Accessing Chemically Differentiated 1,5-dienes Through Palladium Catalyzed Allyl-Allyl Cross-Coupling with Internal Allyl Electrophiles

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ACCESSING CHEMICALLY DIFFERENTIATED 1,5-DIENES THROUGH PALLADIUM CATALYZED ALLYL-ALLYL CROSS-COUPLING WITH INTERNAL ALLYL ELECTROPHILES

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Accessing Chemically Differentiated 1,5-dienes Through Palladium-Catalyzed Allyl-Allyl Cross-Coupling with Internal Allyl Electrophiles

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Thesis Advisor: Professor James P. Morken

Abstract

Internal allyl electrophiles were successfully implemented in a catalytic cross-coupling to allylB(pin) with high regiocontrol to afford multisubstituted 1,5-dienes bearing chemically differentiated olefins. Construction of alkenyl compounds with all carbon quaternary centers and high enantiomeric excess can be achieved in one step without the use of enantiomerically enriched chiral ligands.

Acknowledgments

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To my friends and family, thank you for supporting me physically and emotionally, and for encouraging me to follow my heart. It wasn't easy, but my time at BC gave me the skills and confidence to find my dream job.

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List of Abbreviations

Ac: acyl
App: apparent
B(pin): pinacolato boron
BINAP: 2,2'-bis(diphenylphosphino)1,1'-binapthyl
Bn: benzyl
Boc: *tert*-butyloxycarbonyl
Boc_2O: di-*tert*-butylcarbonate
br: branched
cee: conservation of enantiomeric excess
cod: cyclooctadiene
Cy: cyclohexane
dba: dibenzylidene acetone
DCM: dichloromethane
DMAP: 4-(dimethylamino)pyridine
DPEphos: bis[(2-phenylphosphino)phenyl) ether
dppbenzene: 1,2-bis(diphenylphosphino)benzene
Dppe: 1,2-bis(diphenylphosphino)ethane
dppf: 1,1'-bis(diphenylphosphino)
eq: equation
equiv: equivalent(s)
er: enantiomer ratio
Et_2O: diethyl ether
EtOAc: ethyl acetate
GLC: gas liquid chromatography
h: hours
HPLC: high performance liquid chromatography
HRMS: high resolution mass spectrometry
L*: Chiral Ligand
L: Ligand
Lin: linear
[M]: metal complex
MeO(furyl)BIPHEP: 2,2'- bis(difurylphosphino)-6,6'-dimethoxy-1,1'-biphenyl

OAc: acetate
pin: pinacol
ppm: parts per million
QuinoxP*: 2,3-bis(*tert*-butylmethylphosphino)quinoxaline
regio: regioselectivity
rt: room temperature
S.M.: starting material
TBAF: tetrabutylammonium fluoride
TEA or Et_3N: triethylamine
tol: toluene
xantphos: 4,5-bis(diphenylphosphino)-9,9-dimethylxanthene
y: yield

I. Introduction

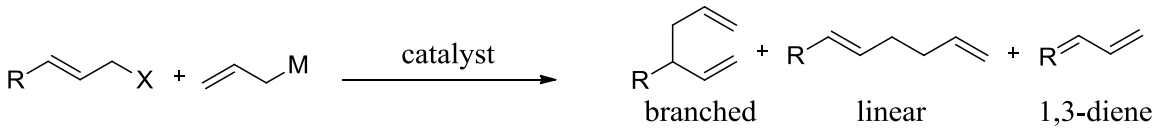
The development of transition metal-catalyzed cross-coupling was a pivotal discovery in synthetic chemistry.[1] Metal catalyzed cross-coupling allows for rapid construction of carbon-carbon bonds in a highly selective manner. Akira Suzuki and Ei-ichi Negishi were awarded the Nobel Prize in chemistry for their work on the cross-coupling of electrophiles bearing aryl, alkyl, and vinyl organometallic reagents. Since their initial discoveries, one motif that has been underexplored in this context is the use of allyl nucleophiles or allyl electrophiles. Several examples of coupling allylmetals with aryl electrophiles have been demonstrated in the literature, [2] but the cross-coupling of allylmetal reagents with allyl electrophiles has been less explored. Two major difficulties inherent to this transformation include control of the regioselectivity, and the propensity for β-hydride elimination from intermediate organopalladium compounds to form1,3-diene byproducts

[1] The Nobel Prize in Chemistry 2010 - Advanced Information". *Nobelprize.org.* Nobel Media AB 2013. Web. 9 Jul 2013. <http://www.nobelprize.org/nobel_prizes/chemistry/laureates/2010/advanced.html>.

[2] Refs for coupling aryl E with allyl metals. Sn: (a)Echavarren, A. M.; Stille, J. K. *J. Am. Chem. Soc.* **1987**, *109*, 5478. (b) Obora,Y.; Tsuji, Y.; Kobayashi, M.; Kawamura, T. *J. Org. Chem.* **1995**, *60*, 4647. (c) Kosugi, M.; Sasazawa, K.; Shimizu, Y.; Migita, T. *Chem. Lett*. **1977**, 301. Si: (d)Hatanaka, Y.; Ebina, Y.; Hiyama, T. *J. Am. Chem. Soc.* **1991**, *113*, 7075. (e) Hatanaka, Y.; Goda, K.; Hiyama, T. *Tetrahedron Lett.* **1994**, *35*, 1279. (f) Hatanaka, Y.; Goda, K.; Hiyama, T. *Tetrahedron Lett.* **1994**, *35*, 6511. B: (g) Kalinin, V. N.; Denisov, F. S.; Bubnov, Y. N. *Mendeleev Commun.* **1996**, 206. (h) Yamamoto, Y.; Takada, S.; Miyaura, N. *Chem. Lett.* **2006**, *35*, 704.

(Figure 1).[3] Initial studies in this field observed mixtures of linear and branched 1,5-diene products (Figure 1).

Figure 1. Allyl-Allyl Coupling Products and Byproducts

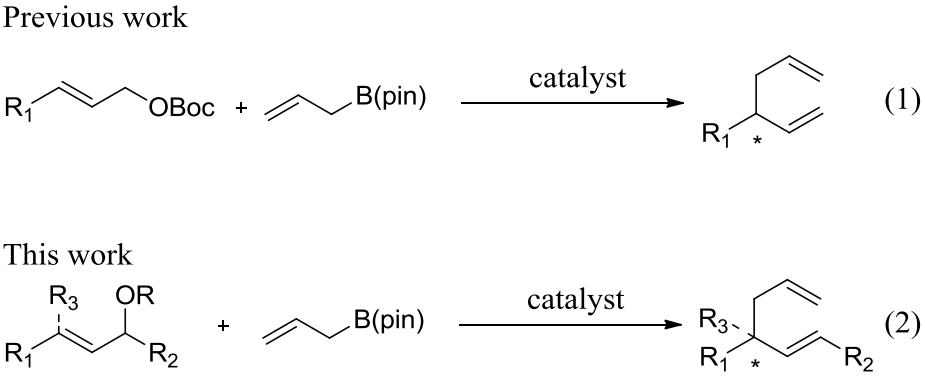


Branch-selective allyl-allyl cross-coupling is an attractive transformation because it allows for the construction of a stereocenter and produces a product with two terminal alkenes. These olefins can be utilized in subsequent reactions to append further complexity to the molecule. In 2010, the Morken group developed the first branch-selective and enantioselective palladium-catalyzed allyl-allyl cross-coupling to form enantioenriched 1,5-dienes (Figure 2, Eq 1).[4] An important feature of this reaction is implementation of allylboronate as the nucleophile. Boron reagents are generally less toxic and less reactive compared to other organometals used in these transformations.[5] For this reason, they are safer to work with and can tolerate a broad range of functional groups.

[3] Keinan, E.; Kumar, S.; Dangur, V.; Vaya, J. *J. Am. Chem. Soc.* **1994**, *116*, 11151.
[4] Zhang, P.; Brozek, L. A.; Morken, J. P. *J. Am. Chem. Soc.* **2010**, *132*, 10686.
[5] Miyaura, N.; Suzuki, A. *Chem. Rev.* **1995**, *95*, 2457.

To expand the utility of the 1,5-diene as a synthetic building block, we sought to construct products with differentiated steric and electronic properties of the alkenes for chemoselective functionalization. We envisioned achieving this through the cross-coupling of internal allyl electrophiles with allylB(pin) and a palladium catalyst (Figure 2, Eq 2). This methodology offers a complement toward other existing modes of diene differentiation, and will be discussed in Section II of this text.[6] We then expanded the scope of the transformation to synthesize all carbon quaternary centers from trisubstituted allyl electrophiles. Finally, the synthesis of enantioenriched chiral quaternary centers using enriched electrophiles and achiral ligands was examined.

Figure 2. Strategy for Improved Chemoselectivity



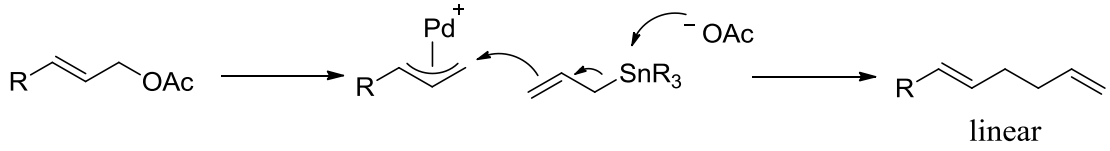
[6](a) Le, H; Kyne, R. E.; Brozek, L. A.; Morken, J. P. *Org. Lett.* **2013**, *15,* 1432. (b) Zhang, P.; Le, H.; Kyne, R. E.; Morken, J. P. *J. Am. Chem. Soc.* **2011**, *133*, 9716.

II. Background on Allyl-Allyl Cross-Coupling

A. Linear Selective Cross-Coupling

The first examples of catalytic, intermolecular cross-coupling of unsymmetrical allyl partners were demonstrated by Trost and Stille. The Trost group coupled substituted allyl stannanes with cinnamyl acetate in the presence of $Pd(PPh_3)_4$ to access 1,5-hexadiene derivatives.[7] They observed that the coupling occurred at the least hindered carbon of the electrophile. In most cases, the allyl from the stannane reacted with inversion through an S_E2' pathway.[8] Thus, they proposed that C-C bond formation occurs *via* an outer-sphere mechanism in which an activated allylstannane directly reacts with the least hindered carbon of the η^3 π-allyl intermediate (Figure 3).

Figure 3. Trost's Outer-Sphere Cross-Coupling



Concurrently, Godschalx and Stille reported a similar coupling of allyl bromides with allylstannanes, catalyzed by a $BnClPd(PPh_3)_2$ complex.[9]

[7] Trost, B. M.; Keinan, E. *Tet. Lett.* **1980**, *21*, 2595.
[8] SE2'in the literature
[9] Godschalx, J.; Stille, J. K. *Tet. Lett.* **1980**, *21*, 2599.

Initially, they hypothesized this reaction would proceed through an inner-sphere mechanism: oxidative addition of the allyl bromide to Pd^0, transmetalation of the allylstannane to Pd^{II}, and reductive elimination to form the linear 1,5-diene (Figure 4). To test this hypothesis, they devised a common intermediate experiment (Figure 5). If an inner-sphere mechanism operated, equations **(3)** and **(4)** would afford the same ratio of products because reductive elimination occurs through a common intermediate. In practice, the experiments produced different product ratios. This result supported an outer sphere coupling mechanism, which is consistent with the observations reported by the Trost group.

Figure 4. Stille's Inner-Sphere Hypothesis

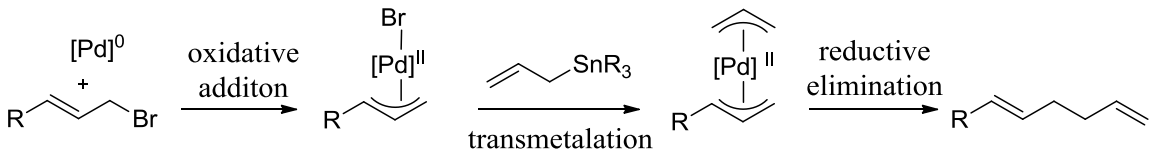
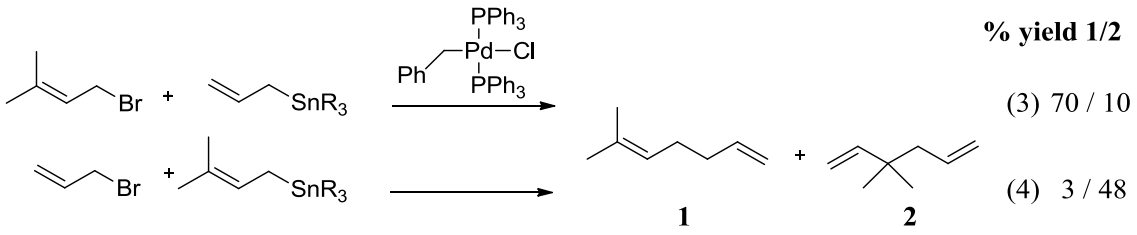
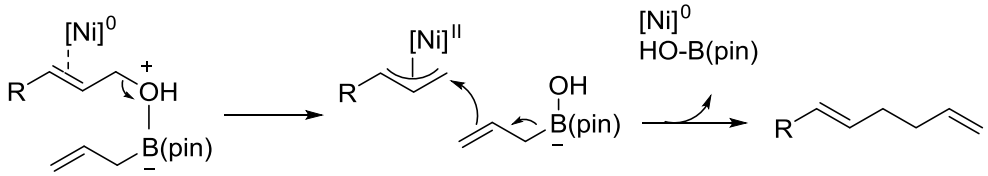


Figure 5. Stille's Mechanistic Experiments



More recently, the Morken group developed the first branch-selective coupling of allyl carbonates with allyl boronates. At the same time, the Kobayashi group developed a linear-selective coupling using the same substrates and metal.[10] The opposite regioselectivity observed by the two groups stems from the choice of phosphine ligand. The Kobayashi group later switched to a $Ni(PPh_3)_4$ catalyst to minimize significant 1,3-diene formation that formed with aliphatic or more hindered carbonates. Nickel has been shown to enhance reductive elimination relative to β-hydride elimination.[11] Using this catalyst, they demonstrated that linear unprotected allyl alcohols could be used in a cross-coupling to afford the linear 1,5-dienes (Figure 6).[12] Based on the observed regioselectivity, they proposed an outer-sphere coupling mechanism similar to that suggested by Trost and Stille.

Figure 6. Kobayashi's Outer-Sphere Ni-Catalyzed Coupling



[10] Schneider, U.; Kobayashi, S. *Chem. Eur. J.* **2009**, *15*, 12247.
[11] (a) Kurosawa, H.; Ohnishi, H.; Emoto, M.; Kawasaki, Y.; Murai, S. *J. Am. Chem. Soc.***1988**, *110*, 6272. (b) Kurosawa, H.; Ohnishi, H.; Emoto, M.; Chatani, N.; Kawasaki, Y.; Murai, S.; Ikeda, I. *Organometallics* **1990**, *9*, 3038.
[12] Jimenez-Aquino, A.; Flegeau, E. F.; Schneider, U.; Kobayashi, S. *Chem. Comm.* **2011**, *47*, 9456.

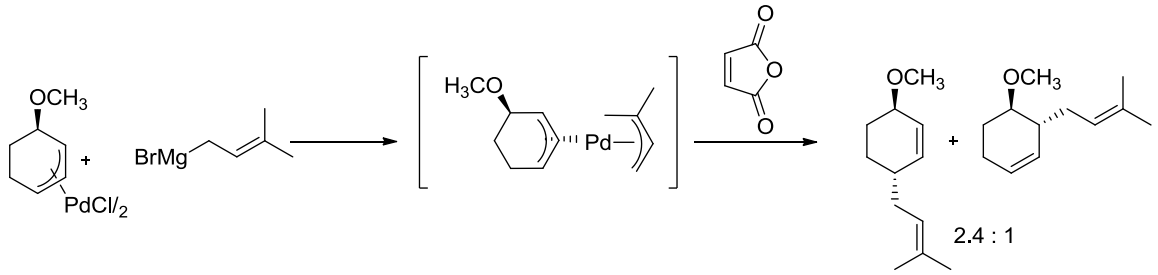
B. Mechanistic Insights into Inner-Sphere Allyl-Allyl Cross-Coupling

Thus far, the mechanistic evidence for allyl-allyl coupling using palladium and nickel catalysts strongly supported an outer sphere mechanism. However, an important study conducted by the Schwartz group suggested that this is not always the case. They observed that allyl palladium dimers can react with allyl Grignard or stannane nucleophiles, forming stable bis(η^3-allyl)Pd intermediates (Figure 7).[13] Isolation of the bis(η^3-allyl)Pd intermediate proved that the allyl stannane moiety could transmetalate onto palladium.[14] In order to induce coupling of the allyl moieties on the Pd-intermediate (*via* reductive elimination), π-acidic ligands such as maleic anhydride or fumaronitrile were required. This coupling was highly selective for C-C bond formation at the least hindered carbon of the allyl units. Unlike the results by Trost and Stille, inversion of prenyl nucleophiles was not observed in either product (Figure 7). In addition, the prenyl group was delivered to the same face as the η^3-bound palladium intermediate. Together, these details support an inner-sphere mechanism. In addition, they concluded that association of π-acidic ligands to the metal

[13] (a) Goliaszewski, A.; Schwartz, J. *J. Am. Chem. Soc.* **1984**, *106*, 5028. (b) Goliaszewski, A.; Schwartz, J. *Tetrahedron*, **1984**, *41*, 5779.
[14] (a) Shi, M.; Nicholas, K.M. *J. Am. Chem. Soc.* **1997**, *119*, 5057. (b) Shirakawa, E.; Yoshida, H.; Nakao, Y.; Hiyama, T. *Org. Lett.* **2000**, *2*, 2209.

promoted the reductive elimination by converting one of the η^3-allyl ligands to the η^1 form (Figure 7). In the prior examples, absence of this ligand type may be the driving force for the well documented outer-sphere mechanism.

Figure 7. Schwartz's Stoichiometric Allyl-Allyl Coupling

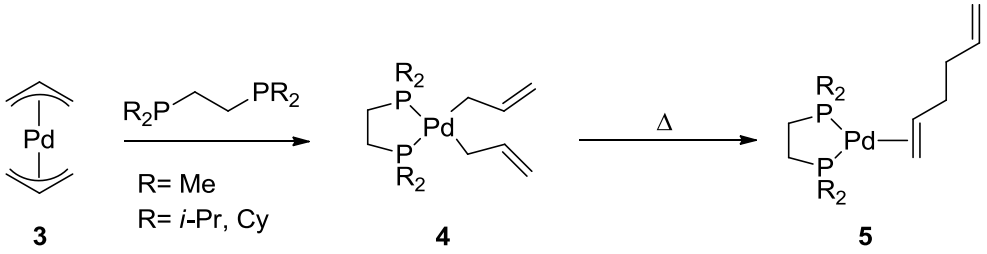


In support of the findings by Schwartz, Jolly[15] and Pörschke[16] demonstrated that bidentate phosphine ligands were also able to promote reductive elimination of bis(allyl)metal intermediates (Figure 8). Isolation of complex **4** at low temperatures suggests that phosphine ligation converts bis(η^3-allyl)Pd complex **3** into the bis(η^1-allyl) form. At ambient temperatures, **4** gives complex **5** *via* reductive elimination. These two reports suggest that a bis(η^1-allyl)Pd conformation such as **4**, may be required for reductive elimination to occur under thermodynamic control. In

[15] Jolly, P. W. *Angew. Chem. Int. Ed.* **1985**, *24*, 283.
[16] Krause, J.; Bonrath, W.; Pörschke, K.-R. *Organometallics.* **1992**, *11*, 1158.

the context of Schwartz's experiment, maleic anhydride could occupy one or two coordination sites around palladium to form a similar intermediate.

Figure 8. Reductive Elimination *via* Bidentate Phosphine Ligands

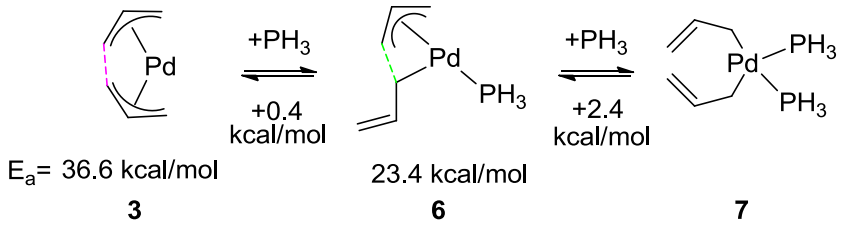


One detail that the prior experiments do not specify is through which carbon atoms the C-C bond formation is occurring. To study the mechanism of the reductive elimination step for bis-allyl systems, Echavarren et al.[17] employed DFT calculations to estimate the activation energies from three plausible intermediates: **3, 6** and **7** (Figure 9). First, his calculations showed that the coordination of ligands around palladium is in equilibrium. Progression from **3** to **6** and **6** to **7** is slightly endothermic by 0.4 and 2.4 kcal/mol respectively. The calculations predicted that reductive elimination from bis(η^3) transition state **3**, has the highest calculated activation energy at

[17] (a) Cuerva, J. M.; Bengoa, E. G-.; Mendez, M.; Echavarren, A. M. *J. Org. Chem.***1997**, *62*, 7540. (b) Cardenas, D. J.; Echavarren, A. M. *Chem. Eur. J.***2002**, *8*, 3620. (c) Cardenas, D. J.; Echavarren, A. *New J. Chem.* **2004**, *28*, 338.

36.6 kcal/mol. This is congruent with the experimental observations demonstrated by Schwartz, Jolly and Porchke[15,16].

Figure 9. Possible Reductive Elimination Intermediates

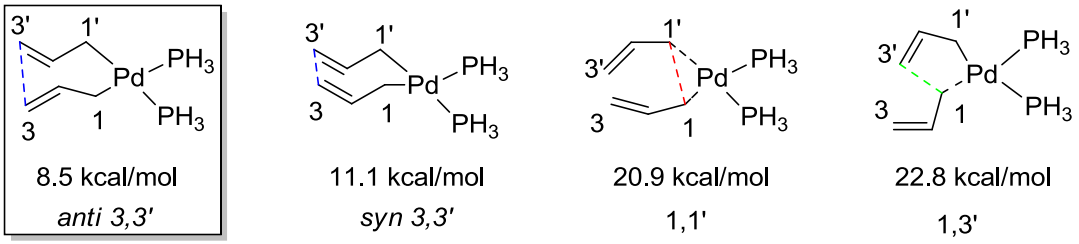


Reductive elimination from transition state **6** was predicted to be lower in energy by 13.6 kcal/mol.[18] There are four available pathways for reductive elimination to proceed from intermediate **7**: 1,1', 1,3', *syn* 3,3', and *anti* 3,3' (Figure 10). The *syn* 3,3' refers to a boat configuration of the seven-membered ring, whereas *anti* 3,3' describes the chair conformation. The calculations predicted that the *anti* 3,3' and *syn* 3,3' pathways have the lowest activation energies. The standard 1,1' pathway was predicted to be higher in energy by 12.4 kcal/mol. The 1,3' pathway was the highest energy pathway from the bis(η^1) intermediate. One plausible hypothesis for this trend is that the formation of double bonds between C1-C2 and C1'-C2' in the 3,3' pathway has a stabilizing interaction with the lone pair electrons on palladium. This is unique for allyl systems as the reductive elimination of

[18] This value includes the energy required to adopt the (η^3)(η^1) binding mode.

aryl and alkyl ligands occurs through the 1,1' mechanism. This unique finding has been confirmed by other groups through computation and experimentation.[19]

Figure 10. Reductive Elimination Energies from Bis(η^1) Intermediates



C. Branch-Selective Allyl-Allyl Cross Coupling

The Morken group capitalized on the 3,3' reductive elimination to develop a number of branch-selective cross-coupling transformations.[4,6,20] Selectivity for the 3,3' elimination was achieved by optimizing the ligand.[21] A screen of bidentate phosphine ligands revealed that ligands with small bite angles favored the branched product while ligands with large bite angles and monodentate ligands were less selective (Scheme 1).[4] One hypothesis for this trend is that the bite angle of the ligand distorts the square planar

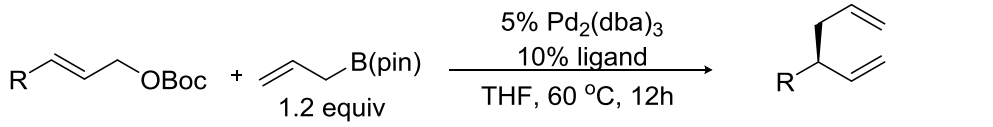
[19] (a) Perez-Rodriguez, M.; Braga, A. A. C.; de Lera, A. R.; Maseras, F.; Alvarez, R.; Expinet, P. *Organometallics.* **2010**, *29*, 4983. For a related experimentally observable h1-allyl-h1-carboxylate, see: (b)Sherden, N. H.; Behenna, D. C.; Virgil, S. C.; Stoltz, B. M. *Angew. Chem., Int. Ed.* **2009**, *48*, 6840.

