ddd, 1H, $J = 17.3$ Hz, 10.3 Hz, 4.6 Hz), 5.05-5.11 (m, 2H), 3.24 (b, 1H), 2.33-2.35 (m, 1H), 2.13 (s, 3H), 1.84 (d, 3H, $J = 2.1$ Hz), 1.81-1.82 (m, 1H), 1.73-1.78 (m, 2H), 1.67-1.69 (m, 2H), 1.59-1.69 (m, 2H), 1.47-1.54 (m, 1H).

$^{13}$C NMR (150 MHz, CDCl$_3$) $\delta$ 169.2, 139.9, 138.5, 125.8, 115.1, 39.6, 31.8, 26.4, 23.3, 21.4, 20.8, 15.5.

GC (cyclosil B, 100 °C): $R_t$ from dpp: 35.003 mins and 36.582 mins; from (S,S-BDPP): 34.844 mins (96%) and 36.738 mins (4%).
HRMS (ESI-MS): \( m/z \) 217.1025 ([M+Na]); exact mass calculated for \( \text{C}_{12}\text{H}_{18}\text{O}_{2}\text{Na} \) 217.1199.

\[ \alpha \] \( ^{23} \)D \( (c = 0.25, \text{CHCl}_3) + 2.4. \) [from (S,S)-BDPP]

\( (E)\)-1-(2-vinylcycloheptylidene)ethyl acetate (9v): \(^1\)H NMR (400 MHz, CDCl\(_3\)) \( \delta \) 5.70 (ddd, 1H, \( J = 17.2 \) Hz, 10.2 Hz, 5.8 Hz), 5.00 (dt, 1H, \( J = 17.2 \) Hz, 1.7 Hz), 4.94 (dt, 1H, \( J = 10.2 \) Hz, 1.7 Hz), 3.06-3.13 (m, 1H), 2.35-2.40 (m, 1H), 2.13 (s, 3H), 1.91-1.99 (m, 1H), 1.83 (s, 3H), 1.71-1.79 (m, 3H), 1.59-1.66 (m, 1H), 1.35-1.44 (m, 1H), 1.17-1.28 (m, 3H).

\(^{13}\)C NMR (100 MHz, CDCl\(_3\)) \( \delta \) 169.5, 141.8, 140.1, 128.7, 112.8, 44.4, 33.2, 31.0, 29.1, 26.1, 25.5, 20.9, 15.9.

GC (cyclosil-B, 65 °C): \( R_t \) from dppp: 457.607 mins and 461.063 mins; from (S,S-BDPP): 456.696 mins (other enantiomer is not visible in GC).

HRMS (ESI-MS): \( m/z \) 231.1356 ([M+Na]); exact mass calculated for \( \text{C}_{13}\text{H}_{20}\text{O}_{2}\text{Na} \) 231.1356.

\[ \alpha \] \( ^{23} \)D \( (c = 0.6, \text{CHCl}_3) - 28.2. \) [from (S,S)-BDPP]

**Typical Procedure for the Hydrolysis of the Silyl Enol Ether**

**Procedure A:** Silyl enol ether (0.1 mmol) and 0.5 mmol 2N aq HCl were charged in a 25mL vial and stirred for a couple of hours. Reaction was monitored by achiral GC (small aliquots had been taken out, quenched with water, extracted with ether, organic
extract was injected in GC). Once all silylenother was consumed, water was added to quench the reaction. The resulting mixture was extracted with ether (5mL X 3). The organic layers were combined, dried over MgSO₄ and concentrated to give the ketone, which was then eluted through a plug of silica with pentane:ether (19:1) to get the pure ketone. Most of the ketones are rotary-evaporated very carefully as these compounds are low-boiling.

**Procedure B:** Silylenolether (0.1mmol), 0.5mmol 5% oxalic acid (aq) and 10% by weight silica gel were charged in a 25mL vial and stirred for 6h at rt. Reaction was monitored by achiral GC (small aliquots had been taken out, quenched with water, extracted with ether, organic extract was injected in GC). Once all silylenother was consumed, water was added to quench the reaction. The resulting mixture was extracted with ether (5mL X 3). The organic layers were combined, dried over MgSO₄ and concentrated to give the ketone, which was then eluted through a plug of silica with pentane:ether (19:1) to get the pure ketone.

**Procedure C:** A 25mL three-necked flask equipped with magnetic stirring bar, stopper, rubber septum and nitrogen inlet was flame dried and purged with argon. The flask was charged with 0.2mmol of BF₃.OEt₂ (freshly distilled) and further diluted with 2mL of DCM and cooled down to -78 °C in dry ice acetone bath. The flask was charged with 0.1mmol of silylenolether dissolved in minimal amount of DCM (0.5mL). 5mL water was added to the reaction mixture very slowly at -78 °C and allowed it to warm up to rt. The resulting mixture was extracted with ether (5mL X 3). The organic layers were
combined, dried over MgSO₄ and concentrated to give the ketone, which was then eluted through a plug of silica with pentane:ether (19:1) to get the pure ketone.

UNLESS OTHERWISE MENTIONED, ALL THE HYDROLYSIS HAS BEEN PERFORMED FOLLOWING PROCEDURE A.

4-Vinyl-2-octanone (11a): $^1$H NMR (500 MHz, CDCl₃) δ 5.85 (ddd, 1H, $J = 2$ Hz, 6.8 Hz, 12 Hz), 4.98 (d, 1H, $J = 6.8$ Hz), 4.95 (d, 1H, $J = 10.4$ Hz), 2.52 (septet, 1H, $J = 2$ Hz), 2.40 (ab quartet, 2H, $J = 3.2$ Hz, 5.2 Hz), 2.09 (s, 3H), 1.18-1.29 (m, 6H), 0.86 (t, 3H, $J = 1.2$ Hz).

$^{13}$C NMR (125 MHz, CDCl₃) δ 208.1, 141.4, 114.7, 49.2, 39.5, 34.3, 30.5, 29.2, 22.6, 13.9.

GC (cyclosil-B, 50 °C): R$_t$ from dppp: 147.99 min and 150.60 min; from (S,S-BDPP): 107.83 min (4.32%) and 108. 28 min (95.68%). From (S,S-DIOP): 148.02 min (>99%).

HRMS (ESI-MS): m/z 177.1227 ([M+Na]); exact mass calculated for C$_{10}$H$_{18}$ONa 177.1250.

$[\alpha]_D^{23}$ (c = 0.852, CHCl₃) − 1.70 [from (S,S-BDPP)]. $[\alpha]_D^{23}$ (c = 1.7, CHCl₃) + 0.3 [from (S,S-DIOP)].

4-Ethyl-2-octanone (12a): (S,S)-BDPP product 11a (>84% ee) was taken further for the hydrogenation reaction. To a Fisher-Porter tube equipped with a magnetic stir bar was added 0.0462 g (0.300 mmol) 11a and 0.0424 g (0.0458 mmol) Wilkinson’s catalyst in 5 mL DCM. The tube was sealed, evacuated and
purged three times with hydrogen gas, and then pressurized to 50 psi of hydrogen gas. The solution stirred at room temperature for 24 h. The gas was evacuated, the solution filtered through a short plug of silica gel to remove the catalyst and the solvent removed. The crude product was purified using 5% diethyl ether / 95% pentanes to get the product as a clear oil 0.0396 g (84% yield).

$^1$H NMR (400 MHz, CDCl$_3$) δ 2.32 (d, 2H, $J = 6.8$ Hz), 2.11 (s, 3H), 1.80 (quintet, 1H, $J = 6.4$ Hz), 1.20-1.32 (m, 8H), 0.81-0.89 (two triplets superimposed, 3H each).

$^{13}$C NMR (100 MHz, CHCl$_3$) δ 209.4, 48.4, 35.3, 33.1, 30.3, 29.7, 28.8, 26.3, 22.9, 14.0, 10.8. (quant. yield).

$[\alpha]_D^{23}$ ($c = 0.264$, CHCl$_3$) + 0.80 [from (S,S-BDPP)]. Lit. value $[\alpha]_D^{23}$ ($c = 2.30$, CHCl$_3$) + 2.70.$^{53}$ This corresponds to $R$-(+)-configuration, which corresponds to (S)-configuration in the starting silyl enol ether 9a.

4-Vinyl-2-decanone (11d): $^1$H NMR (600 MHz, CDCl$_3$) δ 5.60 (ddd, 1H, $J = 8.3$ Hz, 10.3 Hz, 17.1 Hz), 4.99 (ddd, 1H, $J = 1.1$ Hz, 1.6 Hz, 10.7 Hz), 4.97-4.98 (m, 1H), 2.51-2.57 (m, 1H), 2.42 (ab quartet, 2H, $J = 3.2$ Hz, 6.1 Hz), 2.11 (s, 3H), 1.25-1.33 (m, 10H), 0.86-0.89 (m, 3H).

$^{13}$C NMR (150 MHz, CDCl$_3$) δ 208.2, 141.4, 114.7, 49.2, 39.6, 34.7, 31.8, 30.5, 29.2, 26.9, 22.6, 14.0,

GC (cyclosil-B, 70 °C): R$_t$ from dppp: 214.52 min (chiral GC was not able resolve the product into two enantiomers separately); from (S,S-DIOP): 213.70 min.
GC (GTA column, 100 °C): R_t from dppp: 21.59 min and 22.00 min; from (S,S-DIOP): 21.75 min (3%) and 22.03 min (95%).

GC-MS (methyl silicone): m/z 168.28 ([M+]). exact mass calculated for C_{11}H_{20}O 168.15.

[α]_D^{23} (c = 1.4, CHCl_3) + 0.8 [from (S,S-DIOP)]

**4-Cyclohexylhex-5-en-2-one (11e):** \(^1\)H NMR (600 MHz, CDCl_3) δ 5.62 (ddd, 1H, \(J = 8.3\) Hz, 10.3 Hz, 17.2 Hz), 5.00 (dd, 1H, \(J = 1.8\) Hz, 10.3 Hz), 4.95 (ddd, 1H, \(J = 0.5\) Hz, 1.7 Hz, 17.1 Hz), 2.46-2.53 (m, 1H), 2.39-2.43 (m, 1H), 2.11 (s, 3H), 1.62-1.74 (m, 6H), 1.22-1.32 (m, 3H), 0.90-1.02 (m, 2H).

\(^{13}\)C NMR (150 MHz, CDCl_3) δ 208.6, 139.6, 115.6, 46.3, 45.4, 41.6, 30.8, 30.5, 29.7, 26.5, 26.5.

GC (cyclosil-B, 100 °C): R_t from dppp: 66.57 min and 68.28 min; from (S,S-BDPP): 65.97 min (98%) and 68.81 min (2%).

HRMS (ESI-MS): m/z 203.1259 ([M+Na]); exact mass calculated for C_{12}H_{20}ONa 203.1249.

[α]_D^{23} (c = 1.2, CHCl_3) – 1.5 [from (S,S-BDPP)]

**4-Isopropylhex-5-en-2-one (11g):** \(^1\)H NMR (400 MHz, CDCl_3) δ 5.57-5.66 (m, 1H), 5.01 (dd, 1H, \(J = 1.8\) Hz, 10.4 Hz), 4.97 (dd, 1H, \(J = 1.6\) Hz, 17.4 Hz), 2.40-2.49 (m, 3H), 2.11 (s, 3H), 1.57-1.66 (m, 1H), 1.22-1.32 (m, 3H), 0.88 (d, 3H, \(J = 6.7\) Hz), 0.84 (d, 1H, \(J = 6.8\) Hz).
$^{13}$C NMR (150 MHz, CDCl$_3$) $\delta$ 208.3, 139.0, 115.9, 46.4, 45.8, 31.6, 31.5, 30.4, 20.2, 18.8.

GC (cyclosil-B, 50 °C): $R_t$ from dppp: 68.47 min and 69.63 min; from (S,S-BDPP): 70.331 min (>98%).

GC-MS (methyl silicone): $m/z$ 140.22 ([M+]). exact mass calculated for C$_9$H$_{16}$O 140.12.

[$\alpha$]$^D_{23}$ (c = 1.1, CHCl$_3$) + 8.3 [from (S,S-BDPP)]

5-methylhept-6-en-3-one (11i): $^1$H NMR (400 MHz, CDCl$_3$) $\delta$ 5.7365 (ddd, 1H, $J$ = 6.9 Hz, 10.4 Hz, 17.3 Hz), 4.97 (dt, 1H, $J$ = 1.4 Hz, 17.2 Hz), 4.91 (dt, 1H, $J$ = 1.3 Hz, 10.4 Hz), 2.69-2.74 (m, 1H), 2.31-2.46 (m, 4H), 1.03 (t, 3H, $J$ = 7.3 Hz), 1.00 (d, 1H, $J$ = 6.9 Hz).

$^{13}$C NMR (150 MHz, CDCl$_3$) $\delta$ 210.5, 142.9, 112.9, 49.0, 36.5, 33.4, 19.8, 7.6.

GC-MS (methyl silicone): $m/z$ 126.18 ([M+]). exact mass calculated for C$_8$H$_{14}$O 126.10.

(4S,6S)-6,10-Dimethyl-4-vinylundec-9-en-2-one [11j via (S,S-DIOP)CoCl$_2$-catalyzed reaction]: $^1$H NMR (600 MHz, CDCl$_3$) $\delta$ 5.59 (ddd, 1H, $J$ = 8.5 Hz, 10.3 Hz, 17.2 Hz), 5.07-5.10 (m, 1H), 4.96-5.01 (m, 2H), 2.63-2.70 (m, 1H), 2.39 (ab quartet, 2H, $J$ = 5.7 Hz, 15.5 Hz), 2.11 (s, 3H), 1.98-2.04 (m, 1H), 1.89-1.93 (m, 1H), 1.68 (d, 3H, $J$ = 0.9 Hz), 1.60 (m, 3H), 1.37-1.49 (m, 1H), 1.23-1.28 (m, 2H), 1.13-1.17 (m, 1H), 1.05-1.11 (m, 1H), 0.87 (d, 3H, $J$ = 6.6 Hz).

$^{13}$C NMR (150 MHz, CDCl$_3$) $\delta$ 208.1, 141.7, 131.1, 124.8, 114.6, 49.3, 42.4, 37.4, 36.2, 30.6, 29.7, 25.7, 25.2, 20.1, 17.6.
GC (cyclosil-B, 110 °C): R_t from dppp: 72.99 min and 78.10 min; from (S,S)-DIOP: 72.97 min (95%) and 78.63 min (2%) and 82.65 min (2.9%); diastereomeric ratio: 98:2.

HRMS (ESI-MS): m/z 245.1703 ([M+Na]); exact mass calculated for C_{15}H_{26}ONa 245.1706.

\[ \alpha \]_D^{23} (c = 1.2, CHCl_3) – 5.4 [from (S,S-DIOP)]

(4R,6S)-6,10-Dimethyl-4-vinylundec-9-en-2-one [11] via (R,R-DIOP)CoCl_2-catalyzed reaction: ¹H NMR (600 MHz, CDCl_3) δ 5.59 (ddd, 1H, J = 8.5 Hz, 10.3 Hz, 17.2 Hz), 5.06-5.08 (m, 1H), 4.97-5.02 (m, 2H), 2.63-2.69 (b, 1H), 2.40 (ab quartet, 2H, J = 7.6 Hz, 15.5 Hz), 2.11 (s, 3H), 1.89-2.00 (m, 2H), 1.67 (d, 3H, J = 0.9 Hz), 1.59 (m, 3H), 1.38-1.48 (m, 1H), 1.22-1.33 (m, 2H), 1.13-1.19 (m, 1H), 1.06 (ddd, 1H, J = 4.4 Hz, 9.8 Hz, 13.8 Hz), 0.87 (d, 3H, J = 6.5 Hz).

¹³C NMR (150 MHz, CDCl_3) δ 208.1, 141.2, 131.1, 124.8, 114.9, 50.0, 42.1, 37.8, 37.5, 30.6, 29.7, 25.7, 25.4, 18.9, 17.6.

GC (cyclosil-B, 110 °C): R_t dppp: 73.00 min and 78.10 min; from (R,R-DIOP): 73.22 min (1.4%) and 78.10 min (89.8%); diastereomeric ratio: 98:2.

HRMS (ESI-MS): m/z 245.1703 ([M+Na]); exact mass calculated for C_{15}H_{26}ONa 245.1706.

\[ \alpha \]_D^{23} (c = 1.1, CHCl_3) + 1.0 [from (R,R-DIOP)]

1-Phenyl-hex-4-en-3-one (11k): Hydrolysis Procedure B: ¹H NMR (400 MHz, CDCl_3) δ 7.26-7.30 (m, 2H), 7.17-7.21 (m, 3H), 5.91
(ddt, 1H, J = 17 Hz, 10.2 Hz, 7 Hz), 5.18 (dq, 1H, J = 10.2 Hz, 1.3 Hz), 5.12 (dq, 1H, J = 17 Hz, 1.4 Hz), 3.16 (dt, 2H, J = 7 Hz, 1.2 Hz), 2.88-2.92 (m, 2H), 2.75-2.79 (m, 2H).

$^{13}$C NMR (100 MHz, CDCl$_3$) $\delta$ 207.7, 140.9, 130.4, 128.8, 128.3, 126.1, 118.9, 47.9, 43.8, 29.6

HRMS (ESI-MS): m/z 197.0969 ([M+Na]); exact mass calculated for C$_{12}$H$_{14}$ONa 197.0937.

1-((1$R$,2$R$)-2-Vinylcyclohexyl)ethan-1-one (111-cis): Procedure C gives the best diastereomeric ratio for the cis: trans isomers.

$^1$H NMR (600 MHz, CDCl$_3$) $\delta$ 5.87 (ddd, 1H, J = 8.5 Hz, 10.4 Hz, 17.2 Hz), 4.97-5.01 (m, 2H), 2.71-2.75 (m, 1H), 2.52-2.56 (m, 1H), 2.05 (s, 3H), 1.78-1.83 (m, 1H), 1.68-1.73 (m, 1H), 1.57-1.66 (m, 2H), 1.39-1.48 (m, 1H), 1.22-1.29 (m, 1H).

$^{13}$C NMR (150 MHz, CDCl$_3$) $\delta$ 210.6, 137.9, 115.6, 53.8, 41.0, 31.5, 28.6, 24.6, 23.4, 21.6.

GC (cyclosil-B, 70 °C): R$_t$ dppp: 90.25 min and 99.15 min (minor), 115.96 min and 121.13 min (major); from (S,S-BDPP): 90.44 min (0.33%) and 98.89 min (5.95%) [minor] and 117.67 min (4.1%) and 119.74 min (86.8%) [major]; diastereomeric ratio : 14.5 : 1. (91% ee)

LC-MS (ESI-MS): m/z 175.0949 ([M+Na]); exact mass calculated for C$_{10}$H$_{16}$ONa 175.0955.

$[^{23}$D]$_d$ $[^{23}$ (c = 5.5, CHCl$_3$) + 0.9 [from (S,S-BDPP)]
Pure trans-compound has been known in literature.\textsuperscript{41,51-54} Our compound does not match with the trans compound $^{13}\text{C}$ spectra. Minor isomer in the $^{13}\text{C}$ spectra of 11l shows that we have cis as an major isomer and trans as the minor isomer (GC ratio, cis : trans = 13.3:1.0). We have made trans isomer of 11l-trans to confirm the stereochemistry. Absolute stereochemistry has been confirmed by the known literature of compound 12l-trans.\textsuperscript{41,51-54}

\textbf{1-((1S,2R)-2-Vinylcyclohexyl)ethan-1-one (11l-trans):} Compound 11l-cis (25.0 mg, 0.16 mmol) was taken in a sample vial and dissolved in 1:1 ether : pentane mixture (2 mL, ~0.1(M)) and basic alumina (60-325 Mesh, generally added in excess) was added and stirred for 40 h (monitor by GC). The resulting mixture was extracted was then eluted through a plug of silica with pentane:ether (19:1) to get the pure ketone (quantitative yield).

$^{1}$H NMR (600 MHz, CDCl$_3$) $\delta$ 5.61 (ddd, 1H, $J = 7.8$ Hz, 10.4 Hz, 17.3 Hz), 4.97-5.01 (m, 2H), 2.71-2.75 (m, 1H), 2.52-2.56 (m, 1H), 2.05 (s, 3H), 1.78-1.83 (m, 1H), 1.68-1.73 (m, 1H), 1.57-1.66 (m, 2H), 1.39-1.48 (m, 1H), 1.22-1.29 (m,1H).

$^{13}$C NMR (150 MHz, CDCl$_3$) $\delta$ 212.1, 141.4, 114.3, 56.7, 43.6, 31.9, 29.3, 28.8, 25.3, 25.2.

GC (cyclosil-B, 70 °C): 90.20 min (3.3%) and 97.17 min (82.3%) [major] and 123.54 min (12.1%) [minor]; diastereomeric ratio : 7.1 : 1.0 (92% ee)

LC-MS (ESI-MS): $m/z$ 175.0942 ([M+Na]); exact mass calculated for C$_{10}$H$_{16}$ONa 175.0955.
Stereochemistry has been confirmed by known literature.\textsuperscript{51-54} Absolute stereochemistry has been confirmed by the known compound \textit{12l-trans}, which has been described in the literature.

\textbf{1-\((1S,2S)-2\text{-Ethylcyclohexyl})ethan-1-one \textit{(12l-trans)}:} A Fischer-Porter tube equipped with a magnetic stir bar was charged with 25.0 mg (0.16 mmol) of compound \textit{11l-trans} \textit{(trans: cis = 7:0:1)} and 15.6 mg (0.016 mmol) of Wilkinson’s catalyst in 2 mL of dry DCM. The tube was sealed, evacuated and purged three times with hydrogen gas and then filled to 50 psi. A glass shield was placed in front of the tube and the mixture was stirred for 10 h (monitor by GC, opening of the tube should be done very carefully releasing the pressure and tube should be sealed, evacuated and purged every single time). End of the reaction, the solution was filtered through a short pad of silica to remove the catalyst. The product was eluted through a plug of silica with pentane:ether (19:1) to get the pure ketone (77\% yield, NMR shows \textit{trans: cis} = 6.9 :1.0).

\textit{H NMR (600 MHz, CDCl\textsubscript{3})} \(\delta\) 2.18 (td, 1H, \(J = 3.0\) Hz, 11.2 Hz), 2.11 (s, 3H), 1.83-1.90 (m, 1H), 1.72-1.80 (m, 3H), 1.48-1.56 (m, 1H), 1.18-1.35 (m, 5H), 1.01-1.08 (m,1H), 0.84 (t, 3H, \(J = 7.5\) Hz).

\textit{C NMR (150 MHz, CDCl\textsubscript{3})} \(\delta\) 213.4, 57.5, 39.9, 30.1, 29.7, 28.9, 27.3, 25.8, 10.9.

HRMS (ESI-MS): \textit{m/z} 177.1427 ([M+Na]); exact mass calculated for C\textsubscript{10}H\textsubscript{18}ONa 177.1438.
$\alpha_D^{23}$ (c = 1.25, CHCl$_3$) + 4.64 [from (S,S)-BDPP]. This corresponds to [1S,2S(+)] configuration, which corresponds to (R)-configuration in the starting silyl enol ether 9l.

