[Contribution from the Ellen H. Richards Institute of the Pennsylvania State College]

A NUCLEAR SYNTHESIS OF 2-IODOANTHRAQUINONE¹

ROBERT W. HIGGINS, CLIFFORD L. HILTON,² AND SHARADCHANDRA D. DEODHAR

Received April 2, 1951

In the course of preparing materials for an investigation to be carried out within the Department of Chemistry, it became desirable to obtain pure samples of 4-iodophthalic anhydride, 2-benzoyl-4-(?)-iodobenzoic acid, and 2-iodoanthraquinone. A search of the literature revealed no entirely satisfactory method for the preparation of any of these compounds. In fact, no reference to the synthesis of 2-benzoyl-4-(?)-iodobenzoic acid could be found.

The procedure described in this paper for the synthesis of these compounds is based on the method used by Higgins and Chessick (1) for other members of the series. Preparation of 4-iodophthalic anhydride from the readily available 5iodoanthranilic acid using the Sandmeyer reaction followed by hydrolysis of the resulting 2-cyano-5-iodobenzoic acid proved superior to published procedures (2-6). This compound was converted to 2-benzoyl-4-(?)-iodobenzoic acid by a Friedel-Crafts reaction and the latter compound cyclized with sulfuric acid.

Stephens (7) observed that 4-bromophthalic anhydride with benzene and aluminum chloride gave about equal amounts of 2-benzoyl-4-bromobenzoic acid and 2-benzoyl-5-bromobenzoic acid. Proof of structure was accomplished by alkali fusion.

While the presence of isomers is indicated in the case of the condensation of 4-iodophthalic anhydride with benzene, only one isomer has been isolated in pure form. From the crude product melting from 162 to 172° , a product melting from 193 to 193.5° was obtained by recrystallization from toluene. A small fraction, m.p. $148-151^{\circ}$, was also obtained. The latter fraction could not be further purified. The neutralization equivalent of the crude product (m.p. $162-172^{\circ}$) indicated that the impurity was identical with the main product in composition. The structure of the main product has not been determined.

EXPERIMENTAL⁸

4-Iodophthalic acid. To 45 ml. of concentrated sulfuric acid and 200 ml. of water in a 1-lround-bottomed flask equipped with a stirrer and immersed in an ice-salt bath was added. with stirring, 15.8 g. (0.060 mole) of 5-iodoanthranilic acid. [The 5-iodoanthranilic acid was prepared by the method of Wallingford and Krueger (8), but purified by recrystallization of the ammonium salt until the acid had m.p. 224-226°.] When the solution had been cooled to 5°, 11.5 g. (0.167 mole) of sodium nitrite in 30 ml. of water was introduced. After two hours' stirring, the diazonium solution was poured onto 400 g. of crushed ice. Concentrated sodium hydroxide or sodium carbonate was then added slowly to pH 6.5. When sodium hydroxide was used, it was frequently necessary to add additional amounts of ice to maintain the temperature between 5° and 10°.

¹ Presented at the Spring meeting of the Pennsylvania Academy of Science, Muhlenberg College, Allentown, Pennsylvania, March 23, 1951.

² Present Address: Department of Chemistry, The Pennsylvania State College.

³ All melting points are uncorrected.

A complex cyanide solution was prepared by adding 13.0 g. (0.26 mole) of sodium cyanide in 100 ml. of water dropwise to a hot, continuously stirred solution of 16.0 g. (0.064 mole) of hydrated copper sulfate in 150 ml. of water. The clear cyanide complex was then added to the diazonium salt solution. The reaction mixture was allowed to come to room temperature, then heated to 70-80° to insure complete decomposition of the diazonium complex. On cooling and acidifying a solid product was obtained. This crude 2-cyano-5-iodobenzoic acid was hydrolyzed without further purification.

The crude product was added to 175 ml. of water and 50 ml. of concentrated sulfuric acid. The suspension was heated for eight hours with vigorous stirring on a steam-bath. It was cooled by immersion in an ice-salt bath and the crude acid was removed. Purification was effected by solution in the minimum of dilute sodium carbonate and treatment with decolorizing charcoal. Acidification of the alkaline filtrate yielded 16.0 g. of 4-iodophthalic acid (91% over-all). The 4-iodophthalic acid had m.p. 180–184°.

