

Cesium Alkyltrifluoroborates from Asymmetric Boronic Esters

Donald S. Matteson,* Davis Maliakal, Philip S. Pharazyn, Byung Ju Kim

Department of Chemistry, Washington State University, Box 644630, Pullman, WA 99164-4630, USA

Fax +1(509)3358867; E-mail: dmatteson@wsu.edu

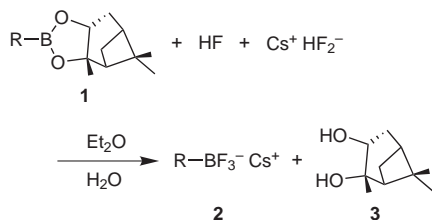
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Abstract: Cesium alkyltrifluoroborates are precipitated in high yields by the reaction of pinanediol (alkyl)boronates in diethyl ether with equivalent amounts of a mixture of aqueous hydrofluoric acid and cesium fluoride.

Key words: boron, asymmetric synthesis, fluorine, cesium, trifluoroborate

Organotrifluoroborates have become of considerable interest for organic synthesis.¹ In previous work we have shown that asymmetric potassium alkyltrifluoroborates can be generated from the corresponding pinanediol or 1,2-dicyclohexylethane-1,2-diol alkylboronates and converted into alkyl dihaloboranes useful in synthesis,² and that tetrachlorosilane in coordinating solvents such as tetrahydrofuran or acetonitrile converts alkyltrifluoroborates into solvent-coordinated alkyl dichloroboranes.³ One of the unsolved problems in this work was the fact that pinanediol alkylboronates **1** are not converted completely into potassium alkyltrifluoroborates and pinanediol (**3**), which exist in equilibrium with a significant fraction of unchanged **1** and potassium bifluoride under the reaction conditions used.²

More efficient conversion of **1** into alkyltrifluoroborate salts was expected if the salts **2** precipitated from the reaction mixture. In a promising preliminary experiment, cesium cyclohexyltrifluoroborate (**2a**) precipitated on addition of cesium fluoride to an aqueous solution of the potassium salt. It was then found that **2** would precipitate in good yields when ethereal solutions of **1** were added to excess preformed aqueous cesium bifluoride. However, this initial procedure was wasteful of cesium fluoride and did not take stoichiometry into account (Equation 1).



Equation 1 Reaction of pinanediol alkylboronates **1** with HF/CsHF₂ in a two-phase system

When the stoichiometric ratio of reactants was used, reactions proved faster and the yields of products **2** and **3** remained as high as before. Several simple cesium alkyltrifluoroborates were prepared as a test of the method. Results are summarized in Table 1.

Table 1 Structures and Yields of Precipitated, Air-Dried **2** from Stoichiometric Amounts of **1** in Diethyl Ether with Concentrated Aqueous HF and CsHF₂

Product	Structure	Yield (%)
2a		97
2b	CH ₃ (CH ₂) ₃ -BF ₃ ⁻ Cs ⁺	90
2c	CH ₃ (CH ₂) ₇ -BF ₃ ⁻ Cs ⁺	85
2d	Ph-BF ₃ ⁻ Cs ⁺	90
2e	Ph-CH ₂ -BF ₃ ⁻ Cs ⁺	96
2f	Ph-CH ₂ CH ₂ -BF ₃ ⁻ Cs ⁺	85
2g		90
2h		72
2i		85
2j		72
2k		70

Precipitated yields were high and ¹H NMR, ¹³C NMR, ¹⁹F NMR, and ¹¹B NMR spectra in CD₃CN were appropriate for the expected structures. The NMR spectra were very clean, showing only traces of tetrafluoroborate anion (¹⁹F NMR: δ = -149 from CFC₃; presumably derived from trialkoxyborane impurities in the boronic esters), which usually disappeared after recrystallization from water. Chemical shifts for ¹H on C adjacent to B as well as ¹⁹F and ¹¹B are summarized in Table 2, and ¹H NMR and ¹³C NMR data are listed in a footnote.⁴

After recrystallization from water, even though NMR spectra failed to indicate significant impurities, only **2a** and **2d** yielded correct C and H analyses. Achiral samples **2b**, **2c**, **2e**, and **2f** were off by 1–2% in carbon content, and the asymmetric compounds were grossly impure. Small

