A Novel α-Hydroxydihydrochalcone from the Heartwood of *Pterocarpus angolensis* D.C.: Absolute Configuration, Synthesis, Photochemical Transformations, and Conversion into α-Methyldeoxybenzoins

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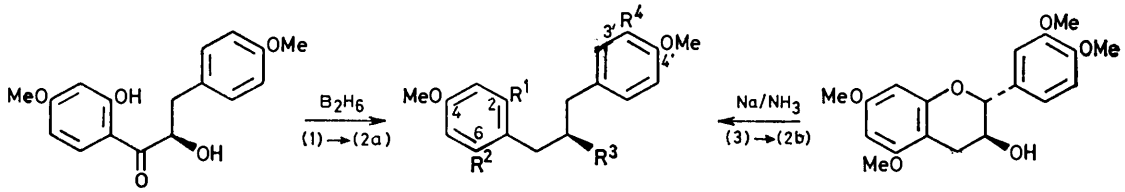
The absolute configuration of (α*R*)-α,2'-dihydroxy-4,4'-dimethoxydihydrochalcone from the heartwood of *Pterocarpus angolensis* D.C. is established. Its structure is substantiated by synthesis and by photochemical conversion of its α-*O*-tosyl derivative into an α-tosyloxymethyldeoxybenzoin and hence to the α-methyldeoxybenzoin analogue. The photochemical step also leads, amongst others, to α-hydroxymethyldeoxybenzoin, β-hydroxydihydrochalcone, and 2-benzylbenzofuran-3-one analogues depending on the conditions of the photolysis.

CONTINUED examination of the heartwood of *Pterocarpus angolensis* D.C. (muninga, kiaat), known for its durability,[1] has shown the presence of a novel α-hydroxydihydrochalcone (1). This class of compound has hitherto been restricted to a single example of unknown absolute configuration, nubigenol [2] (α,2',4,4',6'-pentahydroxydihydrochalcone), from *Podocarpus nubigena*. The new α,2'-dihydroxy-4,4'-dimethoxydihydrochalcone (1) is associated with several α-methyldeoxybenzoins,[3,4] one exhibiting the same dimethoxy-functionality, and also isoflavones [3,5-9] in *P. angolensis*. Conversion of the α-hydroxydihydrochalcone into an α-methyldeoxybenzoin has now been achieved chemically for the first time by means of an initial photochemical step. A similar approach to isoflavonoid synthesis has also been investigated.

The molecular structure of α,2'-dihydroxy-4,4'-dimethoxychalcone (1), $C_{17}H_{18}O_5$, is evident from spectroscopic data and was confirmed by total synthesis (see later). The presence of a chiral centre at C-α is reflected in the magnetic non-equivalence of the adjacent (C-β) methylene protons (δ 2.84 and 3.13) and in its optical activity as illustrated by c.d. spectra. The absolute configuration of the new α-hydroxydihydrochalcone was determined by its reduction with diborane to 1-(2-hydroxy-4-methoxyphenyl)-3-(4-methoxyphenyl)-propan-2-ol (2a) (Scheme 1). This compound bears a close structural resemblance to 3-(3,4-dimethoxyphenyl)-1-(2-hydroxy-4,6-dimethoxyphenyl)propan-2-ol (2b) [of known absolute configuration (2*R*)], obtained by Birch reduction of (2*R*,3*S*)-(+)-catechin 3',4',5,7-tetramethyl ether (3). [10] Comparison of the c.d. spectra of these propanols (2a and b), which exhibit identical Cotton effects, accordingly defines the (α*R*)-configuration of the dihydrochalcone (1).

Synthesis of the latter was accomplished *via* the 4,4'-dimethoxy-2'-methoxymethoxychalcone intermediate (6a), prepared by conventional base-catalysed condensation of the appropriate fragments (4a) and (5a). Epoxidation (H_2O_2–$^-$OH) of this chalcone readily gives the stable chalcone epoxide (7a), which undergoes hydrogenation (Pd–$BaSO_4$) to produce racemic α,2'-dihydroxy-4,4'-dimethoxydihydrochalcone (9) in good yield, after deprotection of the 2'-OH by acid hydrolysis (8a) ⟶ (9). The product thus obtained was shown to be identical to the natural metabolite by mass and n.m.r. spectrometry. The above sequence represents a simple and general method of synthetic access to α-hydroxydihydrochalcones.

Consideration of α-hydroxydihydrochalcones [e.g. (1)] as possible biogenetic precursors to α-methyldeoxybenzoins and isoflavones stems from their observed association in *P. angolensis*,[4] the rearrangement requiring an anionotropic 1,2-shift of the β-phenyl group of the α,2'-dihydroxy-4,4'-dimethoxydihydrochalcone (1). The problems connected with an analogous *in vitro*



(1) (2) (3)

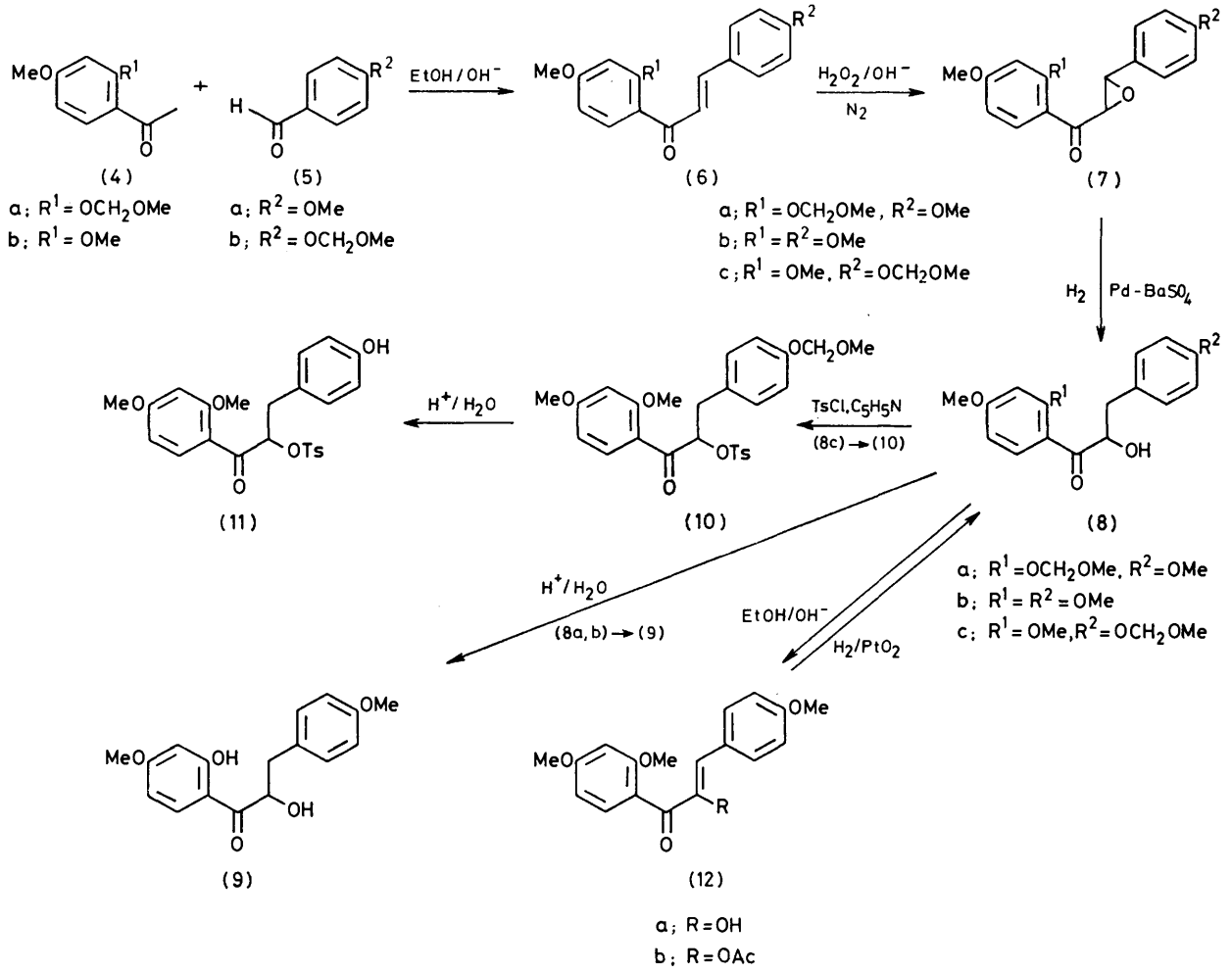
a; $R^2 = R^4 = H$; $R^1 = R^3 = OH$
b; $R^2 = R^4 = OMe$; $R^1 = R^3 = OH$
c; $R^2 = R^4 = H$; $R^1 = R^3 = OAc$
d; $R^2 = R^4 = OMe$; $R^1 = R^3 = OAc$

