

## Environmental Friendly Method for the Iodination of Moderately Active Arenes

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(Received: 22 August 2009;

Accepted: 19 August 2010)

AJC-8982

An effective and environmental friendly method for the iodination of various moderately active methoxy arenes, phenols and anilines using hydrogen peroxide and acidified sodium periodate in aqueous ethanol medium is reported. The extent of iodination is easily controlled by stoichiometry and excellent yields of mono iodinated products are obtained.

**Key Words:** Aromatic iodination, Moderately activated arenes, Sodium periodate, Hydrogen peroxide.

### INTRODUCTION

Aromatic iodides are generally more reactive than the respective chlorides and bromides. Hence, they have found many applications in organic syntheses. They are also useful for the preparation of organometallic reagents and some are potential intermediates for the synthesis of pharmaceutical and bioactive materials. Many different methods<sup>1-12</sup> and their improvements have been reported for the effective preparation of aromatic iodides. But it is still desirable to seek better, *i.e.*, quick, inexpensive, easy and environmentally benign methods. In this paper an efficient, new and eco-friendly method for aromatic iodination is reported.

### EXPERIMENTAL

The melting points for the freshly prepared monoiodinated arenes by this method were uncorrected. All the reagents and solvents were of commercially available (Fluka, Aldrich) and were used without further purification. <sup>1</sup>H and <sup>13</sup>C NMR spectra were acquired on Jeol 270 and 400 MHz and Varian Gemini 300 MHz spectrophotometers. Mass spectra were recorded on a GC-Mass Spec Finnigan MAT 8230MS instrument. Elemental analyses were carried out on a Heraeus CHN-rapid-Elemental analyzer in Organic Research Laboratories.

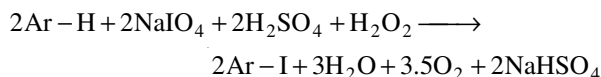
**Typical iodination procedure using NaIO<sub>4</sub>/H<sub>2</sub>O<sub>2</sub>/H<sub>2</sub>SO<sub>4</sub> in aqueous ethanol medium: (TP):** Appropriate arene (10 mmol) and NaIO<sub>4</sub> (2.14 g, 10 mmol) were dissolved in 30 mL of water and 10 mL of ethanol. This mixture was treated with 0.53 mL of conc. sulphuric acid (10 mmol, 0.98 g) slowly. Then, 0.14 mL of 30 % hydrogen peroxide (5 mmol, 0.17 g) was added drop wise and shaken well. The mixture was heated

to 50 °C for the required time. After cooling to room temperature, the reaction mixture was treated with aqueous sodium bisulphite solution and the organic material was extracted with diethyl ether. (3 mL × 30 mL). The combined organic layer was washed with water and dried over MgSO<sub>4</sub>, filtered and concentrated *in vacuo*. The residue was purified by column chromatography using hexane. A set of moderately active arenes were used in this study and the results are discussed below.

### RESULTS AND DISCUSSION

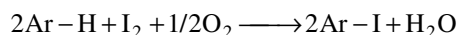
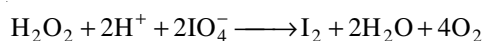
This iodination method was developed using acidified sodium periodate and hydrogen peroxide to iodinate aromatic compounds. It is an interesting one because NaIO<sub>4</sub> and H<sub>2</sub>O<sub>2</sub>, both are oxidants, they would undergo oxidation and reduction reactions. This method was carried in aqueous ethanol medium as an environmental friendly manner.

In this method various moderately active methoxy arenes, phenols and anilines were subjected for iodination procedure (TP) as per stoichiometry.



It is known from the literature that the redox reactions take place between sodium periodate and hydrogen peroxide. It is assumed that NaIO<sub>4</sub> is converted into molecular iodine and oxygen evolved during this reaction may lead to the formation of active I<sup>+</sup> species. From our numerous attempts it was found that these reactions could be enhanced by introducing acid in the reaction media. Hence, based on the reaction

observed, this iodination method was developed. The possible reactions for this system may be described as given below.



This method is suitable for the iodination of methoxy arenes, phenols and anilines and excellent yield of their iodo products were obtained in each case and are listed below.

