[CONTRIBUTION FROM THE CHEMICAL LABORATORY OF THE UNIVERSITY OF ILLINOIS]

POLYHYDROXY-METHYLANTHRAQUINONES.
IX. CONTRIBUTION TO THE STRUCTURE OF RUBIADIN

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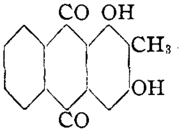
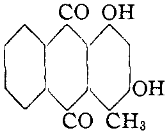
Rubiadin is one of the pigments of madder[2] in which it occurs as a glucoside. Its monomethyl ether has been isolated from *morinda longiflora*[3a] and *morinda citrafolia*.[3b] Rubiadin was first isolated by Schunck and Marchlewski[4] who, after analysis and molecular-weight determinations, assigned to it the composition of a dihydroxy-methylanthraquinone. By oxidation it yielded phthalic acid thus indicating that all of the groups present were in the same ring. There are thus six possible isomers, 1,2-dihydroxy-3-methyl-, 1,2-dihydroxy-4-methyl-, 1,4-dihydroxy-2-methyl-, 2,3-dihydroxy-1-methyl-, 1,3-dihydroxy-2-methyl- and 1,3-dihydroxy-4-methylanthraquinone. The first three are known substances and do not resemble rubiadin; the fourth is not known, but with two adjacent hydroxyl groups it should have reactions similar to those of alizarin and hystazarin, reactions which it does not possess. Rubiadin has, therefore, very probably either the fifth (I) or sixth (II) formula, and is a purpuroxanthin derivative as is indicated also from its color reactions—red with alkali and yellow with concd. sulfuric acid.



I



II

Schunck and Marchlewski synthesized the 1,3-dihydroxy-2-methylanthraquinone and showed that it resembled rubiadin very closely in its color reactions and had the same melting point, 290°. The diacetate of rubiadin, however, melted at 225°, and that of the synthetic product at 217°. As a consequence these investigators assumed rubiadin to be the 1,3-dihydroxy-4-methylanthraquinone.

The monomethyl ether of rubiadin (m. p., 290°), as isolated by Barrowcliff and Tutin from *morinda longiflora*, formed on demethylation a dihydroxy-methylanthraquinone (m. p., 290°), whose diacetate melted

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[1] This communication is an abstract of a portion of a thesis submitted by Florence D. Stouder in partial fulfilment of the requirements for the degree of Doctor of Philosophy in Chemistry in the Graduate School at the University of Illinois.

[2] Perkins and Everest, "Natural Organic Coloring Matters," Longmans, Green and Co., London, **1918**.

[3] (a) Barrowcliff and Tutin, *J. Chem. Soc.*, **91**, 1909 (1907). (b) Simonsen, *ibid.*, **117**, 561 (1920).

[4] Schunck and Marchlewski, *ibid.*, **63**, 969, 1137 (1892); **65**, 182 (1894).

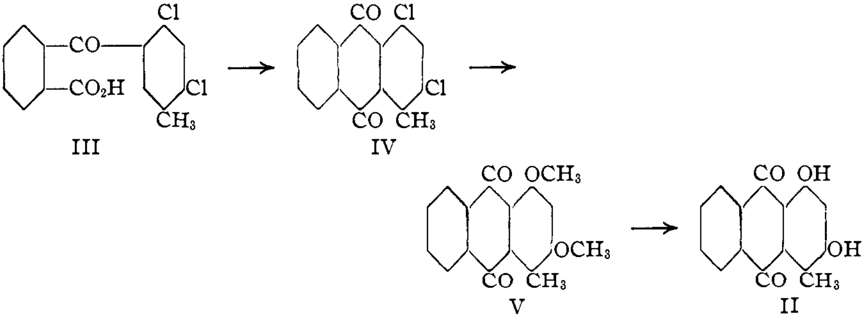
at 225°. Although these are the melting points of rubiadin and its derivative, these investigators assigned to the compound the structure of the monomethyl ether of 1,3-dihydroxy-2-methylanthraquinone, in spite of Schunck and Marchlewski's conclusions.

In this investigation the 1,3-dihydroxy-4-methylanthraquinone (II) and its derivatives have been synthesized and have been shown not to be identical with rubiadin and its derivatives.

	Rubiadin M. p., °C.	1,3-dihydroxy-4-methylanthraquinone M. p., °C.
Anthraquinone	290	251
Dimethyl ether	181	162
Diacetate	225	176.5

The only conclusion that can be drawn is that rubiadin is 1,3-dihydroxy-2-methylanthraquinone and that Schunck and Marchlewski did not obtain the pure diacetate of 1,3-dihydroxy-2-methylanthraquinone synthetically, and consequently found a discrepancy between the melting point of their product and that of the corresponding derivative of the natural product.

