JOC Article

Investigation of Cyclization Reactions of Dicyclohexyl-6-iodo- and -6-tosylhexenylborane. A Facile Radical Cyclization Diverted to a Rearrangement−Cyclization with Base

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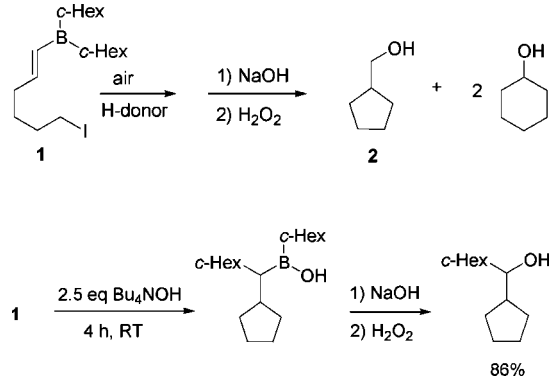

Dicyclohexyl-6-iodohexenylborane efficiently undergoes radical cyclization at room temperature using tri-*n*-butyltin hydride as a hydrogen donor and without the aide of a radical initiator. Efforts to develop environmentally friendly reagents using hypophosphites as substitutes for tin hydrides in this reaction provided a 60% yield of cyclopentanemethanol when tetrabutylammonium hypophosphite was used. Air was necessary as an initiator when hypophosphites were used. During investigations of the radical cyclization reactions, it was discovered that excess tetrabutylammonium hydroxide provided the rearrangement−cyclization product in excellent yield. Since this product was chiral, efforts were focused on achieving enantioselectivity. Oxazaborolidines made from chiral amino alcohols and 6-tosyl-1-hexenylboronic acid were treated with methyllithium to give 1-cyclopentylethanol after oxidation in 60% ee, demonstrating that oxazaborolidines were effective chiral directors for this reaction.

Introduction

Radical reactions offer mild conditions and functional group tolerance and often give different products and have different selectivity from ionic reactions. The use of vinylorganoboranes for radical cyclization processes would provide an organoborane product useful for further manipulation.[1] However, this possibility has not been widely exploited. Cooke[2] in his study of anionic cyclizations of 6-iodohexenylboranes considered the possibility of radical involvement. Using AIBN and Bu_3SnH with dimesityl-6-iodohexenylborane, he obtained 80% yield of the cyclized alkylborane, demonstrating that α-boryl radicals were effective terminators for radical cyclization reactions.[3] Matteson's studies of the α-boryl radical concluded that extra stability is gained from electron delocalization of the radical into the empty p-orbital on boron.[4]

Vinylboronates have also been used for radical cyclizations. Batey used a radical cyclization mechanism in the synthesis of 1−3, 1−4, and 1−5 diols.[5,6] Carboni used alkenylboronates,[7] obtaining good yields of the cyclized pinacolborane as well as cyclized vinyl 9-BBN. Lee also studied radical cyclizations of alkenylboronates.[8]

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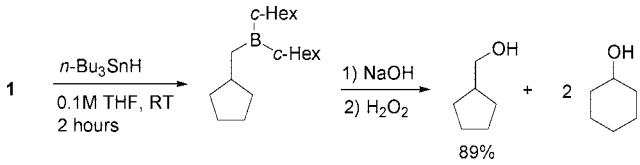
SCHEME 1



Results and Discussion

Efforts began with optimization of the radical cyclization reaction shown in Scheme 1.[9,10] Applying Cooke's methodology (*n*-Bu_3SnH, AIBN, refluxing benzene) to the radical cyclization of dicyclohexyl-6-iodohexenylborane **1** provided good yields of cyclopentanemethanol **2** and cyclohexanol after oxidation.

In order to reduce the temperature of the reaction, the use of oxygen to initiate the reaction was investigated.[11] Repeating the reaction at room temperature with *n*-Bu_3SnH and air at 0.5 mL/min as initiator also gave good yields of alcohol product. Lower flow rates of air provided similar results. Indeed, the reaction proceeded smoothly even in the absence of added air to give yields of 89% **2** and 99% cyclohexanol after 2 h (Scheme 1). Presumably, small traces of air are initiating the reaction as is the case with the 1,4 addition of organoboranes to acrolein.[12]

The major drawback to this reaction is the use of the organotin reagent that is toxic and difficult to remove. There exist several alternatives to tin hydrogen donors, including silanes, cyclohexadienes, and silylated cyclohexadienes, as well as phosphorus compounds.[13−15] The use of hypophosphites was chosen since they are nontoxic, cheap, and generally easy to remove from the reaction mixture (Figure 1).

