Catalytic Asymmetric Claisen Rearrangements. The Development of Ru(II)-Catalyzed Formal [3,3] Sigmatropic Rearrangements and Related Enolate Allylation Reactions

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The Claisen rearrangement, a [3,3] sigmatropic rearrangement, remains an important method for the construction of C-C bonds nearly a century after its discovery. However, methods to affect a catalytic and asymmetric variant of this reaction are rare. A transition metal/Lewis acid co-catalyst system (Ru(II)-B(III)) has been successfully employed to affect an enantioselective, and diastereoselective Claisen rearrangement of simple, achiral, allyl vinyl ethers without the need for auxiliary functionality to assist in substrate-catalyst association. In addition, we have developed a complementary ruthenium catalyzed enolate allylic alkylation reaction that forms Claisen-like products, without the need to synthesize allyl vinyl ethers.

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LIST OF ABBREVIATIONS

COE……...Cyclooctene

Cp……...Cyclopentadienyl

Cp*……..…….. Pentamethylcyclopentadienyl

Cy……Cyclohexyl

DCE……1,2-Dichloroethane

DMAP……..4-Dimethylaminopyridine

DMF……...*N*,*N*-Dimethylformamide

dr……..…..Diastereomer ratio

ee……...Enantiomeric excess

EI……Electron Ionization

equiv……....…….Equivalent

GC……Gas chromatography

HATU……(Dimethylamino)

-*N*,*N*-dimethyl(3*H*-[1,2,3]triazolo[4,5-*b*]pyridin-3-yloxy)methaniminium hexafluorophosphate

HFIP……. Hexafluoroisopropanol

HPLC……High-pressure liquid chromatography

HRMS……..High-resolution mass spectrum

LA……Lewis acid

LDA……Lithium diisopropylamide

MS……...Molecular sieves

NaHMDS……...Sodium hexamethylsilazide

NBS……*N*-Bromosuccinimide

RT……Ambient temperature

THF……..Tetrahydrofuran

TLC……Thin-layer chromatography

TMS……Trimethylsilyl

TMSCl……...Trimethylsilyl chloride

Tf……...……..……Trifluoromethanesulfoyl

PREFACE

I would like to thank my advisor Professor Scott Nelson, for giving me the opportunity to work under his direction. I have enjoyed the time spent in your lab, and you have enabled me to become an independent researcher and a better chemist.

Next, I would like to thank the Nelson group members and the rest of my Chevron friends for all of your help and guidance during my graduate school career. You have provided a fun and supportive environment that made it bearable to come to lab every day. I would specifically like to thank Dr. Robert Dura for working with me on the Claisen project, and Mike Nardone for your collaboration on the enolate allylation project. You have provided me with insightful discussions as well as greatly appreciated laughs.

Finally, I would like to thank my family for supporting me during my time in graduate school. You have believed in me during this entire journey, and have never let me give up on my dreams and aspirations. For that reason, I dedicate this document to you.

1.0 INTRODUCTION TO CATALYZED CLAISEN REARRANGEMENTS

1.1 THE CLAISEN REARRANGEMENT

The Claisen rearrangement, the [3,3] sigmatropic rearrangement of an allyl vinyl ether **1** to a δ, γ- unsaturated aldehyde **3** was discovered in 1912 by Ludwig Claisen.[1] Since then, this rearrangement has become a popular method for carbon-carbon bond formation in organic synthesis.[2] Its utility stems from the fact that the rearrangement proceeds through a highly ordered chair-type transition state **2** providing both a reliable and predictable method for establishing vicinal stereocenters (Figure 1). The popularity of this stereoselective process has resulted in the development of a number of related transformations that include the Carroll (1940),[3] Eschenmoser (1964),[4] Johnson (1970),[5] Ireland (1972),[6] and Reformansky (1973) variants of the Claisen rearrangement.[7]

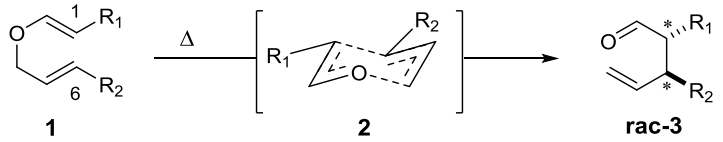


Figure 1. General Claisen Rearrangement

The development of a catalytic asymmetric Claisen rearrangement remains a challenging undertaking. Efforts have been made to accomplish this formidable task by utilizing Lewis

acids and transition metals as two distinct modes of catalysis (Figure 2). Unfortunately, due to the structure of the allyl vinyl ether and its carbonyl containing product, little success has been made. Catalysis by Lewis acids generally requires stoichiometric amounts of reagents due to the greater Lewis basicity of the carbonyl containing product versus the starting allyl vinyl ether.[8,9] In addition, catalysis by transition metals is met with its own problems, specifically the fact that late transition metals generally prefer to bind to the more electron rich vinyl olefin, resulting in strict substrate requirements.[10] As a result of this complication, few catalytic asymmetric variants of the Claisen rearrangement exist today, and they will be discussed herein.

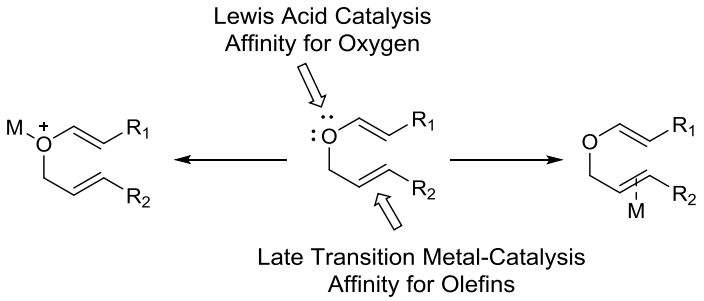


Figure 2. Modes of Catalysis for the Claisen Rearrangement

1.2 MODES OF CATALYSIS FOR THE CLAISEN REARRANGMENT

1.2.1 Lewis Acid Catalysis

1.2.1.1 Origins of Lewis Acid Catalysis

The Claisen rearrangement of simple, aliphatic allyl vinyl ethers is a thermal process that generally requires temperatures of around 200 °C. As a consequence of this thermal restriction, a number of attempts have been made to accelerate these reactions. The earliest endeavors utilize

Lewis acids to coordinate to the oxygen atom of the allyl vinyl ether (Figure 3).[8,9,11, 12] The binding helps to weaken the breaking C-O bond and stabilize the developing negative charge on the oxygen atom of the enolate-like moiety, thus aiding to accelerate the reaction.[13]

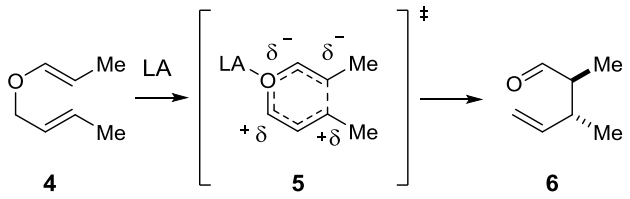
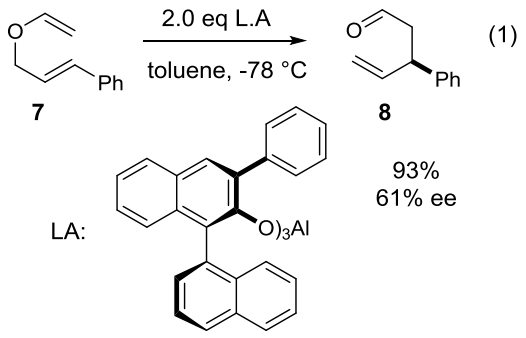


Figure 3. Lewis Acid Catalysis

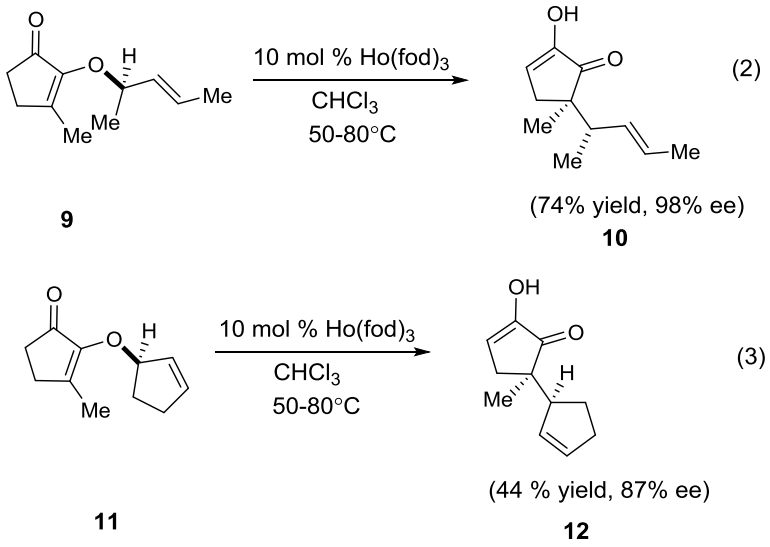
The earliest examples of Lewis acid-catalyzed Claisen rearrangements utilized BF_3,[11] BCl_3[14] and alumina.[15] Although enhancements to the rate of the reaction were observed, yields were poor and a large amount of side reactions were produced. This is thought to be the result of complete ionization of the allyl vinyl ether. The first synthetically useful variant was developed by Yamamoto utilizing a chiral Al(III) complex (eq 1).[8] Unfortunately, multiple equivalents of the Lewis acid were necessary to promote the Claisen reaction due to the increased Lewis basicity of the carbonyl containing product over the allyl vinyl ether. Although the reaction was not catalytic, it demonstrated that Lewis acids in combination with chiral ligands were suitable candidates to enhance the rate of the reaction. This provided a basis for further development of catalytic asymmetric reactions.



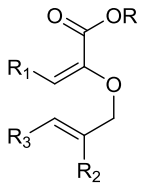
1.2.1.2 Examples of Lewis Acid Catalyzed Claisen Rearrangements

Trost was the first to report a catalytic Claisen rearrangement.[16] He was able to demonstrate that lanthanide(III) cations in combination with 7,7-dimethyl-1,1,1,2,2,3,3-heptafluoro-4,6-octanedionate (FOD) ligands were suitable catalysts for the Claisen rearrangement of cyclic aliphatic allyl vinyl ethers. The correct choice of lanthanide metal proved to be critical to ensure a concerted process.

The Lewis acidity of many of the lanthanide(III) complexes proved to be problematic as they caused the rearrangement to proceed with dissociation and racemization of the starting allyl vinyl ethers. Ultimately, it was determined that (FOD) complexes of Eu and Ho provided the best results overall, with $Ho(FOD)_3$ proving to be the most effective catalyst. Under the optimized conditions, the rearrangement proceeded with up to 98% chirality transfer and yielded a single diastereomer. Trost demonstrated that this catalyst system operated for a variety of allyl vinyl ethers, including acyclic and cyclic substrates, albeit with varying yields and chirality transfers (eq 2 and 3).[16]



Following Trosts discovery that Lewis acids were viable catalysts for mediating Claisen rearrangements, Hiersmann looked to expand this work and develop an improved catalytic, enantioselective Claisen rearrangement utilizing a chiral Lewis acid catalyst.[12,17,18] In doing so, he decided to use 2-alkoxycarbonyl-substituted allyl vinyl ethers such as **13** (Figure 4), due to their ease of synthesis, stability, and inherent reactivity.

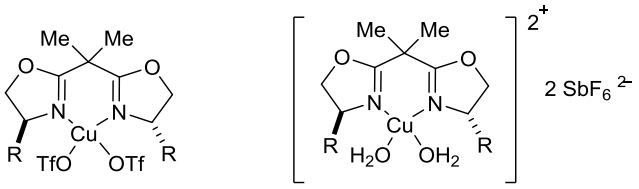


13

Figure 4. 2-Alkoxycarbonyl Substituted Allyl Vinyl Ethers

After performing a Lewis acid screen, he discovered that a variety of metal triflates including Cu(II), Lanthanide(III), and Sc(III), were effective catalysts for mediating the Claisen rearrangement.[12] He determined that $Cu(OTf)_2$ in combination with molecular sieves provided

optimal reactivity, a 99% yield of the Claisen product, and good diastereoselectivity (93:7 *syn*:*anti*). Encouraged by the results, he wanted to further extend his work to produce an enantioselective rearrangement. The observation that $Cu(OTf)_2$ was an efficient catalyst directed his search for a chiral catalyst towards the well known chiral Cu(II) bisoxazoline complexes **14** and **15** (Figure 5).[17, 18]



14 **14a** R= Ph **14b** R= *t*-Bu **15** **15a** R= Ph **15b** R= *t*-Bu

Figure 5. Copper Bisoxazoline Complexes **14** and **15**

Hiersmann utilized copper complexes of the type **14a** in which the bisoxazoline ligand contained a phenyl group or a *t*-butyl group. He demonstrated that these Lewis acids facilitated the rearrangement via bidentate chelation to the substrate **17** (Figure 6), causing an inductive effect that would effectively polarize the transition state. This allowed the reaction to proceed through a lower activation energy than the thermal rearrangement to afford the Claisen product **18**.[18]

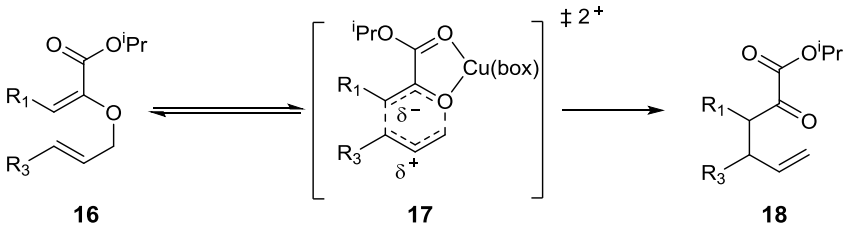


Figure 6. Lewis Acid Mediated Claisen Rearrangement

The use of the Cu(II)bisoxazoline complex **15b** was able to mediate an enantioselective (72-91% ee) and highly diastereoselective rearrangement. Interestingly, the diastereoselectivities were shown to be highly dependent on the configuration of the allyl bond of the starting allyl vinyl ethers. The *Z* configuration provided products with high diastereoselectivities (3:97, *syn*:*anti*) and enantioselectivities of up to 91%. The *E* configuration provided enantioselectivities of up to 72%, but inferior diastereoselectivities (28:72, *syn*:*anti*).[17]

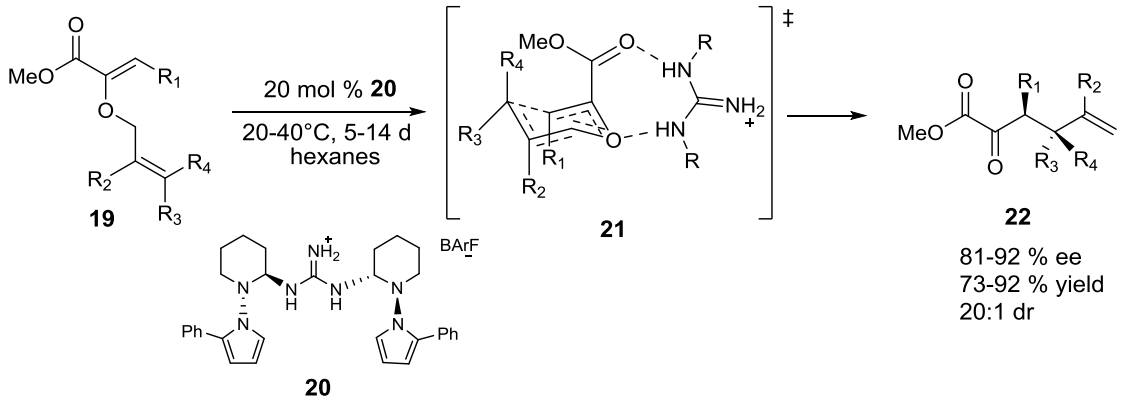
Although both excellent diastereoselectivities and enantioselectivities were observed in the reaction with these copper(II) catalysts, there were severe substrate restrictions. The alkoxycarbonyl moiety at the 2-position of the vinyl ether was absolutely necessary mechanistically for bidentate activation by the copper(II) bisoxazoline Lewis acid. Also, the diastereoselectivity of the reaction was dependent on the allyl ether geometry with the *Z* isomer providing superior results. The limited utility of this methodology showcased the need for catalysts that worked for a wider range of substrates.

1.2.1.3 Hydrogen Bonding Catalysis

Most recently, Jacobsen has developed a catalytic and enantioselective Claisen rearrangement (Scheme 1).[19,20] Rather than using Lewis acid catalysis like Hiersmann, he utilized hydrogen bond donor catalysts to affect the Claisen rearrangement.

Simple unactivated allyl vinyl ethers were the desired target substrate for Jacobsen. However, utilizing chiral guanidinium ion catalysts as bidentate hydrogen bond donors failed to provide sufficient product formation. As a result, the substrate was modified to include an alkoxycarbonyl moiety to aid in substrate activation. With this added modification, Jacobsen was able to affect a catalytic, asymmetric Claisen rearrangement with yields of up to 92% (Scheme 1). More specifically catalyst **20** was able to afford Claisen products of substrates containing methyl and ethyl groups at the R_1 position with high enantioselectivities (up to 92%). In addition, disubstituted ethers provided products of type **22** in high enantioselectivity and diastereoselectivity. This demonstrated that the reaction proceeded though a six-membered chair like transition state **21** that was stabilized from hydrogen bond interactions between the catalyst and both the ether and carbonyl oxygen of the substrate. This showcased the ability of chiral hydrogen bond donors to act as catalysts affecting the Claisen rearrangement, but added functionality on the substrate was still required to aid in the reactions success.

Scheme 1. Hydrogen Bond-Donor Catalysis of the Claisen Rearrangement



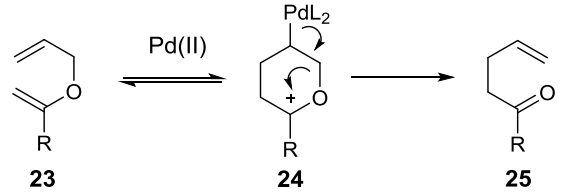
1.2.2 Transition Metal Catalysis of Claisen Rearrangements

1.2.2.1 Mechanism of Catalysis

In sharp contrast to Lewis acid-catalyzed Claisen rearrangements is transition metal-catalysis. The late transition metals are better able to coordinate to the soft C-C multiple bonds of the allyl vinyl ether than the lone pairs of the oxygen atom. This interaction activates the C-C bond towards nucleophilic attack.[21] Capitalizing on this metal-olefin interaction, catalytic Claisen rearrangements have been developed that utilize transition metals such as Pd,[10,21] Hg,[22] and Pt,[23] with Pd(II) catalysis being the most prevalent.

Catalysis by Pd(II) exclusively provides the formal [3,3] Claisen product, suggesting that the mechanism resembles the thermal concerted rearrangement. In order to rationalize this selectivity, it has been proposed that that the reaction proceeds through a "cyclization-induced" rearrangement mechanism in which the Pd(II) coordinates to the allyl olefin of the allyl vinyl ether activating it towards attack by the nucleophilic vinyl olefin (Scheme 2).[10,24] This promotes the formation of a 6-membered cyclic carbonium ion intermediate **24** which rapidly rearranges to the product **25** and regenerates the catalyst.

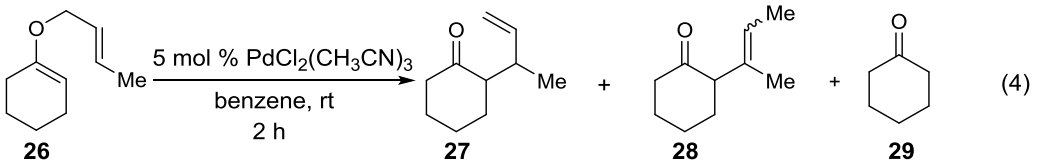
Scheme 2. Cyclization-induced Rearrangement



There is an inherent problem that is associated with transition metal catalysis. The electrophilic metal catalyst can irreversibly bind to the strongly nucleophilic vinyl ether moiety instead if the allylic double bond.[25] As a result, catalysis is often inhibited unless the vinyl ether moiety is blocked.

1.2.2.2 Examples of Transition Metal Catalyzed Claisen Reactions

Van der Baan and Bickelhaupt developed the first known example of a catalytic Claisen rearrangement utilizing a Pd(II) complex.[10] Taking advantage of the "cyclization induced" rearrangement, they subjected a variety of allyl 1-cyclohexenyl ethers such as compound **26**, to $PdCl_2(CH_3CN)_3$ (eq 4). The reaction did produce the desired Claisen product albeit with a few minor side products **28** from double bond isomerization. They were also able to demonstrate that the rearrangement worked efficiently with a variety of other cyclic ethers, except those with trisubstituted allylic ether double bonds. They reasoned that this was most likely attributed to sterics, and prevented the Pd(II) catalyst from binding to the allylic double bond in these congested systems.[10]

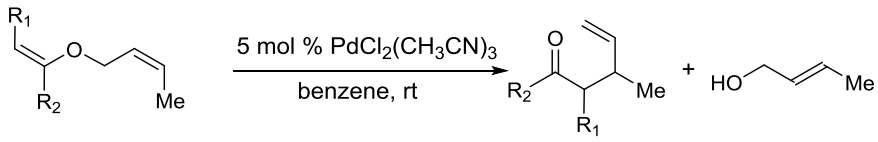


26 **27** **28** **29**

Next, Van der Baan and Bickelhaupt attempted to expand their substrate scope to include acyclic allyl vinyl ethers **30** (Table 1). Unfortunately, these systems were not as compliant as their cyclic counterparts. The allyl vinyl ethers with a highly substituted vinyl group worked well in the rearrangement, providing products with yields greater than 90% on average (Table 1, entry

c). However, when ethers void of substituent's on the vinyl groups were utilized, the reactions yielded large quantities of the corresponding allylic alcohol **32**, with only traces of the desired Claisen product (Table 1, entries a and b). They reasoned that the Pd(II) catalyst preferred to associate with the more electron rich vinyl ether π-system when it was not shielded by alkyl groups, preventing the formation of the desired Claisen product **31**.[10] Although Van der Baan and Bickelhaupt discovered the first catalytic Claisen rearrangement, they realized it would have limited synthetic utility since it was restricted to compounds containing substituted vinyl groups.

Table 1. Van der Baan and Bickelhaupt Substrate Scope Exploration



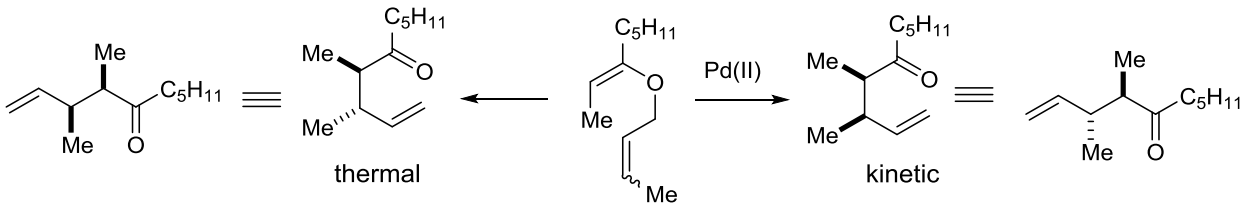
30 **31** **32**

entry	R	Yield
a.	R_1=R_2=H	>2%
b.	R_1=Me; R_2=H	18%
c.	R_1=Me; R_2=Et;	93%

Nakai and co-workers were the next group to investigate the Pd(II) catalyzed Claisen rearrangement.[26-28] They were ultimately responsible for elucidating and defining the stereochemical outcome of Van der Baan and Bickelhaupt's work. They observed that the allyl vinyl ether **33**, in the absence of a palladium catalyst would form the thermal product **35** (Scheme 3). However, in the presence of the palladium catalyst the kinetic product **34** was formed. It was suggested that the kinetic selectivity was due to a Pd(II) bound boat like

transition state whereas the thermal selectivity of the product was due to a chair-like transition state.

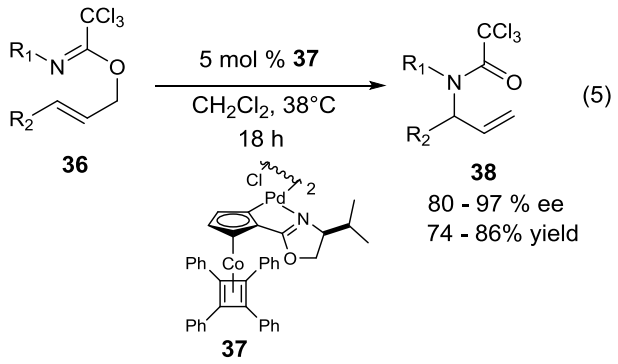
Scheme 3. Stereochemical Outcome of Thermal vs. Pd(II) Catalyzed Rearrangements



Although Nakai and co-workers were able to determine the stereochemical outcome of the palladium catalyzed Claisen rearrangements, they were unable to solve the problem of substrate scope. Ultimately, the strict requirements that Van der Baan and Bickehaupt discovered still prevented this transformation from taking place in a truly catalytic asymmetric manner.

In 1997, Overman discovered the first catalytic asymmetric Pd(II)- catalyzed rearrangement that proceeded without rigid substrate requirements.[29] He discovered that achiral allylic imidates could be converted to enantioenriched allylic amides via a Pd(II)- catalyzed Claisen-like rearrangement. Utilizing palladium(II) complex **37** with allylic imidates of type **36**, provided the allylic amides **38** in high yields (93-99%) and enantioselectivities (93-99%) (eq 5).[30] In addition, he also demonstrated that substitution of the allyl bond (R_2) was tolerated for unbranched substituent's. However, when *t*-butyl or cyclohexyl groups were used the reaction proceeded at a much slower rate. Additionally, it was discovered that (*E*)-allylic trichloroacetimidates were the only viable starting materials as the (*Z*) isomer failed to react in high yields and enantioselectivities. Although the rearrangement of the acetimidates provided

rearrangement products with high enantioselectivities, and good substrate scope, the methodology could not be translated to allyl vinyl ethers.



1.3 LIMITATIONS OF PREVIOUS CATALYTIC CLAISEN REARRANGEMENTS

Lewis acid, hydrogen bond donor and transition metal catalysis has provided an excellent starting point towards the discovery of truly catalytic Claisen rearrangements. They have provided a great deal of insight into the multitude of mechanistic pathways in which these catalyzed reactions are able to operate, however they each have their own respective limitations.

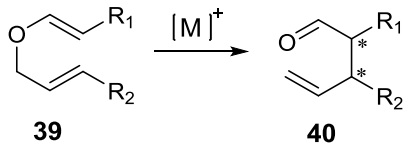
Lewis acids and hydrogen bond donors have been shown to be efficient catalysts for facilitating the Claisen rearrangement, and provide almost complete chirality transfer. Unfortunately, the substrate scopes for these copper(II) bisoxazoline and hydrogen bond donor catalyzed reactions are not that large due to the fact that the alkoxylcarbonyl moiety is necessary for the reaction to take place. In addition, the Pd(II) catalyzed rearrangements provided reactions that are highly diastereoselective, but their substrate scope for allyl vinyl ethers is poor. These reactions are only enantioselective for acetimidates and attempts at enantioselective

transformations of simple allyl vinyl ethers have been met with little success. In order for a more synthetically useful catalytic asymmetric Claisen rearrangement, there is a need for reaction conditions that utilize simple allyl vinyl ethers and provide highly enantioselective, and diastereoselective products.

2.0 DEVELOPMENT OF A CATALYTIC ASYMMETRIC CLAISEN REARRANGEMENT OF STRUCTURALLY SIMPLE, UNACTIVATED ALLYL VINYL ETHERS

2.1 TRANSITION METAL ACTIVATION OF ALLYL VINYL ETHERS

Catalytic asymmetric Claisen rearrangements have been plagued by strict substrate requirements necessary for substrate-catalyst association. As a result, we sought to develop a catalytic asymmetric Claisen rearrangement on structurally simple, unactivated allyl vinyl ethers of type **39**. We envisioned that this could be accomplished utilizing the strategy of olefin activation with late transition metals to produce structurally complex aldehyde products of type **40**, with control of both relative and absolute stereochemistry (eq 6).

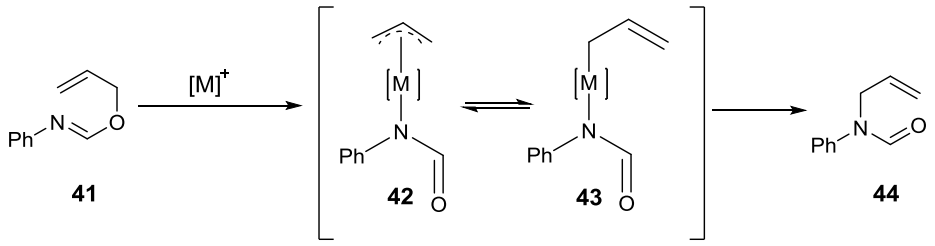


(6)

Transition metal-catalyzed Claisen rearrangements have generally been restricted to rearrangements of allyl imidates rather than simple allyl vinyl ethers.[10,21,29,30] In addition, focus has been placed on rearrangements involving "cyclization induced" mechanisms. However, a report by Bosnich, on the rearrangement of allylic imidates, demonstrated that an alternate

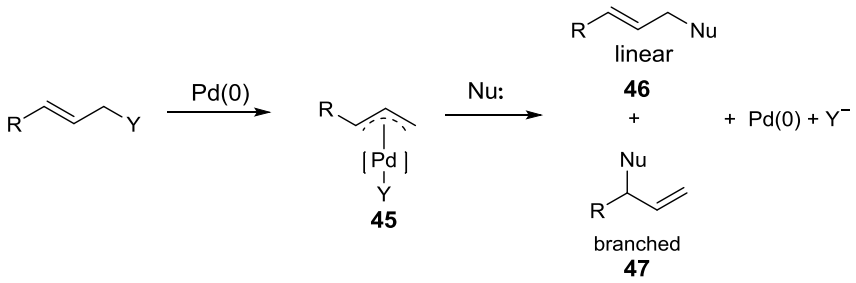
mechanism could be utilized to affect the Claisen rearrangement (Scheme 4).[31] In his report, transition metals such as Ir(I) and Rh(I) were able to oxidatively add to the allylic imidate **41** forming a π-allyl metal complex and amide anion **42**. Upon nucleophilic addition to the π-allyl metal complex, the product **44** of a formal [3,3] rearrangement was formed.

Scheme 4. Late Transition Metal-Mediated Rearrangement of Allyl Imidates



Transition metal π-allyl chemistry is typically seen in allylic alkylation reactions with the most popular being the Tsuji-Trost allylation (Scheme 5).[32] The reaction uses Pd(0) complexes to form the key intermediate metal π–allyl systems of type **45**. However, palladium is not the only metal known to produce these π–allyl systems. Other metals that participate in this type of reaction include iridium,[33] ruthenium,[34] molybdenum,[35] tungsten,[36] and rhodium.[37] Depending on the metal employed, the regiochemical bias of the reaction can be influenced. Generally, Pd(0) complexes prefer to form linear addition products **46**,[32] whereas complexes of Ir(I) and Ru(II) provide a preference for the branched substitution products **47**.[33,34]

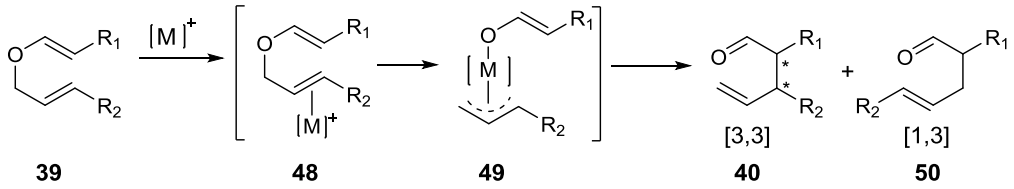
Scheme 5. Tsuji-Trost Allylation



2.2 REACTION DESIGN

Bosnich's research suggested that the archetypical Claisen rearrangement could be catalyzed by transition metals utilizing a π-allyl mechanism (Scheme 6). The late transition metal could oxidatively add across the C-O σ-bond of the allyl vinyl ether **39** with concomitant formation of a metal-bound enolate and allyl cation complex **49**. The metal bound enolate could function as a nucleophile and add to the π-allyl system forming the desired Claisen product **40**.

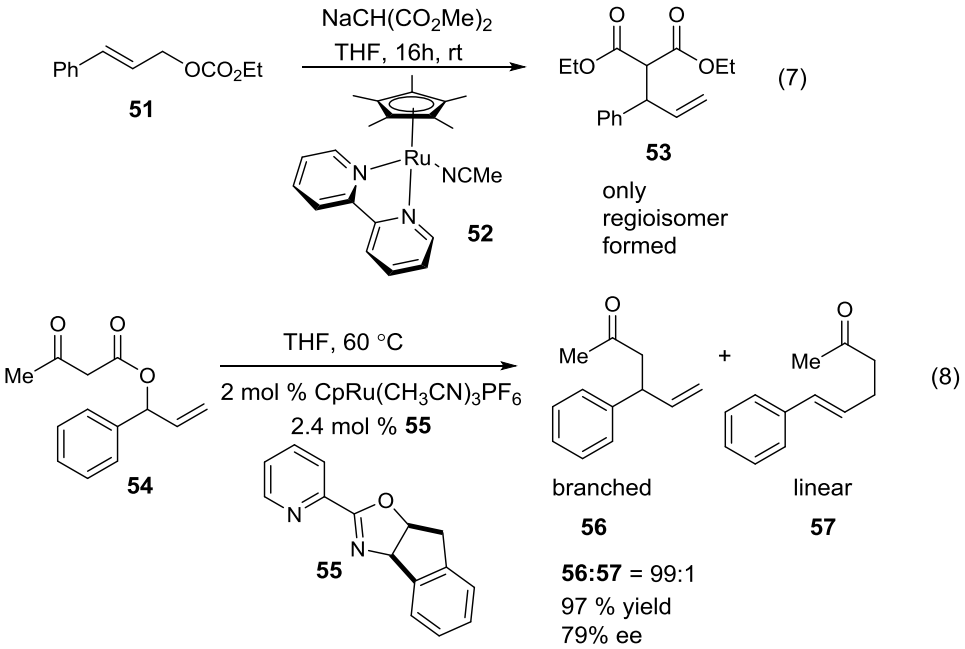
Scheme 6. Desired Late Transition Metal-Catalyzed Asymmetric Claisen Rearrangement



The archetypal Claisen rearrangement proceeds exclusively through a concerted process providing the [3,3] product where as our proposed rearrangement would proceed via an asynchronous mechanism. This could be problematic due to the formation of an asymmetric

metal π-allyl complex **49**, allowing the formation of both the formal [3,3] and [1,3] products **40** and **50**. As a result, our catalyst design needed to be focused on transition metals that were able to labilize allylic C-O σ-bonds and enforce nucleophilic attack at the branched position of the metal-allyl complex.

Complexes of Ir(I) and Ru(II) have been utilized to enforce the formation of the branched substitution products in allylic alkylation reactions.[33,34] More specifically, [Cp*Ru(2,2'-bipyridine)]$^+$ **52** and [CpRu(2,2'-bipyridine)]$^+$ complexes have been shown to exhibit a strong regiochemical bias for producing the desired branched products (eq 7).[34a,38,39] In addition, reactions utilizing these Ru(II) complexes have proven to be enantioselective when using chiral (*N*,*N*)-bidentate ligands of type **55** (eq 8).[39c,d] As a consequence, Ru(II)- complexes were chosen as a starting point for catalyst design.



2.3 PRELIMINARY REACTION DEVELOPMENT

Reaction development commenced with the use of simple allyl vinyl ether **39a**, as a standard test substrate. Utilizing **39a** with 5-10 mol % of CpRu(II) complex **58,** obtained by addition of $[CpRu(CH_3CN)_3]PF_6$ to pyridine oxazoline ligand **55**, in THF at room temperature, provided unreacted starting materials (Figure 7A). This was not surprising as transition metal-based catalysts are expected to have a greater preference to associate with more electron rich olefins.[25,40] In the case of allyl vinyl ethers, the metal would prefer to associate with the vinyl olefin **59** (Figure 7B). As a result of this preference, there exists an unproductive equilibrium as indicated by **48** to **59**, preventing labilization of the C-O σ-bond necessary for the rearrangement to take place.

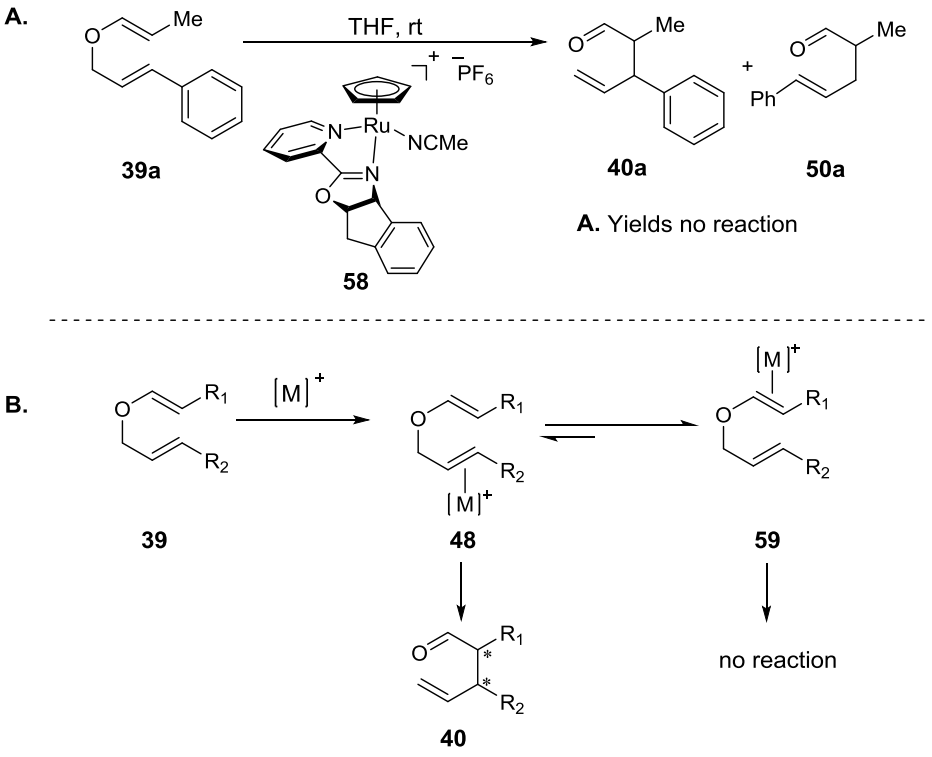
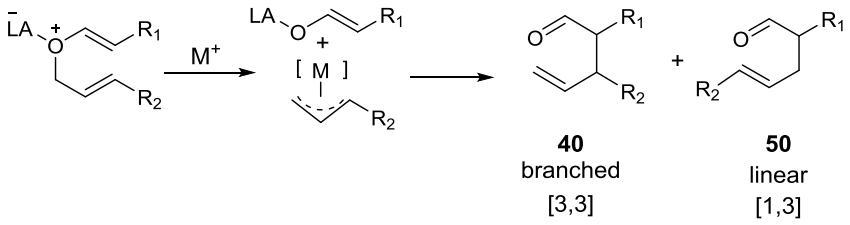


Figure 7. A. Initial Experiment **B.** Possible Limitations of Simple Allyl Vinyl Ethers

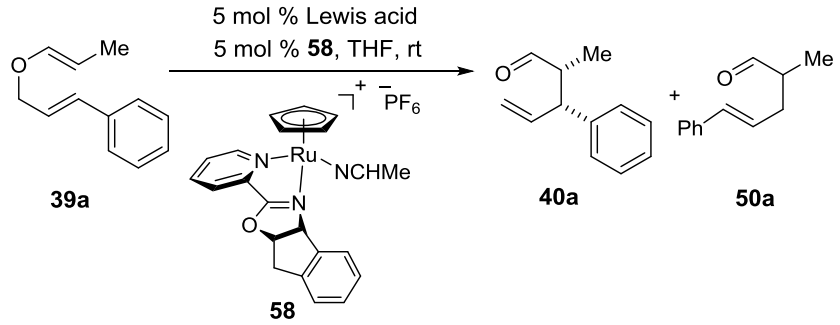
At this juncture, an additional strategy for activating the substrate seemed necessary. The potential of a co-catalyst to assist in allyl vinyl ether activation appeared to be an easily implemented solution to reaction design. In addition, Lewis acids have been shown to assist in the labilization of C-O σ-bonds of allyl vinyl ethers though Lewis acid-base association with the ether oxygen.[8-18] As a result, we wanted to determine if a weak Lewis acid could be used as a co-catalyst in our system, weakening the C-O σ-bond and increasing the potential for oxidative insertion of the ruthenium complex (Scheme **7**). However, the choice of Lewis acid would be critical as we would need to ensure that it did not catalyze the Claisen rearrangement independent of the enantioenriched CpRu(II) complex or degrade the catalyst in anyway.

Scheme 7. General Lewis Acid Activation of Allyl Vinyl Ethers



As a standard test reaction, we used allyl vinyl ether **39a**, 5 mol % CpRu(II) **58**, and a myriad of Lewis acids that are known to be compatible with transition metals (Table 2). Weak Lewis acids that included $ZnCl_2$, CuCl, $NiCl_2$, and Ti(*i*-OPr)$_4$ provided no reaction. Conversely, stronger Lewis acids that included $Cu(OTf)_2$, $Sn(OTf)_2$, $AgPF_6$, and $Al(OTf)_3$ completely converted the starting material **39a** into an inseparable mixture of both Claisen products **40a** and **50a**, and many other unidentified side products. The moderately Lewis acidic $B(OMe)_3$, afforded about 5% of the desired Claisen product **40a**.

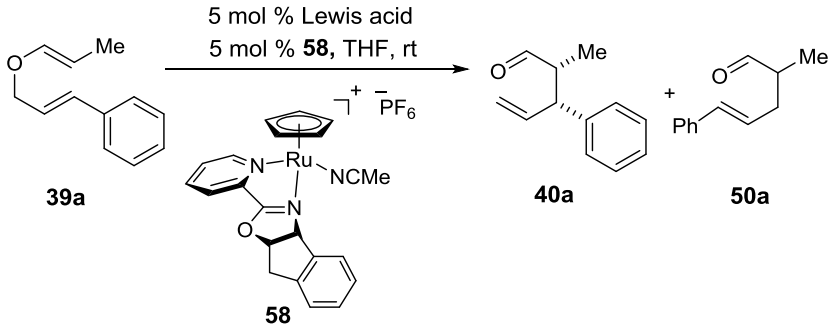
Table 2. Lewis Acid Activation of Allyl Vinyl Ether **39a**



Entry	Lewis acids	Observation
a	$ZnCl_2$, CuCl, $NiCl_2$, and Ti(*i*-OPr)$_4$	No reaction
b	$Cu(OTf)_2$, $Sn(OTf)_2$, $AgPF_6$, and $Al(OTf)_3$	Inseparable mix of **40a** and **40b** and unidentified side products
c	$B(OMe)_3$	5 % **40a**

With $B(OMe)_3$ providing the first positive result, we reasoned that by fine tuning the Lewis acidity of the borate through the alteration of its ligands, we could increase the efficiency of the reaction. The use of more electron withdrawing ligands would increase the borates Lewis acidity and therefore possibly aid in the labilization of the C-O σ-bond. Utilizing 5 mol % of $B(OCH_2CF_3)_3$ afforded a modest increase in reaction conversion of the test reaction to about 10% (Table 3). Employing 5 mol % of $B(OPh)_3$ led to a more dramatic increase in reaction conversion to 63%, with enantioselectivity of the formal [3,3] product approaching synthetically useful levels (81% ee). Although regioselectivity (**40a**:**50a**= 5:1) and diastereoselectivity (**40a**$_{anti}$:**40a**$_{syn}$= 2:1) remained poor, the borate proved to be an effective co-catalyst providing useful levels of conversion to the formal [3,3] product while exhibiting no tendency to mediate the background rearrangement independent of the Ru(II) catalyst.

Table 3. Effect of Boron Lewis Acids on Reaction Conversion



Lewis acid	conversion(%)[a]	**40a**:**50a**	*anti:syn*(**40a**)[a]	ee **40a** (%)[b]
$B(OMe)_3$	5	N.D[c]	-	-
$B(OCH_2CF_3)_3$	10	N.D[c]	-	-
$B(OPh)_3$	63	5:1	2:1	81

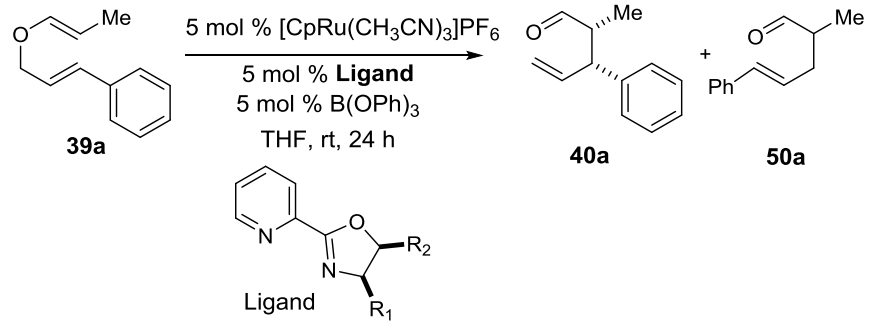
[a]Determined by ^{1}H NMR of the crude product mixture. [b] Determined by Chiral GC.
[c]N.D. = not determined.

2.4 LIGAND SCREEN FOR REACTION OPTIMIZATON

Having found an appropriate co-catalyst for our system, attempts were made to optimize the regio-, diastereo-, and enantioselectivity of the reaction. Capitalizing on the observation that pyridine oxazoline ligands were proficient in Ru-catalyzed reactions,[39c,d] we wanted to determine how modifying the sterics and electronics of the ligand affected the reaction. The steric environment of pyridine oxazoline backbone was first modification made to determine the effect of ligand structure on reaction selectivity (Table 4). Utilizing allyl vinyl ether **39a**, 5 mol % $B(OPh)_3$, and 5 mol % CpRu(II) with pyridine oxazoline ligands **60b-d**, in THF for 24 h provided negligible improvements in reaction selectivity in comparison to the original indanyl ligand **55**. The phenyl substituted ligand **60b** provided an improvement in reaction conversion to

78%, but regioselectivity (**40a:50a**= 4.5:1) and diastereoselectivity (**40a**$_{anti}$:**40a**$_{syn}$= 2:1) remained unchanged from the indanyl ligand, and enantioselectivity decreased dramatically to 53%. The benzyl substituted ligand **60c** provided a small increase in regioselectivity up to about 7:1 (**40a**:**50a**), however the diastereoselectivity (**40a**$_{anti}$:**40a**$_{syn}$ = 1.6:1) and enantioselectivity (71%) proved to be inferior. In addition, isopropyl ligand **60c**, offered no improvements in selectivity compared to indanyl ligand **55** and the sterically hindered tert-butyl ligand **60d** failed to provide any reaction.

Table 4. Pyridine Oxazoline Ligand Screen for Reaction Optimization



Entry	Ligand R_1	R_2	conversion(%)[a]	**40a:50a**[a]	*anti:syn*(**40a**)[a]	ee (**40a**) (%)[b]
a	indanyl (**55**)		63	5:1	2:1	81
b	phenyl (**60b**)	H	78	4.5:1	2:1	53
c	benzyl (**60c**)	H	40	7:1	1.7:1	72
d	isopropyl (**60d**)	H	62	5:1	1.6:1	71
e	tert-butyl (**60e**)	H	0	-	-	-

[a] Determined by ^{1}H NMR of the crude product mixture. [b] Determined by Chiral GC.

