[CONTRIBUTION FROM KENT CHEMICAL LABORATORY, UNIVERSITY OF CHICAGO]

POSITIVE HALOGENS ATTACHED TO CARBON IN THE AROMATIC SERIES. II. IODINE DERIVATIVES OF META-PHENYLENEDIAMINE AND OF RESORCINOL

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Some time ago one of us[2] called attention to the fact that certain compounds containing bromine or iodine in the benzene ring could undergo hydrolysis in such a way that the halogen was replaced by hydrogen, while the solution acquired oxidizing properties evidenced by the liberation of free halogen, or by the formation of more highly halogenated derivatives. Such behavior might be said to constitute the experimental definition of what is here meant by a positive[3] halogen in organic combination.

In the cases previously cited, the halogen which reacted in this manner was always *ortho* or *para* to an amino or hydroxyl group. As these radicals are among the most strongly negative recognized by advocates of modern theories of polar valence[4] as applied to organic compounds, the results are well in accord with those to be deduced from the electronic structure of benzene as depicted by Stieglitz[5] or from the theory of induced alternations in polarity.[6,7] As a further consequence of these theories

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

[2] Nicolet, THIS JOURNAL, **43**, 2081 (1921).

[3] A *relatively* positive halogen (as shown by its reactions) is meant. The "assumption that each atom in a molecule exists in a definite oxidation-reduction stage which can be represented by an integral polar number" [Lewis, "Valence and the Structure of Atoms," A. C. S. Monograph Series, Chemical Catalog Co., New York, **1923**] is here expressly denied. A displacement, probably relatively slight, of the electrons which in terms of the Lewis theory are shared by the atoms in question, could explain the results here described.

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

[5] Ref. 4 b, p. 1293.

[6] (a) Lapworth, *Mem. Manchester Phil. Soc.*, **64** [II], 1 (1920); (b) *J. Chem. Soc.*, **121**, 416 (1922). (c) Kermack and Robinson, *ibid.*, **121**, 427 (1922). (d) Lapworth and Shoesmith, *ibid.*, **121**, 1391 (1922).

[7] It seems of interest to point out that since substituents entering the benzene ring are usually positive (Ref. 5) the data collected by de Lange [*Rec. trav. chim.*, **45**, 19 (1926)] on "The Displacement of Atoms and Groups in the Benzene Nucleus," can in general be interpreted as the replacement of *positive* groups. It will be shown in Paper V of the present series [Nicolet, THIS JOURNAL, **49**, 1810 (1927)] that the existence of reactions by which these polarities can be demonstrated may also be correlated with the possibility of the formation of quinoidal derivatives. Whatever the ultimate fate of the present interpretation may be, at the very least it constitutes a conspicuously efficient mnemonic system for the prediction of such replacements.

and of the interpretation previously given, it was to be expected that two amino or hydroxyl groups, both *ortho* or *para* to the halogens in question, would result in increased reactivity of these halogens in the sense indicated. It is the purpose of this paper to show that suitable iodo derivatives of *m*-phenylenediamine and of resorcinol behave in the anticipated manner.

The preparation of the necessary derivatives, a number of which are new, is described in the Experimental Part. All of them showed liberation of iodine when boiled with 10% hydrochloric acid, the rates varying both with constitution and with the solubilities of the individual substances. It was not thought desirable to estimate quantitatively the rates of iodine liberation, as these were obviously complicated by simultaneous reactions of resubstitution and of oxidation. While the *type* of these side reactions confirms the assumption that halogen is here removed in positive form, their *existence* would make useless any figures on rate of accumulation of oxidizing substances in solution. The type of initial reaction assumed is here indicated.

$$\mathrm{RI} + \underset{(\mathrm{HCl})}{\mathrm{H_2O}} \rightleftharpoons \mathrm{RH} + \underset{(\mathrm{ClI})}{\mathrm{HOI}}$$

