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3-Chloro-1-lithiopropene, a Functional Organolithium Reagent, and Its Reactions with Alkylboronates To Give 3-Alkylprop-1-en-3-ols

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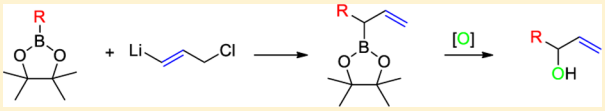
Supporting Information

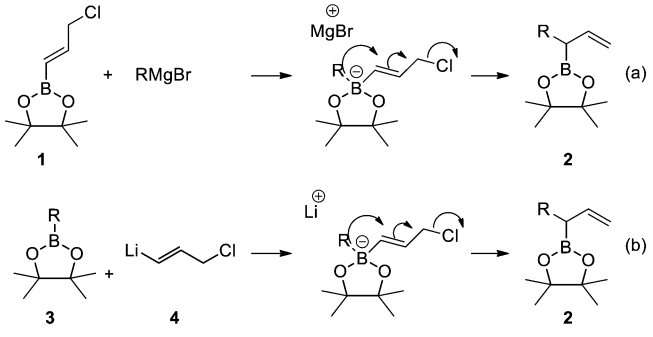
ABSTRACT: The reagent 3-chloro-1-lithiopropene (**4**) can be generated by treating 1-bromo-3-chloropropene with *t*-BuLi. It is unstable but if generated at low temperature in the presence of alkylboronic esters, such as **3**, is trapped in situ to give rearrangement products **2**, which on oxidation give 3-alkylprop-1-en-3-ols in good yields. The reaction works for primary, secondary, benzylic, and even tertiary alkylboronic esters, providing allylic alcohols bearing almost any alkyl group available using organoborane chemistry and incorporating all features of such groups.



Migration of alkyl groups from boron to carbon is important for formation of C−C bonds.[1] Depending on the reaction, trialkylboranes undergo migration of one,[2] two,[3] or all three[4] alkyl groups to a single carbon atom, usually with retention of stereochemical integrity. Furthermore, although boron is commonly removed by oxidation, the immediate product is an organoboron compound and potentially available for further elaboration. Single-migration reactions of trialkylboranes lack efficient use of alkyl groups, and migratory selectivity may be a problem. Alkyldialkoxyboranes (alkylboronate esters) are substantially less electrophilic, and only highly nucleophilic, often unstable reagents such as halomethyllithiums are sufficiently reactive.[5] Even then, migration of *tert*-alkyl groups is difficult, but in a recent investigation, we have extended the range of substrates to include quite hindered *tert*-alkyl groups.[6]

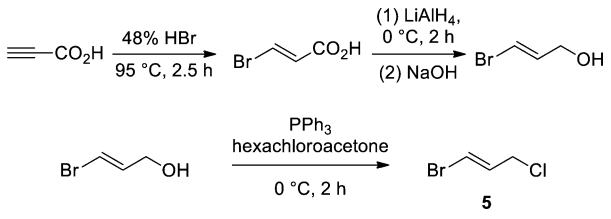
Reactions of 3-chloropropenylboronates such as **1** with Grignard reagents (Scheme 1a)[7] give compounds **2** with high enantiomeric excess under asymmetric catalysis.[8] This important and useful reaction is limited by the availability of appropriate Grignard reagents, which are not tolerant of functionality. By contrast, organoboron derivatives tolerate many functional groups and can be generated by a range of stereospecific processes. Thus, Scheme 1b would be a more generally useful approach to compounds **2** than Scheme 1a. We now report the successful realization of this approach.

Scheme 1. Alternative Approaches to Compounds 2



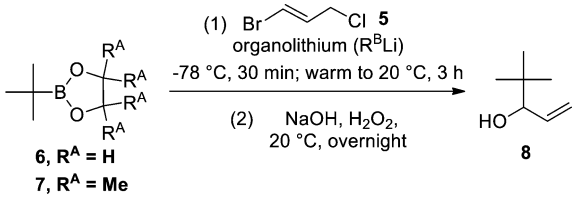
(*E*)-1-Bromo-3-chloroprop-1-ene (**5**) was synthesized by the literature procedure (Scheme 2).[9−12] The final product **5** required careful fractional distillation to provide a clean sample.

Scheme 2. Synthesis of 1-Bromo-3-chloropropene (5)



Reports of reactions like Scheme 1a[7,8] gave no examples of use of *tert*-alkylmagnesium reagents, so we first looked at reactions of *tert*-butylboronic esters and investigated both boronate ester **6** and the more hindered pinacol analogue **7**. Br−Li exchange of **5** to give **4** was attempted with *n*-BuLi and *t*-BuLi; solutions were reacted with **6** or **7** and then oxidized to give 4,4-dimethylpent-1-en-3-ol (**8**) (Scheme 3). Yields were monitored by GC.

