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Palladium-Catalyzed Borylation of Primary Alkyl Bromides

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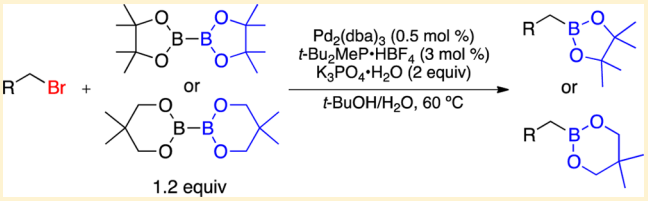
Supporting Information

ABSTRACT: A mild Pd-catalyzed process for the borylation of alkyl bromides has been developed using bis(pinacolato)-diboron as a boron source. This process accommodates the use of a wide range of functional groups on the alkyl bromide substrate. Primary bromides react with complete selectivity in the presence of a secondary bromide. The generality of this approach is demonstrated by its extension to the use of alkyl iodides and alkyl tosylates, as well as borylation reactions employing bis(neopentyl glycolato)diboron as the boron source.



Over the past few decades, the Suzuki–Miyaura cross-coupling reaction has become a workhorse for the construction of carbon–carbon bonds.[1−3] The majority of such reactions involve the use of aryl or vinylboron nucleophiles. In comparison, methods that allow the general use of alkylboron nucleophiles in Suzuki–Miyaura cross-coupling reactions have remained far less developed.[4,5] A major focus of the research in our laboratory is the development of new methods for carbon–carbon bond formation via metal-catalyzed cross-coupling reactions using alkyl nucleophiles.[6−8] For such transformations, alkylboron reagents constitute ideal nucleophiles. The high covalency of the carbon–boron bond typically makes alkylboron reagents air and moisture stable, configurationally stable, and compatible with a diverse range of functional groups.[9,10] Thus, the development of new cross-coupling methods that enable the general use of alkylboron reagents is an attractive synthetic goal.

Classically, organoboron reagents have been generated via borylation of the corresponding lithium or magnesium reagents or via the hydroboration of a terminal olefin.[11] More recently, significant progress has been made toward the development of new, milder methods to generate organoboron reagents for use in synthesis. Particular attention has been focused on the preparation of alkyl and aryl boronic ester derivatives via transition metal-catalyzed processes. Notable examples include the metal-catalyzed hydroboration of alkenes,[12−16] metal-catalyzed C–H activation/borylation sequences,[17−25] and metal-catalyzed β-borylation of α,β-unsaturated compounds.[26−30] With the aim of developing a mild and general method to generate primary alkylboronate esters for use in cross-coupling reactions, we explored the possibility of using bis(pinacolato)diboron as a boron source in the Pd-catalyzed borylation of alkyl halides. An analogous strategy has been successfully applied to the formation of arylboronic esters from aryl halides.[31−33] However, a method to effect the direct Pd-catalyzed borylation of alkyl halides has not been reported.[34−36] Herein, we report a Pd-catalyzed method for the selective borylation of primary alkyl bromides. This process displays excellent functional group tolerance and can be extended to the use of alkyl iodides and alkyl tosylates. Additionally, we have demonstrated that bis(neopentyl glycolato)diboron can be successfully employed as the boron source with nominal variation of the standard reaction conditions.

Initial ligand screening revealed that trialkylphosphines were most effective in the Pd-catalyzed borylation of (3-bromopropyl)benzene. This is consistent with the reported ability of trialkylphosphine-ligated palladium(0) complexes to undergo oxidative addition into primary alkyl halides.[37−39] Products resulting from alkyl halide reduction and β-hydride elimination constituted the major side-products observed during reaction optimization. There was no evidence for protodeboronation of the alkylboronic ester products over the course of the reactions. Our final, optimized conditions are displayed in Table 1. The use of t-$Bu_2MeP{\cdot}HBF_4$ as a supporting ligand resulted in the highest yields. t-BuOH and DMA were the most effective solvents for this transformation. K_3PO_4 was the most effective base, though K_2CO_3 could also be used successfully. While the addition of exogenous water was found to be essential for efficient conversion, only a nominal variation in GC yield was observed when 3 equiv of H_2O was used in place of 15 equiv H_2O.

