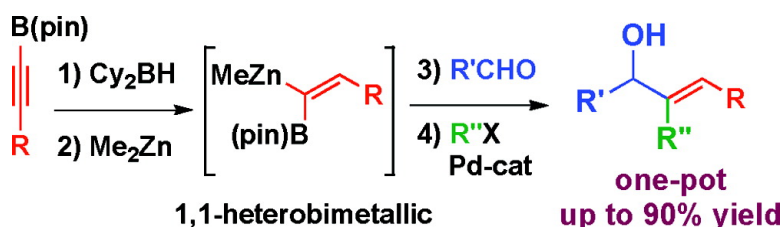**Article**

Generation and Tandem Reactions of 1-Alkenyl-1,1-Heterobimetallics: Practical and Versatile Reagents for Organic Synthesis

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Generation and Tandem Reactions of 1-Alkenyl-1,1-Heterobimetallics: Practical and Versatile Reagents for Organic Synthesis

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Abstract: A practical and straightforward method for generation of versatile 1-alkenyl-1,1-heterobimetallic intermediates and their application to construction of functionalized building blocks are disclosed. Beginning with readily available air-stable 1-alkynyl-1-boronate esters, hydroboration with dicyclohexylborane generates 1-alkenyl-1,1-diboro species. In situ transmetallation with dialkylzinc reagents furnishes 1-alkenyl-1,1-heterobimetallic intermediates. Direct treatment with aldehydes followed by workup allows isolation of B(pin)-substituted allylic alcohols in 70−95% yield. The B(pin)-substituted allylic alcohols react with NBS to afford (*E*)-α,β-unsaturated aldehydes in 51−77% yield via a semipinacol-type rearrangement. In situ treatment of 1-alkenyl-1,1-heterobimetallic intermediates with aldehydes followed by TBHP oxidation enables the preparation of α-hydroxy ketones. Under optimized conditions, addition of 1-alkenyl-1,1-heterobimetallic intermediates to a variety of protected α- and β-hydroxy aldehydes proceeds with good to excellent control over diastereoselectivity to furnish differentially protected dihydroxy ketones. The 1-alkenyl-1,1-heterobimetallic intermediates have also been employed in tandem aldehyde addition/Suzuki cross-coupling reactions to provide densely functionalized allylic alcohols in good to excellent yields.

1. Introduction

The ever-increasing complexity of organic target molecules necessitates the introduction of new methods for the efficient assembly of functionalized intermediates from simple precursors.[1,2] An appealing strategy toward this end is the development of novel tandem reactions whereby sequential transformations can be performed without isolation or purification of intermediates.[3−5] Our approach to this goal entails generation of functionalized 1-alkenyl-1,1-heterobimetallic intermediates, wherein each metal exhibits distinct reactivity that can be selectivity exploited in C−C bond-forming reactions or for installation of functional groups.
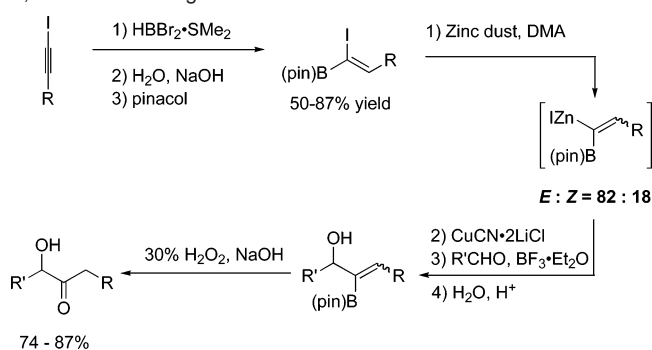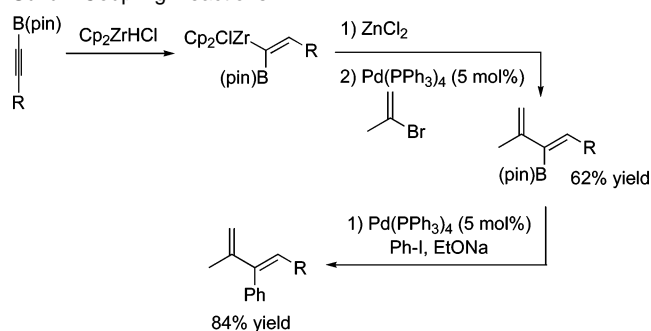
The generation and reactivity of 1-alkenyl-1,1-bimetallics has been of interest for several years; however, relatively few practical applications to stereoselective organic transformations have been reported.[6−14] In pioneering work by Knochel and co-workers,[15] hydroboration of 1-iodoalkynes with HBBr$_2$·SMe$_2$ (Scheme 1) generated vinylboranes that were then hydrolyzed to boronic acids. Subsequent treatment with pinacol and purification by column chromatography gave pinacol boronate esters in 50−80% isolated yields. The 1-iodoalkenyl boronate esters were then exposed to zinc dust in DMA to generate (*Z*)-1-alkenyl-1,1-heterobimetallic compounds. Unfortunately, insertion of zinc into the C−I bond did not proceed with stereochemical fidelity but provided a mixture of double bond isomers (*E:Z* = 82:12), limiting the utility of these 1,1-bimetallic reagents. Reaction of the resulting 1-alkenyl-1,1-zinc boron bimetallics with CuCN resulted in formation of 1,1-copper boron derivatives, which were subjected to a variety of electrophiles. For example, reaction of the 1,1-copper boron bimetallic with aldehydes in the presence of BF$_3$·OEt$_2$ provided the vinyl boronate ester addition products. After standard workup, the resulting *E:Z* mixture of vinyl boronate esters was treated with 30% H$_2$O$_2$ to provide the α-hydroxy ketones in 74−87% yield (50−58% yield from the 1-iodoalkynes, Scheme 1).[15]

In related work, Srebnik and co-workers examined the hydrozirconation of alkynyldioxaborolanes with Schwartz reagent to generate 1-alkenyl-1,1-heterobimetallic intermediates

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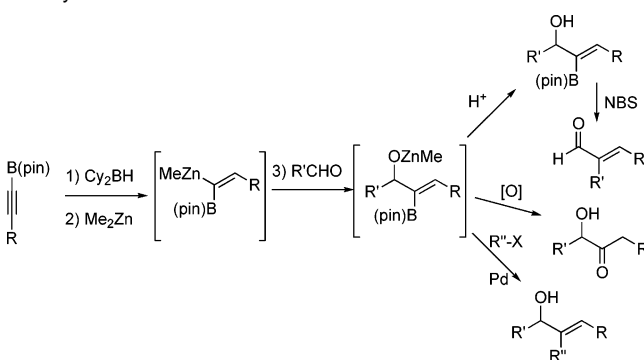(11) Shimizu, M.; Nakamaki, C.; Shimono, K.; Schelper, M.; Kurahashi, T.; Hiyama, T. *J. Am. Chem. Soc.* **2005**, *127*, 12506.
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Scheme 1. Knochel's Synthesis of α-Hydroxy Ketones via 1,1-Bimetallic Reagents

Scheme 2. Srebnik's Preparation of Dienes by Negishi and Suzuki Coupling Reactions

Scheme 3. Application of 1-Alkenyl-1,1-heterobimetallic Intermediates to the Synthesis of Boronate-Substituted Allylic Alcohols, α-Hydroxy Ketones, Dienols, and α,β-Unsaturated Aldehydes

Scheme 4. One-Pot Generation of B(pin)-Substituted Allylic Alcohols

1,1-heterobimetallics can be generated, using our method, from air-stable B(pin)-substituted alkynyl boronate esters and can be employed in further applications without isolation of intermediates.

