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Stereoselective Formation of Trisubstituted Vinyl Boronate Esters by the Acid-Mediated Elimination of α-Hydroxyboronate Esters

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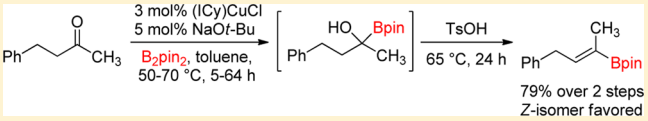
Supporting Information

ABSTRACT: The copper-catalyzed diboration of ketones followed by an acid-catalyzed elimination leads to the formation of 1,1-disubstituted and trisubstituted vinyl boronate esters with moderate to good yields and selectivity. Addition of tosic acid to the crude diboration products provides the corresponding vinyl boronate esters upon elimination. The trisubstituted vinyl boronate esters are formed as the (*Z*)-olefin isomer, which was established by subjecting the products to a Suzuki−Miyaura coupling reaction to obtain alkenes of known geometry.

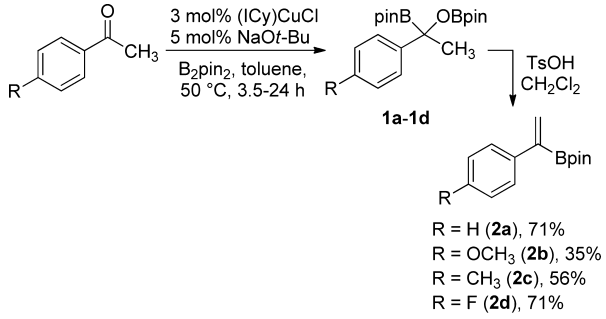


Vinyl boronate esters play a significant role in target-directed synthesis of alkenes through the Suzuki−Miyaura coupling reaction.[1,2] While 1,2-disubstituted vinyl boranes and boronates are readily available through the hydroboration of terminal alkynes,[3−5] methods to access 1,1-disubstituted vinyl boronates are less abundant and have additional limitations,[6−10] particularly in the area of functional group tolerance. Methods to access trisubstituted vinyl boronates typically suffer from poor stereo- or regioselectivity unless the substrate has significant steric or electronic differentiation.[11,12] The absence of a general method[13,14] to access these valuable synthetic intermediates is surprising considering the wealth of natural products and pharmaceutical targets that contain trisubstituted alkenes. If new methods to access the required trisubstituted vinyl boronates with control of stereo- and regioselectivity were established, it would provide a valuable strategy to access many biologically relevant synthetic targets.

In 2010, we reported the copper-catalyzed diboration of ketones, which provides tertiary α-hydroxyboronate esters upon hydrolysis of the O−B bond.[15−17] Recognizing the potential of these intermediates to access vinyl boronate esters by an elimination reaction, we examined α-hydroxyboronates under typical elimination conditions. We herein report the acid-catalyzed elimination of α-hydroxyboronate esters to provide 1,1-disubstituted and trisubstituted vinyl boronate esters in a facile procedure from readily available ketones which requires only one purification process.

Acetophenone-derived α-hydroxyboronate ester (**1a**, R = H, Scheme 1) was chosen as an initial substrate for acid-mediated elimination since the expected carbocation would be stabilized by the phenyl substituent. **1a** was treated with various acids in an effort to promote an E1 elimination reaction. *p*-Toluenesulfonic acid (TsOH) in dichloromethane was found to be particularly effective in promoting the elimination reaction to provide 1,1-disubstituted vinyl boronate **2a** in 71% isolated yield.

Scheme 1. Diboration/Elimination of Acetophenones



Several additional acetophenone derivatives were examined, and it was found that the aryl substituent has a significant influence on the rate of the diboration reaction. Electron-rich 4-methoxyacetophenone was found to be much less reactive than acetophenone in the copper-catalyzed diboration reaction, resulting in 70% conversion to **1b** under similar reaction conditions. Increased reaction time and catalyst loading was successful in obtaining >85% conversion, but a modest 35% yield was obtained upon isolation of the elimination product (**2b**). The low yield likely reflects the combination of inefficient diboration and elimination. In the case of a less electron-donating methyl substituent, the diboration reactivity was largely recovered and elimination product **2c** was isolated in 56% yield. Finally, 4-fluoro-substituted acetophenone was examined, providing rapid diboration, and the corresponding vinyl boronate (**2d**) was isolated in 71% yield.

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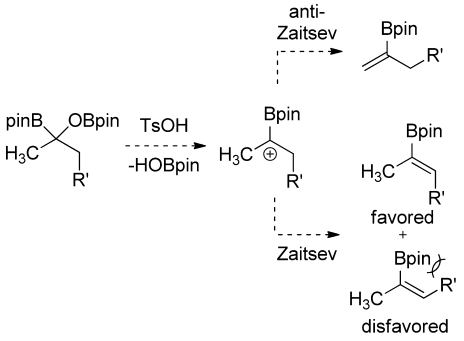
The sensitivity of the diboration reaction toward electronic effects and the potential value of trisubstituted vinyl boronate esters led us to turn our attention to dialkyl ketones. The greatest challenge to the success of this method was the regio- and stereoselectivity of the elimination reaction (Scheme 2).

