Doctoral Dissertation

Development of Copper(I)-Catalyzed Synthesis of γ-Functionalized Allylboronates

Graduate School of Chemical Sciences and Engineering
Hokkaido University

Yuta Takenouchi
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Contents

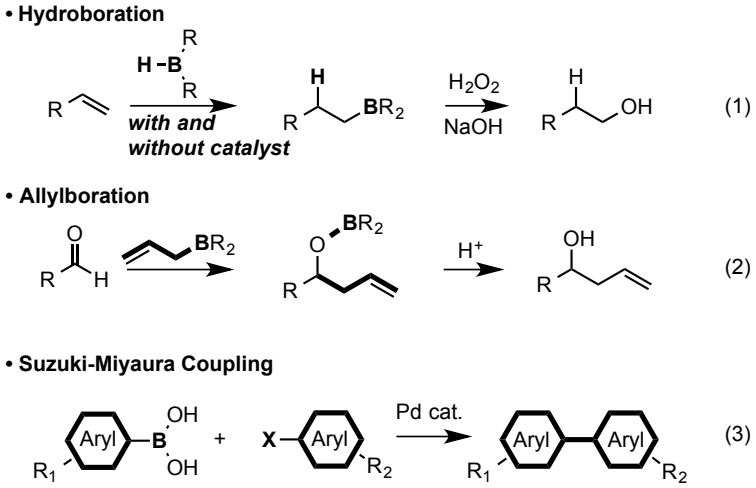
Chapter 1

General Introduction

1.1 Organoboron Compounds

Organoboron compounds are an important and useful organometallic reagent in organic synthetic chemistry (Scheme 1). As shown by the studies of H. C. Brown, who was awarded by Nobel Prize in chemistry in 1979 for his development of the use of boron-containing compounds in organic synthesis, hydroboration and allylboration have been one of the most powerful and reliable carbon–boron or carbon–carbon bond-forming methods in organic chemistry.[1] More recently, combination of organoboron and transition-metal chemistry has become important. Although uncatalyzed-hydroboration of olefins proceeds with *anti*-Markovnikov regioselectivity (Scheme 1, eq. 1), the metal-catalyzed hydroboration provides different chemoselectivity, regioselectivity and diastereoselectivity since the mechanisms of catalyzed and uncatalyzed reactions are different in many cases.[2] As other aspect of development of organoboron chemistry, there is a cross-coupling reaction of organoboron compounds and organic halides in the presence of a palladium catalyst that was reported by A. Suzuki and N. Miyaura in 1979 (Scheme 1, eq. 3).[3] The cross-coupling reaction have been remarkably developed and utilized in academic and industrial fields. Suzuki was also given Nobel Prize in 2010 for development of the Pd-catalyzed coupling reactions.

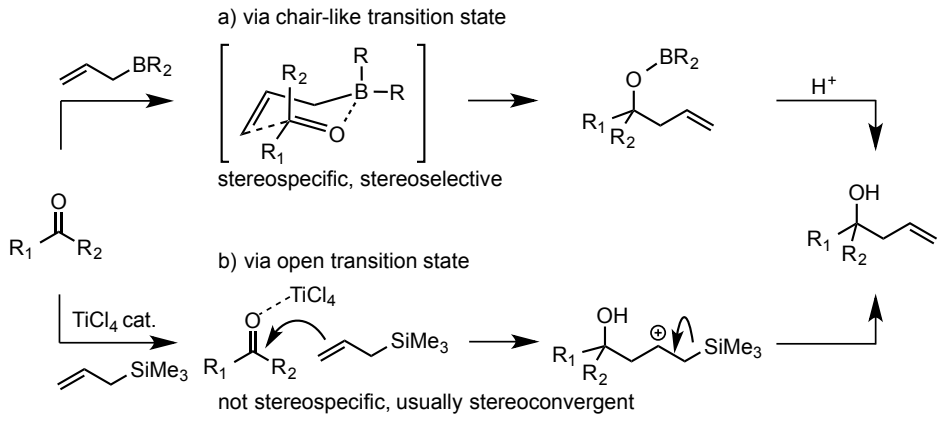
Compared with other organometallic reagents, notable advantages of organoboron compounds are i) stable in air and easy to handling, ii) mild Lewis acidity, iii) low toxicity.[4] Thus, they display unique properties and reactivity that could not be found in other organometallic reagents. For example, although allylboronates are both chemically and configurationally stable under air, they show high reactivity for limited electrophiles such as aldehydes. Furthermore, their reactivity in allylation can be more enhanced by addition of catalytic amount of Lewis/Brønsted acids (Scheme 1, eq. 2).[5] Because of these unique and irreplaceable characters of organoboron compounds, requirement for development of a novel approach to organoboron reagents is increasing in recent years.



Scheme 1. Organoboron Compounds in Organic Synthesis

1.2 Allylation with Allylboron Compounds

Allylboron compounds have been widely used as an allylation reagent for carbonyl compounds or imines. There have been known two types of the mechanisms in the allyl metalation of carbonyl compounds: a) the mechanism with Zimmerman-Traxler chair-like transition state and b) the mechanism with open transition state. For allylboron reagents, the allylation proceed via chair-like transition states because of Lewis acidic ability of the boron atom. Concerted activation of the oxygen atom on the carbonyl moiety and nucleophilic attack from the C=C bond to the carbon atom on the carbonyl moiety would occur in the transition state (Scheme 2a). This pathway includes tightly constrained transition states, resulting the high stereoselectivity. It is significantly important to develop a preparation method for stereodefined allylboronates to take advantage of the high stereo-controlling ability. Compared with allylation with allylboron compounds, other allylmetal reagents have several disadvantages to stereo-, and regioselective allylation. For example, allyllithium or allyl Grignard reagents are not configurationally stable, showing α/γ and *E*/*Z* rearrangement. Allylsilane or allylstannane reagents have been found to be an efficient organometallic reagent because of their stability and reactivity in allylation. The allylation with these reagents usually undergo via an open transition state with external Lewis acids. The reaction proceeds in not stereospecific but stereoconvergent manner in many cases (Scheme 2b).[4]

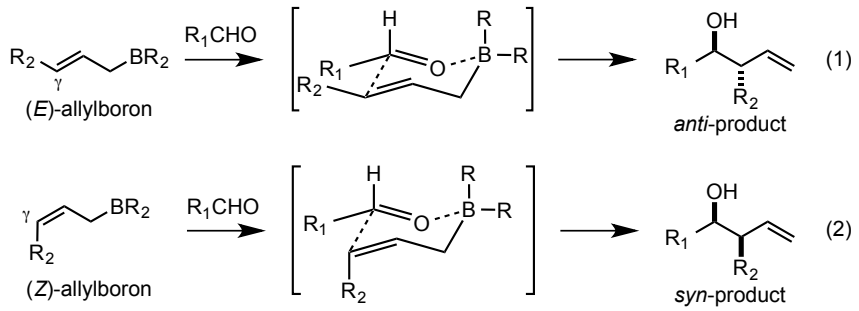


Scheme 2. Allylation of Carbonyl Compounds with Allylboron or -silane Reagents

1.2.1 Effect of Substituents at Allylboron Compounds in Allylboration

1.2.1.1 Allylboration with γ-Subsituted Allylboron Compounds

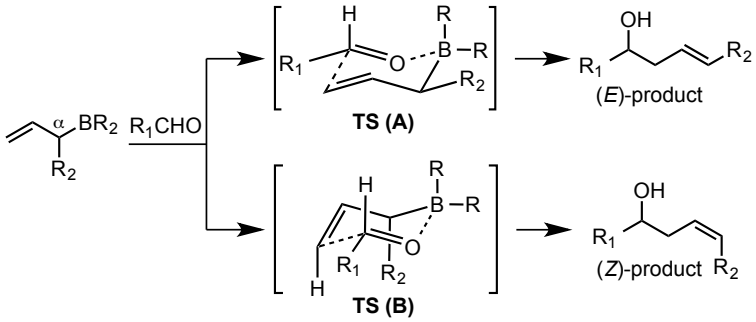
The allylation with the (*E*)- or (*Z*)-allylboron compounds possessing a substituent at their γ-position provide the *anti*- or *syn*-allylated products, respectively. These stereoselectivity have been experimentally investigated using (*E*)- or (*Z*)-crotylboron compounds. It was found that the stereospecificity in the reaction is generally very high.[4] In the transition state of the reaction with (*E*)-allylboron, the γ-substituent R_2 is in the equatorial position as shown in Scheme 3, eq. 1. Thus, *anti*-isomer is obtained selectively. (*Z*)-Allylboron gives *syn*-product, because the γ-substituent R_2 is in the axial position in the transition state (Scheme 3, eq. 2).



Scheme 3. Diastereoselectivity in Aldehyde Allylation with γ-Substituted Allylboron

1.2.1.2 Allylboration with α-Substituted Allylboron Compounds

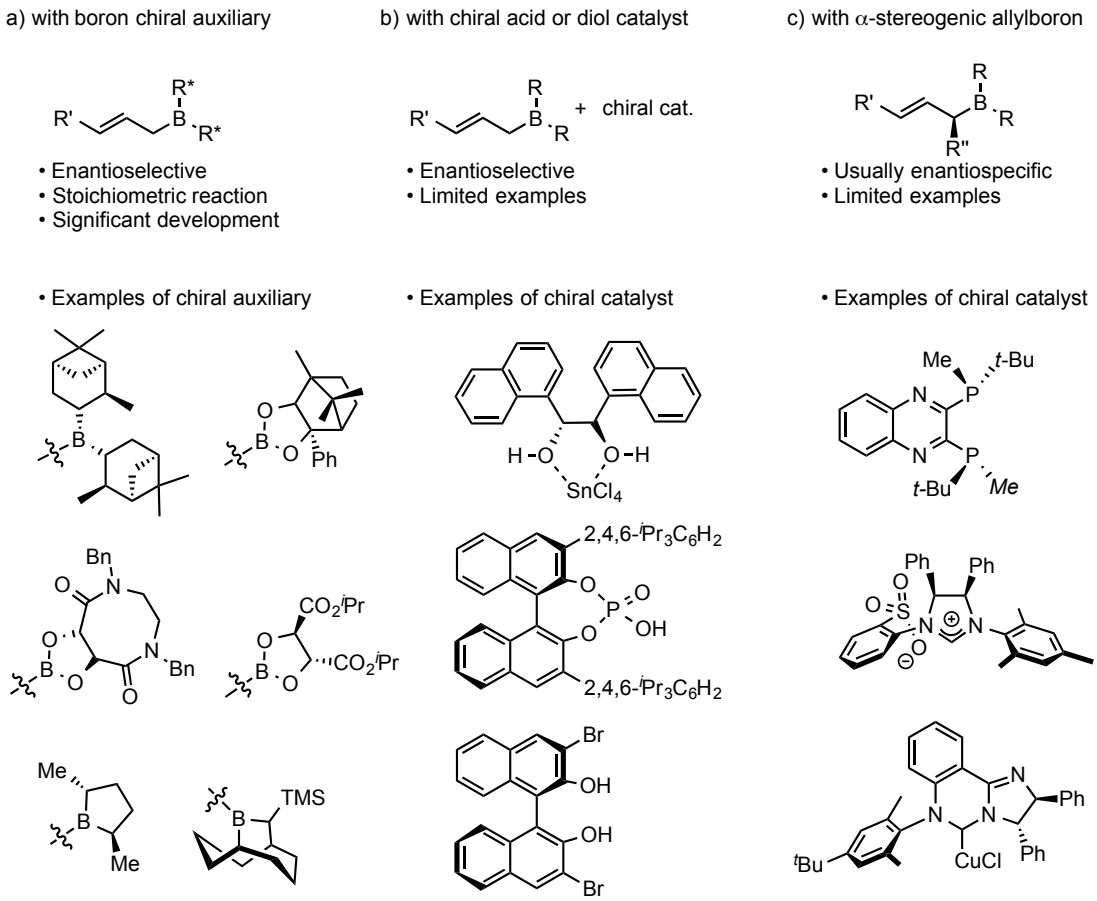
The allylation with allylboron compounds containing a substituent at the α-position can provide (*Z*)- or (*E*)-homoallylalcohol derivatives. When the α-substituent is a nonpolar alkyl group, the *E*/*Z* selectivity can be explained by two competing six-membered transition states (Scheme 4). In the case of the reaction via TS (A), the gauche strain between the α-substituent and the boron moiety would increase the activation energy barrier of the transition state. On the other hands, the 1,3-allylic strain is the major energy increasing factor of the reaction pathway that provides (*Z*)-product via TS (B). The competition of these two factors influences the *E*/*Z* ratio of the allylation product.[4]



Scheme 4. Steric Factors in Diastereoselectivity of Aldehyde Allylation with α-Substituted Allylborons

1.2.2 Asymmetric Allylborations

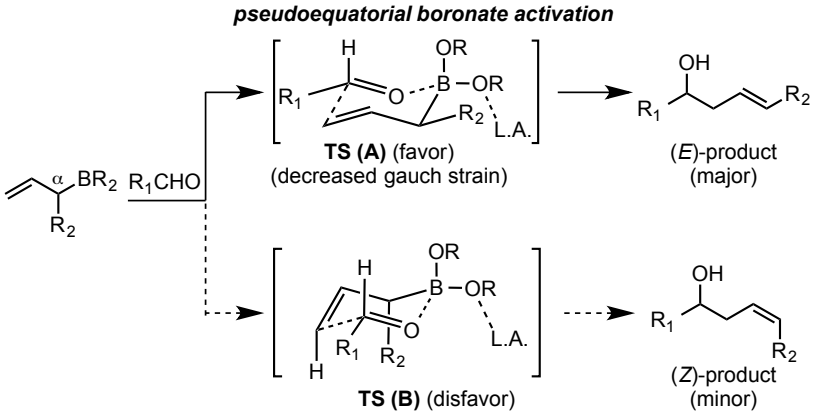
For asymmetric allylation with allylboron compounds, there are three types of approaches (Scheme 5). The first one utilizes a chiral auxiliary on the boron atom (Scheme 5a). Although the reaction proceeds with high enantio- and diastereoselectivity in this case, a stoichiometric amount of the expensive chiral source is required. The second one is the method with chiral Lewis/Brønsted acid or diol as a catalyst in the allylation reaction (Scheme 5b). As compared to the former method, only catalytic amount of the chiral source is required in the asymmetric allylation. However, development of the asymmetric catalysts and the precise reaction controlling are generally difficult. For the third one, optically pure α-stereogenic allylboron compounds are utilized (Scheme 5c). In this case, the chirality transfers from the α-chiral allylboron compound to allylated-product usually occurs with highly stereoselective manner to give optically active product.[4]



Scheme 5. Stereoselectivity in Aldehyde Allylation with α-Substituted Allylboron

1.2.3 Stereoselectivity in Acid-Catalyzed Allylboration

Allylboronate esters are more configurationally stable but are less reactive than allylboranes with alkyl groups on the B atom because of the low Lewis acidity of allylboronates. Addition of catalytic amounts of Brønsted or Lewis acids can enhance reactivity of allylboronates.[4] On the other hands, when acid catalysts coordinate to the oxygen atom of the allylboronate, the activation energy of the transition state becomes significantly low. Furthermore the gauche strain between the substituent at the α-position R_2 and the substituent on the boron atom also becomes low [Scheme 6. TS (A)]. As a result, (*E*)-allylated-product is obtained selectively. These mechanisms were supported by experimental results and density functional theory (DFT) calculations.[5]



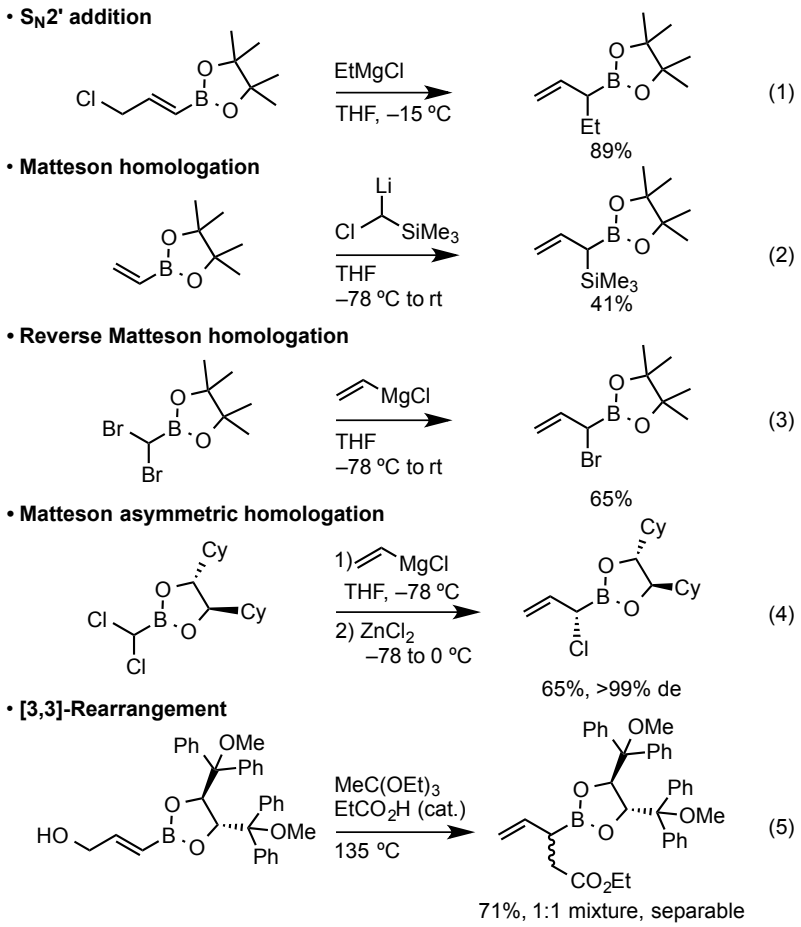
Scheme 6. Stereoselectivity in Acid-Catalyzed Aldehyde Allylation with α-Substituted Allylboron

1.3 Synthesis of Allylboron Compounds

1.3.1 Synthesis of α-Substituted Allylboron Compounds

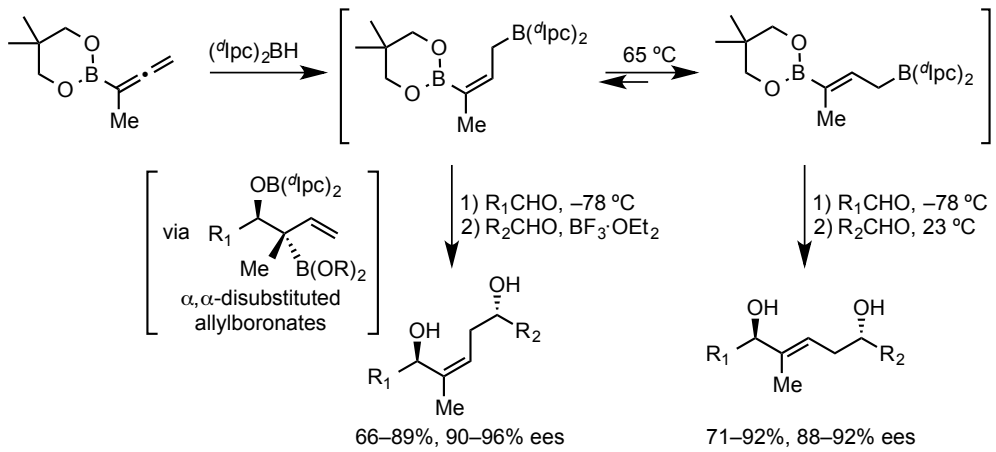
1.3.1.1 Stoichiometric Reactions

Selected examples for synthesis of α-substituted allylboronates are shown in Scheme 7.[6] Selective S_N2' addition and Matteson homologation have been found as an efficient way for preparation of the organoboronate esters. Nucleophilic attack of ethylmagnesium chloride to 3-chloropropenylboronates yielded the desired allylboronates (eq. 1). α-Trimethylsilylallylboronates were synthesized by homologation with vinylboronates (eq. 2). α,α-Dibromomethyl boronates were used as a reverse homologation reagent to afford α-bromoallylboronates (eq. 3). To prepare α-chiral allylboronates, asymmetric homologation of alkenylboronates that have a stoichiometric chiral director was found to be efficient (eq. 4). In 2004, a preparation procedure with [3,3]-rearrangement of chiral 3-hydroxy propenylboronates was reported (eq. 5).



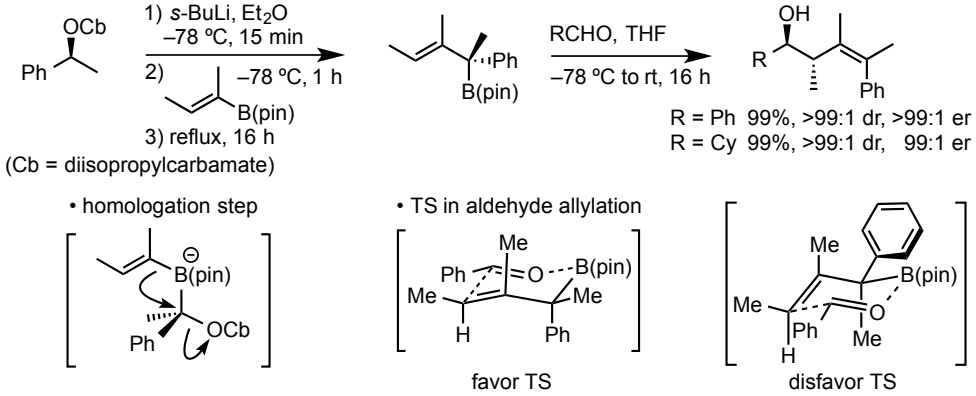
Scheme 7. Syntheses of α-Substituted Allylboronates via Stoichiometric Routes

Roush's group applied the hydroboration/allylation procedure to 1,1-methylborylallene substrates to synthesize the (*Z*)- and (*E*)-2-methyl-1,5-anti-pentenediols (Scheme 8). Kinetically controlled hydroboration of allenylboronates followed by a double aldehyde allylation of the (*Z*)-allylboron gave the corresponding (*Z*)-products when $BF_3{\cdot}OEt_2$ was used as the catalyst in the second allylboration step. The first allylboration provide the stereodefined α,α-disubstituted allylboronates, which are difficult to access by using other preparation methods. The sequential allylations of aldehydes by taking advantage of the reactivity difference between $B(Ipc)_2$ and $B(OR)_2$ moieties yielded (*Z*)- and (*E*)-2-methyl-1,5-*anti*-pentenediols in high yield with excellent stereoselectivity.[7]



Scheme 8. Hydroboration of 1,1-Methylborylallene and Sequential Reactions with Aldehydes

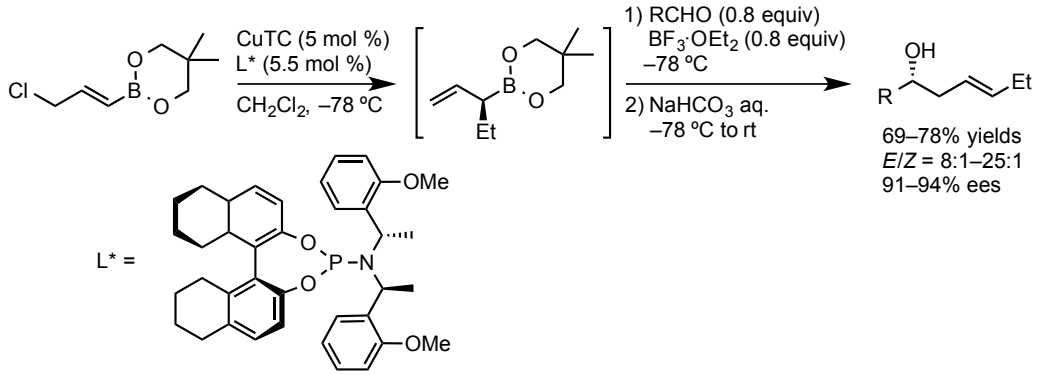
Enantio-enriched β-boryl-α,α-disubstituted allylic boronates were prepared by the homologation of vinyl boronic pinacol esters with chiral secondary lithiated carbamates (Scheme 9).[8] The subsequent aldehyde allylation yielded fully stereodefined homoallylic alcohols bearing trisubstituted alkenes. As a result of the DFT calculations of the transition state in the allylation step, the transition state where the phenyl group occupies the equatorial position lies 2.3 kcal mol^{-1} higher in the free energy than the corresponding axial transition state. The calculation results consistent with experimental results of the high *Z*-selectivity.



Scheme 9. Chiral Allylboron Synthesis via Homologation of Chiral Benzylcarbamate

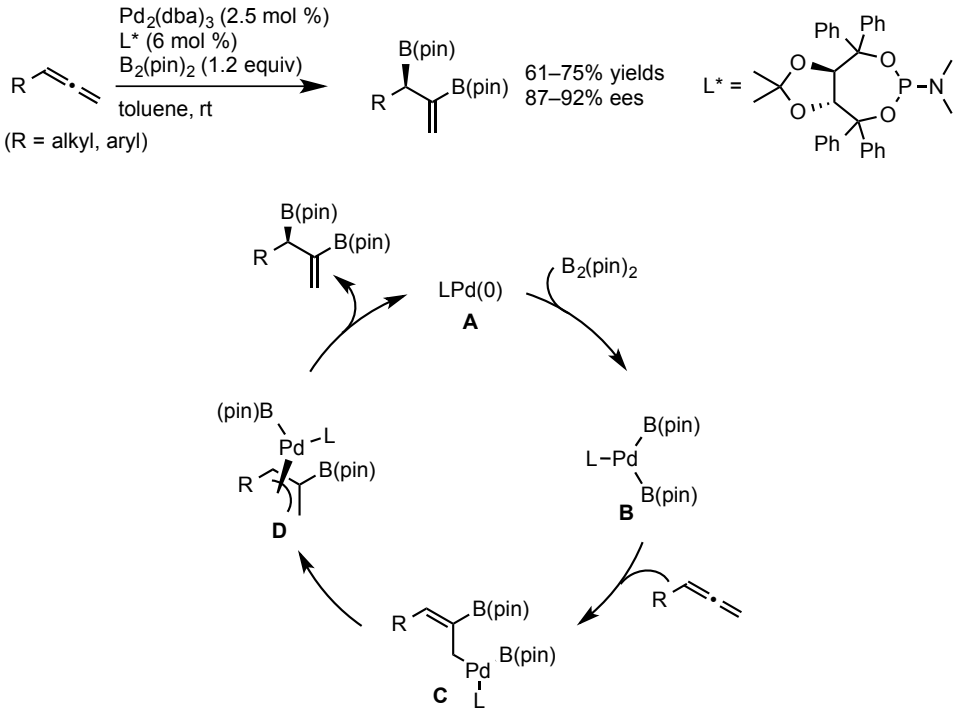
1.3.1.2 Catalytic Reactions

Development of asymmetric catalytic methods for α-chiral allylboronates is an important research subject because of their low requirement of the stoichiometry of the chiral source. Hall and co-workers reported an enantioselective preparation method of α-stereogenic allylboronates and fully diastereo-controlled aldehyde allylation with the boron reagents (Scheme 10).[9] They investigated an asymmetric S_N2' allylic alkylation of 3-halopropenylboronates using chiral phosphoramidite ligands and transition metals. Although allylic Matteson homologation with these substrates would proceed as a background reaction, slow addition of Grignard reagents could suppress the side reactions.



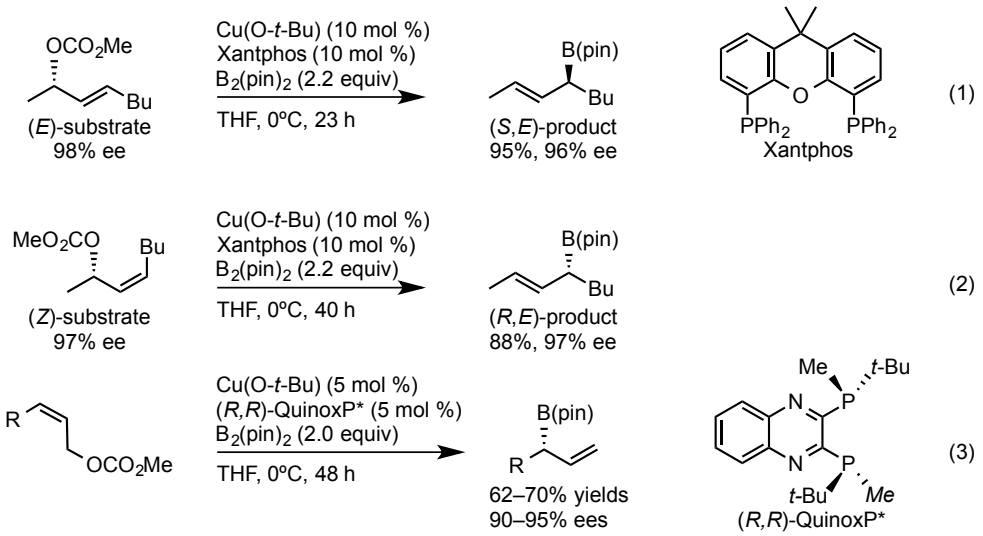
Scheme 10. Asymmetric α-Alkylation of 3-Halopropenylboronates

In 2004 Morken and co-workers reported a Pd-catalyzed enantioselective diboration of allenyl derivatives (Scheme 11).[10] The Pd-catalyzed reaction with the chiral phosphoramidite ligand afforded α-chiral β-boryl allylboronates in moderate yield with high enantioselectivity. The authors conducted the asymmetric borylation, aldehyde allylation and oxidation of boron moiety in one-pot to give the β-hydroxyketone derivatives with high enantioselectivity in 2005. In this reaction, oxidative addition of $B_2(pin)_2$ to the Pd(0)-L* complex (**A**) would be the initial step (**B**). Next, the transfer of both boron groups to the unsaturated substrate is caused by coordination and insertion of the more accessible terminal alkene of the allene substrate to give η^1-allyl palladium complex (**C**). The η^1–η^3 isomerization would afford the π-allyl complex (**D**) and the subsequent reductive elimination provided the desired allylboronates. As a result of the mechanism investigation that was conducted by the same group in 2007, the coordination and insertion of Pd complex (**B**) directly provides the η^3 π-allyl complex (**D**) in a stereospecific, concerted fashion.



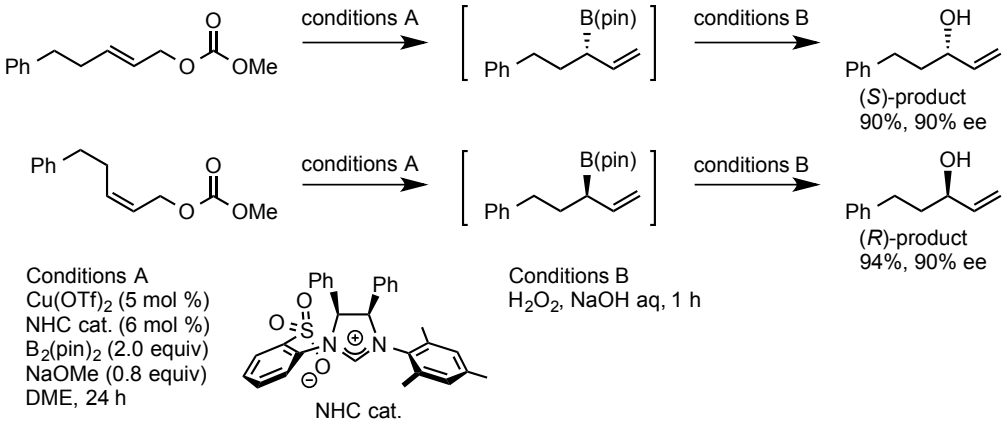
Scheme 11. Pd-Catalyzed Diboration of Allene Derivatives

Copper catalysis has been widely used in nucleophilic introduction of a boron moiety because of their convenient preparation of active borylcopper(I) species from $B_2(pin)_2$ and copper(I) alkoxide via σ-bond metathesis, and excellent regioselectivity in boryl substitution reaction. Ito and co-workers first reported stereospecific boryl substitution of allylic carbonates using Cu(O-*t*-Bu)/Xantphos catalyst system (Scheme 12, eq. 1 and 2).[11a] The reaction using optically active (*E*)- or (*Z*)-substrate yielded (*S*,*E*)- or (*R*,*E*)-product in high stereoselectivity, respectively. The experimental results represented that the copper(I)-catalyzed boryl substitution undergoes via S_N2' pathway. In 2007, the same group reported enantioselective boryl substitution of (*Z*)-allylic carbonates with chiral diphosphine ligand QuinoxP* (Scheme 12, eq. 3).[11b] While the reaction proceeded in high yield with excellent enantioselectivity to give the corresponding α-stereogenic allylboronates, the use of the (*E*)-substrates resulted in poor enantioselectivity.



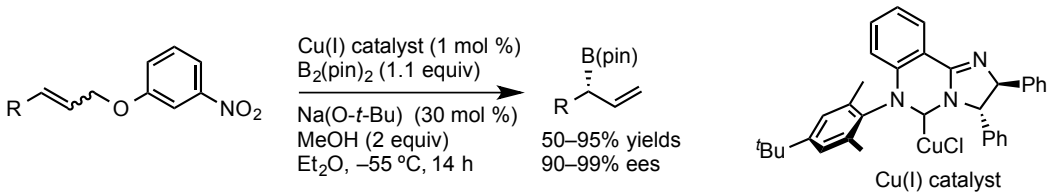
Scheme 12. Copper(I)-Catalyzed γ-Boryl Substitution of Allylic Carbonates

In 2010, Hoveyda group has expanded the substrate scope in the allylic boryl substitution using chiral *N*-heterocyclic carbene as a ligand (Scheme 13).[12] In this reaction, both (*E*)- and (*Z*)-allylic carbonates afforded the desired (*S*)- and (*R*)-products in enantio-enriched form, respectively.



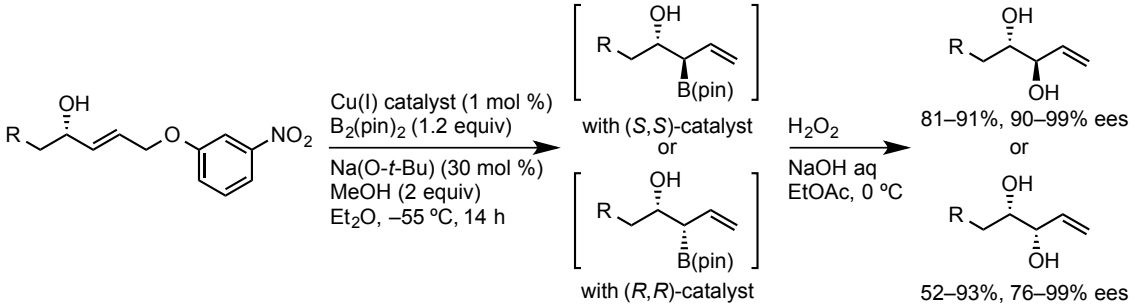
Scheme 13. Asymmetric γ-Boryl Substitution of (*E*)- and (*Z*)-Allylic Carbonates

McQuade and co-workers reported stereoconvergent synthesis of α-chiral allylboronates from an *E*/*Z* mixture of allylic aryl ethers through a Cu(I)–NHC-catalyzed boryl substitution in 2011 (Scheme 14).[29a] Whereas previously reported copper(I)-catalyzed asymmetric allylic boryl substitution reactions are stereodivergent (Schemes 12 and 13), this reaction is stereoconvergent borylation. The *E*/*Z* mixture of allylic ether substrates yielded the α-stereogenic allylboronates as a single isomer in excellent enantioselectivity.



Scheme 14. Copper(I)-Catalyzed Stereodivergent Borylation of Allylic Ether

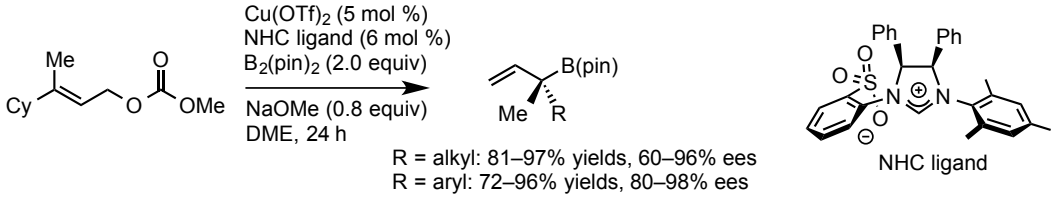
The use of the same Cu(I)-NHC catalyst system enables the catalyst-controlled introduction of a boron moiety to allylic ethers possessing optically active hydroxyl group. The borylation with (*S*,*S*)- and (*R*,*R*)-NHC-Cu(I) catalyst and subsequent oxidation of the boron group afforded *anti*-1,2-diol and *syn*-1,2-diol derivatives in high enantioselectivity, respectively (Scheme 15).[29b] They proposed that allylic boryl substitution and cross-metathesis strategy for the highly diastereoselective preparation of fully stereodefined chiral polyol derivatives.



Scheme 15. Enantioselective Borylation of σ-Chiral Allylic Ether

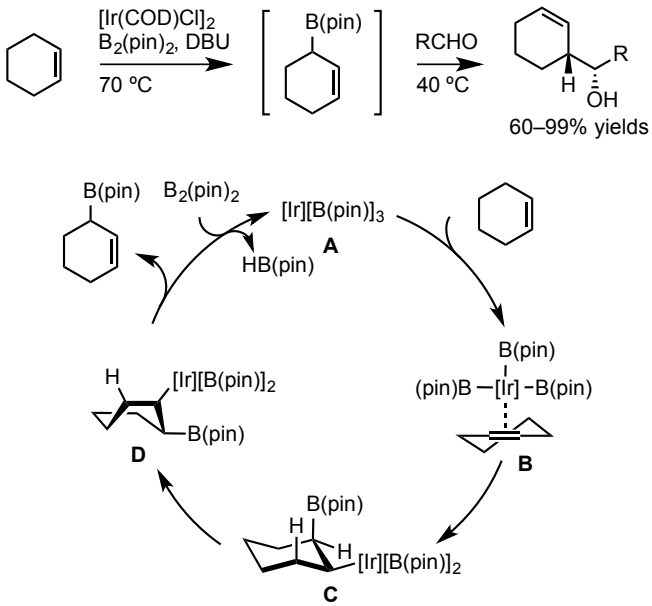
Enantioselective catalytic preparation of α,α-disubstituted allylboronates have been represented as an important and difficult objective. Hoveyda and co-workers achieved asymmetric synthesis of α-substituted allylboronates bearing B-substituted quaternary carbon stereogenic center using the chiral Cu(I)-NHC complex (Scheme 16).[12] However, aldehyde allylation with the allylboronates

resulted the corresponding product as 1:1 mixture of diastereomer.



Scheme 16. Boryl Substitution of γ,γ-Disubstituted Allylic Carbonate

Allylic C–H borylation is a simple, straightforward and promising method to access to allylboron compounds. Szabó and co-workers achieved a selective Ir-catalyzed allylic C–H borylation reaction (Scheme 17).[14a,b] The Ir-catalyzed C–H activation borylation reactions arises from the formation of a tris(boryl)Ir complex (**A**). The coordination of the tris(boryl)Ir complex gives Ir complex (**B**) and the insertion of the active species to alkene moiety of substrate proceeds via a *syn* mechanism to give alkyl-iridium intermediate (**C**). Allylic C–H bond is able to adapt to the *syn* conformation that is required for the β-hydride elimination (**D**). The iridium hydride species that are generated after β-elimination react with bis(pinacolato)diboron (B_2pin_2) to give pinacolborane (HBpin) with regeneration of the catalyst A.

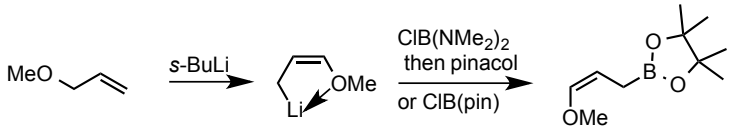


Scheme 17. Catalytic Allylic C–H Borylation of Cyclohexene

1.3.2 Preparation of γ-Alkoxyallylboron Compounds

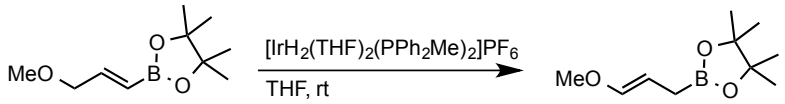
1.3.2.1 Stoichiometric Reactions

Hoffmann and co-workers reported the first synthesis of γ-alkoxyallylboronates in 1981. Following their report, Wuts and co-workers also reported the γ-alkoxyallylboronates in 1982. They used 3-methoxyprop-1-ene as a starting material. The reaction between lithiated allyl ethers and boron electrophiles afforded the desired (*Z*)-γ-alkoxyallylboronates (Scheme 18).[15] The conformation of the allylboronates depends on the conformation of lithiated allyl ethers: the lithiation of allyl ethers with *s*-butyllithium afforded *cis*-organolithium reagent selectively.



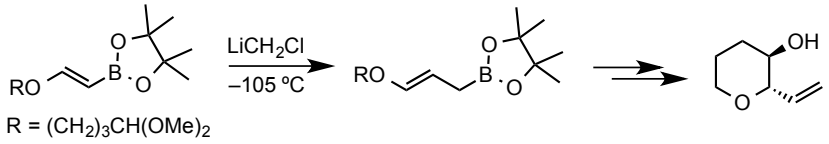
Scheme 18. Selective Preparation of (*Z*)-γ-Alkoxyallylborontes

An efficient approach for (*E*)-γ-alkoxyallylboronates synthesis was found by Miyaura and co-workers (Scheme 19).[16] They applied a transition-metal-catalyzed isomerization of the double bond, which originally reported by Moro-oka and Baudry, to (*E*)-γ-alkoxyvinylboronates. The reaction with Ir catalyst proceeded at room temperature to give the desired (*E*)-γ-alkoxyallylboronates in high yield with excellent *E*/*Z* selectivity.



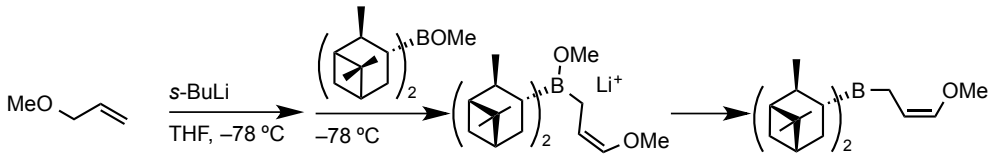
Scheme 19. Ir-Catalyzed Isomerization of γ-Alkoxyvinylboronates

Hoffmann's group reported a homologation reaction with $LiCH_2Cl$ to convert vinylboronates into (*E*)-γ-alkoxyallylboronates. In this report, they used the allylboronates to aldehyde allylation without isolation of the allylboronates (Scheme 20).[17] They applied the boronates for intermolecular allylboration, giving rise to tetrahydropyran.



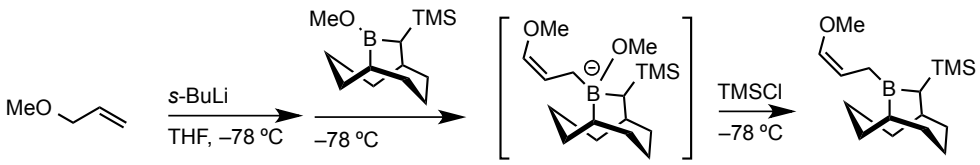
Scheme 20. Homologation Reaction of Vinyl Boronates

Brown and co-workers reported an asymmetric variant to the preparation of the boron compounds in 1988. They used diisopinocampheyl (Ipc) group as the chiral auxiliary. The aldehyde allylation with the allylboron compounds afforded optically active 1,2-diol derivatives in high yield with excellent enantio- and diastereoselectivity (Scheme 21).[18] However the boron reagents are configurationally unstable above –78 ºC.



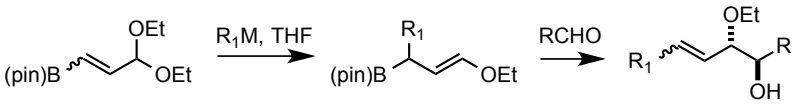
Scheme 21. Selective Synthesis of (*Z*)-(γ-Methoxyallyl)diisopinocampheylboranes

As mentioned above, allylboron compounds have both high reactivity for carbonyl compounds and low configurational stability above low temperature. To address this disadvantage, Soderquist and co-workers used 10-trimethylsilyl-9-borabicyclo[3.3.2]decane (10-TMS-9-BBD) substituted γ-alkoxyallylborons (Scheme 22).[19] The (*Z*)-(γ-methoxyallyl)-10-TMS-9-BBD reagents are more configurationally stable than the corresponding $(Ipc)_2B$ reagents. Furthermore, their compounds showed excellent diastereo- and enantioselectivity in the allylation of aldehydes and imines.



Scheme 22. Selective Synthesis of (*Z*)-(γ-Methoxyallyl)-10-TMS-9-BBD

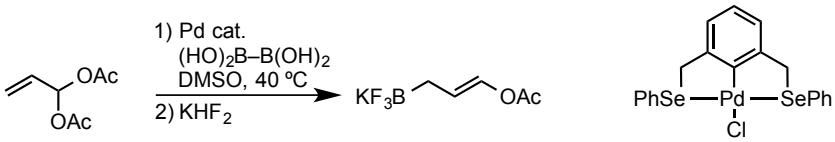
Although α-substituent on the allylboron reagents plays an important role for a convergent synthesis, selective synthesis α-substituted γ-alkoxyallylboronates has been difficult when classical methods are used. Carreaux and co-workers developed a novel approach to α-substituted (*E*)-γ-alkoxyallylboronates. The addition of organometallics to vinylboronates possessing an acetal group in the γ-position underwent via S_N2' reaction pathway to give the desired allylboronates (Scheme 23).[20]



Scheme 23. Stereoselective Synthesis of α-Substituted γ-Alkoxyallylboronates

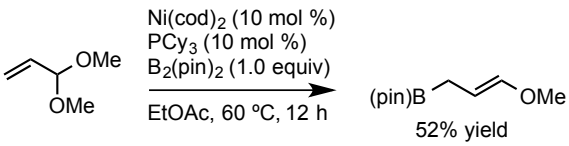
1.3.2.2 Catalytic Reactions

In 2005, Szabó's group reported boryl substitution of allyl acetates using a pincer Pd complex catalyst (Scheme 24).[21] In this reaction, only one of the acetate groups of allylic diacetate substrate is replaced by boronate functionality to give the desired γ-acetoxyallylboron compound. They isolated the desired product after transformation of less stable B(pin) moiety to more stable BF_3K.



Scheme 24. Catalytic Synthesis of γ-Alkoxyallylboronates with Pd Catalyst

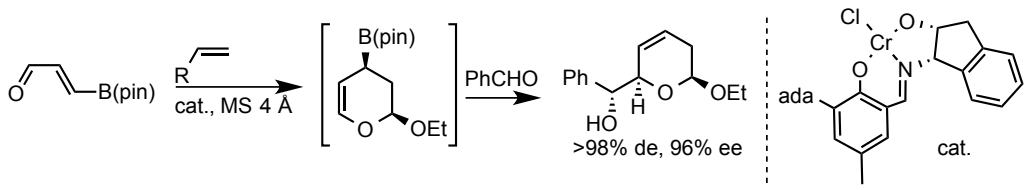
Morken and co-workers developed a Ni-catalyzed method for allylic acetate. The reaction is applicable for the substrate bearing both internal and terminal alkene moiety (Scheme 25).[22] When using $PdCl_2$ catalyst instead of Ni catalyst, the borylation of allylic halides substrates proceeded to give the corresponding allylboronates.



Scheme 25. Catalytic Synthesis of γ-Alkoxyallylboronates with Ni Catalyst

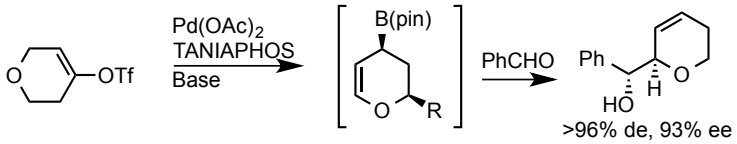
Although numerous preparation methods for γ-alkoxyallylboronates have been reported, especially

for asymmetric reactions, almost all of them are containing a chiral boron auxiliary and bearing an achiral primary C–B bond. Hall and co-workers reported asymmetric syntheses of cyclic α-chiral γ-alkoxyallylboronates (Scheme 26).[24] They applied chiral Cr catalysis, which were found to be a good catalyst for asymmetric inverse electron demand hetero[4+2] reaction that was originally reported by Jacobsen group, to this reaction between 3-boronoacrolein and vinyl ether. The hetero-Diels–Alder reaction gave heterocyclic α-chiral γ-alkoxyallylboronates in high yield with high enantioselectivity.