2. Results and Discussion

Our interest in the application of 1-alkenyl-1,1-heterobimetallics to organic synthesis stems from their potential to serve as versatile multifunctional intermediates in sequential bond-forming reactions. With the goal of developing simple and practical methods employing such heterobimetallics, the following criteria were deemed important. The 1-alkenyl-1,1-heterobimetallics must be easily generated using standard organic laboratory techniques and used without isolation or purification of air-sensitive intermediates.

2.1. Generation and Reactions of 1-Alkenyl-1,1-Hetero-bimetallic Reagents. With the above guidelines in mind, we generated 1-alkenyl-1,1-heterobimetallic reagents via hydroboration of air-stable B(pin)-substituted alkynes with dicyclohexylborane (Scheme 4).[19−24] The resulting 1,1-diboro species exhibited resonances at 30 and 80 ppm in the ^{11}B NMR spectrum, consistent with the proposed structure.[25] Only one regioisomer was observed in the hydroboration reaction, and no isomerization of the double bond was detected by ^{1}H NMR spectroscopy.

Although both B−C bonds of the 1-alkenyl-1,1-diboro compounds in Scheme 4 are similarly unreactive toward most organic electrophiles, we hypothesized that they would display significantly different rates of transmetallation with organozinc reagents. This hypothesis was based on the ease of transmetallation of dialkyl vinylboranes (R$_2$BCH=CHR′) versus aryl boronate esters and acids. Srebnik[26] and Oppolzer[27] demon-

(Scheme 2).[16−18] Transmetallation of the Zr−C bond allowed selective coupling reactions to be performed with retention of the stereochemistry of the alkenyl group. For example, reaction of the 1,1-boron zirconium bimetallic with ZnCl$_2$ generated the 1,1-boron zinc bimetallic. In the presence of 5 mol % Pd(PPh$_3$)$_4$ and a vinyl bromide, a Negishi coupling ensued with formation of the dienyl boronate ester in 62% isolated yield. In the next step, treatment of dienyl boronate ester with PhI, EtONa, and fresh Pd(PPh$_3$)$_4$ (5 mol %) provided the Suzuki coupling product in 84% yield.[16]

Although both of these studies represent important advances in the chemistry of 1,1-heterobimetallics, each has drawbacks in its applications to organic synthesis. The multistep synthesis and the need for isolation of the 1-iodoalkenyl boronate esters in Scheme 1 diminish the synthetic efficiency and attractiveness of these reagents. Furthermore, the loss of stereochemistry in the zinc insertion step gives rise to isomeric mixtures of (E)- and (Z)-products, limiting their synthetic utility. The application of Schwartz reagent, Cp$_2$ZrHCl, on large scale is impractical and prohibitively expensive. We speculate that these limitations have discouraged the adoption of 1-alkenyl-1,1-heterobimetallic reagents by the organic community.

In this report, we outline the generation of practical and synthetically useful 1-alkenyl-1,1-heterobimetallic intermediates that undergo a variety of transformations to provide boronate-substituted allylic alcohols, α-hydroxy ketones, dienols, and α,β-unsaturated aldehydes (Scheme 3). We have also studied additions of 1-alkenyl-1,1-heterobimetallic reagents to chiral aldehydes to furnish *syn* and *anti* protected α,β-dihydroxy ketones with high diastereoselectivity. Importantly, 1-alkenyl-

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Table 1. Preparation of B(pin)-Substituted Allylic Alcohols from Scheme 4

entry	boron alkyne	aldehyde	product	yield (%)
1	(pin)B≡≡n-Bu	PhCHO	Ph, OH, B(pin), n-Bu chain	81
2	(pin)B≡≡t-Bu	PhCHO	Ph, OH, B(pin), t-Bu	91
3	(pin)B≡≡(CH₂)₄Cl	2-Br-benzaldehyde (CHO, Br)	OH, Br, B(pin), (CH₂)₄Cl	93
4	(pin)B≡≡(CH₂)₄Cl	4-Cl-benzaldehyde (CHO, Cl)	OH, Cl, B(pin), (CH₂)₄Cl	91
5	(pin)B≡≡(CH₂)₄Cl	4-Me-benzaldehyde (CHO)	OH, B(pin), (CH₂)₄Cl	70
6	(pin)B≡≡(isopropenyl)	PhCHO	Ph, OH, B(pin), vinyl	79
7	(pin)B≡≡t-Bu	isobutyl-CHO	OH, B(pin), t-Bu	95

strated that dialkyl vinylboranes undergo rapid transmetallation with dialkylzinc reagents at low temperature. In contrast, Bolm reported that B(pin)-substituted aryl groups undergo transmetallation with dialkylzinc reagents only on prolonged heating.[28] Thus, by selective transmetallation of the more reactive alkenyl dicyclohexylborane with dimethylzinc, we believed it would be possible to generate reactive zinc boron heterobimetallic species. We were pleased to find that the Cy₂B group underwent transmetallation with dimethylzinc much faster than the (pin)B and that the resulting boron/zinc heterobimetallic reagent readily added to aldehydes to provide B(pin)-substituted (E)-allylic alcohols in high yields (Scheme 4). We propose that the origin of this reactivity difference stems from the availability of the p orbitals on the borons. Through resonance, the B(pin) oxygens donate electron density to boron, reducing its Lewis acidity. In contrast, the cyclohexyl groups donate electron density through the sigma bonds, leaving the boron p orbital more available to participate in the alkyl/vinyl exchange and lowering the barrier for the transmetallation process at BCy₂. No product derived from methyl addition to the aldehyde was observed.

Table 1 presents representative examples of the synthesis and isolation of B(pin)-substituted allylic alcohols (70−95% isolated yield). Benzaldehyde derivatives with ortho or para substituents and benzaldehyde itself were very good substrates for the vinyl addition reaction (entries 1−6). Furthermore, the aliphatic aldehyde in entry 7 gave 95% yield. Other saturated aldehydes have been used successfully in tandem reactions and are outlined in subsequent sections. A variety of B(pin)-substituted alkynes were employed, including those with small substituents (n-Bu) and bulky groups (t-Bu). In entry 6, the boron alkyne contains a conjugated vinyl group whereas the substrates in entries 3−5 possess chlorides. Importantly, only one isomer of the allylic alcohol was observed in each case, indicating that isomerization

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Scheme 5. NBS Promoted Rearrangement of B(pin)-Substituted Allylic Alcohols

51-77% yield
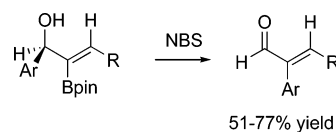
Table 2. Stereospecific Synthesis of (E)-Trisubstituted α,β-Unsaturated Aldehydes from Scheme 5

entry	allylic alcohols	product	yield (%)
1[a]	Ph, OH, B(pin), n-Bu chain	H, O, Ph, n-Bu chain enal	74
2[a]	Ph, OH, B(pin), t-Bu	H, O, Ph, t-Bu enal	51
3	4-Cl-C₆H₄, OH, B(pin), (CH₂)₄Cl	H, O, 4-Cl-C₆H₄, (CH₂)₄Cl enal	59
4	4-Me-C₆H₄, OH, B(pin), (CH₂)₄Cl	H, O, 4-Me-C₆H₄, (CH₂)₄Cl enal	77

[a] Stereochemistry determined by nOe. See the Supporting Information for details.

of the double bond *does not occur* under the transmetallation, addition, or workup conditions. This is particularly impressive in the case of cis t-Bu and B(pin) groups in entries 2 and 7. B(pin)-substituted allylic alcohols are potentially suitable substrates for Suzuki cross-coupling reactions, a topic addressed in Section 2.5.