Using the optimized conditions displayed in Table 1, alkylboronate esters were generated cleanly in high yields from a wide range of functionalized primary alkyl bromides (Table 2). Alkyl bromide substrates bearing functional groups including nitriles, alcohols, ethers, esters, amides, and imides were successfully borylated.[40] The presence of heterocyclic substituents on the alkyl bromide substrate was also well tolerated. 1-Bromo-5-chloropentane underwent selective borylation at the bromide. Although primary alkyl chlorides did not undergo efficient borylation under these conditions, alkyl

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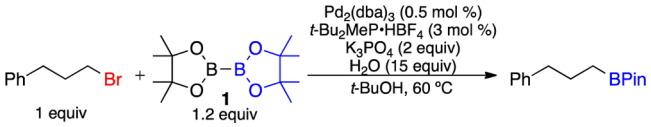
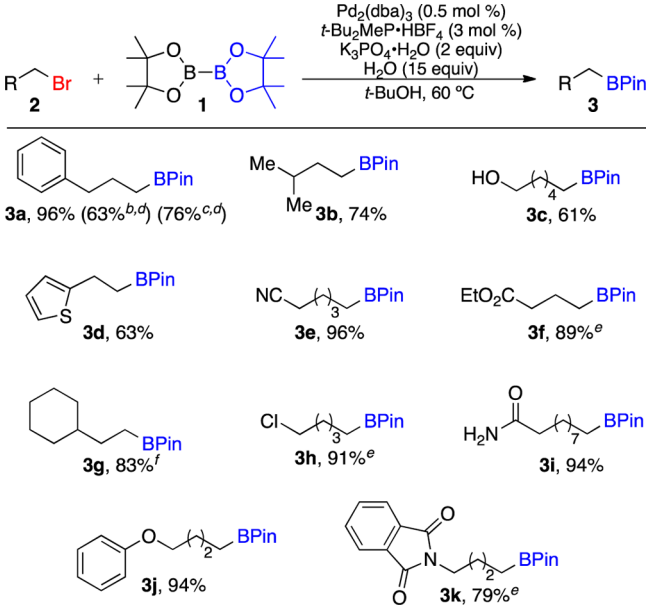
Table 1. Optimization of Standard Reaction Conditions



entry	variation from standard conditions above	yield (%)[a]
1	None	97
2	3 equiv H_2O	93
3	NMP used as solvent, 3 equiv H_2O	29
4	Toluene used as solvent, 3 equiv H_2O	<10
5	DMA used as solvent, 3 equiv H_2O	70
6	DMF used as solvent, 3 equiv H_2O	44
7	DMF used as solvent, no water	<10
8	PCy_3·HBF_4 used as ligand, 3 equiv H_2O	34
9	P*n*–Bu_3·HBF_4 used as ligand, 3 equiv H_2O	<10
10	P*t*–Bu_3·HBF_4 used as ligand, 3 equiv H_2O	<10

[a]Yields and selectivities determined by GC with dodecane as an internal standard.

Table 2. Pd-Catalyzed Borylation of Primary Alkyl Bromides[a]

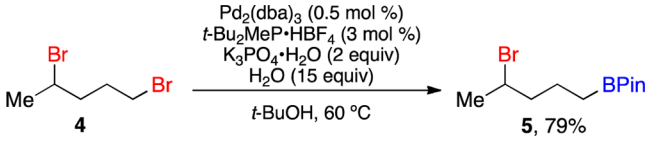


[a]Alkyl bromide (1 mmol), bis(pinacolato)diboron (1.2 mmol); average yield of 2 runs. [b]Using alkyl iodide. [c]Using alkyl tosylate. [d]0.75 mmol scale. [e]3 mol % PCy_3·HBF_4. [f]1.5 mol % $Pd_2(dba)_3$, 9 mol % PCy_3·HBF_4.

iodides and alkyl tosylates were viable electrophiles. As these reactions proceeded, we observed no evidence of transmetalation of the pinacol alkylboronate ester produced in the reaction.

