

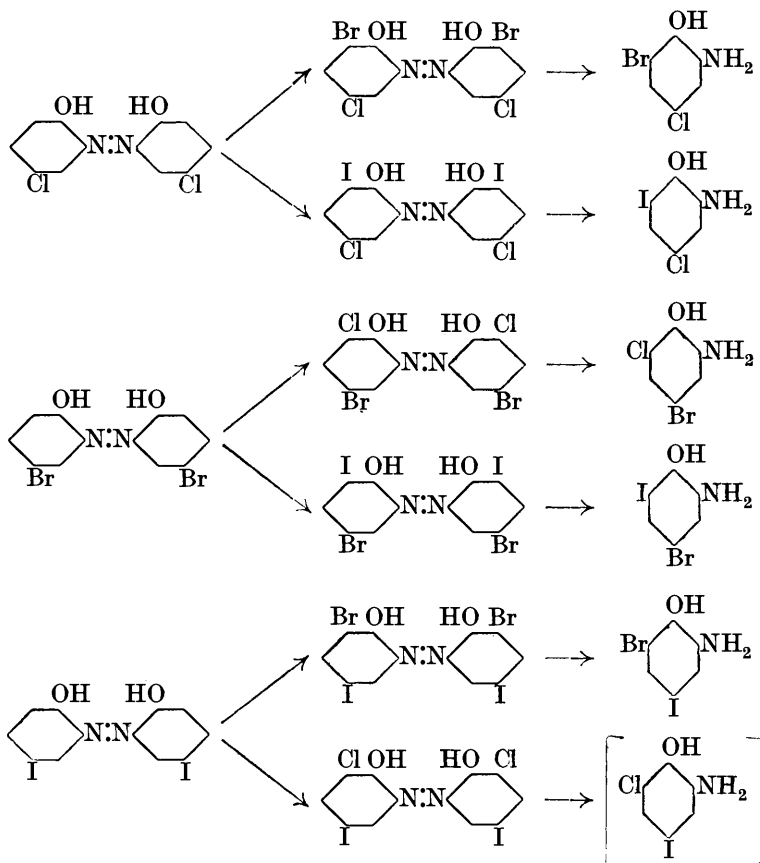
CCLXVIII.—*The Preparation of Some Halogenoamino-phenols. Part I. Mixed Tetrahalogen Derivatives of o-Azophenol. Part II. Halogen Derivatives of p-Hydroxyazobenzene.*

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Part I. Mixed Tetrahalogen Derivatives of o-Azophenol.

THE method employed for the preparation of substituted amino-phenols in this research is based on the ease of reduction of *o*- and *p*-azophenol and their derivatives (see preceding paper). It has been shown (*loc. cit.*) that the primary product of the reaction between two molecules of halogen and one of *o*-azophenol is the 5 : 5'-disubstituted compound, and that further halogenation fills the 3- and 3'-positions. This property allows of the preparation of two isomerides of each of dichlorodibromo-, dichlorodi-iodo-,

and dibromodi-iodo-*o*-azophenol, the reduction of which should give rise to the six theoretically possible mixed 2 : 4-dihalogeno-6-amino-phenols; five are described in this paper.



In the preparation of the mixed tetrahalogeno-*o*-azophenols it was not usually necessary to isolate the dihalogen compound from the solvent medium, since, by using the calculated quantity of halogenating agent, substitution of one halogen for hydrogen could be followed by substitution of a second in the same solution. In the case of the 5 : 5'-di-iodo-compounds, however, preliminary isolation of the di-iodo-stage was essential, since it is usual to employ excess of the iodinating agent, the excess being ultimately removed by addition of sodium sulphite. Use of a further quantity of chloramine in the same solution, whether for chlorination or bromination, would naturally lead to further iodination.

EXPERIMENTAL.

The same methods of halogenation were used as in the preceding work, although in some cases acetochloroamide was employed instead of dichloramine-T as a source of halogen. The advantage of the former is that its product of hydrolysis (acetamide) is soluble in water, and therefore does not contaminate the halogenated material when this is isolated from acetic acid solution by dilution with water. Analyses are expressed as before (*loc. cit.*, analytical note).

