Constituents of Dragon's Blood. Part II.[1] Structure and Oxidative Conversion of a Novel Secobiflavonoid

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A novel secobiflavonoid, (2*S*)-8-*trans*-[2-(6-benzoyloxy-4-hydroxy-2-methoxy-3-methylphenyl)ethenyl]-5-methoxyflavan-7-ol (1a) has been isolated from the resin dragon's blood, and identified by spectra and degradative experiments. Oxidation of (1a) or its derivatives with dichlorodicyanobenzoquinone or silver oxide occurs with ring closure to give new substituted arylfuro[2,3-*h*]benzopyrans or 8-(benzofuran-2-yl)flavans. Oxidation of the furobenzopyran (9b) with hydrogen peroxide–alkali converts the 2-methylphloroglucinol unit into a cyclopent-4-ene-1,3-dione ring.

DRAGON'S BLOOD is a commercially available resin, usually obtained from trees of *Daemonorops draco* (Palmae) in South-east Asia.[2] The resin was investigated by the schools of Brockmann and Robertson,[3] in order to establish the structures of the red pigments dracorhodin and dracorubin. In our hands, however, the resin has revealed itself as a rich source of other new natural substances, namely flavans,[1] biflavonoids,[4] deoxyproanthocyanidins,[4] triflavonoids, chalcones,[1] and terpenoids.[5]

We report here the isolation of a novel example of an oxidised biflavonoid (1a) by careful t.l.c. of a principal fraction from silica gel column chromatography of the crude resin. The phenolic nature of (1a) is shown by

[1] Part I, G. Cardillo, L. Merlini, G. Nasini, and P. Salvadori, *J. Chem. Soc.* (*C*), 1971, 3967.

[2] S. Fränkel and E. David, *Biochem. Z.*, 1927, **187**, 146; F. M. Dean, 'Naturally Occurring Oxygen Ring Compounds,' Butterworths, London, 1963, pp. 412 and 491; W. Spaich and G. Koethke, *Deut. Apoth.-Zeit.*, 1955, **95**, 1193.

[3] H. Brockmann and H. Junge, *Ber.*, 1943, **76**, 751; A. Robertson, and W. B. Whalley, *J. Chem. Soc.*, 1950, 1882; H. A. Olaniyi, J. W. Powell, and W. B. Whalley, *J.C.S. Perkin I*, 1973, 179.

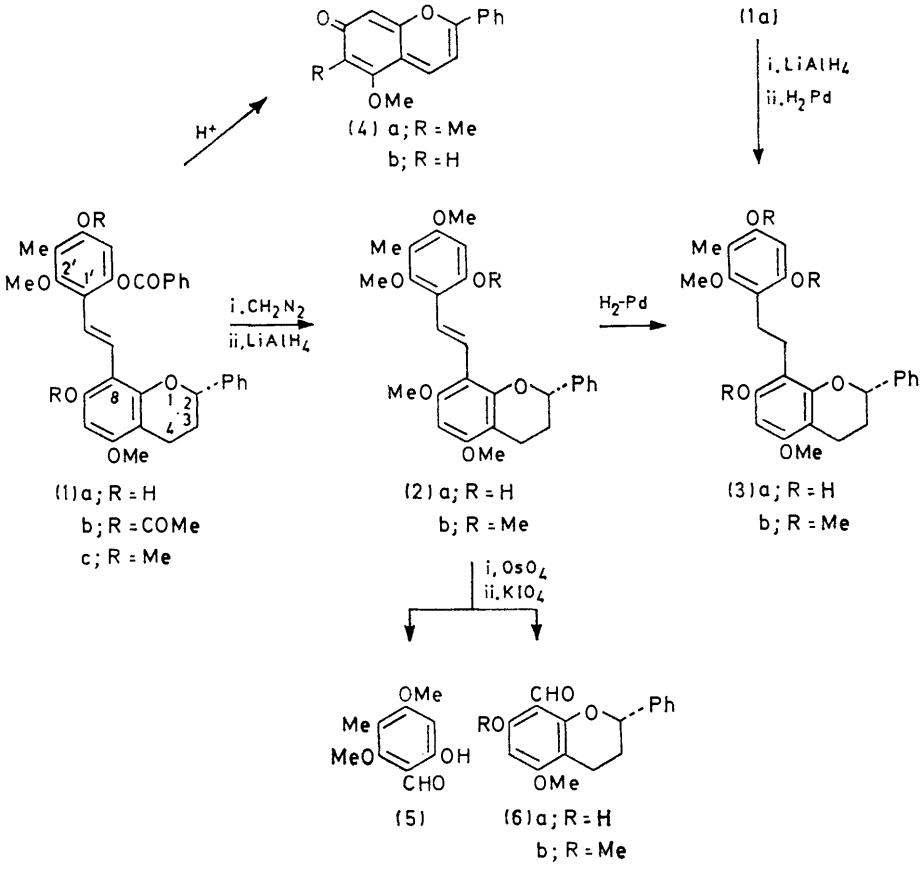
[4] L. Merlini and G. Nasini, Communication to the International Symposium on Polyphenols, Gargnano, Italy, 1975.

[5] F. Piozzi, S. Passannanti, M. P. Paternostro, and G. Nasini, *Phytochemistry*, 1974, **13**, 2231.

the easy formation of a diacetate (1b) and a dimethyl ether (1c). Analytical and spectral data for (1a—c) agreed with the formula $C_{33}H_{30}O_7$ for (1a). The presence of an ester group is shown by the i.r. spectrum, and the n.m.r. spectrum indicates the presence of two aromatic methoxy-groups, an aromatic methyl, two aromatic protons (singlets), the sequence $ArCH(O)\cdot CH_2\cdot CH_2Ar$, and twelve aromatic or olefinic protons. Thus (1a) must have a skeleton of thirty carbon atoms, which suggests a biflavonoid.

