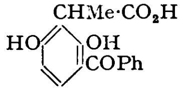
966. *The Pigments of " Dragon's Blood " Resin. Part IV.* The Oxidation of Some Anhydro-7-hydroxybenzopyranols.*

By P. Broadbent, Alexander Robertson, and W. B. Whalley.

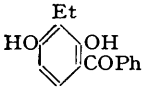
Syntheses of 3- and 5-ethyl-2 : 4-dihydroxy- and of 3-ethyl-2 : 6-dihydroxy-benzophenone are described. Model oxidations of the anhydro-bases from several 7-hydroxy-2 : 4-diphenylbenzopyranols with methanolic alkaline hydrogen peroxide give benzoic acid as the only recognisable product.

On oxidation with alkaline hydrogen peroxide in methanol dracorubin gave, in addition to the dihydric phenol draconol, a monobasic acid, dracoic acid (Brockmann, Haase, and Freiensehner, *Ber.*, 1944, **77**, 279; cf. Robertson, Whalley, and Yates, Part III *) which Brockmann *et al.* originally suggested was represented by a formula of the type (I). Whilst the elucidation of the structure of dracoic acid, *viz.*, (—)-7-hydroxy-5-methoxyflavan-8-carboxylic acid, and of draconol has already been reported (Part III *), the investigations now described were carried out simultaneously in the course of an examination of the earlier formulæ.

On the basis of (I), decarboxylation of dracoic acid would be expected to furnish a *C*-ethylresbenzophenone type (II) having a strong ferric reaction (*i.e.*, an *o*-hydroxybenzophenone), and synthesis of the various isomerides, for use as possible reference compounds, was, therefore, undertaken. Thus, 3- (II) and 5-ethyl-2 : 4-dihydroxybenzophenone (III) were prepared from benzonitrile and 2- and 4-ethylresorcinol respectively by Hoesch's method.



(I)



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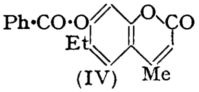

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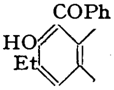

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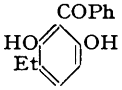
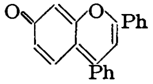


(VI)

The orientation of the product (III) from 4-ethylresorcinol, which could conceivably have been (VI), was confirmed by an unequivocal synthesis of the latter by hydrolytic fission of 8-benzoyl-6-ethyl-7-hydroxy-4-methylcoumarin (V) which was obtained from 7-benzoyloxy-6-ethyl-4-methylcoumarin (IV) by the Fries reaction. Attempts to prepare the remaining *o*-hydroxybenzophenone, *viz.*, 4-ethyl-2 : 6-dihydroxybenzophenone, from 5-ethylresorcinol either by the Hoesch or the Friedel–Crafts reaction gave only intractable resins. The coumarin route to this ketone was excluded by the failure of 7-benzoyloxy-5-ethyl-4-methylcoumarin to undergo the Fries reaction, in keeping with the known



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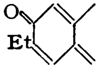

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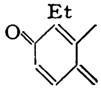
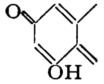


(IX)



(X)

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* Part III, *J.*, 1950, 3117.

peculiar properties of the 5-alkylated resorcinol derivatives (cf. Robertson and Whalley, *J.*, 1949, 3038).

In view of the importance of draconol as a primary degradation product of dracorubin it seemed desirable to undertake model oxidation experiments on anhydro-7-hydroxybenzopyranols with hydrogen peroxide, as information on this topic was not available. Malvin chloride in aqueous solution (Karrer and Widmer, *Helv. Chim. Acta.* 1927, **10**, 729, 758) and 3-methoxyflavylium perchlorate in acetic acid (Quint and Dilthey, *Ber.*, 1931, **64**, 2082; Dilthey and Höschen, *J. pr. Chem.*, 1933, **138**, 42) undergo scission by hydrogen peroxide at the 2 : 3-position of the benzopyrylium nucleus, whilst the mild oxidising agents, perbenzoic acid, monoperphthalic acid, and aqueous ferric chloride oxidise the methyl ethers of pyranols at the 3 : 4-double bond (Karrer and Fatzer, *Helv. Chim. Acta*, 1942, **25**, 1129, 1138; Karrer, Trugenberger, and Hamdi, *ibid.*, 1943, **26**, 2116; Karrer and Trugenberger, *ibid.*, 1945, **28**, 444). No analogy can be easily drawn between the oxidations of ethers of carbinol bases in organic solvents and the oxidation of an anhydro-base in methanol with alkaline hydrogen peroxide.

