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THE PREPARATION OF ALIZARIN FROM PHTHALIC ANHYDRIDE AND ORTHO-DICHLOROBENZENE

By Max Phillips

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The synthesis of anthraquinone from phthalic anhydride and benzene, by the application of the Friedel and Crafts reaction, has of late become commercially important. This synthesis was made commercially feasible by the development in recent years of improved processes for the manufacture of phthalic anhydride and aluminum chloride. The applications of this synthesis are quite general, and a number of derivatives of anthraquinone are thus prepared commercially.

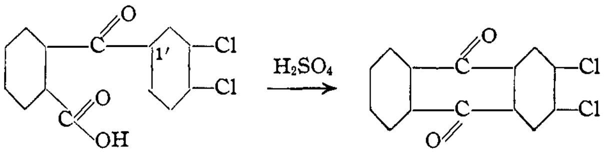
In this paper, experiments are described on the preparation of 2,3-dichloro-anthraquinone from phthalic anhydride and *o*-dichlorobenzene and the conversion of the dichloro-anthraquinone into alizarin.

o-Dichlorobenzene is obtained as a by-product in the chlorination of benzene, particularly in connection with the preparation of *p*-dichlorobenzene. A large quantity of *o*-dichlorobenzene is annually produced in this country and is now utilized only to a limited extent. It was with the view to possible development of a commercial utilization of this product that the investigation described was undertaken.

Sprent and Dodd[1] claim that when phthalic anhydride and *o*-dichlorobenzene are condensed with anhydrous aluminum chloride at 115°, chlorobenzoylbenzoic acid is formed. This they condensed with sulfuric acid into 2-chloro-anthraquinone (β-chloro-anthraquinone). Their claim could not be confirmed. Several experiments were conducted following the directions given in the Sprent and Dodd patent and the only reaction product obtained was 2,3-dichloro-anthraquinone. The *o*-dichlorobenzene which Sprent and Dodd used may have contained monochlorobenzene as an impurity, which would account for the result they obtained.[2]

When *o*-dichlorobenzene is condensed with phthalic anhydride, two isomeric dichlorobenzoylbenzoic acids may be formed (I and II).

The 3 ,4′- and 2′,3′-dichloro-2-benzoylbenzoic acids, upon condensation with concd. sulfuric acid, yield 2,3- and 1,2-dichloro-anthraquinone, respectively, as indicated below.



3′,4′-Dichloro-2-benzoylbenzoic acid 2,3-Dichloro-anthraquinone

I

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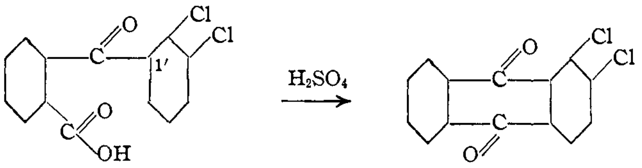
[1] Sprent and Dodd, Brit. pat. 204,528 (1923).

[2] Phillips, *Ind. Eng. Chem.*, **17**, 721 (1925).



2′,3′-Dichloro-2-benzoylbenzoic acid 1,2-Dichloro-anthraquinone

II

The dichlorobenzoylbenzoic acid obtained by the method described in this paper (m. p., 191°, corr.), when heated with sulfuric acid (d., 1.84), was converted into 2,3-dichloro-anthraquinone. It is thus reasonably assured that the dichlorobenzoylbenzoic acid obtained has the structure represented by Formula I. There was no indication of the formation of the other isomeric acid (Formula II).

In the alkali fusion of 2,3-dichloro-anthraquinone one would expect to obtain the 2,3-dihydroxy-anthraquinone (hystazarin). However, Kircher[3] found that dichloro-anthraquinone (m. p., 261°) obtained by the oxidation of dichloro-anthracene, when fused with alkali, was converted into alizarin and from that concluded that the dichloro-anthraquinone at hand must have been the 1,2 derivative. It is now known, however, that 1,2-dichloro-anthraquinone melts at 208° (corr.),[4] so that Kircher's dichloro-anthraquinone was, without doubt, impure 2,3-dichloro-anthraquinone. Furthermore, Grandmougin[5] has recently shown that 2,3-dibromo-anthraquinone, on fusion with alkali, is converted into alizarin and has also proved that the dibromo-anthraquinone used by Graebe and Liebermann[6] in their now classic synthesis of alizarin was the 2,3 compound. That 2,3-dichloro-anthraquinone should yield alizarin instead of hystazarin is, therefore, not at all surprising.

Experimental Part

Materials Used.—The phthalic anhydride used in these experiments was the c. p., sublimed product.

