cracked ice. The olive-green precipitate was extracted with 500 cc. of hot 1% sodium hydroxide solution. After washing with water and drying, the residue was extracted with hot benzene. After cooling and adding petroleum ether, the benzene extract deposited 3.5 g. of yellow needles of 2-methylbenzanthrone, m. p. 198.5–199°, from benzene and petroleum ether. A mixed melting point with 2-methylbenzanthrone prepared from 2-methyl-9-anthrone showed no depression.[5]

Anal. Subs., 0.1033: CO_2, 0.3403; H_2O, 0.0444. Calcd. for $C_{18}H_{12}O$; C, 88.49; H, 4.91. Found: C, 88.35; H, 4.81.

Condensation of Phthalide with Chlorobenzene.—A mixture of 10 g. of phthalide in 55 cc. of chlorobenzene with 20 g. of anhydrous aluminum chloride was heated in an oil-bath at 125–130° for fifteen hours. The resulting product was worked up as before. No pure compound could be isolated.

A portion of the crude condensation product on oxidation with chromic acid gave 2-chloro-anthraquinone, m. p. 206–207°. On attempting to prepare a chlorobenzanthrone, a mixture which could not be separated into its components was obtained.

Summary

1. Phthalide can be condensed with aromatic hydrocarbons and their derivatives with the formation of anthrones.

2. Condensation takes place both through the methylene and the carboxyl residues of phthalide resulting in the formation of a mixture of isomers and rendering the method unsuitable for the synthesis of anthrones of definite structure.

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[CONTRIBUTION FROM THE CHEMICAL LABORATORY OF WASHINGTON UNIVERSITY]

STUDIES IN THE ANTHRONE SERIES.
II. THE SYNTHESIS OF SOME HYDROXYMETHYLANTHRONES[1]

BY AL STEYERMARK WITH JOHN H. GARDNER

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Since the most important of the naturally occurring anthrones are derived from 1,8-dihydroxy-3-methylanthraquinone and some related compounds, it has seemed of interest to study methods for the synthesis of hydroxy- and hydroxymethylanthrones which will afford definite proof of the structures of the products obtained. Most of the work which has been done on the determination of the structure of this class of compounds has been analytical in nature and has not always led to concordant results.[2] The only synthetic method which has been extensively investigated is the phthalaldehyde acid condensation method originated by Bistrzycki, which has been extended and improved by Adams and his students. The

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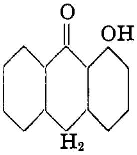
[1] Based upon a portion of a thesis submitted by Al Steyermark, Fellow in Chemistry and Physics, in partial fulfilment of the requirements for the Degree of Doctor of Philosophy in Washington University, June, 1930.

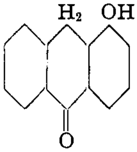
[2] Cross and Perkin, *J. Chem. Soc.*, 292 (1930), and previous papers by Perkin and his co-workers; Green, *ibid.*, 2341 (1927).

number of compounds obtainable in this way is distinctly limited owing to the[3] difficulty of preparing suitable substituted phthalaldehyde acids.

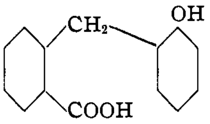
The most commonly used method for the preparation of anthrones has been the reduction of the corresponding anthraquinone with tin and hydrochloric acid in glacial acetic acid solution. This method was applied to 1-hydroxyanthraquinone by Liebermann and Mamlock and by Meyer and Sander,[4] but no satisfactory evidence as to the structure of the product obtained was presented until Cross and Perkin[5] showed that the benzanthrone which was obtained from it could not be methylated with methyl iodide and alkali, indicating that the carbonyl and hydroxyl groups are adjacent to each other. From this it must be concluded that the product is 1-hydroxy-9-anthrone (I). In the same paper they describe the preparation of an isomer, presumably 1-hydroxy-10-anthrone (II), obtained by the reduction of the acetate of 1-hydroxyanthraquinone.[6]



I



II



III

In this work the first step was the confirmation of the conclusions of Cross and Perkin by direct synthesis. *o*-(2-Hydroxybenzoyl)-benzoic acid was reduced to *o*-(2-hydroxybenzyl)-benzoic acid (III), which was in turn dehydrated to 1-hydroxy-10-anthrone. This compound, which formed colorless needles melting at 241–2°, agreed in all of its properties with the compound obtained by Cross and Perkin by the reduction of the acetate of 1-hydroxyanthraquinone. The compound obtained on the reduction of 1-hydroxyanthraquinone itself, however, formed canary yellow needles melting at 137.5–138° and consequently can be only 1-hydroxy-9-anthrone. From this it is concluded that the hydroxyl group in the α-position of the anthraquinone molecule directs the reduction to the carbonyl group farthest removed.

