NEW METHODS FOR STEREOSELECTIVE INCORPORATION OF BORON INTO
MOLECULES UTILIZING 1,1-ORGANODIBORONATE ESTERS

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ABSTRACT

Stephanie Alyce Murray: New Methods for Stereoselective Incorporation of Boron into
Molecules Utilizing 1,1-Organodiboronate Esters
(Under the direction of Simon J. Meek)

I. Enantio- and Diastereoselective 1,2-Additions of 1,1-Diborylalkanes to α-Ketoesters

An enantio- and diastereoselective addition of 1,1-diborylalkanes to α-ketoesters is
reported. The reaction is catalyzed by a copper-phosphoramidite catalyst system and yields
products in up to 70% yield, 99:1 er and >20:1 dr after oxidation to the corresponding diol. The
utility of the products is illustrated through functionalizations including homologation, cross-
metathesis, and tetrahydropyran synthesis.

II. Stereoselective 3-Component Bis-Electrophile Couplings of 1,1-Diborylalkanes

A stereoselective tandem epoxide ring-opening/allylation reaction facilitated by a copper
catalyst is reported. The reaction is tolerant of alkyl and aryl epoxides in good yield (up to 99%)
and diastereoselectivity (up to >20:1). The application of this technique to the synthesis of
polyol motifs is explored. Cross coupling, amination, and alkene functionalization reactions
illustrate the versatility of the products.

III. Synthesis of Stereodefined Alkenyl Boronates from Epoxides and Diborylmethane through Pd-Catalyzed Dehydroboration

The palladium catalyzed synthesis of alkenyl boronate esters from epoxides and
diborylmethane via a dehydroboration process is reported. Products are obtained in up to 75%
yield as single olefin isomer. The substrate scope includes alkyl, aryl, and complex steroid
derived molecules. The products are further functionalized through cross coupling and
cycloproponation procedures.

To the Stonehill College Chemistry department. Without you I would still be drawing five bonds to carbon.

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minute to teach cupcake chemistry. I believe that the discussion in our weekly course instructor meetings was the beginning of my interest in a career focused on improving STEM education.

I came to UNC because from the first moment I stepped on campus it felt like home. The close-knit, friendly, collaborative department reminded me of everything I loved about Stonehill. From my advisor, Simon, I learned more about chemistry than I ever thought possible and for that I am very thankful. To my lab mates and fellow UNC grad students, I can't imagine going through grad school with anyone else. It was our nights out indulging in ridiculous amounts of pasta, drinking blue cups on a Friday after a long group meeting, and playing soccer together on Saturdays that got me through grad school. I am especially thankful to Cortnie and Matt J, you are the both perfect mixture of friend and mentor and I will forever be thankful for all that you have taught me and all of the fun adventures we have had (and will continue to have). I cannot wait to watch you both start your own labs and be the next big names in organometallic chemistry. To Jake, Justin, and Michael, thank you for making sure there was never a dull moment in lab and for increasing my knowledge of video games from nonexistent to "race cars." I also had the great privilege of working with three fantastic undergrad students: Sanita, Amber and Eugenia (aka my "Bristol Girls"). I truly could not have asked for better undergraduates to work with. I loved getting to watch you all improve dramatically throughout the year (and hated having to let you go just as you were becoming great chemists).

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miss having you close by so much but can't wait to come visit (often). Jen, thank you for always (eventually) picking up the phone when I call on my drive home from work. I love our conversations and your visits to NC and I can't wait to be able to come visit you frequently in NH. Cortnie (I know I already mentioned you, but you get two), thank you for getting me out of lab and into the real world. From restaurant week, to basketball games, to the rock quarry, you helped me enjoy life in grad school and I couldn't have asked for a better friend to adventure with.

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2,2-DMP	2,2-dimethoxypropane
[{Ir(cod)Cl$_2$}$_2$]	Bis(1,5-cyclooctadienediiridium(I) dichloride
[Pd(allyl)Cl]$_2$	Allylpalladium(II) chloride dimer
[Pd(Cl)(η^3-C$_3$H$_5$)]$_2$	Allylpalladium(II) chloride dimer
Pd(μ-Br)(P^{t}Bu$_3$)$_2$]$_2$	bromo(tri-*tert*-butylphosphine)palladium(I) dimer
(*R*)-binap	(R)-(+)-2,2'-bis(diphenylphosphino)-1,1'-binaphthyl
(*R*)-Cl-OMe-biphep	(R)-(+)-5,5'-Dichloro-6,6'-dimethoxy-2,2'-bis(diphenylphosphino)1,1'-biphenyl
(*R*)-dtbm-segphos	(R)-(-)5,5'-bis[di(3,5-di-tert-butyl-4-methoxyphenyl)phosphino]-4,4'-bi-1,3-benzodioxole
(*R*)-Monophos	(R)-(-)-(3,5-Dioxa-4-phospha-cyclohepta[2,1-a;3,4-a']dinaphthalen-4-yl)dimethylamine
(*R,R*)-Me-duphos	(-)-1,2-bis[(2R,5R)-2,5-dimethylpholano]benzene
(*R,S*)-josiphos	(R)-(-)-1-[(S)-2 (diphenylphosphino)ferrocenyl]ethyldicyclohexylphosphine
° C	degrees Celsius
Å	angstrom
AgOAC	silver(I) acetate
Ar	generic aryl group
B$_2$(pin)$_2$	bis (pinacolato)diboron
BCl$_3$	boron trichloride
bdpp	(2*S*,4*S*)-2,4-Bis(diphenylphosphino)pentane
Bn	benzyl
Boc	*tert*-butyl dicarbonate
Cbz	carboxybenzyl
CH$_2$	methylene group

CH₂Br₂	dibromomethane
CH₂I₂	diiodomethane
CH₂N₂	diazomethane
conv.	conversion
CSA	camphorsulfonic acid
CsF	cesium fluoride
Cu(MeCN)₄PF₆	tetrakis(acetonitrile)copper hexafluorophosphate
Cu(OAc)₂	copper(II) acetate
Cu(OMe)₂	copper(II) methoxide
Cu(OTf)₂	copper(II) trifluoromethanesulfonate
CuBr.dms	copper(I) bromide dimethylsulfide
CuCl	copper(I) chloride
CuI	copper(I) iodide
CuIMesCl	Chloro[1,3-bis(2,4,6-trimethylphenyl)imidazole-2-ylidene]copper(I)
CuSiAdCl	Chloro[1,2-Bis(1-adamanyl)-4,5-dihydroimidazoliumcopper(I)
CuSiMesCl	Chloro[1,3-bis(2,4,6-trimethylphenyl)-4,5-dihydroimidazole-2-ylidene]copper(I)
Cy	cyclohexyl
dce	1,2-dichloroethane
dme	1,2-dimethoxyethane
dmf	N-N'-dimethylformamide
dmpd	dimethyl-4-phenylenediamine
dppb	1,2-diphenylphosphinobutane
dr	diastereomeric ratio
E⁺	generic electrophile
E	*entgegen*

ee%	enantiomeric excess
eq	equivalent
er	enantiomeric ratio
Et	ethyl group
Et$_3$N	triethylamine
Et$_2$O	diethyl ether
Et$_2$Zn	diethylzinc
Grubbs Gen 2	(1,3-Bis(2,4,6-trimethylphenyl)-2-imidazolidinylidene)dichloro(phenylmethylene)(tricyclohexylphosphine)ruthenium
h	hour(s)
H$_2$O	water
H$_2$O$_2$	hydrogen peroxide
H$_2$	hydrogen (diatomic)
HB(pin)	pinacolborane
HMPA	hexamethylphosphoarmide
HPLC	high pressure liquid chromatography
IMes	1,3-bis(2,4,6-trimethylphenyl)imidazole-2-ylidene
^{i}Pr	isopropyl group
KOH	potassium hydroxide
KOPh	potassium phenoxide
LiOEt	lithium ethoxide
LiO^{t}Am	lithium *tert*-amylate
LiO^{t}Bu	lithium *tert*-butoxide
LiTMP	lithium 2,2,6,6-tetramethylpiperidide
L$_n$	generic ligands on metal center
M$^+$	generic metal

M	molar
Me	methyl group
MeCN	acetonitrile
Me-DuPhos	(-)-1,2-Bis[(2R,5R)-2,5-dimethylpholano]benzene
MeOH	methanol
MeONH$_2$	methoxyamine
Mes	mesityl group (2,4,5-trimethylphenyl_
min	minutes
MOR	generic alkoxide base
n-BuLi	*n*-butyllithium
Na$_2$S$_2$O$_3$	sodium thiosulfate
NaBO$_3$•4H$_2$O	sodium perborate tetrahydrate
NaOH	sodium hydroxide
NaO^{t}Bu	sodium *tert*-butoxide
NHC	N-heterocyclic carbene
NMR	nuclear magnetic resonance
NOESY	nuclear overhauser effect spectroscopy
OAc	acetoxy
OP(OEt)$_3$	triethylphosphate
OR	generic alkoxy group
Pd[P(^{t}Bu$_3$)]$_2$	bis[tri(*tert*-butyl)phosphine]palladium(0)
Pd(dba)$_2$	bis(dibenzylideneacetone)palladium(0)
Pd(PPh$_3$)$_4$	tetrakis(triphenylphosphine)palladium(0)
P(*n*-Bu)$_3$	tri(*n*-butyl)phosphine
Pd/C	palladium supported on activated carbon
Pd(OAc)$_2$	palladium(II) acetate

PdCl$_2$(PPh$_3$)$_2$	bis(triphenylphosphine)palladium(II) dichloride
PCy$_3$	tricyclohexylphosphine
Ph	phenyl group
pin	pinacolato group
PPh$_3$	triphenylphosphine
PPTS	pyridinium p-toluenesulfonate
precat	precatalyst
Pt(PPh$_3$)$_4$	tetrakis(triphenylphosphine)platinum(0)
R	generic organic group
R-Br	generic alkyl halide
Rac-binap	racemic 2,2'-bis(diphenylphosphino)-1,1'-binaphthyl
[Rh(cod)Cl$_2$]	chloro(1,5-cyclooctadiene)rhodium(I)
RuPhos	2-dicyclohexylphosphino-2',6'-diisopeopoxybiphenyl
SegPhos	(*R*)-(+)-5,5'-bis(diphenylphosphino-4,4'-bi-1,3-benzodioxole
SFC	Supercritical Fluid Chromatography
SiMes•HCl	1,2-bis(2,4,6-trimethylphenyl)imidazolinium chloride
TaniaPhos	(*R*$_p$)-1-Dicyclohexylphosphino-2-[(*R*)-α-(dimethylamino)-2-(dicyclohexylphosphino)benzyl]ferrocene
TBDPS	*tert*-butyldiphenylsilyl
TBS	*tert*-butyldimethylsilyl group
*t*Bu	*tert*-butyl group
*t*BuOOH	*tert*-butyl hydroperoxide
*t*BuLi	*tert*-butyl lithium
temp	temperature
TESOK	potassium triethylsilanolate
thf	tetrahydrofuran

thf-d_8	octadeuteriotetrahydrofuran
TIPS	triisopropylsilyl group
TMS	trimethylsilyl
TMSCl	chlorotrimethylsilane
Ts	tosyl
UV	Ultraviolet
V(O)(acac)$_2$	vanadyl acetylacetonate
Xantphos	4,5-bis(diphenylphosphino)-9,9-dimethylxanthene
Z	*zusammen*
ZnCl$_2$	zinc(II) chloride
ZnI$_2$	zinc(II) iodide

Chapter 1 Enantio- and Diastereoselective 1,2-Additions of 1,1-Diborylalkanes to α-Ketoesters[1]

1.1 Introduction

The efficient synthesis of pharmaceutical molecules requires the development of new methodologies in organic chemistry. In particular, stereoselective reactions are important as they allow for the synthesis of biologically active molecules as single enantiomer compounds which is often required for pharmaceuticals. Boronate ester functional groups possess unique reactivity that renders them highly desirable as building blocks for the synthesis of important biologically active molecules. Boronate esters can be easily transformed into a multitude of common functional groups through stereospecific means (Figure 1.1).[1,2] Due to the diverse array of stereospecific transformations that can be carried out on boronate esters, being able to easily access small molecule building blocks that contain stereodefined boronate esters is of great use to the scientific community. Therefore, the development of methods for stereoselective incorporation of boronate esters into molecules is necessary. Methods that incorporate these boronate ester groups via carbon-carbon bond formation are of even greater value to the synthetic community as they allow for fast construction of complex structures by building the carbon framework and simultaneously introducing an easily transformed functional group. Accomplishing this in a stereoselective manner would be very useful for organic synthesis.

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[1] A portion of this chapter appeared as a communication in *Angewandte Chemie International Edition,* the full reference is as follows: Murray, S. A.*; Green, J. C.*; Tailor, S. B.; Meek, S. J. *Angew. Chem. Int. Ed.* **2016**, *55,* 9065-9069 (* indicates authors contributed equally).
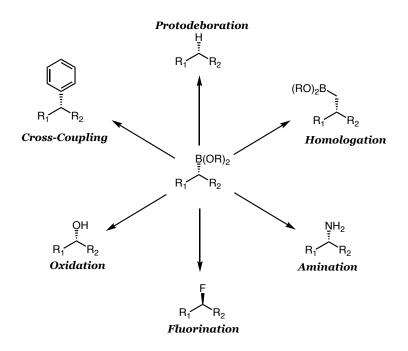
Figure 1.1 Examples of stereoselective functionalizations of boronate esters

1.2 Background

The stereoselective incorporation of boron into molecules via C-B bond forming

reactions has been well studied. Established methods such as hydroboration[2–8], diboration[9–14],

and conjugate boration[15–18] can generate C(sp3)-boryl species in high yield and stereoselectivity.

While these methods provide access to versatile C(sp3)-boryl species that can be further

functionalized, they do not typically generate any additional new functionality beyond the

installation of the boryl group. Therefore, our focus began with the development of methods that

not only stereospecifically introduce a boronate ester but also generate additional functionality

in the molecule. Our initial focus was on the formation of carbon-carbon bonds and alcohol

functional groups. This would allow for rapid construction of highly complex molecular scaffolds

that can be applied towards the total synthesis of important biologically active molecules.
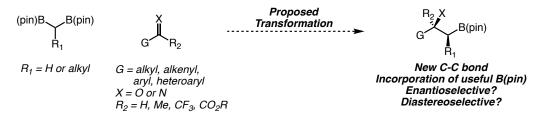
While the previously mentioned methods that install boron into molecules via

hydroboration, diboration, and conjugate boration typically utilize boron sources such as

organo-borane derivatives or diboron species such as bispinacolatodiboron (B₂pin₂), we wanted

to focus on a different boron source that would allow us to incorporate the boron group stereoselectively via C-C bond formation instead of C-B bond formation.

1.2.1 Proposed reaction

In order to accomplish this goal of stereoselective boron incorporation via C-C bond formation, we wanted to employ readily available and bench stable 1,1-diborylmethane or a substituted derivative, as our nucleophile for the addition to carbonyls. Using an 1,1-organodiboronate reagent in a 1,2-addition reaction with a carbonyl substrate had the potential to generate up to two new stereocenters, form a new C-C bond, and install a versatile boron functional group (Scheme 1.1).

Scheme 1.1 General proposed 1,2-addition reaction of 1,1-diborylalkanes and carbonyl or imine electrophiles

1.2.2 Synthesis and use of 1,1-diborylalkanes

Diborylmethane, along with other polyborylated species, was first synthesized in the 1960s by Matteson and coworkers, however its use was severely limited by the methods required to synthesize it (**Figure 1.2a and b**).[19,20] In 2001, Srebnik and co-workers published a new methodology for synthesizing unsubstituted diborylmethane utilizing $B_2(pin)_2$, a platinum catalyst, and diazomethane (**Figure 1.2c**).[21] While this method generated the desired product in high yields and was an improvement over previous methods, the use of highly explosive diazomethane gas is undesirable. In 2009, Shibata and co-workers developed a rhodium catalyzed hydroboration of alkynes for the synthesis of substituted variants of diborylmethane (**Figure 1.2d**).[22] This methodology uses a commercially available metal salt, ligand, and boron source (pinacol borane) and is conducted under ambient temperature and pressure making it a user-friendly approach to the synthesis of 1,1-diborylalkanes. One issue however, is that this

methodology is only applicable for the synthesis of substituted diborylalkanes since the main carbon framework is derived from the alkyne that is used. This method cannot be used to produce the simple unsubstituted 1,1-diborylmethane. Additionally, these substituted variants can already be synthesized from diborylmethane via known methodology that involves deprotonation using lithium 2,2,6,6,-tetramethylpiperidine (LTMP) at the relatively acidic methylene position followed by quenching with the desired electrophile (**Figure 1.2b**).[20]

In 2014, Morken and co-workers published the first truly scalable synthesis of 1,1-diborylmethane (**Figure 1.2e**).[23] Their methodology involves the diboration of 1,1-dibromoalkanes using a copper catalyst, $B_2(pin)_2$ and super-stoichiometric lithium methoxide which serves to activate the $B_2(pin)_2$ for transmetallation to the copper catalyst. While this methodology was a great improvement over those previously developed, a major drawback is the large excess of $B_2(pin)_2$ required as only one boron group from each molecule of $B_2(pin)_2$ can be incorporated into the product which results in poor overall atom economy. While $B_2(pin)_2$ is commercially available, it can be an expensive reagent making this a less than ideal stoichiometry for this reaction.

In 2015, our group disclosed an alternative preparation for 1,1-diborylmethane that allows $B_2(pin)_2$ to serve as the limiting reagent in the synthesis leading to higher atom economy.[24] Utilizing isopropyl magnesium chloride, an α-iodomethyl Grignard can be generated at cryogenic (-78 °C) temperature from insertion into diiodomethane. The α-iodomethyl Grignard can then add to the empty p-orbital on one of the boron groups of $B_2(pin)_2$ forming an -ate complex that then undergoes a borotropic shift releasing the adjacent iodine leaving group, and resulting in the formation of diborylmethane. This methodology allows for the large scale (>10 g) synthesis of diborylmethane using commercially available reagents and in high atom economy relative to the boron starting material as both boron groups from the $B_2(pin)_2$ are incorporated into the product.

(a) Matteson (1969)

(b) Matteson (1981)

(c) Srebnik (2009)
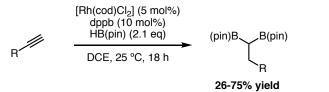
(d) Shibata (2001)

(e) Morken (2014)

(f) Meek (2015)
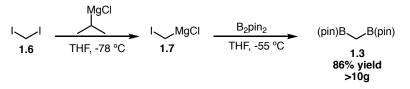
Figure 1.2 Methods for the synthesis of 1,1-diborylalkanes

1.2.3 Applications of 1,1-diborylalkanes in organic synthesis

With a straightforward method of obtaining large quantities of diborylmethane in hand, the focus shifted to the development of new methodologies that utilize this versatile reagent. Initial work by Matteson had illustrated that deprotonated diborylmethane could be added to alkyl halides to generate alkyl substituted 1,1-diborylalkanes (**Figure 1.2b**). Additionally, he showed that these substituted 1,1-diborylalkanes could be deprotonated and added to aldehydes to generate 1,2-hydroxy bisboronate products. These products then undergo a boron-Wittig reaction to yield vinyl boronate esters which can be oxidized to the corresponding ketone (**Figure 1.3**).[25]
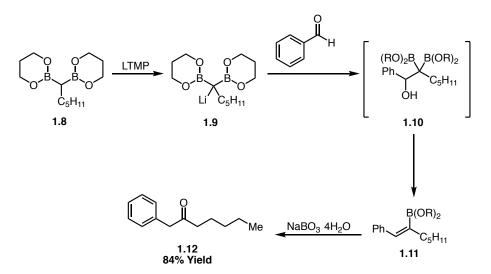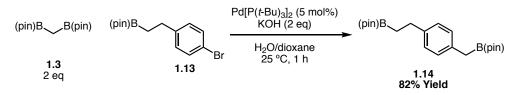
Figure 1.3 1,2-Addition of 1,1-diborylalkanes to aldehydes

This initial work by Matteson focused on deprotonating these diboronate esters at the carbon bound to the two boron groups. The presence of the two boron groups stabilize the resulting carbanion through interactions with the empty p-orbital on the boron moieties. This stabilization lead to the significantly decreased pka at that position (pka ~ 30)[20,25] making these protons easily deprotonated by large amide bases such as LTMP.

In addition to deprotonation, 1,1-diborylalkanes can also be activated via complexation of a Lewis base to the empty p-orbtial of the boron moiety. In 2011, Endo and Shibata took this approach to activating 1,1-diborylalkanes in a palladium-catalyzed Suzuki cross-coupling

reaction (**Scheme 1.2**). They were able to achieve good yields of the cross-coupled products under mild reaction conditions in short reaction times. They also illustrated that the *gem*-diboryl functionality was necessary for this cross coupling to occur as a substrate containing a pendant boronate ester (**1.13**) did not react through this pendant group.[26]

Scheme 1.2 Initial use of 1,1-diborylalkanes in a Suzkui reaction.

In 2014, Morken and coworkers expanded on this initial study with the development of an enantioselective method.[23] In this work, Morken utilizes a palladium phosphoramidite catalyst system and a superstoichiometric amount of potassium hydroxide base to induce enantioselective cross coupling of one of the boron moieties on substituted diborylalkanes with aryl halides. Mechanistic studies revealed that the base does not deprotonate the acidic α-proton on the boron reagent, but instead hydrolyzes the pinacol group on the reactive boron in order for the transmetallation to occur. Additionally, it was shown through isotope labeling experiments and mass spectral techniques that the transmetallation occurs through an invertive process.[23,27] This work was further expanded on by Hall and coworkers.[27] These mechanistic studies illustrate that the α-boryl organopalladium species is generated in high levels of enantioselectivity and is configurationally stable under the reactions conditions.
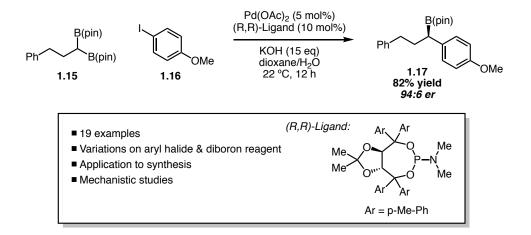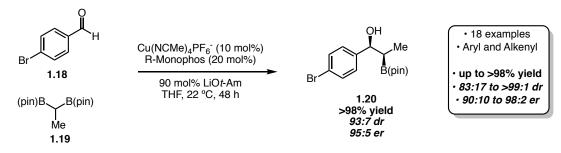
Figure 1.4 Enantioselective cross coupling of 1,1-diborylalkanes by Morken and coworkers

Initial work in the Meek lab pioneered by Matthew Joannou focused on using these 1,1-organodiboronate esters in 1,2-addition reactions with aldehydes. Utilizing a catalyst system comprised of $Cu(NCMe)_4PF_6$ and Monophos with LiO*t*-Am base as activator, the addition of diborylethane (**1.19**) to various aryl aldehydes was accomplished in high yield, enantioselectivity, and diastereoselectivity (**Figure 1.5a**).[24] The *syn*-hydroxyboronates accessible through this methodology can be easily functionalized using known stereospecific boron transformations. Joannou also developed a method for the diastereoselective synthesis of *anti*-hydroxboronate esters using a silver catalyst at decreased temperature (**Figure 1.5b**).[28] Additionally, a broader range of substituted 1,1-diboronate esters could be employed in this methodology. Alkyl aldehydes were tolerated by using slightly modified conditions employing preactivation of the diboron substrate with [n]BuLi. This approach prevented the enolization of the alkyl aldehyde substrate which was problematic in methods utilizing stoichiometric alkoxide base.

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(a) Cu Catalyzed Enantio- and Diastereoselective 1,2-Addition of Diborylmethane

1.18

1.19

Cu(NCMe)$_4$PF$_6^-$ (10 mol%)
R-Monophos (20 mol%)

90 mol% LiOt-Am
THF, 22 °C, 48 h

1.20
>98% yield
93:7 dr
95:5 er

• 18 examples
• Aryl and Alkenyl

• **up to >98% yield**
• *83:17 to >99:1 dr*
• *90:10 to 98:2 er*

(b) Ag Catalyzed Diastereoselective 1,2-Addition of Diborylmethane

i. Aryl Aldehydes

1.18

1.19

AgOAc (10 mol%)
KOt-Bu (1.3 eq)

THF, -25 °C, 24 h

1.21
64% yield
97:3 d.r.

• 25 examples
• Aryl, Alkenyl & Alkyl
• Substituted boron reagents

• **up to 77% yield**
• *47:53 to 99:1 d.r.*

ii. Alkyl Aldehydes

1.22

1.23

AgOAc (10 mol%)
nBuLi (1 eq)

THF, -25 °C, 24 h

1.24
51% yield
95:5 d.r.
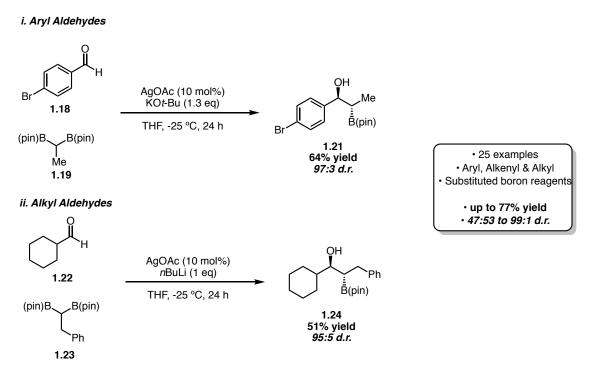
Figure 1.5 1,1-Diborylalkanes in 1,2-addition to aldehydes

The mechanism of the copper catalyzed transformation is outlined in **Figure 1.6**.

Initially, the 1,1-diboronate ester (**1.19**) is activated by the lithium alkoxide base (**1.27**) to

generate the borate species (**1.26**) which is then ready for transmetallation. This activation can

theoretically occur via two different pathways that lead to the same intermediate. The first

involves free lithium alkoxide in solution interacting with the empty p-orbital on one of the

boron moieties to generate the desired borate species (**1.26**) that can then undergo

transmetallation giving **1.28**. The alternative route resembles more of a sigma bond methathesis

mechanism where an alkoxide ligand bound to the copper catalyst (**1.25**) interacts with one of

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the boron moieties resulting in transmetallation of the alkyl fragment to the catalyst. Once the alkyl copper species (**1.28**) is generated, it can partake in 1,2-addition to the carbonyl generating the chiral secondary alcohol via formation of a new C-C bond (**1.30**). The product (**1.31**) can then be released from the catalyst by salt exchange with the lithium base in solution to regenerate the active catalyst (**1.25**). Upon aqueous workup, the desired product is obtained (**1.32**).
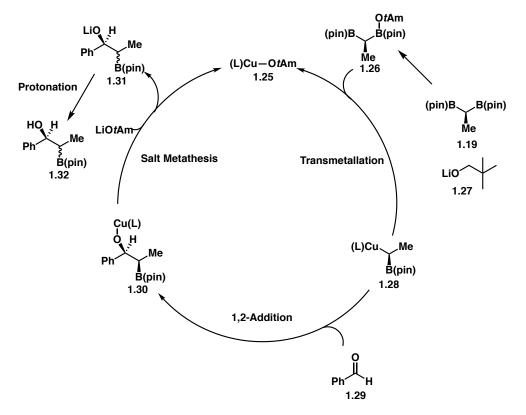
Figure 1.6 Catalytic cycle of the Cu-catalyzed addition of diborylethane to aldehydes.

This method proved to be successful for a variety of aryl aldehydes in good yield and selectivity.[24] The high diastereo- and enantioselectivity observed in this chemistry suggest that, like in Morken's enantioselective cross-coupling reaction, the α-boryl organocopper species (**1.26**) is generated through an enantioselective transmetallation and is configurationally stable under the reaction conditions. To confirm this, the secondary alcohol generated from the carbonyl of a substrate that resulted in low diastereoselectivity was removed and the enantioenrichment of the resulting product was determined. The er remained high and

unchanged (92:8) at the remaining stereocenter suggesting that the α-boryl organocopper species is being formed in high selectivity and the poor diastereoselectivity is a result of poor facial selectivity between the catalyst and the aldehyde.

With this precedent established for the addition of 1,1-organodiboronate esters to carbonyls, the expansion to other carbonyl substrates and diboron reagents was undertaken. In the original work done in the lab, the 1,2-addition reaction generated secondary alcohols via addition to aldehydes. Tertiary alcohols are another useful functional group that can be challenging to synthesize selectively.[29,30] Additionally, if a method can incorporate additional functionality in a single manipulation while setting that tertiary alcohol stereocenter, it will be even more useful as it will allow for the rapid buildup of molecular complexity through an efficient process. Due to the abundance of stereospecific boron-based functionalizations, the development of methods that stereospecifically incorporate boron into molecules is highly desirable.

1.3 Addition of 1,1-diborylalkanes to carbonyls for the generation of tertiary 1,2-hydroxyboronate esters

The first step towards developing this methodology was choosing the correct carbonyl substrate to generate these tertiary alcohol products. Theoretically the simplest transition would be from the aldehydes used previously to ketones. However, this presented many obstacles. The potential difficulty with this class of substrates stems from their ability to enolize under basic conditions. The stoichiometric alkoxide base that is required for activating the diboron reagent can also deprotonate the ketone to generate an enolate which can then undergo a variety of different nonproductive decomposition pathways including aldol chemistry. We had previously shown through NMR studies that, under our reaction conditions, only 21% of the diboron reagent is activated.[24] The remaining base is free in solution. As the activated boron reagent is consumed in the 1,2-addition reaction, more of the diborylethane is activated to maintain the equilibrium between the activated and unactivated species in solution. Since some of the base is

always free in solution, it is possible that it will be able to deprotonate the ketone starting material and lead to destruction of the substrate before it can be used productively.

With these potential problems in mind, ketones were explored under reaction conditions that were successful for aldehydes to see if the product forming pathway would be fast enough to compete with the decomposition of the starting ketone via deprotonation. Using Cu(OMe)$_2$, *R*-Monophos, and LiO*t*Bu as activator in THF with a 1:1 stoichiometry between the acetophenone and diborylmethane did not yield any of the desired product (**Table 1.1, Entry 1**). To try to encourage reactivity the base was switched to NaO*t*Bu, which is typically a stronger activator than the lithium variant. Using an excess of the diborylmethane 14% of the desired product (**1.34**) was obtained (**Table 1.1 Entry 2**). While observing product was a promising result, the enantioselectivity of the reaction was only 59:41 er. In the early reaction screenings for the aldehyde chemistry the authors had found that copper methoxide often led to inconsistent results in the 1,2-addition reactions. Because of this, a similar reaction to entry 2 but using CuCl as the copper source instead of Cu(OMe)$_2$ was attempted, however only 17% conversion to the desired product was observed and an even lower level of selectivity at 52:48 er. (**Table 1.1, Entry 3**). A brief solvent screen was then performed to observe solvent effects on conversion and enantioselectivity, however better results were not obtained in 1,4-dioxane or DME (**Table 1.1, Entries 4&5**). Additionally, all of these reactions showed substantial consumption of the starting materials indicating that further optimization in this type of reaction would be quite challenging.

Table 1.1 Addition of diborylmethane to acetophenone.

Entry	Cu Source	Activator (X eq)	Solvent	Eq. of **1.3**	**1.34** (%)	er
1	Cu(OMe)$_2$	LiOtBu (1)	THF	1	0	-
2	Cu(OMe)$_2$	NaOtBu (1.2)	THF	2	14	59:41
3	CuCl	NaOtBu (1)	THF	1	17	52:48
4	Cu(OMe)$_2$	NaOtBu (1.2)	dioxane	2	18	-
5	Cu(OMe)$_2$	NaOtBu (1.2)	dme	2	0	-

Having established that ketones are not viable substrates under the current reaction manifold, other carbonyl substrates that would produce the desired tertiary alcohol were explored. α-Ketoesters were another class of substrates that seemed promising for 1,2-addition with organodiboronate esters. The adjacent ester group in an α-ketoester eliminates the possibility for enolization. Additionally, the ester would help to make the ketone more reactive towards 1,2-addition than a ketone would be.

1.3.1 Reaction optimization[30]

Initially, the 1,2-addition of diborylmethane to ethyl phenyl glyoxylate was explored under the previously optimized conditions for the addition of diborylethane to aldehydes using LiOtBu as base (**Table 1.2**). At 22 °C, the desired product was observed in 23% yield and 91:9 er (**Table 1.2, Entry 1**) using Cu(MeCN)$_4$PF$_6$ and R-Monophos as the catalyst. No starting ketoester was returned in this reaction, however 11% of product **1.38** derived from boron-Wittig elimination was observed. The boron Wittig reaction occurs when the alkoxide group generated in the 1,2-addition reaction chelates with the adjacent boron which results in the elimination of the O-B(pin) moiety. While this is an undesired reaction product, it is indicative of product

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formation so we speculated that if the elimination reaction can be slowed down then the amount
of desired product formed should increase.

Table 1.2 Optimization of the addition of diborylmethane to ethyl phenyl glyoxylate

Entry[a]	R	Base (X eq)	Temp (°C)	1.37 (%)[b]	1.36 (%)[c]	1.38 (%)	er[d]
1	Et	LiOtBu (1)	22	<2	23	11	91:9
2	Et	LiOtBu (2.05)	22	<2	43	24	91:9
3	Et	LiOtBu (2.05)	4	<2	60	12	92:8
4	Et	LiOtBu (2.05)	-10	<2	74	<2	96:4
5	Et	LiOtBu (2.05)	-25	35	51	<2	95:5
6	tBu	LiOtBu (1)	-10	<2	63	<2	94:6
7	Me	LiOtBu (2.05)	-10	<2	70	<2	93:7
8	Et	LiOtBu (1)	-10	18	26	8	91:9
9	Et	NaOtBu (2.05)	-10	32	37	<2	81:19

(a) Reactions performed under N_2 atm. (b) In all cases >98% conv. of α-ketoester starting material.
(c) Conversions determined by ^{1}H NMR analysis of unpurified mixtures, with DMF as an internal
standard, at either 400 or 600 MHz. (d) Determined by $NaBO_3 \cdot H_2O$ oxidation to diol and HPLC
analysis.

Another important observation made with this first reaction was the identity of the ester.
The α-ketoester substrate used in the reaction contained an ethyl ester moiety, however the
primary product observed in the reaction contained a *tert*-butyl ester obtained from a
transesterification reaction with some of the lithium *tert*-butoxide in solution (**1.36**). This is not
a surprising result as it was previously shown that only a small amount of the diboron reagent
exists as the borate complex at any time in the reaction mixture. This means that the remaining

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LiO*t*Bu is available to transesterify the starting ethyl ester to the *tert*-butyl ester. This process also results in the formation of lithium ethoxide as base and consumes the remaining lithium *tert*-butoxide. This means that in order for the desired reaction to proceed under these reaction conditions, it would be necessary for the lithium ethoxide to activate the diborylmethane for addition to the ketoester. This could be problematic as the less soluble lithium ethoxide might not be a good activator of the diboron reagent. Additionally, the enantioselectivity of the reaction could be affected by the smaller ethoxide activating group.

In order to overcome the issue of multiple alkoxide bases present in solution, the reaction was repeated using 2.05 equivalents of LiO*t*Bu. Under these reaction conditions, the conversion to the desired product increased to 43% and the enantioselectivity remained constant at 91:9 er (**Table 1.2, Entry 2**). The elimination product (**1.38**) increased to 24%. This was a promising result as the elimination product is derived from the desired product, so if that pathway can be shut down then the yield of desired product should increase.

To try to decrease the elimination product, the reaction temperature was lowered to 4 ºC. This resulted in an increase in conversion to the desired product to 60% and a slight increase in enantioselectivity to 92:8 er (**Table 1.2, Entry 3**). A small amount, 12%, of the undesired elimination product was still observed at this temperature. Additional cooling to -10 ºC led to a further increase in conversion to 74% and enantioselectivity to 96:4 er (**Table 1.2, Entry 4**). At -10 ºC no elimination product or returned starting material was observed. Further cooling to -25 ºC did not improve the reaction (**Table 1.2, Entry 5**). At this temperature only 51% conversion to product was observed with an enantioselectivity of 95:5. No elimination product was observed at -25 ºC however starting material in the form of the *tert*-butyl ester (**1.37**) was observed in 35% yield. Reactions conducted at -25 ºC for longer periods of time did not result in an increase in conversion to product. This also indicates that the transesterification reaction is likely faster than the 1,2-addition, and that the starting ketoester is transesterified to the *tert*-butyl ester prior to the addition of the diboron reagent. This is further supported by a control reaction
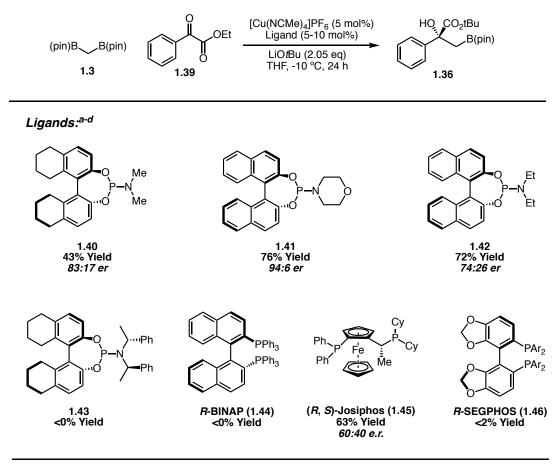
wherein treatment of ethyl phenyl glyoxylate with 2 equivalents of LiO*t*Bu without copper or ligand at -10 °C for 2.5 h resulted in full consumption of the starting ethyl ester and 90% conversion to the *tert*-butyl ester.

With optimized reaction conditions in hand, the role that the identity of the ester plays in the reaction was probed. Starting with the *tert*-butyl ketoester and using only one equivalent of base resulted in a slight decrease in reaction efficiency yielding 63% conversion and 94:6 er (**Table 1.2, Entry 6**). Using the methyl ester, the product was obtained in 70% conversion, however only 91:9 er (**Table 1.2, Entry 7**). Using one equivalent of lithium *tert*-butoxide at -10 °C lead to a complex mixture of all three products in overall low yield (**Table 1.2, Entry 8**). The identity of the base was also explored by switching from the lithium alkoxide base to sodium *tert*-butoxide (**Table 1.2, Entry 9**). The sodium base resulted in a much more complex product distribution even at decreased temperature. At -10 °C, product was observed in only 37% conversion and had a significant decrease in enantioselectivity to an er of only 81:19. The starting material was observed as the *tert*-butyl ester in 32%. These results agree with the previous work with aldehydes in which a lithium alkoxide base was necessary to achieve the desired reactivity and selectivity.

Finally, a variety of phosphine ligands were screened to see if an increase in yield or conversion could be achieved. Bidentate phosphines such as *(R)*-BINAP and *(R)*-dtbm-SEGPHOS both resulted in <2% conversion. A bidentate (*R*,*S*)-Josiphos ligand gave 63% conversion to product however the enantioselectivity diminished to only 60:40 er. Other phosphoramidite ligands were successful in this reaction, however the conversion and selectivity were always comparable to or diminished relative to that of the simple *R*-Monophos variant. The results of the reactions using these ligands are illustrated in **Figure 1.7**.
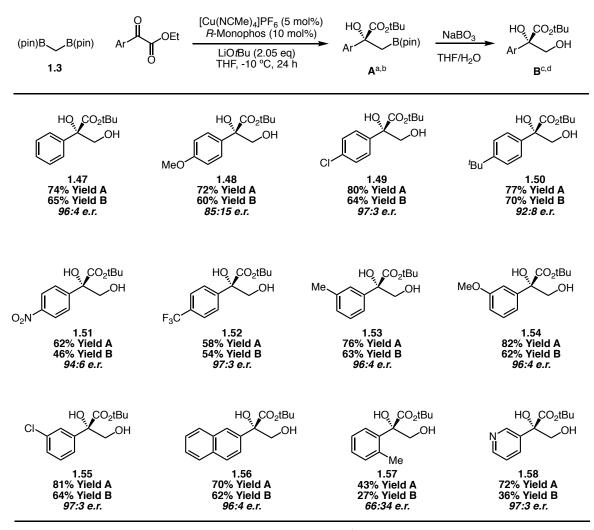
(pin)B B(pin)

1.3

O / OEt (with phenyl, =O)

1.39

[Cu(NCMe)$_4$]PF$_6$ (5 mol%)
Ligand (5-10 mol%)
LiOtBu (2.05 eq)
THF, -10 °C, 24 h

HO CO$_2$tBu
B(pin)

1.36

Ligands:[a-d]

1.40
43% Yield
83:17 er

1.41
76% Yield
94:6 er

1.42
72% Yield
74:26 er

1.43
<0% Yield

R-BINAP (1.44)
<0% Yield

(R, S)-Josiphos (1.45)
63% Yield
60:40 e.r.

R-SEGPHOS (1.46)
<2% Yield

(a) Reactions performed under N$_2$ atm. (b) In all cases >98% conv. of α-ketoester starting material. (c) Conversions determined by ^{1}H NMR analysis of unpurified mixtures, with DMF as an internal standard, at either 400 or 600 MHz. (d) Determined by NaBO$_3$·H$_2$O oxidation to diol and HPLC analysis.

Figure 1.7 Ligand screen for 1,2-addition of diborylmethane to ethyl phenyl glyoxylate.

1.3.3 Substrate scope[30]

With optimized conditions in hand, the substrate scope of the reaction was explored. First, the ketoester was varied. In order to aid in isolation and determination of selectivity, the crude reactions were oxidized to the diol for isolation. **Figure 1.8** illustrates the many aromatic ketoesters were tolerated in this reaction. The *p*-OMe substrate (**1.48**), while being a high yielding reaction, gave product in significantly lower enantioselectivity than most of the other substrates which all tended to be greater than 90:10 e.r. It was postulated that this particularly electron-rich aromatic ring could allow for racemization of the product upon purification by silica gel chromatography. This was ruled out by taking the isolated product and resubjecting it to silica gel chromatography and then checking the level of enantioselectivity obtained in that

re-isolated product. No change in selectivity was observed meaning that the lower enantioselectivity is what is produced in the reaction. A weakly electron withdrawing chloride group in the para position resulted in 64% yield and 97:3 er of the desired diol product (**1.49**). A *tert*-butyl substituent at the para was well tolerated yielding product **1.50** in 70% yield and 92:8 er. Strongly electron withdrawing nitro group (**1.51**) was tolerated at the para position in good er (94:6) and slightly diminished yield (46%). Trifluoromethyl substitution at the para position resulted in 54% isolated yield and 97:3 er (**1.52**).
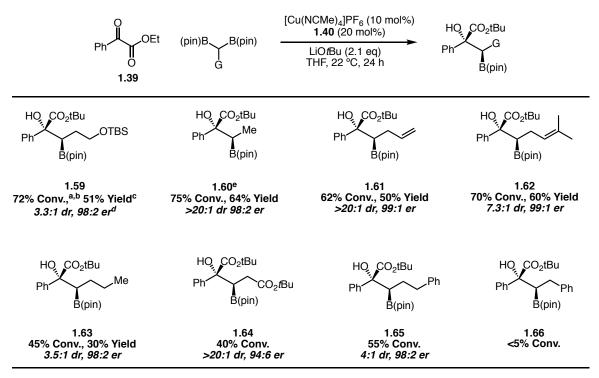
Substitution at the meta position was well tolerated. This was illustrated through methyl (**1.53**, 63% yield, 96:4 er), methoxy (**1.54**, 62% yield, 96:4 er) and chloro (**1.55**, 64% yield, 97:3 er) substitution. Napthyl derived ketoester yielded product **1.56** in 62% yield and 96:4 er. The *o*-Me ketoester showed decreased reactivity and selectivity yielding **1.57** in 27% yield and 66:34 er. This is most likely due to the increase in sterics near the already sterically hindered reactive sight on the ketoester. A pyridine heterocyle (**1.58**) was well tolerated for the initial 1,2-addition reaction as illustrated by the 72% conversion to the corresponding 1,2-hydroxyboronate ester, however upon oxidation only 36% of the desired diol was isolated in 97:3 er.

Figure 1.8 Ketoester substrate scope

The scheme at top shows:

(pin)B–B(pin) **1.3** + Ar–C(=O)–CO₂Et, with [Cu(NCMe)₄]PF₆ (5 mol%), R-Monophos (10 mol%), LiOtBu (2.05 eq), THF, -10 °C, 24 h → **A**[a,b] (Ar–C(OH)(CO₂tBu)–CH₂–B(pin)); then NaBO₃, THF/H₂O → **B**[c,d] (Ar–C(OH)(CO₂tBu)–CH₂OH)

Substrate scope products:

1.47 — 74% Yield A / 65% Yield B / 96:4 e.r.

1.48 (MeO) — 72% Yield A / 60% Yield B / 85:15 e.r.

1.49 (Cl) — 80% Yield A / 64% Yield B / 97:3 e.r.

1.50 (tBu) — 77% Yield A / 70% Yield B / 92:8 e.r.

1.51 (O₂N) — 62% Yield A / 46% Yield B / 94:6 e.r.

1.52 (F₃C) — 58% Yield A / 54% Yield B / 97:3 e.r.

1.53 (Me) — 76% Yield A / 63% Yield B / 96:4 e.r.

1.54 (MeO) — 82% Yield A / 62% Yield B / 96:4 e.r.

1.55 (Cl) — 81% Yield A / 64% Yield B / 97:3 e.r.

1.56 (naphthyl) — 70% Yield A / 62% Yield B / 96:4 e.r.

1.57 (Me) — 43% Yield A / 27% Yield B / 66:34 e.r.

1.58 (pyridyl) — 72% Yield A / 36% Yield B / 97:3 e.r.

[a] In all cases >98% conv. of α-ketoester starting material is consumed. [b] Determined by ¹H-NMR analysis of unpurified mixtures with dmf as internal standard, at either 400 or 600 MHz. [c] Yield of the purified diol (average of 2 runs) [d] Determined by HPLC analysis

The substrate scope was then explored in relation to the 1,1-organodiboronate ester. Initially, 1,1-diborylethane was studied. With an increase in catalyst loading to 10 mol% and an increase in temperature to 22 °C, a 64% yield of the desired product was obtained as a single diastereomer and in 98:2 er (**Figure 1.9**). X-ray crystallographic analysis of the product confirmed that the boron unit and the hydroxyl group are on opposite faces (**Figure 1.10**). When the scope was explored further beyond the simple ethyl substituted diboron reagent, the yields of the desired product dropped dramatically. Jacob Green took over the further optimization of this reaction for other substituted diboron reagents. He found that by switching

the ligand from *R*-Monophos to the partially hydrogenated *R*-H$_8$-Monophos (**1.39 in Figure 1.7**) the yields of the desired products rose significantly. As illustrated in **Figure 1.9**, alkyl, alkenyl, benzyl, and ester substituted diboron reagents all give the desired products in high yields and diastereo- and enantioselectivity.

1.59
72% Conv.,[a,b] 51% Yield[c]
3.3:1 dr, 98:2 er[d]

1.60[e]
75% Conv., 64% Yield
>20:1 dr 98:2 er

1.61
62% Conv., 50% Yield
>20:1 dr, 99:1 er

1.62
70% Conv., 60% Yield
7.3:1 dr, 99:1 er

1.63
45% Conv., 30% Yield
3.5:1 dr, 98:2 er

1.64
40% Conv.
>20:1 dr, 94:6 er

1.65
55% Conv.
4:1 dr, 98:2 er

1.66
<5% Conv.

[a] In all cases >98% conv. of α-ketoester starting material is consumed. [b] Determined by ^{1}H-NMR analysis of unpurified mixtures with dmf as internal standard, at either 400 or 600 MHz. [c] Yield of the purified diol (average of 2 runs). [d]Determined by HPLC analysis. [e] **1.35** used as ligand.

Figure 1.9 Substituted 1,1-diborylalkane substrate scope
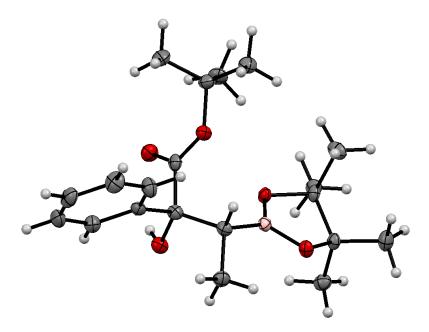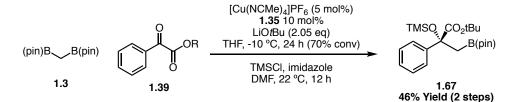
Figure 1.10 X-ray structure of 1.60
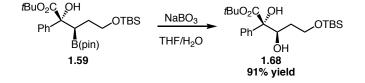
1.3.4 Functionalizations[30]

In order to illustrate the utility of the products generated in these reactions, a series of functionalizations was carried out on both the alcohol and boron moiety (**Figure 1.11**). First, to show that the products can be isolated with the boron moiety in place, the alcohol was protected as the trimethylsilyl ether and the product **1.67** was isolated in 46% overall yield from the starting ketoester. The oxidation of **1.59** resulted in the diol product **1.68** in 91% isolated yield. To illustrate the versatility of the boron moiety, a homologation reaction was carried out on silyl protected **1.69**. Product **1.70** was obtained after one carbon homologation in 50% yield.[32] Next, a cross methathesis reaction was carried out on **1.61** with cis-butenediol as coupling partner.[33] This functionalization results in a 63% yield of **1.71** and a 16:1 *E:Z* ratio illustrating that transformations can be conducted on other parts of the molecule while leaving the boron moiety in place. Lastly, an iodoetherification reaction was performed on the prenyl substituted product to form tetrahydropyran **1.74** in 56% yield and 3:1 d.r.[34]
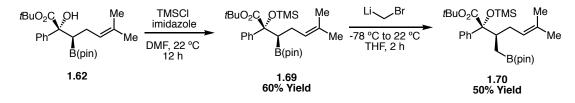
(a) Alcohol Protection

(b) Oxidation
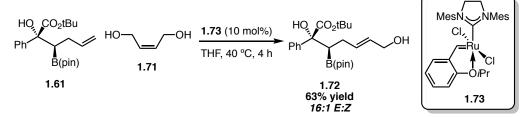
(c) Protection & Homologation

(d) Metathesis

(e) Iodoetherification
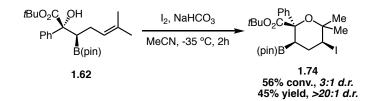
Figure 1.11 Product functionalizations

1.3.5 Mechanism[30]

  Figure 1.12 illustrates the proposed catalytic cycle for this reaction. Transmetallation of diborylethane (**1.19**) to the copper catalyst occurs via coordination to the bound alkoxide ligand (**1.75**) (or activation by free base in solution). The α-boryl copper species (**1.76**) then undergoes

a 1,2-addition reaction with the ketoester (**1.39**) followed by turnover of the catalyst via ligand exchange with the lithium alkoxide base.
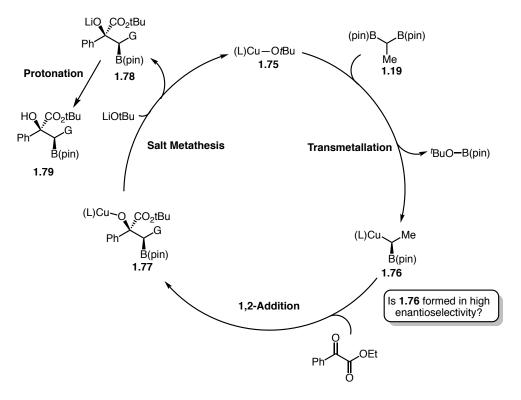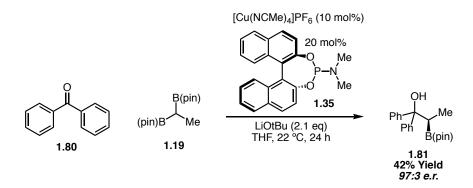
Figure 1.12 Proposed catalytic cycle

In order to gain insight into the stereochemical determining steps of the reaction, the addition of diborylethane to benzophenone was carried out and is illustrated in **Scheme 1.3**. The product of this reaction (**1.73**) is formed in low conversion (42%) however high stereoselectivity (97:4 e.r.). This indicates that the α-boryl copper species **1.76**, is formed in high selectivity, and that the catalyst controls both the selective formation of the α-boryl copper species as well as the facial selectivity of the addition to the ketoester.

Scheme 1.3 1,2-Addition of diborylethane to benzophenone as mechanistic probe

1.4 Conclusions[30]

In summary, a new methodology for the stereoselective synthesis of tertiary alcohols containing a vicinal boronate ester from 1,1-organodiboronate esters and α-ketoesters using a copper phosphoramidite catalyst system was developed. The products are generated in good yield, diastero-, and enantioselectivity. The methodology extends to a variety of α-ketoesters and substituted 1,1-diboronate esters. The versatility of these products was illustrated through multiple functionalizations including oxidation, homologation, and cross coupling. The reaction is proposed to occur via an enantioselective transmetallation and evidence of this was presented in the high level of enantioselectivity that is achieved when benzophenone is used as the carbonyl substrate.

1.5 Experimental[30]

1.5.1 General

All reactions were carried out in oven-dried (150 ˚C) or flame-dried glassware under an inert atmosphere of dried nitrogen unless otherwise noted. Analytical thin-layer chromatography was performed on glass plates coated with 0.25 mm of 60 Å mesh silica gel. Plates were visualized by exposure to UV light (254 nm) and/or immersion into Seebach's or $KMnO_4$ stain followed by heating. Column chromatography using regular silica gel was performed using silica gel P60 (mesh 230-400) supplied by Silicycle. Deactivated silica gel was prepared by mixing silica gel and deionized water (65:35 by weight) followed by vigorous

shaking and stirring until a free-flowing powder was obtained. This was allowed to sit overnight. All solvents were sparged with argon and then purified under a positive pressure of argon through an SG Water, USA Solvent Purification System. Tetrahydrofuran (OmniSolv) was passed successively through two columns of neutral alumina. The ambient temperature in the laboratory was approximately 22 °C. Reactions were run at low temperatures using an isopropanol filled SP Scientific cryobath.

1.5.2 Instrumentation

All ^{1}H NMR spectra were recorded on Bruker Spectrometers (AVANCE-600 and DRX 400). Chemical shifts are reported in ppm from tetramethylsilane and referenced to the residual protio solvent peak (CDCl$_3$: δ 7.26). Data are reported as follows: chemical shift, multiplicity (s = singlet, d = doublet, t = triplet, qu = quartet, quint = quintet, br = broad, m = multiplet, app = apparent), integration, and coupling constants are given in Hz. ^{13}C NMR spectra were recorded on Bruker Spectrometers (AVANCE-600 and DRX-400) with carbon and proton decoupling. Chemical shifts are reported in ppm from tetramethylsilane and referenced to the residual protio solvent peak (CDCl$_3$: δ 77.16). ^{13}B NMR spectra were recorded on a Bruker model 500 MHz spectrometer. All IR spectra were recorded on a Jasco 260 Plus Fourier transform infrared spectrometer. Mass spectrometry samples were analyzed with a hybrid LTQ FT (ICR 7T) (ThermoFisher, Bremen, Germany) mass spectrometer. Samples were introduced via a microelectrospray source at a flow rate of 10 μL/min (solvent composition 10:1 MeOH:H$_2$O). Xcalibur (ThermoFisher, Breman, Germany) was used to analyze the data. Molecular formula assignments were determined with Molecular Formula Calculator (v 1.2.3). Low-resolution mass spectrometry (linear ion trap) provided independent verification of molecular weight distributions. All observed species were singly charged, as verified by unit m/z separation between mass spectral peaks corresponding to the ^{12}C and ^{13}C^{12}C$_{c-1}$ isotope for each elemental composition. Optical rotations were determined using a Jasco P1010 polarimeter and concentrations are reported in g/100mL. Enantiomeric ratios were determined on an Agilent

Technologies 1220 Infinity LC using the following columns: Diacel CHIRALPAK IA (4.6 mm x 250 mmL x 5 μm), Diacel CHIRALPAK IB (4.6 mm x 250 mmL x 5 μm), and Diacel CHIRALPAK IC (4.6 mm x 250 mmL x 5 μm).

1.5.3 Reagents

Ammonium chloride was purchased from Alfa Aesar and used as received.

^{n}Butyl lithium (1.6M in hexanes) was purchased from Strem Chemicals and titrated using *sec*-butanol and phenanthroline prior to use.

Calcium hydride was purchased from Strem Chemicals and used without further purification.

Copper(I) chloride was purchased from Strem Chemicals and kept in a nitrogen filled dry box.

Copper(II) triflate was purchased from Strem Chemicals and kept in a nitrogen filled dry box.

Copper(I) tetrakisacetonitrile hexafluorophosphate was purchased from Sigma-Aldrich and kept in a nitrogen filled dry box.

Chloroform-d$_{3}$ was purchased from Cambridge Isotope Laboratories and used without further purification.

Chlorotrimethylsilane was purchased from Acros, dried over calcium hydride, distilled, stored under nitrogen at 0° C, and used within 2 weeks of distillation.

Diborylmethane was synthesized according to literature procedure and matched literature spectra.[24] It was purified via column chromatography (20:1 hexanes:ethyl acetate) to contain <7% $B_2(pin)_2$ by ^{1}H-NMR spectroscopy and dried via azeotropic distillation from benzene.

Dibromomethane was purchased from Alfa Aesar and passed through a short column of neutral alumina and then sparged with dry nitrogen before use.

Dimethylformamide (dry) was purchased from EMD and used as received.

Ethyl benzoylformate was purchased from Sigma Aldrich and Alfa Aesar, dried via azeotropic distillation with benzene, and stored under nitrogen.

Ethyl 4-nitrophenylglyoxylate was obtained from Lancaster Synthesis, dried via azeotropic distillation with benzene, and stored under nitrogen at -25° C.

Ethyl mesitylglyoxylate was obtained from Lancaster Synthesis, dried via azeotropic distillation with benzene, and stored under nitrogen at -25° C.

Ethyl-3-methylbenzoyl formate was obtained from Reike Specialty Chemicals, dried via azeotropic distillation with benzene, and stored under nitrogen at -25° C.

Hoveyda-Grubbs Catalyst 2nd Generation was obtained from Sigma Aldrich and used as received.

Imidazole was purchased from Alfa-Aesar and used as received.

Iodine was purchased from EM Science and used as received.

Lithium *tert*-butoxide was purchased from Strem Chemicals, stored in a nitrogen filled dry box and used as received.

(*R*)-Monophos (1.35), (*R*)-MorphPhos (1.41), and (*R*)-H$_8$-Monophos (1.40) were synthesized according to published literature procedure and matched literature spectra.[35,36]
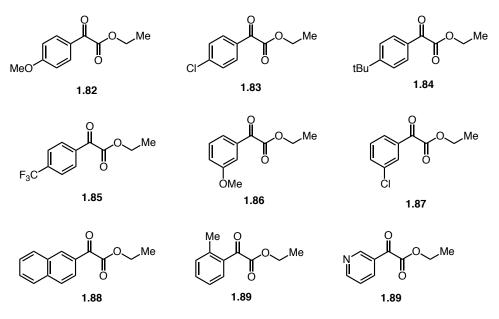
R)-BINAP was purchased from Strem Chemicals and stored in a nitrogen filled dry box.

(R,S)-josiphos (1.45) was purchased from Strem Chemicals and stored in a nitrogen filled dry box.

Sodium bicarbonate was purchased from BDH and used as received.

Sodium perborate tetrahydrate was purchased from Sigma Aldrich and used as received.

1.5.4 Preparation of α-ketoesters

1.82   **1.83**   **1.84**

1.85   **1.86**   **1.87**

1.88   **1.89**   **1.89**

Ketoesters **1.82** – **1.89** were prepared according to literature procedure and matched the known ^{1}H-NMR and ^{13}C-NMR spectra.[37-41] All ketoesters were dried via azeotropic distillation with benzene and stored under nitrogen at -25 °C.

