

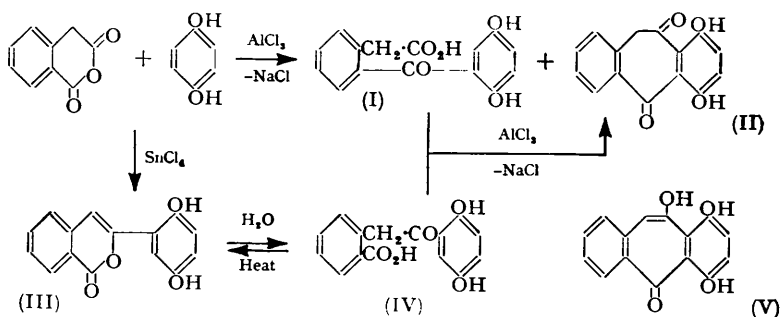
Hydroxybenzotropones. Part III. Synthesis of a Hydroxy dimethoxydibenzotropone.*

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The dimethoxy-1 : 2 : 4 : 5-dibenzocycloheptadienedione (VI) has been obtained *via* a condensation of quinol with homophthalic anhydride. It behaves as an enol-ketone, showing no tropolone characteristics.

In the condensation of quinol and glutacnic acid (see Part I *) the intermediate keto-acid cyclises to a five-membered ring, forming an oxoindanylacetic acid. When homophthalic acid (the aromatic analogue of glutacnic acid) is used a similar ring closure is prohibited and conditions are more favourable for the formation of a seven-membered ring. Thus condensation of homophthalic acid (or anhydride) with quinol in molten sodium chloride-aluminium chloride gave the dione (II) in low yield, and a small amount of the keto-acid (I) which was converted into the dione on further treatment in the fusion mixture. A Friedel-Crafts reaction between homophthalic anhydride and quinol in stannic chloride (Buu-Hoï, *Bull. Soc. chim. France*, 1944, 11, 338) gave the *isocoumarin* (III) which was readily hydrolysed to the keto-acid (IV), isomeric with (I). This acid (IV) is reconverted into the *isocoumarin* when heated, or when dissolved in anhydrous hydrofluoric acid, but on fusion in sodium chloride-aluminium chloride again yields the dione (II).

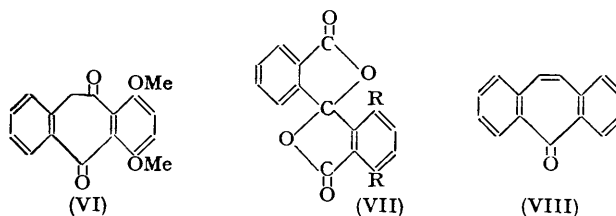


The orange dione (II) forms a diacetate and a trimethyl ether with methyl sulphate, but is not methylated by diazomethane. It also reacts with phenylhydrazine although the product is not a simple hydrazone. It gives a green ferric chloride colour but no colour with boroacetic anhydride, and is extracted from chloroform by a solution of pH 9.8. It forms an orange-red solution in cold aqueous sodium hydroxide and dissolves in hot aqueous sodium carbonate; it is reduced in alkaline solution by sodium dithionite but the addition of hydrogen peroxide does not restore the colour. The infrared spectrum shows that this compound exists as the dione (II) rather than as the hydroxytropone (V). In the $6\text{-}\mu$ region there is a strong band at 1640 cm.^{-1} and a very strong band at 1600 cm.^{-1} , indicating the presence of two unsymmetrical strongly hydrogen-bonded carbonyl groups. In the $3\text{-}\mu$ region there is a broad band at 3000 cm.^{-1} and two sharp but weak bands at 2997 and 3050 cm.^{-1} . The last two are most probably due to aromatic C-H vibrations. There is no band near 3300 cm.^{-1} . All this is in favour of structure (II) but not (V). Moreover the spectrum showed no significant change in carbon tetrachloride solution, showing the hydrogen-bonding to be almost all intramolecular. Some resemblance to quinizarin (1 : 4-dihydroxyanthraquinone) in physical properties might therefore be expected. This is seen again in the ultraviolet absorption where the curve of the diketone (II) is similar in character to that of quinizarin (see Morton and Earlam, *J.*, 1941, 159; Spruit, *Rec. Trav.*

* Parts I and II, the two preceding papers.

chim., 1949, 68, 325), the maxima in the latter case falling at longer wavelengths as would be expected from the more extended conjugation.

