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Catalytic enantioselective transformations of borylated substrates: Preparation and synthetic applications of chiral alkylboronates*

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Abstract: Organoboronic acid derivatives are well-established intermediates for the preparation of alcohols and amines, and in the formation of C–C bonds via different reactions, including homologations, carbonyl allylboration, or transition-metal-catalyzed cross-coupling chemistry. In the past decade, there has been great interest in the development of catalytic enantioselective methods for the preparation of chiral, optically enriched organoboronates as precursors of enantioenriched compounds. While the mainstream strategy remains the late-stage borylation of organic functional groups, our group has focused on an alternate strategy focused on modification of boron-containing substrates. In this way, acyclic and cyclic secondary alkyl- and allyl-boronates were prepared through catalytic enantioselective processes such as [4 + 2] cycloadditions, isomerizations, allylic substitutions, and conjugate additions. The resulting optically enriched boronates have been successfully utilized in the syntheses of complex natural products and drugs. One remaining challenge in the chemistry of secondary alkylboronate derivatives is their cross-coupling, especially with control of stereoselectivity. In this regard, our recent approach featured the conjugate asymmetric borylation of β-boronyl acrylates, providing the first enantioselective preparation of highly optically enriched 1,1-diboronyl derivatives. The chirality of these geminal diboron compounds is conferred through the use of two distinct boronate adducts, which can be coupled chemo- and stereoselectively with a variety of aryl and alkenyl halides under palladium catalysis.

Keywords: asymmetric catalysis; chemoselectivity; cross-coupling reactions; natural products; organoboronates.

INTRODUCTION

Organoboronic acid derivatives are well-established precursors of alcohols and amines, and can participate as intermediates in the formation of C–C bonds via different reactions, including homologative 1,2-rearrangements, carbonyl allylboration, or transition-metal-catalyzed cross-coupling chemistry (Fig. 1) [1]. For instance, the Suzuki–Miyaura cross-coupling is one of the most ubiquitous reactions used in pharmaceutical chemistry for the preparation of substituted aromatic and heteroaromatic compounds [2].

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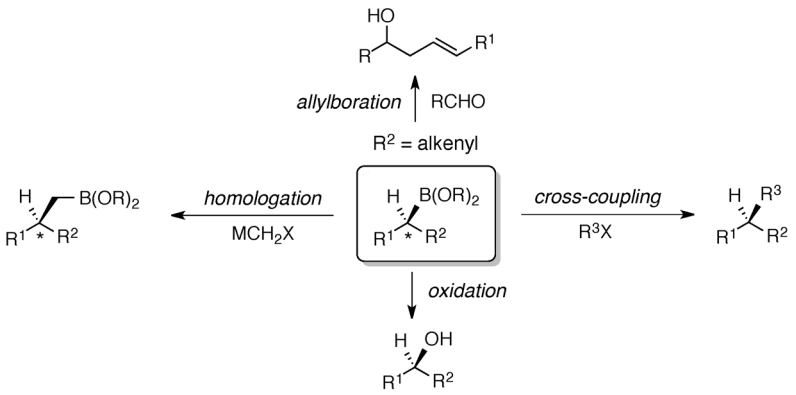


Fig. 1 Synthetic applications of chiral secondary alkylboronic esters.

In the past decade, there has been significant interest in the development of synthetic methods for the preparation of chiral, optically enriched organoboronates as precursors of enantioenriched organic compounds. Early contributions such as Brown's hydroboration methodology [3] and Matteson's asymmetric homologation [4] featured the use of stoichiometric chiral auxiliaries and set an important precedent in this research field (Fig. 2).

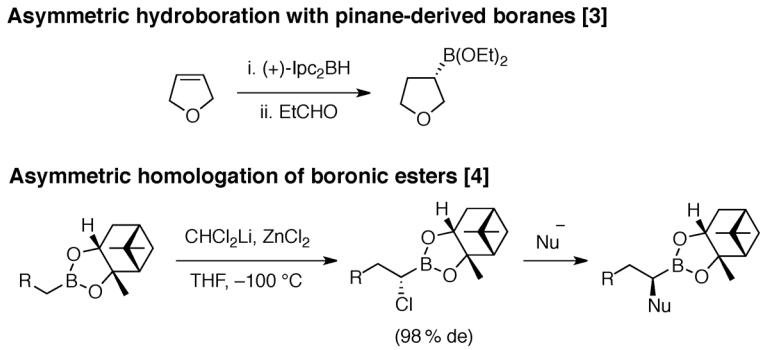


Fig. 2 Classical stoichiometric methods for the preparation of chiral secondary alkylboronic esters.

Recent efforts, however, have focused on more atom-economical strategies that make use of chiral catalysis. With this view, there are two distinct approaches for the preparation of chiral organoboronates: the late-stage borylation of organic functional groups [5], and an alternate strategy focused on modification of boron-containing substrates, i.e., early-stage borylation. The conceptual difference between these two approaches is illustrated in Fig. 3, which compares a catalytic enantioselective hydroboration of an alkene as an example of late-stage borylation [5a], with the catalytic asymmetric hydrogenation of an alkenylboronate as an example of early-stage borylation [6].

While the mainstream strategy to access chiral alkylboronates remains the late-stage borylation of organic functional groups such as alkenes [5], our group has focused on early-stage borylation. Early-stage borylation is advantageous in many ways: first, utilization of a pre-borylated substrate provides a wide selection of well-established asymmetric functionalization reactions. Secondly, a single borylated substrate can generate multiple products by reaction with a simpler and variable type of reagent. In the late-stage borylation approach, a different borylated substrate is required for every desired product. Despite all the above-stated advantages, early-stage borylation is potentially limited by chemoselectiv-

