

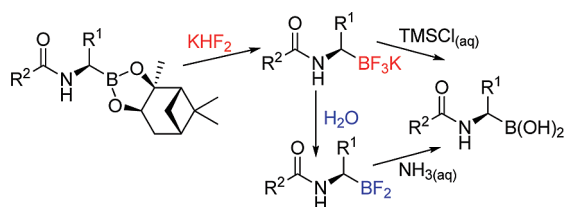
Observations on the Deprotection of Pinanediol and Pinacol Boronate Esters via Fluorinated Intermediates

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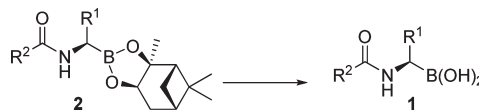
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methods for the synthesis of chiral alkyl boronic acids of general structure **1**, normally involving protection of the boronic acid group as esters of chiral diols (e.g., pinanediol, as illustrated for **2**) (reviewed in Matteson⁹). Deprotection of these esters can be achieved by methods including cleavage with boron trichloride,^{10,11} transesterification with other boronic acids,¹² or acidic hydrolysis.^{3,13,14} The success of these approaches varies for reasons including functional group incompatibilities, impure product mixtures, and difficulties in separation of the free diol from the boronic acid without reformation of the ester (a solid phase technique has been developed to assist with this¹⁵). Although the *N*-methyliminodiacetic acid boronate, an alternative readily removable boronic acid protecting group, has been reported,¹⁶ there remains a need for improved methods for deprotection of pinanediol boronate esters,¹¹ because of the useful chiral induction properties of the pinanediol group.



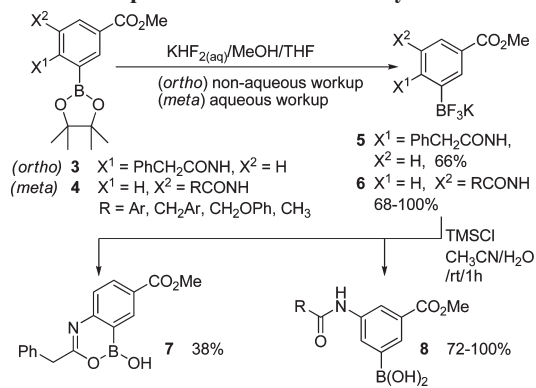
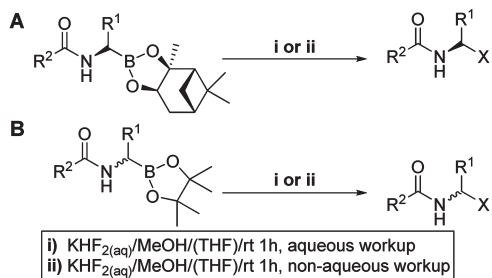
Methods for the deprotection of pinanediol and pinacol esters of various boronic acids via fluoroborane intermediates were evaluated. Treatment of the boronate esters with potassium hydrogen difluoride normally gives trifluoroborate salts; in the case of α -amido alkyl or *o*-amido phenyl boronate esters, aqueous workup gives difluoroboranes. Procedures for transformation of both trifluoroborates and difluoroboranes to free boronic acids are described.

In the course of work on the development of phenylboronic acids as inhibitors of penicillin binding proteins, we evaluated various methods for the deprotection of pinacol phenylboronate esters.⁵ A series of substituted phenylboronic acid pinacol esters **3** and **4** were deprotected in good yields by treatment with potassium hydrogen difluoride (KHF₂) to generate the trifluorinated intermediates **5** and **6** which were hydrolyzed in the presence of trimethylsilyl chloride (TMSCl) to give the boronic acids **7** and **8** (Scheme 1), according to the method of Yuen and Hutton,¹⁷ which was based on the pioneering work of Vedejs et al.¹⁸ Here we report the application of this methodology to the deprotection of other boronate esters including α -amido pinanediol boronate esters. We found that in cases where a neighboring amide carbonyl group can coordinate with the boron, difluoroboranes, instead of trifluoroborates, could be isolated, depending on the workup procedure used. We also report