[20] (a) Brozek, L. A.; Ardolino, M. J.; Morken, J. P. *J. Am. Chem. Soc.* **2011**, *133,* 16778. (b) Ardolino, M. J.; Morken, J. P. J. Am. Chem. Soc. **2012**, *134*, 8770.

[21] (a) Birkholz, M. N.; Freixa, Z.; van Leeuwen, P. W. N. M. *Chem. Soc. Rev.* **2009**, *38*, 1099. (b) van Leeuwen, P. W. N. M.; Kamer, P. C. J.; Reek, J. N. H.; Dierkes, P. *Chem. Rev.* **2000**, *100*, 2741.

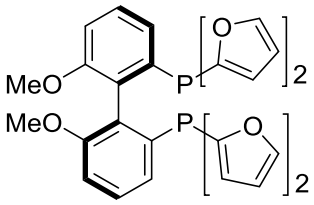
geometry adopted by the bis(η^1-allyl)Pd intermediate. Echavarren calculated the P-Pd-P angles for the 1,1' and 3,3'-eliminations to be 104.9° and 96.6° respectively.[17] Similar reports speculate that small-bite-angle ligands increase the distance between C1 and C1', thereby increasing the activation energy barrier to the 1,1'-reductive elimination pathway.[22] Recent findings show that palladium complexes with large bite-angle ligands react through three coordinate "arm off" structures that favor the linear product.[23]

Scheme 1. Morken's Branch-Selective and Enantioselective Coupling

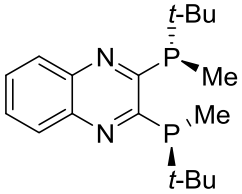


16 examples, 50-90% yield,
up to 99:1 er

Ligand	Bite angle	Branched:Linear
PPh_3	--	1:>20
dppe	85	98:2
dppf	96	94:6
DPEphos	102	72:28



(R)-MeO-furyl-BIPHEP
L1



(R,R)-QuinoxP*
L2

[22] Marcon, J. E.; Moloy, K. G. *J. Am. Chem. Soc.* **1998**, *120*, 8527.
[23] Ardolino, M, J.; Morken, J. P. *Tetrahedron.* **2015**.

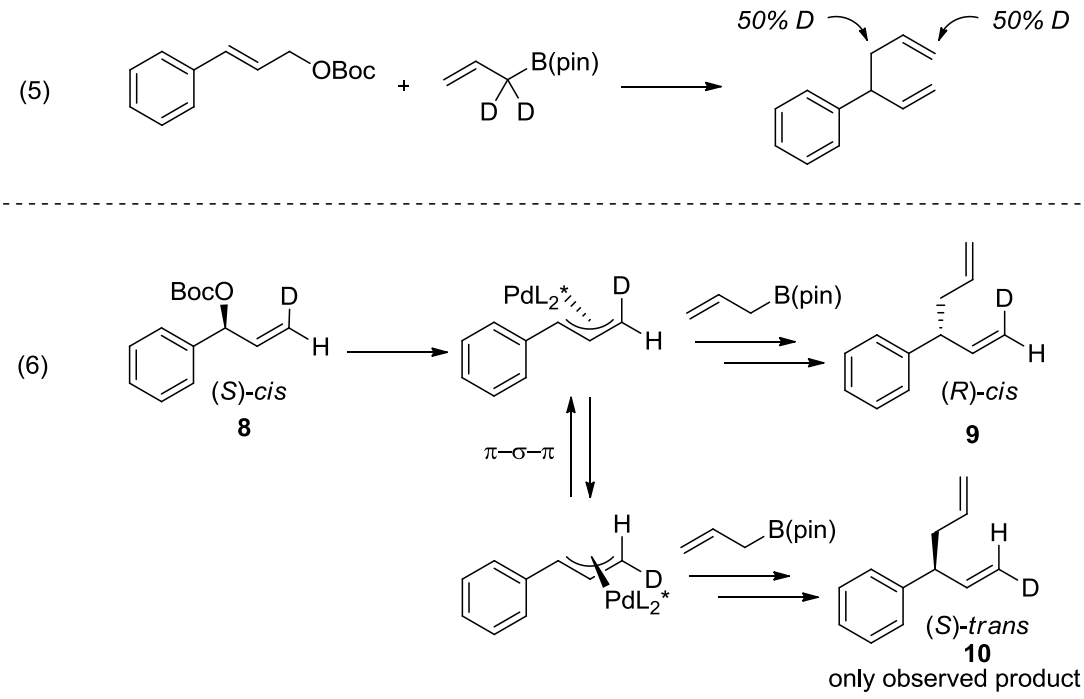
The scope of this reaction was quite broad: sterically encumbered allyl carbonates, heteroaromatics, and even protected allylic and homoallylic alcohols were tolerated with good yields and up to 99:1 *er*.

To verify the proposed inner sphere mechanism, two important experiments were carried out. In the first experiment, isotopically labeled allylB(pin) was employed as the substrate in the allyl-allyl coupling (Figure 11, Eq. 5). Under the normal cross-coupling conditions, the deuterium label was found at both allyl termini in the reaction product (and the recovered allylBpin was unscrambled). If the reaction occurred through an outer-sphere mechanism, in which nucleophilic addition of allylB(pin) to the Pd-allyl intermediate occurs in an S_E2' fashion, deuterium scrambling would not occur, and allyl inversion would be present. The observations made in this experiment are consistent with a mechanism that proceeds by transmetalation, followed by isomerization of the bis(allyl)Pd complex.

In the second experiment, enantiomerically enriched **8** was prepared and subjected to the cross coupling. The only product observed was (*S*)-**10,** which was isolated with 91% *ee* and >20:1 E:Z ratio (Figure 11, Eq 6). Assuming that oxidative addition occurs *anti* to the leaving group, and reductive elimination occurs from the same face as the palladium, the resulting product would be (*R*)-**9**. Surprisingly, this product was not

observed. A plausible explanation for this observation is that the palladium center was able to isomerize to the opposite face of the allyl species *via* rapid π–σ–π isomerization. The favored pathway is dictated by the chiral ligand and produced (*S*)-**10** upon completion of the reaction. This was the first demonstration of catalyst controlled enantioselectivity in a branched selective allyl-allyl cross-coupling.

Figure 11. Deuterium Labeling Mechanistic Studies

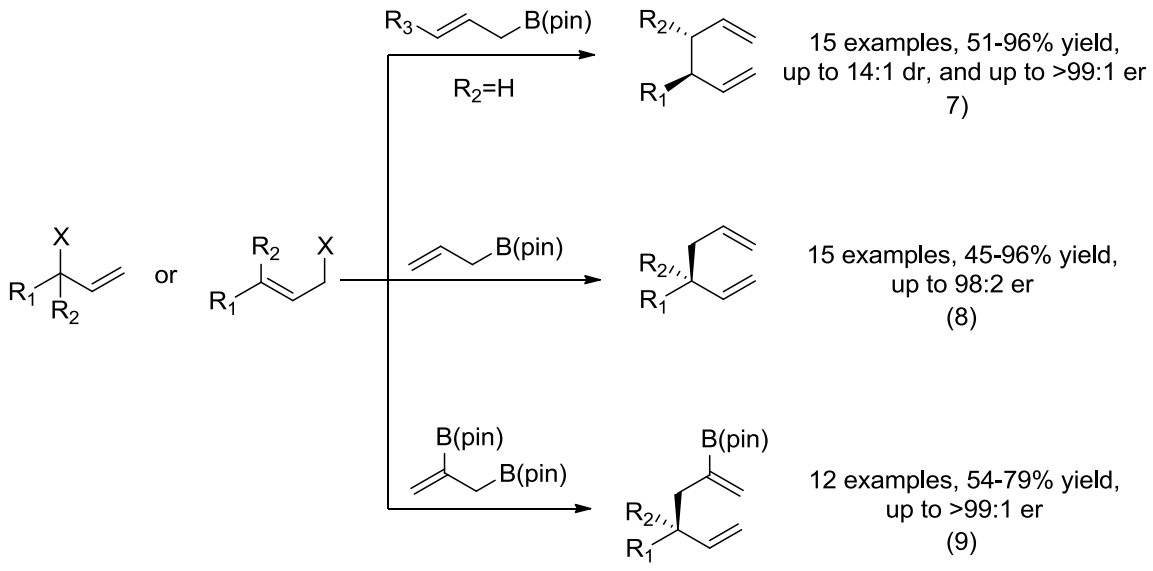


Since this initial publication, the Morken group has expanded the scope of this transformation to access a number of branched 1,5-dienes (Figure 12). In 2011, a diasterioselective transformation utilizing prochiral

γ-substituted allyl boronates and allyl chlorides was developed (Figure 12, Eq 7).[20a] The reaction tolerated silyl ethers, esters, imides, and pendant alkene substituents. Sterically hindered all-carbon quaternary centers were synthesized with high enantioselectivity using racemic trisubstituted or tertiary allyl carbonates in the coupling (Figure 12, Eq 8).[6(b)] Before optimization, significant amounts of β-hydride elimination products were observed. This was later minimized by the addition of CsF[24] and water[25] additives that accelerate the transmetalation with respect to β-hydride elimination. Finally, the Morken group demonstrated that functionalized allyl boronates, including those with an additional boronic ester at the vinylic position, can be employed in the reaction (Figure 12, Eq 9).[6(a)] This type of allyl nucleophile provided 1,5-diene products with differentiated olefins. These developments demonstrate how versatile and powerful the allyl-allyl cross-coupling reaction is for asymmetric carbon-carbon bond formation.

[24] Wright S. W,; Hageman, D. L.; McClure, L. D. *J. Org. Chem*. **1994**, *59*, 6095.
[25] (a) Amatore C, Jutand A, Le Duc G. *Chem. Eur. J.* **2011**, *17*, 2492 (b) Carrow, B.; Hartwig, J. *J. Am. Chem. Soc.* **2011**, *133*, 2116. (c) Suzaki Y, Osakada K. *Organometallics.* **2006**, *25*, 3251.

Figure 12. Morken's Branch-Selective Cross-Couplings



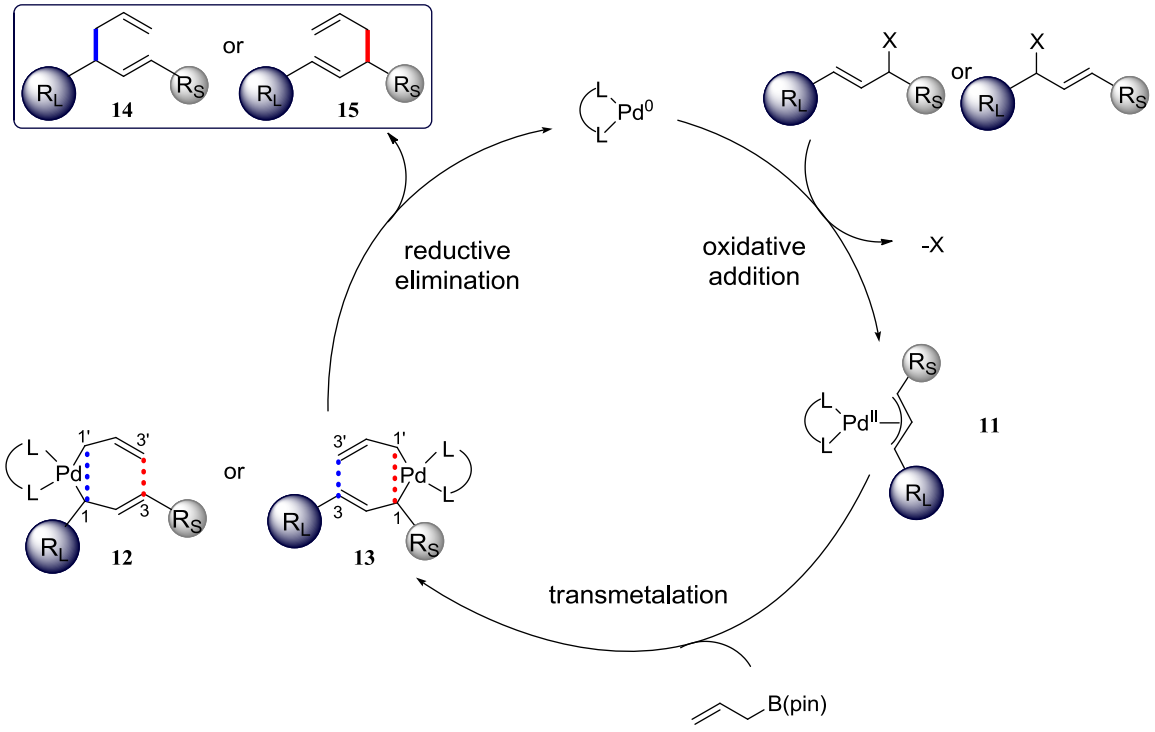
III. Development of the Internal Allyl-Allyl Cross-Coupling

A. The Proposed Catalytic Cycle

Using the previous mechanistic studies of the Morken group as a model, the proposed mechanism for the cross coupling of a disubstituted, internal allyl electrophile with allyl B(pin) is shown in Figure 13. In the first step, oxidative addition of the allyl electrophile to palladium (0) forms Pd(II)-(η^3-allyl) intermediate **11**. Transmetalation of the allyl boron nucleophile to the palladium center can form two possible Pd(II)-(η^1-allyl) intermediates (**12** or **13**). With two intermediates that can eliminate by two different reductive elimination pathways, we expected to observe mixtures of products **14** and **15** (See Figure 10 for reductive elimination pathways).

To elaborate, product **14** can form by 3,3' reductive elimination of **13** or 1,1' reductive elimination of **12**. Similarly, product **15** can form by 3,3' reductive elimination of **12** or 1,1' reductive elimination of **13**.

Figure 13. Proposed Catalytic Cycle for Internal Ally-Allyl Cross-Coupling

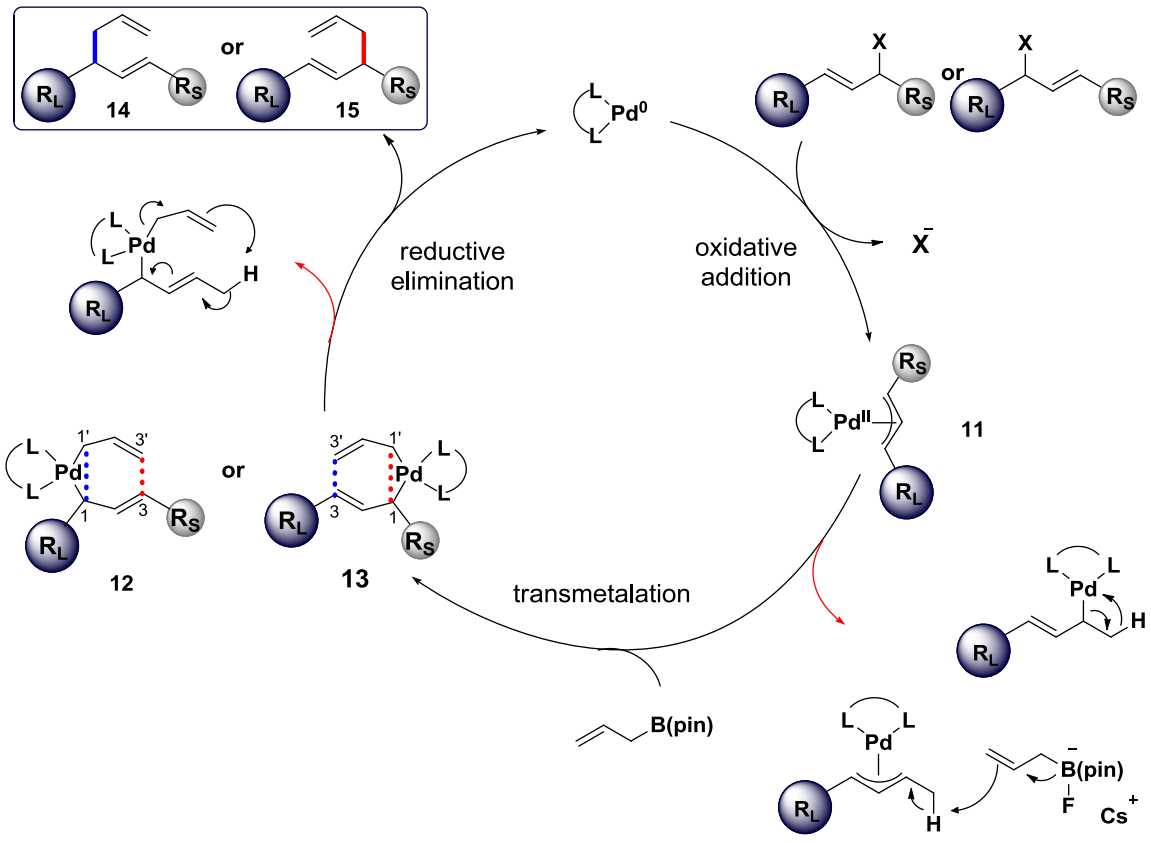


While motifs **14** and **15** are synthetically useful, our aim is to form the C-C bond at the more hindered or substituted carbon atom of the electrophile. We hypothesized that in cases where one substituent was sterically larger than the other $R_L > R_S$, or if an additional substituent was present geminal to R_L, steric repulsions between the ligands on Pd and the substitutents on the allyl electrophile would bias the reductive elimination

from intermediate **13**. By tuning the bite angle on the bidentate phosphine ligand, we predict that 3,3'-reductive elimination from species **13** will afford product **14** with high regioselectivities.

In addition to the complex regioselectivities in this transformation, we were also aware that competing formation of 1,3-diene byproducts through various off cycle β-hydride abstraction and elimination pathways were likely and could affect the yield of our transformation. Possible mechanisms are shown with red arrows in Figure 14.

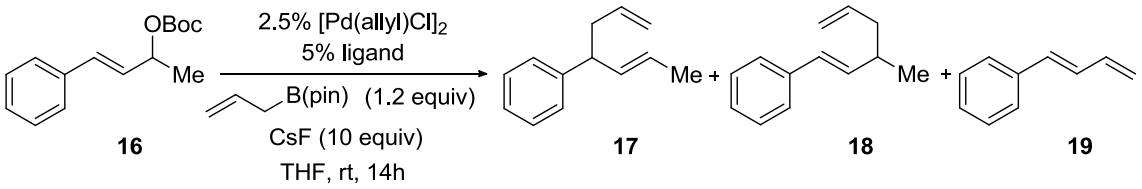
Figure 14. 1,3-Diene Forming Pathways



B. Proof of Concept and Reaction Optimization

We initiated our studies using methyl substituted cinnamyl carbonate **16** as a model substrate (Table 1). This carbonate was chosen for a few reasons: it can be easily prepared from cinnamyl alcohols (see SI for synthesis), the Boc protecting group is tolerable under similar reaction conditions,[4] and the size difference between the phenyl and methyl substituents is enough to reveal any effects of sterics on the regioselectivity. For the initial reaction parameters, we used conditions that were optimized in a previous paper on a similar substrate.[4] Based on our sterics hypothesis, we expected the coupling to favor branched product **17**.

Table 1. Ligand Optimization



16 **17** **18** **19**

entry	ligand	bite angle	**17 : 18**	**(17+18) : 19**	yield (%)[a]
1	PPh_3	-	0:1	1:1	43
2	dpp-benzene	83	4:1	5:1	66
3	*rac*-BINAP	92	2:1	1:6	4
4	dppp	91	0:1	1:4	11
5	dppf	96	1:10	1:10	2
6	DPEphos	102	1:10	1:4	16
7	*rac*-OMe-BIPHEP	87[b]	0:1	1:2	32

[a] combined yield of 1,5 diene products

[b] calculated dihedral angle

For the ligand screen, a variety of commercially available bidentate phosphine ligands were chosen. They are all racemic and range in bite angle[26] and electronic properties (Table 1). A few observations stood out from the ligand screen. First, PPh_3 selectively afforded the undesired regioisomer **18,** while dppbenzene afforded product **17** with good regioselectivity. Second, we expected to see a negative trend between increasing bite angle and selectivity of the 3,3' reductive elimination product **17**. This held true with the exception of dppp and OMe-BIPHEP, which were completely selective for **18** (the 1, 1' reductive elimination product) despite reportedly small bite angles. The third observation was the overall low yields due to increased formation of byproduct **19**.

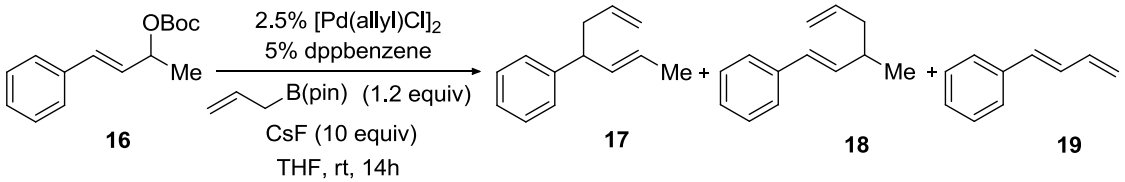
The first observation is in line with our hypothesis that bidentate ligands promote branched product formation *via* 3,3' reductive elimination of the bis(η^1-allyl)Pd intermediate. In contrast, monodentate ligands bias outersphere or 1,1' elimination pathways. Increasing the bite angle of the ligand impacts the energetics of the 3,3' and 1,1' reductive elimination pathways by perturbing the bis (η^1-allyl) intermediate to favor a the 1,1' pathway.[27] Based on the second observation, it is clear that other factors in

[26] Zhang, Z.; Qian, H.; Longmeier, J.; Zhang, X. *J. Org. Chem.* **2000**, *65*, 6223
[27] Van Leeuwen, P. W. N. M; Kamer, P. C. J.; Reek, J. N. H.; Dierkes, P. *Chem. Rev.* **2000**, *100*, 2741

addition to bite angle, such as electronics and sterics of the ligands, also play a role in the observed regioselectivity for this class of substrate. The third observation hints that larger ligands can slow down the transmetalation, allowing the off cycle reactions to form large quantities of **19**.

After identifying dppbenzene as the optimal ligand for branch selectivity, we looked at reoptimizing the reaction conditions to improve 1,5- diene yields and reduce 1,3-diene formation. Increasing the reaction temperature to 60 °C increased both 1,5 and 1,3-diene formation (Table 1, Entry 2). Removal of CsF (Entry 3) led to no 1,5-diene product. Reducing the equivalents of CsF (Entry 4) resulted in lower yields compared to entry 1. Replacing CsF with Cs_2CO_3 provided a higher yield albeit with diminished regioselectivity. The addition of 15 equivalents of water improved yields (Entry 6), but too much was detrimental to the regioselectivity (Entry 7). In entry 9 we demonstrated that the regioisomer of the substrate provides equivalent reactivity and selectivity. This result affirms a common intermediate forms after oxidative addition and it broadens the utility of the reaction.