SCHEME 1

synthesis centre around (i) development of a transient carbocation at C-α, (ii) enhancement of the nucleophilic character of the B-ring in order to facilitate the proposed 1,2-migration, and (iii) previous protection of the 2′-OH, thus preventing undesirable intramolecular attack at C-α. These prerequisites are met by synthesis of 4-hydroxy-2′,4′-dimethoxy-α-tosyloxydihydrochalcone (11) [*cf.* Scheme 2, (4b) + (5b) ⟶ (6c) ⟶ (7c) ⟶ (8c) ⟶ (10) ⟶ (11)] followed by its photolysis.

rearrangements which are presumably all based on the formation of a highly unstable α-carbocation. Notable was the unique demethylation of the 2′-methoxy-function which accompanied cyclization in the first-mentioned process (11) ⟶ (13).

Introduction of water into the reaction mixture had little effect on the yields of the 2-benzylbenzofuranone (13) and chalcone (14), but 4′-hydroxy-2,4-dimethoxy-α-hydroxymethyldeoxybenzoin (19a) formed at the expense

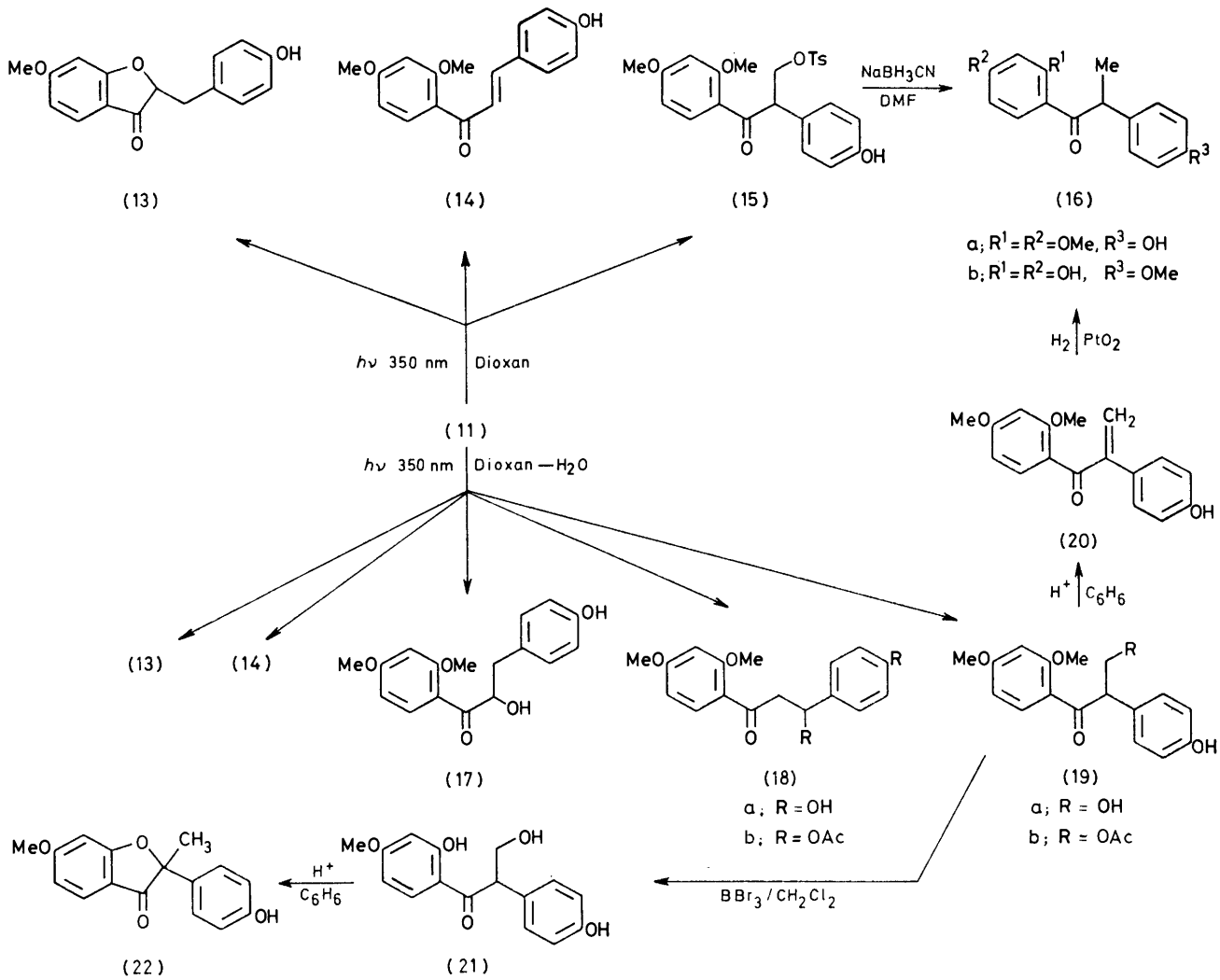


SCHEME 2

Irradiation (350 nm) of the tosylate (11) (*cf.* Scheme 3) in anhydrous dioxan produces 2-(4-hydroxybenzyl)-6-methoxybenzo[*b*]furan-3(2*H*)-one (13), 4-hydroxy-2′,4′-dimethoxychalcone (14), and 4′-hydroxy-2,4-dimethoxy-α-tosyloxymethyldeoxybenzoin (15) in 2, 5, and 10% yields respectively. Structural elucidation of these products was based primarily on ^{1}H n.m.r. data, compound (15) displaying a well-defined ABC system as expected from the vicinal α-methine–methylene arrangement (α-H, δ 4.97; β-CH_2, δ 4.56 and 4.09). These products presumably all follow from heterolytic cleavage of the C_α–O-tosyl bond followed by intramolecular cyclization, elimination, and 1,2-shifts respectively, of the α-tosyloxymethyl derivative (15). These products of photolysis were accompanied by an isomeric pair of α- and β-hydroxydihydrochalcones (17) and (18a), the latter distinguishable from the α-isomer by its spontaneous conversion into the chalcone analogue on addition of acid. Participation of water as a competitive nucleophile during rearrangements was indicated by the formation of both α-hydroxymethyldeoxybenzoin (19a) and the α- and β-hydroxydihydrochalcones (17) and (18a) in good yields (25, 20, and 20% respectively).

