Tetrahedron 65 (2009) 9956–9960

Contents lists available at ScienceDirect

Tetrahedron

journal homepage: www.elsevier.com/locate/tet

Improved method for the conversion of pinacolboronic esters into trifluoroborate salts: facile synthesis of chiral secondary and tertiary trifluoroborates

Viktor Bagutski, Abel Ros, Varinder K. Aggarwal *

School of Chemistry, University of Bristol, Cantock's Close, Bristol BS8 1TS, UK

ARTICLE INFO

Article history:
Received 21 August 2009
Received in revised form
16 September 2009
Accepted 2 October 2009
Available online 8 October 2009

ABSTRACT

A general method for the preparation of virtually any potassium trifluoroborate salt from the corresponding pinacolboronic ester is reported. Thus, conditions for an azeotropic removal of pinacol from the reaction mixture were found to afford the desired potassium trifluoroborates of sufficient purity (>95%) in nearly quantitative yields irrespective of the nature of the product. The utility of this method is illustrated by the preparation of a broad range of enantioenriched secondary and tertiary potassium trifluoroborates.

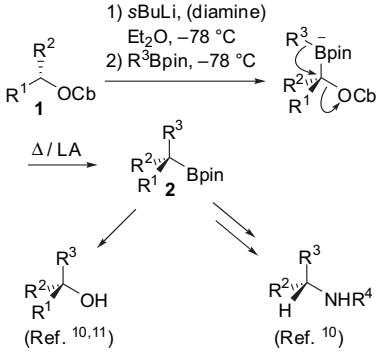
1. Introduction

Organotrifluoroborate salts have emerged in recent years as versatile coupling partners across a broad spectrum of reactions, often showing not only superior reactivity to their boronic ester cousins but also superior stability.[1] For example, whilst primary trifluoroborate salts[2] and alkyl boronic esters both readily participate in Suzuki–Miyaura reactions, the secondary alkyl substrates are limited to the trifluoroborate salts.[3] Rhodium-catalyzed 1,2- and 1,4-additions of organotrifluoroborate salts to aldehydes and Michael acceptors are also well established reactions.[4] Recently, enantioselective organocatalytic Michael additions of vinyl- and heteroaryltrifluoroborates to prochiral enals[5] and α-vinylations of aldehydes with vinyltrifluoroborates[6] have been reported. Furthermore, Matteson has reported the first example of the preparation of chiral secondary trifluoroborates and their conversion into amines.[7] Numerous reports of functional group interconversions in the presence of a trifluoroborate moiety, which remains intact to a broad range of reaction conditions, also add significant synthetic utility to this class of compounds.[8] This considerable research activity has been facilitated by Vedejs' simple protocol[9] for the preparation of organotrifluoroborate salts from the corresponding boronic acids (Scheme 1). Indeed, many salts are now commercially available.[10] However, we encountered a significant problem in the transformation of the α-branched pinacolboronic esters to the trifluoroborate salts using Vedejs' protocol and now report a simple modification which enables the salts to be prepared routinely in high yield and high purity.

Scheme 1. Vedejs' protocol for the preparation of trifluoroborate salts.

2. Results and discussion

We recently reported a new method for the preparation of enantioenriched secondary alcohols and amines[11] as well as chiral tertiary alcohols[12] by homologation of boronic pinacol esters with chiral primary and secondary lithiated carbamates (Scheme 2). The methodology showed broad substrate scope in terms of the carbamates and boronic esters employed.



Scheme 2. Preparation of chiral boronic esters by homologation of boronic esters with chiral α-lithiated primary and secondary carbamates (for R^1–R^3 see Table 1).

In order to enhance the utility of this chemistry further we recognised that transformation of the intermediate boronic esters into the corresponding trifluoroborate salts would open up new

* Corresponding author. Tel.: +44 117 954 6315; fax: +44 117 929 8611.
E-mail address: v.aggarwal@bristol.ac.uk (V.K. Aggarwal).

