Author/s:
Churches, QI;Hooper, JF;Hutton, CA

Title:
A general method for interconversion of boronic acid protecting groups: Trifluoroborates as common intermediates

Date:
2015-06-05

Citation:
Churches, Q. I., Hooper, J. F. & Hutton, C. A. (2015). A general method for interconversion of boronic acid protecting groups: Trifluoroborates as common intermediates. Journal of Organic Chemistry, 80 (11), pp.5428-5435. https://doi.org/10.1021/acs.joc.5b00182.

Persistent Link:
https://hdl.handle.net/11343/57418

A General Method for Interconversion of Boronic Acid Protecting Groups: Trifluoroborates as Common Intermediates

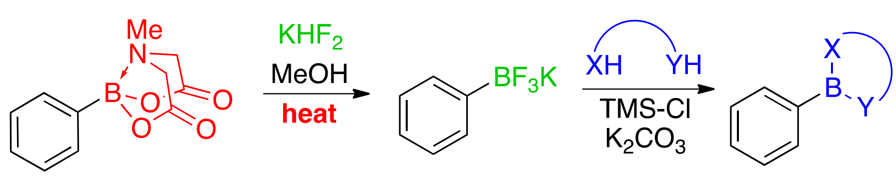
Quentin I. Churches,[†,‡] *Joel F. Hooper*[†] *and Craig A. Hutton*[*,†]

[†] School of Chemistry and Bio21 Molecular Science and Biotechnology Institute, University of Melbourne, Parkville, VIC 3010, Australia

[‡] CSIRO Materials Science and Engineering, Clayton, VIC 3168, Australia

chutton@unimelb.edu.au

ABSTRACT: We have developed a general protocol for the interconversion of diverse protected boronic acids, via intermediate organotrifluoroborates. *N*-Methyliminodiacetyl boronates, which have been hitherto resistant to direct conversion to trifluoroborates, have been shown to undergo fluorolysis at elevated temperatures. Subsequent solvolysis of organotrifluoroborates in the presence of trimethylsilyl chloride and a wide range of bis-nucleophiles enables the generation of a variety of protected boronic acids.



INTRODUCTION

The utility of organoboron compounds in organic synthesis has flourished in recent years,[1] particularly through developments in the Suzuki–Miyaura coupling. Boronic acids are also extremely valuable substrates for other metal-catalyzed reactions,[2] the Petasis reaction,[3] and the iterative synthesis of polyene natural products.[4,5a]

Free boronic acids are often unstable, difficult to handle, or are prone to dehydration to give the corresponding boroxine.[1,4d] Bulky boronate esters such as pinacolyl and hexyleneglycolyl boronate esters have been used extensively as 'blocking' groups that reduce the reactivity of the organoboronate through steric effects.[5b] More recently, true 'protecting' groups for boronic acids have been introduced that modulate reactivity through both steric and electronic effects. Suginome developed the diaminonaphthalenyl (dan) group that diminishes the reactivity of an organoboron compound toward metal-catalyzed cross-couplings.[6] Burke developed the *N*-methyliminodiacetyl (mida) group as a boronic acid protecting group that similarly renders the organoboron unreactive toward cross-coupling reactions.[7] Both the B(dan) and B(mida) protecting groups require removal to regenerate the boronic acid to re-establish reactivity of the organoboron in cross-coupling reactions.

To function as useful protecting groups, the B(dan), B(mida) and other boronate systems must be able to be introduced and removed under mild conditions, preferably in an orthogonal manner. The B(mida) and B(dan) protecting groups employ orthogonal deprotection strategies – mild base[4e] and acid,[6c] respectively. However, problems frequently arise in the introduction of these protecting groups, such as the requirement of high temperatures and long reaction times,[4c] the generation of highly reactive dibromoborane intermediates,[4e] and low yields or conversion efficiency.

Organotrifluoroborate salts, extensively investigated by Molander,[7] have also been used as protecting groups for boronic acids. Organotrifluoroborates are generally easily handled, stable crystalline solids. In the absence of protic solvents they have limited reactivity, though they are readily hydrolyzed to the reactive boronic acid.[8]

We have previously shown that trifluoroborates can be hydrolyzed to the corresponding boronic acid with TMS-Cl in the presence of water.[9] We envisaged that elaboration of the TMS-Cl promoted solvolysis of trifluoroborates, incorporating various bis-nucleophiles in place of water, would enable the generation of a variety of protected boronic acids. Together with a general method for the generation of trifluoroborates from protected boronic acid derivatives, this process would enable the facile interconversion of virtually any combination of boronic acid protecting groups. Such a process would allow the protection of boronic acids under a wide range of reaction conditions such that they could be carried through multi-step processes, a frequent limitation of the use of organoborons in synthesis.[4g]

To establish the generality of this interconversion process, we needed to establish the generality of both the preparation of trifluoroborates from protected boronic acids, and subsequently that of the reverse process; the preparation of protected boronic acids from trifluoroborates.

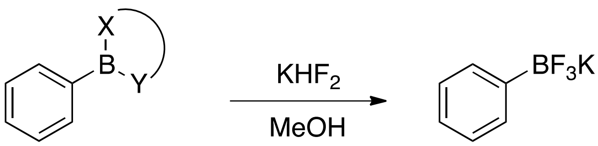
RESULTS AND DISCUSSION

R–BXY to R–BF$_3$K

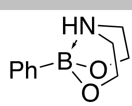
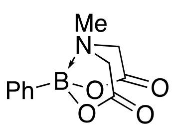
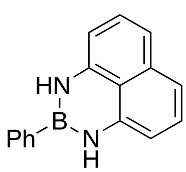
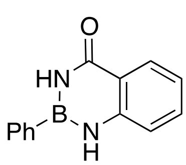
Organotrifluoroborates are readily prepared from boronic acids by treatment with KHF_2,[10] or KF/tartaric acid.[11] The use of KHF_2 also enables the conversion of boronate esters,[9,12,13] boroxines,[7d] trisalkoxyboronates,[14] and diaminoboranes[15] to trifluoroborates, and thus appears quite general. However, no examples of the direct conversion of *N*-based boron protecting groups, such as the important B(mida) or B(dan) groups, to trifluoroborates have been reported. B(mida) groups have been converted to trifluoroborates indirectly, via the corresponding boronic acid intermediates.[16] Several studies of compounds possessing a B(dan) group and a second boronate group suggest the B(dan) group is resistant to conversion to trifluoroborates under these conditions,[17] but this has not been extensively investigated. Accordingly, we sought to determine whether the KHF_2 method was suitable for the preparation of trifluoroborates from B(mida), B(dan) and other *N*-based boronate derivatives.

Phenyl diethanolamine-boronate **1b** was converted to $PhBF_3K$ **1a** in good yield under standard conditions (Table 1, entry 1). However, the other *N*-based boronate derivatives were considerably less reactive. The anthranilamide (aam) boronate[18] **1e** was only partially converted to the corresponding trifluoroborate at room temperature in 1 hour. Nevertheless, heating the reaction to 70 °C did result in complete conversion of PhB(aam) **1e** to the trifluoroborate **1a** (Table 1, entry 4, 72% isolated yield). PhB(mida) **1c** was unreactive to KHF_2 at room temperature, but similarly underwent complete conversion to **1a** at elevated temperature (Table 1, entry 2).

Table 1. Conversion of B–N boronates to trifluoroborates [a]



1b-e **1a**

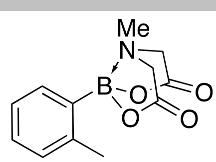
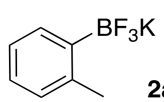
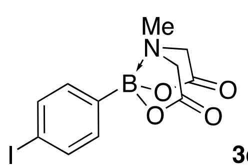
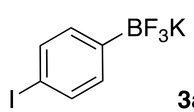
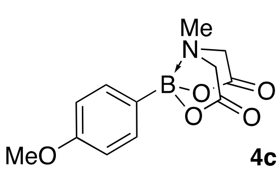
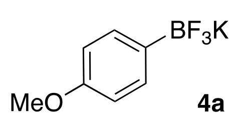
entry	Ph–BXY		yield of **1a** (%)
1		**1b**	85[a,b]
2		**1c**	0[a] 90[c]
3		**1d**	0[a] 0[c]
4		**1e**	29[a] 72[c]

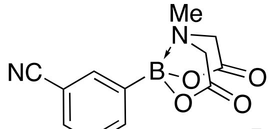
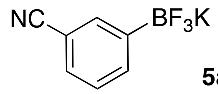
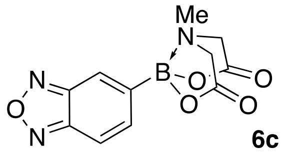
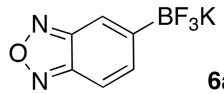
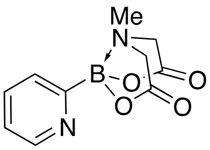
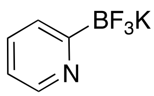
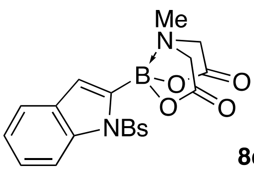
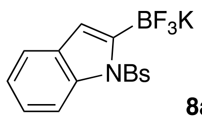
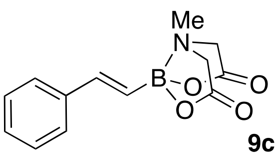
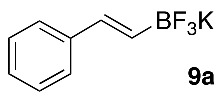
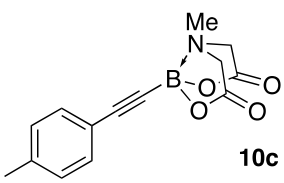
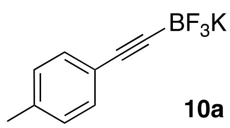
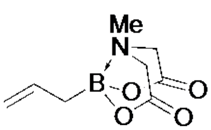
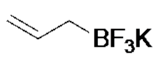
[a] Conditions; 4.5 M KHF_2, MeOH, rt, 1 h. [b] Product contaminated with diethanolamine•HF. [c] Isolated yield upon heating in MeOH at 70 °C.