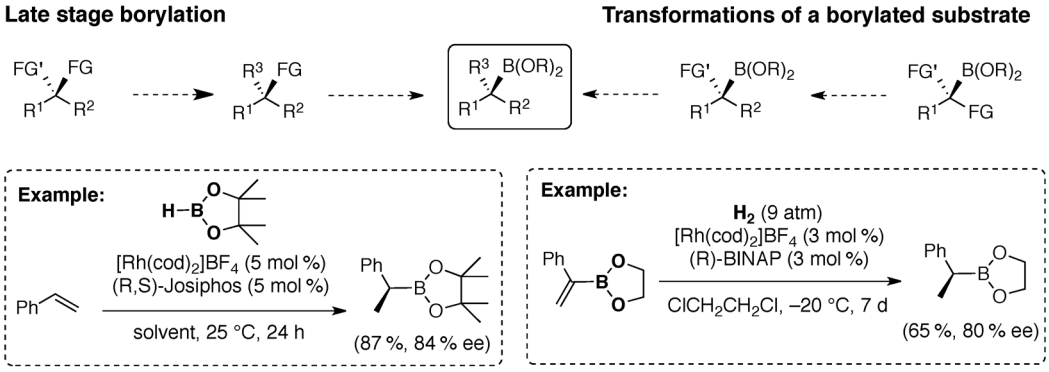
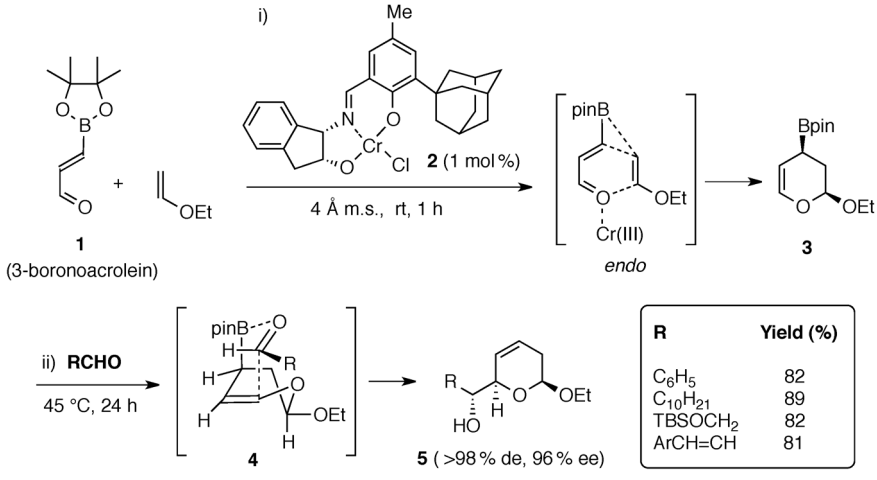


Fig. 3 Conceptual strategies for the catalytic preparation of chiral secondary alkylboronic esters.

ity issues. Methods employed to transform a borylated substrate must be compatible with the boronyl group. For instance, transition-metal catalysts may interfere by insertion into B–C bonds and lead to undesired reaction pathways. Although the preparation of chiral alkylboronates using catalytic enantioselective methods presents several challenges, studies from our group and others have demonstrated that chemoselectivity issues can be avoided with a careful optimization of reaction variables. This way, enantiomerically enriched alkylboronates were prepared successfully using a variety of transformation types described below.

CATALYTIC ENANTIOSELECTIVE HETERO [4 + 2] CYCLOADDITION WITH 3-BORONOACROLEIN

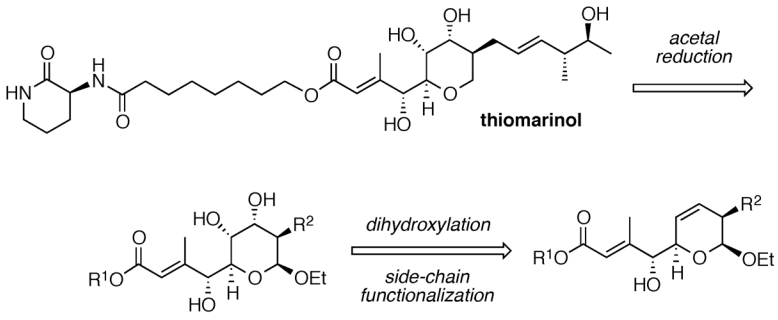
In 2003, we reported the first example of catalytic enantioselective preparation of a chiral α-substituted allylic boronate [7]. When used as a heterodiene, 3-boronoacrolein pinacolate **1** reacted with ethyl vinyl ether via an inverse electron-demand hetero [4 + 2] cycloaddition catalyzed by Jacobsen's chiral Cr(III) salen complex (**2**) to afford cyclic allylboronate **3** in high yield and high enantioselectivity (Scheme 1). Without a change of solvent, the resulting allylic boronate can be treated subsequently with a variety of aldehydes to provide α-hydroxyalkyl pyrans **5** in high diastereoselectivity with perfect transfer of



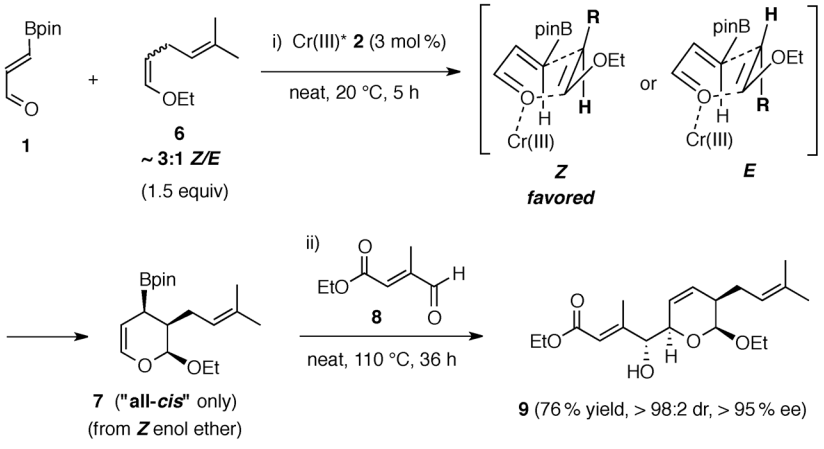
Scheme 1 Preparation of α-hydroxyalkyl dihydropyrans **5** via the chiral allylic boronate **3**.

enantiomeric purity according to the expected chairlike transition state **4**. Key to the success of this multicomponent reaction is the higher temperature required for the allylboration step, which prevented addition of **3** onto the starting boronoacrolein **1**. Furthermore, the borylated heterodiene **1** was found to be significantly more reactive compared to non-borylated analogues like ethyl (*E*)-4-oxobutenoate [7b]. The possibility of using a lower catalyst loading was a benefit of this surprising reactivity.