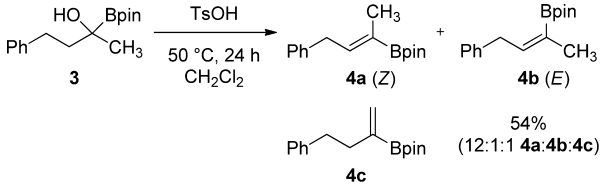
Scheme 2. Expected Selectivity of Elimination from Dialkyl Ketones



Assuming that a carbocation intermediate is formed, the regiochemistry should be governed by Zaitsev's rule,[18] providing differentiation if the two alkyl substituents provide alkenes with different substitution patterns. The stereochemistry of the vinyl boronate was expected to be governed by the steric strain imposed by the pinacolatoboronate ester (Bpin) on a *cis* substituent, which would result in a (*Z*)-alkene.

A study of the elimination reaction was initiated by subjecting α-hydroxyboronate ester **3** to similar conditions used for substrates **1a**–**1d** (Scheme 1). Addition of 2 equiv of *p*-toluenesulfonic acid to **3** in dichloromethane provided complete conversion to **4** after 24 h at 50 °C (Scheme 3).

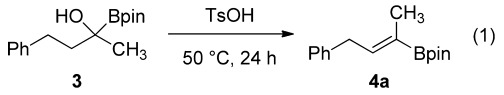
Scheme 3. Acid-Mediated Elimination of Alcohol 3



Under these conditions, **4** was isolated in 54% yield as a 12:1:1 mixture of **4a**/**4b**/**4c**. The major isomer (**4a**) has the expected regio- and stereoselectivity, favoring the *Z*-trisubstituted vinyl boronate ester. To streamline the reaction sequence, the crude diboration product was subjected to the reaction conditions without purification. Under these conditions, **4** was isolated in 63% yield (with identical selectivity) over two steps from 4-phenyl-2-butanone.

In an effort to improve the reaction selectivity, a solvent screen was initiated for the elimination step. Alcohol and ethereal solvents were ineffective in promoting the elimination, providing no reaction (Table 1, entries 1–3). Dimethoxyethane (DME) proved to be an exception, providing unselective formation of **4** (entry 4). Acetonitrile was even less selective than DME (entry 5). Nonpolar solvents, however, provided selectivities nearly as high as dichloromethane (entries 6–8). Recognizing the opportunity to further streamline the synthesis of these vinyl boronate esters by performing the diboration and elimination in one reaction vessel without workup, we optimized the two-step, one-flask diboration/elimination of 4-phenyl-2-butanone using toluene as the solvent for both steps. Simple addition of *p*-toluenesulfonic acid to the reaction mixture after diboration resulted in clean formation of **4** (12:1:1.5 of **4a**/**4b**/**4c**) in 79% isolated yield by heating the elimination reaction to 65 °C for 9 h (Table 2, entry 1). The improved yield and reproducibility of the transformation led to the adoption of this protocol for the remaining substrates.

Table 1. Solvent Screen for the Elimination of 3

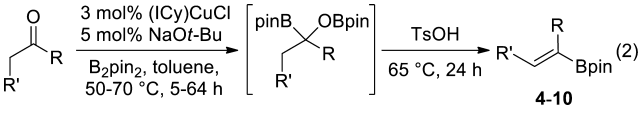


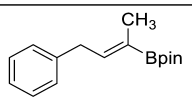
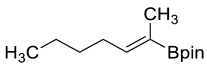
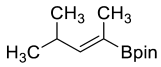
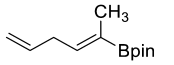
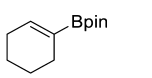
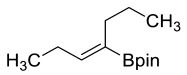
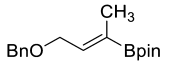
Entry	Solvent	Selectivity (**4a**:**4b**:**4c**)[a]
1	methanol	No Reaction
2	ether	No Reaction
3	tetrahydrofuran	No Reaction
4	dimethoxyethane	41:13:1
5	acetonitrile	7.5:6:1
6	toluene	9:1:1
7	dichloromethane	12:1:1
8	1,2-dichloroethane	9:2:1

[a]Selectivity determined by ^{1}H NMR spectroscopy of the crude reaction mixture with 5 s relaxation delay to ensure integral integrity.

The diboration/elimination protocol was applied to a series of ketones to probe the scope of the transformation. The diboration/elimination of 2-heptanone and 4-methyl-2-pentanone (Table 2, entries 2 and 3) was found to provide similar yield and selectivity as 4-phenyl-2-butanone. 5-Hexen-2-one

Table 2. Substrate Scope for Vinyl Boronate Formation



Entry	Vinyl Boronate	Yield (%)	Selectivity[a]
1		79	12:1:1.5 (**4a**:**4b**:**4c**)
2		63	10:1:1 (**5a**:**5b**:**5c**)
3		63	14.3:1:1.3 (**6a**:**6b**:**6c**)
4		55	18:1:3.6 (**7a**:**7b**:**7c**)
5[b]		57	NA (**8**)
6		54	2:1 (**9a**:**9b**)
7		41	1:0:1.2 (**10a**:**10b**:**10c**)

[a]Selectivity determined by ^{1}H NMR spectroscopy of the crude reaction mixture with 5 s relaxation delay to ensure integral integrity. [b]Dichloromethane used as solvent in place of toluene.

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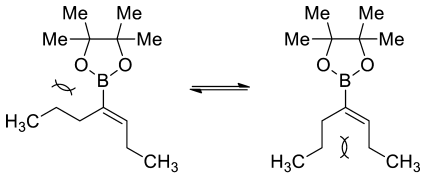
(entry 4) was examined to determine if the pendant alkene would be tolerated under the reaction conditions. The copper-catalyzed diboration was found to be highly selective for the carbonyl over the alkene.[19] Cyclohexanone was also examined, providing vinyl boronate **8** in 57% yield with only one possible isomer (entry 5).

