

113. Dithio- β -isoindigo (Dithiodiphtalimidine) from Phthalonitrile.
Part I. A Condensation Reaction of *o*-Dinitriles.

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Phthalonitrile is quantitatively converted, under the action of hydrogen sulphide in alcoholic ammonia, into a highly coloured, very stable condensation product. The product has been identified as *dithio- β -isoindigo*, which behaves as a tautomeric base, showing the reactions of a di-imine and of a dithiol. It forms intensely coloured pigments with copper and other metals. The paper describes the reactions of this substance and its derivatives. The condensation reaction can be applied also to other *o*-dinitriles.

IN attempting to prepare dithiophthalimide, we found that the interaction of phthalimide and phosphorus pentasulphide gave a mixture of the required substance with *monothio-phthalimide*, and it was decided to attempt to convert phthalonitrile into phthalodithioamide with alcoholic ammonia and hydrogen sulphide, and thence into dithiophthalimide. The reaction succeeds with *iso*- and *tere*-phthalonitrile (Luckenbach, *Ber.*, 1884, **17**, 1431), but the literature indicated that it would probably not do so with phthalonitrile (see Pinner, "Die Imidoäther und ihre Derivate"). Actually, the reaction led to quantitative conversion of phthalonitrile into a crystalline substance (I) having much the appearance of indigo.

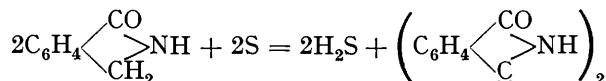
The substance, purplish-black, but red by transmitted light, was remarkably stable to heat and to the action of concentrated hydrochloric or sulphuric acid or of alkali hydroxide; it dissolved in organic bases, giving intensely red solutions, and formed deeply coloured metallic salts.

Analysis gave the empirical formula C_8H_5NS . Oxidation with nitric acid gave sulphur and phthalimide suggesting the presence of a pyrrolidine ring. Alkylation with methyl iodide gave a crystalline orange methyl derivative (II), shown by analysis and determination of molecular weight to have the formula $(C_8H_4NS \cdot CH_3)_2$. This was confirmed by alkylation with ethyl iodide, which gave yellow crystals of a substance (IIA), shown to have the formula $(C_8H_4NS \cdot C_2H_5)_2$.

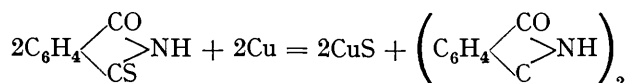
The alkyl derivatives formed unstable red hydrochlorides, which, when boiled with hydrochloric acid, lost a molecular proportion of methyl- or ethyl-thiol, giving in each case a substance (III; IIIA) having the formula $(C_{16}H_9ON_2S \cdot R)$, where $R = CH_3$ or C_2H_5 . Thus it became clear that the alkyl groups were attached to sulphur and that in each case a group SR had been replaced by hydroxyl. Substance (I) must therefore be a dithiol or its tautomeride.

It was then found that more prolonged boiling with aqueous or alcoholic hydrochloric acid removed the second SR group from each of the alkyl derivatives, replacing it as before by hydroxyl and thus giving the same substance (IV) in each case; the product was a yellowish material having the formula $C_{16}H_{10}O_2N_2$, of high decomposition point and insoluble in most solvents. Its properties suggested that it was β -*isoindigo* (diphtalimidine, di*isoindolinone*), a substance prepared by Liebermann and Bistrzycki (*Ber.*, 1893, **26**, 539) by heating *o*-phthalaldehydic acid (*o*-carboxybenzaldehyde) with methyl-alcoholic ammonia at 160° in a sealed tube.

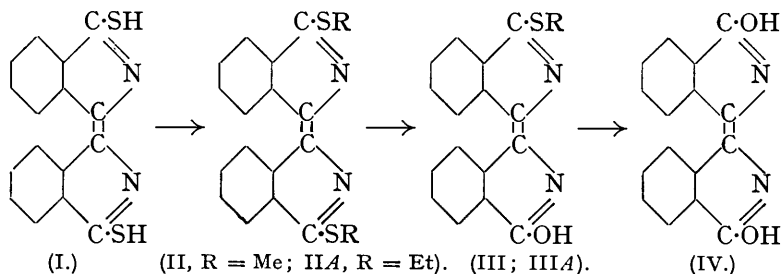
This hypothesis was confirmed when (IV) was obtained in good yield by oxidising phthalimidine with sulphur at 200 – 210° :



