ester obtainable in this temperature range from equimolar concentrations of alcohol and acid is about 88 to 90%.

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[CONTRIBUTION FROM THE DEPARTMENT OF CHEMISTRY OF THE UNIVERSITY OF KANSAS]

THE IODINATION OF PHENOL AND CRESOL ETHERS

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The introduction of iodine into aromatic hydrocarbons such as benzene, toluene, cymene, etc., using nitric acid as an oxidizing agent was first described by La Datta and Chatterjee.[1] The method has been studied in detail in this Laboratory and the following paper is an account of the reaction as applied to the phenol ethers. The free phenols are too reactive and the resulting products consist of nitro rather than the desired iodo compounds. When the phenol ethers are used, the reaction proceeds smoothly and in good yields. The interesting fact was also noted that iodine can be introduced into the nitro-anisoles and nitrophenetoles, although nitrobenzene is unaffected under the same conditions. A description of the general procedure is given in one instance; the other results are tabulated.

Experimental

I. Iodination of Phenetole.—Phenetole (20 g.) and iodine[2] (15 g.) were placed in a small Kjeldahl flask fitted with a ground in glass condenser and heated in an oil-bath at 180°. For higher temperatures a metal-bath can be used. From time to time 2–3-cc. portions of concentrated nitric acid were added through the condenser. After an hour's heating the iodine had practically disappeared. The residue in the flask was washed with alkali and steam distilled. In the iodination of cresol derivatives the alkali dissolves any substituted benzoic acids formed by oxidation. The oil was separated, dried and fractionated at 11 mm. It came over between 120 and 138° and on cooling part of it solidified. This when freed from oil melted at 28° and proved to be *p*-iodophenetole. The major portion of the oil (b. p. 240° at 730 mm.) corresponded in properties to the known *o*-iodophenetole. Additional evidence of its formation was given by the fact that in one run the main product was 2-iodo-4-nitrophenetole (m. p. 96°).[3]

V. 2-Nitro-4-iodo-anisole (m. p. 98°).—Reverdin[4] described this ether as melting at 73° but the following proof of structure would seem to confirm the higher melting point.

The nitration of *p*-acetanisidine and subsequent hydrolysis gave the 2-nitro-4-

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[1] Datta and Chatterjee, THIS JOURNAL, **39**, 435 (1917).

[2] The addition of 3–5 cc. of pyridine increases the yield and lowers the temperature at which the reaction occurs.

[3] Reverdin, *Ber.*, **29**, 2596 (1896).

[4] Reverdin, *ibid.*, **29**, 1003, 2595 (1896); *Bull. soc. chim.*, [3] **15**, 639 (1896); Brenans, *Compt. rend.*, **134**, 360 (1902).

amino-anisole (m. p. 51°),[11] from which was obtained the above 4-iodo compound (m. p. 96°), confirmed by mixed melting point.

Anal. Calcd. for $C_7H_6INO_3$: N, 5.01. Found: N, 4.95, 5.04.

TABLE I

REAGENTS AND PRODUCTS

No.	Subs. iodinated and temperature, °C.	Product (yield)
II	*o*-Cresol methyl ether (140°)	1-Methoxy-2-methyl-4-iodobenzene (85%)[a]
III	*m*-Cresol methyl ether (165°)	1-Methoxy-3-methyl-4-iodobenzene[b]
IV	*o*-Cresol methyl ether (180°)	1-Methoxy-2-iodo-4-methylbenzene[c] (80%)[7]
V	*o*-Nitro-anisole (160–180°)	2-Nitro-4-iodo-anisole
VI	*p*-Nitro-anisole (160–170°)	2-Iodo-4-nitro-anisole[d]
VII	*m*-Nitro-anisole (160–170°)	3-Nitro-4-iodo-anisole[9,e]
VIII	*m*-Amino-anisole[f]	1-Methoxy-3-amino-6-iodobenzene[g] (oil)

[a] Non-volatile with steam. Identical with the ether formed by the methylation of the phenol (m. p. 65°) obtained from 2-amino-5-iodobenzene.[5] [b] Constitution proved by synthesis from 1-methoxy-3-methyl-4-aminobenzene.[6] A little liquid 6-iodo derivative is also formed, as well as some methoxybenzoic acid. [c] Willgerodt isolated the 2- and 3-iodo isomers from the cresol ether and iodine chloride. We found no evidence of the 3-iodo isomer[7] (m. p. 75°). [d] When reduced it gave an amine (m. p. 74°) whose hydrochloride melted at 170°. Calcd.: N, 4.92. Found: N, 4.88. The results agree with the work of Brenans and Reverdin.[8] [e] 3-Nitro-4-iodophenetole was obtained from *m*-nitrophenetole. [f] Heated with iodine, calcium carbonate and water. [g] 2-Iodo-5-nitro-anisole (m. p. 127–128°)[10] on reduction gave an oil whose hydrochloride was identical with the preceding; analysis and mixed m. p.