4-Heptanone (entry 6) and 4-benzyloxy-2-butanone (entry 7) provided the corresponding vinyl boronate ester but in poor selectivity. In the case of 4-heptanone, the loss of selectivity (of *Z* vs *E*) seems to result when a secondary α carbon is present on both sides of the carbonyl. Although one would expect the propyl substituent geminal to the Bpin to have little effect on the preference for *Z* over *E*, the Bpin substituent likely forces the propyl substituent to orient itself toward the ethyl substituent, in an *s-cis* conformation (Scheme 4),[20] which

Scheme 4. Explanation of Stereoselectivity in Formation of 9



cancels most of the added strain observed with the methyl ketone substrates (entries 1–4). The loss of selectivity observed with 4-benzyloxy-2-butanone (entry 7) is not explained as readily. The electronegativity of the benzyloxy substituent seems to be responsible for the decreased rate of **10a** formation compared to **10c**. Further experiments are required to interrogate this decrease in selectivity.

The synthetic utility of the resulting vinyl boronate esters was demonstrated by subjecting them to Suzuki–Miyaura coupling conditions to provide trisubstituted olefins in good yield.[21] Vinyl boronates **4**, **5**, **7**, and **9** were readily coupled with 3-iodotoluene, providing the corresponding (*E*)-alkene in good yield (Table 3, entries 1–4). Bromo-substituted arenes were also used in the coupling reaction, providing high yields (entries 5 and 6). This Suzuki coupling reaction was used to verify the vinyl boronate geometry as *Z* by synthesizing alkenes with known alkene geometry.[22]

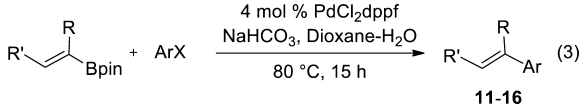
In summary, a diboration/elimination sequence was developed that utilizes tertiary α-hydroxyboronate esters as intermediates to generate 1,1-disubstituted and trisubstituted vinyl boronate esters with good selectivity. Suzuki–Miyaura coupling reactions were used to demonstrate the synthetic utility of the trisubstituted vinyl boronates and to unambiguously assign the stereochemistry of the major product.

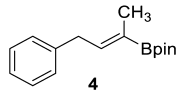
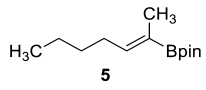
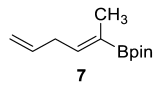
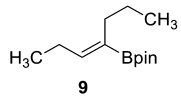
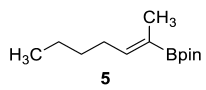
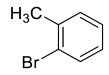
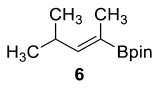
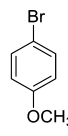
EXPERIMENTAL SECTION

General Methods. All air- and moisture-sensitive materials were handled under dry nitrogen, either in an inert atmosphere glovebox or by standard Schlenk techniques. All solvents were dried and degassed unless used for extraction or purification. In all procedures, concentration was performed by rotary evaporation and through a Shlenk manifold. TLC analysis was performed on 60 Å silica layer fluorescence UV plates. Purification was performed by flash column chromatography with hand-packed columns of silica gel, 40–63 μm, 60 Å.

NMR spectra were collected at 500 or 400 MHz for ^{1}H NMR and 100 or 125 MHz for ^{13}C NMR. ^{1}H NMR spectra were referenced to chloroform-*d* at 7.26 ppm. The ^{1}H NMR spectral data are reported as

Table 3. Suzuki Coupling Reactions of Vinyl Boronates



Entry	Vinyl Boronate	ArX	Yield (%)	Product
1	 **4**		74	**11**
2	 **5**		84	**12**
3	 **7**		60	**13**
4	 **9**		87	**14**
5	 **5**		92	**15**
6	 **6**		92	**16**

follows: chemical shift parts per million, multiplicity (s = singlet, d = doublet, t = triplet, q = quartet, qn = quintet, hex = hextet, sep = septet, oct = octet, m = multiplet), coupling constants (hertz), and integration. ^{13}C NMR spectra were referenced to chloroform-*d* at 77.0 ppm. Attenuated total reflection IR (ATR-IR) spectra and absorptions are reported in cm^{-1}. High-resolution mass spectrometry was obtained by time-of-flight electrospray ionization.

Toluene and benzene-d_6 were dried and distilled from calcium hydride, degassed using freeze, pump, thaw cycles, and stored in an inert atmosphere glovebox. Ketones were purchased from commercial sources and distilled, degassed, and stored in the glovebox before use. *p*-Toluenesulfonic acid was purified by recrystallization (ethyl acetate) and dried by vacuum oven before it was brought into the inert atmosphere glovebox. Chloroform-*d*, bis(pinacolato)diboron, and sodium *tert*-butoxide were purchased and used as received. [1,3-Dicyclohexylimidazol-2-ylidene]copper(I) chloride was made following known procedures.[15,16]