**4-Iodo-1-methoxynaphthalene:** 4-Iodo-1-methoxy naphthalene was prepared from 1-methoxynaphthalene (1.58 g, 10 mmol). Reaction time: 40 min at 50 °C. Column chromatography yielded the product as white crystal (2.41 g, 85 %), m.p. 52 °C (lit. m.p. 52-53 °C). MS (m/e): 284 ( $[\text{M}^+]$  98 %)  $^1\text{H}$  NMR ( $\text{CDCl}_3$ ):  $\delta$  3.99 (s, 3H), 6.67 (d,  $J = 8$  Hz, 1H), 7.26 (d,  $J = 8$  Hz, 1H), 7.58 (td,  $J = 7.6$  and 0.8 Hz, 1H), 7.98 (d,  $J = 8.4$  Hz, 1H), 8.02 (d,  $J = 8.4$  Hz, 1H), 8.23 (d,  $J = 8.4$  Hz, 1H).  $^{13}\text{C}$  NMR ( $\text{CDCl}_3$ ):  $\delta$  55.4, 90.1, 105.8, 123.3, 126.0, 126.7, 128.8, 131.7, 135.7, 140.1, 157.2.  $\text{C}_{11}\text{H}_9\text{OI}$ : C: 46.67; H: 3.38, I: 44.74.

**4-Iodo-1-methoxy-2-methylbenzene:** 4-Iodo-1-methoxy-2-methylbenzene was prepared from 1-methoxy-2-methylbenzene (1.22 g, 10 mmol). Reaction time: 0.5 h at 50 °C. Column chromatography yielded the product as white crystal (2.23 g, 90 %), m.p. 80 °C (lit. m.p. 79-80 °C). MS (m/e): 248 ( $[\text{M}^+]$  99 %),  $^1\text{H}$  NMR ( $\text{CDCl}_3$ ):  $\delta$  2.34 (s, 3H), 3.12 (s, 3H), 6.72 (d,  $J = 8$  Hz, 1H), 7.26 (dd,  $J = 8$  and 2.1 Hz, 1H), 7.73 (d,  $J = 2.1$  Hz, 1H).  $^{13}\text{C}$  NMR ( $\text{CDCl}_3$ ):  $\delta$  15.4, 60.2, 86.9, 110.5, 127.3, 130.3, 135.9, 156.1.  $\text{C}_8\text{H}_9\text{OI}$ : C: 38.67; H: 3.81; I: 51.42.

**1-Iodo-2,3-dimethoxybenzene:** 1-Iodo-2,3-dimethoxybenzene was prepared from 1,2-dimethoxybenzene (1.38 g, 10 mmol). Reaction time: 0.5 h at 50 °C. Column chromatography (hexane) yielded the product as solid (2.48 g, 94 %), m.p. 44 °C (lit. m.p. 43-45 °C). MS (m/e): 264 ( $[\text{M}^+]$  96 %),  $^1\text{H}$  NMR ( $\text{CDCl}_3$ ):  $\delta$  3.79 (s, 3H), 3.84 (s, 3H), 6.38 (d,  $J = 8$  Hz, 1H), 6.64 (d,  $J = 8$  Hz, 1H), 7.13 (t,  $J = 8$  Hz, 1H),  $^{13}\text{C}$  NMR ( $\text{CDCl}_3$ ):  $\delta$  58.7, 60.2, 80.1, 115.5, 122.9, 130.8, 146.7, 147.9.  $\text{C}_8\text{H}_9\text{O}_2\text{I}$ : C: 36.17; H: 3.31; I: 48.12.

**2-Iodo-1,3,5-trimethoxybenzene:** 2-Iodo-1,3,5-trimethoxybenzene was prepared from 1,3,5-trimethoxybenzene (1.68 g, 10 mmol). Reaction time: 0.5 h at 50 °C. Column chromatography (hexane) yielded the product as solid (2.79 g, 95 %), m.p. 119 °C (lit. m.p. 120 °C). MS (m/e): 294 ( $[\text{M}^+]$  96 %),  $^1\text{H}$  NMR ( $\text{CDCl}_3$ ):  $\delta$  3.79 (s, 3H), 3.84 (s, 6H), 6.12 (s, 2H),  $^{13}\text{C}$  NMR ( $\text{CDCl}_3$ ):  $\delta$  55.4, 56.8, 69.6, 88.5, 160.5, 162.4.  $\text{C}_9\text{H}_{11}\text{O}_3\text{I}$ : C: 36.23; H: 3.45; I: 43.23.