Ethylpiperidine hypophosphite (EPHP) has been used with Et_3B as a mediator for carbon−carbon bond formation.[16] Radical cyclizations with EPHP include aryl radical cyclizations to cyclohexenes that proceeded efficiently with 10 equiv of EPHP to form the expected *cis*-fused hexahydrocarbazoles[17] as well as efficient cyclizations to a tricyclic compound[18] and to trisubstituted tetrahydrofurans.[19] An advantage of EPHP is that it may be completely removed by washing with 2 M HCl and then saturated $NaHCO_3$ during the workup procedure.

The reaction in Scheme 1 was further investigated, but instead of tributyltin hydride, EPHP (5 equiv/mol borane) in THF was used in both the presence and absence of air. For the reactions with no air, the yields of **2** were low. With 0.5 mL/min of air, a 2 mmol scale reaction was over in 2.5 h, giving 50% GC yield. When higher flow rates of air were used, the reaction was complete in less time but the yields were lower. The higher flow rates of air led to competitive oxidation of the organoborane. The use of triethylborane as a sacrificial organoborane was of no advantage.[20]

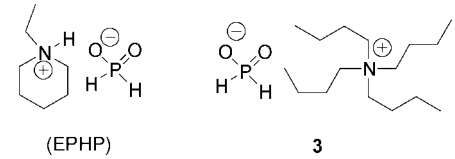
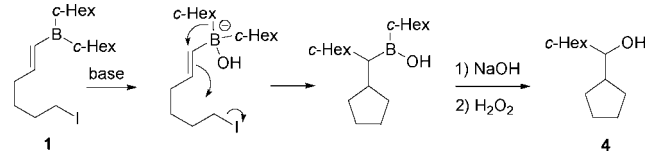


FIGURE 1. Hypophosphites used for the radical cyclization reaction.

SCHEME 2



Other hypophosphites were investigated. Anilinium hypophosphite[21] and sodium hypophosphite[22] (NaH_2PO_2) provided low yields of the desired product. Besides being insoluble, the anilinium salt protonated the vinylborane giving 6-iodohexene as the major product.

Tetrabutylammonium hypophosphite **3** (from tetrabutylammonium hydroxide and hypophosphorous acid) is soluble in THF. The reaction was run with and without air in THF, using 2.5 equiv of **3** per mole of the borane. After 2.5 h, the yield of **2** was 60% with 0.2 mL/min of air and 5% without air (2 mmol reaction). Higher flow rates of air led to lower yields. This reagent was promising since it was inexpensive, easy to prepare, and had good solubility in THF and the byproduct precipitated out during workup.

The effect of excess hypophosphorous acid or tetrabutylammonium hydroxide on the reaction was also explored. The acid could provide the alkene product by protonation of the vinylborane. Excess base could coordinate with the borane and decrease its ability to stabilize the α-radical. When excess acid was added, a slight decrease in the yield of **2** was found, but when excess base was added, a new product, cyclohexylcyclopentylmethanol **4**, was obtained.[9,23] Our hypothesis for the mechanism (Scheme 2) is that the hydroxide adds to the boron, forming an ate complex. Subsequent migration of the cyclohexyl group and cyclization provides the rearranged organoborane that is oxidized to **4**.

A related reaction has been reported by Negishi[24] (Scheme 3) in which the reaction of tosylvinylborane **5** with 1 equiv of *n*-butyllithium gave the alkene products **6** and **7**. However, the alcohol **4** was not reported. The reaction in Scheme 3 presumably proceeds through an ate complex that rearranges with formation of the cyclopentyl ring. Elimination of the alkene can occur by loss of *n*-Bu-*c*-HexBH from the rearranged organoborane. Presumably, elimination of the alkene from the highly hindered organoborane occurs before oxidation. Other ring-forming or rear-

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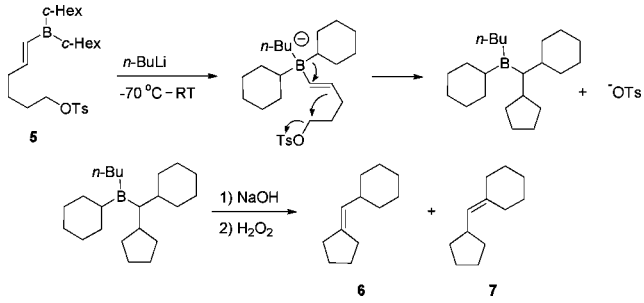
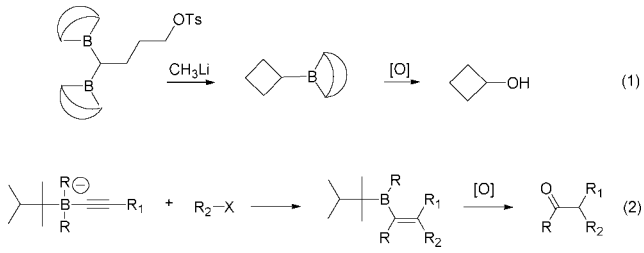
SCHEME 3