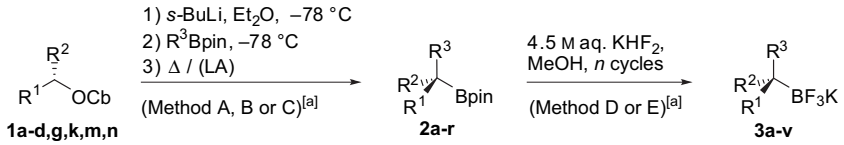
0040-4020/$ – see front matter © 2009 Elsevier Ltd. All rights reserved.
doi:10.1016/j.tet.2009.10.002

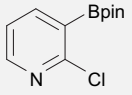
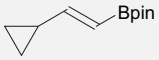
opportunities in synthesis. We therefore decided to first isolate the boronic esters, which were found to be sufficiently stable to silica gel for purification. Thus, following the reaction shown in Scheme 2, neutral aqueous work-up (1 M aqueous KH_2PO_4 was used) and subsequent 'dry-column' flash chromatography[13] gave the pinacolboronic esters in excellent yields, especially for the tertiary boronic esters **2g**–**q** (Table 1, entries 7–17).

derivatives has been achieved by re-crystallization[14] or by distilling off pinacol under vacuum.[15]

These literature procedures were initially employed but problems were invariably encountered. Thus, amongst the boronic esters **2a**–**r**, crystallization of the trifluoroborate salt (acetone/hexane) worked well for boronic ester **2o**, affording the salt **3o** in moderate yield (41%) but this procedure was not general. Hartwig's

Table 1
Synthesis of α-branched boronic esters **2a**–**r** and potassium trifluoroborates **3a**–**r**[a]



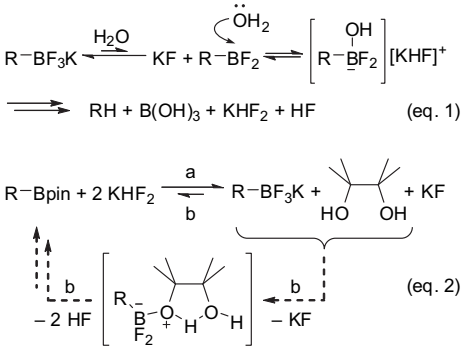
Entry		1a-d,g,k,m,n		R^3Bpin	2a-r		3a-v	
		R^1	R^2	R^3	Method	Yield % (ee)	Method	Yield % (*n*)
1	**a**	H	Me	Ph	A	63 (94)	D	95 (4)
2	**b**	H	Et	Ph	A	75 (92)	D	92 (4)
3	**c**	H	*i*-Pr	Ph	A	67 (92)	D	87 (4)
4	**d**	H	$Ph(CH_2)_2$–	Et	A	87 (94)	D	87 (5)
5	**d**	H	$Ph(CH_2)_2$–	Et	A	87 (94)	E	95 (5)
6	**e**	H	$Ph(CH_2)_2$–	*i*-Pr	A	64 (96)	D	86 (5)
7	**f**	H	$Ph(CH_2)_2$–	Ph	A	91 (94)	D	91 (3)
8	**g**	Ph	Me	Et	B	77 (99)	D	98 (1)
9	**h**	Ph	Me	*i*-Pr	B	93 (90)	D	99 (3)
10	**i**	Ph	Me	Vinyl	B	89 (96)	D	98 (3)
11	**i**	Ph	Me	Vinyl	B	89 (96)	E	97 (4)
12	**j**	Ph	Me	Allyl	B	92 (99)	D	99 (6)
13	**k**	Ph	Et	Allyl	B	90 (n.d.)	D	99 (3)
14	**l**	Ph	Me	Bn	B	78 (97)	D	99 (6)
15	**m**	4-ClC_6H_4–	Me	Et	B	83 (99)	D	98 (6)
16	**n**	4-$MeOC_6H_4$–	Me	Et	C	91 (96)	D	99 (9)
17	**o**	Ph	Me	4-ClC_6H_4–	B	79 (99)	D	95 (8)
18	**p**	Ph	Me	4-$MeOC_6H_4$–	B	70 (99)	D	94 (8)
19	**p**	Ph	Me	4-$MeOC_6H_4$–	B	70 (99)	E	96 (9)
20	**q**	4-$MeOC_6H_4$–	Me	4-ClC_6H_4–	C	76 (96)	D	94 (9)
21	**r**	Ph	Me	3-furyl	B	65 (98)	D	98 (4)
22	**s**						E	96 (3)
23	**t**						E	73 (4)
24	**u**	CH_2=C=CH–Bpin					E	73 (3)
25	**v**	Ph–C≡C–Bpin					E	68 (2)

[a] **Method A**. Primary carbamates (0.2 M in Et_2O) were deprotonated with 1.3 M *sec*-BuLi at −78 °C in the presence of 1 equiv of (−)-sparteine over 5 h and reacted with boronic ester. After formation of ate-complex, 1 equiv of 1 M ethereal solution of $MgBr_2$ was added and the reaction mixture was refluxed for 16 h. **Method B**. Secondary benzylic carbamates (0.25 M in Et_2O) were deprotonated with 1.3 M *sec*-BuLi at −78 °C within 20 min, reacted with an excess of boronic ester. After 30 at −78 °C, the reaction mixture was warmed up at room temperature and stirred for 4 h. **Method C**. Same as Method B except the deprotonation was performed within 5 min in the presence of 1 equiv of TMEDA. **Method D**. 0.2 M soln of boronic ester was treated at ambient temperature with saturated aq soln of KHF_2 (4.5 mmol per 1 mmol of substrate). After solvents removal, the residue was dissolved in aq MeOH, and the solvents were evaporated again. Dissolution–evaporation cycles were repeated *n* times. **Method E**. Method D was followed, except that 2.2 mmol of KHF_2 per 1 mmol of boronic ester was used. For details see Supplementary data and references therein.