In contrast to nickel- and copper-catalyzed processes that can undergo oxidative addition via radical processes,[35,36,41,42] Pd(0) complexes generally undergo oxidative addition with alkyl halides via direct nucleophilic displacement of the halide leaving group.[37−39] As a result, the use of Pd catalysis is generally limited to primary electrophiles. Fortunately, this mechanism for oxidative addition can be exploited to achieve the chemoselective borylation of molecules bearing multiple halide groups. Using 1,4-dibromopentane (**4**) as an electrophile (Scheme 1), we observed that a primary bromide could indeed

Scheme 1. Selective Borylation of Primary Bromide[a]

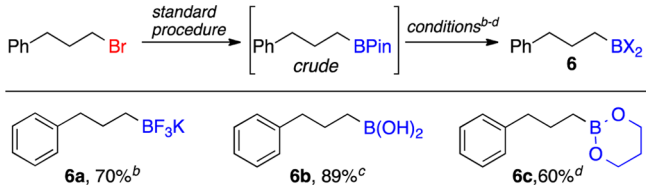


[a]Alkyl bromide (1 mmol), bis(pinacolato)diboron (1.2 mmol); average yield of 2 runs.

be selectively borylated in the presence of a remote secondary bromide. This reaction occurred efficiently, with no detectable trace of borylation at the secondary bromide.

To broaden the utility of our borylation method, we have developed methods to convert the crude pinacol boronate products to other boronate derivatives (Table 3). After

Table 3. Direct Preparation of Boronate Ester Derivatives[a]

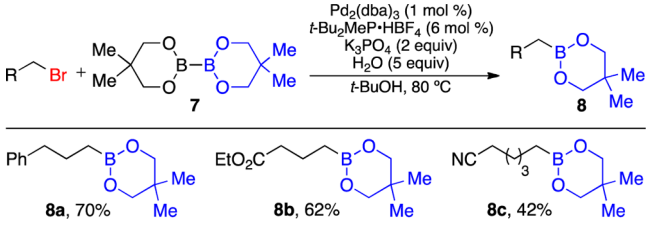


[a]Alkyl bromide (0.75 mmol); average yield of 2 runs. [b]KHF_2, MeOH, rt, 2 h. [c]$NaIO_4$, HCl(aq), THF/H_2O, rt, 3 h. [d]Footnote c, then 1,3-propanediol, benzene, reflux, 12 h.

borylation of (3-bromopropyl)benzene via the standard conditions of Table 1, transformation of the resulting pinacol boronate ester to a trifluoroboronate (**6a**), boronic acid (**6b**), and propylene glycol boronate (**6c**) was readily achieved without isolation of the pinacol boronate intermediate.

It has been demonstrated that transmetalation of an aryl group from a pinacol boronate ester to palladium occurs significantly more slowly than transmetalation of an aryl group from a neopentyl glycol boronate ester.[43] Consistent with this trend, Pd-catalyzed borylation reactions that form pinacol alkylboronate esters showed no sign of postborylation transmetalation of the alkyl group, while neopentyl glycol alkylboronate esters generated by an analogous process displayed evidence of subsequent transmetalation of the alkyl group. However, with minor modifications, we successfully developed a process to achieve the Pd-catalyzed cross-coupling of alkyl bromides and bis(neopentylglycolato)diboron (**7**) with minimal transmetalation of the generated alkylboronate ester (**8**) (Table 4). Although yields for the reactions were lower than those for the formation of the corresponding pinacol

Table 4. Pd-Catalyzed Borylation of Alkyl Bromides Using Bis(neopentylglycolato)diboron[a]



[a]Alkyl bromide (0.2 mmol), bis(pinacolato)diboron (0.22 mmol); average yield of 2 runs.

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alkylboronate esters, the general success of this reaction underscores the broad utility of our process, and suggests that alkyl boronate compounds may be successfully formed from the Pd-catalyzed cross-coupling reaction of alkyl electrophiles with other diboron reagents.

In conclusion, we have developed a mild process for the Pd-catalyzed borylation of primary alkyl electrophiles using bis(pinacolato)diboron as a boron source. The reaction is highly tolerant of reactive functional groups, requires low catalyst loadings, and accommodates the use of alkyl bromide, iodide, and tosylate electrophiles. Primary bromides react with complete selectivity over secondary bromides. The ability to easily convert the pinacol alkylboronate esters directly into boronic acids, trifluoroboronates, and other boronate esters broadens the utility of this method. Finally, we have demonstrated that our borylation process is not exclusive to the use of bis(pinacolato)diboron as a boron source and can be extended to the use of other diboron reagents.