PhB(dan) **1d** was unreactive to KHF_2 treatment, even at elevated temperature (Table 1, entry 3). These results are in accordance with the hydrolytic stabilities determined for protected boronic acid derivatives determined by Suginome,[18] and indicate that the conversion of boronate derivatives to trifluoroborates with KHF_2 appears general for all systems except B-(sp^2)N,-(sp^2)N systems.

With the finding that PhB(mida) **1c** could be converted to the corresponding trifluoroborate **1a** with KHF_2 at elevated temperature, the transformation of a range of aryl, vinyl and alkynyl-B(mida) compounds to the corresponding trifluoroborates was investigated. In general, conversion of the B(mida) compounds to the corresponding trifluoroborates proceeded in good yield, with minimal steric and electronic effects evident (see Table 2). The conversion of the pyridyl-2-B(mida) **7c** to the pyridyl-2-trifluoroborate **7a** was achieved at room temperature, and avoided decomposition of the product that occurred at 70 °C (Table 2, entry 6).

Table 2. Conversion of B(mida) boronates to trifluoroborates [a]

entry	R–B(mida)	R–BF_3K	yield (%)
1	 **2c**	 **2a**	74
2	 **3c**	 **3a**	88
3	 **4c**	 **4a**	87

4	 5c	 5a	80
5	 6c	 6a	71
6	 7c	 7a	~80[b]
7	 8c	 8a	80
8	 9c	 9a	99
9	 10c	 10a	78
10	 11c	 11a	62

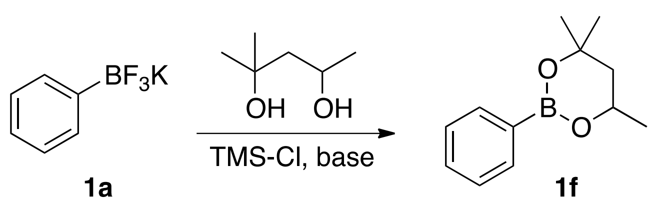
[a] standard conditions; 4.5 M KHF_2, MeOH, 70 °C, 1–1.5 h. [b] rt, 16 h, approx. yield (contaminated with MIDA, see ref. 7e).

R–BF$_3$K to R–BXY

With the conversion of most common boronate protecting groups to trifluoroborates shown to be readily achievable, we next sought to investigate the generality of the complementary conversion of trifluoroborates to a range of boronate derivatives.

We have previously developed a method for the hydrolysis of trifluoroborates to boronic acids by treatment with TMSCl/H_2O.[9] Molander reported a closely related method employing silica gel as the fluorophile.[19] While the conversion of trifluoroborates to organoboron derivatives via the boronic acid derivatives[20] and dichloroboranes[21] has been demonstrated, the direct conversion of trifluoroborates to organoborons other than the boronic acid is rare, and is limited to elaboration of the TMS-Cl method with bis-silyl ethers[22] or esters.[23] Molander has used silica gel in the presence of an alcohol to generate boronate esters from trifluoroborates, though this transformation possibly proceeds via hydrolysis to boronic acid followed by in situ boronate ester formation.[19]

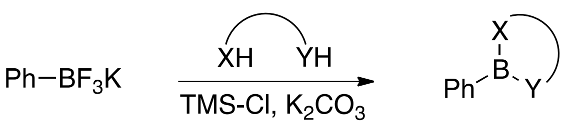
Table 3. Optimization of diol boronate formation



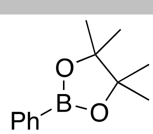
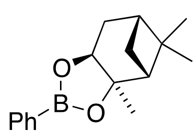
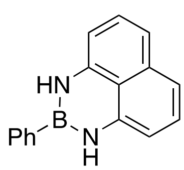
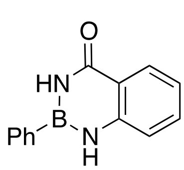
entry	equiv of diol	TMS-Cl equivs.	base	equiv of base	yield (%)
1	1.1	1.1	Et_3N	1	40
2	1.1	1.1	Et_3N	2	59
3	1.1	1.1	Et_3N	3	67
4	1.1	1.1	Et_3N	4	41
6	2	1.1	Et_3N	3	65
7	3	1.1	Et_3N	3	66
8	1.2	1	Et_3N	3	55
9	1.2	2	Et_3N	3	75
10	1.2	3	Et_3N	3	88
11	1.2	3	K_2CO_3	3	93

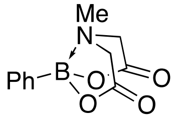
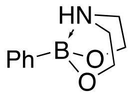
Our initial investigations focused on the direct conversion of trifluoroborates to boronate esters. Conversion of potassium phenyltrifluoroborate **1a** to the corresponding hexyleneglycol boronate **1f** was initially optimized, with variation of the amount of diol and TMS-Cl and the type of base employed. Reasonable yields were obtained under a variety of conditions, with optimum yields for this transformation obtained with a slight excess of diol and 3 equiv of both TMS-Cl and K_2CO_3 (Table 3). This direct method of conversion of trifluoroborates to boronate esters with a diol and TMS-Cl is simpler than the related reaction of diol bis-silyl ethers as prior preparation of the diol bis-silyl ether is not required. The use of pinacol or pinanediol under similar conditions (2 equiv TMS-Cl and K_2CO_3) gave the corresponding boronate esters **1g** and **1h** in excellent yields (Table 4, entries 1,2).

Table 4. Conversion of trifluoroborates to other boronate derivatives [a]



1a **1b-h**

entry	Ph–BXY		yield (%)
1		**1g**	97
2		**1h**	96
3		**1d**	99
4		**1e**	78

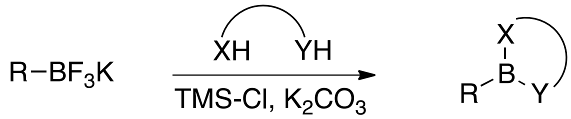
5		**1c**	86[b], 63[c]
6		**1b**	82[b]

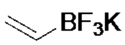
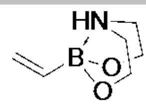
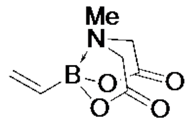
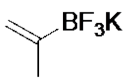
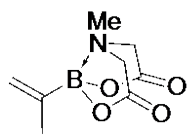
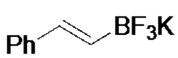
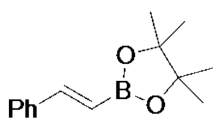
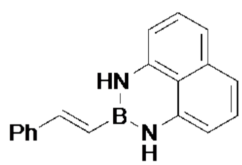
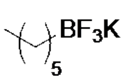
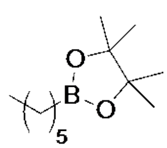
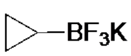
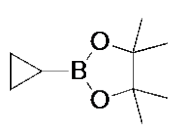
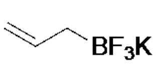
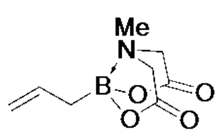
[a] Conditions; nucleophile (1.1 equiv), K_2CO_3 (2 equiv), TMS-Cl (2 equiv), CH_3CN, rt, 2 h. [b] DMF, rt, 18 h. [c] MIDA disodium salt used in place of MIDA/K_2CO_3.

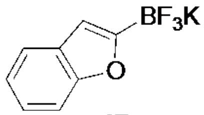
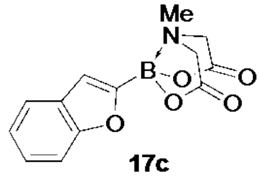
The conversion of phenyltrifluoroborate **1a** to the *N*-based boronate derivatives was next investigated. Incorporating diaminonaphthalene as the bis-nucleophile generated the PhB(dan) derivative **1d** in excellent yield (Table 4, entry 3). The use of anthranilamide, MIDA and diethanolamine also proceeded in good yield to generate the corresponding boronate derivatives **1e**, **1c** and **1b** (Table 4, entries 4–6). The use of MIDA with base (K_2CO_3) provided the PhB(mida) derivative **1c** in greater yield than employing the MIDA disodium salt (Table 4, entry 5).