CONSTANTS AND ANALYTICAL DATA

No.	M. p., °C.	Formula		Analyses, % Calcd.	Analyses, % Found
II	74	C_8H_9IO	I	51.21	51.2
III	75	C_8H_9IO	I	51.21	51.10 51.15
IV	(Oil, b. p. 240°)	C_8H_9IO	I	51.21	51.13
V	98	$C_7H_8INO_2$	N	5.01	5.03 5.09
VI	96	$C_7H_8INO_2$		...	...
VII	62	$C_7H_8INO_2$	N	5.01	4.98
VIII	155–156	$C_7H_8INO\cdot HCl$	HCl	12.78	12.22

When the 2-nitro-4-iodo-anisole was reduced, the amine and its acetyl derivative were identical with the compounds synthesized from *p*-acetanisidine.

1-Methoxy-2-nitrodiphenylurea from phenylisocyanate and the 2-nitro-4-amino-anisole melts at 164°.

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[5] Wheeler and Liddle, *Am. Chem. J.*, **42**, 501 (1909).

[6] Stadel, *Ann.*, **217**, 51 (1883); **259**, 210 (1890); Khotinsky and Jacopson-Jacopmann, *Ber.*, **42**, 3097 (1909); Gibson, *J. Chem. Soc.*, **123**, 1269 (1923).

[7] Willgerodt and Kornblum, *J. prakt. Chem.*, [2] **39**, 296 (1889); Schall and Dralle, *Ber.*, **17**, 2533 (1896).

[8] Brenans, *Compt. rend.*, **134**, 360 (1902); Reverdin, *Ber.*, **29**, 998 (1896); *Bull. soc. chim.*, [3] **15**, 639 (1896).

[9] Reverdin, *Ber.*, **29**, 2597 (1896); *Bull. soc. chim.*, [3] **17**, 115 (1898); Hahle, *J. prakt. Chem.*, [2] **42**, 74 (1891).

[10] Mendola and Eyre, *Chem. Zentr.*, II, 97 (1901).

[11] German patent 101,778; Reverdin and Bucky, *Ber.*, **39**, 2698 (1896).

Anal. Calcd. for $C_{14}H_{13}N_3O_4$: N, 14.63. Found: N, 14.41, 14.70.

VI. The 2-iodo-4-amino-anisole (m. p. 74°) can be easily made directly from *p*-anisidine by heating with calcium carbonate, iodine, water and ether. It must be extracted from the reaction product as it is not volatile with steam. Under like conditions *p*-phenetidine gives the 2-iodo-4-aminophenetole.[12]

The constitution of the 2-iodo-4-nitro-anisole was further proved by diazotizing 4-nitro-*o*-anisidine. The iodine compound melted at 96° and the identity was confirmed by analysis and mixed melting point.

1-Methoxy-4-nitro-2-diphenyl-urea from the nitro-anisidine and phenyl isocyanate melted at 192°.

Anal. Calcd. for $C_{14}H_{13}N_3O_4$: N, 14.63. Found: N, 14.70.

Summary

It has been shown that the methyl cresol ethers and the nitro-anisoles can be iodinated directly at temperatures of 160–180°, using nitric acid as an oxidizing agent. The methoxy group has the main directing influence in the position of the iodine.

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THE CONSTITUTION OF CERTAIN CHLORO-IODO AND BROMO-IODO ANILINES AND BENZENES

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In the course of the study of the effect of halogens on the aromatic amines, it became necessary to prepare certain iodine substitution products of the chloro and bromo substituted anilines. The method of Wheeler was employed, wherein iodine was allowed to react with the amine in the presence of calcium carbonate and water.[1]

In the paper in question[2] the final determination of structure of some of the derivatives was from necessity left unsettled and the present work fills in the lacunae with some additional data.

Experimental

4-Bromo-2,6-di-iodo-aniline.[3]—The iodination of 4-bromo-2-iodo-aniline gave a di-iodo compound (m. p. 148°). When this was diazotized in alcohol solution, the product was the known 1-bromo-3,5-di-iodobenzene (m. p. 140°).[4]

Anal. Calcd. for $C_6H_3BrI_2$: Br, 19.53; I, 62.09. Found: Br, 19.35; I, 62.01.

1-Bromo-3,4,5-tri-iodobenzene was prepared from the bromo-di-iodo-aniline

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[12] Reverdin, *Ber.*, **29**, 2596 (1896).

[1] Wheeler and others, *Am. Chem. J.*, **42**, 441, 448 (1909); **44**, 127, 500 (1910).

[2] Dains, Vaughan and Janney, THIS JOURNAL, **40**, 931–936 (1918).

[3] Ref. 2, p. 932.

[4] Körner and Condardi, *Chem. Zentr.*, II, 1038 (1913); *Atti. Accad. Lincei.*, **22**, 832 (1913).