1.5.5 Preparation of substituted diboryl reagents
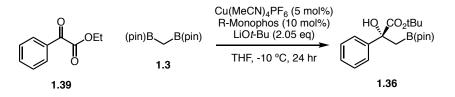
Diboryl reagents used for the synthesis of compounds **1.59** – **1.60** and **1.62** – **1.66** were synthesized following a known synthetic procedure and matched literature spectra.[24,28]

1.90

Diboryl reagent **1.90** was prepared according to a literature procedure.[24,28] In an N_2-filled glove box, an oven-dried 50 mL round-bottom flask was charged with diboryl methane (500 mg, 1.9 mmol) and a magnetic stirbar, capped with a rubber septum, and sealed with electrical tape. A separate oven-dried, 25 mL conical flask was charged with lithium 2,2,6,6-tetramethylpiperidide (288 mg, 1.96 mmol), capped with a rubber septum, and sealed with electrical tape. The two flasks were brought out of the glove box, where the diboryl methane flask was charged with 7.8 mL of dry THF and the LTMP-containing flask was charged with 15.5

mL of dry THF (0.17 M total). Both flasks were allowed to cool to 0 °C (ice/water baths). The LTMP solution was then transferred via cannula to the diboryl methane flask with stirring. After the transfer, the reaction mixture was allowed to stir at 0 °C for 10 min. Allyl bromide (0.403 mL, 4.67 mmol) was added to the reaction via a syringe. The reaction mixture was allowed to warm up to 22 °C over 18 h with stirring. The reaction was quenched with 10 mL of a saturated aqueous solution of NH_4Cl. The biphasic mixture was extracted three times with diethyl ether (150 mL total), and the combined organic extracts were dried over $MgSO_4$, filtered, and concentrated *in vacuo*. The crude reaction mixture was purified by silica gel chromatography (20:1 hexanes:EtOAc, R_f=0.20) to give the desired product as a clear, viscous oil in 77% isolated yield (445 mg). **¹H NMR** (600 MHz, CDCl3) δ 5.87 (ddt, J = 16.6, 10.1, 6.3 Hz, 1H), 4.99 (ddd, J = 17.1, 3.5, 1.7 Hz, 1H), 4.88 – 4.84 (m, 1H), 2.29 (dd, J = 7.8, 6.5 Hz, 2H), 1.22 (s, 12H), 1.21 (s, 12H), 0.85 (t, J = 8.0 Hz, 1H). **¹³C NMR** (151 MHz, CDCl3) δ 140.70, 113.20, 83.07, 29.62, 24.88, 24.52. **IR (υ/cm⁻¹):** 2979 (s), 2931 (s), 1359 (m), 1320 (m), 1141 (s). **LRMS (ESI⁺)** [M+Na] calcd for $C_{16}H_{30}B_2O_4Na$ 331.22, found 331.27.
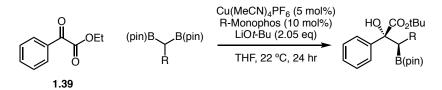
1.5.6 General procedures

General procedure A: Cu-catalyzed 1,2-addition reaction using diborylmethane
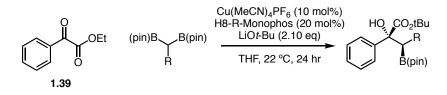
In a nitrogen filled dry box, a stock solution of $Cu(MeCN)_4PF_6$ (0.017 M), *(R)*-Monophos (0.033 M) and LiOtBu (0.017 M) in THF was made in an 8-mL vial equipped with a magnetic stir bar. This was allowed to stir for 45 min at 22 °C. Diborylmethane (40.2 mg, 0.15 mmol) and LiO*t*Bu (16 mg, 0.2 mmol) were weighed into a separate 8-mL vial and dissolved in THF (0.4 mL). An aliquot of the catalyst solution (0.3 mL) and stir bar was then transferred to the vial containing the diborylmethane and LiO*t*-Bu. The vial was sealed with a septa-lined cap, taped, removed from the glovebox, and cooled to -10 °C in a cryobath. After 5 minutes at -10 °C, the

ketoester was added to the vial via syringe. The reaction was kept at -10 °C for 24 hours and agitated periodically. The reaction was quenched with a saturated aqueous solution of NH_4Cl (1.5 mL), and the aqueous layer extracted three times with diethyl ether. The combined organic extracts were dried over $MgSO_4$, filtered, and concentrated *in vacuo*. Conversion was determined by ^{1}H NMR using dimethylformamide as an internal standard. The crude reaction mixture was then taken on to Supplementary Procedure A or C without purification.

General procedure B: Cu-catalyzed 1,2-addition reaction of secondary alkyl boronates

1.39

In a nitrogen filled dry box, an 8-mL vial equipped with a magnetic stir bar was charged with $Cu(MeCN)_4PF_6$ (1.9 mg, 0.005 mmol), *(R)*-Monophos (3.9 mg, 0.010 mmol), and LiOtBu (0.4 mg, 0.005 mmol) and dissolved in THF (0.30 mL, 0.017M). This was allowed to stir for 45 min. Organodiboron reagent (0.15 to 0.20 mmol) and LiOtBu (16 mg, 0.2 mmol) were weighed into a separate 8-mL vial and dissolved in THF (0.4 mL). The catalyst solution and stir bar was then transferred to the vial containing the organodiboron reagent and LiOtBu. The vial was sealed with a septa-lined cap, taped, removed from the glovebox, and placed on a magnetic stir plate at 22 °C. Ethyl benzoyl formate (18 mg, 0.1 mmol) was added to the vial via syringe. The reaction was allowed to stir at room temperature for 24 hours. The reaction was quenched with a saturated aqueous solution of NH_4Cl (1.5 mL), and the aqueous layer extracted three times with diethyl ether. The combined organic extracts were dried over $MgSO_4$, filtered, and concentrated *in vacuo*. Conversion was determined by ^{1}H NMR using dimethylformamide as an internal standard. The product was purified via silica gel chromatography.

General procedure C: Cu-catalyzed 1,2-addition reaction of secondary alkyl boronates

In a nitrogen filled dry box, an 8-mL vial equipped with a magnetic stir bar was charged with

Cu(MeCN)$_4$PF$_6$ (3.8 mg, 0.010 mmol), H$_8$-(R)-Monophos (7.3 mg, 0.020 mmol), and LiOtBu

(0.8 mg, 0.010 mmol) and dissolved in THF (0.60 mL). This was allowed to stir for 45 min.

Organodiboron reagent (0.15 to 0.20 mmol) and LiOtBu (16 mg, 0.2 mmol) were weighed into a

separate 8-mL vial and dissolved in THF (0.1 mL). The catalyst solution and stir bar was then

transferred to the vial containing the organodiboron reagent and LiOtBu. The vial was sealed

with a septa-lined cap, taped, removed from the glovebox, and placed on a magnetic stir plate at

22 °C. Ethyl benzoyl formate (18 mg, 0.1 mmol) was added to the vial via syringe. The reaction

allowed to stir at room temperature for 24 hours. The reaction was quenched with a saturated

aqueous solution of NH$_4$Cl (1.5 mL), and the aqueous layer extracted three times with diethyl

ether. The combined organic extracts were dried over MgSO$_4$, filtered, and concentrated *in*

vacuo. Conversion was determined by ^{1}H NMR using dimethylformamide as an internal

standard. The product was purified via silica gel chromatography.

1.5.7 Supplementary procedures

Supplementary procedure A: synthesis of enantioenriched diols
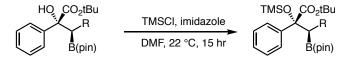
The crude hydroxyboronate was combined with sodium perborate tetrahydrate (77 mg, 0.5

mmol), dissolved in a 1:1 mixture of THF and water (1 mL, 0.1M) and vigorously stirred for 2

hours at 22 °C. The reaction was quenched with a saturated aqueous solution of NH$_4$Cl (1.5 mL),

and the aqueous layer extracted three times with diethyl ether, dried over MgSO$_4$, filtered, and

concentrated *in vacuo*. The product was purified via silica gel column chromatography.

Enantiomeric excess of the diol was determined by HPLC analysis compared to the authentic racemic material.

Supplementary procedure B: synthesis of enantioenriched diols

The crude hydroxyboronate was passed through a silica gel column. The resulting oil was then combined with sodium perborate (77 mg, 0.5 mmol), dissolved in a 1:1 mixture of THF and water (1 mL, 0.1M) and vigorously stirred for 2 hours at 22 °C. The reaction was quenched with a saturated aqueous solution of NH_4Cl (1.5 mL), and the aqueous layer extracted three times with diethyl ether, dried over $MgSO_4$, filtered, and concentrated *in vacuo*. The product was purified via silica gel column chromatography. Enantiomeric excess of the diol was determined by HPLC analysis compared to the authentic racemic material.

Supplementary Procedure C: synthesis of TMS-protected β-hydroxyboronates
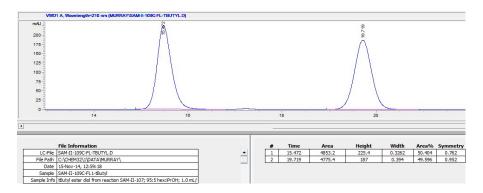
The crude hydroxyboronate (R=H) or purified hydroxyboronate (R=alkyl) was concentrated in an 8 mL vial, capped with a septa-lined cap, and purged with nitrogen for 5 minutes. Imidazole (8 mg, 0.12 mmol) and a magnetic stir bar were quickly added to the vial under a stream of nitrogen. The vial was purged with nitrogen for an addition 2 minutes and then vial was charged with DMF via syringe (0.2 mL, 0.15M). Chlorotrimethylsilane (15 µl, 0.4 mmol) was added via syringe to the vial. The vial was placed on a magnetic stir plate at 22 °C and allowed to stir for 18 hours. The reaction was quenched with saturated NH_4Cl (2 mL), extracted with diethyl ether, washed with saturated sodium bicarbonate solution, washed with brine, dried over $MgSO_4$ and concentrated *in vacuo*. The crude mixture was purified via silica gel column chromatography.

1.5.8 Product characterization
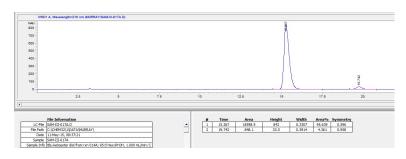
1.47

***Tert*-butyl (*S*)-2,3-dihydroxy-2-phenylpropanoate (1.47).** Following General Procedure A and Supplementary Procedure A, the crude oxidation mixture was purified by silica gel (regular) chromatography (4:1 hexanes:ethyl acetate, gravity) to yield diol **1.47** as a colorless oil in 65% isolated yield (15.5 mg). **¹H NMR** (600 MHz, CDCl₃) δ 7.65 - 7.59 (m, 2H), 7.39 (t, *J* = 7.6 Hz, 2H), 7.34 (m, *J* = 7.2 Hz, 1H), 4.21 (t, *J* = 10.8 Hz, 1H), 4.14 (s, 1H), 3.74 (dd, *J* = 11.4, 3.0 Hz, 1H), 2.39 (dd, *J* = 10.4, 3.5 Hz, 1H), 1.52 (s, 9H). **¹³C NMR** (151 MHz, CDCl₃) δ 172.9, 138.6, 128.3, 128.1, 125.4, 84.0, 79.4, 68.4, 27.9. **HRMS (ESI⁺)** [2M+Na]⁺ calcd for C₂₆H₃₆O₈Na⁺ 499.2308, found 499.2296. **IR (ν/cm⁻¹):** 3446 (m, br), 2976 (m), 1732 (s), 1558 (m), 1541 (m), 1369 (s), 1252 (m), 1140 (m). **[α]²²_D** = -25.6° (*c* = 0.205, CH₂Cl₂, l = 100 mm). **[α]²²_D** = -6.8 (*c* = 0.16, CH₂Cl₂, l = 100 mm). Absolute stereochemistry was confirmed by comparison of the optical rotation to that of the known *R* enantiomer.[42]

Racemic Material

#	Time	Area	Height	Width	Area%	Symmetry
1	15.472	4853.2	225.4	0.3262	50.404	0.762
2	19.719	4775.4	187	0.394	49.596	0.952
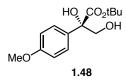
File Information
LC-File: SAM-II-109C-FL-TBUTYL.D
File Path: C:\CHEM32\1\DATA\MURRAY\
Date: 15-Nov-14, 12:59:18
Sample: SAM-II-109C-FL1-tButyl
Sample Info: tButyl ester diol from reaction SAM-II-107; 95:5 hex:iPrOH; 1.0 mL/
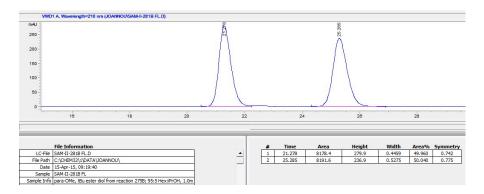
Major: 15.2 min; Minor: 19.8 min; 96:4 e.r.

1.48

***Tert*-butyl (*S*)-2,3-dihydroxy-2-(4-methoxyphenyl)propanoate (1.48).** Following

General Procedure A and Supplementary Procedure A, the crude oxidation mixture was purified

by silica gel (50:50 regular:deactivated, mixed) chromatography (4:1 hexanes: ethyl acetate) to

yield diol **1.48** as a colorless oil in 60% yield (16.1 mg). **¹H NMR** (600 MHz, CDCl$_3$) δ 7.49 (d, *J*

= 8.8 Hz, 2H), 6.88 (d, *J* = 8.8 Hz, 2H), 4.15 (t, *J* = 10.7 Hz, 1H), 4.08 (s, 1H), 3.81 (s, 3H), 3.68

(dd, *J* = 11.6, 2.6 Hz, 1H), 2.34 (dd, *J* = 10.4, 3.5 Hz, 1H), 1.49 (s, 9H). **¹³C NMR** (151 MHz,

CDCl$_3$) δ 173.2, 159.5, 130.8, 126.8, 113.8, 84.0, 79.2, 68.5, 55.4, 28.0. **HRMS (ESI⁺)** [2M+Na]⁺

calcd for C$_{28}$H$_{40}$O$_{10}$Na⁺ 559.2519, found 559.2510. **IR (υ/cm⁻¹):** 3465 (br, m), 2978 (m), 2931

(m), 1718 (s), 1510 (s), 1251 (s), 1159 (s). **[α]²²$_D$** = -25.6 (*c* = 0.435, CH$_2$Cl$_2$, l = 100 mm).

Diacel CHIRALPAK IA Column; 95:5 hexanes:iPrOH; 1.0 mL/min; 210 nm

Racemic Material

Enantioenriched Material

#	Time	Area	Height	Width	Area%	Symmetry
1	21.481	7002.8	239.6	0.4469	85.217	0.778
2	25.548	1214.8	35.7	0.5237	14.783	0.96
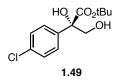
File Information	
LC-File	SAM-III-090A.D
File Path	C:\CHEM32\1\DATA\MURRAY\
Date	15-Jul-15, 14:23:12
Sample	SAM-III-090A
Sample Info	p-OMe ester diol from rxn SAM-III-088A; 95:5 Hex:iPrOH, 1.000 mL

Major: 21.5 min; Minor: 25.5 min; 85:15 e.r.

1.49

Tert-**butyl (*S*)-2-(4-chlorophenyl)-2,3-dihydroxypropanoate (1.49).** Following General Procedure A and Supplementary Procedure A, the crude oxidation mixture was purified by silica gel (50:50 regular:deactivated, mixed) chromatography (6:1 hexanes: ethyl acetate) to yield diol **1.49** as a colorless oil in 64% yield (17.6 mg). **¹H NMR** (600 MHz, CDCl$_3$) δ 7.53 (d, *J* = 8.6 Hz, 2H), 7.33 (d, *J* = 8.6 Hz, 2H), 4.14 (m, *J* = 4.2 Hz, 2H), 3.68 (dd, *J* = 11.4, 2.7 Hz, 1H), 2.33 (dd, *J* = 9.6, 4.3 Hz, 1H), 1.49 (s, 9H). **¹³C NMR** (151 MHz, CDCl$_3$) δ 172.6, 137.2, 134.3, 128.6, 127.1, 84.5, 79.2, 68.4, 28.0. **HRMS (ESI⁺)** [M+Na]⁺ calcd for C$_{13}$H$_{17}$O$_4$ClNa⁺ 295.0713, found 295.0909. **IR (υ/cm⁻¹):** 3449 (m, br), 2978 (m), 1727 (s), 1492 (m), 1370 (m), 1254 (m), 1156 (s), 1094 (s). **[α]²²$_D$** = -21.3 (*c* = 0.455, CH$_2$Cl$_2$, l = 100 mm).

Diacel CHIRALPAK IA Column; 95:5 hexanes:iPrOH; 1.0 mL/min; 210 nm

Racemic Material

		File Information
LC-File	SAM-II-281C FL.D	
File Path	C:\CHEM32\1\DATA\MURRAY\	
Date	15-Apr-15, 09:53:52	
Sample	SAM-II-281C FL	
Sample Info	para-Cl, tBu ester diol from reaction 275C; 95:5 Hex:iPrOH, 1.0mL/r	

#	Time	Area	Height	Width	Area%	Symmetry
1	17.117	8224.2	353.6	0.3563	49.851	0.869
2	18.358	8273.2	330.6	0.3829	50.149	0.858

Enantioenriched Material

		File Information
LC-File	SAM-III-066B.D	
File Path	C:\CHEM32\1\DATA\MURRAY\	
Date	24-Jun-15, 11:43:02	
Sample	SAM-III-066B	
Sample Info	p-Cl ester diol from rxn SAM--III-064B; 95:5 Hex:iPrOH, 1.000 mL/r	

#	Time	Area	Height	Width	Area%	Symmetry
1	17.129	2826.8	122.5	0.3552	97.039	0.948
2	18.37	86.2	3.7	0.3646	2.961	0.931

Major: 17.1 min; Minor: 18.4 min; 97:3 e.r.

1.50

***Tert*-butyl (*S*)-2-(4-(tert-butyl)phenyl)-2,3-dihydroxypropanoate (1.50).** Following

General Procedure A and Supplementary Procedure A, the crude oxidation mixture was purified

by silica gel (50:50 regular:deactivated, mixed) chromatography (6:1 hexanes: ethyl acetate) to

yield diol **1.50** as a white solid in 70% yield (20.6 mg). **¹H NMR** (600 MHz, CDCl₃) δ 7.55 - 7.47

(m, 2H), 7.42 - 7.33 (m, 2H), 4.15 (d, *J* = 10.3 Hz, 1H), 4.06 (s, 1H), 3.70 (d, *J* = 11.3 Hz, 1H),

2.37 (s, 1H), 1.51 (s, 9H), 1.31 (s, 9H). **¹³C NMR** (151 MHz, CDCl₃) δ 173.1, 151.1, 135.8, 125.4,

125.3, 84.0, 79.5, 68.7, 34.6, 31.4, 28.0. **HRMS (ESI⁺)** [2M+Na]⁺ calcd for $C_{34}H_{52}O_8Na^+$

611.3560, found 611.3553. **IR (υ/cm⁻¹):** 3472 (m, br), 2964 (s), 1722 (s), 1369 (m), 1274 (m), 1159 (s), 1112 (m). **[α]²²D** = -25.3 (*c* = 0.680, CH₂Cl₂, l = 100 mm).
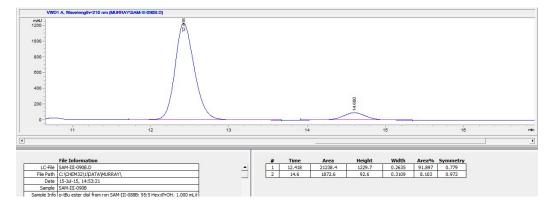
Diacel CHIRALPAK IA Column; 95:5 hexanes:iPrOH; 1.0 mL/min; 210 nm

Racemic Material

#	Time	Area	Height	Width	Area%	Symmetry
1	12.472	1122.3	65.5	0.264	49.382	0.936
2	14.649	1150.4	56.3	0.3143	50.618	0.97

File Information
LC-File SAM-II-281A FL.D
File Path C:\CHEM32\1\DATA\JOANNOU\
Date 15-Apr-15, 08:56:59
Sample SAM-II-281A FL
Sample Info para-tBu, tBu ester diol; 95:5 Hex:iPrOH, 1.0mL/min; Column IA; 21

Enantioenriched Material

#	Time	Area	Height	Width	Area%	Symmetry
1	12.418	21238.4	1229.7	0.2635	91.897	0.779
2	14.6	1872.6	92.6	0.3109	8.103	0.972

File Information
LC-File SAM-III-090B.D
File Path C:\CHEM32\1\DATA\MURRAY\
Date 15-Jul-15, 14:53:21
Sample SAM-III-090B
Sample Info p-tBu ester diol from rxn SAM-III-088B: 95:5 Hex:iPrOH, 1.000 mL/r

Major: 12.4 min; Minor: 14.6 min; 92:8 e.r.

1.51

***Tert*-butyl (*S*)-2,3-dihydroxy-2-(4-nitrophenyl)propanoate (1.51).** Following General Procedure A and Supplementary Procedure A, the crude oxidation mixture was purified by silica gel (50:50 regular:deactivated, mixed) chromatography (4:1 hexanes: ethyl acetate, gravity) to yield diol **1.51** as a yellow oil in 46% yield (13.1 mg). **¹H NMR** (600 MHz, CDCl₃) δ 8.22 (d, *J* = 8.9 Hz, 2H), 7.81 (d, *J* = 8.9 Hz, 2H), 4.26 (s, 1H), 4.18 (d, *J* = 11.3 Hz, 1H), 3.72 (d, *J* = 11.3 Hz,
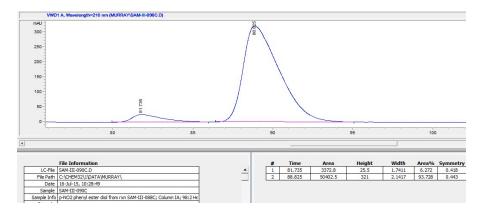
1H), 2.38 (s, 1H), 1.50 (s, 9H). **^{13}C NMR** (151 MHz, CDCl$_3$) δ 171.6, 147.8, 145.6, 126.8, 123.5, 85.1, 79.3, 68.3, 27.8. **HRMS (ESI$^+$)** [M+Na]$^+$ calcd for C$_{13}$H$_{34}$O$_{12}$NNa$^+$ 306.0945, found 306.0945. **IR (υ/cm^{-1}):** 3443 (s), 2979 (w), 1726 (m), 1642 (m), 1522 (s), 1370 (m), 1349 (s), 1156 (m). **[α]^{22}$_D$** = -34.9 (c = 0.53, CH$_2$Cl$_2$, l = 100 mm).

Diacel CHIRALPAK IA Column; 98:2 hexanes:iPrOH; 1.0 mL/min; 210 nm

Racemic Material

#	Time	Area	Height	Width	Area%	Symmetry
1	81.369	4549.1	33.7	1.788	49.793	0.408
2	89.061	4586.9	37.1	1.7122	50.207	0.818

File Information
LC-File: SAM-III-028C_2.D
File Path: C:\CHEM32\1\DATA\MURRAY\
Date: 16-May-15, 15:19:30
Sample: SAM-III-028C_2
Sample Info: p-nitro-tBu-ester diol from rxn 026C; 98:2 Hex:iPrOH, 1.000 mL/min

Enantioenriched Material

#	Time	Area	Height	Width	Area%	Symmetry
1	81.735	3372.8	25.5	1.7411	6.272	0.418
2	88.825	50402.5	321	2.1417	93.728	0.443

File Information
LC-File: SAM-III-090C.D
File Path: C:\CHEM32\1\DATA\MURRAY\
Date: 16-Jul-15, 10:28:49
Sample: SAM-III-090C
Sample Info: p-NO2 phenyl ester diol from rxn SAM-III-088C; Column IA; 98:2 He

Major: 81.7 min; Minor: 88.8 min; 94: 6 e.r.

1.52

***Tert*-butyl (*S*)-2,3-dihydroxy-2-(4-(trifluoromethyl)phenyl)propanoate (1.52).**

Following General Procedure A and Supplementary Procedure A, the crude oxidation mixture was purified by silica gel chromatography (4:1 hexanes: ethyl acetate) to yield diol **1.52** as a

colorless oil in 54% yield (17.1 mg). **¹H NMR** (600 MHz, CDCl$_3$) δ 7.74 (d, J = 8.2 Hz, 2H), 7.62 (d, J = 8.3 Hz, 2H), 4.22 (d, J = 0.9 Hz, 1H), 4.17 (t, J = 10.7 Hz, 1H), 3.71 (dd, J = 11.3, 3.8 Hz, 1H), 2.43 (dd, J = 10.0, 3.9 Hz, 1H), 1.50 (s, 9H). **¹³C NMR** (151 MHz, CDCl$_3$) δ 172.1, 142.5, 126.1, 125.3, 125.3, 125.3, 125.2, 124.9, 123.1, 84.6, 79.3, 68.4, 27.8. **LRMS (ESI⁺)** [M+Na]⁺calcd for C$_{14}$H$_{17}$F$_3$O$_4$Na⁺ 329.10, found 329.18. **IR (υ/cm⁻¹):** 3457 (m, br), 2980 (m), 2934 (m), 1726 (s), 1328 (s). **[α]²²$_D$** = -9.4 (c = 0.91, CH$_2$Cl$_2$, l = 100 mm).

Diacel CHIRALPAK IA Column; 95:5 hexanes:iPrOH; 1.0 mL/min; 210 nm

Racemic Material

#	Time	Area	Height	Width	Area%	Symmetry
1	14.182	2469.7	127.3	0.2984	50.790	1.013
2	15.797	2392.9	112.2	0.3287	49.210	0.985

Enantioenriched Material

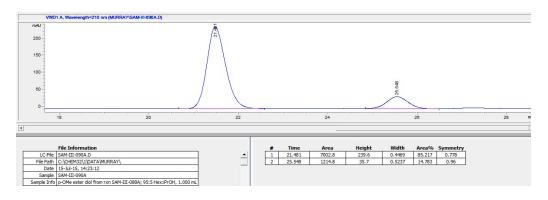| #	Time	Area	Height	Width	Area%	Symmetry
1	14.213	30162.3	1564.2	0.298	96.513	0.996
2	15.838	1089.7	51.9	0.325	3.487	1.005
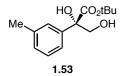
Major: 14.2 min; Minor: 15.8 min; 97:3 e.r.

1.53

***Tert*-butyl (*S*)-2,3-dihydroxy-2-(m-tolyl)propanoate (1.53).** Following General Procedure A and Supplementary Procedure A, the crude oxidation mixture was purified by silica
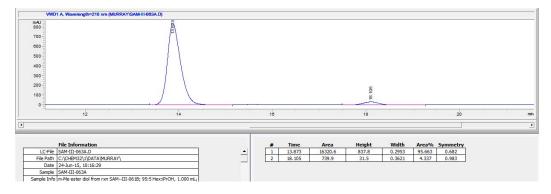
gel (50:50 regular:deactivated, mixed) chromatography (6:1 hexanes: ethyl acetate) to yield diol

1.53 as a colorless oil in 63% yield (16.4 mg). **¹H NMR** (600 MHz, CDCl$_3$) δ 7.41 (d, J = 2.0 Hz,

1H), 7.36 (d, J = 8.4 Hz, 1H), 7.24 (t, J = 7.7 Hz, 1H), 7.12 (d, J = 7.7 Hz, 1H), 4.17 (d, J = 10.5

Hz, 1H), 4.07 (s, 1H), 3.71 (d, J = 11.3 Hz, 1H), 2.36 (s, 3H), 1.49 (s, 9H). **¹³C NMR** (151 MHz,

CDCl$_3$) δ 173.1, 138.7, 138.1, 129.0, 128.3, 126.3, 122.6, 84.0, 79.5, 68.5, 28.0, 21.8. **HRMS**

(ESI⁺) [2M+Na]⁺ calcd for C$_{28}$H$_{40}$O$_8$Na⁺ 527.2621, found 527.2611. **IR (υ/cm⁻¹):** 3469 (m, br),

2978 (m), 1722 (s), 1370 (m), 1275 (m), 1156 (s), 1059 (m). **[α]²²$_D$** = -31.9 (c = 0.625, CH$_2$Cl$_2$, l =

100mm).

Diacel CHIRALPAK IA Column; 95:5 hexanes:iPrOH; 1.0 mL/min; 210 nm

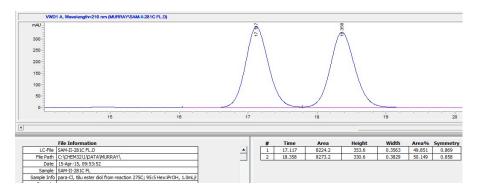### Racemic Material
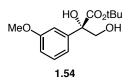
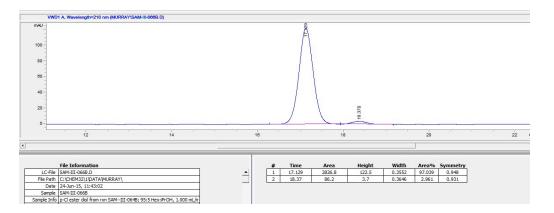### Enantioenriched Material
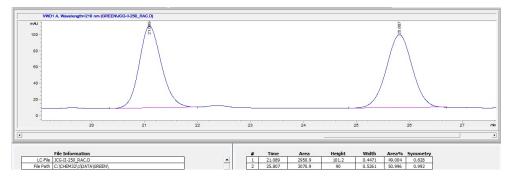
Major: 13.9 min; Minor: 18.1 min; 96:4 e.r.

1.54
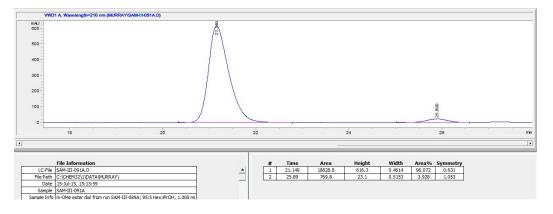
***Tert*-butyl (*S*)-2,3-dihydroxy-2-(3-methoxyphenyl)propanoate (1.54).** Following General Procedure A and Supplementary Procedure A, the crude oxidation mixture was purified by silica gel (50:50 regular:deactivated, mixed) chromatography (4:1 hexanes: ethyl acetate,) to yield diol **1.54** as a colorless oil in 62% yield (16.7 mg). **¹H NMR** (600 MHz, CDCl$_3$) δ 7.30 - 7.24 (m, 1H), 7.19 - 7.13 (m, 2H), 6.85 (ddd, *J* = 8.1, 2.6, 1.0 Hz, 1H), 4.16 (t, *J* = 10.3 Hz, 1H), 4.09 (s, 1H), 3.81 (s, 3H), 3.70 (d, *J* = 11.3 Hz, 1H), 2.32 (d, *J* = 9.8 Hz, 1H), 1.50 (s, 9H). **¹³C NMR** (151 MHz, CDCl$_3$) δ 172.8, 159.6, 140.2, 129.3, 117.8, 113.6, 111.3, 84.0, 79.4, 68.4, 55.2, 27.9. **HRMS (ESI⁺)** [2M+Na]⁺ calcd for C$_{28}$H$_{40}$O$_{10}$Na⁺ 559.2512, found 559.2512. **IR (υ/cm⁻¹):** 3452 (m, br), 2932 (m), 1725 (s), 1602 (m), 1401 (m), 1369 (m), 1255 (s), 1155 (s), 1052 (s). **[α]²²$_D$** = -21.4 (*c* = 0.49, CH$_2$Cl$_2$, l = 100 mm).

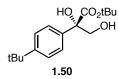*Diacel CHIRALPAK IA Column; 95:5 hexanes:iPrOH; 1.0 mL/min; 210 nm*

Racemic Material

#	Time	Area	Height	Width	Area%	Symmetry
1	21.089	2950.9	101.2	0.4471	49.004	0.828
2	25.807	3070.9	90	0.5261	50.996	0.992

File Information
LC-File JCG-II-250_RAC.D
File Path C:\CHEM32\1\DATA\GREEN\

Enantioenriched Material

File Information
LC-File SAM-III-091A.D
File Path C:\CHEM32\1\DATA\MURRAY\
Date 15-Jul-15, 15:13:59
Sample SAM-III-091A
Sample Info m-OMe ester diol from rxn SAM-III-089A; 95:5 Hex:iPrOH, 1.000 ml

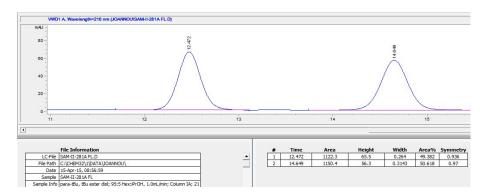| #	Time	Area	Height	Width	Area%	Symmetry
1	21.149	18828.8	616.3	0.4614	96.072	0.631
2	25.89	769.8	23.1	0.5153	3.928	1.053

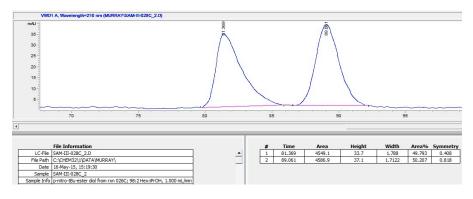*Major: 21.1 min; Minor: 25.9 min; 96:4 e.r.*

1.55
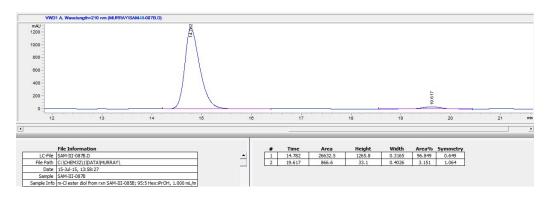
***Tert*-butyl (*S*)-2-(3-chlorophenyl)-2,3-dihydroxypropanoate (1.55).** Following General Procedure A and Supplementary Procedure A, the crude oxidation mixture was purified by silica gel (50:50 regular:deactivated, mixed) chromatography (6:1 hexanes: ethyl acetate) to yield diol **1.55** as a colorless oil in 64% yield (17.6 mg). **¹H NMR** (600 MHz, CDCl$_3$) δ 7.62 (bs, *J* = 1.3 Hz, 1H), 7.50 - 7.44 (m, 1H), 7.33 - 7.27 (m, 2H), 4.29 - 4.00 (m, 2H), 3.69 (dd, *J* = 11.5, 2.9 Hz, 1H), 2.36 (dd, *J* = 10.1, 3.8 Hz, 1H), 1.50 (s, 9H). **¹³C NMR** (151 MHz, CDCl$_3$) δ 172.2, 140.6, 134.3, 129.5, 128.2, 125.9, 123.7, 84.4, 79.0, 68.3, 27.8. **HRMS (ESI⁺)** [2M+Na]⁺ calcd for C$_{26}$H$_{34}$O$_8$Cl$_2$Na⁺ 567.1528, found 567.1517. **IR (υ/cm⁻¹):** 3464 (s, br), 2979 (m), 2929 (m), 1724 (s), 1370 (m), 1287 (m), 1258 (m), 1157 (s), 1079 (m). **[α]²²$_D$** = -32.7 (*c* = 0.725, CH$_2$Cl$_2$, l = 100 mm).

Diacel CHIRALPAK IA Column; 95:5 hexanes:iPrOH; 1.0 mL/min; 210 nm

Racemic Material

#	Time	Area	Height	Width	Area%	Symmetry
1	14.893	16324.1	760.8	0.3223	49.850	0.656
2	19.785	16422.5	626	0.4031	50.150	0.907

File Information	
LC-File	SAM-III-028B.D
File Path	C:\CHEM32\1\DATA\MURRAY\
Date	15-May-15, 17:48:28
Sample	SAM-III-028B
Sample Info	m-chloro-tBu-ester diol from rxn 026B; 95:5 Hex:iPrOH, 1.000 mL/m

Enantioenriched Material

#	Time	Area	Height	Width	Area%	Symmetry
1	14.782	26632.5	1265.8	0.3165	96.849	0.649
2	19.617	866.6	33.1	0.4026	3.151	1.064

File Information

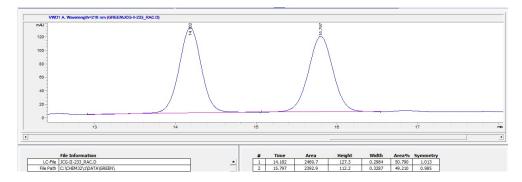| LC-File	SAM-III-087B.D
File Path	C:\CHEM32\1\DATA\MURRAY\
Date	15-Jul-15, 13:58:27
Sample	SAM-III-087B
Sample Info	m-Cl ester diol from rxn SAM-III-085B; 95:5 Hex:iPrOH, 1.000 mL/m

Major: 14.8 min; Minor: 19.6 min; 97:3 e.r.

1.56
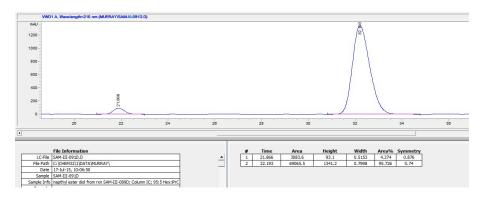
***Tert*-butyl (*S*)-2,3-dihydroxy-2-(napthalen-2-yl)propanoate (1.56).** Following General Procedure A and Supplementary Procedure A, the crude oxidation mixture was purified by silica gel (50:50 regular:deactivated, mixed) chromatography (6:1 hexanes: ethyl acetate, gravity) to yield diol **1.56** as a white solid in 62% yield (17.8 mg). **¹H NMR** (600 MHz, CDCl$_3$) δ 8.12 - 8.07 (m, 1H), 7.90 - 7.81 (m, 3H), 7.68 (dd, *J* = 8.7, 1.9 Hz, 1H), 7.53 - 7.46 (m, 2H), 4.32 (t, *J* = 10.2 Hz, 1H), 4.28 - 4.21 (m, 1H), 3.81 (d, *J* = 11.3 Hz, 1H), 2.43 (d, *J* = 6.9 Hz, 1H), 1.50 (s, 9H). **¹³C NMR** (151 MHz, CDCl$_3$) δ 173.0, 136.2, 133.2, 133.1, 128.5, 128.1, 127.7, 126.5, 126.4, 125.0, 123.4, 84.3, 79.7, 68.5, 28.0. **HRMS (ESI⁺)** [2M+Na] calcd for C$_{34}$H$_{40}$O$_8$Na⁺ 599.2621, found 599.2614. **IR (υ/cm⁻¹):** 3469 (br, m), 2978 (m), 2929 (m), 1721 (s), 1370 (s), 1283 (s), 1249 (s), 1156 (s), 1128 (s). **[α]²²$_D$** = -24.3 (*c* = 0.740, CH$_2$Cl$_2$, l = 100 mm).

Diacel CHIRALPAK IC Column; 95:5 hexanes:iPrOH; 1.0 mL/min; 210 nm

Racemic Material

Enantioenriched Material
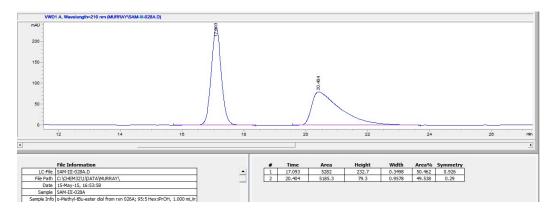
Major: 32.2 min; Minor: 21.9 min; 96:4 e.r.

1.57
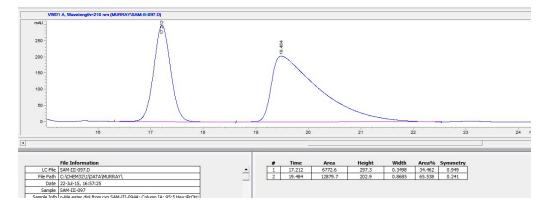
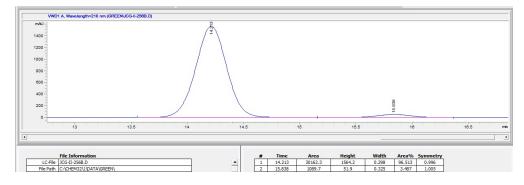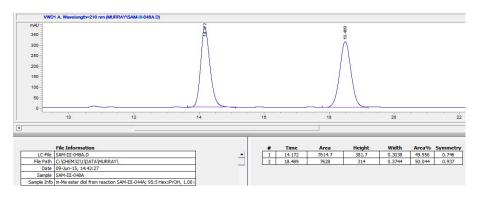***Tert*-butyl (*S*)-2,3-dihydroxy-2-(o-tolyl)propanoate (1.57).** Following General Procedure A and Supplementary Procedure A, the crude oxidation mixture was purified by silica gel (regular) chromatography (4:1 hexanes: ethyl acetate) to yield diol **1.57** as a colorless oil in 27% yield (6.8 mg). **¹H NMR** (400 MHz, CDCl$_3$) δ 7.31 (dd, *J* = 7.6, 1.6 Hz, 1H), 7.23 - 7.13 (m, 3H), 4.33 - 4.20 (m, 1H), 4.11 - 4.02 (m, 2H), 2.39 (s, 3H), 1.43 (s, 9H).). **¹³C NMR** (151 MHz, CDCl$_3$) δ 173.6, 137.2, 136.7, 132.4, 128.3, 126.3, 125.9, 83.7, 79.1, 67.4, 27.9, 20.8. **HRMS (ESI⁺)** [2M+Na] calcd for C$_{28}$H$_{40}$O$_8$Na⁺ 527.2611, found 527.2621. **IR (υ/cm⁻¹):** 3446 (m, br), 2977 (s), 2929 (s), 1725 (s), 1458 (m), 1394 (m), 1369 (s), 1277 (s), 1159 (s), 1114 (s). **[α]²²$_D$** = -10.4 (*c* = 0.410, CH$_2$Cl$_2$, l = 100 mm).

Diacel CHIRALPAK IA Column; 95:5 hexanes:iPrOH; 1.0 mL/min; 210 nm

Racemic Material

#	Time	Area	Height	Width	Area%	Symmetry
1	17.093	5282	232.7	0.3498	50.462	0.926
2	20.404	5185.3	79.3	0.9578	49.538	0.29

File Information
LC-File: SAM-III-028A.D
File Path: C:\CHEM32\1\DATA\MURRAY\
Date: 15-May-15, 16:53:58
Sample: SAM-III-028A
Sample Info: o-Methyl-tBu-ester diol from rxn 026A; 95:5 Hex:iPrOH, 1.000 mL/m

Enantioenriched Material

#	Time	Area	Height	Width	Area%	Symmetry
1	17.212	6772.6	297.3	0.3498	34.462	0.949
2	19.484	12879.7	202.9	0.8685	65.538	0.241

File Information
LC-File: SAM-III-097.D
File Path: C:\CHEM32\1\DATA\MURRAY\
Date: 22-Jul-15, 16:57:25
Sample: SAM-III-097
Sample Info: o-Me ester diol from rxn SAM-III-094A; Column IA; 95:5 Hex:iPrOH;

Major: 17.2 min; Minor: 19.5 min; 66:34.r.
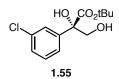

1.58
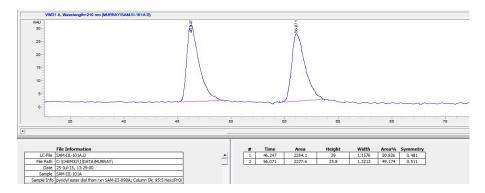
***Tert*-butyl-(*S*)-2,3-dihydroxy-2-(pyridine-2-yl)propanoate (1.58).** Following General

Procedure A and Supplementary Procedure A, the crude oxidation mixture was purified by silica

gel (50:50 regular:deactivated, mixed) chromatography (4:1 hexanes: ethyl acetate) to yield diol

1.58 as a yellow oil in 36% yield (8.6 mg). **¹H NMR** (600 MHz, CDCl$_3$) δ 8.85 (d, *J* = 2.2 Hz,

1H), 8.57 (dd, *J* = 4.9, 1.6 Hz, 1H), 7.94 (dt, *J* = 8.2, 1.9 Hz, 1H), 7.30 (dd, *J* = 8.1, 4.8 Hz, 1H),

4.17 (d, *J* = 11.4 Hz, 1H), 3.73 (d, *J* = 11.3 Hz, 1H), 1.50 (s, 9H). **¹³C NMR** (151 MHz, CDCl$_3$) δ

172.3, 149.5, 147.5, 134.4, 133.7, 123.3, 84.9, 78.3, 68.6, 28.0. **HRMS (ESI⁺)** [M+Na] calcd for

$C_{12}H_{17}NO_4Na^+$ 262.1055, found 262.1054. **IR (υ/cm^{-1}):** 3385 (m, br), 2919 (m), 1730 (s), 1370 (m), 1286 (m), 1251 (m), 1159 (s). **[α]$^{22}_D$** = -39.2 (c = 0.425, CH$_2$Cl$_2$, l = 100 mm).
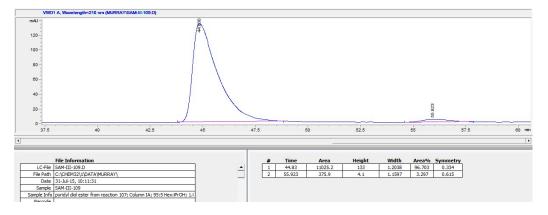
Diacel CHIRALPAK IA Column; 95:5 hexanes:iPrOH; 1.0 mL/min; 210 nm

Racemic Material

#	Time	Area	Height	Width	Area%	Symmetry
1	46.247	2354.1	29	1.1576	50.826	0.481
2	56.071	2277.6	25.8	1.3213	49.174	0.511

File Information
LC-File: SAM-III-101A.D
File Path: C:\CHEM32\1\DATA\MURRAY\
Date: 25-Jul-15, 13:29:00
Sample: SAM-III-101A
Sample Info: pyridyl ester diol from rxn SAM-III-098A; Column IA; 95:5 Hex:iPrOH

Enantioenriched Material

#	Time	Area	Height	Width	Area%	Symmetry
1	44.83	11025.2	133	1.2038	96.703	0.334
2	55.923	375.9	4.1	1.1597	3.297	0.615

File Information
LC-File: SAM-III-109.D
File Path: C:\CHEM32\1\DATA\MURRAY\
Date: 31-Jul-15, 10:11:31
Sample: SAM-III-109
Sample Info: pyridyl diol ester from reaction 107; Column IA; 95:5 Hex:iPrOH; 1.0

Major: 45.2 min; Minor: 56.6 min; 97:3 e.r.

1.67

***Tert*-butyl (*R*)-2-phenyl-3-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)-2 ((trimethylsilyl)oxy)propanoate (1.67).** Following General Procedure A and Supplementary Procedure C, the crude material was purified by silica gel (regular) chromatography (75:1 pentane:diethyl ether) to yield **1.67** as a colorless solid in 46% yield (58 mg). **^{1}H NMR** (600 MHz, CDCl$_3$) δ 7.51 - 7.46 (m, 2H), 7.28 (t, *J* = 7.7 Hz, 2H), 7.24 - 7.19 (m,
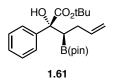
1H), 1.77 (d, J = 15.3 Hz, 1H), 1.70 (d, J = 15.3 Hz, 1H), 1.44 (s, 9H), 1.16 (s, 6H), 1.15 (s, 6H), 0.07 (s, 9H). **¹³C NMR** (151 MHz, CDCl$_3$) δ 173.0, 145.2, 127.7, 127.0, 125.6, 83.0, 81.3, 80.7, 27.9, 24.8, 24.7, 2.2. **HRMS (ESI⁺)** [M+Na]⁺ calcd for C$_{22}$H$_{37}$BO$_5$SiNa⁺ 443.2401, found 443.2389. **IR (υ/cm⁻¹):** 2979 (m), 1738 (s), 1366 (s), 1333 (m), 1248 (m), 1147 (s). **[α]²²$_D$ = +2.8** (c = 0.17, CH$_2$Cl$_2$, l = 100 mm).

1.59
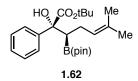
***Tert*-butyl (2*R*,3*R*)-5-((tert-butyldimethylsilyl)oxy)-2-hydroxy-2-phenyl-3-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)pentanoate (1.59).** Following General Procedure C, the crude material was purified by silica gel (80:20 regular:deactivated, layered) chromatography (benzene, gravity) to yield β-hydroxyboronate **1.59** as a colorless oil in 51% isolated yield (25.6 mg). **¹H NMR** (600 MHz, CDCl$_3$) δ 7.56 (d, J = 7.4 Hz, 2H), 7.30 (t, J = 7.7 Hz, 2H), 7.22 (t, J = 7.3 Hz, 1H), 3.98 (s, 1H), 3.60 (ddd, J = 9.9, 8.3, 4.2 Hz, 1H), 3.46 – 3.40 (m, 1H), 2.16 (dd, J = 11.0, 2.9 Hz, 1H), 1.59 – 1.53 (m, 1H), 1.40 (s, 9H), 1.36 – 1.28 (m, 1H), 1.25 (s, 6H), 1.24 (s, 6H), 0.85 (s, 9H), -0.05 (d, J = 11.2 Hz, 6H). **¹³C NMR** (151 MHz, CDCl$_3$) δ 174.6, 141.6, 127.9, 127.0, 126.1, 83.4, 82.4, 80.5, 62.7, 28.6, 27.7, 26.0, 25.0, 24.6, 18.3, -5.3, -5.4. **HRMS (ESI⁺)** [M+Na]⁺ calcd for C$_{27}$H$_{47}$BO$_6$SiNa⁺ 529.3133, found 529.3126. **IR (υ/cm⁻¹):** 3489 (m, br), 2930 (s), 2857 (s), 1719 (m), 1369 (s). **[α]²²$_D$ = -2.5** (c = 1.04, CH$_2$Cl$_2$, l = 100 mm).

1.60

***Tert*-butyl (2*R*,3*R*)-2-hydroxy-2-phenyl-3-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)butanoate (1.60).** Following General Procedure B, the crude material was purified by silica gel (regular) chromatography (15:1 pentane:diethyl ether, gravity) to yield β-hydroxyboronate **1.60** as a white solid in 67% isolated yield (19.1 mg). On a 1.0 g (5.6 mmol)

scale (with respect to ketoester), compound **11b** was isolated in 60% yield (1.21 g, contains 5% diboryl ethane impurity). **¹H NMR** (600 MHz, CDCl$_3$) δ 7.58 - 7.51 (m, 2H), 7.31 (dd, J = 8.4, 7.0 Hz, 2H), 7.25 - 7.20 (m, 1H), 3.86 (s, 1H), 2.08 (q, J = 7.6 Hz, 1H), 1.41 (s, 9H), 1.25 (s, 6H), 1.24 (s, 6H), 0.75 (d, J = 7.6 Hz, 3H). **¹³C NMR** (151 MHz, CDCl$_3$) δ 174.6, 141.5, 127.8, 126.9, 125.8, 83.4, 82.3, 80.2, 27.8, 24.9, 24.6, 9.5. **HRMS (ESI⁺)** [2M+Na]⁺ calcd for C$_{40}$H$_{62}$B$_2$O$_{10}$Na⁺ 747.4427, found 747.4451. **IR (υ/cm⁻¹):** 3401 (m, br), 2979 (s), 1693 (s), 1475 (m), 1373 (s). **[α]²²$_D$** = -1.6 (c = 1.47, CH$_2$Cl$_2$, l = 100 mm).

1.61
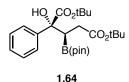
***Tert*-butyl (2*R*,3*R*)-2-hydroxy-2-phenyl-3-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)hex-5-enoate (1.61).** Following General Procedure C, the crude mixture was purified by silica gel (80:20 regular:deactivated, layered) chromatography (benzene, gravity) to yield β-hydroxyboronate **1.61** as a colorless oil in 50% isolated yield (19.3 mg). **¹H NMR** (600 MHz, CDCl$_3$) δ 7.59 - 7.54 (m, 2H), 7.32 (dd, J = 8.4, 7.0 Hz, 2H), 7.26 - 7.22 (m, 1H), 5.77 (ddt, J = 17.1, 10.1, 6.7 Hz, 1H), 4.93 - 4.86 (m, 1H), 4.85 (ddt, J = 10.0, 2.1, 1.0 Hz, 1H), 3.92 (s, 1H), 2.17 - 2.10 (m, 1H), 2.09 (dd, J = 11.3, 2.8 Hz, 1H), 1.41 (s, 9H, 1.25 (s, 6H), 1.24 (s, 6H). **¹³C NMR** (151 MHz, CDCl$_3$) δ 174.3, 141.3, 138.4, 128.4, 127.9, 127.1, 125.9, 114.8, 83.6, 82.5, 80.1, 30.2, 27.8, 24.9, 24.8. **HRMS (ESI⁺)** [M+Na]⁺ calcd for C$_{22}$H$_{33}$BO$_5$Na⁺ 411.2319, found 411.2315. **[α]²²$_D$** = -4.2 (c = 0.37, CH$_2$Cl$_2$, l = 100 mm)

1.62
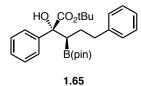
***Tert*-butyl (2*R*,3*R*)-2-hydroxy-6-methyl-2-phenyl-3-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)hept-5-enoate (1.62).** Following General Procedure C, the crude mixture was purified by silica gel (80:20 regular:deactivated, layered) chromatography

(benzene, gravity) to yield β-hydroxyboronate **1.62** as a white solid in 60% isolated yield (24.9

mg). **^{1}H NMR** (600 MHz, CDCl$_3$) δ 7.61 - 7.55 (m, 2H), 7.31 (dd, J = 8.4, 7.1 Hz, 2H), 7.25 - 7.21

(m, 1H), 5.06 (dddd, J = 6.8, 5.4, 2.8, 1.4 Hz, 1H), 3.91 (s, 1H), 2.07 (dd, J = 13.1, 7.8 Hz, 1H),

2.01 (dd, J = 11.6, 3.7 Hz, 1H), 1.60 (s, 3H), 1.42 (d, J = 1.3 Hz, 3H), 1.40 (s, 9H), 1.24 (s, 6H),

1.23 (s, 6H). **^{13}C NMR** (151 MHz, CDCl$_3$) δ 174.4, 141.3, 131.6, 127.8, 127.0, 126.0, 124.0, 83.5,

82.5, 80.0, 27.8, 25.8, 24.9, 24.7, 24.3, 17.7. **HRMS (ESI$^+$)** [2M+Na]$^+$ calcd for C$_{48}$H$_{74}$B$_2$O$_{10}$Na$^+$

855.5366, found 855.5387. **IR (υ/cm^{-1}):** 3489 (m, br), 2978 (s), 2926 (s), 1716 (s), 1370 (m).).

[α]^{22}$_D$ = +8.3 (c = 0.65, CH$_2$Cl$_2$, l = 100 mm).

1.63

***Tert*-butyl (2*R*,3*R*)-2-hydroxy-2-phenyl-3-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-**

2-yl)hexanoate (1.63). Following General Procedure C, the crude mixture was purified by

silica gel (80:20 regular:deactivated, layered) chromatography (benzene, gravity) to yield β-

hydroxyboronate **1.63** as a colorless oil in 30% isolated yield (11.8 mg).) ^{1}H NMR (600 MHz,

CDCl3) δ 7.56 – 7.52 (m, 2H), 7.31 (dd, J = 10.5, 4.8 Hz, 2H), 7.25 – 7.21 (m, 1H), 3.90 (s, 1H),

1.97 (dd, J = 11.2, 3.6 Hz, 1H), 1.39 (s, 9H), 1.38 – 1.32 (m, 2H), 1.26 (s, 6H) 1.26 (s, 6H), 1.14 –

1.05 (m, 1H), 1.00 – 0.92 (m, 1H), 0.74 (t, J = 7.3 Hz, 3H). ^{12}C NMR (151 MHz, CDCl3) δ 174.63,

141.68, 127.79, 126.89, 125.83, 83.42, 82.28, 80.49, 27.76, 27.64, 24.88, 24.78, 22.52, 14.36.

HRMS (ESI$^+$) [2M+Na]$^+$ calcd for C$_{44}$H$_{70}$B$_2$O$_{10}$Na$^+$ 803.5053, found 803.5065. **IR (υ/cm^{-1}):**

3492 (m, br), 2979 (s), 2932 (s), 1715 (s), 1370 (m). **[α]^{22}$_D$** = +14.0 (c = 0.32, CH$_2$Cl$_2$, l = 100

mm).

1.64

Di-*tert*-butyl (2*R*,3*R*)-2-hydroxy-2-phenyl-3-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)pentanedioate (1.64). Following General Procedure C, the crude mixture was purified by silica gel (80:20 regular:deactivated, layered) chromatography (benzene, gravity) to yield β-hydroxyboronate **1.64** as a colorless oil in 14% isolated yield (6.6 mg). **¹H NMR** (600 MHz, CDCl₃) δ 7.61 – 7.56 (m, 2H), 7.31 (dd, *J* = 10.5, 4.8 Hz, 2H), 7.26 – 7.21 (m, 1H), 3.95 (s, 1H), 2.46 (dd, *J* = 11.7, 4.3 Hz, 1H), 2.34 (dd, *J* = 17.2, 11.8 Hz, 1H), 1.89 (dd, *J* = 17.2, 4.3 Hz, 1H), 1.44 (s, J = 7.0 Hz, 9H), 1.36 (s, 9H), 1.25 (s, 6H), 1.21 (s, 6H). **¹³C NMR** (151 MHz, CDCl₃) δ 174.17, 173.76, 141.11, 128.00, 127.19, 126.06, 83.61, 83.07, 79.87, 79.14, 32.04, 28.04, 27.75, 25.01, 24.54. **HRMS (ESI⁺)** [M+Na]⁺ calcd for $C_{25}H_{39}BO_7Na^+$ 485.2687, found 485.2683. **IR (υ/cm⁻¹):** 3482 (m, br), 2979 (s), 1724 (s), 1369 (m), 1141 (m). $[\alpha]^{22}_D$ = -5.7 (*c* = 0.38, CH₂Cl₂, l = 100 mm).


1.65

***Tert*-butyl (2*R*,3*R*)-2-hydroxy-2,5-diphenyl-3-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)pentanoate (1.65).** Following General Procedure C, the crude mixture was purified by silica gel (80:20 regular:deactivated, layered) chromatography (benzene, gravity) to yield β-hydroxyboronate **1.65** as a colorless oil in 33% isolated yield (14.8 mg). **¹H NMR** (600 MHz, CDCl₃) δ 7.48 - 7.42 (m, 2H), 7.30 - 7.25 (m, 2H), 7.24 - 7.20 (m, 1H), 7.18 (d, *J* = 7.6 Hz, 2H), 7.14 - 7.09 (m, 1H), 7.04 - 6.99 (m, 2H), 3.93 (s, 1H), 2.72 (ddd, *J* = 13.6, 10.6, 4.6 Hz, 1H), 2.37 (ddd, *J* = 13.7, 10.2, 7.0 Hz, 1H), 2.03 (dd, *J* = 11.1, 3.4 Hz, 1H), 1.71 (dtd, *J* = 13.2, 10.6, 4.6 Hz, 1H), 1.39 (s, 9H), 1.34 (ddt, *J* = 13.7, 6.6, 3.4 Hz, 1H), 1.29 (s, 6H), 1.28 (s, 6H). **¹³C NMR** (151 MHz, CDCl₃) δ 174.5, 142.7, 141.4, 128.5, 128.4, 128.1, 127.8, 127.0, 125.8,
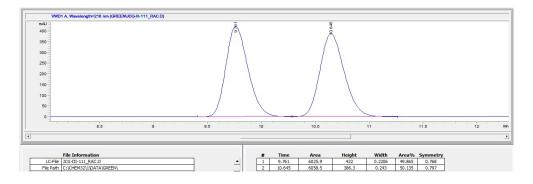
125.5, 83.5, 82.4, 80.5, 35.4, 27.7, 27.2, 25.0, 24.8. **HRMS (ESI⁺)** [M+Na]⁺ calcd for

$C_{27}H_{37}BO_5Na^+$ 475.2632, found 475.2627. **IR (υ/cm⁻¹):** 3524 (m, br), 2979 (s), 2931 (s), 1722

(s), 1369 (m). **[α]²²_D** = +11.1 (c = 0.44, CH_2Cl_2, l = 100 mm).

1.68

***Tert*-butyl (2*S*,3*R*)-5-((tert-butyldimethylsilyl)oxy)-2,3-dihydroxy-2-**
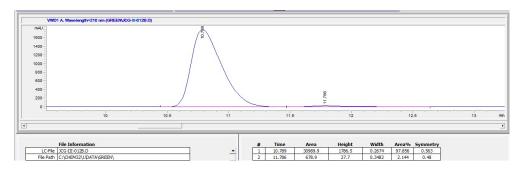
phenylpentanoate (1.68) Following General Procedure C and Supplementary Procedure A,

the crude oxidation mixture was purified by silica gel (regular) chromatography (15:1

hexanes:ethyl acetate, gravity) to yield diol **1.68** as a colorless oil in 91% isolated yield (15.2 mg).

¹H NMR (600 MHz, CDCl₃) δ 7.63 (dd, J = 7.9, 1.4 Hz, 2H), 7.37 - 7.30 (m, 2H), 7.30 - 7.26 (m,

1H), 4.55 (ddd, J = 9.6, 7.0, 1.9 Hz, 1H), 4.00 (s, 1H), 3.78 (ddd, J = 10.2, 7.2, 4.4 Hz, 1H), 3.68

(ddd, J = 10.6, 6.7, 4.8 Hz, 1H), 2.95 (d, J = 7.0 Hz, 1H), 1.47 (s, 9H), 0.88 (s, 9H), 0.02 (d, J =

14.9 Hz, 6H). **¹³C NMR** (151 MHz, CDCl₃) δ 173.4, 138.8, 128.1, 127.6, 125.8, 83.4, 81.1, 75.0,

61.2, 32.6, 27.8, 25.9, 18.2, -5.5, -5.5. **HRMS (ESI⁺)** [2M+Na]⁺ calcd for $C_{42}H_{72}O_{10}Si_2Na^+$

815.4562, found 815.4546. **IR (υ/cm⁻¹):** 3482 (m, br), 2955 (s), 2857 (m), 1723 (s), 1370 (m).