Treatment of the substance (1a) with trifluoroacetic or other acids (Scheme 1) gave a mixture containing the protons in the n.m.r. spectrum of (1a) requires that these two protons must be on different rings. In view of the presence of an ester group, and of the u.v. absorption of (1a) at longer wavelength than that of a simple flavan,[1] the other structural unit of (1a) must be at an oxidation level higher than that of a flavan.

Cleavage of the ester group in the dimethyl ether (1c) with lithium aluminium hydride yielded a new phenol (2a). Comparison of spectral data showed that (1c) is a benzoate ester of (2a). It follows that the flavan part of (1a) is linked to a nine-carbon unit. This unit must have an aromatic ring bearing three OR substituents;



SCHEME 1

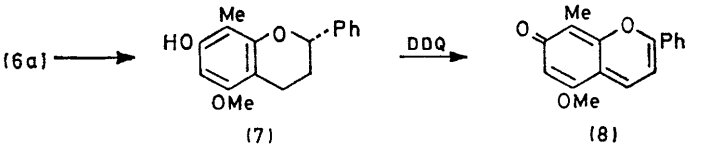
two quinone methides dracorhodin (4a) and nordracorhodin (4b);[1] their formation requires concomitant oxidation, most probably by air. This result indicates that, like other components of the resin,[1,4] compound (1a) is built up from the two flavan units corresponding to (4a) and (4b). In actual fact, the structure (1a) contains only one flavan unit, as shown by the n.m.r. data, and by the loss of only one unit of mass 104 in the mass spectrum (retro-Diels–Alder [6]). As both structures (4a) and (4b) contain two *meta*-substituents on the aromatic ring, the presence of two singlets for the aromatic

[6] S. E. Drewes, 'Chroman and Related Compounds—Mass Spectra, Verlag Chemie, Weinheim, 1974, p. 68.

therefore this ring and the flavan must be linked by a $-CH{=}CH-$ bridge. Moreover, the n.m.r. data (showing one aromatic proton on each ring) require that the aromatic methyl group must be on the single aromatic ring and not on the flavan. These results establish the gross structure of (2a) except for the position of the benzoate. Confirmation of this structure came from catalytic reduction of the methyl ether (2b) to the dihydro-derivative (3b); signals for the new $ArCH_2\cdot CH_2Ar$ group appeared clearly in the n.m.r. spectrum. In structures (1a) and (2a) and their derivatives, n.m.r. signals for the vinylic protons are always masked by the overlapping aromatic proton absorption. Conversely,

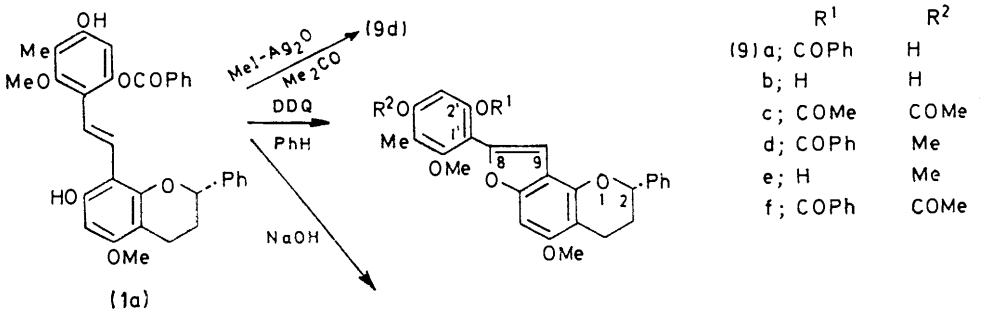
cleavage of the ester group in (1a) by hydride and catalytic reduction of the non-isolated intermediate afforded a triphenol (3a), which was easily methylated to (3b).

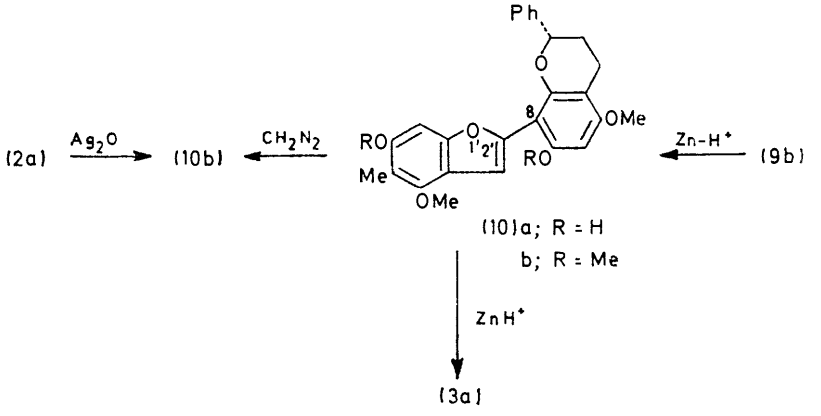
Lemieux–Johnson oxidation of the phenol (2a) afforded two aromatic aldehydes, (5) and (6b), thus confirming the presence of a stilbene double bond. Analytic and spectral data for (6b) are consistent with an 8- or a 6-formyl-5,7-dimethoxyflavan structure. The former was established by the synthesis of (6b) by methylation of the aldehyde (6a), prepared in turn from 5-methoxyflavan-7-ol [1] *via* a Gattermann reaction.[7] Support for this assignment was obtained by reduction (Zn–AcOH) of the aldehyde (6a) to 5-methoxy-8-methylflavan-7-ol,[7] the structure of which was established by oxidation with aldehyde. The mass and u.v. spectra (comparison with 2-hydroxy-4,6-dimethoxybenzaldehyde [8]) spectra are consistent with structure (5). The sequence of the substituents on the aromatic ring of (5) and thus of (1a) and derivatives is also established by the formation of