With the indanyl substituted pyridine oxazoline ligand **55** providing the best results in terms of diastereo- and enantioselectivity (**40a**:**50a**= 5:1, **40a**$_{anti}$:**40a**$_{syn}$= 2:1, 81% ee), we sought to change the electronics of the ligand to improve the reaction regioselectivity. Electron

donation to the metal center is known to increase the activity of the incipient metal complex towards oxidative insertion into adjacent C-O σ-bonds, in systems similar to ours.[38a,39b] Also, it has been shown that increasing the electron density of the metal complex will also help improve regioselectivity in allylic alkylation type reactions due to the asymmetric bonding of the Ru catalyst to the π–allyl system (Figure 8).[41,42]

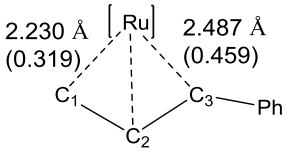
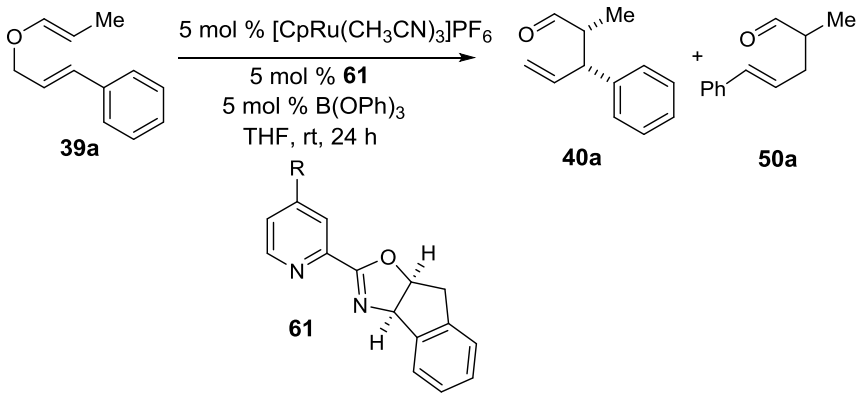


Figure 8. Asymmetric Binding of Ru π-allyl complex

With this knowledge, we decided to synthesize a set of pyridine oxazoline ligands **61a-c** with electron donating groups on the 4-position of the pyridine moiety (Table 5). Utilizing ligand **61a,** containing a methyl group on pyridine, under the standard reaction conditions (5 mol % $B(OPh)_3$, 5 mol % CpRu(II), THF, 24 h) provided a modest increase in regioselectivity to 6.5:1 (**40a**:**50a**), favoring the branched product **40a**. Further increasing the electron density of the ligand by adding a methoxy group to the pyridine ring, ligand **61b**, afforded an even greater preference for the formation of the branched product (**40a**:**50a**= 9:1). In addition, utilization of the highly electron donating dimethylamino group in **61c** provided the best regioselectivity of 12:1 (**40a**:**50a**). These observations demonstrated that modulating the electronics of the ligand provided a viable strategy for influencing regioselectivity.

Table 5. Electronic Effects of Ligands **61a, b,** and **c** on Product Regioselectivity



entry	R	conversion(%)[a]	**40a**:**50a**	*anti:syn*(**40a**)[a]
a	Me (**61a**)	12.9	6.5:1	2.25:1
b	OMe (**61b**)	29	9:1	2:1
c	NMe_2 (**61c**)	44	12:1	1.6:1

[a] Determined by ^{1}H NMR of the crude product mixture.

At this point, changing the electronics and the sterics of the pyridine oxazoline ligand provided no vast improvement in the reaction besides an increase in regioselectivity. It was apparent that we needed to reevaluate ligand design in order to further optimize the reaction selectivity. As a result, the mechanism of the reaction needed to be examined. It was necessary to determine if the reaction was proceeding though an intermolecular mechanism in which the substrate became fragmented into separate nucleophilic and electrophilic species **62** or through an intramolecular mechanism **63** (Figure 9A). For this purpose a double crossover experiment was developed using equimolar amounts of compound **39b** and **39c** in the presence of 5 mol % CpRu(II) complex **58**, 5 mol % $B(OPh)_3$ and THF (Figure 9B). The experiment produced an equimolar amount of four different products **40a**, **40b**, **40b′**, and **40c**, suggesting an intermolecular mechanism. More specifically the reaction showcased that upon oxidative

insertion of the Ru(II) catalyst to the substrate, a Ru-bound π-allyl system was formed with the dissociation of the enolate fragment from the coordination sphere of the metal allowing enolate crossover between substrates **39b** and **39c**.[38c] We hypothesized that if the reaction could be forced to operate via an intramolecular mechanism **63** (Figure 9A) in which the enolate would not dissociate from the coordination sphere of the metal, a highly ordered transition state could be invoked and the Claisen products would be formed with better diastereoselectivity.

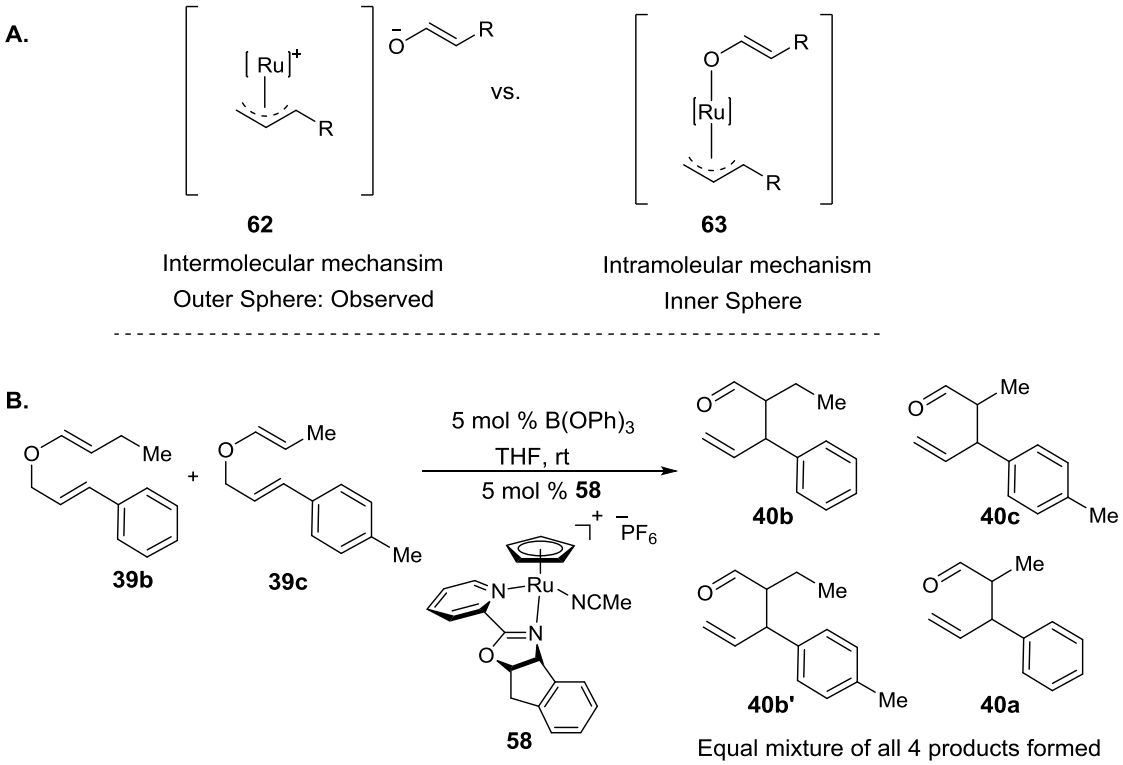


Figure 9. A. Inner vs. Outer-sphere Mechanism **B**. Crossover Experiment

Work reported by Kitamura and co-workers on the Ru(II)-catalyzed hydrolysis of allyl ethers provided valuable insight on the design of catalysts that would enforce an intramolecular mechanism.[43] Kitamura proposed that their reaction proceeded via hydrogen bonding interactions between quinaldic acid and the allyl ether (Figure 10A). We speculated that similar

hydrogen bonding interactions could possibly prevent dissociation of the enolate involved in our Claisen rearrangement, and provide a more ordered transition state that would invoke an intramolecular mechanism. Additionally, enantioenriched equivalents of quinaldic acid were conveniently available via hydrolysis of the pyridine oxazoline ligands, forming amides capable of hydrogen bonding (Figure 10B).

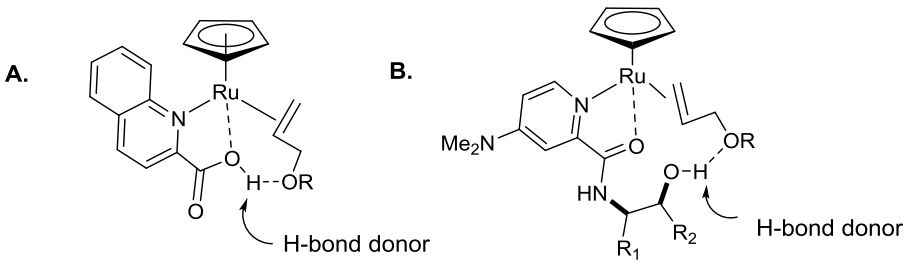
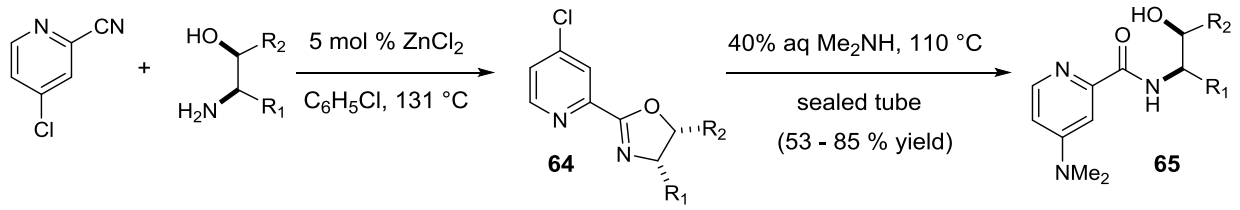


Figure 10. A. Ru(II)-Catalyzed Hydrolysis of Ethers; **B.** Picolinamide Ligands

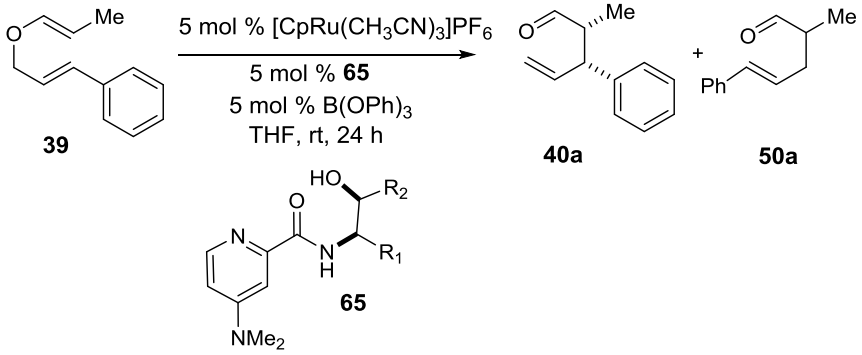
To this end, a variety of enantioenriched picolinamide amide ligands of the type **65** were synthesized with relative ease (Scheme 8). They were prepared by Lewis acid-catalyzed condensation of 4-chloropicolinitrile and various amino alcohols to generate the pyridyloxazolines of type **64**.[44] Heating **64** with aqueous dimethylamine effected nucleophilic aromatic substitution[45] and oxazoline hydrolysis to afford the desired picolinamide ligand **65** in moderate to good yields.

Scheme 8. General Synthesis of Picolinamide Ligands



Having secured an adequate synthesis of our desired ligands, we needed to determine whether they would facilitate an improvement in reaction selectivity via hydrogen bonding interactions with the allyl vinyl ether substrate. When subjected to the standard reaction conditions (5 mol % CpRu(II)-**65**, 5 mol % $B(OPh)_3$, THF), the diastereoselectivity of the reaction increased substantially from 2:1 to over 10:1 (**40a**$_{anti}$:**40a**$_{syn}$) depending on the R groups present on the ligand (Table 6). Ligands **65a-c** provided products with diastereoselectivities of up to 7:1(**40a**$_{anti}$:**40a**$_{syn}$) and enantioselectivities of up to76%. The indanyl substituted ligand **65d** provided the best results in terms of product selectivity that were near synthetically useful levels (**40a**:**50a**= 4:1, **40a**$_{anti}$:**40a**$_{syn}$= 10:1, 89% ee) albeit for substrate conversion at a modest 63%.

Table 6. Picolinamide Ligand Screen for Optimization of Reaction Diastereoselectivity



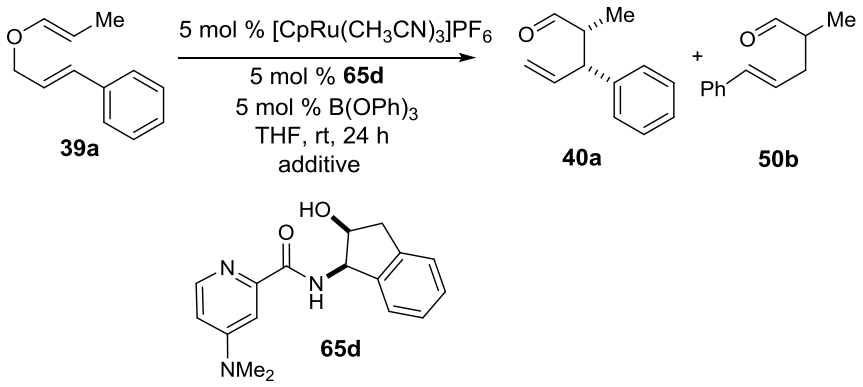
Entry	R_1	R_2	conversion(%)[a]	**40a**:**50a**	*anti:syn*(**40a**)[a]	ee **40a** (%)[b]
a	isopropyl (**65a**)	H	42	4.8:1	6.7:1	76
b	phenyl (**65b**)	H	39	3.2:1	5:1	55
c	benzyl (**65c**)	H	42	4:1	3:1	22
d	**indanyl (65d)**		**63**	**4:1**	**10:1**	**89**

[a] Determined by ^{1}H NMR of the crude product mixture. [b] Determined by Chiral GC.

2.5 REACTION OPTIMIZATION

Having secured adequate enantio- and diastereocontrol in the desired reaction with the use of the picolinamide ligand **65d**, optimization of reaction conversion to levels above 60% was crucial. Catalyst lifetime was thought to be contributing to incomplete substrate conversion. As a result, we sought to avoid catalyst degradation by eliminating the possibility of trace amounts of water with the use of molecular sieves. With the addition of a 1:1 weight/weight ratio of 4Å molecular sieves to substrate **39a** utilizing our standard reaction conditions (5 mol % CpRu(II)-**65d**, 5 mol % $B(OPh)_3$, THF), it was discovered that reaction conversion did increase dramatically to 93% over 24 hours (Table 7, entry a). Surprisingly, there was also an improvement in both diastereo- and regioselectivity (**40a**$_{anti}$:**40a**$_{syn}$= 16:1, **40a**:**50a=** 4.6:1 from **40a**$_{anti}$:**40a**$_{syn}$= 10:1, **40a**:**50a**= 4:1 without 4Å MS). It remains unclear if these improvements are the result of more rigorous water exclusion or are suggestive of a more complex role for the molecular sieves.[46]

Table 7. Evaluation of Additives on Reaction Conversion



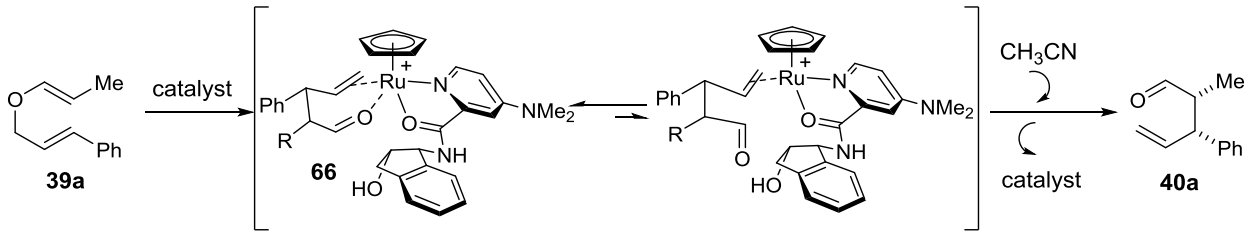
Entry	Additive	Observation
a	4Å MS	93% conversion
b	1 equiv **40a**	decreased conversion
c	20 mol % DMF/ 4Å MS	76% conversion
d	20 mol % acetone/4Å MS	82% conversion
e	**20 mol % MeCN/ 4Å MS**	**100 % conversion/ 20:1 dr**

Another possible source of incomplete reaction conversion can be attributed to product inhibition as the resulting aldehyde product **40a** is more Lewis basic than the allyl vinyl ether **39a**. To determine if this was a problem, we needed to introduce an excess of the Lewis basic aldehyde to our reaction to observe if reaction conversion decreased. Addition of a full equivalent of aldehyde **40a** to our standard reaction conditions (5 mol % CpRu(II)-**65d**, 5 mol % $B(OPh)_3$, 100 wt % 4Å MS, THF) provided a decrease in reaction conversion, however the reaction was not completely inhibited (Table 7, entry b). This showcased that we needed an additional mechanism to help expel the Lewis basic product from the coordination sphere of the metal allowing the active catalyst to be regenerated.

To accelerate catalyst turnover, we envisioned that added amounts of a polar, coordinating solvent could act as a labile ligand to aid in the expulsion of the product from the

coordination sphere of the metal by disrupting the Ru(II)-pentenal chelate **66** formed under the reaction conditions (Scheme 9). Addition of 20 mol % of polar solvents that included DMF, acetonitrile, and acetone under the standard reaction conditions (5 mol % CpRu(II)-**65d**, 5 mol % $B(OPh)_3$, 100 wt % 4Å MS, THF), provided an increase in reaction efficiency (Table 7, entry e). Acetonitrile proved to be the optimal additive, and provided complete conversion to the Claisen product after 24 hours along with small enhancements in enantio-, diastereo-, and regiochemistry (93% ee, $\mathbf{40a}_{anti}$:$\mathbf{40a}_{syn}$ = 20:1, **40a**:**50a**= 5.3:1).

Scheme 9. Product Inhibition and Role of Additives in Catalyst Turnover

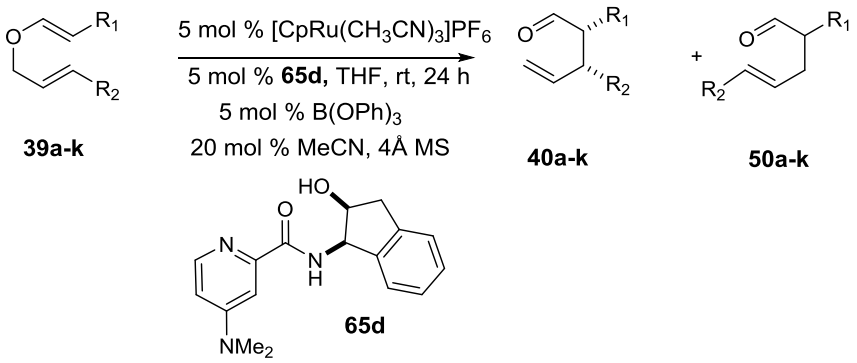


2.6 REACTION SCOPE

Through the use of additives, including 4Å MS and a substoichiometric amount of acetonitrile, we demonstrated that a catalytic, diastereoselective and enantioselective Claisen rearrangement was possible for simple vinyl ether **39a**. Expansion of substrate scope beyond the phenyl substituted allyl vinyl ether **39a** was critical for synthetic utility. To test the substrate scope, a diverse set of C_1-alkyl, C_6-aryl and heteroaryl allyl vinyl ethers were synthesized (Table 8). Under the fully optimized conditions (5 mol % CpRu(II)-**65d**, 5 mol % $B(OPh)_3$, 100 wt % 4Å MS, 20 mol % MeCN, THF), all allyl vinyl ethers afforded the rearranged Claisen products with

high enantioselectivity and *anti*-diastereoselectivity. The steric and electronic differences in the substrate did not affect enantioselectivity, and provided products with greater than 90% ee except for **40f** and **40k** (Table 8, entry f and k). In addition, diastereoselectivity did not seem to be affected by the steric and electronic differences of the C_6-aryl or heteroaryl groups on the substrate, providing products with high *anti*-diastereoselectivity of greater than 10:1 for all *E*,*E*-allyl vinyl ether substrates. The lower diastereoselectivity for compound **40b** (**40b**$_{anti}$:**40b**$_{syn}$= 6.3:1, entry b) can be attributed to a mixture of olefin isomers about the vinyl ether moiety. Regioselectivity on the other hand, varied greatly with the electronics of the C_6-aryl group on the substrate. Aromatic groups that had an electron-donating group on the 4-position of the ring (entry d) provided products with high regioselectivity (**40d**:**50d=** 14:1) compared to aromatic groups with electron withdrawing groups at the 4-position of the ring (entry e) (**40e**:**50e=** 4.7:1). This is not too surprising as the electronics of the phenyl ring will influence the stability of the branched position of the π-allyl system. The electron donating groups will support the partial positive charge on the branched position while electronegative groups will destabilize it resulting in different ratios of the branched and linear products. Additionally, substitution at the 2-position of the aromatic ring also greatly influenced regioselectivity. The regioselectivities were lower when the 2-position of the ring was substituted (entries f and j) compared to the 4-position (entries c-e). Additionally all reaction conversions and yields were excellent, averaging above 80% in most cases.

Table 8. Investigation of Substrate Scope with Optimized Claisen Conditions

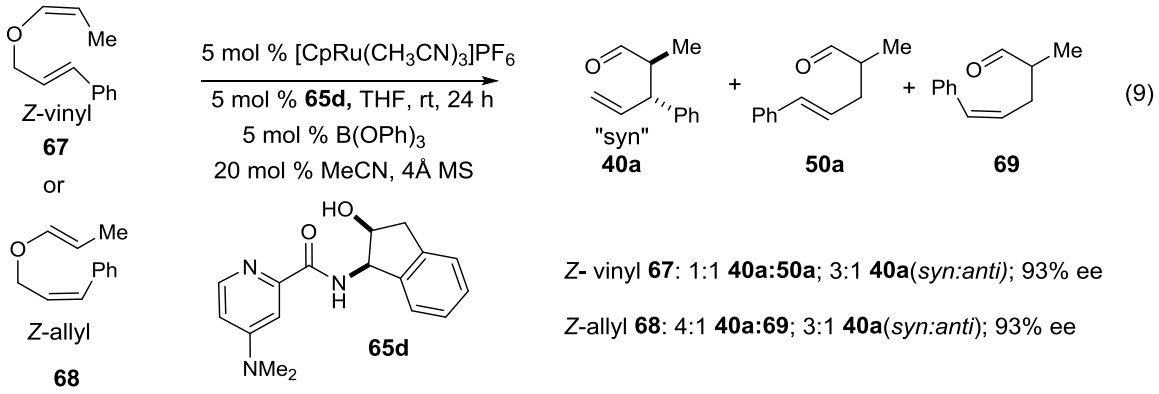


Entry	R_1	R_2	conversion(%)[a]	**40:50**[a]	*anti:syn*(**40**)[a]	ee **40** (%)[b]	yield **40** (%)[c]
a	Me	Ph	100	5.3:1	20:1	93	91
b	Et	Ph	100	3.6:1	6.3:1	99	89
c	Me	Ph, 4-Me	98	7.6:1	17:1	92	90
d	Me	Ph, 4-OMe	95	14:1	18:1	91	86
e	Me	Ph, 4-Br	97	4.7:1	25:1	92	92
f	Me	Ph, 2-OMe	95	4.4:1	11.1:1	78	89
g	Me	Ph, 3-OMe	93	6.5:1	25:1	93	80
h	Me	Ph, 3-Cl	100	4.6:1	16.6:1	96	78
i[d]	Me	2-furyl	98	10:1	20:1	96	63
j	Me	1-napthyl	97	3:1	10:1	96	90
k	Me	2-napthyl	100	7:1	16:1	84	94

[a] Determined by ^{1}H NMR of the crude product mixture, [b]Determined by Chiral GC, [c] Isolated yield after flash chromatography,[d] Reaction was run for 48 hr

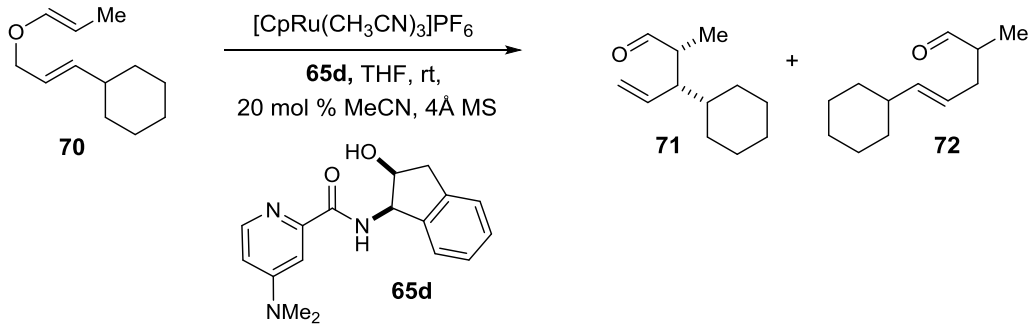
In addition to sterics and electronics of the substrate influencing the reaction, olefin geometry within the allyl vinyl ether had a significant impact on regio- and diastereoselectivity (eq 9). Inverting the geometry of either the vinyl ether or the allyl olefin of the substrate (*Z*-vinyl ether **67**, or *Z*-allyl ether **68**) caused the diastereoselectivity of the formal [3,3] product to invert from *anti* to *syn,* complementary to that of the thermal Claisen rearrangement. The enantioselectivities of the products remained high (93%) which is consistent with the

rearrangement of the *E,E*-allyl vinyl ethers, however both the regioselectivities and diastereoselectivities were eroded. The *Z,E*-vinyl ether provided a 1:1 mixture of the formal [3,3] to [1,3] products, where the *E,Z*- vinyl ether provided a 4:1 mixture. The diastereoselectivities in both cases were low at 3:1 with a preference for the *syn* diastereomer.



Finally, to examine whether aromatic substrates are required, a non-aromatic substrate **70** was synthesized and subjected to the optimized reaction conditions (5 mol % CpRu(II)-**65d**, 5 mol % $B(OPh)_3$, 100 wt % 4Å MS, 20 mol % MeCN, THF) (Table 9, entry a). Substrate **70** proved to be considerably less reactive, and required higher catalyst loadings (10% CpRu(II)-**65d**) and a more Lewis acidic borate (10 mol % $B(O^pC_6H_4F)_3$) in order to achieve some reactivity (Table 9, entry b). Even with the use of the higher catalyst loading, this substrate only provided the linear product **72** rather than the desired branched product **71**, in a modest 44% yield with low enantioselectivity (26%). This may be attributed both to the sterics and electronics of the substrate. The cyclohexane ring is more sterically demanding than the phenyl ring system, possibly preventing nucleophilic attack at the branched position of the π-allyl system.

Table 9. Optimization of Reaction Conditions for Aliphatic Substrate **70**



Entry	Conditions	Observations
a	5 mol % CpRu(II)-**65d,** 5 mol % $(BOPh)_3$, 24h	No Reaction
b	10 % CpRu(II)-**65d**, 10 mol % $B(O^pC_6H_4F)_3$, 48h	Only Linear Product **72** (44% yield), 23% ee

Additionally, computational studies by the group of Bruneau and co-workers revealed that the binding of Ru to π-allyl systems of aliphatic substrates is much more symmetric than that of aromatic substrates (Figure 11).[34a] Therefore, the branched position of the allyl system becomes less distinct relative to the terminal position providing poor regioselectivities in the allylic alkylation chemistry of alkyl allylic substrates.

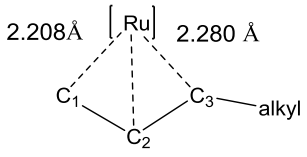


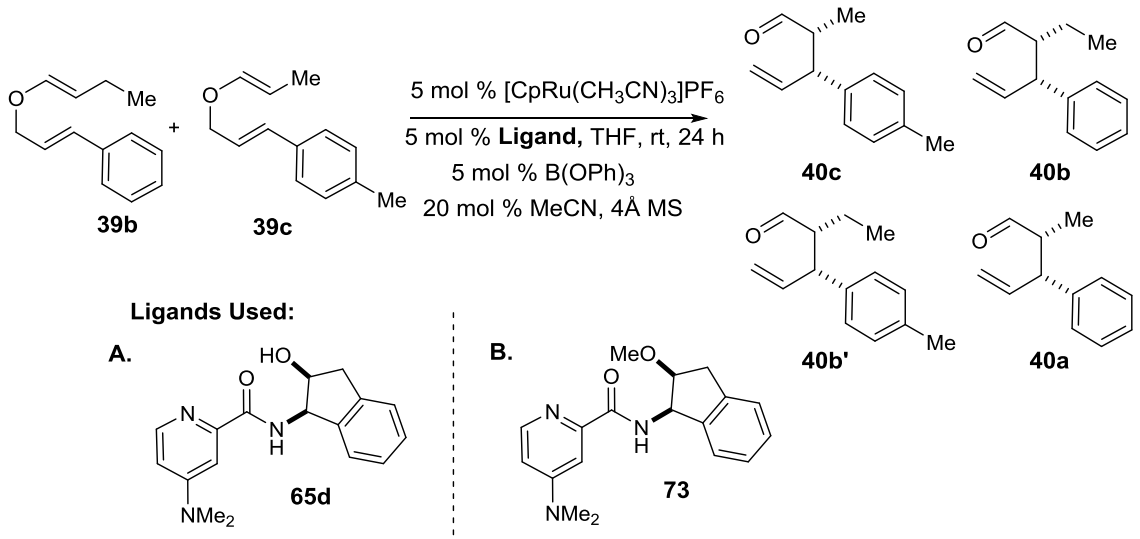
Figure 11. Symmetric Bonding of Ruthenium with Aliphatic Substrates

2.7 CROSSOVER EXPERIMENT AND ELUCIDATION OF THE REACTION MECHANISM

Efforts to elucidate the mechanism of the reaction focused on obtaining a crystal structure of the Ru(II)-**65d** complex. We wanted to determine how the picolinamide ligand **65d** bound to the Ru(II)-complex in order to determine the origin of diastereoselectivity. However, these efforts failed due to the instability of the complex. As an alternative, we decided to develop a crossover experiment to determine whether or not oxidative addition of the Ru(II)-complex was occurring with the release of the enolate fragment, or if it stayed within the coordination sphere of the metal.

Utilizing an equimolar amount of substrates **39b** and **39c** under the optimized reaction conditions (5 mol % CpRu(II)-**65d**, 5 mol % $B(OPh)_3$, 100 wt % 4Å MS, 20 mol % MeCN, THF) provided no crossover products and gave diastereoselectivities identical to those obtained for single-substrate reactions (Scheme 10). In order to determine if this was indeed the result of the hydroxyl moiety on the ligand, we needed to run the exact same crossover experiment utilizing ligand **73**, in which a methyl ether replaces the free alcohol. Utilizing the protected ligand **73** in the crossover experiment of substrates **39b** and **39c** provided an equimolar mixture of four products with poor diastereoselectivity consistent with the rearrangement occurring with dissociation of the enolate moiety from the coordination sphere of the metal. Therefore, we can conclude that the alcohol residue on the ligand both helps to enforce an intramolecular mechanism as well as secure a highly ordered transition state required for stereoselective C-C bond formation.

Scheme 10. Crossover Experiments Utilizing Ligands **65d**, and **73**



Ligand	Product Distribution	% Diastereomeric excess
70d	**40c**:**40b**:**40b'**:**40a** = 1:1:0:0	89 (**40c**), 74 (**40b**)
73	**40c**:**40b**:**40b'**:**40a** = 1:1:1:1	22 (**40c**), 29 (**40b**), 29 (**40b'**), 20 (**40a**)

From these results, along with previously established models pertaining to CpRu(π–allyl) complexes,[34a,38f,41] we were able to provide a potential reaction mechanism (Figure 12). The $B(OPh)_3$ activated allyl vinyl ether **74** could enter the coordination sphere of the metal by replacing the solvent molecule forming complex **75**. Oxidative addition of the ether C-O σ-bond would then be able to occur with the assistance of the Lewis acid, providing an *endo*-(η^3–allyl)Ru(IV) complex **76**. An *exo* conformation is possible, but not likely due to possible steric interactions occurring between the central C-H bond of the allyl system and the Cp ring. The resulting boron enolate stays within the coordination sphere of the metal via interaction with the hydroxyl moiety of the ligand, allowing intramolecular delivery of the enolate to the more substituted end of the allyl ligand affording the Ru-pentenal chelate **66** with *anti*-diastereoselectivity. The product is then released from the coordination sphere of the metal via

disruption of the pentenal chelate via added acetonitrile, affording the desired product **40** and regenerating the active catalyst **77**.

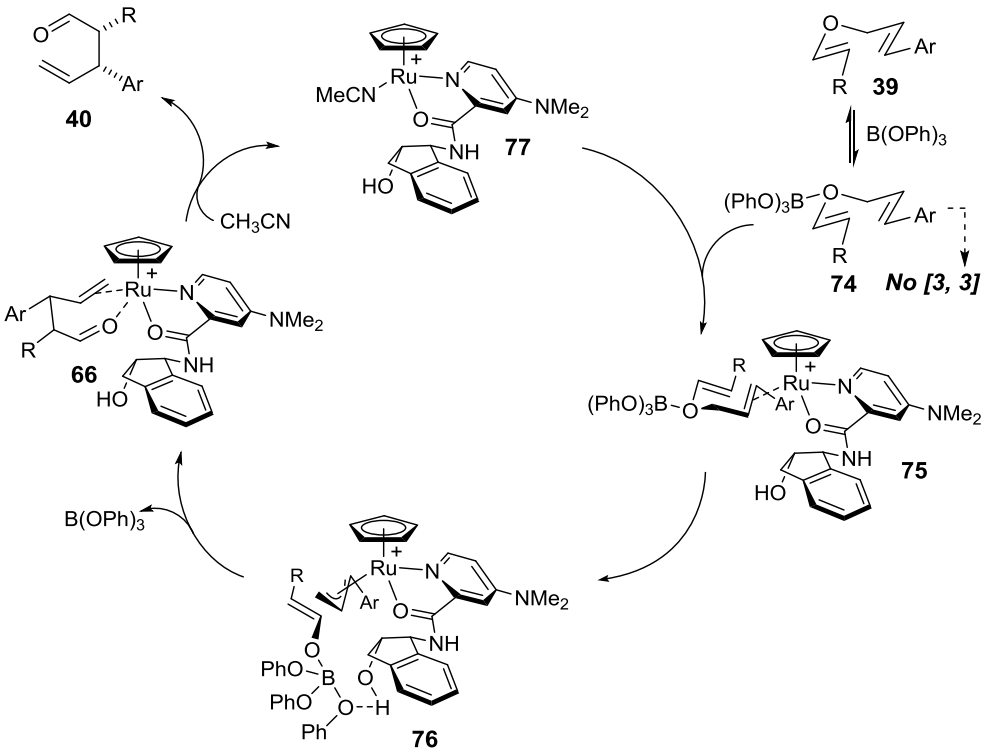
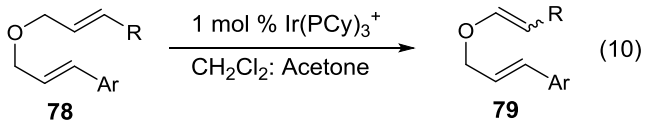


Figure 12. Potential Mechanism for Ru(II)-Catalyzed Claisen Rearrangement

2.8 EXPANSION OF SUBSTRATE SCOPE

In an attempt to expand the substrate scope of the catalytic asymmetric Claisen rearrangement, it became apparent that the synthesis of a more diverse class of allyl vinyl ethers of type **79** was no longer trivial or facile. The use of the $Ir(PCy)_3^+$ isomerization catalyst on diallyl ethers **78** with C_1-alkyl (when R= H or methyl), provided allyl vinyl ethers with high E selectivity (eq 10).[48] However, when the alkyl chain is elongated to an ethyl or a propyl group, a mixture of olefin

isomers formed and the product was isolated in low yields. In addition, when a halogen was present the reaction shut down, and only diallyl ether starting material was recovered. Since a mixture of olefin geometries would erode the diastereoselectivity of the final Claisen product we needed to develop an alternative solution to either the synthesis of allyl vinyl ethers or propose a different method to form the Claisen products.



78 **79** (10)

When R= H or Me, E/Z > 95:5
R= Et, E/Z = 5:1, 38% yield
R= *n*Pr, E/Z= 1:1, 23% yield
R= Cl, No reaction

2.9 CONCLUSIONS

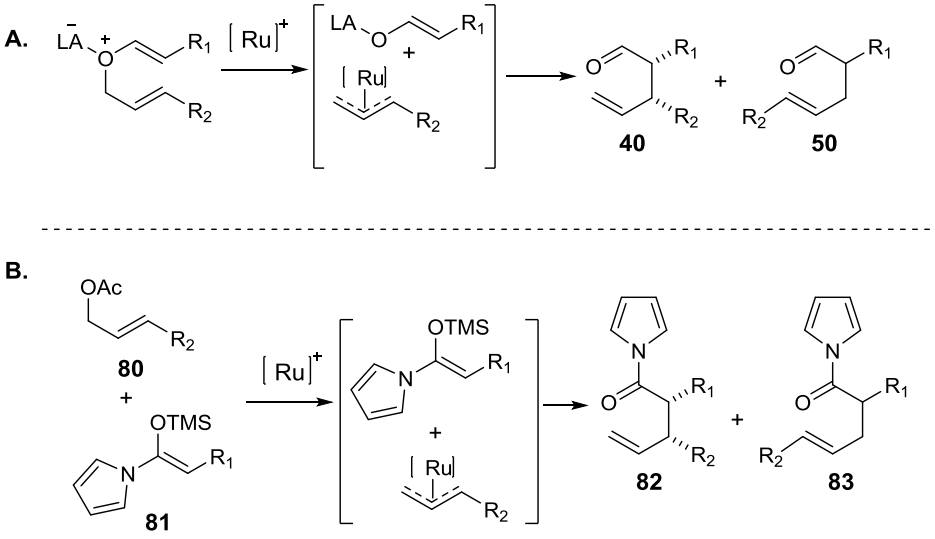
In conclusion, we have developed a transition metal-catalyzed asymmetric Claisen rearrangement for simple allyl vinyl ethers that does not require any additional functionality for substrate-catalyst association and reaction completion. The reaction proceeds under mild conditions with low catalyst loadings and in general, easily accessible starting materials. All reactions proceed with high yields (80%) and good diastereoselectivities (10:1 *anti:syn*) with some as high as 25:1. Enantioselectivities that have been determined are excellent averaging above 90%. Despite the rearrangement being limited to C_6-aryl substrates, it provides easy access to γ, δ- unsaturated carbonyl compounds in a highly asymmetric manner.

3.0 RUTHENIUM-CATALYZED ENOLATE ALLYLIC ALKYLATIONS PROVIDING CLAISEN-LIKE PRODUCTS

3.1 A CLAISEN ALTERNATIVE

Due to the substrate scope limitations encountered utilizing the catalytic asymmetric Claisen rearrangement we wanted to develop a complementary reaction utilizing easily accessible starting materials that would provide the same C-C bond connections and high diastereo- and enantioselectivity as the Claisen rearrangement. Based on the mechanistic studies performed utilizing the asymmetric Claisen conditions, we speculated that the reaction proceeded via oxidative addition to the C-O σ-bond of the allyl vinyl ether with subsequent Ru-bound enolate-allyl cation recombination (Scheme 11A). Due to the intramolecular nature of the reaction, the products of type **40** were formed with vicinal stereocenters in high diastereo- and enantioselectivity. Developing an intermolecular variant of the rearrangement utilizing easily prepared pyrrole silyl enol ethers as the enolate **81,** and allylic acetates **80** as the pro-electrophile, would provide a complimentary strategy to access similar Claisen products of type **82**, but with a larger substrate scope that was inaccessible from our catalytic asymmetric Claisen rearrangement (Scheme 11B).

Scheme 11. A. Catalytic Asymmetric Claisen Reaction; **B.** A Claisen Alternative using Silyl Enol Ethers as Nucleophiles

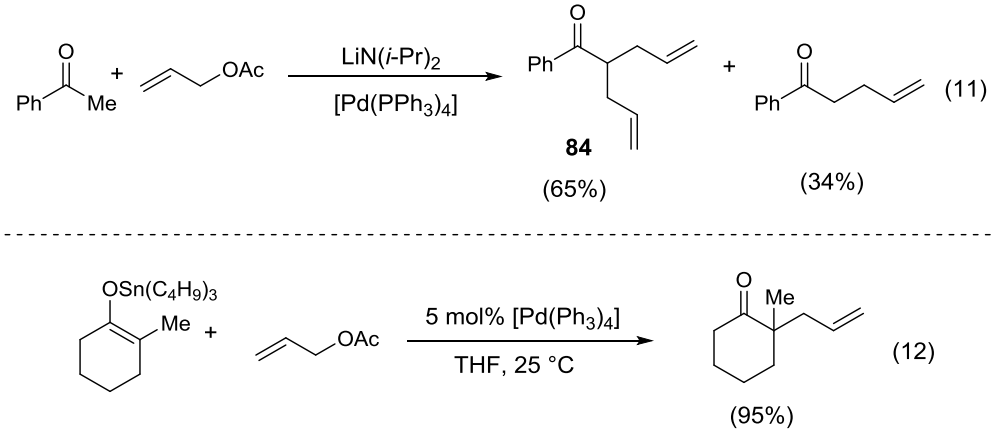


3.2 INTRODUCTION TO ENOLATE ALLYLIC ALKYLATIONS

Transition metal-catalyzed allylic alkylation reactions provide highly versatile C-C bond constructions in a variety of synthetic reactions.[49] In general, the nucleophilic partner in these reactions are stabilized carbon nucleophiles that include malonic esters, β–ketoesters, 1,3 diketones or nitro compounds. While enolates are an important class of nucleophiles; their use in allylic alkylation chemistry has not been fully developed. Trost pioneered the use of enolates in allylic alkylation chemistry in the 1980's.[50] He utilized the lithium enolate of acetophenone as a nucleophile in the palladium catalyzed allylic alkylation of allyl acetate (Scheme 12, eq 11). However, the reaction was plagued by the formation of the double alkylated product **84**. This remained a challenge, especially when the enolate precursor contained more than one acidic proton. Due to these discouraging results, chemists turned to "softer" tin or boron enolates,

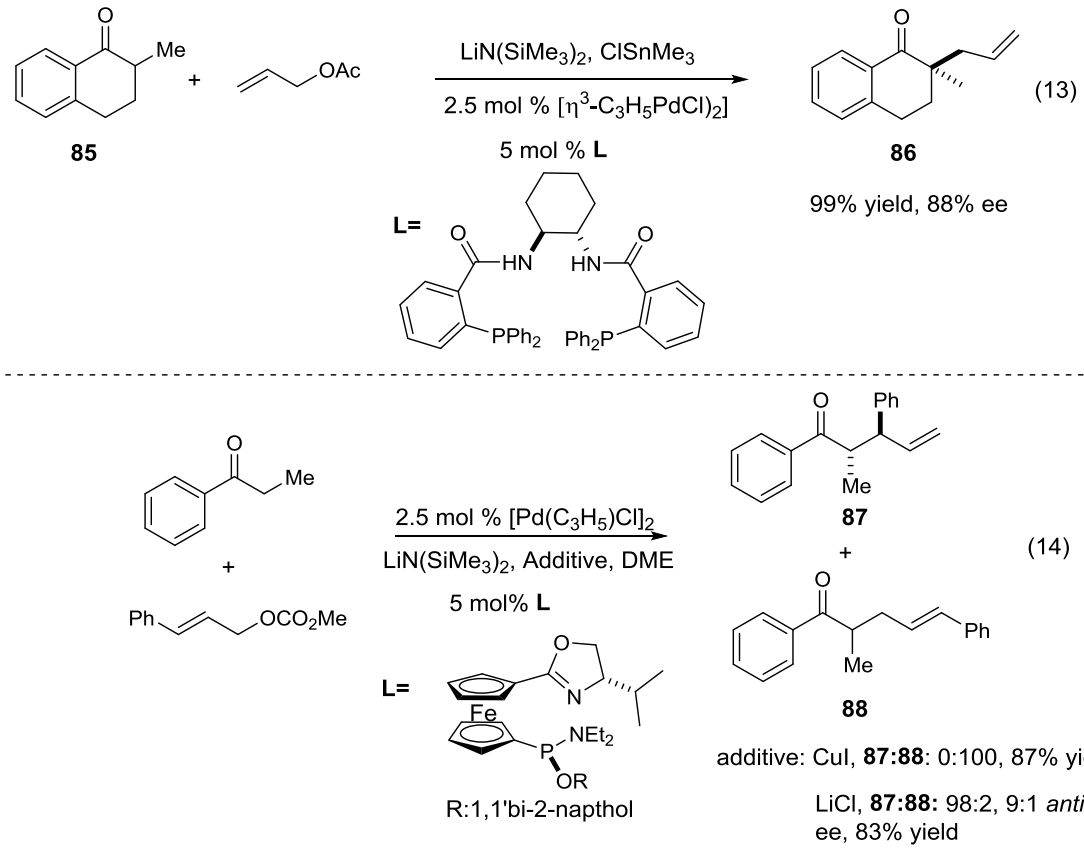
which react more efficiently with the "soft" Pd- π-allyl system.[51] Indeed, this did solve the problem of double alkylation and produced the mono-alkylated product in up to 90% yield in some instances (Scheme 12, eq 12).

Scheme 12. Early Developments in Enolate Allylic Alkylation Chemistry



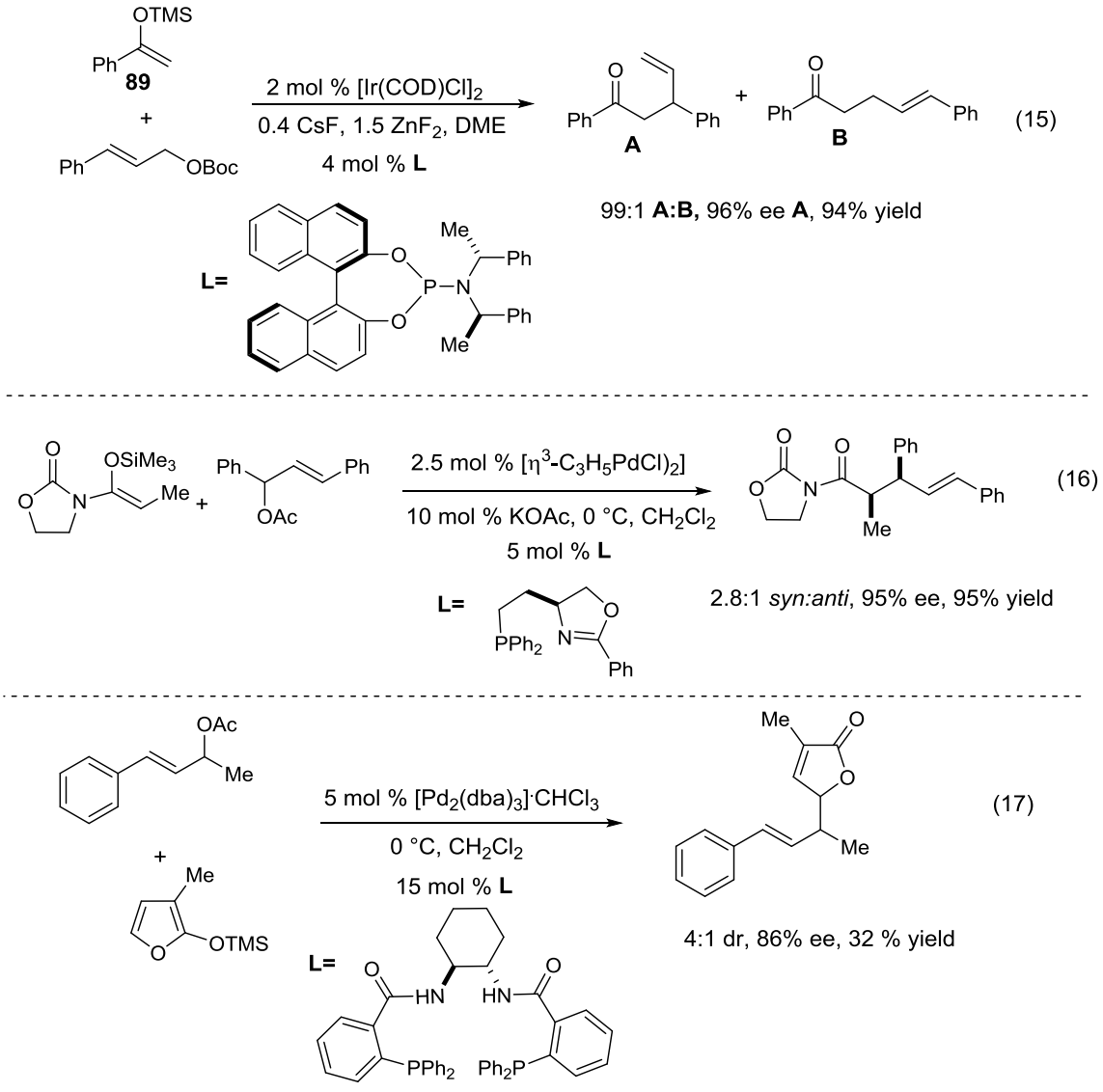
An asymmetric variant of the reaction took much longer to develop due to the intermolecular nature of the reaction. In order for chiral ligands to influence stereochemistry in the reaction, they need to be a part of the bond making and bond breaking process occurring outside of the coordination sphere of the metal. In 1999, Trost developed a Pd-catalyzed asymmetric allylic alkylation utilizing allyl acetate, and the tin enolate of 2-methyl-1-tetralone **85** (Scheme 13, eq 13).[52] This provided the allylated product **86** with a quaternary center in high yield and good enantioselectivity. In addition, a diastereoselective reaction was developed utilizing simple lithium enolates (Scheme 13, eq 14).[53] The choice of metal salt influenced the regioselectivity of the reaction, providing products **87** and **88** with high enantioselectivity, and diastereoselectivities that ranged from 5 to 20:1.

