Chapter 2

Synthesis and Utility of Chiral Allylic Silanes Prepared via Ni-Catalyzed Asymmetric Reductive Cross-Coupling[‡]

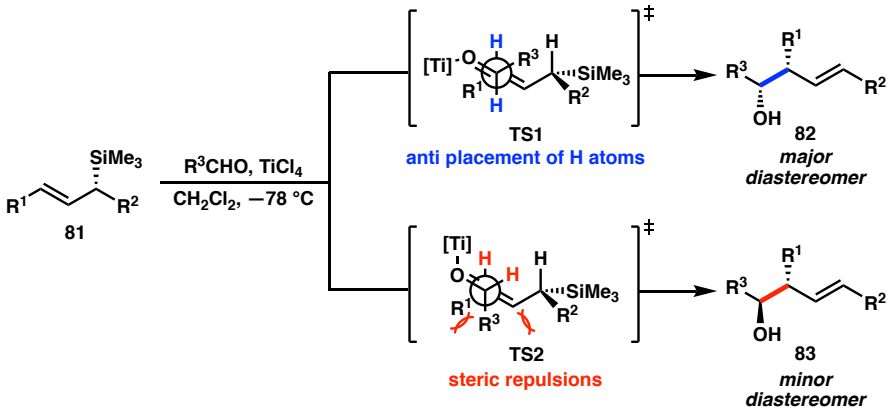
2.1 INTRODUCTION

The synthesis of chiral organosilanes has been an area of recent interest in organic chemistry.[1–3] Organosilanes are not only valuable organic materials with applications in medicinal chemistry[4–6] and materials science,[7] but they are also versatile reagents in organic synthesis.[8–11] In particular, chiral allylic silanes (**81**) engage in highly stereoselective reactions with a variety of electrophiles,[12–18] one example being the Hosomi-Sakurai reaction which is a powerful method for C–C bond constuction (Scheme

[‡] Portions of this chapter have been reproduced from the following communication: Hofstra, J. L.; Cherney, A. H.; Ordner, C. M.; Reisman, S. E. *J. Am. Chem. Soc.* **2018**, *140*, 139, DOI: 10.1021/jacs.7b11707, copyright 2018 American Chemical Society. The research presented in this chapter was completed in collaboration with Alan H. Cherney (graduate student), Ciara M. Ordner (undergraduate student), and Dana Gephart (undergraduate student) in the Reisman group.

2.1).[19–22] The reaction proceeds with excellent diastereoselectivity and transfer of chirality to provide the *syn* homoallylic alcohol (**82**) as the major diastereomer. The *trans* homoallylic alcohol (**83**) is formed as the minor diastereomer. This transformation has not only proven its utility in organic methodology but has also been useful in the total synthesis of natural products.[22–29]

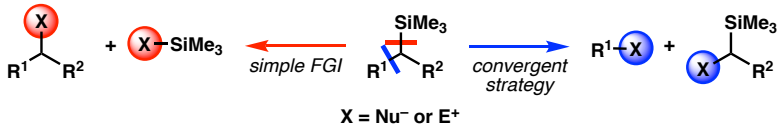
Scheme 2.1 *Open transition state analysis for the Hosomi-Sakurai allylation.*



Despite the utility of chiral allylic silanes, the enantioselective preparation of these reagents often requires multistep sequences or the incorporation of specific functional groups to direct the formation of the C(sp^3)–Si bond. Chiral allylic silanes are most commonly prepared through diastereoselective or stereospecific transformations, which include Claisen rearrangement of vinyl silanes,[30,31] bis-silylation of allylic alcohols,[32] silylene insertion of allylic ethers,[33] and the alkenylation of 1,1-silaboronates.[34,35] In addition, several enantioselective transition metal-catalyzed reactions have been developed, which include the hydrosilylation of dienes,[36,37] the silylboration of allenes,[38] the insertion of metal carbenoids into Si–H bonds,[39,40] and conjugate addition[41,42] and allylic substitution[43] reactions. Notably, while metal-catalyzed cross-coupling methods for

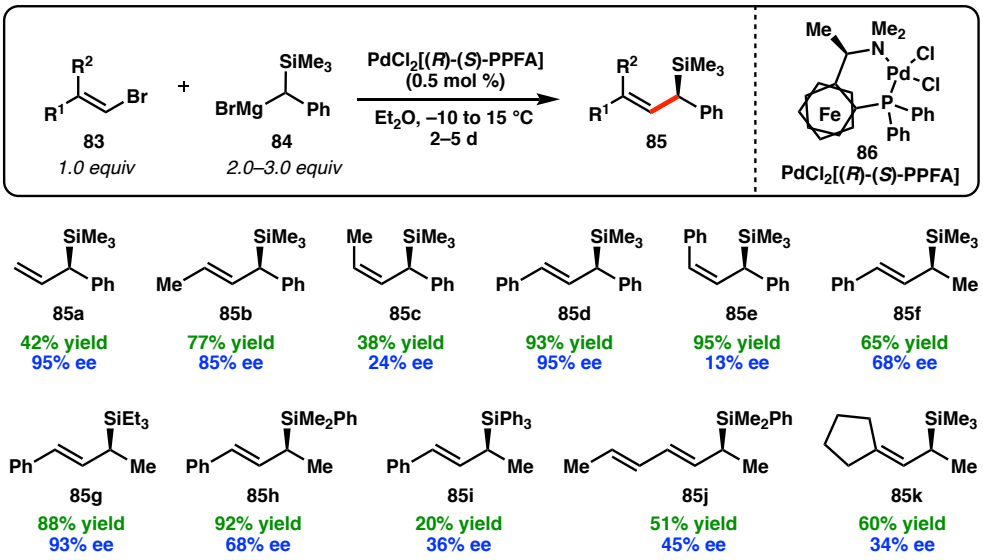
C–Si bond formation have been developed in the racemic sense which allows straight-forward functional group interconversions (FGI), the ability to access chiral stereocenters through C–Si bond formation has yet to be envisioned.[44–49] In contrast, the use of Si-containing nucleophiles or electrophiles in asymmetric transition metal-catalyzed cross-coupling, in which the critical silicon-bearing C(sp^3)-hybridized stereogenic center is established in the C–C bond forming step, represents an alternative and highly modular approach to synthesize chiral allylic silanes (Figure 2.1).

Figure 2.1 *Disconnections to prepare alkyl silanes via cross-coupling.*



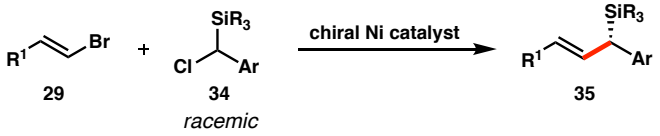
Indeed, the first synthesis of an enantioenriched chiral allylic silane was the Pd-catalyzed asymmetric cross-coupling between α-(trimethylsilyl)benzylmagnesium bromide (**84**) and alkenyl bromides (**83**) reported by Kumada, Hayashi, and coworkers in 1982; these results were followed up with a subsequent study in 1986 (Figure 2.2).[19,21] A variety of alkenyl bromides were evaluated, providing chiral allylic silane products containing alkyl and phenyl substituents (**85a**–**k**). While *Z*-alkenyl and cyclic alkenyl bromides (**85c**, **85e**, and **85k**) successfully provided the desired products, the ee was diminished compared to the use of *E*-alkenyl bromides. Additionally, the identity of the silane was critical to obtaining high ee: $SiEt_3$ > $SiMe_3$ = $SiMe_2Ph$ > $SiPh_3$ (**85g**, **85h**, **85f**, and **85i**). This method, however, employs Grignard reagents as coupling partners which are not stable to long-term storage and decrease the functional group compatibility of the reaction.

Figure 2.2 *Scope of Kumada's cross-coupling to synthesize chiral allyl silanes.*



We envisioned that a Ni-catalyzed asymmetric reductive alkenylation would address the limitation of reagent stability and functional group compatibility, as the required (chlorobenzyl)silanes (**34**) are bench stable compounds and reductive cross-coupling reactions typically exhibit good functional group tolerance (Scheme 2.2).[50,51] Thus, a Ni-catalyzed reductive alkenylation could provide chiral allylic silanes that are not readily accessible by other methods. Herein we describe a Ni-catalyzed asymmetric reductive cross-coupling to directly prepare enantioenriched allylic silanes (**36**) from simple building blocks (**29** and **34**). The resulting chiral allylic silanes are shown to undergo a variety of post-coupling transformations that proceed with high levels of chirality transfer.

Scheme 2.2 *Ni-catalyzed reductive cross-coupling to synthesize chiral allyl silanes.*

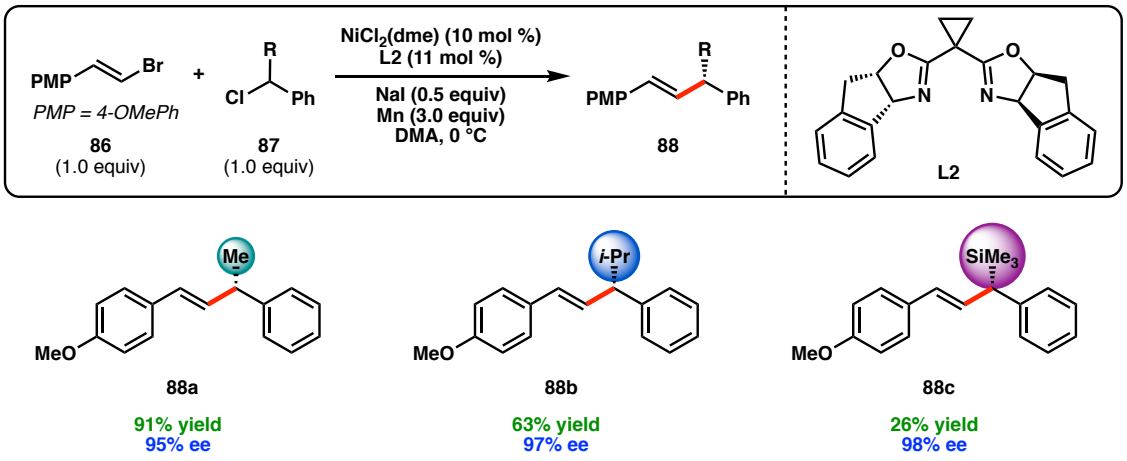


2.2 REACTION OPTIMIZATION EXPAND

2.2.1 Initial Reaction Hit

Our investigations began with the coupling between (*E*)-1-(2-bromovinyl)-4-methoxybenzene (**86**) and (chloro(phenyl)methyl)trimethylsilane (**87**) using $NiCl_2$(dme) and chiral bis(oxazoline) ligand **L2**, which was optimal in our previously developed enantioselective reductive alkenylation reaction (Figure 2.2).[50] When the reaction was conducted at 0 °C with *N,N*-dimethylacetamide (DMA) as the solvent, allylic silane **88c** was formed in a low amount (26% yield) but with a high level of enantioselectivity (98% ee). We hypothesized that the presence of the bulky trimethylsilyl group impeded the oxidative addition of **87** to the Ni catalyst. Indeed, a decrease in product yield was observed when the α-benzyl substituent increased in size (R = Me > *i*-Pr > $SiMe_3$). Evaluation of the reaction profile by ^{1}H NMR revealed full consumption of **87** and formation of benzyl homocoupling product as the major side product; alkenyl bromide **86** was recovered with minimal conversion to homocoupled diene. Although the yield of the cross-coupling

Figure 2.3 *Ni-catalyzed cross-coupling with various benzylic chlorides.*

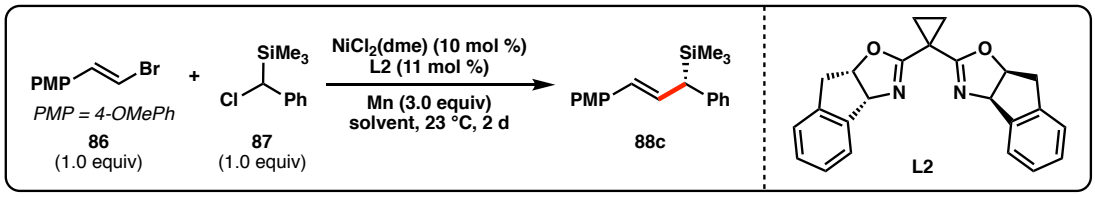


transformation remained to be optimized, the use of chiral bis(oxazoline) ligand **L2** showed remarkable enantioselectivity and was thus retained throughout the duration of reaction optimization. Optimization commenced to discover reaction conditions that mitigate benzyl homocoupling product to afford higher yields of the cross-coupled product (**88c**).

2.2.2 Solvents

A variety of solvents were evaluated in the cross-coupling reaction (Table 2.1) at room temperature (23 °C) in the absence of NaI. Amide solvents such as DMA and *N*-methyl-2-pyrrolidone (NMP) provided **88c** in comparable yields and enantioselectivities (entries 1–2). Dimethyl formamide (DMF) was also found to be a competent solvent in the reaction (entry 3), however both *N*,*N*′-dimethylpropyleneurea (DMPU) and tetrahydrofuran (THF) provided no product (entries 4–5). Further optimization studies were conducted in NMP as the solvent provided **88c** in the highest yield.

Table 2.1. *Evaluation of solvents.*



Entry	Solvent	yield (%)	ee (%)
1	DMA	20	94
2	NMP	23	94
3	DMF	12	90
4	DMPU	0	—
5	THF	0	—

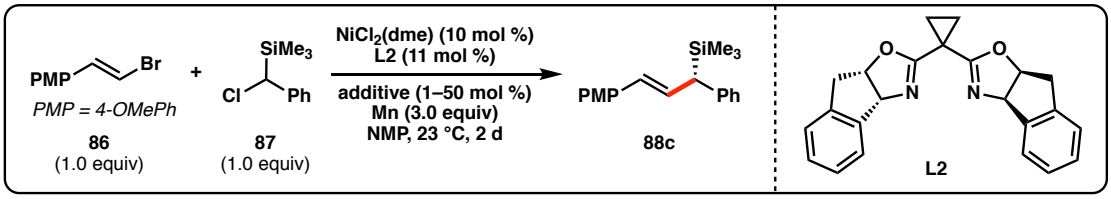
2.2.3 Additives

A variety of additives were then evaluated (Table 2.2). While NaI proved to be an effective additive in our previous alkenylation reaction,[50] possibly through the formation

of reactive alkenyl iodide species, the use of NaI in the synthesis of **88c** did not appreciably improve the reaction yield (entry 2). However, the addition of cobalt(II) phthalocyanine (CoPc), a co-catalyst that also enables the Ni-catalyzed cross-coupling of benzyl mesylates by facilitating alkyl radical generation,[52] was found to significantly improve the yield of **88c** (entry 3). Kinetic studies by Kishi and coworkers found the addition of CoPc in Cr- and Fe-mediated haloallylations of aldehydes increased the reaction rate through the CoPc-mediated formation of catalytically active M-Br species.[53] When similar kinetic studies were conducted on the formation of **88c**, the reaction rate was instead found to decrease upon addition of CoPc. Given these results, we hypothesize that CoPc is used to mitigate benzyl homocoupling formation by sequestering reactive benzyl radical intermediates. This could result in an overall decrease in the rate of consumption of **87**. Therefore the addition of CoPc may be help moderate a mismatch in the rate of oxidative addition between the two electrophiles.

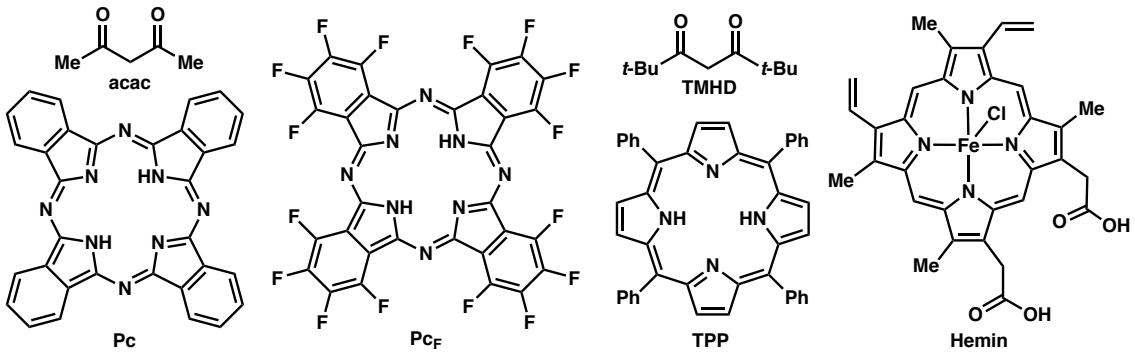
Other Co-containing co-catalysts were also evaluated. Interestingly, the perfluorinated CoPc co-catalyst ($CoPc_F$) did not improve the reaction (entry 4). A variety of other Co sources were also evaluated, many of which concomitantly diminished the ee and the reaction yield of **88c** (entries 5–10). A screen of Fe phthalocyanine and porphyrin co-catalysts were evaluated (entries 11–13), and both Fe(II)Pc and Fe(III)PcCl were found to improve the yield of **88c**. The use of $Fe(TMHD)_3$ provided **88c** in an essentially racemic form (entry 14). Taken together, it is likely that the co-catalyst phthalocyanine scaffold plays a more important role in improving the reaction yield compared to the identity of the coordinated metal center (Co vs. Fe).

Table 2.2. *Evaluation of Co and Fe co-catalysts.*



Entry	Additive	yield (%)	ee (%)
1	—	21	93
2	NaI (50 mol %)	24	94
3	CoPc (1 mol %)	38	96
4	$CoPc_F$ (1 mol %)	23	94
5	$CoCl_2$ (5 mol %)	3	57
6	$CoBr_2$ (5 mol %)	14	86
7	CoI_2 (5 mol %)	17	85

Entry	Additive	yield (%)	ee (%)
8	$Co(PPh_3)_2Cl_2$ (1 mol %)	7	31
9	$Co(acac)_2$ (1 mol%)	12	82
10	CoTPP (1 mol %)	17	88
11	Fe(II)Pc (1 mol %)	28	95
12	Fe(III)PcCl (1 mol %)	33	95
13	Hemin (1 mol %)	17	93
14	$Fe(TMHD)_3$ (1 mol %)	11	6

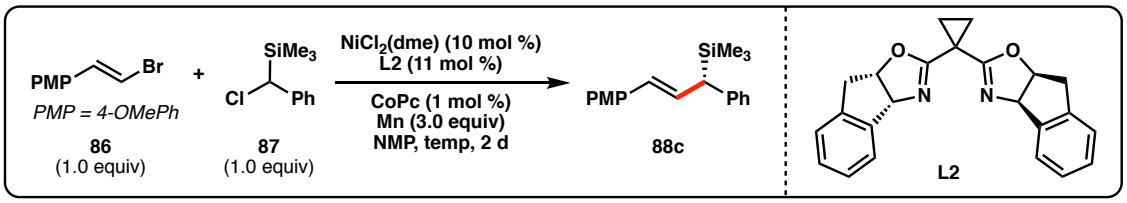


2.2.4 Temperature

In order to maximize our efforts to improve the yield of this transformation, we turned to the use of the Freeslate Core Module system housed within the Caltech Center for Catalysis and Chemical Synthesis. This equipment contained temperature regulated cold wells for reactions to be run at a variety of cryogenic temperatures while providing discrete rotary stirrers for each sample vial, a necessity to promote consistent stirring of heterogeneous reaction mixtures. During the course of reaction optimization, we discovered that decreasing the temperature improved the reaction yield (Table 2.3, entries 1–3), however achieving full conversion was inconsistent when conducted at 0 °C.

Therefore, in order to ensure complete conversion, the reaction was conducted at 5 °C which consistently provided full conversion for reactions run in the Freeslate system as well as in a benchtop cryocool system.

Table 2.3. *Evaluation of temperature.*

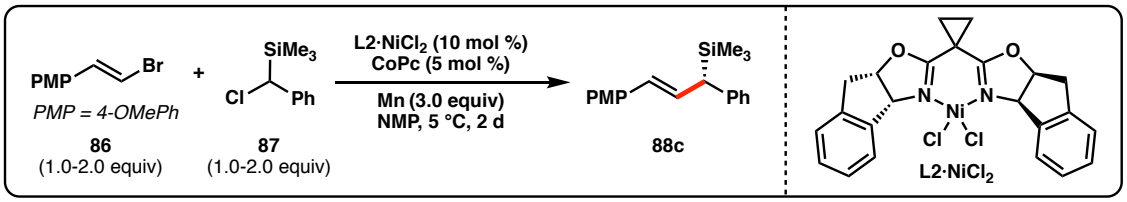


Entry	Temp	yield (%)	ee (%)
1	23 °C	33	96
2	10 °C	46	96
3	0 °C	58	94

2.2.5 Electrophile Equivalents

The electrophile ratio was then evaluated (Table 2.4) with the precomplexed **L2**·$NiCl_2$. The yield of **88c** increased when an excess of either electrophile was used, however excess alkenyl bromide improved the yield most significantly and without loss of enantioselectivity. In some cases, the use of 1.5 equivalents alkenyl bromide was sufficient to improve the reaction, however the use of 2.0 equivalents alkenyl bromide proved most

Table 2.4. *Evaluation of electrophile equivalents.*



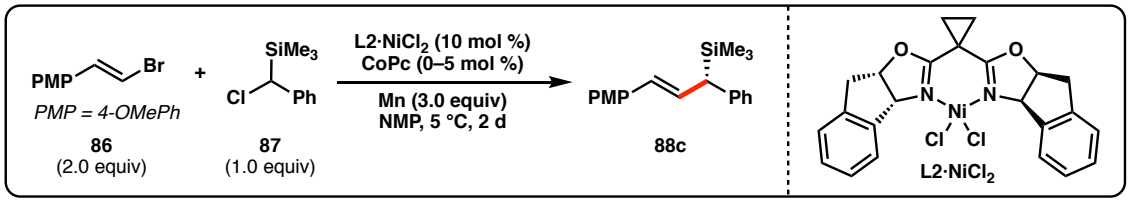
Entry	86 (equiv)	87 (equiv)	yield (%)	ee (%)
1	1.0	2.0	62	91
2	1.0	1.0	51	96
3	2.0	1.0	70	97

robust across a range of substrates (*vide infra*). Similarly, the use of the precomplex **L2**·$NiCl_2$ in place of $NiCl_2$(dme) and **L2** also proved most robust, particularly for low yielding substrates.

2.2.6 CoPc Loading

Evaluation of CoPc loading revealed that the yield of **88c** improved when 3 mol % CoPc was used, and no further increase was observed with 5 mol % or 10 mol % CoPc (Table 2.5, entries 2–5). The optimal amount of CoPc catalyst likely lies between 1 mol % and 3 mol % loading, however low loadings were difficult to weigh on small scale. The use of 5 mol % CoPc, which provided **88c** in 70% yield and 97% ee, was used to evaluate the reaction scope.

Table 2.5. *Evaluation of CoPc loading.*



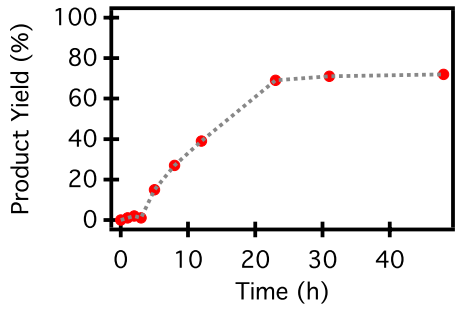
Entry	CoPc (mol %)	yield (%)	ee (%)
1	0	20	96
2	1	56	97
3	3	68	97
4	5	70	97
5	10	69	96

2.2.7 Reaction Time

While our previously developed alkenylation reaction was conducted for 6 hours at 0 °C,[50] the cross-coupling between **86** and **87** shows low conversion after 6 hours at 5 °C due to a lengthy induction period. We typically envision the induction period to be

due to the heterogeneous reduction of Ni(II) to the active nickel catalyst, possibly a Ni(0) species. The yield of **88c** was monitored for 2 days, which revealed that maximum conversion is reached after 24 hours (Figure 2.4). The yield of **88c** is then maintained between 24–48 hours, which demonstrates that no decomposition of **88c** occurs under the reaction conditions. In order to ensure full conversion during substrate scope evaluation, the cross-coupling reaction time was set for a total of 48 hours.

Figure 2.4 *Evaluation of reaction time.*

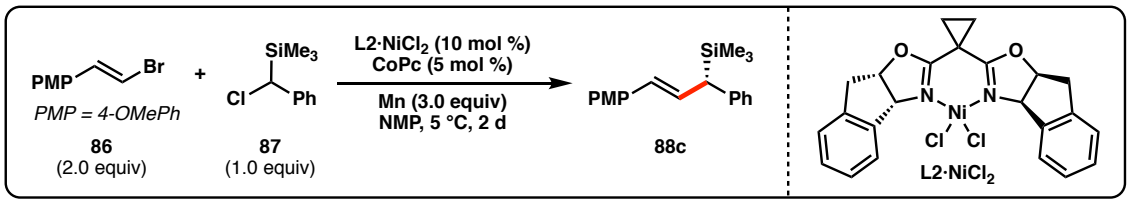


2.2.8 Optimization Summary and Controls

In summary, the cross-coupling between **86** and **87** was improved from our previous alkenylation conditions due to: 1) raising the temperature to 5 °C, 2) running the reaction for 2 days, 3) the addition of 5 mol % CoPc, and 4) increasing the alkenyl bromide to 2.0 equivalents. Control experiments confirmed that $NiCl_2$(dme), ligand, and Mn are all required to form **88c** (Table 2.6, entries 1–4), and other reductants such as Zn and tetrakis(*N*,*N*-dimethylamino)ethylene (TDAE) are deleterious to the yield and enantioselectivity (entries 5–6). While TDAE did afford 39% yield of **88c**, it is formed in only 2% ee. The cross-coupling of **86** and **87** with TDAE in the absence of CoPc shows no conversion (entry 7), indicating that the cross-coupling may be occurring on a reduced

CoPc complex when TDAE is used. The cross-coupling reactions are initially a deep blue upon addition of CoPc; however, upon reaction completion, the solution is a dark green color, indicating reduced CoPc.

Table 2.6. *Control experiments and evaluation of other reductants.*

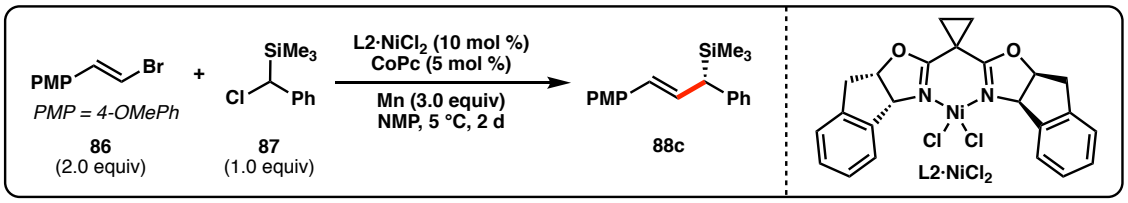


Entry	Deviation from Standard Conditions	yield (%)	ee (%)
1	—	70	97
2	no Mn	0	—
3	L2 (10 mol %), no L2·$NiCl_2$	0	—
4	$NiCl_2$(dme) (10 mol %), no L2·$NiCl_2$	13	—
5	Zn instead of Mn	22	85
6	TDAE instead of Mn	39	2
7	TDAE instead of Mn, no CoPc	0	—

2.2.9 Scalability

With the optimized conditions in hand, the scalability was investigated (Table 2.7). We were pleased to find that the cross-coupling could be set up in a variety of different

Table 2.7. *Evaluation of reaction scalability.*



Entry	Scale (mmol)	Isolated Mass	Reaction Vessel	Setup	Cooling	yield (%)	ee (%)
1	0.2	42 mg	8 mL vial	glovebox	Freeslate	71	95
2	0.5	107 mg	20 mL vial	glovebox	Freeslate	72	96
3	0.5	104 mg	20 mL vial	glovebox	cryocool	70	98
4	0.5	114 mg	10 mL flask	glovebox	cryocool	77	97
5	1.0	211 mg	15 mL flask	bench top	cryocool	71	98
6	6.0	1.31 g	100 mL flask	glovebox	cryocool	74	97

glass containers and be cooled with a traditional laboratory cryocool (entries 3–5). The reaction could also be run directly on the benchtop using standard Schlenk techniques, alleviating the need for a glovebox (entry 5). Finally, we found that the reaction could be run on gram scale, providing an isolated 1.3 g of **88c** in 74% yield and 97% ee (entry 6).

2.2.10 Chiral Ligands

A variety of other chiral ligands were evaluated for the cross-coupling between **86** and **87**, either at room temperature with 1 mol % CoPc (Figure 2.5) or under the optimized reaction conditions (Figure 2.6). Although chiral BOX ligand **L6** provided **88c** in excellent enantioselectivity (90% ee) and in higher yield compared to **L2** at room temperature, upon cooling the reaction to 5 °C, **L2** provided a higher yield of **88c** compared to **L6**. Substitution at the *para* positon on the benzylic arene (**L7**) did not affect the ee of **88c**, however altering the cyclic linker to a cyclobutane (**L5**) or adding methyl groups to the

Figure 2.5 *Evaluation of chiral bidentate ligands at room temperature.*

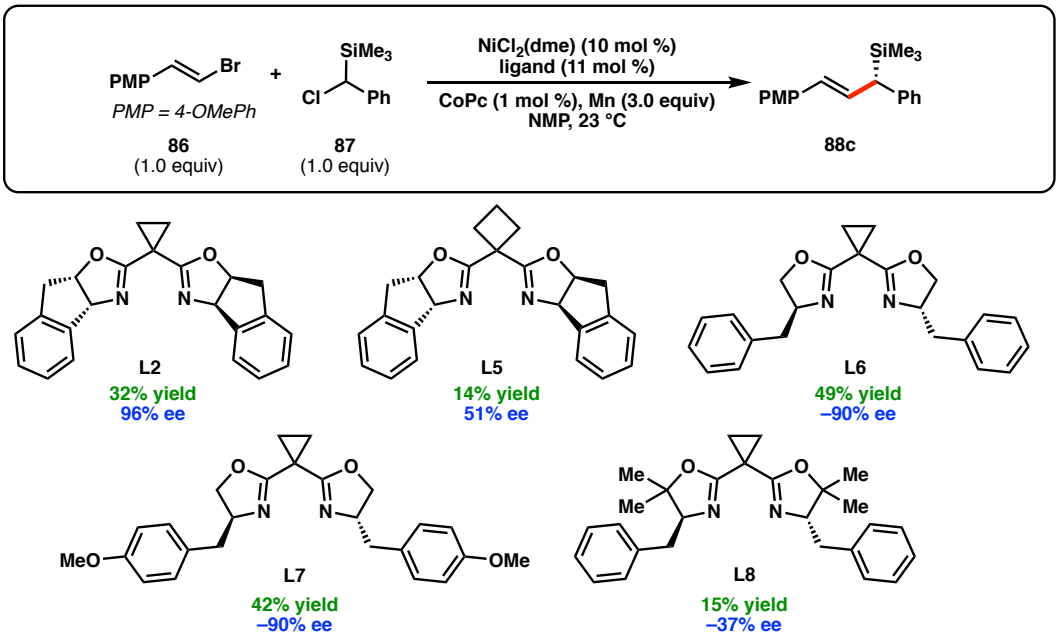
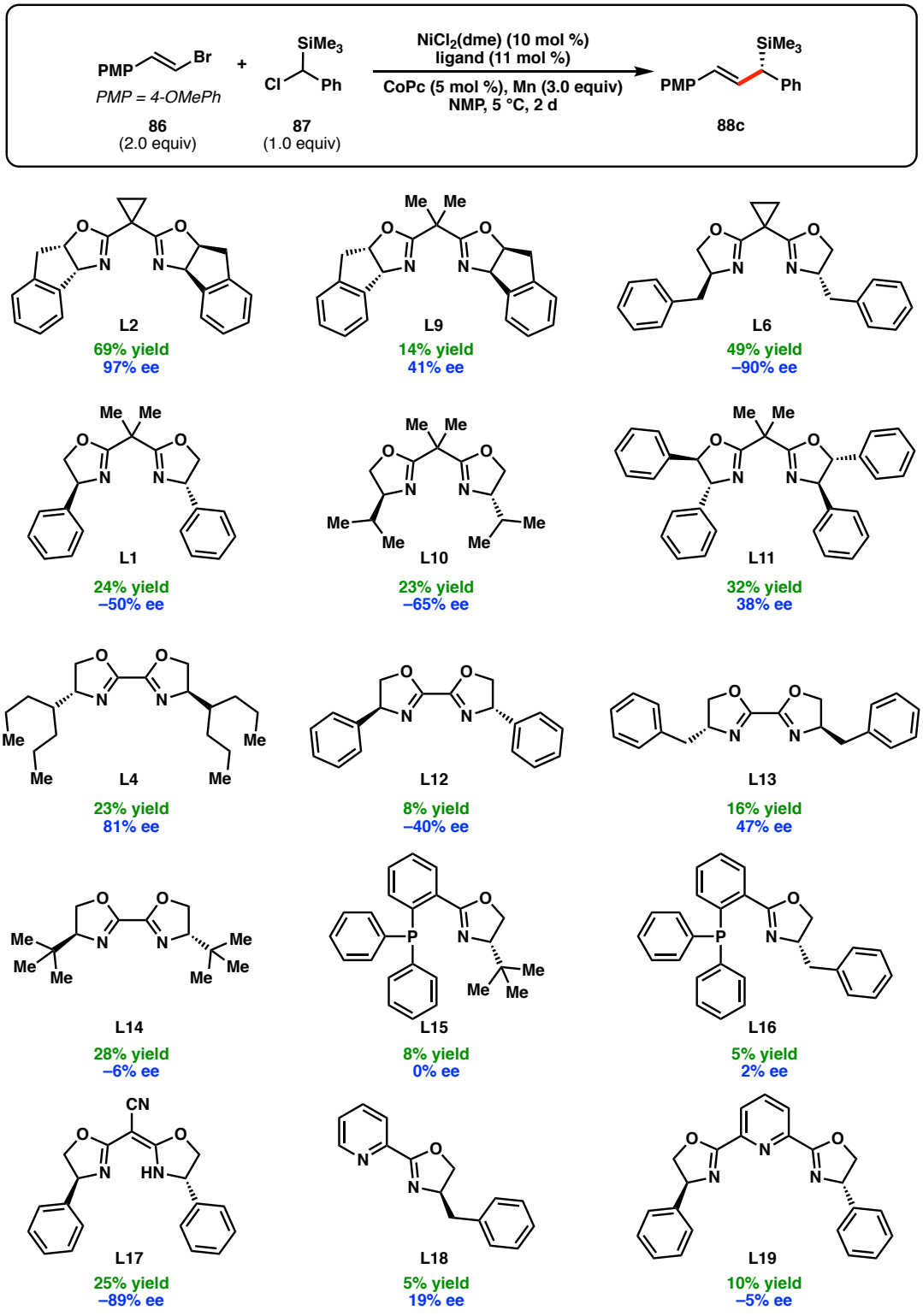


Figure 2.6 *Evaluation of chiral bidentate ligands at low temperature.*



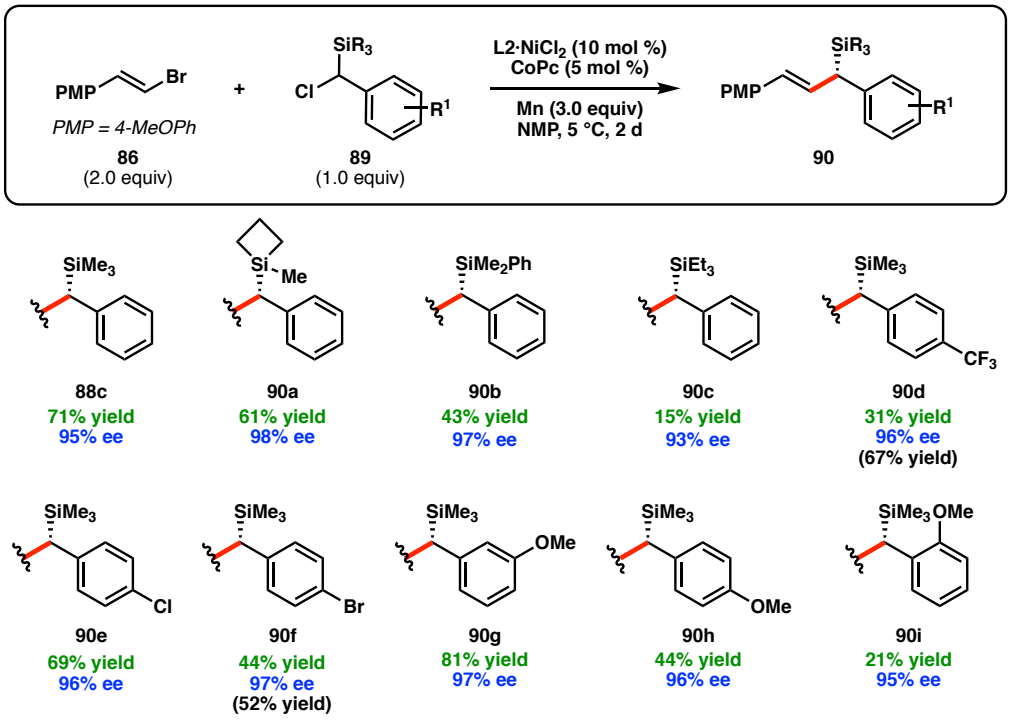
oxazoline (**L8**) diminished the ee. Taken together, these results suggest the bite angle of the oxazoline may contribute important factors in imparting enantioselectivity to **88c**.

A series of other ligand scaffolds were evaluated at 5 °C, and the desired allylic silane was also formed in excellent enantioselectivity when chiral BOX ligand **L6**, BiOx ligand **L4**, and CyanoBOX ligand **L17** were used (90%, 81%, and –89% ee, respectively) (Figure 2.6). Although these ligands provide **88c** in diminished yield, it is worthy to note other ligand scaffolds can be used to access **88c** with good ee. Other ligand scaffolds such as PHOX (**L15**, **L17**), PyOX (**L18**), and PyBOX (**L19**) do not perform well and provide **88c** in low yield.

2.3 SUBSTRATE SCOPE

With the optimized conditions in hand, the scope of the chlorobenzyl silane was investigated (Figure 2.6). Whereas strained silacyclobutane[54] **90a** was prepared in good yield and excellent ee, the corresponding triethylsilane **90c** was formed in poor yield, presumably due to increased steric encumbrance at Si. The dimethylphenyl silane **90b** could also be prepared, albeit in reduced yield. Substrates bearing either electron-withdrawing or electron-donating groups on the arene cross-coupled with universally high ee; however, in some cases the yield was diminished due to instability of the products (**90d**, **90f**). In these cases, special quenching protocols at low temperature were necessary to prevent product decomposition upon workup. While *m*-methoxy substitution provided **90g** in 81% yield, *p*-methoxy and *o*-methoxy substitution significantly decreased the yield of the cross-coupling products (**90h**, **90i**).

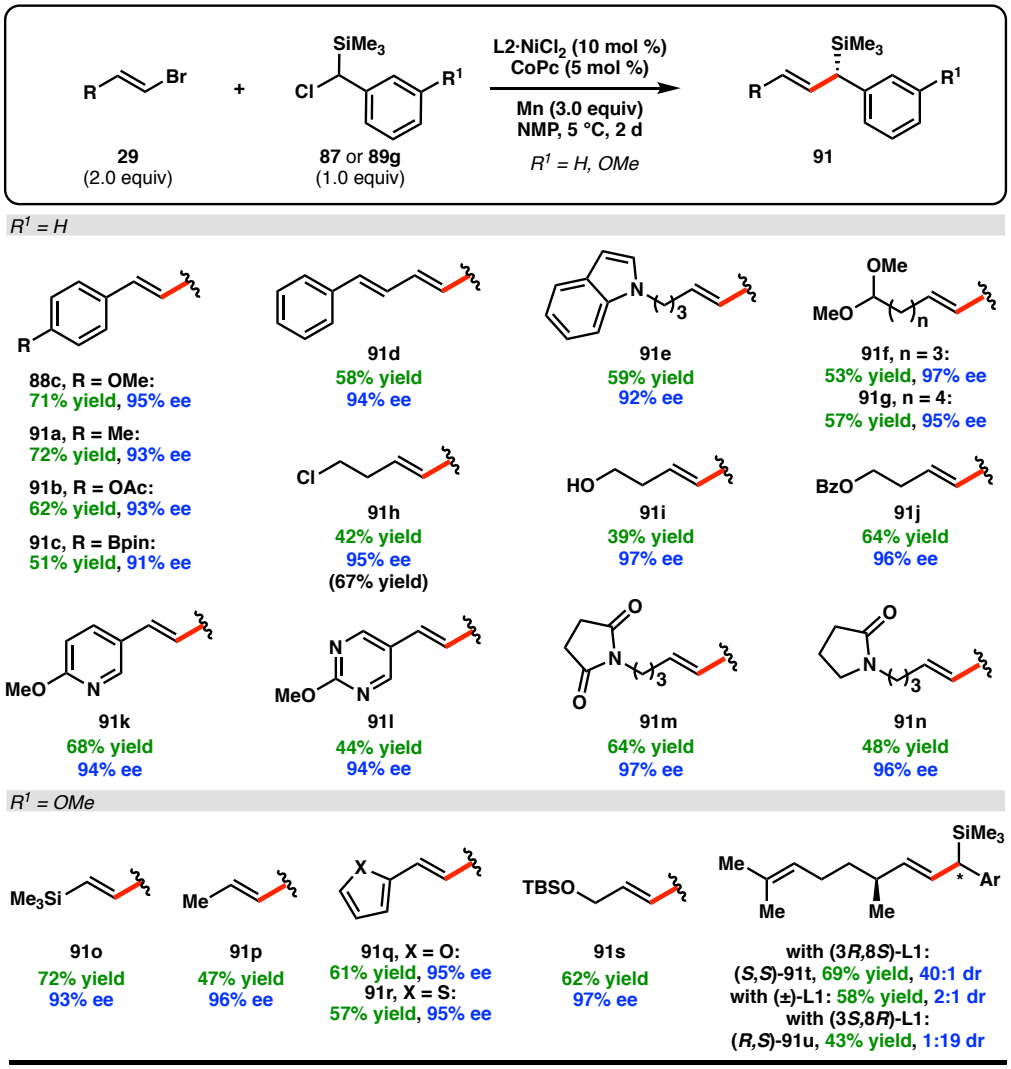
Figure 2.7 *Evaluation of chlorobenzyl silane scope.*



Reactions are conducted on 0.2 mmol scale under N_2. Isolated yields are provided; ee is determined by SFC using a chiral stationary phase. NMR yields of **90d** and **90f** versus an internal standard are provided in parentheses.

The reaction tolerates a diverse array of functional groups on the alkenyl bromide coupling partner (Figure 2.7), including aryl boronates (**91c**), esters (**91b**, **91j**), imides (**91m**), amides (**91n**), alkenyl silanes (**91o**), and alkyl halides (**91h**). For non-polar alkenyl bromide substrates, *m*-methoxy chlorobenzyl silane **89g** was used as the coupling partner to facilitate product purification (**91o**–**91u**). A number of alkyl-substituted alkenyl bromides performed comparably to styrenyl bromides. By changing which enantiomer of **L2**·$NiCl_2$ is employed, diastereomeric polyenes **90t** and **90u** were prepared, although the yield is decreased with the mismatched (3*S*,8*R*)-**L2**·$NiCl_2$ catalyst. Finally, alkenyl bromides bearing furan (**91q**), thiophene (**91r**), pyridine (**91k**), pyrimidine (**91l**), and indole (**91e**) heterocycles could be utilized, giving the corresponding allylic silanes in high ee.

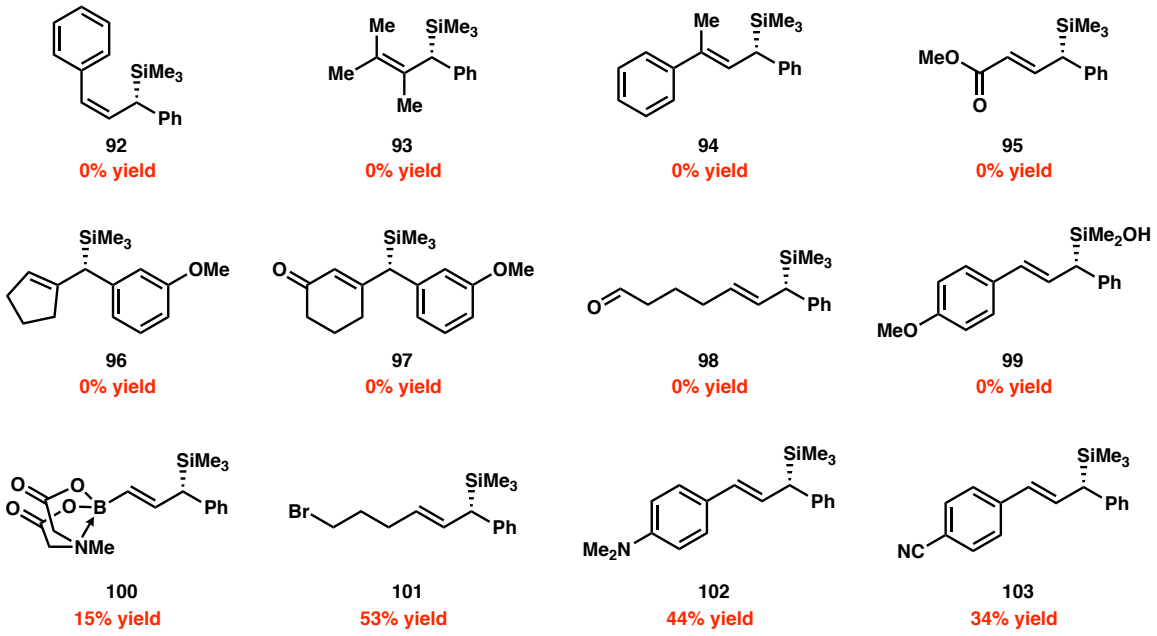
Figure 2.8 *Evaluation of alkenyl bromide scope.*



Reactions are conducted on 0.2 mmol scale under N_2. Isolated yields are provided; ee is determined by SFC or HPLC using a chiral stationary phase. NMR yield of **91h** versus an internal standard is provided in parentheses.

While a number of functional groups are tolerated under these conditions, geometric limitations do exist (Figure 2.9). For example, *Z*-alkenes (**92**) and tri- (**94**, **95**) and tetra-substituted (**93**) alkenyl bromides failed to react to produce the desired coupling products. Activated alkenyl halides (**95**, **97**) also fail in the reaction. The use of chlorobenzyl silane containing a free Si–OH group did not provide the desired product

Figure 2.9 *Limitations on the substrate scope.*

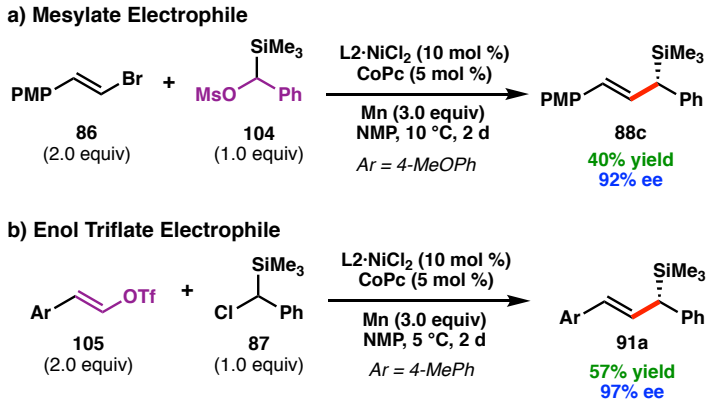


(**99**); rather, the cross-coupled desilylated product was obtained as a mixture of alkene regioisomers. Aldehyde functional groups (**98**) were not tolerated under the reaction conditions, however other functional groups such as MIDA boronates (**100**), alkyl bromides (**101**), dimethyl anilines (**102**), and nitriles (**103**) provided products albeit in low yields.

Although halide electrophiles were the primary focus of this study, oxygen-based electrophiles were also evaluated. We were pleased to find that mesylate **104** provided **88c** in 40% yield and 92% ee when conducted at 10 °C. The slight increase in temperature helped increase conversion of **104** compared to the reaction being run at 5 °C. However, starting material still remained in the reaction after 2 days, which contributed to the lower yield of **88c** (Scheme 2.3a). Attempts to improve the yield with excess **86** or upon addition of NaCl proved unfruitful. When the reaction was run in the absence of CoPc, **88c** was still

formed, albeit in reduced yields; this is in contrast to the cross-coupling of benzylic mesylates and aryl bromides conducted by Weix and coworkers which provide no product in the absence of CoPc. Enol triflate **105** also underwent cross-coupling to afford **91a** in 57% yield, again with excellent enantioselectivity (Scheme 2.3b). Although the yields were modest, we note that these reactions were conducted under conditions developed for the organic halides with minimal re-optimization.

Scheme 2.3 *Reactions with oxygen-based electrophiles.*



2.4 UTILITY OF CHIRAL ALLYLIC SILANES

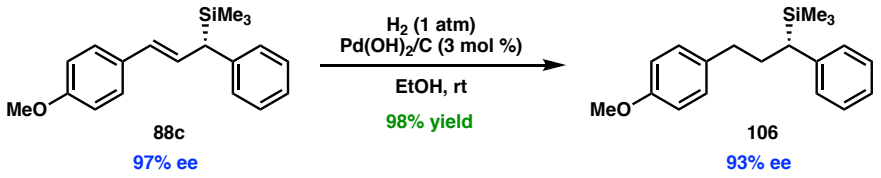
The developed Ni-catalyzed cross-coupling reaction provides rapid access to functionalized chiral allylic silanes that are useful in a variety of synthetic contexts. A few transformations are highlighted in the following section to depict the use of these products as chiral starting materials, particularly for use in the construction of vicinal stereocenters.

2.4.1 Reduction of Allylic Silanes

Chiral alkyl silanes are commonly used as masked alcohols revealed via the Tamao–Fleming oxidation.[55–59] Oestreich and coworkers recently reported an elegant

chiral Ni-catalyzed cross-coupling between α-silyl alkyl iodides and alkyl zinc reagents using a chiral $NiCl_2$·PyBox catalyst generated in situ.[60] One advantage to this method is it does not rely on activated substrates (e.g. benzylic halides) to stabilize potential radical intermediates during the catalytic cycle, however the enantioselectivities of the products are somewhat diminished (60–92% ee). Chiral allylic silanes synthesized via our reductive cross-coupling can be converted into the corresponding alkyl silanes via hydrogenation. To demonstrate this, hydrogenation of **88c** with Pearlman's catalyst in the presence of H_2 provided alkyl silane **106** in 98% yield with only modest erosion of enantioselectivity (Scheme 2.4). The enantiospecificity (es) of this reaction is calculated to be 96% es.

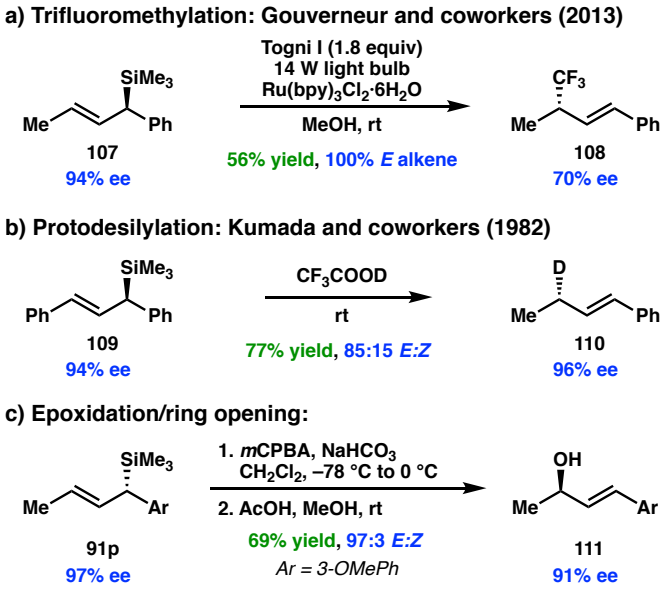
Scheme 2.4 *Hydrogenation of chiral allyl silanes.*



2.4.2 Transposition Reactions

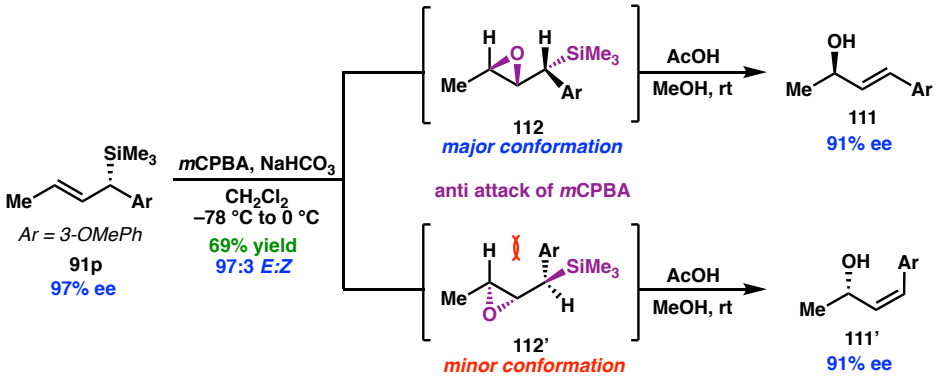
Chiral allylic silanes can also undergo a variety of reactions to transpose the stereocenter and alkene moiety (Scheme 2.5). Gouverneur and coworkers demonstrated that allylic CF_3 products (**108**) can be synthesized from chiral allylic silanes (**107**) via photoredox catalysis with $Ru(bpy)_3Cl_2$ in the presence of Togni's reagent (Scheme 2.5a).[61] The reaction is proposed to proceed through stereospecific trifluoromethyl radical addition to the alkene, followed by elimination of the trimethylsilane. While the reaction proceeds in moderate yield, the stereochemical fidelity, however, is sub-optimal (74% es). In contrast, chiral allylic silanes (**109**) can undergo protodesilylation (Scheme 2.5b) or be

Scheme 2.5 *Transposition reactions of chiral allylic silanes.*



converted to chiral allylic alcohols (**111**) with higher levels of enantiospecificity (Scheme 2.5c). Hayashi and coworkers demonstrated that allylic silanes (**109**) can undergo stereospecific protodesilylation with deuterated acetic acid to form **110** with perfect enantiospecificity (Scheme 2.5b).[62] In a separate report, Hayashi and coworkers showed that epoxidation of the alkene in **91p** with *m*CPBA affords the chiral epoxide, which can undergo acid-catalyzed ring opening to afford the chiral allylic alcohol with only slight

Scheme 2.6 *Stereochemical outcome of chiral allylic silane epoxidation.*

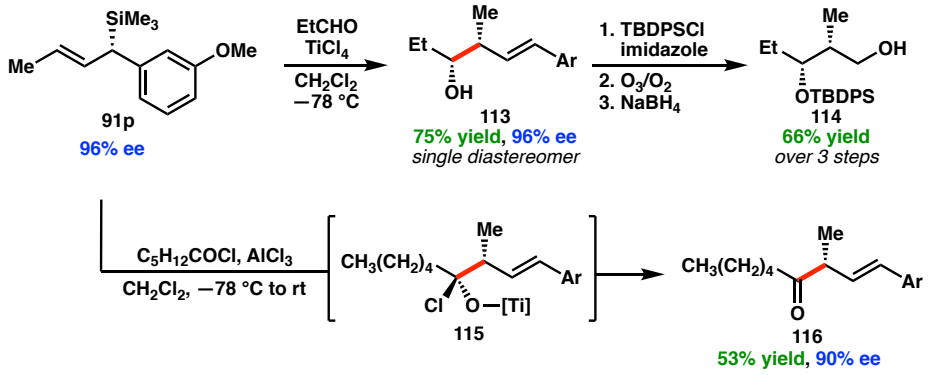


erosion of enantioselectivity. While Hayashi reports obtaining a 98% yield of **111** as an 81:19 mixture of *E*:*Z* isomers with 88% es when Ar = Ph,[63] in our hands, when Ar = 3-OMePh, **111** was obtained in 69% yield and 94% es as a 97:3 mixture of *E*:*Z* alkenes. The *E* and *Z* isomers are generated in opposite enantiomeric series due to anti-attack of *m*CPBA on the major and minor conformations of **112** during the epoxidation reaction (Scheme 2.6), which ultimately requires separation if oxidative cleavage of the alkene is planned.