Scheme 3. Initial Investigative Reactions



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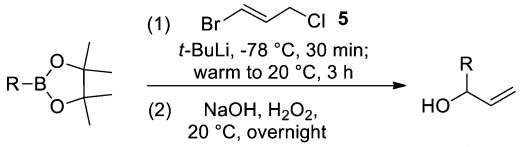
t-BuLi was more effective at generating **4** than *n*-BuLi, probably because of lower competition from other sites of attack. Generating **4** ex situ and adding it to the boronate was not successful, presumably because **4** is unstable and needs trapping immediately. Excess organolithium was deleterious, presumably because of increased competition from direct addition to the boronate, while the more hindered boronate **7** gave higher yields than **6**, presumably because of lower competition from such addition. Use of **5** containing ~5% of pentachloroacetone caused a disproportionate decrease in yield, so purity of **5** is important. However, under the most favored conditions (1.1 equiv of *t*-BuLi and pure **5**, in situ, with **7**), the yield of **8** was almost quantitative.

A representative selection of pinacol alkylboronates **3**, possessing alkyl groups ranging in bulk from *n*-butyl to thexyl (2,3-dimethyl-2-butyl), was tested under the standard conditions (Table 1). Some products were purified from the

Table 1. Syntheses of Allylic Alcohols 9



3 **9**

entry	R	yield of **9** (%)[a]
1	*n*-butyl	90
2	benzyl	75
3	4-methoxybenzyl	84
4	*i*-propyl	94
5	cyclohexyl[b]	83
6	*t*-butyl	98
7	thexyl	34
8	thexyl (use of **11**)[c]	36
9	thexyl (use of **12**)[c]	99

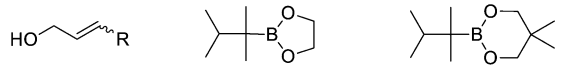
[a]Yield by GC with tetradecane as standard. [b]*E*/*Z* **5** used. [c]Boronic ester **11** or **12** used instead of **3** (R = thexyl).

reaction mixtures; authentic samples of others were prepared from vinylmagnesium bromide and the appropriate aldehyde, so response factors could be calculated and yields monitored by GC to provide true reaction yields (Table 1, entries 1–7).

All but one of the standard reactions (i.e., entries 1–6) provided very good yields of the desired products **9**, none of which contained allylic rearrangement isomers **10**, which have been recorded in earlier reports.[7] Reaction of the 2,2-dimethylpropane-1,3-diol ester of *n*-butylboronic acid did give some rearranged product (78:22 mixture of (*E*/*Z*)-**10**:**9**), but no rearranged products were observed with 2,2-dimethyl-1,3-propanediol esters of more hindered alkylboronic acids or with pinacol boronates of less hindered alkylboronic acids.

As **5** isomerizes to give a mixture of *E* and *Z* isomers in the presence of light,[13] samples had been kept cold and in the dark. In order to check whether precursor **5** needed to be stereochemically pure, a sample was exposed to daylight for several hours to convert it into an *E*/*Z* mixture and then subjected to a standard reaction with **3** (R = cyclohexyl). The yield of **9** (R = cyclohexyl) (Table 1, entry 5) was similar to those obtained for other examples with pure (*E*)-**5**, so synthesis of 1-bromo-3-chloropropene need not be stereoselective.

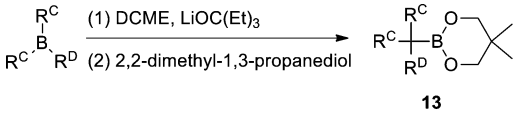
The most hindered pinacol alkylboronic ester (thexyl, entry 7) gave a significantly lower yield than the other alkylboronates **3**. Our experience with halomethyllithium reactions led us to suspect poorer capture of **4** by the more hindered alkylboronate, allowing competitive decomposition of **4**. To try to overcome this, we synthesized the less hindered thexylboronates **11** and **12** from thexylborane and the corresponding diols.



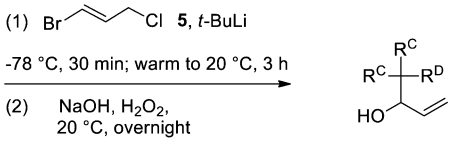
10 **11** **12**

When subjected to the standard conditions, **11** gave 36% of **9** (R = thexyl, entry 8), while **12** gave 99% (entry 9). Similar subtlety was observed in reactions with $BrCH_2Li$, where yields of the corresponding products from **1** (R = thexyl), **11**, and **12** were 35, 80, and 71%.[6] For best results in the present reaction, therefore, it is important that the boronate be sufficiently hindered to inhibit direct reaction between the added organolithium and the boronate or its complex with **4**, but not be so hindered to limit its ability to capture **4**, allowing decomposition of **4** to compete. Pinacol alkylboronates are evidently satisfactory up to the hindrance level of a *t*-butyl group, but for thexyl, the somewhat less hindered 2,2-dimethylpropane-1,3-diol boronate is optimal. To find where the limits of the method lie, standard conditions were applied to alkylboronates incorporating highly hindered *tert*-alkyl groups obtained by use of reactions of trialkylboranes with dichloromethyl methyl ether (DCME, Table 2).

