[CONTRIBUTION FROM THE CHEMICAL LABORATORY OF NORTHWESTERN UNIVERSITY]

Synthesis of Iodinated Benzoylbenzoic Acids and Anthraquinones[1]

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Although many halogenated anthraquinones have been prepared, the known iodine derivatives are limited in number. The 1- and 2-iodoanthraquinones have been obtained from the amines[2] and 1,5-diiodoanthraquinone has been prepared from the diamine.[3] The action of iodine and sodium nitrite in fuming sulfuric acid upon anthracene yields a mixture of mono- and diiodoanthraquinones of unknown structure[4] whose physical properties were not recorded. It has been reported[5] that the action of iodine on anthraquinone in 70% oleum at 180° yields a complex mixture of products of which a tri-, a tetra- and a penta-iodoanthraquinone were isolated. The tetra compound was characterized by its high melting point (500°). The only attempt so far made to prepare an iodinated anthraquinone by a nuclear synthesis was that of Eckert and Klinger.[5] They found that the benzoyltetraiodobenzoic acid obtained from tetraiodophthalic anhydride and benzene when heated with concentrated sulfuric acid at 190–200° lost iodine but nevertheless there resulted a 20% yield of a tetraiodoanthraquinone, m. p. 476° (dec.), which they believed was not the 1,2,3,4-compound. Attempts to bring about ring closure by the use of aluminum chloride resulted in evolution of iodine and hydrogen chloride with formation of a diiodoanthraquinone (m. p. 290–292°) of unknown structure.

Lawrance[6] found that tetraiodophthalic anhydride condensed readily with toluene but ring closure was not attempted. The conversion of benzoyltetrabromobenzoic acid to the anthraquinone[7] has been brought about by heating with 13% oleum and a variety of substituted anthraquinones has been prepared from the benzoylbenzoic acids resulting from the action of tetrachlorophthalic anhydride upon benzene derivatives.[8]

Since Pratt and Perkins[9] have shown that the di- and triiodophthalic anhydrides obtained by partial iodination of phthalic anhydride in oleum can be separated it was decided to investigate the condensation of these with representative aromatic compounds under various conditions. The condensation of the 3,4-, 4,5- and 3,6-di-, and the 3,4,6-triiodophthalic anhydrides with benzene occurs readily in the presence of two molecular equivalents of aluminum chloride. The products from the 3,4- and 4,5-diiodo anhydrides are purified readily by crystallizing their potassium salts from hot water. On the other hand, the potassium salts of the acids obtained from the 3,4,6-triiodo- and tetraiodophthalic anhydrides do not separate from water readily. No effort has so far been made to determine which of the two possible acids results from the 3,4-diiodo anhydride and benzene but the ease of ring closure indicates that it is 2-benzoyl-3,4-diiodobenzoic acid. The 3,4,6-triiodo anhydride yields a mixture in practically equal amounts of the two possible isomeric acids.

Ring closure of the three benzoyldiiodobenzoic acids was effected readily with 100% sulfuric acid. With a lower concentration iodine elimination occurred. The 2,3-diiodoanthraquinone corresponds in melting point to the diiodoanthraquinone obtained by Eckert and Klinger[5] through the action of aluminum chloride upon benzoyltetraiodobenzoic acid. The identity of these acids is reasonable as the iodine atoms in the 1,4-positions are eliminated easily. Attempts to condense phthalic anhydride with *m*-diiodobenzene under a variety of conditions were unsuccessful. It was thought that from the benzoylbenzoic acid so obtained it might be possible to prepare the unknown 1,3-diiodoanthraquinone.

Conversion of the two isomeric benzoyltriiodobenzoic acids into 1,2,4-triiodoanthraquinone occurred under narrowly defined conditions in yields of about 25%. In view of these results various attempts were made to induce a similar reaction with benzoyltetraiodobenzoic acid under conditions where iodine was not eliminated but without success, confirming previous reports.[5]

The results of some preliminary experiments designed to prepare iodinated hydroxyanthraqui-

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(1) Presented before the Organic Division of the American Chemical Society at the Milwaukee meeting September, 1938.