![TMSO](image)

**Conditions**

- TiCl$_4$, slow addition of H$_2$O at -78 °C after 1h
  - 71% yield, dr 3.2:1 (syn : anti)
- BF$_3$: OEt$_2$, after 1h, slow addition of H$_2$O at -78 °C
  - 68% yield, dr 5.7 : 1
- BHT, hexane, -78 °C
  - No reaction
- BHT, hexane, rt, overnight
  - No reaction
- CSA, hexane, slow addition of H$_2$O at -78 °C after 1h
  - Messy reaction from NMR
- TiCl$_4$, BINOL, slow addition of H$_2$O at -78 °C after 1h
  - 66% yield, dr 1.5 : 1
- 2(M) HCl, rt, 4h, ether
  - 75% yield, dr 1.5:1, not clean reaction
- MeLi, THF, 0 °C, slow addition of H$_2$O at -78 °C after 1h
  - 73% yield, dr 2.4:1
- TBAF, ether, -78 °C, slow addition of H$_2$O at -78 °C after 1h
  - 69% yield, dr 1.5:1

[BHT = 2,4-Di-tert-butyl-4-methylphenol, CSA = Camphorsulfonic acid]

1-((1R,2R)-2-Vinylcycloheptyl)ethan-1-one (11m): Procedure C gives the best diastereomeric ratio for the cis:trans isomers. $^1$H NMR (400 MHz, CDCl$_3$) 5.68 (major, ddd, 1H, $J = 17.2$ Hz, 10.2 Hz, 8.1 Hz, minor diastereomer superimposed), 4.97 (minor, ddd, 1H, $J = 16.3$ Hz, 1.8 Hz, 1 Hz), 4.91 (major, ddd, 1H, $J = 17.2$ Hz, 1.6 Hz, 1.1 Hz, minor diastereomer superimposed), 4.87 (major, ddd, 1H, $J = 10.3$ Hz, 1.7 Hz, 0.6 Hz, minor diastereomer superimposed), 2.69-2.80 (minor, m, 2H), 2.42-2.56 (major, m, 2H), 2.09 (major, s, 3H, minor diastereomer superimposed), 1.41-1.80 (major, m, 10H, minor diastereomer superimposed).
\(^{13}\text{C}\) NMR (100 MHz, CDCl\(_3\)) \(\delta\) 211.8, 211.1 (minor), 142.7, 139.5 (minor), 114.8 (minor), 113.3, 58.5, 56.8 (minor), 45.4, 43.9 (minor), 33.6 (minor), 33.3, 29.7 (minor), 29.2, 29.16 (minor), 28.9, 28.7, 28.0 (minor), 26.6, 25.6, 25.0 (minor), 24.6 (minor).

GC (cyclosil-B, 80 °C): \(R_t\) from dppp: 102.45 min and 112.43 min (major), 131.64 min and 139.28 min (minor); from (S,S-BDPP): 111.10 min (major) (76.1%) and 138.01 min (21.4%); diastereomeric ratio : 5.7 : 1 (95% ee for both isomers).

HRMS (ESI-MS): \(m/z\) 189.1260 ([M+Na]); exact mass calculated for C\(_{11}\)H\(_{18}\)ONa 189.1250.

\([\alpha]_D^{23}\) (c = 1.95, CHCl\(_3\)) + 14.7 [from (S,S-BDPP)]

**1-((1R,2R)-2-Vinylecyclooctyl)ethan-1-one (11n):** Procedure C gives the best diastereomeric ratio for the \emph{cis}: \emph{trans} isomers. \(^1\text{H}\) NMR (400 MHz, CDCl\(_3\)) \(\delta\) 5.70 (ddd, 1H, \(J = 7.9\) Hz, 10.4 Hz, 17.2 Hz, minor diastereomer superimposed), 4.95-5.00 (m, 2H, minor diastereomer), 4.91-4.94 (m, 1H), 4.89 (dd, 1H, \(J = 1.6\) Hz, 5.0 Hz), 2.66-2.85 (m, 1H, minor diastereomer), 2.58-2.60 (m, 1H), 2.12 (s, 3H, minor diastereomer), 2.09 (s, 3H), 1.77-1.85 (m, 1H), 1.61-1.76 (m, 6H, minor diastereomer superimposed), 1.44-1.60 (m, 6H, minor diastereomer superimposed).

\(^{13}\text{C}\) NMR (100 MHz, CDCl\(_3\)) \(\delta\) 211.7, 142.3, 113.8, 55.9, 43.3, 29.8, 29.3, 27.8, 27.2, 26.3, 25.4, 25.3.

minor diastereomer peaks: \(\delta\) 139.6, 114.8, 53.0, 43.9, 30.6, 30.3, 28.2, 28.0, 26.2.
GC (cyclosil-B, 90 °C): R_t from dppp: 121.132 min (major) and 136.83 min and 143.34 min (minor); from (S,S-BDPP): 122.08 min (79.9%) [major] and 143.46 min (17.8%) [minor]; diastereomeric ratio : 4.5:1 (99% ee for both isomers).

GC-MS (methyl silicone): m/z 180.22 ([M+]). exact mass calculated for C_{12}H_{22}O 180.29.

[α]_D^{23} (c = 0.975, CHCl_3) + 17.0 [from (S,S-BDPP)]

Typical Procedure for the Bromination of Silyl Enol Ether: Procedure for CuBr_2-Mediated Bromination Reaction of 4-Vinyl-2-trimethylsilyloxy-2(E)-octene (9a):

A three-necked round-bottom equipped with a gas inlet, magnetic stir bar, and septa was flame-dried and purged with argon. A solution of 0.0292 g (0.129 mmol) 9a in 1 mL dry, distilled DMF was added to the flask. Under a strong stream of argon, 0.149 g (0.663 mmol) CuBr_2 was added in one portion, and the mixture stirred at room temperature for 24 h. The solution was poured into 5 mL ice cold distilled water and extracted with (3 x 10 mL) diethyl ether. The organic layers were combined, dried with MgSO_4, filtered to remove the solids and the solvent removed in vacuo. The compound was purified by flash chromatography using silica gel and diethyl ether : pentane mixture (5:95) to get the product as a clear oil 0.0302 g (quantitative yield).

3-Bromo-4-vinyl-2-octanone (13): (S,S-BDPP) product $\delta$-9a (>84% ee) was taken further for the bromination reaction. $^1$H NMR (500 MHz, CDCl_3) δ 5.46-5.90 (two m superimposed, 1H each), 5.08-5.19 (two dd superimposed, 2H each), 4.20 (d, 1H, J = 9 Hz, threo cmpd.), 4.08 (d, 1H, J = 12 Hz erythro cmpd.), 2.52-2.64 (two m superimposed, 1H each), 2.34 (s, 3H), 2.28 (s, 3H),
1.30 – 1.46 (two m superimposed, 4 H each), 0.87 (two t superimposed, 3 H each).

*Erythro* and *threo* can be assigned by analogy to work done by Pitkanen on vicinal proton coupling constants for \(\alpha,\beta\)- and \(\alpha,\gamma\)-dichloroesters.\(^5\)

\(^{13}\)C NMR (125 MHz, CDCl\(_3\)) \(\delta\) 202.3 (201.5), 137.4 (136.9), 118.7 (118.2), 59.7 (59.2), 46.8 (46.7), 32.3 (31.7), 29.2 (29.0), 28.6 (27.2), 26.2 (25.3), 20.7 (18.8).

GC (*cyclosil-*B, 85 °C): \(R_t\) from dppp: 75.17 min (26.63%), 78.28 min (24.27%), 80.32 min (21.53%), 82.57 min (27.65%); from (S,S-BDPP): 75.26 min (47.32%), 78.57 min (2.53%), 80.68 min (2.80%), 82.78 min (47.33%). [ee of the product 88%]

GC-MS (*methyl silicone*): m/z ([M+]) 232.05 and 234.04; exact mass calculated for \(\text{C}_{10}\text{H}_{17}\text{OBr}\) 232.15.

**1-Acetyl-1-bromo-2-vinylcycloheptane (22b):** (S,S-BDPP) product **R-9m**

(96% ee) was taken further for the bromination reaction. \(^1\)H NMR (500 MHz, CDCl\(_3\)) \(\delta\) 5.72-5.80 (two m superimposed, 1H each), 4.90-5.04 (two dd superimposed, 2H each), 3.03 (t, 1H, \(J = 7.5\) Hz), 2.88 (t, 1H, \(J = 8.5\) Hz), 2.38-2.49 (two s 3H each superimposed on one m, 2H), 2.15 – 2.13 (m, 2H), 1.72-1.86 (two m superimposed, 4H each), 1.46 – 1.65 (two m superimposed, 2H each).

\(^{13}\)C NMR (125 MHz, CDCl\(_3\)) \(\delta\) 205.6 (203.7), 140.1 (137.0), 117.7 (115.9), 82.5 (79.9), (53.4) 50.9, 40.4 (37.9) 31.5 (30.2), (29.3) 28.0, (27.6) 27.2, 28.8 (25.3), 15.0 (12.0)

GC (*cyclosil-*B, 125 °C): \(R_t\) from dppp: 26.07 min (33.07%), 26.67 min (33.40%), 29.15 min (16.76%), 30.08 min (16.75%). From (S,S-BDPP): 26.03 min (69.47%), 26.62 min (1.86%), 29.08 min (0.33%), 30.41 min (28.33%). [ee of the product 95%]
GC-MS (*methyl silicone*): m/z ([M+] 244.45 and 246.04; exact mass calculated for C\textsubscript{11}H\textsubscript{17}OBr 244.05

**Typical Procedure for the Hydroxylation of Silyl Enol Ether: Procedure for Methyltrioxorhenium (MTO) Mediated Hydroxylation Reaction of 4-Vinyl-2-trimethylsilyloxy-2(E)-octene (9a):**

A 50-ml flask was charged with 4mL of a 95:5 CH\textsubscript{3}CN: AcOH, 0.71mmol of H\textsubscript{2}O\textsubscript{2} (30% in H\textsubscript{2}O), 0.35mmol of pyridine, and 0.002mmol of methyltrioxorhenium. To this flask, mmol was added slowly and then stirred at room temp for 45 min. The CH\textsubscript{3}CN was then removed *in vacuo*. To the remaining mixture was added 20mL of a saturated solution of KF in MeOH and the reaction was stirred for 5 h. The reaction was diluted with ether and neutralized with saturated NaHCO\textsubscript{3} (aq), then extracted with ether (20mL x 3), washed with water, and dried over Na\textsubscript{2}SO\textsubscript{4} overnight. Product was concentrated and then purified by column chromatography using 30% EtOAc in hexanes, yielding a colorless oil which contained a mixture of diastereomers. (45% yield)

![3-Hydroxy-4-vinylctan-2-one (14)](image)

3-Hydroxy-4-vinylctan-2-one (14): (S,S-BDPP) product *S*-9a (35% ee) was taken further for the hydroxylation reaction. GC diastereomeric ratio: dpdp (2.2:1); (S,S-BDPP) (2.2:1) \textsuperscript{1}H NMR (400 MHz, CDCl\textsubscript{3}) δ 5.82 (major, ddd, 1H, J = 18.4 Hz, 10.8 Hz, 8.8 Hz), 5.59 (minor, ddd, 1H, J = 17.2 Hz, 10.4 Hz, 9.6 Hz), 5.13-5.18 (major, m, 2H), 5.00-5.07 (minor, m, 2H), 4.22 (minor, dd, 1H, J = 4.8 Hz, 2.8 Hz), 4.18 (major, dd, 1H, J = 5.2 Hz, 3.6 Hz), 3.48 (minor, d, 1H, J = 3.6 Hz), 3.41 (major, d, 1H, J = 5.2 Hz), 2.42-2.46 (major, m, 1H, superimposed on minor), 2.23
(major, s, 3H), 2.19 (minor, s, 3H), 1.1-1.42 (major, m, 6H, superimposed on minor), 0.93 (minor, t, 3H, $J = 6.8$ Hz), 0.88 (major, t, 3H, $J = 6.8$ Hz).

$^{13}$C NMR (100 MHz, CDCl$_3$) $\delta$ 209.3, 208.9, 138.9, 136.1, 117.1, 116.5, 80.6, 79.6, 47.4, 47.2, 31.3, 29.5, 29.4, 27.5, 26.1, 25.4, 22.6, 22.5, 14.0, 13.9.

GC: (cyclosil-B, 80°C): $R_t$ from dppp: 85.29 min (14.11%), 87.04 min (31.83%), 94.51 min (14.05%), 99.39 min (31.64%); from (S,S-BDPP): 85.06 min (21.00%), 86.77 min (46.35%), 94.59 min (10.22%), 99.51 min (22.41%) [ee of the product 35%]

HRMS (ESI-MS): m/z 193.1201 ([M + Na]); exact mass calculated for $C_{10}H_{18}O_2Na$ 193.1199.

1-Acetyl-1-hydroxy-2-vinylcycloheptane (22a): (S,S-BDPP) product $R$-9m (96% ee) was taken further for the hydroxylation reaction. GC diastereomeric ratio: from (S,S-BDPP) (1:1), masses of recovered product indicated a ratio of 1:1 for dppp. $^1$HNMR (400 MHz, CDCl$_3$) $\delta$ 5.72 (minor, ddd, 1H, $J = 20.0$ Hz, 10.4 Hz, 7.6 Hz, superimposed on major), 5.67 (major, ddd, 1H, $J = 17.2$ Hz, 10.0 Hz, 9.2 Hz, superimposed on minor), 5.07 (minor, ddt, 2H, $J = 17.2$ Hz, 10.4 Hz, 1.6 Hz), 4.97 (major, ddd, 1H, $J = 17.2$ Hz, 2.0 Hz, 0.8 Hz), 4.93 (major, dd, 1H, $J = 10.0$ Hz, 2.0 Hz), 2.42-2.48 (major, m, 1H, superimposed on minor), 2.20 (major, s, 3H), 2.06 (minor, s, 3H), 1.5-1.9 (major, m, 10H, superimposed on minor). [product was contaminated with trace of ethyl acetate]
$^{13}$C (100 MHz, CDCl$_3$) δ 212.4, 211.6, 171.1, 139.3, 138.6, 115.6, 114.6, 84.3, 82.3, 60.4, 53.0, 51.5, 38.5, 36.9, 30.6, 30.3, 30.2, 29.3, 27.5, 26.6, 26.3, 23.9, 22.4, 22.0, 21.0, 14.2.

[product was contaminated with trace of ethyl acetate]

GC: (cyclosil-B, 120°C): R$_t$ dppp first diastereomer: 25.40 min (50.12%) and 26.94 min (49.88%); dppp second diastereomer: 27.39 min (50.00%) and 28.76 min (50.00%); from (S,S-BDPP): 25.38 min (49.76%) and 28.75 min (50.24%) [minor enantiomers are too small to integrate] [ee of the product >96%]

HRMS (ESI-MS): m/z 205.1221 ([M + Na]); exact mass calculated for C$_{11}$H$_{18}$O$_2$Na 205.1199.

**Typical Procedure for the Mukaiyama-Alkylation Reaction of Silyl Enol Ether:**

**Procedure for Mukaiyama-Alkylation Reaction of 4-Vinyl-2-trimethylsilyloxy-2(E)-octene (9a) with tert-Butyl chloride:**

A 25 mL three-necked flask equipped with magnetic stirring bar, stopper, rubber septum and nitrogen inlet was flame dried and purged with argon. The flask was charged with 0.5 mL of 1(M) TiCl$_4$ (in DCM) [neat TiCl$_4$ does not help for this reaction] and further diluted with 1mL of DCM and cooled down to -45 ºC in cryocooler bath (temperature is very important for alkylation reaction as reaction did not work both at -78 ºC and 0 ºC). tert-butyl chloride (30µL, 0.275mmol, 1.1 eq) was added in the flask. The flask was charged with 0.25mmol of 4-vinyl-2-trimethylsilyloxy-2(E)-octene (0.056g, 0.25mmol) dissolved in minimal amount of DCM (1mL). The solution mixture immediately turned in to brownish-red color. The reaction mixture was allowed to stir at -45 ºC for an hour
(reaction was monitored by TLC). 5mL water was added to the reaction mixture very slowly at -45 °C and allowed it to warm up to rt. The resulting mixture was extracted with ether (5mL X 3). The organic layers were combined, dried over MgSO₄ and concentrated to give the -alkylated product which was then eluted through a plug of silica with hexane-ethylacetate (10:1) to get the pure product.

3-tert-Butyl-4-vinyl-2-octanone (15): (S,S-BDPP) product S-9a (35% ee) was taken further for the alkylation reaction. GC diastereomeric ratio: dppp (6 : 1); from (S,S-BDPP) (5.7 : 1), Compound 15 has some impurity of the corresponding ketone 11a which is very difficult to separate by column chromatography. 

**1H NMR (400 MHz, CDCl₃)** δ 5.51-5.65 (minor, m, 1H), 5.50-5.65 (major, m, 1H), 4.99-5.05 (m, major and minor superimposed, 2H each), 2.42-2.57 (broad, major and minor superimposed, 2H each), 2.27 (s, ketone 11a), 2.16 (major, s, 3H), 2.15 (minor, s, 3H), 1.14-1.33 (m, major and minor superimposed with ketone 11a, 6H each), 0.996 (minor, s, 9H), 0.991 (major, s, 9H), 0.82-0.90 (m, major and minor superimposed with ketone 11a, 3H each).

**13C NMR (100 MHz, CDCl₃)** δ 213.0, 142.6, 135.8, 125.5, 114.9, 65.4, 44.7, 35.0, 34.2, 34.1, 33.9, 32.7, 30.3, 28.7, 22.5, 22.3, 14.1, 14.0

GC (cyclosil-B, 85 °C): Rᵣ from dppp: 64.72 min and 69.91 min (major), 67.96 min and 72.99 min (minor); from (S,S-BDPP): 64.68 min (10.9%) and 69.91 min (73.9%) (major), 67.96 min (13.3%) and 72.99 min (2.0%) (minor). [ee of the product 35%]

HRMS (ESI-MS): *m/z* 233.1893 ([M+Na]); exact mass calculated for C₁₄H₂₆O₁Na 233.1876.
[α]D$^{23}$ (c = 0.55, CHCl$_3$) + 14.7 [from (S,S-BDPP)]

**Typical Procedure for the Mukaiyama-Michael Reaction of Silyl Enol Ether:**

Procedure for Mukaiyama-Michael Reaction of 4-Vinyl-2-trimethylsilyloxy-2(E)-octene (9a) with Methyl Vinyl Ketone:

A 25mL three-necked flask equipped with magnetic stirring bar, stopper, rubber septum and nitrogen inlet was flame dried and purged with argon. The flask was charged with 0.5mL of 1(M) TiCl$_4$ (in DCM) [neat TiCl$_4$ does not help for this reaction] and further diluted with 1mL of DCM and cooled down to -78 °C in dry ice acetone bath. Methyl vinyl ketone (24µL, 0.275mmol, 1.1 eq) was added in the flask as color changed in to pale yellow. The flask was charged with 0.25mmol of 4-vinyl-2-trimethylsilyloxy-2(E)-octene (0.056g, 0.25mmol) dissolved in minimal amount of DCM (1mL). The solution mixture immediately turned in to brownish-red color. The reaction mixture was allowed to stir at -78 °C for an hour (reaction was monitored by TLC). 5 mL water was added to the reaction mixture very slowly at -78 °C and allowed it to warm up to rt. The resulting mixture was extracted with ether (5mL X 3). The organic layers were combined, dried over MgSO$_4$ and concentrated to give the Mukaiyama-Michael product which was then eluted through a plug of silica with hexane-ethylacetate (4:1) to get the pure product.

5-Acetyl-6-vinyl-2-decanone (16): (S,S-BDPP) product S-9a (85% ee) was taken further for the Michael reaction. GC diastereomeric ratio: dppp (5.7 : 1); from (S,S)-BDPP (4.9 : 1), $^1$H NMR (400 MHz, CDCl$_3$) δ 5.57 (minor, ddd, 1H, J = 8.9 Hz, 10.3 Hz, 17.3 Hz), 5.43 (major, ddd, J = 9.2 Hz, 10.2 Hz, 17 Hz), 5.08 (major, dd, 1H, J
= 10.2 Hz, 1.8 Hz), 5.05-5.07 (minor, m, 1H, superimposed on major), 5.01 (major, dd, 1H, J = 17 Hz, 1.5 Hz), 4.96-5.01 (minor, m, 1H, superimposed on major), 2.45-2.49 (minor, m, 1H), 2.34-2.43 (major, m, 2H, minor diastereomer superimposed), 2.15-2.31 (major, m, 2H, minor diastereomer superimposed), 2.13 (major, s, 3H), 2.11 (minor, s, 3H), 2.09 (major, s, 3H, minor diastereomer 3H superimposed), 1.68-1.87 (major, m, 2H, minor diastereomer 2H superimposed), 1.13-1.30 (major, m, 6H, minor diastereomer 6H superimposed), 0.84-0.88 (major, m, 3H, minor diastereomer 3H superimposed).

$^{13}$C NMR (125 MHz, CDCl$_3$) $\delta$ 211.7, 208.1, 139.1, 117.0, 56.4, 46.0, 41.3 (minor), 40.9, 32.5, 30.8 (minor), 30.3 (minor), 29.9, 29.6, 29.5, 29.3 (minor), 22.5, 22.4, 13.98.

GC (cyclosil-B, 115 °C): R$_t$ from dppp: 81.62 min and 82.43 min (major), 86.12 min and 86.77 min (minor); from (S,S-BDPP): 82.27 min (83.2%) (major) and 85.97 min (16.8%) (minor). [ee of the product >85%]

HRMS (ESI-MS): m/z 247.1668 ([M+Na]); exact mass calculated for C$_{14}$H$_{24}$O$_2$Na 247.1669.

$[\alpha]_D^{23}$ (c = 0.95, CHCl$_3$) + 0.63 [from (S,S-BDPP)]

5-Acetyl-6-vinyl-methyldecanoate (17): (S,S-BDPP) product S-9a (85% ee) was taken further for the Michael reaction. GC diastereomeric ratio: from dppp (6.8 : 1); from (S,S)-BDPP (6.5 : 1), $^1$H NMR (400 MHz, CDCl$_3$) $\delta$ 5.59 (minor, ddd, 1H, J = 17 Hz, 10.2 Hz, 9.3 Hz), 5.44 (major, ddd, 1H, J = 17 Hz, 10.1 Hz, 9.5 Hz), 5.08 (major, dd, 1H, J = 10.2 Hz, 1.8 Hz), 5.04-5.06 (minor, m, 1H, minor diastereomer superimposed), 5.00 (major, ddd, 1H, J = 17 Hz, 1.8 Hz, 0.6
Hz), 4.99 (minor, ddd, 1H, $J = 17$ Hz, 1.8 Hz, 0.7 Hz), 3.66 (minor, s, 3H), 3.65 (major, s, 3H), 2.51-2.57 (minor, m, 1H), 2.46 (major, dt, 1H, $J = 8.2$ Hz, 5.0 Hz), 2.23-2.32 (major, m, 2H, minor diastereomer superimposed), 2.17-2.19 (major, m, 1H, minor diastereomer superimposed), 2.15 (major, s, 3H), 2.11 (minor, s, 3H), 1.80-1.87 (major, m, 2H, minor diastereomer superimposed), 1.14-1.34 (major, m, 6H, minor diastereomer superimposed), 0.85-0.88 (major, m, 3H, minor diastereomer superimposed).

$^{13}$C NMR (100 MHz, CDCl$_3$) $\delta$ 211.4, 173.6, 138.9, 117.1, 116.5 (minor), 56.3, 51.6, 46.1, 32.4, 32.0 (minor), 31.7, 30.3 (minor), 29.9, 29.6, 29.5, 23.7, 22.5, 13.98.

GC (cyclosil-B, 100 °C): $R_t$ from dppp: 223.59 min (major, broad, enantiomers tailing over each other) and 226.86 min (minor, broad, enantiomers tailing over each other); from (S,S-BDPP): 223.89 min (86.6%) (major) and 226.44 min (11.3%) (minor). [ee of the product $>$85%]

HRMS (ESI-MS): $m/z$ 263.1605 ([M+Na]); exact mass calculated for $C_{14}H_{24}O_3Na$ 263.1618.

$[\alpha]_D^{23}$ (c = 0.3, CHCl$_3$) + 4.3 [from (S,S-BDPP)]

6-Acetyl-4-butyl-7-vinyl-2-undecanone (18): (S,S-BDPP) product $S$-9a (85% ee) was taken further for the Michael reaction. NMR diastereomeric ratio: dppp (12.5 : 1); from (S,S-BDPP) (13 : 1), $^1$H NMR (400 MHz, CDCl$_3$) $\delta$ 5.66 (minor, dt, 1H, $J = 17.1$ Hz, 9.8 Hz), 5.47 (major, dt, 1H, $J = 17$ Hz, 10 Hz), 5.10 (major, dd, 1H, $J = 10.2$ Hz, 1.9 Hz), 5.04 (major, dd, 1H, $J = 17$ Hz, 1.7 Hz), 5.00-5.5.05 (minor, m, 1H, superimposed over
major), 4.94 (minor, dd, 1H, $J = 17.4$ Hz, 1.8 Hz), 2.70-2.75 (minor, m, 1H), 2.58 (major, dd, 1H, $J = 10.2$ Hz, 3.8 Hz), 2.34-2.53 (major, m, 2H, minor diastereomer superimposed), 2.19-2.27 (major, m, 1H, minor diastereomer superimposed), 2.17 (minor, s, 3H), 2.14 (major, s, 3H), 2.13 (major, s, 3H), 1.53-1.61 (major, m, 1H, minor diastereomer superimposed), 0.96-1.03 (major, m, 12H, minor diastereomer superimposed), 0.82-0.88 (major, m, 6H, minor diastereomer superimposed).

