

acid until no change in the melting point of 290–291° (corr.) was obtained. Even after this extensive purification no very satisfactory analyses could be obtained. The 2,4,6-tribromophenylhydrazine itself loses bromine on standing and it is probable that the hydrazone is also unstable.

Tetrabromophthal-2,4,6-tribromophenylhydrazone is very soluble in pyridine, and somewhat less so in xylene (1 : 50), acetic anhydride (1 : 140), benzene (1 : 100), acetic acid (1 : 400), and acetone. It is insoluble in alcohol and ethyl acetate. It crystallizes in very long, thin needles, resembling cotton batton, possessing a light greenish yellow color. With dimethylaniline a slightly orange color is produced.

Subst. 0.3329, 0.2511. Cc. 0.1 *N* AgNO<sub>3</sub>; 29.27, 22.23.

Calc. for C<sub>14</sub>H<sub>3</sub>O<sub>2</sub>N<sub>2</sub>Br<sub>7</sub>: Br, 70.77. Found: 69.52, 70.00.

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[CONTRIBUTION FROM THE SCHOOL OF CHEMISTRY, UNIVERSITY OF PITTSBURGH.]

## PHTHALIC ACID DERIVATIVES, CONSTITUTION AND COLOR, XV.<sup>1</sup> 3,4,6-TRIIODOPHTHALOXIME AND SOME OF ITS DERIVATIVES.

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Tetraiodophthaloxime failed to give instances of the dimorphism which had been observed with various derivatives of the corresponding tetrachlorophthaloxime.<sup>2</sup> This property of appearing in two distinct crystal forms, one stable, the other unstable at ordinary temperatures, has been found quite characteristic of many substituted phthalimide derivatives. Inasmuch as both phthaloxime itself and tetraiodophthaloxime gave no examples of dimorphism while tetrachlorophthaloxime appeared to be especially adapted constitutionally to show this property, it was thought desirable to prepare the triiodophthaloxime series. The 3 atoms of iodine might correspond in effect to 4 of chlorine in so far as any proximity effects were concerned. It was also desirable to have this new series of substituted phthalic acid derivatives for spectroscopic study.

**3,4,6-Triiodophthaloxime.**—The triiodophthalic anhydride necessary was prepared and purified following the recent methods of Pratt and Perkins.<sup>3</sup> Fifty grams of the yellow crystals were finely powdered and suspended in about 400 cc. of water containing 10 g. of hydroxylamine hydrochloride and 12.1 g. of sodium bicarbonate. The mixture was placed in a briskly boiling water bath and frequently stirred. It

<sup>1</sup> THIS JOURNAL, 40, 412 (1918).

<sup>2</sup> *Ibid.*, 40, 407 (1918).

<sup>3</sup> *Ibid.*, 40, 219 (1918).

soon turned red. A portion of the solution then gave a strong wine color with a drop of dilute ferric chloride showing the formation of hydroxamic acid. The heating was continued until a test portion gave only a slight color with ferric chloride, about two hours being required. The pasty mixture was cooled, acidified with sufficient hydrochloric acid to give a clear yellow, and filtered. The precipitate was washed free from chlorides and recrystallized from alcohol. Yield, nearly theoretical.

3,4,6-Triiodophthaloxime gave long, lemon-yellow needles from alcohol or glacial acetic acid, and decomposed at 224–226° (corr.) with decomposition. The oxime is easily soluble in hot acetic acid and acetone, slightly in alcohol and less in methyl alcohol. From all of these solvents the same type of crystals was always obtained, no evidence of dimorphism being observed.

Subst. 0.2569, 0.2707. Cc. 0.1 N AgNO<sub>3</sub>; 14.19, 14.95.

Calc. for C<sub>8</sub>H<sub>2</sub>O<sub>3</sub>NI<sub>3</sub>: I, 70.40. Found: 70.03, 70.01.

**Ammonium Salt.**—Dry ammonia reacts very slowly and incompletely with powdered oxime, but no difficulty was encountered in making the salt by passing moist ammonia over a weighed sample in a porcelain boat. The color changed at once to a deep red and the increase in weight evidenced complete reaction within a few hours.