This three-component reaction process was applied to a total synthesis of a thiomarinol antibacterial marine natural product (Scheme 2) [8]. To access the core of thiomarinol, the dihydropyran product required a reduction of the acetal and a dihydroxylation of the endocyclic alkene. Furthermore, to make the dihydropyran precursor, the key step required a chiral allylic boronate substituted with a group that would permit the functionalization of the right-hand side chain of thiomarinol. To this end, a *Z* 2-substituted enol ether was required in lieu of ethyl vinyl ether. Although it could only be obtained as a 3:1 *Z*:*E* mixture, it was found that the *Z* isomer of **6** reacted much faster to give chiral allylic boronate **7** in high diastereoselectivity and enantioselectivity (Scheme 3). Following a quick purification, **7** was reacted with the α,β-unsaturated aldehyde **8** to give the allylboration product **9** in 76 % yield. The latter was transformed in 13 more steps into the targeted natural product, thiomarinol.

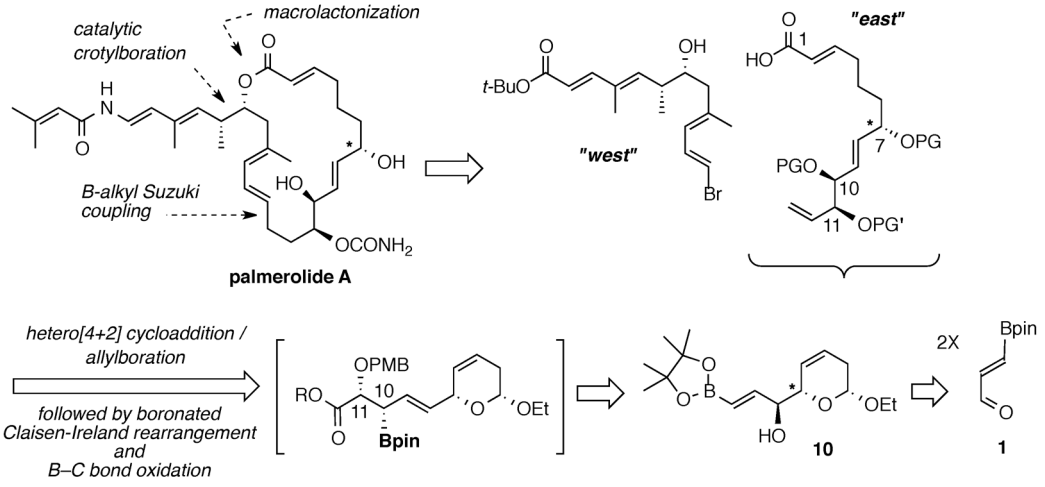


Scheme 2 Retrosynthetic analysis of thiomarinol from a dihydropyran precursor.



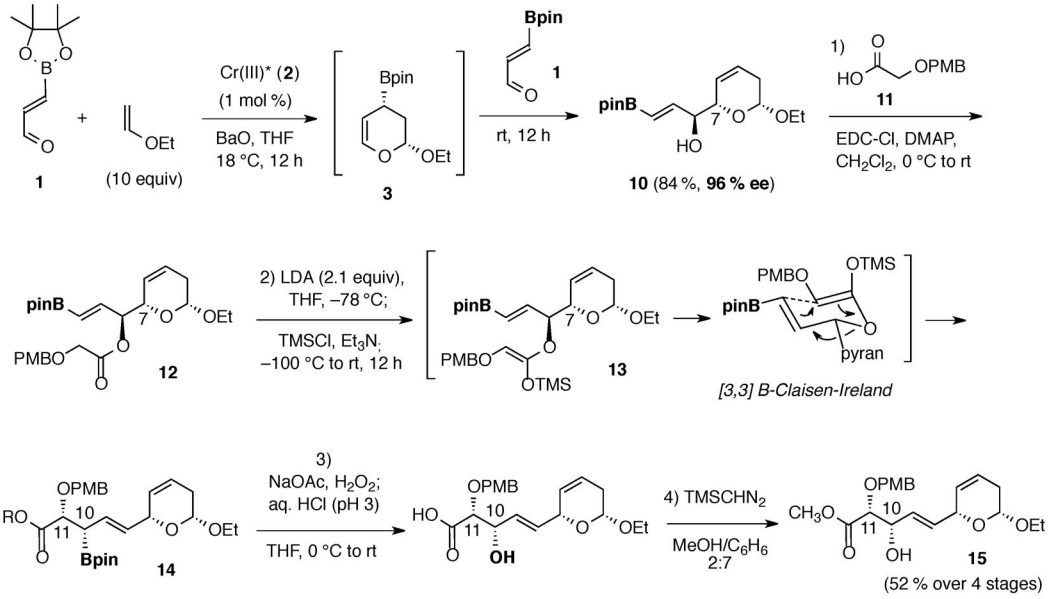
Scheme 3 Total synthesis of thiomarinol using polysubstituted pyranylboronate **7**.

More recently, the [4 + 2] cycloaddition/allylboration methodology was applied successfully to a total synthesis of palmerolide A, a complex macrolide with selective anti-melanoma activity. The construction of the East fragment featured two chiral secondary boronates as key intermediates (Scheme 4) [9].



Scheme 4 Retrosynthetic analysis for the East fragment of palmerolide A.

First, the chiral allylic boronate **3** was generated as described above. This time, however, our synthetic strategy exploited the "self-allylboration" product **10** that was initially feared to be unavoidable in the hetero [4 + 2] cyloaddition between **3** and **1**. In the event, use of an excess of **1** did lead to the desired product **10** via allylic boronate intermediate **3** (Scheme 5). The secondary hydroxyl group was then acylated with **11** to give ester **12**, which set the stage for a Claisen–Ireland rearrangement of silyl enol ether **13** to produce chiral secondary alkylboronate **14** in high diastereoselectivity. Strategically, this synthesis employed boronate **14** as a masked form of hydroxyl group, allowing a selective differentiation of C10 and C11 hydroxyls of palmerolide. This sequence was necessary in order to selectively transform the C11 hydroxyl into a carbamate unit later in the synthesis. Thus, a stereoretentive oxida-



Scheme 5 Application of chiral secondary alkylboronates in the synthesis of an advanced intermediate for the East fragment of palmerolide A.

tion of the B–C bond of **14** was eventually followed by protection of the resulting C10 hydroxyl as a silyl ether to give **15**. The East fragment of palmerolide was completed in 8 more steps, then coupled to the West fragment en route to a completed total synthesis. It is noteworthy that this synthesis featured two very useful stereoselective transformations of chiral boronates: aldehyde allylation and oxidation.