2.4.3 Hosomi-Sakurai Allylations

Most notably, chiral allylic silanes are known for their ability to participate in Hosomi-Sakurai allylations with a wide variety of electrophiles.[9] These reactions can proceed in either an intermolecular or intramolecular manner to set vicinal stereocenters with excellent transfer of chirality. For example, chiral allylic silane **91p** can undergo an intermolecular Hosomi-Sakurai allylation with propanal and $TiCl_4$ to provide **113** in 75% yield as a single diastereomer and with no erosion of enantioselectivity (Scheme 2.7).[19,20] The resulting alcohol can be subsequently protected as the silyl ether and ozonolytic cleavage of the styrene provides primary alcohol **114** upon reduction with $NaBH_4$. In

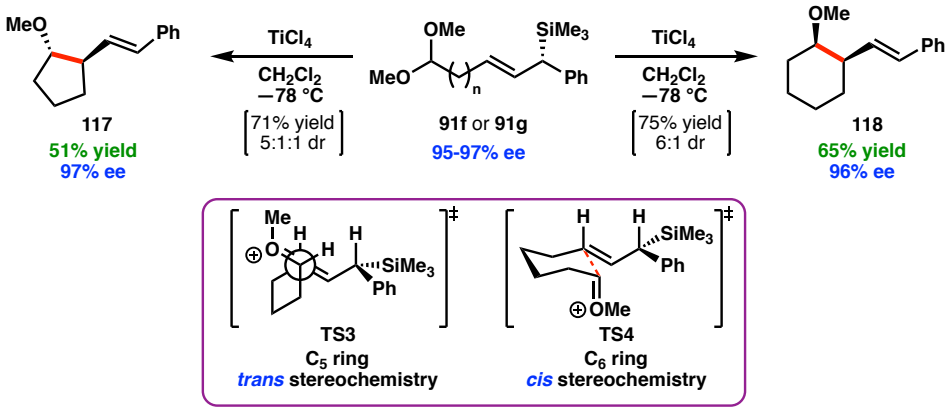
Scheme 2.7 *Intermolecular Hosomi-Sakurai allylations.*



addition, allylation of **91p** with hexanoyl chloride in the presence of $AlCl_3$ directly affords the α-chiral ketone **116** without isomerization into conjugation. This reaction proceeds via displacement of the chloride from intermediate **115**, which leads to the formation of the ketone product.[19,64–68]

Chiral allylic silanes can also be used in intramolecular allylations. For example, allylic silanes **91f** and **91g**, which contain pendant acetals, undergo stereospecific $TiCl_4$-mediated intramolecular cyclization to form the 5- and 6-membered rings **117** and **118**, respectively (Figure 2.10). The observed absolute and relative stereochemistry is consistent with an *anti*-S_E' mode of addition to an oxocarbenium ion through a *syn*-clinal transition state, giving rise to the *trans*-substituted 5-membered ring and the *cis*-substituted 6-membered ring.[69] While these transition states support the stereochemical outcome, it is worthwhile to mention that mechanistic studies by Denmark and coworkers also suggest an S_N2-type mechanism may be consistent with the observed results.[70]

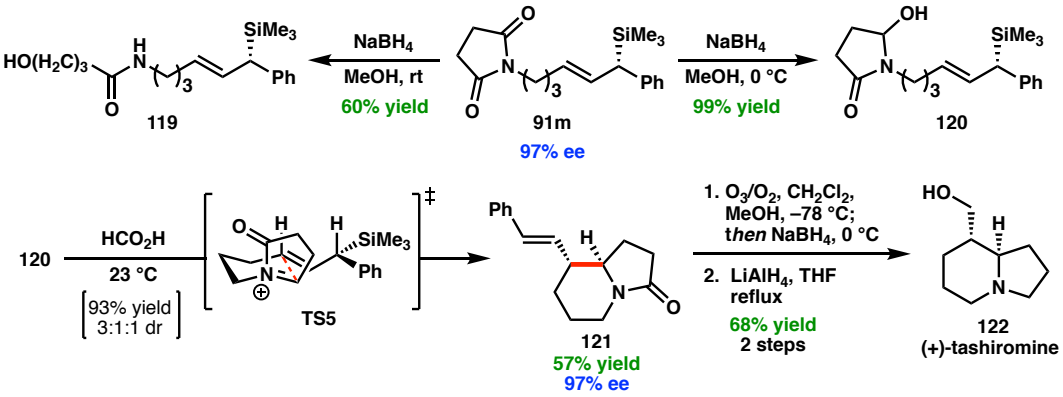
Figure 2.10 *Intramolecular Hosomi-Sakurai allylations.*



The utility of this method was further demonstrated in a concise enantioselective synthesis of (+)-tashiromine (Figure 2.11).[71,72] Sodium borohydride reduction of imide

91m at 0 °C provided aminal **120** in 99% yield as a 1:1 mixture of diastereomers.[73] The reaction temperature was critical for obtaining the desired aminal product; when the reduction was conducted at room temperature, further reduction of **120** afforded the ring-opened product **119**. Exposure of aminal **120** to neat formic acid[74] induced cyclization to form the fused bicycle in a 93% combined yield of a 3:1:1 mixture of isomers. The major isomer **121** was isolated in 57% yield and 97% ee. Finally, ozonolysis of the styrene and reduction of the amide provided (+)-tashiromine (**122**) in 68% yield over two steps.

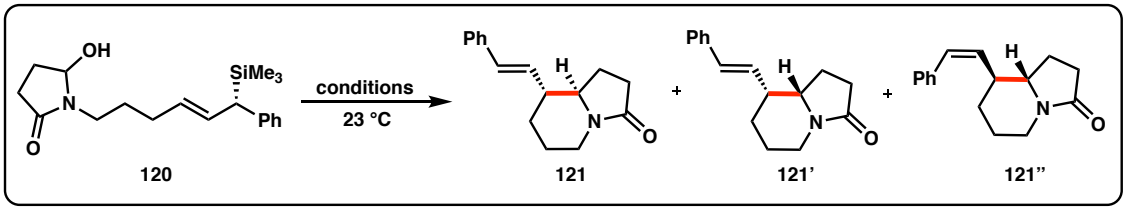
Figure 2.11 *Total synthesis of (+)-tashiromine.*



The selectivity of the acid-catalyzed cyclization of **120** was found to be dependent on the identity of the acid (Table 2.8). When trifluoroacetic acid was added to a solution of **120** in CH_2Cl_2 at room temperature, a 1.0:0.39:0.49 mixture of **121**:**121'**:**121''** was obtained (entry 1), providing the desired product **121** as 53% of the combined isomers. The addition of 4 Å molecular sieves had no effect on this ratio (entry 2). Both $TiCl_4$ and TMSOTf provided a poorer isomeric ratio, affording 44% and 48% of **121** as the major isomer, respectively (entries 3–4). The use of neat formic acid (HCO_2H) provided the best ratio of all acids tested; **121** was obtained as 68% of the total mixture. The absolute and

relative stereochemistry of the minor allylation isomers **121'** and **121''** were assigned based on literature precedent for the related glutarimide analog.[75]

Table 2.8. *Evaluation of acids in the intramolecular allylation of* ***120****.*



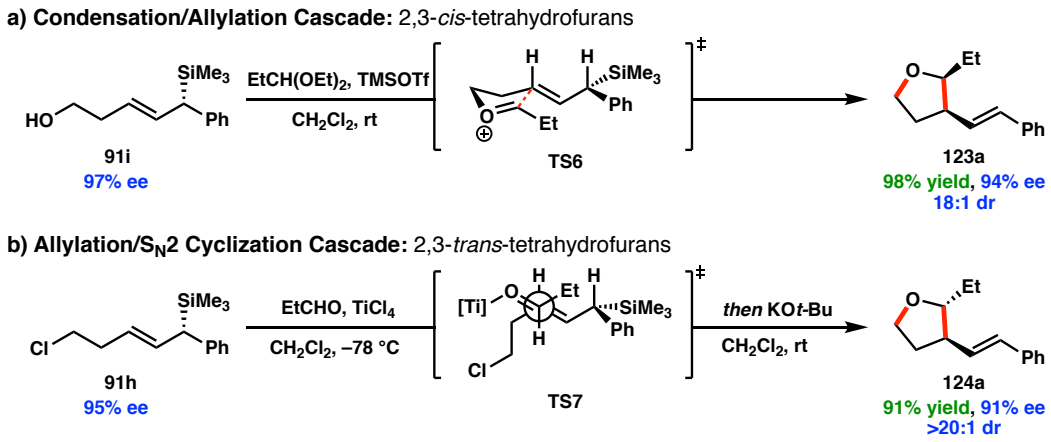
Entry	Conditions	121 :	121' :	121"	121 (%)
1	TFA, CH_2Cl_2	1.0	0.39	0.49	53
2	TFA, 4 Å MS, CH_2Cl_2	1.0	0.37	0.44	55
3	$TiCl_4$, 4 Å MS, CH_2Cl_2	1.0	0.62	0.64	44
4	TMSOTf, CH_2Cl_2	1.0	0.50	0.60	48
5	HCO_2H *(neat)*	1.0	0.30	0.17	68

2.4.4 Synthesis of 2,3-Disubstituted Tetrahydrofurans

Either the 2,3-*cis*- or 2,3-*trans*-disubstituted tetrahydrofurans can be prepared by Lewis acid-mediated cyclizations of alcohol **91i** or chloride **91h**, respectively; both proceed with excellent transfer of chirality (Scheme 2.8). Chiral allylic silane **91i** can undergo a Lewis acid-mediated condensation of acetaldehyde diethyl acetal onto the pendant alcohol to afford **123a**, therefore inducing an intramolecular allylation to set the *cis* stereochemical relationship across the tetrahydrofuran ring (Scheme 2.8a).[76] In contrast, $TiCl_4$-mediated intermolecular Hosomi-Sakurai allylation of **91h** with acetaldehyde proceeds smoothly (Scheme 2.8b). Upon completion, quenching the reaction with water affords the corresponding alcohol; however, addition of a strong base (KO*t*Bu) facilitates removal of Ti from the resulting alkoxide and induces intramolecular S_N2 cyclization to form the

tetrahydrofuran ring (**124a**). The stereochemistry from the intermolecular allylation translates to provide the *trans* stereochemical relationship across the tetrahydrofuran.

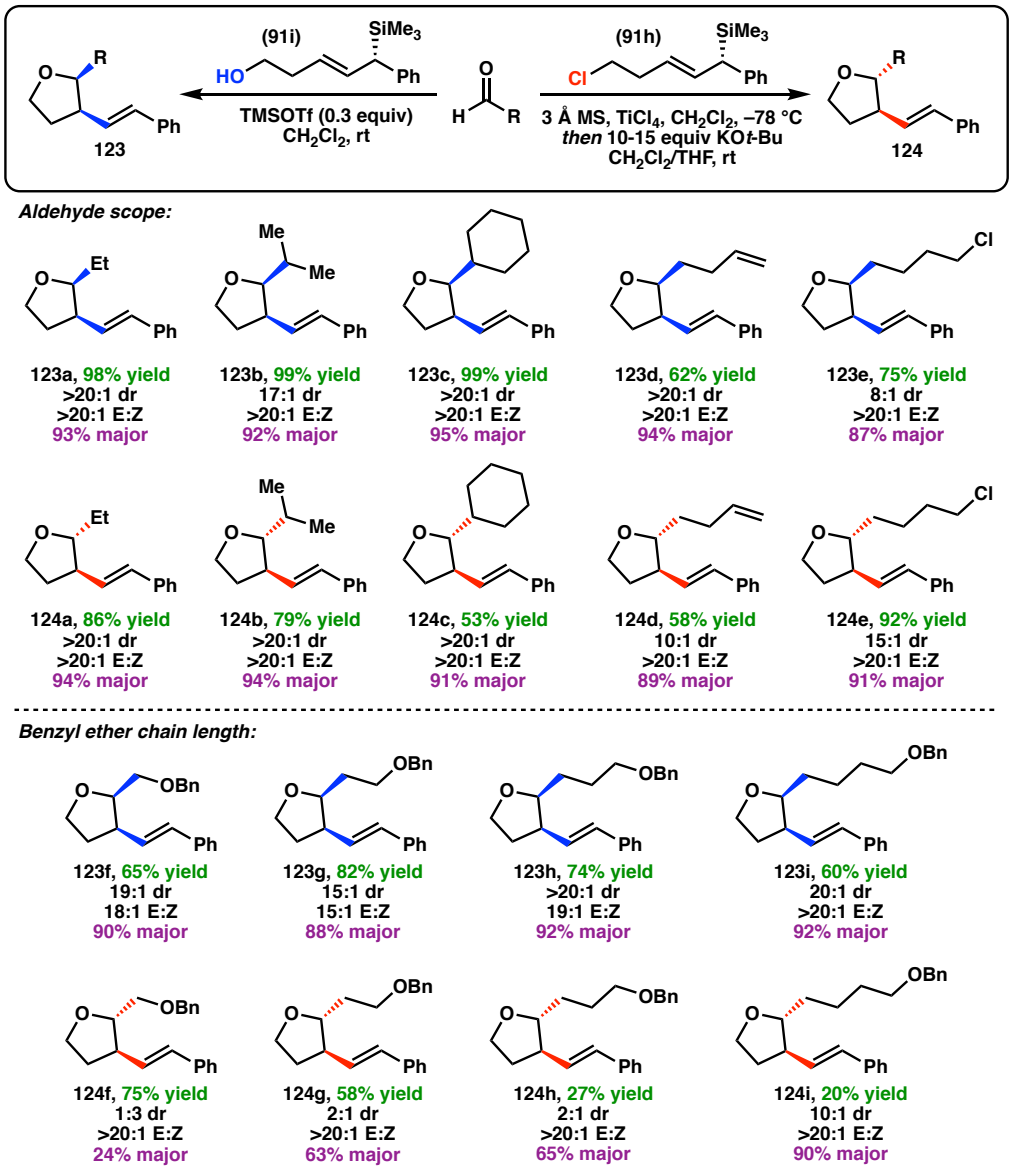
Scheme 2.8 *Synthesis of 2,3-disubstituted tetrahydrofurans.*



A series of aldehydes was then evaluated under these reaction conditions (Figure 2.10). A total of four product isomers are possible in both transformations: 1) *cis* tetrahydrofuran, *E* isomer, 2) *trans* tetrahydrofuran, *E* isomer, 3) *cis* tetrahydrofuran, *Z* isomer, and 4) *cis* tetrahydrofuran, *Z* isomer. Yields are reported for the combined mixture of isomers, and the major isomer as depicted is given as a percentage of the total mixture (representative purity). Excellent diastereoselectivity and *E:Z* ratio of the alkene moiety was observed in most cases, with the exception of decreased dr for **123b**, **123e**, **124d**, and **124e**. Interestingly, tetrahydrofuran **123e** was preferentially formed via S_N2 cyclization to afford the 5-membered heterocycle instead of the 6-membered heterocycle. While alkenes and alkyl chlorides are well-tolerated, the presence of benzyl ethers resulted in diminished dr for the *trans* tetrahydrofurans due to coordination to Ti.[75] While **124g** was formed in a poor 2:1 dr, the major isomer was still obtained as the *trans* product. However, **124f** was formed in a 1:3 ratio of *trans*:*cis*, demonstrating that the proximal benzyl ether can not only

erode dr, but also overturn inherent selectivity. In contrast, benzyl ethers were well-tolerated in the intramolecular allylation to form the *cis* tetrahydrofurans.

Figure 2.12 *Scope of the 2,3-disubstituted tetrahydrofurans.*



2.5 CONCLUSION

In summary, a highly enantioselective Ni-catalyzed cross-coupling reaction has been developed for the preparation of chiral allylic silanes. The reactions proceed under mild conditions and tolerate a variety of functional groups. The enantioenriched allylic silanes undergo several stereospecific transformations with high levels of chirality transfer, which we anticipate will prove useful in an array of synthetic contexts.

2.6 EXPERIMENTAL SECTION

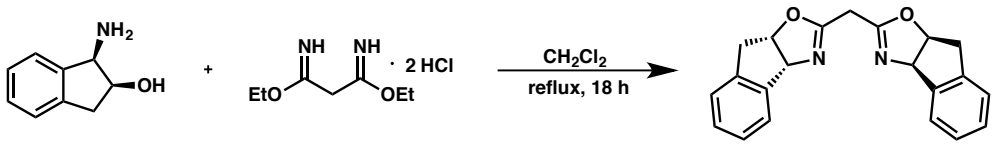
2.6.1 Materials and Methods

Unless otherwise stated, reactions were performed under a N_2 atmosphere using freshly dried solvents. Tetrahydrofuran (THF), diethyl ether (Et_2O), methylene chloride (CH_2Cl_2), toluene (PhMe), hexane, and benzene (C_6H_6) were dried by passing through activated alumina columns. Triethylamine (Et_3N), diisopropylamine (*i*-Pr_2NH), and trimethylsilyl chloride (TMSCl) were distilled over calcium hydride prior to use. Anhydrous *N*,*N*'-dimethylacetamide (DMA) and anhydrous *N*-methylpyrrolidinone (NMP) were purchased from Aldrich and stored under N_2. Manganese powder (–325 mesh, 99.3%) was purchased from Alfa Aesar. Zinc dust (97.5%) was purchased from Strem. Unless otherwise stated, chemicals and reagents were used as received. All reactions were monitored by thin-layer chromatography using EMD/Merck silica gel 60 F254 pre-coated plates (0.25 mm) and were visualized by UV, CAM, or $KMnO_4$ staining. Flash column chromatography was performed as described by Still et al.[77] using silica gel (230-400 mesh, Silicycle) or 10% $AgNO_3$ doped silica gel (+230 mesh, Sigma Aldrich). Purified compounds were dried on

a high vacuum line (0.2 torr) to remove trace solvent. Optical rotations were measured on a Jasco P-2000 polarimeter using a 100 mm path-length cell at 589 nm. ^{1}H and ^{13}C NMR spectra were recorded on a Bruker Avance III HD with Prodigy cryoprobe (at 400 MHz and 101 MHz, respectively), a Varian 400 MR (at 400 MHz and 101 MHz, respectively), or a Varian Inova 500 (at 500 MHz and 126 MHz, respectively). ^{1}H and ^{19}F NMR spectra were also recorded on a Varian Inova 300 (at 300 MHz and 282 MHz, respectively). NMR data is reported relative to internal $CHCl_3$ (^{1}H, $\delta = 7.26$), $CDCl_3$ (^{13}C, $\delta = 77.0$), and C_6F_6 (^{19}F, $\delta = -164.9$). Data for ^{1}H NMR spectra are reported as follows: chemical shift (δ ppm) (multiplicity, coupling constant (Hz), integration). Multiplicity and qualifier abbreviations are as follows: s = singlet, d = doublet, t = triplet, q = quartet, m = multiplet, br = broad. IR spectra were recorded on a Perkin Elmer Paragon 1000 spectrometer and are reported in frequency of absorption (cm^{-1}). Analytical chiral SFC was performed with a Mettler SFC supercritical CO_2 analytical chromatography system (CO_2 = 1450 psi, column temperature = 40 °C) with Chiralcel AD-H, OD-H, AS-H, OB-H, and OJ-H columns (4.6 mm x 25 cm). Analytical chiral HPLC was performed with an Agilent 1100 Series HPLC with a Chiralcel OD-H column (4.6 mm x 25 cm, Daicel Chemical Industries, Ltd.). HRMS were acquired from the Caltech Mass Spectral Facility using fast-atom bombardment (FAB), electrospray ionization (ESI-TOF), or electron impact (EI). X-ray diffraction and elemental analysis (EA) were performed at the Caltech X-ray Crystal Facility.

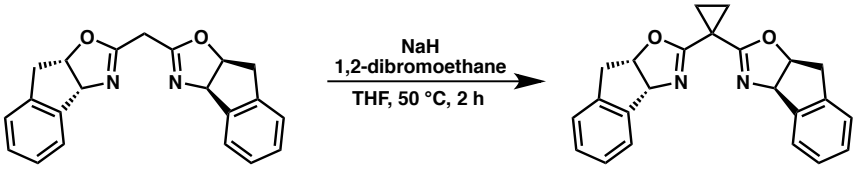
2.6.2 Ni(II) Complex Preparation

Bis((3a*R*,8a*S*)-3a,8a-dihydro-8*H*-indeno[1,2-*d*]oxazol-2-yl)methane (L20)



According to a procedure by Snyder and coworkers,[78] the (*1R*,*2S*)-(+)-cis-1-amino-2-indanol (4.70 g, 31.5 mmol, 2.1 equiv) and diethyl malonimidate dihydrochloride (3.47 g, 15 mmol, 1 equiv) were added to a flame-dried 1 L round bottom flask fitted with a reflux condenser and a magnetic stir bar, and put under an inert atmosphere (N_2). Then CH_2Cl_2 (360 mL) was added and the solution was heated at 45 °C for 18 hours. The reaction was cooled, and then quenched with water (690 mL). The layers were separated, the aqueous layer was extracted with CH_2Cl_2 (4 x 180 mL), and the combined organic layers were dried with $MgSO_4$, filtered, and concentrated. The crude material was purified by recrystallization from cooling hot ethanol to yield 3.30 g (67% yield) of **L20** as a white solid. Spectral data matched those reported in literature.[78]

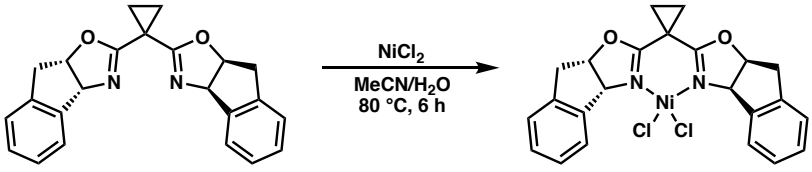
(3a*R*,3a'*R*,8a*S*,8a'*S*)-2,2'-(Cyclopropane-1,1-diyl)bis(3a,8a-dihydro-8*H*-indeno[1,2-*d*]-oxazole) (L2)



Following a procedure by Sibi and coworkers,[79] bis(oxazoline) **L20** (1.65 g, 5.0 mmol, 1 equiv) was added to a flame-dried 200 mL round bottom flask with a magnetic stir bar.

The flask was placed under inert atmosphere (N_2), THF (25 mL) was added, and the solution was cooled to 0 °C. Dry sodium hydride (60 wt % in mineral oil, 601 mg, 15 mmol, 3 equiv) was added in portions. **Note:** Wet NaH resulted in saponification of the oxazoline, which could be removed by column chromatography (silica, 10% MeOH/CH_2Cl_2). The solution was allowed to stir for 30 minutes before 1,2-dibromoethane (517 μL, 6 mmol, 1.2 equiv) was added dropwise over the course of 10 minutes. The reaction was then warmed to 50 °C and stirred for 2 hours. **Note:** Aliquots could be monitored by ^{1}H NMR to ensure complete conversion. The reaction was quenched with aqueous NH_4Cl (25 mL) and extracted with CH_2Cl_2 (2 x 85 mL). The combined organic layers were dried with Na_2SO_4, filtered, and concentrated under reduced pressure. The crude material was purified by recrystallization upon cooling from hot ethanol to yield 1.46 g (82% yield) of **L2** as a light tan solid. Spectral data matched those reported in the literature.[79]

Nickel(II) bis(chloride) (3a*R*,3a'*R*,8a*S*,8a'*S*)-2,2'-(cyclopropane-1,1-diyl)bis(3a,8a-dihydro-8*H*-indeno[1,2-*d*]oxazole) (L2·$NiCl_2$)



Adapted from a procedure by Evans and coworkers.[80] Bis(oxazoline) ligand **L2** (1.07 g, 3.0 mmol, 1 equiv) and anhydrous nickel(II) chloride (390 mg, 3.0 mmol, 1 equiv) were added to a round bottom flask equipped with a magnetic stirring rod and dissolved in a mixture of MeCN (65 mL) and water (0.75 mL). The solution was heated to 80 °C under

an N_2 atmosphere for 6 hours to afford a dark purple solution. The reaction was concentrated under reduced pressure and the obtained solid was dissolved in CH_2Cl_2, filtered through a plug of cotton, dispensed into four 20 mL scintillation vials, and recrystallized by vapor diffusion (CH_2Cl_2/pentane) to afford dark purple crystals suitable for X-ray diffraction. **Notes:** The **L2**·$NiCl_2$ complex can crystallize both as a monomeric species (purple solid, very common) or a trimeric species (orange solid, rare). The monomeric catalyst was used for the entirety of this manuscript, however a control reaction revealed that product **88c** was obtained in comparable yield and ee when the trimeric catalyst was used. To isolate **L2**·$NiCl_2$, the dichloromethane was decanted and the crystals were washed with hexane. The crystals were transferred by spatula to a new vial and crushed to provide a powder. The resulting complex was dried under vacuum to yield 1.3 g (89% yield) of **L2**·$NiCl_2$ as a purple solid. **m.p.** = >300 °C **^{1}H NMR (400 MHz, $CDCl_3$):** δ 94.87 (s, 2H), 47.79 (s, 2H), 20.23 (s, 2H), 11.77 (s, 4H), 11.51 (s, 2H), 10.45 (s, 2H), 5.34 (d, J = 119.5 Hz, 2H), 3.92 (s, 2H), -1.10 (s, 2H). **FTIR (NaCl, thin film, cm^{-1}):** 3611, 3306, 2835, 2214, 1836, 1651, 1479, 1461, 1442, 1367, 1312, 1274, 1247, 1224, 1172, 1154, 1114, 1009, 951, 911, 860, 835. **EA:** Anal. Calc'd. for **L1**·$NiCl_2$, $C_{23}H_{20}Cl_2N_2NiO_2$ (%): C, 56.84; H, 4.15; N, 5.76. Found: C, 56.24; H, 4.14; N, 5.63.

2.6.3 Optimization of Reaction Parameters

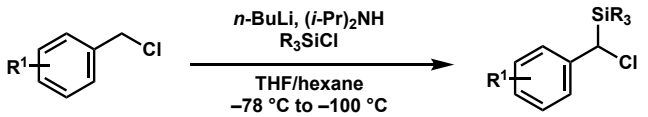
Ligand (0.011 mmol, 0.11 equiv), $NiCl_2$(dme) (0.010 mmol, 0.10 equiv), alkenyl bromide **86** (0.1-0.2 mmol, 1-2 equiv), Mn^0 (0.3 mmol, 3 equiv), and additive (if used, 0.005-0.05 mmol, 0.05-0.5 equiv, as specified) were charged to a vial on the benchtop. In some cases, **L2**·$NiCl_2$ complex (0.010 mmol, 0.10 equiv) was used in place of **L2** and $NiCl_2$(dme). The

vial was brought into a nitrogen-filled glovebox and charged with NMP (0.2 mL, 0.5 M) followed by a mixture of the chlorobenzyl silane (**87**, 20 μL, 0.1 mmol, 1 equiv) and dibenzyl ether (internal standard). The vials were sealed with Teflon caps and stirred at the specified reaction temperature at 250 rpm for 48 hours. The slurry was dissolved in 10% EtOAc/hexanes, loaded onto a silica plug in a glass pipet, and flushed with 8 mL of 10% EtOAc/hexanes into a 20 mL scintillation vial. The solution was concentrated under reduced pressure and analyzed by ^{1}H NMR to obtain the reaction yield. The product was purified by preparative TLC, dissolved in 10% EtOH/hexanes, and analyzed by SFC with chiral stationary phase to obtain the enantiomeric excess (% ee) of the reaction product.

2.6.4 Substrate Preparation

2.6.4.1 Chlorobenzyl Silane Electrophiles

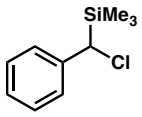
General Procedure 1: Chlorobenzyl Silane Synthesis



Adapted from a procedure by Hashmi and coworkers.[81] A flame-dried round bottom flask equipped with a magnetic stir bar was placed under inert atmosphere (N_2) and charged with diisopropylamine (2.8 mL, 20 mmol, 1.0 equiv) and THF (9 mL). The solution was cooled to –78 °C and stirred for 5 minutes. *n*-Butyllithium was added dropwise (8 mL, 2.5 M in hexane, 20 mmol, 1.0 equiv) and stirred for another 10 minutes, at which time the solution was diluted with hexane (9 mL) and cooled to –100 °C. A mixture of the benzyl chloride (20 mmol, 1.0 equiv) and silyl chloride (24 mmol, 1.2 equiv) in THF (9 mL) was added

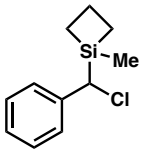
dropwise over the course of 30 minutes via syringe or via cannula. The reaction was stirred for 20 minutes, then warmed to 0 °C and quenched with water (10 mL). The aqueous layer was extracted with ether (3 x 40 mL) and the combined organic layers were washed with 1 M HCl (20 mL), water (20 mL), then dried with $MgSO_4$, filtered, and concentrated under reduced pressure. The product was purified by column chromatography (silica, EtOAc/hexanes) and/or by distillation. For substrates **89c**, **89d**, **89f**, **89h**, and **89j** an inverse addition protocol was used, wherein lithium diisopropylamide (LDA) solution was added dropwise to the mixture of benzyl chloride and R_3SiCl. This procedure minimized the bis-silylated benzyl chloride.

(Chloro(phenyl)methyl)trimethylsilane (87)



Prepared from (chloromethyl)benzene (11.5 mL, 100 mmol) and trimethylsilyl chloride (15.2 mL, 120 mmol) following General Procedure 1. The crude residue was purified by fractional distillation (0.25 Torr, 60 °C) to yield 14.9 g (75% yield) of **87** as a colorless oil. $\mathbf{R_f}$ = 0.61 (silica, hexane, UV). **^{1}H NMR (500 MHz, $CDCl_3$):** δ 7.35 – 7.31 (m, 2H), 7.29 – 7.26 (m, 2H), 7.25 – 7.21 (m, 1H), 4.37 (s, 1H), 0.12 (s, 9H). **^{13}C NMR (126 MHz, $CDCl_3$):** δ 140.3, 128.3, 127.0, 126.7, 53.1, -3.4. **FTIR (NaCl, thin film, cm^{-1}):** 3027, 2959, 1598, 1494, 1450, 1250, 1122, 1074, 912, 863, 844.**HRMS (EI, *m/z*):** calc'd for $C_{10}H_{15}ClSi$ $[M+\cdot]^+$: 198.0632; found: 198.0603.

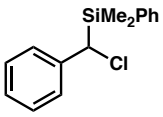
1-(Chloro(phenyl)methyl)-1-methylsiletane (89a)



Prepared from (chloromethyl)benzene (1.15 mL, 10 mmol) and 1-chloro-1-methylsiletane (1.5 mL, 12 mmol) following General Procedure 1 using an

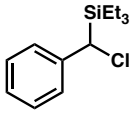
inverse addition protocol. The reaction was also stirred for 1 hour following the addition. The crude residue was purified by column chromatography (silica, hexane), followed by Kugelrohr distillation to yield 594 mg (28% yield) of **89a** as a colorless oil. $\mathbf{R_f}$ = 0.61 (silica, hexane, UV). **^{1}H NMR (500 MHz, $CDCl_3$):** δ 7.36 – 7.30 (m, 4H), 7.27 – 7.21 (m, 1H), 4.56 (s, 1H), 2.04 (dtt, *J* = 12.4, 10.2, 6.1 Hz, 1H), 1.90 (dtt, *J* = 12.7, 10.2, 6.8 Hz, 1H), 1.30 – 1.16 (m, 2H), 1.15 – 0.99 (m, 2H), 0.33 (s, 3H). **^{13}C NMR (126 MHz, $CDCl_3$):** δ 139.5, 128.5, 126.91, 126.86, 51.7, 17.6, 13.8, 13.5, -3.4. **FTIR (NaCl, thin film, cm^{-1}):** 2969, 2927, 1598, 1494, 1450, 1394, 1250, 1121, 1074, 874. **HRMS (EI, *m/z*):** calc'd for $C_{11}H_{15}ClSi$ $[M+\cdot]^+$: 210.0632; found: 210.0607.

(Chloro(phenyl)methyl)dimethyl(phenyl)silane (89b)



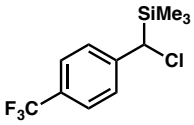
Prepared from (chloromethyl)benzene (2.3 mL, 20 mmol) and chlorodimethyl(phenyl)silane (3.7 mL, 22 mmol) following General Procedure 1 using an inverse addition protocol. The crude residue was purified by fractional distillation (0.25 Torr, 120-153 °C) to yield 2.72 g (52% yield) of **89b** as a light yellow oil. $\mathbf{R_f}$ = 0.22 (silica, hexane, UV). **^{1}H NMR (500 MHz, $CDCl_3$):** δ 7.44 – 7.39 (m, 3H), 7.37 – 7.32 (m, 2H), 7.27 – 7.22 (m, 2H), 7.22 – 7.17 (m, 1H), 7.13 – 7.08 (m, 2H), 4.51 (s, 1H), 0.48 (s, 3H), 0.38 (s, 3H). **^{13}C NMR (126 MHz, $CDCl_3$):** δ 139.7, 135.1, 134.53, 129.8, 128.1, 127.8, 127.3, 126.8, 52.4, -5.06, -5.07. **FTIR (NaCl, thin film, cm^{-1}):** 3070, 3026, 2961, 1494, 1450, 1428, 1250, 1117, 834. **HRMS (FAB, *m/z*):** calc'd for $C_{15}H_{17}ClSi$ $[M–Cl]^+$: 225.1100; found: 225.1104.

(Chloro(phenyl)methyl)triethylsilane (89c)



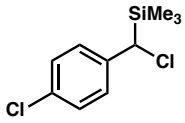
Prepared from (chloromethyl)benzene (2.3 mL, 20 mmol) and triethylsilyl chloride (4.0 mL, 24 mmol) following General Procedure 1. The crude residue was purified by Kugelrohr distillation to yield 3.5 g (73% yield) of **89c** as a light yellow oil. R_f = 0.71 (silica, hexane, UV). ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.34 – 7.28 (m, 4H), 7.24 – 7.19 (m, 1H), 4.48 (s, 1H), 0.96 (t, *J* = 7.9 Hz, 9H), 0.77 – 0.59 (m, 6H). ^{13}C NMR (126 MHz, $CDCl_3$): δ 140.7, 128.4, 127.2, 126.7, 50.9, 7.4, 2.1. FTIR (NaCl, thin film, cm^{-1}): 2955, 2913, 2877, 1598, 1494, 1450, 1414, 1122, 1074, 1009. HRMS (FAB, *m/z*): calc'd for $C_{13}H_{21}ClSi$ $[M+H]^+$: 241.1179; found: 241.1189.

(Chloro(4-(trifluoromethyl)phenyl)methyl)trimethylsilane (89d)



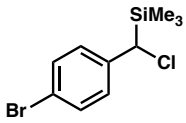
Prepared from 1-(chloromethyl)-4-(trifluoromethyl)benzene (3 mL, 20 mmol) and trimethylsilyl chloride (3 mL, 24 mmol) following General Procedure 1 using an inverse addition protocol. The reaction was also stirred for 1 hour following the addition. The crude residue was purified by fractional distillation (0.25 Torr, 65 °C) to yield 1.29 g (48% yield) of **89d** as a colorless oil. **R_f** = 0.58 (silica, hexane, UV). **^{1}H NMR (500 MHz, $CDCl_3$):** δ 7.58 (d, *J* = 8.2 Hz, 2H), 7.37 (d, *J* = 8.1 Hz, 2H), 4.39 (s, 1H), 0.11 (d, *J* = 0.7 Hz, 9H). **^{13}C NMR (126 MHz, $CDCl_3$):** δ 144.66 (q, J_{C-F} = 1.4 Hz), 128.84 (q, J_{C-F} = 32.5 Hz), 127.1, 125.30 (q, J_{C-F} = 3.8 Hz), 124.32 (q, J_{C-F} = 271.9 Hz), 52.3, -3.6. **^{19}F NMR (282 MHz, $CDCl_3$):** δ -65.6. **FTIR (NaCl, thin film, cm^{-1}):** 2962, 1618, 1415, 1327, 1253, 1166, 1127, 1106, 1069, 1018, 866, 849. **HRMS (FAB, *m/z*):** calc'd for $C_{11}H_{14}ClF_3Si$ $[M+H]^+$: 267.0584; found: 267.0572.

(Chloro(4-chlorophenyl)methyl)trimethylsilane (89e)



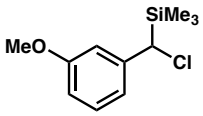
Prepared from 1-chloro-4-(chloromethyl)benzene (800 mg, 5 mmol) and trimethylsilyl chloride (0.76 mL, 6 mmol) following General Procedure 1. The crude residue was purified by column chromatography (silica, hexane) to yield 658 mg (57% yield) of **89e** as a colorless oil. $\mathbf{R_f}$ = 0.58 (silica, hexane, UV). **^{1}H NMR (500 MHz, $CDCl_3$):** δ 7.29 – 7.26 (m, 2H), 7.20 – 7.16 (m, 2H), 4.30 (s, 1H), 0.09 (s, 9H). **^{13}C NMR (126 MHz, $CDCl_3$):** δ 139.0, 132.3, 128.5, 128.3, 52.3, -3.5. **FTIR (NaCl, thin film, cm^{-1}):** 2959, 1490, 1404, 1251, 1122, 1093, 1014, 865, 846. **HRMS (EI, *m/z*):** calc'd for $C_{10}H_{14}Cl_2Si$ $[M+\cdot]^+$: 232.0242; found: 232.0270.

(Chloro(4-bromophenyl)methyl)trimethylsilane (89f)



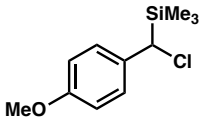
Prepared from 1-chloro-4-(bromomethyl)benzene (1.02 g, 5 mmol) and trimethylsilyl chloride (0.76 mL, 6 mmol) following General Procedure 1 using an inverse addition protocol. The crude residue was purified by fractional distillation (0.25 Torr, 85 °C) to yield 411.6 mg (30% yield) of **89f** as a colorless oil which solidified in the freezer. $\mathbf{R_f}$ = 0.58 (silica, hexane, UV). **m.p.** = 30-31 °C **^{1}H NMR (500 MHz, $CDCl_3$):** δ 7.45 – 7.40 (m, 2H), 7.14 – 7.09 (m, 2H), 4.28 (s, 1H), 0.08 (s, 9H). **^{13}C NMR (126 MHz, $CDCl_3$):** δ 139.5, 131.4, 128.6, 120.3, 52.3, -3.5. **FTIR (NaCl, thin film, cm^{-1}):** 2958, 1487, 1398, 1262, 1271, 1074, 1010, 864, 845, 829. **HRMS (EI, *m/z*):** calc'd for $C_{10}H_{14}BrClSi$ $[M+\cdot]^+$: 275.9737; found: 275.9760.

(Chloro(3-methoxyphenyl)methyl)trimethylsilane (89g)



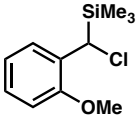
Prepared from 1-(chloromethyl)-3-methoxybenzene (2.9 mL, 20 mmol) and trimethylsilyl chloride (3.05 mL, 24 mmol) following General Procedure 1. The crude residue was purified by fractional distillation (0.25 Torr, 85 °C) to yield 1.2 g (27% yield) of **89g** as a colorless oil. $\mathbf{R}_f$ = 0.59 (silica, 10% EtOAc/ hexane, UV). **^{1}H NMR (500 MHz, $CDCl_3$):** δ 7.24 – 7.19 (m, 1H), 6.82 (ddq, *J* = 4.6, 2.4, 0.8 Hz, 2H), 6.76 (ddd, *J* = 8.2, 2.5, 1.0 Hz, 1H), 4.32 (s, 1H), 3.81 (s, 3H), 0.11 (s, 9H). **^{13}C NMR (126 MHz, $CDCl_3$):** δ 159.6, 141.9, 129.2, 119.5, 112.8, 112.1, 55.3, 53.0, -3.3. **FTIR (NaCl, thin film, cm^{-1}):** 3002, 2958, 1600, 1583, 1489, 1466, 1435, 1296, 1265, 1250, 1148, 1050, 882, 842. **HRMS (FAB, *m/z*):** calc'd for $C_{11}H_{17}ClOSi$ $[M+H]^+$: 229.0816; found: 229.0819.

(Chloro(4-methoxyphenyl)methyl)trimethylsilane (89h)



Prepared from 1-(chloromethyl)-4-methoxybenzene (2.7 mL, 20 mmol) and trimethylsilyl chloride (3.05 mL, 24 mmol) following General Procedure 1 using an inverse addition protocol. The reaction was also stirred for 1 hour following the addition. The crude residue was purified by fractional distillation (0.25 Torr, 85 °C) to yield 1.07 g (47% yield) of **89h** as a colorless oil which solidified in the freezer. Spectral data matched those reported in the literature.[81]

(Chloro(2-methoxyphenyl)methyl)trimethylsilane (89i)

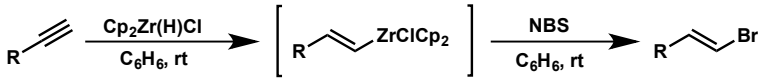


Prepared from 1-(chloromethyl)-2-methoxybenzene (700 μL, 5 mmol) and trimethylsilyl chloride (0.76 mL, 6 mmol) following General Procedure 1. The

crude residue was purified by column chromatography (silica, hexane to 10% Et_2O/hexane) to yield 633 mg (55% yield) of **89i** as a colorless oil. $\mathbf{R_f}$ = 0.67 (silica, 10% EtOAc/hexane, UV). **^{1}H NMR (500 MHz, $CDCl_3$):** δ 7.41 (dd, *J* = 7.6, 1.7 Hz, 1H), 7.18 (ddd, *J* = 8.2, 7.4, 1.7 Hz, 1H), 7.01 – 6.93 (m, 1H), 6.83 (dd, *J* = 8.2, 1.1 Hz, 1H), 4.98 (s, 1H), 3.81 (s, 3H), 0.09 (s, 9H). **^{13}C NMR (126 MHz, $CDCl_3$):** δ 155.5, 129.0, 128.8, 127.4, 120.7, 110.0, 55.3, 46.1, -3.3. **FTIR (NaCl, thin film, cm^{-1}):** 2958, 2837, 1598, 1585, 1488, 1464, 1438, 1289, 1245, 1101, 1051, 1030, 866, 842. **HRMS (EI, *m/z*):** calc'd for $C_{11}H_{17}ClOSi$ $[M+\cdot]^+$: 228.0737; found: 228.0738.

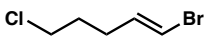
2.6.4.2 Alkenyl Bromide Electrophiles

General Procedure 2: Hydrozirconation/Bromination



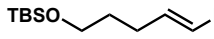
Adapted from a procedure by Zhou, Lin, and coworkers.[82] Schwartz's reagent (2.5 mmol, 1.25 equiv) was added to a flame-dried round bottom flask containing a magnetic stir bar in the glovebox and sealed under inert atmosphere (N_2). C_6H_6 (22 mL) was added via syringe, and the alkyne (2 mmol, 1 equiv) was added dropwise to the stirring mixture. The reaction was stirred for one hour and *N*-bromosuccinimide was added (2.5 mmol, 1.25 equiv). The reaction was stirred for one hour, and then diluted with Et_2O (150 mL). The solution was washed with brine and the organic layer was dried with Na_2SO_4, filtered, and concentrated under reduced pressure. The crude residue was dissolved in a 5% Et_2O/hexane solution, flushed through a silica plug, and concentrated to afford the desired product.

(*E*)-1-bromo-5-chloropent-1-ene (S2)



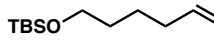
Prepared from 5-chloropent-1-yne (205 mg, 2 mmol, 1 equiv), Schwartz's reagent (645 mg, 2.5 mmol, 1.25 equiv), and N-bromosuccinimide (446 mg, 2.5 mmol, 1.25 equiv) following General Procedure 2. The crude residue was purified by filtration through a pad of silica (5% Et_2O/hexane) to yield 295 mg (80% yield) of **S2** as a colorless oil. Spectral data matched those reported in the literature.[83]

(*E*)-((5-bromopent-4-en-1-yl)oxy)(*tert*-butyl)dimethylsilane (S3)



Prepared from *tert*-butyl(pent-4-yn-1-yloxy)dimethylsilane (3.95 g, 20 mmol, 1 equiv), Schwartz's reagent (7.2 g, 28 mmol, 1.4 equiv), and N-bromosuccinimide (5 g, 28 mmol, 1.4 equiv) following General Procedure 2. The crude residue was purified by filtration through a pad of silica (5% Et_2O/hexane) to yield 4.38 g (79% yield) of **S3** as a colorless oil. $\mathbf{R_f}$ = 0.38 (silica, hexane, $KMnO_4$). **^{1}H NMR (500 MHz, $CDCl_3$):** δ 6.18 (dt, *J* = 13.5, 7.3 Hz, 1H), 6.03 (dt, *J* = 13.5, 1.4 Hz, 1H), 3.61 (t, *J* = 6.2 Hz, 2H), 2.12 (qd, *J* = 7.3, 1.4 Hz, 2H), 1.65 – 1.57 (m, 2H), 0.90 (s, 9H), 0.05 (s, 6H). **^{13}C NMR (126 MHz, $CDCl_3$):** δ 137.9, 104.5, 62.1, 31.7, 29.5, 26.1, 18.5, -5.2. **FTIR (NaCl, thin film, cm^{-1}):** 2954, 2930, 2895, 2858, 1622, 1472, 1463, 1388, 1361, 1256, 1107, 1006, 937, 837. **HRMS (EI, m/z):** calc'd for $C_{11}H_{23}BrOSi$ $[M+H-H_2]^+$: 277.0623; found: 277.0608.

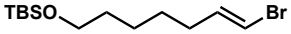
(*E*)-((6-bromohex-5-en-1-yl)oxy)(*tert*-butyl)dimethylsilane (S4)



Prepared from *tert*-butyl(hex-5-yn-1-yloxy)dimethylsilane (2.5 g, 12 mmol, 1 equiv), Schwartz's reagent (4.4 g, 17.1 mmol, 1.45 equiv), and N-

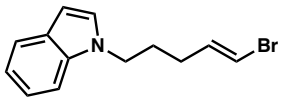
bromosuccinimide (3.05 g, 17.1 mmol, 1.45 equiv) following General Procedure 2. The crude residue was purified by filtration through a pad of silica (5% Et_2O/hexane) to yield 2.5 g (72% yield) of **S4** as a colorless oil. $\mathbf{R_f}$ = 0.38 (silica, hexane, $KMnO_4$). **^{1}H NMR (500 MHz, $CDCl_3$):** δ 6.17 (dt, *J* = 13.8, 7.2 Hz, 1H), 6.02 (dt, *J* = 13.5, 1.2 Hz, 1H), 3.61 (t, *J* = 6.2 Hz, 2H), 2.07 (qd, *J* = 7.2, 1.4 Hz, 2H), 1.56 – 1.49 (m, 2H), 1.49 – 1.41 (m, 2H), 0.90 (d, *J* = 0.6 Hz, 9H), 0.06 (d, *J* = 0.6 Hz, 6H). **^{13}C NMR (126 MHz, $CDCl_3$):** δ 138.2, 104.4, 62.9, 32.9, 32.2, 26.1, 25.1, 18.5, -5.1. **FTIR (NaCl, thin film, cm^{-1}):** 2953, 2930, 2896, 2858, 1621, 1472, 1463, 1388, 1256, 1104, 1006, 938, 836, 812. **HRMS (FAB, *m/z*):** calc'd for $C_{12}H_{25}BrOSi$ $[M+H-H_2]^+$: 291.0780; found: 291.0773.

(*E*)-((7-bromohept-6-en-1-yl)oxy)(*tert*-butyl)dimethylsilane (S5)



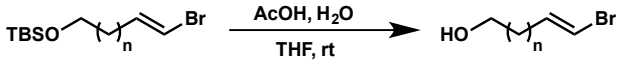
Prepared from *tert*-butyl(hept-6-yn-1-yloxy)dimethylsilane (2.27 g, 10 mmol, 1 equiv), Schwartz's reagent (3.6 g, 14 mmol, 1.4 equiv), and N-bromosuccinimide (2.5 g, 14 mmol, 1.4 equiv) following General Procedure 2. The crude residue was purified by filtration through a pad of silica (5% Et_2O/hexane) to yield 1.6 g (52% yield) of **S5** as a colorless oil. $\mathbf{R_f}$ = 0.28 (silica, hexane, $KMnO_4$). **^{1}H NMR (500 MHz, $CDCl_3$):** δ 6.16 (dt, *J* = 13.4, 7.3 Hz, 1H), 6.01 (dt, *J* = 13.4, 1.4 Hz, 1H), 3.60 (t, *J* = 6.5 Hz, 2H), 2.05 (qd, *J* = 7.2, 1.4 Hz, 2H), 1.55 – 1.48 (m, 2H), 1.46 – 1.38 (m, 2H), 1.38 – 1.30 (m, 2H), 0.90 (s, 9H), 0.05 (s, 6H). **^{13}C NMR (126 MHz, $CDCl_3$):** δ 138.3, 104.3, 63.2, 33.1, 32.7, 28.5, 26.1, 25.3, 18.5, -5.1. **FTIR (NaCl, thin film, cm^{-1}):** 1952, 2930, 2857, 1621, 1472, 1463, 1255, 1101, 938, 836. **HRMS (FAB, *m/z*):** calc'd for $C_{13}H_{27}BrOSi$ $[M+H-H_2]^+$: 305.0936; found: 305.0925.

(*E*)-1-(5-bromopent-4-en-1-yl)-1*H*-indole (29e)



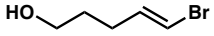
Prepared from 1-(pent-4-yn-1-yl)-1*H*-indole (356 mg, 2 mmol, 1 equiv), Schwartz's reagent (645 mg, 2.5 mmol, 1.25 equiv), and N-bromosuccinimide (451 mg, 2.5 mmol, 1.25 equiv) following General Procedure 2. The crude residue was purified by column chromatography (silica, 0 to 2% Et_2O/hexane) to yield 361 mg (52% yield) of **29e** as a colorless oil. Spectral data matched those reported in the literature.[84]

General Procedure 3: Silyl Ether Deprotection



The alkenyl bromide (1.4 mmol, 1 equiv) was dissolved in a solution of acetic acid (3 mL), water (1 mL), and THF (1 mL) in a round bottom flask equipped with a magnetic stir bar, and stirred overnight at room temperature. The reaction was slowly added to a solution of $NaHCO_3$, extracted with Et_2O, dried with Na_2SO_4, filtered, and concentrated under reduced pressure. The crude material was purified by column chromatography (silica, Et_2O/hexanes).

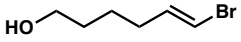
(*E*)-5-bromopent-4-en-1-ol (S6)



Prepared from **S3** (4.8 g, 15 mmol) following General Procedure 3. The crude residue was purified by column chromatography (silica, 30% Et_2O/hexane to 50% Et_2O/hexane) to yield 2.5 g (92% yield) of **S6** as a colorless oil. $\mathbf{R_f}$ = 0.64 (silica, 30% EtOAc/hexane, $KMnO_4$). **^{1}H NMR (500 MHz, $CDCl_3$):** δ 6.17 (dt, *J* = 13.5, 7.2 Hz, 1H), 6.05 (dt, *J* = 13.5, 1.4 Hz, 1H), 3.63 (t, *J* = 6.4 Hz, 2H), 2.14 (qd, *J* = 7.3, 1.4 Hz, 2H), 1.92

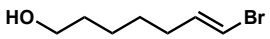
– 1.85 (m, 1H), 1.69 – 1.61 (m, 2H). **^{13}C NMR (126 MHz, $CDCl_3$):** δ 137.4, 104.8, 61.8, 31.5, 29.3. **FTIR (NaCl, thin film, cm^{-1}):** 3338, 2938, 2877, 1621, 1438, 1232, 1059, 940, 911. **HRMS (EI, *m/z*):** calc'd for C_5H_9BrO $[M+\cdot]^+$: 163.9837; found: 163.9846.

(*E*)-6-bromohex-5-en-1-ol (S7)



Prepared from **S4** (2.48 g, 8.5 mmol) following General Procedure 3. The crude residue was purified by column chromatography (silica, 30% Et_2O/hexane) to yield 1.15 g (76% yield) of **S7** as a colorless oil. $\mathbf{R_f}$ = 0.64 (silica, 30% EtOAc/hexane, $KMnO_4$). **^{1}H NMR (500 MHz, $CDCl_3$):** δ 6.17 (dt, *J* = 13.4, 7.2 Hz, 1H), 6.04 (dt, *J* = 13.5, 1.4 Hz, 1H), 3.65 (t, *J* = 6.4 Hz, 2H), 2.09 (qd, *J* = 7.2, 1.4 Hz, 2H), 1.63 – 1.55 (m, 2H), 1.54 – 1.45 (m, 2H), 1.27 (s, 1H). **^{13}C NMR (126 MHz, $CDCl_3$):** δ 137.9, 104.7, 62.7, 32.8, 32.1, 24.9. **FTIR (NaCl, thin film, cm^{-1}):** 3338, 2935, 2861, 1619, 1457, 1438, 1226, 1065, 943. **HRMS (EI, *m/z*):** calc'd for $C_6H_{11}BrO$ $[M+\cdot]^+$: 177.9993; found: 178.0008.

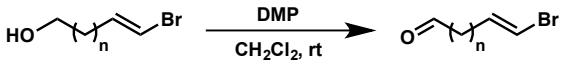
(*E*)-7-bromohept-6-en-1-ol (S8)



Prepared from **S5** (1.5 g, 5 mmol) following General Procedure 3. The crude residue was purified by column chromatography (silica, 30% Et_2O/hexane) to yield 684 mg (72% yield) of **S8** as a colorless oil. $\mathbf{R_f}$ = 0.73 (silica, 30% EtOAc/hexane, $KMnO_4$). **^{1}H NMR (500 MHz, $CDCl_3$):** δ 6.21 (dt, *J* = 13.5, 7.3 Hz, 1H), 6.06 (dt, *J* = 13.4, 1.4 Hz, 1H), 3.68 (t, *J* = 6.6 Hz, 2H), 2.11 (qd, *J* = 7.2, 1.4 Hz, 2H), 1.67 (s, 1H), 1.65 – 1.57 (m, 2H), 1.52 – 1.37 (m, 4H). **^{13}C NMR (126 MHz, $CDCl_3$):** δ 138.1, 104.4, 62.8, 33.0, 32.5, 28.5, 25.2. **FTIR (NaCl, thin film, cm^{-1}):** 3338, 2933, 2858, 1620, 1460, 1436,

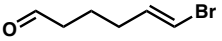
1220, 1073, 1054, 935. **HRMS (FAB, *m/z*):** calc'd for $C_7H_{13}BrO$ $[M+H]^+$: 193.0223; found: 193.0228.

General Procedure 4: Aldehyde Formation



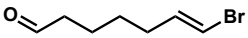
A flame-dried round bottom flask equipped with a magnetic stir bar was placed under inert atmosphere (N_2) and charged with the alcohol (4 mmol, 1 equiv). Anhydrous CH_2Cl_2 (24 mL) was added to the flask, followed by Dess-Martin periodinane (4.8 mmol, 1.2 equiv). The reaction was stirred at room temperature and monitored by TLC until it reached full conversion (approx. 2 hours). The reaction was quenched with aqueous $NaHCO_3$, extracted with Et_2O, dried with Na_2SO_4, filtered over a plug of silica with 50% Et_2O/hexane, and concentrated under reduced pressure to give the crude material.

(*E*)-6-bromohex-5-enal (S9)



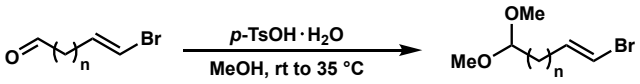
Prepared from **S7** (718 mg, 4 mmol) following General Procedure 4 to yield 689 mg (97% yield) of **S9** as a yellow oil. The crude residue was used in the next step without further purification. $\mathbf{R_f}$ = 0.24 (silica, 10% EtOAc/ hexane, $KMnO_4$). **^{1}H NMR (500 MHz, $CDCl_3$):** δ 9.76 (t, *J* = 1.5 Hz, 1H), 6.16 – 6.10 (m, 1H), 6.05 (dt, *J* = 13.5, 1.2 Hz, 1H), 2.46 (td, *J* = 7.2, 1.5 Hz, 2H), 2.09 (qd, *J* = 7.3, 1.2 Hz, 2H), 1.74 (p, *J* = 7.3 Hz, 2H). **^{13}C NMR (126 MHz, $CDCl_3$):** δ 201.9, 136.9, 105.5, 42.9, 32.2, 21.0. **FTIR (NaCl, thin film, cm^{-1}):** 2936, 2826, 2724, 1817, 1724, 1620, 1440, 1452, 1410, 1390, 1231, 1043, 945. **HRMS (FAB, *m/z*):** calc'd for C_6H_9BrO $[M+H]^+$: 176.9915; found: 176.9909.

(*E*)-7-bromohept-6-enal (S10)



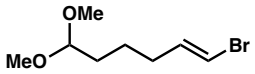
Prepared from **S8** (382 mg, 2 mmol) following General Procedure 4 to yield 413 mg (72% yield) of **S10** as a yellow oil. The crude residue was used in the next step without further purification. $\mathbf{R_f}$ = 0.28 (silica, 10% EtOAc/ hexane, $KMnO_4$). **^{1}H NMR (500 MHz, $CDCl_3$):** δ 9.76 (t, *J* = 1.6 Hz, 1H), 6.15 (dt, *J* = 13.5, 7.2 Hz, 1H), 6.03 (dt, *J* = 13.5, 1.3 Hz, 1H), 2.44 (td, *J* = 7.3, 1.6 Hz, 2H), 2.07 (qd, *J* = 7.3, 1.4 Hz, 2H), 1.68 – 1.59 (m, 2H), 1.47 – 1.39 (m, 2H). **^{13}C NMR (126 MHz, $CDCl_3$):** δ 202.4, 137.5, 104.8, 43.7, 32.8, 28.2, 21.4. **FTIR (NaCl, thin film, cm^{-1}):** 2934, 2722, 1724, 1620, 1459, 1390, 1224, 938. **HRMS (FAB, *m/z*):** calc'd for $C_7H_{11}BrO$ $[M+H]^+$: 191.0072; found: 191.0076.

General Procedure 5: Acetal Formation



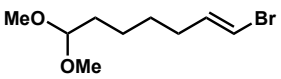
To a 20 mL scintillation vial equipped with a magnetic stir bar were added the aldehyde (2 mmol, 1 equiv), *p*-toluenesulfonic acid monohydrate (1 mmol, 0.5 equiv), and methanol (5.5 mL). The vial was sealed with a Teflon screw-cap, and stirred at 35 °C. The reaction was monitored by TLC until the reaction had reached full completion. The reaction was quenched with aqueous $NaHCO_3$, extracted with Et_2O, dried with $MgSO_4$, filtered, and concentrated under reduced pressure. The crude material was purified by column chromatography (silica, ether/hexanes). *Note: It is important to immediately quench the reaction upon removal from the stir plate. Hydrolysis of the product to the aldehyde proceeds upon standing at room temperature.*

(*E*)-1-bromo-6,6-dimethoxyhex-1-ene (29f)



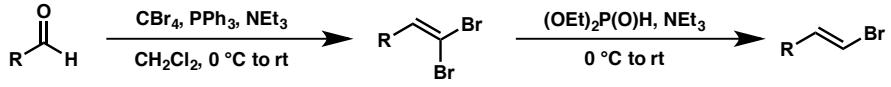
Prepared from **S9** (356 mg, 2 mmol) following General Procedure 5. The crude residue was purified by column chromatography (silica, 10% Et_2O/hexane to 30% Et_2O/hexane) to yield 410 mg (91% yield) of **29f** as a light yellow oil. $\mathbf{R}_f$ = 0.32 (silica, 10% EtOAc/hexane, $KMnO_4$). **^{1}H NMR (500 MHz, $CDCl_3$):** δ 6.15 (dt, *J* = 13.5, 7.2 Hz, 1H), 6.03 (dt, *J* = 13.5, 1.4 Hz, 1H), 4.35 (t, *J* = 5.6 Hz, 1H), 3.31 (s, 6H), 2.07 (qd, *J* = 7.3, 1.4 Hz, 2H), 1.63 – 1.57 (m, 2H), 1.50 – 1.42 (m, 2H). **^{13}C NMR (126 MHz, $CDCl_3$):** δ 137.8, 104.7, 104.3, 52.9, 32.8, 31.9, 23.7. **FTIR (NaCl, thin film, cm^{-1}):** 2949, 2830, 1440, 1621, 1458, 1439, 1386, 1193, 1162, 1128, 1071, 943. **HRMS (EI, *m/z*):** calc'd for $C_8H_{15}BrO_2$ $[M+H–H_2]^+$: 221.0177; found: 221.0172.