Table 2. Parameter Optimization



16 **17** **18** **19**

entry	variation of conditions	**17:18**	(**17+18**):**19**	yield (%)[a]
1	RT	4:1	5:1	66
2	60 °C	3:1	4:1	62
3	no CsF	-	0:1	-
4	CsF (3 equiv)	3:1	4:1	54
5	Cs_2CO_3 (10 equiv)	3:1	6:1	78
6	H_2O (15 equiv)	4:1	9:1	78
7	H_2O (46 equiv)	1:5	3:2	68
8	CsF (3 equiv), H_2O (15 equiv)	1:1	4:1	69
9	1a, H_2O (15 equiv)	4:1	10:1	68

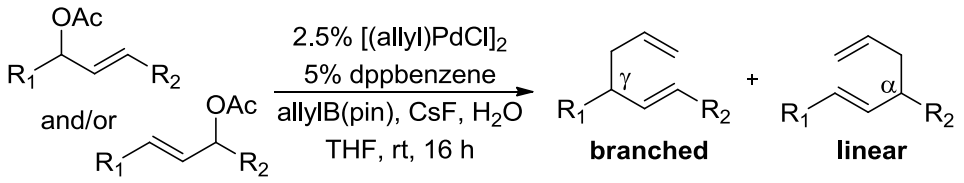
[a] combined yield of 1,5 diene products.

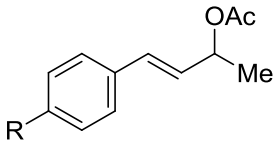
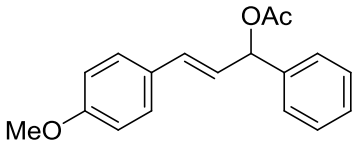
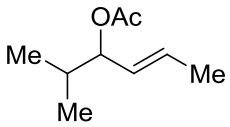
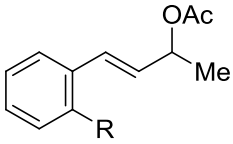
C. Scope of Secondary Allyl Electrophiles

After optimizing the reaction parameters, we explored the scope of the reaction on secondary allyl acetates (Table 3). For these studies the Boc group was replaced with an acetate leaving group because it provided similar reactivity, but improved yields. The lower yields may be attributed to β–hydride abstraction facilitated by tert-Butanol. Compound **20** was coupled to allylB(pin) to afford a 3:1 branched to linear ratio and 88% combined

yield (Table 3, Entry 1). The remaining yield corresponds to 1,3-diene byproducts.

Table 3. Allyl-Allyl Cross-Coupling of Secondary Allyl Acetates



entry	substrate		R	br : lin[b]	yield (%)[c]
1		**20**	H	3:1	88
2		**21**	OMe	1:1	69
3		**22**	Cl	4:1	92
4		**23**	CF_3	10:1	50
5		**24**		1:2	77
6		**25**		2:1	80[d]
7		**26**	Me	7:1	96
8[e]		**27**	OMe	7:1	80

[a]Conditions: 3 equiv of allylB(pin), 10 equiv of CsF, 15 equiv of H_2O, 0.2 M THF. [b] Ratios were determined by ^1H NMR of crude. [c]Yields are the average of two or more experiments and are corrected to account for inseparable elimination product 1,3-diene. [d]Yield determined by ^1H NMR using trimethoxybenzene as internal standard. [e] Starting material is a mixture of regioisomers.

To our surprise, we observed that the electronic properties of the phenyl ring had a measureable impact on the regioselectivity. Electron rich substrate **21** showed increased formation of linear product compared to the

branched (1:1 vs 4:1). In contrast, electron poor substrate **23** showed increased selectivity for the branched product (10:1). To further probe the influence of these forces, we synthesized substrates **24** and **25** whose substituents differ by electronic or steric properties only. The poor selectivity for either product in both examples demonstrates that the both steric and electronic effects are subtle when independent. We postulate that electronic effects can alter the equilibrium of all possible Pd(II)-(η^1-allyl) intermediates. Electron rich substituents (Table 3, entries 2 and 5) can increase electron density at the gamma carbon, resulting in stronger Pd-C coordination at the gamma carbon. This results in more 3,3' reductive elimination at the alpha carbon. In contrast, electron poor substituents will decrease the electron density at the gamma position, weakening the C-Pd σ bond. The result is a bias for Pd intermediate at the alpha carbon and C-C bond formation at the gamma carbon.

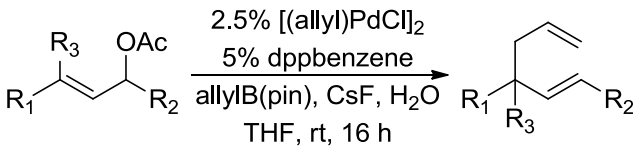
Further enhancing the steric effects with ortho substitution around the ring (Table 3, Entries 7, 8) supported our original hypothesis. These observations suggest that 3,3' reductive elimination is affected by the steric and electronic properties of the substituents on the electrophile, with large and electron poor/withdrawing substituents promoting branch-selective coupling alpha to the large substituent.

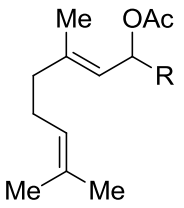
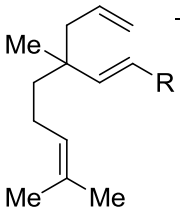
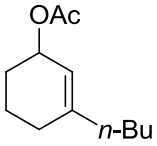
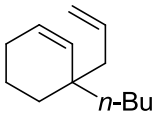
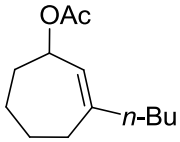
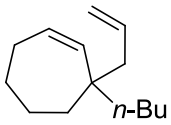
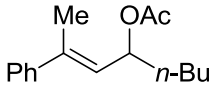
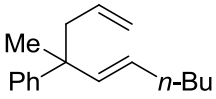
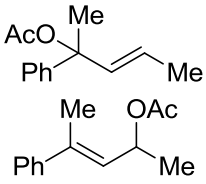
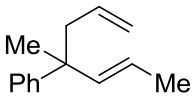
D. Allyl-Allyl Cross-Coupling of Trisubstituted Allyl Acetates

In Table 4, we subjected a variety of tri-substituted allyl electrophiles to the optimized cross-coupling conditions. The steric effect of the R3 substituent led to very high selectivity for the quaternary 1,5-diene. This observation is highlighted in Figure 15; the steric repulsion forces between the R1 and R3 substituents and the ligands on palladium significantly increases the energy of this intermediate. In entries 4-9, the steric bulk of the R2 substituent correlates to increases in 1,3-diene formation, resulting in lower yields.

Despite the high energy barriers of this transformation, the reaction conditions tolerated terpene derived substrates, 6 and 7 membered cyclic substrates as well as aromatic substrates providing very hindered products in 59-90% yield. Regioisomers (Entry 10) and cis olefins (Entry 3) also behaved well under these conditions and formed only one regioisomer.

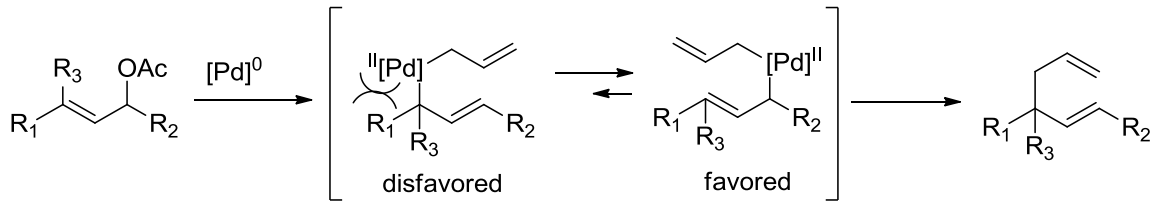
Table 4. Substrate Scope of Trisubstituted Allyl Electrophiles



entry		S.M.	product	R		yield (%)[b]
1	**28**			Me	**29**	80
2	**30**			Me[c]	**29**	90
3	**31**			*n*-Bu	**32**	75
4	**33**			*i*-Pr	**34**	65
5	**35**			Cy	**36**	74
6	**37**			Ph	**38**	55
7	**39**				**40**	58
8	**41**				**42**	78
9	**43**				**44**	86
10	**45**	 (1.3:1 mixture)			**46**	78

[a]Conditions: 3 equiv of allylB(pin), 10 equiv of CsF, 15 equiv of H_2O, 0.2M THF. [b]Yields are the average of two or more experiments and are corrected to account for inseparable elimination product 1,3-diene. [c]Z-allylic acetate was employed.

Figure 15. Regioselectivity Model for Trisubstituted Allyl Electrophiles

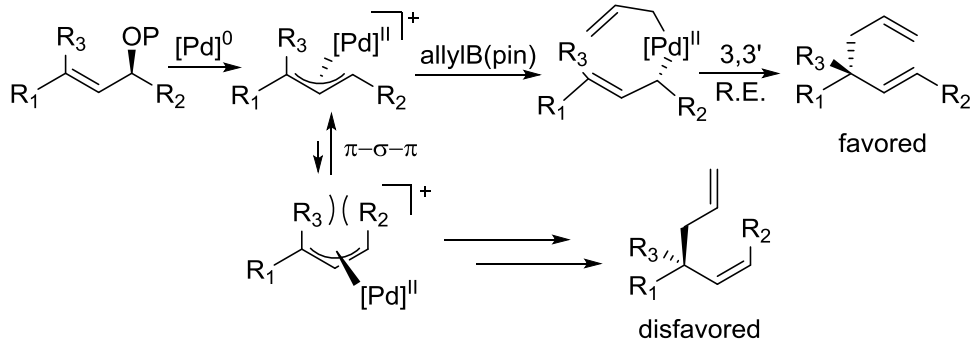


E. Enantioenriched 1,5-Dienes

As discussed throughout the text, the Morken group has demonstrated many branch-selective and enantioselective allyl-allyl cross-couplings with terminal allyl electrophiles. The selectivity observed in these systems is reliant on π-σ-π isomerization of the palladium to both faces of the substrate followed by 3,3' reductive elimination, which are influenced by the chiral bidentate phosphine ligand (Scheme 1 and Figure 11).

As Figure 16 shows, addition of a substituent at R3 renders both allyl termini stereogenic, thus racemization is inhibited. Without racemization, the reaction is subject to catalyst control. We reasoned that enrichment of the substrate would be preserved through the cross-coupling and transferred to the product (Figure 16). This negates the need for chiral bidentate ligands, and would provide a general, stereospecific transformation.

Figure 16. Model for Chirality Transfer with Enriched Trisubstituted Allyl Electrophiles

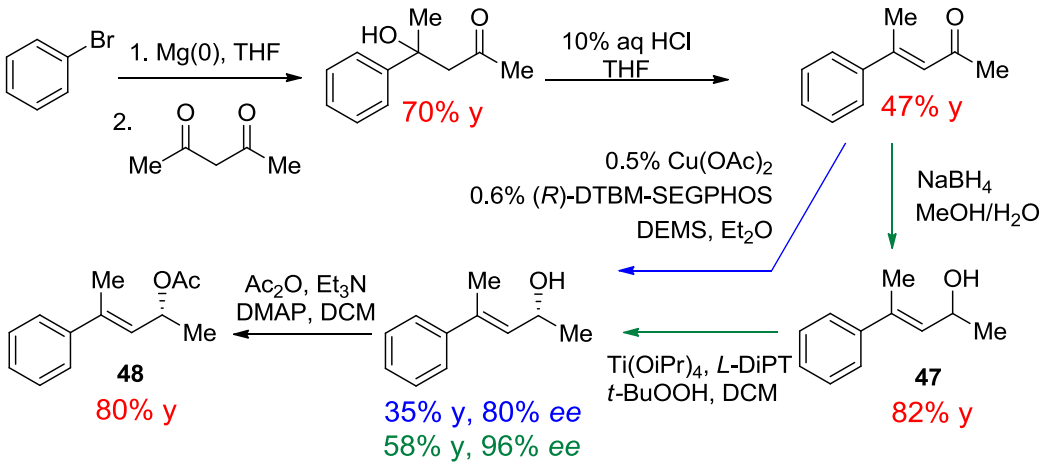


F. Synthesis of Enantioenriched Allyl Electrophiles

To test our chirality transfer process, we synthesized aryl acetate **48**. Achieving the substrate with high ee was accomplished using one of two methods as shown in Scheme 2. Both routes started off with a Grignard reaction with acetic anhydride and aryl bromide. Acid hydrolysis afforded the α,β unsaturated ketone in moderate yield. Under the conditions highlighted in blue, an enantioselective CuH-catalyzed 1,2 addition was performed to give good *ee* albeit low yield.[28] These conditions were unfavorable because they utilized expensive catalysts and were very temperature sensitive.

[28] Voigtritter, K. R.; Isley, N. A.; Moser, R.; Aue, D. H.; Lipshutz, B. H. *Tetrahedron,* **2012**, *68*, 3410

Scheme 2. Synthetic Route Toward Enantioenriched Allyl Acetates

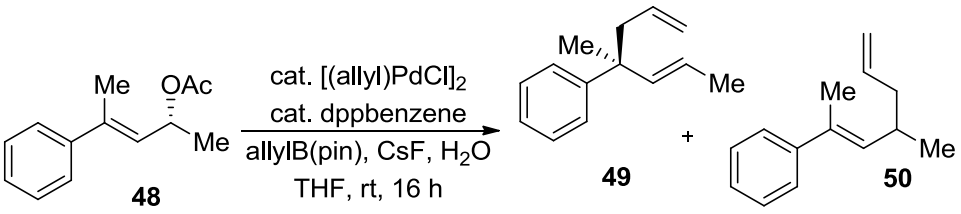


In the second route, highlighted in green, $NaBH_4$ reduction followed by Sharpless kinetic resolution gives the allylic alcohol in high *ee* and in higher yield over the two steps. The final step is acetate protection catalyzed by triethyl amine and DMAP. With the model substrate in hand, we subjected it to the standard reaction conditions for racemic substrates (Table 5, Entry 1). The reaction produced **49** in >20 : 1 regioselectivity and 79% yield. The regioselectivity values were in agreement with what was observed for the racemic analog, but the enantiomeric ratio (*er)* was only 79:21. Factoring in the *ee* of the starting material, this equates to a mere 65% conservation of enantioenrichment (*cee*).

We began to perturb the reaction conditions and observed that lower catalyst loadings afforded higher cee (Table 5). In entry 2, 1 mol% catalyst resulted in 98% *cee* while 10 mol% catalyst resulted in 47% *cee*. Oddly, the

yield of **49** also diminished with increasing *cee* (Entry 2 vs. 5). We found evidence in the literature of this trend in other systems.

Table 5. Effects of Catalyst Loading on Chirality Transfer



entry	% cat	yield (%)[c]	49:50[b]	*er* (%)[d]	*cee* (%)[e]
1	5	79	>20:1	79:21	65
2	1	50	1:1	94:6	98
3	2.5	70	7:1	92:8	90
4	10	72	8:1	71:29	47
5	15	73	9:1	61:39	26

[a]Conditions: 3 equiv of allylB(pin), 10 equiv of CsF, 15 equiv of H_2O, 0.2M THF. [b] Ratios were determined by ^{1}H NMR of crudes. [c] Yields are the average of two or more experiments and are corrected to account for inseparable elimination product 1,3-diene. [d] er ratios were determined using chiral GC or HPLC. Absolute configuration assigned in analogy to known compounds. See the Supporting Information. [e]cee is calculated as follows: cee = (product ee/starting material ee) x 100.

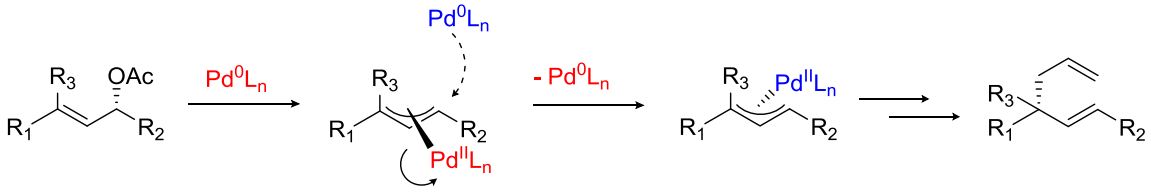
We surmised that the erosion of *ee* observed at higher catalyst loadings could be the result of a redox-transmetalation process involving two palladium intermediates.[29] This has been demonstrated in the literature by Kurosawa, Bäckvall and Amatore. Kurosawa demonstrated that Pd(II)-(η^3 allyl) complexes can undergo transmetalation from an outer sphere Pd^0

[29] (a) Mackenzie, P. B.; Whelan, J.; Bosnich, B. *J. Am. Chem. Soc.* **1985,** *107,* 2046. (b) Kurosawa, H.; Ogoshi, S.; chantani, N.; Kawasaki, Y.; Murai, S.; Ikeda, I. *Chem. Lett.* **1990**, 1745. (c) Bäckvall, J.-E.; Grandberg, K. L.; Heumann, A. *Isr. J. Chem.* **1991**, *31*, 17. (d) Granberg, K. L.; Bäckvall, J.-E.; *J. Am. Chem. Soc.* **1992**, *112*, 6858. € Amatore, c.; Gamez, S.; Jutand, A.; Meyer, G.; Moreno-Mallas, M.; Morral, L.; Pleixtas, R. *Chem. –Eur. J.* **2000**, *6*, 3372. (f) Amatore, C.; Jutand, A.; Mensah, L.; Meyer, G.; Fiaund, J.-C.; Legros, J. Y. *Eur. J. Org. Chem.* **2006**, 1185.

or Pt^0 catalyst. This occurs on the opposite face of the bound Pd(II) resulting in net stereo inversion and both oxidation of the incoming metal and reduction of the eliminated metal.

Figure 17 shows the mechanism of redox transmetalation in the context of substrate **48**. This hypothesis fits the data: the more palladium catalyst present in the system, the more outer sphere transmetalation can occur, resulting in more erosion of the *ee*. In cases where the catalyst loading is low, transmetalation is slow such that 1,3-diene formation increases.

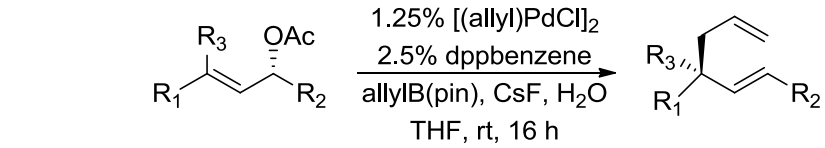
Figure 17. Mechanism for Redox Transmetalation.

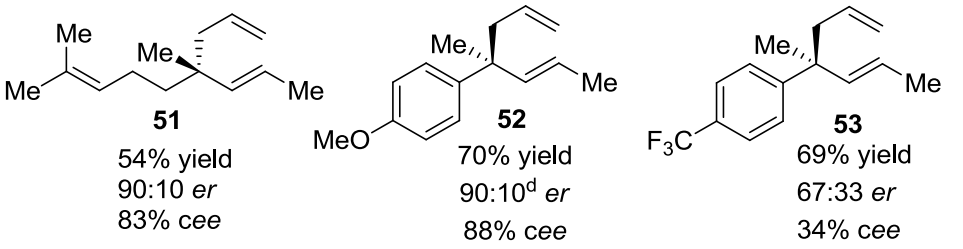


To reduce the effects of redox transmetalation, we reduced the catalyst loading to 2.5% and increased the equivalents of allyl B(pin) and the other additives (to speed up transmetalation). The scope of the reaction was expanded to include alkyl and aryl trisubstituted electrophiles. The cross-coupling of the alkyl acetate gave **51** in modest yield and 83% *cee*. The para- methoxy acetate afforded **52** in good yield, and slightly higher *cee*. The substrate bearing the electron withdrawing group performed poorly under these conditions, affording **53** in 34% *cee*. In this case, the

withdrawing nature of the substrate could increase its reactivity to redox transmetalation. Further mechanistic studies and substrate scope were performed by Hai Le.

Table 6. Scope of Stereo Selective Cross Coupling





In conclusion, we have demonstrated a general cross-coupling method for internal allyl electrophiles and allylboron nucleophiles to afford highly substituted 1,5-dienes bearing tertiary centers, all carbon quaternary centers, and enantioenriched chiral centers. Regioselectivities were high and found to be driven by both steric and electronic properties of the substrate. Internal allyl electrophiles provided an opportunity to differentiate the olefins for more selective subsequent synthesis. Enantioenriched quaternary centers can be formed from enriched acetates under low catalyst conditions without the need for a chiral phosphine ligand.

IV. Experimental Information

A. General information

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

Liquid Chromatography was performed using forced flow (flash chromatography) on silica gel (SiO_2, 230×450 Mesh) purchased from Silicycle. Thin Layer Chromatography was performed on 25 μm silica gel plates purchased from Silicycle. Visualization was performed using ultraviolet light (254 nm), potassium permanganate ($KMnO_4$) in water, ceric

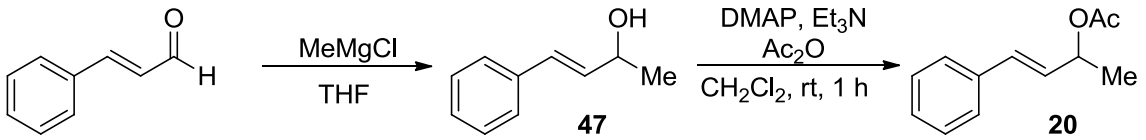
ammonium molybdate (CAM) in water, or phosphomolybdic acid (PMA) in ethanol. Analytical chiral gas liquid chromatography (GLC) was performed on a Hewlett-Packard 6890 Series chromatograph equipped with a split mode capillary injection system, a flame ionization detector, and a Supelco β-Dex 120 column, or a Supelco Asta Chiraldex B-DM with helium as the carrier gas. Analytical chiral supercritical fluid chromatography (SFC) was performed on a Thar SFC equipped with a Waters 2998 photodiode array detector and an analytical-2-prep column oven with methanol as the modifier. Analytical high performance liquid chromatography (HPLC) was performed on an Agilent 1120 compact chromatograph equipped with gradient pump and variable wavelength detector. Optical rotations were measured on a Rudolph Analytical Research Autopol IV Polarimeter.

All reactions were conducted in oven- or flame-dried glassware under an inert atmosphere of nitrogen or argon. Tetrahydrofuran (THF), Toluene (PhMe), and dichloromethane (DCM) were purified using a Pure Solv MD-4 solvent purification system from Innovative Technology Inc. by passing through two activated alumina columns after being purged with argon. Triethylamine (TEA) and Ethyl Acetate (EtOAc) were distilled from calcium hydride. Tetrakis(triphenylphosphine)palladium(0) [$Pd(PPh_3)_4$], bis(cyclopentadienyl)zirconium(IV) dichloride ($ZrCp_2Cl_2$), (*R*)-(−)-5,5′-

Bis[di(3,5-di-*tert*-butyl-4-methoxyphenyl)phosphino]-4,4′-bi-1,3-benzodioxole ((*R*)-(-)-DTBM-Segphos), 1,2-bis(diphenylphosphino)benzene (dpp-Benzene) were purchased from Strem Chemicals Inc. Allylboronic acid pinacol ester [allylB(pin)] was generously donated by Frontier Scientific. All other reagents were purchased from either Fisher or Aldrich and used without further purification.

B. Preparation and Characterization of Starting Materials

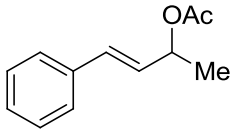
Synthesis and characterization of (*E*)-4-phenylbut-3-en-2-yl acetate (20):



General procedure A: To a flame-dried round-bottomed flask equipped with a stir bar was added 3.0 M methylmagnesium chloride in THF (5.53 mL, 16.5 mmol) and THF (25 mL). The solution was cooled to 0 ºC and cinnamaldehyde (1.88 mL, 14.9 mmol) in THF (5 mL) was added dropwise *via* syringe. The reaction was allowed to stir at 0 ºC for 1 h. The reaction was quenched with water and 0.5 M HCl (aq). The organic layer was separated, and the aq. layer was extracted with ethyl acetate three times.

The combined organics were washed with brine, dried with Na_2SO_4, filtered and concentrated *in vacuo*. **47** was then acetylated using procedure **B**.

