

A Simple and General Route to Aryl Iodides from Arenes

José Barluenga, Pedro J. Campos, José M. González, and Gregorio Asensio
 Departamento de Química Orgánica, Facultad de Química, Universidad de Oviedo, Spain

Mercury(II) oxide–tetrafluoroboric acid reacts with arenes under mild or very mild conditions to afford, after treatment with iodine in a 'one-stage' reaction, the corresponding aryl iodide. The orientation is that expected based on general aromatic substitution theory and hence the *meta*-iodinated derivatives of deactivated arenes are accessible.

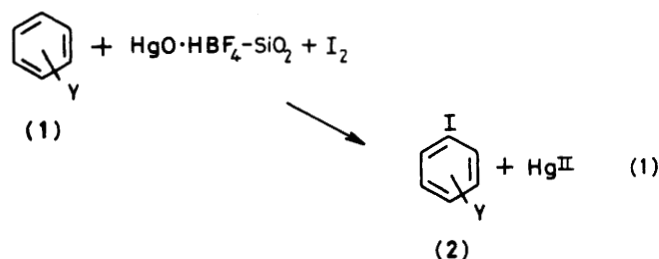
The halogenation with molecular halogen is one of the classic reactions of aromatic substitution and has been thoroughly investigated owing to its theoretical as well as synthetic value.¹ The electrophilic strength of molecular chlorine and bromine allows the direct reaction of these halogens with arenes. Conversely, the reaction of iodine with aromatic rings needs the presence of an activating agent except for a few special cases. The most widely employed strategy consists of the use of a powerful oxidant² in order to produce a strongly electrophilic species I^{+} . The disadvantages of this method lie in the rather drastic conditions employed, due to the oxidizing character of the promoter and/or the elevated temperatures that limit the scope of the iodination of activated arenes and halogenoarenes.

An alternative approach with reversed polarity is the reaction of diazonium salts or triazenes with iodide ion.³ An important drawback of these methods is that an aromatic amine must be used as starting material. On the other hand, the thallation of aromatics followed by reaction of the resulting organothallic derivative with iodide ion, a reaction developed by McKillop and Taylor,⁴ is among the most common methods for performing aromatic iodination. However, the metallation step is very sensitive to the presence of substituents on the arene moiety which are able to co-ordinate with thallium trifluoroacetate and this limits the possibility of synthesizing *meta*- or *para*-substituted iodoarenes. A similar approach has been the mercuriation of arenes with mercury(II) acetate followed by anionic exchange with chloride, isolation of the corresponding chloromercury derivative, and then reaction with iodine. The synthetic potential of this method of iodination is limited to very activated arenes owing to the low mercuriation rate.⁵ Mercury(II) trifluoroacetate under drastic conditions has been used for the polyhalogenation of arenes.⁶

Results and Discussion

In the last few years we have been involved in the study of the utility of $HgO \cdot HBF_4$ in organic synthesis. Owing to the highly electrophilic behaviour of this reagent⁷ we felt that it could be valuable in promoting aromatic iodination.

Now, we have found that the reaction of $HgO \cdot HBF_4$ with aromatic compounds in the presence of iodine leads to monoiodoarenes in a simple 'one-stage' process, which can be carried out at room temperature in dichloromethane (method A, see Experimental section) or at 85 °C in 1,2-dichloroethane (method B, see Experimental section). In these solvents $HgO \cdot HBF_4$ is in the form of a gummy solid that makes stirring difficult, thus decelerating the reaction. To avoid this problem mercury(II) oxide was mixed with silica gel and dissolved in 35% aqueous tetrafluoroboric acid. The mixture was evaporated to dryness under reduced pressure and the resulting $HgO \cdot HBF_4$, supported on silica gel, was used in the iodination reaction. Under these conditions the iodination rate is greatly increased (reaction 1; Table).