(7) (8)

(4a) from treatment of (1a) with acid. This latter reaction requires also that the benzoate ester group is *ortho* to the stilbene double bond, as also confirmed by oxidative reactions (see later). We have no evidence supporting a particular mechanism for the conversion of (1a) into (4a) and (4b), although a vinylogous Fries reaction to reconstitute the C_{15} chain leading to (4a), followed by acid-induced dealkylation of the flavan moiety and by oxidation in air seems attractive.





SCHEME 2

dichlorodicyanobenzoquinone [1] to the quinone methide (8); the product (8) was different (t.l.c. and n.m.r.) from the known 6-methyl isomer, dracorhodin (4a).[1]

The other aldehyde (5) was isolated in only a small amount. However, comparison of the structures (6b) and (2b) requires (5) to be a dimethoxy-methylsalicyl-

The configuration of the stilbene double bond of (1a) was established as *trans* by the 100 MHz n.m.r. spectrum, which showed the signal for one of the two protons as a doublet, J 17 Hz.

The optical activity of (1a) must be due to C-2, which is the only chiral centre. The 2*S*-absolute configuration

[7] A. Robertson, W. B. Whalley, and J. Yates, *J. Chem. Soc.*, 1950, 3117.

[8] F. Santavy, D. Walterowa, and L. Hruban, *Coll. Czech. Chem. Comm.*, 1972, **37**, 1825.

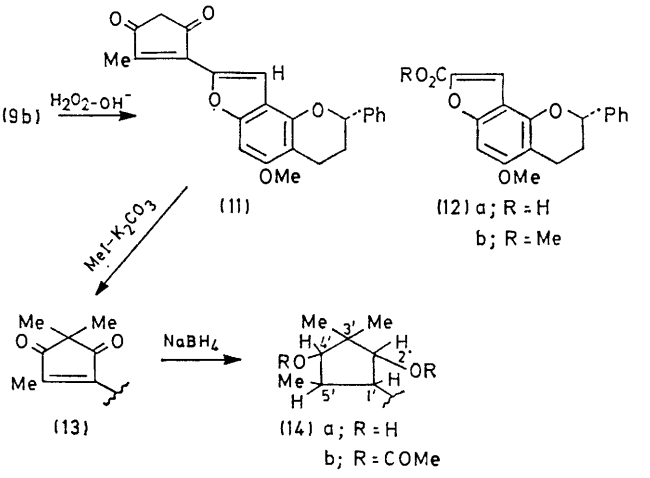
was established by hydrogenolysis of the derivative (9b) (see later) with zinc and sulphuric acid to the known (2*S*)-5-methoxyflavan-7-ol.[1]

The structure (1a) is consistent with biogenesis from a 3,8-linked biflavanoid, by oxidation with cleavage of the 2,3-bond. Although no example of a similar structure in nature has been reported so far, *in vitro* oxidation of a 3-substituted flavonoid with such a cleavage *via* a Baeyer–Villiger reaction has been achieved.[9]

Compound (1a) undergoes some interesting oxidation reactions. Treatment with 2,3-dichloro-5,6-dicyanobenzoquinone (DDQ) in benzene gave compound (9a) in high yield (Scheme 2). The same reaction most probably occurred during attempted methylation of (1a) with methyl iodide and silver oxide, the latter acting as an oxidant to give (9a), which is immediately methylated to give (9d). The formation of a monomethyl ether (9d), and of a monoacetate (9f) of (9a) shows that one OH group of (1a) has taken part in the oxidation reaction. The mass spectrum of (9a) shows a molecular ion at *m/e* 536 [2 mass units less than (1a)], and in the n.m.r. spectrum the number of aromatic protons is two less than in (1a), and a new singlet appears at δ 7.06. The flavan heterocyclic ring appears unaltered (n.m.r. and mass spectra), as is the ester group, which can be cleaved ($LiAlH_4$) to give the phenol (9b). The 2-arylbenzofuran structure (9a) is consistent with these data, and with the course of similar reactions of 2,2′- and 2,4′-dihydroxystilbenes.[10] Also the same mechanism should be operative, *i.e.* oxidation to a phenoxyl radical, which is mesomeric with a β-carbon radical, followed by radical addition to the double bond or by nucleophilic addition of the *ortho*-OH to the quinone methide system of the radical, and oxidation to the benzofuran.[10]

However if (1a) is treated with methanolic potassium hydroxide in order to hydrolyse the ester group, the isomer (10a) of (9b) can be isolated, together with benzoic acid. Again the mass and n.m.r. spectra and the formation of a dimethyl ether (10b) indicate that (10a) has a 2-arylbenzofuran nucleus, and the only possible structure is the one shown. In this case it must be the new *ortho*-OH formed by hydrolysis of the benzoate (1a), which is involved in cyclization, rather than the 7-OH of the flavan. Confirmation of this hypothesis came from synthesis of (10b) by oxidation (Ag_2O) of (2a), in which all the OH groups except for that in position 6′ are protected by methylation. In this latter case a direct redox addition of the phenoxyl radical to the double bond must be invoked.[11] Compound (10b) is identical with the monomethyl ether of (10a) (t.l.c. and spectral comparison). Moreover, direct conversion of (9b) into the isomer (10a) could be achieved, although in low yield, by treatment with zinc and acid. Under more forcing conditions, hydrogenolysis of the benzofuran ring occurred, with formation of (3a).