The 1,3-dihydroxy-4-methylanthraquinone was prepared by condensing phthalic anhydride with 2,4-dichlorotoluene to give 2,4-dichloro-5-methylbenzoyl-*o*-benzoic acid (III), which was converted with sulfuric acid to the corresponding anthraquinone (IV). Upon long treatment with sodium methylate the halogens were replaced by methoxyl groups (V) and the free hydroxyl derivative was obtained by the action of hydrobromic acid.



The synthesis of 1,3-dihydroxy-2-methylanthraquinone is now being studied.

Experimental Part

2,4-Dichlorotoluene.—To 90 cc. of cuprous chloride solution (prepared according to the method of Marvel and McElvain[5]) was added a solution of 20 g. of 2,4-diaminotoluene hydrochloride in 20 g. of concd. hydrobromic acid and 100 cc. of water. The solution was brought to a boil in a flask fitted with a mercury seal stirrer and a reflux

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[5] Marvel and McElvain, "Organic Syntheses," John Wiley and Sons, Inc., New York, Vol. III, **1925**, p. 33.

condenser and then without further heating, 180 cc. of 10% sodium nitrite solution was added, drop by drop. When all was added the mixture was steam distilled and the dichlorotoluene washed with sodium hydroxide solution, water, and then distilled in a vacuum; yield, 11.6 g. of product boiling at 195°. The chief difference between these directions and those which appear in the literature[6] is that a much more dilute solution is employed and a tight container used to prevent volatilization.

2,4-Dichloro-5-methyl-benzoyl-*o*-benzoic Acid. III.—The general procedure used was that described by Fieser[7] for preparing 4-methyl-benzoyl-*o*-benzoic acid. After condensing for eight hours 20 g. of phthalic anhydride, 69 g. of 2,4-dichlorotoluene and 50 g. of anhydrous aluminum chloride, there was obtained a thick, viscous substance which, however, readily crystallized from hot toluene and when pure, melted at 140°; yield, about 60%.

Anal. Subs., 0.1000: 2.15 cc. of 0.1530 *N* NaOH. Calcd. for $C_{15}H_{10}O_3Cl_2$: neut. equiv. 309. Found: 304.

2,4-Dichloro-1-methylanthraquinone. IV.—A mixture of 20 g. of 2,4-dichloro-5-methyl-benzoyl-*o*-benzoic acid with 4 g. of boric acid and 400 cc. of concd. sulfuric acid was heated on a water-bath for two hours. Upon pouring into water, there was obtained 7.5 g. of product which upon purification from chloroform formed bright yellow crystals and melted at 155°.

Anal. Subs., 0.2000; 13.7 cc. of 0.1 *N* $AgNO_3$. Calcd. for $C_{15}H_8O_2Cl_2$: Cl, 24.4. Found: 24.3.

2,4-Dimethoxy-1-methylanthraquinone. V.—A solution of sodium methylate was prepared by adding as much sodium to 250 cc. of absolute methyl alcohol as would dissolve in it at ordinary temperature. To this was added 6 g. of pure 2,4-dichloro-1-methylanthraquinone and the mixture heated under a reflux condenser on a water-bath for 24 hours. Water was then added, the methyl alcohol boiled off and the crude product filtered and dried. Upon purification from chloroform, it formed yellow needles melting at 162°.

Anal. Subs., 0.1500; CO_2, 0.3949; H_2O, 0.0611. Calcd. for $C_{17}H_{14}O_4$: C, 72.4; H, 4.98. Found: C, 72.0; H, 4.6.

2,4-Dihydroxy-1-methylanthraquinone.—The 2,4-dimethoxy-1-methylanthraquinone was refluxed for 12 hours in a mixture of constant-boiling hydrobromic and glacial acetic acids. The product was purified from benzene and then formed pale yellow needles, melting at 251°.

Anal. Subs., 0.1000; CO_2, 0.2612; H_2O, 0.0360. Calcd. for $C_{15}H_{10}O_4$: C, 70.84; H, 3.97. Found: C, 71.26; H, 4.03.

2,4-Diacetoxy-1-methylanthraquinone.—By refluxing 1 g. of 2,4-dihydroxy-1-methylanthraquinone with 20 cc. of acetic anhydride and 2 g. of freshly fused sodium acetate, there was obtained upon treatment with water the diacetyl derivative, which was purified by crystallization from acetic acid. It formed yellow needles melting at 176.5°.

Summary

The synthesis of 1,3-dihydroxy-4-methylanthraquinone has been completed and the substance has been shown not to be identical with rubiadin.

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[6] Erdmann, *Ber.*, **24**, 2771 (1891).

[7] Fieser, Ref. 5, Vol. IV, p. 75.