[α]²²_D = -16.7 (c = 1.03, CH_2Cl_2, l = 100 mm).

Diacel CHIRALPAK IC Column; 97:3 hexanes:iPrOH; 0.75 mL/min; 210 nm

Racemic Material

File Information		#	Time	Area	Height	Width	Area%	Symmetry
LC-File	JCG-III-111_RAC.D	1	9.761	6025.9	422	0.2206	49.865	0.768
File Path	C:\CHEM32\1\DATA\GREEN\	2	10.645	6058.5	386.3	0.243	50.135	0.797

Enantioenriched Material

VWD1 A, Wavelength=210 nm (GREENJCG-III-012B.D)

	File Information	#	Time	Area	Height	Width	Area%	Symmetry
LC-File	JCG-III-012B.D	1	10.789	30989.9	1786.5	0.2674	97.856	0.563
File Path	C:\CHEM32\1\DATA\GREEN\	2	11.786	678.9	27.7	0.3482	2.144	0.48
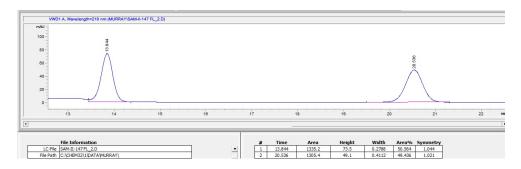
Major: 10.8 min; Minor: 11.8 min; 98:2 e.r.

1.91

***Tert*-butyl (2S,3R)-2,3-dihydroxy-2-phenylbutanoate (1.91).** Following General Procedure B and Supplementary Procedure A, the crude oxidation mixture was purified by silica gel (regular) chromatography (4:1 hexanes:ethyl acetate, gravity) to yield diol **1.91** as a white solid in 40% isolated yield (10.2 mg) over two steps. **^{1}H NMR** (600 MHz, CDCl$_3$) δ 7.61 (dd, *J* = 8.4, 1.3 Hz, 2H), 7.34 (dd, *J* = 8.3, 6.7 Hz, 2H), 7.30 - 7.26 (m, 1H), 4.48 (q, *J* = 6.4 Hz, 1H), 4.03 (s, 1H), 1.48 (s, 9H), 0.95 (d, *J* = 6.5 Hz, 3H). **^{13}C NMR** (151 MHz, CDCl$_3$) δ 173.6, 139.1, 128.2, 127.7, 125.6, 83.8, 81.2, 72.3, 27.8, 17.0. **HRMS (ESI$^+$)** [2M+Na]$^+$ calcd for C$_{28}$H$_{40}$O$_8$Na$^+$ 527.2621, found 527.2609. **IR (υ/cm^{-1}):** 3460 (m, br), 2925 (s), 1716 (s), 1449 (m), 1278 (s). **[α]^{22}$_D$** = -37.2 (*c* = 0.51, CH$_2$Cl$_2$, l = 100 mm).

Diacel CHIRALPAK IA Column; 95:5 hexanes:iPrOH; 1.0 mL/min; 210 nm

Racemic Material

VWD1 A, Wavelength=210 nm (MURRAY\SAM-II-147 FL_2.D)

	File Information	#	Time	Area	Height	Width	Area%	Symmetry
LC-File	SAM-II-147 FL_2.D	1	13.844	1335.2	73.5	0.2788	50.564	1.044
File Path	C:\CHEM32\1\DATA\MURRAY\	2	20.536	1305.4	49.1	0.4112	49.436	1.021
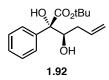
Major: 13.3 min; Minor: 19.9 min; 98:2 e.r.

1.92

***Tert*-butyl (2*S*,3*R*)-2,3-dihydroxy-2-phenylhex-5-enoate (1.92).** Following General

Procedure C and Supplementary Procedure A, the crude oxidation mixture was purified by silica

gel (regular) chromatography (8:1 hexanes:ethyl acetate, pressure) to yield diol **1.92** as a

colorless oil in 34% isolated yield (9.6 mg) over two steps. **¹H NMR** (600 MHz, CDCl$_3$) δ 7.67 -

7.61 (m, 2H), 7.39 - 7.33 (m, 2H), 7.32 - 7.28 (m, 1H), 5.79 (dddd, J = 16.9, 10.2, 7.6, 6.5 Hz, 1H),

5.06 - 5.03 (m, 1H), 5.03 - 4.99 (m, 1H), 4.36 - 4.30 (m, 1H), 4.06 (d, J = 0.7 Hz, 1H), 2.11 - 2.02

(m, 2H), 1.92 (dddd, J = 13.3, 6.6, 2.8, 1.4 Hz, 1H), 1.48 (s, 9H). **¹³C NMR** (151 MHz, CDCl$_3$) δ

173.3, 138.6, 135.0, 128.3, 127.9, 125.7, 117.6, 83.9, 81.0, 75.4, 35.4, 27.8. **HRMS (ESI⁺)**

[2M+Na]⁺ calcd for C$_{32}$H$_{44}$O$_8$Na⁺ 579.2934, found 579.2928. **IR (υ/cm⁻¹):** 3485 (m, br), 2926

(s), 1721 (s), 1278 (s). **[α]²²$_D$** = -20.7 (*c* = 0.44, CH$_2$Cl$_2$, l = 100 mm).

Diacel CHIRALPAK IA Column; 95:5 hexanes:iPrOH; 1.0 mL/min; 210 nm

Racemic Material

#	Time	Area	Height	Width	Area%	Symmetry
1	11.81	7633.9	494.6	0.2381	49.990	0.922
2	27.435	7637.1	210.1	0.5581	50.010	0.796

File Information
LC-File: JCG-III-062B(RAC).D
File Path: C:\CHEM32\1\DATA\GREEN\

Enantioenriched Material

#	Time	Area	Height	Width	Area%	Symmetry
1	11.834	31677.7	1927.1	0.2498	99.284	0.711
2	28.135	228.3	6.1	0.5709	0.716	0.918

File Information
LC-File: JCG-III-071B.D
File Path: C:\CHEM32\1\DATA\GREEN\

Major: 11.8 min; Minor: 28.1 min; 99:1 e.r.

1.93

***Tert*-butyl (2*S*,3*R*)-2,3-dihydroxy-6-methyl-2-phenylhept-5-enoate (1.93).** Following

General Procedure C and Supplementary Procedure A, the crude oxidation mixture was purified

by silica gel (regular) chromatography (15:1 hexanes:ethyl acetate, gravity) to yield diol **1.93** as a

colorless oil in 39% isolated yield (11.8 mg) over two steps. **¹H NMR** (600 MHz, CDCl$_3$) δ 7.67 -

7.61 (m, 2H), 7.38 - 7.32 (m, 2H), 7.32 - 7.26 (m, 1H), 5.14 (dddd, J = 8.1, 6.8, 2.9, 1.4 Hz, 1H),

4.28 (dd, J = 10.2, 2.8 Hz, 1H), 4.06 (s, 1H), 2.09 - 2.01 (m, 1H), 1.86 - 1.79 (m, 1H), 1.66 (d, J =

1.5 Hz, 3H), 1.47 (s, 12H). **¹³C NMR** (151 MHz, CDCl$_3$) δ 173.4, 138.9, 134.6, 128.2, 127.7, 125.7,

120.5, 83.8, 81.1, 76.4, 29.6, 27.8, 25.9, 17.8. **HRMS (ESI⁺)** [2M+Na]⁺ calcd for C$_{36}$H$_{52}$O$_8$Na⁺

635.3560, found 635.3554. **IR (υ/cm⁻¹):** 3475 (m, br), 2977 (s), 2927 (s), 1721 (s), 1159 (s).

[α]²²$_D$ = -3.9 (*c* = 0.65, CH$_2$Cl$_2$, l = 100 mm).

Diacel CHIRALPAK IA Column; 93:7 hexanes:iPrOH; 1.0 mL/min; 210 nm
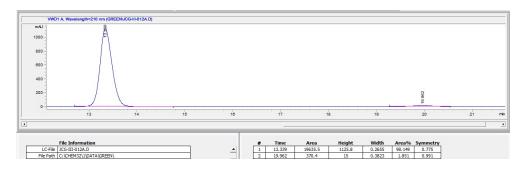
Racemic Material

#	Time	Area	Height	Width	Area%	Symmetry
1	8.82	4694.3	394.6	0.1838	50.080	0.956
2	21.737	4679.2	155.5	0.4631	49.920	0.951

LC-File: JCG-II-298A(II).D
File Path: C:\CHEM32\1\DATA\GREEN\

Enantioenriched Material

#	Time	Area	Height	Width	Area%	Symmetry
1	8.639	52811.7	3473.1	0.2374	99.279	0.635
2	21.397	383.8	13.4	0.4487	0.721	1.004

LC-File: JCG-III-012C(II).D
File Path: C:\CHEM32\1\DATA\GREEN\

Major: 8.8 min; Minor: 21.4 min; 99:1 e.r

1.94

***Tert*-butyl (2*S*,3*R*)-2,3-dihydroxy-2-phenylhexanoate (1.94).** Following General Procedure C and Supplementary Procedure A, the crude oxidation mixture was purified by silica gel (regular) chromatography (4:1 hexanes:ethyl acetate, gravity) to yield diol **1.94** as a white solid. **¹H NMR** (600 MHz, CDCl$_3$) δ 7.61 (dd, *J* = 5.3, 3.4 Hz, 2H), 7.38 – 7.32 (m, 2H), 7.31 – 7.27 (m, 1H), 4.29 – 4.22 (m, 1H), 4.05 (s, 1H), 1.91 (d, *J* = 11.1 Hz, 1H), 1.56 – 1.49 (m, 1H), 1.48 (s, 9H), 1.31 – 1.22 (m, 2H), 1.09 – 1.03 (m, 1H), 0.81 (t, *J* = 7.2 Hz, 3H). **¹³C NMR** (151 MHz, CDCl$_3$) δ 173.7, 139.0, 128.2, 127.7, 125.6, 83.9, 81.4, 75.9, 32.7, 27.8, 19.1, 13.9. **HRMS (ESI⁺)** [2M+Na]⁺ calcd for C$_{44}$H$_{70}$B$_2$O$_{10}$Na⁺ 803.5063, found 803.5065. **IR (υ/cm⁻¹): 3**481 (m, br),

2960 (m), 1869 (s), 1716 (m), 1541 (m), 1507 (m), 1457 (s), 1395 (s), 1371 (s), 1278 (s), 1141 (s), 1069 (s). **[α]^{16}$_D$** = -5.1 (*c* = 0.19, CH$_2$Cl$_2$, l = 100 mm).
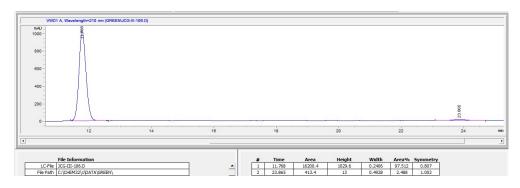
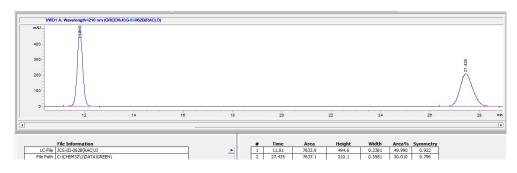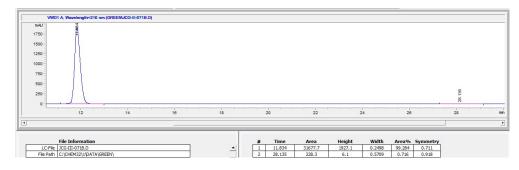*Diacel CHIRALPAK IA Column; 95:5 hexanes:iPrOH; 1.0 mL/min; 210 nm*

Racemic Material

#	Time	Area	Height	Width	Area%	Symmetry
1	11.911	4928.8	308.9	0.2451	50.332	0.95
2	24.541	4863.8	147.3	0.5081	49.668	0.893

File Information
LC-File JCG-III-071A.D
File Path C:\CHEM32\1\DATA\GREEN\

Enantioenriched Material

#	Time	Area	Height	Width	Area%	Symmetry
1	11.768	16200.4	1029.6	0.2406	97.512	0.807
2	23.865	413.4	13	0.4928	2.488	1.002

File Information
LC-File JCG-III-106.D
File Path C:\CHEM32\1\DATA\GREEN\
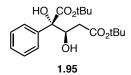
Major: 11.8 min; Minor: 23.9 min; 98:2 e.r.

1.95
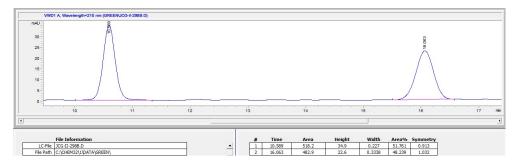
Di-*tert*-butyl (2S,3R)-2,3-dihydroxy-2-phenylpentanedioate (1.95). Following General Procedure C and Supplementary Procedure A, the crude oxidation mixture was purified by silica gel (regular) chromatography (4:1 hexanes:ethyl acetate, gravity) to yield diol **1.95** as a colorless oil in 21% isolated yield (7.5 mg) over two steps. **¹H NMR** (600 MHz, CDCl$_3$) δ 7.68 - 7.62 (m, 2H), 7.39 - 7.32 (m, 2H), 7.32 - 7.27 (m, 1H), 4.73 (dd, *J* = 10.0, 2.7 Hz, 1H), 4.05 - 3.93 (m, 1H), 2.35 (dd, *J* = 16.5, 10.0 Hz, 1H), 2.02 (dd, *J* = 16.6, 2.7 Hz, 1H), 1.48 (s, 9H), 1.41 (s, 9H). **¹³C NMR** (151 MHz, CDCl$_3$) δ 172.7, 172.2, 138.2, 128.3, 128.0, 125.8, 83.9, 81.2, 80.6, 73.0, 36.4,
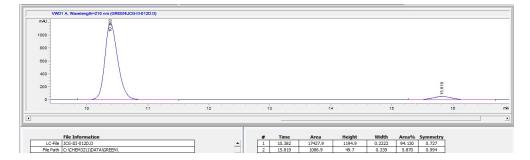
28.1, 27.8. **HRMS (ESI⁺)** [2M+Na]⁺ calcd for $C_{38}H_{66}O_{12}Na^+$ 727.3669, found 727.3658. **IR**

(υ/cm⁻¹): 3486 (m, br), 2978 (s), 2927 (m), 1727 (s), 1154 (s). **[α]²²_D** = -23.7 (*c* = 0.38, CH₂Cl₂, l

= 100 mm).

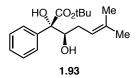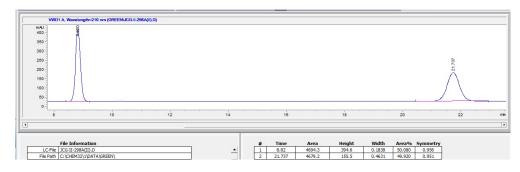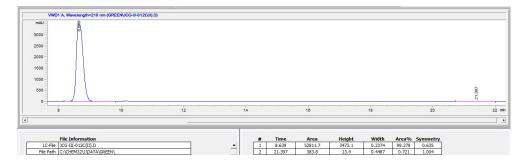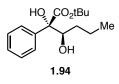*Diacel CHIRALPAK IA Column; 95:5 hexanes:iPrOH; 1.0 mL/min; 210 nm*

Racemic Material

#	Time	Area	Height	Width	Area%	Symmetry
1	10.589	518.2	34.9	0.227	51.761	0.913
2	16.063	482.9	22.6	0.3338	48.239	1.032

LC-File: JCG-II-298B.D
File Path: C:\CHEM32\1\DATA\GREEN\

Enantioenriched Material

#	Time	Area	Height	Width	Area%	Symmetry
1	10.382	17427.9	1194.9	0.2222	94.130	0.727
2	15.819	1086.9	49.7	0.339	5.870	0.994

LC-File: JCG-III-012D.D
File Path: C:\CHEM32\1\DATA\GREEN\

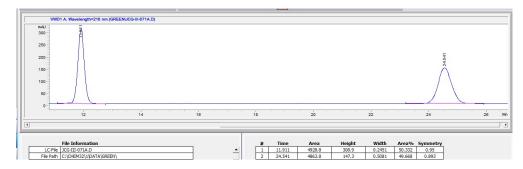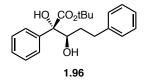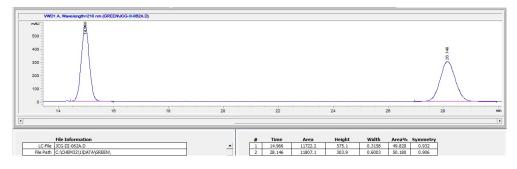### *Major: 10.4 min; Minor: 15.8 min; 94:6 e.r.*

1.96
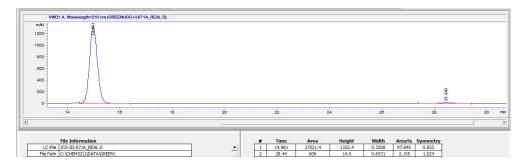
***Tert*-butyl (2*S*,3*R*)-2,3-dihydroxy-2,5-diphenylpentanoate (1.96).** Following General

Procedure C and Supplementary Procedure A, the crude oxidation mixture was purified by silica

gel (regular) chromatography (8:1 hexanes:ethyl acetate) to yield diol **1.96** as a colorless oil in

22% isolated yield (7.5 mg) over two steps. **¹H NMR** (600 MHz, CDCl₃) δ 7.55 - 7.51 (m, 2H),

7.34 - 7.29 (m, 2H), 7.29 - 7.26 (m, 1H), 7.21 (t, *J* = 7.5 Hz, 2H), 7.16 - 7.12 (m, 1H), 7.08 - 7.03

(m, 2H), 4.28 (td, *J* = 10.7, 1.9 Hz, 1H), 4.07 (d, *J* = 0.7 Hz, 1H), 2.86 (ddd, *J* = 14.6, 10.4, 4.8

Hz, 1H), 2.53 (ddd, J = 13.9, 10.1, 6.9 Hz, 1H), 2.06 (d, J = 11.2 Hz, 1H), 1.67 - 1.58 (m, 1H), 1.47 (s, 9H), 1.44 (ddt, J = 10.4, 3.4, 1.7 Hz, 1H). **¹³C NMR** (151 MHz, CDCl$_3$) δ 173.5, 141.9, 138.7, 128.4, 128.2, 128.2, 127.8, 125.7, 125.6, 83.9, 81.3, 75.5, 32.4, 32.2, 27.8. **HRMS (ESI⁺)** [2M+Na]⁺ calcd for $C_{42}H_{52}O_8Na^+$ 707.3560, found 707.3558. **IR (υ/cm⁻¹):** 3460 (m, br), 2926 (m), 1721 (s), 1278 (s). **[α]²²_D** = +11.6 (c = 0.14, CH$_2$Cl$_2$, l = 100 mm).

Diacel CHIRALPAK IA Column; 95:5 hexanes:iPrOH; 1.0 mL/min; 210 nm

Racemic Material

#	Time	Area	Height	Width	Area%	Symmetry
1	14.966	11722.2	575.1	0.3158	49.820	0.932
2	28.146	11807.1	303.9	0.6003	50.180	0.906

Enantioenriched Material

#	Time	Area	Height	Width	Area%	Symmetry
1	14.981	27521.4	1322.4	0.3208	97.845	0.853
2	28.44	606	14.5	0.6531	2.155	1.024
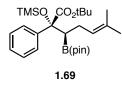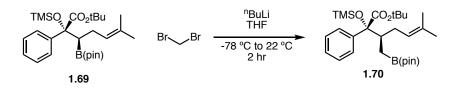
Major: 15.0 min; Minor: 28.4 min; 98:2 e.r.
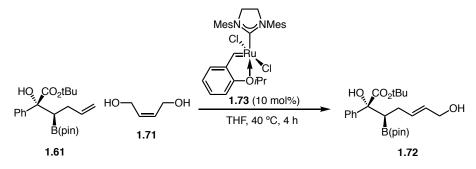
1.69

***Tert*-butyl (2*R*,3*R*)-6-methyl-2-phenyl-3-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)-2-((trimethylsilyl)oxy)hept-5-enoate (1.69).** Following General Procedure C and Supplementary Procedure C, the crude material was purified by silica gel chromatography (50:1 pentane:diethyl ether) to yield **1.69** as a colorless oil in 60% yield (8.8 mg). **¹H NMR** (600

MHz, CDCl$_3$) δ 7.45 (dd, J = 8.5, 1.3 Hz, 2H), 7.28 (t, J = 7.4 Hz, 2H), 7.22 - 7.18 (m, 1H), 5.04 (ddd, J = 8.2, 4.0, 2.4 Hz, 1H), 2.11 - 1.94 (m, 1H), 1.83 - 1.71 (m, 2H), 1.56 (s, 3H), 1.47 (s, 9H) 1.40 (s 3H), 1.19 (s, 6H), 1.18 (s, 6H), 0.17 (s, 9H). **^{13}C NMR** (151 MHz, CDCl$_3$) δ 172.9, 143.9, 130.9, 127.6, 126.9, 126.0, 124.8, 84.2, 82.9, 82.1, 28.1, 25.9, 25.1, 24.9, 24.8, 17.7, 2.9. **HRMS (ESI$^+$)** [M+Na]$^+$ calcd for C$_{27}$H$_{45}$BO$_5$SiNa$^+$ 511.3027, found 511.3013. **IR (υ/cm^{-1}):** 2979 (m), 1735 (s), 1370 (s), 1248 (s), 1146 (s). **[α]^{16}$_D$** = +35.8 (c = 0.2, CH$_2$Cl$_2$, l = 100 mm).
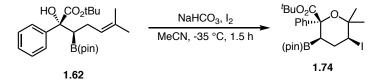
***Tert*-butyl (2*R*,3*R*)-6-methyl-2-phenyl-3-((4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)methyl)-2-((trimethylsilyl)oxy)hept-5-enoate (1.70).** Following a literature procedure,[43] protected hydroxyboronate **1.70** (23.9 mg, 0.05 mmol) was added to an oven dried 8 mL vial containing a stir bar. The vial was purged with nitrogen for 3 minutes. A solution of dibromomethane in THF was made (0.125 mmol, 0.25M) and an aliquot (0.5 mL) was added to the vial via syringe. The vial was cooled to -78 °C (dry ice/acetone bath). A solution of ^{n}BuLi (0.066 mL, 0.11 mmol, 1.67M) in hexanes was added dropwise via syringe. The reaction was allowed to stir at -78 °C for 20 minutes and then allowed to warm to room temperature and stirred for an additional two hours. The reaction was quenched with a saturated solution of ammonium chloride (1.5 mL), extracted with diethyl ether (3x), dried over MgSO$_4$ and concentrated. The crude material was purified via silica gel (regular) chromatography (100:1 pentane:ether, gravity) to yield the desired homologated product **1.70** in 50% yield (12.5 mg). **^{1}H NMR** (400 MHz, CDCl$_3$) δ 7.63 - 7.55 (m, 2H), 7.29 (dd, J = 8.4, 6.7 Hz, 2H), 7.25 - 7.16 (m, 1H), 4.99 - 4.88 (m, 1H), 2.64 (td, J = 9.7, 4.2 Hz, 1H), 1.77 - 1.59 (m, 2H), 1.56 (s, 3H), 1.48 (s, 9H), 1.41 (s, 3H), 1.24 (s, 12H), 0.21 (s, 9H). **^{13}C NMR** (151 MHz, CDCl$_3$) δ 172.8, 142.7, 131.8, 127.8, 127.0, 126.2, 123.6, 87.3, 82.9, 81.8, 43.9, 29.9, 28.0, 26.3, 25.1, 17.8, 3.0. **LRMS**

(ESI+)[M+Na]+ calcd for C28H47BO5SiNa+ 525.3184, found 525.26. IR (υ/cm-1): 2978 (m), 1734 (s), 1457 (m), 1369 (s), 1324 (m), 1248 (s), 1201 (s), 1079 (m), 1055 (m). **[α]^{16}$_D$** = +3.3 (c = 0.42, CH2Cl2, l = 100 mm).

***Tert*-butyl (*E*)-2,7-dihydroxy-2-phenyl-3-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)hept-5-enoate (1.72).** An 8 mL vial containing a magnetic stir bar was charged with allyl hydroxyboronate **1.61** (10.4 mg, 0.027 mmol) and cis-2-butene-1,4-diol **1.71** (4.7 mg, 0.054 mmol, 4.4 μL). The vial was sealed, evacuated, and placed under an inert atmosphere of N2 gas. To a separate, oven-dried 8 mL vial, (1,3-Bis-(2,4,6-trimethylphenyl)-2-imidazolidinylidene)dichloro(o-isopropoxyphenylmethylene)ruthenium (1.7 mg, 0.0027 mmol) was added. The vial was sealed, evacuated and purged with N$_2$. The vial containing the catalyst was then charged with dry THF (200 μL) and purged with N$_2$ gas. The catalyst solution was cannula transferred to the reaction vial containing hydroxyboronate and alkene at room temperature. The green reaction mixture was warmed to 40 °C and allowed to stir for 6 hours. After, the reaction was diluted with wet diethyl ether and concentrated in vacuo. Analysis of the crude mixture revealed formation of desired product in a 6.5:1 E/Z ratio. The resulting brown oil was purified by silica gel chromatography (4:1 hexanes:ethyl acetate) to afford **1.72** (7.1 mg, 0.017 mmol, 63% yield) as a white solid in 94:6 E/Z ratio. **¹H NMR** (600 MHz, CDCl3) δ 7.60 – 7.55 (m, 2H), 7.34 (t, J = 7.7 Hz, 2H), 7.28 – 7.24 (m, 1H), 5.61 (dt, J = 15.0, 6.8 Hz, 1H), 5.52 – 5.46 (m, 1H), 3.98 (d, J = 1.9 Hz, 2H), 3.95 (d, J = 5.1 Hz, 1H), 2.19 – 2.08 (m, 2H), 1.87 – 1.81 (m, 1H), 1.43 (s, 9H), 1.27 (s, 12H), 1.09 (t, J = 5.7 Hz, 1H). **¹³C NMR** (151 MHz, CDCl3) δ 174.3, 141.4, 133.1, 129.2, 127.9, 127.1, 125.9, 83.6, 82.7, 80.1, 63.8, 28.5, 27.8, 25.0, 24.7. **LRMS**

(ESI⁺) [M+Na]⁺ calcd for $C_{23}H_{35}BO_6Na^+$ 441.24, found 441.36. **IR (υ/cm⁻¹):** 3482 (m, br), 2979 (s), 2929 (m), 1716 (s), 1370 (m), 1163 (s). **[α]¹⁶ᴅ** = +4.4 (c = 0.26, CH_2Cl_2, l = 100 mm).

***Tert*-butyl (2*R*,3*R*,5*S*)-5-iodo-6,6-dimethyl-2-phenyl-3-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)tetrahydro-2*H*-pyran-2-carboxylate (1.74).** Following a modified literature procedure,[34] prenyl-substituted hydroxyboronate **1.62** (16.8 mg, 0.040 mmol) was added to an 8 mL amber vial containing a stir bar. The vial was placed under vacuum for ten minutes, then back-filled with nitrogen. The vial was charged with dry acetonitrile (0.4 mL) and cooled to 0 °C in an ice water bath. Sodium bicarbonate (10.1 mg, 0.121 mmol) was added to the vial, the vial was capped, and the resulting suspension was allowed to stir at 0 °C for 15 minutes. The reaction was then transferred to a -35 °C bath, where it was allowed to cool for ten minutes. Iodine (30.7 mg, 0.121 mmol) was added to the vial, and the reaction was kept at -35 °C for 1.5 hours. The reaction mixture was diluted with water and extracted with ethyl acetate (4x). The combined organics were washed with saturated sodium thiosulfate solution, dried over $MgSO_4$, filtered and concentrated *in vacuo*. The crude material was purified via silica gel (regular) chromatography (20:1 hexanes:diethyl ether) to yield the desired cyclized product **1.74** in 45% yield (9.5 mg). **¹H NMR** (600 MHz, CDCl₃) δ 7.41 (dd, *J* = 5.3, 3.4 Hz, 2H), 7.27 (d, *J* = 7.7 Hz, 2H), 7.25 – 7.21 (m, 1H), 4.37 (dd, *J* = 13.2, 3.8 Hz, 1H), 2.70 (dd, *J* = 27.5, 13.4 Hz, 1H), 2.43 (dt, *J* = 14.4, 3.9 Hz, 1H), 1.60 (s, 3H), 1.57 (s, 3H), 1.53 (s, 9H), 1.18 (s, 6H), 1.17 (s, 6H). **¹³C NMR** (151 MHz, CDCl₃) δ 173.7, 143.2, 127.3, 127.1, 126.7, 84.0, 82.8, 82.8, 39.8, 34.0, 31.8, 31.6, 27.8, 25.3, 24.2, 22.7, 22.2, 14.2. **LRMS (ESI⁺)** [M+Na]⁺ calcd for $C_{24}H_{36}BIO_5Na^+$ 565.16, found 565.18. **IR (υ/cm⁻¹):** 2979 (m), 2929 (m), 1715 (s), 1369 (s), 1149 (s). **[α]¹⁶ᴅ** = +13.2 (*c* = 0.28, CH_2Cl_2, l = 100 mm).

1.81
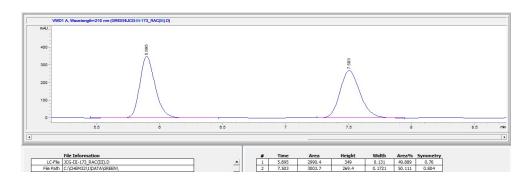
(*R*)-1,1-diphenyl-2-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)propan-1-ol (1.81).

Following General Procedure B, the crude material (42% NMR conversion) was purified by silica

gel (regular) chromatography (20:1 hexanes:diethyl ether) to yield β-hydroxyboronate **20** which

was taken directly on to oxidation (see below). **¹H NMR** (600 MHz, CDCl$_3$) δ 7.57 (dd, J = 8.4,

1.1 Hz, 2H), 7.46 (dd, J = 8.4, 1.1 Hz, 2H), 7.28 – 7.23 (m, 6H), 7.13 (ddd, J = 11.9, 6.0, 2.9 Hz,

2H), 3.61 (s, 1H), 2.40 (q, J = 7.4 Hz, 1H), 1.08 (s, 6H), 0.95 (s, 6H), 0.92 (d, J = 7.4 Hz, 3H).**¹³C

NMR** (151 MHz, CDCl$_3$) δ 149.9, 145.9, 128.2, 128.0, 126.6, 126.1, 125.8, 125.7, 83.7, 78.8, 24.6,

24.2, 10.1.

1.97
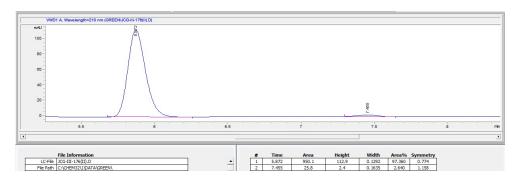
(*R*)-(+)-1,1-Diphenyl-1,2-propanediol. (R)-(+)-1,1-Diphenyl-1,2-propanediol (1.97).

Following General Procedure B and Supplementary Procedure A, the crude oxidation mixture

was purified by silica gel (regular) chromatography (4:1 hexanes:ethyl acetate, gravity) to yield

diol **20** as a white solid in 12% isolated yield (2.7 mg) over two steps. Spectral data aligns with

previously reported results.[44] **[α]²²**$_D$ = +9.7 (c = 0.14, MeOH, l = 100mm).

Diacel CHIRALPAK IC Column; 90:10 hexanes:iPrOH; 1.0 mL/min; 210 nm

Racemic Material

File Information		#	Time	Area	Height	Width	Area%	Symmetry
LC-File	JCG-III-173_RAC(III).D	1	5.895	2990.4	349	0.131	49.889	0.76
File Path	C:\CHEM32\1\DATA\GREEN\	2	7.503	3003.7	269.4	0.1721	50.111	0.804

Enantioenriched Material

VWD1 A, Wavelength=210 nm (GREENJCG-III-176(II).D)

	File Information	
LC-File	JCG-III-176(II).D	
File Path	C:\CHEM32\1\DATA\GREEN\	

#	Time	Area	Height	Width	Area%	Symmetry
1	5.872	950.1	112.9	0.1292	97.360	0.774
2	7.455	25.8	2.4	0.1635	2.640	1.158

Major: 5.9 min; Minor: 7.5 min; 97:3 e.r.

1.5.9 Spectra

1.47
^{1}H NMR (600 MHz, CDCl$_3$)

1.47
^{13}C NMR (151 MHz, CDCl$_3$)

64

1.48
^{1}H NMR (600 MHz, CDCl$_3$)

1.48
^{13}C NMR (151 MHz, CDCl$_3$)

65

1.49
^{1}H NMR (600 MHz, CDCl$_3$)

1.49
^{13}C NMR (151 MHz, CDCl$_3$)

66

1.50

^{1}H NMR (600 MHz, CDCl$_3$)

1.50

^{13}C NMR (151 MHz, CDCl$_3$)

67

1.51
^{1}H NMR (600 MHz, CDCl$_3$)

1.51
^{13}C NMR (151 MHz, CDCl$_3$)

68

1.52
^{1}H NMR (600 MHz, CDCl$_3$)

1.52
^{13}C NMR (151 MHz, CDCl$_3$)

69

1.53
^{1}H NMR (600 MHz, CDCl$_3$)

1.53
^{13}C NMR (151 MHz, CDCl$_3$)

70

1.54

^{1}H NMR (600 MHz, CDCl$_3$)

1.54

^{13}C NMR (151 MHz, CDCl$_3$)

71

1.55
^{1}H NMR (600 MHz, CDCl$_3$)

1.55
^{13}C NMR (151 MHz, CDCl$_3$)

72

1.56
^{1}H NMR (600 MHz, CDCl$_3$)

1.56
^{13}C NMR (151 MHz, CDCl$_3$)

73

1.57

^{1}H NMR (600 MHz, CDCl$_3$)

1.57

^{13}C NMR (151 MHz, CDCl$_3$)

74

1.58
^{1}H NMR (600 MHz, CDCl$_3$)

1.58
^{13}C NMR (151 MHz, CDCl$_3$)

1.67

^{1}H NMR (600 MHz, CDCl$_3$)

1.67

^{13}C NMR (151 MHz, CDCl$_3$)

76

1.90
^{1}H NMR (600 MHz, CDCl$_3$)

1.90
^{13}C NMR (151 MHz, CDCl$_3$)

77

1.59

^{1}H NMR (600 MHz, CDCl$_3$)

1.59

^{13}C NMR (600 MHz, CDCl$_3$)

1.60
^{1}H NMR (600 MHz, CDCl$_3$)

1.60
^{13}C NMR (151 MHz, CDCl$_3$)

79

1.61
^{1}H NMR (600 MHz, CDCl$_3$)

1.61
^{13}C NMR (151 MHz, CDCl$_3$)

80

HO CO₂tBu

B(pin)

1.62
¹H NMR (600 MHz, CDCl₃)

HO CO₂tBu

B(pin)

1.62
¹³C NMR (151 MHz, CDCl₃)

81

1.63

^{1}H NMR (600 MHz, CDCl$_3$)

1.63

^{13}C NMR (151 MHz, CDCl$_3$)

82

1.64
^{1}H NMR (600 MHz, CDCl$_3$)

1.64
^{13}C NMR (151 MHz, CDCl$_3$)

83

1.65

^{1}H NMR (600 MHz, CDCl$_3$)

1.65

^{13}C NMR (151 MHz, CDCl$_3$)

84

1.68

^{1}H NMR (600 MHz, CDCl$_3$)

1.68

^{13}C NMR (151 MHz, CDCl$_3$)

85

1.91

^{1}H NMR (600 MHz, CDCl$_3$)

1.91

^{13}C NMR (151 MHz, CDCl$_3$)

86

1.92
^{1}H NMR (600 MHz, CDCl$_3$)

1.92
^{13}C NMR (151 MHz, CDCl$_3$)

87

1.93
^{1}H NMR (600 MHz, CDCl$_3$)

1.93
^{13}C NMR (151 MHz, CDCl$_3$)

88

1.94

^{1}H NMR (600 MHz, CDCl$_3$)

1.94

^{13}C NMR (151 MHz, CDCl$_3$)

89

1.95
^{1}H NMR (600 MHz, CDCl$_3$)

1.95
^{13}C NMR (151 MHz, CDCl$_3$)

1.96
^{1}H NMR (600 MHz, CDCl$_3$)

1.96
^{13}C NMR (151 MHz, CDCl$_3$)

91

TMSO CO$_2$tBu

B(pin)

1.69
^{1}H NMR (151 MHz, CDCl$_3$)

TMSO CO$_2$tBu

B(pin)

1.69
^{13}C NMR (151 MHz, CDCl$_3$)

TMSO CO₂tBu

1.70
¹H NMR (600 MHz, CDCl₃)

TMSO CO₂tBu

1.70
¹³C NMR (151 MHz, CDCl₃)

1.72

^{1}H NMR (600 MHz, CDCl$_3$)

1.72

^{13}C NMR (151 MHz, CDCl$_3$)

1.74
^{1}H NMR (600 MHz, CDCl$_3$)

1.74
^{13}C NMR (151 MHz, CDCl$_3$)

95

Selective gradient 1D NOESY at 1.426 ppm (H_d)

Selective gradient 1D NOESY at 4.365 ppm (H$_a$)

NOE between H$_d$ and H$_a$ supports assignment of major diastereomer.

1.81
^{1}H NMR (600 MHz, CDCl$_3$)

1.81
^{13}C NMR (151 MHz, CDCl$_3$)

99

1.5.10 Crystal structure data for 1.60

Identification Code: jcg_ii_300a

Empirical Formula: $C_{40}H_{58}B_2O_{10}$

Formula Weight: 720.43

Measurement Temperature: 100(2) K

Radiation Type: CuK\a

Wavelength: 1.54178

Crystal System: triclinic

Space Group: P-1

Unit Cell Dimensions: a = 6.2365(3) Å; α = 101.486(3)°

b = 9.4178(4) Å; β = 93.584(3)°

c = 18.1506(9) Å; γ = 100.833(3)°

Volume: 1020.55(8) Å³

Z: 2

Density (calculated): 1.172 g/cm³

Absorption Correction Coefficient: 0.622 (mm⁻¹)

F(000): 388

Crystal size: 0.035 mm x 0.053 mm x 0.202 mm

Theta Max: 66.61°

Index Ranges: $h_{max} = 7$; $k_{max} = 11$; $l_{max} = 21$

Reflections Collected: 6875

Independent Reflections: 5753

Completeness of Theta: 98

Min:Max Transmission Ratio: 0.8977

Refinement Method: XL

Goodness-of-fit on F2 0: 0.822

R Indicies: R1 = 0.0415; wR2 = 0.0564

Bond lengths for 1.60 (Å)

Number	Atom1	Atom2	Length
1	O1	C17	1.469(3)
2	O1	B1	1.363(3)
3	O2	C16	1.473(3)
4	O2	B1	1.369(3)
5	O5	C9	1.330(3)
6	O5	C22	1.495(3)
7	O3	C7	1.420(3)
8	O3	H3	0.88(4)
9	O4	C9	1.212(3)
10	C17	C19	1.513(4)
11	C17	C16	1.552(3)
12	C17	C20	1.530(4)
13	C7	C9	1.535(4)
14	C7	C1	1.542(4)

15	C7	C12	1.543(3)
16	C19	H19A	0.98
17	C19	H19B	0.979
18	C19	H19C	0.98
19	C16	C21	1.513(4)
20	C16	C18	1.518(4)
21	C1	C2	1.387(4)
22	C1	C6	1.399(4)
23	C12	H12	1
24	C12	C26	1.539(4)
25	C12	B1	1.581(4)
26	C21	H21A	0.98
27	C21	H21B	0.98
28	C21	H21C	0.98
29	C22	C23	1.520(4)
30	C22	C25	1.510(4)
31	C22	C24	1.513(4)
32	C2	H2	0.95
33	C2	C3	1.393(4)
34	C23	H23A	0.981
35	C23	H23B	0.98
36	C23	H23C	0.979
37	C4	H4	0.95
38	C4	C5	1.380(5)
39	C4	C3	1.377(4)

40	C20	H20A	0.979
41	C20	H20B	0.98
42	C20	H20C	0.98
43	C6	H6A	0.95
44	C6	C5	1.383(4)
45	C25	H25A	0.98
46	C25	H25B	0.981
47	C25	H25C	0.98
48	C5	H5	0.949
49	C26	H26A	0.98
50	C26	H26B	0.98
51	C26	H26C	0.98
52	C3	H3A	0.95
53	C18	H18A	0.98
54	C18	H18B	0.979
55	C18	H18C	0.98
56	C24	H24A	0.98
57	C24	H24B	0.98
58	C24	H24C	0.98
59	C34	H34	0.95
60	C34	C37	1.400(4)
61	C34	C41	1.374(4)
62	C38	H38	0.95
63	C38	C37	1.388(4)
64	C38	C39	1.394(4)

65	C37	C42	1.543(4)
66	C40	H40	0.949
67	C40	C41	1.396(4)
68	C40	C39	1.377(5)
69	C41	H41	0.95
70	C39	H39	0.951
71	O6	C42	1.422(3)
72	O6	H6	0.95(4)
73	O7	C50	1.207(3)
74	O8	C49	1.491(3)
75	O8	C50	1.326(3)
76	C49	C54	1.521(4)
77	C49	C53	1.509(4)
78	C49	C52	1.520(4)
79	C43	H43	1
80	C43	C42	1.546(4)
81	C43	C55	1.540(4)
82	C43	B2	1.579(4)
83	C50	C42	1.539(4)
84	C55	H55A	0.981
85	C55	H55B	0.98
86	C55	H55C	0.98
87	C54	H54A	0.98
88	C54	H54B	0.979
89	C54	H54C	0.98

90	C53	H53A	0.98
91	C53	H53B	0.98
92	C53	H53C	0.98
93	C52	H52A	0.98
94	C52	H52B	0.98
95	C52	H52C	0.98
96	O9	B2	1.370(3)
97	O9	C58	1.457(4)
98	O10	B2	1.374(5)
99	O10	C59	1.461(4)
100	C58	C59	1.548(5)
101	C58	C61	1.512(6)
102	C58	C63	1.518(5)
103	C59	C64	1.534(7)
104	C59	C62	1.502(8)
105	C61	H61A	0.98
106	C61	H61B	0.981
107	C61	H61C	0.98
108	C63	H63A	0.98
109	C63	H63B	0.98
110	C63	H63C	0.98
111	C64	H64A	0.98
112	C64	H64B	0.981
113	C64	H64C	0.98
114	C62	H62A	0.98

| 115 | C62 | H62B | 0.981 |
| 116 | C62 | H62C | 0.98 |

Bond angles for 1.60 (º)

Number	Atom1	Atom2	Atom3	Angle
1	C17	O1	B1	106.4(2)
2	C16	O2	B1	106.5(2)
3	C9	O5	C22	121.3(2)
4	C7	O3	H3	110(2)
5	O1	C17	C19	109.5(2)
6	O1	C17	C16	101.9(2)
7	O1	C17	C20	107.0(2)
8	C19	C17	C16	115.1(2)
9	C19	C17	C20	109.9(2)
10	C16	C17	C20	112.8(2)
11	O3	C7	C9	108.4(2)
12	O3	C7	C1	110.0(2)
13	O3	C7	C12	107.6(2)
14	C9	C7	C1	103.8(2)
15	C9	C7	C12	113.9(2)
16	C1	C7	C12	113.0(2)
17	C17	C19	H19A	109.5
18	C17	C19	H19B	109.5
19	C17	C19	H19C	109.5
20	H19A	C19	H19B	109.4
21	H19A	C19	H19C	109.5

22	H19B	C19	H19C	109.5
23	O2	C16	C17	101.8(2)
24	O2	C16	C21	108.7(2)
25	O2	C16	C18	106.5(2)
26	C17	C16	C21	115.1(2)
27	C17	C16	C18	113.0(2)
28	C21	C16	C18	110.9(2)
29	O5	C9	O4	126.2(2)
30	O5	C9	C7	112.0(2)
31	O4	C9	C7	121.7(2)
32	C7	C1	C2	120.2(2)
33	C7	C1	C6	121.7(2)
34	C2	C1	C6	118.0(3)
35	C7	C12	H12	106.6
36	C7	C12	C26	110.6(2)
37	C7	C12	B1	114.1(2)
38	H12	C12	C26	106.5
39	H12	C12	B1	106.6
40	C26	C12	B1	111.9(2)
41	C16	C21	H21A	109.5
42	C16	C21	H21B	109.5
43	C16	C21	H21C	109.5
44	H21A	C21	H21B	109.4
45	H21A	C21	H21C	109.5
46	H21B	C21	H21C	109.5

47	O5	C22	C23	111.3(2)
48	O5	C22	C25	108.0(2)
49	O5	C22	C24	101.5(2)
50	C23	C22	C25	112.9(2)
51	C23	C22	C24	110.9(2)
52	C25	C22	C24	111.6(2)
53	C1	C2	H2	119.6
54	C1	C2	C3	120.9(3)
55	H2	C2	C3	119.5
56	C22	C23	H23A	109.5
57	C22	C23	H23B	109.5
58	C22	C23	H23C	109.4
59	H23A	C23	H23B	109.4
60	H23A	C23	H23C	109.5
61	H23B	C23	H23C	109.5
62	H4	C4	C5	120.4
63	H4	C4	C3	120.4
64	C5	C4	C3	119.2(3)
65	C17	C20	H20A	109.5
66	C17	C20	H20B	109.4
67	C17	C20	H20C	109.4
68	H20A	C20	H20B	109.6
69	H20A	C20	H20C	109.5
70	H20B	C20	H20C	109.4
71	C1	C6	H6A	119.7

72	C1	C6	C5	120.7(3)
73	H6A	C6	C5	119.6
74	C22	C25	H25A	109.4
75	C22	C25	H25B	109.5
76	C22	C25	H25C	109.5
77	H25A	C25	H25B	109.4
78	H25A	C25	H25C	109.5
79	H25B	C25	H25C	109.5
80	C4	C5	C6	120.8(3)
81	C4	C5	H5	119.6
82	C6	C5	H5	119.6
83	C12	C26	H26A	109.4
84	C12	C26	H26B	109.5
85	C12	C26	H26C	109.4
86	H26A	C26	H26B	109.6
87	H26A	C26	H26C	109.5
88	H26B	C26	H26C	109.4
89	C2	C3	C4	120.5(3)
90	C2	C3	H3A	119.8
91	C4	C3	H3A	119.7
92	C16	C18	H18A	109.5
93	C16	C18	H18B	109.5
94	C16	C18	H18C	109.5
95	H18A	C18	H18B	109.5
96	H18A	C18	H18C	109.5

97	H18B	C18	H18C	109.5
98	C22	C24	H24A	109.5
99	C22	C24	H24B	109.5
100	C22	C24	H24C	109.5
101	H24A	C24	H24B	109.5
102	H24A	C24	H24C	109.4
103	H24B	C24	H24C	109.5
104	O1	B1	O2	113.6(2)
105	O1	B1	C12	126.4(2)
106	O2	B1	C12	119.9(2)
107	H34	C34	C37	119.8
108	H34	C34	C41	119.9
109	C37	C34	C41	120.4(2)
110	H38	C38	C37	119.7
111	H38	C38	C39	119.8
112	C37	C38	C39	120.5(3)
113	C34	C37	C38	118.7(2)
114	C34	C37	C42	120.5(2)
115	C38	C37	C42	120.8(2)
116	H40	C40	C41	120.5
117	H40	C40	C39	120.5
118	C41	C40	C39	119.1(3)
119	C34	C41	C40	120.8(3)
120	C34	C41	H41	119.6
121	C40	C41	H41	119.6

122	C38	C39	C40	120.5(3)
123	C38	C39	H39	119.7
124	C40	C39	H39	119.7
125	C42	O6	H6	107(2)
126	C49	O8	C50	121.8(2)
127	O8	C49	C54	109.8(2)
128	O8	C49	C53	109.4(2)
129	O8	C49	C52	101.7(2)
130	C54	C49	C53	112.6(2)
131	C54	C49	C52	111.1(2)
132	C53	C49	C52	111.6(2)
133	H43	C43	C42	107.7
134	H43	C43	C55	107.7
135	H43	C43	B2	107.6
136	C42	C43	C55	111.2(2)
137	C42	C43	B2	109.8(2)
138	C55	C43	B2	112.6(2)
139	O7	C50	O8	126.3(2)
140	O7	C50	C42	121.9(2)
141	O8	C50	C42	111.8(2)
142	C37	C42	O6	110.9(2)
143	C37	C42	C43	111.6(2)
144	C37	C42	C50	107.4(2)
145	O6	C42	C43	106.8(2)
146	O6	C42	C50	107.5(2)

147	C43	C42	C50	112.6(2)
148	C43	C55	H55A	109.5
149	C43	C55	H55B	109.5
150	C43	C55	H55C	109.5
151	H55A	C55	H55B	109.5
152	H55A	C55	H55C	109.5
153	H55B	C55	H55C	109.4
154	C49	C54	H54A	109.4
155	C49	C54	H54B	109.4
156	C49	C54	H54C	109.5
157	H54A	C54	H54B	109.5
158	H54A	C54	H54C	109.5
159	H54B	C54	H54C	109.5
160	C49	C53	H53A	109.5
161	C49	C53	H53B	109.5
162	C49	C53	H53C	109.4
163	H53A	C53	H53B	109.5
164	H53A	C53	H53C	109.5
165	H53B	C53	H53C	109.5
166	C49	C52	H52A	109.5
167	C49	C52	H52B	109.4
168	C49	C52	H52C	109.5
169	H52A	C52	H52B	109.5
170	H52A	C52	H52C	109.5
171	H52B	C52	H52C	109.5

172	B2	O9	C58	108.0(2)
173	B2	O10	C59	107.7(3)
174	C43	B2	O9	122.3(2)
175	C43	B2	O10	125.5(3)
176	O9	B2	O10	112.1(3)
177	O9	C58	C59	102.4(3)
178	O9	C58	C61	106.2(3)
179	O9	C58	C63	109.3(3)
180	C59	C58	C61	113.6(3)
181	C59	C58	C63	114.6(3)
182	C61	C58	C63	110.0(3)
183	O10	C59	C58	102.9(3)
184	O10	C59	C64	105.8(3)
185	O10	C59	C62	110.4(3)
186	C58	C59	C64	112.9(3)
187	C58	C59	C62	115.4(3)
188	C64	C59	C62	109.0(4)
189	C58	C61	H61A	109.5
190	C58	C61	H61B	109.5
191	C58	C61	H61C	109.5
192	H61A	C61	H61B	109.5
193	H61A	C61	H61C	109.4
194	H61B	C61	H61C	109.5
195	C58	C63	H63A	109.4
196	C58	C63	H63B	109.4

197	C58	C63	H63C	109.5
198	H63A	C63	H63B	109.5
199	H63A	C63	H63C	109.5
200	H63B	C63	H63C	109.5
201	C59	C64	H64A	109.5
202	C59	C64	H64B	109.5
203	C59	C64	H64C	109.5
204	H64A	C64	H64B	109.4
205	H64A	C64	H64C	109.5
206	H64B	C64	H64C	109.4
207	C59	C62	H62A	109.5
208	C59	C62	H62B	109.4
209	C59	C62	H62C	109.5
210	H62A	C62	H62B	109.4
211	H62A	C62	H62C	109.5
212	H62B	C62	H62C	109.5

Torsion angles for 1.60 (º)

Number	Atom1	Atom2	Atom3	Atom4	Torsion
1	B1	O1	C17	C19	148.6(2)
2	B1	O1	C17	C16	26.2(2)
3	B1	O1	C17	C20	-92.3(2)
4	C17	O1	B1	O2	-11.8(3)
5	C17	O1	B1	C12	164.7(2)
6	B1	O2	C16	C17	24.6(2)
7	B1	O2	C16	C21	146.6(2)

8	B1	O2	C16	C18	-93.9(2)
9	C16	O2	B1	O1	-9.2(3)
10	C16	O2	B1	C12	174.1(2)
11	C22	O5	C9	O4	0.8(4)
					-
12	C22	O5	C9	C7	175.8(2)
13	C9	O5	C22	C23	-54.3(3)
14	C9	O5	C22	C25	70.1(3)
					-
15	C9	O5	C22	C24	172.4(2)
16	H3	O3	C7	C9	-8(3)
17	H3	O3	C7	C1	105(3)
18	H3	O3	C7	C12	-131(3)
19	O1	C17	C19	H19A	-54.8
20	O1	C17	C19	H19B	-174.8
21	O1	C17	C19	H19C	65.2
22	C16	C17	C19	H19A	59.3
23	C16	C17	C19	H19B	-60.7
24	C16	C17	C19	H19C	179.3
25	C20	C17	C19	H19A	-172.1
26	C20	C17	C19	H19B	68
27	C20	C17	C19	H19C	-52.1
28	O1	C17	C16	O2	-30.5(2)
					-
29	O1	C17	C16	C21	147.9(2)

30	O1	C17	C16	C18	83.2(2)
					-
31	C19	C17	C16	O2	149.0(2)
32	C19	C17	C16	C21	93.6(3)
33	C19	C17	C16	C18	-35.2(3)
34	C20	C17	C16	O2	83.8(2)
35	C20	C17	C16	C21	-33.6(3)
					-
36	C20	C17	C16	C18	162.4(2)
37	O1	C17	C20	H20A	-62.9
38	O1	C17	C20	H20B	177
39	O1	C17	C20	H20C	57.1
40	C19	C17	C20	H20A	55.9
41	C19	C17	C20	H20B	-64.2
42	C19	C17	C20	H20C	175.9
43	C16	C17	C20	H20A	-174.2
44	C16	C17	C20	H20B	65.7
45	C16	C17	C20	H20C	-54.2
					-
46	O3	C7	C9	O5	158.0(2)
47	O3	C7	C9	O4	25.3(3)
48	C1	C7	C9	O5	85.1(3)
49	C1	C7	C9	O4	-91.7(3)
50	C12	C7	C9	O5	-38.2(3)
51	C12	C7	C9	O4	145.0(3)

52	O3	C7	C1	C2	-18.7(3)
53	O3	C7	C1	C6	164.7(2)
54	C9	C7	C1	C2	97.1(3)
55	C9	C7	C1	C6	-79.5(3)
					-
56	C12	C7	C1	C2	139.0(3)
57	C12	C7	C1	C6	44.4(3)
58	O3	C7	C12	H12	-174.2
59	O3	C7	C12	C26	-58.8(3)
60	O3	C7	C12	B1	68.4(3)
61	C9	C7	C12	H12	65.6
					-
62	C9	C7	C12	C26	179.0(2)
63	C9	C7	C12	B1	-51.8(3)
64	C1	C7	C12	H12	-52.5
65	C1	C7	C12	C26	62.9(3)
					-
66	C1	C7	C12	B1	169.9(2)
67	O2	C16	C21	H21A	-50.1
68	O2	C16	C21	H21B	-170
69	O2	C16	C21	H21C	70
70	C17	C16	C21	H21A	63.4
71	C17	C16	C21	H21B	-56.6
72	C17	C16	C21	H21C	-176.6
73	C18	C16	C21	H21A	-166.8

74	C18	C16	C21	H21B	73.3
75	C18	C16	C21	H21C	-46.8
76	O2	C16	C18	H18A	-53.2
77	O2	C16	C18	H18B	-173.2
78	O2	C16	C18	H18C	66.8
79	C17	C16	C18	H18A	-164.1
80	C17	C16	C18	H18B	75.9
81	C17	C16	C18	H18C	-44.1
82	C21	C16	C18	H18A	65
83	C21	C16	C18	H18B	-55
84	C21	C16	C18	H18C	-175
85	C7	C1	C2	H2	3.5
86	C7	C1	C2	C3	-176.5(2)
87	C6	C1	C2	H2	-179.7
88	C6	C1	C2	C3	0.3(4)
89	C7	C1	C6	H6A	-3.5
90	C7	C1	C6	C5	176.5(3)
91	C2	C1	C6	H6A	179.8
92	C2	C1	C6	C5	-0.2(4)
93	C7	C12	C26	H26A	-61.4
94	C7	C12	C26	H26B	178.5
95	C7	C12	C26	H26C	58.6
96	H12	C12	C26	H26A	54
97	H12	C12	C26	H26B	-66.1

98	H12	C12	C26	H26C	174
99	B1	C12	C26	H26A	170.2
100	B1	C12	C26	H26B	50.1
101	B1	C12	C26	H26C	-69.8
102	C7	C12	B1	O1	22.0(4)
103	C7	C12	B1	O2	-161.7(2)
104	H12	C12	B1	O1	-95.3
105	H12	C12	B1	O2	81
106	C26	C12	B1	O1	148.5(3)
107	C26	C12	B1	O2	-35.1(3)
108	O5	C22	C23	H23A	-38.4
109	O5	C22	C23	H23B	-158.4
110	O5	C22	C23	H23C	81.5
111	C25	C22	C23	H23A	-160.1
112	C25	C22	C23	H23B	79.9
113	C25	C22	C23	H23C	-40.1
114	C24	C22	C23	H23A	73.8
115	C24	C22	C23	H23B	-46.2
116	C24	C22	C23	H23C	-166.2
117	O5	C22	C25	H25A	-64.6
118	O5	C22	C25	H25B	175.5
119	O5	C22	C25	H25C	55.4
120	C23	C22	C25	H25A	58.9
121	C23	C22	C25	H25B	-61.1

122	C23	C22	C25	H25C	178.9
123	C24	C22	C25	H25A	-175.4
124	C24	C22	C25	H25B	64.7
125	C24	C22	C25	H25C	-55.3
126	O5	C22	C24	H24A	-55.9
127	O5	C22	C24	H24B	-175.9
128	O5	C22	C24	H24C	64.1
129	C23	C22	C24	H24A	-174.2
130	C23	C22	C24	H24B	65.8
131	C23	C22	C24	H24C	-54.2
132	C25	C22	C24	H24A	59
133	C25	C22	C24	H24B	-61
134	C25	C22	C24	H24C	179
135	C1	C2	C3	C4	-0.1(4)
136	C1	C2	C3	H3A	179.9
137	H2	C2	C3	C4	179.9
138	H2	C2	C3	H3A	-0.1
139	H4	C4	C5	C6	-179.8
140	H4	C4	C5	H5	0.2
141	C3	C4	C5	C6	0.1(4)
142	C3	C4	C5	H5	-179.9
143	H4	C4	C3	C2	179.9
144	H4	C4	C3	H3A	-0.1
145	C5	C4	C3	C2	-0.1(4)
146	C5	C4	C3	H3A	179.9

147	C1	C6	C5	C4	0.1(4)
148	C1	C6	C5	H5	-180
149	H6A	C6	C5	C4	180
150	H6A	C6	C5	H5	0
151	H34	C34	C37	C38	-178.6
152	H34	C34	C37	C42	2.6
153	C41	C34	C37	C38	1.5(4)
154	C41	C34	C37	C42	-177.4(2)
155	H34	C34	C41	C40	179.3
156	H34	C34	C41	H41	-0.8
157	C37	C34	C41	C40	-0.7(4)
158	C37	C34	C41	H41	179.2
159	H38	C38	C37	C34	178.8
160	H38	C38	C37	C42	-2.3
161	C39	C38	C37	C34	-1.2(4)
162	C39	C38	C37	C42	177.7(3)
163	H38	C38	C39	C40	-179.8
164	H38	C38	C39	H39	0.2
165	C37	C38	C39	C40	0.2(4)
166	C37	C38	C39	H39	-179.8
167	C34	C37	C42	O6	175.4(2)
168	C34	C37	C42	C43	56.4(3)
169	C34	C37	C42	C50	-67.4(3)
170	C38	C37	C42	O6	-3.4(3)

171	C38	C37	C42	C43	122.4(3)
172	C38	C37	C42	C50	113.7(3)
173	H40	C40	C41	C34	179.7
174	H40	C40	C41	H41	-0.2
175	C39	C40	C41	C34	-0.3(4)
176	C39	C40	C41	H41	179.8
177	H40	C40	C39	C38	-179.5
178	H40	C40	C39	H39	0.6
179	C41	C40	C39	C38	0.5(4)
180	C41	C40	C39	H39	-179.4
181	H6	O6	C42	C37	96(2)
182	H6	O6	C42	C43	-142(2)
183	H6	O6	C42	C50	-21(2)
184	C50	O8	C49	C54	63.5(3)
185	C50	O8	C49	C53	-60.6(3)
					-
186	C50	O8	C49	C52	178.7(2)
187	C49	O8	C50	O7	-2.7(4)
188	C49	O8	C50	C42	178.9(2)
189	O8	C49	C54	H54A	-68.1
190	O8	C49	C54	H54B	172
191	O8	C49	C54	H54C	51.9
192	C53	C49	C54	H54A	54.2
193	C53	C49	C54	H54B	-65.8

194	C53	C49	C54	H54C	174.1
195	C52	C49	C54	H54A	-179.8
196	C52	C49	C54	H54B	60.3
197	C52	C49	C54	H54C	-59.8
198	O8	C49	C53	H53A	-54.1
199	O8	C49	C53	H53B	-174.2
200	O8	C49	C53	H53C	65.9
201	C54	C49	C53	H53A	-176.6
202	C54	C49	C53	H53B	63.4
203	C54	C49	C53	H53C	-56.5
204	C52	C49	C53	H53A	57.6
205	C52	C49	C53	H53B	-62.4
206	C52	C49	C53	H53C	177.7
207	O8	C49	C52	H52A	-59.5
208	O8	C49	C52	H52B	-179.4
209	O8	C49	C52	H52C	60.6
210	C54	C49	C52	H52A	57.3
211	C54	C49	C52	H52B	-62.6
212	C54	C49	C52	H52C	177.4
213	C53	C49	C52	H52A	-176
214	C53	C49	C52	H52B	64
215	C53	C49	C52	H52C	-56
216	H43	C43	C42	C37	-62.3
217	H43	C43	C42	O6	176.3
218	H43	C43	C42	C50	58.6

219	C55	C43	C42	C37	55.5(3)
220	C55	C43	C42	O6	-65.9(3)
221	C55	C43	C42	C50	176.4(2) -
222	B2	C43	C42	C37	179.2(2)
223	B2	C43	C42	O6	59.4(3)
224	B2	C43	C42	C50	-58.3(3)
225	H43	C43	C55	H55A	53.9
226	H43	C43	C55	H55B	-66.1
227	H43	C43	C55	H55C	173.9
228	C42	C43	C55	H55A	-63.9
229	C42	C43	C55	H55B	176
230	C42	C43	C55	H55C	56.1
231	B2	C43	C55	H55A	172.3
232	B2	C43	C55	H55B	52.3
233	B2	C43	C55	H55C	-67.6
234	H43	C43	B2	O9	-46.8
235	H43	C43	B2	O10	130.7
236	C42	C43	B2	O9	70.2(3) -
237	C42	C43	B2	O10	112.3(3) -
238	C55	C43	B2	O9	165.3(3)
239	C55	C43	B2	O10	12.2(4)

#					Value
					-
240	O7	C50	C42	C37	101.7(3)
241	O7	C50	C42	O6	17.7(3)
242	O7	C50	C42	C43	135.0(3)
243	O8	C50	C42	C37	76.8(3)
					-
244	O8	C50	C42	O6	163.8(2)
245	O8	C50	C42	C43	-46.5(3)
					-
246	C58	O9	B2	C43	171.0(3)
247	C58	O9	B2	O10	11.2(3)
248	B2	O9	C58	C59	-22.8(3)
249	B2	O9	C58	C61	96.6(3)
					-
250	B2	O9	C58	C63	144.8(3)
251	C59	O10	B2	C43	-171.1(3)
252	C59	O10	B2	O9	6.6(4)
253	B2	O10	C59	C58	-20.2(3)
254	B2	O10	C59	C64	98.4(4)
					-
255	B2	O10	C59	C62	143.8(3)
256	O9	C58	C59	O10	25.7(3)
257	O9	C58	C59	C64	-87.8(4)
258	O9	C58	C59	C62	146.0(3)
259	C61	C58	C59	O10	-88.3(4)

260	C61	C58	C59	C64	158.1(4)
261	C61	C58	C59	C62	31.9(5)
262	C63	C58	C59	O10	144.0(3)
263	C63	C58	C59	C64	30.4(5)
264	C63	C58	C59	C62	-95.8(4)
265	O9	C58	C61	H61A	-61.1
266	O9	C58	C61	H61B	178.8
267	O9	C58	C61	H61C	58.8
268	C59	C58	C61	H61A	50.6
269	C59	C58	C61	H61B	-69.4
270	C59	C58	C61	H61C	170.6
271	C63	C58	C61	H61A	-179.3
272	C63	C58	C61	H61B	60.7
273	C63	C58	C61	H61C	-59.4
274	O9	C58	C63	H63A	-66.6
275	O9	C58	C63	H63B	173.4
276	O9	C58	C63	H63C	53.3
277	C59	C58	C63	H63A	179.1
278	C59	C58	C63	H63B	59.1
279	C59	C58	C63	H63C	-60.9
280	C61	C58	C63	H63A	49.6
281	C61	C58	C63	H63B	-70.4
282	C61	C58	C63	H63C	169.5
283	O10	C59	C64	H64A	-69.3
284	O10	C59	C64	H64B	170.8

285	O10	C59	C64	H64C	50.8
286	C58	C59	C64	H64A	42.5
287	C58	C59	C64	H64B	-77.5
288	C58	C59	C64	H64C	162.6
289	C62	C59	C64	H64A	172
290	C62	C59	C64	H64B	52
291	C62	C59	C64	H64C	-67.9
292	O10	C59	C62	H62A	-67.7
293	O10	C59	C62	H62B	172.4
294	O10	C59	C62	H62C	52.4
295	C58	C59	C62	H62A	176.2
296	C58	C59	C62	H62B	56.3
297	C58	C59	C62	H62C	-63.7
298	C64	C59	C62	H62A	48.1
299	C64	C59	C62	H62B	-71.8
300	C64	C59	C62	H62C	168.1

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Chapter 2 Stereoselective 3-Component Bis-Electrophile Couplings of 1,1-Diborylmethane[1]

2.1 Introduction

The development of efficient methodologies that quickly and selectively build up complexity within a molecular scaffold is critical for the synthesis of existing pharmaceuticals and potential new bioactive molecules. This is best accomplished using methods that simultaneously generate new carbon-carbon bonds, which make up the backbone of organic molecules, introduce new functional groups that can serve as handles for further functionalization, and install stereocenters in high selectivity resulting in single enantiomer products. Tandem reactions have the potential to incorporate each of these desirable reaction features into a single transformation. In a tandem reaction, initial reactivity between two reaction components generates a new molecule, with inherently different reactivity than the starting materials, which can then participate in further reactions.[1–4] This type of reaction is attractive for use with 1,1-diboronate ester reagents as they have two different modes of reactivity that could be selectively employed at different points of a reaction sequence. This would allow for the formation of a new carbon-carbon bond, installation of a boronate ester as a functional group, and generation of at least one new stereocenter.