Another unusual oxidation reaction was observed when the benzofuran (9b) was treated with hydrogen peroxide in alkaline medium (Scheme 3). Of the two main products, one was easily identified as furobenzopyrancarboxylic acid (12a), derived from complete

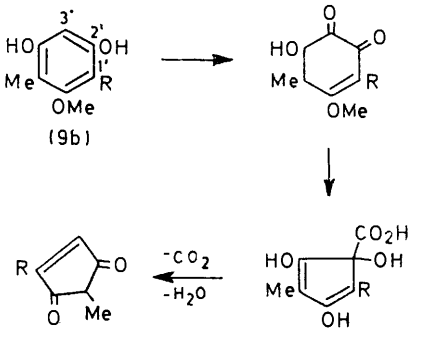


SCHEME 3

oxidation of the dihydroxy-substituted aromatic ring of (9b). The other product (11), $C_{24}H_{20}O_5$, is a yellow solid, with strong carbonyl i.r. bands at 5.80 and 5.90 μm and a highly conjugated chromophore. The n.m.r. spectrum indicates that whereas the furobenzopyran unit has not changed, the ' upper ' part of the molecule has lost two carbon atoms. One is that of the methoxy-group, whereas the vinylic methyl group (uncoupled in the n.m.r.) is still present. Methylation (MeI–K_2CO_3) of (11) introduced two geminal methyl groups. This result, combined with the presence of a CH_2 singlet at δ 2.98 in the n.m.r. spectrum of (11), can be explained in terms of double alkylation of a ·CO·CH_2·CO· system. All the available evidence is consistent with the structures (11) and (13), which are further confirmed by reduction ($NaBH_4$) of (13) to the hexahydro-diol (14a). The main features of the spectrum of this product are a methyl doublet at high field, a signal for a new benzylic proton (1′) with two vicinal couplings, and doublets for the two ·CH·O· units, coupled with H-1′ or H-5′, and both shifted at lower field by acetylation [to (14b)]. The formation of cyclopent-4-ene-1,3-diones by oxidation of orcinol derivatives to *o*-quinones, followed by ring contraction due to a benzylic rearrangement, has been reported.[12] However, this mechanism cannot apply in the oxidation of (9b), as the only free position for oxidation and formation of the quinone is 3′. Therefore one would expect that the ring contraction takes place between C-2′ and -3′or C-3′ and -4′ (Scheme 4). On the contrary, the structure of the oxidation product (11) implies the demethylation of the 6′-OMe, followed by ring contraction between C-1′ and -5′ of (9b). An attractive mechanism for the reaction is that already

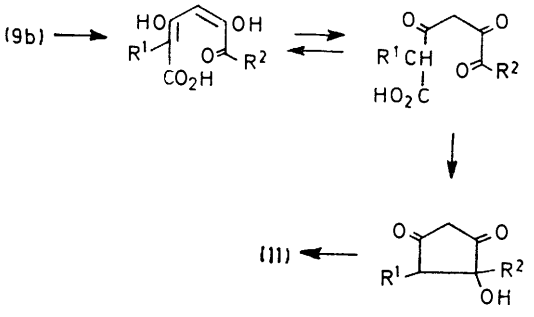
[9] L. Jurd, *Tetrahedron*, 1966, **22**, 2913.
[10] B. Cardillo, M. Cornia, and L. Merlini, *Gazzetta*, 1975, **105**, 1151.
[11] F. Minisci, *Accounts Chem. Res.*, 1975, **8**, 165.
[12] R. K. Haynes and H. Musso, *Chem. Ber.*, 1974, **107**, 3723.

proposed [13] for tetraphenylresorcinol, which involves oxidation to a diradical (on C-1′ and -5′ in this case), followed by coupling and extrusion of CO. The formation, however, of a labile colourless compound in our reaction which is quickly converted into the yellow (11)



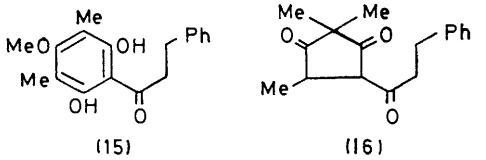
SCHEME 4

by treatment with acid suggests the following sequence: hydrolysis of the 6′-OMe group, followed by oxidation of the 1′,6′- or 5′,6′-double bond with cleavage to give the tautomer of a 1,2,4-triketone, which could condense to give an aldol, in turn easily dehydrated to (11) in acidic medium (Scheme 5).



SCHEME 5

Compounds (15) and (16), related to both (9) and (13) have been found in the plant *Myrica gale*,[14] where an oxidation process similar to that observed by us could



occur. Oxidation of 4,6-dihydroxy-2-methoxy-3-methyldihydrochalcone with alkaline hydrogen peroxide or sodium hydroxide in an attempt to obtain a derivative of (16) was, however, unsuccessful.

[13] H. Güsten, G. Kirsch, and D. Schulte-Frohlinde, *Tetrahedron*, 1968, **24**, 4393.

EXPERIMENTAL

U.v. spectra were measured for solutions in 95% ethanol with a Beckman DK-2 apparatus; n.m.r. spectra were obtained with a Varian A-60 or XL-15-100 instrument. Unless otherwise stated, column chromatography was performed with Merck silica gel (0.05—0.20 mm) and t.l.c. with Merck silica gel HF_{254}.