SCHEME 4



rangement reactions have been reported by Brown[25] (Scheme 4, eq 1), Pelter[26] (Scheme 4, eq 2), and Corey.[27]

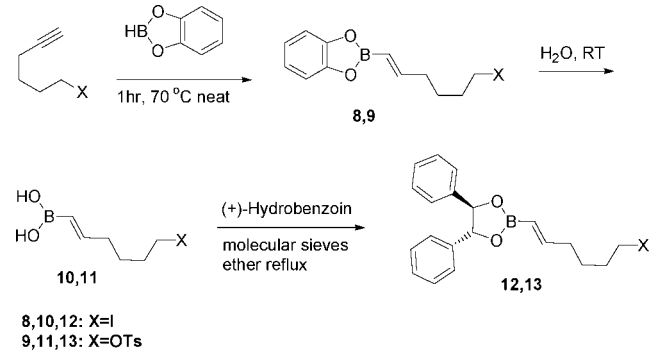
Further studies of the reaction in Scheme 2 showed that the use of 2.5 equiv of tetrabutylammonium hydroxide (40 wt. % solution in water) gave a 92% GC yield (86% isolated yield) of **4** from **1** after 4 h at room temperature. The reaction was repeated using the tosylhexenylborane **5**. The reaction was much slower but after 65 h the GC yield of **4** was 80%.

The reaction of sodium methoxide or sodium *t*-butoxide with **1** provided no **4** after 50 h. With sodium hydroxide, compound **4** slowly formed and after 65 h, the GC yield was 85%.

The rearrangement-cyclization reaction provided **4** in excellent yields, but the product was racemic. In order to obtain optically active product, a chiral auxiliary would be needed. This could be a chiral organoborane but one would have to worry about selective migration of the alkyl groups on boron. Therefore nonmigrating groups such as found in boronic esters were investigated.

Boronic esters of chiral diols have been used effectively to induce high enantiomeric excesses. Matteson used boronic esters of C_2 chiral diols and other chiral diols extensively for homologation of boronic esters with dichloromethyllithium to give α-chloroboronic esters.[28] The α-chloroboronic ester reactions permit efficient sequential syntheses of two or more adjacent chiral centers with absolute control of the configuration of each center while allowing incorporation of a wide variety of functional and hydrocarbon groups. The synthesis of L-(+)-ribose via pinanediol is a classic example of this chemistry.[29] Many other examples exist.[30] Roush found that allylic boronic esters of diisopropyl tartrate yielded high diasteroselectivity with chiral aldehydes.[31]

SCHEME 5



Methyllithium or methylmagnesium bromide was added to alkenyl boronic esters made from chiral diol directors to form an ate complex that would rearrange with cyclization, providing 1-cyclopentylethanol after oxidation. Vinylboronic acids were prepared by heating neat catecholborane with 6-iodo- or 6-tosyl-1-hexyne for 1 h at 70 °C followed by water hydrolysis.[32,33] The esters were made by refluxing the boronic acid with a diol and molecular sieves in ether as shown for hydrobenzoin in Scheme 5. In addition to hydrobenzoin, esters were made from diethyl tartrate, pinanediol and pinacol. The esters were filtered thru Celite and either purified by chromatography or used directly.

It was found that the ethyl ester groups of diethyltartrate boronic ester preferentially reacted with methyllithium. Also, methyllithium preferentially exchanged with the iodide on the iodo boronic esters. For this reason, the tosylate was used for all future studies.

The best yield was obtained with the hydrobenzoin ester **13,** giving 85% GC yield of 1-cyclopentylethanol **(14)** with 3 equiv of methylmagnesium bromide. However, the product was racemic as determined by NMR using the chiral shift reagent, europium tris[3-(heptafluoropropylhydroxymethylene)-(+)-camphorate] ($Eu(hfc)_3$). These results suggested that the Grignard or lithium reagent was displacing an alkoxide from boron, eventually forming the trimethylvinylborate complex that would then undergo cyclization. Since the chiral auxiliary was displaced, the product would be racemic, and thus other chiral directors were sought.

