

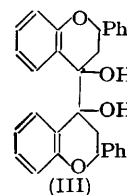
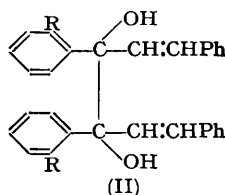
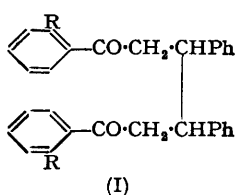
The Structure of Tannins. Part II. The Reduction Products of 2'-Hydroxy- and 2'-Methoxy-chalkones and of Flavanone.*

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The course of reduction of 2'-hydroxy- and 2'-methoxy-chalkones † with zinc and acetic acid resembles closely that of chalcone (Part I *). The main products are (±)- and *meso*-1 : 6-di-*o*-hydroxyphenyl-3 : 4-diphenylhexane-1 : 6-diones (I; R = OH) and their methyl ethers (I; R = OMe), respectively. The *meso*-dione (I; R = OH) is shown to differ from the pinacol (III) of similar m. p. formed by reduction of flavanone.

IN Part I * of this series it was shown that the reduction products obtained from chalcone with zinc dust and acetic acid were *meso*- and (±)-1 : 3 : 4 : 6-tetraphenylhexane-1 : 6-diones (I; R = H), neither isomer having the pinacol structure (II; R = H) suggested for the lower-melting compound by Russell and Todd (*J.*, 1934, 1066). The possibility that 2'-hydroxychalcone might yield a "flavpinacol" (III) remained, however, since it could cyclise to flavanone before reduction, and previous investigators (Freudenberg and Orthner, *Ber.*, 1922, 55, 1748; Geissman and Clinton, *J. Amer. Chem. Soc.*, 1946, 68, 700) had obtained the pinacol (III) by reduction of flavanone. Furthermore, Russell (*J.*, 1934, 218) observed that the reduction products of 2'-hydroxychalcones were insoluble in alkali, in agreement with the structure (III).



In order to obtain reference compounds, the reduction of 2'-methoxychalcone was first studied and, from the mixture of products, *meso*- and (±)-1 : 6-di-*o*-methoxyphenyl-3 : 4-diphenylhexane-1 : 6-dione (I; R = OMe) were isolated and characterised as oximes. Confirmation of the structure of the *meso*-isomer was obtained by its synthesis from di-*o*-methoxyphenylcadmium and *meso*-ββ'-diphenyladipoyl chloride. This reaction also yielded a compound, C₃₂H₂₈O₃, m. p. 224°, which is presumably a dehydration product of the *meso*-dione, but is not identical with *cis*-1-*o*-methoxybenzoyl-2-*o*-methoxyphenyl-4 : 5-diphenylcyclopentene, obtained by treatment of the *meso*-dione with alcoholic hydrochloric acid.

Condensation of (±)-ββ'-diphenyladipoyl chloride with di-*o*-methoxyphenylcadmium did not yield a crystalline product but acid treatment of the crude product afforded *trans*-1-*o*-methoxybenzoyl-2-*o*-methoxyphenyl-4 : 5-diphenylcyclopentene, identical with the dehydration product obtained from the (±)-dione (I; R = OMe).

The reduction of 2'-hydroxychalcone yielded three compounds. Two of these were identified as the *meso*- and (±)-1 : 6-di-*o*-hydroxyphenyl-3 : 4-diphenylhexane-1 : 6-diones (I; R = OH) respectively by methylation to the two diones (I; R = OMe) described above. The (±)-isomer was readily soluble in aqueous alkali and gave a strong ferric reaction; but the *meso*-isomer was not soluble in aqueous alkali and gave no ferric reaction, although it dissolved on addition of alkali to its suspension in acetone or methanol. Possibly Russell's alkali-insoluble reduction products were similar "cryptophenolic" compounds.

* Part I, *J.*, 1950, 3367.

† For numbering see Editorial Report on Nomenclature, *J.*, 1953, 4201.

