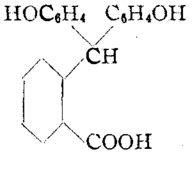
[Contribution from the College of Pharmacy, University of Michigan]

Hydroxy- and Methoxyphenylanthrones. II

By F. F. Blicke and R. A. Patelski[1]

A number of years ago it was stated by Baeyer[2] that phenolphthalin yields 3-hydroxy-9-(4'-hydroxyphenyl)-anthrone-10, or its tautomer, 3,10-dihydroxy-9-(4'-hydroxyphenyl)-anthracene, when treated with sulfuric acid and that the anthrone is converted, by oxidation, into 3,9-di-hydroxy-9-(4'-hydroxyphenyl)-anthrone-10. It has been shown,[3] however, that the two compounds actually obtained by Baeyer were 2,5-di-(*p*-hydroxyphenyl)-3,4-benzofuran and 2-(4''-hydroxybenzoyl)-4'-hydroxybenzophenone.

We have found that if phenolphthalin (I), or its diacetyl derivative, is treated with zinc chloride and acetic anhydride, instead of sulfuric acid, there is produced the triacetyl derivative of 3,10-dihydroxy-9-(4'-hydroxyphenyl)-anthracene (II) which, when oxidized, yields the diacetyl derivative of 3,9-dihydroxy-9-(4'-hydroxyphenyl)-anthrone-10 (III).



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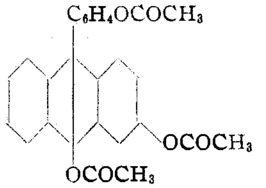

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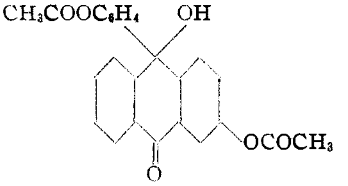

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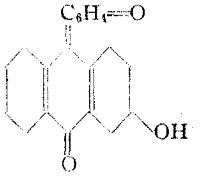

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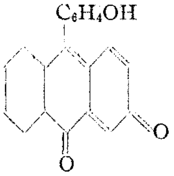

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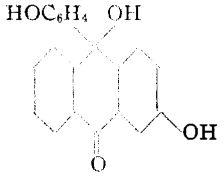

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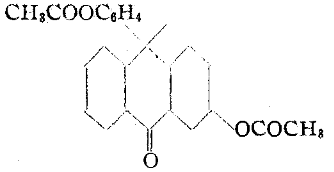

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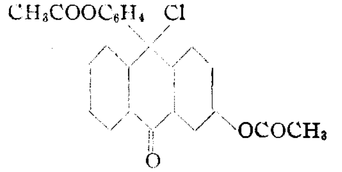

VII

Upon hydrolysis the colorless trihydroxy compound (IV) is obtained. When heated or allowed to come into contact with mineral acids the hydroxy compound is converted into a highly colored fuchsone, either V or VI, or possibly a mixture of the two compounds. The diphenolic ether was obtained upon methylation of the trihydroxy compound (IV).

In order to supply proof of the structure of these compounds the carbinol III was converted into the carbinol chloride, the diacetyl derivative of 3-hydroxy-9-chloro-9-(4'-hydroxyphenyl)-anthrone-10, (VII). A solution of the chloride became deep red instantly when shaken with molecular silver due to the formation of the free radical 3-acetoxy-9-(4'-acetoxyphenyl)-anthronyl-10 (VIII); the red solution decolorized rapidly when exposed to air with the formation of the characteristic peroxide.

2,5-Di-(*p*-anisyl)-3,4-benzofuran (IX) was reduced to 2,5-di-(*p*-anisyl)-2,5-dihydro-3,4-benzofuran (X) with sodium amalgam. Reduction of 2-(4''-methoxybenzoyl)-4'-methoxybenzophenone (XIII) with the same reagent yielded 2-(4''-methoxy-α-hydroxybenzyl)-4'-methoxydiphenylcarbinol (XIV). When treated with zinc chloride in acetic acid solution both X and XIV were converted into 2-methoxy-9-(*p*-anisyl)-anthracene (XI). Upon oxidation the anthracene yielded 2-methoxy-9-hydroxy-9-(*p*-anisyl)-anthrone-10 (XII). The latter condensed with anisole to form 2-methoxy-9,9-di-(*p*-anisyl)-anthrone-10 (XV).