CATALYTIC ENANTIOSELECTIVE BORYLATIVE ISOMERIZATION

The chiral pyranyl boronates described in the previous section are produced as acetals as a result of the cycloaddition process with vinyl ethers. Recognizing that this feature may not be desirable toward synthesizing certain classes of compounds, we sought an alternative method for producing unsubstituted pyranyl boronates. We were intrigued by a report by Masuda and co-workers, which detailed a new procedure for palladium-catalyzed borylation of alkenyl triflates (Fig. 4) [10]. Instead of giving the expected alkenylboronate **17**, substrate **16** gave the isomerized allylic boronate **18** as the main reaction product.

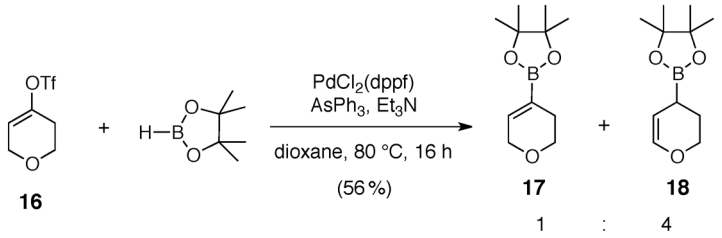
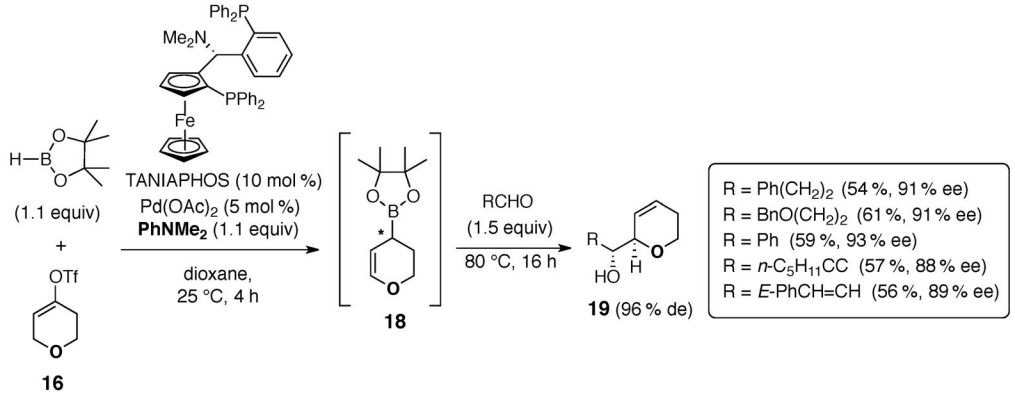
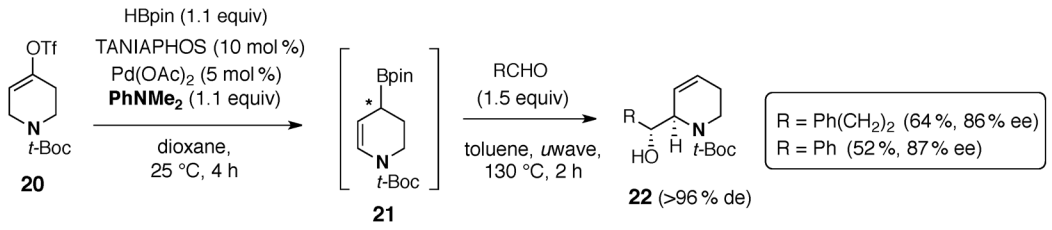


Fig. 4 Borylation of alkenyl triflate **16** with isomerization, as observed by Masuda and co-workers.

We first set out to develop conditions for the exclusive formation of the allylic boronate [11]. Then, careful optimization of the chiral diphosphine ligand and other reaction parameters led to a set of conditions affording chiral secondary allylic boronate **18**, which was followed by a diastereoselective allylboration of aldehydes to give, with high enantio- and diastereoselectivity, the desired α-hydroxyalkyl pyrans **19** devoid of the acetal substituent found in **3** (Scheme 6). From substrate **20**, a similar process was applied to the formation of the corresponding chiral piperidyl boronate **21** and allylation products **22** (Scheme 7). A mechanism was also proposed for this unique method of preparation of chiral cyclic secondary allylic boronates [11].



Scheme 6 Preparation of α-hydroxyalkyl dihydropyrans by catalytic enantioselective isomerization.



Scheme 7 Preparation of α-hydroxyalkyl dihydropiperidines by catalytic enantioselective isomerization.

CATALYTIC ASYMMETRIC ALLYLIC ALKYLATION OF PROPENYLBORONATES

Chiral α-substituted allylic boronates are important reagents for the preparation of optically enriched homoallylic alcohols by addition to achiral aldehydes [12]. The preparation of optically enriched α-substituted allylic boronates **23** and their additions to aldehydes were pioneered by Hoffmann [12]. These reagent-controlled additions proceed with near-perfect transfer of chirality to give two diastereomeric products **25** and **27** (Fig. 5). These *Z* and *E* allylic alcohol products are epimeric, and their ratio is highly dependent on the nature of the α-substituent (X) and the nature of the boronic ester [12]. The ratio of **25** and **27** can be explained in terms of steric and dipolar effects on the two competing transition structures **24** and **26**.

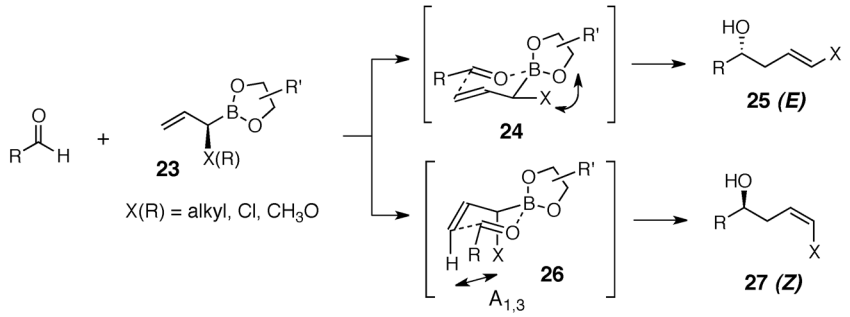


Fig. 5 Postulated competing transition structures in the allylation of aldehydes with chiral α-substituted allylic boronates. Note: A stereodefined reagent is shown to emphasize the stereochemistry of the reaction and the epimeric relationship between products **25** and **27**.

