[Contribution from the Frank C. Whitmore Laboratory of the Pennsylvania State College]

SYNTHESIS OF 3,5-DIIODOPHTHALIC ANHYDRIDE AND 1,3-DIIODOANTHRAQUINONE

ROBERT W. HIGGINS[1] AND JOHN C. CHESSICK[2]

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Of the four theoretically possible diiodophthalic anhydrides only three have been previously reported. Pratt and Perkins (1) obtained 3,4-, 3,6-, and 4,5-diiodophthalic anhydride by the partial iodination of phthalic anhydride in 50% oleum. However, the remaining isomer 3,5-diiodophthalic anhydride was not detected in nor isolated from the reaction mixture. Interest was aroused in the preparation of this compound in order to complete the synthesis of all the isomeric homonuclear diiodoanthraquinones, of which there likewise are four.

Three isomeric homonuclear diiodoanthraquinones of known structure were heretofore reported by Higgins and Suter (2). The 1,2-, 1,4-, and 2,3-diiodoanthraquinones were prepared by the condensation of 3,4-, 3,6-, and 4,5-diiodophthalic anhydride respectively with benzene, followed by ring closure with 100% sulfuric acid. The 2,3-diiodoanthraquinone obtained proved to be identical with a diiodoanthraquinone of unknown structure previously reported by Eckert and Klinger (3).

The procedure for the preparation of 3,5-diiodophthalic anhydride initially involved the iodination of anthranilic acid (4). This step proceeded readily but the replacement of the amino group by the cyano radical and its subsequent hydrolysis gave inconsistent yields. However, yields as high as 86% have been realized in the diazotization. The product obtained is the sodium salt of the iodinated cyanobenzoic acid. It may be hydrolyzed to the desired iodinated phthalic acid without further purification. On refluxing the iodinated phthalic acid in a dry benzene solution, containing acetic anhydride in slight excess of the theoretical amount, the iodinated phthalic anhydride was formed.

It was reported earlier that the benzoylbenzoic acids obtained by the condensation of 3,4- and 4,5-diiodophthalic anhydride with benzene could be readily purified by crystallizing their sodium or potassium salts from hot water (2). However, the benzoylbenzoic acid obtained on condensing 3,5-diiodophthalic anhydride with benzene could not be purified in this manner. At present absolute proof to determine which of the isomeric acids, 2-benzoyl-3,5-diiodobenzoic acid (I) or 2-benzoyl-4,6-diiodobenzoic acid (II), result from the condensation has not been obtained. Work in progress may lead to that end. However, because of the ease in ring closure it is strongly suspected the acid is I.

EXPERIMENTAL[3]

3,5-Diiodoanthranilic acid (4). A solution of 59.0 g. (0.363 mole) of iodine monochloride in 60 ml. of 25% hydrochloric acid was added slowly to a solution, at 80°, of 25.0 g. (0.182

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[1] Present address: Ellen H. Richards Institute, Pennsylvania State College.

[2] Present address: Lehigh University.

[3] All melting points uncorrected.

mole) of anthranilic acid in 500 ml. of 25% hydrochloric acid. The mixture was stirred vigorously for several minutes and then diluted with 2 l. of water, after which the temperature was elevated to 80–90° and maintained there for 20 minutes. The crude product was obtained on cooling and filtering. Purification was effected by dissolving the product in 600 ml. of water to which sufficient ammonium hydroxide was added to maintain alkalinity. A small amount of insoluble material was removed. The yield of product obtained on acidification of the filtrate with dilute hydrochloric acid was 59 g., or 83%. The grayish-white product melted at 230–231°.

2-Cyano-3,5-diiodobenzoic acid.[4] A solution of 50 ml. of water and 75 ml. of concentrated sulfuric acid was added to a 1-l. round-bottom flask which was equipped with a stirrer and immersed in an ice-salt bath. While stirring, 11.7 g. (0.0304 mole) of 3,5-diiodoanthranilic acid was added to this solution. After the solution had been cooled to 5°, 5.6 g. (0.081 mole) of sodium nitrite, previously dissolved in 20 ml. of water, was introduced. After one to two hours stirring, the yellow diazonium solution was diluted with 300 ml. of water, filtered rapidly, and returned to the ice-salt bath. A concentrated solution of sodium hydroxide or sodium carbonate was added slowly until *p*H 6.5 was reached. When sodium hydroxide was used in the neutralization frequent addition of ice was necessary in order to maintain the temperature between 5–10°.