We later found, also, that the action of copper or silver on monothio-phthalimide at 175 – 250° gave a similar result:

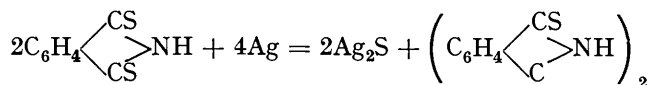


The following scheme then gave a consistent account of the foregoing alkylations of (I) and the subsequent degradations producing (IV) :

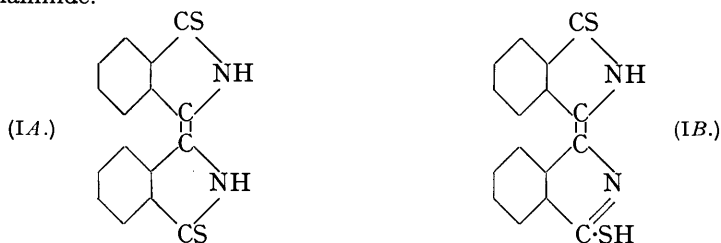


The coloured substance (I) was therefore indicated to be *dithio-β-isoindigo*, which may be regarded as capable also of assuming the forms (IA) and (IB). Similar tautomeric forms are probable also in the case of (IV).

The structure of (I) was confirmed by synthesis in two ways: (i) by heating dithiophthalimide with silver at 175–190° :



and (ii) by the action of alcoholic ammonia, or of alcoholic ammonia and hydrogen sulphide, on dithiophthalimide.

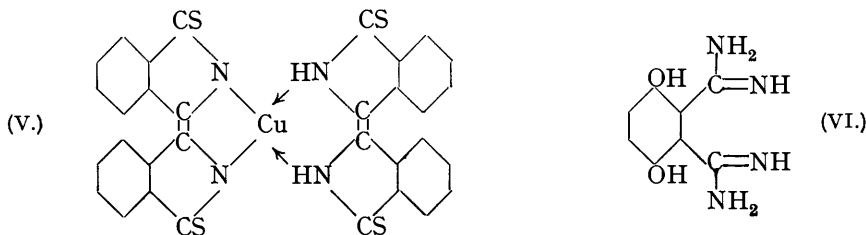


There seems no doubt, therefore, as to the outline structure of (I). Its formation from phthalonitrile, hydrogen sulphide, and ammonia could be expressed in several ways: *e.g.*, dithiophthalimide, which could be formed by the addition of a molecule of hydrogen sulphide at each of the nitrile groups, followed by the loss of a molecule of ammonia from the resulting phthalodithioamide, may actually be an intermediate, since it is now known to be converted into (I) under the conditions of the original preparation. It has been found that the reaction producing (I) from phthalonitrile is not dependent upon the presence of alcohol, though a hydroxylic solvent is essential; thus, an aqueous medium may be employed but the reaction fails in benzene.

There is little to indicate whether (I) is a *cis*- or a *trans*-ethylenic compound, or a mixture of the two forms. The infusibility and insolubility of the substance make it necessary to examine the composition and character of the metallic derivatives for evidence on this point, but only a preliminary study of a few of the salts has been made.

From molecular models it would seem that, with a bivalent metal, any of the three possible *trans*-forms of dithio-β-isoindigo could only form a normal derivative (*i.e.*, one in which both the acidic hydrogen atoms of the organic molecule were replaced by the metal) of polymeric character, with (theoretically) infinite molecular weight; for steric reasons, the metal atom of such a compound would probably not be able to co-ordinate with N or S derived from (I). The same should hold for the *cis*-form of (I); but the *cis*-form of (IB) should be able to form a dimeric normal compound, with one copper atom co-ordinated with two nitrogen atoms and the other copper atom not co-ordinated (unless to an external molecule). On the other hand, the *cis*-form of (IA) should give rise to a monomeric normal compound, which could attach another molecule of the *cis*-form of

(IA) by co-ordinating with the nitrogen atoms as shown (V). We prepared a normal copper compound, soluble in pyridine and not co-ordinated with external molecules, and



also a second copper compound containing a further molecule of dithio- β -isoindigo; the latter may correspond to (V). These compounds are therefore probably derived from a *cis*-form of the organic molecule.