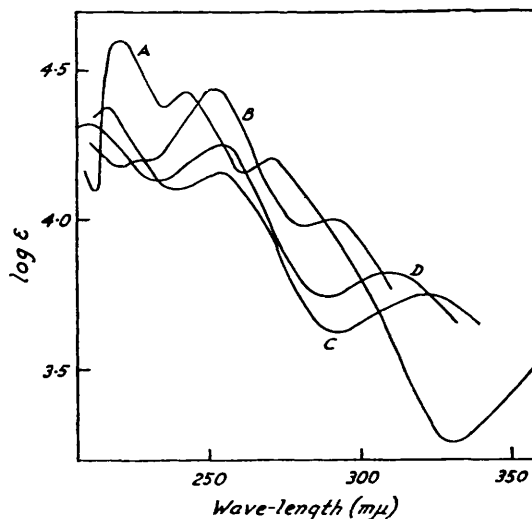
The trimethyl ether (V; OMe in place of OH) is completely stable to alkaline hydrolysis but under acid conditions it gave the dimethyl ether (VI). This is slightly soluble in



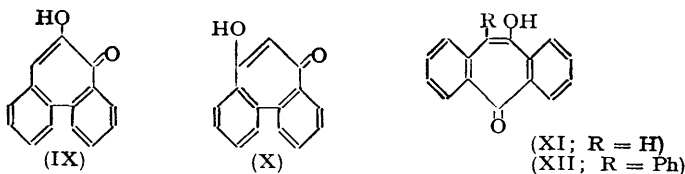
concentrated hydrochloric acid, and soluble in hot caustic alkalis, forming an orange solution, and gives no ferric colour. It formed a 2 : 4-dinitrophenylhydrazone and a 3 : 5-dinitrobenzoate, and reaction with methyl sulphate regenerated the trimethyl ether.

- A, 1' : 4'-Dihydroxy-1 : 2-4 : 5-dibenzocycloheptadiene-3 : 7-dione (II).
 B, Diacetate of (A).
 C, Dimethyl ether (VI) of (A).
 D, Trimethyl ether of (A).

Solvent : methanol.



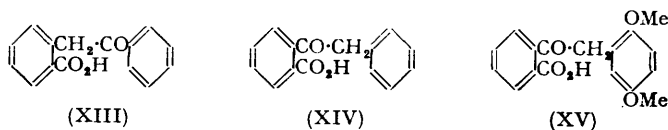
Oxidation of the trimethyl ether with sodium dichromate in acetic acid gave a colourless product, insoluble in hot sodium carbonate solution but dissolving in warm dilute aqueous sodium hydroxide; the original compound was obtained by acidification of the alkaline solution. Quantitative hydrolysis showed the presence of two lactone rings and the oxidation product is considered to be (VII; R = OMe). This is supported by a carbonyl band in the infrared spectrum at the unusually high value of 1787 cm.^{-1} ; Grove (*J.*, 1952, 3345) found the carbonyl band in 3-acetoxypthalides to be as high as 1785 cm.^{-1} . The



dilactone (VII; R = H) was obtained by Treibs and Klinkhammer (*Ber.*, 1951, 84, 671) from dibenzotropone (VIII) on ozonolysis and oxidation of the aldehydo-acid obtained.

It can now be seen that the diketone (II) and its dimethyl ether (VI), like all the other known hydroxydibenzotropones [(IX), Nakasaki, *J. Chem. Soc. Japan*, 1951, 72, 739;

(X), Lucien and Taurins, *Canad. J. Chem.*, 1952, **30**, 208; (XI), Rigaudy and Nedelec, *Compt. rend.*, 1953, **237**, 1097; (XII), Cook, *J.*, 1928, 58], show no characteristic tropolone properties. They behave as enol-ketones. The dimethyl ether of the diketone (II) is the least acidic of the group. This may be due to suppression of enolisation by the *peri*-methoxyl groups (see Part I, *loc. cit.*), although the dimethyl ether seems to exist, at least in methanol solution, in the enol form, the ultraviolet absorption being very similar to that of the trimethyl ether (see Figure). The enol form of the dimethyl ether would be slightly stabilised by hydrogen-bonding whereas chelation inhibits enolisation of the diketone (II). Rigaudy and Nedelec (*loc. cit.*) claim to have isolated the hydroxytropone (XI) in both enol and keto-forms.



After the synthesis of the diketone (II) some further experiments were made to obtain related compounds. Cyclisation of the keto-acids (XIII) and (XIV) by use of fused sodium chloride-aluminium chloride, anhydrous hydrogen fluoride, and polyphosphoric acid gave only the corresponding *isocoumarin* and *phthalide*. More surprising was the failure of the acid (XV) to yield a diketone.