5 : 5'-Dichloro-3 : 3'-dibromo-2 : 2'-dihydroxyazobenzene. — *o*-Azophenol (2 g.) dissolved in stable acetic acid (500 c.c.) was chlorinated to the dichloro-stage by the addition of a solution of dichloramine-T (2.3 g.) in acetic acid (100 c.c.) with the addition of a few drops of dilute hydrochloric acid. When free chlorine could no longer be detected (20 minutes), the solution was reduced to about half its bulk by distillation under reduced pressure. Bromination was then effected by adding to the warmed mixture a solution of dichloramine-T (2.55 g.) in acetic acid (50 c.c.) to which had been added potassium bromide (2.25 g.) in water (10 c.c.). When the mixture was cooled, the *chlorobromo*-compound separated in orange-red prisms. A further quantity was obtained by removing part of the solvent by distillation under diminished pressure. It crystallised from benzene in needles of the same colour, m. p. 259° (decomp.); yield, 3.0 g. (Found: Cl, 15.3; Br, 36.7. $C_{12}H_6O_2N_2Cl_2Br_2$ requires Cl, 16.1; Br, 36.3%).

The *diacetyl* derivative crystallised from alcohol in pale orange needles, m. p. 203°, and the *dibenzoyl* derivative formed fine orange granules, m. p. 212°, from benzene and ligroin.

4-Chloro-6-bromo-2-aminophenol. — The above azophenol was decolorised with a warm mixture of stannous chloride and hydrochloric acid. After removal of tin from the solution with hydrogen sulphide, the residue yielded small white, prismatic crystals of the *aminophenol hydrochloride* (Found: Cl, 27.1; Br, 30.8. $C_6H_5ONClBr, HCl$ requires Cl, 27.4; Br, 30.9%). The *base*, liberated from the hydrochloride by means of aqueous sodium bicarbonate, formed fine white needles, m. p. 89—90°, from aqueous alcohol.

4-Chloro-6-bromo-2-acetamidophenyl acetate formed fine white needles, m. p. 130° (Found: Ag halides/original weight, 107.5. $C_{10}H_9O_3NClBr$ requires 108.1%), and 4-chloro-6-bromo-2-benzamidophenyl benzoate silky white needles, m. p. 180.5° (Found: Ag halides/original weight, 76.38. $C_{20}H_{13}O_3NClBr$ requires 76.98%), from aqueous alcohol.

3 : 3'-Dichloro-5 : 5'-dibromo-2 : 2'-dihydroxyazobenzene, prepared from *o*-azophenol, in a similar manner to its isomeride above, by bromination followed by chlorination, crystallised from benzene in fine orange-red needles, m. p. 263° (Found : Cl, 15.9; Br, 36.4%).

The *diacetyl* derivative crystallised from benzene in silky orange needles, m. p. 199°, and the *dibenzoyl* derivative from benzene and ligroin as an orange powder, m. p. 201°.

6-Chloro-4-bromo-2-aminophenol was obtained as its *hydrochloride* (Found : Cl, 27.4; Br, 31.6%) by reduction of the above azophenol with stannous chloride and hydrochloric acid. The *base* crystallised from aqueous alcohol in white prisms, m. p. 93°.

6-Chloro-4-bromo-2-acetamidophenyl acetate formed white prisms, m. p. 137°, from alcohol (Found : Ag halides/original weight, 108.3%), and 6-chloro-4-bromo-2-benzamidophenyl benzoate crystallised in silky white needles, m. p. 182° (Found : Ag halides/original weight, 76.05%).

