THE DEVELOPMENT OF BIFUNCTIONAL ALLYLBORONATE REAGENTS FOR STEREOSELECTIVE CARBONYL ALLYLBORATION

by

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Abstract

CHAPTER 1

The synthesis of a bifunctional allylboron reagent via Ni-catalyzed borylation of allylic acetate is developed. Subsequent allylation of aldehydes, ketones and cyclic aldimines gave homoallylic alcohols and amines in good yields. The allylsilane moiety in the products serves as a useful handle for subsequent transformations.

CHAPTER 2

The enantioselective *anti*- and *syn*-(borylmethyl)allylation of aldehydes via phosphoric acid catalysis is developed. Both (*E*)- and (*Z*)-γ-borylmethyl allylboronate reagents were prepared via the Cu-catalyzed highly stereoselective protoboration of 1,3-dienylboronate. Chiral phosphoric acid-catalyzed aldehyde allylation with either the (*E*)- or (*Z*)-allylboron reagent provided 1,2-*anti*- or 1,2-*syn*-adducts in good yields with high enantioselectivities. The application to the synthesis of morinol D was accomplished.

CHAPTER 3

A highly stereoselective synthesis of (*E*)-*δ*-boryl-*anti*-homoallylic alcohols is developed. In the presence of a Lewis acid, aldehyde allylation with *α*-boryl-(*E*)-crotylboronate gave *δ*-boryl-anti-homoallylic alcohols in good yields with excellent *E*-selectivity. The *E*-vinylboronate group in the products provides a useful handle for cross-coupling reactions as illustrated in the fragment synthesis of chaxamycins C and D.

CHAPTER 4

Highly stereo- and enantioselective synthesis of (*E*)-δ-hydroxymethyl-anti-homoallylic alcohols is developed. Under the developed conditions, reactions between aldehydes and chiral nonracemic α-borylmethyl-(*E*)-crotylboronate with oxidative workup gave δ-hydroxymethyl-anti-homoallylic alcohols with high *E*-selectivities and enantioselectivities.

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List of Abbreviations

Å	Angstroms
Bn	Benzyl
9-BBN	9-Borabicyclo(3.3.1)nonane
Bpin	Boronic acid pinacol
Bu	Butyl
°C	Degrees celcius
cod	1,5-Cyclooctadiene
$CDCl_3$	Deuterated chloroform
CH_2Cl_2	Dichloromethane
d	Doublet
dba	Dibenzylideneacetone
DCE	1,2-Dichloroethane
dd	Doublet of doublets
ddd	Doublet of doublet of doublets
DMF	Dimethylformamide
dppf	1,1′-Bis(diphenylphosphino)ferrocene
dr	Diastereomeric ratio
E	Electrophile
ee	Enantiomeric excess
Et	Ethyl
Et_2O	Diethylether
EtOAc	Ethyl acetate

eqiuv.	equivalent
h	hour
HPLC	High-performance liquid chromatography
HRMS	Lowest unoccupied molecular orbital
Hz	Hertz
Im	Imidazole
4-iodoanisole	4-Methoxyiodobenzene
^{d}Ipc	Diisopinocampheylborane
^{i}Pr	Isopropyl
IPr•HCl	1,3-Bis-(2,4,6-Tribenzhydrylphenyl)-1H-imidazol-3-ium chloride
J	Coupling constant
L	Ligand
L.A.	Lewis acid
LTMP	Lithium tetramethylpiperidide
2,6-lutidine	2,6-Dimethylpyridine
M	Molar
m	Multiplet
Me	Methyl
MeOH	Methanol
Met	Metallic
mol	Mole
MS	Molecular sieves
ND	Not detected

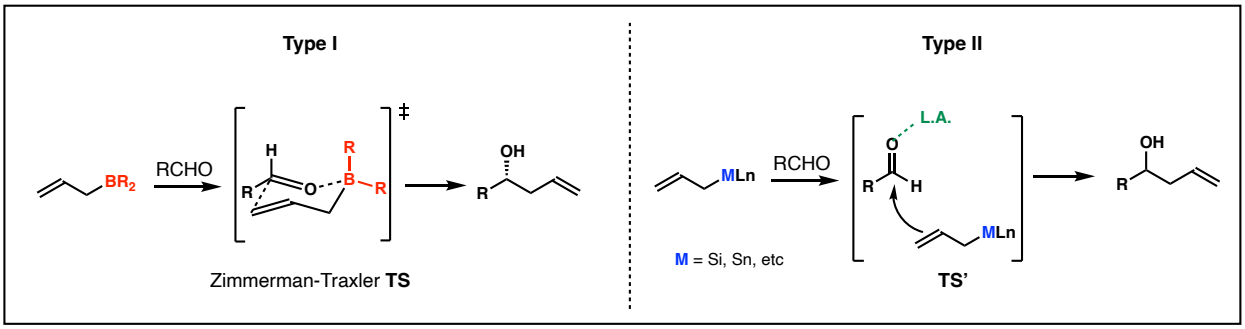
NMR	Nuclear magnetic resonance
NOE	Nuclear Overhauser effect
O_3	Ozone
OAc	Acetate
Ph	Phenyl
PhMe	Toluene
PPh_3	Triphenylphosphine
ppm	Parts per million
rt	Room temperature
s	Singlet
S_E2	Bimolecular electrophilic substitution
SPhos	2-Dicyclohexylphosphino-2′,6′-dimethoxybiphenyl
TS	Transition State
Ts	Toluenesulfonyl
t	Triplet
TBAF	Tetra-n-butylammonium fluoride
TBDPS	*tert*-Butyldiphenylsilyl
TBS	*tert*-Butyldimethylsilyl
^{t}Bu	*tert*-butyl
TES	Triethylsilyl
TFAA	Trifluoroacetic anhydride
THF	Tetrahydrofuran
TIPS	Triisopropylsilyl

TLC	Thin-layer chromatography
TMSOTf	Trimethylsilyl trifluoromethanesulfonate
tol	Toluene
Xantphos	(9,9-Dimethyl-9H-xanthene-4,5-diyl)bis(diphenylphosphane)

Introduction

The formation of carbon-carbon bond is one of the most important reactions in organic synthesis. Carbonyl allylation with allylic organometallics is a powerful method to create the C-C bond.[1-8] Based on the reaction mechanisms, carbonyl allylation with allylic organometallics can be divided into reactions with type I reagents and type II reagents. The carbonyl addition of type II reagents proceeds through acyclic transition states. Hence, the addition of type II reagents to carbonyl compounds is not stereospecific and usually stereoconvergent.[5] By contrast,

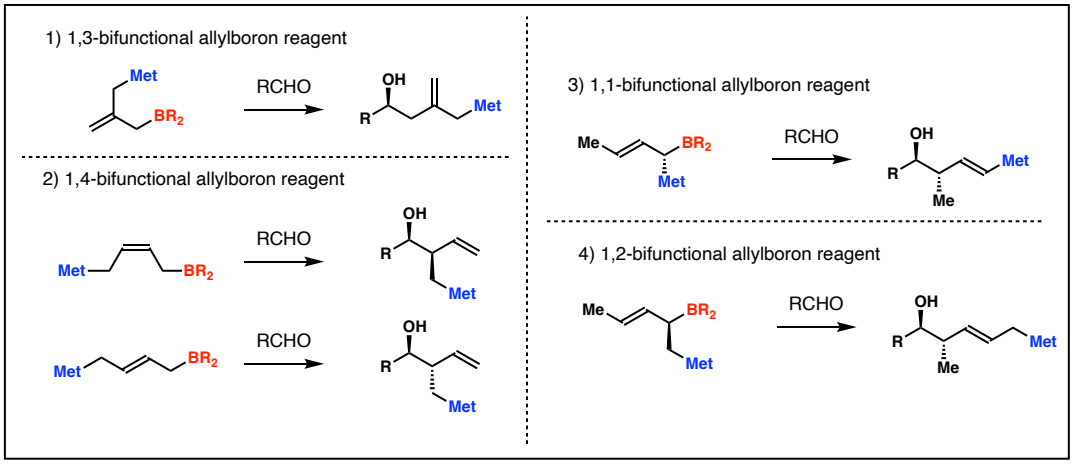
Scheme 1.0. Type I and Type II allylation reagent



carbonyl allylation with type I reagents proceeds with high stereospecificity via the well-established, six-membered Zimmerman-Traxler transition state.[9,10] Allylic boron reagents as one class of type I reagents have recently emerged as versatile reagents in modern organic synthesis owing to the highly predictable stereochemical outcomes. Although allyl boranes are highly reactive toward the carbonyl allylation, they lack the tolerance toward oxygen and moisture, and they often have low thermal stabilities. Allylic boronates can serve as more suitable alternatives because they are usually air- and water-stable.

A fundamentally important problem in organic chemistry is to increase the efficiency of a synthesis sequence, which could enable the expeditious construction of a diverse array of target molecular scaffolds. Toward this end, bifunctional allylation reagents are of great synthetic interest. Compared to the reactions with classic allylation reagents, allylations of electrophiles with these bifunctional reagents generate stereochemically well-defined functionalized homoallylic compounds, which can directly participate in a number of further synthetically useful transformations.

Scheme 1.1 Bifunctional allylboron reagent



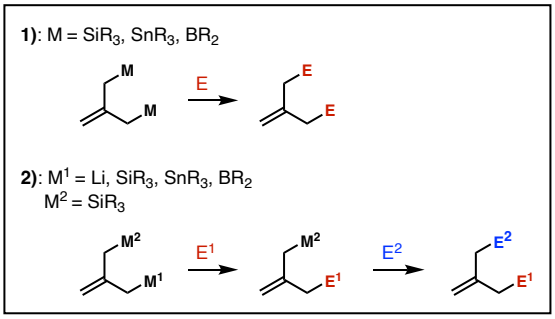
In the following four chapters, four types of developed bifunctional allylboronate reagents, 1,3-, 1,4-, 1,1- and 1,2-bifunctional allylboron reagents, and subsequent stereoselective carbonyl allylboration will be introduced (**Scheme 1.1**).

CHAPTER ONE

1,3-Bifunctional allylboron reagent

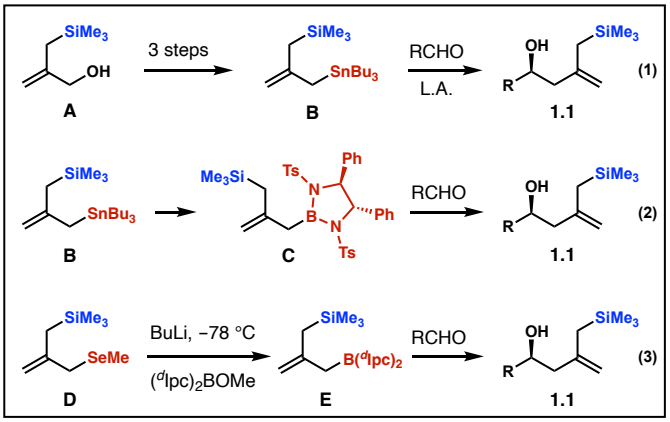
The carbonyl addition of 1,3-bifunctional allylation reagents (**Scheme 1.2**) produces homoallylic alcohols, leaving an untouched allylmetal moiety to engage in an intramolecular allylic transfer reaction to construct versatile building blocks such as 1,5-diols and tetrahydropyrans.[11-17] Additionally, a variety of piperidines can be synthesized from 1,3-bifunctional reagents and imines using the same strategies. 1,3-bifunctional allylation reagents (**Scheme 1.2**, top panel) with two identical allylmetal units can react with two equivalents of electrophiles to furnish symmetrical 1,5-bifunctionalized products.[18] However, in most cases, a stepwise manipulation of bismetallic reagents with different electrophiles would be more synthetically useful. To achieve this goal, the reactivities of two allymetal units should be sufficient different toward the electrophile addition. Several 1,3-bifunctional allylation reagents (**Scheme 1.2**, bottom panel) meeting this requirement have been developed.

Scheme 1.2. 1,3-Bifunctional allylation reagents



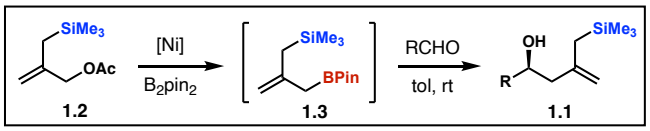
For example, the allylstannane unit in reagent **B** [2-(trimethylsilylmethyl) allyltri-n-butylstannane] selectively reacted with aldehydes to give homoallylic alcohols **1.1** in the presence of a Lewis acid (eq 1, **Scheme 1.3**).[19-24] By taking advantage of the different reactivities of allylboron and allylsilane toward carbonyl addition, Williams and coworkers developed a bifunctional allylation reagent **C** from organotin reagent **B**.[25-27] The reaction of **C** with aldehydes produced the same alcohol products **1.1** (eq 2, **Scheme 1.3**). More recently, 2-(trimethylsilyl-methyl) allylborane reagent **E** was synthesized from the allylselenium precursor **D** by the Kadota group (eq 3, **Scheme 1.3**).[28] Addition of **E** to aldehydes also afforded alcohols **1.1**. All three reactions formed product **1.1** with an allylsilane unit, which can be used as a handle for further transformations. However, these important achievements are not without any drawback. Organoboron reagent **E** is known to be moisture and oxygen sensitive, while the preparation of reagent **C** requires organotin reagent **B**, which is not environmentally benign. The development of less-toxic, air- and moisture-stable reagents to address these disadvantages is therefore valuable.

Scheme 1.3. Approaches to Homoallylic Alcohol 1.1 via Bifunctional Allylation Reagents



With our continuing interest in allylation chemistry, we set a goal to develop a reagent to solve this problem. We chose allylboronate **1.3** (**Scheme 1.4**) as the targeted reagent because of the low toxicity, and stability toward air and moisture. It is quite surprising that such a simple allylboronate reagent has not been synthesized previously. We envisioned to prepare this reagent via a Ni-catalyzed borylation of the commercially available allylic acetate **1.2** (**Scheme 1.4**). Reagent **1.3** should readily react with aldehydes to give homoallylic alcohols **1.1** that have an allylic silane moiety as a useful handle for subsequent transformations.

Scheme 1.4. preparation of reagent 1.3 and subsequent allylation

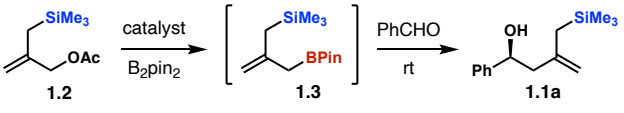


1.1 Preparation of 2-(trimethylsilyl-methyl) allylboronate

We began our studies by developing the reaction conditions for borylation of allylic acetate **1.2**. The initial experiments were conducted with CuCl as the catalyst for allylic borylation.[29] While the reaction did not occur in the absence of a ligand, ^{1}H NMR spectroscopy indicated that allylic acetate **1.2** was fully converted to reagent **1.3** with 5 mol % of Xantphos or dppbz as the ligand. In addition, the combination of $Ni(cod)_2$ and PPh_3 is also an effective catalytic system to convert allylic acetate **1.2** to **1.3**.[30] However, although reagent **1.3** is not moisture and oxygen sensitive, it is not stable enough toward flash column chromatography. Therefore, subsequent experiments were conducted to probe whether the aldehyde allylation step can be carried out in a one-pot manner. After full consumption of allylic acetate **1.2**,

benzaldehyde was added to the same reaction vessel. Gratifyingly, the allylation was complete in 2 h at ambient temperature, and homoallylic alcohol **1.1** was generated from the reaction. The results obtained from the Ni system are superior to those from the conditions under Cu catalysis. And homoallylic alcohol **1.1** was isolated in 73% yield (**Table 1.1**). The Ni catalyst can be removed by simply filtering the crude reaction mixture through a short pad of Celite. The obtained stock solution of reagent **1.3** can be stored at − 20 °C over two weeks with only minimal decomposition (< 10%).

Table 1.1 Evaluation of the reaction conditions for the aldehyde allylboration



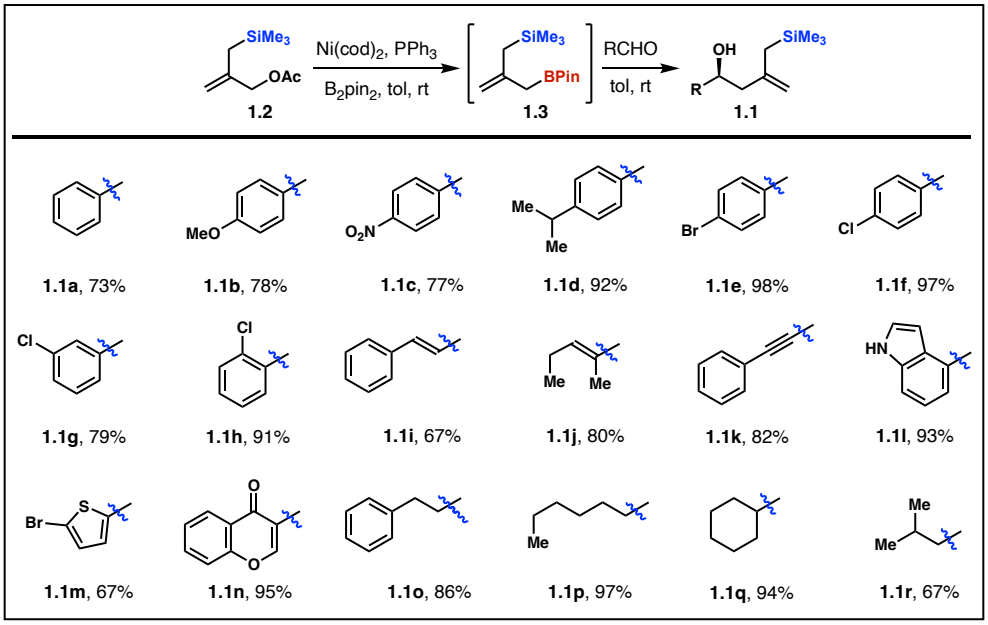
entry	catalyst	ligand	base	yield (**1.1a**) (%)
1	CuCl	no ligand	KO*t*-Bu	ND
2	CuCl	Xantphos	KO*t*-Bu	83
3	CuCl	dppbz	KO*t*-Bu	17
4	$Ni(cod)_2$	PPh_3	no base	73

1.2 Application to the stereoselective allylboration of aldehydes, ketones and amides

The reaction conditions developed for the synthesis of **1.1a** were then applied to reactions with a variety of aldehydes, and the results are summarized in **Scheme 1.5**. Allylation of aromatic aldehydes bearing electron-donating or electron-withdrawing substituents at the *para*-position of the arene provided products **1.1b-d** in 77-92% yields. Halogen-substituted aromatic aldehydes reacted to afford alcohols **1.1e-h** in 79-98% yields. Similar results were obtained with α, β-unsaturated aldehydes, and alcohols **1.1i-k** were formed in 67-82% yields. Reactions with heteroaromatic aldehydes occurred smoothly to furnish products **1.1l-n** in 67-95% yields.

Finally, aliphatic aldehydes are also suitable reaction partners, and alcohols **1.1o-r** were obtained in 67-97% yields. It should be noted that the allylsilane moiety in homoallylic alcohols **1.1** is sensitive to acidic conditions. For instance, homoallylic alcohols **1.1** were decomposed in aged deuterated chloroform within a few minutes. However, they are perfectly stable in d^6-acteone or d^8-toluene.

Scheme 1.5. Synthesis of Homoallylic Alcohols 1.1 via Allylic Borylation and Aldehyde Allylation



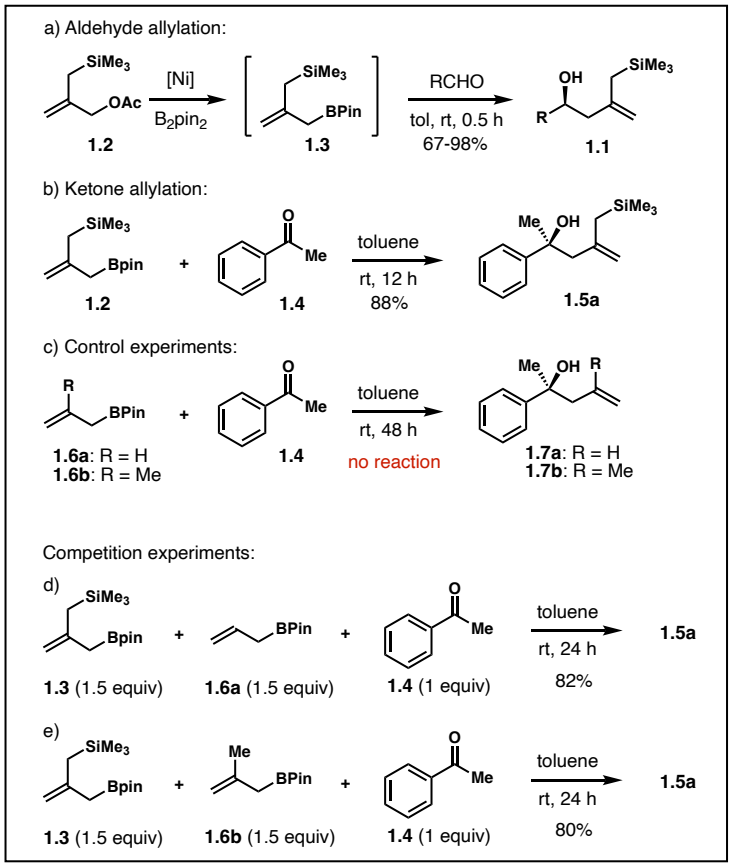
We noticed that the rate of aldehyde allylboration reaction with reagent **1.3** is rather fast; the starting aldehydes were consumed within 10−30 min at ambient temperature. By contrast, reactions of aldehydes with the parent pinacol allylboronates **1.6a** or **1.6b** require a much longer reaction time (several hours typically). The remarkable reactivity of reagent **1.3** is quite surprising, which promoted us to examine the reaction of ketones with allylboronate **1.3**. In the

event, upon exposure to freshly prepared reagent **1.3** (1.5 equiv), acetophenone **1.4** was completely consumed after 12 h at ambient temperature, and allylation product **1.5a** was isolated in 88% yield (eq b, **Scheme 1.6**).

In control experiments, the reaction of acetophenone **1.4** with allylboronate **1.6a** or **1.6b** under identical reaction conditions did not provide any allylation product **1.7a** or **1.7b** at ambient temperature even with prolonged reaction time (eq c, **Scheme 1.6**).

Competition experiments were also conducted to compare the reactivities of reagents **1.3** and **1.6** toward ketone addition. As shown in **Scheme 1.6**, when equal amounts of reagents **1.3** and **1.6a** (1.5 equiv) were added to ketone **1.4** (1 equiv), alcohol **1.5a** was obtained as the only product in 82% yield from the reaction (eq d, **Scheme 1.6**). Similar results were obtained when allylboronate **1.3** and **1.6b** were used, and only **1.5a** was isolated in 80% yield (eq e, **Scheme 1.6**). Again, formation of products **1.7** was not detected in either case. These data indicate that reagent **1.3** is much more reactive than the parent allylboronates **1.6** in reactions with ketones.

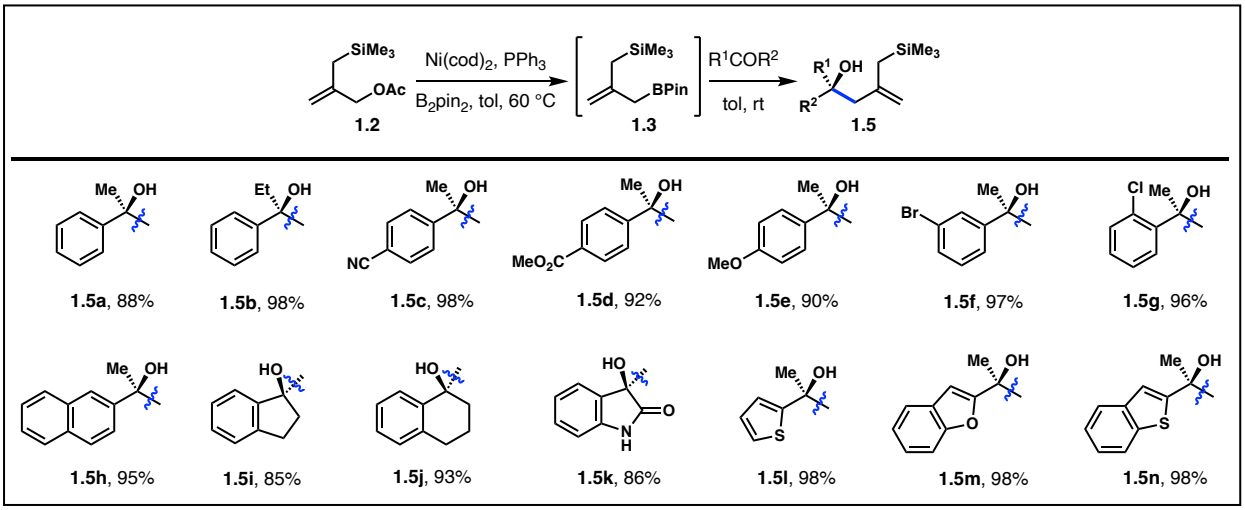
Scheme 1.6. Ketone allylation



To demonstrate the generality of this reaction, we explored the scope of ketone that participated in reactions with reagent **1.3**. As summarized in **Scheme 1.7**, allylboronate **1.3** reacted with various aromatic and heteroaromatic ketones to give tertiary alcohol products in high yields. For instance, allylboration of propiophenone with reagent **1.3** gave alcohol product in 98% yield. Aromatic ketones substituted with an electron-donating or withdrawing group at the *para*-position worked well to form tertiary alcohols in **1.5b-e** 90-98% yield. Reactions of aromatic ketones with various substitution patterns afforded products **1.5f-g** in 96-97% yield. The reaction of **1.3** with 2-acetonaphthone occurred to give product **1.5h** in 95% yields. Cyclic aromatic ketones, such as indanone, tetralone and isatin, reacted with **1.3** to afford tertiary alcohol products **1.5i-k** in 85-93% yields. Heteroaromatic ketones are also suitable substrates for

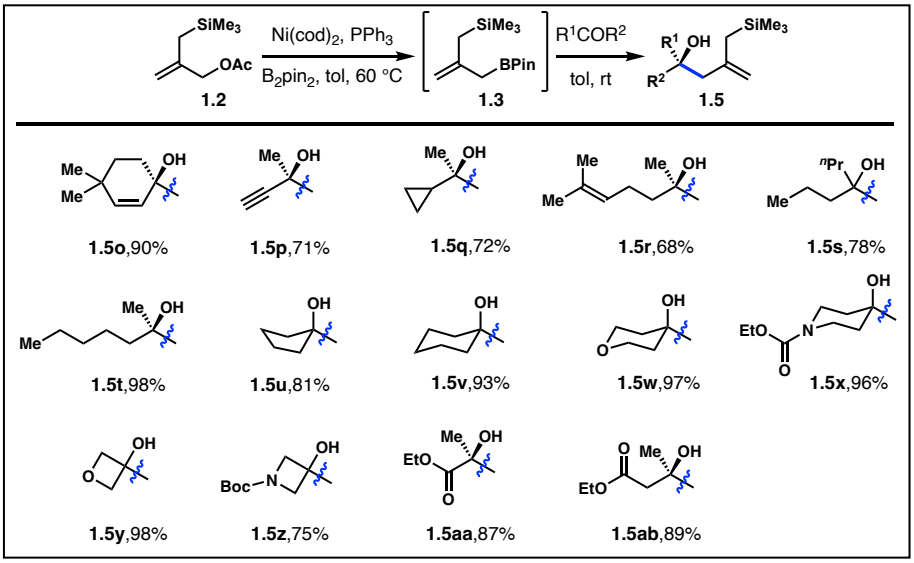
the allylation. Reactions of 2-acetylthiophene, 2-acetylbenzofuran, and 2-acetylthiophene with reagent **1.3** proceeded smoothly to provide tertiary alcohols **1.5l-n** in excellent yields.

Scheme 1.7. Scope of Aromatic and Heteroaromatic Ketone in Reactions with Allylboronate



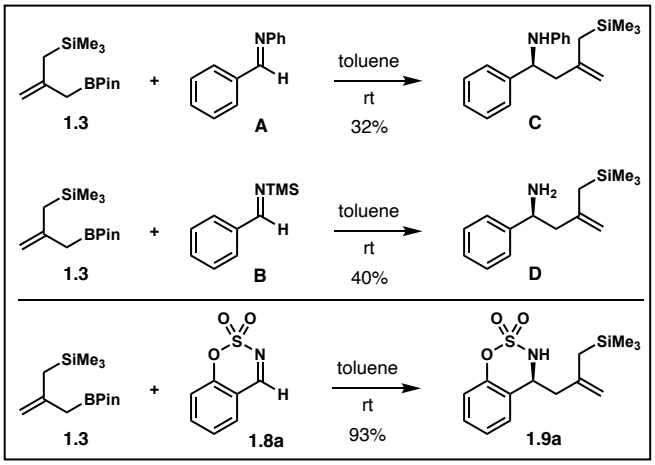
Reactions of allylboronate **1.3** with α, β-unsaturated and aliphatic ketones were also examined and the results are summarized in **Scheme 1.8.** α, β-Unsaturated ketones, such as 4,4-dimethyl-2-cyclohexen-1-one and 3-butyn-2-one, reacted with reagent **1.3** to provide tertiary alcohols **1.5o-p** in 71-90% yields. Reactions with various acyclic aliphatic ketones occurred to deliver allylated products **1.5q-t** in 68-98% yields. Cyclic aliphatic ketones also participated in reactions with allylboronate **1.3** to give tertiary homoallylic alcohols in **1.5u-z** 75-98% yields. Allylation of ketoesters such as ethyl pyruvate and ethyl acetoacetate produced homoallylic alcohols **1.5aa-bb** in 87-89% yields.

Scheme 1.8. Scope of α, β-Unsaturated and Aliphatic Ketone in Reactions with Allylboronate 1.3



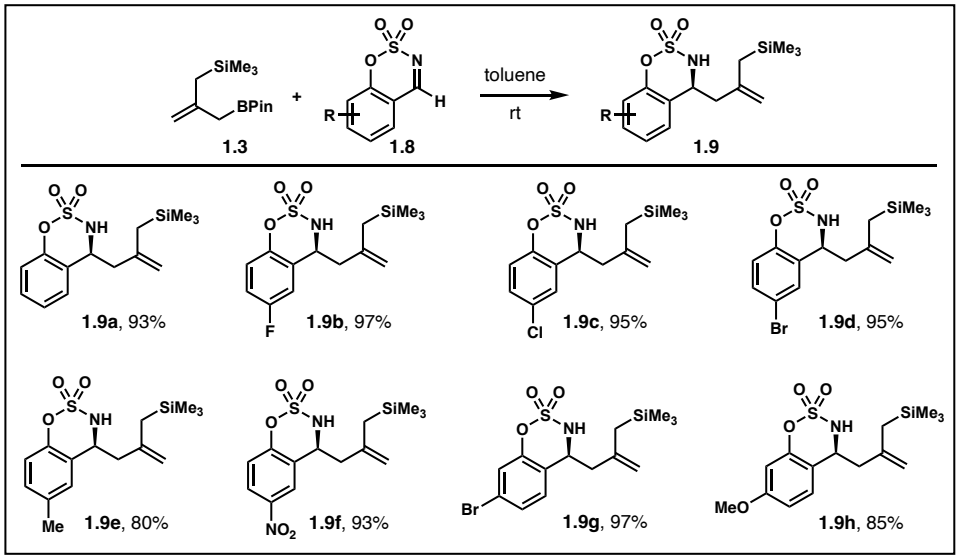
Imine allylation is an important method to access secondary carbinamines. While imines are generally much less reactive compared to aldehydes, we were intrigued whether the highly reactive allylboronate **1.3** could also react with imines to provide amine products. The reactions of allylboronate **1.3** with several imines were examined under standard reaction conditions. As shown in **Scheme 1.9.**, the reaction of imine **A** with allylboronate **1.3** was conducted in toluene at ambient temperature for 24 h, and secondary carbinamine **C** was obtained in 32% yield. Allylboration of imine **B** with reagent **1.3** provided amine product **D** in a similar yield (40%). We suspected that an electron-withdrawing group on the N atom of imines might improve their reactivity toward allyl addition. Gratifyingly, when cyclic aldimine **1.8a** was used, [14] the reaction of **1.3** with **1.8a** produced secondary carbinamine **1.9a** in 93% yield in the absence of any additive at ambient temperature.

Scheme 1.9. Allylation of imines with allylboronate 1.3



The scope of cyclic aldimine **1.8a** that participated in reactions with reagent **1.3** was explored, and the results are summarized in **Scheme 1.10**. A broad range of cyclic aldimines **1.8** with different electronic properties and various substitution patterns reacted with allylboronate **1.3**, and secondary carbinamine products **1.9a-h** were obtained in 80-97% yield. Again, these results further demonstrated the high reactivity of allylboronate **1.3**.

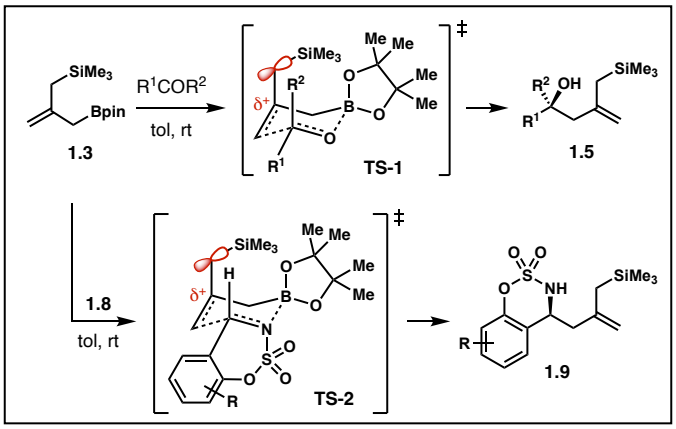
Scheme 1.10. Scope of Cyclic Aldimine in Reactions with Allylboronate 1.3



1.3 Proposed rationale for the high reactivity

The exceptionally high reactivity of allylboronate **1.3** is rather intriguing. Unlike the reaction with type II allylation reagents such as allylsilanes that often involves a carbocation intermediate,[31-33] it is generally considered that carbonyl or imine addition with allylboron reagents (type I allylation reagents) is a concerted process that does not involve any intermediate. However, the high reactivity of allylboron reagent **1.3** (compared to allylboronates **1.6**) indicates that carbonyl addition with allylboronate **1.3** may proceed through a concerted but asynchronous pathway. As such, the partially developed carbocation in **TS-1** or **TS-2** is stabilized by the electrons from the neighboring C-Si bond (β-Si effect)[34-37] to significantly lower the activation energy of the allylboration process (**Scheme 1.11**). By contrast, the parent allylboronates **1.6** do not have the appended trimethylsilyl group and cannot have such a stabilization benefit energetically. Consequently, reactions of allylboronates **1.6** with ketones usually do not occur at ambient temperature.

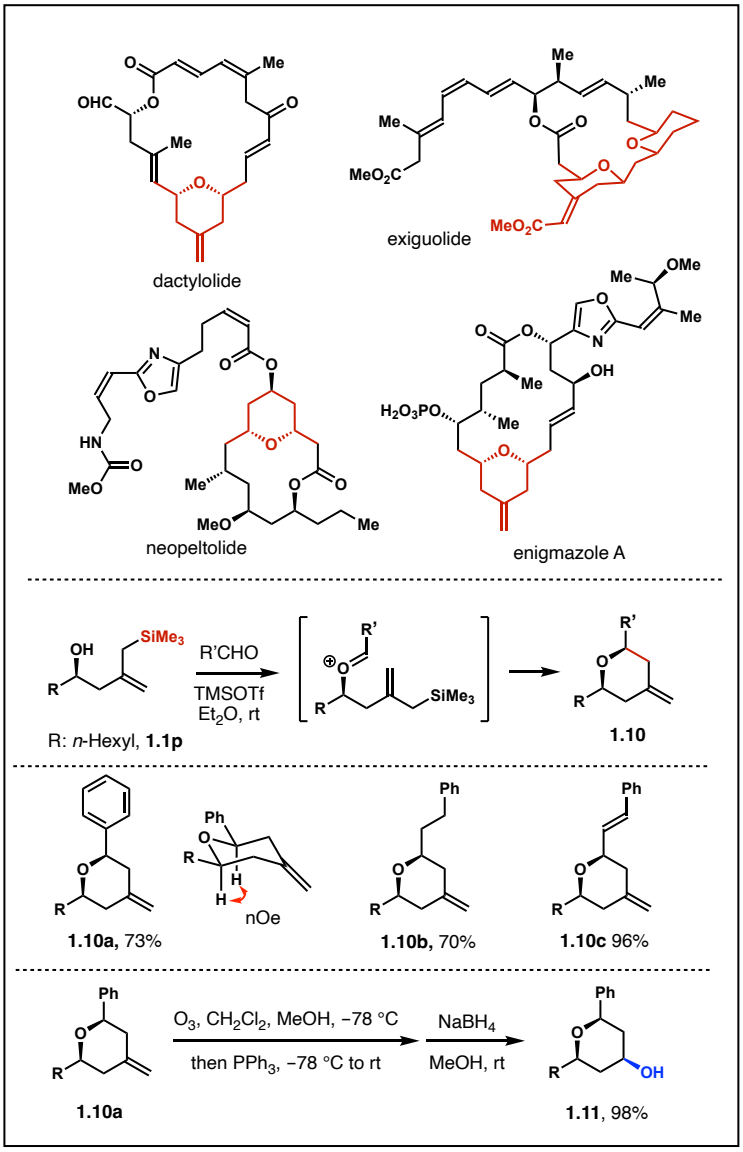
Scheme 1.11. Proposed Rationale for the High Reactivity of 1.3



1.4 Double allylation studies

cis-2,6-Disubstituted tetrahydropyran is a common scaffold in numerous natural products (**Scheme 1.12**).[14,16,38,39] As many strategies have been developed to construct such a structural entity, homoallylic alcohols **1.1** can also be utilized to synthesize tetrahydropyrans. As shown in Scheme **1.12**, in the presence of TMSOTf, reactions of alcohol **1.1q** with a few representative aldehydes gave *cis*-2,6-disubstituted tetrahydropyran products **1.10a-c** in 70-96% yields with >20:1 diastereoselectivities (determined by the nOe studies). In addition, 4-hydroxyl-tetrahydropyran **1.11** was obtained in 98% yield via a one-pot ozonolysis and reduction reaction sequence from **1.10a**. The stereochemistry of the newly formed hydroxyl group was assigned by the nOe studies.

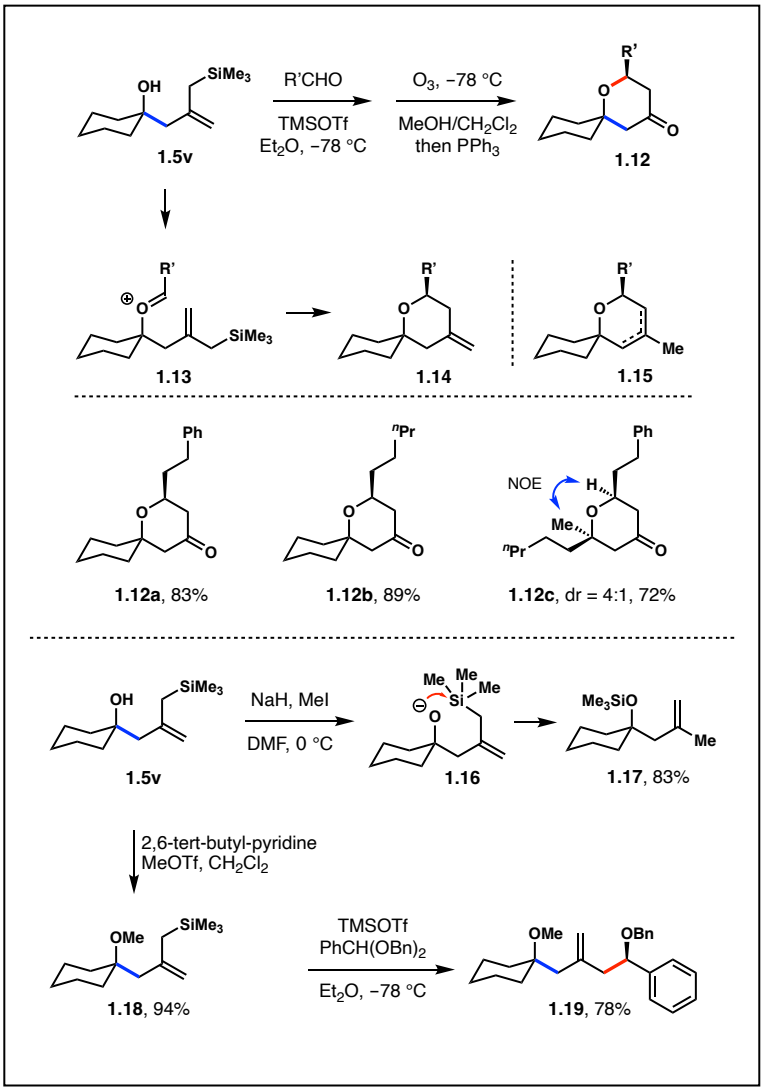
Scheme 1.12. Stereoselective Synthesis of *cis*-2,6-Disubstituted Tetrahydropyran from Homoallylic Alcohol 1.1



The homoallylic alcohol and amine products obtained from this method contain an allylsilane unit, which can be used for a second allylation reaction (**Scheme 1.13**). For example, compound **1.5v** reacted with a few representative aldehydes to give tetrahydropyrans **1.14** via the

intermediacy of oxocarbenium **1.13**. Products **1.14** were contaminated with a small amount of olefin isomerization

Scheme 1.13. Double Allylation Studies



product **1.15** (3-5%) after purification. However, the side products can be separated after ozonolysis, and ketones **1.12** were isolated in 83-89% yield. In the case of **1.12c**, two diastereomers (4:1) were obtained; **1.12c** was isolated as the major diastereomer in 72% yield.

The stereochemistry of **1.12c** was assigned by the nOe analysis. In addition, compound **1.18**, which was synthesized via methylation of **1.5v** with 2,6-tert-butyl-pyridine and MeOTf, reacted with phenyl dibenzyl acetal in the presence of TMSOTf to give benzyl ether **1.19** in 78% yield (methylation of **1.5v** with NaH and MeI gave TMS ether **1.17** through a Brook rearrangement of alkoxide **1.16**). In both types of reactions, bifunctional allylation reagent **1.3** serves as a linchpin to join two distinct carbonyl compounds (**Scheme 1.13**).

1.5 Conclusion

In summary, we developed a Ni-catalyzed borylation of allylic acetate to access 1,3-bifunctional allylation reagent **1.3**. This silyl-allylboron reagent **1.3** readily reacted with a variety of aldehydes to give homoallylic alcohols **1.1** in good yields. The allylsilane unit embedded in product **1.1** serves as a useful handle for additional functional group transformations, as illustrated by the diastereoselective synthesis of cis-2,6-disubstituted tetrahydropyrans. Silyl-allylboron reagent **1.3** can also react with a broad range of ketones or cyclic aldimines gave tertiary alcohols or secondary carbinamines in excellent yields at ambient temperature without any catalyst or additive. The allylsilane moiety in the products underwent a second allylation with aldehydes or acetals to form synthetically useful products.

1.6 Experimental section

General Information

All reaction solvents were purified before use. Tetrahydrofuran, diethyl ether and toluene were purified by passing through a solvent column composed of activated A-1 alumina. Unless indicated otherwise, all reactions were conducted under an atmosphere of argon using flame-dried or oven-dried (120 ˚C) glassware. The term "concentrated under reduced pressure" refers to the removal of solvents and other volatile materials using a rotary evaporator with the water bath temperature below 30 ˚C, followed by the removal of residual solvents at high vacuum (< 0.2 mbar).

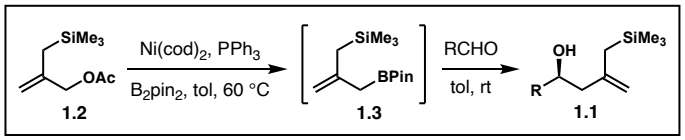
Proton nuclear magnetic resonance (^{1}H NMR) spectra were acquired on commercial instruments (400 and 600 MHz) at Auburn University NMR facility. Carbon-13 nuclear magnetic resonance (^{13}C NMR) spectra were acquired at 101 and 151 MHz. The proton signal for the residual non-deuterated solvent (δ 7.26 for chloroform, δ 2.05 for acetone and δ 2.08 for toluene) was used as an internal reference for ^{1}H NMR spectra. For ^{13}C NMR spectra, chemical shifts are reported relative to the resonance of chloroform (δ 77.36) and acetone (δ 29.84). Coupling constants are reported in Hz. High-resolution mass spectra were recorded on a commercial high-resolution mass spectrometer via the Micro Mass/Analytical Facility operated by the College of Chemistry and Biochemistry, Auburn University.

Analytical thin layer chromatography (TLC) was performed on Kieselgel 60 F254 glass plates precoated with a 0.25 mm thickness of silica gel. The TLC plates were visualized with UV light and/or by staining with Hanessian solution (ceric sulfate and ammonium molybdate in aqueous sulfuric acid) or $KMnO_4$. Column chromatography was generally performed using

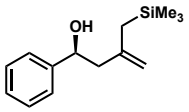
Kieselgel 60 (230-400 mesh) silica gel, typically using a 50-100:1 weight ratio of silica gel to crude product.

Procedure and characterization

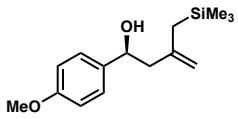
Stereoselective allylboration of aldehydes, ketones and amides



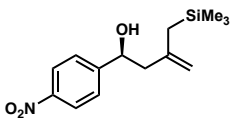
General procedure for synthesis of homoallylic alcohols 1.1: In an Ar-filled glove box, allylic acetate **1.2** (56 mg, 0.3 mmol, 1 equiv), B_2Pin_2 (84 mg, 0.33 mmol, 1.1 equiv), $Ni(cod)_2$ (4 mg, 0.015 mmol, 5 mol %), PPh_3 (4 mg, 0.015 mmol, 5 mol %), toluene (0.5 mL) and a Teflon-coated magnetic stirring bar were sequentially added into a 1-dram vial. The vial was sealed with a cap containing a PTFE-lined silicone septum and removed from the glove box stirring at 60 ˚C for 2 h. After complete consumption of allylic acetate **1.2**, the mixture was filtered through a pad of Celite and the solution was concentrated under reduced pressure. The obtained allylboronate **1.3** was dissolved in anhydrous toluene and was used for aldehyde allylation without further purification. To a reaction vial containing a Teflon-coated magnetic stirring bar was added freshly distilled aldehyde (0.1 mmol, 1.0 equiv) followed by addition of allylboronate **1.3** (0.15 mmol, 0.25 mL of a 0.6 M solution in toluene). The reaction mixture was then allowed to stir at ambient temperature. After complete consumption of the aldehyde, purification of the crude reaction mixture was performed by flash chromatography (gradient elution with hexane and EtOAc) to provide alcohol **1.1**.



***rac*-1-phenyl-3-((trimethylsilyl)methyl)but-3-en-1-ol (1.1a)** Prepared according to the general procedure. The crude mixture was purified by column chromatography to give compound **1.1a** in 73% yield (17 mg) as colorless oil. ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.30 – 7.43 (m, 4H), 7.19 – 7.30 (m, 1H), 4.77 (s, 2H), 4.73 (s, 1H), 2.21 – 2.43 (m, 3H), 1.61 (d, *J* = 13.9 Hz, 1H), 1.56 (d, *J* = 13.4 Hz, 1H), 0.02 (s, 9H). ^{13}C NMR (151 MHz, $CDCl_3$) δ 144.7, 144.2, 128.7, 127.8, 126.1, 111.5, 71.3, 49.5, 26.7, -1.0. HRMS (ESI): m/z for $C_{14}H_{22}OSiNa$ $[M+Na]^+$ calcd. 257.1338, found: 257.1334.

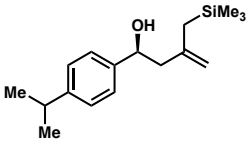


***rac*-1-(4-methoxyphenyl)-3-((trimethylsilyl)methyl)but-3-en-1-ol (1.1b)** Prepared according to the general procedure. The crude mixture was purified by column chromatography to give compound **1.1b** in 78% yield (21 mg) as colorless oil. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.30 (d, *J* = 8.5 Hz, 2H), 6.89 (d, *J* = 8.6 Hz, 2H), 4.77 (s, 1H), 4.76 – 4.74 (m, 1H), 4.73 (s, 1H), 3.81 (s, 3H), 2.34 (d, *J* = 6.7 Hz, 2H), 2.21 (s, 1H), 1.63 (d, *J* = 13.4 Hz, 1H), 1.57 (d, *J* = 14.4 Hz, 1H), 0.04 (s, 9H). ^{13}C NMR (151 MHz, $CDCl_3$) δ 159.2, 144.8, 136.4, 127.3, 114.0, 111.4, 71.0, 55.6, 49.3, 26.7, -1.0. HRMS (ESI): m/z for $C_{15}H_{24}O_2SiNa$ $[M+Na]^+$ calcd. 287.1443, found: 287.1450.

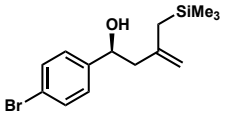


***rac*-1-(4-nitrophenyl)-3-((trimethylsilyl)methyl)but-3-en-1-ol (1.1c)** Prepared according to the general procedure. The crude mixture was purified by column chromatography to give compound **1.1c** in 77% yield (22 mg) as colorless oil. ^{1}H NMR (600 MHz, $CDCl_3$) δ 8.21 (d, *J* = 8.6 Hz, 2H), 7.55 (d, *J* = 8.5 Hz, 2H), 4.94 – 4.84 (m, 1H), 4.80 (s, 2H), 2.49 (s, 1H), 2.37 (dd, *J* = 10.2, 6.0 Hz, 1H), 2.25 (dd, *J* = 13.5, 10.2 Hz, 1H), 1.63 (d, *J* = 13.4 Hz, 1H), 1.56 (d, *J* = 13.4 Hz, 1H), 0.05 (s, 9H). ^{13}C NMR (151 MHz, $CDCl_3$) δ

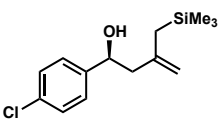
151.7, 147.4, 143.8, 126.8, 124.0, 112.4, 70.3, 49.5, 26.6, -1.1. HRMS (ESI): m/z for $C_{14}H_{21}NO_3SiNa$ $[M+Na]^+$ calcd. 302.1188, found: 302.1187.



***rac*-1-(4-isopropylphenyl)-3-((trimethylsilyl)methyl)but-3-en-1-ol (1.1d)** Prepared according to the general procedure. The crude mixture was purified by column chromatography to give compound **1.1d** in 92% yield (25 mg) as colorless oil. ^{1}H NMR (600 MHz, d^6-acteone) δ 7.29 (d, J = 7.8 Hz, 2H), 7.19 (d, J = 7.8 Hz, 2H), 4.84 – 4.74 (m, 1H), 4.66 (s, 1H), 4.58 (s, 1H), 3.93 (s, 1H), 2.80 – 2.97 (m, 1H), 2.37 (dd, J = 13.5, 8.9 Hz, 1H), 2.33 – 2.20 (m, 1H), 1.65 (d, J = 13.4 Hz, 1H), 1.59 (d, J = 13.4 Hz, 1H), 1.21 (d, J = 6.9 Hz, 6H), 0.03 (s, 9H). ^{13}C NMR (151 MHz, d^6-acteone) δ 148.0, 145.5, 144.3, 126.74, 126.70, 110.27, (110.26), 72.6, (72.5), 49.5, (49.4), 34.5, 27.1, 24.4, -1.2. HRMS (ESI): m/z for $C_{17}H_{28}OSiNa$ $[M+Na]^+$ calcd. 299.1807, found: 299.1815.

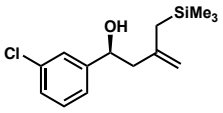


***rac*-1-(4-bromophenyl)-3-((trimethylsilyl)methyl)but-3-en-1-ol (1.1e)** Prepared according to the general procedure. The crude mixture was purified by column chromatography to give compound **1.1e** in 98% yield (31 mg) as colorless oil. ^{1}H NMR (600 MHz, d^6-acteone) δ 7.49 (d, J = 8.2 Hz, 2H), 7.34 (d, J = 8.1 Hz, 2H), 4.78 – 4.90 (m, 1H), 4.62 (s, 1H), 4.57 (s, 1H), 4.22 (s, 1H), 2.38 (dd, J = 13.4, 8.5 Hz, 1H), 2.30 (dd, J = 13.5, 4.0 Hz, 1H), 1.64 (d, J = 13.4 Hz, 1H), 1.59 (d, J = 13.4 Hz, 1H), 0.03 (s, 9H). ^{13}C NMR (151 MHz, d^6-acteone) δ 146.2, 145.0, 131.8, 128.9, 120.7, 110.62, (110.60), 72.2, (72.1), 49.41, (49.35), 27.1, -1.3. HRMS (ESI): m/z for $C_{14}H_{21}BrOSiNa$ $[M+Na]^+$ calcd. 335.0443, found: 335.0435.



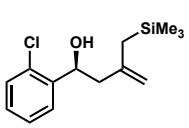
***rac*-1-(4-chlorophenyl)-3-((trimethylsilyl)methyl)but-3-en-1-ol (1.1f)**

Prepared according to the general procedure. The crude mixture was purified by column chromatography to give compound **1.1f** in 97% yield (26 mg) as colorless oil. ^{1}H NMR (600 MHz, d^6-acteone) δ 7.40 (d, J = 8.6 Hz, 2H), 7.34 (d, J = 8.4 Hz, 2H), 4.85 (dt, J = 8.3, 4.4 Hz, 1H), 4.62 (s, 1H), 4.57 (s, 1H), 4.23 (s, 1H), 2.39 (dd, J = 14.0, 8.2 Hz, 1H), 2.30 (dd, J = 14.0, 5.2 Hz, 1H), 1.64 (d, J = 13.5 Hz, 1H), 1.59 (d, J = 13.3 Hz, 1H), 0.02 (s, 9H). ^{13}C NMR (151 MHz, d^6-acteone) δ 145.7, 145.0, 132.6, 128.8, 128.5, 110.6, 72.1, 49.4, 27.1, -1.3. HRMS (ESI): m/z for $C_{14}H_{21}ClOSiNa$ $[M+Na]^+$ calcd. 291.0948, found: 291.0954.



***rac*-1-(3-chlorophenyl)-3-((trimethylsilyl)methyl)but-3-en-1-ol (1.1g)**

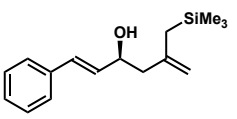
Prepared according to the general procedure. The crude mixture was purified by column chromatography to give compound **1.1g** in 79% yield (21 mg) as colorless oil. ^{1}H NMR (600 MHz, d^6-acteone) δ 7.42 (s, 1H), 7.29 – 7.37 (m, 2H), 7.25 (d, J = 6.2 Hz, 1H), 4.81 – 4.91 (m, 1H), 4.64 (s, 1H), 4.59 (s, 1H), 2.39 (dd, J = 13.6, 8.4 Hz, 1H), 2.32 (dd, J = 13.7, 4.2 Hz, 1H), 1.65 (d, J = 13.4 Hz, 1H), 1.60 (d, J = 13.4 Hz, 1H), 0.03 (s, 9H). ^{13}C NMR (151 MHz, d^6-acteone) δ 149.4, 145.0, 134.2, 130.5, 127.5, 126.7, 125.3, 110.7, (110.6), 72.2, (72.1), 49.4, (49.3), 27.0, -1.3. HRMS (ESI): m/z for $C_{14}H_{21}ClOSiNa$ $[M+Na]^+$ calcd. 291.0948, found: 291.0947.



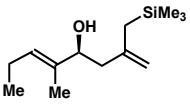
***rac*-1-(2-chlorophenyl)-3-((trimethylsilyl)methyl)but-3-en-1-ol (1.1h)**

Prepared according to the general procedure. The crude mixture was purified by column chromatography to give compound **1.1h** in 91% yield (24 mg) as colorless oil. ^{1}H NMR (600 MHz, d^8-toluene) δ 7.69 (d, J = 7.7 Hz, 1H), 7.06 – 7.12 (m, 1H), 6.94 – 7.00 (m, 1H), 6.78 (dd, J = 7.7 Hz, 7.0 Hz, 1H), 5.11 (d, J = 9.7 Hz, 1H), 4.72 (s, 1H), 4.63 (s, 1H), 2.51 (d, J = 13.8 Hz, 1H), 2.00 (dd, J = 13.7, 10.0 Hz, 1H), 1.90 (d, J = 2.6 Hz, 1H), 1.58 (d, J = 13.4 Hz, 1H),

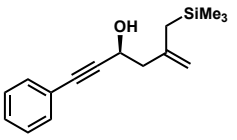
1.49 (d, J = 13.3 Hz, 1H), 0.00 (s, 9H). ^{13}C NMR (151 MHz, d^6-acteone) δ 145.1, 144.2, 131.8, 129.7, 129.0, 128.2, 127.9, 110.4, 69.1, 47.8, 26.9, -1.3. HRMS (ESI): m/z for $C_{14}H_{21}ClOSiNa$ $[M+Na]^+$ calcd. 291.0948, found: 291.0945.



***rac*-(*E*)-1-phenyl-5-((trimethylsilyl)methyl)hexa-1,5-dien-3-ol (1.1i)** Prepared according to the general procedure. The crude mixture was purified by column chromatography to give compound **1.1i** in 67% yield (17 mg) as colorless oil. ^{1}H NMR (600 MHz, d^8-toluene) δ 7.23 (d, J = 7.6 Hz, 2H), 7.06 – 7.13 (m, 2H), 7.00 –7.05 (m, 1H), 6.59 (d, J = 15.9 Hz, 1H), 6.14 (dd, J = 15.9, 5.7 Hz, 1H), 4.72 (s, 1H), 4.65 (s, 1H), 4.25 (dt, J = 10.0, 6.2 Hz, 1H), 2.17 (d, J = 6.6 Hz, 2H), 1.53 (d, J = 3.0 Hz, 1H), 1.50 (d, J = 13.4 Hz, 1H), 1.45 (d, J = 13.4 Hz, 1H), 0.00 (s, 9H). ^{13}C NMR (151 MHz, d^6-acteone) δ 145.2, 138.2, 134.3, 129.3(2C), 128.0, 127.0, 110.2, 71.1, 47.4, 27.3, -1.3. HRMS (ESI): m/z for $C_{14}H_{24}OSiNa$ $[M+Na]^+$ calcd. 283.1494, found: 283.1512.

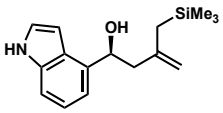


***rac*-(*E*)-5-methyl-2-((trimethylsilyl)methyl)octa-1,5-dien-4-ol (1.1j)** Prepared according to the general procedure. The crude mixture was purified by column chromatography to give compound **1.1j** in 80% yield (18 mg) as colorless oil. ^{1}H NMR (400 MHz, d^6-acteone) δ 5.36 (t, J = 7.0 Hz, 1H), 4.65 (s, 1H), 4.56 (s, 1H), 4.01 – 4.19 (m, 1H), 3.35(d, J = 3.6 Hz, 1H), 2.18 (d, J = 6.6 Hz, 2H), 1.91 – 2.03 (m, 2H), 1.5 – 1.73 (m, 5H), 0.92 (t, J = 7.5 Hz, 3H), 0.03 (s, 9H). ^{13}C NMR (151 MHz, d^6-acteone) δ 145.8, 138.0, 127.4, 109.82, (109.81), 76.2, (76.1), 45.4, (45.3), 26.9, 21.3, 14.4, 11.3, -1.2. HRMS (ESI): m/z for $C_{13}H_{26}OSiNa$ $[M+Na]^+$ calcd. 249.1651, found: 249.1647.

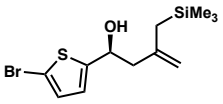


***rac*-1-phenyl-5-((trimethylsilyl)methyl)hex-5-en-1-yn-3-ol (1.1k)** Prepared

according to the general procedure. The crude mixture was purified by column chromatography to give compound **1.1k** in 82% yield (21 mg) as colorless oil. ^{1}H NMR (600 MHz, *d*^{6}-acteone) δ 7.38 – 7.54 (m, 2H), 7.35 (*app.* s, 3H), 4.79 (s, 1H), 4.65 – 4.73 (m, 2H), 4.52 (d, *J* = 5.1 Hz, 1H), 2.48 (dd, *J* = 13.7, 6.6 Hz, 1H), 2.42 (dd, *J* = 13.6, 7.2 Hz, 1H), 1.72 (d, *J* = 13.4 Hz, 1H), 1.68 (d, *J* = 13.4 Hz, 1H), 0.05 (s, 9H). ^{13}C NMR (151 MHz, *d*^{6}-acteone) δ 144.2, 132.1, 129.3, 129.0, 124.0, 110.6, 92.5, 84.3, 61.8, 47.5, 27.3, -1.3. HRMS (EI): m/z for $C_{16}H_{20}Si$ $[M–H_2O]^+$ calcd. 240.1334, found: 240.1326.