Isolation of the Secobiflavonoid (1a).—Powdered commercial dragon's blood resin (200 g) was mixed with 100 g of silica gel, and placed on a silica gel column. After elution with hexane, increasing amounts of ether were added to the eluant; with hexane–ether (1 : 1) a complex mixture was collected. Preparative t.l.c. (benzene–ether, 4 : 1) gave (2S)-8-trans-[2-(6-*benzoyloxy*-4-*hydroxy*-2-*methoxy*-3-*methylphenyl*)*ethenyl*]-5-*methoxyflavan*-7-*ol* (1a), which was detected on t.l.c. plates by spraying with cerium(IV) sulphate in sulphuric acid (brown colour on heating); R_F 0.43 in ether and 0.15 in benzene–ether (9 : 1) on Bakerflex IB-F plates. Compound (1a) has m.p. 115—118° (from ether–hexane), $[\alpha]_D^{20}$ −60° (*c* 0.57 in $CHCl_3$), *m/e* 538, $\lambda_{max.}$ 232.5, 316, and 326sh nm (ε 31 000, 24 900, and 24 300), $\lambda_{max.}$ ($CHCl_3$) 3.0 (OH) and 5.8 μm (OCOPh), δ ($CDCl_3$) 2.10 (s, Me), *ca.* 2.0 (m, H_2-3), *ca.* 2.6 (m, H_2-4), 3.56 and 3.70 (OMe), 4.90 (X of ABX, PhC*H*O), 6.04 (s, H-6), 6.38 (s, H-5′), 6.97 (1 H, *J* 17 Hz), 7.1—8.2 (11 H), and 6.8—7.1 (2 OH).

Acidic Degradation of the Secobiflavonoid (1a).—Compound (1a) (250 mg) was dissolved in trifluoroacetic acid (8 ml) and kept at room temperature for 20 h. Evaporation and chromatography with chloroform–ether gave compounds (4a) (35%) and (4b) (10%), identified by t.l.c. comparison and n.m.r. spectra.[1]

The Diacetate (1b).—Acetylation of (1a) (100 mg) [Ac_2O (5 ml) and AcONa (100 mg) at 60 °C for 30 min] gave the diacetate (1b) as a glassy solid, $[\alpha]_D^{20}$ −47.5° (*c* 0.19 in MeOH), *m/e* 622, $\lambda_{max.}$ 230sh, 289sh, and 316 nm (ε 31 300, 12 800, and 15 100), $\lambda_{max.}$ (alkaline EtOH) 346 nm (ε 16 200), $\lambda_{max.}$ (Nujol) 5.68 (OCOMe) and 5.75 μm (OCOPh), δ ($CDCl_3$) 2.01 (Me), 2.14 and 2.20 (Ac), 1.84—2.10 (H_2-3), 2.59 (m, H_2-4), 3.50 and 3.67 (OMe), 4.84 (H-2), 6.17 (s, H-6), 6.68 (s, H-5′), 7.1—7.5 (10 H), and 7.9—8.0 (2 H).

The Dimethyl Ether (1c).—Compound (1a) was methylated (CH_2N_2–Et_2O for 1 week) to give the *dimethyl ether* (1c) as white crystals, m.p. 179° (from ether) (Found: C, 73.55; H, 6.2. $C_{35}H_{34}O_7$ requires C, 74.2; H, 6.05%), *m/e* 566, $\lambda_{max.}$ 234, 318, and 326sh nm (ε 32 400, 26 000, and 25 700), $\lambda_{max.}$ (KBr) 5.78 μm (OCOPh), δ [$CDCl_3$–$(CD_3)_2CO$ (2 : 1)] 2.12 (Me), 2.0—2.2 (H_2-3), 2.5—2.7 (H_2-4), 3.52 and 3.54 (OMe), 3.82 (2 OMe), 4.97 (H-2), 6.10 (s, H-6), 6.54 (s, H-5′), and 7.3—8.2 (12 H).

The Phenol (2a).—A solution of the dimethyl ether (1c) (200 mg) in dry ether was refluxed for 0.5 h with an excess of lithium aluminium hydride. Treatment with water and dilute acid, extraction with ethyl acetate, and preparative t.l.c. [hexane–AcOEt (2 : 1)] gave the phenol (2a) as a glassy solid, *m/e* 462(100%), 358(37), 343(28), 283(6), 179(37), and 108(3), δ ($CDCl_3$) 1.90 (Me), 1.8—2.2 (H_2-3), 2.64 (H_2-4), 3.42, 3.66, 3.76, and 3.78 (OMe), 5.05 (H-2), 6.12 (s, H-6), 6.26 (s, H-5′), and 7.0—7.6 (7 H).

The *Per-O-methyl Derivative* (2b).—The phenol (2a) was methylated as described for (1a), to give the penta-methoxy-

[14] T. Anthonsen, I. Falkenberg, M. Laake, A. Midelfart, and T. Mortensen, *Acta Chem. Scand.*, 1971, **25**, 1929.

compound (2b), m.p. 118°, *m/e* 476(100%), 372(28), and 357(33), $\lambda_{max.}$ 306 and 329sh nm (ε 15 400 and 10 600).

The Triphenol (3a).—(a) *From the secobiflavonoid* (1a). The reduction product (2a) (not isolated) was hydrogenated in ethyl acetate over 10% palladium–carbon.