Normal *mercuric* and *cadmium* compounds were also obtained, but as these were only sparingly soluble in pyridine the possibility that they are derived from *trans*-forms is not excluded. A crystalline *cobaltous* compound corresponding in composition to (V) was prepared, and this also is probably derived from a *cis*-form. A disilver compound was obtained but only in an impure state.

The data are sufficient to show that both acidic groupings of dithio- β -isoindigo may unite with metallic atoms at the same time. It seems just possible also that dithio- β -isoindigo, as prepared in the initial reaction, contains, or may assume, both the *cis*- and the *trans*-form.

Naphthalo-1:2-dinitrile behaved like phthalonitrile towards alcoholic ammonium hydrosulphide, giving a purplish-black substance resembling (I); so the reaction is capable of extension to other *o*-dinitriles. This point is under examination. 3:6-Dihydroxyphthalonitrile, however, gave only 3:6-dihydroxyphthalodiamidine (VI), which proved more stable than had been expected.

EXPERIMENTAL.

Conversion of Phthalimide into Di- and Mono-thiophthalimide.—The following is an adaptation of the method of Pratt and Brill (*Philippine J. Sci.*, 1914, 9, A, 105): Phthalimide (10 g.) was suspended in boiling xylene (200 c.c., distilled over sodium), and phosphorus pentasulphide (15 g.) added in portions of 3 g. during 6 hours. The xylene, decanted from a sticky residue and allowed to cool, deposited phthalimide (2–3 g.) and inorganic matter; these were removed, the xylene distilled in steam, and the residue extracted five times with boiling water (1 l. in all), part (A) remaining insoluble: on cooling, the extract deposited crude *monothiophthalimide*, which crystallised from glacial acetic acid (the chief impurity, phthalimide, separated first and was removed; addition of water to the mother-liquor then caused the thio-compound to crystallise) in long, bright red needles, m. p. 174° (Found: C, 59.1; H, 3.3; N, 8.8; S, 19.3. C_8H_5ONS requires C, 58.9; H, 3.1; N, 8.6; S, 19.6%). The residue from the extraction with boiling water (A) was crystallised twice from a little glacial acetic acid, giving thin dark-brown (black when pure) needles with bluish tinge, consisting of *dithiophthalimide* (yield, 1.3 g.) (Found: C, 53.9; H, 2.9; N, 8.1; S, 35.9. $C_8H_5NS_2$ requires C, 53.6; H, 2.8; N, 7.8; S, 35.75%); it became red and pasty at 180–184° and then solidified [production of (I)] and did not melt at 350°; it dissolved in aqueous alkali hydroxides to yellow solutions, formed a copper derivative which crystallised from pyridine, and gave a yellow precipitate with methyl iodide in methyl-alcoholic solution. Heated at 200–250° for 1½ hours, dithiophthalimide gave (I) and free sulphur. Mono- and di-thiophthalimide form mixed crystals, or a definite addition product (reddish-brown). [Note. Pratt and Brill obtained dithiophthalimide, but their description of it (“brilliant red needles”) seems to correspond more closely with monothiophthalimide; they did not mention the latter substance.]

Dithio- β -isoindigo (I).—Phthalonitrile (20 g.) was dissolved in warm alcohol (200 c.c.), aqueous ammonia (*d* 0.88; 20 c.c.) added, and hydrogen sulphide passed into the cold mixture; the liquid became yellow and then deep red (10 mins.), and glistening plates, nearly black, began to separate. The mixture was now warmed, and passage of hydrogen sulphide continued until excess was present. The liquid was finally boiled in a beaker to remove the excess of