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[1] A portion of this work appeared as a communication in the *Journal of the American Chemical Society*. The full reference is as follows: Murray, S. A.; Liang, M. Z.; Meek, S. J. *J. Am. Chem. Soc.* **2017**, *139*, 14061-14064.
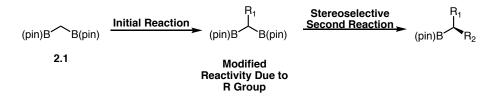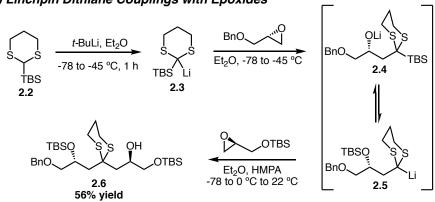
Figure 2.1 General concept for proposed tandem reaction

2.2 Background

2.2.1 Previous work
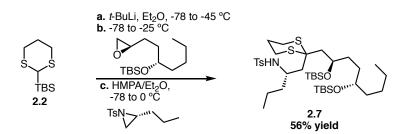
Tandem methodologies which set a new carbon-carbon bond and incorporate new functionality have been widely developed.[1–5] A subsection of this methodology that is even more attractive are methodologies that construct two carbon-carbon bonds at the same carbon center through a single synthetic operation.[6–19] A prototypical example is dithiane anion relay chemistry pioneered by Smith and coworkers. In this work, a dithiane unit can serve as a bis-carbanion surrogate which allows two electrophiles to be coupled at the same carbon center (**Figure 2.2**).[7–10,16–19] While this linchpin methodology is efficient for bond formation, as it generates two new carbon-carbon bonds in a single step, it typically does not introduce new stereocenters into the molecule. Other examples of dianion relay chemistry have been developed by Schaumann and coworkers and Utimoto and coworkers, which utilize silicon-induced multicomponent processes for the synthesis of cyclopentanols[6] and dihalomethylene units in biselectrophile coupling reactions, respectively.[11]

Dual cation/anion methodologies also exist. For example, Johnson and co-workers employ silyl glyoxylates for multicomponent reactions.[12–15] In this approach, the silylglyoxylate reacts first as an electrophile through addition to the carbonyl. This then generates a tetrahedral intermediate poised to undergo a Brook rearrangement and produce a carbanion at the previously electrophilic carbon (**2.14** to **2.15** in Figure 2.2). This carbanion then acts as a nucleophile and reacts with electrophiles such as carbonyls to complete the tandem process. This ultimately generates two new carbon-carbon bonds at the same carbon center and

generates a new stereocenter in the process which is controlled by the chair-like transition states invoked in the second carbon-carbon bond forming event.

(a) Linchpin Dithiane Couplings with Epoxides

(b) Linchpin Dithiane Couplings with Epoxides & Aziridines

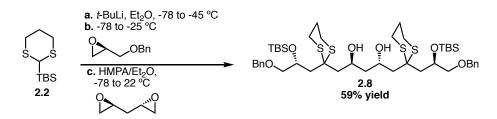**(c) Iterative Couplings for Total Synthesis**

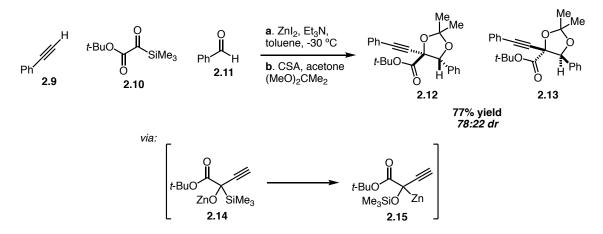**Figure 2.2** Examples of dithiane anion relay chemistry

Figure 2.3 Silyl glyoxylates in multicomponent reactions

2.2.2 Reaction design

There are two different approaches to activating 1,1-diborylakanes: Lewis base activation and deprotonation. For Lewis base activation, a nucleophilic base adds into an empty p-orbital generating a negatively charged borate (left side of **Figure 2.4**). Some examples of bases typically used for boron activation include potassium hydroxide, lithium *tert*-butoxide, *n*-butyl lithium, and cesium fluoride. As the C-B bond of the activated boron unit is polarized towards carbon it can react as a nucleophile and results in loss of the boron-alkoxy group (a net deborylative pathway).

The second method utilizes the increased acidity of the methylene protons of the *gem*-diborylalkane which are markedly more acidic (pKa ~30)[20,21] than those on an all carbon alkyl chain (right side of **Figure 2.4**). This allows for deprotonation of the methylene position followed by addition to an electrophile. In theory, these two modes of reactivity could be employed sequentially in a controlled manner, resulting in the formation of two different carbon-carbon bonds at the same carbon center, thus making 1,1-diborylmethane a dianionic synthon.

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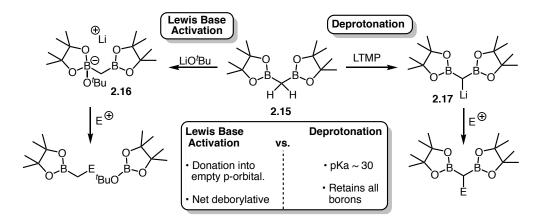
Figure 2.4 Modes of activation of 1,1-diborylalkanes

Epoxides are an attractive electrophile class for this reaction for a variety of reasons. First, epoxides are known to undergo ring opening when treated with organometallic reagents[22–24] such as organolithiums,[25–28] organoborons,[29] organocoppers,[30,31] and Grignard reagents.[32] While some reactivity has also been shown between epoxides and diborylmethane in a deborylative process, this method has many limitations including a very specific substrate scope and selectivity issues.[33]

In the proposed reaction, diborylmethane will be deprotonated with LTMP and the resulting boron stabilized carbanion will be used to open an epoxide (**Figure 2.5**). After the lithiated diboron reagent opens the epoxide, an alkoxide is generated at the 3-position relative to the new carbon-carbon bond that was formed (**A** in **Figure 2.5**). As previously mentioned, the second mode of reactivity of 1,1-diboronate esters is activation of a boryl group through coordination of an alkoxide or hydroxide base to the empty p-orbital on the boron generating a negatively charged borate species. The newly generated alkoxide can intramolecularly activate one of the boronate esters to form the chelated borate intermediate (**B** in **Figure 2.5**). This borate is then nucleophilic at carbon and can directly add to an electrophile or transmetallate to a transition metal catalyst.
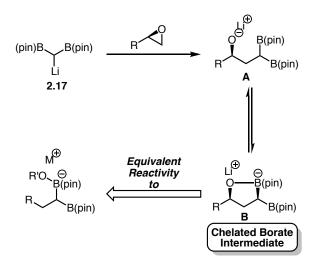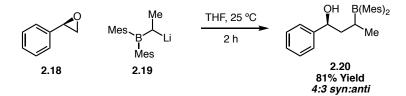
Figure 2.5 Proposed epoxide opening utilizing deprotonated diborylmethane

Precedent for using boron stabilized carbanions to open epoxides can be found in the

work of Pelter and coworkers. As illustrated in **Scheme 2.1**, styrene oxide was efficiently

opened by the boron stabilized carbanion **2.19** to give the 1,3-hydroxy boron compound **2.20** in

81% yield and 4:3 *syn:anti* selectivity as determined by oxidation to the corresponding diol.[29]

This illustrates that boron stabilized carbanions are sufficient nucleophiles for opening epoxides

and therefore that deprotonated diborylmethane should be able to participate in a similar

reaction.

Scheme 2.1 Styrene oxide ring opening with boron stabilized carbanions

Lewis base activation of boronate esters typically occurs through an intermolecular

interaction between the p-orbital on the boron and an external base such as lithium *tert*-

butoxide or potassium hydroxide like what is seen in a Suzuki-Miyaura cross-coupling reaction[34]

or our group's 1,2-addition chemistry with aldehydes[35] and ketoesters[36]. The need for an

external strong base is often a limitation for this chemistry as any substrate used in the reaction

must be tolerant of it. This typically limits substrates to those without enolizable protons or base

labile functional groups. There are also examples of intramolecular activation of boryl moieties as nucleophiles in which an amide serves as the activating group.[37–39] Since the activation will occur through an intramolecular process, this methodology will not have the same limitations present in processes that require stoichiometric strong base.

In addition to facilitating the second carbon-carbon bond forming event, the five membered chelate intermediate (**B** in **Figure 2.5**) formed through the opening of the epoxide has the potential to control stereochemistry in the second step and lead to a diastereoselective process. Stereodefined epoxides are readily available substrates that are easily made through stereoselective oxidation of alkenes[40–43] or resolution of racemic epoxides.[44] Using an enantioenriched epoxide for the ring opening step could theoretically lead to the formation of two diastereomers of the chelated intermediate (**A** and **B** in **Figure 2.6**). By developing reaction conditions that either preferentially formed one diastereomer (selective synthesis of A or B) over the other or that allowed for interconversion between them (equilibrium between A and B) with one preferentially reacting to give product over the other, a highly diastereoselective reaction could be achieved. The identity of the diastereomer of the product that is formed would be dependent on both the reactive chelate intermediate and the reaction pathway followed (invertive or retentive). Additionally, if the mechanism of the second reaction (inversion vs retention) could be controlled, potentially through changing the metal catalyst or reaction conditions,[45] then all potential stereoisomers of the product could easily be obtained which is highly desirable for the synthesis of potentially bioactive molecules.
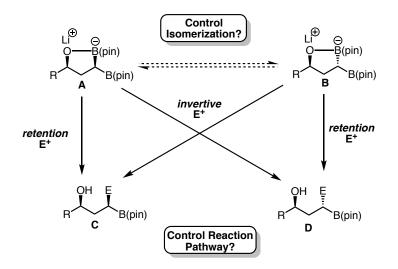
Figure 2.6 Potential reaction pathways to yield product from chelated intermediate

2.3 Allylation of chelated borates derived from ring opening of epoxides by diborylmethane[46]

In order to make use of this potential tandem bis-electrophile coupling reaction, an appropriate secondary reaction must be chosen to pair with the ring opening step. In theory, this reaction can be any of the well-studied, boron-based functionalizations that proceeds via an activated borate intermediate such as allylation, cross-coupling, or 1,2-addition. A reaction sequence consisting of an epoxide ring opening step followed by an allylation reaction was explored first. The goal was to establish a procedure for effectively opening the epoxide with the lithiated diborylmethane as well as conditions for an *in situ* allylation of the resulting chelated borate intermediate.

2.3.1 Reaction development

The initial reaction being studied is illustrated in **Table 2.1**. Treatment of 1,1-diborylmethane with LTMP at 0 °C for 10 minutes results in the formation of the lithiated intermediate **2.17**. This is the same procedure as is used in the formation of the substituted diboron reagents outlined in Chapter 1. After 10 minutes at 0 °C, styrene oxide (**2.18**) was added and the reaction was allowed to stir at 22 °C for fifteen minutes. The solution of the ring opened intermediate was then treated with copper chloride and allyl chloride and allowed to stir at 22 °C for 24 hours (**Table 2.1, Entry 1**). This reaction gave 52% conversion to product **2.21**

and 3:1 d.r. favoring the *anti*-product as illustrated in **Table 2.1, Entry 1**. This was a promising first result as it illustrated that the epoxide can in fact be opened by the carbanion of diborylmethane and that the chelated intermediate is reactive towards copper catalyzed allylation. Increasing the temperature to 45 °C did not result in an increase in conversion to product and produced a lower dr of 2:1 (**Table 2.1, Entry 2**). While the decrease in diastereoselectivity was not desired, the change in the dr did indicate that there was potential to control the diastereoselectivity of the reaction by tuning the reaction conditions. Further heating the reaction to 60 °C increased the conversion to product slightly to 58% and did not affect the dr (**Table 2.1, entry 3**).

In an attempt to increase the conversion and diastereoselectivity of the reaction, the identity of the allyl coupling partner was explored. The use of an allyl phosphate was tolerated in the reaction and gave 45% conversion to product, however the diastereoselectivity further decreased from the allyl chloride result giving a 1:1 mixture of diastereomers (**Table 2.1, Entry 4).** Allyl acetate was completely inactive in the reaction (**Table 2.1, Entry 5**). With allyl bromide as the allylating reagent, the product was formed in 77% conversion to product and 8:1 dr (**Table 2.1, Entry 6**).

With the optimal allylation reagent in hand, the optimization of the catalyst was undertaken. Copper (I) acetate resulted in a slight increase in diastereoselectivity to 10:1 however, a more substantial decrease in conversion to 57% (**Table 2.1, Entry 7**). A similar decrease in yield was observed for copper (I) bromide (8:1 d.r. and 55% conversion) and copper (I) iodide (9:1 d.r. and 62% conversion) (**Table 2.1, Entries 8 & 9**).

Table 2.1 Tandem epoxide opening and allylation optimization studies

entry	X	Cu salt	temp (ºC)	conv. (%)[a]	dr[b]
1	Cl	CuCl	22	52	3:1
2	Cl	CuCl	45	58	2:1
3	Cl	CuCl	60	45	2:1
4	OP(OEt)$_3$	CuCl	60	45	1:1
5	OAc	CuCl	60	<2	-
6	Br	CuCl	60	77	8:1
7	Br	CuOAc	60	57	10:1
8	Br	CuBr.dms	60	55	8:1
9	Br	CuI	60	62	9:1

Reactions performed under N$_2$ atm. [a] Conversion to **2.19**; values determined by analysis of 400, 500 or 600 MHZ ^{1}H NMR spectra of unpurified mixtures with DMF as internal standard. [b] dr determined by oxidation to the corresponding diol and analysis of ^{1}H NMR spectra

The effect of a ligand on the conversion and diastereoselectivity of the reaction was explored next and is illustrated in **Figure 2.7**. While the use of BINAP as a ligand led to the desired product, other bidentate ligands such as Xantphos, dppb, and bdpp shut down reactivity. Interestingly, while the conversion is comparable between *rac*-BINAP and *R*-BINAP, a significant difference in diastereoselectivity was observed between the racemic and enantioenriched forms of the ligand. This suggests that there could be an important matched/mismatched relationship between the chiral intermediates generated in this reaction and the chirality on the ligand. While monodentate phosphines such as *R*-Monophos, triphenylphosphine, and tricyclohexylphosphine yielded product in decent to good yield, the diastereoselectivity decreased with all of these ligands to either 2:1 or 3:1. Lastly, NHC ligands were found to give both decreased yield and selectivity. Since better conditions were not

achieved by changing the catalyst, the conditions in entry 6 of **Table 2.1** that resulted in 77%

conversion and 8:1 d.r. favoring the *anti*-product were deemed the best conditions and further
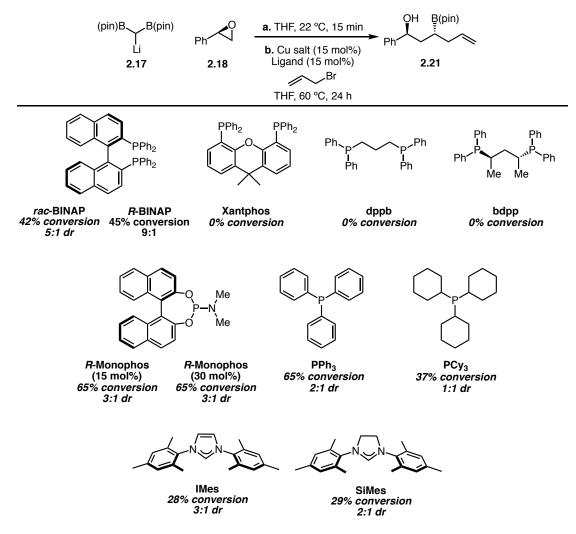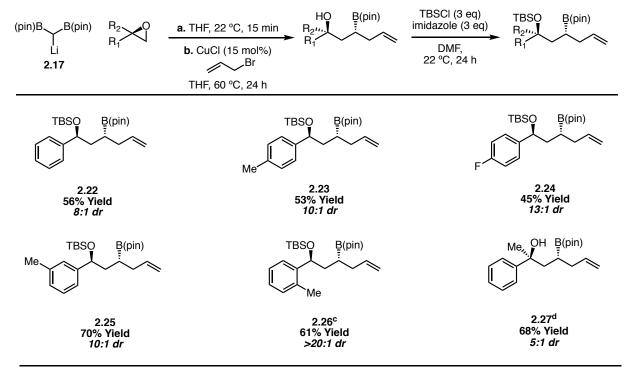
optimization was not undertaken.

a. THF, 22 ºC, 15 min

b. Cu salt (15 mol%)
Ligand (15 mol%)

THF, 60 ºC, 24 h

2.17 **2.18** **2.21**

rac-BINAP
42% conversion
5:1 dr

R-BINAP
45% conversion
9:1

Xantphos
0% conversion

dppb
0% conversion

bdpp
0% conversion

R-Monophos
(15 mol%)
65% conversion
3:1 dr

R-Monophos
(30 mol%)
65% conversion
3:1 dr

PPh₃
65% conversion
2:1 dr

PCy₃
37% conversion
1:1 dr

IMes
28% conversion
3:1 dr

SiMes
29% conversion
2:1 dr

Figure 2.7 Ligand optimization

2.3.2 Substrate scope

Having determined the optimized conditions for this reaction, the scope of the reaction

was explored, first with respect to the epoxide. For ease of purification, the crude reaction

material was subjected to silyl ether protection conditions to yield the resulting OTBS-B(pin)

derivatives which were isolated via silica gel chromatography. A series of aryl epoxides was tried

first (**Figure 2.8**). Substitution at the ortho (**2.26**), meta (**2.25**) and para positions (**2.23** −

2.24) of the ring were all tolerated. While a slight decrease in yield was observed for the para substituted epoxides (**2.23** and **2.24**) an increase in diastereoselectivity was observed at 10:1 and 13:1 respectively. Meta and ortho methyl substituted styrene oxide substrates both gave good yield and diastereoselectivity to the desired products. Di-substituted product **2.27**, derived from α-methyl styrene oxide, was also tolerated in moderate yield, albeit lower diastereoselectivity, likely due the larger methyl group (relative to hydrogen) allowing for less differentiation than can occur when R₂ is H. β-methylstyrene derived epoxide was also explored in this reaction, however this substrate resulted a low yield of a mixture of products with ring opening occurring at both the terminal and internal positions.
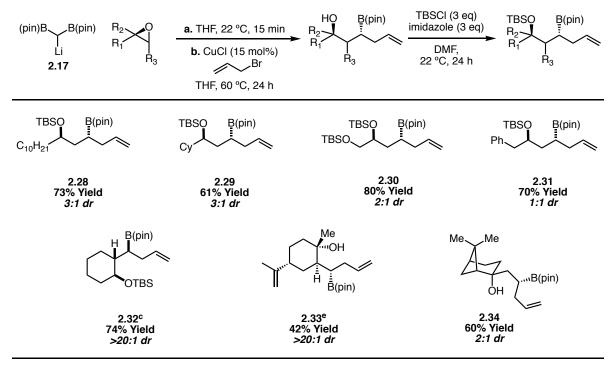
^a Reactions performed under N₂ atm. ^bYield represents isolated yield of purified material and is an average of two experiments. ^cEpoxide opening : 22 °C for 24 h. ^d Isolated as diol after oxidation.

Figure 2.8 Substrate scope - aryl epoxides

One of the benefits of this reaction over previous 1,1-diboronate ester chemistry is the lack of stoichiometric strong alkoxide base in the reaction. In previous work, the presence of external alkoxide base has limited the substrates to aryl and other non-enolizable groups, such as cinnamyl. Since the activation of the diboron reagent in this methodology occurs through an

internal chelate and no strong base (after initial deprotonation of diborylmethane during which the epoxide is not present) is necessary for the reaction to proceed, a wider array of substrates was available for this transformation. Terminal alkyl epoxides (compounds **2.28 − 2.31**) were tolerated in the reaction giving high yields however, slightly diminished diastereoselectivity was observed. This decrease in diastereoselectivity was expected based on the origin of stereocontrol in the reaction. The diastereoselectivity of this reaction is under complete substrate control. The observed selectivity is based on the steric interactions at play in the chelated intermediate and how it proceeds through the allylation step. Because of this, it is reasonable that the smaller alkyl substituted epoxides would give a lower level of diastereoselectivity than the larger, aryl substituted substrates. Simple alkyl substituents such as dodecyl (**2.28**) and cyclohexyl (**2.29**) both gave good yield however low diastereoselectivity. An epoxide containing a silyl protected alcohol yielded product in 80% yield and 3:1 diastereoselectivity (**2.30**).

Cyclohexeneoxide (**2.32**) was the best alkyl derived substrate giving 74% yield as a single diastereomer. The rigid cyclic conformation of the ring likely contributed to the high level of diastereoselectivity observed with this substrate. High diastereoselectivity was found with limonene oxide however the product was only obtained in 42% yield (**2.33**). This is probably partially due to the fact that limonene oxide is sold as a mixture of isomers and one likely reacts faster than the other. Finally, β-pinene (**2.34**) derived epoxide gave a modest 60% yield and only 2:1 dr.
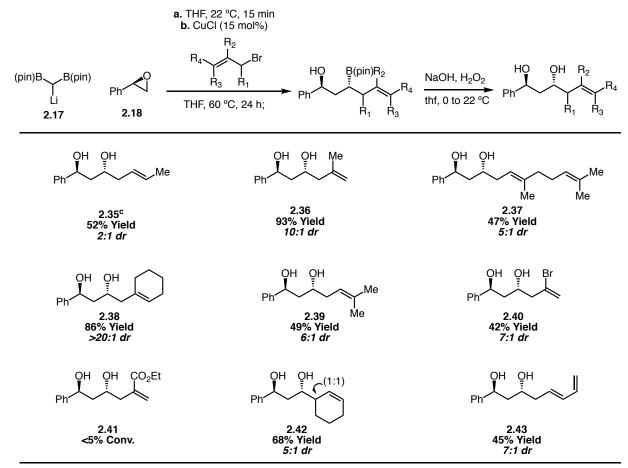
a Reactions performed under N_2 atm. bYield represents isolated yield of purified material and is an average of two experiments. cEpoxide opening : 22 °C for 24 h. dIsolated yield of diol after H_2O_2/NaOH oxidation. eEpoxide opening 45 °C for 24 h.

Figure 2.9 Substrate scope - alkyl epoxides

The scope of the allyl bromide was then explored and is illustrated in **Figure 2.10**. It was observed through this study that the diastereoselectivity was also dependent on the allyl bromide used. Terminal substituted crotyl bromide yielded product **2.35** in modest yield and low diastereoselectivity. The decreased efficiency and selectivity of this reaction is most likely due to competing S_N2 and S_N2' mechanisms which yield different products (both of which were observed). Allyl bromides substituted at the 2-position (**2.36** and **2.40**) gave good to excellent yield and high diastereoselectivity. The same product is achieved when these allyl bromides react through an S_N2 or S_N2' mechanism which most likely helps increase the yield and selectivity. Terminally substituted geranyl and prenyl bromides yielded products **2.37** and **2.39** in moderate yield and diastereoselectivity. The highest selectivity was observed with the internal cyclohexene derived bromide which gave **2.38** in 86% yield as a single diastereomer. Repositioning the olefin one carbon over inside the cyclohexene ring yielded product **2.42** in good yield and moderate dr. Surprisingly, the ester substituted allyl bromide was not a viable

substrate for this reaction and no conversion to **2.41** was observed. Compound **2.43** which is derived from the corresponding bromodiene is obtained in 45% yield and 7:1 dr.
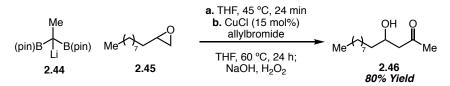
Figure 2.10 Substrate scope - allyl bromides

The last component of this reaction that can be changed to expand the scope of possible products is the diboron reagent. Substituted diboron reagents can be made simply by deprotonating diborylmethane with LTMP and quenching the resulting carbanion with the desired alkyl bromide or iodide.[21,47] Following this protocol, diborylethane **2.42** can be easily synthesized by treatment of the diborylmethane derived carbanion with iodomethane.[20]

The reactivity of diborylethane towards ring opening and allylation was then explored. Dodecene oxide was treated with **2.44** at 45 °C for 24 h followed by addition of allylbromide and copper chloride and an increase in temperature to 60 °C. After 24 hours, the crude reaction

mixture was subjected to hydrogen peroxide oxidation conditions which would result in the diol product if the reaction was successful. As shown in **Scheme 2.2**, β-hydroxyketone **2.46** was obtained instead of the desired diol. This product is the result of the efficient ring opening of the epoxide however a failed allylation step. The ketone is generated when the ring opened diboryl intermediate does not react further with the copper and allylbromide but is stable enough to survive the reaction conditions and then undergo oxidation upon the addition of hydrogen peroxide and sodium hydroxide.

Scheme 2.2 Application of diborylethane in tandem epoxide opening and allylation reaciton

2.3.3 Mechanistic studies

Mechanistic studies were performed by following the progress of the reaction using NMR spectroscopy. Following the normal reaction conditions, diborylmethane was treated with LTMP at 0 °C in deuterated THF. After stirring at 0 °C for 10 minutes, styrene oxide was added and the reaction mixture was transferred to an NMR tube under N_2. The NMR spectra presented in **Figure 2.11** was obtained 10 minutes after addition of the epoxide to the deprotonated diborylmethane (in this time the reaction went from being a heterogeneous mixture to a homogeneous solution). The styrene oxide was completely consumed and the conversion to the chelated species was 73% as determined by comparison to an internal standard. As is shown in **Figure 2.11** and **Figure 2.12**, the dr between the chelated intermediates (labeled **2.47** and **2.48** in **Figure 2.11**) is 56:44.
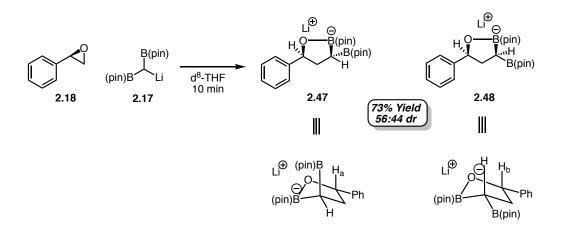
Figure 2.11 NMR reaction of styrene oxide with deprotonated diborylmethane.
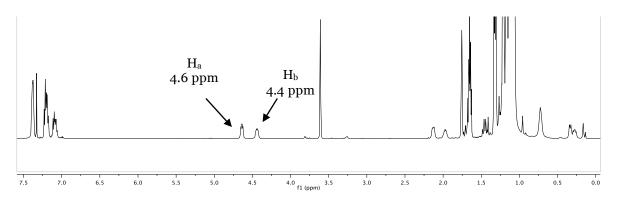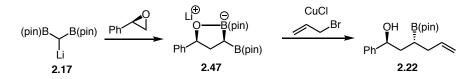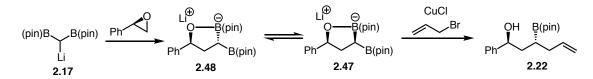

Figure 2.12 NMR spectrum of the reaction shown in **Figure 2.11**

As illustrated in **Figure 2.11**, this chelated intermediate can take on two different diastereomeric forms depending on which boron forms the chelate with the alkoxy group. In theory, the observed high diastereoselectivity of this reaction can result from one of three reaction pathways. In the first path, one of the two diastereomers of the chelated intermediate will be formed selectively over the other and will react to give a single diastereomer of the product. Since both of the diastereomers are formed, as is seen in the NMR experiment, this is not a viable explanation for the high diastereoselectivity.
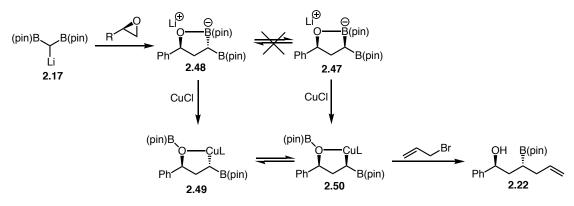
Figure 2.13 Possible mechanistic pathways to achieve high diastereoselectivity

In the second path, both diastereomers are formed but only one of them is reactive to

give the desired product. Due to the high yield observed in many of the examples in the

substrate scope, in order for this to be the case there would also need to be a pathway for

interconversion between the two chelated intermediates. This interconversion would allow for

the high yield and diastereoselectivity to be achieved. It was theorized that interconversion

between the intermediates could be possible at the elevated temperature (60 °C) that the

reaction is conducted at. This was tested by heating the reaction to 60 °C in the NMR

spectrometer. The ratio did not change upon heating the sample to 60 °C in the spectrometer or

after 14 hours at 60 °C (**Figure 2.14**). This data suggests that, under the reaction conditions,

interconversion between the two chelated intermediates is not possible before the addition of
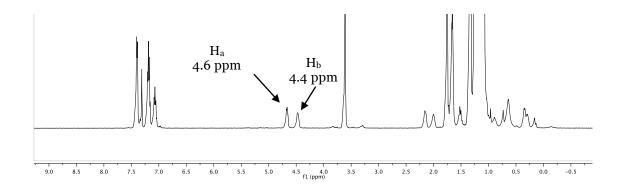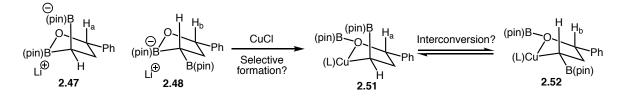
copper.

Figure 2.14 NMR spectra of epoxide opening reaction at 60 °C

Considering all of the NMR data, the observed selectivity must be related to the copper species and not the diboron intermediate. The first possibility is that the selectivity can come from the selective formation of one of the two possible copper chelated intermediates (only forms **2.51** or **2.52**) which then results in the selective formation of the product. The second is that the copper intermediate is not formed selectively and that a Curtin-Hammett situation arises where the selective reaction of one of the intermediate diastereomers leads to product and there is a pathway for interconversion between these two intermediates (interconversion between **2.51** and **2.52**).

An attempt was made to follow the reaction via NMR after the addition of the copper catalyst. It was observed that both diastereomers of the borate intermediate were consumed at similar rates. This further confirmed the hypothesis that the diastereoselectivity was achieved through a copper species. In addition to seeing the disappearance of the two boron intermediates, once the copper was added to the reaction, a multitude of new peaks appeared between 4.6 and 5.2 ppm. This indicated that, upon addition of the copper and allyl chloride, multiple new species were observed. These new species most likely include both diastereomers of the copper intermediate and both diastereomers of the product. Due to the abundance of

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peaks and their overlapping nature, further mechanistic insights about the transmetallation and allylation steps could not be garnered from the NMR data.
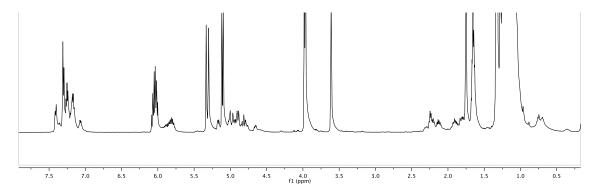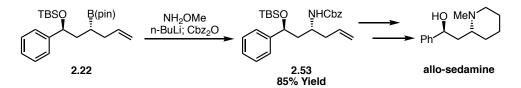

Figure 2.15 NMR spectra after the addition of CuCl and allyl chloride
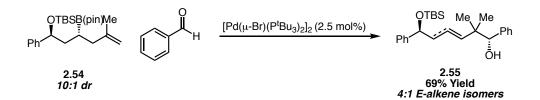
2.3.4 Product functionalizations

In order to illustrate the versatility of the products obtained via this methodology, a variety of product functionalizations were undertaken. First, using conditions developed by Morken and coworkers,[48] the boronate ester group in compound **2.22** was transformed into an amine via treatment with a solution of methoxy amine and *n*-butyl lithium. This afforded compound **2.53** in 85% yield. Compound **2.53** is a known intermediate in the synthesis of the natural product (+)-allo-sedamine which can be used to treat a variety of respiratory problems.[49]

Scheme 2.3 Amination of protected 1,3-hydroxyboronate ester

Next, two carbon-carbon bond forming functionalizations were carried out. The first was an alkene isomerization/allylation reaction. When compound **2.54** was treated with benzaldehyde in the presence of a palladium (I) catalyst, the olefin in **2.54** undergoes isomerization to generate the allyl boronate ester in situ.[50] This species then undergoes a 1,2-addition reaction with benzaldehyde to give product **2.55** in 69% yield in a 4:1 ratio of *E*-alkene isomers.

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Scheme 2.4 Alkene isomerization and allylation of protected 1,3-hydroxyboronate ester

The ability of these products to participate in Suzuki cross-coupling reactions was also explored. For the previous functionalization, the reactions were carried out on the isolated, TBS-protected derivative of the product obtained from the allylation reactions. A different approach was taken for the cross-coupling reactions. Cross-coupling reactions were carried out on the free alcohols obtained as the product of the allylation reaction to show how useful this methodology could be for rapid installation of multiple functional groups in a complex molecule. Following an established cross-coupling procedure,[51] compound **2.22** was treated with an aryl bromide and aqueous potassium hydroxide in the presence of a Pd-RuPhos catalyst system. Products **2.50**, and **2.51** were obtained in 40% and 54% overall yield respectively from the starting epoxide. This sequence makes 3 new carbon-carbon bonds and sets one new stereocenter.
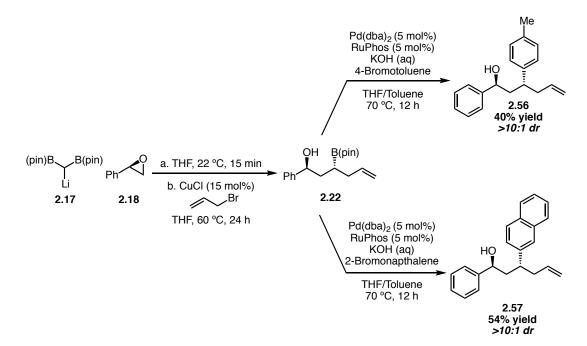

Figure 2.16 Cross coupling of 1,3-hydroxyboronate esters

Lastly, my co-worker Michael Liang carried out a series of sequential tandem coupling reactions in order to illustrate the iterative nature that these reactions can take on for the synthesis of 1,3-polyol motifs. As illustrated in **Figure 2.17**, following the standard ring opening/allylation reaction sequence previously discussed, compound **2.58** was synthesized in 99% yield on a 5 mmol (1.03 g of product) scale. It was found that increasing the scale that the reaction was conducted on led to an increase in the yield of the reaction. This is most likely due to the reaction setup. Since the deprotonation must occur at 0 ºC, a cooled solution of LTMP in THF is cannula transferred to a cooled solution of diborylmethane. After 10 minutes, the epoxide is added to this reaction mixture via syringe. After the reaction has stirred at 22 ºC for a sufficient amount of time to allow for the epoxide to be fully opened by the diborylmethane, the solution is then cannula transferred to a separate vial containing the copper catalyst. The allylbromide is then added via syringe. Increasing the scale of the reaction likely increases the efficiency of these cannula transfers; a small amount being left behind in a transfer will not have as detrimental of an effect on the yield of a 5 mmol scale reaction as it will on a 0.1 mmol scale reaction (the scale at which all reaction optimization and substrates were tested at).

After the isolation of the product from the first ring opening/allylation sequence, a vanadium catalyzed directed epoxidation followed by ketal protection was carried out to yield the terminal epoxide **2.59** in 55% yield and 25:3.5:1 dr. The second ring opening/allylation sequence was then carried out on the ketal epoxide to give the desired product, **2.60**, in 75% yield and 4.5:1 dr as the diol after oxidation. This results in an overall yield of 41% for the formation of 4 carbon-carbon bonds and three stereocenters.
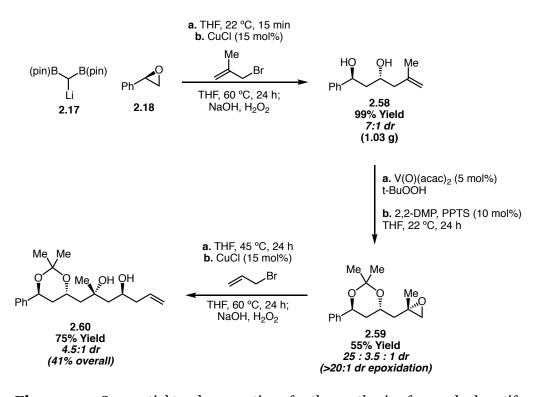
Figure 2.17 Sequential tandem reactions for the synthesis of 1,3-polyol motifs

2.4 Enantioselective tandem allylation of ethylene oxide

The allylation reaction presented thus far relies on substrate control to set the

stereochemistry in the final product. This means that steric interactions within the molecule

determine which diastereomer will be favored and to what degree. As is visible in the substrate

scope, examples with more sterically demanding substituents or rigid ring systems tend to yield

products in higher levels of selectivity than those with less sterically demanding substitution (ie

2.22 vs **2.31**). Another approach to setting stereochemistry is catalyst control. In this case, the

selectivity is dependent upon the interactions between the catalyst and the bound substrate.

This gives the potential for more control over the key interactions that lead to high levels of

selectivity since the catalyst can be altered as needed without changing the identity of the

product obtained from the reaction. Similar modifications to steric interactions present in a

substrate-controlled reaction would typically lead to a different product being formed as the

modifications must be made to the substrate itself.

As shown in **Figure 2.7**, the identity of the catalyst had a profound effect on the diastereoselectivity of the allylation reaction. For example, using a catalyst system comprised of CuCl and *rac*-BINAP, a decrease in conversion and diastereoselectivity to 42% and 5:1 was observed and when a CuCl and triphenylphosphine catalyst system was employed the conversion remained higher at 65% but a substantial decrease in diastereoselectivity to 2:1 was observed (compared to 77% and 8:1 dr with just CuCl). While the decrease in yield and selectivity observed with these catalysts is undesired, the fact that the catalyst changed the selectivity at all was encouraging as it signified that there was the potential for a catalyst controlled system.

One of the challenges with attempting an enantioselective variant of this reaction through a catalyst-controlled method is controlling the many stereoisomers that can be formed throughout the reaction. For example, using a racemic styrene oxide and a chiral catalyst to conduct an enatio- and diastereoselective tandem allylation reaction would be very challenging. The chiral catalyst would introduce another stereochemical component to the reaction therefore leading to four possible diastereomers (and their enantiomers) being formed. Selective formation or reaction through one specific diastereomer would be very difficult to control.

Ethylene oxide was chosen as a model substrate for the development of a catalyst-controlled enantioselective allylation reaction. Starting with ethylene oxide had many benefits. First, as an unsubstituted epoxide, the reaction will simply be an enantioselective reaction as opposed to both an enantio- and diastereoselective reaction. This simplification also decreases the number of possible diastereomers of intermediates in the reaction making it much more manageable as a starting point for a catalyst-controlled reaction. Lastly, the seemingly simple products that would be obtained from the ring opening and enantioselective allylation of ethylene oxide are not easy to make via other methodologies so developing a synthesis of them from simple building blocks such as ethylene oxide, diborylmethane, and allyl bromide is very attractive.

Using ethylene oxide as the model epoxide also presents some challenges. Since it is completely unsubstituted, achieving high levels of enantioselectivity could be quite difficult. A catalyst-controlled reaction relies on interactions between the catalyst and substrate that lead to preferential binding of the substrate in a specific orientation. An unsubstituted epoxide might not be sterically demanding enough to favor a specific binding orientation with the catalyst.

The initial round of screening was conducted to determine the feasibility of the reaction from a reactivity standpoint without focusing on enantioselectivity. A series of chiral phosphine ligands were screened under conditions similar to those disclosed for the diastereoselective allylation reaction and the results are illustrated in **Table 2.2**. The primary modification, other than the catalyst identity, from the previously optimized conditions is the change in the identity of the limiting reagent. In the previous work, the epoxide always served as the limiting reagent with a slight excess (1.5 equivalents) of the diboron reagent. It was found through early reaction screening that this ratio led to the most efficient epoxide ring opening. Ethylene oxide is a gas but can also be used as a solution in a variety of solvents, including THF which is the solvent used for these tandem reactions. While using the solution of ethylene oxide makes the reaction far more user friendly than using the epoxide in its gaseous state, it is still not a perfect solution. Solutions of ethylene oxide in THF are sold under a concentration range as opposed to at a specific concentration. For example, the solution used in this chemistry had a molarity between 2.5 and 3.3M. Because of this, it was difficult to use the ethylene oxide as the limiting reagent because the exact amount present in the reaction was unknown. Additionally, the highly volatile nature of ethylene oxide meant that the solution could easily change concentration from one day to the next. To avoid having to quantify the concentration of ethylene oxide in the solution prior to each reaction the epoxide was used in excess with the diborylmethane serving as the limiting reagent.
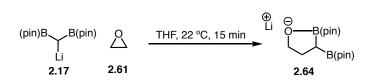
Table 2.2 Catalyst screening for ethylene oxide allylation reaction

entry	Ligand	Conversion
1	*R*-BINAP	29%
2	*R*-OMe-biphep	26%
3	*R,S*-Josiphos (Ph, Cy)	47%
4	*R*-Monophos	0%
5	SegPhos	29%
6	Me-DuPhos	42%
7	TaniaPhos	26%

[a] Reactions performed under N_2 atm. [b]Conversion to **2.55**; values determined by analysis of 400, 500 or 600 MHZ ^{1}H NMR spectra of unpurified mixtures with DMF as internal standard.

As illustrated in **Table 2.2**, a variety of chiral phosphine ligands were initially screened for reactivity in this system. For ease of characterization, the initially formed crude hydroxyboronate ester **2.62** was oxidized *in-situ* to the corresponding diol **2.63**. The highest conversion obtained in this screen was 47% utilizing a Josiphos ligand. Other ligands that gave promising results included BINAP, SegPhos, Me-DuPhos and OMe-biphep. One problem with this reaction that was observed early during reaction optimization was reproducibility. For example, using the same Josiphos ligand across three reactions led to conversions of 47%, 9%, and 7% and OMe-biphep gave 42%, 45% ad 26% over three reactions. This proved to be a problem present with other ligands as well and is most likely due to inconsistent formation of the cyclic borate intermediate.

As mentioned previously, one of the main concerns associated with this reaction was the efficient formation of the chelated intermediate. In previous work, it had been observed that the cyclic borate was typically quite stable prior to the addition of copper. With this in mind, an

attempt was made to make and isolate the cyclic borate derived from ethylene oxide and diborylmethane (**Scheme 2.5**). A cooled solution of LTMP in THF was added to a solution of diborylmethane in THF at 0 °C. After stirring at 0 °C for 10 minutes, a solution of ethylene oxide in THF was added and the reaction was allowed to warm to room temperature and stir for 15 minutes. The solvent was then removed under a stream of dry nitrogen gas and then the reaction vial was brought into the glovebox.

Scheme 2.5 Isolation of chelated intermediate

Inside the glovebox, the resulting solid residue was washed three times with hexanes and dried under vacuum. The ^{1}H-NMR spectrum was obtained in d_8-THF and matched what was expected for the cyclic borate intermediate. Two multiplets centered at 3.5 ppm were indicative of the protons at the base of the oxygen. Two multiplets centered at 1.5 and 1.7 ppm indicated the methylene protons on the carbon between the alcohol and the boron (see experimental for spectrum). The proton at the base of the two borons was found to be a multiplet centered at 0.1 ppm which is in agreement with previous NMR studies conducted for the allylation chemistry. It appeared that the borate had been formed very cleanly on small scale. However, when the reaction was scaled up in an attempt to make enough to use directly in a reaction, it was no longer a clean reaction. Many new peaks were observed by NMR indicating either that the reaction did not go to completion or that other species were also being formed. While further attempts at isolating this species were not undertaken, the initial result shows promise that further optimization could lead to isolation of the cyclic borate intermediate in high yield and purity.

Attempts to separate the enantiomers of the diol via chiral gas chromatography were unsuccessful and the lack of a strong chromophore in the molecule made separation on chiral HPLC or SFC impossible. To overcome this, instead of isolating the product as diol **2.63**, the

crude hydroxyboronate ester was subjected to TBDPS protection conditions to result in the silyl protected hydroxyboronate ester. This approach had two main benefits. The first is that it allowed for easier visualization using the UV detector on an HPLC or SFC for quantification of the level of enantioselectivity of the reaction. Second, the silyl protected products tended to be more stable and easier to handle than the hydroxyboronate esters. While the *tert*-butyldiphenylsilyl group made the product easy to track during chiral separations, it also made the product extremely nonpolar and therefore difficult to separate via HPLC or SFC methods. Oxidation of the silyl-protected 1,3-hydroxyboronate ester to the monoprotected 1,3-diol also did not result in a useful chiral assay.
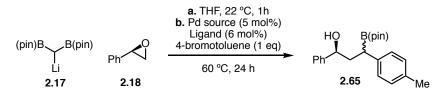
Due to the difficulties associated with developing an appropriate stereochemical assay for this reaction and the success of other projects at the time further exploration of a catalyst controlled, enantioselective allylation reaction was not undertaken. The work here illustrates that this reaction is feasible and further work to develop a good method for quantifying selectivity and further screening of ligands and reaction conditions could lead to improved results.

2.5 Tandem palladium catalyzed cross-coupling reaction

The Suzuki-Miyaura cross coupling reaction is one of the most well-known boron-based transformations in organic chemistry. In 2010 Suzuki shared the Nobel Prize in chemistry for developing the palladium catalyzed cross coupling reaction along with Richard Heck and Ei-ichi Negishi. The Suzuki reaction couples organoboron compounds with aryl halides using a palladium catalyst and a base. The palladium catalyst first undergoes oxidative addition into the aryl or vinyl halide. The base then serves to activate the boron species generating a four-coordinate borate which can undergo transmetallation with the palladium complex to generate an organopalladium intermediate. Reductive elimination then occurs to yield the desired product. Over the years, the scope of this reaction has been expanded dramatically with regards to both the boron reagents and halides that can be used.[34]

Since the Suzuki reaction is facilitated by the formation of a borate species followed by transmetallation to a metal catalyst, it was theorized that the chelated intermediate generated upon addition of the deprotonated diborylmethane **2.17** to an epoxide could participate in a Suzuki cross-coupling reaction. Precedent was set for transmetallation to a metal catalyst through the copper catalyzed allylation work so it was possible that transmetallation to palladium would also be feasible.
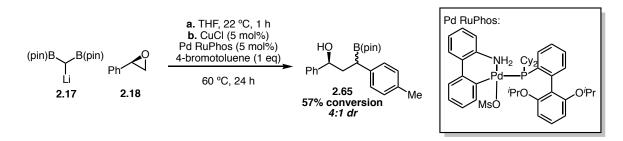
Initially, this reaction was explored using common conditions for Suzuki cross coupling reactions (**Scheme 2.6**). Ligands such as RuPhos, XPhos, and SPhos which are known to work well for Suzuki cross coupling reactions were employed with Pd(dba)₂ as the metal source. Initial catalyst screening without additives did not result in conversion to the desired cross-coupled product. Inclusion of a base additive such as cesium carbonate or potassium phosphate was explored but did not result in the desired product.

Scheme 2.6 Initial tandem cross-couping reaction

The results up to this point suggest that transmetallation to palladium was more difficult than the previously studied transmetallation to copper. Both Semba/Nakao[52] and Brown[45,53] independently showed in 2014 that palladium catalyzed cross coupling reactions could be facilitated by the addition of a copper co-catalyst to the reaction.[54] Since it is already known from the allylation chemistry that the cyclic borate is capable of transmetallating efficiently to copper, and there is precedent for copper and palladium co-catalyzed Suzuki reactions, a copper and palladium dual catalyst system was explored as a secondary reaction in this tandem process.

Treating the *in-situ* generated borate intermediate derived from styrene oxide and diborylmethane with copper chloride, Buchwald's Pd-RuPhos complex, and 4-bromotoluene at 60 °C in THF as illustrated in **Scheme 2.7**, resulted in 57% conversion to the desired product

and 4:1 dr after oxidation to the corresponding diol. A small catalyst screen focusing on the identity of the copper catalyst was then conducted to try to increase both the conversion and the diastereoselectivity of the reaction. It was found that while copper-NHC complexes were capable of catalyzing the reaction, the dr tended to decrease relative to when unligated copper was used. An increase in dr to 8:1 was observed when the loading was decreased to 2.5 mol%. Additionally, the temperature was increased from 60 ºC to 80 ºC to try and increase the conversion. While this did result in a slight increase in conversion, the dr decreased to 2:1.
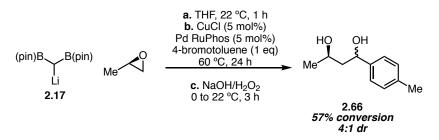

Scheme 2.7 Cu/Pd co-catalyst system for tandem cross-coupling

Table 2.3 Catalyst screen for tandem cross-coupling reaction

entry	Copper Complex	Palladium[b]	Ligand	conv. (%)[c]	dr[d]
1	CuCl	Pd precat	RuPhos	57	4:1
2	CuCl[e]	Pd(dba)$_2$	RuPhos	40	4:1
3	CuCl[f]	Pd(dba)$_2$	RuPhos	35	8:1
4	CuIMesCl	Pd precat	RuPhos	37	2:1
5	CuSiAdCl	Pd precat	RuPhos	47	2:1
6	CuSiMesCl	Pd precat	RuPhos	39	2:1

[a]Reactions performed under N$_2$ atm. [b]Pd precat refers to the palladcycle complex in Figure X. [c]Conversion to **2.58**; values determined by analysis of 400, 500 or 600 MHZ ^{1}H NMR spectra of unpurified mixtures with DMF as internal standard. [d]dr determined via oxidation to the corresponding diol. [e]10 mol% CuCl. [f]2.5 mol% CuCl
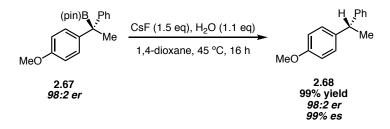
While further optimization of the reaction was not undertaken at this time, these results illustrate that cross coupling of the cyclic borate intermediate is a viable process. To explore whether this process would also be applicable to alkyl epoxides, propylene oxide was subjected to the reaction conditions and the desired product **2.59** was obtained in 57% conversion and 4:1 dr. While the yield and diastereoselectivity are low for both of these examples, the fact that both alkyl and aryl epoxides are tolerated under these unoptimized reaction conditions is promising for future work on this project.

Scheme 2.8 Tandem cross-coupling with propylene oxide

2.6 Diastereoselective protonation of substituted cyclic borate species
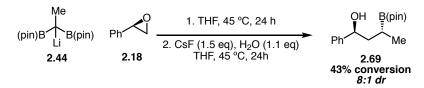
As previously mentioned in section 2.3.2 on the copper-catalyzed tandem allylation reaction, substituted *gem*-diborylalkanes, such as diborylethane, are capable of participating in the ring opening reaction with epoxides at elevated temperatures, however they are incapable of undergoing a subsequent copper catalyzed allylation reaction (**Scheme 2.2**). This does not mean that there are no other reactions that these substituted intermediates can participate in. The addition of the methyl group in diborylethane appears to bring enough additional steric hindrance to the system to prevent reactivity with the copper allyl species. Because of this, in order for a secondary reaction to be feasible on these substituted intermediates, it must utilize a very small, unhindered electrophile. The best reaction to begin with for these systems is therefore a simple diastereoselective protodeboration reaction.

In 2010, Aggarwal and coworkers showed that enantioenriched tertiary boronate esters could participate in a stereospecific protodeboronation reaction to give enantioenriched tertiary alkyl centers.[55] The reaction employs cesium fluoride and water in 1,4-dioxane at 45 °C for 16

hours to give high yields and enantiospecificity of the desired products as illustrated in **Scheme 2.9**. If this reaction could be employed as a secondary reaction in the tandem epoxide opening chemistry it would result in the diastereoselective synthesis of 1,3-hydroxyboronate esters.
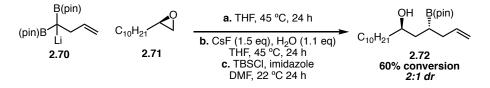

Scheme 2.9 Aggarwal's stereospecific protodeporation

To test this protodeboronation reaction in the tandem system, *R*-styrene oxide was treated with deprotonated diborylethane and heated to 45 °C for 24 hours to facilitate the ring opening reaction (**Scheme 2.10**). This mixture was then transferred to a vial containing cesium fluoride followed by the addition of water. The reaction was again heated to 45 °C for 24 hours. After oxidation, the desired diol product was obtained in 43% conversion and 8:1 dr favoring the *anti*-product (**2.59**) with 28% returned styrene oxide indicating that the reaction could become higher yielding if the ring opening was more efficient. These results illustrated a promising proof of concept for this reaction.

Scheme 2.10 Protodeboration reaction utilizing diborylethane and styrene oxide

Using *gem*-diborylalkane **2.70**, which contains an allyl substituent, in this methodology would yield the same products obtained in the copper catalyzed allylation reaction when diborylmethane was utilized to open the epoxide. It was theorized that using this protonation approach could result in a higher level of diastereoselectivity for some of the alkyl substrates that yielded products in low dr with the copper allylation methodology. To test this, dodecene oxide was treated with deprotonated diborylethane and heated to 25 °C for 24 hours. The

162

mixture was then transferred to a vial containing CsF and water was added to the reaction. After

24 hours at 45 °C, the product was observed in 60% conversion and 2:1 dr. This is both a

decrease in conversion and diastereoselectivity relative to the copper catalyzed methodology

(73% yield, 3:1 dr). The size difference between the dodecyl substituent and the allyl group must

not be significant enough to favor one diastereomer of the chelated intermediate over the other.

Further optimization of the reaction conditions and exploration of the substrate scope will

further develop this initial study into a useful reaction.

Scheme 2.11 Protodeboration reaction utilizing an allyl substituted 1,1-diboronate ester and dodecene oxide

2.7 Conclusions[46]

A method for the stereoselective linchpin coupling of 1,1-diborylmethane with epoxides

and allyl electrophiles was developed. This method takes advantage of the acidity of 1,1-

organodiboronates to generate a reactive boron stabilized carbanion which can undergo a ring

opening reaction with an epoxide. The alkoxy group generated from the ring opening can then

chelate to one of the boronate esters thereby activating it for further reactivity. Introduction of a

copper catalyst and allyl electrophile generated the allylation products in good yield and

diastereoselectivity. The mechanism was studied via NMR spectroscopy and it was determined

that interconversion between the two diastereomers of the boron chelated intermediate does not

occur and that copper plays a role in the high levels of diastereoselectivity observed. The

versatility of the products was illustrated via amination, isomerization/allylation, and cross-

coupling functionalizations. The usefulness of this transformation for iterative processes was

illustrated through the synthesis of a 1,3-polyol motif via sequential ring opening and allylation

reactions. Initial development of an enantioselective, catalyst-controlled tandem ring opening

and allylation reaction utilizing ethylene oxide was explored. Lastly, applications of the cyclic

borate intermediate to other borate based reactions were also studied. The borate species was found to participate in cross-coupling and protodeboronation reactions.