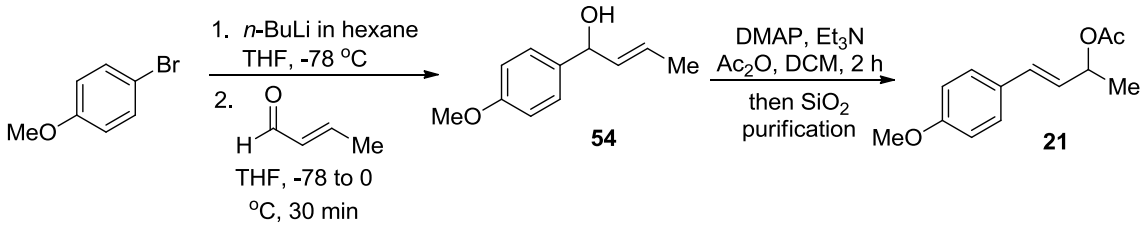
General Procedure B: A 100 mL round-bottomed flask was charged with **47** (2.4 g, 9.5 mmol), 4-dimethylaminopyridine (116 mg, 0.95 mmol) and CH_2Cl_2 (20 mL). Triethylamine (2.7 mL, 19 mmol) was added and the reaction stirred for 20 minutes, followed by the addition of acetic anhydride (1.8 mL, 19 mmol). The reaction was capped with a septum, vented with a needle, and was allowed to stir while warming to room temperature for 1 h. The reaction was then quenched with water. The organic layer was separated and the aqueous layer was extracted with CH_2Cl_2 three times. The organic portions were combined, dried over Na_2SO_4, filtered, and concentrated *in vacuo*. The crude material was purified on silica gel (5% Et_2O/pentane) to afford a colorless oil (88 % yield over 2 steps).



(*E*)-4-phenylbut-3-en-2-yl acetate (20): ^{1}H NMR (500 MHz, $CDCl_3$): δ 1.41 (3H, d, *J* = 6.6 Hz), 2.08 (3H, s), 5.53 (1H, quint, *J* = 6.8 Hz), 6.19 (1H, dd, *J* = 15.9, 6.8 Hz), 6.60 (1H, d, 15.9 Hz), 7.23-7.26 (1H, m), 7.29-7.34 (2H, m), 7.36-7.39 (2H, m); ^{13}C NMR (125 MHz, $CDCl_3$): δ 20.3, 21.4, 71.0, 126.5, 127.9, 128.8, 131.5, 136.3,

170.3; IR (neat): 2980 (w), 1732 (s), 1370 (m), 1235 (s), 1040 (m), 966 (m), 951 (m), 748 (m), 693 (m) cm^{-1}; HRMS (ESI+) for $C_{13}H_{16}O_2$ [M+H]: calculated: 190.0994, found: 190.1002. R_f = 0.25 in 5% EtOAc/hexanes.

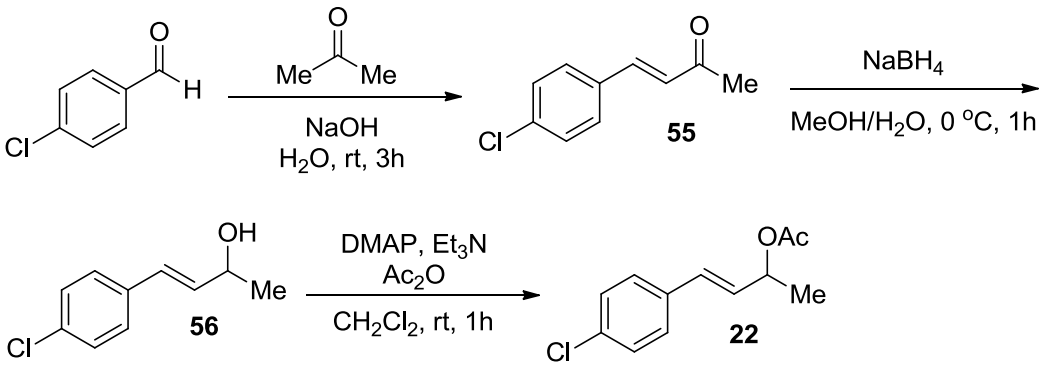
Synthesis and characterization of (*E*)-4-(4-methoxyphenyl)but-3-en-2-yl acetate (21):



General Procedure C: A flame-dried round-bottomed flask under N_2 was equipped with a stir bar and charged with 4-bromoanisole (0.12 mL, 1 mmol) and THF (4 mL). The solution was cooled to -78 °C before adding 2.5 M *n*-butyllithium in hexanes (0.4 mL, 1.0 mmol) dropwise via syringe. The reaction was stirred for 10 minutes before the dropwise addition of crotonaldehyde (0.85 mL, 1.0 mmol) in THF (1 mL). After 10 minutes at –78 ºC, the reaction was warmed to room temperature and was allowed to stir for 30 min. The reaction was diluted with ether (10 mL) before quenching with water (5 mL) at 0 ºC. The aqueous portion was extracted with ether three times and the organic portions were washed with brine, dried over Na_2SO_4, filtered and concentrated *in vacuo* to afford **54**. The alcohol **54** was

then protected following procedure **B**. After purification on SiO_2, the product rearranged to the corresponding regioisomer. Spectral data is in accordance with literature values.[30]

Synthesis and characterization of (*E*)-4-(4-chlorophenyl)but-3-en-2-yl acetate (22): [30]



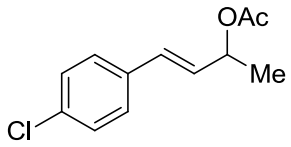
General procedure D:

Step 1: A round-bottom flask equipped with a stir bar was charged with 4-chlorobenzaldehyde (0.56 g, 4.0 mmol) and D.I. water (25.5 mL). A suspension of acetone (1.46 mL, 20.0 mmol) and NaOH (0.58 g, 14.4 mmol) in D.I. water (8.5 mL) was added to the reaction. The mixture was stirred at room temperature for 3 h. The reaction was quenched with water and the aqueous layer was extracted with DCM three times. The organic portion

[30] Akai, S.; Hanada, R.; Fujiwara, N.; Kita, Y.; Egi, M. *Org. Lett.* **2010**, *12*, 4900

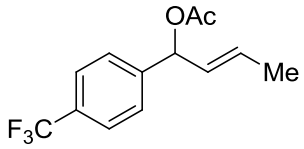
was washed with brine, dried with Na_2SO_4, filtered and concentrated *in vacuo*.

Step 2: A round-bottom flask equipped with a stir bar was charged with **55** (0.63 g, 2.6 mmol), H_2O (0.5 mL) and MeOH (2 mL). The solution was cooled to 0 ^oC before $NaBH_4$ (113.5 mg, 3 mmol) was added. The reaction was stirred at room temperature for 1 h. The reaction was then diluted with CH_2Cl_2 and washed with brine. The aqueous layer was extracted with CH_2Cl_2 three times. The organic portion was dried over Na_2SO_4, filtered, and concentrated *in vacuo.* The allyl alcohol **56** was then protected using general procedure **B**. The crude material was purified on silica gel (5% Et_2O/pentane) to afford a clear colorless oil (60% yield over 2 steps).

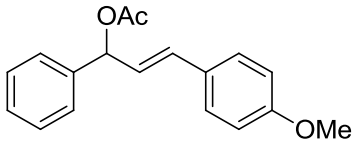


(*E*)-4-(4-chlorophenyl)but-3-en-2-yl acetate (22): ^1H NMR (500 MHz, $CDCl_3$): δ 1.40 (3H, d, *J* = 6.5 Hz), 2.07 (3H, s), 5.50 (1H, app dq, *J* = 13.0, 6.6 Hz), 6.16 (1H, dd, *J*= 15.9, 6.6 Hz), 6.55 (1H, d, *J* = 15.9 Hz), 7.26-7.31 (4H, m); ^{13}C NMR (125 MHz, $CDCl_3$): δ 20.3. 21.3, 701.7, 127.7, 128.7, 129.5, 133.5, 134.8, 170.2; IR (neat): 2981 (w), 1734 (s), 1492 (m), 1371 (m), 1238 (s), 1094 (m), 1042 (m), 1013 (m), 968 (m), 952 (m), 806 (m) cm^{-1}; HRMS (ESI+) for

$C_{12}H_{13}ClO_2$ [M+H]: calculated: 224.0604, found: 224.06115. R_f = 0.24 in 5% EtOAc/hexanes.

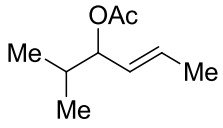


(*E*)-1-(4-(trifluoromethyl)phenyl)but-2-en-1-yl acetate (23): From commercially available 1-Bromo-4-(trifluoromethyl)benzene, procedure **C** and **B** were followed. ^{1}H NMR (500 MHz, $CDCl_3$): δ 1.73 (3H, d, *J* = 6.4 Hz), 2.11 (3H, s), 5.63 (1H, dd, *J* = 15.2, 6.9 Hz), 5.78 (1H, dq, *J* = 15.2, 6.4 Hz), 6.24 (1H, d, *J* = 6.9 Hz), 7.45 (2H, d, *J* = 8.3 Hz), 7.61 (2H, d, *J* = 8.3 Hz); ^{13}C NMR (125 MHz, $CDCl_3$): δ 169.8, 143.7, 130.6, 130.0 (q, $^2J_{CF}$ = 32.4 Hz), 128.9, 127.0, 125.4 (q, $^3J_{CF}$ = 3.6 Hz), 124.0 (q, $^1J_{CF}$ = 271.7 Hz), 75.6, 21.2, 17.7; IR (neat): 2921(br), 1737 (s), 1371 (m), 1323 (s), 1227(s), 1164 (s), 1122 (s), 1065 (s), 1016 (s), 962 (s), 831 (m) cm^{-1}; HRMS (ESI+) for $C_{11}H_{10}F_3$ [M-OAc+H]: calculated 199.0735, found: 199.0783. The crude material was purified on silica gel (5% Et_2O/pentane) to afford a colorless yellow oil (86 % yield over 2 steps). R_f = 0.32 in 5% EtOAc/hexanes.



(*E*)-3-(4-methoxyphenyl)-1-phenylallyl acetate (24): From commercially available 3-(4-methoxyphenyl)-1-phenyl-propenone, general procedure **D,** step 2 was

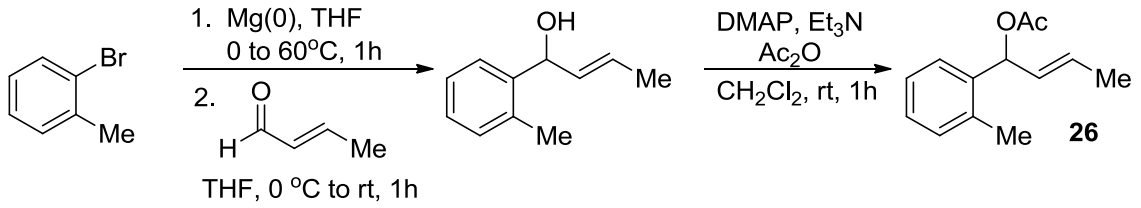
followed. The allyl alcohol was protected using general procedure **B.** ^{1}H NMR (500 MHz, $CDCl_3$): δ 2.13 (3H, s), 3.81 (3H, s), 6.22 (1H, dd, *J* = 16.1, 7.3 Hz), 6.42 (d, *J* = 7.3 Hz), 6.58 (1H, d, *J* = 16.1 Hz), 6.84 (2H, d, *J* = 8.8 Hz), 7.28-7.44 (7H, m); ^{13}C NMR (125 MHz $CDCl_3$): δ 21.4, 45.9, 55.3, 76.4, 114.0, 125.3, 127.0, 127.9, 128.0, 128.6, 128.9, 132.3, 139.5, 159.6, 170.1; IR (neat): 2934 (br), 1735(s), 1607 (m), 1512 (s), 1455 (w), 1370 (m), 1300 (w), 1233 (s), 1176 (m) cm^{-1}; HRMS (ESI+) for $C_{18}H_{18}O_3$ [M]: calculated: 282.1256, found: 282.1267. The crude material was used without purification (83% yield over 2 steps). R_f = 0.33 in 10% EtOAc/hexanes.



(*E*)-2-methylhex-4-en-3-yl acetate (25): From commercially available isopropylmagnesium chloride and crotonaldehyde, general procedure **A** and **B** were followed. ^{1}H NMR (500 MHz, $CDCl_3$): δ 0.88 (6H, app. t, *J* = 6.1 Hz), 1.70 (3H, dd, *J* = 6.6, 1.7 Hz), 1.82 (1H, app octet, *J* = 6.9 Hz), 2.04 (3H, s), 4.98 (1H, t, *J* = 7.1 Hz), 5.39 (1H, ddq, *J* = 15.4, 7.8, 1.7 Hz), 5.70 (1H, dq, *J* = 15.4, 6.6 Hz); ^{13}C NMR (125 MHz, $CDCl_3$): δ 17.8, 18.0, 18.2, 21.3, 32.0, 79.6, 127.8, 129.9, 170.4; IR (neat): 2963 (m), 2934 (w), 2876 (w), 1735 (s), 1469 (w), 1450 (w), 1371 (m), 1236 (s), 1018 (m), 968 (m) cm^{-1}; HRMS (ESI+) for $C_7H_{13}O_2$

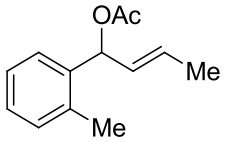
[M -OAc]: calculated: 97.1017, found: 97.1020. The crude material was purified on silica gel (100% pentane) to afford a colorless oil (59% yield over 2 steps). R_f= 0.35 in 5% EtOAc/hexanes.

Synthesis and characterization for (*E*)-4-(*o*-tolyl)but-3-en-2-yl acetate (26):

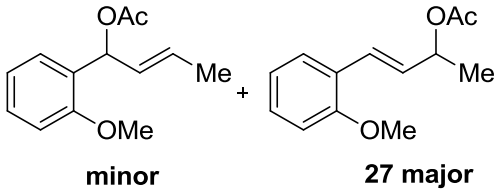


General Procedure E: To a flame-dried round-bottom flask equipped with a stir bar and reflux condenser was added magnesium turnings (280 mg, 11.5 mmol). An additional flame-drying was performed before THF (22 mL) and 2-bromotoluene (1.32 mL, 11 mmol) was added dropwise at 0 ºC. The solution was refluxed at 60 ºC for 1 h, then cooled to 0 ºC before a solution of crotonaldehyde (0.83 mL, 10 mmol) in THF (5 mL) was added dropwise *via* syringe. The reaction was allowed to stir at ambient temperature for 1 h. The reaction was cooled to 0 ºC and quenched with saturated aqueous NH_4Cl. The aqueous layer was extracted with ethyl acetate three times and the combined organics were washed with brine, dried with Na_2SO_4, filtered, and concentrated *in vacuo*. The allyl alcohol was then protected using

general procedure **B**. The crude material was purified on silica gel (5% Et_2O/pentane) to afford **26** as a colorless oil (76% yield over 2 steps).



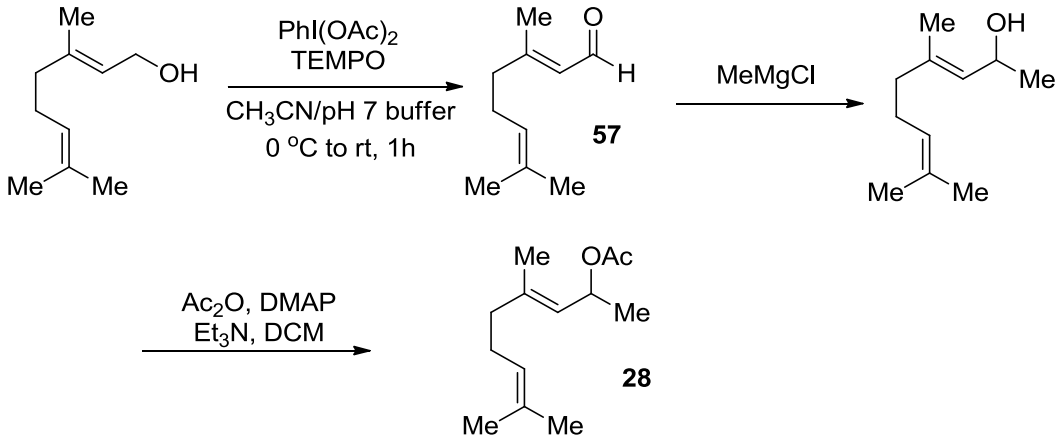
(*E*)-4-(*o*-tolyl)but-3-en-2-yl acetate (26): ^{1}H NMR (500 MHz, $CDCl_3$): δ 1.42 (3H, d, *J* = 6.6 Hz), 2.08 (3H, s), 2.35(3H, s), 5.55 (1H, app q, *J* = 6.6 Hz), 6.07 (1H, dd, *J* = 15.9, 6.8 Hz), 6.82 (1H, d, *J* = 15.8 Hz), 7.13-7.18 (3H, m), 7.41-7.44(1H, m); ^{13}C NMR (125 MHz, $CDCl_3$): δ 19.7, 20.5, 21.4, 71.2, 125.6, 126.0, 127.7, 129.5, 130.1, 130.2, 135.4, 135.6, 170.3; IR (neat): 3019 (w), 2979 (w), 2932 (w), 1734 (s), 1486 (w), 1459 (w), 1370 (m), 1234 (s), 1152 (w), 1039 (m), 966 (m), 950 (m), 749 (m) cm^{-1}; HRMS (ESI-) for $C_{13}H_{16}O_2$ [M+H]: calculated: 205.1138, found: 205.0484. R_f = 0.31 in 5% EtOAc/hexanes.



(*E*)-4-(2-methoxyphenyl)but-3-en-2-yl acetate (27 major – 1h) and (E)-1-(2-methoxyphenyl)but-2-en-1-yl acetate (minor): From commercially available 1-bromo-2-methoxybenzene, general procedure **E** and **B** were followed. The desired starting material isomerized to its regioisomer during silicagel purification. ^{1}H NMR (500 MHz, $CDCl_3$): δ 1.42 (3H, d, *J* = 6.3 Hz, major), 1.69 (3H, d, *J* = 4.9 Hz, minor), 2.07 (3H,

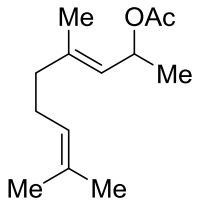
s, major), 2.08 (3H, s, minor), 3.84 (3H, s, minor), 3.85 (3H, s, major), 5.54 (1H, dq, *J* = 6.3, 6.3 Hz, major), 5.62-5.76 (2H, m, minor), 6.22 (1H, dd, *J* = 16.1, 6.8 Hz, major), 6.60 (1H, d, *J* = 5.4 Hz, minor), 6.84-6.99 (3H+1H, m, major+minor), 7.20-7.30 (1H+2H, m, major+minor), 7.36 (1H, d, *J* = 7.4 Hz, minor), 7.42 (1H, d, *J* = 7.4 Hz); ^{13}C NMR (125 MHz, $CDCl_3$): δ 17.7, 20.4, 21.3, 21.4, 55.4, 55.6, 70.7, 71.5, 110.7, 110.8, 120.6, 125.3, 126.5, 127.0, 127.1, 128.2, 128.6, 128.9, 128.9, 129.3, 156.4, 156.9, 169.9, 170.3; IR (neat): 2978 (br), 2937 (br), 2838 (w), 1731 (s), 1598 (m), 1580 (w), 1490 (m), 1463 (m), 1438 (m), 1370 (m), 1232 (s) cm^{-1}; HRMS (ESI+) for $C_{13}H_{16}O_3$ [M +H]: calculated: 220.1099, found: 220.1109. The crude material was purified on silica gel (10% ether/pentane) to afford a clear oil (42%y after 2 steps). R_f = 0.23 in 10% EtOAc/hexanes.

Synthesis and characterization of (*E*)-4,8-dimethylnona-3,7-dien-2-yl acetate (28)

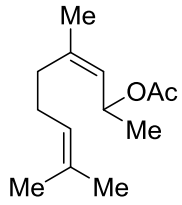


General procedure F: A flame-dried round-bottom flask under N_2 was equipped with a stir bar, and charged with $PhI(OAc)_2$ (44.0 mmol, 14.2 g), TEMPO (4.0 mmol, 270 mg), CH_3CN (34 mL), and aqueous pH 7 buffer (9.6 mL). The solution was cooled to 0 ºC before adding geraniol (40.0 mmol, 6.17 g) *via* syringe. The reaction was allowed to stir while warm to room temperature for 1 h. $Na_2S_2O_3$ was then added. The organic layer was removed and the aqueous layer was extracted with ether three times. The organic portions were dried with Na_2SO_4, filtered and concentrated *in vacuo*. The crude oil was purified on silica gel (10% Et_2O/hexanes) to afford a colorless oil (4.9 g, 80% yield).

57 was subjected to conditions in general procedure **A** and **B** to obtain the desired starting material as a colorless oil (72% yield over 3 steps).

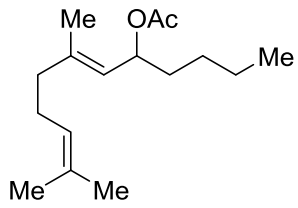


(*E*)-4,8-dimethylnona-3,7-dien-2-yl acetate (28): ^{1}H NMR (500 MHz, $CDCl_3$): δ 1.25 (3H, d, *J* = 6.4 Hz), 1.60 (3H, s), 1.68 (3H, s), 1.70 (3H, d, *J* = 1.3 Hz), 1.97-2.02 (2H, m), 2.01 (3H, s), 2.04-2.12 (2H, m), 5.07 (1H, br. t, *J* = 6.8 Hz), 5.16 (1H, d, *J* = 8.8 Hz), 5.59 (1H, dq, *J* = 15.1, 6.3 Hz); ^{13}C NMR (125 MHz $CDCl_3$): δ 16.6, 17.6, 20.9, 21.4, 25.6, 26.3, 39.4, 68.1, 123.8, 124.7, 131.7, 139.4, 170.4; IR (neat): 2974 (w), 2929 (w),1732 (m), 1447 (w), 1369 (m), 1240 (s), 1144 (w), 1040 (m), 951 (w) cm^{-1}; HRMS (ESI+) for $C_{11}H_{19}$ [M-OAc]: calculated: 151.1492, found: 151.1482. R_f = 0.65 in 10% EtOAc.

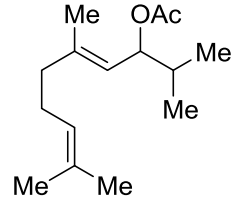


(*Z*)-4,8-dimethylnona-3,7-dien-2-yl acetate (30): From commercially available *cis*-3,7-Dimethyl-2,6-octadien-1-ol (Nerol), general procedure **F**, **A**, and **B** were followed. ^{1}H NMR (500 MHz, $CDCl_3$): δ 1.25 (3H, d, *J* = 6.3 Hz), 1.60 (3H, s), 1.67 (3H, s), 1.72 (3H, d, *J* = 1.4 Hz), 2.00 (3H, s), 2.01-2.17 (3H, m), 2.21-2.22 (1H, m), 5.09 (1H, br t, *J* = 6.8 Hz), 5.17 (1H, d, *J* = 9.3 Hz), 5.59 (1H, dq, *J* = 15.4, 6.1 Hz); ^{13}C NMR (125 MHz $CDCl_3$): δ 17.6, 21.2, 21.4, 23.3, 25.7, 26.5, 32.4, 67.8,123.8, 125.4, 132.0, 139.8, 170.3; IR (neat): 2969 (w), 2930 (w),2860 (w), 1734 (m), 1670 (w), 1447 (w), 1369 (m), 1240 (s), 1035 (m), 950 (w) cm^{-1}; HRMS (ESI+) for $C_{11}H_{19}$ [M-OAc]: calculated: 151.1492,

found: 151.1534. The crude material was purified on silica gel (2% Et_2O/pentane) to afford a colorless oil (55% yield over 4 steps). R_f = 0.34 in 5% EtOAc/hexanes.