In Vedejs' procedure (Scheme 1), a methanolic solution of a boron derivative RBY_2 (Y=OH was originally described but other derivatives have also been used,[1b,c] e.g., Y=halogen, –OR or $–NR_2$) is simply treated with an excess (3–4 equiv) of saturated aqueous solution of KHF_2. After solvents removal and re-crystallization, the trifluoroborate salt is then isolated in pure form. This procedure has been applied to a range of alkyl, alkenyl and aryl substrates but occasionally yields are only moderate, perhaps reflecting problems in finding suitable solvents for re-crystallization. In the case of the popularly used pinacolboronic esters purification of simple aryl

procedure[15] of removing pinacol by distillation in vacuo worked well only for **2g** (50 °C/0.05 mbar, over P_2O_5). When we applied Hartwig's modification of Vedejs' protocol to boronic ester **2k**, the crude trifluoroborate **3k** remained as an oil even after attempted continuous removal of pinacol in a Kugelrohr apparatus at 60 °C and 0.05 mbar. Furthermore, no crystallization of trifluoroborate salt **3k** could be induced even in hexane, in which it seemed soluble! In fact, repeated manipulation of the trifluoroborate salt in different solvents resulted in partial decomposition of **3k** via hydrolytic cleavage of the C–B-bond as well as increased amounts of

the starting boronic ester (Scheme 3, Eq. 1). Evidently, the pinacol by-product inhibited formation of the crystalline trifluoroborate salt and furthermore its presence may cause reformation of the boronic ester to some extent[16] (Scheme 3, Eq. 2).



Scheme 3. Rationale for formation–decomposition of trifluoroborate salts.

Clearly, a more effective method for removal of pinacol was required. After some experimentation, a simple and general solution for the purification of the trifluoroborate salts was discovered. It was found that pinacol could form an azeotrope with water under moderate vacuum, which was sufficiently volatile to be removed from the reaction mixture using a rotary evaporator. Moreover, the trifluoroborates displayed excellent stability against protodeboronation even upon prolonged/repeated treatment with a saturated aqueous-methanolic solution of KHF_2. Presumably, in spite of reversibility of the entire process, the equilibrium is shifted completely towards formation of the trifluoroborate salt due to the presence of excess of fluoride-anion (Scheme 3, Eq. 2). This feature is important when numerous repetitions of evaporation cycles are required. In a typical procedure, to a stirred 0.2 M solution of boronic ester in methanol an excess of saturated aqueous solution of KHF_2 (4.5 mmol per 1 mmol of substrate) was added and after stirring at room temperature all of the volatile materials were removed on a rotary evaporator (T_{bath} 45–50 °C/25–15 mbar). The solid residue was then re-dissolved in 50% aqueous methanol and the volatile materials were evaporated again. This step was repeated until ^{1}H NMR spectra of the crude mixture displayed less than 1 mol % of pinacol remaining [δ (CD_3CN) 1.14 ppm]. Finally, the crude mixture was extracted with acetone followed by filtration and evaporation to give, after drying in vacuo, the trifluoroborate salt in high purity. The number of dissolution–evaporation cycles (n) was found to depend on the physical nature of the product. Thus, for tertiary dialkylaryltrifluoroborates, three cycles were enough to ensure almost complete removal of pinacol (Table 1, entries 9–13; typically, less than 0.5 mol % of pinacol was detected by ^{1}H NMR spectroscopy). Secondary alkylaryl- or dialkyltrifluoroborates required 3–5 cycles (Table 1, entries 1–4, 6 and 7), whereas 6–9 cycles were necessary to remove pinacol contamination from tertiary diarylalkyltrifluoroborates. In general, the following trend was observed: if the crude product was already crystalline, no or few (up to three) dissolution–evaporation cycles were required for its purification (entries 8–10 and 13), whereas if it was a waxy syrup, then up to nine cycles were sometimes necessary (entries 14–18 and 20). Of particular note is that this method was also effective in the preparation of non-crystalline trifluoroborates **3d**, and **3e** (Table 1, entries 4 and 6).