Scheme 26. Enantioselective Synthesis of α-Chiral γ-Alkoxyallylboronates

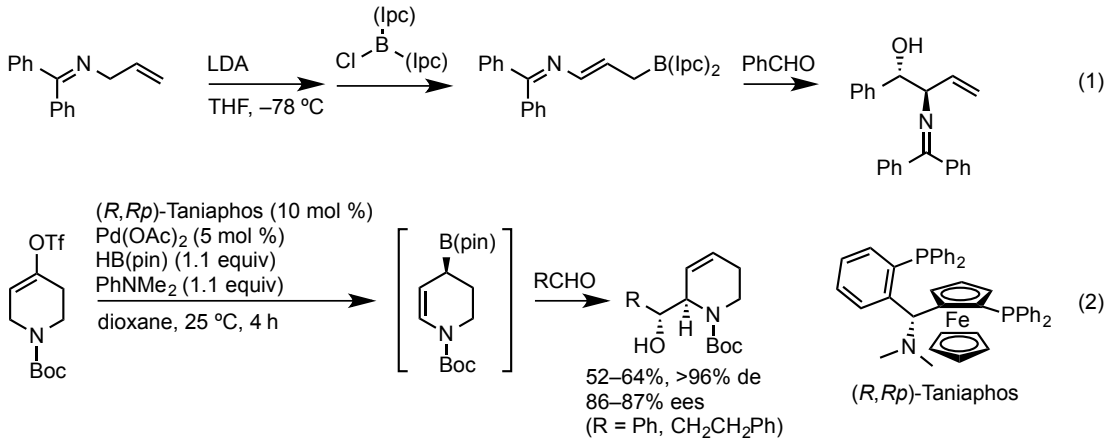
Pd-catalyzed borylation of alkenyl triflate was found to be a novel approach for oxacyclic γ-alkoxyallylboronate by Masuda and co-workers in 2000. Hall's group reported an asymmetric variant to this process in 2009 using chiral (*R,Rp*)-Taniaphos ligand (Scheme 27).[24a] They succeeded in synthesizing heterocyclic α-chiral γ-alkoxyallylboronates in high enantio- and diastereoselectivity.



Scheme 27. Enantioselective Synthesis of α-Chiral γ-Alkoxyallylboronates

1.3.3 Preparation of γ-Amino Allylboron Compounds

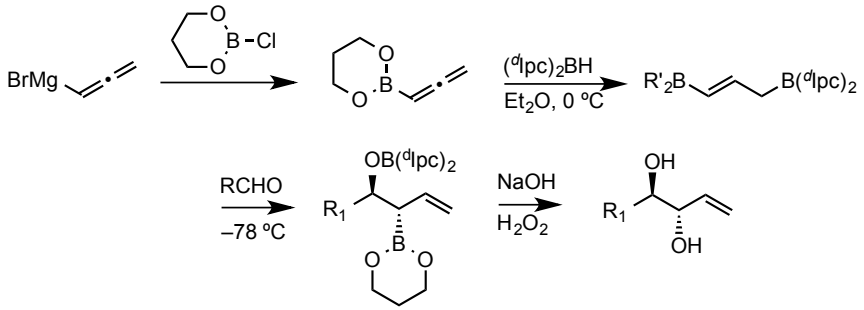
A linear γ-aminoallylboron compounds were prepared via lithiation of allylic amines and subsequent reaction with boron nucleophiles (Scheme 28, eq. 1).[23] The asymmetric borylative isomerization is applicable for *N*-heterocyclic vinyl triflates. The corresponding enantio-enriched products were obtained in moderate yield with excellent enantioselectivity (Scheme 28, eq. 2).[24c]



Scheme 28. Preparation Methods of γ-Alkoxyallylboronates

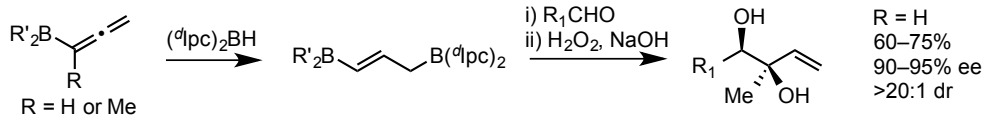
1.3.4 Preparation of γ-Boryl Allylboron Compound

γ-Borylallylboron compounds have been used as an alternative of γ-alkoxyallylboron compounds, because generally the boron moiety can be transformed to a hydroxyl group under mild conditions without degradation of their optical purity. A novel approach for (*E*)-γ-borylallylboron compounds via hydroboration of allenylboronates were reported by Brown and co-workers (Scheme 29).[25] Stereoselective α-borylallylation of aldehydes and stereospecific oxidation of boron group afforded *anti*-1,2-diol derivatives.



Scheme 29. Selective Preparation of (*E*)-γ-Borylallylborontes

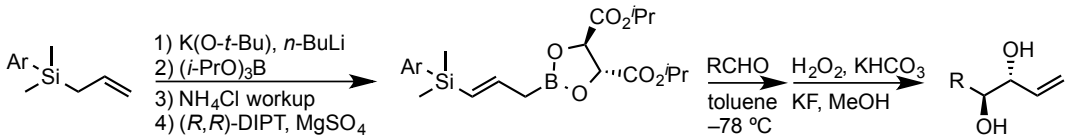
Roush and co-workers improved this allene hydroboration/aldehyde allylation sequence. Stereoselective hydroboration of α-methyl-substituted allenyl boronates and subsequent allylation of aldehydes provided stereo-controlled 2-methyl-1,2-*syn*-diols in high yield with enantioselectivity (Scheme 30). [7,25]



Scheme 30. Selective Preparation of (*E*)-γ-Silylallylboronates

1.3.5 Synthesis of γ-Silylallylboronates

Silyl groups are also regarded as a hydroxyl group equivalent because there is reliable stereospecific oxidation method (Fleming-Tamao oxidation). The preparation of (*E*)-γ-alkoxyallylmetal reagents from (*E*)-γ-alkoxyallyl anion precursors has been difficult because of their configurational instability. Roush and co-workers succeeded in stereoselective synthesis of (*E*)-γ-silylallylboronates through lithiation of allylsilanes and the subsequent reaction with boron electrophiles (Scheme 31).[26]

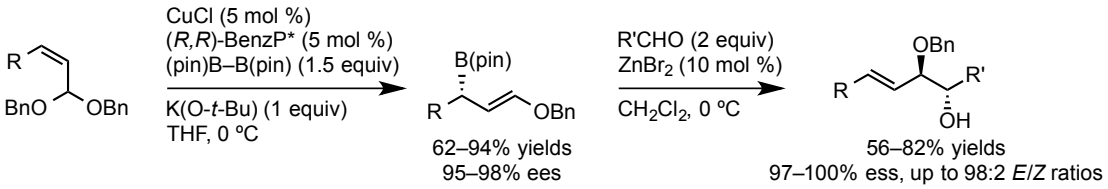


Scheme 31. Selective Preparation of (*E*)-γ-Silylallylboronates

1.4 Survey of This Dissertation

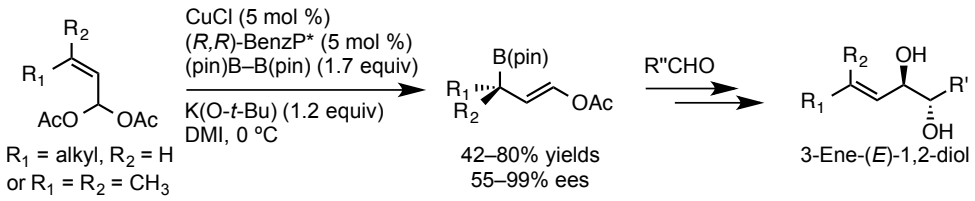
As mentioned in previous sections, allylboron reagents are one of the most powerful tools in synthetic chemistry. Considering the increasing demand for these useful reagents, development of novel and efficient approach for stereodefined and functionalized allylboronates are significantly important.

In chapter 2, the first catalytic enantioselective synthesis of linear or carbocyclic α-chiral (*E*)-γ-alkoxyallylboronates is described. The copper(I)-catalyzed asymmetric boryl substitution of allyl acetals gives the corresponding allylboronates in high yield with excellent enantioselectivity (Scheme 32). This reaction allowed a preparation of highly functionalized products bearing ester, silyl ether, benzyl ether, acetyl ether and cyano group. Highly stereoselective aldehyde allylation with the allylboronates is also demonstrated.



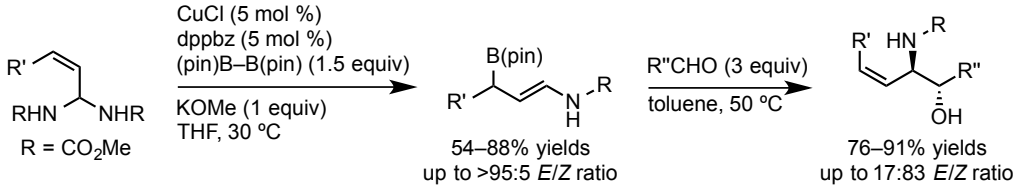
Scheme 32. Asymmetric Borylation/Aldehyde Allylation of Allyl Acetals

In chapter 3, the author shows enantioselective boryl substitution of allyl acylals with a chiral copper catalyst. The reaction represents broad substrate scope and excellent enantioselectivity. Allylation with the synthesized γ-acetoxy allylboronate and deprotection of the allylated under mild conditions are an efficient pathway to 3-ene-1,2-diol unit (Scheme 33).



Scheme 33. Asymmetric Borylation/Aldehyde Allylation of Allyl Acylals

In chapter 4, the first catalytic synthesis of linear α-substituted γ-amino allylboronates is reported. The reaction proceeded with high yield and *E*/*Z* selectivity and subsequent aldehyde allylation using the allylboronates afforded the (*Z*)-*anti*-1,2-amino alcohol derivatives with high stereoselectivity (Scheme 34).



Scheme 34. Asymmetric Borylation/Aldehyde Allylation of Allyl Acylals

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Chapter 2

Copper(I)-Catalyzed Enantioselective Synthesis of α-Chiral Linear or Carbocyclic (*E*)-γ-Alkoxyallylboronates

Abstract: A new method has been developed for the catalytic asymmetric synthesis of α-chiral linear or carbocyclic γ-alkoxyallylboronates via the copper(I)-catalyzed γ-boryl substitution of allyl acetals. This reaction afforded the products in high yields with excellent *E*/*Z* selectivities and enantioselectivities [only (*E*)-product, 91−98% ee] and also exhibited high functional group compatibility. Subsequent allylation of aldehydes with the α-chiral γ-alkoxyallylboronates provided the *anti*-1,2-diol derivatives in a highly stereospecific manner, and the utility of the α-chiral γ-alkoxyallylboronates was further demonstrated by a convergent coupling of a complex polyol derivative using a γ-alkoxyallylboronate and a chiral α-oxyaldehyde. The stereoselective modular construction of a complex 3,3-disubstituted cyclopentene containing three consecutive stereocenters including a quaternary chiral carbon was also reported. Useful transformations of the α-chiral linear γ-alkoxyallylboronates were also demonstrated.

2.1 Introduction

The chiral 1,2-diol structure is important and is often found in natural products such as carbohydrates and polyketides.[1] Consequently, stereoselective coupling reactions constructing chiral 1,2-diol units with concurrent C−C bond formation between two functionalized synthetic fragments can be powerful tools for the efficient convergent synthesis of the complex polyols containing multiple stereocenters.[2] Addition reactions of enantioenriched γ-alkoxyallyl organometallic reagents to a carbonyl compound have been employed for the construction of the stereodefined 3-ene-1,2-diol structure with a concomitant C−C bond formation, and the double bond in the product can be further utilized through a number of selective functionalization reactions.[2n,o,3,4] Among the γ-alkoxyallyl organometallic reagents, γ-alkoxyallylboron compounds are widely used as versatile reagents for asymmetric synthesis because they react both reliably and predictably, exhibiting high levels of stability under atmospheric conditions and low toxicity.[5] Following from the initial studies of Hoffmann[5] and Wuts,[7] the stereoselective allylation of aldehydes with γ-alkoxyallylboron compounds[8] has been used for the synthesis of polyoxygenated natural products and pharmaceuticals.[9] γ-Borylallyl- or γ-silylallylboron compounds were also reported as flexible alternative reagents for the reaction.[10] In most cases, these reactions involve γ-alkoxyallylboron compounds bearing an achiral primary C−B bond with a chiral boron auxiliary, which give 1,2-diol derivatives containing a terminal alkene moiety via aldehyde allylation. Although these known enantioenriched γ-alkoxyallylboron compounds are highly useful, the boron compounds lack the substituent at the α-position and need a stoichiometric chiral auxiliary to construct the stereodefined 3-ene-1,2-diol unit after the aldehyde allylation.

In contrast, aldehyde allylation involving α-chiral (*E*)- or (*Z*)-γ-alkoxyallylboronates affords stereodefined anti- or *syn*-1,2-diols containing an internal alkene moiety, the stereochemistry of which is controlled by the chiral C−B bond structure without the use of a chiral auxiliary.[11,12] This aldehyde allylation of the boronates is expected to be suitable for the convergent synthesis of complex molecules containing 3-ene-1,2-diol structures; it can make a new bond between the functionalized fragments of the boronate and aldehyde moieties through the stereodefined 3-ene-1,2-diol unit in a highly stereospecific manner. However, only a few synthetic methods are available for the asymmetric construction of α-chiral γ-alkoxyallylboronates. In addition, synthetic methods for other related optically active α-chiral γ-alkoxyallyl organometallic reagents such as organostannane[13] or organosilane[14] compounds are also limited. Hall et al. developed two catalytic methods for the construction of the boronates, including a Cr(III)-catalyzed enantioselective inverse

electron demand hetero-[4+2] reaction[15a] and Pd-catalyzed enantioselective boryl substitution.[15b] Furthermore, the utility of these chiral boronates was demonstrated in the synthesis of natural products[16] such as thiomarinol. However, these approaches are limited to six-membered oxacyclic (*Z*)-γ-alkoxyallylboronates. To the best of our knowledge, there have been no reports in the literature pertaining to the catalytic asymmetric synthesis of α-chiral linear or carbocyclic γ-alkoxyallylboronates to date, and the development of an effective method for their synthesis is therefore highly desirable.

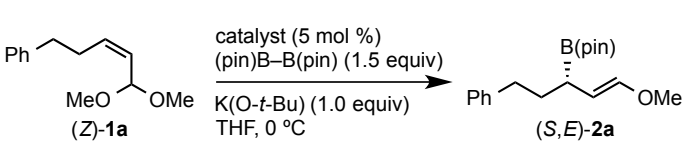
In chapter 2, the author reports a novel approach to enantioenriched α-chiral linear or carbocyclic (*E*)-γ-alkoxyallylboronates via the copper(I)/chiral bisphosphine-catalyzed γ-boryl substitution of allyl acetals and the subsequent conversion of these boronates to the corresponding *anti*-1,2-diol derivatives, which are generally more difficult to prepare than *syn*-1,2-diol derivatives, through a newly developed $ZnBr_2$-catalyzed aldehyde allylation. This borylation/allylation process was found to be effective for the convergent synthesis of a complex polyol derivative with high stereoselectivity and functional group compatibility. The aldehyde allylation with carbocyclic γ-alkoxyallylboronates afforded sterically congested *anti*-1,2-diol derivatives,[17] which were used for the unprecedented stereoselective modular synthesis of complex 3,3-disubstituted cyclopentenes containing three consecutive chiral centers, including a quaternary chiral carbon, via the iterative borylation/aldehyde allylation. We have also demonstrated useful transformations of the α-chiral linear boronates.

2.2 Optimization of Reaction Conditions

Copper(I)-catalyzed borylation has emerged as a powerful method for the synthesis of organoboron compounds.[18] We previously reported a copper(I)-catalyzed asymmetric borylation using diboron that provided optically active allylboronates.[19] Inspired by these successes, we proceeded to investigate the development of a copper(I)-catalyzed asymmetric synthesis of γ-alkoxyallylboronates via the enantioselective γ-boryl substitution of allyl acetals.[20] Pleasingly, while an extensive review of the literature revealed reports concerning the catalytic asymmetric α-substitution of allyl acetals, we could not find any reports describing the catalytic asymmetric γ-substitution of allyl acetals with nucleophiles of any type.[21]

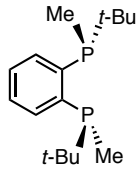
We initially investigated suitable reaction conditions for the reaction of allyl acetal (*Z*)-**1a** with bis(pinacolato)diboron (Table 1). The results revealed that (*R*,*R*)-BenzP* was the best ligand for the reaction.[22] The borylation of (*Z*)-**1a** with CuCl/(*R*,*R*)-BenzP* (5 mol %), bis(pinacolato)diboron (1.5 equiv), and K(O-*t*-Bu) (1.0 equiv) in THF afforded the corresponding (*S*,*E*)-**2a** in excellent yield (95%) and ee (97%) (Table 1, entry 1). This reaction employed CuCl as a catalyst precursor, which can be used without a glovebox.[19e] It is noteworthy that none of the minor (*Z*)-product was observed. The boryl substitution reaction also proceeded smoothly in the presence of 10 mol % K(O-*t*-Bu), although the yield was slightly lower than that of the reaction conducted with a stoichiometric charge of the base and required a longer reaction time (Table 1, entry 2). The use of Cu(O-*t*-Bu) provided reactivity and stereoselectivity levels similar to those observed for CuCl/K(O-*t*-Bu) (Table 1, entry 3). The other ligands gave inferior results (Table 1, entries 4−7). Interestingly, the application of the optimum reaction conditions to (*E*)-**1a** instead of (*Z*)-**1a** resulted in a significantly lower ee (Table 1, entry 8). Recently, Morken et al. reported Ni-catalyzed γ-borylation of alkenyl acetal with a terminal carbon−carbon double bond.[20] We thus tested the Ni-catalyzed reaction of the substrate (*E*)-**1a**, which has an internal carbon−carbon double bond. However, no reaction occurred after 24 h at 60 °C (Table 1, entry 9).

Table 1. Optimization of the Reaction Conditions for the Copper(I)-Catalyzed Enantioselective Boryl Substitution of Allyl Acetal (*Z*)-**1a**[a]

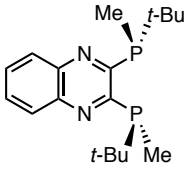


Entry	catalyst	time (h)	yield[b] (%)	ee[c] (%)
1	CuCl/(*R*,*R*)-BenzP*	3	95 (83)	97
2[d]	CuCl/(*R*,*R*)-BenzP*	24	81	96
3[e]	Cu(O-*t*-Bu)/(*R*,*R*)-BenzP*	3	88	97
4	CuCl/(*R*,*R*)-QuinoxP*	8	63	93
5	CuCl/(*R*,*R*)-Me-Duphos	24	14	73
6	CuCl/(*R*)-Segphos	24	38	21
7	CuCl/(*R*,*S*)-Josiphos	45	43	11
8[f]	CuCl/(*R*,*R*)-BenzP*	3	86 (73)	34 (*R*)
9[f,g]	$Ni(cod)_2/PPh_3$	24	0	–

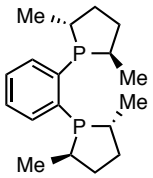
[a]Reagents and conditions: CuCl (0.025 mmol), ligand (0.025 mmol), (*Z*)-**1a** (0.5 mmol), bis(pinacolato)diboron (0.75 mmol), and K(O-*t*- Bu)/THF (1.0 M, 0.5 mL, 0.5 mmol) in THF (0.5 mL) at 0 °C. [b]NMR yield. The isolated yield is shown in parentheses. [c]The ee value of (*S*,*E*)-**2a** was determined by HPLC analysis of the alcohol derived from the product boronate. [d]A 10 mol % concentration of K(O-*t*-Bu) was used. [e]Isolated Cu(O-*t*-Bu) was used, and K(O-*t*-Bu) was not added. [f](*E*)-**1a** (*E*:*Z* = 95:5) was used as the substrate. [g]Reagents and conditions: $Ni(cod)_2$ (10 mol %), PPh_3 (10 mol %), and bis(pinacolato)diboron (0.5 mmol) in EtOAc (0.4 mL) at 60 °C, 24 h.



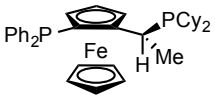
(*R*,*R*)-BenzP*



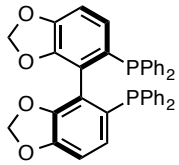
(*R*,*R*)-QuinoxP*



(*R*,*R*)-Me-Duphos



(*R*,*S*)-Josiphos



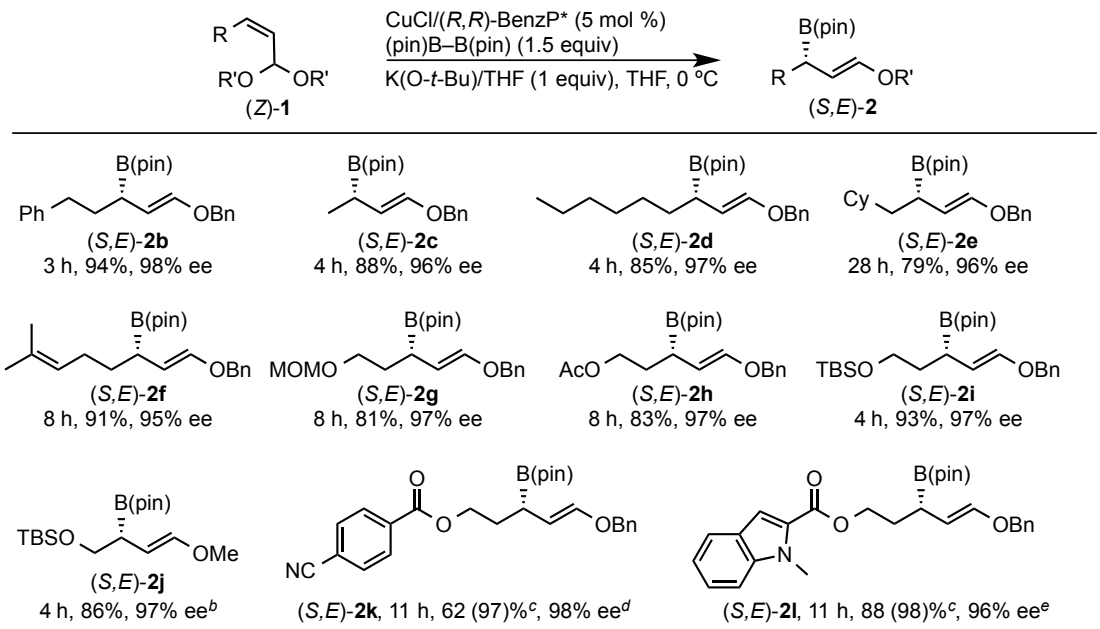
(*R*)-Segphos

2.3 Substrate Scope in Enantioselective Synthesis of Linear γ-Alkoxyallylboronates

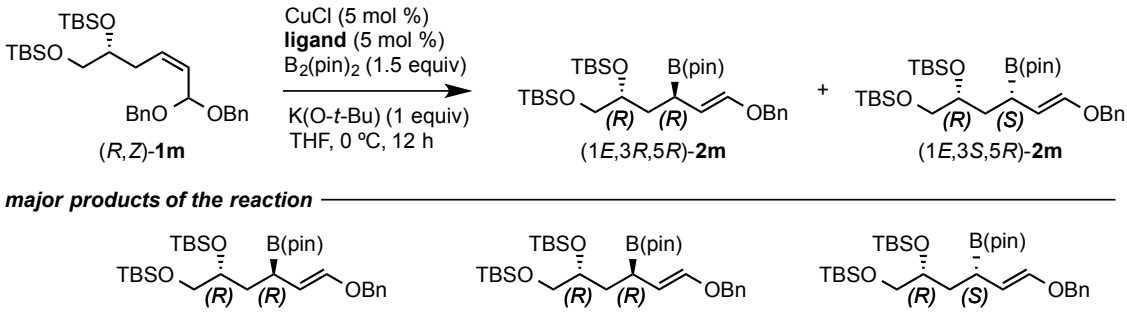
With the optimized conditions in hand, we examined the substrate scope of the reaction (Table 2). The application of the optimized conditions to allyl dibenzyl acetal (*Z*)-**1b** gave the corresponding product (*S*,*E*)-**2b** in 94% yield with 98% ee. Substrates containing a methyl, hexyl, or methylcyclohexyl group [(*Z*)-**1c–e**] also afforded the products in high yields with excellent enantioselectivities [(*S*,*E*)-**2c**, 88% yield, 96% ee; (*S*,*E*)-**2d**, 85% yield, 97% ee; (*S*,***E***)-**2e**, 79% yield, 96% ee]. The γ-alkoxyallylboronate (*S*,*E*)-**2f**, bearing a trisubstituted alkenyl group, was also formed in 91% yield with 95% ee. The allyl acetals (*Z*)-**1g–j**, bearing methoxymethyl ether, acetoxy, and silyl ether groups, respectively, also reacted smoothly to afford the corresponding products in high yields and excellent enantioselectivities [(*S*,*E*)-**2g**, 81% yield, 97% ee; (*S*,*E*)-**2h**, 83% yield, 97% ee; (*S*,*E*)-**2i**, 93% yield, 97% ee; (*R*,*E*)-**2j**, 86% yield, 97% ee]. The use of nitrogen-containing substrates (*Z*)-**1k** and (*Z*)-**1l** provided the corresponding products (*S*,*E*)-**2k** and (*S*,*E*)-**2l** in high yields and excellent enantioselectivities without any degradation of the functional groups [(*S*,*E*)-**2k**, 97% yield, 98% ee; (*S*,*E*)-**2l**, 98% yield, 96% ee]. However, the products could not be fully isolated because of the presence of the byproducts; thus, the derivatizations of the crude products were conducted to check the product structure and yields (62% and 88% isolated yields, respectively).

The reactions of substrate (*R*,*Z*)-**1m** containing an optically active silyl ether moiety are shown in Scheme 4. The use of the Xantphos ligand gave (1*E*,3*R*,5*R*)-**2m** in 80% yield and a diastereomeric ratio of 16:84, which was attributed to the steric effect of the chiral silyl ether group. The reactions of (*R*,*Z*)-**1m** with CuCl/(*S*,*S*)- and (*R*,*R*)-BenzP* proceeded to give the corresponding (1*E*,3*R*,5*R*)-**2m** and (1*E*,3*S*,5*R*)-**2m**, respectively, in good yields and excellent catalyst-controlled stereoselectivity (75% and 75% yields, 0.4:99.6 and 97:3 dr, respectively).

Table 2. Substrate Scope of the Copper(I)-Catalyzed a Enantioselective Boryl Substitution of Allyl Acetal (*Z*)-**1**[a]



[a]Reagents and conditions: CuCl (0.025 mmol), (*R*,*R*)-BenzP* (0.025 mmol), (*Z*)-1 (0.5 mmol), bis(pinacolato)diboron (0.75 mmol), and K(O-*t*-Bu)/THF (1.0 M, 0.5 mL, 0.5 mmol) in THF (0.5 mL) at 0 °C. The ee values of the products were determined by HPLC analysis of the saturated alcohols derived from the corresponding boronates. [b]The ee was determined after derivatization of (*R*,*E*)-**2j** to the related *p*-nitrobenzoyl ester. [c]NMR yield of the boronate in the crude reaction mixture. [d]The hydrogenated derivative was isolated in 62% yield after hydrogenation of crude (*S*,*E*)-**2k**. The ee value was determined by HPLC analysis of the hydrogenated derivative. [e]The alcohol derivative was isolated in 88% yield after hydrogenation of the alkene moiety and subsequent oxidation of the crude (*S*,*E*)-**2l**. The ee value was determined by HPLC analysis of the alcohol derivative.

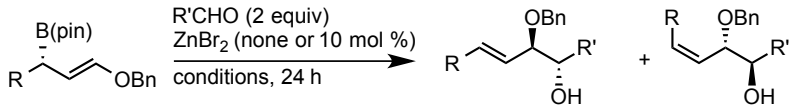


Scheme 1. γ-Borylation of Substrate (*R*,*Z*)-**1m** with CuCl/ Xantphos or Chiral BenzP* Ligands

2.4 Aldehyde Allylation with Linear (*E*)-γ-Alkoxyallylboronates

To date, there have been no reports in the literature describing the allylation of aldehydes with linear enantioenriched α-chiral (*E*)-γ-alkoxyallylboronates to give the corresponding 1,2-diol derivatives with high *E*/*Z* and *anti*:*syn* selectivities and enantioselectivities. With this in mind, we investigated the optimum reaction conditions for the aldehyde allylation with the γ-alkoxyallylboronates (Table 3). Without any catalyst, the allylboronate (*S*,*E*)-**2c** or (*S*,*E*)-**2i** reacted with benzaldehyde in CH_2Cl_2 or THF to afford products with low *E*/*Z* selectivity but high enantiospecificity (es)[23] (Table 3, entries 1−4). It has been reported that the selectivity of aldehyde allylation can be improved by the presence of an acid catalyst. Carreaux reported the $BF_3{\cdot}OEt_2$-catalyzed reaction of racemic (*E*)-γ-alkoxyallylboronates to afford products with high levels of *anti*:*syn* selectivity,[11] although the *E*/*Z* ratios were still in need of improvement. With this in mind, we screened a variety of Lewis acids, including $BF_3{\cdot}OEt_2$, $AlCl_3$, $FeCl_3$, $Sc(OTf)_3$, TMSOTf, and $ZnBr_2$. The results revealed that $ZnBr_2$, which had never been used as a Lewis acid catalyst for the allylation of aldehydes with allylboron reagents,[24,25] turned out to be the most effective Lewis acid catalyst for the highly stereoselective aldehyde allylation with our boron compounds (Table 3, entries 5−13). The stereoselectivities of this aldehyde allylation were in good agreement with the mechanism that had been previously postulated in the literature (see the Supporting Information).[11,25] The use of CH_2Cl_2 solvent is necessary for the high stereoselectivity of this reaction; allylation in THF solvent in the presence of $ZnBr_2$ catalyst gave inferior results, which would be due to the coordination of THF to $ZnBr_2$ catalyst (Table 3, entry 1 vs entry 7, entry 2 vs entry 8). The reaction of (*S*,*E*)-**2i** with octanal, cinnamaldehyde, or 2-octynal also afforded the corresponding alcohol products with high stereoselectivity (Table 3, entries 9−11). The reaction of (*S*,*E*)-**2c** with octanal provided the corresponding product in high selectivity and good *E*/*Z* ratio (Table 3, entry 12). The boronate (*S*,*E*)-**2g** bearing the methoxymethyl group also afforded the product in high es and good *E*/*Z* ratio (Table 3, entry 13, *E*/*Z* = 86:14, 100% es). The reactions in entries 5, 11, and 12 resulted in slightly lower yields than those in other entries, but the *anti*:*syn* ratios were not changed.

Table 3. Aldehyde Allylation with Optically Active γ-Alkoxyallylboronates **2**



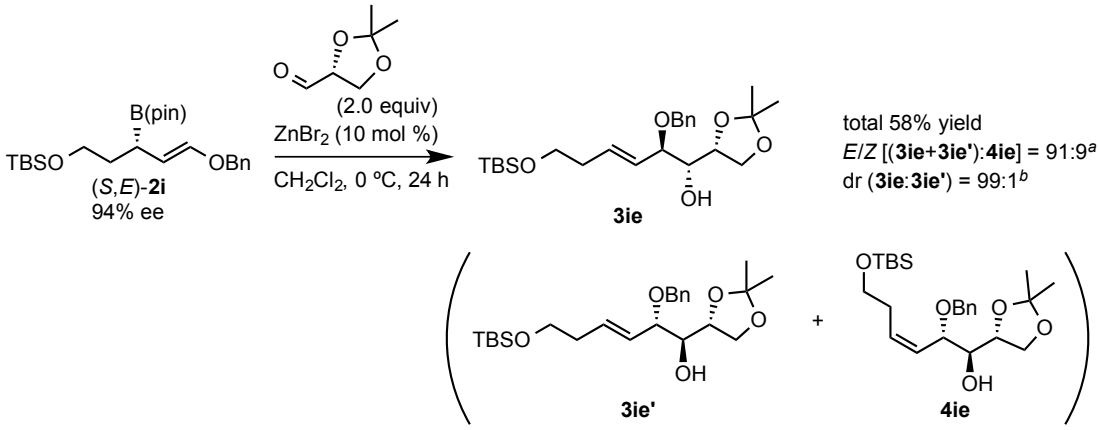
(*S*,*E*)-**2c**, 96% ee (R_1 = Me)
(*S*,*E*)-**2i**, 97% ee (R_1 = CH_2CH_2OTBS)
(*S*,*E*)-**2g**, 97% ee (R_1 = CH_2CH_2OMOM)

(*E*)-*anti*-**3** (*Z*)-*anti*-**4**

Entry	substrate	R_2CHO	solvent	*E*/*Z*[a] (**3**:**4**)	yield[b] (%)	es[c] (%)
1[d,e]	(*S*,*E*)-**2i**	PhCHO	CH_2Cl_2	34:66	94	100
2[d]	(*S*,*E*)-**2c**	PhCHO	CH_2Cl_2	18:82	80	100
3[d]	(*S*,*E*)-**2i**	PhCHO	THF	29:71	80	98
4[d]	(*S*,*E*)-**2c**	PhCHO	THF	15:85	78	100
5[f]	(*S*,*E*)-**2i**	PhCHO	CH_2Cl_2	98:2	68	100
6[f]	(*S*,*E*)-**2c**	PhCHO	CH_2Cl_2	92:8	81	100
7[e,f]	(*S*,*E*)-**2i**	PhCHO	THF	33:67	91	100
8[f]	(*S*,*E*)-**2i**	PhCHO	THF	18:82	89	100
9[f]	(*S*,*E*)-**2i**	$C_7H_{15}CHO$	CH_2Cl_2	96:4	79	97
10[e,f]	(*S*,*E*)-**2i**	cinnamaldehyde	CH_2Cl_2	93:7	79	100
11[e,f]	(*S*,*E*)-**2i**	2-octynal	CH_2Cl_2	87:13	73	98
12[f]	(*S*,*E*)-**2c**	$C_7H_{15}CHO$	CH_2Cl_2	85:15	72	100
13[e,f]	(*S*,*E*)-**2g**	PhCHO	CH_2Cl_2	86:14	81	100

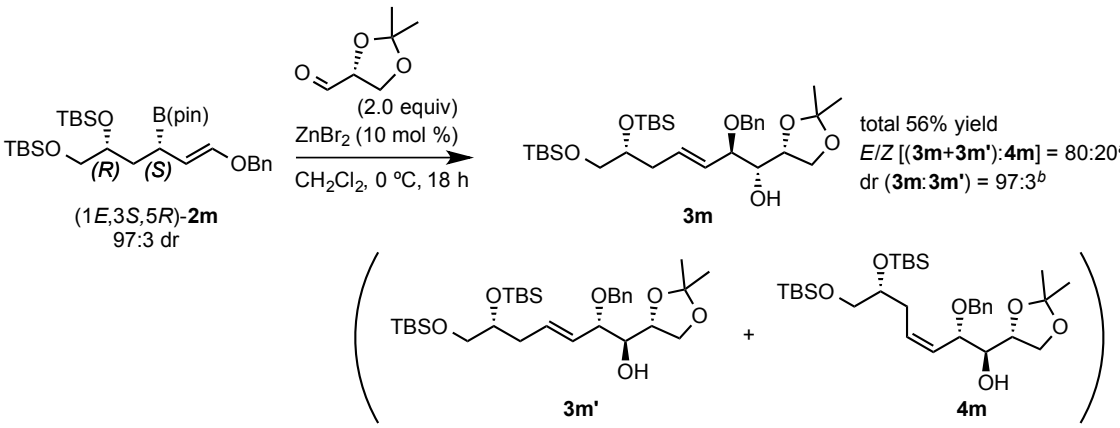
[a]The *E*:*Z* ratios (**3**:**4**) of the *anti*-products were determined by ^{1}H NMR and HPLC analysis. [b]Isolated yield of *anti*-products. The minor *syn*-isomers of **3** and **4** were present in less than trace amounts, which could be determined by ^{1}H NMR analysis of the crude reaction mixtures. [c]See ref 23. The ee values of the major products were determined by HPLC analysis. [d]Reagents and conditions: (*S*,*E*)-**2** (0.2 mmol) and the aldehyde (0.4 mmol) in a solvent (0.4 mL) at 30 °C. e(*S*,*E*)-**2i** with 94% ee was used. [f]Reagents and conditions: (*S*,*E*)-**2** (0.2 mmol), aldehyde (0.4 mmol), and dry $ZnBr_2$ (10 mol %) in a solvent (0.4 mL) at 0 °C. The use of dry $ZnBr_2$ is necessary for the high stereoselectivity.

The reaction conditions were compatible with a chiral α-oxyaldehyde substrate leading to the desired product in 58% yield, high *E*/*Z* ratio, and high dr {Scheme 2, *E*/*Z* [(**3ie**+**3ie′**):**4ie**] = 91:9, dr (**3ie**:**3ie′**) = 99:1}. The dr value [(**3ie**+**3ie′**):**4ie** = 99:1] was higher than the expected value (97:3) based on the enantiomeric purity of (*S*,*E*)-**2i** (94% ee). This would be attributed to the kinetic resolution upon addition of the optically active allylboronate to the chiral α-oxyaldehyde.



Scheme 2. Aldehyde Allylation of (*R*)-Glyceraldehyde Acetonide and Optically Active γ-Alkoxyallylboronate (*S*,*E*)-**2i**

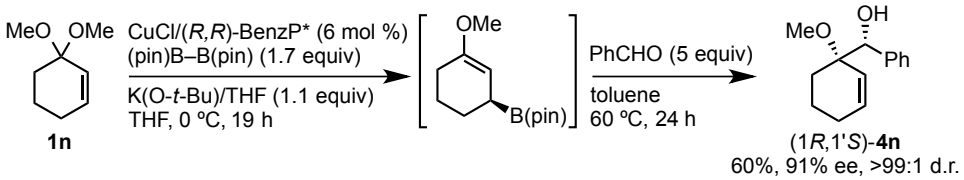
Having established conditions for the aldehyde allylation, we probed the feasibility of the convergent synthesis of complex polyol derivatives using the borylation/aldehyde allylation procedure (Scheme 3). The reaction of the boronate (1*E*,3*S*,5*R*)-**2m** with (*R*)-glyceraldehyde acetonide successfully proceeded to give the desired complex allylation product **3m** in good yield and selectivity {total 56% yield, *E*/*Z* [(**3m**+**3m′**):**4m**] = 80:20, dr (**3m**:**3m′**) = 97:3}.



Scheme 3. Convergent Coupling for Polyol Derivative Synthesis via Aldehyde Allylation of Complex Boronates and Aldehydes

2.5 Enantioselective Synthesis of Carbocyclic γ-Alkoxyallylboronates

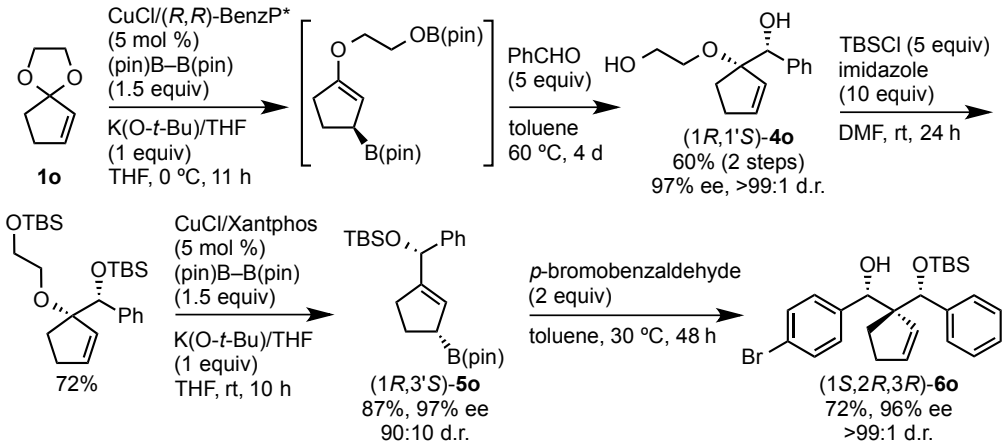
We then proceeded to examine the borylation of cyclic allyl ketals, which could provide access to 1,2-diol derivatives containing sterically congested vicinal stereogenic centers through a subsequent aldehyde allylation (Scheme 4). The boryl substitution of allyl ketal **1n** proceeded smoothly under the standard conditions, although the isolation of the product boronate was not successful. Thus, we carried out borylation of **1n** and sequential allylation of aldehyde without isolation of the allylboronate, which afforded the corresponding product (1*R*,1′*S*)-**4n** in good yield with high levels of diastereo- and enantioselectivity without the need for a Lewis acid catalyst. No proton signals of the minor diastereomer were detected in the ^{1}H NMR spectra of the crude reaction mixture after the allylation step. The single isomeric product was isolated in 60% yield with 91% ee after chromatographic purification.



Scheme 4. Enantioselective Boryl Substitution/Aldehyde Allylation of Allyl Ketal **1n**

The above borylation/aldehyde allylation procedure generated an allyl ether moiety in the products, and it was envisaged that this structural feature could be used as a reactive site for the subsequent copper(I)-catalyzed borylation. With this in mind, we proceeded to investigate the stereoselective modular construction of an optically active 3,3-disubstituted cyclopentene scaffold, which contained three consecutive chiral centers, including a quaternary carbon, using an iterative borylation/aldehyde allylation procedure[19c] (Scheme 5). Substrate **1o** underwent the first borylation/aldehyde allylation to afford the diol (1*R*,1′*S*)-**4o** in good yield, with excellent diastereo- and enantioselectivity (dr of the crude reaction mixture, 98:2; 60% isolated yield after recrystallization as a single isomer with 97% ee). In this reaction, the allylation of benzaldehyde proceeded with high diastereoselectivity. Following TBS protection of the hydroxy groups in (1*R*,1′*S*)-**4o**, a second diastereoselective borylation with the achiral copper(I)/ Xantphos catalyst[19e] was conducted to afford the corresponding allylboronate (1*S*,3′*R*)-**5o** via a *syn*-S_N2' mechanism (90:10 dr), which occurred as a consequence of the steric effect imposed by the bulky silyl group.[26] The configurations of (1*R*,1′*S*)-**4o** and (1*S*,3′*R*)-**5o** were determined by X-ray crystallographic

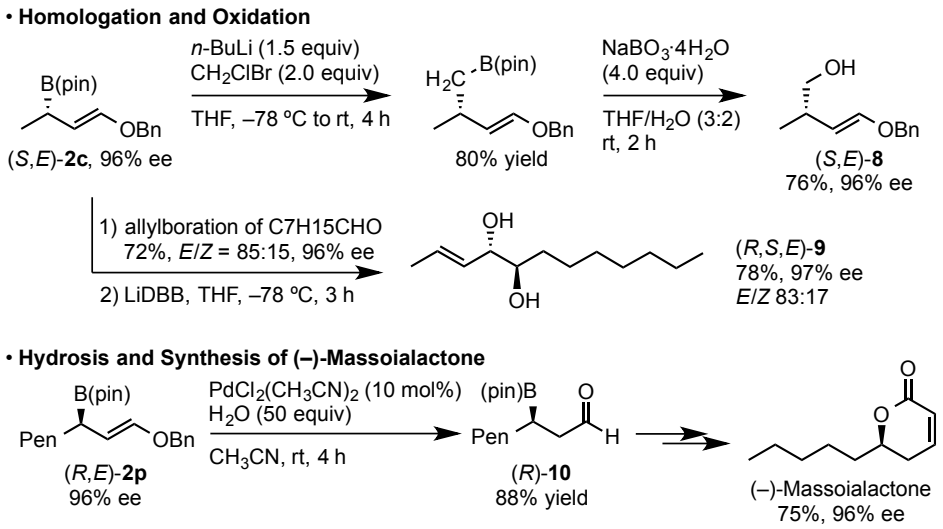
analysis (see the Supporting Information). Finally, a second allylation of *p*-bromobenzaldehyde with (1*S*,3′*R*)-**5o** provided monoprotected 1,3-diol (1*S*,2*R*,3*R*)-**6o** in good yield with high diastereo- and enantioselectivity (72% yield, single diastereomer, 96% ee). During the allylation of *p*-bromobenzaldehyde with (1*S*,3′*R*)-**5o**, the reaction of the major isomer of (1*S*,3′*R*)-**5o** proceeded selectively prior to that of the minor isomer, which led to the observed higher diastereomeric ratio of the product. The absolute configuration of the product (1*S*,2*R*,3*R*)-**6o** was determined by X-ray crystallographic analysis of the corresponding deprotected 1,3-diol (see the Supporting Information). This synthetic method can be used as a general strategy to provide novel functionalized cycloalkene scaffolds for drug discovery.[27]



Scheme 5. Stereoselective Modular Construction of a Complex 3,3-Disubstituted Cyclopentene

2.6 Application of Linear γ-Alkoxyallylboronates

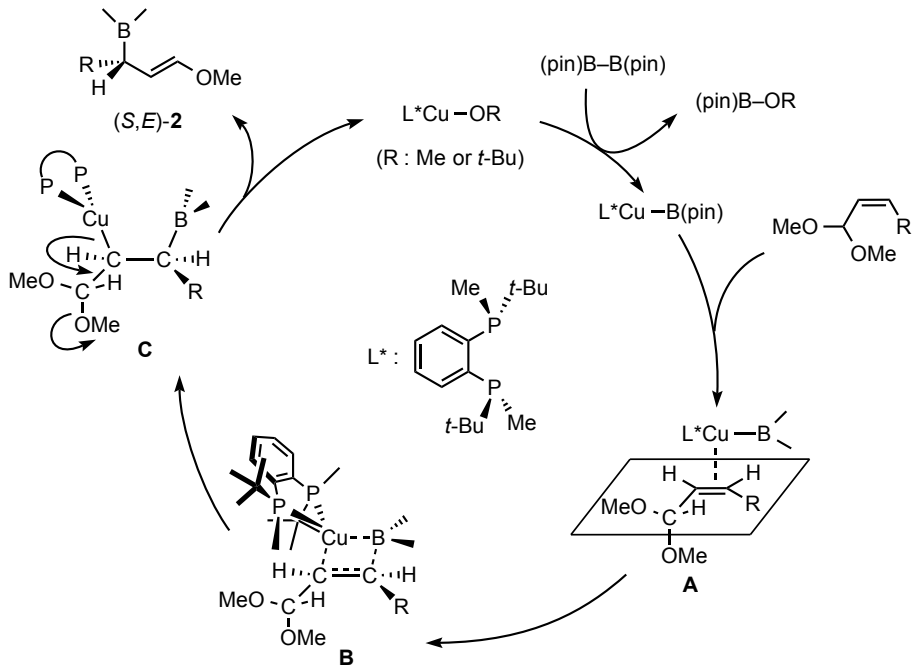
We further demonstrated the transformations of these α-chiral linear (*E*)-γ-alkoxyallylboronates (Scheme 6). The boronate (*S*,*E*)-**2c** underwent homologation to afford the corresponding homoallylboronate (*R*,*E*)-**7** in 80% yield followed by oxidation to afford alcohol (*S*,*E*)-**8** in 76% yield with 96% ee, where the alkenyl ether moiety remained intact. In addition, the feasibility of 3-ene-*anti*-1,2-diols was also confirmed by using lithium di-tert-butylbiphenyl (LiDBB) reagent. Deprotection of the benzyl group in the allylation product from (*S*,*E*)-**2c** and octyl aldehyde gave the corresponding diol in 78% yield without lowering its enantiomeric purity and *anti*:*syn* and *E*/*Z* ratios [97% ee, (*R*,*S*,*E*)-**9**:(*S*,*R*,*Z*)-**9** = 87:13; the *syn*-isomer could not be observed by ^{1}H NMR] . The boronate (*R*,*E*)-**2p** prepared by the present enantioselective borylation was subjected to a Pd-catalyzed hydrolysis[28] to afford the β-boryl aldehyde (*R*)-**10** in 88% yield.[29] We further carried out a total synthesis of (−)-massoialactone from (*R*)-**10**.



Scheme 6. Transformations of α-Chiral Linear (*E*)-γ-Alkoxyallylboronates

2.7 Proposed Mechanism in Asymmetric Boryl Substitution and Aldehyde Allylation

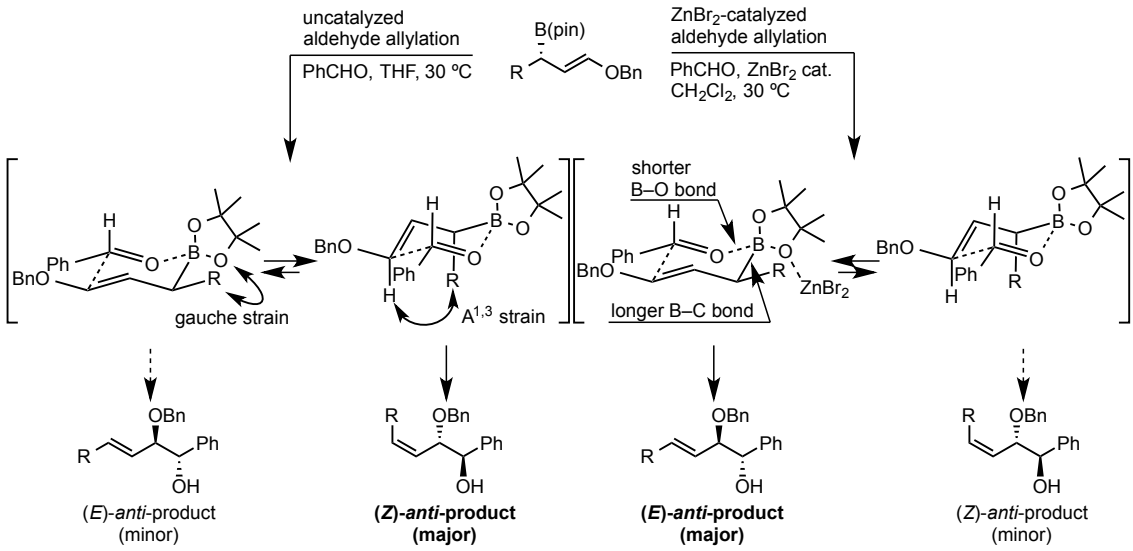
A reaction mechanism has been proposed to account for the stereochemical outcome of this boryl substitution (Scheme 7). The selective enantiofacial addition of the Cu−B bond of the in situ generated borylcopper(I) species to the C−C double bond of the allyl acetal **A** would occur through the transition structure **B** to give the alkylcopper intermediate **C**. The conformation of the allyl acetal would be fixed due to 1,3-allylic strain, which would also account for the observed preferential formation of (*E*)-products. Subsequent β-alkoxy elimination would afford the optically active γ-alkoxyallylboronate (*S*,*E*)-**2**.