EXPERIMENTAL SECTION

Toluene and THF (unstabilized) were transferred to separate 20 L solvent-delivery kegs and vigorously purged with argon for 2 h. The solvents were further purified by passing them under argon pressure through two packed columns of neutral alumina (for THF) or through neutral alumina and copper(II) oxide (for toluene). All other reagents and solvents were used as received unless otherwise noted. Flash chromatography was performed using silica gel (ultra pure grade). Nuclear magnetic resonance spectra were recorded on a 500 MHz instrument. All ^{1}H NMR experiments are reported in δ units, parts per million (ppm), and were measured relative to the signals for residual chloroform (7.26 ppm), dimethyl sulfoxide (2.50 ppm) or acetonitrile (1.94 ppm). All ^{13}C NMR spectra are reported in ppm relative to deuterochloroform (77.2 ppm), dimethyl sulfoxide (39.5 ppm) or acetonitrile (118.3 ppm) and were obtained with ^{1}H decoupling. All GC analyses were performed on a gas chromatograph with an FID detector using a 25 m × 0.20 mm capillary column with cross-linked methyl siloxane as the stationary phase.

General Procedure for Borylation of Primary Alkyl Bromides with Bis(pinacolato)diboron. $Pd_2(dba)_3$ (4.6 mg, 0.005 mmol), di-*tert*-butyl(methyl)phosphonium tetrafluoroborate (7.4 mg, 0.03 mmol), $(BPin)_2$ (305 mg, 1.2 mmol) and $K_3PO_4{\cdot}H_2O$ (460 mg, 2 mmol) were weighed out on the benchtop in an oven-dried 10 mL screw top test tube with stir bar. The test tube was sealed using a screw cap lined with a Teflon septum. With stirring begun, the test tube was evacuated (100 mTorr) and backfilled three times with argon using a needle attached to a vacuum manifold. The alkyl bromide (1 mmol) was then added to the test tube via a microsyringe, followed by degassed tertiary butyl alcohol (3 mL) and degassed water (0.25 mL). If the alkyl bromide was a solid, it was weighed out after $K_3PO_4{\cdot}H_2O$ before evacuating the test tube. The test tube was sealed with electrical tape and the reaction mixture was stirred overnight on the benchtop at 60 °C with no additional argon pressure. *N.B.: Ensure that $K_3PO_4{\cdot}H_2O$ does not clump while the* reaction *is in progress. If clumping becomes problematic, K_2CO_3 may be used in place of $K_3PO_4{\cdot}H_2O$.* The reaction mixture was quenched through the addition of saturated aqueous NH_4Cl (5 mL). The resulting mixture was then poured into a separatory funnel and extracted with diethyl ether (3 × 20 mL). The combined organic layers were washed with brine and dried over Na_2SO_4. The crude product was purified by column chromatography.

General Procedure for Borylation of Primary Alkyl Bromides with Bis(neopentylglycolato)diboron. $Pd_2(dba)_3$ (1.83 mg, 0.002 mmol), di-*tert*-butyl(methyl)phosphonium tetrafluoroborate (3 mg, 0.012 mmol), $(BNeop)_2$ (54 mg, 0.24 mmol) and anhydrous K_3PO_4 (85 mg, 0.4 mmol) were weighed out in the glovebox in an oven-dried 10 mL screw top test tube with stir bar. The test tube was sealed using a screw cap lined with a Teflon septum. The reaction was stirred on a stir plate and alkyl bromide (0.2 mmol) was then added to the vial via a microsyringe. Degassed tertiary butyl alcohol (1 mL) and degassed water (20 μL) were then added under argon, outside of the glovebox. The test tube was sealed with electrical tape and the reaction mixture was stirred for 5 h on the benchtop at 80 °C with no additional argon pressure. The reaction mixture was quenched through the addition of saturated aqueous NH_4Cl (ca. 4 mL). The resulting mixture was then poured into a separatory funnel and extracted with diethyl ether (3 × 10 mL). The combined organic layers were washed with brine and dried over Na_2SO_4. The crude product was purified by column chromatography.

*4,4,5,5-Tetramethyl-2-(3-phenylpropyl)-1,3,2-dioxaborolane (**3a**).*[44] The general procedure was employed. A reddish yellow liquid (236 mg, 96%) was isolated by column chromatography (98:2 Hex/Ether). ^{1}H NMR (500 MHz, $CDCl_3$) δ: 7.27 (t, J = 7.5 Hz, 2H), 7.16−7.20 (m, 3H), 2.63 (t, J = 7.5 Hz, 2H), 1.76 (app. quint., J = 7.5 Hz, 2H), 1.26 (s, 12H), 0.85 (t, J = 7.5 Hz, 2H) ppm. ^{13}C NMR (125 MHz, $CDCl_3$) δ: 142.8, 128.6, 128.3, 125.7, 83.0, 38.69, 26.2, 24.9, 11 (B-CH_2, br) ppm. ^{11}B (MHz, $CDCl_3$) δ: 33.3 ppm.