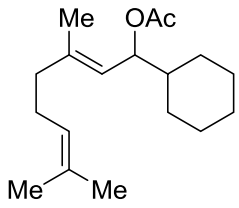


(*E*)-7,11-dimethyldodeca-6,10-dien-5-yl acetate (31): From commercially available geraniol, and *n*-butyllithium, **procedure F, A,** and **B** was followed. ^{1}H NMR (500 MHz, $CDCl_3$): δ 0.89 (3H, t, *J* = 7.0 Hz), 1.17-1.37 (4H, m), 1.44-1.52 (1H, m), 1.60 (3H, s), 1.60-1.66 (1H, m), 1.68 (3H, s), 1.71 (3H, d, *J* = 1.3 Hz), 1.98-2.20 (2H, m), 2.02 (3H, s), 2.06-2.12 (2H, m), 5.04-5.10 (2H, m), 5.47 (1H, dt, *J* = 9.0, 6.8 Hz); ^{13}C NMR (125 MHz $CDCl_3$): δ 7.0, 9.8, 10.7, 14.4, 15.5, 18.6, 19.2, 20.2, 27.7, 32.5, 64.6, 116.7, 116.9, 124.6, 133.2, 163.4; IR (neat): 2959 (w), 2930 (m), 2860 (w), 1734 (s), 1671 (w), 1443 (w), 1369 (m), 1238 (s) cm^{-1}; HRMS (ESI+) for $C_{14}H_{25}$ [M-OAc]: calculated: 193.1962, found: 193.1963. The crude material was purified on silica gel (2% Et_2O/pentane) to afford a clear oil (79% yield over 3 steps). R_f = 0.53 in 5% EtOAc/hexanes.



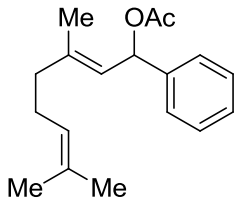
(*E*)-2,5,9-trimethyldeca-4,8-dien-3-yl acetate (33): From commercially available geraniol, and isopropylmagnesium

chloride (2M in THF), general procedure **F, A,** and **B** was followed**.** ^{1}H NMR (500 MHz, $CDCl_3$): δ 0.87 (3H, d, *J* = 12.2 Hz), 0.89 (3H, d, *J* = 6.8 Hz), 1.60 (3H, s), 1.67 (3H, s), 1.72 (3H, d, 1.3 Hz), 1.82 (1H, octet, *J* = 6.8 Hz), 2.01-2.04 (2H, m), 2.03 (3H, s), 2.06-2.14 (2H, m), 5.03-5.12 (1H, m), 5.28 (1H, dd, *J* = 9.5, 7.1 Hz); ^{13}C NMR (125 MHz $CDCl_3$): δ 16.9, 17.7, 17.8, 18.3, 21.3, 25.7, 26.3, 32.5, 39.7, 76.0, 122.0, 124.0, 131.6, 140.8, 170.5; IR (neat): 2964 (w), 2928 (w), 1734 (s), 1671 (w), 1446 (w), 1369 (m), 1239 (s), 1017 (m), 972 (m) cm^{-1}; HRMS (ESI+) for $C_{13}H_{23}$ [M-OAc]: calculated: 179.1805, found: 179.1828. The crude material was purified on silica gel (100% pentane) to afford a colorless oil (68% yield over 3 steps). R_f = 0.4 in 5% EtOAc/hexanes.



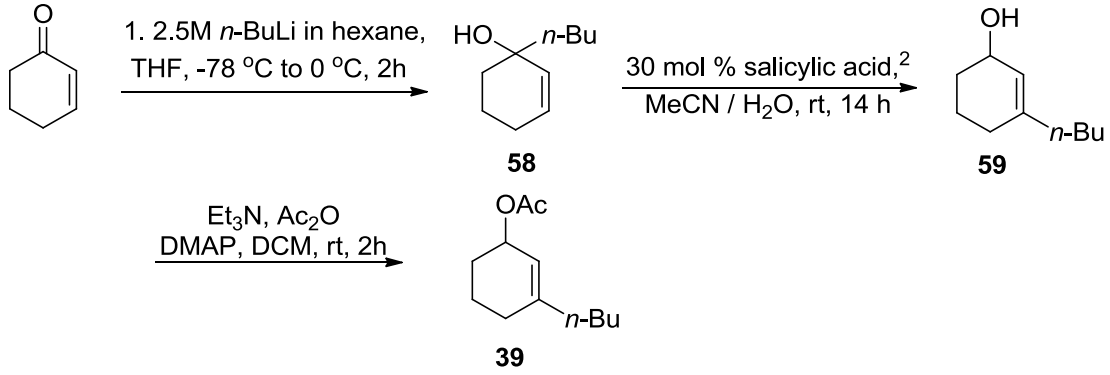
(*E*)-1-cyclohexyl-3,7-dimethylocta-2,6-dien-1-yl acetate (35): From commercially available geraniol, and cyclohexylmagnesium chloride (2M in Et_2O), general procedure **F, A,** and **B** was followed. ^{1}H NMR (500 MHz, $CDCl_3$): δ 0.86-1.02 (2H, m), 1.07-1.28 (4H, m), 1.44-1.54 (1H, m), 1.60 (3H, s), 1.62-1.69(2H, m), 1.65 (3H, s), 1.69-1.78 (2H, m), 1.70, (3H, s), 1.98-2.06 (2H, m), 2.00 (3H, s), 2.08-2.14 (2H, m), 5.01-5.10 (2H, m), 5.28 (1H, m); ^{13}C NMR (125 MHz $CDCl_3$): δ 16.9, 17.7, 21.3, 25.7, 25.9, 26.0, 26.2, 26.4,

28.3, 28.9, 39.7, 42.2, 75.3, 122.4, 124.0, 131.6, 140.6, 170.5; IR (neat): 2926 (s), 2854 (m), 1734 (s), 1450 (m), 1369 (m), 1240 (s), 1016 (m), 973 (m) cm^{-1}; HRMS (ESI+) for $C_{16}H_{27}$ [M-OAc]: calculated: 219.2113, found: 219.2123. The crude material was used without purification to give a clear oil (77% yield over 3 steps). R_f = 0.5 in 5% EtOAc/hexanes.



(*E*)-3,7-dimethyl-1-phenylocta-2,6-dien-1-yl acetate (37): From commercially available geraniol, general procedure **F, C,** and then **B** was followed**.** ^{1}H NMR (500 MHz, $CDCl_3$): δ 1.57 (3H, s), 1.65 (3H, s), 1.81 (3H, s), 2.03-2.11 (4H, m), 2.09 (3H, s), 5.02-5.06 (1H, s), 5.40 (1H, d, *J* = 8.8 Hz), 6.53 (1H, d, *J* = 8.8 Hz), 7.25-7.30 (1H, m), 7.34 (4H, d, *J* = 4.4 Hz); ^{13}C NMR (125 MHz, $CDCl_3$): δ 16.9, 17.6, 21.3, 25.6, 26.2, 39.5, 72.7, 123.3, 1213.7, 126.5, 127.6, 128.4, 131.8, 140.4, 140.7, 170.2; IR (neat): 2966 (w), 1734 (s), 1369 (m), 1230 (s), 1016, (m), 960 (m), 745 (m), 671 (s); HRMS (ESI+) for $C_{16}H_{22}$ $[M\text{-}OAc]^+$: calculated: 214.1722, found: 214.1802. The crude material was purified on silica gel (5% ether/hexanes) to afford a colorless oil (55% yield). R_f = 0.29 in 5% ether/hexanes.

Synthesis and characterization of 3-butylcyclohex-2-en-1-yl acetate (39):



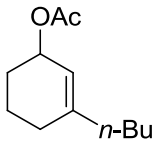
General procedure G:

Step 1: To a flame-dried round-bottomed flask charged with magnetic stir bar, under positive N_2 atmosphere was added by 8 mL THF. The flask was cooled to -78 ^oC, and 2.4 mL *n*-BuLi (2.54 M in hexanes) was added dropwise. Cyclohexenone (0.49 mL, 5.0 mmol in 2 mL THF) was slowly added to the mixture. The flasked was warmed to 0 ^oC and allowed to stir for 2 hours. The reaction was then quenched with H_2O. The organic layer was separated, and the aqueous layer was extracted with Et_2O three times. The organics were combined and condensed *in vacuo* to afford **58**. The crude oil of **58** was used in the next step without further purification.

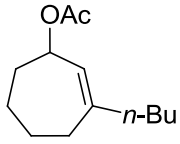
Step 2: [31]To a round-bottomed flask charged with stir bar and the crude oil of **58** was added MeCN (25 mL) and H_2O (D.I., 5 mL), followed by salicylic acid (210 mg, 1.5 mmol). The flask was capped and allowed to stir

[31] McCubbin, J. A.; Voth, S.; Krokhin, O. V. *J. Org. Chem.* **2011**, *76*, 8537

overnight. Saturated $NaHCO_3$ was added to the reaction mixture, the organic layer was separated and the aqueous layer was extracted with Et_2O three times. The combined organics were concentrated *in vacuo* to afford **59** as a light, yellow oil. The crude oil of **59** was subjected directly to acetylation conditions (general procedure **B**).



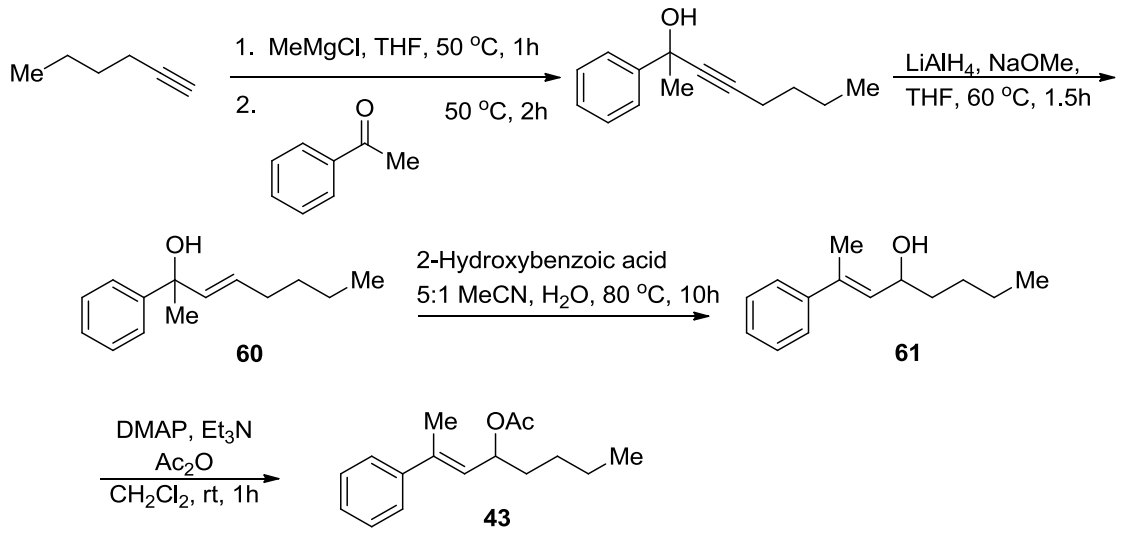
3-butylcyclohex-2-en-1-yl acetate (39): ^{1}H NMR (500 MHz, $CDCl_3$): δ 0.89 (3H, t, J = 6.8 Hz), 1.29 (2H, tq, J = 14.7, 7.4 Hz), 1.36-1.42 (2H, m), 1.54-1.80 (4H, m), 1.88-195 (1H, m), 1.97-2.00 (3H, m), 2.04 (3H, s), 5.27 (1H, br s), 5.44 (1H, br s); ^{13}C NMR (125 MHz, $CDCl_3$): δ 13.9, 19.1, 21.5, 22.4, 28.3, 28.4, 29.6, 37.3, 68.9, 119.3, 144.9, 170.9; IR (neat): 2930 (s), 1730 (s), 1369 (m), 1234 (s), 1057 (m), 909 (m); HRMS (ESI+) for $C_{10}H_{17}$ $[M\text{-}OAc]^+$: calculated: 137.1325, found: 137.1369. The crude material was purified on silica gel (5% ether/hexanes) to afford a colorless oil (78% yield over 3 steps). R_f = 0.33 in 5% ether/hexanes.



3-butylcyclohept-2-en-1-yl acetate (41): Starting from cycloheptenone, general procedure **G** was followed; ^{1}H NMR (500 MHz, $CDCl_3$): δ 0.89 (3H, t, J = 7.1 Hz), 1.25-1.39 (6H, m), 1.59-1.71

(4H, m), 1.78-1.82 (1H, m), 1.88-1.93 (1H, m), 1.94-1.99 (2H, m), 2.05 (3H, s), 2.03-2.18 (2H, m), 5.35-5.40 (2H, m); ^{13}C NMR (125 MHz, $CDCl_3$): δ 13.9, 21.4, 22.3, 26.0, 27.1, 29.8, 32.4, 32.9, 39.8, 74.0, 127.1, 143.9, 170.4; IR (neat): 2926 (m), 1734 (s), 1367 (m), 1237 (s), 1024 (m), 840 (w); HRMS (ESI+) for $C_{11}H_{20}$ $[M\text{-}OAc]^+$: calculated: 152.1565, found: 152.1593. The crude material was purified on silica gel (5% ether/hexanes) to afford a colorless oil. R_f = 0.24 in 5% ether/hexanes.

Synthesis and characterization of (*E*)-2-phenyloct-2-en-4-yl acetate (43):



General Procedure H:

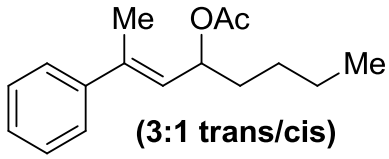
Step 1:[32] A flame-dried 2-neck round-bottom flask equipped with a reflux condenser, stir bar, and rubber septum was charged with THF (4 mL),

[32] Raminelli, C.; Gargalaka, J.; Silveira, C. C.; Comasseto, J. V. *Tetrahedron*, **2007**, *63*, 8801

methylmagnesium chloride (2.16 mL, 4.8 mmol, 2.2 M in THF) and 1-hexyne (0.55 mL, 4.8 mmol). The reaction was heated to 50 ^{o}C for 1 h, at which point the reaction was cooled to room temperature, and aceteophenone (0.47 mL, 4.0 mmol) was added dropwise *via* syringe. The reaction was warmed to 50 ^{o}C, and was allowed to stir for an additional 2 h. The solution was then cooled to room temperature and quenched with saturated aqueous ammonium chloride (10 mL). The organic layer was separated and the aqueous layer was extracted with ethyl acetate three times. The organic portions were combined and washed with brine, dried over Na_2SO_4, filtered, and concentrated *in vacuo*.

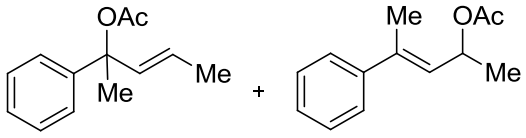
Step 2: Literature procedure was followed to reduce the alkyne and obtain **60**. [30]

The allylic alcohol **61** was subjected to conditions in procedure **G** (step 2) and procedure **B** to afford the desired allylic acetate **43**.



(*E*) & (*Z*)-2-phenyloct-2-en-4-yl acetate (43): ^{1}H NMR (500 MHz, $CDCl_3$): δ 0.77 (3H, t, *J* = 7.0 Hz, *cis*), 0.86 (3H, t, *J* = 7.0 Hz, *trans*), 1.06-1.19 (m), 1.20-1.34 (m), 1.36-1.48 (m), 1.52-1.60 (m), 1.66-1.74 (m), 1.93 (3H, s, *cis*), 1.99 (3H *trans* + 3H *cis*, s), 2.09 (3H, s, *trans*), 5.14 (1H, dt, *J* =

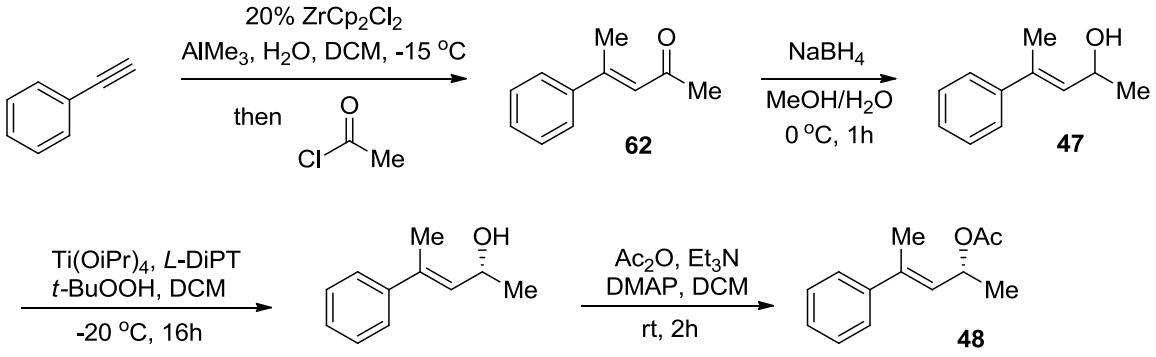
9.3, 6.6 Hz, *cis*), 5.36 (1H, dd, *J* = 9.3, 1.5 Hz, *cis*), 5.56-5.64 (2H, m, *trans*), 7.11-7.15 (m), 7.18-7.22 (m), 7.24-7.30 (m), 7.32-7.36 (m); ^{13}C NMR (125 MHz $CDCl_3$): δ 13.9, 14.0, 16.5, 21.3, 22.4, 22.6, 26.0, 27.1, 27.2, 34.6, 34.7, 71.7, 72.6, 125.9, 125.9, 126.6, 127.0, 127.3, 127.5, 128.2, 128.2, 138.7, 141.0, 141.1, 142.8, 170.1, 170.5; IR (neat): 2957 (w), 2932 (w), 2861 (w), 1732 (s), 1494 (w), 1445 (w), 1369 (m), 1235 (s), 1016 (m), 950(m) cm^{-1}; HRMS (ESI+) for $C_{14}H_{19}$ [M-OAc]: calculated:187.1418, found:187.1491. The crude material was purified on silica gel (10% ether/hexanes) to afford a clear oil (24% yield over 4 steps). R_f = 0.33 in 5% EtOAc/hexanes.



(*E*)-2-phenylpent-3-en-2-yl acetate (major) & (*E*)-4-phenylpent-3-en-2-yl acetate (minor) (45): From commercially available (*E*)-pent-3-en-2-one, procedure **A** and **B** was followed. ^{1}H NMR (500 MHz, $CDCl_3$):1.37 (3H, d, *J* = 6.3 Hz, minor), 1.75 (3H, dd, *J* = 6.4, 1.9 Hz, major), 1.85 (3H, s, major), 2.05 (3H, s, minor), 2.06 (3H, s, major), 2.12 (3H, d, *J* = 1.5 Hz, minor), 5.67 (1H, app dq, *J* = 19.5, 6.4 Hz, major), 5.72-5.79 (2H, m, minor), 5.99 (1H, ddd, J = 15.1, 2.9, 1.4 Hz, major), 7.22-7.28 (1H major + 1 H minor, m), 7.31-7.36 (3H major

+ 3H minor), 7.39-7.41 (1H major + 1H minor, m); ^{13}C NMR (125 MHz, $CDCl_3$): 16.3, 17.9, 20.8, 21.4, 22.3, 26.2, 68.3, 83.2, 125.1, 125.9, 126.2, 126.9, 127.0, 127.1, 127.3, 127.4, 127.5, 128.1, 128.2, 128.3, 134.6, 137.9, 142.7, 144.6, 169.4, 170.4; IR (neat): 3026 (w), 2935 (w), 1736 (s), 1494 (m), 1240 (s), 1119 (m), 913 (m), 760 (m), 699 (m); HRMS (ESI+) for $C_{13}H_{16}O_2$ [M-OAc]: calculated 145.1012, found 145.1003. The crude material was purified on silica gel (5% Et_2O/Pentane) to afford a colorless oil (30% yield over 2 steps). R_f = 0.38 in 5% EtOAc/hexanes.

Synthesis and characterization of (*E*)-4-phenylpent-3-en-2-yl acetate (48)



General Procedure I:

Step 1: Starting from phenylacetylene, literature procedure was followed.[33]

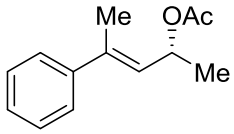
Step 2: General procedure **D**, step 2 was followed.

[33] Dabrowski, J. A.; Haeffner, J.; Hoveyda, A. H. *Angew. Chem., Int. Ed.* **2013**, *52*, 7694

Step 3:[34] A flame dried round bottom flask equipped with a stir bar was charged with **62** (1.2 g, 7.6 mmol), *L*-(-)-DIPT (1.92 mL, 9.2 mmol), and CH_2Cl_2 (76 mL). The mixture was cooled to -20 ^oC and Ti(O*i*-Pr)$_4$ (2.26 mL, 7.6 mmol) was added. The solution stirred for 30 minutes, then 5.5 M. *t*-BuO_2H in decane (0.84 mL, 4.6 mmol) was added slowly *via* syringe. The reaction was stirred for 16 h. The reaction was then quenched with a cold solution of citric acid (6 g) and $FeSO_4 \cdot 7H_2O$ (16 g) in 50 mL D.I. H_2O and was stirred vigorously at room temperature, until the solution was clear. The organic layer was set aside and the aqueous layer was extracted with CH_2Cl_2 three times. The combined organic fractions were concentrated *in vacuo*, and the crude residue was dissolved in diethyl ether (50 mL). To this solution was added a solution of NaOH (20 g) and NaCl (3 g) in H_2O (50 mL) at 0 ^oC. The mixture stirred at 0 ^oC for 1 h before the addition of H_2O (25 mL). The organic layer was removed and the aqueous layer was extracted with ethylacetate three times. The organic portions were combined, dried over Na_2SO_4, filtered, and concentrated *in vacuo*. The crude material was purified on silica gel to afford the enantioenriched alcohol.

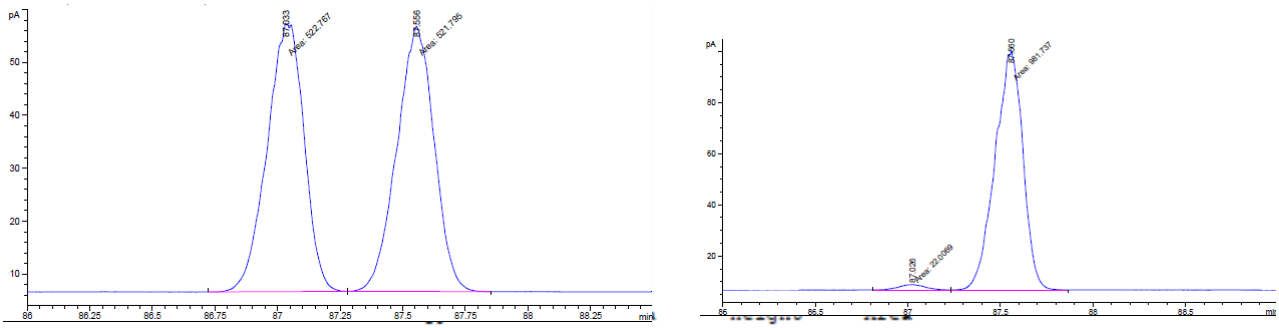
[34] (a) Martin, V. S.; Woodard, S. S.; Katsuki, T.; Yamada, Y.; Ikeda, M.; Sharpless, K. B. *J. Am. Chem. Soc.* **1981**, *103*, 6237; (b) Gao, Y.; Hanson, R. M.; Klunder, J. M.; Ko, S. Y.; Masamune, H.; Sharpless, K. B. *J. Am. Chem. Soc.* **1987**, *109*, 5765; (c) Li, Z.; Parr, B. T.; Davies, H. M. L. *J. Am. Chem. Soc.* **2012**, *134*, 10942.

Step 4: General procedure **B** was followed to obtain the desired starting material **48**.