2.8 Experimental[46]

2.8.1 General

All reactions were carried out in oven-dried (150 °C) or flame dried glassware under inert atmosphere of dried nitrogen unless otherwise noted. Analytical thin-layer chromatography was performed on glass plates coated with 0.25 mm of 60 Å mesh silica gel. Plates were visualized by exposure to UV light (254 nm) and/or immersion into Seebach's or $KMnO_4$ stain followed by heating. Column chromatography using silica gel was performed using P60 (mesh 230-400) supplied by Silicycle. All solvents were sparged with argon and then purified under a positive pressure of argon through an SG Water, USA Solvent Purification System. Tetrahydrofuran (Omnisolv) was passed successively through two columns of neutral alumina. The ambient temperature in the laboratory was approximately 22 °C.

2.8.2 Instrumentation

All ^{1}H NMR spectra were recorded on Bruker Spectrometers (AVANCE-600, Bruker 500, and DRX 400). Chemical shifts are reported in ppm from tetramethylsilane and referenced to the residual protio solvent peak ($CDCl_3$: δ 7.26; C_6D_6: δ 7.16; THF-d_8 δ 3.58). Data are reported as follows: chemical shift, multiplicity (s = singlet, d = doublet, t = triplet, qu = quartet, quint = quintet, br = broad, m = multiplet, app = apparent), integration, and coupling constants are given in Hz. ^{13}C NMR spectra were recorded on Bruker Spectrometers (AVANCE-600 and Bruker 500) with carbon and proton decoupling. Chemical shifts are reported in ppm from tetramethylsilane and referenced to the residual protio solvent peak ($CDCl_3$: δ 77.16; C_6D_6: δ 128.06). ^{11}B NMR spectra were recorded on a Bruker model 500 MHz spectrometer. All IR spectra were recorded on a Jasco 260 Plus Fourier transform infrared spectrometer. Low-resolution mass spectrometry samples were analyzed with a hybrid LTQ FT (ICR 7T) (ThermoFisher, Bremen, Germany) mass spectrometer. Samples were introduced via a

microelectrospray source at a flow rate of 10 μL/min in methanol. Xcalibur (ThermoFisher, Breman, Germany) was used to analyze the data. Molecular formula assignments were determined with Molecular Formula Calculator (v 1.2.3). All observed species were singly charged, as verified by unit m/z separation between mass spectral peaks corresponding to the ^{12}C and $^{13}C^{12}C_{c-1}$ isotope for each elemental composition. High-resolution mass spectrometry samples were analyzed using an HPLC system that consisted of an Agilent 1200 (Agilent, Waldbronn, Germany) binary pump (G1312A) operating at a flow-rate of 0.3 mL min^{-1}. The solvents were degassed using an on-line membrane system (Agilent G1379A). The column was maintained in a thermostated compartment at 40 °C (Agilent G1316A). The diode array detector was an Agilent G1315D operating at three wavelengths of 250, 254 and 280 nm. Separation was performed on a Waters Acquity UPLC BEH C18 column (2.1 x 50 mm, 1.7 um particle size). The injection (5 μL) was performed using an autosampler (Agilent G1329A). LC conditions were set at water with 0.1% formic acid (A) for 1 min before ramping linearly over 5 mins to 100% acetonitrile with 0.1% formic acid (B) and then switched back to 100% A and allowed to re-equilibrate until 10 min. The HPLC system was coupled to the Q-TOF via a dual ESI interface operating in positive ion mode using a capillary voltage of +3.5 kV. The other optimum values of the ESI-TOF parameters were drying gas temperature, 325 °C; drying gas flow, 5 L min^{-1} and nebulizing gas pressure, 15 psi. The detection was carried out considering a mass range of 100–1500 m/z. Prior to acquiring samples, an external instrument calibration was performed using Agilent ESI-L Low Concentration Tuning Mix. MassHunter Quantitative Analysis (Agilent, Waldbronn, Germany) was used to analyze the data. Solutions were dissolved in MeOH at 0.1 mg/mL or less and diluted appropriately based on responsiveness to the ESI mechanism. Molecular formula assignments were determined with Molecular Formula Calculator (v 1.2.3). The success of mass data for molecular ions was considered based on the widely-accepted accuracy threshold for confirmation of elemental compositions established at 5 ppm. All observed species were singly charged, as verified by unit m/z separation between mass spectral

peaks corresponding to the ^{12}C and $^{13}C^{12}C_{c-1}$ isotope for each elemental composition. Optical rotations were determined using a Jasco P1010 polarimeter and concentrations are reported in g/100mL. Enantiomeric ratios were determined on a Waters Acquity UPC^2 instrument at 22 °C using ACQUITY UPC^2 Trefoil CEL2 (2.1mm x 50 mm x 2.5μm) column and Waters PDA detector set to 210 nm.

2.8.3 Reagents

Allylbenzene was purchased from Alfa Aesar and used as received.

Allylbromide was purchased from Sigma Aldrich, plugged through neutral alumina before use and stored under nitrogen in the refrigerator.

Alpha-methylstyrene was purchased from Alfa Aesar and used as received.

Ammonium chloride was purchased from Alfa Aesar and used as received.

Benzene-d$_6$ was purchased from Cambridge Isotope Laboratories and used as received.

(-)-Beta-pinene was purchased from TCI America and used as received.

Bis(dibenzylideneacetone)palladium (0) (Pd(dba)$_2$) was purchased from Strem, stored in a nitrogen filled glovebox, and used as received.

2-bromonapthalene was purchased from Alfa Aesar and used as received.

3-bromo-2-bromomethyl-1-propene was purchased from Sigma Aldrich, plugged through neutral alumina before use, and stored under nitrogen in the refrigerator.

3-bromocyclohexene was purchased from Acros, plugged through neutral alumina before use, and stored under nitrogen in the refrigerator.

3-bromo-2-methylpropene was purchased from Sigma Aldrich, plugged through neutral alumina before use, and stored under nitrogen in the refrigerator.

4-bromotoluene was purchased from Alfa Aesar, recrystallized from ethanol, dried via azeotropic distillation from benzene, and stored in a nitrogen filled dry box.

Bromo(tri-*tert*-butylphosphine)palladium(I) dimer was purchased from Strem, stored in a -20 °C freezer in a nitrogen filled glovebox, and used as received.

Chloroform-d (CDCl₃) was purchased from Cambridge Isotope Laboratories and used as received.

Copper (I) chloride was purchased from Strem Chemicals and kept in a nitrogen filled dry box.

Copper (I) tetrakisacetonitrile hexafluorophosphate was purchased from Sigma Aldrich and kept in a nitrogen filled dry box.

Cyclohexene oxide was purchased from Alfa Aesar and used as received.

2-Dicyclohexylphosphino-2′,6′-diisopropoxybiphenyl (RuPhos) was purchased from Sigma Aldrich, stored in a nitrogen filled glovebox, and used as received.

Trans-crotylbromide was purchased from Acros, plugged through neutral alumina before use, and stored under nitrogen in the refrigerator.

1,2-dichloroethane (DCE) was purchased from Sigma Aldrich, dried over calcium hydride, distilled onto 3Å molecular sieves, and stored in a nitrogen filled glovebox.

1-dodecene was purchased from Alfa Aesar and used as received.

3,3-dimethylallyl bromide was purchased from Sigma Aldrich and plugged through neutral alumina before use.

Dimethylformamide (DMF) (Anhydrous) was purchased from EMD and used as received.

Diborylmethane was prepared according to literature procedures[35] and matched literature spectra. It was purified via silica gel chromatography, dried via azeotropic distillation from benzene, and stored in a nitrogen filled glovebox.

Diborylethane was prepared according to literature procedure[35] and matched literature spectra. It was purified via silica gel chromatography, dried via azeotropic distillation from benzene and stored in a nitrogen filled glovebox.

4-fluorostyrene was purchased from Alfa Aesar and used as received

Geranylbromide was purchased from Sigma Aldrich, plugged through neutral alumina before use, and stored under nitrogen in the refrigerator.

Hydrogen peroxide (30%) was purchased from Fisher Scientific, stored in the freezer, and used as received.

Imidazole was purchased from Alfa Aesar and used as received.

(+)-Limonene oxide, mixture of cis and trans was purchased from Sigma Aldrich and dried via azeotropic distillation from benzene.

Lithium 2,2,6,6-tetramethylpiperidide (LTMP) was purchased from Sigma Aldrich and kept in a nitrogen filled dry box.

2-methylstyrene was purchased from Alfa Aesar and used as received.

3-methylstyrene was purchased from Alfa Aesar and used as received.

4-methylstyrene was purchased from Alfa Aesar and used as received.

Palladium 10% wt on activated carbon (wet) was purchased from Aldrich and used as received.

Pd-RuPhos precataylst was synthesized according to known literature procedure and matched literature spectra.[56]

(R)-BINAP was purchased from Strem Chemicals and stored in a nitrogen filled dry box.

(R)-Styrene oxide was purchased from Sigma Aldrich and dried via azeotropic distillation before use.

Styrene was purchased from Alfa Aesar and used as received.

***Tert*-butyldimethylchlorosilane** was purchased from Alfa Aesar and used as received.

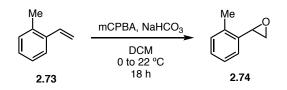**tert-Butyldimethylsilyl (*R*)-(-)-glycidyl ether** was purchased from Sigma Aldrich and used as received.

Vinylcyclohexane was purchased from Alfa Aesar and used as received.
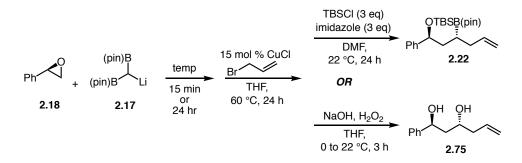
2.8.4 General procedures

General procedure for the synthesis of epoxides

Epoxides yielding products **2.22-2.34** were synthesized according to the following general procedure. All epoxides matched known literature spectra.

Me / mCPBA, NaHCO$_3$ / DCM / 0 to 22 °C / 18 h / Me / O

2.73   **2.74**

2-methylstyrene (2.2 mL, 17 mmol) was dissolved in DCM (100 mL) in a 250 mL single neck

round bottom flask containing a stirbar. Solid NaHCO$_3$ was added to the flask and the reaction

was cooled to 0 °C in an ice bath. The flask was then fitted with an addition funnel containing

mCPBA (6.5g, 18.7 mmol) dissolved in DCM (70 mL). The mCPBA solution was added dropwise

through the addition funnel over 15 minutes. The reaction was then stirred at 0 °C for an

additional 15 minutes and then allowed to warm to room temperature and stirred overnight. The

mixture was then transferred to a separatory funnel and the organics were washed twice with a

saturated solution of sodium carbonate and twice with saturated sodium thiosulfate. The

organics were then dried over sodium sulfate, concentrated, and purified via silica gel

chromatography to give the desired epoxide as a clear oil (1.76 g, 77%). The epoxide was dried

via azeotropic distillation from benzene prior to use.

General procedure for the copper catalyzed three-component allylation reaction

In a nitrogen filled glovebox, diborylmethane (40.2 mg, 0.15 mmol) was weighed into an 8-mL

vial equipped with a magnetic stir bar. The diborylmethane was dissolved in THF (0.4 ml) and

the vial was sealed with a septa-lined cap and taped. Lithium 2,2,6,6-tetramethylpiperidide

(LTMP) (22.8 mg, 0.155 mmol) was weighed into a separate 8-mL vial, dissolved in THF (0.8

mL) and sealed with a septum lined cap and tape. Copper (I) chloride (1.5 mg, 0.015 mmol) was

weighed into a third 8-mL vial with a magnetic stir bar and sealed with a septum lined cap and

tape. The vials were removed from the glovebox and the diborylmethane and LTMP solutions were cooled to 0 °C in an ice water bath. The LTMP solution was transferred via cannula to the diborylmethane solution at 0 °C, and this was solution was allowed to stir at 0 °C for 10 minutes. The epoxide (0.1 mmol) was then added via syringe and the solution was brought to the correct temperature for the epoxide used and stirred for the necessary time. (Monosubstitued epoxides: 15 min at 22 °C; Di- or ortho-substituted epoxides: 24 hr at 22 °C; trisubstituted epoxides: 24 hr at 45 °C). The reaction was then returned to room temperature and transferred via cannula to the vial containing the copper chloride. Allyl bromide (26 μl, 0.3 mmol) was then added to the reaction via syringe. The reaction was then sealed with tape and allowed to stir at 60 °C for 24 h. The mixture was then cooled to room temperature and quenched with a saturated solution of aqueous ammonium chloride, extracted with diethyl ether (x3), dried over magnesium sulfate, filtered, and concentrated *in vacuo*. **For unsubtituted allyl bromides:** Imidazole (20 mg, 0.3 mmol) and a magnetic stir bar were then added to the vial. The vial was sealed wi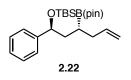th a septum cap and flushed with dry N_2. *Tert*-butyldimethylchlorosilane (45 mg, 0.3 mmol) was quickly added to the vial and the vial was again purged with N_2. Dry dimethylformamide (0.6 mL) was then added through the septum cap via syringe. The reaction was stirred at 22 °C for 24 h. The reaction was then quenched with a saturated solution of ammonium chloride, extracted with diethyl ether, dried over magnesium sulfate, filtered, and concentrated *in vacuo*. The residue was purified via silica gel chromatography (50:1 Hexanes:Et$_2$O, gravity) to yield the desired product. **For substituted allyl bromides:** The crude mixture was dissolved in THF (0.25 mL), a stir bar was added, and the reaction was cooled to 0 °C in an ice water bath. NaOH (3 M, 0.25 mL) and H_2O_2 (30%, 0.16 mL) were added. The reaction was sealed with a septum lined cap that was pierced with a vent needle and allowed to warm to room temperature and stir for 3 hours. The reaction was then cooled to 0 °C in an ice water bath. The reaction was quenched with a saturated solution of sodium thiosulfate, extracted with diethyl ether (x3), dried over magnesium sulfate and
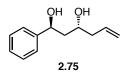
concentrated *in vacuo*. The resulting crude mixture was purified via silica gel chromatography (4:1 hexanes:ethyl acetate to 1:1 hexanes:ethyl acetate). Excess pinacol was then removed via azeotropic distillation on a rotary evaporator using a 1:1 mixture of water and methanol with a 55 °C water bath.

Note: For **Table 2.1** and **Figure**, yields and diastereomeric ratios were determined using DMF as an NMR internal standard. In cases where diastereomeric ratio could not be clearly determined in the crude NMR of the hydroxy boronate ester product, oxidation with sodium hydroxide and hydrogen peroxide was carried out and the ratio was determined using the crude diol obtained.

2.8.5 Product characterization

2.22

***Tert*-butyldimethyl((((1*S*,3*R*)-1-phenyl-3-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)hex-5-en-1-yl)oxy)silane (2.22).** Following the general procedure, protected 1,3-hydroxyboronate ester **2.22** was isolated in 56% yield and 8:1 dr (23.4 mg) as a clear oil.

¹H NMR (600 MHz, C_6D_6) δ 7.46 (dd, J = 8.1, 1.4 Hz, 2H), 7.19 (t, J = 7.7 Hz, 2H), 7.11 - 7.05 (m, 1H), 5.97 (ddt, J = 17.0, 10.2, 6.8 Hz, 1H), 5.12 (dq, J = 17.0, 1.5 Hz, 1H), 5.04 - 4.98 (m, 1H), 4.94 (dd, J = 7.2, 5.8 Hz, 1H), 2.46 - 2.29 (m, 2H), 2.02 (dd, J = 8.3, 5.8 Hz, 2H), 1.71 (m, 1H), 1.07 (s, 6H), 1.07 (s, 6H), 1.02 (s, 8H), 0.20 (s, 3H), -0.05 (s, 3H). **¹³C NMR** (151 MHz, C_6D_6) δ 146.9, 138.8, 128.5, 127.3, 126.3, 115.3, 83.0, 75.7, 43.3, 36.4, 26.3, 25.2, 24.9, 18.5, -4.1, -4.5. **IR (v/cm⁻¹):** 2928(m), 2857 (m), 1381 (m), 1144 (s), 1059 (m), 700 (m). **MS (ESI⁺):** [M+Na]⁺ calcd for $C_{24}H_{41}BO_3SiNa^+$ 439.28, found 439.45. **[α]²²D** = -25.4 (c =0.295, CH_2Cl_2, l = 100 mm).

Relative stereochemistry of **2.22** was determined via conversion of crude hydroxy boronate ester to the diol as follows:
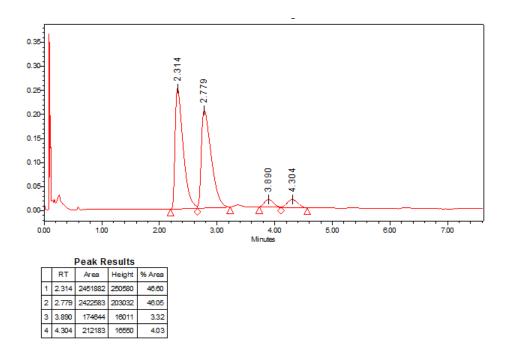
2.75

(1S,3R)-1-phenylhex-5-ene-1,3-diol (2.75). The reaction was performed following the general procedure using (*R*)-styerene oxide (60.1 mg, 0.5 mmol). The crude mixture was dissolved in THF (0.25 mL), a stir bar was added, and the reaction was cooled to 0 °C in an ice water bath. NaOH (3M, 0.25 mL) and H_2O_2 (30%, 0.16 mL) were added. The reaction was sealed with a septum lined cap that was pierced with a vent needle and allowed to warm to room temperature and stir for 3 hours. The reaction was then cooled down to 0 °C in an ice water bath. The reaction was quenched with a saturated solution of sodium thiosulfate, extracted with diethyl ether (x3), dried over magnesium sulfate and concentrated *in vacuo*. The resulting crude mixture was purified via silica gel chromatography (2:1 hexanes:ethyl acetate). Excess pinacol was then removed via azeotropic distillation on the rotary evaporator using a 1:1 mixture of water and methanol with a 55 °C water bath to give diol **2.75** in 56% yield (10.7 mg) and 8:1 dr as a white solid. ^{1}H-NMR spectra matched the literature spectra for the anti-diol.[57]

Major Diastereomer:
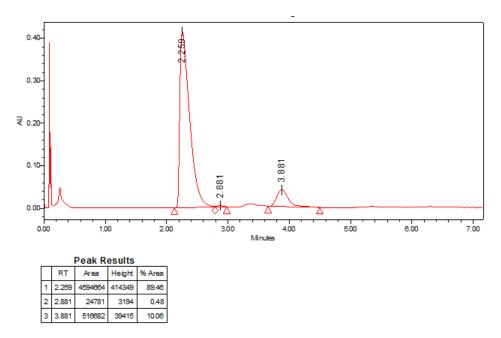
^{1}H NMR (600 MHz, $CDCl_3$) δ 7.50 − 7.34 (m, 4H), 7.34 − 7.29 (m, 1H), 5.87 − 5.69 (m, 1H), 5.26 − 5.13 (m, 2H), 5.09 (dd, *J* = 8.1, 3.4 Hz, 1H), 3.95 (tdd, *J* = 8.0, 4.9, 3.0 Hz, 1H), 3.06 (s, 1H), 2.40 (s, 1H), 2.36 − 2.21 (m, 2H), 2.04 − 1.84 (m, 2H). **[α]$^{22}_D$** = -35.9 (*c* =0.03, CH_2Cl_2, l = 100 mm).

To prove that stereochemistry of the epoxide is maintained throughout the reaction, diol **2.75** was synthesized from both racemic styrene oxide and *R*-styrene oxide. As illustrated by the SFC traces, no erosion of stereochemistry occurs in this reaction.

Trefoil CEL2 (2.1mm x 50 mm x 2.5μm); 98:2 CO₂:iPrOH; 2 mL/min; 210 nm.

Racemic Trace

Peak Results

	RT	Area	Height	% Area
1	2.314	2451882	250580	46.60
2	2.779	2422583	203032	46.05
3	3.890	174644	16011	3.32
4	4.304	212183	16550	4.03

Enantioenriched Material

Peak Results

	RT	Area	Height	% Area
1	2.259	4594664	414349	89.46
2	2.881	24781	3194	0.48
3	3.881	516682	39415	10.06

Anti Diastereomer: Major enantiomer: 2.259 min; Minor enantiomer: 2.881 min; 99.5:0.5 er.
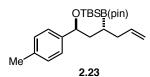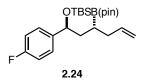
Syn Diasteromer: Major enantiomer: 3.881 min; Minor enantiomer: undetectable; >99:1 er.
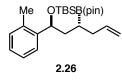
2.23

***Tert*-butyldimethyl((3-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)-1-(*p*-tolyl)hex-5-en-1-yl)oxy)silane (2.23).** Following the general procedure, protected 1,3-hydroxyboronate ester **2.23** was isolated in 53% yield and 10:1 dr (22.7 mg) as a clear oil. **¹H NMR** (600 MHz, CDCl$_3$) δ 7.17 (d, J = 8.0 Hz, 2H), 7.08 (d, J = 7.8 Hz, 2H), 5.77 (ddt, J = 17.0, 10.1, 6.9 Hz, 1H), 4.99 (dt, J = 17.1, 1.7 Hz, 1H), 4.92 (ddd, J = 9.0, 2.3, 1.1 Hz, 1H), 4.62 (t, J = 6.4 Hz, 1H), 2.32 (s, 3H), 2.15 (ddd, J = 5.4, 4.2, 2.4 Hz, 2H), 1.67 (dd, J = 7.8, 6.2 Hz, 2H), 1.24 (s, 12H), 0.86 (s, 9H), 0.01 (s, 3H), -0.20 (s, 3H). **¹³C NMR** (151 MHz, CDCl$_3$) δ 143.6, 138.5, 136.3, 128.8, 125.9, 115.2, 83.1, 83.1, 75.0, 42.7, 36.0, 26.1, 26.1, 25.2, 24.9, 21.3, 18.4, -4.3, -4.7. **IR (ν/cm⁻¹):** 2928 (m), 1381 (s), 1251 (m), 1145 (s), 836 (s). **MS (ESI⁺):** [M+Na]⁺ calcd for C$_{25}$H$_{43}$BO$_3$SiNa⁺ 453.30, found 453.45.

2.24
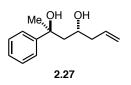
***Tert*-butyl((1-(4-fluorophenyl)-3-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)hex-5-en-1-yl)oxy)dimethylsilane (2.24).** Following the general procedure, protected 1,3-hydroxyboronate ester **2.24** was isolated in 45% yield and 14:1 dr (19.6 mg) as a clear oil.
¹H NMR (600 MHz, CDCl$_3$) δ 7.24 (dd, J = 8.6, 5.6 Hz, 2H), 6.97 (t, J = 8.7 Hz, 2H), 5.76 (ddt, J = 17.0, 10.1, 6.9 Hz, 1H), 4.99 (dd, J = 17.0, 1.8 Hz, 1H), 4.96 - 4.92 (m, 1H), 4.64 (t, J = 6.5 Hz, 1H), 2.23 - 2.08 (m, 2H), 1.65 (dd, J = 8.0, 5.9 Hz, 2H), 1.38 - 1.27 (m, 1H), 1.24 (s, 12H), 0.86 (s, 9H), 0.01 (s, 3H), -0.21 (s, 3H). **¹³C NMR** (151 MHz, CDCl$_3$) δ 161.9 (d, J = 243.8 Hz), 142.3 (d, J = 2.9 Hz), 138.4, 127.5 (d, J = 7.8 Hz), 115.3, 114.9 (d, J = 21.2 Hz), 83.2, 74.5, 42.6, 36.0, 26.0, 25.2, 25.0, 18.3, -4.3, -4.7. **¹⁹F NMR** (376 MHz, CDCl$_3$) δ -116.5 (m). **IR (ν/cm⁻¹):**

2929 (m), 1254 (m), 1144 (m), 835 (s). **MS (ESI⁺):** [M+H]⁺ calcd for $C_{24}H_{41}BFO_3Si^+$ 435.29, found 435.09.

2.25

***Tert*-butyldimethyl((3-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)-1-(*m*-tolyl)hex-5-en-1-yl)oxy)silane (2.25).** Following the general procedure, protected 1,3-hydroxyboronate ester **2.25** was isolated in 70% yield and 10:1 dr (30 mg) as a clear oil.

¹H NMR (600 MHz, CDCl₃) δ 7.16 (t, *J* = 7.5 Hz, 1H), 7.11 – 7.06 (m, 2H), 7.04 – 6.99 (m, 1H), 5.78 (ddt, *J* = 17.0, 10.1, 6.9 Hz, 1H), 4.99 (dd, *J* = 17.1, 1.9 Hz, 1H), 4.96 – 4.89 (m, 1H), 4.62 (dd, *J* = 7.6, 5.2 Hz, 1H), 2.33 (s, 3H), 2.17 (dddd, *J* = 6.8, 5.3, 4.1, 1.3 Hz, 2H), 1.68 (ddd, *J* = 7.2, 5.3, 1.7 Hz, 2H), 1.37 (dq, *J* = 9.0, 6.8 Hz, 1H), 1.25 (s, 12H), 0.87 (s, 9H), 0.02 (s, 3H), -0.20 (s, 3H). **¹³C NMR** (151 MHz, CDCl₃) δ 146.5, 138.5, 137.5, 127.9, 127.6, 126.7, 123.1, 115.2, 83.1, 75.2, 42.7, 36.1, 26.1, 25.3, 24.9, 21.7, 18.4, -4.3, -4.7. **IR (ν/cm⁻¹):** 2928 (b, m), 1471 (m), 1380 (s), 1319 (m), 1254 (s). **MS (ESI⁺)** [M+Na]⁺ calcd for $C_{25}H_{43}BO_3SiNa^+$ 453.30, found 453.45.

2.26

***Tert*-butyldimethyl((3-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)-1-(*o*-tolyl)hex-5-en-1-yl)oxy)silane (2.26).** Following the general procedure, protected 1,3-hydroxyboronate ester **2.26** was isolated in 61% yield and >20:1 dr (26.4 mg) as a clear oil. **¹H NMR** (600 MHz, CDCl₃) δ 7.45 (d, *J* = 7.8 Hz, 1H), 7.19 – 7.13 (m, 1H), 7.10 (td, *J* = 7.4, 1.5 Hz, 1H), 7.08 – 6.99 (m, 1H), 5.78 (ddt, *J* = 17.0, 10.1, 6.9 Hz, 1H), 4.98 (dd, *J* = 17.1, 1.9 Hz, 1H), 4.95 – 4.90 (m, 1H), 4.88 (dd, *J* = 10.1, 2.3 Hz, 1H), 2.34 (s, 3H), 2.23 – 2.12 (m, 2H), 1.70 – 1.59 (m, 1H), 1.53 (m, 2H), 1.27 (s, 6H), 1.26 (s, 6H) 0.87 (s, 9H), 0.01 (s, 3H), -0.23 (s, 3H). **¹³C NMR** (151 MHz, CDCl₃) δ 145.0, 138.5, 129.9, 126.4, 126.1, 125.9, 115.2, 83.2, 41.6, 36.5, 26.1, 25.2, 25.2, 19.3,

18.4, -4.3, -4.8. **IR (v/cm⁻¹):** 2977 (s), 2956 (s), 1380 (s), 1372 (s), 1254 (s), 1144 (s), 1106 (m), 1086 (s), 1057 (m). **MS (ESI⁺)** [M+Na]⁺ calcd for $C_{25}H_{43}BO_3SiNa^+$ 453.30, found 453.45.

2.27

2-phenyl-4-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)hept-6-en-2-ol

(**2.27**). Following the general procedure, 1,3-diol **2.27** was isolated in 58% yield and 5:1 dr (11.9 mg) as a clear oil. **¹H NMR** (600 MHz, CDCl₃) δ 7.43 (dd, J = 8.3, 1.3 Hz, 2H), 7.35 (t, J = 7.7 Hz, 3H), 5.64 (dddd, J = 16.9, 10.3, 7.9, 6.6 Hz, 1H), 5.12 – 5.01 (m, 2H), 4.24 (s, 1H), 3.55 – 3.36 (m, 1H), 2.22 – 2.11 (m, 2H), 2.07 (dd, J = 14.6, 1.9 Hz, 1H), 1.95 (dd, J = 14.6, 10.7 Hz, 1H), 1.52 (s, 3H). **¹³C NMR** (151 MHz, CDCl₃) δ 147.5, 133.9, 128.3, 126.5, 125.0, 118.9, 75.5, 69.0, 48.0, 42.8, 32.7. **IR** (v/cm⁻¹): 3348 (s, br), 2975 (m), 2927 (m), 2360 (m), 1445 (s), 1267 (m). **HRMS** (ESI⁺) [2M+Na]⁺ calcd for $C_{26}H_{36}O_4Na^+$ 435.2512, found 435.2487.

2.28

***tert*-butyldimethyl(((4R,6R)-4-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)hexadec-1-en-6-yl)oxy)silane (2.28).** Following the general procedure, 1,3-hydroxyboronate ester **2.28** was isolated in 73% yield and 3:1 dr (35.0 mg) as a clear oil.

Major Diastereomer

¹H NMR (600 MHz, CDCl₃) δ 5.84 - 5.73 (m, 1H), 5.01 (dd, J = 17.1, 1.9 Hz, 1H), 4.97 - 4.91 (m, 1H), 3.61 (m, 1H), 2.22 - 2.07 (m, 2H), 1.56 (m, 1H), 1.45 - 1.38 (m, 3H), 1.25 – 1.22 (m, 39H), 0.87 (s, 12H), 0.05 (s, 3H), 0.03 (s, 3H). **¹³C NMR** (151 MHz, CDCl₃) δ 138.7, 115.1, 83.1, 72.5, 38.5, 37.9, 36.2, 32.1, 30.0, 29.8, 29.8, 29.8, 29.5, 26.2, 25.8, 25.3, 25.1, 25.0, 24.9, 22.9, 14.3, -4.1 -4.1.

Minor Diastereomer

¹H NMR (600 MHz, CDCl₃) δ 5.84 - 5.73 (m, 1H), 5.01 (dd, J = 17.1, 1.9 Hz, 1H), 4.97 - 4.91 (m, 1H), 3.66 (qd, J = 6.7, 6.0, 4.7 Hz, 1H), 2.22 - 2.07 (m, 2H), 1.56 (m, 1H), 1.45 - 1.38 (m, 3H), 1.25 – 1.22 (m, 39H), 0.87 (s, 12H), 0.05 (s, 3H), 0.03 (s, 3H). **¹³C NMR** (151 MHz, CDCl₃) δ 138.5, 115.2, 83.1, 71.3, 38.6, 36.8, 36.0, 29.9, 29.8, 26.1, 25.8, 25.3, 25.0, 23.0, 18.3, -4.1, -4.3.

IR (ν/cm⁻¹): 2955 (s), 1385 (m), 1321 (m), 1254 (s), 1145 (s), 835 (s). **MS (ESI⁺)** [M+Na]⁺ calcd for C₂₈H₅₇BO₃SiNa⁺ 503.41, found 503.54.

2.29

***tert*-butyl((-1-cyclohexyl-3-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)hex-5-en-1-yl)oxy)dimethylsilane (2.29).** Following the general procedure, 1,3-hydroxyboronate ester **2.29** was isolated in 61% yield and 3:1 d.r. (25.7 mg) as a clear oil.

Major Diastereomer

¹H NMR (600 MHz, CDCl₃) δ 5.78 (ddq, J = 16.9, 10.1, 6.8 Hz, 1H), 5.01 (dq, J = 17.0, 1.5 Hz, 1H), 4.93 (ddd, J = 10.1, 2.2, 1.1 Hz, 1H), 3.53 −3.44 (dt, J = 8.3, 3.6 Hz, 1H), 2.20 – 2.04 (m, 2H), 1.80 – 1.69 (m, 2H), 1.68 – 1.61 (m, 2H), 1.57 – 1.48 (m, 2H), 1.39 – 1.30 (m, 2H), 1.22 (s, 6H), 1.22 (s, 6H), 1.19 – 1.12 (m, 1H), 1.08 (m, 2H), 0.88 (s, 9H), 0.04 (s, 3H), 0.04 (s, 3H). **¹³C NMR** (151 MHz, CDCl₃) δ 138.7, 115.0, 83.0, 76.5, 44.3, 36.4, 34.6, 28.2, 28.0, 27.0, 26.9, 26.9, 26.2, 25.8, 25.1, 25.0.

Minor Diastereomer

¹H NMR (600 MHz, CDCl₃) δ 5.78 (ddq, J = 16.9, 10.1, 6.8 Hz, 1H), 5.01 (dq, J = 17.0, 1.5 Hz, 1H), 4.93 (ddd, J = 10.1, 2.2, 1.1 Hz, 1H), 3.41 – 3.31 (m, 1H), 2.20 – 2.04 (m, 2H), 1.80 – 1.69 (m, 2H), 1.68 – 1.61 (m, 2H), 1.57 – 1.48 (m, 2H), 1.39 – 1.30 (m, 2H), 1.22 (s, 6H), 1.22 (s, 6H), 1.19 – 1.12 (m, 2H), 1.08 (m, 3H), 0.88 (s, 9H), 0.04 (s, 3H), 0.04 (s, 3H). **¹³C NMR** (151 MHz, CDCl₃) δ 138.5, 115.2, 83.1, 75.1, 41.8, 41.6, 36.3, 36.0, 35.1, 30.1, 29.3, 27.2, 27.0, 26.2, 26.01 25.8.

IR (ν/cm⁻¹): 2928 (s), 2855 (m), 1381 (m), 1254 (m), 1145 (s), 1067 (m). **MS (ESI⁺)** [M+Na]⁺ calcd for $C_{24}H_{47}BO_3SiNa^+$ 445.33, found 445.54.

2.30

2,2,3,3,8,8,9,9-octamethyl-5-(2-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)pent-4-en-1-yl)-4,7-dioxa-3,8-disiladecane (2.30). Following the general procedure, 1,3-hydroxyboronate ester **2.30** was isolated in 80% yield and 1.7:1 dr (39.0 mg) as a clear oil.
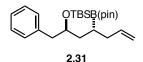
Major Diastereomer

¹H NMR (600 MHz, CDCl₃) δ 5.85 - 5.72 (m, 1H), 5.00 (dd, *J* = 17.1, 1.8 Hz, 1H), 4.97 - 4.90 (m, 1H), 3.69 - 3.63 (m, 1H), 3.54 - 3.46 (m, 2H), 2.25 - 2.09 (m, 2H), 1.53 (m, 1H), 1.35 - 1.27 (m, 1H), 1.22 (s, 12H), 0.90 (s, 9H), 0.87 (s, 9H), 0.07 (s, 3H), 0.06 (s, 3 H) 0.04 (s, 3H), 0.03 (s, 3H). **¹³C NMR** (151 MHz, CDCl₃) δ 138.7, 115.1, 83.0, 73.5, 68.3, 36.4, 35.9, 26.2, 26.2, 25.1, 25.0, 18.6, 18.3, -3.9, -4.5, -5.1, -5.2.

Minor Diastereomer

¹H NMR (600 MHz, CDCl₃) δ 5.85 - 5.72 (m, 1H), 5.00 (dd, *J* = 17.1, 1.8 Hz, 1H), 4.97 - 4.90 (m, 1H), 3.74 - 3.69 (m, 1H), 3.39 (dd, *J* = 10.1, 5.8 Hz, 2H), 2.25 - 2.09 (m, 2H), 1.74 - 1.66 (m, 1H), 1.35 - 1.27 (m, 1H), 1.22 (s, 12H), 0.88 (s, 9H), 0.88 (s, 9H), 0.03- 0.07 (m, 6H). **¹³C NMR** (151 MHz, CDCl₃) δ 138.4, 115.3, 83.1, 72.4, 67.9, 35.4, 35.2, 26.1, 26.1, 25.1, 25.0,18.6, 18.4, -4.0, -4.5, -5.1, -5.1.

IR (ν/cm⁻¹): 2927 (s), 2855 (s), 1380 (m), 1371 (m), 1254 (m), 1146 (s), 1067 (m), 836 (m). **MS (ESI⁺)** [M+H]⁺ calcd for $C_{25}H_{54}BO_4Si^+$ 485.37, found 485.09.

2.31

***Tert*-butyldimethyl((1-phenyl-4-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)hept-6-en-2-yl)oxy)silane (2.31).** Following the general procedure, 1,3-hydroxyboronate ester **2.31** was isolated in 70% yield and 1:1 dr (30.4 mg) as a clear oil.

Major Diastereomer

¹H NMR (600 MHz, CDCl₃) δ 7.24 (dd, *J* = 7.4, 3.2 Hz, 2H), 7.20 – 7.15 (m, 3H), 5.78 (tdd, *J* = 10.0, 6.5, 3.0 Hz, 1H), 5.06 – 4.98 (m, 1H), 4.97 – 4.86 (m, 1H), 3.89 – 3.77 (m, 1H), 2.71 (qd, *J* = 13.4, 6.2 Hz, 2H), 2.53 (dd, *J* = 13.3, 8.2 Hz, 1H), 2.15 (m, 2H), 1.54 (m 1H), 1.48 – 1.39 (m, 2H), 1.18 (s, 6H), 1.18 (s, 6H), 0.84 (s, 9H), -0.02 (s, 3H), -0.19 (s, 3H). **¹³C NMR** (151 MHz, CDCl₃) δ139.6, 138.3, 129.9, 128.1, 126.0, 115.2, 83.1, 73.8, 44.6, 38.4, 36.1, 26.1, 25.8, 25.0, 24.9, 18.2, -4.4, -4.6.
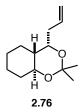
Minor Diastereomer

¹H NMR (600 MHz, CDCl₃) δ 7.24 (dd, *J* = 7.4, 3.2 Hz, 2H), 7.20 – 7.15 (m, 3H), 5.78 (tdd, *J* = 10.0, 6.5, 3.0 Hz, 1H), 5.06 – 4.98 (m, 1H), 4.97 – 4.86 (m, 1H), 3.89 – 3.77 (m, 1H), 2.86 (dd, *J* = 13.3, 3.7 Hz, 1H), 2.15 (m, 2H), 1.70 – 1.63 (m, 1H), 1.64 – 1.54 (m, 2H), 1.26 (s, 6H), 1.26 (s, 6H), 0.80 (s, 9H), -0.12 (s, 3H), -0.35 (s, 3H). **¹³C NMR** (151 MHz, CDCl₃) δ 139.6, 138.3,130.1, 128.0, 125.9, 83.3, 73.4, 43.4, 39.2, 36.2, 25.8, 25.0, 25.0, 18.2, -4.6, -5.1.

IR (ν/cm⁻¹): 2955 (s), 2928 (s), 1380 (s), 1254 (s), 1144 (s), 1081 (s), 836 (s). **MS (ESI⁺)** [M+Na]⁺ calcd for $C_{25}H_{43}BO_3SiNa^+$ 453.30, found 453.45.

2.32
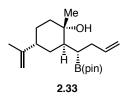
***tert*-butyldimethyl((2-(1-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)but-3-en-1-yl)cyclohexyl)oxy)silane (2.32).** Following the general procedure, 1,3-hydroxyboronate ester **2.32** was isolated in 74% yield and 20:1 dr (29.0 mg) as a clear oil. **¹H NMR** (600 MHz,

179

CDCl$_3$) δ 5.86 - 5.75 (m, 1H), 5.00 (dd, J = 17.1, 1.9 Hz, 1H), 4.94 - 4.88 (m, 1H), 3.54 (td, J = 9.5, 4.3 Hz, 1H), 2.36 - 2.27 (m, 1H), 2.05 - 1.95 (m, 1H), 1.88 - 1.82 (m, 1H), 1.82 - 1.75 (m, 1H), 1.71 (m, 1H), 1.66 (ddd, J = 9.2, 3.7, 1.9 Hz, 1H), 1.60 - 1.55 (m, 1H), 1.41 - 1.30 (m, 1H), 1.22 (m, 2H) 1.22 (s, 6H), 1.21 (s, 6H), 1.14 - 1.05 (m, 1H), 1.02 - 0.95 (m, 1H), 0.88 (m, 9H), 0.09 (s, 3H), 0.06 (s, 3H). **^{13}C NMR** (151 MHz, CDCl$_3$) δ 139.8, 114.4, 82.8, 74.0, 47.2, 36.4, 33.9, 28.4, 26.2, 25.9, 25.3, 25.1, 25.0, 18.3, -3.8, -4.6. **IR (ν/cm^{-1}):** 2929 (s), 2856 (s), 1471 (w), 1387 (m), 1371 (m), 1255 (m), 1144 (m), 1089 (m). **MS (ESI$^+$)** [M+Na]$^+$ calcd for C$_{22}$H$_{43}$BO$_3$SiNa$^+$ 417.47, found 417.45.
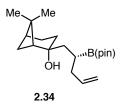

2.76

Stereochemistry of **2.32** was determined via transformation to the corresponding acetonide **2.76** according to the following procedure:[58] Following the general procedure, the crude hydroxy boronate was dissolved in THF (0.25 mL) in an 8 mL vial with a stir bar and septum cap. The vial was cooled to 0 °C in an ice bath. NaOH (3M, 0.25 mL) and H$_2$O$_2$ (30%, 0.16 mL) were added to the reaction at 0 °C. The septa cap was vented with a needle, allowed to warm to room temperature, and stirred for 3 hours. The reaction was then cooled back to 0 °C and quenched with saturated sodium thiosulfate, extracted with diethyl ether, dried over magnesium sulfate, and concentrated *in vacuo*. The crude mixture was then plugged through silica (2:1 hexanes:ethyl acetate) and concentrated *in vacuo*. Pinacol was removed via azeotropic distillation from a 1:1 mixture of methanol and water. The product was then dissolved in DMF (0.6 mL) in an 8 mL vial containing a stir bar and sealed with a septum cap. The vial was purged with nitrogen and 2,2-dimethoxypropane was added (0.069 mL, 10 eq) to the vial. The cap was then quickly removed and pyridinium *p*-toluenesulfonate (0.7 mg, 5 mol%) was added. The vial was then sealed, purged with nitrogen for two minutes, and then allowed to stir at room

temperature for one hour. One drop of triethylamine was added to the reaction followed by a saturated solution of sodium bicarbonate. The mixture was extracted with diethyl ether, dried over magnesium sulfate, and concentrated *in vacuo*. The crude mixture was purified via column chromatography (10:1 hexanes: diethyl ether) to yield the product in 56% yield and >20:1 dr (12.2 mg) as a clear oil. **^{1}H NMR** (600 MHz, C_6D_6) δ 5.99 (ddt, *J* = 17.1, 10.6, 6.7 Hz, 1H), 5.23 – 4.95 (m, 2H), 3.96 (ddd, *J* = 11.1, 7.3, 4.5 Hz, 1H), 3.51 (td, *J* = 10.6, 4.2 Hz, 1H), 2.52 – 2.22 (m, 1H), 2.17 – 1.99 (m, 1H), 1.98 – 1.82 (m, 1H), 1.65 (m, 1H), 1.54 (m, 1H), 1.48 (s, 3H), 1.45 (m, 4H), 1.37 (m, 2H), 1.24 – 1.15 (m, 1H), 1.07 (m, 1H), 0.99 – 0.91 (m, 1H), 0.90 – 0.73 (m, 1H). **^{13}C NMR** (151 MHz, C_6D_6) δ 137.1, 128.4, 116.0, 99.2, 72.2, 69.4, 45.0, 36.2, 33.2, 28.3, 26.4, 26.3, 26.2, 25.0. **IR (v/cm^{-1}):** 3854 (m), 3711 (m), 3566 (m), 2933 (m), 1748 (m), 1540 (s), 1507 (s). **MS (ESI$^+$):** [M+H]$^+$ calcd for $C_{13}H_{24}O_2^+$ 211.17, found 211.18.

2.33

(1*R*,2*S*,4*S*)-1-methyl-4-(prop-1-en-2-yl)-2-((*R*)-1-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)but-3-en-1-yl)cyclohexan-1-ol (2.33). Following the general procedure with 0.2 mmol of limonene oxide, 1,3-hydroxyboronate ester **2.33** was isolated in 42% yield and >20:1 dr. (13.9 mg) as a clear oil. Yield was calculated assuming only one of the isomers of starting material reacts to give product. **^{1}H NMR** (600 MHz, CDCl$_3$) δ 5.78 (ddt, *J* = 17.0, 10.1, 6.8 Hz, 1H), 5.04 (dd, *J* = 17.1, 1.8 Hz, 1H), 4.99 – 4.92 (m, 1H), 4.85 – 4.75 (m, 2H), 2.35 – 2.13 (m, 3H), 1.94 (dddd, *J* = 14.0, 6.0, 3.9, 1.5 Hz, 1H), 1.76 (d, *J* = 8.5 Hz, 1H), 1.72 (s, 3H), 1.67 (dt, *J* = 9.0, 4.3 Hz, 1H), 1.62 – 1.55 (m, 1H), 1.52 (dq, *J* = 9.1, 4.0 Hz, 3H), 1.37 (dt, *J* = 10.2, 5.4 Hz, 1H), 1.23 (s, 6H), 1.22 (s, 6H), 1.21 (s, 3H). **^{13}C NMR** (151 MHz, CDCl$_3$) δ 147.8, 138.8, 115.5, 110.2, 83.2, 73.9, 46.5, 38.7, 37.4, 36.5, 30.4, 26.5, 25.2, 25.2, 24.9, 22.1. **IR (v/cm^{-1}):** 3437 (br, m), 2977 (m), 1388 (m), 1371 (m), 1321 (m), 1143 (s). **HRMS (ESI$^+$)** [2M+Na]$^+$ calcd for $C_{40}H_{70}O_6Na^+$ 691.5257, found 691.5244. **[α]^{22}$_D$** = -10.3 (*c* =-0.7, CH$_2$Cl$_2$, l = 100 mm).

2.34

(1R,2R,5S)-2-((S)-2-hydroxypent-4-en-1-yl)-6,6-dimethylbicyclo[3.1.1]heptan-2-ol

(2.34). Following the general procedure, 1,3-hydroxyboronate ester **2.34** was isolated in 60%
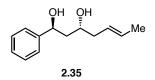
yield in 2:1 d.r. (12.6 mg) as a yellow solid.

Major Disastereomer

¹H NMR (600 MHz, CDCl$_3$) δ 5.88 − 5.76 (m, 1H), 5.14 − 5.09 (m, 2H), 4.12 (dddd, J = 10.5,

7.0, 5.6, 1.6 Hz, 1H), 3.48 (s, 1H), 2.85 (s, 1H), 2.28 − 2.15 (m, 2H), 2.07 − 1.98 (m, 1H), 1.94 (td,

J = 6.0, 3.4 Hz, 1H), 1.91 − 1.72 (m, 4H), 1.38 (dd, J = 14.2, 10.4 Hz, 1H), 1.23 (s, 3H), 1.13 (s,

3H), 1.00 (d, J = 10.4 Hz, 1H). **¹³C NMR** (151 MHz, CDCl$_3$) δ 134.8, 118.1, 79.4, 68.6, 54.0, 47.9,

42.9, 40.8, 38.6, 29.6, 27.9, 27.7, 24.2, 23.7.

Minor Diastereomer
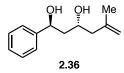
¹H NMR (600 MHz, CDCl$_3$) δ 5.88 − 5.76 (m, 1H), 5.14 − 5.09 (m, 2H), 3.89 (dtd, J = 10.9, 6.2,

1.9 Hz, 1H), 3.48 (s, 1H), 2.85 (s, 1H), 2.28 − 2.15 (m, 2H), 2.07 − 1.98 (m, 1H), 1.94 (td, J = 6.0,

3.4 Hz, 1H), 1.91 − 1.72 (m, 4H), 1.38 (dd, J = 14.2, 10.4 Hz, 1H), 1.26 (s, 3H), 1.13 (s, 3H), 0.92

(d, J = 9.8 Hz, 1H). **¹³C NMR** (151 MHz, CDCl$_3$) δ 134.7, 118.1, 79.1, 68.0, 49.8, 47.2, 42.7, 40.8,

38.1, 28.4, 27.8, 27.7, 24.8, 23.6.

MS (ESI⁺) [M+Na]⁺ calcd for C$_{14}$H$_{24}$O$_2$Na⁺ 247.17, found 247.27.**IR (ν/cm⁻¹):** 3392 (br, s),

2915 (s), 1651 (w), 1540 (s), 1507 (w), 995 (w), 914 (s), 750 (w).

2.35

(1*S*,3*R*,*E*)-1-phenylhept-5-ene-1,3-diol (2.35). Following the general procedure, 1,3-diol

2.35, was isolated in 52% yield (10.7 mg) in 3:1 S$_N$2' (2:1 dr) to S$_N$2 (2:1 dr) ratio. **¹H NMR** (600

MHz, CDCl$_3$) δ 7.47 − 7.36 (m, 7H), 7.33 − 7.28 (m, 2H), 5.82 − 5.63 (m, 1H), 5.63 − 5.52 (m,

1H), 5.48 – 5.33 (m, 1H), 5.10 (m, 1H), 4.97 (m, 1H), 3.94 (m, 1H), 3.88 (m, 1H), 3.77 (m, 1H), 3.66 (m, 1H), 3.17 (s, 1H), 3.08 (s, 1H), 2.87 (s, 1H), 2.48 – 2.13 (m, 5H), 2.09 – 1.85 (m, 0H), 1.71 (d, J = 5.1 Hz, 2H), 1.67 (d, J = 5.1 Hz, 2H), 1.06 (d, J = 6.8 Hz, 1H), 1.03 (d, J = 6.8 Hz, 1H).

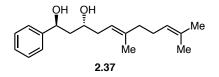**^{13}C NMR (151 MHz, CDCl$_3$)** δ 144.7, 144.7, 144.6, 140.6, 140.3, 129.7, 129.7, 128.6, 128.6, 128.6, 128.6, 127.9, 127.7, 127.4, 127.4, 127.4, 126.7, 125.8, 125.8, 125.7, 125.7, 125.6, 117.1, 115.9, 71.9, 71.9, 71.9, 71.9, 69.0, 68.4, 44.1, 43.9, 41.8, 40.9, 35.1, 25.0, 18.3, 15.1, 13.3. **IR (ν/cm^{-1}):** 3366 (br, s), 2917 (m), 2360 (m), 1452 (m), 1053 (m). **HRMS (ESI$^+$)** [2M+Na]$^+$ calcd for C$_{26}$H$_{36}$O$_4$Na$^+$ 435.2512, found 435.2493.

2.36
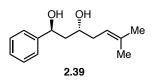
1S,3R)-5-methyl-1-phenylhex-5-ene-1,3-diol (2.36). Following the general procedure, 1,3-diol **2.36**, was isolated in 93% yield in 10:1 d.r. (191.1 mg) as a white solid.

^{1}H NMR (600 MHz, CDCl$_3$) δ 7.40 – 7.26 (m, 5H), 5.09 (dd, J = 8.5, 3.0 Hz, 1H), 4.89 (m, 1H), 4.80 (tq, J = 2.1, 1.0 Hz, 1H), 4.02 (m, 1H), 3.02 (s, 1H), 2.29 – 2.17 (m, 3H), 1.99 – 1.81 (m, 2H), 1.72 (t, J = 1.1 Hz, 3H), 1.59 (d, J = 23.2 Hz, 1H). **^{13}C NMR** (151 MHz, CDCl$_3$) δ 144.7, 142.4, 128.6, 127.4, 125.7, 114.0, 71.7, 66.2, 46.2, 44.6, 22.5. **IR (ν/cm^{-1}):** 3388 (s, br), 3073 (w), 2917 (s), 1646 (m), 1455 (s), 1059 (s), 890 (m), 700 (s). **MS (ESI$^+$)** [M+Na]$^+$ calcd for C$_{13}$H$_{18}$O$_2$Na$^+$ 229.12, found 229.27. **[α]^{22}$_D$** = -8.45 (c = 2.14, CH$_2$Cl$_2$, l = 100 mm).

2.37
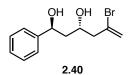
(E)-6,10-dimethyl-1-phenylundeca-5,9-diene-1,3-diol (2.37). Following the general procedure, 1,3-diol **2.37** was isolated in 47% yield in 4:1 dr (11.3 mg) as a clear oil. **^{1}H NMR** (500 MHz, CDCl$_3$) δ 7.36 (td, J = 8.3, 6.2 Hz, 4H), 7.29 – 7.23 (m, 1H), 5.26 – 4.97 (m, 3H), 3.85 (qd, J = 4.9, 1.6 Hz, 1H), 3.21 (s, 1H), 2.27 – 1.85 (m, 8H), 1.67 (s, 3H), 1.63 (s, 3H), 1.59 (s, 3H). **^{13}C NMR** (151 MHz, CDCl$_3$) δ 144.7, 139.6, 132.0, 128.5, 127.3, 125.7, 124.2, 119.7, 71.9, 69.1,

44.0, 40.0, 36.2, 26.6, 25.9, 17.9, 16.4. **IR (ν/cm⁻¹):** 3370 (s, br), 2915 (s), 1452 (m), 1057 (m), 700 (s). **HRMS (ESI⁺)** [2M+Na]⁺ calcd for $C_{38}H_{56}O_4Na^+$ 599.4077, found 599.4064. **[α]²²_D** = -23.5 (*c* =-0.625, CH₂Cl₂, l = 100 mm).

2.38
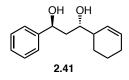
(1S,3R)-4-(cyclohex-1-en-1-yl)-1-phenylbutane-1,3-diol (2.38). Following the general procedure, 1,3-diol **2.38** was recrystallized from pentane and diethyl ether to give 86% yield in >20:1 d.r. (21.2 mg) as a white solid. **¹H NMR** (600 MHz, CDCl₃) δ 7.40 – 7.27 (m, 5H), 5.57 – 5.51 (m, 1H), 5.08 (m, *J* = 8.0, 3.7 Hz, 1H), 3.95 (m, *J* = 11.2, 8.2, 5.0, 2.7 Hz, 1H), 3.18 (d, *J* = 4.3 Hz, 1H), 2.19 (d, *J* = 2.5, 0.9 Hz, 1H), 2.18 – 2.09 (m, 2H), 2.04 – 1.99 (br s, 2fH), 1.89 (m, *J* = 68.8, 14.6, 8.5, 3.1 Hz, 4H), 1.61 (m, *J* = 11.0, 4.8, 2.3 Hz, 1H), 1.57 – 1.52 (m, 1H). **¹³C NMR** (151 MHz, CDCl₃) δ 144.8, 134.4, 128.5, 127.3, 125.7, 71.7, 66.2, 46.5, 44.5, 28.4, 25.4, 22.9, 22.4. **IR (ν/cm⁻¹):** 3365 (br, s), 2924 (s), 1652 (m), 1540 (m), 1455 (s), 1055 (m), 700 (m). **MS (ESI⁺)** [M+Na]⁺ calcd for $C_{16}H_{22}O_2Na^+$ 269.15, found 269.27. **[α]²²_D** = -12.04 (*c* = 0.195, CH₂Cl₂, l = 100 mm).


2.39

(1*S*,3*R*)-6-methyl-1-phenylhept-5-ene-1,3-diol (2.39). Following the general procedure, 1,3-diol **2.39**, was isolated in 49% yield (10.7 mg) in 6:1 dr. **¹H NMR** (600 MHz, CDCl₃) δ 7.45 – 7.35 (m, 4H), 7.30 (m, 1H), 5.23 – 5.12 (m, 1H), 5.09 (dd, *J* = 8.0, 3.4 Hz, 1H), 3.98 – 3.77 (m, 1H), 2.30 (m, 2H), 2.19 (m, 1H), 1.94 (qdd, *J* = 14.6, 8.2, 3.2 Hz, 2H), 1.75 (s, 3H), 1.66 (s, 3H). **¹³C NMR** (151 MHz, CDCl₃) δ 144.7, 135.9, 128.5, 127.4, 1 25.7, 119.7, 71.9, 69.2, 44.1, 36.3, 26.1, 18.2. **IR (ν/cm⁻¹):** 3420 (s, br), 2966 (w), 2915 (w), 1695 (m), 1454 (w), 1054 (m), 755 (m), 700 (m). **MS (ESI⁺)** [M+Na]⁺ calcd for $C_{14}H_{20}O_2Na^+$ 243.14, found 243.27. **[α]²²_D** = -36.5 (*c* =-0.42, CH₂Cl₂, l = 100 mm).
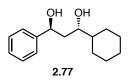
2.40

(1*S*,3*S*)-5-bromo-1-phenylhex-5-ene-1,3-diol (2.40). Following the general procedure, 1,3-diol **2.40** was isolated in 42% yield in 7:1 dr (11.3 mg) as a clear oil. **¹H NMR** (500 MHz, CDCl$_3$) δ 7.40 − 7.34 (m, 4H), 7.29 (ddd, *J* = 9.1, 5.2, 2.3 Hz, 1H), 5.70 (d, *J* = 1.5 Hz, 1H), 5.54 (d, *J* = 1.7 Hz, 1H), 5.08 (dd, *J* = 8.6, 3.2 Hz, 1H), 4.30 − 4.20 (m, 1H), 2.77 (br,s, 1H), 2.66 (ddd, *J* = 14.4, 8.4, 0.9 Hz, 1H), 2.58 (ddd, *J* = 14.4, 4.4, 1.2 Hz, 1H), 2.50 (m, 1H), 1.97 (ddd, *J* = 14.5, 8.6, 3.0 Hz, 1H), 1.89 (ddd, *J* = 14.6, 8.5, 3.3 Hz, 1H). **¹³C NMR** (151 MHz, CDCl$_3$) δ 144.3, 130.3, 128.7, 127.7, 125.7, 120.0, 71.7, 66.8, 49.2, 43.9. **IR (v/cm⁻¹):** 3367 (br, s), 2917 (m), 1630 (s), 1125 (m), 1061 (s), 891 (m). **HRMS (ESI⁺)** [2M+Na]⁺ calcd for C$_{24}$H$_{30}$Br$_2$O$_4$Na⁺ 563.0409, found 563.0376. **[α]²²$_D$** = -31.2 (*c* =-0.475, CH$_2$Cl$_2$, l = 100 mm).

2.41
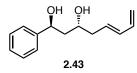
(1*S*,3*S*)-1-(cyclohex-2-en-1-yl)-3-phenylpropane-1,3-diol (2.41). Following the general procedure, 1,3-diol **2.41** was isolated in 68% yield in 5:1 dr with respect to alcohol stereocenters and 1:1 dr of each with respect to the cyclohexane stereocenter (15.8 mg) as a white solid. **¹H NMR** (600 MHz, CDCl$_3$) δ 7.49 − 7.34 (m, 4H), 7.34 − 7.28 (m, 1H), 5.87 (dt, *J* = 10.0, 3.1 Hz, 1H), 5.70 (dd, *J* = 10.2, 2.4 Hz, 1H), 5.56 (dd, *J* = 10.2, 2.4 Hz, 1H), 5.10 (dt, *J* = 5.6, 2.7 Hz, 1H), 3.85 (m, 1H), 3.78 − 3.69 (m, 1H), 2.99 − 2.91 (m, 1H), 2.26 (m, 1H), 2.09 − 1.85 (m, 5H), 1.85 − 1.68 (m, 3H), 1.61 − 1.44 (m, 2H). **¹³C NMR** (151 MHz, CDCl$_3$) δ 144.7, 144.7, 130.9, 130.4, 128.6, 128.6, 128.0, 127.5, 127.4, 126.8, 125.8, 125.7, 125.6, 72.6, 72.0, 72.0, 71.6, 53.6, 42.2, 41.7, 41.6, 41.5, 25.6, 25.4, 23.3, 21.7, 21.4. **IR (v/cm⁻¹):** 3366 (s, br), 2925 (m), 1603 (m), 1450 (m), 1048 (m). **MS (ESI⁺)** [2M+Na]⁺ calcd for C$_{30}$H$_{40}$O$_4$Na⁺ 487.2824, found 487.2816. **[α]²²$_D$** = -21.9 (*c* =-0.425, CH$_2$Cl$_2$, l = 100 mm).

To confirm the diastereoselectivity, **2.41** was hydrogenated according to the following

procedure:

2.77
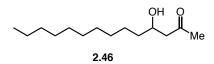
Diol **2.77** (7 mg, 0.03 mmol) was dissolved in MeOH (0.5 mL) in an 8 mL vial containing a stir

bar. The vial was sealed with a septum lined cap and purged with nitrogen. The cap was briefly

removed and 10% palladium on carbon (0.7 mg) was added. The reaction was sealed and the vial

was purged with nitrogen. A balloon of hydrogen was then attached and the reaction was

sparged with hydrogen and then allowed to stir under an atmosphere of hydrogen for 1 hour.

