

Chapter 2

Copper(I)-Catalyzed Direct Boryl Substitution of Unactivated Alkyl Halides

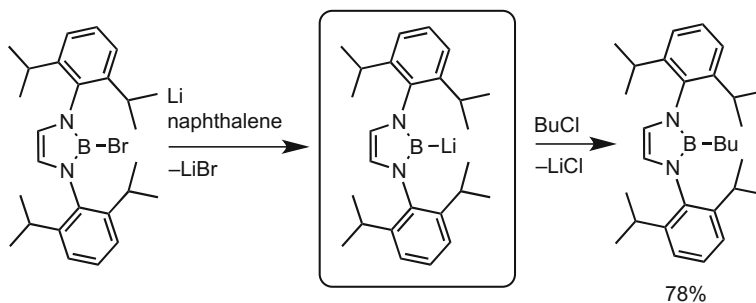
Abstract The borylation substitution of alkyl halides with diboron reagent proceeded in the presence of a copper(I)/Xantphos catalyst and a stoichiometric amount of K(O-*t*-Bu) base. The borylation proceeded with normal and secondary alkyl chlorides, bromides, and iodides, but alkyl sulfonates did not react. Menthyl halides afforded the corresponding borylation product with excellent diastereoselectivity, whereas optically active (*R*)-2-bromo-5-phenylpentane gave a racemic product. The reaction with cyclopropylmethyl bromide resulted in ring-opening products, suggesting that the reaction involves a radical-mediated mechanism.

2.1 Introduction

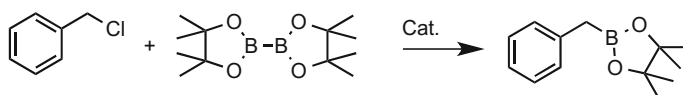
Organoborons are indispensable synthetic reagents in organic synthesis; much effort has therefore been devoted to the development of their efficient preparation [1–39]. Although many attractive and elegant procedures have been reported, direct boryl substitution of alkyl halides is still challenging. In conventional procedures for organoboron synthesis, alkyl halides are the starting materials for the organometallic nucleophiles, such as Grignard or organolithium reagents, which react with boron electrophiles to form a C–B bond. This procedure has significant limitations, especially in the presence of the functional groups often found in structurally complex molecules. Direct borylation of alkyl halides should be quite promising in this respect.

Yamashita and Nozaki recently created a boryllithium species by introducing significant steric hindrance around the boryl atom (Scheme 2.1) [9–12]. Although this species has enough nucleophilicity to react with unactivated alkyl halides, this elaborate reaction is not suitable for many common organic syntheses.

Miyaura and Marder also reported boryl substitutions of activated alkyl halides such as allyl and benzyl chlorides using a palladium and a copper catalysis, respectively; however, there are no general borylation procedures for unactivated alkyl halides (Scheme 2.2) [1–5, 24, 25, 35].



Scheme 2.1 Synthesis of boryllithium: reactivity as a boryl anion



with Pd cat./KOAc: Miyaura and Ishiyama (2002), 85%
 with Cu cat./K(O-*t*-Bu): T. B. Marder (2009), 61%

Scheme 2.2 Transition-metal-catalyzed boryl substitution of activated alkyl halides

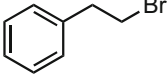
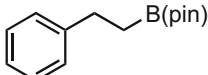
The author reports here the first practical method for boryl substitution that is applicable to a broad range of alkyl halides with various functional groups, offering a direct umpolung pathway for conventional reactions based on carbon nucleophiles generated from alkyl halides.

2.2 Results and Discussion

Recent advances in copper(I)-catalyzed reactions with diboron derivatives [13–39] enable introduction of boryl groups into various organic electrophiles such as $\alpha\beta$ -unsaturated carbonyl compounds [13, 24–32] allylic esters [14, 15, 18, 19, 33, 34], aryl halides [35], allyl and benzyl halides [24, 25, 35], and other substrates [16, 20–23, 36–39]. The author did not anticipate that unactivated alkyl halides could afford boron compounds by copper(I)-catalyzed borylation because previous studies found that alkyl sulfonates, which are good substrates for nucleophilic substitutions, were resistant to direct boryl substitution [20, 40].

In the course of the study, the author accidentally found that an alkyl halide reacted with a diboron compound to produce the corresponding alkylboronate in the presence of a copper(I) catalyst, which is very similar to those our group previously reported [14, 20]. As shown in Table 2.1, entry 1, the reaction between 2-phenylethyl bromide **1a** and bis(pinacolato)diboron **2** proceeded smoothly in the presence of a CuCl/Xantphos catalyst (3 mol%) and a stoichiometric amount of K

Table 2.1 Studies of reaction conditions for copper(I)-catalyzed boryl substitution of alkyl halides **1a**^a