Boronic acids are used as inhibitors of enzymes bearing nucleophilic residues at their active sites. Numerous studies on the synthesis and biological evaluation of boronic acid derivatives as inhibitors of enzymes including serine proteases (for reviews see Walker and Lynas¹ and Yang et al.²), β -lactamases,^{3,4} penicillin binding proteins,^{5–7} and the human proteasome⁸ have been reported. There are established

- (1) Walker, B.; Lynas, J. F. *Cell. Mol. Life Sci.* **2001**, *58*, 596–624.
- (2) Yang, W.; Gao, X.; Wang, B. *Med. Res. Rev.* **2003**, *23*, 346–368.
- (3) Morandi, F.; Caselli, E.; Morandi, S.; Focia, P. J.; Blazquez, J.; Shoichet, B. K.; Prati, F. *J. Am. Chem. Soc.* **2003**, *125*, 685–695.
- (4) Venturelli, A.; Tondi, D.; Cancian, L.; Morandi, F.; Cannazza, G.; Segatore, B.; Prati, F.; Amicosante, G.; Shoichet Brian, K.; Costi, M. P. *J. Med. Chem.* **2007**, *50*, 5644–5654.
- (5) Inglis, S. R.; Zervosen, A.; Woon, E. C. Y.; Gerards, T.; Teller, N.; Fischer, D. S.; Luxen, A.; Schofield, C. J. *J. Med. Chem.* **2009**, *52*, 6097–6106.
- (6) Nicola, G.; Peddi, S.; Stefanova, M.; Nicholas, R. A.; Gutheil, W. G.; Davies, C. *Biochemistry* **2005**, *44*, 8207–8217.
- (7) Pechenov, A.; Stefanova, M. E.; Nicholas, R. A.; Peddi, S.; Gutheil, W. G. *Biochemistry* **2003**, *42*, 579–588.
- (8) Dorsey, B. D.; Iqbal, M.; Chatterjee, S.; Menta, E.; Bernardini, R.; Bernareggi, A.; Cassara, P. G.; D'Arasmo, G.; Ferretti, E.; De Munari, S.; Oliva, A.; Pezzoni, G.; Allievi, C.; Strepponi, I.; Ruggeri, B.; Ator, M. A.; Williams, M.; Mallamo, T. J. *J. Med. Chem.* **2008**, *51*, 1068–1072.

- (9) Matteson, D. S. *Tetrahedron* **1998**, *54*, 10555–10606.
- (10) Kinder, D. H.; Katzenellenbogen, J. A. *J. Med. Chem.* **1985**, *28*, 1917–1925.
- (11) Matteson, D. S.; Jesthi, P. K.; Sadhu, K. M. *Organometallics* **1984**, *3*, 1284–1288.
- (12) Snow, R. J.; Bachovchin, W. W.; Barton, R. W.; Campbell, S. J.; Coutts, S. J.; Freeman, D. M.; Gutheil, W. G.; Kelly, T. A.; Kennedy, C. A.; Krolikowski, D. A.; Leonard, S. F.; Pargellis, C. A.; Tong, L.; Adams, J. *J. Am. Chem. Soc.* **1994**, *116*, 10860–10869.
- (13) Morandi, S.; Morandi, F.; Caselli, E.; Shoichet, B. K.; Prati, F. *Bioorg. Med. Chem.* **2008**, *16*, 1195–1205.
- (14) Thomson, J. M.; Distler, A. M.; Prati, F.; Bonomo, R. A. *J. Biol. Chem.* **2006**, *281*, 26734–26744.
- (15) Pennington, T. E.; Cynantya, K. B.; Hutton, C. A. *Tetrahedron Lett.* **2004**, *45*, 6657–6660.
- (16) Gillis, E. P.; Burke, M. D. *J. Am. Chem. Soc.* **2008**, *130*, 14084–14085.
- (17) Yuen, A. K. L.; Hutton, C. A. *Tetrahedron Lett.* **2005**, *46*, 7899–7903.
- (18) Vedejs, E.; Chapman, R. W.; Fields, S. C.; Lin, S.; Schrimpf, M. R. *J. Org. Chem.* **1995**, *60*, 3020–3027.