The reaction was quenched by passing the mixture over a pad of Celite followed by

concentration *in vacuo*. The crude material was purified via column chromatography (2:1

hexanes:ethyl acetate) to yield the desired hydrogenated product in 94% yield (6.4 mg). The

NMR matched literature spectra and confirmed the 5:1 d.r. at the two alcohol stereocenters.[59] **¹H**

NMR (600 MHz, CDCl$_3$) δ 7.46 − 7.35 (m, 4H), 7.29 (d, J = 3.8 Hz, 1H), 5.10 (t, J = 5.7 Hz, 1H),

3.64 (q, J = 6.1 Hz, 1H), 2.98 (s, 1H), 2.14 (s, 1H), 2.00 − 1.90 (m, 2H), 1.89 − 1.83 (m, 1H), 1.81

− 1.73 (m, 2H), 1.71 − 1.65 (m, 2H), 1.40 (m, 1H), 1.24 (m, 2H), 1.15 (tt, J = 12.8, 3.4 Hz, 1H),

1.05 − 0.91 (m, 2H). **¹³C NMR** (151 MHz, CDCl$_3$) δ 144.8, 128.6, 128.6, 127.4, 125.6, 73.6, 72.0,

43.7, 41.7, 29.1, 28.3, 26.6, 26.3, 26.2.

2.43
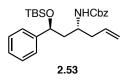
(1S,3R,E)-1-phenylocta-5,7-diene-1,3-diol (2.43). Following the general procedure, 1,3-

diol **2.43** was isolated in 45% yield (10.1 mg) in 8:1 d.r. **¹H NMR** (600 MHz, CDCl$_3$) δ 7.39 −

7.27 (m, 5H), 6.31 (dt, J = 17.0, 10.3 Hz, 1H), 6.14 (dd, J = 15.3, 10.4 Hz, 1H), 5.66 (dt, J = 15.1,

7.5 Hz, 1H), 5.14 (dd, J = 16.8, 1.7 Hz, 1H), 5.07 (d, J = 4.4 Hz, 1H), 5.03 (d, J = 10.1 Hz, 1H),

3.93 (d, J = 6.2 Hz, 1H), 2.93 (s, 1H), 2.39 − 2.22 (m, 3H), 1.91 (qdd, J = 14.5, 8.2, 3.1 Hz, 2H).

¹³C NMR (151 MHz, CDCl₃) δ 144.5, 136.8, 134.7, 130.1, 128.6, 127.5, 125.7, 116.5, 71.9, 68.5, 44.2, 40.9. **IR (ν/cm⁻¹):** 3351 (br, s), 2916 (s), 2297 (w), 1650 (m), 1556 (w), 1454 (m), 1004 (s), 758 (m). **MS (ESI⁺)** [M+Na]⁺ calcd for $C_{14}H_{18}O_2Na^+$ 241.12, found 241.27. **[α]²²_D** = -10.48 (*c* = 0.38, CH₂Cl₂, l = 100 mm).

2.46
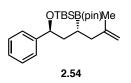
4-hydroxytetradecan-2-one (2.46). In a nitrogen filled glovebox, diborylethane (42.0 mg, 0.15 mmol) was weighed into an 8-mL vial equipped with a magnetic stir bar. The diborylethane was dissolved in THF (0.4 ml) and the vial was sealed with a septa-lined cap and taped. Lithium 2,2,6,6-tetramethylpiperidide (LTMP) (22.8 mg, 0.15 mmol) was weighed into a separate 8-mL vial, dissolved in THF (0.8 mL) and sealed with a septum lined cap and tape. The vials were removed from the dry box and the diborylethane and LTMP were cooled to 0 ºC in an ice water bath. The LTMP solution was transferred via cannula to the diborylethane solution at 0 ºC. This was allowed to stir at 0 ºC for 10 minutes. Dodeceneoxide (0.1 mmol) was then added via syringe and the solution was brought to room temperature and stirred for 24 hours. The reaction was quenched with saturated ammonium chloride, extracted with ether (x3), dried over magnesium sulfate and concentrated *in vacuo*. The resulting crude mixture was dissolved in THF (0.25 mL) and cooled to 0 ºC in an ice water bath. NaOH (0.25 mL, 3M) and H₂O₂ (0.125 mL, 30%) were added and the reaction was allowed to stir and slowly warm to room temperature over two hours. The reaction was then cooled back to 0 ºC in an ice bath and quenched with a saturated solution of sodium thiosulfate. The mixture was warmed to room temperature, extracted with ether (x3), dried over magnesium sulfate, and concentrated *in vacuo* and purified via silica gel chromatography. **2.46** was isolated in 80% yield (18.0 mg) as a white solid. **¹H NMR** (500 MHz, CDCl₃) δ 4.02 (m, 1H), 2.97 (d, *J* = 3.3 Hz, 1H), 2.63 (dd, *J* = 17.7, 2.7 Hz, 1H), 2.52 (dd, *J* = 17.7, 9.2 Hz, 1H), 2.18 (s, 3H), 1.56 – 1.44 (m, 1H), 1.39 (m, 2H), 1.25 (s, 15H), 0.87 (t, *J* = 6.9 Hz, 3H). **¹³C NMR** (151 MHz, CDCl₃) δ 210.3, 67.7, 50.1, 36.5,

32.0, 30.9, 29.8, 29.8, 29.7, 29.7, 29.5, 25.6, 22.8, 14.3. **IR (ν/cm⁻¹):** 3324 (m, br), 3234 (m, br), 2916 (s), 2848 (s), 1708 (s), 1464 (m). **HRMS (ESI⁺)** [2M+Na]⁺ calcd for $C_{38}H_{56}O_4Na^+$ 479.4077, found 479.4060.
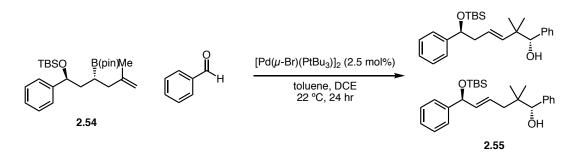

2.53

benzyl ((1S,3R)-1-((tert-butyldimethylsilyl)oxy)-1-phenylhex-5-en-3-yl)carbamate (2.53). Following a literature procedure,[48] a solution of O-methylhydroxylamine in THF (2.5 mL, 1.45 mmol, 0.38 M) and THF (2.7 mL) were added to a flame dried 25 mL single neck round bottom flask containing a stir bar under inert nitrogen atmosphere. The flask was cooled to -78 °C in a dry ice/acetone bath. *n*-BuLi (1.09 mL, 1.45 mmol, 1.33M in hexanes) was added and the solution was allowed to stir at -78 °C for 30 minutes. A separate flame dried 8 mL vial was charged with 1,3-hydroxyboronate ester (**2.53**) (201.3 mg, 0.48 mmol) and diluted with THF (1 mL) under N₂. The solution of 1,3-hydroxyboronate ester was then added dropwise via syringe to the solution of deprotonated O-methylhydroxylamine at -78 °C. The reaction flask was warmed to room temperature and then heated to 60 °C. After stirring at 60 °C for 16 hours, the reaction flask was cooled to room temperature and benzyl chloroformate (0.22 mL, 1.55 mmol) was added. After stirring at room temperature for 1 hour the reaction was quenched with water (10 mL). The layers were separated and the aqueous layer was extracted with EtOAc (3 x 20 mL). The combined organics were dried over sodium sulfate, concentrated, and purified via column chromatography (95:5 hexanes:EtOAc) to give the desired carbamate **31** in 87% yield in 16:1 d.r. (184.2 mg) as a white solid. **¹H NMR** (600 MHz, CDCl₃) δ 7.41 – 7.23 (m, 10H), 5.82 – 5.72 (m, 1H), 5.22 (d, *J* = 8.1 Hz, 1H), 5.17 – 5.02 (m, 4H), 4.83 (dd, *J* = 9.3, 2.8 Hz, 1H), 3.93 – 3.84 (m, 1H), 2.44 – 2.26 (m, 2H), 1.93 (ddd, *J* = 15.3, 10.9, 5.5 Hz, 1H), 1.67 (t, *J* = 14.7, 8.8, 2.9 Hz, 1H), 0.90 (s, 9H), 0.06 (s, 3H), -0.26 (s, 3H). **¹³C NMR** (151 MHz, CDCl₃) δ 155.9, 145.0, 136.9, 134.6, 128.6, 128.4, 128.2, 128.1, 127.4, 125.9, 117.9, 72.7, 66.5, 48.5, 44.6, 39.7, 26.0, 18.2,

-4.4, -5.0. **IR (v/cm⁻¹):** 3326 (m), 3065 (m), 2928 (s), 2856 (s), 1708 (s), 1530 (s), 1256 (m), 1096 (s). **[α]²²_D** = -31.73 (c = 3.32, CH₂Cl₂, l = 100 mm).

2.54
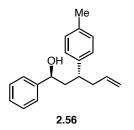
***tert*-butyldimethyl((($1S,3R$)-5-methyl-1-phenyl-3-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)hex-5-en-1-yl)oxy)silane (2.54).** Following the general procedure, 1,3-hydroxyboronate ester **2.54** was isolated in 67% yield in >20:1 d.r. (29.0 mg) as a clear oil. **¹H NMR** (600 MHz, CDCl₃) δ 7.28 (d, J = 4.3 Hz, 4H), 7.20 (h, J = 4.3 Hz, 1H), 4.70 − 4.66 (m, 2H), 4.64 (dd, J = 9.3, 3.4 Hz, 1H), 2.18 (dd, J = 14.3, 7.2 Hz, 1H), 2.02 (dd, J = 14.3, 8.5 Hz, 1H), 1.70 (s, 3H), 1.66 (ddd, J = 13.6, 9.3, 4.4 Hz, 1H), 1.63 − 1.55 (m, 2H), 1.25 (s, 12H), 0.87 (s, 9H), 0.04 (s, 3H), -0.21 (s, 3H). **¹³C NMR** (151 MHz, CDCl₃) δ 146.7, 145.3, 128.1, 126.8, 125.9, 111.0, 83.1, 75.2, 42.5, 39.6, 26.1, 26.0, 25.2, 24.9, 22.2, 18.3, -4.3, -4.7. **IR (v/cm⁻¹):** 2929 (m), 2857 (m), 1386 (s), 1320 (m), 1255 (m), 1144 (s), 776 (s). **HRMS (ESI⁺):** [M+H]⁺ calcd for C₂₅H₄₄BO₃Si⁺ 431.3147, found 431.3138. **[α]²²_D** = -31.67 (c =0.24, CH₂Cl₂, l = 100 mm).
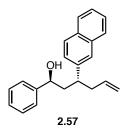
($1R,6S,E$)-6-(($tert$-butyldimethylsilyl)oxy)-2,2-dimethyl-1,6-diphenylhex-3-en-1-ol (2.55). Following a known literature procedure,[50] inside the glovebox, **2.55** (34 mg, 0.08 mmol) and [Pd(μ-Br)(PtBu₃)]₂ (1.6 mg, 0.002 mmol, 2 mol%) were weighed into an 8 mL vial containing a stir bar. The solids were dissolved in toluene (0.040 mL) and DCE (0.040 mL). Benzaldehyde (0.024 mL, 0.24 mmol, 3 equiv.) was added and the reaction was sealed and
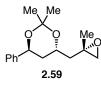
removed from the glovebox. The mixture was allowed to stir at room temperature for 24 hours. The reaction was then diluted in diethyl ether and passed over a pad of celite. The mixture was purified via silica gel chromatography to give a mixture of olefin isomers in 69% yield, 4:1 olefin ratio (22.7 mg). Using silica gel treated with silver nitrate, a small portion of pure **2.55** was obtained (11.8 mg, 29%) and used for NMR characterization. **¹H NMR (600 MHz, CDCl₃)** δ 7.37 − 7.31 (m, 2H), 7.29 − 7.20 (m, 5H), 7.16 − 7.10 (m, 1H), 5.47 (dt, J = 15.5, 7.1 Hz, 1H), 5.34 (dt, J = 15.7, 1.2 Hz, 1H), 4.75 (t, J = 5.8 Hz, 1H), 4.27 (s, 1H), 2.57 − 2.39 (m, 2H), 1.95 (s, 1H), 1.61 (s, 1H), 0.95 (s, 3H), 0.90 (s, 9H), 0.86 (s, 3H), 0.04 (s, 3H), -0.09 (s, 3H). **¹³C NMR (151 MHz, CDCl₃)** δ 144.9, 140.6, 139.3, 128.1, 127.8, 127.4, 127.3, 127.1, 126.2, 125.8, 80.6, 74.9, 44.5, 41.8, 25.9, 25.0, 21.3, 18.4, -4.6, -4.8. **MS (ESI⁺)** [M+Na]⁺ calcd for $C_{26}H_{35}O_2SiNa^+$ 433.25, found 433.36. **IR (ν/cm⁻¹):** 3468 (br, w), 2956 (m), 2928 (m), 2856 (m), 1492 (m), 1255 (m), 1090 (m), 836 (s). **[α]²²_D** = 3.5 (c =0.58, CH₂Cl₂, l = 100 mm).

2.56

(1*S*,3*R*)-1-phenyl-3-(*p*-tolyl)hex-5-en-1-ol (2.56). Following a known literature procedure,[51] in a nitrogen filled dry box, diborylmethane (40.2 mg, 0.15 mmol) was weighed into an 8-mL vial equipped with a magnetic stir bar. The diborylmethane was dissolved in THF (0.4 mL) and the vial was sealed with a septum-lined cap and taped. Lithium 2,2,6,6-tetramethylpiperidide (LTMP) (22 mg, 0.15 mmol) was weighed into a separate 8-mL vial, dissolved in THF (0.8 mL) and sealed with a septum lined cap and tape. Copper (I) chloride (1.5 mg, 0.015 mmol) was weighed into a third 8-mL vial with a magnetic stir bar and sealed with a septum lined cap and tape. The vials were removed from the dry box and the diborylmethane and LTMP were cooled to 0 °C in an ice water bath. The LTMP solution was transferred via cannula to the diborylmethane solution at 0 °C. This was allowed to stir at 0 °C for 10 minutes.

The epoxide (0.1 mmol) was added via syringe and the solution was brought to 22 ºC and stirred for 15 minutes. The reaction was returned to room temperature and transferred via cannula to the vial containing the copper chloride. Allyl bromide (26 μL, 0.3 mmol) was added to the reaction via syringe. The reaction was sealed with tape and allowed to stir at 60 ºC for 24 h. The mixture was then cooled to room temperature and quenched with a saturated solution of aqueous ammonium chloride, extracted with ether, dried over magnesium sulfate, filtered, and concentrated *in vacuo*. The crude mixture was sealed with a septum lined cap and the vial was purged with nitrogen. Inside the glovebox, Pd(dba)$_2$ (0.6 mg, 1 mol%) and RuPhos (0.5 mg, 1 mol%) were weighed into an 8-mL vial and dissolved in toluene (0.5 mL). 4-Bromotoluene was added to a separate vial and dissolved in THF (0.5 mL). These vials were sealed with septum lined caps and removed from the glovebox. The bromotoluene solution was cannula transferred under nitrogen to the crude hydroxyboronate. Once dissolved, this solution was cannula transferred to the catalyst mixture. A solution of nitrogen sparged KOH (aq.) (0.122 mL, 0.4 mmol) was added to the reaction via syringe. The mixture was then stirred at 70 ºC for 14 hours. The reaction was quenched by plugging the mixture over a pad of Celite with ether and concentrated *in vacuo*. The mixture was purified via column chromatography to yield the desired product **2.56** in 40% yield in >10:1 dr (10.6 mg). **¹H NMR** (500 MHz, CDCl$_3$) δ 7.35 – 7.27 (m, 2H), 7.26 – 7.21 (m, 3H), 7.18 – 7.09 (m, 4H), 5.68 (ddt, *J* = 17.1, 10.1, 7.0 Hz, 1H), 5.05 – 4.85 (m, 2H), 4.38 (dd, *J* = 10.4, 2.8 Hz, 1H), 3.02 (dtd, *J* = 11.3, 7.3, 4.0 Hz, 1H), 2.40 – 2.36 (m, 1H), 2.35 (s, 3H), 2.10 (ddd, *J* = 14.3, 10.4, 4.0 Hz, 1H), 1.86 (ddd, *J* = 14.1, 11.3, 2.9 Hz, 1H), 1.70 (s, 1H). **¹³C NMR** (151 MHz, CDCl$_3$) δ 145.5, 141.3, 137.0, 135.9, 129.4, 128.5, 127.9, 127.5, 125.7, 116.3, 71.9, 45.6, 42.0, 21.2. **HRMS (ESI⁺)** [2M+Na]⁺ calcd for C$_{38}$H$_{44}$O$_2$Na⁺ 555.3239, found 555.3230. **IR (ν/cm⁻¹):** 3371 (br, m), 2920 (m), 1639 (m), 1514 (m), 1452 (m), 1050 (m). **[α]²²$_D$** = 16.2 (*c* =0.215, CH$_2$Cl$_2$, l = 100 mm).

2.57
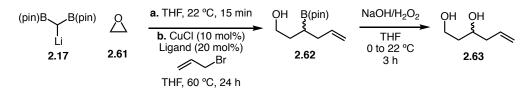
3-allyl-5-methyl-1-phenylhex-4-en-1-ol (2.57). Following the procedure used for the

synthesis of 32 with 2-bromonapthalene instead of 4-bromotoluene, **2.57** was obtained in 54%

yield in >10:1 dr (16.3 mg). **¹H NMR** (600 MHz, CDCl$_3$) δ 7.86 (m, 3H), 7.72 (s 1H), 7.50 (m,

2H), 7.43 (dd, J = 8.4, 1.8 Hz, 1H), 7.32 (tt, J = 6.6, 1.3 Hz, 2H), 7.26 (m, 3H), 5.83 – 5.56 (m,

1H), 5.09 – 4.80 (m, 2H), 4.39 (dd, J = 10.5, 2.7 Hz, 1H), 3.27 (m, 1H), 2.65 – 2.38 (m, 2H), 2.22

(ddd, J = 14.3, 10.5, 3.9 Hz, 1H), 2.01 (ddd, J = 14.3, 11.3, 2.8 Hz, 1H), 1.86 – 1.74 (s, 1H). **¹³C**

NMR (151 MHz, CDCl$_3$) δ 145.4, 141.9, 136.8, 133.7, 132.5, 128.6, 128.4, 127.8, 127.8, 127.6,

126.9, 126.1, 125.9, 125.6, 125.5, 116.4, 71.9, 45.5, 42.7, 41.8. **MS (ESI⁺)** [M+Na]⁺ calcd for

C$_{22}$H$_{22}$ONa⁺ 325.41, found 325.27. **IR (ν/cm⁻¹):** 3393 (m, br), 2975 (m), 2928 (m), 1600 (m),

1507 (m), 1453 (m), 747 (s), 700 (s). **[α]²²_D** = 33.6 (c =0.815, CH$_2$Cl$_2$, l = 100 mm).

2.59

(4S,6S)-2,2-dimethyl-4-(((S)-2-methyloxiran-2-yl)methyl)-6-phenyl-1,3-dioxane

(2.59). Diol **2.58** (1.03 g, 5.0 mmol) was dissolved in DCM (50 mL) in a 100-mL single neck

round bottom flask containing a stir bar under inert nitrogen atmosphere. VO(acac)$_2$ (9.9 mg,

0.04 mmol) was added to the flask and the reaction was cooled to -5 ⁰C in an ice bath. 1.8 mL of

5.5 M tBuOOH (10 mmol) in tBuOH was added dropwise over 1 minute. The reaction was then

stirred at -5 ⁰C for an additional 30 minutes and then allowed to warm to room temperature and

stirred for 8 hours, monitored by TLC. The mixture was then transferred to a separatory funnel

and the organic layer was washed with a saturated solution of sodium thiosulfate. The aqueous

layer was extracted three times with DCM and all organics were combined. The organic layer

was then washed once with a saturated sodium chloride solution. The organics were then dried over magnesium sulfate and concentrated *in vacuo*. The crude product was then dissolved in DMF (32.0 mL) in a 100-mL single neck round bottom flask containing a stir bar and fitted with a rubber septum. The flask was purged with nitrogen and 2,2-dimethoxypropane was added (6.2 mL, 10 eq, 50.0 mmol) to the flask. The septum was then quickly removed and pyridinium *p*-toluenesulfonate (125.6 mg, 10 mol%) was added. The vial was then sealed, purged with nitrogen for two minutes, and then allowed to stir at room temperature for 18 hours. 1.0 mL of triethylamine was added to the reaction followed by a saturated solution of sodium bicarbonate. The mixture was extracted with diethyl ether, dried over magnesium sulfate, and concentrated *in vacuo*. The crude mixture was purified via silica gel chromatography (9:1 hexanes: EtOAc) to yield the product **2.59** in 55% yield and >20:1 dr (721.1 mg) as a clear oil. **¹H NMR** (600 MHz, CDCl₃) δ 7.39 – 7.27 (m, 5H), 4.86 (dd, *J* = 9.7, 6.4 Hz, 1H), 4.04 (tdd, *J* = 9.3, 6.2, 3.7 Hz, 1H), 2.78 (d, *J* = 4.8 Hz, 1H), 2.58 (d, *J* = 4.9 Hz, 1H), 2.04 (dd, *J* = 14.8, 8.8 Hz, 1H), 2.01 – 1.96 (m, 1H), 1.91 (ddd, *J* = 13.0, 9.3, 6.4 Hz, 1H), 1.69 (dd, *J* = 14.8, 3.8 Hz, 1H), 1.46 (s, 3H), 1.45 (s, 3H), 1.37 (s, 3H). **¹³C NMR** (151 MHz, CDCl₃) δ 142.5, 128.6, 127.6, 126.1, 101.1, 68.7, 63.7, 55.3, 53.3, 42.2, 40.6, 30.5, 25.1, 24.8, 22.6. **MS (ESI⁺)** [M+Na]⁺ calcd for $C_{16}H_{22}O_3Na^+$ 285.14, found 285.09. **IR (ν/cm⁻¹):** 2986 (s), 2930 (s), 1716 (w), 1558 (w), 1507 (w), 1378 (s), 1225 (s) 699 (s) [α]²²_D = -36.9 (*c* =0.165, CH₂Cl₂, l = 100 mm).

2.60

(2R,4S)-1-((4S,6S)-2,2-dimethyl-6-phenyl-1,3-dioxan-4-yl)-2-methylhept-6-ene-2,4-diol (2.60). Following the general procedure, 1,3-diol **2.60** was isolated in 75% yield in 4.5:1 d.r. (12.5 mg) as a white solid. **¹H NMR** (600 MHz, CDCl₃) δ 7.39 – 7.26 (m, 5H), 5.86 (ddt, *J* = 17.2, 10.3, 7.1 Hz, 1H), 5.15 – 5.03 (m, 2H), 4.98 – 4.88 (m, 1H), 4.63 (s, 1H), 4.45 (dddd, *J* = 11.2, 8.7, 6.2, 2.4 Hz, 1H), 4.20 (d, *J* = 12.4 Hz, 2H), 4.13 (dtd, *J* = 10.4, 6.2, 1.5 Hz,

1H), 2.35 – 2.26 (m, 1H), 2.22 – 2.14 (m, 1H), 2.06 – 1.92 (m, 2H), 1.89 (dd, J = 14.5, 10.8 Hz,

1H), 1.71 – 1.56 (m, 3H), 1.52 (s, 3H), 1.46 (s, 2H), 1.34 (s, 3H). **13C NMR** (151 MHz, CDCl$_3$) δ

142.1, 135.3, 128.7, 127.7, 126.1, 117.3, 101.3, 74.0, 73.9, 68.6, 67.6, 65.1, 48.1, 47.9, 44.1, 42.5,

40.6, 39.6, 25.1, 25.1, 24.9. **IR (v/cm^{-1}):** 3346 (br, s), 2850 (s), 2360 (s), 2341 (s), 1456 (m),

1226 (m), 752 (w), 668 (w). **MS (ESI$^+$)** [M+Na]$^+$ calcd for C$_{20}$H$_{30}$O$_4$Na$^+$ 357.19, found 357.18.

$[\alpha]^{22}_D$ = -11.0(c = 0.265, CH$_2$Cl$_2$, l = 100 mm).
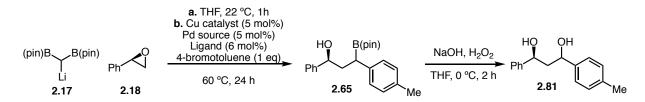
hex-5-ene-1,3-diol (2.63). Inside the glovebox, diborylmethane (26.8 mg, 0.1 mmol) was

weighed into an 8 mL vial containing a stir bar and dissolved in THF (0.25 mL). Lithium

2,2,6,6-tetramethylpiperidide (LTMP) (14.7 mg, 0.1 mmol) was weighed into a separate 8 mL

vial and dissolved in THF (0.5 mL). Copper chloride (1 mg, 0.01 mmol) and ligand (0.02 mmol)

were weighed into a third vial containing a stir bar and dissolved in THF (0.1 mL). The vials

were sealed with septa lined caps and removed from the glovebox. The diborylmethane and

LTMP solutions were cooled to 0 °C and the LTMP was cannula transferred to the

diborylmethane solution. The reaction was stirred at 0 °C for 10 minutes. A solution of ethylene

oxide (40 μL) was added to the vial and the reaction was allowed to warm to 22 °C and stir for

15 minutes. The reaction was then cannula transferred to the vial containing the copper catalyst.

Allyl bromide (26 μL, 0.3 mmol) was added and the reaction was heated to 60 °C for 24 hours.

The reaction was then cooled to 0 °C and a solution of NaOH (0.25 mL, 3M) was added followed

by H$_2$O$_2$ (0.15 mL). The reaction was stirred at 0 °C for two hours and then quenched (dropwise)

with a saturated solution of sodium thiosulfate. The organics were extracted with ethyl acetate

(x3), dried over MgSO$_4$, and concentrated *in vacuo* to yield crude **2.63**. The conversion to

product was determined by 1H-NMR spectroscopy using DMF as an internal standard. The diol

was isolated once to confirm the structure by 1H-NMR and matched known literature spectra.[60]

¹H NMR (600 MHz, CDCl₃) δ 5.92-5.73 (m, 1H), 5.24-5.11 (m, 2H), 4.01-3.80 (m, 2H), 2.43-2.21 (m, 3H), 1.75 (tq, *J*=8.4, 4.1 Hz, 2H).
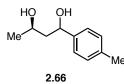
Inside the glovebox, diborylmethane (26.8 mg, 0.1 mmol) was weighed into a vial with a stir bar and dissolved in THF (0.3 mL). Lithium 2,2,6,6-tetramethylpiperidide (LTMP) (15.5 mg, 0.105 mmol) was weighed into a separate vial and dissolved in THF (0.7 mL). The vials were caped with septa lined caps and removed from the glovebox. Outside the glovebox, the vials were cooled to 0 °C and the LTMP solution was cannula transferred to the diborylmethane solution. The reaction was stirred at 0 °C for 10 minutes. Ethylene oxide in THF (80 µL, 0.2 mmol) was added and the reaction was allowed to warm to 22 °C and stir for 15 minutes. The solvent was removed under a stream of dry nitrogen. Once dry, the vial was brought back into the glovebox. The solid residue was washed three times with hexanes and dried under vacuum. **¹H NMR** (500 MHz, THF-d₈) δ 3.53 (m, 1H), 3.46 (m, 1H), 1.73 (m, 1H), 1.61-1.51 (m, 1H), 1.21 (m, 13H), 1.14-0.93 (m, 13H), 0.14 (m, 1H). **¹³C NMR** (126 MHz, THF-d₈) δ 80.8, 64.6, 31.6, 30.0, 22.5, 13.5. **¹¹B NMR** (160 MHz, THF-d₈) δ 12.45.
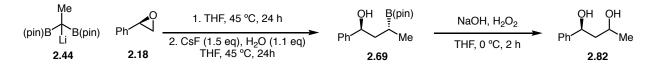
**(1*S*)-1-phenyl-3-(*p*-tolyl)propane-1,3-diol (2.81).** Inside the glovebox, diborylmethane (40.2 mg, 0.15 mmol) was weighed into an 8 mL vial containing a stir bar and dissolved in THF (0.4 mL). Lithium 2,2,6,6-tetramethylpiperidide (LTMP) (22.1 mg, 0.15 mmol) was weighed into a separate 8 mL vial and dissolved in THF (0.8 mL). The desired copper source (0.005 mmol), palladium source (0.005 mmol), the desired ligand (0.006 mmol), and 4-bromotoluene (17.1 mg, 0.1 mmol) were added to a separate vial and dissolved in THF (0.2 mL). The vials were

sealed with septa lined caps and removed from the glovebox. The diborylmethane and LTMP solutions were cooled to 0 °C and the LTMP was cannula transferred to the diborylmethane solution. The reaction was stirred at 0 °C for 10 minutes. *R*-styrene oxide (11 μL, 0.1 mmol) was added and the reaction was allowed to warm to 22 °C and stir for one hour. The reaction was then cannula transferred to the vial containing the catalyst solution and the mixture was heated to 60 °C for 24 hours. After 24 hours, the reaction was cooled to 0 °C and a solution of NaOH (0.25 mL, 3 M) was added followed by H_2O_2. The reaction was stirred (with venting) at 0 °C for 2 hours. The reaction was then quenched (dropwise) at 0 °C with a solution of saturated sodium thiosulfate. The organics were extracted with diethyl ether (x3), dried over magnesium sulfate, and concentrated *in vacuo* to yield the crude diol product. Conversion to product was determined using ^{1}H-NMR spectrometry with DMF as internal standard. The product was isolated via silica gel chromatography and the structure confirmed through ^{1}H-NMR analysis and matched known literature spectra.[61] **^{1}H NMR** (500 MHz, CDCl$_3$) δ 7.43 − 7.33 (m, 5H), 7.32 − 7.24 (m, 4H), 7.18 (dd, *J* = 7.8, 5.9 Hz, 2H), 5.04 (dd, *J* = 10.2, 2.8 Hz, 1H), 5.01 (dt, *J* = 7.3, 3.8, 1H), 4.96 (dd, *J* = 7.4, 4.4, 1H), 3.37 (s, 1H), 3.15 (s, 1H), 2.91 (s, 1H), 2.75 (s, 1H), 2.37 (s, 3H), 2.36 (s, 1H), 2.23 -2.15 (m, 2H).

2.66
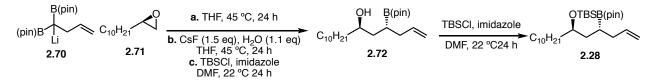
(3*R*)-1-(*p*-tolyl)butane-1,3-diol (2.66) was prepared from propylene oxide according to the same procedure as **2.81**. The conversion was determined using ^{1}H-NMR spectroscopy with DMF as internal standard. The product was isolated via silica gel chromatography and the structure was confirmed using ^{1}H-NMR analysis and comparison to reported literature spectra.[62] **^{1}H NMR** (500 MHz, CDCl$_3$) δ 7.33 − 7.24 (m, 3H), 7.16 (d, *J* = 7.9 Hz, 2H), 5.03 (dd, *J* = 7.9, 3.6 Hz, 1H), 4.91 (dd, *J* = 10.3, 2.9 Hz, 1H), 4.18 − 4.11 (m, 1H), 4.07 (ddd, *J* = 8.2, 6.2, 3.0 Hz, 1H), 2.35 (s, 3H), 1.93 -1.80 (m, 2H), 1.68 − 1.63 (m, 3H), 1.35 -1.31 (m, 4H).

(1S)-1-phenylbutane-1,3-diol (2.82) was prepared following a modified literature

procedure.[55] Inside the glovebox, diborylethane (42.0 mg, 0.15 mmol) was weighed into an 8 mL

vial containing a stir bar and dissolved in THF (0.4 mL). Lithium 2,2,6,6-tetramethylpiperidide

(LTMP) (22.1 mg, 0.15 mmol) was weighed into a separate 8 mL vial and dissolved in THF (0.8

mL). Cesium fluoride (23 mg, 0.15 mmol) was weighed into a third vial containing a stir bar. All

of the vials were sealed with septa lined caps and removed from the glovebox. The LTMP and

diborylethane solutions were cooled to 0 °C and the LTMP solution was cannula transferred to

the diborylethane solution. The reaction was stirred at 0 °C for 10 minutes. Styrene oxide (11 µL,

0.1 mmol) was added and the reaction was heated to 45 °C for 24 hours. After 24 hours, the

reaction was cooled to 22 °C and cannula transferred to the vial containing the cesium chloride.

Water (2 µL, 0.11 mmol) was added to the reaction and it was heated to 45 °C for 24 hours. After

24 hours, the reaction was cooled to 22 °C and quenched with a saturated, aqueous solution of

ammonium chloride. The organics were extracted with diethyl ether (x3), dried over magnesium

sulfate, and concentrated *in vacuo* to yield crude **2.69**. The crude conversion was determined to

be 43% with 8:1 dr by ^{1}H-NMR analysis using DMF as an internal standard. To confirm the

structure of the product, **2.69** was oxidized to **2.81**. Crude **2.69** was dissolved in THF (0.25

mL) and cooled to 0 °C. NaOH (0.25 mL, 3 M) was added followed by hydrogen peroxide (0.15

mL) and the reaction was allowed to stir (with venting) for 2 hours at 0 °C. The reaction was

quenched (dropwise) at 0 °C with a saturated aqueous solution of sodium thiosulfate. The

organics were extracted with diethyl ether (x3), dried over magnesium sulfate, and concentrated

in vacuo to yield crude **2.82**. A sample of the pure diol was isolated via silica gel

chromatography and the structure was confirmed via ^{1}H-NMR analysis and comparison to

known literature values.[63] **^{1}H NMR** (500 MHz, CDCl$_3$) δ 7.55 − 7.35 (m, 4H), 7.35 − 7.23 (m,

1H), 5.09 (dd, *J* = 7.7, 3.7 Hz, 1H), 4.97 (dd, *J* = 10.2, 3.0 Hz, 1H), 4.29 – 4.17 (m, 1H), 4.10 (ddd,

J = 8.2, 6.3, 3.1 Hz, 1H), 1.91 (qdd, *J* = 14.6, 7.9, 3.4 Hz, 2H), 1.27 (m, 3H).
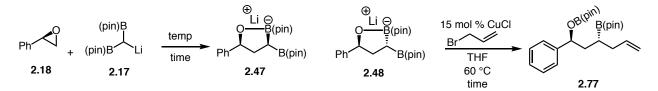
tert-butyldimethyl(((4R,6R)-4-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)hexadec-1-en-6-yl)oxy)silane (2.28). 2.28 was prepared following a modified literature procedure.[55] Inside the glovebox, allyl diboronate ester (23 mg, 0.075 mmol) was weighed into an 8 mL vial containing a stir bar and dissolved in THF (0.2 mL). Lithium 2,2,6,6-tetramethylpiperidide (LTMP) (11 mg, 0.075 mmol) was weighed into a separate 8 mL vial and dissolved in THF (0.4 mL). Cesium fluoride (12 mg, 0.075 mmol) was weighed into a third vial containing a stir bar. All of the vials were sealed with septa lined caps and removed from the glovebox. The LTMP and diborylethane solutions were cooled to 0 °C and the LTMP solution was cannula transferred to the diborylethane solution. The reaction was stirred at 0 °C for 10 minutes. Dodecene oxide (11 µL, 0.05 mmol) was added and the reaction was heated to 45 °C for 24 hours. After 24 hours, the reaction was cooled to 22 °C and cannula transferred to the vial containing the cesium chloride. Water (1 µL, 0.05 mmol) was added to the reaction and it was heated to 45 °C for 24 hours. After 24 hours, the reaction was cooled to 22 °C and quenched with a saturated, aqueous solution of ammonium chloride. The organics were extracted with diethyl ether (x3), dried over magnesium sulfate, and concentrated *in vacuo* to yield crude **2.28**. The crude conversion was determined to be 59% with 3:1 dr by ^{1}H-NMR analysis using DMF as an internal standard. To confirm the structure of the product, the crude mixture was dissolved in DMF (0.3 mL) and treated with TBSCl (23 mg, 0.15 mmol) and imidazole (10 mg, 0.15 mmol). The reaction was stirred for 24 hours at 22 °C and then quenched with a saturated solution of ammonium chloride. The organics were extracted with diethyl ether (x3), dried over magnesium

chloride, and concentrated *in vacuo* to yield the crude product. The structure was confirmed by comparison of the ¹H-NMR spectra to that previously reported.
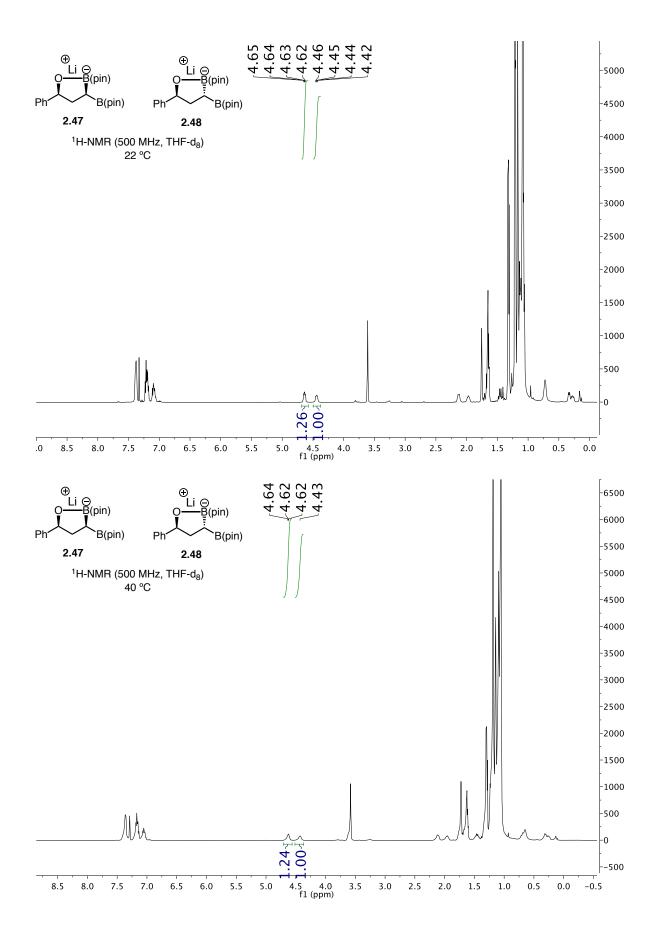
2.8.6 NMR Studies
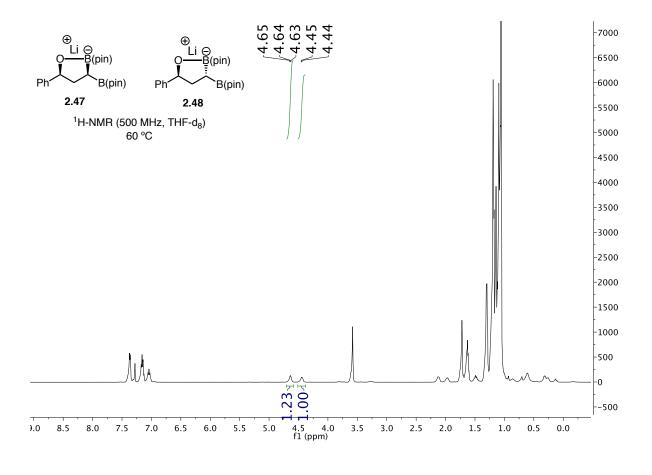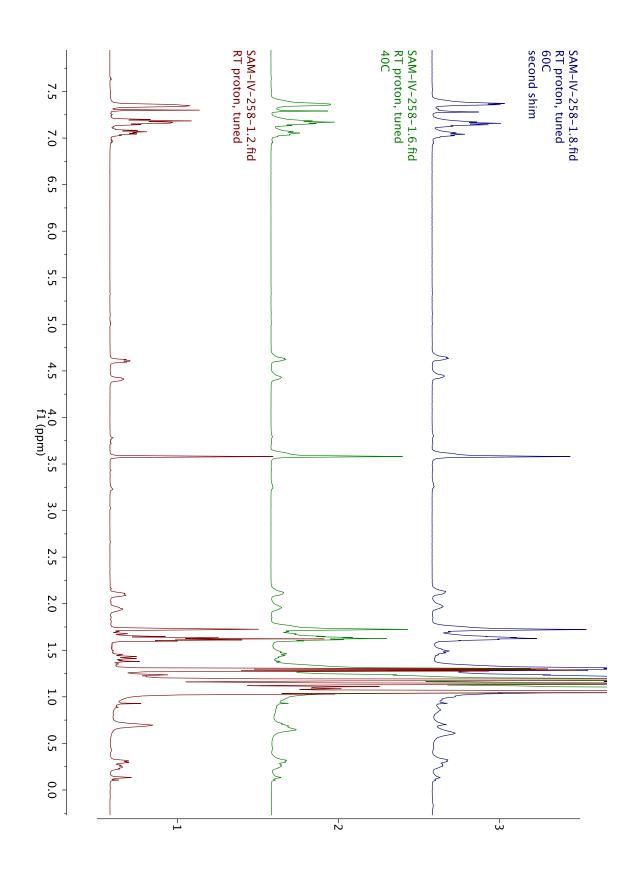
Inside the glovebox, diborylmethane (40.2 mg, 0.15 mmol) was weighed into a vial with a stir bar and dissolved in THF-d_8 (0.4 mL). Lithium 2,2,6,6-tetramethylpiperidide (LTMP) (22 mg, 0.15 mmol) was weighed into a separate vial and dissolved in THF-d_8 (0.8 mL). An NMR tube was sealed inside the glovebox with a septa cap. The vials and NMR tubes we all removed from the glovebox. The diborylmethane and LTMP solutions were cooled to 0 ºC in an ice water bath and the LTMP solution was cannula transferred to the diborylmethane solution. This mixture was allowed to stir at 0 ºC for 10 minutes. (*R*)-styrene oxide was then added via syringe and the reaction was allowed to warm to room temperature until the reaction became homogeneous. The mixture was then canula transferred to the NMR tube. The septa cap of the NMR tube was then sealed tightly with electrical tape. ¹H-NMR spectra were taken at 22 ºC, 40 ºC, and 60 ºC. ¹¹B-NMR spectrum was obtained at 22 ºC. Inside the glovebox CuCl was weighed into a vial. The vial was sealed with a septa cap and removed from the glovebox. A new NMR tube was also sealed with a septa cap inside the glovebox and removed. The reaction mixture was cannula transferred from the NMR tube to the vial containing CuCl. Allyl bromide was added to the vial via syringe. The mixture was then transferred to the new NMR tube and the septa cap of the NMR tube was sealed tightly with electrical tape. The reaction was monitored via ¹H-NMR at 22 ºC, 40 ºC, and 60 ºC and ¹¹B-NMR at 60 ºC.

2.8.7 NMR Spectra

¹H-NMR (500 MHz, THF-d₈)
22 °C

¹H-NMR (500 MHz, THF-d₈)
40 °C

^{1}H-NMR (500 MHz, THF-d$_8$)
60 ºC

2.47

2.48

−30.95
−12.49

2.47   **2.48**

^{11}B-NMR (160 MHz, THF-d$_8$)
22 °C

2.47   **2.48**

^{1}H-NMR (500 MHz, THF-d$_8$)
NOESY at 4.436 ppm

2.47 2.48

^{1}H-NMR (500 MHz, THF-d$_8$)
NOESY at 4.640 ppm

2.77
^{1}H-NMR (500 MHz, THF-d$_8$)
22 °C
After addition of CuCl and allyl bromide

4.63
4.62
4.61
4.42
4.41

1.23
1.00

2.77
^{1}H-NMR (500 MHz, THF-d$_8$)
40 °C, 20 min
After addition of CuCl and allyl bromide

4.62
4.44

1.75
1.00

2.77
^{1}H-NMR (500 MHz, THF-d$_8$)
60 °C, 50 min
After addition of CuCl and allyl bromide

4.62

2.77

^{11}B-NMR (500 MHz, THF-d$_8$)
60 °C, 50 min
After addition of CuCl and allyl bromide

~22.19
12.08
8.43
~4.12

2.22

^{1}H-NMR (600 MHz, C$_6$D$_6$)

2.22

^{13}C-NMR (151 MHz, C_6D_6)

146.9, 138.8, 128.5, 128.4, 128.2 C6D6, 128.1 C6D6, 127.9 C6D6, 127.3, 126.3, 115.3, 83.0, 75.7, 43.3, 36.4, 26.2, 26.2, 25.2, 25.0, 24.9, 18.5, 4.1, 4.5

2.23

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

7.26 CDCl3, 7.17, 7.16, 7.09, 7.08, 5.81, 5.79, 5.79, 5.78, 5.78, 5.77, 5.76, 5.75, 5.75, 5.74, 5.74, 5.73, 5.71, 5.70, 5.00, 5.00, 5.00, 4.97, 4.97, 4.93, 4.93, 4.93, 4.92, 4.91, 4.91, 2.32, 2.17, 2.17, 2.16, 2.16, 2.16, 2.15, 2.15, 2.15, 2.14, 1.68, 1.67, 1.66, 1.66, 1.35, 1.34, 1.32, 1.24, 0.86, 0.01, −0.16, −0.20

OTBSB(pin)

Me

2.23

^{13}C-NMR (151 MHz, CDCl$_3$)

143.6
138.5
136.3
128.7
125.9
115.2
83.1
77.4 CDCl3
77.2 CDCl3
76.9 CDCl3
75.0
42.7
36.0
26.1
26.1
25.2
24.9
21.3
18.4
4.2
4.7

OTBSB(pin)

F

2.24

^{1}H-NMR (600 MHz, CDCl$_3$)

7.26 CDCl3
7.25
7.24
7.24
7.23
6.98
6.97
6.95
5.79
5.77
5.76
5.75
5.75
5.74
5.01
5.01
5.01
5.00
4.98
4.98
4.97
4.95
4.94
4.94
4.93
4.93
4.93
4.92
4.92
4.65
4.64
4.62
2.18
2.18
2.17
2.17
2.16
2.16
2.15
2.15
2.14
2.14
2.14
1.67
1.65
1.65
1.64
1.57
1.33
1.32
1.31
1.31
1.24
1.24
1.23
1.23
0.87
0.86
0.86
0.85
0.01
0.01
-0.16
-0.21
-0.21
-0.22

2.28
2.24
1.00
0.08
2.28
1.12
2.29
1.99
1.10
14.03
10.54
3.42
3.09

OTBSB(pin)

2.24

^{13}C-NMR (151 MHz, CDCl$_3$)

162.7, 161.1, 142.3, 142.3, 138.4, 127.5, 127.4, 115.3, 114.9, 114.8, 83.2, 77.4 CDCl3, 77.2 CDCl3, 76.9 CDCl3, 42.6, 36.0, 26.0, 25.2, 24.9, 18.3, -4.3, -4.7

OTBSB(pin)

2.24

^{19}F-NMR (376 MHz, CDCl$_3$)

-116.41, -116.53, -116.63

2.25

^{1}H-NMR (600 MHz, CDCl$_3$)

2.25

^{13}C-NMR (151 MHz, CDCl$_3$)

Me OTBSB(pin)

2.26

^{1}H-NMR (600 MHz, CDCl$_3$)

Me OTBSB(pin)

2.26

^{13}C-NMR (151 MHz, CDCl$_3$)

2.27

^{1}H-NMR (600 MHz, CDCl$_3$)

2.27

^{13}C-NMR (151 MHz, CDCl$_3$)

212

2.28

^{1}H-NMR (600 MHz, CDCl$_3$)

2.28

^{13}C-NMR (151 MHz, CDCl$_3$)

213

OTBSB(pin)

2.29

^{1}H-NMR (600 MHz, C$_6$D$_6$)

OTBSB(pin)

2.29

^{13}C-NMR (151 MHz, CDCl$_3$)

2.30

^{1}H-NMR (600 MHz, CDCl$_3$)

2.30

^{13}C-NMR (151 MHz, CDCl$_3$)

215

OTBSB(pin)

2.31

¹H-NMR (600 MHz, CDCl₃)

7.26 CDCl3
7.25
7.25
7.24
7.24
7.23
7.18
7.18
7.17
7.17
7.16
7.16
5.80
5.79
5.78
5.78
5.77
5.77
5.76
5.03
5.02
5.01
5.00
4.99
4.99
4.98
4.95
4.95
4.94
4.94
4.93
4.93
4.92
3.85
3.85
3.84
3.84
3.82
2.87
2.85
2.84
2.73
2.72
2.71
2.70
2.55
2.53
2.52
2.51
2.17
2.15
2.14
2.13
2.13
2.12
2.11
1.60
1.59
1.58
1.52
1.43
1.26
1.25
1.19
1.18
0.84
0.80
−0.02
−0.12
−0.19
−0.35

OTBSB(pin)

2.31

¹³C-NMR (151 MHz, CDCl₃)

140.0
139.6
138.6
138.3
130.1
129.9
128.1
128.0
126.0
125.9
115.3
115.2

83.3
83.1
77.4 CDCl3
77.2 CDCl3
76.9 CDCl3
73.8
73.4

44.6
43.4
39.2
38.4
36.2
36.1
26.1
26.1
25.8
25.8
25.1
25.0
25.0
24.9
18.2
18.2
−4.4
−4.6
−5.1

216

2.32

^{1}H-NMR (600 MHz, CDCl$_3$)

2.32

^{13}C-NMR (151 MHz, CDCl$_3$)

2.76

^{1}H -NMR (600 MHz, C$_6$D$_6$)

2.76

^{13}C -NMR (151 MHz, C$_6$D$_6$)

218

2.76
^{1}H -COSY (600 MHz, C$_6$D$_6$)

f2 (ppm)

f1 (ppm)

219

2.76

^{1}H -NOESY (600 MHz, C$_6$D$_6$)

Shows correlation between two H's shown

2.33

^{1}H-NMR (600 MHz, CDCl$_3$)

2.33
^{13}C-NMR (151 MHz, CDCl$_3$)

2.34
^{1}H-NMR (600 MHz, CDCl$_3$)

Me Me

...B(pin)

OH

2.34

^{13}C-NMR (151 MHz, CDCl$_3$)

—134.8
—118.1
—79.4
—68.6
—54.0
—47.9
—42.9
—42.7
—40.8
—38.6
—29.6
—27.9
—27.8
—27.7
—24.2
—23.7
—23.6

OH   OH

Me

2.35

^{1}H-NMR (CDCl$_3$, 600 MHz)

7.38
7.38
7.37
7.37
7.36
7.36
7.35
7.34
7.28
7.27
7.27
7.26 CDCl3
5.56
5.55
5.40
5.39
5.38
5.37
5.09
5.08
5.07
5.07
5.06
5.05
2.24
2.23
2.22
2.22
2.22
2.21
2.21
2.21
2.20
2.20
2.19
2.17
1.94
1.93
1.92
1.92
1.92
1.91
1.91
1.89
1.88
1.87
1.87
1.86
1.69
1.69
1.68
1.67
1.65
1.65
1.64
1.64
1.63
1.62
1.04
1.03
1.01
1.00

7.77
1.83

0.87
1.07
1.49
0.36
2.09
0.20

0.48
1.00
0.31
0.21

1.00
0.38

5.43

4.13
3.48
3.31

0.89
0.58

2.35

^{13}C-NMR (CDCl$_3$, 151 MHz)

Peaks: 144.7, 144.7, 144.6, 140.5, 140.3, 129.7, 129.7, 128.6, 128.6, 128.6, 128.6, 127.9, 127.7, 127.4, 127.4, 127.4, 126.7, 125.8, 125.8, 125.7, 125.6, 125.6, 117.1, 115.9; 77.4 CDCl3, 77.2 CDCl3, 76.9 CDCl3, 71.9, 71.9, 71.8, 69.0, 68.4; 44.1, 43.9, 41.8, 40.9, 35.1; 25.0; 18.2, 15.1, 13.2

f1 (ppm)

2.36

^{1}H-NMR (CDCl$_3$, 600 MHz)

Peaks: 7.39, 7.39, 7.38, 7.38, 7.38, 7.37, 7.37, 7.36, 7.36, 7.36, 7.36, 7.35, 7.34, 7.34, 7.28, 7.27, 7.27, 5.09, 4.89, 4.89, 4.89, 4.81, 4.80, 4.80, 4.80, 4.80, 4.80, 2.26, 2.26, 2.25, 2.25, 2.24, 2.23, 2.22, 2.22, 2.21, 2.21, 2.21, 1.96, 1.95, 1.94, 1.94, 1.88, 1.87, 1.86, 1.86, 1.77, 1.77, 1.77, 1.72, 1.72

Integrations: 3.83, 3.87, 1.00, 1.09, 1.10, 1.02, 0.93, 2.95, 1.08, 1.22, 2.65

f1 (ppm)

2.36

^{13}C-NMR (CDCl$_3$, 151 MHz)

144.7
142.4
128.6
127.4
125.7
114.0
71.7
66.2
46.2
44.6
22.5

3.37

^{1}H-NMR (500 MHz, CDCl$_3$)

7.37
7.37
7.37
7.35
7.35
7.26 CDCl3
5.12
5.12
5.11
5.10
5.09
5.09
5.09
5.08
5.07
5.06
5.06
5.05
5.05
5.04
2.28
2.26
2.18
2.17
2.10
2.09
2.08
2.06
2.06
2.05
2.04
2.03
2.02
1.94
1.94
1.93
1.92
1.92
1.91
1.90
1.90
1.90
1.73
1.72
1.68
1.67
1.66
1.63
1.63
1.62
1.60
1.59

4.87
0.79
3.44
0.21
0.20
1.00
0.86
10.35
0.61
3.56
3.25
3.64

224

2.37
^{13}C-NMR (151 MHz, CDCl$_3$)

144.7, 139.6, 132.0, 128.5, 127.3, 125.7, 124.2, 119.7, 77.4 CDCl3, 77.2 CDCl3, 76.9 CDCl3, 71.9, 69.1, 44.0, 40.0, 36.2, 26.6, 25.9, 17.8, 16.4

2.38
^{1}H-NMR (600 MHz, CDCl$_3$)

7.39, 7.39, 7.37, 7.36, 7.36, 7.35, 7.34, 7.28, 7.27, 7.26, 7.26, 5.55, 5.54, 5.54, 5.09, 5.08, 5.08, 5.07, 3.19, 3.18, 2.20, 2.19, 2.19, 2.15, 2.13, 2.12, 2.02, 2.01, 1.97, 1.96, 1.96, 1.95, 1.94, 1.94, 1.93, 1.93, 1.86, 1.85, 1.84, 1.84, 1.83, 1.83, 1.83, 1.82, 1.62, 1.61, 1.60, 1.59, 1.58, 1.57, 1.56, 1.56, 1.55, 1.55, 1.54

3.95, 2.22, 1.00, 0.98, 0.98, 0.95, 0.98, 2.00, 2.14, 1.96, 2.12, 6.15

2.38

^{13}C-NMR (151 MHz, CDCl$_3$)

144.8
134.3
128.5
127.3
125.7
125.6
71.7
66.2
46.5
44.5
28.4
25.4
22.9
22.4

2.39

^{1}H-NMR (CDCl$_3$, 600 MHz)

2.39

^{13}C-NMR (CDCl$_3$, 151 MHz)

2.40

^{1}H-NMR (500 MHz, CDCl$_3$)

2.40
¹³C-NMR (151 MHz, CDCl₃)

144.3
130.3
128.7
127.7
125.7
120.0
77.4 CDCl3
77.2 CDCl3
76.9 CDCl3
71.7
66.8
49.2
43.9

2.41
¹H-NMR (600 MHz, CDCl₃)

7.39
7.39
7.38
7.38
7.37
7.37
7.37
7.36
7.35
7.34
7.29
7.28
7.27
7.27
7.27
7.26 CDCl3
5.68
5.68
5.54
5.54
5.09
5.08
5.07
5.07
5.06
2.24
2.24
2.23
2.23
2.22
2.22
1.99
1.98
1.98
1.97
1.96
1.96
1.95
1.94
1.94
1.93
1.92
1.91
1.91
1.90
1.89
1.88
1.88
1.77
1.77
1.76
1.76
1.75
1.74
1.74
1.73
1.73
1.72
1.51
1.51
1.51
1.50
1.50
1.49
1.48
1.34

2.41

^{13}C-NMR (151 MHz, CDCl$_3$)

2.79

^{1}H-NMR (600 MHz, CDCl$_3$)

2.79
^{13}C-NMR (151 MHz, CDCl$_3$)

144.8
128.6
128.6
127.4
125.8
125.6
77.4 CDCl3
77.2 CDCl3
76.9 CDCl3
73.5
72.0
43.7
41.7
29.0
28.3
26.6
26.3
26.2

2.43
^{1}H-NMR (600 MHz, CDCl$_3$)

7.41
7.40
7.39
7.38
7.37
7.37
7.32
7.31
7.31
7.31
7.30
7.30
7.30
7.29
6.35
6.32
6.19
6.16
6.15
6.15
5.70
5.69
5.67
5.19
5.18
5.16
5.16
5.11
5.11
5.10
5.07
5.06
5.06
5.05
5.05
3.97
3.96
2.92
2.91
2.36
2.35
2.35
2.34
2.33
2.32
2.32
2.30
2.30
2.30
1.97
1.96
1.95
1.95
1.94
1.94
1.93
1.92

4.28
1.04
1.00
1.02
0.97
1.29
0.97
1.02
0.94
0.80
2.83
2.21

2.43

^{13}C-NMR (151 MHz, CDCl$_3$)

144.5
136.8
134.7
130.0
128.6
127.5
125.7
116.5
71.9
68.5
44.2
40.9

2.53

^{1}H-NMR (600 MHz, CDCl$_3$)

2.53

^{13}C-NMR (151 MHz, CDCl$_3$)

2.54

^{1}H-NMR (600 MHz, CDCl$_3$)

2.54

¹³C-NMR (151 MHz, CDCl₃)

146.7, 145.3, 128.1, 126.8, 125.9, 111.0, 83.1, 77.4 CDCl₃, 77.2 CDCl₃, 76.9 CDCl₃, 75.2, 42.5, 39.6, 26.1, 26.0, 25.2, 24.9, 22.2, 18.3, –4.3, –4.7

2.55

¹H-NMR (600 MHz, CDCl₃)

233

2.55

^{1}H-NMR (600 MHz, CDCl$_3$)

2.55

^{13}C-NMR (151 MHz, CDCl$_3$)

234

2.56

^{1}H-NMR (600 MHz, CDCl$_3$)

2.56

^{13}C-NMR (151 MHz, CDCl$_3$)

235

2.57

^{1}H-NMR (600 MHz, CDCl$_3$)

2.57

^{13}C-NMR (151 MHz, CDCl$_3$)

2.59
^{1}H-NMR (600 MHz, CDCl$_3$)

2.59
^{13}C-NMR (151 MHz, CDCl$_3$)

2.60

¹H-NMR (600 MHz, CDCl₃)

2.60

¹³C-NMR (151 MHz, CDCl₃)

238

2.64
¹H-NMR (500 MHz, THF-d_8)

2.64
¹¹B-NMR (160 MHz, THF-d_8)

239

2.64
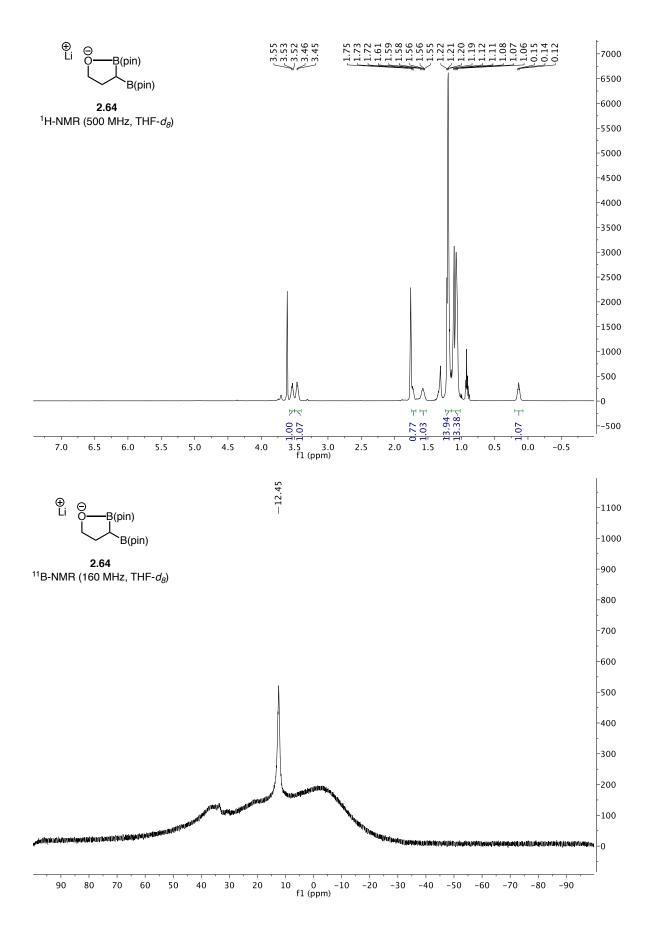^{13}C-NMR (126 MHz, THF-d_8)
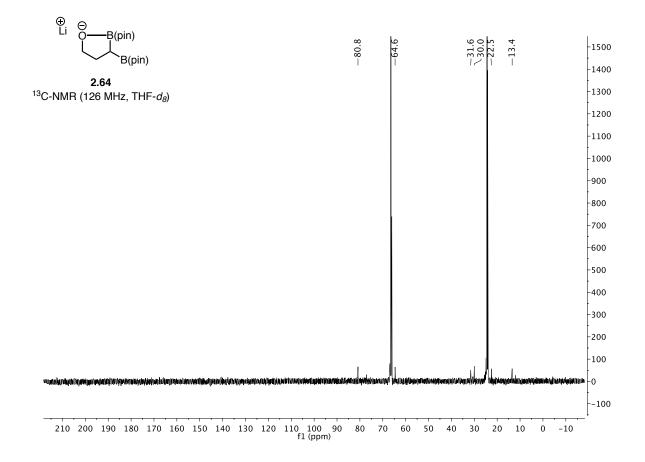
—80.8
—64.6
—31.6
—30.0
—22.5
—13.4

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Chapter 3 Synthesis of Stereodefined Alkenyl Boronates from Epoxides and Diborylmethane through Pd-Catalyzed Dehydroboration[1]

3.1 Introduction

Developing new methods for the synthesis of versatile functional groups is a primary

goal of organic chemistry research. Even when methods exist for making a specific functional

group, new methods that do so more efficiently or from different starting materials are always

useful. In particular, multicomponent or tandem reactions which generate multiple new

functional groups in one reaction from simple, readily available starting materials are attractive

transformations. Tandem reactions increase the efficiency with which important chemical

building blocks are accessed. One class of useful chemical building blocks are alkenyl boronate
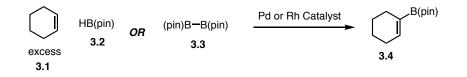
esters.