Scheme 7. Proposed Mechanism in Boryl Substitution

The stereoselectivities of aldehyde allylations with linear (*E*)-γ-alkoxyallylboronates were in good agreement with the mechanism that had been previously postulated in the literature.[33,34] The explanation for the stereochemical outcome of $ZnBr_2$-catalyzed or uncatalyzed aldehyde allylation with the α-chiral γ-alkoxyallylboronates is shown in the scheme 8. In the case of the uncatalyzed reaction, the gauche strain between the α-substituent and the pinacol moiety has large effects on the *E*/*Z* selectivity rather than the $A^{1,3}$ strain, which lead to the formation of (*Z*)-*anti*-product. In contrast, the gauche strain becomes less important in the $ZnBr_2$-catalyzed reactions, because the coordination

of the catalyst to the boron oxygen makes the B−O (aldehyde) bond shorter and the B−C bond longer, which leads the pathway that provides (*E*)-*anti*-product to be more favorable. Allylation of aldehydes with the allylboronate (*S*,*E*)-**2i**, which has a larger substituent at the α-position than that of the allylboronate (*S*,*E*)-**2c**, leads to higher *E*/*Z* selectivity, which occurred as a consequence of the steric effect in the 1,3-allylic strain of the minor transition state.



Scheme 8. Proposed Mechanism and Stereoselectivity in Aldehyde Allylation

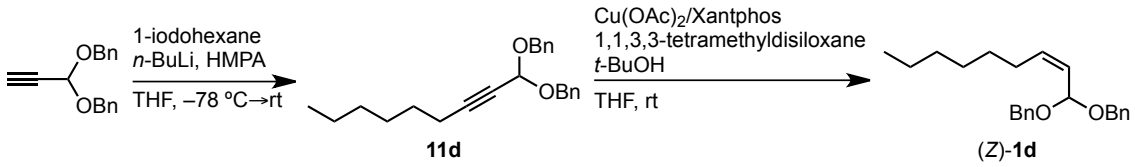
2.7 Conclusion

In conclusion, we have developed a copper(I)-catalyzed enantioselective boryl substitution of allyl acetals, providing a novel approach to optically active α-chiral linear or carbocyclic (*E*)-γ-alkoxyallylboronates. Furthermore, we have developed a highly stereoselective, zinc Lewis acid-catalyzed aldehyde allylation with these boronates. This borylation represents the first example of an enantioselective γ-substitution of allylic acetals. The utility of the borylation/aldehyde allylation procedure has been demonstrated by the convergent synthesis of the complex polyol derivatives and the stereoselective modular construction of a complex cyclopentene scaffold. Furthermore, we have demonstrated the useful transformations of the enantioenriched linear (*E*)-γ-alkoxyallylboronates.

2.8 Experimental Data

Substrate Preparation

Preparation of (*Z*)-1,1-dibenzyloxynon-2-ene [(*Z*)-1d].



In an oven-dried 200 mL two-neck round-bottomed flask, 3,3-dibenzyloxyprop-1-yne (1.76 g, 6.96 mmol), hexamethylphosphoric triamide (4.87 mL, 28 mmol) and dry THF (60 mL) were charged under nitrogen atmosphere and cooled to −78 ºC. A hexane solution of *n*-BuLi (1.60 M, 5.25 mL, 8.4 mmol) was added dropwise to the solution. After 45 min, 1-iodohexane (2.06 mL, 14 mmol) was added and then the reaction mixture was allowed to warm to room temperature and stirred for 5 h. After pouring onto water, the mixture was extracted with Et_2O, and the solvent was removed by evaporation after dried over Na_2SO_4. The residue was purified by flash column chromatography (hexane/EtOAc = 99.5:0.5 to 97:3) to obtain the desired product **11d** as a colorless oil (1.94 g, 5.77 mmol, 83 % isolated yield).

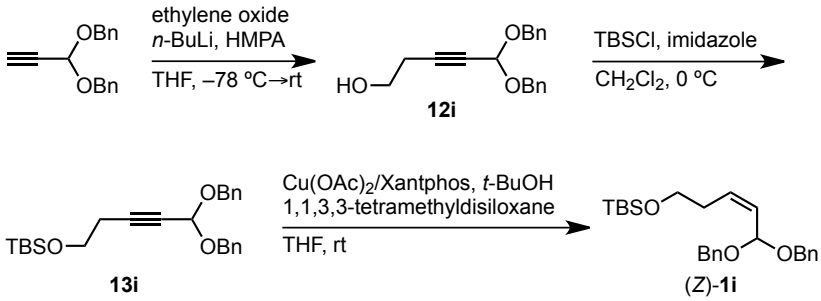
^{1}H NMR (392 MHz, $CDCl_3$, δ): 0.88 (t, *J* = 6.9 Hz, 3H), 1.21–1.44 (m, 6H), 1.53 (quint, *J* = 7.3 Hz, 2H), 2.26 (dt, *J* = 1.8, 7.3 Hz, 2H), 4.62 (d, *J* = 11.8 Hz, 2H), 4.79 (d, *J* = 11.8 Hz, 2H), 5.46 (t, *J* = 1.6 Hz, 1H), 7.25–7.40 (m, 10H). ^{13}C NMR (101 MHz, $CDCl_3$, δ): 13.9 (CH_3), 18.5 (CH_2), 22.4 (CH_2), 28.1 (CH_2), 28.4 (CH_2), 31.1 (CH_2), 67.0 (CH_2), 75.3 (*C*), 87.3 (*C*), 90.9 (*C*H), 127.5 (*C*H), 127.9 (*C*H), 128.2 (*C*H), 137.5 (*C*).

In an oven-dried 20 mL round-bottomed flask, $Cu(OAc)_2$ (13.6 mg, 0.075 mmol) and Xantphos (43.4 mg, 0.075 mmol) were dissolved in dry THF (5 mL) at room temperature under nitrogen atmosphere. 1,1,3,3-Tetramethyldisiloxane (1.8 mL, 10 mmol) and *tert*-butyl alcohol (0.47 mL, 5 mmol) were added to the resulting solution. After stirred for 30 min, **11d** was added to the above solution and the resultant mixture was stirred for 12 h at room temperature. After the completion of the reaction was checked by GC, the mixture was directly filtered through a short silica-gel column to give the crude product. After removal of the solvents under reduced pressure, the crude product was purified with flash chromatography to give the corresponding (*Z*)-allyl acetal **1d**. When

unreacted polysiloxane was found in the product after SiO_2 chromatography, addition of TBAF (1 M in THF, 4 mL, 4 mmol) enabled removal of polysiloxane. After stirring for 1 h, the solvents were removed by evaporation and the residue was purified with flash column chromatography to obtain the desired product (*Z*)-**1d** (468.4 mg, 1.63 mmol, 55% isolated yield).

^{1}H NMR (401 MHz, $CDCl_3$, δ): 0.87 (t, *J* = 6.8 Hz, 3H), 1.19–1.40 (m, 8H), 2.09 (dq, *J* = 1.1, 7.4 Hz, 2H), 4.58 (d, *J* = 12.0 Hz, 2H), 4.67 (d, *J* = 12.0 Hz, 2H), 5.43 (d, *J* = 6.4 Hz, 1H), 5.61 (ddt, *J* = 1.4, 6.4, 10.8 Hz, 1H), 5.70 (ddt, *J* = 0.9, 7.2, 11.5 Hz, 1H), 7.15–7.36 (m, 10H). ^{13}C NMR (100 MHz, $CDCl_3$, δ): 14.0 (CH_3), 22.5 (CH_2), 28.0 (CH_2), 28.8 (CH_2), 29.2 (CH_2), 31.6 (CH_2), 66.8 (CH_2), 96.9 (*C*H), 126.5 (*C*H), 127.5 (*C*H), 127.8 (*C*H), 128.3 (*C*H), 135.7 (*C*H), 138.1 (*C*). HRMS–ESI (*m*/*z*): $[M+Na]^+$ calcd for $C_{23}H_{30}O_2Na$, 361.21380; found, 361.21365. Anal. Calcd for $C_{23}H_{30}O_2$: C, 81.61; H, 8.93. Found: C, 81.46; H, 9.08.

Preparation of (*Z*)-5-(*tert*-Butyldimethylsiloxy)-1,1-dibenzyloxypent-2-ene [(*Z*)-1i].



In an oven-dried 200 mL two-neck round-bottomed flask, 3,3-dibenzyloxyprop-1-yne (7.59 g, 30 mmol), hexamethylphosphoric triamide (22.5 mL, 17 mmol) and dry THF (30 mL) were charged under nitrogen atmosphere and cooled to −78 ºC. A hexane solution of *n*-BuLi (1.65 M, 20 mL, 33 mmol) was added dropwise to the solution. After 30 min, ethylene oxide (1 M solution in THF, 36 mL, 36 mmol) was added. After stirring for 2 h, the reaction mixture was allowed to warm to room temperature and stirred for overnight. The reaction mixture was quenched by the addition of saturated NH_4Cl aq. and extracted with Et_2O. After dried over Na_2SO_4, the solvent was removed by evaporation and the residue was purified by flash column chromatography to give the corresponding alcohol **12i** (6.94 g, 23.4 mmol, 78% isolated yield).

NMR data of **12i**: ^{1}H NMR (396 MHz, $CDCl_3$, δ): 1.73 (t, *J* = 6.1 Hz, 1H), 2.53 (dt, *J* = 1.6, 6.3 Hz, 2H), 3.72 (q, *J* = 6.2 Hz, 2H), 4.62 (d, *J* = 11.9 Hz, 2H), 4.79 (d, *J* = 11.9 Hz, 2H), 5.47 (t, *J* = 1.6 Hz, 1H), 7.24–7.41 (m, 10H). ^{13}C NMR (100 MHz, $CDCl_3$, δ): 22.3 (CH_2), 59.9 (CH_2), 66.8 (CH_2), 76.2 (*C*), 84.1 (*C*), 90.5 (*C*H), 127.3 (*C*H), 127.6 (*C*H), 127.9 (*C*H), 136.9 (*C*).

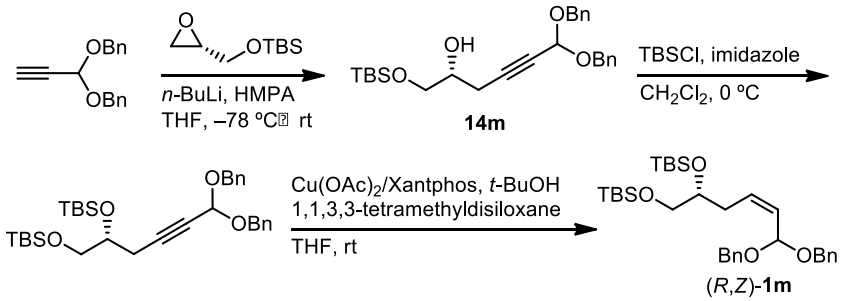
In an oven-dried 100 mL two-neck round-bottomed flask, alcohol **12i** (2.96 g, 10 mmol), imidazole (1.02 g, 15 mmol) and dry CH_2Cl_2 (30 mL) were charged under nitrogen atmosphere and cooled to 0 ºC. Then, a CH_2Cl_2 solution of TBSCl (2.26 g, 15 mmol in 10 mL of CH_2Cl_2) was added to the mixture and stirred for 1.5 h. After that, the reaction was quenched by addition of saturated NH_4Cl aq. and extracted with Et_2O. The solvent is removed by evaporation after dried over Na_2SO_4. The residue was purified by flash column chromatography (hexane/EtOAc = 100:0 to 94:6) to give the TBS protected product **13i** in quantitative yield (4.13 g, 101% isolated yield).

^{1}H NMR (396 MHz, $CDCl_3$, δ): 0.06 (s, 6H), 0.89 (s, 9H), 2.48 (dt, *J* = 1.3, 7.3 Hz, 2H), 3.74 (t, *J* = 7.3 Hz, 2H), 4.61 (d, *J* = 11.5 Hz, 2H), 4.78 (d, *J* = 11.9 Hz, 2H), 5.45 (s, 1H), 7.24–7.39 (m, 10H). ^{13}C NMR (100 MHz, $CDCl_3$, δ): –5.45 (*C*H_3), 18.1 (*C*), 22.9 (*C*H_2), 25.7 (*C*H_3), 61.3 (*C*H_2), 67.0 (*C*H_2), 76.3 (*C*), 84.1 (*C*), 90.7 (*C*H), 127.5 (*C*H), 127.9 (*C*H), 128.2 (*C*H), 137.4 (*C*).

In an oven-dried 20 mL 2-neck round-bottomed flask, $Cu(OAc)_2$ (13.6 mg, 0.075 mmol) and Xantphos (43.4 mg, 0.075 mmol) were dissolved in dry THF (5 mL) at room temperature, then 1,1,3,3-tetramethyldisiloxane (1.8 mL, 10 mmol) and *tert*-butyl alcohol were added to the resulting solution. After stirring for 30 min, **12i** was added to the reaction mixture and the solution was stirred for 12 h. After the completion of the reaction was checked by GC, the mixture was directly filtered through a short silica-gel column to give the crude product. After removal of the solvents under reduced pressure, the residue was purified with flash column chromatography (EtOAc:hexane = 0/100 to 8/92) to obtain desired (*Z*)-**1i** (1.08 g, 2.62 mmol, 44% isolated yield).

^{1}H NMR (401 MHz, $CDCl_3$, δ): 0.03 (s, 6H), 0.88 (s, 9H), 2.35 (q, *J* = 6.5 Hz, 2H), 3.62 (t, *J* = 6.6 Hz, 2H), 4.58 (d, *J* = 11.6 Hz, 2H), 4.66 (d, *J* = 11.2 Hz, 2H), 5.44 (d, *J* = 5.6 Hz, 1H), 5.65–5.79 (m, 2H), 7.23–7.37 (m, 10H). ^{13}C NMR (100 MHz, $CDCl_3$, δ): –5.4 (*C*H_3), 18.2 (*C*), 25.9 (*C*H_3), 31.7 (*C*H_2), 62.3 (*C*H_2), 66.8 (*C*H_2), 97.0 (*C*H), 127.5 (*C*H), 127.8 (*C*H), 128.3 (*C*H), 131.9 (*C*H), 138.1 (*C*). HRMS–ESI (*m*/*z*): $[M+Na]^+$ calcd for $C_{25}H_{36}O_3NaSi$, 435.23259; found, 435.23328. Anal. Calcd for $C_{25}H_{36}O_3Si$: C, 72.77; H, 8.79. Found: C, 72.59; H, 8.71.

Preparation of 1,1-dibenzyloxy-5,6-bis(*tert*-butyldimethylsiloxy)hex-2-ene [(*R*,*Z*)-1m].



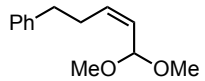
In an oven-dried 300 mL 3-neck round-bottomed flask, 3,3-dibenzyloxyprop-1-yne (8.86 g, 35 mmol) and dry THF (100 mL) were charged under nitrogen atmosphere and cooled to −78 ºC. A hexane solution of *n*-BuLi (1.65 M, 21.2 mL, 35 mmol) was added dropwise to the mixture. After 1 h, a solution of (*S*)-TBS-glycidol ether (10.55 g, 56 mmol, >95% ee) in dry THF (80 mL) was added to the mixture, then the resulting solution was stirred for 15 min. $BF_3 \cdot OEt_2$ (4.32 mL, 35 mmol) was added dropwise to the reaction mixture and then allowed to warm to –30 ºC and stirred for 16 h. The reaction mixture was quenched with saturated Na_2HCO_3 aq. and extracted with EtOAc. The extract was dried over Na_2SO_4 and evaporated under reduced pressure. The residue was purified by flash column chromatography (hexane/EtOAc = 90:10) to give the corresponding alcohol **14m** (7.99 g, 18.1 mmol, 52% isolated yield).

^{1}H NMR (396 MHz, $CDCl_3$, δ): 0.07 (s, 6H), 0.89 (s, 9H), 2.46 (d, *J* = 5.1 Hz, 1H), 2.47–2.53 (m, 2H), 3.60 (dd, *J* = 5.5, 10.3 Hz, 1H), 3.71 (dd, *J* = 4.0, 9.9 Hz, 1H), 3.82 (sex, *J* = 5.5 Hz, 1H), 4.62 (d, *J* = 11.9 Hz, 2H), 4.78 (d, *J* = 11.5 Hz, 2H), 5.46 (s, 1H), 7.25–7.39 (m, 10H). ^{13}C NMR (100 MHz, $CDCl_3$, δ): –5.6 (*C*H_3), 18.1 (*C*), 23.2 (*C*H_2), 25.7 (*C*H_3), 65.4 (*C*H_2), 67.0 (*C*H_2), 69.8 (*C*H), 77.2 (*C*), 83.1 (*C*), 90.7 (*C*H), 127.6 (*C*H), 127.9 (*C*H), 128.2 (*C*H), 137.3 (*C*).

Further TBS protection of the secondary hydroxy group and *Z*-selective reduction of the C≡C bond to C=C bond of **14m** were carried out according to the procedure described above to give the related product (*R*,*Z*)-**1m**.

^{1}H NMR (396 MHz, $CDCl_3$, δ): 0.03 (s, 6H), 0.04 (s, 6H), 0.87 (s, 9H), 0.88 (s, 9H), 2.22–2.32 (m, 1H), 2.36–2.46 (m, 1H), 3.40 (dd, *J* = 6.3, 9.9 Hz, 1H), 3.50 (dd, *J* = 5.5, 9.9 Hz, 1H), 3.71 (quint, *J* = 5.8 Hz, 1H), 4.57 (d, *J* = 11.4 Hz, 2H), 4.66 (dd, *J* = 6.1, 11.7 Hz, 2H), 5.45 (d, *J* = 6.3 Hz, 1H), 5.70 (dd, *J* = 6.3, 10.7 Hz, 1H), 5.76–5.84 (m, 1H), 7.25–7.37 (m, 10H). ^{13}C NMR (101 MHz, $CDCl_3$, δ): –5.41 (*C*H_3), –5.36 (*C*H_3), –4.7 (*C*H_3), –4.4 (*C*H_3), 18.1 (*C*), 18.3 (*C*), 25.8 (*C*H_3), 25.9 (*C*H_3), 33.0 (*C*H_2), 66.5 (*C*H_2), 66.9 (*C*H_2), 72.7 (*C*H), 97.3 (*C*H), 127.5 (*C*H), 127.8 (*C*H), 128.3 (*C*H), 131.8 (*C*H), 138.1 (*C*), 138.2 (*C*). HRMS–ESI (*m*/*z*): $[M+Na]^+$ calcd for $C_{32}H_{52}O_4NaSi_2$, 579.32963; found, 579.33040. Anal. Calcd for $C_{32}H_{52}O_4Si_2$: C, 69.01; H, 9.41. Found: C, 69.04; H, 9.42.

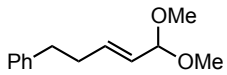
(*Z*)-1,1-Dimethoxy-5-phenylpent-2-ene [(*Z*)-1a].



(*Z*)-**1a**

^{1}H NMR (400MHz, $CDCl_3$, δ): 2.47 (dq, *J* = 1.4, 7.5 Hz, 2H), 2.71 (t, *J* = 7.5 Hz, 2H), 3.26 (s, 6H), 4.99 (dd, *J* = 1.1, 6.6 Hz, 1H), 5.44 (ddt, *J* = 1.6, 6.4, 11.2 Hz, 1H), 5.70 (ddt, *J* =1.2, 7.5, 11.2 Hz, 1H), 7.16–7.32 (m, 5H). ^{13}C NMR (99 MHz, $CDCl_3$, δ): 29.9 (*C*H_2), 35.5 (*C*H_2), 52.3 (*C*H_3), 99.4 (*C*H), 125.9 (*C*H), 127.0 (*C*H), 128.3 (*C*H), 128.4 (*C*H), 134.3 (*C*H), 141.4 (*C*). HRMS-ESI (*m*/*z*): $[M+Na]^+$ calcd for $C_{13}H_{18}O_2Na$, 229.11990; found, 229.11989.

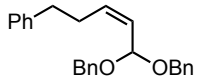
(*E*)-1,1-Dimethoxy-5-phenylpent-2-ene [(*E*)-1a].



(*E*)-**1a**

This substrate contains a small amount of *Z* isomer (*E*/*Z* = 95:5). ^{1}H NMR (401 MHz, $CDCl_3$, δ): 2.47 (q, *J* = 7.8 Hz, 2H), 2.73 (t, *J* = 7.8 Hz, 2H), 3.29 (s, 6H), 4.71 (d, *J* = 5.5 Hz, 1H), 5.49 (dd, *J* = 5.5, 16.1 Hz, 1H), 5.70 (dt, *J* =6.8, 15.9 Hz, 1H), 7.16–7.32 (m, 5H). ^{13}C NMR (100 MHz, $CDCl_3$, δ): 33.5 (*C*H_2), 34.9 (*C*H_2), 52.1 (*C*), 102.7 (*C*H), 125.6 (*C*H), 127.0 (*C*H), 128.05 (*C*H), 128.13 (*C*H), 134.1 (*C*H), 141.1 (*C*). HRMS-ESI (*m/z*): $[M+Na]^+$ calcd for $C_{13}H_{18}O_2Na$, 229.11990; found, 229.12000. Anal. Calcd for $C_{13}H_{18}O_2$: C, 75.69; H, 8.80. Found: C, 75.62; H, 8.84.

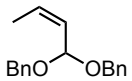
(*Z*)-1,1-Dibenzyloxy-5-phenylpent-2-ene [(*Z*)-1b].



(*Z*)-**1b**

^{1}H NMR (392 MHz, $CDCl_3$, δ): 2.43 (q, *J* = 7.7 Hz, 2H), 2.67 (t, *J* = 7.6 Hz, 2H), 4.51 (d, *J* = 11.5 Hz, 2H), 4.61 (dd, *J* = 11.8 Hz, 2H), 5.35 (d, *J* = 6.5 Hz, 1H), 5.60–5.67 (m, 1H), 5.73 (dt, *J* = 7.5, 11,4 Hz, 1H), 7.09–7.38 (m, 15H). ^{13}C NMR (99 MHz, $CDCl_3$, δ): 29.8 (*C*H_2), 35.8 (*C*H_2), 66.7 (*C*H_2), 97.3 (*C*H), 125.8 (*C*H), 127.38 (*C*H), 127.43 (*C*H), 127.7 (*C*H), 128.17 (*C*H), 128.24 (*C*H), 128.3 (*C*H), 134.3 (*C*H), 138.0 (*C*), 141.2 (*C*). HRMS-EI (*m/z*): $[M–C_7H_7O, –H]^{2+}$ calcd for $C_{18}H_{18}O$, 250.13576; found, 250.13535. Anal. Calcd for $C_{25}H_{26}O_2$: C, 83.76; H, 7.31. Found: C, 83.77; H, 7.45.

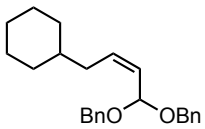
(*Z*)-1,1-Dibenzyloxybut-2-ene [(*Z*)-1c].



(*Z*)-**1c**

^{1}H NMR (392 MHz, $CDCl_3$, δ): 1.68 (dd, *J* = 1.4, 6.9 Hz, 3H), 4.56 (d, *J* = 12.2 Hz, 2H), 4.65 (d, *J* = 11.4 Hz, 2H), 5.45 (d, *J* = 5.9 Hz, 1H), 5.60–5.68 (m, 1H), 5.69–5.80 (m, 1H), 7.21–7.37 (m, 10H). ^{13}C NMR (99 MHz, $CDCl_3$, δ): 13.7 (CH_3), 66.8 (CH_2), 96.8 (*C*H), 127.5 (*C*H), 127.6 (*C*H), 127.8 (*C*H), 128.3 (*C*H), 129.9 (*C*H), 138.1 (*C*). HRMS–ESI (*m*/*z*): $[M+Na]^+$ calcd for $C_{18}H_{20}O_2Na$, 291.13555; found, 291.13542. This product contains small amount of impurities.

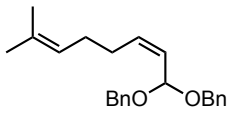
(*Z*)-1,1-Dibenzyloxy-4-cyclohexylbut-2-ene [(*Z*)-1e].



(*Z*)-**1e**

^{1}H NMR (401 MHz, $CDCl_3$, δ): 0.85 (q, *J* = 11.0 Hz, 2H), 1.03–1.35 (m, 4H), 1.59–1.71 (m, 5H), 1.98 (t, *J* = 6.8 Hz, 2H), 4.58 (d, *J* = 12.0 Hz, 2H), 4.66 (d, *J* = 12.0 Hz, 2H), 5.41 (d, *J* = 6.0 Hz, 1H), 5.61–5.76 (m, 2H), 7.25–7.38 (m, 10H). ^{13}C NMR (101 MHz, $CDCl_3$, δ): 26.2 (CH_2), 26.4 (CH_2), 33.0 (CH_2), 35.7 (CH_2), 37.9 (*C*H), 66.8 (CH_2), 96.9 (*C*H), 127.1 (*C*H), 127.5 (*C*H), 127.9 (*C*H), 128.3 (*C*H), 134.4 (*C*H), 138.1 (*C*). HRMS–ESI (*m*/*z*): $[M+Na]^+$ calcd for $C_{24}H_{30}O_2Na$, 373.21380; found, 373.21349. Anal. Calcd for $C_{24}H_{30}O_2$: C, 82.24; H, 8.63. Found: C, 82.10; H, 8.71.

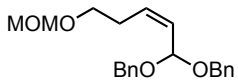
(*Z*)-1,1-Dibenzyloxy-7-methylocta-2,6-diene [(Z)-1f].



(*Z*)-**1f**

^{1}H NMR (392 MHz, $CDCl_3$, δ): 1.58 (s, 3H), 1.67 (s, 3H), 2.05 (q, *J* = 7.3 Hz, 2H), 2.15 (q, *J* = 7.1 Hz, 2H), 4.58 (d, *J* = 11.4 Hz, 2H), 4.66 (d, *J* = 11.4 Hz, 2H), 5.08 (t, *J* = 6.9 Hz, 1H), 5.43 (d, *J* = 5.9 Hz, 1H), 5.62 (dd, *J* = 6.1, 11.2 Hz, 1H), 5.70 (dt, *J* = 6.9, 11.1 Hz, 1H), 7.26–7.38 (m, 10H). ^{13}C NMR (99 MHz, $CDCl_3$, δ): 17.6 (CH_3), 25.5 (CH_3), 27.6 (CH_2), 28.1 (CH_2), 66.6 (CH_2), 96.9 (*C*H), 123.4 (*C*H), 126.8 (*C*H), 127.3 (*C*H), 127.6 (*C*H), 128.1 (*C*H), 131.9 (*C*), 135.0 (*C*H), 138.0 (*C*). HRMS–ESI (*m*/*z*): $[M+Na]^+$ calcd for $C_{23}H_{28}O_2Na$, 359.19815; found, 359.19861.

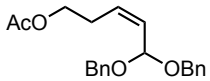
(*Z*)-1,1-Dibenzyloxy-5-(methoxymethoxy)pent-2-ene [(*Z*)-1g].



(*Z*)-**1g**

^{1}H NMR (396 MHz, $CDCl_3$, δ): 2.42 (q, *J* = 6.3 Hz, 2H), 3.33 (s, 3H), 3.54 (t, *J* = 6.5 Hz, 2H), 4.586 (d, *J* = 11.9 Hz, 2H), 4.588 (s, 2H), 4.67 (d, *J* = 11.5 Hz, 2H), 5.45 (d, *J* = 5.1 Hz, 1H), 5.69–5.80 (m, 1H), 5.74 (dd, *J* = 2.8, 4.4 Hz, 1H), 7.26–7.36 (m, 10H). ^{13}C NMR (99 MHz, $CDCl_3$, δ): 28.5 (CH_2), 54.8 (CH_3), 66.5 (CH_2), 66.6 (CH_2), 96.0 (CH_2), 96.8 (*C*H), 127.3 (*C*H), 127.6 (*C*H), 128.1 (*C*H), 128.5 (*C*H), 131.5 (*C*H), 137.9 (*C*). HRMS–ESI (*m*/*z*): $[M+Na]^+$ calcd for $C_{21}H_{26}O_4Na$, 365.17233; found, 365.17260. Anal. Calcd for $C_{21}H_{26}O_4$: C, 73.66; H, 7.65. Found: C, 73.71; H, 7.79.

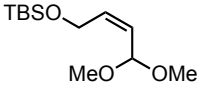
(*Z*)-5-Acetoxy-1,1-dibenzyloxypent-2-ene [(*Z*)-1h].



(*Z*)-**1h**

^{1}H NMR (396 MHz, $CDCl_3$, δ): 2.01 (s, 3H), 2.46 (q, *J* = 6.6 Hz, 2H), 4.08 (t, *J* = 6.9 Hz, 2H), 4.59 (d, *J* = 11.1 Hz, 2H), 4.67 (d, *J* = 11.9 Hz, 2H), 5.44 (d, *J* = 5.5 Hz, 1H), 5.65–5.79 (m, 2H), 7.26–7.38 (m, 10H). ^{13}C NMR (99 MHz, $CDCl_3$, δ): 20.4 (CH_3), 27.2 (CH_2), 62.9 (CH_2), 66.4 (CH_2), 96.6 (*C*H), 127.3 (*C*H), 127.5 (*C*H), 128.0 (*C*H), 129.2 (*C*H), 130.1 (*C*H), 137.7 (*C*), 170.4 (*C*). HRMS–ESI (*m*/*z*): $[M+Na]^+$ calcd for $C_{21}H_{24}O_4Na$, 363.15668; found, 363.15713. Anal. Calcd for $C_{21}H_{24}O_4$: C, 74.09; H, 7.11. Found: C, 74.20; H, 7.20.

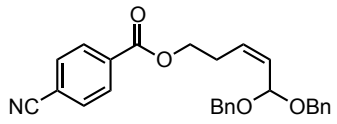
(*Z*)-4-(*tert*-Butyldimethylsiloxy)-1,1-dimethoxybut-2-ene [(*Z*)-1j].



(*Z*)-**1j**

^{1}H NMR (396 MHz, $CDCl_3$, δ): 0.08 (s, 6H), 0.90 (s, 9H), 3.30 (s, 6H), 4.31 (dd, *J* = 1.8, 5.9 Hz, 2H), 5.07 (dd, *J* = 0.9, 5.9 Hz, 1H), 5.45 (ddt, *J* =1.8, 5.9, 11.8 Hz, 1H), 5.77 (ddt, *J* = 1.3, 5.8, 11.6 Hz, 1H). ^{13}C NMR (100 MHz, $CDCl_3$, δ): –5.3 (CH_3), 18.2 (*C*), 25.8 (CH_3), 52.0 (CH_3), 59.8 (CH_2), 99.3 (*C*H), 126.3 (*C*H), 135.1 (*C*H). HRMS-EI (*m*/*z*): $[M–CH_3O, –H]^{2+}$ calcd for $C_{11}H_{22}O_2Si$, 214.13891; found, 214.13839.

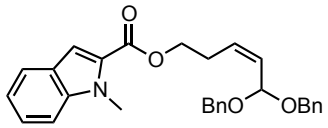
(*Z*)-5,5-Dibenzyloxypent-3-en-1-yl 4-cyanobenzoate [(*Z*)-1k].



(*Z*)-**1k**

^{1}H NMR (401 MHz, $CDCl_3$, δ): 2.62 (q, *J* = 6.5 Hz, 2H), 4.37 (t, *J* = 6.4 Hz, 2H), 4.58 (d, *J* = 11.6 Hz, 2H), 4.67 (d, *J* = 11.2 Hz, 2H), 5.48 (d, *J* = 6.0 Hz, 1H), 5.70–5.86 (m, 2H), 7.26–7.38 (m, 10H), 7.62 (d, *J* = 7.6 Hz, 2H), 8.08 (d, *J* = 7.6 Hz, 2H). ^{13}C NMR (99 MHz, $CDCl_3$, δ): 27.4 (CH_2), 64.3 (CH_2), 66.6 (CH_2), 96.7 (*C*H), 116.1 (*C*), 117.7 (*C*), 127.5 (*C*H), 127.6 (*C*H), 128.2 (*C*H), 129.7 (*C*H), 129.8 (*C*H), 129.9 (*C*H), 132.0 (*C*H), 133.6 (C), 137.7 (*C*), 164.6 (*C*). HRMS–ESI (*m*/*z*): $[M+Na]^+$ calcd for $C_{27}H_{25}O_4NNa$, 450.16758; found, 450.16679. Anal. Calcd for $C_{27}H_{25}NO_4$: C, 75.86; H, 5.89; N, 3.28. Found: C, 75.51; H, 5.96; N, 3.04.

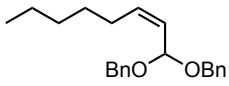
(*Z*)-5,5-Dibenzyloxypent-3-en-1-yl 1-methyl-1*H*-indole-2-carboxylate [(*Z*)-1l].



(*Z*)-**1l**

^{1}H NMR (396 MHz, $CDCl_3$, δ): 2.62 (q, *J* = 5.9 Hz, 2H), 4.05 (s, 3H), 4.34 (t, *J* = 6.5 Hz, 2H), 4.59 (d, *J* = 11.9 Hz, 2H), 4.68 (d, *J* = 11.5 Hz, 2H), 5.50 (d, *J* = 3.6 Hz, 1H), 5.75–5.85 (m, 2H), 7.11–7.18 (m, 1H), 7.22–7.41 (m, 13H), 7.62 (d, *J* = 7.9 Hz, 1H). ^{13}C NMR (99 MHz, $CDCl_3$, δ): 27.7 (CH_2), 31.5 (CH_3), 63.3 (CH_2), 66.8 (CH_2), 96.9 (*C*H), 110.1 (*C*H), 110.2 (*C*H), 120.4 (*C*H), 122.5 (*C*H), 125.0 (*C*H), 125.7 (*C*), 127.5 (*C*H), 127.8 (*C*H), 128.3 (*C*H), 129.5 (*C*H), 130.5 (*C*H), 137.9 (*C*), 139.6 (*C*), 162.0 (*C*). HRMS–ESI (*m*/*z*): $[M+Na]^+$ calcd for $C_{29}H_{29}O_4NNa$, 478.19888; found, 478.19815. Anal. Calcd for $C_{29}H_{29}NO_4$: C, 76.46; H, 6.42; N, 3.07. Found: C, 76.29; H, 6.53; N, 2.83.

(*Z*)-1,1-Dibenzyloxyoct-2-ene. [(*Z*)-1p].



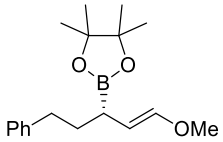
(*Z*)-**1p**

^{1}H NMR (401 MHz, $CDCl_3$, δ): 0.87 (t, *J* = 6.6 Hz, 3H), 1.19–1.40 (m, 6H), 2.08 (q, *J* = 7.3 Hz, 2H), 4.58 (d, *J* = 11.6 Hz, 2H), 4.66 (d, *J* = 11.2 Hz, 2H), 5.43 (d, *J* = 6.4 Hz, 1H), 5.61 (dd, *J* = 6.4, 10.8 Hz, 1H), 5.70 (dt, *J* = 7.2, 11.2 Hz, 1H), 7.25–7.36 (m, 10H). ^{13}C NMR (101 MHz, $CDCl_3$, δ): 14.0 (CH_3), 22.5 (CH_2), 28.1 (CH_2), 29.0 (CH_2), 31.4 (CH_2), 66.9 (CH_2), 97.0 (*C*H), 126.5 (*C*H),

127.6 (*C*H), 127.9 (*C*H), 128.4 (*C*H), 135.9 (*C*H), 138.2 (*C*). HRMS–ESI (*m*/*z*): $[M+Na]^+$ calcd for $C_{22}H_{28}O_2Na$, 347.19815; found, 347.19812. Anal. Calcd for $C_{22}H_{28}O_2$: C, 81.44; H, 8.70. Found: C, 81.31; H, 8.79.

Characterization of Boryl Substitution Products

4,4,5,5-Tetramethyl-2-[(3*S*)-(*E*)-5-phenyl-1-methoxy-1-penten-3-yl]-1,3,2-dioxaborolane [(*S*,*E*-2a)].

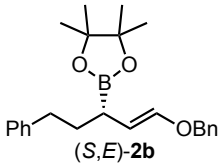


(*S*,*E*)-**2a**

The reaction was performed according to the representative procedure with (*Z*)-**1a** (102.0 mg, 0.49 mmol). The title compound was purified by silica-gel chromatography (EtOAc:hexane = 1/99 to 3/97). 83% isolated yield (123.6 mg, 0.409 mmol), 97% ee.

^{1}H NMR (392 MHz, $CDCl_3$, δ): 1.24 (s, 12H), 1.59–1.72 (m, 2H), 1.78–1.88 (m, 1H), 2.49–2.59 (m, 1H), 2.61–2.71 (m, 1H), 3.52 (s, 3H), 4.72 (dd, *J* = 9.3, 12.9 Hz, 1H), 6.29 (d, *J* = 12.5 Hz, 1H), 7.12–7.28 (m, 5H). ^{13}C NMR (99 MHz, $CDCl_3$, δ): 22.8 (br, B–*C*H), 24.6 (CH_3), 24.7 (CH_3), 33.8 (CH_2), 35.0 (CH_2), 55.9 (CH_3), 83.1 (*C*), 103.3 (*C*H), 125.5 (*C*H), 128.1 (*C*H), 128.4 (*C*H), 142.6 (*C*), 146.9 (*C*H). $[\alpha]_D^{21.4}$ = +6.6 (*c* 1.0, $CHCl_3$). HRMS-EI (*m/z*): [M] calcd for $C_{18}H_{27}BO_3$, 302.20533; found, 229.11989. HRMS-EI (m/z): $[M+H]^+$ calcd for $C_{18}H_{28}BO_3$, 302.21623; found, 302.21661. Anal. Calcd for $C_{18}H_{27}BO_3$: C, 71.54; H, 9.00. Found: C, 71.30; H, 9.12. The ee value of this compound was determined by HPLC analysis after reduction of the C=C bond and following $NaBO_3 \cdot 4H_2O$ oxidation of the boryl group in the product [CHIRALPAK® OD-3, 2-PrOH:hexane = 5/95, 0.5 mL/min, 40 °C, retention time: 20.97 min (major enantiomer) and 27.17 min (minor enantiomer)]. The absolute configuration was determined by the advanced Mosher NMR spectroscopic method.

(*S*,*E*)-2-[1-(Benzyloxy)-5-phenylpent-1-en-3-yl]-4,4,5,5-tetramethyl-1,3,2-dioxaborolane [(*S*,*E*-2b)].

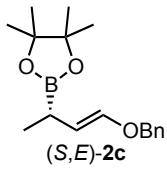


(*S*,*E*)-**2b**

The reaction was performed according to the representative procedure with (*Z*)-**1b** (180.0 mg, 0.50 mmol). The title compound was purified by silica-gel chromatography (EtOAc:hexane). 94% isolated yield (178.3 mg, 0.471 mmol), 98% ee.

^{1}H NMR (392 MHz, $CDCl_3$, δ): 1.23 (s, 12H), 1.59–1.90 (m, 3H), 2.47–2.69 (m, 2H), 4.73 (s, 2H), 4.86 (dd, *J* =9.3, 12.6 Hz, 1H), 6.33 (d, *J* = 12.5 Hz, 1H), 7.12–7.38 (m, 10H). ^{13}C NMR (99 MHz, $CDCl_3$, δ): 22.9 (br, B-*C*H), 24.6 (*C*H_3), 24.7 (*C*H_3), 33.6 (*C*H_2), 35.0 (*C*H_2), 70.9 (*C*H_2), 83.1 (*C*), 105.4 (*C*H), 125.5 (*C*H), 127.5 (*C*H), 127.7 (*C*H), 128.1 (*C*H), 128.3 (*C*H), 128.4 (*C*H), 137.3 (*C*), 142.6 (*C*), 145.7 (*C*H). $[\alpha]_D^{21.4}$ = +13.4 (*c* 1.0, $CHCl_3$, 98% ee). HRMS-EI (*m*/*z*): $[M]^+$ calcd for $C_{24}H_{31}BO_3$, 377.24026; found, 377.24164. Anal. Calcd for $C_{24}H_{31}BO_3$: C, 76.20; H, 8.26. Found: C, 76.19; H, 8.44. The ee value of this compound was determined by HPLC analysis after reduction of the C=C bond and following $NaBO_3{\cdot}4H_2O$ oxidation of the boryl group in the product [CHIRALPAK® OD-3, 2-PrOH:hexane = 10:90, 0.5 mL/min, 40 °C, retention time: 48.72 min (major enantiomer) and 78.11 min (minor enantiomer)].

(*S*,*E*)-2-[4-(Benzyloxy)but-3-en-2-yl]-4,4,5,5-tetramethyl-1,3,2-dioxaborolane [(*S*,*E*)-2c].



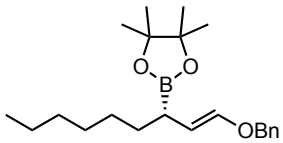
(*S*,*E*)-**2c**

The reaction was performed according to the representative procedure with (*Z*)-**1c** (134.8 mg, 0.5 mmol). The title compound was purified by silica-gel chromatography (EtOAc:hexane). 88% isolated yield (127.1 mg, 0.441 mmol), 96% ee.

^{1}H NMR (401 MHz, $CDCl_3$, δ): 1.07 (d, *J* = 7.2 Hz, 3H), 1.23 (s, 12H), 1.75 (quint, *J* = 7.6 Hz, 1H), 4.71 (s, 2H), 4.96 (dd, *J* = 8.0, 12.8 Hz, 1H), 6.33 (d, *J* = 12.4 Hz, 1H), 7.25–7.37 (m, 5H). ^{13}C NMR (101 MHz, $CDCl_3$, δ): 16.4 (br, B–*C*H), 16.4 (*C*H_3), 24.48 (*C*H_3), 24.53 (*C*H_3), 70.8 (*C*H_2), 82.9 (*C*), 107.3 (*C*H), 127.4 (*C*H), 127.5 (*C*H), 128.2 (*C*H), 137.3 (*C*), 144.7 (*C*H). HRMS-EI (*m*/*z*): [M] calcd for $C_{17}H_{25}BO_3$, 288.18999; found, 288.18951. $[\alpha]_D^{25.8}$ = +6.9 (*c* 1.2 in $CHCl_3$, 96% ee).

The ee value was determined by HPLC analysis of the corresponding alcohol after reduction of the C=C bond and following $NaBO_3 \cdot 4H_2O$ oxidation of the boryl group in the product [Daicel CHIRALPAK® OD-3, 2-PrOH/hexane = 5/95, 0.5 mL/min, 40 °C, retention time: 22.01 min (major enantiomer) and 25.17 min (minor enantiomer)].

(*S*,*E*)-2-[1-(Benzyloxy)non-1-en-3-yl]-4,4,5,5-tetramethyl-1,3,2-dioxaborolane [(*S*,*E*)-2d].

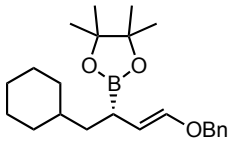


(*S*,*E*)-**2d**

The reaction was performed according to the representative procedure with (*Z*)-**1d** (171.5 mg, 0.507 mmol). The title compound was purified by silica-gel chromatography (EtOAc:hexane = 0.5/99.5 to 3/97). 85% isolated yield (154.1 mg, 0.430 mmol), 97% ee.

^{1}H NMR (401 MHz, $CDCl_3$, δ): 0.87 (t, J = 6.5 Hz, 3H), 1.22 (s, 12H), 1.18–1.40 (m, 9H), 1.42–1.53 (m, 1H), 1.62 (q, J = 8.2 Hz, 1H), 4.71 (s, 2H), 4.84 (dd, J = 9.4, 12.6 Hz, 1H), 6.31 (d, J = 12.8 Hz, 1H), 7.25–7.35 (m, 5H). ^{13}C NMR (100 MHz, $CDCl_3$, δ): 14.1 (CH_3), 22.6 (CH_2), 23.2 (br, B–*C*H), 24.6 (CH_3), 24.7 (CH_3), 28.8 (CH_2), 29.3 (CH_2), 31.8 (CH_2), 31.9 (CH_2), 71.0 (CH_2), 83.0 (*C*), 106.0 (*C*H), 127.5 (*C*H), 127.7 (*C*H), 128.4 (*C*H), 137.5 (*C*), 145.3 (*C*H). HRMS–ESI (*m*/*z*): $[M+Na]^+$ calcd for $C_{22}H_{35}O_3BNa$, 380.26078; found, 380.26070. $[\alpha]_D^{26.1}$ = +14.7 (*c* 1.4 in $CHCl_3$, 97% ee). Anal. Calcd for $C_{22}H_{35}BO_3$: C, 73.74; H, 9.85. Found: C, 73.62; H, 9.94. The ee value was determined by HPLC analysis of the corresponding alcohol after reduction of the C=C bond and following $NaBO_3 \cdot 4H_2O$ oxidation of the boryl group in the product [Daicel CHIRALPAK® OD-3, 2-PrOH/hexane = 3/97, 0.5 mL/min, 40 °C, retention time: 16.11 min (major enantiomer) and 18.95 min (minor enantiomer)].

(*S*,*E*)-2-(4-(Benzyloxy)-1-cyclohexylbut-3-en-2-yl)-4,4,5,5-tetramethyl-1,3,2-dioxaborolane [(*S*,*E*)-2e].



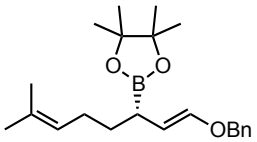
(*S*,*E*)-**2e**

The reaction was performed according to the representative procedure with (*Z*)-**1e** (172.8 mg, 0.49 mmol). The title compound was purified by silica-gel chromatography (EtOAc:hexane = 0.75/99.25

to 3/97). 79% isolated yield (144.0 mg, 0.389 mmol), 96% ee.

^{1}H NMR (401 MHz, $CDCl_3$, δ): 0.70–0.94 (m, 2H), 1.02–1.40 (m, 7H), 1.22 (s, 12 H), 1.58–1.80 (m, 5H), 4.71 (s, 2H), 4.80 (dd, *J* = 9.8, 12.6 Hz, 1H), 6.29 (d, *J* = 12.4 Hz, 1H), 7.25–7.36 (m, 5H). ^{13}C NMR (100 MHz, $CDCl_3$, δ): 20.2 (br, B–*C*H), 24.5 (*C*H_3), 26.2 (*C*H_2), 26.3 (*C*H_2), 26.6 (*C*H_2), 32.7 (*C*H_2), 33.6 (*C*H_2), 36.1 (*C*H), 39.1 (*C*H_2), 70.9 (*C*H_2), 82.9 (*C*), 106.1 (*C*H), 127.4 (*C*H), 127.6 (*C*H), 128.3 (*C*H), 137.4 (*C*), 145.1 (*C*H). HRMS–ESI (*m*/*z*): $[M+Na]^+$ calcd for $C_{23}H_{35}O_3BNa$, 392.26078; found, 392.26125. $[\alpha]_D^{25.9}$ = +27.9 (*c* 1.0 in $CHCl_3$, 96% ee). Anal. Calcd for $C_{23}H_{35}BO_3$: C, 74.59; H, 9.53. Found: C, 74.34; H, 9.48. The ee value was determined by HPLC analysis of the corresponding alcohol after reduction of the C=C bond and following $NaBO_3 \cdot 4H_2O$ oxidation of the boryl group in the product [Daicel CHIRALPAK® OD-3, 2-PrOH/hexane = 1/99, 0.5 mL/min, 40 °C, retention time: 34.27 min (major enantiomer) and 38.32 min (minor enantiomer)].

(*S*,*E*)-2-[1-(Benzyloxy)-7-methylocta-1,6-dien-3-yl]-4,4,5,5-tetramethyl-1,3,2-dioxaborolane [(*S*,*E*)-2f].

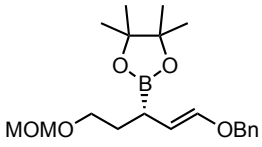


(*S*,*E*)-**2f**

The reaction was performed according to the representative procedure with (*Z*)-**1f** (168.6 mg, 0.50 mmol). The title compound was purified by silica-gel chromatography (EtOAc:hexane = 0/100 to 6/94). 91% isolated yield (162.6 mg, 0.456 mmol), 95% ee.