General Procedure A for the Diboration of Aryl Ketones and Acid-Mediated Elimination. *4,4,5,5-Tetramethyl-2-(1-phenylvinyl)-1,3,2-dioxaborolane (**2a**).*[9] In a glovebox, an oven-dried resealable solvent flask (with PTFE valve) equipped with a stirbar was charged with bis(pinacolato)diboron (0.561 g, 2.20 mmol), NaO*t*-Bu (0.010 g, 0.100 mmol), (ICy)CuCl (0.020 g, 0.060 mmol), and toluene (24 mL), followed by acetophenone (0.240 mL, 2.00 mmol). (The only variation in subsequent reactions is the starting ketone.) The flask was sealed and removed from the glovebox and heated to 50 °C. After 3.5 h, the reaction mixture was concentrated and the resulting residue was dissolved in pentane, filtered through Celite, and concentrated in vacuo. The crude diboronate was combined with *p*-toluenesulfonic acid (0.456 g, 2.4 mmol) followed by 24 mL of CH_2Cl_2. The reaction was stirred at 22 °C for 3.5 h and concentrated in vacuo. Purification by silica gel column chromatography (2:98 ethyl acetate/hexanes) provided vinyl boronate ester **2a** as a white solid (0.326 g, 71%): ^{1}H NMR (500 MHz, $CDCl_3$) δ = 7.48 (d, *J* = 7.3,

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2H), 7.31 (t, J = 7.5, 2H), 7.25 (m, 1H), 6.06 (m, 2H), 1.32 (s, 12H); ^{13}C NMR (125 MHz, benzene-d_6) δ = 152.2, 130.5, 130.4, 127.3, 126.2, 126.0, 83.3, 24.5.

*2-(1-(4-Methoxyphenyl)vinyl)-4,4,5,5-tetramethyl-1,3,2-dioxaborolane (**2b**).*[23] General procedure A was followed with 4′-methoxyacetophenone (0.300 g, 2.00 mmol), 10 mol % of (ICy)CuCl (0.063 g, 0.200 mmol), and 12 mol % of NaO*t*Bu (0.024 g, 0.240 mmol) for 4 h at 50 °C. Purification by silica gel column chromatography (8:92 ethyl acetate/hexanes) provided vinyl boronate ester **2b** as a white solid (0.181 g, 35%): ^{1}H NMR (500 MHz, $CDCl_3$) δ = 7.44 (d, J = 7.0, 2H), 6.86 (d, J = 7.0, 2H), 6.01 (d, J = 3.0, 1H), 5.96 (d, J = 3.0, 1H), 3.80 (s, 3H), 1.32 (s, 12H); ^{13}C NMR (100 MHz, $CDCl_3$) δ = 158.8, 133.9, 129.0, 128.3, 113.6, 83.7, 54.2, 24.8; ^{11}B NMR (160 MHz, benzene-d_6) δ = 30.3; IR (neat) 2987, 1508, 1248, 1141, 1029, 832 cm^{-1}; HRMS (ES) calcd for ($C_{15}H_{21}BO_3$ + Na)$^+$ 261.1665, found 261.1668.

*4,4,5,5-Tetramethyl-2-(1-(p-tolyl)vinyl)-1,3,2-dioxaborolane (**2c**).* General procedure A was followed with 4′-methylacetophenone (0.270 mL, 2.00 mmol) for 18 h at 50 °C. Purification by silica gel column chromatography (3:97 ether/hexanes) yielded **2c** as a white solid (0.273 g, 56%): ^{1}H NMR (500 MHz, $CDCl_3$) δ = 7.38 (d, J = 8.0, 2H), 7.13 (d, J = 8.0, 2H), 6.04 (d, J = 3.2, 1H), 6.00 (d, J = 3.2, 1H), 2.33 (s, 3H), 1.32 (s, 12H); ^{13}C NMR (100 MHz, $CDCl_3$) δ = 138.5, 136.7, 130.0, 128.9, 127.0, 83.7, 24.8, 21.1; ^{11}B NMR (160 MHz, benzene-d_6) δ = 30.2; IR (neat) 2977, 1388, 1184, 850 cm^{-1}; HRMS (ES) calcd for ($C_{15}H_{21}BO_2$ + NH_4)$^+$ 267.1535, found 267.1534.

*2-(1-(4-Fluorophenyl)vinyl)-4,4,5,5-tetramethyl-1,3,2-dioxaborolane (**2d**).* General procedure A was followed with 4′-fluoroacetophenone (0.245 mL, 2.00 mmol) for 24 h at 50 °C. Purification by silica gel column chromatography (8:92 ethyl acetate/hexanes) yielded **2d** as a white crystalline solid (0.352 g, 71%): mp 44−47 °C; ^{1}H NMR (500 MHz, $CDCl_3$) δ = 7.46 (t, J = 9.0, 2H), 7.00 (t, J = 9.0, 2H), 6.04 (m, 2H), 1.32 (s, 12H); ^{13}C NMR (100 MHz, $CDCl_3$) δ = 162.2 (d, J = 244 Hz), 137.3 (d, J = 3.0), 130.7, 128.7 (d, J = 8.0), 114.8 (d, J = 32.0 Hz), 83.9, 24.8; ^{11}B NMR (160 MHz, benzene-d_6) δ = 29.9; IR (neat) 2996, 1505, 1422, 1159, 841 cm^{-1}; HRMS (CI) calcd for ($C_{14}H_{18}BFO_2$ + NH_4)$^+$ 266.1730, found 266.1735.