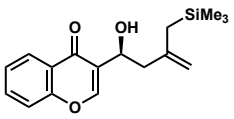


***rac*-1-(1*H*-indol-4-yl)-3-((trimethylsilyl)methyl)but-3-en-1-ol (1.1l)** Prepared according to the general procedure. The crude mixture was purified by column chromatography to give compound **1.1l** in 93% yield (25 mg) as colorless oil. ^{1}H NMR (400 MHz, *d*^{6}-acteone) δ 7.31 (d, *J* = 7.4 Hz, 2H), 7.12 (d, *J* = 7.1 Hz, 1H), 7.06 (dd, *J* = 7.6, 7.6 Hz, 1H), 6.63 (s, 1H), 5.22 (ddd, *J* = 8.7, 4.5, 4.5 Hz, 1H), 4.75 (s, 1H), 4.62 (s, 1H), 3.81 (d, *J* = 3.6 Hz, 1H), 2.43 – 2.57 (m, 2H), 1.73 (d, *J* = 13.4 Hz, 1H), 1.65 (d, *J* = 13.4 Hz, 1H), 0.03 (s, 9H). ^{13}C NMR (151 MHz, *d*^{6}-acteone) δ 146.1, 138.3, 137.2, 126.2, 125.0, 121.9, 116.2, 110.8, 109.9, 100.8, (100.7), 71.8, (71.7), 48.41, (48.35), 27.2, -1.2. HRMS (ESI): m/z for $C_{16}H_{23}NOSiNa$ $[M+Na]^+$ calcd. 296.1447, found: 296.1443.

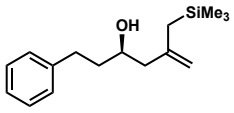


***rac*-1-(5-bromothiophen-2-yl)-3-((trimethylsilyl)methyl)but-3-en-1-ol (1.1m)** Prepared according to the general procedure. The crude mixture was purified by column chromatography to give compound **1.1m** in 67% yield (21 mg) as colorless oil. ^{1}H NMR (600 MHz, *d*^{6}-acteone) δ 6.93 – 7.00 (m, 1H), 6.78 (d, *J* = 2.8 Hz, 1H), 4.99 – 5.11 (m, 1H), 4.71 (d, *J* = 3.6 Hz, 1H), 4.67 (s, 1H), 4.61 (s, 1H), 2.48 (dd, *J* = 13.8, 7.9 Hz, 1H), 2.40 (dd, *J* = 13.9, 5.2 Hz, 1H), 1.65 (d, *J* = 13.4 Hz, 1H), 1.60 (d, *J* = 13.4 Hz, 1H), 0.03 (s, 9H).^{13}C

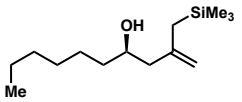
NMR (151 MHz, d^6-acteone) δ 152.6, 143.7, 129.5, 123.5, 110.0, (109.5), 68.4, (68.3), 48.31, (48.26), 26.3, -2.1. HRMS (ESI): m/z for $C_{12}H_{18}BrSSi$ $[M–OH]^+$ calcd. 301.0082, found: 301.0069.



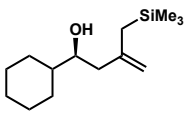
***rac*-3-(1-hydroxy-3-((trimethylsilyl)methyl)but-3-en-1-yl)-4*H*-chromen-4-one (1.1n)** Prepared according to the general procedure. The crude mixture was purified by column chromatography to give compound **1.1n** in 95% yield (29 mg) as colorless oil. ^{1}H NMR (600 MHz, d^6-acteone) δ 8.18 (s, 1H), 8.14 (d, J = 7.9 Hz, 1H), 7.79 (dd, J = 7.7, 7.7 Hz, 1H), 7.58 (d, J = 8.4 Hz, 1H), 7.48 (dd, J = 7.3, 7.3 Hz, 1H), 4.96 – 5.02 (m, 1H), 4.69 (s, 1H), 4.60 (s, 1H), 4.21 (d, J = 3.6 Hz, 1H), 2.61 (d, J = 13.8 Hz, 1H), 2.23 (dd, J = 13.6, 8.7 Hz, 1H), 1.72 (d, J = 13.4 Hz, 1H), 1.66 (d, J = 13.4 Hz, 1H), 0.05 (s, 9H). ^{13}C NMR (151 MHz, d^6-acteone) δ 176.9, 157.1, 154.0, 145.5, 134.6, 128.0, 126.1, 125.9, 124.7, 119.1, 110.4, (110.3), 66.1, (66.0), 46.4, (46.3), 27.0, -1.3. HRMS (ESI): m/z for $C_{17}H_{22}O_3SiNa$ $[M+Na]^+$ calcd. 325.1236, found: 325.1222.



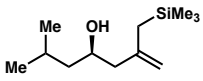
***rac*-1-phenyl-5-((trimethylsilyl)methyl)hex-5-en-3-ol (1.1o)** Prepared according to the general procedure. The crude mixture was purified by column chromatography to give compound **1.1o** in 86% yield (22 mg) as colorless oil. ^{1}H NMR (600 MHz, d^6-acteone) δ 7.26 (dd, J = 7.1, 7.1 Hz, 2H), 7.21 (d, J = 7.0 Hz, 2H), 7.10 – 7.18 (m, 1H), 4.63 (s, 1H), 4.57 (s, 1H), 3.75 (s, 1H), 3.45 (s, 1H), 2.75 – 2.87 (m, 1H), 2.60 – 2.71 (m, 1H), 2.10 – 2.25 (m, 2H), 1.71 – 1.88 (m, 1H), 1.59 – 1.70 (m, 1H), 1.57 (s, 2H), 0.01 (s, 9H). ^{13}C NMR (151 MHz, d^6-acteone) δ 145.9, 143.6, 129.2, 129.1, 126.4, 109.84, (109.82), 69.1, (69.0), 47.53, (47.48), 40.0, 39.9, 32.7, 27.1, -1.3. HRMS (ESI): m/z for $C_{16}H_{26}OSiNa$ $[M+Na]^+$ calcd. 285.1651, found: 285.1647.



***rac*-2-((trimethylsilyl)methyl)dec-1-en-4-ol (1.1p)** Prepared according to the general procedure. The crude mixture was purified by column chromatography to give compound **1.1p** in 97% yield (23 mg) as colorless oil. ^{1}H NMR (600 MHz, d^{6}-acteone) δ 4.63 (s, 1H), 4.57 (s, 1H), 3.70 (s, 1H), 2.10 (d, J = 6.2 Hz, 2H), 1.60 (s, 2H), 1.47 (d, J = 11.8 Hz, 2H), 1.22 – 1.38 (m, 8H), 0.87 (d, J = 6.9 Hz, 3H), 0.02 (s, 9H). ^{13}C NMR (151 MHz, d^{6}-acteone) δ 146.1, 109.71, (109.69), 69.6, (69.5), 47.6, (47.5), 38.02, (37.97), 32.6, 30.2, 27.1, 26.5, 23.3, 14.4, -1.3. HRMS (ESI): m/z for $C_{14}H_{30}OSiNa$ $[M+Na]^{+}$ calcd. 265.1964, found: 265.1958.



***rac*-1-cyclohexyl-3-((trimethylsilyl)methyl)but-3-en-1-ol (1.1q)** Prepared according to the general procedure. The crude mixture was purified by column chromatography to give compound **1.1q** in 94% yield (23 mg) as colorless oil. ^{1}H NMR (400 MHz, d^{6}-acteone) δ 4.66 (s, 1H), 4.60 (s, 1H), 3.58 – 3.40 (m, 1H), 2.94 (d, J = 4.6 Hz, 1H), 2.20 (dd, J = 13.8, 3.4 Hz, 1H), 1.91 – 2.03 (m, 1H), 1.84 (d, J = 11.3 Hz, 1H), 1.69 – 1.78 (m, 2H), 1.55 –1.68 (m, 4H), 0.85 – 1.48 (m, 7H), 0.03 (s, 9H). ^{13}C NMR (151 MHz, d^{6}-acteone) δ 146.4, 109.80, (109.78), 73.5, (73.4), 44.34, (44.31), 44.01, (43.96), 30.2, 28.2, 27.3, 27.2, 27.0, 26.9, 25.1, -1.2. HRMS (ESI): m/z for $C_{14}H_{27}OSi$ $[M-H]^{+}$ calcd. 239.1831, found: 239.1824.

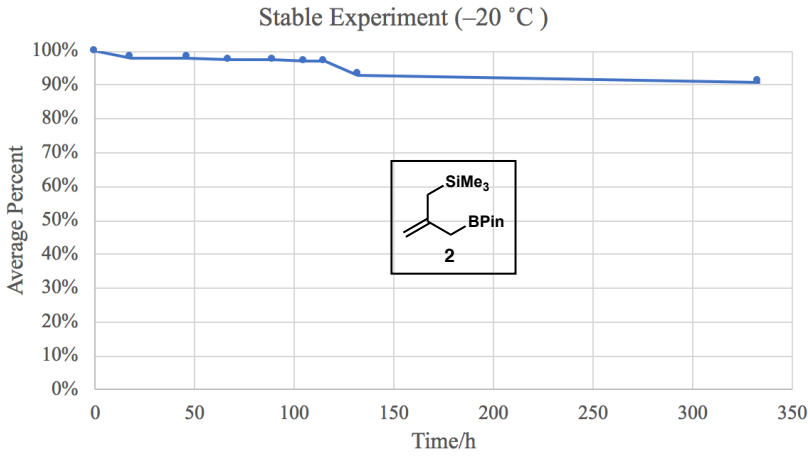


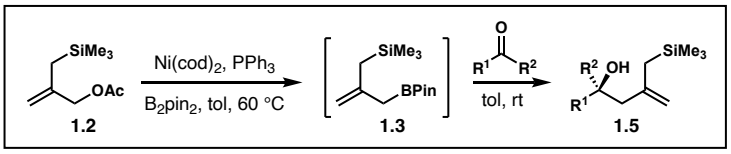
***rac*-6-methyl-2-((trimethylsilyl)methyl)hept-1-en-4-ol (1.1r)** Prepared according to the general procedure. The crude mixture was purified by column chromatography to give compound **1.1r** in 67% yield (14 mg) as colorless oil. ^{1}H NMR (600 MHz, d^{6}-acteone) δ 4.63 (s, 1H), 4.58 (s, 1H), 3.80 (s, 1H), 3.21 (s, 1H), 2.06 – 2.20 (m, 2H), 1.77 –1.92 (m, 1H), 1.60 (s, 2H), 1.26 – 1.40 (m, 1H), 1.12 – 1.26 (m, 1H), 0.89 (dd, J = 6.4, 6.4 Hz, 6H), 0.03 (s, 9H). ^{13}C NMR (151 MHz, d^{6}-acteone) δ 146.0, 109.76, (109.74), 67.6, 67.5,

48.2, (48.1), 47.3, (47.2), 27.1, 25.1, 24.0, 22.1, -1.3. HRMS (ESI): m/z for $C_{12}H_{25}OSi$ $[M-H]^+$ calcd. 213.1675, found: 213.1672.

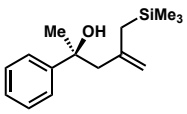
Stability Studies of Allylboronate 1.3 at –20 ℃

Two samples of allylboronate **1.3** (0.1 mmol) were prepared according to the general procedure. 1,3,5-trimethoxybenzene was used as the internal standard. ^{1}H NMR spectra were recorded in toluene-d^8 nine times over the course of two weeks. The percentage is the average of two runs.





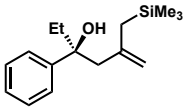
General procedure for synthesis of tertiary homoallylic alcohols 1.5: In an Ar-filled glove box, allylic acetate **1.2** (56 mg, 0.3 mmol, 1 equiv), B_2Pin_2 (84 mg, 0.33 mmol, 1.1 equiv), $Ni(cod)_2$ (4 mg, 0.015 mmol, 5 mol %), PPh_3 (4 mg, 0.015 mmol, 5 mol %), toluene (0.5 mL) and a Teflon-coated magnetic stirring bar were sequentially added into a 1-dram vial. The vial was sealed with a cap containing a PTFE-lined silicone septum and removed from the glove box stirring at 60 ˚C for 2 h. After complete consumption of allylic acetate **1.2**, the mixture was filtered through a short pad of Celite and the resulting solution was concentrated under reduced pressure. The obtained allylboronate **1.3** was dissolved in anhydrous toluene and was used for ketone allylation without further purification. To a reaction vial containing a Teflon-coated magnetic stirring bar was added ketone (0.1 mmol, 1 equiv) followed by addition of allylboronate **1.2** (0.15 mmol, 0.25 mL of a 0.6 M solution in toluene). The reaction mixture was allowed to stir at ambient temperature. After complete consumption of the ketone, purification of the crude reaction mixture was performed by flash chromatography (gradient elution with hexane and EtOAc) to provide alcohol **1.5**.



***rac*-(*S*)-2-phenyl-4-((trimethylsilyl)methyl)pent-4-en-2-ol (1.5a)**

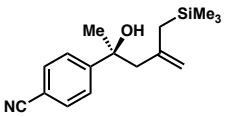
Prepared according to the general procedure. The crude mixture was purified by column chromatography to give compound **1.5a** in 88% yield (22 mg) as colorless oil. ^{1}H NMR (600 MHz, d^6-acteone) δ 7.50 (d, J = 7.4 Hz, 2H), 7.29 (dd, J = 7.6, 7.6 Hz, 2H), 7.18 (dd, J = 7.2, 7.2 Hz, 1H), 4.57 (s, 1H), 4.55 (s, 1H), 3.84 (s, 1H), 2.49 (d, J = 13.4 Hz, 1H), 2.42 (d, J = 13.3 Hz, 1H), 1.54 (s, 3H), 1.44 (s, 2H), -0.04 (s, 9H). ^{13}C NMR (151 MHz, d^6-acteone) δ 150.1,

145.3, 128.4, 126.8, 126.0, 112.0, 74.3, 53.1, 30.1, 28.3, -1.3. HRMS (ESI^+): m/z for $C_{15}H_{24}OSiNa$ $[M+Na]^+$ calcd. 271.1494, found: 271.1506.

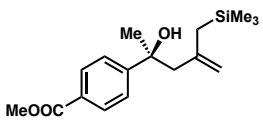


***rac*-(*S*)-3-phenyl-5-((trimethylsilyl)methyl)hex-5-en-3-ol (1.5b)**

Prepared according to the general procedure. The crude mixture was purified by column chromatography to give compound **1.5b** in 98% yield (26 mg) as colorless oil. ^1H NMR (600 MHz, d^6-acteone) δ 7.45 (d, J = 7.6 Hz, 2H), 7.30 (dd, J = 7.7, 7.7 Hz, 2H), 7.18 (dd, J = 7.3, 7.3 Hz, 1H), 4.55 (s, 1H), 4.54 (s, 1H), 3.49 (s, 1H), 2.54 (d, J = 13.4 Hz, 1H), 2.47 (d, J = 13.4 Hz, 1H), 1.89 – 2.0 (m, 1H), 1.76 – 1.89 (m, 1H), 1.44 (d, J = 13.2 Hz, 1H), 1.22 (d, J = 13.2 Hz, 1H), 0.69 (t, J = 7.4 Hz, 3H), -0.06 (s, 9H). ^{13}C NMR (151 MHz, d^6-acteone) δ 147.6, 145.0, 128.3, 126.6 (2C), 112.1, 76.6, 52.1, 35.9, 28.4, 8.2, -1.3. HRMS (EI^+): m/z for $C_{16}H_{26}OSi$ $[M]^+$ calcd. 262.1753, found: 262.1743.

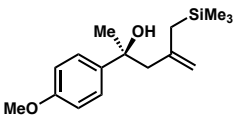


***rac*-(*S*)-4-(2-hydroxy-4-((trimethylsilyl)methyl)pent-4-en-2-yl)benzonitrile (1.5c)** Prepared according to the general procedure. The crude mixture was purified by column chromatography to give compound **1.5c** in 98% yield (27 mg) as colorless oil. ^1H NMR (600 MHz, d^6-acteone) δ 7.56 – 7.86 (m, 4H), 4.56 (s, 1H), 4.50 (s, 1H), 4.23 (s, 1H), 2.52 (d, J = 13.4 Hz, 1H), 2.47 (d, J = 13.4 Hz, 1H), 1.58 (s, 3H), 1.54 (d, J = 13.2 Hz, 1H), 1.44 (d, J = 13.2 Hz, 1H), -0.03 (s, 9H). ^{13}C NMR (151 MHz, d^6-acteone) δ 155.6, 144.7, 132.3, 127.3, 119.6, 112.3, 110.5, 74.7, 52.6, 30.1, 28.3, -1.3. HRMS (ESI^+): m/z for $C_{16}H_{23}NOSiNa$ $[M+Na]^+$ calcd. 296.1447, found: 296.1440.

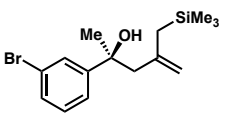


***rac*-methyl (*S*)-4-(2-hydroxy-4-((trimethylsilyl)methyl) pent-4-**

en-2-yl)benzoate (1.5d) Prepared according to the general procedure. The crude mixture was purified by column chromatography to give compound **1.5d** in 92% yield (28 mg) as colorless oil. ^{1}H NMR (600 MHz, d^6-acteone) δ 7.95 (d, J = 8.2 Hz, 2H), 7.64 (d, J = 8.2 Hz, 2H), 4.56 (s, 1H), 4.52 (s, 1H), 4.10 (s, 1H), 3.86 (s, 3H), 2.52 (d, J = 13.4 Hz, 1H), 2.47 (d, J = 13.4 Hz, 1H), 1.58 (s, 3H), 1.51 (d, J = 13.2 Hz, 1H), 1.44 (d, J = 13.2 Hz, 1H), -0.04 (s, 9H). ^{13}C NMR (151 MHz, d^6-acteone) δ 167.1, 155.5, 144.9, 129.6, 128.8, 126.4, 112.2, 74.6, 52.8, 52.2, 30.2, 28.4, -1.3. HRMS (ESI$^+$): m/z for $C_{17}H_{27}O_3Si$ $[M+H]^+$ calcd. 307.1729, found: 307.1717.

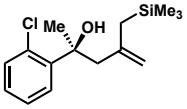


***rac*-(*S*)-2-(4-methoxyphenyl)-4-((trimethylsilyl)methyl)pent-4-en-2-ol (1.5e)** Prepared according to the general procedure. The crude mixture was purified by column chromatography to give compound **1.5e** in 90% yield (25 mg) as colorless oil. ^{1}H NMR (600 MHz, d^6-acteone) δ 7.40 (d, J = 8.7 Hz, 2H), 6.85 (d, J = 8.7 Hz, 2H), 4.57 (s, 1H), 4.53 (s, 1H), 3.60 – 3.90 (m, 4H), 2.46 (d, J = 13.2 Hz, 1H), 2.40 (d, J = 13.0 Hz, 1H), 1.51 (s, 3H), 1.48 (d, J = 13.3 Hz, 1H), 1.44 (d, J = 13.2 Hz, 1H), -0.04 (s, 9H). ^{13}C NMR (151 MHz, d^6-acteone) δ 158.9, 145.5, 142.1, 127.1, 113.6, 111.8, 74.0, 55.3, 53.2, 30.1, 28.3, -1.3. HRMS (ESI$^+$): m/z for $C_{16}H_{25}OSi$ $[M–OH]^+$ calcd. 261.1675, found: 261.1664.

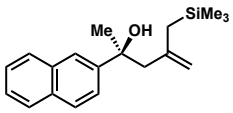


***rac*-(*S*)-2-(3-bromophenyl)-4-((trimethylsilyl)methyl)pent-4-en-2-ol (1.5f)** Prepared according to the general procedure. The crude mixture was purified by column chromatography to give compound **1.5f** in 97% yield (32 mg) as colorless oil. ^{1}H NMR (600 MHz, d^6-acteone) δ 7.71 (s, 1H), 7.48 (d, J = 7.7 Hz, 1H), 7.38 (d, J = 6.9 Hz, 1H), 7.26 (dd, J = 7.8, 7.8 Hz, 1H), 4.58 (s, 1H), 4.54 (s, 1H), 4.07 (s, 1H), 2.49 (d, J = 13.3 Hz, 1H), 2.44 (d, J = 13.4 Hz, 1H), 1.55 (s, 3H), 1.51 (d, J = 13.3 Hz, 1H), 1.45 (d, J = 13.3 Hz, 1H), -

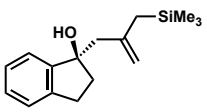
0.03 (s, 9H). ^{13}C NMR (151 MHz, d^6-acteone) δ 152.9, 144.9, 130.5, 129.8, 129.2, 125.1, 122.4, 112.2, 74.3, 52.8, 30.2, 28.3, -1.3. HRMS (CI$^+$): m/z for $C_{15}H_{24}OSiBr$ [M+H]$^+$ calcd. 327.0780, found: 327.0782.



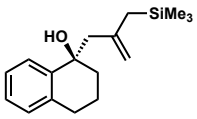
***rac*-(*S*)-2-(2-chlorophenyl)-4-((trimethylsilyl)methyl)pent-4-en-2-ol (1.5g)** Prepared according to the general procedure. The crude mixture was purified by column chromatography to give compound **1.5g** in 96% yield (27 mg) as colorless oil. ^{1}H NMR (600 MHz, d^6-acteone) δ 7.88 (d, J = 7.8 Hz, 1H), 7.36 (d, J = 7.8 Hz, 1H), 7.29 (dd, J = 7.0, 7.0 Hz, 1H), 7.23 (dd, J = 7.5, 7.5 Hz, 1H), 4.59 (s, 1H), 4.53 (s, 1H), 4.07 (s, 1H), 2.95 (d, J = 13.5 Hz, 1H), 2.61 (d, J = 13.5 Hz, 1H), 1.70 (s, 3H), 1.59 (d, J = 13.2 Hz, 1H), 1.32 (d, J = 13.2 Hz, 1H), -0.02 (s, 9H). ^{13}C NMR (151 MHz, d^6-acteone) δ 146.0, 145.2, 131.7, 131.3, 129.4, 129.0, 127.6, 111.9, 74.8, 48.4, 28.3, 28.0, -1.4.



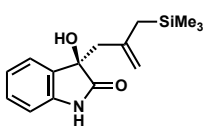
***rac*-(*S*)-2-(naphthalen-2-yl)-4-((trimethylsilyl)methyl)pent-4-en-2-ol (1.5h)** Prepared according to the general procedure. The crude mixture was purified by column chromatography to give compound **1.5h** in 95% yield (28 mg) as colorless oil. ^{1}H NMR (600 MHz, d^6-acteone) δ 8.01 (s, 1H), 7.75 – 7.94 (m, 3H), 7.67 (d, J = 8.5 Hz, 1H), 7.32 – 7.59 (m, 2H), 4.57 (s, 2H), 4.04 (s, 1H), 2.61 (d, J = 13.4 Hz, 1H), 2.54 (d, J = 13.3 Hz, 1H), 1.64 (s, 3H), 1.49 (d, J = 13.2 Hz, 1H), 1.46 (d, J = 13.2 Hz, 1H), -0.05 (s, 9H). ^{13}C NMR (151 MHz, d^6-acteone) δ 147.6, 145.2, 134.1, 133.0, 128.8, 128.2, 127.9, 126.6, 126.2, 125.4, 124.1, 112.0, 74.6, 52.7, 30.2, 28.3, -1.3. HRMS (ESI$^+$): m/z for $C_{19}H_{26}OSiNa$ [M+Na]$^+$ calcd. 321.1651, found: 321.1653.



***rac*-(*R*)-1-(2-((trimethylsilyl)methyl)allyl)-2,3-dihydro-1*H*-inden-1-ol (1.5i)** Prepared according to the general procedure. The crude mixture was purified by column chromatography to give compound **1.5i** in 85% yield (22 mg) as colorless oil. ^{1}H NMR (600 MHz, d^{6}-acetone) δ 7.25 – 7.41(m, 1H), 7.10 – 7.25 (m, 3H), 4.60 (s, 2H), 4.00 (s, 1H), 2.83 – 2.90 (m, 1H), 2.69 – 2.80 (m, 1H), 2.55 (d, *J* = 13.4 Hz, 1H), 2.38 – 2.46 (m, 1H), 2.35 (d, *J* = 13.4 Hz, 1H), 1.96 – 2.13 (m, 1H), 1.73 (d, *J* = 13.1 Hz, 1H), 1.47 (d, *J* = 13.2 Hz, 1H), 0.00 (s, 9H). ^{13}C NMR (151 MHz, d^{6}-acetone) δ 149.9, 145.6, 143.3, 128.3, 126.9, 125.3, 124.0, 111.5, 83.5, 49.3, 40.2, 30.0, 28.2, -1.3. HRMS (ESI^{+}): m/z for $C_{16}H_{24}OSiNa$ $[M+Na]^{+}$ calcd. 283.1494, found: 283.1500.

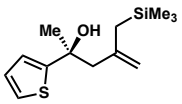


***rac*-(*R*)-1-(2-((trimethylsilyl)methyl)allyl)-1,2,3,4-tetrahydronaphthalen-1-ol (1.5j)** Prepared according to the general procedure. The crude mixture was purified by column chromatography to give compound **1.5j** in 93% yield (25 mg) as colorless oil. ^{1}H NMR (600 MHz, d^{6}-acetone) δ 7.57 (d, *J* = 7.7 Hz, 1H), 7.15 (dd, *J* = 7.4, 7.4 Hz, 1H), 7.10 (dd, *J* = 7.3, 7.3 Hz, 1H), 7.02 (d, *J* = 7.5 Hz, 1H), 4.63 (s, 1H), 4.57 (s, 1H), 3.76 (s, 1H), 2.63 – 2.82 (m, 2H), 2.50 (d, *J* = 13.7 Hz, 1H), 2.42 (d, *J* = 13.7 Hz, 1H), 2.11 – 2.26 (m, 1H), 1.99 (d, *J* = 13.1 Hz, 1H), 1.78 – 1.91 (m, 2H), 1.66 – 1.78 (m, 1H), 1.51 (d, *J* = 13.1 Hz, 1H), 0.02 (s, 9H). ^{13}C NMR (151 MHz, d^{6}-acetone) δ 145.9, 145.1, 136.8, 129.2, 127.7, 127.2, 126.5, 111.8, 72.6, 51.1, 36.3, 30.4, 28.1, 20.9, -1.2. HRMS (ESI^{+}): m/z for $C_{17}H_{26}OSiNa$ $[M+Na]^{+}$ calcd. 297.1651, found: 297.1642.

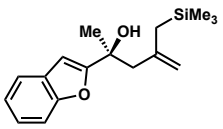


***rac*-(*R*)-3-hydroxy-3-(2-((trimethylsilyl)methyl)allyl)indolin-2-one (1.5k)** Prepared according to the general procedure. The crude mixture was purified

by column chromatography to give compound **1.5k** in 86% yield (24 mg) as white solid. ^{1}H NMR (600 MHz, d^6-acetone) δ 9.27 (s, 1H), 7.37 (d, J = 7.3 Hz, 1H), 7.21 (dd, J = 7.6, 7.6 Hz, 1H), 6.99 (dd, J = 7.2, 7.2 Hz, 1H), 6.85 (d, J = 7.7 Hz, 1H), 4.91 (s, 1H), 4.44 (s, 1H), 4.43 (s, 1H), 2.67 (d, J = 12.8 Hz, 1H), 2.62 (d, J = 12.8 Hz, 1H), 1.40 (d, J = 13.2 Hz, 1H), 1.35 (d, J = 13.3 Hz, 1H), -0.02 (s, 9H). ^{13}C NMR (151 MHz, d^6-acetone) δ 179.5, 143.0, 142.2, 132.2, 129.9, 125.6, 122.3, 112.2, 110.3, 77.2, 46.4, 28.2, -1.4. HRMS (ESI$^+$): m/z for $C_{15}H_{21}NO_2SiNa$ $[M+Na]^+$ calcd. 298.1239, found: 298.1240.

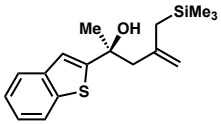


***rac*-(*S*)-2-(thiophen-2-yl)-4-((trimethylsilyl)methyl)pent-4-en-2-ol (1.5l)** Prepared according to the general procedure. The crude mixture was purified by column chromatography to give compound **1.5l** in 98% yield (25 mg) as colorless oil. ^{1}H NMR (600 MHz, d^6-acteone) δ 7.25 (dd, J = 4.4, 1.8 Hz, 1H), 6.79 – 7.03 (m, 2H), 4.63 (s, 1H), 4.59 (s, 1H), 4.34 (s, 1H), 2.54 (d, J = 13.1 Hz, 1H), 2.46 (d, J = 13.1 Hz, 1H), 1.49 – 1.72 (m, 4H), 1.44 (d, J = 13.2 Hz, 1H), -0.02 (s, 9H). ^{13}C NMR (151 MHz, Acetone) δ ^{13}C NMR (151 MHz, d^6-acteone) δ 156.0, 145.1, 127.2, 124.1, 122.9, 112.1, 73.7, 53.8, 30.2, 28.2, -1.3. HRMS (EI$^+$): m/z for $C_{13}H_{23}OSiS$ $[M+H]^+$ calcd. 255.1239, found: 255.1230.

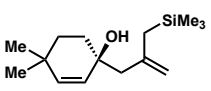


***rac*-(*S*)-2-(benzofuran-2-yl)-4-((trimethylsilyl)methyl)pent-4-en-2-ol (1.5m)** Prepared according to the general procedure. The crude mixture was purified by column chromatography to give compound **1.5m** in 98% yield (28 mg) as colorless oil. ^{1}H NMR (600 MHz, d^6-acteone) δ 7.56 (d, J = 7.6 Hz, 1H), 7.47 (d, J = 8.2 Hz, 1H), 7.25 (dd, J = 8.3, 8.3 Hz, 1H), 7.20 (dd, J = 7.8, 7.8 Hz, 1H), 6.69 (s, 1H), 4.58 (s, 2H), 4.33 (s, 1H), 2.63 (s, 2H), 1.60 (s, 3H), 1.42 (d, J = 13.2 Hz, 1H), 1.39 (d, J = 13.2 Hz, 1H), -

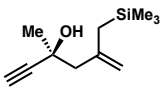
0.04 (s, 9H). ^{13}C NMR (151 MHz, d^6-acteone) δ 163.8, 154.5, 143.8, 128.7, 123.6, 122.6, 120.9, 111.3, 110.8, 101.4, 70.9, 49.2, 27.0, 26.7, -2.2. HRMS (ESI$^+$): m/z for$C_{17}H_{24}O_2SiNa$ [M+Na]$^+$ calcd. 311.1443, found: 311.1418.



***rac*-(*S*)-2-(benzo[*b*]thiophen-2-yl)-4-((trimethylsilyl)methyl)pent-4-en-2-ol (1.5n)** Prepared according to the general procedure. The crude mixture was purified by column chromatography to give compound **1.5n** in 98% yield (30 mg) as colorless oil. ^{1}H NMR (600 MHz, Acetone-d_6) δ ^{1}H NMR (600 MHz, d^6-acteone) δ 7.85 (d, J = 7.8 Hz, 1H), 7.74 (d, J = 7.7 Hz, 1H), 7.32 (dd, J = 7.5, 7.5 Hz, 1H), 7.27 (dd, J = 7.5, 7.5 Hz, 1H), 7.21 (s, 1H), 4.64 (s, 1H), 4.63 (s, 1H), 4.58 (s, 1H), 2.63 (d, J = 13.3 Hz, 1H), 2.55 (d, J = 13.3 Hz, 1H), 1.61 – 1.82 (m, 4H), 1.55 (d, J = 13.2 Hz, 1H), -0.01 (s, 9H). ^{13}C NMR (151 MHz, d^6-acteone) δ 157.0, 144.8, 141.0, 140.0, 124.8, 124.4, 124.0, 122.9, 119.4, 112.3, 74.1, 53.2, 30.1, 28.3, -1.3. HRMS (ESI$^+$): m/z for $C_{17}H_{24}OSSiNa$ [M+Na]$^+$ calcd. 327.1215, found: 327.1215.

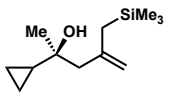


***rac*-(*S*)-4,4-dimethyl-1-(2-((trimethylsilyl)methyl)allyl)cyclohex-2-en-1-ol (1.5o)** Prepared according to the general procedure. The crude mixture was purified by column chromatography to give compound **1.5o** in 90% yield (23 mg) as colorless oil. ^{1}H NMR (600 MHz, d^6-acetone) δ 5.49 (d, J = 10.1 Hz, 1H), 5.37 (d, J = 10.1 Hz, 1H), 4.63 (s, 2H), 3.40 (s, 1H), 2.20 (d, J = 13.6 Hz, 1H), 2.18 (d, J = 13.6 Hz, 1H), 1.70 – 1.94 (m, 3H), 1.56 – 1.70 (m, 2H), 1.36 – 1.53 (m, 1H), 0.97 (s, 3H), 0.93 (s, 3H), 0.02 (s, 9H). ^{13}C NMR (151 MHz, d^6-acetone) δ 145.5, 138.3, 132.5, 111.4, 69.9, 50.6, 34.4, 33.4, 32.3, 29.8, 28.6 (2C), -1.2. HRMS (ESI$^+$): m/z for $C_{15}H_{28}OSiNa$ [M+Na]$^+$ calcd. 275.1807, found: 275.1819.



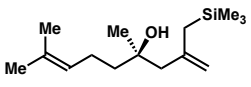
***rac*-(*S*)-3-methyl-5-((trimethylsilyl)methyl)hex-5-en-1-yn-3-ol (1.5p)**

Prepared according to the general procedure. The crude mixture was purified by column chromatography to give compound **1.5p** in 71% yield (14 mg) as colorless oil. ^{1}H NMR (600 MHz, d^{6}-acetone) δ 4.75 (s, 1H), 4.69 (s, 1H), 4.30 (s, 1H), 2.89 (s, 1H), 2.38 (d, J = 13.3 Hz, 1H), 2.34 (d, J = 13.3 Hz, 1H), 1.86 (d, J = 13.3 Hz, 1H), 1.82 (d, J = 13.3 Hz, 1H), 1.43 (s, 3H), 0.03 (s, 9H). ^{13}C NMR (151 MHz, d^{6}-acetone) δ 144.3, 112.2, 89.9, 72.4, 67.1, 51.8, 30.1, 28.2, -1.3. HRMS (CI^{+}): m/z for $C_{11}H_{21}OSi$ $[M+H]^{+}$ calcd. 197.1362, found: 197.1368.



***rac*-(*S*)-2-cyclopropyl-4-((trimethylsilyl)methyl)pent-4-en-2-ol (1.5q)**

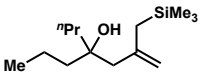
Prepared according to the general procedure. The crude mixture was purified by column chromatography to give compound **1.5q** in 72% yield (15 mg) as colorless oil. ^{1}H NMR (600 MHz, d^{6}-acetone) δ 4.64 (s, 2H), 2.90 (s, 1H), 2.23 (d, J = 12.8 Hz, 1H), 2.18 (d, J = 12.8 Hz, 1H), 1.84 (d, J = 13.1 Hz, 1H), 1.74 (d, J = 13.1 Hz, 1H), 1.15 (s, 3H), 0.75 – 1.04 (m, 1H), 0.39 – 0.58 (m, 1H), 0.30 – 0.39 (m, 1H), 0.15 – 0.30 (m, 2H), 0.02 (s, 9H). ^{13}C NMR (151 MHz, d^{6}-acetone) δ 146.1, 111.4, 70.7, 51.8, 29.1, 27.6, 22.3, 1.2, 0.9, -1.1.



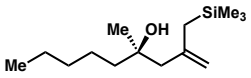
***rac*-(*R*)-4,8-dimethyl-2-((trimethylsilyl)methyl)nona-1,7-dien-4-ol (1.5r)**

Prepared according to the general procedure. The crude mixture was purified by column chromatography to give compound **1.5r** in 68% yield (17 mg) as colorless oil. ^{1}H NMR (600 MHz, d^{6}-acetone) δ 5.11 (t, J = 6.3 Hz, 1H), 4.64 (s, 1H), 4.62 (s, 1H), 3.07 (*app.* d, J = 3.7 Hz, 1H), 2.19 (d, J = 13.2 Hz, 1H), 2.14 (d, J = 13.2 Hz, 1H), 1.94 – 2.11 (m, 2H), 1.81 (d, J = 13.2 Hz, 1H), 1.74 (d, J = 13.2 Hz, 1H), 1.65 (s, 3H), 1.60 (s, 3H), 1.39 – 1.54 (m,

2H), 1.16 (s, 3H), 0.02 (s, 9H). ^{13}C NMR (151 MHz, d^6-acetone) δ 146.1, 131.2, 125.9, 111.2, 72.5, 50.5, 43.3, 28.8, 27.4, 25.9, 23.4, 17.7, -1.2. HRMS (ESI$^+$): m/z for $C_{15}H_{30}OSiNa$ $[M+Na]^+$ calcd. 277.1964, found: 277.1952.

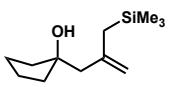


***rac*-4-propyl-2-((trimethylsilyl)methyl)hept-1-en-4-ol (1.5s)** Prepared according to the general procedure. The crude mixture was purified by column chromatography to give compound **1.5s** in 78% yield (19 mg) as colorless oil. ^{1}H NMR (600 MHz, d^6-acetone) δ 4.63 (s, 1H), 4.60 (s, 1H), 2.88 (s, 1H), 2.12 (s, 2H), 1.79 (s, 2H), 1.19 – 1.56 (m, 8H), 0.87 (t, J = 6.4 Hz, 6H), 0.01 (s, 9H). ^{13}C NMR (151 MHz, Acetone) δ ^{13}C NMR (151 MHz, d^6-acetone) δ 146.1, 111.0, 74.3, 47.9, 42.4, 28.6, 17.6, 15.0, -1.2. HRMS (CI$^+$): m/z for $C_{14}H_{31}OSi$ $[M+H]^+$ calcd. 243.2144, found: 243.2141.



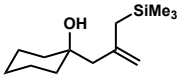
***rac*-(*R*)-4-methyl-2-((trimethylsilyl)methyl)non-1-en-4-ol (1.5t)**

Prepared according to the general procedure. The crude mixture was purified by column chromatography to give compound **1.5t** in 98% yield (24 mg) as colorless oil. ^{1}H NMR (600 MHz, d^8 -toluene) δ 4.70 (s, 1H), 4.67 (s, 1H), 2.13 (d, J = 13.0 Hz, 1H), 2.03 (d, J = 12.9 Hz, 1H), 1.71 (d, J = 13.1 Hz, 1H), 1.63 (d, J = 13.0 Hz, 1H), 1.50 – 1.14 (m, 8H), 1.09 (s, 3H), 0.92 (t, J = 6.7 Hz, 3H), 0.04 (s, 9H). ^{13}C NMR (151 MHz, d^8 -toluene) δ 145.2, 111.4, 71.9, 49.8, 43.0, 33.0, 29.0, 27.2, 24.2, 23.2, 14.4, -1.3. HRMS (CI$^+$): m/z for $C_{14}H_{31}OSi$ $[M+H]^+$ calcd. 243.2144, found: 243.2140.

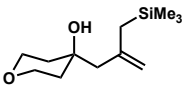


1-(2-((trimethylsilyl)methyl)allyl)cyclopentan-1-ol (1.5u) Prepared according

to the general procedure. The crude mixture was purified by column chromatography to give compound **1.5u** in 81% yield (17 mg) as colorless oil. ^{1}H NMR (400 MHz, d^{6}-acetone) δ 4.65 (s, 1H), 4.62 (s, 1H), 2.94 (s, 1H), 2.27 (s, 2H), 1.68 – 1.86 (m, 4H), 1.45 – 1.68 (m, 6H), 0.03 (s, 9H). ^{13}C NMR (151 MHz, d^{6}-acetone) δ 146.5, 110.6, 81.8, 49.6, 40.2, 28.5, 24.0, -1.3. HRMS (ESI^{+}): m/z for $C_{12}H_{24}OSiNa$ $[M+Na]^{+}$ calcd. 235.1494, found: 235.1483.

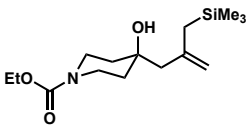


1-(2-((trimethylsilyl)methyl)allyl)cyclohexan-1-ol (1.5v) Prepared according to the general procedure. The crude mixture was purified by column chromatography to give compound **1.5v** in 93% yield (21 mg) as colorless oil. ^{1}H NMR (400 MHz, d^{6}-acetone) δ 4.64 (s, 1H), 4.60 (s, 1H), 2.79 (s, 1H), 2.13 (s, 2H), 1.77 (s, 2H), 1.58 – 1.71 (m, 2H), 1.47 – 1.58 (m, 3H), 1.34 – 1.47 (m, 4H), 1.13 – 1.32 (m, 1H), 0.02 (s, 9H). ^{13}C NMR (151 MHz, d^{8} -toluene) δ 144.7, 111.3, 70.5, 51.1, 38.2, 29.3, 26.3, 22.6, -1.4. HRMS (EI^{+}): m/z for $C_{13}H_{24}Si$ $[M-H_2O]^{+}$ calcd. 208.1647, found: 208.1649.

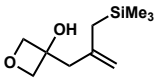


4-(2-((trimethylsilyl)methyl)allyl)tetrahydro-2*H*-pyran-4-ol (1.5w)

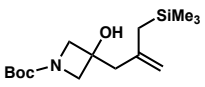
Prepared according to the general procedure. The crude mixture was purified by column chromatography to give compound **1.5w** in 97% yield (22 mg) as colorless oil. ^{1}H NMR (600 MHz, d^{6}-acetone) δ 4.66 (s, 1H), 4.62 (s, 1H), 3.64 – 3.83 (m, 2H), 3.45 – 3.64 (m, 2H), 3.26 (s, 1H), 2.17 (s, 2H), 1.75 (s, 2H), 1.56 – 1.69 (m, 2H), 1.47 (d, J = 12.0 Hz, 2H), 0.02 (s, 9H). ^{13}C NMR (151 MHz, d^{6}-acetone) δ 144.0, 110.7, 68.3, 63.4, 51.1, 37.9, 28.3, -2.1. HRMS (ESI^{+}): m/z for $C_{12}H_{25}O_2Si$ $[M+H]^{+}$ calcd. 229.1624, found: 229.1626.



ethyl 4-hydroxy-4-(2-((trimethylsilyl)methyl)allyl)piperidine-1-carboxylate (1.5x) Prepared according to the general procedure. The crude mixture was purified by column chromatography to give compound **1.5x** in 96% yield (29 mg) as colorless oil. ^{1}H NMR (600 MHz, d^{6}-acetone) δ 4.67 (s, 1H), 4.63 (s, 1H), 3.93 – 4.25 (m, 2H), 3.55 – 3.93 (m, 2H), 3.33 (s, 1H), 3.04 – 3.26 (m, 2H), 2.18 (s, 2H), 1.75 (s, 2H), 1.41 – 1.64 (m, 4H), 1.12 – 1.26 (m, 3H), 0.02 (s, 9H). ^{13}C NMR (151 MHz, d^{6}-acetone) δ 155.6, 144.8, 111.6, 69.8, 61.3, 51.7, 40.6, 40.5, 37.6, 37.4, 29.0, 15.0, -1.3. HRMS (ESI^{+}): m/z for $C_{15}H_{29}NO_3SiNa$ $[M+Na]^{+}$ calcd. 322.1814, found: 322.1814.

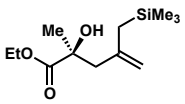


3-(2-((trimethylsilyl)methyl)allyl)oxetan-3-ol (1.5y) Prepared according to the general procedure. The crude mixture was purified by column chromatography to give compound **1.5y** in 98% yield (20 mg) as colorless oil. ^{1}H NMR (600 MHz, Acetone-d_6) δ ^{1}H NMR (600 MHz, d^{6}-acetone) δ 4.68 (s, 1H), 4.64 (s, 1H), 4.60 (s, 1H), 4.47 (d, J = 11.4 Hz, 2H), 4.45 (d, J = 11.4 Hz, 2H), 2.52 (s, 2H), 1.66 (s, 2H), 0.04 (s, 9H). ^{13}C NMR (151 MHz, d^{6}-acetone) δ 144.3, 110.3, 84.2, 74.4, 46.5, 28.2, -1.3.. HRMS (ESI^{+}): m/z for $C_{10}H_{20}O_2SiNa$ $[M+Na]^{+}$ calcd. 223.1130, found: 223.1139.

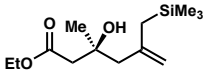


***tert*-butyl 3-hydroxy-3-(2-((trimethylsilyl)methyl)allyl)azetidine-1-carboxylate (1.5z)** Prepared according to the general procedure. The crude mixture was purified by column chromatography to give compound **1.5z** in 75% yield (22 mg) as colorless oil. ^{1}H NMR (600 MHz, d^{6}-acetone) δ 4.72 (s, 1H), 4.66 (s, 1H), 4.61 (s, 1H), 3.84 – 3.87 (m, 2H), 3.71 – 3.75 (m, 2H), 2.43 (s, 2H), 1.69 (s, 2H), 1.40 (s, 9H), 0.03 (s, 9H). ^{13}C

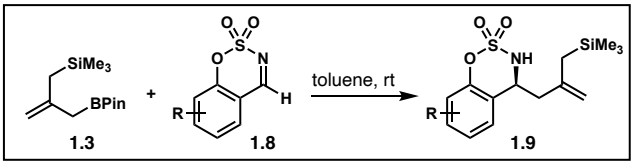
NMR (151 MHz, d^6-acetone) δ 156.9, 144.3, 110.6, 79.1, 70.5, 63.8, 62.6, 47.2, 28.5, 28.2, -1.3. HRMS (ESI^+): m/z for $C_{15}H_{29}NO_3SiNa$ $[M+Na]^+$ calcd. 322.1814, found: 322.1828.



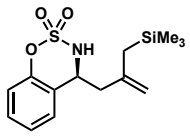
***rac*-ethyl (*S*)-2-hydroxy-2-methyl-4-((trimethylsilyl)methyl)pent-4-enoate (1.5aa)** Prepared according to the general procedure. The crude mixture was purified by column chromatography to give compound **1.5aa** in 87% yield (21 mg) as colorless oil. ^1H NMR (600 MHz, d^6-acetone) δ 4.64 (s, 1H), 4.61 (s, 1H), 4.03 – 4.27 (m, 2H), 3.99 (s, 1H), 2.43 (d, J = 13.6 Hz, 1H), 2.31 (d, J = 13.6 Hz, 1H), 1.71 (d, J = 13.2 Hz, 1H), 1.61 (d, J = 13.2 Hz, 1H), 1.34 (s, 3H), 1.25 (t, J = 6.3 Hz, 3H), 0.01 (s, 9H). ^{13}C NMR (151 MHz, d^6-acetone) δ 176.7, 144.2, 111.5, 75.3, 61.6, 48.5, 28.2, 26.8, 14.5, -1.4. HRMS (ESI^+): m/z for $C_{12}H_{25}O_3Si$ $[M+H]^+$ calcd. 245.1573, found: 245.1585.



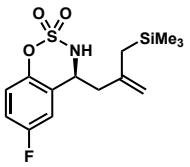
***rac*-ethyl (*S*)-3-hydroxy-3-methyl-5-((trimethylsilyl)methyl) hex-5-enoate (3bb)** Prepared according to the general procedure. The crude mixture was purified by column chromatography to give compound **1.5bb** in 89% yield (23 mg) as colorless oil. ^1H NMR (600 MHz, d^6-acetone) δ 4.66 (s, 1H), 4.64 (s, 1H), 3.98 – 4.25 (m, 2H), 3.67 – 3.89 (m, 1H), 2.52 (d, J = 15.0 Hz, 1H), 2.46 (d, J = 15.0 Hz, 1H), 2.27 (d, J = 13.2 Hz, 1H), 2.23 (d, J = 13.2 Hz, 1H), 1.70 – 1.87 (m, 2H), 0.97 –1.53 (m, 6H), 0.02 (s, 9H). ^{13}C NMR (151 MHz, Acetone) δ ^{13}C NMR (151 MHz, d^6-acetone) δ 172.8, 145.6, 111.8, 71.8, 60.7, 49.9, 46.0, 28.5, 27.8, 14.5, -1.3. HRMS (ESI^+): m/z for $C_{13}H_{27}O_3Si$ $[M+H]^+$ calcd. 259.1708, found: 259.1732.



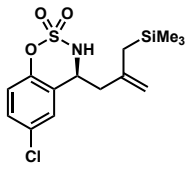
General procedure for synthesis of sulfonamide 1.9: To a reaction vial containing a Teflon-coated magnetic stirring bar was added imine **1.8** (0.1 mmol, 1 equiv) followed by addition of allylboronate **1.3** (0.15 mmol, 0.25 mL of a 0.6 M solution in toluene). The reaction mixture was allowed to stir at ambient temperature. After complete consumption of the imine **1.8**, purification of the crude reaction mixture was performed by flash chromatography (gradient elution with hexane and EtOAc) to provide sulfonamide **1.9**.



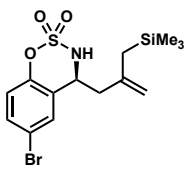
***rac*-(S)-4-(2-((trimethylsilyl)methyl)allyl)-3,4-dihydrobenzo[e][1,2,3] oxathiazine 2,2-dioxide (1.9a)** Prepared according to the general procedure. The crude mixture was purified by column chromatography to give compound **1.9a** in 92% yield (29 mg) as colorless oil. ^{1}H NMR (600 MHz, d^6-acteone) δ 7.45 (d, J = 7.5 Hz, 1H), 7.39 (dd, J = 7.4, 7.4 Hz, 1H), 7.26 (dd, J = 7.1, 7.1 Hz, 1H), 7.05 (d, J = 7.9 Hz, 1H), 5.00 (d, J = 10.3 Hz, 1H), 4.86 (s, 1H), 4.77 (s, 1H), 2.95 (s, 1H), 2.87 (d, J = 14.4 Hz, 1H), 1.75 – 1.85 (dd, J = 13.0, 13.0 Hz, 1H), 1.75 – 1.85 (d, J = 15.3 Hz, 1H), 1.63 – 1.75 (d, J = 13.9 Hz, 1H), 0.09 (s, 9H). ^{13}C NMR (151 MHz, d^6-acteone) δ 152.1, 143.6, 130.1, 127.9, 125.9, 124.0, 119.1, 111.7, 56.1, 43.2, 26.2, -1.3. HRMS (ESI$^+$): m/z for $C_{14}H_{21}NO_3SiSNa$ $[M+Na]^+$ calcd. 334.0909, found: 334.0916.



***rac*-(S)-6-fluoro-4-(2-((trimethylsilyl)methyl)allyl)-3,4-dihydrobenzo [e] [1,2,3]oxathiazine 2,2-dioxide (1.9b)** Prepared according to the general procedure. The crude mixture was purified by column chromatography to give compound **1.9b** in 97% yield (32 mg) as colorless oil. ^{1}H NMR (600 MHz, $CDCl_3$) δ 6.97 – 7.16 (m, 2H), 6.76 – 6.97 (m, 1H), 4.85 – 5.05 (m, 1H), 4.81 (s, 1H), 4.78 (s, 1H), 4.71 (d, *J* = 6.9 Hz, 1H), 2.75 (dd, *J* = 14.5, 4.6 Hz, 1H), 2.60 (dd, *J* = 14.5, 8.9 Hz, 1H), 1.55 (d, *J* = 13.8 Hz, 1H), 1.52 (d, *J* = 13.6 Hz, 1H), 0.07 (s, 9H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 159.7 (d, *J* = 246.5 Hz), 147.2 (d, *J* = 2.6 Hz), 141.9, 124.5 (d, *J* = 7.1 Hz), 121.0 (d, *J* = 8.1 Hz), 116.8 (d, *J* = 23.2 Hz), 113.6, 113.3 (d, *J* = 24.2 Hz), 54.8, 43.3, 26.4, -1.0. HRMS (ESI^+): m/z for $C_{14}H_{21}NO_3SiSF$ $[M+H]^+$ calcd. 330.0995, found: 330.0983.

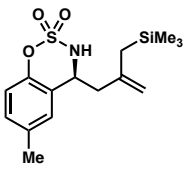


***rac*-(S)-6-chloro-4-(2-((trimethylsilyl)methyl)allyl)-3,4-dihydrobenzo[e] [1,2,3]oxathiazine 2,2-dioxide (1.9c)** Prepared according to the general procedure. The crude mixture was purified by column chromatography to give compound **1.9c** in 95% yield (33 mg) as colorless oil. ^{1}H NMR (600 MHz, *d*^{6}-acteone) δ 7.47 – 7.65 (m, 1H), 7.42 (dd, *J* = 8.8, 1.9 Hz, 1H), 7.10 (d, *J* = 8.8 Hz, 1H), 5.02 (dd, *J* = 10.7, 4.3 Hz, 1H), 4.87 (s, 1H), 4.78 (s, 1H), 2.81 – 3.14 (m, 2H), 2.75 (dd, *J* = 14.4, 10.9 Hz, 1H), 1.76 (d, *J* = 13.7 Hz, 1H), 1.74 (d, *J* = 13.7 Hz, 1H), 0.09 (s, 9H).^{13}C NMR (151 MHz, *d*^{6}-acteone) δ 150.8, 143.5, 130.3, 130.0, 127.8, 126.0, 120.9, 111.9, 56.0, 43.0, 26.1, -1.4. HRMS (ESI^+): m/z for $C_{14}H_{21}NO_3SiSCl$ $[M+H]^+$ calcd. 346.0700, found: 346.0710.

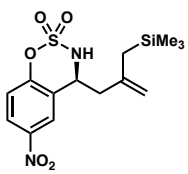


***rac*-(S)-8-bromo-4-(2-((trimethylsilyl)methyl)allyl)-3,4-dihydrobenzo [e][1,2,3]oxathiazine 2,2-dioxide (1.9d)** Prepared according to the general

procedure. The crude mixture was purified by column chromatography to give compound **1.9d** in 95% yield (37 mg) as colorless oil. ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.38 – 7.54 (m, 1H), 7.30 – 7.38 (m, 1H), 6.92 (d, *J* = 8.7 Hz, 1H), 4.85 – 5.06 (m, 1H), 4.81 (s, 1H), 4.77 (s, 1H), 4.73 (d, *J* = 7.6 Hz, 1H), 2.76 (dd, *J* = 14.5, 4.6 Hz, 1H), 2.62 (dd, *J* = 14.5, 8.7 Hz, 1H), 1.53 (d, *J* = 13.7 Hz, 1H), 1.48 (d, *J* = 13.6 Hz, 1H), 0.08 (s, 9H).^{13}C APT NMR (101 MHz, $CDCl_3$) δ 184.7, 150.4, 141.9, 132.8, 129.7, 124.8, 121.2, 118.4, 113.7, 54.6, 43.1, 26.4, -1.0. HRMS (ESI^+): m/z for $C_{14}H_{21}NO_3SiSBr$ $[M+H]^+$ calcd. 390.0195, found: 390.0197.

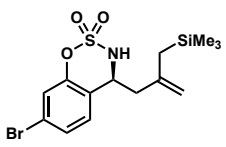


***rac*-(S)-6-methyl-4-(2-((trimethylsilyl)methyl)allyl)-3,4-dihydrobenzo[e][1,2,3]oxathiazine 2,2-dioxide (1.9e)** Prepared according to the general procedure. The crude mixture was purified by column chromatography to give compound **1.9e** in 81% yield (26 mg) as colorless oil. ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.10 (d, *J* = 8.2 Hz, 1H), 6.99 (s, 1H), 6.91 (d, *J* = 8.4 Hz, 1H), 4.83 – 5.07 (m, 1H), 4.79 (s, 1H), 4.77 (s, 1H), 4.66 (d, *J* = 7.3 Hz, 1H), 2.78 (dd, *J* = 14.5, 4.4 Hz, 1H), 2.61 (dd, *J* = 14.5, 8.9 Hz, 1H), 2.34 (s, 3H), 1.54 (d, *J* = 13.8 Hz, 1H), 1.49 (d, *J* = 13.6 Hz, 1H), 0.07 (s, 9H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 149.3, 142.3, 135.4, 130.4, 126.9, 122.4, 119.2, 113.4, 54.9, 43.4, 26.4, 21.2, -1.0. HRMS (ESI^+): m/z for $C_{15}H_{24}NO_3SiS$ $[M+H]^+$ calcd. 326.1246, found: 326.1237.

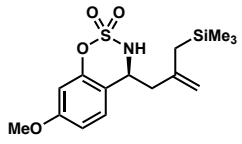


***rac*-(S)-6-nitro-4-(2-((trimethylsilyl)methyl)allyl)-3,4-dihydrobenzo[e][1,2,3]oxathiazine 2,2-dioxide (1.9f)** Prepared according to the general procedure. The crude mixture was purified by column chromatography to give compound **1.9f** in 93% yield (33 mg) as colorless oil. ^{1}H NMR (600 MHz, $CDCl_3$) δ 8.22 (dd, *J* = 9.0, 2.3 Hz, 1H), 8.05 – 8.20 (m, 1H), 7.18 (d, *J* = 9.0 Hz, 1H), 4.95 –5.13 (m, 1H), 4.90 (d, *J*

= 7.7 Hz, 1H), 4.85 (s, 1H), 4.79 (s, 1H), 2.86 (dd, *J* = 14.6, 4.8 Hz, 1H), 2.69 (dd, *J* = 14.6, 8.7 Hz, 1H), 1.57 (d, *J* = 13.8 Hz, 1H), 1.53 (d, *J* = 13.6 Hz, 1H), 0.09 (s, 9H). ^{13}C NMR (101 MHz, $CDCl_3$) δ ^{13}C NMR (101 MHz, $CDCl_3$) δ 155.6, 144.9, 141.6, 125.3, 124.0, 122.9, 120.6, 113.9, 54.8, 43.1, 26.6, -1.0. HRMS (ESI^+): m/z for $C_{14}H_{21}N_2O_5SiS$ $[M+H]^+$ calcd. 357.0940, found: 357.0933.



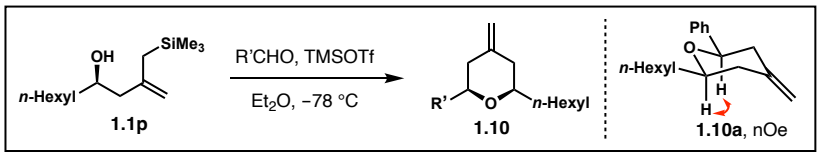
***rac*-(S)-7-bromo-4-(2-((trimethylsilyl)methyl)allyl)-3,4-dihydrobenzo [e][1,2,3]oxathiazine 2,2-dioxide (1.9g)** Prepared according to the general procedure. The crude mixture was purified by column chromatography to give compound **1.9g** in 97% yield (38 mg) as white solid. ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.33 (dd, *J* = 8.4, 1.8 Hz, 1H), 7.20 (d, *J* = 1.7 Hz, 1H), 7.08 (d, *J* = 8.3 Hz, 1H), 4.84 – 5.02 (m, 1H), 4.80 (s, 1H), 4.77 (s, 1H), 4.74 (d, *J* = 7.4 Hz, 1H), 2.76 (dd, *J* = 14.5, 4.6 Hz, 1H), 2.59 (dd, *J* = 14.5, 8.9 Hz, 1H), 1.54 (d, *J* = 13.9 Hz, 1H), 1.52 (d, *J* = 13.7 Hz, 1H), 0.07 (s, 9H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 151.6, 141.9, 128.9, 127.9, 122.6304, 122.6303, 121.9, 113.5, 54.7, 43.3, 26.4, -1.0. HRMS (ESI^+): m/z for $C_{14}H_{21}NO_3SiSBr$ $[M+H]^+$ calcd. 390.0195, found: 390.0186.



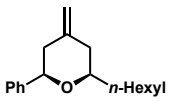
***rac*-(S)-7-methoxy-4-(2-((trimethylsilyl)methyl)allyl)-3,4-dihydrobenz [e][1,2,3]oxathiazine 2,2-dioxide (1.9h)** Prepared according to the general procedure. The crude mixture was purified by column chromatography to give compound **1.9h** in 85% yield (29 mg) as colorless oil. ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.09 (d, *J* = 8.7 Hz, 1H), 6.76 (dd, *J* = 8.6, 2.2 Hz, 1H), 6.55 (d, *J* = 2.3 Hz, 1H), 4.82 – 4.98 (m, 1H), 4.77 (s, 1H), 4.75 (s, 1H), 4.66 (d, *J* = 7.6 Hz, 1H), 3.80 (s, 3H), 2.76 (dd, *J* = 14.5, 4.4 Hz, 1H), 2.56 (dd, *J* = 14.4, 8.9 Hz, 1H), 1.53 (d, *J* = 13.6 Hz, 1H), 1.49 (d, *J* = 13.6

Hz, 1H), 0.06 (s, 9H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 160.5, 152.0, 142.3, 127.3, 114.6, 113.2, 112.6, 104.1, 56.0, 54.5, 43.4, 26.5, -1.0. HRMS (ESI^+): m/z for $C_{15}H_{23}NO_4SiSNa$ $[M+Na]^+$ calcd. 364.1015, found: 364.1019.