With a nonpolar alkyl substituent, steric interactions play a dominant role on the relative energies of these putative transition structures. Transition structure **24** is destabilized by a steric interaction between the boronic ester and the pseudo-equatorial α-substituent. On the other hand, chairlike transition structure **26** features unfavorable allylic interactions due to the pseudo-axial position of the substituent. The use of a hindered ester, such as pinacolate, aggravates interactions between the substituent (X) and the pinacol methyls in **24**, and tends to favor transition structure **26** leading to the *Z*-configured product **27** [13]. With a polar substituent (halogen, alkoxy), dipolar effects tend to dominate and further favor transition structure **26** with the pseudo-axial C–X bond *anti* to the axial B–O bond [12]. Unfortunately, with alkyl substituents, the ratio of products **25**:**27** is usually low. Moreover, established procedures for the preparation of α-alkyl substituted allylic boronates using stoichiometric auxiliaries tend to be tedious.

Transition-metal-catalyzed asymmetric allylic alkylation is a very useful reaction process to generate new C–C bonds in high enantioselectivity [14]. The requirement for a transition-metal catalyst

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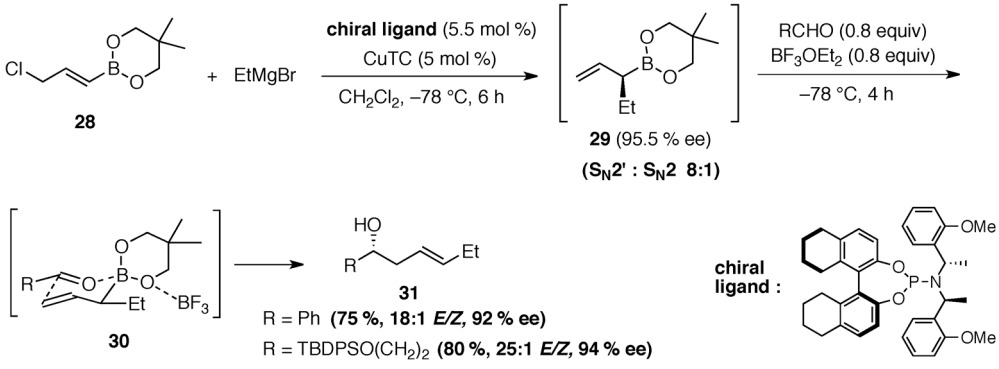
poses a challenge to the use of boronyl-substituted substrates due to the labile B–C bonds, which can undergo oxidative addition and other deboronation pathways.

Despite those apprehensions, we found that iridium catalysis led to the formation of chiral α-substituted allylic boronates with up to 84 % ee and moderate regioselectivities using a chiral monophosphoramidite ligand. These optically enriched α-substituted allylboronates could then undergo Lewis acid-catalyzed aldehyde allylboration, affording various homoallylic alcohols in excellent yields [15]. Later, using conditions developed by Alexakis and co-workers on nonborylated substrates [16], we developed a one-pot, sequential catalytic enantioselective allylic alkylation/aldehyde allylboration reaction with a borylated substrate (Scheme 8) [17]. Thus, (*E*)-3-chloropropenylboronate **28** was reacted with EtMgBr in the presence of a chiral phosphoramidite–Cu(I) complex at –78 °C to give the chiral allylic boronate intermediate **29** in 95.5 % ee and 8:1 regioselectivity favoring the desired product of S_N2' addition. Without isolation, addition of an aldehyde in the presence of boron trifluoride led to secondary alcohol **31** in high ee with a remarkable *E*:*Z* selectivity. The benefit of a Lewis acid-catalyzed allylboration [18] is obvious; without BF_3, a 3:1 *E*:*Z* ratio is obtained. The superior selectivity was attributed to a tighter, more advanced transition state **30** where steric interactions are accentuated.



Scheme 8 Catalytic enantioselective allylic alkylation/allylboration featuring chiral boronate **29**.

CATALYTIC ENANTIOSELECTIVE CONJUGATE ADDITIONS ONTO 3-BORONYL ENOATES

Oxy-Michael reactions are notoriously difficult, thus borylative conjugate additions [19a] as recently demonstrated by the groups of Yun [19b–e], Fernandéz [19f–k], Hoveyda [19l,m], Shibasaki [19n,o], Nishiyama [19p], and others [19q,r] provides an attractive alternative to produce β-hydroxy carboxyesters. We have developed a complementary conceptual approach where the boronate group is preinstalled on a universal α,β-unsaturated ester substrate, which is then subjected to a catalytic asymmetric conjugate addition with unstabilized carbanions (Fig. 6) [20]. This versatile approach is advantageous compared to conjugate borylation because it avoids the preparation of a different 3-substituted enoate for each desired alkylboronate product.

We anticipated that the chemical compatibility of the boronate substituent could be a major challenge in these reactions. Possible undesired pathways include nucleophilic attack of the organometallic reagent onto the boronate substituent (giving a borinic ester), and insertion of the transition metal into the B–C bond leading to deboronative processes. The first round of optimization examined traditional organometallic agents such as organozinc and organomagnesium reagents under copper catalysis. Because pinacol boronates are known to tolerate many reaction conditions, substrate **32** was attempted first. Under all conditions, however, only a low yield of the desired product was observed with Grignard reagents under Cu(I) catalysis.