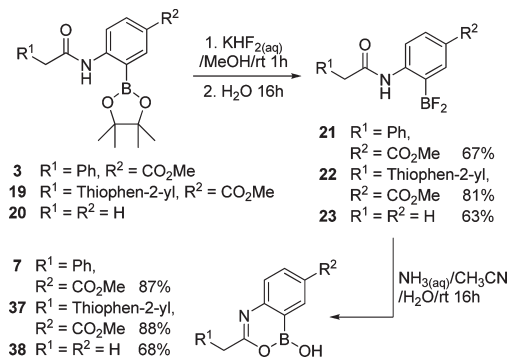
SCHEME 1. Deprotection of Pinacol Phenyl Boronates⁵SCHEME 2. Fluoroboranes from α -Amido Boronates

Sch.	Start. Mat.	R ¹	R ²	Meth.	Prod.	X	Yield %
A	9	$\text{CH}_2\text{CH}(\text{CH}_3)_2$	PhCH_2	i	11	BF_3K	65
A	10	Ph	$(\text{Thiophen-2-yl})\text{CH}_2$	ii	30	BF_3K	17
A	9	$\text{CH}_2\text{CH}(\text{CH}_3)_2$	PhCH_2	i	12	BF_2	39
A	39	$\text{CH}_2\text{CH}(\text{CH}_3)_2$	2,6-Dimethoxyphenyl	i	35	BF_2	60
A	13	$\text{CH}_2\text{CH}(\text{CH}_3)_2$	$(\text{Thiophen-2-yl})\text{CH}_2$	i	15 (17)	BF_2 (BF_3K)	56 (10)
A	13	$\text{CH}_2\text{CH}(\text{CH}_3)_2$	$(\text{Thiophen-2-yl})\text{CH}_2$	ii	17	BF_3K	44
B	14	$\text{CH}_2\text{CH}(\text{CH}_3)_2$	$(\text{Thiophen-2-yl})\text{CH}_2$	i	16	BF_2	77
B	14	$\text{CH}_2\text{CH}(\text{CH}_3)_2$	$(\text{Thiophen-2-yl})\text{CH}_2$	ii	18	BF_3K	91

on the evaluation of procedures for the conversion of the different fluorinated intermediates into free boronic acids.

When preparing trifluoroborate salts from their parent diol esters, both separation of the trifluoroborate salt from the diol and isolation of the trifluoroborate salt from the excess KHF_2 are necessary. The first process can be achieved by washing the crude salt with a nonpolar solvent, while the second can involve either aqueous (washing) or nonaqueous (extraction with hot solvent) procedures (Scheme 1). While the initially reported method¹⁷ used nonaqueous conditions, in application of this method to the preparation of substituted phenyl boronic acids,⁵ we found it easier to use an aqueous procedure in most cases.

Because of the biomedical importance of peptide boronic acids, we investigated the extension of the fluoroborate methodology for the deprotection of α -amido pinanediol boronates (Scheme 2). In initial work on **9** and **10**, we tested both aqueous and nonaqueous workup procedures, and found it was possible to obtain salt **11** from **9** by aqueous workup in good yield, provided that the amount of water used was minimized. When an excess of water was used, it was noted that significant quantities of product were being carried to the filtrate. Instead of the anticipated trifluoroborate salt, this material was identified as the corresponding

SCHEME 3. Deprotection of *o*-Amido Pinacol Phenylboronates via Difluoroboranes

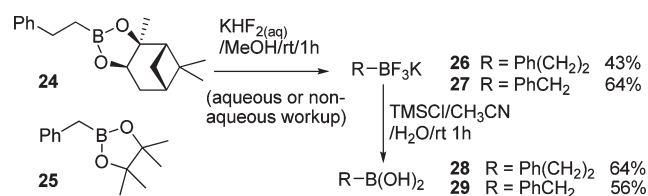
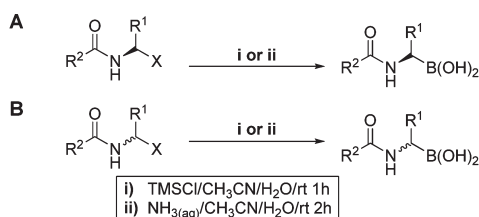
difluoroborane **12** (Scheme 2). Difluoroborane analogues of α -amido alkyl boronic acids have been previously reported, but were prepared from their corresponding boronic acids by treatment with aqueous hydrofluoric acid.¹⁰ Trifluoroborate **11** was converted to the difluoroborane **12** by suspension in water with stirring; almost complete conversion was observed after 1 h (overnight stirring gave complete conversion).