^{1}H NMR (392 MHz, $CDCl_3$, δ): 1.21 (s, 12H), 1.31–1.42 (m, 1H), 1.49–1.70 (m, 2H), 1.57 (s, 3H), 1.66 (s, 3H), 1.97 (nonet, *J* = 7.4 Hz, 2H), 4.69 (s, 2H), 4.84 (dd, *J* = 9.6, 12.7 Hz, 1H), 5.05–5.13 (m, 1H), 6.31 (d, *J* = 12.5 Hz, 1H), 7.21–7.35 (m, 5H). ^{13}C NMR (99 MHz, $CDCl_3$, δ): 17.6 (*C*H_3), 22.8 (br, B–*C*H), 24.5 (*C*H_3), 24.6 (*C*H_3), 25.6 (*C*H_3), 27.2 (*C*H_2), 31.8 (*C*H_2), 70.8 (*C*H_2), 82.9 (*C*), 105.5 (*C*H), 124.5 (*C*H), 127.3 (*C*H), 127.5 (*C*H), 128.2 (*C*H), 131.2 (*C*), 137.3 (*C*), 145.4 (*C*H). HRMS–ESI (*m*/*z*): $[M+H]^+$ calcd for $C_{22}H_{34}O_3B$, 356.26318; found, 356.26357. $[\alpha]_D^{25.9}$ = +11.8 (*c* 1.1 in $CHCl_3$, 95% ee). The ee value was determined by HPLC analysis of the corresponding alcohol after reduction of the C=C bonds and following $NaBO_3 \cdot 4H_2O$ oxidation of the boryl group in the product [Daicel CHIRALPAK® OD-3, 2-PrOH/hexane = 3/97, 0.5 mL/min, 40 °C, retention time: 16.01 min (major enantiomer) and 18.37 min (minor enantiomer)]. This product contains small amount of impurities.

(*S*,*E*)-2-[1-(Benzyloxy)-5-(methoxymethoxy)pent-1-en-3-yl]-4,4,5,5-tetramethyl-1,3,2-dioxaborolane [(*S*,*E*)-2g].

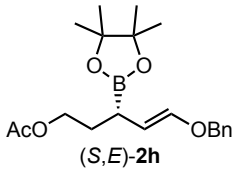


(*S*,*E*)-**2g**

The reaction was performed according to the representative procedure with (*Z*)-**1g** (172.4 mg, 0.504 mmol). The title compound was purified by silica-gel chromatography (EtOAc:hexane = 5/95 to 10/90). 81% isolated yield (148.3 mg, 0.409 mmol), 97% ee.

^{1}H NMR (392 MHz, $CDCl_3$, δ): 1.22 (s, 12H), 1.56–1.68 (m, 1H), 1.72–1.92 (m, 2H), 3.34 (s, 3H), 3.45–3.57 (m, 2H), 4.55–4.62 (m, 2H), 4.71 (s, 2H), 4.84 (dd, *J* = 9.4, 12.5 Hz, 1H), 6.34 (d, *J* = 12.5 Hz, 1H), 7.24–7.37 (m, 5H). ^{13}C NMR (99 MHz, $CDCl_3$, δ): 20.1 (br, B–*C*H), 24.5 (*C*H_3), 24.6 (*C*H_3), 31.7 (*C*H_2), 55.0 (*C*H_3), 66.6 (*C*H_2), 70.9 (*C*H_2), 83.0 (*C*), 96.2 (*C*H_2), 105.0 (*C*H), 127.4 (*C*H), 127.6 (*C*H), 128.3 (*C*H), 137.2 (*C*), 145.7 (*C*H). HRMS–ESI (*m*/*z*): $[M+Na]^+$ calcd for $C_{20}H_{31}O_5BNa$, 384.21931; found, 384.22007. $[\alpha]_D^{25.8}$ = +13.0 (*c* 1.1 in $CHCl_3$, 97% ee). Anal. Calcd for $C_{20}H_{31}BO_5$: C, 66.31; H, 8.63. Found: C, 66.20; H, 8.80. The ee value was determined by HPLC analysis of the corresponding alcohol after reduction of the C=C bond and following $NaBO_3 \cdot 4H_2O$ oxidation of the boryl group in the product [Daicel CHIRALPAK® OD-3, 2-PrOH/hexane = 10/90, 0.5 mL/min, 40 °C, retention time: 13.95 min (major enantiomer) and 15.23 min (minor enantiomer)].

(*S*,*E*)-5-(Benzyloxy)-3-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)pent-4-en-1-yl acetate [(*S*,*E*)-2h].



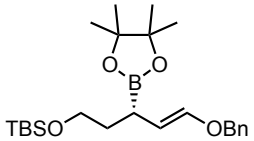
(*S*,*E*)-**2h**

The reaction was performed according to the representative procedure with (*Z*)-**1h** (167.0 mg, 0.491 mmol). The title compound was purified by silica-gel chromatography (EtOAc:hexane = 5/95 to 10/90). 83% isolated yield (147.6 mg, 0.410 mmol), 97% ee.

^{1}H NMR (396 MHz, $CDCl_3$, δ): 1.23 (s, 12H), 1.59–1.90 (m, 3H), 2.03 (s, 3H), 4.00–4.13 (m, 2H), 4.71 (s, 2H), 4.80 (dd, *J* = 9.5, 12.7 Hz, 1H), 6.33 (d, *J* = 12.3 Hz, 1H), 7.25–7.38 (m, 5H). ^{13}C NMR

(100 MHz, $CDCl_3$, δ): 19.3 (br, B–*C*H), 20.8 (*C*H_3), 24.4 (*C*H_3), 24.5 (*C*H_3), 30.1 (*C*H_2), 63.3 (*C*H_2), 70.8 (*C*H_2), 83.1 (*C*), 104.0 (*C*H), 127.2 (*C*H), 127.5 (*C*H), 128.2 (*C*H), 137.0 (*C*), 146.0 (*C*H), 170.8 (*C*). HRMS–ESI (*m*/*z*): $[M+Na]^+$ calcd for $C_{20}H_{29}O_5BNa$, 382.20366; found, 382.20438. $[\alpha]_D^{25.7}$ = +27.1 (*c* 1.4 in $CHCl_3$, 97% ee). Anal. Calcd for $C_{20}H_{29}BO_5$: C, 66.68; H, 8.11. Found: C, 66.71; H, 8.27. The ee value was determined by HPLC analysis of the corresponding alcohol after reduction of the C=C bond and following $NaBO_3 \cdot 4H_2O$ oxidation of the boryl group in the product [Daicel CHIRALPAK® OD-3, 2-PrOH/hexane = 10/90, 0.5 mL/min, 40 °C, retention time: 22.96 min (major enantiomer) and 28.08 min (minor enantiomer)].

(*S*,*E*)-5-(*tert*-Butyldimethylsiloxy)-1-benzyloxy-3-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)pent-1-ene [(*S*,*E*)-2i].

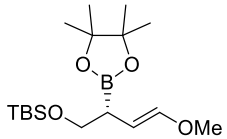


(*S*,*E*)-**2i**

The reaction was performed according to the representative procedure with (*Z*)-**1i** (206 mg, 0.499 mmol). The title compound was purified by silica-gel chromatography (EtOAc:hexane = 1/99 to 5/95). 93% isolated yield (199.4 mg, 0.462 mmol), 97% ee.

^{1}H NMR (396 MHz, $CDCl_3$, δ): 0.03 (s, 6H), 0.89 (s, 9H), 1.21 (s, 12H), 1.48–1.62 (m, 1H), 1.68–1.84 (m, 2H), 3.59 (t, *J* = 6.5 Hz, 2H), 4.70 (s, 2H), 4.81 (dd, *J* = 9.5, 12.7 Hz, 1H), 6.32 (d, *J* = 12.7 Hz, 1H), 7.23–7.35 (m, 5H). ^{13}C NMR (100 MHz, $CDCl_3$, δ): –5.31 (CH_3), –5.29 (CH_3), 18.3 (*C*), 19.0 (br, B–*C*H), 24.5 (CH_3), 24.7 (CH_3), 25.9 (CH_3), 34.4 (CH_2), 62.0 (CH_2), 70.9 (CH_2), 83.0 (*C*), 105.0 (*C*H), 127.4 (*C*H), 127.6 (*C*H), 128.3 (*C*H), 137.3 (*C*), 145.7 (*C*H). HRMS–ESI (*m*/*z*): $[M+Na]^+$ calcd for $C_{24}H_{41}BO_4NaSi$, 454.27957; found, 454.27983. $[\alpha]_D^{25.6}$ = +6.8 (*c* 1.0 in $CHCl_3$, 97% ee). The ee value was determined by HPLC analysis of the corresponding alcohol after reduction of the C=C bond and following $NaBO_3 \cdot 4H_2O$ oxidation of the boryl group in the product [Daicel CHIRALPAK® OD-3, 2-PrOH/hexane = 1/99, 0.5 mL/min, 40 °C, retention time: 20.99 min (major enantiomer) and 22.61 min (minor enantiomer)].

(*R*,*E*)-4-(*tert*-Butyldimethylsiloxy)-1-methoxy-3-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)but-1-ene [(*R*,*E*)-2j].



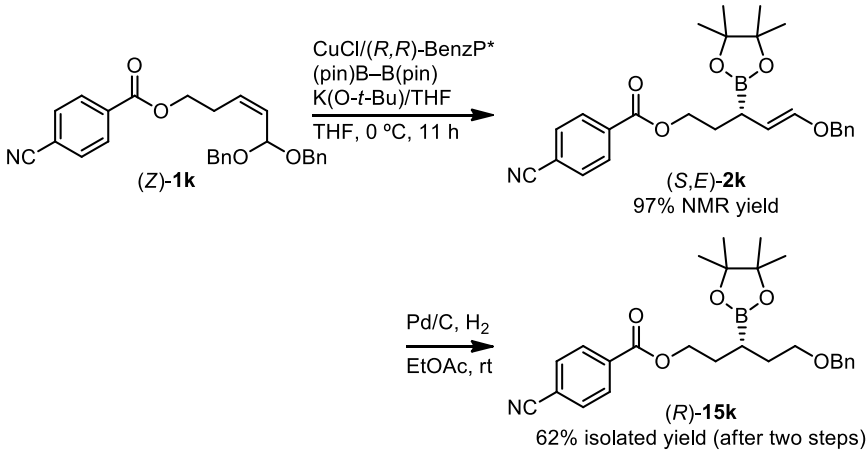
(*R*,*E*)-**2j**

The reaction was performed according to the representative procedure with (*Z*)-**1j** (121.7 mg, 0.49 mmol). The title compound was purified by silica-gel chromatography (EtOAc:hexane). 86% isolated yield (144.8 mg, 0.423 mmol), 97% ee.

^{1}H NMR (392 MHz, $CDCl_3$, δ): 0.030 (s, 3H), 0.035 (s, 3H), 0.88 (s, 9H), 1.24 (s, 12H), 1.93 (q, *J* = 8.1 Hz, 1H), 3.50 (s, 3H), 3.60 (dd, *J* = 7.2, 9.3 Hz, 2H), 3.68 (dd, *J* = 8.1, 9.2 Hz, 2H), 4.68 (dd, *J* =9.5, 12.7 Hz, 1H), 6.33 (d, *J* = 12.9 Hz, 1H). ^{13}C NMR (99 MHz, $CDCl_3$, δ): –5.4 (CH_3), 18.3 (*C*), 24.7 (CH_3), 25.9 (CH_3), 27.5 (br, B–*C*H), 55.7 (CH_3), 65.6 (CH_2), 83.1 (*C*), 99.9 (*C*H), 147.8 (*C*H).

$[\alpha]_D^{21.5}$ = –1.5 (*c* 1.0, $CHCl_3$). HRMS-EI (*m/z*): $[M–C_4H_9]+$ calcd for $C_{13}H_{26}BO_4Si$, 285.16962; found, 285.16933. To determine the ee value, the C=C bond of the product was hydrogenated with Pd/C, then the boryl group was oxidized with $NaBO_3·4H_2O$ followed by esterification with *p*-nitro benzoyl chloride. The ee value of the product was determined by HPLC analysis of the corresponding *p*-nitro benzoyl ester [CHIRALPAK® OD-3, 2-PrOH:hexane = 0.5:99.5, 0.5 mL/min, 40°C, retention time: 45.55 min (major enantiomer) and 63.73 min (minor enantiomer)].

(*S*,*E*)-5-(Benzyloxy)-3-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)pent-4-en-1-yl 4-cyanobenzoate [(*S*,*E*)-2k].

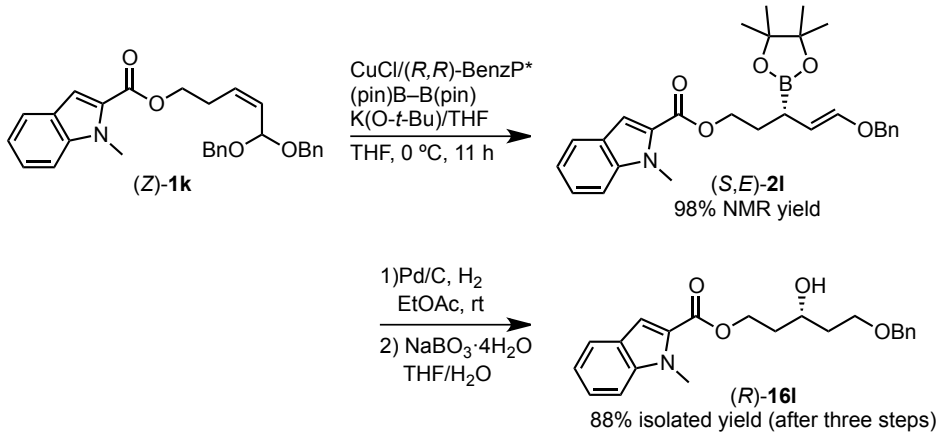


The reaction was performed according to the representative procedure with (*Z*)-**1k** (201.2 mg, 0.47 mmol) and ^{1}H NMR yield of (*S*,*E*)-**2k** was 97%. After the completion of the reaction was checked by ^{1}H NMR, the reaction mixture was directly filtered through a short silica-gel column by hexane/EtOAc (50:50) as an eluent. Because SiO_2 chromatography resulted in a low separation and product purity, the yield and ee were evaluated after derivatization. The crude product was hydrogenated with Pd/C and purified by preparative TLC to give (*R*)-**15k**. After removal of the solvents under reduced pressure, the crude product was hydrogenated with Pd/C. The (*R*)-**15k** was purified by preparative TLC (EtOAc:hexane = 40/60). 62% isolated yield (131.3 mg, 0.292 mmol), 98% ee.

(*S*,*E*)-**15k**: ^{1}H NMR (401 MHz, $CDCl_3$, δ): 1.21 (s, 12H), 1.25–1.33 (m, 1H), 1.73–1.98 (m, 4H), 3.45–3.54 (m, 2H), 4.33–4.45 (m, 2H), 4.50 (s, 2H), 7.24–7.36 (m, 5H), 7.70 (d, *J* = 8.4 Hz, 2H), 8.12 (d, *J* = 8.4 Hz, 2H). ^{13}C NMR (101 MHz, $CDCl_3$, δ): 16.8 (br, B–*C*H), 24.62 (CH_3), 24.66 (CH_3), 29.6 (CH_2), 30.8 (CH_2), 65.2 (CH_2), 69.2 (CH_2), 72.7 (CH_2), 83.1 (*C*), 116.0 (*C*), 117.9 (*C*), 127.3 (*C*H), 127.5 (*C*H), 128.2 (*C*H), 130.0 (*C*H), 132.0 (*C*H), 134.2 (*C*), 138.4 (*C*), 164.8 (*C*). HRMS–ESI (*m/z*): $[M+Na]^+$ calcd for $C_{26}H_{32}O_5NBNa$, 471.23021; found, 471.23010. $[\alpha]_D^{25.5}$ = –3.7

(c 1.1 in $CHCl_3$, 98% ee). The ee value was determined by HPLC analysis of (R)-**15k** [Daicel CHIRALPAK® OZ-3, 2-PrOH/hexane = 2/98, 0.5 mL/min, 40 °C, retention time: 34.67 min (minor enantiomer) and 36.80 min (major enantiomer)].

(*S*,*E*)-5-(Benzyloxy)-3-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)pent-4-en-1-yl 1-methyl-1*H*-indole-2-carboxylate [(*S*,*E*)-2l].

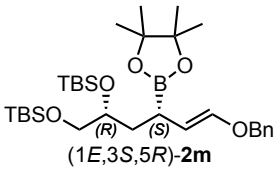


The reaction was performed according to the representative procedure with (Z)-**1l** (226.5 mg, 0.5 mmol) and ^{1}H NMR yield of (S,E)-**2l** was 98%. The reaction mixture was directly subjected to short path of silica-gel column by hexane/EtOAc (50:50) as an eluent. Because SiO_2 chromatography resulted in a low separation and product purity, the yield and ee were evaluated after derivatization. After removal of the solvents under reduced pressure, the crude product was dissolved in EtOAc (2 mL). Then Pd/C (10 wt%, 24 mg) was added to the mixture. The atmosphere in the reaction vessel was replaced by hydrogen and stirred at room temperature for 2 h under hydrogen balloon. After 2 h, the reaction mixture was directly filtered through a short silica-gel column by hexane/EtOAc (50:50) as an eluent to give the crude reduced product. It was then evaporated and dissolved in THF/H_2O (3:2) solvent. To the solution was added $NaBO_3{\cdot}4H_2O$ (153.9 mg, 4 equiv) and stirred for 12 h at rt. Then, the mixture was separated with water and EtOAc, and then extracted three times with EtOAc. The combined organic layer was dried over Na_2SO_4, filtered and evaporated. The crude derivatized compound (R)-**16l** was purified by silica-gel column chromatography (EtOAc:hexane = 10/90 to 25/75). 88% isolated yield (160.8 mg, 0.438 mmol), 96% ee.

^{1}H NMR (401 MHz, $CDCl_3$, δ): 1.73–1.96 (m, 4H), 3.31 (brs, 1H), 3.58–3.74 (m, 2H), 3.99 (s, 3H), 3.95–4.05 (m, 1H), 4.36–4.55 (m, 2H), 4.47 (s, 2H), 7.08–7.15 (m, 1H), 7.20–7.34 (m, 8H), 7.63 (d, J = 8.4 Hz, 1H). ^{13}C NMR (101 MHz, $CDCl_3$, δ): 31.4 (CH_3), 36.3 (CH_2), 36.4 (CH_2), 61.4 (CH_2),

67.7 (*C*H), 68.6 (CH_2), 73.1 (CH_2), 110.0 (*C*H), 110.1 (*C*H), 120.4 (*C*H), 122.4 (*C*H), 124.8 (*C*H), 125.6 (*C*), 127.5 (*C*H), 127.6 (*C*H,*C*), 128.3 (*C*H), 137.7 (*C*), 139.5 (*C*), 162.1 (*C*). HRMS–ESI (*m*/*z*): $[M+Na]^+$ calcd for $C_{22}H_{25}O_4NNa$, 390.16758; found, 390.16703. $[\alpha]_D^{26.0}$ = –13.0 (*c* 1.2 in $CHCl_3$, 96% ee). The ee value was determined by HPLC analysis of the corresponding alcohol after $NaBO_3 \cdot 4H_2O$ oxidation of the borylated product in comparison of the racemic sample [Daicel CHIRALPAK® OZ-3, 2-PrOH/hexane = 20/80, 0.5 mL/min, 40 °C, retention time: 16.29 min (minor enantiomer) and 18.88 min (major enantiomer)].

(1*E*,3*S*,5*R*)-1-Benzyloxy-3-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl) -5,6-bis(*tert*-butyldimethylsiloxy)hex-1-ene [(1*E*,3*S*,5*R*)-2m].

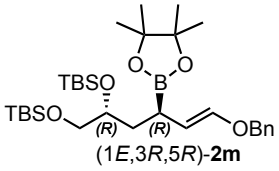


(1*E*,3*S*,5*R*)-**2m**

The reaction was performed according to the representative procedure with (*Z*)-**1m** (270.9 mg, 0.49 mmol) and (*R*,*R*)-BenzP* ligand. The title compound was purified by silica-gel chromatography (EtOAc:hexane = 0/100 to 2/98). 75% isolated yield (210.6 mg, 0.365 mmol), 98:2 dr.

^{1}H NMR (396 MHz, $CDCl_3$, δ): 0.037 (s, 3H), 0.042 (s, 3H), 0.051 (s, 3H), 0.065 (s, 3H), 0.88 (s, 9H), 0.89 (s, 9H), 1.21 (s, 12H), 1.33–1.44 (m, 1H), 1.74–1.88 (m, 2H), 3.41–3.53 (m, 2H), 3.67 (quin, *J* = 5.4 Hz, 1H), 4.70 (s, 2H), 4.86 (dd, *J* = 9.1, 12.7 Hz, 1H), 6.33 (d, *J* = 12.7 Hz, 1H), 7.25–7.36 (m, 5H). ^{13}C NMR (100 MHz, $CDCl_3$, δ): –5.33 (CH_3), –5.27 (CH_3), –4.6 (CH_3), –4.1 (CH_3), 18.2 (*C*), 18.4 (*C*), 19.5 (br, B–*C*H), 24.6 (CH_3), 24.7 (CH_3), 25.99 (CH_3), 26.02 (CH_3), 36.7 (CH_2), 67.7 (CH_2), 70.9 (CH_2), 72.9 (*C*H), 83.0 (*C*), 106.0 (*C*H), 127.5 (*C*H), 127.7 (*C*H), 128.4 (*C*H), 137.4 (*C*), 145.5 (*C*H). HRMS–ESI (*m*/*z*): $[M+Na]^+$ calcd for $C_{31}H_{57}O_5BNaSi_2$, 598.37661; found, 598.37646. $[\alpha]_D^{26.1}$ = +11.5 (*c* 1.0 in $CHCl_3$, 98:2 dr). The diastereomeric ratio was determined by HPLC analysis of the corresponding alcohol after reduction of the C=C bond and following $NaBO_3 \cdot 4H_2O$ oxidation of the boryl group in the product [Daicel CHIRALPAK® OD-3, 2-PrOH/hexane = 0.5/99.5, 0.5 mL/min, 40 °C, retention time: 15.51 min (major diastereomer) and 20.40 min (minor diastereomer)].

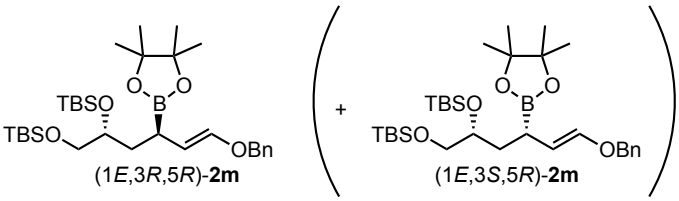
(1*E*,3*R*,5*R*)-1-Benzyloxy-3-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl) -5,6-bis(*tert*-butyldimethylsiloxy)hex-1-ene [(1*E*,3*R*,5*R*)-2m].



The reaction was performed according to the representative procedure with (*Z*)-**1m** (270.2 mg, 0.49 mmol) and (*S*,*S*)-BenzP* ligand. The title compound was purified by silica-gel chromatography (EtOAc:hexane = 0/100 to 2/98). 75% isolated yield (210.5 mg, 0.365 mmol), 0.5:99.5 dr.

^{1}H NMR (401 MHz, $CDCl_3$, δ): 0.034 (s, 3H), 0.040 (s, 3H), 0.046 (s, 6H), 0.88 (s, 9H), 0.89 (s, 9H), 1.21 (s, 12H), 1.50–1.63 (m, 2H), 1.83 (q, *J* = 8.4 Hz, 1H), 3.40–3.54 (m, 2H), 3.64–3.72 (m, 1H), 4.70 (s, 2H), 4.78 (dd, *J* = 9.4, 12.6 Hz, 1H), 6.32 (d, *J* = 12.8 Hz, 1H), 7.25–7.36 (m, 5H). ^{13}C NMR (100 MHz, $CDCl_3$, δ): –5.3 (CH_3), –4.5 (CH_3), –4.1 (CH_3), 18.2 (*C*), 18.4 (*C*), 24.6 (CH_3), 24.7 (CH_3), 26.0 (CH_3), 36.2 (CH_2), 67.9 (CH_2), 71.0 (CH_2), 71.8 (*C*H), 83.0 (*C*), 105.6 (*C*H), 127.5 (*C*H), 127.7 (*C*H), 128.4 (*C*H), 137.4 (*C*), 145.6 (*C*H). The carbon directly attached to the boron atom was not detected, likely due to quadrupolar relaxation.[31,32] HRMS–ESI (*m*/*z*): $[M+Na]^+$ calcd for $C_{31}H_{57}O_5BNaSi_2$, 598.37661; found, 598.37612. $[\alpha]_D^{26.0}$ = –14.8 (*c* 1.3 in $CHCl_3$, 0.5:99.5 dr). The diastereomeric ratio was determined by HPLC analysis of the corresponding alcohol after reduction of the C=C bond and following $NaBO_3 \cdot 4H_2O$ oxidation of the boryl group in the product [Daicel CHIRALPAK® OD-3, 2-PrOH/hexane = 0.5/99.5, 0.5 mL/min, 40 °C, retention time: 16.12 min (minor diastereomer) and 21.60 min (major diastereomer)].

(1*E*,3*R*,5*R*)-1-Benzyloxy-3-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl) -5,6-bis(*tert*-butyldimethylsiloxy)hex-1-ene [(1*E*,3*R*,5*R*)-2m].

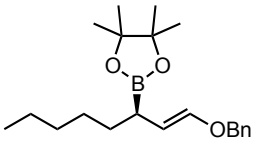


The reaction was performed according to the representative procedure with (*Z*)-**1m** (266.7 mg, 0.48 mmol) and Xantphos ligand. The title compound was purified by silica-gel chromatography (EtOAc:hexane = 0/100 to 2/98). 80% isolated yield (221.5 mg, 0.384 mmol), 16:84 dr.

^{1}H NMR (401 MHz, $CDCl_3$, * indicates signals of the minor diastereomer, δ): 0.02–0.90 (m, 12H), 0.88 (d, *J* = 1.2 Hz, 9H), 0.89 (d, *J* = 0.80 Hz, 9H), 1.22 (s, 12H), 1.51–1.64 (m, 2H), 1.75–1.89 (m,

1H), 3.40–3.55 (m, 2H), 3.68 (quin, J = 5.6 Hz, 1H), 4.70 (s, 2H), 4.78 (dd, J = 9.6, 12.8 Hz, 0.84H), 4.86* (dd, J = 9.2, 13.0 Hz, 0.16H), 6.32 (d, J = 12.4 Hz, 1H), 7.25–7.38 (m, 5H). ^{13}C NMR (101 MHz, $CDCl_3$, δ): –5.3 (CH_3), –4.6* (CH_3), –4.5 (CH_3), –4.1 (CH_3), 18.1 (*C*), 18.4 (*C*), 24.56 (CH_3), 24.64 (CH_3), 24.7* (CH_3), 26.0 (CH_3), 36.2 (CH_2), 36.7* (CH_2), 67.7* (CH_2), 67.9 (CH_2), 70.87* (CH_2), 70.92 (CH_2), 71.8 (CH_2), 72.8* (CH_2), 83.0 (*C*), 105.5 (*C*H), 105.9* (*C*H), 127.4 (*C*H), 127.6 (*C*H), 128.3 (*C*H), 137.4 (*C*), 145.5* (*C*H), 145.6 (*C*H). The carbon directly attached to the boron atom was not detected, likely due to quadropolar relaxation.[31,32] HRMS–ESI (*m*/*z*): $[M+Na]^+$ calcd for $C_{31}H_{57}O_5BNaSi_2$, 598.37661; found, 598.37735. $[\alpha]_D^{25.8}$ = –16.4 (*c* 1.1 in $CHCl_3$, 16:84 dr). The diastereomeric ratio was determined by ^{1}H NMR of the product (84:16 dr).

(*R*,*E*)-2-[1-(Benzyloxy)oct-1-en-3-yl]-4,4,5,5-tetramethyl-1,3,2-dioxaborolane [(*R*,*E*)-2p].



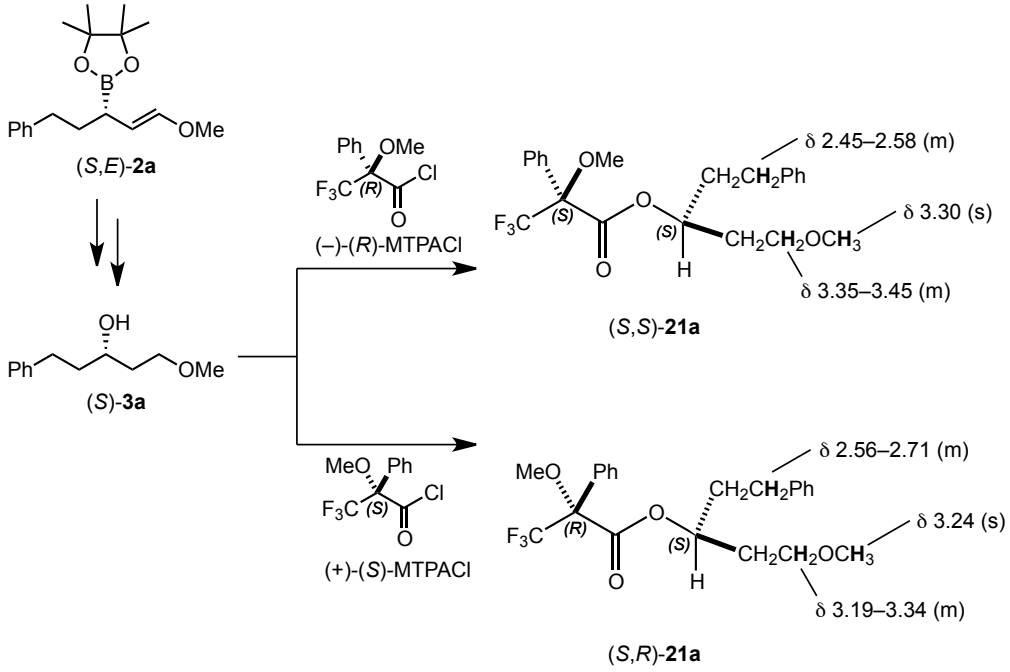
(*R*,*E*)-**2p**

The reaction was performed according to the representative procedure with (*Z*)-**1p** (603.0 mg, 1.86 mmol) and (*S*,*S*)-BenzP* ligand. The title compound was purified by silica-gel chromatography (EtOAc:hexane = 0/100 to 3/97)., 82% isolated yield (522.8 mg, 1.52 mmol), 97% ee.

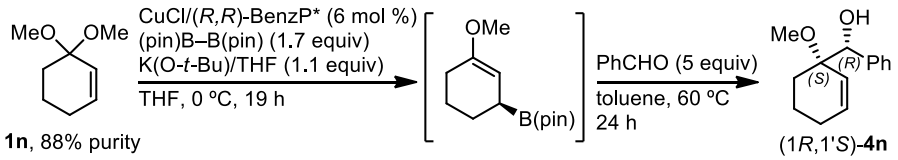
^{1}H NMR (392 MHz, $CDCl_3$, δ): 0.87 (t, J = 7.1 Hz, 3H), 1.23 (s, 12H), 1.16–1.40 (m, 7H), 1.43–1.54 (m, 1H), 1.62 (q, J = 8.0 Hz, 1H), 4.71 (s, 2H), 4.84 (dd, J = 9.8, 12.5 Hz, 1H), 6.31 (d, J = 12.5 Hz, 1H), 7.25–7.36 (m, 5H). ^{13}C NMR (100 MHz, $CDCl_3$, δ): 14.0 (CH_3), 22.5 (CH_2), 23.2 (br, B–*C*H), 24.5 (CH_3), 24.6 (CH_3), 28.4 (CH_2), 31.7 (CH_2), 31.8 (CH_2), 70.9 (CH_2), 82.9 (*C*), 106.0 (*C*H), 127.4 (*C*H), 127.6 (*C*H), 128.3 (*C*H), 137.4 (*C*), 145.3 (*C*H). HRMS–ESI (*m*/*z*): $[M+Na]^+$ calcd for $C_{21}H_{33}O_3BNa$, 366.24513; found, 366.24554. $[\alpha]_D^{25.6}$ = –13.8 (*c* 1.3 in $CHCl_3$, 97% ee). The ee value was determined by HPLC analysis of the corresponding alcohol after reduction of the C=C bond and following $NaBO_3 \cdot 4H_2O$ oxidation of the boryl group in the product [Daicel CHIRALPAK® OD-3, 2-PrOH/hexane = 1/99, 0.5 mL/min, 40 °C, retention time: 35.25 min (minor enantiomer) and 41.65 min (major enantiomer)].

Determination of the absolute configurations of linear γ-alkoxyallylboronates.

The absolute configurations of allylboronate (*S*,*E*)-**2a** was determined by a standard Mosher's procedure. Allylboronate (*S*,*E*)-**2a** was derivatized to the corresponding alcohol (*S*)-**3a** via H_2/Pd-C reduction and subsequent $NaBO_3$ oxidation. The absolute configuration of (*S*)-**3a** was determined by the comparison of the ^{1}H NMR spectra of (+)- and (–)-MTPA esters of (*S*)-**3a** as shown in the following figure. The absolute configurations of other allylboronates were deduced by this result.



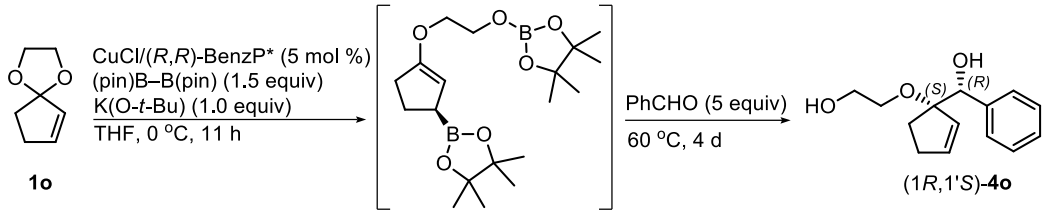
(1*R*,1'*S*)-1-(1-Methoxycyclohex-2-enyl)(phenyl)methanol [(1*R*,1'*S*)-4n].



The copper(I)-catalyzed enantioselective boryl substitution was performed according to the representative procedure with **1n** (69.3 mg, 0.43 mmol). After the reaction completion was checked by ^{1}H NMR, the reaction mixture was directly filtered through a short Florisil® column by hexane/EtOAc (50:50) as an eluent to give crude γ-alkoxyallylboronate as a colorless oil. Then, the crude product was dissolved in dry toluene (0.5 mL) under a nitrogen atomosphere, and benzaldehyde (0.25 mL, 2.5 mmol) was added to the mixture. The resultant solution was stirred for 24 h at 60 ºC. The reaction mixture was quenched by a CH_2Cl_2 solution of triethanolamine (10% v/v, 2.5 mL). The mixture was separated with water and EtOAc, and then extracted three times with EtOAc. The combined organic layer was washed with brine, dried over Na_2SO_4, filtered and evaporated. The crude product was purified by column chromatography (EtOAc:hexane = 5/95 to 15/85). 60% isolated yield (56.5 mg, 0.25 mmol, 91% ee, single isomer).

^{1}H NMR (396 MHz, $CDCl_3$, δ): 1.34–1.45 (m, 1H), 1.54–1.67 (m, 1H), 1.77 (t, *J* = 6.3 Hz, 2H), 1.74–1.86 (m, 1H), 1.90–2.02 (m, 1H), 3.09 (t, *J* = 3.8 Hz, 1H), 3.26 (s, 3H), 4.60 (d, *J* = 4.8 Hz, 1H), 5.44 (dt, *J* = 2.4, 10.7 Hz, 1H), 6.04 (dt, *J* = 3.8, 10.3 Hz, 1H), 7.21–7.38 (m, 5H). ^{13}C NMR (100 MHz, $CDCl_3$, δ): 19.5 (CH_2), 24.9 (CH_2), 27.4 (CH_2), 50.6 (CH_3), 78.0 (*C*), 78.6 (*C*H), 127.0 (*C*H), 127.4 (*C*H), 127.5 (*C*H), 128.2 (*C*H), 134.6 (*C*H), 140.1 (*C*). HRMS–ESI (*m*/*z*): $[M+Na]^+$ calcd for $C_{14}H_{18}O_2Na$, 241.11990; found, 241.11983. $[\alpha]_D^{25.8}$ = +48.0 (*c* 1.0 in $CHCl_3$, 91% ee). The ee value was determined by HPLC analysis [Daicel CHIRALPAK® OD-3, 2-PrOH/hexane = 1/99, 0.5 mL/min, 40 °C, retention time: 35.49 min (major enantiomer) and 42.43 min (minor enantiomer)].

(1*R*,1'*S*)-1-[1-(2-Hydroxyethoxy)cyclopent-2-enyl)(phenyl)methanol [(1*R*,1'*S*)-4o].



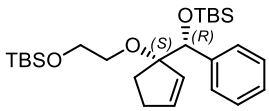
The copper(I)-catalyzed enantioselective boryl substitution was performed according to the representative procedure with **1o** (252.3 mg, 2.0 mmol). After the reaction mixture was stirred for 11

h at 0 ^{o}C, a small amount of the crude sample (ca. 20 mL) was quenched with triethanolamine (10% v/v) and used for checking the completion of the reaction by ^{1}H NMR. In the case of substrate **1o**, short silica-gel column chromatography of the reaction mixture leads to decrease the diastereoselectivity in the next aldehyde allylation step. Therefore, benzaldehyde (252.3 mg, 10 mmol) was added to the reaction mixture directly. Then, the resultant solution was warmed to 60 ^{o}C. After stirring for 4 days, the mixture was directly subjected to silica-gel column chromatography with hexane/EtOAc as an eluent to remove the excess amount of benzaldehyde. The resulting crude mixture was treated with a CH_2Cl_2 solution of triethanolamine (10% v/v, 4.0 mL). Distilled water was added to the solution, then extracted with $CHCl_3$ three times. The combined organic layer was dried over $MgSO_4$ and evaporated under reduced pressure. The crude product was purified with flash chromatography (SiO_2, $CHCl_3$/EtOAc = 100:0 to 1:2), then the resulting crude product was further purified by reprecipitation from hexane/Et_2O solution to give diol (1*R*,1'*S*)-**4o** in 60% isolated yield (281.0 mg, 1.20 mmol, 97% ee, single diastereomer). The crystal of (1*R*,1'*S*)-**4o** for X-ray crystallographic analysis was prepared by recrystallization from MeOH/pentane/Et_2O solution of (1*R*,1'*S*)-**4o**.

^{1}H NMR (396 MHz, $CDCl_3$, δ): 1.82–1.94 (m, 2H), 2.05–2.14 (m, 1H), 2.21–2.32 (m, 1H), 2.44 (brs, 1H), 3.36 (brs, 1H), 3.40–3.45 (m, 2H), 3.66–3.76 (m, 2H), 4.73 (s, 1H), 5.59 (dt, *J* = 2.3, 6.0 Hz, 1H), 6.00 (dt, *J* = 2.4, 5.8 Hz, 1H), 7.22–7.38 (m, 5H). ^{13}C NMR (100 MHz, $CDCl_3$, δ): 29.1 (CH_2), 31.5 (CH_2), 62.2 (CH_2), 63.8 (CH_2), 79.0 (*C*H), 94.6 (*C*), 127.56 (*C*H), 127.58 (*C*), 128.0 (*C*H), 130.2 (*C*H), 137.9 (*C*H), 139.9 (*C*). HRMS–ESI (*m/z*): $[M+Na]^+$ calcd for $C_{14}H_{18}O_3Na$, 257.11482; found, 257.11447. $[a]^{24.1}_{D}$ = –18.0 (*c* 1.0, $CHCl_3$, 97% ee). The ee value was determined by HPLC analysis [Daicel CHIRALPAK® IC-3, 2-PrOH/hexane = 20:80, 40 ^{o}C, retention time: 16.78 min (minor enantiomer) and 17.94 min (major enantiomer)].

The absolute configuration of (1*R*,1'*S*)-**4o** was determined by the single crystal X-ray structural analyses (See chapter 7 in Supporting Information).

TBS protected product (1*R*,1'*S*)-17o.



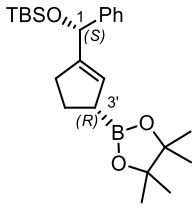
(1*R*,1'*S*)-**17o**

TBSCl (483.7 mg, 3.21 mmol) was added in portion to the stirred solution of diol (1*R*,1'*S*)-**4o** (250.0 mg, 1.07 mmol) and imidazole (436 mg, 6.42 mmol) in dry DMF at rt. The resultant solution was stirred at rt for 25 h. After that, the reaction was quenched with water and extracted with Et_2O

three times. The combined organic solution was dried over Na_2SO_4, then the crude product was purified by silica-gel column chromatography (hexane/Et_2O = 100:0 to 100:2) to give (1*R*,1'*S*)-**17o** in 72% isolated yield (358.4 mg, 0.774 mmol) as a colorless oil.

^{1}H NMR (396 MHz, $CDCl_3$, δ): –0.21 (s, 3H), 0.02 (s, 3H), 0.03 (s, 3H), 0.05 (s, 3H), 0.84 (s, 9H), 0.88 (s, 9H), 1.51 (ddd, *J* = 4.7, 8.9, 13.9 Hz, 1H), 1.82–1.93 (m, 1H), 2.05 (ddd, *J* = 4.1, 9.0, 14.0 1H), 2.16–2.27 (m, 1H), 3.30 (dt, *J* = 6.1, 9.5 Hz, 1H), 3.37 (dt, *J* = 5.9, 9.5 Hz, 1H), 3.65 (t, *J* = 5.9 Hz, 2H), 4.74 (s, 1H), 5.64 (dt, *J* = 2.1, 5.6 Hz, 1H), 5.97 (dt, *J* = 2.4, 5.7 Hz, 1H), 7.17–7.27 (m, 3H), 7.33– 7.38 (m, 2H). ^{13}C NMR (100 MHz, $CDCl_3$, δ): –5.3 (*C*H_3), –4.9 (*C*H_3), –4.6 (*C*H_3), 18.1(*C*), 18.4 (*C*), 25.8 (*C*H_3), 26.0 (*C*H_3), 27.9 (*C*H_2), 31.8(*C*H_2), 63.1 (*C*H_2), 64.2 (*C*H_2), 78.1 (*C*H), 94.5 (*C*), 126.8 (*C*H), 126.9 (*C*H), 128.2 (*C*H), 132.5 (*C*H), 136.2 (*C*H), 141.9 (*C*). HRMS–ESI (*m/z*): $[M+Na]^+$ calcd for $C_{26}H_{46}O_3NaSi_2$, 485.28777; found, 485.28737.

Allylboronate (1*S*,3'*R*)-5o.

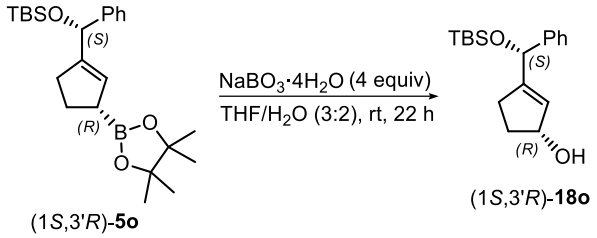


(1*S*,3'*R*)-**5o**

The boryl substitution reaction was carried out according to the representative procedure with substrate (1*R*,1'*S*)-**17o** (232.0 mg, 0.5 mmol) and Xantphos ligand. The title compound was purified by silica-gel chromatography (EtOAc:hexane = 0/100 to 4/100). 87% isolated yield (180.7 mg, 0.436 mmol). 90:10 dr.

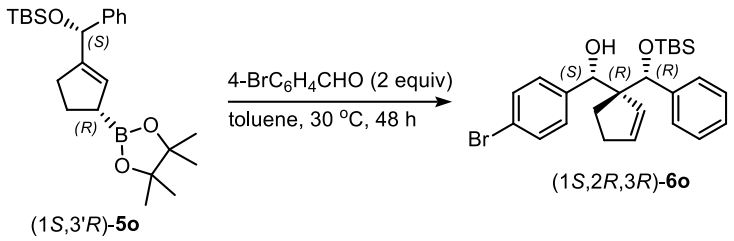
^{1}H NMR (392 MHz, $CDCl_3$, * indicates signals of the minor diastereomer, δ): 0.00 (s, 3H), 0.05 (s, 3H), 0.91 (s, 9H), 1.220 (s, 6H), 1.224 (s, 6H), 1.80–2.00 (m, 2H), 2.00–2.10 (m, 1H), 2.10–2.30 (m, 2H), 5.32 (s, 0.9H), 5.35* (s, 0.1H), 5.59* (s, 0.1H), 5.65 (s, 0.9H), 7.20 (t, *J* = 7.0 Hz, 1H), 7.28 (t, *J* = 7.2 Hz, 2H), 7.33 (d, *J* = 7.5 Hz, 2H) ^{13}C NMR (99 MHz, $CDCl_3$, δ): –5.1 (*C*H_3), –4.8 (*C*H_3), 18.3 (*C*), 24.7 (*C*H_3), 25.8 (*C*H_2), 25.9 (*C*H_3), 28.4–30.4 (B-*C*H), 31.1 (*C*H_2), 73.9 (*C*H), 83.0 (*C*), 126.0 (*C*H), 126.5 (*C*H), 126.6 (*C*H), 127.8 (*C*H), 143.6 (*C*), 146.0 (*C*). HRMS–ESI (*m/z*): $[M–H]^+$ calcd for $C_{24}H_{38}O_3BSi$, 412.27141; found, 412.27155. $[a]^{22.8}_D$ = +50.5 (*c* 1.0, $CHCl_3$, 97% ee, 90:10 dr). The ee value and dr were determined by ^{1}H NMR and HPLC analysis of the corresponding alcohol (1*S*,3'*R*)-**18o** derived from $NaBO_3 \cdot 4H_2O$ oxidation of the boronate (1*S*,3'*R*)-**5o**.

The absolute structure of (1*S*,3'*R*)-**5o** was determined by the single crystal X-ray structural analyses (See chapter 7 in Supporting Information)



^{1}H NMR of alcohol (1*S*,3'*R*)-**18o** (392 MHz, $CDCl_3$, * indicates minor diastereomer, δ): –0.07 (s, 3H), 0.04 (s, 3H), 0.90 (s, 9H), 1.40–1.70 (brs, 1 H), 1.62–1.71 (m, 1H), 2.00–2.13 (m, 1H), 2.19–2.36 (m, 2H), 4.78–4.86 (m, 1H), 5.24–5.30 (m, 1H), 5.67–5.71* (m, 0.1H), 5.67–5.71 (m, 0.9H), 7.20–7.37 (m, 5H). The ee value and dr were determined by HPLC analysis [Daicel CHIRALPAK® OD-3, 2-PrOH/hexane 2:98, 40 ^{o}C, retention time of the major diastereomer: 15.39 min (minor enantiomer) and 18.03 min (major enantiomer), retention time of the minor diastereomer: 14.49 min (major enantiomer) and 23.33 min (minor enantiomer)].

(*S*)-(4-Bromophenyl){(*R*)-1-[(*R*)-(*tert*-butyldimethylsiloxy)(phenyl)methyl]cyclopent-2-en-1-yl} methanol [(1*S*,2*R*,3*R*)-6o].



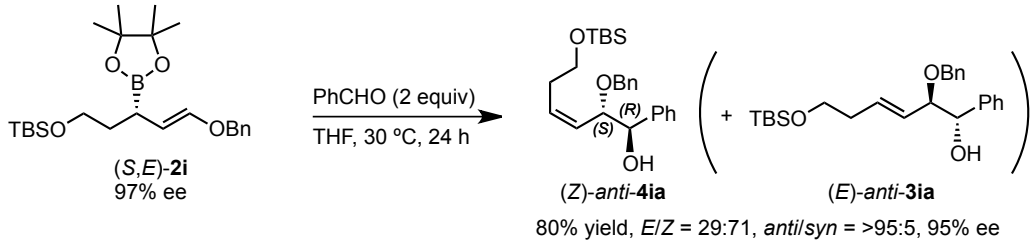
In a vacuum dried 20 mL Schlenk flask, boronate (1*S*,3'*R*)-**5o** (82.9 mg, 0.2 mmol) and *p*-bromobenzaldehyde (80.4 mg, 0.4 mmol) were dissolved in dry toluene (0.2 mL) under nitrogen atmosphere. The resulting solution was then warmed to 30 ^{o}C. After stirring for 48 h, the reaction was quenched with a CH_2Cl_2 solution of triethanolamine (10% v/v, 0.5 mL), then stirred for 2 h at rt. After that, the reaction mixture was concentrated under reduced pressure, and purified by silica-gel column chromatography (hexane/EtOAc = 100:0 to 100:4) to give (1*S*,2*R*,3*R*)-**6o** in 72% isolated yield (68.2 mg, 0.144 mmol, 96% ee, single diastereomer). Analytical sample of (1*S*,2*R*,3*R*)-**6o** was further purified by gel-permeation chromatography to remove a small amount of impurities.

^{1}H NMR (392 MHz, $CDCl_3$, δ): –0.37 (s, 3H), 0.06 (s, 3H), 0.90 (s, 9H) 1.02–1.14 (m, 1H), 1.30–1.46 (m, 2H), 1.54–1.64 (m, 1H), 3.52 (s, 1H), 4.80 (s, 1H), 4.94 (s, 1H), 5.72 (dt, *J* = 2.3, 5.8 Hz, 1H), 5.99 (dt, *J* = 2.0, 5.8 Hz, 1H), 7.18–7.40 (m, 9H). ^{13}C NMR (99 MHz, $CDCl_3$, δ): –5.1 (CH_3), –

4.2 (CH_3), 18.1 (*C*), 25.9 (CH_3), 27.0 (CH_2), 31.3 (CH_2), 64.0 (*C*), 79.2 (*C*H), 81.5 (*C*H), 121.2 (*C*), 127.4 (*C*H), 127.5 (*C*H), 128.6 (*C*H), 129.9 (*C*H), 130.2 (*C*H), 130.3 (*C*H), 135.8 (*C*H), 140.4 (*C*), 141.5 (*C*). HRMS–ESI (*m/z*): $[M–H]^+$ calcd for $C_{25}H_{32}O_2BrSi$, 471.13604; found, 471.13629. $[a]^{24.5}_D$ = –20.5 (*c* 1.0, $CHCl_3$, 96% ee). The ee value and dr were determined by HPLC analysis [Daicel CHIRALPAK® OD-3, 2-PrOH/hexane = 2:98, 40 ^oC, retention time: 10.41 min (major enantiomer) and 18.87 min (minor enantiomer)].