General Procedure B for the Diboration of Alkyl Ketones and Acid-Mediated Elimination. Each of the trisubstituted vinyl boronate esters was synthesized by the following procedure. In a glovebox, an oven-dried resealable solvent flask, equipped with a stirbar, was charged with bis(pinacolato)diboron (0.279 g, 1.10 mmol), NaO*t*-Bu (0.005 g, 0.050 mmol), (ICy)CuCl (0.010 g, 0.030 mmol), and toluene (12 mL), followed by the ketone (1.00 mmol). The flask was sealed and removed from the glovebox and heated in an oil bath at 50−70 °C. After 3−64 h, the solvent flask containing the reaction mixture was taken back into the glovebox, and *p*-toluenesulfonic acid (0.380 g, 2.00 mmol) was added to the reaction mixture. After 24 h at 65 °C, the reaction mixture was concentrated in vacuo. The resulting residue was dissolved in dichloromethane, filtered through a silica plug with 250 mL of ethyl acetate to remove excess toluene sulfonic acid, and was concentrated in vacuo. Purification by flash silica gel column chromatography provided the corresponding vinyl boronate ester.

*(Z)-4,4,5,5-Tetramethyl-2-(4-phenylbut-2-en-2-yl)-1,3,2-dioxaborolane (**4a**).* General procedure B was followed with 1-phenyl-3-butanone (0.150 mL, 1.00 mmol) at 50 °C for 15 h for the diboration reaction. The vinyl boronate ester was formed as a 12:1:1.5 ratio of **4a**/**4b**/**4c** in the crude reaction mixture. Purification by silica gel column chromatography (4:96 ethyl acetate/hexane) provided vinyl boronate ester **4** in a 12.5:1:1.75 ratio of isomers as a pale yellow oil (0.204 g, 79%): R_f = 0.5 (4:96 ethyl acetate/hexanes); (*Z* isomer) ^{1}H NMR (500 MHz, $CDCl_3$) δ = 7.28 (t, J = 7.7, 2H), 7.19 (d, J = 7.6, 3H), 6.47 (t, J = 6.6, 1H), 3.48 (d, J = 7.2, 2H), 1.81 (s, 3H), 1.25 (s, 12H); ^{13}C NMR (125 MHz, $CDCl_3$) δ = 144.2, 128.7, 128.5, 128.3, 125.8, 83.2, 35.0, 24.8, 14.0; (minor isomers) (*E* isomer) ^{1}H NMR (500 MHz, $CDCl_3$) δ = 7.29 (t, J = 9.1, 3H), 7.20 (d, J = 7.8, 2H), 6.19 (t, J = 6.8, 1H), 3.62 (d, J = 7.8, 2H), 1.80 (s, 3H), 1.25 (s, 12H); (1,1-disubstituted) ^{1}H NMR (500 MHz, $CDCl_3$) δ = 7.28 (m, 2H), 7.20 (m, 3H), 5.80 (s, 1H), 5.61 (s, 1H), 2.58 (t, J = 7.3, 2H), 2.42 (t, J = 7.3, 2H), 1.25 (s, 12H); IR (neat) 2979, 1630, 1368, 1304, 1183, 888, 716 cm^{-1}; HRMS (CI) calcd for ($C_{16}H_{23}BO_2$ + NH_4)$^+$ 276.2138, found 276.2144.

*(Z)-4,4,5,5-Tetramethyl-2-(hept-2-en-3-yl)-1,3,2-dioxaborolane (**5a**).* General procedure B was followed with 2-heptanone (0.712 mL, 5.00 mmol) at 70 °C for 64 h. The vinyl boronate ester was formed as a 10:1:1 ratio of **5a**/**5b**/**5c** in the crude reaction mixture. Purification by silica gel column chromatography (4:96 ethyl acetate/hexanes) provided vinyl boronate ester **5** in a 20:1:1.6 ratio of isomers as a pale yellow oil (0.707 g, 63%): R_f = 0.4 (4:96 ethyl acetate/hexanes); (*Z* isomer) ^{1}H NMR (500 MHz, $CDCl_3$) δ = 6.32 (td, J = 7.0, 1.7, 1H), 2.11 (q, J = 6.5, 2H), 1.67 (s, 3H), 1.35 (m, 4H), 1.26 (s, 12H), 0.89 (t, J = 7.0, 3H); ^{13}C NMR (400 MHz, $CDCl_3$) δ = 146.7, 83.0, 31.0, 28.4, 24.8, 22.5, 14.0, 13.9; (minor isomers) (*E* isomer) (characteristic spectral data) ^{1}H NMR (500 MHz, $CDCl_3$) δ = 6.05 (t, J = 7.4, 1H); (1,1-disubstituted) (characteristic spectral data) ^{1}H NMR (500 MHz, $CDCl_3$) δ = 5.75 (d, J = 3.4, 1H), 5.59 (br s, 1H); IR (neat) 2979, 2927, 1632, 1369, 1301, 1140 cm^{-1}; HRMS (CI) calcd for ($C_{13}H_{25}BO_2$ + NH_4)$^+$ 242.2294, found 242.2302.