Table 2. Reactions of *tert*-Alkylboronates 13



13



14

entry	R^C	R^D	yield of **14** (%)[a]
1	Me	*i*-Pr	99[b]
2	Et	Et	25 (31)[c]
3	*n*-C_8H_{17}	*n*-C_8H_{17}	28[d]
4	*c*-Hex	PhCH=CH	0
5	*c*-Pent	*c*-Pent	0[e]

[a]By GC unless otherwise stated. [b]This is the result reported in Table 1, entry 9, for reaction of **12**, which was not obtained by the DCME reaction. [c]Number in parentheses is for a similar reaction with 3 equiv of *t*-BuLi and **5**. [d]Yield estimated by relative integrations in the ^1H NMR spectrum of the crude product. [e]The ethylene glycol boronate was used in this case.

The results were similar to those with bromomethyllithium as reagent.[6] With very hindered triethylmethyl- and trioctylmethylboronates, modest but usable yields of the expected products were formed even without optimization of individual reactions. However, with extremely hindered dicyclohexyl(2-phenylethenyl)methyl- and tricyclopentylmethylboronates, none of the desired products were formed (even with the ethylene glycol boronate in the latter case). Therefore, the

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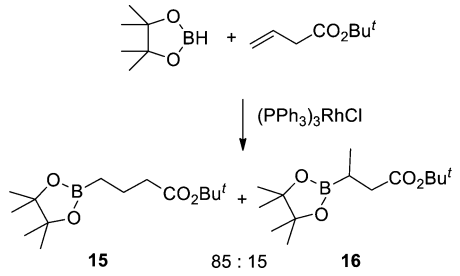
upper limit of steric hindrance for this methodology has been identified.

Several products **9**/**14** were isolated by column chromatography from reactions in Tables 1 and 2 (see Supporting Information). Yields of isolated products were typically 5−20% lower than indicated by GC because of losses during separation. However, additional fractions containing the desired product mixed with other materials were available, and higher yields of isolated product could be achieved if necessary.

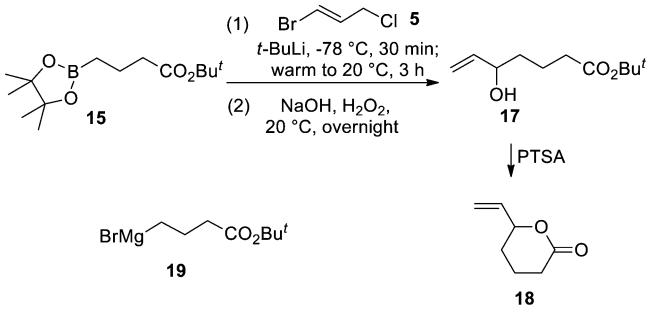
The new methodology is very general, being applicable to alkylboronates with alkyl groups of widely different bulk and potentially possessing functionality incompatible with Grignard or organolithium reagents. To test the ability of the method to tolerate functionality, and to demonstrate applicability to compounds of synthetic interest, we synthesized **15** (Scheme 4).[14] The crude product (91% yield) was a mixture (85:15) of **15** and **16**, which was separated by column chromatography.

Scheme 4. Synthesis of Compound 15



Reaction of **15** with **4** under the standard conditions led to hydroxy ester **17** (96% yield by GC), which was purified by column chromatography. Lactone **18** (100% yield) was obtained by reflux of a benzene solution of **17** with *p*-toluenesulfonic acid monohydrate (PTSA) for 4 h (Scheme 5).[15] It is unlikely that **17** or **18** could be obtained easily by

Scheme 5. Syntheses of Compounds 17 and 18

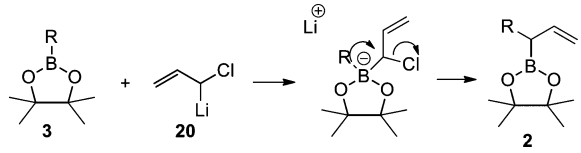


reacting **1** according to Scheme 1a with Grignard reagent **19** because of the lack of stability of such a reagent, and comparable reactions have not been demonstrated with more stable organozinc reagents. Hydroxy esters typified by **17** and lactone **18** have been used in syntheses of prostaglandins,[16] insect pheromones,[17] and other natural products.[18] While there are efficient routes to compound **18**,[19] the present approach is very short and demonstrates the synthetic potential of the new process.

Although we oxidized the intermediate (1-alkylallyl)-boronates (like **2**) to substituted allylic alcohols **9**/**14**/**17**, they are also available for other types of transformations, such as reactions with aldehydes[7,8,20] or protodeboronation.[21]

Products like **2** are potentially available (Scheme 6) by use of 3-chloro-3-lithiopropene (**20**), accessible by deprotonation of

Scheme 6. Generation of 2 from Reagent 20



allyl chloride with LDA.[22] We therefore mixed **1** (R = Bn) with allyl chloride and LDA (to generate **20**) under the conditions developed for reactions of **4**. Compound **9** (R = Bn) was obtained in 40% yield (by GC), showing that this approach is much less efficient than use of **4**. Of course, not all reactions of **4** and **20** will give identical products, so the new reagent is important for other reasons, too.

