Anal. (Carius). Calcd. for $C_8H_9ON_2Br$: Br, 34.89. Found: 35.26, 35.36.

2,3,5-Tribromo-4-amino-acetanilide.—When 2.6 g. (2 molecular proportions) of bromine was aspirated into a solution of 2 g. of 3-bromo-4-amino-acetanilide in 50 cc. of glacial acetic acid, a solid tribromo derivative separated. After being treated with alkali to remove hydrobromic acid and crystallized from alcohol, it formed white needles; m. p., 207°. Smaller amounts of bromine gave the same product but in smaller yields.

Anal. (Carius). Calcd. for $C_8H_7O_6N_2Br_3$: Br, 61.97. Found: 61.99, 61.86.

The structure assigned is the one that would be expected from the method of preparation. By diazotization and reduction, the amino group was replaced by hydrogen. Hydrolysis of the product gave a substance melting somewhat indefinitely from 88 to 90°. The expected product, 2,3,5-tribromo-aniline, melts at 91°.[13]

Summary

1. Some new bromo and iodo derivatives of *p*-phenylenediamine have been described.

2. Determinations of the rate of halogen removal from *o*-iodo-aniline and from iodo- and bromo-*p*-phenylenediamine, under conditions designed to measure the positivity of the halogen in question, gave results in the ratio 69.0:6.9:2.6. These fall in the order predicted by the theory advanced.

CHICAGO, ILLINOIS

[CONTRIBUTION FROM THE KENT CHEMICAL LABORATORY, UNIVERSITY OF CHICAGO]

POSITIVE HALOGENS ATTACHED TO CARBON IN THE AROMATIC SERIES. IV. SELECTIVITY OF HALOGEN REMOVAL

BY BEN H. NICOLET AND REUBEN B. SANDIN[1]

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In previous papers of this series[2] attention has been called to the tendency of bromine or iodine occupying certain specific positions in aromatic compounds to be removed by hydrolysis and replaced by hydrogen. Such halogens are to be found primarily in positions *ortho* or *para* to amino or hydroxyl groups, and their whole behavior is conveniently summed up in the statement that they react as somewhat positive halogens.

In studying the removal of such halogens it has often proved more convenient to perform the hydrolysis in the presence of stannous chloride in order to obviate effects due to resubstitution and to oxidation. It is believed that the presence of this reducing agent does not affect in any important way the primary reaction of halogen removal.[2b]

[13] Claus and Wallbaum, *J. prakt. Chem.*, [2] **56**, 60 (1897).

[1] The material here presented was used by Reuben B. Sandin in partial satisfaction of the requirements for the degree of Doctor of Philosophy at the University of Chicago, 1924.

[2] (a) Nicolet, THIS JOURNAL, **43**, 2081 (1921). (b) Nicolet and Sampey, *ibid.*, **49**, 1796 (1927). (c) Nicolet and Ray, *ibid.*, **49**, 1801 (1927).

The explanation advanced for the behavior of these reactive halogens implies that halogens in other positions in the molecule should show very different behavior and there is a large amount of evidence in the chemical literature to show that this is, at least qualitatively, the case. In the present paper, striking evidence of a more quantitative nature is presented.

3-Iodo-4-aminotoluene readily shows the reactions of positive iodine.[2a,3] 2-Iodo-4-aminotoluene should not and, we find, does not show such reactions. A number of new derivatives of the latter substance, containing bromine or iodine in the 3 or 5 position, have been prepared and their hydrolysis with hydrochloric acid in the presence of stannous chloride has been studied. The results (Table I) indicate that under conditions which cause removal of iodine, or even of bromine, from the 3 or 5 position (with reference to methyl), the 2-iodine is completely unaffected. These results are fully in accord with the original assumptions and are considered, incidentally, as a further justification for the use of stannous chloride in this and earlier work.

A quantitative comparison of the rates of removal of iodine (Table II) from 2-iodo-aniline and from 2,5-di-iodo-4-aminotoluene (only the 5-iodine is removed in the latter case) has been made and the former reaction is found to be about one-third more rapid. Fair constants for the velocity of the reaction have been calculated on the assumption that it is not influenced by changes in the concentration of stannous chloride. The latter, however, is relatively large in these cases. More decisive results on this point[4] have been obtained in other instances.

Experimental Part

2-Iodo-4-nitrotoluene.—*o*-Toluidine was nitrated by a method[5] recommended for the nitration of *p*-toluidine; a 70% yield of crude 2-amino-4-nitrotoluene was obtained. The 2-iodo-4-nitrotoluene was made according to Willgerodt and Kok[6] with a 90% yield. It formed nearly white crystals; m. p., 54°.[7]

2-Iodo-4-aminotoluene.—The nitro compound was reduced with tin and hydrochloric acid and the base recovered by steam distillation; yield, 90%. The pure substance melted at 39° and its acetyl derivative at 130°.[8]

2,5-Di-iodo-4-aminotoluene.[9]—A mixture of 5 g. of 2-iodo-4-aminotoluene, 5.4 g. of iodine, 2.5 g. of calcium carbonate and 10 cc. each of water and ether was refluxed on

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[3] Wheeler and Liddle, *Am. Chem. J.*, **42**, 453 (1909).