Occasionally, a residue remained after the diazotization step in spite of the use of an excess of nitrous acid. In one instance, the small, insoluble fraction was removed and a small portion was taken for examination and was detonated on probing. This showed it to be undissolved diazonium salt. Therefore, the complex cyanide solution should be added to the diazotized solution without filtration.

4-Iodophthalic anhydride. To 150 ml. of dry benzene was added 20 ml. of acetic anhydride and 16.0 g. (0.0548 mole) of 4-iodophthalic acid. The reaction mixture was refluxed until solution had been effected. Upon concentration to 40 ml. and cooling, the anhydride was obtained as pale yellow crystals, m.p. 125-126°. The yield was 13.4 g. (89%).

2-Benzoyl-4-(?)-iodobenzoic acid. In a 500-ml. three-necked, round-bottomed flask fitted with a mercury-sealed stirrer, was placed 10.0 g. (0.0365 mole) of 4-iodophthalic anhydride and 200 ml. of dry thiophene-free benzene. Then 9.7 g. (0.073 mole) of anhydrous aluminum chloride was added during 15 to 20 minutes. The reaction mixture was refluxed and stirred for 24 hours. After cooling to room temperature, the mixture was acidified with concentrated hydrochloric acid and the excess benzene was removed by steam-distillation. The residue was filtered, washed free from mineral acid, and dissolved in dilute sodium carbonate. Acidification was effected by the gradual addition of dilute (1:3) hydrochloric acid with stirring. The yield of crude product, m.p. 162-172°, was 10.9 g. (85%). After several recrystallizations from toluene, 4 g. of product, m.p. 193-193.5°, was obtained. The low-melting isomer could not be obtained in a pure state.

Anal. Calc'd for C₁₄H₁₉IO₃: Neut. equiv., 352.

Found for crude product: Neut. equiv., 351, 342.

for pure product: Neut. equiv., 353, 351.

2-Iodoanthraquinone. To 50 ml. of concentrated sulfuric acid at 140° was added gradually 3.0 g. (0.0085 mole) of pure 2-benzoyl-4-(?)-iodobenzoic acid. The mixture was heated at this temperature for five hours and allowed to cool to room temperature. It was then poured over crushed ice and heated on the steam-bath to coagulate the precipitate. After filtration, washing, and extraction with a dilute sodium carbonate solution, the product was dried at $90-100^{\circ}$. On crystallization from a benzene-toluene mixture, 2.3 g. (81%) of a yellow product, m.p. 175-176°, was obtained. This corresponds exactly with the melting point obtained in the preparation of 2-iodoanthraquinone from 2-aminoanthraquinone via diazotization (9, 10). Dehydration of the crude product rather than the pure product gave a 68% yield.

SUMMARY

1. A new synthesis of 4-iodophthalic acid and its anhydride has been accomplished in good vields.

2. The condensation of 4-iodophthalic anhydride with benzene has been carried out.

3. Dehydration of the resulting 2-benzoyl-4-(?)-iodobenzoic acid gave 2-iodoanthraquinone.

STATE COLLEGE, PENNSYLVANIA

REFERENCES

(1) HIGGINS AND CHESSICK, J. Org. Chem., 16, 243 (1951).

(2) EDINGER, J. prakt. Chem., 53, 386 (1896).

(3) BLICKE AND SMITH, J. Am. Chem. Soc., 51, 1865 (1929).

(4) TWISS AND HEINZELMANN, J. Org. Chem., 15, 496 (1950).

(5) WILLGERODT, Ber., 29, 1575 (1896).

(6) DATTA AND CHATTERJEE, J. Am. Chem. Soc., 41, 294 (1919).

(7) STEPHENS, J. Am. Chem. Soc., 43, 1950 (1921).

(8) WALLINGFORD AND KRUEGER, Org. Syntheses, Coll., Vol. II, 349 (1943).

(9) KAUFLER, Ber., 37, 60 (1904).

(10) SCHOLL AND NEOVIUS, Ber., 44, 1088 (1911).