Relative Ease of Removal of Iodine.—The conditions used have been described. Table I gives the percentage of total iodine present removed after heating at 100° for the lengths of time specified.

Summary

1. The preparation of a number of new iodo derivatives of resorcinol and of *m*-phenylenediamine has been described.

2. A standard method for the removal of iodine from these substances by hydrolysis and mild reduction has been applied and the results have been correlated with the theory presented as to the relatively positive nature of the halogens involved.

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

POSITIVE HALOGENS ATTACHED TO CARBON IN THE AROMATIC SERIES. III. DERIVATIVES OF PARA-PHENYLENEDIAMINE, PARA-NITRO-ANILINE AND MESITYLENE

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As has been more clearly set forth in previous papers[2] a positive character is attributed to such halogens as are removed on hydrolysis to give products other than halides, and are replaced during this reaction by hydrogen. Such behavior has been demonstrated in the case of a number of *o*- or *p*-bromo or iodo derivatives of phenol and of aniline, and corresponding iodo derivatives of resorcinol and of *m*-phenylenediamine have been shown to give similar results with the greater readiness which would be expected if the two negative groups united in enforcing an increased positivity of the halogens in question.

Before reporting the work done with derivatives of *p*-phenylenediamine and *p*-nitro-aniline, some results obtained with iodomesitylene will be discussed briefly. The methyl group is usually considered to be negative, although conspicuously less so than the hydroxyl or amino group. A sufficient number of methyl groups, properly placed, might perhaps cause an iodine atom to show properties similar to those referred to above. The ideal derivative for such a purpose should be iodomesitylene,[3] which

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[1] The material here presented was used by William L. Ray in partial satisfaction of the requirements for the degree of Doctor of Philosophy at the University of Chicago, 1923.

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

[3] Klages [*J. prakt. Chem.*, [2] **61**, 307 (1900)] has shown that iodomesitylene is reduced by hydriodic acid at a considerably lower temperature than that required for iodobenzene. Töhl and Eckel [*Ber.*, **26**, 1099 (1893)] found that iodomesitylene yielded

contains three methyl groups, all *ortho* or *para* to the iodine in question. It was found that while a solution of iodomesitylene in glacial acetic acid containing hydrogen chloride could be heated under reflux without the liberation of appreciable quantities of iodine, such solutions, when heated in sealed tubes at 135 or 150°, showed iodine liberation to a very considerable extent. Under similar conditions phenyl iodide showed, as was expected, no evidence of reaction.

Preparation and Hydrolysis of Iodomesitylene.—The iodination of mesitylene with iodine and iodic acid in acetic acid solution[4] gave better results than the use of sulfur iodide.[5] Owing to the insolubility of iodomesitylene in water, a solution was prepared containing, per 100 cc. of glacial acetic acid, 5.6 g. of iodomesitylene and 6.6 g. of dry hydrogen chloride. Portions of this solution were heated in sealed tubes in a bomb furnace with the results shown in Table I. The liberated iodine was titrated with thiosulfate, and unaltered iodomesitylene was recovered in each case. After the last run no di-iodomesitylene could be found, showing that resubstitution had not occurred to any appreciable extent. Mesitylene was, however, isolated and identified by its boiling point and by the deep red color it gave with diazotized picramide.[6]

TABLE I

LIBERATION OF IODINE FROM IODOMESITYLENE

Time of heating, hours	Temp., °C.	Total iodine liberated, %
1	135	7.8
1	135	9.5
4.5	150	20.0
6	150	42.9

Iodobenzene was heated under conditions parallel to those described. No iodine color developed and no benzene could be detected.

A solution of 2 g. of iodomesitylene and 3.66 g. (2 molecular proportions) of stannous chloride in 7.2 cc. of concd. hydrochloric acid and 34 cc. of acetic acid was heated for 6.5 hours at 135°. The chief product was mesitylene, although a little of the iodo derivative remained.

As a test of the theory as to the importance of the position occupied by the activating groups, as well as of their number and character, it was considered desirable to study the effect on the lability of a bromine or iodine atom in the 2 position relative to an amino group, of additional substituents such as an amino or a nitro group in the 4 position. To this end, suitable derivatives of *p*-nitro-aniline and of *p*-phenylenediamine were prepared and characterized.

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di-iodomesitylene when shaken with concd. sulfuric acid. The latter is, however, too strong an oxidizing agent to make this resubstitution conclusive evidence of positivity.[2a]

[4] Klages and Storp, *J. prakt. Chem.*, [2] **65**, 564 (1902).

[5] Edinger and Goldberg, *Ber.*, **33**, 2881 (1900).

[6] Meyer and Tochtermann, *Ber.*, **54**, 2283 (1921).