2.2. Stereospecific Generation of (E)-Trisubstituted α,β-Unsaturated Aldehydes. With the B(pin)-substituted allylic alcohols in hand, we desired to examine their reactivity toward oxidants such as N-bromosuccinimide (NBS). It is known that vinyl borane derivatives react with electrophilic halide sources to give halodeborylation products with inversion of the double bond stereochemistry.[29,30] In contrast to the reaction of vinyl boranes with halogenating reagents, combination of our B(pin)-substituted benzylic allylic alcohols with NBS resulted in an interesting skeletal rearrangement with formation of (E)-trisubstituted enals (Scheme 5). The (E)-stereochemistry was assigned on the basis of NOE experiments with the enals in entries 1 and 2. Although substrates with aryl carbinols underwent migration to form (E)-trisubstituted enals (Scheme 5), alkyl derivatives resulted in complex mixtures of products under the conditions examined. This observation is most likely related to the greater migratory aptitude of aryl groups.[31] The products of these oxidative rearrangements are listed in Table 2.
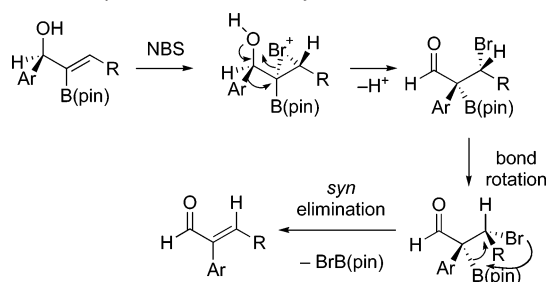
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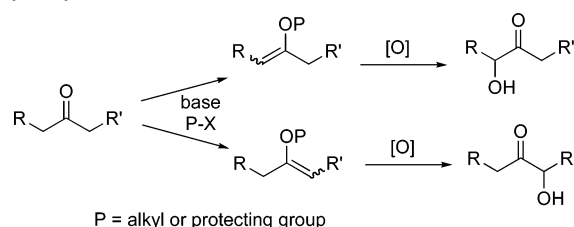(30) Brown, H. C.; Hamaoka, T.; Ravindran, N.; Subrahmanyam, C.; Somayaji, V.; Bhat, N. G. *J. Org. Chem.* **1989**, *54*, 6075.
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Scheme 6. Proposed Reaction Pathway for the Stereospecific Formation of α,β-Unsaturated Aldehydes

A possible reaction pathway for the formation of the enals is illustrated in Scheme 6. Attack of the NBS on the C—C double bond forms a bromonium intermediate. A semipinacol-type rearrangement ensues with migration of the carbinol Ar group, opening of the bromonium ion, and generation of the aldehyde after deprotonation. Finally, after bond rotation, we propose a syn elimination of the boronate ester and the bromide to give the (E)-enal product. The stereoselective synthesis of α,β-unsaturated aldehydes represents a challenge due to the ease of isomerization of the double bond by nucleophiles. As such, these enals would be difficult to prepare with high selectivity by other methods.

2.3. One-Pot Synthesis of α-Hydroxy Ketones. The high isolated yields in the synthesis of B(pin)-substituted allylic alcohols (Table 1) imply that formation of the 1,1-heterobimetallic intermediates and carbonyl additions occur smoothly and that the intermediates in this process might be suitable for further elaboration. We were initially attracted to the preparation of α-hydroxy ketones, which are important intermediates in the synthesis of natural and non-natural products. The synthesis of α-hydroxy ketones has been studied,[15,33−46] with most methods based on the oxidation of enolates or their derivatives.[35,36,47−51] This approach relies on a regio- and stereoselective enolization, which may be difficult to achieve (Scheme 7). Moreover, if the substrate contains pre-existing stereocenters, the facial selectivity of the oxidation becomes crucial. Alternative approaches entail the catalytic asymmetric benzoin[52−56] and the cross silyl benzoin condensations.[57−59] These reactions are elegant and suitable for aromatic substrates but give low yields with aliphatic derivatives.

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Scheme 7. Enolization/Oxidation Strategy for the Synthesis of α-Hydroxy Ketones

P = alkyl or protecting group

Scheme 8. One-Pot Procedure for the Synthesis of α-Hydroxy Ketones
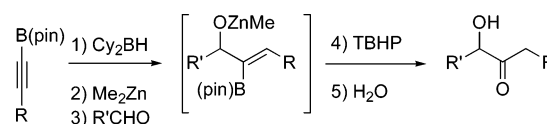
Table 3. One-Pot Preparation of α-Hydroxy Ketones from Scheme 8

entry	boron alkyne	aldehyde	product	yield (%)
1	Bu≡≡B(pin)	X= H	X= H	65[a]
2		X= 2-OMe	X= 2-OMe	80[b]
3		X= 2-Br	X= 2-Br	81[b]
4		X= 4-Cl	X= 4-Cl	83[b]
5	Bu≡≡B(pin)	BnO—CHO		74[b]
6	≡≡B(pin)	PhCHO		40[a]

[a] Five equiv of TBHP as oxidant. [b] One and one-tenth equiv of BF$_3$·OEt$_2$ were added at −78 °C, 10 equiv of TBHP were used as oxidant.

We envisioned a one-pot synthesis of α-hydroxy ketones beginning with hydroboration of B(pin)-substituted alkynes with dicyclohexylborane, transmetallation to zinc to furnish 1-alkenyl-1,1-heterobimetallics, and addition to aldehydes (Scheme 8). The resulting B(pin)-substituted allylic alkoxides are then subjected to in situ oxidation with *tert*-butylhydroperoxide (TBHP) to provide the α-hydroxy ketones. As illustrated in Table 3, this one-pot procedure was successful. Most substrates gave higher yields when BF$_3$·OEt$_2$ was used during the carbonyl addition (entries 2−6). After optimization, B(pin) alkynes were converted into α-hydroxy ketones in good yields for the one-pot 4-step transformation.

Aromatic aldehydes substituted at the 2- or 4-positions successfully underwent the addition/oxidation procedure to afford α-hydroxy ketones in 65−83% yield (entries 1−4). Aliphatic aldehydes, as found in entry 5 and further described below, were also good substrates for the tandem reaction. In entry 6, the enyne addition product isomerized under the reaction and work up conditions to give the conjugated α-hydroxy enone in lower yield (40%).

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Scheme 9. Enolization and Oxidation of Benzyl Isopentyl Ketone
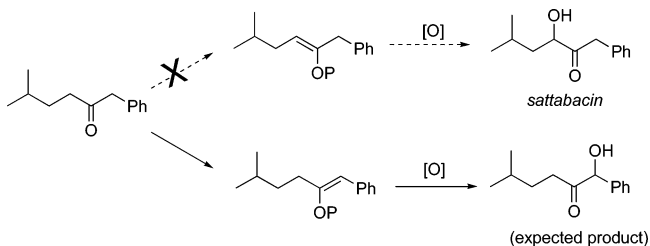
Scheme 10. One-Pot Synthesis of *sattabacin*
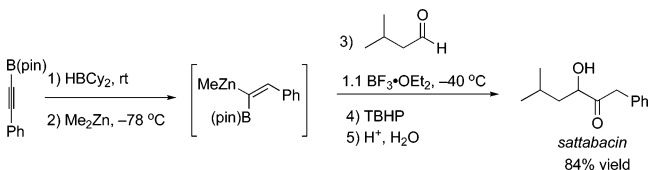
The α-hydroxy ketone in Scheme 9, called *sattabacin*, was isolated from soil and found to exhibit antiviral properties.[60] The generation of this product from benzyl isopentyl ketone by oxidation would be difficult (Scheme 9) because the increased acidity of the benzylic hydrogens and the higher thermodynamic stability of the resulting enolate favors the formation of the isomeric product. Using our 1,1-heterobimetallics, *sattabacin* was obtained with high yield (84%) in a one-pot procedure (Scheme 10).