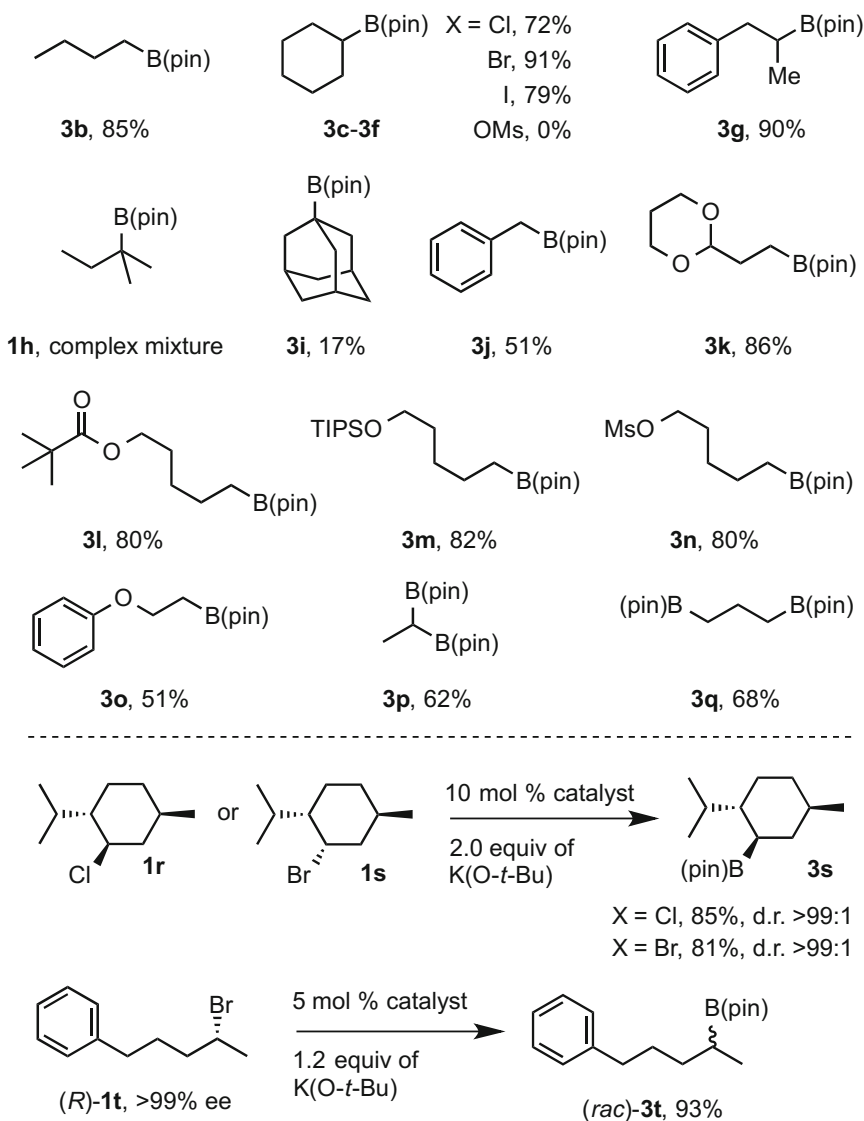
 1a 3 mol % CuCl 3 mol % Xantphos B₂(pin)₂ 2 (1.2 equiv) base (1.0 equiv) THF, rt, 4 h →  3a				
Entry	CuX	Ligand	Base	Yield (%) ^b
1	CuCl	Xantphos	K(O- <i>t</i> -Bu)	94
2	CuCl	Xantphos	none	0
3	none	Xantphos	K(O- <i>t</i> -Bu)	0
4	CuCl	None	K(O- <i>t</i> -Bu)	2
5	CuCl	PPh ₃	K(O- <i>t</i> -Bu)	69
6	CuCl	dppe	K(O- <i>t</i> -Bu)	73
7	CuCl	dppp	K(O- <i>t</i> -Bu)	79
8	CuCl	dppb	K(O- <i>t</i> -Bu)	65
9	CuCl	dppf	K(O- <i>t</i> -Bu)	74
10	CuClIPr		K(O- <i>t</i> -Bu)	13
11	Cu(O- <i>t</i> -Bu)/10 mol%	Xantphos/10 mol%	None	3
12	Cu(O- <i>t</i> -Bu)/100 mol%	Xantphos/10 mol%	None	2
13	CuI	Xantphos	K(O- <i>t</i> -Bu)	70
14	CuCN	Xantphos	K(O- <i>t</i> -Bu)	47
15	Cu(OAc) ₂	Xantphos	K(O- <i>t</i> -Bu)	88
16	CuCl/1 mol%	Xantphos/1 mol%	K(O- <i>t</i> -Bu)	96

^aConditions: **1a** (0.5 mmol), CuX (0.015 mmol), ligand (0.015 mmol), K(O-*t*-Bu)/THF (1.0 M, 0.5 mL), **2** (0.6 mmol)

^bYield was determined by GC analysis of crude mixture with an internal standard

^cCuClIPr: chloro [1,3-bis(2,6-diisopropylphenyl)-imidazole-2-ylidene]copper(I)