*2-Isopentyl-4,4,5,5-tetramethyl-1,3,2-dioxaborolane (**3b**).*[45] The general procedure was employed. A yellow liquid (147 mg, 74%) was isolated by column chromatography (99:1 Hex/Ether). ^{1}H NMR (500 MHz, $CDCl_3$) δ: 1.45 (m, J = 6.5 Hz, 1H), 1.21−1.3 (m, 2H), 1.23 (s, 12H), 0.84 (d, J = 6.5 Hz, 6H), 0.74 (t, J = 8.5 Hz, 2H) ppm. ^{13}C NMR (125 MHz, $CDCl_3$) δ: 83.0, 33.1, 30.4, 25.0, 22.4 ppm. The carbon atom directly attached to the boron atom was not detected, likely due to quadrupolar broadening. ^{11}B (MHz, $CDCl_3$) δ: 33.3 ppm.

*6-(4,4,5,5-Tetramethyl-1,3,2-dioxaborolan-2-yl)hexan-1-ol (**3c**).*[35] The general procedure was employed. A brownish liquid (139 mg, 61%) was isolated by column chromatography (gradient from 80:20 to 75:25 Hex/EtOAc). ^{1}H NMR (500 MHz, $CDCl_3$) δ: 3.63 (app. q, J = 6.5 Hz, 2H), 1.53−1.59 (m, 2H), 1.38−1.45 (m, 2H), 1.29−1.36 (m, 4H), 1.24 (s, 12H), 0.77 (t, J = 7.5 Hz, 2H) ppm. ^{13}C NMR (125 MHz, CDCl3) δ: 83.0, 63.2, 32.8, 32.2, 25.6, 24.9, 24.0 ppm. The carbon atom directly attached to the boron atom was not detected, likely due to quadrupolar broadening. ^{11}B (MHz, $CDCl_3$) δ: 33.2 ppm.

*4,4,5,5-Tetramethyl-2-(2-(thiophen-2-yl)ethyl)-1,3,2-dioxaborolane (**3d**).*[35] The general procedure was employed. An orange-yellow liquid (149 mg, 63%) was isolated by column chromatography (98:2 Hex/Ether). ^{1}H NMR (500 MHz, $CDCl_3$) δ: 7.08 (dd, J = 5 Hz, 1.5 Hz, 1H), 6.88 (m, 1H), 6.79 (m, 1H), 2.96 (t, J = 8 Hz, 2H), 1.24 (m, 14H), ppm. ^{13}C NMR (125 MHz, CDCl3) δ: 147.9, 126.6, 123.5, 122.7, 83.3, 24.9, 24.5 ppm. The carbon atom directly attached to the boron atom was not detected, likely due to quadrupolar broadening. ^{11}B (MHz, $CDCl_3$) δ: 32.9 ppm.

*6-(4,4,5,5-Tetramethyl-1,3,2-dioxaborolan-2-yl)hexanenitrile (**3e**).*[35] The general procedure was employed. A golden yellow liquid (214 mg, 96%) was isolated by column chromatography (gradient from 95:5 to 93:7 Hex/Ether). ^{1}H NMR (500 MHz, CDCl3) δ: 2.30 (t, J = 7 Hz, 2H), 1.63 (quint., J = 7.0 Hz, 2H), 1.40−1.43 (m, 4H), 1.22 (s, 12H), 0.76 (t, J = 7.0 Hz, 2H) ppm. ^{13}C NMR (125 MHz, $CDCl_3$) δ: 119.9, 83.1, 31.3, 25.2, 24.9, 23.2, 17.1, 11 (B-CH_2, br) ppm. ^{11}B (MHz, $CDCl_3$) δ: 33.1 ppm.