EXPERIMENTAL

1' : 4'-Dihydroxy-1 : 2 : 4 : 5-dibenzocycloheptadiene-3 : 7-dione (II).—To a molten mixture of anhydrous aluminium chloride (150 g.) and sodium chloride (30 g.) at 180° was added slowly with stirring, a mixture of homophthalic acid (18 g.) and quinol (11 g.). An orange-brown colour developed as the reaction proceeded and the temperature was not allowed to exceed 195°. The mixture was cooled and decomposed with water (1 l.) and concentrated hydrochloric acid (500 ml.), and the precipitate collected. The dried precipitate was extracted with boiling light petroleum (b. p. 100—120°), and the extract concentrated, filtered (charcoal), and allowed to crystallise. Recrystallisation from the same solvent yielded clusters of orange crystals, m. p. 179° (0.3 g., 1%) which when sublimed *in vacuo* were yellow (Found : C, 70.6; H, 3.95. $C_{15}H_{10}O_4$ requires C, 70.85; H, 3.95%). Light absorption : max. at 220, 242, 270, and 432 $m\mu$ ($\log \epsilon$ 4.60, 4.43, 4.20, and 4.25 respectively) in cyclohexane. When the filtrate from the above reaction was extracted with chloroform, and the latter treated with aqueous sodium hydrogen carbonate, acidification of the aqueous extract afforded o-(2 : 5-dihydroxybenzoyl)phenylacetic acid (I). Recrystallisation from water gave yellow crystals of the *hemihydrate*, m. p. 119° (Found : C, 64.4; H, 4.65. $C_{15}H_{12}O_5 \cdot \frac{1}{2}H_2O$ requires C, 64.1; H, 4.6%). Heating the acid *in vacuo* above its m. p. gave bright yellow needles of the anhydrous acid, m. p. 156° (Found : C, 66.35; H, 4.6. $C_{15}H_{12}O_5$ requires C, 66.1; H, 4.4%). The acid was converted into the dione (II) by the above procedure. It had m. p. and mixed m. p. 178°. 2 : 5-Dihydroxydeoxybenzoin-2'-carboxylic acid (IV) was also converted into the dione (II) by the same treatment. It had m. p. and mixed m. p. 179° (10%). The *diacetate* separated from benzene-light petroleum (b. p. 80—90°) in pale yellow crystals, m. p. 174° (Found : C, 67.7; H, 4.15. $C_{15}H_{14}O_6$ requires C, 67.45; H, 4.15%). Light absorption : max. at 252 and 290 $m\mu$ ($\log \epsilon$ 4.43 and 4.01 respectively) in MeOH. It gave no ferric chloride colour. Reaction of the dione (II) with phenylhydrazine afforded a *product* as orange plates, m. p. 204° (from aqueous alcohol) (Found : C, 74.35; H, 5.75; N, 7.6. $C_{23}H_{20}O_5N_2$ requires C, 74.2; H, 5.4; N, 7.5%). Refluxing the dione (II) in methyl sulphate-acetone-potassium carbonate for 24 hr. gave the *trimethyl ether* as deep yellow crystals, m. p. 188° [from light petroleum (b. p. 100—120°)] (Found : C, 72.85; H, 5.45; OMe, 30.1. $C_{18}H_{16}O_4$ requires C, 72.95; H, 5.4; 3OMe, 31.4%). Light absorption : max. at 210, 255, and 310 $m\mu$ ($\log \epsilon$ 4.35, 4.25 and 3.83 respectively) in MeOH.

Oxidation of the Trimethyl Ether.—The ether (0.15 g.) was dissolved in glacial acetic acid (5 ml.), and sodium dichromate (0.65 g.) in the same solvent (2.5 ml.) was added. After refluxing 30 min. the mixture was poured into water, a voluminous precipitate being formed. The *dilactone*, crystallised from benzene (charcoal), had m. p. 236° (Found : C, 65.2; H, 3.9. $C_{17}H_{12}O_6$ requires C, 65.4; H, 3.85%). Dissolution of 13.5 mg. of the dilactone in warm 0.025N-sodium hydroxide and back-titration with hydrochloric acid showed that 3.24 ml. of alkali were neutralised (required 3.44 ml.).