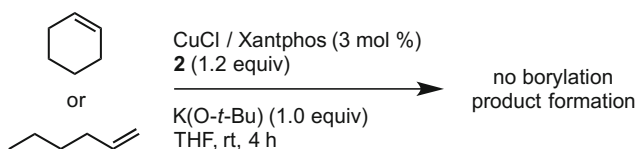
(O-*t*-Bu) base (1.0 equiv). The reaction was complete within 4 h at room temperature and produced the corresponding boronate **3a** in high yield (94%) without any side-product detection (Table 2.1, entry 1). This catalysis requires a K(O-*t*-Bu) base, a copper(I) salt, and a ligand, for the reaction to proceed (entries 2–4). Xantphos provided the best result among the phosphine ligands tested; the reactions with PPh₃, dppe, dppp, dppb, and dppf were slow and incomplete, resulting in moderate yields of the product, even after long reaction times (entries 5–9). Use of a copper(I)/NHC (NHC: *N*-heterocyclic carbene) catalyst gave a much slower initial reaction rate (entry 10). When a catalytic or stoichiometric amount of Cu(O-*t*-Bu) was used instead of a CuCl/K(O-*t*-Bu) combination, only trace amounts of the product were observed (entries 11 and 12). CuI, CuCN, and Cu(OAc)₂ can be used, but longer reaction times were required (entries 13–15) [41]. A lower catalyst loading of 1 mol% also gave an excellent result (96%, 4 h, entry 16).

Table 2.2 Substrate scope

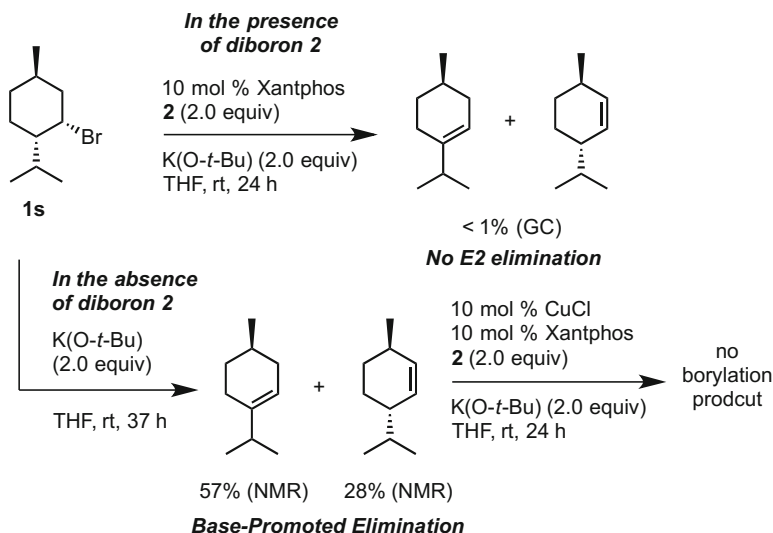
This reaction was then evaluated for various alkyl halides, as summarized in Table 2.2. Unactivated primary and secondary alkyl halides were converted to the corresponding alkylboronates in good yield (entries 1–6). The effects of the leaving group were investigated with cyclohexyl substrates (entries 2–5). Reaction of cyclohexyl bromide **1d** gave the borylation product **3c** in the highest yield, with a

short reaction time (91%, 5 h), among cyclohexyl chloride **1c** and bromide **1e** (72%, 18 h; 79%, 48 h, respectively). In contrast, cyclohexyl mesylate **1f** did not react (entry 5). This inactivity is consistent with our previous studies of related mesylate substrates [20]. The reactions of tertiary alkyl halides **1h** and **1i** were quite sluggish (entries 7 and 8). An activated alkyl halide, benzyl bromide **1j**, also gave the desired product in moderate yield, accompanied by a small amount of a homo-coupling side-product (1,2-diphenylethane, 9%) [35]. This reaction proceeded in the presence of various functional groups; acetal (**1k**), ester (**1l**), silyl ether (**1m**), and sulfonate (**1n**) were compatible under these reaction conditions (entries 9–14). Alkylboronates bearing a beta-alkoxy group were not accessible by Grignard or organolithium methods because the corresponding organometallic compounds with a beta-alkoxy group could not be easily prepared because they readily undergo beta-alkoxy elimination. This method enables direct conversion of alkyl halide **1o** to **3o** (entry 14). Reactions of 1,1- and 1,3-dibromo compounds proceeded smoothly to produce the corresponding bis-boryl products (entries 14 and 15). (1*R*,2*R*,4*R*)-Menthyl boronate **3r** was synthesized with excellent diastereoselectivity (> 99:1) from both (1*S*,2*R*,5*R*)-menthyl chloride **1r** and (1*S*,2*S*,4*R*)-neomenthyl bromide **1s** (entries 16 and 17, 85% and 81%, respectively). The reaction of the optically active secondary alkyl halide (*R*)-**1t** afforded the racemic product **3t** (entry 19). These results indicate that the stereocenter originating from the chiral C(sp³)-X bond undergoes rapid interconversion of configuration during the reaction. This may cause epimerization to a thermodynamically stable product (entries 17 and 18) and complete racemization (entry 19). This is quite different from the results of our previous studies on copper(I)-catalyzed substitution of acyclic allylic carbonates with diboron, where the *anti*-S_N2' reaction proceeded with high stereospecificity [14, 42–46].