The constitution of the third reduction product, $C_{30}H_{24}O_3$, m. p. 144° , is uncertain since pure derivatives have not been obtained from it, but it is probably an *o*-hydroxybenzoyl-*o*-hydroxyphenyldiphenylcyclopentene. It has a strongly hydrogen-bonded and conjugated carbonyl group (infra-red absorption at 1644 cm^{-1} in a mull, 1642 cm^{-1} in chloroform) and also shows the broad hydroxyl absorption (*ca.* 3300 cm^{-1}) characteristic of hydrogen bonding.

The *meso*-dione (I; R = OH) has a melting point very close to that of flavpinacol (III) described by Freudenberg and Orthner and by Geissman and Clinton (*loc. cit.*). However, comparison of the properties of these compounds, shown together with those of the (\pm)-dione (I; R = OH) in the Table, indicates that the structures assigned to them are correct. A mixed melting point also showed a considerable depression.

Reduction products of flavanone and 2'-hydroxychalkone.

Compound	Solution in H_2SO_4	Ultra-violet absorption (in EtOH) λ_{max} (m μ) (log ϵ)	Infra-red absorption (cm. $^{-1}$)	M. p.
Flavpinacol (III)	Red	279 (3.76); 285 (3.75)	No CO band; 3500 (OH)	255—256°
<i>meso</i> -Dione (I; R = OH)	Greenish-yellow	254 (4.35); 328 (3.94)	1637 (CO) *	256—257°
(\pm)-Dione (I; R = OH)	Greenish-yellow	254 (4.29); 328 (3.9)	1634 (CO) *	126°

* No sharp OH band (H-bonded).

Thus it is clear that reduction of 2'-hydroxychalkone with zinc and acetic acid resembles closely that of chalkone (Part I) in forming bimolecular diketones. This is normal with $\alpha\beta$ -unsaturated ketones (Kohler and Thompson, *J. Amer. Chem. Soc.*, 1937, **59**, 887) but, on the other hand, flavpinacol is a normal product of the reduction of the saturated aromatic ketone, flavanone.

So far we have no positive evidence of the interconversion of 2'-hydroxychalkone and flavanone during the reduction with zinc and acetic acid, although Geissman and Clinton (*loc. cit.*) found such interconversion during reductions with sodium amalgam and with magnesium and hydrochloric acid. Thus we cannot be certain that Russell's tannin-like compounds did not contain "flavpinacols," but it seems certain that they must have contained considerable quantities of the bimolecular diketones. Consequently deductions of tannin structure based on other assumed constitutions lack firm foundation.

EXPERIMENTAL

M. p.s are corrected. Some of the analyses are by Dr. Zimmerman, C.S.I.R.O., Melbourne.

Reduction of 2'-Methoxychalkone.—Zinc dust (100 g.) was added in small portions during 1 hr. to a refluxing solution of 2'-methoxychalkone (25 g.; b. p. $226^\circ/11\text{ mm.}$) in alcohol (500 ml.) and acetic acid (75 ml.), and refluxing was continued for 15 min. When the filtered solution was cooled for 2 hr. at 0° , crystals (A; 12 g.) separated. After a further 18 hr. at 0° a second crop (B; 2.8 g.) was obtained. On concentration to 200 ml. a third (C; 1.3 g.) and after 2 days at 0° a fourth crop (D; 0.75 g.) crystallised.

Fractions B and D, after being washed with water to remove zinc acetate, formed hexagonal plates of (\pm)-1 : 6-*di-o-methoxyphenyl*-3 : 4-*diphenylhexane*-1 : 6-*dione* (2.5 g.), m. p. $177\text{--}178^\circ$, from methanol [Found : C, 80.3; H, 6.6; OMe, 12.9%; *M* (Rast), 550. $C_{32}H_{30}O_4$ requires C, 80.3; H, 6.3; 2OMe, 13.0%; *M*, 478.6]. With hydroxylamine hydrochloride and pyridine (*cf.* Part I) it formed a *dioxime*, prisms, m. p. 228° , from aqueous acetic acid (Found : C, 75.5; H, 6.1; N, 5.7. $C_{32}H_{32}O_4N_2$ requires C, 75.6; H, 6.3; N, 5.5%).