Formation of the α-hydroxymethyldeoxybenzoin (19a) and its α-*O*-tosyl derivative (15) both illustrate the desired 1,2-phenyl migration. These compounds were

readily converted into the analogous α-methyldeoxybenzoin (16a) by reduction ($NaBH_3CN$–DMF) of the tosyloxy-function of the latter, or by acid dehydration of the α-hydroxymethyldeoxybenzoin to 1-(4-hydroxyphenyl)-1-(2,4-dimethoxybenzoyl)ethylene (20), followed by catalytic hydrogenation. The resultant 4′-hydroxy-2,4-dimethoxy-α-methyldeoxybenzoin (16a) thus obtained possessed a basic structure (but differing cyclization of the α-hydroxymethyldeoxybenzoin (21), obtained by selective demethylation (BBr_3–CH_2Cl_2) of the 2-*O*-methyl analogue (19a), consistently gave α-cyclization, in contrast with the required β-cyclization. Presumably this results from intramolecular stabilization of the incipient β-carbocation by a 1,2-hydride shift to give the C-α benzylic carbocation, which undergoes cyclization with the 2-hydroxy-group. The product



SCHEME 3

substitution) identical to that of angolensin [3] (16b) and illustrates an α-hydroxychalcone–α-methyldeoxybenzoin relationship which is paralleled in *Pterocarpus angolensis*.

The confirmed natural co-existence of the new α,2′-dihydroxy-4,4′-dimethoxydihydrochalcone (1) and its chalcone analogue, liquiritigenin,[11] with the known isoflavones prunetin,[12] genistein,[13] muningin,[3] and 7-methyltectorigenin [14] in *P. angolensis* also prompted attempts at conversion of the α-tosyloxydihydrochalcone (11) [derived from the dihydrochalcone (8a)] into an isoflavone *via* the α-hydroxymethyldeoxybenzoin (19a), despite predictable difficulties. All attempts at acid thus obtained, the benzo[*b*]furanone (22), was readily characterized by its ^1H n.m.r. spectrum which displayed a total absence of heterocyclic protons, except for a methyl singlet (δ 1.67).

Synthetic α-hydroxy-2′,4,4′-trimethoxydihydrochalcone (8b) (*cf.* Scheme 2) resists, as expected, chemically induced 1,2-phenyl migration under a variety of acidic conditions, giving α- and β-cleavage of the molecule to yield 2,4-dimethoxybenzoic acid and also 2,4-dimethoxyacetophenone. Treatment with ethanolic alkali, however, readily gives an oxidative conversion into the α-hydroxychalcone analogue (12a), a process which is

reversible by catalytic hydrogenation (EtOH–PtO_2). The 4-hydroxy-analogue (17) gives similar results under acid (and alkaline) conditions indicating that the free hydroxy-group on the B-ring does not increase its aptitude for migration under these conditions. The above contrasts with, and emphasises the significance of, the initial photochemical step which not only induces the desired 1,2-shift, but also provides novel access to a number of flavonoid species (*cf.* refs. 15—18).

EXPERIMENTAL

Unless otherwise stated n.m.r. spectra obtained by Fourier transform techniques were recorded for solutions in $CDCl_3$ (Me_4Si as internal reference) and i.r. spectra for solutions in $CHCl_3$. Mass spectra were obtained with a Varian CH-5 instrument, and a JASCO J-20 spectropolarimeter was employed for c.d. determinations (in MeOH). Systems used for separation of components comprised Merck Kieselgel 60 (column chromatography) and Merck Kieselgel 60 PF_{254} (preparative t.l.c.). T.l.c. bands were located by u.v. illumination and/or spray reagents ($HClO_4$–$FeCl_3$ or HCHO–H_2SO_4). Where omitted, n.m.r. and mass-fragmentation spectra of known compounds and of other non-crystalline derivatives are in agreement with the proposed structures.

Isolation of Constituents from P. angolensis.—Drillings (800 g) of the heartwood of *P. angolensis* were extracted with n-hexane (3 × 3 l, 24 h each) followed by MeOH (3 × 3 l, 24 h each) producing, on evaporation of the solvents, an orange-red oil (11.3 g, 1.4%) and a dark brown resin (94.7 g, 11.8%) respectively.

Column chromatography (benzene as eluant; flow rate 20 ml h^{-1}) of a portion (6 g) of the n-hexane extract yielded eleven crude fractions, the last two after limited addition of acetone to the eluant (benzene–acetone, 95 : 5 v/v). Only one of these (fraction 10, retention time 208 h, 615 mg) was further investigated and found to contain α,2′-dihydroxy-4,4′-dimethoxydihydrochalcone (1) following successive purification by column chromatography (n-hexane–acetone, 8 : 2 v/v; flow rate 20 ml h^{-1}, retention time 24 h) and t.l.c. (n-hexane–acetone 9 : 1 v/v, × 5, R_F 0.54).

Twelve crude fractions were obtained by column chromatography (benzene–acetone–MeOH, 7 : 2.5 : 0.5 v/v/v; flow rate 20 ml h^{-1}) of a portion of the MeOH extract (12 g). Column chromatography (1,2-dichloroethane–acetone, 9 : 1 v/v, flow rate 20 ml h^{-1}) of fraction 5 (1.5 g, retention time 88 h) of this separation produced crude prunetin and 7-*O*-methyltectorigenin which both required acetylation prior to further purification due to difficulties in separation. Thus the former was isolated as platelets (23 mg) of pure 4′,5-di-*O*-acetylprunetin, m.p. 223 °C (lit.,[19] 222.5 °C), following column chromatography (1,2-dichloroethane–acetone, 98 : 2 v/v; flow rate 20 ml h^{-1}, retention time 18 h) and t.l.c. (n-hexane–1,2-dichloroethane–acetone, 27 : 70 : 3 v/v/v; R_F 0.24), while 7-*O*-methyltectorigenin similarly yielded needles (51 mg) of the 4′,5-di-*O*-acetyl analogue, m.p. 182—183 °C (lit.,[9] 182—184 °C), by t.l.c. (n-hexane–1,2-dichloroethane–butan-2-one, 50 : 44 : 6 v/v/v; R_F 0.33) after column chromatography (1,2-dichloroethane–acetone, 98 : 2 v/v; flow rate 20 ml h^{-1}, retention time 31 h).