Hydrolyses with Acid Only.—Solutions of the substance in 10% hydrochloric acid were boiled under reflux for suitable periods. After appropriate adjustment of the acidity, these solutions were then titrated with thiosulfate. The results obtained with 2-iodo-4-nitro-aniline are given in Table II, with velocity constants (time in minutes) calculated for a first-order reaction.

Table II

Hydrolysis of 2-Iodo-4-nitro-aniline with Acid Only

Time, min.	Reaction, %	$K \times 10^3$
120	27.6	2.69
205	45.7	2.98
240	51.2	2.99
360	63.3	2.82

The "constants" obtained by this method have, however, relatively little meaning and are given only to illustrate this fact. The accumulation of oxidizing power in the solution (which is what is measured) really represents the difference between hydrolysis on the one hand and resubstitution or oxidations of other types on the other. In the case of iodophenylenediamine, extensive oxidation was evident from the first and the values found were very irregular. With iodonitro-aniline no destructive oxidation was noticed. The extent to which resubstitution took place is unknown, at least no di-iodonitro-aniline could be detected under the conditions described. When, however, iodonitro-aniline was heated under reflux with three parts of glacial acetic acid and one of hydrochloric acid, some 2,6-di-iodo-4-nitro-aniline (m. p., 243°) was isolated, and when 2 g. of the iodonitro-aniline was heated with 20 cc. of concd. hydrochloric acid in a bomb tube for eight hours at 105°, not only was some of the di-iodo derivative formed, but the resulting solution showed very little oxidizing power. In view of the other results described, there can be little question that hydrolysis was here a fairly rapid reaction, but resubstitution must have taken place with almost equal efficiency. The reason for placing little weight on quantitative results obtained in the presence of acid alone is thus apparent.

Hydrolyses in the Presence of Stannous Chloride.—This more accurate method cannot, of course, be applied to nitro compounds, as they would undergo reduction. In making measurements, 2 g. of substance was dissolved in 20 cc. of 10% hydrochloric acid containing 4.0 g. of $SnCl_2.2H_2O$. Such solutions were boiled under reflux for the desired periods, and then cooled. Iodine was determined as described by Nicolet and Sampey.[2b] The results obtained with 2-iodo-*p*-phenylenediamine are given in Table III, together with the velocity constants calculated on the assumption[7] that the reaction rate is proportional only to the concentration of the

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[7] For a justification of this assumption, see Ref. 2b.

organic iodo compound. For comparison, *o*-iodo-aniline was prepared and hydrolyzed under parallel conditions. The percentage of reaction after 15 and 30 minutes was in this case 61.9 and 89.0%, corresponding to $K \times 10^3 = 64.0$ and 74.0, respectively. It is apparent that the 4-amino group decreases the rate of reaction decidedly.

TABLE III

HYDROLYSIS OF IODO-*p*-PHENYLENEDIAMINE, USING STANNOUS CHLORIDE

Time, min.	Total iodine removed, %	$K \times 10^3$, min.
60	29.4	5.9
180	72.9	7.2
240	79.4	7.1
300	89.5	7.5

The hydrolysis of bromo-*p*-phenylenediamine was similarly carried out in the presence of stannous chloride, but the direct determination of small quantities of bromine in the resulting solutions offered too great difficulties, and the progress of reaction was followed in a somewhat rough manner as follows.

After heating for the desired lengths of time, the solutions were cooled, treated with an excess of sodium acetate to remove free hydrochloric acid and then well shaken with 2.5 cc. of acetic anhydride. The precipitates, consisting of a mixture of the diacetyl derivatives of *p*-phenylenediamine and its bromo derivative, with base tin salts, were collected, and the tin salts washed out with dil. hydrochloric acid. Bromine was then determined (Carius) in the residue, and the proportion of the bromo compound calculated. As diacetyl-*p*-phenylenediamine is decidedly less soluble than its bromo derivative, this method somewhat exaggerates the ease of bromine removal. After boiling for six and nine hours the extent of bromine removal was found to be 54.3 and 78.8%, corresponding to values of $K \times 10^3$ (minutes) of 2.3 and 2.9, respectively. As anticipated, bromine is removed less rapidly than iodine.

Experimental Part

2-Iodo-*p*-phenylenediamine.—Ten g. of 2-iodo-4-nitro-aniline[8] was covered with 50 cc. of concd. hydrochloric acid and gently warmed, and 30 g. of $SnCl_2.2H_2O$ in 50 cc. of hydrochloric acid was added slowly with stirring. Stirring and warming were continued until most of the material was dissolved and the yellow color had disappeared. The solution was cooled in ice (a white double salt separated) and cautiously made alkaline with 50% sodium hydroxide solution. After thorough cooling, rapid filtration gave a 75% yield of product which crystallized from water in white needles; m. p., 110.5°.