[4] To be presented later by Dr. J. R. Sampey.

[5] Houben-Weyl, "Die Methoden der organischen Chemie," Georg Thieme, Leipzig, **1924**, vol. 4, p. 139.

[6] Willgerodt and Kok, *Ber.*, **41**, 2077 (1908).

[7] The melting point has previously been given as 58° (Ref. 6) and 51° [Reverdin, *Ber.*, **30**, 3000 (1897)].

[8] Willgerodt and Gartner [*Ber.*, **41**, 2813 (1908)] reduced the nitro compound with ferrous sulfate and ammonia; their base melted at 37°; acetyl derivative, m. p., 130°.

[9] Wheeler, *Am. Chem. J.*, **44**, 501 (1910).

a water-bath for three hours and then made alkaline and subjected to steam distillation. The 2,5-di-iodo derivative came over slowly and separated for the most part in the condenser. It formed needles from alcohol; m. p., 110°.

Anal. (Carius). Calcd. for $C_7H_7NI_2$: I, 70.75. Found: 71.0, 71.2.

One g. of the substance was heated to boiling under reflux for two hours with 10% hydrochloric acid. 2-Iodo-4-aminotoluene was the chief product. Iodine equivalent to 0.3 atom was deposited in the condenser; that in the solution was not determined.

2,5-Di-iodo-4-acetotoluide.—When the base was warmed with acetic anhydride the acetyl derivative was obtained. It formed white needles; m. p., 193°.

Anal. (Carius). Calcd. for $C_9H_9ONI_2$: I, 63.34. Found: 63.37, 63.47.

2-Iodo-5-bromo-4-acetotoluide.—2-Iodo-acetotoluide was dissolved in five parts of glacial acetic acid, treated with one mole of bromine and allowed to stand for 12 hours. The yield was nearly quantitative. The purified product formed white needles; m. p., 165–166°. When treated with additional bromine under similar conditions it did not react further.

Anal. (Carius). Calcd. for C_9H_9ONBrI: AgBr + AgI, 119.4. Found: 118.6, 118.4.

2-Iodo-5-bromo-4-aminotoluene.—The acetyl derivative was refluxed for ten minutes with 20% hydrochloric acid and the base was recovered by steam distillation; m. p., 86–87°.

Anal. (Carius). Calcd. for C_7H_7NBrI: AgBr + AgI, 135.0. Found: 135.7, 135.6.

2-Iodo-3,5-dibromo-4-aminotoluene.—2-Iodo-4-aminotoluene was brominated in glacial acetic acid solution, using two moles of bromine. The use of less bromine leads to the same product, mixed with unaltered material. After steam distillation, the substance crystallized from alcohol in light brown needles; m. p., 109°; yield, 75%.

Anal. (Carius). Calcd. for $C_7H_6NBr_2I$: AgBr + AgI, 164.6. Found: 164.0.

2-Iodo-3,5-dibromo-4-acetotoluide.—As might have been expected, the base did not acetylate readily. Acetic anhydride was without action but heating with acetyl chloride readily gave the acetyl derivative. From alcohol it separated in fine, white needles; m. p., 228–229°.

Anal. (Carius). Calcd. for $C_9H_8ONBr_2I$: AgBr + AgI, 141.0. Found: 140.3, 139.7.

2,3,5-Tri-iodo-4-aminotoluene.—To a solution of 5 g. of 2-iodo-4-aminotoluene in 50 cc. of glacial acetic acid was added 7.8 g. (2 moles) of iodine monochloride, and the mixture allowed to stand for 24 hours. A tarry mass separated. Water was added and the supernatant liquid decanted. On addition of alkali and steam distillation only 2,5-di-iodo-4-aminotoluene came over. When this was removed, the residue was extracted with hot alcohol and the solution decolorized with charcoal. Repeated recrystallizations from a mixture of alcohol and chloroform gave a small yield of light brown needles, melting constantly at 120–121°.

Anal. (Carius). Calcd. for $C_7H_6NI_3$: I, 78.55. Found: 78.42, 78.23.

The base was not acetylated by hot acetic anhydride. As acetyl chloride would probably have caused liberation of iodine, no further attempt at acetylation was made.

Action of Bromine on 2,5-Di-iodo-4-aminotoluene.—The di-iodotoluidine (0.5 g.) was dissolved in 15 cc. of glacial acetic acid. To this was added 0.44 g. (2 molecular proportions) of bromine, also dissolved in acetic acid, and the whole was allowed to stand for 24 hours. Addition of an excess of alkali and steam distillation gave 0.4 g. of a product melting at 108° which, when mixed with pure 2-iodo-3,5-dibromo-4-

aminotoluene, melted at 109°. The more mobile iodine had thus been replaced by bromine while the iodine in the 2 position was unaffected.