To probe further the scope of the boronate interconversion a variety of alkenyl- and alkyl-boron species were investigated. The parent vinyltrifluoroborate **12a** was converted to the corresponding diethanolamine boronate **12b** and B(mida) derivative **12c** in reasonable yield (Table 5, entries 1,2). Although a number of protected vinylboronic acid derivatives are commercially available, vinyltrifluoroborate **12a** is considerably less expensive per mole than all others.[24] Similarly, propenyl trifluoroborate **13a** was converted to the corresponding B(mida) derivative **13c** in excellent yield (entry 3). Styrenyltrifluoroborate **9a** was converted to the corresponding B(pin) and B(dan) derivatives, **9g** and **9d**, in excellent yield (entries 4,5). Hexyl and cyclopropyl trifluoroborates **15a** and **16a** were converted to the corresponding volatile B(pin) derivatives **15g** and **16g** (entries 6,7). Allyl and benzofuran-2-yl trifluoroborates **11a** and **17a**, were converted to the corresponding B(mida) compounds **11c** and **17c** in reasonable to excellent yields (entries 8,9).

Table 5. Scope of boronate interconversions



entry	R–BF_3K	R–BXY	yield (%)
1	 **12a**	 **12b**	74
2		 **12c**	65
3	 **13a**	 **13c**	94
4	 **9a**	 **9g**	91
5		 **9d**	76
6	 **15a**	 **15g**	63[b]
7	 **16a**	 **16g**	33[b]
8	 **11a**	 **11c**	75

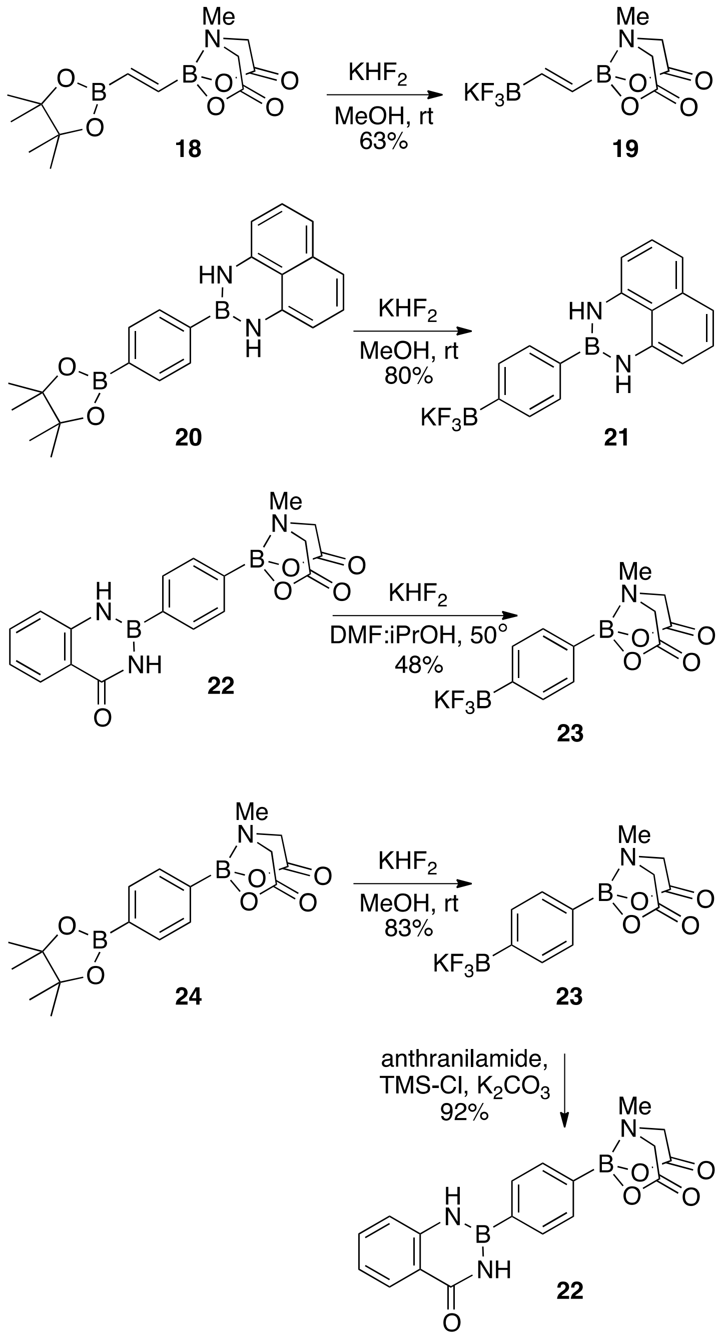
9	 **17a**	 **17c**	89

[a] Conditions; nucleophile (1–1.2 equiv), K_2CO_3 (1–1.2 equiv), TMS-Cl (3 equiv), CH_3CN, rt, 2–18 h. [b] quantitative conversion by TLC; some loss on isolation due to volatility.[25]

Orthogonal interconversion of bisboronates

Given the differential reactivity of the B(mida), B(aam) and B(dan) groups, we next sought to exploit these differences in the orthogonal interconversion of differentially-protected bisboronate systems. Accordingly, treatment of the vinyl-B(pin)/B(mida) bisboronate **18** with KHF_2 underwent selective fluorolysis of the pinacol boronate to give the vinyl-BF_3K/B(mida) bisboronate **19** in 63% yield (Scheme 1), highlighting the stability of the B(mida) group and the orthogonal nature of the B(pin) and B(mida) protecting groups under standard KHF_2 conditions. Further, addition of Bu_4NOH enabled isolation of the more soluble tetrabutylammonium trifluoroborate salt. Similarly, the aryl-B(pin)/B(mida) and aryl-B(pin)/B(dan) bis-boronates, **24** and **20**, respectively, also underwent selective conversion of the B(pin) group to generate the corresponding monotrifluoroborates **23** and **21** with retention of the B(mida) and B(dan) protecting groups, respectively (Scheme 1). Pleasingly, conditions were also found that enabled selective fluorolysis of the B(aam) group in the B(aam)/B(mida) bis-boronate **22**, generating the aryl-BF_3K/B(mida) bisboronate **23** in reasonable yield, despite the B(aam) group being only slightly more reactive under fluorolysis conditions than the B(mida) group. Lastly, following conversion of the aryl-B(pin)/B(mida) bis-boronate **24** to the corresponding monotrifluoroborate **23**, subsequent treatment with TMS-Cl in the presence of anthranilamide gave the corresponding B(aam)/B(mida) bis-boronate **22** in excellent yield, exemplifying the use of this procedure for the orthogonal interconversion of boronate protecting groups.

Scheme 1. Orthogonal interconversion of bisboronates



CONCLUSIONS

In summary, we have developed a general protocol for the interconversion of diverse protected boronic acids, via intermediate organotrifluoroborates. B–N containing boronate derivatives are resistant to direct conversion to trifluoroborates, though B(aam) and B(mida) compounds undergo the conversion at elevated temperatures. Importantly, this allows the selective conversion of differentially protected bisboronates to mono-trifluoroborates. Subsequent solvolysis of organotrifluoroborates in the presence of TMS-Cl and a wide range of bis-nucleophiles allows the general conversion to a wide variety of protected boronic acids.

EXPERIMENTAL SECTION

General Information. ^{1}H NMR spectra were recorded at 400 or 500 MHz. Residual solvent peaks were used as internal references: chloroform (δ 7.26 ppm), d_3-methanol (δ 3.31 ppm), d_5-acetone (δ 2.05 ppm) and d_5-DMSO (δ 2.50 ppm). ^{13}C NMR spectra were recorded at 100 or 125 MHz, with sovent used as an internal reference: d-chloroform (δ 77.00), d_6-acetone (δ 30.83 ppm), d_4-methanol (δ 49.00 ppm) and d_6-DMSO (δ 39.52). IR spectra were obtained as thin films. Mass spectra were recorded on an FT-ICR mass spectrometer by electrospray ionisation in the negative mode, unless otherwise noted.

General Procedure 1; Conversion of B(mida) boronates to trifluoroborates. To a stirred solution of the B(mida) derivative in methanol (40 mL/mmol) was added aq. KHF_2 solution (3–4 equiv., 4.5 M solution) and the mixture was stirred at 70 °C (or at room temperature, see tables) for 1–2 h. The solvent was removed under reduced pressure and the crude residue was thoroughly dried under high vacuum. The solid was extracted with hot acetone, filtered and the solvent evaporated. The crude product was recrystallized (acetone/hexanes) yielding the corresponding potassium trifluoroborate derivative.