Subst. 0.4136, 0.7402. Increase in weight; 0.0130, 0.0244.

Calc. for C<sub>8</sub>H<sub>2</sub>O<sub>3</sub>NI<sub>3</sub>.NH<sub>3</sub>: NH<sub>3</sub>, 3.15. Found: 3.14, 3.30.

The ammonium, sodium, potassium and silver salts are brilliant, red and are insoluble in all solvents.

**Silver Salt.**—The silver salt necessary for preparing various ethers was made by adding an excess of carefully adjusted ammoniacal silver nitrate solution to the oxime dissolved in warm alcohol. The red voluminous product was washed as free from adsorbed silver as possible and a sample dried for analysis. Weighed samples were treated with 6 N nitric acid and the silver nitrate titrated.

Subst. 0.1226, 0.0919. Cc. 0.1 N NH<sub>4</sub>SCN; 1.82, 1.36.

Calc. for C<sub>8</sub>HO<sub>3</sub>NI<sub>3</sub>Ag: Ag, 15.37. Found: 16.02, 15.96.

**3,4,6-Triiodophthaloxime Ethers.**—In preparing ethers of other oximes studied, the general procedure followed has been to suspend the dry silver salt in ethyl ether containing the alkyl halide and boil with a reflux condenser until the red color was removed. It has frequently happened that this conversion, for no apparent reason, proceeded very slowly, days occasionally being required. We have now modified the method in that the silver salt is no longer removed from the alcohol suspension in which it was formed. It is allowed to settle, as much excess alcohol as possible is decanted off, and the alkyl halide added directly to the suspension. A few minutes' shaking suffices to convert the silver salt into

its corresponding ether when an alkyl iodide is used. Bromides and chlorides react more slowly and require refluxing. The yields are approximately quantitative.

**Methyl Ether.**—The ether prepared as above was obtained in the form of ill-shaped tiny clusters of blades and needles. Both forms were canary yellow, the former predominating from chloroform, the latter when alcohol, acetic acid or acetic anhydride was used as solvents. The ether decomposes without melting at  $245\text{--}253^\circ$  (corr.). The prismatic form could not be obtained, hence, considerable difficulty was encountered in purifying this ether, as the modification available did not crystallize at all well.

Subst. 0.2245, 0.2607. Cc. 0.1 *N* AgNO<sub>3</sub>; 12.25, 14.28.

Calc. for C<sub>9</sub>H<sub>8</sub>O<sub>3</sub>NI<sub>3</sub>: I, 68.62. Found: 68.52, 68.78.

**Ethyl Ether.**—The ethyl ether was obtained only as light yellow masses of confused curved needles. No prismatic form was observed. It was recrystallized from chloroform and alcohol mixture until the melting point of  $241.5\text{--}242.5^\circ$  (corr.) remained unchanged.

Subst. 0.3033, 0.2748. Cc. 0.1 *N* AgNO<sub>3</sub>; 16.15, 14.67.

Calc. for C<sub>10</sub>H<sub>8</sub>O<sub>3</sub>NI<sub>3</sub>: I, 66.93. Found: 66.86, 67.03.

**Isopropyl Ether.**—The isopropyl ether is very soluble in chloroform-alcohol, tending toward supersaturation. It was obtained only in the form of cotton-like, yellow needles, melting at  $182\text{--}186^\circ$  (corr.).

Subst. 0.2652, 0.2543. Cc. 0.1 *N* AgNO<sub>3</sub>; 13.76, 13.19.

Calc. for C<sub>11</sub>H<sub>8</sub>O<sub>3</sub>NI<sub>3</sub>: I, 65.31. Found: 65.78, 65.76.

**Allyl Ether.**—The allyl ether was the first that gave the second dimorphic form. It was obtained from chloroform, by the addition of alcohol, as coarse prisms of a fairly deep yellow color. The cotton-like modification was not noticed. The ether melts at  $192\text{--}192.5^\circ$  (corr.).