$^{13}$C NMR (100 MHz, CDCl$_3$) $\delta$ 212.2, 208.3, 140.2, 116.6, 58.5, 45.7, 45.2 (minor), 44.3, 40.0, 34.3, 33.0, 32.8, 30.3, 30.1, 29.7, 29.4, 28.0 (minor), 22.7, 22.5 (minor), 22.49, 14.1, 13.97, 13.88 (minor).

GC (cyclosil-$B$, 120 °C): R$_t$ from dppp: 198.48 min (5.5%), 202.83 min (49.3%) and 205.29 min(45.2%); from (S,S-BDPP): 198.65 min (4.8%), 203.91 min (86.8%), 204.91 min (6.2%) and 207.02 min (2.2%). [ee of the product >85%]

HRMS (ESI-MS): $m/z$ 303.2286 ([M+Na]); exact mass calculated for C$_{18}$H$_{32}$O$_2$Na 303.2295

$[\alpha]_D^{23}$ (c = 2.25, CHCl$_3$) – 8.5 [from (S,S-BDPP)]

4-(1-Acetyl-2-vinylcycloheptyl)butan-2-one (24): (S,S-BDPP) product

$R$-9m (96% ee) was taken further for the Michael reaction. GC diastereomeric ratio: dppp (11.5 : 1); from (S,S-BDPP) (7 : 1), $^1$H NMR (400 MHz, CDCl$_3$) $\delta$ 5.75-5.84 (m, major and minor superimposed, 1H each), 5.02-5.04 (m, major and minor superimposed, 1H each), 4.98-5.01 (m, major and minor superimposed, 1H each), 2.73 (major, quintet, 1H, $J = 5$ Hz), 2.33-2.41 (m, major
and minor superimposed, 1H each), 2.14-2.27 (m, major and minor superimposed, 1H each), 2.12 (minor, s, 3H), 2.11 (major, s, 3H), 2.09 (major, s, 3H), 2.06 (minor, s, 3H), 1.93-2.04 (m, major and minor superimposed, 1H each), 1.79-1.87 (m, major and minor superimposed, 1H each), 1.58-1.76 (m, major and minor superimposed, 6H each), 1.44-11.56 (m, major and minor superimposed, 4H each).

$^13$C NMR (100 MHz, CDCl$_3$) $\delta$ 212.3, 208.4, 139.0, 115.8, 57.0, 47.7, 38.5, 33.5, 30.6, 30.0, 28.1, 27.7, 25.8, 24.4, 23.4.

GC (cyclosil-B, 130 °C): R$_t$ from dppp: 124.37 min and 126.29 min (major), 135.59 min and 137.11 min (minor); from (S,S-BDPP): 127.07 min (87.4%) (major) and 137.33 min (12.6%) (minor). [ee of the product >96%]

HRMS (ESI-MS): $m/z$ 259.1669 ([M+Na]); exact mass calculated for C$_{15}$H$_{24}$O$_2$Na 259.1669.

$[\alpha]_D^{23}$ (c = 0.65, CHCl$_3$) – 12.7 [from (S,S-BDPP)]

**Typical Procedure for the Mukaiyama-Aldol Reaction of Silyl Enol Ether:**

**Procedure for Mukaiyama-Aldol Reaction of 4-Vinyl-2-trimethylsilyloxy-2(E)-octene (9a) with Cyclohexanecarboxaldehyde:**

A 25mL three-necked flask equipped with magnetic stirring bar, stopper, rubber septum and nitrogen inlet was flame dried and purged with argon. The flask was charged with 55µL of BF$_3$.OEt$_2$ and further diluted with 1mL of DCM and cooled down to -78 °C in dry ice acetone bath. Cyclohexanecarboxaldehyde (32µL, 0.265mmol, 1.2 eq) was added in the flask as color changed in to pale yellow. The flask was charged with 0.221 mmol
of 4-Vinyl-2-trimethylsilyloxy-2(\textit{E})-octene (0.050g, 0.221mmol) dissolved in minimal amount of DCM (1mL). The solution mixture immediately turned in to brownish-red color. The reaction mixture was allowed to stir at -78 °C for an hour (reaction was monitored by TLC). 5mL water was added to the reaction mixture very slowly at -78 °C and allowed it to warm up to rt slowly. The resulting mixture was extracted with ether (5mL X 3). The organic layers were combined, dried over MgSO₄ and concentrated to give the Mukaiyama-Aldol product which was then eluted through a plug of silica with hexane-ethylacetate (4:1) to get the pure product.

3-(hydroxy(phenyl)methyl)-4-vinylactan-2-one (19a): \textsuperscript{1}H NMR shows diastereomeric ratio : 1 : 0.4 : 0.3; \textsuperscript{1}H NMR (400 MHz, CDCl₃) δ 7.23-7.32 (all diastereomers, m, 5H), 5.89 (minor, ddd, 1H, J = 17 Hz, 10 Hz, 9.9 Hz), 5.76 (major, ddd, 1H, J = 17.1 Hz, 9.9 Hz, 9.8 Hz), 5.58 (minor, ddd, 1H, J = 17 Hz, 10.1 Hz, 9.5 Hz), 5.23 (minor, dd, 1H, J = 8 Hz, 1.3 Hz), 5.11-5.23 (major, m, 2H, rest diastereomers 2H each superimposed), 4.95 (minor, dd, 1H, J = 7.6 Hz, 3.4 Hz), 4.91 (major, d, 1H, J = 8.2 Hz), 4.83 (minor, d, 1H, J = 9.1 Hz), 3.09 (minor, dd, 1H, J = 9.1 Hz, 4.3 Hz), 3.04 (major, t, 1H, J = 7.6 Hz), 2.87 (minor, dd, 1H, J = 9.7 Hz, 3.6 Hz), 2.59-2.71 (all diastereomers, m, 2H), 1.78 (minor, s, 3H), 1.74 (minor, s, 3H), 1.73 (major, s, 3H), 1.12-1.33 (all diastereomers, m, 6H), 0.84-0.88 (all diastereomers, m, 3H).

\textsuperscript{13}C NMR (100 MHz, CDCl₃) δ 215.1, 210.87 (major), 210.75 (3 diastereomers), 142.93, 142.37, 141.78 (major), 141.46 (major), 139.20, 139.03 (3 diastereomers, 2 carbon), 128.48, 128.38 (major), 127.89 (major) (3 diastereomers), 127.22, 126.81 (major), 126.68
(3 diastereomers), 125.49 (major), 125.24, 117.98, 116.89 (major) (3 diastereomers, 2 carbon), 74.48 (major), 73.47, 72.41 (3 diastereomers), 65.82, 64.83 (major), 63.67 (3 diastereomers), 44.89 (major), 44.23, 43.71 (3 diastereomers), 34.55, 34.21, 33.92, 33.48 (major), 32.74, 32.16, 30.94, 30.31 (major), 29.83, 29.67, 29.54 (major), 22.48 (major), 22.42, 15.24, 13.99 (major), 13.93.

HRMS (ESI-MS): m/z 283.1661 ([M+Na]); exact mass calculated for C₁₇H₂₄O₂Na 283.1669.

3-(Cyclohexyl(hydroxy)methyl)-4-vinloctan-2-one (19b): (S,S-BDPP) product S-9a (85% ee) was taken further for the aldol reaction. ¹H NMR shows diastereomeric ratio : 1 : 0.2 : 0.1; ¹H NMR (400 MHz, CDCl₃) δ 5.86 (minor, ddd, 1H, J = 17.1 Hz, 10 Hz, 10 Hz), 5.72 (major, ddd, 1H, J = 17.1 Hz, 9.8 Hz, 9.6 Hz), 5.47 (minor, ddd, 1H, J = 16.6 Hz, 10.2 Hz, 9.4 Hz), 5.10-5.16 (major, m, 2H, rest diastereomers 1H each superimposed), 4.94-5.01 (minor, m, 1H each superimposed), 3.66 (major, dd, 1H, J = 4.2 Hz, 7.2 Hz), 3.44 (minor, dd, 1H, J = 3.5 Hz, 8.2 Hz), 3.38 (minor, dd, 1H, J = 2.7 Hz, 9.0 Hz), 2.93 (minor, dd, 1H, J = 8.4 Hz, 4.3 Hz), 2.83 (major, t, 1H, J = 7.0 Hz), 2.77 (minor, dd, 1H, J = 9.1 Hz, 3.6 Hz), 2.70 (minor, dd, 1H, J = 9.5 Hz, 2.6 Hz), 2.58-2.64 (minor, m, 1H), 2.48-2.57 (major diastereomer with one minor diastereomer, m, 1H), 2.23 (minor, s, 3H), 2.17 (major, s, 3H), 2.14 (minor, s, 3H), 1.71-1.80 (all diastereomers, m, 4H), 1.58-1.80 (all diastereomers, m, 3H), 1.38-1.46 (all diastereomers, m, 1H), 1.06-1.32 (all diastereomers, m, 9H), 0.83-0.87 (all diastereomers, m, 3H).
$^{13}$C NMR (100 MHz, CDCl$_3$) δ 211.73, 114.76, 116.29, 75.79, 59.77, 44.09, 41.11, 32.55, 31.08, 30.42, 29.62, 26.72, 26.37, 26.30, 26.08, 22.50, 14.00.

Minor diastereomers: 215.51, 211.42, 139.80, 139.57, 117.32, 116.74, 75.47, 75.17, 58.66, 57.05, 44.47, 43.39, 42.49, 41.21, 33.66, 33.28, 32.85, 32.37, 30.54, 29.92, 29.85, 29.52, 26.55, 26.15, 25.96, 25.80.

HRMS (ESI-MS): m/z 289.2104 ([M+Na]); exact mass calculated for C$_{17}$H$_{30}$O$_2$Na 289.2111.

$[\alpha]_D^{23}$ (c = 1.6, CHCl$_3$) + 1.375 [from (S,S-BDPP)]

**Typical Procedure for the Mannich Reaction of Silyl Enol Ether: Procedure for Mannich Reaction of 4-Vinyl-2-trimethylsilyloxy-2(\textit{E})-octene (9a) with N-Ts-Phenylmethanimine:**

A 25mL three-necked flask equipped with magnetic stirring bar, stopper, rubber septum and nitrogen inlet was flame dried and purged with argon. The flask was charged with N-Ts-phenylmethanimine$^{56}$ (35mg, 0.1325mmol, 1.2 eq) and further diluted with 1mL of DCM and cooled down to -78 °C in dry ice acetone bath. 14µL of BF$_3$.OEt$_2$ (35mg, 0.1325mmol, 1.2 eq) was added in the flask slowly using a microliter syringe. 4-Vinyl-2-trimethylsilyloxy-2(\textit{E})-octene (0.025g, 0.11mmol) dissolved in minimal amount of DCM (1mL) was cannula transferred in to the reaction flask keeping the reaction temperature at -78 °C. The reaction mixture was allowed to stir at -78 °C for an hour (reaction was monitored by TLC). 5mL water was added to the reaction mixture very slowly at -78 °C and allowed it to warm up to rt slowly. The resulting mixture was extracted with ether
(5mL X 3). The organic layers were combined, dried over MgSO₄ and concentrated to give the product which was then eluted through a plug of silica with hexane:ether (4:1) to get the pure product.

\[ \text{N-(2-Acetyl-1-phenyl-3-vinylheptyl)-4-methylbenzenesulfonamide (20):} \]

\( \text{(S, S-DIOP) product R-9a (99\% ee) was taken further for the Mannich reaction.} \)

\( ^1 \text{H NMR shows diastereomeric ratio 7:1;} \)

\( ^1 \text{H NMR (400 MHz, CDCl}_3) \)

\( \delta 7.47 \text{ (major, d, } 2\text{H, } J = 8.3 \text{ Hz), } 7.38 \text{ (minor, d, } 2\text{H, } J = 0.3 \text{ Hz), } 7.32 \text{ (minor, d, } 2\text{H, } J = 8.1 \text{ Hz), 6.98-7.09 (major diastereomer superimposed with minor diastereomer, m, 5H), 6.92 (major, dd, } 2\text{H, } J = 1.5 \text{ Hz, 7.4 Hz), 5.74 (minor, ddd, } 1\text{H, } J = 9.2 \text{ Hz, 10.4 Hz, 16.9 Hz), 5.55 (major, ddd, } 1\text{H, } J = 9.5 \text{ Hz, 10.1 Hz, 17.0 Hz), 5.32 (major, minor superimposed, d, } 1\text{H, } J = 8.6 \text{ Hz), 5.11-5.21 (major, minor superimposed, m, 2H), 4.58 (major, t, } 1\text{H, } J = 8.8 \text{ Hz), 3.03 (major, minor superimposed, dd, } 1\text{H, } J = 6.1 \text{ Hz, 9.2 Hz), 2.54-2.61 (major, minor superimposed, m, 1H), 2.32 (major, s, 3H), 2.29 (minor, s, 3H), 1.70 (major, s, 3H), 1.48-1.57 (major, minor superimposed, m, 1H), 1.04-1.31 (major, minor superimposed, m, 6H), 0.84-0.90 (major, minor superimposed, m, 3H).} \)

\( ^{13} \text{C NMR (100 MHz, CDCl}_3) \)

\( \delta 209.3, 143.1, 140.3, 138.9, 137.3, 129.2, 128.3, 127.5, 127.3, 127.1, 117.3, 63.0, 57.4, 43.6, 33.3, 29.8, 29.5, 22.6, 21.4, 14.0. \)

minor diastereomers (which ones are observed separately): 129.7, 129.1, 127.4, 127.1, 126.5, 125.5, 62.3, 34.1, 30.3, 22.3.

HRMS (ESI-MS): \( m/z 436.1915 ([M+Na]) \); exact mass calculated for \( \text{C}_{24}\text{H}_{31}\text{O}_{3}\text{SNa} \)

439.1917.
\[ \alpha \]_{D}^{23} (c = 1.1, \text{CHCl}_3) +18.4 \text{ [from (S,S-DIOP)]}

**Typical Procedure for the Nucleophilic Addition of Silyl Enol Ethers to Aromatic Nitro Compounds:** Procedure for Nucleophilic Addition of 4-Vinyl-2-trimethylsilyloxy-2(\(E\))-octene (9a) to 1-Bromo-4-nitrobenzene:

3-(5-Bromo-2-nitrophenyl)-4-vinyloctan-2-one (21):\(^{14}\) (S,S-DIOP) product \(R-9a\) (99% ee) was taken further for the nucleophilic reaction.

To a mixture of 1-bromo-4-nitrobenzene (40mg, 0.199mmol, 0.95 eq) and 4-vinyl-2-trimethylsilyloxy-2(\(E\))-octene (50mg, 0.221mmol, 1.0 eq) in 1 mL of THF at -78 °C, was cannula transferred 70.0mg of TASF (0.243mmol, 1.1 eq) dissolved in 1ml of acetonitrile: THF mixture (1:1). The solution immediately turned in to greenish color. The cold bath was removed and the reaction was warmed up to -30 °C and maintained at -30 °C for an hour. After the solution was cooled back to -78 °C, 50.2mg of DDQ in 1mL of THF was added dropwise. The cold bath was removed and and the reaction was warmed up to -30 °C and maintained at -30 °C for 4h. Water was added at -30 °C to quench the reaction. The reaction mixture was allowed to warm up to room temperature and extracted with diethyl ether. Isolation by flash chromatography yielded 32mg of 3-(5-bromo-2-nitrophenyl)-4-vinyloctan-2-one (yield 41%) with a diastereomeric ratio 2:1.

\(^1\)H NMR shows diastereomeric ratio (2:1); \(^1\)H NMR (400 MHz, CDCl\(_3\)) \(\delta\) 7.798 (minor, d, 1H, \(J = 2.1\) Hz), 7.60-7.66 (major diastereomer superimposed with minor diastereomer, m, 2H), 7.53 (minor, dd, 2H, \(J = 2.1\) Hz, 8.6 Hz), 7.47 (major, dd, 1H, \(J = 2.1\) Hz, 8.6 Hz), 5.57 (minor, ddd, 1H, \(J = 9.1\) Hz, 10.2 Hz, 17.0 Hz), 5.20 (major, ddd, 1H, \(J = 10\) Hz, 17.0 Hz, 17.0 Hz), 5.06-5.14 (major, minor superimposed, m, 1H), 4.80
(major, minor superimposed, dd, 1H, $J = 1.7$ Hz, 10.2 Hz), 4.70 (major, minor superimposed, dd, 1H, $J = 1.6$ Hz, 17.0 Hz), 4.37 (major, d, 1H, $J = 10.4$ Hz), 4.30 (minor, d, 1H, $J = 10.4$ Hz), 2.66-2.79 (major, minor superimposed, m, 1H), 2.25 (major, s, 3H), 2.21 (minor, s, 3H), 1.19-1.35 (major, minor superimposed, m, 6H), 0.85-0.90 (major, minor superimposed, m, 3H).

$^{13}C$ NMR (100 MHz, CDCl$_3$) δ 206.3, 206.2, 149.9, 149.6, 138.6, 137.9, 133.8, 133.4, 133.3, 133.2, 131.2, 131.1, 127.5, 127.4, 125.5, 125.4, 118.2, 117.8, 56.2, 55.95, 47.9, 47.5, 33.1, 32.2, 31.7, 31.2, 29.3, 28.7, 22.4, 22.2, 13.9, 13.7.

GC (cyclosil-B, 130 °C): $R_t$ from dppp: 139.58 min (23.2%), 141.82 min (23.1%), 145.17 min (28.4%) and 146.35 min (25.2%), diastereomeric ratio = 1:1; from (S,S-DIOP): 141.16 min (33.8%) and 144.56 min (66.2%), diastereomeric ratio = 2:1. [ee of the product 99%]

HRMS (ESI-MS): $m/z$ 376.0508 and 378.1609 ([M+Na]); exact mass calculated for C$_{16}$H$_{20}$O$_3$N$_1$Br$_1$Na 376.0519.

$[\alpha]_D^{23}$ (c = 0.5, CHCl$_3$) + 93.6 [from (S,S-DIOP)]
Typical Procedure for the Allylation of the Silyl Enol Ether: Procedure for Allylation of \((E)\)-Trimethyl(1-(2-vinylcycloheptylidene)ethoxy)silane (9m) with Allyl Bromide:

In a flame-dried 25 mL flask under argon was combined 0.36 mmol silyl enol ether and 0.58 mmol allyl bromide in 1 mL dry THF and the flask was cooled to 0 °C. A suspension of 0.42 mmol TASF was added dropwise and the reaction was allowed to warm to rt and stir overnight. The reaction was quenched with saturated NaHCO₃(aq), extracted with ether (10mL x 3), and dried over Na₂SO₄ overnight. Product was concentrated and then purified by column chromatography using 5% EtOAc in hexanes, yielding a colorless oil which contained a mixture of diastereomers. (25% yield)

1-((1S,2R)-1-allyl-2-vinylcycloheptyl)ethan-1-one (23): \((S,S\text{-BDPP})\)

Product R-9m (96% ee) was taken further for the allylation reaction. GC diastereomeric ratio: dppp (2.8:1); \((S,S\text{-BDPP})\) (2.6:1). \(^1\)H (400 MHz, CDCl₃) δ 5.79-5.89 (major and minor superimposed, m, 1H each), 5.62-5.72 (major and minor superimposed, m, 1H each), 5.02-5.11 (major and minor superimposed, m, 1H each), 2.79 (septet, 1H, \(J = 10\) Hz, 6.4 Hz, 3.6 Hz), 2.33-2.47 (major and minor superimposed, m, 2H each), 2.14 (major, s, 3H), 2.06 (minor, s, 3H), 1.45-1.74 (major and minor superimposed, m, 10H each). [product was contaminated with ethyl acetate and hexanes]

\(^{13}\)C (100 MHz, CDCl₃) δ 212.4, 212.1, 140.2, 139.3, 134.5, 134.1, 118.0, 117.4, 115.8, 115.5, 60.4, 57.9, 57.6, 51.2, 48.1, 41.1, 40.1, 33.8, 31.6, 31.4, 30.5, 30.0, 28.6, 28.2,
27.7, 26.3, 25.3, 25.2, 23.5, 22.6, 22.3, 21.0, 14.2 [product was contaminated with ethyl acetate and hexanes]

GC: (cyclosil-B, 100 °C): R_t from dppp: 104.98 min (13.79%), 108.67 min (36.15%), 110.19 min (36.26%), 112.46 min (13.80%); from (S,S-BDPP): 105.08 min (0.08%), 108.79 min (0.38%), 110.31 min (73.87%), 112.56 min (26.67%). GC diastereomeric ratio: (S,S-BDPP) (2.6:1). [ee of the product 95%]

HRMS (ESI-MS): m/z 229.1568 ([M + Na]); exact mass calculated for C_{14}H_{22}ONa 229.1563.

Typical Procedure for the Preparation of Enol Triflates via Hydrovinylation of Siloxydienes: Procedure for Generation of Enolate of 4-Vinyl-2-trimethylsilyloxy-2(E)-octene (9a) for the Preparation of Vinyl triflate (E)-4-Vinylct-2-en-2-yl trifluoromethanesulfonate (25):

A 25mL three-necked flask equipped with magnetic stirring bar, stopper, rubber septum and nitrogen inlet was flame dried and purged with argon. The flask was charged with 4-vinyl-2-trimethylsilyloxy-2(E)-octene (500mg, 2.2mmol, achiral or enantiopure substrate) and further diluted with 2mL of THF and cooled down to 0 °C in an ice bath. 1.7 mL of 1.6(M) MeLi in ether (2.65mmol, 1.2 eq) was added in the flask slowly as color changed in to pale yellow. The reaction mixture was allowed to warm up to ambient room temperature for an hour to generate the lithium enolate. The reaction mixture was cooled back to -78 °C and a solution of PhN(Tf)_2 (950mg, 2.65mmol, 1.2 eq) in 4 mL THF was added to the reaction mixture slowly. The resulting mixture was allowed to warm up to room temperature over 6 h and rotaevaporated to remove all the solvent from
the vinyl triflate product which was then eluted through a plug of silica with pentane to
get the pure product.

*(E)-4-Vinyloct-2-en-2-yl trifluoromethanesulfonate (25):* \(^1\)H NMR

\(\text{OTf} \)

\[(400 \text{ MHz, CDCl}_3) \delta 5.69 \text{ (ddd, 1H, } J = 6.5 \text{ Hz, } 10.0 \text{ Hz, } 17.4 \text{ Hz)},
5.39 \text{ (dd, 1H, } J = 0.7 \text{ Hz, } 10.0 \text{ Hz}), 5.04 \text{ (ddd, 1H, } J = 1.4 \text{ Hz, } 2.8 \text{ Hz, } 3.6 \text{ Hz}), 5.01 \text{ (ddd, } 1H, J = 1.3 \text{ Hz, } 2.7 \text{ Hz, } 3.8 \text{ Hz}), 2.75-2.83 \text{ (m, } 1H), 2.04 \text{ (d, } 3H, J = 0.8 \text{ Hz}), 1.47 – 1.56 \text{ (m, } 1H), 1.22-1.42 \text{ (m, } 5H), 0.87-0.91 \text{ (m, } 3H).\]

\(\text{^13C NMR} (100 \text{ MHz, CDCl}_3) \delta 146.4, 139.3, 124.4, 120.1, 114.8, 41.6, 34.8, 29.1, 22.5, 16.3, 13.9.\)

GC (*cyclosil B, 50 °C*): \(R_t\) from dppp: 342.994 min and 346.68 min; from (S,S-DIOP): 341.42 min (>99%).

HRMS (ESI-MS): \(m/z 308.9703 ([M+Na])\); exact mass calculated for C\(_{11}\)H\(_{17}\)O\(_3\)F\(_3\)SNa 308.9934.