*Ethyl 4-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)butanoate (**3f**).* The general procedure was employed with following modification: The ligand used in this reaction is tricyclohexylphosphonium tetrafluoroborate (11 mg, 0.03 mmol). A bright yellow liquid (215 mg, 89%) was isolated by column chromatography (95:5 Hex/Ether). ^{1}H NMR (500 MHz, CDCl3) δ: 4.10 (q, J = 7 Hz, 2H), 2.31 (t, J = 7.5 Hz, 2H), 1.74 (app. quint., J = 7.5 Hz, 2H), 1.23−1.26 (m, 15H), 0.81 (t, J = 8 Hz, 2H) ppm. ^{13}C NMR (125 MHz, CDCl3) δ: 173.8, 83.1, 60.2, 36.7, 24.8, 19.8, 14.4, 11 (B-CH_2, br) ppm. ^{11}B (MHz, $CDCl_3$) δ: 32.8 ppm. HRMS (EI^+): Calcd ($C_{12}H_{23}BO_4^+$) 242.1689; Found 242.1700.

*2-(2-Cyclohexylethyl)-4,4,5,5-tetramethyl-1,3,2-dioxaborolane (**3g**).*[46] The general procedure was employed with following modifications: $Pd_2(dba)_3$ (14 mg, 0.015 mmol), tricyclohexylphosphonium tetrafluoroborate ligand (33 mg, 0.09 mmol). A pale yellow liquid (198 mg, 83%) was isolated by column chromatography (98:2 Hex/Ether). ^{1}H NMR (500 MHz, $CDCl_3$) δ: 1.61−1.72 (m, 5H), 1.11−1.31 (m, 18H), 0.83 (app. q, J = 12 Hz, 2H), 0.75 (t, J = 8.5 Hz,

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2H) ppm. ^{13}C NMR (125 MHz, $CDCl_3$) δ: 83.0, 40.1, 33.1, 31.5, 26.9, 26.6, 24.9, 20 (B-CH_2, br) ppm. ^{11}B (MHz, $CDCl_3$) δ: 33.4 ppm.

*2-(5-Chloropentyl)-4,4,5,5-tetramethyl-1,3,2-dioxaborolane (**3h**).*[47] The general procedure was employed with following modification: The ligand used in this reaction is tricyclohexylphosphonium tetrafluoroborate (11 mg, 0.03 mmol). A yellowish orange liquid (211 mg, 91%) was isolated by column chromatography (98:2 Hex/Ether) ^{1}H NMR (500 MHz, $CDCl_3$) δ: 3.50 (t, J = 7 Hz, 2H), 1.75 (app. quint., J = 7 Hz, 2H), 1.41 (m, 4H), 1.23 (s, 12H), 0.77 (t, J = 7 Hz, 2H) ppm. ^{13}C NMR (125 MHz, $CDCl_3$) δ: 83.1, 45.2, 32.6, 29.6, 24.9, 23.4, 11 (B-CH_2, br) ppm. ^{11}B (MHz, $CDCl_3$) δ: 32.9 ppm.

*10-(4,4,5,5-Tetramethyl-1,3,2-dioxaborolan-2-yl)decanamide (**3i**).* The general procedure was employed. A white solid (279 mg, 94%) was isolated by column chromatography (95:5 CH_2Cl_2/MeOH). ^{1}H NMR (500 MHz, $CDCl_3$) δ: 5.32 (broad d, 2H), 2.21 (t, J = 7.5 Hz, 2H), 1.60−1.66 (m, 2H), 1.22−1.26 (m, 22H), 0.76 (t, J = 7.5 Hz, 2H) ppm. ^{13}C NMR (125 MHz, $CDCl_3$) δ: 175.6, 83.0, 36.1, 32.6, 29.62, 29.50, 29.46, 29.38, 25.7, 25.0, 24.1 ppm. The carbon atom directly attached to the boron atom was not detected, likely due to quadrupolar broadening. ^{11}B (MHz, $CDCl_3$) δ: 33.7 ppm. Anal. Calcd. for $C_{16}H_{32}BNO_3$: C, 64.65; H, 10.85. Found: C, 64.41; H, 10.99.

*4,4,5,5-Tetramethyl-2-(4-phenoxybutyl)-1,3,2-dioxaborolane (**3j**).*[48] The general procedure was employed. A bright yellow liquid (259 mg, 94%) was isolated by column chromatography (99:1 Hex/Ether). ^{1}H NMR (500 MHz, $CDCl_3$) δ: 7.26 (dt, J = 7.5 Hz, 1 Hz, 2H), 6.88−6.93 (m, 3H), 3.95 (t, J = 6.5 Hz, 2H), 1.80 (quint., J = 6.5 Hz, 2H), 1.59 (quint., J = 8 Hz, 2H), 1.25 (s, 12H), 0.86 (t, J = 8 Hz, 2H) ppm. ^{13}C NMR (125 MHz, $CDCl_3$) δ: 159.3, 129.5, 120.5, 114.6, 83.1, 67.8, 31.9, 25.0, 20.7 ppm. The carbon atom directly attached to the boron atom was not detected, likely due to quadrupolar broadening. ^{11}B (MHz, $CDCl_3$) δ: 33.1 ppm.