Initial separation of fraction 7 from the MeOH extract (709 mg, retention time 94 h) by column chromatography (1,2-dichloroethane–acetone, 85 : 15 v/v, flow rate 20 ml h^{-1}) gave crude genistein (retention time 12 h) which was purified by t.l.c. (1,2-dichloroethane–acetone, 64 : 4 v/v; × 2). Acetylation gave 4′,5,7-tri-*O*-acetylgenistein which was isolated as platelets (10 mg), m.p. 199 °C (lit.,[20] 198 °C). Liquiritigenin was obtained as needles (15 mg), m.p. 204 °C (lit.,[11] 207 °C), from fraction 8 of the MeOH extract (315 mg, retention time 109 h) by successive column chromatography (chloroform–acetone, 4 : 1 v/v; flow rate 20 ml h^{-1}, retention time 7 h) and t.l.c. (chloroform–acetone, 4 : 1 v/v; × 2, R_F 0.67) followed by a final purification based on the selective solubility of the compound in chloroform.

Muningen crystallized as cubes (120 mg), m.p. 289 °C (decomp.) [lit.,[3] 285 °C (decomp.)], from fraction 11 (380 mg, retention time 175 h) obtained from the MeOH extract.

α,2′-Dihydroxy-4,4′-dimethoxydihydrochalcone (1) crystallized from EtOH as needles (71 mg), m.p. 89.5 °C (Found: C, 67.4; H, 6.0. $C_{17}H_{18}O_5$ requires C, 67.5; H, 6.0%); *m/e* 302 (M^+, 5.8%), 285 (15), 284 (75), 181 (24), 167 (28), 152 (24), 151 (85), 149 (76), 122 (53), 121 (100), and 108 (14); c.d. (*c* 0.052 0) $[\theta]_{225}$ 0, $[\theta]_{230}$ −3.79 × 10^3, $[\theta]_{237}$ 0, $[\theta]_{246}$ 3.48 × 10^3, $[\theta]_{269}$ 0, $[\theta]_{310}$ −10.9 × 10^3, $[\theta]_{370}$ 0; δ 10.47 (s, 2′-OH), 7.50 (d, *J* 10.0 Hz, H-6′), 7.00 (d, *J* 8.8 Hz, H-2 and -6), 6.72 (d, *J* 8.8 Hz, H-3 and -5), 6.41 (dd, *J* 10.0 and 2.5 Hz, H-5′), 6.41 (d, *J* 2.5 Hz, H-3′), 5.16 (m, H-α), 3.81 and 3.72 (s, 2 × OCH_3), 3.47 (d, *J* 7.8 Hz, α-OH), and 3.13 (dd, *J* 13.8 and 5.0 Hz) and 2.84 (dd, *J* 13.8 and 6.6 Hz) (β-CH_2); $\nu_{max.}$ 1 640 cm^{-1} (C=O).

1-(*2-Hydroxy-4-methoxyphenyl*)-3-(*4-methoxyphenyl*)-*propan-2-ol* (2a).—Diborane [generated by the action of 3% (w/v) benzoic acid–H_2SO_4 (50 ml) on powdered $NaBH_4$ (5 g)] was passed through an agitated solution of α,2′-dihydroxy-4,4′-dimethoxydihydrochalcone (1) (100 mg) in tetrahydrofuran (THF) (10 ml; dried over $LiAlH_4$) at 0 °C for 2½ h and subsequently at ambient temperature for 10 h. The reaction was left to stand for 12 h prior to termination by the addition of a 10% (v/v) H_2SO_4–ice mixture (*ca.* 20 ml) and extraction with ether (3 × 15 ml). The combined extracts were washed with 2% (w/v) aqueous $NaHCO_3$ (2 × 10 ml) and H_2O (3 × 10 ml), dried (Na_2SO_4), and evaporated. T.l.c. (1,2-dichloroethane–acetone, 75 : 25 v/v, R_F 0.84) and crystallization from light petroleum (b.p. 40—60 °C)–benzene (7 : 3) gave (2a) as *prisms* (44 mg), m.p. 87 °C (Found: C, 71.0; H, 7.0. $C_{17}H_{20}O_4$ requires C, 70.8; H, 7.0%); *m/e* 288 (M^+, 17%); c.d. (*c* 0.056 1) $[\theta]_{200}$ 0, $[\theta]_{205}$ −1.8 × 10^3, $[\theta]_{207}$ 0, $[\theta]_{210}$ 5.15 × 10^3, $[\theta]_{214}$ 0, $[\theta]_{215}$ −2.3 × 10^3, $[\theta]_{220}$ −2.68 × 10^3, $[\theta]_{225}$ −5.45 × 10^3, $[\theta]_{242}$ 0, $[\theta]_{250}$ 0.21 × 10^3, $[\theta]_{262}$ 0; δ 8.17br (s, 2-OH), 7.00 (d, *J* 8.8 Hz, H-2′ and -6′), 6.81 (d, *J* 7.5 Hz, H-6), 6.73 (d, *J* 8.8 Hz, H-3′ and -5′), 6.20 (d, *J* 2.5 Hz, H-3), 6.28 (dd, *J* 7.5 and 2.5 Hz, H-5), 4.02 (m, C*H*OH), 3.72 and 3.69 (s, 2 × OCH_3), 3.36 (m, CHO*H*), and 2.69 (m, 2 × CH_2). The compound formed a diacetate (2c).

3-(*3,4-Dimethoxyphenyl*)-1-(*2-hydroxy-4,6-dimethoxyphenyl*)*propan-2-ol* (2b).[10]—Reduction of tetra-*O*-methyl-(+)-catechin (3) was performed according to the method of Birch *et al.*[10] to yield an amorphous solid (8 mg), *m/e* 348 (M^+, 41%); c.d. (*c* 0.054 2) $[\theta]_{200}$ 0, $[\theta]_{210}$ −7.3 × 10^3, $[\theta]_{213}$ 0, $[\theta]_{216}$ 9.69 × 10^3, $[\theta]_{221}$ 0, $[\theta]_{228}$ −10.6 × 10^3, $[\theta]_{230}$ −4.5 × 10^3, $[\theta]_{250}$ −0.64 × 10^3, $[\theta]_{262}$ −0.51 × 10^3, $[\theta]_{274}$ 0; δ 8.00br (s, 2-OH), 6.66 (d, *J* 2.5 Hz, H-5′ and -6′), 6.59 (d, *J* 2.5 Hz, H-2′), 6.09 (d, *J* 2.5 Hz, H-3), 5.98 (d, *J* 2.5 Hz, H-5), 4.05 (m, C*H*OH), 3.78 (s, 2 × OCH_3), 3.69 (s, 2 × OCH_3), 3.12—2.34 (m, 2 × CH_2), and 2.34br (s, CHO*H*). The compound formed a diacetate (2d).

α,2′-Dihydroxy-4,4′-dimethoxydihydrochalcone (9).—4,4′-Dimethoxy-2′-methoxymethoxychalcone epoxide,[21] m.p.