Procedures of Aldehyde Allylations and Characterization of Products

Allylation of benzaldehyde with allylboronate (*S*,*E*)-2i (Table3, entry 1).



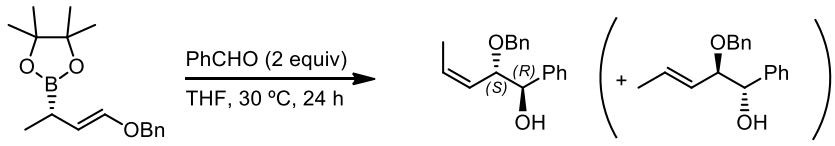
Representative procedures for allylation of aldehyde without Lewis acid catalyst.

In a vacuum dried reaction tube, (*S*,*E*)-**2i** (85.3 mg, 0.197 mmol) was dissolved in dry THF (0.4 mL) under N_2 atmosphere. Benzaldehyde (40.8 μL, 0.4 mmol) was successively added to the mixture, and stirred for 24 h at 30 ºC. The reaction mixture was quenched by a CH_2Cl_2 solution of triethanolamine (10% v/v, 2.5 mL). The mixture was separated with water and EtOAc, and then extracted three times with EtOAc. The combined organic layer was dried over Na_2SO_4, filtered and evaporated. The crude product was purified by silica-gel chromatography (EtOAc:hexane = 3/97 to 9/91) to give the corresponding *anti*-1,2-diol derivatives as a colorless oil. 80% isolated yield (65.3 mg, 0.158 mmol), 95% ee, *E*/*Z* = 29:71.

^{1}H NMR (396 MHz, $CDCl_3$, * indicates signals of the minor diastereomer, δ): 0.01 (s, 4.7H), 0.04* (s, 1.3H), 0.87 (s, 7.1H), 0.88* (s, 1.9H), 1.89–2.01 (m, 0.79H), 2.04–2.16 (m, 0.79H), 2.21–2.31* (m, 0.42H), 2.60* (d, *J* = 3.6 Hz, 0.21H), 2.72 (d, *J* = 3.6 Hz, 0.79H), 3.31–3.45 (m, 1.58H), 3.58* (t, *J* = 6.5 Hz, 0.42H), 3.88* (dd, *J* = 5.0, 8.1 Hz, 0.21H), 4.27 (dd, *J* = 5.0, 9.7 Hz, 0.79H), 4.33 (d, *J* = 12.3 Hz, 0.79H), 4.34* (d, *J* = 11.9 Hz, 0.21H), 4.59 (d, *J* = 11.9 Hz, 0.79H), 4.60* (d, *J* = 11.9 Hz, 0.21H), 4.77* (dd, *J* = 3.6, 5.3 Hz, 0.21H), 4.82 (dd, *J* = 3.6, 4.6 Hz, 0.79H), 5.39–5.54 (m, 2H), 5.62* (dt, *J* = 6.9, 15.6 Hz, 0.21H), 5.74 (dt, *J* = 7.4, 11.2 Hz, 0.79H), 7.16–7.37 (m, 10H). ^{13}C NMR (100 MHz, $CDCl_3$, δ): –5.3 (CH_3), 18.29* (*C*), 18.35 (*C*), 25.9 (CH_3), 31.4 (CH_2), 36.0* (CH_2), 62.4 (CH_2), 62.5* (CH_2), 70.1 (CH_2), 75.6* (*C*H), 75.7 (*C*H), 78.2 (*C*H), 83.9* (*C*H), 126.9 (*C*H), 127.2 (*C*H), 127.4 (*C*H), 127.45* (*C*H), 127.52 (*C*H), 127.6* (*C*H), 127.7 (*C*H), 127.8* (*C*H), 127.9 (*C*H), 128.3 (*C*H), 133.1 (*C*H), 134.0* (*C*H), 138.2 (*C*), 140.3 (*C*), 140.5* (*C*). HRMS–ESI (*m*/*z*): $[M+Na]^+$ calcd for $C_{25}H_{36}O_3NaSi$, 435.23259; found, 435.23277. $[\alpha]_D^{22.9}$ = +9.2 (*c* 1.0 in $CHCl_3$, 95% ee). Anal. Calcd for $C_{25}H_{36}O_3Si$: C, 72.77; H, 8.79. Found: C, 72.57; H, 8.83. The ee value and the *E*/*Z* ratio was determined by HPLC analysis {Daicel CHIRALPAK® OZ-3, 2-PrOH/hexane = 1/99, 0.5 mL/min, 40 °C, retention time: 20.11 min [(*Z*)-*anti*-**4ia** major enantiomer], 27.55 min [(*Z*)-*anti*-**4ia** minor enantiomer], 23.17 min [(*E*)-*anti*-**3ia** major enantiomer) and 18.81 min

[(*E*)-*anti*-**3ia** minor enantiomer]}.

Allylation of benzaldehyde with allylboronate (*S*,*E*)-2c (Table 3, entry 2).

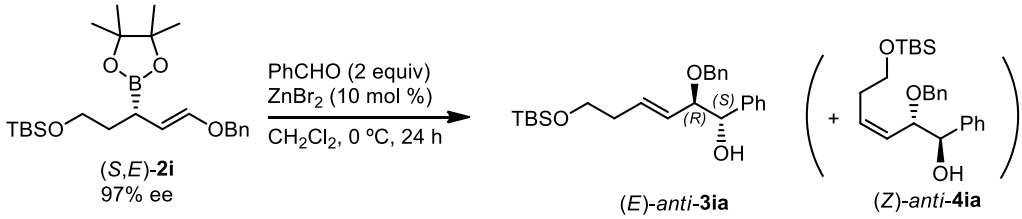


78% yield, *E*/*Z* = 15:85, *anti*/*syn* = >95:5, 96% ee

The reaction was performed according to the representative procedure with (*S*,*E*)-**2c** (59.4 mg, 0.206 mmol). The title compound was purified by silica-gel chromatography (EtOAc:hexane = 3/97 to 9/91). 78% isolated yield (43.3 mg, 0.161 mmol), 96% ee, *E*/*Z* = 15:85.

^{1}H NMR (401 MHz, $CDCl_3$, * indicates signals of the minor diastereomer, δ): 1.37 (dd, *J* = 1.8, 7.0 Hz, 2.55H), 1.71* (dd, *J* = 1.8, 6.6 Hz, 0.45H), 2.54* (dd, *J* = 1.0, 3.4 Hz, 0.15H), 2.59–2.62 (m, 0.85H), 3.88* (dd, *J* = 5.2, 8.4 Hz, 0.15H), 4.33 (ddd, *J* = 0.8, 4.4, 9.6 Hz, 0.85H), 4.36 (d, *J* = 12.0 Hz, 1H), 4.59* (d, *J* = 11.6 Hz, 0.15H), 4.61 (d, *J* = 12.0 Hz, 0.85H), 4.77* (dd, *J* = 3.2, 5.2 Hz, 0.15H), 4.85 (t, *J* = 4.0 Hz, 0.85H), 5.41 (ddq, *J* = 1.8, 9.4, 11.2 Hz, 1H), 5.64* (dt, *J* = 6.4, 15.6 Hz, 0.15H), 5.80 (ddq, *J* = 0.8, 6.8, 11.2 Hz, 0.85H), 7.16–7.38 (m, 10H). ^{13}C NMR (101 MHz, $CDCl_3$, δ): 13.3 (CH_3), 17.9* (CH_3), 70.0 (CH_2), 75.7 (*C*H), 77.6 (*C*H), 83.8* (*C*H), 126.4 (*C*H), 126.8 (*C*H), 126.9* (*C*H), 127.0* (*C*H), 127.3 (*C*H), 127.4* (*C*H), 127.5 (*C*H), 127.6* (*C*H), 127.7 (*C*H), 127.8 (*C*H), 128.3 (*C*H), 131.0 (*C*H), 132.3* (*C*H), 138.2 (*C*), 140.2 (*C*), 140.5* (*C*). HRMS–ESI (*m*/*z*): $[M+Na]^+$ calcd for $C_{18}H_{20}O_2Na$, 291.13555; found, 291.13566. $[\alpha]_D^{22.9}$ = +25.7 (*c* 1.1 in $CHCl_3$, 96% ee). Anal. Calcd for $C_{18}H_{20}O_2$: C, 80.56; H, 7.51. Found: C, 80.53; H, 7.56. The ee value and the *E*/*Z* ratio was determined by HPLC analysis {Daicel CHIRALPAK® OZ-3, 2-PrOH/hexane = 2/98, 0.5 mL/min, 40 °C, retention time: 19.51 min [(*Z*)-*anti*-**4ca** major enantiomer], 27.99 min [(*Z*)-*anti*-**4ca** minor enantiomer], 22.68 min [(*E*)-*anti*-**3ca** major enantiomer] and 18.63 min [(*E*)-*anti*-**3ca** minor enantiomer]}.

$ZnBr_2$-catalyzed allylation of benzaldehyde with allylboronate (*S*,*E*)-2i (Table 3, entry 3).



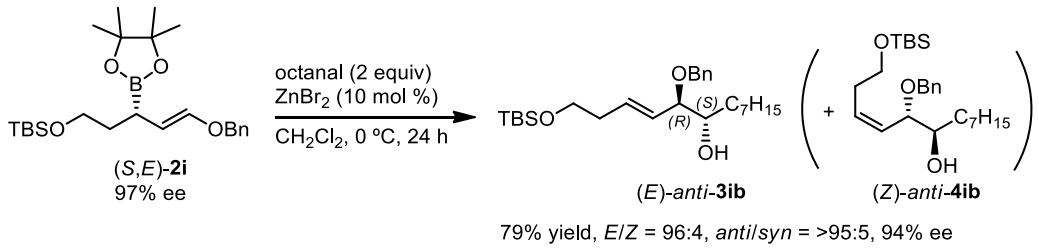
68% yield, *E*/*Z* = 98:2, *anti*/*syn* = >95:5, 98% ee

Representative procedures for $ZnBr_2$-catalyzed allylation of aldehyde.

$ZnBr_2$ (4.3 mg, 10 mol %) was added to a reaction vial sealed with a screw cap containing a silicon-coated rubber septum in the globe box under argon. After the reaction vial was removed from the globe box, it was connected to a vacuum/nitrogen manifold through a needle. Dry CH_2Cl_2 (0.4 mL), (*S*,*E*)-**2i** (84.5 mg, 0.196 mmol) and benzaldehyde (40.8 mL, 0.4 mmol) was successively added to the vial, and stirred for 24 h at 0 ºC. The use of dry $ZnBr_2$ is necessary for the high stereoselectivity of this aldehyde allylation. The reaction mixture was quenched by a CH_2Cl_2 solution of triethanolamine (10% v/v, 2.5 mL). The mixture was separated with water and EtOAc, and then extracted three times with EtOAc. The combined organic layer was dried over Na_2SO_4, filtered and evaporated. The crude product was purified by silica-gel chromatography (EtOAc:hexane = 3/97 to 9/91) to give the corresponding *anti*-1,2-diol derivatives as a colorless oil. 68% isolated yield (54.7 mg, 0.133 mmol), 98% ee and *E*/*Z* = 98:2.

^{1}H NMR (401 MHz, $CDCl_3$, δ): 0.03 (s, 6H), 0.88 (s, 9H), 2.17–2.34 (m, 2H), 2.67 (d, *J* = 3.2 Hz, 1H), 3.57 (t, *J* = 6.6 Hz, 2H), 3.87 (dd, *J* = 5.0, 8.2 Hz, 1H), 4.32 (d, *J* = 11.6 Hz, 1H), 4.58 (d, *J* = 12.0 Hz, 1H), 4.75 (dd, *J* = 3.0, 5.0 Hz, 1H), 5.43 (dd, *J* = 8.0, 15.6 Hz, 1H), 5.60 (dt, *J* = 6.8, 15.3 Hz, 1H), 7.14–7.34 (m, 10H). ^{13}C NMR (101 MHz, $CDCl_3$, δ): –5.3 (CH_3), 18.3 (*C*), 25.9 (CH_3), 36.0 (CH_2), 62.5 (CH_2), 70.1 (CH_2), 75.6 (*C*H), 83.9 (*C*H), 126.9 (*C*H), 127.4 (*C*H), 127.5 (*C*H), 127.6 (*C*H), 127.8 (*C*H), 127.9 (*C*H), 128.3 (*C*H), 134.1 (*C*H), 138.2 (*C*), 140.4 (*C*). HRMS–ESI (*m*/*z*): $[M+Na]^+$ calcd for $C_{25}H_{36}O_3NaSi$, 435.23259; found, 435.23260. $[\alpha]_D^{22.6}$ = –8.8 (*c* 1.1 in $CHCl_3$, 98% ee). Anal. Calcd for $C_{25}H_{36}O_3Si$: C, 72.77; H, 8.79. Found: C, 72.61; H, 8.79. The ee value and the *E*/*Z* ratio was determined by HPLC analysis {Daicel CHIRALPAK® OZ-3, 2-PrOH/hexane = 1/99, 0.5 mL/min, 40 °C, retention time: 24.79 min [(*E*)-*anti*-**3ia** major enantiomer), 19.79 min [(*E*)-*anti*-**3ia** minor enantiomer] and 21.67 min [(*Z*)-*anti*-**4ia** major enantiomer]}. Minor enantiomer of (*Z*)-*anti*-**4ia** was not detected by HPLC analysis.

$ZnBr_2$-catalyzed allylation of octanal with allylboronate (*S*,*E*)-2i (Table 3, entry 4).

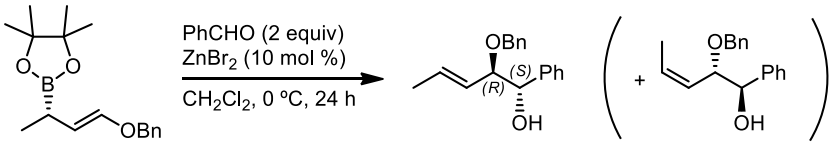


The reaction was performed according to the representative procedure with (*S*,*E*)-**2i** (86.4 mg, 0.20 mmol). The title compound was purified by silica-gel chromatography (EtOAc:hexane = 3/97 to

10/90). 79% isolated yield (68.6 mg, 0.158 mmol), 94% ee, *E*/*Z* = 96:4.

^{1}H NMR (401 MHz, $CDCl_3$, δ): 0.06 (s, 6H), 0.87 (t, *J* = 6.8 Hz, 3H), 0.90 (s, 9H), 1.18–1.35 (m, 10H), 1.35–1.50 (m, 2H), 2.33 (q, *J* = 6.5 Hz, 2H), 3.62–3.73 (m, 4H), 4.36 (d, *J* = 11.6 Hz, 1H), 4.61 (d, *J* = 12.0 Hz, 1H), 5.53 (dd, *J* = 8.0, 15.6 Hz, 1H), 5.73 (dt, *J* = 7.0, 15.5 Hz, 1H), 7.24–7.37 (m, 5H). ^{13}C NMR (101 MHz, $CDCl_3$, δ): –5.3 (CH_3), 14.1 (CH_3), 18.3 (*C*), 22.6 (CH_2), 25.7 (CH_2), 25.9 (CH_3), 29.2 (CH_2), 29.6 (CH_2), 31.8 (CH_2), 32.2 (CH_2), 36.1 (CH_2), 62.7 (CH_2), 69.9 (CH_2), 73.3 (*C*H), 83.1 (*C*H), 127.5 (*C*H), 127.7 (*C*H), 127.9 (*C*H), 128.3 (*C*H), 133.9 (*C*H), 138.5 (*C*). HRMS–ESI (*m*/*z*): $[M+Na]^+$ calcd for $C_{26}H_{46}O_3NaSi$, 457.31084; found, 457.31088. $[\alpha]_D^{22.9}$ = –26.1 (*c* 1.1 in $CHCl_3$, 94% ee). Anal. Calcd for $C_{26}H_{46}O_3Si$: C, 71.83; H, 10.67. Found: C, 70.44; H, 10.55. The ee value and the *E*/*Z* ratio was determined by HPLC analysis after deprotection of TBS ether in the product {Daicel CHIRALPAK® IC-3, 2-PrOH/hexane = 3/97, 0.5 mL/min, 40 °C, retention time: 53.63 min [(*E*)-*anti*-**3ib** major enantiomer], 42.80 min [(*E*)-*anti*-**3ib** minor enantiomer] and 34.13 min [(*Z*)-*anti*-**4ib** major enantiomer]}. Minor enantiomer of (*Z*)-*anti*-**4ib** was not detected by HPLC analysis.

$ZnBr_2$-catalyzed allylation of benzaldehyde with allylboronate (*S*,*E*)-2c (Table 3, entry 5).



(*S*,*E*)-**2c** 96% ee

(*E*)-*anti*-**3ca** (*Z*)-*anti*-**4ca**

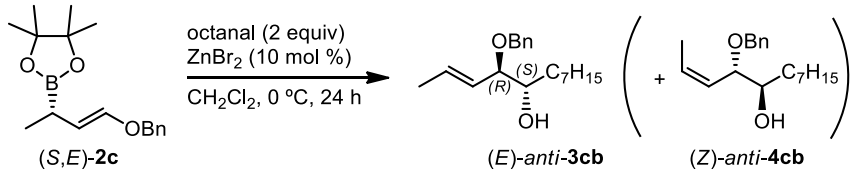
81% yield, *E*/*Z* = 92:8, *anti*/*syn* = >95:5, 96% ee

The reaction was performed according to the representative procedure with (*S*,*E*)-**2c** (57.5 mg, 0.20 mmol). The title compound was purified by silica-gel chromatography (EtOAc:hexane = 3/97 to 9/91). 81% isolated yield (43.4 mg, 0.162 mmol), 96% ee, *E*/*Z* = 92:8.

^{1}H NMR (401 MHz, $CDCl_3$, * indicates signals of the minor diastereomer, δ): 1.35* (dd, *J* = 1.6, 7.2 Hz, 0.24H), 1.69–1.71 (m, 2.76H), 2.58–2.63 (m, 0.92H), 2.64–2.69* (m, 0.08H), 3.87 (dd, *J* = 5.0, 8.2 Hz, 1H), 4.32 (d, *J* = 11.6 Hz, 0.92H), 4.34* (d, *J* = 18.4 Hz, 0.08H), 4.58 (d, *J* = 12.4 Hz, 0.92H), 4.60* (d, *J* = 12.0 Hz, 0.08H), 4.76 (dd, *J* = 3.6, 5.2 Hz, 0.92H), 4.83* (t, *J* = 3.6 Hz, 0.08H), 5.40 (ddq, *J* = 1.2, 8.4, 15.6 Hz, 1H), 5.62 (dq, *J* = 6.4, 15.6 Hz, 0.92H), 5.73–5.83 (m, 0.08H), 7.14–7.36 (m, 10H). ^{13}C NMR (101 MHz, $CDCl_3$, δ): 13.3* (CH_3), 17.9 (CH_3), 70.0 (CH_2), 75.7 (*C*H), 77.6* (*C*H), 83.8 (*C*H), 126.4* (*C*H), 126.8* (*C*H), 126.94 (*C*H), 126.97* (*C*H), 127.37 (*C*H), 127.43 (*C*H), 127.6 (*C*H), 127.7* (*C*H), 127.9 (*C*H), 128.2 (*C*H), 131.0* (*C*H), 132.3 (*C*H), 138.2 (*C*), 140.5 (*C*). HRMS–ESI (*m*/*z*): $[M+Na]^+$ calcd for $C_{18}H_{20}O_2Na$, 291.13555; found, 291.13565. $[\alpha]_D^{22.7}$ = –19.4 (*c* 1.0 in $CHCl_3$, 96% ee). Anal. Calcd for $C_{18}H_{20}O_2$: C, 80.56; H, 7.51. Found: C,

80.32; H, 7.55. The ee value and the *E*/*Z* ratio was determined by HPLC analysis {Daicel CHIRALPAK® OZ-3, 2-PrOH/hexane = 2/98, 0.5 mL/min, 40 °C, retention time: 22.87 min [(*E*)-*anti*-**3ca** major enantiomer], 19.17 min [(*E*)-*anti*-**3ca** minor enantiomer] and 20.85 min [(*Z*)-*anti*-**4ca** major enantiomer]}. Minor enantiomer of (*Z*)-*anti*-**4ca** was not detected by HPLC analysis.

$ZnBr_2$-catalyzed allylation of octanal with allylboronate (*S*,*E*)-2c (Table 3, entry 6).



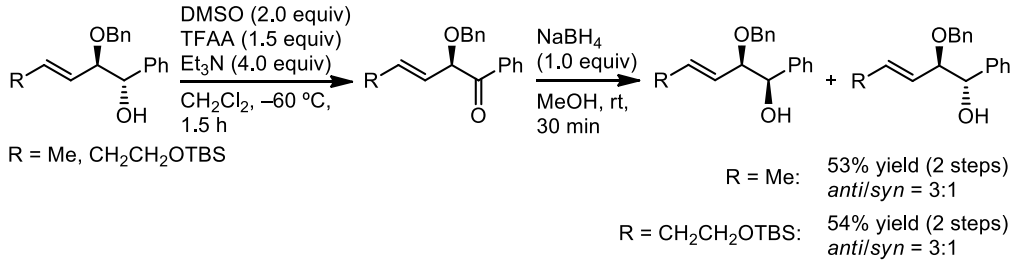
72% yield, *E*/*Z* = 85:15, *anti*/*syn* = >95:5, 96% ee

The reaction was performed according to the representative procedure with (*S*,*E*)-**2c** (56.9 mg, 0.197 mmol). The title compound was purified by silica-gel chromatography (EtOAc:hexane = 4/96 to 11/89). 72% isolated yield (41.4 mg, 0.143 mmol), 96% ee, *E*/*Z* = 85:15.

^{1}H NMR (396 MHz, $CDCl_3$, * indicates signals of the minor diastereomer, δ): 0.87 (t, *J* = 6.7 Hz, 3H), 1.18–1.35 (m, 10H), 1.35–1.52 (m, 2H), 1.61–1.68* (m, 0.45H), 1.78 (dd, *J* = 1.2, 6.3 Hz, 2.55H), 2.13 (d, *J* = 3.6 Hz, 1H), 3.62–3.77 (m, 1H), 3.65 (dd, *J* = 4.0, 8.7 Hz, 0.85H), 4.13* (dd, *J* = 4.0, 9.9 Hz, 0.15H), 4.35 (d, *J* = 11.9 Hz, 0.85H), 4.37* (d, *J* = 12.3 Hz, 0.15H), 4.609 (d, *J* = 11.5 Hz, 0.85H), 4.614* (d, *J* = 11.9 Hz, 0.15H), 5.43–5.54 (m, 1H), 5.73 (dt, *J* = 6.4, 15.4 Hz, 0.85H), 5.84–5.94* (m, 0.15H), 7.23–7.38 (m, 5H). ^{13}C NMR (100 MHz, $CDCl_3$, δ): 13.7* (CH_3), 14.1 (CH_3), 18.0 (CH_3), 22.6 (CH_2), 25.7 (CH_2), 25.8* (CH_2), 29.2 (CH_2), 29.6 (CH_2), 31.8 (CH_2), 32.1* (CH_2), 32.2 (CH_2), 69.78 (CH_2), 69.84* (CH_2), 73.4 (*C*H), 83.1 (*C*H), 126.9* (*C*H), 127.2 (*C*H), 127.49 (*C*H), 127.55* (*C*H), 127.7 (*C*H), 127.8* (*C*H), 128.3 (*C*H), 130.5* (*C*H), 131.9 (*C*H), 138.5 (*C*). HRMS–ESI (*m*/*z*): $[M+Na]^+$ calcd for $C_{19}H_{30}O_2Na$, 313.21380; found, 313.21367. $[\alpha]_D^{22.7}$ = –34.2 (*c* 1.0 in $CHCl_3$, 96% ee). Anal. Calcd for $C_{19}H_{30}O_2$: C, 78.57; H, 10.41. Found: C, 78.46; H, 10.51. The ee value and the *E*/*Z* ratio was determined by HPLC analysis {Daicel CHIRALPAK® OZ-3, 2-PrOH/hexane = 0.25/99.75, 0.5 mL/min, 40 °C, retention time: 48.72 min [(*E*)-*anti*-**3cb** major enantiomer], 45.81 min [(*E*)-*anti*-**3cb** minor enantiomer], 52.72 min [(*Z*)-*anti*-**4cb** major enantiomer] and 56.64 min [(*Z*)-*anti*-**4cb** major enantiomer]}.

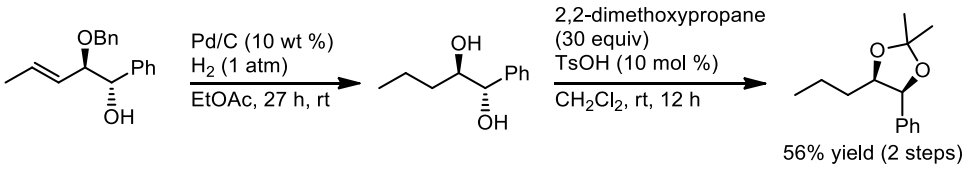
Determination of *anti*/*syn* ratios of allylation products.

The *syn*-products of aldehyde allylation were synthesized according to the following scheme and purified by silica-gel column chromatography. The *anti*/*syn* ratios of the aldehyde allylation products were determined by the comparison of ^{1}H NMR spectra of the crude reaction mixture and the corresponding *anti*- and *syn*-products.

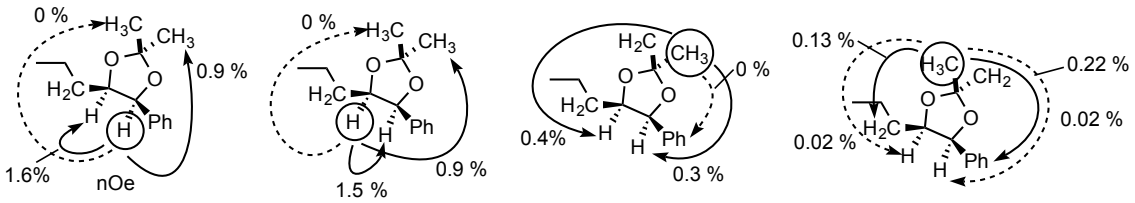


Determination of the relative configurations of the products of aldehyde allylation with γ-alkoxyallylboronates.

The relative configuration of allylation product (*E*)-*anti*-**3ca** was determined by NOE measurements after derivatization to the corresponding cyclic acetal as shown in the following scheme.



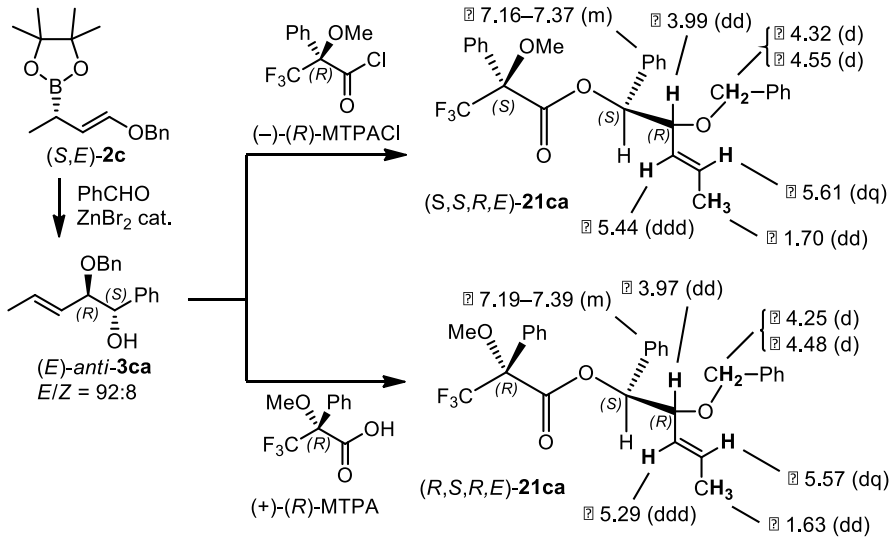
NOE experiments of the cyclic acetal derived from (*E*)-*anti*-**3ca** also supports the proposed relative stereochemistry as shown in the following figure. The relative structures of other products of aldehyde allylation with g-alkoxyallylboronates were deduced by these results.



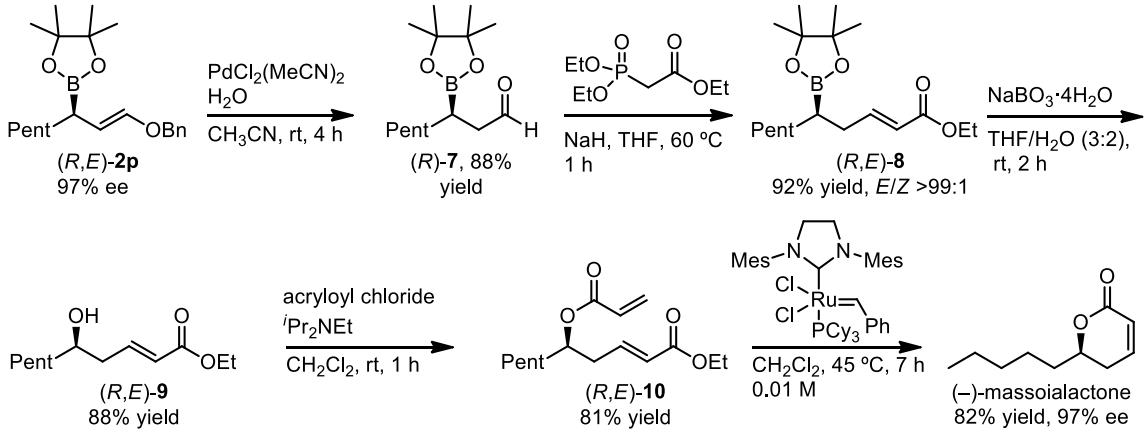
Determination of absolute configuration of products.

The absolute configuration of allylation product (*E*)-*anti*-**3ca** was determined by a standard Mosher's procedure. Comparison of ^{1}H NMR spectra of (+) and (–)-MTPA ester of (*E*)-*anti*-**3ca** as shown in the following figure indicates the absolute configuration of C1 in (*E*)-*anti*-**3ca** is *S*

configuration. The absolute configurations of other aldehyde allylation products were deduced by this result.



Asymmetric Synthesis of (–)-Massoialactone



H_2O (0.90 mL) was added to a solution of (*R*,*E*)-**2p** (378.4 mg, 1.10 mmol) and $PdCl_2(MeCN)_2$ (28.5 mg, 0.11 mmol) in CH_3CN (55 mL) at room temperature. After stirring for 4 h, the reaction mixture was directly extracted with hexane five times. The combined organic layer was dried over Na_2SO_4. The solvents were removed by evaporation. The residue was purified by flash column chromatography (EtOAc/hexane = 1/99 to 7/93) to give the desired aldehyde (*R*)-**7** (269.7 mg, 0.96 mmol, 88% isolated yield).

^{1}H NMR (396 MHz, $CDCl_3$, δ): 0.87 (t, *J* = 6.7 Hz, 3H), 1.14–1.53 (m, 21H), 2.46–2.66 (m, 2H), 9.76 (s, 1H). ^{13}C NMR (100 MHz, $CDCl_3$, δ): 13.8 (CH_3), 17.1 (br, B–*C*H), 22.3 (CH_2), 24.4 (CH_3), 24.5 (CH_3), 28.2 (CH_2), 30.2 (CH_2), 31.7 (CH_2), 45.7 (CH_2), 82.9 (*C*), 202.3 (*C*H).

Ethyl 2-(diethoxyphosphoryl)acetate (0.223 mL, 1.02 mmol) was added dropwise to a suspension of NaH (60%, dispersion in liquid paraffin) (41.8 mg, 1.02 mmol) in THF (1.86 mL) at 0 °C. After gas evolution stopped, (*R*)-**7** (236.9 mg, 0.85 mmol) was added dropwise with stirring at 0 °C. The reaction mixture was then warmed to 60 ºC and stirred for 1 h. The reaction was quenched by addition of H_2O and extracted three times with EtOAc. The combined organic layer was dried over Na_2SO_4. After filtration, the solvents were removed by evaporation. The crude mixture was purified by silica-gel chromatography (EtOAc/hexane = 1/99 to 5/95) to afford the corresponding ester (251.4 mg, 0.78 mmol, 92% isolated yield) as a colorless oil.

^{1}H NMR (396 MHz, $CDCl_3$, δ): 0.87 (t, *J* = 6.5 Hz, 3H), 1.05–1.49 (m, 12H), 1.23 (s, 12H), 2.27 (nonet, *J* = 7.2 Hz, 2H), 4.17 (q, *J* = 7.1 Hz, 2H), 5.81 (d, *J* = 15.9 Hz, 1H), 6.96 (dt, *J* = 7.5, 15.4 Hz, 1H). ^{13}C NMR (100 MHz, $CDCl_3$, δ): 13.8 (CH_3), 14.0 (CH_3), 22.3 (CH_2), 22.6 (br, B–*C*H), 24.5 (CH_3), 28.3 (CH_2), 30.6 (CH_2), 31.7 (CH_2), 33.6 (CH_2), 59.6 (CH_2), 82.9 (*C*), 121.4 (*C*H), 149.0 (*C*H), 166.3 (*C*).

(*R*,*E*)-**8** (135.1 mg, 0.417 mmol) was dissolved in THF/H_2O (3:2) solvent. $NaBO_3 \cdot 4H_2O$ (153.9 mg, 4.83 equiv) was added to the solution and stirred for 12 h at rt. Then, the mixture was separated with water and EtOAc, and then extracted with EtOAc four times. The combined organic layer was dried over Na_2SO_4, filtered and evaporated. The crude mixture was purified by silica-gel column chromatography (EtOAc:hexane = 10/90 to 20/80) to give the corresponding alcohol (*R*,*E*)-**9** (78.3 mg, 0.365 mmol, 88% isolated yield).

^{1}H NMR (396 MHz, $CDCl_3$, δ): 0.90 (t, *J* = 6.3 Hz, 3H), 1.24–1.40 (m, 8H), 1.40–1.55 (m, 3H), 2.26–2.47 (m, 2H), 3.71–3.81 (m, 1H), 4.19 (q, *J* = 7.1 Hz, 2H), 5.91 (dd, *J* = 1.2, 15.8 Hz, 1H), 6.98 (dt, *J* = 7.9, 15.8 Hz, 1H). ^{13}C NMR (99 MHz, $CDCl_3$, δ): 13.8 (CH_3), 14.0 (CH_3), 22.4 (CH_2), 25.1 (CH_2), 31.6 (CH_2), 36.9 (CH_2), 40.0 (CH_2), 60.1 (CH_2), 70.2 (*C*H), 123.3 (*C*H), 145.7 (*C*H), 166.4 (*C*).

Acryloyl chloride (113.1 mL, 1.4 mmol) was added dropwise to a solution of (*R*,*E*)-**9** (75.5 mg, 0.353 mmol) and *N*,*N*-diisopropylethylamine (279.4 mL, 1.6 mmol) in CH_2Cl_2 (1.2 mL) at 0 °C. Then, the reaction mixture was warmed to room temperature and stirred for 1 h. The reaction mixture was diluted with CH_2Cl_2, successively washed with HCl aq. and saturated $NaHCO_3$ aq., dried over Na_2SO_4. After filtration, the solvents were removed by evaporation. The crude mixture was purified by silica-gel chromatography (EtOAc/hexane = 5/95) to afford the desired product (*R*,*E*)-**10** (76.6 mg, 0.285 mmol, 81% isolated yield) as a colorless oil.

^{1}H NMR (396 MHz, $CDCl_3$, δ): 0.88 (t, *J* = 6.9 Hz, 3H), 1.21–1.40 (m, 9H), 1.50–1.69 (m, 2H), 2.43–2.57 (m, 2H), 4.19 (q, *J* = 7.1 Hz, 2H), 4.99–5.09 (m, 1H), 5,80–5.91 (m, 2H), 6.11 (dd, *J* =

10.5, 17.2 Hz, 1H) , 6.40 (dd, J = 1.4, 17.2 Hz, 1H) , 6.89 (dt, J = 7.9, 15.0 Hz, 1H). ^{13}C NMR (100 MHz, $CDCl_3$, δ): 13.7 (CH_3), 14.0 (CH_3), 22.3 (CH_2), 24.7 (CH_2), 31.3 (CH_2), 33.4 (CH_2), 36.5 (CH_2), 60.0 (CH_2), 72.4 (*C*H), 124.0 (*C*H), 128.4 (*C*H), 130.5 (CH_2), 143.3 (*C*H), 165.4 (*C*), 165.9 (*C*).

In a vacuum dried 100 mL round bottomed flask, Grubbs second generation catalyst (8.7 mg, 0.01 mmol) was dissolved in CH_2Cl_2 (20 mL) at room temperature under N_2 atmosphere. (*R*,*E*)-**10** (55.7 mg, 0.208 mmol) was added to the solution and then warmed to 45 ºC. After stirred for 7 h, the solvent of the reaction mixture was removed by evaporation. The crude mixture was purified by silica-gel chromatography (EtOAc/hexane = 2/98 to 10/90) to afford the desired (–)-massoialactone (28.5 mg, 0.17 mmol, 82% isolated yield, 97% ee). ^{1}H and ^{13}C NMR spectra of this product were in agreement with the literature data.[35] Analytical sample of this product was further purified by gel-permeation chromatography to remove a small amount of impurities.

^{1}H NMR (396 MHz, $CDCl_3$, δ): 0.90 (t, J = 7.1 Hz, 3H), 1.24–1.59 (m, 6H), 1.59–1.73 (m, 1H), 1.74–1.86 (m, 1H), 2.26–2.42 (m, 2H), 4.37–4.47 (m, 1H), 5.99–6.05 (m, 1H), 6.85–6.92 (m, 1H). ^{13}C NMR (100 MHz, $CDCl_3$, δ): 13.9 (CH_3), 22.5 (CH_2), 24.4 (CH_2), 29.3 (CH_2), 31.5 (CH_2), 34.8 (CH_2), 78.0 (*C*H), 121.4 (*C*H), 145.0 (*C*H), 164.6 (*C*). HRMS–ESI (*m*/*z*): $[M+Na]^+$ calcd for $C_{10}H_{16}O_2Na$, 191.10425; found, 191.10422. $[\alpha]_D^{25.7}$ = –146.5 (*c* 1.0 in $CHCl_3$, 97% ee). The ee value was determined by HPLC analysis [Daicel CHIRALPAK® OD-3, 2-PrOH/Hexane = 0.5/99.5, 0.5 mL/min, 40 °C, retention time: 62.37 min (major enantiomer) and 58.91 min (minor enantiomer)]. The absolute configuration was determined by comparison of the optical rotation to the literature value for (–)-massoialactone: $[\alpha]_D^{27}$ = –103.7 (*c* 0.20 in $CHCl_3$, 90% ee)**.**

Single Crystal X-Ray Structural Analyses

Single crystal X-ray structural analyses were carried out on a Rigaku R-AXIS RAPID diffractometer using graphite monochromated Mo-K_a radiation. The structures were solved by direct methods and expanded using Fourier techniques. Non-hydrogen atoms were refined anisotropically. Hydrogen atoms were refined using the riding model. All calculations were performed using the CrystalStructure crystallographic software package except for refinement, which was performed using SHELXL-97.[36]

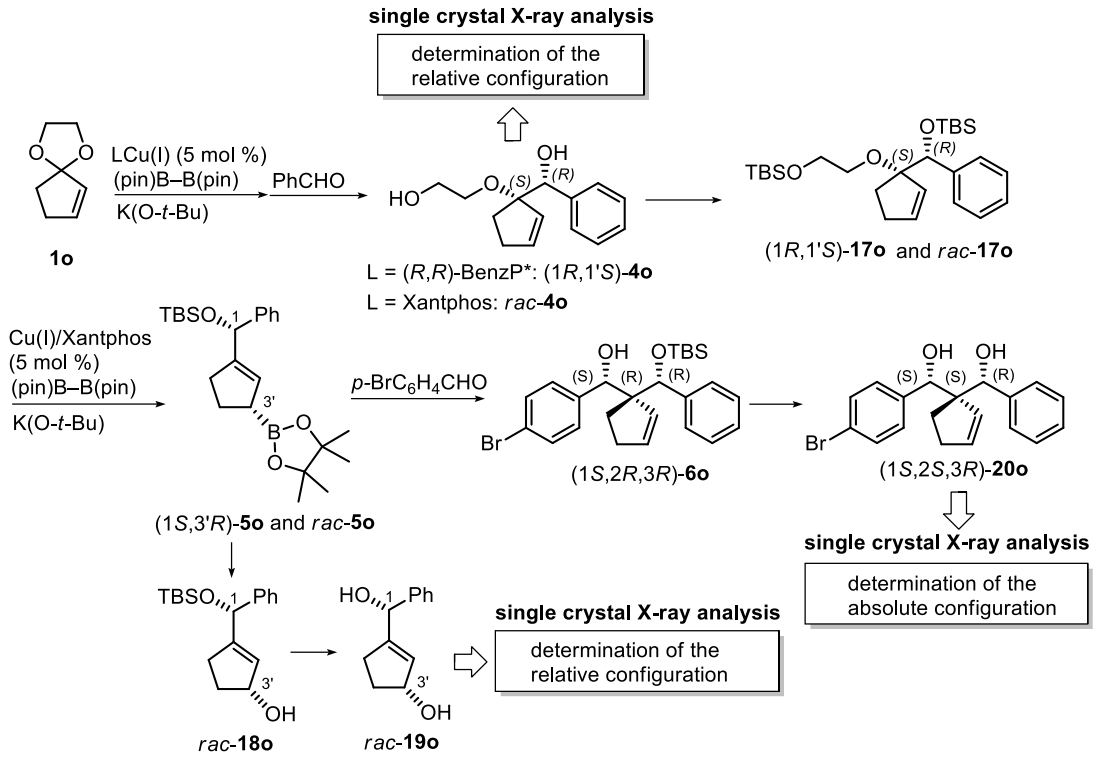
The determination of the stereochemistry of (1*R*,1'*S*)-**4o**, (1*S*,3'*R*)-**5o** and (1*S*,2*S*,3*R*)-**20o** was carried out according to the following scheme.

The absolute stereochemistry of (1*R*,1'*S*)-**4o** was determined by the comparison of the two single crystal X-ray analyses. The absolute stereochemistry of C1 in (1*R*,1'*S*)-**4o** was determined by the

single crystal X-ray analysis of (1*S*,2*S*,3*R*)-**20o**, which was derived from (1*R*,1'*S*)-**4o**. The relative stereochemistry between C1 and C1' in (1*R*,1'*S*)-**4o** was then determined by the single crystal X-ray analysis of (1*R*,1'*S*)-**4o**.

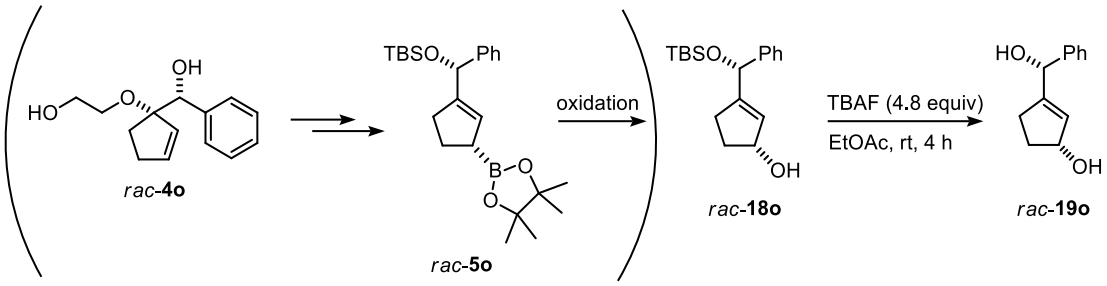
The absolute stereochemistry of (1*S*,3'*R*)-**5o** was determined by the comparison of the two single crystal X-ray analyses of (1*S*,2*S*,3*R*)-**20o**, which was derived from (1*S*,3'*R*)-**5o**. The relative stereochemistry between C1 and C3' in (1*S*,3'*R*)-**5o** was then determined by the single crystal X-ray analysis of *rac*-**19o**, derived from *rac*-**5o**.

The absolute stereochemistry of (1*S*,2*R*,3*R*)-**6o** was determined by the single crystal X-ray analysis of (1*S*,2*S*,3*R*)-**20o** derived from (1*S*,2*R*,3*R*)-**6o** using anomalous scattering of X-rays.



Preparation of *rac*-19o and 1,3-diol 20o for X-ray crystallographic analyses.

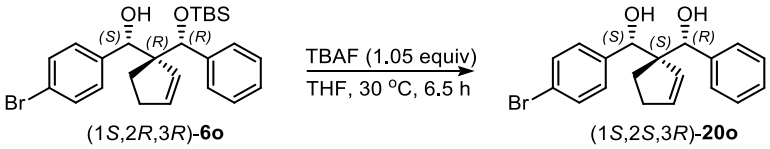
3-[Hydroxy(phenyl)methyl]cyclopent-2-enol (*rac*-19o).



In a 10 mL Schlenk flask, *rac*-**18o** (51 mg, 0.167 mmol) were dissolved in EtOAc (0.5 mL). TBAF (1.0 M in THF, 400 mL) was added to the mixture. The resulting solution was stirred for 2 h at rt. After that, TBAF (1.0 M in THF, 400 mL) was added to the reaction mixture and the solution was stirred for additional 2 h at rt. Then, the reaction mixture was directly subjected to silica-gel column chromatography (hexane/EtOAc = 90:10 to 0:100) to give *rac*-**19o** in 73% isolated yield (23.3 mg, 0.122 mmol). The crystal of *rac*-**19o** for X-ray crystallographic analysis was prepared by recrystallization from MeOH/pentane/Et_2O solution of *rac*-**19o**.

^{1}H NMR (396 MHz, CD_3OD, δ): 1.71–1.61 (m, 1H), 2.10–2.00 (m, 1H), 2.17–2.27 (m, 1H), 2.31–2.40 (m, 1H), 4.76–4.83 (m, 1H), 5.26 (s, 1H), 5.72–5.76 (m, 1H), 7.22–7.28 (m, 1H), 7.28–7.38 (m, 4H). ^{13}C NMR (100 MHz, $CDCl_3$, δ): 31.0 (CH_2), 34.5 (CH_2), 74.4 (*C*H), 77.8 (*C*H), 127.7 (*C*H), 128.5 (*C*H), 128.8 (*C*H), 129.3 (*C*H), 143.8 (*C*), 151.9 (*C*).

(*S*)-(4-Bromophenyl){(*S*)-1-[(*R*)-hydroxy(phenyl)methyl]cyclopent-2-en-1-yl}methanol [(1*S*,2*S*,3*R*)-20o].



In a vacuum dried 25 mL flask, (1*S*,2*R*,3*R*)-**6o** (45.3 mg, 0.0957 mmol) were dissolved in dry THF (2 mL) under nitrogen atmosphere. To the resulting solution was added TBAF (1 M solution in THF, 105 mL, 0.105 mmol) at 0 °C, then the reaction mixture was warmed to 30 °C and stirred for 6.5 h. After that, SiO_2 was added to the reaction mixture and the solvent was removed under reduced pressure. The resultant crude product absorbed onto SiO_2 particles was purified by silica-gel column chromatography (hexane/EtOAc = 10:1 to 5:1) to give (1*S*,2*S*,3*R*)-**20o** in 96% isolated yield (32.9 mg, 0.916 mmol). Analytical sample of (1*S*,2*S*,3*R*)-**20o** was further purified by gel-permeation chromatography to remove a small amount of impurities. The ee value of (1*S*,2*S*,3*R*)-**20o** (98% ee) was determined after recrystallization from its MeOH solution and this single crystal of (1*S*,2*S*,3*R*)-**20o** was used for X-ray analysis.

^{1}H NMR (396 MHz, $CDCl_3$, δ): 1.27–1.34 (m, 2H), 1.50 (t, *J* = 7.1 Hz, 2H), 2.61 (d, *J* = 1.5 Hz, 1H), 2.98 (d, *J* = 1.4 Hz, 1H), 4.90 (d, *J* = 1.1 Hz, 1H), 4.94 (s, 1H), 5.83 (dt, *J* = 2.4, 5.7 Hz, 1H), 6.03 (dt, *J* = 2.2, 5.8 Hz, 1H), 7.23–7.32 (m, 5H), 7.32–7.38 (m, 2H), 7.38–7.43 (m, 2H). ^{13}C NMR (100 MHz, $CDCl_3$, δ): 26.1 (CH_2), 31.4 (CH_2), 63.6 (*C*), 78.9 (*C*H), 79.7 (*C*H), 121.5 (*C*), 127.6 (*C*H), 127.7 (*C*H), 128.2 (*C*H), 129.3 (*C*H), 130.0 (*C*H), 130.6 (*C*H), 137.4 (*C*H), 140.3 (*C*), 141.1 (*C*). HRMS–ESI (*m/z*): $[M–H]^+$ calcd for $C_{19}H_{18}O_2Br$, 357.04957; found, 357.05025 $[a]^{23.5}_D = –1.7$

(*c* 1.5, MeOH, 98% ee). The ee value was determined by HPLC analysis [Daicel CHIRALPAK® IC-3, 2-PrOH/hexane = 5:95, 40 ^{o}C, Retention time; 54.59 min (major enantiomer) and 58.75 min (minor enantiomer)].

