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Triolborates: water-soluble complexes of arylboronic acids as precursors to iodoarenes

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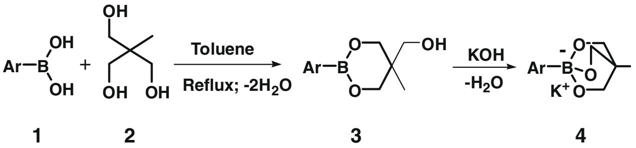
ABSTRACT

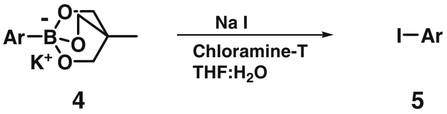
A facile synthesis of aryl and heteroaryl iodides from water-soluble complexes of aryl- and heteroarylboronic acids has been developed.

Haloarenes are versatile synthetic intermediates in organic chemistry.[1] They are also very important compounds in medicinal chemistry, radiochemistry, and pharmaceutical research.[2] Electrophilic halogenation of metal and metalloid precursors to obtain haloarenes is well documented in the literature but its utility, particularly in radiochemistry, is somewhat restricted due to the high reactivity and toxic properties of many of the precursors and reagents.[3–5] Arylboronic acids, esters, and potassium aryltrifluoroborates can all be used to prepare aryl iodides or aryl bromides using either sodium iodide or sodium bromide in the presence of a mild oxidant.[6] We wish to report a very facile preparation of aryl and heteroaryl iodides from triolborates, water-soluble complexes of arylboronic acids using sodium iodide and chloramine-T. The water solubility of these borate complexes is of great importance in radiochemistry as the final products can be rapidly purified by removal of the excess starting material using simple extraction techniques.

The requisite cyclic triolborates **4** are prepared from the corresponding commercially available boronic acids, **1**.[7] Typically, **1** and 1,1,1-tris(hydroxymethyl)ethane (**2**) are refluxed in toluene and the water generated is removed azeotropically to obtain boronate ester **3** which is then treated with potassium hydroxide to afford cyclic triolborate **4**.[8]



The iodination of triolborate **4** with sodium iodide in the presence of chloramine-T in a solvent mixture of THF/H_2O provides iodoarene **5**.[9]



A variety of iodoarenes have been prepared from the corresponding aryl triolborates. The results of these iodinations are summarized in Table 1. The new chemistry is tolerant of a wide range of functional groups and provides the iodinated products in good to excellent yields. Substrates containing electron-donating groups undergo iodination rapidly at ambient temperature. Those containing electron-withdrawing groups require longer reaction times and higher temperatures. Ortho substituents do not hinder the reaction which takes place in a very high yield (entry 10). Heteroaryl triolborates also undergo iodination smoothly (entries 8 and 9).

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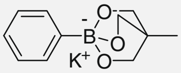
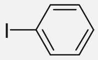
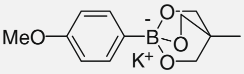
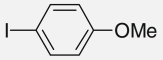
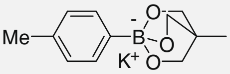
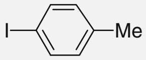
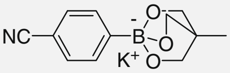
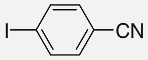
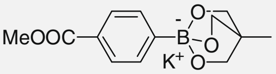
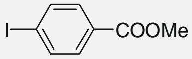
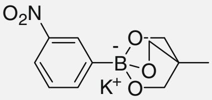
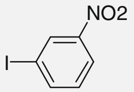
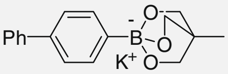
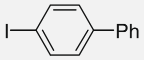
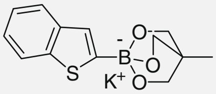
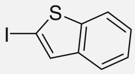
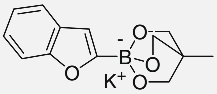
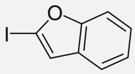
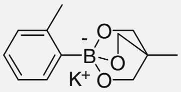
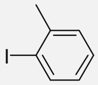
Table 1
Synthesis of aryl iodides from triolborates[a]

Entry	Substrate	Product	Time (min)	Yield[b] (%)
1			20	75
2			20	89
3			20	85
4			30	68[c]
5			30	64[c]
6			90	52[c]
7			20	80
8			20	72
9			20	68
10			20	80

[a] All products were characterized by ^{1}H, ^{13}C NMR spectroscopy and compared to standards.
[b] Isolated yields.
[c] Reaction was conducted at 50 °C.

