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Simple and regioselective oxyiodination of aromatic compounds with ammonium iodide and Oxone®☆

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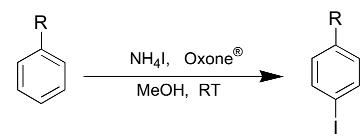
Abstract—A simple method for the iodination of aromatic compounds using NH_4I as the iodine source and Oxone® as the oxidant is described.

1. Introduction

In the 1960s the homolytic cleavage of the carbon–iodine bonds of iodoarenes was found to proceed with ease under the influence of UV radiation. This reaction immediately found wide application in organic synthesis.[1] In recent years, direct iodination methods have been intensively developed by using iodonium donating systems, such as iodine–mercury(II) oxides,[2] iodine–tetrabutylammonium peroxydisulfate,[3] BuLi–F_3CCH_2I,[4] NIS–CF_3SO_3H,[5] iodine–F–TEDA–BF_4,[6] NIS,[7] bis(*syn*-collidine)iodine(I) hexafluorophosphate,[8] iodine monochloride,[9] bis(pyridine)iodonium(I) tetra fluoroborate–CF_3SO_3H,[10] iodine–$(NH_4)_2S_2O_8$–$CuCl_2$–Ag_2SO_4,[11] iodine–silver sulfate[12] and iodine–mercury salts.[13] However, most of these methods require hazardous or toxic reagents or high reaction temperature for a long reaction time. Organometallic reagents are convenient precursors for the preparation of aryl iodides but their use is somewhat restricted due to the high reactivity and toxic properties of many reagents.[14–16] We have designed a practical and regioselective method for direct aromatic iodination. Our method is based on generation of electrophilic iodine in situ from NH_4I as the iodine source and Oxone® as the oxidant (Scheme 1). Oxone® is a stable ternary composite of $KHSO_5 \cdot KHSO_4$ and K_2SO_4 in 2:1:1 molar ratio and its use has been demonstrated for a variety of organic reactions.[17–22]



Scheme 1.

Our results are summarized in Table 1. As can be seen, this iodination generally proceeds well with high yields and regioselectivity. Iodination of methoxy aromatic derivatives takes place in high yields at room temperature. Surprisingly, iodinations of mesitylene, 1,2,4-trimethylbenzene and *m*-xylene proceed at room temperature in 24 h in high yields whereas *o*-xylene only gave a lower yield after 48 h. 2-Methoxynaphthalene gave 1-iodo-2-methoxynaphthalene. Nitrobenzene and benzoic acid were not iodinated even under severe conditions and were recovered without change. Iodination was *para*-directed whenever possible, otherwise it occurred in the *ortho*-position. *O*-Iodination occurred when the *p*-position was blocked with a substituent (Table 1, entries 3 and 4). The regioselectivity was deduced from the observation that iodination occurred at the more electron rich and less sterically hindered positions. The iodination proceeded highly *para*-selectively to a substituent, especially an alkoxy group and for *m*-xylene, even though in the cases of phenols and *o*-xylene the selectivities were only moderate. All products were characterized by NMR and mass spectra.

We have also checked the influence of solvent on the reactivity. When this reaction was performed using

Keywords: Iodination; Ammonium iodide; Oxone®; Aromatic compounds; Regioselectivity.

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Table 1. Regioselective oxyiodination of aromatics with NH_4I and Oxone®[a]

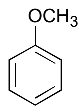
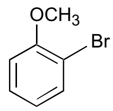
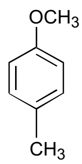
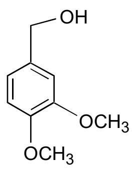
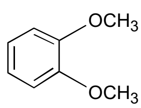
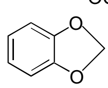
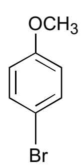
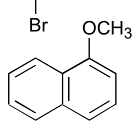
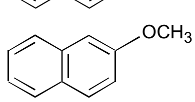
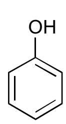
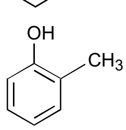
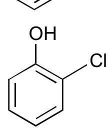
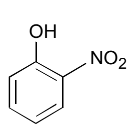
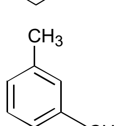
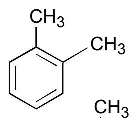
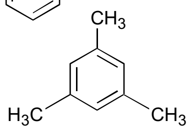
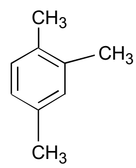
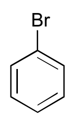
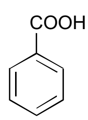
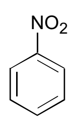
Entry	Substrate	*T*/h	Conversion (%)	Selectivity[b] (%)			
				ortho	*para*	Di-iodination	Other products
1		8	99	5	95	—	—
2		48	88	—	99	—	—
3		20	99	99	—	—	—
4		8	98	—	99	—	—
5		8	97	—	99	—	—
6		24	73	—	99	—	—
7		24	36	99	—	—	—
8		24	93	2	94	4	—
9		24	99	96	—	—	4
10		8	88	42	51	7	—
11		6	97	20	70	10	—
12		24	48	7	93	—	—
13		24	70	14	53	33	—
14		24	99	—	99	—	—

Table 1 (*continued*)

Entry	Substrate	*T*/h	Conversion (%)	Selectivity[b] (%)			
				ortho	*para*	Di-iodination	Other products
15		48	63	—	88	—	12
16		24	99	—	99	—	—
17		24	90	—	99	—	—
18		24	—	—	—	—	—
19		24	—	—	—	—	—
20		24	—	—	—	—	—

[a] Substrate (2 mmol), NH_4I (2.2 mmol), Oxone® (2.2 mmol), methanol (10 mL), rt.
[b] The products were characterized by NMR, mass spectra and yields were quantified by GC.

carbon tetrachloride, hexane, dichloromethane or acetonitrile, the reactivity observed was lower than in MeOH.

A typical oxyiodination of aromatic compounds in the presence of Oxone® proceeded according to the stoichiometry of Eq. 1.

$$ArH + NH_4I + 2KHSO_5 \cdot KHSO_4 \cdot K_2SO_4 \rightarrow ArI + NH_4OH + K_2S_2O_8 \cdot KHSO_4 \cdot K_2SO_4 + H_2O \quad (1)$$

In conclusion, the regiospecific nuclear iodination of aromatic compounds can be achieved efficiently with NH_4I–Oxone® in MeOH.

2. General procedure for the iodination of aromatic compounds

Oxone® (2.2 mmol) was added to a well-stirred solution of NH_4I (2.2 mmol) and substrate (2.0 mmol) in methanol (10 mL) and the reaction mixture was allowed to stir at room temperature. The reaction was monitored by thin layer chromatography (TLC). After completion of the reaction, the reaction mixture was filtered and solvent evaporated under reduced pressure. The products were purified by column chromatography over silica gel (finer than 200 mesh) with 5–30% ethyl acetate in hexane as eluent. All the structures of the products were confirmed by NMR and mass spectra.[13,23–28]

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