In conclusion, the novel organolithium reagent **4** has been generated from 1-bromo-3-chloropropene and *t*-BuLi at −78 °C. In the presence of pinacol alkylboronates (**3**), it is trapped to form complexes that rearrange to (α-alkylallyl)boronates **2**, in good yields except for ones with extremely hindered alkyl groups, which require less hindered diol units. Direct oxidation of **2**, without isolation, gives the corresponding allylic alcohols **9** in good yields.

EXPERIMENTAL SECTION

General Experimental Details. Melting point determinations were performed by the open capillary method and are reported uncorrected. ^{1}H and ^{13}C NMR chemical shifts (δ) are reported in parts per million (ppm) relative to TMS, and coupling constants *J* are reported to the nearest 0.1 Hz. C, CH, CH_2, or CH_3 ^{13}C signals are assigned from DEPT-90 and 135 spectra. In a number of cases, carbon atoms attached to boron gave very broad peaks in ^{13}C NMR spectra, and these could not always be distinguished. Hydrogen atoms attached to these carbons were not always observed in ^{1}H NMR spectra. Low- and high-resolution mass spectra were recorded on a time-of-fight mass spectrometer using electron impact (EI). High-resolution mass spectra were recorded only for new compounds. IR spectra were recorded on a FT-IR spectrometer as a thin film (liquid samples) or applied as a solution in chloroform, and the chloroform was allowed to evaporate (solid samples). Column chromatography was carried out using 60A (35−70 μm) silica. GC determinations were performed using a gas chromatograph fitted with a ZB-5 column (30 m, 0.32 mm inner diameter, 1.0 μm film thickness). The carrier gas was He at 69.3 kPa, and a split injection mode was used. The oven temperature was increased from 70 to 260 °C at 6 °C min^{-1} and then held for 4 min. Authentic samples of products were used to determine response factors relative to tetradecane, a known amount of which was added to reaction mixtures to allow quantification of product yields.

Synthesis of 1-Bromo-3-chloroprop-1-ene (5). *Synthesis of (E)-3-Bromoacrylic Acid:*[9] A mixture of propiolic acid (8.79 mL, 0.143 mol) and aq HBr (48%, 40 mL) was heated at 95 °C for 2.5 h, then left to cool. The crude product was filtered, washed with cold water (3 × 25 mL), and dried in air to give (*E*)-3-bromoacrylic acid as colorless needles (13.49 g, 63%); mp 120−121.5 °C (lit.[23] mp 117.5−118.5 °C).

Synthesis of (E)-3-Bromoprop-2-en-1-ol:[10] A two-necked round-bottomed flask equipped with a magnetic stirrer bar, septum, and septum-capped dropping funnel was assembled hot and flushed with N_2. (*E*)-3-Bromoacrylic acid (8.00 g, 53 mmol) was dissolved in dry diethyl ether (40 mL) and transferred via syringe to the dropping funnel. Powdered $LiAlH_4$ (4.02 g, 106 mmol) was transferred quickly to the reaction flask, and dry diethyl ether (40 mL) was added. The reaction mixture was cooled in an ice bath, and the solution of 3-bromoacrylic acid was added dropwise via the dropping funnel with

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vigorous stirring. The mixture was stirred for 2 h, then water (2.5 mL) was added dropwise, followed by 15% NaOH (5.25 mL) and more water (7.4 mL). The resulting salts were washed with diethyl ether (3 × 50 mL), and the combined extracts were dried over sodium sulfate and concentrated under reduced pressure to give fairly pure (*E*)-3-bromoprop-2-en-1-ol as a yellow liquid (4.16 g, 57%).

Synthesis of (E)-1-bromo-3-chloroprop-1-ene[11,12] ***(5):*** A 50 mL round-bottomed flask equipped with a magnetic stirrer bar was charged with (*E*)-3-bromoprop-2-en-1-ol (3.52 g, 25.7 mmol) and cooled using an ice bath. Hexachloroacetone (7.79 mL, 51.4 mmol) was added and the solution stirred for 5 min. Powdered triphenylphosphine (6.74 g, 25.7 mmol) was added portionwise over a period of 25 min. The mixture was stirred for 2 h at 0 °C, then fractionally distilled under reduced pressure to give 90% pure (*E*)-1-bromo-3-chloroprop-1-ene, which was fractionally distilled a second time to give pure (*E*)-1-bromo-3-chloroprop-1-ene (**5**) as a colorless liquid (0.52 g, 13%): ^{1}H (500 MHz, $CDCl_3$) δ 6.48 (1H, dt, J = 13.5, 1.1 Hz), 6.34 (1H, dt, J = 13.5, 7.1 Hz), 4.02 (2H, dd, J = 7.1, 1.1 Hz); ^{13}C (125 MHz, $CDCl_3$) δ 133.1 (CH), 110.8 (CH), 43.6 (CH_2).