5 : 5'-Dichloro-3 : 3'-di-iodo-2 : 2'-dihydroxyazobenzene. — *o*-Azophenol (2 g.) was chlorinated to the dichloro-stage, the solvent acetic acid (600 c.c.) was reduced by distillation to one-third of its bulk, and the dichloro-compound was then iodinated without isolation by the addition of a solution of iodine chloride (2.33 mols.) prepared by dissolving acetochloroamide (2.35 g.) and potassium iodide (4.2 g.) in acetic acid (150 c.c.). The whole solution was made up to 500 c.c. with acetic acid and warmed on a water-bath, specimens of 5 c.c. being withdrawn at 5-minute intervals. After 90 minutes the titre showed that two molecules of iodine chloride had been used, and the solution was cooled and the excess of iodine destroyed by the addition of aqueous sodium sulphite. On removal of the bulk of the solvent by distillation, the dichlorodi-iodo-compound separated as a brown precipitate. A further quantity was obtained by diluting the filtrate with water. It formed orange-yellow needles (4.1 g.) from benzene, which on heating rapidly had m. p. 272° (decomp.) (Found : Cl, 13.1; I, 47.4. $C_{12}H_6O_2N_2Cl_2I_2$ requires Cl, 13.3; I, 47.5%).

The *diacetyl* derivative crystallised from benzene in silky orange needles, m. p. 205°, and the *dibenzoyl* derivative in light brownish needles, m. p. 254°.

4-Chloro-6-iodo-2-aminophenol was obtained, by the reduction of the above azophenol, in the form of its *hydrochloride*, which crystallised from water in small white prisms (Found : Cl, 23.3; I, 40.6. C_6H_5ONClI, HCl requires Cl, 23.2; I, 41.5%). The *base* formed white needles from aqueous alcohol, having no definite melting point but charring at about 90°.

4-Chloro-6-iodo-2-acetamidophenyl acetate formed silky white

needles, m. p. 169°, from aqueous alcohol (Found : Ag halides/original weight, 107.9. $C_{10}H_9O_3NCl_2$ requires 107.1%).

5 : 5'-Dibromo-3 : 3'-di-iodo-2 : 2'-dihydroxyazobenzene was prepared from *o*-azophenol by bromination followed by iodination as in the preceding example. It crystallised from alcohol in light brown needles (yield, 83%), m. p. 255° (decomp.) (Found : Ag halides/original weight, 134.8. $C_{12}H_6O_2N_2Br_2I_2$ requires 135.6%).

The *diacetyl* derivative crystallised from benzene and ligroin in pale orange needles, m. p. 186°, and the *dibenzoyl* derivative in pale brown needles, m. p. 252°.

4-Bromo-6-iodo-2-aminophenol hydrochloride, produced by the reduction of the above dibromodi-iodo-compound, formed creamy white flakes (Found : Cl, 10.1; Br, 22.95; I, 35.8. C_6H_5ONBrI, HCl requires Cl, 10.1; Br, 22.8; I, 36.2%). The *base* crystallised from alcohol in fine white needles which decomposed before melting.

4-Bromo-6-iodo-2-acetamidophenyl acetate crystallised from alcohol in silky white needles, m. p. 190° (decomp.) (Found : Ag halides/original weight, 106.7. $C_{10}H_9O_3NBrI$ requires 106.3%), and 4-bromo-6-iodo-2-benzamidophenyl benzoate from aqueous alcohol in white prisms, m. p. 185° (Found : Ag halides/original weight, 80.9. $C_{20}H_{13}O_3NBrI$ requires 81.02%).

3 : 3'-Dibromo-5 : 5'-di-iodo-2 : 2'-dihydroxyazobenzene. — 5 : 5'-Di-iodo-2 : 2'-dihydroxyazobenzene was isolated as described in the previous paper. It was then brominated with two equivalents of the brominating agent, and the dibromodi-iodo-compound was isolated as orange-red needles, m. p. 256°, after three crystallisations from benzene (Found : Br, 25.9; I, 40.2. $C_{12}H_6O_2N_2Br_2I_2$ requires Br, 25.6; I, 40.7%).

The *diacetyl* derivative crystallised from benzene in golden needles, m. p. 217°, and the *dibenzoyl* derivative in orange-red prisms, m. p. 215°.