*(Z)-4,4,5,5-Tetramethyl-2-(1,3-dimethyl-1-butenyl)-1,3,2-dioxaborolane (**6a**).* General procedure B was followed with 2-methyl-4-heptanone (0.250 mL, 2.00 mmol) at 70 °C for 24 h. The vinyl boronate ester was formed as a 14.3:1:1.3 ratio of **6a**/**6b**/**6c** in the crude reaction mixture. Purification by silica gel column chromatography (4:96 ethyl acetate/hexanes) provided vinyl boronate ester **6** in a 11:1:1 ratio of isomers as a pale yellow oil (0.265 g, 63%): R_f = 0.43 (4:96 ethyl acetate/hexanes); (*Z* isomer) ^{1}H NMR (500 MHz, $CDCl_3$) δ = 6.12 (dd, J = 9.1, 1.6, 1H), 2.68 (m, 1H), 1.69 (d, J = 1.6, 3H), 1.26 (s, 12H), 0.97 (d, J = 6.7, 6H); ^{13}C NMR (400 MHz, $CDCl_3$) δ = 153.4, 83.1, 27.5, 24.8, 22.2, 13.7; (minor isomers) (*E* isomer) (characteristic spectral data) ^{1}H NMR (500 MHz, $CDCl_3$) δ = 5.79 (d, J = 3.7, 1H); (1,1-disubstituted) (characteristic spectral data) ^{1}H NMR (500 MHz, $CDCl_3$) δ = 5.84 (d. J = 9.5, 1H), 5.56 (s, 1H); IR (neat) 2961, 2869, 1633, 1368, 1301, 1144 cm^{-1}; HRMS (CI) calcd for ($C_{12}H_{23}BO_2$ + NH_4)$^+$ 228.2137, found 228.2138.

*(Z)-2-(Hexa-2,5-dien-2-yl)-4,4,5,5-tetramethyl-1,3,2-dioxaborolane (**7a**).* General procedure B was followed with 5-hexen-2-one (0.354 mL, 3.00 mmol) at 70 °C for 24 h. The vinyl boronate ester was formed as a 18:1:3.6 ratio of **7a**/**7b**/**7c** in the crude reaction mixture. Purification by silica gel column chromatography (4:96 ethyl acetate/hexanes) provided vinyl boronate ester **7** in a 16.7:1:1.7 ratio of isomers as a pale yellow oil (0.343 g, 55%): R_f = 0.43 (4:96 ethyl acetate/hexanes); (*Z* isomer) ^{1}H NMR (500 MHz, benzene-d_6) δ = 6.79 (td, J = 7.3, 2.0, 1H), 5.75 (ddt, J = 16.6, 10.2, 6.3, 1H), 5.05 (dq, J = 17.1, 1.9, 1H), 4.94 (dq, J = 10.3, 1.7, 1H), 2.83 (t, J = 6.3, 2H), 1.9 (s, 3H), 1.08 (s, 12H); ^{13}C NMR (125 MHz, $CDCl_3$) δ = 144.2, 136.8, 128.8, 115.8, 83.7, 33.9, 25.5, 14.7; (*E* isomer) ^{1}H NMR (500 MHz, benzene-d_6) δ = 6.26 (td, J = 7.1, 2.0, 1H), 5.75 (ddt, J = 16.6, 10.2, 6.3, 1H), 5.10 (d, J = 2.0, 1H), 4.99 (J = dq, 10.3, 1.7, 1H), 3.42 (t, J = 6.3, 2H), 2.1 (s, 3H), 1.08 (s, 12H); (1,1-disubstituted) ^{1}H NMR (500 MHz, benzene-d_6) δ = 6.2 (s, 1H), 6.0 (s, 1H), 5.73 (ddt, J = 16.6, 10.2, 6.3, 1H), 5.10 (dq, J = 17.1, 1.9, 1H), 4.99 (dq, J = 10.3, 1.7, 1H), 2.42 (t, J = 6.8, 2H) 2.38 (t, J = 6.8, 2H) 1.05 (s, 12H); IR (neat) 2976, 1388, 1285, 1204, 1122, 982, 847 cm^{-1}; HRMS (CI) calcd for ($C_{12}H_{21}BO_2$ + NH_4)$^+$ 226.1981, found 226.1974.

*2-(Cyclohex-1-en-1-yl)-4,4,5,5-tetramethyl-1,3,2-dioxaborolane (**8**).*[24] In a glovebox, an oven-dried resealable solvent flask, equipped with a stirbar, was charged with bis(pinacolato)diboron (0.561 g, 2.2 mmol), NaO*t*-Bu (0.010 g, 0.100 mmol), (ICy)CuCl (0.020 g, 0.060 mmol), and toluene (24 mL), followed by cyclohexanone (0.207 mL, 2.00 mmol). The flask was sealed, removed from the glovebox, and heated to 50 °C. After 22 h, the reaction mixture was filtered through Celite and concentrated in vacuo. *p*-Toluenesulfonic acid (0.760 g, 4.0 mmol) was added to a flask containing the crude diboronate followed by 24 mL of CH_2Cl_2. The reaction was equipped with a reflux condenser and heated to 50 °C for 24 h. After 24 h, the reaction mixture was filtered through a silica plug and concentrated in vacuo. Purification by silica gel column chromatography (4:96 ethyl acetate/hexanes) provided **8** as a colorless oil (0.237 g, 57%): ^{1}H NMR (500

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MHz, benzene-d_6) δ = 6.97 (t, J = 6.8, 1H), 2.42 (m, 2H), 1.98 (m, 2H), 1.56 (m, 2H), 1.49 (m, 2H), 1.09 (s, 12H); ^{13}C NMR (125 MHz, benzene-d_6) δ = 143.9, 83.5, 27.5, 27.2, 25.5, 23.2; ^{11}B NMR (160 MHz, benzene-d_6) δ = 29.9; IR (neat) 2925, 1632, 1427, 1144, 862 cm^{-1}.