ammonia and hydrogen sulphide. The precipitate was collected, washed with boiling water and with alcohol, and then extracted (Soxhlet) with carbon disulphide to remove free sulphur [1 part of free sulphur was present to 4 parts of (I), indicating reduction of 1 mol. of nitrile by 1 mol. of hydrogen sulphide]. The residue consisted of (I) in a nearly pure state, the yield being 96%. For analysis and for the principal reactions, the substance was extracted twice with boiling nitrobenzene (100 c.c. in all), in which it was sparingly soluble (1 g. in 200 c.c.), washed with boiling benzene, and dried at 110°; or it was dissolved in aqueous sodium hydroxide and reprecipitated with glacial acetic acid (Found: C, 65.6, 65.5; H, 3.5, 3.8; N, 9.8, 9.9; S, 21.9. $C_{16}H_{10}N_2S_2$ requires C, 65.3; H, 3.4; N, 9.55; S, 21.75%). It formed purplish-black flattened needles, red by transmitted light or when powdered, and unchanged up to 350°; it was insoluble in all low-boiling solvents, but appreciably soluble in hot aniline, pyridine, and other organic bases, to intensely red solutions; it was slightly soluble in aqueous ammonia, more soluble in aqueous alkali hydroxides, and very soluble in aqueous-alcoholic alkali hydroxides. It was unaffected by prolonged boiling with concentrated hydrochloric acid or with alcoholic potassium hydroxide, or by heating for a minute with concentrated sulphuric acid near the b. p. It was violently oxidised and completely dissolved on being warmed with concentrated nitric acid, dilution with water causing precipitation of phthalimide in large yield; oxidation with nitric acid under other conditions produced free sulphur. Unlike dithiophthalimide (*q.v.*), it was not reduced by boiling aniline, but alcoholic hydrazine removed its sulphur as hydrogen sulphide; sodium amalgam, or zinc and sodium hydroxide, caused reduction only after prolonged boiling; with hydrazine, it gave the dihydrazone of β-isoindigo (see later). It readily formed metallic salts, usually purplish-black and appreciably soluble in pyridine; the normal mercuric and cupric salts were obtained pure, and a preliminary examination was made of others:

Mercuric dithio-β-isoindigo. When (I) (0.2 g.) was heated under reflux with a solution of an excess of mercuric cyanide in pyridine (10 c.c.), a microcrystalline red powder, not melting below 350°, was obtained, which was washed with pyridine, water, and alcohol, and dried at 110° (Found: C, 38.7; H, 2.5. $C_{16}H_8N_2S_2Hg$ requires C, 39.0; H, 1.6%). Under other conditions, using mercuric chloride, an unstable *addition product* (green tablets) of this salt with mercuric chloride and pyridine was formed; this lost its pyridine over sulphuric acid, becoming red. When the green salt (Found: N, 7.6. $C_{16}H_8N_2S_2Hg.HgCl_2.4C_5H_5N$ requires N, 7.8%) was extracted with boiling water, pyridine and mercuric chloride were removed and the red normal salt (above) was left (Found: loss on washing, 54.0. Calc., 54.3%).

Cupric dithio-β-isoindigo. A warm solution of an excess of cupric acetate in alcoholic ammonia was added to a filtered solution of (I) in the same solvent; very small, almost black crystals separated on cooling; the salt was purified by dissolving it in pyridine (violet-red solution), partly precipitating it with water (it did not retain pyridine), and drying at 100° (Found: C, 54.05; H, 2.65; Cu, 17.65. $C_{16}H_8N_2S_2Cu$ requires C, 54.0; H, 2.25; Cu, 17.9%).

Dithio-β-isoindigo cupric dithio-β-isoindigo (V) was obtained as a nearly black powder when a solution of (I) in pyridine was heated with aqueous cupric chloride or acetate. It appeared to be cupric dithio-β-isoindigo with the metal atom co-ordinated with a further molecule of (I); it was free from pyridine and appeared to be a tetrahydrate (Found: C, 53.3; H, 3.8; Cu, 9.0. $C_{32}H_{18}N_4S_4Cu.4H_2O$ requires C, 53.2; H, 3.6; Cu, 8.8%), but water was not lost at 100° and the purity of the substance is open to doubt.

Dithio-β-isoindigo cobaltous dithio-β-isoindigo was prepared as in the foregoing example; it consisted of almost black microcrystals (purplish-red streak), soluble in pyridine but insoluble in cold alcohol; it contained no pyridine; analysis (after drying at 100°) suggested that it was a dihydrate, but the purity is in doubt (Found: C, 56.25, 56.4; H, 3.45, 3.4; Co, 9.4, 8.85. $C_{32}H_{18}N_4S_4Co.2H_2O$ requires C, 56.4; H, 3.2; Co, 8.7%).