Overall, our procedure for the synthesis of α-hydroxy ketones represents a significant improvement over previous methods, because it is not necessary to isolate or purify the intermediates and the entire procedure can be conveniently conducted in a single reaction vessel. These promising results inspired us to develop methods for the addition of 1,1-heterobimetallic reagents to chiral aldehydes to prepare highly oxygenated enantioenriched building blocks that would be of value in natural product synthesis.

2.4. Diastereoselective Additions of 1-Alkenyl-1,1-hetero-bimetallic Reagents to Chiral Aldehydes. Diastereoselective C−C bond-forming reactions are crucial to the successful elaboration of intermediates in natural product synthesis. Toward our goal of developing synthetically useful 1,1-heterobimetallic reagents, we next focused on stereoselective additions of 1-alkenyl-1,1-heterobimetallic reagents to chiral aldehydes bearing protected α- or β-hydroxy groups that permit chelation, such as benzyl, or that traditionally disfavor chelation, such as trialkylsilyl.

2.4.1. Diastereoselective Additions to Chiral Propanals. Treatment of racemic 2-phenyl-propionaldehyde with our boron/zinc 1,1-heterobimetallic reagent followed by oxidation with TBHP resulted in formation of the α-hydroxy ketone in 72% yield with 1:6 dr (Scheme 8 above, Table 4, entry 1). In this case, the stereochemistry has not been determined, but the reaction is assumed to proceed by Felkin addition to give the predicted product.[61]

Chiral aldehydes with α- or β-hydroxy groups are among the most useful substrates for the synthesis of polyhydroxylated products. The enantioenriched TBS protected α-hydroxy aldehyde gave *syn*-products derived from Felkin addition (Scheme

11, P = protecting group) in good yields (77−84%), but with modest dr (1:3−5, entries 2 and 3, Table 4). Increasing the size of the protecting group to TBDPS and TIPS gave high dr's of 1:11 and 1:14, respectively, favoring the expected Felkin addition products (entries 4 and 5). The stereochemical assignments were based on either X-ray analysis of the major diastereomer or on ¹H NMR studies using the modified Mosher method[62] (see Table footnotes and Supporting Information).

To prepare the diastereomer, enantioenriched α-hydroxy aldehydes protected with benzyl and PMB groups were examined. Addition of 1,1-heterobimetallics to benzyl and PMB protected α-hydroxy aldehydes gave the expected *anti*-Felkin or Cram products via chelation control with high dr ≥ 15:1. A variety of B(pin) alkynes were employed resulting in formation of α,β-dioxygenated ketones with yields between 70−87% (entries 6−10). Thus, as outlined in Table 4, our method enables synthesis of both diastereomeric α,β-dioxygenated ketones with excellent control over diastereoselectivity (up to 1:14 favoring Felkin and 20:1 favoring *anti*-Felkin addition).

Early in our reaction optimization efforts outlined in Table 4 (entry 2), we had occasion to examine the effect of several Lewis acids on the addition of 1,1-heterobimetallics to silyl protected α-hydroxy propanals. Surprisingly, addition of the Lewis acid BF₃·OEt₂ resulted in a reversal of the diastereoselectivity (Table 5). In the absence of Lewis acids, addition to the TBS protected aldehyde provided the Felkin addition product (Table 5, entry 1). In contrast, in toluene or dichloromethane with 1.1−2.5 equiv of BF₃·OEt₂ the anti-Felkin addition products were formed with 6:1 to 20:1 dr (entries 2−5).[63] Although diastereoselectivities were better in dichloromethane, yields were higher in toluene and with less BF₃·OEt₂. In the case of the TBDPS-protected aldehyde, the dr went from 1:11 favoring Felkin addition in the absence of BF₃·OEt₂ to 1:1 in its presence. The highest dr in the absence of Lewis acids was with the TIPS derivative, which furnished product with 1:14 dr favoring Felkin addition (entry 9). When the addition with the TIPS protected aldehyde was conducted in the presence of BF₃·OEt₂, the anti-Felkin product was obtained with 8:1 to 20:1 dr (entries 10−13). Thus, use of the TIPS protected α-hydroxy aldehydes with and without BF₃·OEt₂ enabled synthesis of α,β-dihydroxyketones with dr's between 16:1 and 1:14. Such high levels of diastereocontrol with the same substrate increase the flexibility and attractiveness of these methods.

The unexpected diastereofacial selectivities in Table 5 are not consistent with current models used to predict diastereoselectivity in additions to silyl-protected α-hydroxy aldehydes. First, monodentate Lewis acids, such as BF₃·OEt₂, are expected to increase the proportion of *Felkin addition product*, exactly the opposite of our observations (Table 5). Furthermore, although there are some examples of silyl-protected α-hydroxy aldehydes that do undergo chelation controlled addition reactions,[64,65] the silyl groups in these reports are significantly smaller than TIPS, such as TMS and TBS. Chelation controlled addition to these substrates, however, is observed with Lewis acids possessing *two open coordination sites*.

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Table 4. Diastereoselective Addition of 1,1-Heterobimetallic Complexes to Chiral Aldehydes from Scheme 11

entry	boron alkyne	aldehyde	major product	dr[c]	yield[d] (%)
1	n-Bu—≡—B(pin)	(H, O / Ph, Me)	(structure)	1 : 6	72
2	n-Bu—≡—B(pin)	(H, O / OTBS, Me)	(structure)	1 : 3[b]	83
3	Ph—≡—B(pin)		(structure, Ph / OTBS, Me)	1 : 5	85
4	n-Bu—≡—B(pin)	(H, O / OTBDPS, Me)	(structure)	1 : 11	54
5	n-Bu—≡—B(pin)	(H, O / OTIPS, Me)	(structure)	1 : 14	68
6	n-Bu—≡—B(pin)	(H, O / OBn, Me)	(structure)	20 : 1	80
7	Cl(CH$_2$)$_4$—≡—B(pin)		(structure, Cl / OBn, Me)	20 : 1	87
8	t-Bu—≡—B(pin)	(H, O / OPMB, Me)	(structure)	20 : 1[a]	70
9	n-Bu—≡—B(pin)		(structure, OPMB, Me)	20 : 1	79
10	(cyclohexenyl)—≡—B(pin)		(structure, OPMB, Me)	>15 : 1	79

[a] Absolute configurations of products were determined by X-ray crystallography. [b] Absolute configurations of products were determined by analysis of the Mosher esters. [c] Anti-Felkin:Felkin; determined by ¹H NMR. [d] Isolated yield.

Scheme 11. Diastereoselective Additions of 1,1-Heterobimetallics to Protected α-Hydroxy Propanals

(reaction scheme): B(pin) on alkyne R, 1) Cy$_2$BH, 2) Me$_2$Zn → [MeZn, R, B(pin)], 3) aldehyde (H, O, OP, Me), 4) TBHP → R—C(O)—CH$_2$... OH, OP, Me (*anti*-Felkin) + R... OH, OP, Me (Felkin)
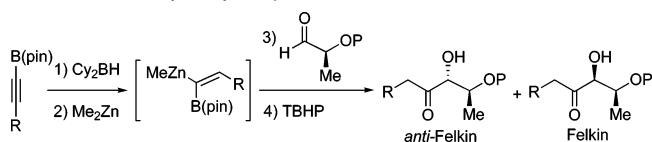
Examples of chelation-controlled additions have been reported by Evans and co-workers employing AlMe$_2$Cl and AlMeCl$_2$, which have a single open coordination site but can undergo chloride abstraction to generate a chelating cationic Lewis acid (Scheme 12).[66] Similar behavior was not observed with BF$_3$·OEt$_2$ under the Evans conditions, however. A halide abstraction mechanism analogous to the aluminum system has been proposed by Crimmins with TiCl$_4$ and a tridentate substrate.[67,68] At this time, we do not have sufficient experimental evidence to introduce a model to explain the unexpected Lewis acid effect

observed in Table 5. Studies to shed light on the origin of stereoselectivity in these reactions are ongoing in our laboratory.

