

An Expeditious and General Aromatic Iodination Procedure

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The reaction of IPy_2BF_4 with an arene and an acid (HBF_4 or $\text{CF}_3\text{SO}_3\text{H}$), in CH_2Cl_2 at room temperature, provides a mild and efficient entry to the preparation of iodinated arenes.

Aromatic electrophilic substitution is a major class of reaction in organic chemistry, halogenation being a representative example.¹ Molecular bromine or chlorine and a Lewis acid are the reagents commonly used to carry out the corresponding halogenation. However, iodoaromatic compounds cannot be made in the same way.² To overcome this limitation alternative conditions have been developed,^{3,4} although many of the reported procedures are not general.[†] In this communication we report a new approach to tackling this problem, based on the reactivity of bis(pyridine) iodonium(1) tetrafluoroborate (IPy_2BF_4) as a mild source of electrophilic iodine.⁵

A methylene chloride solution containing arene-iodonium salt-tetrafluoroboric acid (1:1.1:2.2 ratio, respectively), is

stirred at room temperature for 15 min and, after isolation, affords the corresponding iodinated derivative[‡] (Scheme 1).

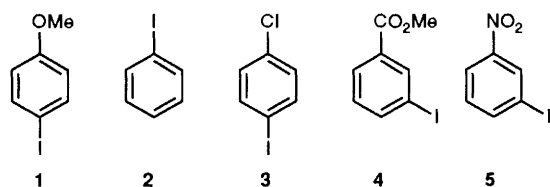
Following this reaction scheme, the fairly electron-activated aromatic ring of anisole can, cleanly and selectively, be converted into the iodo-containing derivative in quantitative yield. (^1H and ^{13}C) NMR inspection and GC-EM analysis of the crude reaction mixture reveals the formation of the



Scheme 1 Reagents and conditions: $\text{i IPy}_2\text{BF}_4$, 2HBF_4 (or $\text{CF}_3\text{SO}_3\text{H}$) in CH_2Cl_2 , room temp.

[†] More specifically, most of the reported methods either failed to provide examples of successful direct iodination of aromatics having strong electron-withdrawing substituents (*i.e.* an ester or a nitro group), or require harsh conditions resulting in polyiodination or other unwanted side reactions.

[‡] All iodinated compounds prepared show satisfactory analytical data, matching previously reported physical and spectroscopic properties. Yields have not been systematically optimized yet.



4-iodo-substituted regioisomer **1**. Similarly, less reactive benzene leads to a 48% isolated yield of iodobenzene **2**, again without any evidence of polyiodination taking place at a competitive rate. A more sluggish reaction occurs in the case of chlorobenzene and the yield is as low as 28% as a mixture of regioisomers (*para*:*ortho* = 93:7 by GC-EM), from which pure *para* isomer **3** can be isolated. The reaction failed to iodinate more deactivated aromatic compounds as methyl benzoate or nitrobenzene. Longer reaction times or higher temperatures do not increase the yield.

A possible modification of the nature and the stability⁶ of the iodinating agent could be achieved by switching the nature of the counteranion of the acid added to the medium. Remarkably, when trifluoromethanesulfonic acid (triflic acid) is used to generate the electrophilic source of iodine rather than tetrafluoroboric acid, efficient iodination of either methyl benzoate or nitrobenzene occurs at room temperature. Only the 3-regioisomer is obtained in each case; 51% of pure 3-iodinated derivative **4** was isolated (70% by ¹H NMR from the crude) for methyl benzoate, and a 27% of **5** in the case of nitrobenzene (45% by ¹H NMR from the crude). Chlorobenzene can also be iodinated by the iodonium salt-triflic acid mixture, giving a significant improvement of the yield to 78%.

In conclusion, a general method using very simple and mild conditions is described to perform the iodination of aromatic rings. Products are obtained according to the rules for aromatic electrophilic substitution. These are the mildest reported conditions to iodinate nitrobenzene.⁷ However, no problems are foreseen in iodination of activated compounds, such as anisole.^{4d} The procedure has not shown limitations concerning the nature of the substituents. Indeed, examples of

iodination of aromatic compounds having electron-withdrawing substituents are reported (featuring a halogen, an ester and a nitro group). The examples reported herein broach the possibility of establishing a unique entry into the preparation of iodoarenes based on this reagent.

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