86 °C (7a, 200 mg) was hydrogenated (1 atm) in MeOH (25 ml) at ambient temperatures for 10 h, utilizing freshly prepared [22] Pd–$BaSO_4$ as catalyst. Filtration and evaporation of the solvent, followed by t.l.c. (chloroform–acetone, 99 : 1 v/v), yielded *α-hydroxy-4,4′-dimethoxy-2′-methoxymethoxydihydrochalcone* (8a, R_F 0.44) as a pale yellow oil (180 mg) (Found: *m/e*, 328.129. $C_{19}H_{22}O_6$ requires *M* − H_2O, 328.131); δ 7.47 (d, *J* 8.8 Hz, H-6′), 7.00 (d, *J* 8.8 Hz, H-2 and -6), 6.72 (d, *J* 8.8 Hz, H-3 and -5), 6.72 (d, *J* 2.5 Hz, H-3′), 6.59 (dd, *J* 8.8 and 2.5 Hz, H-5′), 5.22 (m, OCH_2OCH_3), 5.22br (s, H-α), 3.81 (s, OCH_3), 3.81br (s, α-OH), 3.72 (s, OCH_3), 3.44 (s, OCH_2OCH_3), and 3.11 (dd, *J* 14.4 and 4.4 Hz) and 2.69 (dd, *J* 14.4 and 6.9 Hz) (β-CH_2). The dihydrochalcone (8a) (40 mg) in MeOH (1 ml) was refluxed on a water-bath in the presence of 3M-HCl (0.2 ml) for 20 min. Dilution with H_2O (2 ml), extraction into ether (2 × 3 ml), and t.l.c. (chloroform–acetone, 24 : 1 v/v; R_F 0.67) followed by evaporation and crystallization from EtOH gave the *α-hydroxydihydrochalcone* (9) as needles (36 mg), m.p. 88.5 °C (Found: C, 67.4; H, 6.0. $C_{17}H_{18}O_5$ requires C, 67.5; H, 6.0%); *m/e* 302 (M^+, 2.4%); δ 10.47 (s, 2′-OH), 7.50 (d, *J* 10.0 Hz, H-6′), 6.97 (d, *J* 8.8 Hz, H-2 and -6), 6.72 (d, *J* 8.8 Hz, H-3 and -5), 6.44 (dd, *J* 10.0 and 2.5 Hz, H-5′), 6.44 (d, *J* 2.5 Hz, H-3′), 5.16 (m, H-α), 3.81 and 3.72 (s, 2 × OCH_3), 3.50 (d, *J* 8.8 Hz, α-OH), and 3.13 (dd, *J* 13.8 and 5.0 Hz) and 2.84 (dd, *J* 13.8 and 6.9 Hz) (β-CH_2); $\nu_{max.}$ 1 640 cm^{-1} (C=O).

Synthesis and Reactions of α-Hydroxy-2′,4,4′-trimethoxydihydrochalcone (8b).—*2′,4,4′-Trimethoxychalcone* (6b).[23] Condensation of 2,4-dimethoxyacetophenone (4b) (2 g) with anisaldehyde (5a) (2.1 g) gave the chalcone (6b) by the method described above. Crystallization from ethanol yielded yellow needles (2.15 g), m.p. 78 °C (lit.,[23] 88 °C), *m/e* 298 (M^+, 90%); δ 7.66 (d, *J* 8.8 Hz, H-6′), 7.59 (d, *J* 16.3 Hz, H-β), 7.47 (d, *J* 8.8 Hz, H-2 and -6), 7.28 (d, *J* 16.3 Hz, H-α), 6.84 (d, *J* 8.8 Hz, H-3 and -5), 6.50 (dd, *J* 8.8 and 2.5 Hz, H-5′), 6.44 (s, H-3′), and 3.84, 3.81, and 3.78 (s, 3 × OCH_3).

αβ-Epoxy-2′,4,4′-trimethoxydihydrochalcone (7b). When prepared, as previously indicated, from the chalcone (6b) (2 g), the epoxide (7b) crystallized from the reaction mixture as *needles* (1.9 g), m.p. 102 °C (Found: C, 68.7; H, 5.7. $C_{18}H_{18}O_5$ requires C, 68.8; H, 5.8%); *m/e* 314 (M^+, 44%); δ 7.81 (d, *J* 8.8 Hz, H-6′), 7.22 (d, *J* 8.8 Hz, H-2 and -6), 6.81 (d, *J* 8.8 Hz, H-3 and -5), 6.50 (dd, *J* 8.8 and 2.5 Hz, H-5′), 6.31 (d, *J* 2.5 Hz, H-3′), 4.27 (d, *J* 2.5 Hz, H-α), 3.84 (d, *J* 2.5 Hz, H-β), and 3.78, 3.75, and 3.53 (s, 3 × OCH_3).

α-Hydroxy-2′,4,4′-trimethoxydihydrochalcone (8b). Catalytic hydrogenation (Pd–$BaSO_4$) of the epoxide analogue (7b) (1.1 g) and purification by t.l.c. (chloroform–acetone, 19 : 1 v/v) yields the α-hydroxydihydrochalcone (8b) (R_F 0.64) which crystallized from EtOH as *platelets* (850 mg), m.p. 64 °C (Found: C, 68.5; H, 6.3. $C_{18}H_{20}O_5$ requires C, 68.3; H, 6.4%); *m/e* 298 (M^+ − H_2O, 60%); δ 7.81 (d, *J* 8.8 Hz, H-6′), 7.03 (d, *J* 8.8 Hz, H-2 and -6), 6.72 (d, *J* 8.8 Hz, H-3, and -5), 6.56 (dd, *J* 8.8 and 2.5 Hz, H-5′), 6.44 (d, *J* 2.5 Hz, H-3′), 5.25 (m, H-α), 3.91 (s, α-OH), 3.88, 3.84, and 3.72 (s, 3 × OCH_3), and 3.06 (dd, *J* 13.8 and 3.8 Hz) and 2.63 (dd, *J* 13.8 and 7.5 Hz) (β-CH_2); $\nu_{max.}$ 1 665 cm^{-1} (C=O).

α-Hydroxy-2′,4,4′-trimethoxychalcone (12a). α-Hydroxy-2′,4,4′-trimethoxydihydrochalcone (8b) (400 mg), 1M-NaOH (10 ml), and EtOH (4 ml) were stirred at 45 °C for 7 h,[24] and the mixture was then diluted with ice–water (*ca.* 75 ml), acidified (3M-HCl; 4 ml), and extracted with ethyl acetate (3 × 50 ml). Acid was removed by washing with H_2O (5 × 50 ml). Drying (Na_2SO_4), evaporation of the solvent, and preparative t.l.c. (n-hexane–benzene–acetone, 5 : 4 : 1 v/v/v; × 2) gave the α-hydroxychalcone (12a) (R_F 0.49) which crystallized from EtOH as *platelets* (114 mg), m.p. 99 °C (Found: C, 68.9; H, 5.8. $C_{18}H_{18}O_5$ requires C, 68.8; H, 5.8%); *m/e* 314 (M^+, 1.6%); δ 7.69 (d, *J* 8.8 Hz, H-6′), 7.08 (d, *J* 8.8 Hz, H-2 and -6), 6.75 (d, *J* 8.8 Hz, H-3 and -5), 6.47 (dd, *J* 8.8 and 2.5 Hz, H-5′), 6.28 (d, *J* 2.5 Hz, H-3′), 3.94—3.91 (m, CH_2), and 3.77, 3.72, and 3.57 (s, 3 × OCH_3); $\nu_{max.}$ 1 670 and 1 730 cm^{-1} (C=O). The compound gave a monoacetate.