Hydrolysis and Reduction with Hydrochloric Acid and Stannous Chloride.—As some of the halogenated toluidines described above were difficultly soluble in hot hydrochloric acid, they were dissolved in a mixture of equal volumes of concd. hydrochloric acid and glacial acetic acid. The amount of amine was so chosen that the solution was approximately 0.055 M in each case. An excess of stannous chloride (2 moles for each atom of halogen present) was then added and the solutions were heated under reflux to active boiling for the times indicated in Table I.

In the last column of Table I are listed the products isolated in each case. These were identified by the melting points of the free base or acetyl derivative or both. In each instance the identification was confirmed by determining the melting point of a mixture of the product with a known sample of the pure substance. Large samples were not used and the difference between the reported totals and 100% represents losses in recovery and separation, rather than side reactions. In no case was there any indication of the removal of iodine in the 2 position with formation of *p*-toluidine.

TABLE I

REACTION WITH HYDROCHLORIC ACID AND STANNOUS CHLORIDE

Substance used	Time of hydrolysis, hours	Products recovered
2-Iodo-4-aminotoluene	8.0	Unaltered material only
2,5-Di-iodo-4-aminotoluene	0.5	20% unaltered; 30% of 2-iodo-4-aminotoluene
2,3,5-Tri-iodo-4-aminotoluene	1.5	No unaltered material; 50% of 2-iodo-4-aminotoluene
	1.5	2-Iodo-4-aminotoluene only
2-Iodo-5-bromo-4-aminotoluene	8.0	5% unaltered; 70% of 2-iodo-4-aminotoluene
2-Iodo-3,5-dibromo-4-aminotoluene	4.0	50% of 2-iodo-5-bromo-4-aminotoluene
	8.0	Chiefly 2-iodo-4-aminotoluene; a little 2-iodo-5-bromo derivative.

Quantitative Comparison of the Rates of Removal of Iodine from 2,5-Di-iodo-4-aminotoluene and 2-Iodo-aniline.—To a solution of 0.00066 mole of substance in 10 cc. of glacial acetic acid was added 5 cc. of 10% hydrochloric acid containing 0.5 g. of $SnCl_2.2H_2O$. In each experiment such a mixture was heated in a rapidly boiling water-bath for the time indicated, then quickly cooled and diluted with water. An extraction with chloroform at this point removed a small amount of material which otherwise gave an interfering color in the subsequent titration. Iodine was determined[2b] by the method of Fresenius. The atomic % of iodine removed in each case, together with the values of K calculated on the assumption that the reaction is of the first order, are given in Table II.

TABLE II

RATE OF IODINE REMOVAL

Time, min.	2-Iodo-aniline Reaction, %	2-Iodo-aniline K	2,5-Di-iodo-4-aminotoluene[a] Reaction, %	2,5-Di-iodo-4-aminotoluene[a] K
5	7.82	0.0165	6.72	0.0137
15	25.18	.0194	23.13	.0169
30	49.18	.0226	36.22	.0150
60	75.19	.0232	61.46	.0161
120	93.23	.0225	83.50	.0150

[a] Only one iodine is reactive.

Summary

1. A number of new halogen derivatives of 2-iodo-4-aminotoluene have been prepared.
2. A study of the selectivity and rate of halogen removal in these compounds offers striking confirmation of predictions based on a consideration of the removable halogens as positive.

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[CONTRIBUTION FROM THE KENT CHEMICAL LABORATORY, UNIVERSITY OF CHICAGO]

POSITIVE HALOGENS ATTACHED TO CARBON IN THE AROMATIC SERIES. V. ANALOGY BETWEEN POSITIVE AND NEGATIVE HALOGENS

BY BEN H. NICOLET

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The pronounced reactivity toward all alkaline reagents of the halogens in 2,4- and 2,6-dinitrophenyl halides is well known. The halogens are removed as halide ion and replaced by —OH, —NH_2, etc. Very few chemists have hesitated to attribute this increase in reactivity to an increase in the negative character of the halogen in question by the nitro groups, which in turn are usually conceded, in recent years at least,[1] to be positive in character. The fact that no case was known in which a halogen attached to carbon in a benzene ring was given a conspicuously negative character by substituents occupying only positions *meta* to it, appears to have caused little apprehension.

Recent papers[2] from this Laboratory have discussed as positive certain halogens (bromine and, more conspicuously, iodine) which, when occupying positions *ortho* or *para* to one or more amino or hydroxyl groups, were

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[1] Fry, "Electronic Conception of Valence," Longmans, Green and Co., **1921**, p. 122. Stieglitz, THIS JOURNAL, **44**, 1305 (1922). Shoesmith, Hetherington and Slater, *J. Chem. Soc.*, **125**, 1314 (1924).

[2] (a) Nicolet, THIS JOURNAL, **43**, 2081 (1921). (b) Nicolet and Sampey, *ibid.*, **49**, 1796 (1927). (c) Nicolet and Ray, *ibid.*, **49**, 1801 (1927). (d) Nicolet and Sandin, *ibid.*, **49**, 1806 (1927).