*Potassium phenyltrifluoroborate (**1a**)*. Prepared from PhB(mida) derivative **1c** (70 mg, 0.3 mmol) and aq. KHF_2 solution (0.2 mL, 0.9 mmol, 4.5 M) at 70°C for 1 h, according to General Procedure 1. The product was purified by recrystallization (acetone/hexanes) yielding a white solid (50.1 mg, 90 %). ^{1}H NMR (400 MHz, acetone-d_6) δ 7.45 (d, J = 7.2 Hz, 2H), 7.17–6.71 (m, 3H).[11]

*Potassium 2-tolyltrifluoroborate (**2a**).* Prepared from *o*-tolyl-B(mida) derivative **2c** (74 mg, 0.3 mmol) and aq. KHF_2 solution (0.2 mL, 0.9 mmol, 4.5 M) according to General Procedure 1 at 70 °C for 90 minutes. The crude residue was extracted with hot acetone and the mixture was filtered, the filtrate was concentrated in vacuo and the crude residue recrystallised from a minimal amount of hot acetone and pet. spirits, to afford the potassium trifluoroborate as a white powder (42 mg, 71 %). ^{1}H NMR (400 MHz, acetone-d_6) δ 7.48 (d, J = 6.7 Hz, 1H), 7.05–6.75 (m, 3H), 2.40 (s, 3H). ^{13}C NMR (100 MHz, acetone-d_6) δ 141.8, 132.8, 129.1, 126.2, 124.2, 22.1 (carbon bearing boron substituent not observed).[26]

*Potassium 4-iodophenyltrifluoroborate (**3a**).* Prepared from 4-iodophenyl-B(mida) derivative **3c** (108 mg, 0.3 mmol) and aq. KHF_2 solution (0.2 mL, 0.9 mmol, 4.5 M) according to General Procedure 1 at 70 °C for 1 h. The product was purified by recrystallization (acetone/hexanes) yielding a white solid (82 mg, 88 %). ^{1}H NMR (400 MHz, acetone-d_6) δ 7.34 (ddd, J = 7.9, 1.2, 0.7 Hz, 2H), 7.14 (d, J = 7.9 Hz, 2H). ^{13}C NMR (100 MHz, acetone-d_6) δ 135.3, 134.1, 90.9 (carbon bearing boron substituent not observed).[27]

*Potassium 4-methoxyphenyltrifluoroborate (**4a**).* Prepared from 4-methoxyphenyl-B(mida) derivative **4c** (79 mg, 0.3 mmol) and aq. KHF_2 solution (0.2 mL, 0.9 mmol, 4.5 M) according to General Procedure 1 at 70 °C for 60 minutes. The crude residue was extracted with hot acetone and the mixture was filtered, the filtrate was concentrated in vacuo and the crude residue recrystallised from a minimal amount of hot acetone and pet spirits, to afford a white solid (56 mg, 87 %). ^{1}H NMR (400 MHz, acetone-d_6) δ 7.57–7.21 (m, 2H), 6.78–6.49 (m, 2H), 3.72 (s, 3H). ^{13}C NMR (100 MHz, acetone-d_6) δ 158.8, 133.4, 112.7, 55.0 (carbon bearing boron substituent not observed).[26]

*Potassium 3-cyanophenyltrifluoroborate (**5a**).* Prepared from 3-cyanophenyl-B(mida) derivative **5c** (77 mg, 0.3 mmol) and aq. KHF_2 solution (0.2 mL, 0.9 mmol, 4.5 M) according to General Procedure 1 at 70 °C for 60 minutes. The crude residue was extracted with hot acetone and the mixture was filtered, the filtrate was concentrated in vacuo and the crude residue recrystallised from a minimal amount of hot acetone and pet. spirits, to afford a white solid (56 mg, 87 %). ^{1}H NMR (400 MHz, acetone-d_6) δ 7.72 (dt, J = 4.4, 2.3 Hz, 2H), 7.39 (dt, J = 7.6, 1.6 Hz, 1H), 7.33–7.16 (m, 1H). ^{13}C NMR (100 MHz, acetone-d_6) δ 137.0 (q, J = 1.8 Hz), 136.0 (q, J = 1.9 Hz), 129.6 , 128.00 , 121.0 , 111.0.[7c]

*Potassium 5-benzofurazantrifluoroborate (**6a**).* Prepared from 5-benzofurazan-B(mida) derivative **6c** (82.5 mg, 0.3 mmol) and aq. KHF_2 solution (0.2 mL, 0.9 mmol, 4.5 M) according to General Procedure 1 at 70 °C for 60 minutes. The crude residue was extracted with hot acetone and the mixture was filtered, the filtrate was concentrated in vacuo and the crude residue recrystallised from a minimal amount of hot acetone and pet. spirits, to afford a white powder (50 mg, 80 %). ^{1}H NMR (400 MHz, acetone-d_6) δ 7.72 (dt, J = 4.4, 2.3 Hz, 2H), 7.39 (dt, J = 7.6, 1.6 Hz, 1H), 7.25 (m, 1H). ^{13}C NMR (100 MHz, acetone-d_6) δ 150.5 , 150.1, 138.7 , 115.9 (q, J = 2.8 Hz), 113.2. Spectral data matched that of an authentic commercial sample.

*Potassium pyridine-2-trifluoroborate (**7a**).* To a stirred solution of pyridyl-2-B(mida) derivative **7c** (140 mg, 0.6 mmol) in methanol (6 mL) was added aq. KHF_2 solution (0.4 mL, 1.8 mmol, 4.5 M) and the mixture was stirred at room temperature for 16 h. The solvent was removed under reduced pressure and the crude residue was thoroughly dried under high vacuum. The crude solid was extracted with methanol, filtered and the solvent evaporated. The residue was extracted with a small amount of methanol which was evaporated to afford the corresponding potassium pyridine-2-trifluoroborate **7a** and methyliminodiacetic acid as a 1:1 mixture (79.8 mg, 80 %). ^{1}H NMR (400 MHz, methanol-d_4) δ 8.58 (br d, J = 6.0 Hz, 1H), 8.36 (td, J = 7.7, 1.2 Hz, 1H), 8.01 (br d, J = 7.8 Hz, 1H), 7.81 (ddd, J = 7.6, 6.0, 1.5 Hz, 1H); MIDA peaks appear at δ 3.71 (s, 4H), 2.95 (s, 3H). ^{13}C NMR (100 MHz, methanol-d_4) δ 144.8, 140.5, 131.3, 125.6.[7e]

*Potassium N-(phenylsulfonyl)indolyl-2-trifluoroborate (**8a**).* Prepared from N-phenylsulfonylindolyl-B(mida) derivative **8c** (124 mg, 0.3 mmol) and aq. KHF_2 solution (0.2 mL, 0.9 mmol, 4.5 M) according to General Procedure 1 at 70 °C for 90 minutes. The crude residue was extracted with hot acetone and the mixture was filtered, the filtrate was concentrated in vacuo and the crude residue recrystallised from a minimal amount of hot acetone and pet. spirits, to afford a white powder (110 mg, 100%). ^{1}H NMR (400 MHz, acetone-d_6) δ 8.20–8.10 (m, 2H), 8.10–8.03 (m, 1H), 7.56–7.48 (m, 1H), 7.48–7.38 (m, 3H), 7.22–7.05 (m, 2H), 6.78 (d, J = 0.9 Hz, 1H). ^{13}C NMR (100 MHz, acetone-d_6) δ 140.4, 138.7, 133.9, 132.7, 129.5, 127.9 (q, J = 1.8 Hz), 123.4 , 123.3 , 120.9, 116.2 (q, J = 3.1 Hz), 115.1. HRMS: *m/z* calculated for $C_{14}H_{10}BF_3NO_2S$ ([M–K^+]$^-$), 324.0477; found *m/z* 324.0474.

*Potassium trans-styrenyltrifluoroborate (**9a**).* Prepared from *trans*-styrenyl-B(mida) derivative **9c** (78 mg, 0.3 mmol) and aq. KHF_2 solution (0.2 mL, 0.9 mmol, 4.5 M) according to General Procedure 1 at 70 °C for 1 h. The product was purified by recrystallization (acetone/hexanes) yielding a white solid (45 mg, 71%). ^{1}H NMR (400 MHz, acetone-d_6) δ 7.37–7.32 (m, 2H), 7.22 (app dd, J = 8.4, 6.9 Hz, 2H), 7.09 (app tt, J = 7.3, 3.5 Hz, 1H), 6.67 (d, J = 18.2 Hz, 1H), 6.32 (dq, J = 18.3, 3.7 Hz, 1H). ^{13}C NMR (100 MHz, acetone-d_6) δ 140.9, 133.9, 128.1, 125.7, 125.6 (carbon bearing boron substituent not observed).[11]

*Potassium 2-(4-tolyl)-ethynyltrifluoroborate (**10a**).* Prepared from 4-methylphenylethynyl-B(mida) derivative **10c** (49 mg, 0.18 mmol) and aq. KHF_2 solution (0.2 mL, 0.9 mmol, 4.5 M) according to General Procedure 1 at 70 °C for 60 minutes. The crude residue was extracted with hot acetone and the mixture was filtered, the filtrate was concentrated in vacuo and the crude residue recrystallised from a minimal amount of hot acetone and pet. spirits, to afford a white powder (31 mg, 78%). ^{1}H NMR (400 MHz, acetone-d_6) δ 7.29–7.13 (m, 2H), 7.11–6.91 (m, 2H), 2.27 (s, 3H). ^{13}C NMR (100 MHz, acetone-d_6) δ 136.0, 131.1, 128.6, 123.5, 89.1, 20.4.[28]

*Potassium allyltrifluoroborate (**11a**).* Prepared from allyl-B(mida) derivative **11c** (100 mg, 0.57 mmol)) and aq. KHF_2 solution (0.33 mL, 4.5M, 1.52 mmol) at room temperature for 1 h according to General Procedure 1. The product was collected by filtration to yield the product **11a** (52 mg, 62%) as a white crystalline solid. ^{1}H NMR (400 MHz, acetone-d_6) δ 5.94 (dq, J = 10.0, 7.9 Hz, 1H), 4.64 (m, 2H), 1.14 (br s, 2H); ^{13}C NMR (100 MHz, acetone-d_6) δ 142.1, 109.2 (carbon bearing boron substituent not observed).