\([\alpha]^{23}_D (c =0.75, \text{CHCl}_3) – 2.9 \text{ [from (S,S-DIOP)].}\)

NOESY NMR confirms *(E)-25* due to observed nOe between allyl-CH\(_3\) with newly
installed vinyl group.

*(E)-4-Vinyldec-2-en-2-yl trifluoromethanesulfonate (26):* \(^1\)H

\(\text{NMR} (400 \text{ MHz, CDCl}_3) \delta 5.69 \text{ (ddd, 1H, } J = 6.5 \text{ Hz, } 10.0 \text{ Hz,}
17.4 Hz), 5.39 (dd, 1H, J = 0.7 Hz, 10.1 Hz), 5.04 (ddd, 1H, J = 1.3 Hz, 2.8 Hz, 3.7 Hz), 5.01 (ddd, 1H, J = 1.3 Hz, 2.6 Hz, 3.7 Hz), 2.76-2.83 (m, 1H), 2.04 (d, 3H, J = 0.8 Hz), 1.44-1.52 (m, 1H), 1.23-1.33 (m, 9H), 0.87-0.90 (m, 3H).

$^{13}$C NMR (100 MHz, CDCl$_3$) δ 146.4, 139.3, 124.4, 120.1, 114.8, 41.6, 35.1, 34.1, 31.7, 29.1, 26.9, 22.5, 22.3, 16.3, 14.0.

GC (cyclosil B, 70 °C): R$_t$ from dppp: 417.05 min.

HRMS (ESI-MS): m/z 337.1045 ([M+Na]); exact mass calculated for C$_{13}$H$_{21}$O$_3$F$_3$SNa 337.1056.

$[\alpha]_D^{23}$ (c =0.85, CHCl$_3$) – 5.2 [from (S,S-DIOP)]

(27): $^1$H NMR (400 MHz, CDCl$_3$) δ 5.68 (ddd, 1H, J = 7.3 Hz, 10.3 Hz, 17.4 Hz), 5.47 (dd, 1H, J = 0.8 Hz, 10.4 Hz), 5.05 (dt, 1H, J = 1.3 Hz, 10.3 Hz), 4.998 (dt, 1H, J = 1.3 Hz, 17.2 Hz), 2.57-2.63 (m, 1H), 2.03 (d, 3H, J = 0.9 Hz), 1.63-1.75 (m, 5H), 1.10-1.38 (m, 6H).

$^{13}$C NMR (100 MHz, CDCl$_3$) δ 146.4, 138.1, 123.1, 120.1, 115.7, 48.1, 42.2, 30.9, 29.9, 26.4, 26.3, 26.3, 16.4.

GC (cyclosil B, 90 °C): R$_t$ from dppp: 188.53 min and 192.07 min. from (S,S-BDPP): 188.84 min (2%) and 190.01 min (98%).

HRMS (ESI-MS): m/z 335.0894 ([M+Na]); exact mass calculated for C$_{13}$H$_{19}$O$_3$F$_3$SNa 335.0899.
[\alpha]D^{23} (c =0.80, CHCl₃) + 11.25 [from (S,S-BDPP)].

(E)-4-Isopropylhexa-2,5-dien-2-yl trifluoromethanesulfonate (28):

\[
\begin{align*}
\text{H NMR (400 MHz, CDCl₃)} & \delta 5.70 \text{ (ddd, 1H, } J = 7.0 \text{ Hz, 10.3 Hz, 17.3 Hz)}, 5.47 \text{ (dd, 1H, } J = 0.6 \text{ Hz, 10.4 Hz)}, 5.07 \text{ (dt, 1H, } J = 1.2 \text{ Hz, 10.3 Hz)}, 5.02 \text{ (dt, 1H, } J = 1.4 \text{ Hz, 17.2 Hz)}, 2.56-2.64 \text{ (m, 1H)}, 2.04 \text{ (d, 3H, } J = 0.8 \text{ Hz)}, 1.70 \text{ (septet, 1H, } J = 6.8 \text{ Hz)}, 0.92 \text{ (d, 1H, } J = 6.7 \text{ Hz)}, 0.89 \text{ (d, 1H, } J = 6.8 \text{ Hz}).
\end{align*}
\]

\[13C\text{ NMR (100 MHz, CDCl₃)} \delta 146.7, 138.1, 122.7, 120.2, 115.8, 48.6, 32.5, 20.2, 19.2, 16.3.\]

GC (cyclosil B, 50 °C): Rₜ from dppp: 149.84 min and 154.13 min. from (S,S-BDPP): 152.91 min (3%) and 154.66 min (97%).

HRMS (ESI-MS): m/z 295.0577 ([M+Na]); exact mass calculated for C₁₀H₁₅O₃F₃SNa 295.0586.

\[\text{[\alpha]D}^{23} (c =1.8, CHCl₃) + 2.8 \text{ [from (S,S-BDPP)]} \]

(E)-1-(2-Vinylcyclohexyldene)ethyl trifluoromethanesulfonate (29):

\[
\begin{align*}
\text{H NMR (400 MHz, CDCl₃)} & \delta 5.83 \text{ (ddd, 1H, } J = 4.7 \text{ Hz, 10.4 Hz, 17.4 Hz)}, 5.12 \text{ (ddd, 1H, } J = 1.4 \text{ Hz, 2.1 Hz, 10.4 Hz)}, 5.02 \text{ (ddd, 1H, } J = 1.4 \text{ Hz, 2.1 Hz, 17.3 Hz)}, 3.22 \text{ (b, 1H)}, 2.67-2.72 \text{ (m, 1H)}, 2.05 \text{ (d, 3H, } J = 2.2 \text{ Hz)}, 1.85-2.05 \text{ (m, 2H)}, 1.76-1.83 \text{ (m, 1H)}, 1.43-1.67 \text{ (m, 4H}).
\end{align*}
\]

\[13C\text{ NMR (100 MHz, CDCl₃)} \delta 139.5, 138.7, 132.2, 120.0, 115.9, 40.2, 31.7, 26.2, 22.3, 21.0, 15.9.\]
GC (cyclosil B, 100 °C): R<sub>t</sub> from dppp: 33.67 min and 39.48 min. from (S,S-BDPP): 33.56 min (>95%).

HRMS (ESI-MS): <i>m/z</i> 307.0593 ([M+Na]); exact mass calculated for C<sub>11</sub>H<sub>13</sub>O<sub>3</sub>F<sub>3</sub>SNa 307.0586.

[<i><i>[α]</i></i><sub>D</sub>]<sup>23</sup> (c =1.0, CHCl<sub>3</sub>) – 15.2 [from (S,S-BDPP)]

OTf (E)-1-(2-Vinylcycloheptylidene)ethyl trifluoromethanesulfonate (30): <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>) <i>δ</i> 5.67 (ddd, 1H, <i>J</i> = 5.8 Hz, 10.4 Hz, 17.1 Hz), 4.997 (dt, 1H, <i>J</i> = 1.4 Hz, 6.7 Hz), 4.96 (dt, 1H, <i>J</i> = 1.5 Hz, 13.4 Hz), 3.06-3.12 (m, 1H), 2.65-2.70 (m, 1H), 2.03 (b, 3H), 1.88-2.00 (m, 2H), 1.77-1.85 (m, 3H), 1.41-1.51 (m, 1H), 1.14-1.38 (m, 3H).

<sup>13</sup>C NMR (100 MHz, CDCl<sub>3</sub>) <i>δ</i> 142.6, 138.9, 134.9, 119.9, 113.7, 45.0, 32.9, 30.5, 28.9, 26.11, 26.09, 16.2.

GC (cyclosil B, 120 °C): R<sub>t</sub> from dppp: 20.72 min and 21.55 min. from (S,S-BDPP): 20.70 min (97%) and 21.56 min (3%).

HRMS (ESI-MS): <i>m/z</i> 321.0743 ([M+Na]); exact mass calculated for C<sub>12</sub>H<sub>17</sub>O<sub>3</sub>F<sub>3</sub>SNa 321.0743.

[<i><i>[α]</i></i><sub>D</sub>]<sup>23</sup> (c =0.75, CHCl<sub>3</sub>) – 43.4 [from (S,S-BDPP)]

(4<i>R</i>,6<i>S</i>,<i>E</i>)-6,10-Dimethyl-4-vinylundeca-2,9-dien-2-yl trifluoromethanesulfonate (31a): <sup>1</sup>H NMR (600 MHz, CDCl<sub>3</sub>) <i>δ</i> 5.68 (ddd, 1H, <i>J</i> = 6.4 Hz, 10.3 Hz, 17.0 Hz), 5.33 (dd, 1H, <i>J</i> = 0.5 Hz, 10.1...
Hz), 5.07-5.09 (m, 1H), 5.03 (dt, 1H, $J = 1.3$ Hz, 10.4 Hz), 5.01-5.02 (m, 1H), 2.89-2.94 (m, 1H), 2.05 (d, 3H, $J = 0.8$ Hz), 1.91-2.02 (m, 2H), 1.68 (d, 3H, $J = 0.8$ Hz), 1.60 (b, 3H), 1.38-1.42 (m, 2H), 1.25-1.33 (m, 2H), 1.15-1.21 (m, 1H), 0.88 (d, 3H, $J = 6.5$ Hz).

$^{13}$C NMR (125 MHz, CDCl$_3$) $\delta$ 146.4, 139.6, 131.4, 124.5, 124.4, 119.6, 114.5, 42.3, 39.2, 37.3, 29.8, 29.7, 25.6, 25.3, 19.3, 17.6, 16.3.

GC (cyclosil $B$, 130 °C): $R_t$ dppp: 36.87 min and 38.76 min. from (S,S)-DIOP: 36.87 min (96%) and 38.49 mins (3%).

HRMS (ESI-MS): $m/z$ 376.9350 ([M+Na]); exact mass calculated for C$_{16}$H$_{25}$O$_3$F$_3$SNa 376.9347.

$[\alpha]_D^{23}$ (c =0.55, CHCl$_3$) – 26.4 [from (S,S-DIOP)]

(4S,6S,E)-6,10-Dimethyl-4-vinylundeca-2,9-dien-2-yl trifluoromethanesulfonate (31b): $^1$H NMR (600 MHz, CDCl$_3$) $\delta$ 5.64 (ddd, 1H, $J = 6.48$ Hz, 10.0 Hz, 17.2 Hz), 5.38 (dd, 1H, $J = 0.7$ Hz, 10.0 Hz), 5.00-5.10 (m, 3H), 2.86-2.94 (m, 1H), 2.05 (d, 3H, $J = 0.8$ Hz), 1.81-2.02 (m, 2H), 1.68 (d, 3H, $J = 0.9$ Hz), 1.60 (b, 3H), 1.40-1.54 (m, 2H), 1.24-1.37 (m, 2H), 1.10-1.16 (m, 1H), 0.86-0.90 (m, 3H).

$^{13}$C NMR (125 MHz, CDCl$_3$) $\delta$ 146.2, 139.2, 131.4, 124.7, 124.5, 114.8, 42.5, 39.4, 31.6, 29.7, 25.7, 25.3, 19.7, 17.6, 16.3.

GC (cyclosil $B$, 130 °C): $R_t$dppp: 36.87 min and 38.76 min. from (R,R)-DIOP: 36.571 min (4%) and 38.649 mins (93%).
HRMS (ESI-MS): \( m/z \) 376.9350 ([M+Na]); exact mass calculated for \( \text{C}_{16}\text{H}_{25}\text{O}_{3}\text{F}_{3}\text{SNa} \) 376.9347.

\[ [\alpha]_D^{23} (c =0.25, \text{CHCl}_3) – 6.4 \text{ [from (R,R-DIOP)]} \]

**Procedures for Cross-Coupling Reactions**

\((E)-3\text{-Methyl-5-vinylnon-3-ene (32)}\): A 25mL three-necked flask equipped with magnetic stirring bar, stopper, rubber septum and nitrogen inlet was flame dried and purged with argon. The flask was charged with \((\text{dppp})\text{NiCl}_2\) (9.5mg, 0.0175mmol, 0.2 eq) and 1.0mL of distilled, dried THF was added at room temperature. \((E)-4\text{-vinylct-2-en-2-yl trifluoromethanesulfonate (25.0 mg, 0.09mmol, 1.0 eq)}\) and 0.3mL of 1(M) of ethylmagnesium bromide (0.27 mmol, 3.0 eq) were added in the flask slowly as color changed in to brownish. The reaction mixture was allowed to stir at room temperature for 1h. The suspension was further diluted with diethylether and washed with water and brine. The organic layer was dried over \(\text{MgSO}_4\) and concentrated to yellow oil, which was then further purified by flash column chromatography (100% pentane) to give pure \((E)-3\text{-methyl-5-vinylnon-3-ene (9.0mg, yield 61%)}\).

\(^1\text{H NMR (400 MHz, CDCl}_3\) } \delta \ 5.69 \text{ (ddd, 1H, } J = 7.0 \text{ Hz, 10.2 Hz, 17.2 Hz), 4.96 (ddd, 1H, } J = 1.4 \text{ Hz, 2.0 Hz, 5.8 Hz), 4.88-4.93 (m, 2H), 2.84-2.91 (m, 1H), 2.01 (dq, 2H, } J = 0.96 \text{ Hz, 7.4 Hz), 1.61 (d, 3H, } J = 1.3 \text{ Hz), 1.36-1.44 (m, 1H), 1.21-1.32 (m, 5H), 0.99 (t, 3H, } J = 7.4 \text{ Hz), 0.88 (t, 3H, } J = 6.9 \text{ Hz).}^

\(^{13}\text{C NMR (100 MHz, CDCl}_3\) } \delta \ 142.4, 137.1, 125.8, 112.4, 42.2, 35.3, 32.5, 29.4, 22.3, 16.3, 14.0, 12.9.
GC (cyclosil B, 90 °C): R_t from dppp: 8.99 min and 9.16 min. from (S,S-DIOP): 8.98 min (92%) and 9.15 min (2%).

HRMS (ESI-MS): m/z 197.0795 ([M+Na]); exact mass calculated for C_{12}H_{22}Na 197.0789.

[α]_D^{23} (c =0.5, CHCl_3) + 15.4 [from (S,S-DIOP)]

(E)-3-Methyl-5-vinylnon-3-en-2-one (33a): A 25mL three-necked flask equipped with magnetic stirring bar, stopper, reflux condensor and nitrogen inlet was flame dried and purged with argon and taken inside the glove box. The flask was charged with Pd(PPh_3)_4 (40.0mg, 0.035mmol, 0.1 eq) and anhydrous LiCl (75.0mg, 1.75mmol, 5.0 eq) inside the glove box. The flask was removed from the glove box with the flow-control inlet closed, placed on a vacuum line, and the stopcock opened to vacuum to remove the nitrogen, and subsequently purged with argon. Distilled, dried THF (4.0 mL) was added at room temperature. (E)-4-vinylcot-2-en-2-yl trifluoromethanesulfonate (100.0 mg, 0.35mmol, 1.0 eq) and tributyl(1-ethoxyvinyl)tin (126mg, 0.35 mmol, 1.0 eq) were added in the flask slowly as color changed in to pale yellow. The reaction mixture was allowed to stir at 65 °C for 24 h. The reddish suspension was further diluted with diethylether and washed a 5% aqueous ammonium hydroxide solution, water and brine. The organic layer was dried over MgSO_4 and concentrated to yellow oil.

The crude compound was dissolved in 2mL THF and 2mL of 2(N) HCl and stirred at room temperature for 10 h. The reaction mixture was washed with water and diethylether. The organic layers were dried over MgSO_4 and concentrated to give a light yellow oil,
which was then further purified by flash column chromatography (hexane: ether 19:1) to give pure \((E)\)-3-methyl-5-vinylnon-3-en-2-one (39.0mg, yield 61%).

\[
{^1}H\text{ NMR (400 MHz, CDCl}_3\text{) } \delta 6.42 (dq, 1H, J = 2.0 Hz, 9.5 Hz), 5.66-5.75 (m, 1H), 5.04 (b, 1H), 5.01 (dt, 1H, J = 1.1 Hz, 5.8 Hz), 3.07-3.15 (m, 1H), 2.32 (s, 1H), 1.79 (d, 3H, J = 1.3 Hz), 1.61-1.68 (m, 1H), 1.48-1.58 (m, 1H), 1.25-1.42 (m, 5H), 0.92 (t, 3H, J = 7.3 Hz).
\]

\[
{^{13}}C\text{ NMR (100 MHz, CDCl}_3\text{) } \delta 199.9, 145.1, 139.4, 137.2, 114.8, 43.5, 29.3, 27.9, 26.8, 25.5, 17.5, 13.6, 11.4.
\]

GC (cyclosil B, 100 °C): \(R_t\) from dppp: 32.92 min and 33.21 min. From (S,S-DIOP): 32.91 min (99%).

HRMS (ESI-MS): \(m/z\) 203.1402 ([M+Na]); exact mass calculated for \(C_{12}H_{20}O_{1}Na\) 203.1406.

\([\alpha]_D^{23} (c = 1.325, \text{CHCl}_3) = -15.4 \text{ [from (S,S-DIOP)]}\)

\((E)\)-3-methyl-5-vinylnona-1,3-diene (33b): A 25mL three-necked flask equipped with magnetic stirring bar, stopper, reflux condensor and nitrogen inlet was flame dried and purged with argon and taken inside the glove box. The flask was charged with \(\text{Pd(PPh}_3\text{)}_4\) (4.0mg, 0.0035mmol, 0.05 eq) and anhydrous \(\text{LiCl}\) (9.0mg, 0.21mmol, 3.0 eq) inside the glove box. The flask was removed from the glove box with the flow-control inlet closed, placed on a vacuum line, and the stopcock opened to vacuum to remove the nitrogen, and subsequently purged with argon. Distilled, dried \(\text{THF}\) (1.0 mL) was added at room temperature. \((E)\)-4-vinyloct-2-en-2-yl
trifluoromethanesulfonate (20.0 mg, 0.7mmol, 1.0 eq) and tributyl(vinyl)tin (21mg, 0.066 mmol, 0.95 eq) were added in the flask slowly as color changed in to pale yellow. The reaction mixture was allowed to stir at 65 °C for 24 h. The reddish suspension was further diluted with diethylether and washed a 5% aqueous ammonium hydroxide solution, water and brine. The organic layer was dried over MgSO₄ and concentrated to yellow oil (8.0 mg, 67% yield).

\(^1\)H NMR (600 MHz, CDCl₃) δ 6.39 (ddd, 1H, \(J = 0.7\) Hz, 10.7 Hz, 17.4 Hz), 5.70 (ddd, 1H, \(J = 7.0\) Hz, 10.2 Hz, 17.2), 5.31 (d, 1H, \(J = 9.2\) Hz), 5.10 (m, 1H), 4.92-4.99 (m, 3H), 2.99-3.07 (m, 1H), 1.75 (d, 1H, \(J = 1.2\) Hz), 1.40-1.50 (m, 1H), 1.34-1.38 (m, 1H), 1.24-1.33 (m, 4H), 0.88 (t, 3H, \(J = 7.4\) Hz).

\(^{13}\)C NMR (125 MHz, CDCl₃) δ 141.63, 141.29, 135.5, 133.9, 113.3, 110.9, 42.6, 35.1, 29.4, 22.7, 14.0, 12.0.

GC (cyclosil B, 75 °C): \(R_f\) from dppp: 27.298 min and 27.950 mins from (S,S-DIOP): 27.309 min (95%) and 28.025 min (2%).

GC-MS (methyl silicone): \(m/z\) ([M+]) 164.10; exact mass calculated for C₁₀H₂₀ 164.16.

\((E)\)-1-(but-3-en-2-ylidene)-2-vinylcycloheptane (33c): \(^1\)H NMR (400 MHz, CDCl₃) δ 6.88 (dd, 1H, \(J = 11.0\) Hz, 17.2 Hz), 5.75-5.66 (m, 1H), 5.18 (dd, 1H, \(J = 1.6\) Hz, 17.2 Hz), 5.01 (dd, 1H, \(J = 1.5\) Hz, 11.0 Hz), 4.92 (d, 1H, \(J = 1.6\) Hz), 4.89 (dt, 1H, \(J = 1.6\) Hz, 6.4 Hz), 3.34-3.40 (m, 1H), 2.66-2.71 (m, 1H), 1.82-1.99 (m, 3H), 1.71-1.80 (m, 2H), 1.77 (s, 3H), 1.40-1.49 (m, 1H), 1.34-1.38 (m, 1H), 1.21-1.33 (m, 2H).
$^{13}$C NMR (100 MHz, CDCl$_3$) $\delta$ 141.96, 140.64, 135.90, 128.62, 112.38, 111.62, 46.48, 32.95, 30.82, 29.90, 26.82, 26.17, 12.87.

GC (cyclosil B, 110 °C): R$_t$ from dppp: 19.404 min and 20.127 mins from (S,S-BDPP): 19.420 min (2%) and 20.034 min (94%).

GC-MS (methyl silicone): m/z ([M+]) 176.30; exact mass calculated for C$_{13}$H$_{20}$ 176.16.

**(E)-(4-Vinyloct-2-en-2-yl)benzene (34):** A 25mL three-necked flask equipped with magnetic stirring bar, stopper, reflux condensor and nitrogen inlet was flame dried and purged with argon and taken inside the glove box. The flask was charged with Pd(PPh$_3$)$_4$ (10.0mg, 0.009mmol, 0.1 eq) and anhydrous K$_3$PO$_4$ (28.0mg, 0.135mmol, 1.5 eq) inside the glove box. The flask was removed from the glove box with the flow-control inlet closed, placed on a vacuum line, and the stopcock opened to vacuum to remove the nitrogen, and subsequently purged with argon. Distilled, dried dioxane (2.0 mL) was added at room temperature. (E)-4-vinyloct-2-en-2-yl trifluoromethanesulphonate (25.0 mg, 0.09mmol, 1.0 eq) and phenylboronic acid (12.8mg, 0.1 mmol, 1.1 eq) were added in the flask at one portion. The reaction mixture was allowed to reflux at 85 °C for 24 h. The reaction mixture was further diluted with diethylether and washed a saturated ammonium chloride solution, water and brine. The organic layer was dried over MgSO$_4$ and concentrated to yellow oil, which was then further purified by flash column chromatography (100% pentane) to give pure (E)-(4-vinyloct-2-en-2-yl)benzene (13.0mg, yield 67%).

$^1$H NMR (600 MHz, CDCl$_3$) $\delta$ 7.38-7.40 (m, 2H), 7.29-7.32 (m, 2H), 7.20-7.23 (m, 1H), 5.77 (ddd, 1H, $J = 6.9$ Hz, 10.2 Hz, 17.2 Hz), 5.60 (dq, 1H, $J = 1.3$ Hz, 9.2 Hz), 5.03 (dt, 1H), 4.89 (ddd, 1H, $J = 10.2$ Hz, 17.2 Hz, 17.2 Hz), 3.90 (ddd, 1H, $J = 6.9$ Hz, 10.2 Hz, 17.2 Hz), 3.70 (ddd, 1H, $J = 6.9$ Hz, 10.2 Hz, 17.2 Hz), 3.50 (ddd, 1H, $J = 6.9$ Hz, 10.2 Hz, 17.2 Hz), 3.30 (ddd, 1H, $J = 6.9$ Hz, 10.2 Hz, 17.2 Hz), 3.10 (ddd, 1H, $J = 6.9$ Hz, 10.2 Hz, 17.2 Hz), 2.90 (ddd, 1H, $J = 6.9$ Hz, 10.2 Hz, 17.2 Hz), 2.70 (ddd, 1H, $J = 6.9$ Hz, 10.2 Hz, 17.2 Hz), 2.50 (ddd, 1H, $J = 6.9$ Hz, 10.2 Hz, 17.2 Hz), 2.30 (ddd, 1H, $J = 6.9$ Hz, 10.2 Hz, 17.2 Hz), 2.10 (ddd, 1H, $J = 6.9$ Hz, 10.2 Hz, 17.2 Hz), 1.90 (ddd, 1H, $J = 6.9$ Hz, 10.2 Hz, 17.2 Hz), 1.70 (ddd, 1H, $J = 6.9$ Hz, 10.2 Hz, 17.2 Hz), 1.50 (ddd, 1H, $J = 6.9$ Hz, 10.2 Hz, 17.2 Hz), 1.30 (ddd, 1H, $J = 6.9$ Hz, 10.2 Hz, 17.2 Hz), 1.10 (ddd, 1H, $J = 6.9$ Hz, 10.2 Hz, 17.2 Hz), 0.90 (ddd, 1H, $J = 6.9$ Hz, 10.2 Hz, 17.2 Hz), 0.70 (ddd, 1H, $J = 6.9$ Hz, 10.2 Hz, 17.2 Hz), 0.50 (ddd, 1H, $J = 6.9$ Hz, 10.2 Hz, 17.2 Hz), 0.30 (ddd, 1H, $J = 6.9$ Hz, 10.2 Hz, 17.2 Hz), 0.20 (ddd, 1H, $J = 6.9$ Hz, 10.2 Hz, 17.2 Hz).
1H, $J = 1.5$ Hz, 17.2 Hz), 4.97 (dt, 1H, $J = 1.1$ Hz, 10.3 Hz), 3.06-3.11 (m, 1H), 2.05 (d, 
1H, $J = 1.3$ Hz), 1.49-1.57 (m, 1H), 1.40-1.46 (m, 1H), 1.29-1.33 (m, 4H), 0.87-0.91 (m, 
3H).