Subst. 0.2572, 0.2722. Cc. 0.1 *N* AgNO<sub>3</sub>; 13.43, 14.26.

Calc. for C<sub>11</sub>H<sub>8</sub>O<sub>3</sub>NI<sub>3</sub>: I, 65.55. Found: 66.20, 66.41.

**Benzyl Ether.**—4.5 g. of dry silver salt was boiled with benzyl chloride until the red color disappeared. The hot solution was filtered and alcohol added to abundant precipitation. The crude ether was recrystallized from chloroform and alcohol until the melting point of  $217.0\text{--}217.5^\circ$  (corr.) remained unchanged. An excellent yield of glistening, broad, canary yellow plates was obtained. No other form was observed.

Subst. 0.2711, 0.3384. Cc. 0.1 *N* AgNO<sub>3</sub>; 13.00, 16.18.

Calc. for C<sub>15</sub>H<sub>8</sub>O<sub>3</sub>NI<sub>3</sub>: I, 60.35. Found: 60.79, 60.62.

**Acetate.**—3,4,6-Triiodophthaloxime was boiled gently for 30 minutes with just enough acetic anhydride to effect solution. The acetate that crystallized out on cooling was washed with alcohol and recrystallized until pure from chloroform. It was obtained as light yellow, lenticular blades, melting at  $223.0\text{--}224.0^\circ$  (corr.).

Subst. 0.2729, 0.2238. Cc. 0.1 *N* AgNO<sub>3</sub>; 14.01, 16.56.

Calc. for C<sub>10</sub>H<sub>4</sub>O<sub>4</sub>N<sub>2</sub>: I, 65.22. Found: 65.08, 65.14.

**Benzoate.**—A sample of pure oxime was dissolved in 4 times its weight of benzoyl chloride at about 140° and the solution held at this temperature for 30 minutes. It was then diluted with alcohol, allowed to stand until the odor of benzoyl chloride disappeared and filtered. The crude benzoate was washed with alcohol and ether and recrystallized from a chloroform alcohol mixture until the melting point of 224–225° (corr.) remained unchanged. Clusters of deep yellow lenticular crystals were obtained.

Subst. 0.3011, 0.2851. Cc. 0.1 *N* AgNO<sub>3</sub>; 14.35, 13.64.

Calc. for C<sub>15</sub>H<sub>6</sub>O<sub>4</sub>N<sub>2</sub>: I, 59.04. Found: 60.42, 60.65.

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## THE PREPARATION OF PIPERAZINE.

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Piperazine, or diethylenediamine,  $\text{HN} \begin{array}{c} \diagup \text{CH}_2 \cdot \text{CH}_2 \\ \diagdown \text{CH}_2 \cdot \text{CH}_2 \end{array} \text{NH}$  has been used ex-

tensively in cases of gout and arthritis with such success that its absence from the market justified a rather extended search for methods which might be employed in preparing it.<sup>1</sup> Several important modifications of procedure, as disclosed in the patent literature, have been found which it is believed will materially aid anyone attempting to prepare piperazine commercially.

The ease with which ethylene bromide condenses with aniline to form diphenyl piperazine appears to offer the best starting point in the preparation. This reaction can be carried out under proper conditions to give practically a theoretical yield suitable without further purification for the purpose. Unfortunately, it does not seem possible to replace the two phenyl radicals with hydrogen to give piperazine directly.

However, nitrous acid reacts with diphenyl piperazine, and this derivative can be hydrolyzed. According to German patent No. 60,547, boiling with alkalis accomplishes the desired result.

The conversion of diphenyl piperazine into its dinitroso derivative involves difficulties which are not disclosed in this or other patents. The addition of sodium nitrite to a suspension of diphenyl piperazine in acidulated cold water results in the formation of sticky, green tars which give no traces of piperazine on boiling with aqueous or alcoholic alkali. Many

<sup>1</sup> The value of piperazine in certain types of nephritis has been studied extensively by Dr. E. E. Mayer, who will report his results in the near future.