(*E*)-1-bromo-7,7-dimethoxyhept-1-ene (29g)



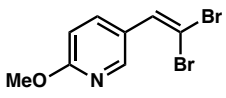
Prepared from **S10** (382 mg, 2 mmol) following General Procedure 5. The crude residue was purified by column chromatography (silica, 10% Et_2O/hexane to 30% Et_2O/hexane) to yield 421 mg (89% yield) of **29g** as a light yellow oil. $\mathbf{R}_f$ = 0.32 (silica, 10% EtOAc/hexane, $KMnO_4$). **^{1}H NMR (500 MHz, $CDCl_3$):** δ 6.21 (dt, *J* = 13.5, 7.2 Hz, 1H), 6.06 (dt, *J* = 13.5, 1.4 Hz, 1H), 4.40 (t, *J* = 5.7 Hz, 1H), 3.36 (s, 6H), 2.10 (qd, *J* = 7.2, 1.4 Hz, 2H), 1.68 – 1.61 (m, 2H), 1.52 – 1.36 (m, 4H). **^{13}C NMR (126 MHz, $CDCl_3$):** δ 138.0, 104.5, 104.4, 52.8, 33.0, 32.3, 28.6, 24.1. **FTIR (NaCl, thin film, cm^{-1}):** 2986, 2944, 2860, 2830, 1621, 1459, 1386, 1364, 1192, 1158, 1128, 1076, 1052, 937. **HRMS (EI, *m/z*):** calc'd for $C_9H_{17}BrO_2$ $[M+H–H_2]^+$: 235.0334; found: 235.0311.

General Procedure 6: Alkenyl Bromides from Aldehydes



General Procedure 6, Part A: Following a procedure by Alexakis and coworkers,[85] a flame dried round bottom flask equipped with a magnetic stir bar was charged with tetrabromomethane (20 mmol, 2 equiv) and triphenylphosphine (40 mmol, 4 equiv) while under inert atmosphere (N_2). The flask was cooled to 0 °C and CH_2Cl_2 (30 mL) was added, followed by the triethylamine (10 mmol, 1 equiv). The aldehyde (10 mmol, 1 equiv) was dissolved in CH_2Cl_2 (5 mL) and added dropwise to the reaction mixture. The reaction was warmed to room temperature and stirred for 90 minutes. The reaction was removed from the stir plate and slowly added to a vigorously stirring solution of Et_2O (150 mL) and hexane (150 mL), filtered, and concentrated under reduced pressure. The crude residue was purified by column chromatography (silica, ether/hexanes) to afford the dibromoalkene.

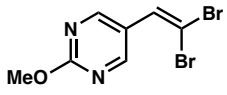
5-(2,2-dibromovinyl)-2-methoxypyridine (S11)



Prepared from 6-methoxynicotinaldehyde (1.36 g, 10 mmol) following General Procedure 6A. The crude residue was purified by column chromatography (silica, 1% Et_2O/hexane to 10% Et_2O/hexane) to yield 570 mg (20% yield) of **S11** as a yellow oil. $\mathbf{R_f}$ = 0.48 (silica, 10% EtOAc/hexane) **^{1}H NMR (500 MHz, $CDCl_3$):** δ 8.25 (dt, *J* = 2.4, 0.6 Hz, 1H), 7.90 (ddd, *J* = 8.7, 2.5, 0.6 Hz, 1H), 7.37 (q, *J* = 0.6 Hz, 1H), 6.74 (dt, *J* = 8.7, 0.5 Hz, 2H), 3.94 (s, 3H) **^{13}C NMR (126 MHz, $CDCl_3$):** δ 163.8, 147.6, 137.8, 133.5, 124.9, 110.7, 89.3, 53.8 **FTIR (NaCl, thin film, cm^{-1}):** 2982, 2946,

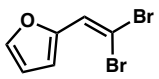
1603 1595, 1561, 1491, 1381, 1309, 1289, 1254, 1132, 1024, 1014, 867, 819 **HRMS (ESI-TOF, m/z):** calc'd for $C_8H_7NOBr_2$ $[M+H]^+$: 291.8973; found: 291.8967.

5-(2,2-dibromovinyl)-2-methoxypyrimidine (S12)



Prepared from 2-methoxypyrimidine-5-carbaldedyde (966 mg, 7 mmol) following General Procedure 6A. The crude residue was purified by column chromatography (silica, 30% Et_2O/hexane to 50% Et_2O/hexane) to yield 1.5 g (74% yield) of **S12** as a light yellow solid. $\mathbf{R_f}$ = 0.63 (silica, 25% EtOAc/ hexane, UV). **m.p.** = 62-63 °C **^{1}H NMR (500 MHz, $CDCl_3$):** δ 8.70 (d, *J* = 0.6 Hz, 2H), 7.33 (t, *J* = 0.6 Hz, 1H), 4.03 (s, 3H). **^{13}C NMR (126 MHz, $CDCl_3$):** δ 164.8, 158.7, 130.4, 123.8, 92.1, 55.4. **FTIR (NaCl, thin film, cm^{-1}):** 2991, 1589, 1549, 1524, 1473, 1412, 1391, 1338, 1291, 1233, 1046, 1028, 951, 812, 835. **HRMS (ESI-TOF, m/z):** calc'd for $C_7H_6N_2OBr_2$ $[M+H]^+$: 292.8920; found: 292.8950.

2-(2,2-dibromovinyl)furan (S13)

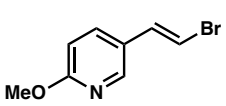


Prepared from furfural (1.9 g, 20 mmol) following General Procedure 6A. The crude residue was purified by column chromatography (silica, hexane) to yield 3.3 g (66% yield) of **S13** as a yellow oil. Spectral data matched those reported in the literature.[86]

General Procedure 6, Part B: The dibromoalkene (1.7 mmol, 1 equiv) and diethyl phosphite (5.1 mmol, 3 equiv) were added to a vial with a magnetic stirring rod and placed under an inert atmosphere (N_2). The solution was cooled to 0 °C and triethylamine (5.1 mmol, 3 equiv) was added dropwise. The reaction was warmed to room temperature and

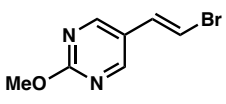
stirred overnight. The reaction was quenched with water (5 mL) and extracted with CH_2Cl_2 (20 mL). The organic layer was washed with brine (5 mL), dried with Na_2SO_4, filtered, and concentrated under reduced pressure. The crude residue was purified by column chromatography (silica, ether/hexanes) to afford the vinyl bromide.

(*E*)-5-(2-bromovinyl)-2-methoxypyridine (29k)



Prepared from **S11** (500 mg, 1.7 mmol) following General Procedure 6B. The crude residue was purified by column chromatography (silica, 2% Et_2O/hexane to 5% Et_2O/hexane) to yield 314 mg (86% yield, 96:4 *E*:*Z*) of **29k** as a white solid. $\mathbf{R_f}$ = 0.46 (silica, 10% EtOAc/hexane). **m.p.** = 53-56 °C **^{1}H NMR (500 MHz, $CDCl_3$):** δ 8.05 (d, *J* = 2.5 Hz, 1H), 7.54 (ddd, *J* = 8.7, 2.5, 0.4 Hz, 1H), 7.02 (dq, *J* = 14.0, 0.5 Hz, 1H), 6.70 (dt, *J* = 8.7, 0.6 Hz, 1H), 6.65 (d, *J* = 14.0 Hz, 1H), 3.93 (s, 3H). **^{13}C NMR (126 MHz, $CDCl_3$):** δ 164.0, 145.3, 135.3, 133.5, 125.5, 111.4, 105.5, 53.7. **FTIR (NaCl, thin film, cm^{-1}):** 3061, 2943, 1613, 1598, 1562, 1490, 1385, 1303, 1285, 1258, 1238, 1026, 1015, 947, 837. **HRMS (ESI-TOF, m/z):** calc'd for C_8H_8NOBr $[M+H]^+$: 213.9868; found: 213.9858.

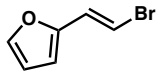
(*E*)-5-(2-bromovinyl)-2-methoxypyrimidine (29l)



Prepared from **S12** (880 mg, 3 mmol) following General Procedure 6B. The crude residue was purified by column chromatography (silica, 5% Et_2O/hexane to 30% Et_2O/hexane) to yield 473 mg (73% yield, 97:3 *E*:*Z*) of **29l** as a white solid. $\mathbf{R_f}$ = 0.60 (silica, 25% EtOAc/ hexane, UV). **m.p.** = 89-90 °C **^{1}H NMR (500 MHz, $CDCl_3$):** δ 8.46 (s, 2H), 6.99 (dt, *J* = 14.2, 0.5 Hz, 1H), 6.79 (d, *J* = 14.2 Hz, 1H),

4.01 (d, J = 0.5 Hz, 3H). **^{13}C NMR (126 MHz, $CDCl_3$):** δ 165.2, 156.5, 130.2, 124.1, 107.7, 55.3. **FTIR (NaCl, thin film, cm^{-1}):** 3057, 2993, 1593, 1553, 1479, 1414, 1388, 1339, 1290, 1248, 1186, 1049, 1030, 951, 909, 803. **HRMS (ESI-TOF, m/z):** calc'd for $C_7H_7N_2OBr$ $[M+H]^+$: 214.9820; found: 214.9803.

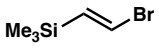
(*E*)-2-(2-bromovinyl)furan (29q)



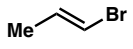
Prepared from **S13** (3.3 g, 13.1 mmol) following General Procedure 6B. The crude residue was purified by column chromatography (silica, hexane) to yield 400 mg (18% yield, *E* isomer) of **29q** as a yellow oil. **Note:** It is possible to separate the E and Z vinyl bromide isomers by column chromatography. The E isomer has a higher R_f than the Z isomer. Careful column separation eliminates the need for base mediated isomerization of the Z olefin, a lower yielding procedure (8% yield), typically employed in previous studies.[50] Spectral data matched those reported in the literature.[85]

Other Alkenyl Bromides

Alkenyl bromides **29o** and **29p** were purchased from commercial sources (Sigma Aldrich).

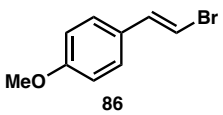


29o

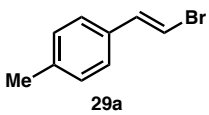


29p

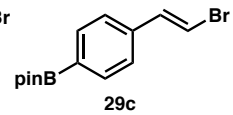
Alkenyl bromides **86**, **29a**, **29c**, **29d**, **29i**, and **29j** were prepared according to literature procedures reported and referenced by Reisman and coworkers.[50]



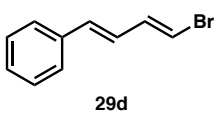
86



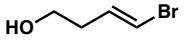
29a



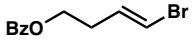
29c



29d

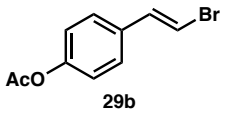


29i



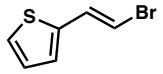
29j

Alkenyl bromide **29b** was prepared according to a literature procedure reported by Buchwald and coworkers.[87]



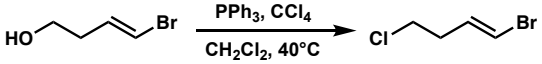
29b

Alkenyl bromide **29r** was prepared according to a literature procedure reported by Roy and coworkers.[88]



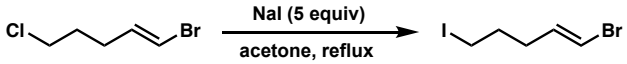
29r

(*E*)-1-bromo-4-chlorobut-1-ene (S14)



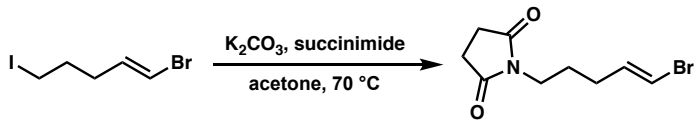
To a 10 mL round bottom flask equipped with a magnetic stir bar was added (*E*)-4-bromobut-3-en-1-ol (363 mg, 2.4 mmol, 1.0 equiv), PPh_3 (944 mg, 3.6 mmol, 1.5 equiv), CCl_4 (480 mL, 4.8 mmol, 2.0 equiv) and 2 mL of CH_2Cl_2. The reaction was stirred at overnight at 40 °C for 10 hours. After cooling to room temperature, the crude mixture was poured into pentane, filtered through a plug of silica gel with additional pentane, and concentrated under reduced pressure to afford 276 mg (68% yield) of **S14** as a colorless oil. $\mathbf{R_f}$ = 0.49 (silica, hexane, $KMnO_4$). **^{1}H NMR (500 MHz, $CDCl_3$):** δ 6.24 – 6.16 (m, 2H), 3.54 (t, *J* = 6.7 Hz, 2H), 2.57 – 2.47 (m, 2H). **^{13}C NMR (126 MHz, $CDCl_3$):** δ 133.7, 107.7, 43.0, 36.0. **FTIR (NaCl, thin film, cm^{-1}):** 3066, 2960, 1622, 1444, 1425, 1300, 1283, 1247, 1232, 1218, 937, 906. **HRMS (EI, *m/z*):** calc'd for C_4H_6BrCl $[M+\cdot]^+$: 169.9312; found: 169.9299.

(*E*)-1-bromo-5-iodopent-1-ene (S15)



Alkyl chloride **S2** (1.96 g, 10.5 mmol, 1 equiv) and sodium iodide (7.49 g, 50 mmol, 5 equiv) were added to a 100 mL round bottom flask equipped with a magnetic stir bar and dissolved in 30 mL acetone. The reaction was refluxed overnight for 14 hours and then cooled to room temperature. Hexanes was added to the reaction to precipitate out the remaining NaI, and the mixture was filtered through a plug of silica gel with additional hexane. The solution was concentrated to obtain 2.47 g (90% yield) of **S15** as a yellow oil (*approximately 9% alkyl chloride remains*). $\mathbf{R_f}$ = 0.31 (silica, hexane, $KMNO_4$). **^{1}H NMR (500 MHz, $CDCl_3$):** δ 6.17 – 6.05 (m, 2H), 3.18 (t, *J* = 6.8 Hz, 2H), 2.18 (dddd, *J* = 7.4, 5.9, 4.3, 1.9 Hz, 2H), 1.91 (p, *J* = 6.7 Hz, 2H). **^{13}C NMR (126 MHz, $CDCl_3$):** δ 135.8, 105.9, 33.5, 31.9, 5.8. **FTIR (NaCl, thin film, cm^{-1}):** 2933, 2838, 1622, 1427, 1312, 1293, 1268, 1231, 1202, 1166, 936. **HRMS (FAB, *m/z*):** calc'd for C_5H_8BrI $[M+\cdot]^+$: 273.8854; found: 273.8862.

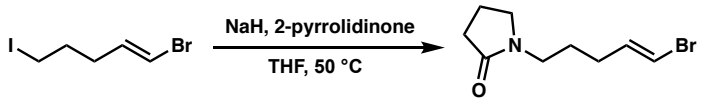
(*E*)-1-(5-bromopent-4-en-1-yl)pyrrolidine-2,5-dione (29m)



Alkyl iodide **S15** (275 mg, 1.0 mmol, 1.0 equiv), succinimide (99 mg, 1.0 mmol, 1.0 equiv), and K_2CO_3 (691 mg, 5.0 mmol, 5.0 equiv) were added to 20 mL scintillation vial equipped with a cross-shaped stir bar and dissolved in 3 mL of acetone. The vial was sealed with a Teflon cap and stirred at 70 °C for 4 hours. The reaction was cooled to room temperature,

quenched with H_2O, and extracted with EtOAc (2x). The combined organic layers were dried with Na_2SO_4, filtered, and concentrated under reduced pressure. The crude residue was purified by column chromatography (silica, hexane to 40% acetone/hexanes) to yield 169 mg (69% yield) of **29m** as a colorless oil. $\mathbf{R_f}$ = 0.47 (silica, 30% acetone/hexane, CAM). **^{1}H NMR (500 MHz, $CDCl_3$):** δ 6.13 (dt, *J* = 13.6, 6.8 Hz, 1H), 6.07 (dt, *J* = 13.5, 1.1 Hz, 1H), 3.51 (dd, *J* = 7.7, 6.7 Hz, 2H), 2.70 (s, 4H), 2.10 – 2.03 (m, 2H), 1.69 (p, *J* = 7.2 Hz, 2H). **^{13}C NMR (126 MHz, $CDCl_3$):** δ 177.4, 136.6, 105.4, 38.2, 30.5, 28.3, 26.4. **FTIR (NaCl, thin film, cm^{-1}):** 2941, 1774, 1697, 1621, 1438, 1402, 1343, 1250, 1206, 1151, 1104, 940, 820. **HRMS (FAB, *m/z*):** calc'd for $C_9H_{12}BrNO_2$ $[M+H]^+$: 246.0130; found: 246.0123.

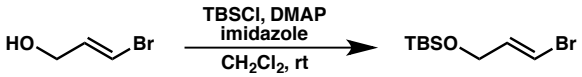
(*E*)-1-(5-bromopent-4-en-1-yl)pyrrolidin-2-one (29n)



In the glovebox, sodium hydride (91 mg, 95% in mineral oil, 3.6 mmol, 1.2 equiv) was added to a flame-dried 50 mL round bottom flask equipped with a stir bar and sealed with a rubber septum. The flask was removed from the glovebox, 10 mL THF was added under an inert (N_2) atmosphere, and the solution was cooled to 0 °C. 2-pyrrolidinone (225 mg, 228 mL, 3.0 mmol, 1.0 equiv) was added dropwise and stirred for 10 minutes. Alkyl iodide **S15** (825 mg, 3.0 mmol, 1.0 equiv) was added and the reaction was heated to 50 °C and stirred for 15 hours. The reaction was cooled to room temperature, quenched with H_2O, and extracted with EtOAc (2x). The combined organic layers were dried with Na_2SO_4, filtered, and concentrated under reduced pressure. The crude residue was purified by

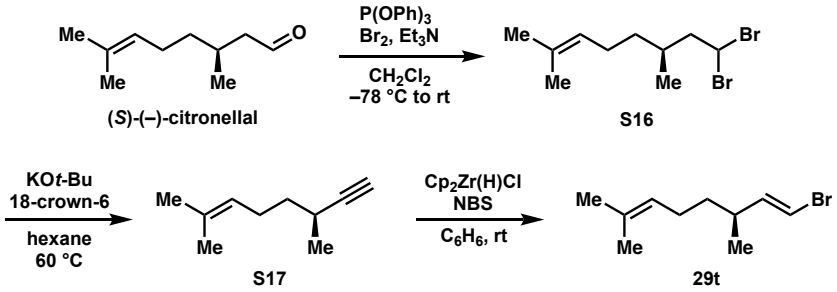
column chromatography (silica, hexane to 40% acetone/hexanes) to yield 476 mg (68% yield) of **29n** as a colorless oil. $\mathbf{R_f}$ = 0.31 (silica, 30% acetone/hexane, CAM). **^{1}H NMR (500 MHz, $CDCl_3$):** δ 6.12 (dt, *J* = 13.4, 7.1 Hz, 1H), 6.03 (dt, *J* = 13.5, 1.3 Hz, 1H), 3.36 – 3.31 (m, 2H), 3.25 (t, *J* = 7.2 Hz, 2H), 2.35 (t, *J* = 8.1 Hz, 2H), 2.06 – 1.95 (m, 4H), 1.64 – 1.56 (m, 2H). **^{13}C NMR (126 MHz, $CDCl_3$):** δ 175.1, 136.9, 105.1, 47.2, 41.9, 31.1, 30.4, 26.2, 17.9. **FTIR (NaCl, thin film, cm^{-1}):** 2928, 2863, 1682, 1620, 1494, 1462, 1426, 1287, 1262, 940. **HRMS (FAB, *m/z*):** calc'd for $C_9H_{14}BrNO$ $[M+H]^+$: 232.0337; found: 232.0333.

(*E*)-((3-bromoallyl)oxy)(*tert*-butyl)dimethylsilane (29s)



To a round bottom flask were added *tert*-butyldimethylsilyl chloride (514 mg, 3.3 mmol, 1.1 equiv), 4-dimethylaminopyridine (48 mg, 0.3 mmol, 0.1 equiv), imidazole (409 mg, 6 mmol, 2 equiv), and (*E*)-3-bromoprop-2-en-1-ol (411 mg, 3 mmol, 1 equiv) and the flask was placed under N_2. The solids were dissolved in CH_2Cl_2 (8 mL) and stirred overnight at room temperature. The reaction was quenched with aqueous NH_4Cl (3 mL), diluted with pentane (12 mL), and the layers were separated. The organic layer was washed with water (2 x 3 mL) and brine (3 mL), then dried with $MgSO_4$, filtered, and concentrated under reduced pressure. The crude material was purified by column chromatography (silica, pentane) to yield 684 mg of **29s** (91% yield) as a colorless oil. Spectral data matched those reported in the literature.[89]

(*S*,*E*)-1-bromo-3,7-dimethylocta-1,6-diene (29t)



Similar to a route by Shenvi and co-workers,[90] the alkenyl bromide **29t** was prepared in three steps from enantiomerically pure (*S*)-(–)-citronellal.

Part A: Triphenylphosphite (9.8 mL, 37.5 mmol, 1.5 equiv) was added to a flame-dried 1 L flask with a magnetic stir bar and dissolved in anhydrous CH_2Cl_2 under an inert atmosphere (N_2). The flask was cooled to –78 °C and bromine (1.7 mL, 32.5 mmol, 1.3 equiv) and triethylamine (10.5 mL, 75 mmol, 3 equiv) were successively added dropwise. Citronellal (4.5 mL, 25 mmol, 1 equiv) was dissolved in CH_2Cl_2 (25 mL) and added dropwise. The reaction was warmed to room temperature and stirred for 2 hours then was concentrated under reduced pressure. Pentane was added to the crude residue and filtered through a pad of silica with pentane. The solution was concentrated under reduced pressure to yield 6.7 g (90% yield) of **S16** as a mixture of the dibromide and *cis*/*trans* vinyl bromide. The crude material was used in the next step without further purification. The ^{1}H NMR spectrum of the dibromide **S16** matches that reported in the literature.[90]

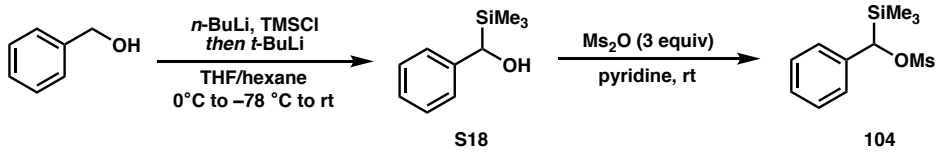
Part B: A flame-dried 500 mL round bottom flask with a magnetic stir bar was charged with potassium *tert*-butoxide (3.37 g, 30 mmol, 3 equiv) and sealed under inert atmosphere (N_2). Dry hexanes (250 mL) and 18-crown-6 (220 mg, 0.8 mmol, 0.08 equiv) were added

and the suspension was vigorously stirred. Dibromide **S16** (2.98 g, 10 mmol, 1 equiv) was added and the reaction was heated to 60 °C and refluxed for 8 hours. The reaction was quenched with water, extracted with hexane, and concentrated under reduced pressure. The crude material was filtered through a pad of silica with pentane to afford 1.15 g (85% yield) of **S17** as a mixture of the alkyne and vinyl bromide (>99% *E*-isomer). The crude material was used in the next step without further purification. The ^{1}H NMR spectra of **S17** matches that which is reported in the literature.[90]

Part C: Prepared from **S17** (1.15 g, 8.4 mmol, 1 equiv), Schwartz's reagent (2.7 g, 10.5 mmol, 1.25 equiv), and N-bromosuccinimide (1.87 g, 10.5 mmol, 1.25 equiv) following General Procedure 2. The crude residue was purified by column chromatography (silica, hexane) to yield 862 mg (47% yield, 95% pure) of **29t** as a colorless oil. $\mathbf{R_f}$ = 0.77 (silica, hexane, $KMnO_4$). $[\boldsymbol{\alpha}]_{\boldsymbol{D}}^{\mathbf{25}}$ = +54° (c = 1.0, $CHCl_3$). **^{1}H NMR (500 MHz, $CDCl_3$):** δ 6.06 (dd, *J* = 13.5, 8.1 Hz, 1H), 5.98 (dd, *J* = 13.6, 0.6 Hz, 1H), 5.06 (tdq, *J* = 7.2, 2.9, 1.5 Hz, 1H), 2.18 (ddt, *J* = 14.8, 13.6, 6.8 Hz, 1H), 1.96 (ddddd, *J* = 9.3, 8.2, 7.1, 2.1, 1.1 Hz, 2H), 1.69 (p, *J* = 1.5 Hz, 3H), 1.60 (d, *J* = 1.3 Hz, 3H), 1.37 – 1.30 (m, 2H), 1.01 (d, *J* = 6.8 Hz, 3H). **^{13}C NMR (126 MHz, $CDCl_3$):** δ 143.6, 131.8, 124.0, 103.2, 37.4, 36.4, 25.7, 25.6, 20.0, 17.8. **FTIR (NaCl, thin film, cm^{-1}):** 2964, 2926, 2916, 2871, 2853, 1618, 1458, 1376, 1278, 1206, 1108, 941. **HRMS (EI, m/z):** calc'd for $C_{10}H_{17}Br$ $[M+\cdot]^+$: 216.0514; found: 216.0510.

2.6.4.3 Oxygen-Based Electrophiles

Phenyl(trimethylsilyl)methyl methanesulfonate (104)

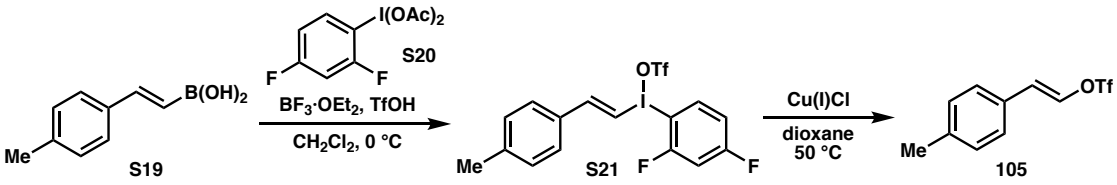


Part A: Adapted from a procedure by Maleczka and coworkers.[91] Benzyl alcohol (1 mL, 10 mmol, 1 equiv) was added to a flame-dried 200 mL round bottom flask and dissolved in 20 mL of THF. The reaction was cooled to 0 °C and *n*-BuLi (4.4. mL, 2.5 M in hexane, 11 mmol, 1.1 equiv) was added dropwise. The reaction was stirred for 15 min, then TMSCl (1.4 mL, 11.0 mmol, 1.1 equiv) was added dropwise and stirred for an additional 15 min. The flask was cooled to –78 °C and *t*-BuLi (7.5 mL, 1.7 M in pentane, 13.0 mmol, 1.3 equiv) was added dropwise. The reaction was warmed to room temperature and stirred for 1 hour. The reaction was quenched with sat. NH_4Cl (40 mL) and extracted with Et_2O (80 mL). The organic layer was washed with water (40 mL) and brine (40 mL), then dried with $MgSO_4$, filtered, and concentrated under reduced pressure. The crude material was purified by column chromatography (silica, 0 to 15% EtOAc/ hexane) to yield 1.3 g (73% yield) of **S188** as a colorless oil. Spectral data matched those reported in the literature.[91]

Part B: The benzyl alcohol **S18** (288 mg, 1.6 mmol, 1 equiv) was added to a 10 mL round bottom flask containing a magnetic stir bar and put under an inert atmosphere (N_2). Pyridine (1.0 mL) was added followed by methanesulfonic anhydride (442 mg, 2.5 mmol, 1.7 equiv). The reaction was stirred for 4 hours at room temperature, at which time an additional portion of methanesulfonic anhydride (1.3 equiv) was added, and the reaction

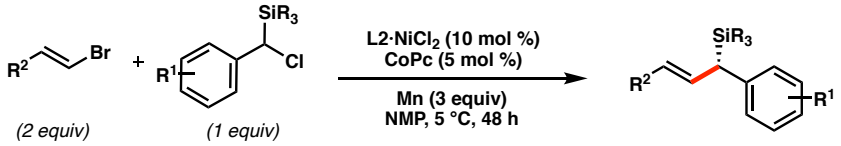
was stirred two more hours. The milky suspension was quenched with water (5 mL) and extracted with EtOAc (2 x 10 mL). The combined organic layers were washed with water (10 mL) and brine (2 x 10 mL), dried with $MgSO_4$, filtered, and concentrated under reduced pressure. The crude material was purified by column chromatography (florisil, 0 to 10% EtOAc/hexane) to yield 176 mg (43% yield) of **104** as a white solid. $\mathbf{R_f}$ = 0.19 (silica, 10% EtOAc/hexane, CAM). **m.p.** = 71-72 °C **^{1}H NMR (500 MHz, $CDCl_3$):** δ 7.38 – 7.33 (m, 2H), 7.28 – 7.24 (m, 1H), 7.23 – 7.19 (m, 2H), 5.38 (s, 1H), 2.66 (s, 3H), 0.09 (s, 9H). **^{13}C NMR (126 MHz, $CDCl_3$):** δ 137.8, 128.9, 127.5, 125.9, 81.0, 39.2, -4.0. **FTIR (NaCl, thin film, cm^{-1}):** 2959, 1357, 1251, 1174, 973, 933, 913, 864, 844, 827. **HRMS (FAB, *m/z*):** calc'd for $C_{11}H_{18}O_3SSi$ $[M+H-H_2]^+$: 257.0668; found: 257.0670.

(*E*)-4-methylstyryl trifluoromethanesulfonate (105)



The alkenyl triflate was prepared from the corresponding alkenyl boronic acid according to a procedure by Sigman and coworkers.[92] Spectral data matched those reported in the literature.[92]

2.6.5 Enantioselective Reductive Cross-Couplings



General Procedure 7: Reaction on 0.2 mmol scale.

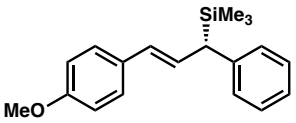
On the bench-top, a 2 dram vial was equipped with a stir bar and the alkenyl bromide (0.4 mmol, 2 equiv), **L2**·$NiCl_2$ complex (9.7 mg, 0.02 mmol, 0.10 equiv), Mn powder (33.0 mg, 0.6 mmol, 3 equiv), and cobalt phthalocyanine (5.7 mg, 0.01 mmol, 0.05 equiv) were added. The vial was brought into a N_2-filled glovebox and the vial was charged with NMP (0.4 mL, 0.5 M) and the chlorobenzyl silane (0.2 mmol, 1 equiv). The vial was sealed with a Teflon cap and stirred at 250 rpm at 5 °C in a temperature-controlled well plate for 2 days. The crude reaction was brought out of the glove box, diluted with 2 mL H_2O, slowly quenched with 1 mL of 1 M HCl, and further diluted with water (10 mL). The aqueous layer was extracted with diethyl ether (3 x 20 mL) and the combined organic layers were washed with brine (15 mL), dried with $MgSO_4$, filtered, and concentrated under reduced pressure. The crude material was purified by column chromatography to afford the desired product. **Notes:** In order to efficiently remove the viscous contents from the vial, it is useful to fill the vial ¾ full with an extraction solvent, screw on the Teflon cap, and shake vigorously with the stir bar inside. Removal of blue CoPc stains from glassware was accomplished by scrubbing with Alconox soap solution. Removal of blue CoPc stains from stir bars was accomplished using conc. HNO_3.

Assignment of Absolute Stereochemistry

The absolute stereochemistry of **91c** was assigned by single crystal X-ray diffraction. The absolute stereochemistry of **S22** was assigned by comparing the optical rotation of the purified product to the literature value. All other chiral allylic silane products were assigned by analogy.

Characterization of Reaction Products

(*S*,*E*)-(3-(4-methoxyphenyl)-1-phenylallyl)trimethylsilane (88c)



From (chloro(phenyl)methyl)trimethylsilane 87. Prepared from (*E*)-1-(2-bromovinyl)-4-methoxybenzene (**86**, 85.2 mg, 0.4 mmol) and (chloro(phenyl)methyl)trimethylsilane (**87**, 39.8 mg, 0.2 mmol) according to General Procedure 7. The crude residue was purified by column chromatography (silica, 0 to 2% Et_2O/hexane) to yield **88c** (42.4 mg, 71% yield) in 95% ee as a colorless oil. $\mathbf{R_f}$ = 0.61 (silica, 10% EtOAc/hexane, UV). **Chiral SFC:** (AD-H, 2.5 mL/min, 20% IPA in CO_2, λ = 280 nm): t_R (minor) = 3.0 min, t_R (major) = 3.9 min. $[\boldsymbol{\alpha}]_{\boldsymbol{D}}^{\mathbf{25}}$ = +27° (c = 1.0, $CHCl_3$). **^{1}H NMR (500 MHz, $CDCl_3$):** δ 7.36 – 7.29 (m, 4H), 7.21 – 7.13 (m, 3H), 6.91 – 6.84 (m, 2H), 6.49 (dd, *J* = 15.6, 9.9 Hz, 1H), 6.35 (d, *J* = 15.6 Hz, 1H), 3.82 (d, *J* = 0.5 Hz, 3H), 3.13 (d, *J* = 9.8 Hz, 1H), 0.05 (d, *J* = 0.6 Hz, 9H). **^{13}C NMR (126 MHz, $CDCl_3$):** δ 158.6, 142.7, 131.1, 128.5, 128.3, 127.7, 127.3, 127.0, 124.8, 114.0, 55.4, 43.8, -2.7. **FTIR (NaCl, thin film, cm^{-1}):** 3024, 2955, 2898, 1607, 1510, 1493, 1465, 1450, 1441, 1295, 1286, 1249, 1175, 1106, 1055, 1035, 963, 876, 861, 838. **HRMS (TOF-ESI, *m/z*):** calc'd for $C_{19}H_{24}OSi$ $[M+H]^+$: 297.1675; found: 297.1687.

From phenyl(trimethylsilyl)methyl methanesulfonate 104. Prepared from with (*E*)-1-(2-bromovinyl)-4-methoxybenzene (**87**, 85.2 mg, 0.4 mmol) and phenyl(trimethylsilyl)-methyl methanesulfonate (**104**, 51.7 mg, 0.2 mmol) according to General Procedure 7, but at 10 °C and with the addition of an internal standard. **Note:** The increased temperature provided slightly higher yield (~5%). The crude material was dissolved in 10% EtOAc/hexane and filtered through a pad of silica in place of the acidic aqueous workup.

The yield of **88c** was determined to be 40% yield by ^{1}H NMR, and the enantioselectivity was determined to be 92% ee following purification by preparative TLC.

Preparative Scale: Reaction on a 6.0 mmol scale:

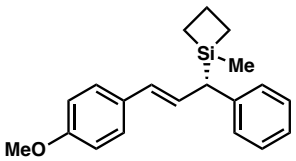
On a bench-top to a 100 mL round bottom flask (with 24/40 joint) equipped with a medium-size egg-shaped stir bar was added alkenyl bromide **86** (2.56 g, 12 mmol, 2 equiv), **L2**·$NiCl_2$ (293 mg, 0.6 mmol, 0.10 equiv), Mn^0 powder (990 mg, 18 mmol, 3 equiv), and cobalt phthalocyanine (172 mg, 0.3 mmol, 0.05 equiv). Under an inert atmosphere in a glovebox, the flask was charged with NMP (12 mL, 0.5 M) followed by chlorobenzyl silane **L2** (1.19 g, 6 mmol, 1 equiv). The round bottom flask was sealed with an unpunctured large septum, wrapped with electrical tape, and brought out of the glovebox. The flask was stirred (at 450 rpm) at 5 °C in a bench-top cryocool by submerging it in an isopropanol bath cooled with a Thermo Scientific EK90 Immersion Cooler for 3 days. The reaction was diluted with 70 mL of water, slowly quenched with 30 mL of M HCl, and transferred to a separatory funnel with 100 mL water and 300 mL diethyl ether. The layers were separated and the aqueous layer was extracted with diethyl ether (2 x 400 mL). The combined organic layers were washed with brine, dried with $MgSO_4$, filtered, and concentrated under reduced pressure. The crude residue was purified by column chromatography (silica, 0 to 2% Et_2O/hexane) to yield **88c** (1.3 g, 74% yield) in 97% ee as a colorless oil.

Glovebox-free, Bench-top Setup:

On a bench-top to a 15 mL round bottom flask equipped with a small egg-shaped stir bar was added alkenyl bromide **86** (426 mg, 2.0 mmol, 2 equiv), **L2**·$NiCl_2$ (49 mg, 0.10 mmol,

0.10 equiv), Mn^0 powder (165 mg, 3.0 mmol, 3 equiv), and cobalt phthalocyanine (29 mg, 0.05 mmol, 0.05 equiv). The flask was sealed with a rubber septum and connected to a Schlenk line via a large gauge needle. The flask was evacuated and backfilled with N_2 (3 times). The NMP (2 mL, 0.5 M) and chlorobenzyl silane **87** (199 mg, 1.0 mmol, 1 equiv) were added via syringe. The N_2 needle was removed, the septum was sealed with electrical tape, and the reaction was stirred at 5 °C in a bench-top cryocool 2 days. The reaction was diluted (5 mL water + 5 mL of Et_2O) and stirred while quenched via slow addition of 1 M HCl (2 mL). The solution was transferred to a separatory funnel, diluted with additional water (35 mL) and Et_2O (35 mL), and the layers were separated. The aqueous layer was extracted with Et_2O (2 x 50 mL). The combined organic layers were dried with $MgSO_4$, filtered, and concentrated under reduced pressure. The crude residue was purified by column chromatography (silica, 0 to 30% PhMe/hexane) to yield **88c** (211 mg, 71% yield) in 98% ee as a colorless oil.

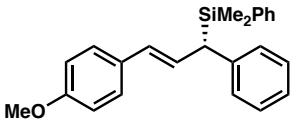
(*S*,*E*)-1-(3-(4-methoxyphenyl)-1-phenylallyl)-1-methylsiletane (90a)



Prepared from (*E*)-1-(2-bromovinyl)-4-methoxybenzene (**86**, 85.2 mg, 0.4 mmol) and 1-(chloro(phenyl)methyl)-1-methylsiletane (**89a**, 42.2 mg, 0.2 mmol) according to General Procedure 7. The crude residue was purified by column chromatography (silica, 0 to 3% Et_2O/hexane) to yield **90a** (37.6 mg, 61% yield) in 98% ee as a colorless oil. $\mathbf{R_f}$ = 0.58 (silica, 10% EtOAc/hexane, UV). **Chiral SFC:** (AD-H, 2.5 mL/min, 20% IPA in CO_2, λ = 280 nm): t_R (minor) = 4.8 min, t_R (major) = 6.0 min. $[\alpha]_D^{25}$ = +41° (c = 1.0, $CHCl_3$). **^{1}H NMR (500 MHz, $CDCl_3$):** δ 7.37 – 7.30 (m, 4H), 7.25 – 7.20 (m, 2H), 7.20 – 7.15 (m,

1H), 6.90 – 6.85 (m, 2H), 6.52 (ddd, *J* = 15.7, 9.4, 1.0 Hz, 1H), 6.42 (d, *J* = 15.7 Hz, 1H), 3.82 (d, *J* = 0.9 Hz, 3H), 3.39 (d, *J* = 9.3 Hz, 1H), 2.11 – 1.91 (m, 2H), 1.25 – 1.13 (m, 2H), 1.10 – 0.97 (m, 2H), 0.25 (d, *J* = 0.9 Hz, 3H). **^{13}C NMR (126 MHz, $CDCl_3$):** δ 158.7, 141.7, 131.0, 128.7, 128.3, 127.3, 127.2, 127.1, 125.1, 114.1, 55.4, 43.1, 17.8, 13.9, 13.7, -2.9. **FTIR (NaCl, thin film, cm^{-1}):** 3023, 2960, 2929, 1607, 1510, 1491, 1450, 1293, 1429, 1175, 1118, 1074, 1035, 962, 867. **HRMS (TOF-ESI, *m/z*):** calc'd for $C_{20}H_{24}OSi$ $[M+H]^+$: 309.1675; found: 309.1667.

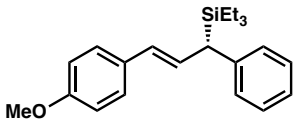
(*S*,*E*)-(3-(4-methoxyphenyl)-1-phenylallyl)dimethyl(phenyl)silane (90b)



Prepared from (*E*)-1-(2-bromovinyl)-4-methoxybenzene (**86**, 85.2 mg, 0.4 mmol) and (chloro(phenyl)methyl)dimethyl-(phenyl)silane (**89b**, 52.2 mg, 0.2 mmol) according to General Procedure 7. The crude residue was purified by column chromatography (silica, 0 to 30% PhMe/hexane) to yield **90b** (30.7 mg, 43% yield) in 97% ee as a colorless oil. $\mathbf{R}_f$ = 0.48 (silica, 10% EtOAc/hexane, UV). **Chiral SFC:** (AD-H, 2.5 mL/min, 20% IPA in CO_2, λ = 280 nm): t_R (minor) = 3.7 min, t_R (major) = 4.2 min. $[\alpha]_D^{25}$ = +22° (c = 1.0, $CHCl_3$). **^{1}H NMR (500 MHz, $CDCl_3$):** δ 7.40 – 7.37 (m, 3H), 7.35 – 7.31 (m, 2H), 7.26 – 7.19 (m, 4H), 7.15 – 7.09 (m, 1H), 7.03 – 6.98 (m, 2H), 6.84 (d, *J* = 8.7 Hz, 2H), 6.37 (dd, *J* = 15.6, 9.7 Hz, 1H), 6.24 (d, *J* = 15.6 Hz, 1H), 3.82 (s, 3H), 3.29 (d, *J* = 9.7 Hz, 1H), 0.32 (s, 6H). **^{13}C NMR (126 MHz, $CDCl_3$):** δ 158.6, 142.0, 136.8, 134.5, 131.1, 129.3, 128.3, 128.1, 128.0, 127.6, 127.6, 127.0, 124.9, 114.0, 55.4, 43.4, -4.0, -4.5. **FTIR (NaCl, thin film, cm^{-1}):** 3024, 2956, 1606, 1510, 142, 1287, 1249, 1175, 1113, 1035, 831, 814. **HRMS (FAB, *m/z*):** calc'd for $C_{24}H_{26}OSi$ $[M+\cdot]^+$: 358.1753; found: 358.1749.

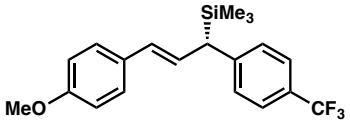
The reaction was also conducted on a larger reaction scale using alkenyl bromide **86** (1.70 g, 8.0 mmol), chlorobenzyl silane **86b** (1.044 g, 4.0 mmol), **L2**·$NiCl_2$ (194 mg, 0.4 mmol), Mn powder (660 mg, 12 mmol), and cobalt phthalocyanine (114 mg, 0.2 mmol) in 8 mL NMP. The reaction was stirred at 5 °C for 2 days and subsequently purified by column chromatography (silica, 0 to 30% PhMe/hexane) to yield **90b** (600 mg, 42% yield) in 97% ee as a yellow oil.

(*S*,*E*)-(3-(4-methoxyphenyl)-1-phenylallyl)triethylsilane (90c)



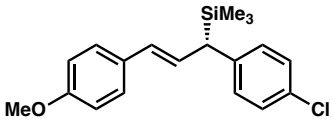
Prepared from (*E*)-1-(2-bromovinyl)-4-methoxybenzene (**86**, 85.2 mg, 0.4 mmol) and (chloro(phenyl)methyl)triethylsilane (**89c**, 48.2 mg, 0.2 mmol) according to General Procedure 7. The crude residue was purified by column chromatography (silica, 0 to 2% Et_2O/hexane) to yield **90c** (10.9 mg, 16% yield, 93% clean, contains 7% unidentified silyl isomer) in 93% ee as a colorless oil. The yield is adjusted accordingly to (16 x 0.93 = 15% yield). $\mathbf{R_f}$ = 0.61 (silica, 10% EtOAc/hexane, UV). **Chiral SFC:** (AD-H, 2.5 mL/min, 20% IPA in CO_2, λ = 280 nm): t_R (minor) = 3.0 min, t_R (major) = 3.5 min. $[\boldsymbol{\alpha}]_{\boldsymbol{D}}^{\mathbf{25}}$ = +73° (c = 0.3, $CHCl_3$). **^{1}H NMR (500 MHz, $CDCl_3$):** δ 7.30 – 7.23 (m, 4H), 7.19 – 7.15 (m, 2H), 7.14 – 7.09 (m, 1H), 6.86 – 6.81 (m, 2H), 6.47 (dd, *J* = 15.6, 10.0 Hz, 1H), 6.30 (d, *J* = 15.6 Hz, 1H), 3.80 (s, 3H), 3.25 (d, *J* = 10.0 Hz, 1H), 0.92 (t, *J* = 7.9 Hz, 9H), 0.61 – 0.56 (m, 6H). **^{13}C NMR (126 MHz, $CDCl_3$):** δ 158.6, 142.8, 131.2, 128.9, 128.5, 127.5, 127.1, 127.0, 124.8, 114.0, 55.4, 41.0, 7.6, 2.6. **FTIR (NaCl, thin film, cm^{-1}):** 3024, 2953, 2875, 1936, 2910, 1607, 1510, 1493, 1467, 1456, 1294, 1286, 1249, 115, 1036, 1010, 963. **HRMS (TOF-ESI, *m/z*):** calc'd for $C_{22}H_{30}OSi$ $[M+H–H_2]^+$: 337.1988; found: 337.1964.

(*S*,*E*)-(3-(4-methoxyphenyl)-1-(4-(trifluoromethyl)phenyl)allyl)trimethylsilane (90d)



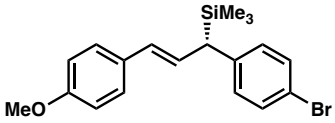
Prepared from (*E*)-1-(2-bromovinyl)-4-methoxybenzene (**86**, 85.2 mg, 0.4 mmol) and (chloro(4-trifluoromethyl-phenyl)methyl)-trimethylsilane (**89d**, 53.4 mg, 0.2 mmol) according to General Procedure 7. The crude material was dissolved in chilled (0 °C) 10% EtOAc/hexane while it was still cold, and filtered through a pad of silica in place of the acidic aqueous workup. **Note**: Complete decomposition of the product was observed when the crude reaction was warmed to room temperature and subjected to aqueous work up. The crude residue was purified by preparative TLC (silica, hexane to 20% toluene/hexane) to yield **90d** (22.5 mg, 31% yield) in 96% ee as a colorless oil. When the reaction was conducted with an internal standard, the yield was determined to be 67% yield by ^{1}H NMR. $\mathbf{R}_f$ = 0.56 (silica, 10% EtOAc/hexane). **Chiral SFC:** (AD-H, 2.5 mL/min, 20% IPA in CO_2, λ = 280 nm): t_R (minor) = 2.6 min, t_R (major) = 3.5 min. $[\alpha]_D^{25}$ = +25° (c = 1.0, $CHCl_3$). **^{1}H NMR (500 MHz, $CDCl_3$):** δ 7.53 (d, *J* = 7.8 Hz, 2H), 7.30 (d, *J* = 8.6 Hz, 2H), 7.24 (d, *J* = 7.9 Hz, 2H), 6.86 (d, *J* = 8.7 Hz, 2H), 6.43 (dd, *J* = 15.6, 9.7 Hz, 1H), 6.33 (d, *J* = 15.5 Hz, 1H), 3.81 (s, 3H), 3.19 (d, *J* = 9.7 Hz, 1H), 0.02 (s, 9H). **^{13}C NMR (126 MHz, $CDCl_3$):** δ 158.8, 147.2 (q, $J_{C\text{-}F}$ = 1.2 Hz), 130.7, 128.5, 127.3, 127.13 (q, $J_{C\text{-}F}$ = 32.2 Hz), 127.12, 126.9, 125.39 (q, $J_{C\text{-}F}$ = 3.8 Hz), 124.6 (q, $J_{C\text{-}F}$ = 271.5 Hz), 114.1, 55.4, 44.0, -2.8. **^{19}F NMR (282 MHz, $CDCl_3$):** δ -65.3. **FTIR (NaCl, thin film, cm^{-1}):** 2957, 2837, 1615, 1578, 1511, 1466, 1420, 1327, 1290, 1250, 1163, 1121, 1070, 1036, 1016, 962, 866, 846. **HRMS (FAB, *m/z*):** calc'd for $C_{20}H_{23}F_3OSi$ $[M+\cdot]^+$: 364.1470; found: 364.1480.

(*S*,*E*)-(1-(4-chlorophenyl)-3-(4-methoxyphenyl)allyl)trimethylsilane (90e)



Prepared from (*E*)-1-(2-bromovinyl)-4-methoxybenzene (**86**, 85.2 mg, 0.4 mmol) and (chloro(4-chlorophenyl)methyl)-trimethylsilane (**89e**, 46.6 mg, 0.2 mmol) according to General Procedure 7. The crude residue was purified by column chromatography (silica, 0 to 2% Et_2O/hexane) to yield **90e** (45.7 mg, 69% yield) in 96% ee as a colorless oil. $\mathbf{R_f}$ = 0.58 (silica, 10% EtOAc/hexane, UV). **Chiral SFC:** (OJ-H, 2.5 mL/min, 10% IPA in CO_2, λ = 280 nm): t_R (major) = 5.0 min, t_R (minor) = 7.9 min. $[\boldsymbol{\alpha}]_D^{25}$ = +21° (c = 1.0, $CHCl_3$). **^{1}H NMR (500 MHz, $CDCl_3$):** δ 7.32 – 7.28 (m, 2H), 7.28 (s, 2H), 7.11 – 7.06 (m, 2H), 6.89 – 6.84 (m, 2H), 6.40 (dd, *J* = 15.5, 9.5 Hz, 1H), 6.32 (d, *J* = 15.6 Hz, 1H), 3.81 (s, 3H), 3.09 (d, *J* = 9.5 Hz, 1H), 0.03 (d, *J* = 0.5 Hz, 9H). **^{13}C NMR (126 MHz, $CDCl_3$):** δ 158.7, 141.3, 130.9, 130.3, 128.53, 128.52, 128.1, 127.5, 127.1, 114.06, 55.4, 43.2, -2.8. **FTIR (NaCl, thin film, cm^{-1}):** 3029, 2956, 1899, 2835, 1608, 1510, 1490, 1292, 1249, 1176, 1092, 1036, 1013, 963, 864, 841, 803. **HRMS (TOF-ESI, *m/z*):** calc'd for $C_{19}H_{23}ClOSi$ $[M+H-H_2]^+$: 329.1128; found: 329.1138.

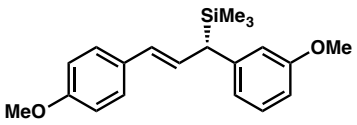
(*S*,*E*)-(1-(4-bromophenyl)-3-(4-methoxyphenyl)allyl)trimethylsilane (90f)



Prepared from (*E*)-1-(2-bromovinyl)-4-methoxybenzene (**86**, 85.2 mg, 0.4 mmol) and (chloro(4-bromophenyl)methyl)-trimethylsilane (**89f**, 55.5 mg, 0.2 mmol) according to General Procedure 7. The crude material was dissolved in chilled (0 °C) 10% EtOAc/hexane while it was still cold, and filtered through a pad of silica in place of the acidic aqueous workup. **Note:** Warming the reaction to room temperature and conducting an acidic workup resulted in unidentified side

products that could not be separated from the desired product by column chromatography. The crude residue was purified by column chromatography (silica, hexane to 20% toluene/hexane) to yield **90f** (32.7 mg, 44% yield) in 97% ee as a colorless oil. When the reaction was conducted with an internal standard, the yield was determined to be 52% yield by ^{1}H NMR analysis of the crude reaction mixture. $\mathbf{R}_f$ = 0.59 (silica, 10% EtOAc/hexane, UV). **Chiral SFC:** (AD-H, 2.5 mL/min, 20% IPA in CO_2, λ = 280 nm): t_R (minor) = 6.9 min, t_R (major) = 9.4 min. $[\boldsymbol{a}]_D^{25}$ = +15° (c = 1.0, $CHCl_3$). **^{1}H NMR (500 MHz, $CDCl_3$):** δ 7.39 (d, *J* = 8.5 Hz, 2H), 7.28 (d, *J* = 8.3 Hz, 2H), 7.01 (d, *J* = 8.2 Hz, 2H), 6.84 (d, *J* = 8.8 Hz, 2H), 6.37 (dd, *J* = 15.6, 9.5 Hz, 1H), 6.30 (d, *J* = 15.6 Hz, 1H), 3.81 (s, 3H), 3.06 (d, *J* = 9.4 Hz, 1H), 0.01 (s, 9H). **^{13}C NMR (126 MHz, $CDCl_3$):** δ 158.7, 141.8, 131.5, 130.9, 129.0, 128.1, 127.4, 127.1, 118.3, 114.1, 55.5, 43.2, -2.8. **FTIR (NaCl, thin film, cm^{-1}):** 3022, 2954, 1898, 1606, 1510, 1486, 1464, 1291, 1248, 1175, 1035, 1008, 962, 862, 840, 802. **HRMS (TOF-ESI, *m/z*):** calc'd for $C_{19}H_{23}BrOSi$ $[M+H-H_2]^+$: 373.0623; found: 373.0615.

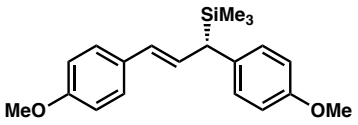
(*S*,*E*)-(1-(3-methoxyphenyl)-3-(4-methoxyphenyl)allyl)trimethylsilane (90g)



Prepared from (*E*)-1-(2-bromovinyl)-4-methoxybenzene (**86**, 85.2 mg, 0.4 mmol) and (chloro(3-methoxyphenyl)-methyl)-trimethylsilane (**89g**, 45.8 mg, 0.2 mmol) according to General Procedure 7. The crude residue was purified by column chromatography (silica, 0 to 3% Et_2O/hexane) to yield **90g** (53.0 mg, 81% yield) in 97% ee as a colorless oil. $\mathbf{R}_f$ = 0.45 (silica, 10% EtOAc/hexane, UV). **Chiral SFC:** (AD-H, 2.5 mL/min, 25% IPA in CO_2, λ = 280 nm): t_R (minor) = 2.8 min, t_R (major) = 3.7 min. $[\boldsymbol{a}]_D^{25}$ = +16° (c = 1.0, $CHCl_3$). **^{1}H NMR (500**

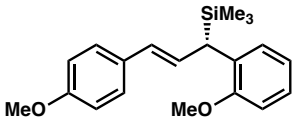
MHz, $CDCl_3$): δ 7.34 – 7.28 (m, 2H), 7.22 (t, *J* = 7.9 Hz, 1H), 6.88 – 6.84 (m, 2H), 6.79 – 6.74 (m, 1H), 6.74 – 6.68 (m, 2H), 6.45 (dd, *J* = 15.6, 9.8 Hz, 1H), 6.33 (d, *J* = 15.6 Hz, 1H), 3.82 (s, 3H), 3.81 (s, 3H), 3.10 (d, *J* = 9.8 Hz, 1H), 0.05 (s, 9H). **^{13}C NMR (126 MHz, $CDCl_3$):** δ 159.7, 158.6, 144.4, 131.1, 129.3, 128.1, 127.7, 127.0, 119.9, 114.0, 113.3, 109.7, 55.4, 55.2, 43.9, -2.6. **FTIR (NaCl, thin film, cm^{-1}):** 3000, 2955, 2834, 1607, 1579, 1510, 1464, 1438, 1299, 1287, 1248, 1174, 1148, 1038, 963, 838, 819. **HRMS (TOF-ESI, *m/z*):** calc'd for $C_{20}H_{26}O_2Si$ $[M+H-H_2]^+$: 325.1624; found: 325.1673.

(*S*,*E*)-(1,3-bis(4-methoxyphenyl)allyl)trimethylsilane (90h)



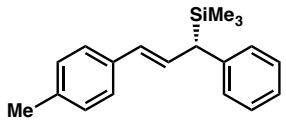
Prepared from (*E*)-1-(2-bromovinyl)-4-methoxybenzene (**86**, 85.2 mg, 0.4 mmol) and (chloro(4-methoxyphenyl)-methyl)-trimethylsilane (**89h**, 45.8 mg, 0.2 mmol) according to General Procedure 7. The crude residue was purified by preparative TLC (silica, 10% EtOAc/hexane) to yield **90h** (28.9 mg, 44% yield) in 96% ee as a colorless oil. $\mathbf{R_f}$ = 0.45 (silica, 10% EtOAc/hexane, UV). **Chiral SFC:** (AD-H, 2.5 mL/min, 20% IPA in CO_2, λ = 280 nm): t_R (minor) = 5.6 min, t_R (major) = 6.8 min. $[\alpha]_D^{25}$ = +21° (c = 1.0, $CHCl_3$). **^{1}H NMR (500 MHz, $CDCl_3$):** δ 7.31 – 7.26 (m, 2H), 7.10 – 7.05 (m, 2H), 6.88 – 6.83 (m, 4H), 6.41 (dd, *J* = 15.6, 9.6 Hz, 1H), 6.30 (d, *J* = 15.6 Hz, 1H), 3.81 (s, 3H), 3.80 (s, 3H), 3.05 (d, *J* = 9.6 Hz, 1H), 0.03 (s, 9H). **^{13}C NMR (126 MHz, $CDCl_3$):** δ 158.6, 157.1, 134.6, 131.2, 128.8, 128.2, 127.4, 127.0, 114.0, 113.9, 55.43, 55.37, 42.5, -2.6. **FTIR (NaCl, thin film, cm^{-1}):** 3000, 2954, 2834, 1608, 1509, 1464, 1441, 1297, 1289, 1248, 1175, 1036, 964, 863, 839. **HRMS (TOF-ESI, *m/z*):** calc'd for $C_{20}H_{26}O_2Si$ $[M+H-H_2]^+$: 325.1624; found: 325.1605.