Fractions A and C, after removal of zinc acetate with boiling water, yielded *meso*-1 : 6-*di-o-methoxyphenyl*-3 : 4-*diphenylhexane*-1 : 6-*dione* (2.5 g.), m. p. $197\text{--}198^\circ$, in the less soluble fractions from methanol [Found : C, 80.7; H, 6.1; OMe, 12.4%; *M* (Rast), 360] and a further crop (0.4 g.) of the (\pm)-isomer from the more soluble fractions. The *meso*-isomer formed a *dioxime*, rectangular plates, m. p. 262° from methanol-pyridine (20 : 1) (Found : C, 75.7; H, 6.4; N, 5.3%).

Both diones were stable to bromine in carbon tetrachloride and to permanganate in acetone.

meso-1 : 6-*Di-o-methoxyphenyl*-3 : 4-*diphenylhexane*-1 : 6-*dione*.—To the Grignard reagent prepared from *o*-bromoanisole (2 g.), ether (12.5 ml.), and magnesium turnings (0.25 g.), dry cadmium chloride (1.4 g.) was added during 90 min., with stirring. Thirty minutes later a solution of *meso*- $\beta\beta'$ -diphenyladipoyl chloride (0.3 g.) in warm benzene was added and after removal of the ether the mixture was stirred while refluxing for 2 hr. Ice and dilute hydrochloric acid were added and the mixture was distilled with steam. 2 : 2'-Dimethoxydiphenyl, m. p. 155°, separated from the distillate and a resinous solid (0.4 g.) from the residue. After extraction of the latter with ether, the residue (70 mg.) formed crystals, m. p. 224°, from chloroform-ethanol (1 : 4) (Found : C, 83.6; H, 6.6. $C_{32}H_{28}O_3$ requires C, 83.5; H, 6.1%). The ether-soluble material was chromatographed on alumina (activity IV), and from the light petroleum-benzene (1 : 2) eluate prisms of *meso*-1 : 6-*di-o-methoxyphenyl*-3 : 4-*diphenylhexane*-1 : 6-*dione* separated, having m. p. 194–195° raised to 196–197° on admixture with the reduction product (m. p. 197°) of 2'-methoxychalkone.

trans-1-*o-Methoxybenzoyl*-2-*o-methoxyphenyl*-4 : 5-*diphenylcyclopentene*.—(\pm)-1 : 6-*Di-o-methoxyphenyl*-3 : 4-*diphenylhexane*-1 : 6-*dione* (0.2 g.) was dissolved in boiling methanol, and hydrochloric acid was added to faint turbidity and then enough methanol to form a clear solution, which was refluxed for 2 hr. *trans*-1-*o-Methoxybenzoyl*-2-*o-methoxyphenyl*-4 : 5-*diphenylcyclopentene* (40 mg.) separated from the hot solution and a further 120 mg. on cooling. It formed hexagonal plates, m. p. 148–149°, from chloroform-methanol [Found : C, 82.9; H, 6.2, 6.1; OMe, 13.6; *M* (Rast), 429, 449. $C_{32}H_{28}O_3$ requires C, 83.4; H, 6.1; 2OMe, 13.5%; *M*, 460.5].

The same compound (m. p. and mixed m. p.) was obtained from the reaction between *di-o-methoxyphenyl*cadmium and (\pm)- $\beta\beta'$ -diphenyladipoyl chloride, followed by treatment of the amorphous non-volatile product with alcoholic hydrogen chloride. It decolorises bromine in carbon tetrachloride quite rapidly.

cis-1-*o-Methoxybenzoyl*-2-*o-methoxyphenyl*-4 : 5-*diphenylcyclopentene*.—The *meso*-*dione* (0.2 g.), treated with alcoholic hydrogen chloride, yielded *cis*-1-*o-methoxybenzoyl*-2-*o-methoxyphenyl*-4 : 5-*diphenylcyclopentene* (0.1 g.) which formed prisms, m. p. 155°, from methanol [Found : C, 83.4; H, 6.2%; *M* (Rast), 328] and decolorised bromine in carbon tetrachloride.