(b) *From the benzofuran* (10a). A solution of (10a) (50 mg) in methanolic 10% sulphuric acid was refluxed for 15 h with an excess of zinc powder. The reaction was monitored by t.l.c. Evaporation, treatment with aqueous sodium carbonate, extraction with ether, and preparative t.l.c. gave the triphenol (3a) as a glassy solid, *m/e* 436, $\lambda_{max.}$ 280 nm (ε 3 580), $\lambda_{max.}$ (alkaline EtOH) 290 nm (ε 8 000), δ [$(CH_3)_2CO$] 2.0 (Me), 1.9—2.2 (H_2-3), 2.5—2.8 (H_2-4 and $ArCH_2{\cdot}CH_2Ar$), 3.57 and 3.73 (OMe), 5.03 (H-2), 6.15 and 6.27 (s, H-5′ and H-6), 7.3—7.6 (5 H), 7.71 (OH), and 7.81 (2 OH).

The Pentamethoxy-compound (3b).—Reduction of (2b) over 10% palladium–carbon in ethyl acetate or methylation of (3a) with methyl iodide–potassium carbonate in acetone gave the *methyl ether* (3b), m.p. 120°, $[\alpha]_D^{20}$ −42° (*c* 0.52 in $CHCl_3$) (Found: C, 72.55; H, 7.5. $C_{29}H_{34}O_6$ requires C, 72.8; H, 7.15%), *m/e* 478(68%), 284(90), 283(100), 209(95), 195(100), 179(18), 165(68), and 104(59), δ ($CDCl_3$) 2.03 (Me), 2.0—2.2 (H_2-3), 2.6—2.9 (H_2-4), 2.78 ($ArCH_2{\cdot}CH_2Ar$), 3.50 3.55, 3.74, 3.80, and 3.82 (OMe), 4.92 (H-2), 6.10 and 6.15 (H-5′ and H-6), and 7.15—7.5 (5 H).

(2S)-7-*Hydroxy*-5-*methoxyflavan*-8-*carbaldehyde* (6a).—*Compound* (6a) was synthesized as reported [7] from (2*S*)-5-methoxyflavan-7-ol and had m.p. 125°, *m/e* 284(47%), 193(100), 152(33), and 104(53) (Found: C, 71.8; H, 5.8. $C_{17}H_{16}O_4$ requires C, 71.8; H, 5.65%), $[\alpha]_D^{20}$ −97.5° (*c* 0.53 in $CHCl_3$), $\lambda_{max.}$ 296 and 330sh nm (ε 19 500 and 3 840), δ ($CDCl_3$) 7.45 (s, ArCHO).

Oxidation of the Phenol by Osmium Tetraoxide.—Osmium tetraoxide (100 mg) dissolved in dry ether was added dropwise to a stirred solution of (2a) (30 mg) in dry dioxan (5 ml); the reaction was monitored with t.l.c. until the starting material had disappeared, then water (2 ml) and an excess of potassium periodate were added, and stirring was continued for 20 min. Evaporation, dilution, extraction with ether, and preparative t.l.c. with hexane–ethyl acetate (2 : 1) gave 6-hydroxy-2,4-dimethoxy-3-methylbenzaldehyde (5), $\lambda_{max.}$ 231, 236sh, 286, and 330 nm, *m/e* 196(100%), 181(41), 178(42), and 150(76); and (2*S*)-5,7-dimethoxyflavan-8-carbaldehyde (6b), m.p. 95—100°, *m/e* 298(48%), 207(100), 194(71), and 136(38), $\lambda_{max.}$ 229, 290, and 320sh nm (ε 12 700, 12 400, and 4 000), identical (t.l.c. and mass and n.m.r. spectra) with a specimen obtained by methylation of (6a) (MeI–Ag_2O in Me_2CO for 0.5 h at reflux).

(2S)-5-*Methoxy*-8-*methylflavan*-7-*ol* (7).—Prepared from (6a) by the reported [7] method, the *flavanol* (7) had m.p. 140—143° (Found: C, 75.65; H, 6.95. $C_{17}H_{18}O_3$ requires C, 75.55; H, 6.7%), *m/e* 270. Oxidation of (7) with 2 mol. equiv. of DDQ in benzene at reflux for 2 h gave the quinone methide (8), m.p. 170°, *m/e* 266(44%), 251(100), 223(6), 181(6), and 152(8), $\lambda_{max.}$ 272, 320, 330sh, 378, and 500 nm (ε 11 000, 8 500, 7 200, 4 450, and 6 700).

(2S)-8-(2-*Benzoyloxy*-4-*hydroxy*-5-*methyl*-6-*methoxyphenyl*)-3,4-*dihydro*-5-*methoxy*-2-*phenyl*-2H-*furo*[2,3-h]-1-*benzopyran* (9a).—A solution of the secobiflavonoid (1a) (500 mg) in dry benzene (30 ml) was treated with an excess of DDQ, and stirred for 1 h at room temperature. Filtration, evaporation, and preparative t.l.c. gave the *furobenzopyran* (9a) (50%), m.p. 120°, $[\alpha]_D^{20}$ −52° (*c* 0.40 in $CHCl_3$) (Found: C 73.1; H, 5.35. $C_{33}H_{28}O_7$ requires C, 73.85; H, 5.25%), *m/e* 536, 432 (*M* − 104), 328, 327 (432 − 105), 300, and 284, $\lambda_{max.}$ 286sh and 305 nm (ε 9 900 and 10 800), $\lambda_{max.}$ (alkaline EtOH) 320 nm (ε 10 600), $\lambda_{max.}$ (Nujol) 3.0br (OH) and 5.75 μm (OCOPh), δ ($CDCl_3$) 2.14 (Me), 2.0—2.3 (H-3), 2.70 (m, H_2-4), 3.62 and 3.66 (OMe), 5.09 (X of ABX, H_2-2), 6.09 (s, H-3′), 6.55 (H-6), 7.06 (s, H-9), and 7.3—8.2 (10 H).