A comparison of the different workup procedures was made with the use of α -amido pinanediol boronate **13** and pinacol ester **14** (Scheme 2). For both **13** and **14**, use of aqueous or nonaqueous workup procedures gave the difluoroboranes (**15** and **16**) and the trifluoroborate products (**17** and **18**), respectively. Yields were lower in the cases of reaction of **13**. In the case of the nonaqueous procedure, this is probably due to the poor solubility of product **17** in hot acetone during workup in the presence of pinanediol. In the case of the aqueous procedure, this is probably due to loss of material because of partial solubility in water (some **17** later crystallized from the aqueous phase).

We have prepared the trifluoro *o*-amido phenylborate salt **5** from its parent pinacol ester **3** via the nonaqueous workup procedure⁵ (Scheme 1); however, the product **5** was difficult to isolate. In contrast, a series of *m*-amido pinacol phenylboronates of general structure **4** were converted into the corresponding trifluoroborates **6** in good yields and purities with use of the aqueous workup procedure⁵ (Scheme 1). We were then interested in whether application of the aqueous workup could serve as an improvement to the procedure for formation of trifluoroborates of *o*-amido phenylboronic acids. Following treatment of **3**, **19**, and **20** with KHF_2 , exposure of the isolated intermediates to water led to formation of the difluoroboranes **21**, **22**, and **23** in good yields (Scheme 3) in a manner similar to that used for the α -amido alkyl compounds (Scheme 2). Generation of the difluoroborane **21** as described here gives an improvement in the yield, purity, and ease of application compared to the preparation of the corresponding trifluoroborate salt **5**.⁵

The conversion of simple pinanediol and pinacol alkylboronates into potassium trifluoroborates was also investigated (Scheme 4). When applying this methodology to **24** and **25**, it was found that the nonaqueous workup procedure was preferable because of the relatively high solubility of the products in water, leading to lower yields for the aqueous procedure; this highlights a limitation of the

SCHEME 4. Deprotection of Simple Alkyl Boronates

SCHEME 5. Conversion of α -Amido Fluoroboranes into Boronic Acids

Sch.	Start. Mat.	R ¹	R ²	X	Meth.	Prod.	Yield %
A	11	CH ₂ CH(CH ₃) ₂	PhCH ₂	BF ₃ K	i	31	51
A	30	Ph	(Thiophen-2-yl)CH ₂	BF ₃ K	i	32	52
A	12	CH ₂ CH(CH ₃) ₂	PhCH ₂	BF ₂	ii	31	81
A	35	CH ₂ CH(CH ₃) ₂	2,6-Dimethoxyphenyl	BF ₂	ii	36	41 ^a
A	15	CH ₂ CH(CH ₃) ₂	(Thiophen-2-yl)CH ₂	BF ₂	ii	34	85
B	18	CH ₂ CH(CH ₃) ₂	(Thiophen-2-yl)CH ₂	BF ₃ K	i	33	77
B	18	CH ₂ CH(CH ₃) ₂	(Thiophen-2-yl)CH ₂	BF ₃ K	ii	33	78 ^b
B	16	CH ₂ CH(CH ₃) ₂	(Thiophen-2-yl)CH ₂	BF ₂	ii	33	77
B	16	CH ₂ CH(CH ₃) ₂	(Thiophen-2-yl)CH ₂	BF ₂	i	33	80 ^c

^aPrior to optimization. ^bOvernight reaction. ^cReaction 50% complete.

aqueous workup method. Notably, the trifluoroborates **26** and **27** were isolated in these cases, even after exposure of the products to water.