*Potassium trans-2-trifluoroboryl-1-vinyl-B(mida) (**19**).* To a solution of *trans*-2-B(pin)-vinyl-B(mida) derivative **18** (105 mg, 0.34 mmol) in methanol (1 mL) was added aqueous KHF_2 solution (0.43 mL, 4.5 M, 1.93 mmol). The resulting white slurry was stirred at room temperature for 1 h and then concentrated *in vacuo*. The crude solid obtained was extracted exhaustively with anhydrous hot acetone (product poorly soluble). The extract was filtered and the filtrate concentrated in vacuo. The crude residue obtained was recrystallised from a minimal amount of hot acetone and ether (5 mL), to afford an amorphous solid (62 mg, 63%). ^{1}H NMR (400 MHz, DMSO-d_6) δ 6.09 (dq, *J* = 20.5, 3.4 Hz, 1H), 5.63 (d, *J* = 20.6 Hz, 1H), 4.09 (d, *J* = 17.1 Hz, 2H), 3.86 (d, *J* = 17.0 Hz, 2H), 2.67 (s, 3H). ^{13}C NMR (100 MHz, DMSO-d_6) δ 169.5, 61.0, 46.5 (carbon bearing boron substituents not observed). ^{11}B NMR (128 MHz, DMSO-d_6) δ 12.3, 2.51. HRMS: *m/z* calculated for $C_7H_9B_2F_3NO_4$ ([M–K$^+$]$^-$), 250.0670; found *m/z* 250.0669. IR (neat, cm^{-1}) 526, 545, 556, 567, 592, 607, 633, 648, 675, 737, 763, 823, 850, 892, 1004, 1025, 1050, 1073, 1221, 1294, 1333, 1374, 1460, 1633, 1727, 3265, 3324, 3348.

Tetrabutylammonium trans-2-trifluoroboryl-1-vinyl-B(mida). To a solution of *trans*-2-B(pin)-vinyl-B(mida) derivative **18** (0.50 g, 1.62 mmol) in methanol (1 mL) was added aqueous KHF_2 (1.05 mL,4.5 M, 4.6 mmol, 3.1 eq). After stirring for 30 min, $Bu_4N^+OH^-$ (1.10 mL, 40 % aq. solution, 1.62 mmol) was added dropwise and the mixture stirred for 1 h. The reaction was diluted with DCM (10 mL) and the aqueous layer was extracted with DCM (5 × 10 mL). The combined organic layers were dried ($MgSO_4$), filtered and the solvent evaporated to afford the tetrabutylammonium trifluoroborate salt (0.560 g, 70%, ~90% purity) contaminated with tetrabutyl ammonium species. Careful washing with minimal tetrahydrofuran was able to remove excess tetrabutylammonium salts with minor loss of product. ^{1}H NMR (400 MHz, DMSO-d_6) δ 6.09 (dq, *J* = 20.5, 3.4 Hz, 1H), 5.63 (d, *J* = 20.6 Hz, 1H), 4.09 (d, *J* = 17.1 Hz, 2H), 3.86 (d, *J* = 17.0 Hz, 2H), 2.67 (s, 3H). ^{13}C NMR (100 MHz, DMSO-d_6) δ 169.9, 61.8, 59.1, 46.9, 46.8, 24.3, 20.2, 13.8 (carbon bearing boron substituents not observed). ^{11}B NMR (128 MHz, DMSO-d_6) δ 12.3, 2.51. HRMS: *m/z* calculated for $C_7H_9B_2F_3NO_4$ ([M–Bu_4N^+]$^-$), 250.0670; found *m/z* 250.0669.

*Potassium 4-trifluoroborylphenyl-B(dan) (**21**).* To a solution of B(pin)/B(dan) 1,4-benzenebisboronate **20** (51.7 mg, 0.139 mmol) in methanol (1 mL) was added aqueous KHF_2 (0.43 mL, 4.5 M, 1.93 mmol). The resulting white slurry was stirred at room temperature for 15 min, the solvent was then removed under reduced pressure and the residue extracted with hot acetone. The mixture was filtered, the filtrate was concentrated in vacuo and the residue recrystallised from a minimal amount of hot acetone and pet. spirits, to afford a light purple powder (39 mg, 80 %). ^{1}H NMR (400 MHz, acetone-d_6) δ 7.63 (d, *J* = 7.4 Hz, 2H), 7.54 (d, *J* = 7.4 Hz, 2H), 7.50 (s, 2H), 7.08 (t, *J* = 7.8 Hz, 2H), 6.62 (d, *J* = 7.6 Hz, 2H). ^{13}C NMR (100 MHz, acetone-d_6) δ 143.7, 137.6, 132.4, 131.2, 128.5, 121.0, 117.5, 106.6 (carbon bearing boron substituents not observed). ^{11}B NMR (128 MHz, acetone-d_6) δ 32.04, 5.59. IR (neat, cm^{-1}) 629, 701, 755, 824, 890, 965, 1005, 1024, 1047, 1092, 1179, 1196, 1234, 1272, 1304, 1389, 1449, 1513, 1585, 1596, 1613, 1649, 2854, 2925, 2966, 3219, 3294, 3308, 3327, 3334. HRMS: *m/z* calculated for $C_{16}H_{12}B_2F_3N_2$ ([M–K^{+}]$^{-}$), 311.1139; found *m/z* 311.1142.

*Potassium 4-trifluoroborylphenyl-B(mida) (**23**).*

from 4-B(pin)-phenyl-B(mida) ***24****;* Prepared from B(pin)/B(mida) 1,4-benzenebisboronate **24** (500mg, 1.46 mmol) and aq. KHF_2 solution (0.92 mL, 4.5M, 4.14 mmol) at room temperature for 1 h according to General Procedure 1. The precipitate was collected by filtration to yield the product **23** (415 mg, 83%) as a white solid. ^{1}H NMR (400 MHz, acetone-d_6) δ 7.30 (s, 2H), 7.15 (s, 2H), 4.25 (d, *J* = 17 Hz, 2H) 4.03 (d, *J* = 17 Hz, 2H), 2.42 (s, 3H); ^{13}C NMR (100 MHz, acetone-d_6) δ 170.0, 131.3, 130.8, 130.1, 62.0, 47.9 (carbon bearing boron substituent not observed); ^{11}B NMR (128 MHz, acetone-d_6) δ 16.6, 7.9; IR (neat, cm^{-1}) 3302, 1741, 1657, 1620, 1338, 1302, 1231, 1035, 983, 817; HRMS: *m/z* calculated for $C_{11}H_{11}B_2F_3NO_4$ ([M–K^{+}]$^{-}$), 300.0826; found *m/z* 300.0856.

from 4-B(aam)-phenyl-B(mida) ***22****;* To a solution of B(aam)/B(mida) 1,4-benzenebisboronate **22** (41mg, 0.11 mmol) in a mixture of 2-propanol and DMF (1:1) was added aq. KHF_2 solution (73 μL, 4.5M, 0.33 mmol). The mixture was heated to 50 ˚C for 1 h and cooled to room temperature. The solution was cooled to –20 ˚C overnight, and the product was collected by filtration to yield **23** (18 mg, 48%) as a white solid.

General Procedure 2; conversion of trifluoroborates to boronate ester derivatives. To a mixture of the potassium trifluoroborate, potassium carbonate (2 equiv.), and diol (1 equiv.) in acetonitrile was added TMS-Cl (1.5 eq) and the reaction stirred 2 h. The reaction was diluted with ether, filtered and the solvent evaporated under reduced pressure. The crude residue obtained was purified by passage through a silica plug eluting with ethyl acetate/hexane yielding the corresponding boronate ester.

*Hexyleneglycolyl phenylboronate (**1f**).* Prepared from phenyltrifluoroborate **1a** (138 mg, 0.747 mmol) and 2,4-hexylene glycol (90 mg, 0.76 mmol) according to General Procedure 2. The boronate ester was isolated by column chromatography on silica gel (hexanes/ethyl acetate = 1:4). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.81 (dd, *J* = 8.0, 1.5 Hz, 2H), 7.50–7.24 (m, 3H), 4.32 (dqd, *J* = 11.5, 6.2, 3.0 Hz, 1H), 1.83 (dd, *J* = 13.9, 3.0 Hz, 1H), 1.69–1.48 (m, 1H), 1.36 (s, 3H), 1.34 (s, 3H), 1.33 (d, *J* = 6.2 Hz, 3H).[29]

*Pinacolyl phenylboronate (**1g**).* Prepared from phenyltrifluoroborate **1a** (138 mg, 0.747 mmol) and pinacol (90 mg, 0.76 mmol) according to General Procedure 2. The boronate ester was isolated by column chromatography on silica gel (hexanes/ethyl acetate = 1:4) yielding a white solid (148 mg, 97 %).[30]

