A convenient procedure for the iodination of arenes

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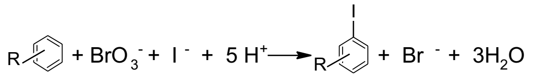
Two different procedures for the iodination of various arenes using potassium bromate and potassium iodide in the presence of hydrochloric acid are presented. Iodination of benzene, naphthalene and deactivated arenes were carried out in aqueous acetic acid medium and good yields of iodoarenes were obtained. Activated arenes, such as anisole, substituted phenols and anilines underwent excellent conversion to their iodinated products in an aqueous methanol medium.

Keywords: aromatic iodination, potassium bromate, potassium iodide, arenes

Iodoarenes are valuable synthetic products and are used in the preparation of many natural products and bioactive compounds.[1] Aromatic iodo derivatives have also been used in metal catalysed cross-coupling reactions[2] which are applied in the synthesis of complex molecules.

Aromatic iodination is of interest because iodine is the least reactive among the halogens and therefore, it needs activation for effective electrophilic substitution. Iodination reactions are usually carried out either by diiodine in the presence of an oxidising agent or by using the iodonium ion donating reagents. Several useful methods have been reported including I_2–chromium oxide,[3] I_2–silver sulfate,[4] I_2–diiodine pentoxide,[5] I_2–mercury salts,[6] I_2–nitrogen dioxide,[7] I_2–peracetic acid,[8] I_2–potassium permanganate,[9] iodine-tetra butyl ammonium peroxydisulfate,[1°] iodine monochloride,[11] N-iodosuccinimide (NIS),[12] BuLi-F_3CCH_2I,[13] NaI/chloramine-T in methanol.[14] Herein, we report $KBrO_3$/KI in hydrochloric acid as an efficient reagent for the iodination of various arenes.

In the context of our interest in iodination reactions, the use of potassium bromate and potassium iodide for the preparation of iodoarenes was examined. It was found that this mixture in the presence of hydrochloric acid reacted with various aromatic compounds, both activated and deactivated ones according to the stoichiometry Eqn (1), gave their corresponding iodo products in high yields.



(1)

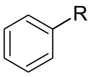
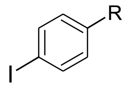
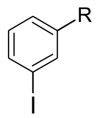
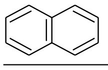
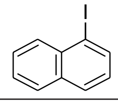
First, we have attempted iodination of benzene, naphthalene and deactivated arenes in aqueous acetic acid medium at 80°C (Procedure 1). All the chosen substrates gave mono iodo products in good yields. The results are shown in Table 1.

In case of the iodination of activated arenes such as substituted phenols and anilines, with this system-$KBrO_3$/KI/H^+, it was found that iodination was effective in aqueous methanol. Hence reactions were carried on various activated arenes in aqueous methanol medium at 60°C (Procedure 2**).** In each case, excellent yields of the iodoproduct was obtained and the results are given in Table 2.

In this system, the possible iodination reactions can be explained as follows. When potassium bromate is treated with potassium iodide in the presence of hydrochloric acid iodine is evolved shown by the immediate change of the colourless reaction mixture to a dark red colour. The iodine formed *in situ* may undergo oxidation with the to the more reactive iodonium ion species which can affect aromatic iodination.

In conclusion, the iodination of various arenes were achieved effectively by $KBrO_3$/KI in the presence of hydrochloric acid in aqueous acetic acid and aqueous methanol medium. The iodinating procedures are simple and the reagents used are easily available and non-hazardous in nature. The yields of the iodo products are good and no harmful by-products were observed.

Table 1 Iodination of arenes by $KBrO_3$/KI/H^+ using procedure 1

Substrate	Time/h	Product[a]	M.p. (lit.[15])/°C	Yield/%[b]
				
R = H	3	R = H	B.p. 187 (189)	91
R = Cl	4	R = Cl	55 (56–57)	83
R = Br	4	R = Br	90 (89–91)	80
				
R = NO_2	4	R = NO_2	B.p. 280 (280)	82
R_1 =COOH	5	R = COOH	187 (187–188)	71
	3		B.p. 304 (305)	90

[a]Products were characterised by their m.p. or b.p., mass, ^1H NMR and ^{13}C NMR and elemental analysis 1 ± 0.3%.
[b]Yield refer to pure isolated products.