(*E*)-4-phenylpent-3-en-2-yl acetate (48): Spectral data is in accordance with literature values.[35]

Analysis of stereo chemistry: The enantiopurity was determined using chiral GLC (Chiral β-dex, Supelco, 60 ^{o}C for 5 minutes, ramp 1 ^{o}C / min to 140 ^{o}C, hold at 140 ^{o}C for 20 minutes, 20 psi, sr = 35:1). The absolute stereochemistry was determined by analogy to reported literature.[34]

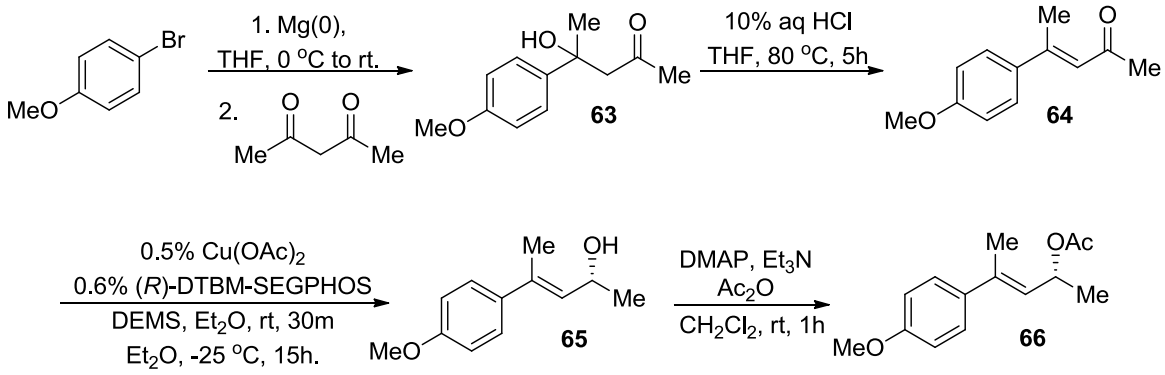


#	[min]		[min]	[pA*s]	[pA]	%
1	87.026	MM	0.1676	22.00691	2.18899	2.19248
2	87.560	MM	0.1748	981.73694	93.59392	97.80752

Totals : 1003.74385 95.78291

[35] Voigtritter, K. R.; Isley, N. A.; Moser, R.; Aue, H. D.; Lipshutz, B. H. *Tetrahedron* **2012**, *68*, 3410

Synthesis and characterization of (*E*)-4-(4-methoxyphenyl)pent-3-en-2-yl acetate (66):



General procedure K:

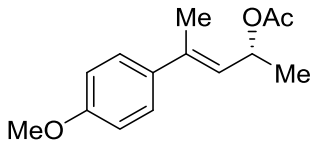
Step 1: Starting with 4-bromoanisole, **63** was obtained following literature procedure.[36]

Step 2: Adapted from literature procedure.[6] A round-bottomed flask was equipped with a stir bar and reflux condenser. The flask was charged with **63** (3.94 g, 16 mmol), THF (48 mL) and 10% HCl in H_2O (16 mL). The reaction was stirred at 80 °C for 1 h. The reaction was then diluted with H_2O and extracted with ethyl acetate three times. The organic portion was washed with brine, dried with Na_2SO_4, filtered, and concentrated *in vacuo*. The crude material was purified on column chromatography (SiO_2, 20% EtOAc/hex) to afford ketone **64** as a white solid.

[36] Guthrie, J. P.; Wang, X.-P. *Can. J. Chem.* **1992**, *70*, 1055.

Step 3[35]: In the dry-box, an oven-dried 2-dram vial equipped with a stir bar was charged with anhydrous $Cu(OAc)_2$ (4.63 mg, 0.026 mmol) and (*R*)-DTBM-SEGPHOS (30.08 mg, 0.026 mmol). The vial was capped with a rubber septum and brought out of the box. At room temperature, dry ethyl ether (2 mL) and diethoxymethyl silane (2.45 mL, 15.3 mmol) were added under N_2. After stirring for 10 min, the reaction mixture was cooled to -25 ^oC. A solution of **64** (0.82 g, 5.1 mmol) in dry ethyl ether (1 mL) was added slowly *via* syringe. The mixture was stirred for 15 h at -25 ^oC. To the mixture was added 1.0 M TBAF in THF (15.3 mL) and the reaction was stirred for an additional 1 h. MeOH (10 mL) was then added, and the reaction was warmed to room temperature, concentrated *in vacuo*, and filtered through a short SiO_2 plug. The crude material was then purified using column chromatography (SiO_2, 20% EtOAc/hexanes) to afford clean **66** as a colorless oil (814.2 mg, 83% yield).

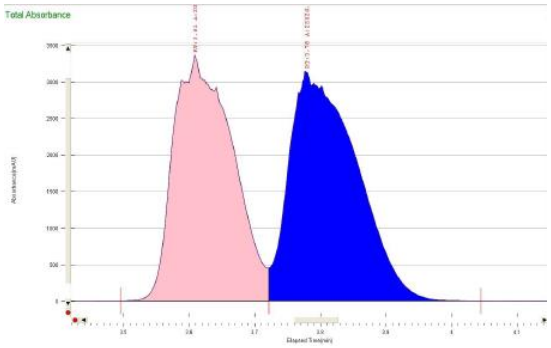
Step 4: General procedure **B** was followed to obtain the desired starting material.



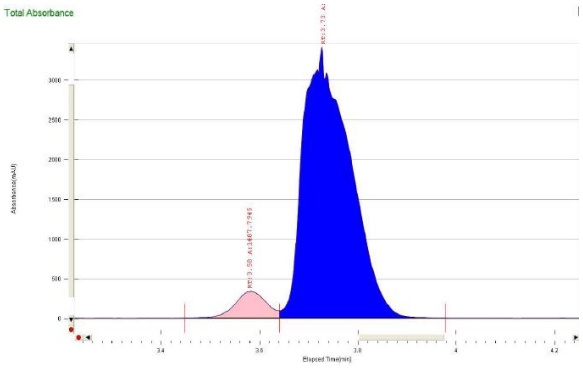
(E)-4-(4-methoxyphenyl)pent-3-en-2-yl acetate (66): ^1H NMR (500 MHz, $CDCl_3$): δ 1.36 (3H, d, *J* = 6.3 Hz), 2.05 (3H,s), 2.10 (3H, s), 3.81 (3H, s), 5.67 (1H, d, *J* = 8.8 Hz), 5.76 (1H, dq, *J* = 8.8, 6.3 Hz), 6.86 (2H, d, *J* = 8.8 Hz), 7.34 (2H, d, *J* = 8.8

Hz); ^{13}C NMR (125 MHz, $CDCl_3$): δ 16.3, 20.9, 21.4, 55.3, 68.4, 113.6, 125.9, 126.9, 135.1, 137.3, 159.1, 170.4; IR (neat): 2977(br), 2932 (br), 2837 (w), 1732 (m), 1607 (w), 1513 (m), 1444 (w), 1370 (w), 1289 (w), 1242 (s), 1181 (w), 1036 (m) cm^{-1}; HRMS (ESI+) for $C_{14}H_{19}O_3$ [M+H]: calculated: 235.1334, found: 235.1321. The crude material was purified on silica gel (7% ether/pentane) to afford a corlorless oil (15% yield over 4 steps). R_f = 0.12 in 5% EtOAc/hexanes.

Analysis of stereo chemistry: The enantiopurity was determined on alohol **66** using chiral SFC (OJ-H, Chiralpak, 3mL/min, 4% isopropanol, 100 bar, 35 °C). The absolute stereochemistry was determined by analogy to reported literature.[35]



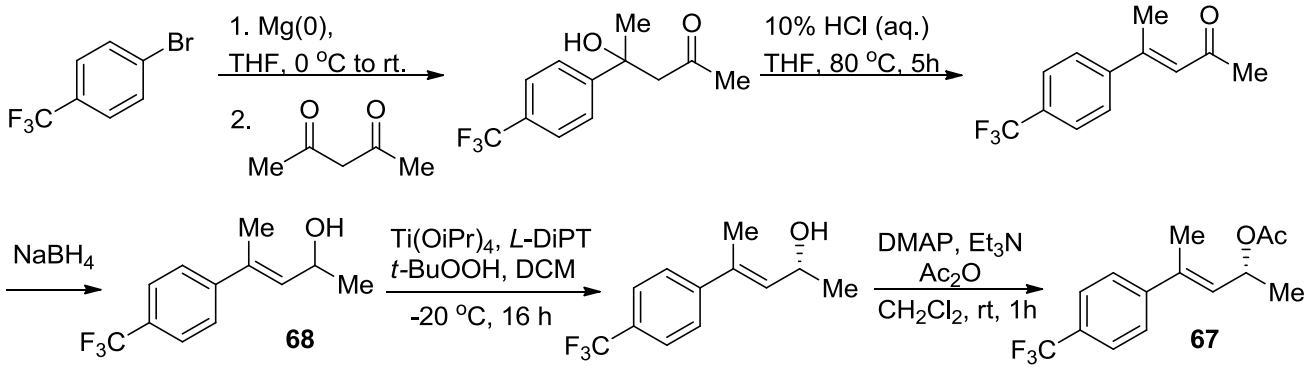
Racemic

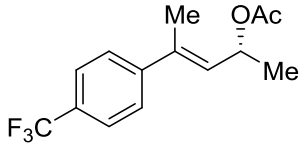


Reaction product

Peak No	% Area	Area	RT (min)
1	6.1967	1487.7945	3.58
2	93.8033	22521.5346	3.73
Total:	100	24009.3291	

Synthesis and characterization of (*E*)-4-(4-(trifluoromethyl)phenyl)pent-3-en-2-yl acetate (67):

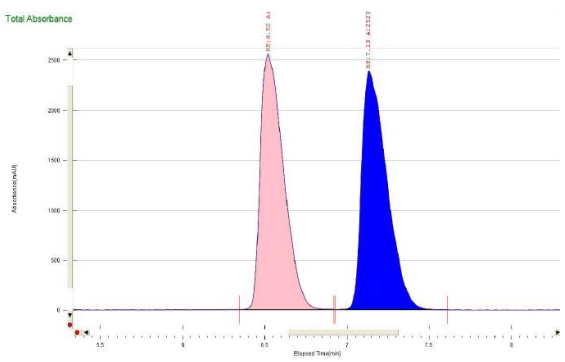




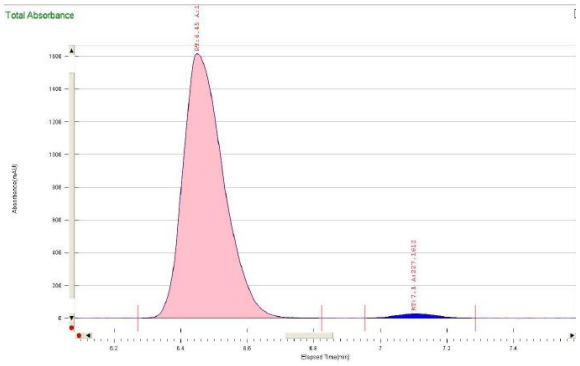
(*E*)-4-(4-(trifluoromethyl)phenyl)pent-3-en-2-yl acetate (67): From commercially available 4-bromobenzotrifluoride, procedure **K**, step 1 and 2 was followed, then procedure **I** step 3 and 4 and procedure **B** was followed. ^{1}H NMR (500 MHz, $CDCl_3$): δ 1.40 (3H, d, J = 5.9 Hz), 2.05 (3H, s), 2.14 (3H, d, J = 1.5 Hz), 5.73-5.80 (2H, m), 7.43 (2H, d, J = 8.3 Hz), 7.57 (2H, d, J = 8.3 Hz); (125 MHz, $CDCl_3$): δ 16.3, 20.6, 21.3, 68.1, 123.1, 125.1, 125.2, 125.3, 125.4, 126.2, 129.4 (q, $^{2}J_{CF}$ = 32.4 Hz), 136.7, 146.2, 170.4; IR (neat): 2979 (br), 1738 (m), 1616 (w), 1371 (w), 1326 (s), 1240 (m), 1165 (m), 1124 (m), 1072 (m), 1042 (w), 1014 (w), 946 (w) cm^{-1}; HRMS (ESI+) for $C_{14}H_{15}F_3O_2$ [M+H]: calculated: 273.1102, found: 273.1099. The crude material was

purified on silica gel (10% ether/pentane) to afford a colorless oil. R_f = 0.22 in 5% EtOAc/hexanes.

Analysis of stereo chemistry: The enantiopurity was determined on alohol **67** using chiral SFC (OD-H, Chiralpak, 3mL/min, 3% Isopropanol, 100 bar, 35 ^{o}C). The absolute stereochemistry was determined by analogy to reported literature.[34]



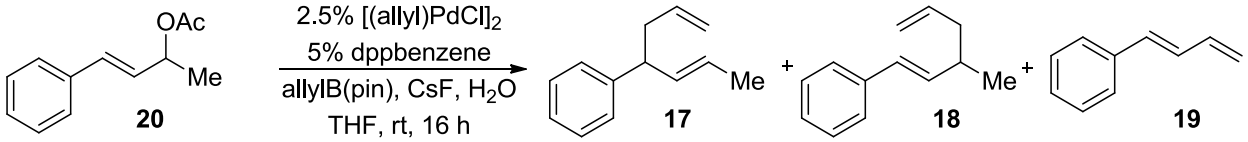
Racemic



Reaction product

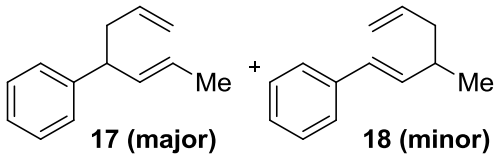
Peak No	% Area	Area	RT (min)
1	98.3578	13605.9216	6.45
2	1.6422	227.1612	7.1
Total:	100	13833.0828	

C. Synthesis and Characterization of the Allyl-Allyl Coupling Products



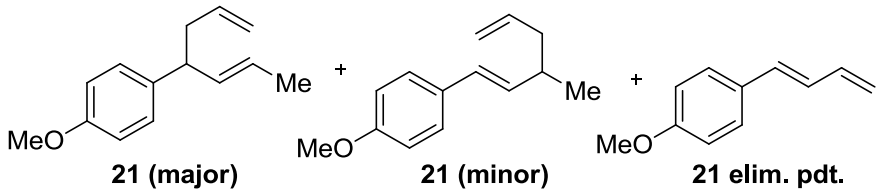
General procedure L: In the dry-box, an oven dried 2-dram vial equipped with a stir bar was charged with (η^3-allylPdCl)$_2$ (1.4 mg, 0.0038 mmol), dppbenzene (4.6 mg, 0.0075 mmol), and THF (0.25 mL). The resulting solution was allowed to stir at room temperature for 5 min. At this time, the vial was sequentially charged with **20** (37.2 mg, 0.15 mmol), allylB(pin) (75.6 mg, 0.45 mmol), CsF (228 mg, 1.5 mmol), and THF (0.75 mL). The vial was tightly capped with a rubber septum, removed from the dry-box, and placed under a positive pressure of N_2. Degassed H_2O was then added (40 µL) *via* a glass syringe. The rubber septum was rapidly exchanged with a polypropylene cap, sealed with tape, and the reaction was allowed to stir at room temperature for 16 h. The slurry was diluted with water, the organic layer was separated and the aqueous layer was extracted three times with Et_2O. The organic portion was dried with Na_2SO_4 filtered, and concentrated under reduced pressure. The crude material was purified by silica gel chromatography (100% pentane) to yield a 6:2:1 mixture of **17 and 18**, and

elimination product **19**. The combined yield of **17** and **18** was calculated to be 88%. **19** can be removed by treating the mixture with maleic anhydride (30mg, 0.3 mmol) in THF at 60 ^{o}C for 3 h.



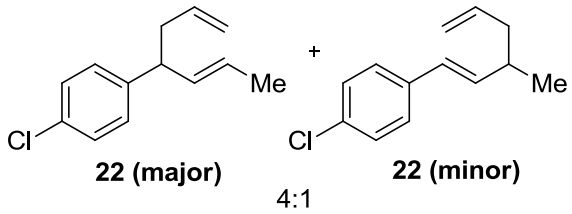
17 (major) **18 (minor)**

(*E*)-hepta-1,5-dien-4-ylbenzene (17, major) & (*E*)-(3-methylhexa-1,5-dien-1-yl)benzene (18, minor): ^{1}H NMR (500 MHz, $CDCl_3$): δ 1.11 (3H, d, *J* = 6.8 Hz, minor), 1.66 (3H, d, *J* = 5.6 Hz, major), 2.10-2.26 (2H, m, minor), 2.36-2.54 (2H+1H, m, major+minor), 3.70 (1H, q, *J* = 8.3 Hz, major), 4.95-5.09 (2H+2H, m, major+minor), 5.50-5.61(2H, m, major), 5.70-5.87(1H+1H, m, major+minor), 6.16 (1H, dd, *J* = 15.9, 7.3 Hz, minor), 6.37 (1H, d, *J* = 15.9 Hz, minor), 7.17-7.38 (5H + 5H, m, major + minor); ^{13}C NMR (125 MHz $CDCl_3$): δ 13.2, 19.9, 36.9, 41.1, 41.4, 43.0, 115.9,116.0, 124.0, 126.0, 126.0, 126.8, 127.3, 128.2, 128.4, 128.5, 133.8, 136.0,136.7, 137.0, 137.8, 144.9); IR (neat): 3077(m), 3026 (m), 2976 (m), 2922 (m), 1640 (m), 1600 (w), 1493(m), 1451 (m), 1072 (w), 1030 (w), 994(s) cm^{-1}; HRMS (ESI+) for $C_{13}H_{17}$ [M +H]: calculated: 173.1330, found: 173.1333. The crude material was purified on silica gel (100% pentane) to afford a colorless oil. R_f = 0.81 in 5% EtOAc/hexanes.



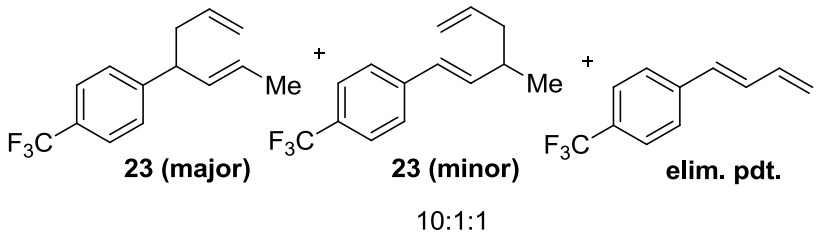
(*E*)-1-(hepta-1,5-dien-4-yl)-4-methoxybenzene (21, major) & (*E*)-1-methoxy-4-(3-methylhexa-1,5-dien-1-yl)benzene (21, minor): Prepared using general procedure **L**. ^{1}H NMR (500 MHz, $CDCl_3$): δ 1.09 (3H, d, *J* = 6.8 Hz, minor), 1.65 (3H, d, *J* = 4.9 Hz, major), 2.06-2.24 (2H, m, minor), 2.33-2.49 (2H, m, major), 2.82-2.89 (1H, m, minor), 3.65 (1H, td, *J* = 8.3, 6.6 Hz, major), 3.79 (3H, s, major), 3.81 (3H, s, minor), 3.82 (3H, s, elim. pdt.), 4.95-5.06 (2H minor + 2H elim. pdt., m), 4.97 (1H, d, *J* = 10.3 Hz, major), 5.03 (1H, d, *J* = 17.1 Hz, major), 5.47-5.57 (2H, m, major), 5.74 (1H, ddt, *J* = 17.1, 10.3, 6.8 Hz, major), 5.82 (1H, ddt, *J* = 17.1, 9.8, 7.3 Hz, minor), 6.01 (1H, dd, *J* = 15.6, 7.3 Hz, minor), 6.29-6.32 (1H, m, elim. pdt.), 6.82-6.88 (2H major + 2H minor, m), 7.11-7.16 (2H major + 2H elim. pdt., m), 7.21 (2H elim. pdt., m), 7.29 (2H minor, m); ^{13}C NMR (125 MHz $CDCl_3$): δ 13.1, 41.2, 42.1, 55.2, 113.8, 115.8, 123.7, 128.2, 134.1, 136.8, 137.1, 157.8; IR (neat): 3074 (w), 3007 (w), 2914 (w), 2835 (w), 1609(w), 1510 (s), 1463 (w), 1441 (w), 1302 (w), 1247 (s), 1177 (m), 996 (m) cm^{-1}; HRMS (ESI+) for $C_{14}H_{18}O_1$ [M +H]: calculated: 203.1435, found: 203.1443. The crude material was purified on silica gel

(1% ether/pentane) to afford a colorless oil (22mg, 70% combined yield for **21 major** and **minor**). R_f= 0.52 in 5% ether/hex



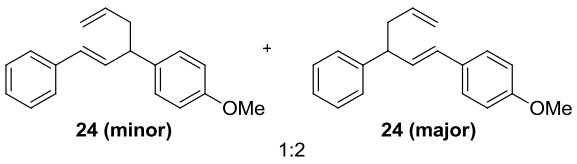
(*E*)-1-chloro-4-(hepta-1,5-dien-4-yl)benzene (22, major) & (*E*)-1-chloro-4-(3-methylhexa-1,5-dien-1-yl)benzene (22, minor): Prepared using general procedure **L**. ^{1}H NMR (500 MHz, $CDCl_3$): δ 1.11 (3H, d, *J* = 6.8 Hz, minor), 1.65 (3H, d, *J* = 5.3 Hz, major), 2.09-2.23 (2H, m, minor), 2.34-2.49 (2H + 1H, m, major+minor), 3.67 (1H, q, *J* = 7.5 Hz, major), 4.99 (1H, d, *J* = 10.3 Hz, major), 5.03 (1H, d, *J* = 17.1 Hz, major), 4.96-5.08 (2H, m, minor),5.49-5.47 (2H, m, major), 5.71 (1H, ddt, *J* = 17.2, 10.3, 6.9 Hz, major), 5.81 (1H, ddt, *J* = 17.1, 10.1, 7.1 Hz, minor), 6.14 (1H, dd, *J* = 15.9, 7.5 Hz, minor), 6.32 (1H, d, *J* = 15.6 Hz, minor), 7.10-7.30 (4H major + 4H minor, m); ^{13}C NMR (125 MHz, $CDCl_3$): δ 13.2, 19.8, 36.9,41.1, 41.3, 42.4, 116.1, 116.3, 124.5,127.1, 127.2, 128.5, 128.6, 128.7, 131.6, 133.3, 136.2, 136.8, 143.4; IR (neat): 3077(w), 3013 (w), 2977 (w), 2922 (w), 1640 (w), 1491 (s), 1439 (m), 1371 (w), 1092 (s), 1014 (s), 994 (m), 967 (m), 913(s) cm^{-1}; HRMS (ESI+) for $C_{13}H_{15}Cl$ [M +H]: calculated: 207.0948, found: 207.0941. The crude material was purified on silica gel (100% pentane) to afford a

colorless oil (28mg, 92% combined yield for **22 major** and **minor**). R_f = 0.93 in 5% EtOAc/hexanes.



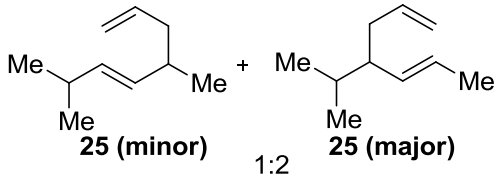
(*E*)-1-(hepta-1,5-dien-4-yl)-4-(trifluoromethyl)benzene (23, major) & (*E*)-1-(3-methylhexa-1,5-dien-1-yl)-4-(trifluoromethyl)benzene (23, minor) & (E)-1-(buta-1,3-dien-1-yl)-4-(trifluoromethyl)benzene (elim. pdt.): Prepared using general procedure **L**. ^{1}H NMR (500 MHz, $CDCl_3$): δ 1.11 (3H, d, *J* = 6.9 Hz, elim. pdt.), 1.64 (3H, d, *J* = 5.4 Hz, major), 1.68 (3H, d, *J* = 6.4 Hz, minor), 2.11-2.25 (1H, m, minor), 2.37-2.52 (2H+1H, m, major + minor), 3.14 (1H, ap. t, *J* = 8.0 Hz, minor), 3.67 (1H, q, *J* = 7.4 Hz, major), 4.94-5.08 (6H, m, major + minor + elim. pdt.), 5.46 (1H, dq, *J* = 15.6, 6.4 Hz, minor), 5.51-5.62 (2H+1H, m, major + minor), 5.64-5.75 (2H, m, major + minor), 5.75-5.85 (1H, m, elim. pdt.), 6.25 (1H, dd, *J* = 16.1, 7.8 Hz, elim. pdt.), 6.39(1H, d, *J* = 15.7 Hz, elim. pdt.); ^{13}C NMR (125 MHz, $CDCl_3$): δ 13.2, 14.0, 17.9, 19.7, 22.3, 29.7, 34.1, 36.9, 40.1, 40.9, 41.2, 42.9, 48.6, 116.2, 116.4, 116.5, 119.4, 125.0, 125.2, 125.3 (q, $^3J_{CF}$ = 3.8 Hz), 126.1, 126.5, 127.1, 127.7, 127.8, 127.9, 128.1, 128.2, 128.4, 132.8, 133.5, 135.9, 136.2, 136.6, 138.8,

149.0; IR (neat): 3026 (w), 2917 (w), 1639 (w), 1598 (w), 1493 (m), 1445 (m), 1375 (w), 973 (s), 912 (s) cm^{-1}; HRMS (ESI+) for $C_{14}H_{15}F_3$ [M +H]: calculated: 241.1204, found: 241.1197. The crude material was purified on silica gel (100% pentane) to afford a colorless oil (17.4mg, 50% combined yield for **23 major** and **minor**). R_f = 0.8 in 5% ether/hexanes.



