Notes

Synthesis of Organic Bromides via Organotrifluoroborates

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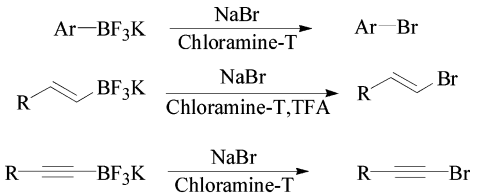
Summary: Organotrifluoroborates are rapidly converted into organic bromides under mild conditions, using sodium bromide in the presence of chloramine-T. The reactions are highly regioselective, are stereospecific, and proceed in excellent yields.

Organic bromides are valuable intermediates in a variety of organic syntheses,[1] including palladium-catalyzed coupling reactions[2] and free-radical chemistry.[3] They are also important in pharmaceutical research[4] and in the preparation of biocidal agents.[5] Organometallic reagents are convenient precursors for preparing organic bromides, but their use is somewhat restricted due to their high reactivity and toxic properties.[6] Organoboronic acids and esters can be brominated under conditions that tolerate a wide variety of functional groups, using sodium bromide and an oxidizing agent, but the reactions generally require the addition of base or acid.[7]

Potassium organotrifluoroborates are more nucleophilic than the corresponding boronic acids. They are also air and moisture stable and can be readily synthesized from boronic acids by addition of KHF_2.[8] Recent studies indicate that trifluoroborate salts are versatile synthetic intermediates.[9] We recently reported that potassium organotrifluoborates are rapidly converted to organic iodides under mild conditions using sodium iodide in the presence of chloramine-T.[10] We now wish to report that organotrifluoroborates can be brominated under similar conditions in excellent yields.[11,12]

Scheme 1



Potassium aryl-, alkenyl-, and alkynyltrifluoroborates are readily brominated. The method tolerates a wide

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(1) (a) Hofmeister, H.; Annen, K.; Lauren, H.; Weichert, R. *Angew. Chem., Int. Ed. Engl.* **1984**, *23*, 727. (b) Shair, M. D.; Yoon, T.; Danishefsky, J. S. *J. Org. Chem.* **1994**, *59*, 3755. (c) Michael, A.; Rassat, A. *Tetrahedron Lett.* **1999**, *40*, 8579.

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(5) Jeffrey, T. *Chem. Commun.* **1998**, 909.

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(7) (a) Brown, H. C.; Lane, C. F. *J. Am. Chem. Soc.* **1970**, *92*, 6660. (b) Kabalka, G. W.; Sastry, K. A. R.; Hsu, H. C.; Hylarides, M. D. *J. Org. Chem.* **1981**, *46*, 3113. (c) Kabalka, G. W.; Sastry, K. A. R.; Sastry, M.; Somayaji, V. *Org. Prep. Proc. Int.* **1982**, *14*, 359.

(8) (a) Vedejs, E.; Chapman, R. W.; Fields, S. C., Schrimpf, M. R. *J. Org. Chem.* **1995**, *60*, 3020. (b) Petasis, N. A.; Yudin, A. K.; Zavialov, I. A.; Prakash, G. K. S.; Olah, G. A. *Synlett* **1997**, 606. (c) Darses, S.; Genet, J.-P.; Brayer, J. L.; Demoute, J.-L. *Tetrahedron Lett.* **1997**, *38*, 4393.

(9) (a) Darses, S.; Michaud, G.; Genet, J.-P. *Tetrahedron Lett.* **1998**, *39*, 5045. (b) Batey, R. A.; Quach, T. D. *Tetrahedron Lett.* **2001**, *42*, 9099. (c) Molander, G. A.; Ito, T. *Org. Lett.* **2001**, *3*, 393. (d) Molander, G. A.; Biolattp, B. *Org. Lett.* **2002**, *4*, 1867. (e) Pucheault, M.; Darses, S.; Genet, J.-P. *Eur. J. Org. Chem.* **2002**, 3552. (f) Molander, G. A.; Rivero, M. R. *Org. Lett.* **2002**, *4*, 107. (g) Kabalka, G. W.; Venkataiah, B.; Dong, G. *Org. Lett.* **2003**, *5*, 3803.

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(11) General procedure: to a solution of potassium organotrifluoroborate (1.0 mmol) in 50% aqueous tetrahydrofuran (5 mL), contained in a round-bottomed flask, was added chloramine-T (1.2 mmol), followed by sodium bromide (1.2 mmol). The resulting solution was stirred at room temperature for the required length of time (Tables 1−3). The mixture was extracted into ethyl acetate (3 × 25 mL), and the combined organic extracts were washed with water (20 mL) and brine (20 mL), dried over anhydrous sodium sulfate, and concentrated under reduced pressure. The product was purified by column chromatography over silica gel using petroleum ether/ethyl acetate (98/2). The products were identified by comparison of physical and spectral properties with literature values. (Note that 0.03 mmol of trifluoroacetic acid was added for entries 5 and 6 (Table 1) and entries 1−5 (Table 2).)