Synthesis of Boronate Esters. Boronate esters **3** where R = Bn and 4-MeOBn were purchased from Sigma-Aldrich and TCI, respectively, and used without further purification. Boronate esters **3** where R = Bu, *i*-Pr, and cyclohexyl were prepared from the reaction of their corresponding boronic acids with pinacol in pentane in 73, 36, and 32% yields, respectively. Boronate ester **3** where R = *tert*-Bu was prepared by the literature method from pinacolborane and *tert*-BuMgCl in 40% yield.[24] Boronate ester **3** where R = thexyl was prepared by the method previously described from the monohydroboration of 2,3-dimethyl-2-butene and subsequent reaction with pinacol, while boronate esters **11** and **12** were also prepared as described previously.[6]

Boronate esters **13** were prepared by the DCME reaction with the appropriate trialkylboranes. The procedure for preparation of **13** (R^C = *c*-Hex, R^D = PhCH=CH) is typical. Characterization details of the other boronate esters **13** can be found in our previous publication.[6]

Boronate Ester ***13*** *(R^C = c-Hex, R^D = PhCH=CH):* Dicyclohexylborane was prepared by the dropwise addition of cyclohexene (2.12 mL, 20.9 mmol) to borane dimethyl sulfide complex (10 M, 1.00 mL, 10.0 mmol). The mixture was stirred at room temperature for 2 h, dry THF (10 mL) was added, then the mixture was kept at 0 °C during the dropwise addition of phenylacetylene (1.15 mL, 10.5 mmol). The mixture was stirred for 1 h at 0 °C and 1 h at room temperature then recooled to 0 °C. Dichloromethyl methyl ether (1.36 mL, 15.0 mmol) was added dropwise, followed by a freshly prepared solution of lithium triethylcarboxide (dropwise addition of *n*-BuLi (1.6 M in hexanes, 9.38 mL, 15.0 mmol) to a solution of 3-ethyl-3-pentanol (2.12 mL, 15.0 mmol) in THF (10 mL)) dropwise via a cannula over a 20 min period. The ice bath was removed and the mixture left to stir for a further 1 h. 2,2-Dimethyl-1,3-propanediol (1.57 g, 15.0 mmol) in dry THF (5 mL) was added and the reaction mixture left to stir overnight at room temperature. The crude product following workup was separated by column chromatography on silica (petroleum ether) to give pure (*E*)-2-(1,1-dicyclohexyl-3-phenylallyl)-5,5-dimethyl-1,3,2-dioxaborinane (1.19 g, 20%) as cubic crystals: mp 188−189 °C; ^{1}H (400 MHz, $CDCl_3$) δ 7.40 (2H, d, J = 7.2 Hz), 7.29 (2H, app t, J = 7.6 Hz), 7.16 (1H, t, J = 7.3 Hz), 6.36 (1H, d, J = 16.7 Hz), 6.25 (1H, d, J = 16.7 Hz), 3.65 (4H, s), 0.91−1.82 (22H, m), 1.01 (6H, s); ^{13}C (125 MHz, $CDCl_3$) (*quat C next to boron not seen*) δ 139.4 (quat C), 135.9 (CH), 129.0 (CH), 128.4 (CH), 126.2 (CH), 126.1 (CH), 71.9 (CH_2), 41.1 (CH), 31.4 (quat C), 30.5 (CH_2), 29.2 (CH_2), 27.7 (CH_2), 27.4 (CH_2), 27.3 (CH_2), 22.6 (CH_3); ^{11}B{^{1}H} (96.2 MHz, $CDCl_3$) δ 29.3; HR-EI$^+$ MS m/z (%) calcd for $C_{26}H_{39}{}^{11}BO_2$ 394.3043, found 394.3049 (M^+, 39%).

Reactions of Alkylboronic Esters with 5 and *tert*-BuLi: General Procedure. A mixture of the appropriate boronic ester **3**, **11**, **12**, or **13** (1 equiv), 1-bromo-3-chloroprop-1-ene (**5**, 1.1 equiv), and dry THF in a dry 50 mL round-bottomed flask equipped with a magnetic stirrer bar and septum was cooled to −78 °C, and *t*-BuLi in hexanes (1.1 equiv) was added dropwise with vigorous stirring, and the mixture was stirred for an additional 30 min. The cooling bath was removed and the reaction mixture left to warm to 20 °C over 3 h. An accurately weighed amount of tetradecane (~0.2 mL) was added as a standard to enable GC determination of the amount of desired product formed following workup. The reaction mixture was cooled to 0 °C, then oxidized by dropwise addition of excess NaOH (0.6 g in 5 mL of H_2O), followed by hydrogen peroxide (30% by weight, 3 mL). Once the initial exothermic reaction subsided, the cooling bath was removed and the mixture left to stir overnight at room temperature. Diethyl ether (10 mL) was added, the aqueous layer saturated with sodium chloride, and a small aliquot taken from the organic phase for GC analysis. The mixture was extracted with diethyl ether (2 × 25 mL). The extract was washed with water (10 mL) and brine (10 mL), then dried over $MgSO_4$ to give a crude product containing the desired 3-alkylprop-1-en-3-ol **9** or **14**, which was estimated by GC. In some cases (see below), mixtures were separated by column chromatography on silica (prewashed with 3% triethylamine in petroleum ether, petroleum ether/ethyl acetate 95:5 through 85:15) to provide the pure products.