The anhydrous aluminum chloride used was the commercial article.

The *o*-dichlorobenzene was a commercial product obtained from The Niagara Alkali Company, Niagara Falls, New York.

When subjected to distillation, 89% distilled at 175–180°, 3% below 175° and 8% above 180°. It was used directly, without previous distillation.

Method.—In a preliminary experiment 37 g. (0.25 mole) of phthalic anhydride, 184 g. of *o*-dichlorobenzene (1.25 moles) and 73 g. of anhydrous aluminum chloride (0.27 mole) were placed in a flask provided with a reflux condenser at the top of which was inserted a calcium chloride tube. The mixture was heated in an oil-bath first at

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[3] Kircher, *Ann.*, **238,** 348 (1887).

[4] Ullmann and Billig, *Ann.*, **381,** 27 (1911).

[5] Grandmougin, *Compt. rend.*, **173,** 717 (1921).

[6] Graebe and Liebermann, *Ann. Suppl.*, **7,** 289 (1870).

120° and subsequently heated to the boiling point of the mixture (temperature of the oil-bath, 175°). After two hours' heating, the reaction mixture, which was black, was allowed to cool, and was poured into ice water; 100 cc. of concd. hydrochloric acid was added to this mixture and the *o*-dichlorobenzene removed by distillation in a current of steam. The black, tarry residue was digested on the steam-bath with a 20% sodium carbonate solution. The greater part of the tarry matter remained undissolved. The filtrate from this was boiled with animal charcoal, filtered and acidified with sulfuric acid. The dichlorobenzoylbenzoic acid was filtered off and dried at 120°. The yield, before crystallization, amounted to 15 g., or 20.3%. It was crystallized twice from hot benzol and obtained as colorless, prismatic crystals; m. p., 191.2° (corr.). It is readily soluble in chloroform, ethyl alcohol and glacial acetic acid; it is difficultly soluble in carbon tetrachloride and practically insoluble in petroleum ether.

Anal. Subs., 0.1971, 0.1934: CO_2, 0.4128, 0.4037; H_2O, 0.0558, 0.0505. Subs., 0.1837, 0.1692: AgCl, 0.1800, 0.1661. Calcd. for $C_{14}H_8O_3Cl_2$: C, 56.96; H, 2.76; Cl, 24.03. Found: C, 57.11, 56.92; H, 3.16, 2.92; Cl, 24.24, 24.28.

Conversion of 3′, 4′-Dichloro-2-benzoylbenzoic Acid into 2,3-Dichloro-anthraquinone.—Fourteen g. of the acid obtained as described above was treated with 20 times its weight of sulfuric acid (d., 1.84) and heated at 150° for four hours. The reaction mixture, after being cooled to room temperature, was poured into ice water, filtered and washed with water, then with sodium carbonate solution, and again with water. The dichloro-anthraquinone precipitate was dried at 120°; yield, 13 g. It was crystallized from glacial acetic acid, separating out as light yellow, needle-like crystals; m. p., 267° (corr.). The yield of the crystallized product amounted to 9 g. (69.2% of the theoretical, calculated on the dichlorobenzoylbenzoic acid taken). This product is identical with the 2,3-dichloro-anthraquinone described by Ullmann and Billig.[7]

Inasmuch as in the preliminary experiment just described, the yield of the 3′,4′-dichloro-2-benzoylbenzoic acid was far from satisfactory, owing to the formation of a tarry matter, experiments were conducted for the purpose of increasing this yield, if possible. Several preliminary experiments showed that if the condensation were conducted at 100°, the formation of tarry matter would be entirely avoided. It was also indicated that the proportion of aluminum chloride used was an important factor in determining the yield. Accordingly, a series of experiments was conducted at the reaction temperature of 100°, in which the ratio of aluminum chloride to phthalic anhydride was the only variable. In all of the experiments an excess of *o*-dichlorobenzene was used (5 moles of *o*-dichlorobenzene to 1 mole of phthalic anhydride). The procedure was, briefly, as follows.