Double Allylation Studies



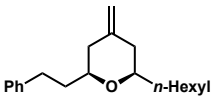
General procedure for stereoselective synthesis of tetrahydropyrans 1.10: To a solution of β-Hydroxyallylsilicane **1.1p** (24mg, 0.1 mmol, 1.0 equiv) in diethyl ether (2.0 mL), aldehyde (0.2 mmol, 2 equiv) was added, and the mixture was cooled to –78 ˚C. TMSOTf (27 μL, 0.15 mmol, 1.5 equiv) was added and the mixture was stirred for 20 min. Aqueous 1N NaOH solution (1 mL) was added and the mixture was brought to rt, then transferred to a separatory funnel. The layers were separated and the aqueous layer was extracted with Et_2O (3 x 1 mL). The combined organic layers were dried over anhydrous magnesium sulfate, filtered, and concentrated under reduced pressure. Purification of the crude product was performed by flash chromatography (gradient elution with hexane and EtOAc) to provide product **1.10**.



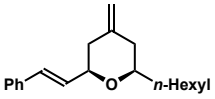
***rac*-(2*R*,6*R*)-2-hexyl-4-methylene-6-phenyltetrahydro-2*H*-pyran (1.10a)**

Prepared according to the general procedure. The crude mixture was purified by column chromatography to give compound **1.10a** in 73% yield (19 mg) as colorless oil. ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.39 (d, J = 7.1 Hz, 2H), 7.35 (t, J = 7.4 Hz, 2H), 7.19 – 7.30 (m, 1H), 4.79 (s, 2H), 4.23 – 4.40 (m, 1H), 3.24 – 3.60 (m, 1H), 2.46 (d, J = 13.3 Hz, 1H), 2.29 (d, J = 13.2 Hz,

1H), 2.22 (dd, *J* = 12.1 Hz, 12.1 Hz, 1H), 2.02 (dd, *J* = 12.1 Hz, 12.1 Hz, 1H), 1.63 – 1.78 (m, 1H), 1.49 – 1.56 (m, 1H), 1.41 – 1.49 (m, 1H), 1.34 – 1.41 (m, 1H), 1.09 – 1.34 (m, 6H), 0.76 – 0.99 (m, 3H). ^{13}C NMR (151 MHz, $CDCl_3$) δ 145.4, 143.0, 128.6, 127.7, 126.2, 109.0, 80.3, 79.2, 43.1, 40.8, 36.7, 32.2, 29.7, 25.7, 23.0, 14.5. HRMS (ESI): m/z for $C_{18}H_{26}O$ $[M+H]^+$ calcd. 259.2062, found: 259.2051.

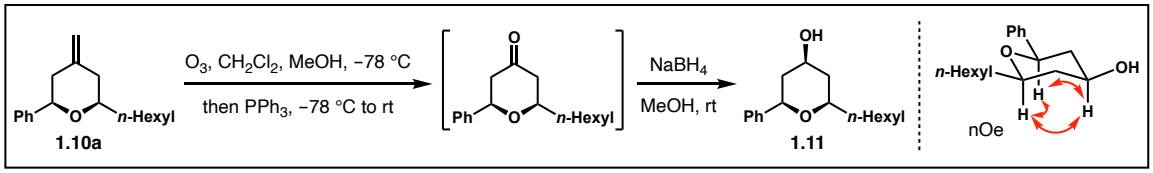


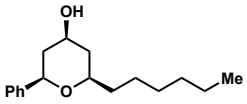
***rac*-(2*R*,6*S*)-2-hexyl-4-methylene-6-phenethyltetrahydro-2*H*-pyran (1.10b)** Prepared according to the general procedure. The crude mixture was purified by column chromatography to give compound **1.10b** in 70% yield (20 mg) as colorless oil. ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.23 – 7.39 (m, 2H), 7.19 (d, *J* = 6.8 Hz, 3H), 4.68 (s, 1H), 4.66 (s, 1H), 3.03 – 3.34 (m, 2H), 2.76 – 2.92 (m, 1H), 2.61 – 2.76 (m, 1H), 2.20 (d, *J* = 13.4 Hz, 1H), 2.17 (d, *J* = 13.6 Hz, 1H), 1.81 – 2.03 (m, 3H), 1.66 –1.79 (m, 1H), 1.07 – 1.65 (m, 10H), 0.76 – 1.00 (m, 3H). ^{13}C NMR (151 MHz, $CDCl_3$) δ 145.5, 142.5, 128.9, 128.6, 126.0, 108.5, 78.6, 77.3, 41.4, 41.3, 38.2, 36.7, 32.2, 32.1, 29.7, 26.0, 23.0, 14.5. HRMS (ESI): m/z for $C_{20}H_{31}O$ $[M+H]^+$ calcd. 287.2375, found: 287.2361.



***rac*-(2*R*,6*R*)-2-hexyl-4-methylene-6-((*E*)-styryl)tetrahydro-2*H*-pyran (1.10c)** Prepared according to the general procedure. The crude mixture was purified by column chromatography to give compound **1.10c** in 96% yield (27 mg) as colorless oil. ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.39 (d, *J* = 7.2 Hz, 2H), 7.31 (dd, *J* = 7.2 Hz, 7.2 Hz, 2H), 7.23 (dd, *J* = 6.5 Hz, 6.5 Hz, 1H), 6.61 (d, *J* = 16.0 Hz, 1H), 6.27 (dd, *J* = 16.0, 5.8 Hz, 1H), 4.77 (s, 2H), 3.85 – 4.04 (m, 1H), 3.23 – 3.45 (m, 1H), 2.34 (d, *J* = 13.2 Hz, 1H), 2.26 (d, *J* = 13.3 Hz, 1H), 2.15 (dd, *J* = 12.2 Hz, 12.2 Hz, 1H), 1.96 (dd, *J* = 12.2 Hz, 12.2 Hz, 1H), 1.61 – 1.72 (m,

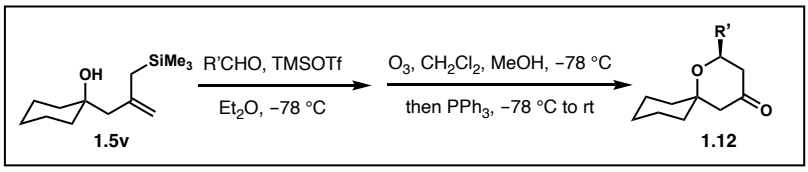
1H), 1.41 – 1.55 (m, 2H), 1.13 – 1.40 (m, 7H), 0.78 – 0.97 (m, 3H). ^{13}C NMR (151 MHz, $CDCl_3$) δ 144.8, 137.1, 130.7, 130.4, 128.8, 127.9, 126.8, 109.1, 79.1, 78.8, 41.3, 40.9, 36.7, 32.1, 29.7, 25.8, 23.0, 14.5. HRMS (ESI): m/z for $C_{20}H_{29}O$ $[M+H]^+$ calcd. 285.2218, found: 285.2207.





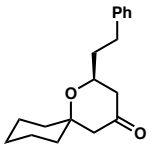
***rac*-(2*R*,4*S*,6*R*)-2-hexyl-6-phenyltetrahydro-2*H*-pyran-4-ol (1.11)** To a solution of tetrahydropyran **1.10a** (13 mg, 0.05 mmol, 1.0 equiv) in dichloromethane and methanol (2.00 mL, 1:1), 1 mg Sudan III was added as indicator. Then the mixture was cooled to –78 ˚C and treated with a stream of ozone generated from O_2. The bright red solution became purple after 10 min, which indicated complete consumption of tetrahydropyran **1.10a**. Turn off the ozone generator, and allow oxygen to purge the reaction mixture of ozone for 5 min. Then PPh_3 (18 mg, 0.07 mmol, 1.4 equiv) was added in the mixture. The mixture was warmed to ambient temperature and stirred for 30 min. The resulting solution was concentrated under reduced pressure. The concentrated solution was diluted in 2 mL EtOH. Then $NaBH_4$ (5.7 mg, 3.0 equiv, 0.15 mmol) was added in the solution. After complete consumption of ketone intermediate, the reaction was quenched by saturated NH_4Cl solution and transferred to a separatory funnel. The layers were separated and the aqueous layer was extracted with EtOAc (3 x 1 mL). The combined organic layers were dried over anhydrous magnesium sulfate, filtered, and concentrated under reduced pressure. Purification of the crude product was performed by flash chromatography (gradient elution with hexane and EtOAc) to provide product **1.11** in 98% yield (13 mg) as colorless oil .^{1}H NMR (600 MHz, $CDCl_3$) δ 7.30 – 7.43 (m,

3H), 7.20 – 7.30 (m, 2H), 4.36 (d, J = 10.7 Hz, 1H), 3.84 – 4.08 (m, 1H), 3.40 – 3.56 (m, 1H), 2.22 (d, J = 10.7 Hz, 1H), 2.03 (d, J = 11.9 Hz, 1H), 1.60 – 1.74 (m, 1H), 1.13 – 1.60 (m, 12H), 0.76 – 0.98 (m, 3H). ^{13}C NMR (151 MHz, $CDCl_3$) δ 142.5, 128.7, 127.8, 126.2, 77.6, 76.3, 69.0, 43.2, 41.1, 36.4, 32.1, 29.7, 25.8, 23.0, 14.5. HRMS (ESI): m/z for $C_{17}H_{27}O_2$ $[M+H]^+$ calcd. 263.2011, found: 263.2007.

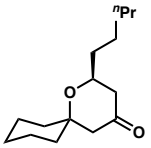


General procedure for synthesis of compound 1.12: To a solution of alcohol **1.5v** (23 mg, 0.1 mmol, 1.0 equiv) in diethyl ether (2.0 mL), was added aldehyde (0.2 mmol, 2 equiv). The reaction mixture was placed in a dry ice/acetone bath and cooled to –78 ˚C. TMSOTf (27 µL, 0.15 mmol, 1.5 equiv) was added and the mixture was stirred at –78 ˚C for 12 h. Then saturated aqueous $NaHCO_3$ solution (1 mL) was added and the mixture was allowed to warm to ambient temperature. The reaction mixture was transferred into a separatory funnel. The organic layer was separated and the aqueous layer was extracted with Et_2O (3 x 1 mL). The combined organic layers were dried over anhydrous magnesium sulfate, filtered, and concentrated under reduced pressure to give crude tetrahydropyran **10**. The crude product was dissolved in dichloromethane and methanol (2.00 mL, 1:1). The reaction vessel was placed in a dry ice/acetone bath and cooled to –78 ˚C. Then the reaction mixture was treated with a stream of ozone (generated from air). The reaction progress was monitored by TLC. After complete consumption of the tetrahydropyran intermediate, the reaction mixture was purged with N_2 for 5 min. Then PPh_3 (36 mg, 0.14 mmol, 1.4 equiv) was added. The reaction mixture was warmed to ambient temperature

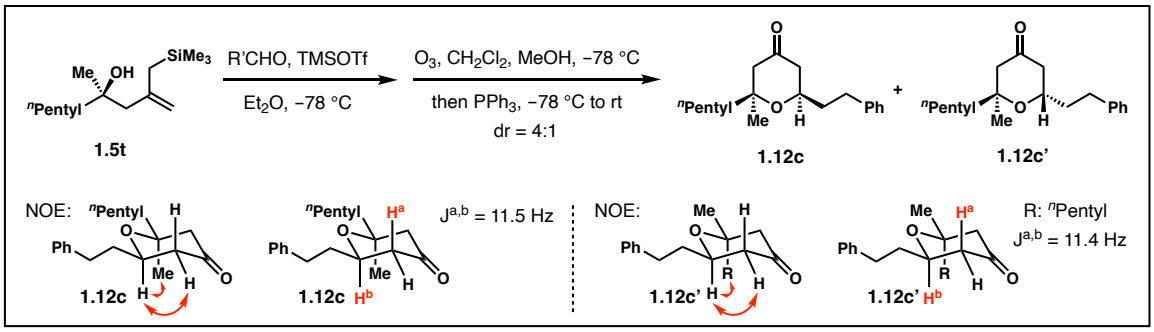
and stirred for additional 30 min. The resulting solution was concentrated under reduced pressure. Purification of the crude product was performed by flash chromatography (gradient elution with hexane and EtOAc) to provide product **8**.

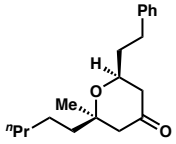


2-phenethyl-1-oxaspiro[5.5]undecan-4-one (1.12a) Prepared according to the general procedure. The crude mixture was purified by flash column chromatography to give compound **1.12a** in 83% yield (23 mg) as colorless oil. ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.24 – 7.44 (m, 2H), 7.07 – 7.24 (m, 3H), 3.67 – 3.93 (m, 1H), 2.81 – 3.25 (m, 1H), 2.65 – 2.81 (m, 1H), 2.48 – 2.81 (m, 4H), 1.90 – 2.08 (m, 1H), 1.80 – 1.90 (m, 1H), 1.68 – 1.81 (m, 3H), 1.33 – 1.55 (m, 4H), 0.99 – 1.33 (m, 3H). ^{13}C NMR (151 MHz, $CDCl_3$) δ 208.9, 142.1, 128.73, 128.68, 126.2, 76.3, 69.3, 53.2, 48.2, 39.8, 39.0, 32.4, 32.0, 25.7, 22.0, 21.4. HRMS (ESI$^+$): m/z for $C_{18}H_{25}O_2$ $[M+H]^+$ calcd. 273.1855, found: 273.1847.

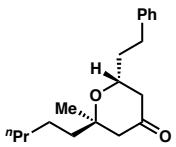


2-pentyl-1-oxaspiro[5.5]undecan-4-one (1.12b) Prepared according to the general procedure. The crude mixture was purified by flash column chromatography to give compound **1.12b** in 89% yield (21 mg) as colorless oil. ^{1}H NMR (600 MHz, $CDCl_3$) δ 3.61 – 3.86 (m, 1H), 2.30 (d, J = 13.7 Hz, 2H), 2.24 (d, J = 13.6 Hz, 1H), 2.10 – 2.21 (m, 1H), 1.68 – 2.00 (m, 3H), 1.57 – 1.68 (m, 1H), 1.51 – 1.57 (m, 1H), 1.45 – 1.51 (m, 2H), 1.37 – 1.45 (m, 3H), 1.26 – 1.37 (m, 5H), 1.06 – 1.26 (m, 3H), 0.89 (t, J = 6.6 Hz, 3H). ^{13}C NMR (151 MHz, $CDCl_3$) δ 209.3, 76.1, 69.9, 53.4, 48.4, 39.7, 37.3, 32.1, 31.9, 30.1, 25.7, 22.9, 22.0, 21.3, 14.5. HRMS (ESI$^+$): m/z for $C_{15}H_{27}O_2$ $[M+H]^+$ calcd. 239.2011, found: 239.2019.

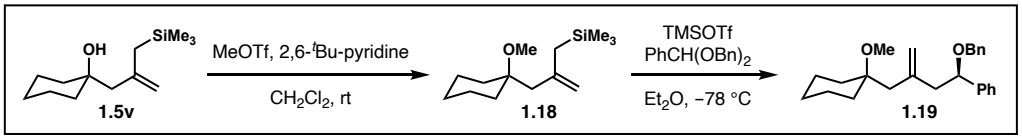




***rac*-(2*R*,6*S*)-2-methyl-2-pentyl-6-phenethyltetrahydro-4*H*-pyran-4-one (1.12c)** Prepared according to the general procedure with **1.5t** as the starting material. The crude mixture was purified by column chromatography to give compound **1.12c** in 72% yield (21 mg) as colorless oil. ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.23 – 7.43 (m, 2H), 7.08 – 7.23 (m, 3H), 3.61 – 3.93 (m, 1H), 2.75 – 2.93 (m, 1H), 2.58 – 2.75 (m 1H), 2.38 (d, *J* = 13.6 Hz, 1H), 2.28 (d, *J* = 13.7 Hz, 1H), 2.18 – 2.25 (m, 2H), 1.86 – 2.05 (m, 1H), 1.68 – 1.86 (m, 1H), 1.50 – 1.68 (m, 2H), 1.23 – 1.50 (m, 6H), 1.09 (s, 3H), 0.91 (t, *J* = 7.0 Hz, 3H). ^{13}C NMR (151 MHz, $CDCl_3$) δ 209.3, 141.9, 128.8, 128.7, 126.2, 77.3, 69.5, 52.4, 48.2, 44.1, 38.6, 32.5, 31.9, 23.3, 23.0, 22.2, 14.5. HRMS (ESI^+): m/z for $C_{19}H_{29}O_2$ $[M+H]^+$ calcd. 289.2168, found: 289.2162.



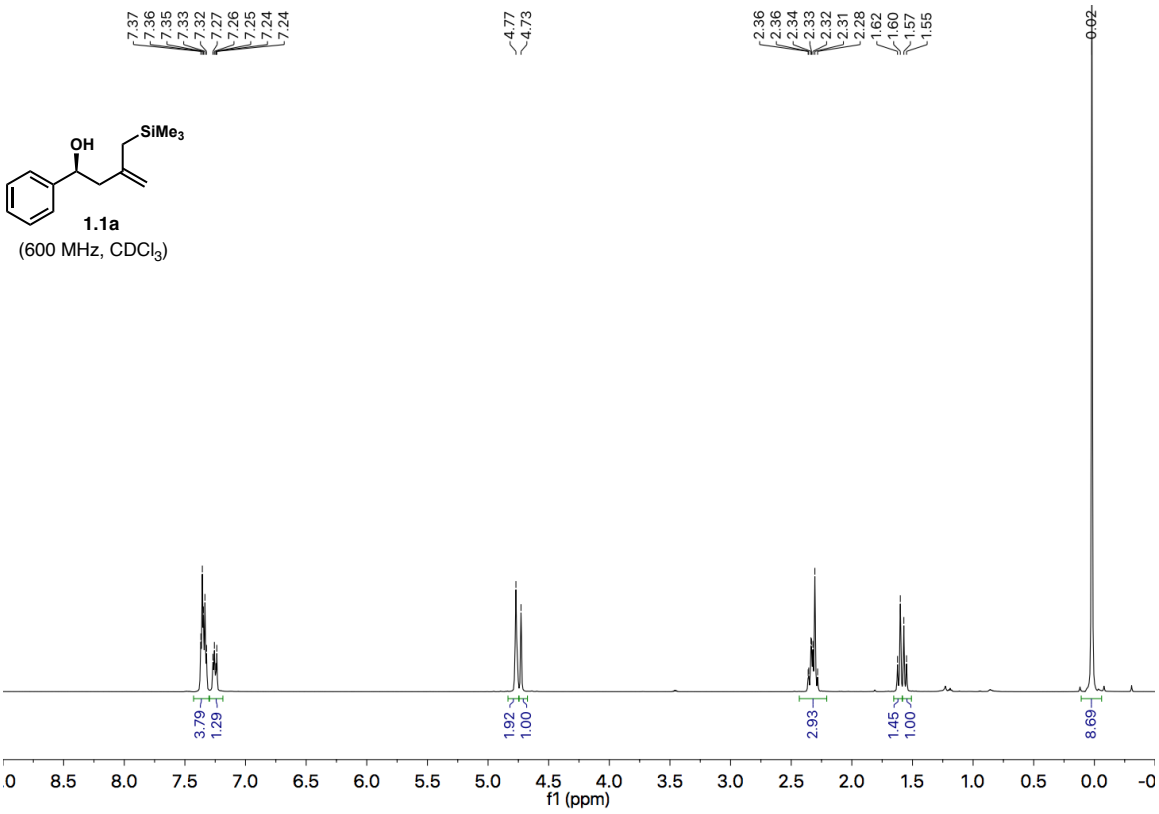
***rac*-(2*R*,6*R*)-2-methyl-2-pentyl-6-phenethyltetrahydro-4*H*-pyran-4-one (1.12c')** Compound **1.12c'** was isolated in 18% yield (5 mg) as colorless oil. ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.23 – 7.38 (m, 2H), 7.17 – 7.23 (m, 3H), 3.59 – 3.87 (m, 1H), 2.75 – 3.01 (m, 1H), 2.47 – 2.75 (m, 1H), 2.39 (d, *J* = 13.8 Hz, 1H), 2.26 – 2.35 (m, 2H), 2.22 (dd, *J* = 14.1, 11.2 Hz, 1H), 1.89 – 2.05 (m, 1H), 1.73 – 1.88 (m, 1H), 1.46 – 1.52 (m, 1H), 1.30 (s, 3H), 1.11 – 1.29 (m, 7H), 0.87 (t, *J* = 7.1 Hz, 3H). ^{13}C NMR (151 MHz, $CDCl_3$) δ 208.9, 141.9, 128.72, 128.67, 126.3, 77.3, 69.8, 53.4, 47.7, 38.6, 36.2, 32.3, 32.0, 27.7, 22.9, 22.7, 14.4. HRMS (EI^+): m/z for $C_{19}H_{28}O_2$ $[M]^+$ calcd. 288.2089, found: 288.2092.



***rac*-(*R*)-(1-(benzyloxy)-3-((1-methoxycyclohexyl)methyl)but-3-en-1-yl)benzene (1.19)** To a solution of alcohol **1.5v** (23 mg, 0.1 mmol, 1.0 equiv) in dichloromethane (2.0 mL), was added 2,6-*tert*-butyl-pyridine (0.4 mmol, 4 equiv) and MeOTf (0.25 mmol, 2.5 equiv). The mixture was stirred for 12 h at ambient temperature. After complete consumption of alcohol **1.5v**, the reaction mixture was concentrated under reduced pressure. The residue was purified by column chromatography (gradient elution with hexane and EtOAc) to give methyl ether **1.18** in 94% yield. ^{1}H NMR (600 MHz, d^{6}-acetone) δ 4.62 (s, 1H), 4.62 (s, 1H), 3.13 (s, 3H), 2.10 (s, 2H), 1.73 (d, J = 13.1 Hz, 2H), 1.65 (s, 2H), 1.44 – 1.59 (m, 3H), 1.34 – 1.44 (m, 2H), 1.27 (t, J = 12.3 Hz, 2H), 1.11 – 1.23 (m, 1H), 0.02 (s, 9H). ^{13}C NMR (151 MHz, $CDCl_3$) δ 143.9, 111.3, 76.1, 48.5, 43.9, 34.5, 28.6, 26.9, 22.2, -1.1.

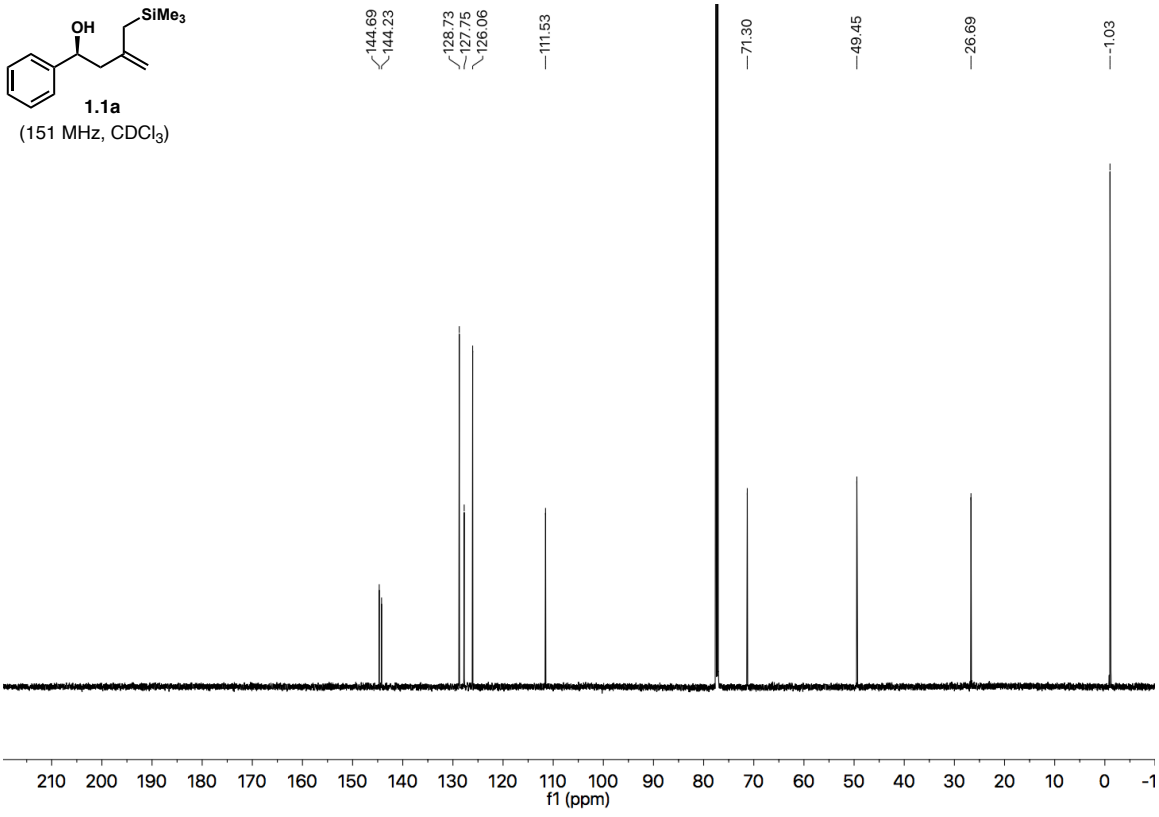
To a solution **1.18** in diethyl ether (2.0 mL), benzaldehyde dibenzyl acetal (61 mg, 0.2 mmol, 2 equiv) was added. The mixture was cooled to –78 ˚C, TMSOTf (27 μL, 0.15 mmol, 1.5 equiv) was added and the mixture was stirred at –78 ˚C for 12 h. Then saturated aqueous $NaHCO_3$ solution (1 mL) was added and the mixture was allowed to warm to ambient temperature. The reaction mixture was transferred into a separatory funnel. The organic layer was separated and the aqueous layer was extracted with Et_2O (3 x 1 mL). The combined organic layers were dried over anhydrous magnesium sulfate, filtered, and concentrated under reduced pressure The crude mixture was purified by flash chromatography to give compound **1.19** as colorless oil in 78% yield (27 mg). ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.32 – 7.43 (m, 5H), 7.21 – 7.32 (m, 5H), 4.89 (s, 1H), 4.82 (s, 1H), 4.34 – 4.58 (m, 2H), 4.24 (d, J = 11.9 Hz, 1H), 3.11(s,

3H), 2.65 (dd, *J* = 14.3, 8.4 Hz, 1H), 2.42 (dd, *J* = 14.4, 5.1 Hz, 1H), 2.14 (d, *J* = 14.3 Hz, 1H), 2.02 (d, *J* = 14.3 Hz, 1H), 1.62 – 1.78 (m, 2H), 1.43 – 1.55 (m, 3H), 1.32– 1.43 (m, 2H), 1.08 – 1.31 (m, 3H). ^{13}C NMR (151 MHz, $CDCl_3$) δ 142.8, 142.6, 138.8, 128.7, 128.6, 128.1, 127.9, 127.8, 127.2, 116.5, 80.8, 75.9, 70.6, 48.5, 46.5, 41.9, 34.4, 26.0, 22.21, 22.17. HRMS (ESI^+): m/z for $C_{25}H_{32}O_2Na$ $[M+Na]^+$ calcd. 387.2300, found: 387.2302.



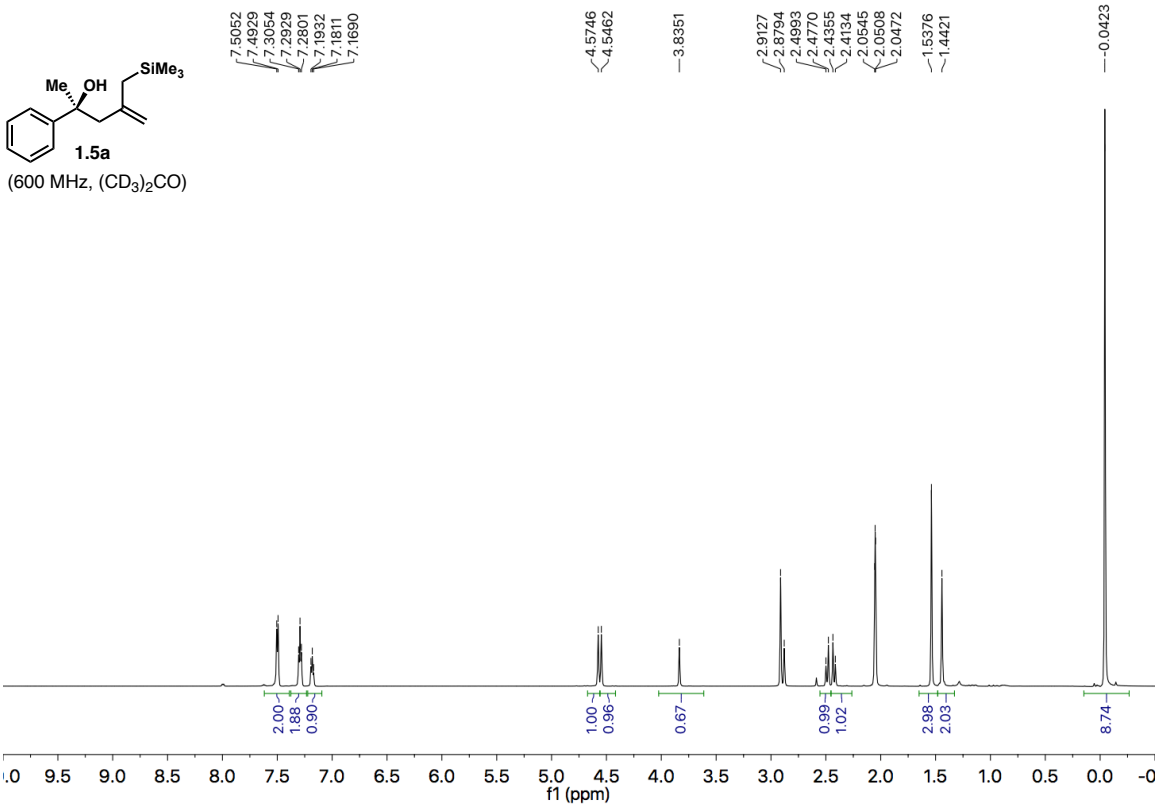
1.1a

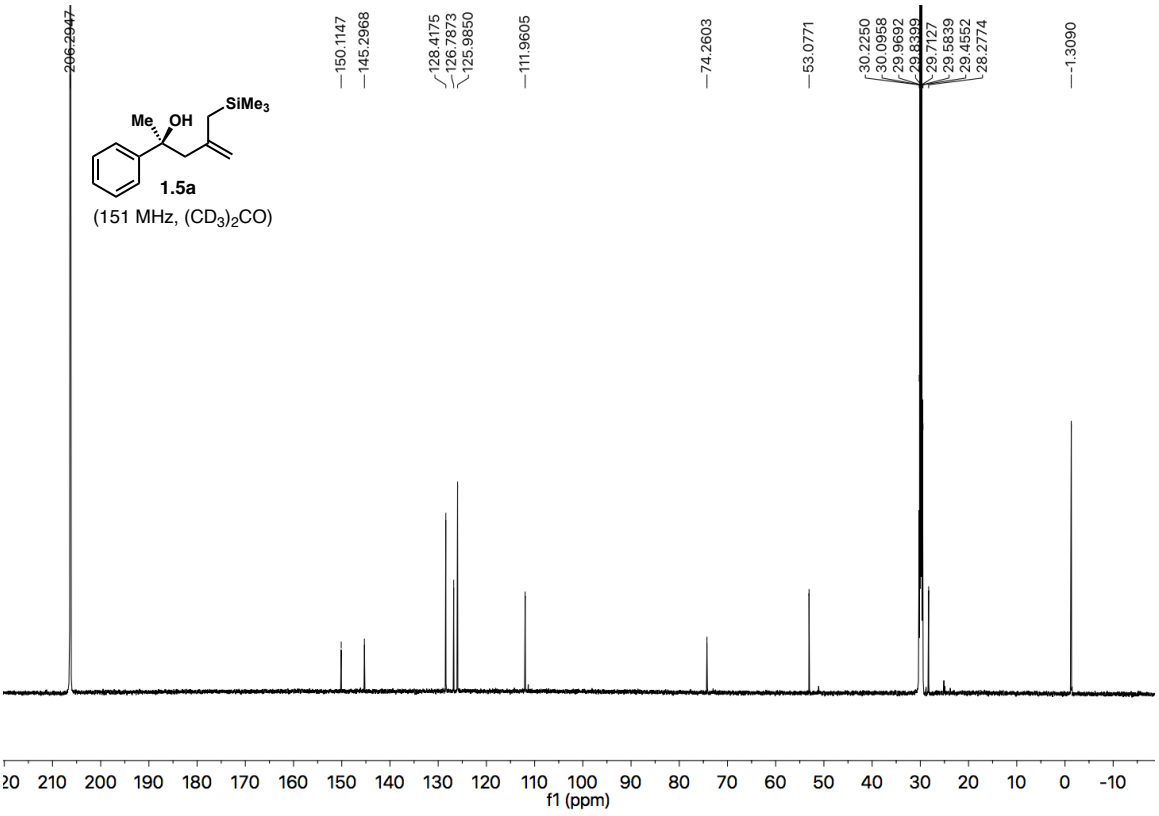
(600 MHz, $CDCl_3$)



1.1a

(151 MHz, $CDCl_3$)


7.5052
7.4929
7.3054
7.2929
7.2801
7.1932
7.1811
7.1690
4.5746
4.5462
3.8351
2.9127
2.8794
2.4993
2.4770
2.4355
2.4134
2.0545
2.0508
2.0472
1.5376
1.4421
-0.0423
2.00
1.88
0.90
1.00
0.96
0.67
0.99
1.02
2.98
2.03
8.74
f1 (ppm)


206.2947
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128.4175
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125.9850
111.9605
74.2603
53.0771
30.2250
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29.9692
29.8399
29.7127
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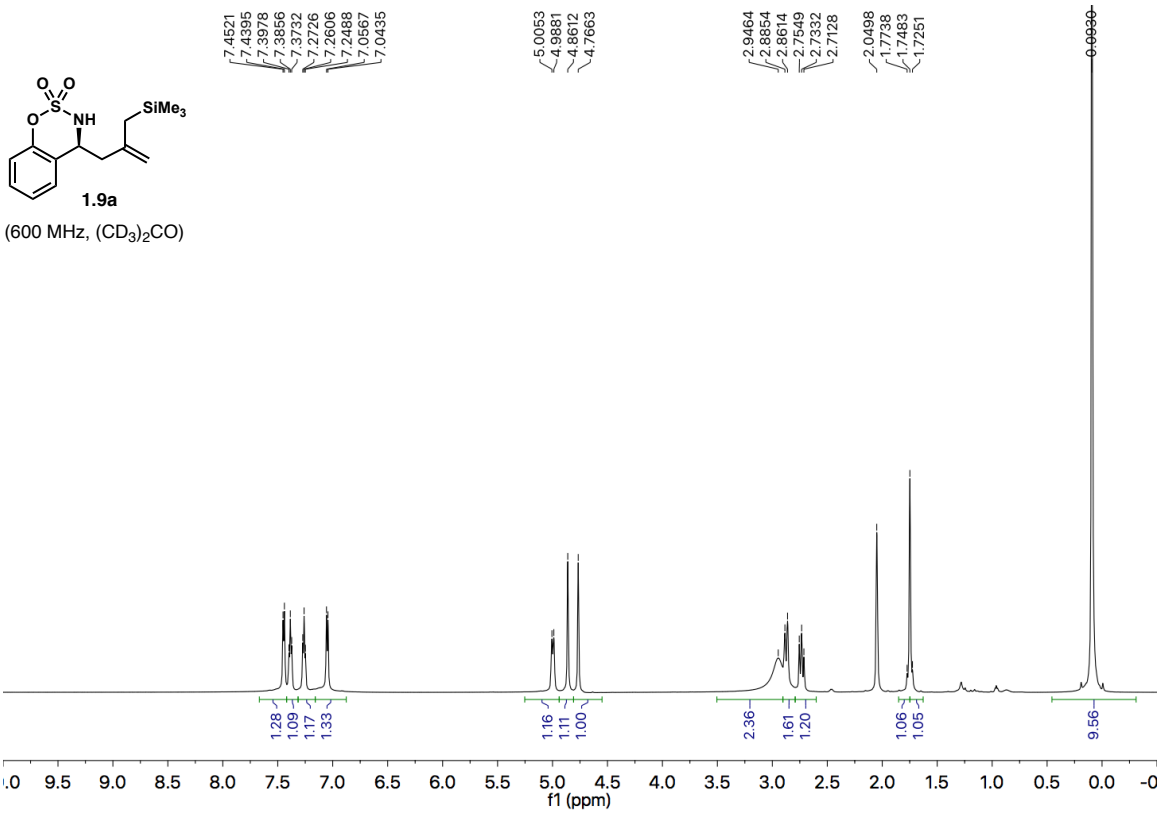
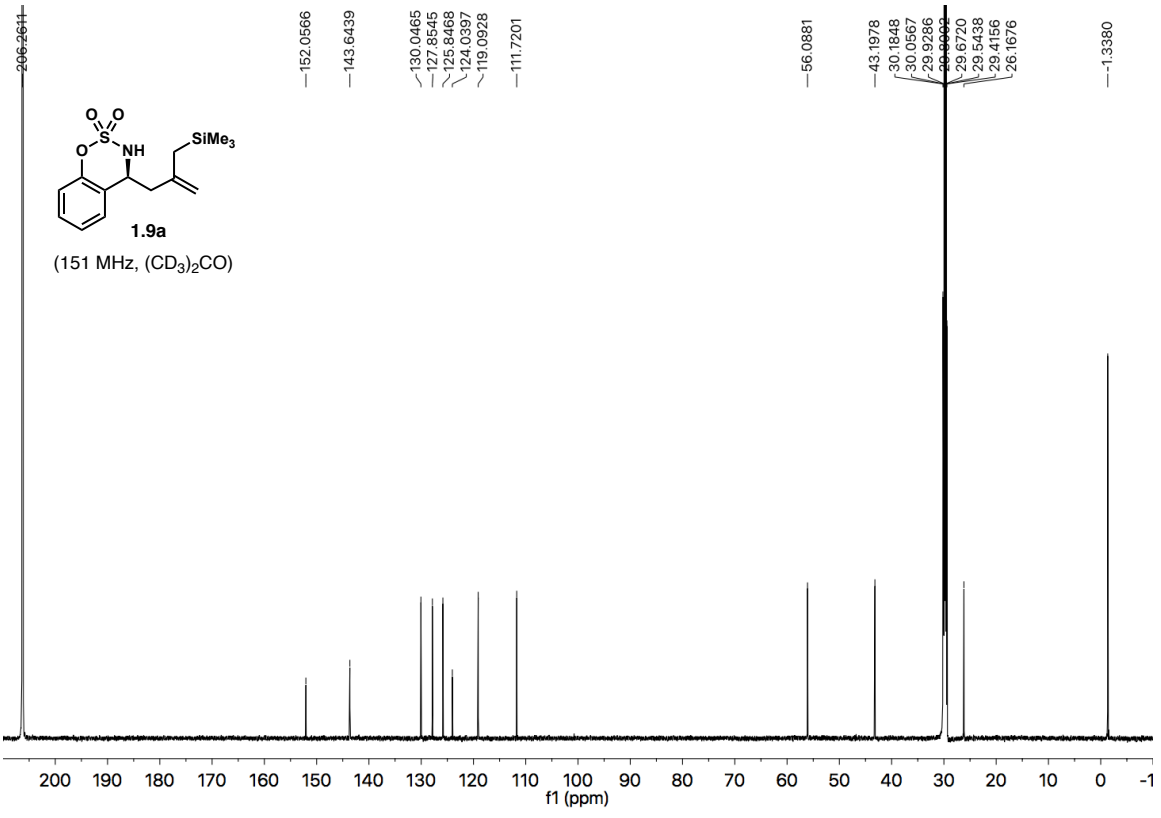
29.4552
28.2774
-1.3090
f1 (ppm)



1.9a

(600 MHz, $(CD_3)_2CO$)



1.9a

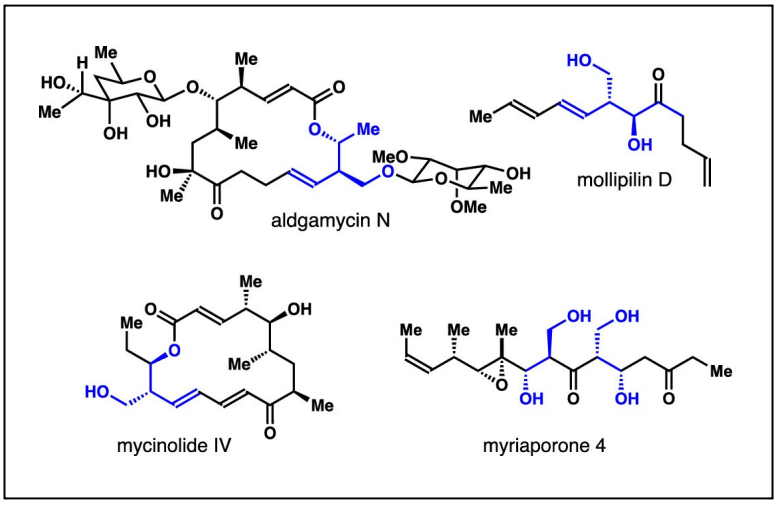
(151 MHz, $(CD_3)_2CO$)

CHAPTER TWO

1,4-Bifunctional allylboron reagents

Chiral, nonracemic 1,2-*anti*- and 1,2-*syn*-2-hydroxymethyl-3-ene-1-ols (highlighted in blue in **Figure 2.1**) are common structural motifs in many biologically active natural products.[40-72] Diastereo- and enantioselective syntheses of these structural entities are therefore important objectives in organic synthesis. Several approaches are available to generate these molecules in a racemic form with good *anti/syn* selectivities.[73-81] However, methods that allow for their enantioselective syntheses are much underdeveloped.

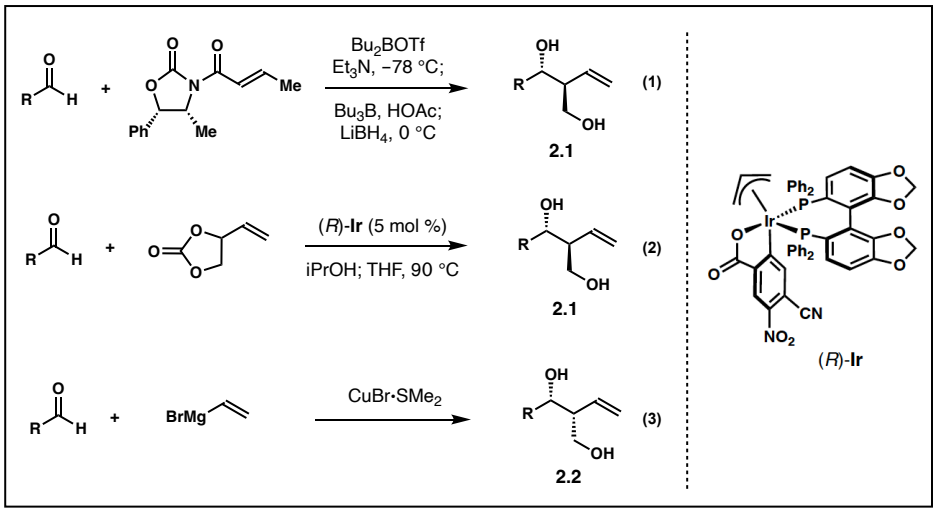
Figure 2.1. Selected natural products containing 1,2-*syn*- or *anti*-hydroxymethyl-1,3-diols



As shown in **Scheme 2.1**, Evans reported a chiral auxiliary-based aldol/reduction reaction sequence to generate enantioenriched 1,2-anti-isomer **2.1** (eq 1, **Scheme 1.14**).[82] This method has been widely adopted in the syntheses of natural products that contain such a structural motif.[82-88] More recently, a catalytic variant of this method was disclosed by the Shibasaki

group.[89,90] Using a cyclic carbonate as the allyl donor, Krische and coworkers reported an elegant Ir-catalyzed *anti*-(hydroxymethyl)allylation strategy to access enantioenriched diol **2.1** (eq 2, **Scheme 1.14**).[91] By contrast, asymmetric synthesis of 1,2-*syn*-isomer **2.2** mainly relies on vinyl Grignard addition to enantioenriched epoxy alcohols (eq 3, **Scheme 2.1**).[92-96] The development of catalytic methods that allow for the entry to enantioenriched *syn*-isomer **2.2** would be desirable.

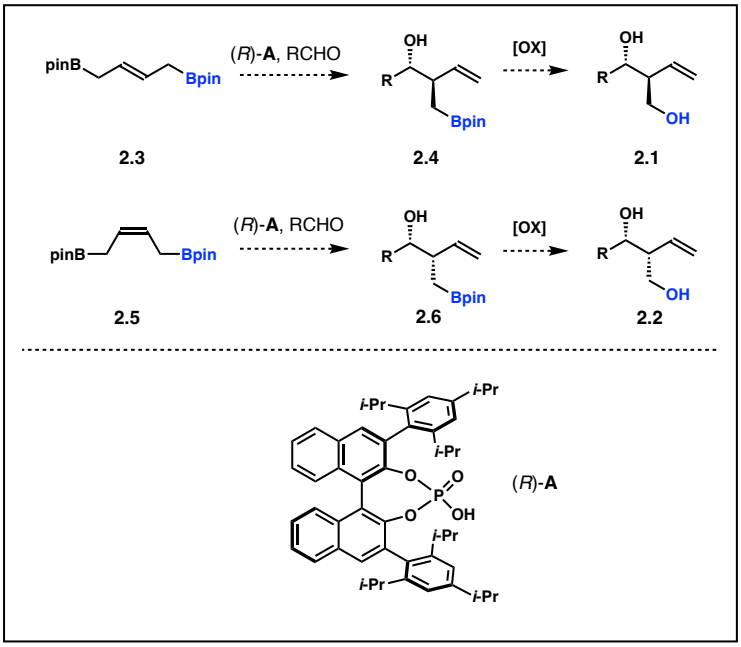
Scheme 2.1 Approaches for Enantioselective Syntheses of 1,2-*anti*- and 1,2-*syn*-2-hydroxymethyl-3-ene-1-ols



Pioneered by the Antilla group, chiral phosphoric acid catalyzed enantioselective aldehyde addition with unsaturated organoboron compounds has emerged as a powerful method to access enantioenriched homoallylic, allenic and homopropargylic alcohols.[97-124] Inspired by these prior studies, we envisioned a chiral phosphoric acid-catalyzed asymmetric aldehyde allylboration strategy to synthesize both 1,2-*anti*- and 1,2-*syn*-2- hydroxymethyl-3-ene-1-ols, **2.1** and **2.2**. As shown in **Scheme 2.2**, based on the well-established chair-like transition state typically involved in allylboration chemistry, we anticipate that chiral phosphoric acid (R)-**A** catalyzed aldehyde addition with (*E*)-γ-borylmethyl allylboronate **2.3** should provide 1,2-*anti*-

adduct **2.4** with high diastereo- and enantioselectivity. Similarly, the reaction with (*Z*)-reagent **2.5** should generate 1,2-*syn*-adduct **2.6** selectively. Subsequent oxidation of the Bpin group in **2.4** and **2.6** should produce enantioenriched, mono-protected 1,2-*anti*- and 1,2-*syn*-2-hydroxymethyl-3-ene-1-ols (**2.1** and **2.2**, **Scheme 1.15**). Moreover, the Bpin group in intermediates **2.4** and **2.6** should be amenable to a variety of transformations besides oxidation.[125-127]

Scheme 2.2. proposed asymmetric synthetic route for 1,3-syn/anti-diols

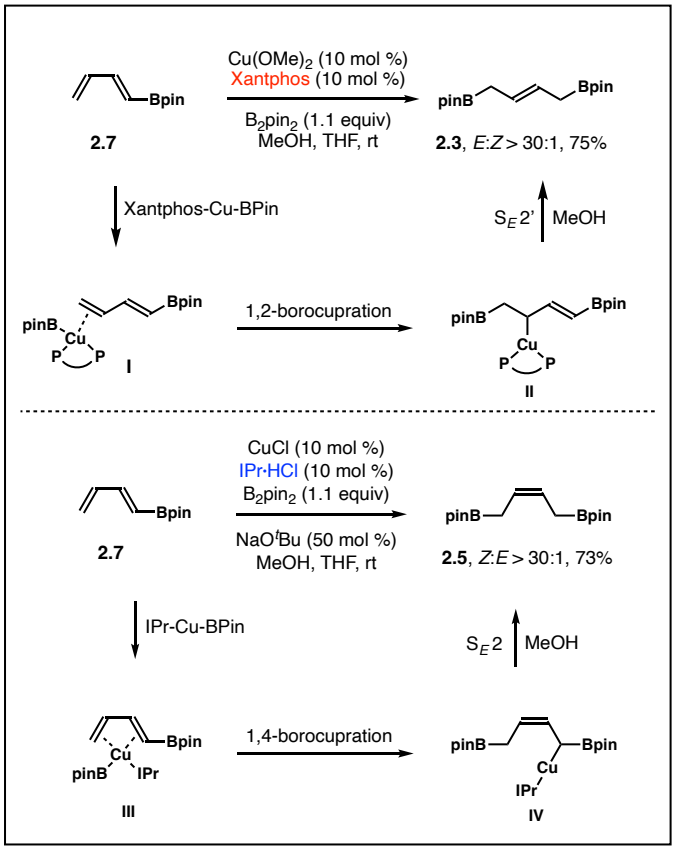


2.1 Preparation of (E)- and (Z)-γ-borylmethyl allylboronate reagents

Based on the proposed synthetic strategy, we began our studies by developing suitable methods for stereoselective syntheses of (*E*)- and (*Z*)-γ-borylmethyl allylboronate reagents **2.3** and **2.5**.[128-136] After initial experimentations, a Cu-catalyzed diene protoboration approach was identified for stereoselective syntheses of **2.3** and **2.5**.[137-140] We discovered that, in the presence of a bidentate phosphine ligand Xantphos, Cu-catalyzed protoboration of 1,3-dienylboronate **2.7**

gave (*E*)-γ-borylmethyl allylboronate **2.3** in 75% yield with > 30:1 *E*-selectivity (**Scheme 2.3**). The (*Z*)-

Scheme 2.3 Stereoselective syntheses of (E)- and (Z)-γ-Borylmethyl allylboronates



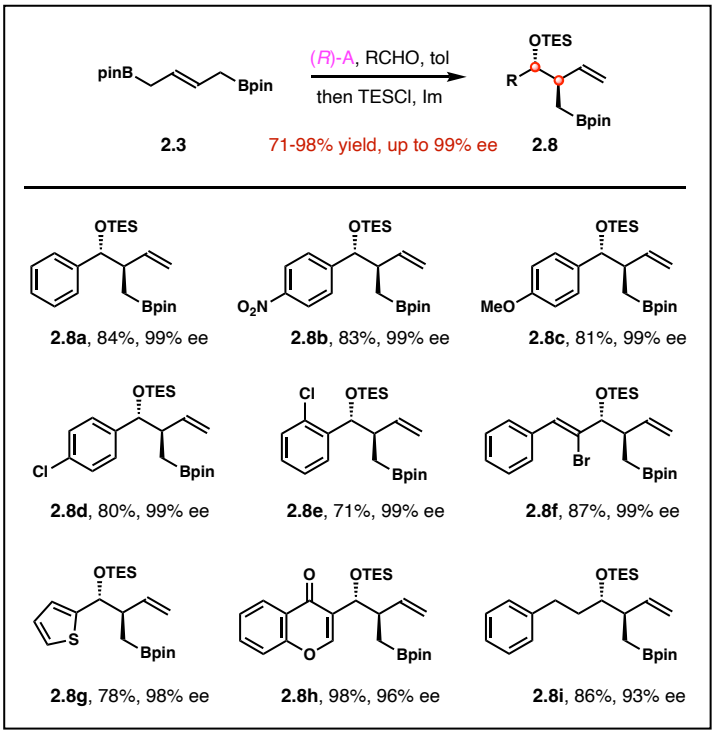
isomer **2.5** was synthesized with high *Z*-selectivity from 1,3-dienylboronate **2.7** simply by replacing Xantphos with a monodentate NHC ligand, IPr. And (*Z*)-γ-borylmethyl allylboronate **2.5** was obtained in 73% yield with >30:1 *Z*-selectivity. The rationale for *E*- or *Z*-selective protoboration is shown in **Scheme 2.3.** We propose that Xantphos-ligated Cu-Bpin complex coordinates to one alkene unit of diene **2.7** to form Cu-complex **I**, which undergoes 1,2-borocupration to give allylcopper intermediate **II**. Subsequent protonation of allylcopper **II**

proceeds via an S_E2' pathway to give (*E*)-γ-borylmethyl allylboronate **2.3** with high *E*-selectivity. On the other hand, IPr-ligated Cu-Bpin forms complex **III** with diene **2.7**. Then a 1,4-addition borocupration occurs to give allylcopper species **IV**. Direct S_E2 protonation of allylcopper **VI** produces (*Z*)-γ-borylmethyl allylboronate **2.5** selectively.

2.2 Enantioselective allylboration of aldehydes via Brønsted acid catalysis

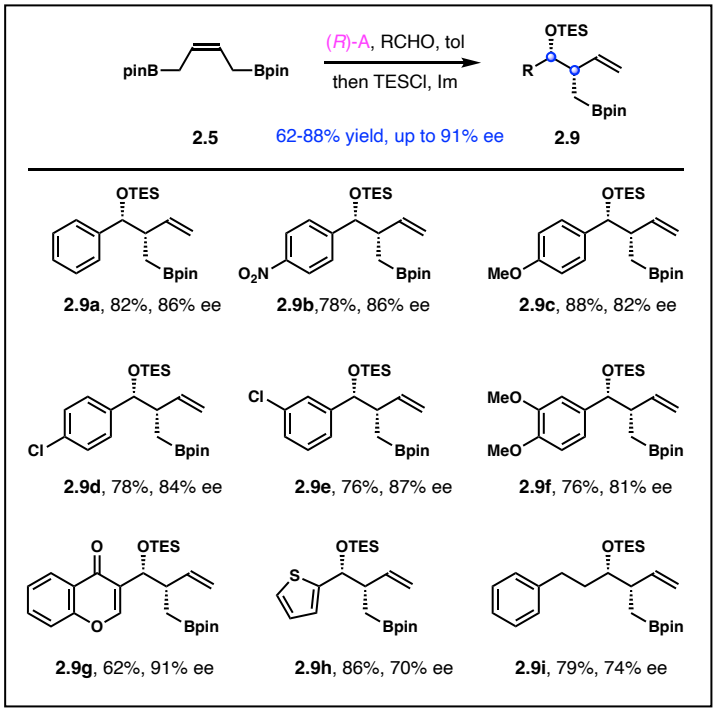
To access enantioenriched 1,2-*anti* and 1,2-*syn* products **2.8** or **2.9**, asymmetric allylations with boronate **2.3** or **2.5** were conducted in the presence of chiral phosphoric acid (R)-**A**. As shown in **Scheme 2.4**, the reaction between benzaldehyde and (*E*)-allylboronate **2.3** with 5 mol % of (R)-**A** as the catalyst occurred at −45 °C in toluene. After the *in situ* protection of the secondary alcohol group, *anti*-adduct **2.8a** was obtained in 85% yield with 99% ee. Using this protocol, a collection of aldehydes, ortho-substituted aromatic aldehydes and aliphatic aldehydes in particular, reacted with allylboronate **2.3** to give *anti*-products **2.8b-i** in 72-97% yields with 90-99% ee.[141-143]

Scheme 2.4. Enantioselective allylboration of aldehydes with (*E*)-allylboronate 2.3



Asymmetric aldehyde allylation with the *Z*-reagent **2.5** turned out to be more challenging. We noticed that (*Z*)-allylboronate **2.5** is less reactive than the (*E*)-isomer **2.3** toward aldehyde addition. And the enantioselectivities of *syn*-adducts **2.9** are generally lower than the optical purity of *anti*-adducts **2.5**, presumably owing to the uncatalyzed background reactions. Nevertheless, reactions of **2.5** with several representative aldehydes occurred to give *syn*-adducts **2.9a-g** in 62-88% yields with 81-91% ee as summarized in **Scheme 2.5**. Reactions with 2-thiophene carboxaldehyde and hydrocinnamaldehyde gave products in 79-86% yields with moderate enantioselectivities (70-74% ee). The *anti*- and *syn*-relative configuration of **2.8** and **2.9** are assigned by coupling constant analyses of the corresponding acetonides.

Scheme 2.5. Enantioselective allylboration of aldehydes with (*Z*)-allylboronate 2.5

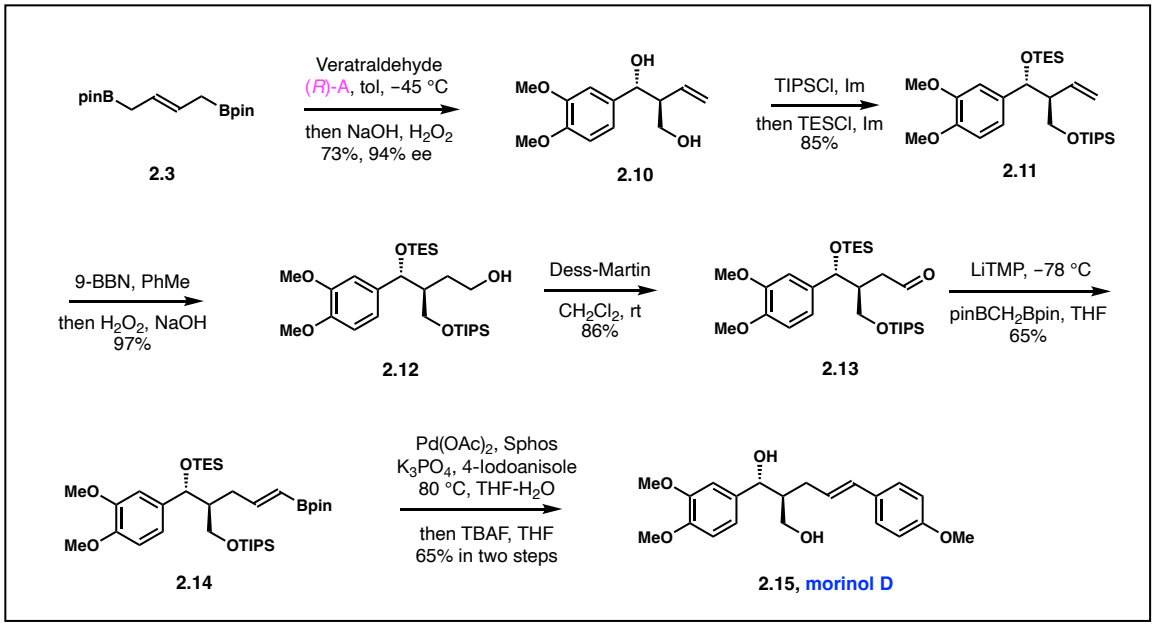


2.3 Application to the synthesis of morinol D

To demonstrate the synthetic utility of this method, total synthesis of natural product morinol D were conducted.[144,145] As shown in **Scheme 2.6**, asymmetric allylation of veratraldehyde with (*E*)-allylboronate **2.3** followed by oxidative workup gave *anti*-hydroxymethyl-1,3-diol **2.10** in 73% yield with 94% ee. Protection of the alcohol groups in **2.10** with excess TIPSCl only occurred at the primary alcohol group. Then the secondary OH group of **2.10** was converted to a TES ether by adding TESCl to the reaction mixture, affording product **2.11** in 85% yield. Hydroboration-oxidation of **2.11** with 9-BBN produced alcohol **2.12** in 97% yield, which underwent Dess-Marin oxidation to give **2.13** in 86% yield. Aldehyde **2.13** was transformed to vinyl boronate **2.14** in 65% yield and > 30:1 *E*-selectivity by using the olefination protocol developed by the Morken group.[146] Pd-catalyzed Suzuki coupling of **2.14** with 4-

iodoanisole followed by deprotection of the silyl ethers with TBAF gave morinol D (**2.15**) in 64% yield over two steps.