*4,4,5-Trimethylhex-1-en-3-ol (**9**, R = 1,1,2-Trimethylpropyl, i.e., Thexyl):* From **3** (R = thexyl) (0.564 g, 2.66 mmol), **5** (0.416 g, 2.68 mmol), THF (15 mL), and *t*-BuLi in hexanes (1.9 M, 1.41 mL, 2.68 mmol) (note that the excess of **5** and organolithium reagent was smaller in this example); colorless oil (0.105 g, 28%); ^{1}H (400 MHz, $CDCl_3$) δ 5.94 (1H, ddd, J = 17.2, 10.5, 6.7 Hz), 5.23 (1H, d, J = 17.2 Hz), 5.18 (1H, d, J = 10.5 Hz), 4.01 (1H, d, J = 6.7 Hz, *C*HOH), 1.73 (1H, app sept, J = 7.0 Hz), 1.47 (1H, br s), 0.87 (3H, d, J = 6.9 Hz), 0.85−0.82 (6H, m), 0.73 (3H, s); ^{13}C (125 MHz, $CDCl_3$) δ 138.5 (CH), 116.5 (CH_2), 78.1 (CH), 39.6 (quat C), 32.9 (CH), 19.0 (CH_3), 18.6 (CH_3), 17.5 (CH_3), 17.4 (CH_3); HRMS (EI$^+$) m/z calcd for $C_9H_{18}O$ 124.1252, found 124.1252 ($M^+ - H_2O$).

*4,4-Diethylhex-1-en-3-ol (**14**, R^C = R^D = Et):* From **13** (R^C = R^D = Et) (0.335 g, 1.58 mmol), **5** (0.274 g, 1.76 mmol), dry THF (10 mL), and *t*-BuLi in hexanes (1.6 M, 1.09 mL, 1.74 mmol); colorless liquid (0.042 g, 17%); ^{1}H (500 MHz, $CDCl_3$) δ 6.02 (1H, ddd, J = 17.2, 10.5, 6.6 Hz), 5.24 (1H, app dt, J = 17.2, 1.6 Hz), 5.16 (1H, app dt, J = 10.5, 1.6 Hz), 4.00−3.96 (1H, m), 1.41−1.28 (6H, m), 0.84 (9H, t, J = 7.6 Hz); ^{13}C (125 MHz, $CDCl_3$) δ 138.8 (CH), 115.9 (CH_2), 78.4 (CH), 41.7 (quat C), 26.0 (CH_2), 8.5 (CH_3); HRMS (EI$^+$) m/z calcd for $C_{10}H_{20}O$ 156.1514, found 156.1509 (M^+).

*1-Phenylbut-3-en-2-ol (**9**, R = Benzyl):*[25] From **3** (R = Bn) (0.280 g, 1.28 mmol), **5** (0.226 g, 1.45 mmol), dry THF (10 mL), and *t*-BuLi in hexanes (1.5 M, 0.97 mL, 1.46 mmol); colorless oil (0.097 g, 52%); ^{1}H (400 MHz, $CDCl_3$) δ 7.24 (2H, app t, J = 6.9 Hz), 7.19−7.15 (3H, m), 5.86 (1H, ddd, J = 17.2, 10.5, 5.8 Hz), 5.18 (1H, app dt, J = 17.2, 1.4 Hz), 5.06 (1H, app dt, J = 10.5, 1.3 Hz), 4.31−4.24 (1H, m), 2.82 (1H, dd, J = 13.6, 5.1 Hz), 2.72 (1H, dd, J = 13.6, 8.0 Hz), 1.64 (1H, br s); ^{13}C (125 MHz, $CDCl_3$) δ 140.2 (CH), 137.8 (quat C), 129.7 (CH), 128.6 (CH), 126.7 (CH), 115.1 (CH_2), 73.8 (CH), 43.9 (CH_2); LRMS (EI$^+$) m/z 148 (M^+, 4%).

*1-(4-Methoxyphenyl)but-3-en-2-ol (**9**, R = 4-Methoxybenzyl):*[26] From 4-methoxybenzylboronic acid pinacol ester (0.292 g, 1.18 mmol), **5** (0.210 g, 1.35 mmol), dry THF (10 mL), and *t*-BuLi in hexanes (1.5 M, 0.84 mL, 1.26 mmol); colorless oil (0.185 g, 52%); ^{1}H (400 MHz, $CDCl_3$) δ 7.15 (2H, d, J = 8.7 Hz), 6.86 (2H, d, J = 8.7 Hz), 5.93 (1H, ddd, J = 17.2, 10.5, 5.8 Hz), 5.24 (1H, app dt, J = 17.2, 1.4 Hz), 5.13 (1H, app dt, J = 10.5, 1.4 Hz), 4.34−4.27 (1H, m), 3.79 (3H, s), 2.83 (1H, dd, J = 13.7, 5.1 Hz), 2.73 (1H, dd, J = 13.7, 7.9 Hz), 1.65 (1H, br s); ^{13}C (125 MHz, $CDCl_3$) δ 158.4 (quat C), 140.3 (CH), 130.5 (CH), 129.7 (quat C), 114.8 (CH_2), 114.0 (CH), 73.7 (CH), 55.3 (CH_3), 42.9 (CH_2); LRMS (EI$^+$) m/z 178 (M^+, 45%).