This reaction does not include base-promoted elimination/alkene hydroboration pathway. The following experiments exclude this mechanism. (1) Alkenes did not undergo hydroboration under the reaction conditions presented in Table 2.1 and 2.2 (Schemes 2.3 and 2.4). (2) Base-promoted elimination of alkylhalides proceeded quickly in the presence of *t*-BuOK; however, by addition of **2**, base-promoted elimination was completely inhibited (Scheme 2.4). Complexation of *t*-BuOK and Lewis acidic **2** would reduce the basicity of *t*-BuOK significantly. (3) Our boryl substitution of secondary alkyl halides was regiospecific (Table 2.2, entries 6, 17, 18, and 19). However, elimination products of secondary alkyl halides should give regioisomers in term of double bond (Scheme 2.4). It is difficult to assume product convergence in hydroboration of regio isomeric alkenes. In addition, the



Scheme 2.3 Attempts of copper(I)-catalyzed hydroboration of alkenes with diboron **2**

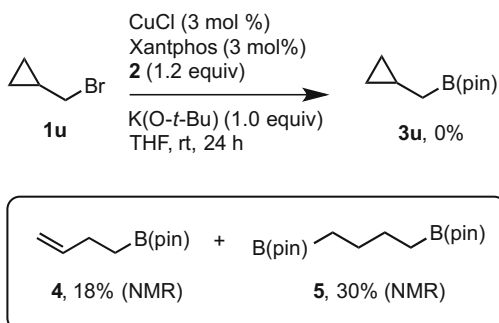


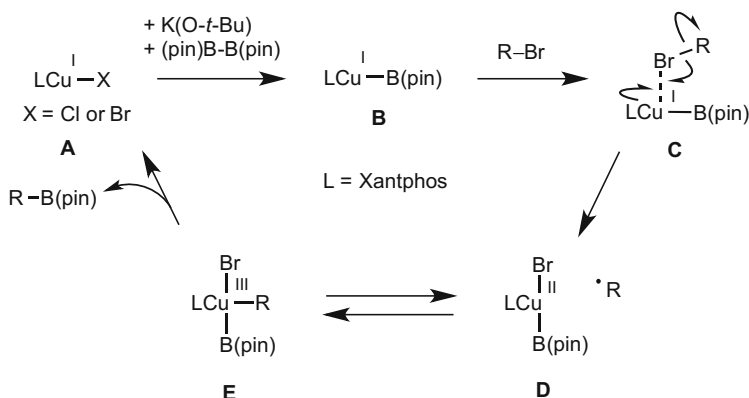
Scheme 2.4 Experiments for exclusion of elimination/hydroboration pathway of **1s**

base-promoted elimination products from **1s** did not undergo hydroboration under the conditions for our copper(I)-catalyzed boryl substitution of alkyl halides (Scheme 2.4).

In order to probe the reaction mechanism further, the author also carried out the copper(I)-catalyzed borylation of cyclopropylmethyl bromide (**1u**), as illustrated in Scheme 2.5. 3-Butenylboronate **4** (18%) and bis-boryl product **5** (30%), which could be derived from **4** through further borylation of the terminal double bond, were found in the reaction mixture, but the simple boryl substitution product **3u** was not detected. The formation of the ring-opening products suggests that this reaction could include a radical pathway; this assumption is not inconsistent with the stereochemical outcomes observed in entries 17–19, Table 2.2 [47–50].

Scheme 2.5 Copper(I)/xantphos-catalyzed borylation of cyclopropylmethyl bromide (**1u**)





Scheme 2.6 Proposed reaction mechanism

The proposed reaction mechanism of the current borylation reaction is shown in Scheme 2.6. First, copper(I) salt **A** reacts with K(O-*t*-Bu) base and a diboron compound to form active species **B**. The single electron transfer between a borylcopper(I) and alkylhalide occurs to generate copper(II) intermediate **D** and alkyl radical species. Further single electron transfer proceeds to give the copper (III) complex **E** and then subsequent reductive elimination provides the corresponding boryl substituted product and copper(I) halide **A**.

2.3 Summary

In summary, the author has developed a novel copper(I)-catalyzed reaction as the first practical procedure for boryl substitution of unactivated alkyl halides [51]. This reaction offers a direct umpolung pathway for the conventional carbon nucleophile method, and has high functional group compatibility and interesting stereochemical-controlling properties. The author believes that this procedure will be a powerful synthetic method for a broad range of alkylboronates, including those that could not be synthesized by previous methods.

2.4 Experimental

2.4.1 General

Materials were obtained from commercial suppliers and purified by the standard procedure unless otherwise noted. Solvents were purchased from commercial suppliers, degassed via three freeze-pump-thaw cycles, and further dried on MS 4A.

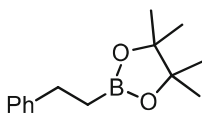
NMR spectra were recorded on JEOL JNM-ECX400P spectrometer (^1H : 400 MHz and ^{13}C : 100 MHz) Tetramethylsilane (^1H) and CDCl_3 (^{13}C) were employed as external standards, respectively. CuCl (ReagentPlus® grade, 224332-25G, $\geq 99\%$) and $\text{K}(\text{O}-t\text{-Bu})/\text{THF}$ (1.0 M, 328650-50ML) were purchased from Sigma-Aldrich Co. and used as received. Mesitylene or 1,1,2,2-tetrachloroethane was used as the internal standard for determining NMR yield. GLC analysis was conducted with Shimadzu GC-2014 or GC-2025 equipped with ULBON HR-1 glass capillary column (Shinwa Chemical Industries) and a FID detector HPLC analyses with chiral stationary phase were carried out using Hitachi LaChrome Elite HPLC system with L-2400 UV detector. Recycle preparative gel permeation chromatography was conducted with JAI LC-9101 using CHCl_3 as the eluent. Low- and high-resolution mass spectra were recorded at the Center for Instrumental Analysis, Hokkaido University.