Table 2 Selected NMR δ Values for Cesium Alkyltrifluoroborates

Compd	BCH (300 MHz) ^a	¹⁹ F NMR (282 MHz) ^{b,c}	¹¹ B NMR (160 MHz) ^d
2a	0.07 (1 H)	−144.3	5.1
2b	0.05 (2 H)	−135.7	5.5
2d	–	−136.5	5.4
2e	1.60 (2 H)	−137.6	3.7
2f	0.39 (2 H)	−134.9	4.6
2g	3.21 (1 H)	−136.9	5.2
2h	0.51 (1 H)	−146.7	–
2i	3.10 (1 H)	−143.8	5.5
2j	2.94 (1 H)	−145.4	3.7
2k	2.60 (1 H)	−141.9	3.7

^a Broadened by ¹¹B or ¹⁰B, split by ¹⁹F and ¹H, unresolved.^b Referenced to internal standard CFC1₃; all partially resolved 1:1:1:1 quartets.^c *J* values for ¹¹B–¹⁹F are all ca. 60 (±10) Hz and imprecise because of line broadening.^d Reference to external standard BF₃·OEt₂; all partially resolved 1:3:3:1 quartets.

proportions of the trifluoroborate salts may hydrolyze in aqueous solutions, or drying may have been incomplete. Asymmetric samples **2i**, **2j**, and **2k** recrystallized once from acetonitrile or acetonitrile/diethyl ether, after filtering any insoluble contaminant, yielded satisfactory C and H analyses.⁵

The choice of cesium as the cation was prompted not only by the expected lower water solubility of the cesium salts but also their anticipated higher solubility in polar organic solvents. Tetrabutylammonium ion was also tested, but its analogue of **2f** failed to precipitate under the conditions used with cesium salts. The potassium analogue of **2k** likewise failed to precipitate. Presumably, the potassium salt could be isolated from the water phase, but this has not yet been tested.

Tetrabutylammonium cyclohexyltrifluoroborate precipitated when an aqueous solution of the potassium salt was treated with tetrabutylammonium fluoride. The solubility of tetrabutylammonium salts in polar organic solvents could be useful for some purposes. A limitation on utility is suggested by the observation that the tetrabutylammonium cation was cleaved to tributylamine haloborane complex when the cyclohexyltrifluoroborate was treated with boron trichloride in dichloromethane in an attempt to generate unsolvated cyclohexylboron dichloride.

With regard to experimental procedures, in spite of the exothermic reaction of hydrofluoric acid and cesium fluoride, it is essential that these components be mixed before the ethereal solution of boronic ester is introduced. An alternative procedure in which the hydrofluoric acid and

ethereal solution of the boronic ester were stirred together before introduction of the cesium fluoride resulted in grossly incomplete conversion of the fluoride into bifluoride and lowered yields of product contaminated with substantial amounts of unchanged cesium fluoride. It appears likely that hydrofluoric acid is soluble in the ether phase and thus of limited availability for reaction with solid cesium fluoride. This interpretation is consistent with the observation that no reaction of **1f** was observed when pentane was used in place of diethyl ether as the organic solvent, excluding HF from the organic phase.

Although all of the reported examples precipitated under the reaction conditions, extension to more complex structures has led to examples that do not. The aqueous phase can be more sharply differentiated from the ether phase by addition of pentane, and it appears that the cesium salts remain in aqueous solution. It may be noted that yields of **2h**, **2j**, and **2k** are significantly lower than the others, and water solubility may be the problem. There is also some evidence that such functionalized salts may be soluble in diethyl ether saturated with water and containing some HF, a problem that can be avoided by adding pentane to the ether phase before separation. It should also be noted that **2k** contains ca. 10% of its diastereomer at the C adjacent to B because pinanediol is not a selective stereodirector for its methylboronic ester and was not expected to provide the usual 99% stereoselectivity⁶ with its ethylboronic ester, as indeed it did not.

All of the pinanediol esters reported here as well as several others yielded precipitates of the corresponding cesium trifluoroborates. However, preliminary evidence indicates that a few functionalized cesium alkyltrifluoroborates are too water-soluble to precipitate. Recovery of an example of these from the aqueous phase has not yet been carried out.

The data presented here are all for pinanediol esters because they are the hardest chiral boronic esters to cleave. 1,2-Dicyclohexylethane-1,2-diol boronic esters can be converted into cesium alkyltrifluoroborates under similar conditions, but the diol is only slightly soluble in diethyl ether and coprecipitates with the salt. This problem can be solved either by using a large volume of ethyl acetate for the organic phase or by extraction of the solid product with a large volume of anhydrous diethyl ether, in which the cesium salts are not appreciably soluble. Formation of cesium alkyltrifluoroborates from pinacol boronic esters, as expected, is facile, rapid, and efficient.