The Diphenol (9b).—A solution of the furobenzopyran (9a) (100 mg) in ether was treated with lithium aluminium hydride in the usual way, and gave the diphenol (9b) as a glassy solid, m.p. 63—65°, *m/e* 432, $\lambda_{max.}$ 256.5, 287sh, 300, 308sh, and 330sh nm (ε 8 000, 11 700, 12 500, 12 400, and 7 200), δ ($CDCl_3$) 2.12 (Me), 2.0—2.4 (H_2-3), 2.65—2.95 (H_2-4), 3.60 and 3.82 (OMe), 5.10 (H-2), 6.25 (s, H-3′), 6.62 (s, H-6), and 7.14 (s, H-9), δ [$(CH_3)_2CO$] 2.11 (Me), 3.58 and 3.84 (OMe), 4.64 (OH), 5.16 (H-2), 6.20 (s, H-3′), 6.77 (s, H-6), 6.95 (s, H-9), and 7.2—7.6 (5 H).

Hydrogenolysis of the Diphenol (9b).—To the diphenol (9b) (150 mg) dissolved in methanol 10% sulphuric acid (8 ml) an excess of zinc was added, and the mixture was refluxed for 20 h. The usual work-up and preparative t.l.c. gave 8-ethyl-5-methoxyflavan-7-ol and (2*S*)-5-methoxyflavan-7-ol, identified by mass and n.m.r. spectra and optical rotation.[1]

The Diacetate (9c).—Acetylation [Ac_2O–pyridine] of the diphenol (9b) gave the diacetate (9c), m.p. 155—157°, *m/e* 516(90%), 474(38), 432(24), 370(75), and 328(100), $\lambda_{max.}$ (Nujol) 5.70 μm (OCOMe), δ ($CDCl_3$) 2.12 (Me), 2.20 and 2.30 (Ac), 2.0—2.8 (4 H), 3.60 and 3.86 (OMe), 5.13 (H-2), 6.65 and 6.75 (H-3′ and H-6), 7.05 (s, H-9), and 7.20—7.60 (5 H).

The Methoxy-benzoate (9d).—A solution of the secobiflavonoid (1a) (250 mg) in acetone was refluxed for 10 h with methyl iodide (1.5 ml) and silver oxide (250 mg). The usual work-up and t.l.c. afforded the methoxy-benzoate (9d) [which was also prepared quantitatively by treating (9a) (400 mg) with methyl iodide–potassium carbonate in acetone] as pale yellow crystals, m.p. 80—85°, *m/e* 550(53%), 446(35), 341(5), 313(15), 298(13), and 105(100), $\lambda_{max.}$ 306 nm (ε 3 300), $\lambda_{max.}$ ($CHCl_3$) 5.8 μm (OCOPh), δ ($CDCl_3$) 2.20 (Me), 1.9—2.9 (4 H), 3.62, 3.66, and 3.85 (OMe), 5.10 (H-2), 6.10 (s, H-3′), 6.62 (s, H-6), 7.05 (s, H-9), and 7.2—8.3 (10 H).

The Methoxy-phenol (9e).—The methoxy-benzoate (9d) was treated with lithium aluminium hydride as described above to give the phenol (9e) as a glassy solid, *m/e* 446, δ ($CDCl_3$) 2.12 (Me), 3.64, 3.72, and 3.88 (OMe), 5.17 (H-2), 6.50 (s, H-6), 6.70 (s, H-3′), and 7.20 (s, H-9).

The Acetate (9f).—The hydroxy-benzoate (9a) was acetylated [Ac_2O–pyridine] to give the acetate (9f) as a glass, δ ($CDCl_3$) 2.17 (Me), 2.33 (Ac), 3.64 and 3.67 (OMe), 5.10 (H-2), 6.14 (s, H-3′), 6.92 (s, H-6), and 7.15 (s, H-9) (the assignment of the two last signals is based on the nuclear Overhauser effect between 5-OMe and H-6 in benzene solution).

(2S)-8-(6-*Hydroxy*-4-*methoxy*-5-*methylbenzofuran*-2-*yl*)-5-*methoxyflavan*-7-*ol* (10a).—The secobiflavonoid (1a) (200 mg) in methanolic 2N-potassium hydroxide (10 ml) was heated for 30 min on a steam-bath; dilution, acidification, extraction with ether, and preparative t.l.c. gave benzoic acid and the benzofuran (10a), m.p. 215—218° (from ether), *m/e* 432(95%), 328(100), 313(55), 299(4), and 164(31), $\lambda_{max.}$ 310sh, 320, and 333sh nm (ε 22 300, 25 400, and 16 800), $\lambda_{max.}$ (alkaline EtOH) 332 nm (ε 13 800), δ [$(CD_3)_2CO$] 2.10 (Me), 2.0—2.2 (H_2-3), 2.70 (m, H_2-4), 3.50 and 3.80 (OMe), 5.05 (H_2), 6.20 (s, H-6), 6.80 (s, H-7′), 7.05 (s, H-3′), 7.2—7.6

(5 H), and 8.25 (OH). A few mg of (10a), identified by u.v. spectrum and t.l.c. comparison, were also obtained by treatment of (9b) (10 mg) with zinc in methanolic 5% sulphuric acid for 30 min at reflux.