Twenty-nine and six-tenths g. (0.2 mole) of finely-ground phthalic anhydride and 147 g. (1 mole) of *o*-dichlorobenzene were placed in an Erlenmeyer flask provided with an inverted condenser, at the end of which was attached a calcium chloride tube; the requisite amount of powdered aluminum chloride was added and the mixture heated on the steam-bath until there was no further evolution of hydrogen chloride (about 14 hours). To the reaction mixture, after cooling to room temperature, water and 100 cc. of concd. hydrochloric acid were added and the mixture was distilled in a current of steam to remove the excess of *o*-dichlorobenzene. The residue was filtered off, washed with hot water and successively digested on the steam-bath with sodium carbonate solution

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[7] Ref. 4, p. 11.

until free from 3′,4′-dichloro-2-benzoylbenzoic acid. This sodium carbonate solution was boiled with animal charcoal, filtered and made acid with dil. sulfuric acid, whereupon the 3′,4′-dichloro-2-benzoylbenzoic acid separated out as a grayish, crystalline precipitate, which was filtered off, dried at 110° and weighed.

The result thus obtained is recorded in Table I, under the heading "Yield of 3′,4′-dichloro-2-benzoylbenzoic acid (crude)." This material was crystallized once from boiling benzene, giving a colorless, crystalline product which was dried at 110° and weighed. This result is recorded in Table I, under the heading "Yield of 3′,4′-dichloro-2-benzoylbenzoic acid (pure)." The purity of the 3′,4′-dichloro-2-benzoylbenzoic acid was determined by titrating with 0.1 *N* sodium hydroxide solution. The yield of this pure 3′,4′-dichloro-2-benzoylbenzoic acid was calculated on the basis of the phthalic anhydride taken.

TABLE I

EFFECT OF QUANTITY OF ALUMINUM CHLORIDE ON THE YIELD OF 3′,4′-DICHLORO-2-BENZOYLBENZOIC ACID

Temperature, 100°; molal ratio of phthalic anhydride to *o*-dichlorobenzene, 1:5 (29.6 g. of phthalic anhydride and 147 g. of *o*-dichlorobenzene).

Expt.	Molal ratio of phthalic anhydride to $AlCl_3$	*o*-Dichlorobenzene recovered, g.	Yield of 3′,4′-dichloro-2-benzoylbenzoic acid, g.		Purity %	Calcd. yield of 3′,4′-dichloro-2-benzoylbenzoic acid, %
			Crude	Pure		
1	1:0.5	137	0	0	0	0
2	1:1	107	34.9	30.5	100	51.7
3	1:1.1	106	50.6	36.6	98.7	62.0
4	1:1.2	104	46.1	36.6	100	62.0
5	1:1.5	99	51.4	41.3	100	70.0
6	1:2	91	60.4	43.1	98.8	73.0

It will be observed from Table I that practically the maximum yield of dichlorobenzoylbenzoic acid was obtained when the molal ratio of phthalic anhydride to aluminum chloride was 1:1.5.

Determination of the Quantity of Sulfuric Acid to Be Used for the Conversion of 3′,4′-Dichloro-2-Benzoylbenzoic Acid into 2,3-Dichloroanthraquinone

In the preliminary experiment previously described, the 3′,4′-dichloro 2-benzoylbenzoic acid was condensed into 2,3-dichloro-anthraquinone, using a rather large excess of concd. sulfuric acid. The reaction was complete after heating for four hours at 150°. In order to determine the minimum quantity of sulfuric acid necessary in this condensation, experiments were conducted in which the proportion of sulfuric acid (d., 1.84) to 3′,4′-dichloro-2-benzoylbenzoic acid was the only variable. The procedure was briefly as follows.

Eight and eighty-five hundredths (8.85) g. (0.03 mole) of 3′,4′-dichloro-2-benzoylbenzoic acid and the requisite amount of sulfuric acid (d., 1.84) were heated together at 150° for four hours. The reaction mixture was subsequently cooled to room temperature and then poured into several times its volume of cold water. The precipitated 2,3-dichloro-anthraquinone was filtered off, washed with dil. sodium carbonate solution, then with water, and finally dried at 110°. The product thus obtained was pure, as is indicated by the chlorine determination recorded in Table II.

TABLE II

EFFECT OF VARYING THE QUANTITY OF SULFURIC ACID

Temperature, 150°; 0.03 mole of 3′,4′-dichloro-2-benzoylbenzoic acid (8.85 g.); reaction period, four hours.

Expt.	Ratio of 3′,4′-dichloro-2-benzoylbenzoic acid to sulfuric acid	Yield of 2,3-dichloro-anthraquinone, g.	Cl,[a] %	Calcd. yield of 2,3-dichloro-anthraquinone, %
1	1:2	7.94	25.67	95.6
2	1:4	8.15	25.61	98.0
3	1:6	8.17	25.58	98.3
4	1:8	8.34	25.20	98.4
5	1:10	8.27	25.50	98.6

[a] Calcd. for $C_{14}H_6O_2Cl_2$: Cl, 25.60.