(*S*,*E*)-(1-(2-methoxyphenyl)-3-(4-methoxyphenyl)allyl)trimethylsilane (90i)



Prepared from (*E*)-1-(2-bromovinyl)-4-methoxybenzene (**86**, 85.2 mg, 0.4 mmol) and (chloro(2-methoxyphenyl)methyl)-trimethylsilane (**89i**, 45.8 mg, 0.2 mmol) according to General Procedure 7. The crude residue was purified by preparative TLC (silica, 10% EtOAc/hexane) to yield **90i** (13.4 mg, 21% yield) in 95% ee as a colorless oil. $\mathbf{R}_f$ = 0.52 (silica, 10% EtOAc/hexane, UV). **Chiral SFC:** (AD-H, 2.5 mL/min, 20% IPA in CO_2, λ = 280 nm): t_R (minor) = 2.5 min, t_R (major) = 3.5 min. $[\boldsymbol{a}]_D^{25}$ = +9° (c = 1.0, $CHCl_3$). **^{1}H NMR (500 MHz, $CDCl_3$):** δ 7.31 – 7.27 (m, 2H), 7.21 (dd, *J* = 7.6, 1.7 Hz, 1H), 7.10 (ddd, *J* = 8.0, 7.3, 1.7 Hz, 1H), 6.93 (td, *J* = 7.5, 1.2 Hz, 1H), 6.87 – 6.82 (m, 3H), 6.48 (ddd, *J* = 15.6, 10.0, 0.6 Hz, 1H), 6.33 (d, *J* = 15.6 Hz, 1H), 3.82 (s, 3H), 3.81 (s, 3H), 3.65 (d, *J* = 10.1 Hz, 1H), 0.00 (s, 9H). **^{13}C NMR (126 MHz, $CDCl_3$):** δ 158.5, 156.0, 131.4, 131.3, 128.5, 127.5, 127.0, 125.4, 120.6, 114.0, 110.4, 55.4, 55.2, 35.3, -2.6. **FTIR (NaCl, thin film, cm^{-1}):** 2951, 2901, 2834, 1608, 1510, 1490, 1464, 1439, 1289, 1246, 1174, 1032, 964, 837. **HRMS (FAB, *m/z*):** calc'd for $C_{20}H_{26}O_2Si$ $[M+H]^+$: 327.1780; found: 327.1795.

(*S*,*E*)-trimethyl(1-phenyl-3-(*p*-tolyl)allyl)silane (91a)

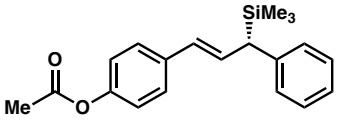


From (E)-1-(2-bromovinyl)-4-methylbenzene 86. Prepared from (*E*)-1-(2-bromovinyl)-4-methylbenzene (**29a**, 78.8 mg, 0.4 mmol) and (chloro(phenyl)methyl)trimethylsilane (**87**, 39.8 mg, 0.2 mmol) according to General Procedure 7. The crude residue was purified by column chromatography (silica, 0 to 3% Et_2O/hexane) to yield **91a** (40.5 mg, 72% yield) in 93% ee as a colorless oil. $\mathbf{R}_f$ = 0.24 (silica, hexane). **Chiral SFC:** (OJ-H, 2.5 mL/min, 7% IPA in CO_2, λ = 245 nm): t_R

(major) = 3.9 min, t_R (minor) = 9.5 min. $[\boldsymbol{a}]_D^{25}$ = +28° (c = 1.0, $CHCl_3$). **^{1}H NMR (500 MHz, $CDCl_3$):** δ 7.36 – 7.27 (m, 4H), 7.22 – 7.12 (m, 5H), 6.59 (dd, *J* = 15.6, 10.0 Hz, 1H), 6.38 (d, *J* = 15.6 Hz, 1H), 3.16 (d, *J* = 9.9 Hz, 1H), 2.37 (s, 3H), 0.06 (s, 9H). **^{13}C NMR (126 MHz, $CDCl_3$):** δ 142.6, 136.4, 135.5, 129.5, 129.3, 128.5, 128.1, 127.30, 125.9, 124.8, 43.9, 21.3, -2.7. **FTIR (NaCl, thin film, cm^{-1}):** 3023, 2955, 1639, 1595, 1512, 1496, 1450, 1248, 1211, 1183, 1106, 1077, 1056, 963, 905, 840. **HRMS (FAB, *m/z*):** calc'd for $C_{19}H_{24}Si$ $[M+\cdot]^+$: 280.1647; found: 280.1648.

From (E)-4-methylstyrenyl trifluoromethanesulfonate 105. Prepared from (*E*)-4-methylstyryl trifluoromethanesulfonate (**105**, 0.4 mmol, 2 equiv) and (chloro(phenyl)methyl)trimethylsilane (**87**, 39.8 mg, 0.2 mmol) according to General Procedure 7, but with the addition of an internal standard. The crude material was dissolved in 10% EtOAc/hexane and filtered through a pad of silica in place of the acidic aqueous workup. The yield of **91a** was determined to be 57% yield by ^{1}H NMR, and the enantioselectivity was determined to be 97% ee following purification by preparative TLC.

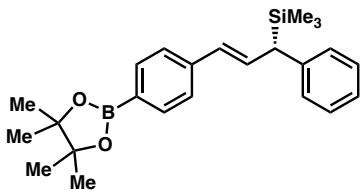
(*S*,*E*)-4-(3-phenyl-3-(trimethylsilyl)prop-1-en-1-yl)phenyl acetate (91b)



Prepared from (*E*)-4-(2-bromovinyl)phenyl acetate (**29b**, 96.4 mg, 0.4 mmol) and (chloro(phenyl)methyl)trimethylsilane (**87**, 39.8 mg, 0.2 mmol) according to General Procedure 7. The crude residue was purified by column chromatography (silica, 0 to 4% Et_2O/hexane) to yield **91b** (40.3 mg, 62% yield) in 93% ee as a colorless oil. $\mathbf{R}_f$ = 0.39 (silica, 10% EtOAc/hexane, UV). **Chiral SFC:** (AD-H, 2.5 mL/min, 20% IPA in CO_2, λ = 280 nm): t_R (minor) = 3.2 min, t_R (major) = 3.8 min.

$[\boldsymbol{\alpha}]_D^{25}$ = +18° (c = 1.0, $CHCl_3$). **^{1}H NMR (500 MHz, $CDCl_3$):** δ 7.39 – 7.35 (m, 2H), 7.30 (dd, *J* = 8.3, 7.1 Hz, 2H), 7.18 – 7.12 (m, 3H), 7.06 – 7.01 (m, 2H), 6.57 (dd, *J* = 15.6, 9.9 Hz, 1H), 6.36 (d, *J* = 15.6 Hz, 1H), 3.14 (d, *J* = 9.9 Hz, 1H), 2.31 (s, 3H), 0.03 (s, 9H). **^{13}C NMR (126 MHz, $CDCl_3$):** δ 169.7, 149.4, 142.3, 136.1, 130.9, 128.5, 127.3, 127.2, 126.8, 124.9, 121.7, 43.9, 21.3, -2.7. **FTIR (NaCl, thin film, cm^{-1}):** 3024, 2956, 1761, 1600, 1505, 1369, 1248, 1211, 1196, 1166, 1015, 910, 838. **HRMS (TOF-ESI, *m/z*):** calc'd for $C_{20}H_{24}O_2Si$ $[M+H-H_2]^+$: 323.1467; found: 323.1471.

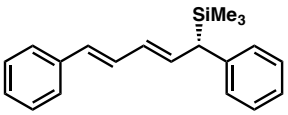
(*S*,*E*)-trimethyl(1-phenyl-3-(4-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)phenyl)-allyl)-silane (91c)



Prepared from (*E*)-1-(4-(2-bromovinyl)phenyl)-3,3,4,4-tetra-methylborolane (**29c**, 123.6 mg, 0.4 mmol) and (chloro(phenyl)-methyl)trimethylsilane (**87**, 39.8 mg, 0.2 mmol) according to General Procedure 7. The crude residue was purified by column chromatography (silica, 0 to 3% Et_2O/hexane) to yield **91c** (40.3 mg, 51% yield) in 91% ee as a white solid. Crystals of **91c** were grown by vapor diffusion (CH_2Cl_2, pentane) to provide colorless needles suitable for X-ray crystallography. $\mathbf{R_f}$ = 0.52 (silica, 10% EtOAc/hexane, UV). **m.p.** = 138-142 °C **Chiral SFC:** (AD-H, 2.5 mL/min, 20% IPA in CO_2, λ = 280 nm): t_R (minor) = 3.8 min, t_R (major) = 6.5 min. $[\boldsymbol{\alpha}]_D^{25}$ = +12° (c = 1.0, $CHCl_3$). **^{1}H NMR (500 MHz, $CDCl_3$):** δ 7.81 – 7.73 (m, 2H), 7.41 – 7.35 (m, 2H), 7.35 – 7.28 (m, 2H), 7.21 – 7.12 (m, 3H), 6.70 (dd, *J* = 15.6, 10.0 Hz, 1H), 6.39 (d, *J* = 15.6 Hz, 1H), 3.16 (d, *J* = 10.0 Hz, 1H), 1.36 (s, 12H), 0.03 (s, 9H). **^{13}C NMR (126 MHz, $CDCl_3$):** δ 142.2, 141.0, 135.2, 131.9, 128.5, 128.2, 127.3, 125.3, 124.9, 83.8, 44.2, 25.00, 24.97, -2.7. *(C*

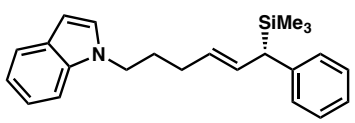
bonded to boron not observed) **FTIR (NaCl, thin film, cm^{-1}):** 2976, 2955, 2915, 1607, 1398, 1361, 1321, 1268, 1248, 1144, 1091, 964, 860, 839. **HRMS (TOF-ESI, *m/z*):** calc'd for $C_{24}H_{33}BO_2Si$ $[M+H-H_2]^+$: 391.2265; found: 391.2242.

((*S*,2*E*,4*E*)-1,5-diphenylpenta-2,4-dien-1-yl)trimethylsilane (91d)



Prepared from ((1*E*,3*E*)-4-bromobuta-1,3-dien-1-yl)benzene (**29d**, 83.6 mg, 0.4 mmol) and (chloro(phenyl)methyl)-trimethylsilane (**87**, 39.8 mg, 0.2 mmol) according to General Procedure 7. The crude residue was purified by column chromatography (silica, hexane) to yield **91d** (33.7 mg, 58% yield) in 94% ee as a colorless oil. $\mathbf{R_f}$ = 0.73 (silica, 10% EtOAc/hexane, UV). **Chiral SFC:** (AD-H, 2.5 mL/min, 10% IPA in CO_2, λ = 280 nm): t_R (minor) = 6.1 min, t_R (major) = 7.6 min. $[\boldsymbol{a}]_{\boldsymbol{D}}^{\mathbf{25}}$ = +23° (c = 1.0, $CHCl_3$). **^{1}H NMR (500 MHz, $CDCl_3$):** δ 7.43 – 7.38 (m, 2H), 7.35 – 7.28 (m, 4H), 7.24 – 7.19 (m, 1H), 7.18 – 7.12 (m, 3H), 6.89 – 6.82 (m, 1H), 6.45 (d, *J* = 15.6 Hz, 1H), 6.28 – 6.18 (m, 2H), 3.12 – 3.07 (m, 1H), 0.03 (s, 9H). **^{13}C NMR (126 MHz, $CDCl_3$):** δ 142.2, 137.9, 135.2, 129.7, 129.5, 129.1, 128.7, 128.5, 127.3, 127.1, 126.1, 124.8, 44.1, -2.7. **FTIR (NaCl, thin film, cm^{-1}):** 3081, 3059, 3022, 2955, 1632, 1597, 1495, 1448, 1248, 1074, 1056, 986, 840. **HRMS (TOF-ESI, *m/z*):** calc'd for $C_{20}H_{24}Si$ $[M+H-H_2]^+$: 291.1569; found: 291.1566.

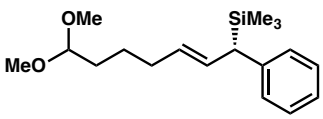
(*S*,*E*)-1-(6-phenyl-6-(trimethylsilyl)hex-4-en-1-yl)-1*H*-indole (91e)



Prepared from (*E*)-1-(5-bromopent-4-en-1-yl)-1*H*-indole (**29e**, 105.7 mg, 0.4 mmol) and (chloro(phenyl)methyl)-trimethylsilane (**87**, 39.8 mg, 0.2 mmol) according to General Procedure 7. The crude

residue was purified by column chromatography (silica, 0 to 6% Et_2O/hexane) to yield **91e** (45.1 mg, 65% yield) in 92% ee as a faint blue oil (trace CoPc impurity). The ^{1}H NMR spectrum shows minor impurities in the aryl region, therefore the purity of **91e** was determined by quantitative NMR to be 90% pure. The yield is adjusted accordingly to (65 x 0.90 = 59% yield). $\mathbf{R}_f$ = 0.59 (silica, 10% EtOAc/hexane, UV). **Chiral SFC:** (OJ-H, 2.5 mL/min, 15% IPA in CO_2, λ = 280 nm): t_R (minor) = 7.7 min, t_R (major) = 10.0 min. $[\boldsymbol{a}]_D^{25}$ = +10° (c = 1.0, $CHCl_3$). **^{1}H NMR (500 MHz, $CDCl_3$):** δ 7.71 – 7.68 (m, 1H), 7.37 (dq, *J* = 8.1, 0.9 Hz, 1H), 7.34 – 7.29 (m, 2H), 7.27 – 7.23 (m, 1H), 7.18 – 7.11 (m, 5H), 6.55 (dd, *J* = 3.1, 0.8 Hz, 1H), 5.89 (ddt, *J* = 15.0, 9.9, 1.4 Hz, 1H), 5.48 – 5.41 (m, 1H), 4.16 (t, *J* = 7.1 Hz, 2H), 2.96 (d, *J* = 9.9 Hz, 1H), 2.16 – 2.09 (m, 2H), 2.00 – 1.93 (m, 2H), 0.02 (s, 9H). **^{13}C NMR (126 MHz, $CDCl_3$):** δ 142.9, 136.0, 130.8, 128.7, 128.4, 127.9, 127.5, 127.2, 124.7, 121.4, 121.0, 119.3, 109.5, 101.0, 45.8, 43.0, 30.4, 30.2, -2.8. **FTIR (NaCl, thin film, cm^{-1}):** 2955, 1597, 1511, 1464, 1316, 1247, 1083, 968, 839. **HRMS (FAB, *m/z*):** calc'd for $C_{23}H_{29}NSi$ $[M+H]^+$: 348.2148; found: 348.2162.

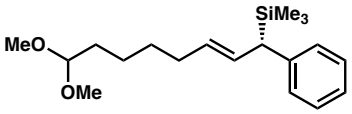
(*S*,*E*)-(7,7-dimethoxy-1-phenylhept-2-en-1-yl)trimethylsilane (91f)



Prepared from (*E*)-1-bromo-6,6-dimethoxyhex-1-ene (**29f**, 89.2 mg, 0.4 mmol) and (chloro(phenyl)methyl)trimethylsilane (**87**, 39.8 mg, 0.2 mmol) according to General Procedure 7. The crude material was dissolved in Et_2O and filtered through a pad of silica in place of the acidic aqueous workup. The crude residue was purified by column chromatography (silica, 0 to 4% Et_2O/hexane) to yield **91f** (32.7 mg, 53% yield) in 97% ee as a colorless oil. $\mathbf{R}_f$ = 0.41 (silica, 10% EtOAc/hexane, CAM). **Chiral SFC:** (OJ-H, 2.5 mL/min, 1% IPA in CO_2, λ = 235 nm): t_R

(minor) = 6.1 min, t_R (major) = 6.7 min. $[\alpha]_D^{25}$ = +22° (c = 1.0, $CHCl_3$). **^{1}H NMR (500 MHz, $CDCl_3$):** δ 7.24 (ddd, *J* = 8.1, 7.2, 1.4 Hz, 2H), 7.11 – 7.04 (m, 3H), 5.80 (ddt, *J* = 15.0, 9.9, 1.4 Hz, 1H), 5.39 (dtd, *J* = 14.9, 6.8, 0.9 Hz, 1H), 4.37 (t, *J* = 5.7 Hz, 1H), 3.31 (s, 6H), 2.89 (d, *J* = 9.9 Hz, 1H), 2.07 (td, *J* = 7.4, 6.0 Hz, 2H), 1.64 – 1.58 (m, 2H), 1.48 – 1.39 (m, 2H), -0.04 (s, 9H). **^{13}C NMR (126 MHz, $CDCl_3$):** δ 143.2, 129.8, 128.7, 128.3, 127.2, 124.5, 104.6, 52.7, 42.9, 32.8, 32.1, 24.9, -2.8. **FTIR (NaCl, thin film, cm^{-1}):** 3024, 2951, 2898, 2829, 1598, 1493, 1450, 1385, 1248, 1128, 1070, 966, 839. **HRMS (FAB, *m/z*):** calc'd for $C_{18}H_{30}O_2Si$ $[M+H-H_2]^+$: 305.1937; found: 305.1940.

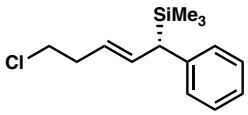
(*S*,*E*)-(8,8-dimethoxy-1-phenyloct-2-en-1-yl)trimethylsilane (91g)



Prepared from (*E*)-1-bromo-7,7-dimethoxyhept-1-ene (**29g**, 94.9 mg, 0.4 mmol) and (chloro(phenyl)methyl)trimethylsilane (**87**, 39.8 mg, 0.2 mmol) according to General Procedure 7. The crude material was dissolved in Et_2O and filtered through a pad of silica in place of the acidic aqueous workup. The crude residue was purified by column chromatography (silica, 0 to 4% Et_2O/hexane) to yield **91g** (36.7 mg, 57% yield) in 95% ee as a colorless oil. $\mathbf{R}_f$ = 0.41 (silica, 10% EtOAc/hexane, CAM). **Chiral SFC:** (OJ-H, 2.5 mL/min, 1% IPA in CO_2, λ = 210 nm): t_R (minor) = 6.0 min, t_R (major) = 7.1 min. $[\alpha]_D^{25}$ = +18° (c = 1.0, $CHCl_3$). **^{1}H NMR (500 MHz, $CDCl_3$):** δ 7.31 – 7.25 (m, 2H), 7.15 – 7.07 (m, 3H), 5.82 (ddt, *J* = 15.0, 9.9, 1.3 Hz, 1H), 5.43 (dtd, *J* = 14.9, 6.8, 0.9 Hz, 1H), 4.39 (t, *J* = 5.7 Hz, 1H), 3.35 (s, 3H), 3.34 (s, 3H), 2.92 (d, *J* = 9.9 Hz, 1H), 2.15 – 2.04 (m, 2H), 1.69 – 1.60 (m, 2H), 1.49 – 1.35 (m, 4H), 0.00 (s, 9H). **^{13}C NMR (126 MHz, $CDCl_3$):** δ 143.2, 129.5, 129.0, 128.3, 127.2, 124.5, 104.6, 52.70, 52.65, 42.9, 32.8, 32.4, 29.8, 24.3, -2.9. **FTIR (NaCl, thin film, cm^{-}**

^{1}): 3024, 2948, 2859, 2829, 1597, 1493, 1450, 1248, 1127, 1079, 1054, 965, 839. **HRMS (FAB, *m/z*):** calc'd for $C_{19}H_{32}O_2Si$ $[M+\cdot]^+$: 320.2172; found: 320.2166.

(*S*,*E*)-(5-chloro-1-phenylpent-2-en-1-yl)trimethylsilane (91h)

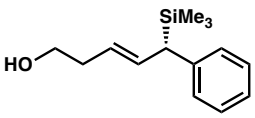


Prepared from (*E*)-1-bromo-4-chlorobut-1-ene (**29h**, 67.8 mg, 0.4 mmol) and (chloro(phenyl)methyl)trimethylsilane (**87**, 39.8 mg, 0.2 mmol) according to General Procedure 7. The crude residue was purified by column chromatography (silica, hexane) to yield **91h** (21.3 mg, 42% yield) in 95% ee as a colorless oil. When the reaction was conducted with an internal standard, the yield was determined to be 67% yield by ^{1}H NMR. $\mathbf{R_f}$ = 0.25 (silica, hexane, $KMnO_4$). **Chiral SFC:** (OD-H, 2.5 mL/min, 1% IPA in CO_2, λ = 210 nm): t_R (major) = 5.2 min, t_R (minor) = 5.9 min. $[\boldsymbol{\alpha}]_{\boldsymbol{D}}^{\mathbf{25}}$ = +25° (c = 1.0, $CHCl_3$). **^{1}H NMR (500 MHz, $CDCl_3$):** δ 7.29 – 7.23 (m, 2H), 7.13 – 7.09 (m, 1H), 7.09 – 7.05 (m, 2H), 5.94 (ddt, *J* = 15.1, 10.0, 1.3 Hz, 1H), 5.40 (dddd, *J* = 15.0, 7.4, 6.6, 1.0 Hz, 1H), 3.58 – 3.48 (m, 2H), 2.94 (d, *J* = 9.9 Hz, 1H), 2.59 – 2.46 (m, 2H), -0.02 (s, 9H). **^{13}C NMR (126 MHz, $CDCl_3$):** δ 142.6, 133.2, 128.4, 127.2, 124.7, 124.1, 44.8, 43.2, 36.2, -2.9. **FTIR (NaCl, thin film, cm^{-1}):** 3025, 2956, 2898, 159, 1494, 1450, 1248, 1081, 968, 840. **HRMS (FAB, *m/z*):** calc'd for $C_{14}H_{21}ClSi$ $[M+H]^+$: 253.1179; found: 253.1175.

The reaction was also conducted on a larger reaction scale using alkenyl bromide **29h** (3.39 g, 20.0 mmol), chlorobenzyl silane **87** (1.99 g, 10.0 mmol), **L2**·$NiCl_2$ (486 mg, 1.0 mmol), Mn powder (1.64 g, 30.0 mmol), and cobalt phthalocyanine (286 mg, 0.5 mmol) in 20 mL NMP. The reaction was stirred at 5 °C for 4 days and subsequently purified by column

chromatography (silica, hexane) to yield **91h** (1.11 g, 44% yield) in 97% ee as a colorless oil. The remaining mixed fractions were not further purified.

(*S*,*E*)-5-phenyl-5-(trimethylsilyl)pent-3-en-1-ol (91i)

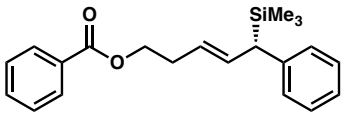


Prepared from (*E*)-4-bromobut-3-en-1-ol (**29i**, 60.4 mg, 0.4 mmol) and (chloro(phenyl)methyl)trimethylsilane (**87**, 39.8 mg, 0.2 mmol) according to General Procedure 7. The crude residue was purified by column chromatography (silica, 0 to 20% EtOAc/hexane) to yield **91i** (20.5 mg, 39% yield) in 97% ee as a faint blue oil (trace CoPc impurity). $\mathbf{R}_f$ = 0.54 (silica, 25% EtOAc/hexane, CAM). **Chiral SFC:** (OJ-H, 2.5 mL/min, 2% MeOH in CO_2, λ = 210 nm): t_R (major) = 6.5 min, t_R (minor) = 8.5 min. $[\boldsymbol{\alpha}]_D^{25}$ = +45° (c = 1.0, $CHCl_3$). **^{1}H NMR (500 MHz, $CDCl_3$):** δ 7.28 – 7.23 (m, 2H), 7.12 – 7.08 (m, 1H), 7.08 – 7.04 (m, 2H), 5.93 (ddt, *J* = 15.1, 10.0, 1.3 Hz, 1H), 5.37 (dtd, *J* = 15.0, 7.1, 0.9 Hz, 1H), 3.62 (t, *J* = 6.4 Hz, 2H), 2.94 (d, *J* = 9.9 Hz, 1H), 2.35 – 2.30 (m, 2H), 1.51 (s, 1H), -0.03 (s, 9H). **^{13}C NMR (126 MHz, $CDCl_3$):** δ 142.8, 133.2, 128.4, 127.2, 124.7, 124.5, 62.4, 43.3, 36.4, -2.9. **FTIR (NaCl, thin film, cm^{-1}):** 3340, 3024, 2954, 289, 1597, 1494, 1450, 1258, 1248, 1081, 1062, 1048, 1032, 967, 866, 839. **HRMS (FAB, *m/z*):** calc'd for $C_{14}H_{22}OSi$ $[M+H]^+$: 235.1518; found: 235.1528.

The reaction was also conducted on a larger reaction scale using alkenyl bromide **29i** (300 mg, 2.0 mmol), chlorobenzyl silane **87** (199 mg, 1.0 mmol), **L2**·$NiCl_2$ (49 mg, 0.1 mmol), Mn powder (165 mg, 3.0 mmol), and cobalt phthalocyanine (29 mg, 0.05 mmol) in 2 mL NMP. The reaction was stirred at 5 °C for 2 days and subsequently purified by column

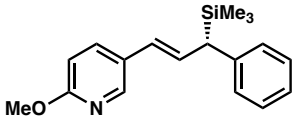
chromatography (silica, 5 to 30% Et_2O/hexane) to yield **91i** (97 mg, 41% yield) in 97% ee as a faint blue oil.

(*S*,*E*)-5-phenyl-5-(trimethylsilyl)pent-3-en-1-yl benzoate (91j)



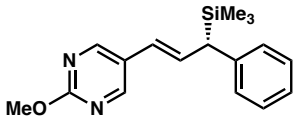
Prepared from (*E*)-4-bromobut-3-en-1-yl benzoate (**29j**, 102.0 mg, 0.4 mmol) and (chloro(phenyl)methyl)trimethylsilane (**87**, 39.8 mg, 0.2 mmol) according to General Procedure 7. The crude residue was purified by column chromatography (silica, 0 to 6% Et_2O/hexane) to yield **91j** (44.9 mg, 66% yield) in 96% ee as a colorless oil. The ^{1}H NMR spectrum shows minor impurities in the aryl region, therefore the purity of **91j** was determined by quantitative NMR to be 97% pure. The yield is adjusted accordingly to (66 x 0.97 = 64% yield). $\mathbf{R_f}$ = 0.52 (silica, 10% EtOAc/hexane, UV). **Chiral SFC:** (OJ-H, 2.5 mL/min, 10% IPA in CO_2, λ = 230 nm): t_R (major) = 3.1 min, t_R (minor) = 4.4 min. $[\boldsymbol{a}]_D^{25}$ = +15° (c = 1.0, $CHCl_3$). **^{1}H NMR (500 MHz, $CDCl_3$):** δ 8.08 – 8.04 (m, 2H), 7.60 – 7.55 (m, 1H), 7.47 – 7.42 (m, 2H), 7.31 – 7.25 (m, 2H), 7.16 – 7.12 (m, 1H), 7.12 – 7.07 (m, 2H), 6.00 (ddq, *J* = 15.1, 10.0, 1.2 Hz, 1H), 5.49 (dtt, *J* = 14.8, 6.9, 0.8 Hz, 1H), 4.38 (t, *J* = 6.6 Hz, 2H), 2.97 (d, *J* = 9.9 Hz, 1H), 2.56 (qd, *J* = 6.5, 1.1 Hz, 2H), -0.02 (d, *J* = 0.6 Hz, 9H). **^{13}C NMR (126 MHz, $CDCl_3$):** δ 166.6, 142.6, 132.8, 132.7, 130.4, 129.6, 128.3 (2C), 127.1, 124.6, 123.8, 64.7, 43.1, 32.4, -2.99. **FTIR (NaCl, thin film, cm^{-1}):** 2956, 1722, 1601, 1493, 1452, 1314, 1275, 1176, 1114, 1070, 1027, 967, 839. **HRMS (TOF-ESI, *m/z*):** calc'd for $C_{21}H_{26}O_2Si$ $[M+H]^+$: 339.1780; found: 339.1755.

(*S*,*E*)-2-methoxy-5-(3-phenyl-3-(trimethylsilyl)prop-1-en-1-yl)pyridine (91k)



Prepared from (*E*)-5-(2-bromovinyl)-2-methoxypyridine (**29k**, 85.6 mg, 0.4 mmol) and (chloro(phenyl)methyl)trimethylsilane (**87**, 39.8 mg, 0.2 mmol) according to General Procedure 7. The crude residue was purified by column chromatography (silica, 0 to 4% Et_2O/hexane) to yield **91k** (40.6 mg, 68% yield) in 94% ee as a colorless oil. $\mathbf{R_f}$ = 0.45 (silica, 10% EtOAc/hexane, UV). **Chiral SFC:** (OB-H, 2.5 mL/min, 1% IPA in CO_2, λ = 280 nm): t_R (minor) = 7.8 min, t_R (major) = 9.4 min. $[\alpha]_D^{25}$ = +35° (c = 1.0, $CHCl_3$). **^{1}H NMR (500 MHz, $CDCl_3$):** δ 8.07 (dt, *J* = 2.6, 0.6 Hz, 1H), 7.64 (ddd, *J* = 8.6, 2.5, 0.5 Hz, 1H), 7.32 – 7.26 (m, 2H), 7.17 – 7.11 (m, 3H), 6.70 (dt, *J* = 8.6, 0.6 Hz, 1H), 6.48 (dd, *J* = 15.7, 9.9 Hz, 1H), 6.29 (d, *J* = 15.6 Hz, 1H), 3.93 (s, 3H), 3.12 (d, *J* = 9.9 Hz, 1H), 0.02 (s, 9H). **^{13}C NMR (126 MHz, $CDCl_3$):** δ 163.1, 144.7, 142.3, 135.3, 130.1, 128.5, 127.4, 127.2, 124.9, 124.2, 110.8, 53.6, 44.0, -2.7. **FTIR (NaCl, thin film, cm^{-1}):** 3022, 2951, 2899, 1600, 1567, 1492, 1384, 1287, 1249, 1028, 959, 838. **HRMS (FAB, *m/z*):** calc'd for $C_{18}H_{23}NOSi$ $[M+H]^+$: 298.1627; found: 298.1616.

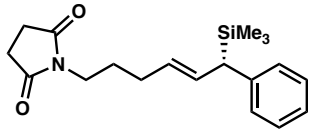
(*S*,*E*)-2-methoxy-5-(3-phenyl-3-(trimethylsilyl)prop-1-en-1-yl)pyrimidine (91l)



Prepared from (*E*)-5-(2-bromovinyl)-2-methoxypyrimidine (**29l**, 86.0 mg, 0.4 mmol) and (chloro(phenyl)methyl)trimethylsilane (**87**, 39.8 mg, 0.2 mmol) according to General Procedure 7. The crude residue was purified by column chromatography (silica, 0 to 20% Et_2O/hexane) to yield **91l** (26.2 mg, 44% yield) in 94% ee as a faint blue oil (trace CoPc impurity). $\mathbf{R_f}$ = 0.18 (silica, 10% EtOAc/hexane, UV). **Chiral SFC:** (OJ-H, 2.5 mL/min, 5% IPA in CO_2, λ = 254 nm): t_R

(minor) = 11.7 min, t_R (major) = 13.2 min. $[\alpha]_D^{25}$ = +34° (c = 1.0, $CHCl_3$). **^{1}H NMR (500 MHz, $CDCl_3$):** δ 8.47 (s, 2H), 7.32 – 7.27 (m, 2H), 7.17 – 7.10 (m, 3H), 6.56 (dd, *J* = 15.8, 9.9 Hz, 1H), 6.21 (d, *J* = 16.0 Hz, 1H), 4.00 (s, 3H), 3.12 (dd, *J* = 9.9, 1.0 Hz, 1H), 0.02 (s, 9H). **^{13}C NMR (126 MHz, $CDCl_3$):** δ 164.5, 156.2, 141.6, 132.6, 128.7, 127.2, 125.7, 125.1, 120.5, 55.0, 44.4, -2.7. **FTIR (NaCl, thin film, cm^{-1}):** 3023, 2956, 2899, 1593, 1553, 1473, 1410, 1330, 1248, 1047, 1030, 963, 840. **HRMS (FAB, *m/z*):** calc'd for $C_{17}H_{22}N_2OSi$ $[M+H]^+$: 299.1580; found: 299.1591.

(*S*,*E*)-1-(6-phenyl-6-(trimethylsilyl)hex-4-en-1-yl)pyrrolidine-2,5-dione (91m)

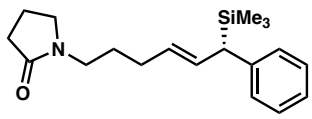


Prepared from (*E*)-1-(hex-4-en-1-yl)pyrrolidine-2,5-dione (**29m**, 98.4 mg, 0.4 mmol) and (chloro(phenyl)methyl)-trimethylsilane (**87**, 39.8 mg, 0.2 mmol) according to General Procedure 7. The crude residue was purified by column chromatography (silica, 0 to 30% acetone/hexane) to yield **91m** (42.0 mg, 64% yield) in 97% ee as a faint blue oil (trace CoPc impurity). $\mathbf{R_f}$ = 0.53 (silica, 30% acetone/hexane, CAM). **Chiral SFC:** (OJ-H, 2.5 mL/min, 5% IPA in CO_2, λ = 210 nm): t_R (minor) = 6.0 min, t_R (major) = 6.4 min. $[\alpha]_D^{25}$ = +15° (c = 1.0, $CHCl_3$). **^{1}H NMR (500 MHz, $CDCl_3$):** δ 7.23 (tt, *J* = 7.9, 1.8 Hz, 2H), 7.10 – 7.06 (m, 1H), 7.06 – 7.03 (m, 2H), 5.82 (ddt, *J* = 15.1, 10.0, 1.4 Hz, 1H), 5.36 (dtd, *J* = 15.1, 6.7, 0.9 Hz, 1H), 3.53 – 3.49 (m, 2H), 2.88 (d, *J* = 10.0 Hz, 1H), 2.63 (q, *J* = 1.4 Hz, 4H), 2.11 – 2.02 (m, 2H), 1.73 – 1.58 (m, 2H), -0.05 (s, 9H). **^{13}C NMR (126 MHz, $CDCl_3$):** δ 177.4, 143.0, 130.4, 128.3, 127.4, 127.2, 124.6, 43.0, 38.7, 30.2, 28.2, 27.7, -2.9. **FTIR (NaCl, thin film, cm^{-}**

[1]): 2950, 1774, 1703, 1437, 1402, 1369, 1344, 1248, 1158, 1129, 840. **HRMS (FAB, *m/z*):** calc'd for $C_{19}H_{27}NO_2Si$ $[M+H]^+$: 330.1889; found: 330.1880.

The reaction was also conducted on a larger reaction scale using alkenyl bromide **29m** (492 mg, 2.0 mmol), chlorobenzyl silane **87** (199 mg, 1.0 mmol), **L2**·$NiCl_2$ (49 mg, 0.1 mmol), Mn^0 powder (165 mg, 3.0 mmol), and cobalt phthalocyanine (29 mg, 0.05 mmol) in 2 mL NMP. The reaction was stirred at 5 °C for 4 days and subsequently purified by column chromatography (silica, 0 to 30% acetone/hexane) to yield **91m** (196 mg, 59% yield) in 97% ee as a faint blue oil.

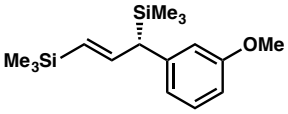
(*S*,*E*)-1-(6-phenyl-6-(trimethylsilyl)hex-4-en-1-yl)pyrrolidin-2-one (91n)



Prepared from (*E*)-1-(5-bromopent-4-en-1-yl)pyrrolidin-2-one (**29n**, 92.8 mg, 0.4 mmol) and (chloro(phenyl)methyl)-trimethylsilane (**87**, 39.8 mg, 0.2 mmol) according to General Procedure 7. The crude residue was purified by column chromatography (silica, 0 to 30% acetone/hexane) to yield **91n** (30.6 mg, 48% yield) in 96% ee as a faint blue oil (trace CoPc impurity). $\mathbf{R_f}$ = 0.44 (silica, 30% acetone/hexane, CAM). **Chiral SFC:** (OB-H, 2.5 mL/min, 5% IPA in CO_2, λ = 210 nm): t_R (major) = 6.4 min, t_R (minor) = 8.6 min. $[\boldsymbol{a}]_{\boldsymbol{D}}^{\mathbf{25}}$ = +26° (c = 0.5, $CHCl_3$). **^{1}H NMR (500 MHz, $CDCl_3$):** δ 7.26 – 7.21 (m, 2H), 7.11 – 7.06 (m, 1H), 7.06 – 7.03 (m, 2H), 5.81 (ddt, *J* = 15.1, 10.0, 1.4 Hz, 1H), 5.38 (dtd, *J* = 14.8, 6.8, 0.9 Hz, 1H), 3.39 – 3.33 (m, 2H), 3.28 (t, *J* = 7.4 Hz, 2H), 2.89 (d, *J* = 10.0 Hz, 1H), 2.37 (t, *J* = 8.1 Hz, 2H), 2.09 – 2.03 (m, 2H), 2.00 (ddd, *J* = 14.2, 8.1, 6.9 Hz, 2H), 1.59 (qt, *J* = 7.8, 3.4 Hz, 2H), -0.04 (s, 9H). **^{13}C NMR (126 MHz, $CDCl_3$):** δ 175.0, 143.1, 130.2, 128.4, 127.8, 127.2,

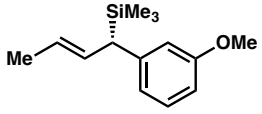
124.6, 47.3, 43.0, 42.4, 31.2, 30.3, 27.7, 18.0, -2.8. **FTIR (NaCl, thin film, cm^{-1}):** 2923, 2862, 1690, 1494, 1462, 1426, 1285, 1247, 839. **HRMS (FAB, *m/z*):** calc'd for $C_{19}H_{29}NOSi$ $[M+H]^+$: 316.2087; found: 316.2097.

(*S*,*E*)-(3-(3-methoxyphenyl)prop-1-ene-1,3-diyl)bis(trimethylsilane) (91o)



Prepared from (*E*)-(2-bromovinyl)trimethylsilane (**29o**, 71.7 mg, 0.4 mmol) and (chloro(3-methoxyphenyl)methyl)trimethylsilane (**89g**, 45.8 mg, 0.2 mmol) according to General Procedure 7. The crude residue was purified by column chromatography (silica, 0 to 15% toluene/hexane) to yield **91o** (42.0 mg, 72% yield) in 93% ee as a colorless oil. $\mathbf{R_f}$ = 0.69 (silica, 5% Et_2O/hexane, CAM). **Chiral HPLC:** (OD-H, 1.0 mL/min, hexane, λ = 230 nm): t_R (minor) = 4.5 min, t_R (major) = 4.8 min. $[\boldsymbol{\alpha}]_{\boldsymbol{D}}^{\mathbf{25}}$ = +26° (c = 1.0, $CHCl_3$). **^{1}H NMR (500 MHz, $CDCl_3$):** δ 7.20 (t, *J* = 7.9 Hz, 1H), 6.73 – 6.63 (m, 3H), 6.33 (dd, *J* = 18.3, 9.4 Hz, 1H), 5.57 (dd, *J* = 18.4, 1.1 Hz, 1H), 3.81 (s, 3H), 3.02 (dd, *J* = 9.3, 1.0 Hz, 1H), 0.08 (s, 9H), -0.02 (s, 9H). **^{13}C NMR (126 MHz, $CDCl_3$):** δ 159.7, 145.8, 144.0, 129.3, 127.8, 119.9, 113.3, 109.6, 55.2, 48.4, -0.9, -2.8. **FTIR (NaCl, thin film, cm^{-1}):** 2954, 2898, 2834, 1596, 1486, 1466, 1451, 1436, 1284, 1248, 1148, 1054, 988, 868, 838. **HRMS (EI, *m/z*):** calc'd for $C_{16}H_{28}OSi_2$ $[M+\cdot]^+$: 292.1679; found: 292.1690.

(*S*,*E*)-(1-(3-methoxyphenyl)but-2-en-1-yl)trimethylsilane (91p)

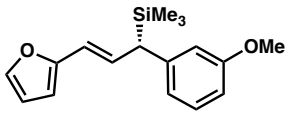


Prepared from (*E*)-1-bromoprop-1-ene (**29p**, 48.4 mg, 0.4 mmol) and (chloro(3-methoxyphenyl)methyl)trimethylsilane (**89g**, 45.8 mg, 0.2 mmol) according to General Procedure 7. The crude residue was purified by

column chromatography (silica, 0 to 10% toluene/hexane) to yield **91p** (22.1 mg, 47% yield) in 96% ee as a colorless oil. $\mathbf{R_f}$ = 0.63 (silica, 5% Et_2O/hexane, CAM). **Chiral SFC:** (OD-H, 2.5 mL/min, 3% IPA in CO_2, λ = 235 nm): t_R (major) = 3.4 min, t_R (minor) = 4.4 min. $[\boldsymbol{\alpha}]_D^{25}$ = +20° (c = 1.0, $CHCl_3$). **^{1}H NMR (500 MHz, $CDCl_3$):** δ 7.20 – 7.13 (m, 1H), 6.69 – 6.60 (m, 3H), 5.78 (ddq, *J* = 14.9, 10.0, 1.6 Hz, 1H), 5.41 (dqd, *J* = 15.0, 6.4, 0.9 Hz, 1H), 3.79 (s, 3H), 2.86 (d, *J* = 10.0 Hz, 1H), 1.70 (ddd, *J* = 6.4, 1.6, 0.6 Hz, 3H), -0.04 (s, 9H). **^{13}C NMR (126 MHz, $CDCl_3$):** δ 159.6, 145.0, 130.2, 129.2, 123.7, 119.9, 113.2, 109.6, 55.2, 43.1, 18.3, -2.8. **FTIR (NaCl, thin film, cm^{-1}):** 2956, 2917, 1598, 1579, 1487, 1436, 1290, 1258, 1247, 1149, 1050, 851, 838. **HRMS (TOF-ESI, *m/z*):** calc'd for $C_{14}H_{22}OSi$ $[M+H]^+$: 235.1518; found: 235.1498.

The reaction was also conducted with 1-bromoprop-1-ene (3:1 *cis* and *trans* mixture) (96.8 mg, 0.8 mmol, 4 equiv) and (chloro(3-methoxyphenyl)methyl)trimethylsilane (**89g**, 45.8 mg, 0.2 mmol) according to General Procedure 7. The crude residue was purified by column chromatography (silica, 0 to 20% toluene/hexane) to yield **91p** (12.5 mg, 27% yield) as a mixture of isomers (approx. 4 compounds, *E* allylic silane is the major product).

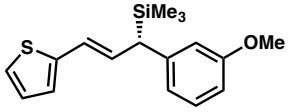
(*S*,*E*)-(3-(furan-2-yl)-1-(3-methoxyphenyl)allyl)trimethylsilane (91q)



Prepared from (*E*)-2-(2-bromovinyl)furan (**29q**, 69.2 mg, 0.4 mmol) and (chloro(3-methoxyphenyl)methyl)trimethylsilane (**89g**, 45.8 mg, 0.2 mmol) according to General Procedure 7. The crude residue was purified by column chromatography (silica, 0 to 20% toluene/hexane) to yield **91q** (35.2 mg, 61% yield) in 95% ee as a yellow oil. $\mathbf{R_f}$ = 0.38 (silica, 5% Et_2O/hexane, UV). **Chiral SFC:**

(OJ-H, 2.5 mL/min, 1% IPA in CO_2, λ = 280 nm): t_R (minor) = 9.3 min, t_R (major) = 10.3 min. $[\boldsymbol{a}]_D^{25}$ = +13° (c = 1.0, $CHCl_3$). **^{1}H NMR (500 MHz, $CDCl_3$):** δ 7.31 (dd, *J* = 1.9, 0.7 Hz, 1H), 7.20 (td, *J* = 7.6, 1.0 Hz, 1H), 6.76 – 6.72 (m, 1H), 6.71 – 6.66 (m, 2H), 6.54 (dd, *J* = 15.6, 10.0 Hz, 1H), 6.35 (dd, *J* = 3.2, 1.8 Hz, 1H), 6.17 (dd, *J* = 15.6, 1.0 Hz, 1H), 6.10 (d, *J* = 3.2 Hz, 1H), 3.81 (s, 3H), 3.04 (d, *J* = 9.8 Hz, 1H), 0.03 (s, 9H). **^{13}C NMR (126 MHz, $CDCl_3$):** δ 159.7, 153.6, 143.9, 141.2, 129.43, 129.38, 120.0, 116.8, 113.4, 111.2, 109.9, 105.8, 55.3, 44.0, -2.6. **FTIR (NaCl, thin film, cm^{-1}):** 2956, 2899, 2835, 1598, 1580,1488, 1452, 1465, 1436, 1289, 1250, 1150, 1049, 1012, 960, 839. **HRMS (FAB, *m/z*):** calc'd for $C_{17}H_{22}O_2Si$ $[M+\cdot]^+$: 286.1389; found: 286.1377.

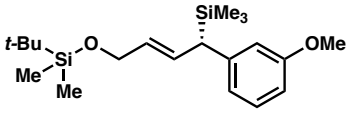
(*S*,*E*)-(1-(3-methoxyphenyl)-3-(thiophen-2-yl)allyl)trimethylsilane (91r)



Prepared from (*E*)-2-(2-bromovinyl)thiophene (**29r**, 75.6 mg, 0.4 mmol) and (chloro(3-methoxyphenyl)methyl)trimethylsilane (**89g**, 45.8 mg, 0.2 mmol) according to General Procedure 7. The crude residue was purified by column chromatography (silica, 0 to 20% toluene/hexane) to yield **91r** (34.3 mg, 57% yield) in 95% ee as a yellow oil. $\mathbf{R}_f$ = 0.44 (silica, 5% Et_2O/hexane, UV). **Chiral SFC:** (OJ-H, 2.5 mL/min, 5% IPA in CO_2, λ = 280 nm): t_R (minor) = 4.4 min, t_R (major) = 5.5 min. $[\boldsymbol{a}]_D^{25}$ = +27° (c = 1.0, $CHCl_3$). **^{1}H NMR (500 MHz, $CDCl_3$):** δ 7.25 – 7.18 (m, 1H), 7.08 (dt, *J* = 5.1, 0.9 Hz, 1H), 6.94 (dd, *J* = 5.1, 3.5 Hz, 1H), 6.87 – 6.84 (m, 1H), 6.76 – 6.71 (m, 1H), 6.71 – 6.66 (m, 2H), 6.49 (d, *J* = 15.6 Hz, 1H), 6.42 (dd, *J* = 15.4, 9.2 Hz, 1H), 3.81 (s, 3H), 3.06 (d, *J* = 9.2 Hz, 1H), 0.04 (s, 9H). **^{13}C NMR (126 MHz, $CDCl_3$):** δ 159.7, 143.8, 143.4, 130.5, 129.4, 127.4, 124.0, 122.9, 121.5, 119.9, 113.4, 109.9, 55.3, 43.9, -2.6. **FTIR (NaCl, thin film, cm^{-1}):** 3021, 2998, 2954, 2834, 1604, 1598, 1580, 1488,

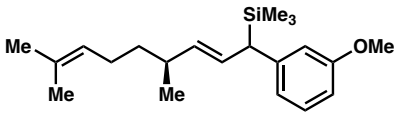
1465, 1451, 1435, 1288, 1258, 1248, 1148, 1048, 952, 838. **HRMS (FAB, *m/z*):** calc'd for $C_{17}H_{22}OSSi$ $[M+\cdot]^+$: 302.1161; found: 302.1168.

(*S*,*E*)-*tert*-butyl((4-(3-methoxyphenyl)-4-(trimethylsilyl)but-2-en-1-yl)oxy)dimethylsilane (91s)



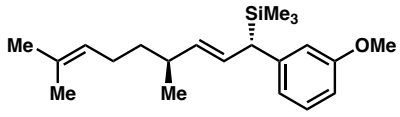
Prepared from (*E*)-((3-bromoallyl)oxy)(*tert*-butyl)dimethylsilane (**29s**, 100.5 mg, 0.4 mmol) and (chloro(3-methoxyphenyl)methyl)-trimethylsilane (**89g**, 45.8 mg, 0.2 mmol) according to General Procedure 7. The crude residue was purified by column chromatography (10% $AgNO_3$ on silica, 0 to 4% Et_2O/hexane) to yield **91s** (45.1 mg, 62% yield) in 97% ee as a colorless oil. $\mathbf{R_f}$ = 0.47 (silica, 5% Et_2O/hexane, CAM). **Chiral SFC:** (OD-H, 2.5 mL/min, 2% IPA in CO_2, λ = 210 nm): t_R (major) = 5.1 min, t_R (minor) = 7.4 min. $[\boldsymbol{\alpha}]_D^{25}$ = +14° (c = 1.0, $CHCl_3$). **^{1}H NMR (500 MHz, $CDCl_3$):** δ 7.17 (t, *J* = 7.9 Hz, 1H), 6.69 – 6.60 (m, 3H), 6.01 (ddt, *J* = 15.1, 9.9, 1.5 Hz, 1H), 5.52 (dtd, *J* = 15.0, 5.4, 1.0 Hz, 1H), 4.17 (dd, *J* = 5.4, 1.5 Hz, 2H), 3.79 (s, 3H), 2.93 (d, *J* = 9.9 Hz, 1H), 0.92 (s, 9H), 0.07 (s, 6H), -0.02 (s, 9H). **^{13}C NMR (126 MHz, $CDCl_3$):** δ 159.6, 144.3, 130.3, 129.2, 127.9, 119.9, 113.7, 109.8, 64.1, 55.2, 42.9, 26.1, 18.5, -2.8, -4.93, -4.95. **FTIR (NaCl, thin film, cm^{-1}):** 2955, 2930, 2896, 2857, 1599, 1580, 1488, 1464, 1249, 1149, 1031, 1102, 1050, 967, 837. **HRMS (FAB, *m/z*):** calc'd for $C_{20}H_{36}O_2Si_2$ $[M+H-H_2]^+$: 363.2176; found: 363.2193.

((4*S*,*E*)-1-(3-methoxyphenyl)-4,8-dimethylnona-2,7-dien-1-yl)trimethylsilane ((*rac*)-91tu)



Prepared from (*S*,*E*)-1-bromo-3,7-dimethylocta-1,6-diene (**29t**, 86.9 mg, 0.4 mmol) and (chloro(3-methoxyphenyl)methyl)-trimethylsilane (**89g**, 45.8 mg, 0.2 mmol) according to General Procedure 7, with the exception of racemic **L2** (7.8 mg, 0.022 mmol) and $NiCl_2$(dme) (4.4 mg, 0.02 mmol) in place of (*3R*,*8S*)-**L2**·$NiCl_2$. The crude residue was purified by column chromatography (silica, 0 to 15% toluene/hexane) to yield **(***1-rac,4S***)-91tu** (38.3 mg, 58% yield) in 2:1 dr (determined by NMR analysis of the purified product) as a colorless oil. Spectral data for each diastereomer are reported below. $\mathbf{R}_f$ = 0.63 (silica, 5% Et_2O/hexane, CAM). $[\alpha]_D^{25}$ = +26° (c = 1.0, $CHCl_3$). **FTIR (NaCl, thin film, cm^{-1}):** 2958, 2913, 1598, 1580, 1487, 1451, 1436, 1258, 1248, 1148, 1048, 966, 837. **HRMS (FAB, *m/z*):** calc'd for $C_{21}H_{34}OSi$ $[M+H]^+$: 331.2457; found: 331.2455.

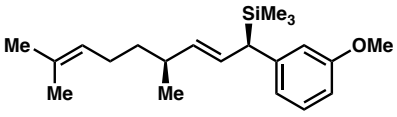
((1*S*,4*S*,*E*)-1-(3-methoxyphenyl)-4,8-dimethylnona-2,7-dien-1-yl)trimethylsilane ((*S*,*S*)-91t)



Prepared from (*S*,*E*)-1-bromo-3,7-dimethylocta-1,6-diene (**29t**, 86.9 mg, 0.4 mmol) and (chloro(3-methoxyphenyl)methyl)-trimethylsilane (**89g**, 45.8 mg, 0.2 mmol) according to General Procedure 7. The crude residue was purified by column chromatography (silica, 0 to 15% toluene/hexane) to yield (*1S*,*4S*)-**91t** (45.8 mg, 69% yield) in 40:1 dr (determined by NMR analysis of the purified product) as a colorless oil. $[\alpha]_D^{25}$ = +43° (c = 1.0, $CHCl_3$). **^{1}H NMR (500 MHz, $CDCl_3$):** δ 7.21 – 7.14 (m, 1H), 6.70 – 6.62 (m, 3H), 5.73 (ddd, *J* = 15.1, 10.0,

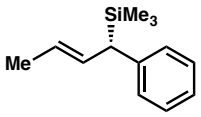
1.0 Hz, 1H), 5.26 (ddd, *J* = 15.0, 8.0, 0.9 Hz, 1H), 5.14 (tdq, *J* = 7.2, 2.9, 1.4 Hz, 1H), 3.80 (s, 3H), 2.87 (d, *J* = 9.9 Hz, 1H), 2.19 – 2.09 (m, 1H), 2.08 – 1.91 (m, 2H), 1.71 (q, *J* = 1.3 Hz, 3H), 1.62 (d, *J* = 1.3 Hz, 3H), 1.36 – 1.29 (m, 2H), 0.98 (d, *J* = 6.7 Hz, 3H), -0.02 (s, 9H). **^{13}C NMR (126 MHz, $CDCl_3$):** δ 159.6, 145.1, 135.3, 131.3, 129.2, 127.5, 124.9, 119.9, 113.2, 109.5, 55.2, 43.0, 37.6, 37.1, 26.2, 25.9, 21.3, 17.9, -2.7.

((1*R*,4*S*,*E*)-1-(3-methoxyphenyl)-4,8-dimethylnona-2,7-dien-1-yl)trimethylsilane ((*R*,*S*)-91u)



Prepared from (*S*,*E*)-1-bromo-3,7-dimethylocta-1,6-diene (**29t**, 86.9 mg, 0.4 mmol) and (chloro(3-methoxyphenyl)methyl)-trimethylsilane (**89g**, 45.8 mg, 0.2 mmol) according to General Procedure 7, with the exception of the (*3S,8R*)-**L2**·$NiCl_2$ catalyst (9.7 mg, 0.02 mmol) in place of the (*3R*,*8S*)-**L2**·$NiCl_2$ catalyst. The crude residue was purified by column chromatography (silica, 0 to 15% toluene/hexane) to yield (*1R*,*4S*)-**91u** (28.4 mg, 43% yield) in 1:19 dr (determined by NMR analysis of the purified product) as a colorless oil. $[\alpha]_D^{25}$ = –9° (c = 1.0, $CHCl_3$). **^{1}H NMR (500 MHz, $CDCl_3$):** δ 7.19 – 7.13 (m, 1H), 6.69 – 6.60 (m, 3H), 5.75 – 5.67 (m, 1H), 5.28 (ddd, *J* = 15.1, 7.7, 0.9 Hz, 1H), 5.08 (tdq, *J* = 7.2, 2.9, 1.5 Hz, 1H), 3.79 (s, 3H), 2.87 (d, *J* = 9.9 Hz, 1H), 2.18 – 2.08 (m, 1H), 1.98 – 1.90 (m, 2H), 1.67 (q, *J* = 1.3 Hz, 3H), 1.55 (d, *J* = 0.8 Hz, 3H), 1.33 – 1.25 (m, 2H), 1.00 (d, *J* = 6.7 Hz, 3H), -0.04 (s, 9H). **^{13}C NMR (126 MHz, $CDCl_3$):** δ 159.6, 145.1, 135.2, 131.3, 129.1, 127.3, 124.9, 119.9, 113.2, 109.5, 55.2, 42.9, 37.5, 36.7, 26.1, 25.9, 21.2, 17.8, -2.8.