Scheme 2.6. Enantioselective Synthesis of Morinol D

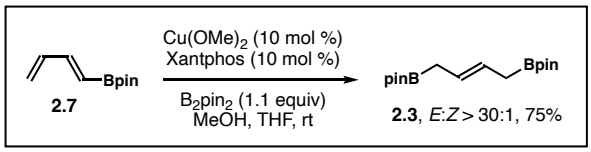


2.4 Conclusion

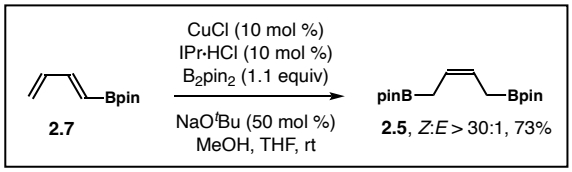
(*E*)- and (*Z*)-γ-borylmethyl allylboronate reagents were developed. A chiral phosphoric acid-catalyzed enantioselective *anti*- and *syn*-(borylmethyl)allylation of aldehydes was achieved. Reagents **1.22** and **1.24** were synthesized via a Cu-catalyzed stereoselective protoboration of 1,3-dienylboronate **1.26** with either a bidentate phosphine ligand or a monodentate NHC ligand. In the presence of a catalytic amount of chiral phosphoric acid (R)-**A**, asymmetric aldehyde allylation with (*E*)-reagent **1.22** gave *anti*-adducts **1.20** in good yields with excellent enantioselectivities. Allylation reactions with (*Z*)-reagent **1.24** also proceeded to deliver *syn*-adducts **1.21** in good yields and enantioselectivities. The synthetic utility of the method was demonstrated by the total synthesis of morinol D.

2.5 Experimental section

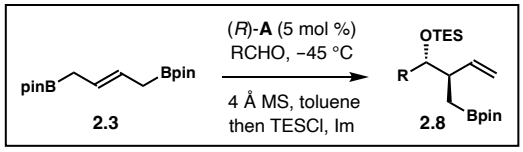
Enantioselective allyboration of aldehydes via Brønsted acid catalysis



(*E*)-1,4-bis(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)but-2-ene (2.3): In an Ar-filled glove box, $Cu(OMe)_2$ (10 mg, 0.08 mmol, 10 mol %), Xantphos (46 mg, 0.08 mmol, 10 mol %), a Teflon-coated magnetic stir bar, and THF (1.5 mL) were sequentially added into a 1-dram vial. The mixture was stirred for 15 min at ambient temperature in the glove box. B_2Pin_2 (211 mg, 0.83 mmol, 1.1 equiv) was added and the mixture was stirred for 5 min. Then dienylboronate **2.7** (135 mg, 0.75 mmol, 1.0 equiv) and MeOH (30 μL, 0.75 mmol, 1.0 equiv) were added to the mixture sequentially and the resulting mixture was kept stirring at ambient temperature. After complete consumption of diene **2.7**, Et_2O (2 mL) was added to the vial, and the reaction mixture was filtered through a pad of Celite. The solution was concentrated under reduced pressure. Purification of the crude product was performed by flash chromatography (gradient elution with hexane and ethyl acetate, 30:1 to 10:1) to give product **2.3** in 75% yield (173 mg, *E*:*Z* > 30:1) as a white solid. ^{1}H NMR (600 MHz, $CDCl_3$) δ 5.39 – 5.45 (m, 2H), 1.64 (*app.* s, 4H), 1.23 (s, 24H). ^{13}C NMR (151 MHz, $CDCl_3$) δ 125.6, 83.4, 25.1, 16.5. HRMS (ESI$^+$): *m*/*z* for $C_{16}H_{31}B_2O_4$ $[M+H]^+$ calcd. 309.2413, found 309.2408.

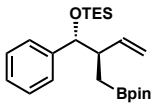


(*Z*)-1,4-bis(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)but-2-ene (2.5): In an Ar-filled glove box, CuCl (7 mg, 0.08 mmol, 10 mol %), IPr·HCl (32 mg, 0.08 mmol, 10 mol %), NaO^{t}Bu (37 mg, 0.38 mmol, 50 mol %), a Teflon-coated magnetic stir bar, and THF (1.5 mL) were sequentially added to a 1-dram vial. The mixture was stirred for 15 min at ambient temperature in the glove box. B_2Pin_2 (211 mg, 0.83 mmol, 1.1 equiv) was added and the mixture was stirred for 5 min. Then dienylboronate **2.7** (135 mg, 0.75 mmol, 1.0 equiv) and MeOH (60 μL, 1.5 mmol, 2.0 equiv) were added to the mixture sequentially and the resulting mixture was kept stirring at ambient temperature. After complete consumption of diene **2.7**, Et_2O (2 mL) was added to the vial, and the reaction mixture was filtered through a pad of Celite. The solution was concentrated under reduced pressure. Purification of the crude product was performed by flash chromatography (gradient elution with hexane and ethyl acetate, 30:1 to 10:1) to give the product **2.5** in 73% yield (169 mg, *Z*:*E* > 30:1) as a white solid. ^{1}H NMR (500 MHz, $CDCl_3$) δ 5.47 – 5.54 (m, 2H), 1.65 (d, *J* = 4.6 Hz, 4H), 1.23 (s, 24H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 124.5, 83.5, 25.1, 11.7. HRMS (ESI$^+$): *m*/*z* for $C_{16}H_{31}B_2O_4$ $[M+H]^+$ calcd. 309.2413, found 309.2408.

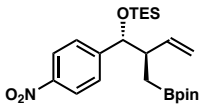


General procedure for synthesis of chiral TES-protected homoallylic alcohols 2.8: To a reaction flask containing a stir bar, freshly activated 4 Å MS (25 mg) and phosphoric acid (*R*)-**A** (3.8 mg, 0.005 mmol), allylboronate **2.3** (0.1 mmol) and toluene (0.3 mL) was added to the flask. The mixture was placed in a −45℃ cold bath and stirred for 5 min. Then freshly distilled aldehyde (0.2 mmol, if it is a liquid) was added slowly to the reaction mixture *via* a microliter syringe. The mixture was kept at −45℃ and stirred for 48 h. After complete consumption of the

allylboronate **2.3**, TESCl (23 mg, 0.15 mmol, 1.5 equiv), imidazole (14 mg, 0.2 mmol, 2.0 equiv) and DMF (0.2 ml) were added to the mixture. The reaction mixture was stirred at ambient temperature for additional 4 h. Then diethyl ether (1 mL) and brine (1 mL) was added. The organic layer was separated and the aqueous layer was extracted with Et_2O (2 mL x 3). The combined organic extracts were dried over anhydrous sodium sulfate, filtered, and concentrated under reduced pressure. Purification of the crude product was performed by flash chromatography (gradient elution with hexane and ethyl acetate) to give product **2.8**.

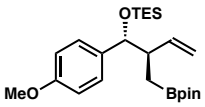


Triethyl(((1R,2R)-1-phenyl-2-((4,4,5,5-tetramethyl-1,3,2-dioxaborolan -2-yl) methyl) but-3-en-1-yl)oxy)silane (2.8a) Prepared according to the general procedure. The crude mixture was purified by column chromatography (hexane:ethyl acetate = 80:1 to 60:1) to give compound **2.8a** in 84% yield (34 mg) as colorless oil. The enantiomeric excess was determined by HPLC analysis to be 99% ee (254 nm, 25 °C); t_1 = 11.9 min, t_2 = 13.0 min [(Chiralpak IA) hexane/i-PrOH, 99.6:0.4, 1.0 mL/min]; $[\alpha]_D^{25}$ = 3.14 (c 0.42, $CHCl_3$). ^1H NMR (600 MHz, $CDCl_3$) δ 7.24 – 7.26 (m, 4H), 7.17 – 7.21 (m, 1H), 5.80 (ddd, *J* = 17.7, 10.3, 8.1 Hz, 1H), 4.93 (d, *J* = 10.3 Hz, 1H), 4.89 (d, *J* = 17.3 Hz, 1H), 4.58 (d, *J* = 5.3 Hz, 1H), 2.52 – 2.57 (m, 1H), 1.21 (s, 6H), 1.19 (s, 6H), 0.84 – 0.90 (m, 10H), 0.77 (dd, *J* = 15.3, 10.2 Hz, 1H), 0.44 – 0.53 (m, 6H). ^{13}C NMR (151 MHz, $CDCl_3$) δ 144.4, 140.6, 127.8, 127.3, 127.1, 115.3, 83.3, 79.4, 48.4, 25.3, 25.1, 13.8, 7.2, 5.2. HRMS (ESI^+): m/z for $C_{23}H_{40}BO_3Si$ $[M+H]^+$ calcd. 403.2840, found: 403.2825.



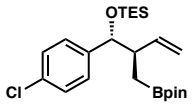
Triethyl(((1R,2R)-1-(4-nitrophenyl)-2-((4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)methyl)but-3-en-1-yl)oxy)silane (2.8b) Prepared

according to the general procedure. The crude mixture was purified by column chromatography (hexane:ethyl acetate = 80:1 to 60:1) to give compound **2.8b** in 83% yield (37 mg) as colorless oil. The enantiomeric excess of mono-TES protected diol (benzylic) was determined by HPLC analysis to be 99% ee (254 nm, 25 °C); t_1 = 9.05 min, t_2 = 9.47 min [(Chiralpak ID) hexane/i-PrOH, 98:2, 1.0 mL/min]; $[\alpha]_D^{25}$ = 0.06 (c 0.33, $CHCl_3$). ^{1}H NMR (600 MHz, $CDCl_3$) δ 8.13 (d, *J* = 8.5 Hz, 2H), 7.42 (d, *J* = 8.4 Hz, 2H), 5.67 – 5.74 (m, 1H), 4.93 (d, *J* = 10.2 Hz, 1H), 4.80 (d, *J* = 17.2 Hz, 1H), 4.74 (d, *J* = 4.2 Hz, 1H), 2.50 – 2.54 (m, 1H), 1.22 (s, 6H), 1.20 (s, 6H), 0.95 (dd, *J* = 15.4, 4.9 Hz, 1H), 0.87 (t, *J* = 7.9 Hz, 9H), 0.81 (dd, *J* = 15.4, 9.9 Hz, 1H), 0.38 – 0.55 (m, 6H). ^{13}C NMR (151 MHz, $CDCl_3$) δ 152.2, 147.3, 139.1, 127.8, 123.3, 116.3, 83.5, 78.4, 48.5, 25.3, 25.1, 13.8, 7.1, 5.2. HRMS (ESI^+): m/z for $C_{23}H_{39}BO_5NSi$ $[M+H]^+$ calcd. 448.2691, found: 448.2709.

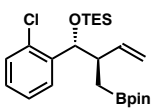


Triethyl(((1*R*,2*R*)-1-(4-methoxyphenyl)-2-((4,4,5,5-tetramethyl-1, 3, 2-dioxaborolan-2-yl)methyl)but-3-en-1-yl)oxy)silane (2.8c) Prepared according to the general procedure. The crude mixture was purified by column chromatography (hexane:ethyl acetate = 80:1 to 60:1) to give compound **2.8c** in 81% yield (35 mg) as colorless oil. The enantiomeric excess of mono-TES protected diol (benzylic) was determined by HPLC analysis to be 99% ee (254 nm, 25 °C); t_1 = 8.06 min, t_2 = 8.52 min [(Chiralpak IA) hexane/i-PrOH, 98:2, 1.0 mL/min]; $[\alpha]_D^{25}$ = 0.83 (c 0.80, $CHCl_3$). ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.17 (d, *J* = 8.5 Hz, 2H), 6.79 (d, *J* = 8.5 Hz, 2H), 5.79 (ddd, *J* = 17.7, 10.4, 8.1 Hz, 1H), 4.93 (d, *J* = 10.4 Hz, 1H), 4.90 (d, *J* = 18.0 Hz, 1H), 4.51 (d, *J* = 5.5 Hz, 1H), 3.79 (s, 3H), 2.49 – 2.53 (m, 1H), 1.20 (s, 6H), 1.19 (s, 6H), 0.78 – 0.87 (m, 10H), 0.73 (dd, *J* = 15.2, 10.3 Hz, 1H), 0.34 – 0.49 (m, 6H). ^{13}C NMR (151 MHz, $CDCl_3$) δ 158.8, 140.9, 136.7, 128.3, 115.2, 113.2, 83.2, 79.0, 55.5,

48.5, 25.3, 25.1, 13.7, 7.2, 5.2. HRMS (ESI$^+$): m/z for $C_{24}H_{41}BO_4NaSi$ $[M+Na]^+$ calcd. 455.2765, found: 455.2785.

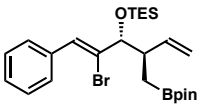


(((1R,2R)-1-(4-chlorophenyl)-2-((4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)methyl)but-3-en-1-yl)oxy)triethylsilane (2.8d) Prepared according to the general procedure. The crude mixture was purified by column chromatography (hexane:ethyl acetate = 80:1 to 60:1) to give compound **2.8d** in 80% yield (35 mg) as colorless oil. The enantiomeric excess was determined by HPLC analysis to be 99% ee (254 nm, 25 °C); t_1 = 15.1 min, t_2 = 16.2 min [(Chiralpak IA) hexane/i-PrOH, 99.6:0.4, 1.0 mL/min]; $[\alpha]_D^{25}$ = 2.69 (c 0.87, $CHCl_3$). . ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.23 (d, *J* = 8.5 Hz, 2H), 7.19 (d, *J* = 8.4 Hz, 2H), 5.74 (ddd, *J* = 17.1, 10.3, 8.2 Hz, 1H), 4.93 (d, *J* = 10.7 Hz, 1H), 4.86 (d, *J* = 17.3 Hz, 1H), 4.57 (d, *J* = 5.1 Hz, 1H), 2.47 – 2.51 (m, 1H), 1.21 (s, 6H), 1.19 (s, 6H), 0.84 – 0.90 (m, 10H), 0.76 (dd, *J* = 15.3, 10.0 Hz, 1H), 0.33 – 0.53 (m, 6H). ^{13}C NMR (151 MHz, $CDCl_3$) δ ^{13}C NMR (151 MHz, $CDCl_3$) δ 143.0, 140.1, 132.7, 128.5, 128.0, 115.7, 83.3, 78.7, 48.4, 25.3, 25.1, 13.7, 7.2, 5.2. HRMS (ESI$^+$): m/z for $C_{23}H_{38}BO_3NaSiCl$ $[M+Na]^+$ calcd. 459.2270, found: 459.2259.

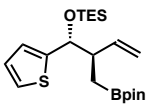


(((1*R*,2*R*)-1-(2-chlorophenyl)-2-((4,4,5,5-tetramethyl-1,3,2-dioxaborolan -2-yl)methyl)but-3-en-1-yl)oxy)triethylsilane (2.8e) Prepared according to the general procedure. The crude mixture was purified by column chromatography (hexane:ethyl acetate = 80:1 to 60:1) to give compound **2.8** in 71% yield (31 mg) as colorless oil. The enantiomeric excess of mono-TES protected diol (benzylic) was determined by HPLC analysis to be 90% ee (254 nm, 25 °C); t_1 = 11.9 min, t_2 = 13.0 min [(Chiralpak IA) hexane/i-PrOH, 99.6:0.4, 1.0 mL/min]; $[\alpha]_D^{25}$ = 1.98 (c 1.38, $CHCl_3$). ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.22 – 7.26 (m, 1H),

7.15 – 7.20 (m, 2H), 7.13 (d, *J* = 6.8 Hz, 1H), 5.74 (ddd, *J* = 17.5, 10.3, 8.2 Hz, 1H), 4.94 (d, *J* = 10.1 Hz, 1H), 4.87 (d, *J* = 17.3 Hz, 1H), 4.57 (d, *J* = 5.0 Hz, 1H), 2.48 – 2.53 (m, 1H), 1.21 (s, 6H), 1.20 (s, 6H), 0.90 (dd, *J* = 15.6, 4.8 Hz, 1H), 0.86 (t, *J* = 7.9 Hz, 9H), 0.77 (dd, *J* = 15.3, 10.1 Hz, 1H), 0.34 – 0.53 (m, 6H). ^{13}C NMR (151 MHz, $CDCl_3$) δ 146.6, 140.0, 133.8, 129.1, 127.30, 127.26, 125.4, 115.7, 83.4, 78.7, 48.4, 25.3, 25.1, 13.7, 7.1, 5.2. HRMS (ESI$^+$): m/z for $C_{23}H_{39}BClO_3Si$ $[M+H]^+$ calcd. 437.2450, found: 437.2383.

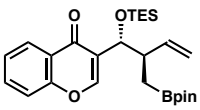


(((3*R*,4*R*,*Z*)-2-bromo-1-phenyl-4-((4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)methyl)hexa-1,5-dien-3-yl)oxy)triethylsilane (2.8f) Prepared according to the general procedure. The crude mixture was purified by column chromatography (hexane:ethyl acetate = 80:1 to 60:1) to give compound **2.8f** in 87% yield (44 mg) as colorless oil. The enantiomeric excess of mono-TES protected diol (benzylic) was determined by HPLC analysis to be 99% ee (254 nm, 25 °C); t_1 = 13.8 min, t_2 = 15.1 min [(Chiralpak IA) hexane/i-PrOH, 99.6:0.4, 1.0 mL/min]; $[\alpha]_D^{25}$ = 2.16 (c 1.23, $CHCl_3$). ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.56 (d, *J* = 7.5 Hz, 2H), 7.35 (dd, *J* = 7.5, 7.5 Hz, 2H), 7.28 (dd, *J* = 7.4, 7.4 Hz, 1H), 7.00 (s, 1H), 5.84 (ddd, *J* = 17.4, 10.3, 8.1 Hz, 1H), 5.04 (d, *J* = 17.3 Hz, 1H), 5.01 (d, *J* = 10.3 Hz, 1H), 4.25 (d, *J* = 5.3 Hz, 1H), 2.78 – 2.83 (m, 1H), 1.234 (s, 6H), 1.228 (s, 6H), 0.87 – 0.99 (m, 11H), 0.51 – 0.68 (m, 6H). ^{13}C NMR (151 MHz, $CDCl_3$) δ 139.4, 136.1, 129.9, 129.4, 128.43, 128.41, 128.1, 116.0, 83.4, 82.2, 44.1, 25.3, 25.2, 14.4, 7.3, 5.3. HRMS (ESI$^+$): m/z for $C_{25}H_{40}BO_3NaSiBr$ $[M+Na]^+$ calcd. 529.1921, found: 529.1932.



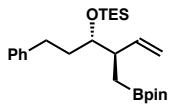
Triethyl(((1*R*,2*R*)-2-((4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)methyl)-1-(thiophen-2-yl)but-3-en-1-yl)oxy)silane (2.8g) Prepared according to the general

procedure. The crude mixture was purified by column chromatography (hexane:ethyl acetate = 80:1 to 60:1) to give compound **2.8g** in 78% yield (32 mg) as colorless oil. The enantiomeric excess of mono-TES protected diol (benzylic) was determined by HPLC analysis to be 98% ee (254 nm, 25 °C); t_1 = 15.9 min, t_2 = 17.6 min [(Chiralpak IA) hexane/i-PrOH, 99.6:0.4, 1.0 mL/min]; $[\alpha]_D^{25}$ = 2.80 (c 1.40, $CHCl_3$). ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.16 (d, *J* = 4.9 Hz, 1H), 6.89 – 6.90 (m, 1H), 6.85 (d, *J* = 3.3 Hz, 1H), 5.81 – 5.87 (m, 1H), 4.98 – 5.01 (m, 2H), 4.85 (d, *J* = 5.8 Hz, 1H), 2.57 – 2.62 (m, 1H), 1.21 (s, 6H), 1.20 (s, 6H), 0.93 (dd, *J* = 15.5, 4.3 Hz, 1H), 0.88 (t, *J* = 7.9 Hz, 9H), 0.78 (dd, *J* = 15.4, 10.2 Hz, 1H), 0.53 (q, *J* = 7.7 Hz, 6H). ^{13}C NMR (151 MHz, $CDCl_3$) δ 148.8, 140.5, 126.2, 124.04, 123.99, 115.7, 83.3, 75.6, 48.9, 25.3, 25.1, 13.5, 7.2, 5.2. HRMS (ESI^+): m/z for $C_{21}H_{37}BO_3NaSiS$ $[M+Na]^+$ calcd. 431.2223, found: 431.2234.

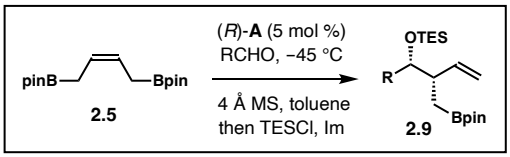


3-((1R,2R)-2-((4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)methyl)-1-((triethylsilyl)oxy)but-3-en-1-yl)-4H-chromen-4-one (2.8h) Prepared according to the general procedure. The crude mixture was purified by column chromatography (hexane:ethyl acetate = 80:1 to 60:1) to give compound **2.8h** in 98% yield (46 mg) as colorless oil. The enantiomeric excess of mono-TES protected diol (benzylic) was determined by HPLC analysis to be 96% ee (254 nm, 25 °C); t_1 = 6.29 min, t_2 = 7.11 min [(Chiralpak IC) hexane/i-PrOH, 98:2, 1.0 mL/min]; $[\alpha]_D^{25}$ = 5.63 (c 1.62, $CHCl_3$). ^{1}H NMR (600 MHz, $CDCl_3$) δ 8.21 (d, *J* = 7.9 Hz, 1H), 7.85 (s, 1H), 7.63 (dd, *J* = 8.4, 8.4 Hz, 1H), 7.43 (d, *J* = 8.4 Hz, 1H), 7.38 (dd, *J* = 7.5, 7.5 Hz, 1H), 5.73 (ddd, *J* = 17.5, 9.7, 9.7 Hz, 1H), 5.06 (d, *J* = 3.1 Hz, 1H), 4.93 (dd, *J* = 10.3, 1.7 Hz, 1H), 4.81 (d, *J* = 17.3 Hz, 1H), 2.61 – 2.66 (m, 1H), 1.20 (s, 6H), 1.18 (s, 6H), 1.09 (dd, *J* = 15.1, 10.8 Hz, 1H), 1.01 (dd, *J* = 15.1, 4.2 Hz, 1H), 0.91 (t, *J* = 8.0 Hz, 9H), 0.59 (q, *J* =

7.9 Hz, 6H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 176.5, 156.6, 154.9, 139.2, 133.6, 127.0, 126.3, 125.2, 124.2, 118.4, 116.5, 83.3, 71.0, 45.7, 25.3, 25.1, 7.3, 5.2. HRMS (ESI^+): m/z for $C_{26}H_{39}BO_5NaSi$ $[M+Na]^+$ calcd. 493.2558, found: 493.2552.

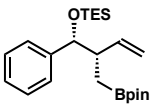


Triethyl(((3*S*,4*R*)-1-phenyl-4-((4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)methyl)hex-5-en-3-yl)oxy)silane (2.8i) Prepared according to the general procedure. The crude mixture was purified by column chromatography (hexane:ethyl acetate = 80:1 to 60:1) to give compound **2.8i** in 86% yield (37 mg) as colorless oil. The enantiomeric excess of the corresponding diol was determined by HPLC analysis to be 93% ee (254 nm, 25 °C); t_1 = 7.01 min, t_2 = 7.62 min [(Chiralpak ID) hexane/i-PrOH, 90:10, 1.0 mL/min]; $[\alpha]_D^{25}$ = − 0.92 (c 0.87, $CHCl_3$). ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.27 (dd, *J* = 8.0, 7.1 Hz, 2H), 7.15 – 7.18 (m, 3H), 5.77 – 5.83 (m, 1H), 5.04 (d, *J* = 17.3 Hz, 1H), 5.01 (d, *J* = 10.2 Hz, 1H), 3.67 – 3.69 (m, 1H), 2.64 – 2.67 (m, 1H), 2.57 – 2.60 (m, 1H), 2.48 – 2.51 (m, 1H), 1.69 – 1.74 (m, 2H), 1.223 (s, 6H), 1.218 (s, 6H), 0.98 – 1.02 (m, 10H), 0.91 (dd, *J* = 15.5, 10.2 Hz, 1H), 0.61 (q, *J* = 7.9 Hz, 6H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 143.1, 140.6, 128.7, 128.6, 125.9, 115.3, 83.3, 76.3, 45.2, 36.8, 32.6, 25.3, 25.1, 7.4, 5.7. HRMS (ESI^+): m/z for $C_{25}H_{44}BO_3Si$ $[M+H]^+$ calcd. 431.3153, found: 431.3172.

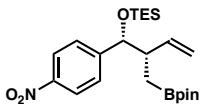


General procedure for synthesis of chiral TES-protected homoallylic alcohols 2.9: To a reaction flask containing a stir bar, freshly activated 4 Å MS (25 mg) and phosphoric acid (*R*)-**A** (3.8 mg, 0.005 mmol), allylboronate **2.5** (0.1 mmol) and toluene (0.3 mL) was added to the flask.

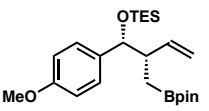
The mixture was placed in a −45 °C cold bath and stirred for 5 min. Then freshly distilled aldehyde (0.2 mmol, if it is a liquid) was added slowly to the reaction mixture *via* a microliter syringe. The mixture was kept at −45 °C and stirred for 48 h. After complete consumption of the allylboronate **2.5**, TESCl (23 mg, 0.15 mmol, 1.5 equiv), imidazole (14 mg, 0.2 mmol, 2.0 equiv) and DMF (0.2 ml) were added to the mixture. The reaction mixture was stirred at ambient temperature for additional 4 h. Then diethyl ether (1 mL) and brine (1 mL) was added. The organic layer was separated and the aqueous layer was extracted with Et_2O (2 mL x 3). The combined organic extracts were dried over anhydrous sodium sulfate, filtered, and concentrated under reduced pressure. Purification of the crude product was performed by flash chromatography (gradient elution with hexane and ethyl acetate) to give product **2.9**.



Triethyl(((1*R*,2*S*)-1-phenyl-2-((4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)methyl)but-3-en-1-yl)oxy)silane (2.9a) Prepared according to the general procedure. The crude mixture was purified by column chromatography (hexane:ethyl acetate = 80:1 to 60:1) to give compound **2.9a** in 82% yield (33 mg) as colorless oil. The enantiomeric excess of the corresponding diol was determined by HPLC analysis to be 86% ee (254 nm, 25 °C); t_1 = 17.6 min, t_2 = 18.7 min [(Chiralpak IE) hexane/i-PrOH, 95:5, 1.0 mL/min]. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.26 – 7.28 (m, 4H), 7.18 – 7.23 (m, 1H), 5.69 (ddd, *J* = 17.7, 10.9, 8.2 Hz, 1H), 4.89 – 4.93 (m, 2H), 4.52 (d, *J* = 6.0 Hz, 1H), 2.56 – 2.64 (m, 1H), 1.23 (s, 6H), 1.21 (s, 6H), 1.07 (dd, *J* = 15.2, 4.4 Hz, 1H), 0.84 – 0.90 (m, 10H), 0.44 – 0.55 (m, 6H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 144.1, 140.9, 127.8, 127.4, 127.1, 115.1, 83.2, 79.2, 48.3, 25.3, 25.1, 7.2, 5.2. HRMS (ESI^+): m/z for $C_{23}H_{40}BO_3Si$ $[M+H]^+$ calcd. 403.2840, found: 403.2837.

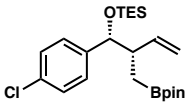


Triethyl(((1*R*,2*S*)-1-(4-nitrophenyl)-2-((4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)methyl)but-3-en-1-yl)oxy)silane (2.9b) Prepared according to the general procedure. The crude mixture was purified by column chromatography (hexane:ethyl acetate = 80:1 to 60:1) to give compound **2.9b** in 78% yield (35 mg) as colorless oil. The enantiomeric excess of the corresponding alcohol after oxidation was determined by HPLC analysis to be 86% ee (254 nm, 25 °C); t_1 = 13.4 min, t_2 = 14.2 min [(Chiralpak IA) hexane/i-PrOH, 98:2, 1.0 mL/min]; $[\alpha]_D^{25} = -0.10$ (c 0.80, $CHCl_3$). ^{1}H NMR (600 MHz, $CDCl_3$) δ 8.13 (d, *J* = 8.6 Hz, 2H), 7.42 (d, *J* = 8.5 Hz, 2H), 5.64 (ddd, *J* = 17.8, 10.4, 7.9 Hz, 1H), 4.92 (d, *J* = 10.3 Hz, 1H), 4.87 (d, *J* = 17.2 Hz, 1H), 4.63 (d, *J* = 5.9 Hz, 1H), 2.55 – 2.60 (m, 1H), 1.21 (s, 6H), 1.20 (s, 6H), 0.96 (dd, *J* = 15.3, 5.1 Hz, 1H), 0.83 – 0.87 (m, 10H), 0.44 – 0.55 (m, *J* = 7.5 Hz, 6H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 151.7, 147.4, 139.7, 128.1, 123.2, 116.2, 83.5, 78.3, 48.3, 25.3, 25.1, 7.1, 5.1. HRMS (ESI^+): m/z for $C_{23}H_{39}BNO_5Si$ $[M+H]^+$ calcd. 448.2691, found: 448.2694.

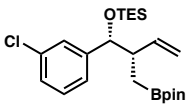


Triethyl(((1*R*,2*S*)-1-(4-methoxyphenyl)-2-((4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)methyl)but-3-en-1-yl)oxy)silane (2.9c) Prepared according to the general procedure. The crude mixture was purified by column chromatography (hexane:ethyl acetate = 80:1 to 60:1) to give compound **2.9c** in 88% yield (38 mg) as colorless oil. The enantiomeric excess of the corresponding diol was determined by HPLC analysis to be 82% ee (254 nm, 25 °C); t_1 = 15.9 min, t_2 = 16.9 min [(Chiralpak IG) hexane/i-PrOH, 90:10, 1.0 mL/min]. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.16 (d, *J* = 8.4 Hz, 2H), 6.79 (d, *J* = 8.4 Hz, 2H), 5.66 (ddd, *J* = 17.7, 10.4, 8.4 Hz, 1H), 4.86 – 4.90 (m, 2H), 4.45 (d, *J* = 6.1 Hz, 1H), 3.78 (s, 3H), 2.52 – 2.59 (m, 1H), 1.21 (s, 6H), 1.20 (s, 6H), 1.06 (dd, *J* = 15.3, 4.7 Hz, 1H), 0.79 – 0.87 (m,

10H), 0.42 – 0.52 (m, 6H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 158.8, 141.0, 136.3, 128.5, 115.0, 113.2, 83.2, 78.8, 55.5, 48.4, 25.3, 25.1, 7.2, 5.2. HRMS (ESI^+): m/z for $C_{24}H_{41}BO_4NaSi$ $[M+Na]^+$ calcd. 455.2765, found: 455.2766.

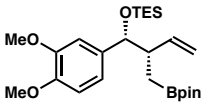


(((1*R*,2*S*)-1-(4-chlorophenyl)-2-((4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)methyl)but-3-en-1-yl)oxy)triethylsilane (2.9d) Prepared according to the general procedure. The crude mixture was purified (hexane:ethyl acetate = 80:1 to 60:1) to give compound **2.9d** in 78% yield (34 mg) as colorless oil. The enantiomeric excess of mono-TES protected diol (benzylic) was determined by HPLC analysis to be 84% ee (254 nm, 25 °C); t_1 = 12.0 min, t_2 = 13.2 min [(Chiralpak IA) hexane/i-PrOH, 99.6:0.4, 1.0 mL/min]; $[\alpha]_D^{25}$ = 0.72 (c 0.74, $CHCl_3$). ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.23 (d, *J* = 8.4 Hz, 2H), 7.18 (d, *J* = 8.3 Hz, 2H), 5.64 (ddd, *J* = 18.2, 10.4, 7.9 Hz, 1H), 4.87 – 4.90 (m, 2H), 4.49 (d, *J* = 5.9 Hz, 1H), 2.51 – 2.56 (m, 1H), 1.21 (s, 6H), 1.19 (s, 6H), 1.00 (dd, *J* = 15.4, 4.8 Hz, 1H), 0.80 – 0.84 (m, 10H), 0.43 – 0.53 (m, 6H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 142.6, 140.5, 132.7, 128.7, 128.0, 115.5, 83.3, 78.5, 48.3, 25.3, 25.1, 7.2, 5.2. HRMS (ESI^+): m/z for $C_{23}H_{38}BO_3NaSiCl$ $[M+Na]^+$ calcd. 459.2270, found: 459.2292.

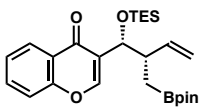


(((1R,2S)-1-(3-chlorophenyl)-2-((4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)methyl)but-3-en-1-yl)oxy)triethylsilane (2.9e) Prepared according to the general procedure. The crude mixture was purified by column chromatography (hexane:ethyl acetate = 80:1 to 60:1) to give compound **2.9e** in 76% yield (33 mg) as colorless oil. The enantiomeric excess of the corresponding diol was determined by HPLC analysis to be 87% ee (254 nm, 25 °C); t_1 = 17.3 min, t_2 = 22.6 min [(Chiralpak IA) hexane/i-PrOH, 98:2, 1.0 mL/min].

^{1}H NMR (600 MHz, $CDCl_3$) δ 7.25 (d, *J* = 1.8 Hz, 1H), 7.14 – 7.17 (m, 2H), 7.10 – 7.13 (m, 1H), 5.65 (ddd, *J* = 16.8, 10.6, 7.8 Hz, 1H), 4.88 – 4.91 (m, 2H), 4.48 (d, *J* = 5.9 Hz, 1H), 2.51 – 2.56 (m, 1H), 1.20 (s, 6H), 1.18 (s, 6H), 1.00 (dd, *J* = 15.4, 4.7 Hz, 1H), 0.81 – 0.86 (m, 10H), 0.42 – 0.52 (m, 6H). ^{13}C NMR (151 MHz, $CDCl_3$) δ 146.3, 140.4, 133.8, 129.1, 127.5, 127.3, 125.6, 115.6, 83.3, 78.5, 48.3, 25.3, 25.0, 11.8, 7.1, 5.2. HRMS (ESI^+): m/z for $C_{23}H_{38}BO_3NaSiCl$ $[M+Na]^+$ calcd. 459.2270, found: 459.2291.

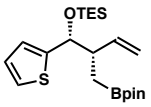


(((1R,2S)-1-(3,4-dimethoxyphenyl)-2-((4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)methyl)but-3-en-1-yl)oxy)triethylsilane (2.9f) Prepared according to the general procedure. The crude mixture was purified by column chromatography (hexane:ethyl acetate = 80:1 to 60:1) to give compound **2.9f** in 76% yield (35 mg). The enantiomeric excess of the corresponding diol was determined by HPLC analysis to be 81% ee (254 nm, 25 °C); t_1 = 25.4 min, t_2 = 28.2 min [(Chiralpak IG) hexane/i-PrOH, 90:10, 1.0 mL/min]; ^{1}H NMR (500 MHz, $CDCl_3$) δ 6.87 (s, 1H), 6.74 (d, *J* = 8.4 Hz, 1H), 6.72 (d, *J* = 8.3 Hz, 1H), 5.63 – 5.70 (m, 1H), 4.88 – 4.91 (m, 2H), 4.44 (d, *J* = 6.0 Hz, 1H), 3.87 (s, 3H), 3.86 (s, 3H), 2.53 – 2.58 (m, 1H), 1.21 (s, 6H), 1.20 (s, 6H), 1.08 (dd, *J* = 15.3, 4.6 Hz, 1H), 0.81 – 0.87 (m, 10H), 0.42 – 0.54 (m, 6H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 148.6, 148.1, 141.0, 136.9, 119.6, 115.0, 110.4, 110.3, 83.3, 79.0, 56.1(two overlapping carbon signals), 48.4, 25.3, 25.1, 7.2, 5.2. HRMS (ESI^+): m/z for $C_{25}H_{43}BO_5NaSi$ $[M+Na]^+$ calcd. 485.2871, found: 485.2868.

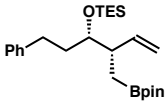


3-((1*R*,2*S*)-2-((4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)methyl)-1-((triethylsilyl)oxy)but-3-en-1-yl)-4*H*-chromen-4-one (2.9g) Prepared according to the general procedure. The crude mixture was purified by column chromatography

(hexane:ethyl acetate = 80:1 to 60:1) to give compound **2.9g** in 62% yield (29 mg) as colorless oil. The enantiomeric excess of the corresponding alcohol after oxidation was determined by HPLC analysis to be 91% ee (254 nm, 25 °C); t_1 = 17.9 min, t_2 = 19.9 min [(Chiralpak IA) hexane/i-PrOH, 98:2, 1.0 mL/min]; $[\alpha]_D^{25} = -2.95$ (c 0.86, $CHCl_3$). ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.21 (d, *J* = 8.1 Hz, 1H), 7.91 (s, 1H), 7.64 (dd, *J* = 7.8, 7.8 Hz, 1H), 7.44 (d, *J* = 8.4 Hz, 1H), 7.38 (dd, *J* = 7.5, 7.5 Hz, 1H), 5.84 – 5.93 (m, 1H), 5.05 – 5.11 (m, 2H), 5.00 (d, *J* = 10.4 Hz, 1H), 2.65 – 2.71 (m, 1H), 1.15 (s, 12H), 0.89 – 0.99 (m, 10H), 0.83 (dd, *J* = 15.4, 10.4 Hz, 1H), 0.57 (q, *J* = 7.8 Hz, 6H).^{13}C NMR (101 MHz, $CDCl_3$) δ 176.6, 156.6, 154.7, 141.0, 133.6, 126.8, 126.4, 125.2, 124.3, 118.4, 115.6, 83.2, 70.1, 45.8, 25.3, 24.9, 7.2, 5.1. HRMS (ESI^+): m/z for $C_{26}H_{40}BO_5Si$ $[M+H]^+$ calcd. 471.2738, found: 471.2727.

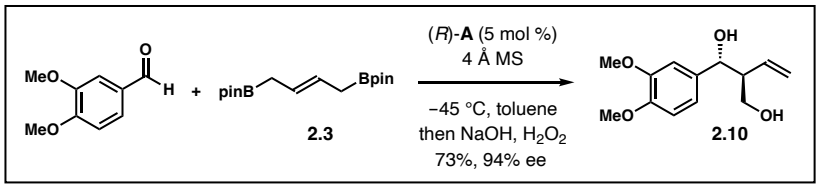


Triethyl(((1*R*,2*S*)-2-((4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)methyl)-1-(thiophen-2-yl)but-3-en-1-yl)oxy)silane (2.9h) Prepared according to the general procedure. The crude mixture was purified by column chromatography (hexane:ethyl acetate = 80:1 to 60:1) to give compound **2.9h** in 86% yield (35 mg) as colorless oil. The enantiomeric excess of the corresponding diol was determined by HPLC analysis to be 70% ee (254 nm, 25 °C); t_1 = 10.5 min, t_2 = 11.2 min [(Chiralpak IG) hexane/i-PrOH, 90:10, 1.0 mL/min]. ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.16 (d, *J* = 4.9 Hz, 1H), 6.88 (dd, *J* = 3.8, 4.5 Hz 1H), 6.83 (d, *J* = 2.9 Hz, 1H), 5.72 (ddd, *J* = 17.6, 10.2, 7.9 Hz, 1H), 4.93 – 4.97 (m, 2H), 4.81 (d, *J* = 6.3 Hz, 1H), 2.61 – 2.67 (m, 1H), 1.23 (s, 6H), 1.21 (s, 6H), 1.11 (dd, *J* = 15.5, 5.0 Hz, 1H), 0.86 – 0.91 (m, 10H), 0.47 – 0.58 (m, 6H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 148.3, 140.2, 126.1, 124.19, 124.15, 115.6, 83.3, 75.3, 48.6, 25.3, 25.1, 12.5, 7.2, 5.2. HRMS (ESI^+): m/z, $C_{21}H_{37}BO_3NaSiS$ $[M+Na]^+$ calcd. 431.2223, found: 431.2208.



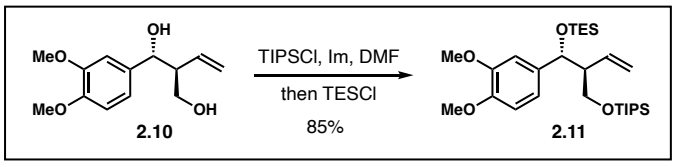
Triethyl(((3*S*,4*S*)-1-phenyl-4-((4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)methyl)hex-5-en-3-yl)oxy)silane (2.9i) Prepared according to the general procedure. The crude mixture was purified by column chromatography (hexane:ethyl acetate = 80:1 to 60:1) to give compound **2.9i** in 79% yield (34 mg) as colorless oil. The enantiomeric excess of the corresponding diol was determined by HPLC analysis to be 74% ee (254 nm, 25 °C); t_1 = 7.00 min, t_2 = 7.60 min [(Chiralpak IC) hexane/i-PrOH, 90:10, 1.0 mL/min]. ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.21 – 7.41 (dd, *J* = 7.5, 7.5 Hz, 2H), 7.16 – 7.17 (m, 3H), 5.84 (ddd, *J* = 17.8, 10.3, 7.8 Hz, 1H), 5.06 (d, *J* = 17.3 Hz, 1H), 5.01 (d, *J* = 10.3 Hz, 1H), 3.65 – 3.68 (m, 1H), 2.73 – 2.78 (m, 1H), 2.50 – 2.59 (m, 2H), 1.65 – 1.77 (m, 2H), 1.23 (s, 6H), 1.22 (s, 6H), 0.95 – 1.01 (m, 10H), 0.83 (dd, *J* = 15.3, 9.5 Hz, 1H), 0.65 (q, *J* = 7.9 Hz, 6H). ^{13}C NMR (151 MHz, $CDCl_3$) δ 143.3, 141.1, 128.7, 128.6, 125.9, 114.9, 83.3, 76.1, 45.3, 36.0, 32.1, 25.3, 25.1, 7.4, 5.7. HRMS (ESI$^+$): m/z for $C_{25}H_{44}BO_3Si$ $[M+Na]^+$ calcd. 431.3153, found: 431.3165.

Synthesis of morinol D



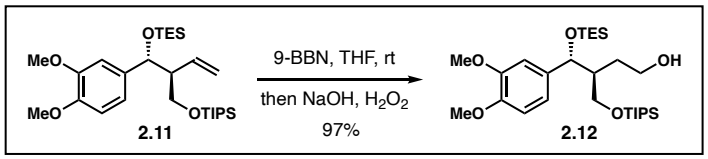
(1*R*,2*S*)-1-(3,4-dimethoxyphenyl)-2-vinylpropane-1,3-diol (2.10) To a reaction flask containing a stir bar, freshly activated 4 Å MS (25 mg) and phosphoric acid (*R*)-**A** (3.8 mg, 0.005 mmol), allylboronate **2.3** (246 mg, 0.80 mmol) and toluene (2 mL) was added to the flask. The mixture was placed in a −45 °C cold bath and stirred for 5 min. Then veratraldehyde (1.6 mmol,

264 mg) was added slowly to the reaction mixture *via* a microliter syringe. The mixture was kept at −45 °C and stirred for 48 h. After complete consumption of the allylboronate **2.3**, NaOH (3N aqueous, 3 mL) was added to the reaction mixture followed by slow addition of 30% H_2O_2 (3 mL) at 0 °C. The reaction was stirred vigorously for 6 h; then EtOAc (5 mL) and brine (5 mL) was added. The organic layer was separated and the aqueous layer was extracted with EtOAc (5 mL x 3). The combined organic extracts were dried over anhydrous sodium sulfate, filtered, and concentrated under reduced pressure. Purification of the crude product was performed by flash chromatography (gradient elution with hexane and ethyl acetate 2:1 to 1:1) to give product diol **2.10** in 73% yield (139 mg). The enantiomeric excess of the corresponding mono-TES protected diol (benzylic) was determined by HPLC analysis to be 94% ee (254 nm, 25 °C); t_1 = 16.6 min, t_2 = 17.7 min [(Chiralpak IA) hexane/i-PrOH, 98:2, 1.0 mL/min]; ^{1}H NMR (600 MHz, $CDCl_3$) δ 6.91 (d, *J* = 1.7 Hz, 1H), 6.87 (dd, *J* = 8.2, 1.8 Hz, 1H), 6.84 (d, *J* = 8.2 Hz, 1H), 5.84 (ddd, *J* = 17.4, 10.3, 8.8 Hz, 1H), 5.30 (dd, *J* = 10.4, 1.5 Hz, 1H), 5.22 (d, *J* = 17.3 Hz, 1H), 4.75 (d, *J* = 6.3 Hz, 1H), 3.89 (s, 3H), 3.88 (s, 3H), 3.63 (dd, *J* = 10.7, 5.5 Hz, 1H), 3.58 (dd, *J* = 10.7, 6.2 Hz, 1H), 2.57 – 2.61 (m, 1H), 2.37 (bs, 1H), 1.58 (bs, 1H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 149.4, 148.9, 136.0, 135.0, 120.1, 119.1, 111.2, 109.8, 75.2, 64.1, 56.3, 56.2, 54.1. HRMS (ESI^+): m/z for $C_{13}H_{18}O_4Na$ $[M+Na]^+$ calcd. 261.1103, found: 261.1104.



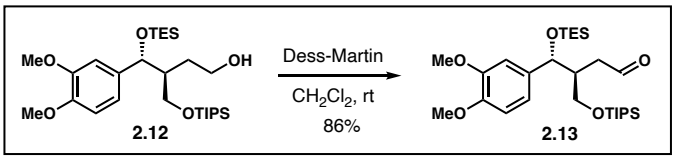
(6*S*,7*R*)-7-(3,4-dimethoxyphenyl)-9,9-diethyl-3,3-diisopropyl-2-methyl-6-vinyl-4,8-dioxa-3,9-disilaundecane 2.11: To a reaction vial containing a Teflon-coated magnetic stirring bar were added diol **2.10** (119 mg, 0.50 mmol, 1.0 equiv) and DMF (0.7 mL) followed by addition of

TIPSCl (192 mg, 1.0 mmol, 2.0 equiv) and imidazole (88 mg, 1.25 mmol, 2.5 equiv). The reaction mixture was then allowed to stir at ambient temperature for 2 h. Then TESCl (151 mg, 1.0 mmol, 2.0 equiv) and imidazole (88 mg, 1.25 mmol, 2.5 equiv) were added to the reaction mixture. The reaction was stirred for 1 h. Then diethyl ether (1 mL) and brine (1 mL) was added. The organic layer was separated and the aqueous layer was extracted with ethyl ether (2 mL x 3). The combined organic extracts were dried over anhydrous sodium sulfate, filtered, and concentrated under reduced pressure. Purification of the crude product was performed by flash chromatography (gradient elution with hexane and ethyl acetate 50:1 to 30:1) to give product TES-protected homoallylic alcohol **2.11** in 85% yield (216 mg). ^{1}H NMR (500 MHz, $CDCl_3$) δ 6.86 (s, 1H), 6.77 (app.s, 2H), 5.87 (ddd, *J* = 17.9, 9.6, 9.6 Hz,1H), 5.03 (d, *J* = 10.4 Hz, 1H), 4.98 – 4.99 (m, 1H), 4.90 (d, *J* = 17.4 Hz, 1H), 3.863 (s, 3H), 3.859 (s, 3H), 3.77 (dd, *J* = 8.4, 8.4 Hz, 1H), 3.51 (dd, *J* = 9.3, 5.2 Hz, 1H), 2.29 – 2.34 (m, 1H), 1.07 – 1.13 (m, 21H), 0.87 (t, *J* = 7.9 Hz, 9H), 0.51 (q, *J* = 8.0 Hz, 6H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 148.6, 148.0, 137.6, 136.4, 118.9, 117.7, 110.6, 110.1, 73.4, 64.6, 56.5, 56.13, 56.05, 18.4, 12.4, 7.2, 5.2. HRMS (ESI^+): m/z for $C_{28}H_{52}O_4NaSi_2$ $[M+Na]^+$ calcd. 531.3302, found: 531.3279.



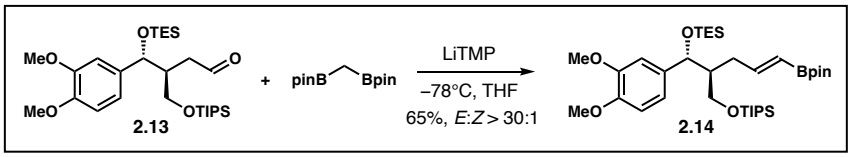
(3*S*,4*R*)-4-(3,4-dimethoxyphenyl)-4-((triethylsilyl)oxy)-3-(((triisopropylsilyl)oxy) methyl)butan-1-ol 2.12: In an Ar-filled glove box, **2.11** (203 mg, 0.40 mmol, 1.0 equiv), THF (0.7 mL), 9-BBN (73 mg, 0.60 mmol, 1.5 equiv) and a Teflon-coated magnetic stir bar were sequentially added to a 1-dram vial. And the mixture was stirred for 2 h at ambient temperature in the glove box. After complete consumption of **2.11**, the vial was removed from glove box.

Then NaOH (3N aqueous, 0.5 mL) was added to the reaction mixture followed by slow addition of 30% H_2O_2 (0.5 mL) at ambient temperature for 1 h. Then diethyl ether (1 mL) and brine (1 mL) was added. The organic layer was separated and the aqueous layer was extracted with Et_2O (2 mL x 3). The combined organic extracts were dried over anhydrous sodium sulfate, filtered, and concentrated under reduced pressure. Purification of the crude product was performed by flash chromatography (gradient elution with hexane and ethyl acetate 20:1 to 10:1) to give product TES-protected homoallylic alcohol **2.12** in 97% yield (204 mg). ^{1}H NMR (500 MHz, $CDCl_3$) δ 6.87 (d, *J* = 1.4 Hz, 1H), 6.77 – 6.78 (m, 2H), 4.70 (d, *J* = 5.5 Hz, 1H), 3.873 (s, 3H), 3.868 (s, 3H), 3.74 (dd, *J* = 10.0, 4.7 Hz, 1H), 3.62 (t, *J* = 5.6 Hz, 2H), 3.47 (dd, *J* = 9.9, 7.0 Hz, 1H), 3.18 (bs, 1H), 1.85 – 1.93 (m, 2H), 1.55 – 1.65 (m, 1H), 0.98 – 1.11 (m, 21H), 0.87 (t, *J* = 7.9 Hz, 9H), 0.45 – 0.58 (m, 6H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 149.0, 148.4, 136.7, 119.1, 110.8, 109.8, 75.5, 65.2, 61.9, 56.2, 56.1, 49.0, 32.0, 18.3, 12.3, 7.1, 5.1. HRMS (ESI$^+$): m/z for $C_{28}H_{54}O_5Si_2Na$ $[M+Na]^+$ calcd. 549.3408, found: 549.3420.



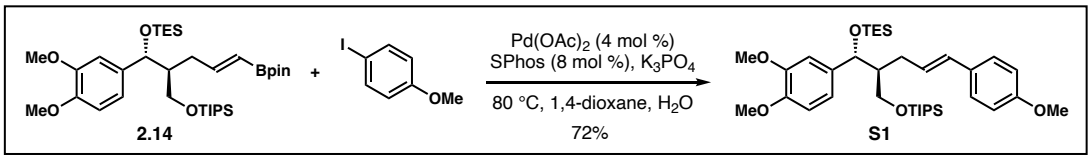
(3*S*,4*R*)-4-(3,4-dimethoxyphenyl)-4-((triethylsilyl)oxy)-3-(((triisopropylsilyl)oxy) methyl)butanal 2.13: To a reaction vial containing a Teflon-coated magnetic stirring bar were added alcohol **2.12** (158 mg, 0.30 mmol, 1.0 equiv) and DCM (1.0 mL) followed by addition of DMP (191 mg, 0.45 mmol, 1.5 equiv). The reaction mixture was then allowed to stir at ambient temperature for 2 h. After complete consumption of **2.12**, the reaction mixture was diluted with diethyl ether (1 mL) and filtered through a pad of silica gel. After concentrated under reduced pressure, purification of the crude product was performed by flash chromatography (gradient

elution with hexane and ethyl acetate 30:1 to 10:1) to give aldehyde **2.13** in 86% yield (135 mg). ^{1}H NMR (600 MHz, $CDCl_3$) δ 9.71 (t, *J* = 2.2 Hz, 1H), 6.86 (s, 1H), 6.78 – 6.80 (m, 2H), 4.75 (d, *J* = 6.4 Hz, 1H), 3.88 (s, 6H), 3.63 (dd, *J* = 9.9, 5.2 Hz, 1H), 3.47 (dd, *J* = 9.9, 6.1 Hz, 1H), 2.61 (ddd, *J* = 16.7, 5.7, 2.1 Hz, 1H), 2.48 (ddd, *J* = 16.7, 7.0, 2.3 Hz, 1H), 2.36 – 2.41 (m, 1H), 1.01 – 1.07 (m, 21H), 0.86 (t, *J* = 7.9 Hz, 9H), 0.42 – 0.53 (m, 6H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 203.1, 149.2, 148.6, 136.5, 119.2, 110.9, 109.7, 74.5, 63.9, 56.2, 56.1, 46.7, 42.8, 18.3, 12.3, 7.1, 5.1. HRMS (ESI$^+$): m/z for $C_{28}H_{52}O_5Si_2Na$ $[M+Na]^+$ calcd. 547.3251, found: 547.3243.



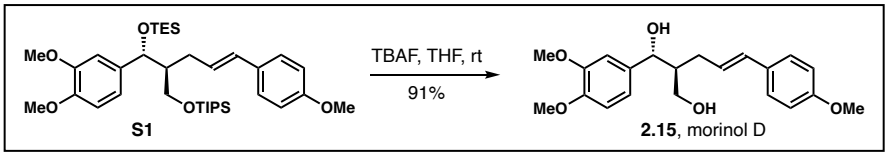
(6*S*,7*R*)-7-(3,4-dimethoxyphenyl)-9,9-diethyl-3,3-diisopropyl-2-methyl-6-((*E*)-3-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)allyl)-4,8-dioxa-3,9-disilaundecane 2.14: A Teflon-coated magnetic stirring bar, LiTMP (88 mg, 0.60 mmol, 2.0 equiv) and THF (1.0 mL) were added to an Ar-filled reaction vial. The reaction mixture was then allowed to stir at 0 °C for 5 min. Then 1,1-diborylmethane (161 mg, 0.60 mmol, 2.0 equiv) was added to the mixture and stirred at 0 °C for 5 min. Then reaction mixture was cooled to −78 °C and aldehyde **2.13** (157 mg, 0.30 mmol, 1.0 equiv) was added. The reaction mixture was stirred at −78 °C for 4 h. After complete consumption of aldehyde **2.13**, the reaction mixture was quenched with sat. NH_4Cl aqueous and extracted with Et_2O (2 mL x 3). The combined organic extracts were dried over anhydrous sodium sulfate, filtered, and concentrated under reduced pressure. Purification of the crude product was performed by flash chromatography (gradient elution with hexane and ethyl acetate 30:1 to 10:1) to give vinylboronate **2.14** in 65% yield (126 mg). ^{1}H NMR (600 MHz, $CDCl_3$) δ 6.87 (s, 1H), 6.79 (d, *J* = 7.6 Hz, 1H), 6.77 (d, *J* = 7.9 Hz, 1H), 6.58 (ddd, *J* = 17.5, 6.8,

6.8 Hz, 1H), 5.40 (d, *J* = 17.9 Hz, 1H), 4.89 (d, *J* = 4.6 Hz, 1H), 3.863 (s, 3H), 3.857 (s, 3H), 3.63 – 3.65 (m, 1H), 3.41 (dd, *J* = 9.9, 4.3 Hz, 1H), 2.35 – 2.39 (m, 1H), 2.16 – 2.22 (m, 1H), 1.79 – 1.84 (m, 1H), 1.24 (s, 12H), 0.94 – 1.11 (m, 21H), 0.87 (t, *J* = 7.9 Hz, 9H), 0.51 (q, *J* = 8.2 Hz, 6H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 154.7, 148.8, 148.1, 137.4, 119.0, 110.7, 109.9, 83.2, 73.6, 62.8, 56.2, 56.0, 50.3, 32.7, 25.1, 18.4, 12.4, 7.2, 5.2. HRMS (ESI$^+$): m/z for $C_{35}H_{65}O_6BSi_2Na$ $[M+Na]^+$ calcd. 671.4310, found: 671.4327.

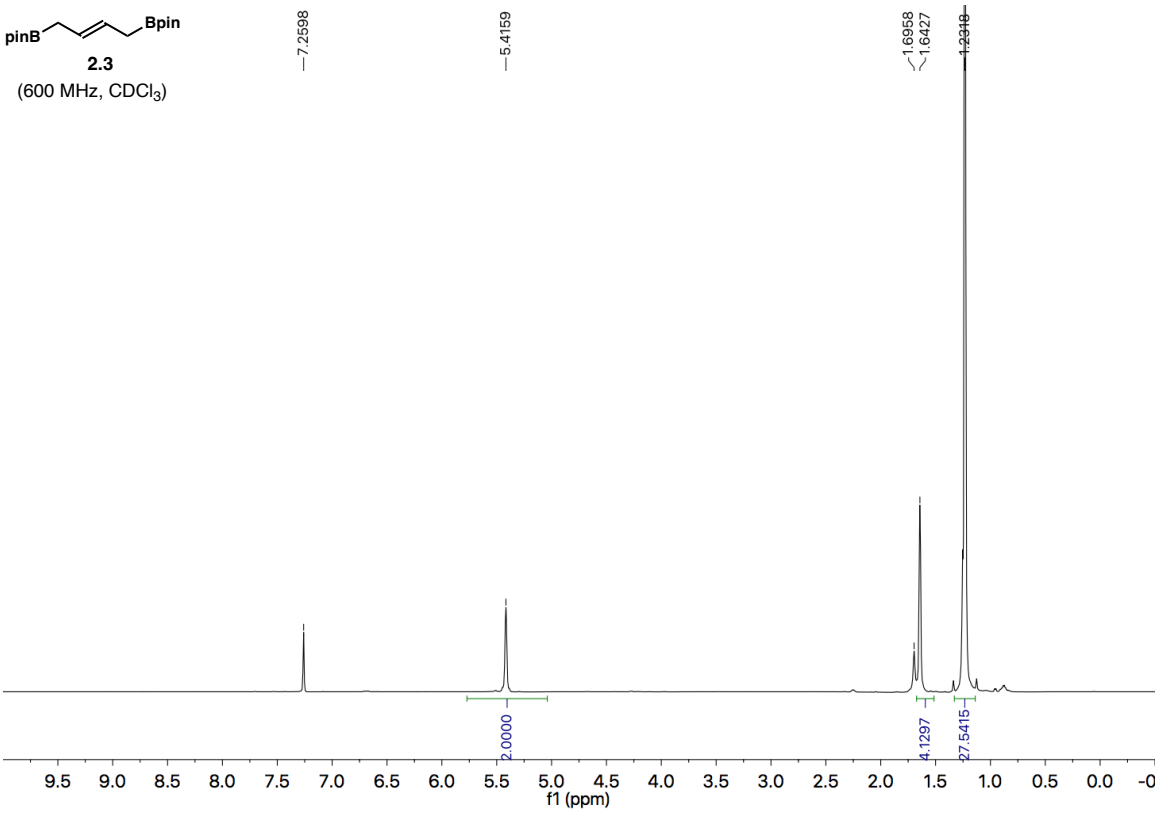


(6*S*,7*R*)-7-(3,4-dimethoxyphenyl)-9,9-diethyl-3,3-diisopropyl-6-((*E*)-3-(4-methoxyphenyl)allyl)-2-methyl-4,8-dioxa-3,9-disilaundecane S1: A Teflon-coated magnetic stirring bar, $Pd(OAc)_2$ (2 mg, 0.008 mmol, 4 mol %), SPhos (7 mg, 0.016 mmol, 8 mol %), K_3PO_4 (64 mg, 0.60 mmol, 3.0 equiv) and 1,4-dioxane (0.7 mL) were added to an Ar-filled reaction vial. Then vinylboronate **2.14** (130 mg, 0.2 mmol, 1.0 equiv), 4-iodoanisole (51 mg, 0.22 mmol, 1.1 equiv) and H_2O (6 μL) were added to the reaction vial. Then reaction mixture was heated to 80 °C and stirred for 12 h. After complete consumption of vinylboronate **2.14**, the reaction mixture was diluted with diethyl ether (1 mL) and filtered through a pad of silica gel. After concentrated under reduced pressure, purification of the crude product was performed by flash chromatography (gradient elution with hexane and ethyl acetate 30:1 to 10:1) to give **S1** in 72% yield (91 mg). ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.21 (d, *J* = 8.5 Hz, 2H), 6.90 (s, 1H), 6.79 – 6.83 (m, 4H), 6.30 (d, *J* = 15.8 Hz, 1H), 6.01 (ddd, *J* = 15.4, 7.3, 7.3 Hz, 1H), 4.90 (d, *J* = 5.5 Hz, 1H), 3.871 (s, 3H), 3.866 (s, 3H), 3.79 (s, 3H), 3.65 (dd, *J* = 9.8, 6.3 Hz, 1H), 3.46 (dd, *J* = 10.0, 4.8 Hz, 1H), 2.41 – 2.46 (m, 1H), 2.24 – 2.30 (m, 1H), 1.79 – 1.85 (m, 1H), 0.94 – 1.03 (m, 21H),

0.89 (t, J = 7.9 Hz, 9H), 0.48 – 0.58 (m, 6H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 158.9, 148.9, 148.1, 137.6, 131.2, 130.7, 128.2, 127.2, 119.1, 114.2, 110.8, 109.9, 73.8, 62.7, 56.2, 56.1, 55.6, 51.0, 29.7, 18.4, 12.4, 7.3, 5.2. HRMS (ESI$^+$): m/z for $C_{36}H_{60}O_5Si_2Na$ $[M+Na]^+$ calcd. 651.3877, found: 651.3896.