3.2 Background

Alkenylboronate esters are an attractive functional group for organic synthesis as they

can be used to install a wide variety of functionality into a molecule. For example, new C-C

bonds can be formed utilizing cross-coupling methodologies.[1–4] Additionally, transformation

such as cycloproponation[5,6], hydroboration[7], allylation[8], and enantioselective diboration[9] can be

conducted on the olefinic component. The abundance of functional groups that are easily

accessible from vinyl boronate esters makes them useful moieties for the synthesis of complex

molecules.

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[1] A portion of this work appeared as a communication in Organic Letters. The full reference is as follows: Murray, S. A.; Luc, E. C. M.; Meek, S. J. *Org Lett.* **2018**, *20*, 469-471.

3.2.1 Current methods for preparation of alkenyl boronates

A variety of methodologies for the synthesis of akenylboronate esters currently exist. **Figure 3.1** highlights some of these methods including olefin C-H borylation,[10-15] alkyne hydroboration,[16,17] cross-metathesis,[18-20] cross-coupling,[21,22] and boron-Wittig.[23-31] Each of these methodologies have their own benefits and limitations. Alkene C-H borylation methods include rhodium, iridium, and palladium catalyzed approaches. One of the major challenges in these methodologies is selective incorporation of only a single boron unit as opposed to polyborylation.[10-15] Alkyne hydroboration is a well-studied area of organic chemistry and can be catalyzed by a multitude of metals including copper, iron, rhodium, zirconium, and cobalt. Additionally, metal free methodologies also exist. While these methodologies have been widely studied and are often used, they are not always the most attractive approach for two reasons: it can be difficult to achieve selective monoboylation at the desired position and the borane derivatives required are highly reactive and air sensitive making them difficult to work with.[16,17]

Cross metathesis using ruthenium, molybdenum or tungsten based catalysts can be a useful way to make vinyl boronate esters in both good yield and olefin geometry selectivity which is dependent upon the identity of the catalyst. The main drawback of these methodologies is the inability to make tri and tetra-substituted alkenyl boronate esters.[18-20] Cross coupling has been studied as well using a palladium catalyst to couple together $B_2(pin)_2$ and either vinyl bromides or vinyl triflates.[21,22]

(a) Olefin C-H Borylation

(b) Hydroboration of Alkynes

(c) Cross Metathesis

• Z-Selective

• E-Selective
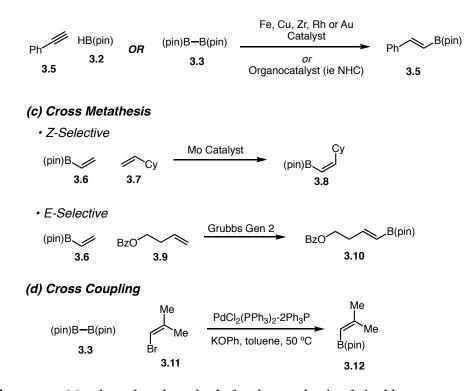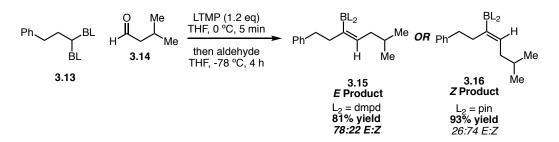

(d) Cross Coupling

Figure 3.1 Metal catalyzed methods for the synthesis of vinyl boronate esters

The boron-Wittig reaction is one method for synthesizing vinyl boronic acid pinacol esters that does not require a metal catalyst. The boron-Wittig reaction was pioneered by Matteson[23–26] and recently presented as a method for the synthesis of vinyl boronate esters by Morken and coworkers (**Scheme 3.1**).[30] The reaction couples together aldehydes and 1,1-organodiboron compounds to produce the desired olefinic products. The diboron reagent is first treated with LTMP to deprotonate the methylene unit forming the reactive boron-stabilizd carbanion. This carbanion then adds to the carbonyl carbon of the aldehyde generating a 1,2-hydroxy-bisboryl species. The resulting negatively charged oxygen species can then chelate to

one of the adjacent boron groups creating a 4-membered borate containing ring. The formation of this borate will induce a Wittig type elimination to occur expelling the LiOB(pin) group and forming the desired olefin. Morken's methodology enables the synthesis of vinyl boronates with a variety of substitution patterns depending on the conditions used. For example, the use of the pinacol derived diboron reagent typically yields the *Z* product in moderate selectivity while switching to the dimethyl pentanediol (dmpd) protected boron reagent leads the *E* product in moderate selectivity. While the boron-Wittig elimination process is a useful means of forming alkenyl boronates, it does come with the drawback that the useful alcohol functional group that is generated from the initial attack from the diboronate ester onto the carbonyl is removed from the product in the elimination step.

Scheme 3.1 Synthesis of vinyl boronate esters via boron-Wittig elimination

3.2.2 Synthesis of enantioenriched β-hydroxy alkenyl boronates

A straightforward approach to synthesizing enantioenriched β-hydroxy alkenyl boronates is the metathesis reaction of a vinyl boronate ester and a stereodefined allylic alcohol as illustrated in **Figure 3.2**. Vinyl boronate ester **3.6** is commercially available, however the necessary chiral allylic alcohol coupling partner typically need to be synthesized. There are several ways to make the allylic alcohols in high levels of enantioselectivity. The first is an iridium-catalyzed allylic substitution methodology developed by Carreira and Helmchen.[32–34] This method utilizes an iridium phosphoramidite catalyst system to convert linear allylic carbonates to stereodefined secondary allylic alcohols under mild conditions. Enzymatic methods also exist to resolve racemic mixtures of secondary allylic alcohols. This methodology typically is a resolution that converts one enantiomer to the acetate and leaves the other

enantiomer as the secondary alcohol.[35] Additionally, Hoveyda and coworkers have develop a methodology that employs a copper-NHC catalyst for the enantioselective allylic substitution of allylic carbonates to secondary allylic boronates which can then be stereospecifically oxidized to yield the desired enantioenriched allylic alcohols.[36] Of particular note, this methodology can be utilized for the enantioselective synthesis of tertiary allylic alcohols.

(a) Cross Metathesis

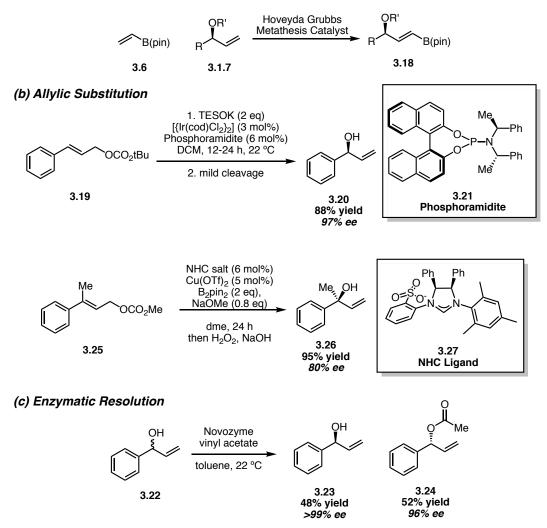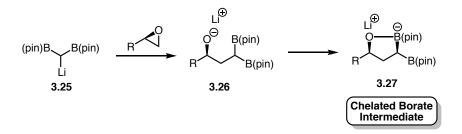**(b) Allylic Substitution**

(c) Enzymatic Resolution

Figure 3.2 Synthesis of enantioenriched allylic alcohols

While methodologies to make these molecular scaffolds do exist, there are some drawbacks that are illustrated in the previous examples. While the methods to obtain enantioenriched allylic alcohols for use in metathesis exist, this approach is not the most efficient since an additional step must be undertaken. Additionally, enzymatic resolution

pathways are often substrate dependent so the breadth of scope of available starting materials is limited. Therefore, the development of new methodologies for the synthesis of enantioenriched β-hydroxy alkenyl boronates that take a different synthetic approach and can potentially utilize more commercially available starting materials would be useful to the synthetic community.

3.2.3 Synthesis of β-hydroxy alkenyl boronates via dehydroboration

Epoxides are an attractive class of molecules to use in the synthesis of β-hydroxy alkenyl boronates since many enantioenriched epoxides are commercially available and the synthesis and resolution of epoxides is a well-developed field. Using deprotonated 1,1-organodiboronate esters to open epoxides generates the compound **3.27** shown in **Scheme 3.2**. Since previous work had illustrated that this intermediate is reactive in boron based functionalization, it had potential to be a useful intermediate for the synthesis of β-hydroxy alkenyl boronates.

Scheme 3.2 Epoxide opening with diborylmethane to generate a chelated borate intermediate

In order to use intermediate **3.27** as a means of forming alkenyl boronates, an approach different from the boron-Wittig reaction must be taken. The reasoning for this is two-fold. First, the alcohol is a desirable functional group and incorporating it into the product would be very useful. Additionally, intermediate **3.27** can be achieved with defined stereochemistry at the alcohol position through the use of an enantioenriched epoxide starting material. This then allows for the incorporation of a chiral alcohol into the product. Secondly, the 1,3 relationship between the alcohol and the boron will allow for a chelate to form, however it will not allow for the Wittig type elimination to occur. The boron-Wittig elimination requires a 1,2 orientation between the boron and oxygen in order to occur. The previous work on the copper-catalyzed

allylation of intermediate **3.27** illustrated that the activation of the boron by the coordinating oxygen is enough to facilitate transmetallation to a copper catalyst. It was therefore plausible that transmetallation to other metal catalysts could be achieved.

3.2.4 Precedent for Pd-catalyzed formation of olefins via dehydrogenation

In 2015, Newhouse and coworkers reported the palladium-catalyzed dehydrogenation of esters and nitriles.[37] Up to this point, dehydrogenation of strongly electron withdrawing groups such as esters and nitriles could not be accomplished in a single synthetic step. Newhouse's work presented a methodology to achieve the formation of carbon-carbon double bonds adjacent to electron withdrawing groups in a single step using a palladium catalyst. Using a strong base such as LTMP and a zinc additive, an alkyl ester is deprotonated at the β-position. This alkyl zinc (**3.33**) can then undergo transmetallation to the palladium catalyst (**3.32**). This alkyl palladium species (**3.34**) can then undergo β-hydride elimination to release the desired product (**3.29**). This methodology proved to be suitable for a variety of alkyl esters and nitriles. Later in 2016, this work was extended to include amides and was even viable in the presence of free alcohols and amines.[38]

A similar mechanistic approach can be envisioned for transforming intermediate **3.27** into a β-hydroxy alkenyl boronate ester. The boron participating in the oxygen chelate is ready for transmetallation to palladium. If the intermediate can successfully transmetallate to palladium, the resulting alkyl palladium species will behave analogously to intermediate **3.34** in the mechanism proposed by Newhouse resulting in a β-hydride elimination to furnish the desired alkenyl boronate ester. This proposed reaction is outlined in **Scheme 3.3.**
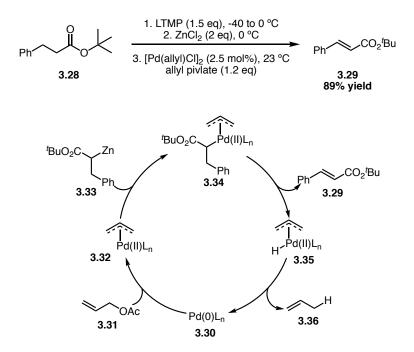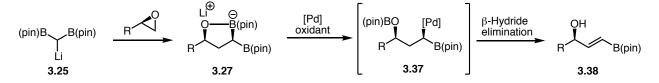
Figure 3.3 Pd-catalyzed ester dehydrogenation developed by Newhouse and coworkers

Scheme 3.3 Proposed reaction

3.3 Synthesis of alkenyl boronates via Pd-catalyzed dehydroboration[39]

3.3.1 Reaction optimization

Initial reaction screening was completed using a palladium allyl chloride dimer as catalyst, allyl chloride as the oxidant, and styrene oxide at 20 °C for 24 hours which did not result in the generation of product (**Table 3.1**, **Entry 1**). Increasing the temperature to 40 °C afforded the desired product in 42% yield (**Table 3.1**, **Entry 2**) and further warming to 60 °C increased the conversion to 63% (**Table 3.1, Entry 3**). Initially, it appeared that the product was formed as a mixture of olefin isomers as two pairs of doublets were visible for the olefin in the ^{1}H-NMR spectra of the compound. However, upon purification via silica gel chromatography only the trans-olefin isomer was isolated. Revisiting the crude ^{1}H-NMR spectra of the compound showed that the two pairs of doublets had almost identical coupling constants indicating that

the two compounds being formed were not likely to be olefin isomers as a significant difference in coupling constants would be expected. It was then proposed that the two observed compounds were the desired product and a related compound where the B(pin) group was still bound to the oxygen. This coordination of boron to the oxygen occurs in the catalytic cycle but should be substituted out by a proton during the aqueous ammonium chloride workup conditions that the reaction is subjected to. It was theorized that the ammonium chloride quench followed by immediate extraction was not sufficiently protonating the alcohol in the product. To overcome this, the workup was modified to include a 30-minute stir of the crude reaction with a solution of saturated aqueous ammonium chloride. This resulted in the formation of a single product as the free alcohol under all reaction conditions.

Table 3.1 Reaction optimization

Reaction scheme:
3.39 (Ph epoxide) + 3.25 ((pin)B–CH(Li)–B(pin)) → 1. THF, 22 °C, 1 h; 2. [Pd] 2.5 mol%, allyl chloride, THF, temp, 24 h → 3.40 (Ph–CH(OH)–CH=CH–B(pin)) and 3.41 (Ph–CH(O-allyl)–CH2–CH(B(pin))–B(pin))

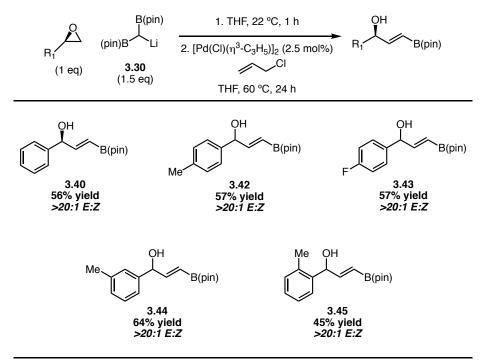| entry[a]	Pd catalyst	temp °C	conv[b] (%); **3.31:3.32**	E:Z
1	[Pd(allyl)Cl]₂	20	<5: -	
2	[Pd(allyl)Cl]₂	40	42; >98:2	>20:1
3	[Pd(allyl)Cl]₂	60	63; >98:2	>20:1
4	Pd(PPh₃)₄	60	59; <2:98	
5	PdCl₂(dppb)	60	76; <2:98	
6	PdCl₂(dppf)	60	46; <2:98	
7	Pd(dba)₂, binap	60	63; <2:98	
8[c]	[Pd(allyl)Cl]₂	60	62; >98:2	>20:1
9[d]	[Pd(allyl)Cl]₂	60	60; >98:2	>20:1

[a]Reactions performed under N_2 atm. [b]Values determined by analysis of 400 or 600 MHz ^{1}H NMR spectra of unpurified mixtures with DMF as internal standard. [c]Reaction run at [0.16M]. [d]Reaction run at [0.05M]

Both monodentate and bidentate ligands were then explored to try to increase the conversion to the desired alkenyl boronate product, however Pd complexes with phosphine ligands did not yield the desired product. Triphenylphosphine, dppb, dppf, and binap (**Table**

3.1, Entries 4-7) all provided moderate to good yields of the O-allylated product **3.41** instead of the desired alkenyl boronate ester **3.40**. Lastly, the role that concentration played in the reaction was explored by conducting the reaction at both an increased and decreased concentration however no major change in conversion was observed (**Table 3.2, Entries 8 & 9**). Allyl acetate was also studied as the oxidant instead of allyl chloride since it is the best oxidant in the work by Newhouse and coworkers[37,38] however, it resulted in a decrease in conversion to 54%.

3.3.2 Substrate scope

Aryl epoxides were the first class of epoxides applied to this reaction. Substitution at the ortho, meta, and para positions were all tolerated as illustrated in **Figure 3.4** with compounds **3.40** and **3.42 – 3.45**. It was also illustrated using the unsubstituted styrene oxide that the defined alcohol stereocenter derived from the epoxide remains enriched in the product by determining the enantiomeric excess of product **3.31** via chiral HPLC separation. After proving that the stereocenter is maintained throughout the reaction with model substrate **3.31**, most other substrates explored in this scope were racemic. When enantioenriched epoxides were used as substrates the stereochemistry is clearly illustrated in the product.
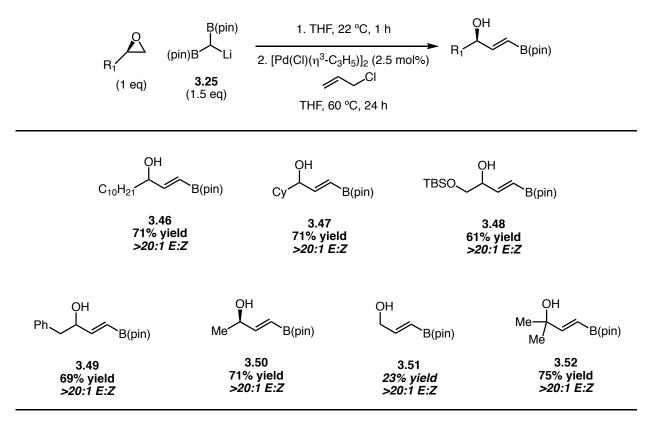
Figure 3.4 Substrate scope - aryl epoxides

A variety of simple alkyl epoxides were also successful in this reaction and typically gave better yields than what was observed with the aryl epoxides. Dodecyl and cyclohexyl substituted epoxides both yielded the desired alkenyl boronate in 71% yield as a single olefin isomer. The reaction to yield product **3.48** was completed on a gram scale in 61% yield. Benzyl substituted epoxide **3.49** also fared well giving the desired product in 69% yield as a single diastereomer. The simplest epoxide available, ethylene oxide, was successful in the reaction albeit in lower yield at only 23%. In the optimized reaction, the boron reagent is present in excess (1.5 eq) but due to the volatile nature of ethylene oxide, excess ethylene oxide was used in this reaction which most likely contributed to the decreased yield.

The simple transition from ethylene oxide to propylene oxide (**3.50**) resulted in a dramatic increase in yield to 71%. Propylene oxide is a liquid at room temperature and therefore the optimized stoichiometry could be employed. Additional substitution to isobutylene oxide

(**3.52**) yielded a similar result to propylene oxide at 75%. Both of these products were obtained as single olefin isomers.
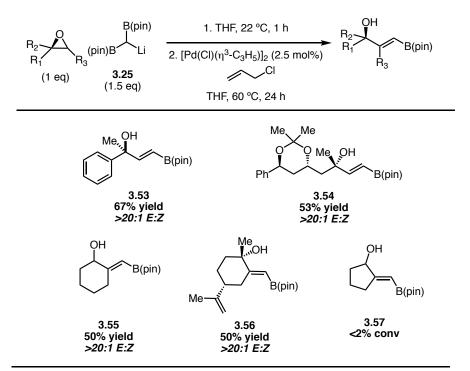

Reactions performed under N_2 atm. Yield represents isolated yield of purified material and is an average of two runs.

Figure 3.5 Substrate scope - alkyl epoxides

In addition to isobutylene oxide, other 1,1-disubsituted epoxides were also tolerated such as α-methyl styrene oxide (**3.53**). Product **3.54** which was obtained in 53% yield was derived from the previous work through a ring opening, allylation, epoxidation, and protection sequence which was explained in detail in Chapter 2. Both of these products were isolated as single olefin isomers.

The reaction was also tolerant of epoxides fused on 6-membered rings. Cyclohexene oxide opened in 50% yield (**3.55**) as a single olefin isomer with the boron unit trans to the alcohol substituent as expected. The more complex limonene oxide (**3.56**) led to a diminished 34% conversion. Interestingly, cyclopentene oxide (**3.57**) was not a viable substrate for this
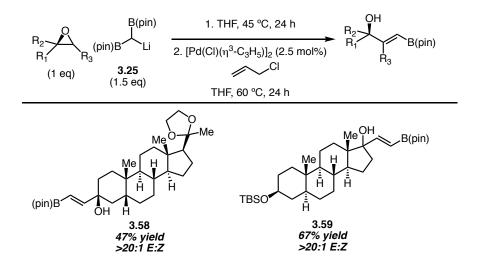
reaction. The epoxide did not appear to undergo ring opening under the optimized reaction conditions or at increased temperature.

Figure 3.6 Substrate scope - di & trisubstituted epoxides

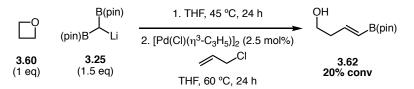The last epoxide substrates explored for this reaction were complex steroid derived molecules. In particular, a progesterone derived epoxide which led to product **3.58** in 47% yield as a single olefin isomer and an androsterone derived epoxide which yielded product **3.59** in 67% yield and 5:1 dr as a single olefin isomer. The dr for the androsterone based product is the same dr as the starting epoxide.

Figure 3.7 Substrate scope - steroid derived epoxides

After successfully exploring the substrate scope with respect to the epoxide, further expansion of the substrate scope was explored. Oxetanes, the four-membered analogs of epoxides, can also undergo ring opening when treated with a nucleophile such as a Grignard reagent.[40,41] Exposing an oxetane to the lithiated diborylmethane species should result in ring opening and the formation of a chelate similar to that with the epoxides. In this case, the chelate would be a six-membered ring instead of the five-membered ring generated from reaction with an epoxide. Six membered rings are an energetically favorable ring size so forming this chelate should be possible. Treating trimethylene oxide with **3.25** in THF at 45 °C for 24 hours followed by addition of palladium and allyl chloride and increasing the reaction temperature to 60 °C for an additional 24 hours resulted in a 20% NMR conversion to the desired alkenyl boron compound **3.62** as a single olefin isomer. In an attempt to increase the yield, an excess of oxetane was used however this did not result in an improved reaction.

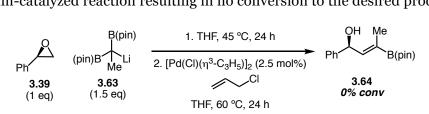**Scheme 3.4** Substrate scope – oxetane

There are a couple of possible reasons why the reaction with the oxetane is not as high yielding as the epoxide reactions. First, trimethylene oxide is a completely unsubstituted oxetane and the most comparable epoxide would be ethylene oxide. As previously discussed, ethylene oxide is a very poor substrate for this reaction producing a yield that is quite comparable to that observed with oxetane. With the epoxides, the addition of a simple methyl group was enough to dramatically increase the conversion from 23% to 71%. It is possible that this increase is simply due to the highly volatile nature of ethylene oxide or that the presence of substitution on the ring helps to improve the efficiency of the ring opening or stability of the chelated intermediate. Applying this reaction to more substituted oxetanes could result in an increase in yield.

Another possible reason for the decrease in reactivity could be the change in shape from epoxide to oxetane. The bond angles in a four-membered ring are significantly bigger (around 90°) than those in a three-membered ring (around 60°) and the approach of the nucleophile to the ring might need to occur differently than in the epoxide chemistry. This could be similar to the reaction with cyclopentene oxide in which the epoxide did not open most likely due to conformational or steric restraints. One more possible explanation is derived from the size of the chelate. As is illustrated by the increased temperature (60 °C) required to give appreciable product yields in this reaction, transmetallation from the chelated intermediate to the palladium is potentially a challenging mechanistic step. The transmetallation from the six-membered chair-like chelate formed from opening the oxetane might be an even more difficult ring to break than the five-membered chelate which could contribute to the decreased yield.

The other component to the scope of the reaction is with respect to the boron reagent. When diborylethane, **3.63**, was used in place of diborylmethane no product was observed. It was known from previous work (see Chapter 2) that the lithiated derivative of diborylethane is reactive enough to open dodecene oxide at 45 °C over 24 hours, however this ring opened

intermediate had not been reactive towards allylation chemistry. This same trend was observed in this palladium-catalyzed reaction resulting in no conversion to the desired product.
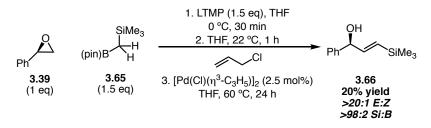

Scheme 3.5 Substrate scope – diborylethane

Another potential modification to expand the scope of the reaction would be to substitute one of the boron moieties for a different group. This would potentially allow for the chelate to still exist through the remaining boron and allow for transmetallation to the palladium, however instead of eliminating to form an alkenyl boronate ester, an alkene with a different terminal group would be formed. In order for this to work, a derivative of diborylmethane is needed that was easy to synthesize, stable, and sufficiently acidic at the methylene protons to allow for easy deprotonation. In 1982 Matteson and coworkers reported the synthesis of mixed boron silicon reagents such as compound **3.65**.[42] In their work, they illustrated the synthesis for this reagent and conducted deprotonation studies to explore the relative acidity of the methylene unit. Their work suggested that this reagent could be viable in our reaction as the methylene position could be deprotonated by LTMP with TMEDA as activator.[42] This reagent could either generate the alkenyl silane via boron transmetallation to palladium followed by elimination or generate an undesired 1,4-Brook rearrangement side product.

To test the viability of **3.65** in this reaction, it was treated with LTMP at 0 °C for 30 minutes followed by addition of styrene oxide and warming to room temperature for one hour. After one hour at room temperature the reaction mixture was transferred to the Pd catalyst and allyl chloride was added. The reaction was heated to 60 °C for 24 hours and a 20% yield of a single olefin isomer was observed. Additionally, 23% of the ring opened but not eliminated product was observed. The vinyl silane product was the only elimination product observed, no vinyl boron product was formed. This indicates that transmetallation to palladium is faster than

both the dehydrosilylation reaction and the 1,4-Brook rearrangement. Adding TMEDA to the

deprotonation step to emulate Matteson's conditions[42] did not yield any of the desired product.

This is most likely due to the TMEDA ligating to the palladium catalyst generating a species that
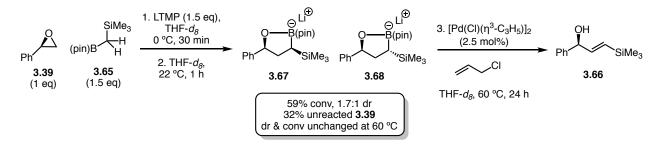
is not catalytically competent.

Scheme 3.6 Substrate scope - mixed boron silicon reagent

3.3.3 Mechanistic studies of vinyl silane formation

To gain additional insight into why this reaction was so low yielding relative to the

diborylmethane variant, an NMR study was undertaken. **3.65** was treated with LTMP in

deuterated THF followed by addition of styrene oxide. Following the reaction via ^{1}H NMR

revealed a 59% conversion to cyclic borates **3.67** and **3.68** in a 1.7:1 ratio. This is slightly lower

yielding and slightly more diastereoselective than what is oberserved via ^{1}H NMR when the

reaction is conducted with diborylmethane (see Chapter 2). Additionally, 32% of unreacted **3.39**

was observed. The ratio and quantity of the cyclic borates did not change upon heating the

reaction mixture to 60 °C in the spectrometer. Upon addition of the palladium and allyl

chloride, a complex mixture was observed. Both of the cyclic borates began to be consumed, the

olefin peaks of the product began to grow in, and a multitude of unidentifiable peaks grew in

(see Experimental). This complex spectrum prevented further analysis of the reaction after the

addition of the palladium catalyst and allyl chloride. However, since the conversion to the cyclic

borates is significantly higher than the conversion to the final product, the decreased efficiency

must be related to the dehydroboration step. This was further confirmed through a separate

control reaction in which **3.65** was deprotonated with LTMP under these conditions and the

resulting anion was quenched with allyl bromide. The resulting allyl product was obtained in

65% conversion with 26% returned starting material (see Experimental). This supports the theory that the difficult step is the dehydroboration reaction since the conversion to allyl product is comparable to the amount of cyclic borate seen in the NMR experiment.

Scheme 3.7 Mechanistic studies

2.3.4 Product Functionalizations

To illustrate the versatility of the products two types of functionalizations were undertaken. First, the application of these alkenyl boronates to cross coupling was studied (**Figure 3.8**). Using cross coupling conditions employing tetrakis(triphenylphosphine)palladium as catalyst and cesium carbonate as a base additive in a mixture of toluene and water at 80 °C, good yields of cross coupled product were obtained. Compound **3.47** was successfully coupled to a vinyl bromide to yield diene **3.70** in 65% yield as well as with 3-bromopyridine to yield the heterocyclic product **3.73** in 59% yield. Notably, these cross couplings could be carried out directly on the alkenyl boronates without protection of the alcohol.
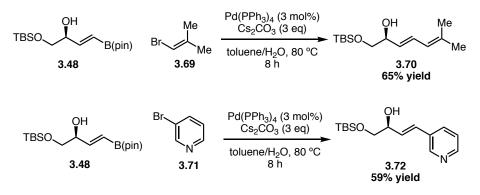

Figure 3.8 Cross coupling of alkenyl boronate products

The second functionalization studied employed the adjacent hydroxyl group as a directing group in a diastereoselective Simmons-Smith cycloproponation following conditions developed by Shi and coworkers.[5,6] Taking vinyl boronate **3.74** and treating it with an excess of diethylzinc and diiodomethane in a mixture of trifluoroethanol and hexanes at 22 °C for 24 hours resulted in the cycloproponation of the olefin in 65% yield as a single diastereomer (**3.75**).
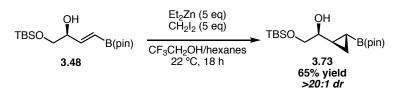

Figure 3.9 Cycloproponation of alkenyl boronate ester

3.4 Conclusion

In summary, an efficient synthesis of alkenyl boronates from 1,1-diborylmethane and epoxides utilizing a simple palladium catalyst system and allyl chloride as a sacrificial hydride acceptor was developed. This reaction gives the desired hydroxy alkenyl boronates in good yield as a single olefin isomer for both alkyl and aryl epoxides. The readily available nature of enantioenriched epoxides makes this an attractive method for the synthesis of these compounds as single enantiomers. Further application of this methodology to oxetanes and mixed boron-silicon reagents was explored with minimal success resulting in about 20% yield to the desired products in both cases. ^{1}H-NMR studies indicated that the epoxide was undergoing ring opening with the boron-silican reagent in higher yields (59%), therefore the reason for the decreased efficiency must be related to the dehydroboration step. The complex mixture obtained upon the addition of palladium and allyl chloride to the ^{1}H-NMR reaction prevented further study of the mechanism. Versatility of the products was demonstrated through cross coupling of the alkenyl boronate bearing the unprotected hydroxyl group as well as directed Simmons-Smith cycloproponation.

3.5 Experimental[39]

3.5.1 General

All reactions were carried out in oven-dried (150 °C) or flame dried glassware under inert atmosphere of dried nitrogen unless otherwise noted. Analytical thin-layer chromatography was performed on glass plates coated with 0.25 mm of 60 Å mesh silica gel. Plates were visualized by exposure to UV light (254 nm) and/or immersion into Seebach's or $KMnO_4$ stain followed by heating. Column chromatography using silica gel was performed using P60 (mesh 230-400) supplied by Silicycle. All solvents were sparged with argon and then purified under a positive pressure of argon through an SG Water, USA Solvent Purification System. Tetrahydrofuran (Omnisolv) was passed successively through two columns of neurtral alumina. The ambient temperature in the laboratory was approximately 22 °C.

3.5.2 Instrumentation

All ^{1}H NMR spectra were recorded on Bruker Spectrometers (AVANCE-600, Bruker 500, and DRX 400). Chemical shifts are reported in ppm from tetramethylsilane and referenced to the residual protio solvent peak ($CDCl_3$: δ 7.26; C_6D_6: δ 7.16; THF-d_8 δ 3.58). Data are reported as follows: chemical shift, multiplicity (s = singlet, d = doublet, t = triplet, qu = quartet, quint = quintet, br = broad, m = multiplet, app = apparent), integration, and coupling constants are given in Hz. ^{13}C NMR spectra were recorded on Bruker Spectrometers (AVANCE-600 and Bruker 500) with carbon and proton decoupling. Chemical shifts are reported in ppm from tetramethylsilane and referenced to the residual protio solvent peak ($CDCl_3$: δ 77.16; C_6D_6: δ 128.06, THF-d_8 δ 67.21). ^{11}B NMR spectra were recorded on a Bruker model 500 MHz spectrometer. All IR spectra were recorded on a Jasco 260 Plus Fourier transform infrared spectrometer. High-resolution mass spectrometry samples were analyzed with a hybrid LTQ FT (ICR 7T) (ThermoFisher, Bremen, Germany) mass spectrometer. Samples were introduced via a microelectrospray or APPI source at a flow rate of 10 μL/min in methanol or acetone. Xcalibur (ThermoFisher, Breman, Germany) was used to analyze the data. Molecular formula

assignments were determined with Molecular Formula Calculator (v 1.2.3). All observed species were singly charged, as verified by unit m/z separation between mass spectral peaks corresponding to the ^{12}C and $^{13}C^{12}C_{c-1}$ isotope for each elemental composition. MassHunter Quantitative Analysis (Agilent, Waldbronn, Germany) was used to analyze the data. Solutions were dissolved in MeOH at 0.1 mg/mL or less and diluted appropriately based on responsiveness to the ESI mechanism. Molecular formula assignments were determined with Molecular Formula Calculator (v 1.2.3). The success of mass data for molecular ions was considered based on the widely-accepted accuracy threshold for confirmation of elemental compositions established at 5 ppm. All observed species were singly charged, as verified by unit m/z separation between mass spectral peaks corresponding to the ^{12}C and $^{13}C^{12}C_{c-1}$ isotope for each elemental composition. Optical rotations were determined using a Jasco P1010 polarimeter and concentrations are reported in g/100mL. Enantiomeric ratios were determined on an Agilent Technologies 1220 Infinity LC using a Diacel CHIRALPAK IA (4.6 mm x 250 mm x 5µm) column. Melting points were determined using a Mel-Temp® apparatus.

3.5.3 Reagents

Allylbenzene was purchased from Alfa Aesar and used as received.

Allylchloride was purchased from Sigma Aldrich, plugged through neutral alumina before use and stored under nitrogen.

Allyl palladium(II) chloride dimer ([Pd(allyl)Cl]₂) was purchased from Strem, stored at -20 ºC in a nitrogen filled glovebox and used as received.

α-methylstyrene was purchased from Alfa Aesar and used as received.

Ammonium chloride was purchased from Alfa Aesar and used as received.

Benzene-d₆ was purchased from Cambridge Isotope Laboratories and used as received.

Bis(dibenzylideneacetone)palladium (0) (Pd(dba)₂) was purchased from Strem and stored in a nitrogen filled glovebox.

1,4-Bis(diphenylphosphino)butane (dppb) was purchased from Strem and stored in a nitrogen filled glovebox.

[1,1'-Bis(diphenylphosphino)ferrocene]dichloropalladium (II) (Pd(dppf)Cl$_2$) was purchased from Strem and stored in a nitrogen filled glovebox.

3-Bromopyridine was purchased from Alfa Aesar and used as received.

^{n}Butyl Lithium was purchased from Strem and used as received.

^{i}Butylene oxide was purchased from Alfa Aesar and used as received.

Chloroform-d (CDCl$_3$) was purchased from Cambridge Isotope Laboratories and used as received.

3-Chloroperbenzoic acid (50-55% wt in water) was purchased from Alfa Aesar and used as received.

Cyclohexene oxide was purchased from Alfa Aesar and used as received.

Dibromomethane was purchased from Alfa Aesar and passed through a plug of neutral alumina prior to use.

Diethyl zinc (1M in Hexanes) was purchased from Sigma Aldrich and used as received.

1-Dodecene was purchased from Alfa Aesar and used as received.

Dimethylformamide, anhydrous (DMF) was purchased from EMD and used as received.

Diborylmethane was prepared according to literature procedures[43] and matched literature spectra. It was purified via silica gel chromatography, dried via azeotropic distillation from benzene, and stored in a nitrogen filled glovebox.

Ethylene glycol was purchased from BDH and used as received.

Ethylene oxide was purchased from Sigma Aldrich and used as received.

4-Fluorostyrene was purchased from Alfa Aesar and used as received

Imidazole was purchased from Alfa Aesar and used as received.

(+)-Limonene oxide, mixture of cis and trans was purchased from Sigma Aldrich and dried via azeotropic distillation from benzene.

Lithium 2,2,6,6-tetramethylpiperidide (LTMP) was purchased from Sigma Aldrich and stored in a nitrogen filled dry box.

2-Methylstyrene was purchased from Alfa Aesar and used as received.

3-Methylstyrene was purchased from Alfa Aesar and used as received.

4-Methylstyrene was purchased from Alfa Aesar and used as received.

Palladium (II) Dichloride was purchased from Strem and stored in a nitrogen filled dry box.

Potassium *tert*-Butoxide was purchased from Strem Chemicals, stored in a desiccator, and used as received.

Progesterone was purchased from Sigma Aldrich and used as received.

***(R)*-Propylene oxide** was purchased from Alfa Aesar and used as received.

***p*-Toluenesulfonic acid monohydrate** was purchased from Sigma Aldrich and used as received.

***(R)*-BINAP** was purchased from Strem Chemicals and stored in a nitrogen filled dry box.

***(R)*-Styrene oxide** was purchased from Sigma Aldrich and dried via azeotropic distillation before use.

tert-Butyldimethylsilyl (*R*)-(-)-glycidyl ether was purchased from Sigma Aldrich and used as received.

tert-Butyldimethylsilyl chloride was purchased from Alfa Aesar and used as received.

***trans*-Androsterone** was purchased from Sigma Aldrich and used as received.

Tetrakis (triphenylphosphine)palladium (0) was purchased from Strem and stores a 0 °C in a nitrogen filled dry box.

Trifluoroethanol was purchased from Sigma Aldrich, dried over calcium sulfate, distilled, and sparged with N_2 prior to use.
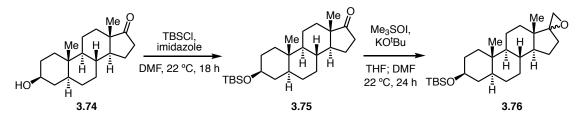
Trimethyl((4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)methyl)silane (8) was synthesized according to known literature methods.[42]

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Trimethylsulfoxonium iodide was purchased from Bean Town Chemical and used as received.

Vinylcyclohexane was purchased from Alfa Aesar and used as received.

3.5.4 General Procedures

General Procedure for the Synthesis of Epoxides – Epoxides yielding products **3.42-3.47**, **3.49** and **3.53 – 3.54** were synthesized according to the following general procedure as previously disclosed (Chapter 2).[44]

Trans-androsterone (500 mg, 1.7 mmol, 1 eq) was dissolved in DMF (18 mL) in a round bottom flask containing a stir bar. Imidazole (347 mg, 5.1 mmol, 3 equiv) was then quickly added and the flask was purged with N_2. tert-Butyldimethylsilyl chloride (769 mg, 5.1 mmol, 3 equiv) was then quickly added as a solid and the flask was again purged with N_2. The reaction was allowed to stir overnight at 22 °C upon which it turned into a thick white slurry. The reaction was cooled to 0 °C, quenched with aqueous ammonium chloride, extracted with diethyl ether, dried over magnesium sulfate, and concentrated *in vacuo*. The crude reaction mixture was purified via silica gel chromatography to yield the desired silyl protected steroid **3.75** in 86% yield (594 mg) which matched known literature spectra.[45]

Epoxide **S3** was synthesized following a procedure reported by Hamilton *et al.*[46] **3.75** (250 mg, 0.62 mmol, 1eq), potassium *tert*-butoxide (278.3 mg, 2.48 mmol, 4 equiv), and trimethylsulfoxonium iodide (546 mg, 2.48 mmol, 4 equiv) were weighed into an 8 mL vial containing a stir bar. The flask was sealed with a septum and purged with N_2. The solids were slurried in THF (1.5 mL) and DMF (1.5 mL) and stirred at 22 °C for 24 hours. The slurry was then cooled to 0 °C, diluted with water, and filtered through a fritted funnel. The solids were

collected and purified via silica gel chromatography to give the desired epoxide **3.76** in 52%

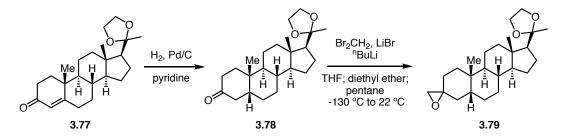yield (134 mg) and 2:1 dr.

Major Diastereomer

¹H NMR (600 MHz, CDCl₃) δ 3.54 (tt, J = 11.0, 4.6 Hz, 1H), 2.89 (d, J = 5.1 Hz, 1H), 2.59 (d,

J = 5.1 Hz, 1H), 1.97 (ddd, J = 14.2, 11.0, 2.1 Hz, 1H), 0.88 (s, 9H), 0.87 (s, 3H), 0.81 (s, 3H),

0.05 (s, 6H).

Minor Diastereomer

¹H NMR (600 MHz, CDCl₃) δ 3.54 (tt, J = 11.0, 4.6 Hz, 1H), 2.73 (d, J = 4.5 Hz, 1H), 2.66 (d,

J = 4.5 Hz, 1H), 2.26 (ddd, J = 15.3, 10.5, 2.3 Hz, 1H), 0.88 (s, 9H), 0.81 (s, 3H), 0.80 (s, 3H),

0.05 (s, 6H).

¹³C NMR (151 MHz, CDCl₃) δ 72.3, 70.7, 70.2, 54.7, 54.4, 53.8, 53.1, 52.9, 47.5, 45.3, 45.2,

41.7, 40.3, 38.8, 38.8, 37.4, 35.8, 35.8, 35.8, 35.7, 34.2, 32.1, 32.1, 32.1, 31.8, 30.4, 30.1, 29.2,

28.8, 28.8, 26.1, 26.1, 24.2, 23.7, 20.8, 20.4, 18.4, 16.3, 14.5, 12.5, -4.4.

HRMS (APCI⁺) [M(-OH)]⁺ calcd for $C_{26}H_{45}OSi^+$ 401.3234, found 401.3200. **IR (ν/cm⁻¹):**

2928 (s), 2855 (s), 1470 (m), 1449 (m), 1376 (m), 1359 (m), 1249 (s), 1096 (s), 1081 (s). **Melting**

Point: 129-131 ⁰C.
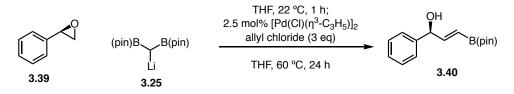
Compound **3.78** was synthesized using a known literature procedure and matched literature

spectra.[47] **3.77** (200 mg, 0.56 mmol, 1 equiv) was weighed into an 8 mL vial containing a stir

bar. Palladium on carbon (20 mg, 10% wt/wt) was added to the vial. The solids were dissolved in

degassed pyridine, the vial was sealed with a septum lined cap, and the vial was purged with N_2.

The atmosphere was replaced with hydrogen by purging the reaction with a balloon of hydrogen

(x3) and the reaction was allowed to stir under a balloon pressure of hydrogen for two hours.

The mixture was then filtered over a plug of celite with ethyl acetate. The organics were washed with a solution of copper acetate to remove the pyridine. The organics were dried over magnesium sulfate and concentrated *in vacuo* to give the crude product. The mixture was purified vial silica gel chromatography to yield the desired product in 77% yield (155 mg) and >20:1 dr favoring the *cis* decalin.[48,49] **^{1}H NMR (500 MHz, CDCl$_3$)** δ 4.06 – 3.98 (m, 1H), 3.95 (td, *J* = 7.2, 5.9 Hz, 1H), 3.89 (p, *J* = 7.2 Hz, 2H), 2.70 (dd, *J* = 15.1, 13.5 Hz, 1H), 2.34 (td, *J* = 14.6, 5.4 Hz, 1H), 2.18 – 2.13 (m, 1H), 2.10 – 1.97 (m, 3H), 1.96 – 1.79 (m, 3H), 1.77 – 1.68 (m, 2H), 1.64 (dt, *J* = 7.1, 4.8 Hz, 1H), 1.55 – 1.32 (m, 6H), 1.30 (s, 3H), 1.25 (ddd, *J* = 9.6, 4.5, 2.2 Hz, 3H), 1.17 – 1.07 (m, 3H), 1.02 (s, 3H), 0.78 (s, 3H). **^{13}C NMR (126 MHz, CDCl$_3$)** δ 213.6, 112.0, 65.4, 63.4, 58.5, 56.5, 44.5, 42.5, 42.3, 40.9, 39.9, 37.4, 37.2, 35.2, 35.1, 26.8, 25.9, 24.7, 23.9, 23.1, 22.8, 21.1, 13.2. **HRMS (ESI$^+$)** [2M+Na]$^+$ calcd for C$_{46}$H$_{72}$O$_6$Na 743.5227, found 743.5204. **IR (v/cm^{-1}):** 2939 (s), 2878 (m), 1716 (s), 1540 (m), 1455 (m). **[α]$^{22}_D$** = 31.6 (*c* = 0.185, CH$_2$Cl$_2$, l = 100 mm). **Melting Point:** 171 ºC

Following a modified literature procedure,[50] inside a glovebox LiBr (22 mg, 0.25 mmol, 1.1 equiv) was weighed into an 8 mL vial containing a stir bar. The solid was then dissolved in THF (1 mL), diethyl ether (0.2 mL), and pentane (0.1 mL). The vial was sealed with a septum lined cap and removed from the glovebox. Dibromomethane (0.018 mL, 0.25 mmol, 1.1 equiv) was added via syringe. The mixture was then cooled to -130 ºC in a pentane/liquid N$_2$ bath. ^{n}BuLi (0.156 mL, 0.25 mmol, 1.1 equiv) was added dropwise via syringe. The mixture was allowed to stir at -130 ºC for 30 minutes. A solution of **3.78** (82 mg, 0.23 mmol, 1 equiv) in a minimal amount of THF was added via cannula to the cooled reaction mixture. The reaction was stirred at -130 ºC for 90 minutes and then allowed to warm to room temperature slowly. The reaction was quenched with saturated ammonium chloride, extracted with diethyl ether (x3), dried over magnesium sulfate, and concentrated *in vacuo*. The crude reaction mixture was purified via silica gel chromatography to yield the desired product in 54% yield (46 mg) and >20:1 dr.
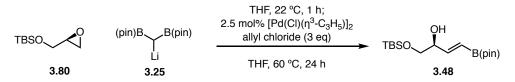
¹H NMR (600 MHz, CDCl₃) δ 4.02 (dt, J = 7.6, 6.5 Hz, 1H), 3.97 (td, J = 7.2, 6.0 Hz, 1H), 3.94 – 3.86 (m, 2H), 2.69 – 2.60 (m, 2H), 2.41 (t, J = 13.8 Hz, 1H), 2.07 (dt, J = 12.3, 3.0 Hz, 1H), 2.01 – 1.88 (m, 2H), 1.32 (s, 3H), 1.03 (s, 3H), 0.79 (s, 3H). **¹³C NMR (151 MHz, CDCl₃)** δ 112.1, 65.4, 63.4, 59.4, 58.6, 56.7, 53.7, 42.3, 40.9, 40.3, 40.1, 35.3, 34.8, 34.4, 33.7, 28.3, 26.6, 26.3, 24.7, 23.9, 23.6, 23.2, 21.1, 13.2. **IR (ν/cm⁻¹):** 2930 (s), 2869 (s), 1540 (m), 1472 (m), 1455 (m), 1446 (m), 1374 (m), 1260 (m), 1244 (m), 1216 (m), 1052 (m). **HRMS (APCI⁺)** [M+H]⁺ calcd for $C_{24}H_{39}O_3^+$ 375.2899, found 375.2868. **[α]²²_D** = 17.1 (c = 0.540, CH₂Cl₂, l = 100 mm).

Melting Point: 156-163 °C

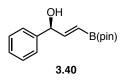### *General procedure for dehydroboration reactions*

Inside of a nitrogen filled dry box, diborylmethane (40.2 mg, 0.15 mmol, 1.5 equiv) was weighed into an 8-mL vial containing a magnetic stir bar. The solids were dissolved in THF (0.4 mL) and sealed with a septum lined cap. Lithium 2,2,6,6-piperidine (LTMP) (22.0 mg, 0.15 mmol, 1.5 equiv) was added to a separate 8-mL vial, dissolved in THF (0.8 mL) and sealed with a septum lined cap. Palladium (allyl)chloride dimer ([Pd(allyl)Cl]₂) (0.9 mg, 0.0025 mmol, 2.5 mol%) was weighed into a third 8-mL vial containing a stir-bar. The vials were sealed with a septum lined cap and all vials were removed from the glovebox. The vial containing diborylmethane and LTMP were cooled to 0 °C in an ice water bath. The LTMP solution was then cannula transferred under nitrogen to the diborylmethane solution at 0 °C. The mixture was allowed to stir at 0 °C for 10 min (30 minutes for **3.65**) after which epoxide (0.1 mmol, 1 equiv) was added via syringe. The solution was then allowed to warm to 22 °C and stirred at the necessary temperature for the required time period based on the epoxide used (monosubstituted epoxides: 22 °C, 1h; disubstituted epoxides: 22 °C, 24 h; trisubstituted epoxides, **3.54**, **3.58 & 3.59**: 45 °C, 24 h). The reaction mixture was then cannula transferred under nitrogen to the vial

containing the palladium catalyst. Allyl chloride (24 µL, 0.3 mmol, 3 equiv) was added to the vial via syringe and the vial was sealed with Teflon tape. The reaction was stirred at 60 °C for 24 h then allowed to cool to 22 °C and quenched with a saturated aqueous solution of ammonium chloride. The biphasic mixture was rapidly stirred for 30 minutes. The organics were then extracted three times with diethyl ether, dried over magnesium sulfate and concentrated *in vacuo* to yield the crude product. The product was purified via silica gel chromatography (8:1 to 2:1 Hexanes:Ethyl Acetate; visualized with Seebach stain).

General procedure for gram scale dehydroboration reactions

Inside of a nitrogen filled dry box, diborylmethane (2.2 g, 8.15 mmol, 1.5 equiv) was weighed into a round bottom flask containing a magnetic stir bar. The solids were dissolved in THF (22 mL) and sealed with a septum. Lithium 2,2,6,6-piperidine (LTMP) (1.2 g, 8.15 mmol, 1.5 equiv) was added to a separate round bottom flask, dissolved in THF (43 mL) and sealed with a septum. Palladium (allyl)chloride dimer ([Pd(allyl)Cl]₂) (50.0 mg, 0.14 mmol, 2.5 mol%) was weighed into a third flask containing a stir-bar. The flasks containing diborylmethane and LTMP were cooled to 0 °C in an ice water bath. The LTMP solution was then cannula transferred under nitrogen to the diborylmethane solution at 0 °C. The mixture was allowed to stir at 0 °C for 10 min after which epoxide (1.2 mL, 5.43 mmol, 1 equiv) was added via syringe. The solution was then allowed to warm to 22 °C and stirred at 22 °C for 1 hour. The reaction mixture was then cannula transferred under nitrogen to the flask containing the palladium catalyst. Allyl chloride (1.3 mL, 16.8 mmol, 0.3 equiv) was added to the flask via syringe. The reaction was stirred at 60 °C for 24 h then allowed to cool to 22 °C and quenched with a saturated aqueous solution of ammonium chloride. The biphasic mixture was rapidly stirred for 30 minutes. The organics were then extracted three times with diethyl ether, dried over magnesium sulfate and

concentrated *in vacuo* to yield the crude product. The product was purified via silica gel chromatography (10:1 Hexanes:Ethyl Acetate; visualized with Seebach stain) to yield **3h** in 61% (1.14 g) and >20:1 *E:Z* as a yellow oil.
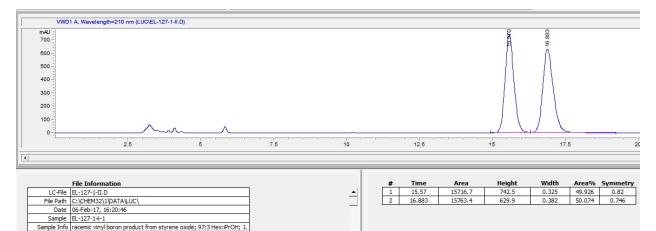
3.5.5 Product characterization

3.40

(*S,E*)-1-phenyl-3-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)prop-2-en-1-ol (3.40). Following the general procedure, vinyl boronate ester **3.40** was isolated in 56% yield and >20:1 *E:Z* (14.4 mg) as a white solid. **¹H NMR** (400 MHz, CDCl$_3$) δ 7.46 – 7.35 (m, 4H), 7.31 (dd, *J* = 5.6, 3.1 Hz, 1H), 6.78 (dd, *J* = 18.0, 5.3 Hz, 1H), 5.77 (dd, *J* = 18.0, 1.6 Hz, 1H), 5.27 (d, *J* = 5.3 Hz, 1H), 2.08 – 1.93 (m, 1H), 1.28 (s, 12H). **¹³C NMR** (151 MHz, CDCl$_3$) δ 153.7, 142.0, 128.7, 128.0, 126.6, 83.5, 76.3, 24.9, 24.9. **HRMS (ESI⁺)** [M+Na]⁺ calcd for C$_{15}$H$_{21}$BONa⁺ 283.1481, found 283.1471. **IR (ν/cm⁻¹):** 3446 (m, br), 2978 (m), 1639 (s), 1358 (s), 1144 (s), 849 (m), 700 (m). **[α]²²$_D$** = -28.7 (*c* = 0.755, CH$_2$Cl$_2$, l = 100 mm). **Melting Point:** 108-110 °C.
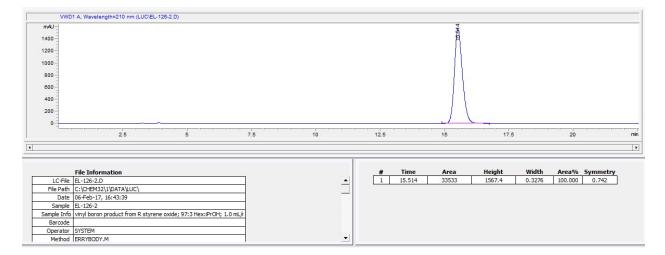
Retention of stereochemistry was confirmed by comparing the chiral HPLC traces of the product made with racemic styrene oxide to that made with *R*-styrene oxide. *Daicel CHIRALPAK IA; 97:3 Hex:iPrOH; 1.0 mL/min; 210 nm*

Racemic Material

VWD1 A, Wavelength=210 nm (LUC\EL-127-1-II.D)

File Information	
LC-File	EL-127-1-II.D
File Path	C:\CHEM32\1\DATA\LUC\
Date	06-Feb-17, 16:20:46
Sample	EL-127-1-ii-1
Sample Info	racemic vinyl boron product from styrene oxide; 97:3 Hex:iPrOH; 1.

#	Time	Area	Height	Width	Area%	Symmetry
1	15.57	15716.7	742.5	0.325	49.926	0.82
2	16.883	15763.4	629.9	0.382	50.074	0.746

Enantioenriched Material

VWD1 A, Wavelength=210 nm (LUC\EL-126-2.D)

File Information	
LC-File	EL-126-2.D
File Path	C:\CHEM32\1\DATA\LUC\
Date	06-Feb-17, 16:43:39
Sample	EL-126-2
Sample Info	vinyl boron product from R styrene oxide; 97:3 Hex:iPrOH; 1.0 mL/r
Barcode	
Operator	SYSTEM
Method	ERRYBODY.M

#	Time	Area	Height	Width	Area%	Symmetry
1	15.514	33533	1567.4	0.3276	100.000	0.742

Major: 15.5 min; Minor:16.9 min; >99:1 e.r.

3.41

(*E*)-3-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)-1-(*p*-tolyl)prop-2-en-1-ol (3.41).

Following the general procedure, vinyl boronate ester **3.41** was isolated in 57% yield and >20:1

E:Z (15.7 mg) as a white solid. **¹H NMR** (500 MHz, CDCl$_3$) δ 7.28 (d, *J* = 4.3 Hz, 2H), 7.18 (d, *J*

= 7.8 Hz, 2H), 6.77 (dd, *J* = 18.0, 5.2 Hz, 1H), 5.76 (dd, *J* = 17.9, 1.5 Hz, 1H), 5.24 (d, *J* = 5.2 Hz,

1H), 2.36 (s, 3H), 1.99 (s, 1H), 1.27 (s, 12H). **¹³C NMR** (151 MHz, CDCl$_3$) δ 153.9, 137.7, 129.4,

126.6, 83.5, 76.1, 24.9, 24.9, 21.3. **HRMS (ESI⁺)** [M+Na]⁺ calcd for C$_{16}$H$_{23}$BONa⁺ 297.1638,
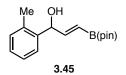
found 297.1629. **IR (v/cm⁻¹):** 3446 (m, br), 2978 (m), 1640 (s), 1322 (s), 1144 (s), 970 (m), 950 (m), 900 (m), 849 (m). **Melting Point:** 83 °C.

3.42

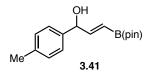**(*E*)-1-(4-fluorophenyl)-3-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)prop-2-en-1-ol (3.42).** Following the general procedure, vinyl boronate ester **3.42** was isolated in 57% yield and >20:1 *E:Z* (15.7 mg) as a clear oil. **¹H NMR** (600 MHz, CDCl₃) δ 7.37 – 7.26 (m, 3H), 7.03 (t, *J* = 8.7 Hz, 2H), 6.71 (dd, *J* = 18.0, 5.3 Hz, 1H), 5.73 (dd, *J* = 18.0, 1.5 Hz, 1H), 5.23 (m, 1H), 2.03 (d, *J* = 3.6 Hz, 1H), 1.26 (s, 12H). **¹³C NMR** (151 MHz, CDCl₃) δ 162.5 (d, *J* = 246.0 Hz), 153.5, 137.7 (d, *J* = 3.0 Hz), 128.3 (d, *J* = 8.3 Hz), 115.5 (d, *J* = 21.2 Hz), 83.6, 75.6, 24.9, 24.9. **HRMS (ESI⁺)** [M+Na]⁺ calcd for $C_{15}H_2BFONa^+$ 301.1387, found 301.1376. **IR (v/cm⁻¹):** 3435 (m, br), 2979 (m), 1642 (m), 1509 (s), 1390 (s), 1358 (s), 1324 (s), 1221 (m), 1143 (s), 970 (m).