We then considered adducts that were recently shown to suppress the normal reactivity of boronic acids (Fig. 6). Thus, we prepared the *N*-methyldiaminoacetic acid (MIDA) adduct **33** [21], the trifluoroborate salt **34** [22], and the 1,8-diaminonaphthalene (dan) derivative **35** [23] and evaluated their use in the Cu(I)-catalyzed addition of EtMgBr using Loh's conditions for β-alkyl α,β-unsaturated esters with Tol-BINAP as the chiral ligand [24]. Substrate **33** was found to be insoluble in most reaction solvents, and borate salt **34** gave incomplete conversion to a complex mixture. The dan adduct **35**, however, gave very promising results, and further optimization of this reaction focused on the stoichiometry of reagents and the temperature, which led to the conditions of Fig. 7 [20]. A selection of products is displayed in Fig. 7 to illustrate the scope of this conjugate addition procedure. To the exception of methyl, unbranched aliphatic reagents provided high yields of product **37** with ee's over 95 % and slightly lower selectivities for branched ones. It is known that thioester derivatives are more reactive and can provide

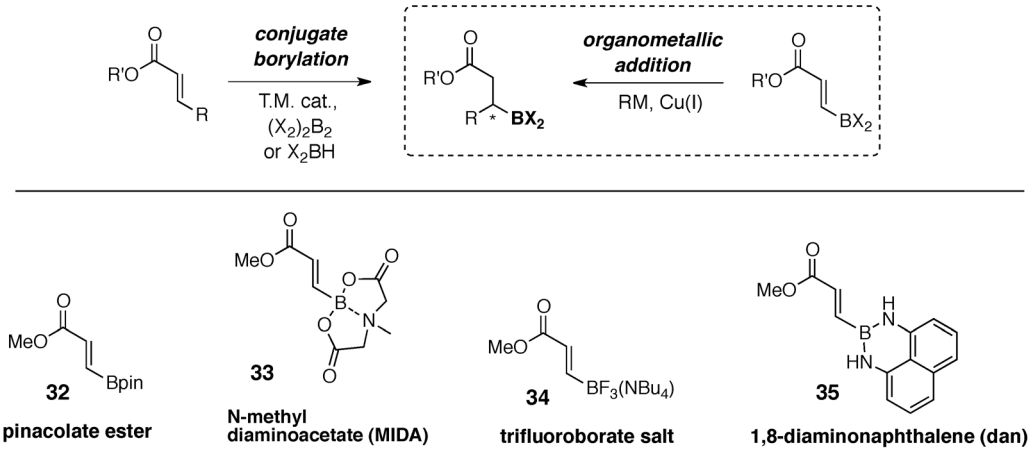


Fig. 6 Two different conjugate addition strategies for the preparation of chiral alkylboronates.

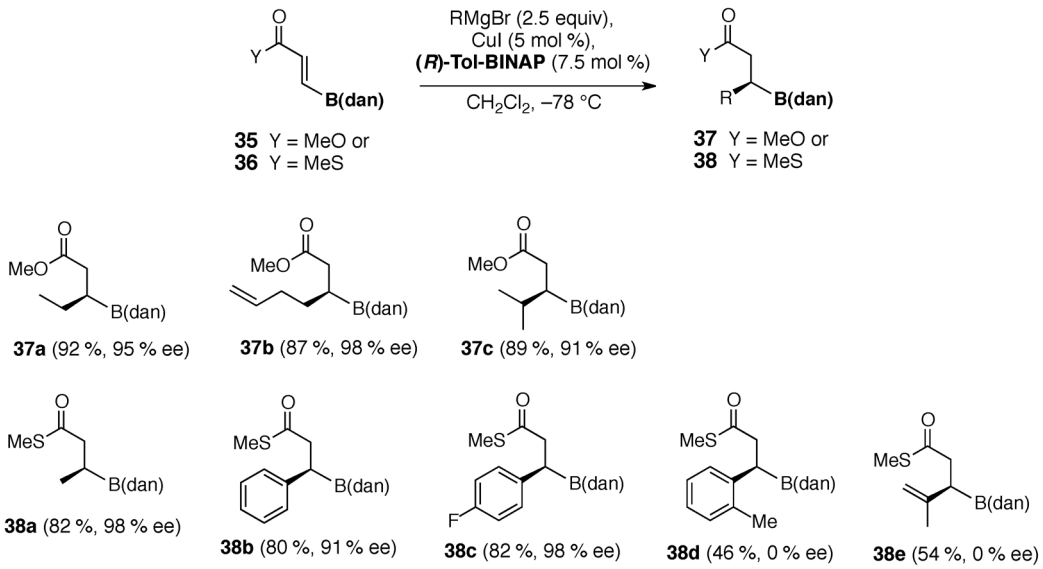


Fig. 7 Chiral secondary alkylboronates by catalytic enantioselective conjugate additions onto dan adducts **35** and **36**.

improvements of yields and selectivities with less reactive organomagnesium reagents [25]. In the event, the methyl thioester derivative **36** led to a substantial improvement of both yields and enantioselectivity with MeMgBr and aromatic Grignard reagents. Hindered reagents led only to racemic products (e.g., **38d**, **38e**).

As part of our ongoing search for new ways to access chiral secondary boronates, we reasoned that the corresponding copper-catalyzed enantioselective conjugate reduction of β-boronyl-β-alkyl α,β-unsaturated esters would provide a useful conceptual alternative to the conjugate addition of Grignard reagents onto **35** and **36**. Using conditions developed by Buchwald and co-workers using polymethylhydrosiloxane (PMHS) as stoichiometric hydride source [26], excellent yields and high ee's were obtained for all cases of β-primary alkyl substrates **39** (Fig. 8) [27].

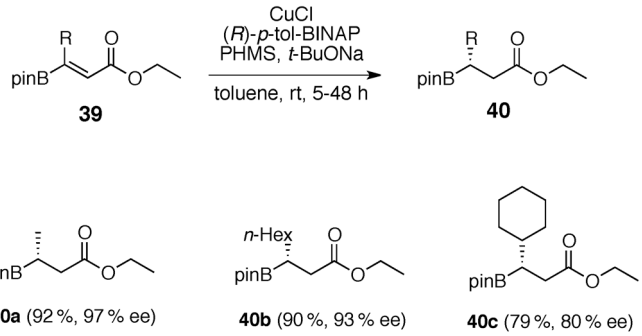


Fig. 8 Chiral secondary alkylboronates by catalytic enantioselective conjugate reduction onto β-alkyl-substituted β-pinacolatoboronyl enoates.

Recently, we expanded this methodology for the syntheses of various optically enriched β-aryl-β-boronyl enoates [28]. As shown with the example of Fig. 9, the asymmetric conjugate reduction of enoates such as **41** afforded the corresponding enantioenriched secondary boronate with an excellent yield and a good ee. The β,β-disubstituted enoate **41** could be synthesized through Heck coupling from the Bdan derivative **35** in a good yield. The key for the improved reactivity and ee on this substrate is the utilization of 1,8-diaminonaphthalene as a planar masking group over the bulky pinacol protecting group.