Experimental Part

Triacetyl Derivative of 3,10-Dihydroxy-9-(4'-hydroxyphenyl)-anthracene (II).—Twenty grams of phenolphthalin (I), or an equivalent amount of its diacetyl derivative, and 8 g. of anhydrous zinc chloride, dissolved in 35 cc. of acetic anhydride, were heated on a steam-bath for fifteen minutes and then poured into a mixture of water and ice which contained a small amount of hydrochloric acid. The crystalline product was digested with hot alcohol, filtered and recrystallized from a mixture of benzene and petroleum ether (90–100°); yield 19 g.; m. p. 188–189°.

Anal. Calcd. for $C_{26}H_{20}O_6$: C, 72.87; H, 4.71. Found: C, 73.04; H, 4.88.

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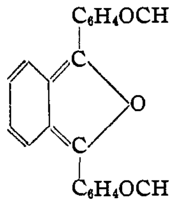
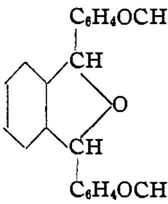
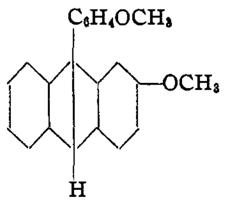
[1] Monsanto–Pfizer Research Associate.

[2] Baeyer, *Ann.*, **202**, 100 (1880).

[3] Blicke and Weinkauff, This Journal, **54**, 1454 (1932).


IX


X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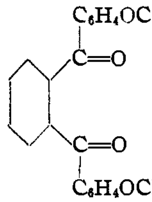
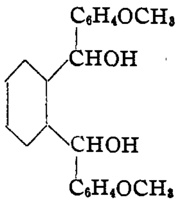
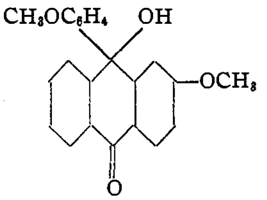
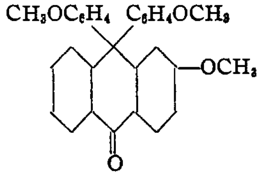

XIII


XIV


XII


XV

The compound exhibits an intense purple fluorescence when dissolved in organic solvents and a red-brown color when moistened with concd. sulfuric acid.

Diacetyl Derivative of 3,9-Dihydroxy-9-(4′-hydroxyphenyl)-anthrone-10 (III).—To 10 g. of the triacetate, dissolved in 50 cc. of acetic acid, there was added 7 g. of sodium dichromate, dissolved in 6 cc. of hot water. The mixture soon began to boil; after it had been heated on a steam-bath for two hours and poured into 500 cc. of water the crystalline product was recrystallized from benzene; yield 8 g.; m. p. 186–187°.

Anal. Calcd. for $C_{24}H_{18}O_6$: C, 71.61; H, 4.51. Found: C, 71.45; H, 4.67.

Solutions of this product in organic solvents do not fluoresce. The material turns purple when treated with concd. sulfuric acid.

3,9-Dihydroxy-9-(4′-hydroxyphenyl)-anthrone-10 (IV).—A mixture of 5 g. of the diacetate, 20 cc. of 10% sodium hydroxide solution and 5 cc. of alcohol was heated on a steam-bath for five minutes, cooled, diluted with 25 cc. of water and 50 cc. of saturated ammonium chloride solution. The pale pink precipitate was dissolved in cold alcohol, treated with charcoal at room temperature, filtered and the solution diluted with water. After precipitation by water from an alcoholic solution the practically colorless, crystalline product melted at 127–128° with the formation of a deep red liquid. The compound, dried in a desiccator over calcium chloride for two weeks prior to analysis, contained water of crystallization.

Anal. Calcd. for $C_{20}H_{14}O_4 \cdot H_2O$: C, 71.43; H, 4.80. Found: C, 71.41; H, 4.87.

In addition to the development of the deep color, the loss of an amount of water which corresponds closely to that calculated for fuchsone formation demonstrates the conversion of IV into V or VI. Thus, when 0.5219 g. of the colorless anthrone was heated at 130° for twenty-four hours, the deep red sample obtained weighed 0.4669 g.; calcd. wt. 0.4660 g. ($C_{20}H_{14}O_4 \cdot H_2O - 2H_2O$).