Cadmium dithio-β-isoindigo was obtained from a solution of (I) in pyridine and aqueous cadmium chloride; it was violet-black, with greenish-bronze reflex, and was insoluble in alcohol and only sparingly soluble in boiling pyridine; it was dried over phosphoric oxide (Found: C, 43.75; H, 2.85. $C_{16}H_8N_2S_2Cd.2H_2O$ requires C, 43.6; H, 2.7%).

A purplish-black disilver salt was also prepared. It was not obtained pure, but analysis showed that it contained two atoms of silver to sixteen atoms of carbon.

SS'-Dimethyldithio-β-isoindigo (II).—A cold solution of (I) (3 g.) and sodium hydroxide (2 g.) in water (5 c.c.) was treated with alcohol (15 c.c.), and methyl iodide (2 c.c.) in a few c.c. of alcohol was run in; crystals began to separate at once. After 1 hour, the liquid was diluted with water to 200 c.c. and the crystals were collected, dried, and recrystallised from boiling benzene (200 c.c.); the yield was nearly quantitative. The substance separated from benzene

or pyridine in flat needles, m. p. 258°, which were orange- or brownish-yellow according to the concentration of the crystallising solution [Found : C, 67.0, 67.2; H, 4.6, 4.6; N, 9.0, 9.1; S, 19.7; *M* (micro-Rast, in camphor), 316. $C_{18}H_{14}N_2S_2$ requires C, 67.05; H, 4.4; N, 8.7; S, 19.9%; *M*, 322]. It dissolved to yellow solutions in pyridine, chloroform, and benzene. It did not give rise to metallic salts, but formed an addition compound with mercuric chloride in pyridine. It was oxidised by nitric acid to phthalimide, which was free from *N*-methylphthalimide. Boiling with concentrated hydrochloric acid changed (II) into (III) and then into (IV).

S-Methylthio- β -isoindigo (III).—When (II) was boiled for a few minutes with concentrated hydrochloric acid, methylthiol was evolved. The liquid was diluted with an equal volume of water; minute yellow crystals then separated, m. p. 297° (after recrystallisation from pyridine and from glacial acetic acid); the mother-liquor was free from methylamine. The substance contained sulphur (Found : C, 69.8, 69.6; H, 4.2, 4.3; N, 10.0. $C_{17}H_{12}ON_2S$ requires C, 69.85; H, 4.1; N, 9.6%). It formed a bright red hydrochloride, which was hydrolysed by boiling water. *S*-Methylthio- β -isoindigo was converted into β -isoindigo and methylthiol on being boiled further with concentrated hydrochloric acid.

β -isoIndigo (IV).—This was prepared by boiling (II) with a mixture of equal volumes of alcohol and concentrated hydrochloric acid under reflux for 24 hours; methylthiol was evolved, and β -isoindigo separated as a powder, which was precipitated from solution in hot concentrated sulphuric acid, or extracted with boiling pyridine, in which it was only slightly soluble, to remove impurities; it was free from sulphur. It formed pale yellow or greenish needles from aniline or from phenol-*p*-cresol, not melted at 350° (Found : C, 73.2; H, 4.2; N, 11.1. Calc. for $C_{16}H_{10}O_2N_2$: C, 73.3; H, 3.8; N, 10.7%). It dissolved to a yellow solution in hot rather concentrated aqueous sodium hydroxide and was reprecipitated unchanged by glacial acetic acid. β -isoIndigo was prepared also (i) from *SS'*-diethyldithio- β -isoindigo and (ii) from phthalimidine, as described later. Each of these samples of β -isoindigo, when warmed with bromine and then boiled with water, gave a yellow residue showing a blue fluorescence in alcohol.

SS'-Diethyldithio- β -isoindigo (IIA).—This was prepared in the manner described for (II); the temperature must not be allowed to rise during the reaction. It formed silky, yellow, flat needles, m. p. 162°, from pyridine [Found : C, 68.9; H, 5.4; N, 8.3; *M* (micro-Rast, in camphor), 341. $C_{20}H_{18}N_2S_2$ requires C, 68.6; H, 5.15; N, 8.0%; *M*, 350]. It behaved towards boiling concentrated hydrochloric acid in the same way as (II), giving ethylthiol and (successively) *S*-ethylthio- β -isoindigo (below) and β -isoindigo.