Anal. (Carius). Calcd. for $C_6H_7N_2I$: I, 54.24. Found: 54.03, 53.93.

2,5-Diacetylamino-iodobenzene.—This was readily obtained by the action of acetic anhydride and crystallized from acetic acid; m. p., 211.5°.

Anal. (Carius). Calcd. for $C_{10}H_{11}O_2N_2I$: I, 39.91. Found: 39.80.

2,5-Dibenzoylamino-iodobenzene.—The base was benzoylated by the Schotten-Baumann method. The product, slightly soluble in the commoner solvents, was crystallized from nitrobenzene; m. p., 254°.

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[8] Willgerodt and Arnold, *Ber.*, **34**, 3351 (1901).

Anal. (Carius). Calcd. for $C_{20}H_{15}O_2N_2I$: I, 28.71. Found: 28.86.

Acetylation of 2,6-Di-iodo-4-nitro-aniline.—Körner and Contardi[9] reported an acetyl derivative melting at 249°, prepared by the action of acetic anhydride on the amine. When the base was refluxed for an hour with an excess of anhydride, with or without fused sodium acetate, we obtained a product melting at 248°, which was only exceptionally pure di-iodonitro-aniline.

Anal. (Carius). Calcd. for $C_6H_4O_2N_2I$: I, 65.11. Found: 64.97.

When 10 g. of the base was warmed with 35 cc. of anhydride containing five drops of concd. sulfuric acid, the N-diacetyl derivative melting at 169°[10] was formed.

Anal. (Carius). Calcd. for $C_{10}H_8O_4N_2I_2$: I, 53.55. Found: 53.40, 53.45.

2-Bromo-4-nitro-aniline.—This substance has been made by a number of indirect methods.[11] The direct bromination has been stated[9] to give a mixture difficult to separate, of mono- and dibromo derivatives. The following procedure was found effective. Seventy-five g. of *p*-nitro-aniline was dissolved by heating in 1000 cc. of concd. hydrochloric acid and the solution rapidly cooled to room temperature. The aspiration through the solution of 87 g. of bromine was begun promptly and completed during two hours with frequent agitation. The solution was then filtered and the solid agitated with a liter of water to hydrolyze the hydrochloride. The insoluble base was crystallized from 600 cc. of 65% alcohol. The yield, including two crops after concentration of the solution, was 81%; m. p., 104.5°. When the bromine was dissolved in concd. hydrochloric acid and added in this form, the yield was reduced and some of the dibromo derivative was formed.

2-Bromo-4-nitro-acetanilide.—Attempts to brominate *p*-nitro-acetanilide in acetic acid solution were not successful even when iron wire was added as catalyst. Acetylation of bromonitro-aniline is moderately difficult. Chattaway and Orton[12] heated it with acetyl chloride at 130° and obtained a mono-acetyl derivative melting at 129°, but Körner and Contardi[9] speak of an acetyl derivative (m. p., 114°) and a diacetyl derivative (m. p., 132°). To a mixture of 10 g. of bromonitro-aniline and 5 cc. of glacial acetic acid containing 5 drops of concd. sulfuric acid, was added 5 cc. of acetic anhydride and the whole was warmed until the yellow color disappeared. The nearly white product (10.5 g.) melted at 129–130°. It was also obtained when the base was boiled for an hour with acetic anhydride alone. Analysis showed it to be the mono-acetyl derivative.

2-Bromo-*p*-phenylenediamine.—The bromonitro-aniline was reduced as already described for the iodo compound, and the base extracted with ether. The product (yield, 75%) crystallized from carbon tetrachloride in white needles; m. p., 76°.

Anal. (Carius). Calcd. for $C_6H_7N_2Br$: Br, 42.73. Found: 42.86, 42.95.

2,5-Diacetylaminobromobenzene.—The acetylation offered no difficulty. The product melted at 200°.

Anal. (Carius). Calcd. for $C_{10}H_{11}O_2N_2Br$: Br, 29.48. Found: 29.61.

2-Bromo-4-amino-acetanilide.—Bromonitro-acetanilide was suspended in twice its weight of concd. hydrochloric acid and treated with 3 moles of $SnCl_2.2H_2O$ in the same solvent. The mixture, which became somewhat warm, was stirred for half an hour, cooled and made alkaline with 50% sodium hydroxide solution. The gummy mass which separated gave crystals from benzene; m. p., 123°.

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[9] Körner and Contardi, *Atti accad. Lincei*, **22** [I], 825 (1913); *C. A.*, **8**, 73 (1914).

[10] Körner and Contardi (Ref. 9) give 171°.

[11] Hübner, *Ber.*, **10**, 1709 (1877); *Jahresber.*, 305, 350, **1875**, Ref. 9.

[12] Chattaway and Orton, *Ber.*, **33**, 2398 (1900).

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.

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

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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).