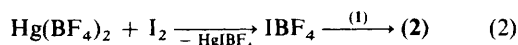
Two alternative mechanisms can be envisaged for the $HgO \cdot HBF_4$ -promoted iodination of aromatics. (a) A first

Table. Synthesis of iodoarenes (2) (see reaction 1)

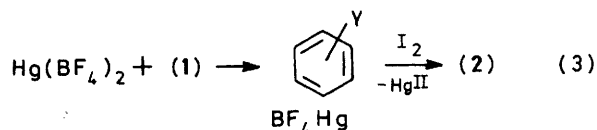
Aromatic compound	Method	Reaction time (h)	Product	Yield (%)	Composition			Literature ref. or molecular formula
					<i>ortho</i> (%)	<i>meta</i> (%)	<i>para</i> (%)	
Benzene	(1a)	A	4	(2a)	54			a
Toluene	(1b)	B	0.5	(2b)	73	40		60
t-Butylbenzene	(1c)	A	0.5	(2c)	78			>99
Mesitylene	(1d)	A	0.5	(2d)	74			
Pentamethylbenzene	(1e)	A	0.1	(2e)	60			
Chlorobenzene	(1f)	B	2.5	(2f)	51	16		84
Bromobenzene	(1g)	B	3	(2g)	49	10		90
Anisole	(1h)	A	0.3	(2h)	87			>99
Benzoic acid	(1i)	B	20	(2i)	35		>99	
Methyl benzoate	(1j)	B	21	(2j)	37		>99	
Nitrobenzene	(1k)	B	260	(2k)	12		>99	

^a Beilstein, E II, 5, p. 165; ^b Beilstein, E III, 5, p. 721; ^c Beilstein, E III, 5, p. 722; ^d Beilstein, E I, 5, p. 200; ^e R. M. Keefer and L. J. Andrews, *J. Am. Chem. Soc.*, 1956, 78, 5623; ^f Beilstein, E I, 5, p. 119; ^g Beilstein, E II, 5, p. 167; ^h Beilstein, E II, 5, p. 167; ⁱ Beilstein, E II, 5, p. 168; ^j Beilstein, E III, 6, p. 774; ^k Beilstein, E II, 9, p. 240; ^l Beilstein, H, 9, p. 365; ^m Beilstein, E II, 5, p. 191.

interaction between iodine and mercury(II) cation to give the active iodine tetrafluoroborate responsible for the iodination (reaction 2).



(b) An aromatic mercuriation by the highly electrophilic $\text{HgO}\cdot\text{HBF}_4$, followed by displacement of mercury by iodine (reaction 3).



As the iodination proceeds, the solution is decolourized and a pale red solid precipitates. By contrast, no change can be observed when a mixture of $\text{HgO}\cdot\text{HBF}_4$ -silica gel and iodine in dichloromethane is stirred for 48 h at room temperature. On these grounds route *b* seems to be the most likely one. The mercuriation appears to be the rate-determining step since we found that it determines the time required for the iodination. For instance, when mesitylene (**1d**) was treated with $\text{HgO}\cdot\text{HBF}_4$ until a negative test for free mercury(II) was obtained, the observed mercuriation time was similar to that of iodination when $\text{HgO}\cdot\text{HBF}_4$ and iodine were added at once. However, the possible existence of a minor amount of iodine tetrafluoroborate in equilibrium with iodine and mercury(II) tetrafluoroborate cannot be definitively ruled out and then the iodination by iodine tetrafluoroborate could occur (circumstantially) at a similar rate to mercuriation.*

The mercuriation of aromatics with $\text{HgO}\cdot\text{HBF}_4$ supported on silica gel is very fast if compared with the rate when using other mercury(II) salts. For instance, mesitylene is completely mercuriated in 25 min in dichloromethane while the same process with mercury(II) acetate in methanol-acetic acid takes up to seven days.⁸

The steric factors affect, to a considerable extent, the mercuriation process and hence the iodination. Thus, anisole leads almost exclusively to the *para*-substituted isomer while a 16:84 or 10:90 *ortho:para* isomer ratio is obtained from chloro- or bromo-benzene respectively. This selectivity lies in the same order as that observed for the thallium(III) trifluoroacetate-promoted iodination.⁴ No polyhalogenation products were ever found in our experiments. A remarkable difference with the thallium-based method is that in our case substituents carrying a negative charge or lone electron-pairs do not direct the mercuriation-iodination to the *ortho* position. Thus, typical electron-withdrawing substituents such as the carboxy or nitro groups give *meta*-orientation in the iodination as expected (Table).