*2-(4-(4,4,5,5-Tetramethyl-1,3,2-dioxaborolan-2-yl)butyl)-isoindoline-1,3-dione (**3k**).* The general procedure was employed with following modification: tricyclohexylphosphonium tetrafluoroborate (11 mg, 0.03 mmol) was used as ligand. A brown liquid (260 mg, 79%) was isolated by column chromatography (gradient from 85:15 to 80:20 Hex/Ether). ^{1}H NMR (500 MHz, $CDCl_3$) δ: 7.80 (dd, J = 8.5 Hz, 3 Hz, 2H), 7.67 (dt, J = 8.5 Hz, 2.5 Hz, 2H), 3.64 (t, J = 7.5 Hz, 2H), 1.66 (quint., J = 7.5 Hz, 2H), 1.44 (quint., J = 8 Hz, 2H), 1.20 (s, 12H), 0.79 (t, J = 7.5 Hz, 2H) ppm. ^{13}C NMR (125 MHz, $CDCl_3$) δ: 168.5, 133.9, 132.3, 123.2, 83.1, 38.0, 31.2, 24.9, 21.4, 11 (B-CH_2, br) ppm. ^{11}B (MHz, $CDCl_3$) δ: 33.0 ppm. Anal. Calcd. for $C_{18}H_{24}BNO_4$: C, 65.67; H, 7.35. Found: C, 65.45; H, 7.28.

*2-(4-Bromopentyl)-4,4,5,5-tetramethyl-1,3,2-dioxaborolane (**5**).* The general procedure was employed. A bright-yellow liquid (219 mg, 79%) was isolated by column chromatography (98:2 Hex/Ether). ^{1}H NMR (500 MHz, $CDCl_3$) δ: 4.13 (app. sextet, J = 6.5 Hz, 1H), 1.82−1.90 (m, 1H), 1.73−1.80 (m, 1H), 1.70 (d, J = 7 Hz, 3H), 1.48−1.66 (m, 2H), 1.24 (s, 12H), 0.73−0.84 (m, 2H) ppm. ^{13}C NMR (125 MHz, $CDCl_3$) δ: 83.1, 51.6, 43.8, 26.5, 24.9, 22.3, 10 (B-CH_2, br) ppm. ^{11}B (160 MHz, $CDCl_3$) δ: 33.2 ppm. HRMS (EI^+): Calcd ($C_{11}H_{22}BBrO_2 - CH_3^+$) 261.0661; Found 261.0656.

*Potassium 3-Phenyl-trifluoroboratopropane (**6a**).*[35] The general procedure was employed. A white solid (118 mg, 70%) was isolated. ^{1}H NMR (500 MHz, DMSO) δ: 7.20−7.23 (t, J = 7.5 Hz, 4H), 7.08−7.12 (m, 3H), 2.45 (t, J = 8.0 Hz, 2H), 1.40 (app. quint., J = 7.5 Hz, 2H), 0.02 (m, 2H) ppm. ^{13}C NMR (125 MHz, DMSO) δ: 144.1, 128.3, 127.9, 124.9, 28.25, 28.24, 20 (B-CH_2, br) ppm. ^{11}B (160 MHz, DMSO) δ: 9.3 ppm.

*3-Phenylpropylboronic Acid (**6b**).*[49] The general procedure was employed. A yellowish white solid (109 mg, 89%) was isolated. ^{1}H NMR (500 MHz, DMSO) δ: 7.40 (s, 2H), 7.25 (t, J = 8 Hz, 2H), 7.13−7.16 (m, 3H), 2.50 (m, 2H), 1.60 (app. quint., J = 7.5 Hz, 2H), 0.60 (t, J = 8.0 Hz, 2H) ppm. ^{13}C NMR (125 MHz, CD_3CN) δ: 143.9, 129.4, 129.1, 126.5, 39.2, 27.3 ppm. The carbon atom directly attached to the boron atom was not detected, likely due to quadrupolar broadening. ^{11}B (160 MHz, CD_3CN) δ: 37.0 ppm.