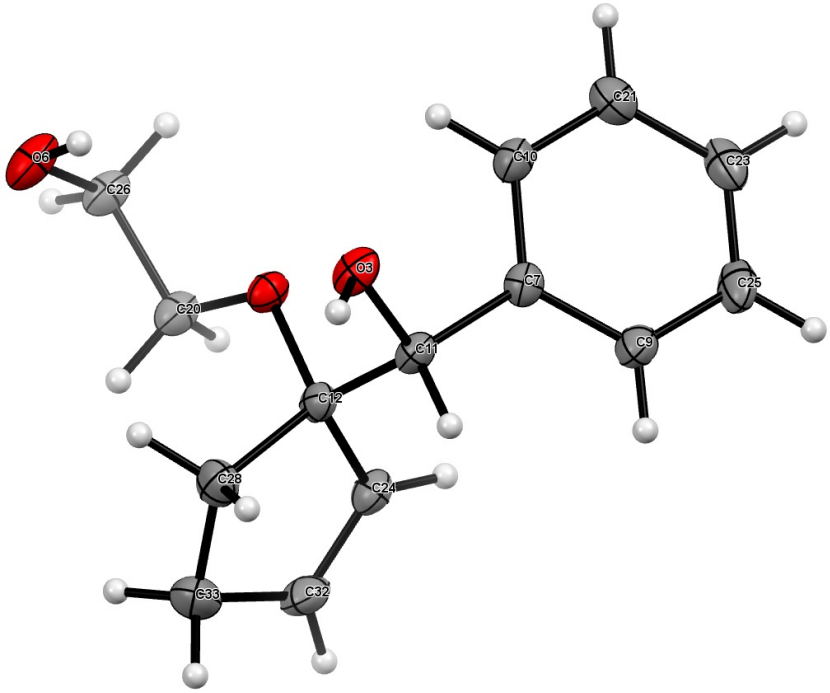


Figure S1. ORTEP structure of (1*R*,1'*S*)-**4o**. Thermal ellipsoids are drawn at the 50% probability level.

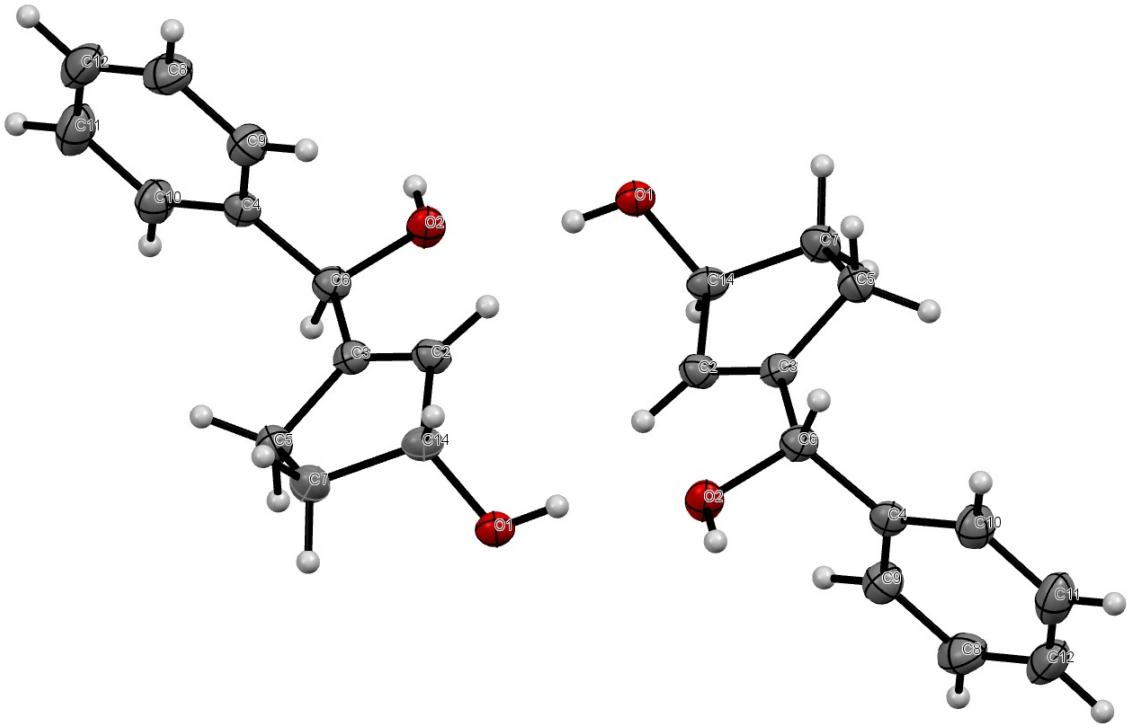


Figure S2. ORTEP structure of *rac*-**19o**. Thermal ellipsoids are drawn at the 50% probability level.

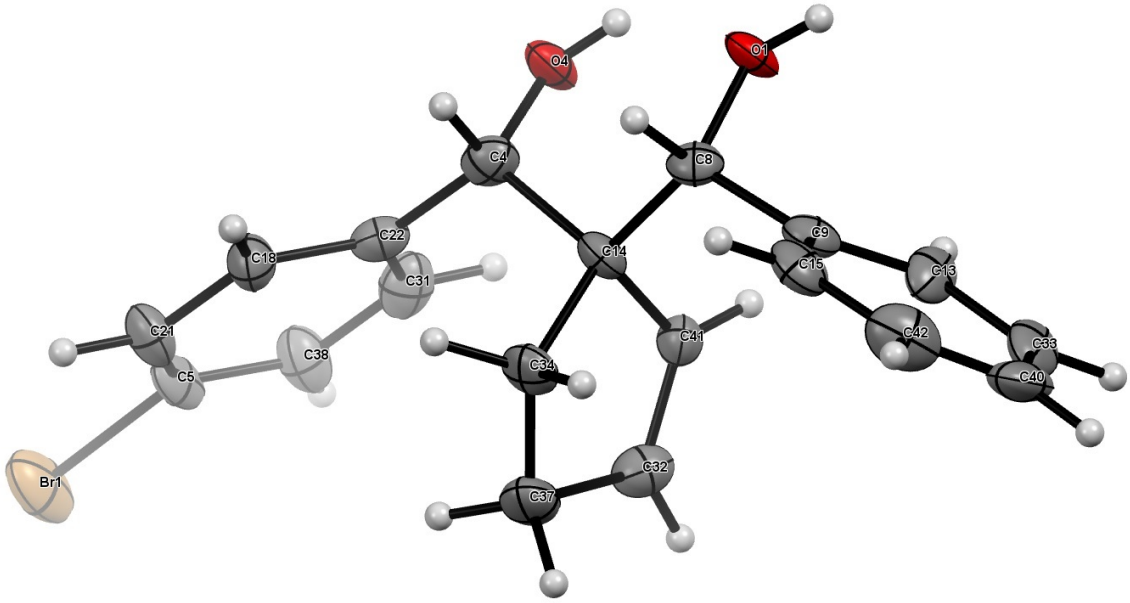


Figure S2. ORTEP structure of (1*S*,2*S*,3*R*)-**20o**. Thermal ellipsoids are drawn at the 50% probability level.

Table S1. Summary of X-ray crystallographic data for (1*R*,1'*S*)-**4o**, *rac*-**19o** and (1*S*,2*S*,3*R*)-**20o**.

Compound	(1*R*,1'*S*)-**4o**	*rac*-**19o**	(1*S*,2*S*,3*R*)-**20o**
CCDC Name	CCDC 967534	CCDC 967535	CCDC 967533
Deteremined Configuration	relative	relative	absolute
Empirical Formula	$C_{14}H_{18}O_3$	$C_{12}H_{14}O_2$	$C_{19}H_{19}BrO_2$
Formula Weight	234.29	190.24	359.26
Crystal System	triclinic	monoclinic	triclinic
Crystal Size / mm	0.524 × 0.442 × 0.194	0.680 × 0.278 × 0.095	0.654 × 0.241 × 0.218
a / Å	7.858(2)	11.5695(9)	7.6581(5)
b / Å	7.905(2)	6.0722(4)	10.9491(8)
c / Å	11.434(2)	15.1263(9)	11.8918(9)
a / °	74.344(4)	90.0000	76.123(2)
b / °	87.755(4)	110.659(2)	82.045(3)
g / °	65.930(3)	90.0000	70.713(2)
V / Å^3	622.4(2)	994.3(1)	911.8(1)
Space Group	*P*1 (#1)	$P2_1/c$ (#14)	*P*1 (#1)
Z value	2	4	2
D_{calc} / g cm^{-3}	1.250	1.271	1.308
Temperature / K	123	123	123
$2q_{max}$ / °	55.0	55.0	54.9
m (MoK$_a$) / cm^{-1}	0.865	0.850	22.648
No. of Reflections Measured	Total : 6107 Unique : 4623 (R_{int} = 0.0142)	Total : 9131 Unique : 2258 (R_{int} = 0.0384)	Total : 8923 Unique : 6791 (R_{int} = 0.0518) Friedel pairs:2663
No. of Observations (All reflections)	4623	2258	6791
Residuals: R_1 (I > 2.00s (I))	0.0352	0.0418	0.0588
Residuals: wR_2 (All reflections)	0.1065	0.1134	0.1599
Goodness of Fit Indicator (*GOF*)	1.086	1.075	1.134
Maximum peak in Final Diff. Map / Å^3	–0.28 e$^-$	0.31 e$^-$	1.24 e$^-$
Minimum peak in Final Diff. Map / Å^3	–0.23 e$^-$	–0.19 e$^-$	–0.79 e$^-$
Flack parameter	*	–	0.023(13)

*We did not obtain the Flack parameter because the purpose of this analysis is to determine the relative configuration of **4o**.

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Chapter 3

Copper(I)-Catalyzed Enantioselective Borylation of Allyl Acylals: A Novel Approach for α-Chiral γ-Acetoxyallylboronates

Abstract: A novel approach has been developed for the enantioselective synthesis of α-chiral γ-acetoxyallylboronates via the copper(I)-catalyzed γ-boryl-substitution of allyl acylals. This reaction proceeded with high *E*/*Z* selectivity and enantioselectivity (*E*/*Z* = >99:1, up to 80% yield, up to 99% ee). The subsequent allylation of aldehyde with the allylboronate afforded the mono-protected *anti*-1,2-diol derivative with high stereoselectivity.

3.1 Introduction

The asymmetric aldehyde allylation with allylboronates is a useful transformation in organic synthesis because of the high synthetic utility of the 1,2-diol products.[1] Allylboronates bearing a substituent at their γ-position relative of the boron atom are especially important organometallic reagents for the construction of consecutive chiral centers via C–C bond forming reactions because they can react with aldehydes in a highly stereospecific manner through a six-membered transition state.[2] In particular, optically active γ-alkoxyallylboronates have been widely used for the preparation of chiral 1,2-diol moieties, which can be found in a wide range of natural products and synthetic drugs.[3] However, the synthetic methods used for the construction of these boronates typically require a boron source bearing stoichiometric chiral auxiliary.[4]

Previously, we reported the first catalytic synthesis of α-chiral linear or carbocyclic γ-alkoxyallylboronates via the copper(I)-catalyzed γ-boryl substitution of allyl acetals.[5] Although our reaction showed high enantioselectivity and broad substrate scope in terms of its functional group compatibility, it was not amenable to sterically hindered substrates because they exhibited poor reactivity toward the boryl copper nucleophile. In addition, this reaction required harsh reaction conditions to allow for the removal of the benzyl groups from the mono-protected 1,2-diols, which were obtained by the aldehyde allylation with the corresponding γ-alkoxyallylboronates. Furthermore, the route required for the synthesis of the dibenzyl acetal substrates showed limited substrate scope, as well as being a laborious and time-consuming procedure.[6]

To address these issues, we focused on allyl acylals as alternative substrates for the copper-catalyzed boryl substitution reaction. Allyl acylals have been shown to be well suited to nucleophilic substitution reactions, such as palladium-catalyzed asymmetric alkylations[7] or Lewis acid-catalyzed cyanation.[8] We therefore expected that allyl acylals would be more reactive than allyl acetals toward nucleophilic boryl substitution reactions because the acetoxy group in the former is more electron withdrawing than the ether group in the latter, making the LUMO of the allyl acylal substrate lower in energy and more reactive toward a nucleophilic boryl copper intermediate. Furthermore, acetyl groups can be removed under milder conditions than those required to remove ether groups, making this process more efficient than our previous method.[9] Notably, a facile synthetic method has been reported for the direct construction of allyl acylals from aldehydes and acetic anhydride using an acid catalyst.[10]

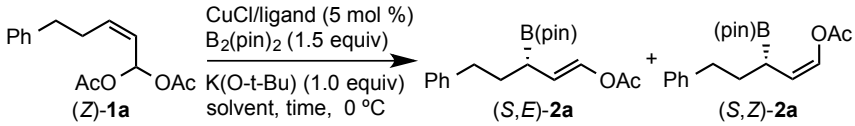
Herein, we report the enantioselective synthesis of α-chiral γ-acetoxyallylboronates using a chiral copper catalyst and bis(pinacolato)diboron as a boron source. Notably, this reaction was successfully

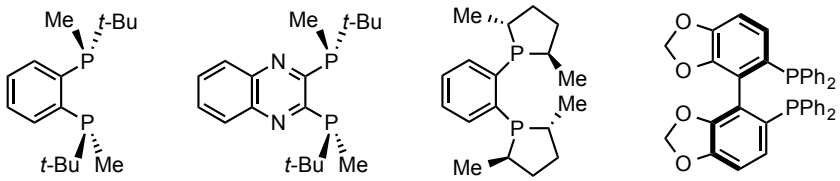
applied to a wide range of allyl acylal substrates, including sterically hindered compounds, to afford the desired products in good yields.

3.2 Optimization of Reaction Conditions

Initial optimization studies focused on the *E*/*Z* selectivity and enantioselectivity of the copper(I)-catalyzed boryl substitution of an allyl acylal to afford the corresponding allylboronate. The reaction of acylal (*Z*)-**1a** with $B_2(pin)_2$ in the presence of CuCl/(*R*,*R*)-BenzP* as a ligand (5 mol %) and K(O-*t*-Bu) as a base (1 equiv) in THF or toluene afforded mixtures of the corresponding (*E*)- and (*Z*)-products (Table 1, entries 1 and 2).[11] In our previous study involving the borylation of allyl acetals, we only ever observed the formation of the (*E*)-isomer as a single product, which we attributed to the substrate undergoing an *anti*-S_N2' reaction mechanism with a fixed conformation because of the 1,3-allylic strain of the substrate (see Electronic Supplementary Information).[5,12] The use of 1,3-dimethyl-2-imidazolidinone (DMI) as a solvent provided the (*E*)-product with high *E*/*Z* selectivity and excellent enantioselectivity (73% yield, *E*/*Z* = 98:2, 89% ee; Table 1, entry 3). Several other chiral ligands, including (*R*,*R*)-QuinoxP*, (*R*)-Segphos and (*R*,*R*)-Me-Duphos, were also tested, but resulted in poor yields and *E*/*Z* selectivities (Table 1, entries 4–6). The amounts of base and $B_2(pin)_2$ added to the reaction also had a considerable impact in the reactivity. For example, the use of a catalytic amount of K(O-*t*-Bu) (10 mol %) yielded a trace amount of the desired product, whereas the use of small excesses of K(O-*t*-Bu) (1.5 equiv) and $B_2(pin)_2$ (2.0 equiv) resulted in high yield with excellent *E*/*Z*- and enantioselectivity (79% yield, *E*/*Z* = >99:1, 95% ee; Table 1, entry 8).

Table 1. Optimization of the Reaction Conditions for the Copper(I)-Catalyzed Enantioselective Boryl Substitution of Allyl Acylal (*Z*)-**1a**[a]





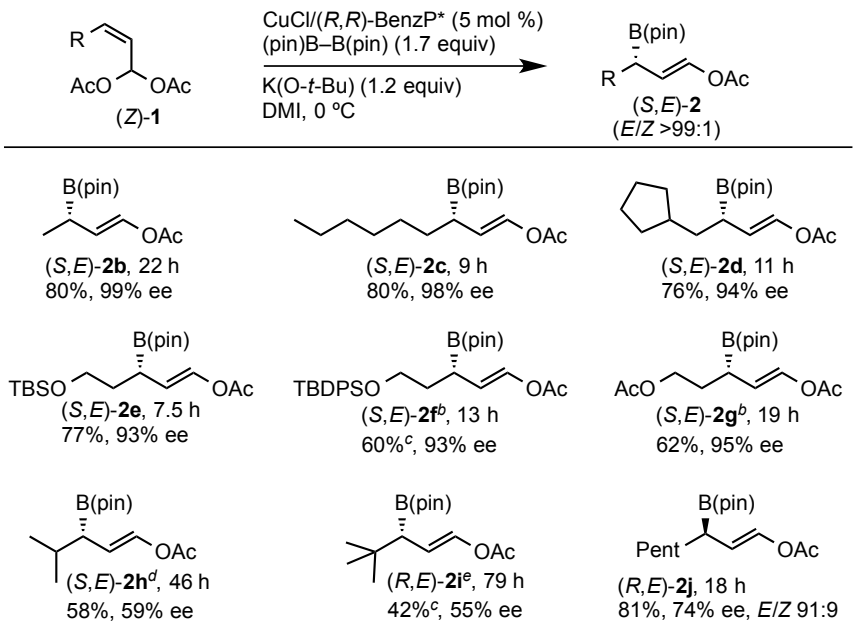
Entry	Solvent	Ligand	time (h)	*E*/*Z*[b]	yield (%)[c]	ee[d]
1	THF	(*R*,*R*)-BenzP*	30	82:18	78	93
2	toluene	(*R*,*R*)-BenzP*	48	76:24	74	92
3	DMI	(*R*,*R*)-BenzP*	45	98:2	73	89
4	DMI	(*R*,*R*)-QuinoxP*	24	90:10	30	–
5	DMI	(*R*)-Segphos	24	87:13	23	–
6	DMI	(*R*,*R*)-Me-Duphos	24	79:21	30	–
7[e]	DMI	(*R*,*R*)-BenzP*	24	–	trace	–
8[f]	DMI	(*R*,*R*)-BenzP*	28	>99:1	79	95

[a]Reagents and conditions: CuCl (0.01 mmol), ligand (0.01 mmol), (*Z*)-**1a** (0.2 mmol), bis(pinacolato)diboron (0.3 mmol), and K(O-*t*-Bu) (0.2 mmol) in solvent (0.4 mL) at 0 °C. [b]The E/*Z* selectivity was determined by GC. [c]NMR yield. [d]The ee values of the products were determined by HPLC analysis. [e]The ee value of the major product was difficult to determine using HPLC analysis because both SiO_2 and chiral column chromatography resulted in an insufficient separation of the major product and the unconsumed substrate.[f]10 mol % of K(O-*t*-Bu) was used. [g]2.0 equiv. of $B_2(pin)_2$ and 1.5 equiv. of K(O-*t*-Bu) were used. 0.5 mmol scale.

3.3 Substrate Scope of The Copper(I)-Catalyzed Borylation of Allyl Acylals

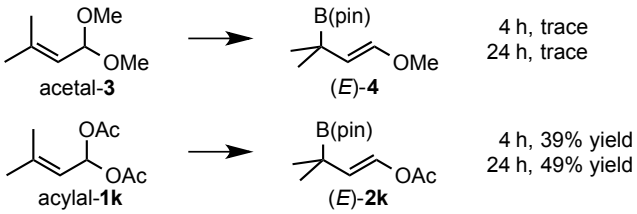
As shown in Table 2, various α-chiral γ-acetoxyallylboronates were obtained in high yields and enantioselectivities under the optimized reaction conditions. Furthermore, several optically active products bearing an alkyl substituent (e.g., R = methyl, hexyl, methylcyclopentyl) were obtained in high yields and enantioselectivities [(*S*,*E*)-**2b**, 80% yield, 99% ee; (*S*,*E*)-**2c**, 80% yield, 98% ee; (*S*,*E*)-**2d**, 76% yield, 94% ee]. This reaction also showed good functional group tolerance, as exemplified by the boryl substitution of substrates bearing a silyl ether or acetoxy group, which proceeded in high yield and excellent enantioselectivity without any degradation of the functional groups [(*S*,*E*)-**2e**, 77% yield, 93% ee; (*S*,*E*)-**2f**, 60% yield, 93% ee; (*S*,*E*)-**2g**, 62% yield, 95% ee]. σ-Branched allyl acylals [(*Z*)-**1h** and (*Z*)-**1i**], which have steric congestion around their C=C bond, also reacted smoothly to give the corresponding borylated products (58 and 42% yield, respectively), but the enantiomeric excess of these products were unfortunately low (59 and 55% ee, respectively), compared with (*S*,*E*)-**2b** and (*S*,*E*)-**2c**. The borylation of the (*E*)-substrate (*E*)-**1j** (*E*/*Z* = 95:5) proceeded with poor enantioselectivity to give the corresponding product with the opposite absolute configuration for the boron atom [(*R*,*E*)-**2j**, 81% yield, 74% ee, *E*/*Z* = 91:9].

Table 2. Substrate Scope of the Copper(I)-Catalyzed Enantioselective Boryl Substitution of Allyl Acylal (*Z*)-**1**[a]



[a]Reagents and conditions: CuCl (0.025 mmol), (*R*,*R*)-BenzP* (0.025 mmol), (*Z*)-**1** (0.5 mmol), bis(pinacolato)diboron (0.85 mmol) and K(O-*t*-Bu) (0.6 mmol) in DMI (1.0 mL) at 0 °C. The ee values of the products were determined by HPLC analysis. [b]1.5 equiv. of K(O-*t*-Bu) and 2.0 equiv. of $B_2(pin)_2$ were used. [c]NMR yield. [d]THF (0.3 mL) and DMI (0.3 mL) were used as a solvent. 10 mol % of CuCl and (*R*,*R*)-BenzP* were used. [e]THF (1.0 mL) was used as a solvent. 15 mol % of CuCl and (*R*,*R*)-BenzP* were used. 0.2 mmol scale.

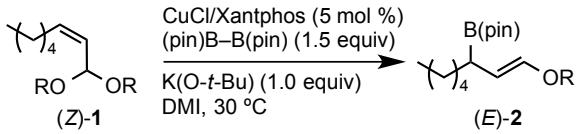
We then proceeded to compare the reactivities of the allyl acetal and acylal substrates. Ally acetal **3** and acylal **1k**, which both have a tri-substituted alkene moiety, were selected as model substrates. The boryl substitution of acetal **3** provided only a trace amount of the corresponding borylated product (*E*)-**4** in 4 h. Even after an extended reaction time (>24 h), the allyl acetal **3** remained largely intact. The low conversion of the acetal substrate was attributed to steric hindrance around the C–C double bond of the substrate and the poor leaving group ability of the methyl ether group compared with the acetyl group. In contrast, the acylal substrate **1k** reacted much more effectively than the acetal to give the borylated product in 49% yield after 24 h (Scheme 1). These results therefore demonstrate that acylal substrates can undergo allyl substitution much more effectively than the corresponding acetals.

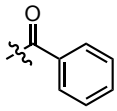


Reaction Conditions:
CuCl/Xantphos (5 mol %), $B_2(pin)_2$ (1.5 equiv)
K(O-*t*-Bu) (1.0 equiv), THF, 30 ºC

Scheme 1. γ-Borylation of Trisubstituted Allyl Acetal and Acylal with CuCl/Xantphos Catalyst System[a]

Effect of leaving group of substrates in this borylation was investigated (Scheme 2). The borylation of the allylic geminal diacetate proceeded smoothly to give the corresponding product in high yield (entry 1). On the other hands, both borylations of the allylic geminal dipivalate and dibenzoate proceeded with long reaction times to provide the corresponding products in low yield, respectively (entries 2 and 3).

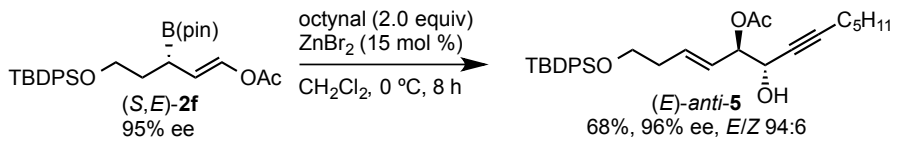


entry	R	time (h)	yield (%)
1		6	69
2		41	42
3		51	5

Scheme 2. Impact of Leaving Group in γ-Borylation of Allyl Acylals with Cu(I) Catalyst[a]

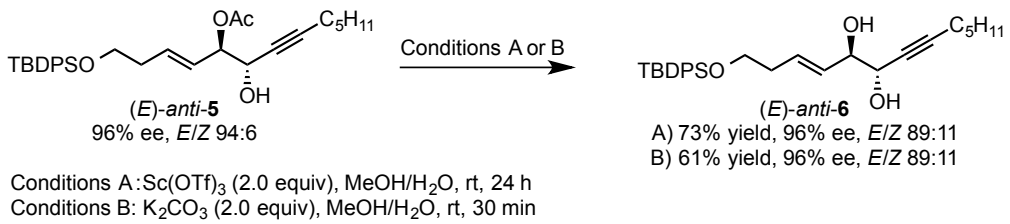
3.4 Aldehyde Allylation with Linear γ-Acetoxyallylboronates and Deprotection of the Product

The allylboronates (*S,E*)-**2f** prepared using our new method were subsequently applied to the stereoselective aldehyde allylation (Scheme 3). Octynal was successfully allylated with boronate (*S,E*)-**2f** in the presence of $ZnBr_2$, which was added as a Lewis acid catalyst.[13,14] We previously found that $ZnBr_2$ is an efficient catalyst for enhancing the stereoselectivity and accelerating the reaction rate for the allylation of aldehydes with γ-alkoxyallylboronates.[5] With this in mind, we investigated the reaction of octynal with (*S,E*)-**2f** in the presence of $ZnBr_2$. Pleasingly, this reaction provided the desired product in high stereoselectivity and good *E*/*Z* selectivity [(*E*)-*anti*-**5**, 68% yield, 100% es, *E*/*Z* = 94:6].



Scheme 3. Aldehyde Allylation with Optically Active γ-Acetoxyallylboronate (*S,E*)-**2f**[a]

The acetyl group in the allylation product (*E*)-*anti*-**5** was readily removed under acidic conditions (Scheme 4, Conditions A) to give the corresponding diol in 73% yield without lowering its enantiomeric purity. The acetyl group was also removed under basic conditions to afford the desired product (*E*)-*anti*-**6** in good yield without any degradation of the functional group or loss of optical purity (Scheme 4, Conditions B).



Scheme 4. Deprotection of the Acetyl Group in the Allylation Products under Acidic and Basic Conditions

3.5 Conclusion

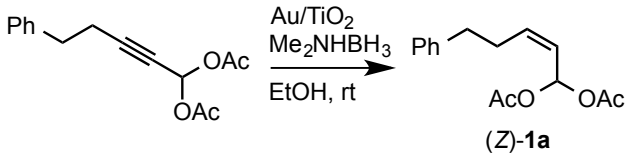
In summary, we have developed a new method for the asymmetric synthesis of chiral γ-acetoxyallylboronates via the copper(I)-catalyzed boryl substitution of allyl acylals. The resulting allylboronates were used to achieve the highly stereoselective aldehyde allylation. Furthermore, the acetyl group of the allylated product was readily removed under basic and acidic conditions to give the corresponding (*E*)-1,2-diol. This reaction therefore represents a useful method for the synthesis of 3-(*E*)-alkenyl-*anti*-1,2-diols.

3.6 Experimental Data

Preparation of Allyl Acylal Substrates

The allyl acylal **1k** and allyl acetal **3** were synthesized according to the literature procedure. [16,17]

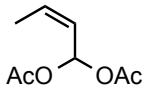
Preparation of (*Z*)-5-phenylpent-2-ene-1,1-diyl diacetate [(*Z*)-1a].[15]



Propargyl diacetate was synthesized through the reaction of propargyl aldehyde and acetic anhydride according to the literature procedure.[18] To an oven-dried 50 mL two-neck round bottomed flask, 5-phenylpent-2-yne-1,1-diyl diacetate (1.4353 g, 5.51 mmol) and dry EtOH (13 mL) were charged under nitrogen atmosphere at room temperature. After addition of Me_2NHBH_3 (603.1 mg, 10.2 mmol), Au/TiO_2 (653.5 mg) were added immediately to the solution. After the completion of the reaction was checked by GLC, the mixture was directly filtered through a short silica-gel column with ethyl acetate/hexane (10:90) as the eluent. After removal of the solvents under reduced pressure, the crude product was purified with flash column chromatography (SiO_2, ethyl acetate/hexane, 1:99–6:94) to give the corresponding (*Z*)-allyl acylal **1a** as a colorless oil (514.9 mg, 1.96 mmol, 36% isolated yield).

^{1}H NMR (392 MHz, $CDCl_3$, δ): 2.05 (s, 6H), 2.55–2.64 (m, 2H), 2.70 (t, *J* = 7.4 Hz, 2H), 5.49 (ddt, *J* = 1.4, 8.3, 11.0 Hz, 1H), 5.76 (dt, *J* = 7.6, 10.8 Hz, 1H), 7.14–7.30 (m, 5H), 7.38 (d, *J* = 9.0 Hz, 1H). ^{13}C NMR (99 MHz, $CDCl_3$, δ): 20.8 (CH_3), 29.7 (CH_2), 35.3 (CH_2), 86.0 (*C*H), 123.3 (*C*H), 125.9 (*C*H), 128.3 (*C*H), 128.5 (*C*H), 136.6 (*C*H), 141.0 (*C*), 168.6 (*C*). HRMS-ESI (*m*/*z*): $[M+Na]^+$ calcd for $C_{15}H_{18}O_4Na$, 285.10973; found, 285.10964.

(*Z*)-But-2-ene-1,1-diyl diacetate [(*Z*)-1b].

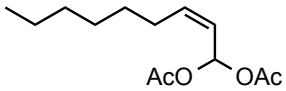


(*Z*)-**1b**

^{1}H NMR (392 MHz, $CDCl_3$, δ): 1.84 (dd, *J* = 1.8, 7.3 Hz, 3H), 2.09 (s, 6H), 5.51 (ddq, *J* = 1.8, 8.7, 10.6 Hz, 1H), 5.84 (ddq, *J* = 0.8, 7.1, 10.9 Hz, 1H), 7.48 (dd, *J* = 0.8, 8.6 Hz, 1H). ^{13}C NMR (99 MHz, $CDCl_3$, δ): 13.7 (CH_3), 20.9 (CH_3), 86.0 (*C*H), 123.8 (*C*H), 132.5 (*C*H), 168.7 (*C*). HRMS-EI

(*m*/*z*): $[M–CH_3]^+$ calcd for $C_7H_9O_4$, 157.05008; found, 157.05005.

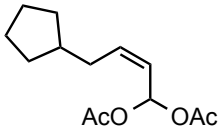
(*Z*)-Non-2-ene-1,1-diyl diacetate [(*Z*)-1c].



(*Z*)-**1c**

^{1}H NMR (392 MHz, $CDCl_3$, δ): 0.88 (t, *J* = 6.9 Hz, 3H), 1.21–1.43 (m, 8H), 2.08 (s, 6H), 2.24 (dq, *J* = 1.4, 7.7 Hz, 2H), 5.48 (ddt, *J* = 1.5, 8.3, 11.2 Hz, 1H), 5.74 (dt, *J* = 7.6, 11.8 Hz, 1H), 7.46 (dd, *J* = 1.0, 8.0 Hz, 1H). ^{13}C NMR (99 MHz, $CDCl_3$, δ): 14.0 (CH_3), 20.8 (CH_3), 22.5 (CH_2), 28.0 (CH_2), 28.8 (CH_2), 29.2 (CH_2), 31.6 (CH_2), 86.1 (*C*H), 122.7 (*C*H), 138.2 (*C*H), 168.6 (*C*). HRMS-ESI (*m*/*z*): $[M+Na]^+$ calcd for $C_{13}H_{22}O_4Na$, 265.14103; found, 265.14106.

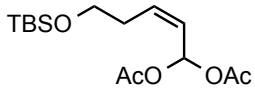
(*Z*)-4-Cyclopentylbut-2-ene-1,1-diyl diacetate [(*Z*)-1d].



(*Z*)-**1d**

^{1}H NMR (392 MHz, $CDCl_3$, δ): 1.08–1.19 (m, 2H), 1.45–1.67 (m, 4H), 1.69–1.79 (m, 2H), 1.83 (sex, *J* = 7.4 Hz, 1H), 2.08 (s, 6H), 2.26 (dt, *J* = 1.7, 7.4 Hz, 2H), 5.50 (ddt, *J* = 1.5, 8.2, 11.0 Hz, 1H), 5.77 (dt, *J* = 7.4, 11.5 Hz, 1H), 7.46 (dd, *J* = 0.8, 8.2 Hz, 1H). ^{13}C NMR (99 MHz, $CDCl_3$, δ): 20.8 (CH_3), 24.9 (CH_2), 32.1 (CH_2), 33.9 (CH_2), 39.7 (*C*H), 86.1 (*C*H), 122.8 (*C*H), 137.4 (*C*H), 168.6 (*C*). HRMS-ESI (*m*/*z*): $[M+Na]^+$ calcd for $C_{13}H_{20}O_4Na$, 263.12538; found, 263.12506.

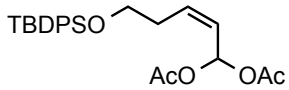
(*Z*)-5-[(*tert*-Butyldimethylsilyl)oxy]pent-2-ene-1,1-diyl diacetate [(*Z*)-1e].



(*Z*)-**1e**

^{1}H NMR (392 MHz, $CDCl_3$, δ): 0.04 (s, 6H), 0.88 (s, 9H), 2.08 (s, 6H), 2,48 (dq, *J* = 1.7, 6.6 Hz, 2H), 3.66 (t, *J* = 6.3 Hz, 2H), 5.57 (ddt, *J* = 1.5, 8.4, 11.2 Hz, 1H), 5.84 (dt, *J* = 7.4, 10.8 Hz, 1H), 7.43 (dd, *J* = 0.6, 8.4 Hz, 1H). ^{13}C NMR (99 MHz, $CDCl_3$, δ): –5.4 (CH_3), 18.2 (*C*), 20.8 (CH_3), 25.8 (CH_3), 31.4 (CH_2), 62.1 (CH_2), 86.1 (*C*H), 124.0 (*C*H), 134.5 (*C*H), 168.6 (*C*). HRMS-ESI (*m*/*z*): $[M+Na]^+$ calcd for $C_{15}H_{28}O_5NaSi$, 339.15982; found, 339.16010.

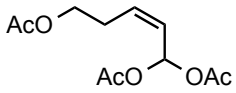
(*Z*)-5-[(*tert*-Butyldiphenylsilyl)oxy]pent-2-ene-1,1-diyl diacetate [(*Z*)-1f].



(*Z*)-**1f**

^{1}H NMR (392 MHz, $CDCl_3$, δ): 1.03 (s, 9H), 2.05 (s, 6H), 2.54 (dq, *J* = 1.6, 13.7 Hz, 2H), 3.71 (t, *J* = 6.3 Hz, 2H), 5.58 (ddt, *J* = 1.5, 8.2, 11.1 Hz, 1H), 5.87 (dt, *J* = 7.4, 11.2 Hz, 1H), 7.34–7.47 (m, 7H), 7.62–7.69 (m, 4H). ^{13}C NMR (99 MHz, $CDCl_3$, δ): 19.2 (*C*), 20.9 (CH_3), 26.7 (CH_3), 31.3 (CH_2), 62.9 (CH_2), 86.2 (*C*H), 124.1 (*C*H), 127.6 (*C*H), 129.6 (*C*H), 133.6 (*C*), 134.7 (*C*H), 135.5 (*C*H), 168.6 (*C*). HRMS-ESI (*m*/*z*): $[M+Na]^+$ calcd for $C_{25}H_{32}O_5NaSi$, 463.19112; found, 463.19195.

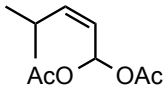
(*Z*)-Pent-2-ene-1,1,5-triyl triacetate [(*Z*)-1g].



(*Z*)-**1g**

^{1}H NMR (392 MHz, $CDCl_3$, δ): 2.04 (s, 3H), 2.09 (s, 6H), 2.62 (dq, *J* = 1.5, 6.9 Hz, 2H), 4,11 (t, *J* = 6.7 Hz, 2H), 5.62 (ddt, *J* = 1.5, 8.2, 11.0 Hz, 1H), 5.75 (dt, *J* = 7.5, 11.1 Hz, 1H), 7.43 (dd, *J* = 1.2, 7.8 Hz, 1H). ^{13}C NMR (99 MHz, $CDCl_3$, δ): 20.8 (CH_3), 27.4 (CH_2), 63.0 (CH_2), 85.9 (*C*H), 125.3 (*C*H), 132.7 (*C*H), 168.6 (*C*), 170.9 (*C*). HRMS-ESI (*m*/*z*): $[M+Na]^+$ calcd for $C_{11}H_{16}O_6Na$, 267.08391; found, 267.08394.

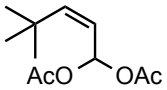
(*Z*)-4-Methylpent-2-ene-1,1-diyl diacetate [(*Z*)-1h].



(*Z*)-**1h**

^{1}H NMR (392 MHz, $CDCl_3$, δ): 0.98 (d, *J* = 6.7 Hz, 6H), 2.08 (s, 6H), 2.78–2.93 (m, 1H), 5.37 (dd, *J* = 8.2, 11.0 Hz, 1H), 5.55 (t, J = 10.6 Hz, 1H), 7.47 (d, J = 7.5 Hz, 1H). ^{13}C NMR (99 MHz, $CDCl_3$, δ): 20.9 (CH_3), 22.8 (CH_3), 27.5 (*C*H), 86.2 (*C*H), 120.3 (*C*H), 144.9 (*C*H), 168.6 (*C*). HRMS-ESI (*m*/*z*): $[M+Na]^+$ calcd for $C_{10}H_{16}O_4Na$, 223.09408; found, 223.09427.

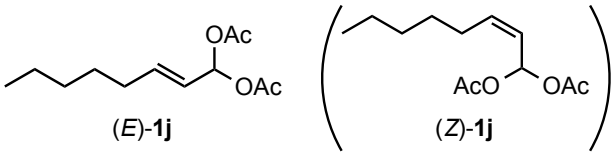
(*Z*)-4,4-Dimethylpent-2-ene-1,1-diyl diacetate [(*Z*)-1i].



(*Z*)-**1i**

^{1}H NMR (392 MHz, $CDCl_3$, δ): 1.17 (s, 9H), 2.08 (s, 6H), 5.29 (dd, *J* = 9.0, 12.2 Hz, 1H), 5.67 (dd, *J* = 1.2, 12.7 Hz, 1H), 7.71 (dd, *J* = 0.8, 9.0 Hz, 1H). ^{13}C NMR (99 MHz, $CDCl_3$, δ): 20.9 (CH_3), 30.7 (CH_3), 34.2 (*C*), 85.8 (*C*H), 120.6 (*C*H), 147.0 (*C*H), 168.6 (*C*). HRMS-ESI (*m*/*z*): $[M+Na]^+$ calcd for $C_{11}H_{18}O_4Na$, 237.10973; found, 237.10982.

(*E*)-Oct-2-ene-1,1-diyl diacetate [(*E*)-1j].



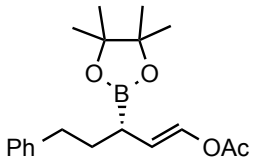
(*E*)-**1j** (*Z*)-**1j**

(*E*)-Allyl acylal was synthesized from the corresponding α,β-unsaturated aldehyde.[2]

^{1}H NMR (392 MHz, $CDCl_3$, * indicates signals of the minor isomer, δ): 0.73* (t, *J* = 7.1 Hz, 3H), 0.89 (t, *J* = 6.7 Hz, 3H), 1.21–1.36 (m, 6H), 1.40 (quint, *J* = 7.4 Hz, 2H), 2.09 (s, 6H), 5.22–5.29* (m, 1H), 5.35–5.42* (m, 1H), 5.53 (dd, *J* = 6.5, 15.5 Hz, 1H), 6.03 (dt, *J* = 6.7, 15.3 Hz, 1H), 7.10 (d, *J* = 6.7 Hz, 1H), 7.37* (d, *J* = 12.5 Hz, 1H). ^{13}C NMR (99 MHz, $CDCl_3$, δ): 13.9 (CH_3), 20.8 (CH_3), 21.1* (CH_3), 22.3 (CH_2), 24.6* (CH_2), 28.0 (CH_2), 31.2 (CH_2), 31.3* (CH_2), 31.8 (CH_2), 34.5* (CH_2), 71.2* (*C*H), 89.7 (*C*H), 112.8* (*C*H), 123.0 (*C*H), 138.2 (*C*H), 138.7* (*C*H), 168.6 (*C*). HRMS-ESI (*m*/*z*): $[M+Na]^+$ calcd for $C_{12}H_{20}O_4Na$, 251.12538; found, 251.12566.

Characterization of Boryl Substitution Products

(*S*,*E*)-5-Phenyl-3-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)pent-1-en-1-yl acetate [(*S*,*E*)-2a].

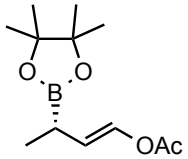


(*S*,*E*)-**2a**

The reaction was performed according to the representative procedure with (*Z*)-**1a** (129.5 mg, 0.494 mmol) and ^{1}H NMR yield of (*S*,*E*)-**2a** was 79%. The title compound was purified by silica-gel chromatography (Et_2O:hexane = 0/100 to 10/90). 52% isolated yield (84.8 mg, 0.257 mmol), 95% ee.

^{1}H NMR (392 MHz, $CDCl_3$, δ): 1.25 (s, 12H), 1.63–1.93 (m, 3H), 2.11 (s, 3H), 2.52–2.71 (m, 2H), 5.45 (dd, *J* = 9.4, 12.5 Hz, 1H), 7.09 (d, *J* = 12.2 Hz, 1H), 7.13–7.31 (m, 5H). ^{13}C NMR (99 MHz, $CDCl_3$, δ): 20.7 (CH_3), 22.9 (br, B–*C*H), 24.6 (CH_3), 24.7 (CH_3), 32.8 (CH_2), 35.0 (CH_2), 83.4 (*C*), 115.4 (*C*H), 125.6 (*C*H), 128.2 (*C*H), 128.4 (*C*H), 135.2 (*C*H), 142.3 (*C*), 168.1 (*C*). HRMS-EI (*m*/*z*): $[M]^+$ calcd for $C_{19}H_{27}BO_4$, 329.20387; found, 329.20481. $[\alpha]_D^{22.2}$ = +5.4 (*c* 1.0, $CHCl_3$, 95% ee). The ee value was determined by HPLC analysis [Daicel CHIRALPAK® OD-3, 2-PrOH:hexane = 0.25:99.75, 0.5 mL/min, 40 °C, retention time: 25.44 min (major enantiomer) and 24.83 min (minor enantiomer)].

(*S*,*E*)-3-(4,4,5,5-Tetramethyl-1,3,2-dioxaborolan-2-yl)but-1-en-1-yl acetate [(*S*,*E*)-2b].



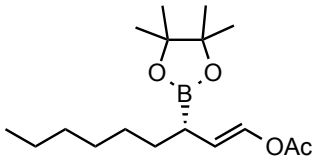
(*S*,*E*)-**2b**

The reaction was performed according to the representative procedure for (*Z*)-**1b** (86.4 mg, 0.502 mmol). The title compound was purified by silica-gel chromatography (Et_2O:hexane = 4/96 to 7/93). 80% isolated yield (96.7 mg, 0.403 mmol), 99% ee.

^{1}H NMR (392 MHz, $CDCl_3$, δ): 1.11 (d, *J* = 7.1 Hz, 3H), 1.24 (s, 12H), 1.84 (quint, *J* = 7.4 Hz, 1H), 2.10 (s, 3H), 5.54 (dd, *J* = 8.6, 12.5 Hz, 1H), 7.06 (dd, *J* = 1.4, 12.7 Hz, 1H). ^{13}C NMR (99 MHz, $CDCl_3$, δ): 15.2 (CH_3), 16.7 (br, B–*C*H), 20.7 (CH_3), 24.6 (CH_3), 83.4 (*C*), 117.4 (*C*H), 134.3

(*C*H), 168.2 (*C*). HRMS-EI (*m*/*z*): $[M]^+$ calcd for $C_{12}H_{21}BO_4$, 239.15692; found, 239.15697. $[\alpha]_D^{24.9}$ = –19.8 (*c* 1.0, $CHCl_3$, 99% ee). To determine the ee value, the C=C bond of the product was hydrogenated with Pd/C, then the boryl group was oxidized with $NaBO_3 \cdot 4H_2O$ followed by esterification with *p*-nitro benzoyl chloride. The ee value of the product was determined by HPLC analysis of the corresponding *p*-nitro benzoyl ester [Daicel CHIRALPAK® OD-3, 2-PrOH:hexane = 1:99, 0.5 mL/min. 40 °C, retention time: 60.99 min (major enantiomer) and 8.22 min (minor enantiomer)].

(*S*,*E*)-3-(4,4,5,5-Tetramethyl-1,3,2-dioxaborolan-2-yl)non-1-en-1-yl acetate [(*S*,*E*)-2c].

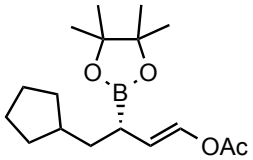


(*S*,*E*)-**2c**

The reaction was performed according to the representative procedure with (*Z*)-**1c** (123.0 mg, 0.508 mmol). The title compound was purified by silica-gel column chromatography (EtOAc:hexane = 1/99 to 5/95). 80% isolated yield (126.0 mg, 0.406 mmol), 98% ee.

^{1}H NMR (392 MHz, $CDCl_3$, δ): 0.87 (t, *J* = 6.9 Hz, 3H), 1.18–1.44 (m, 9H), 1.24 (s, 12H), 1.48–1.62 (m, 1H), 1.73 (q, *J* = 8.2 Hz, 1H), 2.10 (s, 3H), 5.41 (dd, *J* = 9.8, 12.5 Hz, 1H), 7.06 (dd, *J* = 1.0, 12.7 Hz, 1H). ^{13}C NMR (99 MHz, $CDCl_3$, δ): 14.0 (CH_3), 20.7 (CH_3), 22.6 (CH_2), 23.2 (br, B–*C*H), 24.6 (CH_3), 24.7 (CH_3), 28.8 (CH_2), 29.2 (CH_2), 30.9 (CH_2), 31.7 (CH_2), 83.2 (*C*), 115.8 (*C*H), 134.7 (*C*H), 168.1 (*C*). HRMS-EI (*m*/*z*): $[M]^+$ calcd for $C_{17}H_{31}BO_4$, 309.23517; found, 309.23560. $[\alpha]_D^{25.3}$ = –7.4 (*c* 1.0, $CHCl_3$, 98% ee). The ee value was determined by HPLC analysis [Daicel CHIRALPAK® OZ-3, 2-PrOH:hexane = 0.1:99.9, 0.5 mL/min, 40 °C, retention time: 29.60 min (major enantiomer) and 28.15 min (minor enantiomer). The UV light having wavelength in 220 nm was used to detect the product.].

(*S*,*E*)-4-Cyclopentyl-3-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)but-1-en-1-yl acetate [(*S*,*E*)-2d].

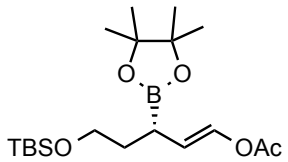


(*S*,*E*)-**2d**

The reaction was performed according to the representative procedure with (*Z*)-**1d** (121.9 mg, 0.507 mmol). The title compound was purified by silica-gel column chromatography (EtOAc:hexane = 0/100 to 4/96). 76% isolated yield (119.1 mg, 0.386 mmol), 94% ee.

^{1}H NMR (396 MHz, $CDCl_3$, δ): 0.99–1.13 (m, 2H), 1.24 (s, 12H), 1.38–1.64 (m, 6H), 1.67–1.85 (m, 4H), 2.09 (s, 3H), 5.39 (dd, *J* = 9.9, 12.3 Hz, 1H), 7.06 (dd, *J* = 0.8, 12.3 Hz, 1H). ^{13}C NMR (100 MHz, $CDCl_3$, δ): 20.7 (CH_3), 22.4 (br, B–*C*H), 24.6 (CH_3), 25.0 (CH_2), 25.2 (CH_2), 32.1 (CH_2), 32.8 (CH_2), 37.1 (CH_2), 39.0 (*C*H), 83.2 (*C*), 115.9 (*C*H), 134.6 (*C*H), 168.1 (*C*). HRMS-ESI (*m*/*z*): $[M+Na]^+$ calcd for $C_{17}H_{29}BO_4Na$, 330.20874; found, 330.20889. $[\alpha]_D^{27.3}$ = +11.4 (*c* 0.7, $CHCl_3$, 94% ee). To determine the ee value, the C=C bond of the product was hydrogenated with Pd/C, then the boryl group was oxidized with $NaBO_3 \cdot 4H_2O$ followed by esterification with *p*-nitro benzoyl chloride. The ee value of the product was determined by HPLC analysis of the corresponding *p*-nitro benzoyl ester [Daicel CHIRALPAK® OZ-3, 2-PrOH:hexane = 1:99, 0.5 mL/min. 40 °C, retention time: 69.55 min (major enantiomer) and 135.57 min (minor enantiomer)].

(*S*,*E*)-5-[(*tert*-Butyldimethylsilyl)oxy]-3-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)pent-1-en-1-yl acetate [(*S*,*E*)-2e].