Data are presented showing relative rates of formation of iodide ion when the substances described are boiled with acid in the presence of sufficient acetic acid to dissolve them, and of an excess of stannous chloride, to prevent oxidation and resubstitution. The use of stannous chloride in the estimation of the positivity of halogens under such conditions has already been suggested.[1] Experience seems to have justified its use.[8] The use of hydriodic acid as reducing agent in such tests has recently become somewhat common.[9] While we are inclined to believe that the rate of removal of halogen atoms by reduction with hydriodic acid is probably related to the positivity of the halogen in question, there are few halogens which are not replaced by hydrogen under the influence of hydriodic acid at higher temperatures;[10] there is also the further disturbing factor, particularly in the work quoted,[9] that the reaction[11]

[8] Three lines of evidence may be mentioned. (a) The halogens removed, as recorded in chemical literature and as found in these experiments, are those, and only those, whose removal would be predicted on the basis of the theory here presented. (b) No evidence is known that stannous chloride can act like certain metals (in other words, magnesium in the Grignard reagents) to form an intermediate compound of a type which would be expected to hydrolyze in such a way as to give the results obtained. Burton and Kenner [*J. Chem. Soc.*, **121**, 680 (1922)] suggest the formation of an intermediate compound which they assume would act in this way; we doubt their interpretation, for reasons given in this note, particularly under (c). (c) In certain analogous cases, evidence has been obtained (as yet unpublished) that the *rate* of removal of halogen is not proportional to the concentration of stannous chloride present.

[9] Ref. 6 d. Shoesmith, *J. Chem. Soc.*, **123**, 2828 (1923). Ref. 4 c.

[10] Klages, *J. prakt. Chem.*, [2] **61**, 307 (1900).

[11] Conant, Kirner and Hussey, THIS JOURNAL, **47**, 488 (1925), and earlier papers there cited.

RBr + HI = RI + HBr continually changes, to an uncontrolled extent, the nature of the halogen being removed. We are, therefore, much inclined to prefer stannous chloride as a diagnostic reagent. Its rather extreme specificity will be further illustrated in Paper IV of this series.

Experimental Part

4-Iodoresorcinol.[12]—It was not found possible to prepare this substance by the method of Stenhouse.[13] Several attempts to modify his conditions led also to mixtures in which, after benzoylation, it was possible to identify only derivatives of resorcinol and di-iodoresorcinol. The action of iodine chloride in ether, acetic acid or hydrochloric acid gave similar results. Attempts to obtain it from 5-iodo-2,4-dihydroxybenzoic acid or from 4-iodo-3-hydroxyphenyl benzoate also failed. Finally, monomercurized resorcinol was prepared by the method of Dimroth;[14] the yield was very poor. Replacement of the mercury by iodine took place normally, and Stenhouse's 4-iodoresorcinol[15] resulted.

4,6-Di-iodoresorcinol.—To 5 g. of resorcinol dissolved in 185 cc. of 20% hydrochloric acid was added 7.3 g. (2 moles) of iodine monochloride. A precipitate appeared immediately. After fifteen minutes, the excess of iodine was removed with sodium sulfite, the solution filtered, and the solid dried and crystallized from benzene; yield, 80%. The substance forms colorless crystals, m. p. 145°, readily soluble in ether, alcohol and benzene, less so in chloroform and hot water, and nearly insoluble in cold water and ligroin.

Anal. (Carius). Calcd. for $C_6H_4O_2I_2$: I, 70.1. Found: 69.9.

The same substance was also made by the method of Stenhouse[13] but a pure product was more difficult to obtain by this procedure.

4,6-Di-iododibenzoylresorcinol.—The di-iodoresorcinol was dissolved in 10% sodium hydroxide solution, and benzoylated by the Schotten-Baumann method. The product decomposed at 195–200°.

Anal. (Carius). Calcd. for $C_{20}H_{12}O_4I_2$: I, 44.6. Found: 45.0.