3.44
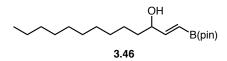
 **(*E*)-3-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)-1-(*m*-tolyl)prop-2-en-1-ol (3.44).** Following the general procedure, vinyl boronate ester **3.44** was isolated in 64% yield and >20:1 *E:Z* (17.5 mg) as a white solid. **¹H NMR** (600 MHz, CDCl₃) δ 7.23 (t, *J* = 7.6 Hz, 1H), 7.17 (s, 1H), 7.15 (d, *J* = 7.7 Hz, 1H), 7.09 (d, *J* = 7.5 Hz, 1H), 6.75 (dd, *J* = 18.0, 5.3 Hz, 1H), 5.74 (dd, *J* = 18.0, 1.6 Hz, 1H), 5.21 (dd, *J* = 5.3, 1.5 Hz, 1H), 2.35 (s, 3H), 1.25 (s, 12H). **¹³C NMR** (151 MHz, CDCl₃) δ 153.9, 142.0, 138.4, 128.7, 128.6, 127.2, 123.6, 83.5, 76.3, 24.9, 24.9, 21.6. **HRMS (ESI⁺)** [M+Na]⁺ calcd for $C_{16}H_{23}BONa^+$ 297.1638, found 297.1628. **IR (v/cm⁻¹):** 3432 (m, br), 2979 (m), 1638 (m), 1390 (s), 1357 (s), 1322 (s), 1270 (m), 1144 (s), 970 (m). **Melting Point:** 70-72 °C.

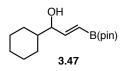**(*E*)-3-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)-1-(*o*-tolyl)prop-2-en-1-ol (3.45).**

Following the general procedure, vinyl boronate ester **3.45** was isolated in 45% yield and >20:1 *E:Z* (12.3 mg) as a clear oil. **¹H NMR** (600 MHz, CDCl₃) δ 7.45 (dd, *J* = 7.5, 1.5 Hz, 1H), 7.24 (td, *J* = 7.5, 1.6 Hz, 1H), 7.21 (td, *J* = 7.4, 1.6 Hz, 1H), 7.17 − 7.14 (m, 1H), 6.75 (ddd, *J* = 18.1, 5.2, 0.7 Hz, 1H), 5.75 (dd, *J* = 18.1, 1.5 Hz, 1H), 5.49 (d, *J* = 5.1 Hz, 1H), 2.37 (s, 3H), 2.00 − 1.91 (m, 1H), 1.28 (s, 12H). **¹³C NMR** (151 MHz, CDCl₃) δ 152.9, 139.9, 135.5, 130.6, 127.8, 126.5, 126.2, 83.5, 72.9, 24.9, 24.9, 19.4. **HRMS (ESI⁺)** [M+Na]⁺ calcd for C₁₆H₂₃BONa⁺ 297.1638, found 297.1627. **IR (ν/cm⁻¹):** 3446 (br, m), 2978 (m), 2929 (m), 1638 (m), 1357 (s), 1322 (s), 1144 (s), 970 (m), 849 (m).

(*E*)-1-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)tridec-1-en-3-ol (3.46). Following the general procedure, vinyl boronate ester **3.46** was isolated in 71% yield and >20:1 *E:Z* (22.9 mg) as a clear oil. **¹H NMR** (600 MHz, CDCl₃) δ 6.64 (dd, *J* = 18.1, 5.3 Hz, 1H), 5.64 (dd, *J* = 18.2, 1.4 Hz, 1H), 4.17 (m, 1H), 1.55 (m, 3H), 1.28 (m, 27H), 0.99 − 0.80 (m, 3H). **¹³C NMR** (151 MHz, CDCl₃) δ 155.5, 83.4, 73.9, 36.8, 32.1, 29.8, 29.7, 29.5, 25.5, 24.9, 24.9, 24.9, 22.8, 14.3. **HRMS (ESI⁺)** [M+Na]⁺ calcd for C₁₉H₃₇BONa⁺ 347.2733, found 347.2723. **IR (ν/cm⁻¹):** 3435 (br, m), 2977 (m), 2925 (s), 2854 (s), 1643 (m), 1466 (m), 1389 (s), 1359 (s), 1321 (s), 1145 (s).

(*E*)-1-cyclohexyl-3-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)prop-2-en-1-ol (3.47). Following the general procedure, vinyl boronate ester **3.47** was isolated in 71% yield and >20:1 *E:Z* (18.9 mg) as a clear oil. **¹H NMR** (600 MHz, CDCl₃) δ 6.61 (dd, *J* = 18.1, 5.6 Hz, 1H),

5.61 (dd, J = 18.1, 1.4 Hz, 1H), 3.91 (t, J = 5.9 Hz, 1H), 1.89 − 1.56 (m, 5H), 1.42 (m, 1H), 1.27 (s, 12H), 1.24 − 1.10 (m, 4H), 1.02 (m, 2H). **¹³C NMR** (151 MHz, CDCl₃) δ 154.2, 83.4, 78.4, 43.3, 29.1, 28.1, 26.6, 26.3, 26.2, 24.9, 24.9. **HRMS (ESI⁺)** [M+Na]⁺ calcd for C₁₅H₂₇BONa⁺ 289.1951, found 289.1939. **IR (ν/cm⁻¹):** 3437 (br, m), 2978 (m), 2926 (s), 2852 (m), 1642 (m), 1450 (m), 1389 (s), 1359 (s), 1321 (s), 1144 (s).

3.48

(*R*,*E*)-1-((*tert*-butyldimethylsilyl)oxy)-4-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)but-3-en-2-ol (3.48). Following the general procedure, vinyl boronate ester **3.48** was isolated in 61% yield and >20:1 *E:Z* (1.14 g) as a yellow oil. **¹H NMR** (500 MHz, CDCl₃) δ 6.54 (dd, J = 18.2, 4.8 Hz, 1H), 5.76 (dd, J = 18.2, 1.7 Hz, 1H), 4.23 (m, 1H), 3.69 (dd, J = 10.1, 3.6 Hz, 1H), 3.45 (dd, J = 10.1, 7.8 Hz, 1H), 2.57 (d, J = 3.6 Hz, 1H), 1.26 (s, 12H), 0.89 (s, 9H), 0.06 (s, 6H). **¹³C NMR** (151 MHz, CDCl₃) δ 150.8, 83.4, 73.8, 66.7, 26.0, 24.9, 24.9, 24.8, 18.5, -5.2, -5.2. **HRMS (ESI⁺)** [2M+Na]⁺ calcd for C₃₂H₆₆B₂O₈Si₂Na⁺ 679.4380, found 679.4355. **IR (ν/cm⁻¹):** 3481 (br, m), 2979 (m), 2955 (m), 2929 (m), 2857 (m), 1644 (m), 1471 (m), 1389 (m), 1354 (s), 1324 (s), 1257 (m), 1145 (s), 1109 (s). **[α]²²_D** = 4.0 (*c* = 0645, CH₂Cl₂, l = 100 mm).

3.49
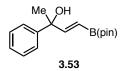
(*E*)-1-phenyl-4-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)but-3-en-2-ol (3.49). Following the general procedure, vinyl boronate ester **3.49** was isolated in 69% yield and >20:1 *E:Z* (18.9 mg) as a clear oil. **¹H NMR** (600 MHz, CDCl₃) δ 7.31 (m, 2H), 7.24 (m, 3H), 6.71 (dd, J = 18.1, 4.9 Hz, 1H), 5.69 (dd, J = 18.2, 1.5 Hz, 1H), 4.43 − 4.32 (m, 1H), 2.92 (dd, J = 13.7, 4.3 Hz, 1H), 2.73 (dd, J = 13.7, 8.8 Hz, 1H), 1.68 (s, 1H), 1.27 (s, 12H). **¹³C NMR** (151 MHz, CDCl₃) δ 154.1, 137.9, 129.6, 128.7, 126.8, 83.5, 74.3, 43.4, 24.9, 24.9. **HRMS (ESI⁺)** [M+Na]⁺ calcd for

$C_{16}H_{23}BO_3SiNa^+$ 297.1638, found 297.1627. **IR (v/cm⁻¹):** 3436 (br, m), 2978 (m), 2928 (m), 1642 (s), 1390 (s), 1359 (s), 1321 (s), 1144 (s).

3.50

**(R,E)-4-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)but-3-en-2-ol (3.50).** Following the general procedure, vinyl boronate ester **3.50** was isolated in 71% yield and >20:1 *E:Z* (14.0 mg) as a clear oil.[51] **¹H NMR** (600 MHz, CDCl₃) δ 6.65 (dd, *J* = 18.1, 5.0 Hz, 1H), 5.61 (dd, *J* = 18.1, 1.5 Hz, 1H), 4.34 (qdd, *J* = 6.6, 4.9, 1.5 Hz, 1H), 1.28 (m, 15H). **¹³C NMR** (151 MHz, CDCl₃) δ 156.3, 83.5, 69.8, 24.9, 22.8. **[α]²²_D** = -5.6 (*c* = 0.67, CH₂Cl₂, l = 100 mm).
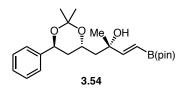
3.51

(E)-3-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)prop-2-en-1-ol (3.51). Following the general procedure, vinyl boronate ester **3.51** was isolated in 23% yield and >20:1 *E:Z* (4.3 mg) as a clear oil.[52] **¹H NMR** (600 MHz, CDCl₃) 6.74 (dt, *J* = 18.2, 4.2 Hz, 1H), 5.71 (dt, *J* = 18.2, 1.9 Hz, 1H), 4.24 (dd, *J* = 4.3, 1.9 Hz, 2H), 1.27 (s, 12H). **¹³C NMR** (151 MHz, CDCl₃) δ 151.8, 83.5, 64.7, 24.9.

3.52

(E)-2-methyl-4-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)but-3-en-2-ol (3.52). Following the general procedure, vinyl boronate ester **3.52** was isolated in 76% yield and >20:1 *E:Z* (16.1 mg) as a clear oil.[53] **¹H NMR** (500 MHz, CDCl₃) δ 6.71 (d, *J* = 18.2 Hz, 1H), 5.61 (d, *J* = 18.2 Hz, 1H), 1.49 (s, 1H), 1.31 (s, 6H), 1.27 (s, 12H). **¹³C NMR** (126 MHz, CDCl₃) δ 159.9, 83.4, 71.9, 29.3, 24.9. **HRMS (ESI⁺)** [M+Na]⁺ calcd for $C_{11}H_{21}BO_3Na^+$ 235.1481, found 235.1471. **IR (v/cm⁻¹):** 3436 (br, m), 2977 (m), 1638 (m), 1458 (m), 1372 (s), 1348 (s), 1320 (s), 1215 (m), 1144 (s), 970 (m).

3.53

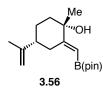**(*E*)-2-phenyl-4-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)but-3-en-2-ol (3.53).**

Following the general procedure, vinyl boronate ester **3.53** was isolated in 67% yield and >20:1

E:Z (18.4 mg) as a clear oil.[54] **¹H NMR** (500 MHz, CDCl$_3$) δ 7.51 – 7.41 (m, 2H), 7.33 (dd, *J* =

8.5, 7.0 Hz, 2H), 7.26 – 7.22 (m, 1H), 6.86 (d, *J* = 18.1 Hz, 1H), 5.69 (d, *J* = 18.1 Hz, 1H), 1.97 (s,

1H), 1.66 (s, 3H), 1.26 (s, 12H). **¹³C NMR** (151 MHz, CDCl$_3$) δ 158.2, 145.9, 128.4, 127.1, 125.4,

83.5, 75.5, 29.3, 25.0, 24.9. **HRMS (ESI⁺)** [M+Na]⁺ calcd for $C_{16}H_{23}BO_3Na^+$ 297.1638, found

297.1627. **IR (v/cm⁻¹):** 3459 (br, m), 2978 (m), 1635 (m), 1388 (m), 1372 (m), 1348 (s), 1322

(m), 1165 (m), 1144 (s).

3.54
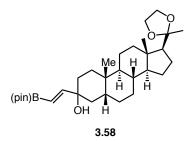
(*S*,*E*)-1-((4*S*,6*S*)-2,2-dimethyl-6-phenyl-1,3-dioxan-4-yl)-2-methyl-4-(4,4,5,5-

tetramethyl-1,3,2-dioxaborolan-2-yl)but-3-en-2-ol (3.54). Following the general

procedure, vinyl boronate ester **3.54** was isolated in 53% yield and >20:1 *E:Z* (10.5 mg) as a

clear oil. **¹H NMR** (500 MHz, CDCl$_3$) δ 7.45 – 7.31 (m, 4H), 7.29 – 7.27 (m, 1H), 6.65 (d, *J* = 18.1

Hz, 1H), 5.68 (d, *J* = 18.0 Hz, 1H), 4.88 (dd, *J* = 9.7, 6.3 Hz, 1H), 4.37 (dq, *J* = 10.2, 3.3 Hz, 1H),

3.61 (s, 1H), 2.01 (ddd, *J* = 13.2, 9.7, 6.3 Hz, 1H), 1.92 (ddd, *J* = 13.1, 9.1, 6.3 Hz, 1H), 1.85 (dd, *J*

= 14.7, 10.3 Hz, 1H), 1.69 (dd, *J* = 14.8, 2.7 Hz, 1H), 1.49 (s, 3H), 1.45 (s, 3H), 1.34 (s, 3H), 1.27

(s, 12H). **¹³C NMR** (151 MHz, CDCl$_3$) δ 159.3, 142.2, 128.6, 127.7, 126.1, 101.3, 83.3, 73.3, 68.7,

64.9, 46.1, 40.6, 26.7, 25.1, 25.0, 24.9. **HRMS (ESI⁺)** [M+Na]⁺ calcd for $C_{46}H_{70}B_2O_{10}Na_2^+$

827.5053, found 827.5037. **IR (v/cm⁻¹):** 3514 (br, w), 2979 (m), 2929 (m), 1639 (m), 1495 (m),

1454 (m), 1379 (s), 1349 (s), 1320 (m), 1225 (m), 1166 (m), 1144 (s). **[α]²²$_D$** = -34.7 (*c* = 0.525,

CH$_2$Cl$_2$, l = 100 mm). **Melting Point:** 105-109 ⁰C.
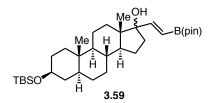
(*E*)-2-((4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)methylene)cyclohexan-1-ol

(3.55). Following the general procedure, vinyl boronate ester **3.55** was isolated in 50% yield and >20:1 *E:Z* (12.0 mg) as a clear oil. **^{1}H NMR** (600 MHz, CDCl$_3$) δ 5.32 (s, 1H), 4.07 − 4.02 (m, 1H), 3.13 − 3.06 (m, 1H), 2.16 − 1.95 (m, 2H), 1.83 − 1.75 (m, 1H), 1.70 (ddt, *J* = 9.8, 5.0, 3.0 Hz, 1H), 1.63 (s, 1H), 1.56 − 1.45 (m, 1H), 1.39 (dddd, *J* = 20.8, 12.5, 10.6, 4.0 Hz, 3H), 1.26 (s, 12H). **^{13}C NMR** (151 MHz, CDCl$_3$) δ 167.0, 83.0, 74.5, 37.1, 31.5, 28.2, 25.0, 24.9, 24.3. **HRMS (ESI$^+$)** [M+Na]$^+$ calcd for C$_{13}$H$_{23}$BONa$^+$ 261.1638, found 261.1628. **IR (ν/cm^{-1}):** 3421 (br, m), 2977 (m), 2931 (m), 2857 (m), 1645 (s), 1371 (s), 1328 (s), 1144 (s).

**(1*S*,4*R*,*E*)-1-methyl-4-(prop-1-en-2-yl)-2-((4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)methylene)cyclohexan-1-ol (3.56).** Following the general procedure, vinyl boronate ester **3.56** was isolated in 34% yield and >20:1 *E:Z* (9.9 mg) as a clear oil. **^{1}H NMR** (500 MHz, CDCl$_3$) δ 5.32 (d, *J* = 1.0 Hz, 1H), 4.80 − 4.67 (m, 1H), 3.10 (ddd, *J* = 12.9, 3.5, 2.0 Hz, 1H), 2.38 (ddd, *J* = 12.9, 11.7, 1.1 Hz, 1H), 1.98 (ddt, *J* = 11.5, 7.0, 3.6 Hz, 1H), 1.89 (dt, *J* = 13.2, 3.5 Hz, 1H), 1.83 (ddd, *J* = 12.9, 3.9, 1.3 Hz, 1H), 1.77 (s, 2H), 1.64 − 1.56 (m, 2H), 1.51 − 1.42 (m, 1H), 1.38 (s, 3H), 1.33 (s, 1H), 1.27 (d, 6H), 1.27 (d, 6H), 1.26 − 1.24 (m, 1H). **^{13}C NMR** (151 MHz, CDCl$_3$) δ 167.0, 149.6, 108.8, 83.2, 46.9, 40.4, 35.0, 27.7, 26.7, 25.1, 24.9, 24.9, 21.4. **HRMS (ESI$^+$)** [M+Na]$^+$ calcd for C$_{17}$H$_{29}$BO$_3$Na$^+$ 315.2107, found 315.2098. **IR (ν/cm^{-1}):** 3419 (br, w), 2977 (m), 2932 (m), 1637 (s), 1371 (s), 1325 (s), 1261 (m), 1144 (s). **[α]^{22}$_D$** = 32.4 (*c* = 0.495, CH$_2$Cl$_2$, l = 100 mm). **Melting Point:** 41-43 °C.

3.58

(5R,8R,9S,10S,13S,14S,17S)-10,13-dimethyl-17-(2-methyl-1,3-dioxolan-2-yl)-3-((E)-2-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)vinyl)hexadecahydro-1H-cyclopenta[a]phenanthren-3-ol (3.58). Following the general procedure (0.04 mmol scale), vinyl boronate ester **3.58** was isolated in 47% yield (9.6 mg), >20:1 *E:Z* and >20:1 dr.

¹H NMR (600 MHz, CDCl₃) δ 6.68 (d, *J* = 18.2 Hz, 1H), 5.64 (d, *J* = 18.2 Hz, 1H), 4.00 (dt, *J* = 7.5, 6.5 Hz, 1H), 3.95 (td, *J* = 7.2, 5.9 Hz, 1H), 3.92 – 3.84 (m, 2H), 1.30 (s, 3H), 1.28 (s, 12H), 0.74 (s, 3H). **¹³C NMR (151 MHz, CDCl₃)** δ 161.1, 112.1, 83.4, 73.6, 65.4, 63.3, 58.6, 56.7, 42.3, 40.0, 39.9, 38.1, 37.5, 35.3, 34.7, 31.8, 31.6, 26.7, 26.4, 25.0, 25.0, 24.7, 23.9, 23.8, 23.1, 21.0, 13.2. **HRMS (APCI⁺)** [M(-OH)]⁺ calcd for $C_{31}H_{50}BO_4^+$ 497.3797, found 497.37501. **IR (ν/cm⁻¹):** 3480 (br, m), 2975 (s), 2931 (s), 2883 (m), 1637 (m), 1446 (m), 1387 (s), 1371 (s), 1348 (s), 1320 (s), 1270 (m), 1145 (s), 1052 (s). **[α]²²_D** = 20.7 (*c* = 0.48, CH₂Cl₂, l = 100 mm). **Melting Point:** 185-187 °C.

3.59

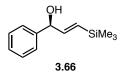**(3S,5S,8R,9S,10S,13S,14S)-3-((*tert*-butyldimethylsilyl)oxy)-10,13-dimethyl-17-((E)-2-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)vinyl)hexadecahydro-1H-cyclopenta[a]phenanthren-17-ol (3.59).** Following the general procedure (0.05 mmol scale), vinyl boronate ester **3.59** was isolated in 67% yield (18.6 mg) and >20:1 *E:Z,* and 5:1 dr.

Major Diastereomer

¹H NMR (600 MHz, CDCl₃) δ 6.77 (d, *J* = 18.2 Hz, 1H), 5.55 (d, *J* = 18.2 Hz, 1H), 3.61 – 3.40 (m, 1H), 1.29 (s, 12H), 0.89 (s, 3H), 0.88 (s, 9H), 0.80 (s, 3H), 0.04 (s, 6H).
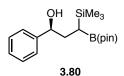
Minor Diastereomer

¹H NMR (600 MHz, CDCl₃) δ 6.77 (d, *J* = 18.2 Hz, 1H), 5.66 (d, *J* = 18.2 Hz, 1H), 3.61 – 3.40 (m, 1H), 1.29 (s, 12H), 0.89 (s, 3H), 0.88 (s, 9H), 0.80 (s, 3H), 0.04 (s, 6H).

¹³C NMR (151 MHz, CDCl₃) δ 157.7, 85.1, 83.4, 72.3, 54.2, 50.3, 47.1, 45.3, 38.8, 37.4, 36.6, 36.4, 35.8, 32.7, 32.1, 31.9, 28.9, 26.1, 25.0, 24.9, 24.9, 23.9, 21.0, 18.4, 14.5, 12.5, -4.4. **HRMS (APCI⁺)** [M(-OH)]⁺ calcd for $C_{33}H_{58}BO_3^+$ 541.4243, found 541.4243. **IR (ν/cm⁻¹):** 3498 (m), 2928 (s), 2855 (s), 1632 (m), 1348 (s), 1144 (m), 1093 (m), 1068 (m), 1006 (m). **Melting Point:** 194-195 ⁰C.

3.62

(*E*)-4-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)but-3-en-1-ol (3.62). Following the general procedure, vinyl boronate **3.62** was obtained in 20% yield calculated via comparison to a known amount of DMF used as an internal standard. A small quantity was obtained via silica gel chromatography for proof of identity and matched literature spectra.[55] **¹H NMR (500 MHz, CDCl₃)** δ 6.60 (dt, *J* = 18.0, 6.7 Hz, 1H), 5.56 (d, *J* = 18.0 Hz, 1H), 3.73 (t, *J* = 6.3 Hz, 2H), 2.44 (qd, *J* = 6.4, 1.5 Hz, 2H), 1.26 (s, 12H).

3.66

(*S*,*E*)-1-phenyl-3-(trimethylsilyl)prop-2-en-1-ol (3.66). Following the general procedure, vinyl silane **3.66** was isolated in 20% yield (3.9 mg) and >20:1 *E:Z* as a colorless oil and matched known literature spectra.[56] A trace amount of product with B(pin) bound to the alcohol is also present. **¹H NMR (500 MHz, CDCl₃)** δ 7.36 (d, *J* = 5.2 Hz, 4H), 7.29 (q, *J* = 1.0 Hz, 1H), 6.20 (dd, *J* = 18.6, 5.2 Hz, 1H), 6.00 (dd, *J* = 18.7, 1.4 Hz, 1H), 5.19 (d, *J* = 4.9 Hz, 1H), 1.94 (s, 1H), 0.07 (s, 9H).

3.80

(S,E)-1-phenyl-3-(trimethylsilyl)prop-2-en-1-ol (3.80). Compound **3.80** was isolated in

23% yield (7.7 mg) as a byproduct of the dehydroboration reaction shown in **Scheme 3.7**.

Major Diastereomer

^{1}H NMR (500 MHz, CDCl$_3$) δ 7.43 – 7.29 (m, 4H), 7.23 (m, 1H), 4.83 – 4.67 (m, 1H), 2.31 (s,

1H), 2.12 – 1.89 (m, 2H), 1.25 (s, 6H), 1.24 (s, 6H), 0.54 (dd, J = 12.4, 2.7 Hz, 1H), 0.01 (s, 9H).

Minor Diastereomer
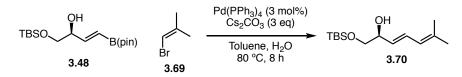
^{1}H NMR (500 MHz, CDCl$_3$) δ 7.43 – 7.29 (m, 4H), 7.23 (m, 1H), 4.52 (m, 1H), 2.45 (d, J = 4.6

Hz, 1H), 1.84 – 1.71 (m, 2H), 1.27 (s, 6H), 1.27 (s, 6H), 0.31 (dd, J = 12.4, 2.7 Hz, 1H), 0.02 (s,

9H).

^{13}C NMR (151 MHz, CDCl$_3$) δ 144.9, 128.5, 128.4, 127.5, 127.1, 126.1, 125.8, 83.2, 83.1, 77.6,

75.6, 66.0, 35.9, 35.7, 29.9, 25.3, 25.2, 25.1, 25.0, 15.4, -1.4, -1.4. **HRMS (ESI$^+$)** [M+Na]$^+$ calcd

for $C_{18}H_{31}BO_3SiNA^+$ 357.2033, found 357.2022. **IR (ν/cm^{-1}):** 3838 (br, m), 3459 (m), 1379 (s),

1351 (s), 1247 (s), 1143 (s), 1066 (s).
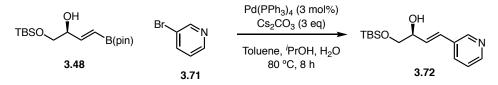
3.5.6 Product functionalizations

Procedures for cross-coupling reactions

(S,E)-1-((*tert*-butyldimethylsilyl)oxy)-6-methylhepta-3,5-dien-2-ol (3.70). Inside a

glovebox vinyl boron **3.48** (39 mg, 0.12 mmol), Pd(PPh$_3$)$_4$ (3.5 mg, 0.003 mmol, 3 mol%), and

Cs$_2$CO$_3$ (97.7 mg, 0.3 mmol, 3 eq) were weighed into an 8 mL vial with a stir bar and dissolved in

toluene (0.120 mL). The vial was sealed with a septum lined cap and removed from the

glovebox. Outside the glovebox, 1-bromo-2-methyl-1-propene (0.010 mL, 0.1 mmol, 1 eq) was

added via syringe followed by degassed water (0.080 mL). The reaction was then heated to 80
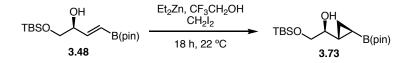
ºC and stirred for 8 hours after which the reaction was cooled to 22 ºC and quenched with a saturated solution of ammonium chloride. The organics were extracted with diethyl ether (x3), dried over magnesium sulfate, and concentrated *in vacuo*. The crude product was purified via silica gel chromatography (20:1 hexanes:diethyl ether) in 65% yield and a single olefin isomer of **3.70** (16.6 mg) as a clear oil. **¹H NMR** (500 MHz, CDCl$_3$) δ 6.52 (ddd, *J* = 15.3, 11.0, 1.2 Hz, 1H), 5.81 (dd, *J* = 10.9, 1.2 Hz, 1H), 5.48 (dd, *J* = 15.2, 6.6 Hz, 1H), 4.20 (m, 1H), 3.64 (dd, *J* = 10.0, 3.6 Hz, 1H), 3.43 (dd, *J* = 10.0, 8.1 Hz, 1H), 2.61 (d, *J* = 2.7 Hz, 1H), 1.77 (s, 3H), 1.76 (s, 3H), 0.90 (s, 9H), 0.08 (s, 6H). **¹³C NMR** (126 MHz, CDCl$_3$) δ 136.5, 128.9, 128.2, 124.5, 73.0, 67.4, 26.2, 26.0, 24.9, 18.5, 18.5, -5.2, -5.2. **HRMS (ESI⁺)** [2M+Na]⁺ calcd for C$_{28}$H$_{56}$NO$_4$Si$_2$⁺ 535.3615, found 535.3587. **IR (ν/cm⁻¹):** 3446 (br, m), 2955 (m), 2928 (s), 2857 (m), 1472 (m), 1254 (s), 1110 (s), 1061 (m). **[α]²²$_D$** = -8.1 (*c* = 0.84, CH$_2$Cl$_2$, l = 100 mm).

(*S,E*)-1-((*tert*-butyldimethylsilyl)oxy)-4-(pyridin-3-yl)but-3-en-2-ol (3.72). Inside the glovebox vinyl boron **3.48** (39 mg, 0.12 mmol), Pd(PPh$_3$)$_4$ (3.5 mg, 0.003 mmol, 3 mol%), and Cs$_2$CO$_3$ (97.7 mg, 0.3 mmol, 3 eq) were weighed into an 8 mL vial with a stir bar and dissolved in toluene (0.120 mL). The vial was sealed with a septum lined cap and removed from the glovebox. Outside the glovebox, 3-bromopyridine (0.010 mL, 0.1 mmol, 1 eq) was added via syringe followed by dry isopropyl alcohol (0.040 mL) and degassed water (0.040 mL). The reaction was then heated to 80 ºC and stirred for 8 hours after which the reaction was cooled to 22 ºC and quenched with a saturated solution of ammonium chloride. The organics were extracted with diethyl ether (x3), dried over magnesium sulfate, and concentrated *in vacuo*. The crude product was purified via silica gel chromatography to yield the desired product **3.72** (2:1 hexanes:ethyl acetate; pinacol removed via azeotropic distillation on a rotovap with MeOH:water (1:1) and 50 ºC water bath) in 59% yield and >20:1 *E:Z* (16.8 mg) as a clear oil.
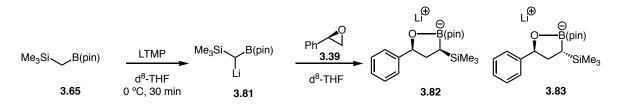
¹H NMR (600 MHz, CDCl₃) δ 8.60 (d, *J* = 2.2 Hz, 1H), 8.46 (dd, *J* = 4.8, 1.6 Hz, 1H), 7.68 (dt, *J* = 7.9, 2.0 Hz, 1H), 7.24 (ddd, *J* = 7.9, 4.8, 0.8 Hz, 1H), 6.68 (dd, *J* = 16.1, 1.4 Hz, 1H), 6.25 (dd, *J* = 16.1, 5.8 Hz, 1H), 4.42 – 4.31 (m, 1H), 3.75 (dd, *J* = 10.0, 3.8 Hz, 1H), 3.54 (dd, *J* = 10.0, 7.6 Hz, 1H), 2.82 (s, 1H), 0.91 (s, 9H), 0.10 (s, 3H), 0.09 (s, 3H). **¹³C NMR** (151 MHz, CDCl₃) δ 148.8, 148.5, 133.1, 132.5, 130.5, 128.1, 123.6, 72.7, 67.1, 26.0, 18.5, -5.2, -5.2. **HRMS (ESI⁺)** [M+H]⁺ calcd for $C_{23}H_{35}BO_5Na^+$ 280.1733, found 280.1719. **IR (ν/cm⁻¹):** 3243 (m, br), 2953 (m), 2857 (m), 1472 (s), 1418 (m), 1253 (s), 1112 (s), 1060 (m). **[α]²²_D** = -2.9 (*c* = 0.97, CH₂Cl₂, l = 100 mm).

Procedure for cycloproponation reaction
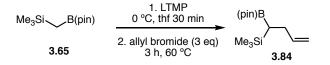
(*S*)-2-((*tert*-butyldimethylsilyl)oxy)-1-((1*R*,2*R*)-2-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)cyclopropyl)ethan-1-ol (3.73). Following the procedure by Walsh and coworkers,[5] vinyl boronate ester **3.48** (33.0 mg, 0.1 mmol, 1 eq) was weighed into a 8 mL vial containing a stir bar inside the glovebox. The vial was sealed with a septum lined cap and removed from the glovebox. The reaction was cooled to 0 °C in an ice water bath and a solution of diethyl zinc (0.5 mL, 0.5 mmol, 1M in hexanes, 5 eq) was added dropwise followed by trifluoroethanol (0.036 mL, 0.5 mmol, 5 eq) and diiodomethane (0.040 mL, 0.5 mmol, 5 eq). The reaction was allowed to warm to room temperature and wrapped in aluminum foil to exclude light. After 18 hours, the reaction was cooled to 0 °C in an ice water bath and quenched with ethyl acetate and aqueous ammonium chloride. The organics were extracted with ethyl acetate (x3), dried over magnesium sulfate, and concentrated *in vacuo* to give crude product. The product was purified via silica gel chromatography to yield **3.73** in 65% yield (22.1 mg) and >20:1 d.r. **¹H NMR (600 MHz, CDCl₃)** δ 3.71 (dd, *J* = 10.0, 3.3 Hz, 1H), 3.54 (dd, *J* = 10.0, 6.8 Hz, 1H), 3.03 – 2.86 (m, 1H), 2.47 (d, *J* = 3.8 Hz, 1H), 1.21 (s, 12H), 1.10 (tt, *J* = 7.9, 5.3 Hz, 1H), 0.90 (s, 9H), 0.74 (ddd, *J* = 7.7, 6.2, 3.5 Hz, 1H), 0.70 (ddd, *J* = 9.7, 5.2, 3.5 Hz, 1H), 0.07

(d, J = 3.1 Hz, 6H), -0.24 (dt, J = 9.6, 5.9 Hz, 1H). **^{13}C NMR (151 MHz, CDCl$_3$)** δ 83.2, 76.5, 67.0, 26.0, 24.8, 24.8, 19.9, 18.4, 9.0, -5.2, -5.2. **HRMS (ESI$^+$)** [M+Na]$^+$ calcd for C$_{17}$H$_{35}$BO$_4$SiNa$^+$ 365.2295, found 365.2291. **IR (ν/cm^{-1}):** 3481 (br, m), 2978 (s), 2955 (s), 2929 (s), 1471 (s), 1436 (s), 1372 (s), 1319 (s), 1145 (s), 1113 (s). **[α]^{22}$_D$** = 18.1 (c = 1.14, CH$_2$Cl$_2$, l = 100 mm).

3.5.7 Mechanistic studies
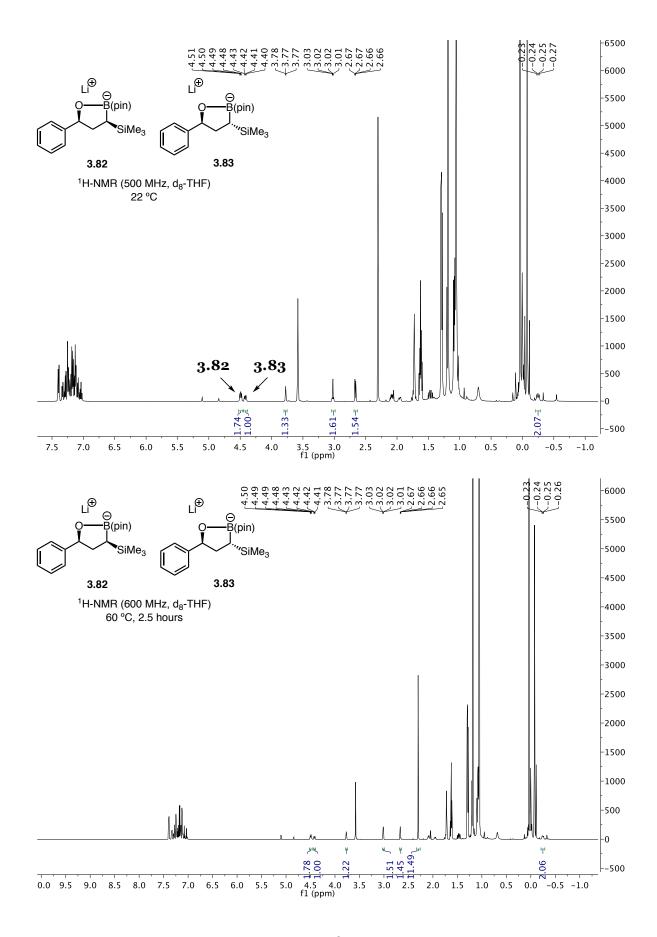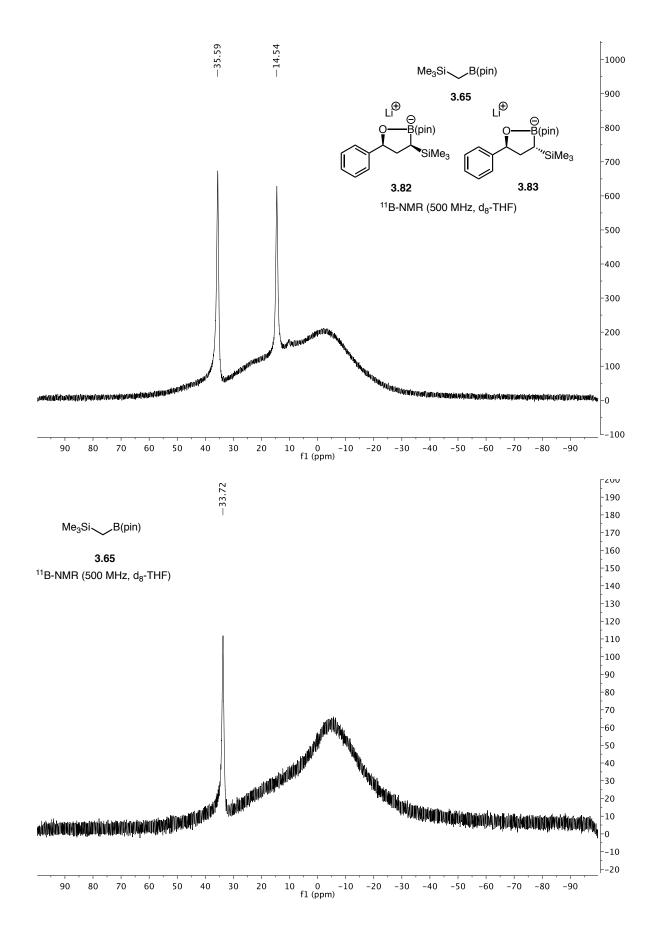
Inside a glovebox, compound **3.65** (0.019 mL, 0.075 mmol, 1.5 eq) was weighed into an 8 mL vial containing a stir bar and dissolved in d^8-THF (0.2 mL). LTMP (11 mg, 0.075 mmol, 1.5 eq) was weighed into a separate 8 mL vial and dissolved in d^8-THF (0.4 mL). Both vials were sealed with septa lined caps and removed from the glovebox. Outside the glovebox, the solutions were cooled to 0 ºC in an ice water bath. The LTMP solution was then cannula transferred under N$_2$ to the solution of **3.65**. The reaction was allowed to stir at 0 ºC for 30 minutes. Styrene oxide (0.005 mL, 0.05 mmol, 1 eq) and dry toluene (internal standard, 0.004 mL) were added via syringe. The reaction was than cannula transferred to an NMR tube sealed under N$_2$ with a septa lined cap. NMR spectroscopy indicated 59% conversion to **3.82** and **3.83** in a 1.7 to 1 ratio and 32% unopened **2**. This conversion and ratio did not change upon heating to 60 ºC for 2.5 hours. ^{11}B NMR indicated the presence of only two boron containing species, **3.65** and **3.82/3.83** indicating that further ring opening was unlikely to occur as there was no **3.81** remaining in the reaction. 1D-NOESY spectroscopy identified an nOe interaction between the benzylic hydrogen and methine hydrogen at the base of the boron and silicon groups in the major diastereomer which was used to assign the proposed structures.

Me₃Si–B(pin) → (pin)B, Me₃Si

1. LTMP
0 °C, thf 30 min

2. allyl bromide (3 eq)
3 h, 60 °C

3.65

3.84
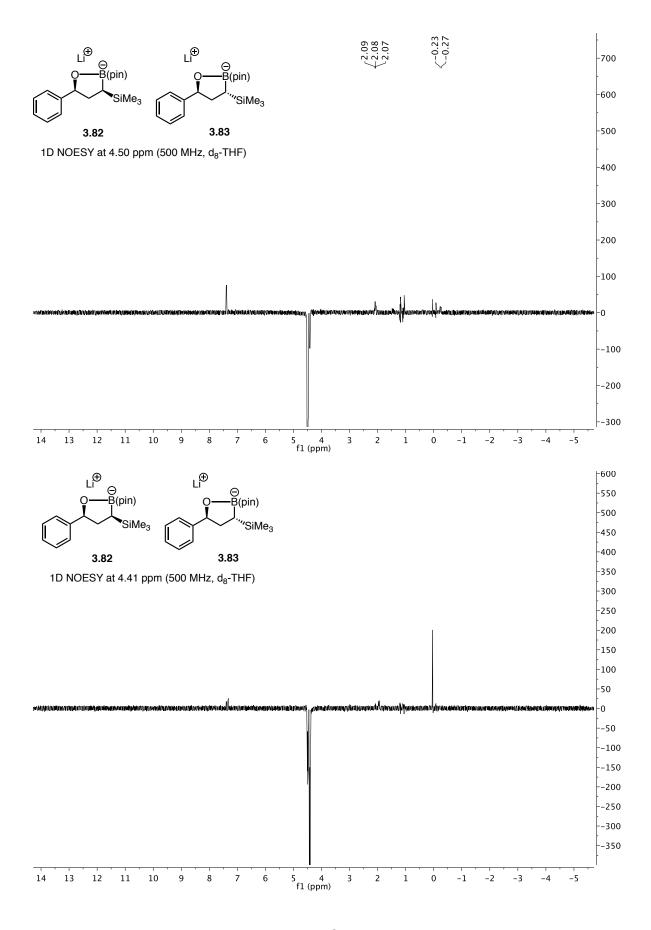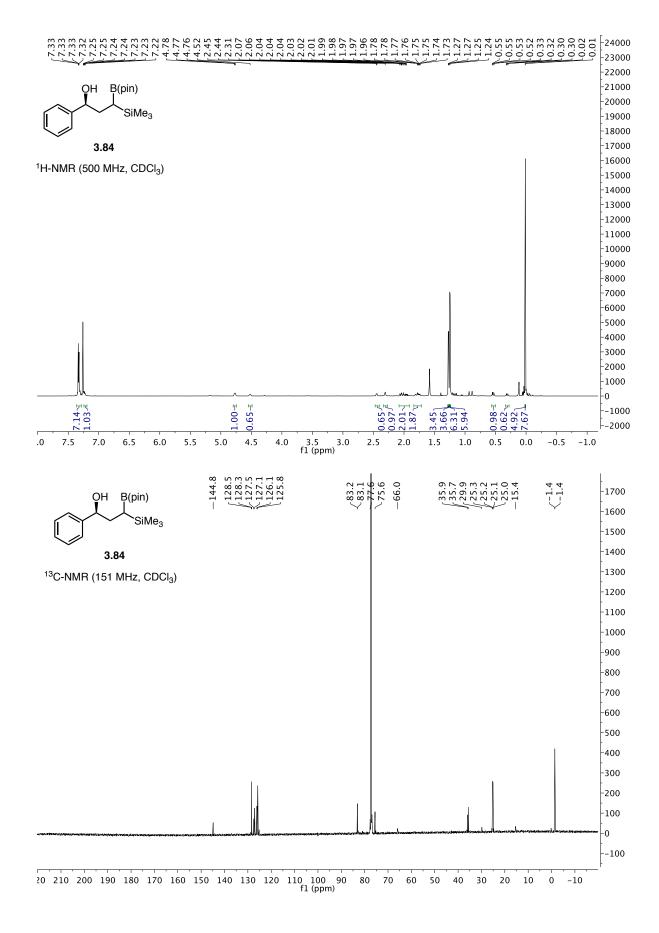
Inside the glovebox compound **3.65** (0.019 mL, 0.075 mmol, 1 eq) was dissolved in THF (0.2 mL) in an 8 mL vial containing a stir bar. LTMP (11 mg, 0.075 mmol, 1 eq) was dissolved into a separate 8 mL vial and dissolved in THF (0.4 mL). The vials were sealed with septa lined caps, removed from the glovebox, and cooled to 0 °C in an ice water bath. The LTMP solution was then cannula transferred to the solution of **3.65**. The mixture was allowed to stir at 0 °C for 30 minutes after which allyl bromide (0.019 mL, 0.225 mmol, 3 eq) was added via syringe. The reaction was heated to 60 °C for 3 hours, then allowed to cool to 22 °C and quenched with a saturated solution of aqueous ammonium chloride. The organics were extracted three times with diethyl ether, dried over magnesium sulfate, and concentrated *in vacuo* to give the crude product **3.84**. Using an internal standard (DMF, 0.004 mL) and the known ^{1}H chemical shifts of the product and starting material[41,57] the conversion to product was determined to be 65% with 26% starting material remaining.

3.5.8 Spectra

¹H-NMR (500 MHz, d₈-THF)
22 °C

¹H-NMR (600 MHz, d₈-THF)
60 °C, 2.5 hours

^{11}B-NMR (500 MHz, d$_8$-THF)

35.59
14.54

Me$_3$Si—B(pin)

3.65

3.82

3.83

Me$_3$Si—B(pin)

3.65

^{11}B-NMR (500 MHz, d$_8$-THF)

33.72

3.82 3.83

1D NOESY at 4.50 ppm (500 MHz, d$_8$-THF)

3.82 3.83

1D NOESY at 4.41 ppm (500 MHz, d$_8$-THF)

289

3.84

^{1}H-NMR (500 MHz, CDCl$_3$)

3.84

^{13}C-NMR (151 MHz, CDCl$_3$)

Me₃Si⌒B(pin)

3.65

(pin)B
|
Me₃Si⌒⌒

3.84

¹H-NMR (500 MHz, CDCl₃)

Me
Me H
H
TBSO H

3.76

¹H-NMR (600 MHz, CDCl₃)

3.76

^{13}C-NMR (151 MHz, CDCl$_3$)

3.78

^{1}H-NMR (500 MHz, CDCl$_3$)

3.78
^{13}C-NMR (126 MHz, CDCl$_3$)

3.79
^{1}H-NMR (600 MHz, CDCl$_3$)

3.79

^{13}C-NMR (151 MHz, CDCl$_3$)

3.41

^{1}H-NMR (400 MHz, CDCl$_3$)

3.41
^{13}C-NMR (151 MHz, CDCl$_3$)

153.7
142.0
128.7
128.0
126.6
83.5
76.3
24.9
24.9

3.42
^{1}H-NMR (500 MHz, CDCl$_3$)

7.28
7.28
7.19
7.17
6.80
6.78
6.76
6.75
5.78
5.77
5.74
5.74
5.24
5.23
2.36
1.99
1.27

1.93
2.05
1.00
1.02
1.02
3.20
0.92
12.90

3.42
^{13}C-NMR (151 MHz, CDCl$_3$)

153.9
137.7
129.4
126.6
83.5
76.1
24.9
24.9
21.3

3.43
^{1}H-NMR (600 MHz, CDCl$_3$)

7.33
7.33
7.32
7.31
7.26
7.04
7.04
7.03
7.01
6.73
6.72
6.70
6.69
5.75
5.74
5.72
5.71
5.24
5.23
5.23
2.04
2.03
1.60
1.26

3.43
^{13}C-NMR (151 MHz, CDCl$_3$)

163.3, 161.6, 153.5, 137.7, 137.7, 128.4, 128.3, 115.6, 115.5, 83.6, 75.6, 24.9, 24.9

3.44
^{1}H-NMR (600 MHz, CDCl$_3$)

7.25, 7.23, 7.22, 7.17, 7.17, 7.15, 7.14, 7.10, 7.10, 7.10, 7.09, 7.09, 6.77, 6.76, 6.74, 6.73, 5.76, 5.76, 5.73, 5.21, 5.21, 5.21, 5.20, 2.35, 1.25

3.44

^{13}C-NMR (151 MHz, CDCl$_3$)

3.45

^{1}H-NMR (600 MHz, CDCl$_3$)

3.45
^{13}C-NMR (151 MHz, CDCl$_3$)

152.9
139.9
135.5
130.6
127.8
126.5
126.2
83.5
72.9
24.9
24.9
19.4

3.46
^{1}H-NMR (600 MHz, CDCl$_3$)

6.66
6.65
6.63
6.62
5.66
5.66
5.63
5.63
4.18
4.17
1.58
1.57
1.57
1.56
1.56
1.55
1.55
1.54
1.54
1.53
1.53
1.30
1.28
1.27
0.91
0.90
0.90
0.89

3.46
^{13}C-NMR (151 MHz, CDCl$_3$)

155.5

83.4
73.9

36.8
32.1
29.8
29.7
29.5
25.5
24.9
24.9
24.9
22.8
14.3

3.47
^{1}H-NMR (600 MHz, CDCl$_3$)

6.65
6.64
6.62
6.61
5.65
5.65
5.62
5.62
3.94
1.83
1.78
1.77
1.77
1.76
1.76
1.76
1.75
1.75
1.74
1.74
1.70
1.68
1.68
1.68
1.67
1.67
1.66
1.66
1.65
1.65
1.29
1.26
1.25
1.25
1.24
1.24
1.23
1.23
1.22
1.21
1.20
1.20
1.19
1.17
1.15
1.09
1.08
1.07
1.06
1.04
1.03
1.02
1.01

0.99
0.99
1.00
5.72
1.06
5.26
2.15

3.47
^{13}C-NMR (151 MHz, CDCl$_3$)

3.48
^{1}H-NMR (600 MHz, CDCl$_3$)

3.48
^{13}C-NMR (151 MHz, CDCl$_3$)

150.8
83.4
73.8
66.7
26.0
24.9
24.9
24.8
18.5
5.2
5.2

3.49
^{1}H-NMR (600 MHz, CDCl$_3$)

7.32
7.31
7.31
7.30
7.30
7.25
7.24
7.24
7.23
6.73
6.72
6.70
6.69
5.70
5.70
5.67
5.67
4.40
4.40
4.39
2.93
2.93
2.91
2.90
2.75
2.74
2.73
2.72
1.68
1.27

3.49
^{13}C-NMR (151 MHz, CDCl$_3$)

154.1
137.8
129.6
128.7
126.8
83.5
74.3
43.4
24.9
24.9

3.50
^{1}H-NMR (600 MHz, CDCl$_3$)

6.67
6.66
6.64
6.63
5.63
5.63
5.60
5.60
4.36
4.36
4.36
4.35
4.35
4.34
4.34
4.34
4.33
4.33
4.33
4.32
4.32
1.28
1.27
1.27

1.00
1.01
1.01
15.60

3.50
^{13}C-NMR (151 MHz, CDCl$_3$)

156.3
83.5
69.8
24.9
22.8

3.51
^{1}H-NMR (600 MHz, CDCl$_3$)

6.76, 6.76, 6.75, 6.73, 6.73, 6.72
5.72, 5.72, 5.72, 5.69, 5.69, 5.69
4.25, 4.24, 4.24, 4.24
1.27

1.00
1.02
1.99
12.30

3.51
^{13}C-NMR (151 MHz, CDCl$_3$)

3.52
^{1}H-NMR (500 MHz, CDCl$_3$)

3.52
^{13}C-NMR (126 MHz, CDCl$_3$)

3.53
^{1}H-NMR (500 MHz, CDCl$_3$)

3.53

^{13}C-NMR (151 MHz, CDCl$_3$)

Peaks: 158.2, 145.9, 128.4, 127.1, 125.4, 83.5, 75.5, 29.3, 25.0, 24.9

3.54

^{1}H-NMR (500 MHz, CDCl$_3$)

Peaks: 7.35, 7.34, 7.34, 7.28, 7.28, 7.27, 7.26, 6.67, 6.63, 5.69, 5.66, 4.89, 4.88, 4.87, 4.86, 4.37, 4.37, 4.36, 4.35, 3.61, 2.01, 2.00, 1.99, 1.98, 1.95, 1.94, 1.94, 1.93, 1.92, 1.92, 1.91, 1.88, 1.85, 1.85, 1.83, 1.71, 1.70, 1.68, 1.67, 1.49, 1.45, 1.34, 1.27

Integrations: 4.18, 0.66, 1.00, 0.94, 0.99, 0.94, 0.82, 1.00, 1.06, 0.84, 1.04, 3.13, 3.06, 3.21, 12.82

3.54
^{13}C-NMR (151 MHz, CDCl$_3$)

3.55
^{1}H-NMR (600 MHz, CDCl$_3$)

3.55
^{13}C-NMR (151 MHz, CDCl$_3$)

3.56
^{1}H-NMR (500 MHz, CDCl$_3$)

3.56

^{13}C-NMR (151 MHz, CDCl$_3$)

3.58

^{1}H-NMR (600 MHz, CDCl$_3$)

3.58
^{13}C-NMR (151 MHz, CDCl$_3$)

3.59
^{1}H-NMR (600 MHz, CDCl$_3$)

311

3.59
^{13}C-NMR (151 MHz, CDCl$_3$)

3.62
^{1}H-NMR (500 MHz, CDCl$_3$)

3.66
^{1}H-NMR (500 MHz, CDCl$_3$)

3.70
^{1}H-NMR (600 MHz, CDCl$_3$)

313

3.70

¹³C-NMR (151 MHz, CDCl₃)

~136.5
128.9
128.2
124.5

73.0
67.4

26.2
26.0
24.9
18.5
18.5

5.2
5.2

3.72

¹H-NMR (600 MHz, CDCl₃)

8.60
8.59
8.47
8.46
8.46
8.46
7.69
7.68
7.68
7.67
7.67
7.25
7.25
7.24
7.23
7.23
7.22
6.70
6.70
6.67
6.67
6.27
6.26
6.24
6.23
4.38
4.38
4.37
4.37
4.37
3.76
3.76
3.75
3.74
3.56
3.54
3.54
3.53
2.82

−0.91

0.10
0.09

1.00
0.98

1.03

0.99

0.98

1.00

0.99

1.01
1.03

0.91

9.26

2.32
2.59

3.72

^{13}C-NMR (151 MHz, CDCl$_3$)

148.8, 148.5, 133.1, 132.5, 130.5, 128.1, 123.6, 72.7, 67.1, 26.0, 18.5, 5.2, -5.2

3.73

^{1}H-NMR (600 MHz, CDCl$_3$)

3.72, 3.72, 3.71, 3.70, 3.70, 3.55, 3.54, 3.54, 3.53, 2.97, 2.96, 2.95, 2.47, 2.47, 1.21, 1.12, 1.11, 1.11, 1.10, 1.10, 1.09, 1.09, 1.08, 1.08, 0.90, 0.76, 0.75, 0.75, 0.75, 0.74, 0.74, 0.73, 0.71, 0.71, 0.70, 0.70, 0.70, 0.69, 0.68, 0.07, 0.07, -0.22, -0.23, -0.23, -0.24, -0.24, -0.25

1.00, 0.98, 0.92, 0.85, 11.86, 1.01, 9.27, 0.93, 0.94, 5.95, 0.92

TBSO
OH
B(pin)

3.73
^{13}C-NMR (151 MHz, CDCl$_3$)

83.2
76.5
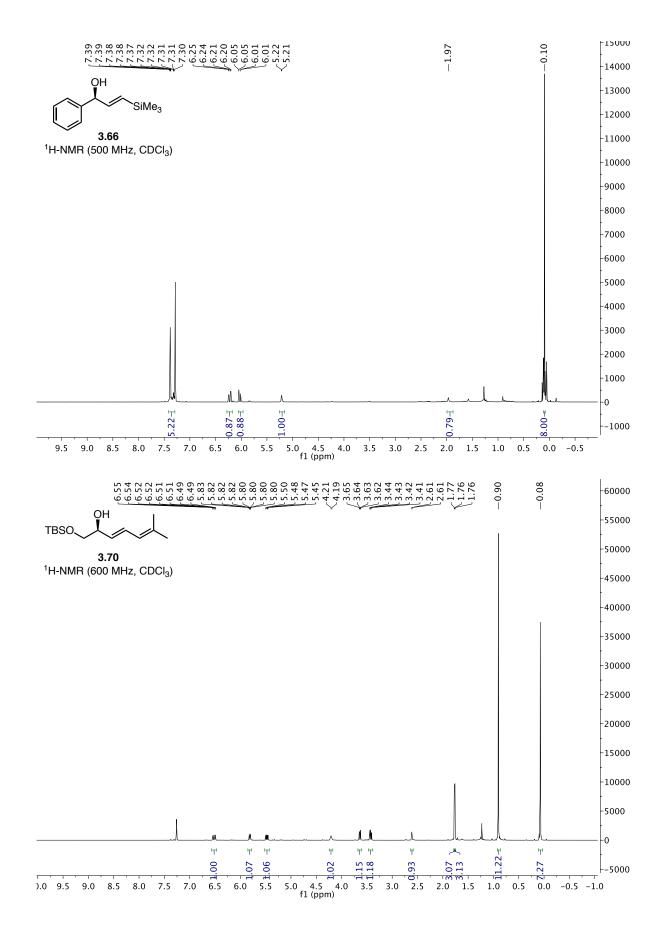67.0
26.0
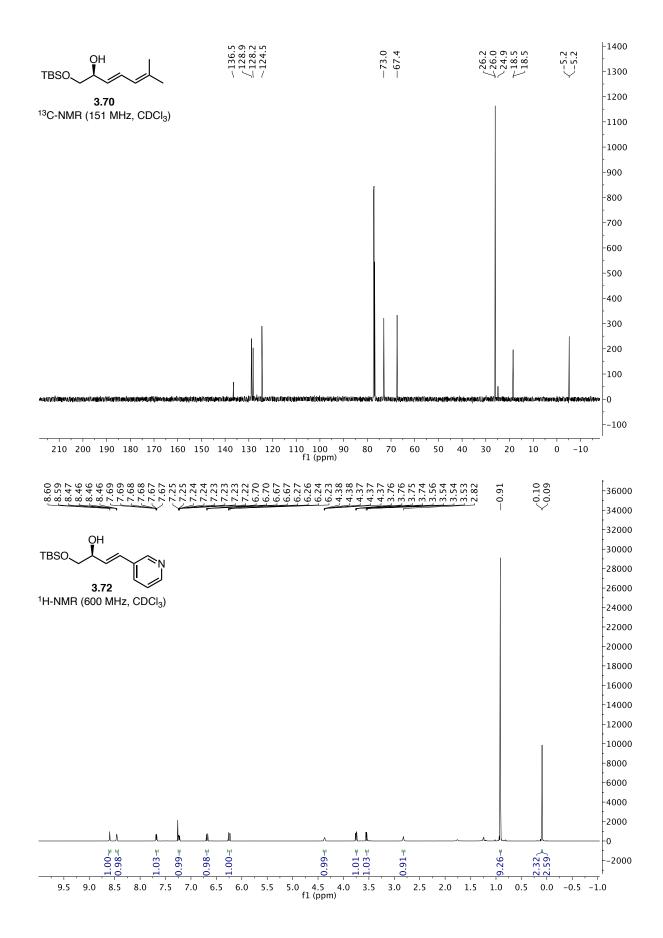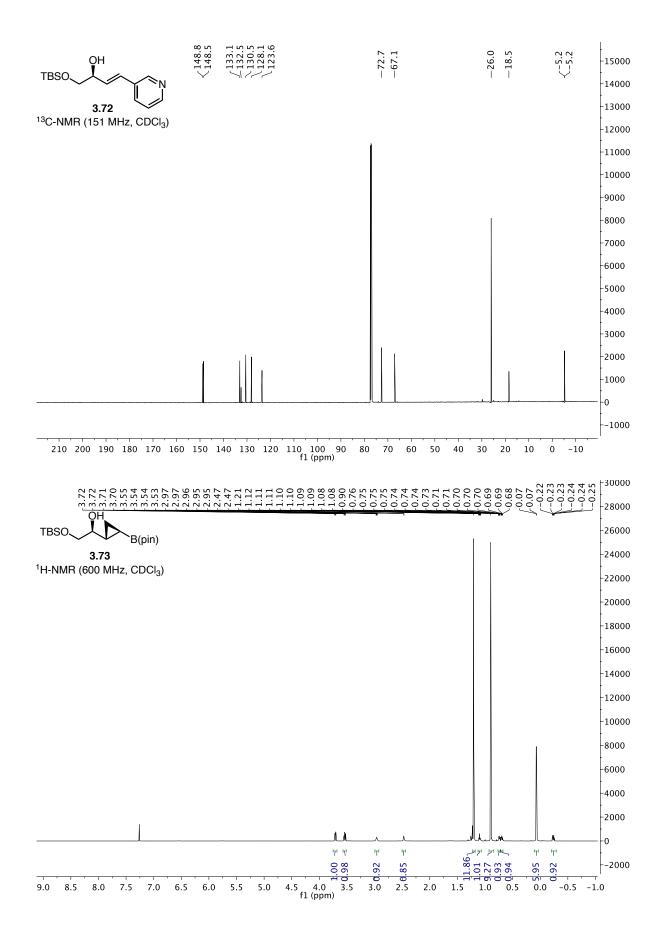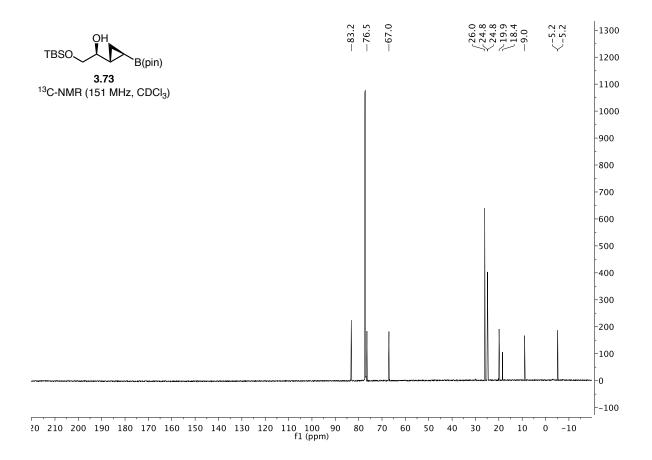24.8
24.8
19.9
18.4
9.0
-5.2
-5.2

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