*(Z)-4,4,5,5-Tetramethyl-2-(hept-3-en-4-yl)-1,3,2-dioxaborolane (**9a**).* General procedure B was followed with 4-heptanone (0.143 mL, 1.00 mmol) at 70 °C for 24 h. The vinyl boronate ester was formed as a 2:1 ratio of **9a**/**9b** in the crude reaction mixture. Purification by silica gel column chromatography (4:96 ethyl acetate/hexane) provided vinyl boronate ester **9** in a 2.6:1 ratio of isomers as a pale yellow oil (0.121 g, 54%): (*Z* isomer) R_f = 0.4 (4:96 ethyl acetate/hexanes); ^{1}H NMR (500 MHz, $CDCl_3$) δ = 6.29 (t, J = 7.1, 1H), 2.17−2.09 (m, 4H), 1.36 (hex, J = 7.5, 2H), 1.25 (s, 12H), 0.99 (t, J = 7.6, 3H), 0.88 (t, J = 7.4, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ = 147.6, 110.0, 82.9, 30.3, 29.8, 24.8, 23.3, 21.7, 14.0; (minor isomer) (*E* isomer) (characteristic spectral data) R_f = 0.4 (4:96 ethyl acetate/hexanes); ^{1}H NMR (500 MHz, $CDCl_3$) δ = 5.98 (t, J = 7.6, 1H); IR (neat) 1509, 1366, 1178, 1141, 1029, 853 cm^{-1}; HRMS (CI) calcd for ($C_{13}H_{25}BO_2$ + NH_4)$^+$ 242.2294, found 242.2296.

*(Z)-4,4,5,5-Tetramethyl-2-(1-methyl-3-phenylmethoxy-1-propenyl)-1,3,2-dioxaborolane (**10a**).* General procedure B was followed with 4-(benzyloxy)-2-butanone (0.174 mL, 1.00 mmol) at 70 °C for 23 h. The vinyl boronate ester was formed as a 1:1.2 ratio of **10a**/**10c** in the crude reaction mixture. Purification by silica gel column chromatography (4:96 ethyl acetate/hexanes) provided **10** as a 1:2.5 mixture of **10a**/**10c** as a pale yellow oil (0.117 g, 41%): R_f = 0.2 (4:96 ethyl acetate/hexanes); (*Z* isomer) (characteristic spectral data) ^{1}H NMR (500 MHz, $CDCl_3$) δ = 6.48 (t, J = 5.7, 1H), 4.53 (s, 2H), 4.17 (d, J = 6.0, 2H), 1.69 (s, 3H), 1.26 (s, 12H); (1,1-disubstituted) (characteristic spectral data) ^{1}H NMR (500 MHz, $CDCl_3$) δ = 5.85 (d, J = 3.3, 1H), 5.70 (s, 1H), 4.51 (s, 2H), 3.56 (t, J = 7.0, 2H), 2.49 (t, J = 6.9, 2H), 1.24 (s, 12H); IR (neat) 2979, 2921, 2853, 1744, 1369, 1309, 1141 cm^{-1}; HRMS (ES) calcd for ($C_{17}H_{25}BO_3$ + Na)$^+$ 311.1798, found 311.1793.

General Procedure C for Suzuki Cross-Coupling of Vinyl Boronate Esters.[21] In a glovebox, an oven-dried round-bottom flask, equipped with a stir bar, was charged with a vinyl boronate ester (1.00 mmol), an aryl halide (1.00 mmol), $NaHCO_3$ (0.318 g, 3.79 mmol), 1,4-dioxane (10.3 mL), H_2O (4.1 mL), and $PdCl_2$(dppf) (0.031 g, 0.038 mmol). The flask was removed from the glovebox, and the reaction mixture was stirred at 80 °C under positive nitrogen pressure. After 15 h, the reaction mixture was quenched with H_2O (5 mL). The aqueous layer was extracted with EtOAc (20 mL), and the organic extract was washed with brine (4 × 25 mL), dried over $MgSO_4$, filtered, and concentrated in vacuo. Purification by silica gel chromatography provided the corresponding Suzuki coupling product.

*(E)-3-(3-Methylphenyl)-1-phenyl-2-butene (**11**).* General procedure C was followed with vinyl boronate ester **4a** (0.258 g, 1.00 mmol) and purification by silica gel column chromatography (1:99 ethyl acetate/hexanes) provided **11** as a yellow oil (0.165 g, 74%): R_f = 0.54 (1:99 ethyl acetate/hexanes); ^{1}H NMR (500 MHz, $CDCl_3$) δ = 7.31−7.28 (m, 2H), 7.23−7.19 (m, 6H), 7.05−7.04 (m, 1H), 5.95 (td, J = 7.4, 1.3, 1H), 3.56 (d, J = 7.4, 2H), 2.34 (s, 3H), 2.13 (d, J = 0.7, 3H); ^{13}C NMR (400 MHz, $CDCl_3$) δ = 143.6, 141.1, 137.7, 135.8, 128.47,128.45, 128.1, 127.5, 126.53, 126.51, 125.9, 122.9, 35.0, 21.5, 16.0; IR (neat) 3026, 2920, 1603, 1494, 1452 cm^{-1}; HRMS (CI) calcd for ($C_{17}H_{18}$ + H)$^+$ 223.1487, found 223.1486.