We recognised that it would also be desirable to reduce the stoichiometry of KHF_2 if possible since its acidic character might interfere with basic functional groups. In fact our established method worked just as well when a slight excess (10%, i.e., 2.2 equiv instead of 4.5 equiv initially used) of KHF_2 was used, affording trifluoroborates **3d**,**i**,**p** (entries 5, 11 and 19) in similarly high yields.

Having developed an improved and simple procedure for the synthesis of α-branched secondary and tertiary trifluoroborates in nearly quantitative yields, we were encouraged to expand its scope towards other classes of trifluoroborate salts. Thus, the synthetically useful (2-chloro-3-pyridyl) pinacolboronic ester **1s** was converted into (2-chloro-3-pyridyl)trifluoroborate **3s** in excellent yield (entry 22). We also tested challenging boronic esters that are prone to decomposition/protodeboronation which included vinyl-, allenyl- and alkynyl substrates. These were converted into the corresponding substituted trifluoroborates in good yields (entries 23–25), showing that the new method has broad scope.

3. Conclusions

In conclusion, we have developed a general method for the conversion of virtually any pinacolboronic ester into the corresponding potassium trifluoroborate irrespective of its physical nature. With the increasing application of trifluoroborate salts in synthesis, this improved route to their preparation should facilitate such developments in the future. Further work in this area is ongoing in our laboratories.

4. Experimental section[17]

4.1. General procedure for the preparation of chiral secondary pinacolboronic esters (GP1A, Method A, Table 1)

To a stirred solution of alkylcarbamate (7.5 mmol) and freshly distilled (−)-sparteine (1.76 g, 7.5 mmol) in anhyd Et_2O (40 mL) chilled below −75 °C (dry ice/acetone bath) was added *sec*-BuLi (5.8 mL of 1.3 M solution in cyclohexane/hexane, 92:8, 7.5 mmol) at such a rate to keep the reaction temperature below −70 °C (~10–20 min). The reaction mixture was stirred at −78 °C for 5 h, and then the respective boronic ester (5 mmol, dissolved in 10 mL of anhyd Et_2O) was added at such a rate to keep the reaction temperature below −70 °C (~5–10 min). The reaction mixture was stirred at this temperature for an additional 30 min, the cooling bath was then removed, and ~0.5 M ethereal solution of $MgBr_2$ (10 mL; prepared prior use from 273 mg of Mg and 650 μL of 1,2-dibromoethane) was added all at once. The reaction mixture was stirred under reflux overnight, then cooled to 0–5 °C (ice-water bath) and 1 M aqueous $KHSO_4$ (20 mL) was added by vigorous stirring (*Caution! Gas evolution!*). After stirring at ambient temperature for an additional 10 min, the layers were separated, and the aqueous one was extracted with Et_2O (3×20 mL). The combined organic phases were washed with water (25 mL), brine (50 mL) and dried ($MgSO_4$). A crude product left after solvents removal was purified by flash chromatography, eluting with PE/EtOAc, 100:1→50:1 to give the pure secondary boronic ester.

*4.1.1. (R)-2-(1-Phenylethyl)-4,4,5,5-tetramethyl-1,3,2-dioxaborolane (**2a**).* According to GP1A, carbamate **1a** (1.82 g, 10.5 mmol) reacted with phenylboronic acid pinacol ester (1.43 g, 7.0 mmol) to give, after flash chromatography, 1.02 g (63%) of pure **2a** as a colourless oil. Oxidation of an aliquot of **2a** according to GP2[17] gave the corresponding alcohol in 94% ee. HPLC separation conditions: CHIRALCEL OD column, hexane/2-propanol (97.5:2.5), flow rate: 1.0 mL/min, T 20 °C; t_R 14.0 min for (*R*)-enantiomer (major) and 18.6 min for (*S*)-enantiomer (minor). The spectroscopic data have matched the previously published ones.[18] $[\alpha]_D^{20}$ −12.0 (c 1.5, $CHCl_3$).