$^{13}$C NMR (125 MHz, CDCl$_3$) $\delta$ 143.96, 141.5, 134.8, 130.96, 128.1, 126.6, 125.7, 113.2, 
43.0, 35.3, 29.5, 22.8, 16.1, 14.1.

GC (cyclosil B, 110 °C): $R_t$ from dppp: 93.66 min and 94.68 min. from (S,S-DIOP): 
94.73 min (99%).

HRMS (ESI-MS): $m/z$ 237.1617 ([M+Na]); exact mass calculated for C$_{16}$H$_{22}$Na 
237.1614.

$[\alpha]_D^{23}$ (c = 1.0, CHCl$_3$) – 3.2 [from (S,S-DIOP)]

**Typical Procedure for Selective Reduction of Vinyl Group of Hydrovinyalted Product:**

A 25mL three-necked flask equipped with magnetic stirring bar, stopper, rubber septum 
and nitrogen inlet was flame dried and purged with argon. The flask was charged with 
CoCl$_2$(i-Pr-PDI) catalyst (13.5mg, 0.022 mmol, 0.1 eq), further diluted with 2mL of 
toluene and cooled down to -78 °C in an dry ice-acetone bath. The substrate 4-vinyl-2-
trimethylsilyloxy-2(E)-octene (50mg, 0.22mmol, achiral or enantiopure substrate) was 
added to the reaction mixture by a microliter syringe, followed by addition of NaEt$_3$BH 
(1 M in toluene, 45µL, 0.44mmol, 0.2 eq) and diethoxymethylsilane [(OEt)$_2$Si(H)(Me)] 
(43µL, 0.26mmol, 1.2 eq). Dry ice-acetone bath has been removed and the reaction 
mixture was allowed to warm up to room temperature over 6 h (reaction was constantly
monitored by GC). Once gas chromatogram showed full consumption of starting material, reaction mixture was rotaevaporated carefully to remove the solvent from the reduced product, which was then further purified over preparative TLC (with pentane) to yield the purified product.

\[ (E)-((4\text{-ethyloct-2-en-2-yl})\text{oxy})\text{trimethylsilane (35):} \]

\[ ^1H \text{NMR (400 MHz, CDCl}_3\text{)} \delta 4.35 \text{ (dq, 1H,} J = 0.8 \text{ Hz, 10.1 Hz), 1.84-1.95 (m, 1H), 1.72 (d, 3H,} J = 0.9 \text{ Hz), 1.21-1.44 (m, 5H), 1.08-1.18 (m, 3H), 0.82-0.90 (m, 6H), 0.18 (s, 9H).} \]

\[ ^13C \text{NMR (100 MHz, CDCl}_3\text{)} \delta 147.4, 114.2, 39.7, 36.1, 29.7, 29.4, 22.9, 18.3, 14.1, 11.9, 0.3. \]

GC (cyclosil B, 50 °C): R_t from dppp: 225.307 min and 230.856 min; from (S,S-DIOP): 225.168 min (92%) and 230.070 min (8%).

GC-MS (methyl silicone): m/z ([M+] 228.30; exact mass calculated for C_{13}H_{28}OSi 228.19.

\[ (E)-((4\text{-ethyloct-2-en-2-yl})\text{oxy})\text{triethylsilane (37):} \]

\[ ^1H \text{NMR (400 MHz, CDCl}_3\text{)} \delta 4.36 \text{ (dq, 1H,} J = 0.8 \text{ Hz, 10.1 Hz), 1.85-1.93 (m, 1H), 1.74 (d, 3H,} J = 0.8 \text{ Hz), 1.20-1.45 (m, 5H), 1.07-1.19 (m, 3H), 1.00 (t, 3H,} J = 8.0 \text{ Hz), 0.99 (t, 9H,} J = 8.0 \text{ Hz), 0.83-0.91 (m, 7H), 0.67 (q, 6H,} J = 8.0 \text{ Hz).} \]

\[ ^13C \text{NMR (100 MHz, CDCl}_3\text{)} \delta 147.5, 113.3, 39.6, 36.1, 29.71, 29.67, 29.39, 18.2, 14.1, 11.9, 6.7, 5.1. \]
GC (HP methyl silicone, 140 °C): R, 4.308 min (achiral GC).

GC-MS (methyl silicone): m/z ([M+] 270.40; exact mass calculated for C_{16}H_{34}OSi 270.24.

4-Ethyl-2-octanone (12a): \(^1\)H NMR (400 MHz, CDCl\(_3\)) \(\delta\) 2.32 (d, 2H, \(J = 6.8\) Hz), 2.11 (s, 3H), 1.80 (quintet, 1H, \(J = 6.4\) Hz), 1.20-1.32 (m, 8H), 0.81-0.89 (two triplets superimposed, 3H each).

\(^{13}\)C NMR (100 MHz, CDCl\(_3\)) \(\delta\) 209.4, 48.4, 35.3, 33.1, 30.3, 29.7, 28.8, 26.3, 22.9, 14.0, 10.8.

GC-MS (methyl silicone): m/z 156.30 ([M+]). exact mass calculated for C\(_{10}\)H\(_{20}\)O 156.27.

HPLC (chiracel ODH): temp 35 °C, flow rate: 0.1 mL/min, hexane: isopropanol = 99:1, \(\text{R}_t\) from dppp: 31.353 min and 31.900 min; from (S,S-DIOP): 31.164 min.

\([\alpha]_D^{23}\) (c = 0.264, CHCl\(_3\)) + 0.80 [from (S,S-BDPP)].

\((E)-(1-(2-ethylcycloheptylidene)ethoxy)trimethyilsilane (36): \(^1\)H NMR (400 MHz, CDCl\(_3\)) \(\delta\) 2.48-2.53 (m, 1H), 2.22-2.30 (m, 1H), 1.86-1.93 (m, 1H), 1.79 (s, 3H), 1.60-1.76 (m, 4H), 1.43-1.49 (m, 1H), 1.18-1.36 (m, 3H), 1.06-1.13 (m, 2H), 0.82 (t, 3H, \(J = 7.4\) Hz).

\(^{13}\)C NMR (100 MHz, CDCl\(_3\)) \(\delta\) 141.7, 122.8, 41.8, 33.9, 31.6, 29.09, 29.07, 26.1, 24.7, 18.4, 12.0, 0.8.

GC (cyclosil-B, 90 °C): \(\text{R}_t\) from dppp: 73.675 min and 74.592 min; from (S,S-BDPP): 73.674 min (98%) and 74.729 min (2%).
GC-MS (methyl silicone): m/z ([M+]) 240.40; exact mass calculated for C_{14}H_{28}OSi 240.19.

4.11. Organic Syntheses Procedure for Hydrovinylation Reaction (~5 g, 25.0 mmol scale)

A. Synthesis of CoCl$_2$(dppp): Anhydrous CoCl$_2$ (1) (1.495 g, 11.52 mmol) was added to a previously flame-dried 250-mL round two-necked bottom flask fitted with a flow control gas inlet and magnetic stir-bar loaded in a glove box under nitrogen. The nitrogen atmosphere was removed and the flask purged with dry argon. Freshly distilled, degassed THF (2) (40 mL) was added, and upon stirring at room temperature for 30 min, a clear deep blue solution formed. A solution of 1,3-Bis(diphenylphosphino)propane (5.0 g, 12.1 mmol) (1) in freshly distilled, degassed ether (2) (40 mL) was added dropwise to yield a blue turbid solution. After stirring at room temperature for 15 h, 80 mL freshly distilled, degassed hexane (2) was added in one portion to yield a blue precipitate. The resulting
precipitate was filtered on a sintered glass fret under argon atmosphere (3), and washed with diethyl ether and hexane (1:1) mixture (3 X 5 mL) to remove any unreacted 1,3-Bis(diphenylphosphino)propane, resulting in 5.8 g (10.70 mmol, 93% yield) of a light blue solid, which was used with no further purification.

**B. Synthesis of CoCl$_2$[(+)-DIOP]:** Anhydrous CoCl$_2$ (0.25 g, 1.90 mmol) was added to a previously flame-dried 50-mL round schlenk flask fitted with a flow control gas inlet and magnetic stir-bar loaded in a glove box under nitrogen. The nitrogen atmosphere was removed and the flask purged with dry argon. Freshly distilled, degassed THF (5 mL) was added, and upon stirring at room temperature for 30 min, a clear deep blue solution formed. A solution of (+)-2,3-O-Isopropylidene-2,3-dihydroxy-1,4-bis(diphenylphosphio)butane (2 and 4) (1.0 g, 2.00 mmol) in freshly distilled, degassed ether (~5 mL) was added dropwise to yield a blue turbid solution. After stirring at room temperature for 15 h, 20 mL freshly distilled, degassed hexane was added in one portion to yield a deep blue precipitate (5). The resulting precipitate was filtered on a sintered glass fret under argon atmosphere, and washed with diethyl ether and hexane (1:1) mixture (3 X 5 mL) to remove any unreacted (+)-2,3-O-Isopropylidene-2,3-dihydroxy-1,4-bis(diphenylphosphio)butane, resulting in 1.10 g (1.75 mmol, 92% yield) of a deep blue solid crystals, which was used with no further purification (6).

**C. Synthesis of Methylaluminoxane (MAO):** A 250–mL, three-necked, round-bottomed flask equipped with a rubber septum, a Teflon-taped flow-controlled argon inlet, a reflux condenser, and a magnetic stirring bar is flame-dried and purged with argon. Under argon from a schlenk line, the flask is then charged with aluminum sulfate
hydrate (7) (5.25 g, 8.3 mmol) and anhydrous toluene (8) (18 mL). The flask is then cooled to −5 °C in a ice/salt bath, at which time trimethylaluminum (2M in toluene) (9 and 10) (28 mL, 55.5 mmol) is added via syringe with stirring. The cold bath is removed and the reaction mixture is allowed to warm to 0 °C gradually (ca. 15 min), then to ambient temperature over another 15 min. The reaction mixture is stirred at ambient temperature for another 7 h and then the reaction mixture is placed over a silicone oil bath and gradually heated to 65 °C for next 9 h (11). After the heating period, the mixture is slowly brought to ambient room temperature. A schlenk filter (12” column fitted with male ground joints and a microporous fret in the center) and a 250 mL single-necked round bottom is flame dried and quickly attached to the 250 mL three-necked reaction flask (12). The solution was filtered to remove the aluminum salt with a slow vacuum (or positive pressure of argon) and the filtrate in 250 mL single necked flask is put under vacuum pump (<0.1mm of Hg) attached with a liquid nitrogen trap to remove all the toluene. The solid is then dried under vacuum for 12 h to afford 1.3 g (40%) of the Methylalumoxane (MAO) as a free-flowing, fine, white solid. Typically, the salt is stored at freezer (−8 °C) inside the glove-box (13). COMMERCIALY AVAILABLE MAO DOES NOT HAVE THE SAME REACTIVITY OF OUR IN-HOUSE PREPARATION.

D. Synthesis of 2-Trimethylsilyloxy-1,3-octadiene: A 250 mL three-necked round-bottom flask equipped with a magnetic stir bar, a gas inlet, and septa was flame-dried and purged with argon. The flask was charged with 8.4 mL (6.0 g, 59.43 mmol) freshly distilled diisopropylamine (14) and 100 mL dry, distilled THF. The mixture was chilled to -78 °C and 23 mL of n-butyllithium (2.5 M solution in hexanes) (15) was added
slowly. The mixture stirred for 1 h, and then a solution of 3-octene-2-one (15) (5.0 g, 39.62 mmol) in 25 mL of THF was added slowly and allowed to stir for 2 h at -78 °C. To the enolate mixture, 7.6 mL (6.5 g, 59.43 mmol) freshly distilled trimethylsilyl chloride (14) was added rapidly, the cooling bath was removed, and the mixture allowed to warm to room temperature and stir for ~10 h (small aliquots has been taken out, quenched by saturated solution of NH₄Cl, organic phase has been injected in GC to monitor the reaction). The reaction was quenched with a saturated solution of NH₄Cl (aq) and extracted with (3 x 40 mL) ether. The combined organic layer was dried with MgSO₄, filtered to remove the solid, and the solvent removed in vacuo to give the crude product (7.4 g, 35.8 mmol, 94% yield) that was purified by bulb-to-bulb distillation to get the product as a clear oil (7.25 g, 36.55 mmol, 92% yield). The purity of the compound was ascertained by gas chromatography, ¹H NMR and ¹³C NMR.

E. Typical Procedure for Asymmetric Co(II)-Catalyzed Hydrovinylation Using Methylaluminoxane as Cocatalyst. [CoCl₂(+)-DIOP] Catalyzed Hydrovinylation of 2-Trimethylsilyloxy-1,3-octadiene: To a flame-dried three-necked round-bottom flask equipped with a flow-control gas inlet, a rubber septum, a magnetic stir-bar and a temperature probe inlet, [CoCl₂(+)-DIOP] catalyst (0.1584 g, 0.2520 mmol, 0.01 equivalents) and methylaluminoxane (2.93 g, 50.4 mmol, 2.0 equivalents with respect to the substrate, assuming a standard weight of 58.08 g/mol) were added while inside a glove box filled with nitrogen. The flask was removed from the glovebox with the flow-control inlet closed, placed on a vacuum line, and the stopcock opened to vacuum to remove the nitrogen, and subsequently purged with argon. Distilled, dried dichloromethane (25.0 mL) was added at room temperature to make a 0.5 M solution
with respect to the substrate, and upon addition of dichloromethane, the solution turned dark red (with lot of fumes generation), indicating the formation of the organo-cobalt species. The reaction mixture was allowed to stir at room temperature for next 10 min (the temperature probe shows slight increase of temperature inside the reaction). The flow control valve was closed to argon and an ethylene balloon was added through the septum. Five 60 mL volumes of gas were removed with a syringe (16) while a high stream of ethylene entered the flask. After stirring under ethylene for five minutes, dried 2-trimethylsilyloxy-1,3-octadiene (5.0 g, 25.2 mmol) was added in 25.0 mL dry, distilled dichloromethane slowly via syringe to the catalyst and the mixture was stirred at room temperature (23 – 25 °C) for 4 h. Upon completion (reaction aliquot has been taken out after every 2 h and injected in achiral methylsilicone column GC to monitor the reaction), the flow-control stopcock was opened to air, and the solution was carefully diluted with 50 mL of pentane and quenched at room temperature with 10.0 mL of MeOH (17). The solution was further diluted with 50 mL pentanes and filtered through a plug of celite on a fretted funnel, washing with (4 x 25 mL) portions of pentanes. The solvent was removed in vacuo to give the product as clear oil (5.1 g, 22.68 mmol, >99% conversion by GC to 1,4-E-hydrobvinylation product, 90% isolated yield of the product). Purity of the product was ascertained by gas chromatography, $^1$H NMR and $^{13}$C NMR (18).

Important Points For these Protocols:

1. Anhydrous CoCl$_2$, 1,3-Bis(diphenylphosphino)propane and (+)-2,3-O-Isopropylidene-2,3-dihydroxy-1,4-bis(diphenylphosphino)butane were purchased from Strem Chemicals.
2. THF and Ether were distilled over sodium and hexane was distilled over calcium hydride, all the solvents were degassed by freeze thaw method.

3. High pressure of argon was used to filter the cobalt complexes on a sintered glass fret.

4. (+)-2,3-O-Isopropylidene-2,3-dihydroxy-1,4-bis(diphenylphosphio)butane was not highly soluble in ether, it was vigorously stirred inside a pear shaped flask with a stir bar under argon atmosphere before the addition to the anhydrous CoCl$_2$ solution.

5. After addition of hexane, the solution was allowed to settle down for an hour. CoCl$_2$[(+)-DIOP] started crystalize out slowly inside the schlenk flask.

6. CoCl$_2$[(+)-DIOP] can be further recrystallized from a saturated CHCl$_3$ solution by slow vapor diffusion of pentane at room temperature.

7. Aluminum sulfate hydrate is purhcased from Sigma Aldrich.

8. Toluene (Sigma Aldrich Company) is distilled under nitrogen over calcium hydride for the use.

9. 2M Trimethylaluminum in toluene is purchased from Sigma Aldrich. It is always stored under refrigerator. Trimethylaluminum should be taken out from refrigerator and kept in ambient temperature for 30 mins before use.

10. Trimethylaluminum is extremely pyrophoric, extreme caution should be maintained through out the experiment. During its slow addition to aluminum sulfate hydrate, fumes are generated inside the reaction vessel. After the addition all the left over inside syringes are diluted with toluene and washed by hexane properly.
11. Reaction temperature was strictly maintained at 65°C. Glass stopper should replace rubber septum during heating. Overheating changes the polymeric ratio and reactivity of MAO.

Figure 4.8. Picture Diagram of Setting up MAO

Step 1: Stir at rt for 6 h
Step 2: After heating keep ready the flame dried schlenk filter
Step 3: Schlenk filter was quickly attached to the reaction flask

Step 4: Reaction mixture was filtered under argon
Step 5: Toluene was removed by a cold trap
Step 6: Kept under vacuum pump

12. Pictures (Figure 4.8) were attached to show the synthesis of MAO. Quick removal of toluene is extremely important for the synthesis of MAO. Toluene should be removed as quickly as possible as MAO is not very stable in toluene medium.
13. MAO has been characterized by $^1$H and $^{13}$C NMR in C$_6$D$_6$.

14. Diisopropylamine and trimethylsilyl chloride were freshly distilled before use.

15. $n$-butyllithium (2.5 M solution in hexanes) and 3-octene-2-one were purchased from Sigma-Aldrich.

16. 60 mL teflon syringe was used to remove the argon gas. 60 mL syringe was pulled minimum 5 times to remove the argon gas inside the flask and increase the ethylene pressure.

17. Addition of MeOH was done very slowly and carefully as it was highly exothermic reaction.

18. Pictures (Figure 4.9 and 4.10) were attached to show the hydrovinylation reaction step-wise.
Figure 4.9. Picture Diagram of Setting up Hydrovinylation Reaction (1st part)

FLAME DRIED 3-NECK FLASK, TOOK INSIDE THE GLOVE BOX

CATALYST WAS TAKEN OUT FROM THE BOX, FLASHED WITH ARGON

DCM WAS ADDED INSIDE THE FLASK, GENERATION OF FUME

STIR FOR COUPLE OF MINS AT ROOM TEMP

ETHYLENE BALLOON WAS INTRODUCED AND A 30 mL SYRINGE WAS USED TO REMOVE ARGON FROM THE FLASK

SUBSTRATAE WAS ADDED, SLIGHT INCREASE OF TEMP
Figure 4.10. Picture Diagram of Setting up Hydrovinylation Reaction (2nd part)

REACTION WAS MONITORED BY GC (NEEDS AROUND 1 HR)

DILUTED WITH PENTANE

ADDITION OF MeOH TO QUENCH THE REACTION

VACUUM FILTRATION OVER CELITE
4.12. References


(32) See experimental section for details.


CHAPTER 5

Cobalt-Catalyzed Enantiodivergent Hydrovinylation Reaction

5.1. Introduction

While enantioselective kinetic resolution\(^{1,2}\) has been a major approach towards the preferential generation of one enantiomer over the other from racemic starting materials, an alternative approach involving divergent reactions of the individual isomers of the racemic starting material, has received only limited attention.\(^{3-5}\) A possible advantage of this approach over kinetic resolution is that 100% of the racemic mixture can be transformed into a set of resolved products, often as diastereomers, separable by traditional methods such as column chromatography. Based on the chiral catalyst and reaction mechanism, the individual isomers of the racemic mixture can undergo these reactions either in regiodivergent ways to produce two constitutionally different products (where separation of the products are relatively easier) or simply stereodivergent ways (where separation of products are relatively more difficult to achieve) to produce two different diastereomeric products.\(^6\)

5.2. Yttrium Catalyzed Regio- divergent Ring Opening of Aziridines

RajanBabu group has been involved with regiodivergent ring opening reactions of racemic aziridines and epoxides and recently, a yttrium-salen catalyzed regiodivergent additions of azides to racemic aziridines was reported in excellent yields and
enantioselectivities (Figure 5.1, a). In presence of a chiral yttrium-salen complex (Figure 5.1, [Y]), the nucleophilic attack of azide occurs at the primary position of (R)-1a of the racemic aziridine, leading to azidoamide 2a as one of the product (42% yield, >99% ee).

**Figure 5.1. Enantiodivergent Reactions in Literature**

![Chemical Structures](image)

**Figure 5.1. a.** Regiodivergent ring opening of chiral aziridines with yttrium-salen catalyst. **b.** Regiodivergent ring opening of oxabicyclic systems with Rh(I) complex. **c.** Regiodivergent ring opening of epoxides with titanocene catalyst.
whereas the other enantiomer (S)-1a exclusively opens up at the secondary position to form product 2b in high yield and enantiomeric excess (46% yield, 99% ee). Apart from this work, Lautens and coworkers utilized a strained [2.2.1]-bicyclic ether for regiodivergent opening by methanol to two regio-isomeric products with a Rh-catalyst system (Figure 5.1, b). Gansäuer and coworkers developed a regiodivergent parallel kinetic ring opening and subsequent reduction of epoxides to give alcohols using a titanocene catalyst (Figure 5.1, c). While metal catalyzed enantiodivergent ring openings and Diels-Alder reactions have been demonstrated by different groups, there are very few reports on carbon-carbon bond forming enantiodivergent reactions in the literature.

5.3. Co(II)-Catalyzed Hydrovinylation of 1-Vinylecloalkenes

RajanBabu group has long been involved in hydrovinylation reaction of readily available prochiral precursors vinylarenes, 1,3-dienes and 1-vinylecloalkenes. While the well-established Ni-based-protocols gave unsatisfactory results for the hydrovinylation of 1,3-dienes, 1,n-bis-diphenylphosphinoalkane-complexes of cobalt(II) gave highly chemoselective 1,4-hydrovinylated products with excellent yields and enantioselectivites. Similarly, another set of substrates that gave a mixture of 1,2- and 1,4-adducts in Ni-protocol, viz., 1-vinylcloalkenes gave highly chemoselective 1,4-hydrovinylated products with high yields and enantioselectivities (Scheme 5.1).

From a completely different perspective, based on our results on enantiodivergent ring opening of racemic aziridines, we are interested to explore Co(II)-catalyzed asymmetric hydrovinylation on racemic 4-substituted-1-vinylcloalkenes and follow the
possible enantiodivergent incorporation of vinyl group into the axial and/or equatorial C2-
positions.

Our studies began with an examination of Co(II)-catalyzed hydrovinylation of 4-t-
butyl-1-vinylcyclohex-1-ene (7, Scheme 5.1). After optimization of reaction conditions
using various combinations of (L)CoCl2/methylaluminoxane (L = dppm, dppe, dppp,
dppb), temperatures, and solvents, it was found that, in sharp contrast to Ni(II)-catalyzed
hydrovinylation reaction (Scheme 5.1, 7 to 8),26 the (dppp)CoCl2/methylaluminoxane
catalyst combination gave almost exclusively 1,4-adducts as a mixture of cis (9a) and
trans (9b) isomers [3.2 : 1].