Scheme 13. Initial Examples of Asymmetric Enolate Allylic Alkylations



The use of nonstabilized silyl enol ethers as nucleophiles in allylic alkylation reactions has remained underdeveloped due to their lack of reactivity. Hartwig and co-workers developed the first iridium-catalyzed, enantioselective reaction with silyl enol ethers (Scheme 14, eq 15).[54] However, they discovered that the reaction required an activator for the silyl enol ether **89**. With the addition of catalytic amounts of metal fluorides, such as CsF and ZnF_2, the reaction was able to proceed with good yields enantioselectivities of up to 96%. However, the development of a regio-, diastereo- and enantioselective allylic alkylation utilizing silyl enol ethers as a nucleophile remains elusive to this day. There are a few diastereoselective examples, but the selectivities are generally poor or the yields are low (Scheme 14, eq 16 and 17).[55,56]

Scheme 14. Silyl Enol Ethers as Nucleophiles in Enolate Allylic Alkylations

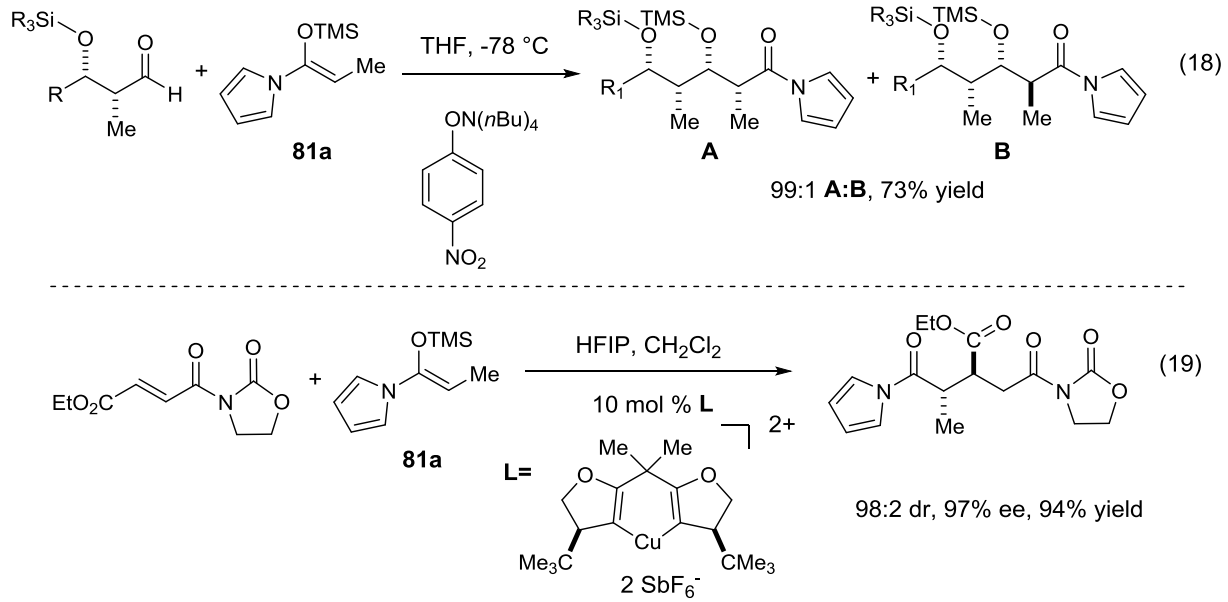


3.3 INITIAL STUDIES TOWARDS THE RUTHENIUM CATALYZED ENOLATE ALLYLIC ALKYLATION

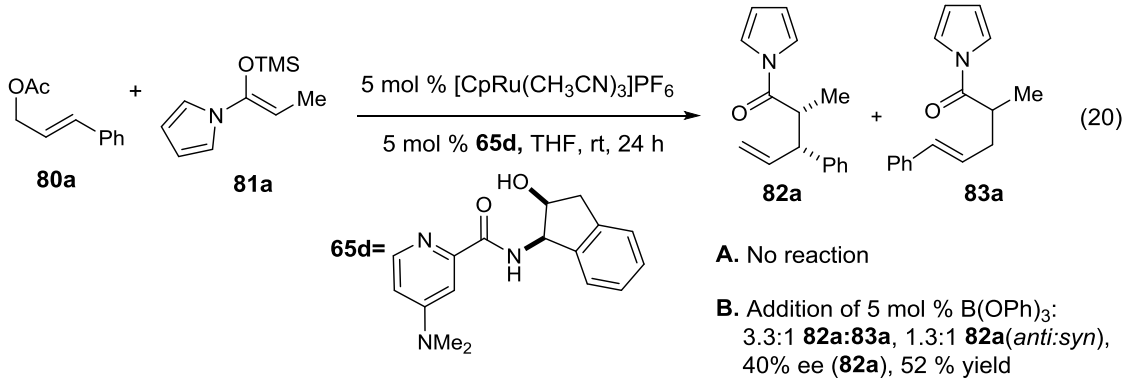
Reaction design commenced with the choice of appropriate substrates. Mono-substituted allylic acetates **80** were chosen as the electrophilic substrate based on their rich history in allylic

alkylation chemistry, including Ru- based methodologies, as well as their ability to readily form Ru(IV)(π-allyl) complexes capable of providing branched addition products.[34,38,39] In addition, they are easily synthesized from either commercially available or easily prepared allylic alcohols. The *N*-acyl pyrrole derived silyl enol ether **81a** was selected based on its ability to act as an ester or amide enolate that can be prepared in high yields with almost exclusive *Z*-configuration.[57] Additionally, it has proven to be synthetically useful in a variety of reaction methodologies. For example, it was shown to be a good nucleophile in Lewis base catalyzed Mukaiyama aldol additions developed in the Nelson lab (Scheme 15, eq 18).[58] Also it served as a nucleophile in the Mukaiyama-Michael additions developed by Evans providing products with high diastereoselectivities and yields (Scheme 15, eq 19).[59] Although these pyrrole silyl enol ethers have never been used to capture metal π-allyl complexes, their increased nucleophilicity relative to ketone derived silyl enol ethers, and ability to induce high diastereoselectivity, makes them an attractive nucleophile for our system.

Scheme 15. Examples of Pyrrole Silyl Enol Ethers as Nucleophiles



After the selection of potential reaction partners, the viability of the reaction was probed utilizing our previously developed Claisen conditions as a starting point. Initial exposure of cinnamyl acetate **80a** and pyrrole silyl enol ether **81a** to our established Claisen conditions, 5 mol % of the Ru(II) complex generated in situ through the reaction of $[CpRu(CH_3CN)_3]PF_6$ with ligand **65d**, gave no reaction after 24 hours (eq 20). With the addition of 5 mol % Lewis acid co-catalyst $B(OPh)_3$ to activate the allylic acetate, the reaction afforded the desired branched acyl pyrrole product **82a**. However, consistent with the preliminary Claisen experiments, it was formed in low yield, and with poor selectivity (**82a**:**83a=** 3.3:1, $\mathbf{82a}_{anti}$:$\mathbf{82a}_{syn}$= 1.3:1, 40% ee, 52% yield).

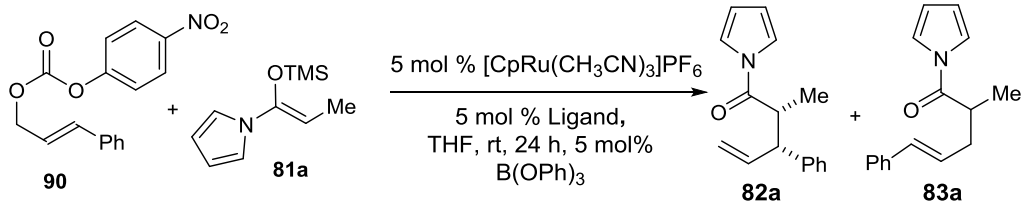


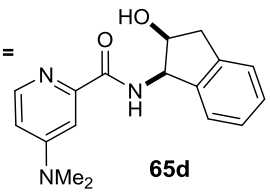
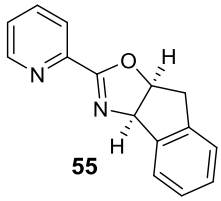
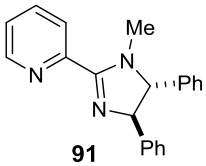
Due to the poor reaction yields and incomplete consumption of starting materials, it appeared that either the allylic acetate was not sufficiently activated enough to undergo oxidative addition by the Ru(II)-catalyst or the pyrrole silyl enol ether **81a** was not a strong enough nucleophile to add to the π-allyl system. If oxidative addition to the allylic acetate was indeed problematic, the leaving group could be easily altered or a stronger Lewis acid could be used to further activate the allylic substrate. To this end, we decided to probe the impact of leaving group structure on reaction efficiency as better leaving groups should increase the rate of

oxidative addition.[60] As a result we replaced the acetate leaving group with *p*-NO_2 phenylcarbonate. Utilizing substrate **90** under the Claisen conditions, (5 mol % CpRu(II) salt, 5 mol % **65d**, 5 mol % $B(OPh)_3$, THF, 24 h) the desired product was formed in 86% yield, but with negligible selectivity (**82a**:**83a=** 3.4:1, **82a**$_{anti}$:**82a**$_{syn}$= 1:1, 0% ee **82a**)(Table 10).

Having achieved an improvement in reaction yield to 86% with the use of a better leaving group, we turned our attention to reaction selectivity, more specifically regioselectivity. Our previous research demonstrated that regioselectivity was affected by ligand electronics. As a result, we wanted to employ a more electron donating ligand, such as the pyridine oxazoline ligand **55**. This ligand did lead to a dramatic increase in both regioselectivity and enantioselectivity, yet diastereoselectivity remained poor at 1:1 (**82a**$_{anti}$:**82a**$_{syn}$) (Table 10). Next, we chose to investigate the imidazoline ligand **91** due to its structural similarity to the oxazoline ligand. The imidazoline moiety contains a nitrogen atom in place of the oxygen which allows for an increase in basicity over the oxazoline moiety.[61] Utilizing imidazoline ligand **91** under the same reaction conditions as above, regioselectivity remained unchanged despite the increase in electron density; surprisingly, diastereoselectivity increased to 3:1 (**82a**$_{anti}$:**82a**$_{syn}$).

Table 10. Ligand Screen Utilizing Allylic *p*- NO_2-phenyl Carbonates as a Substrate

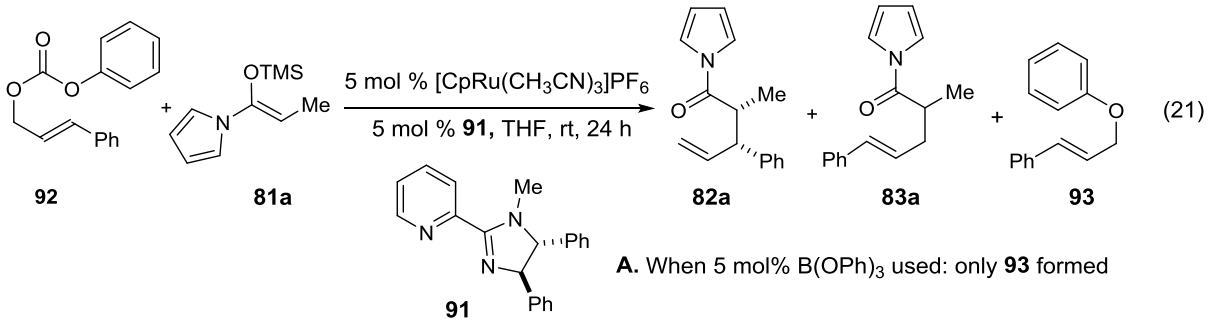


Ligand =  65d	 55	 91
regio (**82a:83a)**[a] 3.4:1	10:1	10:1
anti:syn (**82a**)[a] 1:1	1.3:1	3:1
% yield 86	95	85
% ee[b] (**82a**) 0	68	88

[a] Determined by ^{1}H NMR; [b] Determined by chiral GLC

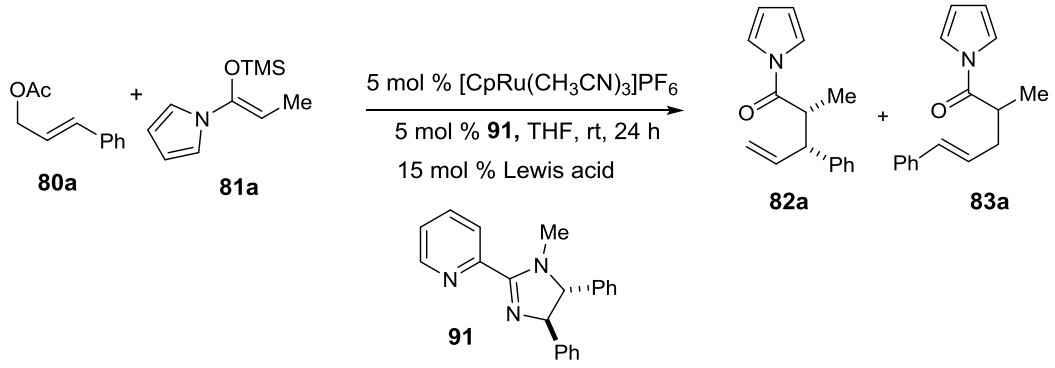
Having secured selectivities nearing synthetically useful levels with the use of imidazoline ligand **91** it became apparent that the *p*-NO_2 phenyl carbonate was not a desirable leaving group from a synthetic point of view. As a result, we wanted to determine if we could achieve similar selectivities and reactivity with alternative leaving groups. Additionally, we thought that a less activated leaving group could result in better reaction selectivity. As a result the *p*-NO_2 phenyl carbonate was replaced with phenyl carbonate (eq 21). However, utilizing substrate **92** under optimized reaction conditions (5 mol % CpRu(II) salt, 5 mol % **91**, 5 mol % $B(OPh)_3$, THF, 24 h), lead primarily to the formation of aryl ether **93**, from nucleophilic addition of the phenoxide leaving group to the π-allyl complex. In order to prevent nucleophilic addition of the phenoxide from occurring, we decided to utilize the stronger Lewis acid, $B(O^pC_6H_4F)_3$, as

a means to both activate the substrate, and help to sequester the phenoxide. However, in order to prevent the aryl ether from forming, up to 30 mol % of the borate was needed. Ultimately, the use of the phenyl carbonate leaving group did substantially improve the diastereoselectivity of the reaction to 6:1 (**82a**$_{anti}$:**82a**$_{syn}$) from 3:1; however the difficulty associated with this substrate required us to re-evaluate the leaving group once again.



Having found that the increased Lewis acidity of B($O^pC_6H_4F$)$_3$ provided better activation of the allylic carbonate substrate **92** compared to B(OPh)$_3$, it became apparent that B($O^pC_6H_4F$)$_3$ could be used to increase the reactivity of the original allylic acetate substrate **80a**. Utilizing 15 mol % B($O^pC_6H_4F$)$_3$ under the optimized Ru(II)-imidazoline catalyst conditions (5 mol % Ru(II) salt, 5 mol % **91**, THF, 24 h) provided a marked improvement in reaction efficiency (86% yield) along with an increase in regio-, diastereo-, and enantioselectivity (**82a**:**83a**= 13:1, **82a**$_{anti}$:**82a**$_{syn}$= 7:1, 92% ee) (Table 11). However, utilization of stronger Lewis acids including B($O^pC_6H_4CF_3$)$_3$ and B($O^pC_6H_4NO_2$)$_3$, proved to be detrimental to diastereoselectivity. We can conclude that not only does ligand structure affect reaction selectivity but leaving group ability seems to have a profound effect on diastereoselectivity.

Table 11. Effect of Lewis Acid on Product Diastereoselectivity



Entry	Lewis Acid	Results
a	$B(O^pC_6H_4F)_3$	13:1 **82a:83a**, 7:1 **82a** (*anti:syn*), 92% ee (**82a**), 86% yield
b	$B(O^pC_6H_4CF_3)_3$	4:1 **82a** (*anti:syn*)
c	$B(O^pC_6H_4NO_2)_3$	2.3:1 **82a** (*anti:syn*)

3.4 LIGAND MODIFICATIONS

Having secured reaction conditions that provided our desired Claisen-like products with good selectivities (**82a**:**83a**= 13:1, $\mathbf{82a}_{anti}$:$\mathbf{82a}_{syn}$= 7:1, 92% ee), we decided to further probe the imidazoline ligand structure to determine if greater product selectivites could be achieved. This was easily done as the ligand could be synthesized via a condensation reaction between an aldehyde of type **94**, and diamine **95** to form the imidazoline moiety in **96**, followed by protection of the resulting free amine (eq 22).[62] This left three distinct ways to modify the ligand: 1) protecting group manipulations on the free amine, 2) steric and electronic adjustments of the pyridine ring, and 3) alteration of the sterics of the diamine backbone (Table 12). The structural modifications could be used to systematically alter the binding of the π-allyl complex

and therefore probe the origins of regioselectivity and enantioselectivity in the reaction in order to elucidate the optimal ligand for reaction success.

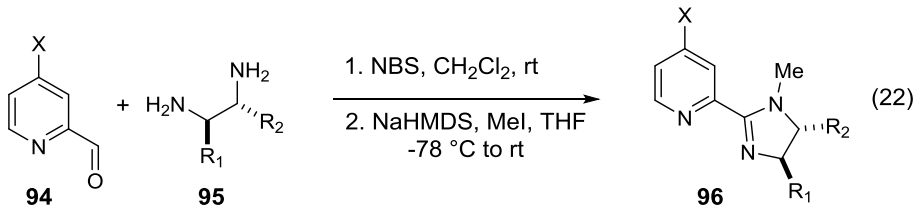
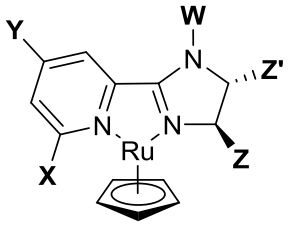


Table 12. Structural Modifications on the Imidazoline Ligand and their Anticipated Effects

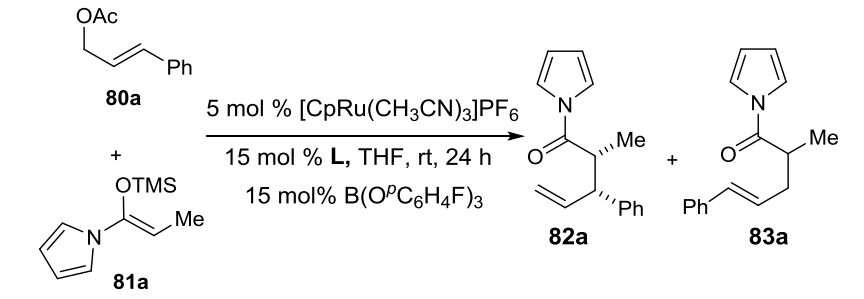


Variable/Region	Influence	Anticipated Effect
W	Increase or decrease sterics at N_{amine}	Stereoelectronic effect that influences regioselectivity
X	Increase steric enviroment of pyridine ring	influence binding of π-allyl system: enantioselectivity
Y	Enhanced electron donation to ruthenium	Influence regioselectivity through asymmetry in π-allyl system
Z	Increase steric enviroment about the imidazoline ring	influence binding of π-allyl system: enantioselectivity

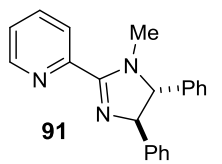
Ligand modifications began with the protecting group on the amine. We reasoned that the electronic nature of the imidazoline ligand could be altered through the manipulation of the the protecting group. Three ligands were synthesized with different protecting groups: methyl

protected **91**, benzyl protected **97,** and non-protected **98** (Table 13). In comparing the results of the standard reaction (5 mol % Ru(II) salt, 5 mol % ligand, 15 mol % $B(O^pC_6H_4F)_3$, THF, 24 h), we found that the methyl protected ligand **91** provided the best selectivity (**82a**:**83a**= 13:1, $\mathbf{82a}_{anti}$:$\mathbf{82a}_{syn}$= 7:1, 92% ee, 86% yield). The benzyl protected ligand **97** provided slightly diminished selectivies compared to the methyl protected version (**82a**:**83a**= 11:1, $\mathbf{82a}_{anti}$:$\mathbf{82a}_{syn}$= 5:1, 88% ee). We believe this may be due to the increased steric nature of the benzyl group causing less efficient electron donation to the imine moiety of the ligand.[61,63,64] The free amine ligand **98** also provided inferior results with a dramatic decrease in regioselectivity and yield (**82a**:**83a**= 6:1, $\mathbf{82a}_{anti}$:$\mathbf{82a}_{syn}$= 5:1, 81% ee, and 50% yield). The decrease in yield implies that oxidative addition to the allylic acetate is not as facile, suggesting that the free amine moiety in ligand **98** may be sequestering the borate Lewis acid. Since the methyl group proved to be the optimal protecting group, we chose to utilize it for the remainder of the ligand modifications.

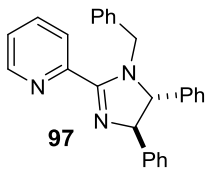
Table 13. Modifications to the Amine Protecting Group on the Imidazoline Ligand



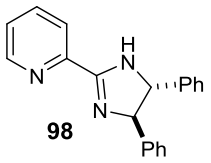
L=



82a:83a[a] = 13:1
7:1 *anti:syn*[a] (**82a**),
92% ee[b], 86% yield



82a:83a[a] = 11:1
5:1 *anti:syn*[a] (**82a**),
88% ee[b], 87% yield



82a:83a[a] = 6.4:1
5:1 *anti:syn*[a] (**82a**),
81% ee[b], 50% yield

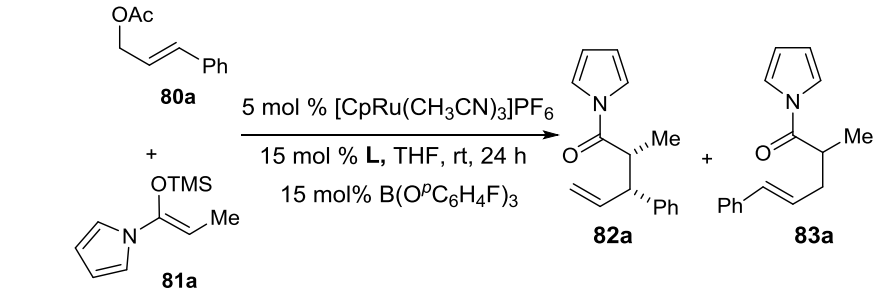
[a] Determined by ^{1}H NMR; [b] Determined by chiral GLC

The next set of alterations to the ligand began with the sterics and electronics of the pyridine moiety. We hoped to gain insight on how the π-allyl complex bound to the Ru(II) complex and therefore optimize enantioselectivity. Investigations of the sterics were focused on the 5- and 6-position of the pyridine ring, as they offered the greatest potential of increasing selectivity. Attachment of a methyl group to the 6-position of the pyridine ring in ligand **99** proved detrimental to reaction conversion, providing the desired product **82a** in only 20% yield (Table 14). However, diastereoselectivity, regioselectivity and enantioselectivity remained consistent at (**82a**:**83a**= 13:1, and $\mathbf{82a}_{anti}$:$\mathbf{82a}_{syn}$= 5:1, 88% ee). Utilization of a quinoline moiety, to add sterics to both the 5-, and 6-position on the pyridine ring in ligand **100**, also proved detrimental to the reaction outcome, causing diastereoselectivity, enantioselectivity and yield to decrease dramatically ($\mathbf{82a}_{anti}$:$\mathbf{82a}_{syn}$=2.5:1, 75% ee, 50 % yield). This led us to believe that steric constraints on the pyridine ring prevented the π-allyl complex from efficiently binding to the catalyst, providing low yields and poor selectivities of the desired product.

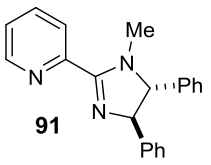
Given that increasing the sterics of the pyridine moiety offered no improvements to the reaction selectivity, the electronics of the ring were probed. We hoped that increasing the electronics of the pyridine ring would increase its σ-basicity, therefore possibly influencing the asymmetric nature of the π-allyl complex and increasing regioselectivity of the rearrangement.[42] Placement of a methoxy group at the 4-position of the pyridine ring in ligand **101**, provided the desired product with about the same regio-, diastereo- and enantioselectivity as the parent imidazoline ligand **91** (**82a**:**83a**= 13:1, $\mathbf{82a}_{anti}$:$\mathbf{82a}_{syn}$= 7:1, 90% ee, 82% yield). However, by further increasing the electron density of the pyridine ring, by replacing the methoxy group with the pyrrolidine moiety in **102**, a modest improvement in both regioselectivity (**82a**:**83a**= 18:1

from **82a**:**83a**= 13:1) and diastereoselectivity (**82a**$_{anti}$:**82a**$_{syn}$= 9:1 from **82a**$_{anti}$:**82a**$_{syn}$= 7:1) was observed.

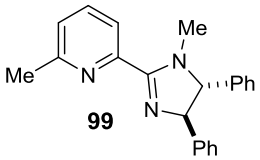
Table 14. Ligand Screen for Reaction Optimization: Alteration of the Sterics and Electronics of the Pyridine Ring



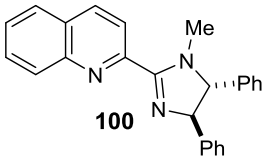
L=



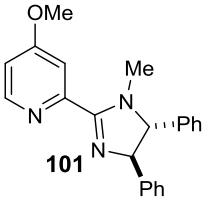
82a:83a[a] = 13:1
7:1 *anti:syn*[a] (**82a**),
92% ee[b], 86% yield



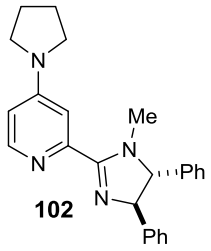
82a:83a[a] = 13:1
5:1 *anti:syn*[a] (**82a**),
88% ee[b],19% yield



82a:83a[a] = 10:1
2.5:1 *anti:syn*[a] (**82a**),
88% ee[b], 50% yield



82a:83a[a] = 13:1
7:1 *anti:syn*[a] (**82a**),
90% ee[b], 82% yield



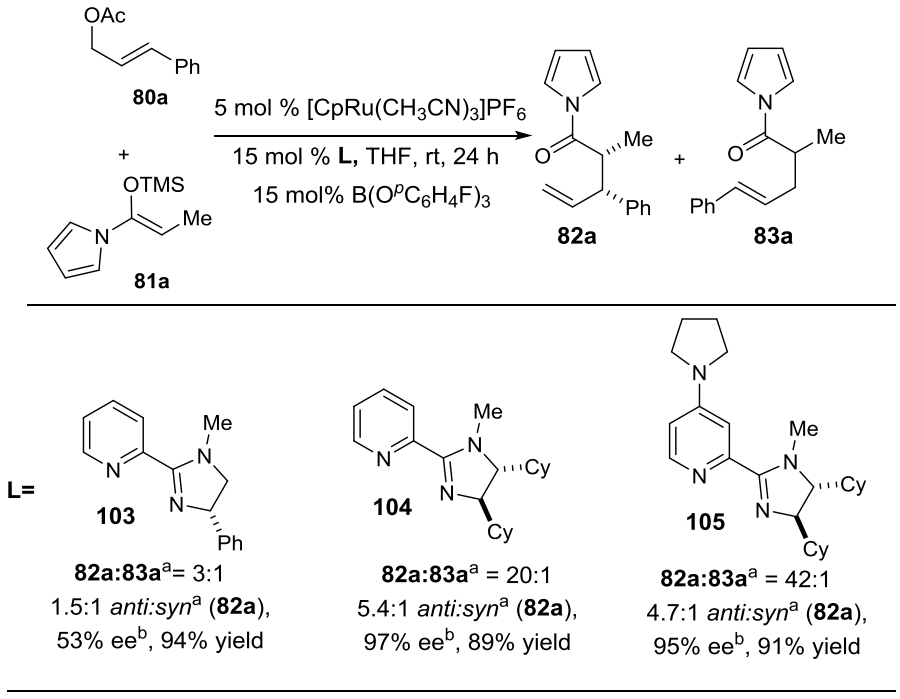
82a:83a[a] = 18:1
9:1 *anti:syn*[a] (**82a**),
91% ee[b], 88% yield

[a] Determined by ^{1}H NMR; [b] Determined by chiral GLC

Following alterations to the pyridine ring of the ligand, the diamine backbone of the imidazoline ring was examined to try and optimize enantioselectivity. We wondered if both phenyl groups were necessary for reaction selectivity, as molecular models showed that the

phenyl group adjacent to the amine moiety pointed away from the coordination sphere of the catalyst. Surprisingly, utilizing ligand **103**, where the phenyl group adjacent to the methyl amine was replaced with a hydrogen, the regio-, diastereo-, and enantioselectivity of the reaction decreased dramatically (**82a**:**83a**= 3:1, **82a**$_{anti}$:**82a**$_{syn}$= 1.5:1, 53% ee) (Table 15). Since this observation suggested that both rings were necessary for increased reaction selectivity, increasing the steric environment was probed. The phenyl groups were replaced with the bulkier cyclohexane rings in ligand **104**. This modification provided the product with increased regio- and enantioselectivity (**82a**:**83a**= 20:1, 97% ee), albeit a small decrease in diastereoselectivity (**82a**$_{anti}$:**82a**$_{syn}$= 5.4:1 from **82a**$_{anti}$:**82a**$_{syn}$= 7:1). Upon discovering that the dicyclohexyl backbone provided an increase in regioselectivity and enantioselectivity, we wondered if placing the electron-donating pyrrolidine ring on the pyridine moiety would further enhance its selectivity as it had with the diphenyl substituted ligand **102** (Table 14). Indeed, using ligand **105** the regioselectivity of the reaction increased dramatically to 42:1, but diastereoselectivity dropped to 4.5:1(**82a**$_{anti}$:**82a**$_{syn}$) and enantioselectivity remained constant (95% ee).

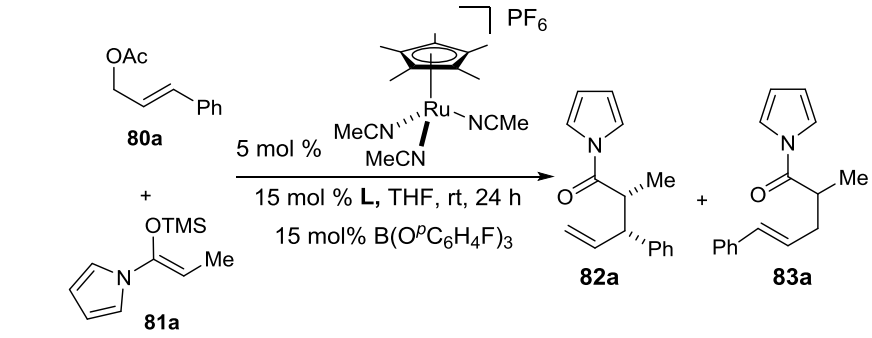
Table 15. Steric Alterations of the Imidazoline Ring

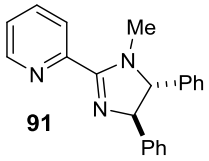
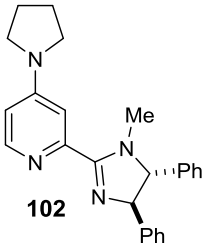
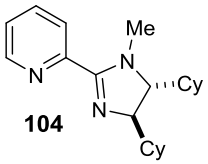
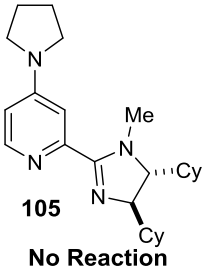


[a] Determined by ^{1}H NMR; [b] Determined by chiral GLC

In order to further investigate the effect of increased sterics and electronics on the system, [Cp*Ru(CH_3CN)$_3$]PF_6 salt was used as the precatalyst (Table 16). In general, the Cp*Ru(II) complexes are largely preferred over the CpRu(II) complexes because they are more electron rich and catalytically more active, providing products with greater regioselectivities in favor of the branched substitution product.[34,38] Surprisingly, the reaction provided products with opposite diastereo-and enantioselectivity compared with the CpRu(II)-imidazoline catalyst with ligands **91** and **104** (**82a**$_{anti}$:**82a**$_{syn}$= 1:3 compared to **82a**$_{anti}$:**82a**$_{syn}$= 7:1). In addition, the products were formed with substantially decreased regio- and diastereoselectivity. Moreover, utilization of the ligands **102** and **105** with substitution at the 4-position of the pyridine, failed to produce any reaction turnover. This may be attributed to an increase in the steric environment due to the bulkier Cp* ring system, preventing efficient binding of the substrate to the catalyst.

Table 16. Reaction Results using Cp*Ru(II) Complex



L=	91	102	104	105
				
	82a:83a[a] = 7:1 1:3 *anti:syn*[a] (**82a**), 98% ee[b], 81% yield	**No Reaction**	**82a:83a**[a]= 21:1 1:1.5 *anti:syn*[a] (**82a**), 40% yield	**No Reaction**

[a] Determined by ^{1}H NMR; [b] Determined by chiral GLC

3.5 REACTION SCOPE

Although, the Cp*Ru(II) complex provided interesting results, the diastereoselectivities and regioselectivities could not be improved further. The CpRu(II) complexes with ligands **102** and **104** ultimately provided superior results. At this juncture, with ligand **102** providing higher diastereoselectivities and ligand **104** providing better regioselectivities and enantioselectivities, we needed to determine how they performed on a larger substrate scope.

Various aryl and heteroaryl allylic acetates along with a variety of silyl pyrrole enol ethers were synthesized and subjected to the optimized reaction conditions (5 mol % CpRu(II) salt, 5 mol % **102** or **104**, 15 mol % $B(O^pC_6H_4F)_3$, THF, 16 h). The substrates afforded the

Claisen-type products with generally high yields of up to 99% with a few exceptions (Table 17 and 18). The use of additional borate was required to increase the yield of the *n*-propyl silyl enol ether to useful levels for unknown reasons (Table 17 and 18, entry c). The borate is thought to only aid in the activation of the allylic acetate, however this demonstrates that it may also play a role in the activation of the silyl enol ether. In addition, the Cl-substituted enolate only provided the desired product in about 38% yield (Table 17, entry f). Increasing the catalytic loading of the borate proved ineffective possibly due to the decreased nucleophilicity of this enolate. The Cl-substituted product was also susceptible to substitution by the acetate leaving group of the substrate. Although this contributed to a lower yield in the reaction, it showcased that the product could be easily derivitized at R_1. Also it is important to note that the bulky isopropyl group of silyl enol ether **81d** (Table 17 and 18, entry d) provided no reaction, showing that the enolate is sensitive to substitution at the α-position.

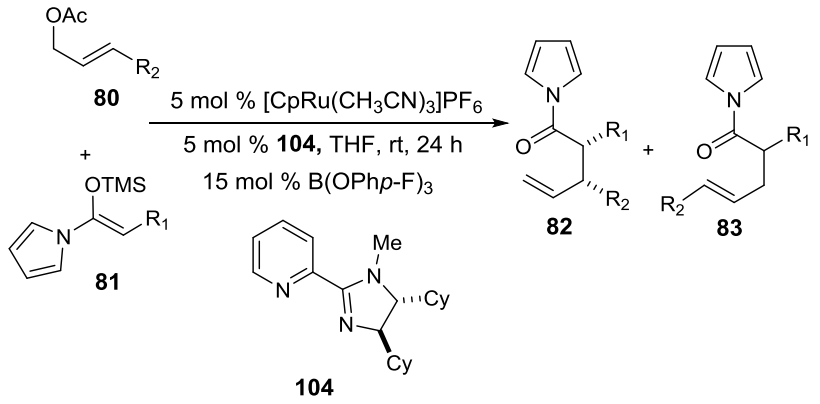
Despite the range of yields being dependent upon enolate sterics and electronics, the products of all of the reactions were formed with consistently high regioselectivities [**82a**:**83a** >19:1 for ligand **104** (Table 17) and > 8:1 with ligand **102** (Table 18)]. The only exception being for the highly electron deficient *p*-NO_2-phenyl allylic acetate which gave moderate regioselectivity (**82a**:**83a=** 5:1) (Table 17, entry j). This is likely due to the fact that the benzylic position is destabilized relative to the rest allylic acetates.

Enantioselectivities utilizing ligand **104** (Table 17), were consistently above 93% for all enolates and allylic acetates. In general, the major *anti* diastereomer was formed in higher ee than the *syn* diastereomer, however the variation was not that substantial (>93% ee *anti*, >85% ee *syn*). There was more variation in enantioselectivity when ligand **102** was used (Table 18). The ee was highly dependent on the enolate with a high of R_1=Me (95% ee) and a low of R_1=Cl (34%

ee) for the *anti* diastereomer. In addition, the *syn* diastereomer was formed with substantially lower enantioselectivities independent of enolate substitution.

Diastereoselectivity showed some dependence on both the substitution of the aryl allylic acetate and the pyrrole silyl enol ether. For example, the more sterically hindered *o*-methoxyphenyl allylic acetate (entry g) provided decreased diastereoselectivity (**82a**$_{anti}$:**82a**$_{syn}$= 3.3:1) when compared to the other substrates providing up to 9:1 (**82a**$_{anti}$:**82a**$_{syn}$) diastereoselectivity. Pyrrole silyl enol ether substitution had a greater impact on diastereoselectivity providing a range marked with a high of R_1 = methyl (**82a**$_{anti}$:**82a**$_{syn}$= 9:1) (Table 18, entry a) and a low of R_1 = Cl (**82a**$_{anti}$:**82a**$_{syn}$= 1.3:1) (Table 17, entry f). This may be attributed to the fact that the Cl atom is quite small in comparison to the rest of the substituents. In addition, the diphenyl substituted ligand **102**, provided consistently higher diastereoselectivities in comparison to ligand **104** for reasons that are unclear at this time.

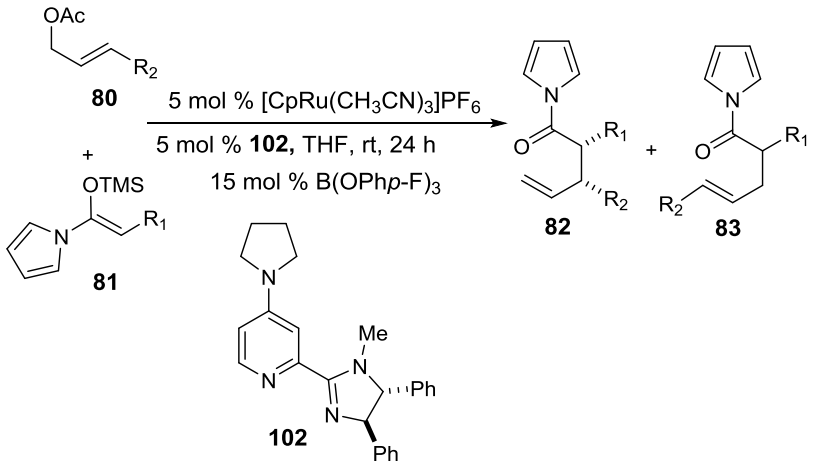
Table 17. Enolate Allylic Alkylation Reaction Scope Using Ligand **104**



entry	R_1	R_2	**82:83**	*anti:syn* (**82**)[a]	% ee[b] **82** *anti:syn*	% yield[c]
a	Me	Ph	20:1	5.4:1	97, 91	89
b	H	Ph	25:1	-	95	82
c[d]	*n*-propyl	Ph	19:1	6:1	96, 97	82
d	*i*-propyl	Ph	no reaction	-	-	-
e	OBn	Ph	>33:1	4:1	96, 89	75
f	Cl	Ph	32:1	1.3	97, N.D.[e]	38
	OAc (pdt)		16:1	2:1	99, 97	10
g	Me	Ph, 4-OMe	>33:1	5:1	94, 89	79
h	Me	Ph, 2-OMe	>33:1	3.3:1	98, 85	79
i	Me	2-furyl	20:1	4.3:1	95, 93	99
j	Me	Ph, 4-NO_2	5:1	4:1	94, 94	88

[a] Determined by ^{1}H NMR, [b]Determined by Chiral GC, [c] Isolated yield after flash chromatography,
[d] 1.0 equivalent $B(O^pC_6H_4F)_3$, [e]N.D. = not determined.

Table 18. Enolate Allylic Alkylation Reaction Scope Utilizing Ligand **102**

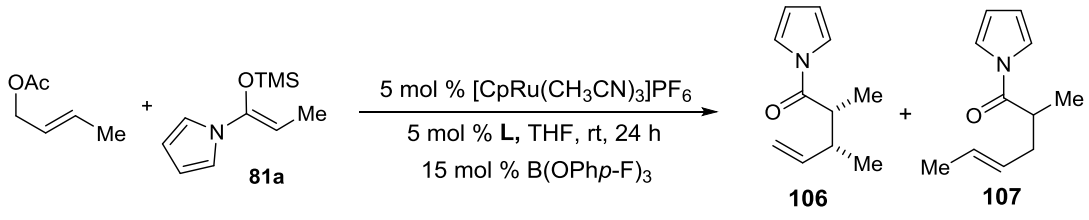


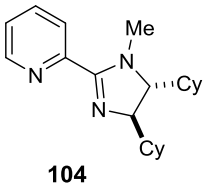
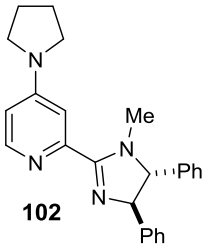
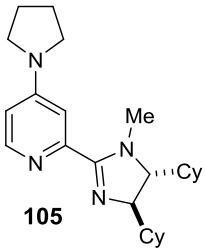
entry	R_1	R_2	**82:83**	*anti:syn*(**82**)[a]	% ee[b] **82** *anti:syn*	% yield[c]
a	Me	Ph	18:1	9:1	95, 79	88
b	H	Ph	14:1	-	68	82
c[d]	*n*-propyl	Ph	13:1	7:1	89, 59	82
d	*i*-propyl	Ph	no reaction	-	-	-
e	OBn	Ph	11:1	4:1	90, 53	80
f	Cl	Ph	32:1	1.3:1	34,-	21
	OAc (pdt)	Ph	32:1	1.3:1	N.D.[e]	5
g	Me	Ph, 4-OMe	>33:1	8:1	91, 67	92
h	Me	Ph, 2-OMe	8:1	4:1	89, 45	81
i	Me	2-furyl	17:1	8:1	89, 54	89
j	Me	Ph, 4-NO_2	4:1	5:1	88, 47	53

[a] Determined by ^{1}H NMR, [b]Determined by Chiral GC, [c] Isolated yield after flash chromatography,
[d] 1.0 equivalent $B(O^pC_6H_4F)_3$, [e]N.D.= not determined.

The optimized catalyst system for the aryl and heteroaryl allylic acetates (5 mol % CpRu(II) salt, 5 mol % **102** or **104**, 15 mol % $B(O^pC_6H_4F)_3$, THF, 16 h) did not translate to the corresponding alkyl allylic acetates (Table 19). The catalyzed rearrangement of crotyl acetate provided the desired products **106** and **107** in very low yields using both ligands **104** (37 % yield) and **102** (36 % yield), with low regioselectivities especially in the case of ligand **104** (**106**:**107** 1.4:1). The reaction required the more electron rich ligand **105** to provide the product with a synthetically useful regioselectivity of 6:1 favoring the branched product **106**.

Table 19. Optimization of Reaction Conditions for Aliphatic Substrates



L=			
	104	**102**	**105**
	106:107[a]**=** 1.4:1 7:1 *anti:syn*[a] (**106**), 67% ee[b], 37% yield	**106:107**[a]**=**4:1 4:1 *anti:syn*[a] (**106**), 36% yield	**106:107**[a]**=**6:1 4:1 *anti:syn*[a] (**106**), 80% ee[b], 37% yield

[a] Determined by ^{1}H NMR; [b] Determined by chiral GLC

3.6 PROPOSED REACTION MECHANISM

The reaction mechanism is postulated to commence with association of the activated allylic acetate **108** to the CpRu(II)-imidazoline active catalyst **112**, forming complex **109** (Figure 13A). The reaction can then proceed via oxidative addition of the CpRu(II)-imidazoline across the allylic acetate C-O σ-bond with assistance from the Lewis acidic $B(O^pC_6H_4F)_3$ to form a Ru(IV) π–allyl complex **110**. Following oxidative addition, the resulting acetate leaving group could function to activate the latent enolate nucleophile **81a** through Lewis acid-base interaction with the silicon residue.[58,65] The resulting highly reactive enolate could then easily add to the π-allyl intermediate with a bias for attack at the more substituted carbon, forming the chelated product complex **111** with a preference for the *anti*- diastereomer. With the addition of acetonitrile, the Claisen-like product **82** gets expelled from the coordination sphere of the Ru-complex regenerating the active catalyst **112**.

Ruthenium-catalyzed allylic alkylation chemistry is generally known to proceed through π-allyl intermediates which should provide the *anti* and *syn* diastereomers (**82**$_{syn}$ and **82**$_{anti}$) with the same enantioselectivity. However, since the enantioselectivities of the *anti* and *syn* diastereomers were quite different, especially when utilizing the diphenyl substituted ligand **102** (95% ee **82a**$_{anti}$, 79% ee **82a**$_{syn}$) (See Table 18), we could not fully discount the possibility that the reaction proceeds through a metal-mediated S_N2' reaction mechanism.[66] In this case, the Ru(II)-complex would oxidatively add to the allylic acetate and form a Ru(II) σ-bonded enyl complex **114** or **115** (Figure 13B)**.** To further elucidate the exact nature of the mechanism we utilized the branched allylic acetate **113** under the optimized reaction conditions to determine if the opposite regioisomer was formed due to the formation of enyl complex **115**. However, the

substrate **113** provided the same branched substitution product **82a** as the linear allylic acetate **80a** (Figure 13B). This showcased that both the branched and linear substrates most likely proceed through the same Ru(IV)-π-allyl intermediate.