The anthrone turns an intense purple when moistened with concd. sulfuric acid or a mixture of acetic and hydrochloric acid. When an acetic acid solution of the anthrone is warmed it turns bright red.

The 3,9-dimethyl ether of the anthrone was obtained when 3.2 g. of the anthrone, dissolved in 35 cc. of 20% sodium hydroxide solution, was treated with 8 cc. of dimethyl sulfate at 80–90°. After recrystallization from alcohol the ether melted at 155–156°.

Anal. Calcd. for $C_{22}H_{18}O_4$: C, 76.27; H, 5.24. Found: C, 76.01; H, 5.42.

The ether is colored an intense blue by concd. sulfuric acid.

Diacetyl Derivative of 3-Hydroxy-9-chloro-9-(4′-hydroxyphenyl)-anthrone-10 (VII).—A hot mixture of 3,9-dihydroxy-9-(4′-hydroxyphenyl)-anthrone-10 diacetate, 75 cc. of benzene and 5 cc. of acetyl chloride was treated with a stream of hydrogen chloride for two hours, the solvent removed under reduced pressure and the oily residue covered with petroleum ether (90–100°). After twelve hours the crystalline material was recrystallized from a mixture of benzene and petroleum ether; m. p. 128–129°.

Anal. Calcd. for $C_{24}H_{17}O_5Cl$: Cl, 8.43. Found: Cl, 8.25.

Peroxide of Free Radical 3-Acetoxy-9-(4′-acetoxyphenyl)-anthronyl-10 (VIII).—A mixture of 1.5 g. of the 9-chloro compound, 15 cc. of benzene and 4 g. of molecular silver was shaken for one hour. An intense red color developed immediately upon the addition of the silver. The mixture was filtered. The filtrate decolorized rapidly upon exposure to air and the peroxide precipitated upon the addition of petroleum ether; m. p. 195–200° with decomposition.

Anal. Calcd. for $C_{48}H_{34}O_{12}$: C, 71.79; H, 4.27. Found: C, 72.09; H, 4.42.

2,5-Di-(*p*-anisyl)-2,5-dihydro-3,4-benzofuran (X).—Ten grams of 2,5-di-(*p*-anisyl)-3,4-benzofuran was suspended in 600 cc. of absolute alcohol and 250 g. of 5% sodium amalgam added in portions. After the initial vigorous reaction had subsided, the mixture was heated for five hours on a steam-bath, filtered while hot and the precipitate of colorless, iridescent crystals recrystallized from alcohol; m. p. 115–116°; yield 7 g. Upon dilution of the mother liquor with water 2 g. more of material was obtained.

Anal. Calcd. for $C_{22}H_{20}O_3$: C, 79.17; H, 6.07. Found: C, 78.92; H, 6.12.

The colorless acetic acid solution becomes green when warmed and exhibits a green fluorescence.

When dissolved in acetic acid and oxidized with sodium dichromate, 2-(4″-methoxybenzoyl)-4′-methoxybenzophenone was produced; it was recrystallized from alcohol; mixed m. p. 157–159°.[4]

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[4] The same melting point was reported by Blicke and Weinkauff, THIS JOURNAL, 54, 1458 (1932).

2-(4″-Methoxy-α-hydroxybenzyl)-4′-methoxydiphenylcarbinol (XIV).—To 3.5 g. of 2-(4″-methoxybenzoyl)-4′-methoxybenzophenone, dissolved in 150 cc. of absolute alcohol, there was added 100 g. of 5% sodium amalgam. After several hours the reaction mixture was heated on a steam-bath for two hours, filtered while hot and the filtrate concentrated to one-half its original volume. Water was added gradually until the solution became turbid, the solution cooled and the crystalline precipitate recrystallized from alcohol; m. p. 139–140°; yield 2.8 g.

Anal. Calcd. for $C_{22}H_{22}O_4$: C, 75.39; H, 6.33. Found: C, 75.08; H, 6.39.

One and seven-tenths grams of the carbinol, dissolved in 20 cc. of acetic acid, was oxidized to 2-(4″-methoxybenzoyl)-4′-methoxybenzophenone with 2 g. of sodium dichromate, dissolved in 10 cc. of acetic acid; mixed m. p. 157–159°; yield 1.3 g.