Cesium Alkyltrifluoroborates

Boronic esters of pinanediol were prepared via well-established procedures.^{6–8} The samples used had undergone Et₂O/aqueous work-up and evaporation of Et₂O, and the residual boronic esters were used without further purification. In a screw-capped polyethylene bottle, a solution of CsF (1.52 g, 10 mmol) in 48% aq HF (0.83 g, 20 mmol HF contained) [CAUTION: exothermic, toxic]⁹ was stirred with a solution of 10 mmol of **1** in 4 mL of Et₂O for 2 h. Precipitation usually began within a few minutes. The precipitates were usually very fine and were collected by gravity filtration with

Whatman No. 1 or by suction filtration with Whatman No. 42 filter paper. The precipitates were washed freely with Et₂O, air dried, and washed again with Et₂O.¹⁰

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References and Notes

- (1) (a) Vedejs, E.; Chapman, R. W.; Fields, S. C.; Lin, S.; Schrimpf, M. R. *J. Org. Chem.* **1995**, *60*, 3020.
(b) Thadani, A. N.; Batey, R. A. *Tetrahedron Lett.* **2003**, *44*, 8051.
(c) Quach, T. D.; Batey, R. A. *Org. Lett.* **2003**, *5*, 1381.
(d) Molander, G. A.; Ito, T. *Org. Lett.* **2001**, *3*, 393.
(e) Molander, G. A.; Fumagalli, T. *J. Org. Chem.* **2006**, *71*, 5743.
(f) Molander, G. A.; Ham, J. *Org. Lett.* **2006**, *8*, 2767.
Reviews: (g) Darses, S.; Genet, J.-P. *Eur. J. Org. Chem.* **2003**, 4313.
(h) Molander, G. A.; Figueroa, R. *Aldrichimica Acta* **2005**, *38*, 49.
- (2) Matteson, D. S.; Kim, G. Y. *Org. Lett.* **2002**, *4*, 2153.
- (3) Kim, B. J.; Matteson, D. S. *Angew. Chem. Int. Ed.* **2004**, *43*, 3056; *Angew. Chem.* **2004**, *116*, 3118.
- (4) ¹H NMR and ¹³C NMR data: data are for CD₃CN solutions; ¹H NMR, 300 MHz; ¹³C NMR, 75.47 MHz, broad BC resonance was usually not detected.
Compound **2a**: ¹H NMR: δ = 0.07 (m, 1 H), 0.95 (m, 2 H), 1.15 (m, 3 H), 1.61 (m, 5 H). ¹³C NMR: δ = 27.3, 28.2, 27.4.
Compound **2b**: ¹H NMR δ = 0.05 (m, 2 H), 0.86 (t, *J* = 7.1 Hz, 3 H), 1.20 (m, 4 H). ¹³C NMR: δ = 14.8, 27.4, 29.2 (d or unresolved q, *J*_{CF} = ca. 2.3 Hz).
Compound **2c**: ¹H NMR: δ = 0.02 (m, 2 H), 0.89 (t, 3 H, *J* = 6.9 Hz), 1.27 (m, 12 H). ¹³C NMR: δ = 14.5, 23.5, 26.9, 30.4, 30.9, 32.9, 34.7.
Compound **2d**: ¹H NMR: δ = 7.16 (m, 3 H), 7.45 (m, 2 H). ¹³C NMR: δ = 126.5, 127.7, 132.4.
Compound **2e**: ¹H NMR: δ = 1.60 (m, 2 H), 6.97 (m, 1 H), 7.12 (m, 4 H). ¹³C NMR: δ = 51 (br), 122.2, 127.1, 128.5.
Compound **2f**: ¹H NMR: δ = 0.39 (m, 2 H), 2.51 (m, 2 H), 7.10 (m, 1 H), 7.20 (m, 4 H). ¹³C NMR: δ = 33.2, 125.5, 128.9.
Compound **2g**: ¹H NMR: δ = 2.67 (dd, *J* = 15.0, 12.3 Hz, 1 H), 3.13 (dd, *J* = 15.0, 2.5 Hz, 1 H), 3.21 (m, 1 H), 7.15 (m, 1 H), 7.25 (m, 4 H).
Compound **2h**: ¹H NMR: δ = 0.51 (m, 1 H), 0.58 (d, 3 H, *J* = 6.0 Hz), 2.06 (dd, *J* = 13.5, 11.1 Hz, 1 H), 2.84 (dd, *J* = 13.5, 3.3 Hz, 1 H), 7.10 (m, 1 H), 7.20 (m, 4 H). ¹³C NMR: δ = 15.4, 40.6, 125.5, 128.7, 130.0, 147.2.