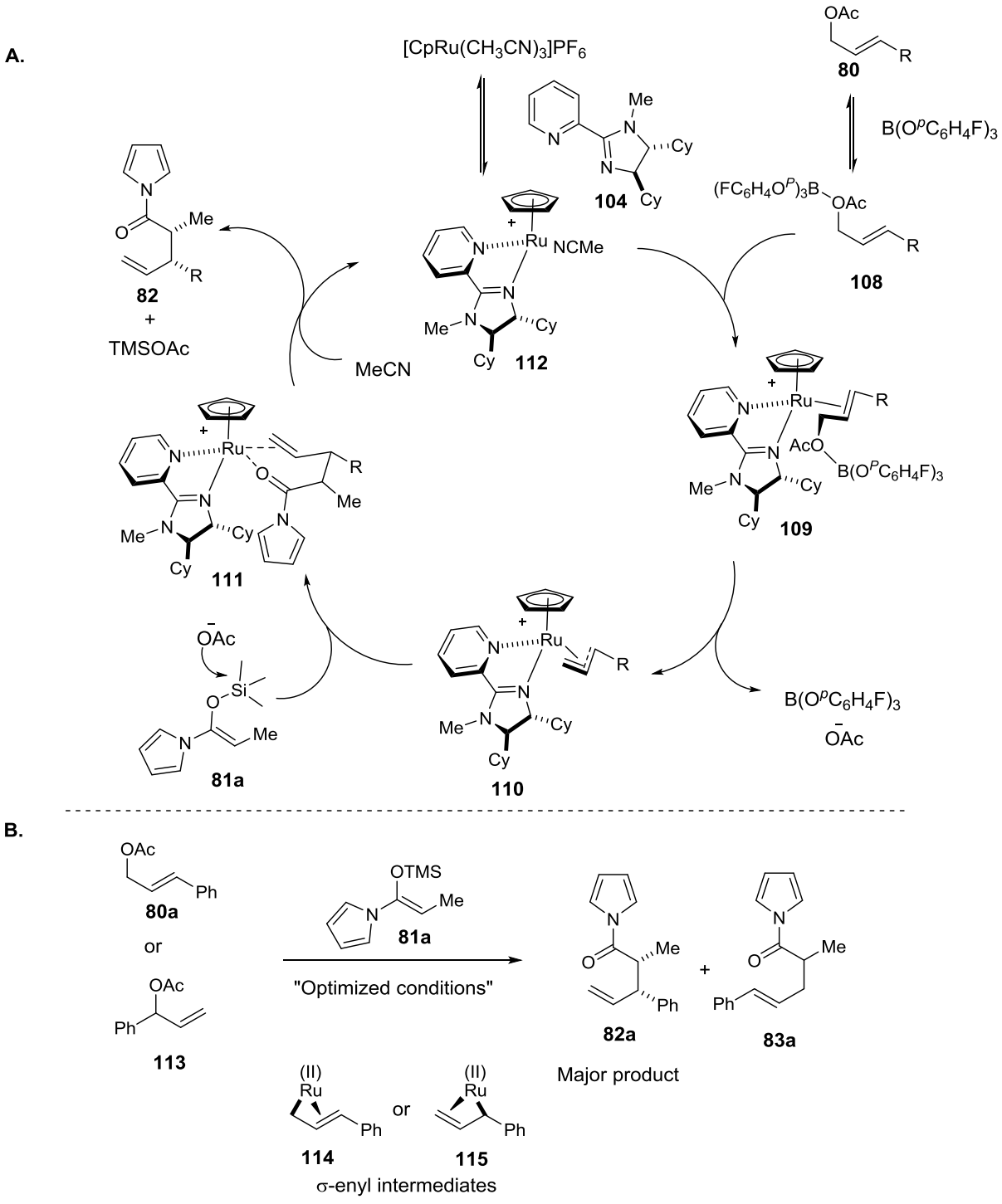


Figure 13. A. Proposed Reaction Mechanism; **B.** Evidence for a π-allyl Mechanism

The major product in our enolate allylic alkylation reaction is formed with a preference for the *anti*-diastereomer. Since the reaction proceeds through an intermolecular mechanism, there is no intrinsic mechanism for enforcing a highly ordered transition state. However, upon inspection of both possible antiperiplanar **116** and synclinal **117** transition states (Figure 14) there appears to be a lower energy conformer that could explain the observed *anti*-diastereomer. Both the antiperiplanar and synclinal transition states suffer from destabilizing gauche interactions, however, the antiperiplanar transition state **116** appears to be a lower energy conformer due to the presence of only two gauche interactions to the three observed in the synclinal transition state. As a result, this may be the reason the *anti*-diastereomer is formed in preference to the *syn*-diastereomer albeit without a high degree of selectivity. However, these transition states do not take into account the Ru(II) catalyst, therefore it is unclear if there are other steric and electronic interactions in play that affect the formation of the *anti* diastereomer.

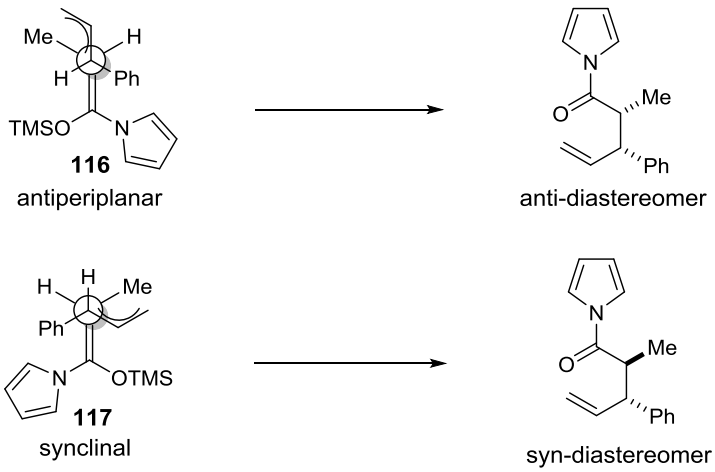


Figure 14. Antiperiplanar and Synclinal Transition States

3.7 CONCLUSIONS

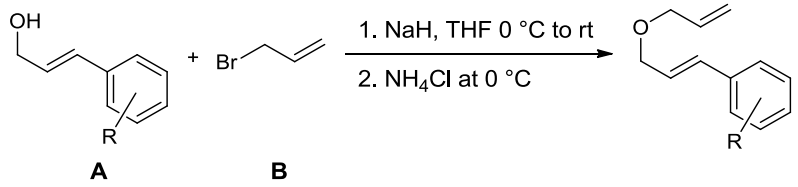
A highly regioselective, diastereoselective, and enantioselective ruthenium-catalyzed enolate allylic alkylation reaction that tolerates a variety of aromatic allylic acetates and pyrrole silyl enol ether nucleophiles has been developed. This reaction methodology provides a superior way to access a variety of Claisen-like products that were recently inaccessible due to trouble accessing allyl vinyl ethers. In addition, just about any aryl allylic acetate can be paired with a pyrrole silyl enol ether to provide an even greater substrate scope than listed in the above table. In addition, the resulting acyl pyrrole products can be easily derivatized to methyl esters, carboxylic acids and alcohols in a highly efficient manner, providing the potential for the products to be used in the construction of natural products.

4.0 EXPERIMENTAL

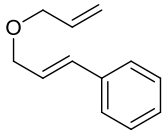
4.1 RUTHENIUM CATALYZED CLAISEN REARRANGEMENT

General Information: Unless otherwise stated, all reactions were performed in dry glassware under an atmosphere of oxygen-free nitrogen using standard inert atmosphere techniques for the manipulation of both solvents and reagents. Anhydrous solvents were obtained by passage through successive alumina- and Q5-packed columns on a solvent purification system. Acetone was distilled from Drierite and stored under nitrogen over 4 Å MS. Sodium hydride (60% dispersion in mineral oil) was purchased from Sigma-Aldrich and used as is. Crotyl and allyl bromide were purchased from Sigma-Aldrich and purified by distillation over CaH_2. $[Ir(COE)Cl]_2$, and PCy_3 were purchased from Strem, $[CpRu(CH_3CN)_3]PF_6$ from Sigma-Aldrich; these reagents were stored and weighed out in a nitrogen-filled glove box. NMR spectra were recorded on a Bruker Avance-300 (300 MHz) spectrometer with chemical shifts reported relative to residual $CHCl_3$ (7.26 ppm) for ^1H and $CDCl_3$ (77.00 ppm) for ^{13}C NMR spectra. High resolution mass spectra were obtained on a VG-7070 or Fisons Autospec high-resolution magnetic sector mass spectrometer. Analytical thin layer chromatography (TLC) was performed on EM Reagent 0.25 mm silica gel 60-F plates. Flash chromatography was performed over EM silica gel 60 (230-240 mesh). Analytical gas chromatography (GC) was performed using a Varian 3900 gas chromatograph with a flame ionization detector and split mode capillary

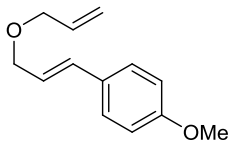
injection system using Varian Chirasil-Dex CB WCOT Fused Silica 25M x 0.25MM column (CP 7502).



General Procedure for the Synthesis of di(allyl) ethers (General Procedure A): Sodium hydride (2.5 eq, 60% suspension in mineral oil) was added to a 0 °C solution of alcohol **A** (1.0 equiv) in THF (0.5 M) and the reaction was stirred 30 min. Allylic bromide **B** (1.4 equiv) was added and the resulting suspension was warmed to ambient temperature and stirred for 3 h. A saturated solution of NH_4Cl (equal in volume to the reaction mixture) was added slowly at 0 °C to quench the reaction and the resulting mixture extracted with Et_2O (3x the initial volume of the reaction mixture). The combined organic extracts were dried over anhydrous $MgSO_4$, solvent removed *in vacuo*, and the residue purified as indicated in the text.

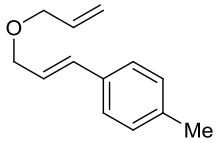


(*E*)-[3-(Allyloxy)prop-1-en-1-yl]benzene: This compounds characterization materials match the data provided in the following publication: Kerrigan, N. J.; Bungard, C. J.; Nelson, S. G. *Tetrahedron* **2008** (*64)* 6863-6869.

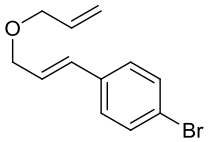


(*E*)-1-[3-(Allyloxy)prop-1-enyl]-4-methoxybenzene: General procedure A was followed employing (*E*)-3-(4-methoxyphenyl)prop-2-en-1-ol (1.0 g, 6.1 mmol) and allyl bromide (0.79 mL, 8.5 mmol) in THF. The crude product was

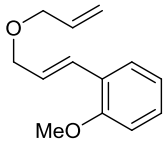
purified by flash chromatography over silica gel (1:1 Et_2O/hexanes) to yield 0.85 g (68%) of the title compound as a colorless oil. ^1H NMR (300 MHz, $CDCl_3$): δ 7.33 (d, *J* = 8.7, 2H), 6.85 (d, *J* = 6.6 Hz, 2H), 6.55 (d, *J* = 15.9 Hz, 1H), 6.17 (dt, *J* = 15.9, 6.3 Hz, 1H), 5.95 (app ddt, *J* = 15.9, 10.5, 5.7 Hz, 1H), 5.31 (dq, *J* = 17.1, 1.5 Hz, 1H), 5.23-5.18 (m, 1H) 4.13 (dd, 6.0, 1.2 Hz, 2H), 4.03 (dt, *J* = 5.4, 1.5 Hz, 1H), 3.80 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$): δ 159.1, 134.6, 132.0, 129.3, 127.5, 123.6, 116.9, 113.8, 70.89, 70.80, 55.1; IR ν_{max}^{neat} cm^{-1}: 3075, 2934, 2839, 1723, 1603, 1513, 1251, 1174, 1110, 833; HRMS (EI) *m/z* calcd for $C_{13}H_{16}O_2$ $(M)^+$: 204.1150; found: 204.1145.



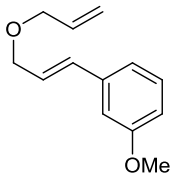
(*E*)-1-[3-(Allyloxy)prop-1-en-1-yl]-4-methylbenzene: This compounds characterization materials match the data provided in the following publication: Nishina, N. and Yamamoto, Y. *Tetrahedron Letters* **2008** (*49)* 4908-4911.



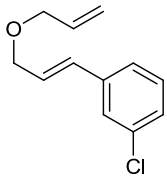
(*E*)-1-[3-(Allyloxy)prop-1-enyl]-4-bromobenzene: General procedure A was followed employing (*E*)-3-(4-bromophenyl)prop-2-en-1-ol (1.0 g, 4.7 mmol) and allyl bromide (0.49 mL, 5.7 mmol) in THF. The crude product was purified by flash chromatography over silica gel (1:1 Et_2O/hexanes) to yield 1.1 g (92%) of the title compound as a yellow oil. ^1H NMR (300 MHz, $CDCl_3$): δ 7.34 (d, *J* = 8.4 Hz, 2H), 7.25 (d, *J* = 8.1 Hz, 2H), 6.56 (d, *J* = 15.9 Hz, 1H), 6.29 (dt, *J* = 15.9, 5.7 Hz, 1H), 5.95 (ddt, *J* = 17.1, 10.5, 5.7 Hz, 1H), 5.32 (dd, *J* = 15.6, 1.5 Hz, 1H), 5.22 (dd, *J* = 10.2, 1.5 Hz, 1H), 4.14 (dd, *J* = 6.0, 1.2 Hz, 2H), 4.04 (dt, *J* = 5.7, 1.2 Hz, 2H); ^{13}C NMR (75 MHz, $CDCl_3$): δ 135.7, 134.6, 131.6, 130.9, 127.9, 126.9, 121.3, 117.1, 71.2, 70.4; IR ν_{max}^{neat} cm^{-1}: 2924, 2853, 1723, 1587, 1487, 1401, 1020, 819, 757; HRMS (EI) *m/z* calcd for $C_{12}H_{13}BrO$ $(M)^+$: 252.0149; found: 252.0151.



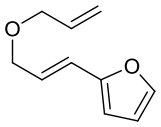
(*E*)-1-[3-(Allyloxy)prop-1-enyl]-2-methoxybenzene: General procedure A was followed employing (*E*)-3-(2-methoxyphenyl)prop-2-en-1-ol (3.0 g, 18 mmol) and allyl bromide (1.9 mL, 22 mmol) in THF. The crude product was purified by flash chromatography over silica gel (1:1 Et_2O/hexanes) to yield 3.5 g (94%) of the title compound as a colorless oil. ^{1}H NMR (300 MHz, $CDCl_3$): δ 7.46 (dd, *J* = 7.5, 1.2 Hz, 1H), 7.24 (t, *J* = 7.2 Hz, 1H), 6.97-6.86 (m, 3H), 6.32 (dt, *J* = 16.2, 6.3 Hz, 1H), 5.56 (ddt, *J* = 16.2, 10.8, 5.7 Hz, 1H), 5.32 (dd, *J* = 17.4, 1.5 Hz, 1H), 5.21 (dd, *J* = 10.2, 1.0 Hz, 1H), 4.18 (d, *J* = 6.0 Hz, 2H), 4.05 (d, *J* = 5.7 Hz, 2H), 3.85 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$): δ 156.6, 134.8, 128.6, 127.5, 126.9, 126.6, 125.6, 120.5, 117.0, 110.7, 71.2, 70.9, 55.3; IR ν_{max}^{neat} cm^{-1}: 3005, 2837, 1647, 1597, 1489, 1483, 1463, 1387.3, 1243, 975, 926, 752; HRMS (EI) *m/z* calcd for $C_{13}H_{16}O_2$ $(M)^+$: 204.1150; found: 204.1146.



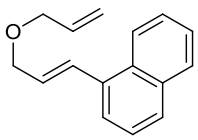
(*E*)-1-[3-(Allyloxy)prop-1-enyl]-3-methoxybenzene: General procedure A was followed employing (*E*)-3-(3-methoxyphenyl)prop-2-en-1-ol (1.9 g, 11 mmol) and allyl bromide (1.4 mL, 16 mmol) in THF. The crude product was purified by flash chromatography over silica gel (1:1 Et_2O/hexanes) to yield 2.1 g (91%) of the title compound as a colorless oil. ^{1}H NMR (300 MHz, $CDCl_3$): δ 7.23 (t, *J* = 15.6, 1H), 6.99 (d, *J* = 7.8 Hz, 1H), 6.93 (s, 1H), 6.81 (dd, *J* = 8.1, 2.5 Hz, 1H), 6.61 (d, *J* = 16.0 Hz, 1H), 6.34-6.25 (m, 2H), 4.88 (s, *J* = 6.6 Hz, 1H), 4.34 (dd, *J* = 6.0, 1.0 Hz, 2H), 3.81 (s, 3H), 1.58 (dd, *J* = 7.0, 1.5 Hz, 3H); ^{13}C NMR (75 MHz, $CDCl_3$): δ 159.6, 138.1, 134.6, 132.1, 129.4, 126.3, 119.8, 117.0, 113.2, 111.6, 71.0, 70.5, 55.1; IR ν_{max}^{neat} cm^{-1}: 3002, 2836, 1599, 1582, 1269, 1156, 1112, 1047, 969, 775, 689; HRMS (EI) *m/z* calcd for $C_{13}H_{16}O_2$ $(M)^+$: 204.1150; found: 204.1144.



(*E*)-1-[3-(Allyloxy)prop-1-enyl]-3-chlorobenzene: General procedure A was followed employing (*E*)-3-(3-chlorophenyl)prop-2-en-1-ol (2.6 g, 15 mmol) and allyl bromide (2.0 mL, 21 mmol) in THF. The crude product was purified by flash chromatography over silica gel (1:1 Et_2O/hexanes) to yield 2.8 g (88%) of the title compound as a pale orange oil. ^{1}H NMR (300 MHz, $CDCl_3$): δ 7.37 (s, 1H), 7.27-7.19 (m, 3H), 6.56 (d, *J* = 17.1 Hz, 1H), 6.31 (dt, *J* = 15.9, 6.0 Hz, 1H), 6.02-5.89 (m, 1H), 5.32 (dq, *J* = 17.1, 1.5 Hz, 1H), 5.22 (dq, *J* = 10.5, 1.5 Hz, 1H), 4.16 (dd, *J* = 5.7, 1.2 Hz, 2H), 4.05 (dt, *J* = 5.4, 1.5 Hz, 2H); ^{13}C NMR (75 MHz, $CDCl_3$): δ 138.5, 134.5, 134.4, 130.6, 129.7, 127.6, 127.4, 126.3, 124.5, 117.1, 71.2, 70.3; IR ν_{max}^{neat} cm^{-1}: 3078, 2849, 1739, 1593, 1565, 1473, 1425, 1356, 1077, 965, 772, 682; HRMS (EI) *m/z* calcd for $C_{12}H_{13}ClO$ $(M)^+$: 208.0653; found: 208.0654.

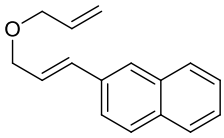


(*E*)-2-[3-(Allyloxy)prop-1-enyl]furan: General procedure A was followed employing (*E*)-3-(Furan-2-yl)prop-2-en-1-ol (2.0 g, 16 mmol) and allyl bromide (2.1 mL, 23 mmol) in THF. The crude product was purified by flash chromatography over silica gel (1:1 Et_2O/hexanes) to yield 2.5 g (93%) of the title compound as a pale yellow oil. ^{1}H NMR (300 MHz, $CDCl_3$): δ 7.34 (d, *J* = 1.2 Hz, 1H), 6.44 (d, *J* = 15.9 Hz, 1H), 6.35 (dd, *J* = 3.3, 1.8 Hz, 1H), 6.26-6.17 (m, 2H), 6.00-5.87 (m, 1H), 5.30 (dq, 17.1, 1.5 Hz, 1H), 5.22-5.18 (m, 1H); ^{13}C NMR (75 MHz, $CDCl_3$): δ 152.3, 141.9, 134.6, 124.6, 120.3, 116.9, 111.1, 107.8, 71.0, 70.0; IR ν_{max}^{neat} cm^{-1}: 2848, 1489, 1354, 1255, 1111, 1075, 1013, 961, 926, 735, 594; HRMS (EI) *m/z* calcd for $C_{16}H_{16}O$ $(M)^+$: 164.0837; found: 164.0835.

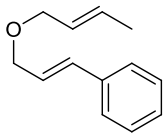


(*E*)-1-[3-(Allyloxy)prop-1-enyl]naphthalene: General procedure A was followed employing (*E*)-3-(Naphthalen-1-yl)prop-2-en-1-ol (0.50 g, 2.7 mmol)

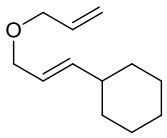
and allyl bromide (0.28 mL, 3.3 mmol) in THF. The crude product was purified by flash chromatography over silica gel (1:1 Et_2O/hexanes) to yield 376 mg (62%) of the title compound as a pale yellow oil. ^1H NMR (300 MHz, $CDCl_3$): δ 8.14-8.11 (m, 1H), 7.87-7.82 (m, 1H), 7.78 (d, *J* = 8.1 Hz, 1H), 7.62 (d, *J* = 7.2 Hz, 1H), 7.54-7.42 (m, 3H), 7.39 (d, *J* = 19.8 Hz, 1H), 6.34 (dt, *J* = 15.6, 5.7, 1H), 6.00 (ddt, *J* = 17.1, 10.5, 5.7 Hz, 1H), 5.36 (dq, *J* = 17.4, 1.8 Hz, 1H), 5.25 (dq, *J* = 10.2, 1.2 Hz, 1H), 4.28 (dd, *J* = 6.0, 1.5 Hz, 2H), 4.12 (dt, *J* = 5.4, 1.2 Hz, 2H); ^{13}C NMR (75 MHz, $CDCl_3$): δ 134.7, 134.5, 133.6, 131.1, 129.4, 129.3, 128.5, 127.9, 126.0, 125.7, 125.6, 123.9, 123.7, 117.1, 71.2, 70.8; IR ν_{max}^{neat} cm^{-1}: 3051, 2920, 1723, 1687, 1510, 1108, 778; HRMS (EI) *m/z* calcd for $C_{16}H_{16}O$ $(M)^+$: 224.1201; found: 224.1200.



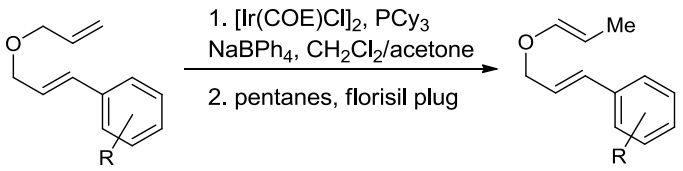
(*E*)-2-[3-(Allyloxy)prop-1-enyl]naphthalene: General procedure A was followed employing (*E*)-3-(Naphthalen-2-yl)prop-2-en-1-ol (798 mg, 4.33 mmol) and allyl bromide (0.56 mL, 6.1 mmol) in THF. The crude product was purified by flash chromatography over silica gel (1:1 Et_2O/hexanes) to yield 800 mg (82%) of the title compound as a white semisolid. ^1H NMR (300 MHz, $CDCl_3$): δ 7.80 (t, *J* = 4.5 Hz, 2H), 7.75 (d, *J* = 10.2 Hz, 2H), 7.61 (dd, *J* = 8.7, 1.2 Hz, 1H), 7.48-7.41 (m, 2H), 6.78 (d, *J* = 15.9 Hz, 1H), 6.43 (dt, *J* = 15.9, 6.0 Hz, 1H), 5.98 (ddd, *J* = 22.8, 11.1, 5.7 Hz, 1H), 5.34 (d, *J* = 17.1 Hz, 1H), 5.23 (d, *J* = 10.5 Hz, 1H), 4.21 (d, *J* = 6.0 Hz, 2H), 4.08 (d, *J* = 5.4 Hz, 2H); ^{13}C NMR (75 MHz, $CDCl_3$): δ 134.6, 134.1, 133.4, 132.9, 132.4, 128.1, 127.9, 127.6, 126.4, 126.3, 126.1, 125.8, 123.5, 117.1, 71.1, 70.7; IR ν_{max}^{neat} cm^{-1}:2923, 2849, 1664, 1623, 1122, 967, 859, 747; HRMS (EI) *m/z* calcd for $C_{16}H_{16}O$ $(M)^+$: 224.1201; found: 224.1198.



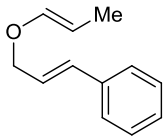
{(*E*)-3-[(*E*)-But-2-enyloxy]prop-1-enyl}benzene: General procedure A was followed employing cinnamyl alcohol (3.0 g, 22 mmol) and (*E*)-1-bromobut-2-ene (2.8 mL, 29 mmol) in THF. The crude product was purified by flash chromatography over silica gel (1:1 Et_2O/hexanes) to yield 3.3 g (79%) of the title compound as a pale yellow oil. ^{1}H NMR (300 MHz, $CDCl_3$): δ 7.44-7.24 (m, 5H), 6.64 (d, *J* = 15.9 Hz, 1H), 6.39-6.29 (m, 1H), 5.84-5.62 (m, 2H), 4.16 (app dq, *J* = 6.6, 1.5 Hz, 2H), 3.99 (dt, *J* = 6.0, 1.0 Hz, 2H), 3.53 (dd, *J* = 6.0, 1.0 Hz, 3H); ^{13}C NMR (75 MHz, $CDCl_3$): δ 136.6, 132.3, 132.2, 129.7, 128.4, 127.9, 127.5, 127.4, 126.7, 126.3, 126.1, 65.3, 17.7; IR ν_{max}^{neat} cm^{-1}: 3025, 2916, 2849, 1671, 1599, 1494, 1448, 1358, 1103, 1051, 966, 739, 692; HRMS (EI) *m/z* calcd for $C_{13}H_{16}O$ $(M)^+$: 188.1201; found: 188.1193.



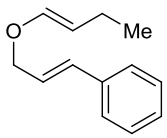
(*E*)-[3-(Allyloxy)prop-1-enyl]cyclohexane: General Procedure C was followed employing (*E*)-3-Cyclohexylprop-2-en-1-ol (2.6 g, 17 mmol) and allyl bromide (1.7 mL, 20 mmol) in THF. The crude product was purified by flash chromatography over silica gel (1:1 Et_2O/hexanes) to yield 3.0 g (99%) of the title compound as a pale orange oil. ^{1}H NMR (300 MHz, $CDCl_3$): δ 5.92 (ddt, *J* = 16.2, 10.8, 5.7 Hz, 1H), 5.65 (dd, *J* = 15.6, 6.3 Hz, 1H), 5.50 (dt, *J* = 15.3, 6.0 Hz, 1H), 5.27 (dd, *J* = 17.4, 1.5 Hz, 1H), 5.17 (d, *J* = 10.5 Hz, 1H), 3.96 (d, *J* = 5.7 Hz, 2H), 3.93 (d, *J* = 6.0 Hz, 2H), 1.97-1.91 (m, 1H), 1.74-1.62 (m, 5H), 1.33-1.01 (m, 4H), 0.88-0.83 (m, 1H); ^{13}C NMR (75 MHz, $CDCl_3$): δ 140.5, 134.9, 123.5, 116.9, 71.1, 70.8, 40.3, 32.7, 26.1, 26.0; IR ν_{max}^{neat} cm^{-1}: 2925, 2851, 1667, 1647, 1448, 1351, 1098, 970, 921; HRMS (EI) *m/z* calcd for $C_{12}H_{20}O$ $(M)^+$: 180.1514; found 180.1517.



General Procedure B. Synthesis of Allyl Vinyl Ethers 39a-k,67,68,70: $[Ir(cC_8H_{14})_2Cl]_2$ (0.5 mol %), PCy_3 (3 mol %) and $NaBPh_4$ (3 mol %) were combined in a flame dried flask in a nitrogen-filled glovebox. The flask was removed from the glovebox and a mixture of CH_2Cl_2/acetone (25:1, 0.67 M final concentration of the diallyl ether substrate) was added. The resulting yellow-orange solution was stirred for 5 min at ambient temperature. The diallyl ether (1.0 equiv) was added to the catalyst solution in a minimal amount of CH_2Cl_2 (≤5% of the total solvent volume) and the reaction was stirred for 10-60 min (until complete consumption of the starting material as monitored by TLC. The reaction mixture was concentrated under a stream of N_2 then pentanes (4x the reaction volume) were added and the resulting heterogeneous mixture was filtered through a Florisil® plug eluting with additional pentanes. The eluent was concentrated to afford the allyl vinyl ethers that were used in the subsequent reaction without further purification.

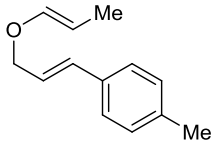


{(*E*)-3-[(*E*)-Prop-1-en-1-yloxy]prop-1-en-1-yl}benzene (39a): This compound's characterization materials match the data provided in the following publication: Kerrigan, N. J.; Bungard, C. J.; Nelson, S. G. *Tetrahedron* **2008**, *64*, 6863-6869.

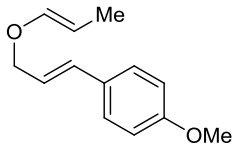


{(*E*)-3-[(*E*)-But-1-enyloxy]prop-1-enyl}benzene (39b): General procedure B was followed employing 1.0 g of ((*E*)-3-((*E*)-but-2-enyloxy)prop-1-enyl)benzene (5.3 mmol), 24 mg $[Ir(cC_8H_{14})_2Cl]_2$ (0.02 mmol), 45 mg of PCy_3 (0.16 mmol), and 36 mg of

$NaBPh_4$ (0.11 mmol). After 2 h the reaction mixture was filtered through a plug of Florisil® and purified further over silica gel (99:1 hexanes/Et_2O) to yield 0.38 g (38%) of the compound as a pale yellow oil. ^1H NMR (300 MHz, $CDCl_3$): δ 7.42-7.23 (m, 5H), 6.65 (d, *J* = 15.9 Hz, 1H), 6.36-6.28 (m, 2H), 4.91 (dt, *J* = 14.1, 7.2 Hz), 4.35 (dd, *J* = 6.0, 1.5 Hz, 2H), 1.96 (app dquin, *J* = 7.5, 1.5 Hz, 2H), 0.99 (t, *J* = 7.5 Hz, 3H); ^{13}C NMR (75 MHz, $CDCl_3$): δ 145.0, 143.7, 136.5, 132.6, 128.5, 127.7, 126.5, 124.8, 109.3, 106.9, 72.2, 69.7, 21.0, 15.2; IR ν_{max}^{neat} cm^{-1}: 3027, 2961, 2927, 2869, 2852, 1651, 1494, 1450, 1376, 1172, 1066, 965, 929, 739, 692; HRMS (EI) *m/z* calcd for $C_{13}H_{16}O$ $(M)^+$: 188.1201; found: 188.1193.

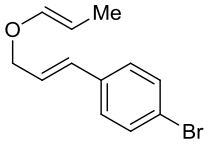


1-Methyl-4-{(*E*)-3-[(*E*)-prop-1-enyloxy]prop-1-enyl}benzene (39c): General procedure B was followed employing 2.1 g of (*E*)-1-(3-(allyloxy)prop-1-enyl)-4-methylbenzene (11 mmol), 50 mg $[Ir(cC_8H_{14})_2Cl]_2$ (0.060 mmol), 92 mg of PCy_3 (0.33 mmol), and 75 mg of $NaBPh_4$ (0.22 mmol). After 30 min the reaction mixture was filtered through a plug of Florisil® to yield 1.7 g (81%) of the compound as a pale yellow waxy solid. ^1H NMR (300 MHz, $CDCl_3$): δ 7.30 (d, *J* = 8.1 Hz, 2H), 7.14 (d, *J* = 8.1 Hz, 2H), 6.61 (d, *J* = 15.9 Hz, 1H) 6.31-6.22 (m, 2H), 4.88 (dq, *J* = 13.2, 6.6 Hz, 1H), 4.34 (dd, *J* = 6.0, 1.2 Hz, 2H), 2.34 (s, 3H), 1.58 (dd, *J* = 6.9, 1.5 Hz, 3H); ^{13}C NMR (75 MHz, $CDCl_3$): δ 146.0, 137.6, 133.6, 132.7, 129.2, 129.0, 126.4, 123.8, 99.4, 69.9, 21.1, 12.5; IR ν_{max}^{neat} cm^{-1}: 2930, 2900, 2855, 1654, 1512, 1457, 1377, 1186, 967, 939, 796; HRMS (EI) *m/z* calcd for $C_{13}H_{16}O$ $(M)^+$: 188.1201; found: 188.1196.

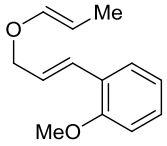


1-Methoxy-4-{(*E*)-3-[(*E*)-prop-1-enyloxy]prop-1-enyl}benzene (39d): General procedure B was followed employing 450 mg of (*E*)-1-[3-

(allyloxy)prop-1-enyl]-4-methoxybenzene (2.2 mmol), 20 mg $[Ir(cC_8H_{14})_2Cl]_2$ (0.020 mmol), 37 mg of PCy_3 (0.13 mmol), and 16 mg of $NaBPh_4$ (0.04 mmol). After 30 min the reaction mixture was filtered through a plug of Florisil® to yield 400 mg (89%) of the title compound as a flaky white solid. ^{1}H NMR (300 MHz, $CDCl_3$): δ 7.32 (d, *J* = 8.7 Hz, 2H), 6.85 (d, *J* = 8.7 Hz, 2H), 6.57 (d, *J* = 15.9 Hz, 1H), 6.26 (dd, *J* = 17.6, 1.5 Hz, 1H), 6.16 (dt, *J* = 15.9, 6.3 Hz, 1H), 4.86 (s, *J* = 6.6 Hz, 1H), 4.31 (dd, *J* = 6.0, 1.2 Hz, 2H), 3.80 (s, 3H), 1.56 (dd, *J* = 6.6, 1.5 Hz, 3H); ^{13}C NMR (75 MHz, $CDCl_3$): δ 159.2, 145.9, 132.3, 129.1, 127.6, 122.5, 113.8, 99.2, 69.9, 55.1, 12.5; IR ν_{max}^{neat} cm^{-1}: 3053, 2958, 2899, 2855, 1654, 1607, 1512, 1251, 1180, 966, 755; HRMS (EI) *m/z* calcd for $C_{13}H_{16}O_2$ $(M)^+$: 204.1150; found: 204.1146.

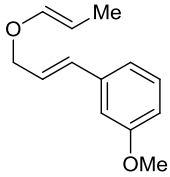


1-Bromo-4-{(*E*)-3-[(*E*)-prop-1-enyloxy]prop-1-enyl}benzene (39e): General procedure B was followed employing 2.7 g of (*E*)-1-[3-(Allyloxy)prop-1-enyl]-4-bromobenzene (11 mmol), 47 mg $[Ir(cC_8H_{14})_2Cl]_2$ (0.05 mmol), 88 mg of PCy_3 (0.31 mmol), and 72 mg of $NaBPh_4$ (0.21 mmol). After 30 min the reaction mixture was filtered through a plug of Florisil® to yield 2.0 g (75%) of the compound as a white waxy solid. ^{1}H NMR (300 MHz, $CDCl_3$): δ 7.44 (d, *J* = 8.4 Hz, 2H), 7.25 (d, *J* = 6.9 Hz, 2H), 6.57 (d, *J* = 16.2, 1H), 6.34-6.23 (m, 2H), 4.87 (dq, *J* = 13.5, 6.6 Hz, 1H), 4.33 (dd, *J* = 5.7, 1.2 Hz, 2H), 1.57 (dd, *J* = 6.6, 1.5 Hz, 3H); ^{13}C NMR (75 MHz, $CDCl_3$): δ 145.9, 135.4, 131.6, 131.2, 127.9, 125.7, 121.5, 99.5, 69.5, 12.5; IR ν_{max}^{neat} cm^{-1}: 2901, 2856, 1654, 1486, 1371, 1178, 969, 853, 799; HRMS (EI) *m/z* calcd for $C_{12}H_{13}BrO$ $(M)^+$: 252.0149; found: 252.0138.

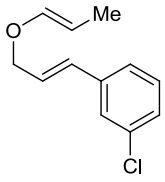


1-Methoxy-2-{(*E*)-3-[(*E*)-prop-1-enyloxy]prop-1-enyl}benzene (39f): General procedure B was followed employing 2.0 g of (*E*)-1-[3-(allyloxy)prop-1-enyl]-2-

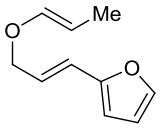
methoxybenzene (9.8 mmol), 44 mg $[Ir(cC_8H_{14})_2Cl]_2$ (0.05 mmol), 82 mg of PCy_3 (0.29 mmol), and 67 mg of $NaBPh_4$ (0.19 mmol). After 30 min the reaction mixture was filtered through a plug of Florisil® to yield 1.1 g (56%) of the compound as a colorless oil. ^{1}H NMR (300 MHz, $CDCl_3$): δ 7.45 (dd, *J* = 7.5, 1.2 Hz, 1H), 7.26-7.21 (m, 1H), 6.98-6.86 (m, 3H), 6.38-6.26 (m, 2H), 4.87 (dq, *J* = 13.5, 6.9 Hz, 1H), 4.36 (d, *J* = 6.9 Hz, 2H) 3.86 (s, 3H), 1.58 (dd, *J* = 6.6, 1.5 Hz, 3H); ^{13}C NMR (75 MHz, $CDCl_3$): δ 156.7, 146.0, 128.8, 127.8, 127.0, 125.5, 125.4, 120.5, 110.7, 99.2, 70.3, 55.3, 12.6; IR ν_{max}^{neat} cm^{-1}: 3031, 2934, 2052, 1897, 1784, 1656, 1597, 1490, 1244, 1174, 1028, 973, 927, 751; HRMS (EI) *m/z* calcd for $C_{12}H_{16}O_2$ $(M)^+$: 204.1150; found: 204.1145.



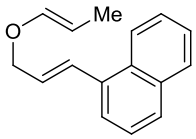
1-Methoxy-3-{(*E*)-3-[(*E*)-prop-1-enyloxy]prop-1-enyl}benzene (39g): General procedure B was followed employing 1.0 g of (*E*)-1-[3-(Allyloxy)prop-1-enyl]-3-methoxybenzene (4.9 mmol), 44 mg $[Ir(cC_8H_{14})_2Cl]_2$ (0.04 mmol), 82 mg of PCy_3 (0.29 mmol), and 36 mg of $NaBPh_4$ (0.09 mmol). After 30 min the reaction mixture was filtered through a plug of Florisil® to yield 0.80 g (80%) of the compound as a waxy colorless solid. ^{1}H NMR (300 MHz, $CDCl_3$): δ 7.26-7.21 (m, 1H), 6.95 (d, *J* = 7.8 Hz, 1H), 6.93 (s, 1H), 6.81 (dd, *J* = 8.1, 2.4 Hz, 1H), 6.61 (d, *J* = 16.0 Hz, 1H), 6.34-6.25 (m, 2H), 4.88 (sextet, *J* = 6.6 Hz, 1H), 4.34 (dd, *J* = 6.0, 1.0 Hz, 2H), 3.81 (s, 3H), 1.58 (dd, *J* = 7.0, 1.5 Hz, 3H); ^{13}C NMR (75 MHz, $CDCl_3$): δ 159.7, 145.9, 137.9, 132.4, 129.4, 125.2, 119.1, 113.4, 111.7, 99.4, 69.7, 55.1, 12.5; IR ν_{max}^{neat} cm^{-1}: 2935, 1656, 1599, 1581, 1489, 1455, 1263, 1172, 1047, 968, 927, 772, 688; HRMS (EI) *m/z* calcd for $C_{13}H_{16}O_2$ $(M)^+$: 243.0787; found: 243.0783.



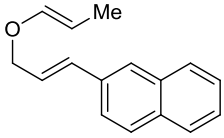
1-Chloro-3-{(*E*)-3-[(*E*)-prop-1-enyloxy]prop-1-enyl}benzene (39h): General procedure B was followed employing 1.0 g of (*E*)-1-[3-(Allyloxy)prop-1-enyl]-3-chlorobenzene (4.8 mmol), 43 mg $[Ir(cC_8H_{14})_2Cl]_2$ (0.04 mmol), 81 mg of PCy_3 (0.29 mmol), and 36 mg of $NaBPh_4$ (0.09 mmol). After 30 min the reaction mixture was filtered through a plug of Florisil® to yield 0.91 g (91%) of the compound as a colorless liquid. ^{1}H NMR (300 MHz, $CDCl_3$): δ 7.25-7.20 (m, 4H), 6.59 (dt, *J* = 16.2, 1.2 Hz, 1H), 6.36-6.24 (m, 2H), 4.88 (sextet, *J* = 6.6 Hz, 1H), 4.35 (dd, *J* = 5.7, 1.5 Hz, 2H), 1.59 (dd, *J* = 10.2, 3.3 Hz, 3H); ^{13}C NMR (75 MHz, $CDCl_3$): δ 145.9, 134.6, 133.1, 129.6, 128.76, 128.74, 127.8, 126.9, 126.8, 99.5, 69.6, 12.5; IR ν_{max}^{neat} cm^{-1}: 3060, 2923, 2858, 1656, 1593, 1565, 1397, 1176, 965, 927, 771, 682; HRMS (EI) *m/z* calcd for $C_{12}H_{13}ClO$ $(M)^+$: 208.0654; found: 208.0650.



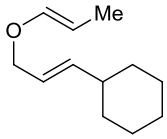
2-{(*E*)-3-[(*E*)-Prop-1-enyloxy]prop-1-enyl}furan (39i): General procedure B was followed employing 500 mg of (*E*)-2-[3-(Allyloxy)prop-1-enyl]furan (3.0 mmol), 27 mg $[Ir(cC_8H_{14})_2Cl]_2$ (0.04 mmol), 51 mg of PCy_3 (0.18 mmol), and 22 mg of $NaBPh_4$ (0.06 mmol). After 30 min the reaction mixture was filtered through a plug of Florisil® to yield 400 mg (80%) of the compound as an orange oil. ^{1}H NMR (300 MHz, $CDCl_3$): δ 7.34 (d, *J* = 1.5 Hz, 1H), 6.44, (d, *J* = 15.9 Hz, 1H), 6.36 (dd, *J* = 3.3, 1.8 Hz, 1H), 6.26-6.17 (m, 2H), 4.85 (sextet, *J* = 6.6 Hz, 1H), 4.31 (dd, *J* = 6.0, 1.2 Hz, 2H), 1.56 (dd, *J* = 6.6, 1.5 Hz, 3H); ^{13}C NMR (75 MHz, $CDCl_3$): δ 146.0, 142.1, 123.5, 120.6, 111.2, 108.2, 99.5, 59.3, 12.5; IR ν_{max}^{neat} cm^{-1}: 3059, 2925, 2858, 1657, 1489, 1457, 1377, 1175, 960, 926, 735; HRMS (EI) *m/z* calcd for $C_{10}H_{12}O_2$ $(M)^+$: 164.0837; found: 164.0833.



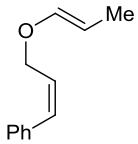
1-{(*E*)-3-[(*E*)-Prop-1-enyloxy]prop-1-enyl}naphthalene (39j): General procedure B was followed employing 854 mg of (*E*)-1-[3-(Allyloxy)prop-1-enyl]naphthalene (3.8 mmol), 17 mg $[Ir(cC_8H_{14})_2Cl]_2$ (0.02 mmol), 32 mg of PCy_3 (0.11 mmol), and 26 mg of $NaBPh_4$ (0.07 mmol). After 30 min the reaction mixture was filtered through a plug of Florisil® to yield 720 mg (85%) of the compound as a pale white waxy solid. ^{1}H NMR (300 MHz, $CDCl_3$): δ 8.13-8.09 (m, 1H), 7.87-7.84 (m, 1H), 7.79 (d, *J* = 8.1 Hz, 1H), 7.61 (d, *J* = 7.2 Hz, 1H), 7.55-7.45 (m, 3H), 7.40 (d, *J* = 15.9 Hz, 1H), 6.33 (app dq, *J* = 15.6, 5.7 Hz, 2H), 4.93 (dq, *J* = 13.2, 6.6 Hz, 1H), 4.46 (dd, *J* = 5.7, 1.2 Hz, 2H), 1.60 (dd, *J* = 6.6, 1.5 Hz, 3H); ^{13}C NMR (75 MHz, $CDCl_3$): δ 146.0, 134.3, 133.5, 131.1, 129.7, 128.4, 128.1, 128.0, 126.0, 125.7, 125.5, 123.9, 123.7, 99.5, 69.8, 12.5; IR ν_{max}^{neat} cm^{-1}: 3058, 2922, 2886, 2857, 1655, 1508, 1454, 1381, 1173, 965, 926, 776; HRMS (EI) *m/z* calcd for $C_{16}H_{16}O$ $(M)^+$: 224.1201; found: 224.1206.



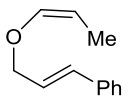
2-{(*E*)-3-[(*E*)-Prop-1-enyloxy]prop-1-enyl} naphthalene (39k): General procedure B was followed employing 760 mg of (*E*)-2-[3-(Allyloxy)prop-1-enyl]naphthalene (3.4 mmol), 30 mg $[Ir(cC_8H_{14})_2Cl]_2$ (0.03 mmol), 56 mg of PCy_3 (0.20 mmol), and 25 mg of $NaBPh_4$ (0.06 mmol). After 30 min the reaction mixture was filtered through a plug of Florisil® to yield 700 mg (93%) of the compound as a waxy colorless solid. ^{1}H NMR (300 MHz, $CDCl_3$): δ 7.82-7.75 (m, 4H), 7.61 (dd, *J* = 8.4, 1.5 Hz, 1H), 7.50-7.42 (m, 2H), 6.80 (d, *J* = 15.9 Hz, 1H), 6.43 (dt, *J* = 15.9, 6.0 Hz, 1H), 6.33-6.28 (m, 1H), 4.91 (sextet, 6.6 Hz, 1H), 4.40 (dd, *J* = 5.7, 1.2 Hz, 2H), 1.60 (dd, *J* = 6.6, 1.5 Hz, 3H); ^{13}C NMR (75 MHz, $CDCl_3$): δ 146.0, 133.9, 133.4, 133.0, 132.6, 128.1, 127.9, 127.6, 126.5, 126.2, 125.9, 125.2, 123.4, 99.4, 69.8, 12.5; IR ν_{max}^{neat} cm^{-1}: 3044, 2950, 2888, 1654, 1175, 966, 814, 740; HRMS (EI) *m/z* calcd for $C_{16}H_{16}O$ $(M)^+$: 224.1201; found: 224.1209.



{(*E*)-3-[(*E*)-Prop-1-enyloxy]prop-1-enyl}cyclohexane (70): General procedure B was followed employing 1.0 g of (*E*)-[3-(Allyloxy)prop-1-en-1-yl]cyclohexane (5.5 mmol), 25 mg $[Ir(cC_8H_{14})_2Cl]_2$ (0.02 mmol), 46 mg of PCy_3 (0.16 mmol), and 38 mg of $NaBPh_4$ (0.11 mmol). After 2 min the reaction mixture was filtered through a plug of Florisil® and purified further over silica gel (99:1 hexanes/Et_2O) to yield 0.21 g (21%) of the compound as a pale yellow oil. ^{1}H NMR (300 MHz, $CDCl_3$): δ 6.21 (dd, *J* = 9.6, 1.5 Hz, 1H), 5.65 (dd, 15.6, 6.6 Hz, 1H), 5.52 (dtd, *J* = 21.6, 6.0, 1.2 Hz, 1H), 4.80 (dq, *J* = 13.5, 6.6 Hz, 1H), 1.99-1.93 (m, 1H), 1.74-1.58 (m, 5H), 1.55 (dd, *J* = 6.6, 1.5 Hz, 3H), 1.33-1.01 (m, 4H), 0.90-0.86 (m, 1H); ^{13}C NMR (75 MHz, $CDCl_3$): δ 146.0, 141.0, 122.5, 98.9, 70.2, 40.3, 33.1, 32.5, 26.1, 25.9, 12.5; IR ν_{max}^{neat} cm^{-1}: 2925, 2852, 1657, 1448, 1382, 1264, 1179, 970, 929, 777; HRMS (EI) *m/z* calcd for $C_{12}H_{20}O$ $(M)^+$: 180.1514; found: 180.1517.

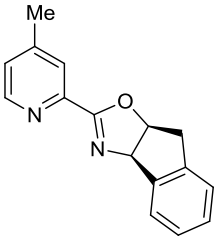


{(*Z*)-3-[(*E*)-Prop-1-enyloxy]prop-1-enyl}benzene (68): General procedure B was followed employing 470 mg of (*Z*)-[3-(Allyloxy)prop-1-enyl]benzene (2.7 mmol), 12 mg $[Ir(cC_8H_{14})_2Cl]_2$ (0.02 mmol), 23 mg of PCy_3 (0.08 mmol), and 19 mg of $NaBPh_4$ (0.05 mmol). After 30 min, the reaction mixture was filtered through a plug of Florisil® and further purified over silica gel (99:1 hexanes/Et_2O) to yield 340 mg (72%) of the compound as a clear colorless oil. ^{1}H NMR (300 MHz, $CDCl_3$): δ 7.41-7.22 (m, 5H), 6.66 (d, *J* = 11.7 Hz, 1H), 6.26 (dq, *J* = 12.6, 1.5 Hz, 1H), 5.89 (dt, *J* = 12.3, 6.3 Hz, 1H), 4.81 (app dq, *J* = 13.5, 6.6 Hz, 1H), 4.48 (dd, *J* = 6.3, 1.8 Hz, 2H), 1.57 (dd, *J* = 6.6, 1.5 Hz, 3H); ^{13}C NMR (75 MHz, $CDCl_3$): δ 145.9, 136.4, 131.9, 128.7, 128.3, 127.8, 127.3, 99.2, 65.8, 12.6; IR ν_{max}^{neat} cm^{-1}: 3026, 2924, 1657, 1493, 1169, 982; HRMS (EI) *m/z* calcd for $C_{12}H_{14}O$ $(M)^+$: 174.1044; found: 174.1038.