(2) Laube, *Ber.*, **40**, 3566 (1907); **37**, 60 (1904).

(3) Scholl, Hass, Meyer and Seer, *ibid.*, **62B**, 107 (1929).

(4) Varma and Subramanyam, *C. A.*, **25**, 2994 (1931).

(5) Eckert and Klinger, *J. prakt. Chem.*, [2] **121**, 281 (1929).

(6) Lawrance, THIS JOURNAL, **43**, 2577 (1921).

(7) Hofmann, *Monatsh.*, **36**, 805 (1915).

(8) For examples see Ruggli and Brunner, *Helv. Chim. Acta*, **8**, 155 (1925); Waldmann, *J. prakt. Chem.*, **147**, 331 (1937); Underwood and Walsh, THIS JOURNAL, **57**, 940 (1935).

(9) Pratt and Perkins, *ibid.*, **40**, 219 (1918).

nones may be mentioned. Although phthalic anhydride condenses with veratrole and with 4-chloroveratrole without undue difficulty, so far it has not been possible to bring about reaction of either of these ethers with 4,5-diiodophthalic anhydride or the tetraiodo compound. On the other hand, anisole and the methyl ethers of *o*- and *m*-cresol react readily with both anhydrides. Further work on this aspect of the investigation is in progress.

Considerable difficulty was encountered in the analysis of iodinated anthraquinones for iodine. The usual procedure with the Parr bomb gave only partial decomposition of the compounds. The Stepanow method using sodium and alcohol gave erratic results which were high until it was found that digestion of the silver iodide precipitate for several hours with dilute nitric acid gave consistent results on both known compounds and the iodinated anthraquinones. The intermediate benzoylbenzoic acids were titrated in aqueous alcohol solution with standard alkali using thymol blue as the indicator.

Experimental

Iodophthalic Acids.—Iodination of phthalic anhydride was conducted according to the procedures of Pratt and Perkins.[9] The low temperature iodination gave the more satisfactory results. In the original directions where separation of the 4,5-diiodophthalic acid is effected by precipitation with a definite volume of "acetic acid," the volume given refers to 6 *N* acid; the use of 100% acetic acid gave a mixture of iodinated acids. In the precipitation of the 3,4,6-triiodo acid 18 cc. of 6 *N* acetic acid gave better results than the 10 cc. specified in the original. The volumes of concentrated hydrochloric acid found necessary in the later stages of the separation checked those specified by Pratt and Perkins. The precipitates obtained by this separation procedure required considerable purification before the products gave satisfactory melting points and the yields of iodophthalic anhydrides isolated were distinctly lower than the amounts of nearly pure acids obtained in the original preparation would suggest. From 780 g. of phthalic anhydride, 1270 g. of iodine, and 2500 g. of 50% oleum after heating for six days at 70–80° were obtained 100 g. of 4,5-diiodophthalic anhydride, m. p. 215–216°, 147 g. of the 3,4,6-triiodo anhydride, m. p. 220–223° (further crystallization raised this to 226–227°); 325 g. of the 3,4-diiodo anhydride, m. p. 194–196° and 395 g. of 3,6-diiodo anhydride, m. p. 228–231°. In addition, smaller amounts of the compounds having somewhat lower melting points were isolated.

2-Benzoyl-4,5-diiodobenzoic Acid.—A mixture of 5 g. of diiodophthalic anhydride, 3.65 g. (10% excess over two molecular equivalents) of aluminum chloride and 40 ml. of benzene was refluxed for twenty-four hours, poured into cold water and the benzene steam distilled out. The water-insoluble residue was filtered and then treated with hot potassium carbonate solution which left only a trace of undissolved material. The solution upon cooling deposited the potassium benzoylbenzoate which was redissolved in hot water and the solution acidified. Crystallizing the precipitate from dilute alcohol gave 4.8 g. of product melting[10] at 244–245°. This corresponds to an 80% yield.