2.4.2 Starting Materials

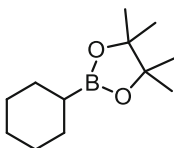
1f and **1n** were prepared from the corresponding alcohols and methanesulfonyl chloride by a standard procedure. **1l** and **1m** were synthesized from the 5-bromopentanol by standard esterification and silylation procedures. **1s** was synthesized by bromination of (–)-menthol with $\text{CBr}_4/\text{PPh}_3$ reagents [52]. Other alkyl halide substrates were purchased from commercial suppliers. The purchased starting materials were not subjected to further purification but dried over MS4A before use.

2.4.3 Representative Procedure for Borylation

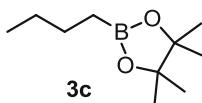
Copper chloride (1.5 mg, 0.015 mmol) and bis(pinacolato)diboron (152.4 mg, 0.6 mmol), Xantphos (8.7 mg, 0.015 mmol) were placed in an oven-dried reaction vial. The vial was sealed with a screw cap containing a Teflon-coated rubber septum. The vial was connected to a vacuum/nitrogen manifold through a needle, evacuated and backfilled with nitrogen. THF (0.5 mmol) and $\text{K}(\text{O}-t\text{-Bu})/\text{THF}$ (1.0 M, 0.25 mL, 0.25 mmol) were added in the vial through the rubber septum. Then alkyl halide **1** (0.5 mmol) was added dropwise. After the reaction was complete, the reaction mixture was passed through a short silica column eluting with ethyl acetate/hexane (10:90). The crude mixture was further purified by flash column chromatography (SiO_2 , ethyl acetate/hexane, 0.5:99.5–2.5:97.5). The flash column chromatography is completed within 10 min. to minimize decomposition of the product.

2.4.3.1 4,4,5,5-Tetramethyl-2-phenethyl-1,3,2-dioxaborolane (3a) [53]**3a**

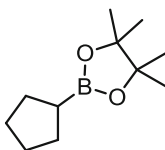
^1H NMR (400 MHz, CDCl_3 , δ): 1.14 (t, $J = 8.2$ Hz, 2H), 1.22 (s, 12H), 2.75 (t, $J = 8.4$ Hz, 2H), 7.13–7.29 (m, 5H). ^{13}C NMR (100 MHz, CDCl_3 , δ): 13.0 (br, B–CH₂), 24.7 (CH₃), 29.9 (CH₂), 83.0 (C), 125.4 (CH), 127.9 (CH), 128.1 (CH), 144.3 (C). HRMS–EI (m/z): $[\text{M}]^+$ calcd for $\text{C}_{14}\text{H}_{21}\text{BO}_2$, 232.1636; found, 232.1635. Anal. Calcd for $\text{C}_{14}\text{H}_{21}\text{BO}_2$: C, 72.44; H, 9.12. Found: C, 72.68; H, 9.31.

2.4.3.2 4,4,5,5-Tetramethyl-2-cyclohexyl-1,3,2-dioxaborolane (3b) [54]**3b**

^1H NMR (400 MHz, CDCl_3 , δ): 0.94–1.05 (m, 1H), 1.24 (s, 12H), 1.25–1.39 (m, 4H), 1.59–1.67 (m, 6H). ^{13}C NMR (100 MHz, CDCl_3 , δ): 22.0 (br, B–CH₂), 24.7 (CH₃), 26.7 (CH₂), 27.1 (CH₂), 27.9 (CH₂), 82.6 (C). HRMS–EI (m/z): $[\text{M}]^+$ calcd for $\text{C}_{12}\text{H}_{23}\text{BO}_2$, 210.1791; found, 210.1802.

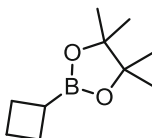
2.4.3.3 4,4,5,5-Tetramethyl-2-butyl-1,3,2-dioxaborolane (3c) [55]**3c**

^1H NMR (400 MHz, CDCl_3 , δ): 0.78 (t, $J = 7.8$ Hz, 2H), 0.88 (t, $J = 7.3$ Hz, 3H), 1.24 (s, 12H), 1.28–1.43 (m, 4H). ^{13}C NMR (100 MHz, CDCl_3 , δ): 10.5 (br, B–CH₂), 13.8 (CH₃), 24.7 (CH₃), 25.4 (CH₂), 26.2 (CH₂), 82.8 (C). HRMS–EI (m/z): $[\text{M}]^+$ calcd for $\text{C}_{10}\text{H}_{21}\text{BO}_2$, 184.1635; found, 184.1644.

