eliminated by the addition of acetyl bromide to the reaction mixtures. Under such conditions the reaction is of first order with respect to ether and of second order with respect to hydrogen bromide in toluene, chlorobenzene, or (presumably) in excess ether; of three-halves order with respect to both reactants in chloroform; and of first order with respect to both reactants in acetic acid. The significance of these results and their bearing on the mechanism of solvolysis of alkyl halides are discussed.

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[CONTRIBUTION FROM THE AVERY LABORATORY OF CHEMISTRY OF THE UNIVERSITY OF NEBRASKA]

Nuclear Iodination of Aromatic Amines

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Previous studies on the reaction between aromatic amines and iodine have been carried out by Hodgson and Marsden,[1] who found that aniline and iodine reacted at various temperatures to produce mixtures of *p*-iodoaniline, 2,4-diiodoaniline, and an aposafranine. Wheeler and Liddle[2] and later Hann and Berliner[3] reported the successful iodination of the toluidines with iodine. Iodine monochloride also has been used to effect nuclear iodination.[4,5]

In the present study the reaction between the hydroacetates of aromatic amines and iodine in aqueous solution has been shown to yield nuclear substitution in active positions. At 15° the position para to the amine group is iodinated; at higher temperatures ortho substitution may also take place. The simplicity of the procedure offers advantages over other methods of iodination.

The reaction has been used to prepare the series of compounds shown in Table I. Iodination of *p*-aminoacetophenone, *p*-nitroaniline, and acetanilide was not effected under comparable conditions: complete recovery of the starting material resulted.

TABLE I

Compound	Reaction temp., °C.	Yield in %	M. p., °C.	Nitrogen, % Calcd.	Nitrogen, % Found
4-Iodoaniline[1,a]	15	30–40	63	6.35	6.35
2,4-Diiodoaniline[b]	70–80	Small	95	4.06	4.10
2-Amino-5-iodobenzoic acid[c]	15	50	210	5.33	5.35
4-Iododimethylaniline[d]	15	Very small	80	5.67	5.66
4-Amino-3-iodobenzene sulfonamide[5]	80–90	20–25	182	9.40	9.28
4-Iodo-2-methylaniline[2,3d]	15	40–45	86–88	6.01	5.90

[a] 4-Iodoaniline is best purified by way of its hydrogen sulfate salt which is sparingly soluble in water. The salt decomposes readily upon suspension in sodium carbonate solution at 50°. [b] The crude is purified by dissolving in hot glacial acetic acid, decolorizing, and diluting with one third the volume of water to precipitate, followed by final crystallization from 60% acetic acid. [c] Purified by way of the ammonium salt.[4] [d] Purified by dissolving in alcohol, precipitating by the addition of water, and crystallizing from 50% alcohol.

Experimental

General Procedure.—The aromatic amine (0.03 to 0.1 mole) was dissolved in 200 ml. of water by the addition of sufficient amounts of glacial acetic acid. An equimolecular amount of iodine (or twice this amount in the preparation of diiodoaniline) was added during the course of one hour with continuous stirring at the temperature indicated in Table I. After an additional thirty minute stirring period, the excess iodine was destroyed with a sodium thiosulfate solution. The dark reaction products were removed by filtration, treated with activated charcoal and crystallized from alcohol or acetic acid.

To get the best yields of *p*-iodoaniline, the reaction mixture should be made alkaline subsequent to the addition of thiosulfate.

4-Amino-3-iodobenzenesulfonamide.—Sulfanilamide (5 g.) was dissolved in 10 ml. of glacial acetic acid and heated to 80–90°. Iodine (6.5 g.) was added in small amounts and the solution kept hot for an additional hour with continuous stirring. The excess iodine was destroyed with sodium bisulfite and the solution diluted with 100 ml. of water. The product which separated was collected and crystallized from 30% alcohol.

Summary

Aniline, *o*-toluidine and anthranilic acid react with iodine in aqueous acetic acid to give mononuclear iodo compounds. Small yields were obtained with dimethylaniline while iodination did not occur with *p*-aminoacetophenone, *p*-nitroaniline and acetanilide. Sulfanilamide reacts in glacial acetic acid at eighty degrees.

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[1] Hodgson and Marsden, *J. Chem. Soc.*, 1365 (1937).

[2] Wheeler and Liddle, *Am. Chem. J.*, **43**, 498 (1909).

[3] Hann and Berliner, THIS JOURNAL, **47**, 1709 (1925).

[4] "Organic Syntheses," Vol. 19, John Wiley and Sons, Inc., New York, N. Y., 1939, p. 53.

[5] Scudi, THIS JOURNAL, **59**, 1481 (1937).