**2-Iodo-4-nitroanisole:** 2-Iodo-4-nitroanisole was prepared from 4-nitroanisole (1.53 g, 10 mmol). Reaction time: 0.5 h at 50 °C. Column chromatography (hexane) yielded the product as solid (2.25 g, 81 %), m.p. 98 °C (lit. m.p. 96-98 °C). MS (m/e): 279 ( $[\text{M}^+]$  96 %),  $^1\text{H}$  NMR ( $\text{CDCl}_3$ ):  $\delta$  3.79 (s, 3H), 6.62 (d,  $J = 8.1$  Hz, 1H), 6.78 (dd,  $J = 8.1$  and 2.3 Hz, 1H), 7.21 (d,  $J = 2.3$  Hz, 1H),  $^{13}\text{C}$  NMR ( $\text{CDCl}_3$ ):  $\delta$  55.4, 86.5, 111.4, 124.5, 134.7, 141.8, 163.4.  $\text{C}_7\text{H}_6\text{NO}_3\text{I}$ : C: 30.45; H: 2.09; I: 45.31.

**2-Iodo-N,N-dimethyl-4-nitroaniline:** 2-Iodo-N,N-dimethyl-4-nitroaniline was prepared from N,N-dimethyl-4-nitroaniline (1.66 g, 10 mmol). Reaction time: 0.5 h at 50 °C.

Column chromatography (hexane) yielded the product as yellow oil. (2.54 g, 87 %). MS (m/e): 292 ( $[\text{M}^+]$  96 %).  $^1\text{H}$  NMR ( $\text{CDCl}_3$ ):  $\delta$  2.95 (s, 6H), 6.98 (d,  $J = 9.0$  Hz, 1H), 8.16 (dd,  $J = 9.0$  and 2.0 Hz, 1H), 8.79 (d,  $J = 2.0$  Hz, 1H),  $^{13}\text{C}$  NMR ( $\text{CDCl}_3$ ):  $\delta$  44.4, 90.6, 118.6, 124.8, 136.4, 138.4, 160.7.  $\text{C}_8\text{H}_9\text{N}_2\text{O}_2\text{I}$ : C: 32.68; H: 3.05; I: 43.23.

**4-Amino-3-iodobenzonitrile:** 4-Amino-3-iodobenzonitrile was prepared from 4-aminobenzonitrile (1.18 g, 10 mmol). Reaction time, 0.5 h at 50 °C. Column chromatography yielded the product as pale white solid (2.02 g, 83 %), m.p. 108 °C (lit. m.p. 109 °C). MS (m/e): 244 ( $[\text{M}^+]$  97 %),  $^1\text{H}$  NMR ( $\text{CDCl}_3$ ):  $\delta$  4.43 (brs, 2H), 6.62 (d,  $J = 8$  Hz, 1H), 7.31 (dd,  $J = 8$  Hz and 1.8 Hz, 1H), 7.80 (d,  $J = 1.8$  Hz, 1H).  $^{13}\text{C}$  NMR ( $\text{CDCl}_3$ ):  $\delta$  82.2, 102.6, 113.2, 119.1, 133.6, 141.2, 156.0.  $\text{C}_7\text{H}_5\text{N}_2\text{I}$ : C: 34.76; H: 2.12; I: 51.97.

**4-Iodo-3-chloroaniline:** 4-Iodo-3-chloroaniline was prepared from 3-chloroaniline (1.27 g, 10 mmol). Reaction time: 0.5 h at 50 °C. Column chromatography yielded the product as colourless needles (2.17 g, 86 %), m.p. 72 °C (lit. m.p. 70-72 °C). MS (m/e): 253 ( $[\text{M}^+]$ , 97 %).  $^1\text{H}$  NMR ( $\text{CDCl}_3$ ):  $\delta$  4.13 (brs, 2H), 6.27 (d,  $J = 8.5$  Hz, 1H), 6.76 (dd,  $J = 8.5$  and 2.7 Hz, 1H), 7.48 (d,  $J = 2.7$  Hz, 1H).  $^{13}\text{C}$  NMR ( $\text{CDCl}_3$ ):  $\delta$  85.1, 115.1, 115.9, 138.6, 141.7, 147.9.  $\text{C}_6\text{H}_5\text{NCI}_2$ : C: 28.67; H: 1.78; I: 50.67.