4.2. General procedure for the preparation of chiral tertiary pinacolboronic esters (GP1B, Method B, Table 1)

To a stirred solution of a benzylcarbamate (5 mmol) in anhyd Et_2O (20 mL) chilled below −75 °C (dry ice/acetone bath) was

added *sec*-BuLi (4.3 mL of 1.3 M solution in cyclohexane/hexane, 92:8, 5.6 mmol) at such a rate to keep the reaction temperature below −70 °C (~10 min). The reaction mixture was stirred at this temperature for an additional 15 min, and the respective boronic ester (6–10 mmol, neat if it is a liquid, or as a 2 M solution in anhyd Et_2O when solid) was added by vigorous stirring at such a rate to keep the reaction temperature below −70 °C (~10 min). The reaction mixture was stirred at this temperature for an additional 30 min, the cooling bath was then removed and stirring was continued at ambient temperature for 4 h. After work-up with 1 M aq KH_2PO_4 (3 mL/mmol of carbamate; see Method A), the crude product was purified by 'dry-column' flash chromatography,[13] eluting with PE/MTBE, 50:1→30:1 to give the pure tertiary boronic ester.

4.3. GP1C (Method C, Table 1)

GP1B was followed, except that the deprotonation of a carbamate was performed in the presence of 1.1 equiv of TMEDA within 5 min.

*4.3.1. (S)-2-(2-Phenylbut-3-en-2-yl)-4,4,5,5-tetramethyl-1,3,2-dioxaborolane (**2i**).* According to GP1B, carbamate **1g** (748 mg, 3 mmol) reacted with vinylboronic acid pinacol ester (2.3 mL of 2 M solution in Et_2O, 4.6 mmol) to give, after flash chromatography and Kugelrohr distillation, 689 mg (89%) of pure **2i** as a colourless oil. Oxidation of an aliquot of **2i** according to GP2[17] gave the corresponding alcohol in 96% ee. For HPLC separation conditions see Ref. 11. ^{1}H NMR ($CDCl_3$, 400 MHz): δ 7.32–7.27 (m, 4H), 7.25–7.22 (m, 4H), 7.17 (tt, J=7.2, 1.5 Hz, 1H), 6.27 (dd, J=17.4, 10.6 Hz, 1H), 5.15 (dd, J=10.6, 1.4 Hz, 1H), 5.05 (dd, J=17.4, 1.4 Hz, 1H), 1.44 (s, 3H), 1.25 (s, 6H), 1.23 (s, 6H) ppm; ^{13}C NMR ($CDCl_3$, 75 MHz) δ 146.6, 144.1, 128.2, 127.3, 125.5, 112.3, 83.6, 24.5, 24.4, 22.2 ppm; ^{11}B NMR ($CDCl_3$, 96 MHz) δ 32.3 (s) ppm; IR (neat) nu(tilde) 3084, 3055, 2978, 2931, 2866, 1629, 1600, 1492, 1457, 1445, 1410, 1372, 1358, 1319, 1272, 1214, 1166, 1143, 1115, 1103, 1070, 1030, 1008, 965, 904, 869, 850, 762, 698, 671 cm^{-1}; MS (EI, 70 eV) *m*/*z* (%) 258 (87) [M$^+$], 243 (9), 231 (2), 201 (9), 185 (9), 172 (4), 158 (94), 142 (37), 131 (59), 115 (24), 105 (19), 101 (26), 91 (25), 84 (100), 77 (10), 69 (22), 55 (17); HRMS (EI) calcd for $C_{16}H_{23}BO_2$ [M]$^+$ 258.1791, found 258.1790; $[\alpha]_D^{23}$ −15.6 (*c* 10, CH_2Cl_2).

4.4. General procedure for preparation of chiral secondary and tertiary potassium alkyltrifluoroborates from pinacolboronic esters (GP3A, Method C, Table 1)

To a stirred solution of boronic ester (2 mmol) in methanol (10 mL) was added KHF_2 (2 mL of 4.5 M saturated aqueous solution, 9 mmol, 4.5 equiv, 2.25-fold excess) dropwise at ambient temperature and the reaction mixture was stirred for 30 min. Then, all of the volatile materials were removed on a rotary evaporator (50→15 mbar/45–50 °C; undesirable bumping of the mixture can be significantly minimized by adjusting the rotation speed), the residue was re-dissolved in 50% aq MeOH (12 mL) and all volatile materials were evaporated again. Evaporation–dissolution cycles were repeated until ^{1}H NMR analysis of an aliquot of the reaction mixture showed less than 1 mol % of pinacol (δ 1.14 [s, 12H]) ppm in acetonitrile-d_3; exact number of repetitions for any particular case is given in Table 1. The solid residue was then triturated with dry acetone (8 mL), the liquid phase was carefully decanted, and the residual inorganic salts were washed with additional acetone (3×2 mL). The combined washings were collected and concentrated in vacuo to give the desired trifluoroborate as a colourless crystalline or amorphous solid, which was finally dried over P_2O_5 (50 °C/0.1 mbar) overnight. Yields were typically quantitative; some minor loss of product is mainly associated with evaporation/drying/substance transfer manipulations.