Oxazaborolidines were shown by Itsuno in the 1980s to be chiral catalysts for the borane-mediated enantioselective reduction of a wide variety of achiral ketones.[34] Corey's studies on this discovery included defining the structure of Itsuno's ligand and the mechanism of the reaction pathway and led to a new and powerful catalytic version of the original stoichiometric Itsuno reduction.[35,36]

In general, for the preparation of the *B*-alkyl- and *B*-aryl-substituted oxazaborolidines, a solution of the aminoalcohol and the corresponding boronic acid were refluxed in toluene for 12−24 h with azeotropic removal of water.[37]

Vinyl oxazaborolidines were prepared from (*S*)-2-amino-3-phenyl-1-propanol or from (*S*)-prolinol and the vinyl boronic acid using the Gamsey[38] method of refluxing overnight in THF

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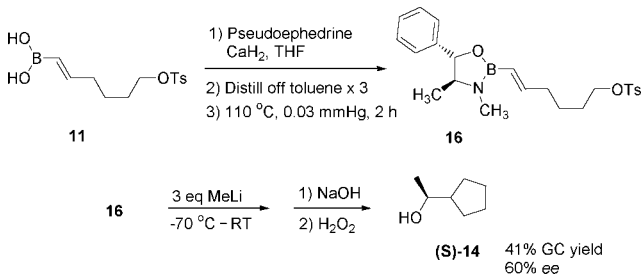
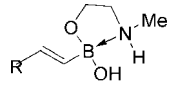
SCHEME 6



over CaH_2. However, the amine reacted with the tosylate, and these oxazaborolidines were easily hydrolyzed.

When (1*S*,2*R*)-(+)-2-amino-1,2-diphenylethanol[39] was used to make the oxazaborolidine equivalent **15**, and 2 equiv of MeMgBr was added, a 60% GC yield of (*S*)-**14** with 20% ee was obtained. Attempts to purify the vinyl oxazaborolidine by recrystallization or distillation were unsuccessful.

It appeared that a more hindered oxazaborolidine was needed. Pseudoephedrine was chosen as a suitable and readily available amino alcohol. The Gamsey[38] method at room temperature was used to make the pseudoephedrine oxazaborolidine **16**, and this greatly reduced the reaction of the amine with the tosylate. A 14% GC yield of 1-cyclopentylethanol was obtained after addition of 1 equiv of MeMgBr. Since all of the water may not be removed at room temperature (either by CaH_2 or molecular sieves) due to formation of a hydroxy/amine ate complex (**17**),[40] more drastic methods for water removal were explored. The standard conditions of distillation with a Dean−Stark trap and further heating under vacuum were used.[37,40] The preparation of **16** from pseudoephedrine is shown in Scheme 6.



17

This time, 3 equiv of MeLi was added and a 41% yield and 60% ee of (*S*)-**14** was obtained. Thus, the oxazaborolidine from pseudoephedrine showed promise toward obtaining good enantioselectivities.

Conclusion

In conclusion, the radical cyclization of **1** proceeded smoothly when *n*-Bu_3SnH was used as a hydrogen donor, even in the absence of an initiator. The use of hypophosphite alternatives to the organotin reagent also provided the cyclization product, although the yields were lower and a radical initiator (oxygen) was needed. Higher flow rates of air led to competitive oxidation of the organoborane. Presumably, the chain-carrying steps were not as efficient for the alternative reagents. During these investigations, a new reaction was discovered in which adding excess base to **1** gave excellent yields of the rearrangement−cyclization product **4**. Further studies aimed at the enantioselective synthesis of **14** showed that using chiral boronic esters as chiral directors were ineffective, giving racemic products. Oxazaborolidines made from chiral amino alcohols with a secondary alcohol and secondary amine did provide selectivity. Using the pseudoephedrine oxazaborolidine **16** with methyllithium, ee's of 60% were obtained.

Experimental Section

Iodohexyne[41] and anilinium hypophosphite[21] were prepared from standard procedures. The airflow apparatus was set up using a peristaltic pump (Low Flow (II), Model 3385 from Fischer, made by Control Company), and ambient air was pumped through a bubbler and into the reaction mixture with a needle attached to tubing filled with a drying agent. 5-Iodohexyne,[41] dicyclohexyl-6-iodohexenylborane **1**,[42] and hex-5-yne-1-yl *p*-toluene-4-sulfonate[43] were prepared from standard procedures. GC yields were determined using a Supelco Carbowax-10 column, with dodecane and pentanol as internal standards.