By a similar method, Barnett and Goodway[7] showed that the reduction of 2-methylanthraquinone yields a mixture of both possible isomeric methylanthrones. A repetition and extension of their work indicates that by far the major part of the product is 2-methyl-10-anthrone (IV) since only 2-methylbenzanthrone (V) can be obtained from the crude mix-

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[3] Brubaker and Adams, This Journal, **49**, 2279 (1927), give a bibliography of the work in this field.

[4] Liebermann and Mamlock, *Ber.*, **38**, 1784 (1905); Meyer and Sander, *Ann.*, **420**, 113 (1920).

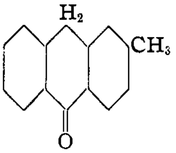
[5] Cross and Perkin, *J. Chem. Soc.*, 292 (1930).

[6] Ref. 5, p. 306.

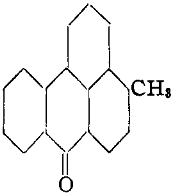
[7] Barnett and Goodway, *ibid.*, 1754 (1929).

ture. Using pure 2-methyl-10-anthrone there was no increase in the yield of 2-methylbenzanthrone.[4] Consequently, we may conclude that the methyl group in the β-position in the anthraquinone molecule directs the reduction to the carbonyl group in the meta position of its ring.

Since the reduction of 1-hydroxyanthraquinone yields a single product and that of 2-methylanthraquinone a mixture, it would be expected that when the orienting influences of the two groups conflict, the hydroxyl group would dominate. This could be tested in the reduction of 1-hydroxy-2-methylanthraquinone.

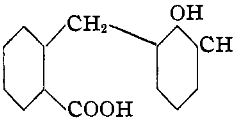


IV

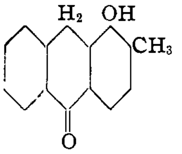


V

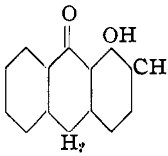
By the reduction of *o*-(2-hydroxy-3-methylbenzoyl)-benzoic acid, there was obtained *o*-(2-hydroxy-3-methylbenzyl)-benzoic acid (VI). This compound, by treatment with sulfuric acid, yielded 1-hydroxy-2-methyl-10-anthrone (VII) as colorless needles melting at 207.2–208°. On reducing 1-hydroxy-2-methylanthraquinone there was obtained an anthrone which crystallized in the form of yellow needles melting at 136.2–137° and which must be 1-hydroxy-2-methyl-9-anthrone (VIII), showing that the hydroxyl group has a stronger directive influence in the reduction of the carbonyl group of an anthraquinone derivative than does the methyl group, as was expected.



VI



VII

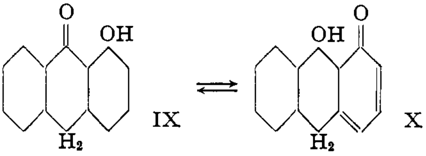


VIII

In the same way, the reduction of 1-hydroxy-3- and 4-methylanthraquinone was investigated. In each case the corresponding methyl-1-hydroxy-9-anthrone was obtained. Both of these anthrones crystallized as canary yellow needles.

By dehydration of *o*-(2-hydroxy-4-methylbenzyl)- and *o*-(2-hydroxy-5-methylbenzyl)-benzoic acid, there were obtained 1-hydroxy-3- and 1-hydroxy-4-methyl-10-anthrone, both forming light colored or colorless needles melting at much higher temperatures than the isomeric 1-hydroxy-9-anthrones.

It is of interest to note that the 1-hydroxy-9-anthrones are in every case colored while the isomeric 1-hydroxy-10-anthrones are, with one exception, colorless. 1-Hydroxy-3-methyl-10-anthrone could never be obtained entirely colorless, but the best samples which were obtained appeared to be slightly impure and it is believed that the color would be removed on complete purification. It seems reasonable to believe that the color of the 1-hydroxy-9-anthrones may be due to a benzenoid–quinoid tautomerism such as has been suggested for the hydroxyanthraquinones and demonstrated in one case,[8] the two forms represented by Formulas IX and X being in equilibrium.