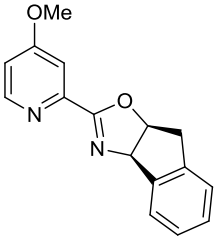


{(*E*)-3-[(*Z*)-Prop-1-en-1-yloxy]prop-1-en-1-yl}benzene (67): This

compound's characterization materials match the data provided in the following publication: Wipf, P.; Waller, D. L.; Reeves, J. T. *J. Org. Chem.* **2005**, *20*, 8096-8102.

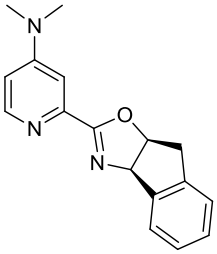


(3a*R*,8a*S*)-2-(4-Methylpyridin-2-yl)-8,8a-dihydro-3a*H*-indeno[1,2-d]oxazole (61a): (1*R*,2*S*)-1-Amino-2,3-dihydro-1*H*-inden-2-ol (0.95g, 4.2 mmol), 4-Methyl-2-cyanopyridine (0.50g, 4.2 mmol), $ZnCl_2$ (0.03 g, 0.21 mmol) and 8.5 mL of chlorobenzene were added to a round bottom flask fitted with a reflux condenser under an inert atmosphere of N_2. The reaction was heated to 130 °C for 24 h at which time the heat was removed and the mixture was allowed to slowly cool to ambient temperature. The chlorobenzene was removed *in vacuo* and the crude material purified over silica gel (0-3% $MeOH/CH_2Cl_2$) to yield a gray solid. This solid was triturated with cold Et_2O and filtered to provide 0.15 g (14%) of the title compound as a white solid. $[\alpha]_D^{19}$ +98.2 (*c* 1.11, $CHCl_3$); ^1H NMR (300 MHz, $CDCl_3$): δ 8.51 (d, *J* = 5.1 Hz, 1H), 7.89 (d, *J* = 0.6 Hz, 1H), 7.57-7.53 (m, 1H), 7.27-2.26 (m, 3H), 7.18 (dd, *J* = 5.1, 0.9 Hz, 1H), 6.89-6.78 (m, 3H), 5.80 (d, *J* = 7.8 Hz, 1H), 5.74 (ddd, *J* = 8.4, 6.0, 2.4 Hz, 1H), 3.55-3.39 (m, 2H), 2.33 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$): δ 163.6, 149.1, 148.2, 141.2, 139.7, 128.6, 127.4, 126.6, 125.3, 116.5, 115.7, 115.4, 84.0, 76.6, 39.5, 20.8; IR ν_{max}^{neat} cm^{-1}: 3068, 2945, 2908, 1640, 1510, 1458, 1354, 1196, 1098, 833, 749; HRMS (ES+) *m/z* calcd for $C_{16}H_{15}N_2O$ $(M + H)^+$: 251.1183; found: 251.1185.



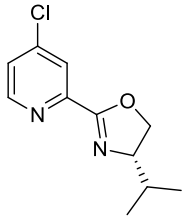
(3a*R*,8a*S*)-2-(4-Methoxypyridin-2-yl)-8,8a-dihydro-3a*H*-indeno[1,2-d]oxazole (61b) : (1*R*,2*S*)-1-amino-2,3-dihydro-1*H*-inden-2-ol (0.33g, 2.2 mmol), 4-Methoxy-2-cyanopyridine (0.20g, 2.2 mmol), $ZnCl_2$

(0.01 g, 0.08 mmol) and 5.0 mL of chlorobenzene were added to a round bottom flask fitted with a reflux condenser under an inert atmosphere of N_2. The reaction was heated to 130 °C for 24 h at which time the heat was removed and the mixture was allowed to slowly cool to ambient temperature. The chlorobenzene was removed *in vacuo* and the crude material purified over silica gel (0-3% MeOH/CH_2Cl_2) to 0.16 g (40%) of a gray solid. $[\alpha]_D^{19}$ +129 (*c* 1.03, $CHCl_3$); ^{1}H NMR (300 MHz, $CDCl_3$): δ 8.46 (d, *J* = 5.7 Hz, 1H), 7.57 (dd, *J* = 6.6, 3.0 Hz, 2H), 7.26 (d, *J* = 2.4 Hz, 3H), 6.86 (dd, *J* = 5.7, 2.7 Hz, 1H), 5.79 (d, *J* = 7.8 Hz, 1H), 5.57 (ddd, *J* = 8.1, 5.7, 2.7 Hz, 1H), 3.86 (s, 3H), 3.56-3.42 (m, 2H); ^{13}C NMR (75 MHz, $CDCl_3$): δ 165.9, 163.2, 150.7, 148.4, 141.5, 139.8, 128.5, 127.4, 125.6, 125.3, 112.3, 109.4, 83.9, 55.4, 39.6; IR ν_{max}^{neat} cm^{-1}: 3060, 3015, 2925, 1642, 1529, 1484, 1360, 1305, 1216, 1078, 1038, 750; HRMS (ES+) *m/z* calcd for $C_{16}H_{15}N_2O_2$ $(M + H)^+$: 267.1134; found: 267.1144.

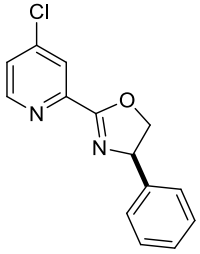


(3a*R*,8a*S*)-2-[4-(Pyrrolidin-1-yl)pyridin-2-yl]-8,8a-dihydro-3a*H*-indeno[1,2-d]oxazole (61c): (3a*R*,8a*S*)-2-(4-Chloropyridin-2-yl)-8,8a-dihydro-3a*H*-indeno[1,2-d]oxazole (0.10 g, 0.37 mmol) was added to a medium pressure reaction vessel along with pyrrolidine (1.2 mL, 15 mmol). The vessel was sealed and heated at 110 °C for 4 h. At this time the reaction vessel was removed from the oil bath and allowed to slowly cool to ambient temperature. The reaction was quenched with an equal volume of saturated NH_4Cl, and extracted (3 x equal volume of CH_2Cl_2), dried over anhydrous $MgSO_4$, and concentrated. The crude product was purified over silica gel (1-5% MeOH/CH_2Cl_2) to yield 0.63 g (56%) of the title compound as a foamy, tan solid. $[\alpha]_D^{19}$ +36 (*c* 0.94, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$):): δ 8.27(d, J = 6.0 Hz, 1H), 7.60–7.58 (m, 1H), 7.29–7.27 (m, 4H), 6.51 (dd, J = 6.0, 2.8 Hz, 1H), 5.78 (d, J = 8.0 Hz, 1H), 5.58–5.54 (m, 1H),

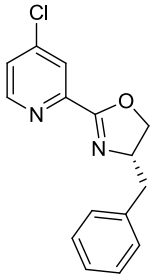
3.50–3.49 (m, 2H), 3.02 (s, 6H);^{13}C NMR (100 MHz, $CDCl_3$): δ 164.3, 154.7, 149.8, 147.0, 141.9, 140.1, 128.6, 127.5, 125.9, 125.5, 108.1, 107.0, 83.87, 77.2, 39.9, 39.4, 29.9; IR ν_{max}^{neat} cm^{-1}: 3031, 2922, 1601, 1511, 1378, 994; HRMS (ES+) *m/z* calcd for $C_{17}H_{17}N_3ONa$ (M)+: 302.1269; found: 302.1265



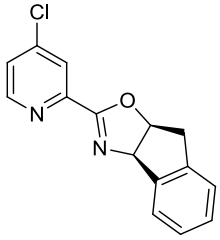
(*S*)-2-(4-Chloropyridin-2-yl)-4-isopropyl-4,5-dihydrooxazole: Characterization materials match the data provided in the following publication: Chelucci, G.; Deiru, S. P.; Saba, A.; Valenti, R. *Tetrahedron: Asymm.* **1999**, *10*, 1457-1464.



(*R*)-2-(4-Chloropyridin-2-yl)-4-phenyl-4,5-dihydrooxazole: Characterization materials match the data provided in the following publication: Chelucci, G.; Deiru, S. P.; Saba, A.; Valenti, R. *Tetrahedron: Asymm.* **1999**, *10*, 1457-1464.

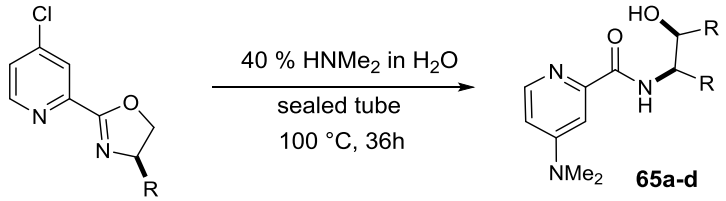


(*S*)-4-Benzyl-2-(4-chloropyridin-2-yl)-4,5-dihydrooxazole: Characterization materials match the data provided in the following publication: Chelucci, G.; Deiru, S. P.; Saba, A.; Valenti, R. *Tetrahedron: Asymm.* **1999**, *10*, 1457-1464.

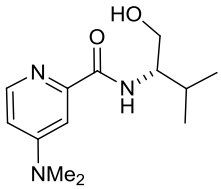


(8*R*,8a*S*)-8,8a-Dihydro-2-(4-chloropyridin-2-yl)-3a*H*-indeno[1,2-*d*]oxazole: 1.6 g of (1*R*,2*S*)-1-Amino-2,3-dihydro-1*H*-inden-2-ol (7.2 mmol), 1.0 g 4-Chloropicolinonitrile (7.2 mmol), 50 mg of $ZnCl_2$ (0.36 mmol) and 15 mL of chlorobenzene were added to a round bottom flask fitted with a reflux condenser under an inert atmosphere of N_2. The reaction was heated to 130 °C for 24 h at which time the heat was

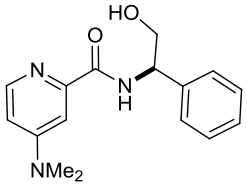
removed and the mixture was allowed to slowly cool to ambient temperature. The chlorobenzene was removed *in vacuo* and the crude material purified over silica gel (0-3% MeOH/CH_2Cl_2) to yield a gray solid. This solid was triturated with cold Et_2O and filtered to provide 1.5 g (76%) of the title compound as a white solid. MP 158-161 °C (dec). $[\alpha]_D^{19}$ +140. (*c* 1.03, $CHCl_3$); ^{1}H NMR (300 MHz, $CDCl_3$): δ 8.56 (d, *J* = 5.4 Hz, 1H), 8.06 (d, *J* = 1.8 Hz, 1H), 7.57 (dd, *J* = 5.4, 2.7 Hz, 1H), 7.36 (dd, *J* = 5.1, 1.8 Hz, 1H), 7.31-7.26 (m, 3H), 5.81 (d, *J* = 7.8 Hz, 1H), 5.61-5.56 (m, 1H), 3.53 (dd, *J* = 18.0, 6.3 Hz, 1H), 3.44 (dd, *J* = 18.0, 2.1 Hz, 1H); ^{13}C NMR (75 MHz, $CDCl_3$): δ 162.1, 150.3, 148.0, 144.6, 141.1, 139.5, 128.6, 127.4, 125.6, 125.5, 125.2, 124.3, 84.1, 39.5; IR ν_{max}^{neat} cm^{-1}: 3054, 1634, 1573, 1554, 1460, 1413, 1342, 1293, 1240, 1084, 997, 843, 751, 711, 690; HRMS (EI) *m/z* calcd for $C_{15}H_{11}ClN_2O$ $(M)^+$: 270.0555; found: 270.0549.



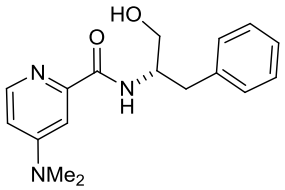
General Procedure for Dimethyl Amine Substituted Ligands (General Procedure C): Chloro-oxazoline ligand precursor was added to a medium pressure reaction vessel along with a 40% dimethylamine solution in H_2O. The vessel was sealed and heated at 110 °C for 36 h. At this time the reaction vessel was removed from the oil bath and allowed to slowly cool to ambient temperature. During this time a thick white precipitate formed. The crude reaction mixture was filtered, the solid collected and dried under high vacuum. Purification over silica gel as described in the text.



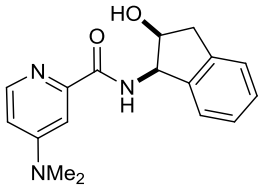
(*S*)-4-(Dimethylamino)-*N*-(1-hydroxy-3-methylbutan-2-yl)picolinamide (65a): General procedure C was followed employing (*S*)-2-(4-Chloropyridin-2-yl)-4-isopropyl-4,5-dihydrooxazole (0.40 g, 1.8 mmol) and dimethyl amine solution (8.0 mL). The crude material was purified over silica gel (97:3 CH_2Cl_2/MeOH) to yield 360 mg (85%) of the title compound as a white foam. $[\alpha]_D^{18}$ -36.2 (*c* 1.22, $CHCl_3$); ^{1}H NMR (300 MHz, $CDCl_3$): δ 8.26 (d, *J* = 8.1 Hz, 1H), 8.11 (d, *J* = 6.0 Hz, 1H), 7.41 (d, *J* = 2.7, 1H), 6.51 (dd, *J* = 6.0, 2.7 Hz, 1H), 3.91-3.72 (m, 2H), 3.03 (s, 6H), 2.03 (octet,*J* = 6.6Hz, 1H), 1.0 (app t, *J* = 6.6 Hz, 6H); ^{13}C NMR (75 MHz, $CDCl_3$): δ 166.2, 155.2, 149.8, 148.2, 107.9, 105.2, 64.3, 57.8, 39.2, 29.1, 19.6, 18.7; IR ν_{max}^{neat} cm^{-1}: 3365, 2959, 2868, 1657, 1613, 1525, 1446, 1377, 1225, 995; HRMS (EI) *m/z* calcd for $C_{13}H_{19}N_3O$ $(M)^+$: 233.1528; found: 233.1526.



(*R*)-4-(Dimethylamino)-*N*-(2-hydroxy-1-phenylethyl)picolinamide (65b): General procedure C was followed employing (*R*)-2-(4-Chloropyridin-2-yl)-4-phenyl-4,5-dihydrooxazole (0.10 g, 0.39 mmol) and dimethyl amine solution (2.0 mL). The crude material was purified over silica gel (97:3 CH_2Cl_2/MeOH) to yield 35 mg (34%) of the title compound as a white waxy solid. $[\alpha]_D^{18}$ + 2.84 (*c* 1.41, $CHCl_3$); ^{1}H NMR (300 MHz, $CDCl_3$): δ 8.71 (d, *J* = 7.2 Hz, 1H), 8.08 (d, *J* = 6.0 Hz, 1H), 7.43-7.35 (m, 5H), 7.30-7.25 (m, 1H), 6.51 (dd, *J* = 6.0, 2.7 Hz, 1H), 5.28-5.20 (m, 1H), 4.03-3.93 (m, 2H), 3.02 (s, 6 H); ^{13}C NMR (75 MHz, $CDCl_3$): δ 165.8, 155.1, 149.6, 148.1, 139.0, 128.7, 127.7, 126.8, 108.0, 105.3, 66.8, 56.4, 39.2; IR ν_{max}^{neat} cm^{-1}: 3371, 3060, 2928, 1665, 1589, 1522, 1464, 1289, 1072, 998, 750; HRMS (EI) *m/z* calcd for $C_{16}H_{17}N_3O$ $(M)^+$: 267.1371; found: 267.1369.

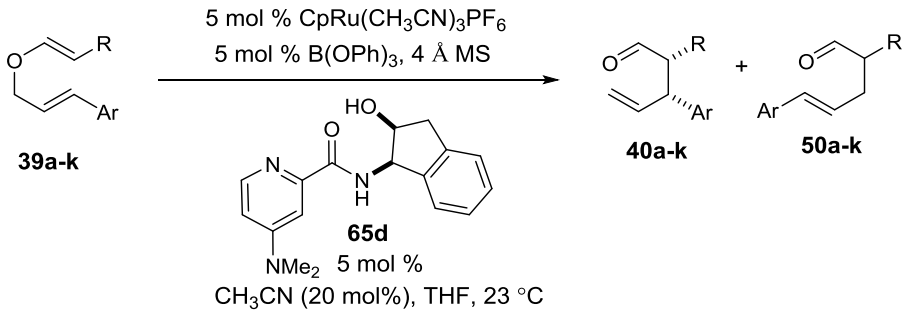


(*S*)-4-(Dimethylamino)-*N*-(1-hydroxy-3-phenylpropan-2-yl)picolinamide (65c): General procedure C was followed employing (*S*)-4-Benzyl-2-(4-chloropyridin-2-yl)-4,5-dihydrooxazole (0.27 g, 0.99 mmol) and dimethyl amine solution (4.5 mL). The crude material was purified over silica gel (97:3 CH_2Cl_2/MeOH) to yield 150 mg (53%) of the title compound as a white foam. $[\alpha]_D^{17}$ - 67.6 (*c* 1.05, $CHCl_3$); ^{1}H NMR (300 MHz, $CDCl_3$): δ 8.37 (d, *J* = 8.1 Hz, 1H), 8.07 (d, *J* = 6.0 Hz, 1H), 7.39 (d, *J* = 2.7 Hz, 1H), 7.29-7.27 (m, 1H), 7.25-7.16 (m, 1H), 6.47 (dd, *J* = 6.0, 2.7 Hz, 1H), 4.40-4.29 (m, 1H), 3.78 (dd, *J* = 11.4, 3.9 Hz, 1H), 3.69 (dd, *J* = 11.1, 5.1 Hz, 1H), 3.00 (s, 6H); ^{13}C NMR (75 MHz, $CDCl_3$): δ 165.5, 155.0, 149.7, 148.0, 137.9, 129.2, 128.4, 126.3, 107.6, 105.1, 63.7, 53.2, 39.1, 37.1; IR ν_{max}^{neat} cm^{-1}: 3365, 3026, 2927, 1657, 1605, 1523, 1443, 1377, 996; HRMS (ES+) *m/z* calcd for $C_{17}H_{22}N_3O_2$ $(M+H)^+$: 300.1534; found: 300.1540.



(1*R*,2*S*)-*N*-(2,3-Dihydro-2-hydroxy-1H-inden-1-yl)picolinamide (65d): General procedure C was followed employing (8*R*,8a*S*)-8,8a-Dihydro-2-(4-chloropyridin-2-yl)-3a*H*-indeno[1,2-*d*]oxa-zole (prepared above) 4.5 mL of a 40% dimethylamine solution in H_2O. The crude material was purified by column chromatography (SiO_2, 0-3% MeOH/CH_2Cl_2 gradient) to afford 150 mg (76%) of the title compound as a colorless solid. mp 214-216 °C (dec); $[\alpha]_D^{19}$ –52 (*c* 0.60, $CHCl_3$); ^{1}H NMR (300 MHz, $CDCl_3$): δ 8.63 (d, *J* = 8.4 Hz, 1H), 8.11 (d, *J* = 6.0 Hz, 1H), 7.50 (d, *J* = 2.7 Hz, 1H), 7.34 (d, *J* = 6.6 Hz, 1H), 7.29-7.21 (m, 4H), 6.54 (dd, *J* = 5.7, 2.7 Hz, 1H), 5.56 (dd, *J* = 8.7, 5.1 Hz, 1H), 4.76 (dt, *J* = 5.1, 2.7 Hz, 1H), 3.22 (dd, *J* = 16.5, 5.4 Hz, 1H), 3.07 (s, 6H), 3.07-2.99 (m, 1H); ^{13}C NMR (75 MHz, $CDCl_3$): δ 166.1, 155.1, 149.7, 148.3, 140.5, 140.2, 128.1, 127.1, 125.2, 124.7, 108.1, 105.3, 74.0, 57.8, 39.5, 39.2 (2C); IR ν_{max}^{neat} cm^{-1}: 2915, 1656, 1605, 1520,

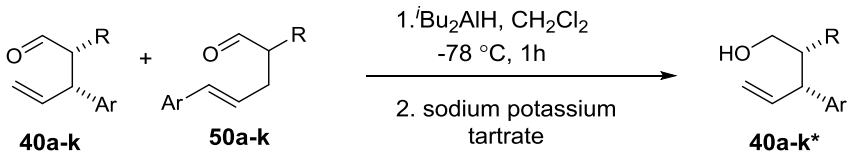
1377, 1225, 1057, 996, 911, 820, 733, 584; HRMS (EI) *m/z* calcd for $C_{17}H_{17}N_3O_2$ $(M)^+$: 297.1477; found: 297.1371.



General Procedure D. Catalytic Asymmetric Claisen Rearrangements of 39a-k: $[CpRu(CH_3CN)_3]PF_6$ (5 mol %) and picolinamide **65d** (5 mol %) were combined in a 2 dram vial inside a nitrogen-filled glovebox. The THF (0.5 M final concentration of the allyl vinyl ether substrate) was added and the reaction mixture was periodically shaken over 30 min. The resulting solution was added to another 2 dram vial containing the allyl vinyl ether (1 equiv), 4 Å MS (100 wt % relative to the allyl vinyl ether), $B(OPh)_3$ (5 mol %) and a Teflon-coated stir bar. The vial was sealed with a threaded cap containing a rubber septum inlet. Immediately after removal from the glovebox, CH_3CN (20 mol %) was added to the reaction mixture via syringe. The mixture was then stirred at ambient temperature for the indicated time (24-48 h). After this time, the vial was opened and the reaction mixture was concentrated under a stream of N_2. Pentanes (4x the reaction volume) were added and the resulting heterogeneous mixture was filtered through a Florisil® plug eluting with additional pentanes. The filtrate was concentrated and the resulting mixture of the *anti*/*syn* [3,3] products (**40a-k**) and [1,3] regioisomer (**50a-k**) was analyzed by ^1H NMR and chiral stationary phase GLC.

Enantiomer ratio determination: Enantiomer ratios of the [3,3] products (**40a-k**) were determined by chiral stationary phase GLC (Varian Chirasil-Dex CB WCOT Fused Silica CP 7502 column, 25 m x 0.25 mm) using authentic samples of racemic *syn* and *anti* diastereomers of the Claisen products for comparison. The racemic samples were prepared by thermal [3,3] rearrangement of the achiral allyl vinyl ethers that provided mixtures of the *syn* and *anti* Claisen diastereomers (+/–)-**40a-k**. The relative stereochemistry of the racemic samples was assigned by comparison to the know compounds (+/–)-*anti*-**40a**[67,68] or (+/–)-syn-**40a***.[68] The relative stereochemistry of the remaining racemic samples was assigned by analogy to these determinations and the widely precedented preference for thermal [3,3] rearrangements to afford the *syn* Claisen adducts as the major diastereomers.

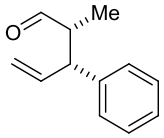
Compound characterization: Effective separation of the *anti* & *syn* [3,3] (**40a-k**) and [1,3] (**40a-k**) products of the catalyzed Claisen rearrangements could not be achieved using routine chromatography. Accordingly, full compound characterization was obtained for homogeneous samples of the primary alcohols obtained by hydride-mediated reduction of the mixture of aldehyde products (see General Procedure E).



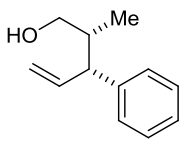
40a-k **50a-k** **40a-k***

General Procedure E. Reduction of Claisen Rearrangement-derived Aldehydes: The crude product mixtures obtained from General Procedure C were dissolved in CH_2Cl_2 (1 M) and cooled to −78 °C under an atmosphere of N_2. A 1.0 M heptane solution of $^{i}Bu_2AlH$ (1.5 equiv)

was added dropwise over 15 min and the reaction mixture was stirred an additional 2 h at −78 °C. The reaction was quenched by adding a saturated aqueous solution of sodium potassium tartrate (100% v/v relative to reaction volume) and the resulting biphasic mixture was warmed to ambient temperature. The mixture was stirred until two homogeneous phases were obtained and the phases were separated. The aqueous phase was extracted with diethyl ether (3x) and the combined organic portions were dried (Na_2SO_4) and concentrated. The crude product mixture was purified by flash chromatography over silica gel (10% ethyl acetate in hexanes eluent).

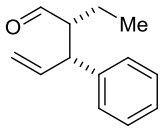


(2*R*,3*R*)-2-Methyl-3-phenylpent-4-enal (40a): General Procedure D was followed employing 100 mg (0.57 mmol) {(*E*)-3-[(*E*)-prop-1-enyloxy]prop-1-enyl}benzene (**39a**), 8.0 mg (0.028 mmol) ligand **65d**, 12.4 mg (0.028 mmol) $[CpRu(CH_3CN)_3]PF_6$, 8.3 mg (0.028 mmol) $B(OPh)_3$, 100 mg 4 Å MS, 6.0 μL (0.12 mmol) CH_3CN and 1.1 mL THF. The reaction mixture was stirred for 24 h at which time it was concentrated under a stream of N_2, filtered through a plug of Florisil® and concentrated to yield 91 mg (91%) of the product mixture containing compounds **40a** and **50a** as the only detectable materials. Separating the stereoisomers of **40a** by GLC {flow rate 1.5 mL/min, method: 90 °C for 10 min, ramp @ 0.7 °C/min to 160 °C, hold for 5 min; T_r (min) = 41.2 [(2*S*,3*S*)-**40a**$_{anti}$], 41.4 (**40a**$_{syn1}$), 42.3 (**40a**$_{syn2}$), 42.6 [(2*R*,3*R*)-**40a**$_{anti}$] (ratio = 11.7:1:19.3:317)} provided the enantiomer ratio (2*S*,3*S*)-**40a**$_{anti}$:(2*R*,3*R*)-**40a**$_{anti}$ = 3.6:96.4 (93% ee).

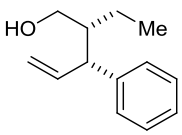


(2*R*,3*R*)-2-Methyl-3-phenylpent-4-en-1-ol (40a*): General Procedure E was followed employing 60 mg (0.34 mmol) of the aldehyde mixture obtained above and 0.52 mL of 1 M heptanes solution of $^{i}Bu_2AlH$ (0.52 mmol) in 0.4 mL CH_2Cl_2. The crude

product mixture was purified by column chromatography (SiO_2, 10% EtOAc/hexanes) to yield 38 mg (63%) of **40a*** as a colorless oil. $[\alpha]_D^{19}$ +100 (*c* 0.880, $CHCl_3$); ^1H NMR (300 MHz, $CDCl_3$): δ 7.33-7.26 (m, 2H), 7.22-7.18 (m, 3H), 6.02 (ddd, *J* = 18.0, 15.6, 9.6 Hz, 1H), 5.11 (dd, *J* = 6.0, 1.8 Hz, 1H), 5.06 (s, 1H), 3.49-3.45 (m, 1H), 3.33-3.29 (m, 1H), 3.22 (t, *J* = 9.0 Hz, 1H), 2.01 (septet, 6.9 Hz, 1H), 1.00 (d, *J* = 6.9 Hz, 3H); ^{13}C NMR (75 MHz, $CDCl_3$): δ 143.5, 139.7, 128.6, 127.6, 126.2, 115.8, 66.2, 53.0, 40.2, 14.6; IR ν_{max}^{neat} cm^{-1}: 3342, 3027, 2962, 1637, 1452, 1029, 913, 701; HRMS (EI) *m/z* calcd for $C_{12}H_{16}O$ $(M)^+$: 176.1201; found: 176.1196.

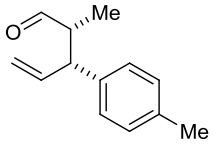


(2*R*,3*R*)-2-Ethyl-3-phenylpent-4-enal (40b): General Procedure D was followed employing 100 mg (0.53 mmol) {(*E*)-3-[(*E*)-but-1-enyloxy]prop-1-enyl}benzene (**39b**), 7.4 mg (0.026 mmol) ligand **65d**, 11.5 mg (0.026 mmol) $[CpRu(CH_3CN)_3]PF_6$, 7.7 mg (0.026 mmol) $B(OPh)_3$, 100 mg 4 Å MS, 5.6 μL (0.11 mmol) CH_3CN and 1.1 mL THF. The reaction mixture was stirred for 48 h at which time it was concentrated under a stream of N_2, filtered through a plug of Florisil® and concentrated to yield 89 mg (89%) of the product mixture containing compounds **40b** and **50b** as the only detectable materials. Separating the stereoisomers of **40b** by GLC {flow rate 0.6 mL/min, method: 105 °C for 10 min, ramp @ 0.7 °C/min to 160 °C, hold for 5 min; T_r (min) = 42.3 (**40b**$_{syn1}$), 42.9 (**40b**$_{syn2}$), 43.7 [(2*R*,3*R*)-**40b**$_{anti}$] (ratio = 1:16.5:94.5)} provided an ee of >99% for (2*R*,3*R*)-**40b**$_{anti}$ [(2*S*,3*S*)-**40b**$_{anti}$ not detected].

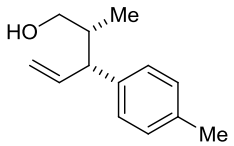


(2*R*,3*R*)-2-Ethyl-3-phenylpent-4-en-1-ol (40b*): General Procedure E was followed employing 64 mg (0.34 mmol) of the aldehyde mixture obtained above and 0.51 mL of 1 M heptanes solution of $^iBu_2AlH$ (0.51 mmol) in 0.40 mL CH_2Cl_2. The crude product mixture was purified by column chromatography (SiO_2, 10% EtOAc/hexanes) to yield

50 mg (77%) of the title compound as a colorless oil. $[\alpha]_D^{22}$ +76.7 (*c* 1.03, $CHCl_3$); ^1H NMR (300 MHz, $CDCl_3$): δ 7.34-7.29 (m, 2H), 7.26-7.18 (m, 3H), 6.03 (dt, *J* = 19.2, 9.9 Hz, 1H), 5.16-5.04 (m, 2H), 3.53 (dd, *J* = 11.1, 4.8 Hz, 1H), 3.41 (dd, *J* = 11.1, 4.5 Hz, 1H), 3.36 (t, *J* = 9.0 Hz, 1H), 1.80 (octet, *J* = 3.9 Hz, 1H), 1.62 (d sextets, *J* = 7.8, 3.9 Hz, 1H); 1.47-1.32 (m, 1H), 0.94 (t, *J* = 7.5 Hz, 3H); ^{13}C NMR (75 MHz, $CDCl_3$): δ 143.4, 140.3, 128.5, 127.7, 126.2, 115.6, 62.0, 51.7, 46.4, 20.6, 11.3; IR ν_{max}^{neat} cm^{-1}: 3354, 3077, 2961, 1636, 1600, 1454, 1033, 913; HRMS (EI) *m/z* calcd for $C_{13}H_{18}O$ $(M)^+$: 190.1357; found: 190.1352.

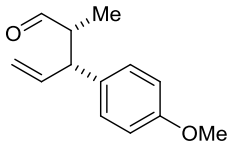


(2*R*,3*R*)-2-Methyl-3-*p*-tolylpent-4-enal (40c): General Procedure D was followed employing 100 mg (0.53 mmol) 1-methyl-4-{(*E*)-3-[(*E*)-prop-1-enyloxy]prop-1-enyl}benzene (**39c**), 7.4 mg (0.026 mmol) ligand **65d**, 12 mg (0.026 mmol) $[CpRu(CH_3CN)_3]PF_6$, 7.7 mg (0.026 mmol) $B(OPh)_3$, 100 mg 4 Å MS, 5.5 μL (0.11 mmol) CH_3CN and 1.1 mL THF. The reaction mixture was stirred for 24 h at which time it was concentrated under a stream of N_2, filtered through a plug of Florisil® and concentrated to yield 90 mg (90%) of the product mixture containing compounds **40c** and **50c** as the only detectable materials. Separating the stereoisomers by GLC {flow rate 1.5 mL/min, method: 90 °C for 10 min, ramp @ 0.7 °C/min to 160 °C, hold for 5 min; T_r (min) = 52.8 [(2*S*,3*S*)-**40c**$_{anti}$], 53.1 (**40c**$_{syn1}$), 54.3 (**40c**$_{syn2}$), 54.6 [(2*R*,3*R*)-**40c**$_{anti}$] (ratio = 4.8:1:11.7:90.7)} provided the enantiomer ratio (2*S*,3*S*)-**40c**$_{anti}$:(2*R*,3*R*)-**40c**$_{anti}$ = 5:95 (90% ee).

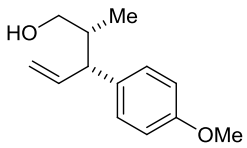


(2*R*,3*R*)-2-Methyl-3-*p*-tolylpent-4-en-1-ol (40c*): General Procedure E was followed employing 203 mg (1.07 mmol) of the aldehyde mixture obtained above and 1.6 mL of 1 M heptanes solution of $^iBu_2AlH$ (1.60 mmol) in 1.0 mL CH_2Cl_2. The crude product mixture was purified by column chromatography (SiO_2, 10% EtOAc/hexanes) to

yield 130 mg (63%) of the title compound as a colorless oil. $[\alpha]_D^{21}$ +76.6 (*c* 1.07, $CHCl_3$); ^1H NMR (300 MHz, $CDCl_3$): δ 7.14-7.08 (m, 4H), 6.00 (ddd, *J* = 18.0, 16.5, 9.3 Hz, 1H), 5.09 (d, *J* = 5.7 Hz, 1H), 5.04 (s, 1H), 3.48 (dd, *J* = 10.8, 4.8 Hz, 1H), 3.32 (dd, *J* = 10.8, 6.0 Hz, 1H), 3.17 (t, *J* = 9.0 Hz, 1H), 3.12 (s, 3H), 1.99 (septet, 6.9 Hz, 1H), 1.00 (d, *J* = 6.6 Hz, 3H); ^{13}C NMR (75 MHz, $CDCl_3$): δ 140.3, 140.0, 135.8, 129.3, 127.5, 115.2, 66.3, 52.7, 40.1, 20.9, 14.7; IR ν_{max}^{neat} cm^{-1}: 3344, 3075, 2923, 1637, 1512, 1456, 1030, 912; HRMS (EI) *m/z* calcd for $C_{13}H_{18}OK$ $(M+K)^+$: 229.0095; found: 229.1005.

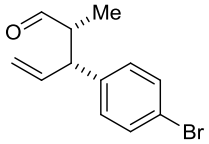


(2*R*,3*R*)-3-(4-Methoxyphenyl)-2-methylpent-4-enal (40d): General Procedure D was followed employing 100 mg (0.49 mmol) 1-methoxy-4-{(*E*)-3-[(*E*)-prop-1-enyloxy]prop-1-enyl}benzene (**39d**), 6.8 mg (0.024 mmol) ligand **65d**, 11 mg (0.024 mmol) $[CpRu(CH_3CN)_3]PF_6$, 7.1 mg (0.024 mmol) $B(OPh)_3$, 100 mg 4 Å MS, 5.1 μL (0.098 mmol) CH_3CN and 0.98 mL THF. The reaction mixture was stirred for 24 h at which time it was concentrated under a stream of N_2, filtered through a plug of Florisil® and concentrated to yield 86 mg (86%) of the product mixture containing compounds **40d** and **50d** as the only detectable materials. Separating the stereoisomers of **40d** by GLC {flow rate 0.4 mL/min, method: 105 °C for 10 min, ramp @ 0.7 °C/min to 160 °C, hold for 5 min; T_r (min) = 80.0 (**40d**$_{syn1}$), 80.2 [(2*S*,3*S*)-**40d**$_{anti}$], 80.6 (**40d**$_{syn2}$), 81.1 [(2*R*,3*R*)-**40d**$_{anti}$] (ratio = 1:2.0:7.2:39)} provided the enantiomer ratio (2*S*,3*S*)-**40d**$_{anti}$:(2*R*,3*R*)-**40d**$_{anti}$ = 4.9:95.1 (90% ee).

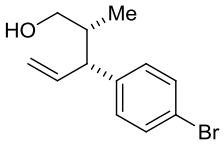


(2*R*,3*R*)-3-(4-Methoxyphenyl)-2-methylpent-4-en-1-ol (40d*): General Procedure E was followed employing 240 mg (1.17 mmol) of the aldehyde mixture obtained above and 1.76 mL of 1 M heptanes solution of $^iBu_2AlH$ (1.76 mmol) in 1.1 mL CH_2Cl_2. The

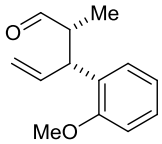
crude product mixture was purified by column chromatography (SiO_2, 10% EtOAc/hexanes) to yield 168 mg (70%) of the title compound as a colorless oil. $[\alpha]_D^{23}$ +90.3 (*c* 1.03, $CHCl_3$); ^1H NMR (300 MHz, $CDCl_3$): δ 7.12 (dt, *J* = 9.6, 3.0 Hz, 2H), 6.85 (dt, *J* = 9.6, 3.0 Hz, 2H), 5.99 (ddd, *J* = 18.9, 13.8, 9.3 Hz, 1H), 5.09-5.03 (m, 2H), 3.77 (s, 3H), 3.45 (dd, *J* = 10.5, 4.8 Hz, 1H), 3.27 (dd, *J* = 10.8, 6.3 Hz, 1H), 3.18 (t, *J* = 8.7 Hz, 1H), 2.03-1.89 (m, 2H), 0.99 (d, *J* = 6.6 Hz, 3H); ^{13}C NMR (75 MHz, $CDCl_3$): δ 157.7, 139.9, 135.4, 128.4, 115.3, 113.8, 65.9, 55.0, 51.9, 40.0, 14.5; IR ν_{max}^{neat} cm^{-1}: 3358, 2956, 2932, 1610, 1511, 1463, 1245, 1034, 913, 829; HRMS (EI) *m/z* calcd for $C_{13}H_{18}O_2$ (M): 206.1307; found: 206.1298.



(2*R*,3*R*)-3-(4-Bromophenyl)-2-methylpent-4-enal (40e): General Procedure D was followed employing 100 mg (0.39 mmol) 1-bromo-4-{(*E*)-3-[(*E*)-prop-1-enyloxy]prop-1-enyl}benzene (**39e**), 5.5 mg (0.019 mmol) ligand **65d**, 8.6 mg (0.019 mmol) $[CpRu(CH_3CN)_3]PF_6$, 5.6 mg (0.019 mmol) $B(OPh)_3$, 100 mg 4 Å MS, 4.1 μL (0.079 mmol) CH_3CN and 0.8 mL THF. The reaction mixture was stirred for 24 h at which time it was concentrated under a stream of N_2, filtered through a plug of Florisil® and concentrated to yield 92 mg (92%) of the product mixture containing compounds **40e** and **50e** as the only detectable materials. Separating the stereoisomers by GLC {flow rate 0.6 mL/min, method: 105 °C for 10 min, ramp @ 0.7 °C/min to 160 °C, hold for 5 min; T_r (min) = 79.6 (**40e**$_{syn1}$), 80.0 [(2*S*,3*S*)-**40e**$_{anti}$], 80.9 (**40e**$_{syn2}$), 81.1 [(2*R*,3*R*)-**40e**$_{anti}$] (ratio = 1:3.7:15.4:86.1)} provided the enantiomer ratio (2*S*,3*S*)-**40e**$_{anti}$:(2*R*,3*R*)-**40e**$_{anti}$ = 4:96 (92% ee).

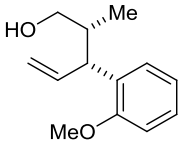


(2*R*,3*R*)-3-(4-Bromophenyl)-2-methylpent-4-en-1-ol (40e*): General Procedure E was followed employing 183 mg (0.72 mmol) of the aldehyde mixture obtained above and 1.09 mL of 1 M heptanes solution of $^{i}Bu_2AlH$ (1.09 mmol) in 0.7 mL CH_2Cl_2. The crude product mixture was purified by column chromatography (SiO_2, 10% EtOAc/hexanes) to yield 111 mg (60%) of the title compound as a colorless oil. $[\alpha]_D^{23}$ +62.5 (*c* 1.04, $CHCl_3$); ^1H NMR (300 MHz, $CDCl_3$): δ 7.42 (dt, *J* = 9.0, 3.0 Hz, 2H), 7.08 (dt, *J* = 9.0, 3.0 Hz, 2H), 6.01-5.90 (m, 1H), 5.11 (s, 1H), 5.07 (ddd, *J* = 7.5, 1.8, 1.0 Hz, 1H), 3.45 (dd, *J* = 10.8, 5.1 Hz, 1H), 3.30 (dd, *J* = 10.8, 6.0 Hz, 1H), 3.23 (t, *J* = 8.7 Hz, 1H), 2.03-1.90 (m, 1H), 0.98 (d, *J* = 6.9 Hz, 3H); ^{13}C NMR (75 MHz, $CDCl_3$): δ 142.5, 138.9, 131.5, 129.4, 119.8, 116.3, 65.8, 52.0, 40.0, 14.3; IR ν_{max}^{neat} cm^{-1}: 3340, 2962, 2926, 2877, 1637, 1487, 1402, 1073, 1030; HRMS (EI) *m/z* calcd for $C_{12}H_{15}BrO$ $(M)^+$: 254.0306; found: 254.0301.

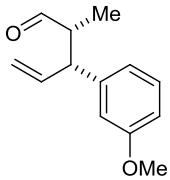


(2*R*,3*R*)-3-(2-Methoxyphenyl)-2-methylpent-4-enal (40f): General Procedure D was followed employing 100 mg (0.49 mmol) 1-methoxy-2-{(*E*)-3-[(*E*)-prop-1-enyloxy]prop-1-enyl}benzene (**39f**), 6.8 mg (0.024 mmol) ligand **65d**, 11 mg (0.024 mmol) $[CpRu(CH_3CN)_3]PF_6$, 7.1 mg (0.024 mmol) $B(OPh)_3$, 100 mg 4 Å MS, 5.1 μL (0.098 mmol) CH_3CN and 0.98 mL THF. The reaction mixture was stirred for 24 h at which time it was concentrated under a stream of N_2, filtered through a plug of Florisil® and concentrated to yield 89 mg (89%) of the product mixture containing compounds **40f** and **50f** as the only detectable materials. Separating the stereoisomers of **40f** by GLC {flow rate 0.6 mL/min, method: 105 °C for 10 min, ramp @ 0.7 °C/min to 160 °C, hold for 5 min, T_r (min) = 55.6 [(2*R*,3*R*)-**40f**$_{anti}$], 56.8 [(2*S*,3*S*)-**40f**$_{anti}$+**40f**$_{syn1}$), 57.3 (**40f**$_{syn2}$) (ratio = 35.4:4.0:1)} provided the enantiomer ratio (2*S*,3*S*)-**40f**$_{anti}$:(2*R*,3*R*)-**40f**$_{anti}$) = 89:11 (78% ee). The diastereomer ratio **40f**$_{anti}$:**40f**$_{syn}$ = 11:1)

was determined by integrating the aldehyde proton resonances (–C**H**O; *syn* δ 9.71, *anti* δ 9.52) in the ^{1}H NMR of the crude product mixture. Using this data, the contribution of the *syn* diastereomer to the unresolved GLC peak at T_r = 56.8 min could be calculated allowing the contribution of (2*S*,3*S*)-**40f**$_{anti}$ to be similarly calculated. This data was used in determining the enantiomer ratio [(2*S*,3*S*)-**40f**$_{anti}$:(2*R*,3*R*)-**40f**$_{anti}$)].

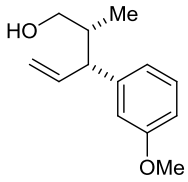


(2*R*,3*R*)-3-(2-Methoxyphenyl)-2-methylpent-4-en-1-ol (40f*): General Procedure E was followed employing 60 mg (0.29 mmol) of the aldehyde mixture obtained above and 0.44 mL of 1 M heptanes solution of ^{i}Bu$_2$AlH (0.44 mmol) in 0.3 mL CH_2Cl_2. The crude product mixture was purified by column chromatography (SiO_2, 10% EtOAc/hexanes) to yield 43 mg (71%) of the title compound as a colorless oil. $[\alpha]_D^{21}$ +30.4 (*c* 1.25, $CHCl_3$); ^{1}H NMR (300 MHz, $CDCl_3$): δ 7.21-7.14 (m, 2H), 6.97-6.86 (m, 2H), 6.09 (ddd, *J* = 17.1, 9.9, 9.3 Hz, 1H), 5.13-5.04 (m, 2H), 3.85 (s, 3H), 3.66 (t, 9.3 Hz, 1H), 3.38 (d, *J* = 10.8 Hz, 1H), 3.28 (dd, *J* = 11.1, 4.5 Hz, 1H), 2.00-1.88 (m, 1H), 1.06 (d, *J* = 6.9 Hz, 3H); ^{13}C NMR (75 MHz, $CDCl_3$): δ 156.3, 139.7, 131.9, 128.2, 127.1, 121.0, 115.7, 110.8, 66.1, 55.5, 45.0, 39.8, 15.2; IR ν_{max}^{neat} cm^{-1}: 3364, 3073, 2960, 2933, 2876, 1636, 1597, 1491, 1462, 1241, 1029, 753; HRMS (EI) *m/z* calcd for $C_{13}H_{18}O_2$ $(M)^+$: 206.1306; found: 206.1297.

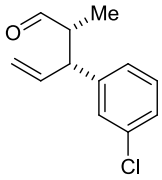


(2*R*,3*R*)-3-(3-Methoxyphenyl)-2-methylpent-4-enal (40g): General Procedure D was followed employing 100 mg (0.49 mmol) 1-methoxy-3-{(*E*)-3-[(*E*)-prop-1-enyloxy]prop-1-enyl}benzene (**39g**), 6.8 mg (0.024 mmol) ligand **65d**, 11 mg (0.024 mmol) $[CpRu(CH_3CN)_3]PF_6$, 7.0 mg (0.024 mmol) $B(OPh)_3$, 100 mg 4 Å MS, 5.1 μL (0.097 mmol) CH_3CN and 0.97 mL THF. The reaction mixture was stirred for 24 h at which

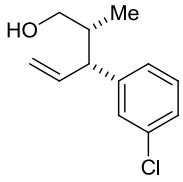
time it was concentrated under a stream of N_2, filtered through a plug of Florisil® and concentrated to yield 93 mg (93%) of the product mixture containing compounds **40g** and **50g** as the only detectable materials. Separating the stereoisomers of **40g** by GLC {flow rate 0.6 mL/min, method: 105 °C for 10 min, ramp @ 0.7 °C/min to 160 °C, hold for 5 min; T_r (min) = 63.8 (**40g**$_{syn1}$), 64.1 [(2*S*,3*S*)-**40g**$_{anti}$], 64.3 (**40g**$_{syn2}$), 64.8 [(2*R*,3*R*)-**40g**$_{anti}$] (ratio = 1:6.1:15.6:175)} provided the enantiomer ratio (2*S*,3*S*)-**40g**$_{anti}$:(2*R*,3*R*)-**40g**$_{anti}$ = 3.4:96.6 (93% ee).



(2*R*,3*R*)-3-(3-Methoxyphenyl)-2-methylpent-4-en-1-ol (40g*): General Procedure E was followed employing 150 mg (0.73 mmol) of the aldehyde mixture obtained above and 1.10 mL of 1 M heptanes solution of $^{i}Bu_2AlH$ (1.10 mmol) in 0.8 mL CH_2Cl_2. The crude product mixture was purified by column chromatography (SiO_2, 10% EtOAc/hexanes) to yield 100 mg (66%) of the title compound as a colorless oil. $[\alpha]_D^{22}$ +68.5 (*c* 1.08, $CHCl_3$); ^{1}H NMR (300 MHz, $CDCl_3$): δ 7.25-7.19 (m, 1H), 6.81-6.73 (m, 3H), 5.99 (ddd, *J* = 16.2, 10.8, 9.3 Hz, 1H), 5.10 (ddd, *J* = 7.5, 1.8, 0.6 Hz, 1H), 5.06 (s, 1H), 3.79 (s, 3H), 3.47 (dd, *J* = 10.8, 5.1 Hz, 1H), 3.32 (dd, *J* = 10.8, 6.0 Hz, 1H), 3.18 (t, *J* = 9.0 Hz, 1H), 2.07-1.94 (m, 1H), 1.00 (d, *J* = 6.9 Hz, 3H); ^{13}C NMR (75 MHz, $CDCl_3$): δ 159.7, 145.1, 139.5, 129.5, 120.0, 115.8, 113.6, 111.2, 66.2, 55.0, 53.0, 40.1, 14.6; IR ν_{max}^{neat} cm^{-1}: 3361, 3075, 2960, 1600, 1488, 1316, 1157, 1041, 916; HRMS (EI) *m/z* calcd for $C_{13}H_{18}O_2Na$ $(M+Na)^+$: 229.1204; found: 229.1208.