(*S*,*E*)-trimethyl(1-phenylbut-2-en-1-yl)silane (S22)



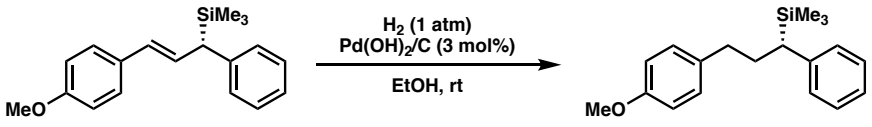
Prepared from (*E*)-1-bromoprop-1-ene (**29p**, 48.4 mg, 0.4 mmol) and (chloro(phenyl)methyl)trimethylsilane (**87**, 39.8 mg, 0.2 mmol) according to General Procedure 7. The reaction provided the desired product in 54% yield by ^{1}H NMR with an internal standard. The crude residue was purified by column chromatography (column 1 – silica, hexane and column 2 – 5% $AgNO_3$ doped silica, 1% Et_2O/hexane) to yield 7.5 mg (18% yield) of **S22** as a colorless oil. Spectral data matched those reported in the literature.[61]

The product was analyzed by optical rotation to give $[\boldsymbol{\alpha}]_{\boldsymbol{D}}^{\mathbf{25}}$ = +23° (c = 0.75, $CHCl_3$) and by comparison to a known literature value (R-isomer (94% ee), $[\boldsymbol{\alpha}]_{\boldsymbol{D}}^{\mathbf{25}}$ = –40.1° (c = 2.0, $CHCl_3$)) we have assigned our product as the S-isomer.[61]

2.6.6 Derivatization of Enantioenriched Allylic Silanes

2.6.6.1 Products from Allylic Silanes

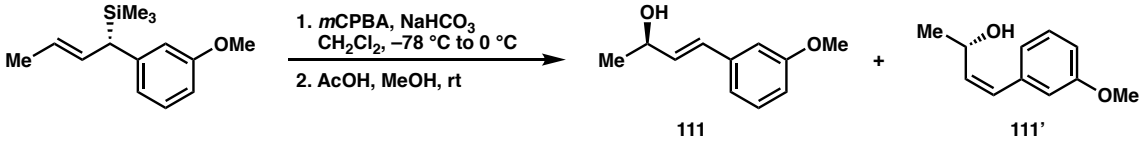
(*S*)-(3-(4-methoxyphenyl)-1-phenylpropyl)trimethylsilane (106)



The allylic silane **88c** (267 mg, 0.9 mmol, 1.0 equiv, 97% ee) was added to a 10 mL round bottom flask and dissolved in 2 mL of EtOH. $Pd(OH)_2$/C (18 mg, 0.03 mmol, 0.03 equiv, 20% Pd on carbon) was added, the flask was sealed with a rubber septum, and the headspace was purged with H_2. The reaction stirred at room temperature for 2 hours under 1 atm of H_2, and was then removed from the stir plate and filtered over a plug of silica

while eluting with Et_2O. The solution was concentrated under reduced pressure to afford 262.9 mg (98% yield) of **106** in 93% ee as a colorless oil. $\mathbf{R}_f$ = 0.34 (silica, 10% EtOAc/hexane, UV). **Chiral SFC:** (AD-H, 2.5 mL/min, 5% IPA in CO_2, λ = 210 nm): t_R (minor) = 2.6 min, t_R (major) = 3.0 min. $[\alpha]_D^{25}$ = +4° (c = 1.0, $CHCl_3$). **^{1}H NMR (500 MHz, $CDCl_3$):** δ 7.35 – 7.30 (m, 2H), 7.20 – 7.15 (m, 1H), 7.09 (ddd, *J* = 15.9, 7.4, 1.8 Hz, 4H), 6.89 – 6.85 (m, 2H), 3.83 (s, 3H), 2.66 (ddd, *J* = 13.6, 9.3, 4.0 Hz, 1H), 2.41 (ddd, *J* = 13.5, 8.7, 7.2 Hz, 1H), 2.21 – 2.00 (m, 3H), -0.01 (s, 9H). **^{13}C NMR (126 MHz, $CDCl_3$):** δ 157.7, 143.4, 134.8, 129.5, 128.3, 127.9, 124.5, 113.8, 55.3, 36.5, 34.5, 31.7, -2.9. **FTIR (NaCl, thin film, cm^{-1}):** 2953, 2934, 1612, 1512, 1451, 1247, 1177, 1039, 858, 836. **HRMS (FAB, *m/z*):** calc'd for $C_{19}H_{26}OSi$ $[M+H]^+$: 299.1831; found: 299.1834.

(*R*,*E*)-4-(3-methoxyphenyl)but-3-en-2-ol (111)

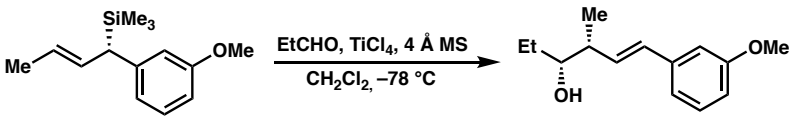


Similar to a procedure by Hayashi and coworkers,[63] the allylic silane **91p** (46.9 mg, 0.2 mmol, 1 equiv, 97% ee) and sodium bicarbonate (20 mg, 0.2 mmol, 1 equiv) were added to a 2 dram vial fitted with a magnetic stir bar and a septum. The vial was purged with N_2 and then 1.0 mL of CH_2Cl_2 was added. The mixture was cooled to –78 °C. A solution of *m*CPBA (54 mg, 77 wt%, 0.24 mmol, 1.2 equiv) in CH_2Cl_2 (1.0 mL) was added to the reaction. The vial was warmed to 0 °C and stirred for one hour, and then concentrated under reduced pressure. The crude residue was dissolved in MeOH (2.0 mL) and acetic acid (140 μL), and stirred at room temperature for 20 minutes, before being diluted with

Et_2O (0.2 mL), washed with 20% NaOH (10 mL) and water (10 mL), dried with $MgSO_4$, filtered, and concentrated under reduced pressure. The crude residue was purified by column chromatography (silica, 0 to 30% Et_2O/hexane) to yield 24.7 mg of **111**+**111'** (69% yield) as a 93:7 mixture of *E*:*Z* isomers (both in 91% ee) as a colorless oil. The stereochemistry of the alcohol is opposite for each *E*:*Z* isomer.[63] Absolute stereochemistry was assigned based on literature precedence.[63] $\mathbf{R}_f$ = 0.32 (silica, 30% EtOAc/hexane, UV). **Chiral SFC:** (OB-H, 2.5 mL/min, 10% IPA in CO_2, λ = 254 nm): *Z*-olefin, t_R (minor) = 2.8 min, t_R (major) = 3.3 min; *E*-olefin, t_R (minor) = 4.5 min, t_R (major) = 5.1 min. $[\boldsymbol{a}]_D^{25}$ = +14° (c = 1.0, $CHCl_3$). **FTIR (NaCl, thin film, cm^{-1}):** 3370, 2969, 2928, 2835, 1598, 1579, 1490, 1465, 1454, 1432, 1319, 1289, 1269, 1156, 1048, 970, 945, 868. **HRMS (FAB, *m/z*)**: calc'd for $C_{11}H_{14}O_2$ $[M+\cdot]^+$: 178.0994; found: 178.0999.

Major isomer (*R*-enantiomer, *E*-olefin): ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.23 (t, *J* = 7.9 Hz, 1H), 6.97 (dt, *J* = 7.6, 1.2 Hz, 1H), 6.92 (dd, *J* = 2.6, 1.6 Hz, 1H), 6.80 (ddd, *J* = 8.3, 2.6, 0.9 Hz, 1H), 6.53 (dd, *J* = 15.9, 1.1 Hz, 1H), 6.26 (dd, *J* = 15.9, 6.4 Hz, 1H), 4.52 – 4.45 (m, 1H), 3.81 (s, 3H), 1.83 (s, 1H), 1.37 (d, *J* = 6.4 Hz, 3H). **^{13}C NMR (126 MHz, $CDCl_3$):** δ 159.9, 138.2, 134.0, 129.7, 129.3, 119.2, 113.4, 111.8, 69.0, 55.3, 23.5.

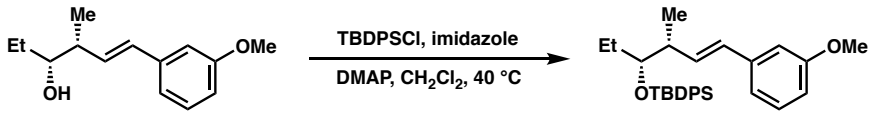
(3*R*,4*R*,*E*)-6-(3-methoxyphenyl)-4-methylhex-5-en-3-ol (113)



To a 2 dram vial equipped with a magnetic stir bar was added **91p** (46.9 mg, 0.2 mmol, 1 equiv, 97% ee) and 100 mg oven-dried 4 Å molecular sieves, and then placed under inert

atmosphere (Ar). The allylic silane was dissolved in 2.0 mL anhydrous CH_2Cl_2 (0.1 M) and the freshly distilled propionaldehyde (29 μL, 0.4 mmol, 2.0 equiv) was added via syringe. The reaction was cooled to –78 °C and stirred for 5 minutes, before the $TiCl_4$ (240 μL, 1.0 M in CH_2Cl_2, 0.24 mmol, 1.2 equiv) was added dropwise down the side of the vial. The reaction continued to stir at –78 °C for 10 minutes, before being quenched with H_2O (0.4 mL) at –78 °C and warmed to room temperature. The aqueous layer was extracted with Et_2O (3 x 20 mL), and the combined organic layers were dried with Na_2SO_4, filtered, and concentrated under reduced pressure. The crude material was purified by column chromatography (silica, 0 to 20% Et_2O/hexane) to yield 33.2 mg of **113** (75% yield) in 97% ee as a colorless oil. Absolute and relative stereochemistry was assigned based on literature precedence.[20] $\mathbf{R_f}$ = 0.48 (silica, 30% EtOAc/hexane, UV). **Chiral SFC:** (OB-H, 2.5 mL/min, 10% IPA in CO_2, λ = 254 nm): t_R (minor) = 4.8 min, t_R (major) = 6.2 min. $[\boldsymbol{\alpha}]_{\boldsymbol{D}}^{\mathbf{25}}$ = +47° (c = 1.0, $CHCl_3$). **^{1}H NMR (500 MHz, $CDCl_3$):** δ 7.22 (t, *J* = 7.9 Hz, 1H), 6.97 (ddt, *J* = 7.7, 1.5, 0.7 Hz, 1H), 6.91 (dd, *J* = 2.6, 1.6 Hz, 1H), 6.78 (ddd, *J* = 8.2, 2.6, 0.9 Hz, 1H), 6.41 (dt, *J* = 15.9, 0.7 Hz, 1H), 6.18 (dd, *J* = 15.9, 8.0 Hz, 1H), 3.82 (s, 3H), 3.49 (ddd, *J* = 8.9, 5.3, 3.7 Hz, 1H), 2.45 (dqdd, *J* = 8.0, 6.8, 5.3, 1.2 Hz, 1H), 1.62 (dqd, *J* = 13.9, 7.5, 3.8 Hz, 1H), 1.58 (s, 1H), 1.48 – 1.38 (m, 1H), 1.14 (d, *J* = 6.8 Hz, 3H), 1.00 (t, *J* = 7.4 Hz, 3H). **^{13}C NMR (126 MHz, $CDCl_3$):** δ 159.9, 139.0, 133.3, 130.3, 129.6, 118.9, 112.9, 111.5, 76.8, 55.3, 42.9, 27.3, 15.1, 10.5. **FTIR (NaCl, thin film, cm^{-1}):** 3401, 2962, 2935, 2875, 2835, 1599, 1579, 1489, 1464, 1457, 1433, 1375, 1318, 1289, 1264, 1157, 1048, 971. **HRMS (FAB, *m/z*):** calc'd for $C_{14}H_{20}O_2$ $[M+H]^+$: 221.1542; found: 221.1531.

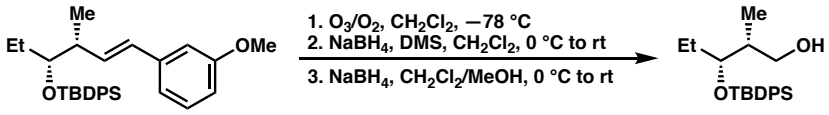
tert-butyl(((3_R_,4_R_,_E_)-6-(3-methoxyphenyl)-4-methylhex-5-en-3-yl)oxy)diphenyl-silane (S23)



Alcohol **113** (24.2 mg, 0.11 mmol, 1 equiv) was added to a 20 mL scintillation vial equipped with a magnetic stir bar, placed under inert atmosphere (N_2), and dissolved in 2 mL CH_2Cl_2. The *tert*-butyldiphenylchlorosilane (TBDPSCl, 84 µL, 0.33 mmol, 3 equiv), imidazole (30 mg, 0.44 mmol, 4 equiv), and 4-dimethylaminopyridine (DMAP, 1.3 mg, 0.011 mmol, 0.10 equiv) were added, and the reaction was heated to 40 °C and stirred for 24 hours. The reaction was then cooled to room temperature, quenched with aq. NH_4Cl (20 mL), and extracted with pentane (3 x 20 ml). The combined organic layers were dried with $MgSO_4$, filtered, and concentrated under reduced pressure. The crude material was purified by column chromatography (silica, 0 to 3% Et_2O/hexane) to yield 47.6 mg of **S23** (97% yield) as a colorless oil. $\mathbf{R_f}$ = 0.42 (silica, 5% Et_2O/hexane, UV). $[\boldsymbol{a}]_D^{25}$ = +99° (c = 1.0, $CHCl_3$). **^{1}H NMR (500 MHz, $CDCl_3$):** δ 7.73 – 7.69 (m, 4H), 7.46 – 7.40 (m, 2H), 7.40 – 7.32 (m, 4H), 7.22 (t, *J* = 7.9 Hz, 1H), 6.90 (dt, *J* = 7.7, 1.2 Hz, 1H), 6.87 (dd, *J* = 2.6, 1.6 Hz, 1H), 6.78 (ddd, *J* = 8.2, 2.6, 0.9 Hz, 1H), 6.37 – 6.28 (m, 2H), 3.82 (s, 3H), 3.69 (ddd, *J* = 6.3, 5.4, 4.0 Hz, 1H), 2.55 – 2.47 (m, 1H), 1.57 – 1.41 (m, 2H), 1.10 (s, 9H), 1.09 (d, *J* = 6.9 Hz, 3H), 0.76 (t, *J* = 7.4 Hz, 3H). **^{13}C NMR (126 MHz, $CDCl_3$):** δ 159.8, 139.5, 136.22, 136.17, 134.9, 134.7, 134.4, 129.6, 129.53, 129.50, 129.0, 127.6, 127.5, 118.9, 112.7, 111.2, 78.6, 55.3, 41.1, 27.3, 27.0, 19.7, 14.6, 10.0, 1.2. **FTIR (NaCl, thin film, cm^{-1}):** 3071, 3048, 2963, 2932, 2857, 1598, 1579, 1488, 1464, 1428, 1377, 1288, 1265,

1192, 1157, 1110, 1049, 1018, 970, 821. **HRMS (FAB, *m/z*):** calc'd for $C_{30}H_{38}O_2Si$ $[M+H–H_2]^+$: 457.2563; found: 457.2556.

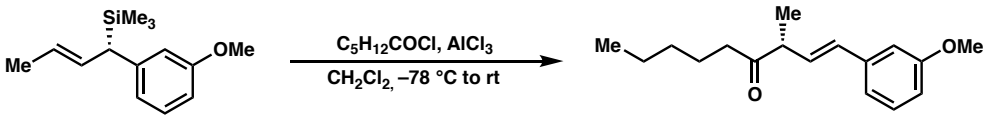
(2*R*,3*R*)-3-((*tert*-butyldiphenylsilyl)oxy)-2-methylpentan-1-ol (114)



Alkene **S23** (45.9 mg, 0.1 mmol, 1 equiv) was dissolved in 10 mL of CH_2Cl_2 in a 25 mL round bottom flask, cooled to –78 °C, and O_2 was bubbled through the solution for 2 minutes. The ozone generator was turned on and a mixture of O_3/O_2 was bubbled through the reaction until the complete consumption of **S23** by TLC (*approx. 20 minutes, at which time the solution turned blue*). The ozone generator was turned off and N_2 was bubbled through the solution for 2 minutes. Sodium borohydride (75.6 mg, 2.0 mmol, 20 equiv) and dimethylsulfide (145 μL, 2.0 mmol, 20 equiv) were added, the reaction was stirred overnight at room temperature, then quenched with aq. NH_4Cl (10 mL) and extracted with Et_2O (3 x 10 mL). The combined organic layers were dried with $MgSO_4$, filtered, and concentrated. The crude material was dissolved in 5.0 mL of CH_2Cl_2 and 5.0 mL of MeOH, cooled to 0 °C, and sodium borohydride (37.8 mg, 1.0 mmol, 10 equiv) was added. The reaction was stirred at 0 °C and warmed to room temperature over the course of 3 hours. The reaction was quenched with aq. NH_4Cl (10 mL) and extracted with Et_2O (3 x 10 mL). The combined organic layers were dried with $MgSO_4$, filtered, and concentrated under reduced pressure. The crude residue was purified by column chromatography (silica, 0 to 25% Et_2O/hexane) to yield 24.4 mg of **114** (68% yield) as a colorless oil. $\mathbf{R}_f$ = 0.42 (silica, 20% EtOAc/hexane, UV/anisaldehyde (stains dark blue)). $[\alpha]_D^{25}$ = –8° (c = 1.0, $CHCl_3$). **^{1}H**

NMR (500 MHz, $CDCl_3$): δ 7.75 – 7.66 (m, 4H), 7.48 – 7.36 (m, 6H), 3.75 (ddd, *J* = 7.3, 6.1, 2.5 Hz, 1H), 3.66 (t, *J* = 9.3 Hz, 1H), 3.51 (dt, *J* = 10.3, 4.9 Hz, 1H), 1.95 – 1.87 (m, 1H), 1.86 (s, 1H), 1.59 – 1.45 (m, 2H), 1.07 (s, 9H), 0.86 (d, *J* = 7.0 Hz, 3H), 0.64 (t, *J* = 7.5 Hz, 3H). **^{13}C NMR (126 MHz, $CDCl_3$):** δ 136.1, 134.6, 133.8, 129.9, 129.7, 127.8, 127.6, 76.8, 66.1, 38.8, 27.2, 26.4, 19.6, 10.8, 10.6. **FTIR (NaCl, thin film, cm^{-1}):** 3372, 3071, 3049, 2964, 2932, 2857, 1472, 1427, 1389, 1361, 1110, 1050, 1021, 938, 821. **HRMS (FAB, *m/z*):** calc'd for $C_{22}H_{32}O_2Si$ $[M+H-H_2]^+$: 357.2250; found: 357.2258.

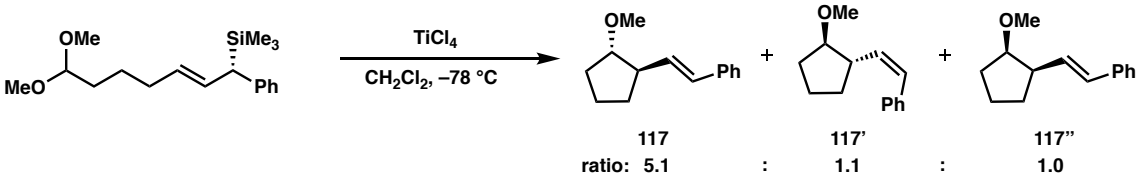
(*R*,*E*)-1-(3-methoxyphenyl)-3-methylnon-1-en-4-one (116)



To a 2 dram vial equipped with a magnetic stir bar was added **91p** (46.9 mg, 0.2 mmol, 1 equiv, 97% ee) and then placed under inert atmosphere (N_2). Anhydrous CH_2Cl_2 (2.0 mL, 0.1 M) and cooled to –78 °C. Aluminum trichloride (32 mg, 0.24 mmol, 1.2 equiv) and hexanoyl chloride (42 μL, 0.3 mmol, 1.5 equiv) were added sequentially and stirred for 10 minutes. The dry ice/acetone bath was removed and the reaction was slowly warmed for 5 minutes until the reaction turned yellow-brown. The reaction was then quenched with H_2O (0.4 mL), and the aqueous layer was extracted with Et_2O (3 x 20 mL). The combined organic layers were dried with $MgSO_4$, filtered, and concentrated under reduced pressure. The crude material was purified by column chromatography (silica, 0 to 4% Et_2O/hexane) to yield 27.8 mg of **116** (53% yield) in 90% ee as a colorless oil. Absolute stereochemistry was assigned based on mechanistic precedence in the literature.[1969] $\mathbf{R}_f$ = 0.41 (silica, 10% EtOAc/hexane, UV). **Chiral SFC:** (OB-H, 2.5 mL/min, 5% IPA in CO_2, λ = 254 nm): t_R

(minor) = 7.1 min, t_R (major) = 8.9 min. $[\alpha]_D^{25}$ = –139° (c = 1.0, $CHCl_3$). **^{1}H NMR (500 MHz, $CDCl_3$):** δ 7.23 (dd, *J* = 8.1, 7.6 Hz, 1H), 6.97 – 6.94 (m, 1H), 6.91 – 6.89 (m, 1H), 6.79 (ddd, *J* = 8.2, 2.6, 0.9 Hz, 1H), 6.48 (dd, *J* = 15.8, 0.8 Hz, 1H), 6.16 (dd, *J* = 15.8, 8.7 Hz, 1H), 3.82 (s, 3H), 3.37 (dtd, *J* = 8.6, 6.9, 5.8 Hz, 1H), 2.59 – 2.44 (m, 2H), 1.61 – 1.54 (m, 2H), 1.35 – 1.21 (m, 7H), 0.88 (t, *J* = 7.1 Hz, 3H). **^{13}C NMR (126 MHz, $CDCl_3$):** δ 211.8, 159.9, 138.4, 131.9, 129.7, 129.6, 119.0, 113.4, 111.5, 55.3, 50.8, 41.1, 31.5, 23.5, 22.6, 16.5, 14.1. **FTIR (NaCl, thin film, cm^{-1}):** 2957, 2932, 2871, 1713, 1599, 1580, 1489, 1454, 1433, 1317, 1289, 1266, 1157, 1047, 970. **HRMS (FAB, *m/z*):** calc'd for $C_{17}H_{24}O_2$ $[M+H]^+$: 261.1855; found: 261.1844.

((*E*)-2-((1*R*,2*S*)-2-methoxycyclopentyl)vinyl)benzene (117)



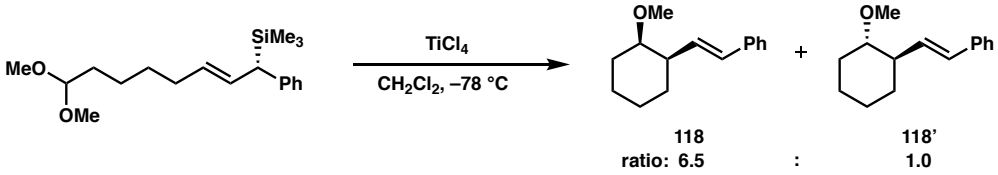
Allylic silane **91f** (23.3 mg, 0.076 mmol, 1 equiv, 97% ee) was added to a 2 dram vial equipped with a magnetic stir bar and placed under inert atmosphere (N_2). Anhydrous CH_2Cl_2 (2.0 mL, 0.038 M) was added and the reaction was cooled to –78 °C. $TiCl_4$ (91 µL, 1.0 M in CH_2Cl_2, 0.091 mmol, 1.2 equiv) was added dropwise down the side of the vial. The reaction continued to stir at –78 °C for 5 minutes, and then was quenched with H_2O (0.4 mL) at –78 °C and slowly warmed to room temperature. **Note:** If the reaction was warmed to room temperature before quenching with H_2O, the corresponding alkyl chloride was isolated. The aqueous layer was extracted with Et_2O (3 x 20 mL), and the combined organic layers were dried with $MgSO_4$, filtered, and concentrated under reduced pressure.

The crude material was purified by column chromatography (silica, 0 to 4% Et_2O/hexane) to yield 10.9 mg of **117**+**117'**+**117''** (71% yield) in 5.1:1.1:1.0 dr as determined by ^{1}H NMR analysis. The mixture of diastereomers was further purified by preparative TLC to isolate 7.8 mg (51% yield) of the major diastereomer (*E*-olefin, **117**) in 97% ee as a colorless oil, and 3.3 mg (21% yield) of a mixture of the minor diastereomers **117'**+**117''** in a 1.0:1.2 ratio as a colorless oil. Both diastereomers with the *E*-olefin (**117** and **117''**) were assigned based on comparison of ^{1}H NMR spectra to that of synthetically prepared standards. The absolute stereochemistry of **117** was assigned by optical rotation. The observed diastereoselectivity is consistent with the literature precedence on the intramolecular allylation of allylic silanes onto pendant aldehydes.[69]

Major diastereomer (*trans*-product, *E*-olefin, 117): R_f = 0.49 (silica, 10% EtOAc/hexane, UV). **Chiral SFC:** (OB-H, 2.5 mL/min, 5% IPA in CO_2, λ = 254 nm): t_R (minor) = 5.3 min, t_R (major) = 5.7 min. $[\boldsymbol{a}]_{\boldsymbol{D}}^{\mathbf{25}}$ = +80° ± 18° (c = 0.5, $CHCl_3$). **Note:** This optical rotation has a high standard deviation. **^{1}H NMR (500 MHz, $CDCl_3$):** δ 7.36 (dtd, *J* = 7.6, 1.6, 0.9 Hz, 2H), 7.29 (dd, *J* = 8.5, 6.9 Hz, 2H), 7.22 – 7.17 (m, 1H), 6.47 – 6.42 (m, 1H), 6.20 (dd, *J* = 15.8, 8.0 Hz, 1H), 3.62 – 3.57 (m, 1H), 3.35 (s, 3H), 2.70 – 2.63 (m, 1H), 2.02 – 1.90 (m, 2H), 1.81 – 1.65 (m, 3H), 1.55 – 1.46 (m, 1H). **^{13}C NMR (126 MHz, $CDCl_3$):** δ 137.7, 133.2, 129.5, 128.6, 127.1, 126.1, 88.0, 57.4, 49.5, 31.3, 30.9, 22.5. **FTIR (NaCl, thin film, cm^{-1}):** 3058, 3025, 2957, 2872, 2821, 1599, 1494, 1449, 1365, 1201, 1116, 964. **HRMS (FAB, *m/z*):** calc'd for $C_{14}H_{18}O$ $[M+\cdot]^+$: 202.1358; found: 202.1361.

Mixture of minor diastereomers (*trans*-product, *Z*-olefin, 117' + *cis*-product, *E*-olefin, 117''): R_f = 0.51 (silica, 10% EtOAc/hexane, UV). **^{1}H NMR (500 MHz, $CDCl_3$):** δ 7.40 – 7.27 (m, 9H), 7.25 – 7.16 (m, 2H), 6.46 – 6.39 (m, 3H), 5.56 (dd, *J* = 11.6, 10.3 Hz, 1H), 3.73 (td, *J* = 4.9, 2.7 Hz, 1H), 3.58 (dt, *J* = 6.5, 5.2 Hz, 1H), 3.30 (s, 3H), 3.29 (s, 3H), 3.12 – 3.04 (m, 1H), 2.68 – 2.60 (m, 1H), 2.02 – 1.90 (m, 2H), 1.89 – 1.78 (m, 5H), 1.78 – 1.60 (m, 6H), 1.47 – 1.38 (m, 1H). **^{13}C NMR (126 MHz, $CDCl_3$):** δ 138.0, 137.5, 135.7, 131.0, 129.9, 129.0, 128.9, 128.6, 128.3, 126.9, 126.8, 126.2, 88.9, 85.7, 57.3, 57.2, 48.5, 44.7, 32.0, 31.4, 30.8, 30.2, 29.9, 22.5, 22.2.

((*E*)-2-((1*R*,2*R*)-2-methoxycyclohexyl)vinyl)benzene (118)



Allylic silane **91g** (28.0 mg, 0.087 mmol, 1 equiv, 95% ee) was added to a 2 dram vial equipped with a magnetic stir bar and placed under inert atmosphere (N_2) before 2.0 mL of anhydrous CH_2Cl_2 (0.044 M) was added and the reaction was cooled to –78 °C. $TiCl_4$ (104 µL, 1.0 M in CH_2Cl_2, 0.104 mmol, 1.2 equiv) was added dropwise down the side of the vial. The reaction was stirred at –78 °C for 5 minutes, and then was quenched with H_2O (0.4 mL) at –78 °C and slowly warmed to room temperature. The aqueous layer was extracted with Et_2O (3 x 20 mL), and the combined organic layers were dried with $MgSO_4$, filtered, and concentrated under reduced pressure. The crude material was purified by column chromatography (silica, 0 to 10% Et_2O/hexane) to yield 14.2 mg of **118**+**118'** (75% yield) in 6.5:1.0 dr as determined by ^{1}H NMR analysis. The mixture of diastereomers was

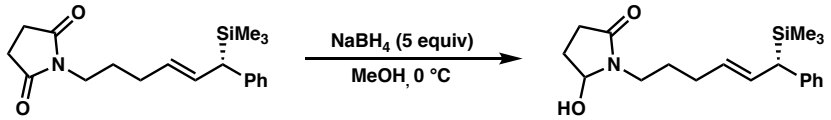
further purified by preparative TLC to isolate 12.3 mg (65% yield) of the major diastereomer (**118**) in 96% ee as a colorless oil, and 1.5 mg (8% yield) of the minor diastereomer (**118'**) in 96% ee as a colorless oil. The minor diastereomer (*trans*-product, **118'**) was assigned based on comparison of ^{1}H NMR spectra to that of a synthetically prepared standard; absolute stereochemistry was assigned by analogy (to the 5-membered ring product **117**). The absolute and relative stereochemistry of the major diastereomer (*cis*-product, **118**) was assigned by analogy (relative – to **118'**; absolute – to product **117**).

Major diastereomer (*cis*-product, 118): R_f = 0.58 (silica, 10% EtOAc/hexane, UV). **Chiral SFC:** (OB-H, 2.5 mL/min, 2% IPA in CO_2, λ = 280 nm): t_R (major) = 5.3 min, t_R (minor) = 8.4 min. $[\alpha]_D^{25}$ = –0.7° ± 0.7° (c = 1.0, $CHCl_3$). **Note:** This compound shows low optical rotation. **^{1}H NMR (500 MHz, $CDCl_3$):** δ 7.39 – 7.36 (m, 2H), 7.31 – 7.27 (m, 2H), 7.21 – 7.17 (m, 1H), 6.44 – 6.39 (m, 2H), 3.39 (dt, *J* = 6.0, 2.9 Hz, 1H), 3.33 (s, 3H), 2.51 – 2.45 (m, 1H), 1.95 – 1.86 (m, 1H), 1.75 (dtd, *J* = 13.2, 9.6, 3.8 Hz, 1H), 1.70 – 1.59 (m, 2H), 1.58 – 1.51 (m, 1H), 1.50 – 1.38 (m, 2H), 1.38 – 1.31 (m, 1H). **^{13}C NMR (126 MHz, $CDCl_3$):** δ 138.1, 132.7, 129.6, 128.5, 126.9, 126.2, 80.0, 56.5, 44.2, 28.23, 28.19, 24.3, 21.4. **FTIR (NaCl, thin film, cm^{-1}):** 3025, 2931, 2857, 2821, 1599, 1494, 1448, 1364, 1192, 1143, 1097, 1072, 966, 943. **HRMS (FAB, *m/z*):** calc'd for $C_{15}H_{20}O$ $[M+\cdot]^+$: 216.1514; found: 216.1509.

Minor diastereomer (*trans*-product, 118'): R_f = 0.52 (silica, 10% EtOAc/hexane, UV). **Chiral SFC:** (AD-H, 2.5 mL/min, 5% IPA in CO_2, λ = 280 nm): t_R (major) = 5.0 min, t_R (minor) = 6.1 min. $[\alpha]_D^{25}$ = +21° ± 8° (c = 0.1, $CHCl_3$). **Note:** This optical rotation has a

high standard deviation due to the low concentration value. **^{1}H NMR (500 MHz, $CDCl_3$):** δ 7.39 – 7.35 (m, 2H), 7.31 – 7.27 (m, 2H), 7.21 – 7.17 (m, 1H), 6.42 (d, *J* = 16.0 Hz, 1H), 6.27 (dd, *J* = 16.0, 7.5 Hz, 1H), 3.35 (s, 3H), 2.95 (td, *J* = 9.7, 4.0 Hz, 1H), 2.24 – 2.17 (m, 1H), 2.17 – 2.11 (m, 1H), 1.87 – 1.77 (m, 2H), 1.69 (tdd, *J* = 4.7, 3.1, 1.4 Hz, 1H), 1.32 – 1.19 (m, 4H). **^{13}C NMR (126 MHz, $CDCl_3$):** δ 138.1, 133.8, 129.4, 128.6, 126.9, 126.2, 83.3, 56.7, 47.3, 31.7, 30.8, 25.3, 24.7. **FTIR (NaCl, thin film, cm^{-1}):** 3025, 2928, 2856, 2820, 1600, 1493, 1448, 1361, 1190, 1123, 1100, 962. **HRMS (FAB, *m/z*):** calc'd for $C_{15}H_{20}O$ $[M+\cdot]^+$: 216.1514; found: 216.1519.

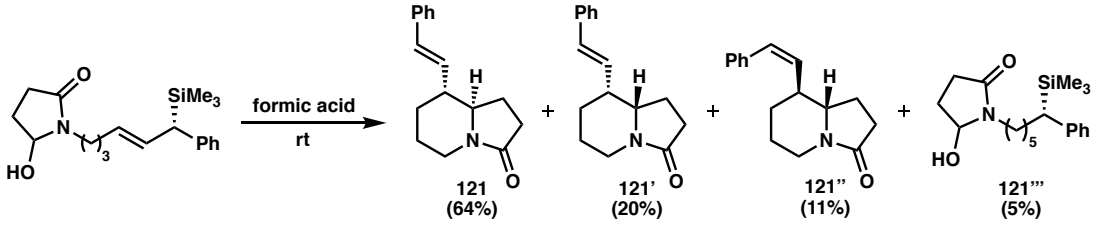
5-hydroxy-1-((*S*,*E*)-6-phenyl-6-(trimethylsilyl)hex-4-en-1-yl)pyrrolidin-2-one (120)



Similar to a procedure by Speckamp and coworkers,[73] allylic silane **91m** (49.9 mg, 0.15 mol, 1.0 equiv, 97% ee) was added to a 2 dram vial equipped with a magnetic stir bar, dissolved in 1 mL of MeOH, and cooled to 0 °C. Sodium borohydride (28.4 mg, 0.75 mmol, 5.0 equiv) was added and the reaction was stirred at 0 °C for 1 hour, then diluted with 4 mL Et_2O and quenched with 4 mL cold (0 °C) H_2O. The layers were separated and the aqueous layer was extracted with Et_2O (3 x 10 mL). The combined organic layers were dried with K_2CO_3, filtered, and concentrated under reduced pressure to afford 49.9 mg (99% yield, ~1:1 mixture of diastereomers) of **120** as a colorless oil. $\mathbf{R}_f$ = 0.26 (silica, 30% acetone/hexane, $KMnO_4$). $[\alpha]_D^{25}$ = +19° (c = 1.0, $CHCl_3$). **^{1}H NMR (500 MHz, $CDCl_3$):** δ 7.26 – 7.21 (m, 2H), 7.10 – 7.06 (m, 1H), 7.06 – 7.02 (m, 2H), 5.81 (dddd, *J* = 15.0, 10.0, 2.4, 1.3 Hz, 1H), 5.42 – 5.34 (m, 1H), 5.16 (s, 1H), 4.11 (s, 1H), 3.47 (dddd, *J* = 17.2, 8.8,

7.2, 3.8 Hz, 1H), 3.13 (ddt, *J* = 13.9, 8.9, 5.3 Hz, 1H), 2.88 (d, *J* = 10.0 Hz, 1H), 2.50 (dtdd, *J* = 12.4, 9.2, 7.0, 3.5 Hz, 1H), 2.31 – 2.19 (m, 2H), 2.05 (q, *J* = 7.2 Hz, 2H), 1.90 – 1.82 (m, 1H), 1.71 – 1.53 (m, 1H), -0.05 (s, 9H). **^{13}C NMR (126 MHz, $CDCl_3$):** δ (175.03, 175.02), 143.0, (130.17, 130.14), 128.3, (127.79, 127.76), 127.1, 124.6, (83.31, 83.29), (42.96, 42.93), (39.76, 39.72), (30.42, 30.40), (29.05, 29.02), 28.3, (27.95, 27.87), -2.9. **FTIR (NaCl, thin film, cm^{-1}):** 3333, 3024, 2954, 2866, 1668, 1652, 1493, 1464, 1422, 1262, 1247, 1072 968, 839. **HRMS (FAB, *m/z*):** calc'd for $C_{19}H_{29}NO_2Si$ $[M+H]^+$: 332.2046; found: 332.2023.

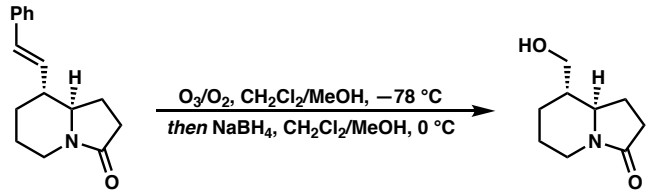
(8*R*,8a*R*)-8-((*E*)-styryl)hexahydroindolizin-3(2*H*)-one (121)



Similar to a procedure by Speckamp and coworkers,[74] allylic silane **120** (39.4 mg, 0.116 mol, 1.0 equiv) was added to a 2 dram vial equipped with a magnetic stir bar, dissolved in 1.5 mL of formic acid, and stirred at room temperature for 1 hour. The reaction was placed in a 50 °C water bath and concentrated under a gentle stream of N_2. The residue was dissolved in 10 mL CH_2Cl_2 and quenched with 6 mL aq. $NaHCO_3$. The aqueous layer was extracted with CH_2Cl_2 (3 x 10 mL). The combined organic layers were dried with K_2CO_3, filtered, and concentrated under reduced pressure to afford 28.6 mg (99% yield) of the crude mixture **121**+**121'**+**121''**+**121'''** (93% combined yield of allylation isomers **121**+**121'**+**121''**). The crude material was purified by column chromatography (silica, 14

cm diameter x 9 cm height, column repeated twice on mixed fractions, 5 to 40% acetone/hexanes) to afford 16.0 mg (57% yield) of the major diastereomer (*E*-olefin) **121** in 97% ee as a colorless oil. A portion of the minor diastereomer and *Z*-olefin were further purified by preparative TLC to remove the reduced alkene product (4.0 mg isolated). The absolute and relative stereochemistry of the minor allylation isomers **121'** and **121''** were assigned based on literature precedent for the related glutarimide analog.[75] **Major diastereomer (*E*-olefin, 121): R_f** = 0.18 (silica, 30% acetone/hexane, UV). **Chiral SFC:** (OD-H, 2.5 mL/min, 30% IPA in CO_2, λ = 254 nm): t_R (minor) = 4.4 min, t_R (major) = 4.8 min. $[\alpha]_D^{25}$ = +116° (c = 1.0, $CHCl_3$). **^{1}H NMR (400 MHz, $CDCl_3$):** δ 7.38 – 7.28 (m, 4H), 7.26 – 7.20 (m, 1H), 6.48 (d, *J* = 15.9 Hz, 1H), 6.01 (dd, *J* = 15.9, 8.1 Hz, 1H), 4.16 (ddt, *J* = 13.2, 4.5, 1.5 Hz, 1H), 3.24 (dt, *J* = 9.9, 7.2 Hz, 1H), 2.68 – 2.57 (m, 1H), 2.44 – 2.29 (m, 2H), 2.23 – 2.12 (m, 1H), 2.04 – 1.87 (m, 2H), 1.80 – 1.75 (m, 1H), 1.75 – 1.67 (m, 1H), 1.55 – 1.36 (m, 2H). **^{13}C NMR (101 MHz, $CDCl_3$):** δ 173.8, 137.1, 131.5, 130.0, 128.7, 127.6, 126.2, 61.1, 48.3, 39.9, 30.9, 30.4, 24.2, 23.9. **FTIR (NaCl, thin film, cm^{-1}):** 3025, 2932, 2854, 1683, 1493, 1436, 1421, 1370, 1315, 1295, 1267, 1143, 968. **HRMS (FAB, *m/z*):** calc'd for $C_{16}H_{19}NO$ $[M+H]^+$: 242.1545; found: 242.1520.

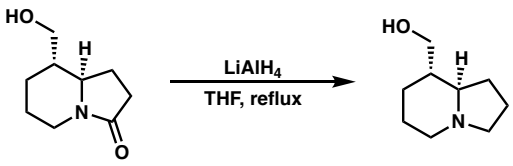
(8*S*,8a*R*)-8-(hydroxymethyl)hexahydroindolizin-3(2*H*)-one (S24)



Alkene **121** (16.0 mg, 0.066 mmol, 1.0 equiv) was added to a 25 mL round bottom flask equipped with a stir bar and dissolved in 4 mL CH_2Cl_2 and 4 mL MeOH. The flask was

cooled to –78 °C and O_2 was bubbled through the solution for 2 minutes. The ozone generator was turned on and a mixture of O_3/O_2 was bubbled through the reaction (approx. 10 minutes, at which time the solution turned blue). The ozone generator was turned off and the headspace was purged with argon. Sodium borohydride (12.5 mg, 0.33 mmol, 5 equiv) was added. The reaction was warmed to 0 °C and continued to stir for 1 hour. The solution was quenched with 4 mL sat. NH_4Cl, diluted 4 mL H_2O, and the layers were separated. The aqueous layer was extracted with 20% MeOH/CH_2Cl_2 (5 x 15 mL). The combined organic layers were dried with Na_2SO_4, filtered, and concentrated under reduced pressure. The crude material was purified by column chromatography (silica, 0 to 10% MeOH/CH_2Cl_2) to afford 7.6 mg of **S24** (68% yield) as a white solid. The NMR spectra matched those previously reported in literature.[93] $\mathbf{R_f}$ = 0.11 (silica, 5% MeOH/CH_2Cl_2, CAM (*very faint*)). $[\alpha]_D^{25}$ = +63° (c = 0.5, $CHCl_3$). **^{1}H NMR (400 MHz, $CDCl_3$):** δ 4.12 (ddt, *J* = 13.3, 4.8, 1.8 Hz, 1H), 3.67 (dd, *J* = 10.9, 4.5 Hz, 1H), 3.58 (dd, *J* = 10.8, 5.4 Hz, 1H), 3.25 (dt, *J* = 10.0, 7.4 Hz, 1H), 2.63 – 2.50 (m, 1H), 2.39 – 2.24 (m, 3H), 1.93 (dqd, *J* = 12.8, 3.1, 1.6 Hz, 1H), 1.82 – 1.66 (m, 3H), 1.47 – 1.21 (m, 3H). **^{13}C NMR (101 MHz, $CDCl_3$):** δ 174.0, 64.5, 59.1, 46.1, 40.1, 30.7, 27.1, 24.7, 24.2. **FTIR (NaCl, thin film, cm^{-1}):** 3373, 2929, 2860, 1662, 1462, 1445, 1423, 1268, 1146, 1091, 1052. **HRMS (FAB, *m/z*):** calc'd for $C_{16}H_{19}NO_2$ $[M+H]^+$: 170.1181; found: 170.1184.

(+)-Tashiromine (122)



Amide **S24** (7.8 mg, 0.045 mol, 1.0 equiv) was added to a 2 dram vial equipped with a magnetic stir bar under an atmosphere of argon and dissolved in 0.5 mL of THF. The $LiAlH_4$ (45 µL, 0.045 mmol, 1.0 equiv, 1M in Et_2O) was added to the reaction at room temperature via syringe, which was then heated to 65 °C for 15 minutes. After cooling to room temperature, the reaction was quenched with 2 µL H_2O, 2 µL 15% NaOH, and 6 µL H_2O. The mixture was filtered through a plug of celite, eluted with additional THF, and concentrated under reduced pressure to afford 7.0 mg (99% yield) of **122** as a light yellow oil. The NMR spectra matched those previously reported in literature.[71,94] $[\boldsymbol{a}]_{\boldsymbol{D}}^{\mathbf{25}}$ = +29° (c = 0.5, $CHCl_3$). **^{1}H NMR (400 MHz, $CDCl_3$):** δ 3.64 (dd, *J* = 10.8, 4.6 Hz, 1H), 3.47 (dd, *J* = 10.8, 6.5 Hz, 1H), 3.13 – 2.99 (m, 2H), 2.06 (q, *J* = 9.1 Hz, 1H), 2.00 – 1.83 (m, 3H), 1.83 – 1.59 (m, 5H), 1.59 – 1.53 (m, 1H), 1.53 – 1.40 (m, 2H), 1.04 (tdd, *J* = 12.9, 11.7, 4.6 Hz, 1H). **^{13}C NMR (101 MHz, $CDCl_3$):** δ 66.5, 65.9, 54.3, 52.8, 44.8, 29.2, 27.7, 25.3, 20.9. **FTIR (NaCl, thin film, cm^{-1}):** 3392, 2930, 2876, 2794, 1671, 1461, 1445, 1385, 1331, 1279, 1217, 1186, 1165, 1123, 1091, 1050. HRMS (FAB, m/z): calc'd for $C_9H_{17}NO$ $[M+H]^+$: 156.1388; found: 156.1377.

The product was analyzed by optical rotation to give $[\boldsymbol{a}]_{\boldsymbol{D}}^{\mathbf{25}}$ = +29° (c = 0.5, $CHCl_3$), therefore the absolute configuration is assigned opposite of that which is reported in the Jacobsen paper $[\boldsymbol{a}]_{\boldsymbol{D}}^{\mathbf{25}}$ = –41° (c = 2.0, EtOH).[71]

Table 2.9. *Comparison of ^{1}H NMR spectroscopic data for natural and synthetic tashiromine (**122**).*

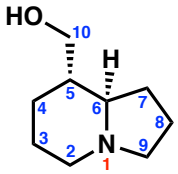
carbon number	**Natural tashiromine**[94] ^{1}H NMR, $CDCl_3$	**Jacobsen (–)-tashiromine**[71] ^{1}H NMR, $CDCl_3$	**Synthetic (+)-tashiromine** ^{1}H NMR, 400 MHz, $CDCl_3$
10	3.64 (dd, *J* = 10.0, 4.0 Hz, 1H)	3.63 (dd, *J* = 4.5, 10.5 Hz, 1H)	3.64 (dd, *J* = 10.8, 4.6 Hz, 1H)
10	3.48 (dd, *J* = 10.0, 6.0, 1H)	3.46 (dd, *J* = 7.0, 11.0 Hz, 1H)	3.47 (dd, *J* = 10.8, 6.5 Hz, 1H)
2,9	Not reported	3.03–3.10 (m, 2H),	3.13 – 2.99 (m, 2H)
9		2.05 (q, *J* = 9.0 Hz, 1H)	2.06 (q, *J* = 9.1 Hz, 1H)
2,4,7		1.43–1.97 (m, 11H)	2.00 – 1.83 (m, 3H)
8,3,10-OH			1.83 – 1.59 (m, 5H)
6			1.59 – 1.53 (m, 1H)
5,4			1.53 – 1.40 (m, 2H)
7		1.03 (qd, *J* = 5.0, 11.5 Hz, 1H)	1.04 (tdd, *J* = 12.9, 11.7, 4.6 Hz, 1H)

Table 2.10. *Comparison of ^{13}C NMR spectroscopic data for natural and synthetic tashiromine (**122**).*

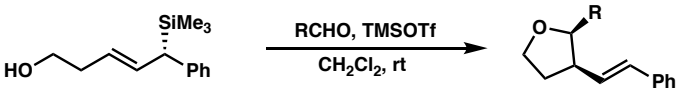
carbon number	**Natural tashiromine**[94] ^{13}C NMR, $CDCl_3$	**Jacobsen (–)-tashiromine**[71] ^{13}C NMR, $CDCl_3$	**Synthetic (+)-tashiromine** ^{13}C NMR, 101 MHz, $CDCl_3$	**Δ** from isolation	**Δ** from Jacobsen
2	52.7	52.7	52.3	-0.4	0.4
3	25.2	25.1	25.3	0.1	-0.2
4	29.2	29.1	29.2	0.0	-0.1
5	44.7	44.6	44.8	0.1	-0.2
6	66.4	66.3	66.5	0.1	-0.2
7	27.6	27.6	27.7	0.1	-0.1
8	20.3	20.7	20.9	0.6	-0.2
9	54.2	54.2	54.3	0.1	-0.1
10	65.9	65.7	65.9	0.0	-0.2

Note: The reported ^{13}C line list in the Jacobsen report is incorrect due to copy/paste error from the synthesis of compound (+)-epilupinine, however the provided ^{13}C spectrum contains the correct ^{13}C peaks for (–)-tashiromine as reported.

Tashiromine (**122**) carbon numbering as reported by Ohmiya and coworkers.[94]

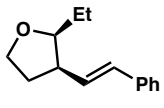


General Procedure 9: Condensation/Allylation for cis-2,3-tetrahydrofurans



On a bench-top open to an atmosphere of air, the allylic silane (0.22 mmol, 1.1 equiv), aldehyde (0.2 mmol, 1.0 equiv) and CH_2Cl_2 (2 mL, 0.1M) were added to a 25 mL round bottom flask equipped with a stir bar. The TMSOTf (0.06 mmol, 0.03 equiv) was added to the flask and the reaction was allowed to stir at room temperature for 5 minutes before being diluted with CH_2Cl_2 (6 mL). Celite (500 mg) was added to the crude mixture and the solution was concentrated under reduced pressure. The resulting powder was then loaded onto a silica column and purified via column chromatography to yield the desired product.

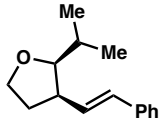
(2*S*,3*R*)-2-ethyl-3-((*E*)-styryl)tetrahydrofuran (123a)



Prepared from (*S*,*E*)-5-phenyl-5-(trimethylsilyl)pent-3-en-1-ol (**91i**, 51.6 mg, 1.1 equiv, 0.22 mmol, 98% ee) and propionaldehyde (11.6 mg, 1.0 equiv, 0.2 mmol) according to General Procedure 9. The crude residue was purified by

column chromatography (silica, 0 to 5% Et_2O/hexanes) to yield 39.6 mg of **123a** (98% yield, >20:1 dr, >20:1 *E*:*Z*, 93% major isomer) as a colorless oil. $\mathbf{R_f}$ = 0.36 (silica, 10% EtOAc/hexane, UV). $[\boldsymbol{a}]_D^{25}$ = +28° (c = 1.0, $CHCl_3$). **^{1}H NMR (500 MHz, $CDCl_3$):** δ 7.39 – 7.34 (m, 2H), 7.34 – 7.27 (m, 2H), 7.25 – 7.19 (m, 1H), 6.41 (d, *J* = 15.8 Hz, 1H), 6.18 (dd, *J* = 15.8, 9.7 Hz, 1H), 4.05 (td, *J* = 8.3, 5.9 Hz, 1H), 3.86 – 3.73 (m, 2H), 2.95 (ddt, *J* = 12.5, 10.0, 5.2 Hz, 1H), 2.22 (dddd, *J* = 12.5, 8.4, 7.5, 5.9 Hz, 1H), 1.89 (dddd, *J* = 12.6, 8.1, 6.4, 4.7 Hz, 1H), 1.62 – 1.42 (m, 2H), 0.96 (t, *J* = 7.4 Hz, 3H). **^{13}C NMR (126 MHz, $CDCl_3$):** δ 137.5, 130.7, 129.7, 128.7, 127.3, 126.2, 126.2, 84.0, 66.6, 45.7, 32.9, 24.5, 10.9. **FTIR (NaCl, thin film, cm^{-1}):** 3026, 2964, 2934, 2874, 1494, 1463, 1450, 1359, 1101, 1063, 1033, 970, 750, 694.

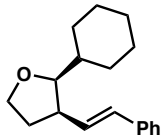
(2*S*,3*R*)-2-isopropyl-3-((*E*)-styryl)tetrahydrofuran (123b)



Prepared from (*S*,*E*)-5-phenyl-5-(trimethylsilyl)pent-3-en-1-ol (**91i**, 51.6 mg, 1.1 equiv, 0.22 mmol, 98% ee) and isobutylaldehyde (14.4 mg, 1.0 equiv, 0.2 mmol) according to General Procedure 9. The crude residue was purified by column chromatography (silica, 0 to 5% Et_2O/hexanes) to yield 44.0 mg of **123b** (99% yield, 17:1 dr, >20:1 *E*:*Z*, 92% major isomer) as a colorless oil. $\mathbf{R_f}$ = 0.45 (silica, 10% EtOAc/hexane, UV). $[\boldsymbol{a}]_D^{25}$ = +58° (c = 1.0, $CHCl_3$). **^{1}H NMR (400 MHz, $CDCl_3$):** δ 7.40 – 7.35 (m, 2H), 7.35 – 7.29 (m, 2H), 7.25 – 7.19 (m, 1H), 6.40 (s, 1H), 6.24 (dd, *J* = 15.8, 10.0 Hz, 1H), 4.06 (q, *J* = 8.0 Hz, 1H), 3.86 (ddd, *J* = 9.4, 8.4, 4.6 Hz, 1H), 3.33 (dd, *J* = 9.8, 4.5 Hz, 1H), 2.97 – 2.89 (m, 1H), 2.27 (ddt, *J* = 12.6, 9.4, 7.5 Hz, 1H), 1.88 (dddd, *J* = 12.5, 7.9, 4.6, 2.0 Hz, 1H), 1.81 – 1.70 (m, 1H), 1.05 (d, *J* = 6.5 Hz, 3H), 0.87 (d, *J* = 6.6 Hz, 3H). **^{13}C NMR (101 MHz, $CDCl_3$):** δ 137.5, 130.4, 129.6, 128.7, 127.2, 126.2, 88.8,

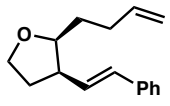
66.4, 45.0, 33.5, 29.5, 20.7, 18.9. **FTIR (NaCl, thin film, cm^{-1}):** 2958, 2872, 1494, 1450, 1388, 1066, 970, 754, 694.

(2*S*,3*R*)-2-cyclohexyl-3-((*E*)-styryl)tetrahydrofuran (123c)



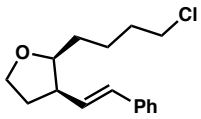
Prepared from (*S*,*E*)-5-phenyl-5-(trimethylsilyl)pent-3-en-1-ol (**91i**, 51.6 mg, 1.1 equiv, 0.22 mmol, 98% ee) and cyclohexanecarbaldehyde (22.4 mg, 1.0 equiv, 0.2 mmol) according to General Procedure 9. The crude residue was purified by column chromatography (silica, 0 to 5% Et_2O/hexanes) to yield 50.6 mg of **123c** (99% yield, >20:1 dr, >20:1 *E*:*Z*, 95% major isomer) as a colorless oil which crystallized upon standing. Crystals suitable for X-ray diffraction were grown from hexane upon standing in the freezer (–20 °C). $\mathbf{R_f}$ = 0.43 (silica, 10% EtOAc/hexane, UV). $[\boldsymbol{\alpha}]_D^{25}$ = +81° (c = 1.0, $CHCl_3$). **^{1}H NMR (400 MHz, $CDCl_3$):** δ 7.40 – 7.35 (m, 2H), 7.32 (dd, *J* = 8.5, 6.7 Hz, 2H), 7.26 – 7.20 (m, 1H), 6.41 (d, *J* = 15.8 Hz, 1H), 6.24 (dd, *J* = 15.9, 9.9 Hz, 1H), 4.04 (q, *J* = 8.0 Hz, 1H), 3.84 (ddd, *J* = 9.5, 8.4, 4.6 Hz, 1H), 3.39 (dd, *J* = 9.7, 4.5 Hz, 1H), 2.93 (dddd, *J* = 9.6, 6.8, 4.5, 1.9 Hz, 1H), 2.25 (ddt, *J* = 12.6, 9.4, 7.5 Hz, 1H), 2.08 – 1.99 (m, 1H), 1.87 (dddd, *J* = 12.5, 7.9, 4.6, 2.0 Hz, 1H), 1.77 – 1.68 (m, 2H), 1.68 – 1.60 (m, 2H), 1.48 (dddd, *J* = 13.2, 8.1, 7.0, 3.5 Hz, 1H), 1.32 – 1.12 (m, 3H), 1.05 (tdd, *J* = 12.5, 10.9, 3.5 Hz, 1H), 0.97 – 0.82 (m, 1H). **^{13}C NMR (101 MHz, $CDCl_3$):** δ 137.7, 130.4, 129.7, 128.6, 127.2, 126.2, 87.3, 66.2, 44.6, 38.9, 33.4, 31.0, 28.9, 26.6, 25.9, 25.8. **FTIR (NaCl, thin film, cm^{-1}):** 2924, 2851, 1492, 1449, 1062, 970, 884, 753, 693.

(2*S*,3*R*)-2-(but-3-en-1-yl)-3-((*E*)-styryl)tetrahydrofuran (123d)



Prepared from (*S*,*E*)-5-phenyl-5-(trimethylsilyl)pent-3-en-1-ol (**91i**, 51.6 mg, 1.1 equiv, 0.22 mmol, 98% ee) and pent-4-enal (16.8 mg, 1.0 equiv, 0.2 mmol) according to General Procedure 9. The crude residue was purified by column chromatography (silica, 0 to 5% Et_2O/hexanes) to yield 28.4 mg of **123d** (62% yield, >20:1 dr, >20:1 *E*:*Z*, 94% major isomer) as a colorless oil. $\mathbf{R_f}$ = 0.43 (silica, 10% EtOAc/hexane, UV). $[\boldsymbol{a}]_D^{25}$ = +49° (c = 1.0, $CHCl_3$). **^{1}H NMR (400 MHz, $CDCl_3$):** δ 7.39 – 7.34 (m, 2H), 7.34 – 7.29 (m, 2H), 7.25 – 7.20 (m, 1H), 6.42 (d, *J* = 15.8 Hz, 1H), 6.17 (dd, *J* = 15.8, 9.6 Hz, 1H), 5.82 (ddt, *J* = 16.9, 10.2, 6.7 Hz, 1H), 5.06 – 4.92 (m, 2H), 4.05 (td, *J* = 8.3, 5.7 Hz, 1H), 3.90 – 3.78 (m, 2H), 3.01 – 2.91 (m, 1H), 2.28 – 2.17 (m, 2H), 2.17 – 2.05 (m, 1H), 1.89 (dddd, *J* = 12.8, 8.1, 6.6, 5.0 Hz, 1H), 1.67 – 1.48 (m, 2H). **^{13}C NMR (101 MHz, $CDCl_3$):** δ 138.6, 137.4, 130.7, 129.6, 128.7, 127.3, 126.2, 126.2, 114.8, 81.7, 67.0, 45.9, 32.9, 30.9, 30.8. **FTIR (NaCl, thin film, cm^{-1}):** 3026, 2974, 2937, 2871, 1640, 1449, 1066, 1051, 969, 911, 750, 694.