The results in Table II show that the conversion of 3′,4′-dichloro-2-benzoylbenzoic acid into 2,3-dichloro-anthraquinone is practically quantitative, using four parts by weight of concd. sulfuric acid to one part of 3′,4′-dichloro-2-benzoylbenzoic acid.

Condensation of Phthalic Anhydride and *o*-Dichlorobenzene According to the Method of Sprent and Dodd

Inasmuch as the results obtained were at variance with those claimed in the patent of Sprent and Dodd,[1] an experiment was carried out following the description of their method as given in the patent. The reaction product consisted entirely of 2,3-dichloro-anthraquinone (m. p., 267°, corr.). It was not possible to find any 2-chloro-anthraquinone which, according to Sprent and Dodd, is supposed to be the chief product of this reaction.

Alkali Fusion of 2,3-Dichloro-anthraquinone into Alizarin

In a typical experiment, 20 g. of 2,3-dichloro-anthraquinone, 80 g. of potassium hydroxide and 20 cc. of water were heated in a nickel crucible which was inserted in an oil-bath. At 225° (thermometer in the reaction mixture) a reaction took place and the fusion mass became dark blue. This temperature was maintained for 20 minutes and the reaction product then allowed to cool. The cold melt was dissolved in water, heated to boiling and filtered. No insoluble residue was left on the filter paper. The filtrate was acidified with dil. sulfuric acid, and the orange precipitate was filtered off, washed and dried; yield, 5.4 g., or 31.2%. The alizarin was purified by sublimation and identified through its melting point and also spectrophotometrically.[8]

Summary

(1) A synthesis of alizarin from phthalic anhydride and *o*-dichlorobenzene is brought about by the condensation of phthalic anhydride,

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[8] The spectrophotometric measurements were made by Mr. W. C. Holmes of the Color Laboratory.

o-dichlorobenzene and anhydrous aluminum chloride into 3′,4′-dichloro-2-benzoylbenzoic acid, and the conversion of this acid, by means of sulfuric acid, into 2,3-dichloro-anthraquinone. Upon fusion with alkali the dichloro-anthraquinone is converted into alizarin.

(2) The claim of Sprent and Dodd[1] that 2-chloro-anthraquinone is obtained by the condensation of phthalic anhydride and *o*-dichlorobenzene could not be confirmed.

WASHINGTON, D. C.

[CONTRIBUTION FROM THE DEPARTMENT OF RESEARCH IN PURE CHEMISTRY, MELLON INSTITUTE OF INDUSTRIAL RESEARCH, UNIVERSITY OF PITTSBURGH]

THE PREPARATION OF CRYSTALLINE *d*-TALONIC ACID

BY OSCAR F. HEDENBURG AND LEONARD H. CRETCHER

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Introduction

In 1885 Kiliani[1] prepared crystalline *d*-galactonic acid. So far as the authors are aware, this is the only crystalline hexonic acid described in the literature. Later, Nef and one of us[2] made a study of the substance and prepared some of its derivatives.

It is known that when a freshly prepared, aqueous solution of *d*-gluconic acid, or its epimer *d*-mannonic acid, is rapidly concentrated at low temperature and pressure, the resulting gum yields on trituration with absolute alcohol the so-called β-lactone of the corresponding acid.[3]

When, however, a freshly prepared solution of *d*-galactonic acid is treated in the same manner, crystalline *d*-galactonic acid is obtained.[4]

This work was undertaken to determine whether the epimer of *d*-galactonic acid, that is, *d*-talonic acid, on treatment as described above, would yield a β-lactone or an acid. Our results have shown that talonic acid solutions, similarly to solutions of galactonic acid, yield a crystalline acid on evaporation. From an examination of the space formulas of the hexose sugars it is evident that they may be classified in two series on the basis of the configuration of the groups attached to Carbon Atoms 3 and 4. One of these series, characterized by the fact that the hydroxyl groups, in the conventional representation of the sugar molecule, are found on opposite sides of the carbon atoms, may be called the glucose series. It includes also mannose, idose and gulose. The other series, characterized by hydroxyl groups on the same side of the carbon atoms, may be termed the galactose series and embraces also talose, allose and altrose. The monobasic acids corresponding to glucose and mannose-gluconic and

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[1] Kiliani, *Ber.*, **18**, 1551 (1885).

[2] (a) Nef, *Ann.*, **403**, 277 (1914). (b) Hedenburg, THIS JOURNAL, **37**, 364 (1915).

[3] Ref. 2 a, pp. 310, 323; 2 b, pp. 347, 355.

[4] Ref. 2 b, p. 364.