A complex cyanide solution was prepared by adding 6.5 g. (0.13 mole) of sodium cyanide, dissolved in 50 ml. of water, dropwise to a hot solution of 75 ml. of water and 8.0 g. (0.032 mole) of hydrated copper sulfate. The clear cyanide complex was then added to the diazonium salt solution. The reaction mixture was allowed to stand until room temperature was reached, after which it was heated at 70–80° until there was no longer evidence of gas evolution. On cooling the diazotized solution to 10°, a crystalline product appeared. It did not melt but seemed to char at 180°. The yield of the sodium salt of 2-cyano-3,5-diiodobenzoic acid was 11 g., or 86%.

Approximately 1 g. of the product was dissolved in 200 ml. of water. The solution after filtering was acidified. The precipitate obtained was crystallized from a benzene-ethanol solution. A white product melting from 195–197° was obtained.

Anal. Calc'd for $C_8H_3I_2NO_2$: Neut. equiv., 399. Found: Neut. equiv., 400, 399.

3,5-Diiodophthalic acid. The sodium salt of 2-cyano-3,5-diiodobenzoic acid was added to a solution of 50 ml. of water and 100 ml. of concentrated sulfuric acid. The suspension was stirred vigorously and heated on the steam-bath for six to eight hours. It was poured onto crushed ice and the precipitated acid was purified by dissolving the crude product in dilute sodium carbonate solution and decolorizing with bone charcoal. Acidification of the alkaline filtrate yielded the desired product. From 10 g. of the cyano acid salt, the yield of iodinated phthalic acid was 6.5 g., or 65%. The pure white acid had m.p. 219–220°.

Anal. Calc'd for $C_8H_4I_2O_4$: Neut. equiv., 209. Found: Neut. equiv., 208, 209.

3,5-Diiodophthalic anhydride. To 150 ml. of dry benzene was added 2.5 g. of acetic anhydride and 8 g. of the iodinated phthalic acid. The reaction mixture was refluxed until solution had been effected. A small residue generally remained which was removed on filtering. On concentrating the filtrate to a small volume (20–30 ml.) and cooling, the anhydride was obtained as slender pale yellow crystals. The yield of product melting from 144–146° was 6 g., or 80%.

Anal. Calc'd for $C_8H_2I_2O_3$: C, 24.01; H, 0.51.
Found: C, 24.09, 24.26; H, 0.62, 0.69.

2-Benzoyl-3,5(?)-diiodobenzoic acid. A mixture of 50 ml. of thiophene-free benzene, 6.5 g. (0.016 mole) of 3,5-diiodophthalic anhydride, and 4.29 g. (0.0322 mole) of anhydrous aluminum chloride was refluxed and stirred for 16 hours. Then ice and hydrochloric acid were added and the excess benzene removed by distillation. The dark solid material remaining was filtered, washed free of mineral acid and dissolved in dilute sodium carbonate solution. The filtrate from the sodium carbonate extraction, on acidification with dilute

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[4] Yield improved on diazotization by Layman, Senior Thesis, Pennsylvania State College.

hydrochloric acid yielded the condensation product. Upon crystallization from an ethanol-water mixture, 4.9 g. of white granular crystals was obtained. Concentration of the mother liquor yielded an additional 1.5 g. of the condensation product. The total yield of product, m.p. 237–239°, was 6.4 g., or 82%.

Anal. Calc'd for $C_{14}H_8I_2O_3$: Neut. equiv., 478. Found: Neut. equiv., 475, 477.

1,3-Diiodoanthraquinone. To 30 ml. of 100% sulfuric acid at 130° was added gradually 2.5 g. of 2-benzoyl-3,5(?)-diiodobenzoic acid. The reaction mixture was heated at this temperature for one hour, cooled to approximately 70°, and poured over crushed ice. The precipitate was filtered and washed free of mineral acid. It was extracted with warm dilute sodium carbonate solution to remove any uncyclized organic acid. The insoluble portion, on crystallizing from a benzene-toluene mixture, was bright orange in color, m.p. 230–232°. The yield was 1.9 g., or 80%.

Anal. Calc'd for $C_{14}H_6I_2O_2$: C, 36.52; H, 1.30.
Found: C, 36.47, 36.88; H, 1.51, 1.47.

SUMMARY

1. 3,5-Diiodophthalic acid and anhydride have been prepared in good yields.
2. The condensation of 3,5-diiodophthalic anhydride with benzene has been accomplished.
3. 1,3-Diiodoanthraquinone has been characterized.

STATE COLLEGE, PENNA.

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