Compound **2i**: ¹H NMR: δ = 1.71 (s, 3 H), 2.46 (dd, *J* = 13.9, 10.1 Hz, 1 H), 2.78 (dd, *J* = 13.9, 4.4 Hz, 1 H), 3.10 (m, 1 H), 5.89 (m, 1 H), 7.10 (m, 1 H), 7.20 (m, 4 H). ¹³C NMR: δ = 23.6, 38.9, 125.9, 128.6, 130.27, 144.5, 169.8.
Compound **2j**: ¹H NMR: δ = 2.75 (m, 2 H), 2.94 (m, 1 H), 4.26 (d, *J* = 11.9 Hz, 1 H), 4.42 (d, *J* = 11.9 Hz, 1 H), 7.20 (m, 10 H). ¹³C NMR: δ = 39.3, 72.7, 125.9, 127.7, 128.5, 128.7, 129.0, 130.4, 142.1, 145.4.
Compound **2k**: ¹H NMR: δ = 0.93 (t, 3 H, *J* = 7.3 Hz), 1.51 (m, 2 H), 2.60 (m, 1 H), 4.46 (d, *J* = 11.9 Hz, 1 H), 4.52 (d, *J* = 11.9 Hz, 1 H), 7.3 (m, 5 H). ¹³C NMR: δ = 11.5, 23.9, 71.6, 127.3, 128.2, 128.6, 141.6.
- (5) **Analysis Data** (Desert Analytics, Tucson, AZ)
Compound **2a**: Anal. Calcd for C₆H₁₁BCsF₃: C, 25.39; H, 3.91; B, 3.81; Cs, 46.82; F, 20.08. Found: C, 25.40, 25.17; H, 3.71, 3.93; B, 3.79; F, 18.95.
Compound **2d**: Anal. Calcd for C₆H₅BCsF₃: C, 25.94; H, 1.81; B, 3.89; Cs, 47.84; F, 20.52. Found: C 25.82, H 1.90, B 3.80, Cs 47.86, F 20.69.
Compound **2i**: Anal. Calcd for C₁₀H₁₂BCsF₃NO: C, 33.09; H, 3.33; N, 3.86. Found: C, 33.22; H, 3.15; N, 3.82.
Compound **2j**: Anal. Calcd for C₁₅H₁₅BCsF₃O: C, 43.73; H, 3.67. Found: C, 43.73; H, 3.36.
Compound **2k**: Anal. Calcd for C₁₀H₁₃BCsF₃O: C, 34.32; H, 3.74; B, 3.09. Found: C, 34.40; H, 3.59; B, 3.16. Cs and F were inexplicably low: Cs calcd, 37.98; found 36.94; F calcd, 16.29; found 14.64.
Tetrabutylammonium cyclohexyltrifluoroborate: Anal. Calcd for C₂₂H₄₇BF₃N: C, 67.16; H, 12.04; B, 2.75; F, 14.49; N, 3.56. Found: C, 67.49; H, 12.01; B, 2.79; F, 14.00.
- (6) Matteson, D. S.; Ray, R.; Rocks, R. R.; Tsai, D. J. S. *Organometallics* **1983**, *2*, 1536.
- (7) Matteson, D. S.; Sadhu, K. M.; Peterson, M. L. *J. Am. Chem. Soc.* **1986**, *108*, 810.
- (8) (a) Matteson, D. S. *Tetrahedron* **1998**, *54*, 10555.
(b) Matteson, D. S. *Chem. Rev.* **1989**, *89*, 1535.
(c) Matteson, D. S.; Sadhu, K. M.; Lienhard, G. E. *J. Am. Chem. Soc.* **1981**, *103*, 5241.
- (9) It is convenient to prepare a stock solution. CsF (1 mol) was added in small portions to stirred 48% aq HF (2 mols) in a polyethylene bottle cooled with an ice-water bath. [CAUTION: exothermic. Also, HF is highly toxic and contact with skin or breathing of vapors must be strictly avoided]. The density of the resulting solution of CsHF₂ and HF is ca. 2.23, and the weight of 10 mmol is 2.35 g.
- (10) The (1-benzyloxypropyl)trifluoroborate (**2k**) was prepared by a slightly modified procedure. The reaction was allowed to proceed for 24 h, though the effect of reaction time was not investigated. In addition to the 70% yield indicated in Table 1, 17% more of slightly impure **2k** was obtained by concentration of the H₂O/saturated ether phase from the original reaction mixture followed by treatment of the residue with pentane to remove the pinanediol. However, **2k** was not appreciably soluble in anhyd Et₂O.