2-Methoxy-9-(*p*-anisyl)-anthracene (XI).—To 1.5 g. of anhydrous zinc chloride, dissolved in a mixture of 7.5 cc. of acetic anhydride and 7.5 cc. of acetic acid, there was added 5.0 g. of 2,5-di-(*p*-anisyl)-2,5-dihydro-3,4-benzofuran. The furan dissolved with evolution of heat and the crystalline anthracene soon began to precipitate. After one hour the mixture was diluted with 50 cc. of water and the anthracene recrystallized from acetic acid; yield 3.9 g.; m. p. 177–179°.[5] Solutions of this compound exhibit a blue fluorescence.

Five grams of 2-(4″-methoxy-α-hydroxybenzyl)-4′-methoxydiphenylcarbinol was treated with zinc chloride in the manner described above. After one hour the crystalline anthracene was separated and recrystallized from acetic acid; yield 3.8 g.; m. p. 177–179°.

2-Methoxy-9-hydroxy-9-(*p*-anisyl)-anthrone-10 (XII).—Five grams of 2-methoxy-9-(*p*-anisyl)-anthracene, suspended in 25 cc. of acetic acid, was heated for two hours on a steam-bath with 4 g. of sodium dichromate, dissolved in 4 cc. of hot water. The mixture was diluted with an equal volume of water and the precipitated, crystalline anthrone recrystallized from acetic acid; yield 4.5 g.; m. p. 202–203°.[6]

2-Methoxy-9,9-di-(*p*-anisyl)-anthrone-10 (XV).—Two grams of 9-hydroxy-9-(*p*-anisyl)-anthrone-10, 6.0 g. of anisole and two drops of concd. sulfuric acid were heated for two hours on a steam-bath, the mixture treated with hot alcohol and the crystalline product recrystallized from acetic acid; yield 1.5 g.; m. p. 182–184°.[7]

Summary

It has been shown that a hydroxy- and a methoxyphenylanthrone can be obtained from a phthalin, from a benzofuran and from a benzoylbenzophenone.

A free radical of the anthraquinone type has been described.

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[5] Blicke and Weinkauff [THIS JOURNAL, **54**, 1463 (1932)] found 175–176°.

[6] Blicke and Weinkauff [*ibid.*, **54**, 1463 (1932)] reported 199–201°.

[7] Blicke and Patelski, [*ibid.*, **60**, 2640 (1938)] found 183–184°.

[CONTRIBUTION FROM THE CHEMICAL LABORATORY OF BRYN MAWR COLLEGE]

The Introduction of Substituted Vinyl Groups. I. Isopropenyl Alkyl Malonic Esters

BY ARTHUR C. COPE AND EVELYN M. HANCOCK

The wide application of the malonic ester synthesis to organic preparations has resulted in the description of a large number of mono- and dialkyl malonic esters, containing both saturated and unsaturated groups. While β,γ-unsaturated (allyl) groups and groups with the double bond further removed from the point of attachment are readily introduced into malonic ester by the ordinary method, α,β-unsaturated (vinyl) groups cannot be introduced directly, because of the inactivity of the vinyl and alkyl substituted vinyl halides. Indirect methods for the introduction of vinyl groups are difficult and give poor yields,[1] and as a result very few vinyl substituted derivatives of malonic ester have been prepared. In this paper a practical method is described for preparing disubstituted malonic esters in which one of the substituent groups is the isopropenyl or 1-methylvinvyl ($CH_2{=}C(CH_3)$—) group.

Kon and his associates,[2] in the course of their investigation of three-carbon tautomerism, methylated isopropylidene malonic ester, which forms a sodium derivative through migration of a hydrogen from the γ-carbon atom.

$$(CH_3)_2C{=}C(COOEt)_2 + NaOEt \longrightarrow$$

$$EtOH + \underset{(I)}{[CH_2{=}C(CH_3)C(COOEt)_2]^- \, Na^+} \xrightarrow{CH_3I}$$

$$CH_2{=}C(CH_3)C(CH_3)(COOEt)_2 + NaI$$

This reaction was employed to prove that the sodium enolate was derived from the isomeric β,γ-unsaturated ester $CH_2{=}C(CH_3)CH(COOEt)_2$, and was not extended as a possible synthetic method. The application of the reaction ap-

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[1] *Cf.* Cope and McElvain, THIS JOURNAL, **54**, 4311 (1932).

[2] Kon and Speight, *J. Chem. Soc.*, 2727 (1926).