4-Iodo-3-hydroxyphenyl Benzoate.—Monobenzoylresorcinol[16] was dissolved in glacial acetic acid, and treated with 1 mole of iodine chloride in the same solvent, avoiding rise in temperature. After 15 minutes water was added and the excess of iodine was removed with sodium sulfite. The insoluble material (yield, 65%) was crystallized from benzene. It decomposed at 153–155°.

Anal. (Rosanoff).[17] Calcd. for $C_{13}H_9O_3I$: I, 37.3. Found: 37.4.

5-Iodo-2,4-dihydroxybenzoic Acid.—Resorcinic acid[18] was iodinated with one mole

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[12] No proof is here offered as to the positions assigned to iodine in the products described. The structures given seem logical and further work in progress appears likely to confirm them.

[13] Stenhouse, *Ann.*, **171**, 311 (1874).

[14] Dimroth, *Ber.*, **35**, 2865 (1902).

[15] Richter, "Lexikon der Kohlenstoff-Verbindungen" gives 167° as the melting point of this substance. That given by Stenhouse (67°) is correct.

[16] Kauffmann and Kugel, *Ber.*, **44**, 753 (1911).

[17] Drogin and Rosanoff, THIS JOURNAL, **38**, 711 (1916).

[18] Bistrzycki and Kostanecki, *Ber.*, **18**, 1984 (1855).

of iodine monochloride in ether solution. The product (yield, 44%), after crystallization from dilute acetone, melted at 172°. Attempts to prepare it by the method of Stenhouse[13] gave a mixture of mono- and di-iodinated acids.

Anal. (Carius). Calcd. for $C_7H_5O_4I$: I, 45.4. Found: 45.7.

3,5-Di-iodo-2,4-dihydroxybenzoic Acid.—To a solution of 11 g. of resorcinic acid and 36 g. (2 equivalents) of iodine in 100 cc. of ether, was added 75 g. of litharge, and the whole was refluxed for two hours. After evaporation of the ether, the residue was extracted with alcoholic alkali, and the crude di-iodo acid recovered from the extract by dilution with water, acidification and treatment with sodium sulfite; yield, 50%. The product decomposed at 193–196°.

Anal. (Carius). Calcd. for $C_7H_4O_4I_2$: I, 62.3. Found: 62.9.

4-Chloro-6-iodo-*m*-phenylenediamine.—4-Chloro-*m*-phenylenediamine was iodinated in cold, absolute methyl alcohol solution with 1 mole of iodine and an excess of litharge. After three hours, the solution was filtered, the residue washed with methyl alcohol and the product recovered from the combined filtrates by dilution with water; yield, 80%; m. p., 98°.

Anal. (Carius). Calcd. for $C_6H_6N_2ClI$: AgCl, AgI, 140.2. Found: 139.9.

The same substance was obtained by refluxing a mixture of the chlorodiamine and iodine with water, ether and calcium carbonate. The yield, however, was less good. Iodination with iodine monochloride was unsatisfactory, as oxidation of the amine occurred.

4-Iododiacetyl-*m*-phenylenediamine.—*m*-Nitro-acetanilide was reduced with iron and acetic acid.[19] The solution was filtered from the excess of iron and tarry impurities before making alkaline with sodium carbonate. After salting out and filtering, repeated extraction of the solid with hot benzene gave 70% of the calculated quantity of *m*-amino-acetanilide. Into 5 g. of this, dissolved in 200 cc. of 5% hydrochloric acid, was slowly aspirated 4.9 g. (1 mole) of iodine chloride as vapor. The crude iodo-mono-acetyldiamine was dried, and triturated in a mortar with 2 g. of fused sodium acetate and 3 cc. of acetic anhydride, to form the diacetyl derivative. After crystallization from benzene and from chloroform, the 4-iododiacetyl-*m*-phenylenediamine decomposed at 175–180°.

Anal. (Carius). Calcd. for $C_{10}H_{11}O_2N_2I$: I, 35.5. Found: 36.0.