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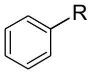
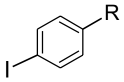
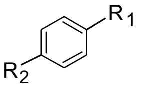
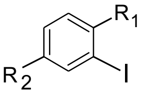
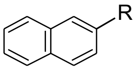
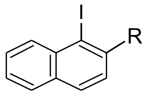
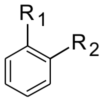
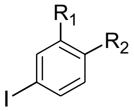
Table 2 Iodination of arenes by $KBrO_3/KI/H^+$ using procedure 2

Substrate	Time/h	Product[a]	M.p. (lit.[15])/°C	Yield/%[b]
				
R = OMe	1.5	R = OMe	54 (53)	94
R = NH_2	1.0	R = NH_2	64 (63)	81
R = OH	1.0	R = OH	92 (93–94)	80
				
$R_1 = NH_2$ $R_2 = NO_2$	2.0	$R_1 = NH_2$ $R_2 = NO_2$	106 (105–109)	89
$R_1 = NH_2$ R_2 =Cl	2.0	$R_1 = NH_2$ R_2 = Cl	41 (39–43)	90
R_1 = OH $R_2 = NO_2$	2.0	R_1 = OH $R_2 = NO_2$	88 (87)	88
R_1 = OH R_2 =Cl	2.0	R_1 = OH R_2 = Cl	76 (78)	90
				
R = NH_2	2.0	R = NH_2	140 (139)	84
R = OH	2.0	R = OH	91 (92)	92
				
R_1 =COOH R_2 = OH	2.0	R_1 =COOH R_2 = OH	197 (196)	81

[a] Products were characterised by their melting points, mass, ^1H NMR and ^{13}C NMR.
[b] Isolated yield.

Experimental

The purity of the iodoproduct was checked by TLC technique on silica gel-G coated aluminium plate, using hexane as eluent. The chromatogram was developed under a mixture of 1% vanillin and 5% ethanolic sulfuric acid as reagent. Melting points were obtained on a Thomas–Hoover apparatus in open capillary tubes and are uncorrected. Elemental analysis were performed at Organic Research Laboratories. ^1H NMR and ^{13}C NMR spectra were acquired on JEOL 270 and 400 MHz and Varian Gemini 300 MHz Spectrometers. Mass spectra were recorded on GC-MASS SPEC FINNIGAN MAT 8230MS Spectrometers.

Procedure 1, applicable for benzene, naphthalene and some deactivated arenes

A solution of naphthalene (1.28 g, 10 mmol), potassium bromate (1.67 g, 10 mmol), potassium iodide (1.66 g, 10 mmol) was prepared in 30 ml acetic acid and 20 ml water. To this colourless solution, 50 mmol of hydrochloric acid was added and stirred. Instantly, the solution was changed into dark red colour due to the liberation of iodine. This reaction mixture was then heated to 80° C for 3 h. After completion of the reaction, ether (4 × 10 ml) was added to the reaction mixture. The combined ether extract was separated and washed with dilute sodium thiosulfate (5%), water and dried over anhydrous Na_2SO_4. Removal of solvent gave dark brown colour liquid which was then purified through a short column packed with silica gel using hexane as eluent. All the spectroscopic analysis (mass, ^1H NMR and ^{13}C NMR) confirmed the formation of 1-iodonaphthalene, (2.28 g, 90%), b.p. 304°C (lit.[15] b.p. 305°C), MS $m/z = 254$, ^1H NMR ($CDCl_3$): δ 6.85 (t, 1H), 7.25 (t, 1H), 7.29 (t, 1H), 7.43 (d, 1H), 7.47 (d, 1H), 7.85 (d, 1H), 7.93 (d, 1H). ^{13}C NMR ($CDCl_3$): 99.54, 126.5, 126.56, 127.51, 128.34, 128.81, 131.9, 133.8, 134.19, 137.21. All the other substrates (Table. 1) were iodinated in good yield by using this procedure 1.

Procedure 2, applicable to anisole, substituted phenols and anilines

A solution of 2-naphthol (1.44 g, 10 mmol), potassium bromate (1.67 g, 10 mmol) and potassium iodide (1.66 g, 10 mmol) was prepared in 10 ml methanol and 40 ml water. 50 mmol of hydrochloric acid was added to this mixture and heated at 60°C for 2 h. The reaction mixture was extracted with diethyl ether (40 ml). The ethereal layer was separated and washed with dilute sodium thiosulfate (5%), water and dried over anhydrous Na_2SO_4. The residue was collected after removal of solvent which was then purified through a short column packed with silica gel using hexane as eluent to afford 1-iodo-2-naphthol (2.48 g, 92%), m.p. 92°C (lit.[15] m.p. 92°C), MS $m/z = 270$. ^1H NMR ($CDCl_3$): δ 7.98 (d, 1 H, $J = 9$ Hz, 8-H), 7.75 (overlapping doublets, 2 H, 4-H and 5-H), 7.58 (t, I H, $J = 8$ Hz, 7-H), 7.35 (t, 1 H, $J = 8$ Hz, 6-H), 7.22 (d, 1 H, $J = 8$ Hz, 3-H); ^{13}C NMR ($CDCl_3$): δ 154.8, 135.6, 131.8, 130.7, 130.5, 126.95, 126.9, 125.0, 117.2, 86.8.

The same procedure was applied to the other substrates mentioned in Table 2 and an excellent yield of iodoproduct were achieved in each case.

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