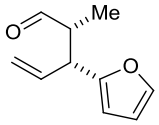


(2*R*,3*R*)-3-(3-Chlorophenyl)-2-methylpent-4-enal (40h): General Procedure D was followed employing 100 mg (0.48 mmol) 1-chloro-3-{(*E*)-3-[(*E*)-prop-1-enyloxy]prop-1-enyl}benzene (**39h**), 6.7 mg (0.024 mmol) ligand **65d**, 11 mg (0.024 mmol) $[CpRu(CH_3CN)_3]PF_6$, 6.9 mg (0.024 mmol) $B(OPh)_3$, 100 mg 4 Å MS, 5.0 μL (0.098 mmol) CH_3CN and 0.96 mL THF. The reaction mixture was stirred for 24 h at which time it was concentrated under a stream of N_2, filtered through a plug of Florisil® and concentrated to yield 78 mg (78%) of the product mixture containing compounds **40h** and **50h** as the only detectable materials. Separating the stereoisomers of **40h** by GLC {flow rate 0.6 mL/min, method: 105 °C for 10 min, ramp @ 0.7 °C/min to 160 °C, hold for 5 min; T_r (min) = 59.1 (**40h**$_{syn1}$), 59.8 [(2*S*,3*S*)-**40h**$_{anti}$], 59.8 (**40h**$_{syn2}$), 60.6 [(2*R*,3*R*)-**40h**$_{anti}$] (ratio = 1:2.6:19.7:146)} provided the enantiomer ratio (2*S*,3*S*)-**40h**$_{anti}$:(2*R*,3*R*)-**40h**$_{anti}$ = 1.8:98.2 (96% ee).

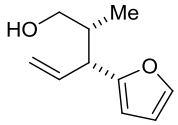


(2*R*,3*R*)-3-(3-Chlorophenyl)-2-methylpent-4-en-1-ol (40h*): General Procedure E was followed employing 60 mg (0.28 mmol) of the aldehyde mixture obtained above and 0.43 mL of 1 M heptanes solution of $^{i}Bu_2AlH$ (0.43 mmol) in 0.3 mL CH_2Cl_2. The crude product mixture was purified by column chromatography (SiO_2, 10% EtOAc/hexanes) to yield 42 mg (69%) of the title compound as a colorless oil. $[\alpha]_D^{23}$ +68.8 (*c* 1.60, $CHCl_3$); ^1H NMR (300 MHz, $CDCl_3$): δ 7.28-7.17 (m, 3H), 7.10 (dt, *J* = 7.2, 1.8 Hz, 1H), 5.98 (ddd, *J* = 16.2, 10.5, 9.3 Hz, 1H), 5.14 (s, 1H), 5.09 (dd, *J* = 7.8, 1.8 Hz, 1H), 3.48 (dd, *J* = 10.8, 4.8 Hz, 1H), 3.33 (dd, *J* = 10.8, 6.0 Hz, 1H), 3.26 (t, *J* = 9.0 Hz, 1H), 2.07-1.94 (m, 1H), 1.00 (d, *J* = 6.9 Hz, 3H); ^{13}C NMR (75 MHz, $CDCl_3$): δ 145.6, 138.8, 134.2, 129.7, 127.8,

126.3, 125.9, 116.5, 65.9, 52.3, 40.6, 14.3; IR ν_{max}^{neat} cm^{-1}: 3331, 2963, 1594, 1475, 1030, 918; HRMS (EI) *m/z* calcd for $C_{12}H_{15}ClO$ $(M)^+$: 210.0811; found: 210.0803.

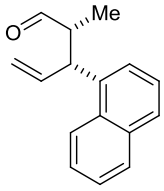


(2*R*,3*R*)-3-(Furan-2-yl)-2-methylpent-4-enal (40i): General Procedure D was followed employing 100 mg (0.61 mmol) 2-{(*E*)-3-[(*E*)-prop-1-enyloxy]prop-1-enyl}furan (**39i**), 8.5 mg (0.031 mmol) ligand **65d**, 13 mg (0.031 mmol) $[CpRu(CH_3CN)_3]PF_6$, 8.8 mg (0.031 mmol) $B(OPh)_3$, 100 mg 4 Å MS, 6.4 μL (0.121 mmol) CH_3CN and 1.2 mL THF. The reaction mixture was stirred for 48 h at which time it was concentrated under a stream of N_2, filtered through a plug of Florisil® and concentrated to yield 68 mg (68%) of the product mixture containing compounds **40i** and **50i** as the only detectable materials. The stereoisomers of **40i** could not be adequately resolved by GLC so the product mixture was reduced (General Procedure D) and the resulting mixture of alcohols used for determining the stereoisomer ratio.

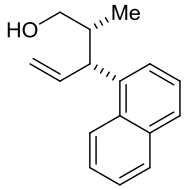


(2*R*,3*R*)-3-(Furan-2-yl)-2-methylpent-4-en-1-ol (40i*): General Procedure E was followed employing 95 mg (0.58 mmol) of the aldehyde mixture obtained above and 0.87 mL of 1 M heptanes solution of $^iBu_2AlH$ (0.87 mmol) in 0.6 mL CH_2Cl_2. The crude product mixture was purified by column chromatography (SiO_2, 10% EtOAc/hexanes) to yield 62 mg (65%) of the title compound as a colorless oil. Analyzing the crude product mixture by GLC (flow rate 3.5 mL/min, method: 80 °C for 10 min, ramp @ 0.5 °C/min to 130 °C, hold for 5 min, T_r (min) = 56.3 [(2*S*,3*S*)-**40i***], 56.6 (**40i***$_{syn1}$), 57.4 (**40i***$_{syn2}$), 58.2 [(2*S*,3*S*)-**40i***] (ratio = 1:4.7:1:53.8)} provided the diastereomer ratio **40i***$_{anti}$:**40i***$_{syn}$ = 10:1 and the enantiomer ratio (2*S*,3*S*)-**40i***:(2*R*,3*R*)-**40i*** = 1.8:98.2 (96% ee). $[\alpha]_D^{22}$ +92.6 (*c* 1.08, $CHCl_3$); ^1H NMR (300 MHz, $CDCl_3$): δ 7.33 (d, *J* = 1.2 Hz, 1H), 6.29 (dd, *J* = 3.0, 1.8 Hz, 1H), 6.04 (d, *J* = 3.0 Hz,

1H), 5.93 (ddd, *J* = 16.8, 10.2, 9.3 Hz, 1H), 5.17-5.10 (m, 2H) 3.54-3.38 (m, 3H), 2.12 (septet, *J* = 6.6 Hz, 1H), 0.91 (d, *J* = 6.9 Hz, 3H); ^{13}C NMR (75 MHz, $CDCl_3$): δ 156.3, 141.0, 136.0, 117.2, 110.0, 105.4, 65.9, 45.6, 38.8, 13.7; IR ν_{max}^{neat} cm^{-1}: 3342, 3078, 2930, 1639, 1504, 1420, 1222, 1148, 1032, 922; HRMS (EI) *m/z* calcd for $C_{12}H_{16}O$ $(M+K)^+$: 205.0631; found: 205.0646.

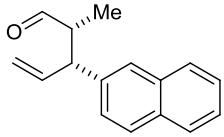


(2*R*,3*R*)-2-Methyl-3-(naphthalen-1-yl)pent-4-enal (40j): General Procedure D was followed employing 100 mg (0.46 mmol) 1-{(*E*)-3-[(*E*)-prop-1-enyloxy]prop-1-enyl}naphthalene (**39j**), 6.5 mg (0.023 mmol) ligand **65d**, 9.9 mg (0.023 mmol) $[CpRu(CH_3CN)_3]PF_6$, 6.7 mg (0.023 mmol) $B(OPh)_3$, 100 mg 4 Å MS, 4.8 μL (0.092 mmol) CH_3CN and 0.93 mL THF. The reaction mixture was stirred for 24 h at which time it was concentrated under a stream of N_2, filtered through a plug of Florisil® and concentrated to yield 90 mg (90%) of the product mixture containing compounds **40j** and **50j** as the only detectable materials. Separating the stereoisomers of **40j** by GLC {flow rate 1.0 mL/min, method: 105 °C for 10 min, ramp @ 0.7 °C/min to 200 °C, hold for 5 min; T_r (min) = 88.2 (**40j**$_{syn1}$), 86.6 (**40j**$_{syn2}$), 89.5 [(2*R*,3*R*)-**40j**$_{anti}$], 90.0 [(2*S*,3*S*)-**40j**$_{anti}$] (ratio = 11.3:1.4:73:1)} provided the enantiomer ratio (2*R*,3*R*)-**40j**$_{anti}$:(2*S*,3*S*)-**40j**$_{anti}$ = 98.6:1.4 (97% ee).

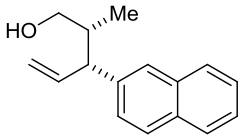


(2*R*,3*R*)-2-Methyl-3-(naphthalen-1-yl)pent-4-en-1-ol (40j*): General Procedure E was followed employing 65 mg (0.29 mmol) of the aldehyde mixture obtained above and 0.45 mL of 1 M heptanes solution of $^{i}Bu_2AlH$ (0.45 mmol) in 0.4 mL CH_2Cl_2. The crude product mixture was purified by column chromatography (SiO_2, 10% EtOAc/hexanes) to yield 37 mg (56%) of the title compound as a colorless oil. $[\alpha]_D^{23}$ –14.5 (*c* 1.45, $CHCl_3$); ^{1}H NMR (300 MHz, $CDCl_3$): δ 8.24 (d, *J* = 8.4 Hz, 1H), 7.88 (d, *J* = 9.0

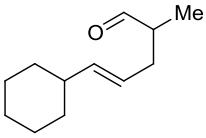
Hz, 1H), 7.74 (d, *J* = 7.8 Hz, 1H), 7.57-7.41 (m, 4H), 6.23 (dt, *J* = 19.5, 9.9 Hz, 1H), 5.32-5.13 (m 2H), 4.24 (t, *J* = 8.4 Hz, 1H), 3.51 (dd, *J* = 10.8, 5.7 Hz, 1H), 3.38 (dd, *J* = 10.5, 5.7 Hz, 1H), 2.25 (septet, *J* = 6.6 Hz, 1H), 1.04 (d, *J* = 6.9 Hz, 3H); ^{13}C NMR (75 MHz, $CDCl_3$): δ 139.7, 138.7, 134.1, 131.3, 128.9, 126.7, 125.9, 125.4, 125.3, 124.5, 123.2, 116.5, 66.2, 46.4, 39.9, 14.1; IR ν_{max}^{neat} cm^{-1}: 3346, 3048, 2926, 1635, 1596, 1460, 1029, 779; HRMS (EI) *m/z* calcd for $C_{16}H_{18}O$ $(M)^+$: 226.1357; found: 226.1368.



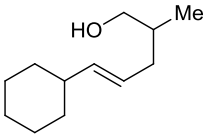
(2*R*,3*R*)-2-Methyl-3-(naphthalen-2-yl)pent-4-enal (40k): General Procedure D was followed employing 100 mg (0.46 mmol) 2-{(*E*)-3-[(*E*)-Prop-1-enyloxy]prop-1-enyl}naphthalene (**39k**), 6.5 mg (0.023 mmol) ligand **65d**, 9.9 mg (0.023 mmol) $[CpRu(CH_3CN)_3]PF_6$, 6.7 mg (0.023 mmol) $B(OPh)_3$, 100 mg 4 Å MS, 4.8 μL (0.092 mmol) CH_3CN and 0.93 mL THF. The reaction mixture was stirred for 24 h at which time it was concentrated under a stream of N_2, filtered through a plug of Florisil® and concentrated to yield 94 mg (94%) of the product mixture. Separating the stereoisomers of **40k** by GLC {flow rate 2.5 mL/min, method: 105 °C for 10 min, ramp @ 0.7 °C/min to 200 °C, hold for 5 min; T_r (min) = 80.1 (**40k**$_{syn1}$), 80.7 (**40k**$_{syn2}$ + (2*S*,3*S*)-**40k**$_{anti}$), 81.5 [(2*R*,3*R*)-**40k**$_{anti}$], (ratio = 76.4:10.9:1)}provided the enantiomer ratio (2*R*,3*R*)-**40k**$_{anti}$:(2*S*,3*S*)-**40k**$_{anti}$ = 92:8 (84% ee). The diastereomer ratio **40k**$_{anti}$:**40k**$_{syn}$ = 16:1 was determined by integrating the aldehyde proton resonances (–C**H**O; *syn* δ 9.74, *anti* δ 9.58) in the ^{1}H NMR of the crude product mixture. Using this data, the contribution of the *syn* diastereomer to the unresolved GLC peak at T_r = 80.7 min could be calculated allowing the contribution of (2*S*,3*S*)-**40k**$_{anti}$ to be similarly calculated. This data was used in determining the enantiomer ratio [(2*S*,3*S*)-**40k**$_{anti}$:(2*R*,3*R*)-**40k**$_{anti}$)].



(2*R*,3*R*)-2-Methyl-3-(naphthalen-2-yl)pent-4-en-1-ol (40k*): General Procedure E was followed employing 92 mg (0.41 mmol) of the aldehyde mixture and 0.63 mL $^{i}Bu_2AlH$ (0.63 mmol) in 0.5 mL CH_2Cl_2. The reaction was purified by column chromatography (SiO_2, 10% EtOAc/hexanes) to yield 44 mg (48%) of the title compound as a colorless oil. $[\alpha]_D^{21}$ +89.8 (*c* 1.27, $CHCl_3$); ^{1}H NMR (300 MHz, $CDCl_3$): δ 7.83-7.79 (m, 3H), 7.65 (s, 1H), 7.51-7.42 (m, 2H), 7.38 (dd, *J* = 8.7, 1.8 Hz, 1H), 6.13 (ddd, *J* = 19.5, 10.2, 9.3 Hz, 1H), 5.17 (d, *J* = 6.9 Hz, 1H), 5.13 (app s, 1H), 3.50 (dd, *J* = 10.8, 4.8 Hz, 1H), 3.42 (app t, *J* = 8.7 Hz, 1H), 3.35 (dd, *J* = 10.5, 6.0 Hz, 1H), 2.10-2.08 (m, 1H), 1.06 (d, *J* = 6.6 Hz, 3H); ^{13}C NMR (75 MHz, $CDCl_3$): δ 140.9, 139.5, 133.5, 132.1, 128.1, 127.5, 126.0, 126.0, 125.9, 125.3, 116.1, 66.19, 52.9, 39.9, 14.6; IR ν_{max}^{neat} cm^{-1}: 3347, 3055, 2962, 1633, 1599, 1507, 1458, 1372, 1029; HRMS (EI) *m/z* calcd for $C_{16}H_{18}O$ $(M)^+$: 249.1255; found: 249.1275.

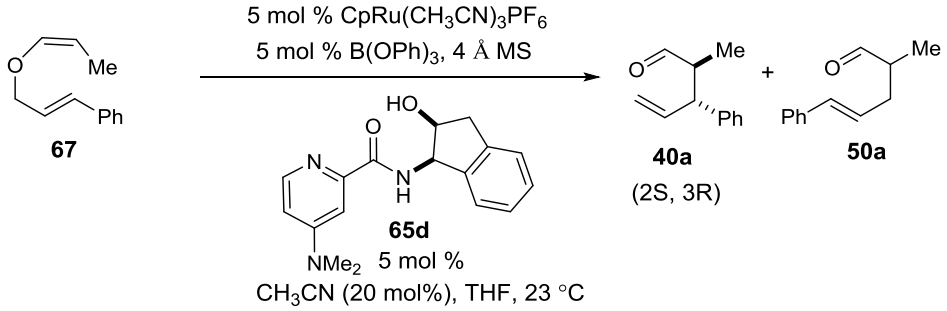


(*E*)-5-Cyclohexyl-2-methylpent-4-enal (72): General Procedure D was followed using $B(O^pC_6H_4F)_3$ in place of $B(OPh)_3$ and using the following quantities of reagents: 50 mg (0.27 mmol) {(*E*)-3-[(*E*)-Prop-1-enyloxy]prop-1-enyl}cyclohexane (**70**), 8.2 mg (0.027 mmol) ligand **65d**, 12.0 mg (0.027 mmol) $[CpRu(CH_3CN)_3]PF_6$, 9.5 mg (0.027 mmol) $B(O^pC_6H_4F)_3$, 50 mg 4 Å MS, 3.0 μL (0.055 mmol) CH_3CN and 0.60 mL THF. The reaction mixture was stirred for 24 h at which time it was concentrated under a stream of N_2, filtered through a plug of Florisil® and concentrated to yield 34 mg (70%) of the product mixture containing compound **72** as the only detectable material.



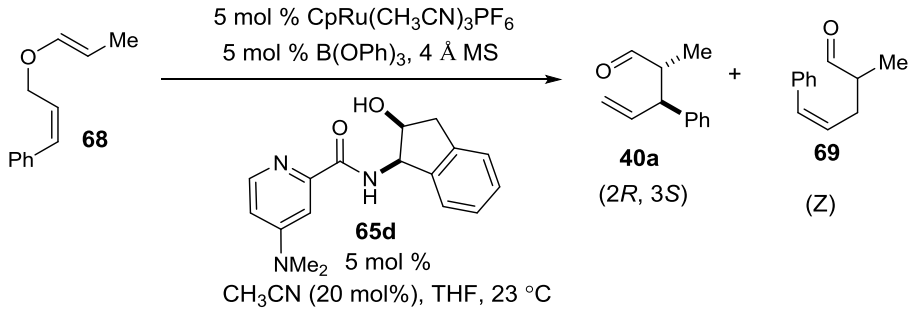
(*E*)-5-Cyclohexyl-2-methylpent-4-en-1-ol (72*): General Procedure E was followed employing 20 mg (0.11 mmol) of the aldehyde mixture obtained

above and 0.17 mL of 1 M heptanes solution of $^{i}Bu_2AlH$ (0.17 mmol) in 0.4 mL CH_2Cl_2. The crude product mixture was purified by column chromatography (SiO_2, 15% EtOAc/hexanes) to yield the title compound as a colorless oil. $[\alpha]_D^{30}$ –2.04 (*c* 1.16, $CHCl_3$); ^1H NMR (300 MHz, $CDCl_3$): δ 5.37 (m, 2H), 3.47 (dddd, *J* = 10.5, 6.3 Hz, 2H), 2.06 (m, 1H), 1.89 (m, 2H), 1.67 (m, 6H), 1.41 (bs, 1H), 1.26 (m, 3H), 1.07 (m, 2H), 0.89 (d, *J* = 6.9 Hz, 3H); ^{13}C NMR (75 MHz, $CDCl_3$): δ 138.4, 125.4, 68.1, 40.7, 36.7, 36.0, 33.2, 26.2, 26.1, 16.5; IR ν_{max}^{neat} cm^{-1}: 3337, 2973, 2851, 1448, 1083 ; HRMS (EI) *m/z* calcd for $C_{12}H_{22}O$ $(M)^+$: 182.1671; found: 182.1664. The enantiomer ratio was determined by converting **72*** to the corresponding (*S*)-*O*-methylmandelate ester and integrating the resonances corresponding to the C_2 methyl substituent (26% ee). [69]



Catalyzed rearrangement of {(*E*)-3-[(*Z*)-prop-1-enyloxy]prop-1-enyl}benzene (67): General Procedure D was followed employing 100 mg (0.57 mmol) {(*E*)-3-[(*Z*)-prop-1-enyloxy]prop-1-enyl}benzene (**67**), 8.0 mg (0.028 mmol) ligand **65d**, 12.4 mg (0.028 mmol) $[CpRu(CH_3CN)_3]PF_6$, 8.3 mg (0.028 mmol) $B(OPh)_3$, 100 mg 4 Å MS, 6.0 μL (0.115 mmol) CH_3CN and 1.1 mL THF. The reaction mixture was stirred for 24 h at which time it was concentrated under a stream of N_2, filtered through a plug of Florisil® and concentrated to yield

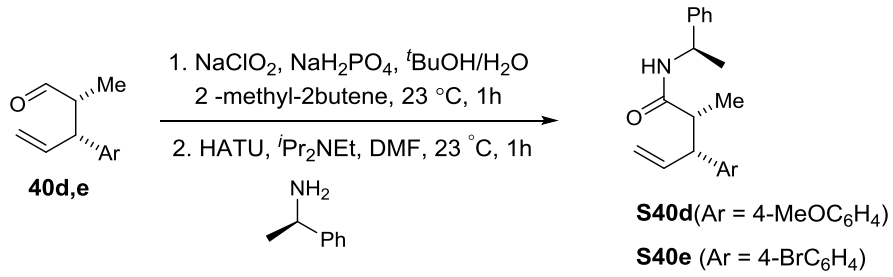
90 mg (90%) of the product mixture containing compounds **40a**$_{anti}$, **40a**$_{syn}$ and **50a** as the only detectable materials; **40a**:**50a** = 1:1 as determined by ^{1}H NMR analysis of the crude product mixture. Separating the stereoisomers of **40a** by GLC {flow rate 1.5 mL/min, method: 90 °C for 10 min, ramp @ 0.7 °C/min to 160 °C, hold for 5 min; T_r (min) = 41.2 [(2*S*,3*S*)-**40a**$_{anti}$], 41.4 [(2*R*,3*S*)-**40a**$_{syn}$], 42.3 [(2*S*,3*R*)-**40a**$_{syn}$], 42.6 [(2*R*,3*R*)-**40a**$_{anti}$] (ratio = 1:1:27.6:7.1)} provided the enantiomer ratio (2*R*,3*S*)-**40a**$_{syn}$:(2*S*,3*R*)-**40a**$_{syn}$ = 3.5:96.5 (93% ee), (2*S*,3*S*)-**40a**$_{anti}$:(2*R*,3*R*)-**40a**$_{anti}$ = 12.5:87.5 (75% ee) and a diastereomer ratio *syn*:*anti* = 3.5:1.



Catalyzed rearrangement of {(*Z*)-3-[(*E*)-prop-1-enyloxy]prop-1-enyl}benzene (68): General Procedure D was followed employing 100 mg (0.57 mmol) {(*Z*)-3-[(*E*)-prop-1-enyloxy]prop-1-enyl}benzene (**68**), 8.0 mg (0.028 mmol) ligand **65d**, 12.4 mg (0.028 mmol) [CpRu(CH_3CN)$_3$]PF_6, 8.3 mg (0.028 mmol) $B(OPh)_3$, 100 mg 4 Å MS, 6.0 μL (0.115 mmol) CH_3CN and 1.1 mL THF. The reaction mixture was stirred for 48 h at which time it was concentrated under a stream of N_2, filtered through a plug of Florisil® and concentrated; **40a**:**69** = 4:1 as determined by ^{1}H NMR analysis of the crude product mixture. The crude product mixture was purified by column chromatography (SiO_2, 3% EtOAc/hexanes) to yield 44 mg (44%) of the product mixture containing compounds **40a** and **69**. Separating the stereoisomers of **40a** by

GLC {flow rate 1.5 mL/min, method: 90 °C for 10 min, ramp @ 0.7 °C/min to 160 °C, hold for 5 min; T_r (min) = 41.2 [(2*S*,3*S*)-**40a**$_{anti}$], 41.4 [(2*R*,3*S*)-**40a**$_{syn}$], 42.3 [(2*S*,3*R*)-**40a**$_{syn}$], 42.6 [(2*R*,3*R*)-**40a**$_{anti}$] (ratio = 7.1:26.3:1:2)} provided the enantiomer ratio (2*R*,3*S*)-**40a**$_{syn}$:(2*S*,3*R*)-**40a**$_{syn}$ = 96.5:3.5 (93% ee), (2*S*,3*S*)-**40a**$_{anti}$:(2*R*,3*R*)-**40a**$_{anti}$ = 78:22 (56% ee) and a diastereomer ratio *syn*:*anti* = 3:1.

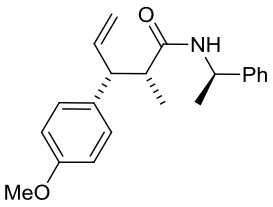
Stereochemical Proofs for Claisen Products. The absolute and relative stereochemistry of compounds (2*R*,3*R*)-**40d**$_{anti}$ and (2*R*,3*R*)-**40e**$_{anti}$ was unambiguously determined by converting these compounds to the corresponding (*R*)-α-methylbenzylamides **S40d** and **S40e** (General Procedure E), respectively, and X-ray diffraction analysis. The absolute stereochemistry of compounds **40a-k** was assigned by analogy to these determinations.



General Procedure F. Oxidation and amidation of aldehydes 40d$_{anti}$ **and 40e**$_{anti}$**:** To a magnetically-stirred solution of aldehyde **40d**$_{anti}$ or **40e**$_{anti}$ (1.0 equiv) and 2-methyl-2-butene (15 equiv) in *t*-BuOH (0.3 M in **40d,e**) was added a solution of $NaClO_2$ (3 equiv) and NaH_2PO_4 (2.6 equiv) in H_2O (1 M in $NaClO_2$) dropwise via syringe at ambient temperature. The reaction was stirred for 3 h whereupon a saturated aqueous solution of NH_4Cl (100% v/v to reaction volume) was added and the resulting mixture was extracted with Et_2O (3x). The combined organic

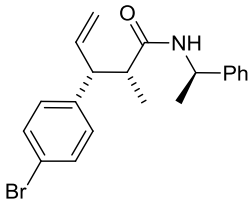
extracts were combined, dried ($MgSO_4$) and concentrated to provide the corresponding carboxylic acid that was used without purification in the next reaction.

To a solution of 2-(7-aza-1H-benzotriazide-1-yl)-1,1,3,3-tetramethyluronium hexafluorophosphate (HATU; 2 equiv) and *i*Pr_2NEt (2 equiv) in DMF (0.1 M) was added the carboxylic acid prepared above as a solution in a small volume of DMF. The reaction was stirred for 1 h at ambient temperature before (*R*)-α-methylbenzylamine (1 equiv) was added. The reaction was stirred for 24 h whereupon 1 M HCl (100% v/v to reaction volume) and the resulting mixture was extracted with Et_2O (3x). The combined organic extracts were dried ($MgSO_4$) and concentrated. The crude product mixture was purified by column chromatography (SiO_2, 20% EtOAc in hexanes) to yield the amides **S40d** and **S40e** as white solids; recrystallization provided X-ray-quality crystals (See appendix A and B).



(2*R*,3*R*)-3-(4-Methoxyphenyl)-2-methyl-*N*-{(*R*)-1-phenyl-ethyl}pent-4-enamide (S40d): General Procedure F was followed employing 168 mg (0.823 mmol) (2*R*,3*R*)-**40d**, 1.26 mL (11.9 mmol) 2-methyl-2-butene, 2.5 mL *t*BuOH, 223 mg (2.46 mmol) $NaClO_2$, 256 mg (2.14 mmol) NaH_2PO_4 and 2.5 mL of H_2O to yield 175 mg (97%) of the crude acid as a colorless oil. The crude acid (80 mg, 0.363) was combined with 226 mg (0.726 mmol) HATU, 100 μL (0.726 mmol) *i*Pr_2NEt and 46 μL (0.363 mmol) (*R*)-α-methylbenzylamine in 3.63 mL of DMF. Purifying the crude product mixture yielded 100 mg (85% over 2 steps) of the title compound as a colorless solid. Recrystallizing **S40d** from petroleum ether/EtOAc yielded crystals suitable for X-ray diffraction analysis (See Appendix A). mp 123.5-127 °C; ^{1}H NMR (300 MHz, $CDCl_3$): δ 7.16-7.13 (m, 3H), 7.07 (d, *J* = 9.0 Hz, 2H), 6.75 (d, *J* = 9.0 Hz, 2H), 6.70 (d, *J* = 2.0 Hz, 1H), 6.68 (d, *J* = 4.0

Hz, 1H) 5.89 (dt, *J* = 15.0, 12.0 Hz, 2H), 5.29 (d, *J* = 6.0 Hz, 1H), 5.12-5.05 (m, 2H), 4.90 (quintet, *J* = 6.0 Hz, 1H), 3.77 (s, 3H), 3.41 (t, *J* = 9.0 Hz, 1H) 2.40 (dq, *J* = 12.0, 6.0 Hz, 1H), 1.34 (d, *J* = 6.0 Hz, 3H), 1.24 (d, *J* = 6.0 Hz, 3H) ; ^{13}C NMR (75 MHz, $CDCl_3$): δ 173.8, 158.1, 142.5, 139.3, 134.9, 128.5, 128.2, 126.8, 125.9, 116.2, 114.0, 55.1, 53.2, 47.7, 47.5, 21.2, 16.6; IR ν_{max}^{neat} cm^{-1}: 3300, 3066, 2976, 2929, 1639, 1542, 1452, 1249, 1035, 923, 829, 699; HRMS (EI) *m/z* calcd for $C_{21}H_{25}NO_2$ $(M)^+$: 323.1882; found: 323.1885.

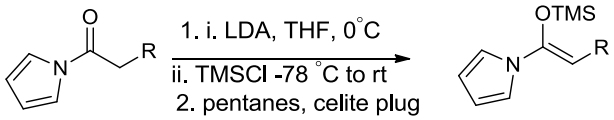


(2*R*,3*R*)-3-(4-Bromophenyl)-2-methyl-*N*-{(*R*)-1-phenylethyl} pent-4-enamide (S40e): General Procedure F was followed employing 238 mg (0.944 mmol) (2*R*,3*R*)-**40e**, 1.45 mL (13.7 mmol) 2-methyl-2-butene, 3.3 mL *t*BuOH, 256 mg (2.83 mmol) $NaClO_2$, 295 mg (2.45 mmol) NaH_2PO_4 and 3.3 mL of H_2O to yield 254 mg (100%) of the crude acid as a colorless oil. The crude acid (100 mg, 0.373) was combined with 283 mg (0.746 mmol) HATU, 105 μL (0.746 mmol) *i*Pr_2NEt and 47 μL (0.373 mmol) (*R*)-α-methylbenzylamine in 3.73 mL of DMF. Purifying the crude product mixture yielded 104 mg (75% over 2 steps) of the title compound as a colorless solid. Recrystallizing **S40e** from petroleum ether/EtOAc yielded crystals suitable for X-ray diffraction analysis (See Appendix B). mp 160-161.5 °C; ^{1}H NMR (300 MHz, $CDCl_3$): δ 7.32 (d, *J* = 8.4 Hz, 2H), 7.27-7.22 (m, 3H), 7.02 (d, *J* = 8.1 Hz, 2H), 6.71 (dd, *J* = 7.8, 2.4 Hz, 2H), 5.87 (dt, *J* = 18.9, 9.6 Hz, 1H), 5.30 (d, *J* = 7.8 Hz, 1H), 5.14 (d, *J* = 4.2 Hz, 1H), 5.09 (s, 1H), 4.89 (quintet, *J* = 7.2 Hz, 1H), 3.44 (t, *J* = 9.9 Hz, 1H), 2.37 (dq, J= 10.8, 6.6 Hz, 1H), 1.36 (d, *J* = 6.9 Hz, 3H), 1.26 (d, *J* = 6.6 Hz, 3H); ^{13}C NMR (75 MHz, $CDCl_3$): δ 173.4, 142.3, 141.8, 138.3, 131.6, 129.4, 128.4, 127.0, 125.7, 120.3, 117.1, 53.3, 47.9, 47.4, 21.1, 16.7; IR ν_{max}^{neat} cm^{-1}: 3300, 3066, 2976, 1639,

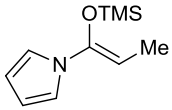
1542, 1512, 1452, 1249, 1035, 923, 829, 699; HRMS (EI) *m/z* calcd for $C_{20}H_{22}BrNONa$ $(M+Na)^+$: 394.0799; found: 394.0807.

4.2 RUTHENIUM CATALYZED ENOLATE ALLYLIC ALKYLATIONS

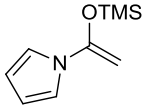
General Information: Unless otherwise indicated, all reactions were performed in dry glassware under an atmosphere of oxygen-free nitrogen using standard inert atmosphere techniques for the manipulation of both solvents and reagents. Anhydrous solvents were obtained by passage through successive alumina- and Q5-packed columns on a solvent purification system. $[CpRu(CH_3CN)_3]PF_6$ was synthesized according to the published procedure[70] and was stored and weighed out in a nitrogen-filled glove box. NMR spectra were recorded at the indicated magnetic field strengths with chemical shifts reported relative to residual C**H**Cl_3 (7.26 ppm) for ^{1}H and **C**DCl_3 (77.0 ppm) for ^{13}C spectra. Analytical thin layer chromatography (TLC) was performed on 0.25 mm silica gel 60-F plates. Flash chromatography was performed over silica gel (230-240 mesh). Analytical gas chromatography (GC) was performed using a flame ionization detector and split mode capillary injection system using Varian Chirasil-Dex CB WCOT fused silica 25 m x 0.25 mm column (CP 7502). Analytical high-performance liquid chromatography (HPLC) was performed using a variable wavelength UV detector (deuterium lamp, 190-600 nm) using a Chiracel OD-H column and HPLC-grade isopropanol and hexanes as the eluting solvents. Melting points were obtained on a Laboratory Devices Mel-Temp apparatus and are uncorrected.



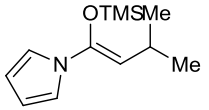
General Procedure A. Synthesis of pyrrole silyl enol ethers 81a-f: To a 0 °C solution of diisopropylamine (1.0 equiv) in THF (1.6M relative to diisopropylamine) was added a solution of 1.6M *n*-BuLi in hexanes (1.1 equiv). The reaction was allowed to stir at 0 °C for 10 min and then cooled to -78 °C. Next, a 0.8M solution of acylpyrrole (1.0 equiv) in THF was added dropwise to the reaction vessel over 5 min and the resulting solution was allowed to stir at -78 °C for 30 min. TMSCl (1.1 equiv) was added dropwise over 5 min, and the reaction was allowed to stir an additional 20 min at -78 °C. The dry ice/acetone bath was removed and the reaction was allowed to stir for an additional 1 h. Next, the reaction was diluted with pentane (4x the reaction volume), and the heterogeneous mixture was filtered through a plug of celite and concentrated. The final product was purified via kugelrohr distillation.



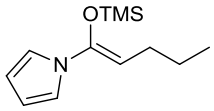
(*Z*)-1-{1-[(Trimethylsilyl)oxy]prop-1-en-1-yl}-1H-pyrrole (81a): Characterization materials match the data provided in the following publication: Evans, D. A.; Johnson, D. S.; *Org. Lett.* **1999**, *1*, 595-598.



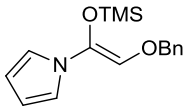
1-{1-[(trimethylsilyl)oxy]vinyl}-1H-pyrrole (81b): Characterization materials match the data provided in the following publication: Frick, U.; Simchen, G. *Liebigs Ann.* **1987**, *10*, 839-845.



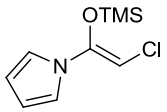
(*Z*)-1-{3-Methyl-1-[(trimethylsilyl)oxy]but-1-en-1-yl}-1H-pyrrole (81c): Characterization materials match the data provided in the following publication : Evans, D. A.; Johnson, D. S.; *Org. Lett.* **1999**, *1*, 595-598.



(*Z*)-1-{1-[(Trimethylsilyl)oxy]pent-1-en-1-yl}-1H-pyrrole (81d): General procedure A was followed employing 1.87 mL of diisopropylamine (13.2 mmol), 9.07 mL of 1.6 M *n*-BuLi (14.5 mmol), 2.0 g 1-(1*H*-pyrrol-1-yl)- 1-Pentanone (13.2 mmol), 1.84 mL TMSCl (1.1 mmol) in 30 mL THF. The reaction was purified via kugelrohr distillation at 1 mm Hg. The product distilled between 70 and 80 ^{o}C (2.14 g, 73%) as a clear colorless oil. ^{1}H NMR (500 MHz, $CDCl_3$): δ 6.86 (t, *J*= 2.0 Hz, 2H), 6.16 (t, *J*= 2.0 Hz, 2H), 4.68 (t, *J*= 7.5 Hz, 1H), 2.09 (q, *J*= 7.5 Hz, 2H), 1.43 (sextet, *J*= 7.5 Hz, 2H), 0.96 (t, *J*= 7.5 Hz, 3H), 0.15 (s, 9H) ; ^{13}C NMR (125 MHz, $CDCl_3$): δ 143.0, 119.0, 108.8, 97.8, 27.4, 23.1, 13.8, -0.15; IR ν_{max}^{neat} cm^{-1}: 2959, 2932, 2871, 1682, 1478, 1368, 1254, 1155, 1101, 1078, 1040, 960, 849, 737, 726; HRMS (EI) *m/z* calcd for $C_{12}H_{21}NOSi$ $(M + H)^+$: 224.1471; found: 224.1480.

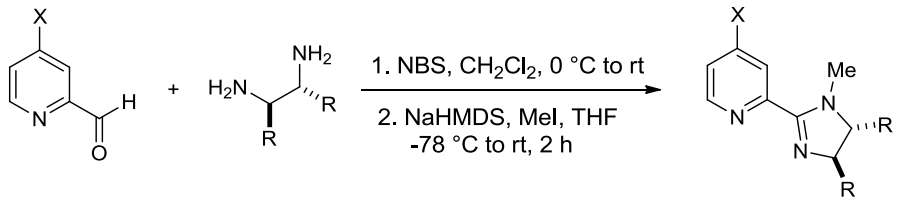


(*Z*)-1-{2-(Benzyloxy)-1-[(trimethylsilyl)oxy]vinyl}-1H-pyrrole (81e): Characterization materials match the data provided in the following publication: Evans, D. A.; Scheidt, K. A.; Johnson, J. N.; Willis, M. C. *J. Am. Chem. Soc.* **2001**, *123*, 4480-4491.



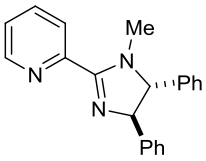
(*Z*)-1-{2-Chloro-1-[(trimethylsilyl)oxy]vinyl}-1H-pyrrole (81f): General procedure A was followed employing 1.49 mL of diisopropylamine (10.5 mmol), 7.19 mL of 1.6 M *n*-BuLi (11.5 mmol), 1.5 g 2-Chloro-1-(1*H*-pyrrol-1-yl)-Ethanone (10.5

mmol), 1.46 mL TMSCl in 30 mL THF. The reaction was purified via kugelrohr distillation at 1 mm Hg. The product distilled between 75 and 80 ^{o}C (1.85 g, 82%) as a clear colorless oil. ^{1}H NMR (500 MHz, $CDCl_3$): δ 6.85 (t, *J*= 2.0 Hz, 2H), 6.23 (t, *J*= 2.0 Hz, 2H), 5.53 (s, 1H), 0.27 (s, 9H); ^{13}C NMR (125 MHz, $CDCl_3$): δ 145.3, 118.9, 110.1, 89.0, 0.06; IR ν_{max}^{neat} cm^{-1}: 3108, 2961, 2900, 1723, 1655, 1562, 1475, 1353, 1258, 1134, 1078, 961, 887, 789, 728; HRMS (EI) *m/z* calcd for $C_9H_{14}ClNOSi$ $(M + H)^+$: 216.0611; found: 216.0619.

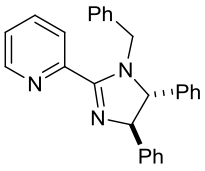


General Procedure B.[62] Synthesis of imidazolylpyridine ligands 91, 97-105: To a solution of picolinaldehyde (1.0 equiv) in CH_2Cl_2 (0.10 M relative to picolinaldehyde) was added the diamine (1.05 equiv). The reaction was allowed to stir for 30 min before N-bromosuccinimide (1.05 equiv) was added as a solid. The resulting solution was stirred overnight. The reaction was quenched with 10% NaOH/H_2O solution of equivalent volume. Organics were extracted with CH_2Cl_2 (3x the reaction volume), dried with $MgSO_4$, and concentrated in vacuo. The crude product was then subjected to methylation conditions without purification. A solution of the crude product in THF (0.10 M) was cooled to -78ºC. To this was added sodium bis(trimethylsilyl)amide (NaHMDS) as a 1.0M solution in THF (1.3 equiv). After stirring for 30 min, iodomethane (1.1 equiv) was added. The reaction flask was then allowed to warm to room temperature and stir for 2 h. Next, the reaction was quenched with an equivalent volume of H_2O and the organics were extracted with CH_2Cl_2 (3x the reaction volume). The extract was dried

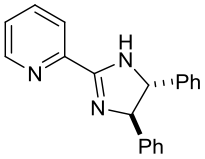
with $MgSO_4$ and concentrated in vacuo. The product mixture was purified by column chromatography.



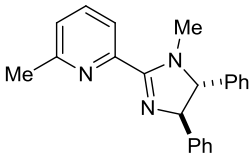
2-[(4*R*,5*R*)-1-Methyl-4,5-diphenyl-4,5-dihydro-1H-imidazol-2-yl]pyridine (91): Characterization materials match the data provided in the following publication : Bastero, A.; Claver, C.; Ruiz, A.; Castillon, S.; Daura, E.; Bo, C.; Zangrando, E. *Chem. Eur. J.* **2004**, *10*, 3747-3760.



2-[(4*R*,5*R*)-1-Benzyl-4,5-diphenyl-4,5-dihydro-1H-imidazol-2-yl]pyridine (97): Characterization materials match the data provided in the following publication : Bastero, A.; Claver, C.; Ruiz, A.; Castillon, S.; Daura, E.; Bo, C.; Zangrando, E. *Chem. Eur. J.* **2004**, *10*, 3747-3760.

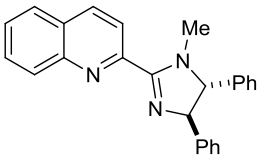


2-[(4*R*,5*R*)-4,5-Diphenyl-4,5-dihydro-1H-imidazol-2-yl]pyridine (98): Characterization materials match the data provided in the following publication : Bastero, A.; Claver, C.; Ruiz, A.; Castillon, S.; Daura, E.; Bo, C.; Zangrando, E. *Chem. Eur. J.* **2004**, *10*, 3747-3760.



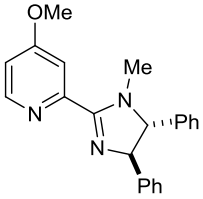
2-Methyl-6-[(4*R*,5*R*)-1-methyl-4,5-diphenyl-4,5-dihydro-1H-imidazol-2-yl]pyridine (99): General procedure B was followed employing 163 mg of 6-methylpicolinaldehyde (1.34 mmol), 300 mg (1*R*,2*R*)-diphenylethylenediamine (1.41 mmol), 252 mg *N*-bromosuccinimide (1.41 mmol), in 13.0 mL CH_2Cl_2. After workup, 429 mg (1.37 mmol) crude product was recovered. The crude product

was then subjected to methylation conditions employing 1.78 mL of NaHMDS (1.0M in THF, 1.78 mmol) and 94.0 µL iodomethane (1.51 mmol) in 13.0 mL THF. The reaction mixture was purified by column chromatography (SiO_2, 5% MeOH/CH_2Cl_2) to afford 256 mg (57%) of the title compound as a pale brown oil*:* $[\alpha]_D^{19}$ +0.209 (*c* 4.12, $CHCl_3$); ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.93 (d, *J*= 7.5 Hz, 1H), 7.69 (t, *J*= 8.0 Hz, 1H), 7.42-7.22 (m, 11H), 5.00 (d, *J* = 10.5 Hz, 1H), 4.39 (d, *J* = 10.5 Hz, 1H), 3.00 (s, 3H), 2.64 (s, 3H); ^{13}C NMR (125 MHz, $CDCl_3$): δ164.3, 157.5, 149.8, 143.3, 140.8, 136.8, 128.8, 128.4, 127.9, 127.4, 127,1, 126.9, 124.2, 122.0, 34.2, 24.5; IR ν_{max}^{neat} cm^{-1}:3060, 2922, 1591, 1569, 1453, 1388, 1302, 1277, 1222, 1156, 1080, 913, 808, 752; HRMS (EI) *m/z* calcd for $C_{22}H_{21}N_3$ $(M + H)^+$: 328.1814; found: 328.1813.

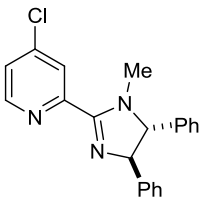


2-[(4*R*,5*R*)-1-Methyl-4,5-diphenyl-4,5-dihydro-1H-imidazol-2-yl]quinoline (100): General procedure B was followed employing 106 mg of quinoline-2-carbaldehyde (0.67 mmol), 150 mg (1*R*,2*R*)-diphenylethylenediamine (0.71 mmol), 125 mg N-bromosuccinimide (0.70 mmol), in 7.0 mL CH_2Cl_2. After workup, 104 mg (0.30 mmol) crude product was recovered. The crude product was then subjected to methylation conditions employing 0.39 mL of NaHMDS (1.0M in THF, 0.39 mmol) and 24 µL iodomethane (0.33 mmol) in 3.0 mL THF. The reaction mixture was purified by column chromatography (SiO_2, 5% MeOH/CH_2Cl_2) to afford 94 mg (86%) of the title compound as a pale brown oil*:* $[\alpha]_D^{19}$ -1.86 (*c* 2.01, $CHCl_3$); ^{1}H NMR (500 MHz, $CDCl_3$): δ 8.27 (dd, *J*= 14.5, 9.0 Hz, 2H), 8.20 (d, *J*= 8.5 Hz, 1H), 7.88 (d, *J*= 8.5 Hz, 1H), 7.77 (ddd, *J*= 8.5, 7.0, 1.5 Hz, 1H), 7.61 (ddd, *J*= 8.0, 1.0 Hz, 1H), 7.44-7.28 (m, 10H), 5.06 (d, *J* = 10.5 Hz, 1H), 4.44 (d, *J* = 10.5 Hz, 1H), 3.20 (s, 3H); ^{13}C NMR (125 MHz, $CDCl_3$): δ 164.0, 150.5, 147.0, 143.3, 140.9, 136.4, 129.9, 129.7, 128.8, 128.5, 128.2, 127.9, 127.6, 127.4, 127.2, 127.1,

122.1, 79.2, 77.4, 34.6; IR ν_{max}^{neat} cm^{-1}: 3059, 3028, 2926, 1600, 1555, 1491, 1392, 1277, 1067, 839, 755; HRMS (EI) *m/z* calcd for $C_{25}H_{21}N_3$ $(M + H)^+$: 364.1814; found: 364.1808.

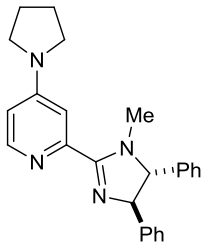


4-Methoxy-2-[(4*R*,5*R*)-1-methyl-4,5-diphenyl-4,5-dihydro-1H-imidazol-2-yl]pyridine (101): General procedure B was followed employing 355 mg of 4-methoxypicolinaldehyde (2.59 mmol), 577 mg (1*R*,2*R*)-diphenylethylenediamine (2.59 mmol), 461 mg *N*-bromosuccinimide (2.59 mmol), in 26.0 mL CH_2Cl_2. After workup, 861 mg (2.61 mmol) crude product was recovered. The crude product was then subjected to methylation conditions employing 3.40 mL of NaHMDS (1.0M in THF, 3.40 mmol) and 42 µL iodomethane (0.67mmol) in 6.0 mL THF. The reaction mixture was purified by column chromatography (SiO_2, 0-2% MeOH/CH_2Cl_2 gradient) to afford 836 mg (72%) of the title compound as a pale brown oil*:* $[\alpha]_D^{22}$ +0.995 (*c* 2.21, $CHCl_3$); ^{1}H NMR (500 MHz, $CDCl_3$): δ 8.50 (d, *J*= 5.5 Hz, 1H), 7.68 (d, *J*= 2.5 Hz, 1H), 7.40-7.26 (m, 10H), 6.91 (dd, *J* = 6.0, 2.5 Hz, 1H), 4.99 (d, *J* = 10.5 Hz, 1H), 4.39 (d, *J*= 10.5 Hz, 1H), 3.93 (s, 3H), 3.01 (s, 3H); ^{13}C NMR (125 MHz, $CDCl_3$): δ 166.2, 164.3, 151.8, 149.8, 143.0, 140.6, 128.8, 126.9, 111.9, 110.2, 78.8, 76.9, 55.5, 34.3; IR ν_{max}^{neat} cm^{-1}: 3060, 2939, 1593, 1562, 1474, 1435, 1376, 1304, 1280, 1190, 1070, 977, 866, 756; HRMS (EI) *m/z* calcd for $C_{22}H_{21}N_3O$ $(M + H)^+$: 344.1763; found: 344.1765.