6-Bromo-4-iodo-2-aminophenol was obtained by reduction of the above azophenol with stannous chloride and hydrochloric acid, removal of the tin, and decolorisation of the solution by boiling with animal charcoal, as its *hydrochloride* (Found : Ag halides/original weight, 162.9. C_6H_5ONBrI, HCl requires 161.5%), white, crystalline flakes. The *base* formed needles, m. p. 90°, from alcohol.

6-Bromo-4-iodo-2-acetamidophenyl acetate crystallised from aqueous alcohol in pearl-white, silky needles, m. p. 196° (Found : Ag halides/original weight, 106.7. $C_{10}H_9O_3NBrI$ requires 106.3%), and 6-bromo-4-iodo-2-benzamidophenyl benzoate in fine white needles, m. p. 194—195° (Found : Ag halides/original weight, 80.67. $C_{20}H_{13}O_3NBrI$ requires 81.02%).

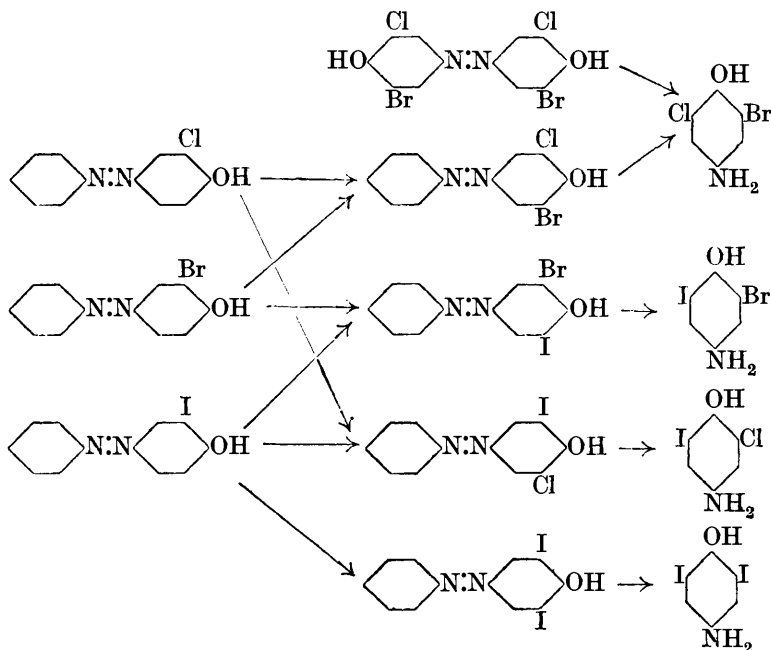
3 : 3'-Dichloro-5 : 5'-di-iodo-2 : 2'-dihydroxyazobenzene.—Repeated

attempts to chlorinate 5:5'-di-iodo-2:2'-dihydroxyazobenzene as described above, with two equivalents of chlorinating agent, yielded a dark brown, amorphous powder which could not be crystallised, and decomposed above 200° without melting. Although its analysis approximated to that calculated for $C_{12}H_8O_2N_2Cl_2I_2$, it was not considered sufficiently pure to be used for the preparation of derivatives, or for reduction to the corresponding aminophenol.

Part II. Halogen Derivatives of p-Hydroxyazobenzene.

As iodo-*p*-azophenols could not be prepared (preceding paper), iodine-substituted *p*-aminophenols were obtained by reducing the iodo-derivatives of *p*-hydroxyazobenzene, which are readily accessible; they were separated from the aniline simultaneously formed by means of the difference in solubility of the hydrochlorides.

Direct halogenation of *p*-hydroxyazobenzene gave the 3:5-dihalogeno-compounds (compare Hewitt and Aston, J., 1900, 77, 712, 810). The monohalogen derivatives were therefore synthesised by coupling diazotised aniline with the *o*-halogenophenols.



The duplicate methods of preparation of the mixed dihalogeno-compounds (see scheme) place beyond doubt their constitution and that of the aminophenols derived from them.

EXPERIMENTAL.

The dihalogen derivatives of *p*-hydroxyazobenzene described below were prepared by the chloroamine method.

