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New synthesis of diaryliodonium sulfonates from arylboronic acids

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Abstract

Diaryliodonium salts, precursors to [^{18}F]fluoroaromatics, have been prepared, in a regioselective manner, from readily available arylboronic acids eliminating the need for acid sensitive and toxic organotin intermediates. © 2000 Elsevier Science Ltd. All rights reserved.

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Iodine, like the other halogens, is found typically in monovalent form (oxidation state: –1). However, due to its large size and polarisability, it is able to form stable polycoordinate, multivalent compounds. Compounds of this type, containing hypervalent iodine, have been known for over a century and have received considerable attention. The ability of these compounds to act as both selective reagents and intermediates has formed the basis for this interest.[1–3]

Our interest in the most numerous member of this group, the diaryliodonium salts, arose from the demonstration that they are suitable precursors for the formation of fluoroarenes by the action of fluoride ion.[4,5] We have extended this methodology to the introduction of the fluorine-18 label ($t_{\frac{1}{2}} = 109.7$ min) in the form of [^{18}F]fluoride ion.[6,7] This methodology has distinct advantages over conventional electrophilic procedures, which employ molecular [^{18}F]F_2, as [^{18}F]fluoride can be produced in higher amounts and higher specific radioactivity by several orders of magnitude.[8] This is an important consideration for ^{18}F-labelled organics employed as radioligands for positron emission tomography (PET) ,[9] a well established clinical research tool, in for example, the use of L-6-[^{18}F]fluoro-DOPA[10,11] in the study of brain dopaminergic neuron density in movement disorders such as Parkinson's disease.

We have recently reported the regioselective preparation of diaryliodonium salts using aryltrialkylstannanes as intermediates.[12,13] Although successful, this methodology raised a number of concerns: the use of toxic organostannane intermediates in the production of radioligands for use

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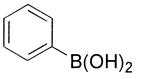
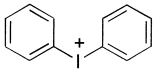
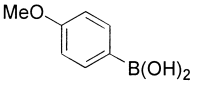
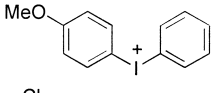
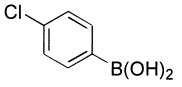
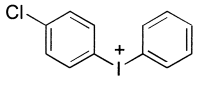
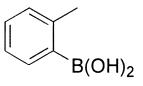
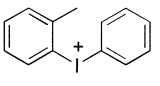
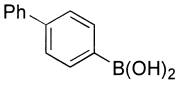
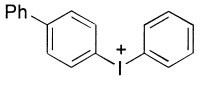
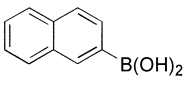
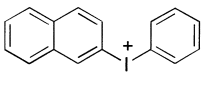
in PET and the susceptibility of electron-rich aryltrialkylstannanes to protolysis which makes their purification arduous and also introduces a source of contamination by formation of the diaryliodonium salt.

As a result, we sought an alternative procedure which would address these concerns, yet still provide an efficient and highly regioselective method for the production of our targets. A recent report demonstrated that treatment of $PhI(OAc)_2$ with $BF_3{\cdot}Et_2O$ followed by the addition of a vinylborane and then aqueous $NaBF_4$ was an efficient method for the preparation of vinylaryliodonium tetrafluoroborates.[14] It was also briefly mentioned that arylboronic acids may also be employed under these conditions and we decided to investigate this class of substrate.

Unavoidable dilution of the isotopic fluorine label occurs when tetrafluoroborate salts are used and as such they are not appropriate precursors for the preparation of ^{18}F-labelled compounds in high specific activity.[15,16] We therefore turned our attention to the preparation of salts which possessed counter ions compatible with the radiofluoridation process, in this case diaryliodonium triflates† and tosylates.‡ The reaction of phenylboronic acid with $PhI(OAc)_2{\cdot}2TfOH$, in dichloromethane at room temperature, gave diphenyliodonium triflate in 92% yield (Table 1: entry 1).