The iodination of very deactivated arenes was carried out by method B (see Experimental section). The use of a slight excess of arene is advisable since it accelerates the reaction. Although yields are lowered in these cases there is no alternative method of *meta*-iodination in a simple and direct 'one-stage' reaction.

The convenience of all the reagents, their ease of handling, and the simplicity of the procedure for the isolation of the resulting iodoarenes make our method of aromatic iodination valuable from the preparative point of view.

Experimental

N.m.r. spectra were recorded on a Varian EM-390 or a Varian FT-80A spectrometer. Chemical shifts are reported in p.p.m. (δ)

downfield from tetramethylsilane. I.r. spectra were recorded on a Pye-Unicam SP-1000 instrument.

Mercury(II) Oxide-Tetrafluoroboric Acid supported on Silica Gel.—To stirred 35% aqueous tetrafluoroboric acid (5.02 g, 20 mmol) was added yellow mercury(II) oxide (2.16 g, 10 mmol) to give a yellow solution. Silica gel 60 (Merck; 2.16 g) was added to the solution and the mixture was evaporated under reduced pressure (10^{-2} Torr) until constant weight to yield a white, granular solid which was directly used for the preparation of iodoarenes.

Synthesis of Iodoarenes (2).—*Method A.* To a rapidly stirred solution of an arene (**1**) (20 mmol) in dichloromethane (20 ml) were added successively mercury(II) oxide-tetrafluoroboric acid-silica gel (4.95 g) and iodine (2.53 g, 10 mmol). When the solution had decolourized the precipitated mercury(II) salts were filtered off and the filtrate was treated with an aqueous sodium thiosulphate, extracted with dichloromethane, and dried (anhydrous Na_2SO_4). Solvents were eliminated at reduced pressure and the resulting mixture was distilled or sublimed to purify the compounds (**2**). Yields of compounds (**2**) are summarized in the Table.

Method B. A solution of an arene (**1**) (40 mmol) in 1,2-dichloroethane (25 ml) was successively treated with mercury(II) oxide-tetrafluoroboric acid-silica gel (4.95 g) and iodine (2.53 g, 10 mmol). The mixture was heated at 85 °C (oil-bath) until the solution had decolourized. After the work-up described above, the iodoarenes (**2**) were isolated. Yields of compounds (**2**) are summarized in the Table.

Known compounds were characterized by n.m.r. spectroscopy by comparison with reported data.⁹ (**2d**) $\delta_{\text{C}}(\text{CCl}_4)$ 19.85, 28.50, 103.51, 126.96, 136.26, and 140.31; (**2e**) $\delta_{\text{C}}(\text{CDCl}_3)$ 16.04, 17.69, 27.43, 108.41, 132.32, 133.94, and 135.99; (**2i**) $\delta_{\text{C}}(\text{CDCl}_3)$ 93.96, 128.93, 130.67, 131.47, 138.12, 142.61, and 170.14.

Compound (2e) had $\delta_{\text{H}}(\text{CCl}_4)$ 1.27 (9 H, s), 6.89–7.50 (4 H, m); δ_{C} (neat cap. D_2O) 32.83, 35.63, 92.57, 128.52, 138.57, and 151.75; ν_{max} (film) 835 cm^{-1} (Found: C, 46.1; H, 5.0. $\text{C}_{10}\text{H}_{13}\text{I}$ requires C, 46.17; H, 5.04%).

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