IX X

Experimental

2-Methyl-10-anthrone.—2-Methylanthraquinone was reduced to the mixture of anthrones by the method of Barnett and Goodway.[9] After five recrystallizations from alcohol there was obtained an 8.8% yield of 2-methyl-10-anthrone, m. p. 101–102°.

2-Methyl-9-anthrone.—The isomeric 2-methyl-9-anthrone was obtained from *p*-toluyl-*o*-benzoic acid by the method of Limpricht.[10] The product melted at 102–103° and showed the same solubilities in alcohol, benzene, petroleum ether and various other solvents as 2-methyl-10-anthrone, explaining the extreme difficulty found in the separation of the two isomers.

2-Methylbenzanthrone.—Three grams of the crude mixture of methylanthrones obtained in the reduction of 2-methylanthraquinone was converted into the benzanthrone by the method of Scholl and Seer.[11] After recrystallization from a mixture of benzene and petroleum ether there was obtained 1 g. of 2-methylbenzanthrone, m. p. 198–199°. None of the isomeric 6-methylbenzanthrone could be isolated. Using pure 2-methyl-10-anthrone did not increase the yield.

***o*-(2-Hydroxybenzoyl)-benzoic Acid and its Homologs.**—Phthalic anhydride was condensed with phenol and with the three cresols according to the procedure of Ullmann and Schmidt.[12] In this way there were obtained *o*-(2-hydroxybenzoyl)-benzoic acid and the three isomeric *o*-(2-hydroxymethylbenzoyl)-benzoic acids. It was noted, however, that, contrary to the results of Ullmann and Schmidt, on condensing phthalic anhydride with phenol and with *o*-cresol, there was formed a larger proportion of the benzoylbenzoic acid in which the condensation had taken place in the position para to the hydroxyl group than that in which the condensation had taken place in the ortho position.

Conversion of the Benzoylbenzoic Acids into Anthraquinone Derivatives.—One part of each of the benzoylbenzoic acids was mixed with two parts of boric acid and dissolved in 15–20 parts of fuming sulfuric acid of a suitable concentration. The solutions were heated for varying times and at various temperatures and were then poured onto cracked ice. The resulting yellow precipitates were coagulated by warming and filtered off. The anthraquinone derivatives were purified by solution in 10% sodium carbonate, precipitation with carbon dioxide and crystallization from alcohol. All

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[8] Zahn and Ochwat, *Ann.*, **462**, 72 (1928).

[9] Barnett and Goodway, *J. Chem. Soc.*, 1754 (1929).

[10] Limpricht, *Ann.*, **314**, 237 (1901).

[11] Scholl and Seer, *ibid.*, **394**, 111 (1912).

[12] Ullmann and Schmidt, *Ber.*, **52**, 2098 (1919).

formed yellow needles. The details are given in Table I. All of these compounds had been prepared previously and their properties agree with those given by previous investigators.

TABLE I

PREPARATIVE DATA

( )-Anthraquinone	% Excess SO_3	Temp., °C.	Time, minutes	Yield, %	M. p., °C.
1-Hydroxy-	20	150	5	52	191–2.5[a]
1-Hydroxy-2-methyl-	10	100	5	62	184–5[b]
1-Hydroxy-3-methyl-	20	150	25	88	177–8[c]
1-Hydroxy-4-methyl-	0	100	30	72	174–5[d]

[a] Birukoff, *Ber.*, **20**, 2438 (1887), and Ullmann and Conzetti, *ibid.*, **53**, 828 (1920), give m. p. 193°. [b] Bentley, Gardner and Weizmann, *J. Chem. Soc.*, 91, 1626 (1907), Copisarow, *ibid.*, 117, 209 (1920), and Keimatsu and Hirano, *Chem. Abstracts*, **23**, 3464 (1929), give the same value. [c] Bentley, Gardner and Weizmann, ref. *b*, and Römer and Link, *Ber.*, **16**, 700 (1883), give the same value. [d] Ullmann and Schmidt, *ibid.*, **52**, 2098 (1919), give 175°.

o-Benzylbenzoic Acids.—To a solution of one part of the benzoylbenzoic acid in three parts of water and 18–20 parts of concentrated ammonium hydroxide there was added three parts of zinc dust. The mixture was then heated gently for ten to twelve hours with mechanical stirring, ammonium hydroxide being added from time to time to maintain the concentration. The solution was filtered from the zinc and the *o*-benzylbenzoic acid precipitated by acidification with hydrochloric acid. The products were purified by solution in ammonium hydroxide, precipitation with hydrochloric acid and recrystallization from 50% methyl or ethyl alcohol, using decolorizing carbon, and from a mixture of benzene and petroleum ether. All of the acids were obtained as colorless needles. The yields and properties are given in Table II.