4.5. General procedure for the preparation of potassium alkyltrifluoroborates from pinacolboronic esters using stoichiometric amounts of KHF_2 (GP3B, Method E, Table 1)

Method GP3A was followed, except that 0.5 mL of 4.5 M aqueous KHF_2 per 1 mmol of boronic ester was used (2.25 equiv, 1.1-fold excess).

*4.5.1. Potassium (R)-1-phenylethyltrifluoroborate (**3a**).* According to GP3A, boronic ester **2a** (3.9 mmol, 900 mg) was subjected to four evaporation cycles to afford 780 mg (95%) of pure **3a** as a colourless solid. ^{1}H NMR (CD_3CN, 400 MHz): δ 7.15–7.11 (m, 4H), 7.99–6.95 (m, 1H), 1.73 (m, 1H), 1.13 (d, J=7.3 Hz, 3H) ppm; ^{13}C NMR (CD_3CN, 100 MHz) δ 153.0, 128.7, 128.3, 123.9, 17.3 ppm; ^{11}B NMR (CD_3CN, 96.2 MHz): δ 3.7 (br s) ppm; ^{19}F NMR (CD_3CN, 283 MHz): δ −145.8 (br s) ppm; IR (neat) nu(tilde) 2966, 2878, 1609, 1491, 1220, 956, 915 cm^{-1}; HRMS (ESI) calcd for $C_8H_9BF_3$ [M−K$^+$] 173.0755, found 173.0759; $[\alpha]_D^{20}$ +4.0 (*c* 1.0, CH_3CN).

*4.5.2. Potassium (S)-(2-phenylbut-3-en-2-yl)trifluoroborate (**3i**).* According to GP3A, boronic ester **2i** (410 mg, 1.59 mmol) was subjected to three evaporation cycles to afford 373 mg (98%) of pure **3i** as a colourless solid. Alternatively, racemic boronic ester **2i** (516 mg, 2 mmol) subjected to four evaporation cycles according to GP3B, afforded 462 mg (97%) of pure **3i**. ^{1}H NMR (CD_3CN, 400 MHz): δ 7.40–7.38 (m, 2H), 7.19–7.15 (m, 2H), 6.99 (tt, J=7.3, 1.3 Hz, 2H), 6.41 (dd, J=17.5, 10.8 Hz, 1H), 4.79 (dd, J=10.8, 2.5 Hz, 1H), 4.75 (dd, J=17.5, 2.5 Hz, 1H), 1.21 (s, 3H) ppm; ^{13}C NMR (CD_3CN, 100 MHz): δ 153.1, 151.7, 128.6, 128.0, 124.1, 107.6, 21.2 ppm; ^{11}B NMR (CD_3CN, 96.2 MHz): δ 4.6 (q, J_{B-F}=60 Hz) ppm; ^{19}F NMR (CD_3CN, 282 MHz): δ −146.1 (q, J_{F-B}=60 Hz) ppm; IR (neat) nu(tilde) 3084, 2967, 2873, 1627, 1597, 1576, 1493, 1467, 1443, 1410, 1370, 1318, 1223, 1175, 1148, 1071, 954, 923, 905, 885, 837, 825, 757, 704, 688, 656 cm^{-1}; HRMS (ESI) [M−K$^+$] calcd for $C_{10}H_{11}BF_3$, 199.0906, found 199.0911; $[\alpha]_D^{24}$ −77.0 (*c* 4.8, CD_3CN).

*4.5.3. Potassium (2-chloropyrid-3-yl)trifluoroborate (**3s**).* According to GP3B, boronic ester **2s** (481 mg, 2 mmol) was subjected to three evaporation cycles to afford 423 mg (96%) of sufficiently pure **3s** (^{1}H NMR has shown <0.4 mol % of starting material **2s** and <0.1 mol % of pinacol) as a colourless crystals. ^{1}H NMR (CD_3CN, 300 MHz) δ 8.12 (dd, J=4.8, 2.1 Hz, 1H), 7.86 (br m, 1H), 7.11 (dd, J=7.3, 4.8 Hz, 1H) ppm; ^{13}C NMR (CD_3CN, 125.7 MHz) δ 156.3 (C), 148.6 (CH), 144.3 (CH), 123.0 (CH) ppm; ^{11}B NMR (CD_3CN, 96.2 MHz) δ 2.7 (q, J_{B-F}=48 Hz) ppm; ^{19}F NMR (CD_3CN, 282 MHz) δ −142.8 (q, J_{F-B}=48 Hz) ppm; IR (neat) nu(tilde) 3073, 1576, 1560, 1379, 1261, 1234, 1215, 1184, 1120, 1089, 1044, 1013, 982, 970, 951, 939, 881, 796, 753, 670 cm^{-1}; HRMS (ESI) [M−K$^+$] calcd for $C_5H_3BClF_3N$ 180.0005/181.9975, found 180.0008/181.9973.