Synthesis of GC Standards from Aldehydes and Vinylmagnesium Bromide: General Procedure. An oven-dried 50 mL round-bottomed flask equipped with a magnetic stirrer bar and septum was flushed with N_2. Vinylmagnesium bromide solution in THF (0.7 M, 1.2 equiv) was added, and the mixture was cooled to 0 °C. The appropriate aldehyde (1 equiv) was added dropwise, and the mixture was stirred for 15 min. Distilled water (10 mL) was added and the product extracted with diethyl ether (3 × 20 mL). The combined organic extracts were washed with water (2 × 10 mL), dried over

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magnesium sulfate, filtered, and concentrated under reduced pressure to give the product.

*Hept-1-en-3-ol (**9**, R = n-Bu):*[27] From vinylMgBr (0.7 M, 20 mL, 14 mmol) and valeraldehyde (1.24 mL, 11.7 mmol); light yellow liquid (0.73 g, 55%); ^{1}H (400 MHz, $CDCl_3$) δ 5.86 (1H, ddd, J = 17.2, 10.5, 6.3 Hz), 5.21 (1H, app dt, J = 17.2, 1.4 Hz), 5.09 (1H, app dt, J = 10.5, 1.4 Hz), 4.08 (1H, app q, J = 6.7 Hz), 1.77 (1H, br s), 1.60−1.44 (2H, m), 1.41−1.23 (4H, m), 0.89 (3H, app t, J = 7.2 Hz); ^{13}C (125 MHz, $CDCl_3$) δ 141.5 (CH), 114.6 (CH_2), 73.4 (CH), 36.9 (CH_2), 27.6 (CH_2), 22.8 (CH_2), 14.1 (CH_3).

*4-Methylpent-1-en-3-ol (**9**, R = i-Pr):*[28] From vinylMgBr (0.7 M, 30 mL, 21 mmol) and isobutyraldehyde (1.60 mL, 17.5 mmol); colorless liquid (1.49 g, 85%); ^{1}H (500 MHz, $CDCl_3$) δ 5.86 (1H, ddd, J = 17.2, 10.5, 6.4 Hz), 5.22 (1H, app dt, J = 17.2, 1.5 Hz), 5.15 (1H, app dt, J = 10.5, 1.5 Hz), 3.86 (1H, app t, J = 6.1 Hz), 1.78−1.67 (1H, m), 1.58 (1H, br s), 0.93 (3H, d, J = 6.8 Hz), 0.90 (3H, d, J = 6.8 Hz); ^{13}C (125 MHz, $CDCl_3$) δ 139.7 (CH), 115.7 (CH_2), 78.4 (CH), 33.8 (CH), 18.3 (CH_3), 17.9 (CH_3).

*1-Cyclohexylprop-2-en-1-ol (**9**, R = Cyclohexyl):*[29] From vinylMgBr (0.7 M, 10 mL, 7 mmol) and cyclohexanecarboxaldehyde (0.71 mL, 5.9 mmol); colorless liquid (0.50 g, 61%); ^{1}H (500 MHz, $CDCl_3$) δ 5.86 (1H, ddd, J = 17.2, 10.4, 6.6 Hz), 5.20 (1H, app dt, J = 17.2, 1.6 Hz), 5.14 (1H, app dt, J = 10.4, 1.6 Hz), 3.84 (1H, app t, J = 6.4 Hz), 1.88−1.81 (1H, m), 1.79−1.70 (2H, m), 1.70−1.62 (2H, m), 1.55 (1H, br s), 1.44−0.93 (6H, m); ^{13}C (125 MHz, $CDCl_3$) δ 140.0 (CH), 115.6 (CH_2), 77.9 (CH), 43.7 (CH), 28.9 (CH_2), 28.5 (CH_2), 26.7 (CH_2), 26.3 (CH_2), 26.2 (CH_2).