3-Chloro-4-hydroxyazobenzene was obtained (yield, 70%) by coupling benzenediazonium chloride with *o*-chlorophenol. It crystallised from aqueous alcohol in yellow prisms, m. p. 88.5° (Farmer and Hantzsch, *Ber.*, 1899, **32**, 3089, give m. p. 88°).

3-Bromo-4-hydroxyazobenzene.—Carefully purified *o*-bromophenol was coupled with the required quantity of diazotised aniline, the mixture being kept strongly alkaline to prevent precipitation of the hydrochloride of the azo-compound. When coupling was complete, the solution was cautiously neutralised by the addition during some hours of dilute acetic acid; rapid neutralisation precipitated the azo-compound as an oil. The solid product crystallised from light petroleum in fine yellow needles, m. p. 80°; yield, 90% (Found: Br, 28.7. $C_{12}H_9ON_2Br$ requires Br, 28.9%). It gave a purple-brown crystalline *hydrochloride*, m. p. 159°. The *acetyl* derivative formed yellow-brown plates, m. p. 98° (Found: Br, 24.9. $C_{14}H_{11}O_2N_2Br$ requires Br, 25.1%), and the *benzoyl* derivative crystallised from aqueous alcohol in brown needles, m. p. 113° (Found: Br, 21.0. $C_{19}H_{13}O_2N_2Br$ requires Br, 21.0%).

3-Iodo-4-hydroxyazobenzene, prepared (yield, 85%) by a method analogous to that described for the bromo-compound, crystallised from light petroleum as yellow flakes, m. p. 77–78°, darkening somewhat on exposure (Found: I, 39.1. $C_{12}H_9ON_2I$ requires I, 39.2%). It formed a blue-black *hydrochloride*, m. p. 172° (decomp.); an *acetyl* compound, crystallising in slender orange needles, m. p. 103–104° (Found: I, 34.9. $C_{14}H_{11}O_2N_2I$ requires I, 34.7%); and a *benzoyl* derivative, crystallising from alcohol in pale orange needles, m. p. 105° (Found: I, 30.1. $C_{19}H_{13}O_2N_2I$ requires I, 29.7%).

3-Chloro-5-bromo-4-hydroxyazobenzene. — (a) 3-Chloro-4-hydroxyazobenzene (1.5 g.) was dissolved in stable acetic acid (40 c.c.) and treated with a solution of acetochloroamide (0.6 g.) in acetic acid (30 c.c.) to which had been added potassium bromide (1.5 g.) in water (10 c.c.). The *chlorobromo*-compound soon began to separate in fine orange needles, which crystallised from aqueous acetic acid in the same form, m. p. 125.5°. A further crop was obtained by diluting the mixture with water; total yield, 1.6 g. (Found: Ag halides/original weight, 105.9. $C_{12}H_8ON_2ClBr$ requires 106.4%).

(b) A solution of 5-bromo-4-hydroxyazobenzene (4.0 g.) in acetic acid (35 c.c.) was chlorinated by the addition of a solution of dichloramine-T (1.8 g.) in acetic acid (15 c.c.) and a few drops of dilute hydrochloric acid. Separation of the product commenced

immediately, and chlorination was complete in $\frac{1}{2}$ hour. A further crop was obtained by diluting the solution with an equal volume of water; total yield, 3.5 g., m. p. 125°. A mixture with the substance prepared by method (a) had m. p. 125.0°.

The *acetyl* derivative crystallised from aqueous alcohol in orange-brown needles, m. p. 133.5° (Found: Ag halides/original weight, 93.43. $C_{14}H_{10}O_2N_2ClBr$ requires 93.76%), and the *benzoyl* derivative from benzene and ligroin in orange prisms, m. p. 118.5° (Found: Ag halides/original weight, 79.12. $C_{19}H_{12}O_2N_2ClBr$ requires 79.75%).

As a final proof of the constitution of the chlorobromo-*p*-hydroxyazobenzene, specimens reduced with stannous chloride and hydrochloric acid yielded 2-chloro-6-bromo-4-aminophenol, m. p. 177° (decomp.), identical with the substance prepared as described on p. 2055.