Dicyclohexyl-1-hexenyl-6-iodoborane (1). The vinylborane was made according to the standard method:[42] Borane−methyl sulfide complex (BMS) (0.2 mL, 2 mmol) in dry THF (4 mL) was cooled in an ice/water bath. Cyclohexene (0.42 mL, 4.2 mmol) was added, the mixture was stirred for 3 h at 0 °C, and a white solid formed. Then, 1-iodo-5-hexyne (1.04 g, 2.0 mmol) in THF (2 mL) at 0 °C was added. The ice bath was removed, and the mixture slowly came to rt while stirring for 1 h. The clear solution was used immediately "as is": ^{1}H NMR (300 MHz, $CDCl_3$) δ 6.68 (t,d, J = 6.2, 17.4 Hz, =C*H*CH_2), 6.21 (d,t, J = 17.4, 1.3 Hz, BC*H*=), 3.21 (t, J = 7.0 Hz, CH_2I), 2.25 (q,d, J = 7.0, 1.2 Hz, CH_2CH), 1.86 (quint, J = 7.2 Hz, 2-H), 1.74 (br d, 6-H), 1.58 (m, 2-H), 1.49 (br d, 4-H,), 1.26 (m, 12-H); ^{13}C NMR (300 MHz, $CDCl_3$) δ 152.8, 133.3 (br), 35.4, 29.6, 26.1, 6.9, 34.5, 27.9, 27.8, 27.4.

Standard Oxidation Procedure of the Organoborane.[1] To 1 mmol of borane was added 3 M NaOH (0.3 mL, 1 mmol), followed by 30% H_2O_2 (0.3 mL, 3 mmol) below 40 °C. The mixture was heated at 50 °C for 1 h. After cooling, ether was added, and solid K_2CO_3 was added to remove the aqueous components. The ether/THF was poured off and washed with brine. The brine was back-extracted with ether, and the combined organic layers were dried with K_2CO_3.

Cyclopentanemethanol (2). To the vinylborane **1** (2 mmol) in 20 mL of THF was added *n*-Bu_3SnH (0.6 mL, 2.2 mmol) and the mixture stirred at rt for 1 h. Then 3 M NaOH (2.0 mL, 6.0 mmol) and 30% H_2O_2 (1.0 mL, 8.9 mmol) were added to oxidize the borane to obtain 89% of **2**. Excess base was used to facilitate removal of the organotin reagents:[44] ^{1}H NMR (300 MHz, $CDCl_3$) δ 3.48 (d, J = 7.03 Hz, 2-H, CH_2OH), 2.22 (br s, 1-H, O*H*), 2.06 (septet, J = 7.47, 1-H, C*H*CH_2OH), 1.71 (m, 2-H), 1.55 (m, 4-H), 1.22 (m, 2-H); ^{13}C NMR (300 MHz, $CDCl_3$) δ 67.4, 42.2, 29.2, 25.6.

Tetrabutylammonium Hypophosphite (3).[45] Aqueous tetrabutylammonium hydroxide (40 wt %, 13.625 g, 21 mmol) was added to a flask containing H_3PO_2 (50 wt %, 2.788 g, 21 mmol). The pH was tested with pH paper, and additional drops of either solution were added until pH 7 was obtained. The water was removed under vacuum (0.3 mmHg) while warming to 70 °C to obtain white crystals. The removal of water was completed by freezing with acetone/CO_2 and continued pumping (lyophilization) to afford 100% of a white solid (7.17 g, 21 mmol): ^{1}H NMR (300 MHz, DMSO-d_6) δ 7.05 (d, J = 450 Hz, 2-H, P*H*), 3.18 (t, J = 8.23, 8-H, CH_2N),

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1.57 (m, 8-H), 1.31 (sextet, $J = 7.35$, 8-H), 0.93 (t, $J = 7.30$, 12-H); ^{13}C NMR (300 MHz, DMSO-d_6) δ 57.4, 23.0, 19.1, 13.4; ^{31}P NMR (300 MHz, DMSO-d_6) δ 1.275 (t, $J_{P-H} = 519$ Hz).

General Procedure for the Radical Cyclization Using Hypophosphite and Air. The reaction with EPHP is representative. To a stirred solution of vinylborane **1** (2 mmol) in THF was added EPHP (1.8 g, 10 mmol), followed by air at 0.5 mL/min for 2.5 h, after which the mixture was oxidized by the standard procedure, except after the solid K_2CO_3 was added, the THF/ether was poured off and the remainder extracted with 2 M HCl (2 × 5 mL), $NaHCO_3$ (5 mL), and then brine (5 mL). The aqueous layers were back-extracted with ether (3 mL) at each step, and the combined extracts were dried with K_2CO_3 and filtered to give 50% GC yield.

Radical Cyclization Using 3. Hypohosphite **3** (1.5 g, 5 mmol) was dissolved in 5 mL of THF, and the stirred solution was added via cannula to 2 mmol of the vinylborane in 5 mL of THF. Air was added at 0.2 mL/min for 2.5 h, and the solution was oxidized, providing 60% GC yield of **2**.