Although transformation of pinanediol alkylboronates to potassium^{19,20} and cesium²¹ trifluoroborate salts has been reported (reviewed in Darses and Genet²²), conversion of these compounds into free boronic acids was not included as part of these investigations. As reported,¹⁷ an effective method for the conversion of phenyltrifluoroborates into boronic acids is by treatment with TMSCl in aqueous acetonitrile (as illustrated for **7** and **8** in Scheme 1). Application of this method to the simple trifluoroborates **26** and **27** gave the boronic acids **28** and **29** (Scheme 4). When applied to α -amido trifluoroborates **11** and **30**, the respective boronic acids **31** and **32** were obtained in modest yields and variable purity, as judged by ¹H NMR spectroscopy (Scheme 5); however, the analytically pure trifluoroborate **18** was converted to the boronic acid **33** in high yield and purity by this method (Scheme 5).

We then investigated the hydrolysis of the difluoroborane intermediates. One example of conversion of a simple (non α -amido) difluoroborane into a boronic acid has been

reported; however, this was mediated by lithium aluminum hydride.²³ Treatment of the difluoroborane **16** with TMSCl in aqueous acetonitrile only resulted in 50% conversion to the boronic acid after 1 h (Scheme 5). When **12** was treated with either aqueous lithium hydroxide (5 equiv) or potassium carbonate (1.5 equiv) at room temperature overnight, no reaction was observed. It has been reported that difluoroboranes are readily hydrolyzed to free boronic acids in tris(hydroxymethyl)aminomethane (tris) buffer.¹⁰ Studies on difluoroborane **15** in D₂O/CD₃CN involving ¹H and ¹⁹F NMR spectroscopy (Figure S-41, Supporting Information) revealed this difluoroborane was not hydrolyzed rapidly in water alone. Addition of dilute aqueous ammonia led to efficient hydrolysis of the difluoroborane to give **34**. This reaction may proceed via initial reaction of ammonia on the boron atom; an analogous mechanism is plausible in tris buffer.¹⁰

Treatment of difluoroboranes **12**, **15**, **16**, and **35** with aqueous ammonia on a preparative scale led to their conversion to the boronic acids **31**, **34**, **33**, and **36**, respectively, in good yields (Scheme 5). ¹⁹F NMR confirmed the products were free of fluorine. To verify that the deprotection procedures did not affect optical purity, the boronic acid **31** was reconverted to its pinanediol boronate ester **9**; the optical rotation was consistent with that of an original enantiopure sample of **9** (Scheme S-1, Supporting Information). Treatment of the *o*-amido aryl difluoroboranes **21**–**23** with aqueous ammonia solution also mediated hydrolysis to give the benzoxazaborinines **7**, **37**, and **38**, respectively, in good yields (Scheme 3). We had previously prepared **7** from its trifluoroborate precursor by treatment with TMSCl (Scheme 1);⁵ however, the overall yield was low. The two-step procedure presented here is an improved method for the preparation of this class of boronic acids from their pinacol protected precursors. For comparison with the difluoroboranes, we investigated the hydrolysis of a *m*-amido phenyl trifluoroborate **6** (Scheme 1) with aqueous ammonia by ¹H and ¹⁹F NMR spectroscopy, as described above for **15**. These studies revealed the trifluoroborate was hydrolyzed under these conditions (data not shown), but at a slower rate than the TMSCl procedure. Similarly, the α -amido alkyl trifluoroborate, **18**, was converted to boronic acid **33** by aqueous ammonia treatment, but at a comparatively much slower rate than with the difluoroboranes (Scheme 5).

The different behavior of the α -amido alkyl and *o*-amido phenylboronic acids, with respect to trifluoroborate or difluoroborane isolation, compared with the unfunctionalized alkyl and *m*-amido phenylboronic acids, on exposure of their trifluoroborate salts to water, suggests that neighboring group participation is important for conversion to the difluoroborane. This is likely to involve the amido carbonyl oxygen atom reacting with the boron intramolecularly. Where this interaction cannot occur, the trifluoroborate is obtained independent of the workup procedure employed. Where neighboring group participation occurs, we propose that the partially water-soluble trifluoroborate salt loses a fluoride ion, leading to precipitation of the relatively water insoluble difluoroborane (Figure 1).

(19) Kim, B. J.; Matteson, D. S. *Angew. Chem., Int. Ed.* **2004**, *43*, 3056–3058.

(20) Matteson, D. S.; Kim, G. Y. *Org. Lett.* **2002**, *4*, 2153–2155.