*(E)-2-(3-Methylphenyl)-2-heptene (**12**).* General procedure C was followed with vinyl boronate ester **5a** (0.224 g, 1.00 mmol) and purification by silica gel column chromatography with hexanes provided **12** as a pale yellow oil (0.158 g, 84%): R_f = 0.6 (hexanes); ^{1}H NMR (500 MHz, $CDCl_3$) δ = 7.19 (m, 3H), 7.03 (m, 1H), 5.76 (t, J = 7.2, 1H), 2.35 (s, 3H), 2.19 (q, J = 7.0, 2H), 2.02 (s, 3H), 1.41 (m, 4H), 0.93 (t, J = 3H); ^{13}C NMR (400 MHz, $CDCl_3$) δ = 144.1, 137.6, 134.5, 128.6, 128.0, 127.2, 126.4, 122.7, 31.8, 28.5, 22.5, 21.5, 15.8, 14.1; IR (neat) 2955, 2924, 2858, 1604, 1465, 1377 cm^{-1}; HRMS (CI) calcd for ($C_{14}H_{20}$ + H)$^+$ 189.1643, found 189.1642.

*(E)-2-(3-Methylphenyl)-2,5-hexadiene (**13**).* General procedure C was followed by vinyl boronate ester **7** (0.069 g, 0.33 mmol), and purification by silica gel column chromatography with hexanes provided **13** as a pale yellow oil (0.034 g, 60%): R_f = 0.65 (hexanes); ^{1}H NMR (500 MHz, $CDCl_3$) δ = 7.19 (d, J = 5.9, 3H), 7.05 (m, 1H), 5.88 (m, 1H), 5.78 (td, J = 7.4, 1.3, 1H), 5.09 (dq, J = 17.1, 1.7, 1H), 5.02 (dq, J = 10.1, 1.6, 1H), 2.95 (t, J = 6.8, 2H), 2.35 (s, 3H), 2.03 (s, 3H); ^{13}C NMR (400 MHz, $CDCl_3$) δ = 143.8, 137.7, 136.7, 136.1, 128.1, 127.4, 126.5, 125.0, 122.8, 114.8, 33.0, 29.7, 21.5; IR (neat) 2922, 2852, 1637, 1603, 1581, 1442 cm^{-1}; HRMS (CI) calcd for ($C_{13}H_{16}$ + H)$^+$ 173.1330, found 173.1333.

*(E)-4-(3-Methylphenyl)-3-heptene (**14**).* General procedure C was followed with vinyl boronate ester **9** (0.162 g, 0.725 mmol), and purification by silica gel column chromatography with hexanes provided **14** as a pale yellow oil (0.093 g, 87%): R_f = 0.63 (hexanes); ^{1}H NMR (500 MHz, $CDCl_3$) δ = 7.21−7.11 (m, 3H), 7.02 (m, 1H), 5.63 (t, J = 7.2, 1H), 2.45 (t, J = 7.6, 2H), 2.34 (s, 3H), 2.20 (qn, J = 7,4, 2H), 1.35 (hex, J = 7.5, 2H), 1.05 (t, J = 7.5, 3H), 0.88 (t, J = 7.4, 3H); ^{13}C NMR (400 MHz, $CDCl_3$) δ = 143.4, 139.4, 137.6, 130.7, 128.0, 127.1, 127.1, 123.4, 31.7, 21.9, 21.6, 14.5, 14.0; IR (neat) 3019, 2957, 2926, 2870, 1603, 1581, 1457, 1376 cm^{-1}; HRMS (CI) calcd for ($C_{14}H_{20}$ + H)$^+$ 189.1643, found 189.1649.

*(E)-2-(2-Methylphenyl)-2-heptene (**15**).* General procedure C was followed with vinyl boronate ester **5** (0.224 g, 1.00 mmol) and purification by silica gel column chromatography with hexanes provided **15** as a colorless oil (0.172 g, 92%): R_f = 0.75 (hexanes); ^{1}H NMR (500 MHz, $CDCl_3$) δ = 7.16−7.10 (m, 3H), 7.06 (m, 1H), 5.28 (t, J = 7.3, 1H), 2.27 (s, 3H), 2.16 (q, J = 7.1, 2H), 1.90 (s, 3H), 1.40 (m, 4H), 0.93 (t, J = 6.8, 3H); ^{13}C NMR (400 MHz, $CDCl_3$) δ = 145.9, 135.8, 134.8, 129.9, 129.8, 128.3, 126.3, 125.5, 31.8, 28.0, 22.4, 19.9, 17.9, 14.1; IR (neat) 2957, 2925, 2857, 1487, 1457, 1377 cm^{-1}; HRMS (CI) calcd for ($C_{14}H_{20}$)$^+$ 188.1565, found 188.1567.

*(E)-1-(1,3-Dimethyl-1-butenyl)-4-methoxybenzene (**16**).* General procedure C was followed with vinyl boronate ester **6** (0.164 g, 0.780 mmol) and purification by silica gel column chromatography with hexanes provided **16** as a pale yellow oil (0.137 g, 92%): R_f = 0.2 (4:96 ethyl acetate/hexanes); ^{1}H NMR (500 MHz, $CDCl_3$) δ = 7.32 (m, 2H), 6.85 (m, 2H), 5.53 (d, J = 8.7, 1H), 3.81 (s, 3H), 2.68 (m, 1H), 2.02 (d, J = 0.9, 3H), 1.04 (d, J = 6.7, 6H); ^{13}C NMR δ = 158.3, 136.5, 134.6, 131.6, 126.6, 113.4, 55.3, 27.9, 23.1, 15.8; IR (neat) 2955, 2931, 2867, 2835, 1607, 1576, 1510, 1243 cm^{-1}; HRMS (CI) calcd for ($C_{13}H_{18}O$ + H)$^+$ 191.1436, found 191.1429.

■ ASSOCIATED CONTENT

Ⓢ Supporting Information

^{1}H NMR spectra for all new compounds and a discussion of the assignment of alkene stereochemistry (with associated experimental procedures). 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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