(1*R*,2*S*)-1-(3,4-dimethoxyphenyl)-2-((*E*)-3-(4-methoxyphenyl)allyl)propane-1,3-diol (2.15, morinol D**):** A Teflon-coated magnetic stirring bar, compound **S1** (31 mg, 0.05 mmol, 1.0 equiv), THF (0.5 mL) and TBAF·H_2O (65 mg, 0.25 mmol, 5.0 equiv) were added to a reaction vial. Then reaction mixture was stirred at ambient temperature for 12 h. After complete consumption of compound **S1**, ethyl acetate (1 mL) and brine (1 mL) was added. The organic layer was separated and the aqueous layer was extracted with ethyl acetate (2 mL x 3). The combined organic extracts were dried over anhydrous sodium sulfate, filtered, and concentrated under reduced pressure. Purification of the crude product was performed by flash chromatography (gradient elution with hexane and ethyl acetate 2:1 to 1:1) to give morinol D (**2.15**) in 91% yield (16 mg). ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.24 (d, J = 8.6 Hz, 2H), 6.95 (app. s, 1H), 6.91 (d, J = 8.3 Hz, 1H), 6.87 (d, J = 8.2 Hz, 1H), 6.83 (d, J = 8.4 Hz, 2H), 6.35 (d, J = 15.7 Hz, 1H), 6.02 (ddd, J = 15.3, 7.3, 7.3 Hz, 1H), 4.98 (d, J = 4.0 Hz, 1H), 3.90 (s, 3H), 3.89 (s, 3H), 3.80 (s, 3H), 3.71 – 3.77 (m, 2H), 2.68 (d, J = 3.0 Hz, 1H), 2.29 (dd, J = 7.1, 7.1 Hz 2H), 2.03 – 2.09 (m, 1H), 1.97 (t, J = 5.2 Hz, 1H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 159.2, 149.3, 148.7, 135.4, 131.5, 130.6, 127.4, 126.7, 118.8, 114.3, 111.3, 109.7, 76.7, 64.3, 56.29, 56.27, 55.6, 47.4, 29.7. HRMS (ESI$^+$): m/z for $C_{21}H_{26}O_5Na$ $[M+Na]^+$ calcd. 381.1678, found: 381.1677.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(600 MHz, CDCl3)
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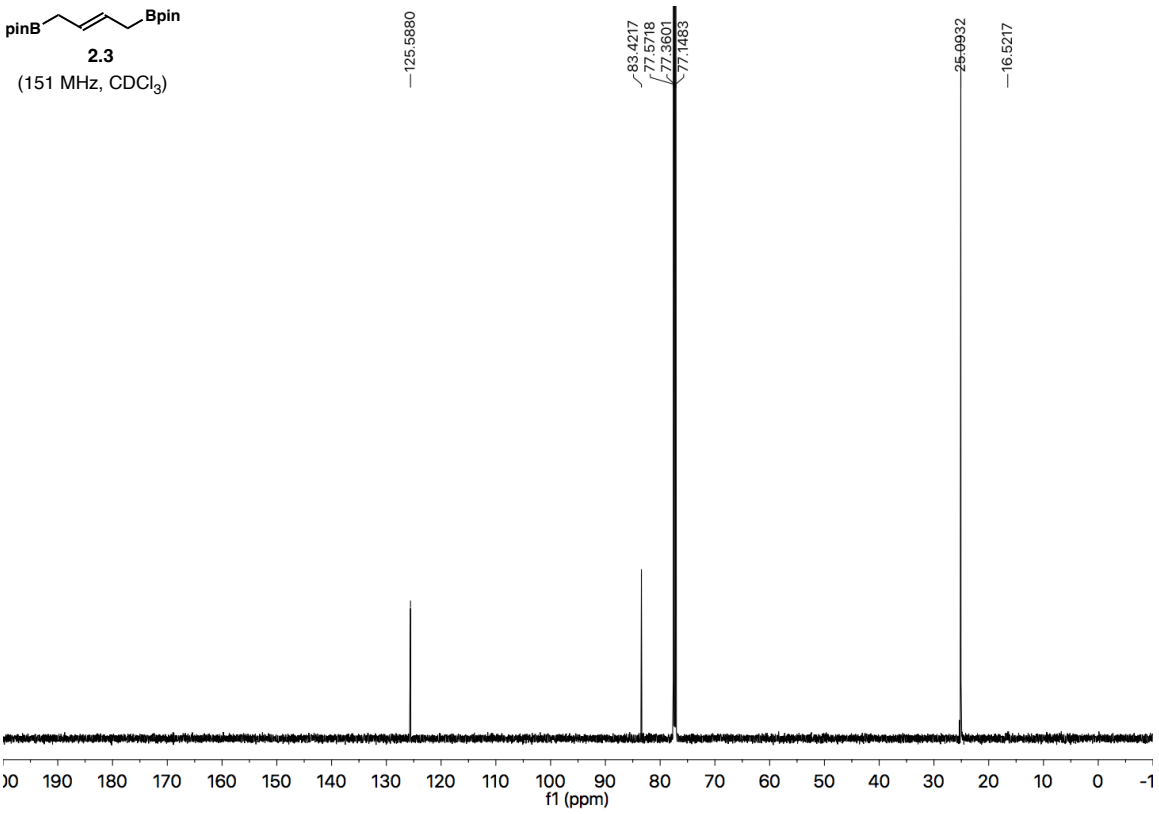
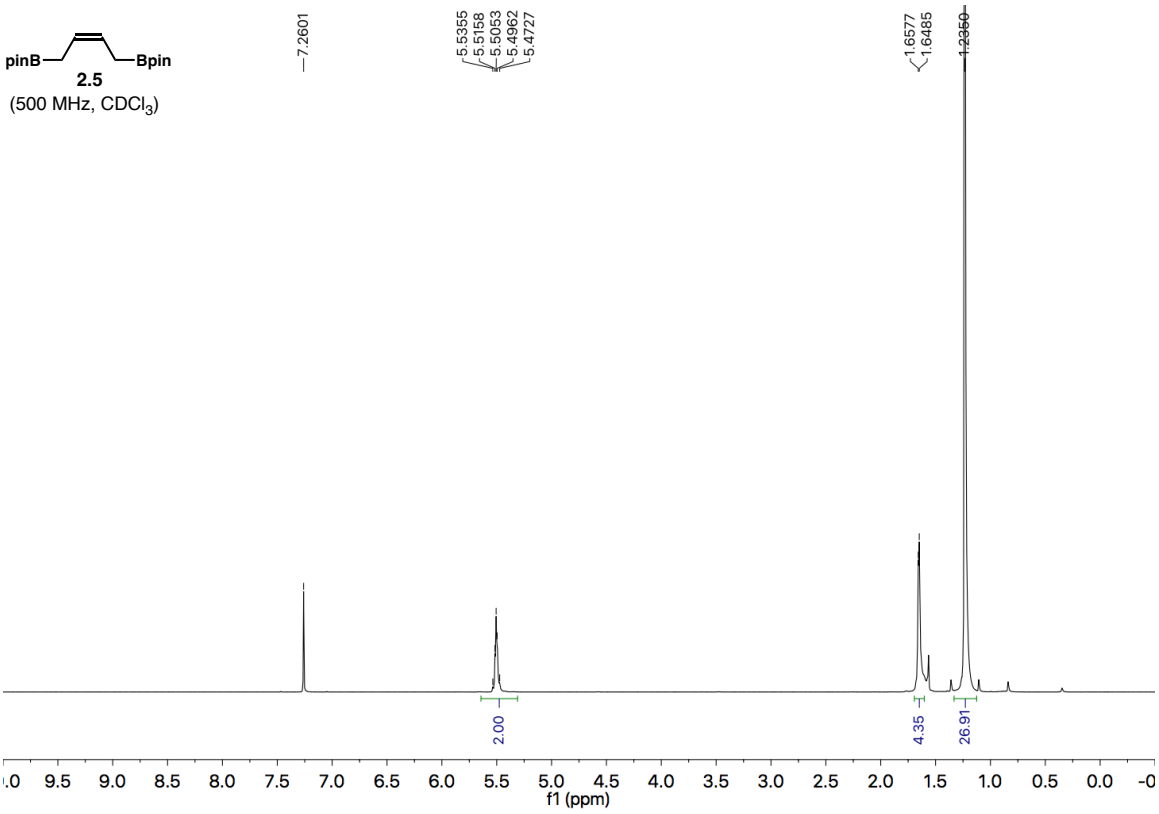
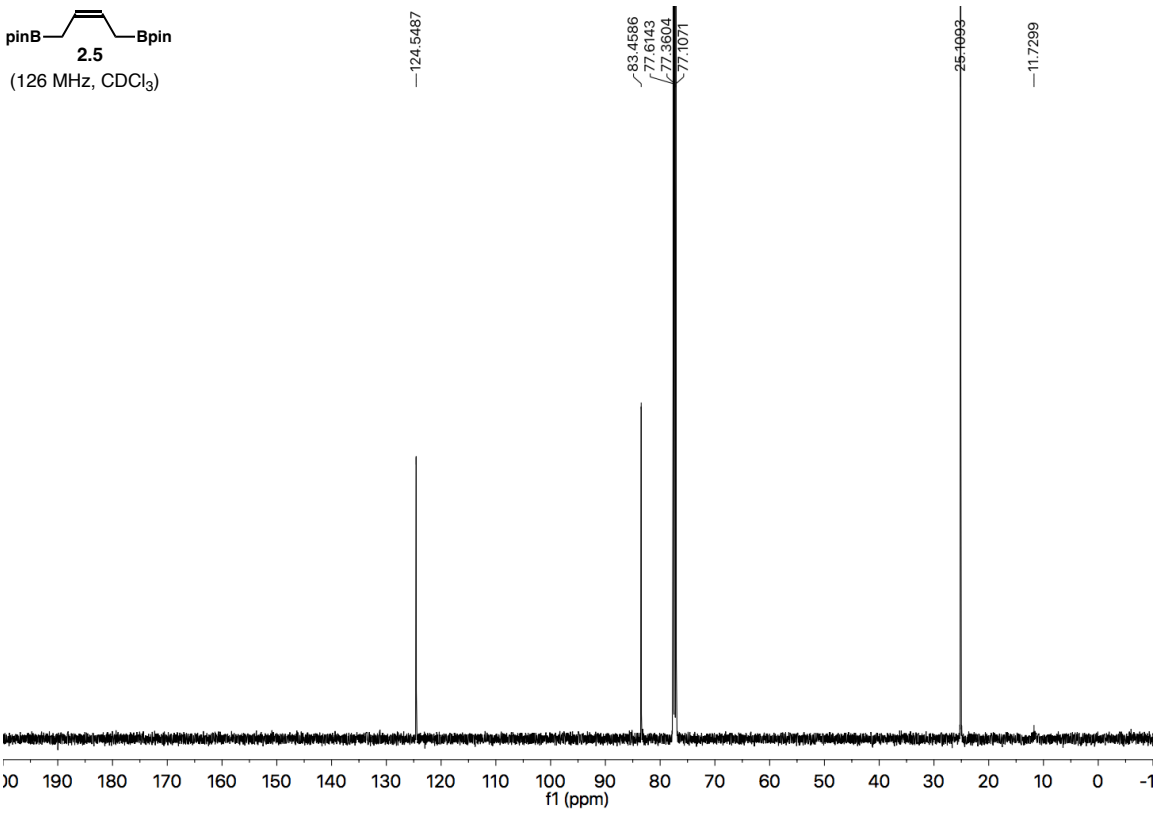
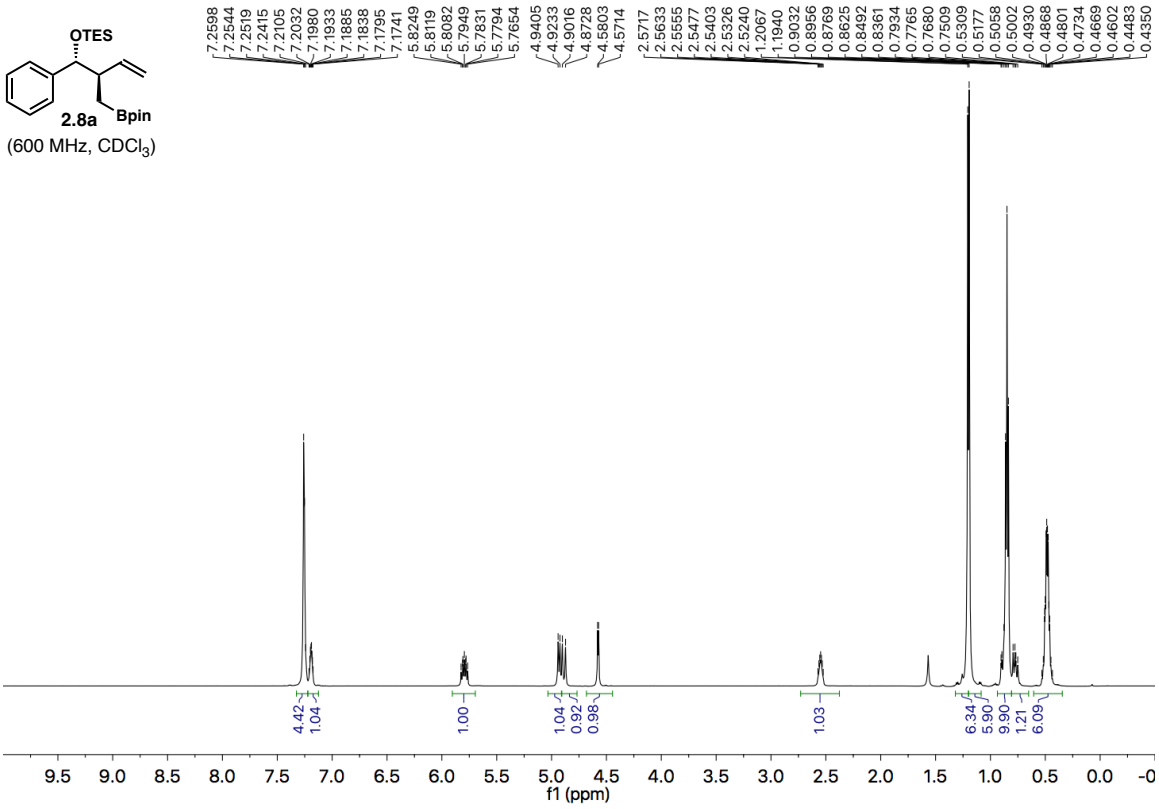
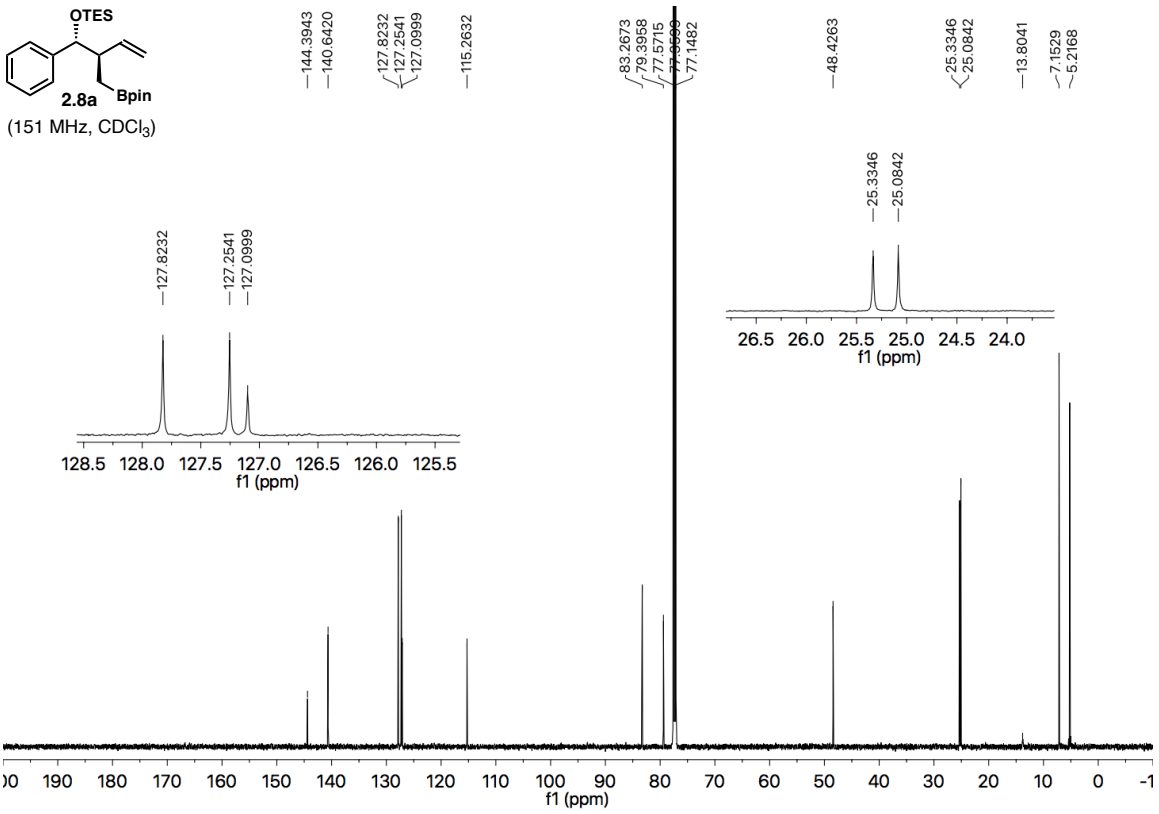
1.6427
1.2318
2.0000
4.1297
7.5415
f1 (ppm)

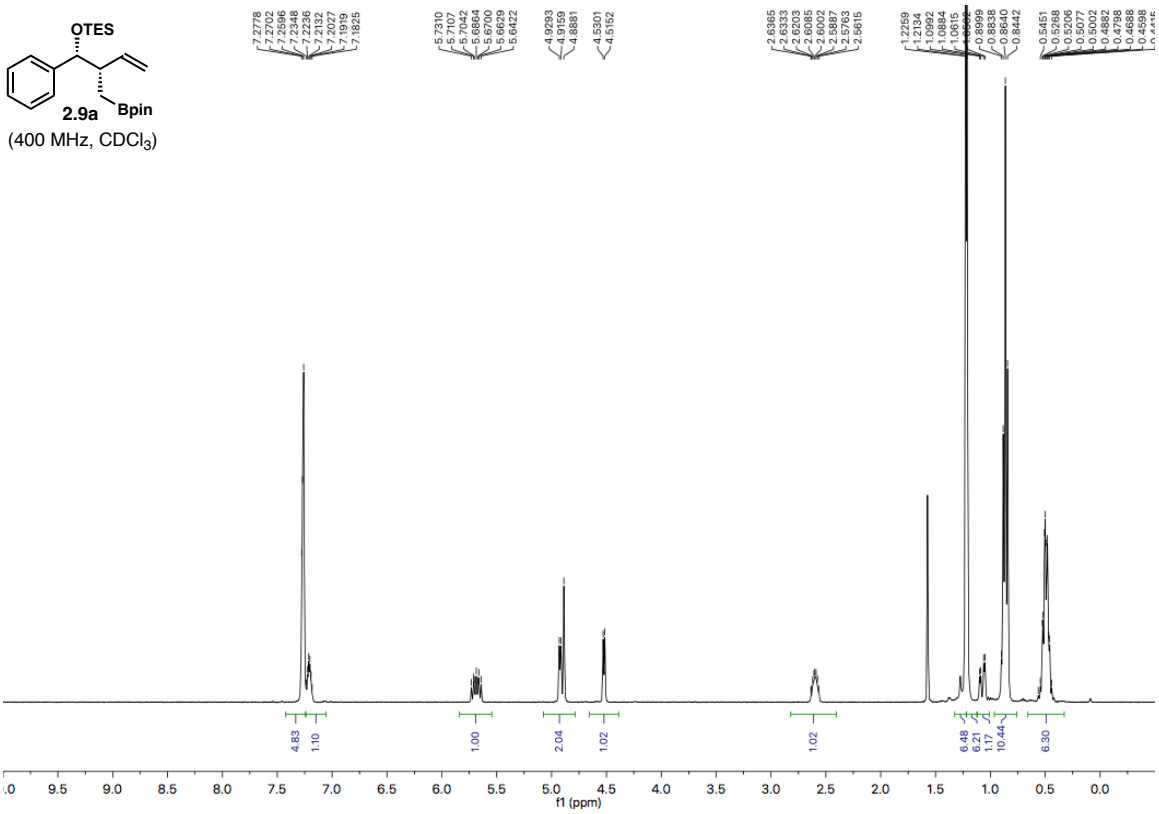

pinB
Bpin
2.3
(151 MHz, CDCl3)
125.5880
83.4217
77.5718
77.3601
77.1483
25.0932
16.5217
f1 (ppm)

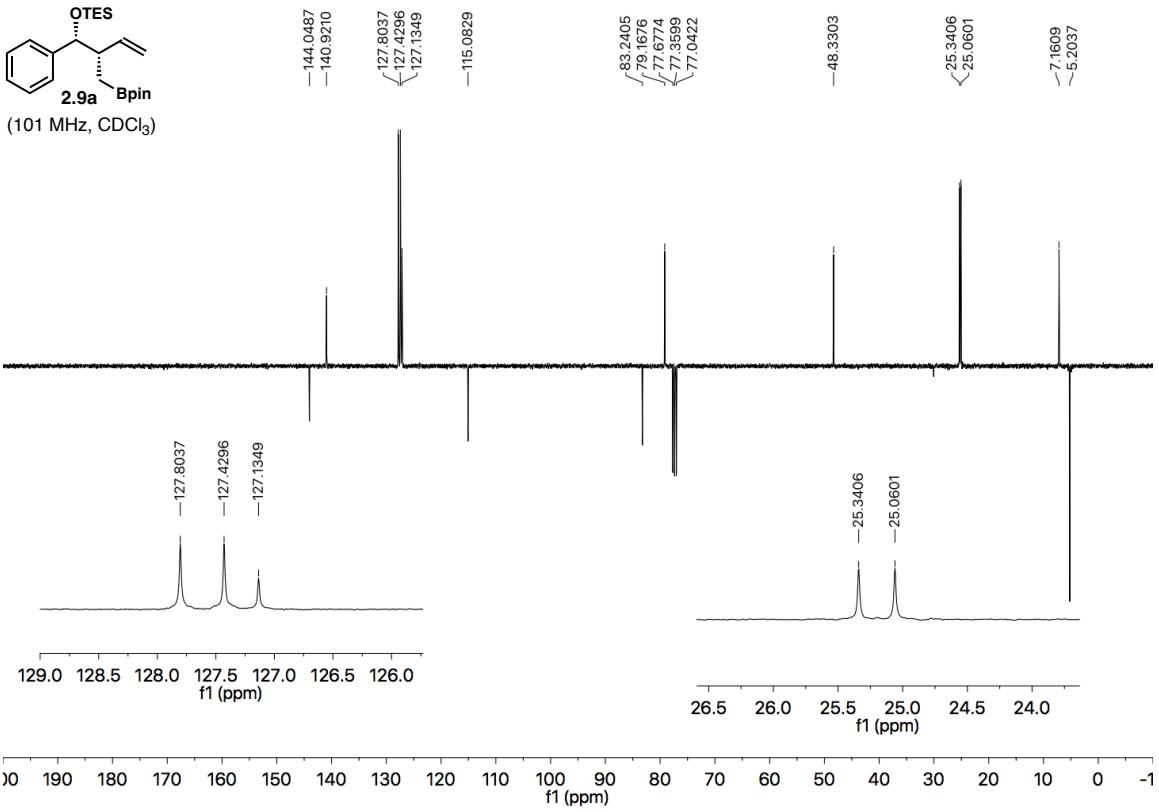

pinB
Bpin
2.5
(500 MHz, CDCl3)
7.2601
5.5355
5.5158
5.5053
5.4962
5.4727
1.6577
1.6485
1.2360
2.00
4.35
26.91
f1 (ppm)


pinB
Bpin
2.5
(126 MHz, CDCl3)
124.5487
83.4586
77.6143
77.3604
77.1071
25.1093
11.7299
f1 (ppm)


OTES
Bpin
2.8a
(600 MHz, CDCl3)
f1 (ppm)


OTES
Bpin
2.8a
(151 MHz, CDCl3)
f1 (ppm)


OTES
Bpin
2.9a
(400 MHz, CDCl3)
f1 (ppm)

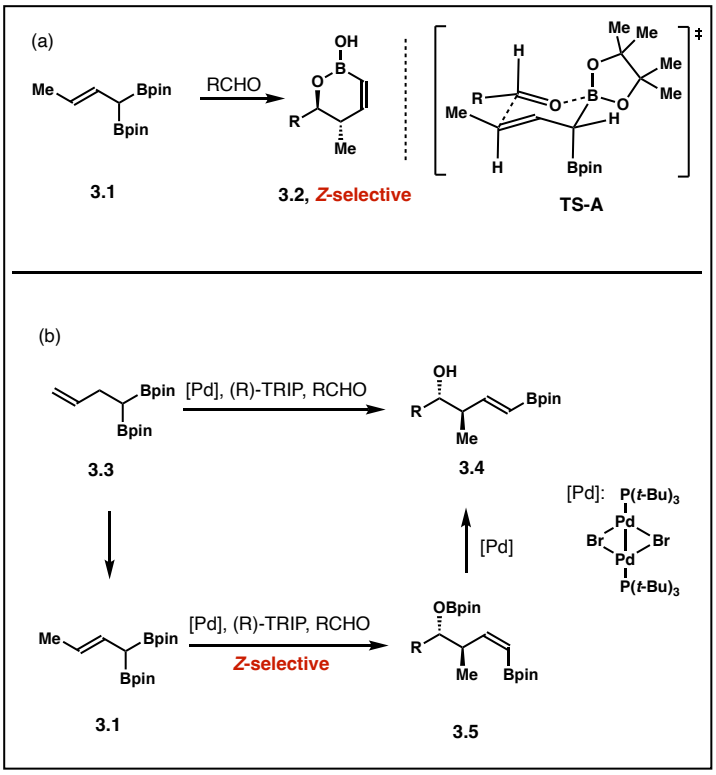

OTES
Bpin
2.9a
(101 MHz, CDCl3)
f1 (ppm)

CHAPTER THREE

1,1-Bifunctional allylboron reagent

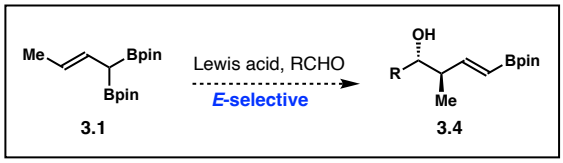
An emerging topic in allylation chemistry is carbonyl addition with 1,1-bismetallic allylation reagents.[147-158] In particular, allylation with (*E*)-α-boryl-crotylboronate **3.1** has recently attracted significant attention. As shown in **Scheme 3.1**, the reaction of reagent **3.1** with aldehydes proceeds via transition state **TS-A** to give *anti*-1,2-oxaborinan-3-enes **3.2** with high *Z*-selectivities. It was proposed that the α-Bpin group of **3.1** is oriented in a pseudoaxial position in **TS-A** to minimize steric interactions. The Murakami group disclosed that enantioenriched δ-boryl-substituted *anti*-homoallylic alcohols **3.4** can be generated from boronate **3.3** via a one-pot reaction sequence.[153] The Pd-catalyzed olefin transposition of **3.3** generates reagent **3.1** *in situ*, which undergoes asymmetric allylation to give the *Z*-adduct **3.5**. The same Pd complex then catalyzes alkene isomerization to form δ-boryl-*anti*-homoallylic alcohols **3.4**.

Scheme 3.1. *Z*-selective Allylboration with *α*-boryl-(*E*)-crotylboronate 3.1



As part of our program on allylation chemistry, we are interested in developing alternative approaches to access *E*-isomer **3.4** from reagent **3.1**. As shown in **Scheme 3.2**, we envisioned that, in the presence of a Lewis acid,[159-161] the addition of reagent **3.1** to aldehydes should provide *δ*-boryl-*anti*-homoallylic alcohols **3.4** with *E*-selectivities. The inherent *Z*-selectivity of aldehyde addition with boronate **3.1** could be inverted by using a Lewis acid catalyst. Moreover, the reaction forms alcohols **3.4** with a functionalized alkene group, which can directly engage in a C–C bond-forming event.

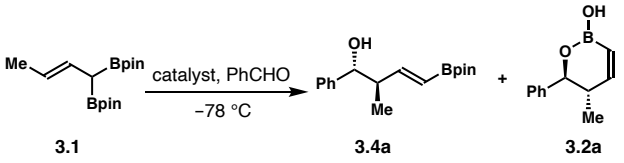
Scheme 3.2. *E*-selective Allylboration with α-boryl-(E)-crotylboronate 3.1



3.1 Evaluation of the reaction conditions for *E*-selective allylation

We initiated our studies by identifying a proper Lewis acid catalyst for the *E*-selective allylation of benzaldehyde with α-boryl-(*E*)-crotylboronate **3.1**. As shown in **Table 3.1**, the reaction without any catalyst gave a 1:10 mixture of **3.4a** and **3.2a** in a combined 96% yield, with *Z*-isomer **3.2a** as the major product (entry 1). The data confirm the strong inherent pseudo axial preference of the α-Bpin group of reagent **3.1** in the allylation transition state (**TS-A**, Scheme 1). When 10 mol % $Sc(OTf)_3$ was utilized as the catalyst, a 2:1 mixture of **3.4a** and **3.2a** was obtained in 78% yield with *E*-isomer **3.4a** as the major product (entry 2). The reaction with 10 mol % $Cu(OTf)_2$ as the catalyst provided a 1:2 mixture of **3.4a** and **3.2a**, slightly favoring *Z*-isomer **3.2a** (entry 3). The *E*-selectivity was improved to 10:1 when the reaction was conducted in the presence of 10 mol % BF_3•OEt_2 (entry 4). However, the yield was only moderate (57%). Doubling the loading of the BF_3•OEt_2 catalyst (20 mol%) significantly improved the yield (90%), again with a high *E*-selectivity (10:1, entry 5). Finally, further enhancement of the *E*-selectivity was achieved by adding 4 Å molecular sieves. The reaction between benzaldehyde and reagent **3.1** with 20 mol% BF_3•OEt_2 at −78 °C provided *E-anti*-adduct **3.44a** as a single isomer in 97% yield (*E*:*Z* > 20:1, entry 6).

Table 3.1. Evaluation of the Reaction Conditions for *E*-Selective Allylation with α-Boryl-(*E*)-crotylboronate 3.1



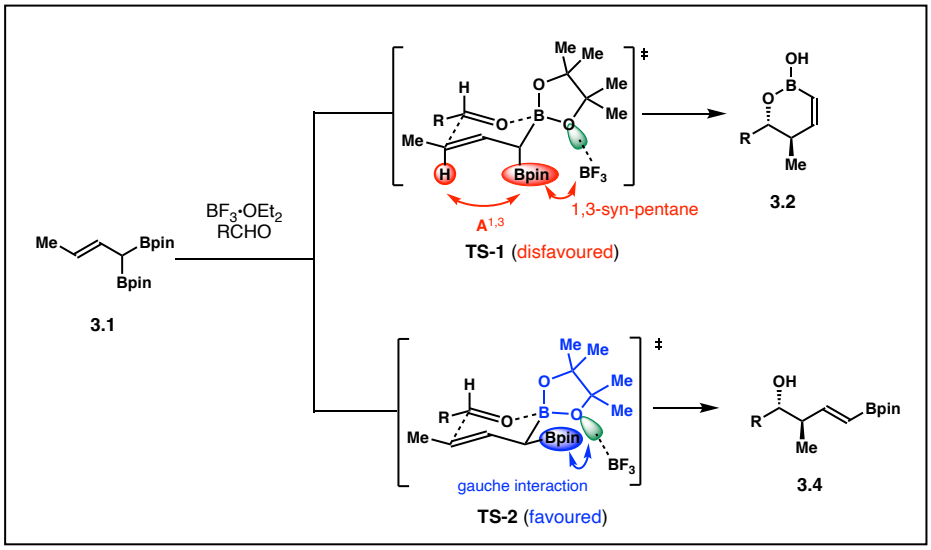
3.1 **3.4a** **3.2a**

entry	catalyst	solvent	**3.4a**:**3.2a**	yield (%)
1	no catalyst, rt	CH_2Cl_2	1:10	96
2	$Sc(OTf)_3$ (10 mol %)	CH_2Cl_2	1.5:1	78
3	$Cu(OTf)_2$ (10 mol %)	CH_2Cl_2	1:1.7	42
4	BF_3•OEt_2 (10 mol %)	CH_2Cl_2	10:1	57
5	BF_3•OEt_2 (20 mol %)	CH_2Cl_2	10:1	90
6	BF_3•OEt_2 (20 mol %), 4 Å MS	CH_2Cl_2	> 20:1	97

3.2 Analyses of the origin of the *E*-selectivity in BF_3•OEt_2-catalyzed allylation

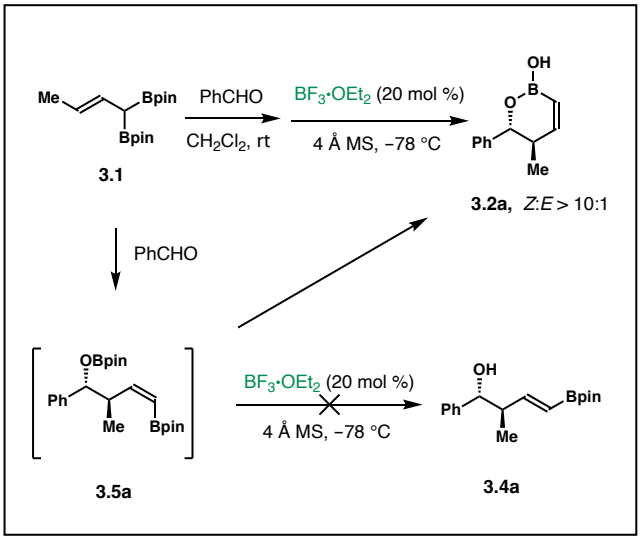
The rationale of the observed *E*-selectivity is outlined in **Scheme 3.3**. **TS-1** and **TS-2** are the two competing transition states with the BF_3 catalyst coordinating to the most accessible lone pair of electrons of the oxygen atoms (shown in light green in **Scheme 3.3**). In **TS-1** that leads to **3.2**, 1,3-*syn*-pentane interactions are developed between the pseudo axially positioned Bpin group and the BF_3 catalyst. Moreover, **TS-1** has an $A^{1,3}$ allylic strain between pseudoaxial H atom the Bpin group. Although gauche interactions between two Bpin groups of reagent **3.1** are present in **TS-2**, such gauche interactions are much weaker compared to the 1,3-*syn*-pentane interactions in **TS-1**.[51] Consequently, the BF_3•OEt_2-catalyzed allylation with boronate **3.1** proceeds via the favored transition state **TS-2**, delivering alcohol **3.4** with high *E*-selectivity.

Scheme 3.3. Transition State Analyses of BF_3•OEt_2-Catalyzed Allylation



We also considered whether the *E*-selectivity originates from the BF_3-catalyzed alkene isomerization of the initial allylation *Z*-adduct **3.5a** (**Scheme 3.4**). To rule out this potential pathway, the reaction of boronate **3.1** with benzaldehyde was conducted in the absence of the BF_3•OEt_2 catalyst. When benzaldehyde was fully consumed, 20 mol% of BF_3•OEt_2 was added to the reaction mixture. After stirring at −78 °C for 12 h, a 10:1 mixture was obtained with *Z*-isomer **3.2a** as the major product. The selectivity is identical to the one from the uncatalyzed reaction (entry 1, **Table 3.1**). Therefore, it is evident that the reaction does not involve a BF_3-catalyzed *Z*-alkene isomerization pathway to generate *E*-isomer **3.4a**.

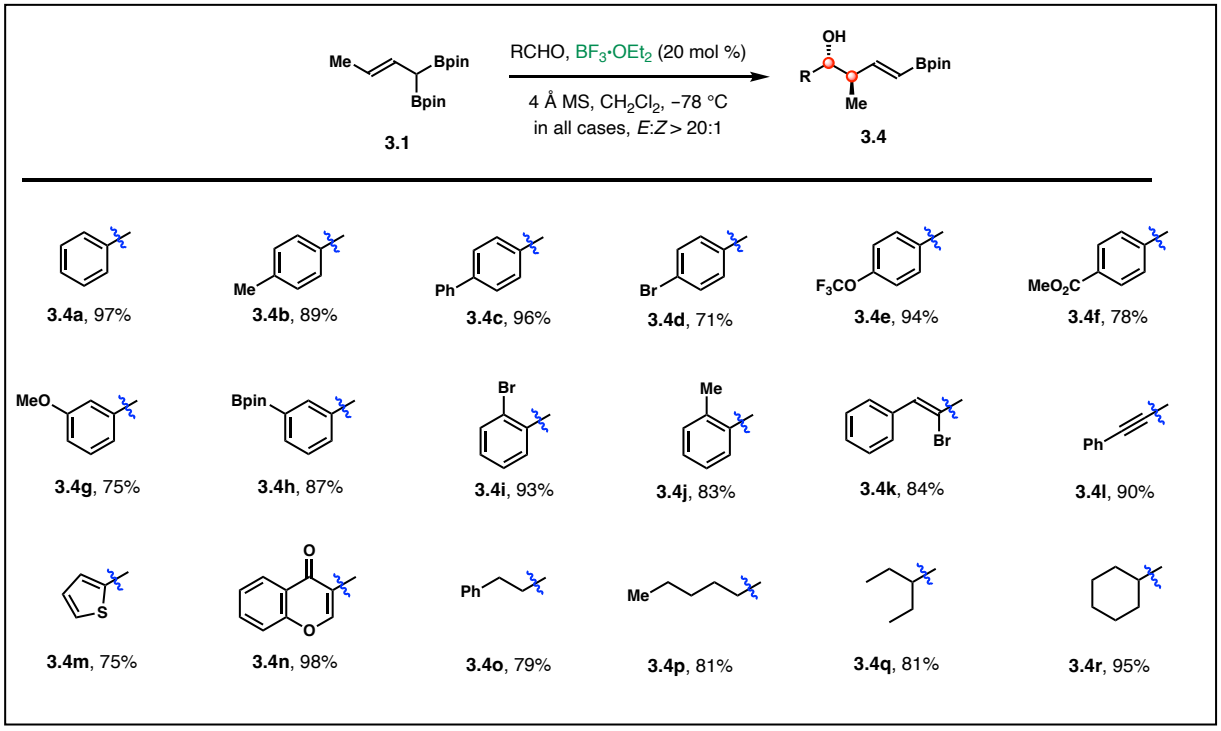
Scheme 3.4. Analyses of the origin of E-selectivity



3.3 Allylboration of aldehydes with crotylboronate 3.1

The reaction scope was explored next and the results are summarized in **Scheme 3.5**. Under the developed conditions, a wide variety of aldehydes participated in the reaction to give (*E*)-*δ*-boryl-*anti*-homoallylic alcohols **3.4** in good yields with excellent *E*-selectivities. Aromatic aldehydes with an alkyl or aryl group at the para-position reacted with boronate **3** to afford products **3.4b-c** in 89–96% yields with >20:1 *E*-selectivities. Aldehydes with a Br atom, an OCF_3 group or an electron-withdrawing CO_2Me group at the para-position are suitable substrates for the reaction. Alcohols **3.4d–f** were obtained in 71–94% yields with excellent *E*-selectivities. Reactions of aromatic aldehydes with diverse substituents at the meta- or ortho-position proceeded smoothly to form alcohols **3.4g–j** in 75–93% yields with >20:1 *E*-selectivities. The reaction tolerates *α*,*β*-unsaturated aldehydes and substrates that contain a heterocycle, forming alcohols **3.4k–n** in 75–98% yields with >20:1 *E*-selectivities. Notably, BF_3•OEt_2-catalyzed reactions of several aliphatic aldehydes with boronate **3.11** delivered products **3.4o–r** in 79–95% yields with excellent *E*-selectivities (> 20:1).

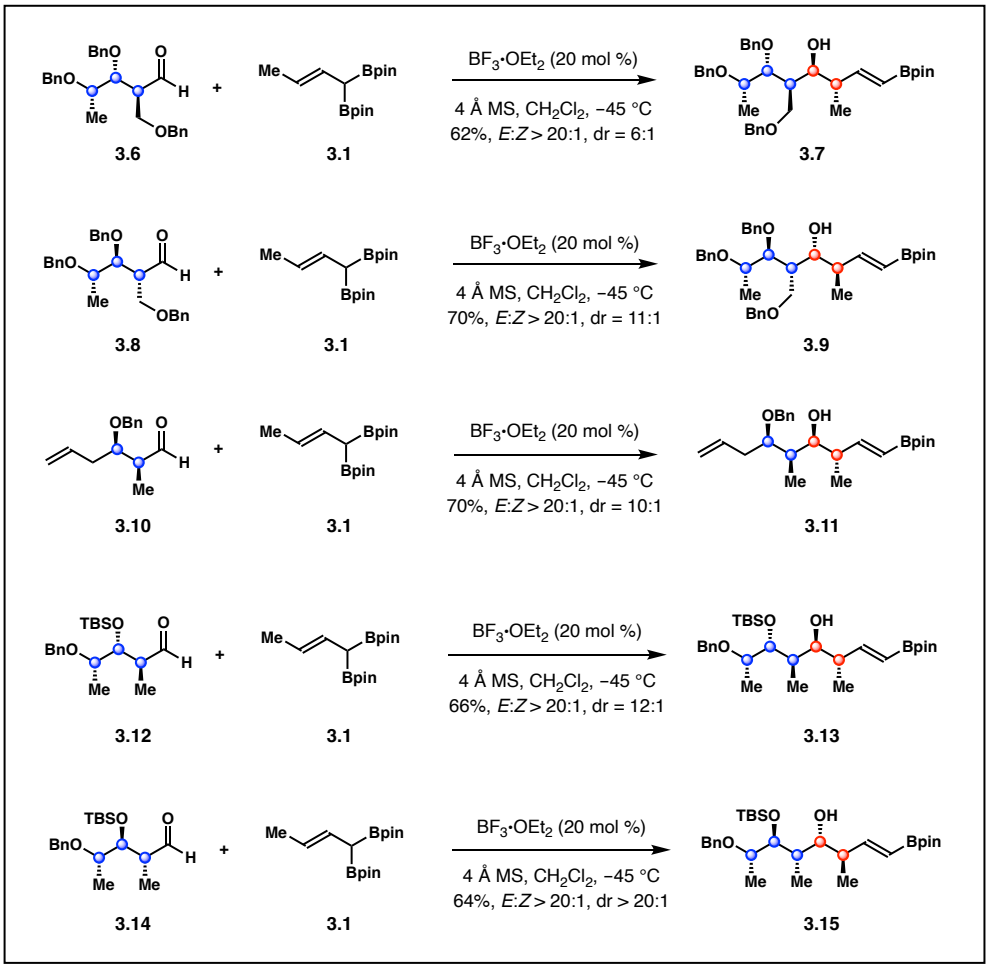
Scheme 3.5. Scope of $BF_3.OEt_2$-catalyzed *E*-selective allylation with α-boryl-(*E*)-crotylboronate



To explore whether the *E*-selective allylation can be used in reactions with chiral, nonracemic aldehydes to generate allylated products diastereoselectively, we synthesized a collection of enantioenriched aldehydes and conducted BF_3•OEt_2-catalyzed allylation studies with reagent **3.1**. As shown in **Scheme 3.6**, the reaction of aldehyde **3.6** with reagent **3.1** was slow at −78 °C. However, upon elevating the reaction temperature to −45 °C, product **3.7** was formed in 62% yield with >20:1 *E*-selectivity and 6:1 diastereoselectivity. Formation of any product with *Z*-olefin geometry was not detected. The reaction of aldehyde **3.8** under the same conditions gave product **3.9** in 70% yield with >20:1 *E*-selectivity and 11:1 d.r. Similar results were obtained from aldehyde **3.10**; adduct **3.11** was afforded in 70% yield with >20:1 *E*-selectivity and 10:1 d.r. Excellent *E*-selectivities were also achieved in the reactions with chiral

aldehydes **3.12** and **3.14**. Allylated products **3.13** and **3.15** were obtained in 66% and 64% yield with 12:1 and 20:1 d.r., respectively. The diastereoselectivities in these reactions are governed by the inherent Felkin–Anh preference of the aldehydes,[13] while the BF_3•OEt_2 catalyst dictates the *E*-selectivity of the reactions.

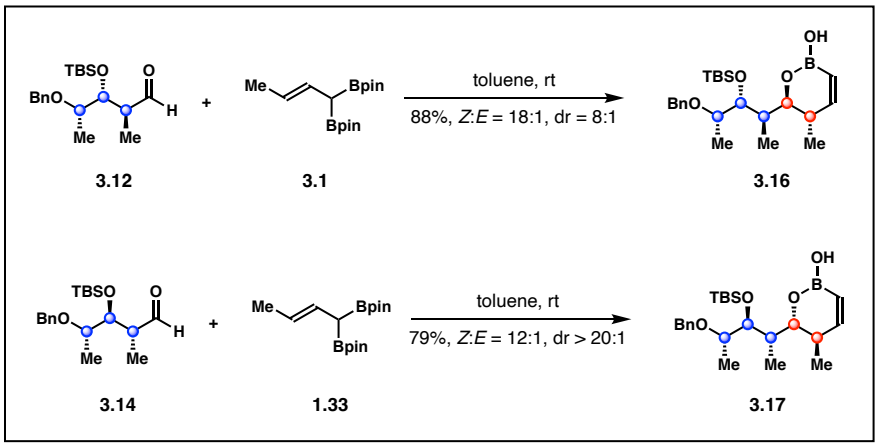
Scheme 3.6. Allylation with enantioenriched aldehydes



As shown in **Scheme 3.7**, it is worth noting that the reactions of chiral aldehydes **3.12** and **3.14** with boronate **3.1** in the absence of the BF_3•OEt_2 catalyst produced *Z* isomers **3.16** and **3.17** with 18:1 and 12:1 *Z*-selectivities, respectively. The inherent *Z* preferences were overridden

in the reactions of **3.12** and **3.14** with the BF_3•OEt_2 catalyst, affording alcohols **3.13** and **3.15** with excellent *E*-selectivities.

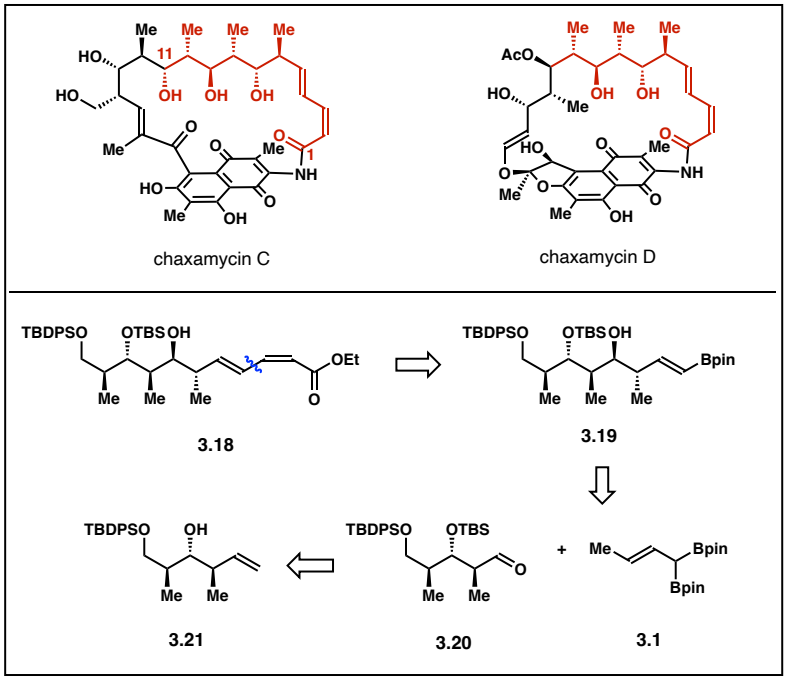
Scheme 3.7. Allylation with enantioenriched aldehydes in the absence of BF_3•OEt_2



3.4 Synthesis of the C(1)–C(11) fragment of chaxamycins C and D

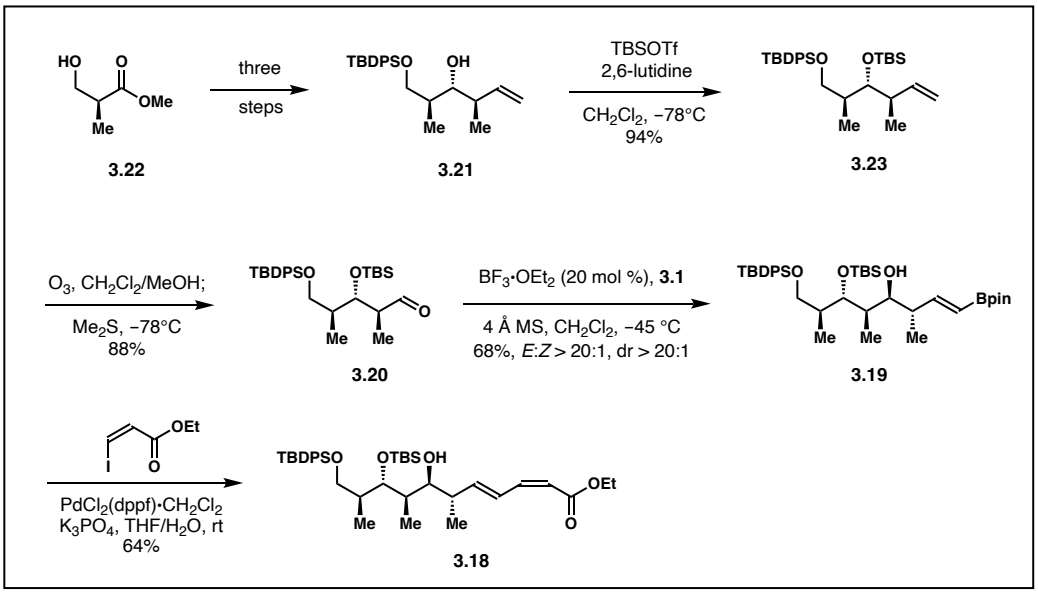
To highlight the synthetic utility of the developed *E*-selective allylation, stereoselective synthesis of a fragment of chaxamycins C and D was pursued.[162] As shown in **Scheme 3.8**, the C(1)–C(11) fragment (**3.18**) of the chaxamycins can be assembled via a Suzuki coupling between vinylboronate **3.19** and ethyl *Z*-iodo-acrylate. Boronate **3.19** can be obtained via the *E*-selective allylation of aldehyde **3.20**, which can be synthesized from known compound **3.21.**[163,164]

Scheme 3.8. Retrosynthetic route of the C(1)–C(11) fragment of chaxamycins.



The synthesis of the C(1)–C(11) fragment of chaxamycins C and D is shown in Scheme **3.9**. Known alcohol **3.21** was synthesized from a Roche ester **3.22** in three steps.[163,164] Alcohol silylation of **3.21** formed TBS-ether **3.23** in 94% yield. Ozonolysis of **3.23** under standard conditions gave aldehyde **3.20** in 88% yield. The BF_3•OEt_2-catalyzed allylation of aldehyde **3.20** with reagent **3.1** afforded alcohol **3.19** in 68% yield with 20:1 *E*-selectivity and diastereoselectivity. The Pd-catalyzed Suzuki coupling of **3.19** with ethyl *Z*-iodo-acrylate furnished diene **3.18**, which represents the C(1)–C(11) fragment of chaxamycins C and D.

Scheme 3.9. Synthesis of the C(1)–C(11) fragment of chaxamycins.

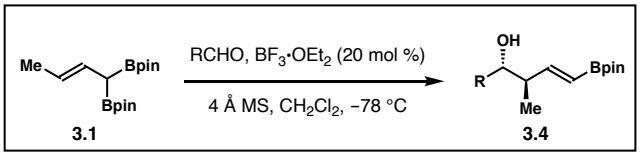


3.5 Conclusion

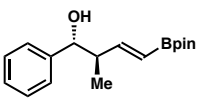
We developed BF_3•OEt_2-catalyzed highly *E*-selective allylation with α-boryl-(*E*)-crotylboronate to give δ-boryl-anti-homoallylic alcohols. The reactions with a collection of enantioenriched aldehydes gave allylated products with excellent *E*-selectivities and high diastereoselectivities, which highlights the synthetic utility of the method in assembling stereochemically rich intermediates. Moreover, the *E*-vinylboronate group in the products provides a handle for transition metal-catalyzed cross-coupling reactions as illustrated in the fragment synthesis of chaxamycins C and D. Similar coupling strategy was also applied in the fragment synthesis of cryptophycin D and dictyostatin.

3.6 Experimental Section

$BF_3.OEt_2$-catalyzed E-selective allylation

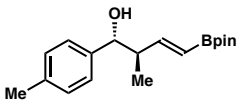


General procedure for synthesis of homoallylic alcohols 3.4: Allylic boronate **3.1** (40 mg, 0.13 mmol, 1.3 equiv), freshly activated 4 Å MS (50 mg), a Teflon-coated magnetic stirring bar and dichloromethane (1 mL) were sequentially added into a reaction flask. The mixture was placed in a −78 ℃ acetone/dry ice bath and stirred for 5 min. Then freshly distilled aldehyde (0.1 mmol, 1.0 equiv, if it is a liquid) was added slowly to the reaction mixture *via* a microliter syringe at −78 ℃. Then $BF_3{\cdot}Et_2O$ (20 mol %) was added slowly to the reaction mixture *via* a microliter syringe at −78 ℃. The mixture was kept at −78 ℃ and stirred for 4 h. After complete consumption of the aldehyde, sat. $NaHCO_3$ (1.0 mL) was added to the reaction mixture. The organic layer was separated and the aqueous layer was extracted with Et_2O (2 mL x 3). The combined organic extracts were dried over anhydrous sodium sulfate, filtered, and concentrated under reduced pressure. Purification of the crude product was performed by flash chromatography (gradient elution with hexane and ethyl acetate) to give alcohol **3.4**.

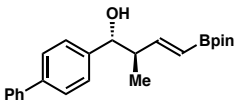


***rac*-(1*R*,2*R*,*E*)-2-methyl-1-phenyl-4-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)but-3-en-1-ol (3.4a)** Prepared according to the general procedure. The crude mixture was purified by column chromatography to give compound **3.4a** in 97% yield (28 mg) as colorless oil. ^1H NMR (600 MHz, $CDCl_3$) δ 7.06 – 7.53 (m, 5H), 6.62 (dd,

J = 18.0, 8.1 Hz, 1H), 5.62 (d, J = 18.0 Hz, 1H), 4.37 (d, J = 8.5 Hz, 1H), 2.36 – 2.81 (m, 1H), 2.23 (s, 1H), 1.27 (s, 12H), 0.82 (d, J = 6.8 Hz, 3H). ^{13}C NMR (151 MHz, $CDCl_3$) δ 156.1, 142.5, 128.6, 128.1, 127.3, 121.2, 83.6, 78.2, 48.6, 25.1, 16.7. HRMS (ESI^+): m/z for $C_{17}H_{25}BO_3Na$ $[M+Na]^+$ calcd. 311.1794, found: 311.1805.

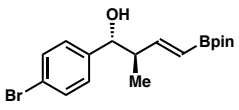


***rac*-(1*R*,2*R*,*E*)-2-methyl-4-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)-1-(*p*-tolyl)but-3-en-1-ol (3.4b)** Prepared according to the general procedure. The crude mixture was purified by column chromatography to give compound **3.4b** in 90% yield (27 mg) as colorless oil. ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.22 (d, J = 7.7 Hz, 2H), 7.15 (d, J = 7.6 Hz, 2H), 6.62 (dd, J = 18.0, 8.1 Hz, 1H), 5.62 (d, J = 18.0 Hz, 1H), 4.33 (d, J = 8.2 Hz, 1H), 2.43 – 2.72 (m, 1H), 2.34 (s, 3H), 2.08 (s, 1H), 1.28 (s, 12H), 0.81 (d, J = 6.7 Hz, 3H). ^{13}C NMR (151 MHz, $CDCl_3$) δ 156.3, 139.5, 137.8, 129.3, 127.2, 83.6, 78.0, 48.6, 25.14, 25.13, 21.5, 16.8. HRMS (ESI^+): m/z for $C_{18}H_{27}BO_3Na$ $[M+Na]^+$ calcd. 325.1951, found: 325.1959.

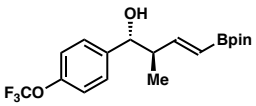


***rac*-(1*R*,2*R*,*E*)-1-([1,1'-biphenyl]-4-yl)-2-methyl-4-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)but-3-en-1-ol (3.4c)** Prepared according to the general procedure. The crude mixture was purified by column chromatography to give compound **3.4c** in 98% yield (36 mg) as colorless oil. ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.59 (d, J = 7.6 Hz, 2H), 7.57 (d, J = 8.1 Hz, 2H), 7.44 (t, J = 7.6 Hz, 2H), 7.41 (d, J = 8.0 Hz, 2H), 7.35 (t, J = 7.3 Hz, 1H), 6.64 (dd, J = 18.0, 8.1 Hz, 1H), 5.66 (d, J = 18.0 Hz, 1H), 4.42 (d, J = 8.2 Hz, 1H), 2.49 – 2.69 (m, 1H), 2.16 (d, J = 1.9 Hz, 1H), 1.29 (s, 12H), 0.87 (d, J = 6.7 Hz, 3H). ^{13}C NMR (151 MHz, $CDCl_3$) δ 156.0, 141.5, 141.1, 140.9, 129.1, 127.7, 127.6, 127.41, 127.39, 83.6, 77.89,

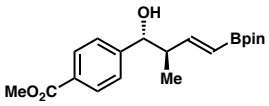
48.7, 25.1, 16.8. HRMS (ESI$^+$): m/z for $C_{23}H_{29}BO_3Na$ $[M+Na]^+$ calcd. 387.2107, found: 387.2092.



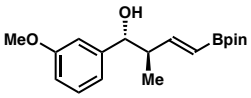
***rac*- (1*R*,2*R*,*E*)-1-(4-bromophenyl)-2-methyl-4-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)but-3-en-1-ol (3.4d)** Prepared according to the general procedure. The crude mixture was purified by column chromatography to give compound **3.4d** in 71% yield (26 mg) as colorless oil. ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.46 (d, *J* = 8.3 Hz, 2H), 7.21 (d, *J* = 8.3 Hz, 2H), 6.56 (dd, *J* = 18.0, 8.1 Hz, 1H), 5.61 (d, *J* = 18.0 Hz, 1H), 4.35 (d, *J* = 8.3 Hz, 1H), 2.29 – 2.66 (m, 1H), 1.74 (s, 1H), 1.28 (s, 12H), 0.83 (d, *J* = 6.8 Hz, 3H). ^{13}C NMR (151 MHz, $CDCl_3$) δ 155.4, 141.4, 131.7, 129.0, 121.9, 83.7, 77.43, 48.7, 25.1, 16.5. HRMS (ESI$^+$): m/z for $C_{17}H_{24}BO_3NaBr$ $[M+Na]^+$ calcd. 389.0900, found: 389.0903.



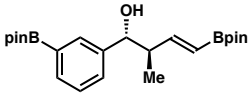
***rac*-(1*R*,2*R*,*E*)-2-methyl-4-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)-1-(4-(trifluoromethoxy)phenyl)but-3-en-1-ol (3.4e)** Prepared according to the general procedure. The crude mixture was purified by column chromatography to give compound **3.4e** in 94% yield (35 mg) as colorless oil. ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.36 (d, *J* = 8.6 Hz, 2H), 7.19 (d, *J* = 8.2 Hz, 2H), 6.57 (dd, *J* = 18.0, 8.2 Hz, 1H), 5.63 (d, *J* = 18.0 Hz, 1H), 4.39 (d, *J* = 8.2 Hz, 1H), 2.39 – 2.61 (m,1H), 2.20 (s, 1H), 1.28 (s, 12H), 0.83 (d, *J* = 6.8 Hz, 3H). ^{13}C NMR (151 MHz, $CDCl_3$) δ 155.4, 148.9, 141.1, 128.7, 121.9, 121.2, 120.7 (q, *J* = 257.2 Hz), 83.7, 77.2, 48.8, 25.1, 16.6. HRMS (ESI$^+$): m/z for $C_{18}H_{24}BO_4F_3Na$ $[M+Na]^+$ calcd. 395.1617, found: 395.1614.