*2-(3-Phenylpropyl)-1,3,2-dioxaborinane (**6c**).*[50] The general procedure was employed. (92 mg, 60%) ^{1}H NMR (500 MHz, CD_3CN) δ: 7.24−7.27 (m, 2H), 7.13−7.18 (m, 3H), 3.95 (t, J = 5.0 Hz, 4H), 2.58 (t, J = 7.5 Hz, 2H), 1.90 (quint., J = 6.0 Hz, 2H), 1.68 (quint., J = 8.0 Hz, 2H), 0.73 (t, J = 8.0 Hz, 2H) ppm. ^{13}C NMR (125 MHz, CD_3CN) δ: 143.1, 128.7, 128.2, 125.6, 61.7, 38.7, 27.5, 26.1, 11 (B-CH_2, br) ppm. ^{11}B (160 MHz, $CDCl_3$) δ: 29.9 ppm.

*5,5-Dimethyl-2-(3-phenylpropyl)-1,3,2-dioxaborinane (**8a**).* The general procedure was employed. A yellowish liquid (32 mg, 70%) was isolated by column chromatography (90:10 Hex/Ether). ^{1}H NMR (500 MHz, CD_3CN) δ: 7.24−7.27 (m, 2H), 7.14−7.19 (m, 3H), 3.57 (s, 4H), 2.60 (t, J = 8 Hz, 2H), 1.70 (app. quint., J = 8 Hz, 2H), 0.95 (s, 6H), 0.76 (t, J = 8 Hz, 2H) ppm. ^{13}C NMR (125 MHz, CD_3CN) δ: 143.1, 128.7, 128.3, 125.6, 72.1, 38.9, 31.8, 29.9, 26.3, 22.0, 15 (B-CH_2, br) ppm. ^{11}B (160 MHz, $CDCl_3$) δ: 29.7 ppm. Anal. Calcd. for $C_{14}H_{21}BO_2$: C, 72.44; H, 9.12. Found: C, 72.45; H, 9.23.

*Ethyl 4-(5,5-Dimethyl-1,3,2-dioxaborinan-2-yl)butanoate (**8b**).* The general procedure was employed. A yellow liquid (28 mg, 62%) was isolated by column chromatography (90:10 Hex/Ether). ^{1}H NMR (500 MHz, CD_3CN) δ: 4.11 (q, J = 7 Hz, 2H), 3.58 (s, 4H), 2.29 (t, J = 7.5 Hz, 2H), 1.70 (app. quint., J = 7.5 Hz, 2H), 1.25 (t, J = 7 Hz, 3H), 0.95 (s, 6H), 0.75 (t, J = 8 Hz, 2H) ppm. ^{13}C NMR (125 MHz, CD_3CN) δ: 174.1, 72.1, 60.2, 36.9, 31.8, 29.8, 22.0, 19.9, 14.4, 14 (B-CH_2, br) ppm. ^{11}B (160 MHz, $CDCl_3$) δ: 29.4 ppm. HRMS (FAB^+): Calcd (for $C_{11}H_{21}BO_4 + H^+$) 229.1611; Found 229.1622.

*6-(5,5-Dimethyl-1,3,2-dioxaborinan-2-yl)hexanenitrile (**8c**).* The general procedure was employed. A yellow liquid (18 mg, 42%) was isolated by column chromatography (90:10 Hex/Ether). ^{1}H NMR (500 MHz, $CDCl_3$) δ: 3.59 (s, 4H), 2.32 (t, J = 7.5 Hz, 2H), 1.65 (app. quint., J = 7 Hz, 2H), 1.37−1.47 (m, 4H), 0.95 (s, 6H), 0.72 (t, J = 8 Hz, 2H) ppm. ^{13}C NMR (125 MHz, $CDCl_3$) δ: 120.1, 72.1, 31.8, 31.4, 29.8, 25.4, 23.3, 22.0, 17.2, 14 (B-CH_2, br) ppm. ^{11}B (160 MHz, $CDCl_3$) δ: 29.4 ppm. HRMS (FAB^+) Calcd (for $C_{11}H_{20}BNO_2 + H^+$) 210.1665; Found 210.1660.

■ ASSOCIATED CONTENT

Ⓢ Supporting Information

^{1}H, ^{13}C, and ^{11}B NMR spectra for all products. 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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