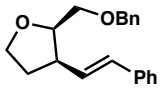
(2*S*,3*R*)-2-(4-chlorobutyl)-3-((*E*)-styryl)tetrahydrofuran (123e)



Prepared from (*S*,*E*)-5-phenyl-5-(trimethylsilyl)pent-3-en-1-ol (**91i**, 51.6 mg, 1.1 equiv, 0.22 mmol, 98% ee) and 5-chloropentanal (24.1 mg, 1.0 equiv, 0.2 mmol) according to General Procedure 9. The crude residue was purified by column chromatography (silica, 0 to 10% Et_2O/hexanes) to yield 39.9 mg of **123e** (75% yield, 8:1 dr, >20:1 *E*:*Z*, 87% major isomer) as a colorless oil. $\mathbf{R_f}$ = 0.27 (silica, 10% EtOAc/hexane, UV). $[\boldsymbol{a}]_D^{25}$ = +29° (c = 0.5, $CHCl_3$). **^{1}H NMR (400 MHz, $CDCl_3$):** δ 7.40 – 7.35 (m, 2H), 7.35 – 7.29 (m, 2H), 7.25 – 7.20 (m, 1H), 6.42 (d, *J* = 15.8 Hz, 1H), 6.16

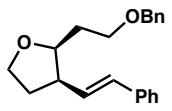
(dd, *J* = 15.8, 9.6 Hz, 1H), 4.05 (td, *J* = 8.2, 5.8 Hz, 1H), 3.87 – 3.77 (m, 2H), 3.51 (t, *J* = 6.7 Hz, 2H), 2.95 (ddt, *J* = 10.1, 7.4, 5.3 Hz, 1H), 2.22 (dddd, *J* = 12.4, 8.4, 7.5, 5.8 Hz, 1H), 1.89 (dddd, *J* = 12.7, 8.1, 6.5, 4.8 Hz, 1H), 1.84 – 1.72 (m, 2H), 1.66 – 1.41 (m, 4H). **^{13}C NMR (101 MHz, $CDCl_3$):** δ 137.4, 130.9, 129.5, 128.7, 127.3, 126.2, 82.2, 66.7, 45.9, 45.1, 32.8, 32.7, 30.8, 24.1. **FTIR (NaCl, thin film, cm^{-1}):** 2934, 2867, 1493, 1449, 1073, 1043, 970, 752, 694.

(2*R*,3*R*)-2-((benzyloxy)methyl)-3-((*E*)-styryl)tetrahydrofuran (123f)



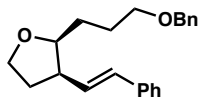
Prepared from (*S*,*E*)-5-phenyl-5-(trimethylsilyl)pent-3-en-1-ol (**91i**, 51.6 mg, 1.1 equiv, 0.22 mmol, 98% ee) and 2-(benzyloxy)acetaldehyde (30.0 mg, 1.0 equiv, 0.2 mmol) according to General Procedure 9. The crude residue was purified by column chromatography (silica, 0 to 15% Et_2O/hexanes) to yield 38.2 mg of **123f** (65% yield, 19:1 dr, 18:1 *E*:*Z*, 90% major isomer) as a colorless oil. $\mathbf{R_f}$ = 0.17 (silica, 10% EtOAc/hexane, UV). $[\alpha]_D^{25}$ = +29° (c = 1.0, $CHCl_3$). **^{1}H NMR (400 MHz, $CDCl_3$):** δ 7.38 – 7.21 (m, 10H), 6.45 (d, *J* = 15.8 Hz, 1H), 6.20 (dd, *J* = 15.8, 9.4 Hz, 1H), 4.55 (q, *J* = 12.1 Hz, 2H), 4.18 – 4.10 (m, 2H), 3.87 (q, *J* = 7.8 Hz, 1H), 3.59 – 3.50 (m, 2H), 3.09 (dq, *J* = 9.4, 6.9 Hz, 1H), 2.20 (dtd, *J* = 12.5, 7.6, 4.9 Hz, 1H), 1.98 (dtd, *J* = 12.3, 7.7, 6.4 Hz, 1H) **^{13}C NMR (101 MHz, $CDCl_3$):** δ 138.3, 137.3, 131.2, 128.8, 128.6, 128.4, 127.8, 127.6, 127.4, 126.2, 80.9, 73.6, 71.1, 67.8, 45.3, 32.9. **FTIR (NaCl, thin film, cm^{-1}):** 3027, 2919, 2861, 1495, 1451, 1361, 1076, 1027, 970, 748, 695.

(2*S*,3*R*)-2-(2-(benzyloxy)ethyl)-3-((*E*)-styryl)tetrahydrofuran (123g)



Prepared from (*S*,*E*)-5-phenyl-5-(trimethylsilyl)pent-3-en-1-ol (**91i**, 51.6 mg, 1.1 equiv, 0.22 mmol, 98% ee) and 3-(benzyloxy)propanal (32.8 mg, 1.0 equiv, 0.2 mmol) according to General Procedure 9. The crude residue was purified by column chromatography (silica, 0 to 15% Et_2O/hexanes) to yield 50.3 mg of **123g** (82% yield, 15:1 dr, 15:1 *E*:*Z*, 88% major isomer) as a colorless oil. $\mathbf{R_f}$ = 0.20 (silica, 10% EtOAc/hexane, UV). $[\boldsymbol{a}]_D^{25}$ = +49° (c = 1.0, $CHCl_3$). **^{1}H NMR (400 MHz, $CDCl_3$):** δ 7.39 – 7.20 (m, 10H), 6.40 (d, *J* = 15.8 Hz, 1H), 6.17 (dd, *J* = 15.8, 9.5 Hz, 1H), 4.57 – 4.48 (m, 2H), 4.10 – 4.02 (m, 2H), 3.83 (td, *J* = 8.3, 6.7 Hz, 1H), 3.62 (td, *J* = 6.7, 3.6 Hz, 2H), 2.97 (ddt, *J* = 9.6, 7.3, 5.5 Hz, 1H), 2.30 – 2.14 (m, 1H), 1.90 (dddd, *J* = 12.1, 8.2, 6.7, 5.1 Hz, 1H), 1.82 (q, *J* = 6.8 Hz, 2H). **^{13}C NMR (101 MHz, $CDCl_3$):** δ 138.6, 137.3, 131.0, 129.4, 128.6, 128.4, 127.8, 127.6, 127.3, 126.2, 79.2, 73.2, 68.0, 66.8, 45.9, 32.7, 31.9. **FTIR (NaCl, thin film, cm^{-1}):** 3027, 2927, 2946, 2861, 1495, 1453, 1363, 1092, 1028, 970, 750, 737, 696.

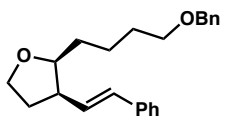
(2*S*,3*R*)-2-(3-(benzyloxy)propyl)-3-((*E*)-styryl)tetrahydrofuran (123h)



Prepared from (*S*,*E*)-5-phenyl-5-(trimethylsilyl)pent-3-en-1-ol (**91h**, 51.6 mg, 1.1 equiv, 0.22 mmol, 98% ee) and 4-(benzyloxy)butanal (35.6 mg, 1.0 equiv, 0.2 mmol) according to General Procedure 9. The crude residue was purified by column chromatography (silica, 0 to 15% Et_2O/hexanes) to yield 47.4 mg of **123h** (74% yield, >20:1 dr, 19:1 *E*:*Z*, 92% major isomer) as a colorless oil. $\mathbf{R_f}$ = 0.17 (silica, 10% EtOAc/hexane, UV). $[\boldsymbol{a}]_D^{25}$ = +33° (c = 1.0, $CHCl_3$). **^{1}H NMR (400 MHz, $CDCl_3$):** δ 7.43 – 7.20 (m, 10H), 6.43 (d, *J* = 15.8 Hz, 1H), 6.19 (dd, *J* = 15.8, 9.6 Hz, 1H), 4.49 (s, 2H),

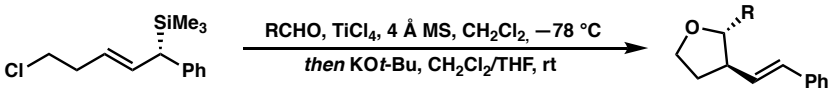
4.06 (td, *J* = 8.3, 5.7 Hz, 1H), 3.92 – 3.78 (m, 2H), 3.49 (qt, *J* = 9.3, 6.4 Hz, 2H), 3.02 – 2.92 (m, 1H), 2.22 (dtd, *J* = 13.4, 7.9, 5.6 Hz, 1H), 1.96 – 1.85 (m, 1H), 1.85 – 1.76 (m, 1H), 1.76 – 1.65 (m, 1H), 1.58 (q, *J* = 7.1 Hz, 2H). **^{13}C NMR (101 MHz, $CDCl_3$):** δ 138.7, 137.4, 130.8, 129.6, 128.6, 128.4, 127.7, 127.5, 127.3, 126.2, 82.2, 72.8, 70.3, 66.7, 45.9, 32.8, 28.2, 26.9. **FTIR (NaCl, thin film, cm^{-1}):** 3027, 2934, 2855, 1495, 1452, 1362, 1100, 1073, 1028, 970, 749, 737, 696.

(2*S*,3*R*)-2-(4-(benzyloxy)butyl)-3-((*E*)-styryl)tetrahydrofuran (123i)



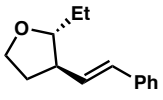
Prepared from (*S*,*E*)-5-phenyl-5-(trimethylsilyl)pent-3-en-1-ol (**91i**, 51.6 mg, 1.1 equiv, 0.22 mmol, 98% ee) and 5-(benzyloxy)pentanal (38.5 mg, 1.0 equiv, 0.2 mmol) according to General Procedure 9. The crude residue was purified by column chromatography (silica, 0 to 15% Et_2O/hexanes) to yield 40.1 mg of **123i** (60% yield, 20:1 dr, >20:1 *E*:*Z*, 92% major isomer) as a colorless oil. $\mathbf{R_f}$ = 0.23 (silica, 10% EtOAc/hexane, UV). $[\alpha]_D^{25}$ = +38° (c = 1.0, $CHCl_3$). **^{1}H NMR (400 MHz, $CDCl_3$):** δ 7.38 – 7.21 (m, 10H), 6.41 (d, *J* = 15.8 Hz, 1H), 6.17 (dd, *J* = 15.8, 9.6 Hz, 1H), 4.47 (s, 2H), 4.05 (td, *J* = 8.2, 5.8 Hz, 1H), 3.89 – 3.78 (m, 2H), 3.46 (t, *J* = 6.5 Hz, 2H), 2.99 – 2.88 (m, 1H), 2.22 (dddd, *J* = 12.5, 8.4, 7.5, 5.8 Hz, 1H), 1.88 (dddd, *J* = 12.7, 8.1, 6.4, 4.7 Hz, 1H), 1.69 – 1.39 (m, 6H). **^{13}C NMR (101 MHz, $CDCl_3$):** δ 138.8, 137.5, 130.7, 129.7, 128.7, 128.4, 127.7, 127.5, 127.3, 126.2, 82.4, 72.9, 70.4, 66.6, 45.9, 32.9, 31.3, 29.9, 23.3. **FTIR (NaCl, thin film, cm^{-1}):** 3027, 2936, 2860, 1495, 1452, 1361, 1102, 1073, 970, 750, 736, 696.

General Procedure 8: Allylation/Cyclization for trans-2,3-tetrahydrofurans



On a bench-top, a 10 mL round bottom flask equipped with a stir bar was sealed with a septum and electrical tape, then flame dried with a propane torch and backfilled with argon. Then 100 mg of oven-dried 3 Å molecular sieves were quickly added to the flask, which was subsequently evacuated and backfilled with argon. The allylic silane (0.22 mmol, 1.1 equiv), aldehyde (0.2 mmol, 1 equiv), and anhydrous CH_2Cl_2 (2.0 mL, 0.1 M) were added to the flask via syringe while under an Ar atmosphere. The reaction mixture was cooled to –78 °C and $TiCl_4$ solution (0.24 mmol, 1.2 equiv, 1 M in DCM) was added via syringe. After stirring for 10 minutes, anhydrous KOtBu solution (2 mmol, 10 equiv, 1 M in THF) was slowly added to the flask via syringe, the reaction was allowed to warm to room temperature, and continued to stir for 2 hours. The crude reaction was filtered through a plug of celite (approx. 4 cm in diameter and 1 cm thick), flushed with 50 mL of Et_2O, and concentrated under reduced pressure. The crude residue was purified by column chromatography to yield the desired product.

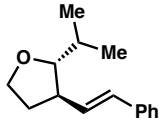
(2*R*,3*R*)-2-ethyl-3-((*E*)-styryl)tetrahydrofuran (124a)



Prepared from (*S*,*E*)-(5-chloro-1-phenylpent-2-en-1-yl)trimethylsilane (**91h**, 55.6 mg, 1.1 equiv, 0.22 mmol, 98% ee) and propionaldehyde (14.4 µl, 1.0 equiv, 0.2 mmol) according to General Procedure 8. The crude residue was purified by column chromatography (silica, 0 to 5% Et_2O/hexanes) to yield 34.6 mg of **124a** (86% yield, >20:1 dr, >20:1 *E*:*Z*, 94% major isomer) as a colorless oil. $\mathbf{R}_f$ = 0.39 (silica, 10%

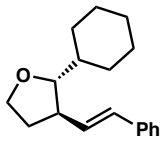
EtOAc/hexane, UV). $[\alpha]_D^{25}$ = +48° (c = 0.5, $CHCl_3$). **^{1}H NMR (500 MHz, $CDCl_3$):** δ 7.40 – 7.34 (m, 2H), 7.32 (ddd, *J* = 7.8, 6.7, 1.2 Hz, 2H), 7.25 – 7.20 (m, 1H), 6.45 (d, *J* = 15.8 Hz, 1H), 6.12 (dd, *J* = 15.8, 8.7 Hz, 1H), 3.92 (dd, *J* = 8.1, 5.9 Hz, 2H), 3.52 (td, *J* = 7.9, 4.1 Hz, 1H), 2.62 – 2.51 (m, 1H), 2.19 (ddt, *J* = 12.0, 8.1, 5.9 Hz, 1H), 1.89 (ddt, *J* = 12.4, 9.0, 8.1 Hz, 1H), 1.73 – 1.63 (m, 1H), 1.54 (dt, *J* = 13.9, 7.4 Hz, 1H), 1.01 (t, *J* = 7.4 Hz, 3H). **^{13}C NMR (126 MHz, $CDCl_3$):** δ 137.3, 131.0, 130.9, 128.7, 127.6, 126.2, 85.3, 67.3, 48.9, 33.9, 26.9, 10.8. **FTIR (NaCl, thin film, cm^{-1}):** 2964, 2932, 2875, 1493, 1450, 1116, 1020, 965, 746, 693.

(2*R*,3*R*)-2-isopropyl-3-((*E*)-styryl)tetrahydrofuran (124b)



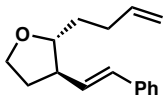
Prepared from (*S*,*E*)-(5-chloro-1-phenylpent-2-en-1-yl)trimethylsilane (**91h**, 55.6 mg, 1.1 equiv, 0.22 mmol, 98% ee) and isobutylaldehyde (18.2 µl, 1.0 equiv, 0.2 mmol) according to General Procedure 8. The crude residue was purified by column chromatography (silica, 0 to 5% Et_2O/hexanes) to yield 34.3 mg of **124b** (79% yield, >20:1 dr, >20:1 *E*:*Z*, 94% major isomer) as a colorless oil. $\mathbf{R}_f$ = 0.46 (silica, 10% EtOAc/hexane, UV). $[\alpha]_D^{25}$ = +46° (c = 1.0, $CHCl_3$). **^{1}H NMR (400 MHz, $CDCl_3$):** δ 7.39 – 7.28 (m, 4H), 7.25 – 7.19 (m, 1H), 6.43 (d, *J* = 15.8 Hz, 1H), 6.14 (dd, *J* = 15.8, 8.8 Hz, 1H), 3.93 – 3.83 (m, 2H), 3.45 (dd, *J* = 7.7, 5.5 Hz, 1H), 2.74 (p, *J* = 8.2 Hz, 1H), 2.16 (dddd, *J* = 12.0, 8.1, 6.6, 5.1 Hz, 1H), 1.92 – 1.77 (m, 2H), 0.98 (dd, *J* = 6.8, 1.0 Hz, 6H). **^{13}C NMR (101 MHz, $CDCl_3$):** δ 137.4, 132.1, 130.4, 128.7, 127.3, 126.1, 88.9, 67.5, 46.3, 34.6, 31.8, 19.7, 18.2. **FTIR (NaCl, thin film, cm^{-1}):** 3026, 2961, 2933, 2872, 1493, 1486, 1449, 1387, 1071, 1051, 965, 747, 693.

(2*R*,3*R*)-2-cyclohexyl-3-((*E*)-styryl)tetrahydrofuran (124c)



Prepared from (*S*,*E*)-(5-chloro-1-phenylpent-2-en-1-yl)trimethylsilane (**91h**, 55.6 mg, 1.1 equiv, 0.22 mmol, 98% ee) and cyclohexanecarbaldehyde (22.4 mg, 1.0 equiv, 0.2 mmol) according to General Procedure 8. The crude residue was purified by column chromatography (silica, 0 to 5% Et_2O/hexanes) to yield 27.1 mg of **124c** (53% yield, >20:1 dr, 20:1 *E*:*Z*, 91% major isomer) as a colorless oil. $\mathbf{R_f}$ = 0.42 (silica, 10% EtOAc/hexane, UV). $[\boldsymbol{a}]_D^{25}$ = +78° (c = 1.0, $CHCl_3$). **^{1}H NMR (400 MHz, $CDCl_3$):** δ 7.40 – 7.34 (m, 2H), 7.34 – 7.28 (m, 2H), 7.25 – 7.19 (m, 1H), 6.43 (d, *J* = 15.7 Hz, 1H), 6.13 (dd, *J* = 15.7, 8.8 Hz, 1H), 3.93 – 3.79 (m, 2H), 3.44 (dd, *J* = 7.6, 5.7 Hz, 1H), 2.78 (p, *J* = 8.2 Hz, 1H), 2.19 – 2.09 (m, 1H), 1.85 (dq, *J* = 12.3, 7.8 Hz, 2H), 1.79 – 1.69 (m, 3H), 1.68 – 1.61 (m, 1H), 1.49 (tdt, *J* = 11.7, 6.1, 3.3 Hz, 1H), 1.30 – 1.04 (m, 5H). **^{13}C NMR (101 MHz, $CDCl_3$):** δ 137.5, 132.1, 130.3, 128.7, 127.3, 126.1, 88.3, 67.4, 46.0, 41.9, 34.6, 30.1, 28.7, 26.7, 26.5, 26.3. **FTIR (NaCl, thin film, cm^{-1}):** 2925, 2852, 1492, 1449, 1085, 1066, 965, 887, 748, 694.

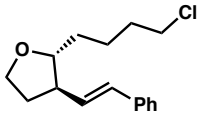
(2*R*,3*R*)-2-(but-3-en-1-yl)-3-((*E*)-styryl)tetrahydrofuran (124d)



Prepared from (*S*,*E*)-(5-chloro-1-phenylpent-2-en-1-yl)trimethylsilane (**91h**, 55.6 mg, 1.1 equiv, 0.22 mmol, 98% ee) and pent-4-enal (16.8 mg, 1.0 equiv, 0.2 mmol) according to General Procedure 8. The crude residue was purified by column chromatography (silica, 0 to 5% Et_2O/hexanes) to yield 26.5 mg of **124d** (58% yield, 10:1 dr, >20:1 *E*:*Z*, 89% major isomer) as a colorless oil. $\mathbf{R_f}$ = 0.39 (silica, 10% EtOAc/hexane, UV). $[\boldsymbol{a}]_D^{25}$ = +69° (c = 1.0, $CHCl_3$). **^{1}H NMR (400 MHz, $CDCl_3$):** δ 7.40 – 7.35 (m, 2H), 7.35 – 7.28 (m, 2H), 7.26 – 7.20 (m, 1H), 6.46 (d, *J* = 15.7 Hz, 1H), 6.11

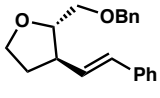
(dd, *J* = 15.8, 8.8 Hz, 1H), 5.84 (ddt, *J* = 16.8, 10.1, 6.6 Hz, 1H), 5.09 – 4.92 (m, 2H), 3.97 – 3.89 (m, 2H), 3.58 (td, *J* = 8.3, 3.7 Hz, 1H), 2.56 (p, *J* = 8.2 Hz, 1H), 2.35 – 2.10 (m, 3H), 1.89 (ddt, *J* = 12.3, 9.0, 8.1 Hz, 1H), 1.73 (dddd, *J* = 13.7, 10.0, 6.2, 3.7 Hz, 1H), 1.60 (dddd, *J* = 13.8, 9.7, 8.1, 5.3 Hz, 1H). **^{13}C NMR (101 MHz, $CDCl_3$):** δ 138.6, 137.3, 131.2, 130.6, 128.7, 127.4, 126.2, 114.7, 83.4, 67.3, 49.5, 33.9, 33.4, 30.8. **FTIR (NaCl, thin film, cm^{-1}):** 3026, 2974, 2931, 2868, 1640, 1493, 1449, 1071, 966, 911, 747, 693.

(2*R*,3*R*)-2-(4-chlorobutyl)-3-((*E*)-styryl)tetrahydrofuran (124e)



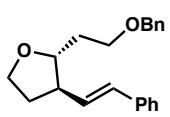
Prepared from (*S*,*E*)-(5-chloro-1-phenylpent-2-en-1-yl)trimethylsilane (**91h**, 55.6 mg, 1.1 equiv, 0.22 mmol, 98% ee) and 5-chloropentanal (24 µl, 1.0 equiv, 0.2 mmol) according to General Procedure 8. The crude residue was purified by column chromatography (silica, 0 to 6% Et_2O/hexanes) to yield 48.6 mg of **124e** (92% yield, 15:1 dr, >20:1 *E*:*Z*, 91% major isomer) as a colorless oil. $\mathbf{R_f}$ = 0.36 (silica, 10% EtOAc/hexane, UV). $[\alpha]_D^{25}$ = +64° (c = 1.0, $CHCl_3$). **^{1}H NMR (400 MHz, $CDCl_3$):** δ 7.40 – 7.28 (m, 4H), 7.25 – 7.20 (m, 1H), 6.46 (d, *J* = 15.8 Hz, 1H), 6.10 (dd, *J* = 15.7, 8.8 Hz, 1H), 3.95 – 3.88 (m, 2H), 3.59 – 3.50 (m, 3H), 2.60 – 2.49 (m, 1H), 2.20 (dddd, *J* = 12.0, 8.1, 6.4, 5.3 Hz, 1H), 1.94 – 1.85 (m, 1H), 1.85 – 1.75 (m, 2H), 1.70 – 1.62 (m, 2H), 1.57 – 1.47 (m, 2H). **^{13}C NMR (101 MHz, $CDCl_3$):** δ 137.2, 131.3, 130.5, 128.7, 127.4, 126.2, 83.7, 67.3, 49.4, 45.1, 33.8, 33.2, 32.8, 24.1. **FTIR (NaCl, thin film, cm^{-1}):** 2938, 2867, 1492, 1449, 1071, 1029, 1017, 966, 748, 693.

(2*S*,3*R*)-2-((benzyloxy)methyl)-3-((*E*)-styryl)tetrahydrofuran (124f)



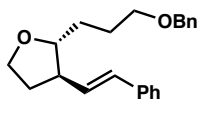
Prepared from (*S*,*E*)-(5-chloro-1-phenylpent-2-en-1-yl)trimethylsilane (**91h**, 55.6 mg, 1.1 equiv, 0.22 mmol, 98% ee) and 2-(benzyloxy)acetaldehyde (30.0 mg, 1.0 equiv, 0.2 mmol) according to General Procedure 8 with the exception that 2.0 equivalents $TiCl_4$ and 15.0 equivalents KOtBu were used in this procedure. The crude residue was purified by column chromatography (silica, 0 to 20% Et_2O/hexanes) to yield 44.2 mg of **124f** (75% yield, 1:3 dr (**Note:** trans is the minor diastereomer), >20:1 *E*:*Z*, 24% major isomer) as a yellow oil. $\mathbf{R_f}$ = 0.18 (silica, 10% EtOAc/hexane, UV). $[\boldsymbol{\alpha}]_D^{25}$ = +41° (c = 1.0, $CHCl_3$). **^{1}H NMR (400 MHz, $CDCl_3$): Note:** mixture of diastereomers, contains additional impurity: δ 7.39 – 7.16 (m, 10.00H), 6.50 – 6.34 (m, 0.74H), 6.25 – 6.07 (m, 0.75H), 4.68 – 4.46 (m, 1.88H), 4.18 – 4.03 (m, 1.36H), 4.01 – 3.92 (m, 0.42H), 3.92 – 3.79 (m, 0.94H), 3.66 (dd, *J* = 10.5, 2.9 Hz, 0.24H), 3.63 – 3.46 (m, 1.87H), 3.44 – 3.32 (m, 0.51H), 3.08 (dq, *J* = 9.4, 6.9 Hz, 0.57H), 2.80 (p, *J* = 8.5 Hz, 0.15H), 2.63 (dddt, *J* = 7.2, 4.3, 2.9, 1.4 Hz, 0.19H), 2.19 (dtd, *J* = 12.5, 7.6, 4.9 Hz, 0.74H), 2.03 – 1.85 (m, 0.83H). **^{13}C NMR (101 MHz, $CDCl_3$): Note:** mixture of diastereomers, contains additional impurity: δ 138.25, 137.19, 131.33, 131.07, 130.05, 128.74, 128.56, 128.51, 128.35, 128.33, 128.27, 127.73, 127.65, 127.56, 127.52, 127.37, 127.29, 126.16, 126.11, 80.81, 73.52, 70.99, 70.96, 67.93, 67.67, 45.23, 45.20, 36.24, 33.57, 32.81, 28.68, 27.59. **FTIR (NaCl, thin film, cm^{-1}):** 3027, 2973, 2930, 2866, 1495, 1452, 1364, 1197, 1092, 1028, 969, 748, 696.

(2*R*,3*R*)-2-(2-(benzyloxy)ethyl)-3-((*E*)-styryl)tetrahydrofuran (124g)



Prepared from (*S*,*E*)-(5-chloro-1-phenylpent-2-en-1-yl)trimethylsilane (**91h**, 55.6 mg, 1.1 equiv, 0.22 mmol, 98% ee) and 3-(benzyloxy)propanal (32.8 mg, 1.0 equiv, 0.2 mmol) according to General Procedure 8 with the exception that 2.0 equivalents $TiCl_4$ and 15.0 equivalents KOtBu were used in this procedure. The crude residue was purified by column chromatography (silica, 0 to 15% Et_2O/hexanes) to yield 35.7 mg of **124g** (58% yield, 2:1 dr, >20:1 *E*:*Z*, 63% major isomer) as a pale yellow oil. $\mathbf{R_f}$ = 0.18 (silica, 10% EtOAc/hexane, UV). $[\boldsymbol{\alpha}]_{\boldsymbol{D}}^{\mathbf{25}}$ = +38° (c = 1.0, $CHCl_3$). **^{1}H NMR (400 MHz, $CDCl_3$): Note:** mixture of diastereomers: δ 7.39 – 7.19 (m, 10H), 6.51 – 6.32 (m, 1H), 6.23 – 6.04 (m, 1H), 4.58 – 4.42 (m, 2H), 4.10 – 3.98 (m, 0.7H), 3.97 – 3.88 (m, 1.2H), 3.81 (td, *J* = 8.4, 6.7 Hz, 0.4H), 3.76 – 3.52 (m, 3H), 3.36 (t, *J* = 6.3 Hz, 0.3H), 3.01 – 2.90 (m, 0.3H), 2.59 (p, *J* = 8.4 Hz, 0.6H), 2.29 – 2.13 (m, 1H), 2.05 – 1.92 (m, 0.7H), 1.92 – 1.75 (m, 2.3H). **^{13}C NMR (101 MHz, $CDCl_3$): Note:** mixture of diastereomers: δ 138.63, 137.35, 137.25, 131.35, 131.08, 130.28, 129.46, 128.67, 128.47, 128.45, 127.83, 127.79, 127.64, 127.60, 127.41, 127.35, 126.22, 81.05, 79.21, 73.21, 73.18, 68.04, 67.91, 67.36, 66.80, 49.59, 45.97, 34.28, 33.76, 32.72, 31.95, 28.79, 27.71. **FTIR (NaCl, thin film, cm^{-1}):** 3027, 2969, 2930, 2865, 1495, 1453, 1363, 1198, 1099, 1028, 967, 748, 696.

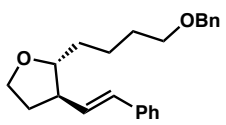
(2*R*,3*R*)-2-(3-(benzyloxy)propyl)-3-((*E*)-styryl)tetrahydrofuran (124h)



Prepared from (*S*,*E*)-(5-chloro-1-phenylpent-2-en-1-yl)trimethylsilane (**91h**, 55.6 mg, 1.1 equiv, 0.22 mmol, 98% ee) and 4-(benzyloxy)butanal (35.6 mg, 1.0 equiv, 0.2 mmol) according to General Procedure 8 with the exception that 2.0 equivalents $TiCl_4$ and 15.0 equivalents KOtBu were used in this procedure. The crude

residue was purified by column chromatography (silica, 0 to 20% Et_2O/hexanes) to yield 17.5 mg of **124h** (27% yield, 2:1 dr, >20:1 *E*:*Z*, 65% major isomer) as a yellow oil. $\mathbf{R_f}$ = 0.22 (silica, 10% EtOAc/hexane, UV). $[\boldsymbol{a}]_D^{25}$ = +13° (c = 1.0, $CHCl_3$). **^{1}H NMR (400 MHz, $CDCl_3$): Note:** mixture of diastereomers: δ 7.41 – 7.19 (m, 10.0H), 6.66 – 6.36 (m, 1H), 6.26 – 5.89 (m, 1H), 4.49 (d, *J* = 8.5 Hz, 2H), 4.04 (td, *J* = 8.2, 5.7 Hz, 0.4H), 3.97 – 3.88 (m, 1.4H), 3.88 – 3.70 (m, 0.7H), 3.59 (td, *J* = 8.2, 3.3 Hz, 0.7H), 3.55 – 3.41 (m, 2H), 3.02 – 2.89 (m, 0.3H), 2.56 (p, *J* = 8.5 Hz, 0.6H), 2.28 – 2.12 (m, 1H), 1.98 – 1.66 (m, 3.6H), 1.63 – 1.50 (m, 1.4H). **^{13}C NMR (101 MHz, $CDCl_3$): Note:** mixture of diastereomers: δ 138.75, 138.73, 137.45, 137.28, 131.17, 130.85, 130.60, 129.61, 128.68, 128.52, 128.44, 128.43, 128.37, 127.73, 127.71, 127.56, 127.40, 127.30, 126.24, 126.21, 83.78, 82.21, 72.90, 72.84, 72.79, 70.39, 70.30, 67.27, 66.70, 49.38, 45.96, 33.88, 32.84, 30.71, 28.19, 26.91, 26.77. **FTIR (NaCl, thin film, cm^{-1}):** 3060, 3027, 2933, 2857, 1495, 1453, 1363, 1203, 1100, 1073, 1028, 967, 747, 696.

(2*R*,3*R*)-2-(4-(benzyloxy)butyl)-3-((*E*)-styryl)tetrahydrofuran (124i)

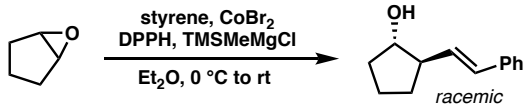


Prepared from (*S*,*E*)-(5-chloro-1-phenylpent-2-en-1-yl)trimethylsilane (**91h**, 55.6 mg, 1.1 equiv, 0.22 mmol, 98% ee) and 5-(benzyloxy)pentanal (38.5 mg, 1.0 equiv, 0.2 mmol) according to General Procedure 8 with the exception that 2.0 equivalents $TiCl_4$ and 15.0 equivalents KOtBu were used in this procedure. The crude residue was purified by column chromatography (silica, 0 to 15% Et_2O/hexanes) to yield 13.7 mg of **124i** (20% yield, 10:1 dr, >20:1 *E*:*Z*, 90% major isomer) as a colorless oil. $\mathbf{R_f}$ = 0.18 (silica, 10% EtOAc/hexane, UV). $[\boldsymbol{a}]_D^{25}$ = +48° (c = 1.0, $CHCl_3$). **^{1}H NMR (400 MHz, $CDCl_3$):** δ 7.39 – 7.12 (m, 10H), 6.44 (d, *J* = 15.7 Hz, 1H),

6.10 (dd, *J* = 15.8, 8.8 Hz, 1H), 4.48 (s, 2H), 3.90 (d, *J* = 8.1 Hz, 2H), 3.56 (td, *J* = 7.8, 3.3 Hz, 1H), 3.46 (td, *J* = 6.5, 2.8 Hz, 2H), 2.53 (p, *J* = 8.6 Hz, 1H), 2.19 (dddd, *J* = 12.0, 8.1, 6.5, 5.3 Hz, 1H), 1.93 – 1.82 (m, 1H), 1.69 – 1.45 (m, 6H). **^{13}C NMR (101 MHz, $CDCl_3$):** δ 138.8, 137.3, 131.1, 130.7, 128.7, 128.4, 127.7, 127.6, 127.4, 126.2, 84.0, 73.0, 70.5, 67.3, 49.4, 33.9, 33.9, 30.0, 23.3. **FTIR (NaCl, thin film, cm^{-1}):** 3027, 2935, 2860, 1495, 1454, 1363, 1102, 1028, 1017, 966, 747, 696.

2.6.6.2 Synthesis of Standards

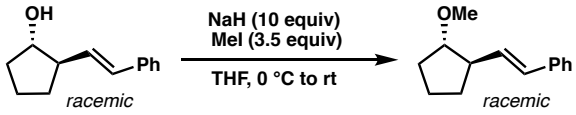
(*trans*)-2-((*E*)-styryl)cyclopentan-1-ol (S25)



According to a procedure by Oshima and coworkers,[95] 1,6-bis(diphenylphosphino)hexane ligand (DPPH, 154 mg, 0.34 mmol, 0.085 equiv) was added to a round bottom flask equipped with a stir bar and pumped into the glovebox filled with an N_2 atmosphere. Cobalt(II) bromide (61 mg, 0.28 mmol, 0.07 equiv) was added, followed by 4 mL of Et_2O. The flask sealed with a septum, and stirred for 1 hour forming a green solution. The round bottom flask was removed from the glovebox and cooled to 0 °C. Cyclopentene oxide (524 µL, 6 mmol, 1.5 equiv), styrene (460 µL, 4 mmol, 1 equiv), and (trimethylsilyl)methyl-magnesium chloride (10 mL, 1 M in Et_2O, 10 mmol, 2.5 equiv) were added sequentially. The reaction was warmed to room temperature and stirred overnight, then quenched with aq. NH_4Cl and extracted with EtOAc (2 x 80 mL). The combined organic layers were dried with $MgSO_4$, filtered, and concentrated under reduced pressure. The crude material was

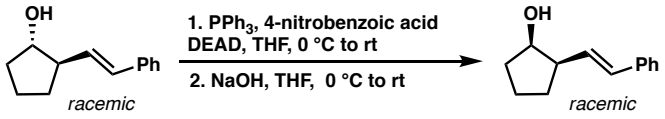
purified by column chromatography (silica, 0 to 30% EtOAc/hexane) to yield 325.6 mg of **S25** (43% yield) as a yellow oil. Spectral data matched those reported in the literature.[95]

((*E*)-2-((*trans*)-2-methoxycyclopentyl)vinyl)benzene (117)



Alcohol **S25** (10.0 mg, 0.055 mmol, 1 equiv) was added to a 1 dram vial, dissolved in THF (0.55 mL), and cooled to 0 °C. Sodium hydride (22 mg, 60 wt% in mineral oil, 0.55 mmol, 10 equiv) and methyl iodide (10.5 µl, 0.165 mmol, 3 equiv) were subsequently added, and the reaction was stirred for 30 minutes at room temperature. The reaction was quenched with aq. NH_4Cl and extracted with Et_2O. The organic layer was dried with $MgSO_4$, filtered, and concentrated under reduced pressure. The crude material was purified by preparative TLC (silica, 10% EtOAc/hexane) to yield 8.3 mg of **117** (77% yield) as a colorless oil.

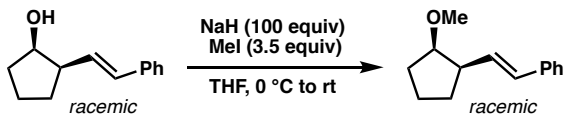
(*cis*)-2-((*E*)-styryl)cyclopentan-1-ol (S26)



Alcohol **S25** (10.0 mg, 0.055 mmol, 1 equiv) was added to a 1 dram vial, sealed with a screw-cap septum, and purged with N_2 before 0.6 mL of THF, triphenylphosphine (57 mg, 0.21 mmol, 3.8 equiv), and 4-nitrobenzoic acid (38 mg, 0.23 mmol, 4.1 equiv) were added. The vial was cooled to 0 °C, diethyl azodicarboxylate (108 mg, 40 wt% in PhMe, 4.5 equiv) was added, and the reaction was stirred at room temperature overnight. The reaction was quenched with 2 mL of 1 M HCl and extracted with Et_2O (2 x 10 mL). The combined

organic layers were dried with $MgSO_4$, filtered, and concentrated under reduced pressure to afford the crude ester product, which was carried forward without further purification. The *para*-nitrobenzoate was then added to a 1 dram vial, dissolved in 0.7 mL THF, and cooled to 0 °C. Then 5% aqueous NaOH (0.6 mL) was added and the reaction was stirred at room temperature for 8 hours. The reaction was diluted with chloroform (5 mL) and washed with H_2O (5 mL), 1 M HCl (5 mL), and brine (5 mL). The organic layer was dried with $MgSO_4$, filtered, and concentrated under reduced pressure. The crude material was purified by preparative TLC (silica, 20% EtOAc/hexane) to yield 5.7 mg of **S26** (57% yield over 2 steps) as a colorless oil. $\mathbf{R_f}$ = 0.36 (silica, 20% EtOAc/hexane, UV). **^{1}H NMR (500 MHz, $CDCl_3$):** δ 7.40 – 7.37 (m, 2H), 7.33 – 7.29 (m, 2H), 7.24 – 7.19 (m, 1H), 6.54 – 6.49 (m, 1H), 6.36 (dd, *J* = 16.0, 7.4 Hz, 1H), 4.25 (td, *J* = 4.5, 2.1 Hz, 1H), 2.67 – 2.59 (m, 1H), 1.99 – 1.89 (m, 2H), 1.87 – 1.80 (m, 2H), 1.79 – 1.71 (m, 1H), 1.71 – 1.62 (m, 1H), 1.43 (s, 1H). **^{13}C NMR (126 MHz, $CDCl_3$):** δ 137.4, 132.0, 129.4, 128.7, 127.4, 126.2, 76.1, 49.5, 34.4, 28.5, 22.3. **FTIR (NaCl, thin film, cm^{-1}):** 3405, 3081, 3058, 3025, 2959, 1599, 1495, 1448, 1327, 1154, 1121, 1073, 1027, 968. **HRMS (FAB, *m/z*):** calc'd for $C_{13}H_{16}O$ $[M+H]^+$: 189.1279; found: 189.1272.

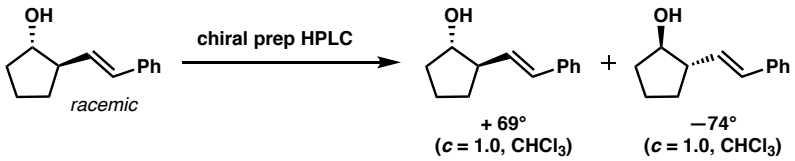
((*E*)-2-((*cis*)-2-methoxycyclopentyl)vinyl)benzene (117'')



Alcohol **S26** (5.7 mg, 0.03 mmol, 1 equiv) was added to a 1 dram vial, dissolved in THF (0.5 mL), and cooled to 0 °C. Sodium hydride (120 mg, 60 wt% in mineral oil, 3.0 mmol,

100 equiv) and methyl iodide (7 µl, 0.105 mmol, 3.5 equiv) were subsequently added, and the reaction was stirred for 30 minutes at room temperature. The reaction was quenched with aq. NH_4Cl and extracted with Et_2O. The organic layer was dried with $MgSO_4$, filtered, and concentrated under reduced pressure. The crude material was purified by preparative TLC (silica, 10% EtOAc/hexane) to yield 2.5 mg of **117''** (41% yield) as a colorless oil. The ^{1}H NMR of the purified product matches the **minor** diastereomer **117''**. $\mathbf{R_f}$ = 0.49 (silica, 10% EtOAc/hexane, UV). **^{1}H NMR (500 MHz, $CDCl_3$):** δ 7.40 – 7.36 (m, 2H), 7.31 – 7.27 (m, 2H), 7.21 – 7.16 (m, 1H), 6.46 – 6.37 (m, 2H), 3.72 (tq, *J* = 4.8, 2.4 Hz, 1H), 3.30 (s, 3H), 2.67 – 2.60 (m, 1H), 1.88 – 1.77 (m, 4H), 1.77 – 1.67 (m, 1H), 1.66 – 1.59 (m, 1H). **^{13}C NMR (126 MHz, $CDCl_3$):** δ 138.0, 131.0, 129.9, 128.6, 126.9, 126.2, 85.7, 57.2, 48.5, 30.8, 30.2, 22.2. **FTIR (NaCl, thin film, cm^{-1}):** 3025, 2926, 2821, 1599, 1495, 1448, 1356, 1128, 1094, 1073, 965, 747. **HRMS (FAB, *m/z*)**: calc'd for $C_{14}H_{18}O$ $[M+\cdot]^+$: 202.1358; found: 202.1374.

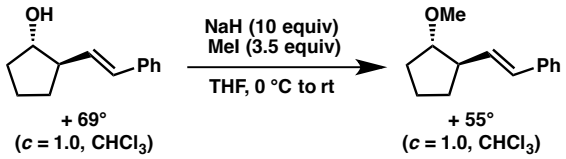
(1*S*,2*R*)-2-((*E*)-styryl)cyclopentan-1-ol and (1*R*,2*S*)-2-((*E*)-styryl)cyclopentan-1-ol



Approximately 60 mg of the racemic alcohol **S25** was separated via preparative HPLC using a chiral AD-H column and 20% isopropanol/hexane to provide 28 mg of the (+)-1*S*,2*R* enantiomer and 24 mg of the (–)-1*R*,2*S* enantiomer. The (+) enantiomer was measured to have an optical rotation of $[\boldsymbol{a}]_D^{25}$ = +69° (c = 1.0, $CHCl_3$) whereas the (–) enantiomer was measured to have an optical rotation of $[\boldsymbol{a}]_D^{25}$ = –74° (c = 1.0, $CHCl_3$). The

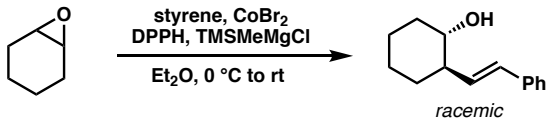
optical rotation of the (+) enantiomer has been previously reported in the literature, which allowed for the appropriate assignment of the two chiral products.[96]

((*E*)-2-((1*R*,2*S*)-2-methoxycyclopentyl)vinyl)benzene (117)



Enantioenriched alcohol **117** ($[\boldsymbol{a}]_D^{25}$ = +69°, 28 mg, 0.15 mmol, 1 equiv) was added to a 20 mL vial, dissolved in THF (2.5 mL), and cooled to 0 °C. Sodium hydride (60 mg, 60 wt% in mineral oil, 1.5 mmol, 10 equiv) and methyl iodide (35 µl, 0.53 mmol, 3.5 equiv) were subsequently added, and the reaction was allowed to stir for 2 hours at room temperature. The reaction was quenched with aq. NH_4Cl and extracted with Et_2O. The organic layer was dried with $MgSO_4$, filtered, and concentrated under reduced pressure. The crude material was purified by column chromatography (silica, hexane to 10% EtOAc/hexane) to yield 24 mg of **117** (80% yield) as a colorless oil. The enantiopure product was measured to have an optical rotation of $[\boldsymbol{a}]_D^{25}$ = +55° (c = 1.0, $CHCl_3$).

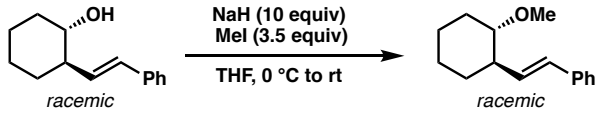
(*trans*)-2-((*E*)-styryl)cyclohexan-1-ol (S27)



According to a procedure by Oshima and coworkers,[95] 1,6-bis(diphenylphosphino)hexane ligand (DPPH, 154 mg, 0.34 mmol, 0.085 equiv) was added to a round bottom flask equipped with a stir bar and pumped into the glovebox filled with an N_2 atmosphere.

Cobalt(II) bromide (61 mg, 0.28 mmol, 0.07 equiv) was added, dissolved in 4 mL of Et_2O, sealed with a septum, and stirred for 1 hour forming a green solution. The round bottom flask was removed from the glovebox and cooled to 0 °C before cyclohexene oxide (608 µL, 6 mmol, 1.5 equiv), styrene (460 µL, 4 mmol, 1 equiv), and (trimethylsilyl)methylmagnesium chloride (10 mL, 1 M in Et_2O, 10 mmol, 2.5 equiv) were added sequentially. The reaction was warmed to room temperature and stirred overnight, then quenched with aq. NH_4Cl and extracted with EtOAc (2 x 80 mL). The combined organic layers were dried with $MgSO_4$, filtered, and concentrated under reduced pressure. The crude material was purified by column chromatography (silica, 0 to 30% EtOAc/hexane) to yield 191 mg of **S27** (24% yield) as a yellow oil. Spectral data matched those reported in the literature.[97]

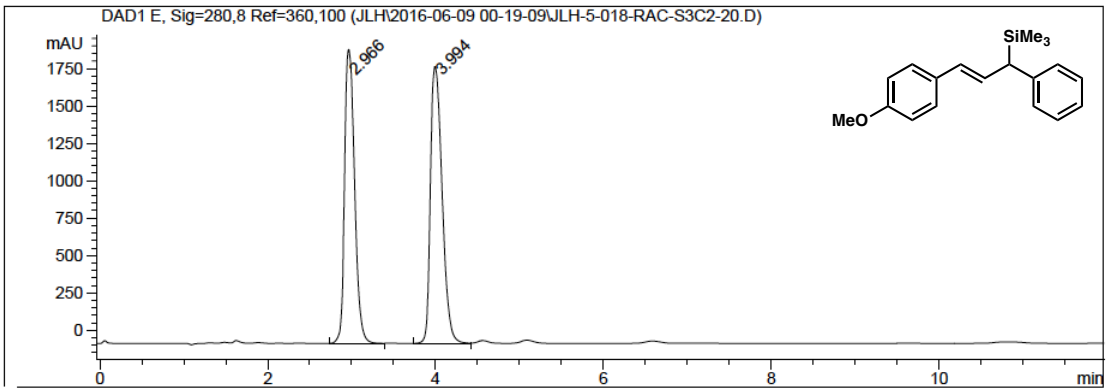
((*E*)-2-((*trans*)-2-methoxycyclohexyl)vinyl)benzene (118')



Alcohol **S27** (12.4 mg, 0.06 mmol, 1 equiv) was added to a 1 dram vial, dissolved in THF (1.0 mL), and cooled to 0 °C. Sodium hydride (240 mg, 60 wt% in mineral oil, 6.0 mmol, 100 equiv) and methyl iodide (14 µl, 0.210 mmol, 3.5 equiv) were subsequently added, and the reaction was allowed to stir for 30 minutes at room temperature. The reaction was quenched with aq. NH_4Cl and extracted with Et_2O. The organic layer was dried with $MgSO_4$, filtered, and concentrated under reduced pressure. The crude material was purified by preparative TLC (silica, 10% EtOAc/hexane) to yield 7.3 mg of **118'** (55% yield) as a colorless oil. The ^1H NMR of the purified product matches the **minor** diastereomer **118'**.

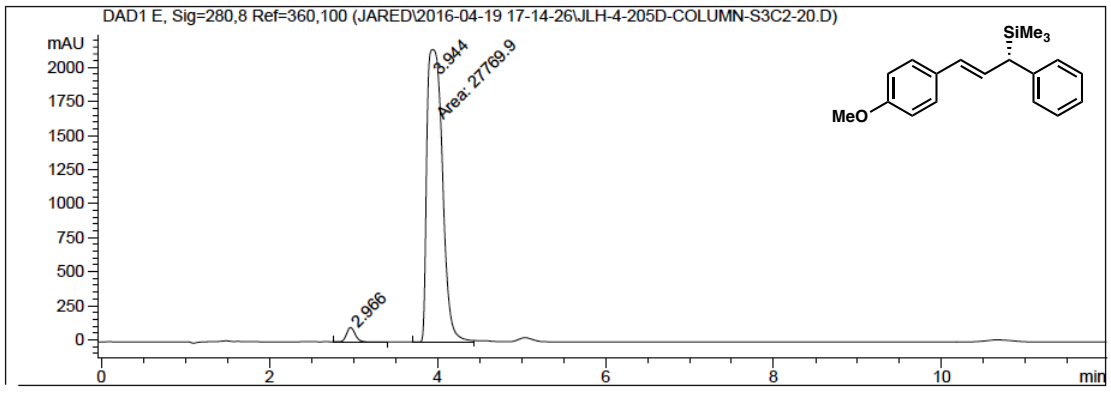
2.6.7 SFC and HPLC Traces of Racemic and Enantioenriched Products

88c (Figure 2.7): racemic



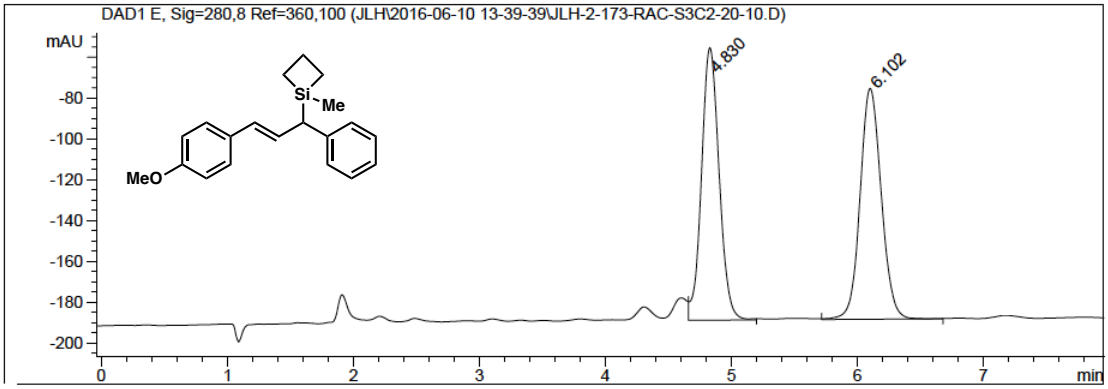
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	2.966	BV	0.1332	1.63275e4	1960.21167	47.6290
2	3.994	BV	0.1534	1.79530e4	1847.51770	52.3710

88c (Figure 2.7): enantioenriched, 95% ee



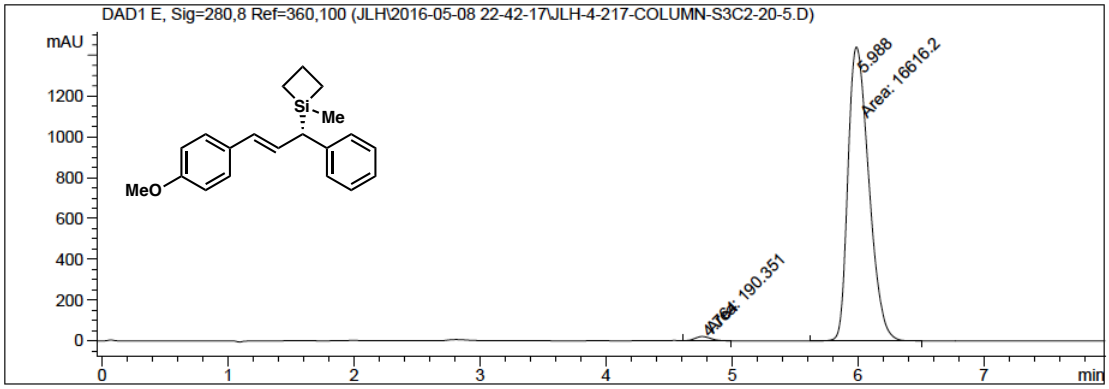
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	2.966	VB	0.1140	779.79077	105.83328	2.7313
2	3.944	MM	0.2154	2.77699e4	2149.07568	97.2687

90a (Figure 2.7): racemic



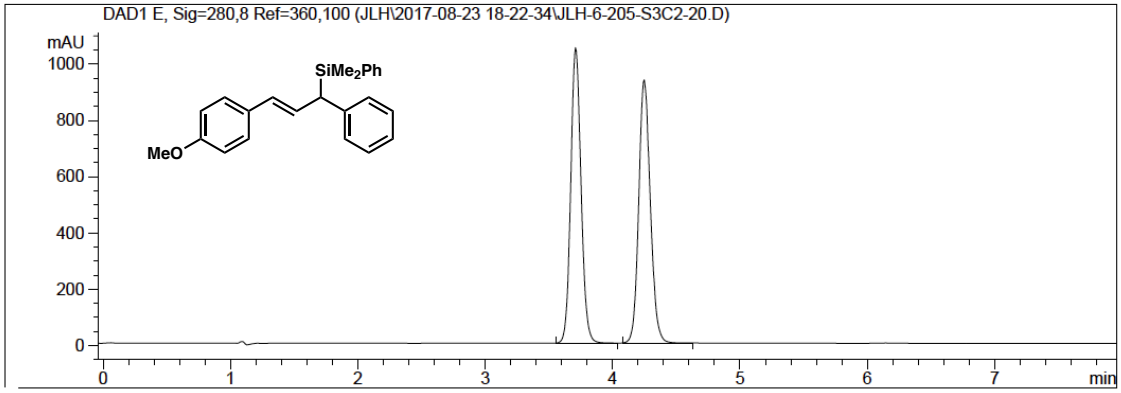
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	4.830	VB	0.1536	1297.76147	133.29198	49.5648
2	6.102	BB	0.1805	1320.54907	112.90835	50.4352

90a (Figure 2.7): enantioenriched, 98% ee



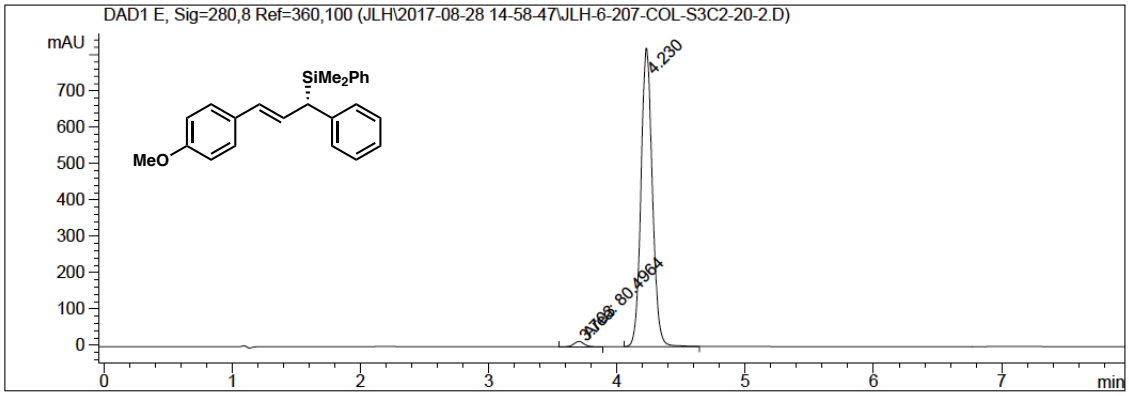
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	4.764	MM	0.1484	190.35126	21.37501	1.1326
2	5.988	MM	0.1922	1.66162e4	1440.68481	98.8674

90b (Figure 2.7): racemic



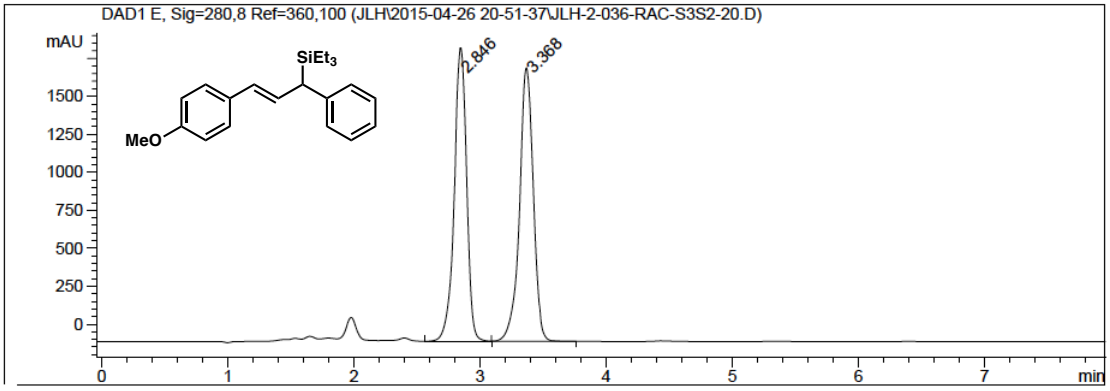
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	3.710	BB	0.0900	5919.53662	1045.89319	49.9092
2	4.248	BB	0.0985	5941.06885	930.83258	50.0908

90b (Figure 2.7): enantioenriched, 97% ee



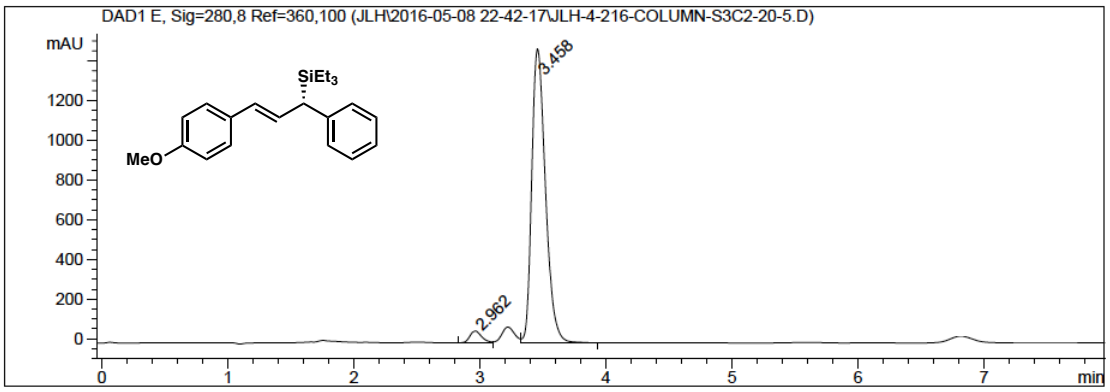
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	3.703	MM	0.0913	80.49639	14.69651	1.5530
2	4.230	BB	0.0965	5102.88428	821.41608	98.4470