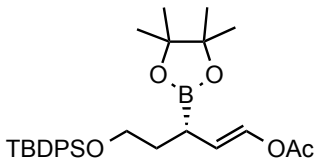
(*S*,*E*)-**2e**

The reaction was performed according to the representative procedure with (*Z*)-**1e** (158.4 mg, 0.501 mmol). The title compound was purified by silica-gel column chromatography (EtOAc:hexane = 2/98 to 4.5/95.5). 77% isolated yield (147.3 mg, 0.383 mmol), 93% ee.

^{1}H NMR (392 MHz, $CDCl_3$, δ): 0.04 (s, 6H), 0.88 (s, 9H), 1.24 (s, 12H), 1.53–1.65 (m, 1H), 1.79 (sex, *J* = 6.7 Hz, 1H), 1.84–1.94 (m, 1H), 2.10 (s, 3H), 3.60 (t, *J* = 6.7 Hz, 2H), 5.40 (dd, *J* = 9.8,

12.5 Hz, 1H), 7.07 (dd, J = 0.8, 12.5 Hz, 1H). ^{13}C NMR (99 MHz, $CDCl_3$, δ): –5.4 (CH_3), –5.3 (CH_3), 18.3 (C), 19.1 (br, B–CH), 20.7 (CH_3), 24.6 (CH_3), 24.7 (CH_3), 25.9 (CH_3), 33.5 (CH_2), 61.9 (CH_2), 83.3 (C), 115.1 (CH), 135.1 (CH), 168.0 (C). HRMS-EI (m/z): $[M–CH_3]^+$ calcd for $C_{18}H_{34}BO_5Si$, 368.23049; found, 368.23094. $[\alpha]_D^{24.4}$ = +5.5 (c 1.0, $CHCl_3$, 93% ee). To determine the ee value, the C=C bond of the product was hydrogenated with Pd/C, then the boryl group was oxidized with $NaBO_3 \cdot 4H_2O$ followed by esterification with p-nitro benzoyl chloride. The ee value of the product was determined by HPLC analysis of the corresponding p-nitro benzoyl ester [Daicel CHIRALPAK® OD-3, 2-PrOH:hexane = 3:97, 0.5 mL/min. 40 °C, retention time: 17.16 min (major enantiomer) and 19.12 min (minor enantiomer)].

(*S*,*E*)-5-[(*tert*-Butyldiphenylsilyl)oxy]-3-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)pent-1-en-1-yl acetate [(*S*,*E*)-2f].

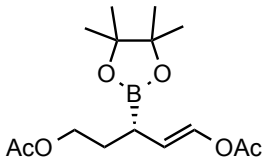


(*S*,*E*)-**2f**

The reaction was performed according to the representative procedure with (*Z*)-**1f** (221.3 mg, 0.502 mmol) and ^{1}H NMR yield of (*S*,*E*)-**2f** was 60%. The title compound was purified by silica-gel column chromatography (Et_2O:hexane = 5/95 to 7.5/92.5). 11% isolated yield (28.8 mg, 0.0566 mmol), 93% ee.

^{1}H NMR (392 MHz, $CDCl_3$, δ): 1.04 (s, 9H), 1.19 (s, 6H), 1.20 (s, 6H), 1.59–1.70 (m, 1H), 1.86 (sex, J = 6.7 Hz, 1H), 1.93–2.02 (m, 1H), 2.09 (s, 3H), 3.65 (t, J = 6.7 Hz, 2H), 5.38 (dd, J = 9.8, 12.5 Hz, 1H), 7.07 (d, J = 12.5 Hz, 1H), 7.32–7.44 (m, 6H), 7.63–7.69 (m, 4H). ^{13}C NMR (99 MHz, $CDCl_3$, δ): 19.2 (C), 20.7 (CH_3), 24.6 (CH_3), 24.7 (CH_3), 26.8 (CH_3), 33.4 (CH_2), 62.6 (CH_2), 83.4 (C), 115.2 (CH), 127.5 (CH), 129.4 (CH), 133.9 (C), 134.0 (C), 135.1 (CH), 135.5 (CH), 168.0 (C). The carbon directly attached to the boron atom was not detected, likely due to quadrupolar relaxation.[5,6] HRMS-ESI (m/z): $[M+Na]^+$ calcd for $C_{29}H_{41}O_5BNaSi$, 530.27448; found, 530.27482. $[\alpha]_D^{26.4}$ = +5.7 (c 0.6, $CHCl_3$, 93% ee). To determine the ee value, the C=C bond of the product was hydrogenated with Pd/C. The ee value of the product was determined by HPLC analysis of the corresponding alkyl boronate. [Daicel CHIRALPAK® OD-3, 2-PrOH:hexane = 0.25:99.75, 0.5 mL/min. 40 °C, retention time: 16.48 min (major enantiomer) and 15.60 min (minor enantiomer)].

(*S*,*E*)-3-(4,4,5,5-Tetramethyl-1,3,2-dioxaborolan-2-yl)pent-1-ene-1,5-diyl diacetate [(*S*,*E*)-2g].

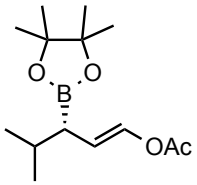


(*S*,*E*)-**2g**

The reaction was performed according to the representative procedure with (*Z*)-**1g** (122.9 mg, 0.503 mmol). The title compound was purified by silica-gel column chromatography (EtOAc:hexane = 9/91 to 14/86). 62% isolated yield (96.7 mg, 0.310 mmol), 91% ee.

^{1}H NMR (392 MHz, $CDCl_3$, δ): 1.24 (s, 12H), 1.64–1.77 (m, 1H), 1.82–1.96 (m, 2H), 2.04 (s, 3H), 2.10 (s, 3H), 3.98–4.16 (m, 2H), 5.39 (dd, *J* = 9.6, 12.3 Hz, 1H), 7.09 (d, *J* = 12.2 Hz, 1H). ^{13}C NMR (99 MHz, $CDCl_3$, δ): 19.6 (br, B–*C*H), 20.6 (*C*H_3), 20.9 (*C*H_3), 24.55 (*C*H_3), 24.63 (*C*H_3), 29.4 (*C*H_2), 63.3 (*C*H_2), 83.5 (*C*), 114.3 (*C*H), 135.4 (*C*H), 167.9 (*C*), 171.0 (*C*). HRMS-ESI (*m*/*z*): $[M+Na]^+$ calcd for $C_{15}H_{25}O_6BNa$, 334.16727; found, 334.16773. $[\alpha]_D^{27.6}$ = +28.6 (*c* 1.0, $CHCl_3$, 91% ee). The ee value was determined by HPLC analysis [Daicel CHIRALPAK® OJ-3, 2-PrOH:hexane = 3:97, 0.5 mL/min, 40 °C, retention time: 11.07 min (major enantiomer) and 10.69 min (minor enantiomer). The UV light having wavelength in 220 nm was used to detect the product.].

(*S*,*E*)-4-Methyl-3-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)pent-1-en-1-yl acetate [(*S*,*E*)-2h].



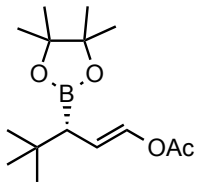
(*S*,*E*)-**2h**

The reaction was performed according to the representative procedure with (*Z*)-**1h** (38.6 mg, 0.193 mmol). The title compound was purified by silica-gel column chromatography. 58% isolated yield (29.8 mg, 0.111 mmol), 59% ee.

^{1}H NMR (392 MHz, $CDCl_3$, δ): 0.89 (d, *J* = 7.1 Hz, 3H), 0.93 (d, *J* = 6.7 Hz, 3H), 1.24 (s, 12H), 1.52 (dd, *J* = 7.6, 10.8 Hz, 1H), 1.82 (sept, *J* = 6.9 Hz, 1H), 2.10 (s, 3H), 5.40 (dd, *J* = 11.0, 12.1 Hz, 1H), 7.05 (d, *J* = 12.5 Hz, 1H). ^{13}C NMR (99 MHz, $CDCl_3$, δ): 20.8 (*C*H_3), 21.5 (*C*H_3), 22.3 (*C*H_3), 24.7 (*C*H_3), 29.6 (*C*H), 31.5 (br, B–*C*H), 83.2 (*C*), 114.3 (*C*H), 135.3 (*C*H), 168.1 (*C*). HRMS-EI (*m*/*z*): $[M]^+$ calcd for $C_{14}H_{25}BO_4$, 268.18485; found, 268.18509. $[\alpha]_D^{22.5}$ = +20.7 (*c* 1.0, $CHCl_3$, 59%

ee). The ee value was determined by HPLC analysis [Daicel CHIRALPAK® OZ-3, 2-PrOH:hexane = 0.5:99.5, 0.5 mL/min, 40 °C, retention time: 10.23 min (major enantiomer) and 9.19 min (minor enantiomer). The UV light having wavelength in 220 nm was used to detect the product.].

(*R*,*E*)-4,4-Dimethyl-3-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)pent-1-en-1-yl acetate [(*R*,*E*)-2i].

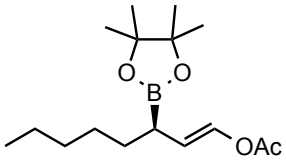


(*R*,*E*)-**2i**

The reaction was performed according to the representative procedure with (*Z*)-**1i** (108.1 mg, 0.505 mmol) and ^{1}H NMR yield of (*R*,*E*)-**2i** was 42%. The title compound was purified by silica-gel column chromatography (Et_2O:hexane = 2/98 to 10/90). 20% isolated yield (28.6 mg, 0.101 mmol), 55% ee.

^{1}H NMR (392 MHz, $CDCl_3$, δ): 0.94 (s, 9H), 1.24 (s, 12H), 1.54–1.65 (m, 1H), 2.11 (s, 3H), 5.49 (dd, *J* = 11.4, 12.2 Hz, 1H), 7.02 (d, *J* = 12.5 Hz, 1H). ^{13}C NMR (99 MHz, $CDCl_3$, δ): 20.8 (CH_3), 20.9 (br, B–*C*H), 24.7 (CH_3), 24.8 (CH_3), 29.2 (CH_3), 32.4 (*C*), 83.1 (*C*), 113.6 (*C*H), 135.4 (*C*H), 168.1 (*C*). HRMS-ESI (*m*/*z*): $[M+Na]^+$ calcd for $C_{15}H_{27}O_4BNa$, 304.19309; found, 304.19284. $[\alpha]_D^{26.5}$ = +13.8 (*c* 1.0, $CHCl_3$, 55% ee). The ee value was determined by HPLC analysis [Daicel CHIRALPAK® OZ-3, 2-PrOH:hexane = 0.5:99.5, 0.5 mL/min, 40 °C, retention time: 9.22 min (major enantiomer) and 8.63 min (minor enantiomer). The UV light having wavelength in 220 nm was used to detect the product.].

(*R*,*E*)-3-(4,4,5,5-Tetramethyl-1,3,2-dioxaborolan-2-yl)oct-1-en-1-yl acetate [(*R*,*E*)-2j].

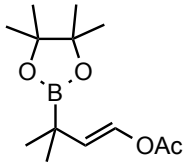


(*R*,*E*)-**2j**

The reaction was performed according to the representative procedure with (*E*)-**1j** (*E*/*Z* 95:5, 111.6 mg, 0.489 mmol). The title compound was purified by silica-gel column chromatography (Et_2O:hexane = 1:99 to 6:94). 81% isolated yield (118.0 mg, 0.398 mmol), 74% ee, *E*/Z 91:9.

^{1}H NMR (392 MHz, $CDCl_3$, * indicates signals of the minor isomer, δ): 0.87 (t, J = 6.7 Hz, 3H), 1.14–1.30 (m, 7H), 1.24 (s, 12H), 1.46–1.59 (m, 1H), 1.64–1.77 (m, 1H), 2.10 (s, 3H), 2.13* (s, 3H), 4.85* (dd, J = 6.3, 9.8 Hz, 1H), 5.41 (dd, J = 9.6, 12.3 Hz, 1H), 7.01* (d, J = 6.3 Hz, 1H), 7.06 (d, J = 12.5 Hz, 1H). ^{13}C NMR (99 MHz, $CDCl_3$, δ): 14.0 (CH_3), 20.7 (CH_3), 22.4 (CH_2), 23.2 (br, B–*C*H), 24.57 (CH_3), 24.63 (CH_3), 28.4 (CH_2), 28.6* (CH_2), 30.7* (CH_2), 30.8 (CH_2), 31.7 (CH_2), 83.2 (*C*), 115.3* (*C*H), 115.8 (*C*H), 133.4* (*C*H), 134.7 (*C*H), 168.0 (*C*). HRMS-EI (*m*/*z*): $[M]^+$ calcd for $C_{16}H_{29}BO_4$, 295.21952; found, 295.22001. $[\alpha]_D^{27.0}$ = –14.2 (*c* 1.0, $CHCl_3$, 74% ee). To determine the ee value, the C=C bond of the product was hydrogenated with Pd/C, then the boryl group was oxidized with $NaBO_3 \cdot 4H_2O$ followed by esterification with *p*-nitro benzoyl chloride. The ee value of the product was determined by HPLC analysis of the corresponding *p*-nitro benzoyl ester [Daicel CHIRALPAK® OD-3, 2-PrOH:hexane = 1.5:98.5, 0.5 mL/min. 40 °C, retention time: 44.13 min (major enantiomer) and 28.69 min (minor enantiomer)].

(*E*)-3-Methyl-3-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)but-1-en-1-yl acetate [(*E*)-2k].



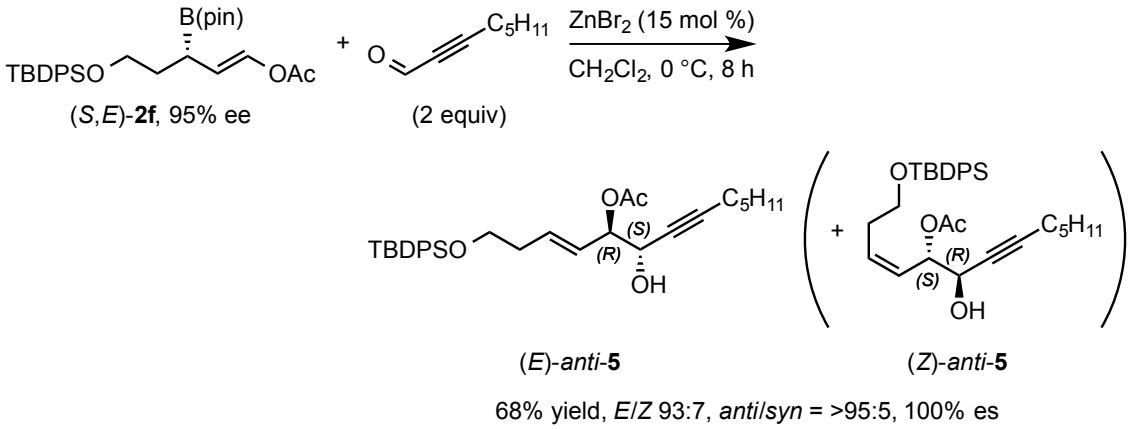
(*E*)-**2k**

The reaction was performed according to the representative procedure with **1k** (93.2 mg, 0.501 mmol) using Xantphos as a ligand instead of (*R*,*R*)-BenzP* and ^{1}H NMR yield of (*E*)-**2k** in 4 h and 24 h were 39% and 49%, respectively. The title compound was purified by silica-gel column chromatography (EtOAc:hexane = 1:99 to 5:95). 3% isolated yield (3.5 mg, 0.0138 mmol).

^{1}H NMR (392 MHz, $CDCl_3$, δ): 1.09 (s, 6H), 1.23 (s, 12H), 2.10 (s, 3H), 5.57 (d, J = 12.5 Hz, 1H), 7.03 (d, J = 12.5 Hz, 1H). ^{13}C NMR (99 MHz, $CDCl_3$, δ): 20.8 (CH_3), 24.1 (CH_3), 24.6 (CH_3), 83.4 (*C*), 123.2 (*C*H), 133.5 (*C*H), 168.3 (*C*). The carbon directly attached to the boron atom was not detected, likely due to quadrupolar relaxation.[19.20] HRMS-ESI (*m*/*z*): $[M+Na]^+$ calcd for $C_{13}H_{23}O_4BNa$, 276.16179; found, 276.16163.

Procedures of Aldehyde Allylation and Characterization of the Product

$ZnBr_2$-catalyzed allylation of 2-octynal with allylboronate (*S*,*E*)-2f



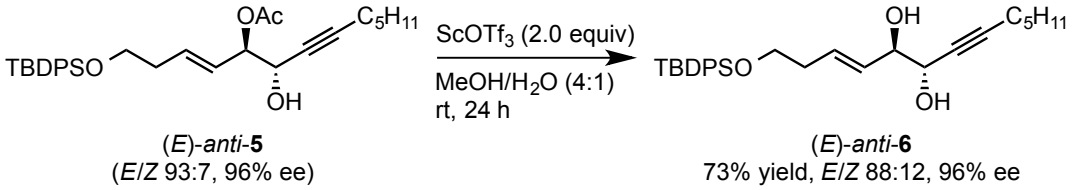
Dry $ZnBr_2$ (7.0 mg, 15 mol %) was added to a reaction vial sealed with a screw cap containing a silicon-coated rubber septum in the glove box under argon atmosphere. After the reaction vial was removed from the glove box, it was connected to a vacuum/nitrogen manifold through a needle. Dry CH_2Cl_2 (0.4 mL), (*S*,*E*)-**2f** (97.5 mg, 0.192 mmol) and 2-octynal (50.8 mg, 0.409 mmol) was successively added to the vial using a syringe, and stirred for 10 h at 0 °C. The use of dry $ZnBr_2$ is necessary for the high stereoselectivity of this aldehyde allylation. The reaction mixture was quenched by a CH_2Cl_2 solution of triethanolamine (10% v/v, 2.5 mL). The mixture was separated with water and EtOAc, and then extracted three times with EtOAc. The combined organic layer was dried over Na_2SO_4, filtered and evaporated. The crude product was purified by silica-gel chromatography (EtOAc:hexane = 11/89 to 14/86) to gve the corresponding *anti*-1,2-diol derivatives as a colorless oil. 68% isolated yield (66.3 mg, 0.131 mmol), 96% ee (100% es) and *E*/*Z* = 93:7.

^{1}H NMR (392 MHz, $CDCl_3$, * indicates signals of the minor isomer, δ): 0.89 (t, *J* = 7.3 Hz, 3H), 1.04 (s, 9H), 1.18–1.40 (m, 4H), 1.42–1.54 (m, 2H), 2.06–2.15 (m, 1H), 2.09 (s, 3H), 2.18 (dt, *J* = 2.0, 7.1 Hz, 2H), 2.27–2.43 (m, 1.72H), 2.44–2.54* (m, 0.28 H), 3.71 (t, *J* = 6.5 Hz, 2H), 4.17–4.24* (m, 0.07H), 4.31–4.37 (m, 0.07H), 4.38–4.48 (m, 0.86H), 5.31 (q, *J* = 3.4 Hz, 0.86H), 5.34–5.38* (m, 0.14H), 5.62 (dd, *J* = 6.9, 15.5Hz, 1H, Signals of minor isomer are hidden in those of major isomer.), 5.88 (ddt, *J* = 0.8, 7.1, 14.6Hz, 1H, Signals of minor isomer are hidden in those of major isomer.), 7.34–7.47 (m, 6H), 7.62–7.70 (m, 4H). ^{13}C NMR (99 MHz, $CDCl_3$, δ): 14.0 (CH_3), 18.6 (CH_2), 19.2 (*C*), 21.0* (CH_3), 21.2 (CH_3), 22.1 (CH_2), 26.8 (CH_3), 28.1 (CH_2), 29.7* (CH_2), 30.9 (CH_2), 31.6* (CH_2), 35.8 (CH_2), 63.1 (CH_2), 63.2* (CH_2), 64.6 (*C*H), 64.8* (*C*H), 76.8 (*C*H), 77.2 (*C*), 87.8 (*C*), 124.7* (*C*H), 125.1 (*C*H), 125.8* (*C*H), 127.6 (*C*H), 129.0* (*C*H), 129.6 (*C*H), 131.7* (*C*H), 133.5*

(*C*H), 133.6 (*C*H), 133.7 (*C*), 135.5 (*C*H), 170.2 (*C*). HRMS-ESI (*m*/*z*): $[M+Na]^+$ calcd for $C_{31}H_{42}O_4NaSi$, 529.27446; found, 529.27532. $[\alpha]_D^{25.3} = -3.4$ (*c* 1.0, $CHCl_3$, 96% ee). The ee value and *E*/*Z* ratio was determined by HPLC analysis after derivatization to the *p*-nitrobenzoic acid ester {Daicel CHIRALPAK® OD-3, 2-PrOH:hexane = 0.75:99.25, 0.5 mL/min. 40 °C, retention time: 41.17 min [(*E*)-*anti*-**5** major enantiomer], 37.89 min [(*E*)-*anti*-**5** minor enantiomer], and 30.53 min [(*Z*)-*anti*-**5** major enantiomer]}. Minor enantiomer of (*Z*)-*anti*-**5** was not detected by HPLC analysis.

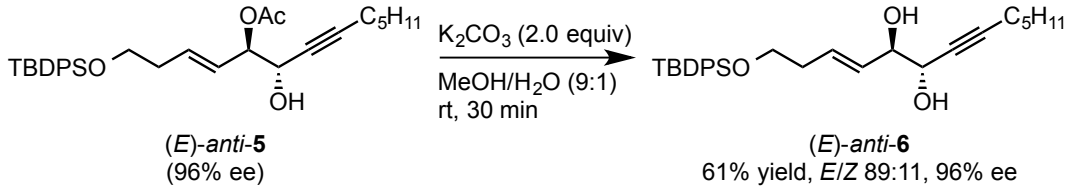
Deprotection of Acetyl Group in the Allylation Product

Deprotection of the acetyl group in the allylation products under acidic condition (Condition A).



(*E*)-*anti*-**5** (10.9 mg, 0.0215 mmol) was dissolved in MeOH/H_2O (4:1) solvent. $Sc(OTf)_3$ (19.7 mg, 0.0400 mmol) was added to the solution and stirred for 24 h at room temperature. Then, the mixture was separated with water and EtOAc, and then extracted with EtOAc for two times. The combined organic layer was dried over Mg_2SO_4, filtered and evaporated. The crude mixture was purified by silica-gel column chromatography (EtOAc: hexane = 10/90 to 25/75) to give the corresponding *anti*-1,2-diol (*E*)-*anti*-**6** (7.3 mg, 0.0157 mmol, 73% isolated yield).

Deprotection of the acetyl group in the allylation products under basic condition (Condition B).



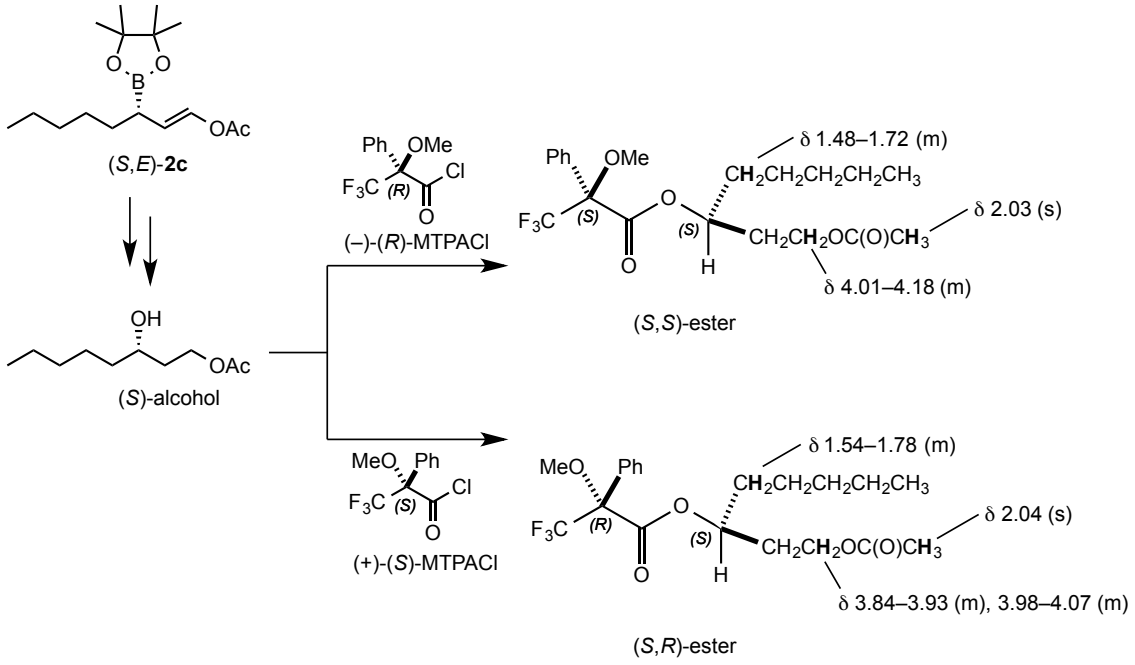
(*E*)-*anti*-**5** (10.7 mg, 0.0211 mmol) was dissolved in MeOH/H_2O (9:1) solvent. K_2CO_3 (6.2 mg, 0.0449 mmol) was added to the solution and stirred for 30 min at rt. Then, the mixture was separated with water and EtOAc, and then extracted with EtOAc for two times. The combined organic layer

was dried over Mg_2SO_4, filtered and evaporated. The crude mixture was purified by silica-gel column chromatography (EtOAc: hexane = 10/90 to 25/75) and gel-permeation chromatography to give the corresponding *anti*-1,2-diol (*E*)-*anti*-**6** (6.0 mg, 0.0129 mmol, 61% isolated yield).

^{1}H NMR (392 MHz, $CDCl_3$, * indicates signals of the minor isomer, δ): 0.89 (t, *J* = 6.9 Hz, 3H), 1.05 (s, 9H), 1.17–1.40 (m, 5H), 1.44–1.55 (m, 2H), 1.90–2.08 (m, 0.89H), 2.20 (dt, *J* = 2.0, 7.2 Hz, 2H), 2.34 (q, *J* = 6.7 Hz, 2H), 3.72 (t, *J* = 6.7 Hz, 2H), 3.83–3.88* (m, 0.11H), 4.08–4.19 (m, 0.89H), 4.25–4.36 (m, 1.11H), 4.81* (dt, *J* = 5.1, 9.5 Hz, 0.11H), 5.61 (dd, *J* = 6.5, 15.5 Hz, 0.89H), 5.65–5.76* (m, 0.11H), 5.82 (dt, *J* = 7.3, 14.9 Hz, 0.89H), 7.33–7.46 (m, 6H), 7.62–7.69 (m, 4H). ^{13}C NMR (99 MHz, $CDCl_3$, δ): 14.0 (CH_3), 18.7 (CH_2), 19.2 (*C*), 22.1 (CH_2), 26.8 (CH_3), 28.2 (CH_2), 31.0 (CH_2), 35.8 (CH_2), 63.3 (CH_2), 66.4 (*C*H), 75.2 (*C*H), 77.2 (*C*), 88.1 (*C*), 127.6 (*C*H), 129.5 (*C*H), 129.6 (*C*H), 131.6 (*C*H), 133.8 (*C*), 135.6 (*C*H). HRMS-ESI (*m*/*z*): $[M+Na]^+$ calcd for $C_{29}H_{40}O_3NaSi$, 487.26389; found, 487.26495. $[\alpha]_D^{24.9}$ = +24.2 (*c* 0.6, $CHCl_3$, 96% ee). The ee value and the *E*/*Z* ratio was determined by HPLC analysis {Daicel CHIRALPAK® OZ-3, 2-PrOH:hexane = 7:93, 0.5 mL/min. 40 °C, retention time: 15.57 min [(*E*)-*anti*-**6** major enantiomer], 20.95 min [(*E*)-*anti*-**6** minor enantiomer], and 19.05 min [(*Z*)-*anti*-**6** major enantiomer]}. Minor enantiomer of (*Z*)-*anti*-**6** was not detected by HPLC analysis.

Determination of the absolute configurations of linear γ-acetoxyallylboronates.

The absolute configrations of allylboronate (*S*,*E*)-**2c** was determined by a standard Mosher's procedure. Allylboronate (*S*,*E*)-**2c** was derivatized to the corresponding alcohol (*S*)-alcohol via H_2/Pd-C reduction and subsequent $NaBO_3$ oxidation. The absolute configuration of (*S*)-alcohol was determined by the comparison of the ^{1}H NMR spectra of (+)- and (–)-MTPA esters of (*S*)-alcohol as shown in the following figure. The absolute configurations of other allylboronates were deduced by this result.



3.7 References

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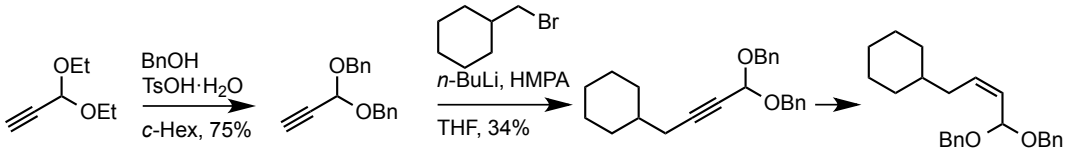
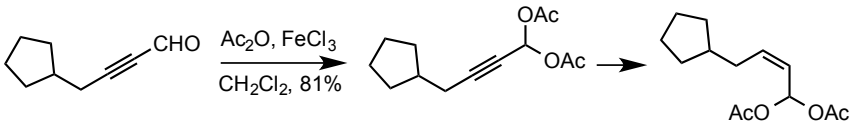
(6) Representative examples of the routes used to synthesize the acetal and acylal substrates

a) A synthesis of (*Z*)-allyl dibenzyl acetal



The allyl acetal substrates were synthesized over several steps (a). The synthesis started from commercially available propargyl diethyl acetal, which was subjected to an acid-catalyzed acetal exchange reaction with benzyl alcohol to give the corresponding dibenzyl acetal. The subsequent deprotonation of the alkyne moiety, followed by the alkylation of the alkynyl lithium and partial reduction of the carbon-carbon triple bond gave the allyl acetal substrate. Although the exchange reaction generally proceeded in high yield, the subsequent alkylation of the terminal alkyne with an alkyl halide was typically low yielding.

b) A synthesis of (*Z*)-allyl acylal



In contrast to the acetal substrates, the acylal substrates were much easier to prepare (b). The formylation of a terminal alkyne, followed by the *gem*-diacetylation of the resulting carbonyl moiety provided the corresponding propargyl acylals in moderate to high yields. The subsequent *Z*-selective reduction of the alkyne moiety in these propargyl acylals yielded the desired allylic substrates.

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Chapter 4

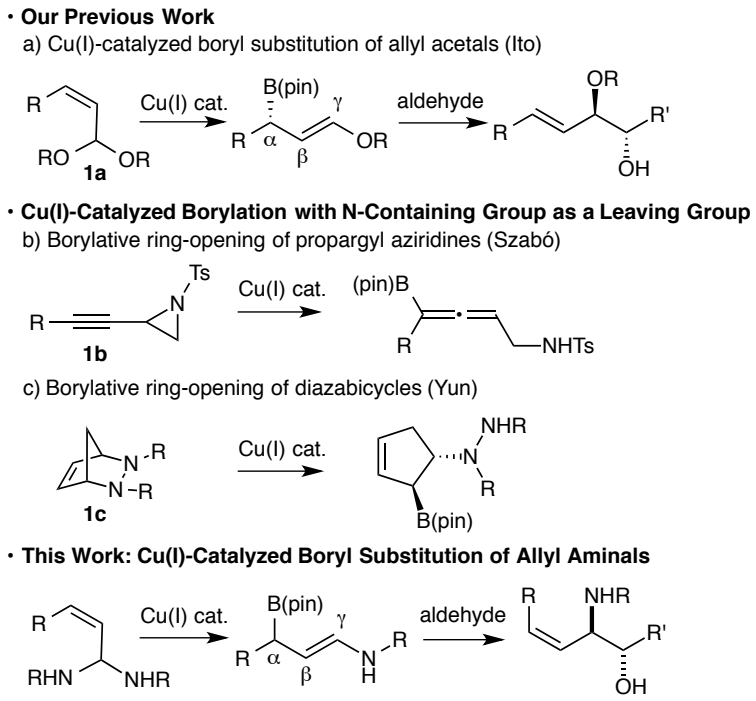
Copper(I)-Catalyzed Boryl Substitution of Allyl Aminals: Selective Synthesis of Linear γ-Aminoallylboronates

Abstract: A novel approach has been developed for the selective synthesis of α-substituted γ-aminoallylboronates through the copper(I)-catalyzed γ-boryl-substitution of allyl aminals. The reaction proceeded with high yield and *E*/*Z* selectivity (*E*/*Z* = >99:1, up to 74% yield). The subsequent aldehyde allylation using the allylboronates afforded the (*Z*)-*anti*-1,2-aminoalcohol derivatives with high stereoselectivity. The borylation/allylation procedure is concise and straightforward approach for construction of vicinal amino alcohol moiety together with new C–C bond formation.

4.1 Introduction

1,2-Aminoalcohols are common structural motifs in natural products and pharmaceutics.[1] Efficient synthesis of this structure is an important challenge and various synthetic approaches have been developed to obtain vicinal amino alcohols.[2] Among them, the approaches involving formation of amino alcohol moiety together with new C–C bond are particularly attractive in the convergent synthesis of 1,2-aminoalcohol derivertives that have a complex carbon skeleton.[3] Although the allylation of carbonyl compounds with γ-amino-substituted allylboron compounds have great potential to access stereodefined vicinal aminoalcohol derivatives because of their high level of chemo- and diastereoselectivities, the synthetic routes to γ-aminoallylboron compounds have been limited.[4] Recently, Pd-catalyzed method for synthesis of the boronates has been reported.[5] Although this method yielded enantio-enriched the γ-aminoallylboronates, this is limited to the synstheis of six-membered heterocyclic products. Development of catalytic method for preparation of linear γ-aminoallylboronates has been desired.

Copper(I)-catalyzed nucleophilic boryl substitution is an efficient way to obtain allylboron compounds because of their high regioselectivity and functional tolerance. Recently, our group succeeded in development of enantioselective boryl substitution of allyl acetals **1a** to give enantio-enriched γ-alkoxyallylboronates.[6] In this reaction, we have been achieved highly stereoselective allylation of aldehydes with the γ-alkoxyallylborontes to afford chiral 1,2-diol derivatives (Scheme 1, a). Extending scope of the boryl substitution/aldehyde allylation procedure, we focused on easily available allyl aminals as a substrate in copper(I)-catalyzed boryl substitution for the synthesis of γ-aminoallylboronates. When the one of the amino group in allyl aminasl act as the leaving group of the copper(I)-catalyzed allylic boryl substitution, the γ-aminoallylboronates can be synthesized. Although the copper catalysis has been widely used for nucleophilic boryl substitution of allyl- or propargyl carbonate[7], ethers[8], sulfonate[9] or phosphate[10], to the best of our knowledge, the reaction using a nitrogen-containing functinal group as a leaving group has been limited to strained compounds such as propargyl aziridines **1b**[11] or diazabicycles **1c**[12] (Scheme 1, b and c). It was not clear whether the amino group act as the leaving group, but we anticipated the appropriate catalysis optimization can achieve this.



Scheme 1. Copper(I)-Catalyzed Boryl Substitution of Allyl Aminals

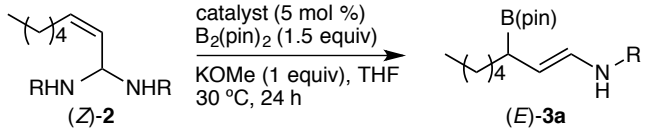
Herein, we report a novel synthetic approach for the linear γ-aminoallylboronates via copper(I)-catalyzed boryl substitution of allyl aminals. The borylation of *N*-methylcarbamate-protected allyl aminals afforded the corresponding boronates in high yield and *E*/*Z* selectivity (54–88% yield, up to >95:5 *E*/*Z* ratio). The allylation of aldehydes with the allylboronates afforded the desired 1,2-aminoalcohol derivatives in good yield and *E*/*Z* selectivity (76–91% yield, up to 17:83 *E*/*Z* ratio).

4.2 Optimization of Reaction Conditions

Allyl aminal bearing *N*-methyl carbamate groups as protection of amino groups [(*Z*)-**2a**] was conducted to reaction optimization. The allyl aminals were easy to prepare using Maruoka's method.[13] The reaction of aminal (*Z*)-**2a** with $B_2(pin)_2$ in the presence of CuCl/dppbz as a catalyst (5 mol %) and KOMe as a base (1 equiv) in THF afforded the desired allylboronate (*E*)-**3a** in high yield and *E*/*Z* selectivity (Table 1, entry 1, 89%).[14] The borylation of (*Z*)-**2a** in the absence of a ligand provided the corresponding product in poor yield (entry 2). The reaction with Xantphos ligand, which is an effective diphosphine ligand in many copper(I)-catalyzed borylation reactions,[7–10] was found to give the product in poor yield (entry 3). When other bidentate phosphine ligands

such as dppe, DPEphos or dmpe were used, the reaction resulted in poor to moderate yields (entries 4–6). The use of a phenanthroline or NHC ligand afforded inferior results compared with that of dppbz ligand (entries 7 and 8). The reaction with monodentate PPh_3 ligand provided a small amount of the product (entry 9). Addition of proton source such as MeOH or *t*-BuOH is necessary for protonation of in situ generated amino-copper species in the borylative ring-opening (Scheme 1, b and c).[11,12] Thus we investigated efficiency of addition of alcohol in this reaction; the addition of MeOH afforded a trace mount of product (entry 10). Efffect of the base on the reactivity was next investigated; the use of K(O-*t*-Bu) or NaOMe resulted in moderate yield (entries 11 and 12). Finally, the impact of the protecting group of the substrate was evaluated by the borylation reactions of *N*-Boc-protected aminal (*Z*)-**2b** or *N*-Cbz-protected aminal (*Z*)-**2c**. These substrates afforded the corresponding product in poor yield (entries 13 and 14).

Table 1. Optimization of the Reaction Conditions for the Copper(I)-Catalyzed Boryl Substitution of Allyl Aminals (*Z*)-**1**[a]



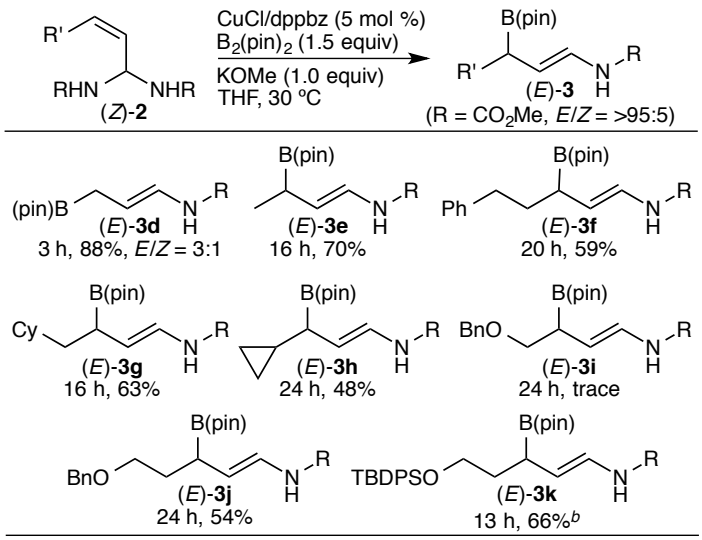
Entry	R	Catalyst	base	yield[b] (%)
1	CO_2Me	CuCl/dppbz	KOMe	89 (71)[c]
2	CO_2Me	CuCl/Xantphos	KOMe	22
3	CO_2Me	CuCl/dppe	KOMe	47
4	CO_2Me	CuCl/DPEphos	KOMe	38
5	CO_2Me	CuCl/dmpe	KOMe	8
6	CO_2Me	CuCl/phen	KOMe	4
7	CO_2Me	IPrCuCl	KOMe	34
8[d]	CO_2Me	CuCl/PPh_3	KOMe	10
9	CO_2Me	CuCl/none	KOMe	16
10[e]	CO_2Me	CuCl/dppbz	KOMe	2
11	CO_2Me	CuCl/dppbz	K(O-*t*-Bu)	59
12	CO_2Me	CuCl/dppbz	NaOMe	63
13	Boc	CuCl/dppbz	KOMe	26[f]
14[g]	Cbz	CuCl/dppbz	KOMe	28[f]

[a]Reagents and conditions: CuCl (0.0125 mmol), ligand (0.0125 mmol), (*Z*)-**1** (0.25 mmol), bis(pinacolato)diboron (0.375 mmol) and base (0.25 mmol) in solvent (0.75 mL) at 30 °C. [b]GC yield.[c] Isolated yield. [d]10 mol % of PPh_3 was used. [e]0.3 equiv of KOMe and 2.0 equiv of MeOH were used.[f]NMR yield. [g]54 h.

4.3 Substrate Scope of Boryl Substitution and Aldehyde Allylation

With optimized conditions in hand, we then start to explore the scope of animals. Various γ-aminoallylboronates were obtained under the optimization conditions (Scheme 2). The borylation of aminal (*Z*)-**2d**, which has a terminal olefin, proceeded in high yield and poor *E*/*Z* selectivity (88% yield, *E*/*Z* = 3:1). The poor *E*/*Z* selectivity was caused by unfixed conformation of the substrate.[6] The methyl group played a sufficient role in enhancement of the *E*/*Z* selectivity: the boryl substitution of (*Z*)-**2e** yielded the corresponding product in high yield and perfect *E*/*Z* selectivity (70% yield). The boronate (*E*)-**3f** possessing an aromatic ring was obtained in high yield (59% yield). The borylation of the substrates (*Z*)-**2g** and (*Z*)-**2h**, which have a branched structure at ε- and σ-position respectively, afforded the desired products in high yield (63% and 72% yield, respectively). The substrate including benzyloxy group at their σ-position (*Z*)-**2i** was subjected to the reaction to give only a trace amount of the product. On the other hands, the borylation of the substrate possessing BnO- and TBDPSO- group at the ε-position afforded the corresponding products (*E*)-**3j** and (*E*)-**3k** in high yield (54% and 66% yield, respectively).

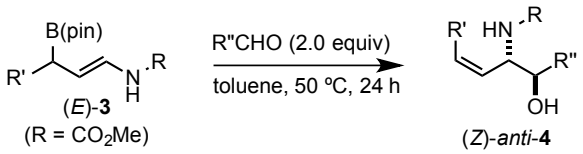
Scheme 2. Substrate Scope of the Copper(I)-Catalyzed Boryl Substitution of Allyl Aminals (Z)-**1**[a]



[a]Reagents and conditions: CuCl (0.0125 mmol), ligand (0.0125 mmol), (*Z*)-**1** (0.25 mmol), bis(pinacolato)diboron (0.375 mmol) and base (0.25 mmol) in solvent (0.75 mL) at 30 °C. [b]10 mol % of CuCl and dppbz were used. K(O-*t*-Bu) was used instead of KOMe.

To demonstrate the usefulness of the γ-aminoallylboronate, we investigated the allylation of aldehyde (Table 2). We carried out the allylation of aromatic aldehyde with (*E*)-**3a** to give the desired (*Z*)-*anti*-1,2-aminoalcohol derivatives in good yield and *E*/*Z* selectivity (82% yield, *E*/*Z* = 17:83). The allylation of aliphatic or conjugated aldehyde were conducted to afford the corresponding products (entry 2, 84% yield, *E*/*Z* = 23:77; entry 3, 91% yield, *E*/*Z* = 19:81, respectively). The use of Cbz-protected γ-aminoallylboronates (*E*)-**3c** showed good yield and *E*/*Z* selectivity in the aldehyde allylation (76% yield, *E*/*Z* = 17:83). The allylation with (*E*)-**3j** that have benzyloxy group afforded the corresponding (*Z*)-*anti*-1,2-aminoalcohol in good yield and moderate *E*/*Z* selectivity (84% yield, *E*/*Z* = 27:73).

Table 2. Aldehyde Allylation with γ-Aminoallylboronates (*E*)-**3**[a]



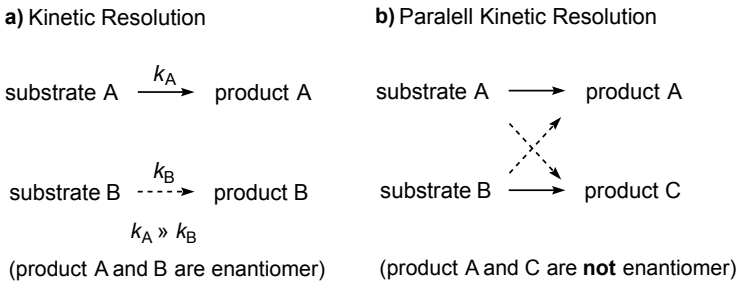
Entry	substrate	R"CHO	*E*/*Z*	yield (%)
1	(*E*)-**2a**	4-nitrobenzaldehyde	17:83	82
2	(*E*)-**2a**	3-phenylpropionaldehyde	23:77	84
3	(*E*)-**2a**	cinnamaldehyde	19:81	91
4	(*E*)-**2c**	4-nitrobenzaldehyde	17:83	76
5	(*E*)-**2j**	4-nitrobenzaldehyde	27:73	84

[a]Reagents and conditions: (*E*)-2 (0.15–0.2 mmol), aldehydes (0.6 mmol) in toluene at 50 ºC. The *E*/*Z* ratios of the *anti*-product were determined by ^{1}H NMR and HPLC analyses.

In summary, we have been succeeded to develop a novel approach for synthesis of the linear γ-aminoallylboronates via copper(I)-catalyzed boryl substitution of allyl aminals. The allylation of aldehyde have been demonstrated with the synthesized boronates to afford (*Z*)-*anti*-1,2-aminoalcohol derivatives in high yield and good *E*/*Z* selectivity. The borylation/allylation procedure is a concise and straightforward approach for vicinal aminoalcohol unit with a concomitant formation of a new carbon-carbon bond.

4.4 Various Kinetic Resolution of Cyclic *N*,*O*-Acetals

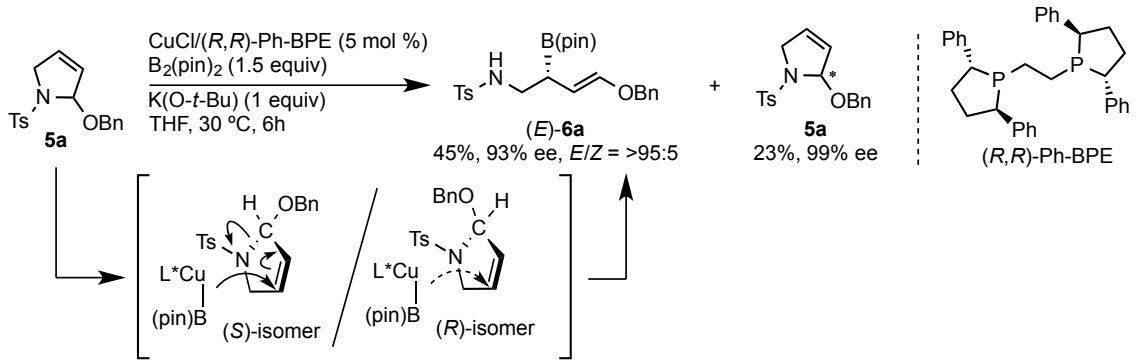
Kinetic resolution is one of asymmetric synthesis and optical resolution methods. When the reaction rate of one enantiomer of the racemic starting material is significantly higher than the other, one enantiomer would be converted selectively to give an enantio-enriched product (Scheme 3a). The other enantiomer of the starting material would remain unreacted and its enantiomeric excess (ee) is usually high. In parallel kinetic resolution (PKR), the racemic mixture is consumed to give two non-enantiomeric products via completely different reaction pathways (Scheme 3b).



Scheme 3. Kinetic Resolution and Parallel Kinetic Resolution of Racemic Substrates

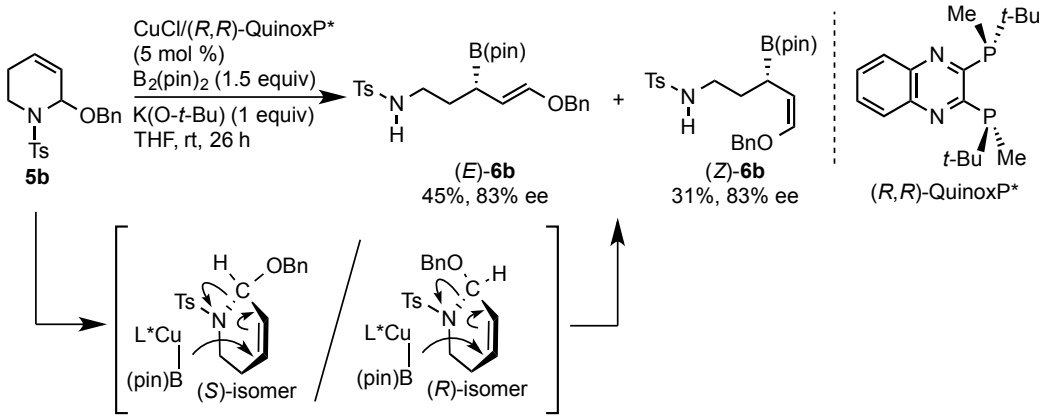
As menthioned above chapters, we achieved development of γ-boryl substitution of allylic acetals, acylals and aminals. Various oxygen- and nitrogen-containing moieties behaved as a leaving group in the borylation, but studies for leaving ability of these moieties remain obscure. Thus, several cyclic allyl *N*,*O*-actals were synthesized and subjected to the copper(I)-catalyzed asymmetric boryl substitution for the investigation of leaving ability in asymmetric copper(I)-catalyzed boryl substitution.