2-Chloro-6-bromo-4-acetamidophenyl acetate crystallised from alcohol in fine white needles, m. p. 168.5° (Found: Ag halides/original weight, 107.1. $C_{10}H_9O_3NClBr$ requires 107.9%), and *2-chloro-6-bromo-4-benzamidophenyl benzoate* in white platelets, m. p. 111–112° (Found: Ag halides/original weight, 76.65. $C_{20}H_{13}O_3NClBr$ requires 76.81%).

3-Chloro-5-iodo-4-hydroxyazobenzene. — (a) The chlorination of 5-iodo-4-hydroxyazobenzene was conducted in the usual way in acetic acid solution, dichloramine-T (1 equiv.) being used in the presence of a few drops of dilute hydrochloric acid. The product (yield, 60%) crystallised from ligroin as a fine brown powder, m. p. 110.5° (Found: Cl, 9.5; I, 35.5. $C_{12}H_8ON_2ClI$ requires Cl, 9.9; I, 35.4%).

(b) 3-Chloro-4-hydroxyazobenzene (5 g.) dissolved in acetic acid (150 c.c.) was treated with a solution of iodine chloride (1 mol.) generated by shaking together acetochloroamide (2.75 g.), finely powdered potassium iodide (4 g.), and acetic acid (100 c.c.). The mixture was warmed on the water-bath until the titre had fallen to one-quarter of the original value. The excess of iodine was removed by sodium sulphite, the bulk of the solvent distilled off under diminished pressure, and the residue diluted with water (100 c.c.). The product precipitated crystallised from ligroin in fine brown granules, m. p. 110°; yield, 5.3 g.

A mixture of the two specimens melted at 110°. *3-Chloro-5-iodo-4-acetoxiazobenzene* crystallised from alcohol in fine orange-red needles, m. p. 124° (Found: Ag halides/original weight, 94.77. $C_{14}H_{10}O_2N_2ClI$ requires 94.5%), and *3-chloro-5-iodo-4-benzoyloxyazobenzene* from benzene in orange prisms, m. p. 115° (Found: Ag halides/original weight, 82.04. $C_{19}H_{12}O_2N_2ClI$ requires 81.9%).

2-Chloro-6-iodo-4-aminophenol was obtained together with aniline

by the reduction of the above chloroiodo-*p*-hydroxyazobenzene with stannous chloride. On removal of the tin from the resulting mixture, the less soluble 2-chloro-6-iodo-4-aminophenol hydrochloride (Found : Ag halides/original weight, 170.2. C_6H_5ONCl, HCl requires 170.6%) separated in white needles, from which the base was obtained by treatment with sodium bicarbonate in silky white prisms, m. p. 169° (decomp.).

2-Chloro-6-iodo-4-acetamidophenyl acetate, m. p. 155° (Found : Ag halides/original weight, 106.7. $C_{10}H_9O_3NCl$ requires 107.1%), and 2-chloro-6-iodo-4-benzamidophenyl benzoate, m. p. 157° (Found : Ag halides/original weight, 80.28. $C_{20}H_{13}O_3NCl$ requires 79.93%), crystallised from aqueous alcohol in needles.

3-Bromo-5-iodo-4-hydroxyazobenzene. — (a) 5-Iodo-4-hydroxyazobenzene was treated with one equivalent of the brominating agent prepared by mixing the required quantities of aqueous potassium bromide and an acetic acid solution of dichloramine-T. The halogen soon disappeared, and dilution with water then precipitated the bromoiodo-compound, which crystallised from ligroin in orange-brown needles, m. p. 128.5° (Found : Br, 19.8; I, 31.4. $C_{12}H_8ON_2BrI$ requires Br, 19.9; I, 31.5%).

(b) A solution of 3-bromo-4-hydroxyazobenzene was treated in acetic acid solution on the water-bath with iodine chloride (1 mol.) prepared as before, until the titre showed that one equivalent of iodinating agent had been used. Dilution of the solution with water, and crystallisation of the amorphous precipitate from alcohol, followed by ligroin, afforded an orange-brown, crystalline material, m. p. 128.5°. Mixed with the specimen obtained above, it melted at 128°.