***rac*-methyl 4-((1*R*,2*R*,*E*)-1-hydroxy-2-methyl-4-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)but-3-en-1-yl)benzoate (3.4f)** Prepared according to the general procedure. The crude mixture was purified by column chromatography to give compound **3.4f** in 77% yield (27 mg) as colorless oil. ^{1}H NMR (600 MHz, $CDCl_3$) δ 8.01 (d, *J* = 8.0 Hz, 2H), 7.40 (d, *J* = 8.1 Hz, 2H), 6.56 (dd, *J* = 18.0, 8.1 Hz, 1H), 5.61 (d, *J* = 18.0 Hz, 1H), 4.45 (d, *J* = 7.8 Hz, 1H), 3.91 (s, 3H), 2.39 – 2.66 (m, 1H), 2.25 (s, 1H), 1.28 (s, 12H), 0.83 (d, *J* = 6.7 Hz, 3H). ^{13}C NMR (151 MHz, $CDCl_3$) δ 167.3, 155.2, 147.6, 129.9, 129.8, 127.3, 121.9, 83.7, 77.6, 52.5, 48.6, 25.1, 16.5. HRMS (ESI$^+$): m/z for $C_{19}H_{27}BO_5Na$ $[M+Na]^+$ calcd. 369.1849, found: 369.1835.

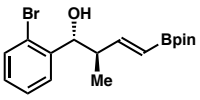


***rac*-(1*R*,2*R*,*E*)-1-(3-methoxyphenyl)-2-methyl-4-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)but-3-en-1-ol (3.4g)** Prepared according to the general procedure. The crude mixture was purified by column chromatography to give compound **1.36g** in 76% yield (24 mg) as colorless oil. ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.18 – 7.32 (m, 1H), 6.86 – 6.99 (m, 2H), 6.82 (dd, , *J* = 8.2, 1.7 Hz, 1H), 6.61 (dd, *J* = 18.0, 8.1 Hz, 1H), 5.62 (d, *J* = 18.0 Hz, 1H), 4.35 (d, *J* = 8.4 Hz, 1H), 3.81 (s, 3H), 2.47 – 2.61 (m, 1H), 2.12 (s, 1H), 1.28 (s, 12H), 0.83 (d, *J* = 6.8 Hz, 3H). ^{13}C NMR (151 MHz, $CDCl_3$) δ 159.9, 156.0, 144.2, 129.6, 119.7, 113.7, 112.4, 83.6, 78.1, 55.6, 48.5, 25.1, 16.7. HRMS (EI$^+$): m/z for $C_{18}H_{27}BO_4$ $[M]^+$ calcd. 318.2002, found: 318.2008.

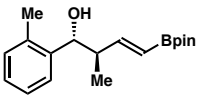


***rac*-(1*R*,2*R*,*E*)-2-methyl-4-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)-1-(3-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)phenyl)but-3-en-1-ol (3.4h)** Prepared according to the general procedure. The crude mixture was purified by

column chromatography to give compound **3.4h** in 87% yield (36 mg) as colorless oil. ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.73 (d, *J* = 8.6 Hz, 2H), 7.45 (d, *J* = 7.7 Hz, 1H), 7.36 (dd, *J* = 7.4, 7.4 Hz, 1H), 6.61 (dd, *J* = 18.0, 8.2 Hz, 1H), 5.63 (d, *J* = 18.0 Hz, 1H), 4.38 (dd, *J* = 8.5, 2.0 Hz, 1H), 2.49 – 2.70 (m, 1H), 2.10 (d, *J* = 2.3 Hz, 1H), 1.34 (s, 12H), 1.28 (s, 12H), 0.82 (d, *J* = 6.8 Hz, 3H). ^{13}C NMR (151 MHz, $CDCl_3$) δ 156.2, 141.8, 134.7, 133.6, 130.3, 128.2, 84.2, 83.6, 78.2, 48.6, 25.21, 25.17, 25.14, 16.9. HRMS (ESI^+): m/z for $C_{23}H_{36}B_2O_5Na$ $[M+Na]^+$ calcd. 437.2647, found: 437.2667.

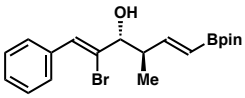


***rac*-(1*R*,2*R*,*E*)-1-(2-bromophenyl)-2-methyl-4-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)but-3-en-1-ol (3.4i)** Prepared according to the general procedure. The crude mixture was purified by column chromatography to give compound **3.4i** in 92% yield (34 mg) as colorless oil^{1}H NMR (600 MHz, $CDCl_3$) δ 7.51 (d, *J* = 7.9 Hz, 1H), 7.48 (d, *J* = 6.9 Hz, 1H), 7.33 (dd, *J* = 7.3, 7.3 Hz, 1H), 7.12 (dd, *J* = 7.4, 7.4 Hz, 1H), 6.65 (dd, *J* = 18.0, 7.8 Hz, 1H), 5.57 (d, *J* = 18.0 Hz, 1H), 4.97 (dd, *J* = 7.3, 2.9 Hz, 1H), 2.48 – 2.77 (m, 1H), 2.23 (d, *J* = 2.7 Hz, 1H), 1.27 (s, 12H), 0.97 (d, *J* = 6.9 Hz, 3H). ^{13}C NMR (151 MHz, $CDCl_3$) δ 155.2, 141.9, 132.8, 129.3, 128.7, 128.0, 123.5, 121.4, 83.6, 75.7, 47.9, 25.11, 25.10, 16.5. HRMS (ESI^+): m/z for $C_{17}H_{24}BO_3NaBr$ $[M+Na]^+$ calcd. 389.0900, found: 389.0897.

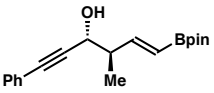


***rac*-(1*R*,2*R*,*E*)-2-methyl-4-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)-1-(*o*-tolyl)but-3-en-1-ol (3.4j)** Prepared according to the general procedure. The crude mixture was purified by column chromatography to give compound **3.4j** in 83% yield (25 mg) as colorless oil. ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.41 (d, *J* = 7.7 Hz, 1H), 7.23 (dd, *J* = 7.4, 7.4 Hz, 1H), 7.17 (dd, *J* = 7.3, 7.3 Hz, 1H), 7.13 (d, *J* = 7.4 Hz, 1H), 6.67 (dd, *J* = 18.0, 8.1 Hz,

1H), 5.64 (d, *J* = 18.0 Hz, 1H), 4.72 (dd, *J* = 8.5, 1.9 Hz, 1H), 2.53 – 2.72 (m, 1H), 2.35 (s, 3H), 2.02 (d, *J* = 2.1 Hz, 1H), 1.28 (s, 12H), 0.85 (d, *J* = 6.8 Hz, 3H). ^{13}C NMR (151 MHz, $CDCl_3$) δ 156.3, 140.7, 135.9, 130.6, 127.7, 126.7, 126.6, 121.4, 83.6, 73.5, 48.5, 25.1, 20.0, 16.5. HRMS (ESI^+): m/z for $C_{18}H_{27}BO_3Na$ $[M+Na]^+$ calcd. 325.1951, found: 325.1964.

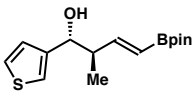


***rac*-(1*Z*,3*R*,4*R*,5*E*)-2-bromo-4-methyl-1-phenyl-6-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)hexa-1,5-dien-3-ol (3.4k)** Prepared according to the general procedure. The crude mixture was purified by column chromatography to give compound **3.4k** in 84% yield (33 mg) as white solid. ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.61 (d, *J* = 7.5 Hz, 2H), 7.37 (dd, *J* = 7.5, 7.5 Hz, 2H), 7.32 (t, *J* = 7.3 Hz, 1H), 7.02 (s, 1H), 6.64 (dd, *J* = 18.0, 7.9 Hz, 1H), 5.64 (d, *J* = 18.0 Hz, 1H), 3.97 (dd, *J* = 8.3, 5.4 Hz, 1H), 2.62 – 2.84 (m, 1H), 2.13 (d, *J* = 5.3 Hz, 1H), 1.28 (s, 12H), 1.02 (d, *J* = 6.8 Hz, 3H). ^{13}C NMR (151 MHz, $CDCl_3$) δ 154.5, 135.2, 130.6, 129.5, 128.6, 128.52, 128.49, 121.5, 83.6, 81.2, 45.0, 25.1, 16.7. HRMS (ESI^+): m/z for $C_{19}H_{26}BO_3NaBr$ $[M+Na]^+$ calcd. 415.1056, found: 415.1045.

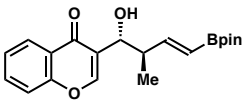


***rac*-(3*R*,4*R*,*E*)-4-methyl-1-phenyl-6-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)hex-5-en-1-yn-3-ol (3.4l)** Prepared according to the general procedure. The crude mixture was purified by column chromatography to give compound **3.4l** in 89% yield (28 mg) as colorless oil. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.37 – 7.50 (m, 2H), 7.28 – 7.37 (m, 3H), 6.63 (dd, *J* = 18.1, 7.3 Hz, 1H), 5.62 (d, *J* = 18.1 Hz, 1H), 4.48 (dd, *J* = 6.0, 6.0 Hz, 1H), 2.53 – 2.74 (m, 1H), 1.98 (d, *J* = 5.4 Hz, 1H), 1.28 (s, 12H), 1.22 (d, *J* = 6.8 Hz, 3H). ^{13}C NMR (151 MHz, $CDCl_3$) δ 154.2, 132.1, 128.8, 128.6, 123.0, 88.8, 86.4, 83.6, 66.8,

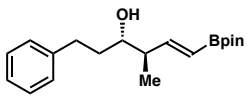
46.8, 25.2, 25.1, 15.6. HRMS (ESI$^+$): m/z for $C_{19}H_{25}BO_3Na$ $[M+Na]^+$ calcd. 335.1794, found: 335.1779.



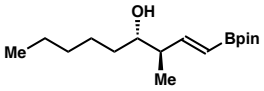
***rac*-(1*R*,2*R*,*E*)-2-methyl-4-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)-1-(thiophen-3-yl)but-3-en-1-ol (3.4m)** Prepared according to the general procedure. The crude mixture was purified by column chromatography to give compound **3.4m** in 76% yield (22 mg) as colorless oil. ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.29 (dd, *J* = 4.9, 3.0 Hz, 1H), 7.19 (d, *J* = 2.6 Hz, 1H), 7.08 (d, *J* = 4.9 Hz, 1H), 6.61 (dd, *J* = 18.0, 7.8 Hz, 1H), 5.61 (d, *J* = 18.0 Hz, 1H), 4.55 (dd, *J* = 7.9, 2.6 Hz, 1H), 2.46 – 2.71 (m, 1H), 2.04 (d, *J* = 3.0 Hz, 1H), 1.28 (s, 12H), 0.90 (d, *J* = 6.8 Hz, 3H). ^{13}C NMR (151 MHz, $CDCl_3$) δ 155.6, 144.1, 126.3, 126.2, 122.2, 83.6, 74.2, 47.9, 25.2, 16.5. HRMS (EI$^+$): m/z for $C_{15}H_{23}BO_3S$ $[M]^+$ calcd. 294.1461, found: 294.1455.



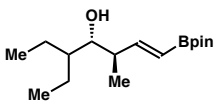
***rac*-3-((1*R*,2*R*,*E*)-1-hydroxy-2-methyl-4-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)but-3-en-1-yl)-4*H*-chromen-4-one (3.4n)** Prepared according to the general procedure. The crude mixture was purified by column chromatography to give compound **3.4n** in 98% yield (35 mg) as colorless oil. ^{1}H NMR (600 MHz, $CDCl_3$) δ 8.19 (d, *J* = 7.9 Hz, 1H), 7.87 (s, 1H), 7.69 (dd, *J* = 7.3, 7.3 Hz, 1H), 7.47 (d, *J* = 8.4 Hz, 1H), 7.42 (dd, *J* = 7.5, 7.5 Hz, 1H), 6.68 (dd, *J* = 18.1, 7.4 Hz, 1H), 5.54 (d, *J* = 18.1 Hz, 1H), 4.46 (dd, *J* = 7.3, 7.3 Hz, 1H), 3.43 (d, *J* = 7.5 Hz, 1H), 2.71 – 3.02 (m, 1H), 1.26 (s, 12H), 1.02 (d, *J* = 6.8 Hz, 3H). ^{13}C NMR (151 MHz, $CDCl_3$) δ 178.3, 156.4, 155.2, 153.7, 134.2, 126.0, 125.6, 124.2, 124.1, 120.7, 118.5, 83.5, 73.3, 45.3, 25.13, 25.08, 17.1. HRMS (ESI$^+$): m/z for $C_{20}H_{25}BO_5Na$ $[M+Na]^+$ calcd. 379.1693, found: 379.1676.



***rac*-(3*S*,4*R*,*E*)-4-methyl-1-phenyl-6-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)hex-5-en-3-ol (3.4o)** Prepared according to the general procedure. The crude mixture was purified by column chromatography to give compound **3.4o** in 78% yield (25 mg) as colorless oil. ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.24 – 7.36 (m, 2H), 7.13 – 7.24 (m, 3H), 6.53 (dd, *J* = 18.0, 7.9 Hz, 1H), 5.52 (d, *J* = 18.0 Hz, 1H), 3.38 – 3.57 (m, 1H), 2.77 – 2.94 (m, 1H), 2.55 – 2.75 (m, 1H), 2.21 – 2.45 (m, 1H), 1.78 – 1.88 (m, 1H), 1.65 – 1.77 (m, 1H), 1.57 (d, *J* = 4.4 Hz, 1H), 1.27 (s, 12H), 1.03 (d, *J* = 6.7 Hz, 3H). ^{13}C NMR (151 MHz, $CDCl_3$) δ 155.5, 142.5, 128.8, 128.7, 126.1, 83.6, 74.2, 46.6, 36.3, 32.5, 25.2, 25.1, 16.1. HRMS (ESI^+): m/z for $C_{19}H_{27}BO_2$ $[M\text{-}H_2O]^+$ calcd. 298.2104, found: 298.2116.

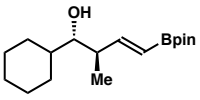


***rac*-(3*R*,4*S*,*E*)-3-methyl-1-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)non-1-en-4-ol (3.4p)** Prepared according to the general procedure. The crude mixture was purified by column chromatography to give compound **3.4p** in 82% yield (23 mg) as colorless oil. ^{1}H NMR (600 MHz, $CDCl_3$) δ 6.55 (dd, *J* = 18.1, 7.8 Hz, 1H), 5.51 (d, *J* = 18.1 Hz, 1H), 3.41 – 3.53 (m, 1H), 2.18 – 2.45 (m, 1H), 1.42 – 1.52 (m, 3H), 1.13 – 1.41 (m, 18H), 1.03 (d, *J* = 6.7 Hz, 3H), 0.88 (t, *J* = 6.5 Hz, 3H). ^{13}C NMR (151 MHz, $CDCl_3$) δ 155.7, 120.7, 83.5, 75.0, 46.2, 34.4, 32.2, 25.8, 25.2, 25.1, 23.0, 16.1, 14.5. HRMS (EI^+): m/z for $C_{16}H_{29}BO_2$ $[M–H_2O]^+$ calcd. 264.2261, found: 264.2256.

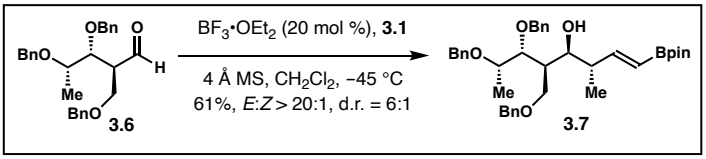


***rac*-(3*R*,4*S*,*E*)-5-ethyl-3-methyl-1-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)hept-1-en-4-ol (3.4q)** Prepared according to the general procedure. The crude mixture was purified by column chromatography to give compound **3.4q** in 83% yield (23

mg) as colorless oil. ^{1}H NMR (600 MHz, $CDCl_3$) δ 6.56 (dd, *J* = 18.0, 8.1 Hz, 1H), 5.53 (d, *J* = 18.0 Hz, 1H), 3.26 – 3.47 (m, 1H), 2.29 – 2.59 (m, 1H), 1.48 – 1.57 (m, 1H), 1.41 – 1.48 (m, 1H), 1.35 – 1.41 (m, 1H), 1.34 (d, *J* = 4.8 Hz, 1H), 1.27 (s, 14H), 1.00 (d, *J* = 6.7 Hz, 3H), 0.84 – 0.92 (m, 6H). ^{13}C NMR (151 MHz, $CDCl_3$) δ 156.5, 83.5, 75.6, 43.6, 42.9, 25.14, 25.11, 22.4, 20.4, 17.0, 12.0, 11.6. HRMS (EI^+): m/z for $C_{16}H_{29}BO_2$ $[M–H_2O]^+$ calcd. 264.2261, found: 264.2257.

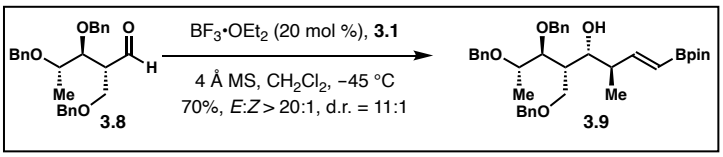


***rac*-(1*S*,2*R*,*E*)-1-cyclohexyl-2-methyl-4-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)but-3-en-1-ol (3.4r)** Prepared according to the general procedure. The crude mixture was purified by column chromatography to give compound **3.4r** in 94% yield (28 mg) as colorless oil. ^{1}H NMR (600 MHz, $CDCl_3$) δ 6.57 (dd, *J* = 18.1, 8.0 Hz, 1H), 5.51 (d, *J* = 18.1 Hz, 1H), 2.93 – 3.30 (m, 1H), 2.30 – 2.63 (m, 1H), 1.71 – 1.90 (m, 3H), 1.52 – 1.68 (m, 2H), 1.33 – 1.46 (m, 2H), 1.08 – 1.32 (m, 16H), 0.91 – 1.08 (m, 4H). ^{13}C NMR (151 MHz, $CDCl_3$) δ 155.8, 120.7, 83.5, 79.3, 42.7, 40.5, 30.3, 27.3, 26.8, 26.7, 26.4, 25.2, 25.1, 17.0. HRMS (EI^+): m/z for $C_{17}H_{29}BO_2$ $[M–H_2O]^+$ calcd. 276.2261, found: 276.2250.

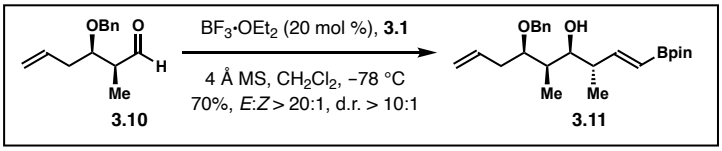


Synthesis of vinyl boronate 3.7: Prepared according to the general procedure. The crude mixture was purified by column chromatography to give compound **3.7** in 61% yield (37 mg) as colorless oil. ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.23 – 7.34 (m, 13H), 7.19 – 7.21 (m, 2H), 6.67 (dd, *J* = 18.0, 7.6 Hz, 1H), 5.48 (d, *J* = 18.1, 1H), 4.83 (d, *J* = 11.0 Hz, 1H), 4.63 (d, *J* = 11.6 Hz, 1H), 4.53 (d, *J* = 11.6 Hz, 1H), 4.49 (d, *J* = 10.9 Hz, 1H), 4.45 (d, *J* = 11.9 Hz, 1H), 4.36 (d, *J* = 12.1 Hz, 1H), 3.94 (dd, *J* = 7.1, 3.5 Hz, 1H), 3.77 – 3.81 (m, 1H), 3.74 (app. d, *J* = 8.9 Hz, 1H), 3.69

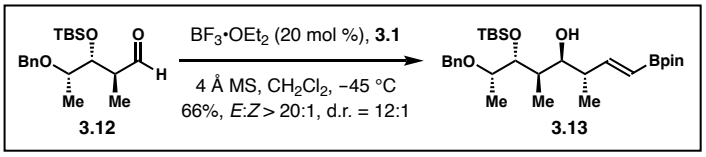
(d, J = 2.4 Hz, 1H), 3.67 (dd, J = 9.7, 7.9 Hz, 1H), 3.63 (dd, J = 9.7, 4.3 Hz, 1H), 2.36 – 2.42 (m, 1H), 2.05 – 2.08 (m, 1H), 1.24 (s, 12H), 1.18 (d, J = 6.3 Hz, 3H), 0.94 (d, J = 6.8 Hz, 3H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 157.8, 138.9, 138.7, 138.4, 128.8, 128.73, 128.72, 128.4, 128.22, 128.20, 128.1, 128.0, 127.9, 83.46, 83.34, 77.64(DEPT 135), 76.23, 74.31, 73.62, 72.06, 66.99, 43.71, 41.32, 25.17, 16.98, 16.79. HRMS (ESI$^+$): m/z for $C_{37}H_{49}BO_6Na$ $[M+Na]^+$ calcd. 623.3520, found: 623.3494.



Synthesis of vinyl boronate 3.9: Prepared according to the general procedure. The crude mixture was purified by column chromatography to give compound **3.9** in 70% yield (42 mg) as colorless oil. ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.30 – 7.34 (m, 8H), 7.24 – 7.30 (m, 7H), 6.67 (dd, J = 18.0, 7.8 Hz, 1H), 5.47 (d, J = 18.0 Hz, 1H), 4.67 (d, J = 11.0 Hz, 1H), 4.61 (d, J = 11.7 Hz, 1H), 4.47 – 4.50(m, 2H), 4.45 (d, J = 11.7 Hz, 1H), 4.39 (d, J = 11.8 Hz, 1H), 3.94 (dd, J = 5.6, 4.0 Hz, 1H), 3.92 (ddd, J = 8.7, 2.3, 2.1 Hz, 1H), 3.73 – 3.77 (m, 1H), 3.64 – 3.71 (m, 2H), 3.34 (d, J = 2.6 Hz, 1H), 2.35 – 2.41 (m, 1H), 2.21–2.24 (m, 1H), 1.30 (d, J = 6.2 Hz, 3H), 1.24 (s, 12H), 0.92 (d, J = 6.8 Hz, 3H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 157.9, 138.9, 138.5, 138.4, 128.8, 128.7(two overlapping carbon signals), 128.3, 128.2, 128.09, 128.05, 128.0, 127.9, 83.3, 82.6, 75.6, 75.0, 74.3, 73.6, 71.0, 67.5, 43.9, 41.4, 25.2, 17.2, 16.4. HRMS (ESI$^+$): m/z for $C_{37}H_{49}BO_6Na$ $[M+Na]^+$ calcd. 623.3520, found: 623.3533.



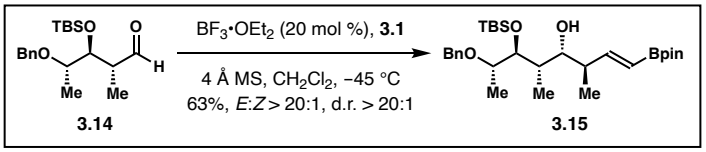
Synthesis of chiral homoallylic alcohol 3.11: Prepared according to the general procedure. The crude mixture was purified by column chromatography to give compound **3.11** in 70% yield (28 mg) as colorless oil. ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.24 – 7.35 (m, 2H), 7.15 – 7.24 (m, 3H), 6.55 (dd, *J* = 18.0, 8.0 Hz, 1H), 5.64 – 5.88 (m, 1H), 5.44 (d, *J* = 18.0 Hz, 1H), 5.07 (dd, d, *J* = 17.1, 1.5 Hz 1H), 5.02 (d, *J* = 9.6 Hz, 1H), 4.61 (d, *J* = 11.3 Hz, 1H), 4.39 (d, *J* = 11.3 Hz, 1H), 3.52 – 3.64 (m, 1H), 3.38 – 3.52 (m, 1H), 2.63 (d, *J* = 1.9 Hz, 1H), 2.40 – 2.53 (m, 1H), 2.31 – 2.39 (m, 1H), 2.24 – 2.31 (m, 1H), 1.70 – 1.89 (m, 1H), 1.20 (s, 12H), 0.92 (d, *J* = 7.0 Hz, 3H), 0.86 (d, *J* = 6.8 Hz, 3H). ^{13}C NMR (151 MHz, $CDCl_3$) δ 157.3, 138.5, 134.9, 128.8, 128.1, 128.0, 117.7, 83.4, 83.4, 77.5, 71.8, 44.2, 37.2, 35.7, 25.18, 25.15, 16.6, 7.0. HRMS (ESI^+): m/z for $C_{24}H_{37}BO_4Na$ $[M+Na]^+$ calcd. 423.2683, found: 423.2694.



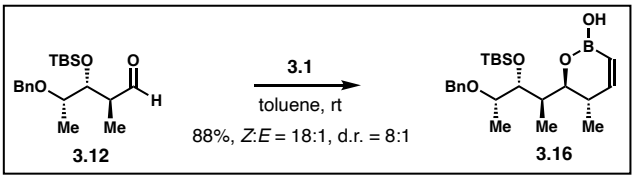
Synthesis of vinyl boronate 3.13: Prepared according to the general procedure. The crude mixture was purified by column chromatography to give compound **3.13** in 66% yield (34 mg) as colorless oil. ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.31 – 7.34 (m, 4H), 7.26 – 7.29 (m, 1H), 6.68 (dd, *J* = 18.0, 7.5 Hz, 1H), 5.51 (d, *J* = 18.0 Hz, 1H), 4.58 (d, *J* = 11.6 Hz, 1H), 4.46 (d, *J* = 11.6 Hz, 1H), 3.80 (app.d, *J* = 8.8 Hz, 1H), 3.74 (dd, *J* = 4.9, 4.4 Hz, 1H), 3.60 – 3.64 (m, 1H), 2.93 (app. s, 1H), 2.31– 2.37 (m, 1H), 1.90 – 1.95 (m, 1H), 1.26 (s, 12H), 1.22 (d, *J* = 6.2 Hz, 3H), 0.93 (d, *J* = 7.2 Hz, 3H), 0.88 – 0.90 (m, 12H), 0.09 (s, 6H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 158.0, 138.7,

128.7, 128.1, 127.9, 83.3, 80.6, 76.7, 74.8, 71.1, 43.6, 37.2, 26.5, 25.2, 18.6, 16.6, 16.2, 10.6, −3.6, −3.7.

HRMS (ESI$^+$): m/z for $C_{29}H_{51}BO_5NaSi$ $[M+Na]^+$ calcd. 541.3497, found: 541.3521.

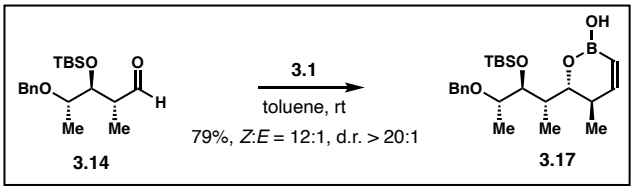


Synthesis of vinyl boronate 3.15: Prepared according to the general procedure. The crude mixture was purified by column chromatography to give compound **3.15** in 63% yield (33 mg) as colorless oil. ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.32 – 7.36 (m, 4H), 7.26 – 7.30 (m, 1H), 6.74 (dd, *J* = 18.1, 7.3 Hz, 1H), 5.53 (dd, *J* = 18.1, 0.8 Hz, 1H), 4.59 (d, *J* = 11.9 Hz, 1H), 4.50 (d, *J* = 11.9 Hz, 1H), 3.72 – 3.74 (m, 2H), 3.64 – 3.69 (m, 1H), 3.55 (app. s, 1H), 2.33 – 2.39 (m, 1H), 1.90 – 1.93 (m, 1H), 1.27 (s, 12H), 1.15 (d, *J* = 6.2 Hz, 3H), 1.05 (d, *J* = 7.1 Hz, 3H), 0.93 (d, *J* = 6.9 Hz, 3H), 0.88 (s, 9H), 0.08 (s, 3H), 0.00 (s, 3H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 158.1, 139.2, 128.6, 127.9, 127.7, 83.3, 81.7, 78.4, 74.9, 71.3, 43.3, 35.1, 26.5, 25.2, 18.7, 16.4, 15.9, 11.6, –3.7, –4.4. HRMS (ESI$^+$): m/z for $C_{29}H_{51}BO_5NaSi$ $[M+Na]^+$ calcd. 541.3497, found: 541.3513.



Synthesis of vinyl boronate 3.16: To a solution of aldehyde **3.12** (34 mg, 0.1 mmol, 1.0 equiv) in toluene (0.3 mL), Allylic boronate **3.1** (40 mg, 0.13 mmol, 1.3 equiv), was added at ambient temperature. The reaction mixture was stirred at ambient temperature for 12 h. After complete consumption of aldehyde **3.12**, Et_2O (2 mL) was added and the resulting mixture was filtered

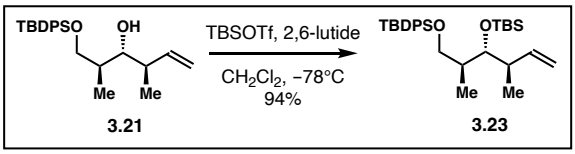
through a pad of silica gel. The solvent was removed under reduced pressure and the residue was purified by flash column chromatography (n-hexane/ethyl acetate) to give product **3.16** (37 mg, 88% yield) as a colorless oil. ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.32 – 7.36 (m, 4H), 7.25 – 7.28 (m, 1H), 6.68 (dd, *J* = 12.0, 1.6 Hz, 1H), 5.62 (dd, *J* = 12.1, 2.6 Hz, 1H), 4.55 (d, *J* = 12.3 Hz, 1H), 4.52 (d, *J* = 12.2 Hz, 1H), 4.16 (dd, *J* = 10.7, 1.8 Hz, 1H), 3.96 (dd, *J* = 9.3, 1.6 Hz, 1H), 3.81 (s, 1H), 3.61 (qd, *J* = 6.3, 1.6 Hz, 1H), 2.39 – 2.45 (m, 1H), 1.53 – 1.59 (m, 1H), 1.13 (d, *J* = 6.3 Hz, 3H), 0.97 (d, *J* = 7.2 Hz, 3H), 0.87 (s, 9H), 0.78 (d, *J* = 6.9 Hz, 3H), 0.08 (s, 3H), 0.03 (s, 3H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 159.0, 139.4, 128.6, 128.0, 127.6, 78.0, 76.6, 74.6, 70.8, 38.8, 34.7, 26.6, 18.9, 17.7, 13.1, 10.2, −3.2, −4.7. HRMS (ESI$^+$): m/z for $C_{23}H_{39}BO_4NaSi$ $[M+Na]^+$ calcd. 441.2608, found: 441.2591.



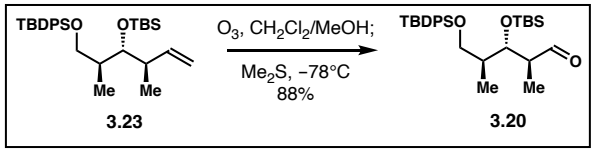
Synthesis of vinyl boronate 3.17: To a solution of aldehyde **3.14** (34 mg, 0.1 mmol, 1.0 equiv) in toluene (0.3 mL), Allylic boronate **3.1** (40 mg, 0.13 mmol, 1.3 equiv), was added at ambient temperature. The reaction mixture was stirred at ambient temperature for 12 h. After complete consumption of aldehyde **3.14**, Et_2O (2 mL) was added and the resulting mixture was filtered through a pad of silica gel. The solvent was removed under reduced pressure and the residue was purified by flash column chromatography (n-hexane/ethyl acetate) to give product **3.17** (33 mg, 79% yield) as a colorless oil. ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.32 – 7.35 (m, 4H), 7.26 – 7.28 (m, 1H), 6.69 (dd, *J* = 12.1, 1.3 Hz, 1H), 5.61 (dd, *J* = 12.1, 2.7 Hz, 1H), 4.59 (d, *J* = 12.0 Hz, 1H), 4.57 (d, *J* = 12.0 Hz, 1H), 4.04 (dd, *J* = 11.0, 1.6 Hz, 1H), 3.90 (dd, *J* = 9.4, 2.9 Hz, 1H), 3.79 (s,

1H), 3.65 (qd, *J* = 6.5, 2.9 Hz, 1H), 2.44 – 2.50 (m, 1H), 1.81 – 1.86 (m, 1H), 1.21 (d, *J* = 6.5 Hz, 3H), 0.98 (d, *J* = 7.2 Hz, 3H), 0.95 (d, *J* = 6.9 Hz, 3H), 0.85 (s, 9H), 0.02 (s, 3H), 0.01 (s, 3H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 159.4, 139.4, 128.6, 127.73, 127.68, 78.5, 78.4, 72.5, 71.1, 37.4, 34.5, 26.3, 18.5, 17.7, 14.1, 9.4, −3.9, −4.2. HRMS (ESI$^+$): m/z for $C_{23}H_{39}BO_4NaSi$ $[M+Na]^+$ calcd. 441.2608, found: 441.2588.

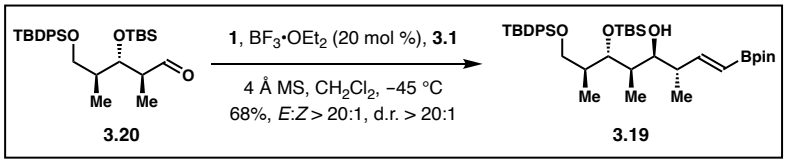
Synthesis of the C(1)–C(11) fragment of chaxamycins C and D



Synthesis of TBS ether 3.23: A 25-mL, pear-shaped flask equipped with a rubber septum and an argon inlet needle was charged with alcohol **3.21** (191 mg, 0.5 mmol, 1.0 equiv) and anhydrous CH_2Cl_2 (8 mL). The solution was cooled to −78 °C, and 2,6-lutidine (134 mg, 1.25 mmol, 2.5 equiv) was added. After 10 min, tert-butyldimethylsilyl trifluoromethanesulfonate (264 mg, 1.0 mmol, 2.0 equiv) was added at −78 °C. The reaction mixture was stirred at –78°C for 1 h. After complete consumption of alcohol **3.21**, Et_2O (5 mL) was added and the resulting mixture was filtered through a pad of silica gel. The solvent was removed under reduced pressure and the residue was purified by flash column chromatography (n-hexane/ethyl acetate) to give TBS ether **3.23** (234 mg, 94% yield) as a colorless oil. ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.64 – 7.66 (m, 4H), 7.39 – 7.42 (m, 2H), 7.35 – 7.38 (m, 4H), 5.84 – 5.90 (m, 1H), 4.88 – 4.91 (m, 2H), 3.76 (dd, *J* = 10.0, 6.0 Hz, 1H), 3.55 (dd, *J* = 5.6, 3.3 Hz, 1H), 3.42 (dd, *J* = 9.9, 7.9 Hz, 1H), 2.32 – 2.37 (m, 1H), 1.90 – 1.97 (m, 1H), 1.06 (s, 9H), 0.97 (d, *J* = 7.0 Hz, 3H), 0.90 (d, *J* = 6.9 Hz, 3H), 0.82 (s, 9H), 0.00 (s, 3H), –0.10 (s, 3H).

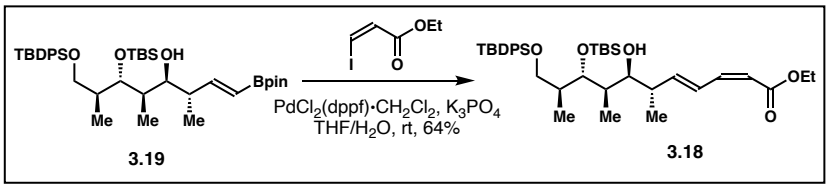


Synthesis of aldehyde 3.20: A stream of ozone in air was bubbled through a solution (initially light red, with Sudan III as the indicator) of TBS ether **3.23** (149 mg, 0.3 mmol) in dichloromethane (4 mL) and MeOH (1 mL) at −78 °C until the light red solution became colorless. The solution was sparged with nitrogen to remove any excess ozone; then dimethylsulfide (5 mL) was added at −78 °C. The reaction mixture was allowed to warm to ambient temperature and stirred for 5 h. The reaction mixture was filtrated through a pad of Celite. The solution was concentrated under reduced pressure. Purification of the crude product was performed by flash column chromatography (n-hexane/ethyl acetate), which provided aldehyde **3.20** (132 mg, 88% yield) as a colorless oil. ^{1}H NMR (600 MHz, $CDCl_3$) δ 9.77 (d, J = 2.6 Hz, 1H), 7.64 – 7.66 (m, 4H), 7.41 – 7.45 (m, 2H), 7.37 – 7.40 (m, 4H), 4.05 (dd, J = 4.9, 3.5 Hz, 1H), 3.68 (dd, J = 10.2, 7.3 Hz, 1H), 3.52 (dd, J = 10.3, 6.5 Hz, 1H), 2.52 – 2.57 (m, 1H), 2.01 – 2.07 (m, 1H), 1.11 (d, J = 7.0 Hz, 3H), 1.07 (s, 9H), 0.87 (d, J = 7.0 Hz, 3H), 0.85 (s, 9H), 0.06 (s, 3H), 0.00 (s, 3H).



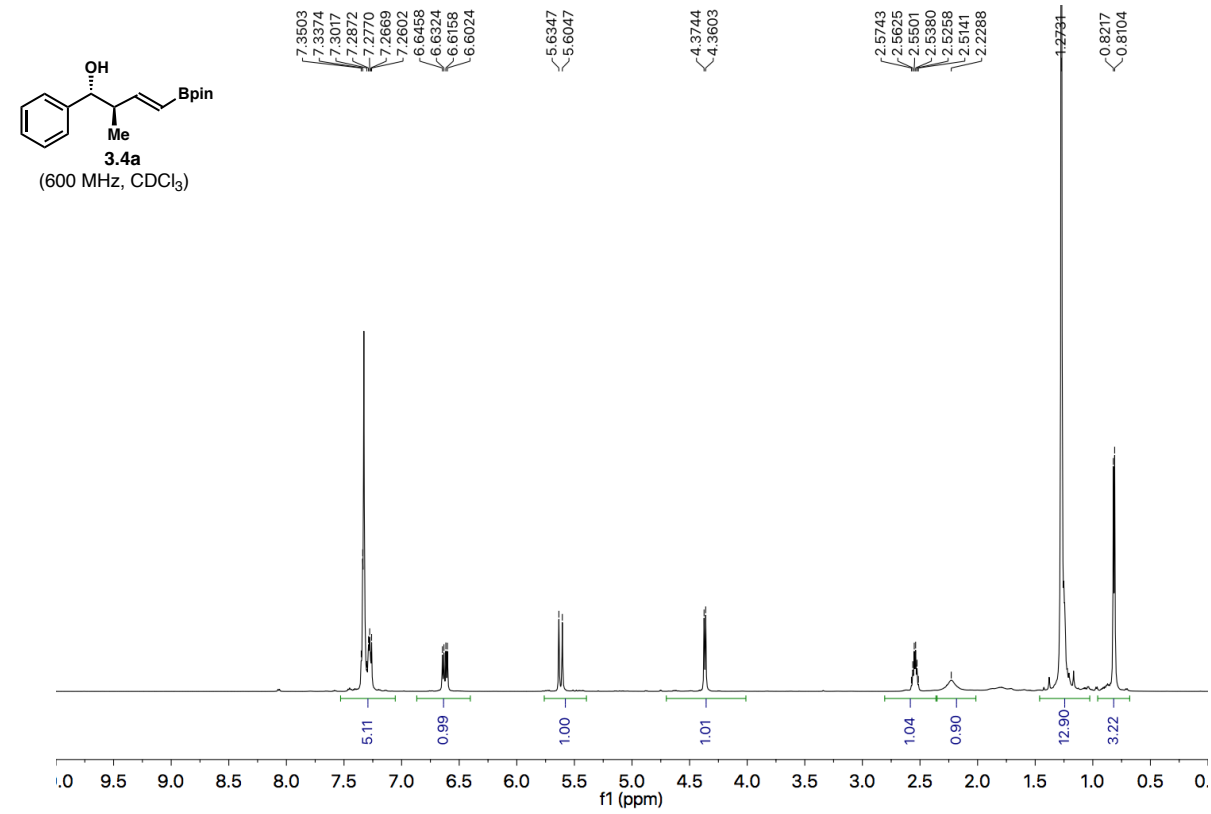
Synthesis of vinyl boronate 3.19: Prepared according to the general procedure. The crude mixture was purified by column chromatography to give compound **3.19** in 68% yield (46 mg) as colorless oil. ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.63 – 7.65 (m, 4H), 7.41 – 7.44 (m, 2H), 7.36 –

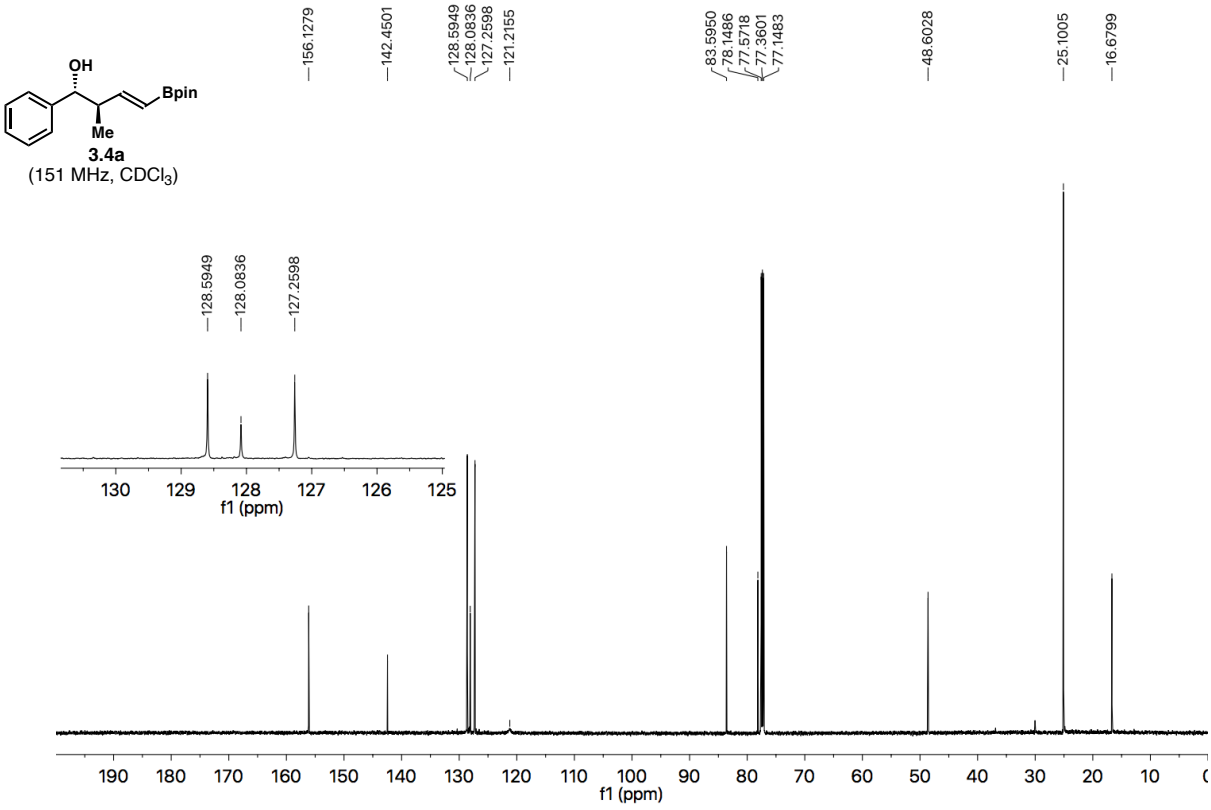
7.39 (m, 4H), 6.69 (dd, *J* = 18.1, 7.4 Hz, 1H), 5.50 (d, *J* = 18.1 Hz, 1H), 3.79 (d, *J* = 9.3 Hz, 2H), 3.71 (dd, *J* = 9.9, 6.3 Hz, 1H), 3.45 (dd, *J* = 9.9, 7.4 Hz, 1H), 3.29 (s, 1H), 2.26 – 2.33 (m, 1H), 2.07 – 2.15 (m, 1H), 1.81 – 1.85 (m, 1H), 1.25 (s, 12H), 1.06 (s, 9H), 0.97 (d, *J* = 7.1 Hz, 3H), 0.93 (d, *J* = 7.0 Hz, 3H), 0.85 (d, *J* = 6.9 Hz, 3H), 0.81 (s, 9H), 0.06 (s, 3H), –0.07 (s, 3H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 158.3, 136.0(two overlapping carbon signals), 134.1, 134.0, 130.02, 129.96, 128.02, 127.99, 83.3, 80.3, 74.9, 66.7, 43.4, 41.0, 35.0, 27.3, 26.5, 25.21, 25.18, 19.6, 18.5, 16.6, 13.9, 12.3, –3.5, –4.0. HRMS (ESI$^+$): m/z for $C_{39}H_{66}BO_5Si_2$ $[M+H]^+$ calcd. 681.4542, found: 681.4532.



Synthesis of compound 3.18: In an Ar-filled glove box, $PdCl_2(dppf)\cdot CH_2Cl_2$ (4 mg, 0.005 mmol, 10 mol %), K_3PO_4 (28 mg, 0.13 mmol, 2.6 equiv), THF (0.5 mL), vinylboronate **3.19** (34 mg, 0.05 mmol, 1.0 equiv), and a Teflon-coated magnetic stirring bar were sequentially added into a 1-dram vial. The vial was sealed with a rubber septum and removed from glove box. Then vinyl iodide (16 mg, 0.07 mmol, 1.3 equiv) and 50 µL H_2O were added to the mixture under argon. The reaction was kept stirring at ambient temperature for 48 h. After complete consumption of boronate **3.19**, Et_2O (2 mL) was added and the resulting mixture was filtered through a short pad of Celite. Brine (5 mL) and Et_2O (1 mL) were added to the filtrate, the organic layer was separated, and the aqueous layer was extracted with Et_2O (3 x 1 mL). The combined organic layers were dried over anhydrous magnesium sulfate, filtered, and concentrated under reduced pressure. Purification of the crude product was performed by flash chromatography to provide

product **3.18** in 64% yield (21 mg) as colorless oil. ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.63 – 7.65 (m, 4H), 7.40 – 7.44 (m, 3H), 7.35 – 7.39 (m, 4H), 6.59 (dd, *J* = 11.8, 11.3 Hz, 1H), 6.22 (dd, *J* = 15.5, 7.4 Hz, 1H), 5.56 (d, *J* = 11.4 Hz, 1H), 4.18 (q, *J* = 7.1 Hz, 2H), 3.81 (dd, *J* = 6.8, 2.5 Hz, 1H), 3.76 (dd, *J* = 9.2, 1.2 Hz, 1H), 3.72 (dd, *J* = 10.0, 6.4 Hz, 1H), 3.45 – 3.48 (m, 2H), 2.38 – 2.44 (m, 1H), 2.09 – 2.16 (m, 1H), 1.84 – 1.88 (m, 1H), 1.29 (t, *J* = 7.1 Hz, 3H), 1.06 (s, 9H), 0.99 (d, *J* = 7.1 Hz, 3H), 0.95 (d, *J* = 7.0 Hz, 3H), 0.92 (d, *J* = 6.8 Hz, 3H), 0.82 (s, 9H), 0.07 (s, 3H), –0.06 (s, 3H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 167.0, 149.4, 145.9, 136.0(two overlapping carbon signals), 134.01, 133.99, 130.04, 130.00, 128.02, 128.00, 126.6, 116.1, 80.5, 75.7, 66.7, 60.2, 41.0, 40.8, 35.0, 27.3, 26.4, 19.6, 18.5, 16.4, 14.7, 13.9, 12.4, –3.50, –4.0. HRMS (ESI^+): m/z for $C_{38}H_{61}O_5Si_2$ $[M+H]^+$ calcd. 653.4058, found: 653.4080.


OH
Bpin
Me
3.4a
(600 MHz, CDCl3)
7.3503
7.3374
7.3017
7.2872
7.2770
7.2669
7.2602
6.6458
6.6324
6.6158
6.6024
5.6347
5.6047
4.3744
4.3603
2.5743
2.5625
2.5501
2.5380
2.5258
2.5141
2.2288
1.2731
0.8217
0.8104
5.11
0.99
1.00
1.01
1.04
0.90
12.90
3.22
f1 (ppm)


OH
Bpin
Me
3.4a
(151 MHz, CDCl3)
156.1279
142.4501
128.5949
128.0836
127.2598
121.2155
83.5950
78.1486
77.5718
77.3601
77.1483
48.6028
25.1005
16.6799
f1 (ppm)

Chapter Four

1,2-Bifunctional allylboron reagent

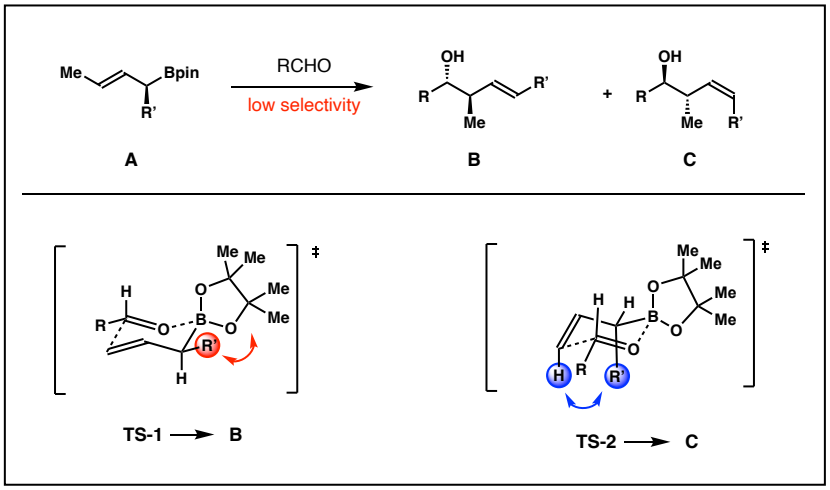
Carbonyl addition with chiral nonracemic α-substituted crotyl metal reagents is a valuable method to synthesize homoallylic alcohols with high enantiopurity.[165,166] Compared to the well developed crotylation chemistry that generates homoallylic alcohols with a terminal alkene unit, crotylation with an α-substituted crotyl metal reagent forms alcohol products with a functionalized olefin. However, the majority of α-substituted crotyl organometallic reagents lack stability owing to the facile reversible 1,3-metallo shifts. By contrast, α-substituted crotylboronate reagents (e.g., **A**) are stable and will not participate in 1,3-boratropic shifts at ambient temperature.[167] The reactions with such boron reagents proceed through the well-defined, cyclic Zimmerman-Traxler transition state. In addition, other attractive features of these boronate reagents are their low toxicities in general, and remarkable stabilities toward oxygen and moisture.

Several challenges are present for developing asymmetric allylation chemistry with α-substituted crotylboronates.[8] First, such boron reagents are chiral, and their enantioselective syntheses, particularly in a practical and efficient manner, are often difficult.[29,168-174] Because the reactions with these reagents proceed via chirality transfer, the enantiomeric excess of the boron reagents will dictate the enantiopurity of the products. Therefore, to be more synthetically relevant, it is critically important to synthesize such reagents in a highly enantioenriched form.

Another challenge in asymmetric reactions with α-substituted crotylboronates is the stereochemical control of the reactions.[175-177] As shown in Scheme **4.1**, the reaction of an aldehyde with α-substituted crotylboronate **A** proceeds with two competing transition states, **TS-**

1 and **TS-2**. Product **B** with *E*-olefin geometry is formed via **TS-1** with the α-substituent occupying a pseudo equatorial position. This transition state typically suffers gauche interactions between the pseudo equatorially oriented R' group and the pinacol unit of boronate **A**. In the competing transition state **TS-2** that forms product **C** with *Z*-olefin geometry, the α-substituent was placed in a pseudo axial position. As such, nonbonding $A^{1,3}$ allylic stain is developed between the H atom and the axially oriented R' group. In general, the energies of these two competing transition states are close to each other when the α-substituent R' is an alkyl group. The reactions often generate a mixture of two products, **B** and **C**, with low selectivities (~1:2 in many cases). Therefore, properly controlling the orientation of the α-substituent of reagent **A** in the reaction transition state is the key to achieve high stereoselectivity of the reaction.

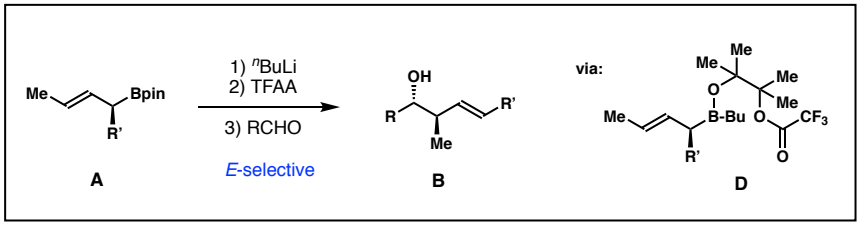
Scheme 4.1. Asymmetric aldehyde addition with enantioenriched α-substituted-(*E*)-crotylboronates



The Aggarwal group disclosed an elegant solution for highly *E*-selective asymmetric allylation with α-substituted crotylboronates.[178,179] As shown in **Scheme 4.2**, by using a three-

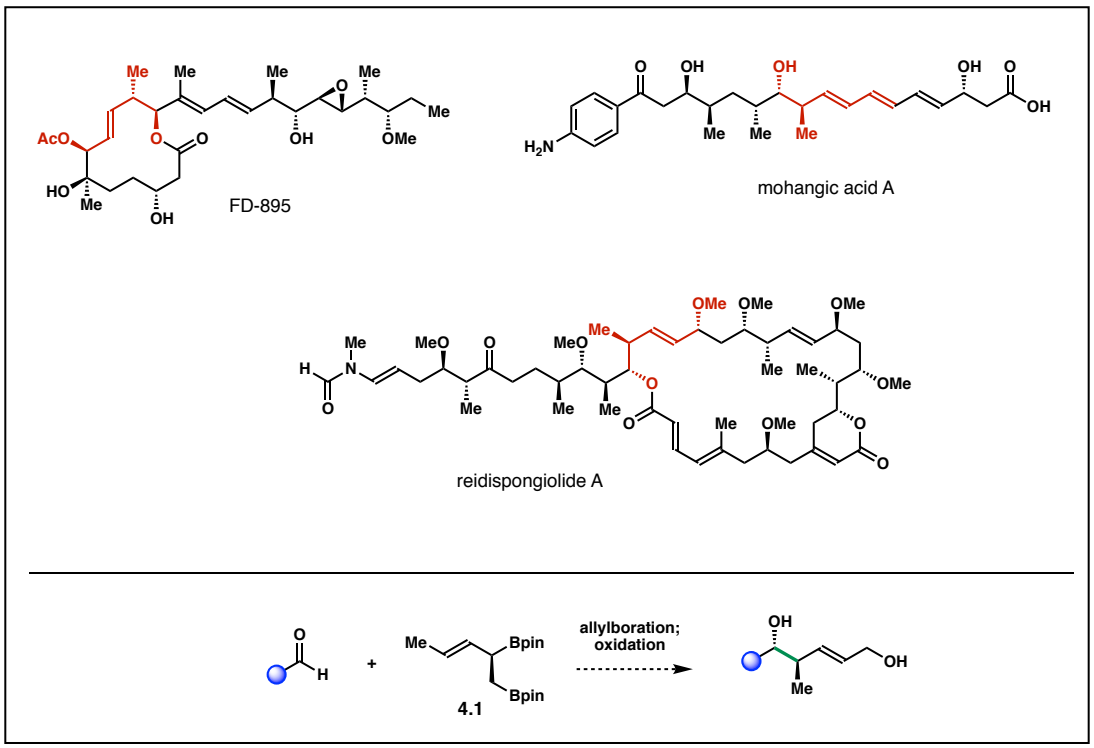
step reaction sequence, δ-substituted homoallylic alcohols **B** were obtained with high *E*-selectivity from reagent **A**. The reaction proceeded via the intermediacy of allylborinate **D** that is substantially more reactive than allylboronates. More importantly, the acyclic nature of allylborinate **D** is structurally flexible, which permits the α-substituent (R' group) of reagent **A** to adopt a pseudo equatorial position with minimal steric repulsion. Consequently, alcohol product **B** was obtained with high *E*-selectivity from reagent **A** using this protocol.

Scheme 4.2. Previous Asymmetric Aldehyde Addition with Enantioenriched α -Substituted-(*E*)-crotylboronates



As part of our ongoing program in organoboron chemistry, we envisioned the *E*-selective aldehyde allylation with α-borylmethyl substituted crotylboronate **4.1** to deliver homoallylic alcohols with high *E*-selectivity and enantioselectivity (bottom panel, **Figure 4.1**). When enantioenriched aldehyde substrates are employed, allylation products can be obtained with excellent *E*-selectivities and diastereoselectivities. Moreover, the reactions with crotylboronate **4.1** generate homoallylic alcohol products (upon oxidative workup) bearing a hydroxymethyl-substituted alkene group that can be used for further C-C bond-forming reactions. The method enables rapid construction of valuable intermediates for the syntheses of bioactive natural products (**Figure 4.1**).

Figure 4.1. Selective bioactive natural products and designed synthetic strategy

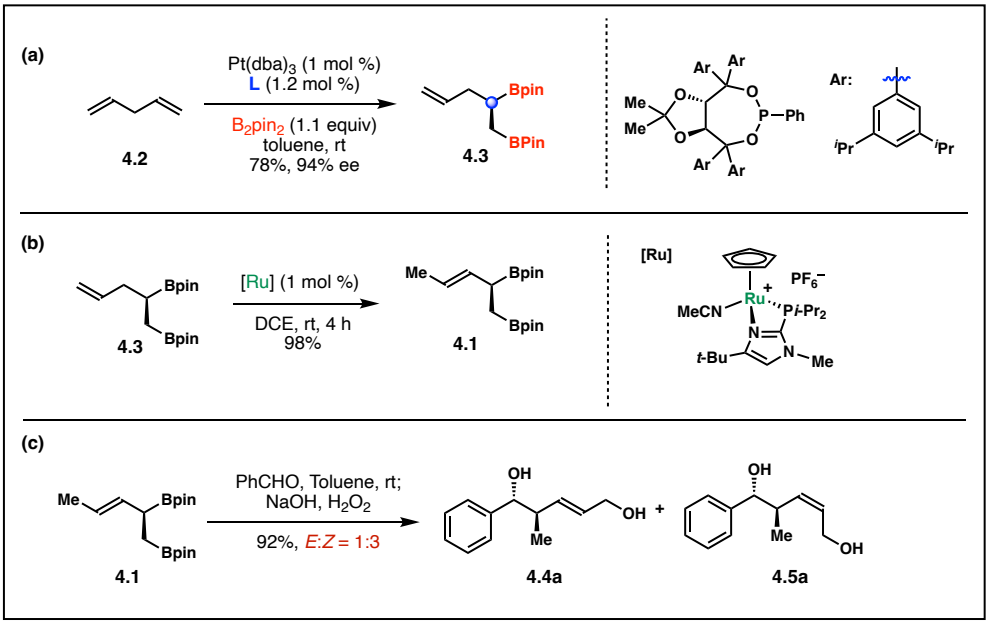


4.1 Enantioselective Synthesis of α-Borylmethyl-(*E*)-crotylboronate 1 and Initial Allylboration Studies

Enantioselective synthesis of α-borylmethyl substituted crotylboronate **4.1** is depicted in Scheme **4.3**. Starting from commercially available 1,4-pentadiene **4.2**, asymmetric diboration of one alkene group gave diboronate **4.3** in 90% yield with 94% ee.[180,181] Subsequent Ru-catalyzed alkene transposition gave the desired reagent **4.1** in 97% yield with >50:1 *E*-selectivity.[182] The enantiopurity of intermediate **4.3** was perfectly transferred to reagent **4.1** in the alkene transposition process. After securing reagent **4.1**, we conducted the reaction of benzaldehyde with **4.1** to assess the inherent *E*/*Z* selectivity of the allylation. As shown in **Scheme 4.3**, the

reaction of **4.1** with benzaldehyde in the absence of any catalyst gave a 1:3 mixture of **4.4a** and **4.5a** in a combined 92% yield, with *Z*-isomer **4.5a** as the major product. The data indicate a 3:1 pseudoaxial preference of the α-CH_2Bpin group of reagent **4.1** in the allylation transition state.