General Procedure for the Rearrangement−Cyclization Reaction Using 1 or 3. Tetrabutylammonium hydroxide (40 wt % solution in water) (8.10 g, 12.5 mmol) was added to 5 mmol of the vinylborane in 20 mL of THF. After 4 h, it was oxidized by adding 3 M NaOH (1.7 mL, 5 mmol) and then 30% H_2O_2, (1.7 mL, 15 mmol) at below 40 °C and then heated at 50 °C for 1 h. After cooling, ether and solid K_2CO_3 were added to remove the aqueous components. The ether/THF was poured off, the remainder was washed with brine and back-extracted with ether, and the combined organic layers were dried with K_2CO_3, filtered, and analyzed by GC to give 92% of **4** (from **1**) and 86% of **4** (0.78 g, 4.3 mmol) after purification by silica gel chromatography (9:1 hexane/ethyl acetate): ^{1}H NMR (300 MHz, $CDCl_3$) δ 3.20 (d,d, $J = 7.21$, 4.20 Hz, 1-H, CHOH), 2.02 (sextet, 1-H, CHCHOH), 1.78 (m, 4-H) 1.40−1.65 (m, 8-H), 1.30−1.40 (m, 2-H), 1.05−1.30 (m, 6-H); ^{13}C NMR (300 MHz, $CDCl_3$) δ 80.1, 43.1, 42.1, 30.5, 29.3, 28.7, 26.7, 26.7, 26.4, 25.7, 25.7.

General Procedure for the Hydroboration of the Alkyne with Catecholborane. Procedures by Brown[32] and Lane[33] were modified, and the conversion of 1-iodo-5-hexyne into (*E*)-2-(6-iodo-1-hexenyl)-1,3,2-benzodioxaborole **8** is representative. A mixture of 1-iodo-5-hexyne (5.62 g, 27 mmol) and neat catecholborane (3.2 g, 27 mmol) was stirred under nitrogen at 70 °C for 1 h, after which a 20% excess of catecholborane (0.64 g, 5.3 mmol) was added. After an additional 0.5 h of stirring, the NMR revealed the reaction to be complete by the absence of the α-alkynyl protons, and the product was used without further purification.

(*E*)-2-(6-Iodo-1-hexenyl)-1,3,2-benzodioxaborole (8): ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.24 (m, 2-H, aryl *H*), 7.10 (m, 2-H, aryl *H*), 7.04 (d,t, $J = 18.08$, 6.49, 1-H, BCHC*H*), 5.84 (d,t, $J = 18.03$, 1.32, 1-H, BC*H*CH), 3.24 (t, $J = 6.93$, 2-H, CH_2I), 2.35 (q,d, $J = 7.07$, 1.41, 2-H, CHCHCH_2), 1.91 (m, 2-H), 1.66 (m, 2-H).

(*E*)-6-(Benzo[*d*][1,3,2]dioxaborol-2-yl)hex-5-enyl 4-Methylbenzenesulfonate (9): ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.80 (d, $J = 8.31$, 2-H, aryl *H*), 7.34 (d, $J = 8.20$, 2-H, aryl *H*), 7.21 (m, 2-H, aryl *H*), 7.07 (m, 2-H, aryl *H*), 6.93 (d,t, $J = 18.04$, 6.49, 1-H, BCHC*H*), 5.74 (d,t, $J = 18.03$, 1.37, 1-H, BC*H*CH), 4.06 (t, $J = 6.26$, 2-H, CH_2OSO$_2$), 2.44 (s, 3-H, aryl methyl), 2.24 (q,d, $J = 7.04$, 1.44, 2-H, CHCHCH_2), 1.69 (m, 2-H), 1.54 (m, 2-H).

General Procedure for the Preparation of the Alkenylboronic Acids.[32] Illustrated for (*E*)-6-iodo-1-hexenylboronic acid **10**. Water (20 mL) was added to **8** (2.3 g, 7.0 mmol) and stirred at 25 °C overnight. The white crystalline product that formed was filtered and recrystallized from hexane/THF, giving 84% (1.5 g, 5.9 mmol) of **10**: ^{1}H NMR (300 MHz, $CDCl_3$) δ 6.50 (d,t, $J = 17.94$, 6.42, 1-H, BCHC*H*), 5.44 (d, $J = 17.92$, 1-H, BC*H*CH), 3.20 (t, $J = 6.91$, 2-H, CH_2I), 2.21 (q,d, $J = 6.85$, 1.37, 2-H, CHCHCH_2), 1.85 (m, 2-H), 1.59 (s, 2-H, O*H*), 1.57 (m, 2-H).