α-Hydroxy-2′,4,4′-trimethoxydihydrochalcone (8b). Catalytic hydrogenation (1 atm.) of the α-hydroxychalcone (12a) (30 mg) in EtOH (5 ml) for 3 h over active PtO_2 (10 mg) yielded the corresponding α-hydroxydihydrochalcone (8b), after purification by t.l.c. (n-hexane–benzene–acetone, 5 : 4 : 1 v/v/v; × 2, R_F 0.51), identical to the sample prepared *via* the epoxide (7b).

Synthesis and Reactions of 4-Hydroxy-2′,4′-dimethoxy-α-tosyloxydihydrochalcone (11).—*2′,4′-Dimethoxy-4-methoxymethoxychalcone* (6c). Condensation of *p*-methoxymethoxybenzaldehyde (5b) (1.1 g) with 2,4-dimethoxyacetophenone (4b) (1 g), as described previously, yielded the chalcone (6c). Crystallization from EtOH gave *yellow needles* (1.79 g), m.p. 85 °C (Found: M^+, 328.132. $C_{19}H_{20}O_5$ requires *M*, 328.131); δ 7.59 (d, *J* 8.1 Hz, H-6′), 7.53 (d, *J* 15.0 Hz, H-β), 7.41 (d, *J* 8.8 Hz, H-2 and -6), 7.25 (d, *J* 15.0 Hz, H-α), 6.91 (d, *J* 8.8 Hz, H-3 and -5), 6.44 (dd, *J* 8.1 and 2.5 Hz, H-5′), 6.36 (s, H-3′), 5.09 (s, OCH_2OCH_3), 3.81 and 3.78 (s, 2 × OCH_3), and 3.41 (s, OCH_2OCH_3).

αβ-Epoxy-2′,4′-dimethoxy-4-methoxymethoxydihydrochalcone (7c). Alkaline peroxidation of the chalcone (6c) (1.0 g) under the above conditions gave the epoxide (7c) which crystallized from the reaction mixture as *needles* (980 mg), m.p. 105 °C (Found: M^+, 344.125. $C_{19}H_{20}O_6$ requires *M*, 344.126); δ 7.73 (d, *J* 8.1 Hz, H-6′), 7.17 (d, *J* 8.8 Hz, H-2 and -6), 6.91 (d, *J* 8.8 Hz, H-3 and -5), 6.44 (dd, *J* 8.1 and 2.5 Hz, H-5′), 6.28 (d, *J* 2.5 Hz, H-3′), 5.09 (s, OCH_2OCH_3), 4.22 (d, *J* 2.5 Hz, H-α), 3.84 (d, *J* 2.5 Hz, H-β), 3.78 and 3.53 (s, 2 × OCH_3), and 3.41 (s, OCH_2OCH_3).

α-Hydroxy-2′,4′-dimethoxy-4-methoxymethoxydihydrochalcone (8c). Catalytic hydrogenation (MeOH; 4 h) of the epoxide (7c) (1.0 g) over Pd–$BaSO_4$ gave the α-hydroxydihydrochalcone (8c) which was purified by t.l.c. (chloroform–acetone, 19 : 1 v/v; R_F 0.66) and crystallized from EtOH as *needles* (1.0 g), m.p. 72 °C (Found: C, 65.8; H, 6.4. $C_{19}H_{22}O_6$ requires C, 65.9; H, 6.4%); *m/e* 346 (M^+, 0.9%); δ 7.81 (d, *J* 8.1 Hz, H-6′), 7.03 (d, *J* 8.8 Hz, H-2 and -6), 6.85 (d, *J* 8.8 Hz, H-3 and -5), 6.53 (dd, *J* 8.1 and 2.5 Hz, H-5′), 6.41 (d, *J* 2.5 Hz, H-3′), 5.20 (m, H-α), 5.09 (s, OCH_2OCH_3), 3.87 and 3.84 (s, 2 × OCH_3), 3.44 (s, OCH_2OCH_3), 3.06 (dd, *J* 13.8 and 3.8 Hz), and 2.59 (dd, *J* 13.8 and 7.5 Hz, β-CH_2); $\nu_{max.}$ 1 665 cm^{-1} (C=O).

2′,4′-Dimethoxy-4-methoxymethoxy-α-tosyloxydihydrochalcone (10). The α-hydroxydihydrochalcone (8c) (1.0 g), pyridine (20 ml, dried over NaOH), and toluene-*p*-sulphonyl chloride (1.5 g) were stirred at room temperature for 24 h. After dilution with H_2O (150 ml), the reaction mixture was extracted with ether (3 × 50 ml) and the extract was washed with H_2O (50 ml). Evaporation followed by crystallization from MeOH gave *triangular platelets* (750 mg), m.p. 109 °C (Found: C, 62.3; H, 5.6; S, 6.5. $C_{26}H_{28}O_8S$ requires C, 62.4; H, 5.6; S, 6.4%);

m/e 329 (M^+ —OTs, 16%); δ 7.66 (d, *J* 8.8 Hz, H-6′), 7.42 [d, *J* 8.8 Hz, H-2 and -6 (Ts)], 7.00 [d, *J* 8.8 Hz, H-3 and -5 (Ts)], 6.89 (d, *J* 8.8 Hz, H-2 and -6), 6.70 (d, *J* 8.8 Hz, H-3 and -5), 6.44 (dd, *J* 8.8 and 2.5 Hz, H-5′), 6.31 (d, *J* 2.5 Hz, H-3′), 5.91 (dd, *J* 8.1 and 3.8 Hz, H-α), 5.06 (s, OCH_2OCH_3), 3.83 and 3.78 (s, 2 × OCH_3), 3.41 (s, OCH_2OCH_3), 3.06 (dd, *J* 14.4 and 3.8 Hz) and 2.78 (dd, *J* 14.4 and 8.1 Hz, β-CH_2), and 2.31 [s, CH_3(Ts)]; $\nu_{max.}$ 1 685 cm^{-1} (C=O).

4-Hydroxy-2′,4′-dimethoxy-α-tosyloxydihydrochalcone (11). Hydrolysis of the 4-*O*-protecting group of the α-tosyloxydihydrochalcone (10) (200 mg) was carried out in a mixture of 3M-HCl (4 ml) and MeOH (10 ml), and the product was isolated by extraction with ethyl acetate (3 × 5 ml). Preparative t.l.c. (n-hexane–benzene–acetone, 4 : 4 : 2 v/v/v; R_F 0.29), followed by crystallization from benzene–MeOH (19 : 1 v/v) yielded *needles* (135 mg), m.p. 127 °C (Found: C, 63.1; H, 5.3; S, 7.1. $C_{24}H_{24}O_7S$ requires C, 63.1; H, 5.3; S, 7.0%); *m/e* 285 (M^+ — OTs, 4.9%); δ 7.66 (d, *J* 8.1 Hz, H-6′), 7.44 [d, *J* 8.1 Hz, H-2, and -6 (Ts)], 7.00 [d, *J* 8.1 Hz, H-3 and -5 (Ts)], 6.81 (d, *J* 8.8 Hz, H-2 and -6), 6.50 (d, *J* 8.8 Hz, H-3 and -5), 6.42 (dd, *J* 8.1 and 2.5 Hz, H-5′), 6.31 (d, *J* 2.5 Hz, H-3′), 5.92 (dd, *J* 8.1 and 3.8 Hz, H-α), 5.47br (s, 4-OH), 3.84 and 3.78 (s, 2 × OCH_3), 3.06 (dd, *J* 13.8 and 3.8 Hz) and 2.77 (dd, *J* 13.8 and 8.1 Hz) (β-CH_2), and 2.31 [s, CH_3(Ts)]; $\nu_{max.}$ 1 730 cm^{-1} (C=O).