Scheme 5.1. 1,2- vs 1,4-Hydrovinylation of 4-tert-Butyl-1-vinylcyclohexene

5.4. Co(II)-Catalyzed Asymmetric Hydrovinylation of 4-Substituted-1-
vinylcycloalkenes: Enantiodivergent Hydrovinylation Reaction

Asymmetric hydrovinylation of such a chiral substrate would test this reaction in
two important ways: will the Co(II)-catalyzed asymmetric hydrovinylation conditions be
compatible with these type of racemic substrates to give 1,4-adducts? More importantly,
will we be able to observe any kinetic resolution or an enantiodivergent reaction of these
racemic substrates, if so, is it possible to override the inherent substrate selectivity by a
chiral catalyst? Following previous hydrovinylation studies on simple 1,3-dienes,22,23 our attention was focused on chiral 2,4-bis-diphenylphosphinopentane (BDPP) ligand, which is structurally very similar (similar bite angle) to the achiral ligand dppp. To our delight, substrate 7 gave exclusively 1,4-hydrovinylation reaction with standard [(R,R)-BDPP]CoCl2/methylaluminoxane condition with quantitative yield and cis and trans ratio [1.1 : 1] (Figure 5.2). Most strikingly, we noticed very high enantioselectivities of both cis (ent-9a, 2R,4S, 91% ee) and trans (ent-9b, 2R,4R, 98% ee) isomers at the end of our reaction. The exceptionally high enantioselectivities in the formation of both diastereomeric products from the racemic substrate 7 clearly revealed that the individual isomers of the racemic mixture of 7 reacted with in divergent pathways to form highly enantioselective diastereomeric products (we will discuss formation of individual diastereomers via enantiodivergent pathway in later part of our discussion).
Figure 5.2. Enantiodivergent Asymmetric Hydrovinylation of Racemic 4-tert-Butyl-1-vinylcyclohexene

5.4.1. Enantiodivergent Asymmetric Hydrovinylation of Chiral [(S)-4-(Prop-1-en-2-yl)-1-vinylcyclohexene]

Before we investigated racemic substrate 7 in detail, we wanted to understand the enantiodivergent pathways better on a chiral non-racemic starting material, which would simplify the analysis. We started our investigation on the enantiopure substrate 11, which was prepared from commercially available (−)-perillaldehyde via a Wittig reaction. Under standard conditions using an achiral catalyst, the hydrovinylation, which is highly chemoselective for the 1,3-diene, gave two products cis-12a (2R,4S) and trans-12b.
(2S,4S) (Figure 5.3, equation a) with a ratio 3.9 : 1. In this substrate, the 4-propenyl group occupies the equatorial position, during the reaction, addition of ethylene can occur leading to an equatorial position or an axial position for the entering vinyl group (Figure 5.3, 1). Addition from the top-face of the η³-intermediate is favored, as it minimizes the 1,3-diaxial interactions between the forming vinyl moiety and the ring substituents to give cis-12a (2R,4S) as the major product. Addition from bottom-face leads to unfavorable axial incorporation of the vinyl group leading to trans-12b (2S,4S) (Figure 5.3, equation a, cis 12a : trans 12b = 4 : 1). Like previous example of substrate 7, we turned our attention to the asymmetric hydrovinylation of S-11. Based on the total absence of the 1,2-adduct in the product mixture, when [(R,R)-BDPP]CoCl₂ is used, this complex appears to be the matching catalyst for this substrate (i. e., for the formation of the 1,4-adducts) and only 1,4-adducts are obtained. It favored the cis-12a (2R,4S) product over trans-12b (2S,4S) product (with a ratio 4 : 1, Figure 5.3. equation b). However, the hydrovinylation of S-11 with the opposite enantiomer of the catalyst, [(S,S)-BDPP]CoCl₂ suggested a complete mismatch substrate-catalyst pair for the 1,4-addition and it reacted on a divergent pathway with S-11 to introduce the vinyl group at the thermodynamically unfavorable axial location to give trans-12b (2S,4S) as the major product (with a ratio of cis : trans = 1 : 12, Figure 5.3. equation c). When the mismatched [(S,S)-BDPP]CoCl₂ catalyst was used, we also observed 33% of 1,2-HV product (the formation of which has much less barrier to ethylene incorporation across the diene vis-a-vis axial incorporation to give trans-12b). Note that use of the matching catalyst [(R,R)-BDPP]CoCl₂ results in 0% of the 1,2-adduct!
Figure 5.3. Enantiodivergent Asymmetric Hydrovinylation of Chiral [((S)-4-(Prop-1-en-2-yl)-1-vinylcyclohexene]

Using the S-11 hydrovinylation as a model, the results of the asymmetric hydrovinylation of substrate 7 can now be fully understood (Figure 5.2). Chiral catalyst [(R,R)-BDPP]CoCl₂ selectively recognizes the individual enantiomers of the racemic substrate 7 and reacts preferentially with (S)-7 to introduce the vinyl group to the
thermodynamically favorable equatorial position to form the product \textit{ent-cis-9a} (2R, 4S) with 91\% ee (Figure 5.2. part b). The exceptionally high enantioselectivity of the product implies that the chiral catalyst \([(R,R)-\text{BDPP})\text{CoCl}_2]\) does not react with the opposite enantiomer (\textit{R})-7 in an mirror image pathway [we did not observe any \textit{cis-9a} (2R, 4S)], rather it places the vinyl group in the thermodynamically unfavorable axial position on (\textit{R})-7 to form the diastereomeric product \textit{ent-trans-9b} (2R, 4R) with >98\% ee. Again very high enantioselectivity of product \textit{ent-trans-9b} (2R, 4R) confirms the fact that chiral catalyst \([(R,R)-\text{BDPP})\text{CoCl}_2]\) effects an efficient enantiodivergent parallel kinetic resolution\textsuperscript{6} during the hydrovinylation reaction. Careful comparison of the studies with the achiral ligand (DPPP) reveals that chiral catalyst \([(R,R)-\text{BDPP})\text{CoCl}_2]\) makes the matching pair with enantiomer (\textit{S})-7, reacts much faster compared to the other enantiomer to form the product \textit{ent-cis-9a} (2R, 4S), whereas enantiomer (\textit{R})-7 is the mismatching pair with this catalyst, reacts much slowly with the catalyst to make the product \textit{ent-trans-9b} (2R, 4R) [a reaction profile with function of time will be discussed in next section]

At this point our attention turned to outcome of hydrovinylation of \textit{rac-7} with the opposite enantiomer of the catalyst. Under standard hydrovinylation conditions, \textit{rac-7} reacts with \([(S,S)-\text{BDPP})\text{CoCl}_2]\) to give \textit{cis-9a} (2S,4R) and \textit{trans-9b} (2S,4S) as the major diastereomeric products (Figure 5.2. part a). Not unexpectedly, we observed very high enantioselectivities for both of products (>98\% ee for both \textit{cis} and \textit{trans} products). Based on our previous observation, we identified that \([(S,S)-\text{BDPP})\text{CoCl}_2]\) makes the matching pair with (\textit{R})-7 to form the thermodynamically favorable equatorial product \textit{cis-9a} (2S,4R) and mismatching pair with (\textit{S})-7 to form the \textit{trans-9b} (2S,4S) product.
Noticeably, we observed this enantiodivergent chemistry on racemic substrate 7 only with (BDPP)CoCl₂ catalyst. Changing the chiral catalyst to (DIOP)CoCl₂ gave exclusive 1,2-hydrovinylation product with no enantioselectivity (Scheme 5.2. 7 to 8).

Scheme 5.2. Ligand Effect on Asymmetric Hydrovinylation of Racemic 4-tert-Butyl-1-vinylcyclohexene

![Scheme 5.2](image)

5.5. Substrate Scope of Co(II)-Catalyzed Enantiodivergent Hydrovinylation Reactions

A number of structurally different dienes were subjected to the hydrovinylation conditions and the results are listed in Table 5.1. Under the optimized conditions [1 atmosphere ethylene, Co(II)-catalyst (0.05 equiv.), MAO (2 equiv.), CH₂Cl₂], the reactions proceed at room temperature giving excellent yields of 1,4-hydrovinylation products with achiral catalyst. The structures of all products have been rigorously established by spectroscopic techniques. Isopropyl substitution (entry 1) at C₄ results in 94% 1,4-HV product with a cis : trans ratio 2.7 : 1. This results further support the conclusion that thermodynamically favorable equatorial addition makes the major product over the less favorable axial addition, in absence of any catalyst control (DPPP...
does not have any control on substrate selectivity). Introducing a phenyl substituent (entry 3) at C₄ needs more active trimethylaluminum as an activator (MAO suffers with poor conversion) and yields 97% 1,4-HV product with a cis : trans ratio 2.7 : 1. Conformationally flexible methyl substituent (entry 3) at C₄ also gives predominantly 1,4-HV with a cis : trans ratio 2.2 : 1. Introducing methyl substituent at the C₂-position of the diene backbone again needs trimethylaluminum as an activator (MAO suffers with poor conversion) and gave exclusively 1,4-HV product with a cis : trans ratio 2.7 : 1 (entry 4).
Table 5.1. Scope of Substrates in the (DPPP)CoCl$_2$-Catalyzed Enantiodivergent Hydrovinylation Reaction$^a$

<table>
<thead>
<tr>
<th>Entry</th>
<th>Starting material (R)</th>
<th>(S)</th>
<th>Products from (dppp)CoCl$_2$ (0.05 equiv.) MAO (2 equiv.)</th>
<th>Yield (%)</th>
<th>1,4-cis: 1,4-trans (1,2-HV)$^b$</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>(R)-13</td>
<td>(S)-13</td>
<td>$cis$-17a (2S,4R) $ent$-cis-17a (2R,4S) $trans$-17b (2S,4S) $ent$-trans-17b (2R,4R)</td>
<td>95</td>
<td>2.7 : 1 (6%)</td>
</tr>
<tr>
<td>2$^c$</td>
<td>(R)-14</td>
<td>Ph (S)-14</td>
<td>$cis$-18a (2S,4R) $ent$-cis-18a (2R,4S) $trans$-18b (2S,4S) $ent$-trans-18b (2R,4R)</td>
<td>88</td>
<td>2.7 : 1 (3%)</td>
</tr>
<tr>
<td>3</td>
<td>(R)-15</td>
<td>(S)-15</td>
<td>$cis$-19a (2S,4R) $ent$-cis-19a (2R,4S) $trans$-19b (2S,4S) $ent$-trans-19b (2R,4R)</td>
<td>93</td>
<td>2.2 : 1 (2%)</td>
</tr>
<tr>
<td>4$^c$</td>
<td>(R)-16</td>
<td>(S)-16</td>
<td>$cis$-20a (2S,4R) $ent$-cis-20a (2R,4S) $trans$-20b (2S,4S) $ent$-trans-20b (2R,4R)</td>
<td>85</td>
<td>2.7 : 1 (1%)</td>
</tr>
</tbody>
</table>

$^a$ See Scheme 5.2 for reaction conditions  
$^b$ See Figure 5.2 for the structure of 1,2-HV product  
$^c$ Instead of methylaluminoxane as an activator  
Trimethylaluminum (in CH$_2$Cl$_2$) was used as activator (2 equiv.)
After the initial studies with achiral catalysts, our focus turned to the effect of chiral catalysts on hydrovinylation of substrates 13-16. Predictably, reaction with each enantiomer of (BDPP)CoCl₂ catalyst with the racemic substrate produce a pair of products corresponding to the matching and mismatching combinations of substrates and catalysts. The results of these studies are summarized in Table 5.2. The 4-substituted-1-vinylcycloalkenes (entries 1-4) lead to exclusive formation of the cis and trans 1,4-hydrovinylation products with very high enantioselectivities (90-99% ee). Chiral catalyst [(R,R)-BDPP]CoCl₂ recognizes very specifically each enantiomer of the racemic starting materials (entries 1-4, column 2) to form diastereomeric products ent-cis-(17-20)a (2R,4S) and ent-trans-(17-20)b (2R,4R) with very high enantioselectivities of both diastereomers. Catalyst [(R,R)-BDPP]CoCl₂ forms the matching pair with (S)-enantiomer of the starting material to introduce the vinyl group to the thermodynamically favorable equatorial position, whereas it forms a mismatch pair with (R)-enantiomer of the racemic starting material to form the unfavorable axial diastereomer. As expected from our substrate study of rac-7 and S-11, the other enantiomer of the catalyst [(S,S)-BDPP]CoCl₂ behaves in a predictable fashion to form diastereomeric products cis-(17-20)a (2S,4R) and trans-(17-20)b (2S,4S), again with exceptionally high enantioselectivities of both diastereomers. What is clearly evident from the high enantioselectivities of these diastereomers is that the chiral catalyst is capable of distinguishing the C₄ center of the racemic starting material. It overcomes the substrate selectivity (what we observed with our achiral catalyst, see Table 5.1) of addition of vinyl group from equatorial position in preference to axial position.
Table 5.2. Substrate Scope of Asymmetric Enantiodivergent Hydrovinylation Reaction

<table>
<thead>
<tr>
<th>Entry</th>
<th>Starting material</th>
<th>Products from (R,R)BDPPCoCl₂ (ee)</th>
<th>Products from (S,S)BDPPCoCl₂ (ee)</th>
<th>Yield (%)</th>
<th>1,4-cis: 1,4-trans (1,2-HV)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>(R,R)-BDPP</td>
</tr>
<tr>
<td>1</td>
<td><img src="image1" alt="Chemical Structure" /></td>
<td><img src="image2" alt="Chemical Structure" /></td>
<td><img src="image3" alt="Chemical Structure" /></td>
<td><img src="image4" alt="Chemical Structure" /></td>
<td>93</td>
</tr>
<tr>
<td></td>
<td><img src="image5" alt="Chemical Structure" /></td>
<td><img src="image6" alt="Chemical Structure" /></td>
<td><img src="image7" alt="Chemical Structure" /></td>
<td><img src="image8" alt="Chemical Structure" /></td>
<td></td>
</tr>
<tr>
<td>2&lt;sup&gt;cd&lt;/sup&gt;</td>
<td><img src="image9" alt="Chemical Structure" /></td>
<td><img src="image10" alt="Chemical Structure" /></td>
<td><img src="image11" alt="Chemical Structure" /></td>
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<td>88</td>
</tr>
<tr>
<td>3</td>
<td><img src="image13" alt="Chemical Structure" /></td>
<td><img src="image14" alt="Chemical Structure" /></td>
<td><img src="image15" alt="Chemical Structure" /></td>
<td><img src="image16" alt="Chemical Structure" /></td>
<td>94</td>
</tr>
<tr>
<td>4&lt;sup&gt;cd&lt;/sup&gt;</td>
<td><img src="image17" alt="Chemical Structure" /></td>
<td><img src="image18" alt="Chemical Structure" /></td>
<td><img src="image19" alt="Chemical Structure" /></td>
<td><img src="image20" alt="Chemical Structure" /></td>
<td>85</td>
</tr>
</tbody>
</table>

<sup>a</sup> See scheme 5.2 for reaction conditions  <sup>b</sup> See figure 5.2 for the structure of 1,2-HV product  <sup>c</sup> Instead of methylaluminoxane as an activator Trimethylaluminum (in CH₂Cl₂) was used as activator (2 equiv.)  <sup>d</sup> 10 mol% (BDPP)CoCl₂ catalyst loading was used  <sup>e</sup> GC overlaps with the other enantiomer
5.6. Rate Differences of Co(II)-Catalyzed Asymmetric Enantiodivergent Hydrovinylation

The rate differences of the individual enantiomers of the racemic starting material with the chiral catalyst are of significant interest in understanding these reactions. We started examining the progress of the reactions using gas chromatographic analysis. A typical kinetic experiment was run by following the peak areas in chromatograms of reaction mixtures at varying time intervals. The starting material and products are well-separated on a chiral cyclosil-B column. A three-necked round bottom flask was charged with the catalyst (0.02 mmol, 0.05 equiv.) and activator (0.66 mmol, 2 equiv.) in 0.1 M dichloromethane (3 mL) under argon atmosphere. The reaction mixture was stirred for 2-3 minutes before ethylene balloon was attached to the reaction flask. After stirring under ethylene for five minutes, substrate rac-13 (0.05 g, 0.33 mmol) was added in one portion via syringe to the reaction mixture and the mixture was allowed to stir at room temperature (23 – 25 °C) (equation 5.1).

\[
\begin{align*}
\text{(S)} & \quad \text{CoCl}_2(R,R)-\text{BDPP} \\
\text{(R)} & \quad \text{CH}_2\text{Cl}_2, \rt, 6\ h, \text{ethylene (1 atm)} \\
\text{ent-cis-9a (2R,4S)} & \quad >98\% \text{ ee} \\
\text{ent-trans-9b (2R,4R)} & \quad >98\% \text{ ee}
\end{align*}
\]
Figure 5.4. Gas Chromatogram Profile of Enantiodivergent of Hydrovinylation of Rac-13 as a Function of Time

An aliquot of the reaction mixture (0.1 mL) was taken out after every 30 mins, diluted with 2 mL of n-pentane and passed over small pad of celite before injecting to the chiral-cyclosil GC column. As can be seen in Figure 5.4, snapshot a, there are only racemic starting material (S)-13 (peak I) and (R)-13 (peak II) at beginning of the reaction (0 mins). As reaction progresses, product peaks start appearing as a function of time. What is really distinctive is that (S)-13 reacts significantly faster than the other enantiomer (R)-13 (Figure 5.4, snapshot b, compare peaks I and II). Chiral catalyst [(R,R)-BDPP]CoCl₂ identifies the (S)-13 as the matching pair and reacts extremely fast to yield product (2R, 4S) (peak IV). Whereas [(R,R)-BDPP]CoCl₂] reacts with (R)-13 much slowly, mostly because it has to overcome unfavorable 1,3-diaxial interaction to form product (2R, 4R) (peak III). After 240 mins (Figure 5.4, snapshot c), the GC trace of the reaction aliquot shows complete consumption of (S)-13 (peak I is completely consumed), whereas mismatch enantiomer (R)-13 is still showing slow progress towards...
product \((2R, 4R)\). Finally, after 480 mins (Figure 5.4, snapshot \(d\)), mismatch enantiomer \((R)-13\) shows complete consumption to product \((2R, 4R)\) (peak III). These gas chromatographic profiles provide strong support for the efficient enantiodivergent parallel kinetic resolution with our \((BDPP)\text{CoCl}_2\) catalyst. An almost identical (but mirror image) gas chromatographic profile was observed with \([((S,S)-BDPP)]\text{CoCl}_2\] and substrate \(rac-13\) as a function of time. We have monitored the entire substrate library [Table 5.2 \((13-16)\)] with gas chromatographic analysis as a function of time and all our gas chromatographic profiles (with both catalyst \([((S,S)-BDPP)]\text{CoCl}_2\] and \([((R,R)-BDPP)]\text{CoCl}_2\)) confirm the observations on Figure 5.4 of reactivity difference of individual enantiomers of racemic starting materials. However, in these of parallel kinetic resolutions, relative rates of individual enantiomers do not matter as long as there is complete catalyst control on the reaction.

5.7. Catalyst Control on Hydrovinylation of Enantiopure 1,3-Dienes

Substrates 7, 11 and 13-16 show a class of compounds where one of the double bond is embedded in a cycloalkane and have a tether at C\(_4\), which allows for the enantiodivergent pathways for the individual enantiomers of the starting material. We turned our attention for the hydrovinylation of racemic linear 1,3-dienes to examine any possible catalyst control on the inherent substrate selectivity. We started our investigation on the enantiopure substrate \((S)-21\), which was prepared from commercially available \((S)\)-citronellal via a modified Wittig reaction.\(^{27}\) We have carefully chosen citronellal as our starting material for making diene, primarily because both the enantiomers, along with racemic diene could be made, starting with the corresponding
commercially available enantio-pure and racemic citronellals. Under standard optimized hydrovinylation conditions using achiral (DPPP)CoCl₂ catalysts, (S)-21 yields two products syn-22 (6S, 8R) and anti-23 (6S, 8S) with very little inherent selectivity (syn : anti = 1 : 1.3) (Scheme 5.3. equation 5.2). Having recognized DIOP to be an excellent catalyst for asymmetric hydrovinylation of 1,3-dienes, our studies started with an examination of the hydrovinylation of enantiopure substrate (S)-21 with [(S,S)-DIOP]CoCl₂ with methylaluminoxane as an activator. Chiral gas chromatographic analysis shows complete conversion of (S)-21 within 30 mins to two diastereomeric products syn-22 (6S, 8R) and anti-23 (6S, 8S). Most strikingly, [(S,S)-DIOP]CoCl₂ completely overcomes substrate selectivity favoring syn-22 diastereomer predominantly (syn : anti = 88:4, with 8% 1,4-linear product observed) (Scheme 5.3. equation 5.3). Not unexpectedly, [(R,R)-DIOP]CoCl₂ yields anti-23 diastereomer as the major product (syn : anti = 5:87, with 8% 1,4-linear product observed) under similar hydrovinylation condition (Scheme 5.3. equation 5.4).
Having recognized the high catalyst selectivity over the substrate, we focused the study on the other enantiomer of the diene, \((R)\)-21. Under standard optimized hydrovinylation conditions using the achiral ligand DPPP, \((R)\)-21 yields two products \textit{syn}-24 (6\(R\), 8\(R\)) and \textit{anti}-25 (6\(R\), 8\(S\)) with very little substrate selectivity (\(\text{syn} : \text{anti} = 1 : 1.25\)) (Scheme 5.4. equation 5.5). The reaction is highly diastereoselective with the formation of products \textit{anti}-24 (6\(R\), 8\(R\)) and \textit{syn}-25 (6\(R\), 8\(S\)) where \([(S,S)\text{-DIOP}]\text{CoCl}_2\) favors primarily \textit{anti}-24 (6\(R\), 8\(R\)) [anti : \text{syn} = 79:5, with 8% 1,4-linear product observed] (Scheme 5.4. equation 5.6) as the major diastereomer. The catalyst \([(R,R)\text{-DIOP}]\text{CoCl}_2\) produces \textit{syn}-25 (6\(R\), 8\(S\)) as the major product under optimized condition [anti : \text{syn} = 4:88, with 8% 1,4-linear product observed] (Scheme 5.4. equation 5.7).
Scheme 5.4. Catalyst Controlled Selectivity on Hydrovinylation of Enantiopure Linear 1,3-Diene (R)-21

5.8. $^1$H NMR and $^{13}$C Studies on Hydrovinylation of Enantiopure 1,3-Dienes

The high specificity of these products was further confirmed by rigorous NMR and gas chromatogram studies (Figure 5.5). For simplicity, we mostly focused our attention on the vinyl region of the $^1$H NMR (400 MHz) and $^{13}$C NMR (100 MHz) spectra. Starting with enantiopure (S)-21, which predominantly forms anti-23 ($6S$, $8S$) with $[(R,R)$-DIOP]$\text{CoCl}_2$ has the following features: the -CH peak of the vinyl group appears at $\delta$ 5.663 ppm in $^1$H NMR (Figure 5.5, spectra a) and $\delta$ 141.72 ppm in $^{13}$C NMR (Figure 5.5, spectra e). Under identical conditions, when $[(R,R)$-DIOP]$\text{CoCl}_2$ was reacted with (R)-21, it completely prevails the substrate selectivity, instead of making the enantiomer of anti-23 ($6S$, $8S$), it predominantly forms syn-25 ($6R$, $8S$). This product was further
confirmed by the -CH peak of the vinyl group at $\delta$ 5.705 ppm in $^1$H NMR (Figure 5.5, spectra c) and $\delta$ 142.229 ppm in $^{13}$C NMR (Figure 5.5, spectra g). Question arises what will happen when (S)-21 will undergo hydrovinylation with [(S,S)-DIOP]CoCl$_2$? We identified the product spectra is exactly identical with $^1$H and $^{13}$C NMR spectra of c and g (Figure 5.5). Additionally, chirality at C$_6$ in the hydrovinylation product is fixed from citronellal (here absolute configuration at C$_6$ is (S)). The only possible product of hydrovinylation of (S)-21 with [(S,S)-DIOP]CoCl$_2$ is syn-22 (6S, 8R) which also matches with the following NMR spectra [$\delta$ 5.705 ppm in $^1$H NMR (Figure 5.5, spectra b) and $\delta$ 142.229 ppm in $^{13}$C NMR (Figure 5.5, spectra f)]. Next, we looked at the $^1$H and $^{13}$C NMR spectra of the hydrovinylation reaction of (R)-21 with [(S,S)-DIOP]CoCl$_2$ and identified the product as anti-24 (6R, 8R) [$\delta$ 5.663 ppm in $^1$H NMR (Figure 5.5, spectra d) and $\delta$ 141.725 ppm in $^{13}$C NMR (Figure 5.5, spectra h)]. This exquisite selectivity on the product confirms the absolute control of (DIOP)CoCl$_2$ catalyst on our hydrovinylation reaction. The chiral catalyst introduces the vinyl group with fixed configuration on the C-C bond-forming step, and most significantly, without considering the substrate chirality. With the help of $^1$H, $^{13}$C NMR and gas chromatographic analysis of all possible four diastereomers of the hydrovinylation of (S)-21 and (R)-21 (equation 3,4,6,7), it can be assigned that [(S,S)-DIOP]CoCl$_2$ exclusively introduces (R)-stereochemistry in the vinyl addition whereas [(R,R)-DIOP]CoCl$_2$ assigned the (S)-stereochemistry across the linear 1,3-dienes irrespective of the configuration of C$_6$. 
Figure 5.5. $^1$H and $^{13}$C spectra of Hydrovinylation of Linear 1,3-dienes (S)-21 and (R)-21
5.9. Catalyst Control on Hydrovinylation of Racemic 1,3-Dienes