*Pinanediolyl phenylboronate (**1h**).* Prepared from phenyltrifluoroborate **1a** (138 mg, 0.747 mmol) and (1R,2R,3S,5R)-(–)-pinanediol (129 mg, 0.760 mmol) according to General Procedure 2. The boronate ester was isolated by column chromatography on silica gel (hexanes/ethyl acetate = 1:4) yielding a viscous oil which solidified upon standing (183 mg, 96%). ^{1}H NMR (200 MHz, $CDCl_3$) δ 7.82 (dd, *J* = 7.9, 1.6 Hz, 3H), 7.57–7.28 (m, 3H), 4.46 (dd, *J* = 8.7, 1.9 Hz, 1H), 2.59–2.09 (m, 3H), 2.08–1.85 (m, 2H), 1.49 (s, 3H), 1.32 (s, 3H), 1.23 (d, *J* = 10.5 Hz, 1H), 0.90 (s, 3H). ^{13}C NMR (50 MHz, $CDCl_3$) δ 134.9, 131.3, 127.9, 86.4, 51.6, 39.7, 38.4, 35.8, 28.9, 27.3, 26.7, 24.2.[31]

*Pinacolyl trans-styrenylboronate (**9g**).* Prepared from potassium *trans*-styrenyltrifluoroborate **9a** (102 mg, 0.747 mmol) and pinacol (90 mg, 0.760 mmol) according to General Procedure 2. The product was isolated by column chromatography on silica gel (hexanes/ethyl acetate = 1:4) yielding a colourless liquid (156 mg, 91% yield). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.54–7.21 (m, 6H), 6.15 (d, *J* = 18.5 Hz, 1H), 1.30 (s, 12H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 149.7, 137.6, 129.0, 128.7, 127.2, 83.5, 25.0 (carbon bearing boron substituent not observed).[32]

*Pinacolyl 1-hexylboronate (**15g**).* Prepared from potassium *n*-hexane-1-trifluoroborate **15a** (143 mg, 0.747 mmol) and pinacol (90 mg, 0.760 mmol) according to General Procedure 2. The product was isolated by column chromatography on silica gel (hexanes/ethyl acetate = 9:1) yielding a clear liquid (100 mg, 63%). ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.44–1.30 (m, 2H), 1.31–1.13 (m, 18H), 0.82 (t, J = 6.9 Hz, 3H), 0.72 (t, J = 7.8 Hz, 2H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 82.9, 32.2, 31.7, 24.9, 24.0, 22.7, 14.2 (carbon bearing boron substituent not observed).[30]

*Pinacolyl cyclopropylboronate (**16g**).* Prepared from potassium cyclopropyltrifluoroborate **16a** (111 mg, 0.747 mmol) and pinacol (90 mg, 0.760 mmol) according to General Procedure 2. The product was isolated by column chromatography on silica gel (hexanes/ethyl acetate = 1:4) as a colourless liquid (42 mg, 33%; *unoptimized, compound lost due to volatility).* ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.21 (s, 12H), 0.60 (ddd, J = 9.2, 6.1, 3.3 Hz, 2H), 0.49 (td, J = 6.0, 3.3 Hz, 2H), –0.20 (tt, J = 9.3, 6.1 Hz, 1H).[33]

General Procedure 3; conversion of trifluoroborates to B(aam) or B(dan) derivatives. To a mixture of potassium carbonate (103 mg, 0.747 mmol), potassium phenyltrifluoroborate (69 mg, 0.374 mmol) in acetonitrile (7.5 mL) was added TMS-Cl (132 µL, 1.12 mmol, 3 eq) and anthranilamide or 1,8-diaminonaphthalene (0.380 mmol) and the reaction stirred for 30 min. The reaction was diluted with ethyl acetate (20 mL), filtered and the solvent evaporated under reduced pressure. The crude residue obtained was purified by column chromatography (silica, eluting with ethyl acetate/petroleum spirits) yielding the product as a white-purple solid.

*PhB(dan) (**1d**).* Prepared from phenyltrifluoroborate **1a** (69 mg, 0.374 mmol) and 1,8-diaminonaphthalene (59 mg, 0.374 mmol) according to General Procedure 3. The product was isolated by column chromatography on silica gel (eluting with 1:4 hexanes/ethyl acetate then 1:1 hexanes/ethyl acetate) yielding **1d** (91 mg, 100 %) as a white-purple solid. ^{1}H NMR (200 MHz, $CDCl_3$) δ 7.72–7.60 (m, 2H), 7.55–7.41 (m, 3H), 7.26–7.00 (m, 4H), 6.43 (dd, J = 7.0, 1.3 Hz, 2H), 6.03 (br s, 2H). ^{13}C NMR (50 MHz, $CDCl_3$) δ 141.2 (2C), 136.5, 131.5 (2C), 130.4, 128.4 (2C), 127.7 (2C) 120.1, 118.0 (2C), 106.2 (2C) (carbon bearing boron substituent not observed).[34]

*PhB(aam) (**1e**).* Prepared from phenyltrifluoroborate **1a** (138 mg, 0.747 mmol) and anthranilamide (104 mg, 0.760 mmol) according to General Procedure 3. The product was isolated by column chromatography on silica gel (hexanes/ethyl acetate = 1:1) yielding **1e** (130 mg, 78%) as a white-purple solid. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.26 (dd, *J* = 8.0, 1.6 Hz, 1H), 7.76–7.66 (m, 2H), 7.66–7.44 (m, 5H), 7.18 (ddd, *J* = 8.1, 7.2, 1.1 Hz, 1H), 7.12 (dd, *J* = 8.1, 0.5 Hz, 1H), 6.82 (br s, 1H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 166.6, 144.2, 133.9, 131.8 (2C), 131.1, 129.2, 128.6 (2C), 121.9, 117.6, 115.0 (carbon bearing boron substituent not observed).[18]

*trans-styrenyl-B(dan) (**9d**).* Prepared from potassium *trans*-styrenyl trifluoroborate **9a** (101.0 mg, 0.747 mmol) and 1,8-diaminonaphthalene (60 mg, 0.380 mmol) according to General Procedure 3. The product was isolated by column chromatography on silica gel (hexanes/ethyl acetate = 3:1) yielding the product **9d** (77 mg, 76 %) as a white-purple solid. ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.55–7.51 (m, 2H), 7.43–7.37 (m, 2H), 7.34 (d, *J* = 7.5 Hz, 1H), 7.20–7.10 (m, 3H), 7.05 (dd, *J* = 8.4, 0.9 Hz, 2H), 6.38 (dd, *J* = 7.3, 1.0 Hz, 2H), 6.34 (d, *J* = 18.6 Hz, 1H), 5.86 (br s, 2H). ^{13}C NMR (125 MHz, $CDCl_3$) δ 143.9, 141.4, 137.8, 136.6, 128.94, 128.92, 127.8, 127.0, 120.1, 117.9, 106.0 (carbon bearing boron substituent not observed).[6a]

General Procedure 4; conversion of trifluoroborates to B(mida) derivatives. To a stirred solution of trifluoroborate salt (0.374 mmol), *N*-methyliminodiacetic acid (59 mg, 0.4 mmol) and potassium carbonate (104 mg, 0.747 mmol) in dimethylformamide (5 mL) under an atmosphere of nitrogen was added TMS-Cl (132 µL, 1.12 mmol) and the mixture was stirred overnight. Ethyl acetate (20 mL) was added and the solution was filtered, and the flask rinsed with a small amount of ethyl acetate. For small scale reactions, the solvent was removed under reduced pressure. For large scale reactions an aqueous workup was employed to remove the DMF; the solution was washed with brine (20 mL), water (20 mL x 2), brine (20 mL) and then dried ($MgSO_4$). The solvent was removed under reduced pressure and the product was purified by recrystallization (ethyl acetate–petroleum spirits) to give the product.

*PhB(mida) (**1c**).* Prepared from phenyltrifluoroborate **1a** (68.8 mg, 0.374 mmol) and *N*-methyliminodiacetic acid (58.9 mg, 0.4 mmol) according to General Procedure 4. The crude residue was recrystallised (ethyl acetate/petroleum spirits) yielding **1c** (75 mg 86 %) as a white solid. ^{1}H NMR (400 MHz, DMSO-d_6) δ 7.45–7.36 (m, 2H), 7.36–7.26 (m, 3H), 4.29 (d, *J* = 17.2 Hz, 2H), 4.07 (d, *J* = 17.2

Hz, 2H), 2.45 (s, 3H). ^{13}C NMR (101 MHz, DMSO-d_6) δ 169.4, 132.3, 128.9, 127.7, 61.8, 47.6 (carbon bearing boron substituent not observed). ^{11}B NMR (128 MHz, DMSO-d_6) δ 13.44.[35]

*Allyl-B(mida) (**11c**).* Prepared from potassium allyltrifluoroborate **11a** (55 mg, 0.374 mmol) and *N*-methyliminodiacetic acid (59 mg, 0.4 mmol) according to General Procedure 4. The crude residue was recrystallised (ethyl acetate/petroleum spirits) yielding **11** (110 mg, 75%) as a white solid. ^{1}H NMR (400 MHz, acetone-d_6) δ 5.89 (ddt, *J* = 17.0, 10.2, 7.6 Hz, 1H), 5.00 (ddt, *J* = 17.1, 2.5, 1.6 Hz, 1H), 4.90 (ddt, *J* = 10.2, 2.5, 1.2 Hz, 1H), 4.21 (d, *J* = 16.9 Hz, 2H), 3.99 (d, *J* = 16.8 Hz, 2H), 2.54 (s, 3H), 1.66 (d, *J* = 7.6 Hz, 2H). ^{13}C NMR (100 MHz, acetone-d_6) δ 168.7, 137.0, 115.3, 62.9, 46.3, 41.3. ^{11}B NMR (128 MHz, acetone-d_6) δ 12.16. Spectral data matched that of an authentic commercial sample.