S-Ethylthio- β -isoindigo (IIIA) separated from pyridine in long yellow needles, m. p. 252° (Found : C, 70.6; H, 4.8; N, 9.45. $C_{18}H_{14}ON_2S$ requires C, 70.6; H, 4.6; N, 9.15%); it was almost insoluble in alcohol, but dissolved in hydrochloric acid to a yellow solution. Prolonged boiling with alcoholic hydrochloric acid gave ethylthiol and β -isoindigo.

Condensation of Dithiophthalimide to Dithio- β -isoindigo.—This was effected by heating with silver or copper. Silver gave a much better reaction, as follows: an intimate mixture of dithiophthalimide (1 g.) and dry silver powder (1 g.; from silver nitrate and hydrazine) was heated on an oil-bath at 175° for $\frac{1}{4}$ hr. and then at 190° for 1 hr. The product was extracted with alcohol to remove any unchanged dithiophthalimide, and the residue then extracted with boiling nitrobenzene (100 c.c.) or with aqueous sodium hydroxide (10%; 10 c.c.) mixed with alcohol (5 c.c.); in either case, the filtered extract contained (I), which was isolated in the manner before described (yield, nearly quantitative). The product was characterised by its general properties and by conversion into its methyl and ethyl derivatives.

A similar condensation with thiophthalimide, silver or copper being used at 175–250°, gave β -isoindigo; the residue after extraction with alcohol and pyridine was purified by means of aqueous sodium hydroxide, as before described. Phthalimide also was produced in this condensation, which was less uniform than the preceding.

Condensation of Phthalimidine to β -isoIndigo.—Phthalimidine (4 g.) and sulphur (3 g.) were intimately mixed and heated on an oil-bath at 200–220° for 1 hour; hydrogen sulphide was vigorously evolved and the molten mixture finally became solid. The powdered product was extracted with carbon disulphide to remove sulphur, and then with hot concentrated hydrochloric acid (to remove any phthalimidine). The yellow residue had the properties of β -isoindigo and appeared to be pure; a sample recrystallised from aniline and another purified through the orange needles of the sodium salt were analysed (Found : C, 72.9, 73.0; H, 3.6, 3.7; N, 10.6. Calc. for $C_{16}H_{10}O_2N_2$: C, 73.3; H, 3.8; N, 10.7%).

Condensation of Dithiophthalimide to Dithio- β -isoindigo.—Dithiophthalimide was dissolved in alcohol, a little aqueous ammonia (*d* 0.88) added, and hydrogen sulphide passed in.

Dithio- β -isoindigo soon separated, and was isolated and purified as already described under the preparation of (I); the yield was nearly quantitative. The product was identified by its general properties and by methylation. Addition of aqueous ammonia to an alcoholic solution of dithiophthalimide also gave (I) in a pure state, after a few minutes (Found : C, 65.1; H, 3.9%).

Action of Hydrazine upon Dithio- β -isoindigo.—A mixture of (I) (1 g.) and an excess of hydrazine hydrate (1 g.) in alcohol (10 c.c.) was heated under reflux for 3 hrs.; an intensely red solution was produced, which soon evolved hydrogen sulphide and gave a crystalline precipitate. The crystals were separated from the hot solution and washed with alcohol. They consisted of β -isoindigodihydrazone (Found : C, 66.5; H, 5.2; N, 28.7, 29.3. $C_{16}H_{14}N_6$ requires C, 66.2; H, 4.8; N, 28.95%), brownish-red microcrystals, frothing and melting at 260°, after darkening from 240°; it was slightly soluble in pyridine (yellow solution), and was soluble in aqueous-alcoholic sodium hydroxide (wine-red solution).

3 : 6-Dihydroxyphthalodiamidine (VI).—To a solution of 3 : 6-dihydroxyphthalonitrile (Thiele and Meisenheimer, *Ber.*, 1900, **33**, 675) (2 g.) in alcohol was added alcoholic ammonia; a yellow powder was precipitated. Crystallised from water (greenish-blue fluorescence), the powder gave bright yellow needles of the *diamidine*, which decomposed and became black between 210° and 270°, but did not melt (Found : C, 49.6; H, 5.7; N, 29.2. $C_8H_{10}O_2N_4$ requires C, 49.5; H, 5.15; N, 28.9%). Dilute acids hydrolysed it to 3 : 6-dihydroxyphthalic acid, but concentrated sulphuric acid gave 3 : 6-dihydroxyphthalimide; it was unchanged by alcoholic hydrogen sulphide in presence of ammonia.

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