Anal. Calcd. for $C_{14}H_8O_3I_2$: neut. equiv., 478. Found: neut. equiv., 481, 481.

2-Benzoyl-3,4-(?)-diiodobenzoic Acid.—By a procedure exactly analogous to that used in the preceding section, there was obtained a 65% yield of the benzoylbenzoic acid from the 3,4-anhydride. The m. p. was 223–224°. Only one product was isolated. When the time of heating was shortened to nine hours the yield was about the same.

Anal. Calcd. for $C_{14}H_8O_3I_2$: neut. equiv., 478. Found: neut. equiv., 476, 478, 481.

2-Benzoyl-3,6-diiodobenzoic Acid.—The potassium salt of the benzoylbenzoic acid from the 3,6-anhydride did not crystallize readily from aqueous solution. Acidification of the solution and crystallization of the precipitate from dilute alcohol gave a 60% yield of acid of m. p. 218–220°.

Anal. Calcd. for $C_{14}H_8O_3I_2$: neut. equiv., 478. Found: neut. equiv., 482, 482, 476.

2-Benzoyl-3,4,6- and 3,5,6-triiodobenzoic Acids.—From 32.6 g. (0.061 mole) of 3,4,6-triiodophthalic anhydride, 18.1 g. (0.136 mole) of aluminum chloride and 200 ml. of benzene after twenty-one hours of refluxing was obtained 37 g. of product soluble in potassium carbonate solution. Heating the product in concentrated hydrochloric acid did not produce a yellow color, indicating that no appreciable amount of anhydride was unreacted. Refluxing the product with 400 ml. of 95% alcohol for forty-five minutes left an insoluble residue amounting to 20 g. which melted at 252–262°. This residue was extracted with hot dioxane, leaving a small amount (2.4 g.) of inorganic material. Concentrating and cooling the dioxane solution gave 13.5 g. of acid melting at 257–258° and a second crop of 2.8 g. melting at 254–257°.

Cooling the alcohol solution gave 10.7 g. of the low melting isomer, m. p. 224–227°, and then further smaller fractions which were practically pure. A total of 16.3 g. of the high melting and 14.4 g. of the low-melting isomer were obtained. The purest samples of these melted at 257–258° and 225–227°, respectively.

Anal. Calcd. for $C_{14}H_7O_3I_3$ (m. p. 257–258°): neut. equiv., 604. Found: neut. equiv., 607, 602.

Anal. Calcd. for $C_{14}H_7O_3I_3$ (m. p. 225–227°): neut. equiv., 604. Found: neut. equiv., 600, 613.

2,3-Diiodoanthraquinone.—To 40 g. of 100% sulfuric acid at 140° was added gradually over thirty minutes with stirring 2 g. of 2-benzoyl-4,5-diiodobenzoic acid. The mixture was then cooled to 70–80° and diluted slowly by adding small pieces of ice. The mixture was filtered and the precipitate warmed with aqueous potassium carbonate to remove any unreacted acid. The insoluble portion was crystallized from benzene and acetic acid and then melted at 291–292°. The yield was 1.6 g. or 80% of the theoretical amount.

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[10] All melting points are corrected.

Anal. Calcd. for $C_{14}H_6O_2I_2$: I, 55.21. Found: I, 55.0, 55.3.

1,2-Diiodoanthraquinone.—This was prepared in a manner similar to that used with the 2,3-isomer. It crystallized in orange-red plates from a benzene–toluene mixture and melted at 236–237°.

Anal. Calcd. for $C_{14}H_6O_2I_2$: I, 55.21. Found: I, 55.6, 55.6.

1,4-Diiodoanthraquinone.—From heating 2 g. of 2-benzoyl-3,6-diiodobenzoic acid with 75 g. of 100% sulfuric acid at 100° for two hours, was obtained 1.1 g. (60%) of the anthraquinone. After crystallizing from alcohol it melted at 218–219°.

Anal. Calcd. for $C_{14}H_6O_2I_2$: I, 55.21. Found: I, 55.4, 55.3, 55.7.