(*E*)-6-(Tosyloxy)hex-1-enylboronic Acid (11) Trimer. The hydrolysis of **7** was similarly carried out, and the foamy crude mixture became completely hydrolyzed during purification by silica gel chromatography (1:1 hexane/ethyl acetate) to give (75%) (1.5 g, 5 mmol) of a clear gel, existing as the trimer, $(BOR)_3$, which was converted to the acid by adding 0.1 mL of water to the flask during storage: ^{1}H NMR (300 MHz, acetone-d_6) δ 7.73 (d, $J = 8.30$, 2-H, aryl *H*), 7.44 (d, $J = 8.06$, 2-H, aryl *H*), 6.43 (d,t, $J = 17.90$, 6.48, 1-H, BCHC*H*), 5.34 (d,t, $J = 17.82$, 1.26, 1-H, BC*H*CH), 4.01 (t, $J = 6.32$, 2-H, CH_2OSO$_2$), 2.39 (s, 3-H, aryl methyl), 2.00 (q,d, $J = 7.08$, 1.31, 2-H, CHCHCH_2), 1.58 (m, 2-H), 1.35 (m, 2-H); ^{13}C NMR (300 MHz, acetone-d_6) δ 151.8, 146.9, 134.6, 131.7, 129.3, 126.2 (br), 72.5, 36.0, 29.6, 25.6, 22.3.

General Procedure for the Preparation of the 6-Iodohexenyl- and 6-Tosylhexenylboronic Esters.[46] The preparation of (4*R*,5*R*,*E*)-2-(6-iodohex-1-enyl)-4,5-diphenyl-1,3,2-dioxaborolane **12** is representative. (*R,R*)-(+)-Hydrobenzoin (0.39 g, 1.8 mmol), **10** (0.46 g, 1.8 mmol), and 240 mg of 4 Å molecular sieves were refluxed in 8 mL of dry diethyl ether overnight, after which time the reaction mixture was filtered through a pad of Celite, washed with ether, and used immediately: ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.43−7.24 (m, 10-H, aryl *H*), 6.85 (d,t, $J = 17.97$, 6.46, 1-H, BCHC*H*), 5.67 (d,t, $J = 18.00$, 1.38 1-H, BC*H*CH), 5.19 (s, 2-H, C*H*OB), 3.23 (t, $J = 6.98$, 2-H, CH_2I), 2.20 (q,d, $J = 6.82$, 1.43, 2-H, CHCHCH_2), 1.90 (m, 2-H), 1.61 (m, 2-H).

(*E*)-6-((4*R*,5*R*)-4,5-Diphenyl-1,3,2-dioxaborolan-2-yl)hex-5-enyl 4-Methylbenzenesulfonate (13). Purification by silica gel chromatography (3:1 hexane/ethyl acetate) gave 71% (3.3 g, 7.0 mmol) of a clear gel: ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.81 (d, $J = 8.20$, 2-H, aryl *H*), 7.44−7.24 (m, 12-H, aryl *H*), 6.77 (d,t, $J = 17.98$, 6.43, 1-H, BCHC*H*), 5.60 (d,t, $J = 17.95$, 1.37, 1-H, BC*H*CH), 5.18 (s, 2-H, C*H*OB), 4.06 (t, $J = 6.35$, 2-H, CH_2OSO$_2$), 2.45 (s, 3-H, aryl methyl), 2.20 (q,d, $J = 6.94$, 1.32, 2-H, CHCHCH_2), 1.72 (m, 2-H), 1.51 (m, 2-H).

General Reaction of the Boronic Esters and Oxazaborolidines with Methyllithium or Methylmagnesium Bromide. Modified from the procedure by Negishi,[24] the reaction of (*E*)-6-((4*S*,5*S*)-3,4-dimethyl-5-phenyl-1,3,2-oxazaborolidin-2-yl)hex-5-enyl 4-methylbenzenesulfonate **16** with methyllithium is representative: To a stirred solution of the oxazaborolidine (0.34 g, 0.80 mmol) in 5 mL of THF at −78 °C, 3 equiv of methyllithium (1.5 mL, 1.6 M) was added dropwise. After 0.5 h, it was slowly brought to rt and stirred for a total of 3 h. It was oxidized by adding 3 M NaOH (0.4 mL, 1.2 mmol) followed by 30% H_2O_2 (0.50 mL, 4.4 mmol) and heated at 50 °C for 1 h. Ten milliliters of 1 M HCl was added after cooling, and the mixture was extracted three times with 10 mL ether, washed with brine, and back-extracted with ether. The organic phase was dried with K_2CO_4 and then filtered. After GC analysis (41%), the solvent was removed under reduced pressure, and after silica gel chromatography (3:1 hexane/ethyl acetate), 38% (34 mg, 0.30 mmol) of **12** was obtained. The product was evaluated by NMR (300 MHz, $CDCl_3$) using the chiral shift reagent Eu(hfc)$_3$ to determine that it was 60% ee. The configuration of the major isomer was determined to be (*S*)-1-cyclopentylethanol by analogy[47] to an NMR shift study of an authentic sample of (*R*)-1-cyclohexylethanol.[48]