Table 1
Preparation of aryl(phenyl)iodonium salts

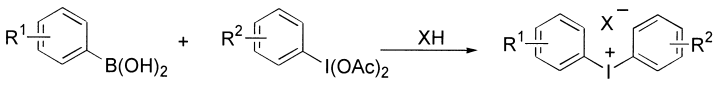
Entry	Arylboronic acid	Diaryliodonium triflate[a]	Yield (%)
1			92
2			97
3			79
4			86
5			74
6			47[b]

[a] All salts were characterised by ^1H, ^{13}C NMR, FT-IR, mp, MS, HRMS and elemental analysis.
[b] Tosylate

† *Typical procedure for the formation of diaryliodonium triflates*: Trifluoromethanesulfonic acid (0.88 ml, 10 mmol) was added dropwise, at –30°C, to a stirred suspension of diacetoxyiodobenzene (1.61 g, 5 mmol) in dichloromethane (50 ml). After 30 min the mixture was allowed to warm to room temperature and stirred for a further hour when it was recooled (–30°C) and the arylboronic acid (5 mmol) added. The resulting mixture was allowed to warm to room temperature overnight when the solvent was removed in vacuo to give the crude product.

‡ *Typical procedure for the formation of diaryliodonium tosylates*: The arylboronic acid (5 mmol) was added to a stirred suspension of hydroxy(tosyloxy)iodobenzene–Koser's Reagent (1.96 g, 5 mmol) in dichloromethane (50 ml). The resulting mixture was stirred at room temperature overnight when the solvent was removed in vacuo to give the crude product.

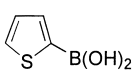
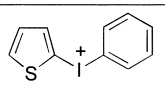
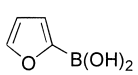
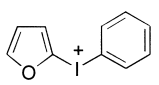
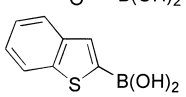
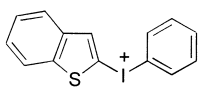
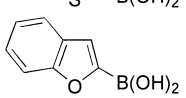
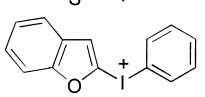
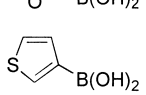
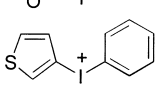
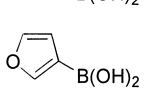
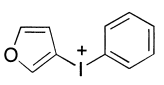
This success prompted us to determine the generality of the process and we found that a range of diaryliodonium salts could indeed be prepared in good yield, from the appropriate arylboronic acid, under these conditions (Scheme 1; Table 1). The efficiency of the iodine–boron exchange was evident as in all cases, analysis of the crude reaction mixture indicated near quantitative formation of the desired diaryliodonium salt. However, small amounts of highly coloured by-products were generated in the process making multiple recrystallisations necessary to obtain the products as analytically pure white crystalline solids. This 'darkening' of the reaction mixture was more pronounced for the electron rich substrates (Table 1: entries 2 and 6) suggesting that the by-products are a result of internal redox processes.



Scheme 1.

Our recent investigation, into the selectivity of the fluoridation process of heteroaryl(phenyl)-iodonium salts, required the use of a range of heteroaryltrialkylstannanes as intermediates in their formation.[13] Although readily prepared using conventional procedures the sensitivity of these materials as described above was a problem exacerbated by the electron rich nature of the heteroaromatic ring. Electron rich arylboronic acids do not suffer from such pronounced sensitivity and were therefore investigated as suitable precursors in the formation of heteroaryl(aryl)-iodonium salts. In a manner analogous to that used above 2-thiopheneboronic acid was added to $PhI(OAc)_2 \cdot 2TfOH$ and gave 2-thienyl(phenyl)iodonium triflate, however, as with the electron rich examples above an analytical sample could not be obtained from the highly coloured reaction

Table 2
Preparation of heteroaryl(phenyl)iodonium salts

Entry	Heteroarylboronic acid	Heteroaryliodonium tosylate[a]	Yield (%)
1			90
2			88
3			74
4			85
5			46
6			70

[a] All salts were characterised by ^1H, ^{13}C NMR, FT-IR, mp, MS, HRMS and elemental analysis.

mixture. Other heteroarylboronic acids behaved in a similar fashion and as a result the less reactive hydroxy(tosyloxy)iodobenzene–Koser's reagent[17] was studied. The use of this reagent greatly reduced the level of contamination and thereby allowed the successful isolation of 2-thienyl-(phenyl)iodonium tosylate (90% yield) and other heteroaryl(phenyl)iodonium tosylates (Table 2).

In summary we have demonstrated a mild and regioselective preparation of diaryliodonium salts, including heteroaryl(phenyl)iodonium salts, from the appropriate arylboronic acids. This eliminates the need for toxic and acid sensitive organostannanes as precursors to these materials.

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