*Vinyl-B(mida) (**12c**).* Prepared from potassium vinyltrifluoroborate **12a** (51 mg, 0.374 mmol) and *N*-methyliminodiacetic acid (59 mg, 0.4 mmol) according to General Procedure 4. The crude residue was recrystallised (ethyl acetate/petroleum spirits) yielding **12c** (45 mg, 65%) as a white solid. ^{1}H NMR (500 MHz, $CDCl_3$) δ 6.11–5.94 (m, 2H), 5.92–5.77 (m, 1H), 3.84 (d, *J* = 16.3 Hz, 2H), 3.69 (d, *J* = 16.3 Hz, 2H), 2.85 (s, 3H).[4e]

*2-Propenyl-B(mida) (**13c**).* Prepared from potassium isopropenyltrifluoroborate **13a** (55 mg, 0.374 mmol) and *N*-methyliminodiacetic acid (118 mg, 0.8 mmol) according to General Procedure 4. The crude residue was recrystallised (ethyl acetate/petroleum spirits) yielding **13c** (55 mg, 94 %) as a white solid. ^{1}H NMR (400 MHz, acetone-d_6) δ 5.45 (br s, 1H), 5.31 (d, *J* = 2.5 Hz, 1H), 4.23 (d, *J* = 17.0 Hz, 2H), 4.04 (d, *J* = 17.0 Hz, 2H), 3.00 (s, 3H), 1.78 (br s, 3H).[4c]

*2-Benzofuranyl-B(mida) (**17c**).* Prepared from potassium 2-benzofuranyltrifluoroborate **17a** (84 mg, 0.374 mmol) and *N*-methyliminodiacetic acid (59 mg, 0.4 mmol) according to General Procedure 4. The crude residue was recrystallised (ethyl acetate/petroleum spirits) yielding **17c** (91 mg, 89%) as a white solid. ^{1}H NMR (400 MHz, DMSO-d_6) δ 7.64 (app d, *J* = 7.1 Hz, 1H), 7.57 (app d, *J* = 8.2 Hz, 1H), 7.29 (td, *J* = 8.3, 7.7, 1.4 Hz, 1H), 7.22 (td, *J* = 7.5, 1.0 Hz, 1H), 7.07 (br s, 1H), 4.41 (d, *J* = 17.2 Hz, 2H), 4.17 (d, *J* = 17.2 Hz, 2H), 2.69 (s, 3H).[4d]

*4-B(aam)-phenyl-B(mida) (**22**).* Prepared from potassium trifluoroborate salt **23** (50mg, 0.147 mmol) and anthranilamide (21 mg, 0.147 mmol) according to General Procedure 4. The crude product was purified by flash chromatography (10% MeOH/EtOAc), to give **24 (**51mg, 92%) as a colourless solid. ^{1}H NMR (400 MHz, acetone-d_6) 9.66 (s, 1H), 9.31 (s, 1H), 8.04–7.99 (m, 3H), 7.75 (d, *J* = 8 Hz, 1H), 7.55 (m, 1H), 7.50 (d, *J* = 8 Hz, 2H), 7.40 (d, *J* = 8 Hz, 2H), 7.09 (t, *J* = 11 Hz, 1H); 4.34 (d, *J* = 17 Hz, 2H), 4.13 (d, *J = 17* Hz, 2H), 2.52 (s, 3H); ^{13}C NMR (100 MHz, acetone-d_6) δ 169.8, 166.7, 145.9, 133.6, 131.8, 128.4, 121.2, 119.2, 118.6 (carbon bearing boron substituent not observed); ^{11}B NMR (128 MHz, acetone-d_6) δ 15.8; IR (neat, cm^{-1}) 3303, 1743, 1658, 1620, 1538, 1339, 1303, 1241, 1037, 988, 716, 725; HRMS: *m/z* calculated for $C_{18}H_{18}B_2N_3O_5$ ($[M+H]^+$), 378.1433; found *m/z* 378.1446.

General Procedure 5; conversion of trifluoroborates to diethanolamine boronate derivatives. To a stirred solution of potassium phenyltrifluoroborate (69 mg, 0.374 mmol), diethanolamine (42 mg, 0.4 mmol) and K_2CO_3 (56 mg, 0.4 mmol) in acetonitrile (5 mL) under an atmosphere of nitrogen was added TMS-Cl (132 µL, 1.12 mmol) and the mixture was stirred for 2 h. Dichloromethane (20 mL) was added to the reaction and the solution was filtered, and the precipitate was washed with dichloromethane (3 x 20 mL). The filtrate was evaporated under reduced pressure and the crude solid residue was purified by recrystallization (dichloromethane/ether).

*Diethanolaminyl phenylboronate (**1b**).* Prepared from phenyltrifluoroborate **1a** (69 mg, 0.374 mmol) and diethanolamine (42 mg, 0.4 mmol) according to General Procedure 5. The product was recrystallised (dichloromethane/ether) yielding **1b** (59 mg, 82%) as a white solid. ^{1}H NMR (400 MHz, DMSO-d_6) δ 7.44 (dd, *J* = 7.8, 1.7 Hz, 2H), 7.24–7.14 (m, 3H), 6.88 (br s, 1H), 3.87 (td, *J* = 9.2, 5.4 Hz, 2H), 3.78 (ddd, *J* = 9.6, 6.6, 3.5 Hz, 2H), 3.13–3.01 (m, 2H), 2.87–2.76 (m, 2H).[36]

*Diethanolaminyl vinylboronate (**12b**).* Prepared from potassium vinyltrifluoroborate **12a** (50 mg, 0.374 mmol) and diethanolamine (40 mg, 0.38 mmol) according to General Procedure 5. The product was recrystallised (dichloromethane/ether) yielding **12b** (39 mg, 74%) as a white solid. ^{1}H NMR (400 MHz, DMSO-d_6) δ 6.72 (s, 1H), 5.83 (dd, *J* = 19.5, 13.2 Hz, 1H), 5.50–5.24 (m, 2H), 4.01–3.66 (m, 2H), 3.65–3.46 (m, 2H), 3.16–2.84 (m, 2H), 2.84–2.59 (m, 2H). ^{13}C NMR (100 MHz, DMSO-d_6) δ 122.5, 62.3, 50.4 (carbon bearing boron substituent not observed).[37]

4-B(pin)-phenyl-B(mida) ***24***. To a solution of 4-bromophenyl-B(mida) boronate (1.11g, 3.53 mmol), KOAc (690 mg, 7.1 mmol) and bispinacolatodiboron (3.58 g, 14.1 mmol) in DMF (40 mL) was added Pd(dppf)Cl_2 (128 mg, 0.17 mmol). The solution was heated to 90 °C overnight and cooled to room temperature. The solvent was removed *in vacuo,* and the residue was purified by flash chromatography (20–50% EtOAc/pet. spirits), followed by recrystallisation (CH_2Cl_2/pet. spirits) to give **24 (**950 mg, 75%) as a colourless crystalline solid. ^1H NMR (400 MHz, acetone-d_6) δ 7.75 (d, J = 7.5 Hz, 2H), 7.56 (d, J = 7.5 Hz, 2H), 4.36 (d, J = 17 Hz, 2H), 4.15 (d, J = 17 Hz, 2H), 2.68 (s, 3H), 1.30 (s, 12H). ^{13}C NMR (100 MHz, acetone-d_6) δ 168.4, 133.9, 131.8, 83.6, 61.9, 47.4, 24.3 (carbon bearing boron substituent not observed). ^{11}B NMR (128 MHz, acetone-d_6) δ 30.5, 11.6. IR (neat, cm^{-1}) 1745, 1657, 1615, 1391, 1363, 1337, 1300, 1220, 1036, 990, 961, 816. HRMS: *m/z* calculated for $C_{17}H_{24}B_2NO_6$ ($[M+H]^+$), 360.1790; found *m/z* 360.1799.

ASSOCIATED CONTENT

Supporting Information

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

AUTHOR INFORMATION

Corresponding Author

*Email: chutton@unimelb.edu.au (C.A.H.).

Notes

The authors declare no competing financial interest.

ACKNOWLEDGMENTS

The Australian Research Council is acknowledged for support.

REFERENCES

(1) *Boronic Acids*, 2nd ed.; Hall, D. G., Ed.; Wiley-VCH: Singapore, **2011**.

(2) (a) Beenen, M. A.; Weix, D. J.; Ellman, J. A. *J. Am. Chem. Soc.* **2006**, *128*, 6304. (b) Beisel, T.; Manolikakes, G. *Org. Lett.* **2013**, *15*, 6046. (c) Vogt, A. P.; Trouillet, V.; Greiner, A. M.; Kaupp, M.; Geckle, U.; Barner, L.; Hofe, T.; Barner-Kowollik, C. *Macromol. Rapid Commun.* **2012**, *33*, 1108. (d) Miura, T.; Takahashi, Y.; Murakami, M. *Org. Lett.* **2007**, *9*, 5075. (e) Nishikata, T.; Yamamoto, Y.; Miyaura, N. *Angew. Chem. Int. Ed.* **2003**, *42*, 2768. (f) Lam, P. Y. S.; Clark, C. G.; Saubern, S.; Adams, J.; Winters, M. P.; Chan, D. M. T.; Combs, A. *Tetrahedron Lett.* **1998**, *39*, 2941. (g) Evans, D. A.; Katz, J. L.; West, T. R. *Tetrahedron Lett.* **1998**, *39*, 2937.