90c (Figure 2.7): racemic



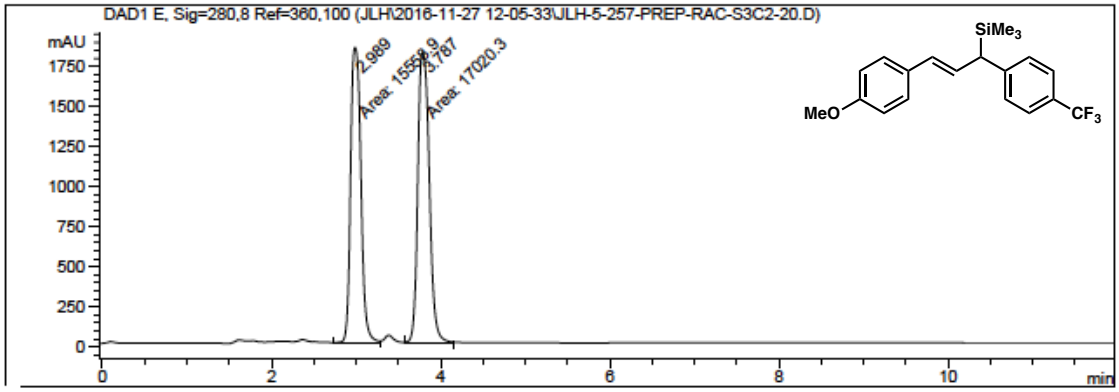
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	2.846	VV	0.1057	1.32271e4	1937.00806	49.0137
2	3.368	VB	0.1170	1.37594e4	1803.53308	50.9863

90c (Figure 2.7): enantioenriched, 93% ee



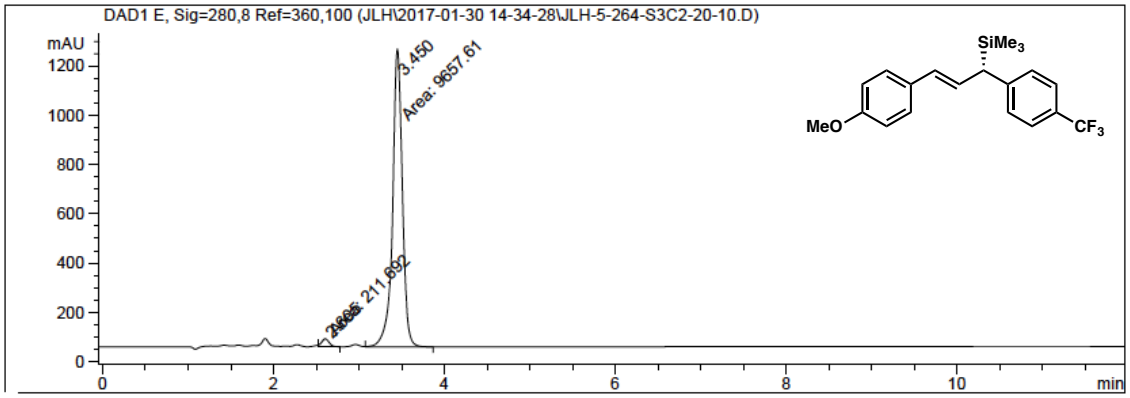
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	2.962	VV	0.0992	386.79767	59.99361	3.3328
2	3.458	VB	0.1164	1.12188e4	1481.32935	96.6672

90d (Figure 2.7): racemic



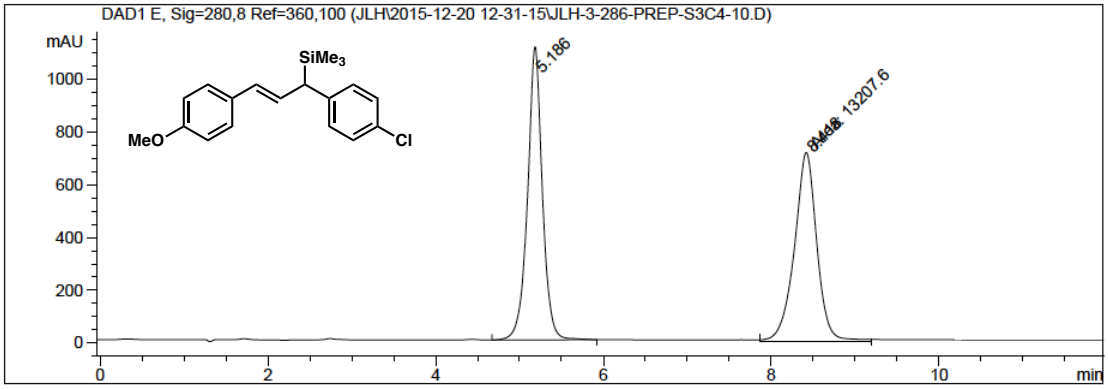
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	2.989	MM	0.1406	1.55589e4	1844.16211	47.7570
2	3.787	MM	0.1563	1.70203e4	1814.95007	52.2430

90d (Figure 2.7): enantioenriched, 96% ee



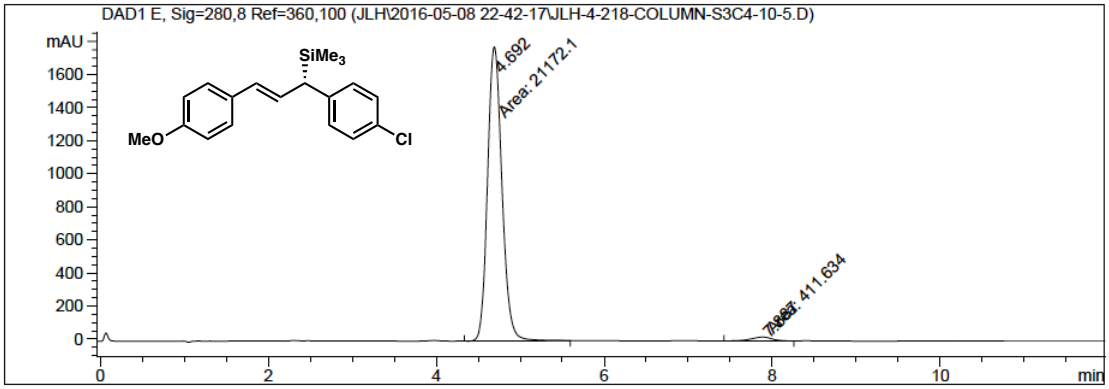
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	2.605	MM	0.1056	211.69177	33.39671	2.1450
2	3.450	MM	0.1330	9657.60938	1210.65833	97.8550

90e (Figure 2.7): racemic



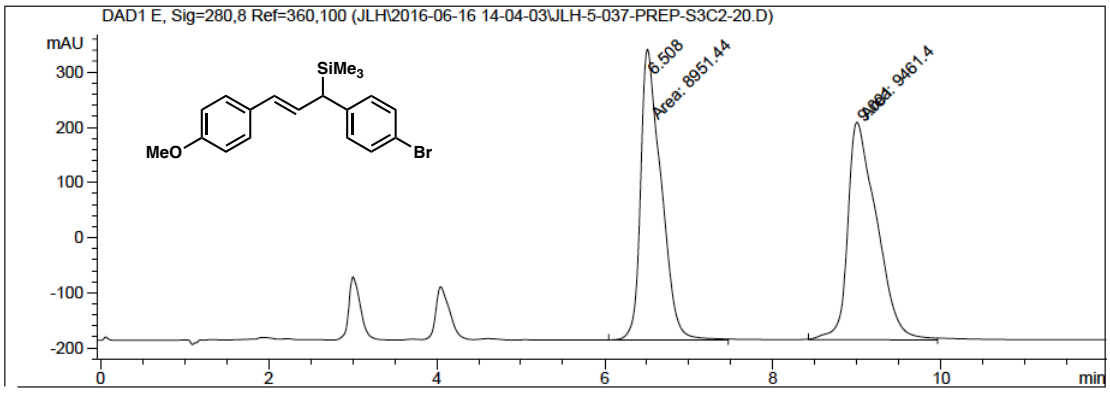
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	5.186	VB	0.1774	1.36628e4	1111.58838	50.8470
2	8.418	MM	0.3079	1.32076e4	714.82355	49.1530

90e (Figure 2.7): enantioenriched, 96% ee



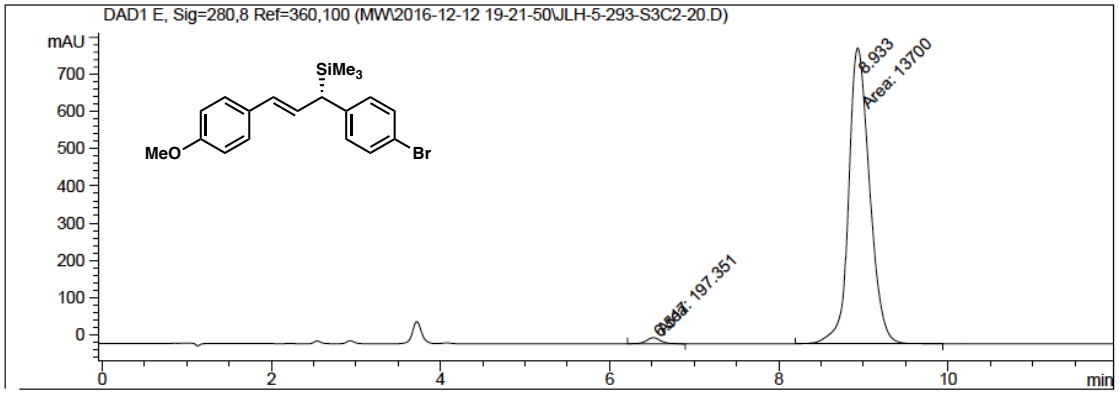
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	4.692	MM	0.1983	2.11721e4	1779.80176	98.0929
2	7.887	MM	0.2914	411.63358	23.54672	1.9071

90f (Figure 2.7): racemic



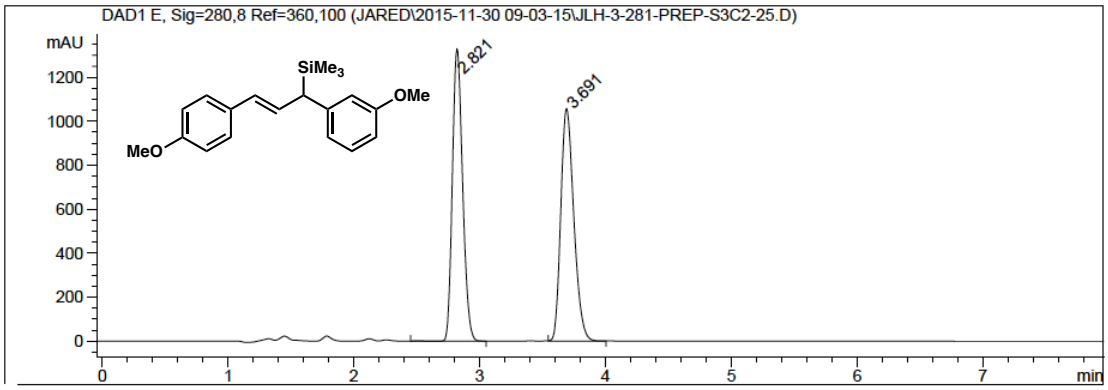
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	6.508	MM	0.2827	8951.43945	527.74286	48.6152
2	9.001	MM	0.3993	9461.40332	394.91501	51.3848

90f (Figure 2.7): enantioenriched, 97% ee



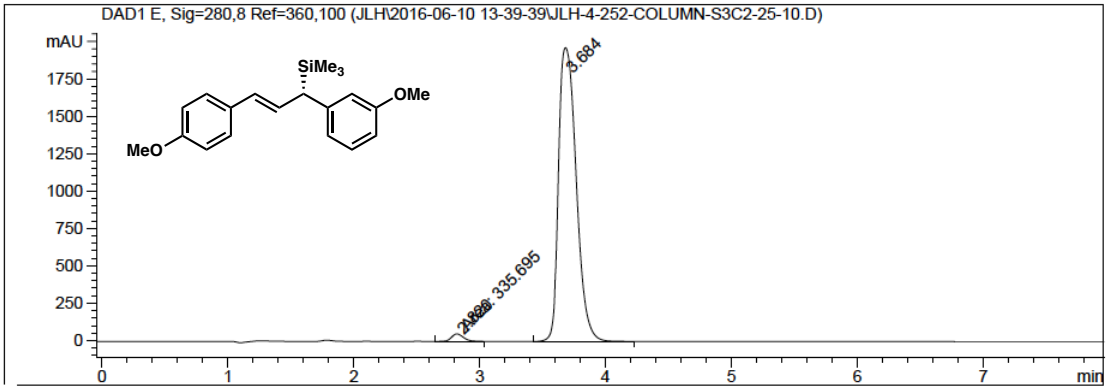
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	6.517	MM	0.1995	197.35112	16.48802	1.4201
2	8.933	MM	0.2865	1.37000e4	796.90198	98.5799

90g (Figure 2.7): racemic



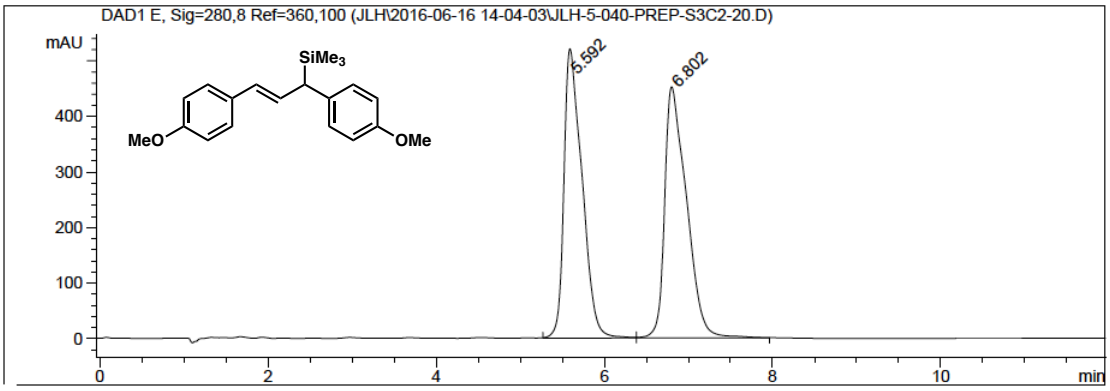
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	2.821	BB	0.0880	7524.96826	1330.39319	49.6931
2	3.691	BB	0.1120	7617.91406	1058.05420	50.3069

90g (Figure 2.7): enantioenriched, 97% ee



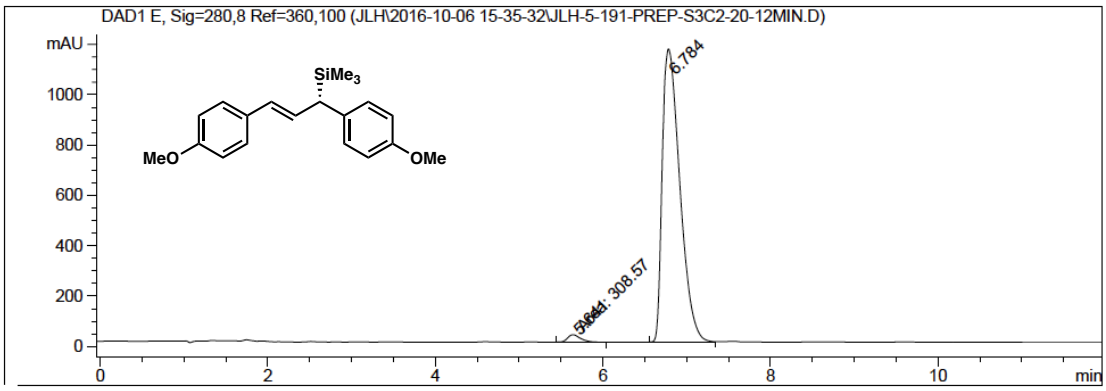
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	2.820	MM	0.1102	335.69470	50.78532	1.7209
2	3.684	BB	0.1578	1.91711e4	1964.58142	98.2791

90h (Figure 2.7): racemic



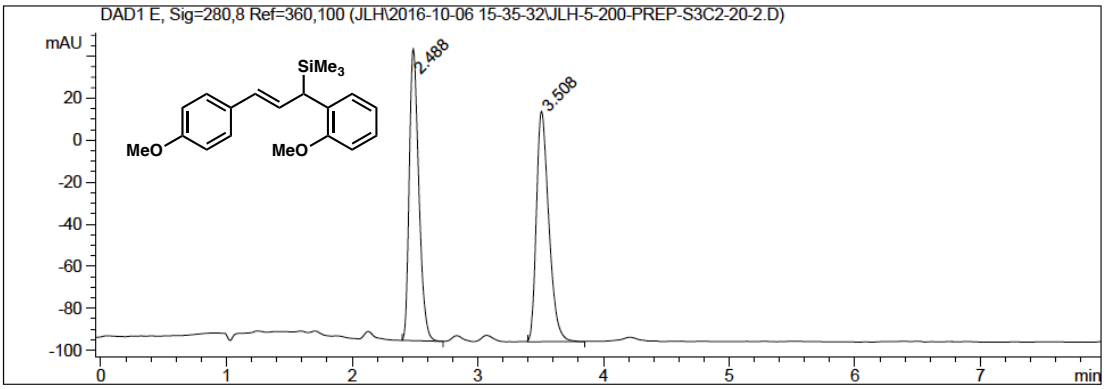
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	5.592	BV	0.2107	7794.18457	520.59595	48.8511
2	6.802	VB	0.2549	8160.78564	451.39059	51.1489

90h (Figure 2.7): enantioenriched, 96% ee



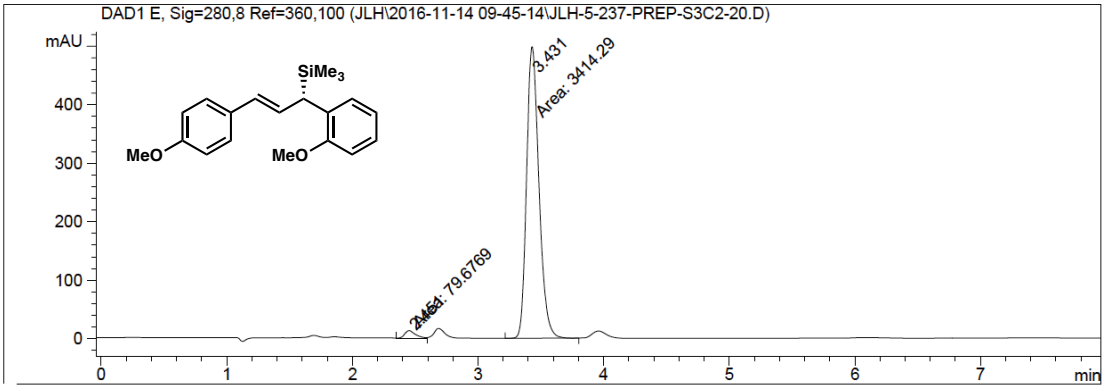
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	5.641	MM	0.1755	308.56979	29.30574	1.7776
2	6.784	BV	0.2270	1.70501e4	1163.17297	98.2224

90i (Figure 2.7): racemic



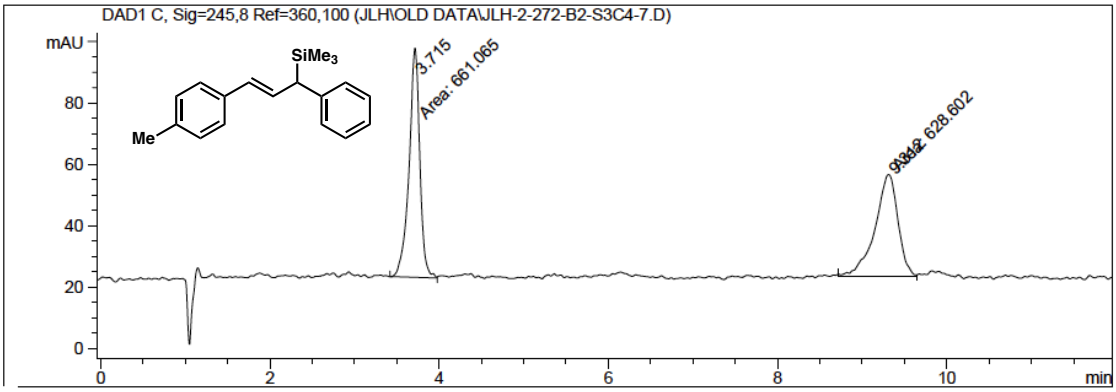
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	2.488	BV	0.0821	734.53345	137.91168	49.3425
2	3.508	BB	0.1042	754.10883	109.69971	50.6575

90i (Figure 2.7): enantioenriched, 95% ee



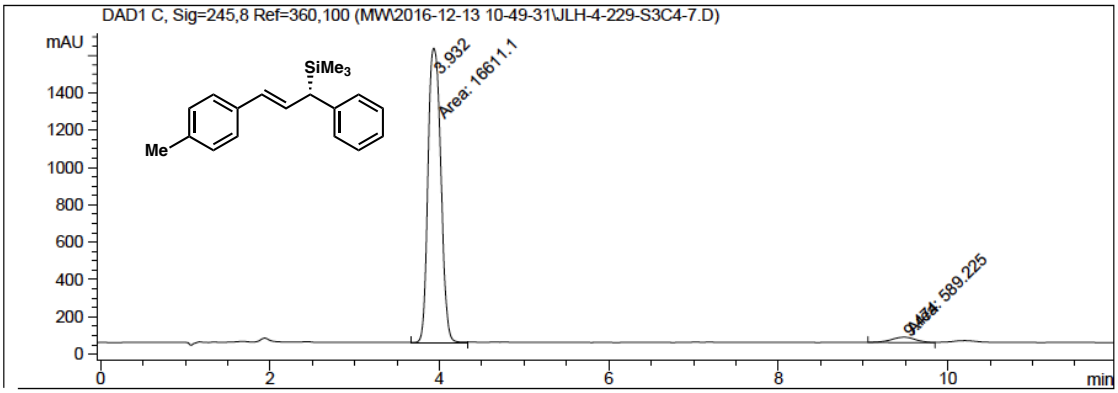
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	2.451	MM	0.1004	79.67693	13.23026	2.2804
2	3.431	MM	0.1137	3414.29102	500.48816	97.7196

91a (Figure 2.8): racemic



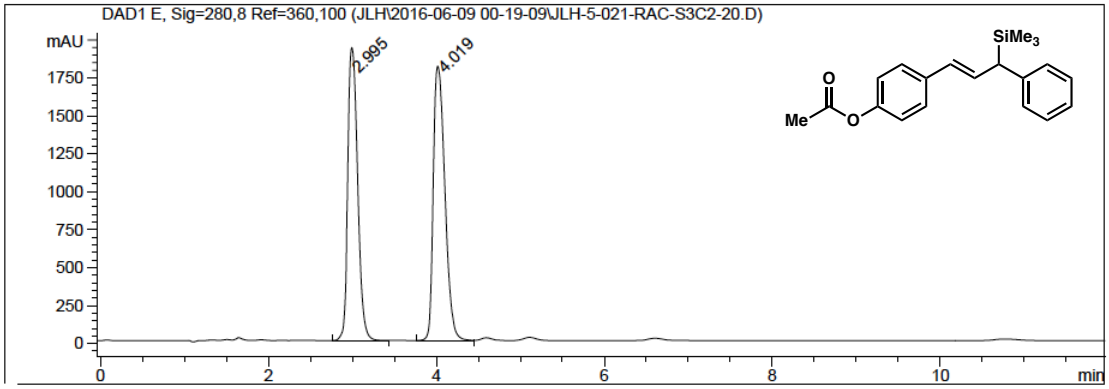
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	3.715	MM	0.1469	661.06458	74.99195	51.2586
2	9.312	MM	0.3153	628.60205	33.22607	48.7414

91a (Figure 2.8): enantioenriched, 93% ee



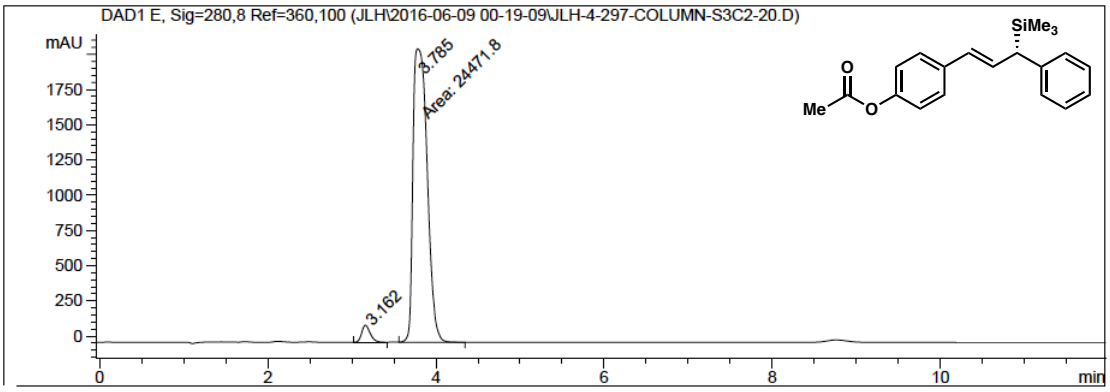
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	3.932	MM	0.1754	1.66111e4	1578.40051	96.5743
2	9.474	MM	0.3380	589.22534	29.05238	3.4257

91b (Figure 2.8): racemic



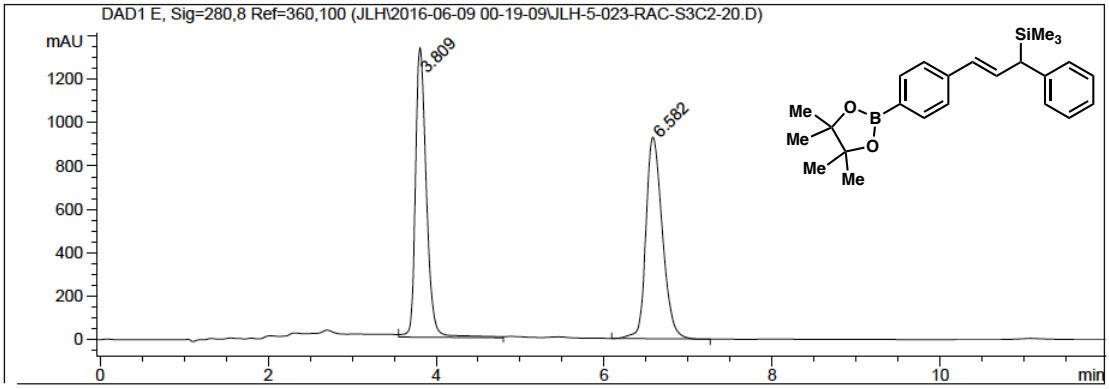
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	2.995	BV	0.1317	1.57998e4	1925.37463	47.5626
2	4.019	BV	0.1526	1.74192e4	1804.08923	52.4374

91b (Figure 2.8): enantioenriched, 93% ee



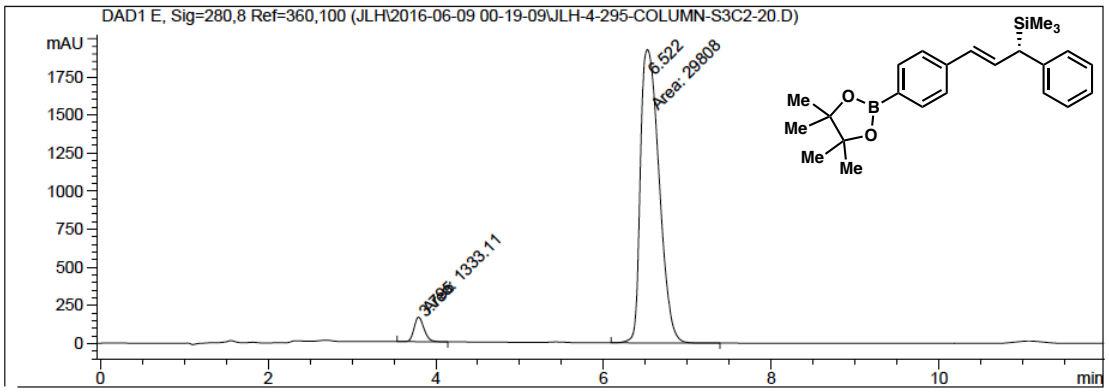
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	3.162	BB	0.1112	861.72925	120.86167	3.4015
2	3.785	MM	0.1958	2.44718e4	2083.04150	96.5985

91c (Figure 2.8): racemic



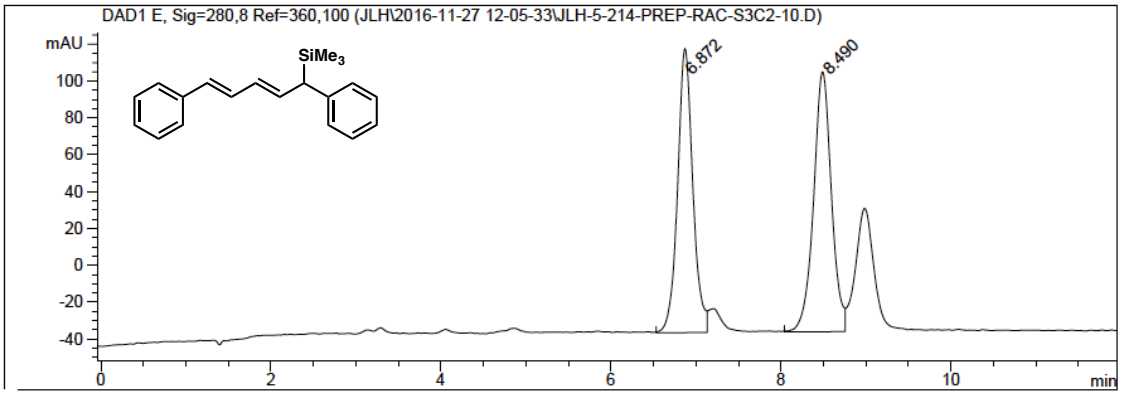
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	3.809	VV	0.1422	1.21206e4	1330.88916	48.9675
2	6.582	VB	0.2109	1.26317e4	927.68268	51.0325

91c (Figure 2.8): enantioenriched, 91% ee



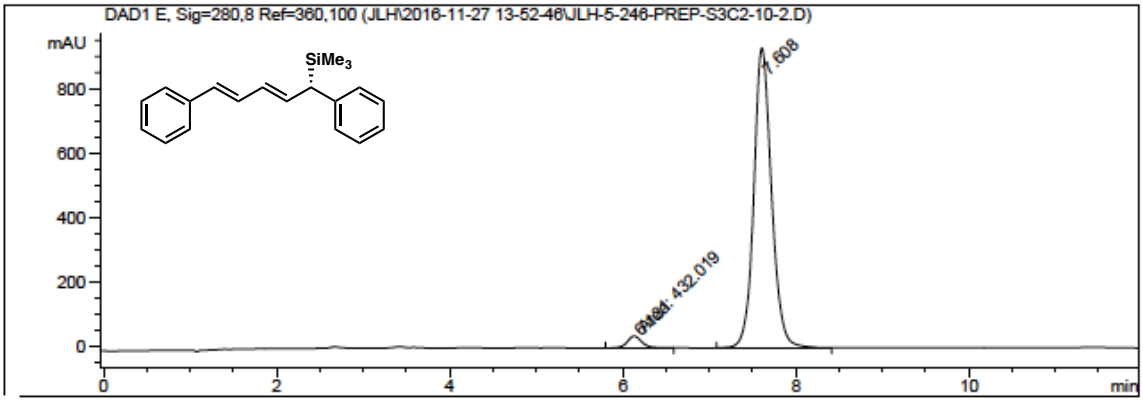
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	3.795	MM	0.1374	1333.10791	161.69827	4.2809
2	6.522	MM	0.2579	2.98080e4	1926.34448	95.7191

91d (Figure 2.8): racemic



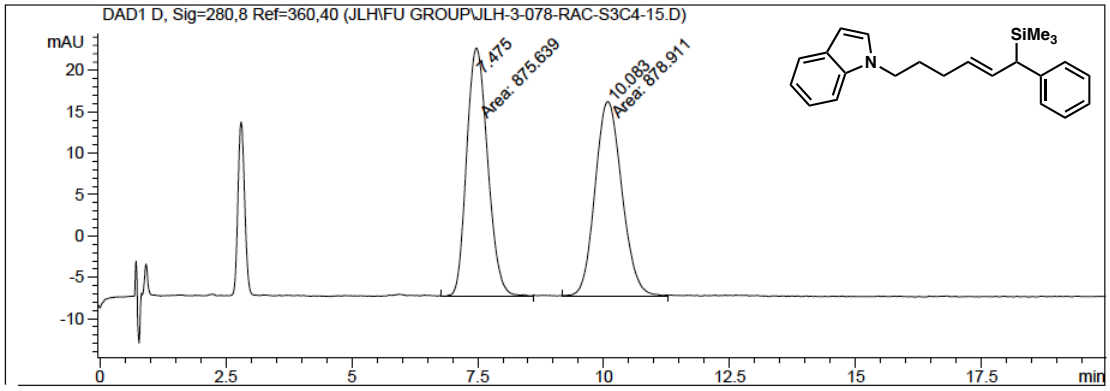
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	6.872	BV	0.1856	1922.17102	154.03583	48.2717
2	8.490	BV	0.2185	2059.81567	140.98209	51.7283

91d (Figure 2.8): enantioenriched, 94% ee



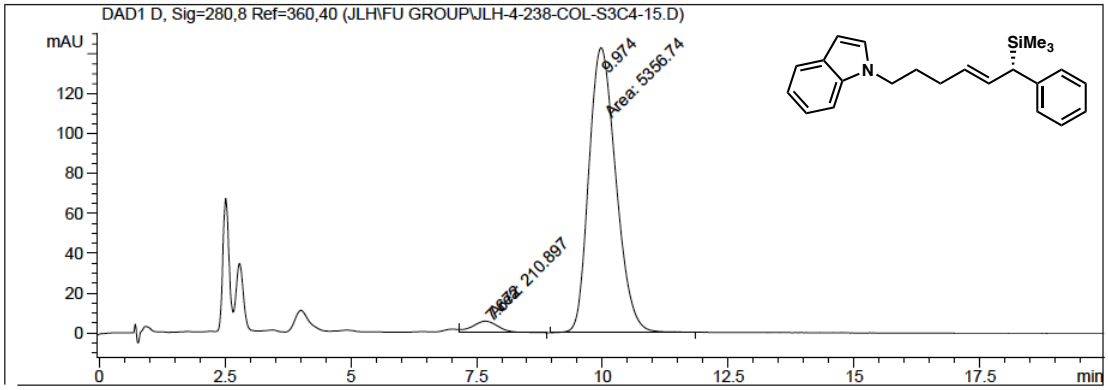
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	6.131	MM	0.1950	432.01929	36.92301	3.1471
2	7.608	BV	0.2189	1.32957e4	929.16394	96.8529

91e (Figure 2.8): racemic



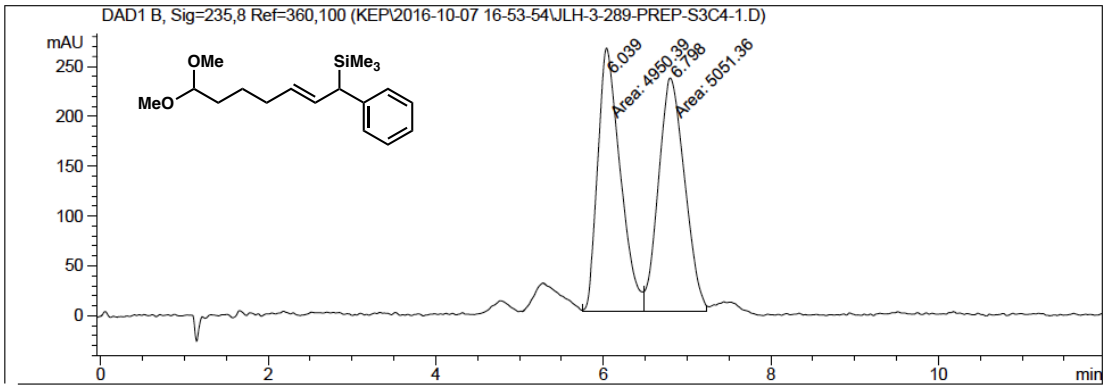
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	7.475	MM	0.4862	875.63855	30.01655	49.9068
2	10.083	MM	0.6219	878.91064	23.55369	50.0932

91e (Figure 2.8): enantioenriched, 92% ee



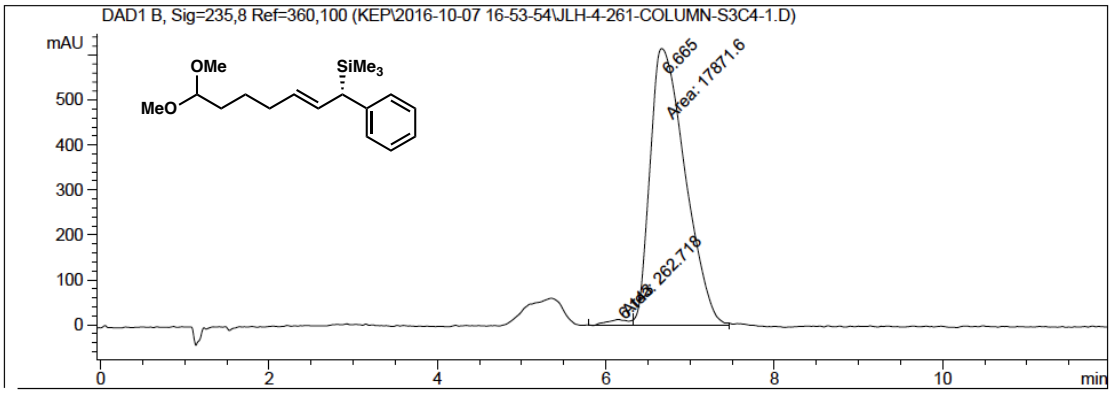
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	7.672	MM	0.6110	210.89684	5.75319	3.7879
2	9.974	MM	0.6244	5356.73975	142.97990	96.2121

91f (Figure 2.8): racemic



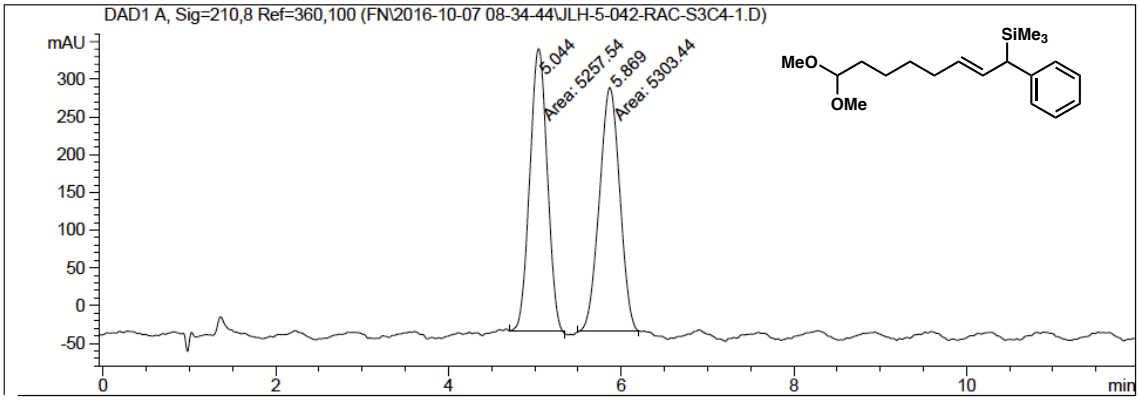
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	6.039	MM	0.3128	4950.39160	263.80368	49.4952
2	6.798	MM	0.3601	5051.36084	233.77972	50.5048

91f (Figure 2.8): enantioenriched, 97% ee



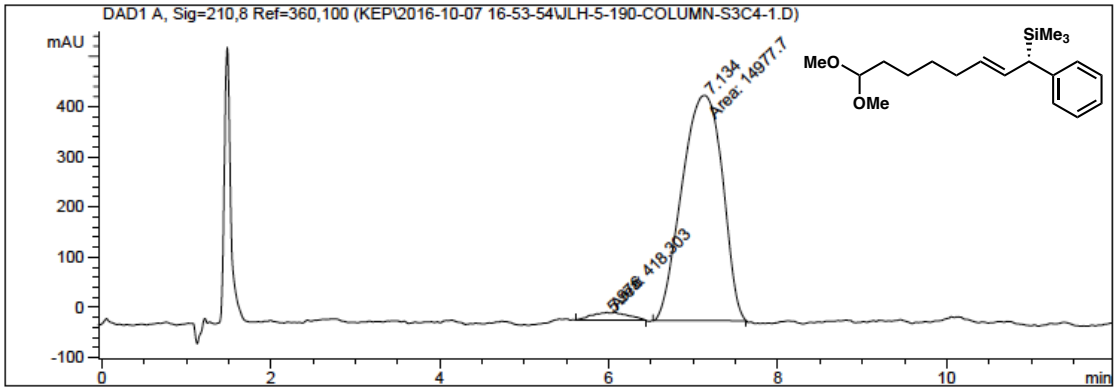
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	6.143	MM	0.3226	262.71774	13.57335	1.4487
2	6.665	MM	0.4833	1.78716e4	616.27795	98.5513

91g (Figure 2.8): racemic



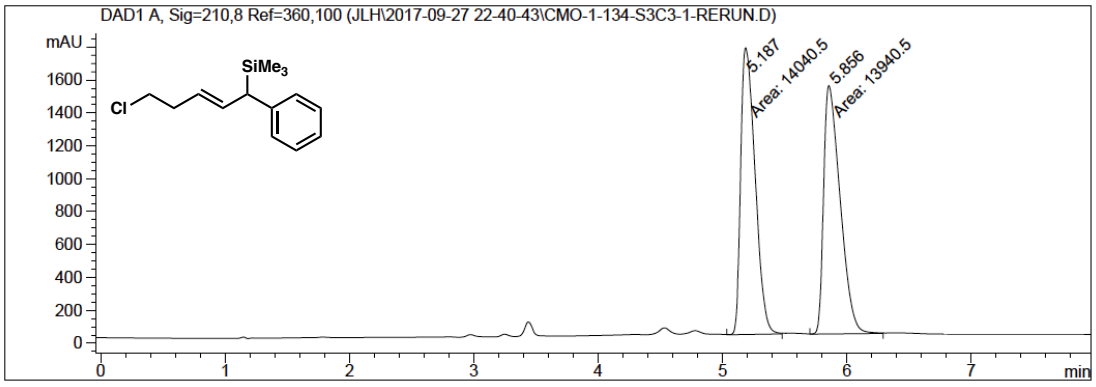
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	5.044	MM	0.2336	5257.54492	375.13754	49.7827
2	5.869	MM	0.2734	5303.44434	323.33304	50.2173

91g (Figure 2.8): enantioenriched, 95% ee



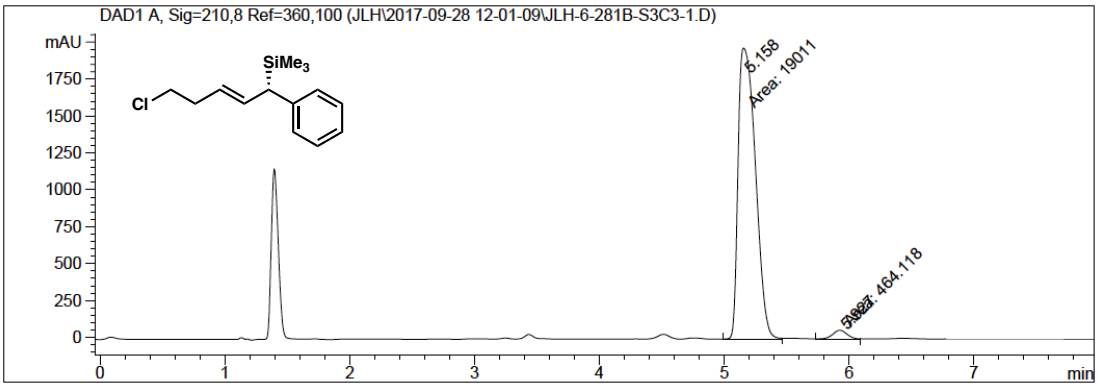
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	5.976	MM	0.4692	418.30276	14.85876	2.7170
2	7.134	MM	0.5565	1.49777e4	448.60516	97.2830

91h (Figure 2.8): racemic



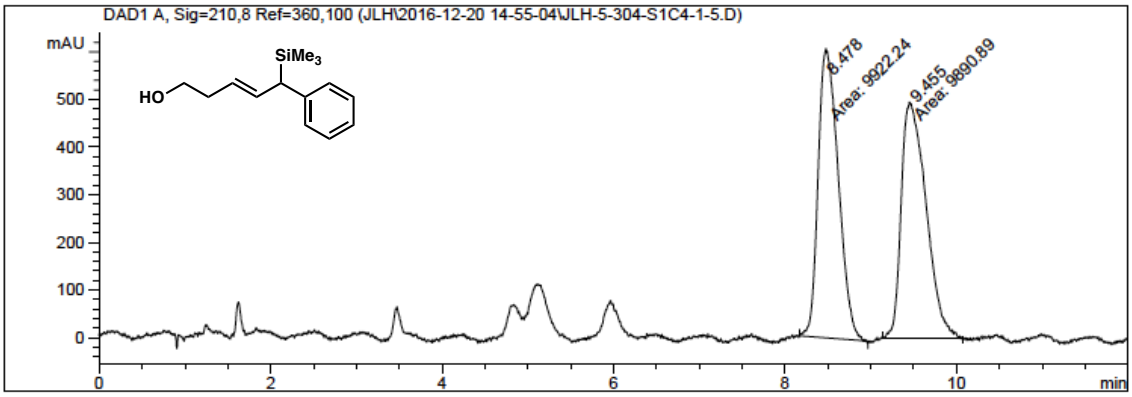
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	5.187	MM	0.1333	1.40405e4	1755.09863	50.1787
2	5.856	MM	0.1533	1.39405e4	1515.26782	49.8213

91h (Figure 2.8): enantioenriched, 95% ee



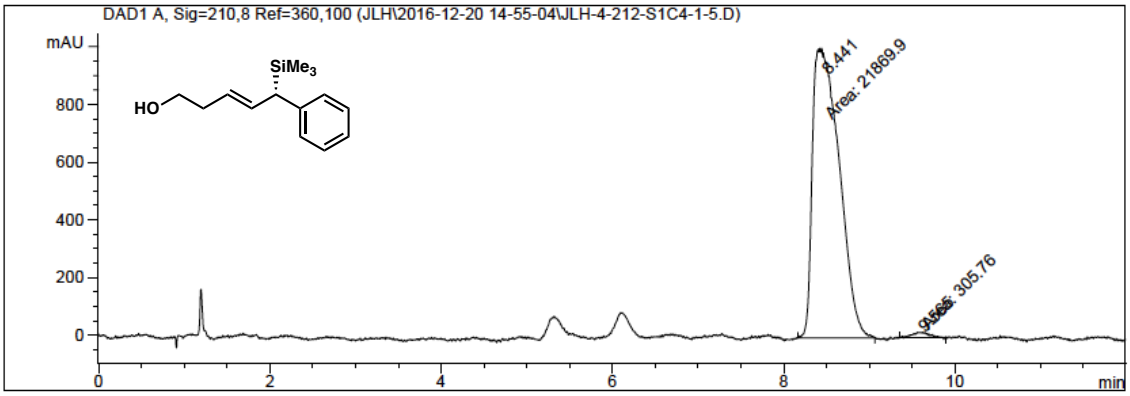
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	5.158	MM	0.1605	1.90110e4	1974.68127	97.6169
2	5.927	MM	0.1312	464.11768	58.96592	2.3831

91i (Figure 2.8): racemic



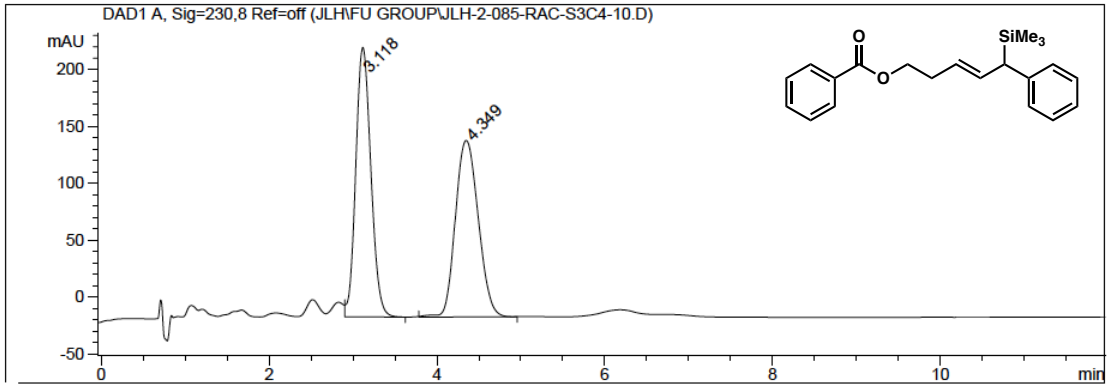
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	8.478	MM	0.2718	9922.24219	608.50598	50.0791
2	9.455	MM	0.3338	9890.89258	493.89984	49.9209

91i (Figure 2.8): enantioenriched, 97% ee



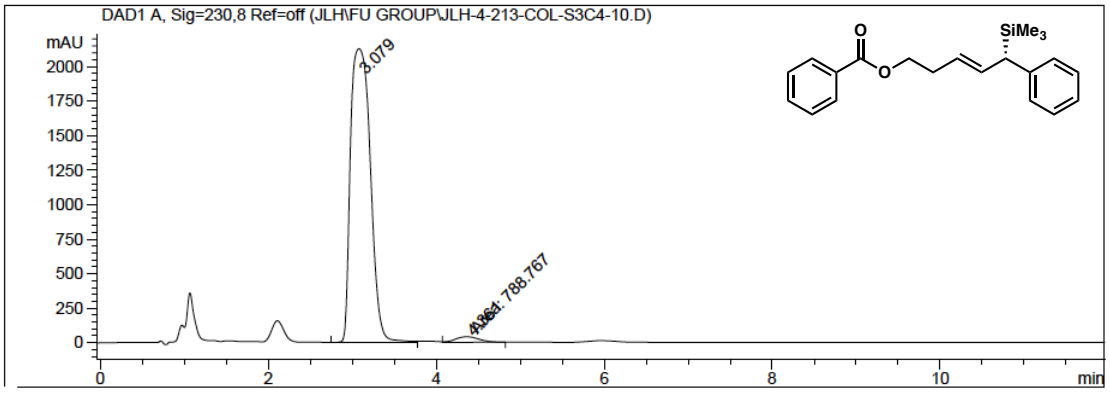
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	8.441	MM	0.3621	2.18699e4	1006.71216	98.6212
2	9.565	MM	0.2544	305.75977	20.02871	1.3788

91j (Figure 2.8): racemic



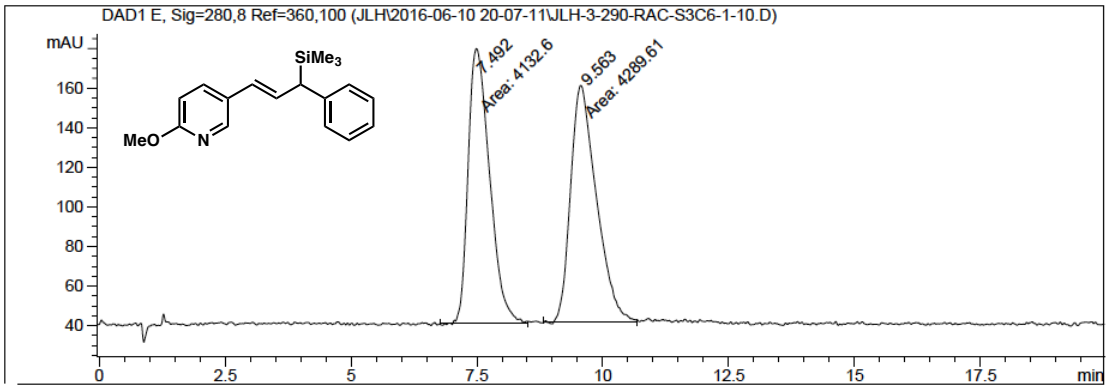
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	3.118	VB	0.1985	2974.74390	236.89671	50.2506
2	4.349	BB	0.3012	2945.07666	155.31581	49.7494

91j (Figure 2.8): enantioenriched, 96% ee



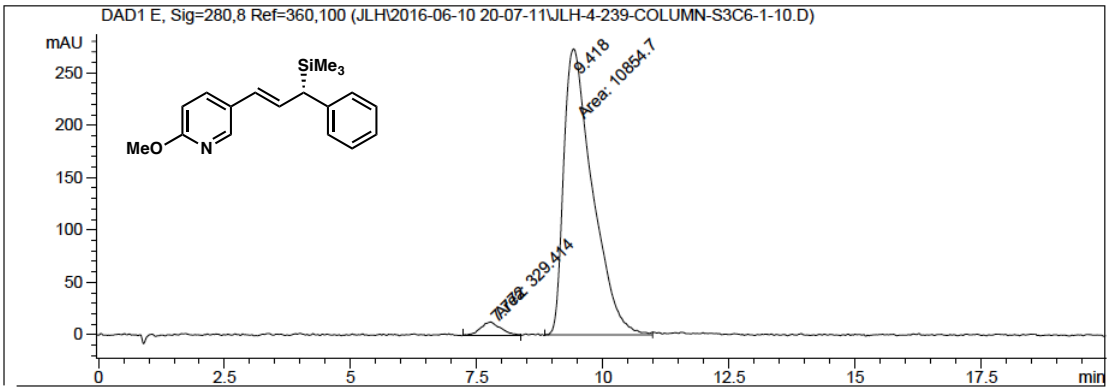
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	3.079	VV	0.2723	3.50735e4	2127.52100	97.8006
2	4.361	MM	0.3241	788.76727	40.55814	2.1994

91k (Figure 2.8): racemic



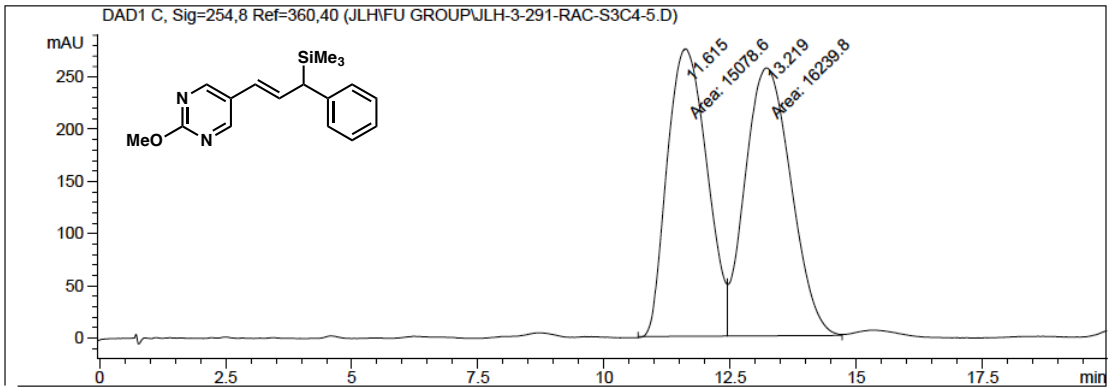
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	7.492	MM	0.4961	4132.59570	138.82385	49.0679
2	9.563	MM	0.5976	4289.60547	119.63455	50.9321

91k (Figure 2.8): enantioenriched, 94% ee



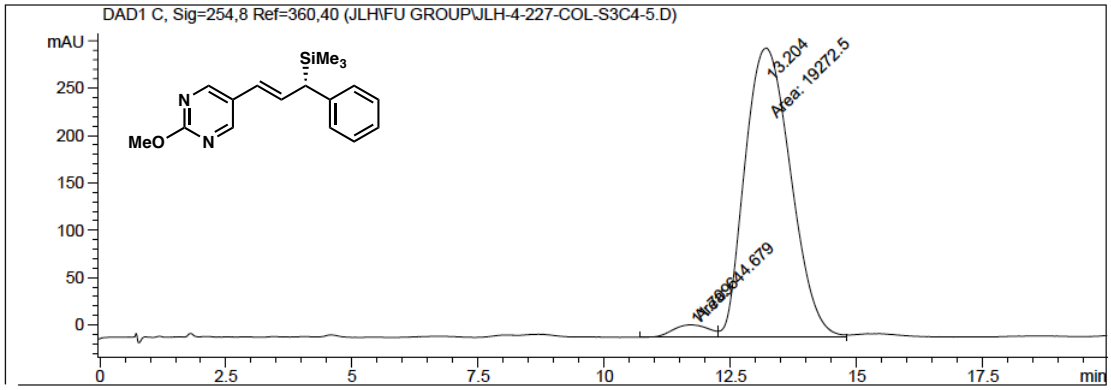
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	7.772	MM	0.4447	329.41449	12.34658	2.9454
2	9.418	MM	0.6623	1.08547e4	273.13736	97.0546