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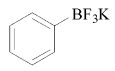
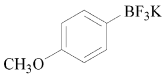
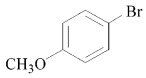
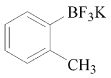
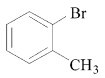
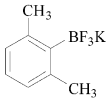
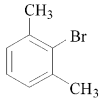
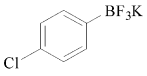
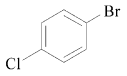
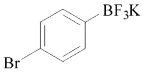
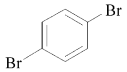
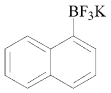
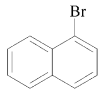
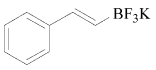
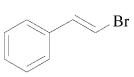
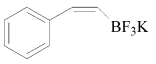
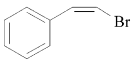
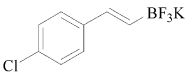
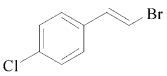
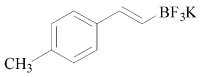
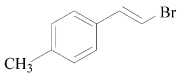
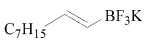
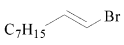
Table 1. Synthesis of Aryl Bromides from Potassium Aryltrifluoroborates[a,b]

Entry	Substrate	Product	Time (min)	Yield (%)[c]
1			10	76
2			10	87
3			10	72
4			15	83
5			15	78[d]
6			15	79[d]
7			10	86
8			10	65

[a] Reaction conditions: trifluoroborate (1.0 mmol), sodium bromide (1.20 mmol), and chloramine-T (1.2 mmol) in aqueous THF (50%). [b] All products were identified by ^{1}H and ^{13}C NMR spectroscopy and by comparison to authentic samples. [c] Isolated yields. [d] Trifluoroacetic acid (0.03 mmol) was added.

Table 2. Synthesis of Alkenyl Bromides from Potassium Alkenyltrifluoroborates[a,b]

Entry	Substrate	Product	Time (min)	Yield (%)[c]
1			10	92
2			10	89
3			10	90
4			10	94
5			10	72

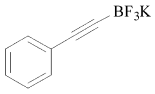
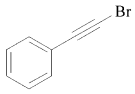
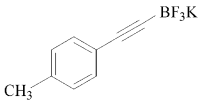
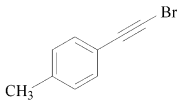
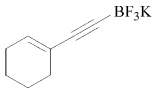
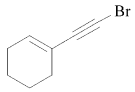
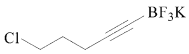
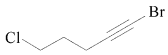
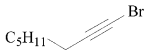
[a] Reaction conditions: trifluoroborate (1.0 mmol), trifluoroacetic acid (0.03 mmol), sodium bromide (1.2 mmol) and chloramine-T (1.2 mmol) in aqueous THF (50%). [b] All products were identified by ^{1}H and ^{13}C NMR spectroscopy and by comparison to authentic samples. [c] Isolated yields.

variety of functional groups and affords the products in excellent yields (Scheme 1). Tables 1−3 contain the results of this study. Sterically hindered potassium aryltrifluoroborates such as (1-methylphenyl)- and (2,6-dimethylphenyl)trifluoroborate readily react at room temperature. Reagents containing electron-withdrawing groups also react at room temperature but require a catalytic amount of trifluoroacetic acid. It is interesting to note that thienyltrifluoroborate also readily participates in the reaction.

Alkenyltrifluoroborates are rapidly converted to alkenyl bromides with retention of stereochemistry in the presence of a catalytic amount of trifluoroacetic acid,

(12) Example of large-scale procedure: to a solution of potassium naphthyltrifluoroborate (25.0 mmol, 5.89 g) in 50% aqueous tetrahydrofuran (100 mL), contained in a round-bottomed flask, was added chloramine-T (30.0 mmol, 8.50 g) followed by sodium bromide (30.0 mmol, 3.10 g). The resultant solution was stirred at room temperature for 10 min, and then the mixture was extracted into toluene (3 × 50 mL). The combined abstracts were washed with water (20 mL) and brine (20 mL), dried over anhydrous sodium sulfate, and concentrated under reduced pressure to yield essentially pure 1-bromonaphthylene. Vacuum distillation produced 4.34 g (84%) of analytically pure product.

Table 3. Synthesis of 1-Bromoalkynes from Potassium Alkynyltrifluoroborates[a,b]

Entry	Substrate	Product	Time (min)	Yield (%)[c]
1			20	87
2			20	92
3			20	78
4			20	79
5			20	79

[a] Reaction conditions: trifluoroborate (1.0 mmol), sodium bromide (1.2 mmol), and chloramine-T (1.2 mmol) in aqueous THF (50%). [b] All products were identified by ^{1}H and ^{13}C NMR spectroscopy and by comparison to authentic samples. [c] Isolated yields.

providing ready access to either (*E*)- or (*Z*)-alkenyl bromides. The reaction is also suitable for preparing 1-bromoalkynes. To our knowledge, this is the first report of an alkynylboron derivative being used as a precursor to bromoalkynes.

In conclusion, we report a convenient procedure for preparing aryl, alkenyl, and alkynyl bromides from potassium organotrifluoroborates.

Acknowledgment. We thank the National Institutes of Health and the Robert H. Cole Foundation for financial support of this research.

Supporting Information Available: Text giving ^{13}C and ^{1}H spectroscopic data and figures giving ^{1}H NMR spectra for all compounds. This material is available free of charge via the Internet at http://pubs.acs.org.

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