Even though asymmetric hydrovinylation on enantiopure 1,3-dienes shows exquisite catalyst-dependent selectivity in the C-C bond-forming step, from more practical point of view, we were really interested on the catalyst selectivity on racemic 1,3-dienes because this would provide a potential route to enantiopure intermediates from readily available racemic compounds (making the reasonable assumption that the diastereomers can be separated by chromatography). From our last discussion on hydrovinylation of 4-substituted-1-vinylcycloalkenes and enantiopure 1,3-dienes (Scheme 5.3 and Scheme 5.4), we could expect a similar stereodivergent reaction on racemic 1,3-diene (rac-21), and may not necessarily involve a kinetic resolution. Under standard optimized achiral hydrovinylation (DPPP) condition, (rac)-21 yields all four diastereomers, syn-22 (6S, 8R), anti-23 (6S, 8S), anti-24 (6R, 8R) and syn-25 (6R, 8S) with no inherent selectivity (syn : anti = 1 : 1) (Scheme 5.5. equation 5.8). It is important to note that there is almost no diastereomeric preference on the product distribution at the end of achiral hydrovinylation on rac-21. However, chiral catalyst [(S,S)-DIOP]CoCl₂ recognizes very specifically individual enantiomers of the racemic starting material (Scheme 5.5. equation 5.9) to form only two diastereomeric products syn-22 (6S, 8R) and anti-24 (6R, 8R) with very high enantioselectivities of both diastereomers (along with ~5% linear product). This can be explained by exquisite selectivity possessed by the chiral catalyst [(S,S)-DIOP]CoCl₂, which completely overrides the substrate control and proceeds by the stereoselective addition of vinyl group across the 1,3-diene of both the enantiomers of rac-21. Overriding any substrate control,
Scheme 5.5. Catalyst Controlled Selectivity on Hydrovinylation of Linear 1,3-Diene

(rac)-21

\[
\begin{align*}
\text{rac-21} & \xrightarrow{\text{CoCl}_2(\text{DPPE}) (0.05 \text{ equiv.}), \\
& \quad \text{MAO (2 equiv.), } \text{CH}_2\text{Cl}_2, \\
& \quad \text{rt, 15 mins, ethylene (1 atm)}} \\
\text{E} & \quad \text{89\% yield} \\
\end{align*}
\]

\[
\begin{align*}
\text{[(S,S)-DIOP]CoCl}_2 \text{ exclusively introduces (}R\text{-)stereochemistry in the vinyl addition of both enantiomers of rac-21. While we could not conclude this highly selective catalyst control as an enantiodivergent reaction (as we concluded in our racemic 1-vinylcycloalkenes), it is a perfect example of catalyst control on diastereomeric product selectivity. The reaction commenced with the selective introduction of (S-)stereochemistry in the vinyl addition of both enantiomers of rac-21 with [(R,R)-DIOP]CoCl}_2 \text{ (Scheme 5.5. equation 5.10). The overall result distinctly recognized the complete control of catalyst on the vinyl addition of hydrovinylation reaction in excellent yields and enantioenrichment. It is also noticeable that we never observed any}} \\
\text{253}
\end{align*}
\]
conventional kinetic resolution in our system, both enantiomers of the substrate react with the chiral catalyst at almost the same rate (see Figure 5.4 for the rate differences) to form diastereomeric products in high yields and enantiomeric purity.

5.10. Selective Reduction of Vinyl Groups of Hydrovinylated Products

Selective reduction of the vinyl group of our hydrovinylated products would expand the potential utility of the products. We choose standard hydrovinylated substrates 17a as the model substrate to conduct the hydrogenation reaction. In early optimization studies we recognized that Wilkinson catalyst (0.1 equiv.) gave us satisfactory results on our hydrovinylated product (Figure 5.6, equation 5.12). However, it required high pressure of H₂ and use of Fischer-porter tube (35 psi of H₂) for 24 h. On the other hand, relatively weak reducing agent, methyldiethoxysilane, in presence of Co(II)-bisimiopyridine complexes gave excellent yields to selectively reduced products (Figure 5.6, equation 5.12). Most excitingly, with our newly developed Co-catalyzed reducing conditions,²⁸ diastereomeric mixture of ent-cis-17a (2R, 4S) and ent-trans-17b (2R, 4R) undergoes highly selective reduction to yield ent-cis-26a (2S, 4S) and ent-trans-26b (2S, 4R) in quantitative yield with no erosion of enantiomeric excess (equation 5.13). We did not observe any isomerization or reduction of substituted double bond in the products. We also identified similar results with another set of diasteromers, cis-17a (2S, 4R) and trans-17b (2S, 4S) (equation 5.14) with very high conversion to reduced products in excellent enantioselectivities.
Figure 5.6. Selective Reduction of Vinyl Groups of Hydrovinylated Products

\[
\begin{align*}
13 \text{ (racemic)} \quad & \quad \text{L} = \text{DPPP} \\
\text{cis} \, 17\text{a} : \text{trans} \, 17\text{b} = 2.7 : 1 \\
1,4 \, 1,2 \, \text{HV} : 94 : 6 \\
\text{L} = (S,S)-\text{BDPP} \\
\text{cis} \, 17\text{a} : \text{trans} \, 17\text{b} = 1.1 : 1 \\
1,4 \, 1,2 \, \text{HV} = >99 : <1 \\
\text{L} = (R,R)-\text{BDPP} \\
\text{cis-ent} \, 17\text{a} : \text{trans-ent} \, 17\text{b} = 1.2 : 1 \\
1,4 \, 1,2 \, \text{HV} = 98 : 2 \\
\end{align*}
\]
5.11. Discussion

In summary, based on our initial work on the hydrovinylation of racemic 4-tert-butyl-1-vinylcyclohexene, a set of racemic 4-substituted-1-vinylcycloalkenes were synthesized and tested for the generality of enantiodivergent hydrovinylation processes using the catalytic cobalt system. The reactions showed highest order of stereodivergent vinyl addition on the individual enantiomers of the racemic dienes with excellent yields and strikingly high enantiomeric excess for both the diastereomeric products. The catalyst developed for the hydrovinylation reaction is also critical for this enantiodivergent processes. Specifically, when we changed our catalytic system from (BDPP)CoCl$_2$ to (DIOP)CoCl$_2$ in the HV of 1-vinylcycloalkenes, we observed only 1,2-HV product (Scheme 5.2). In addition, linear 1,3-dienes shows better selectivity towards 1,4-Z-HV product (compared to 1,4-linear HV product) with (DIOP)CoCl$_2$ in comparison to (BDPP)CoCl$_2$.

In asymmetric hydrovinylation of 1-vinylcycloalkenes, chiral catalyst identifies one enantiomer of the racemic diene as its matched pair and introduces the vinyl group in a much faster rate than the other pair. The other enantiomer of the diene forms the mismatch pair with the catalyst, reacts much slowly along with formation different regio-isomeric hydrovinylated products (e.g. 1,2-HV product for cycloalkenes, 1,4-linear HV product for linear 1,3-dienes). The rate of this reaction also depends on the thermodynamic preference of vinyl addition on the cyclohexane conformers.

The highly selective catalytic system accelerates the hydrovinylation reaction of both enantiomers of a racemic mixture on divergent pathways on a carbon-carbon bond-
forming step. This example belongs to a very rare class of enantiodivergent reactions. The exact origin of this catalyst selectivity remains to be established. Derivatization of these enantiopure diastereomers to synthetically more useful intermediates is currently underway.

5.12. Experimental Section

**General Methods** Air-sensitive reactions were conducted under an inert atmosphere of argon using Schlenk techniques or a Vacuum Atmospheres glovebox. Solvents were distilled from the appropriate drying agents under nitrogen. Ethylene (99.5%) was purchased from Matheson, Inc., and passed through Drierite® and potassium hydroxide before use. Analytical TLC was performed on Siliccycle pre-coated (0.25 mm) silical gel 60 F254 plates. Flash column chromatography was carried out on silica gel 40 (Sorbtech Chemicals), Gas chromatographic analysis was conducted on an Agilent 7820A using hydrogen as the carrier gas, equipped with a methyl silicone column (30 m X 0.32 mm, 0.25 µm film thickness). Enantiomeric excess of chiral compounds were determined by chiral stationary phase gas chromatographic (CSP GC) analysis, which were performed on an Agilent 7820A using hydrogen as the carrier gas, equipped with a Cyclosil-B (30 m X 0.25 mm, 0.25 µm film thickness), capillary GC columns purchased from Agilent. Each GC was equipped with FID detectors and integrators or a computer.

**Synthesis of Cobalt Complexes:** For detailed discussion on synthesis of cobalt complexes, please see chapter 4, experimental section.
Typical Procedure for Synthesis of Methylaluminoxane (MAO): For detailed discussion on synthesis of methylaluminoxane, please see chapter 4, experimental section.

General procedure to synthesize 4-substitued-1-vinylcycloalkenes

A 100 mL three-necked round-bottom flask equipped with a magnetic stir bar, septum stopper, and gas inlet were flame-dried and purged with argon. The flask was chilled to 0 °C and 20 mL of a 1 M solution (20.0 mmol, 1 equivalent) of vinylmagnesium bromide in THF was introduced. The respective cyclic ketone (20.0 mmol, 1 equivalent) was dissolved in 10 mL dry, distilled THF, and added slowly to the Grignard solution over a period of one hour using a syringe pump to aid in the addition. The solution was then allowed to warm slowly to room temperature by removing the ice bath, and subsequently stirred for 2 hours at room temperature. The yellow solution was quenched with saturated NH₄Cl (aq), and the aqueous layer extracted with (3 x 30 mL) ether. The combined organic extracts were dried with MgSO₄, the solids were filtered off, and the solvent removed in vacuo, yielding a crude alcohol.

A new 100 mL three-necked round-bottom flask was flame dried and purged with argon. The crude alcohol was introduced as a solution in 20 mL dry, distilled pyridine. The
mixture was cooled to 0 °C and 2.80 mL (4.60 g, 30.0 mmol) phosphoryl chloride was
introduced dropwise. The solution was kept in the ice bath and allowed to warm to room
temperature overnight. The brown mixture was carefully transferred slowly to a 125 mL
erlenmeyer flask containing crushed ice to quench the remaining phosphoryl chloride.
The ice was allowed to melt, and then the resulting aqueous mixture was extracted by (3
x 30 mL) pentanes. The combined aqueous layers was washed with 10% CuSO₄ (aq)
until no discoloration of the aqueous layer was seen to remove any extracted pyridine,
and then washed with distilled water, dried over MgSO₄, the solids filtered off, and the
solvent removed very carefully in vacuo without the use of a water bath to prevent loss of
the volatile products. The crude product was purified by bulb-to-bulb distillation using a
dry ice / acetone cooling bath to give the product as a clear oil. The oil was stored in a
freezer to prevent evaporation.

4-(tert-butyl)-1-vinylcyclohex-1-ene (7): $^1$H NMR (600 MHz, CDCl₃) δ

```
6.36 (dd, 1H, J = 10.7 Hz, 17.5 Hz), 5.76-5.77 (m, 1H), 5.05 (d, 1H, J = 17.5 Hz),
4.89 (d, 1H, J = 10.7 Hz), 2.32-2.35 (m, 1H), 2.14-2.18 (m, 1H), 2.00-2.10 (m, 1H), 1.88-1.93 (m, 2H), 1.24-1.34 (m, 2H), 0.88 (s, 9H).
```

$^{13}$C NMR (150 MHz, CDCl₃) δ 139.7, 135.9, 130.0, 109.7, 44.3, 32.2, 27.4, 27.2, 25.1, 23.7

GC (cyclodex-B, 110 °C): Rₜ 29.724 min and 30.018 min.

4-isopropyl-1-vinylcyclohex-1-ene (13): $^1$H NMR (400 MHz, CDCl₃) δ

```
6.36 (dd, 1H, J = 10.7 Hz, 17.5 Hz), 5.74-5.76 (m, 1H), 5.05 (d, 1H, J = 17.5 Hz),
```
4.89 (d, 1H, J = 10.7 Hz), 2.27-2.33 (m, 1H), 2.12-2.20 (m, 1H), 2.03-2.11 (m, 1H), 1.83-1.90 (m, 2H), 1.46-1.54 (m, 1H), 1.18-1.36 (m, 2H), 0.89-0.91 (m, 6H).

$^{13}$C NMR (150 MHz, CDCl$_3$) δ 139.8, 135.9, 129.7, 109.7, 40.3, 32.2, 29.5, 25.9, 24.4, 19.9, 19.6

GC (cyclosil-$B$, 80 °C): R$_t$ 43.298 min and 45.810 min.

![Chemical Structure](14)

4-phenyl-1-vinylcyclohex-1-ene (14): $^1$H NMR (400 MHz, CDCl$_3$) δ 6.36 (dd, 1H, J = 10.8 Hz, 17.5 Hz), 5.72-5.73 (m, 1H), 5.06 (d, 1H, J = 17.5 Hz), 4.89 (d, 1H, J = 10.7 Hz), 2.05-2.32 (m, 4H), 1.62-1.82 (m, 3H), 0.97 (d, 3H, J = 6.4 Hz)

$^{13}$C NMR (150 MHz, CDCl$_3$) δ 139.9, 135.7, 129.4, 109.7, 34.3, 30.6, 28.6, 23.8, 21.7

GC (cyclosil-$B$, 75 °C): R$_t$ 12.675 min and 12.926 min.

![Chemical Structure](15)

4-methyl-1-vinylcyclohex-1-ene (15): $^1$H NMR (400 MHz, CDCl$_3$) δ 6.36 (dd, 1H, J = 10.8 Hz, 17.5 Hz), 5.72-5.73 (m, 1H), 5.06 (d, 1H, J = 17.5 Hz), 4.89 (d, 1H, J = 10.7 Hz), 2.05-2.32 (m, 4H), 1.62-1.82 (m, 3H), 0.97 (d, 3H, J = 6.4 Hz)

$^{13}$C NMR (150 MHz, CDCl$_3$) δ 139.9, 135.7, 129.4, 109.7, 34.3, 30.6, 28.6, 23.8, 21.7

GC (cyclosil-$B$, 75 °C): R$_t$ 12.675 min and 12.926 min.

![Chemical Structure](16)

4-(tert-butyl)-1-(prop-1-en-2-yl)cyclohex-1-ene (16): $^1$H NMR (400 MHz, CDCl$_3$) δ 5.88-5.90 (m, 1H), 4.94 (b, 1H), 4.83 (b, 1H), 2.37-2.42 (m, 1H), 2.11-
2.22 (m, 2H), 1.87-1.96 (m, 2H), 1.90 (b, 3H), 1.12-1.30 (m, 2H), 0.88 (s, 9H).

$^{13}$C NMR (150 MHz, CDCl$_3$) δ 143.5, 136.5, 125.2, 109.6, 43.9, 32.1, 27.5, 27.2, 27.0, 24.2, 20.6

GC (cyclosil-B, 100 °C): R, 54.608 min and 56.811 min.

(S)-4-(prop-1-en-2-yl)-1-vinylcyclohex-1-ene (S-11): A 50 mL three-necked round-bottom flask equipped with a magnetic stir bar, flow control gas inlet, and septa was flame dried and purged with argon. 2.85 g (8.00 mmol) Triphenylphosphonium bromide was added to the flask under a strong stream of argon, 40 mL dry, distilled diethyl ether was added to make a slurry, and the mixture chilled to 0 °C. To the slurry, 3.00 mL (7.50 mmol) of a 2.5 M n-butyllithium solution in hexanes was added over a period of 30 mins, and then the ice bath removed to allow the salt to completely dissolve. 1.00 g (6.66 mmol) perillaldehyde was dissolved in 2.5 mL dry, distilled ether and added dropwise to the ylide, and stirred for 2 hours. The solution was poured into 150 mL pentanes and the solids filtered off through celite. The solvent was carefully removed in vacuo due to volatility of the product and the residue purified by bulb-to-bulb distillation to get the product as a clear oil 0.630 g (53% yield).

$^1$H NMR (500 MHz, CDCl$_3$) δ 6.35 (dd, 1H, $J = 6.5$ Hz, 17.5 Hz), 5.77 (bd, 1H, $J = 5$ Hz), 5.07 (d, 1H, $J = 17.5$ Hz), 4.91 (d, 1H, $J = 11$ Hz), 4.74 (d, 2H, $J = 5$ Hz), 2.00-2.40 (m, 6H), 1.91 (m, 1H), 1.76 (s, 3H), 1.50 (m, 1H).

$^{13}$C NMR (133 MHz, CDCl$_3$) δ 149.7, 139.7, 135.8, 129.1, 110.0, 108.7, 41.2, 31.2, 27.3, 24.3, 20.8.
GC (cyclosil-B, 100 °C): R, 17.024 min.

\((S,E)\)-6,10-dimethylundeca-1,3,9-triene (S-21):\(^{27}\) A 50 mL three-necked round-bottom flask equipped with a magnetic stir bar, flow control gas inlet, and septa was flame dried and purged with argon. 0.67 mL (3.9 mmol) diethyl allylphosphonate was added to the flask under a strong stream of argon, 6 mL dry, distilled THF was added, and the mixture chilled to -78 °C. To the solution, 1.4 mL (3.6 mmol) of a 2.5 M n-butyllithium solution in hexanes was added over a period of 10 mins. 0.5 g (3.24 mmol) (S)-citronellal was dissolved in 1.0 mL dry, distilled hexamethylphosphoramide and added dropwise to the ylide at -78 °C, and stirred for 2 hours at -78 °C, and then allowed to warm up to r.t. before quenching with saturated aqueous NH\(_4\)Cl solution. The mixture was extracted with ether (3 X 10 mL) and the combined organic phases were washed with brine, dried over MgSO\(_4\), concentrated to afford the crude product. The crude product was purified by flash column chromatography (100% pentane) to get the product as a clear oil 0.52 g (90% yield).

\(^{1}\)H NMR (600 MHz, CDCl\(_3\)) \(\delta\) 6.32 (ddd, 1H, \(J = 10.2\) Hz, 10.3 Hz, 17.0 Hz), 6.04 (dd, 1H, \(J = 10.4\) Hz, 15.2 Hz), 5.69 (ddd, 1H, \(J = 7.4\) Hz, 7.5 Hz, 15.2 Hz), 5.07-5.11 (m, 2H), 4.95 (dd, 1H, \(J = 1.1\) Hz, 10.2 Hz), 2.08-2.12 (m, 1H), 1.90-2.04 (m, 3H), 1.68 (d, 3H, \(J = 1.0\) Hz), 1.60 (b, 3H), 1.50-1.55 (m, 1H), 1.31-1.38 (m, 1H), 1.12-1.18 (m, 1H), 0.88 (d, 3H, \(J = 6.7\) Hz).

\(^{13}\)C NMR (133 MHz, CDCl\(_3\)) \(\delta\) 137.3, 134.1, 132.1, 131.2, 124.8, 114.6, 40.0, 36.7, 32.8, 25.7, 25.6, 19.5, 17.6.
GC (cyclosil-B, 80 °C): (\(S,E\))-6,10-dimethylundeca-1,3,9-triene (\(S-21\)) \(R_t\) 69.395 min (\(E\)) and 73.362 min (\(Z\)). (\(R,E\))-6,10-dimethylundeca-1,3,9-triene (\(R-21\)) \(R_t\) 69.252 min (\(E\)) and 72.579 min (\(Z\)). racemic-6,10-dimethylundeca-1,3,9-triene (21) \(R_t\) 69.907 min and 70.470 min.

**Typical Procedure for Co(II)-Catalyzed Hydovinylation of 4-Substituted-1-vinylcycloalkenes Using Methylaluminoxane as Co-catalyst:** For detailed discussion on hydovinylation procedure, please see chapter 4, experimental section.

\[
\begin{align*}
\text{trans-9b (2S,4S)} & \quad \text{cis-9a (2S,4R)} \\
\end{align*}
\]

\((2S,4S, Z)-4-(\text{tert-butyl})-1\text{-ethylidene-2-vinylcyclohexane (trans-9b)}\) and \((2S,4R, Z)-4-(\text{tert-butyl})-1\text{-ethylidene-2-vinylcyclohexane (cis-9a)}\): These two diastereomers merge together in the \(^1H\) NMR and \(^{13}C\) NMR spectra.

\(^1H\) NMR (600 MHz, CDCl\(_3\)) \(\delta\) 5.81-5.89 (m, 1H each), 5.26-5.31 (m, 1H each), 4.91-5.02 (m, 2H each), 3.47 (b, 1H, \(\text{trans-9b}\)), 2.97-3.01 (m, 1H, \(\text{cis-9a}\)), 2.15-2.22 (m, 1H each), 2.07 (dt, 1H, \(J = 2.8\) Hz, \(13.8\) Hz, one diastereomer), 1.98 (ddd, 1H, \(J = 4.7\) Hz, 7.4 Hz, 11.9 Hz, one diastereomer), 1.85-1.88 (m, 1H, one diastereomer), 1.75-1.79 (m, 1H, one diastereomer), 1.68-1.71 (m, 1H, one diastereomer), 1.60-1.65 (m, 1H, one diastereomer), 1.58 (d, 3H, \(J = 6.5\) Hz, one diastereomer), 1.58 (d, 3H, \(J = 6.7\) Hz, one diastereomers), 1.27-1.34 (m, 3H, both diastereomers merged), 0.94-1.04 (m, 1H, one diastereomer), 0.84 (s, 9H, one diastereomer), 0.837 (s, 9H, one diastereomer).

\(^{13}C\) NMR (150 MHz, CDCl\(_3\)) \(\delta\) 141.02, 140.95, 140.11, 139.70, 118.52, 117.20, 113.96, 112.08, 44.20, 43.85, 42.77, 39.22, 33.32, 32.99, 32.51, 32.23, 31.98, 31.46, 28.92, 27.47, 27.18, 26.05, 22.69, 22.33, 14.10, 14.05, 13.30, 12.45.
GC (cyclodex-B, 110 °C): See attached GC spectra for diastereomeric ratio and ee.