According to Brockmann *et al.* (*loc. cit.*) the dracoic acid residue was derived from an anhydro-7-hydroxy-2 : 4-diphenylpyranol system present in dracorubin and hence the oxidation of anhydro-2 : 4-diphenylbenzopyranols, types (X), seemed to constitute a close analogy with that of dracorubin. Thus the anhydro-bases derived from 7-hydroxy- (VII), 6-ethyl-7-hydroxy- (VIII), 8-ethyl-7-hydroxy- (IX), and 5 : 7-dihydroxy-2 : 4-diphenylbenzopyranol (X) were oxidised under the conditions employed for dracorubin, but as was expected, the only product which could be isolated in addition to intractable resins was benzoic acid in about one molecular proportion; oxidation of the *C*-ethylresbenzophenones gave about 0·75 mol. of benzoic acid, whilst a comparable experiment with anhydro-7-hydroxybenzopyranol furnished an 0·5 mol. Accordingly, therefore, it seemed clear that in the oxidation of anhydrobenzopyranols the part of the molecule having a structure of type (I) could hardly be expected to survive, a view in agreement with the conclusions described in Part III (*loc. cit.*).

EXPERIMENTAL

3-*Ethyl*-2 : 4-*dihydroxybenzophenone*.—A solution of 2-ethylresorcinol (Russell, Frye, and Mauldin, *J. Amer. Chem. Soc.*, 1940, **62**, 1441) (4 g.) and phenyl cyanide (3·5 ml.) in ether (60 g.), containing zinc chloride (1 g.), was saturated with hydrogen chloride and 6 days later the viscous oil was separated, well washed with ether, and dissolved in water (200 ml.). After having been almost neutralised with sodium hydrogen carbonate, this solution was heated under reflux for 3 hours, and on cooling gave 3-*ethyl*-2 : 4-*dihydroxybenzophenone* which distilled in a high vacuum and then crystallised from dilute acetic acid as pale yellow plates (3·5 g.), m. p. 195° (Found : C, 74·2; H, 6·0. $C_{15}H_{14}O_3$ requires C, 74·4; H, 5·8%). This ketone, which is moderately soluble in the usual solvents, had a red-brown ferric reaction in alcohol. The 2 : 4-*dinitrophenylhydrazone*, which was formed but slowly, separated from alcohol in red hexagonal prisms, m. p. 268° (Found : N, 13·5. $C_{21}H_{18}O_6N_4$ requires N, 13·3%). The oxime could not be obtained either by the sodium acetate or by the pyridine method.

5-*Ethyl*-2 : 4-*dihydroxybenzophenone*.—Interaction of 4-ethylresorcinol (Robinson and Shah, *J.*, 1934, 1491) (4 g.), phenyl cyanide (3·5 ml.), and zinc chloride (1 g.) in ether (60 ml.), saturated with hydrogen chloride, for 7 days furnished a solid which on hydrolysis with water (100 ml.) (excess of hydrochloric acid neutralised with sodium hydrogen carbonate) for 3 hours, gave an oil. When water (125 ml.) was added slowly to a solution of this product in methanol (25 ml.) 5-ethyl-2 : 4-dihydroxybenzophenone was deposited and, on crystallisation from methanol and distillation in a high vacuum followed by recrystallisation from light petroleum, was obtained in pale yellow prisms (3 g.), m. p. 106°, readily soluble in the usual solvents except light petroleum, and having a red-brown ferric reaction (Found : C, 74·4; H, 5·9. Calc. for $C_{15}H_{14}O_3$: C, 74·4; H, 5·8%) [cf. Rosenmund, Buchwald, and Deligiannis, *Arch. Pharm.*, 1933, **271**, 342, who give m. p. 68° (indefinite) for a specimen prepared by an alternative route]. The *oxime* separated from chloroform–light petroleum (b. p. 60—80°) in very pale yellow needles, m. p. 142° (Found : C, 70·2; H, 6·1; N, 5·3. $C_{15}H_{15}O_3N$ requires C, 70·0; H, 5·9; N, 5·4%), and the 2 : 4-*dinitrophenylhydrazone* from ethanol in red plates, m. p. 242° (Found : N, 13·1. $C_{21}H_{18}O_6N_4$ requires N, 13·3%).

3-*Ethyl*-2 : 6-*dihydroxybenzophenone*.—In this work it was found that 8-benzoyl-6-ethyl-7-hydroxy-4-methylcoumarin separated from alcohol in pale yellow prisms, m. p. 159° (Found : C, 73·8; H, 5·4. Calc. for $C_{19}H_{16}O_4$: C, 74·0; H, 5·2%) (Thakor and Shah, *J. Indian Chem. Soc.*, 1946, **23**, 423, give m. p. 133°). Obtained by the alkaline hydrolysis of this coumarin, 3-ethyl-2 : 6-dihydroxybenzophenone formed yellow plates, m. p. 123°, from light petroleum (Thakor and Shah, *loc. cit.*, give m. p. 125—126°, and Desai and Mavani, *Proc. Indian Acad. Sci.*, 1947, **25**, *A*, 341, record m. p. 128°). The 2 : 4-*dinitrophenylhydrazone* separated from alcohol in rosettes of red needles, m. p. 221° (decomp.) after darkening at 150° (Found : N, 13·5. $C_{21}H_{18}O_6N_4$ requires N, 13·3%). The oxime could not be prepared.