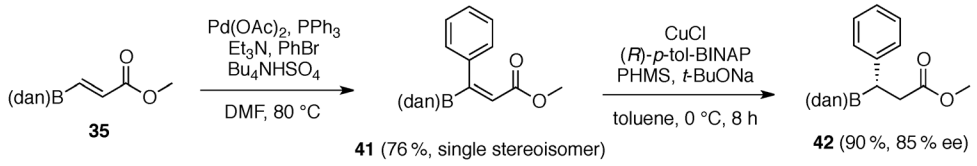


Fig. 9 Preparation of β-(dan)boronyl-β-phenyl enoate and the subsequent Cu(I)-catalyzed enantioselective conjugate reduction [28].

CATALYTIC ENANTIOSELECTIVE PREPARATION AND STEREOSELECTIVE CROSS-COUPLING OF 1,1-DIBORON COMPOUNDS

It is only very recently that notable advances have been reported for the transition-metal-catalyzed cross-coupling of chiral alkylboronates other than cyclopropylboronic esters [29]. The first stereospecific cross-coupling of optically enriched benzylic boronates was demonstrated by Crudden and co-workers [30]. Suginome and co-workers extended those findings to α-(acylamino)benzylboronic

esters [31]. More recently, Molander and co-workers provided the first example of stereospecific cross-coupling of a non-benzylic, secondary alkylboron derivative [32]. An attractive evolution of this concept toward preparing secondary alkylboronates would consist in achieving stereospecific coupling of optically pure 1,1-diboronyl esters (i.e., geminal alkyldiboronic esters). Shibata and co-workers demonstrated that achiral 1,1-diboronyl esters undergo cross-coupling in a chemoselective fashion, affording only the mono-coupled product (as a racemate) (eq. 1, Fig. 10) [33]. These important results suggested that one boronate group can serve as an activating group for cross-coupling of the other boronate. Realizing that the carbon atom of 1,1-diboronyl esters could be made stereogenic through the use of two different boronate adducts, we envisioned the possibility to achieve chemoselective, stereospecific cross-coupling of optically pure 1,1-diboronyl esters.

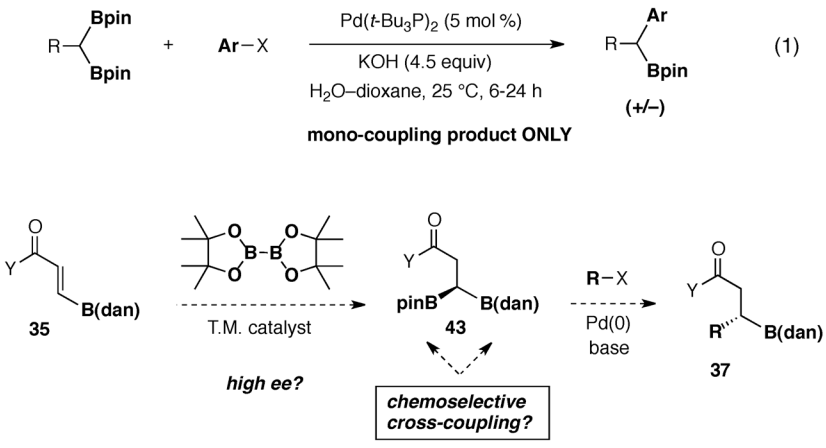


Fig. 10 Strategy for catalytic enantioselective conjugate borylation of β-boronyl acrylate derivatives.

With a view to exploiting pre-borylated substrates, we envisaged a new approach to chiral alkylboronates via a stereoselective mono-cross-coupling of diborylated substrates such as 1,1-diboryl compounds **43** (Fig. 10). Based on our experience with the preparation of optically pure boronic esters via a copper-catalyzed conjugate addition of organomagnesium reagents onto (dan)-3-boronyl enoate **35** (see the previous section), we envisioned that an asymmetric conjugate borylation of **35** with B_2pin_2 could deliver the desired, chiral 1,1-diboronyl ester **43** with high enantioselectivity (Fig. 10) [34]. Upon screening several known reaction conditions, we realized that the protocol developed by Yun and co-workers [19c] allowed access to the desired 3,3-diboronyl carboxyester **43** with a good yield, albeit with a low enantioselectivity when using (*R*)-(*S*)-Josiphos as the diphosphine ligand (Fig. 11). Following a more thorough evaluation of various chiral diphosphine ligands, the trifluoromethyl-substituted Walphos ligand was found to provide the desired enantioenriched 3,3-diboronyl carboxyester **43** with 99 % ee. The enantioenriched 3,3-diboronyl carboxyester **43** is stable to silica column chromatography, and a derivative could be recrystallized to give X-ray quality crystals that allowed the confirmation of the (*R*) absolute stereochemistry of 3,3-diboronyl carboxyester **43** when using the (*R*)-(*R*)-CF_3-Walphos ligand [34].

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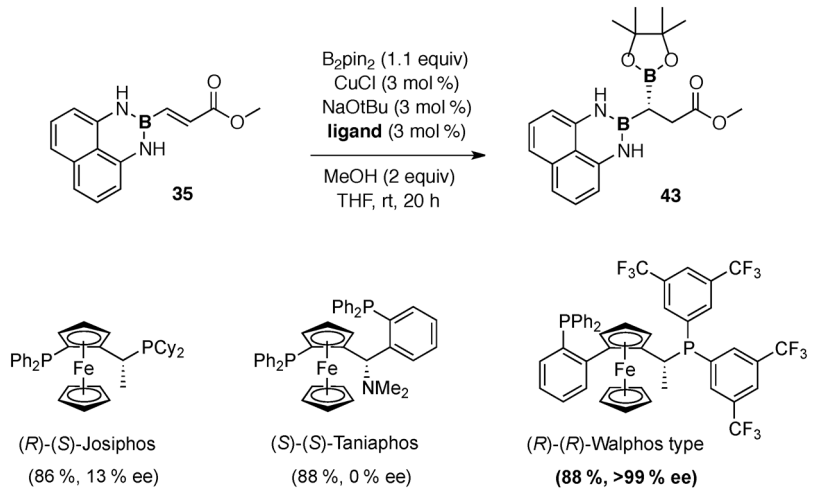

Fig. 11 Optimization of catalytic enantioselective conjugate borylation of β-boronyl acrylate derivative **35**.