2.4.3.4 2-cyclopentyl-4,4,5,5-tetramethyl-1,3,2-dioxaborolane (3d)**3d**

^1H NMR (400 MHz, CDCl_3 , δ): 1.13-1.19 (m, 1H), 1.24 (s, 12H), 1.40-1.54 (m, 4H), 1.58-1.64 (m, 2H), 1.71-1.80 (m, 2H). ^{13}C NMR (100 MHz, CDCl_3 , δ): 21.8 (br, B-CH), 24.6 (CH₃), 26.8 (CH₂), 28.4 (CH₂), 82.7 (C). HRMS-EI (m/z): $[\text{M}-\text{CH}_3]^+$ calcd for $\text{C}_{10}\text{H}_{18}\text{BO}_2$, 181.13998; found, 181.13998.

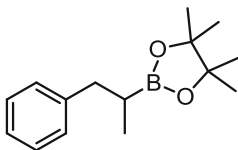
2.4.3.5 2-cyclobutyl-4,4,5,5-tetramethyl-1,3,2-dioxaborolane (3e)



3e

^1H NMR (400 MHz, CDCl_3 , δ): 1.26 (s, 12H), 1.88-2.12 (m, 7H). ^{13}C NMR (100 MHz, CDCl_3 , δ): 17.9 (br, B-CH), 22.6 (CH₂), 23.8 (CH₂), 24.7 (CH₃), 82.8 (C). HRMS-EI (m/z): $[\text{M}-\text{CH}_3]^+$ calcd for $\text{C}_9\text{H}_{16}\text{BO}_2$, 167.12422; found, 167.12445.

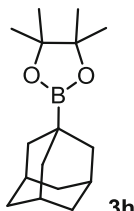
2.4.3.6 4,4,5,5-Tetramethyl-2-(2-phenylpropan-2-yl)-1,3,2-dioxaborolane (3f) [56]



3f

^1H NMR (400 MHz, CDCl_3 , δ): 0.96 (d, $J = 7.3$ Hz, 3H), 1.19 (s, 12H), 1.37 (q, $J = 7.8$ Hz, 1H), 2.54 (dd, $J = 8.7$ and 13.7 Hz, 1H), 2.81 (dd, $J = 7.8$ and 13.7 Hz, 1H), 7.13-7.26 (m, 5H). ^{13}C NMR (100 MHz, CDCl_3 , δ): 15.1 (CH₃), 19.5 (br, B-CH), 24.6 (CH₃), 38.9 (CH₂), 82.9 (C), 125.5 (CH), 127.9 (CH), 128.8 (CH), 142.2 (C). HRMS-EI (m/z): $[\text{M}]^+$ calcd for $\text{C}_{15}\text{H}_{23}\text{BO}_2$, 246.1791; found, 246.1791.

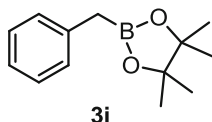
2.4.3.7 2-Adamantyl-4,4,5,5-tetramethyl-1,3,2-dioxaborolane (3h)



3h

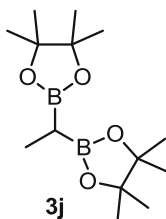
^1H NMR (400 MHz, CDCl_3 , δ): 1.21 (s, 12H), 1.73–1.77 (br, 12H), 1.82–1.87 (br, 3H). ^{13}C NMR (100 MHz, CDCl_3 , δ): 24.6 (CH₃), 27.5 (CH), 37.5 (CH₂), 37.9 (CH₂), 82.6 (C). The carbon directly attached to the boron atom was not detected, likely due to quadropolar relaxation. HRMS–EI (m/z): $[\text{M}]^+$ calcd for $\text{C}_{16}\text{H}_{27}\text{BO}_2$, 262.2104; found, 262.2109.

2.4.3.8 2-Benzyl-4,4,5,5-tetramethyl-1,3,2-dioxaborolane (3i). [57]



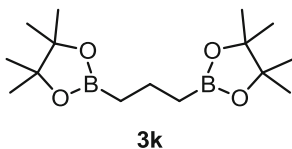
^1H NMR (400 MHz, CDCl_3 , δ): 1.23 (s, 12H), 2.29 (s, 2H), 7.09–7.25 (m, 5H). ^{13}C NMR (100 MHz, CDCl_3 , δ): 20.0 (br, B–CH₂), 24.7 (CH₃), 83.3 (C), 124.8 (CH), 128.2 (CH), 128.9 (CH), 138.6 (C). HRMS–EI (m/z): $[\text{M}]^+$ calcd for $\text{C}_{13}\text{H}_{19}\text{BO}_2$, 218.1478; found, 218.1478.

2.4.3.9 1,1-Bis(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)ethane (3j) [58]



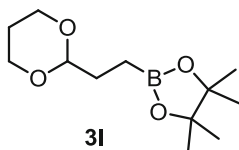
^1H NMR (400 MHz, CDCl_3 , δ): 0.73 (q, $J = 7.4$ Hz, 1H), 1.05 (d, $J = 7.7$ Hz, 3H), 1.227 (s, 12H), 1.234 (s, 12H). ^{13}C NMR (100 MHz, CDCl_3 , δ): 0.2 (br, B–CH₂), 9.0 (CH₃), 24.5 (CH₃), 24.5 (CH₃), 82.8 (C). HRMS–EI (m/z): $[\text{M}]^+$ calcd for $\text{C}_{14}\text{H}_{28}\text{B}_2\text{NaO}_4$, 305.2067; found, 305.2066.