2.4.2. Diastereoselective Additions to Protected β-Hydroxy Propanals. Chiral protected β-hydroxy aldehydes are useful precursors in synthesis because the product 1,3-diol is a common structural motif in natural products. Chelation-controlled additions to these substrates are more challenging, because the additional carbon separating the carbonyl and protected hydroxyl makes chelation less favorable. The similarity in size of the α-substituents also reduces diastereoselectivity in Felkin additions. The most difficult substrates in this class, however, are those that are protected with bulky silyl groups, which disfavor chelation due to the reduced propensity of such silyl ethers to bind to Lewis acids.

Our initial efforts focused on addition of 1,1-heterobimetallics to benzyl protected β-hydroxy aldehydes (Scheme 13) with the goal of controlling diastereoselectivity through chelation. In the absence of additional Lewis acids, the dr of the α-hydroxy ketone product was very low (1.5:1, entry 1, Table 6) favoring anti-Felkin addition. Lewis acids with the potential to chelate, such as ZnBr$_2$, MgBr$_2$, and AlMe$_2$Cl, resulted in formation of

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Table 5. Examination of the Effect of BF$_3$·OEt$_2$ on the Diastereomeric Ratio in the Addition of 1,1-Heterobimetallics to Silyl Protected α-Hydroxy Propanals

entry	aldehyde	major product	BF$_3$·OEt$_2$ (equiv)	sol	dr[a]	yield (%)
1			none	tol.	1:3	83
2			1.1	tol.	6:1	79
3			2.5	tol.	13:1	45
4			1.1	CH$_2$Cl$_2$	10:1	62
5			2.2	CH$_2$Cl$_2$	20:1	39
6			none	tol.	1:11	54
7			1.1	CH$_2$Cl$_2$	~1:1	80
8			2.2	CH$_2$Cl$_2$	~1:1	60
9			none	tol.	1:14	68
10			1.1	tol.	8:1	86
11			2.5	tol.	16:1	67
12			1.1	CH$_2$Cl$_2$	15:1	64
13			2.2	CH$_2$Cl$_2$	20:1	18

[a] Anti-Felkin:Felkin.

Scheme 12. Chelation-Controlled Addition Model Proposed by Evans and Co-workers

	anti-Felkin		Felkin
OP = OBn	90	:	10
OP = OTBS	97	:	3

proposed intermediate
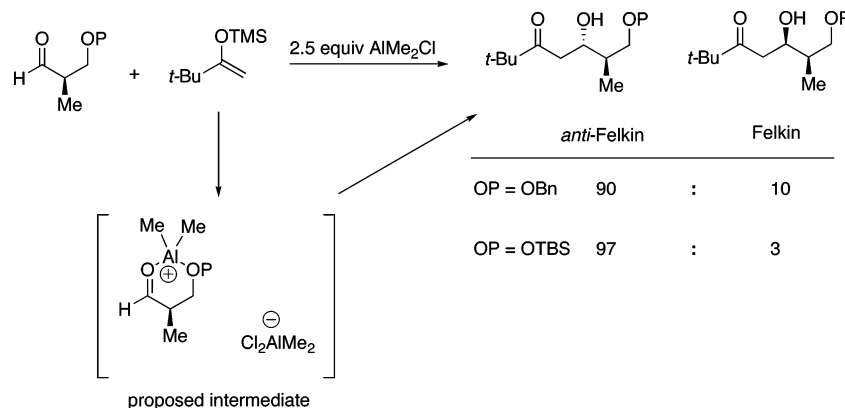
Scheme 13. Diastereoselective Addition of 1,1-Bimetallics to Protected β-Hydroxy Aldehydes
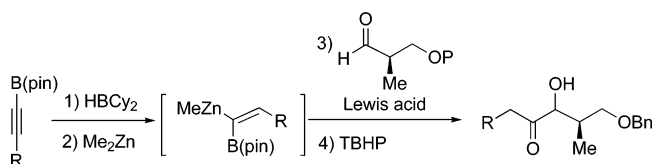
the chelation-controlled addition products with dr's as high as 6:1 (entries 2–4, Table 6). We were again surprised and gratified to find that addition of BF$_3$·OEt$_2$ resulted in excellent control of the diastereoselectivity, with the anti-Felkin product formed in 93% yield with a dr of 20:1 (entry 5). Similar dr's were obtained with other B(pin) alkynes (entries 6 and 7).

We next examined the challenging chiral TBS-protected β-hydroxy aldehydes. Employing B(pin) alkynes, unacceptably low dr's (~1:2) were obtained in the absence of Lewis acids and in the presence of ZnBr$_2$ or BF$_3$·OEt$_2$ (entries 1–3, Table 7). We next examined the size of the boron-containing group on the alkyne (BX$_2$ in Table 7), because it is known that changing the size of the nucleophile impacts diastereoselectivity. Thus, we examined the use of boron alkynes based on 1,3-propane diol, 9-BBN, and isopropoxide. In this study, it was found that the bulky diisopropoxy boronate ester exhibited high dr (11:1) favoring the anti-Felkin addition product (entry 10).

The high diastereofacial selectivities observed with both benzyl and TBS protected β-hydroxy aldehydes in the presence of BF$_3$·OEt$_2$ are surprising because BF$_3$·OEt$_2$ is considered to

Table 6. Optimization of 1,1-Heterobimetallic Addition to Benzyl Protected β-Hydroxy Aldehydes

entry	boron alkynes	major product	Lewis acid (equiv)	dr[b]	yield[c] (%)
1	*n*-Bu━≡━B(pin)		—	1.5 : 1	74
2	*n*-Bu━≡━B(pin)		ZnBr$_2$ (1.1)	5 : 1	–
3	*n*-Bu━≡━B(pin)		MgBr$_2$ (1.1)	1.8 : 1	–
4	*n*-Bu━≡━B(pin)		Me$_2$AlCl (2.5)	~6 : 1	–
5	*n*-Bu━≡━B(pin)		BF$_3$·OEt$_2$ (1.1)	20:1	93
6	Cl(CH$_2$)$_4$━≡━B(pin)		BF$_3$·OEt$_2$ (1.1)	20:1	91
7	Ph━≡━B(pin)		BF$_3$·OEt$_2$ (1.1)	20:1[a]	76

a Absolute configurations of products were determined by X-ray crystallography. *b* Anti-Felkin:Felkin; determined based on ^{1}H NMR analysis. *c* Yields not determined in reactions that gave low dr. Yields listed are isolated.