91l (Figure 2.8): racemic



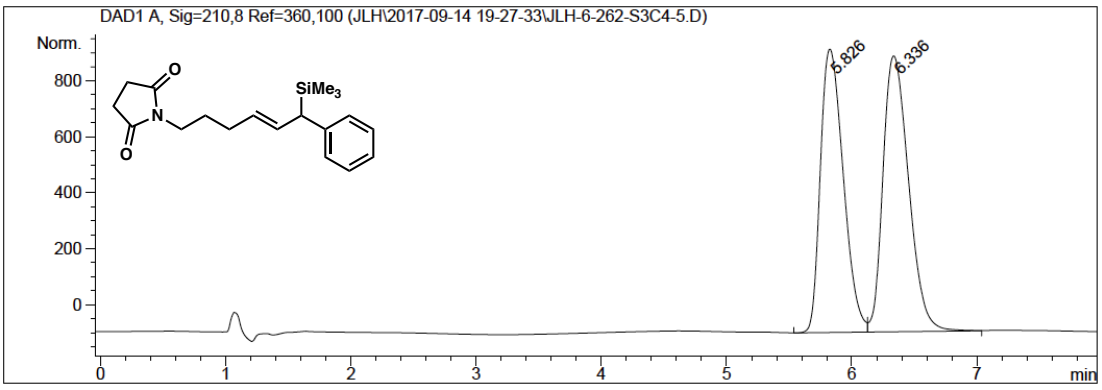
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	11.615	MF	0.9132	1.50786e4	275.19785	48.1463
2	13.219	FM	1.0553	1.62398e4	256.47855	51.8537

91l (Figure 2.8): enantioenriched, 94% ee



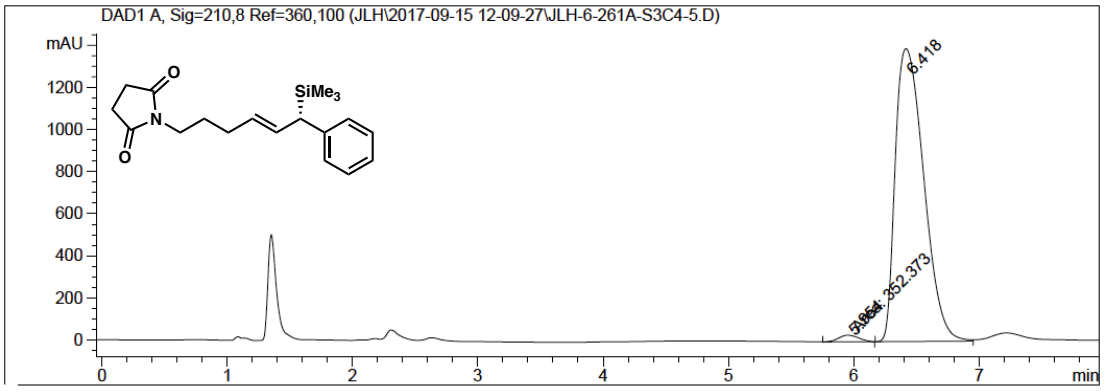
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	11.709	MF	0.8228	644.67889	13.05884	3.2368
2	13.204	FM	1.0519	1.92725e4	305.36429	96.7632

91m (Figure 2.8): racemic



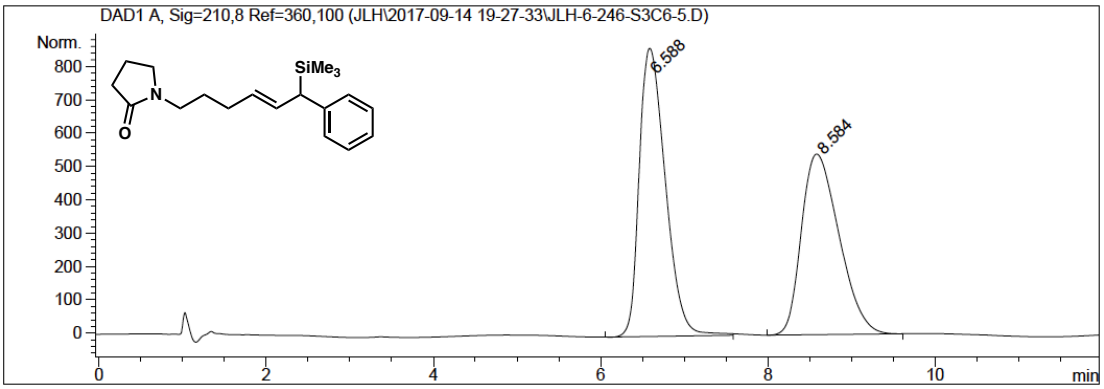
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	5.826	VV	0.2023	1.28826e4	1013.52417	47.7844
2	6.336	VB	0.2265	1.40773e4	986.41656	52.2156

91m (Figure 2.8): enantioenriched, 97% ee



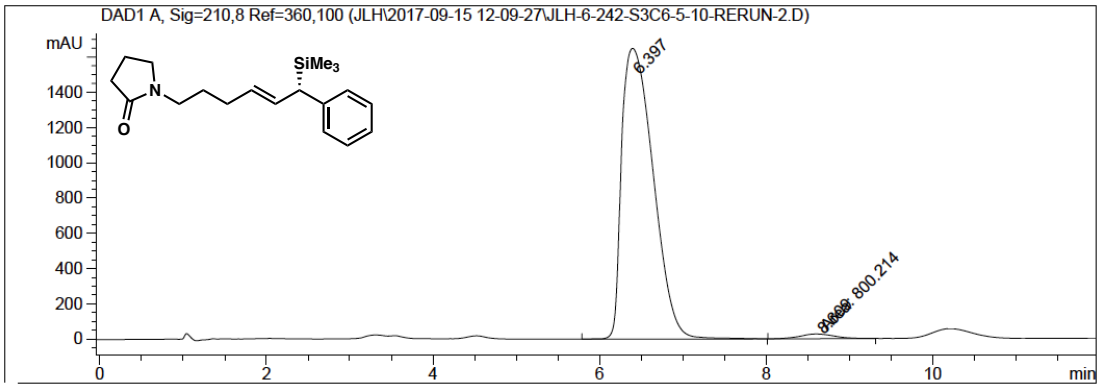
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	5.954	MM	0.1863	352.37341	31.52633	1.5768
2	6.418	VV	0.2565	2.19949e4	1390.66895	98.4232

91n (Figure 2.8): racemic



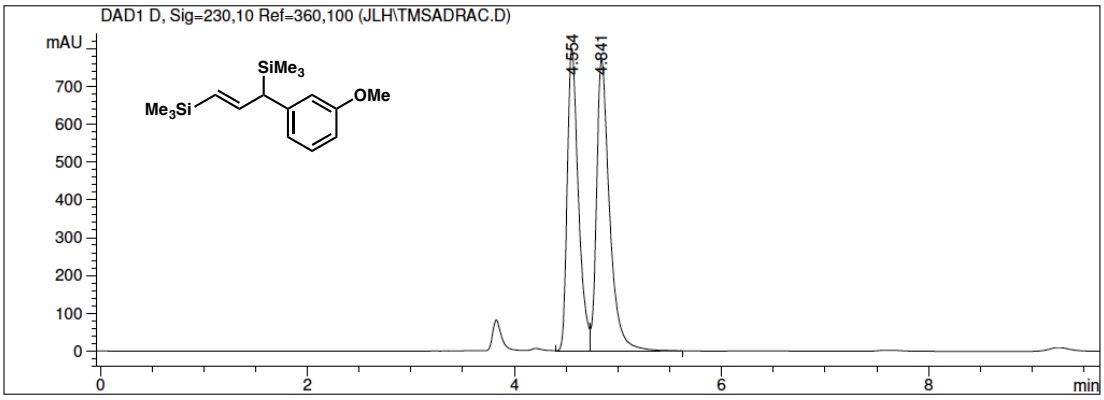
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	6.588	VB	0.3437	1.88022e4	864.66400	52.6067
2	8.584	BB	0.4907	1.69389e4	541.81793	47.3933

91n (Figure 2.8): enantioenriched, 96% ee



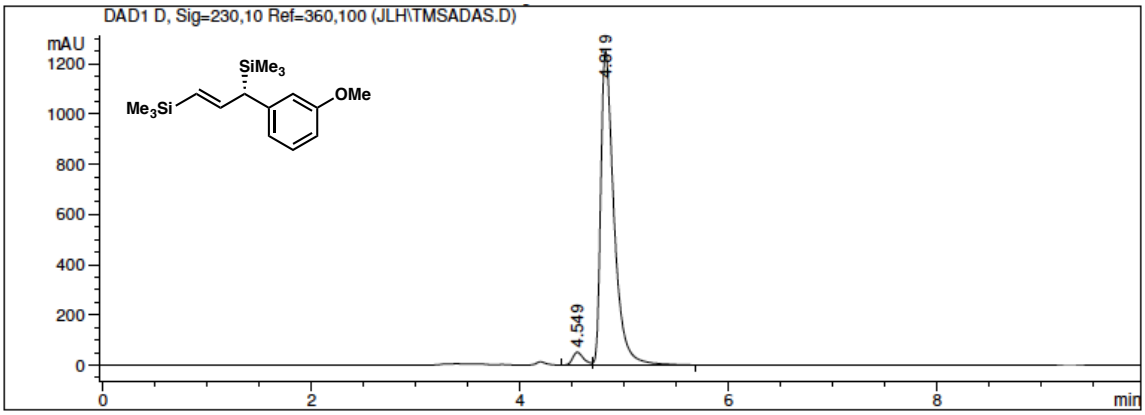
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	6.397	BV	0.4280	4.35448e4	1649.31226	98.1955
2	8.609	MM	0.4921	800.21442	27.09959	1.8045

91o (Figure 2.8): racemic



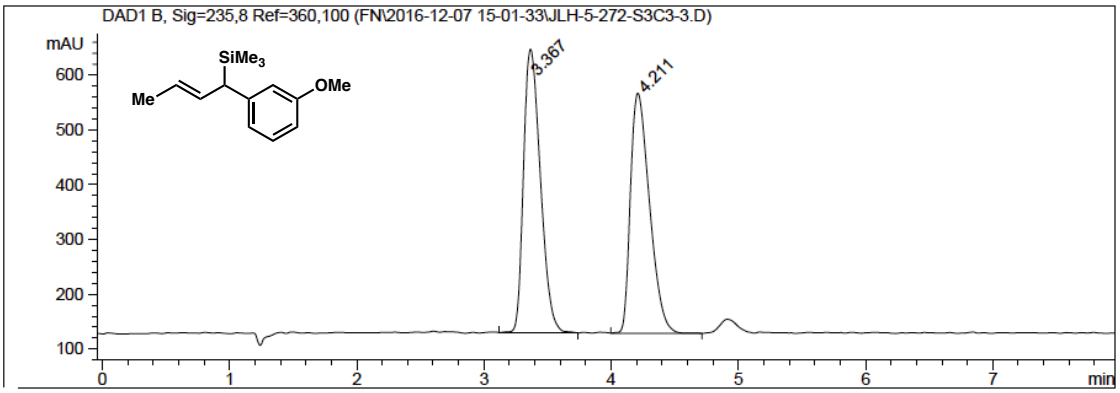
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	4.554	VV	0.1129	5969.46826	801.09521	46.9286
2	4.841	VB	0.1299	6750.85742	772.95972	53.0714

91o (Figure 2.8): enantioenriched, 93% ee



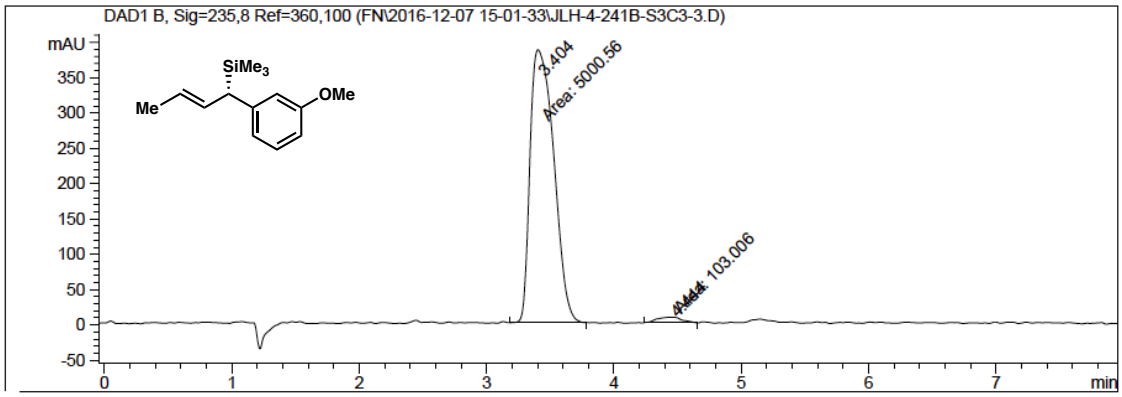
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	4.549	VV	0.1082	370.31830	51.32189	3.2662
2	4.819	VB	0.1323	1.09674e4	1251.31555	96.7338

91p (Figure 2.8): racemic



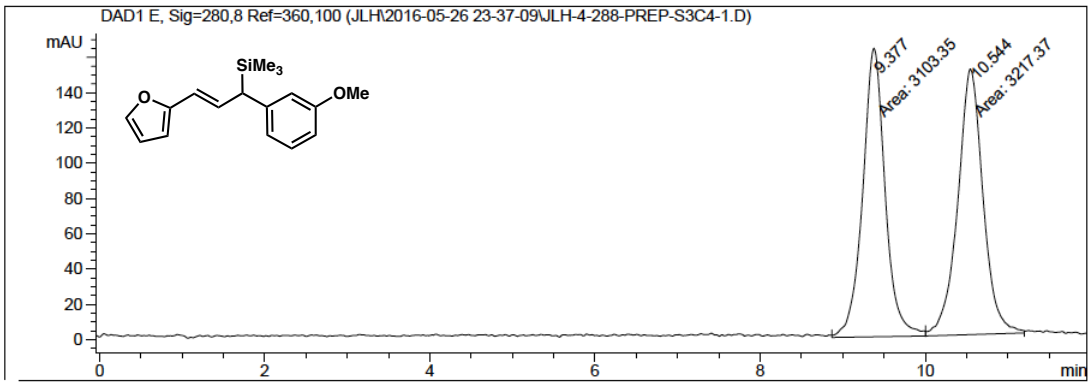
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	3.367	VV	0.1447	4823.06299	517.59222	51.3268
2	4.211	VV	0.1618	4573.71729	438.16852	48.6732

91p (Figure 2.8): enantioenriched, 96% ee



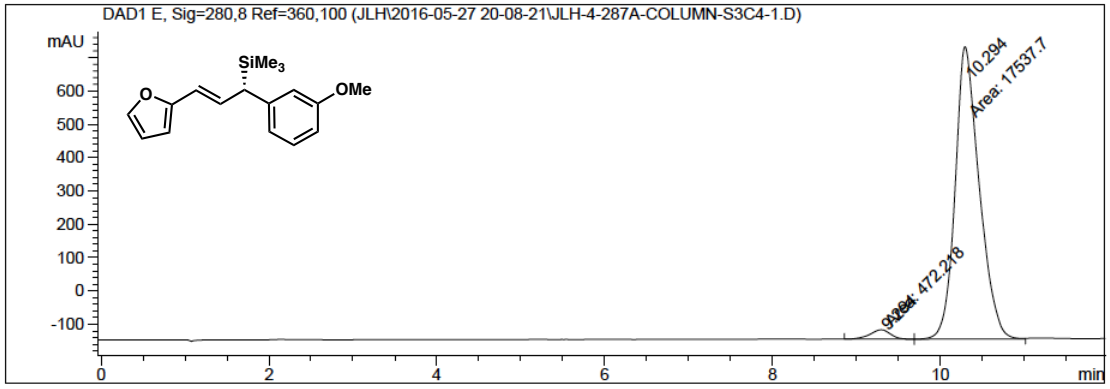
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	3.404	MM	0.2153	5000.55615	387.10941	97.9817
2	4.444	MM	0.2190	103.00621	7.83907	2.0183

91q (Figure 2.8): racemic



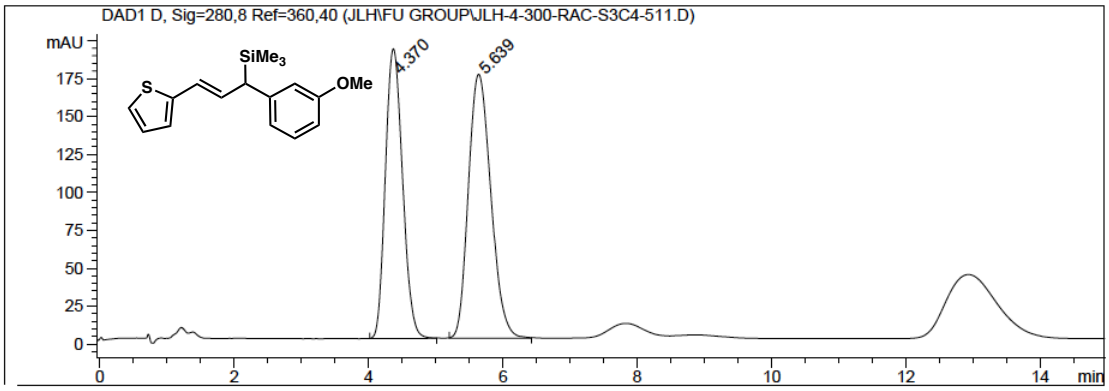
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	9.377	MM	0.3160	3103.34863	163.69301	49.0980
2	10.544	MM	0.3557	3217.37183	150.74971	50.9020

91q (Figure 2.8): enantioenriched, 95% ee



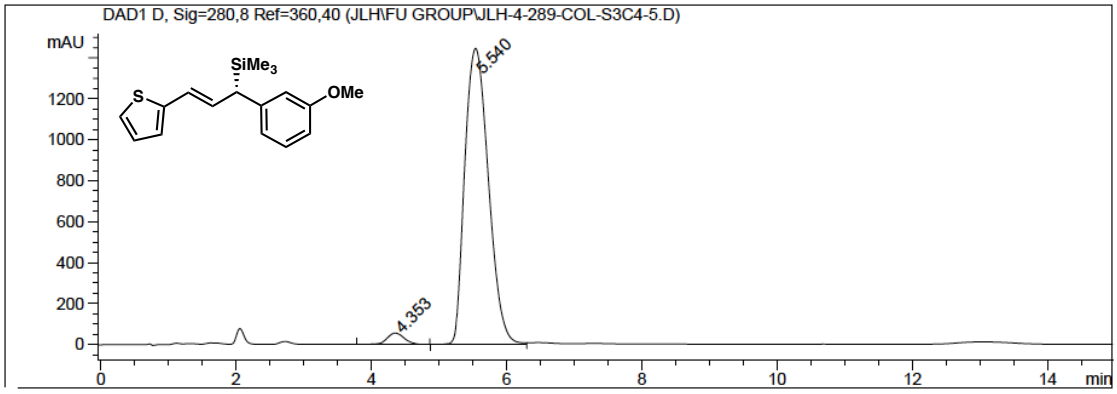
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	9.294	MM	0.2809	472.21768	28.02045	2.6220
2	10.294	MM	0.3330	1.75377e4	877.67529	97.3780

91r (Figure 2.8): racemic



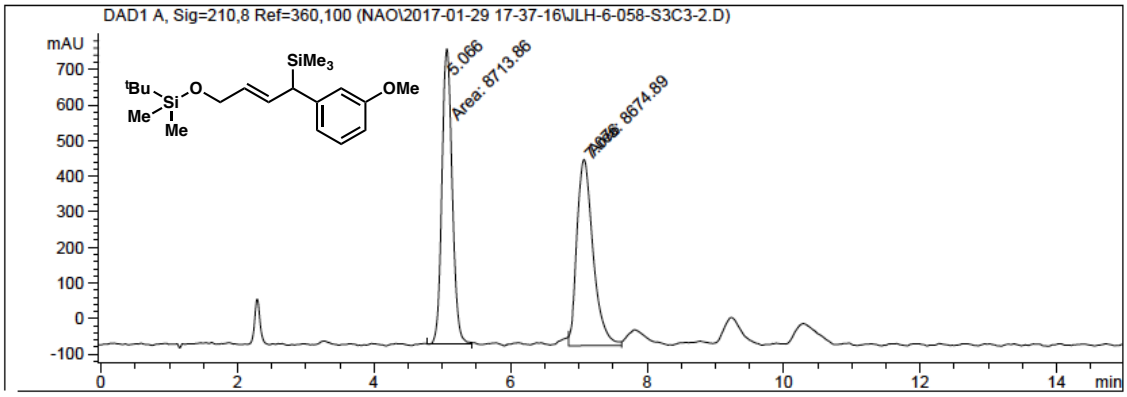
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	4.370	BB	0.2795	3393.40796	190.79709	45.5995
2	5.639	BB	0.3634	4048.35034	174.02675	54.4005

91r (Figure 2.8): enantioenriched, 95% ee



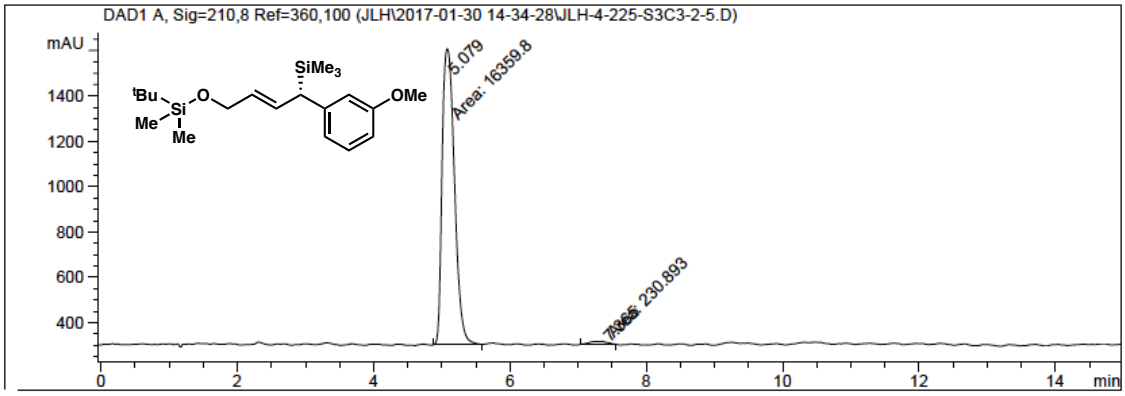
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	4.353	BV	0.2785	972.86749	54.97358	2.6947
2	5.540	VV	0.3956	3.51307e4	1445.08362	97.3053

91s (Figure 2.8): racemic



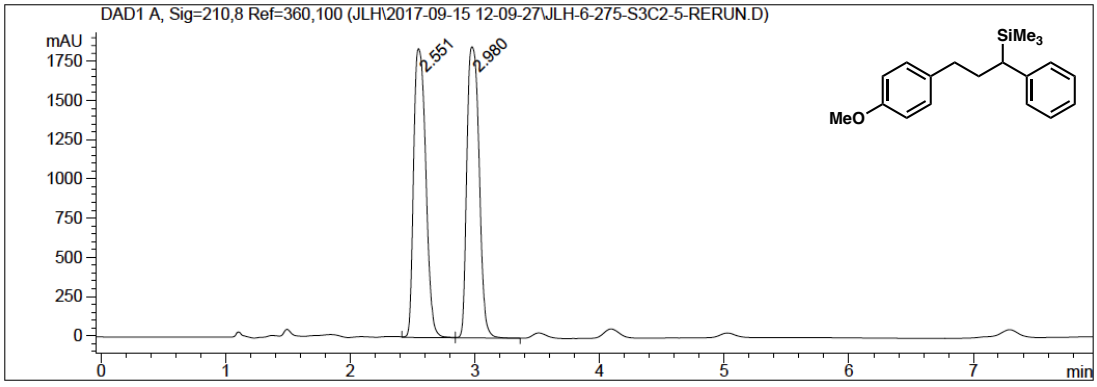
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	5.066	MM	0.1746	8713.86035	831.57080	50.1121
2	7.076	MM	0.2759	8674.88574	524.05389	49.8879

91s (Figure 2.8): enantioenriched, 97% ee



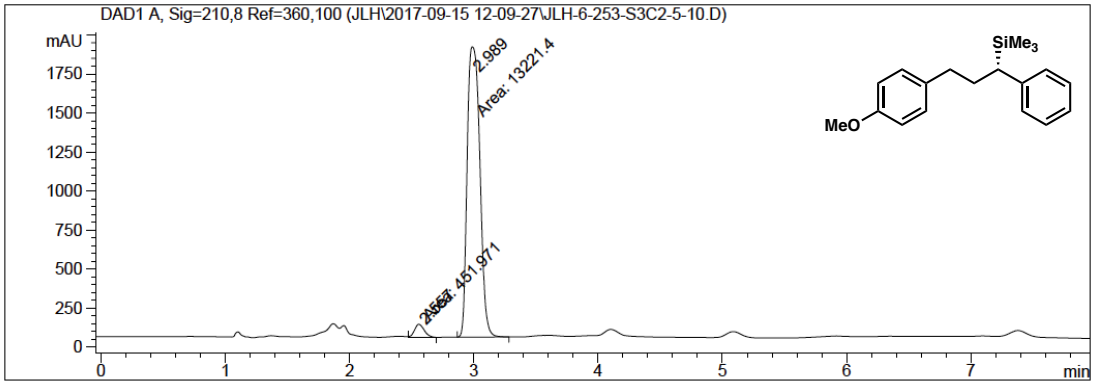
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	5.079	MM	0.2092	1.63598e4	1303.59607	98.6083
2	7.365	MM	0.2925	230.89261	13.15635	1.3917

106 (Scheme 2.4): racemic



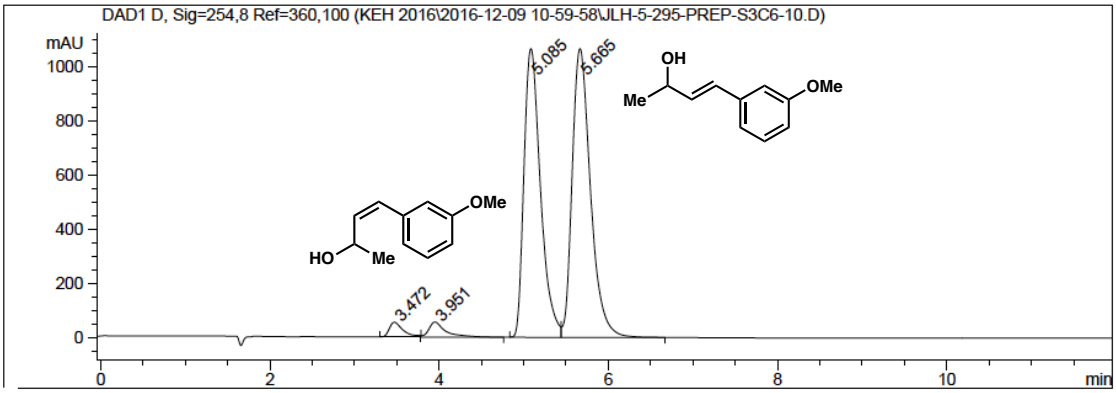
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	2.551	VV	0.1113	1.24955e4	1838.88037	49.5922
2	2.980	VV	0.1118	1.27010e4	1857.98621	50.4078

106 (Scheme 2.4): enantioenriched, 93% ee



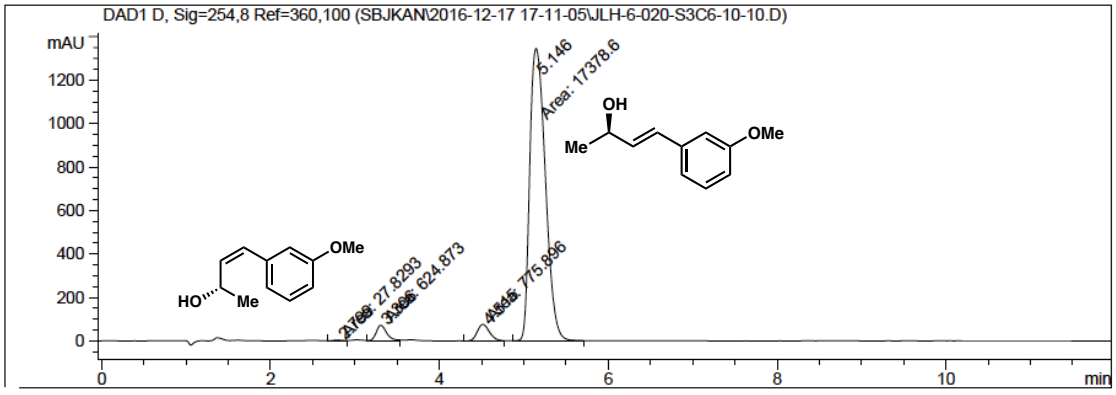
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	2.557	MM	0.0898	451.97076	83.84869	3.3055
2	2.989	MM	0.1184	1.32214e4	1860.47168	96.6945

111 (Scheme 2.6): racemic



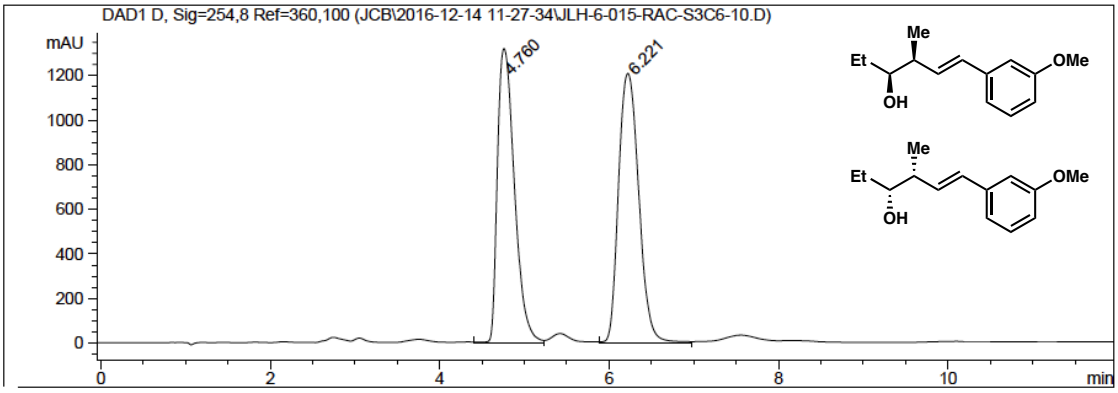
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	3.472	VV	0.1639	618.88599	54.74337	1.9391
2	3.951	VB	0.1983	774.84723	55.69344	2.4277
3	5.085	BV	0.2106	1.44659e4	1063.92664	45.3241
4	5.665	VB	0.2320	1.60569e4	1064.43738	50.3091

111 (Scheme 2.6): enantioenriched, both *E*/*Z*-isomers, 91% ee



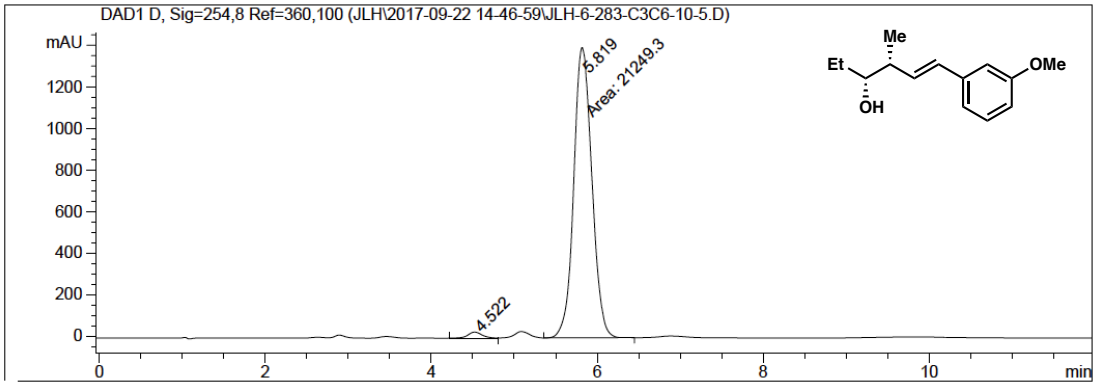
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	2.799	MM	0.1206	27.82935	3.84628	0.1480
2	3.306	MM	0.1454	624.87256	71.64183	3.3225
3	4.515	MM	0.1686	775.89587	76.70793	4.1255
4	5.146	MM	0.2151	1.73786e4	1346.51550	92.4040

113 (Scheme 2.7): racemic



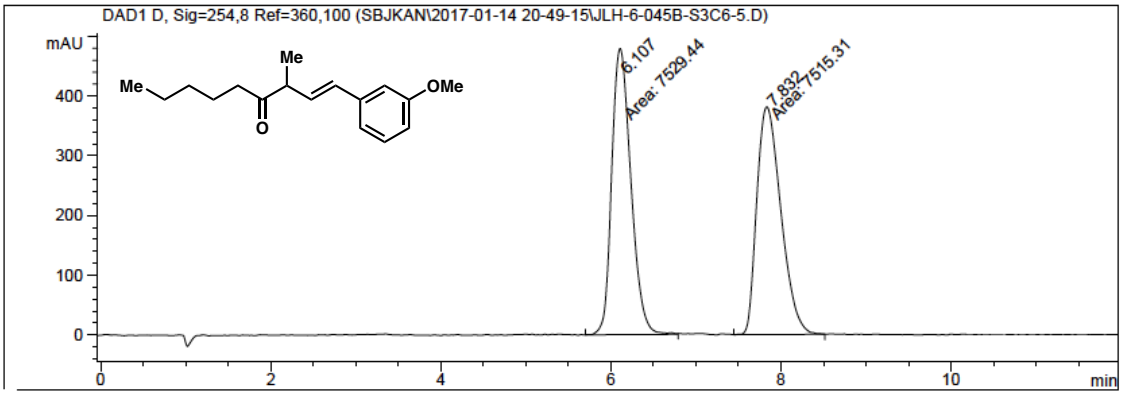
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	4.760	VV	0.2185	1.83661e4	1318.21326	47.8907
2	6.221	VV	0.2651	1.99840e4	1207.41687	52.1093

113 (Scheme 2.7): enantioenriched, 97% ee



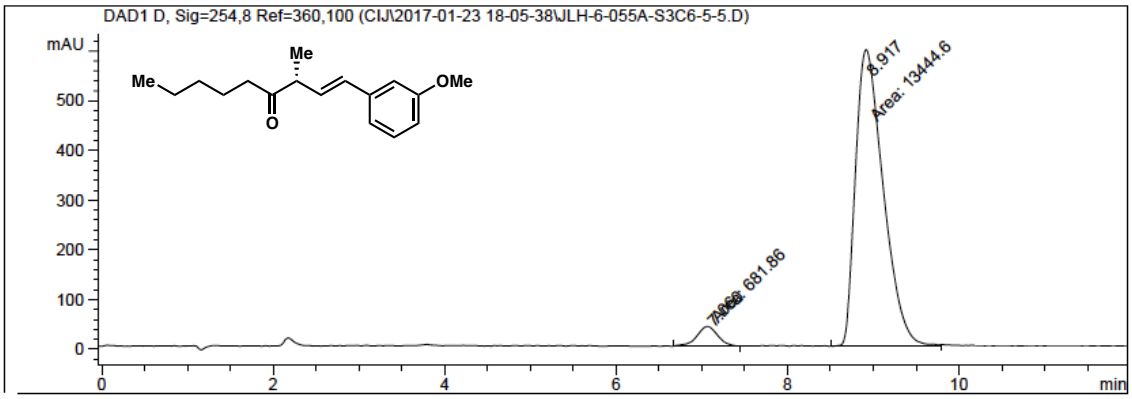
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	4.522	BV	0.1773	341.61523	29.02138	1.5822
2	5.819	MM	0.2530	2.12493e4	1399.80737	98.4178

116 (Scheme 2.7): racemic



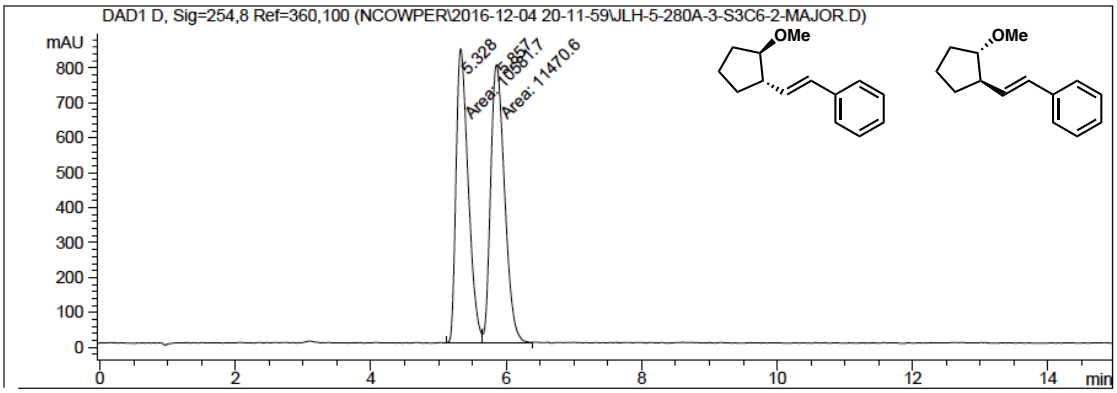
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	6.107	MM	0.2617	7529.43945	479.46429	50.0470
2	7.832	MM	0.3282	7515.30908	381.61700	49.9530

116 (Scheme 2.7): enantioenriched, 90% ee



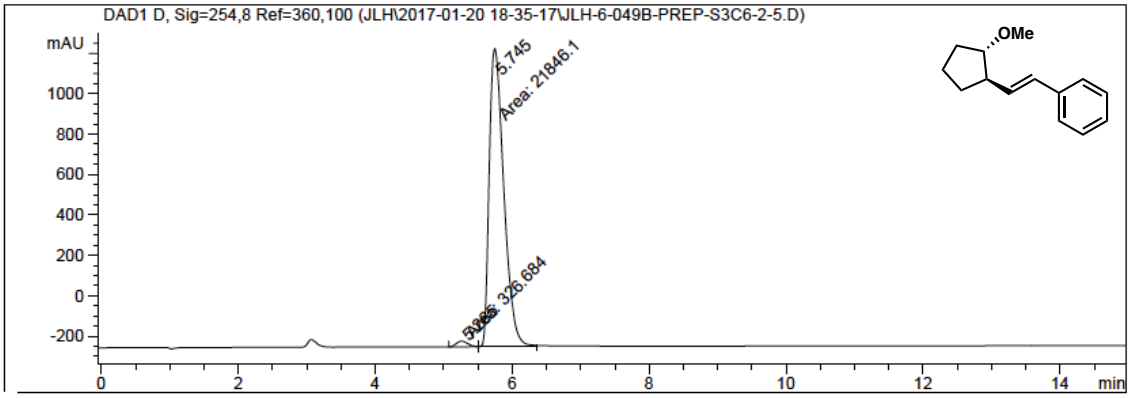
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	7.060	MM	0.2842	681.85974	39.98673	4.8268
2	8.917	MM	0.3756	1.34446e4	596.64233	95.1732

117 (Figure 2.10): racemic, *trans*-product



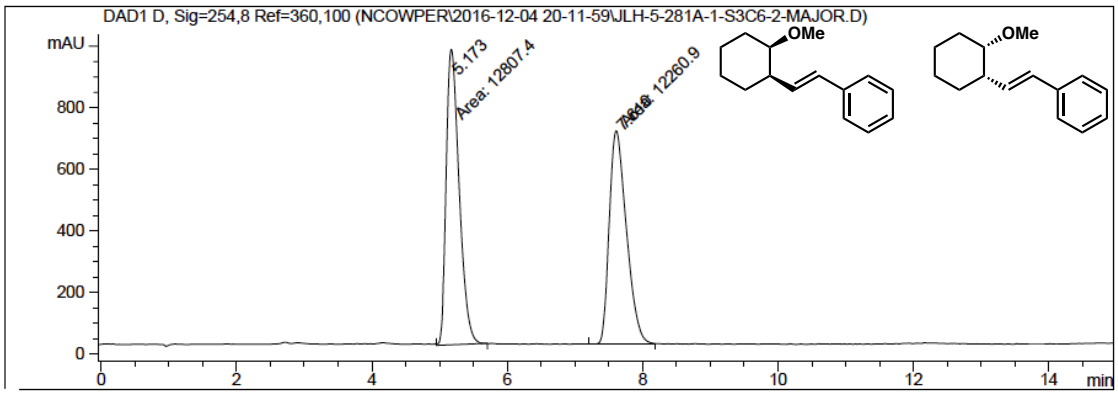
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	5.328	MM	0.2089	1.05817e4	844.24554	47.9846
2	5.857	MM	0.2395	1.14706e4	798.26849	52.0154

117 (Figure 2.10): enantioenriched, 97% ee



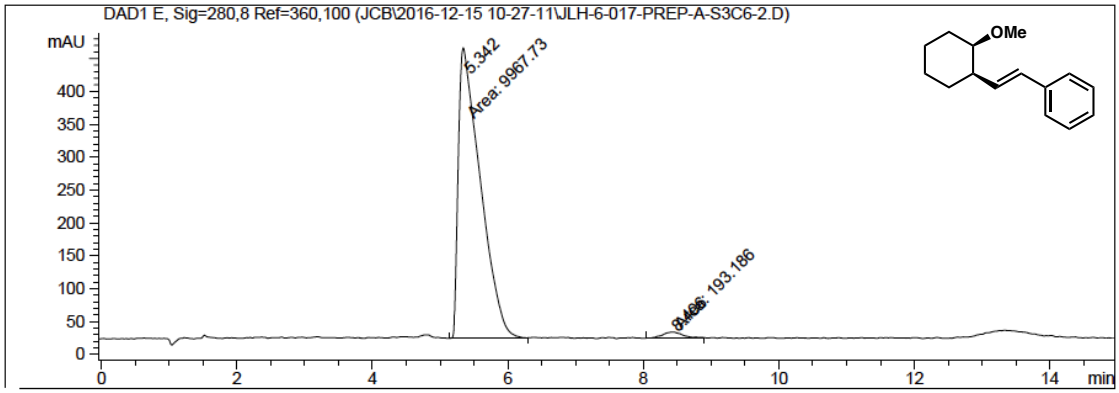
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	5.265	MM	0.1917	326.68356	28.39545	1.4734
2	5.745	MM	0.2466	2.18461e4	1476.56323	98.5266

118(Figure 2.10): racemic, *cis*-product



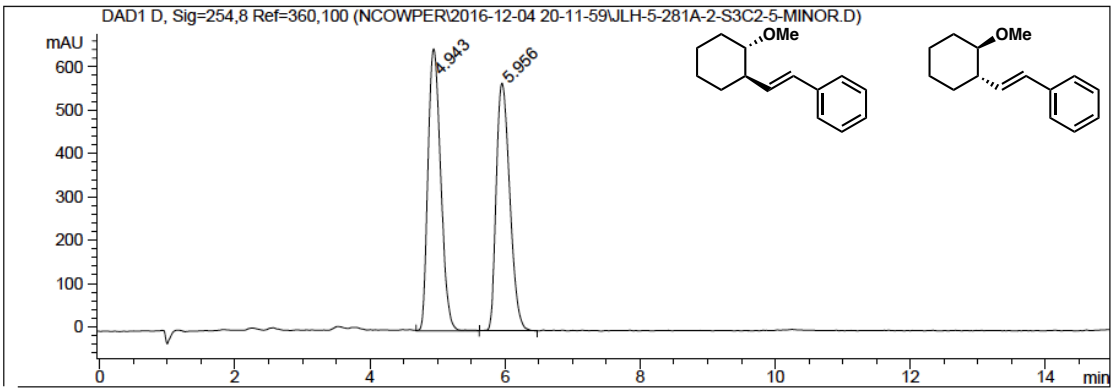
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	5.173	MM	0.2222	1.28074e4	960.75812	51.0900
2	7.610	MM	0.2944	1.22609e4	694.19666	48.9100

118 (Figure 2.10): enantioenriched, 96% ee



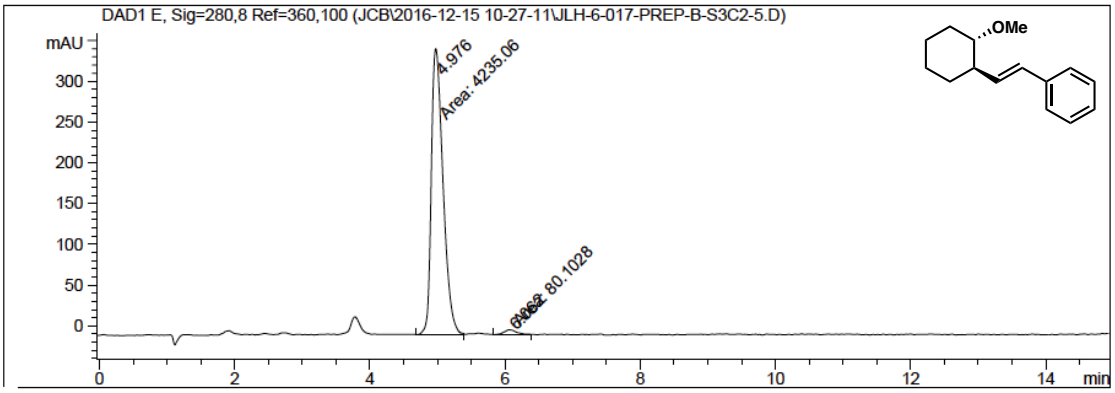
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	5.342	MM	0.3759	9967.73145	442.00150	98.0987
2	8.406	MM	0.3517	193.18593	9.15547	1.9013

118' (Figure 2.10): racemic, *trans*-product



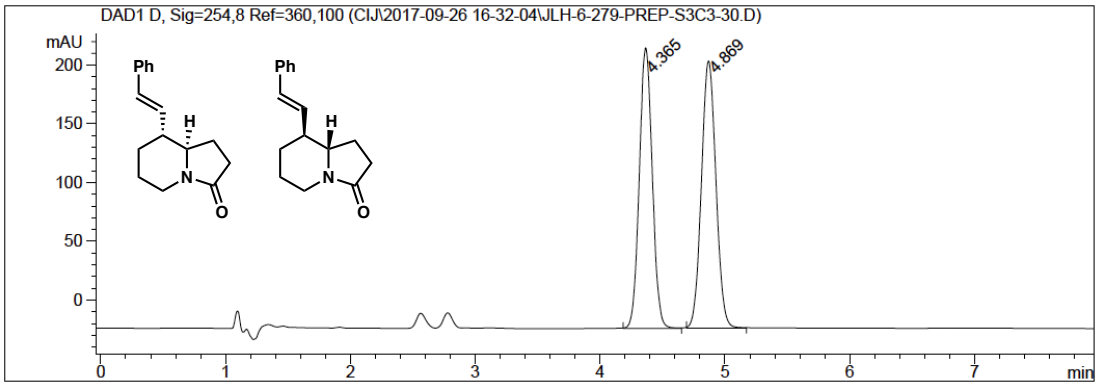
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	4.943	VV	0.2092	8538.20312	650.19324	51.7336
2	5.956	VV	0.2227	7965.97852	571.36676	48.2664

118' (Figure 2.10): enantioenriched, 96% ee



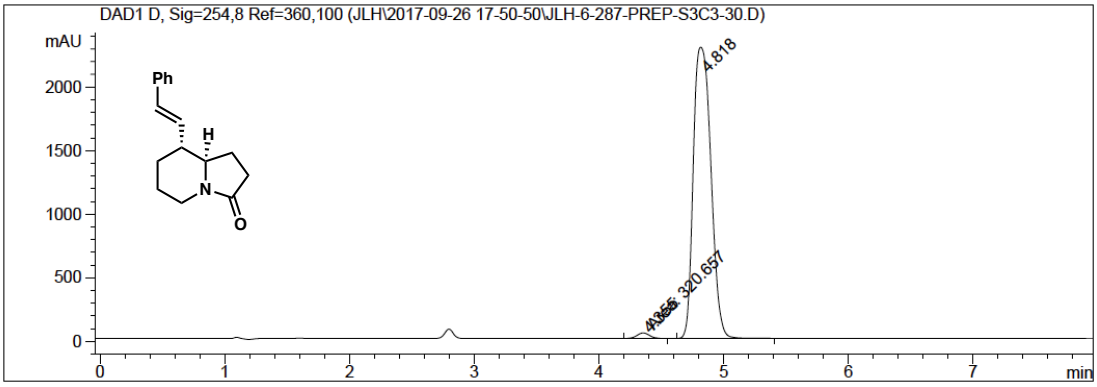
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	4.976	MM	0.2009	4235.05713	351.38831	98.1437
2	6.062	MM	0.2212	80.10277	6.03670	1.8563

121 (Figure 2.11): racemic



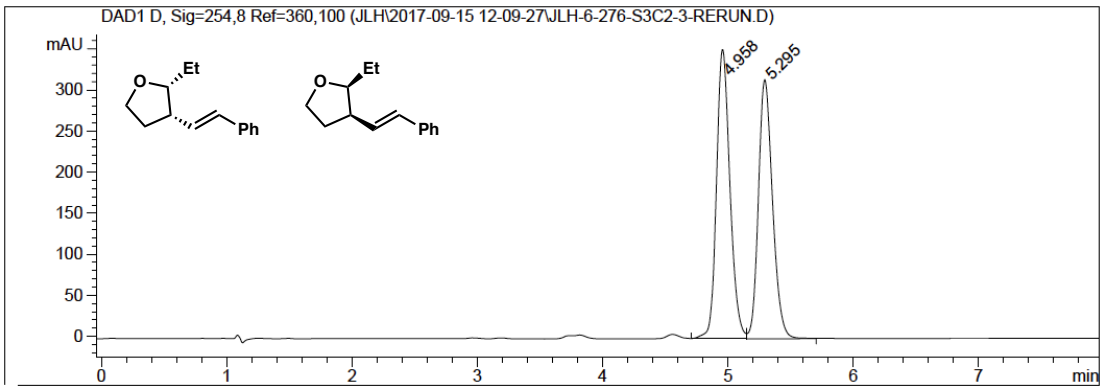
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	4.365	BB	0.1164	1725.97961	238.47392	48.3867
2	4.869	BB	0.1265	1841.07483	227.26039	51.6133

121 (Figure 2.11): enantioenriched, 97% ee



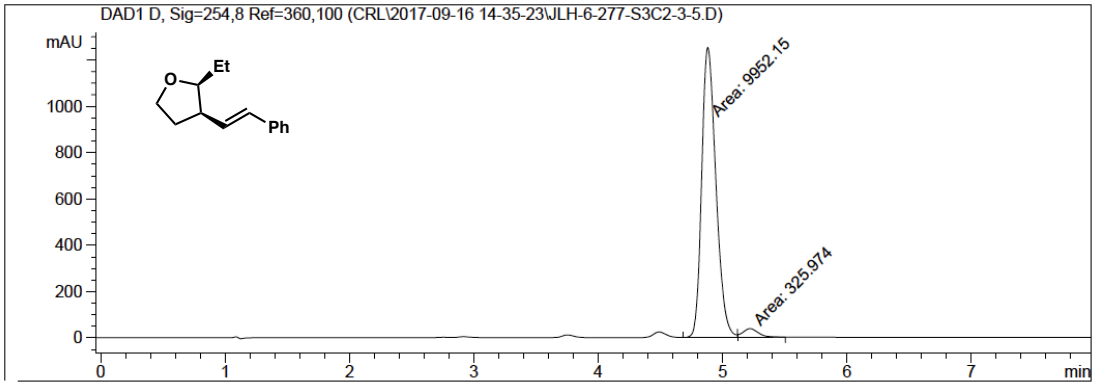
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	4.355	MM	0.1195	320.65738	44.71091	1.4017
2	4.818	BB	0.1586	2.25552e4	2295.60620	98.5983

123a (Scheme 2.8): racemic



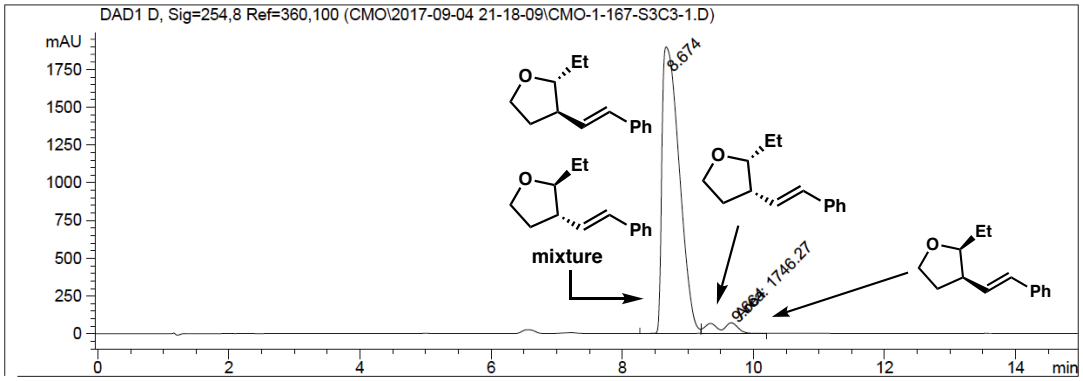
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	4.958	VV	0.1153	2631.88892	351.65015	51.5197
2	5.295	VB	0.1197	2476.61987	314.98431	48.4803

123a (Scheme 2.8): enantioenriched, 94% ee



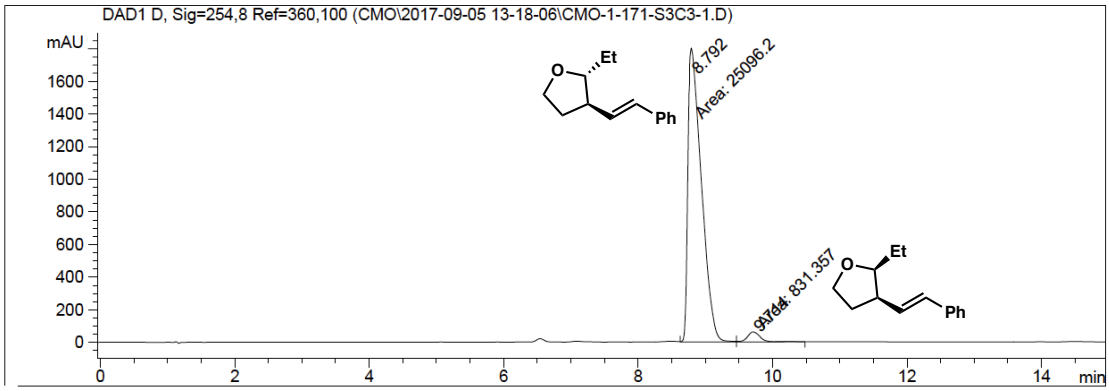
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	4.881	MM	0.1319	9952.15039	1257.06738	96.8285
2	5.220	MM	0.1437	325.97403	37.80476	3.1715

124a (Scheme 2.8): racemic (*OD-H column, separates diastereomers*), 20:1 dr



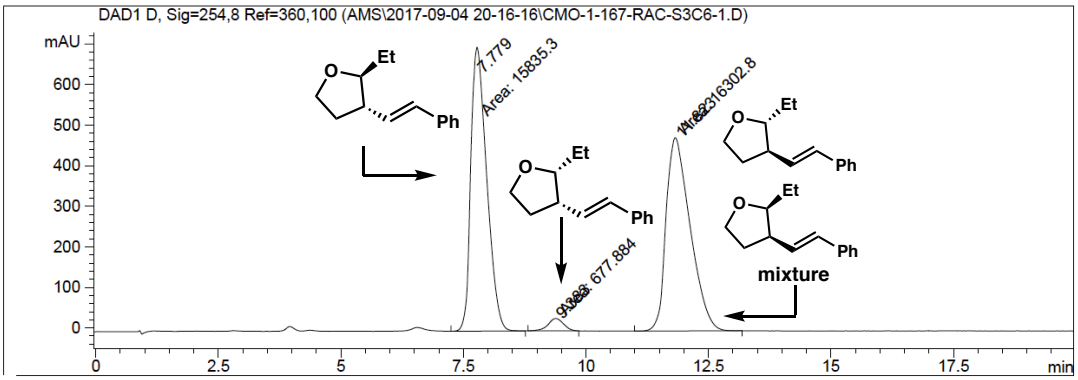
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	8.674	BV	0.2905	3.48916e4	1897.94568	95.2337
2	9.664	MM	0.4156	1746.26965	70.03025	4.7663

124a (Scheme 2.8): enantioenriched (*OD-H column, separates diastereomers*), 30:1 dr



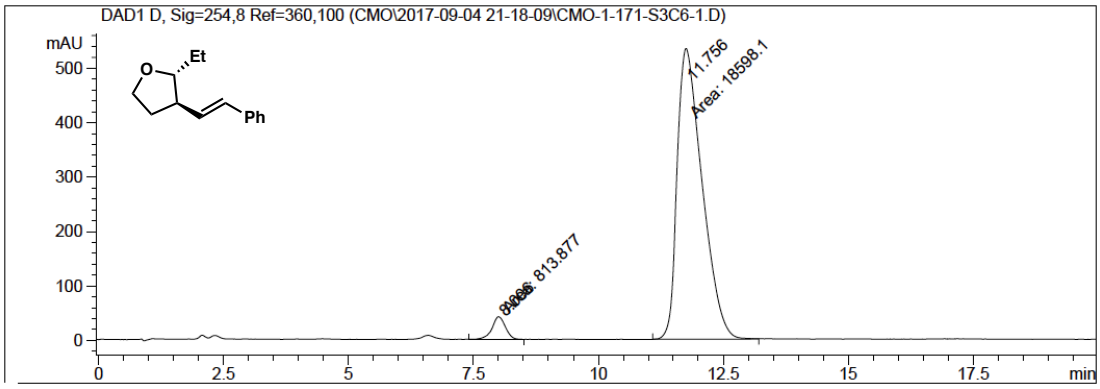
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	8.792	MM	0.2318	2.50962e4	1804.12939	96.7935
2	9.714	MM	0.2231	831.35657	62.09455	3.2065

124a (Scheme 2.8): racemic (*OB-H column, separates enantiomers*)



Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	7.779	MM	0.3770	1.58353e4	700.04340	48.2548
2	9.383	MM	0.3664	677.88428	30.83868	2.0657
3	11.823	MM	0.5703	1.63028e4	476.39767	49.6795

124a (Scheme 2.8): enantioenriched (*OB-H column, separates enantiomers*), 91% ee



Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	8.006	MM	0.3198	813.87683	42.41827	4.1927
2	11.756	MM	0.5799	1.85981e4	534.51337	95.8073

raw % ee = 95.8073 – 4.1927 = 91.61% ee
remove minor diastereomer: remove 3.2% of total area from peak 2 → new area = 17977
adjusted % ee = 95.6745 – 4.3255 = 91.35% ee

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