The Methyl Ether (10b).—Treatment of the phenol (2a) with silver oxide in acetone for 1 h at reflux, or methylation of (10a) with diazomethane, yielded the methyl ether (10b), m.p. 75—83°, *m/e* 460(70%), 341(35), 283(5), and 178(24), $\lambda_{max.}$ 320sh and 332 nm (ε 18 000 and 20 000), δ ($CDCl_3$) 2.16 (Me), 2.1—2.3 (H_2-3), 2.75 (H_2-4), 3.82, 3.88, and 3.92 (OMe), 5.08 (H-2), 6.15 (s, H-6), 6.75 (s, H-7'), 6.90 (s, H-3'), and 7.2—7.4 (5 H).

(2S)-5-*Methoxy*-8-(2-*methyl*-3,5-*dioxocyclopent*-1-*enyl*)-3,4-*dihydro*-2-*phenyl*-2H-*furo*[2,3-h]-1-*benzopyran* (11).—The furobenzopyran (9b) (300 mg) was added to a stirred solution containing methanolic N-potassium hydroxide (20 ml), water (2 ml), and hydrogen peroxide (1 ml) during 10 min at room temperature. Dilution, treatment with dilute hydrochloric acid, and extraction with chloroform gave a mixture which was separated on a column of silica gel (chloroform–methanol as solvent). Elution with $CHCl_3$–MeOH (100 : 1) gave compound (11); use of a ratio of 100 : 50 gave compound (12a) (see below) and a ratio of 50 : 50 gave a few mg of a very polar compound which on acidification with concentrated hydrochloric acid gave compound (11). The *cyclopentenedione* (11) formed yellow crystals, m.p. 228—232° (Found: *m/e* 388.1281 ± 0.004. $C_{24}H_{20}O_5$ requires *M*, 388.1311), $\lambda_{max.}$ 267.5, 279sh, and 407 nm (ε 14 200, 11 850, and 22 000), $\lambda_{max.}$ (alkaline EtOH) 270sh, 297, and 500sh nm (ε 8 900, 13 200, and 2 500), $\lambda_{max.}$ (Nujol) 5.8 and 5.9 μm (CO conj.), δ ($CDCl_3$) 2.24 (m, H_2-3), 2.46 (Me), 2.77 (m, H_2-4), 2.98 (s, CO·CH_2·CO), 3.87 (OMe), 5.15 (H-2), 6.60 (s, H-6), 7.90 (s, H-9), and 7.35—7.50 (5 H).

The dimethyl derivative (13). The cyclopentenedione (150 mg) was refluxed for 2 h with methyl iodide (0.5 ml) and potassium carbonate (200 mg) in dry acetone (20 ml). Filtration, concentration, and precipitation with ether gave the dimethyl derivative (13), m.p. 223—225°, *m/e* 416(66%), 312(100), and 297(10), $\lambda_{max.}$ 268.5, 277sh, and 410 nm (ε 14 200, 12 500, and 23 400), $\lambda_{max.}$ (Nujol) 5.8 and 5.9 μm (CO conj.), δ ($CDCl_3$) 1.18 (s, CMe_2), 2.42 (Me), 2.0—2.3 (m, H_2-3), 2.6—2.8 (H_2-4), 3.82 (OMe), 5.08 (H-2), 6.57 (s, H-6), 7.92 (s, H-9), and 7.2—7.5 (5 H).

The hexahydro-diol (14a). The dione (13) (200 mg) was reduced with methanolic sodium borohydride; the usual work-up gave the diol (14a), m.p. 80—83°, *m/e* 422(99%), 318(100), 216(31), 198(99), and 98(36), $\lambda_{max.}$ 258, 264sh, 298, 306, and 320 nm (ε 18 150, 15 500, 1 980, 1 590, and 1 390), δ ($CDCl_3$) 1.02 and 1.12 (Me), 1.22 (d, CH·CH_3, *J* 7.0 Hz), 2.08—2.90 (H_2-3, H_2-4, and H-1'), 3.10 (H-5', *J* $J_{4',5'}$ 5, $J_{1',5'}$ 11 Hz), 3.30 and 3.80 (d, *H*COH), 3.82 (OMe), 5.09 (H-2), 6.59 and 6.61 (s, H-6 and H-9), and 7.26—7.50 (5 H).

The diacetate (14b). Acetylation of the diol (14a) (150 mg) with pyridine and acetic anhydride gave the diacetate, m.p. 55—60°, δ ($CDCl_3$) 0.94 and 1.22 (Me), 1.14 (d, Me), 1.88 and 2.11 (Ac), 2.0—2.8 (H_2-3, H_2-4, and H-1'), 3.19 (H-5'), 3.83 (OMe), 5.12 and 4.66 (d, H-4' and 2'), 5.10 (H-2), 6.51 and 6.59 (s, H-6 and H-9), and 7.3—7.5 (5 H).

(2*S*)-3,4-Dihydro-5-methoxy-2-phenyl-2*H*-furo[2,3-*h*]-1-benzopyran-8-carboxylic acid (12a) had m.p. 300° (decomp.), *m/e* 324, $\lambda_{max.}$ 288 and 299sh nm (ε 13 300 and 1 400). The methyl ester (12b) (made with diazomethane) had m.p. 160—162°, *m/e* 338(34%) and 234(100), δ ($CDCl_3$) 3.85 and 3.80 (OMe), 6.84 (s, H-6), and 7.54 (s, H-9).

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