2.4.3.10 1,1-Bis(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)propane (3k)



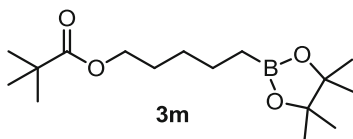
^1H NMR (400 MHz, CDCl_3 , δ): 0.81 (t, $J = 8.1$ Hz, 4H), 1.24 (s, 24H), 1.54 (quint, $J = 8.1$ Hz, 2H). ^{13}C NMR (100 MHz, CDCl_3 , δ): 14.0 (br, B–CH₂), 18.5 (CH₂), 24.7 (CH₃), 82.7 (C). HRMS–EI (m/z): $[\text{M} + \text{Na}]^+$ calcd for $\text{C}_{15}\text{H}_{30}\text{B}_2\text{NaO}_4$, 319.2228; found, 319.2223.

2.4.3.11 2-(2-(1,3-Dioxan-2-yl)ethyl)-4,4,5,5-tetramethyl-1,3,2-dioxaborolane (3l)



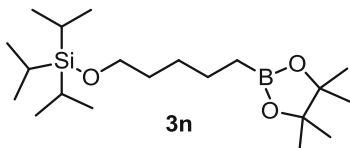
^1H NMR (400 MHz, CDCl_3 , δ): 0.83 (t, $J = 7.9$ Hz, 2H), 1.23 (s, 12H), 1.28–1.36 (m, 1H), 1.72 (dt, $J = 7.7$ and 5.1 Hz, 2H), 2.00–2.12 (m, 1H), 3.774 (m, 2H), 4.1 (m, 2H), 4.47 (t, $J = 5.1$ Hz, 1H). ^{13}C NMR (100 MHz, CDCl_3 , δ): 5.3 (br, B–CH₂), 24.6 (CH₃), 25.7 (CH₂), 29.3 (CH₂), 66.6 (CH₂), 82.7 (C), 102.9 (CH). HRMS–EI (m/z): $[\text{M} - \text{H}]^+$ calcd for $\text{C}_{12}\text{H}_{22}\text{BO}_4$, 241.1611; found, 241.1619. Anal. Calcd for $\text{C}_{12}\text{H}_{23}\text{BO}_4$: C, 59.53; H, 9.57. Found: C, 59.77; H, 9.67.

2.4.3.12 5-(4,4,5,5-Tetramethyl-1,3,2-dioxaborolan-2-yl)pentyl pivalate (3m)

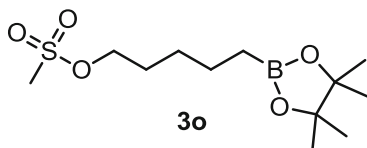


^1H NMR (400 MHz, CDCl_3 , δ): 0.79 (t, $J = 7.7$ Hz, 2H), 1.19 (s, 9H), 1.24 (s, 12H), 1.32–1.49 (m, 4H), 1.59–1.66 (m, 2H), 4.04 (t, $J = 6.8$ Hz, 2H). ^{13}C NMR (100 MHz, CDCl_3 , δ): 10.5 (br, B–CH₂), 23.5 (CH₂), 24.7 (CH₃), 27.1 (CH₃), 28.3 (CH₂), 28.5 (CH₂), 38.5 (C), 64.3 (CH₂), 82.7 (C), 178.4 (C). HRMS–EI (m/z): $[\text{M}]^+$ calcd for $\text{C}_{16}\text{H}_{31}\text{BNaO}_4$, 321.2208; found, 321.2208.

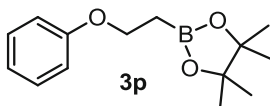
2.4.3.13 4,4,5,5-Tetramethyl-5-tri(isopropyl)silyloxy-1,3,2-dioxaborolane (3n)



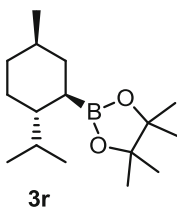
^1H NMR (400 MHz, CDCl_3 , δ): 0.78 (t, $J = 7.9$ Hz, 2H), 1.02–1.13 (m, 21H), 1.24 (s, 12H), 1.30–1.47 (m, 4H), 1.50–1.59 (m, 1H), 3.66 (t, $J = 6.9$ Hz, 2H). ^{13}C NMR (100 MHz, CDCl_3 , δ): 11.1 (br, B–CH₂), 11.9 (CH), 18.0 (CH₃), 23.9 (CH₂), 24.7 (CH₃), 28.6 (CH₂), 32.9 (CH₂), 63.5 (CH₂), 82.8 (C). HRMS–EI (m/z): $[\text{M} - \text{CH}_3]^+$ calcd for $\text{C}_{19}\text{H}_{40}\text{BO}_3\text{Si}$, 355.2840; found, 355.2843. Anal. Calcd for $\text{C}_{20}\text{H}_{43}\text{BO}_3\text{Si}$: C, 64.84; H, 11.70. Found: C, 64.66; H, 11.88.