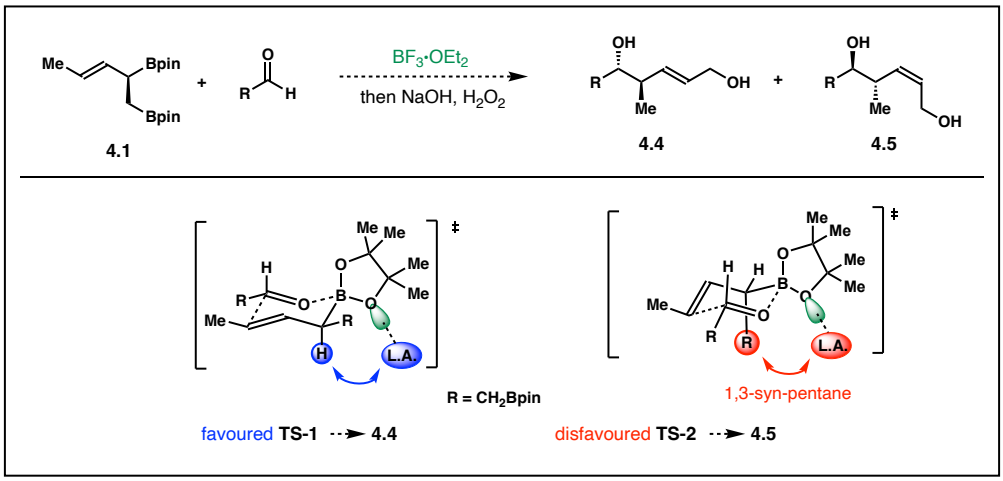
Scheme 4.3. Preparation of enantioenriched α-borylmethyl substituted crotyl-boronates



To achieve *E*-selective allylation, it is imperative to bias the reaction kinetics such that the transition state with α-CH_2Bpin group occupying a pseudo equatorial position is favored. On the basis of the work discussed in **Chapter 3**, we envisaged a Lewis acid-catalyzed allylation approach to achieve *E*-selective allyl addition with reagent **4.1**. As depicted in Scheme **4.4**, we anticipated that the Lewis acid catalyst should coordinate to the most accessible lone pair of electrons of the oxygen atoms (shown in green in **Scheme 4.4**). In **TS-2** that leads to product **4.5**, 1,3-*syn*-pentane interactions are developed between the pseudo axially positioned CH_2Bpin group and the catalyst (shown with a red arrow in **TS-2**). In contrast, such 1,3-*syn*-pentane

interactions in transition state **TS-1** are substantially minimized because only a small hydrogen atom occupies the pseudo axial position (shown with a blue arrow in **TS-1**). Although gauche interactions between the CH_2Bpin group and the pinacol moiety are present in **TS-1**, such gauche interactions should be weaker compared to the 1,3-*syn*-pentane interactions in **TS-2**. Consequently, it is anticipated that Lewis acid-catalyzed allylation with boron reagent **4.1** should proceed via the more favorable transition state **TS-1** to form alcohol **4.4** with *E*-alkene geometry selectively.

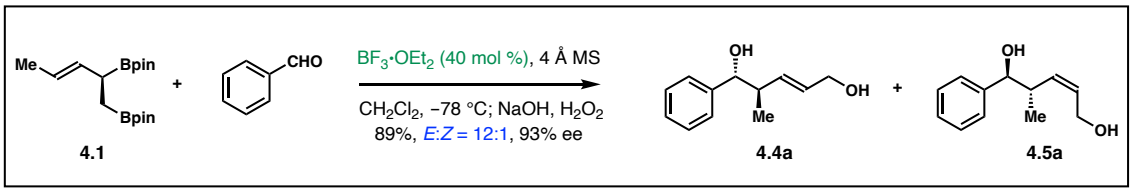
Scheme 4.4. Transition State Analyses for BF_3•OEt_2- Catalyzed *E*-Selective Allylboration with Reagent 4.1



In the event, Lewis acid BF_3•OEt_2 was selected as the catalyst to evaluate *E*-selective allylation of benzaldehyde with α-boryl-(*E*)-crotylboronate **4.1**. As shown in **Scheme 4.5**, in the presence of 4 Å molecular sieves and 40 mol % BF_3•OEt_2, the reaction of benzaldehyde with crotylboronate **4.1** at −78 °C provided *E*-adduct **4.4a** in 89% yield with 12:1 *E*-selectivity. The data support our analysis that the added Lewis acid catalyst can control the stereochemical

outcomes of the reaction. By positioning the α-CH_2Bpin group in a pseudo equatorial position in the favored reaction transition state **TS-1**, *E*-isomer **4.4a** was generated with good selectivity.

Scheme 4.5. Initial study on BF3•OEt_2- Catalyzed *E*-Selective Allylboration

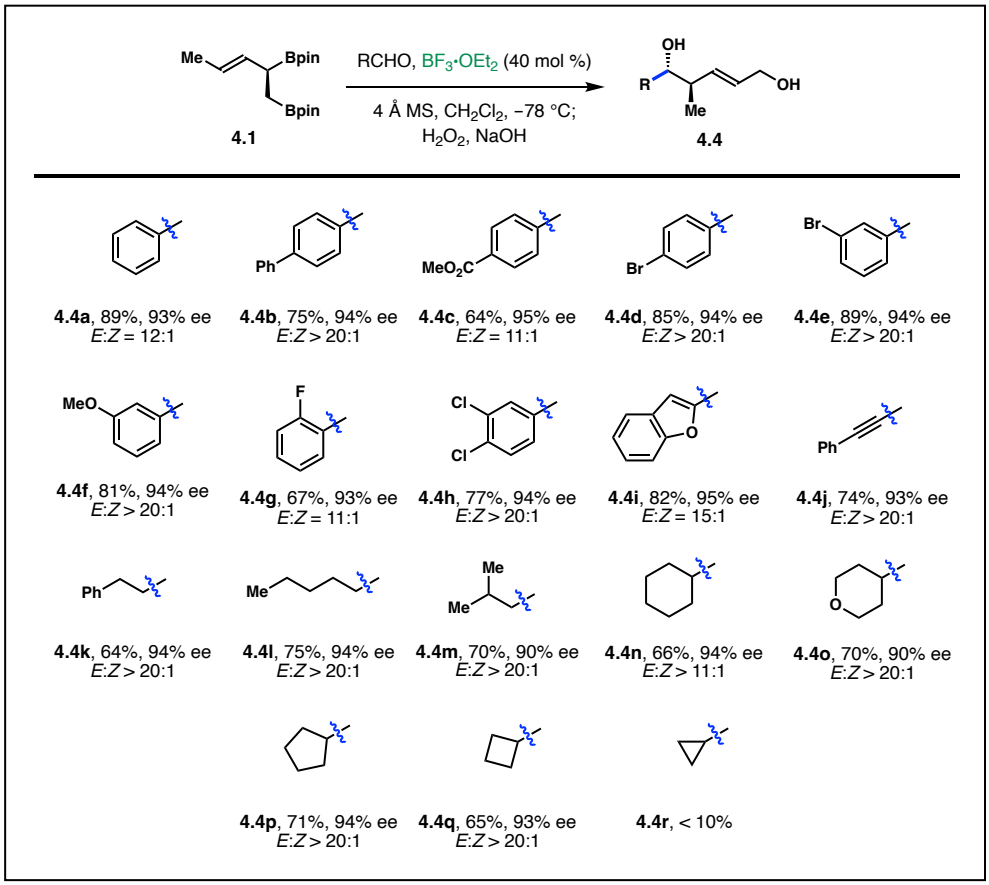


4.2 Asymmetric syntheses of (*E*)-δ-hydroxymethyl-*anti*-homoallylic alcohols

The scope of aldehyde that underwent BF_3•OEt_2-catalyzed *E*-selective allylation with crotylboronate **4.1** is summarized in **Scheme 4.6**. Under the developed reaction conditions, a wide array of aldehydes with diverse electronic properties participated in the reaction to give (*E*)-δ-hydroxymethyl-*anti*-homoallylic alcohols **4.4** in good yields with high *E*-selectivities. Aromatic aldehydes with a substituent at the para-position reacted with reagent **4.1** to afford products **4.4b-d** in 64-85% yields with 11-20:1 *E*-selectivities and 94-95% ee. Reactions of aromatic aldehydes with diverse substituents at the meta- or ortho-position proceeded smoothly to form alcohols **4.4e-h** in 67-89% yields with 11-20:1 *E*-selectivities and 93-94% ee. The reaction conditions also tolerate α, β-unsaturated aldehydes and aldehydes that contain a heterocycle; and alcohols **4.4i-j** were produced in 74-82% yields with 15-20:1 *E*-selectivities and 93-95% ee. Importantly, BF_3•OEt_2-catalyzed reactions of crotylboronate **4.1** with a variety of aliphatic aldehydes delivered products **4.4k-q** in 64-75% yields with 11-20:1 *E*-selectivities and

90-94% ee. It is interesting to note that the reaction with cyclopropyl aldehyde formed a complex mixture, with product **4.4r** in <10% yield.

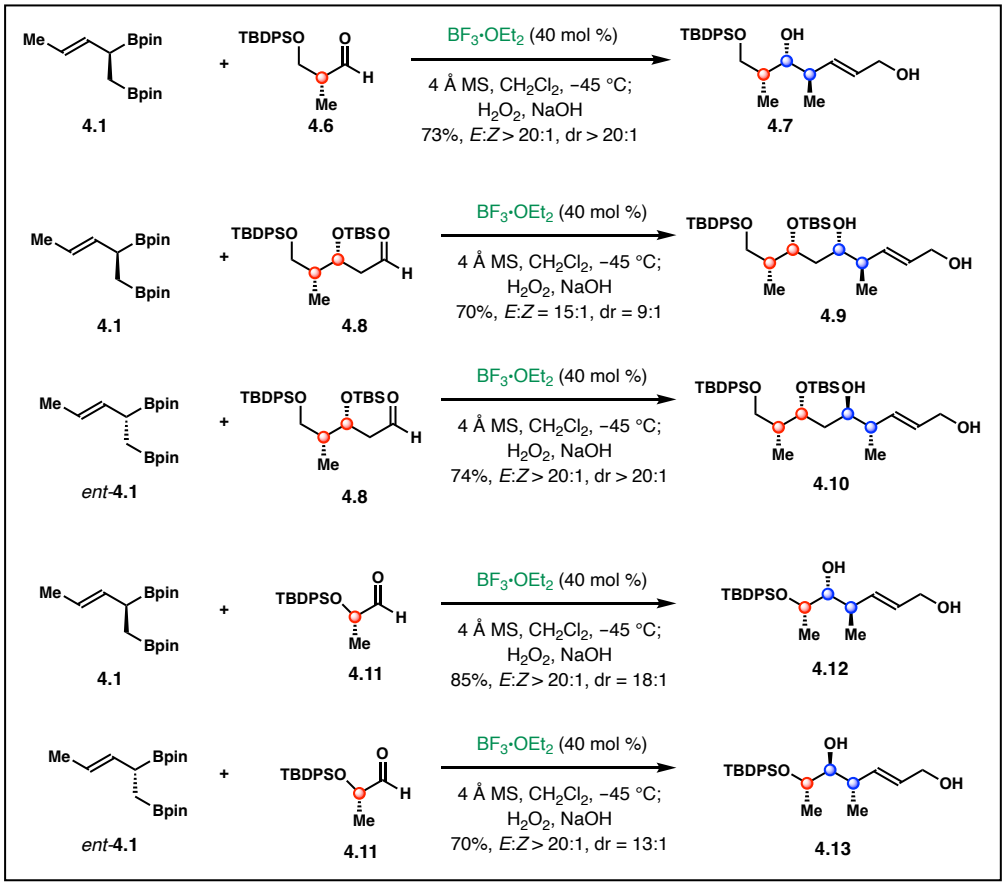
Scheme 4.6. Scope of BF_3•OEt_2-Catalyzed *E*-Selective Allylation



To investigate whether the allylation process could be employed in double stereodifferentiation reactions[183-184] to generate allylated products diastereoselectively while maintaining high *E*-selectivities, the reactions of several chiral, nonracemic aldehydes with boronate **4.1** were conducted. The reaction rates were quite slow at −78 °C with 40 mol % BF_3•OEt_2. Therefore, the reactions with the chiral aldehydes were conducted at −45 °C. As

shown in **Scheme 4.7**, the reaction of aldehyde **4.6** with crotylboronate **4.1** generated product **4.7** in 73% yield with >20:1 *E*-selectivity and diastereoselectivity. Formation of any product with *Z*-olefin geometry was not detected. The reaction of aldehyde **4.8** under the same conditions gave product **4.9** in 70% yield with 15:1 *E*-selectivity and 9:1 diastereoselectivity. When the enantiomeric reagent *ent*-**4.1** was used, product **4.10** was obtained in 74% yield with >20:1 *E*-selectivity and diastereoselectivity. In the case of lactate-derived aldehyde **4.11**, the reaction with reagent **4.1** afforded product **4.12** in 85% yield with >20:1 *E*-selectivity and 18:1 diastereoselectivity. Similar results were obtained from the reaction between **4.11** and reagent *ent*-**4.1**; adduct **4.13** was isolated in 70% yield with >20:1 *E*-selectivity and 13:1 diastereoselectivity.

Scheme 4.7. BF_3•OEt_2-Catalyzed E-Selective Diastereoselective Allylation with Enantioenriched Aldehydes

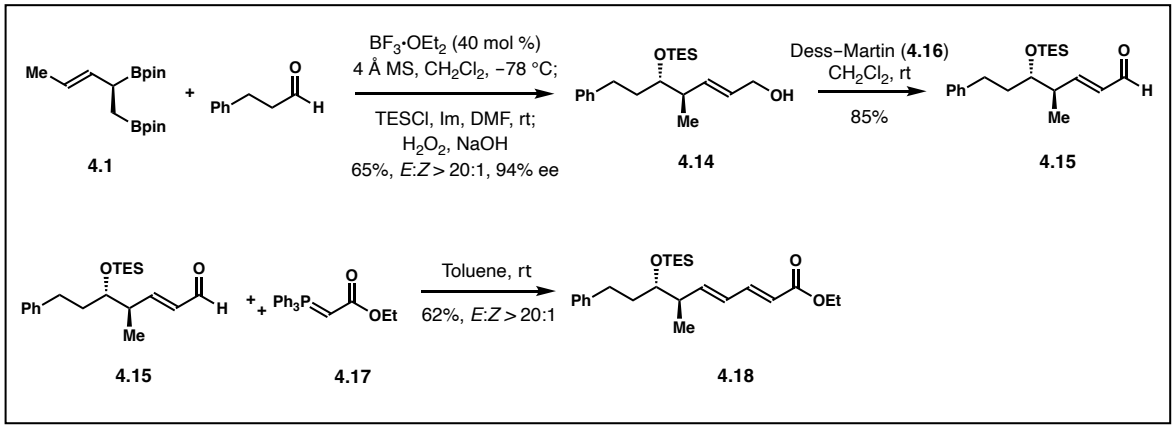


4.3 Transformations of (*E*)-δ-hydroxymethyl-*anti*-homoallylic alcohols

The products obtained under standard reaction conditions are diols. By slightly modifying the reaction conditions, mono-protected diols can be obtained. As shown in **Scheme 4.8**, the reaction of hydrocinnamic aldehyde with reagent **4.1** was conducted under the BF_3•OEt_2-catalyzed reaction conditions. After completion of the reaction, TESCl and imidazole were added before final oxidative workup. This reaction sequence generated mono-protected diol **4.14** in 65% yield. Dess-Martin oxidation of **4.14** delivered aldehyde **4.15** in 85% yield. Aldehyde **4.15** is a

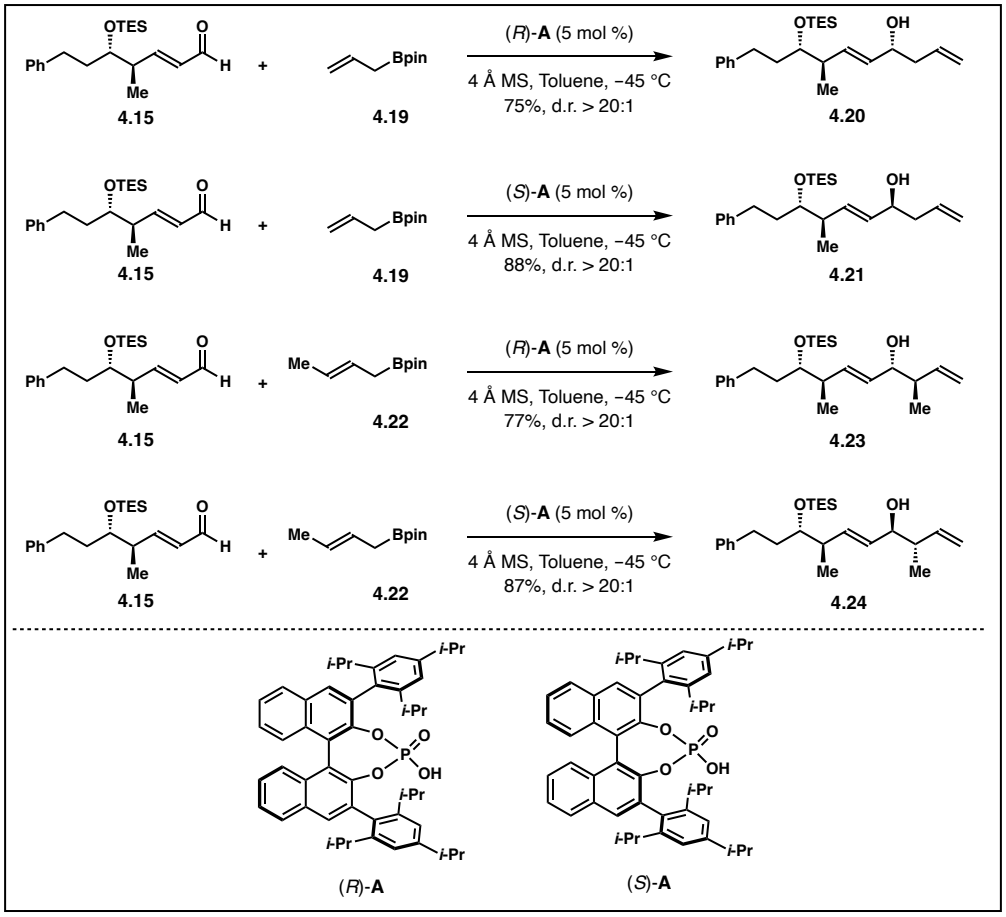
versatile intermediate for further derivatization. For example, Wittig olefination of aldehyde **4.15** with reagent **4.17** afforded ester **4.18** in 62% yield with excellent *E*-selectivity.

Scheme 4.8. Synthesis of aldehyde 13 and subsequent Wittig reaction



With 5 mol % of chiral phosphoric acid (*R*)-**A** as the catalyst,[97-124] allylation of aldehyde **4.15** with allylboronate **4.19** formed product **4.20** in 75% yield with >20:1 diastereoselectivity. When the enantiomeric catalyst (*S*)-**A** is employed, the reaction generated product **4.21** in 88% yield with >20:1 diastereoselectivity. Similar results were observed in asymmetric crotylation with reagent **4.22**. Products **4.23** and **4.24** were obtained in 77-87% yields with >20:1 diastereoselectivities. The results summarized in **Schemes 4.8** and **4.9** highlight the synthetic potential of the method in rapid generation of valuable stereochemically rich intermediates for complex molecule synthesis.

Scheme 4.9. Enantioselective aldehyde allylboration of aldehyde 4.15

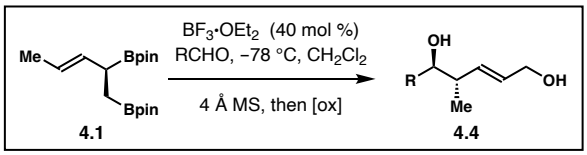


4.4 Conclusion

we developed a Lewis acid-catalyzed highly *E*-selective allylboration with α-borylmethyl-(*E*)-crotylboronate. In the presence of the BF_3•OEt_2 catalyst, aldehyde addition with the boron reagent delivered δ-hydroxymethyl-*anti*-homoallylic alcohols with high *E*-selectivities and enantioselectivities. The reactions with several enantioenriched aldehydes also proceeded to give allylated products with high *E*-selectivities and diastereoselectivities. The homoallylic alcohol products generated from the reactions (upon oxidative workup) contain a hydroxymethyl-substituted alkene group that can be used for further C-C bond-forming reactions.

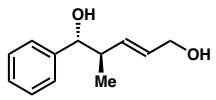
4.5 Experimental Section

$BF_3.OEt_2$-catalyzed E-selective allylation

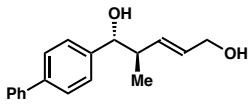


General procedure for crotylboration of aldehydes with reagent 4.4: To a reaction flask containing a stirring bar, crotylboronate **4.1** (48 mg, 0.15 mmol, 1.5 equiv), freshly activated 4 Å MS (25 mg) and dichloromethane (0.4 mL) were added. The mixture was placed in a −78 ºC dry ice/acetone bath. Then freshly prepared solution of BF_3•OEt_2 (0.8 M in DCM, 50 µL, 0.04 mmol, 0.4 equiv) was added to the reaction mixture *via* a microliter syringe at −78 ºC. The mixture was kept at −78 ºC and stirred for 20 min. Then freshly distilled aldehydes (0.1 mmol, 1.0 equiv, if it is a liquid) were dissolved in dichloromethane (0.2 mL) and added slowly to the flask. The reaction mixture was kept stirring at −78 ºC. After complete consumption of the aldehyde, 3N NaOH (0.5 mL) was added to the reaction mixture followed by slow addition of 30% H_2O_2 (0.5 mL) at 0 ºC. The reaction was stirred vigorously for 3 h; then diethyl ether (1 mL) and brine (1 mL) were added. The organic layer was separated and the aqueous layer was extracted with ethyl acetate (2 mL x 3). The combined organic extracts were filtered through a pad of silica gel and concentrated under reduced pressure. The crude reaction product was dissolved in Et_2O (1.0 mL), followed by addition of water (1.0 mL) and $NaIO_4$ (107 mg, 0.5 mmol, 5.0 equiv). The resulting mixture was stirred at ambient temperature for 2 h. Brine (1 mL) and ethyl acetate (0.5 mL) were added; the organic layer was separated and the aqueous layer was extracted with ethyl acetate (3 x 1 mL). The combined organic layers were dried over anhydrous sodium sulfate, filtered, and

concentrated under reduced pressure. Purification of the crude product was performed by flash chromatography to give diol **4.4**.

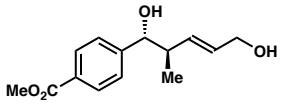


(4*R*,5*R*,*E*)-4-methyl-5-phenylpent-2-ene-1,5-diol (4.4a) Prepared according to the general procedure. The crude mixture was purified by column chromatography to give the title compound as colorless oil in 89% yield (17 mg, *E*:*Z* = 12:1). Enantiomeric excess was determined by HPLC analysis to be 93% ee (254 nm, 25 ˚C); t_1 = 10.6 min, t_2 = 11.7 min [(Chiralpak IA) hexane/i-PrOH, 90:10, 1.0 mL/min]; $[\alpha]_D^{20}$ = +114.9˚ (c 0.75, $CHCl_3$); ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.31 – 7.36 (m, 4H), 7.26 – 7.30 (m, 1H), 5.79 (dt, *J* = 15.6, 5.2 Hz, 1H), 5.72 (dd, *J* = 15.5, 7.9 Hz, 1H), 4.38 (d, *J* = 7.8 Hz, 1H), 4.16 (d, *J* = 5.5 Hz, 2H), 2.48 – 2.54 (m, 1H), 1.57 (brs, 2H), 0.88 (d, *J* = 6.8 Hz, 3H). ^{13}C NMR (151 MHz, $CDCl_3$) δ 142.9, 134.8, 131.5, 128.6, 128.1, 127.1, 78.7, 63.8, 45.0, 17.3. HRMS (ESI^+): *m*/*z* for $C_{12}H_{16}O_2Na$ $[M+Na]^+$ calcd. 215.1048, found 215.1039.

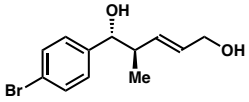


(4*R*,5*R*,*E*)-5-([1,1'-biphenyl]-4-yl)-4-methylpent-2-ene-1,5-diol (4.4b) Prepared according to the general procedure. The crude mixture was purified by column chromatography to give the title compound as colorless oil in 75% yield (20 mg, *E*:*Z* > 20:1). Enantiomeric excess was determined by HPLC analysis to be 94% ee (254 nm, 25 ˚C); t_1 = 12.9 min, t_2 = 15.2 min [(Chiralpak IA) hexane/i-PrOH, 90:10, 1.0 mL/min]; $[\alpha]_D^{20}$ = +119.1˚ (c 1.15, $CHCl_3$); ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.57 – 7.61 (m, 4H), 7.42 – 7.45 (m, 2H), 7.39 – 7.41 (m, 2H), 7.33 – 7.36 (m, 1H), 5.82 (dt, *J* = 15.8, 5.3 Hz, 1H), 5.75 (dd, *J* = 15.5, 7.9 Hz, 1H), 4.44 (d, *J* = 7.8 Hz, 1H), 4.18 (d, *J* = 5.5 Hz, 2H), 2.53 – 2.59 (m, 1H), 1.52 (brs, 2H), 0.94 (d, *J* = 6.8 Hz, 3H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 141.9, 141.2, 141.0, 134.6, 131.6, 129.1,

127.64, 127.58, 127.41, 127.39, 78.4, 63.8, 45.0, 17.3. HRMS (ESI$^+$): *m*/*z* for $C_{18}H_{20}O_2Na$ $[M+Na]^+$ calcd. 291.1361, found 291.1374.

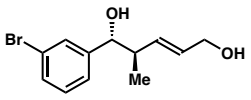


Methyl 4-((1*R*,2*R*,*E*)-1,5-dihydroxy-2-methylpent-3-en-1-yl) benzoate (4.4c) Modified procedure: $NaBO_3$•$4H_2O$ (31 mg, 0.2 mmol, 2.0 equiv) were used for the oxidation step. The crude mixture was purified by column chromatography to give the title compound as colorless oil in 64% yield (16 mg, *E*:*Z* = 11:1). Enantiomeric excess was determined by HPLC analysis to be 95% ee (254 nm, 25 ˚C); t_1 = 9.12 min, t_2 = 12.4 min [(Chiralpak ID) hexane/i-PrOH, 80:20, 1.0 mL/min]; $[\alpha]_D^{20}$ = –2.2˚ (c 1.20, $CHCl_3$); ^{1}H NMR (600 MHz, $CDCl_3$) δ 8.02 (d, *J* = 8.3 Hz, 2H), 7.40 (d, *J* = 8.2 Hz, 2H), 5.77 (dt, *J* = 15.5, 5.5 Hz, 1H), 5.68 (dd, *J* = 15.5, 8.0 Hz, 1H), 4.47 (dd, *J* = 7.4, 2.7 Hz, 1H), 4.15 (dd, *J* = 5.6, 5.6 Hz, 2H), 3.92 (s, 3H), 2.48 – 2.54 (m, 1H), 2.12 (d, *J* = 2.9 Hz, 1H), 1.33 (t, *J* = 5.8 Hz, 1H), 0.91 (d, *J* = 6.8 Hz, 3H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 167.3, 148.0, 133.8, 132.0, 129.9, 129.9, 127.1, 78.1, 63.7, 52.5, 45.1, 17.1. HRMS (ESI$^+$): *m*/*z* for $C_{14}H_{18}O_4Na$ $[M+Na]^+$ calcd. 273.1103, found 273.1095.



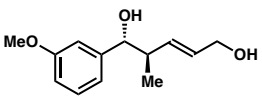
(4*R*,5*R*,*E*)-5-(4-bromophenyl)-4-methylpent-2-ene-1,5-diol (4.4d) Prepared according to the general procedure. The crude mixture was purified by column chromatography to give the title compound as colorless oil in 85% yield (23 mg, *E*:*Z* > 20:1). Enantiomeric excess was determined by HPLC analysis to be 94% ee (254 nm, 25 ˚C); t_1 = 11.0 min, t_2 = 12.4 min [(Chiralpak ID) hexane/i-PrOH, 90:10, 1.0 mL/min]; $[\alpha]_D^{20}$ = +71.5˚ (c 1.15, $CHCl_3$); ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.47 (d, *J* = 8.4 Hz, 2H), 7.20 (d, *J* = 8.3 Hz, 2H), 5.78 (dt, *J* = 15.5, 5.5 Hz, 1H), 5.67 (dd, *J* = 15.5, 8.1 Hz, 1H), 4.35 (d, *J* = 7.6 Hz, 1H),

4.15 (d, *J* = 5.4 Hz, 2H), 2.43 – 2.49 (m, 1H), 2.13 (brs, 1H), 1.45 (brs, 1H), 0.88 (d, *J* = 6.8 Hz, 3H). ^{13}C NMR (151 MHz, $CDCl_3$) δ 141.7, 134.1, 131.9, 131.7, 128.9, 121.8, 77.9, 63.7, 45.2, 17.2. HRMS (ESI^+): *m*/*z* for $C_{12}H_{15}O_2BrNa$ $[M+Na]^+$ calcd. 293.0153, found 293.0164.



(4*R*,5*R*,*E*)-5-(3-bromophenyl)-4-methylpent-2-ene-1,5-diol (4.4e)

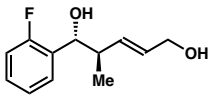
Prepared according to the general procedure. The crude mixture was purified by column chromatography to give the title compound as colorless oil in 89% yield (24 mg, *E*:*Z* > 20:1). Enantiomeric excess was determined by HPLC analysis to be 94% ee (254 nm, 25 ˚C); t_1 = 11.5 min, t_2 = 14.7 min [(Chiralpak ID) hexane/i-PrOH, 90:10, 1.0 mL/min]; $[\alpha]_D^{20}$ = +40.6˚ (c 0.95, $CHCl_3$); ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.50 (dd, *J* = 1.7, 1.7 Hz, 1H), 7.41 (ddd, *J* = 7.6, 2.0, 1.4 Hz, 1H), 7.23 – 7.26 (m, 1H), 7.21 (dd, *J* = 7.7, 7.7 Hz, 1H), 5.78 (dt, *J* = 15.9, 5.7 Hz, 1H), 5.68 (dd, *J* = 15.5, 8.1 Hz, 1H), 4.36 (d, *J* = 7.6 Hz, 1H), 4.16 (d, *J* = 5.2 Hz, 2H), 2.45 – 2.51 (m, 1H), 2.10 (brs, 1H), 1.36 (brs, 1H), 0.91 (d, *J* = 6.8 Hz, 3H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 145.2, 133.8, 132.1, 131.1, 130.20, 130.17, 125.9, 122.8, 77.8, 63.7, 45.2, 17.2. HRMS (ESI^+): *m*/*z* for $C_{12}H_{15}O_2BrNa$ $[M+Na]^+$ calcd. 293.0153, found 293.0141.



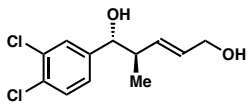
(4*R*,5*R*,*E*)-5-(3-methoxyphenyl)-4-methylpent-2-ene-1,5-diol (4.4f)

Prepared according to the general procedure. The crude mixture was purified by column chromatography to give the title compound as colorless oil in 81% yield (18 mg, *E*:*Z* >20:1). Enantiomeric excess was determined by HPLC analysis to be 94% ee (254 nm, 25 ˚C); t_1 = 6.68 min, t_2 = 7.61 min [(Chiralpak IA) hexane/i-PrOH, 90:10, 1.0 mL/min]; $[\alpha]_D^{20}$ = +85.3˚ (c 0.90, $CHCl_3$); ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.24 – 7.27 (m, 1H), 6.90 (d, *J* = 7.5 Hz, 2H), 6.83 (ddd, *J* = 8.3, 2.5, 1.0 Hz, 1H), 5.79 (dt, *J* = 15.6, 5.5 Hz, 1H), 5.71 (dd, *J* = 15.5, 7.9

Hz, 1H), 4.36 (d, *J* = 7.7 Hz, 1H), 4.16 (d, *J* = 5.5 Hz, 2H), 3.82 (s, 3H), 2.47 – 2.53 (m, 1H), 2.05 (brs, 1H), 1.53 (brs, 1H), 0.90 (d, *J* = 6.8 Hz, 3H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 160.0, 144.6, 134.6, 131.5, 129.6, 119.6, 113.5, 112.6, 78.6, 63.9, 55.6, 45.0, 17.3. HRMS (ESI^+): *m*/*z* for $C_{13}H_{18}O_3Na$ $[M+Na]^+$ calcd. 245.1154, found 245.1144.

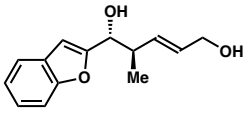


(4*R*,5*R*,*E*)-5-(2-fluorophenyl)-4-methylpent-2-ene-1,5-diol (4.4g) Prepared according to the general procedure. The crude mixture was purified by column chromatography to give the title compound as colorless oil in 67% yield (14 mg, *E*:*Z* = 11:1). Enantiomeric excess was determined by HPLC analysis to be 93% ee (254 nm, 25 ˚C); t_1 = 9.63 min, t_2 = 11.0 min [(Chiralpak IE) hexane/i-PrOH, 90:10, 1.0 mL/min]; $[\alpha]_D^{20}$ = +6.0˚ (c 0.50, $CHCl_3$); ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.43 (dd, *J* = 7.5, 1.8 Hz, 1H), 7.24 – 1.27 (m, 1H), 7.15 (dd, *J* = 7.5, 1.2 Hz, 1H), 7.02 (ddd, *J* = 10.6, 8.2, 1.2 Hz, 1H), 5.77 (dt, *J* = 15.5, 5.1 Hz, 1H), 5.72 (dd, *J* = 15.6, 7.4 Hz, 1H), 4.78 (d, *J* = 7.6 Hz, 1H), 4.15 (d, *J* = 5.0 Hz, 2H), 2.54 – 2.59 (m, 1H), 1.52 (brs, 2H), 0.96 (d, *J* = 6.9 Hz, 3H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 160.5 (d, *J* = 245.3 Hz), 134.2, 131.8, 130.0 (d, *J* = 12.9 Hz), 129.4 (d, *J* = 8.3 Hz), 128.4 (d, *J* = 4.5 Hz), 124.6 (d, *J* = 3.5 Hz), 115.6 (d, *J* = 22.2 Hz), 71.9, 63.8, 44.5, 16.9.

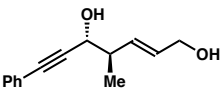


(4*R*,5*R*,*E*)-5-(3,4-dichlorophenyl)-4-methylpent-2-ene-1,5-diol (4.4h) Prepared according to the general procedure. The crude mixture was purified by column chromatography to give the title compound as colorless oil in 77% yield (20 mg, *E*:*Z* > 20:1). Enantiomeric excess was determined by HPLC analysis to be 94% ee (254 nm, 25 ˚C); t_1 = 8.69 min, t_2 = 9.91 min [(Chiralpak IE) hexane/i-PrOH, 90:10, 1.0 mL/min]; $[\alpha]_D^{20}$ = +4.9˚ (c 0.65, $CHCl_3$); ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.44 (d, *J* = 1.9 Hz, 1H), 7.41 (d, *J* = 8.2

Hz, 1H), 7.16 (dd, *J* = 8.2, 2.0 Hz, 1H), 5.78 (dt, *J* = 15.5, 5.4 Hz, 1H), 5.66 (dd, *J* = 15.5, 8.2 Hz, 1H), 4.36 (d, *J* = 7.4 Hz, 1H), 4.16 (dd, *J* = 4.6, 4.6 Hz, 2H), 2.42 – 2.48 (m, 1H), 2.11 (d, *J* = 2.5 Hz, 1H), 1.35 (t, *J* = 5.4 Hz, 1H), 0.92 (d, *J* = 6.8 Hz, 3H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 143.1, 133.3, 132.8, 132.5, 131.9, 130.5, 129.1, 126.5, 77.3, 63.6, 45.2, 17.1.

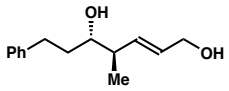


(4*R*,5*R*,*E*)-5-(benzofuran-2-yl)-4-methylpent-2-ene-1,5-diol (4.4i) Prepared according to the general procedure. The crude mixture was purified by column chromatography to give the title compound as colorless oil in 82% yield (19 mg, *E*:*Z* = 15:1). Enantiomeric excess was determined by HPLC analysis to be 95% ee (254 nm, 25 ˚C); t_1 = 12.9 min, t_2 = 14.1 min [(Chiralpak ID) hexane/i-PrOH, 90:10, 1.0 mL/min]; $[\alpha]_D^{20}$ = +105.8˚ (c 0.90, $CHCl_3$); ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.54 (d, *J* = 7.7 Hz, 1H), 7.46 (d, *J* = 8.2 Hz, 1H), 7.26 – 7.28 (m, 1H), 7.22 (dd, *J* = 7.4, 7.4 Hz, 1H), 6.65 (s, 1H), 5.84 (dt, *J* = 15.6, 5.4 Hz, 1H), 5.74 (dd, *J* = 15.5, 7.7 Hz, 1H), 4.60 (dd, *J* = 6.6, 3.3 Hz, 1H), 4.16 (d, *J* = 3.1 Hz, 2H), 2.83 – 2.89 (m, 1H), 2.14 (d, *J* = 4.2 Hz, 1H), 1.33 (brs, 1H), 1.05 (d, *J* = 6.8 Hz, 3H). ^{13}C NMR (151 MHz, $CDCl_3$) δ 158.1, 155.1, 133.5, 132.0, 128.4, 124.5, 123.2, 121.4, 111.6, 104.4, 72.5, 63.7, 42.2, 17.0. HRMS (ESI^+): *m*/*z* for $C_{14}H_{16}O_3Na$ $[M+Na]^+$ calcd. 255.0997, found 255.0990.

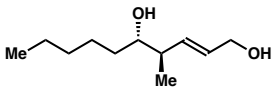


(4*R*,5*R*,*E*)-4-methyl-7-phenylhept-2-en-6-yne-1,5-diol (4.4j) Prepared according to the general procedure. The crude mixture was purified by column chromatography to give the title compound as colorless oil in 74% yield (16 mg, *E*:*Z* > 20:1). Enantiomeric excess was determined by HPLC analysis to be 93% ee (254 nm, 25 ˚C); t_1 = 10.3 min, t_2 = 11.7 min [(Chiralpak IB) hexane/i-PrOH, 90:10, 1.0 mL/min]; $[\alpha]_D^{20}$ = +19.1˚ (c 0.70, $CHCl_3$); ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.42 – 7.45 (m, 2H), 7.29 – 7.33 (m, 3H), 5.83 (dt, *J* =

15.6, 5.5 Hz, 1H), 5.77 (dd, *J* = 15.5, 7.3 Hz, 1H), 4.45 (d, *J* = 6.2 Hz, 1H), 4.17 (d, *J* = 5.5 Hz, 2H), 2.56 – 2.61 (m, 1H), 1.92 (brs, 1H), 1.52 (brs, 1H), 1.22 (d, *J* = 6.8 Hz, 3H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 133.2, 132.1, 131.7, 128.8, 128.7, 122.9, 88.8, 86.4, 67.2, 63.9, 43.6, 16.1. HRMS (ESI$^+$): *m*/*z* for $C_{14}H_{16}O_2Na$ $[M+Na]^+$ calcd. 239.1048, found 239.1039.

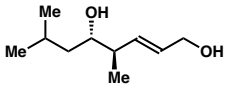


(4*R*,5*S*,*E*)-4-methyl-7-phenylhept-2-ene-1,5-diol (4.4k) Prepared according to the general procedure. The crude mixture was purified by column chromatography to give the title compound as colorless oil in 64% yield (14 mg, *E*:*Z* > 20:1). Enantiomeric excess was determined by HPLC analysis to be 94% ee (254 nm, 25 ˚C); t_1 = 9.02 min, t_2 = 9.62 min [(Chiralpak IB) hexane/i-PrOH, 90:10, 1.0 mL/min]; $[\alpha]_D^{20}$ = – 0.5˚ (c 0.60, $CHCl_3$); ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.27 – 7.30 (m, 2H), 7.17 – 7.22 (m, 3H), 5.73 (dt, *J* = 15.6, 5.3 Hz, 1H), 5.64 (dd, *J* = 15.5, 8.1 Hz, 1H), 4.14 (d, *J* = 5.6 Hz, 2H), 3.42 – 3.46 (m, 1H), 2.81 – 2.87 (m, 1H), 2.64 – 2.70 (m, 1H), 2.22 – 2.29 (m, 1H), 1.79 – 1.86 (m, 1H), 1.66 – 1.74 (m, 1H), 1.53 (brs, 2H), 1.04 (d, *J* = 6.9 Hz, 3H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 142.5, 134.1, 131.3, 128.82, 128.75, 126.2, 74.7, 63.9, 43.2, 36.6, 32.5, 17.0. HRMS (ESI$^+$): *m*/*z* for $C_{14}H_{20}O_2Na$ $[M+Na]^+$ calcd. 243.1361, found 243.1353.

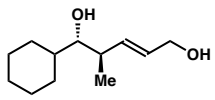


(4*R*,5*S*,*E*)-4-methyldec-2-ene-1,5-diol (4.4l) Prepared according to the general procedure. The crude mixture was purified by column chromatography to give the title compound as colorless oil in 75% yield (14 mg, *E*:*Z* > 20:1). Enantiomeric excess was determined by HPLC analysis to be 94% ee (254 nm, 25 ˚C); t_1 = 6.70 min, t_2 = 7.21 min [(Chiralpak ID) hexane/i-PrOH, 90:10, 1.0 mL/min]; $[\alpha]_D^{20}$ = + 0.5˚ (c 0.60, $CHCl_3$); ^{1}H NMR (500 MHz, $CDCl_3$) δ 5.72 (dt, *J* = 15.5, 5.3 Hz, 1H), 5.65 (dd, *J* = 15.5, 7.8 Hz,

1H), 4.14 (d, J = 5.2 Hz, 2H), 3.39 – 3.43 (m, 1H), 2.20 – 2.27 (m, 1H), 1.43 – 1.52 (m, 4H), 1.24 – 1.41 (m, 6H), 1.04 (d, J = 6.9 Hz, 3H), 0.89 (t, J = 6.9 Hz, 3H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 134.4, 131.0, 75.4, 64.0, 42.9, 34.7, 32.3, 25.8, 23.0, 17.1, 14.4. HRMS (ESI$^+$): m/z for $C_{11}H_{22}O_2Na$ $[M+Na]^+$ calcd. 209.1517, found 209.1511.

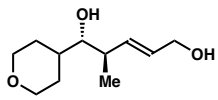


(4*R*,5*S*,*E*)-4,7-dimethyloct-2-ene-1,5-diol (4.4m) Prepared according to the general procedure. The crude mixture was purified by column chromatography to give the title compound as colorless oil in 70% yield (12 mg, E:Z > 20:1). Enantiomeric excess was determined by HPLC analysis to be 90% ee (254 nm, 25 ˚C); t_1 = 4.22 min, t_2 = 4.49 min [(Chiralpak IB) hexane/i-PrOH, 90:10, 1.0 mL/min]; $[\alpha]_D^{20}$ = – 0.4˚ (c 0.70, $CHCl_3$); ^{1}H NMR (600 MHz, $CDCl_3$) δ 5.72 (dt, J = 15.6, 5.4 Hz, 1H), 5.66 (dd, J = 15.5, 7.8 Hz, 1H), 4.14 (d, J = 5.4 Hz, 2H), 3.49 – 3.52 (m, 1H), 2.17 – 2.23 (m, 1H), 1.76 – 1.85 (m, 1H), 1.45 (brs, 2H), 1.32 – 1.37 (m, 1H), 1.22 – 1.26 (m, 1H), 1.05 (d, J = 6.9 Hz, 3H), 0.94 (d, J = 6.7 Hz, 3H), 0.91 (d, J = 6.6 Hz, 3H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 134.3, 131.1, 73.3, 64.0, 44.1, 43.4, 25.0, 24.1, 22.1, 17.0. HRMS (ESI$^+$): m/z for $C_{10}H_{21}O_2$ $[M+H]^+$ calcd. 173.1542, found 173.1541.

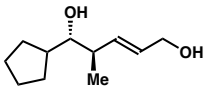


(4*R*,5*S*,*E*)-5-cyclohexyl-4-methylpent-2-ene-1,5-diol (4.4n) Prepared according to the general procedure. The crude mixture was purified by column chromatography to give the title compound as colorless oil in 66% yield (13 mg, E:Z = 11:1). Enantiomeric excess was determined by HPLC analysis to be 94% ee (254 nm, 25 ˚C); t_1 = 7.06 min, t_2 = 7.56 min [(Chiralpak IB) hexane/i-PrOH, 90:10, 1.0 mL/min]; $[\alpha]_D^{20}$ = + 1.8˚ (c 0.50, $CHCl_3$); ^{1}H NMR (500 MHz, $CDCl_3$) δ 5.66 – 5.75 (m, 2H), 4.14 (d, J = 4.3 Hz, 2H), 3.12 (dd, J

= 5.8, 5.9 Hz, 1H), 2.37 – 2.44 (m, 1H), 1.80 – 1.84 (m, 1H), 1.73 – 1.79 (m, 2H), 1.60 – 1.68 (m, 2H), 1.49 (brs, 2H), 1.36 – 1.43 (m, 1H), 1.06 – 1.29 (m, 5H), 1.04 (d, J = 6.9 Hz, 3H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 134.4, 130.9, 79.6, 64.0, 40.8, 39.3, 30.3, 27.6, 26.83, 26.75, 26.4, 17.8. HRMS (ESI^+): m/z for $C_{12}H_{22}O_2Na$ $[M+Na]^+$ calcd. 221.1517, found 221.1516.

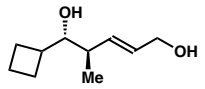


(4*R*,5*S*,*E*)-4-methyl-5-(tetrahydro-2*H*-pyran-4-yl)pent-2-ene-1,5-diol (4.4o) Prepared according to the general procedure. The crude mixture was purified by column chromatography to give the title compound as colorless oil in 70% yield (14 mg, E:Z = 20:1). Enantiomeric excess was determined by HPLC analysis to be 90% ee (254 nm, 25 ˚C); t_1 = 9.21 min, t_2 = 10.4 min [(Chiralpak ID) hexane/i-PrOH, 90:10, 1.0 mL/min]; $[\alpha]_D^{20}$ = – 1.84˚ (c 0.25, $CHCl_3$); ^{1}H NMR (600 MHz, $CDCl_3$) δ 5.67 – 5.75 (m, 2H), 4.15 (d, J = 4.3 Hz, 2H), 3.97 – 4.03 (m, 2H), 3.34 – 3.40 (m, 2H), 3.16 (dd, J = 6.2, 5.4, 1H), 2.38 – 2.43 (m, 1H), 1.70 – 1.74 (m, 1H), 1.61 – 1.68 (m, 1H), 1.42 – 1.56 (m, 5H), 1.08 (d, J = 6.9 Hz, 3H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 133.3, 131.3, 79.0, 68.3, 68.1, 63.9, 38.9, 38.4, 29.8, 28.4, 17.9. HRMS (ESI^+): m/z for $C_{11}H_{21}O_3$ $[M+H]^+$ calcd. 201.1491, found 201.1489.

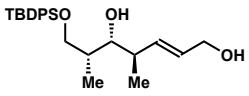


(4*R*,5*S*,*E*)-5-cyclopentyl-4-methylpent-2-ene-1,5-diol (4.4p) Prepared according to the general procedure. The crude mixture was purified by column chromatography to give the title compound as colorless oil in 71% yield (13 mg, E:Z > 20:1). Enantiomeric excess was determined by HPLC analysis to be 94% ee (254 nm, 25 ˚C); t_1 = 10.9 min, t_2 = 11.9 min [(Chiralpak ID) hexane/i-PrOH, 95:5, 1.0 mL/min]; $[\alpha]_D^{20}$ = + 1.3˚ (c 0.15, $CHCl_3$); ^{1}H NMR (600 MHz, $CDCl_3$) δ 5.68 – 5.75 (m, 2H), 4.14 (d, J = 4.2 Hz, 2H), 3.26 (dd, J = 7.7, 4.2 Hz, 1H), 2.30-2.36 (m, 1H), 1.91-1.98 (m, 1H), 1.74-1.79 (m, 1H), 1.66 – 1.72 (m, 1H),

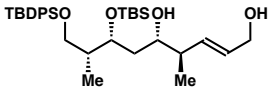
1.59-1.65 (m, 2H), 1.50 – 1.57 (m, 3H), 1.32 – 1.41 (m, 2H), 1.19 – 1.26 (m, 1H), 1.09 (d, J = 6.9 Hz, 3H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 133.9, 130.8, 79.8, 64.1, 44.2, 41.2, 29.5, 28.9, 26.0, 25.9, 18.1.



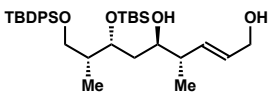
(4*R*,5*S*,*E*)-5-cyclobutyl-4-methylpent-2-ene-1,5-diol (4.4q) Prepared according to the general procedure. The crude mixture was purified by column chromatography to give the title compound as colorless oil in 65% yield (11 mg, E:Z > 20:1). Enantiomeric excess was determined by HPLC analysis to be 93% ee (254 nm, 25 ˚C); t_1 = 6.07 min, t_2 = 6.46 min [(Chiralpak IC) hexane/i-PrOH, 95:5, 1.0 mL/min]; $[\alpha]_D^{20}$ = + 0.7˚ (c 0.45, $CHCl_3$); ^{1}H NMR (600 MHz, $CDCl_3$) δ 5.63 – 5.70 (m, 2H), 4.13 (d, J = 4.5 Hz, 2H), 3.35 (dd, J = 7.7, 4.8 Hz, 1H), 2.40 – 2.47 (m, 1H), 2.19 – 2.24 (m, 1H), 1.96 – 2.01 (m, 1H), 1.80 – 1.95 (m, 4H), 1.75 – 1.80 (m, 1H), 1.38 (brs, 2H), 1.04 (d, J = 6.9 Hz, 3H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 134.2, 130.7, 79.4, 64.0, 40.6, 39.6, 25.3, 24.9, 18.5, 17.4.



(4*R*,5*R*,6*R*,*E*)-7-((*tert*-butyldiphenylsilyl)oxy)-4,6-dimethylhept-2-ene-1,5-diol (4.7) Prepared according to the general procedure. The crude mixture was purified by column chromatography to give the title compound as colorless oil in 73% yield (30 mg, E:Z > 50:1, d.r. > 50:1). $[\alpha]_D^{20}$ = – 0.3˚ (c 1.20, $CHCl_3$); ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.65 – 7.68 (m, 4H), 7.42 – 7.45 (m, 2H), 7.37 – 7.40 (m, 4H), 5.68 – 5.75 (m, 2H), 4.13 (d, J = 4.7 Hz, 2H), 3.69 – 3.74 (m, 2H), 3.60 (dd, J = 8.3, 2.7 Hz, 1H), 2.47 (brs, 1H), 2.28 – 2.33 (m, 1H), 1.79 – 1.85 (m, 1H), 1.55 (brs, 1H), 1.06 (s, 9H), 0.96 (d, J = 3.2 Hz, 3H), 0.94 (d, J = 3.4 Hz, 3H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 136.1, 136.0, 135.9, 133.7, 133.5, 130.2, 130.12, 130.09, 128.07, 128.06, 77.1(DEPT 135), 69.0, 64.0, 40.5, 36.9, 27.2, 19.6, 17.4, 10.0.

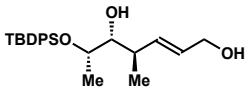


(4*R*,5*S*,7*R*,8*R*,*E*)-7-((*tert*-butyldimethylsilyl)oxy)-9-((*tert*-butyldiphenylsilyl)oxy)-4,8-dimethylnon-2-ene-1,5-diol (4.9) Prepared according to the general procedure. The crude mixture was purified by column chromatography to give the title compound as colorless oil in 70% yield (40 mg, *E*:*Z* = 15:1, d.r. = 9:1). $[\alpha]_D^{20}$ = – 0.5˚ (c 2.00, $CHCl_3$); ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.64 – 7.67 (m, 4H), 7.40 – 7.43 (m, 2H), 7.36 – 7.39 (m, 4H), 5.63 – 5.71 (m, 2H), 4.11 (d, *J* = 4.5 Hz, 2H), 4.00 – 4.02 (m, 1H), 3.69 (dd, *J* = 9.9, 5.8 Hz, 1H), 3.54 (dd, *J* = 9.9, 6.9 Hz, 1H), 3.45 – 3.48 (m, 1H), 2.31 (brs, 1H), 2.18 – 2.24 (m, 1H), 1.83 – 1.87 (m, 1H), 1.62 (ddd, *J* = 14.3, 6.4, 2.4 Hz, 1H), 1.53 (brs, 1H), 1.47 (ddd, *J* = 14.3, 9.6, 7.4 Hz, 1H), 1.06 (s, 9H), 1.03 (d, *J* = 6.9 Hz, 3H), 0.87 (d, *J* = 6.9 Hz, 3H), 0.84 (s, 9H), 0.07 (s, 3H), 0.01 (s, 3H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 136.0 (two overlapping carbon signal), 134.5, 134.3, 134.2, 130.6, 130.0 (two overlapping carbon signal), 128.0, 127.9, 74.0, 73.1, 65.7, 64.1, 43.1, 40.8, 37.7, 27.3, 26.2, 19.6, 18.3, 16.6, 12.1, – 4.0, – 4.1.

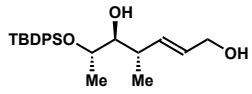


(4*S*,5*R*,7*R*,8*R*,*E*)-7-((*tert*-butyldimethylsilyl)oxy)-9-((*tert*-butyldiphenylsilyl)oxy)-4,8-dimethylnon-2-ene-1,5-diol (4.10) Prepared according to the general procedure. The crude mixture was purified by column chromatography to give the title compound as colorless oil in 74% yield (42 mg, *E*:*Z* = 25:1, d.r. > 20:1). $[\alpha]_D^{20}$ = – 0.2˚ (c 1.90, $CHCl_3$); ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.64 – 7.67 (m, 4H), 7.40 – 7.44 (m, 2H), 7.36 – 7.39 (m, 4H), 5.60 – 5.68 (m, 2H), 4.08 (dd, *J* = 5.0, 5.0 Hz, 2H), 4.00 – 4.03 (m, 1H), 3.63 (dd, *J* = 10.0, 5.0 Hz, 2H), 3.53 (dd, *J* = 10.0, 6.0 Hz, 1H), 2.62 (d, *J* = 2.9 Hz, 1H), 2.10 – 2.15 (m, 1H), 1.87 – 1.93 (m, 1H), 1.52 – 1.55 (m, 2H), 1.22 (t, *J* = 5.9 Hz, 1H), 1.05 (s, 9H), 0.99 (d, *J* = 6.9 Hz, 3H), 0.97 (d, *J* = 6.9 Hz, 3H), 0.87 (s, 9H), 0.08 (s, 3H), 0.04 (s, 3H). ^{13}C

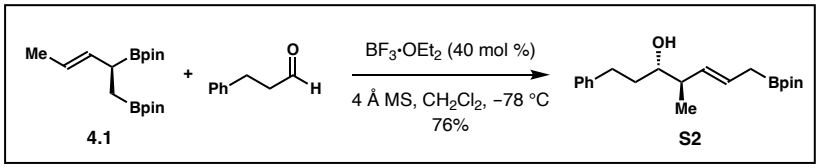
NMR (126 MHz, $CDCl_3$) δ 135.97, 135.95, 134.7, 134.2, 134.1, 130.6, 130.0 (two overlapping carbon signal), 127.0 (two overlapping carbon signal), 72.34, 72.33, 65.9, 64.1, 43.1, 40.8, 37.8, 27.2, 26.3, 19.6, 18.4, 16.7, 13.7, – 4.0, – 4.2.



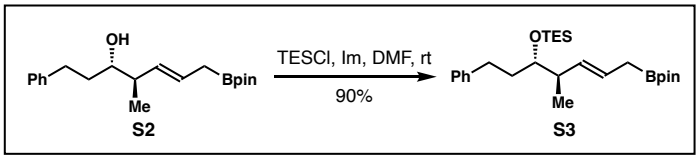
(4*R*,5*R*,6*S*,*E*)-6-((*tert*-butyldiphenylsilyl)oxy)-4-methylhept-2-ene-1,5-diol (4.12) Prepared according to the general procedure. The crude mixture was purified by column chromatography to give the title compound as colorless oil in 85% yield (34 mg, *E*:*Z* > 40:1, d.r. = 18:1). $[\alpha]_D^{20}$ = – 1.4˚ (c 1.70, $CHCl_3$); ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.66 (d, *J* = 6.7 Hz, 4H), 7.44 (t, *J* = 7.3 Hz, 2H), 7.39 (dd, *J* = 7.1, 7.4 Hz, 4H), 5.61 – 5.69 (m, 2H), 4.09 (d, *J* = 3.5 Hz, 2H), 3.87 – 3.92 (m, 1H), 3.31 (dd, *J* = 8.1, 3.3 Hz, 1H), 2.35 (brs, 1H), 2.18 – 2.25 (m, 1H), 1.26 (brs, 1H), 1.05 – 1.07 (m, 12H), 0.75 (d, *J* = 6.9 Hz, 3H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 136.2, 136.1, 135.4, 134.3, 133.9, 130.2, 130.1, 129.6, 128.1, 127.9, 78.6, 70.8, 64.1, 38.4, 27.4, 19.5, 16.5, 16.4.



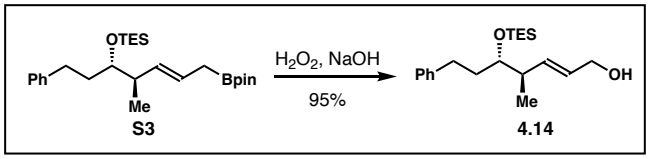
(4*S*,5*S*,6*S*,*E*)-6-((*tert*-butyldiphenylsilyl)oxy)-4-methylhept-2-ene-1,5-diol (4.13) Prepared according to the general procedure. The crude mixture was purified by column chromatography to give the title compound as colorless oil in 70% yield (28 mg, *E*:*Z* = 67:1, d.r. = 13:1). $[\alpha]_D^{20}$ = – 0.2˚ (c 1.25, $CHCl_3$); ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.69 (d, *J* = 7.6 Hz, 4H), 7.42 – 7.46 (m, 2H), 7.37 – 7.40 (m, 4H), 5.65 (dd, *J* = 15.5, 8.4 Hz, 1H), 5.53 (dt, *J* = 15.5, 5.8 Hz, 1H), 4.01 (d, *J* = 5.8 Hz, 2H), 3.76 – 3.80 (m, 1H), 3.21 (dd, *J* = 5.4, 5.5 Hz, 1H), 2.51 (brs, 1H), 2.26 – 2.31 (m, 1H), 1.38 (brs, 1H), 1.07 (s, 9H), 1.02 (d, *J* = 6.2 Hz, 3H), 0.98 (d, *J* = 6.9 Hz, 3H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 136.4, 136.2, 134.6, 134.3, 133.7, 130.2, 130.1, 129.9, 128.1, 127.9, 79.8, 71.3, 64.1, 39.1, 27.4, 20.4, 19.7, 18.2.



(3*S*,4*R*,*E*)-4-methyl-1-phenyl-7-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)hept-5-en-3-ol (S2) To a reaction flask containing a stirring bar, crotylboronate **4.1** (145 mg, 0.45 mmol, 1.5 equiv), freshly activated 4 Å MS (25 mg) and dichloromethane (0.7 mL) were added. The mixture was placed in a −78 ºC dry ice/acetone bath. Then freshly prepared solution of BF_3•OEt_2 (0.8 M in DCM, 150 µL, 0.12 mmol, 0.4 equiv) was added to the reaction mixture *via* a microliter syringe at −78 ºC. The mixture was kept at −78 ºC and stirred for 20 min. Then freshly distilled 3-phenylpropionaldehyde (40 mg, 0.3 mmol, 1.0 equiv) were dissolved in dichloromethane (0.3 mL) and added slowly to the flask. The reaction mixture was kept stirring at −78 ºC. After complete consumption of the aldehyde, saturated aqueous $NaHCO_3$ (1.0 mL) was added to the reaction mixture at 0 ºC. Then organic layer was separated and the aqueous layer was extracted with diethyl ether (2 mL x 3). The combined organic extracts were filtered through a pad of silica gel and concentrated under reduced pressure. Purification of the crude product was performed by flash chromatography to give allylboronate **S2** as white solid (*E*:*Z* > 20:1, 75 mg, 76%). ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.26 – 7.29 (m, 2H), 7.22 (d, *J* = 7.0 Hz, 2H), 7.17 (t, *J* = 7.3 Hz, 1H), 5.60 (dt, *J* = 15.1, 7.5 Hz, 1H), 5.25 (dd, *J* = 15.3, 8.6 Hz, 1H), 3.29 (m, 1H), 2.83 – 2.88 (m, 1H), 2.65 – 2.70 (m, 1H), 2.11 – 2.17 (m, 1H), 1.98 (brs, 1H), 1.82 – 1.88 (m, 1H), 1.64 – 1.71 (m, 3H), 1.24 (s, 12H), 0.98 (d, *J* = 6.8 Hz, 3H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 143.0, 132.4, 128.9, 128.64, 128.63, 126.0, 83.7, 74.5, 43.9, 36.5, 32.5, 25.1, 17.1.