Reduction of 2'-Hydroxychalkone.—2'-Hydroxychalkone (15 g.) was reduced by the method described for 2'-methoxychalkone. The mixture was poured into water and extracted with ether and the ethereal solution extracted with 5% aqueous sodium hydroxide. Acidification of the alkaline solution yielded (\pm)-1 : 6-*di-o-hydroxyphenyl*-3 : 4-*diphenylhexane*-1 : 6-*dione* (3.15 g.) which formed long hexagonal plates, m. p. 126°, from chloroform-methanol [Found : C, 80.4, 80.2; H, 5.7, 5.9%; *M* (Rast), 422, 413. $C_{30}H_{26}O_4$ requires C, 80.0; H, 5.8%; *M*, 450.5]. It gave a red colour with ferric chloride but did not decolorise bromine in carbon tetrachloride and reacted only very slowly with permanganate in acetone. On methylation with methyl sulphate and sodium hydroxide in aqueous-methanolic acetone it formed (\pm)-1 : 6-*di-o-methoxyphenyl*-3 : 4-*diphenylhexane*-1 : 6-*dione*, identical (m. p. and mixed m. p.) with the material described above.

Treatment of (\pm)-1 : 6-*di-o-hydroxyphenyl*-3 : 4-*diphenylhexane*-1 : 6-*dione* with acetic anhydride and pyridine afforded the *diacetate*, fine needles, m. p. 144°, from 95% ethanol (Found : C, 76.6; H, 5.9. $C_{34}H_{30}O_6$ requires C, 76.4; H, 5.7%). It showed carbonyl absorption bands at 1760 and 1697 cm^{-1} .

The ethereal solution yielded a product (1.6 g.), which formed short rods, m. p. 144°, from chloroform-methanol [Found : C, 83.2, 83.4; H, 5.6, 5.5; active H, 0.39%; *M* (Rast), 449, 463. Calc. for $C_{30}H_{24}O_3$: C, 83.3; H, 5.6; 2 active H, 0.47%; *M*, 432.5]. It gave a brown ferric reaction and reacted rapidly with bromine and with permanganate.

The insoluble residue, after removal of zinc acetate with hot water, was extracted continuously for 10 hr. with boiling benzene. From the cooled extract, *meso*-1 : 6-*di-o-hydroxyphenyl*-3 : 4-*diphenylhexane*-1 : 6-*dione* (3.75 g.) separated; this formed long prisms, m. p. 256–257°, from methylene chloride-methanol [Found : C, 79.9; H, 6.1%; *M* (Rast), 560]. A further crop (0.2 g.) was obtained on concentration of the benzene extract. It was sparingly soluble in methanol, ethanol, acetone, and benzene but on addition of potassium hydroxide to a suspension in methanol or acetone it dissolved readily. It gave no ferric reaction.

On acetylation with acetic anhydride and pyridine at the b. p. for 15 min. it yielded a *diacetate*, which formed needles, m. p. 241–242°, from chloroform-methanol (Found : C, 76.3; H, 5.55%). This showed carbonyl bands at 1745 and 1686 cm^{-1} , characteristic of the acetate-carbonyl and the carbonyl attached to a benzene ring, respectively.

On methylation with methyl sulphate and potassium hydroxide in acetone *meso*-1 : 6-*di-o*-

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methoxyphenyl-3 : 4-diphenylhexane-1 : 6-dione was obtained, having m. p. 196—196.5° undepressed on admixture with the reduction product (m. p. 197—198°) of 2'-methoxychalkone.

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