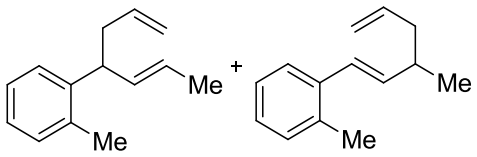
(*E*)-1-methoxy-4-(1-phenylhexa-1,5-dien-3-yl)benzene (24, minor) & (*E*)-1-methoxy-4-(3-phenylhexa-1,5-dien-1-yl)benzene (24, major): Prepared using general procedure **L**. ^{1}H NMR (500 MHz, $CDCl_3$): δ 2.54-2.62 (2H major + 2H minor, m), 3.50 (1H major + 1H minor, app dt, J = 14.7, 7.3 Hz), 3.79 (3H major, s), 3.80 (3H minor, s), 4.98 (1H major + 1H minor, d, *J* = 10.4 Hz), 5.05 (1H major + 1 H minor, d = 17.1 Hz), 5.72-5.82 (1H major + 1H minor, m), 6.22 (1H major, dd, *J* = 15.7, 7.3 Hz), 6.31-6.38 (1H major + 2H minor, m), 6.83 (2H major, d, *J* = 8.3 Hz), 6.87 (2H minor, d, *J* = 8.8 Hz), 7.16-7.36 (7H major + 7H minor, m); ^{13}C NMR (150 MHz, $CDCl_3$): δ 40.2, 40.3, 48.1, 49.0, 55.2, 55.3, 113.9, 116.3, 126.2, 126.3, 127.1, 127.3, 127.4, 127.8, 128.2, 128.5, 128.6, 128.7, 129.2, 129.5, 129.9, 130.3, 131.4, 133.9, 135.9, 136.7, 137.5, 144.1, 158.1, 158.9; IR (neat): 3001 (w), 1639 (m), 1510 (s), 1463 (m), 1247 (s), 1175 (m), 1035 (m), 993

(m), 699 (m); HRMS (ESI+) for $C_{19}H_{20}O$ $[M+H]^+$: calculated: 265.1592, found: 265.1580. The crude material was purified on silica gel (2% ether/pentane) to afford a clear oil (29 mg, 75% combined yield for **24 major** and **minor**). R_f = 0.5 in 2% ether/hexanes.



(*E*)-4,7-dimethylocta-1,5-diene (25, minor) and (*E*)-4-isopropylhepta-1,5-diene (25, major): Prepared using general procedure **L**. ^{1}H NMR (500 MHz, $CDCl_3$): δ 0.84 (3H, d, *J* = 6.8 Hz, major), 0.89 (3H, d, *J* = 6.8 Hz, major), 0.92-0.98 (3H, m, minor), 0.94 (6H, d, *J* = 6.4 Hz, minor), 1.58 (3H, dd, *J* = 6.8, 2.0 Hz, major), 1.61 (1H, m, major), 1.98 (2H, m, major), 2.04-2.30 (4H, m, major+minor), 2.48-2.62 (2H, m, minor), 4.91-5.05 (4H, m, major+minor), 5.12 (1H, d, *J* = 10.2 Hz, minor), 5.17 (1H, t, *J* = 10.8 Hz, major), 5.53 (1H, dq, *J* = 10.3 Hz, 6.8 Hz, major), 5.70-5.81 (1H major + 1 H minor, m); ^{13}C NMR (125 MHz $CDCl_3$): δ 13.3, 18.7, 20.7, 21.1, 23.3, 23.5, 26.8, 31.7, 32.0, 37.4, 41.9, 42.8, 115.0, 115.4, 124.3, 132.8, 133.0, 136.2, 137.4, 137.9; IR (neat): 2960 (w), 2923 (br), 1465 (w), 1384 (w), 903 (s), 724 (s), 650 (m) cm^{-1}; HRMS (ESI+) for $C_{10}H_{17}$ [M-H]: calculated: 137.1330, found: 137.1328. The crude material

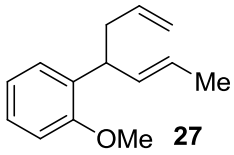
was purified on silica gel (100% pentane) to afford a colorless oil. R_f = 0.49 in 5% EtOAc/hexanes.



2g (major) 7:1 3g (minor)

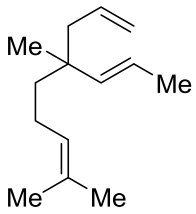
(*E*)-1-(hepta-1,5-dien-4-yl)-2-methylbenzene (26, major) & (*E*)-1-methyl-2-(3-methylhexa-1,5-dien-1-yl)benzene (26, minor): Prepared using general procedure **L**. ^{1}H NMR (500 MHz, $CDCl_3$): δ 1.15 (3H, d, *J* = 6.6 Hz, minor), 1.66 (3H, d, *J* = 4.9 Hz, major), 2.12-2.26 (2H, m, minor), 2.34 (3H, s, minor), 2.36 (3H, s, major), 2.38-2.49 (2H, m, major), 3.84-3.93 (1H, m, major), 4.96-5.08 (2H major + 2H minor, m), 5.48-5.56 (2H, m, major), 5.76 (1H, ddt, 17.1, 10.3, 7.1 Hz, major), 5.83 (1H, ddt, *J* = 17.1, 10.0, 7.1 Hz, minor), 6.10 (1H, dd, *J* = 15.7, 7.6 Hz, minor), 6.55 (1H, d, *J* = 15.9 Hz, minor), 7.06-7.20 (m, major and minor), 7.23 (1H, d, *J* = 7.8 Hz, major), 7.41 (1H, d, *J* = 7.1 Hz minor); ^{13}C NMR (125 MHz, $CDCl_3$): δ major (143.2, 136.9, 135.4, 133.8, 130.3, 126.3, 126.2, 125.7, 123.9, 115.9, 40.7, 38.7, 19.7, 13.3) minor (137.5, 137.0, 135.0, 130.1, 126.7, 126.1, 126.0, 125.5, 115.9, 41.5, 37.2, 20.1, 19.8); IR (neat): 3074 (m), 3017 (m), 2975 (m), 2860 (m), 1640 (m), 1603 (w), 1488 (m), 1461 (m), 1440 (m), 912 (s), 751(s), 726 (s) cm^{-1}; HRMS (ESI+) for $C_{14}H_{18}$ [M +H]: calculated: 187.1482, found: 187.1487.

The crude material was purified on silica gel (100% pentane) to afford a colorless oil (26 mg, 94 % combined yield for **26 major** and **26 minor**). R_f = 0.71 in 5% EtOAc/hexanes.

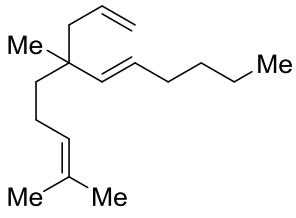


27

(*E*)-1-(hepta-1,5-dien-4-yl)-2-methoxybenzene (27): Prepared using general procedure **L**. ^{1}H NMR (500 MHz, $CDCl_3$): δ 1.65 (3H, d, *J* = 6.8 Hz), 2.38 (1H, app dt, *J* = 14.2, 7.3 Hz), 2.46 (1H, app dt, *J* = 13.7, 5.9 Hz), 3.84 (3H, s), 4.13 (1H, app q, *J* = 6.3 Hz), 4.94 (1H, d, *J* = 10.2 Hz), 5.00 (1H, d, *J* = 17.1 Hz), 5.46-5.53 (1H, m), 5.56-5.61 (1H, m), 5.76 (1H, ddt, *J* = 17.1, 10.2, 6.9 Hz), 6.86 (1H, d, *J* = 8.1 Hz), 6.91 (1H, t, *J* = 7.5), 7.14-7.21 (2H, m); ^{13}C NMR (125 MHz, $CDCl_3$): δ 13.2, 36.1, 40.0, 55.4, 120.6, 124.1, 126.8, 127.7, 133.3, 133.6, 137.2, 156.8; IR (neat): 3073 (w), 3007 (w), 2918 (w), 2835 (w), 1639 (w), 1599 (w), 1490 (s), 1463 (m), 1438 (m), 1238 (s), 1031 (m), 808 (s) cm^{-1}; HRMS (ESI+) for $C_{14}H_{18}O_1$ [M+H]: calculated: 203.1429, found: 203.1436. The crude material was purified on silica gel (2% ether in pentane) to afford a clear oil (21 mg, 70% yield for **27**). R_f = 0.74 in 5% EtOAc/hexanes.

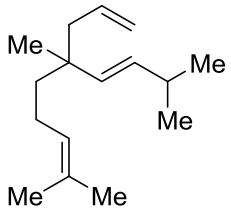


(*E*)-4,8-dimethyl-4-(prop-1-en-1-yl)nona-1,7-diene (29): Prepared using general procedure **L**. ^{1}H NMR (500 MHz, $CDCl_3$): δ 0.94 (3H, s), 1.24-1.29 (2H, m), 1.58 (3H, s), 1.68 (3H, s), 1.69 (3H, s), 1.88 (2H, app dt, *J* = 15.9, 7.3 Hz), 1.99-2.08 (2H, m), 4.90 (1H, d, *J* = 17.6 Hz), 5.00 (1H, s), 5.08 (1H, t, *J* = 7.3 Hz), 5.27-5.37 (2H, m), 5.76 (1H, ddt, *J* = 18.1, 11.0, 7.6 Hz); ^{13}C NMR (125 MHz $CDCl_3$): δ 17.5, 18.2, 22.8, 23.5, 25.7, 38.6, 40.9, 45.7, 116.5, 121.8, 125.1, 130.8, 135.7, 139.5; IR (neat): 2964 (m), 2916 (m), 2856 (m), 1639 (w), 1450 (m), 1439 (m), 1377 (m), 995 (m), 972 (s), 911 (s) cm^{-1}; HRMS (ESI+) for $C_{14}H_{25}$ [M+H]: calculated: 193.1956, found: 193.1948. The crude material was purified on silica gel (100% pentane) to afford a colorless oil (23 mg, 80% yield). R_f = 0.89 in 5% EtOac/hexanes.

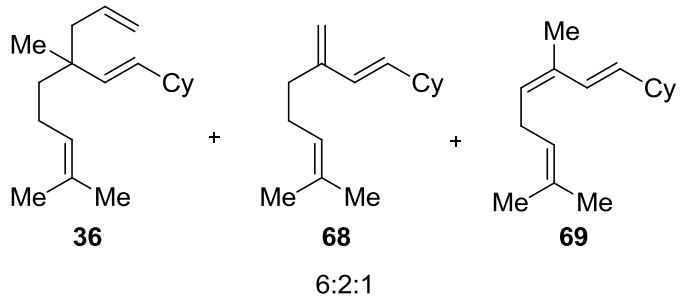


(*E*)-6-allyl-2,6-dimethyldodeca-2,7-diene (32): Prepared using general procedure **L**. ^{1}H NMR (500 MHz, $CDCl_3$): δ 0.89 (3H, t, *J* = 6.8 Hz), 0.94 (3H, s), 1.20-1.38 (6H, m), 1.58 (3H, s), 1.67 (3H, s), 1.87 (2H, app dt, *J* = 16.3, 7.8 Hz), 1.98-2.90 (4H, m), 2.22-2.31 (1H, m), 4.98 (1H, d, *J* = 5.4 Hz), 4.99 (1H, s), 5.09 (1H, t, *J* = 7.3 Hz), 5.24-5.34 (2H, m), 5.75 (1H, ddt, *J* = 16.1,10.7, 7.3); ^{13}C NMR (125 MHz $CDCl_3$): δ 13.9, 17.5, 22.1, 22.9, 23.4,

25.7, 32.0, 32.5, 38.5, 41.0, 45.8, 116.5, 125.2, 127.6, 130.9, 135.7, 138.3; IR (neat): 2959 (s), 2924 (s), 2872 (m), 2856 (m), 1639 (s), 1457 (m), 1377 (m), 995 (m), 974 (s) 911 (s) cm^{-1}; HRMS (ESI+) for $C_{17}H_{31}$ [M+H]: calculated: 235.2426, found: 235.2430. The crude material was purified on silica gel (100% pentane) to afford a colorless oil (28 mg, 79% yield). R_f = 0.87in 5% EtOAc/hexanes.

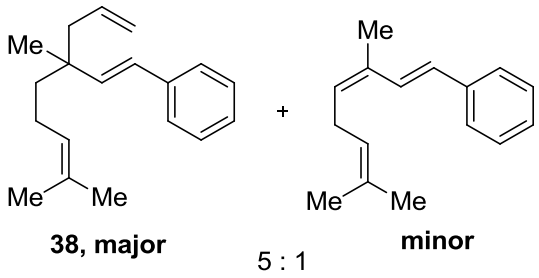


(*E*)-6-allyl-2,6,9-trimethyldeca-2,7-diene (34): Prepared using general procedure **L**. ^{1}H NMR (500 MHz, $CDCl_3$): δ 0.93 (3H, s), 0.97 (6H, d, *J* = 6.6 Hz), 1.20-1.32 (2H, m), 1.59 (3H, s), 1.68 (3H, s), 1.87 (2H, app dt, *J* = 16.4, 7.6 Hz), 2.03 (2H, m), 2.22-2.31 (1H, m), 4.98 (1H, d, *J* = 8.3 Hz), 5.00 (1H, s), 5.08-5.12 (1H, m), 5.24-5.26 (2H, m), 5.69-5.79 (1H, m); ^{13}C NMR (125 MHz $CDCl_3$): δ 17.5, 22.8, 23.0, 23.0, 23.4, 25.7, 31.4, 38.2, 41.0, 45.8, 116.4, 125.2, 130.9, 134.9, 135.2, 135.7; IR (neat): 2960 (s), 2923 (m), 2867 (m), 1638 (w), 1509 (m), 1377 (m), 1102 (w), 995 (m), 974 (s), 911 (s) cm^{-1}; HRMS (ESI+) for $C_{16}H_{29}$ [M+H]: calculated: 221.2269, found: 221.2278. The crude material was purified on silica gel (100% pentane) to afford a colorless oil (21 mg, 63% yield). R_f = 0.9 in 5% EtOAc/hexanes.



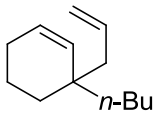
(*E*)-(3-allyl-3,7-dimethylocta-1,6-dien-1-yl)cyclohexane (36); (*E*)-(7-methyl-3-methyleneocta-1,6-dien-1-yl)cyclohexane (68); ((1*E*, 3*Z*)-3,7-dimethylocta-1,3,6-trien-1-yl)cyclohexane (69): Prepared using general procedure **L**. ^{1}H NMR (500 MHz, $CDCl_3$): δ 0.92 (**36**, 3H, s), 1.05-1.21 (**36** + **68**+ **69**, m), 1.22-1.34 (**36** + **68**+ **69**, m), 1.58 (**36**, 3H, s), 1.61 (**68**, 3H, s), 1.63-1.78 (**36** + **68**+ **69**, m), 1.79 (**69**, 3H, s), 1.83-1.96 (**36** + **68**+ **69**, m), 1.97-2.09 (**36**, 2H, m), 2.12-2.24 (2H **68**+ 1H **69**, m), 2.84 (**69**, 2H, br t, *J* = 7.4 Hz), 4.86 (**68**, 1H, s), 4.90 (**S-28**, 1H, s), 4.97 (**36**, 1H, d, *J* = 6.3 Hz), 4.99 (**36**, 1H, s), 5.06-5.14 (**36**, 1H, m), 5.14-5.18 (**68**, 1H, m), 5.19-5.23 (**69**, 1H, m), 5.24 (**68**, 1H, d, *J* = 5.9 Hz), 5.25 (**36**, 1H, s), 5.62 (**69**, 1H, dd, *J* = 15.1, 6.8 Hz), 5.64 (**68**, 1H, dd, *J* = 15.7, 6.9 Hz), 5.72-5.79 (**36**, 1H, m), 6.02 (**68**, 1H, d, *J* = 15.7 Hz), 6.42 (**36**, 1H, d, *J* = 15.1 Hz); ^{13}C NMR (125 MHz, $CDCl_3$): δ 17.5, 17.7, 20.6, 22.9, 23.4, 25.7, 26.0, 26.1, 26.1, 26.2, 26.2, 26.4, 27.0, 29.7, 32.3, 33.2, 33.5, 33.5, 38.3, 41.0, 41.4, 45.9, 113.1, 116.4, 122.9, 124.4, 125.2, 127.2, 129.3, 130.9, 131.7,131.9, 133.6, 135.7, 136.7; IR (neat): 3073 (w), 2962 (m), 2921 (s), 2851 (s), 1679 (br), 1639 (w), 1448 (s), 1377 (m), 1259 (w), 1103 (br), 995 (m), 971 (s), 910 (s) cm^{-1}; HRMS (ESI+) for $C_{19}H_{33}$ [M

+H]: calculated: 261.2582, found: 261.2589. The crude material was purified on silica gel eluted with (100% pentane) to afford a colorless oil (30 mg, 77% yield for **36**). R_f = 0.94 in 5% EtOAc/hexanes.

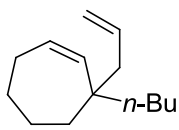


(*E*)-(3-allyl-3,7-dimethylocta-1,6-dien-1-yl)benzene (38, major) & ((1*E*,3*Z*)-3,7-dimethylocta-1,3,6-trien-1-yl)benzene (minor): Prepared using general procedure **L** ^{1}H NMR (500 MHz, $CDCl_3$): δ 1.09 (3H major, s), 1.36-1.46 (2H major, m), 1.58 (3H major, s), 1.67 (3H major, s), 1.69 (3H minor, s), 1.72 (3H minor, s), 1.89-1.99 (2H major, m), 1.94 (3H minor, s), 2.15 (1H major, dd, *J* = 13.2, 5.4 Hz), 2.20 (1H major, dd, *J* = 13.2, 5.4 Hz), 2.97 (2H minor, br t, *J* = 6.9 Hz), 5.02 (1H major, s), 5.06 (1H major, d, *J* = 8.3 Hz), 5.07-5.12 (1H major, m), 5.13-5.18 (1H minor, m), 5.43 (1H minor, br t, *J* = 7.3 Hz), 5.75-5.83 (1H major, m), 6.16 (1H major, d, *J* = 16.2 Hz), 6.28 (1H major, d, *J* = 16.6 Hz), 6.56 (1H minor, d, *J* = 16.1 Hz), 7.17-7.23 (1 H major + 1 H minor, m), 7.28-7.33 (2 H major, m), 7.35-7.38 (2 H major + 2 H minor, m), 7.44 (2H minor, d, *J* = 7.7 Hz); ^{13}C NMR (125 MHz, $CDCl_3$): δ 17.6, 17.8, 20.5, 23.0, 23.3, 25.7, 26.7, 30.3, 39.2, 41.0, 45.7, 117.0, 122.5, 124.8, 125.9, 126.0, 126.4, 126.8, 127.0, 127.2, 128.3, 128.5,

128.6, 130.4, 131.2, 135.2, 138.0, 139.1, 145.5; IR (neat): 2966 (m), 1718 (w), 1493 (s), 1377 (s), 1027 (s), 912 (s), 747 (s), 694 (s); HRMS (ESI+) for $C_{19}H_{26}$ $[M+H]^+$ (major): calculated: 253.1944, found: 253.1956. The crude material was purified on silica gel (pentane) to afford a colorless oil (21 mg, 55% yield for **38**). R_f = 0.80 in pentane.

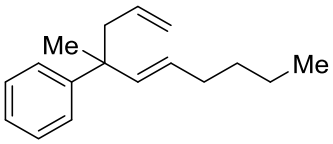


3-allyl-3-butylcyclohex-1-ene (40): Prepared using general procedure **L**, ^{1}H NMR (500 MHz, $CDCl_3$): δ 0.89 (3H, t, *J* = 6.9 Hz), 1.19-1.37 (6H, m), 1.41-1.46 (2H, m), 1.58-1.62 (2H, m), 1.93 (2H, dddd, *J* = 10.3, 6.4, 4.0, 2.5 Hz), 2.05 (2H, d, *J* = 7.8 Hz), 4.97-5.00 (1H, m), 5.01-5.03 (1H, m); 5.42 (1H, d , *J* = 10.3 Hz), 5.64 (1H, dt, *J* = 9.8, 3.5 Hz), 5.77 (1H, dddd, J = 17.6, 16.6, 10.3, 7.3 Hz); ^{13}C NMR (125 MHz, $CDCl_3$): 14.1, 19.0, 22.7, 23.6, 25.1, 32.1, 32.3, 39.6, 44.3, 116.6, 126.1, 135.5, 135.6; IR (neat): 2923 (s), 1638 (m), 1455 (s), 1377 (w), 994 (m), 911 (s), 689 (w); HRMS (ESI+) for $C_{13}H_{22}$ $[M+H]^+$: calculated: 179.1755, found: 179.1693. The crude material was purified on silica gel (pentane) to afford a colorless oil (16 mg, 59% yield). R_f = 0.89 in pentane.



3-allyl-3-butylcyclohept-1-ene (42): Prepared using general procedure **L**, ^{1}H NMR (500 MHz, $CDCl_3$): δ 0.90 (3H, t, *J* =

6.8 Hz), 1.18-1.39 (6H, m), 1.41-1.60 (4H, m) 1.62-1.77 (2H, m), 2.08-2.18 (4H, m), 4.99-5.02 (2H, m), 5.40 (1H, d, J = 11.7 Hz), 5.63 (1H, dt, J = 11.8, 5.9 Hz), 5.76-5.84 (1H, m); ^{13}C NMR (125 MHz, $CDCl_3$): δ 14.1, 23.6, 24.8, 25.9, 28.2, 29.7, 35.7, 39.0, 42.5, 44.2, 116.7, 129.2, 135.7, 140.1; IR (neat): 2923 (s), 1670 (m), 1457 (m), 1377 (w), 995 (w), 912 (m), 727 (w); HRMS (ESI+) for $C_{14}H_{24}$ $[M+H]^+$: calculated: 193.1956, found: 193.1948. The crude material was purified on silica gel (pentane) to afford a colorless oil (21.9 mg, 78% yield). R_f= 0.88 in pentane.



(*E*)-(4-methyldeca-1,5-dien-4-yl)benzene (44): Prepared using general procedure **L**. ^{1}H NMR (500 MHz, $CDCl_3$): δ 0.91 (3H, t, J = 7.0 Hz), 1.29-1.42 (7H, m), 2.07 (2H, dd, J = 7.0 Hz), 2.46-2.56 (2H, m), 4.94 (H, d, J = 9.5 Hz), 5.01 (H, d, J = 17.9 Hz), 5.43 (1H, app dt, J = 13.4, 6.8 Hz), 5.56-5.66 (2H, m), 7.16-7.20 (1H, m), 7.28-7.35 (4H, m); ^{13}C NMR (125 MHz, $CDCl_3$): δ 13.9, 25.6, 31.8, 32.5, 43.2, 46.2, 116.9, 125.7, 126.7, 128.0, 135.5, 148.0; IR (neat): 3075 (w), 2959 (s), 2925 (s), 1639 (w), 1599 (w), 1494 (m), 1458 (m), 1444 (m), 1374 (m), 975 (m), 912 (s), 762 (s), 698 (s) cm^{-1}; HRMS (ESI+) for $C_{17}H_{25}$ [M+H]: calculated: 229.1956, found: 229.1948. The crude material was

purified on SiO_2 eluted with (100% pentane) to afford a colorless oil (30 mg, 86% yield). R_f = 0.8 in 5% EtOAc/hexanes.