TABLE II

YIELDS AND PROPERTIES

α-( )-benzoic acid	M. p., °C.	Yield, %	Calcd., % C	Calcd., % H	Found, % C	Found, % H
(2-Hydroxyphenyl)-	133.8–4.5	98	73.66	5.30	73.31	5.09
(2-Hydroxy-3-methylbenzyl)-	158.2–159	88	74.36	5.83	74.11	5.60
(2-Hydroxy-4-methylbenzyl)-	123–4	77.6	74.36	5.83	73.97	5.61
(2-Hydroxy-5-methylbenzyl)-	129–130	84.5	74.36	5.83	74.01	5.58

1-Hydroxy-9-anthrones.—To a solution of one part of the anthraquinone derivative in 40–50 parts of glacial acetic acid in a flask fitted with a reflux condenser there was added two to three parts of granulated tin. The solution was heated to boiling and three to four parts of concentrated hydrochloric acid was added in small portions during forty-five minutes. After the last addition of hydrochloric acid, the contents were boiled for an hour and then filtered while hot. Upon cooling, the filtrate deposited yellow needles of the anthrone. A further quantity was obtained by the addition of very dilute hydrochloric acid. The anthrones were purified by recrystallization from alcohol. The yields and properties are given in Table III.

1-Hydroxy-10-anthrone.—One part of the *o*-benzylbenzoic acid was dissolved in 20 parts of cold concentrated sulfuric acid and allowed to stand at room temperature for two hours, except that the preparation of 1-hydroxy-3-methyl-10-anthrone required fifteen hours. The resulting anthrones were precipitated by pouring the sulfuric acid solutions over cracked ice. They were purified by crystallization from alcohol and then

TABLE III

YIELDS AND PROPERTIES

-9-Anthrone	M. p., °C.	Yield, %	Calcd., % C	H	Found, % C	H
1-Hydroxy-	137.5–8[a]	89	...	..	...	..
1-Hydroxy-2-methyl-	136.2–7	94	80.47	5.39	80.59	5.54
1-Hydroxy-3-methyl-	158.2–9	85	80.47	5.39	80.38	5.19
1-Hydroxy-4-methyl-	167.4–8.2	94	80.47	5.39	80.11	5.13

[a] Liebermann and Mamlock, *Ber.*, **38**, 1784 (1905), give 138°; Meyer and Sander, *Ann.*, **420**, 113 (1920), give 133–135°.

from a mixture of benzene and petroleum ether. All of the anthrones were colorless needles except 1-hydroxy-3-methyl-10-anthrone, which remained light tan in color after a number of recrystallizations. The yields and properties are given in Table IV.

TABLE IV

YIELDS AND PROPERTIES

-10-Anthrone	M. p. °C.	Yield, %	Calcd., % C	H	Found, % C	H
1-Hydroxy-	241–2[a]	82	79.97	4.80	79.69	4.65
1-Hydroxy-2-methyl-	207.2–8	93	80.47	5.39	80.10	5.20
1-Hydroxy-3-methyl-	258–9	66	80.47	5.39	79.99	5.11
1-Hydroxy-4-methyl-	226.2–7	97.5	80.47	5.39	80.25	5.22

[a] Cross and Perkin, *J. Chem. Soc.*, 306 (1930), give 240–242°.

Summary

1. The reduction of 1-hydroxyanthraquinone and its homologs yields only the corresponding 1-hydroxy-9-anthrone.

2. 1-Hydroxy-10-anthrone and its homologs can be obtained from suitable *o*-benzoylbenzoic acids by reduction to the corresponding *o*-benzylbenzoic acids and dehydration.

3. 1-Hydroxy-9-anthrone and its homologs are bright yellow, while 1-hydroxy-10-anthrone and its homologs are colorless, suggesting the possibility of benzenoid–quinoid tautomerism in the former case.

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