Table 7. Optimization of 1,1-Heterobimetallic Addition to TBS-Protected β-Hydroxy Aldehydes
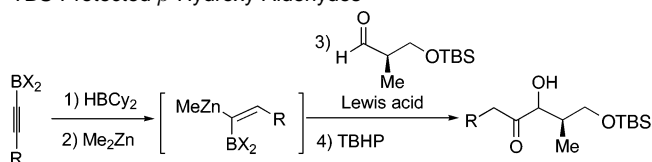
entry	boronalkyne	Lewis acid (equiv)	dr[a]	yield (%)[b]
1	*n*-Bu━≡━B(pin type)	—	1 : 1.2	60
2		ZnBr$_2$ (1.1)	1 : 2.1	–
3		BF$_3$•OEt$_2$ (1.1)	1.5 : 1	–
4	*n*-Bu━≡━B	—	1 : 1.4	–
5		ZnBr$_2$ (1.1)	~2 : 1	–
6	*n*-Bu━≡━B	ZnBr$_2$ (1.1)	~2 : 1	–
7		BF$_3$•OEt$_2$ (2.5)	~2 : 1	–
8	*n*-Bu━≡━B	—	1 : 1.7	–
9		ZnBr$_2$ (1.1)	6 : 1	–
10		BF$_3$•OEt$_2$ (2.5)	11 : 1	61

a Anti-Felkin:Felkin. *b* Yields not determined in reactions that gave low dr. Yields listed are isolated.

be a monodentate Lewis acid. Excellent models have been proposed by Evans to rationalize the observation of anti-Felkin addition products with protected α,β-disubstituted β-hydroxy aldehydes.[69,70] In these cases, the conformation of the aldehyde is controlled by the dipole interactions between the Lewis acid-bound carbonyl group and the protected β-hydroxy group (Scheme 14). The larger R group of the β-stereocenter is situated in the least sterically hindered position, oriented away from the

aldehyde carbonyl group. When the dipole interactions are greater than the cost of attack of the nucleophile over the medium size group on the α-carbon (methyl), anti-Felkin addition products are obtained. This model, however, cannot be used to explain our results, because there is no β-stereocenter on our substrates. Thus, the dipole interactions can be minimized in conformations leading to both the Felkin and anti-Felkin addition pathways using the Evans model (Scheme 14).

One speculative reaction pathway to rationalize the highly diastereoselective formation of anti-Felkin addition products in Table 7 involves binding of BF$_3$ to the carbonyl followed by removal of one of the fluorides by a second molecule of BF$_3$ to give a chelating boron species, as outlined in Scheme 15.[71–73] As mentioned earlier, a somewhat related mechanism has been proposed by Crimmins in the diastereoselective aldol reaction in the presence of excess TiCl$_4$[67,68] and by Evans in the aldol and allyl additions to β-alkoxy aldehydes promoted by dimethylaluminum chloride and methylaluminum dichloride.[66,74,75] We do not currently have experimental evidence for or against this model but note that it does serve to predict the observed stereochemistry in Table 7.

The high diastereoselectivities obtained with both α- and β-hydroxy aldehydes in Tables 4−7 indicate that the 1-alkenyl-1,1-heterobimetallic intermediates outlined herein have significant potential utility in the stereoselective formation of C−C bonds.

2.5. One-Pot Tandem Carbonyl Additions/Cross-Coupling Reactions. Vinyl boronate esters are useful substrates for a variety of transformations, most notably Suzuki cross-coupling reactions.[18,76,77] With this in mind, we explored the possibility

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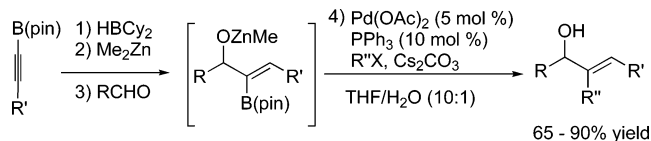
Scheme 14. Evans Model for Additions to α,β-Disubstituted β-Hydroxy Aldehydes (Above) and Application of This Model to the Results in Table 7 (Below)
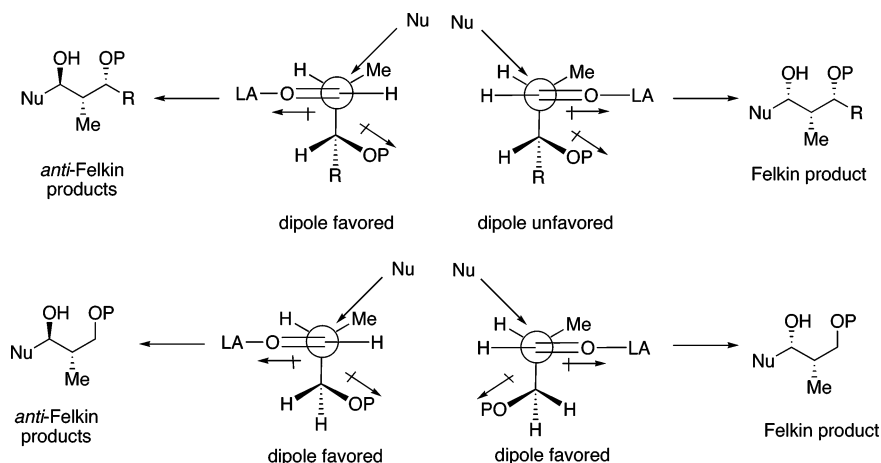
Scheme 15. Possible Reaction Pathway to Rationalize the Observed anti-Felkin Addition Products in Table 7
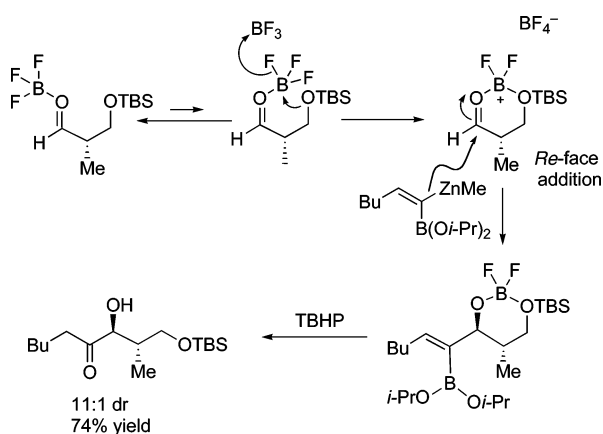
Scheme 16. One-Pot Addition/Cross-Coupling Reaction to Generate Functionalized Allylic Alcohols (Table 8)

Table 8. Tandem Addition/Cross-Coupling Reaction of 1-Alkenyl-1,1-heterobimetallics to Generate Functionalized Allylic Alcohols from Scheme 16

entry	boron alkyne	R''X	product	yield (%)
1	n-Bu—≡—B(pin)	Br⟍⟍		82
2	n-Bu—≡—B(pin)	PhI		90
3	⟍⟍≡—B(pin)	PhI		84
4	n-Bu—≡—B(pin)	n-Bu—≡—Br		65
5	n-Bu—≡—B(pin)			66

of tandem reactions involving initial carbonyl addition of the Zn—C bond, followed by subsequent palladium-mediated cross-coupling of the B—C bond.

As outlined in Scheme 16, steps 1–3 are identical to the synthesis of B(pin) allylic alcohols (Scheme 4). After completion of the carbonyl addition step, Pd(OAc)$_2$ (5 mol %), PPh$_3$ (10 mol %), Cs$_2$CO$_3$ (3 equiv), and the coupling partner were added. The reactions were heated to reflux and the progress followed by TLC. When product formation ceased, the reactions were quenched and subjected to column chromatography on silica gel. The results are presented in Table 8.

The intermediate allylic alkoxy boronate esters were found to undergo coupling with a variety of vinyl and aryl halides. For example, coupling with 2-bromopropene resulted in formation of the dienol product with 82% yield (entry 1). Iodobenzene also proved to be a successful coupling partner for vinyl and dienyl boronate esters, generating allylic alcohol and dienol products in 90 and 84% yield, respectively (entries 2 and 3). Use of 1-bromohexyne in the Suzuki reaction resulted in

formation of the enyne product in 65% yield in the one-pot procedure. The enone 2-iodo-2-cyclohexenone underwent coupling to give the dienone product with 66% yield (entry 5). The results in Table 8 indicate that the 1-alkenyl-1,1-heterobimetallic species generated in the carbonyl additions can be easily employed in further C—C bond-forming reactions.