Synthesis of *tert*-Butyl 4-(4,4,5,5-Tetramethyl-1,3,2-dioxaborolan-2-yl)butanoate (15). Borane dimethyl sulfide (10 M, 1.94 mL, 19.4 mmol) was added to a 50 mL round-bottomed flask equipped with a stirrer bar and under N_2. The flask was cooled in an ice bath, and a solution of pinacol (2.29 g 19.4 mmol) in dry dichloromethane (10 mL) was added dropwise over a period of 10 min. The reaction mixture was stirred for an hour at 0 °C and a further hour at room temperature before being transferred dropwise via cannula to a 100 mL round-bottomed flask equipped with a stirrer bar and a suspension of Wilkinson's catalyst (0.16 g, 0.17 mmol, 1 mol %) in dry dichloromethane (5 mL). The reaction mixture was stirred for 5 min, then *tert*-butyl but-3-enoate (2.50 g, 17.6 mmol) was added dropwise over a period of 10 min. The mixture was stirred overnight at room temperature then concentrated under reduced pressure. Hexane (20 mL) was added, the mixture was filtered, and the filtrate was concentrated to give the crude product (4.30 g, 91%), which consisted of boronic esters **15** and **16** (85:15 by relative integrations by ^{1}H NMR). This was separated by column chromatography on silica (98:2 petroleum ether/ethyl acetate, followed by 95:5, 90:10, and finally 85:15) to give boronate ester **15** as a colorless oil (1.80 g, 50%): ^{1}H (400 MHz, $CDCl_3$) δ 2.21 (2H, t, J = 7.6 Hz), 1.69 (2H, app pent, J = 7.7 Hz), 1.43 (9H, s), 1.23 (12H, s), 0.79 (2H, t, J = 7.8 Hz); ^{13}C (125 MHz, $CDCl_3$) δ 173.1 (quat C), 83.1 (quat C), 80.0 (quat C), 38.0 (CH_2), 28.3 (CH_3), 24.9 (CH_3), 19.9 (CH_2), 10.7 (br, CH_2B); ^{11}B{^{1}H} (96.2 MHz, $CDCl_3$) δ 32.8; HR-EI$^+$ MS m/z (%) calcd for $C_{10}H_{18}{}^{11}BO_3$ 197.1349, found 197.1353 (M^+ − $OC(CH_3)_3$, 41%).

Synthesis of *tert*-Butyl 5-Hydroxyhept-6-enoate (17). *tert*-Butyl-5-hydroxyhept-6-enoate (**17**, 96% yield by GC) was prepared under the standard conditions (see section on reactions of alkylboronic esters with **5** and *tert*-BuLi; general procedure) from boronate ester **15** (0.631 g, 2.34 mmol), **5** (0.423 g, 2.72 mmol), dry THF (10 mL), and *t*-BuLi in hexanes (1.5 M, 1.81 mL, 2.72 mmol), except that after oxidation of the organoboron compound with alkaline hydrogen peroxide the mixture was made acidic (pH ∼3) by addition of HCl, prior to saturation with sodium chloride and extraction. The crude product was separated by column chromatography on silica gel (90:10 petroleum ether/ethyl acetate, followed by 85:15) to give **17** as a colorless oil (0.183 g, 39%): ^{1}H (400 MHz, $CDCl_3$) δ 5.84 (1H, ddd, J = 17.2, 10.4, 6.2 Hz), 5.21 (1H, dt, J = 17.2, 1.4 Hz), 5.09 (1H, dt, J = 10.4, 1.4 Hz), 4.09 (1H, app q, J = 6.6 Hz), 2.24 (2H, app t, J = 7.5 Hz), 2.01 (1H, br), 1.72−1.57 (2H, m), 1.59−1.48 (2H, m), 1.42 (12H, s); ^{13}C (125 MHz, $CDCl_3$) δ 173.1 (quat C), 140.9 (CH), 114.8 (CH_2), 80.3 (quat C), 72.7 (CH), 36.3 (CH_2), 35.2 (CH_2), 28.1 (CH_3), 20.8 (CH_2); HR-EI$^+$ MS m/z (%) calcd for $C_7H_{11}O_2$ 127.0759, found 127.0759 (M^+ − $OC(CH_3)_3$, 92%).

Synthesis of 6-Vinyltetrahydro-2*H*-pyran-2-one (18).[19] *tert*-Butyl 5-hydroxyhept-6-enoate (**17**, 0.069 g, 0.345 mmol), dry benzene (10 mL), and *p*-toluenesulfonic acid monohydrate (0.018 g, 0.093 mmol) were added to a 25 mL round-bottomed flask equipped with a stirrer bar and a condenser. The reaction mixture was heated to reflux (bath temperature = 100 °C) for 4 h. The reaction mixture was concentrated under reduced pressure, hexane (20 mL) was added, and the mixture was filtered. The filtrate was concentrated under reduced pressure to give lactone **18** as a light yellow oil (0.044 g, 100%): ^{1}H (500 MHz, $CDCl_3$) δ 5.86 (1H, ddd, J = 17.2, 10.6, 5.5 Hz), 5.34 (1H, dt, J = 17.2, 1.4 Hz), 5.23 (1H, dt, J = 10.6, 1.4 Hz), 4.84−4.79 (1H, m), 2.62−2.55 (1H, m), 2.52−2.44 (1H, m), 2.02−1.81 (3H, m), 1.70−1.61 (1H, m); ^{13}C (125 MHz, $CDCl_3$) δ 171.2 (quat C), 136.1 (CH), 117.0 (CH_2), 80.4 (CH), 29.7 (CH_2), 28.0 (CH_2), 18.2 (CH_2); HR-EI$^+$ MS m/z (%) calcd for $C_7H_{10}O_2$ 126.0681, found 126.0678 (M^+, 20%).

■ ASSOCIATED CONTENT

Ⓢ Supporting Information

^{1}H and ^{13}C and where relevant ^{11}B NMR spectra for all compounds. This material is available free of charge via the Internet at http://pubs.acs.org.

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Notes

The authors declare no competing financial interest.

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