*4.5.4. Potassium (2-cyclopropylethenyl)trifluoroborate (**3t**).* According to GP3B, boronic ester **2t** (194 mg, 1 mmol) was subjected to four evaporation cycles to afford 127 mg (73%) of sufficiently pure **3t** as a colourless crystals. ^{1}H NMR (CD_3CN, 300 MHz) δ 5.38 (ddt, J=17.6, 7.6, 3.7 Hz, 1H), 5.15 (J=17.6, 8.1 Hz, 1H), 1.30–1.23 (m, 1H), 0.61–0.52 (m, 2H), 0.29–0.21 (m, 2H) ppm; ^{13}C NMR (CD_3CN, 75.4 MHz) δ 140.2 (CH), 17.2 (CH), 7.1 (2 CH_2) ppm; ^{11}B NMR (CD_3CN, 96.2 MHz) δ 1.7 (q, J_{B-F}=55.9 Hz) ppm; ^{19}F NMR (CD_3CN, 282 MHz) δ −140.7 (q, J_{F-B}=55.9 Hz) ppm; IR (neat) nu(tilde) 3080, 3005, 2961, 1640, 1451, 1427, 1359, 1309, 1258 cm^{-1}; HRMS (ESI) [M−K$^+$] calcd for $C_5H_7BF_3$ 135.0598, found 135.0602.

Acknowledgements

We thank EPSRC for support of this work and Frontier Scientific for their generous donation of boronic esters. We also thank Merck for unrestricted support. V.K.A. thanks the Royal Society for

a Wolfson Research Merit Award and EPSRC for a Senior Research Fellowship. A.R. thanks the European Union for a Marie Curie Intra-European Postdoctoral Fellowship within the 7th European Community Framework Program.

Supplementary data

Complete experimental procedures and characterisations are provided. Supplementary data associated with this article can be found in the online version, at doi:10.1016/j.tet.2009.10.002.