The X-ray crystallographic structure of **43** revealed that the carbonyl oxygen of the methyl ester is much closer to the boron atom of the more Lewis acidic pinacolate unit, with a distance of 2.94 Å, than to the boron atom of the Bdan unit (with a distance of 4.41 Å). These observations and the reported inertness of the Bdan unit in cross-coupling reactions [23] made us confident that the pinacol boronate unit could be cross-coupled selectively with aryl halides. Unfortunately, although we were able to obtain the desired product in a good yield, under all conditions attempted we were only able to obtain the desired cross-coupled product as a racemate. Since trifluoroborate salts are known to be potent cross-coupling partners, we prepared the corresponding trifluoroborate salt **44** from the 3,3-diboronyl carboxyester **43** in hand. Using a modification of conditions developed by Molander and co-workers [32], we were glad to isolate products **37** stereospecifically with preservation of stereochemical integrity (Fig. 12).

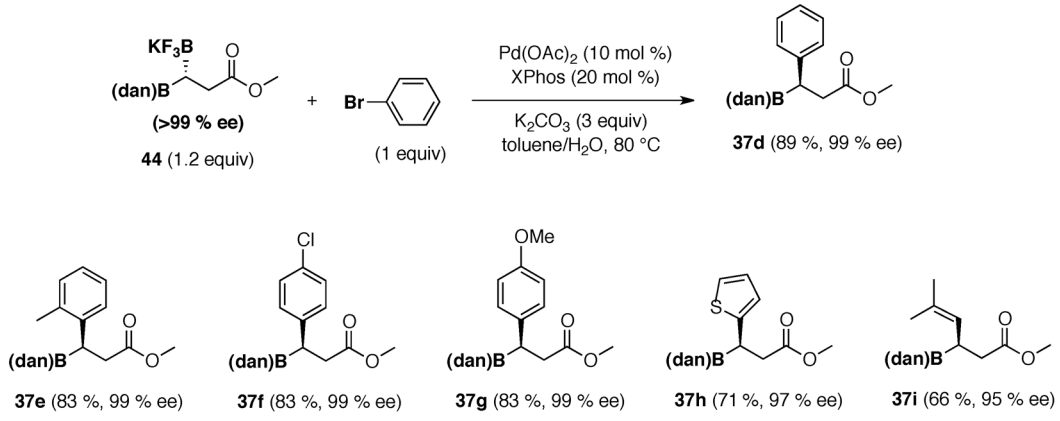

Fig. 12 Stereoinvertive cross-coupling of 1,1-diboryl compound **44**.

The absolute configuration of **37** was confirmed to be (*R*) through comparison with the reported optical rotation of the corresponding alcohol. Combining this result with the (*R*) stereochemistry of 3,3-diboronyl carboxyester **43** (vide supra), it ensures that the observed cross-coupling product **37**

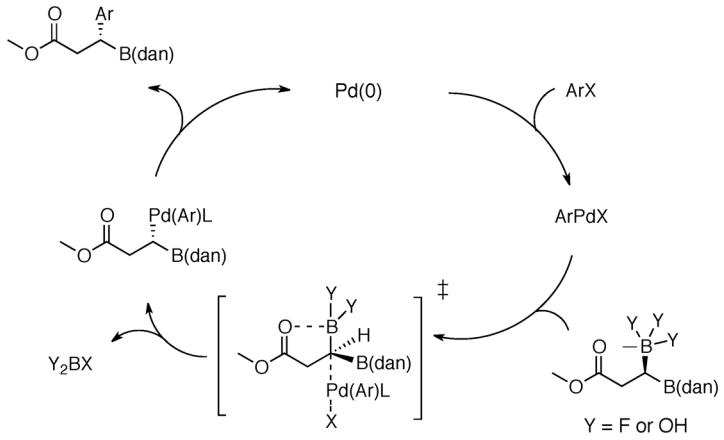

Fig. 13 Proposed mechanistic cycle for stereoinvertive cross-coupling of 1,1-diboryl compound **44**.

underwent a complete inversion of stereochemistry similar to that observed in the Suginome [31] and Molander examples [32] (Fig. 13).

In their communication [32], Molander and co-workers mentioned that the direct cross-coupling reaction with a β-boronyl carboxy ester was not possible, and a stronger coordinating amide was necessary. Consequently, our results with 3,3-diboronyl carboxyesters demonstrate that a strong cooperative effect is at play, which facilitates the transmetallation step through both the coordination of the methyl ester to the boron atom and the stabilization of the α-borylated, Pd(II) intermediate (Fig. 13). Using this optimized procedure, we examined the scope of substrates for cross-coupling reactions with the 3,3-diboryl carboxyester **44**. Most of the coupling reactions with aryl electrophiles proceeded efficiently, leading to high yield and almost complete enantiomeric inversion while tolerating various functional groups (Fig. 12). The reaction tolerates various *ortho*- or *meta*-substituted aryl electrophiles, demonstrating that sterics is not a limiting factor in these cross-coupling reactions. Furthermore, heteroaromatics such as thiophene can also undergo the desired reactions to give the corresponding products in good yields. To our satisfaction, not only aryl electrophiles, but also alkenyl electrophiles could be cross-coupled with the diboronyl reagent, thus affording a new way of preparing enantioenriched allylic boronates.

CONCLUSION

This review described recent developments in the use of catalytic enantioselective methods for the preparation of chiral, optically enriched organoboronates using the strategy of early-stage borylation. In contrast with the mainstream strategy of late-stage borylation of organic functional groups, transformations of boron-containing substrates can generate multiple products by reaction of a single borylated substrate with a simple and variable type of reagent. In this way, acyclic and cyclic secondary alkyl- and allyl-boronates were prepared through catalytic enantioselective processes such as [4 + 2] cycloadditions, isomerizations, allylic substitutions, and conjugate additions. The resulting optically enriched boronates have been successfully utilized in the syntheses of complex natural products such as thiomarinol and palmerolide A. This work on the preparation of chiral alkylboronates by catalytic enantioselective transformations of borylated substrates demonstrates that potential chemoselectivity issues can be avoided with a careful optimization of reaction conditions and a judicious choice of boronyl derivative. The same concept led to the first enantioselective preparation of highly optically enriched 1,1-diboronyl derivatives by a conjugate asymmetric borylation of β-boronyl acrylates. These geminal diboron compounds can be coupled chemo- and stereoselectively with a variety of aryl and alkenyl

halides under palladium catalysis providing a new and efficient method to prepare chiral optically enriched secondary alkylboronates that were difficult to obtain using other methods.

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