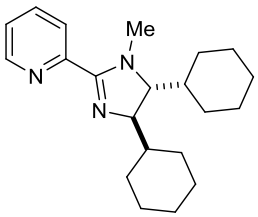
4-Chloro-2-[(4R,5R)-1-methyl-4,5-diphenyl-4,5-dihydro-1H-imidazol-2-yl]pyridine: General procedure B was followed employing 223 mg of 4-chloropicolinaldehyde[71] (1.57 mmol), 351 mg 1*R*,2*R*-diphenylethylenediamine (1.65 mmol), 294 mg N-bromosuccinimide (1.65 mmol), in 15.0 mL CH_2Cl_2. After workup, 590

mg (1.74 mmol) crude product was recovered. Then the crude product was subjected to methylation employing 2.30 mL of NaHMDS (1.0M in THF, 2.26 mmol) and 121 µL iodomethane (1.91 mmol) in 18.0 mL THF. The reaction mixture was purified by column chromatography (SiO_2, 0-2% MeOH/CH_2Cl_2 gradient) to afford 440 mg (72%) of the title compound as a pale brown oil*:* $[\alpha]_D^{19}$ +0.369 (*c* 2.22, $CHCl_3$); ^{1}H NMR (500 MHz, $CDCl_3$): δ 8.59 (dd, *J*= 5.0, 0.5 Hz, 1H), 8.19 (d, *J*= 1.5 Hz, 1H), 7.41-7.33 (m, 11H), 4.99 (d, *J* = 10.5 Hz, 1H), 4.38 (d, *J* = 10.5 Hz, 1H), 3.01 (s, 3H); ^{13}C NMR (125 MHz, $CDCl_3$): δ 163.2, 152.0, 149.3, 144.8, 143.1, 140.7, 128.9, 128.5, 127.9, 127.3, 127.2, 126.9, 125.3, 124.9, 79.0, 77.5, 34.3; IR ν_{max}^{neat} cm^{-1}:3059, 3028, 2855, 1575, 1550, 1491, 1407, 1343, 1277, 1075, 972, 834; HRMS (EI) *m/z* calcd for $C_{21}H_{18}ClN_3$ $(M + H)^+$: 348.1268; found: 348.1250.

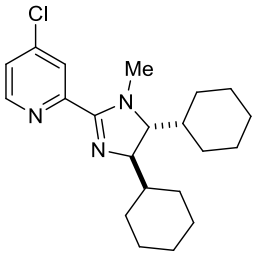


2-[(4*R*,5*R*)-1-Methyl-4,5-diphenyl-4,5-dihydro-1H-imidazol-2-yl]-4-(pyrrolidin-1-yl)pyridine (102): 4-Chloro-2-[(4*R*,5*R*)-1-methyl-4,5-diphenyl-4,5-dihydro-1H-imidazol-2-yl]pyridine (prepared above), 440 mg (1.27 mmol) was added to a medium pressure reaction vessel along with 4.2 mL neat pyrrolidine (50.6 mmol). The vessel was sealed and heated to 90°C for 24 h. At this time the reaction vessel was removed from the oil bath and allowed to cool to ambient temperature and then concentrated in vacuo. The crude reaction mixture was purified by column chromatography (SiO_2, 2-10% MeOH/CH_2Cl_2 gradient) to afford 256 mg (53%) of the title compound as an off-white solid*:* decomposition 62-65°C; $[\alpha]_D^{19}$ -1.57 (*c* 1.08, $CHCl_3$); ^{1}H NMR (500 MHz, $CDCl_3$): δ 8.28 (d, *J*= 5.5 Hz, 1H), 7.38-7.26 (m, 10H), 7.19 (br s, 1H), 6.44 (dd, *J*= 6.0, 2.5 Hz, 1H), 4.99 (d, *J* = 10.0 Hz, 1H), 4.36 (d, *J* = 10.0 Hz, 1H), 3.40 (d, *J*= 2.0 Hz, 4H), 2.98 (s, 3H), 2.04 (p, *J*= 7.0 Hz, 4.0 Hz, 4H) ; ^{13}C NMR (125 MHz, $CDCl_3$): δ 152.2, 148.7, 128.7, 128.4, 127.9, 127.3,

127.2, 126.9, 107.7, 78.7, 47.1, 34.2, 25.3; IR ν_{max}^{neat} cm^{-1}: 3029, 2969, 2855, 1600, 1538, 1495, 1455, 1346, 1275, 1219, 1157, 1082, 1007, 813, 753; HRMS (EI) *m/z* calcd for $C_{25}H_{26}N_4$ $(M + H)^+$: 383.2236; found: 383.2248.

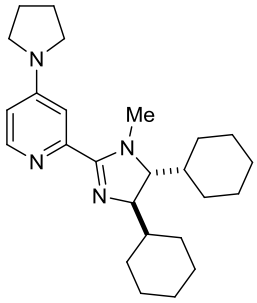


2-[(4*R*,5*R*)-4,5-dicyclohexyl-1-methyl-4,5-dihydro-1*H*-imidazol-2-yl]pyridine (104): General procedure B was followed employing 83 μL picolinaldehyde (0.87 mmol), 186 mg (1*R*,2*R*)-dicyclohexylethylenediamine[72] (0.83 mmol), and 155 mg *N*-bromosuccinimide (0.87 mmol) in 9.0 mL of CH_2Cl_2. After workup, 233 mg (0.75 mmol) of the crude product was recovered. Then the crude product was subjected to methylation employing 0.97 mL NaHMDS (1.0M in THF, 0.97 mmol) and 51 μL iodomethane (0.82 mmol) in 7.0 mL of THF. The reaction mixture was purified by column chromatography (SiO_2, 5-10% MeOH/CH_2Cl_2 gradient then 10% MeOH/2% Et_3N/8% CH_2Cl_2) to afford 202 mg (83%) the title product, an orange/brown viscous oil; $[\alpha]_D^{18}$ +11.3 (*c* 1.15, $CHCl_3$); ^1H NMR (500 MHz, $CDCl_3$): δ 8.64 (dd, *J*= 4.5, 0.5 Hz, 1H), 7.99 (d, *J*= 7.0 Hz, 1H), 7.75 (dt, *J*= 7.5, 1.5Hz, 1H), 7.32 (ddd, *J*= 7.5, 5.0, 1.0 Hz, 1H), 3.69 (t, *J* = 5.0 Hz, 1H), 3.14 (t, *J* = 4.0 Hz, 1H), 3.04 (s, 3H), 1.79-1.60 (m, 11H), 1.28-0.99 (m, 11H) ; ^{13}C NMR (125 MHz, $CDCl_3$): δ 162.7, 148.7, 136.7, 125.3, 124.6, 71.2, 43.4, 41.2, 34.7, 28.6, 28.5, 27.2, 26.6, 26.5, 26.4, 26.3, 26.2; IR ν_{max}^{neat} cm^{-1}: 2923, 2851, 1589, 1563, 1448, 1397, 1318, 1259, 1069, 1044, 799, 748; HRMS (EI) *m/z* calcd for $C_{21}H_{31}N_3$ $(M + H)^+$: 326.2596; found: 326.2588.



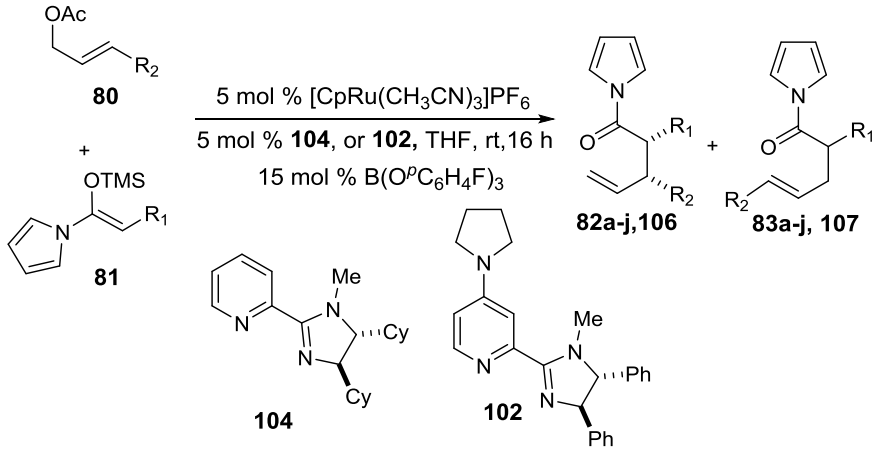
4-Chloro-2-[(4*R*,5*R*)-4,5-dicyclohexyl-1-methyl-4,5-dihydro-1H-imidazol-2-yl]pyridine: General procedure B was followed employing 147 mg 4-chloropicolinaldehyde (1.00 mmol), 213 mg (1*R*,2*R*)-

dicyclohexylethylenediamine (0.95 mmol), and 178 mg *N*-bromosuccinimide (1.00 mmol) in 10.0 mL of CH_2Cl_2. After workup, 319 mg (0.924 mmol) of the crude product was recovered. Then the crude product was subjected to methylation employing 1.20 mL NaHMDS (1.0 M in THF, 1.20 mmol) and 63.3 µL iodomethane (1.02 mmol) in 10.0 mL of THF. The reaction mixture was purified by column chromatography (SiO_2, 3-10% MeOH/ CH_2Cl_2 gradient) to afford 203 mg (61%) of the title compound as a viscous, orange oil; $[\alpha]_D^{19}$ +10.6 (*c* 0.870, $CHCl_3$); ^{1}H NMR (500 MHz, $CDCl_3$): δ 8.52 (d, *J*= 5.0 Hz, 1H), 8.17 (br s, 1H), 7.35 (dd, *J*= 3.5, 1.5 Hz, 1H), 3.73 (br s, 1H), 3.24 (br s, 1H), 3.09 (s, 3H), 1.79-1.70 (m, 5H), 1.67-1.56 (m, 6H), 1.28-0.95 (m, 11H) ; ^{13}C NMR (125 MHz, $CDCl_3$): δ 161.2, 149.6, 145.1, 126.1, 125.5, 71.3, 43.1, 40.7, 34.5, 28.3, 28.2, 28.1, 26.4, 26.3, 26.2, 26.1, 26.0; IR ν_{max}^{neat} cm^{-1}: 2924, 2851, 1574, 1550, 1447, 1409, 1315, 1262, 1070, 981, 893, 843, 752 ; HRMS (EI) *m/z* calcd for $C_{21}H_{30}ClN_3$ $(M + H)^+$: 360.2210; found: 360.2207.



2-[(4*R*,5*R*)-4,5-Dicyclohexyl-1-methyl-4,5-dihydro-1H-imidazol-2-yl]-4-(pyrrolidin-1-yl)pyridine (104): 4-Chloro-2-[(4*R*,5*R*)-4,5-dicyclohexyl-1-methyl-4,5-dihydro-1H-imidazol-2-yl]pyridine (prepared above), 203 mg (0.57 mmol) was added to a medium pressure reaction vessel along with 1.86 mL neat pyrrolidine (22.6 mmol). The vessel was sealed and heated to 90°C for 24 h. At this time the reaction vessel was removed from the oil bath and allowed to cool to ambient temperature and then concentrated in vacuo. The crude reaction mixture was purified by column chromatography (SiO_2, 5-8% MeOH/CH_2Cl_2 gradient) to afford 229 mg of the unmethylated HCl salt. The HCl salt was reexposed to the methylation procedure employing 187 mg of the salt (0.45 mmol), 1.12 mL NaHMDS (1.0 M in THF, 1.12 mmol), and 31 µL

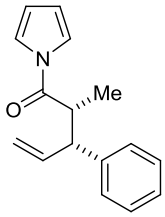
iodomethane (0.49 mmol) in 6 mL THF. The crude reaction mixture was purified by column chromatography (SiO_2, 5-10% MeOH/ CH_2Cl_2 gradient then 10% MeOH/1% Et_3N/9% CH_2Cl_2) to afford 157 mg (89%) of the title compound as a pale yellow oil: $[\alpha]_D^{19}$ +7.07 (*c* 0.990, $CHCl_3$); ^1H NMR (500 MHz, $CDCl_3$): δ 8.18 (d, *J*= 6.0 Hz, 1H), 6.90 (br s, 1H), 6.31 (d, *J*= 5.5 Hz, 1H), 3.61 (t, *J*= 4.5 Hz, 1H), 3.30 (br s, 4H), 3.01 (br s, 1H), 2.94 (s, 3H), 1.96 (t, *J*= 6.0 Hz, 4H), 1.72-1.52 (m, 11H), 1.24-0.98 (m, 11H); ^{13}C NMR (125 MHz, $CDCl_3$): δ 164.0, 151.9, 150.8, 148.6, 107.5, 107.0, 71.5, 70.5, 46.9, 43.4, 41.2, 34.4, 28.6, 28.4, 28.3, 27.2, 26.7, 26.6, 26.4, 26.4, 26.3, 26.2, 25.2; IR ν_{max}^{neat} cm^{-1}: 2922, 2850, 1600, 1539, 1484, 1460, 1388, 1349, 1315, 1262, 1181, 1073, 1006, 811, 750; HRMS (EI) *m/z* calcd for $C_{25}H_{38}N_4$ $(M + H)^+$: 395.3175; found: 395.3201.



General Procedure C. Catalytic Asymmetric Enolate Allylic Alkylations: $[CpRu(CH_3CN)_3]PF_6$ (5 mol %) and ligand **104** or **102** (5 mol %) were combined in a 2 dram vial inside a nitrogen-filled glovebox. The THF (0.5 M final concentration of the allylic acetate substrate) was added and the reaction mixture was periodically shaken over 15 min. The resulting solution was then added to another 2 dram vial containing the allylic acetate (1 equiv),

pyrrole silyl enol ether (1.05 equiv), $B(O^pC_6H_4F)_3$[73] (15 mol %) and a Teflon-coated stir bar. The vial was sealed with a threaded cap containing a rubber septum inlet. The vial was removed from the glovebox, and the mixture was stirred at ambient temperature for 16h. After this time, the vial was opened and the reaction mixture was concentrated under a stream of N_2. Pentanes (4x the reaction volume) were added and the resulting heterogeneous mixture was filtered through a Florisil® plug eluting with additional pentanes. The filtrate was concentrated and the resulting mixture of the *anti*/*syn* [3,3] products (**82a-j, 106**) and [1,3] regioisomer (**83a-j, 107**) was analyzed by ^{1}H NMR and chiral stationary phase GC.

Enantiomer ratio determination: Enantiomer ratios of the branched products (**82a-j**) were determined by chiral stationary phase GLC (Varian Chirasil-Dex CB WCOT Fused Silica CP 7502 column, 25 m x 0.25 mm) or analytical high-performance liquid chromatography (HPLC) using a variable wavelength UV detector (deuterium lamp, 190-600 nm), a Chiracel OD-H column and HPLC-grade isopropanol and hexanes as the eluting solvents. Authentic samples of racemic *syn* and *anti* diastereomers of the products were used for comparison.

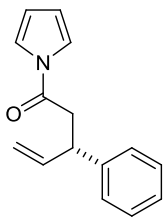


(2*R*,3*R*)-2-Methyl-3-phenyl-1-(1H-pyrrol-1-yl)pent-4-en-1-one (82a): General Procedure C was followed employing 75 mg (0.43 mmol) cinnamyl acetate, 87 mg (0.45 mmol) (*Z*)-1-{1-[(trimethylsilyl)oxy]prop-1-en-1-yl}-1H-pyrrole, 6.9 mg (0.021 mmol) ligand **104**, 9.2 mg (0.021 mmol) $[CpRu(CH_3CN)_3]PF_6$, 22 mg (0.064 mmol) $B(O^pC_6H_4F)_3$, and 0.80 mL THF. The reaction mixture was stirred for 16 h at which time it was concentrated under a stream of N_2, filtered through a plug of Florisil® and concentrated. The crude product was purified by column chromatography (SiO_2, 3% Et_2O/hexanes) to yield 90 mg

(89%) as a mixture of diastereomers. Separating the stereoisomers of **82a** by GLC {flow rate 1.5 mL/min, method: 105 °C for 10 min, ramp @ 0.2 °C/min to 155 °C, hold for 5 min; T_r (min) = 116.5 [(2*S*,3*S*)-**82a**$_{anti}$], 117.2 [(2*R*,3*R*)-**82a**$_{anti}$], 134.3 (**82a**$_{syn1}$), 135.4 (**82a**$_{syn2}$), (ratio = 2.1:129.5:1:20.9)} provided the enantiomer ratio (2*S*,3*S*)-**82a**$_{anti}$:(2*R*,3*R*)-**82a**$_{anti}$ = 1.5:98.4 (97% ee), and (**82a**$_{syn1}$): (**82a**$_{syn2}$) = 4.5:95.4 (91% ee).

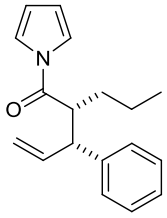
Anti diastereomer (white crystalline solid)*:* mp 49-51 °C; $[\alpha]_D^{23}$ +6.67 (*c* 2.34, $CHCl_3$); ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.26-7.20 (m, 6H), 7.16-7.12 (m, 1H), 6.22 (dd, *J* = 2.0 Hz, 2H), 6.00 (dt, *J* = 16.5, 9.5, Hz, 1H), 5.19 (m, 2H), 3.76 (t, *J* = 10.0 Hz, 1H), 3.51 (dq, *J* = 10.0, 7.0 Hz, 1H), 1.38 (d, *J* = 6.5 Hz, 3H); ^{13}C NMR (125 MHz, $CDCl_3$): δ 173.1, 142.0, 138.3, 128.6, 127.4, 126.7, 118.9, 117.3, 113.0, 53.3, 43.2, 16.8; IR ν_{max}^{neat} cm^{-1}: 3150, 3027, 1708, 1637, 1491, 1301, 1096, 915, 433; HRMS (EI) *m/z* calcd for $C_{16}H_{17}NO$ $(M + H)^+$: 240.1388; found: 240.1404.

Syn diastereomer (pale yellow oil)*:* $[\alpha]_D^{23}$ +7.57 (*c* 1.06, $CHCl_3$); ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.37-7.32 (m, 4H), 7.26-7.22 (m, 3H), 6.32 (app t, *J* = 2.0 Hz, 2H), 5.97 (ddd, *J* = 18.0, 10.0, 8.0 Hz, 1H), 5.02 (dt, *J* = 17.0, 1.0 Hz, 1H), 4.97 (d, *J* = 10.0 Hz, 1H), 3.72 (t, *J* = 10.0 Hz, 1H), 3.46 (dq, *J* = 10.5, 7.0 Hz, 1H), 1.08 (d, *J*= 7.0 Hz, 3H); ^{13}C NMR (125 MHz, $CDCl_3$): δ 173.5, 140.8, 138.9, 128.8, 128.3, 127.0, 119.0, 116.2, 113.3, 53.1, 43.3, 17.0; IR ν_{max}^{neat} cm^{-1}:3027, 2930, 1711, 1600, 1467, 914, 742; HRMS (EI) *m/z* calcd for $C_{16}H_{17}NO$ $(M + H)^+$: 240.1388; found: 240.1373.



(S)-3-phenyl-1-(1H-pyrrol-1-yl)pent-4-en-1-one (82b): General Procedure C was followed employing 75 mg (0.43 mmol) cinnamyl acetate, 81 mg (0.45

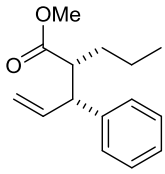
mmol) 1-{1-[(trimethylsilyl)oxy]vinyl}-1H-pyrrole, 6.9 mg (0.021 mmol) ligand **104**, 9.2 mg (0.021 mmol) $[CpRu(CH_3CN)_3]PF_6$, 22 mg (0.064 mmol) $B(O^pC_6H_4F)_3$, 0.80 mL THF. The reaction mixture was stirred for 16 h at which time it was concentrated under a stream of N_2, filtered through a plug of Florisil® and concentrated. The crude product was purified via column chromatography (SiO_2, 3% Et_2O/hexanes) to yield 78 mg (82%) of the product as a colorless oil. Separating the stereoisomers of **82b** by GLC {flow rate 1.5 mL/min, method: 105 °C for 10 min, ramp @ 0.3 °C/min to 175 °C, hold for 5 min; T_r (min) = 120.4 [(3*S*-(**82b**)], 120.9 [3*R*-(**82b**)], (ratio = 1:37.4)} provided an ee of 95%. $[\alpha]_D^{23}$ +0.940 (*c* 0.830, $CHCl_3$); ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.33-7.29 (m, 4H), 7.27-7.21 (m, 3H), 6.28 (app t, *J* = 2.0 Hz, 2H), 6.06 (ddd, *J* = 24.0,10.5, 7.0 Hz, 1H), 5.10 (m, 2H), 4.10 (dd, *J* = 14.5, 7.0 Hz, 1H), 3.24 (dq, *J* = 16.0, 7.5 Hz, 2H); ^{13}C NMR (125 MHz, $CDCl_3$): δ168.6, 142.3, 139.9, 128.7, 127.6, 126.9, 119.0, 115.3, 113.2, 44.8, 40.3; IR ν_{max}^{neat} cm^{-1}:3148, 3028, 2921, 1717, 1638, 1600, 1468, 1338, 1275, 1073, 922, 740; HRMS (EI) *m/z* calcd for $C_{15}H_{15}NO$ $(M + H)^+$ 226.1232; found: 226.1224.



(2*R*,3*R*)-3-Phenyl-2-propyl-1-(1H-pyrrol-1-yl)pent-4-en-1-one (82c): General Procedure C was followed employing 75 mg (0.43 mmol) cinnamyl acetate, 100 mg (0.45 mmol) (Z)-1-{1-[(trimethylsilyl)oxy]pent-1-en-1-yl}-1H-pyrrole (**81c**), 6.9 mg (0.021 mmol) ligand **104**, 9.2 mg (0.021 mmol) $[CpRu(CH_3CN)_3]PF_6$, 146 mg (0.43 mmol) $B(O^pC_6H_4F)_3$, 0.80 mL THF. The reaction mixture was stirred for 16 h at which time it was concentrated under a stream of N_2, filtered through a plug of Florisil® and concentrated. The crude product was purified via column chromatography (SiO_2, 3% Et_2O/hexanes) to yield 93 mg (82%) of the product (**82c**) as a mixture of diastereomers.

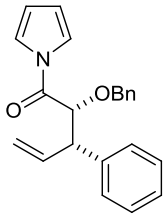
Anti diastereomer (white crystalline solid)*:* mp 81-83 °C; $[\alpha]_D^{22}$ +6.40 (*c* 4.56, $CHCl_3$); ^1H NMR (500 MHz, $CDCl_3$): δ 7.20-7.15 (m, 5H), 7.10 (m, 1H), 6.16 (app t, *J* = 2.0 Hz, 2H), 6.02 (ddd, *J* = 17.0, 9.5 Hz, 1H), 5.17 (m, 2H), 3.71 (t, *J*= 9.5 Hz, 1H), 3.41 (dt, *J*= 10.0, 4.0 Hz, 1H), 3.14 (dt, *J* = 10.0, 4.0 Hz, 1H), 1.83-1.74 (m, 2H), 1.34-1.18 (m, 2H), 0.88 (t, *J*= 7.0 Hz, 3H); ^{13}C NMR (125 MHz, $CDCl_3$): δ 173.0, 141.8, 138.5, 128.6, 127.5, 126.7, 119.0, 117.2, 112.9, 53.3, 49.3, 33.7, 20.4, 14.1; IR ν_{max}^{neat} cm^{-1}: 3148, 3029, 2927, 1694, 1638, 1468, 1345, 1274, 1110, 1048, 924, 758; HRMS (EI) *m/z* calcd for $C_{18}H_{21}NO$ $(M + H)^+$: 268.1701; found: 268.1720.

Syn diastereomer (pale yellow oil)*:* $[\alpha]_D^{22}$ +1.67 (*c* 1.28, $CHCl_3$); ^1H NMR (500 MHz, $CDCl_3$): δ 7.38 (br s, 2H), 7.34 (t, *J*= 7.5 Hz, 2H), 7.23 (dd, *J* = 10.0, 8.5 Hz, 3H), 6.31 (app t, *J* = 2.0 Hz, 2H), 5.93 (ddd, *J* = 19.0, 10.5, 8.3 Hz, 1H), 5.00 (d, *J* = 17.0 Hz, 1H), 4.92 (d, *J* = 10.0 Hz, 1H), 3.68 (t, *J* = 9.0 Hz, 1H), 3.42 (dt, *J*= 10.0, 3.5 Hz, 1H), 1.70-1.63 (m, 1H), 1.34-1.28 (m, 1H), 1.25-1.20 (m, 1H), 1.20-1.17 (m, 1H), 0.74 (t, *J*= 7.0 Hz, 3H); ^{13}C NMR (125 MHz, $CDCl_3$): δ173.3, 141.2, 138.5, 128.8, 128.0, 126.9, 119.0, 116.4, 113.3, 53.4, 49.3, 33.7, 20.5, 14.0; IR ν_{max}^{neat} cm^{-1}: 3150, 3027, 2924, 1709, 1466, 1371, 1114, 1073, 742; HRMS (EI) *m/z* calcd for $C_{18}H_{21}NO$ $(M + H)^+$: 268.1701; found: 268.1720.



Methyl (2*R*,3*R*)-3-phenyl-2-propylpent-4-enoate (82c*):The above compound was derivatized to the methyl ester **82c*** for ee determination. General procedure: To a solution of acyl pyrrole **82c** (1.0 equiv) in MeOH (0.1M) was added NaOMe(10.0 equiv). The reaction was allowed to stir at rt for 24 h, and then quenched with saturated ammonium chloride. The reaction was extracted 3 times with Et_2O, dried over $MgSO_4$, and concentrated to yield **82c*** as the methyl ester. Separating the stereoisomers of **82c*** by GLC {flow rate 2.0 mL/min, method: 80 °C for 10 min, ramp @ 0.4 °C/min to 160 °C, hold for 5 min;

T_r (min) = 60.0 [(2*R*,3*R*)-**82c***$_{anti}$], 60.7 [(2*S*,3*S*)-**82c***$_{anti}$], 81.2 (**82c***$_{syn1}$), 82.4 (**82c***$_{syn2}$), (ratio = 374:7.4:1:65.9)} provided the enantiomer ratio (2*R*,3*R*)-**82c***$_{anti}$:(2*S*,3*S*)-**82c***$_{anti}$ = 98.0:1.9 (96% ee), and (**82c***$_{syn1}$): (**82c***$_{syn2}$) = 1.5:98.5 (97% ee).

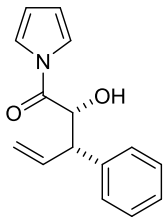


(2*R*,3*S*)-2-(Benzyloxy)-3-phenyl-1-(1H-pyrrol-1-yl)pent-4-en-1-one (82e): General Procedure C was followed employing 100 mg (0.57 mmol) cinnamyl acetate, 171 mg (0.59 mmol) (*Z*)-1-{2-(benzyloxy)-1-[(trimethylsilyl)oxy]vinyl}-1H-pyrrole, 9.2 mg (0.028 mmol) ligand **104**, 12 mg (0.028 mmol) $[CpRu(CH_3CN)_3]PF_6$, 29 mg (0.085 mmol) $B(O^pC_6H_4F)_3$, 1.0 mL THF. The reaction mixture was stirred for 16 h at which time it was concentrated under a stream of N_2, filtered through a plug of Florisil® and concentrated. The crude product was purified via column chromatography (SiO_2, 5% Et_2O/hexanes) to yield 141 mg (75%) of the product **82e** as a mixture of diastereomers.

Anti diastereomer (white solid)*:* mp 77-79 °C; $[\alpha]_D^{22}$ +5.00 (*c* 0.280, $CHCl_3$); ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.37 (br s, 2H), 7.32-7.16 (m, 10H), 6.30-6.23 (m, 3H), 5.20 (d, *J* = 10.5 Hz, 1H), 5.08 (d, *J*= 17.0 Hz, 1H), 4.70 (m, 2H), 4.41 (d, *J*= 11.5Hz, 1H), 3.90 (t, *J*= 7.0 Hz, 1H); ^{13}C NMR (125 MHz, $CDCl_3$): δ168.7, 139.2, 136.3, 136.1, 128.6, 128.4, 128.3, 128.1, 128.0, 127.3, 119.5, 117.9, 113.2, 83.3, 72.5, 53.4; IR ν_{max}^{neat} cm^{-1}: 3083, 3029, 2859, 1715, 1688, 1466, 1329, 1289, 1096, 1019, 926, 739; HRMS (EI) *m/z* calcd for $C_{22}H_{21}NO_2$ $(M + H)^+$: 332.1651; found: 332.1640.

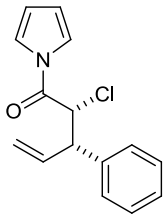
Syn diastereomer (yellow oil): $[\alpha]_D^{18}$ +2.5 (*c* 0.08, $CHCl_3$); ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.48 (t, *J*= 2.5 Hz, 2H), 7.33-7.28 (m, 3H), 7.23-7.20 (m, 5H), 6.97 (m, 2H), 6.28 (t, *J* = 2.5 Hz, 2H), 5.95 (ddd, *J* = 9.0, 10, 17 Hz, 1H), 4.98 (m, 2H), 4.63 (d, *J* = 9.0 Hz, 1H), 4.57 (d, *J*= 9.0 Hz, 1H), 4.23 (d, *J*= 9.0, 1H), 3.89 (t, *J*= 9 Hz, 1H); ^{13}C NMR (125 MHz, $CDCl_3$): δ169.4, 139.6,

136.3, 135.6, 128.5, 128.3, 127.9, 127.1, 119.5, 118.0, 113.3, 83.7, 72.4, 54.2; IR ν_{max}^{neat} cm^{-1}: 2956, 2926, 2867, 1712, 1602, 1505, 1468, 1409, 1344, 1255, 1088, 926, 820.0, 745; HRMS (EI) *m/z* calcd for $C_{18}H_{21}NO$ $(M + Na)^+$: 354.1470; found: 254.1467.



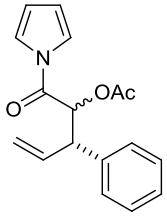
(2*R*,3*S*)-2-Hydroxy-3-phenyl-1-(1H-pyrrol-1-yl)pent-4-en-1-one (82e*):The benzyl ether protecting group of the compound above **82e** was removed for ee determination. General Procedure: To a -78 °C solution of compound **82e** (1.0 equiv) in CH_2Cl_2 (0.1M) was added a 1.0M solution of BCl_3 in CH_2Cl_2 dropwise. The reaction was allowed to stir at -78 °C for 3 h at which time it was quenched with an equal volume of MeOH. The reaction was allowed to warm to rt and then concentrated in vacuo to yield **82e*** as the free alcohol.

Separating the stereoisomers of **82e*** by GLC {flow rate 1.0 mL/min, method: 105 °C for 10 min, ramp @ 0.7 °C/min to 200 °C, hold for 5 min; T_r (min) = 99.3 (**82e***$_{syn1}$), 99.9 (**82e***$_{syn2}$) 100.9 [(2*S*,3*S*)-**82e***$_{anti}$], 101.5 [(2*R*,3*R*)-**82e***$_{anti}$], (ratio = 1:17:2:104)} provided the enantiomer ratio (2*S*,3*S*)-**82e***$_{anti}$:(2*R*,3*R*)-**82e***$_{anti}$ = 1.9:98.1 (96% ee), and (**82e***$_{syn1}$): (**82e***$_{syn2}$) = 5.6:94.4 (89% ee).



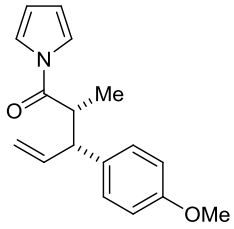
(2*R*,3*S*)-2-Chloro-3-phenyl-1-(1H-pyrrol-1-yl)pent-4-en-1-one (82f): General Procedure C was followed employing 100 mg (0.57 mmol) cinnamyl acetate, 128 mg (0.59 mmol) (*Z*)-1-{2-chloro-1-[(trimethylsilyl)oxy]vinyl}-1H-pyrrole (**81f**), 9.2 mg (0.028 mmol) ligand **104**, 12 mg (0.028 mmol) $[CpRu(CH_3CN)_3]PF_6$, 29 mg (0.085 mmol) $B(O^pC_6H_4F)_3$, 1.0 mL THF. The reaction mixture was stirred for 16 h at which time it was concentrated under a stream of N_2, filtered through a plug of Florisil® and concentrated. The

crude product was purified via column chromatography (SiO_2, 3% Et_2O/hexanes) to yield 56 mg (38%) of the product (**82f**) as an inseparable mixture of diastereomers. In addition, 16 mg (10%) of the OAc substituted product (**82f′**)was collected eluting with 10% Et_2O/hexanes. Separating the stereoisomers of **82f** by GLC {flow rate 1.5 mL/min, method: 105 °C for 10 min, ramp @ 0.3 °C/min to 175 °C, hold for 5 min; T_r (min) = 140.6 [(2*S*,3*S*)-**82f**$_{anti}$], 141.2 [(2*R*,3*R*)-**82f**$_{anti}$], (ratio = 66.1:1)} provided an ee of 97%. The *syn* stereoisomers could not be separated. Diastereomer ratio*(anti:syn)* = 1.0: 0.80 (pale yellow oil); $[\alpha]_D^{23}$ +4.17 (*c* 5.72, $CHCl_3$); ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.43-7.23 (m, 9H), 6.40 (t, *J*= 2.5 Hz, 2H), 6.29 (t, *J*= 2.0 Hz, 1.5H), 6.23 (ddd, *J* = 18.5, 10.5, 2.0 Hz, 0.8H), 6.01 (ddd, *J*= 17.5, 11.0, 6.5 Hz, 1H), 5.32 (d, *J*= 10.0 Hz, 0.8H), 5.25 (dt, *J*= 17.0, 10.0 Hz, 0.8H), 5.18 (d, *J*= 1.0 Hz, 1H), 5.15 (d, *J*= 6.5 Hz, 1H), 5.12 (d, *J*= 10.0 Hz, 0.8H), 5.09 (d, *J*= 10.5 Hz, 1H), 4.21 (dd, *J*= 17.5, 7.5 Hz, 1.8H); ^{13}C NMR (125 MHz, $CDCl_3$): δ 164.5, 165.1, 138.9, 138.6, 136.2, 135.8, 128.9, 128.8, 128.5, 128.1, 127.6, 127.6, 119.4, 119.3, 119.1, 118.9, 114.2, 113.9, 57.4, 57.1, 53.1, 52.8; IR ν_{max}^{neat} cm^{-1}: 3150, 3063, 3029, 1638, 1600, 1547, 1411, 1364, 1318, 1265, 1233, 1076, 988, 860, 742; HRMS (EI) *m/z* calcd for $C_{15}H_{14}ClNO$ $(M + H)^+$: 260.0842; found: 260.0825.



(3*S*)-1-Oxo-3-phenyl-1-(1*H*-pyrrol-1-yl)pent-4-en-2-yl acetate (82f′): Separating the stereoisomers of **82f′** by GLC {flow rate 1.5 mL/min, method: 105 °C for 10 min, ramp @ 0.2 °C/min to 155 °C, hold for 5 min; T_r (min) = 172.7 [(2*R*,3*S*)-**82f′**$_{syn}$], 174.1 [(2*S*,3*R*)-**82f′**$_{syn}$], 176.3 (**82f′**$_{anti1}$), 178.9 (**82f′**$_{anti2}$), (ratio = 1.1:112.6:79.9:1)} provided the enantiomer ratio (2*R*,3*S*)-**82f′**$_{syn}$:(2*S*,3*R*)-**82f′**$_{syn}$ = 1.0:99.0 (98% ee), and (**82f′**$_{anti1}$): (**82f′**$_{anti2}$) = 1.5:98.7 (97% ee). *Anti* diastereomer: *Syn* diastereomer = 1.0: 0.80 (pale yellow oil); $[\alpha]_D^{23}$ +3.31 (*c* 1.16, $CHCl_3$); ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.38-7.20 (m,

13H), 6.33 (app t, *J*= 2.5 Hz, 1.4H), 6.25 (app t, *J*= 2.5 Hz, 2H), 6.17 (ddd, *J* = 17.0, 10.0, 8.5 Hz, 1.3H), 5.99 (ddd, *J*= 17.0, 10.0, 8.5 Hz, 0.8H), 5.94 (m, 0.8H), 5.92 (s, 1H), 5.22 (d, *J*= 10.0 Hz, 1.1H), 5.12 (m, 2.8H), 4.02 (m, 1.8H), 2.16 (s, 3H), 1.96 (s, 2H); ^{13}C NMR (125 MHz, $CDCl_3$): δ170.2, 170.0, 166.5, 166.1, 138.3, 138.1, 135.0, 134.6, 128.8, 128.6, 128.4, 128.1, 127.6, 127.5, 119.2, 119.1, 118.7, 118.6, 113.9, 113.7, 74.1, 73.9, 51.9, 51.7, 20.6, 20.3; IR ν_{max}^{neat} cm^{-1}: 3150, 3030, 2923, 1722, 1640, 1601, 1470, 1415, 1373, 1323, 1294, 1234, 1123, 1073, 926, 817, 744; HRMS (EI) *m/z* calcd for $C_{15}H_{14}ClNO$ $(M + Na)^+$: 306.1106; found: 306.1124.

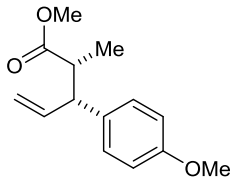


(2*R*,3*R*)-3-(4-Methoxyphenyl)-2-methyl-1-(1H-pyrrol-1-yl)pent-4-en-1-one (82g): General Procedure C was followed employing 100 mg (0.49 mmol) (*E*)-3-(4-methoxyphenyl)allyl acetate, 99 mg (0.51 mmol) (*Z*)-1-{1-[(trimethylsilyl)oxy]prop-1-en-1-yl}-1H-pyrrole, 7.9 mg (0.024 mmol) ligand **104**, 11 mg (0.024 mmol) $[CpRu(CH_3CN)_3]PF_6$, 25 mg (0.073 mmol) $B(O^pC_6H_4F)_3$, 1.0 mL THF. The reaction mixture was stirred for 16 h at which time it was concentrated under a stream of N_2, filtered through a plug of Florisil® and concentrated. The crude product was purified via column chromatography (SiO_2, 5% Et_2O/hexanes) to yield 103 mg (79%) of the product (**82g**) as a mixture of diastereomers.

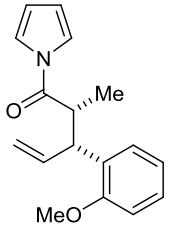
Anti diastereomer (white crystalline solid)*:* mp 56-59 °C; $[\alpha]_D^{22}$ +0.291 (*c* 1.10, $CHCl_3$); ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.22 (br s, 2H), 7.11 (d, *J*= 9 Hz, 2H), 6.76 (d, *J*= 8.5 Hz, 2H), 6.22 (app t, *J* = 2.0 Hz, 2H), 5.97 (ddd, *J*= 18.0, 16.5, 9.0 Hz, 1H), 5.15 (m, 2H), 3.73 (s, 3H), 3.71 (m, 1H), 3.46 (dq, *J*= 9.5, 7.0 Hz, 1H), 1.36 (d, *J*= 7.0 Hz, 3H); ^{13}C NMR (125 MHz, $CDCl_3$): δ 173.1, 158.2, 138.5, 134.2, 128.4, 118.9, 116.9, 114.0, 113.0, 55.1, 52.4, 43.4, 16.9; IR ν_{max}^{neat} cm^{-1}:

3149, 3074, 2935, 2836, 1714, 1636, 1491, 1467, 1366, 1273, 1125, 1072, 995, 896, 742; HRMS (EI) *m/z* calcd for $C_{17}H_{19}NO_2$ $(M + H)^+$: 270.1494; found: 270.1501.

Syn diastereomer (clear colorless oil)*:* $[\alpha]_D^{22}$ +9.74 (*c* 0.310, $CHCl_3$); ^1H NMR (500 MHz, $CDCl_3$): δ 7.38 (br s, 2H), 7.14 (d, *J*= 8.5 Hz, 2H), 6.89 (d, *J* = 8.5 Hz, 2H), 6.32 (app t, *J* = 2.5 Hz, 2H), 5.96 (ddd, *J* = 17.5, 10.5, 8.0 Hz, 1H), 4.98 (m, 2H), 3.81 (s, 3H), 3.68 (t, *J* = 8.0 Hz, 1H), 3.41 (dq, *J*= 10.0, 3.5 Hz, 1H), 1.08 (d, *J*= 7.0 Hz, 3H); ^{13}C NMR (125 MHz, $CDCl_3$): δ173.6, 158.5, 139.1, 132.8, 129.2, 119.0, 115.8, 114.2, 113.3, 55.3, 52.2, 43.4, 16.9; IR ν_{max}^{neat} cm^{-1}: 2930, 2360, 1709, 1492, 1466, 1371, 1274, 1120, 1073, 914, 743; HRMS (EI) *m/z* calcd for $C_{17}H_{19}NO_2$ $(M + H)^+$: 270.1494; found: 270.1479.



Methyl-(2*R*,3*R*)-3-(4-methoxyphenyl)-2-methylpent-4-enoate (82g*): The above compound **82g** was derivatized to the methyl ester **82g*** for ee determination. General procedure: To a solution of acyl pyrrole **82g** (1.0 equiv) in MeOH (0.1M) was added NaOMe (10.0 equiv). The reaction was allowed to stir at rt for 24 h, and then quenched with saturated ammonium chloride. The reaction was extracted 3 times with Et_2O, dried over $MgSO_4$, and concentrated to yield product **82g*** as the methyl ester. Separating the stereoisomers of **82g*** by GLC {flow rate 2.0 mL/min, method: 80 °C for 10 min, ramp @ 0.4 °C/min to 160 °C, hold for 5 min; T_r (min) = 112.9 [(2*S*,3*S*)-**82g***$_{anti}$], 113.9 [(2*R*,3*R*)-**82g***$_{anti}$], 123.4 (**82g***$_{syn1}$), 123.7 (**82g***$_{syn2}$), (ratio = 2.2:66.8:1:16.6)} provided the enantiomer ratio (2*S*,3*S*)-**82g***$_{anti}$:(2*R*,3*R*)-**82g***$_{anti}$ = 3.2:96.8 (94% ee), and (**82g***$_{syn1}$): (**82g***$_{syn2}$) = 5.6:94.3 (89% ee).

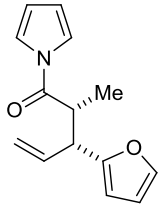


(2*R*,3*R*)-3-(2-Methoxyphenyl)-2-methyl-1-(1H-pyrrol-1-yl)pent-4-en-1-one (82h): General Procedure C was followed employing 100 mg (0.49 mmol) (*E*)-3-(2-methoxyphenyl)allyl acetate, 99 mg (0.51 mmol) (*Z*)-1-{1-[(trimethylsilyl)oxy]prop-1-en-1-yl}-1H-pyrrole, 7.9 mg (0.024 mmol) ligand **104**, 11 mg (0.024 mmol) $[CpRu(CH_3CN)_3]PF_6$, 25 mg (0.073 mmol) $B(O^pC_6H_4F)_3$, 1.0 mL THF. The reaction mixture was stirred for 16 h at which time it was concentrated under a stream of N_2, filtered through a plug of Florisil® and concentrated. The crude product was purified via column chromatography (SiO_2, 5% Et_2O/hexanes) to yield 104 mg (80%) of the product (**82h**) as a mixture of diastereomers. Separating the stereoisomers of **82h** by GLC {flow rate 1.5 mL/min, method: 105 °C for 10 min, ramp @ 0.2 °C/min to 155 °C, hold for 5 min; T_r (min) = 170.9 [(2*S*,3*S*)-**82h**$_{anti}$], 172.4 [(2*R*,3*R*)-**82h**$_{anti}$], 186.4 (**82h**$_{syn1}$), 187.9 (**82h**$_{syn2}$), (ratio = 1:84.2:19.0:1.5)} provided the enantiomer ratio (2*S*,3*S*)-**82h**$_{anti}$:(2*R*,3*R*)-**82h**$_{anti}$ = 1.2:98.8 (98% ee), and (**82h**$_{syn1}$): (**82h**$_{syn2}$) = 92.7:7.3 (85% ee).

Anti diastereomer (white crystalline solid)*:* mp 50-52 °C; $[\alpha]_D^{22}$ +7.83 (*c* 2.84, $CHCl_3$); ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.36 (dd, *J*= 2.0 Hz, 2H), 7.17-7.14 (m, 2H), 6.86 (app t, *J*= 7.0, 7.0 Hz, 1H), 6.82 (d, *J* = 8.0 Hz, 1H), 6.24 (t, *J*= 2.0 Hz, 2H), 6.21 (m, 1H), 5.10 (m, 2H), 4.03 (t, *J*= 9.0Hz, 1H), 3.87 (s, 3H), 3.81 (ddd, *J*= 7.0 Hz, 1H), 1.25 (d, *J*= 7.0 Hz, 3H); ^{13}C NMR (125 MHz, $CDCl_3$): δ 173.3, 156.5, 136.4, 129.9, 129.2, 127.8, 120.7, 119.1, 117.6, 112.6, 110.8, 55.2, 49.1, 41.1, 15.0; IR ν_{max}^{neat} cm^{-1}: 3151, 3004, 2905, 2835, 1701, 1611, 1513, 1469, 1376, 1278, 1179, 835, 743 ; HRMS (EI) *m/z* calcd for $C_{17}H_{19}NO_2$ $(M + Na)^+$: 292.1313; found: 292.1310.

Syn diastereomer (clear colorless oil)*:* $[\alpha]_D^{22}$ +5.74 (*c* 0.380, $CHCl_3$); ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.38 (br s, 2H), 7.23 (dt, *J*= 8.0, 1.5 Hz, 1H), 7.16 (dd, *J* = 7.5, 1.5 Hz, 1H), 6.93 (dt, *J*

= 7.5, 1.0 Hz, 1H), 6.89 (d, *J* = 8.5 Hz, 1H), 6.30 (app t, *J*= 2.0 Hz, 2H), 6.10 (ddd, *J*= 18.5, 10.0, 8.0 Hz, 1H), 5.04 (dt, *J* = 17.0, 1.0 Hz, 1H), 4.94 (dd, *J*= 10.0, 0.5 Hz, 1H), 4.04 (t, *J*= 9.0 Hz, 1H), 3.85 (s, 3H), 3.75 (dq, *J*= 9.5, 7.0 Hz, 1H), 1.08 (d, *J*= 6.5 Hz, 3H); ^{13}C NMR (125 MHz, $CDCl_3$): δ 173.9, 157.2, 138.0, 129.7, 129.0, 128.0, 120.8, 119.1, 116.2, 113.0, 111.0, 55.4, 48.9, 41.5, 16.5; IR ν_{max}^{neat} cm^{-1}: 2930, 2835, 1711, 1637, 1511,1466, 1408, 1320, 1269, 1178, 1115, 1073, 993, 828, 742; HRMS (EI) *m/z* calcd for $C_{17}H_{19}NO_2$ $(M + H)^+$: 270.1494; found: 270.1531.