3-Bromo-5-iodo-4-acetoxyazobenzene crystallised from alcohol in silky, orange needles, m. p. 127—128° (Found : Ag halides/original weight, 95.32. $C_{14}H_{10}O_2N_2BrI$ requires 95.08%), and 3-bromo-5-iodo-4-benzoyloxyazobenzene in brown prisms, m. p. 85° (Found : Ag halides/original weight, 82.56. $C_{19}H_{12}O_2N_2BrI$ requires 83.43%).

2-Bromo-6-iodo-4-aminophenol.—Loss of iodine resulted on boiling the above bromoiodo-*p*-hydroxyazobenzene with acid stannous chloride, but smooth reduction was achieved by treatment of the azo-compound with an acetic acid solution of stannous chloride prepared by passing dry hydrogen chloride into a mixture of tin and acetic acid until the tin had dissolved. The aminophenol was isolated in the usual way as its hydrochloride (Found : Cl, 10.05; Br, 22.8; I, 36.0. C_6H_5ONBrI, HCl requires Cl, 10.1; Br, 22.8; I, 36.2%), from which the base was obtained by the action of sodium bicarbonate in short white prisms, m. p. 185° (decomp.).

2-Bromo-6-iodo-4-acetamidophenyl acetate crystallised from aqueous

alcohol in slender needles, m. p. 186° (Found : Ag halides/original weight, 105.9. $C_{10}H_9O_3NBrI$ requires 106.3%), and 2-bromo-6-iodo-4-benzamidophenyl benzoate in plates, m. p. 148° (Found : Ag halides/original weight, 80.52. $C_{20}H_{13}O_3NBrI$ requires 81.02%).

3 : 5-Di-iodo-4-hydroxyazobenzene.—Attempts to prepare this compound by direct iodination of *p*-hydroxyazobenzene were not successful, oxidation as well as iodination resulting.

To a solution of 3-iodo-4-hydroxyazobenzene (see p. 2064) (4 g.) in acetic acid (65 c.c.) was added a solution of iodine chloride (1 mol.) prepared by mixing together dichloramine-T (2 g.) in acetic acid (35 c.c.) and powdered potassium iodide (2.8 g.). The mixture was heated on the water-bath until the titre showed that one equivalent of iodinating agent had been used (6 minutes). The excess of iodine was then removed by aqueous sodium sulphite, and the product precipitated by the addition of water (100 c.c.). It crystallised from alcohol in brown needles, m. p. 128—129°; yield, 3.1 g. (Found : I, 56.9. $C_{12}H_8ON_2I_2$ requires I, 56.5%).

3 : 5-Di-iodo-4-acetoxiazobenzene crystallised from aqueous alcohol in orange-brown prisms, m. p. 162° (Found : I, 51.6. $C_{14}H_{10}O_2N_2I_2$ requires I, 51.6%), and 3 : 5-di-iodo-4-benzoyloxyazobenzene from acetic acid in fine, yellow needles, m. p. 137—139° (Found : I, 46.1. $C_{19}H_{12}O_2N_2I_2$ requires I, 45.8%).

Reduction of 3 : 5-di-iodo-4-hydroxyazobenzene. Cautious treatment of the azo-compound with an acetic acid solution of stannous chloride and hydrochloric acid afforded 2 : 6-di-iodo-4-aminophenol hydrochloride, from which the base was obtained by the addition of a saturated solution of sodium bicarbonate. It formed long white needles, m. p. 173°, from alcohol (Found : I, 70.3. Calc. : I, 70.4%). Raiford, Taft, and Lankelma (*J. Amer. Chem. Soc.*, 1924, **46**, 2051) give m. p. 169—171°.

3 : 5-Di-iodo-4-acetamidophenyl acetate forms silky, white needles, m. p. 209°, from alcohol (Found : I, 57.0. $C_{10}H_9O_3NI_2$ requires I, 57.1%).

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