The asymmetric borylation of 5-membered *N*-Ts protected *N*,*O*-acetal **5a** with chiral (*R*,*R*)-Ph-BPE ligand afforded enantio-enriched linear γ-alkoxyallylboronate (*E*)-**6a** bearing tosylamide group and optically active reactant substrate **5a** in moderate yield with high enantioselectivity (Scheme 4). In this case, asymmetric borylation proceeded as kinetic resolution to give the optically active allylboronate and the optically active starting material. The absolute configuration of (*E*)-**6a** was determined by a standard Mosher's procedure. The allylboronate (*E*)-**6a** was derivatized to the corresponding alcohol via H_2Pd/C reduction, subsequent Boc-protection of the amine group and $NaBO_3$ oxidation of the boronate group. The absolute configuration of the alcohol derivative was determined by the comparison of the ^{1}H NMR spectra of (+)- and (–)-MTPA esters of the alcohol.



Scheme 4. Kinetic Resolution of 5-Membered Ts-Protected *N*,*O*-Acetal

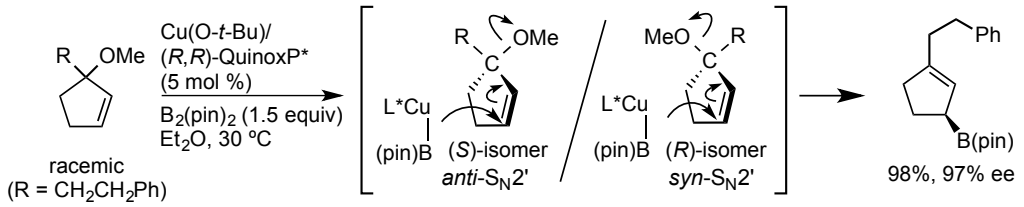
6-Membered Tosyl-protected *N*,*O*-acetal was conducted to the asymmetric borylation with copper catalyst system with chiral ligand (*R*,*R*)-QuinoxP* to give (*E*)- and (*Z*)-γ-alkoxyallylboronates [(*E*)-**6b** and (*Z*)-**6b**] in moderate yield with high enantioselectivity, respectively (Scheme 5). When the boryl-copper intermediate attacked to (*S*)-isomer and (*R*)-isomer of the substrate **5b**, –NTs group would be the leaving group in the both case. The absolute configurations of (*E*)- and (*Z*)-**6b** were determined by a standard Mosher's procedure. The allylboronate **6b** were derivatized to the corresponding alcohol via H_2Pd/C reduction, subsequent Boc-protection of the amine group and $NaBO_3$ oxidation of the boronate group. The absolute configuration of the alcohol derivative was determined by the comparison of the ^{1}H NMR spectra of (+)- and (–)-MTPA esters of the alcohol.



Scheme 5. Parallel Kinetic Resolution of 6-Membered Ts-Protected *N*,*O*-Acetal

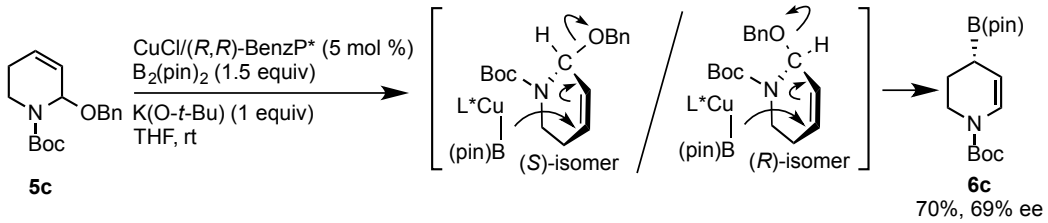
Direct enantio-convergent transformation (DECT) is the reaction that each enantiomer of a racemic mixture is transformed to the same enantiomer of the product via different reaction pathways. The DECT-type borylation with copper(I) catalyst was reported by Ito in 2010 (Scheme 6).[14] In the borylation, one enantiomer of the substrate reacts via an *anti*-S_N2' path way whereas the

other enantiomer undergoes a *syn*-S_N2'-type reaction to give the enantio-enriched product in high yield.



Scheme 6. Direct Enantio-Convergent Borylation of Cyclic Allyl Ether

When N-Boc protected *N*,*O*-acetal **5c** was used as a substrate in the copper(I)-catalyzed borylation, DECT-type borylation proceeded to give the corresponding cyclic γ-aminoallylboronate **6c** (Scheme 7). Both the yield and enantioselectivity of the reaction was moderate but only **6c** was obtained as a single product. The absolute configuration of **6c** was determined by comparison of comparison of the optical rotation of the literature value.[5]



Scheme 7. Direct Enantio-Convergent Borylation of Cyclic *N*,*O*-Acetal

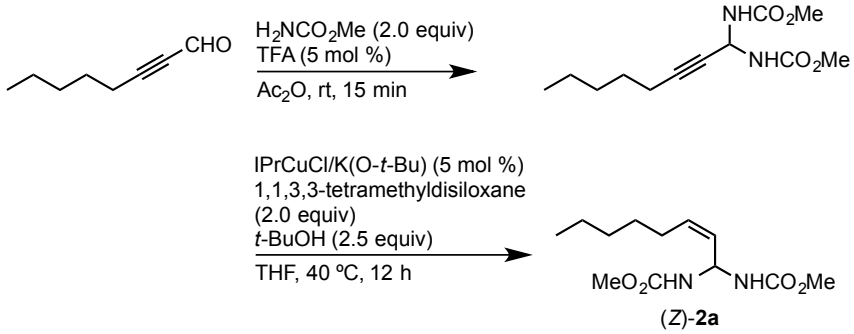
4.5 Conclusion

In summary, we have been succeeded to develop a novel approach for synthesis of the linear γ-aminoallylboronates via copper(I)-catalyzed boryl substitution of allyl aminals. The enantioselective synthesis of the boronate have been achieved with copper(I)/chiral ligand catalyst system. The allylation of aldehyde have been demonstrated with synthesized boronate to afford chiral *anti*-1,2-aminoalcohol in high stereoselectivety. It was a challenging theme to construct a stereodefined 1,2-amino moiety with a concominant C–C bond formation. The borylation/allylation procedure is a concise and straightforward approach for chiral 1,2-aminoalcohol derivatives.

4.6 Experimental Data

Preparation of Allyl Aminal Substrates

Preparation of (*Z*)-dimethyl (oct-2-ene-1,1-diyl)dicarbamate [(*Z*)-2a].

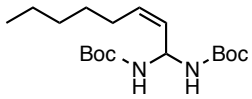


In an oven-dried 30 mL two-neck round-bottomed flask, octynal (4.28 mL, 30 mmol), methylcarbamate (3.60 g, 48 mmol) and acetic anhydride (7.0 mL) were charged under nitrogen atmosphere. Trifluoroacetic acid (0.2 mL) was added to the suspension and the mixture was stirred for 15 min. The product was solidified in acetic anhydride solvent as a white solid. The solid was filtered in vacuum, washed with hexane and purified by column chromatography (SiO_2, hexane/AcOEt = 70:30 to 40:60) to give the product as a white powder (3.53 g, 46% yield).

In screw-capped test tube, IPrCuCl (48.7 mg, 0.1 mmol) and K(O-*t*-Bu) (11.2 mg, 0.1 mmol) were dissolved in dry THF (1.2 mL) under a nitrogen atmosphere. The catalyst solution was allowed to stir vigorously for 20 min and added to a solution of propargyl aminal (530.7 mg, 2.1 mmol), 1,1,3,3-tetramethyldisiloxane (742.3 μL, 4.2 mmol), *t*-BuOH (505.4 μL, 5.25 mmol) and THF (3.0 mL). The mixture was directly filtered through a short silica-gel column with Et_2O as the eluent. After removal of the solvents under reduced pressure, the crude product was purified by flash chromatography (SiO_2, hexane/AcOEt/CH_2Cl_2 = 50:30:20) to give the product (*Z*)-**2a** (271.4 mg, 51% yield).

^{1}H NMR (401 MHz, $CDCl_3$, δ): 0.88 (t, *J* = 6.8 Hz, 3H), 1.18–1.42 (m, 6H), 2.13 (q, *J* = 7.1 Hz, 2H), 3.68 (s, 6H), 5.30–5.90 (m, 4H), 5.55 (dt, *J* = 7.4, 9.6 Hz, 1H). ^{13}C NMR (100 MHz, $CDCl_3$, δ): 13.9 (CH_3), 22.4 (CH_2), 27.6 (CH_2), 28.8 (CH_2), 31.3 (CH_2), 52.1 (CH_3), 56.8 (*C*H), 126.3 (*C*H), 133.9 (*C*H), 155.9 (*C*). HRMS-ESI (*m*/*z*): $[M+Na]^+$ calcd for $C_{12}H_{22}O_4N_2Na$, 281.14718; found, 281.14719.

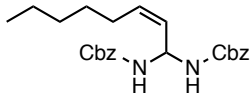
(*Z*)-Di-*tert*-butyl (oct-2-ene-1,1-diyl)dicarbamate [(*Z*)-2b].



(*Z*)-**2b**

^{1}H NMR (401 MHz, $CDCl_3$, δ): 0.89 (t, *J* = 6.8 Hz, 3H), 1.19–1.41 (m, 6H), 1.44 (s, 18H), 2.12 (q, *J* = 6.8 Hz, 2H), 5.37 (br s, 2H), 5.50 (dt, *J* = 7.5, 9.8 Hz, 1H), 5.45–5.65 (m, 1H), 5.55–5.90 (m, 1H). ^{13}C NMR (100 MHz, $CDCl_3$, δ): 13.8 (CH_3), 22.4 (CH_2), 27.5 (CH_2), 28.2 (CH_3), 28.8 (CH_2), 31.2 (CH_2), 56.2 (*C*H), 79.4 (*C*), 127.3 (*C*H), 132.8 (*C*H), 154.7 (*C*). HRMS-ESI (*m*/*z*): $[M+Na]^+$ calcd for $C_{18}H_{34}O_4N_2Na$, 365.24108; found, 365.24103.

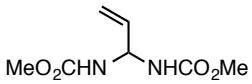
(*Z*)-Dibenzyl (oct-2-ene-1,1-diyl)dicarbamate [(*Z*)-2c].



(*Z*)-**2c**

^{1}H NMR (401 MHz, $CDCl_3$, δ): 0.87 (t, *J* = 7.0 Hz, 3H), 1.19–1.41 (m, 6H), 2.11 (q, *J* = 7.0 Hz, 2H), 5.10 (s, 4H), 5.55 (dt, *J* = 7.8, 9.6 Hz, 1H), 5.51–5.92 (m, 4H), 7.27–7.40 (m, 10H). ^{13}C NMR (100 MHz, $CDCl_3$, δ): 13.9 (CH_3), 22.4 (CH_2), 27.6 (CH_2), 28.8 (CH_2), 31.2 (CH_2), 56.8 (*C*H), 66.7 (CH_2), 126.2 (*C*H), 127.96 (*C*H), 128.02 (*C*H), 128.4 (*C*H), 133.9 (*C*H), 136.1 (*C*), 155.2 (*C*). HRMS-ESI (*m*/*z*): $[M+Na]^+$ calcd for $C_{24}H_{30}O_4N_2Na$, 433.20978; found, 433.20981.

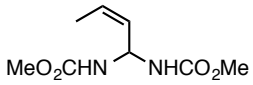
Dimethyl (prop-2-ene-1,1-diyl)dicarbamate [(*Z*)-2d].



(*Z*)-**2d**

^{1}H NMR (401 MHz, $CDCl_3$, δ): 3.69 (s, 6H), 5.25 (d, *J* = 10.4 Hz, 1H), 5.34 (d, *J* = 17.6 Hz, 1H), 5.40–5.88 (m, 3H), 5.89–6.10 (m, 1H). ^{13}C NMR (100 MHz, $CDCl_3$, δ): 52.3 (CH_3), 60.6 (*C*H), 116.7 (CH_2), 135.2 (*C*H), 156.0 (*C*). HRMS-ESI (*m*/*z*): $[M+Na]^+$ calcd for $C_7H_{12}O_4N_2Na$, 211.06893; found, 211.06932.

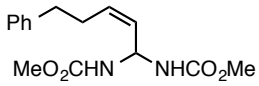
(*Z*)-Dimethyl (but-2-ene-1,1-diyl)dicarbamate [(*Z*)-2e].



(*Z*)-**2e**

^{1}H NMR (401 MHz, $CDCl_3$, δ): 1.72 (d, *J* = 5.6 Hz, 3H), 3.68 (s, 6H), 5.63 (dt, *J* = 7.1, 9.9 Hz, 1H), 5.15–6.00 (m, 4H). ^{13}C NMR (100 MHz, $CDCl_3$, δ): 13.3 (CH_3), 52.2 (CH_3), 56.6 (*C*H), 127.4 (*C*H), 128.0 (*C*H), 156.0 (*C*). HRMS-ESI (*m*/*z*): $[M+Na]^+$ calcd for $C_8H_{14}O_4N_2Na$, 225.08458; found, 225.08465.

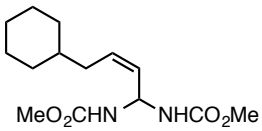
(*Z*)-Dibenzyl (oct-2-ene-1,1-diyl)dicarbamate [(*Z*)-2f].



(*Z*)-**2f**

^{1}H NMR (400 MHz, $CDCl_3$, δ): 2.47 (q, *J* = 7.1 Hz, 2H), 2.68 (t, *J* = 7.6 Hz, 2H), 3.64 (s, 6H), 5.55 (dt, *J* = 7.6, 10.6 Hz, 1H), 5.20–5.90 (m, 4H), 7.15–7.22 (m, 3H), 7.23–7.31 (m, 2H). ^{13}C NMR (100 MHz, $CDCl_3$, δ): 29.5 (CH_2), 35.3 (CH_2), 52.1 (CH_3), 56.8 (*C*H), 125.9 (*C*H), 127.0 (*C*H), 128.3 (*C*H), 128.5 (*C*H), 132.2 (*C*H), 141.2 (*C*), 155.9 (*C*). HRMS-ESI (*m*/*z*): $[M+Na]^+$ calcd for $C_{15}H_{20}O_4N_2Na$, 315.13153; found, 315.13132.

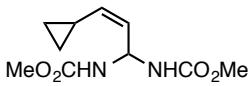
(*Z*)-Dimethyl (4-cyclohexylbut-2-ene-1,1-diyl)dicarbamate [(*Z*)-2g].



(*Z*)-**2g**

^{1}H NMR (401 MHz, $CDCl_3$, δ): 0.81–1.11 (m, 2H), 1.15–1.38 (m, 4H), 1.58–1.74 (m, 5H), 2.01 (t, *J* = 6.6 Hz, 2H), 3.68 (s, 6H), 5.56 (dt, *J* = 7.7, 10.4 Hz, 1H), 5.29–5.91 (m, 4H). ^{13}C NMR (101 MHz, $CDCl_3$, δ): 26.1 (CH_2), 26.2 (CH_2), 32.8 (CH_2), 35.2 (CH_2), 37.7 (CH_3), 51.9 (*C*H), 56.6 (*C*H), 126.8 (*C*H), 131.9 (*C*H), 155.9 (*C*). HRMS-ESI (*m*/*z*): $[M+Na]^+$ calcd for $C_{14}H_{24}O_4N_2Na$, 307.16283; found, 307.16263.

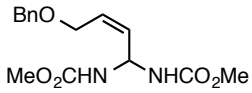
(*Z*)-Dimethyl (3-cyclopropylprop-2-ene-1,1-diyl)dicarbamate [(*Z*)-2h].



(*Z*)-**2h**

^{1}H NMR (401 MHz, $CDCl_3$, δ): 0.40 (dt, *J* = 4.5, 6.6 Hz, 2H), 0.82 (dt, *J* = 4.4, 6.4 Hz, 2H), 1.53–1.67 (m, 1H), 3.69 (s, 6H), 4.89 (t, *J* = 10.2 Hz, 1H), 5.20–5.78 (m, 3H), 5.87 (q, *J* = 7.2 Hz, 1H). ^{13}C NMR (100 MHz, $CDCl_3$, δ): 7.3 (CH_2), 10.0 (*C*H), 52.2 (CH_3), 57.3 (*C*H), 124.3 (*C*H), 137.9 (*C*H), 156.0 (*C*). HRMS-ESI (*m*/*z*): $[M+Na]^+$ calcd for $C_{10}H_{16}O_4N_2Na$, 251.10023; found, 251.10025.

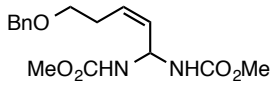
(*Z*)-Dimethyl (4-(benzyloxy)but-2-ene-1,1-diyl)dicarbamate [(*Z*)-2i].



(*Z*)-**2i**

^{1}H NMR (401 MHz, $CDCl_3$, δ): 3.67 (s, 6H), 4.15 (dd, *J* = 1.2, 6.0 Hz, 2H), 4.52 (s, 2H), 5.73 (dt, *J* = 6.0, 17.0 Hz, 1H), 5.35–5.80 (m, 2H), 5.81–6.05 (m, 2H), 7.26–7.40 (m, 5H). ^{13}C NMR (100 MHz, $CDCl_3$, δ): 52.0 (CH_3), 56.7 (*C*H), 65.7 (CH_2), 72.3 (CH_2), 127.5 (*C*H), 127.6 (*C*H), 128.2 (*C*H), 129.1 (*C*H), 129.2 (*C*H), 137.7 (*C*), 155.8 (*C*). HRMS-ESI (*m*/*z*): $[M+Na]^+$ calcd for $C_{15}H_{20}O_5N_2Na$, 331.12644; found, 331.12625.

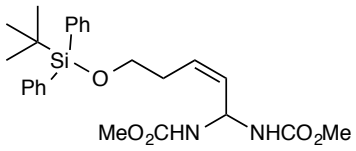
(*Z*)-Dimethyl (5-(benzyloxy)pent-2-ene-1,1-diyl)dicarbamate [(*Z*)-2j].



(*Z*)-**2j**

^{1}H NMR (401 MHz, $CDCl_3$, δ): 2.47 (q, *J* = 6.4 Hz, 2H), 3.50 (t, *J* = 6.4 Hz, 2H), 3.67 (s, 6H), 4.94 (s, 2H), 5.60 (dt, *J* = 7.5, 10.0 Hz, 1H), 5.65–5.88 (m, 2H), 5.89–6.28 (m, 2H), 7.22–7.38 (m, 5H). ^{13}C NMR (100 MHz, $CDCl_3$, δ): 28.0 (CH_2), 51.9 (CH_3), 56.6 (*C*H), 68.9 (CH_2), 72.5 (CH_2), 127.3 (*C*H), 127.4 (*C*H), 128.1 (*C*H), 128.3 (*C*H), 129.4 (*C*H), 138.0 (*C*), 155.8 (*C*). HRMS-ESI (*m*/*z*): $[M+Na]^+$ calcd for $C_{16}H_{22}O_5N_2Na$, 345.14209; found, 345.14182.

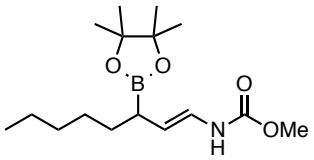
(*Z*)-Dimethyl {5-[(*tert*-butyldiphenylsilyl)oxy]pent-2-ene-1,1-diyl}dicarbamate [(*Z*)-2k].



^{1}H NMR (401 MHz, $CDCl_3$, δ): 1.04 (s, 9H), 2.40 (q, *J* = 6.3 Hz, 2H), 3.66 (s, 6H), 3.68 (t, *J* = 6.4 Hz, 2H), 5.20–5.70 (m, 2H), 5.61 (dt, *J* = 7.4, 10.7 Hz, 1H), 5.70–5.98 (m, 2H), 7.36–7.48 (m, 6H), 7.62–7.70 (m, 4H). ^{13}C NMR (101 MHz, $CDCl_3$, δ): 19.1 (*C*), 26.7 (CH_3), 30.9 (CH_2), 52.0 (CH_3), 56.8 (*C*H), 62.9 (CH_2), 127.5 (*C*H), 128.0 (*C*H), 129.5 (*C*H), 129.9 (*C*H), 133.5 (*C*), 135.4 (*C*H), 155.9 (*C*). HRMS-ESI (*m*/*z*): $[M+Na]^+$ calcd for $C_{25}H_{34}O_5N_2NaSi$, 493.21292; found, 493.21277.

Characterization of Boryl Substitution Products

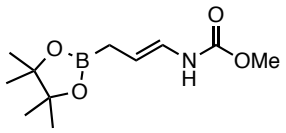
Methyl (*E*)-[3-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)oct-1-en-1-yl]carbamate [(*E*)-3a]



(*E*)-**3a**

^{1}H NMR (401 MHz, $CDCl_3$, δ): 0.87 (t, *J* = 6.6 Hz, 3H), 1.19–1.41 (m, 7H), 1.23 (s, 12H), 1.44–1.54 (m, 1H), 1.64–1.77 (m, 1H), 3.69 (s, 3H), 4.96 (dd, *J* = 9.2, 14.4 Hz, 1H), 6.19 (d, *J* = 10.4 Hz, 1H), 6.43 (dd, *J* = 10.6, 13.8 Hz, 1H). ^{13}C NMR (100 MHz, $CDCl_3$, δ): 14.0 (CH_3), 22.5 (CH_2), 24.58 (CH_3), 24.64 (CH_3), 25.3 (br, B–*C*H), 28.5 (CH_2), 31.2 (CH_2), 31.8 (CH_2), 52.2 (CH_3), 83.1 (*C*), 111.7 (*C*H), 122.8 (*C*H), 154.1 (*C*). HRMS-ESI (*m*/*z*): $[M+Na]^+$ calcd for $C_{16}H_{30}O_4BNa$, 333.21964; found, 333.22026.

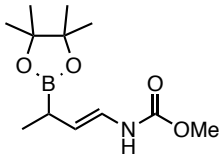
Methyl (*E*)-[3-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)prop-1-en-1-yl]carbamate [(*E*)-3d].



(*E*)-**3d**

^{1}H NMR (400 MHz, $CDCl_3$, * indicates signals of the minor *Z*-isomer, δ): 1.248 (s, 12H), 1.254* (s, 12H), 1.54* (d, *J* = 8.0 Hz, 2H), 1.62 (d, *J* = 7.6 Hz, 2H), 3.69 (s, 3H), 3.73* (s, 3H), 4.74* (q, *J* = 8.0 Hz, 1H), 5.04 (dt, *J* = 7.2, 14.3 Hz, 1H), 6.21 (d, *J* = 8.4 Hz, 1H), 6.44 (t, *J* = 12.4 Hz, 1H). ^{13}C NMR (100 MHz, $CDCl_3$, * indicates signals of the minor *Z*-isomer, δ): 12.4 (B–CH_2), 24.6* (CH_3), 24.7 (CH_3), 52.2 (CH_3), 52.3* (CH_3), 83.3 (*C*), 103.3* (*C*H), 105.9 (*C*H), 122.9* (*C*H), 123.6 (*C*H), 154.1 (*C*), 154.4* (*C*). The carbon directly attached to the boron atom was not detected, likely due to quadrupolar relaxation.[3,4] HRMS-ESI (*m*/*z*): $[M+Na]^+$ calcd for $C_{11}H_{20}O_4NBNa$, 263.14139; found, 263.14176.

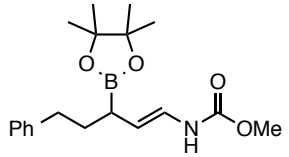
Methyl (*E*)-[3-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)but-1-en-1-yl]carbamate [(*E*)-3e].



(*E*)-**3e**

^{1}H NMR (401 MHz, $CDCl_3$, only major isomer is shown, δ): 1.09 (d, *J* = 7.2 Hz, 3H), 1.21 (s, 12H), 1.74–1.88 (m, 1H), 3.69 (s, 3H), 5.12 (q, *J* = 7.4 Hz, 1H), 6.10–6.28 (m, 1H), 6.42 (dd, *J* = 11.6, 13.2 Hz, 1H). ^{13}C NMR (100 MHz, $CDCl_3$, δ): 15.5 (CH_3), 18.4 (br, B–*C*H), 24.6 (CH_3), 52.2 (CH_3), 83.2 (*C*), 113.2 (*C*H), 122.0 (*C*H), 154.1 (*C*). HRMS-ESI (*m*/*z*): $[M+Na]^+$ calcd for $C_{12}H_{22}O_4NBNa$, 277.15704; found, 277.15732.

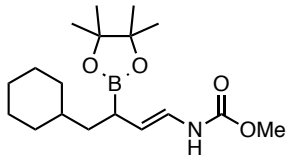
Methyl (*E*)-[5-phenyl-3-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)]pent-1-en-1-ylcarbamate [(*E*)-3f].



(*E*)-**3f**

^{1}H NMR (400 MHz, $CDCl_3$, δ): 1.24 (s, 12H), 1.60–1.72 (m, 1H), 1.73–1.91 (m, 2H), 2.50–2.70 (m, 2H), 3.70 (s, 3H), 5.00 (dd, *J* = 9.2, 14.0 Hz, 1H), 6.22 (d, *J* = 10.8 Hz, 1H), 6.47 (dd, *J* = 10.8, 13.6 Hz, 1H), 7.17 (d, *J* = 6.4 Hz, 3H), 7.22–7.30 (m, 2H). ^{13}C NMR (100 MHz, $CDCl_3$, δ): 24.6 (CH_3), 24.7 (CH_3), 24.9 (br, B–*C*H), 33.2 (CH_2), 35.1 (CH_2), 52.2 (CH_3), 83.2 (*C*), 111.1 (*C*H), 123.3 (*C*H), 125.6 (*C*H), 128.2 (*C*H), 128.4 (*C*H), 142.5 (*C*), 154.0 (*C*). HRMS-ESI (*m*/*z*): $[M+Na]^+$ calcd for $C_{19}H_{28}O_4NBNa$, 367.20399; found, 367.20465.

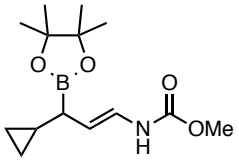
Methyl (*E*)-[4-cyclohexyl-3-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)but-1-en-1-yl] carbamate [(*E*)-3g].



(*E*)-**3g**

^{1}H NMR (399 MHz, $CDCl_3$, δ): 0.70–0.94 (m, 2H), 1.04–1.44 (m, 7H), 1.23 (s, 12H), 1.57–1.76 (m, 4H), 1.76–1.92 (m, 1H), 3.69 (s, 3H), 4.92 (dd, *J* = 9.0, 14.2 Hz, 1H), 6.18 (d, *J* = 10.4 Hz, 1H), 6.42 (dd, *J* = 11.0, 14.2 Hz, 1H). ^{13}C NMR (100 MHz, $CDCl_3$, δ): 22.4 (br, B–*C*H), 24.6 (CH_3), 26.2 (CH_2), 26.3 (CH_2), 26.6 (CH_2), 32.7 (CH_2), 33.6 (CH_2), 36.2 (*C*H), 38.7 (CH_2), 52.2 (CH_3), 83.1 (*C*), 111.8 (*C*H), 122.6 (*C*H), 154.0 (*C*). HRMS-ESI (*m*/*z*): $[M+Na]^+$ calcd for $C_{18}H_{32}O_4NBNa$, 359.23529; found, 359.23615.

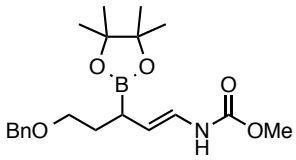
Methyl (*E*)-[3-cyclopropyl-3-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)prop-1-en-1-yl] carbamate [(*E*)-3h].



(*E*)-**3h**

^{1}H NMR (399 MHz, $CDCl_3$, δ): 0.02–0.10 (m, 1H), 0.11–0.21 (m, 1H), 0.44 (d, *J* = 7.2 Hz, 2H), 0.76–0.85 (m, 1H), 1.12–1.35 (m, 1H), 1.25 (s, 12H), 3.70 (s, 3H), 5.09 (d, *J* = 7.5 Hz, 1H), 6.34 (brs, 1H), 6.50 (t, *J* = 12.4 Hz, 1H). ^{13}C NMR (100 MHz, $CDCl_3$, δ): 3.8 (CH_2), 4.3 (CH_2), 12.2 (*C*H), 24.6 (CH_3), 29.5 (br, B–*C*H), 52.3 (CH_3), 83.2 (*C*), 110.8 (*C*H), 122.9 (*C*H), 154.1 (*C*). HRMS-ESI (*m*/*z*): $[M+Na]^+$ calcd for $C_{14}H_{24}O_4NBNa$, 303.17269; found, 303.17313.

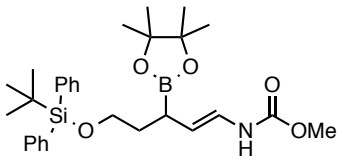
Methyl (*E*)-[5-(benzyloxy)-3-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)pent-1-en-1-yl] carbamate [(*E*)-3j].



(*E*)-**3j**

^{1}H NMR (399 MHz, $CDCl_3$, δ): 1.20 (s, 12H), 1.59–1.74 (m, 1H), 1.80–1.94 (m, 2H), 3.38–3.52 (m, 2H), 3.69 (s, 3H), 4.48 (s, 2H), 4.97 (dd, *J* = 8.8, 13.6 Hz, 1H), 6.26 (d, *J* = 9.2 Hz, 1H), 6.45 (dd, *J* = 10.6, 13.8 Hz, 1H), 7.20–7.40 (m, 5H). ^{13}C NMR (100 MHz, $CDCl_3$, δ): 22.1 (br, B–*C*H), 24.6 (CH_3), 24.7 (CH_3), 31.2 (CH_2), 52.3 (CH_3), 69.2 (CH_2), 72.8 (CH_2), 83.2 (*C*), 110.9 (*C*H), 123.2 (*C*H), 127.4 (*C*H), 127.7 (*C*H), 128.3 (*C*H), 138.6 (*C*), 154.0 (*C*). HRMS-ESI (*m*/*z*): $[M+Na]^+$ calcd for $C_{20}H_{30}O_5NBNa$, 397.21456; found, 397.21508.

Methyl (*E*)-[5-((*tert*-butyldiphenylsilyl)oxy)-3-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl) pent-1-en-1-yl]carbamate [(*E*)-3k].

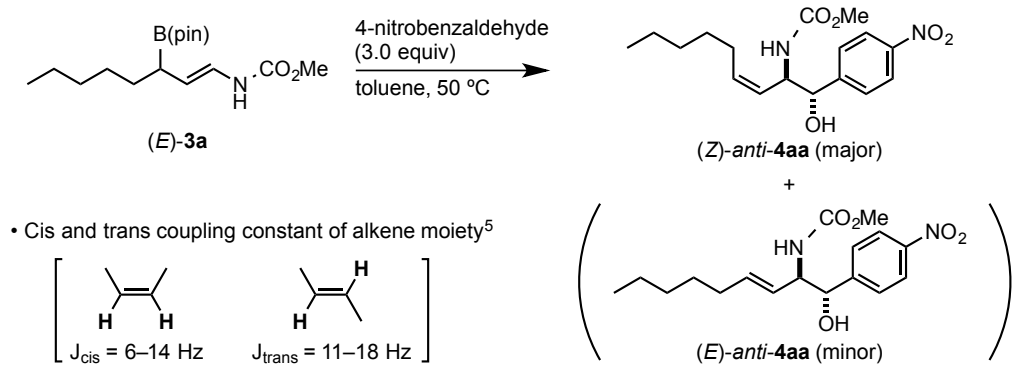


(*E*)-**3k**

^{1}H NMR (399 MHz, $CDCl_3$, only major isomer is shown, δ): 1.04 (s, 9H), 1.18 (s, 6H), 1.19 (s, 6H), 1.56–1.71 (m, 1H), 1.84 (sextet, *J* = 6.8 Hz, 1H), 1.96 (q, *J* = 8.0 Hz, 1H), 3.64 (t, *J* = 6.6 Hz, 2H), 3.70 (s, 3H), 4.89 (dd, *J* = 9.2, 14.0 Hz, 1H), 6.17 (d, *J* = 10.3 Hz, 1H), 6.43 (dd, *J* = 10.8, 14.0 Hz, 1H), 7.36–7.46 (m, 6H), 7.66 (dd, *J* = 1.4, 7.8 Hz, 4H). ^{13}C NMR (100 MHz, $CDCl_3$, only major isomer is shown, δ): 19.2 (*C*), 21.2 (br, B–*C*H), 24.6 (CH_3), 24.7 (CH_3), 26.8 (CH_3), 33.9 (CH_2), 52.3 (CH_3), 62.8 (CH_2), 83.2 (*C*), 111.0 (*C*H), 123.2 (*C*H), 127.5 (*C*H), 129.4 (*C*H), 134.0 (*C*), 135.5 (*C*H), 153.9 (*C*). HRMS-ESI (*m*/*z*): $[M+Na]^+$ calcd for $C_{29}H_{42}O_5NBNaSi$, 545.28538; found, 545.28624.

Aldehyde Allylation and Characterization of Products

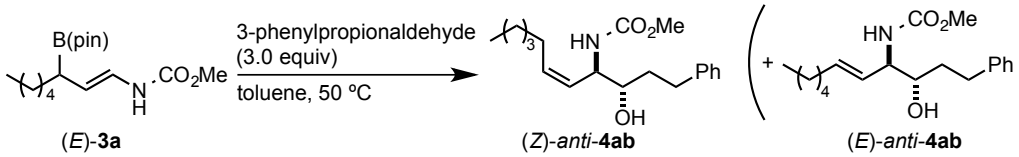
Representative procedure for non-catalyzed allylation of aldehyde (Table 2, entry 1)



The allylboronate (*E*)-**3a** (62.1 mg, 0.2 mmol) was dissolved in toluene (0.4 mL). Then 4-nitrobenzaldehyde (90.7 mg, 0.6 mmol) was added to the mixture and stirred for 24 h at 50 °C. The reaction mixture was quenched by a CH_2Cl_2 solution of triethanolamine (10% v/v, 2.5 mL). The crude product was purified by silica-gel chromatography (EtOAc:hexane = 10/90 to 30/70) to give the corresponding product (*Z*)-*anti*-**4aa** as a colorless oil, 82% isolated yield (55.2 mg, 0.164 mmol) and *E*/*Z* = 17:83. The *E*-*Z* configuration of the products derided from the reaction of (*E*)-**3a** and 4-nitrobenzaldehyde was confirmed from coupling constant of alkene moiety of the product. The *E*/*Z* ratio of the *anti*-product was determined by ^{1}H NMR and HPLC analysis. The *syn* isomers of the products were not observed in ^{1}H NMR analysis of the crude reaction mixture.

^{1}H NMR (401 MHz, $CDCl_3$, * indicates signals of the minor *E*-isomer, δ): 0.82 (t, *J* = 7.2 Hz, 3H), 0.83–0.89* (m, 3H), 0.96–1.33 (m, 6H), 1.65–1.81 (m, 1H), 1.84–2.01 (m, 1H), 3.19 (brs, 1H), 3.71* (s, 3H), 3.72 (s, 3H), 4.70 (brs, 1H), 4.86 (d, *J* = 7.6 Hz, 1H), 4.94* (d, *J* = 7.2 Hz, 1H), 5.00–5.12 (m, 1H), 5.18–5.32 (m, 1H), 5.55 (dt, *J* = 7.5, 10.7 Hz, 1H), 7.54 (d, *J* = 8.4 Hz, 2H), 8.20 (d, *J* = 8.8 Hz, 2H). ^{13}C NMR (99 MHz, $CDCl_3$, * indicates signals of the minor *E*-isomer, δ): 13.8 (CH_3), 13.9* (CH_3), 22.3 (CH_2), 27.6 (CH_2), 28.5* (CH_2), 28.7 (CH_2), 31.1* (CH_2), 31.2 (CH_2), 32.1* (CH_2), 52.4 (CH_3), 54.2 (*C*H), 75.4 (*C*H), 122.5 (*C*H), 123.1 (*C*H), 123.2* (*C*H), 127.2* (*C*H), 127.3 (*C*H), 135.9 (*C*H), 136.0* (*C*H), 147.2 (*C*), 148.1 (*C*), 157.0 (*C*). HRMS-ESI (*m*/*z*): $[M+Na]^+$ calcd for $C_{17}H_{24}O_5N_2Na$, 359.15771; found, 359.15774.

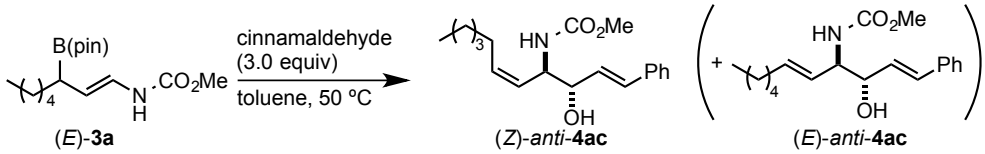
Allylation of 3-phenylpropionaldehyde with allylboronate (*E*)-3a (Table 2, entry 2)



The reaction was performed according to the representative procedure. The ^{1}H NMR and HPLC analysis gave *E*/*Z* ratio of 23:77.

^{1}H NMR (401 MHz, $CDCl_3$, * indicates signals of the minor *E*-isomer, δ): 0.867 (t, *J* = 7.0 Hz, 3H), 0.872* (t, *J* = 6.8 Hz, 3H), 1.18–1.42 (m, 6H), 1.63–1.83 (m, 2H), 1.98–2.23 (m, 2H), 2.60–2.73 (m, 1H), 2.78–2.91 (m, 1H), 3.67 (s, 3H), 3.71 (brs, 1H), 4.15* (brs, 1H), 4.45 (brs, 1H), 4.89 (brs, 1H), 5.04* (brs, 1H), 5.32 (t, *J* = 10.0 Hz, 1H), 5.40* (dd, *J* = 7.2, 15.2 Hz, 1H), 5.65 (dt, *J* = 7.4, 10.9 Hz, 1H), 5.70* (dd, *J* = 6.4, 10.9 Hz, 1H), 7.20 (d, *J* = 6.4 Hz, 2H), 7.24–7.32 (m, 3H). ^{13}C NMR (100 MHz, $CDCl_3$, * indicates signals of the minor *E*-isomer, δ): 13.9 (CH_3), 22.4* (CH_2), 22.5 (CH_2), 27.9 (CH_2), 28.7* (CH_2), 29.1 (CH_2), 31.3* (CH_2), 31.4 (CH_2), 32.1 (CH_2), 32.4* (CH_2), 35.0 (CH_2), 35.4* (CH_2), 52.2 (CH_3), 52.9 (*C*H), 73.4 (*C*H), 124.3 (*C*H), 124.6* (*C*H), 125.8 (*C*H), 128.4 (*C*H), 135.2 (*C*H), 135.4 (*C*H), 141.7 (*C*), 156.7 (*C*). HRMS-ESI (*m*/*z*): $[M+Na]^+$ calcd for $C_{19}H_{29}O_3NNa$, 342.20404; found, 342.20396.

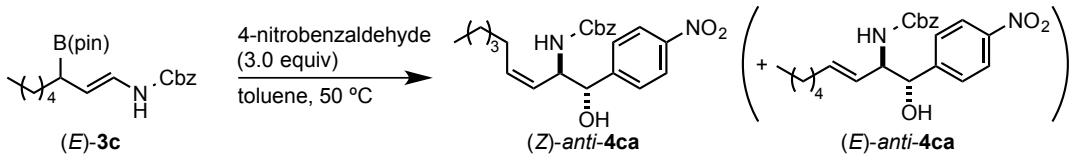
Allylation of cinnamaldehyde with allylboronate (*E*)-3a (Table 2, entry 3)



The reaction was performed according to the representative procedure. The ^{1}H NMR and HPLC analysis gave *E*/*Z* ratio of 19:81.

^{1}H NMR (401 MHz, $CDCl_3$, * indicates signals of the minor *E*-isomer, δ): 0.78–0.92 (m, 3H), 1.18–1.42 (m, 6H), 2.00–2.22 (m, 2H), 2.55 (brs, 1H), 3.69 (s, 3H), 4.42 (brs, 1H), 4.63 (brs, 1H), 4.94 (brs, 1H), 5.35 (t, *J* = 10.2 Hz, 1H), 5.44* (dd, *J* = 6.4, 15.2 Hz, 1H), 5.66 (dt, *J* = 7.5, 11.1 Hz, 1H), 6.17 (dd, *J* = 6.8, 16.0 Hz, 1H), 6.66 (d, *J* = 16.0 Hz, 1H), 7.20 (m, 5H). ^{13}C NMR (100 MHz, $CDCl_3$, * indicates signals of the minor *E*-isomer, δ): 13.92 (CH_3), 13.95* (CH_3), 22.4 (CH_2), 27.9 (CH_2), 28.7* (CH_2), 29.1 (CH_2), 31.3* (CH_2), 31.4 (CH_2), 32.3* (CH_2), 52.25 (CH_3), 53.33 (*C*H), 74.7* (*C*H), 75.0 (*C*H), 124.4 (*C*H), 124.9* (*C*H), 126.5 (*C*H), 127.7 (*C*H), 127.8 (*C*H), 127.9* (*C*H), 128.5 (*C*H), 131.8* (*C*H), 132.1 (*C*H), 134.8* (*C*H), 135.2 (*C*H), 136.4 (*C*), 156.9 (*C*). HRMS-ESI (*m*/*z*): $[M+Na]^+$ calcd for $C_{19}H_{27}O_3NNa$, 340.18823; found, 340.18831.

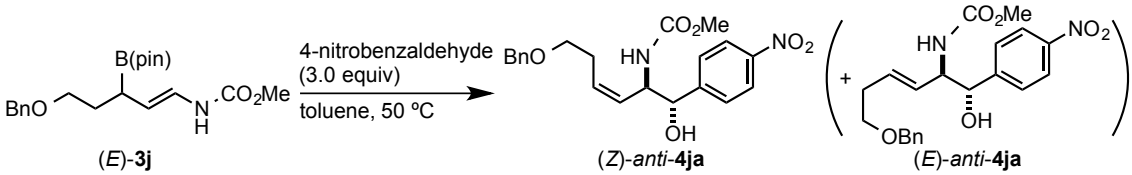
Allylation of 4-nitrobenzaldehyde with allylboronate (*E*)-3c (Table 2, entry 4)



The reaction was performed according to the representative procedure. The ^{1}H NMR and HPLC analysis gave *E*/*Z* ratio of 17:83.

^{1}H NMR (401 MHz, $CDCl_3$, * indicates signals of the minor *E*-isomer, δ): 0.82 (t, *J* = 7.2 Hz, 3H), 0.85* (t, *J* = 6.8 Hz, 3H), 0.96–1.32 (m, 6H), 1.67–1.83 (m, 1H), 1.84–2.01 (m, 1H), 3.20 (brs, 1H), 4.73 (brs, 1H), 4.91 (d, *J* = 6.8 Hz, 1H), 4.96–5.08 (m, 1H), 5.08–5.19 (m, 2H), 5.23 (t, *J* = 10.2 Hz, 1H), 5.26–5.31* (m, 1H), 5.56 (dt, *J* = 7.4, 10.8 Hz, 1H), 7.54 (m, 5H), 7.50 (d, *J* = 8.0 Hz, 2H), 8.16 (d, *J* = 8.8 Hz, 2H), 8.17* (d, *J* = 8.4 Hz, 2H). ^{13}C NMR (99 MHz, $CDCl_3$, * indicates signals of the minor *E*-isomer, δ): 13.86 (CH_3), 13.92* (CH_3), 22.4 (CH_2), 27.7 (CH_2), 28.4* (CH_2), 28.7 (CH_2), 31.1* (CH_2), 31.2 (CH_2), 32.2* (CH_2), 54.3 (*C*H), 67.2 (CH_2), 75.6 (*C*H), 122.5 (*C*H), 123.1 (*C*H), 127.2* (*C*H), 127.3 (*C*H), 128.1 (*C*H), 128.3 (*C*H), 128.5 (*C*H), 136.0 (*C*H), 136.1* (*C*H), 147.2 (*C*), 147.9 (*C*), 156.4 (*C*). HRMS-ESI (*m*/*z*): $[M+Na]^+$ calcd for $C_{23}H_{28}O_5N_2Na$, 435.18894; found, 435.18904.

Allylation of 4-nitrobenzaldehyde with allylboronate (*E*)-3j (Table 2, entry 5)



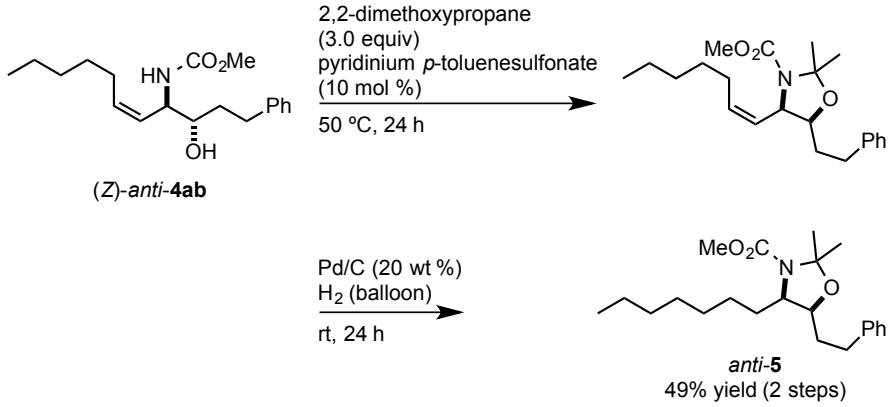
The reaction was performed according to the representative procedure. The ^{1}H NMR and HPLC analysis gave *E*/*Z* ratio of 27:73.

^{1}H NMR (399 MHz, $CDCl_3$, * indicates signals of the minor *E*-isomer, δ): 2.15–2.35 (m, 2H), 3.28–3.46 (m, 2H), 3.55 (brs, 1H), 3.65 (s, 3H), 3.71* (s, 3H), 4.46 (s, 2H), 4.47* (s, 2H), 4.66 (brs, 1H), 4.97 (brs, 2H), 5.32* (dd, *J* = 7.0, 15.4 Hz, 1H), 5.39 (dd, *J* = 9.4, 10.6 Hz, 1H), 5.58* (q, *J* = 7.4 Hz, 1H), 5.65 (dt, *J* = 7.8, 10.9 Hz, 1H), 7.24–7.40 (m, 5H), 7.44* (d, *J* = 8.8 Hz, 2H), 7.49 (d, *J* = 8.8 Hz, 2H), 8.11–8.18 (m, 2H). ^{13}C NMR (99 MHz, $CDCl_3$, * indicates signals of the minor *E*-isomer, δ): 28.5 (CH_2), 32.7* (CH_2), 52.5 (*C*H), 54.5 (*C*H), 58.7* (*C*H), 68.7 (CH_2), 69.0* (CH_2), 72.96* (CH_2), 73.02 (CH_2), 75.3 (CH_3), 123.2 (*C*H), 123.3* (*C*H), 125.5* (*C*H), 125.6 (*C*H), 127.2* (*C*H), 127.4 (*C*H), 127.7 (*C*H), 128.4 (*C*H), 132.0* (*C*H), 132.1 (*C*H), 137.8 (*C*), 138.0* (*C*), 147.3 (*C*), 147.8* (*C*), 148.1 (*C*), 157.0 (*C*). HRMS-ESI (*m*/*z*): $[M+Na]^+$ calcd for $C_{21}H_{24}O_6N_2Na$, 423.15256;

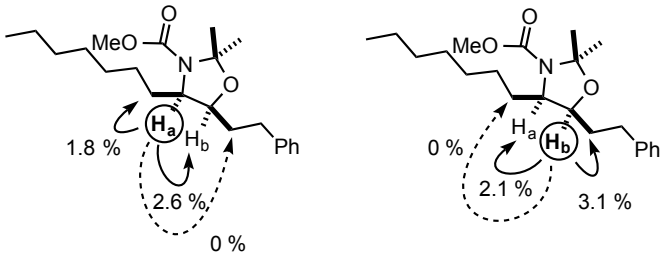
found, 423.15266.

Determination of the relative configurations of the products of aldehyde allylation with γ-aminoallylboronates

The relative configuration of allylation product (*Z*)-*anti*-**4ab** was determined by NOE measurements after derivatization to the corresponding cyclic aminoalcohol as shown in the following scheme.



NOE experiments of the cyclic aminoalcohol *anti*-**5** also support the proposed relative stereochemistry as shown in the following figure. The relative structures of other products of aldehyde allylation with γ-aminoallylboronates were deduced by these results.



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List of Publications

Chapter 2 "Copper(I)-Catalyzed Enantioselective Synthesis of α-Chiral Linear or Carbocyclic (E)-(γ-Alkoxyallyl)boronates"
Eiji Yamamoto, Yuta Takenouchi, Taichi Ozaki, Takanori Miya, Hajime Ito*
J. Am. Chem. Soc. **2014**, *136*, 16515–16521.

Chapter 3 Copper(I)-Catalyzed Enantioselective Boryl Substitution of Allyl Acylals: An Efficient Approach for Enantioenriched α-Chiral γ-Acetoxyallylboronates
Yuta Takenouchi, Ryoto Kojima, Riko Momma, Hajime Ito*
Synlett **2017***, 28,* 270–274.

Chapter 4 Selective Synthesis of Linear α-Substituted (*E*)-γ-Aminoallylboronates via Copper(I)-Catalyzed Borylation of Allyl Aminals
Yuta Takenouchi, Hajime Ito*
to be submitted

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Yuta Takenouchi

Graduate School of Chemical Sciences and Engineering

Hokkaido University

March, 2017