(3) (a) Candeias, N. R.; Montalbano, F.; Cal, P. M. S. D.; Gois, P. M. P. *Chem. Rev.* **2010**, *110*, 6169. (b) Kaiser, P. F.; Churches, Q. I.; Hutton, C. A. *Aust. J. Chem.* **2007**, *60*, 799.

(4) (a) Woerly, E. M.; Roy, J.; Burke, M. D. *Nat. Chem.* **2014**, *6*, 484. (b) Fujii, S.; Chang, S. Y.; Burke, M. D. *Angew. Chem. Int. Ed. Engl.* **2011**, *50*, 7862. (c) Woerly, E. M.; Cherney, A. H.; Davis, E. K.; Burke, M. D. *J. Am. Chem. Soc.* **2010**, *132*, 6941. (d) Knapp, D. M.; Gillis, E. P.; Burke, M. D. *J. Am. Chem. Soc.* **2009**, *131*, 6961. (e) Uno, B. E.; Gillis, E. P.; Burke, M. D. *Tetrahedron* **2009**, *65*, 3130. (f) Gillis, E. P.; Burke, M. D. *Aldrichimica Acta* **2009**, *42*, 17. (g) Gillis, E. P.; Burke, M. D. *J. Am. Chem. Soc.* **2008**, *130*, 14084. (h) Lee, S. J.; Gray, K. C.; Paek, J. S.; Burke, M. D. *J. Am. Chem. Soc.* **2008**, *130*, 466. (i) Gillis, E. P.; Burke, M. D. *J. Am. Chem. Soc.* **2007**, *129*, 6716.

(5) (a) Lightfoot, A. P.; Twiddle, S. J. R.; Whiting, A. *Org. Biomol. Chem.* **2005**, *3*, 3167. (b) Lightfoot, A. P.; Maw, G.; Thirsk, C.; Twiddle, S. J. R.; Whiting, A. *Tetrahedron Lett.* **2003**, *44*,

7645.

(6) (a) Iwadate, N.; Suginome, M. *Org. Lett.* **2009**, *11*, 1899. (b) Noguchi, H.; Shioda, T.; Chou, C.-M.; Suginome, M. *Org. Lett.* **2008**, *10*, 377. (c) Noguchi, H.; Hojo, K.; Suginome, M. *J. Am. Chem. Soc.* **2007**, *129*, 758.

(7) (a) Darses, S.; Genet, J.-P. *Chem. Rev.* **2008**, *108*, 288. (b) Molander, G. A.; Ellis, N. *Acc. Chem. Res.* **2007**, *40*, 275. (c) Molander, G. A.; Fumagalli, T. *J. Org. Chem.* **2006**, *71*, 5743. (d) Molander, G. A.; Yun, C.-S.; Ribagorda, M.; Biolatto, B. *J. Org. Chem.* **2003**, *68*, 5534. (e) Molander, G. A.; Biolatto, B. *J. Org. Chem.* **2003**, *68*, 4302.

(8) (a) Lennox, A. J. J.; Lloyd-Jones, G. C. *J. Am. Chem. Soc.* **2012**, *134*, 7431. (b) Butters, M.; Harvey, J. N.; Jover, J.; Lennox, A. J. J.; Lloyd-Jones, G. C.; Murray, P. M. *Angew. Chem. Int. Ed.* **2010**, *49*, 5156.

(9) Yuen, A. K. L.; Hutton, C. A. *Tetrahedron Lett.* **2005**, *46*, 7899.

(10) Vedejs, E.; Chapman, R.; Fields, S.; Lin, S.; Schrimpf, M. *J. Org. Chem.* **1995**, *60*, 3020.

(11) Lennox, A. J. J.; Lloyd-Jones, G. C. *Angew. Chem. Int. Ed.* **2012**, *51*, 9385.

(12) Murphy, J. M.; Tzschucke, C. C.; Hartwig, J. F. *Org. Lett.* **2007**, *9*, 757.

(13) Kim, B. J.; Matteson, D. S. *Angew. Chem. Int. Ed. Engl.* **2004**, *43*, 3056.

(14) Kolomeitsev, A. A.; Kadyrov, A. A.; Szczepkowska-Sztolcman, J.; Milewska, M.; Koroniak, H.; Bissky, G.; Barten, J. A.; Roschenthaler, G.-V. *Tetrahedron Lett.* **2003**, *44*, 8273.

(15) Molander, G. A.; Pfeiffer, D. *Org. Lett.* **2001**, *3*, 361.

(16) Parsons, A. T.; Senecal, T. D.; Buchwald, S. L. *Angew. Chem. Int. Ed.* **2012**, *51*, 2947.

(17) (a) Lee, J. C. H.; McDonald, R.; Hall, D. G. *Nat. Chem.* **2011**, *3*, 894. (b) Lee, J. C. H.; Hall, D. G. *J. Am. Chem. Soc.* **2010**, *132*, 5544.

(18) Ihara, H.; Koyanagi, M.; Suginome, M. *Org. Lett.* **2011**, *13*, 2662.

(19) Molander, G. A.; Cavalcanti, L. N.; Canturk, B.; Pan, P.-S.; Kennedy, L. E. *J. Org. Chem.* **2009**, *74*, 7364.

(20) (a) Pei, W.; Krauss, I. J. *J. Am. Chem. Soc.* **2011**, *133*, 18514. (b) Mitra, S.; Gurrala, S. R.;

Coleman, R. S. *J. Org. Chem.* **2007**, *72*, 8724.

(21) (a) Hohn, E.; Paleček, J.; Pietruszka, J.; Frey, W. *Eur. J. Org. Chem.* **2009**, 3765. (b) Hohn, E.; Paleček, J.; Pietruszka, J. *Synlett* **2008**, 971.

(22) (a) Touchet, S.; Carreaux, F.; Molander, G. A.; Carboni, B.; Bouillon, A. *Adv. Synth. Catal.* **2011**, *353*, 3391. (b) Inglis, S. R.; Woon, E. C. Y.; Thompson, A. L.; Schofield, C. J. *J. Org. Chem.* **2010**, *75*, 468. (c) Yamamoto, Y.; Hattori, K.; Ishii, J.-I.; Nishiyama, H. *Tetrahedron* **2006**, *62*, 4294.

(23) Noda, H.; Bode, J. W. *Chem. Sci.* **2014**, *5*, 4328.

(24) Potassium vinyltrifluoroborate AUD$2915/mol, vinyl MIDA boronate AUD$5124/mol, Sigma-Aldrich, May 15, 2015.

(25) Brown, H. C.; Park, W. S.; Cha, J. S.; Cho, B. T.; Brown, C. A. *J. Org. Chem.* **1986**, *51*, 337.

(26) Molander, G. A.; Trice, S. L. J.; Dreher, S. D. *J. Am. Chem. Soc.* **2010**, *132*, 17701.

(27) Molander, G. A.; Ellis, N. M. *J. Org. Chem.* **2006**, *71*, 7491.

(28) Mundal, D. A.; Lutz, K. E.; Thomson, R. J. *J. Am. Chem. Soc.* **2012**, *134*, 5782.

(29) Murata, M.; Oda, T.; Watanabe, S.; Masuda, Y. *Synthesis* **2007**, *2007*, 351.

(30) Clary, J. W.; Rettenmaier, T. J.; Snelling, R.; Bryks, W.; Banwell, J.; Wipke, W. T.; Singaram, B. *J. Org. Chem.* **2011**, *76*, 9602.

(31) Morandi, F.; Caselli, E.; Morandi, S.; Focia, P. J.; Blázquez, J.; Shoichet, B. K.; Prati, F. *J. Am. Chem. Soc.* **2003**, *125*, 685.

(32) Southwood, T. J.; Curry, M. C.; Hutton, C. A. *Tetrahedron* **2006**, *62*, 236.

(33) Yang, C.-T.; Zhang, Z.-Q.; Tajuddin, H.; Wu, C.-C.; Liang, J.; Liu, J.-H.; Fu, Y.; Czyzewska, M.; Steel, P. G.; Marder, T. B.; Liu, L. *Angew. Chem. Int. Ed.* **2012**, *51*, 528.

(34) Kaupp, G.; Naimi-Jamal, M. R.; Stepanenko, V. *Chem. Eur. J.* **2003**, *9*, 4156.

(35) Mancilla, T.; Contreras, R. *J. Organomet. Chem.* **1986**, *307*, 1.

(36) Jabbour, A.; Steinberg, D.; Dembitsky, V. M.; Moussaieff, A.; Zaks, B.; Srebnik, M. *J. Med. Chem.* **2004**, *47*, 2409.

(37) Aronovich, P. M.; Mikhailov, B. M. *Izv. Akad. Nauk SSSR, Ser. Khim.* **1968**, 2745.