4,6-Di-iodo-3-acetylamino-aniline.—Four g. of *m*-amino-acetanilide was dissolved in 200 cc. of warm 10% hydrochloric acid, and 8 g. (2 equivalents) of iodine chloride was added. After 15 minutes, sodium sulfite was added to remove the excess of iodine and then sufficient caustic alkali to liberate the amine. The product, crystallized from methyl alcohol, melted at 172–174°.

Anal. (Carius). Calcd. for $C_8H_8ON_2I_2$: I, 60.6. Found: 60.5.

Method of Hydrolysis and Analysis.—All of the substances which have been described liberate iodine when boiled with hydrochloric acid. Some, however, are only slightly soluble in this reagent. Moreover, the iodine liberated causes variable amounts of resubstitution and of oxidation. It was therefore decided to measure the reactivity of iodine in the respective substances by adding sufficient acetic acid to bring them into solution and also an excess of stannous chloride to remove the liberated iodine (as iodide ion) from further reaction. The procedure was as follows.

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[19] By the method used for the *para* compound by Nietzki, *Ber.*, **17**, 343 (1884).

The halogen compound (0.125 g.) was dissolved in 10 cc. of hot glacial acetic acid. To this solution, heated in a bath of boiling water, was added 5 cc. of a hot solution containing 10% each of hydrochloric acid and of $SnCl_2.2H_2O$. Heating was then continued for the time desired, and the solution was removed from the bath, rapidly cooled in water, and analyzed for iodide.

The analytical procedure was based on a method of Fresenius[20] and may be thus outlined.

To the sample to be analyzed, 15 cc. of chloroform was added. Then a 10% solution of sodium nitrite was added, drop by drop, with thorough mixing until the chloroform layer began to be colored; an additional 0.5 cc. was then added; the chloroform was separated and the solution extracted with two more 15cc. portions of chloroform. The combined chloroform extracts were then washed with several small portions of water. After the addition of a few drops of sodium bicarbonate solution, the iodine in the chloroform layer was titrated with 0.02 *N* sodium thiosulfate solution. Special tests in each case showed that the action of nitrous acid under the conditions described did not liberate disturbing amounts of iodine from any of the organic substances used.

TABLE I

RELATIVE RATES OF IODINE REPLACEMENT

Compound used	Time of reaction, minutes	Total iodine removed, %
4-Iodoresorcinol	5	87
4,6-Di-iodoresorcinol	7	66.8
	7	66.5
4-Iodo-3-hydroxyphenyl benzoate	30	11.6
	60	20.0
4,6-Di-iododibenzoylresorcinol	60	2.5
	60	2.7
5-Iodo-2,4-dihydroxybenzoic acid	30	42.4
3,5-Di-iodo-2,4-dihydroxybenzoic acid	30	39.8
4-Iodo-*m*-phenylenediamine[a]	5	66.8
	5	66.0
4,6-Di-iodo-*m*-phenylenediamine[a,b]	5	86.6
	5	85.5
4-Iododiacetyl-*m*-phenylenediamine	20	66.0
4-Iodo-6-chloro-*m*-phenylenediamine	5	98.0
	5	97.5
2-Iodo-*p*-phenylenediamine[c]	60	25.6
	60	25.2
3-Iodo-4-aminotoluene	30	22.0

[a] The corresponding acetyl derivatives were heated for two hours with an excess of 3% sodium hydroxide in 80% alcohol, and the solution was filtered hot to remove a small amount of tar. Water was then added and the alcohol removed by distillation. After cooling, white crystals remained which were separated and dried.

[b] Morgan and Wootton [*J. Chem. Soc.*, **87**, 938 (1905)] have described this substance. They found it rather unstable, and state that "the hydrochloride is decomposed by boiling water."

[c] We are indebted to Dr. W. L. Ray for a sample of this compound.

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[20] Treadwell and Hall, "Analytical Chemistry," John Wiley and Sons, New York, vol. 2, **1919**, p. 657.

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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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