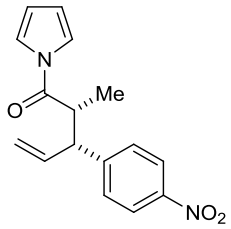


(2*R*,3*R*)-3-(Furan-2-yl)-2-methyl-1-(1H-pyrrol-1-yl)pent-4-en-1-one (82i): General Procedure C was followed employing 100 mg (0.60 mmol) (*E*)-3-(furan-2-yl)allyl acetate, 123 mg (0.63 mmol) (*Z*)-1-{1-[(trimethylsilyl)oxy]prop-1-en-1-yl}-1H-pyrrole, 9.8 mg (0.030 mmol) ligand **104**, 13 mg (0.030 mmol) $[CpRu(CH_3CN)_3]PF_6$, 31 mg (0.090 mmol) $B(O^pC_6H_4F)_3$, 1.2 mL THF. The reaction mixture was stirred for 16 h at which time it was concentrated under a stream of N_2, filtered through a plug of Florisil® and concentrated. The crude product was purified via column chromatography (SiO_2, 3% Et_2O/hexanes) to yield 136 mg (99%) of the product **82i** as a mixture of diastereomers. Separating the stereoisomers of **82i** by GLC {flow rate 2.0 mL/min, method: 80 °C for 10 min, ramp @ 0.4 °C/min to 160 °C, hold for 5 min; T_r (min) = 105.3 [(2*S*,3*S*)-**82i**$_{anti}$], 106.0 [(2*R*,3*R*)-**82i**$_{anti}$], 108.0 (**82i**$_{syn1}$), 109.2 (**82i**$_{syn2}$), (ratio = 1.1:43.1:1:28.9)} provided the enantiomer ratio (2*S*,3*S*)-**82i**$_{anti}$:(2*R*,3*R*)-**82i**$_{anti}$ = 2.4:97.5 (95% ee), and (**82i**$_{syn1}$): (**82i**$_{syn2}$) = 3.3:96.7 (93% ee)

Anti diastereomer (off white, waxy solid)*:* mp 26-28 °C; $[\alpha]_D^{22}$ +3.24 (*c* 4.64, $CHCl_3$); ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.31 (br s, 2H), 7.25 (m, 1H), 6.27 (app t, *J*= 2.5 Hz, 2H), 6.21 (dd, *J* = 3.0, 2.0 Hz, 1H), 6.01 (d, *J*= 3.5 Hz, 1H), 5.92 (ddd, *J*= 17.0, 10.0, 9.5 Hz, 1H), 5.24 (dd, *J*=

10.0, 1.0 Hz, 1H), 5.18 (d, *J*= 17.0Hz, 1H), 3.88 (t, *J*= 9.0 Hz, 1H), 3.57 (dq, *J*= 8.5, 7.0 Hz, 1H), 1.29 (d, *J*= 7.0 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 172.9, 154.6, 141.5, 134.7, 119.1, 118.7, 113.1, 110.2, 106.0, 46.7, 41.5, 15.4; IR ν_{max}^{neat} cm^{-1}: 3149, 2980, 1714, 1503, 1468, 1364, 1321, 1272, 1096, 994, 734; HRMS (EI) *m/z* calcd for $C_{14}H_{15}NO_2$ $(M + H)^+$: 230.1181; found: 230.1183.

Syn diastereomer (light yellow oil)*:* $[\alpha]_D^{22}$ +3.03 (*c* 1.79, $CHCl_3$); ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.37 (dd, *J*= 2.0, 1.0 Hz, 1H), 7.35 (br s, 2H), 6.32 (m, 3H), 6.15 (d, *J* = 3.0 Hz, 1H), 5.95 (ddd, *J* = 18.5, 10.5, 8.0 Hz, 1H), 5.08 (dt, *J*= 17.0, 1.0 Hz, 1H), 5.04 (d, *J*= 10.0 Hz, 1H), 3.85 (t, *J* = 9.0 Hz, 1H), 3.56 (dq, *J*= 9.5, 6.5 Hz, 1H), 1.16 (t, *J*= 7.0 Hz, 3H); ^{13}C NMR (125 MHz, $CDCl_3$): δ 172.9, 153.8, 141.8, 135.9, 119.1, 117.4, 113.3, 110.2, 107.3, 46.5, 42.1, 16.8; IR ν_{max}^{neat} cm^{-1}: 2978, 2929, 1712, 1639, 1503, 1467, 1409, 1318, 1274, 1148, 1073, 1010, 994, 909, 806, 737; HRMS (EI) *m/z* calcd for $C_{14}H_{15}NO_2$ $(M + H)^+$: 230.1181; found: 230.1183.

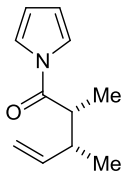


(2*R*,3*R*)-2-Methyl-3-(4-nitrophenyl)-1-(1H-pyrrol-1-yl)pent-4-en-1-one (82j): General Procedure C was followed employing 100 mg (0.45 mmol) (*E*)-3-(4-nitrophenyl)allyl acetate, 93 mg (0.48 mmol) (*Z*)-1-{1-[(trimethylsilyl)oxy]prop-1-en-1-yl}-1H-pyrrole, 7.4 mg (0.023 mmol) ligand **104**, 9.8 mg (0.023 mmol) $[CpRu(CH_3CN)_3]PF_6$, 23 mg (0.068 mmol) $B(O^pC_6H_4F)_3$, 0.90 mL THF. The reaction mixture was stirred for 16 h at which time it was concentrated under a stream of N_2, filtered through a plug of Florisil® and concentrated. The crude product was purified via column chromatography (SiO_2, 6% Et_2O/hexanes) to yield 112 mg (88%) of the product as a mixture of diastereomers. Separating the enantiomers by chiral HPLC [Daicel Chiralpak OD-H column, flow rate 1.0 ml/min, 1% *i*PrOH, 99% hexane; T_r (min) = 13.3

[(2*S*,3*S*)-**82j**$_{anti}$], 14.3 [(2*R*,3*R*)-**82j**$_{anti}$], 15.9 (**82j**$_{syn1}$), 17.0 (**82j**$_{syn2}$), (ratio = 1:30.4:6.7:220.9)} provided the enantiomer ratio (2*S*,3*S*)-**82j**$_{anti}$:(2*R*,3*R*)-**82j**$_{anti}$ = 3.2:96.8 (94% ee), and (**82j**$_{syn1}$): (**82j**$_{syn2}$) = 2.9:97.1 (94% ee)

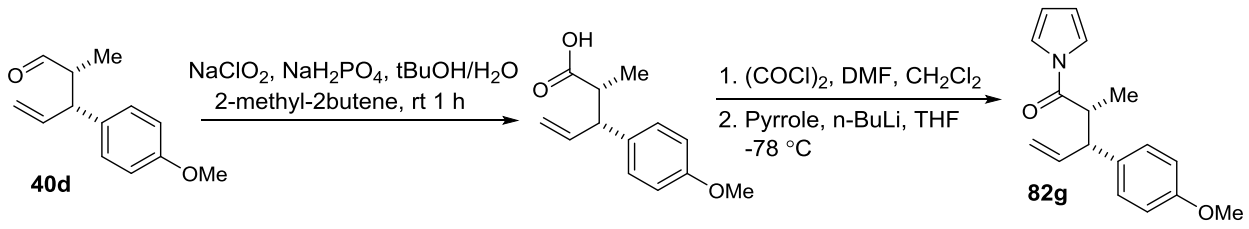
Anti diastereomer (off white solid)*:* mp 93-95 °C; $[\alpha]_D^{22}$ +8.71 (*c* 1.84, $CHCl_3$); ^{1}H NMR (500 MHz, $CDCl_3$): δ 8.09 (d, *J*= 8.5 Hz, 2H), 7.36 (d, *J*= 9.0 Hz, 2H), 7.18 (m, 2H), 6.24 (dd, *J* = 2.5 Hz, 2H), 5.94 (m, 1H), 5.23 (m, 2H), 3.86 (t, *J*= 10.0 Hz, 1H), 3.50 (dq, *J*= 10.0, 7.0 Hz, 1H), 1.42 (d, *J*= 7.0 Hz, 3H); ^{13}C NMR (125 MHz, $CDCl_3$): δ 172.4, 149.8, 146.7, 137.0, 128.4, 123.9, 118.8, 118.7, 113.6, 53.1, 43.1, 17.3; IR ν_{max}^{neat} cm^{-1}: 3148, 3078, 2927, 1709, 1638, 1598, 1467, 1408, 1298, 1235, 1094, 994, 919, 893, 822, 743, 704; HRMS (EI) *m/z* calcd for $C_{16}H_{16}N_2O_3$ $(M + H)^+$: 285.1239; found: 285.1211.

Syn diastereomer (clear, colorless oil)*:* $[\alpha]_D^{22}$ +2.63 (*c* 0.950, $CHCl_3$); ^{1}H NMR (500 MHz, $CDCl_3$): δ 8.22 (d, *J*= 9.0 Hz, 2H), 7.41 (d, *J*= 8.5 Hz, 2H), 7.36 (br s, 2H), 6.35 (app t, *J* = 2.0 Hz, 2H), 5.96 (ddd, *J* = 18.0, 10.5, 7.5 Hz, 1H), 5.07 (m, 2H), 3.90 (t, *J*= 9.5 Hz, 1H), 3.50 (dq, *J* = 10.0, 7.0 Hz, 1H), 1.10 (t, *J*= 7.0 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 172.5, 148.5, 147.1, 137.3, 129.2, 124.0, 119.0, 117.8, 113.7, 52.7, 43.0, 16.9; IR ν_{max}^{neat} cm^{-1}: 2927, 1711, 1602, 1519, 1467, 1409, 1346, 1322, 1273, 1113, 1073, 914, 852, 740, 702; HRMS (EI) *m/z* calcd for $C_{16}H_{16}N_2O_3$ $(M + H)^+$: 285.1239; found: 285.1241.



(2*R*,3*R*)-2,3-Dimethyl-1-(1H-pyrrol-1-yl)pent-4-en-1-one (106): General Procedure C was followed employing 50 mg (0.44 mmol) (*E*)-but-2-en-1-yl acetate, 90 mg (0.46 mmol) (*Z*)-1-{1-[(trimethylsilyl)oxy]prop-1-en-1-yl}-1H-pyrrole, 8.7 mg (0.022 mmol) ligand **105**, 9.5 mg (0.022 mmol) $[CpRu(CH_3CN)_3]PF_6$, 23 mg (0.066 mmol) $B(O^pC_6H_4F)_3$, 0.80 mL THF. The reaction mixture was stirred for 16 h at which time it was

concentrated under a stream of N_2, filtered through a plug of Florisil® and concentrated. The crude product was purified via column chromatography (SiO_2, 1% Et_2O/hexanes) to yield 29 mg (37%) of the product as an inseparable mixture of diastereomers **106** and regioisomers **107**. The mixture of products was saponified to the carboxylic acid (to a solution of 11 mg compound **107** (0.061 mmol) in 0.60 mL THF was added a solution of 0.60 mL of 1.0M NaOH. The solution was allowed to stir over night. The THF was evaporated and the aqueous layer was basified with the addition of an equal volume of saturated sodium bicarbonate. The aqueous layer was extracted 3x CH_2Cl_2 and discarded. The aqueous layer was then acidified to pH=1 with 1M HCl and extracted 3x CH_2Cl_2, dried over $MgSO_4$ and concentrated) which matched literature data. For *Anti* product see: Metz, P.; Hungerhoff, B. *J. Org. Chem.* **1997**, *62*, 4442-4448, for *Syn* product see: Rye, C. E.; Barker, D. *J. Org. Chem.* **2011**, *76*, 6636-6648, and for linear product see: Deyo, D. T.; Aebi, J. D.; Rich, D. H. *Synthesis* **1988**, *8*, 608-610.



Stereochemical Proof for Products (82a-j): (2*R*,3*R*)-3-(4-Methoxyphenyl)-2-methylpent-4-enal **82d** was prepared according to the catalytic asymmetric Claisen rearrangement utilizing procedure D, in which the absolute stereochemistry was determined via X-ray crystallography (See compound **S40d**).

To a magnetically-stirred solution of aldehyde **40d** 64 mg (0.32 mmol) and 2-methyl-2-butene 0.48 mL (4.5 mmol) in 1.0 mL *t*-BuOH (0.3 M) was added a solution of $NaClO_2$ 85 mg

(0.94 mmol) and NaH_2PO_4 113 mg (0.94 mmol) in 1 mL H_2O (1 M in $NaClO_2$) dropwise via syringe at ambient temperature. The reaction was stirred for 3 h whereupon a saturated aqueous solution of NH_4Cl (100% v/v to reaction volume) was added and the resulting mixture was extracted with Et_2O (3x). The combined organic extracts were combined, dried (MgSO4) and concentrated to provide 85 mg of the corresponding carboxylic acid that was used without purification in the next reaction.

To a rt solution of carboxylic acid 50 mg (0.23 mmol) in 1 mL CH_2Cl_2 was added thionyl chloride 30 μL (0.34 mmol) dropwise followed by 1 drop DMF. The reaction was allowed to stir for 1h until evolution of gas ceased. The reaction was then concentrated and redissolved in 0.5 mL of THF. The THF solution was added dropwise to a -78 °C solution of pyrrole 16 μL (0.23 mmol) and 0.18 mL of 1.4M *n*-BuLi (0.25 mmol) in 0.5 mL of THF. The reaction was allowed to gradually warm to rt and stir overnight. The reaction was quenched with H_2O (100% v/v to reaction volume), extracted with Et_2O (3x), dried over $MgSO_4$ and concentrated to yield **82g**.

The product of this reaction matched the 1H NMR and GLC of compound **82g**$_{anti}$. The absolute stereochemistry of compounds **82a-j** was assigned by analogy to this determination.

APPENDIX A. X-RAY CRYSTAL DATA FOR (2*R*,3*R*)-3-(4-METHOXYPHENYL)-2-METHYL-N-[(*R*)-1-PHENYLETHYL]PENT-4-ENAMIDE S40D

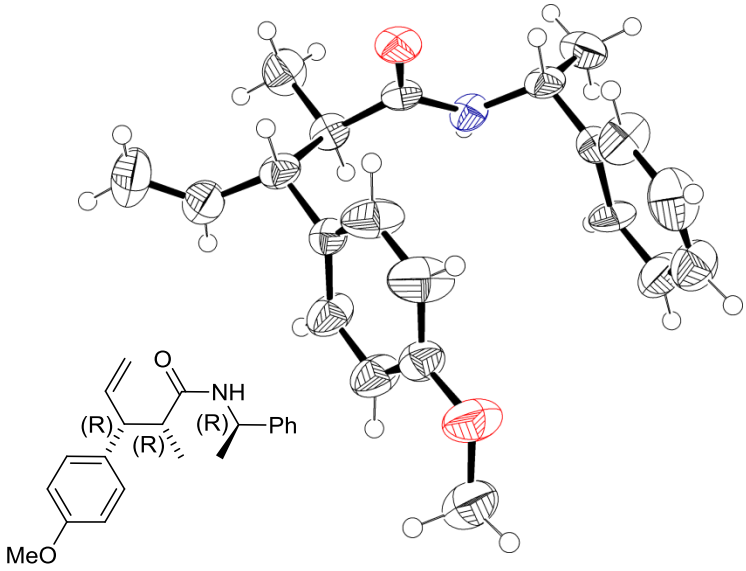


Figure 15. X-Ray Crystal Structure of **S40d**

ORTEP and line structure of (2*R*,3*R*)-3-(4-Methoxyphenyl)-2-methyl-N-[(R)-1-phenylethyl]pent-4-enamide. The molecular structure is drawn with 50% probability displacement ellipsoids; hydrogen atoms are drawn with an artificial radius.

Table 20. CIF information for Compound **S40d**

Identification code	dura2s
Empirical formula	C21 H25 N O2
Formula weight	323.42
Temperature	203(2) K

Wavelength	0.71073 Å	
Crystal system	Orthorhombic	
Space group	P 21 21 21	
Unit cell dimensions	a = 5.0151(18) Å	a= 90°.
	b = 16.013(6) Å	b= 90°.
	c = 22.861(8) Å	g = 90°.
Volume	1835.9(11) $Å^3$	
Z	4	
Density (calculated)	1.170 Mg/m^3	
Absorption coefficient	0.074 mm^{-1}	
F(000)	696	
Crystal size	0.32 x 0.03 x 0.03 mm^3	
Theta range for data collection	1.78 to 24.99°.	
Index ranges	-5<=h<=5, -19<=k<=19, -27<=l<=27	
Reflections collected	14062	
Independent reflections	1899 [R(int) = 0.1244]	
Completeness to theta = 24.99°	99.9 %	
Absorption correction	Semi-empirical from equivalents	
Max. and min. transmission	0.9978 and 0.9766	
Refinement method	Full-matrix least-squares on F^2	
Data / restraints / parameters	1899 / 16 / 257	
Goodness-of-fit on F^2	1.046	
Final R indices [I>2sigma(I)]	R1 = 0.0739, wR2 = 0.1629	
R indices (all data)	R1 = 0.1151, wR2 = 0.1812	
Absolute structure parameter	?	
Largest diff. peak and hole	0.220 and -0.223 $e.Å^{-3}$	

Table 21. Atomic coordinates (x 104) and equivalent isotropic displacement parameters (Å2x 103) for **S40d**

U(eq) is defined as one third of the trace of the orthogonalized U^{ij} tensor.

	x	y	z	U(eq)
N	2011(9)	5768(3)	1827(2)	40(1)
O(1)	-2299(6)	5935(2)	1579(2)	48(1)
O(2)	541(10)	2033(2)	1082(2)	72(1)
C(3)	2607(14)	3029(4)	2897(3)	65(2)
C(6)	1900(10)	4710(3)	2594(2)	38(1)
C(1')	4400(20)	4307(6)	2505(5)	52(3)
C(2')	4750(20)	3473(6)	2657(4)	68(4)
C(4')	170(20)	3373(7)	2939(5)	74(4)
C(5')	-150(20)	4202(6)	2798(5)	60(3)
C(1'')	2320(19)	4136(6)	2186(5)	44(3)
C(2'')	2630(19)	3300(6)	2337(4)	49(3)
C(4'')	2040(30)	3634(5)	3325(4)	56(3)
C(5'')	1770(20)	4475(6)	3176(4)	52(3)
C(7)	1539(10)	5623(3)	2441(2)	41(1)
C(8)	114(10)	5897(3)	1430(2)	35(1)
C(9)	941(10)	6027(3)	809(2)	39(1)
C(10)	-677(11)	5437(3)	412(2)	43(1)
C(11)	-1960(14)	4143(4)	970(3)	68(2)
C(12)	-1620(16)	3322(4)	1133(3)	78(2)
C(13)	414(12)	2850(3)	897(2)	49(2)
C(14)	2020(13)	3205(4)	505(3)	60(2)
C(15)	1711(12)	4038(4)	347(3)	59(2)
C(16)	-264(10)	4522(3)	579(2)	37(1)
C(17)	3246(14)	6200(4)	2809(2)	61(2)
C(18)	581(14)	6937(3)	643(2)	62(2)
C(19)	-148(14)	5586(3)	-222(2)	56(2)
C(20)	-1841(17)	5864(4)	-606(3)	80(2)
C(21)	2474(15)	1512(4)	824(3)	73(2)

Table 22. Bond lengths [Å] and angles [°] for **S40d**

N-C(8)	1.331(6)
N-C(7)	1.442(7)
N-H(1N)	0.78(8)
O(1)-C(8)	1.259(6)
O(2)-C(13)	1.378(7)
O(2)-C(21)	1.408(8)
C(3)-C(4')	1.346(9)
C(3)-C(2'')	1.352(8)
C(3)-C(2')	1.402(9)
C(3)-C(4'')	1.406(8)
C(3)-H(3)	0.9400
C(6)-C(1'')	1.327(11)
C(6)-C(5'')	1.384(8)
C(6)-C(5')	1.391(8)
C(6)-C(1')	1.424(11)
C(6)-C(7)	1.514(7)
C(1')-C(2')	1.392(9)
C(1')-H(1')	0.9400
C(2')-H(2')	0.9400
C(4')-C(5')	1.374(9)
C(4')-H(4')	0.9400
C(5')-H(5')	0.9400
C(1'')-C(2'')	1.390(9)
C(1'')-H(1'')	0.9400
C(2'')-H(2'')	0.9400
C(4'')-C(5'')	1.395(9)
C(4'')-H(4'')	0.9400
C(5'')-H(5'')	0.9400
C(7)-C(17)	1.515(7)
C(7)-H(7A)	0.9900
C(8)-C(9)	1.494(6)
C(9)-C(18)	1.515(7)
C(9)-C(10)	1.542(7)

C(9)-H(9A)	0.9900
C(10)-C(19)	1.493(8)
C(10)-C(16)	1.528(7)
C(10)-H(10A)	0.9900
C(11)-C(16)	1.374(8)
C(11)-C(12)	1.378(8)
C(11)-H(11A)	0.9400
C(12)-C(13)	1.379(9)
C(12)-H(12A)	0.9400
C(13)-C(14)	1.332(8)
C(14)-C(15)	1.391(8)
C(14)-H(14A)	0.9400
C(15)-C(16)	1.365(7)
C(15)-H(15A)	0.9400
C(17)-H(17A)	0.9700
C(17)-H(17B)	0.9700
C(17)-H(17C)	0.9700
C(18)-H(18A)	0.9700
C(18)-H(18B)	0.9700
C(18)-H(18C)	0.9700
C(19)-C(20)	1.298(8)
C(19)-H(19A)	0.9400
C(20)-H(20A)	0.9400
C(20)-H(20B)	0.9400
C(21)-H(21A)	0.9700
C(21)-H(21B)	0.9700
C(21)-H(21C)	0.9700
C(8)-N-C(7)	124.8(4)
C(8)-N-H(1N)	114(5)
C(7)-N-H(1N)	119(5)
C(13)-O(2)-C(21)	117.8(5)
C(4')-C(3)-C(2'')	86.8(8)
C(4')-C(3)-C(2')	121.2(8)
C(2'')-C(3)-C(2')	57.3(6)
C(4')-C(3)-C(4'')	58.8(8)
C(2'')-C(3)-C(4'')	116.0(7)

C(2')-C(3)-C(4'')	94.5(8)
C(4')-C(3)-H(3)	119.4
C(2'')-C(3)-H(3)	127.4
C(2')-C(3)-H(3)	119.4
C(4'')-C(3)-H(3)	116.6
C(1'')-C(6)-C(5'')	119.6(7)
C(1'')-C(6)-C(5')	86.9(7)
C(5'')-C(6)-C(5')	59.0(7)
C(1'')-C(6)-C(1')	56.3(6)
C(5'')-C(6)-C(1')	93.1(7)
C(5')-C(6)-C(1')	115.6(7)
C(1'')-C(6)-C(7)	121.7(5)
C(5'')-C(6)-C(7)	118.7(6)
C(5')-C(6)-C(7)	123.7(6)
C(1')-C(6)-C(7)	120.7(6)
C(2')-C(1')-C(6)	120.9(10)
C(2')-C(1')-H(1')	119.6
C(6)-C(1')-H(1')	119.6
C(1')-C(2')-C(3)	119.0(10)
C(1')-C(2')-H(2')	120.5
C(3)-C(2')-H(2')	120.5
C(3)-C(4')-C(5')	118.9(10)
C(3)-C(4')-H(4')	120.5
C(5')-C(4')-H(4')	120.5
C(4')-C(5')-C(6)	123.9(10)
C(4')-C(5')-H(5')	118.0
C(6)-C(5')-H(5')	118.0
C(6)-C(1'')-C(2'')	120.7(9)
C(6)-C(1'')-H(1'')	119.6
C(2'')-C(1'')-H(1'')	119.6
C(3)-C(2'')-C(1'')	122.9(9)
C(3)-C(2'')-H(2'')	118.5
C(1'')-C(2'')-H(2'')	118.5
C(5'')-C(4'')-C(3)	121.0(8)
C(5'')-C(4'')-H(4'')	119.5
C(3)-C(4'')-H(4'')	119.5

C(6)-C(5")-C(4") 119.6(9)
C(6)-C(5")-H(5") 120.2
C(4")-C(5")-H(5") 120.2
N-C(7)-C(6) 111.2(4)
N-C(7)-C(17) 110.4(4)
C(6)-C(7)-C(17) 113.1(4)
N-C(7)-H(7A) 107.3
C(6)-C(7)-H(7A) 107.3
C(17)-C(7)-H(7A) 107.3
O(1)-C(8)-N 120.7(5)
O(1)-C(8)-C(9) 121.1(5)
N-C(8)-C(9) 118.1(4)
C(8)-C(9)-C(18) 109.8(4)
C(8)-C(9)-C(10) 109.1(4)
C(18)-C(9)-C(10) 112.3(4)
C(8)-C(9)-H(9A) 108.5
C(18)-C(9)-H(9A) 108.5
C(10)-C(9)-H(9A) 108.5
C(19)-C(10)-C(16) 111.9(4)
C(19)-C(10)-C(9) 112.3(4)
C(16)-C(10)-C(9) 111.7(4)
C(19)-C(10)-H(10A) 106.8
C(16)-C(10)-H(10A) 106.8
C(9)-C(10)-H(10A) 106.8
C(16)-C(11)-C(12) 121.4(6)
C(16)-C(11)-H(11A) 119.3
C(12)-C(11)-H(11A) 119.3
C(11)-C(12)-C(13) 120.5(6)
C(11)-C(12)-H(12A) 119.7
C(13)-C(12)-H(12A) 119.7
C(14)-C(13)-O(2) 125.8(6)
C(14)-C(13)-C(12) 118.5(5)
O(2)-C(13)-C(12) 115.7(5)
C(13)-C(14)-C(15) 121.1(6)
C(13)-C(14)-H(14A) 119.4
C(15)-C(14)-H(14A) 119.4

C(16)-C(15)-C(14)121.6(6)
C(16)-C(15)-H(15A)119.2
C(14)-C(15)-H(15A)119.2
C(15)-C(16)-C(11)116.9(5)
C(15)-C(16)-C(10)123.0(5)
C(11)-C(16)-C(10)120.1(5)
C(7)-C(17)-H(17A)109.5
C(7)-C(17)-H(17B)109.5
H(17A)-C(17)-H(17B)
C(7)-C(17)-H(17C)109.5
H(17A)-C(17)-H(17C)
H(17B)-C(17)-H(17C)
C(9)-C(18)-H(18A)109.5
C(9)-C(18)-H(18B)109.5
H(18A)-C(18)-H(18B)
C(9)-C(18)-H(18C)109.5
H(18A)-C(18)-H(18C)
H(18B)-C(18)-H(18C)
C(20)-C(19)-C(10)126.4(6)
C(20)-C(19)-H(19A)116.8
C(10)-C(19)-H(19A)116.8
C(19)-C(20)-H(20A)120.0
C(19)-C(20)-H(20B)120.0
H(20A)-C(20)-H(20B)
O(2)-C(21)-H(21A)109.5
O(2)-C(21)-H(21B)109.5
H(21A)-C(21)-H(21B)
O(2)-C(21)-H(21C)109.5
H(21A)-C(21)-H(21C)
H(21B)-C(21)-H(21C)

Symmetry transformations used to generate equivalent atoms:

Table 23. Anisotropic displacement parameters (Å2x 103) for **S40d**

The anisotropic displacement factor exponent takes the form: $-2p^2[\ h^2\ a^{*2}U^{11} + ... + 2\ h\ k\ a^*\ b^*\ U^{12}\ ]$

U^{11}	U^{22}	U^{33}	U^{23}	U^{13}	U^{12}	
N 20(2)	49(3)	51(3)	6(2)	2(2)	1(2)	
O(1)18(2)	66(3)	59(2)	-6(2)	9(2)	6(2)	
O(2)81(3)	43(2)	92(3)	3(2)	18(3)	8(2)	
C(3)65(5)	60(4)	69(4)	14(4)	3(4)	-2(4)	
C(6)24(3)	51(3)	38(3)	-2(3)	0(2)	0(2)	
C(1')	36(7)	49(7)	70(7)	-4(6)	8(6)	19(5)
C(2')	69(9)	61(8)	74(9)	22(7)	10(8)	20(8)
C(4')	65(10)	88(11)	71(9)	17(8)	13(8)	-26(9)
C(5')	34(6)	61(8)	84(8)	25(7)	16(6)	-11(6)
C(1'')	35(6)	50(7)	47(6)	4(6)	-7(5)	-4(6)
C(2'')	34(6)	58(8)	56(7)	-9(6)	1(6)	14(6)
C(4'')	67(9)	56(8)	44(6)	19(6)	14(7)	2(7)
C(5'')	47(7)	46(7)	62(7)	2(6)	-3(6)	4(6)
C(7)22(3)	49(3)	52(3)	-3(3)	3(2)	10(2)	
C(8)27(3)	29(3)	50(3)	-4(2)	4(2)	-1(2)	
C(9)23(3)	42(3)	51(3)	1(2)	1(2)	-5(2)	
C(10)	27(3)	47(3)	55(3)	-3(3)	-3(2)	7(2)
C(11)	61(4)	43(4)	98(5)	0(3)	34(4)	1(3)
C(12)	86(5)	49(4)	100(5)	6(4)	50(5)	-5(4)
C(13)	51(4)	38(3)	59(3)	-2(3)	-3(3)	0(3)
C(14)	48(4)	58(4)	74(4)	10(3)	12(3)	14(3)
C(15)	44(3)	65(4)	67(4)	18(3)	17(3)	17(3)
C(16)	24(3)	43(3)	45(3)	-5(2)	-8(2)	0(2)
C(17)	60(4)	63(4)	61(3)	-19(3)	4(3)	5(3)
C(18)	76(5)	50(4)	61(4)	8(3)	3(4)	-10(3)
C(19)	56(4)	53(4)	59(4)	2(3)	-6(3)	1(3)
C(20)	88(6)	82(5)	70(4)	16(4)	-30(4)	-1(5)
C(21)	72(5)	53(4)	94(5)	-3(4)	-16(4)	6(4)

Table 24. Hydrogen coordinates (x 10^4) and isotropic displacement parameters ($Å^2$x 10^3) for **S40d**

	x	y	z	U(eq)
H(1N)	3410(160)	5910(50)	1730(30)	80(30)
H(3)	2876	2480	3030	78
H(1')	5821	4608	2341	62
H(2')	6413	3211	2601	82
H(4')	-1297	3053	3064	89
H(5')	-1852	4439	2842	71
H(1'')	2408	4295	1791	53
H(2'')	2867	2907	2036	59
H(4'')	1826	3469	3717	67
H(5'')	1513	4878	3469	62
H(7A)	-347	5767	2520	49
H(9A)	2854	5884	772	46
H(10A)	-2584	5564	479	52
H(11A)	-3382	4451	1129	81
H(12A)	-2784	3081	1407	94
H(14A)	3385	2887	332	72
H(15A)	2891	4274	73	70
H(17A)	2923	6774	2694	92
H(17B)	5113	6066	2749	92
H(17C)	2796	6129	3218	92
H(18A)	1633	7284	903	93
H(18B)	-1286	7087	677	93
H(18C)	1167	7021	243	93
H(19A)	1581	5468	-358	67
H(20A)	-3595	5991	-492	96
H(20B)	-1311	5937	-997	96
H(21A)	2354	957	993	109
H(21B)	4236	1739	896	109
H(21C)	2164	1479	406	109

APPENDIX B. X-RAY CRYSTAL DATA FOR (2*R*,3*R*)-3-(4-BROMOPHENYL)-2-METHYL-N-[(*R*)-1-PHENYLETHYL]PENT-4-ENAMIDE S40E

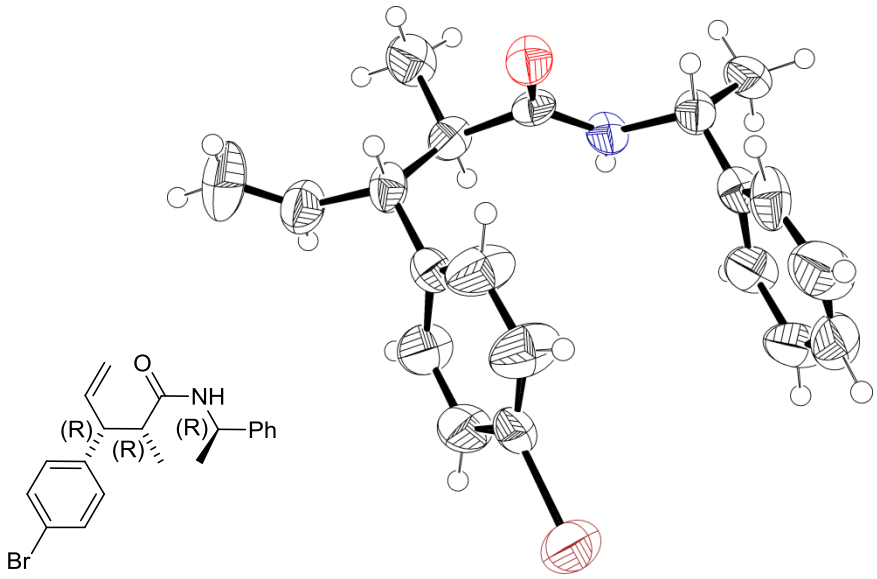


Figure 16. X-Ray Crystal Structure of Compound **S40e**

ORTEP and line structure of (2*R*,3*R*)-3-(4-bromophenyl)-2-methyl-N-[(*R*)-1-phenylethyl]pent-4-enamide (**S40e**). The molecular structure is drawn with 50% probability displacement ellipsoids; hydrogen atoms are drawn with an artificial radius.

Table 25. CIF information for **S40e**

Identification code	mgn114s
Empirical formula	C20 H22 Br N O
Formula weight	372.30

Temperature	203(2) K	
Wavelength	0.71073 Å	
Crystal system	Orthorhombic	
Space group	P2(1)2(1)2(1)	
Unit cell dimensions	a = 5.0268(12) Å	a= 90°.
	b = 15.831(4) Å	b= 90°.
	c = 22.862(6) Å	g = 90°.
Volume	1819.4(8) $Å^3$	
Z	4	
Density (calculated)	1.359 Mg/m^3	
Absorption coefficient	2.264 mm^{-1}	
F(000)	768	
Crystal size	0.26 x 0.05 x 0.01 mm^3	
Theta range for data collection	1.56 to 24.99°.	
Index ranges	-5<=h<=5, -18<=k<=18, -27<=l<=27	
Reflections collected	14271	
Independent reflections	3185 [R(int) = 0.1035]	
Completeness to theta = 24.99°	100.0 %	
Absorption correction	None	
Max. and min. transmission	0.9690 and 0.5906	
Refinement method	Full-matrix least-squares on F^2	
Data / restraints / parameters	3185 / 17 / 253	
Goodness-of-fit on F^2	0.920	
Final R indices [I>2sigma(I)]	R1 = 0.0616, wR2 = 0.1287	
R indices (all data)	R1 = 0.1138, wR2 = 0.1470	
Absolute structure parameter	0.03(2)	
Largest diff. peak and hole	0.705 and -0.268 $e.Å^{-3}$	

Table 26. Atomic coordinates (x 104) and equivalent isotropic displacement parameters (Å2x 103) for **S40e**

U(eq) is defined as one third of the trace of the orthogonalized U^{ij} tensor.

	x	y	z	U(eq)
Br	12121(2)	6656(1)	6010(1)	74(1)
O	7561(8)	10845(3)	6530(2)	52(1)
N	11845(12)	10742(4)	6777(2)	42(2)
C(3)	12698(18)	7995(4)	7889(3)	69(2)
C(6)	11846(11)	9675(4)	7550(2)	41(2)
C(1')	11600(30)	9471(6)	8133(6)	64(4)
C(2')	12010(30)	8629(5)	8281(4)	72(5)
C(4')	12840(30)	8255(6)	7309(3)	53(3)
C(5')	12640(30)	9091(5)	7131(4)	43(3)
C(1'')	9900(30)	9102(8)	7769(5)	56(4)
C(2'')	10090(20)	8270(8)	7958(6)	84(5)
C(4'')	14750(20)	8418(6)	7604(7)	75(5)
C(5'')	14225(17)	9251(7)	7451(6)	61(5)
C(7)	11433(12)	10584(4)	7399(3)	45(2)
C(8)	9912(12)	10855(4)	6399(3)	38(2)
C(9)	10715(14)	10988(4)	5757(3)	46(2)
C(10)	9322(13)	10341(4)	5367(3)	47(2)
C(11)	8586(15)	9005(5)	5925(4)	77(3)
C(12)	9205(15)	8183(4)	6087(4)	77(2)
C(13)	11293(14)	7794(4)	5829(3)	50(2)
C(14)	12708(15)	8202(5)	5429(3)	66(2)
C(15)	12092(17)	9035(5)	5281(3)	65(2)
C(16)	10025(12)	9450(4)	5527(3)	41(2)
C(17)	13137(17)	11166(4)	7763(3)	64(2)
C(19)	9823(16)	10532(5)	4728(3)	63(2)
C(20)	8100(20)	10704(5)	4338(4)	99(3)
C(18)	10100(17)	11899(4)	5612(3)	66(2)

Table 27. Bond lengths [Å] and angles [°] for **S40e**

Br-C(13)	1.895(7)
O-C(8)	1.220(7)
N-C(8)	1.313(8)
N-C(7)	1.460(8)
N-H(1N)	0.67(5)
C(3)-C(4')	1.3893(11)
C(3)-C(2'')	1.3895(11)
C(3)-C(4'')	1.3900(11)
C(3)-C(2')	1.3903(11)
C(3)-H(3)	0.947(10)
C(6)-C(1')	1.376(13)
C(6)-C(5')	1.3895(11)
C(6)-C(5'')	1.3900(11)
C(6)-C(1'')	1.424(14)
C(6)-C(7)	1.493(9)
C(1')-C(2')	1.3900(11)
C(1')-H(1'A)	0.9400
C(2')-H(2'A)	0.9400
C(4')-C(5')	1.3896(11)
C(4')-H(4'A)	0.9400
C(5')-H(5'A)	0.9400
C(1'')-C(2'')	1.3897(11)
C(1'')-H(1''A)	0.9400
C(2'')-H(2''A)	0.9400
C(4'')-C(5'')	1.3900(11)
C(4'')-H(4''A)	0.9400
C(5'')-H(5''A)	0.9400
C(7)-C(17)	1.507(9)
C(7)-H(7A)	0.9900
C(8)-C(9)	1.536(8)
C(9)-C(18)	1.511(9)
C(9)-C(10)	1.528(9)

C(9)-H(9A)	0.9900
C(10)-C(16)	1.500(9)
C(10)-C(19)	1.512(9)
C(10)-H(10A)	0.9900
C(11)-C(16)	1.359(9)
C(11)-C(12)	1.388(10)
C(11)-H(11A)	0.9400
C(12)-C(13)	1.352(9)
C(12)-H(12A)	0.9400
C(13)-C(14)	1.328(9)
C(14)-C(15)	1.395(10)
C(14)-H(14A)	0.9400
C(15)-C(16)	1.352(10)
C(15)-H(15A)	0.9400
C(17)-H(17A)	0.9700
C(17)-H(17B)	0.9700
C(17)-H(17C)	0.9700
C(19)-C(20)	1.274(10)
C(19)-H(19A)	0.9400
C(20)-H(20A)	0.9400
C(20)-H(20B)	0.9400
C(18)-H(18A)	0.9700
C(18)-H(18B)	0.9700
C(18)-H(18C)	0.9700
C(8)-N-C(7)	124.1(6)
C(8)-N-H(1N)	119(5)
C(7)-N-H(1N)	117(5)
C(4')-C(3)-C(2'')	93.8(9)
C(4')-C(3)-C(4'')	51.1(8)
C(2'')-C(3)-C(4'')	126.9(9)
C(4')-C(3)-C(2')	114.5(8)
C(2'')-C(3)-C(2')	57.6(8)
C(4'')-C(3)-C(2')	98.0(8)
C(4')-C(3)-H(3)	118(3)
C(2'')-C(3)-H(3)	103(5)
C(4'')-C(3)-H(3)	128(4)

C(2')-C(3)-H(3) 125(3)
C(1')-C(6)-C(5') 122.5(8)
C(1')-C(6)-C(5'') 97.0(9)
C(5')-C(6)-C(5'') 47.1(7)
C(1')-C(6)-C(1'') 56.6(7)
C(5')-C(6)-C(1'') 90.8(8)
C(5'')-C(6)-C(1'') 109.9(8)
C(1')-C(6)-C(7) 115.9(6)
C(5')-C(6)-C(7) 121.4(6)
C(5'')-C(6)-C(7) 123.2(6)
C(1'')-C(6)-C(7) 126.8(7)
C(6)-C(1')-C(2') 116.6(11)
C(6)-C(1')-H(1'A) 121.7
C(2')-C(1')-H(1'A)121.7
C(1')-C(2')-C(3) 124.9(10)
C(1')-C(2')-H(2'A)117.5
C(3)-C(2')-H(2'A) 117.5
C(3)-C(4')-C(5') 123.9(8)
C(3)-C(4')-H(4'A) 118.1
C(5')-C(4')-H(4'A)118.1
C(6)-C(5')-C(4') 117.0(8)
C(6)-C(5')-H(5'A) 121.5
C(4')-C(5')-H(5'A)121.5
C(2'')-C(1'')-C(6) 131.8(12)
C(2'')-C(1'')-H(1''A)114.1
C(6)-C(1'')-H(1''A)114.1
C(3)-C(2'')-C(1'') 109.0(11)
C(3)-C(2'')-H(2''A)125.5
C(1'')-C(2'')-H(2''A)125.5
C(3)-C(4'')-C(5'') 115.8(10)
C(3)-C(4'')-H(4''A)122.1
C(5'')-C(4'')-H(4''A)122.1
C(4'')-C(5'')-C(6) 125.4(10)
C(4'')-C(5'')-H(5''A)117.3
C(6)-C(5'')-H(5''A)117.3
N-C(7)-C(6) 111.8(5)

N-C(7)-C(17)	110.6(6)
C(6)-C(7)-C(17)	112.5(5)
N-C(7)-H(7A)	107.2
C(6)-C(7)-H(7A)	107.2
C(17)-C(7)-H(7A)	107.2
O-C(8)-N	123.6(6)
O-C(8)-C(9)	119.4(6)
N-C(8)-C(9)	117.0(6)
C(18)-C(9)-C(10)	114.7(6)
C(18)-C(9)-C(8)	106.6(6)
C(10)-C(9)-C(8)	110.2(5)
C(18)-C(9)-H(9A)	108.4
C(10)-C(9)-H(9A)	108.4
C(8)-C(9)-H(9A)	108.4
C(16)-C(10)-C(19)	112.6(6)
C(16)-C(10)-C(9)	112.3(5)
C(19)-C(10)-C(9)	110.7(6)
C(16)-C(10)-H(10A)	106.9
C(19)-C(10)-H(10A)	106.9
C(9)-C(10)-H(10A)	106.9
C(16)-C(11)-C(12)	123.0(7)
C(16)-C(11)-H(11A)	118.5
C(12)-C(11)-H(11A)	118.5
C(13)-C(12)-C(11)	119.1(7)
C(13)-C(12)-H(12A)	120.5
C(11)-C(12)-H(12A)	120.5
C(14)-C(13)-C(12)	119.6(7)
C(14)-C(13)-Br	119.8(5)
C(12)-C(13)-Br	120.6(6)
C(13)-C(14)-C(15)	120.5(7)
C(13)-C(14)-H(14A)	119.7
C(15)-C(14)-H(14A)	119.7
C(16)-C(15)-C(14)	122.0(7)
C(16)-C(15)-H(15A)	119.0
C(14)-C(15)-H(15A)	119.0
C(15)-C(16)-C(11)	115.8(6)

C(15)-C(16)-C(10)122.4(6)
C(11)-C(16)-C(10)121.8(6)
C(7)-C(17)-H(17A)109.5
C(7)-C(17)-H(17B)109.5
H(17A)-C(17)-H(17B)
C(7)-C(17)-H(17C)109.5
H(17A)-C(17)-H(17C)
H(17B)-C(17)-H(17C)
C(20)-C(19)-C(10)127.2(8)
C(20)-C(19)-H(19A)116.4
C(10)-C(19)-H(19A)116.4
C(19)-C(20)-H(20A)120.0
C(19)-C(20)-H(20B)120.0
H(20A)-C(20)-H(20B)
C(9)-C(18)-H(18A)109.5
C(9)-C(18)-H(18B)109.5
H(18A)-C(18)-H(18B)
C(9)-C(18)-H(18C)109.5
H(18A)-C(18)-H(18C)
H(18B)-C(18)-H(18C)

Symmetry transformations used to generate equivalent atoms:

Table 28. Anisotropic displacement parameters(Å2x 103) for **S40e**

The anisotropic displacement factor exponent takes the form: $-2p^2[\ h^2\ a^{*2}U^{11} + ... + 2\ h\ k\ a^*\ b^*\ U^{12}\ ]$

U^{11}	U^{22}	U^{33}	U^{23}	U^{13}	U^{12}	
Br81(1)	56(1)	85(1)	4(1)	-12(1)	11(1)	
O 30(3)	75(3)	50(3)	2(2)	2(2)	4(2)	
N 23(3)	64(4)	40(4)	-2(3)	10(3)	3(3)	
C(3)110(7)	43(4)	54(5)	9(4)	-2(6)	-13(5)	
C(6)25(3)	58(4)	40(4)	-2(3)	7(3)	-7(3)	
C(1')	101(13)	60(9)	30(8)	1(6)	17(8)	-2(9)
C(2')	115(14)	51(8)	51(9)	19(7)	46(10)	-13(10)
C(4')	54(9)	42(8)	61(9)	-24(7)	1(7)	-5(8)
C(5')	48(8)	48(8)	34(7)	-5(6)	-17(7)	-21(7)
C(1'')	42(8)	89(12)	38(9)	7(8)	-7(7)	-12(9)
C(2'')	102(15)	70(12)	79(13)	-11(11)	16(11)	-5(13)
C(4'')	84(12)	55(10)	87(13)	-12(10)	27(11)	5(11)
C(5'')	89(14)	36(9)	59(11)	6(8)	27(10)	-12(9)
C(7)33(4)	64(4)	39(4)	2(3)	4(3)	5(3)	
C(8)24(4)	40(4)	50(4)	-1(3)	-1(3)	5(3)	
C(9)39(4)	51(4)	47(4)	11(3)	7(3)	3(3)	
C(10)	48(4)	59(4)	34(4)	10(3)	0(3)	-2(4)
C(11)	70(5)	67(5)	95(7)	26(5)	39(5)	20(4)
C(12)	79(5)	53(5)	99(6)	32(5)	35(5)	5(4)
C(13)	57(5)	51(4)	42(4)	-14(3)	-10(3)	1(4)
C(14)	66(5)	76(5)	56(4)	2(4)	27(4)	21(5)
C(15)	70(5)	64(5)	62(5)	16(4)	24(5)	7(5)
C(16)	38(4)	45(4)	39(4)	-6(3)	-1(3)	-8(3)
C(17)	75(5)	62(4)	54(4)	-21(3)	-8(4)	14(4)
C(19)	63(5)	78(5)	49(5)	13(4)	-1(4)	9(4)
C(20)	116(8)	119(7)	63(6)	38(5)	-29(6)	-17(7)
C(18)	89(6)	55(5)	53(5)	12(3)	16(4)	-6(4)

Table 29. Hydrogen coordinates (x 10^4) and isotropic displacement parameters ($Å^2$x 10^3) for **S40e**

	x	y	z	U(eq)
H(3)	12570(140)	7409(10)	7970(20)	56(18)
H(1'A)	11177	9880	8416	76
H(2'A)	11798	8478	8676	87
H(4'A)	13097	7840	7020	63
H(5'A)	13018	9255	6745	52
H(1"A)	8175	9328	7789	68
H(2"A)	8685	7946	8109	100
H(4"A)	16383	8157	7521	91
H(5"A)	15594	9553	7264	74
H(7A)	9554	10720	7487	54
H(9A)	12660	10903	5723	55
H(10A)	7387	10406	5433	56
H(11A)	7104	9266	6099	93
H(12A)	8188	7901	6371	92
H(14A)	14136	7928	5243	79
H(15A)	13146	9315	5003	78
H(17A)	12786	11747	7652	96
H(17B)	14999	11037	7696	96
H(17C)	12721	11087	8173	96
H(19A)	11607	10522	4605	76
H(20A)	6281	10722	4437	119
H(20B)	8635	10813	3952	119
H(18A)	10589	12013	5209	99
H(18B)	11105	12267	5870	99
H(18C)	8213	12002	5664	99
H(1N)	13090(100)	10690(30)	6680(20)	9(16)

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