1,2,4-Triiodoanthraquinone.—A. Two grams of the high-melting benzoyltriiodobenzoic acid was added to 60 g. of 100% sulfuric acid kept at 105° over a thirty-minute period with stirring and the mixture heated and stirred for thirty minutes longer. It was then cooled and poured on ice and the resulting colloidal suspension coagulated by heating on the steam-bath. The precipitate was then treated with dilute sodium hydroxide. The red residue upon crystallization from acetic acid yielded 0.5 g. of product melting at 202–204°. This is about 25% of the theoretical amount. Alterations in these conditions did not improve the yield.

B. From treatment of the low-melting benzoyltriiodobenzoic acid as in A was obtained 0.4 g. of the anthraquinone. After two crystallizations from acetic acid the m. p. was 202–203.5°.

Anal. Calcd. for $C_{14}H_5O_2I_3$: I, 64.84. Found: I, 64.9, 65.0.

Summary

1. The condensation of di- and triiodophthalic anhydrides with benzene and aluminum chloride gives good yields of the benzoylbenzoic acids.

2. Ring closure of benzoyldiiodobenzoic acids is readily effected by treatment with 100% sulfuric acid. The triiodo compounds give smaller yields of the triiodoanthraquinones.

3. Veratrole and 4-chloroveratrole do not condense readily with iodinated phthalic anhydrides. Work upon the synthesis of iodinated hydroxyanthraquinones is being continued.

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3,3′-Dimethyl-4,4′-dihydroxybenzophenone

BY MAX H. HUBACHER

During the progress of some work being carried out recently, it became necessary to prepare a quantity of 3,3′-dimethyl-4,4′-dihydroxybenzophenone. This was done by a caustic potash fusion of *o*-cresolphthalein.[1]

Since the properties of the compound prepared from *o*-cresolphthalein did not agree with those recorded by Doebner and Schroeder,[2] an investigation of this discrepancy was made in order to determine the true properties of this material. These chemists obtained a compound which they designated as dioxydimethylbenzophenone, melting at 138°, by caustic potash fusion of *o*-cresolbenzein. For an analysis they report, calculated for $C_{15}H_{14}O_3$: C, 78.51; found, 78.19. Evidently, an error was made in calculation as the value for carbon is 74.36.

A caustic potash fusion of *o*-cresolbenzein produced no trace of a compound melting at 138°. Instead, a product melting at 247° was obtained which was identical with that from *o*-cresolphthalein. That the compound of melting point 247° was the expected 3,3′-dimethyl-4,4′-dihydroxybenzophenone was confirmed by analysis and the preparation of the diacetyl derivative and the mono and dimethyl ethers. On prolonged fusion with caustic potash, the benzophenone was converted into *o*-cresol and 3-methyl-4-hydroxybenzoic acid.

Experimental[3]

3,3′ - Dimethyl - 4,4′ - dihydroxybenzophenone (I).—Seventy grams of potassium hydroxide was heated in a nickel crucible to 260–265° (oil-bath temperature) and 10 g. of *o*-cresolphthalein of m. p. 224–225° was stirred in. After ten minutes, the melt was poured into 1.5 liters of water and acidified with hydrochloric acid. The 6.60 g. of crude was crystallized from 75 cc. of glacial acetic acid; 4.85 g. (69.3%) of (I), melting at 246–247° was obtained. A second crystallization or a sublimation *in vacuo*[4] at 180° gave a pure product, melting point 247.0–247.8°. It formed colorless needles from 20% ethanol and rectangular plates from acetic acid. It dissolved in both sodium hydroxide or concd. sulfuric acid with yellow color.

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(1) A. v. Baeyer, *Ann.*, **202**, 126 (1880); W. R. Orndorff and W. R. Barrett, THIS JOURNAL, **46**, 2488 (1924).

(2) O. Doebner and G. Schroeder, *Ann.*, **257**, 74 (1890).

(3) All melting points are corrected.

(4) All the sublimations were done in a vacuum produced by a CenCO-HyvAC pump guaranteed to produce a vacuum of 0.3 micron.