2.4.3.14 5-(4,4,5,5-Tetramethyl-1,3,2-dioxaborolan-2-yl)pentyl methanesulfonate (3o)


^1H NMR (400 MHz, CDCl_3 , δ): 0.79 (t, $J = 7.5$ Hz, 2H), 1.23 (s, 12H), 1.34–1.48 (m, 4H), 1.75 (quint, $J = 7.1$ Hz, 2H), 3.00 (s, 3H), 4.20 (t, $J = 6.8$ Hz, 2H). ^{13}C NMR (100 MHz, CDCl_3 , δ): 10.9 (br, B–CH₂), 23.3 (CH₂), 24.7 (CH₃), 27.8 (CH₂), 28.7 (CH₂), 37.2 (CH₃), 70.1 (CH₂), 82.8 (C). HRMS–EI (m/z): $[\text{M} + \text{Na}]^+$ calcd for $\text{C}_{12}\text{H}_{25}\text{BNaO}_5\text{S}$, 315.1413; found, 315.1408. Anal. Calcd for $\text{C}_{12}\text{H}_{25}\text{BO}_5\text{S}$: C, 49.33; H, 8.62. Found: C, 49.35; H, 8.64.

2.4.3.15 4,4,5,5-Tetramethyl-2-(2-phenoxyethyl)-1,3,2-dioxaborolane (3p)


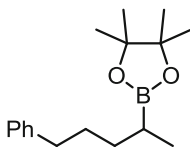
^1H NMR (400 MHz, CDCl_3 , δ): 1.26 (s, 12H), 1.37 (t, $J = 7.9$ Hz, 2H), 4.11 (t, $J = 8.0$ Hz, 2H), 6.89–6.94 (m, 3H), 7.24–7.29 (m, 2H). ^{13}C NMR (100 MHz, CDCl_3 , δ): 12.3 (br, B–CH₂), 24.7 (CH₃), 64.7 (CH₂), 83.3 (C), 114.5 (CH), 120.3 (CH), 129.3 (CH), 159.0 (C). HRMS–EI (m/z): $[\text{M}]^+$ calcd for $\text{C}_{14}\text{H}_{21}\text{BO}_3$, 248.1584; found, 248.1579.

2.4.3.16 2-[(1*R*,2*R*,5*R*)-2-Isopropyl-5-methylcyclohexyl]-4,4,5,5-tetramethyl-1,3,2-dioxaborolane (3r)


^1H NMR (400 MHz, CDCl_3 , δ): 0.72–1.00 (m, 4H), 0.77 (d, $J = 6.9$ Hz, 3H), 0.84 (d, $J = 6.9$ Hz, 3H), 0.90 (d, $J = 6.9$ Hz, 3H), 1.21–1.32 (m, 14H), 1.56–1.72 (m, 4H). ^{13}C NMR (100 MHz, CDCl_3 , δ): 16.4 (CH₃), 21.6 (CH₃), 22.7 (CH₃), 24.6 (CH₃), 24.7 (CH₃), 25.8 (CH₂), 28.0 (br, B–CH), 32.0 (CH), 33.4 (CH), 35.3 (CH₂), 37.1 (CH₂), 43.7 (CH), 82.6 (C). HRMS–EI (m/z): $[\text{M}]^+$ calcd for

C₁₆H₃₁BO₂, 266.2417; found, 266.2415. Anal. Calcd for C₁₆H₃₁BO₂: C, 72.18; H, 11.74. Found: C, 72.31; H, 11.74. [α]_D^{20.5} -2.00 (deg cm³ g⁻¹ dm⁻¹) (c 0.0583 in CHCl₃).

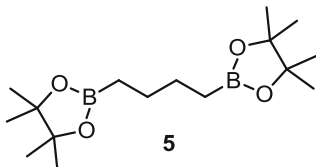
2.4.3.17 4,4,5,5-Tetramethyl-2-(5-phenylpentan-2-yl)-1,3,2-dioxaborolane (3t)



3t

¹H NMR (400 MHz, CDCl₃, δ): 0.96 (d, J = 7.0 Hz, 3H), 1.00–1.09 (m, 1H), 1.23 (s, 12H), 1.30–1.39 (m, 1H), 1.47–1.56 (m, 1H), 1.59–1.69 (m, 2H), 2.60 (t, J = 7.9 Hz, 2H), 7.14–7.18 (m, 3H), 7.25–7.28 (m, 2H). ¹³C NMR (100 MHz, CDCl₃, δ): 15.4 (CH₃), 16.8 (br, B–CH), 24.6 (CH₃), 24.7 (CH₃), 30.8 (CH₂), 32.9 (CH₂), 36.1 (CH₂), 82.7 (C), 125.4 (CH), 128.1 (CH), 128.3 (CH), 142.8 (C). HRMS–EI (m/z): [M]⁺ calcd for C₁₇H₂₇BO₂, 274.2104; found, 274.2104.

2.4.3.18 1,4-Bis(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)butane (5)



5

¹H NMR (400 MHz, CDCl₃, δ): 0.77 (t, J = 7.3 Hz, 4H), 1.24 (s, 24H), 1.39–1.42 (m, 4H). ¹³C NMR (100 MHz, CDCl₃, δ): 10.8 (br, B–CH₂), 24.8 (CH₃), 26.9 (CH₂), 82.8 (C). [M–CH₃]⁺ calcd for C₁₅H₂₉B₂O₄, 295.2252; found, 293.2250.

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