7-*Benzoyloxy*-5-*ethyl*-4-*methylcoumarin*.—5-Ethylresorcinol (1 g.) and ethyl acetoacetate (1 ml.) in concentrated sulphuric acid (5 ml.) gave, in 24 hours, 5-*ethyl*-7-*hydroxy*-4-*methylcoumarin* (1 g.) which was precipitated with ice (30 g.) and crystallised from alcohol, forming colourless prisms (1 g.), m. p. 188° (Found : C, 70·7; H, 6·0. $C_{12}H_{12}O_3$ requires C, 70·6; H, 5·9%). Benzoylation of this compound in 5% aqueous sodium hydroxide gave the 7-*benzoate*, colourless prisms, m. p. 167° (from alcohol) (Found : C, 74·0; H, 5·2. $C_{19}H_{16}O_4$ requires C, 74·0; H, 5·2%). Application of the Fries reaction to this benzoate gave an amorphous solid which on hydrolysis yielded an intractable tar.

6-*Ethyl*-7-*hydroxy*-4-*phenylflavylium Chloride*.—4-Ethylresorcinol (1·4 g.) and dibenzoylmethane (2·3 g.) in ethyl acetate (20 ml.), saturated with hydrogen chloride at 0°, gave 6-ethyl-7-hydroxy-4-phenylflavylium chloride (3·2 g.) which separated from 10% hydrochloric acid–alcohol (1 : 1) as a *dihydrate* in orange prisms, decomp. 255° (Found : C, 69·4; H, 5·8. $C_{23}H_{19}O_2Cl,2H_2O$ requires C, 69·3; H, 5·8%). The *ferrichloride* formed yellow rhombic prisms, m. p. 210° (decomp.), from acetic acid (Found : C, 52·5; H, 3·7; Fe, 10·7. $C_{23}H_{19}O_2Cl_4Fe$ requires C, 52·6; H, 3·6; Fe, 10·6%), and the *perchlorate* in yellow irregular prisms, decomp. >154—156° (Found : C, 64·9; H, 4·6. $C_{23}H_{19}O_6Cl$ requires C, 64·7; H, 4·5%).

Decomposition of 6-ethyl-7-hydroxy-4-phenylflavylium chloride with excess of water or a little aqueous sodium acetate furnished the *anhydro-base*, which crystallised from methanol in crimson prisms or from benzene in dark red plates, m. p. 219° (decomp.) (Found : C, 84·8; H, 5·7. $C_{23}H_{18}O_2$ requires C, 84·7; H, 5·6%).

8-*Ethyl*-7-*hydroxy*-4-*phenylflavylium chloride*, prepared from 2-ethylresorcinol, crystallised from 10% hydrochloric acid–ethanol (1 : 1), forming orange hexagonal plates, m. p. 120° (Found : C, 76·0; H, 5·4; Cl, 9·9. $C_{23}H_{19}O_2Cl$ requires C, 76·2; H, 5·3; Cl, 9·8%). The *ferrichloride* separated from acetic acid in deep yellow prisms, decomp. 210—220° (Found : C, 52·6; H, 3·9; Fe, 10·6. $C_{23}H_{19}O_2Cl_4Fe$ requires C, 52·6; H, 3·7; Fe, 10·6%), and the *perchlorate* in yellow prisms, m. p. 261° (decomp.) (Found : C, 65·5; H, 4·3. $C_{23}H_{19}O_6Cl$ requires C, 64·6; H, 4·5%).

Decomposition of the chloride with aqueous sodium acetate furnished the *anhydro-base*, deep red prisms, m. p. 211° [from methanol or benzene–light petroleum (b. p. 60—80°)] (Found : C, 84·4; H, 5·7. $C_{23}H_{18}O_2$ requires C, 84·6; H, 5·5%).

Oxidation of Anhydro-7-*hydroxy- and Anhydro*-5 : 7-*dihydroxy*-2 : 4-*diphenylbenzopyranol*.—A solution of this base (Bulow and Sicherer, *Ber.*, 1901, **34**, 2368) (0·5 g.) in methanol (20 ml.) containing 3N-aqueous potassium hydroxide (5 ml.) was treated with hydrogen peroxide (1·5 ml.; 100-vol.), added in 6 portions during 3 days. The bright red solution became orange and, after being acidified (Congo-red) with 2N-sulphuric acid and then basified with sodium hydrogen carbonate, was extracted with ether. Evaporation of the dried ethereal extracts left an orange intractable oil. From the residual aqueous liquors which had been acidified an orange solid was isolated with ether and from this product benzoic acid (0·15 g.) was extracted with boiling light petroleum (b. p. 60—80°).

When anhydro-5 : 7-dihydroxy-2 : 4-diphenylbenzopyranol (0·5 g.) (Bulow and Sicherer, *loc. cit.*) was oxidised under the same conditions benzoic acid (0·11 g.) was separated from an intractable solid phenolic product.

UNIVERSITY OF LIVERPOOL.

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