In conclusion, the present study describes a convenient method for preparing iodoarenes from triolborates. The water solubility of these triolborates facilitates the rapid isolation of the desired product from the unreacted starting material.

Acknowledgments

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References and notes

1. (a) Diederich, F.; Stang, P. J. *Metal Catalyzed Cross Coupling Reactions*; Wiely-VCH: Weinheim, Germany, 1998; (b) Miyaura, N.; Yamada, K.; Suginome, H.; Suzuki, A. *J. Am. Chem. Soc.* **1985**, *107*, 972.
2. (a) *Chemistry of Radiopharmaceuticals*; Heindel, N. D., Burns, H. D., Honds, T., Brandy, L. W., Eds.; Masson: New York, 1997; (b) Nicolaou, K. C. *Angew. Chem., Int. Ed.* **1993**, *32*, 1377.
3. Larock, R. C. *Tetrahedron* **1982**, *38*, 1713.
4. Burnett, D. A.; Caplen, M. A.; Domalski, M. S.; Brownw, M. E.; Davis, H. R., Jr.; Clader, J. W. *Bioorg. Med. Chem. Lett.* **2002**, *12*, 311.
5. Pomilio, A. B.; Baroli, M. G. *J. Label. Compd. Radiopharm.* **1997**, *39*, 827.
6. (a) Kabalka, G. W.; Akula, M. R.; Zhang, J. H. *Nucl. Med. Biol.* **2002**, *29*, 841; (b) Kabalka, G. W.; Akula, M. R.; Zhang, J. H. *Nulc. Med. Biol.* **2003**, *30*, 369; (c) Kabalka, G. W.; Mereddy, A. R. *Tetrahedron Lett.* **2004**, *45*, 343.
7. Yamamoto, Y.; Takizawa, M.; Yu, X.; Miyaura, N. *Angew. Chem.* **2008**, *47*, 928.
8. *Representative triolborate procedure* (*preparation of potassium p-tolyl triolborate*): *p*-tolylboronic acid (0.41 g, 3.0 mmol) and 1,1,1-tris(hydroxymethyl)ethane (0.36 g, 3.0 mmol) are mixed in toluene (6 mL). Water is removed by azeotropic distillation using a Dean-Stark apparatus over a period of 4 h. The solvent is then removed to provide the boronate ester. The crude boronate ester and KOH (0.16 g, 2.8 mmol) are suspended in toluene (5 mL) and the mixture is heated at reflux for 4 h; water is removed using a Dean-Stark apparatus. The precipitated potassium triolborate is collected by filtration, thoroughly washed with acetone, and dried under reduced pressure to afford potassium *p*-tolyl triolborate as a white crystalline solid: yield = 0.22 g (84%); ^{1}H NMR (250 MHz, DMSO-d_6) δ = 0.46 (s, 3H), 2.16 (s, 3H), 3.55 (s, 6H), 6.80 (d, 2H, J = 7.5 Hz) and 7.18 (d, 2H, J = 7.5 Hz). ^{13}C NMR (250 MHz, DMSO-d_6) δ = 16.5, 28.4, 73.9, 124.2, 125.7 and 132.4.
9. *Representative iodination procedure* (*preparation of p-iodotoluene*): to a solution of potassium *p*-tolyl triolborate (0.26, 1.0 mmol) in 50% aqueous tetrahydrofuran (5 mL) in a 25 mL round-bottomed flask (shielded from light), chloramine-T (0.28 g, 1.0 mmol) is added accompanied by sodium iodide (0.16 g, 1.1 mmol). The resulting mixture is stirred at room temperature for 20 min. After the reaction is complete, 10% aqueous sodium thiosulfite (2 mL) is added to decompose excess iodine. The mixture is extracted into ethyl acetate (2 × 25 mL), the combined organic extracts are washed with water (20 mL), brine (20 mL), dried over anhydrous sodium sulfate, and concentrated under reduced pressure. The product is purified by column chromatography on silica gel (100–200 mesh) using 98:2 petroleum ether/ethyl acetate to obtain *p*-iodotoluene as a colorless oil: yield = 0.17 g (80%).