(21) Matteson, D. S.; Maliakal, D.; Pharezyn, P. S.; Kim, B. J. *Synlett* **2006**, 3501–3503.

(22) Darses, S.; Genet, J.-P. *Eur. J. Org. Chem.* **2003**, 4313–4327.

(23) Al-Juaid, S. S.; Eaborn, C.; El-Kheli, M. N. A.; Hitchcock, P. B.; Lickiss, P. D.; Molla, M. E.; Smith, J. D.; Zora, J. A. *J. Chem. Soc., Dalton Trans.* **1989**, 447–452.

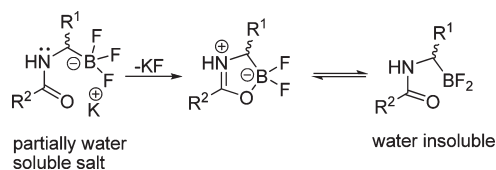


FIGURE 1. Possible mechanism for the formation of difluoroboranes from trifluoroborates.

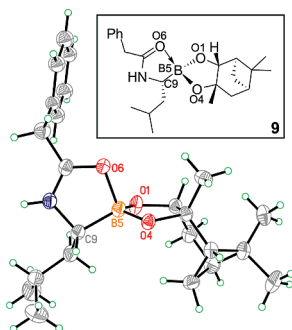


FIGURE 2. Thermal ellipsoid plot of **9** showing the tetrahedral coordination at boron; B5 lies 0.376 Å out of the plane defined by O1, O4, and C9. Selected bond lengths: B5–O1 1.418(3) Å, B5–O4 1.438(3) Å, B5–O6 1.638(3) Å, B5–C9 1.629(3) Å, compared with B–O = 1.37(3) Å; B–C = 1.56(3) Å for three-coordinate boron in CBO₂ motifs reported in the Cambridge Structural Database.^{28,29} Ellipsoids are drawn at the 50% probability and the minor component of the disorder is omitted for clarity.

Evidence for neighboring group participation came from a crystal structure of the pinanediol boronate **9** (Figure 2),²⁴ which reveals reaction of the α -amido oxygen atom with boron, causing the boron atom to have tetrahedral character. Related structures have been reported.^{12,25–27} The IR spectrum of **9** in the solid state contained a band at 1599 cm⁻¹, which is low for an amide CO stretch. This band was shifted to 1651 cm⁻¹ in the solution IR spectrum of **9**, suggesting that the intramolecular reaction is less important in solution. IR spectra of the difluoroboranes (e.g., **12** and **15**) typically displayed amide bands in the region 1635 and 1610 cm⁻¹ for the solid and liquid states, respectively, consistent

(24) The structure was determined from single-crystal X-ray diffraction data collected at low temperature with an Oxford Cryosystems Cryostream N₂ open-flow cooling device.³⁰ Data were collected with an Enraf-Nonius KappaCCD diffractometer (Mo K α radiation; $\lambda = 0.71073$ Å) and processed with the DENZO-SMN package,³¹ including interframe scaling (which was carried out with Scalepack within DENZO-SMN). The structure was solved with SIR92.³² Refinement was carried out with full-matrix least squares within the CRYSTALS suite³³ on F^2 . For further details see the crystallographic information file (CIF).³⁴

(25) Besong, G.; Jarowicki, K.; Kocienski, P. J.; Sliwinski, E.; Boyle, F. T. *Org. Biomol. Chem.* **2006**, *4*, 2193–2207.

(26) Lange, H.; Beirgander, K.; Frohlich, R.; Kehr, S.; Nakamura, S.; Shibata, N.; Toru, T.; Hoppe, M. *Chem.—Asian J.* **2008**, *3*, 88–101.

(27) Matteson, D. S.; Michnick, T. J.; Willett, R. D.; Patterson, C. D. *Organometallics.* **1989**, *8*, 726–729.

(28) Allen, F. H. *Acta Crystallogr. B* **2002**, *58*, 380–388.

(29) Bruno, I. J.; Cole, J. C.; Edgington, P. R.; Kessler, M.; Macrae, C. F.; McCabe, P.; Pearson, J.; Taylor, R. *Acta Crystallogr. B* **2002**, *58*, 389–397.

