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IODINATION OF AROMATIC AMINES WITH IODINE AND SILVER SULFATE

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Abstract: Iodination of aromatic amines with iodine / silver sulfate at room temperature gives iodo-products in good (46-96%) yield.

Earlier work in our laboratory has shown that iodine / silver nitrite is a mild iodination reagent¹. This has proven to be effective for the iodination of alkylbenzenes; however, for alkoxybenzenes such as anisole, possessing a strong electron releasing group, nitro-compounds were found as by-products. Recently, it has been found that iodine / silver sulfate is a better iodination reagent for alkyl and alkoxybenzenes², having the advantages of speed and excellent yield.

The iodine / silver sulfate system has now been applied to the syntheses of iodo-aromatic amines. The results are presented in this report.

























Iodination of aniline can be performed easily by using iodine and aqueous sodium bicarbonate or carbonate to give 4-iodoaniline in good yield³. However, iodination of other aromatic amines usually requires stronger reaction conditions.

Reagents such as iodine / glacial acetic acid⁴, iodine - morpholine complex⁵, iodine / silver trifluoroacetate⁶, iodine / potassium iodide / 1,2-ethanediamine⁷, 1,3-diiodo-5,5-dimethylhydantoin⁸, iodine dimethylsulfoxide⁹, iodine / potassium iodate / sulfuric acid¹⁰ and iodomono-chloride¹¹ have been used. These reagents often give low yield or produce polysubstituted products. Benzyltrimethylammonium dichloriodate was found to be a good iodination reagent for more active aromatic amines but failed to iodinate less reactive nitroanilines¹².

In the present study, it was found that aromatic amines can be iodinated with iodine / silver sulfate at room temperature in ethanol. Deactivated aromatic amines gave iodo-products in excellent yield; under similar conditions, however, aniline and activated aromatic amines gave iodo-products only in moderate yield. Attempts to improve the yields of the latter products using this reagent did not succeed. A higher yield (80%) was obtained on iodinating m-toluidine using iodine / silver acetate as the iodination reagent. Nevertheless, the iodine / silver acetate system is not as effective as iodine / silver sulfate for the iodination of nitroanilines as demonstrated in the iodination of p-nitroaniline, where the reaction was completed within 0.5 hour using the latter reagent, whereas starting material remained after a prolonged reaction time (24 hour) when using the former.

Results are summarized in the Table. A representative iodination was performed as follows:

Table. Iodination of aromatic amines with iodine / silver sulfate

	Amine	Reaction time (min.)	Yield (%)	Product(s) ¹³
1		30	91	
2		30	87	
3		210	90	 (3) :  (1) :  (1) :  (trace)
4		150	79	
5		40	96	 (4) :  (1)
6		80	88	
7		50	91	
8		15	84	
9		40	46	
10		40	50	

4-Nitroaniline (138 mg, 1mM) was added to a mixture of iodine (254 mg, 1mM) and silver sulfate (311mg, 1mM) in ethanol (20 mL) at room temperature. The mixture was stirred for 30 minutes. After this time, the yellow solid was removed by filtration and the filtrate was evaporated to dryness under reduced pressure. The residue was dissolved in dichloromethane and washed with aqueous 5% NaOH solution, then with water. After separation, the organic layer was dried over sodium sulfate and evaporated to dryness. The residue was chromatographed on silica gel and eluted with chloroform to give pure 2-iodo-4-nitroaniline (240 mg, 91%).

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