(*E*)-6-((4*R*,5*R*)-4,5-Diphenyl-1,3,2-dioxaborolan-2-yl)hex-5-enyl 4-Methylbenzenesulfonate (13). With 3 equiv of methylmagnesium bromide: 85% GC yield of **14**.

(E)-6-((4R,5S)-4,5-Diphenyl-1,3,2-oxazaborolidin-2-yl)hex-5-enyl 4-Methylbenzenesulfonate (15). With 2 equiv of MeMgBr: 60% GC yield of (*S*)-**14**, 20% ee.

General Procedure for the Synthesis of Hexenyloxazaborolidines. The combined procedures of Mathre,[37] Gamsey,[38] and Brown[40] were modified as follows, and the preparation of pseudoephedrine oxazaborolidine **16** is representative. A flame-dried

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50-mL flask equipped with a condenser and stir bar was charged with vinylboronic acid (0.79 g, 2.7 mmol) and (+)-pseudoephedrine (0.44 g, 2.7 mmol) and dissolved in THF (10 mL). Calcium hydride (0.25 g, 6 mmol) was added, and the solution was stirred overnight at room temperature. The solution was filtered through Celite under argon and transferred to a dry flask via cannula. The THF was concentrated at 1 atm to ~5 mL, and 20 mL of toluene was added. The solution was stirred at 135 °C for 2 h and then concentrated to ~5 mL. Toluene (20 mL) was added, and the solution was concentrated again. This process was repeated once more, and the remaining solvent was removed under reduced pressure. The residue was heated at 110 °C under vacuum (0.03 mmHg) for 2 h and used "as is".

(*E*)-6-((4*R*,5*S*)-4,5-Diphenyl-1,3,2-oxazaborolidin-2-yl)hex-5-enyl 4-Methylbenzenesulfonate (15). The following peaks are representative of product formation: ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.75 (d, J = 8.27, 2-H, aryl *H*), 7.36−6.87 (m, 12-H, aryl *H*), 6.57 (d,t, J = 17.93, 6.43, 1-H, BCHC*H*), 5.77 (d, J = 8.36, 1-H, C*H*OB), 5.67 (d,t, J = 17.99, 1.32, 1-H, BC*H*CH), 5.01 (d, J = 8.33, 1-H, C*H*NB), 4.07 (t, J = 6.36, 2-H, CH_2OSO_2), 2.45 (s, 3-H, aryl methyl), 2.20 (q, J = 7.08, 1.42, 2-H, CHCHCH_2), 1.71 (m, 2-H), 1.52 (m, 2-H).

(*E*)-6-((4*S*,5*S*)-3,4-Dimethyl-5-phenyl-1,3,2-oxazaborolidin-2-yl)hex-5-enyl 4-Methylbenzenesulfonate (16): ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.73 (d, J = 8.23, 2-H, aryl *H*), 7.29−7.18 (m, 7-H, aryl *H*), 6.40 (t,d, J = 6.47, 17.80, 1-H, BCHC*H*), 5.53 (d,t, J = 17.81, 1.20, 1-H, BC*H*CH), 4.72 (d, J = 6.89, 1-H, C*H*OB), 3.97 (t, J = 6.38, 2-H, CH_2OSO_2), 3.22 (quintet, J = 6.33, 1-H, C*H*NB), 2.62 (s, 3-H, NCH_3), 2.37 (s, aryl methyl), 2.08 (q,t, J = 6.86, 1.22, 2-H, CHCHCH_2), 1.62 (m, 2-H), 1.40 (m, 2-H), 1.18 (d, J = 6.16, 3-H); ^{13}C NMR (300 MHz, $CDCl_3$) δ 149.7, 144.8, 143.3, 133.3, 130.0, 128.0, 127.8, 127.7, 125.8, 120.0 (br), 86.2, 70.6, 65.4, 35.3, 29.9, 28.4, 24.4, 21.5, 19.1.

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Supporting Information Available: Experimental details and characterization data for known compounds. NMR spectra (^{1}H and ^{13}C NMR) for all new compounds. This material is available free of charge via the Internet at http://pubs.acs.org.

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