R<sub>t</sub> from dppp:

\[
\text{trans-9b (2S,4S)} \quad 31.663 \text{ min} \\
\text{ent-trans-9b (2R,4R)} \quad 32.666 \text{ mins} \\
\text{cis-9a (2S,4R)} \quad 33.687 \text{ min} \\
\text{ent-cis-9a (2R,4S)} \quad 34.018 \text{ min}
\]

R<sub>t</sub> from (R,R-BDPP):

\[
\text{ent-trans-9b (2R,4R)} \quad 32.612 \text{ min} \\
\text{ent-cis-9a (2R,4S)} \quad 33.935 \text{ min} \\
\text{10 1,2-HV} \quad 44.734-45.700 \text{ min}
\]

R<sub>t</sub> from (S,S-BDPP):

\[
\text{trans-9b (2S,4S)} \quad 31.539 \text{ min} \\
\text{cis-9a (2S,4R)} \quad 33.370 \text{ min} \\
\text{10 1,2-HV} \quad 44.112 \text{ min}
\]

1,2-Hydrovinylation Products from 4-t-Butyl-1-vinylcyclohexene (8):

\[
^1\text{H NMR (500 MHz, CDCl}_3\text{)} \delta 5.70 – 5.80 (ddd, 1H, J = 3.0, 3.5, 4.0 Hz), 5.34 (br, 1H), 4.96 (d, 1H, J = 17.5 Hz), 4.24 (d, 1H, J = 10.5 Hz), 2.69
\]
(qn, 1H, J = 7.0 Hz, bis-allylic H), 2.02 (d, 2H, J = 16.5 Hz), 1.95 (d, 2H, J = 5.5 Hz), 1.75 – 1.85 (m, 3H), 1.07 (d, 3H, J = 7.0 Hz), 0.86 (s, 9 H).

$^{13}$C NMR (133 MHz, CDCl$_3$) $\delta$ 143.2, 140.6, 120.9, 112.8, 44.6, 44.5, 32.2, 27.9, 27.3, 27.0, 24.5, 17.9. (additional peaks due to the diastereomer: 143.1, 140.8, 120.6, 112.9, 44.4, 28.0, 27.0, 24.5, 18.6). NMR spectra of this compound has been described in the literature.$^{25,26}$

(2S,4S,Z)-4-(iso-propyl)-1-ethyldene-2-vinylcyclohexane (trans-17b) and (2S,4R,Z)-4-(iso-propyl)-1-ethyldene-2-vinylcyclohexane (cis-17a): These two diastereomers merge together in the $^1$H NMR and $^{13}$C NMR spectra.

$^1$H NMR (600 MHz, CDCl$_3$) $\delta$ 5.85-5.93 (m, 1H each), 5.26-5.31 (m, 1H each), 4.91-5.02 (m, 2H each), 3.46 (b, 1H, trans-17b), 3.00-3.04 (m, 1H, cis-17a), 2.17-2.24 (m, 1H each), 2.06 (dt, 1H, J = 2.9 Hz, 13.8 Hz, one diastereomer), 1.97 (dt, 1H, J = 5.8 Hz, 16.7 Hz, one diastereomer), 1.79 (dq, 1H, J = 2.5 Hz, 12.8 Hz, one diastereomer), 1.69-1.73 (m, 1H, one diastereomer), 1.65-1.68 (m, 1H, one diastereomer), 1.60-1.64 (m, 1H, one diastereomer), 1.58 (d, 3H, J = 6.7 Hz, one diastereomer), 1.58 (d, 3H, J = 6.7 Hz, one diastereomers), 1.47-1.53 (m, 1H, one diastereomer), 1.35-1.44 (m, 1H, one diastereomer), 1.34-1.21 (m, 3H, both diastereomers merged), 0.96-1.02 (m, 1H, one diastereomer), 0.86 (dd, 3H, J = 6.8 Hz, 9.9 Hz, one diastereomers), 0.85 (dd, 3H, J = 5.3 Hz, 6.7 Hz, one diastereomers).
$^{13}$C NMR (150 MHz, CDCl$_3$) δ 141.42, 141.01, 140.23, 139.87, 118.28, 117.34, 113.91, 112.07, 43.56, 40.81, 39.22, 38.90, 35.38, 34.11, 33.09, 32.64, 32.33, 31.95, 31.08, 28.64, 20.14, 19.82, 19.79, 19.60, 13.32, 12.46.

GC (cyclosil-B, 80 °C): See attached GC spectra for diastereomeric ratio and ee.

$R_t$ from dppp:

- trans-17b (2S,4S) 45.859 min
- ent-trans-17b (2R,4R) 48.630 min
- cis-17a (2S,4R) 52.343 min
- ent-cis-17a (2R,4S) 54.096 min

$R_t$ from (R,R-BDPP):

- ent-trans-17b (2R,4R) 48.123 min
- ent-cis-17a (2R,4S) 53.819 min

$R_t$ from (S,S-BDPP):

- trans-17b (2S,4S) 45.391 min
- cis-17a (2S,4R) 52.136 min

(2S,4S,Z)-4-phenyl-1-ethylidene-2-vinylcyclohexane

(trans-18b) and (2S,4R,Z)-4-phenyl-1-ethylidene-2-
**vinylcyclohexane (cis-18a):** These two diastereomers merge together in the $^1$H NMR and $^{13}$C NMR spectra.

$^1$H NMR (600 MHz, CDCl$_3$) $\delta$ 7.27-7.31 (m, 5H, both diastereomers merged), 7.17-7.24 (m, 7H, both diastereomers merged), 5.94-6.00 (m, 1H each), 5.35-5.40 (m, 1H each), 5.10 (dt, 1H, $J$ = 2.0 Hz, 10.3 Hz, one diastereomer), 5.01-5.07 (m, 1H each), 4.95 (ddd, 1H, $J$ = 1.1 Hz, 1.8 Hz, 10.2 Hz, one diastereomer), 3.56 (b, 1H, *trans*-18b), 3.13-3.17 (m, 1H, cis-18a), 2.84 (tt, 1H, $J$ = 3.3 Hz, 12.6 Hz, one diastereomer), 2.69-2.75 (m, 1H, one diastereomer), 2.34-2.43 (m, 1H each), 2.11-2.19 (m, 1H each), 1.94-2.02 (m, 1H each), 1.88-1.94 (m, 1H each), 1.69-1.79 (m, 1H each), 1.66-1.67 (m, 5H, both diastereomers merged), 1.63 (dd, 3H, $J$ = 2.2 Hz, 6.7 Hz, one diastereomer).

$^{13}$C NMR (150 MHz, CDCl$_3$) $\delta$ 147.09, 147.07, 141.09, 140.37, 138.99, 138.84, 128.33, 126.88, 126.85, 125.94, 125.89, 119.04, 118.43, 114.58, 112.44, 44.68, 41.45, 39.56, 39.46, 39.27, 38.66, 35.44, 33.90, 33.77, 33.15, 13.67, 12.52.

GC (*cyclosil*-B, 130 °C): See attached GC spectra for diastereomeric ratio and ee.

$R_t$ from dppp:

<table>
<thead>
<tr>
<th>Compound</th>
<th>$R_t$ (min)</th>
</tr>
</thead>
<tbody>
<tr>
<td><em>trans</em>-18b (2S,4S)</td>
<td>52.205</td>
</tr>
<tr>
<td><em>ent</em>-trans-18b (2R,4R)</td>
<td>53.065</td>
</tr>
<tr>
<td><em>cis</em>-18a (2S,4R)</td>
<td>59.739</td>
</tr>
<tr>
<td><em>ent</em>-cis-18a (2R,4S)</td>
<td>61.074</td>
</tr>
</tbody>
</table>

$R_t$ from (*R,R*-BDPP):
R<sub>t</sub> from (S,S-BDPP):

(2S,4S,Z)-4-methyl-1-ethylidene-2-vinylcyclohexane
(trans-19b) and (2S,4R,Z)-4-methyl-1-ethylidene-2-vinylcyclohexane (cis-19a): These two diastereomers merge together in the <sup>1</sup>H NMR and <sup>13</sup>C NMR spectra.

<sup>1</sup>H NMR (600 MHz, CDCl<sub>3</sub>) δ 5.88 (ddd, 1H, <i>J</i> = 6.5 Hz, 10.2 Hz, 16.9 Hz, one diastereomer), 5.82 (ddd, 1H, <i>J</i> = 5.3 Hz, 10.3 Hz, 17.2 Hz, one diastereomer), 5.20-5.25 (m, 1H each), 4.90-4.93 (m, 1H each), 4.87 (dt, 1H, <i>J</i> = 2.0 Hz, 6.2 Hz, one diastereomer), 4.84 (dt, 1H, <i>J</i> = 1.7 Hz, 10.2 Hz, one diastereomer), 3.35 (b, 1H, <i>trans-19b</i>), 3.00-3.03 (m, 1H, <i>cis-19a</i>), 2.12-2.20 (m, 1H each), 1.93-1.96 (m, 1H, one diastereomer), 1.87 (dt, 1H, <i>J</i> = 5.8 Hz, 13.6 Hz, one diastereomer), 1.68-1.71 (m, 1H, one diastereomer), 1.56-1.65 (m, 6H, both diastereomers merged), 1.50-1.52 (m, 6H, both diastereomers merged), 1.14-1.21 (m, 3H, both diastereomers merged), 0.88 (d, 3H, <i>J</i> = 6.5 Hz, one diastereomer), 0.79 (d, 3H, <i>J</i> = 6.4 Hz, one diastereomer).
$^{13}$C NMR (150 MHz, CDCl$_3$) $\delta$ 142.16, 140.92, 139.76, 139.69, 118.20, 117.63, 113.86, 111.98, 42.77, 40.75, 39.46, 39.44, 36.65, 33.01, 32.15, 31.62, 29.47, 27.93, 22.48, 21.44, 13.23, 12.47.

GC (cyclosil-B, 75 °C): See attached GC spectra for diastereomeric ratio and ee.

$R_t$ from dppp:

\[
\begin{align*}
\text{trans-19b (2S,4S)} & : 15.216 \text{ min} \\
\text{ent-trans-19b (2R,4R)} & : 16.097 \text{ min} \\
\text{cis-19a (2S,4R)} & : 21.271 \text{ min} \\
\text{ent-cis-19a (2R,4S)} & : 20.981 \text{ min}
\end{align*}
\]

$R_t$ from ($R,R$-BDPP):

\[
\begin{align*}
\text{ent-trans-19b (2R,4R)} & : 15.179 \text{ min} \\
\text{ent-cis-19a (2R,4S)} & : 20.978 \text{ min}
\end{align*}
\]

$R_t$ from ($S,S$-BDPP):

\[
\begin{align*}
\text{trans-19b (2S,4S)} & : 15.950 \text{ min} \\
\text{cis-19a (2S,4R)} & : 21.106 \text{ min}
\end{align*}
\]

$(2S,4R)$-4-(tert-butyl)-1-(propan-2-ylidene)-2-vinylcyclohexane ($cis$-$20a$) and $(2S,4S)$-4-(tert-butyl)-1-(propan-2-ylidene)-2-vinylcyclohexane ($trans$-$20b$): These two diastereomers merge together in the $^1$H NMR and $^{13}$C NMR spectra.
$^1$H NMR (600 MHz, CDCl$_3$) $\delta$ 5.85 (ddd, 1H, $J = 5.1$ Hz, 10.3 Hz, 17.2 Hz, one diastereomer), 5.73 (ddd, 1H, $J = 6.6$ Hz, 10.2 Hz, 17.0 Hz, one diastereomer), 4.98 (dt, 1H, $J = 2.1$ Hz, 10.3 Hz, one diastereomer), 4.88-4.94 (m, 3H, both diastereomers merged), 3.51 (b, 1H, trans-20b), 3.05-3.11 (m, 1H, cis-20a), 2.56-2.62 (m, 1H, one diastereomer), 2.39 (ddd, 1H, $J = 1.3$ Hz, 7.7 Hz, 13.9 Hz, one diastereomer), 1.99-2.12 (m, 3H, both diastereomers merged), 1.74-1.94 (m, 7H, both diastereomers merged), 1.68-1.70 (m, 6H, one diastereomer), 1.66 (d, 3H, $J = 2.1$ Hz, one diastereomer), 1.63-1.65 (m, 2H, both diastereomers merged), 1.61 (d, 3H, $J = 1.8$ Hz, one diastereomer), 0.84 (s, 9H, one diastereomer), 0.83 (s, 9H, one diastereomer).

$^{13}$C NMR (150 MHz, CDCl$_3$) $\delta$ 141.69, 140.98, 131.75, 130.92, 124.51, 122.68, 113.53, 111.68, 43.69, 43.06, 42.45, 40.90, 33.21, 32.52, 32.19, 30.25, 28.23, 27.45, 27.18, 27.07, 26.19, 24.60, 23.55, 20.36, 20.15, 19.83.

GC (cyclodex-B, 100 °C): See attached GC spectra for diastereomeric ratio and ee.

$R_t$ from dppp:

trans-19b (2S,4S) 84.078 min
ent-trans-19b (2R,4R) 84.978 min
cis-19a (2S,4R) 77.716 min
ent-cis-19a (2R,4S) 78.413 min

$R_t$ from (R,R-BDPP):
R<sub>t</sub> from (S,S-BDPP):

\[
\begin{align*}
\text{ent-cis-20a (2R,4S)} & : 77.716 \text{ min} \\
\text{ent-trans-20b (2R,4R)} & : 84.933 \text{ min}
\end{align*}
\]

\[
\begin{align*}
\text{cis-20a (2S,4R)} & : 78.039 \text{ min} \\
\text{trans-20b (2S,4S)} & : 83.989 \text{ min}
\end{align*}
\]

\[
(4S,Z)-1\text{-ethylidene-4-(prop-1-en-2-yl)-2-vinylcyclohexane [cis-12a (2R,4S) + trans-12b (2S,4S)]: Cis and trans diastereomers merge together in the } ^1\text{H NMR and } ^{13}\text{C NMR spectra.}
\]

\[
^1\text{H NMR (500 MHz, CDCl}_3\text{) } \delta 5.92 \text{ (m, 1H), 5.29 (q, 1H, } J = 5 \text{ Hz), 4.93 (dd, 2H, } J = 5 \text{ Hz, 10 Hz), 4.66 (d, 2H } J = 5 \text{ Hz), 3.05 (ddd, 1H), 2.24 (q, 1H, } J = 10 \text{ Hz), 2.10 (br, 2H), 1.70-1.80 \text{ (br, 5H), 1.59 (d, 3H, } J = 8.0 \text{ Hz), 1.35 – 1.55 (br, 2H) [minor isomer 3.45 (br, 1H); peaks at } \delta 3.05 \text{ (2,4-cis) and } \delta 3.45 \text{ (2,4-trans) together integrate to 1 H].}
\]

Additionally, the 1,2-hydrovinylation can be identified by the \(^1\text{H NMR with the following peaks: } \delta 5.70 – 5.80 \text{ (m, 1H corresponding to internal vinyl proton), 5.45 – 5.48 (br, 1H corresponding to proton on endocyclic alkene), 2.72 (m, 1H corresponding to HV proton adjacent to methyl group), 1.09 (d, 3H corresponding to HV methyl group).}
$^{13}$C NMR (125 MHz, CDCl$_3$) [major isomer]: $\delta$ 149.98, 141.16, 139.28, 118.71, 110.35, 108.44, 44.13, 42.00, 35.89, 33.14, 30.70, 20.78, 13.50 [minor isomer]: $\delta$ 150.38, 140.50, 118.05, 114.33, 108.36, 40.36, 39.07, 37.11, 33.06, 32.95, 29.71, 20.84, 12.47.

GC ($cyclosil$-$B$, 100 °C): See attached GC spectra for diastereomeric ratio and ee.

$R_t$ from dppp:

$$
\text{cis-12a (2R,4S)}\quad 22.526 \text{ min} \\
\text{trans-12b (2S,4S)}\quad 18.304 \text{ min}
$$

cis (major): 22.51 mins. (77%); trans (minor): 18.30 mins. (20%).

$R_t$ from ($R,R$-BDPP):

$$
\text{cis-12a (2R,4S)}\quad 22.443 \text{ min} \\
\text{trans-12b (2S,4S)}\quad 18.271 \text{ min}
$$

$R_t$ from ($S,S$-BDPP):

$$
\text{cis-12a (2R,4S)}\quad 22.130 \text{ min} \\
\text{trans-12b (2S,4S)}\quad 18.204 \text{ min} \\
\text{13 (1,2-HV)}\quad 29.812 \text{ min} \\
\quad 30.451 \text{ min}
$$
(6S,8R,Z)-2,6-dimethyl-8-vinylundeca-2,9-diene  (syn-22):

From [(S,S)-DIOP]CoCl₂

1H NMR (400 MHz, CDCl₃) δ 5.70 (ddd, 1H, J = 6.8 Hz, 10.2 Hz, 17.1 Hz), 5.46-5.54 (m, 1H), 5.13-5.19 (m, 1H), 5.06-5.12 (m, 1H), 4.98 (dt, 1H, J = 1.5 Hz, 17.2 Hz), 4.92 (ddd, 1H, J = 1.2 Hz, 1.8 Hz, 10.2 Hz), 3.11-3.19 (m, 1H), 1.88-2.07 (m, 2H), 1.68 (d, 3H, J = 1 Hz), 1.63 (dd, 3H, J = 1.8 Hz, 6.8 Hz), 1.60 (b, 3H), 1.40-1.50 (m, 1H), 1.28-1.38 (m, 2H), 1.12-1.23 (m, 2H), 0.90 (d, 3H, J = 6.5 Hz).

13C NMR (150 MHz, CDCl₃) δ 142.1, 133.2, 131.0, 124.9, 123.9, 112.6, 42.6, 38.9, 37.4, 29.9, 25.7, 25.5, 19.5, 17.6, 13.0.

GC (cyclosil-B, 80 °C): See attached GC spectra for diastereomeric ratio and ee.
\[
\text{syn-22 (6S, 8R)} : \text{anti-23 (6S, 8S)} = 1:1.3
\]
with 40% 1,4-linear HV product

\[
\text{syn-22 (6S, 8R)} : \text{anti-23 (6S, 8S)} = 88:4
\]
with 8% 1,4-linear HV product

\[
\text{syn-22 (6S, 8R)} : \text{anti-23 (6S, 8S)} = 5:87
\]
with 8% 1,4-linear HV product
CoCl₂(DPPP) (0.05 equiv.), MAO (2 equiv.), CH₂Cl₂, rt, 15 mins, ethylene (1 atm)

anti-24 (6R, 8R) : syn-25 (6R, 8S) = 1 : 1.25 with 15% 1,4-linear HV product

[(S,S)-DIOP]CoCl₂ (0.05 equiv.), MAO (2 equiv.), CH₂Cl₂, rt, 15 mins, ethylene (1 atm)

anti-24 (6R, 8R) : syn-25 (6R, 8S) = 79 : 5 with 8% 1,4-linear HV product

[(R,R)-DIOP]CoCl₂ (0.05 equiv.), MAO (2 equiv.), CH₂Cl₂, rt, 15 mins, ethylene (1 atm)

anti-24 (6R, 8R) : syn-25 (6R, 8S) = 4 : 88 with 8% 1,4-linear HV product
Typical Procedure for Selective Reduction of Vinyl Group of Hydrovinylated Product:

A 25mL three-necked flask equipped with magnetic stirring bar, stopper, rubber septum and nitrogen inlet was flame dried and purged with argon. The flask was charged with CoCl$_2$(i-Pr-PDI) catalyst (6.8mg, 0.011 mmol, 0.1 eq), further diluted with 2mL of toluene and cooled down to -78°C in an dry ice-acetone bath. The substrate 17a and 17b (20mg, 0.11mmol, achiral or enantiopure substrate) was added to the reaction mixture by a microliter syringe, followed by addition of NaEt$_3$BH (1 M in toluene, 23µL, 0.44mmol, 0.2 eq) and diethoxymethylsilane [(OEt)$_2$Si(H)(Me)] (22µL, 0.13mmol, 1.2 eq). Dry ice-acetone bath has been removed and the reaction mixture was allowed to warm up to room
temperature over 6 h (reaction was constantly monitored by GC). Once gas chromatogram showed full consumption of starting material, reaction mixture was rotaevaporated carefully to remove the solvent from the reduced product, which was then further purified over preparative TLC (with pentane) to yield the purified product.

(2S,4S,E)-2-ethyl-1-ethylidene-4-isopropylcyclohexane (ent-cis-26a) and (2S,4R,E)-2-ethyl-1-ethylidene-4-isopropylcyclohexane (ent-trans-26b): These two diastereomers merge together in the $^1$H NMR and $^{13}$C NMR spectra.

$^1$H NMR (600 MHz, CDCl$_3$) $\delta$ 5.19-5.23 (m, 1H each), 2.62-2.65 (m, 1H, ent-trans-26b), 2.35-2.40 (m, 1H, ent-cis-26a), 2.13-2.20 (m, 1H each), 1.99 (dt, 1H, $J = 3.2$ Hz, 13.6 Hz, one diastereomer), 1.91 (ddd, 1H, $J = 2.7$ Hz, 8.0 Hz, 13.3 Hz, one diastereomer), 1.66-1.74 (m, 2H, both diastereomers merged), 1.56-1.58 (m, 6H, both diastereomers merged), 1.52-1.54 (m, 1H, one diastereomer), 1.49-1.52 (m, 1H, one diastereomer), 1.44-1.48 (m, 2H, both diastereomers merged), 1.34-1.42 (m, 3H, both diastereomers merged), 1.28-1.33 (m, 3H, both diastereomers merged), 1.10-1.18 (m, 2H, both diastereomers merged), 0.94-1.03 (m, 2H, both diastereomers merged), 0.89 (q, 3H each, $J = 7.5$ Hz, both diastereomers merged), 0.82-0.86 (m, 12H, both diastereomers merged).

$^{13}$C NMR (150 MHz, CDCl$_3$) $\delta$ 142.87, 142.32, 116.95, 116.16, 39.82, 39.25, 38.26, 37.21, 34.88, 32.81, 32.74, 32.38, 32.33, 31.59, 30.54, 28.12, 25.37, 22.33, 20.18, 19.88, 19.70, 14.05, 13.15, 12.76, 12.21, 11.96.

GC (cyclodex-B, 110 °C): See attached GC spectra for diastereomeric ratio and ee.
$R_t$ from dppp:

$R_t$ from $(R,R)$-BDPP:

$R_t$ from $(S,S)$-BDPP:
5.14. References

(9) Webster, R.; Boing, C.; Lautens, M. J. Am. Chem. Soc. 2009, 131, 444-+
(28) Unpublished results of Balaram Raya, The Ohio State University (2015)
Chapter 1:


(22) Iwamoto, M.; Yuguchi, S. Chem. Commun. 1968, 28-29.


Chapter 2:
(9) The ratios of products in this and other reactions reported in this paper are best determined by gas chromatography where baseline separations of isomers are observed. Since full characterization of all compounds reported in this paper have been documented before (see Supporting Information for citations) only gas chromatograms for the various experiments are included in the Supporting Information.

Chapter 3:
(8) Several examples of metal and ligand-dependent isomerization of alkenes to seemingly less stable isomers have been described in the literature. (a) Ni-catalyzed isomerization of allyl ethers to (Z)-vinyl ethers: Wille, A.; Tomm, S.; Frauenrath, H.

(9) Precise proportion of isomeric compounds were determined by gas chromatography and NMR. See Supporting Information for details including chromatograms of products from various reactions.

(10) At higher temperatures (-10 °C, 1 atm ethylene) (DPPB)CoCl₂/MAO converts both (Z) and (E)-8 to racemic 9 in quantitative yield.

(11) We have carried out Co-catalyzed asymmetric HV of E/Z-mixtures of 16 and 17 and observed results similar to what is documented in Table 3.1 for E/Z-8.


(14) We have carried out high-level DFT calculations (Gaussian 09, geometries optimized with the 6-31G* basis set in conjunction with the B3LYP) on two of the molecules (8) and (16). Not surprisingly, the E-isomer is the more stable one (Kₑ/ᵢ = 3924 and 24.8 respectively, 298 K) and both isomers exist almost exclusively in the s-trans form. The Z-isomer, once generated, will also exist exclusively in the s-trans conformation (Kₛ/ᵢₛ = 1998 and 612 respectively), preventing a stable η⁴-coordination to Co(II).

(16) We have also observed up to 69% conversion of a (Z/E)-mixture (46:54) of 16 to a product of 1,5-H-shift (15, R = C₇H₁₄) by using (DPPE)CoBr₂ (20 mol%)/Zn/ZnI₂ (40 mol%) for 72 h.


Chapter 4:


(32) See experimental section for details.


Chapter 5:
APPENDICES: SUPPLEMENTAL FILES

Please see the supplemental files in the appendices attached to this submission that start on page 290.