3. Summary and Outlook

We have introduced a straightforward and reliable method for the generation of 1-alkenyl-1,1-heterobimetallic species based on hydroboration of readily available B(pin)-substituted alkynes with dicyclohexylborane. The resulting 1-alkenyl-1,1-diboro intermediates are used in situ. The B-vinyl bond of the dicyclohexyl alkenyl borane undergoes rapid and chemoselective transmetallation with the dialkylzinc reagents to generate 1,1-heterobimetallic complexes. These boron/zinc heterobimetallics undergo addition of the more reactive Zn—C bonds to aldehydes to generate the key B(pin)-substituted alkoxide intermediates. Simple protonation furnishes B(pin)-substituted allylic alcohols

in high isolated yield. Treatment of isolated B(pin)-substituted allylic alcohols with NBS induces a novel semipinacol-type rearrangement to form (*E*)-trisubstituted α,β-unsaturated aldehydes with excellent control over the stereochemistry of the double bond. The aldehyde products prepared by this procedure would be challenging to synthesize by other methods.

The B(pin)-substituted allylic alkoxides formed in situ can be treated with TBHP to afford α-hydroxy ketones in high yields. When enantioenriched protected α- or β-hydroxy aldehydes are employed, the diastereoselectivity can be controlled by the proper choice of protecting group and by addition of Lewis acids. For example, with TIPS protected 2-hydroxypropanal, the Felkin addition product can be obtained with 14:1 dr. Addition of $BF_3 \cdot OEt_2$, however, results in a reversal of diastereoselectivity with the anti-Felkin product formed in 16:1 dr. As expected, benzyl protected α-hydroxy aldehydes provide the anti-Felkin products via chelation control in 70−87% yield with >15:1 dr. Benzyl-protected β-hydroxy aldehydes also lead to anti-Felkin products with excellent dr (>20:1) in the presence of $BF_3 \cdot OEt_2$. Thus, with protected α- or β-hydroxy aldehydes, three of the four possible diastereomers have been prepared with good to excellent control over the diastereoselectivity.

Finally, we have advanced a one-pot procedure wherein B(pin)-substituted allylic alkoxides formed in situ can be directly employed in Suzuki cross-coupling reactions with vinyl, phenyl, and alkynyl halides to provide functionalized allylic alcohols and dienols with good yields. Our tandem reaction allows rapid construction of a variety of densely functionalized synthetic intermediates from readily available precursors. These products would be difficult to prepare in an efficient manner using other methods. We anticipate that the ease of generation, the versatility, and the mild nature of our 1,1-heterobimetallic species will make them useful in the synthesis of a wide range of natural and unnatural products.

Experimental Section

General Methods. All reactions were carried out under a nitrogen atmosphere with oven-dried glassware. All manipulations involving dicyclohexylborane and dimethylzinc were carried out under an inert atmosphere in a Vacuum Atmospheres drybox with an attached MO-40 Dritrain or by using standard Schlenk or vacuum line techniques. All chemicals were obtained from Aldrich, Acros, or GFS Chemicals unless otherwise specified. All solvents were purchased from Fischer Scientific. Toluene, dichloromethane, diethyl ether, and hexanes were dried through activated alumina columns. All liquid substrates were distilled prior to use. Dimethylzinc (1.0 or 2.0 M in toluene) was prepared and stored in a Vacuum Atmospheres drybox. NMR spectra were obtained on a Brüker 300, 400, or 500 MHz Fourier transform spectrometer at the University of Pennsylvania NMR facility. $^{13}C\{^1H\}$ NMR spectra were referenced to residual solvent. ^{11}B NMR spectra were referenced to $BF_3 \cdot OEt_2$. The infrared spectra were obtained using a Perkin-Elmer 1600 series spectrometer. Thin-layer chromatography was performed on Whatman precoated silica gel 60 F-254 plates and visualized by ultraviolet light or by staining with ceric ammonium molybdate or phosphomolybdic acid solutions. Silica gel (230−400 mesh, Silicycle) was used for air-flashed chromatography.

B(pin)-substituted alkynes[19,22,23,78] and chiral aldehydes were prepared by literature methods.[79−83]

General Procedure A: Preparation of B(pin)-Substituted Allylic Alcohols. To a suspension of $HBCy_2$ (107 mg, 0.60 mmol) in toluene (2.0 mL) under N_2 was added alkyne-4,4,5,5-tetramethyl-[1,3,2]-

dioxaborolane (0.60 mmol), and the reaction mixture was stirred for 30 min at rt, after which it was homogeneous. The reaction mixture was cooled to −78 °C and treated with Me_2Zn (0.30 mL, 2.0 M in toluene, 0.60 mmol) for 30 min. The solution was then warmed to −10 °C, and an aldehyde (0.50 mmol) was added. The reaction mixture was stirred at −10 °C until TLC showed complete consumption of the aldehyde. The reaction mixture was diluted with EtOAc (4 mL), quenched with H_2O (2 mL), extracted with EtOAc (3 × 40 mL), dried over $MgSO_4$, and concentrated. The residue was purified by flash chromatography on silica gel.

Preparation of 1-Phenyl-2-(4,4,5,5-tetramethyl-[1,3,2]dioxaborolan-2-yl)-hept-2-en-1-ol (entry 1, Table 1). The product was prepared by General Procedure A using benzaldehyde (51 µL, 0.5 mmol), 2-hex-1-ynyl-4,4,5,5-tetramethyl-[1,3,2]dioxaborolane (125 mg, 0.6 mmol). The crude product was purified by flash column chromatograghy on silica gel (hexanes/EtOAc, 96:4) as an oil (81% yield). ^1H NMR (CDCl₃, 500 MHz) δ 0.86 (t, J = 7.2 Hz, 3H), 1.03 (s, 6H), 1.09 (s, 6H), 1.29−1.37 (m, 4H), 2.32−2.36 (m, 2H), 3.02 (s, 1H), 5.11 (br, 1H), 6.22 (t, J = 7.5 Hz, 1H), 7.12−7.15 (m, 1H), 7.21−7.24 (m, 2H), 7.29−7.31 (m, 2H) ppm; $^{13}C\{^1H\}$ NMR (CDCl₃, 125 MHz) δ 14.1, 22.5, 24.5, 25.0, 30.9, 32.1, 79.1, 83.5, 126.4, 126.9, 128.1, 144.8, 148.2 ppm; ^{11}B NMR (CDCl₃, 128 MHz) 27.7 ppm; IR (neat) 1449, 1603, 1635, 2859, 3029, 3454 cm⁻¹; HRMS *m/z* 299.2172 [(M−OH)⁺; calcd for $C_{19}H_{28}BO_2$: 299.2183].

General Procedure B: Synthesis of (*E*)-Trisubstituted α,β-Unsaturated Aldehydes. To the solution of B(pin)-substituted allylic alcohol in 2 mL of CH_3CN/1 mL of H_2O was added slowly NBS (*N*-bromosuccinimide) in 2 mL CH_3CN at rt. The reaction mixture was stirred for 10 h, or until TLC showed complete consumption of starting material. The volatile materials were evaporated under reduced pressure. Next, water was added (4 mL), the solution was extracted with EtOAc (3 × 40 mL), and the combined organic layer was dried over $MgSO_4$ and concentrated. The residue was purified by flash chromatography on silica gel.