**4-Hydroxy-3-iodo-benzonitrile:** 4-Hydroxy-3-iodo benzonitrile was prepared from 4-hydroxybenzonitrile (1.2 g, 10 mmol). Reaction time, 0.5 h at 50 °C. Column chromatography (hexane) yielded the product as colourless solid (1.96 g, 80 %), m.p. 145 °C (lit. m.p. 145-146 °C). MS (m/e): 245 ( $[\text{M}^+]$  98 %),  $^1\text{H}$  NMR ( $\text{CDCl}_3$ ):  $\delta$  6.29 (d,  $J = 8$  Hz, 1H), 7.32 (dd,  $J = 8.0$  and 2.2 Hz, 1H), 7.82 (d,  $J = 2.2$  Hz, 1H), 10.56 (s, br, 1H),  $^{13}\text{C}$  NMR ( $\text{CDCl}_3$ ):  $\delta$  84.9, 106.8, 115.9, 118.7, 133.2, 142.9, 160.6.  $\text{C}_7\text{H}_4\text{NOI}$ : C: 33.56; H: 1.57; I: 51.87.

**2-Chloro-4-iodophenol:** 2-Chloro-4-iodophenol was prepared from 2-chlorophenol (1.28 g, 10 mmol). Reaction time, 0.5 h at 50 °C. Column chromatography (hexane) yielded the product as colourless solid (2.19 g, 79 %), m.p. 54 °C (lit. m.p. 55 °C). MS (m/e): 243 ( $[\text{M}^+]$  96 %),  $^1\text{H}$  NMR ( $\text{CDCl}_3$ ):  $\delta$  6.79 (d,  $J = 9$  Hz, 1H), 7.47 (dd,  $J = 9.0$  and 2.2 Hz, 1H), 7.72 (d,  $J = 2.2$  Hz, 1H).  $^{13}\text{C}$  NMR ( $\text{CDCl}_3$ ):  $\delta$  80.8, 119.9, 122.7, 137.2, 138.9, 157.6.  $\text{C}_6\text{H}_4\text{OClI}$ : C: 28.45; H: 1.47; I: 49.71.

**Methyl-3-iodo-4-hydroxybenzoate:** Methyl-3-iodo-4-hydroxybenzoate was prepared from 4-hydroxybenzoate (1.52 g, 10 mmol). Reaction time, 45 min at 50 °C. Column chromatography yielded the product as colourless solid (2.22 g, 80 %), m.p. 159 °C (lit. m.p. 158 °C). MS (m/e): 278 ( $[\text{M}^+]$  98 %),  $^1\text{H}$  NMR ( $\text{CDCl}_3$ ):  $\delta$  3.74 (s, 3H), 6.82 (d,  $J = 8.4$  Hz, 1H), 7.72 (dd,  $J = 8.4$  and 2.2 Hz, 1H), 8.25 (d,  $J = 2.2$  Hz, 1H), 10.56 (s, br, 1H).  $^{13}\text{C}$  NMR ( $\text{CDCl}_3$ ):  $\delta$  83.9, 116.8, 125.8, 131.2, 140.9, 160.6, 166.7.  $\text{C}_8\text{H}_7\text{O}_3\text{I}$ : C: 34.76; H: 2.45; I: 45.76.

**2-Hydroxy-5-iodopyridine:** 2-Hydroxy-5-iodopyridine was prepared from 2-hydroxypyridine (0.95 g, 10 mmol). Reaction time, 45 min at 50 °C. Column chromatography yielded the product as colourless solid (2.47 g, 86 %), m.p. 190 °C (lit. m.p. 191 °C). MS (m/e): 221 ( $[\text{M}^+]$  98 %).  $^1\text{H}$  NMR ( $\text{CDCl}_3$ ):  $\delta$  6.34 (d,  $J = 11$  Hz, 1H), 7.59 (dd,  $J = 11$  and 2 Hz, 1H), 7.72 (d,  $J = 2$  Hz, 1H).  $^{13}\text{C}$  NMR ( $\text{CDCl}_3$ ):  $\delta$  66.4, 121.8, 142.3, 148.2, 161.7.  $\text{C}_5\text{H}_4\text{O}_2\text{I}$ : C: 27.51; H: 1.75; I: 57.28.

**Conclusion**

In conclusion a fast, simple and environmental friendly iodination method was reported for moderately active arenes. Excellent yields of iodinated products were obtained in short reaction times.

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