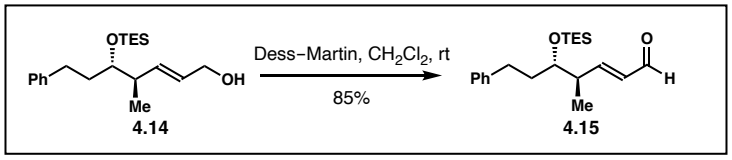


Triethyl(((3*S*,4*R*,*E*)-4-methyl-1-phenyl-7-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)hept-5-en-3-yl)oxy)silane (S3) To a reaction flask containing a stirring bar, allylboronate **S2** (165 mg, 0.5 mmol, 1.0 equiv) and DMF (1.0 mL) were added. Then imidazole (102 mg, 1.5 mmol, 3.0 equiv.) and TESCl (188 mg, 1.25 mmol, 2.5 equiv.) were added to the reaction mixture sequentially. The reaction mixture was kept stirring for at ambient temperature. The reaction process was monitored by TLC. After complete consumption of **S2**, diethyl ether (5 mL) was added and the resulting mixture was filtered through a pad of silica gel. The solvent was removed under reduced pressure. Purification of the crude product by flash chromatography (gradient elution with hexane and ethyl acetate) gave product **S3** as a colorless oil (200 mg, 90%). ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.25 – 7.27 (m, 2H), 7.15 – 7.18 (m, 3H), 5.47 (dt, *J* = 16.1, 7.1 Hz, 1H), 5.36 (dd, *J* = 15.4, 7.7 Hz, 1H), 3.59 – 3.62 (m, 1H), 2.67 – 2.72 (m, 1H), 2.50 – 2.55 (m, 1H), 2.29 – 2.34 (m, 1H), 1.70 – 1.75 (m, 1H), 1.62 – 1.68 (m, 3H), 1.23 (s, 6H), 1.22 (s, 6H), 0.98 (m, 12H), 0.61 (q, *J* = 7.9 Hz, 6H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 143.2, 133.1, 128.7, 128.6, 125.9, 125.4, 83.5, 76.5, 42.8, 35.7, 32.9, 25.10, 25.07, 15.8, 7.4, 5.6.



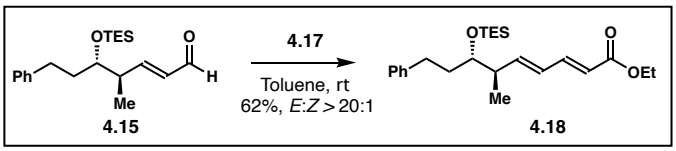
(4*R*,5*S*,*E*)-4-methyl-7-phenyl-5-((triethylsilyl)oxy)hept-2-en-1-ol (4.14) To a reaction flask containing a stirring bar, allylboronate **S3** (222 mg, 0.5 mmol) and diethyl ether (2.0 mL) were added. Then 3N NaOH (0.5 mL) was added to the reaction mixture followed by slow addition of

30% H_2O_2 (0.5 mL) at 0 ºC. The reaction was stirred vigorously for 3 h at room temperature. The organic layer was separated and the aqueous layer was extracted with diethyl ether (2 mL x 3). The solvent was removed under reduced pressure. Purification of the crude product by flash chromatography (gradient elution with hexane and ethyl acetate) gave product **4.14** as a colorless oil (159 mg, 95%). ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.26 – 7.29 (m, 2H), 7.16 – 7.19 (m, 3H), 5.61 – 5.70 (m, 2H), 4.11 (d, *J* = 4.4 Hz, 2H), 3.62 – 3.66 (m, 1H), 2.68 – 2.74 (m, 1H), 2.51 – 2.57 (m, 1H), 2.35 – 2.41 (m, 1H), 1.67 – 1.72 (m, 2H), 1.22 (brs, 1H), 1.02 (d, *J* = 6.9 Hz, 3H), 0.98 (t, *J* = 7.9 Hz, 9H), 0.62 (q, *J* = 7.9 Hz, 6H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 142.9, 135.3, 129.5, 128.7 (two overlapping carbon signal), 126.1, 76.0, 64.3, 42.3, 36.1, 32.6, 15.8, 7.4, 5.6.

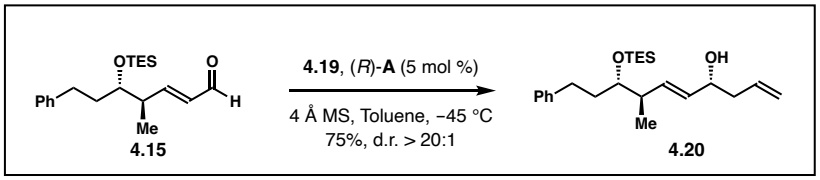


(4*R*,5*S*,*E*)-4-methyl-7-phenyl-5-((triethylsilyl)oxy)hept-2-enal (4.15) To a reaction flask containing a stirring bar and allylic alcohol **4.14** (167 mg, 0.5 mmol, 1.0 equiv) dichloromethane, Dess-Martin periodinane (DMP, 318 mg, 0.75 mmol, 1.5 equiv) and 1 drop of water were added sequentially. The reaction mixture was stirred at room temperature for 1 h. After complete consumption of allylic alcohol, diethyl ether (5 mL) was added and the resulting mixture was filtered through a pad of silica gel. The solvent was removed under reduced pressure. Purification of the crude product by flash chromatography (gradient elution with hexane and ethyl acetate) gave product **4.15** as a colorless oil (141 mg, 85%). $[\alpha]_D^{20}$ = + 0.8˚ (c 0.50, $CHCl_3$); ^{1}H NMR (500 MHz, $CDCl_3$) δ 9.53 (d, *J* = 7.9 Hz, 1H), 7.28 (dd, *J* = 7.5, 7.6 Hz, 2H), 7.19 (t, *J* = 7.4 Hz, 1H), 7.16 (d, *J* = 7.2 Hz, 2H), 6.88 (dd, *J* = 15.8, 7.8 Hz, 1H), 6.12 (dd, *J* = 15.8, 7.9 Hz, 1H), 3.73 – 3.76 (m, 1H), 2.63 – 2.71 (m, 2H), 2.56 – 2.62 (m, 1H), 1.75 – 1.83 (m, 1H),

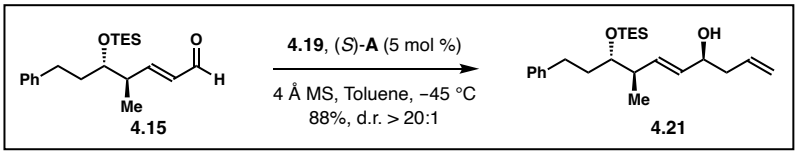
1.65 – 1.73 (m, 1H), 1.14 (d, J = 6.8 Hz, 3H), 0.98 (t, J = 7.9 Hz, 9H), 0.63 (q, J = 8.0 Hz, 6H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 194.5, 160.8, 142.2, 133.2, 128.8, 128.6, 126.3, 75.4, 42.7, 37.1, 32.1, 15.9, 7.3, 5.5. HRMS (ESI$^+$): m/z for $C_{20}H_{33}O_2Si$ $[M+H]^+$ calcd. 333.2250, found 333.2256.



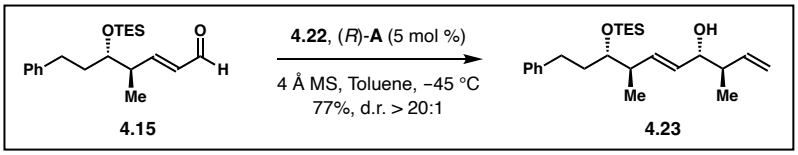
Ethyl (2*E*,4*E*,6*R*,7*S*)-6-methyl-9-phenyl-7-((triethylsilyl)oxy)nona-2,4-dienoate (4.18) To a reaction flask containing a stirring bar, aldehyde **4.15** (33 mg, 0.1 mmol, 1.0 equiv), ethyl (triphenylphosphoranylidene)acetate **4.17** (70 mg, 0.2 mmol, 2.0 equiv) and Toluene (0.5 mL) were added sequentially. The reaction mixture was stirred at room temperature for 3 days. After complete consumption of aldehyde **4.15**, diethyl ether (5 mL) was added and the resulting mixture was filtered through a pad of silica gel. The solvent was removed under reduced pressure. Purification of the crude product by flash chromatography (gradient elution with hexane and ethyl acetate) gave product **4.18** as a colorless oil (E:Z > 20:1, 25 mg, 62%). ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.24 – 7.29 (m, 3H), 7.15 – 7.19 (m, 3H), 6.16 (dd, J = 15.3, 9.8 Hz, 1H), 6.11 (dd, J = 15.2, 7.1 Hz, 1H), 5.80 (d, J = 15.4 Hz, 1H), 4.20 (q, J = 7.1 Hz, 2H), 3.65 – 3.68 (m, 1H), 2.65 – 2.71 (m, 1H), 2.52 – 2.58 (m, 1H), 2.44 – 2.50 (m, 1H), 1.63 – 1.76 (m, 2H), 1.29 (t, J = 7.1 Hz, 3H), 1.06 (d, J = 6.9 Hz, 3H), 0.97 (t, J = 7.9 Hz, 9H), 0.61 (q, J = 7.9 Hz, 6H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 167.6, 146.6, 145.4, 142.7, 128.74, 128.67, 128.65, 126.1, 120.0, 75.8, 60.6, 43.1, 36.6, 32.4, 15.9, 14.7, 7.4, 5.6.



(4*R*,7*R*,8*S*,*E*)-7-methyl-10-phenyl-8-((triethylsilyl)oxy)deca-1,5-dien-4-ol (4.20) To a reaction flask containing a stir bar and freshly activated 4 Å MS (50 mg) was added phosphoric acid (*R*)-**A** (4 mg, 0.005 mmol, 0.005 equiv), prepared aldehyde **4.15** (33 mg, 0.1 mmol, 1.0 equiv), toluene (0.2 mL) were added to the flask. The mixture was placed in a −45 ºC cold bath and stirred for 5 min. Then allylboronate **4.19** (25 mg, 0.15 mmol, 1.5 equiv) in toluene (0.1 mL) was added slowly to the reaction mixture *via* a syringe. The mixture was kept at −45 ºC and stirred for 24 h. After complete consumption of the aldehyde, diethyl ether (5 mL) was added and the resulting mixture was filtered through a pad of silica gel. The solvent was removed under reduced pressure. Purification of the crude product by flash chromatography (gradient elution with hexane and ethyl acetate) gave product **4.20** as a colorless oil (d.r. > 20:1, 28 mg, 75%). $[\alpha]_D^{20}$ = + 0.5˚ (c 1.05, $CHCl_3$); ^{1}H NMR (500 MHz, CDCl3) δ 7.26 – 7.29 (m, 2H), 7.16 – 7.19 (m, 3H), 5.75 – 5.84 (m, 1H), 5.66 (dd, *J* = 15.6, 7.3 Hz, 1H), 5.49 (dd, *J* = 15.6, 7.1 Hz, 1H), 5.10 – 5.15 (m, 2H), 4.11 – 4.16 (m, 1H), 3.63 – 3.66 (m, 1H), 2.50 – 2.57 (m, 1H), 2.34 – 2.41 (m, 1H), 2.25 – 2.34 (m, 1H), 2.34 – 2.11 (m, 2H), 1.66 – 1.71 (m, 2H), 1.57 (d, *J* = 3.9 Hz, 1H), 1.01 (d, *J* = 6.9 Hz, 3H), 0.98 (t, *J* = 7.9 Hz, 9H), 0.62 (q, *J* = 7.9 Hz, 6H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 142.9, 134.7, 134.2, 132.6, 128.7 (two overlapping carbon signal), 126.1, 118.4, 75.9, 72.3, 42.4, 42.2, 35.9, 32.7, 15.5, 7.4, 5.6.

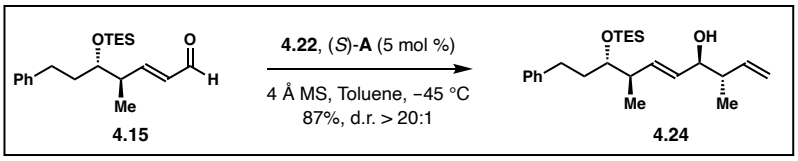


(4*S*,7*R*,8*S*,*E*)-7-methyl-10-phenyl-8-((triethylsilyl)oxy)deca-1,5-dien-4-ol (4.21) To a reaction flask containing a stir bar and freshly activated 4 Å MS (50 mg) was added phosphoric acid (*S*)-**A** (4 mg, 0.005 mmol, 0.005 equiv), prepared aldehyde **4.15** (33 mg, 0.1 mmol, 1.0 equiv), toluene (0.2 mL) were added to the flask. The mixture was placed in a −45 ºC cold bath and stirred for 5 min. Then allylboronate **4.19** (25 mg, 0.15 mmol, 1.5 equiv) in toluene (0.1 mL) was added slowly to the reaction mixture *via* a syringe. The mixture was kept at −45 ºC and stirred for 24 h. After complete consumption of the aldehyde, diethyl ether (5 mL) was added and the resulting mixture was filtered through a pad of silica gel. The solvent was removed under reduced pressure. Purification of the crude product by flash chromatography (gradient elution with hexane and ethyl acetate) gave product **4.21** as a colorless oil (d.r. > 20:1, 33 mg, 88%). $[\alpha]_D^{20}$ = – 0.8˚ (c 0.37, $CHCl_3$); ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.26 – 7.29 (m, 2H), 7.16 – 7.19 (m, 3H), 5.76-5.84 (m, 1H), 5.65 (dd, *J* = 15.6, 7.7 Hz, 1H), 5.49 (dd, *J* = 15.6, 6.5 Hz, 1H), 5.10 – 5.15 (m, 2H), 4.13-4.17 (m, 1H), 3.61-3.65 (m, 1H), 2.66 – 2.72 (m, 1H), 2.50 – 2.56 (m, 1H), 2.34 – 2.39 (m, 1H), 2.25 – 2.33 (m, 2H), 1.66 – 1.70 (m, 2H), 1.02 (d, *J* = 6.9 Hz, 3H), 0.97 (t, *J* = 7.9 Hz, 9H), 0.61 (q, *J* = 7.9 Hz, 6H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 142.9, 134.7, 134.2, 132.7, 128.68, 128.67, 126.1, 118.5, 76.0, 72.1, 42.4, 42.2, 36.1, 32.6, 15.9, 7.4, 5.6.



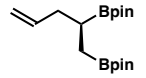
(3*R*,4*S*,7*R*,8*S*,*E*)-3,7-dimethyl-10-phenyl-8-((triethylsilyl)oxy)deca-1,5-dien-4-ol (4.23) To a reaction flask containing a stir bar and freshly activated 4 Å MS (50 mg) was added phosphoric acid (*R*)-**A** (4 mg, 0.005 mmol, 0.005 equiv), prepared aldehyde **4.15** (33 mg, 0.1 mmol, 1.0

equiv), toluene (0.2 mL) were added to the flask. The mixture was placed in a −45 ºC cold bath and stirred for 5 min. Then crotylboronate **4.22** (27 mg, 0.15 mmol, 1.5 equiv) in toluene (0.1 mL) was added slowly to the reaction mixture *via* a syringe. The mixture was kept at −45 ºC and stirred for 24 h. After complete consumption of the aldehyde, diethyl ether (5 mL) was added and the resulting mixture was filtered through a pad of silica gel. The solvent was removed under reduced pressure. Purification of the crude product by flash chromatography (gradient elution with hexane and ethyl acetate) gave product **4.23** as a colorless oil (d.r. > 20:1, 30 mg, 77%). $[\alpha]_D^{20}$ = + 0.7˚ (c 0.95, $CHCl_3$);^{1}H NMR (500 MHz, $CDCl_3$) δ 7.25 – 7.28 (m, 2H), 7.16 – 7.19 (m, 3H), 5.72 – 5.79 (m, 1H), 5.66 (dd, *J* = 15.6, 7.3 Hz, 1H), 5.44 (dd, *J* = 16.3, 7.3 Hz, 1H), 5.11 – 5.15 (m, 2H), 3.82 (dd, *J* = 7.2, 7.3 Hz, 1H), 3.64 – 3.67 (m, 1H), 2.68 – 2.74 (m, 1H), 2.51 – 2.57 (m, 1H), 2.37 – 2.43 (m, 1H), 2.20 – 2.27 (m, 1H), 1.67 – 1.71 (m, 2H), 1.66 (brs, 1H), 1.02 (d, *J* = 6.9 Hz, 3H), 0.96 – 0.99 (m, 12H), 0.62 (q, *J* = 7.9 Hz, 6H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 142.9, 140.9, 135.7, 131.1, 128.7 (two overlapping carbon signal), 126.0, 116.7, 76.7, 75.8, 44.9, 42.3, 35.9, 32.8, 16.5, 15.4, 7.4, 5.6.

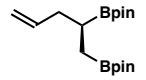


(3*S*,4*R*,7*R*,8*S*,*E*)-3,7-dimethyl-10-phenyl-8-((triethylsilyl)oxy)deca-1,5-dien-4-ol (4.24) To a reaction flask containing a stir bar and freshly activated 4 Å MS (50 mg) was added phosphoric acid (*S*)-**A** (4 mg, 0.005 mmol, 0.005 equiv), prepared aldehyde **4.15** (33 mg, 0.1 mmol, 1.0 equiv), toluene (0.2 mL) were added to the flask. The mixture was placed in a −45 ºC cold bath and stirred for 5 min. Then crotylboronate **4.22** (27 mg, 0.15 mmol, 1.5 equiv) in toluene (0.1 mL) was added slowly to the reaction mixture *via* a syringe. The mixture was kept at −45 ºC and

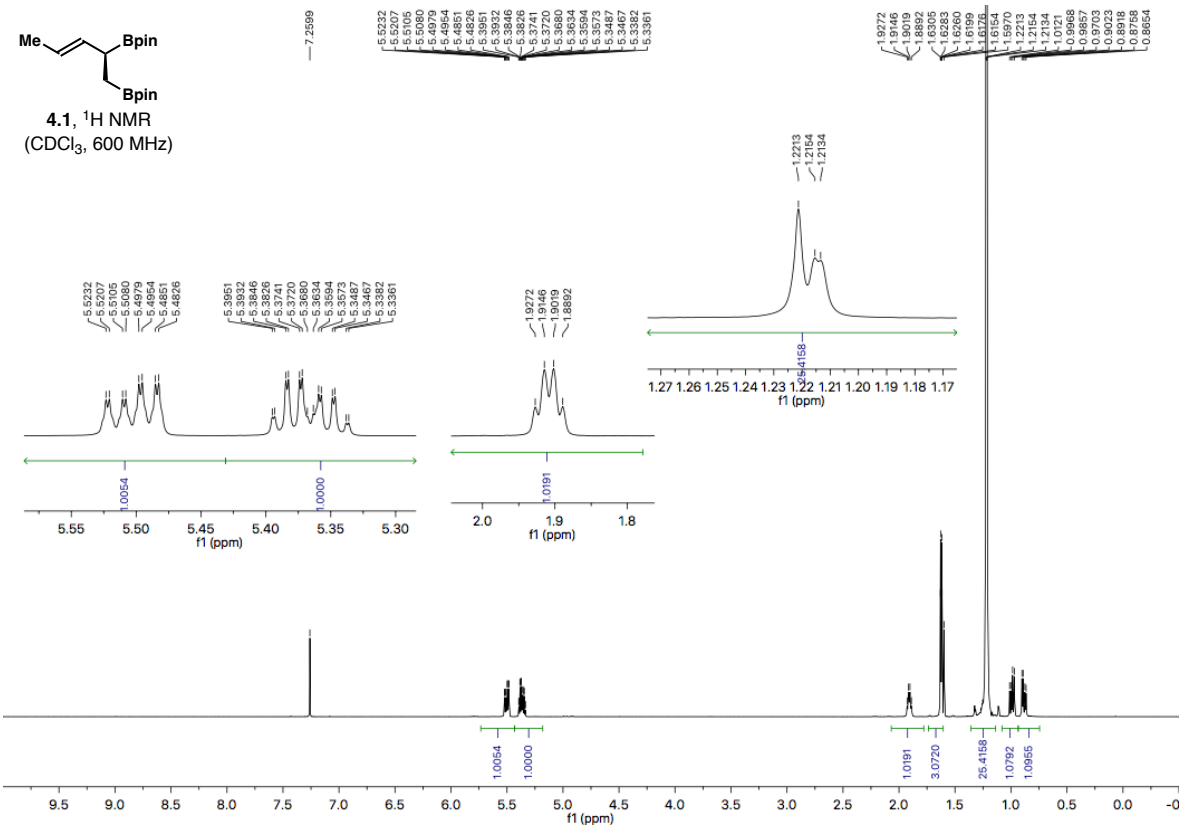
stirred for 24 h. After complete consumption of the aldehyde, diethyl ether (5 mL) was added and the resulting mixture was filtered through a pad of silica gel. The solvent was removed under reduced pressure. Purification of the crude product by flash chromatography (gradient elution with hexane and ethyl acetate) gave product **4.24** as a colorless oil (d.r. > 20:1, 34 mg, 87%). $[\alpha]_D^{20}$ = – 1.0˚ (c 0.95, $CHCl_3$);^{1}H NMR (500 MHz, $CDCl_3$) δ 7.25 – 7.28 (d, *J* = 4.6 Hz, 2H), 7.15 – 7.19 (m, 3H), 5.72 – 5.79 (m, 1H), 5.65 (dd, *J* = 15.6, 7.7 Hz, 1H), 5.44 (dd, *J* = 15.6, 7.2 Hz, 1H), 5.11 – 5.14 (m, 2H), 3.83 (dd, *J* = 7.1, 7.1 Hz, 1H), 3.62 – 3.65 (m, 1H), 2.66 – 2.72 (m, 1H), 2.50 – 2.56 (m, 1H), 2.35 – 2.42 (m, 1H), 2.21 – 2.28 (m, 1H), 1.67 – 1.71 (m, 2H), 1.65 (brs, 1H), 1.03 (d, *J* = 6.9 Hz, 3H), 0.96 – 1.00 (m, 12H), 0.62 (q, *J* = 7.9 Hz, 6H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 142.9, 140.8, 135.7, 131.3, 128.68, 128.65, 126.1, 116.7, 76.6, 76.1, 44.9, 42.3, 36.1, 32.7, 16.5, 15.9, 7.4, 5.6.



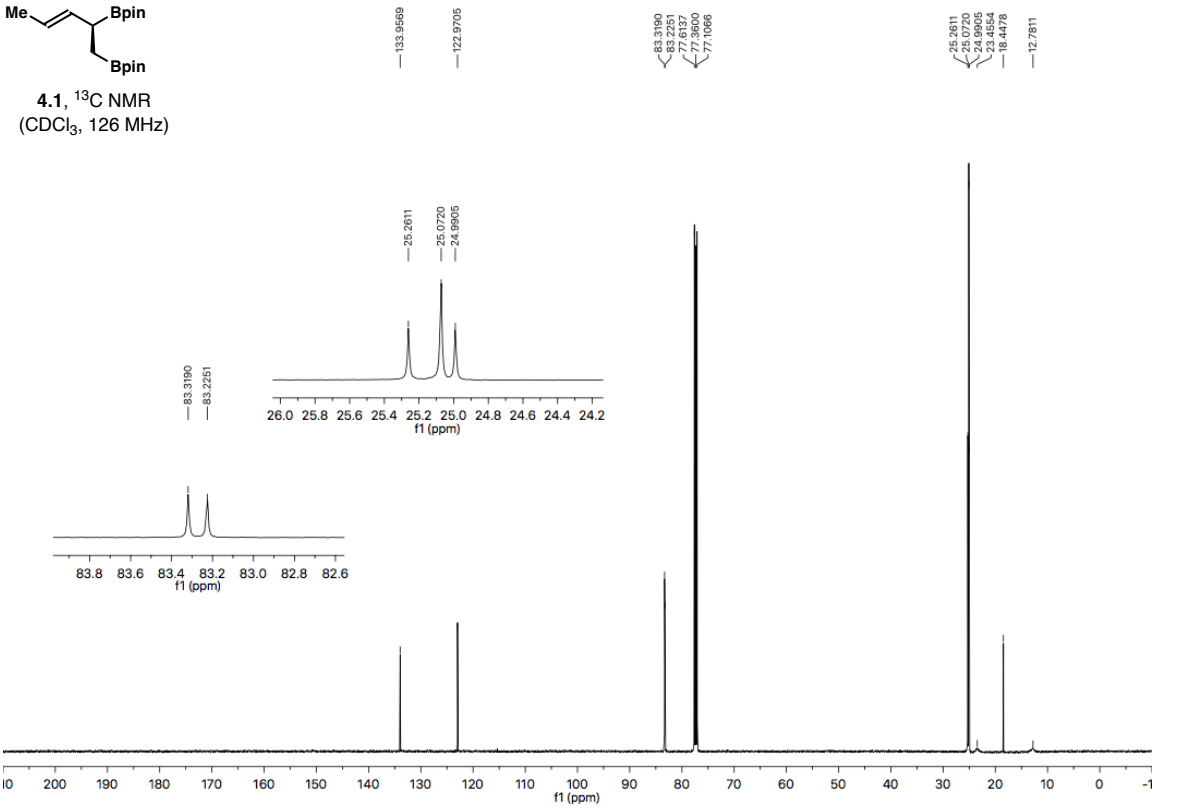
4.3, ^{1}H NMR
($CDCl_3$, 600 MHz)



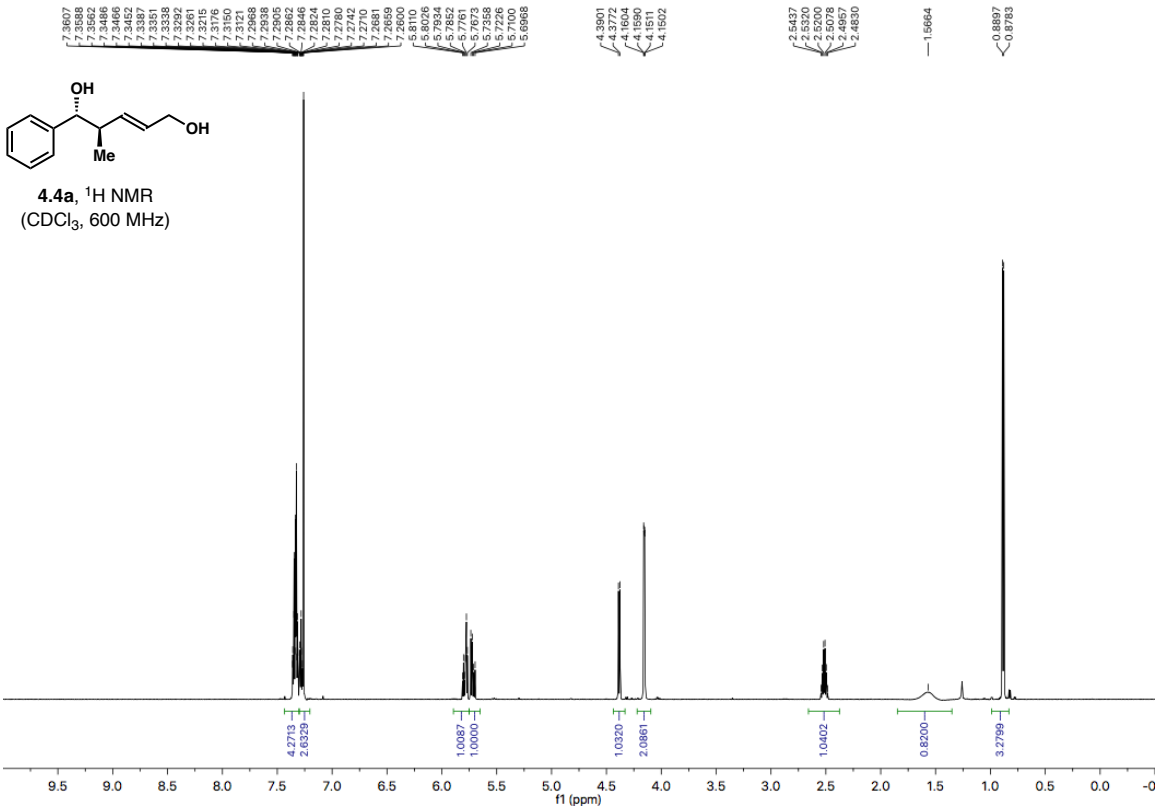
4.3, ^{13}C NMR
($CDCl_3$, 151 MHz)



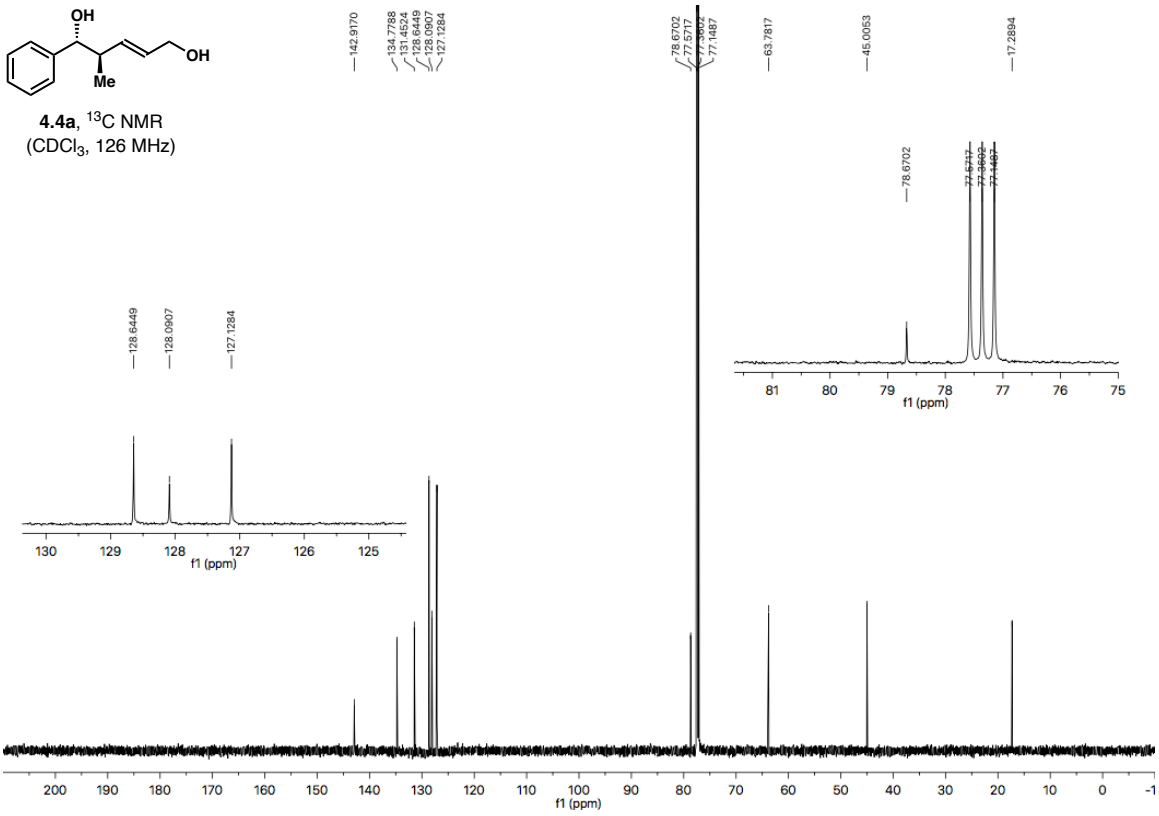
4.1, ^{1}H NMR
($CDCl_3$, 600 MHz)



4.1, ^{13}C NMR
($CDCl_3$, 126 MHz)



4.4a, ^{1}H NMR
($CDCl_3$, 600 MHz)



4.4a, ^{13}C NMR
($CDCl_3$, 126 MHz)

References

(1) Yamamoto, Y.; Asao, N. *Chem. Rev.* **1993**, *93*, 2207.

(2) Denmark, S. E.; Almstead, N. 788 G. In *Modern Carbonyl Chemistry*; Otera, J., Ed.; Wiley-VCH: Weinheim, Germany, 2000; p 299.

(3) Chemler, S. R.; Roush, W. R. In *Modern Carbonyl Chemistry*; Otera, J., Ed.; Wiley-VCH: 791 Weinheim, Germany, 2000; p 403.

(4) Denmark, S. E.; Fu, J. *Chem. Rev.* **2003**, *103*, 2763.

(5) Lachance, H.; Hall, D. G. *Org. React.* **2009**, *73*, 1.

(6) Yus, M.; Gonzaĺez-Goḿez, J. C.; Foubelo, F. *Chem. Rev.* **2011**, *111*, 7774.

(7) Yus, M.; Gonzaĺez-Goḿez, J. C.; Foubelo, F. *Chem. Rev.* **2013**, *113*, 5595.

(8) Diner, C.; Szabó, K. J. *J. Am. Chem. Soc.* **2017**, *139*, 2.

(9) Zimmerman, H. E.; Traxler, M. D. *J. Am. Chem. Soc.* **1957**, *79*, 1920.

(10) Hoffmann, R. W. *Angew. Chem., Int. Ed. Engl.* **1982**, *21*, 555.

(11) Keck, G. E.; Poudel, Y. B.; Cummins, T. J.; Rudra, A.; Covel, J. A. *J. Am. Chem. Soc.* **2011**, *133*, 744.

(12) Lu, Y.; Woo, S. K.; Krische, M. J. *J. Am. Chem. Soc.* **2011**, *133*, 13876.

(13) Lemaire-Audoire, S.; Vogel, P. *J. Org. Chem.* **2000**, *65*, 3346.

(14) Oku, N.; Takada, K.; Fuller, R. W.; Wilson, J. A.; Peach, M. L.; Pannell, L. K.; McMahon, J. B.; Gustafson, K. R. *J. Am. Chem. Soc.* **2010**, *132*, 10278.

(15) Meissner, A.; Kishi, T.; Fujisawa, Y.; Murai, Y.; Takamura, H.; Kadota, I. *Tetrahedron Lett.* **2018**, *59*, 4492.

(16) Wright, A. E.; Cook Botelho, J.; Guzmán, E.; Harmody, D.; Linley,P.; McCarthy, P. J.; Pitts, T. P.; Pomponi, S. A.; Reed, J. K. *J. Nat. Prod.* **2007**, *70*, 412.

(17) Meissner, A.; Tanaka, N.; Takamura, H.; Kadota, I. *Tetrahedron Lett.* **2019**, *60*, 432.

(18) Kang, Y.-T.; Kim, E. H.; Kim, W. J.; Song, N. S.; Shin, J. K.; Cho, B. Y. *Synlett* **1998**, 921.

(19) Yu, C.-M.; Lee, J.-Y.; So, B.; Hong, J. *Angew. Chem., Int. Ed.* **2002**, *41*, 161.

(20) Keck, G. E.; Covel, J. A.; Schiff, T.; Yu, T. *Org. Lett.* **2002**, *4*, 1189.

(21) Keck, G. E.; Truong, A. P. *Org. Lett.* **2005**, *7*, 2153.

(22) Sanchez, C. C.; Keck, G. E. *Org. Lett.* **2005**, *7*, 3053.

(23) Wender, P. A.; Verma, V. A. *Org. Lett.* **2008**, *10*, 3331.

(24) Lee, B.; Kwon, J.; Yu, C.-M. *Synlett* **2009**, *2009*, 1498.

(25) Williams, D. R.; Claeboe, C. D.; Liang, B.; Zorn, N.; Chow, N. S. C. *Org. Lett.* **2012**, *14*, 3866.

(26) Barrett, A. G. M.; Braddock, D. C.; de Koning, P. D.; White, A. J. P.; Williams, D. J. *J. Org. Chem.* **2000**, *65*, 375.

(27) Kissounko, D. A.; Sita, L. R. *J. Am. Chem. Soc.* **2004**, *126*, 5946.

(28) Tanaka, T.; Murai, Y.; Kishi, T.; Takamura, H.; Kadota, I. *Tetrahedron Lett.* **2018**, *59*, 763.

(29) Ito, H.; Kawakami, C.; Sawamura, M. *J. Am. Chem. Soc.* **2005**, *127*, 16034.

(30) Zhang, P.; Roundtree, I. A.; Morken, J. P. *Org. Lett.* **2012**, *14*, 1416.

(31) Fleming, I.; Dunogueѐs, J.; Smithers, R. *Org. React.* **1989**, *37*, 57.

(32) Masse, C. E.; Panek, J. S. *Chem. Rev.* **1995**, *95*, 1293.

(33) Fleming, I.; Barbero, A.; Walter, D. *Chem. Rev.* **1997**, *97*, 2063.

(34) Fleming, I.; Pearce, A.; Snowden, R. L. *J. Chem. Soc., Chem. Commun.* **1976**, 182.

(35) Wierschke, S. G.; Chandrasekhar, J.; Jorgensen, W. L. *J. Am. Chem. Soc.* **1985**, *107*, 1496.

(36) Blumenkopf, T. A.; Overman, L. E. *Chem. Rev.* **1986**, *86*, 857.

(37) Lambert, J. B.; Wang, G. T.; Finzel, R. B.; Teramura, D. H. *J. Am. Chem. Soc.* **1987**, *109*, 7838.

(38) Cutignano, A.; Bruno, I.; Bifulco, G.; Casapullo, A.; Debitus, C.; Gomez-Paloma, L.; Riccio, R. Dactylolide, *Eur. J. Org. Chem.* **2001**, *2001*, 775.

(39) Ohta, S.; Uy, M. M.; Yanai, M.; Ohta, E.; Hirata, T.; Ikegami, S. Exiguolide, *Tetrahedron Lett.* **2006**, *47*, 1957.

(40) Schmitz, F. J.; Gunasekera, S. P.; Yalamanchili, G.; Hossain, M. B.; van der Helm, D. *J. Am. Chem. Soc.* **1984**, *106*, 7251.

(41) Fusetani, N.; Sugawara, T.; Matsunaga, S.; Hirota, H. *J. Org. Chem.* **1991**, *56*, 4971.

(42) Yamauchi, S.; Uno, H. *Org. Biomol. Chem.* **2003**, *1*, 1323.

(43) Zhu, Y.; Lv, Z.-P.; Xue, C.-B.; Wu, W.-S. *Helv. Chim. Acta* **2009**, *92*, 536.

(44) Rateb, M. E.; Houssen, W. E.; Arnold, M.; Abdelrahman, M. H.; Deng, H.; Harrison, W. T. A.; Okoro, C. K.; Asenjo, J. A.; Andrews, B. A.; Ferguson, G.; Bull, A. T.; Goodfellow, M.; Ebel, R.; Jaspars, M. *J. Nat. Prod.* **2011**, *74*, 1491.

(45) Asai, T.; Morita, S.; Shirata, N.; Taniguchi, T.; Monde, K.; Sakurai, H.; Ozeki, T.; Oshima, Y. *Org. Lett.* **2012**, *14*, 5456.

(46) Takahashi, M.; Suzuki, N.; Ishikawa, T.; Huang, H.-Y.; Chang, H.-S.; Chen, I.-S. *J. Nat. Prod.* **2014**, *77*, 2585.

(47) Wang, C.-X.; Ding, R.; Jiang, S.-T.; Tang, J.-S.; Hu, D.; Chen, G.-D.; Lin, F.; Hong, K.; Yao, X.-S.; Gao, H. *J. Nat. Prod.* **2016**, *79*, 2446.

(48) Nicolaou, K. C.; Pavia, M. R.; Seitz, S. P. *J. Am. Chem. Soc.* **1982**, *104*, 2027.

(49) Masamune, S.; Lu, L. D. L.; Jackson, W. P.; Kaiho, T.; Toyoda, T. *J. Am. Chem. Soc.* **1982**, *104*, 5523.

(50) Grieco, P. A.; Inanaga, J.; Lin, N. H.; Yanami, T. *J. Am. Chem. Soc.* **1982**, *104*, 5781.

(51) Suzuki, K.; Matsumoto, T.; Tomooka, K.; Matsumoto, K.; Tsuchihashi, G.-i. *Chem. Lett.* **1987**, *16*, 113.

(52) Matsumoto, T.; Maeta, H.; Suzuki, K.; Tsuchihashi, G.-i. *Tetrahedron Lett.* **1988**, *29*, 3575.

(53) Peŕez,M.;del Pozo, C.; Reyes, F.; Rodríguez, A.; Francesch, A.; Echavarren, A. M.; Cuevas, C. *Angew. Chem., Int. Ed.* **2004**, *43*, 1724.

(54) Fleming, K. N.; Taylor, R. E. *Angew. Chem., Int. Ed.* **2004**, *43*, 1728.

(55) Julian, L. D.; Newcom, J. S.; Roush, W. R. *J. Am. Chem. Soc.* **2005**, *127*, 6186.

(56) Ehrlich, G.; Hassfeld, J.; Eggert, U.; Kalesse, M. *J. Am. Chem. Soc.* **2006**, *128*, 14038.

(57) Smith, A. B., III; Lee, D. *J. Am. Chem. Soc.* **2007**, *129*, 10957.

(58) Dunetz, J. R.; Julian, L. D.; Newcom, J. S.; Roush, W. R. *J. Am. Chem. Soc.* **2008**, *130*, 16407.

(59) Yamada, K.; Tatematsu, H.; Unno, R.; Hirata, Y.; Hirono, I. *Tetrahedron Lett.* **1978**, *19* (46), 4543.

(60) Mohanraj, S.; Kulanthaivel, P.; Subramanian, P.; Herz, W. *Phytochemistry* **1981**, *20*, 1991.

(61) Shi, B.-J.; Xiong, A.-Z.; Zheng, S.-S.; Chou, G.-X.; Wang, Z.-T. *Nat. Prod. Res.* **2010**, *24*, 1897.

(62) Tatsuta, K.; Takahashi, H.; Amemiya, Y.; Kinoshita, M. *J. Am. Chem. Soc.* **1983**, *105*, 4096.

(63) Ito, H.; Ikeuchi, Y.; Taguchi, T.; Hanzawa, Y.; Shiro, M. *J. Am. Chem. Soc.* **1994**, *116*, 5469. (64) Denmark, S. E.; Thorarensen, A.; Middleton, D. S. *J. Am. Chem. Soc.* **1996**, *118*, 8266.

(65) Masuyama, Y.; Takahara, J. P.; Kurusu, Y. *J. Am. Chem. Soc.* **1988**, *110*, 4473.

(66) Fujimura, O.; Takai, K.; Utimoto, K. *J. Org. Chem.* **1990**, *55*, 1705.

(67) Takahara, J. P.; Masuyama, Y.; Kurusu, Y. *J. Am. Chem. Soc.* **1992**, *114*, 2577.

(68) Nakajima, M.; Saito, M.; Hashimoto, S. *Chem. Pharm. Bull.* **2000**, *48* (2), 306.

(69) Araki, S.; Kameda, K.; Tanaka, J.; Hirashita, T.; Yamamura, H.; Kawai, M. *J. Org. Chem.* **2001**, *66*, 7919.

(70) Bandini, M.; Cozzi, P.G.; Licciulli, S.; Umani-Ronchi, A. *Synthesis* **2004**, 409.

(71) Gagliardo,M.;Selander, N.; Mehendale, N. C.; van Koten, G.; Klein Gebbink, R. J. M.; Szabo, K. J. *Chem. - Eur. J.* **2008**, *14*, 4800.

(72) Fujioka, K.; Yokoe, H.; Inoue, A.; Soga, K.; Tsubuki, M.; Shishido, K. *J. Org. Chem.* **2014**, *79*, 7512.

(73) Masuyama, Y.; Takahara, J. P.; Kurusu, Y. *J. Am. Chem. Soc.* **1988**, *110*, 4473.

(74) Fujimura, O.; Takai, K.; Utimoto, K. *J. Org. Chem.* **1990**, *55*, 1705.

(75) Takahara, J. P.; Masuyama, Y.; Kurusu, Y. *J. Am. Chem. Soc.* **1992**, *114*, 2577.

(76) Nakajima, M.; Saito, M.; Hashimoto, S. *Chem. Pharm. Bull.* **2000**, *48* (2), 306.

(77) Araki, S.; Kameda, K.; Tanaka, J.; Hirashita, T.; Yamamura, H.; Kawai, M. *J. Org. Chem.* **2001**, *66*, 7919.

(78) Bandini, M.; Cozzi, P.G.; Licciulli,S.; Umani-Ronchi, A. *Synthesis* **2004**, 409.

(79) Gagliardo, M.; Selander, N.; Mehendale, N. C.; van Koten, G.; Klein Gebbink, R. J. M.; Szabo, K. J. *Chem. - Eur. J.* **2008**, *14*, 4800.

(80) Fujioka, K.; Yokoe, H.; Inoue, A.; Soga, K.; Tsubuki, M.; Shishido, K. *J. Org. Chem.* **2014**, *79*, 7512.

(81) Lopez-Martínez, J. L.; Torres-García, I.; Rodríguez-García, I.; Muñoz-Dorado, M.; Álvarez-Corral, M. *J. Org. Chem.* **2019**, *84*, 806.

(82) Evans, D. A.; Sjogren, E. B.; Bartroli, J.; Dow, R. L. *Tetrahedron Lett.* **1986**, *27*, 4957.

(83) Chiang, Y. C. P.; Yang, S. S.; Heck, J. V.; Chabala, J. C.; Chang, M. N. *J. Org. Chem.* **1989**, *54*, 5708.

(84) Evans, D. A.; Dow, R. L.; Shih, T. L.; Takacs, J. M.; Zahler, R. *J. Am. Chem. Soc.* **1990**, *112*, 5290.

(85) Roush, W. R.; Bannister, T. D.; Wendt, M. D.; Jablonowski, J. A.; Scheidt, K. A. *J. Org. Chem.* **2002**, *67*, 4275.

(86) Reynolds, A. J.; Scott, A. J.; Turner, C. I.; Sherburn, M. S. *J. Am. Chem. Soc.* **2003**, *125*, 12108.

(87) Hamel, C.; Prusov, E. V.; Gertsch, J.; Schweizer, W. B.; Altmann, K.-H. *Angew. Chem., Int. Ed.* **2008**, *47*, 10081.

(88) Kister, J.; Ess, D. H.; Roush, W. R. *Org. Lett.* **2013**, *15*, 5436.

(89) (a) Cui, J.; Ohtsuki, A.; Watanabe, T.; Kumagai, N.; Shibasaki, M. *Chem. - Eur. J.* **2018**, *24*, 2598.

(90) Takeuchi, T.; Kumagai, N.; Shibasaki, M. *J. Org. Chem.* **2018**, *83*, 5851.

(91) Zhang, Y. J.; Yang, J. H.; Kim, S. H.; Krische, M. J. *J. Am. Chem. Soc.* **2010**, *132*, 4562.

(92) Roush, W. R.; Ando, K.; Powers, D. B.; Palkowitz, A. D.; Halterman, R. L. *J. Am. Chem. Soc.* **1990**, *112*, 6339.

(93) Horita, K.; Tanaka, K.; Yonemitsu, O. *Chem. Pharm. Bull.* **1993**, *41*, 2044.

(94) Richardson, T. I.; Rychnovsky, S. D. *J. Am. Chem. Soc.* **1997**, *119*, 12360.

(95) Hanazawa, T.; Koiwa, M.; Hareau, G. P.-J.; Sato, F. *Tetrahedron Lett.* **2000**, *41*, 2659.

(96) Iwata, Y.; Tanino, K.; Miyashita, M. *Org. Lett.* **2005**, *7*, 2341.

(97) (a) Akiyama, T.; Itoh, J.; Yokota, D.; Fuchibe, K. *Angew. Chem., Int. Ed.* **2004**, *43*, 1566.

(98) Uraguchi, D.; Terada, M. *J. Am. Chem. Soc.* **2004**, *126*, 5356.

(99) Akiyama, T. *Chem. Rev.* **2007**, *107*, 5744.

(100) Terada, M. *Chem. Commun.* **2008**, 4097.

(101) Akiyama, T.; Mori, K. *Chem. Rev.* **2015**, *115*, 9277.

(102) Jain, P.; Antilla, J. C. *J. Am. Chem. Soc.* **2010**, *132*, 11884.

(103) Miura, T.; Nishida, Y.; Morimoto, M.; Murakami, M. *J. Am. Chem. Soc.* **2013**, *135*, 11497.

(104) Incerti-Pradillos, C. A.; Kabeshov, M. A.; Malkov, A. V. *Angew. Chem., Int. Ed.* **2013**, *52* (20), 5338.

(105) Huang, Y.; Yang, X.; Lv, Z.; Cai, C.; Kai, C.; Pei, Y.; Feng, Y. *Angew. Chem., Int. Ed.* **2015**, *54*, 7299.

(106) Barrio, P.; Rodríguez, E.; Saito, K.; Fustero, S.; Akiyama, T. *Chem. Commun.* **2015**, *51*, 5246.

(107) Clot-Almenara, L.; Rodríguez-Escrich, C.; Osorio-Planes, L.; Pericaș, M. A. *ACS Catal.* **2016**, *6*, 7647.

(108) Miura, T.; Nakahashi, J.; Murakami, M. *Angew. Chem., Int. Ed.* **2017**, *56*, 6989.

(109) Miura, T.; Nakahashi, J.; Zhou, W.; Shiratori, Y.; Stewart, S. G.; Murakami, M. *J. Am. Chem. Soc.* **2017**, *139*, 10903.

(110) Gao, S.; Chen, M. *Org. Lett.* **2018**, *20*, 6174.

(111) Miura, T.; Oku, N.; Murakami, M. *Angew. Chem., Int. Ed.* **2019**, *58*, 14620.

(112) Gao, S.; Chen, M. *Org. Lett.* **2020**, *22*, 400.

(113) Gao, S.; Duan, M.; Houk, K. N.; Chen, M. *Angew. Chem., Int. Ed.* **2020**, *59*, 10540.

(114) Chen, J.; Chen, M. *Org. Lett.* **2020**, *22*, 7321.

(115) Gao, S.; Duan, M.; Shao, Q.; Houk, K. N.; Chen, M. *J. Am. Chem. Soc.* **2020**, *142*, 18355.

(116) Liu, Y.; Mazet, C. A. *J. Org. Chem.* **2020**, *85*, 5638.

(117) Yuan, J.; Jain, P.; Antilla, J. C. *J. Org. Chem.* **2020**, *85*, 12988.

(118) Jain, P.; Wang, H.; Houk, K. N.; Antilla, J. C. *Angew. Chem., Int. Ed.* **2012**, *51*, 1391.

(119) Chen, M.; Roush, W. R. *J. Am. Chem. Soc.* **2012**, *134*, 10947.

(120) Reddy, L. R. *Org. Lett.* **2012**, *14*, 1142.

(121) Tsai, A. S.; Chen, M.; Roush, W. R. *Org. Lett.* **2013**, *15*, 1568.

(122) Wang, M.; Khan, S.; Miliordos, E.; Chen, M. *Org. Lett.* **2018**, *20*, 3810.

(123) Reddy, L. R. *Chem. Commun.* **2012**, *48*, 9189.

(124) Wang, M.; Khan, S.; Miliordos, E.; Chen, M. *Adv. Synth. Catal.* **2018**, *360*, 4634.

(125) Sadhu, K. M.; Matteson, D. S. *Organometallics* **1985**, *4*, 1687.

(126) Matteson, D. S. *Chem. Rev.* **1989**, *89*, 1535.

(127) Collins, B. S. L.; Wilson, C. M.; Myers, E. L.; Aggarwal, V. K. *Angew. Chem., Int. Ed.* **2017**, *56*, 11700.

(128) Ishiyama, T.; Yamamoto, M.; Miyaura, N. *Chem. Commun.* **1996**, 2073.

(129) Goldberg, S. D.; Grubbs, R. H. *Angew. Chem., Int. Ed.* **2002**, *41*, 807.

(130) Yamamoto, Y.; Takahashi, M.; Miyaura, N. *Synlett* **2002**, *2002* (01), 0128.

(131) Jiang, A. J.; Zhao, Y.; Schrock, R. R.; Hoveyda, A. H. *J. Am. Chem. Soc.* **2009**, *131*, 16630.

(132) Marinescu, S. C.; Schrock, R. R.; Müller, P.; Takase, M. K.; Hoveyda, A. H. *Organometallics* **2011**, *30*, 1780.

(133) Keitz, B. K.; Endo, K.; Herbert, M. B.; Grubbs, R. H. *J. Am. Chem. Soc.* **2011**, *133*, 9686.

(134) Keitz, B. K.; Endo, K.; Patel, P. R.; Herbert, M. B.; Grubbs, R. H. *J. Am. Chem. Soc.* **2012**, *134*, 693.

(135) Occhipinti, G.; Törnroos, K. W.; Jensen, V. R. *Organometallics* **2017**, *36*, 3284.

(136) Li, C.; Yang, Z.; Wang, L.; Guo, Y.; Huang, Z.; Ma, S. *Angew. Chem., Int. Ed.* **2020**, *59*, 6278.

(137) Sasaki, Y.; Zhong, C.; Sawamura, M.; Ito, H. *J. Am. Chem. Soc.* **2010**, *132*, 1226.

(138) Semba, K.; Shinomiya, M.; Fujihara, T.; Terao, J.; Tsuji, Y. *Chem. - Eur. J.* **2013**, *19*, 7125.

(139) Gao, S.; Wang, M.; Chen, M. *Org. Lett.* **2018**, *20*, 7921.

(140) Perry, G. J. P.; Jia, T.; Procter, D. *ACS Catal.* **2020**, *10*, 1485.

(141) Xing, C.-H.; Liao, Y.-X.; Zhang, Y.; Sabarova, D.; Bassous, M.; Hu, Q.-S. *Eur. J. Org. Chem.* **2012**, *2012*, 1115.

(142) Hessler, F.; Betík, R.; Kadlcǐkova,́ A.; Belle, R.; Kotora, M. *Eur. J. Org. Chem.* **2014**, *2014*, 7245.

(143) Rodríguez, E.; Grayson, M. N.; Asensio, A.; Barrio, P.; Houk, K. N.; Fustero, S. *ACS Catal.* **2016**, *6*, 2506.

(144) Su, B.-N.; Takaishi, Y.; Kusumi, T. *Tetrahedron* **1999**, *55*, 14571.

(145) Yamauchi, S.; Uno, H. *Org. Biomol. Chem.* **2003**, *1*, 1323.

(146) Coombs, J. R.; Zhang, L.; Morken, J. P. *Org. Lett.* **2015**, *17*, 1708.

(147) Diner, C.; Szabó, K. J. *J. Am. Chem. Soc.* **2017**, *139*, 2.

(148) Shimizu, M.; Kitagawa, H.; Kurahashi, T.; Hiyama, T. *Angew. Chem. Int. Ed.* **2001**, *40*, 4283.

(149) Chen, M.; Ess, D. H.; Roush, W. R. *J. Am. Chem. Soc.* **2010,** *132*, 7881.

(150) Chen, M.; Roush, W. R. *J. Am. Chem. Soc.* **2011**, *133*, 5744.

(151) Chen, M.; Roush, W. R. *J. Am. Chem. Soc.* **2012**, *134*, 3925. (f) Chen, M.; Roush, W. R. *Org. Lett.* **2013**, *15*, 1662.

(152) Miura, T.; Nakahashi, J.; Murakami, M. *Angew. Chem. Int. Ed.* **2017**, *56*, 6989.

(153) Miura, T.; Nakahashi, J.; Zhou, W.; Shiratori, Y.; Stewart, S. G.; Murakami, M. *J. Am. Chem. Soc.* **2017**, *139*, 10903.

(154) Park, J.; Choi, S.; Lee, Y.; Cho, S. H. *Org. Lett.* **2017**, *19*, 4054.

(155) Gao, S.; Chen, J.; Chen, M. *Chem. Sci.* **2019**, *10*, 3637.

(156) Miura, T.; Nakahashi, J.; Sasatsu, T.; Murakami, M. *Angew. Chem., Int. Ed.* **2019**, *58*, 1138.

(157) Wang, M.; Gao, S.; Chen, M. *Org. Lett.* **2019**, *21*, 2151.

(158) Shin, M.; Kim, M.; Hwang, C.; Lee, H.; Kwon, H.; Park, J.; Lee, E.; Cho, S. H. *Org. Lett.* **2020**, *22*, 2476.

(159) Kennedy, J. W. J.; Hall, D. G. *J. Am. Chem. Soc.* **2002**, *124*, 11586.

(160) Ishiyama, T.; Ahiko, T.; Miyaura, N. *J. Am. Chem. Soc.* **2002**, *124*, 12414.

(161) Sakata, K.; Fujimo- to, H. *J. Am. Chem. Soc.* **2008**, *130*, 12519.

(162) Rateb, M. E.; Houssen, W. E. ; Arnold, M. ; Abdelrahman, M. H. ; Deng, H. ; Harrison, W. T. A. ; Okoro, C. K. ; Asenjo, J. A. ; Andrews, B. A. ; Ferguson, G.; Bull, A. T. ; Goodfellow, M. ; Ebel, R. ; Jaspars, M. *J. Nat. Prod.*, **2011**, *74*, 1491.

(163) Hale, K. J.; Dimopoulos, P.; Cheung, M. L. F. ; Frigerio, M. ; Steed J. W. ; Levett, P. C. *Org. Lett.* **2002**, *4*, 897.

(164) Pasqua, A. E.; Ferrari, F. D.; Hamman, C.; Liu, Y.; Crawford, J. J.; Marquez, R. *J. Org. Chem.* **2012**, *77*, 6989.

(165) Marshall, J. A. *Chem. Rev.* **1996**, *96*, 31.

(166) Shibasaki, M.; Kanai, M. *Chem. Rev.* **2008**, *108*, 2853.

(167) Lachance, H.; Hall, D. G. *Org. React.* **2008**, *73*, 1.

(168) Peng, F.; Hall, D. G. *J. Am. Chem. Soc.* **2007**, *129*, 3070.

(169) Ito, H.; Ito, S.; Sasaki, Y.; Matsuura, K.; Sawamura, M. *J. Am. Chem. Soc.* **2007**, *129*, 14856.

(170) Althaus, M.; Mahmood, A.; Suarez, J. R.; Thomas, S. P.; Aggarwal, V. K. *J. Am. Chem. Soc.* **2010**, *132*, 4025.

(171) Edelstein, E. K.; Namirembe, S.; Morken, J. P. *J. Am. Chem. Soc.* **2017**, *139*, 5027.

(172) Kojima, R.; Akiyama, S.; Ito, H. *Angew. Chem., Int. Ed.* **2018**, *57*, 7196.

(173) Akiyama, S.; Ku- bota, K.; Mikus, M. S.; Paioti, P. H. S.; Romiti, F.; Liu, Q.; Zhou, Y.; Hoveyda, A. H.; Ito, H. *Angew. Chem., Int. Ed.* **2019**, *58*, 11998.

(174) Paioti, P. H. S.; del Pozo, J.; Mikus, M. S.; Lee, J.; Koh, M. J.; Ro- miti, F.; Torker, S.; Hoveyda, A. H. *J. Am. Chem. Soc.* **2019**, *141*, 19917.

(175) Hoffmann, R. W.; Weidmann, U. *J. Organomet. Chem.* **1980**, *195*, 137.

(176) Andersen, M.; Hildebrandt, B.; Koester, G.; Hoffmann, R. W. *Chem. Ber.* **1989**, *122*, 1777.

(177) Hoffmann, R. W.; Wolff, J. J. *Chem. Ber.* **1991**, *124*, 563.

(178) Chen, J. L.-Y.; Scott, H. K.; Hesse, M. J.; Willis, C. L.; Aggarwal, V. K. *J. Am. Chem. Soc.* **2013**, *135*, 5316.

(179) Chen, J. L.-Y.; Aggarwal, V. K. *Angew. Chem. Int. Ed.*, **2014**, *53*, 10992.

(180) Kliman, L. T.; Mlynarski, S. N.; Morken, J. P. *J. Am. Chem. Soc*. **2009**, *131*, 13210.

(181) Coombs, J. R.; Haeffner, F.; Kliman, L. T.; Morken, J. P. *J. Am. Chem. Soc*. **2013**, *135*, 11222.

(182) Grotjahn, D. B.; Larsen, C. R.; Gustafson, J. L.; Nair, R.; Sharma, A. *J. Am. Chem. Soc.* **2007**, *129*, 9592.

(183) Masamune, S.; Choy, W.; Petersen, J. S.; Sita, L. R. *Angew. Chem. Int. Ed. Engl.* **1985**, *24*, 1.

(184) Roush, W. R. *J. Org. Chem.* **1991**, *56*, 4151.