Preparation of (*E*)-2-Phenyl-hept-2-enal (Entry 2, Table 2). The product was prepared by General Procedure B using 1-phenyl-2-(4,4,5,5-tetramethyl-[1,3,2]dioxaborolan-2-yl)-hept-2-en-1-ol (84 mg, 0.265 mmol) and NBS (47 mg, 0.265 mmol). The crude product was purified by flash column chromatograghy on regular silica gel (hexanes/EtOAc, 97:3) as an oil (74% yield). ^1H NMR (CDCl₃, 500 MHz) δ 0.90 (t, J = 7.3 Hz, 3H), 1.32−1.39 (m, 2H), 1.49−1.54 (m, 2H), 2.35−2.42 (td, J = 7.5, 7.5 Hz, 2H), 6.75 (t, J = 7.5 Hz, 1H), 7.16−7.20 (m, 2H), 7.36−7.42 (m, 3H), 9.64 (s, 1H) ppm; $^{13}C\{^1H\}$ NMR (CDCl₃, 125 MHz) δ 14.2, 22.8, 29.9, 31.3, 128.3, 128.6, 129.8, 144.4, 156.9, 194.1 ppm; NOE NMR (CDCl₃, 500 MHz); IR (neat) 1450, 1600, 1694, 2872, 2960, 3060 cm⁻¹; HRMS-CI *m/z* 188.1196 [M⁺; calcd for $C_{13}H_{16}O$: 188.1201].

General Procedure C: Synthesis of α-Hydroxy Ketones in One-Pot. To a suspension of $HBCy_2$ (155 mg, 0.60 mmol) in toluene (2.0 mL) under N_2 was added alkyne-4,4,5,5-tetramethyl-[1,3,2]dioxaborolane (0.60 mmol) and the reaction mixture was stirred for 30 min at rt, after which it was homogeneous. The reaction mixture was cooled to −78 °C and treated with Me_2Zn (0.30 mL, 2.0 M in toluene, 0.60 mmol) for 30 min. The solution was then warmed to −10 °C, and an aldehyde (0.50 mmol) was added. The reaction mixture was stirred at −10 °C until TLC showed complete consumption of the aldehyde. TBHP (0.27−0.45 mL, 5.5 M in octane, 1.5−2.5 mmol) was added slowly into the reaction solution. The reaction was stirred at 0 °C for 20−40 h. The reaction mixture was diluted with EtOAc (4 mL), quenched with H_2O (2 mL), extracted with EtOAc (3 × 40 mL), dried over

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MgSO$_4$, and concentrated. The residue was purified by flash chromatography on deactivated silica gel (Et$_3$N/SiO$_2$ = 2.5% V/V).

General Procedure D: Synthesis of α-Hydroxy Ketones with BF$_3$·OEt$_2$. To a suspension of HBCy$_2$ (64 mg, 0.36 mmol) in toluene (2.0 mL) under N$_2$ was added alkyne-4,4,5,5-tetramethyl-[1,3,2]-dioxaborolane (0.36 mmol), and the reaction mixture was stirred for 30 min at rt, after which it was homogeneous. The reaction mixture was cooled to −78 °C and treated with Me$_2$Zn (0.18 mL, 2.0 M in toluene, 0.36 mmol) for 30 min. BF$_3$·OEt$_2$ (1.1 or 2.5 equiv) was then added to the reaction mixture at −78 °C, followed by the aldehyde (0.30 mmol). The reaction mixture was warmed to −40 °C and stirred between −40 and −20 °C until TLC showed complete consumption of the aldehyde. TBHP (0.54 mL, 5.5 M in octane, 3.0 mmol) was added into the reaction mixture. The solution was stirred at 0 °C for 20−40 h. Workup is the same as in General Procedure C.

General Procedure E: Synthesis of α-Hydroxy Ketones with BF$_3$·OEt$_2$. To a suspension of HBCy$_2$ (64 mg, 0.36 mmol) in toluene (2.0 mL) under N$_2$ was added alkyne-4,4,5,5-tetramethyl-[1,3,2] dioxaborolane (0.36 mmol), and the reaction mixture was stirred for 30 min at rt, after which it was homogeneous. The reaction mixture was cooled to −78 °C and treated with Me$_2$Zn (0.18 mL, 2.0 M in toluene, 0.36 mmol) for 30 min. In a separate flask, the aldehyde (0.30 mmol) and BF$_3$·OEt$_2$ (1.1 or 2.5 equiv) were premixed at −78 °C and for 2 min in 1 mL toluene, then transferred to the Schlenk flask that contained vinylzinc at −78 °C. The reaction mixture was warmed to −40 °C and stirred between −40 and −20 °C until TLC showed complete consumption of the aldehyde. TBHP (0.54 mL, 5.5 M in octane, 3.0 mmol) was added into the reaction solution. The reaction was stirred at 0 °C for 20−40 h. Workup is the same as in General Procedure C.

General Procedure F: Synthesis of Trisubstituted Allylic Alcohols in One-Pot. To a suspension of HBCy$_2$ (86 mg, 0.48 mmol) in toluene (2.0 mL) under N$_2$ was added 2-hex-1-ynyl-4,4,5,5-tetramethyl-[1,3,2]dioxaborolane (100 mg, 0.48 mmol), and the reaction mixture was stirred for 30 min at rt, after which it was homogeneous. The reaction mixture was cooled to −78 °C and treated with Me$_2$Zn (0.30 mL, 2.0 M in toluene, 0.60 mmol) for 30 min. The solution was then warmed to −10 °C, and the aldehyde (0.50 mmol) was added. The

reaction mixture was stirred at −10 °C until TLC showed complete consumption of the aldehyde. The volatile materials were evaporated under reduced pressure followed by the addition of 2 mL of THF/H$_2$O (10:1) at 0 °C. The resulting solution was stirred for 5 min, and Pd-(OAc)$_2$ (4.5 mg, 5 mol %), PPh$_3$ (11 mg, 10 mol %), RX (2.0 equiv, 0.8 mmol), and Cs$_2$CO$_3$ (391 mg, 1.2 mmol, 3 equiv) were added. The reaction mixture was then refluxed at 75 °C for 10 h. The resulting solution was diluted with water (2 mL) and extracted with EtOAc (3 × 40 mL). The combined organic layer was washed with brine, dried over MgSO$_4$, and concentrated under reduced pressure. The remaining residue was purified by flash chromatography on silica gel.

Preparation of 2-Isopropenyl-1-phenyl-hept-2-en-1-ol (Entry 3, Table 8). The product was prepared by General Procedure F using benzaldehyde (51 μL, 0.5 mmol), 2-hex-1-ynyl-4,4,5,5-tetramethyl-[1,3,2]dioxaborolane (125 mg, 0.60 mmol), and 2-bromopropene (89 μL, 1.0 mmol). The crude product was purified by flash column chromatography on silica gel (hexanes/EtOAc, 97:3) to give the title compound as an oil (84% yield). ^{1}H NMR (CDCl$_3$, 500 MHz) δ 0.82−0.85 (t, *J* = 6.9 Hz, 3H), 1.21−1.32 (m, 4H), 1.55 (s, 3H), 1.97−2.04 (m, 2H+1OH), 4.54 (s, 1H), 4.94 (s, 1H), 5.16 (s, 1H), 5.44−5.47 (t, *J* = 7.3 Hz, 1H), 7.17−7.20 (m, 1H), 7.24−7.30 (m, 4H) ppm; ^{13}C-{^{1}H} NMR (CDCl$_3$, 125 MHz) δ 14.2, 22.6, 23.9, 28.6, 32.3, 77.0, 115.9, 126.8, 127.5, 127.8, 128.3, 142.6, 142.8, 144.8 ppm; IR (neat) 1452, 1494, 1628, 2856, 2926, 2958, 3029, 3400 cm^{-1}; HRMS-CI *m/z* 212.1562 [(M−H$_2$O)$^+$; calcd for C$_{16}$H$_{20}$: 212.1566].

Supporting Information Available: Procedures and full characterization, stereochemical assignments, and X-ray determinations of new compounds. This material is available free of charge via the Internet at http://pubs.acs.org.

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