Photochemical conversions of 4-hydroxy-2′,4′-dimethoxy-α-tosyloxydihydrochalcone (11). Irradiation of the tosylate (11) (200 mg) in dioxan (200 ml) at 350 nm for 45 min, gives three prominent products, (13) (R_F 0.54), (14) (R_F 0.46), and 15 (R_F 0.39), after extraction with ethyl acetate (3 × 50 ml) and preparative t.l.c. (n-hexane–benzene–acetone, 8 : 9 : 3 v/v/v; ×3). 2-(*4-Hydroxybenzyl*)-6-*methoxybenzo*[b]*furan*-3(2H)-*one* (13) was isolated as a yellow oil (6 mg) (Found: M^+, 270.089. $C_{16}H_{14}O_4$ requires *M*, 270.089); δ 7.37 (d, *J* 7.5 Hz, H-4), 7.00 (d, *J* 8.8 Hz, H-2′ and -6′), 6.61 (d, *J* 8.8 Hz, H-3′ and -5′), 6.45 (dd, *J* 7.5 and 2.5 Hz, H-5), 6.34 (d, *J* 2.5 Hz, H-7), 5.53br (s, 4′-OH), 4.66 (dd, *J* 7.5 and 3.8 Hz, H-2), 3.78 (s, OCH_3), and 3.23 (dd, *J* 14.4 and 3.8 Hz) and 2.87 (dd, *J* 14.4 and 7.5 Hz) (CH_2); $\nu_{max.}$ 1 710 cm^{-1} (C=O). *4-Hydroxy-2′,4′-dimethoxychalcone* (14) crystallized from EtOH as yellow needles (20 mg), m.p. 138 °C (Found: M^+, 284.106. $C_{17}H_{16}O_4$ requires *M*, 284.105); δ 7.58 (d, *J* 7.5 Hz, H-6′), 7.55 (d, *J* 15.6 Hz, H-β), 7.31 (d, *J* 8.8 Hz, H-2 and -6), 7.20 (d, *J* 15.6 Hz, H-α), 6.78 (d, *J* 8.8 Hz, H-3 and -5), 6.41 (dd, *J* 8.8 and 2.5 Hz, H-5′), 6.34 (s, H-3′), and 3.78 and 3.75 (s, 2 × OCH_3); $\nu_{max.}$ 1 655 cm^{-1} (C=O). *4′-Hydroxy-2,4′-dimethoxy-α-tosyloxymethyldeoxybenzoin* (15), purified by t.l.c. (1,2-dichloroethane–acetone, 9 : 1 v/v; R_F 0.54) was a highly unstable white amorphous compound (57 mg), *m/e* 285 (M^+ — OTs, 2.5%), 284 (3.8), 270 (6.4), 172 (62), 166 (14), 165 (100), 155 (11), 151 (46), 138 (48), 135 (10), 122 (13), 120 (10), 109 (22), 108 (37), 107 (66), 95 (16), 92 (20), and 91 (100); δ 7.59 (d, *J* 8.1 Hz, H-6), 7.33 [d, *J* 8.8 Hz, H-2 and -6 (Ts)], 7.12 [d, *J* 8.8 Hz, H-3 and -5 (Ts)], 6.89 (d, *J* 8.8 Hz, H-2′ and -6′), 6.55 (d, *J* 8.8 Hz, H-3′ and -5′), 6.34 (dd, *J* 8.1 and 2.5 Hz, H-5), 6.20 (d, *J* 2.5 Hz, H-3), 5.05br (s, 4′-OH), 4.97 (dd, *J* 7.5 and 6.3 Hz, H-α), 4.56 (dd, *J* 9.4 and 7.5 Hz) and 4.09 (dd, *J* 9.4 and 6.3 Hz) (CH_2OTs), 3.72 and 3.70 (s, 2 × OCH_3), and 2.36 [s, CH_3-(Ts)].

Irradiation of the tosylate (11) (200 mg) in dioxan–water (4 : 1 v/v) at 350 nm for 90 min, followed by extraction with ethyl acetate (3 × 70 ml) and preparative t.l.c. (n-hexane–benzene–acetone, 4 : 4 : 2 v/v/v; ×2), gave five products, (13) (R_F 0.59), (14) (R_F 0.50), (17) (R_F 0.40), (18a) (R_F 0.28), and 19a (R_F 0.20). The benzofuranone (13) (8 mg) and the chalcone (14) (21 mg) were identical to those described above. *α,4-Dihydroxy-2′,4′-dimethoxydihydrochalcone* (17) crystallized from benzene–EtOH (14 : 1 v/v) as prisms (40 mg), m.p. 143 °C (Found: C, 67.5; H, 6.0. $C_{17}H_{18}O_5$ requires C, 67.5; H, 6.0%); *m/e* 302 (M^+, 4.1%); δ 7.73 (d, *J* 8.1 Hz, H-6′), 6.87 (d, *J* 8.8 Hz, H-2 and -6), 6.53 (d, *J* 8.8 Hz, H-3 and -5), 6.48 (dd, *J* 8.1 and 2.5 Hz, H-5′), 6.34 (d, *J* 2.5 Hz, H-3′), 5.22 (dd, *J* 7.5 and 3.8 Hz, H-α), 4.06br (s, α-OH), 3.86 and 3.81 (s, 2 × OCH_3), and 3.03 (dd, *J* 13.1 and 3.8 Hz) and 2.53 (dd, *J* 13.1 and 7.5 Hz) (β-CH_2); $\nu_{max.}$ 1 715 cm^{-1} (C=O). *β,4-Dihydroxy-2′,4′-dimethoxydihydrochalcone* (18a) crystallized from H_2O–EtOH (9 : 1 v/v) as brown needles (40 mg), m.p. 113 °C (Found: C, 67.4; H, 5.9. $C_{17}H_{18}O_5$ requires C, 67.5; H, 6.0%); *m/e* 302 (M^+, 20%); δ 7.70 (d, *J* 8.1 Hz, H-6′), 7.16 (d, *J* 8.8 Hz, H-2 and -6), 6.67 (d, 8.8 Hz, H-3 and -5), 6.42 (dd, *J* 8.1 and 2.5 Hz, H-5′), 6.31 (d, *J* 2.5 Hz, H-3′), 5.09 (dd, *J* 7.5 and 5.0 Hz, H-β), 3.77 (s, 2 × OCH_3), 3.64br (s, 2 × OH), and 3.31—3.22 (m, α-CH_2); $\nu_{max.}$ 1 710 cm^{-1} (C=O). The compound gave a diacetate (18b). *4′-Hydroxy-α-hydroxymethyl-2,4-dimethoxydeoxybenzoin* (19a) was purified by t.l.c. (1,2-dichloroethane–acetone, 9 : 1 v/v; R_F 0.17) and crystallized from EtOH as needles (50 mg), m.p. 156 °C (Found: C, 67.5; H, 6.0. $C_{17}H_{18}O_5$ requires C, 67.5; H, 6.0%); *m/e* 284 (M^+ — H_2O, 42%); δ 7.64 (d, *J* 8.1 Hz, H-6), 6.91 (d, *J* 8.8 Hz, H-2′ and -6′), 6.55 (d, *J* 8.8 Hz, H-3′ and -5′), 6.33 (dd, *J* 8.1 and 2.5 Hz, H-5), 6.19 (d, *J* 2.5 Hz, H-3), 5.84br (s, 4′-OH), 4.72 (dd, *J* 8.1 and 5.0 Hz, H-α), 4.07—3.78 (m, CH_2OH), 3.72 and 3.66 (s, 2 × OCH_3), and 2.66br (s, CH_2OH); $\nu_{max.}$ 1 660 cm^{-1} (C=O). The compound gave a diacetate.