(30) Cosier, J.; Glazer, A. M. *J. Appl. Crystallogr.* **1986**, *19*, 105–107.

(31) Otwinowski, Z.; Minor, W. Processing of X-ray Diffraction Data Collected in Oscillation Mode. In *Methods Enzymology*; Carter, C. W., Sweet, R. M., Eds.; Academic Press: New York, 1997; Vol. 276.

(32) Altomare, A.; Casciarano, G.; Giacovazzo, G.; Guagliardi, A.; Burla, M. C.; Polidori, G.; Camalli, M. *J. Appl. Crystallogr.* **1994**, *27*, 435.

(33) Betteridge, P. W.; Carruthers, J. R.; Cooper, G. I.; Prout, C. K.; Watkin, D. J. *J. Appl. Crystallogr.* **2003**, *36*, 1487–1487.

with the intramolecular reactions observed for crystals of **9**, suggesting an intramolecular stabilization of the difluoroboranes.

In summary, both α -amido alkyl pinanediolboronates, and *o*-amido pinacol phenylboronates can be deprotected to their free boronic acids via trifluoroborate or difluoroborane intermediates, by using different workup procedures. The choice of either the nonaqueous or aqueous procedure depends on the solubility properties of the fluorinated intermediates (in organic solvents or water) and the ease with which the different products will crystallize or precipitate. In our experience, the success of the nonaqueous method to prepare trifluoroborate salts may also be influenced by the purity of the starting material; in contrast, it is possible for crude starting materials, carried through several steps without purification, to be converted into analytically pure difluoroboranes by the aqueous procedure. The difluoroboranes are best converted into boronic acids by treatment with aqueous ammonia, while trifluoroborates are best converted to the same by treatment with TMSCl. These observations should assist in the sometimes problematic deprotection of pinanediol and pinacol boronate esters, providing a new tool in the synthesis of biologically important boronic acids.

Experimental Section

Example procedures are given below (full experimental details are provided in Supporting Information).

***N*-[(1*R*)-1-(Difluoroboryl)-3-methylbutyl]-2-(2-thienyl)acetamide, **15**.** To a stirred solution of boronate **13** (0.336 g, 0.863 mmol) in methanol (9 mL) was added 4.5 M KHF_{2(aq)} (1.8 mL, 8.10 mmol). {**Note:** KHF₂ is corrosive and discolors glassware after prolonged exposure.} The resulting mixture was stirred for 1 h at rt, then concentrated to dryness. The resulting solid was collected by filtration and washed with hot ether (5 \times 15 mL). The remaining solid was suspended in water (25 mL) and stirred overnight. The solid was collected, washed with a little water, and dried to give **15** (0.126 g, 56%) as a white powder, mp 125–135 °C. Anal. Calcd for C₁₁H₁₆BF₂NOS: C, 50.99; H, 6.22; N, 5.41. Found: C, 50.91; H, 6.15; N, 5.39.

{(1*R*)-3-Methyl-1-[(phenylacetyl)amino]butyl}boronic Acid, **31.** Difluoroborane **12** (100 mg, 0.39 mmol) was stirred in CH₃CN (7.5 mL) and water (5 mL) before addition of an 8% NH_{3(aq)} solution (1.5 mL). The mixture was stirred at rt for 2 h before being concentrated carefully under vacuum to a volume of \sim 3 mL, at which point precipitation was observed. The mixture was extracted with ethyl acetate; the combined extracts were washed with brine and dried (Na₂SO₄), and the solvent was removed to give **31** (80 mg, 81%) as a white solid, mp 85–100 °C. Anal. Calcd for C₁₃H₂₀BNO₃: C, 62.68; H, 8.09; N, 5.62. Found: C, 62.72; H, 8.03; N, 5.49.

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Supporting Information Available: Full experimental details, NMR spectra, and NMR studies on the hydrolysis of difluoroboranes. This material is available free of charge via the Internet at <http://pubs.acs.org>.

(34) Crystallographic data for compound **9** have been deposited with the Cambridge Crystallographic Data Centre, CCDC 749874, which can be obtained free of charge via the Internet at www.ccdc.cam.ac.uk/data_request/cif.