References and notes

1. For reviews on preparation and use of trifluoroborates, see: (a) Darses, S.; Genêt, J.-P. *Eur. J. Org. Chem.* **2003**, 4313–4327; (b) Molander, G. A.; Figueroa, R. *Aldrichimica Acta* **2005**, *38*, 49–56; (c) Molander, G. A.; Ellis, N. *Acc. Chem. Res.* **2007**, *40*, 275–286; (d) Darses, S.; Genêt, J.-P. *Chem. Rev.* **2008**, *108*, 288–325; (e) For seminal contributions to the area see: Darses, S.; Genêt, J.-P.; Brayer, J.-L.; Demoute, J.-P. *Tetrahedron Lett.* **1997**, *38*, 4393–4396; (f) Darses, S.; Michaud, G.; Genêt, J.-P. *Tetrahedron Lett.* **1998**, *39*, 5045–5048.
2. (a) Molander, G. A.; Ito, T. *Org. Lett.* **2001**, *3*, 393–396; (b) Molander, G. A.; Yun, C.-S.; Rigaborda, M.; Biolatto, B. *J. Org. Chem.* **2003**, *68*, 5534–5539.
3. (a) Dreher, S. D.; Dormer, P. G.; Sandrock, D. L.; Molander, G. A. *J. Am. Chem. Soc.* **2008**, *130*, 9257–9259; (b) Van den Hoogenband, A.; Lange, J. H. M.; Terpstra, J. W.; Koch, M.; Visser, G. M.; Visser, M.; Korstanje, T. J.; Jastrzebski, J. T. B. H. *Tetrahedron Lett.* **2008**, *49*, 4122–4124; (c) For a recent breakthrough in the Suzuki–Miyaura coupling of secondary benzylic boronic esters see: Imao, D.; Glasspoole, B. W.; Laberge, V. S.; Crudden, C. M. *J. Am. Chem. Soc.* **2009**, *131*, 5024–5025.
4. (a) Batey, R. A.; Thadani, A. N.; Smil, D. V. *Org. Lett.* **1999**, *1*, 1683–1686; (b) Pucheault, M.; Darses, S.; Genêt, J.-P. *Tetrahedron Lett.* **2002**, *43*, 6155–6157; (c) Pucheault, M.; Darses, S.; Genêt, J.-P. *Eur. J. Org. Chem.* **2002**, 3552–3557; (d) Pucheault, M.; Darses, S.; Genêt, J.-P. *Chem. Commun.* **2005**, 4714–4716; (e) Lalic, G.; Corey, E. J. *Org. Lett.* **2007**, *9*, 4921–4923; (f) Lalic, G.; Corey, E. J. *Tetrahedron Lett.* **2008**, *49*, 4894–4896 for a recent example of the coupling of secondary and tertiary benzylic trifluoroborates with aldehydes see: (g) Ros, A.; Aggarwal, V. K. *Angew. Chem., Int. Ed.* **2009**. doi:10.1002/anie.200901900
5. Lee, S.; MacMillan, D. W. C. *J. Am. Chem. Soc.* **2007**, *129*, 15438–15439.
6. Kim, H.; MacMillan, D. W. C. *J. Am. Chem. Soc.* **2008**, *130*, 398–399.
7. Matteson, D. S.; Kim, G. Y. *Org. Lett.* **2002**, *4*, 2153–2155.
8. Epoxidation of double bond: (a) Molander, G. A.; Rigaborda, M. *J. Am. Chem. Soc.* **2003**, *125*, 11148–11149; Oxidation of hydroxymethyl group: (b) Molander, G. A.; Petrillo, D. E. *J. Am. Chem. Soc.* **2006**, *128*, 9634–9635; 'Click-chemistry': (c) Molander, G. A.; Ham, J. *Org. Lett.* **2006**, *8*, 2767–2770; Lithiations: (d) Molander, G. A.; Ellis, N. *J. Org. Chem.* **2006**, *71*, 7491–7493; Nucleophilic substitutions: (e) Molander, G. A.; Ham, J. *Org. Lett.* **2006**, *8*, 2031–2034; (f) Molander, G. A.; Febo-Ayala, W.; Ortega-Guerra, M. *J. Org. Chem.* **2008**, *73*, 6000–6002; Ozonolysis of double bond: (g) Molander, G. A.; Cooper, D. J. *J. Org. Chem.* **2007**, *72*, 3558–3560; HWE reactions: (h) Molander, G. A.; Figueroa, R. *J. Org. Chem.* **2006**, *71*, 6135–6140.
9. (a) Vedejs, E.; Chapman, R. W.; Fields, S. C.; Lin, S.; Schrimpf, M. R. *J. Org. Chem.* **1995**, *60*, 3020–3027; (b) Vedejs, E.; Fields, S. C.; Hayashi, R.; Hitchcock, S. R.; Powell, D. R.; Schrimpf, M. R. *J. Am. Chem. Soc.* **1999**, *121*, 2460–2470; (c) Darses, S.; Michaud, G.; Genêt, J.-P. *Eur. J. Org. Chem.* **1999**, 1875–1883.
10. According to SciFinder, 135 organic trifluoroborates are currently commercially available.
11. Stymiest, J. L.; Dutheuil, G.; Mahmood, A.; Aggarwal, V. K. *Angew. Chem., Int. Ed.* **2007**, *46*, 7491–7494.
12. Stymiest, J. L.; Bagutski, V.; French, R. M.; Aggarwal, V. K. *Nature* **2008**, *456*, 778–782.
13. (a) Harwood, L. M. *Aldrichimica Acta* **1985**, *18*, 25; (b) Pedersen, D. S.; Rosenbohm, C. *Synthesis* **2001**, 2431–2434.
14. Yuen, A. K. L.; Hutton, C. A. *Tetrahedron Lett.* **2005**, *46*, 7899–7903.
15. Murphy, J. M.; Tzschucke, C. C.; Hartwig, J. F. *Org. Lett.* **2007**, *9*, 757–760.
16. Although after one cycle the ^{11}B NMR spectra of the reaction mixture from **2k** showed no starting boronic ester **2k**, the final ^{1}H NMR spectra of the oil obtained after numerous manipulations (vide supra) showed the following: 64 mol % of **3k**, 16 mol % of **2k** and 20 mol % of pinacol. Direct evidence for reversibility of the reaction of boronic ester with KHF_2 was obtained by ^{11}B NMR monitoring of reaction of trifluoroborate **3k** with an excess of neat pinacol. Thus, at 50 °C, 12% of **3k** was converted into **2k** after 20 h, whereas, after 12 h at 80 °C, the conversion reached 40%. It is also worthy to note that **3k** could eventually be recrystallised (10% acetone in hexane, ~0.1 g/mL) after three evaporation–dissolution cycles had been applied, though the yield decreased significantly.
17. See Supplementary data.
18. Chen, A.; Ren, L.; Crudden, C. M. *J. Org. Chem.* **1999**, *64*, 9704–9710.