4-Hydroxy-2′,4′-dimethoxychalcone (14).—Dehydration of β,4-dihydroxy-2′,4′-dimethoxydihydrochalcone (18a) (10 mg) was accomplished by refluxing with toluene-*p*-sulphonic acid (5 mg) in benzene (3 ml) for 1 h. The mixture was diluted with H_2O (5 ml) and extracted with ether (3 × 5 ml). Evaporation gave the chalcone (14) which was purified by t.l.c. (n-hexane–benzene–acetone, 5 : 4 : 1 v/v/v; R_F 0.15). It crystallized from EtOH as yellow needles (5 mg). This product was identical to the chalcone obtained by photolysis of the tosylate (11).

4′-Hydroxy-2,4-dimethoxy-α-methyldeoxybenzoin (16a).—(*i*) 4′-Hydroxy-2,4-dimethoxy-α-tosyloxymethyldeoxybenzoin (15) (5 mg), $NaBH_3CN$ (1 mg), and *NN*-dimethylformamide (2 ml) were stirred at room temperature for 8 h.[25] Water (4 ml) and 3M-HCl (0.5 ml) was added and the solution was extracted with ether (3 × 5 ml). The extract was washed free of acid with water (4 × 3 ml), evaporated, and purified by t.l.c. (n-hexane–benzene–acetone, 4 : 4 : 2 v/v/v) to yield the deoxybenzoin (16a) (R_F 0.41) which crystallized from EtOH as *platelets* (2 mg), m.p. 142 °C (Found: C, 71.2; H, 6.3. $C_{17}H_{18}O_4$ requires C, 71.3; H, 6.3%); *m/e* 286 (M^+, 1.6%), 167 (20), 166 (10), 165 (100), 149 (49), 122 (12), 121 (22), and 91 (28); δ 7.50 (d, *J* 7.5 Hz, H-6), 6.97 (d, *J* 8.8 Hz, H-2′ and -6′), 6.59 (d, *J* 8.8 Hz, H-3′ and -5′), 6.34 (dd, *J* 8.8 and 2.5 Hz, H-5), 6.28 (s, H-3), 4.66br (s, 4′-OH), 4.62 (q, *J* 6.3 Hz, H-α), 3.75 and 3.73 (s, 2 × OCH_3), and 1.41 (d, *J* 6.3 Hz, α-CH_3); $\nu_{max.}$ 1 670 cm^{-1} (C=O).

(*ii*) The deoxybenzoin (19a) (15 mg), toluene-*p*-sulphonic acid (1 mg), and dry benzene (5 ml) were heated on a water-bath for 5 min. The mixture was poured into water (3

ml), extracted with ethyl acetate (3 × 4 ml), and the extract washed free of acid with water (5 × 2 ml). Following evaporation of the solvent, the α-methyldeoxybenzoin (16a) (4 mg) was obtained by catalytic hydrogenation (1 atm) over PtO_2 (10 mg) in MeOH (5 ml) for 20 min followed by preparative t.l.c. (1,2-dichloroethane–acetone, 95 : 5 v/v; R_F 0.38). The product was identical to that obtained by procedure (*i*).

2,4′-Dihydroxy-α-hydroxymethyl-4-methoxydeoxybenzoin (21).—A solution of the deoxybenzoin (19a) (20 mg) in dry dichloromethane (2 ml) containing BBr_3 (0.3 ml) was stirred for 12 h.[26] The reaction was terminated by addition of ice–water (5 ml) and the mixture was extracted with ether (2 × 2 ml). Evaporation followed by preparative t.l.c. (1,2-dichloroethane–ethyl acetate, 95 : 5 v/v; R_F 0.52) gave a yellow *oil* (8 mg) (Found: *m/e*, 270.087. $C_{16}H_{16}O_5$ requires $M - H_2O$, 270.089); *m/e* 270 ($M^+ - H_2O$, 19%), 151 (53), and 120 (100); δ 9.86 (s, 2-OH), 7.53 (d, *J* 7.0 Hz, H-6), 7.08 (d, *J* 7.0 Hz, H-2′ and -6′), 6.66 (d, *J* 7.0 Hz, H-3′ and -5′), 6.28 (d, *J* 2.0 Hz, H-3), 6.27 (dd, *J* 7.0 and 2.0 Hz, H-5), 4.77br (s, 4′-OH), 4.77 (dd, *J* 8.0 and 4.0 Hz, H-α), 4.03 (dd, *J* 8.0 and 8.0 Hz) and 3.45 (dd, *J* 8.0 and 4.0 Hz) (CH_2OH), 3.72 (s, OCH_3), and 1.53 (s, CH_2OH).

2-(4-Hydroxyphenyl)-6-methoxy-2-methylbenzo[b]*furan-3*(2H)*-one* (22).—A solution of toluene-*p*-sulphonic acid (10 mg) and the deoxybenzoin (21) (20 mg) in dry benzene (5 ml) was refluxed for 12 h. Following evaporation of the solvent, preparative t.l.c. (1,2-dichloroethane–ethyl acetate, 19 : 1 v/v) gave the benzofuranone (22) (R_F 0.22) which crystallized from benzene–n-hexane (minimal hexane) as *cubes* (5 mg), m.p. 140 °C (Found: C, 71.2; H, 5.2. $C_{16}H_{14}O_4$ requires C, 71.1; H, 5.2%); *m/e* 270 (M^+, 81%); δ 8.19 (s, 4′-OH), 7.37 (d, *J* 7.0 Hz, H-4), 7.20 (d, *J* 7.0 Hz, H-2′ and -6′), 6.73 (d, *J* 2.0 Hz, H-7), 6.69 (d, *J* 7.0 Hz, H-3′ and -5′), 6.59 (dd, *J* 7.0 and 2.0 Hz, H-5), 3.87 (s, OCH_3), and 1.69 (s, 2-CH_3); $\nu_{max.}$ 1 710 cm^{-1} (C=O).

Financial support was received from the South African Council of Scientific and Industrial Research, Pretoria, and the Sentrale Navorsingsfonds of this University. One of us (B. C. B. B.) acknowledges the tenure of a C.S.I.R. research assistantship.

[9/2001 *Received*, 18*th December*, 1979]

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