1' : 4'-Dimethoxy-1 : 2-4 : 5-dibenzocycloheptadiene-3 : 7-dione (VI).—The above trimethyl ether (0.1 g.) was dissolved in glacial acetic acid (10 ml.) containing sulphuric acid (5 ml.; 2N). After 4 hr. on a steam-bath, the mixture was diluted with water and the precipitate collected. Crystallisation from light petroleum (b. p. 100—120°) gave yellow *dione*, m. p. 170° (40 mg.) (Found : C, 72.0; H, 4.9; OMe, 20.5. $C_{17}H_{14}O_4$ requires C, 72.3; H, 4.95; OMe, 22.0%). Light absorption : max. at 216, 255, and 320 μ ($\log \epsilon$ 4.38, 4.15, and 3.76 respectively) in MeOH. Remethylation with methyl sulphate gave the trimethyl ether, m. p. and mixed m. p. 188°. The 2 : 4-dinitrophenylhydrazine crystallised as the orange-yellow *dihydrate*, m. p. 240°, from aqueous alcohol (Found : C, 55.2; H, 4.5. $C_{23}H_{18}O_7N_4 \cdot 2H_2O$ requires C, 55.4; H, 4.4%). The lemon-yellow 3 : 5-dinitrobenzoate, crystallised from benzene (charcoal), had m. p. 253° (Found : C, 60.3; H, 3.1. $C_{24}H_{16}O_8N_2$ requires C, 60.5; H, 3.35%).

3-(2 : 5-Dihydroxyphenyl)isocoumarin (III).—A mixture of homophthalic anhydride (8 g.), quinol (6 g.), and anhydrous stannic chloride (25 g.) was heated with stirring at 120° for 1 hr. After cooling, the rust-brown paste was warmed with dilute hydrochloric acid (1 : 1) for a short time, then cooled, and the precipitated isocoumarin was collected and crystallised from aqueous acetic acid (charcoal), forming lustrous brown needles, m. p. 256° (2 g., 15%) which dissolved in hot aqueous sodium carbonate and gave an orange-brown precipitate with ferric chloride (Found : C, 70.55; H, 4.25. $C_{15}H_{10}O_4$ requires C, 70.85; H, 3.95%).

2 : 5-Dihydroxydeoxybenzoin-2'-carboxylic Acid (IV).—The above isocoumarin was warmed for 5 min. in aqueous 10% sodium hydroxide, cooled, and acidified. The precipitated *acid* crystallised from aqueous methanol (charcoal) in cream needles, m. p. 193° (90%) (Found : C, 66.0; H, 4.4. $C_{15}H_{12}O_5$ requires C, 66.1; H, 4.4%). The acid gave a green ferric colour and was reconverted into the isocoumarin in 10 min. at 250° or on treatment with cold anhydrous hydrogen fluoride.

3-(2 : 5-Dimethoxyphenyl)isocoumarin.—This was obtained from homophthalic anhydride and quinol dimethyl ether as for (III). The crude oil obtained was washed in ether with aqueous sodium carbonate, and with water, and evaporated. The remaining oil then solidified when dried *in vacuo*. Several crystallisations from aqueous methanol (charcoal) afforded pale yellow needles, m. p. 112° (Found : C, 72.4; H, 5.2. $C_{17}H_{14}O_4$ requires C, 72.4; H, 5.0%).

(2 : 5-Dimethoxybenzylidene)phthalide.—2 : 5-Dimethoxyphenylacetic acid (17 g.), phthalic anhydride (13 g.), and anhydrous potassium acetate (1 g.) were heated together at 240° for 2 hr. When cold, the solid residue was extracted with boiling glacial acetic acid (charcoal). The *phthalide* separated on cooling and recrystallised from ethanol in bright yellow needles, m. p. 159° (12 g., 49%) (Found : C, 72.15; H, 4.95. $C_{17}H_{14}O_4$ requires C, 72.35; H, 4.95%).

2' : 5'-Dimethoxydeoxybenzoin-2-carboxylic Acid (XV).—The above phthalide (5 g.) was heated with potassium hydroxide (2 g.) in water (15 ml.) until dissolution was complete. Acidification of the ice-cold solution gave a sticky precipitate which was taken into ether. Evaporation of the solvent left a gum which solidified *in vacuo*. After being washed with a little ethyl acetate and then benzene, it crystallised from light petroleum (b. p. 50—60°) in clusters, m. p. 90° (2.5 g., 46%) (Found : C, 67.8; H, 5.1. $C_{17}H_{16}O_5$ requires C, 68.0; H, 5.35%). Heating this *acid* above its m. p. regenerated the phthalide.

(2 : 5-Dihydroxybenzylidene)phthalide.—(a) (2 : 5-Dimethoxybenzylidene)phthalide (0.5 g.) was refluxed for 3 hr. with hydriodic acid (5 ml.; *d* 1.7) in glacial acetic acid (2 ml.). Dilution with water then gave a precipitate which crystallised from aqueous alcohol (charcoal) in pale yellow plates, m. p. 224° (Found : C, 71.0; H, 3.95. $C_{15}H_{10}O_4$ requires C, 70.85; H, 3.95%). (b) By the same procedure 2' : 5'-dimethoxydeoxybenzoin-2-carboxylic acid also gave the phthalide, m. p. and mixed m. p. 224°.

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