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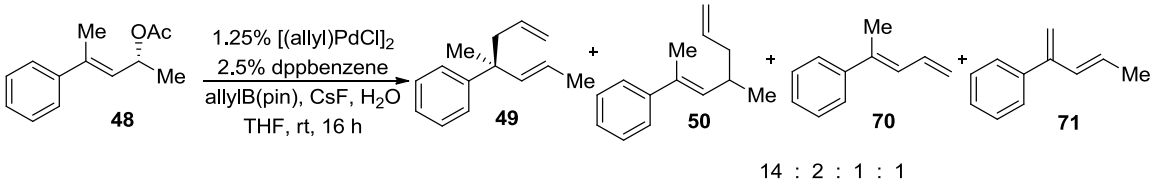
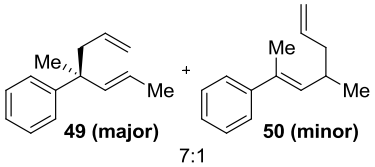


General procedure M: In the dry-box, $(\eta^3\text{-allylPdCl})_2$ in solution of THF (25.5 μL, 0.00188 mmol) and dppbenzene in solution of THF (43 μL, 0.00375 mmol) was added to an oven dried 2-dram vial equipped with a stir bar. The resulting solution was allowed to stir at room temperature for 5 min. At this time, the vial was sequentially charged with **48** (24.3 mg, 0.15 mmol), allylB(pin) (75.6 mg, 0.45 mmol), CsF (228 mg, 1.5 mmol), and THF (0.75 mL). The vial was tightly capped with a rubber septum, removed from the dry-box, and placed under a positive pressure of N_2. Degassed, D.I. water was then added (40 μL) *via* a micro syringe. The rubber septum was rapidly exchanged with a polypropylene cap, sealed with electrical tape, and the reaction was allowed to stir at room temperature for 16 h. The slurry was then diluted with water, the organic layer was separated and the aqueous layer was extracted three times with Et_2O. The organic portion was combined and dried with Na_2SO_4, filtered, and concentrated under reduced

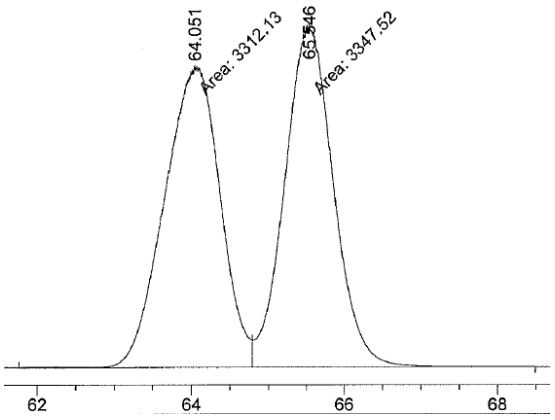
pressure. The crude material was purified by silica gel chromatography (100% pentane) to yield a mixture of 14:2:1:1 of **48**, **49**, **70**, **71**, respectively. The combined yield of **48** and **49** was calculated to be 70% yield (19.5 mg). **70** and **71** can be removed by treating the mixture with maleic anhydride (30 mg, 0.3 mmol) in THF at 60 ^{o}C for 3 h.



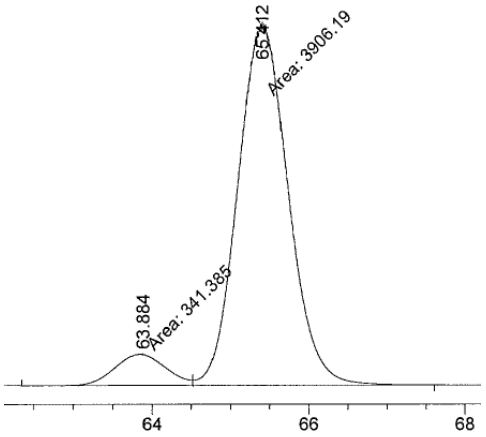
(*E*)-(4-methylhepta-1,5-dien-4-yl)benzene (49, major) & (*E*)-(4-methylhepta-2,6-dien-2-yl)benzene (50, minor): Prepared using general procedure **M**. ^{1}H NMR (500 MHz, $CDCl_3$): δ 1.05 (3H, d, *J* = 6.8 Hz, minor), 1.34 (3H, s, major), 1.73 (3H, dd, *J* = 6.9, 2.0 Hz, major), 2.04 (3H, d, *J* = 1.5 Hz), 2.11-2.16 (2H, m, minor), 2.44-2.57 (2H major + 1H minor, m), 2.57-2.69 (1H, m, minor), 4.94-5.07 (2H major + 2H minor, m), 5.44 (1H, dq, *J* = 15.7, 6.4 Hz), 5.56-5.64 (2H, m, major+minor), 5.67 (1H, dq, *J* = 15.2, 1.5 Hz, major), 5.82 (1H, ddt, *J* = 17.1, 10.3, 7.3 Hz, minor), 7.16-7.40 (8H, m, major+minor); ^{13}C NMR (125 MHz, $CDCl_3$): δ major: 16.0, 18.1, 20.5, 25.5, 33.2, 41.8, 43.2, 46.1, 115.7, 117.0, 122.3, 125.7, 125.9, 126.5, 126.7, 128.0, 128.1, 133.5, 134.3, 135.4, 137.2, 139.6, 144.0, 147.9; IR (neat): 3075 (w), 3058 (w), 3026 (w), 2966 (m), 2916 (m), 2856 (w), 1639 (w), 1598 (w), 1494 (m), 1445 (m), 1375 (m), 1028 (w), 995 (m), 971 (m) cm^{-1}; HRMS

(ESI+) for $C_{14}H_{19}$ [M+H]: calculated: 187.1487, found: 187.1478. The crude material was purified on silica gel (100% pentane) to afford a colorless oil (19.5 mg, 70% combined yield). R_f = 0.78 in 5% EtOAc/hexanes.

Analysis of stereo chemistry: The enantiomer ratio of **49** was determined using chiral GLC (CD-BDM, Supelco, 80 ^{o}C for 70 minutes, 15 psi, sr = 35:1). The absolute stereo chemistry was determined by analogy to **52**.

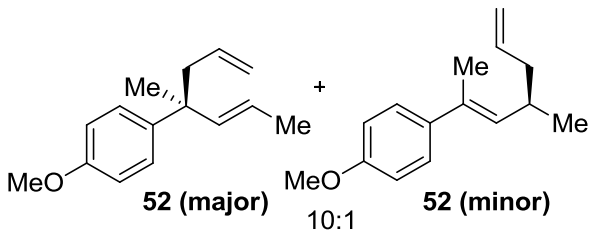


Racemic



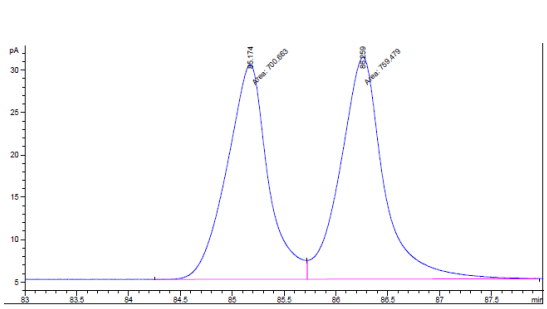
Reaction Product

Peak #	RetTime [min]	Type	Width [min]	Area [pA*s]	Height [pA]	Area %
1	63.884	MF	0.7383	341.38510	7.70674	8.03718
2	65.412	FM	0.7424	3906.18921	87.69042	91.96282

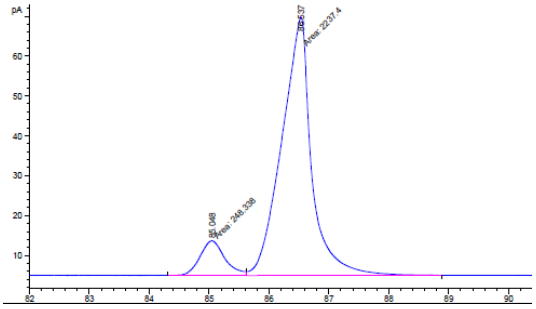


(*E*)-1-methoxy-4-(4-methylhepta-1,5-dien-4-yl)benzene (18, major) & (*R*,*E*)-1-methoxy-4-(4-methylhepta-2,6-dien-2-yl)benzene (52, minor): Prepared using general procedure **M**. ^{1}H NMR (500 MHz, $CDCl_3$): δ 1.05 (3H, d, *J*= 6.8 Hz, minor), 1.33 (3H, s, major), 1.73 (3H, dd, *J* = 6.3, 2.0 Hz, major), 2.03 (3H, d, *J* = 1.5 Hz, minor), 2.42-2.55 (2H major + 2H minor, m), 2.58-2.67 (1H, m, minor), 3.81 (3H, s, major), 3.82 (3H, s, minor), 4.94-5.08 (2H major + 2H minor, m), 5.44 (1H, dq, *J* = 15.6, 6.3 Hz, major), 5.52 (1H, d, *J* = 9.3 Hz, minor), 5.56-5.68 (2H, m, major), 5.82 (1H, ddt, *J* = 17.1, 9.8, 6.8 Hz, minor), 6.83-6.88 (2H, m, minor), 6.86 (2H, d, *J* = 8.8 Hz, major), 7.25 (2H, d, *J* = 8.8 Hz), 7.34 (2H, d, *J* = 8.8 Hz, minor); ^{13}C NMR (125 MHz, $CDCl_3$): δ major: 16.1, 18.1, 20.5, 25.6, 33.1, 41.9, 42.6, 46.2, 55.2, 55.3, 113.3, 113.5, 115.6, 116.9, 122.0, 126.7, 127.6, 127.4, 129.4, 132.8, 135.5, 137.3, 139.9, 140.0, 157.5; IR (neat): 3138 (w), 3001 (m), 2962 (m), 2834 (w), 1638 (w), 1609 (m), 1580 (w), 1511 (s), 1463 (m), 1441 (m), 1374 (w), 1293 (m), 1248 (s), 1182 (m), 1035 (m) cm^{-1}; HRMS (ESI+) for $C_{15}H_{21}O_1$ [M+H]: calculated: 217.1592, found: 217.1591. The crude material was purified on silica gel (100% pentane) to afford a colorless oil (22.7 mg, 86% combined yield). R_f = 0.33 in 5% EtOAc/hexanes.

Analysis of stereo chemistry: The enantiomer ratio of **52** was determined using chiral GLC (CD-BDM, Supelco, 80 ^{o}C, ramp 0.5 ^{o}C/min to 115 ^{o}C, hold at 115 ^{o}C for 30 minutes, 20 psi, sr = 35:1).



Racemic

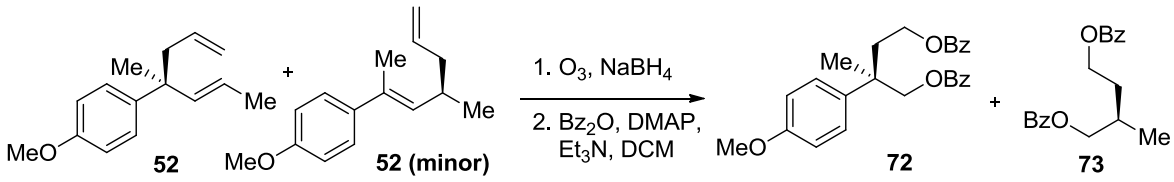


Reaction product

Peak #	RetTime [min]	Type	Width [min]	Area [pA*s]	Height [pA]	Area %
1	85.048	MF	0.4782	248.33794	8.65465	9.99050
2	86.537	FM	0.5764	2237.40283	64.69248	90.00950
Totals :				2485.74077	73.34713	

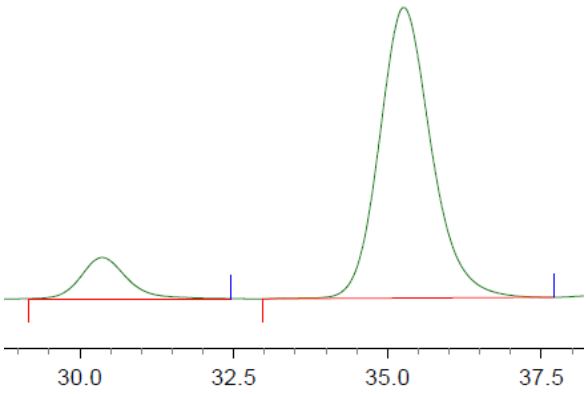
Proof of stereo chemistry:

Mixture of **52 major** and **minor** was treated with ozonolysis/reduction contitions, followed by alcohol protection with benzyl group to obtain **72** and **73**, which can be easily separated.



Absolute stereochemistry of **52** was determined by comparing the HPLC chromatogram of **72** with that of compound reported previously.[37]

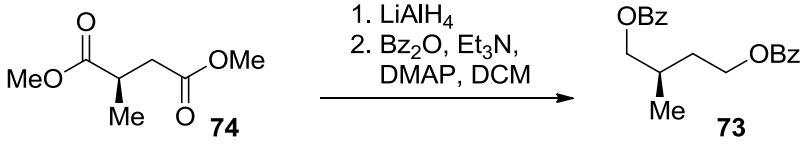
Chiral HPLC: AD-H, Chiralpak, 1.0 mL/min, 2% isopropanol/hex, 254 nm



VWD: Signal A, 254 nm Results

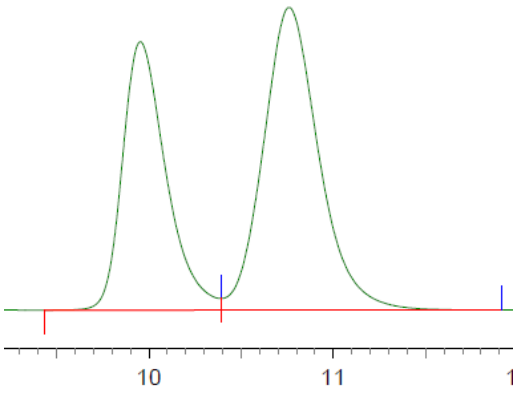
Retention Time	Area	Area %	Height	Height %
30.363	7602484	11.13	145838	12.39
35.263	60721550	88.87	1030928	87.61
Totals	68324034	100.00	1176766	100.00

Absolute stereochemistry of the minor isomer was determined by comparing with authentic sample of dimethyl (*R*)-(+)-methylsuccinate (**74**) via intermediate **73**.

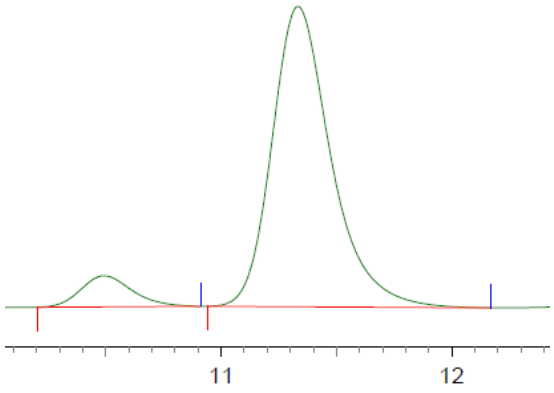


Chiral HPLD: AD-H, Chiralpak, 1.0 ml/min, 1% isopropanol/hex, 254 nm.

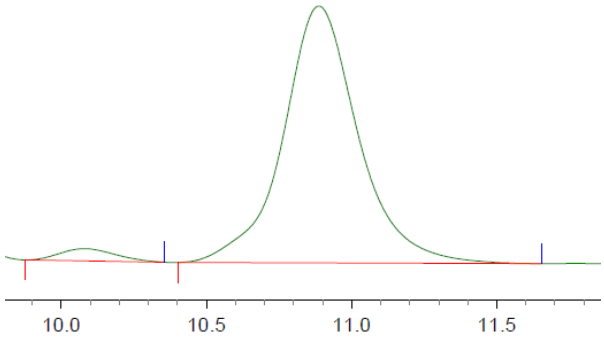
[37] Zhang, P.; Le, H.; Kyne, R. E.; Morken J. P. *J. Am. Chem. Soc.* **2011**, *133*, 9716



Racemic 73 from racemic 74



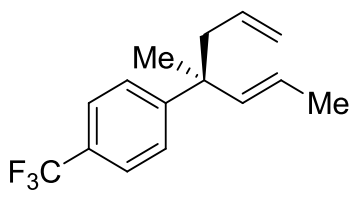
73 from authentic 74



73 derived from 52

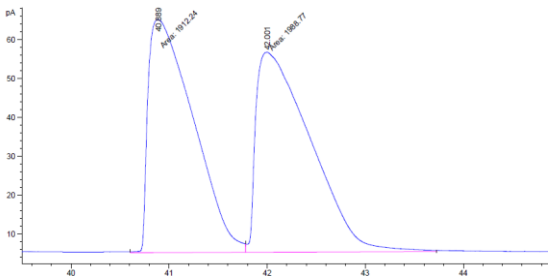
VWD: Signal A,
254 nm Results

Retention Time	Area	Area %	Height	Height %
10.080	424634	3.37	32151	4.54
10.887	12193245	96.63	675793	95.46
Totals	12617879	100.00	707944	100.00

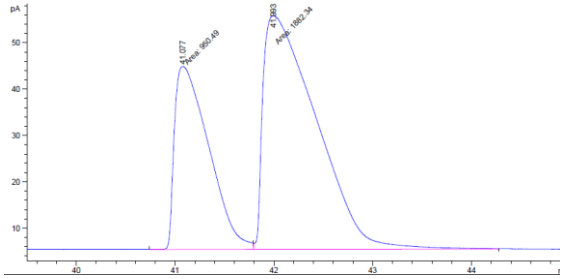


(*E*)-1-(4-methylhepta-1,5-dien-4-yl)-4-(trifluoromethyl)benzene (53): Prepared using general procedure **M**. ^{1}H NMR (500 MHz, $CDCl_3$): δ 1.36 (3H, s), 1.73 (3H, dd, *J* = 6.8, 2.0 Hz), 2.45-2.57 (1H, m), 4.86-5.04 (2H, m), 5.46 (1H, dq, *J* = 15.6, 6.3 Hz), 5.56 (1H, ddt, *J* = 17.1, 9.8, 6.3 Hz), 5.64 (1H, d, *J* = 15.6 Hz), 7.42 (2H, d, *J*= 8.3 Hz), 7.54 (2H, d, *J* = 8.3 Hz); ^{13}C NMR (125 MHz, $CDCl_3$): δ 18.1, 25.4, 43.4, 46.0, 117.6, 123.2, 124.7, 124.8, 124.9, 127.1, 127.5 (p, $^{1}J_{CF}$ = 32.3 Hz), 134.6, 138.7, 152.0; IR (neat): 2922 (w), 1640 (w), 1617 (w), 1451 (w), 1410 (w), 1326 (s), 1165 (m), 1124 (s), 1071(m), 1016 (m) cm^{-1}; HRMS (ESI+) for $C_{15}H_{18}F_3$ [M+H]: calculated: 255.13606, found: 255.13573. The crude material was purified on silica gel (100% pentane) to afford a clolorless oil (27mg, 69% yield). R_f = 0.8 in 5% EtOAc/hexanes.

Analysis of stereo chemistry: The enantiomer ratio of **53** was determined using chiral GLC (CD-BDM, Supelco, 80 ^{o}C, ramp 0.5 ^{o}C/min to 110 ^{o}C, hold at 110 ^{o}C for 10 minutes, 20 psi, sr = 35:1). Absolute stereochemistry was determined by analogy to **52**.

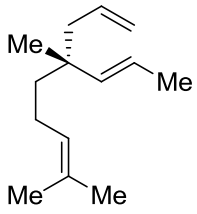


Racemic



Reaction product

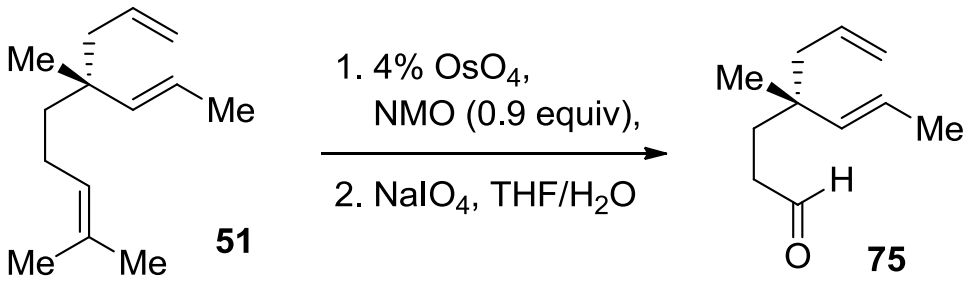
Peak #	RetTime [min]	Type	Width [min]	Area [pA*s]	Height [pA]	Area %
1	41.077	MF	0.4012	950.49042	39.48108	33.55262
2	41.993	FM	0.6216	1882.34460	50.47442	66.44738
Totals :				2832.83502	89.95550	



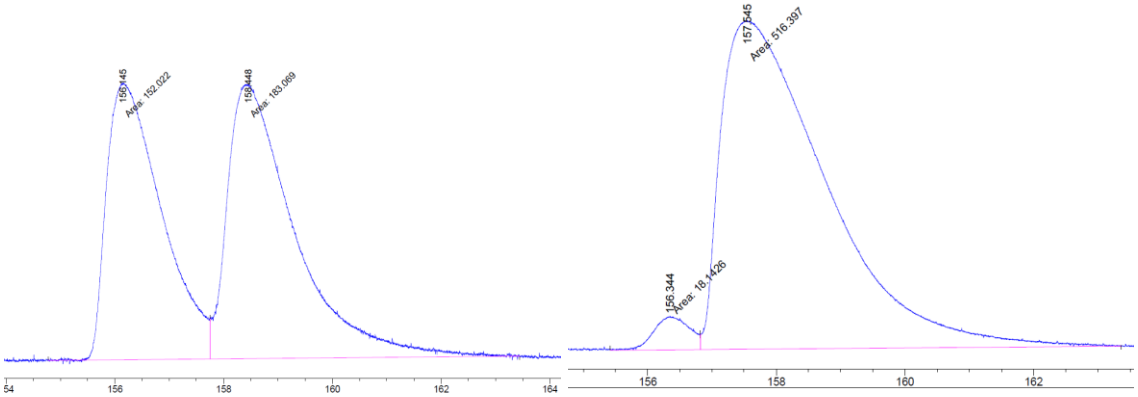
(*R*,*E*)-4,8-dimethyl-4-(prop-1-en-1-yl)nona-1,7-diene (**51**): Prepared using general procedure **M**. All spectral information match with the analogous racemic product **29**. The crude material was purified on silica gel (pentane) to afford a colorless oil (14 mg, 50% yield). R_f = 0.90 in pentane.

Analysis of stereochemistry:

Product **51** was treated with catalytic OsO_4, and NMO followed by $NaIO_4$ diol cleavage to afford **75** for GLC analysis. The analogous racemic material was prepared from racemic product **29**. The absolute stereochemistry was determined by analogy to **52**.



Chiral GLC (CD-BDM, Supelco, 40 °C, ramp 0.15 °C to 90 °C, 90 °C for 30 minutes, 20 psi, sr: 35:1)



Racemic **75** **75** from reaction product

Peak #	RetTime [min]	Type	Width [min]	Area [pA*s]	Height [pA]	Area %
1	156.344	MF	0.6451	18.14260	4.68757e-1	3.39406
2	157.545	FM	1.8869	516.39673	4.56115	96.60594
Totals :				534.53933	5.02991	

For HNMR and CNMR spectra, see Supporting Information:
H. Le, A. Batten and J. P. Morken *Org. Lett*. **2014**, *16*, 2096.