The Structures of the Trihydroxyflavans from the Acid-catalyzed Rearrangement and Dimerization of 3-Carene-2,5-dione[1]

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The structures of the trimethyl ethers of three of the four mechanistically probable trihydroxyflavans derived by acid-catalyzed rearrangement and dimerization of 3-carene-2,5-dione have been assigned on spectroscopic grounds and by analogy with earlier results obtained under conditions which precluded dimerization. Confirmation of these assignments has been obtained by the unambiguous synthesis of two of the isomeric trimethyl ethers from simple aromatic precursors.

Les structures des triméthyl éthers de trois parmi les quatre trihydroxyflavanes possibles quant au mécanisme, et qui dérivent d'une transposition acido-catalysée et d'une dimérisation du carène-3 dione-2,5, ont été attribuées en se fondant sur des données spectroscopiques et par analogie avec des résultats précédents obtenus dans des conditions qui excluent toute dimérisation. La confirmation de ces attributions a été obtenue par une synthèse non ambigüe de deux des triméthyl éthers isomères, à partir de progéniteurs aromatiques simples.

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As part of our investigation of the chemistry of the bicyclo[4.1.0]heptane derivative, 3-carene-2,5-dione (**1**) (1–3) we examined the effect of concentrated hydrochloric acid at room temperature. After a very brief interval a pale brown solid precipitated in 77% yield from the initially clear yellow solution. The same product was obtained on similar treatment of **1** with concentrated sulfuric acid, albeit in lower yield. The nature of this solid product, actually a mixture of isomers, is the subject of the present study.

Preliminary i.r. examination of the solid product revealed intense hydrogen-bonded hydroxyl absorption in the range 3600–3100 and a moderately strong band at 1600 cm^{-1} indicative of aromatic character. A bathochromic shift in the u.v. absorption maximum from 295 to 312 nm on addition of potassium hydroxide to a methanolic solution, and the ready solubility in aqueous alkali provided further indications of the presence of a phenolic group or groups in the product, although ferric chloride tests were consistently negative. The mass spectrum of the product showed an apparent molecular weight of 328, with major fragment ions occurring at *m/e* 165 and 164. The n.m.r. spectrum showed two main sets of broad resonances, in the aromatic region at δ 6.5–8.0 and in the region 0.9–3.2 p.p.m. From the complexity of the spectra in general and from the difficulty in obtaining analytical samples of reproducible melting point, we concluded that we were probably dealing with a mixture of at least two components. Furthermore, because of solubility problems we felt that conversion of the dimeric rearrangement product to a more tractable derivative would be rewarding.

Various attempts at esterification of the product were unsuccessful but methylation with excess methyl sulfate under mild conditions produced a viscous yellow oil which contained only traces of unreacted hydroxyl. A preliminary analysis of this oil by t.l.c. indicated that there were at least three major components present. The mass spectrum of the mixture revealed an apparent molecular weight of 370, indicating the presence of three hydroxyl groups in the original product, all presumably phenolic in nature from the ease of methylation. Column chromatography of the methylated product, using a large ratio of adsorbent (Grade I alumina) to substrate, led to the elution in ether–hexane of four isomeric products, referred to subsequently in the order of elution as methylated dimers **A**–**D**. Relative yields of **A**–**D** and details of the n.m.r. and mass spectra appear in Table 1.

The n.m.r. spectra of **A**, **C**, and **D** confirmed in each case the presence of three methoxyl

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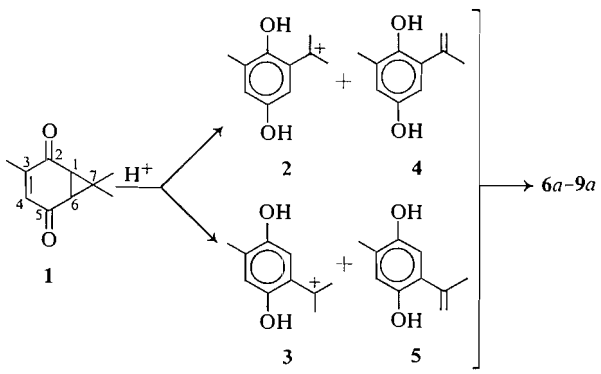
TABLE 1. Spectral data for methylated dimers **A**, **C**, and **D**

Dimer	n.m.r. (δ) in CCl_4				Mass spectra (relative intensity)†	
	Aromatic	OCH_3	CH_2	CH_3		
A (15%)	6.83 (1H, s)	3.77	2.82 (1H, d)	2.12	370	(27)
(*p, p*-)*	6.75 (1H, s)	3.68	1.88 (1H, d)	2.07	192	(100)
	6.55 (1H, s)	3.51	($J = -14$ Hz)	1.58	179	(31)
	6.48 (1H, s)			1.21	178	(23)
				0.66		
B (8%)‡						
(*p, m*-)*						
C (41%)	6.81 (1H, d)	3.72	2.72 (1H, d)	2.20	370	(49)
(*m, p*-)*	6.74 (1H, s)	3.64	1.96 (1H, d)	2.11	192	(100)
	6.50 (1H, s)	3.48	($J = -14$ Hz)	1.63	191	(24)
	6.45 (1H, d)			1.23	179	(73)
	($J = 3$ Hz)			0.69	178	(79)
					177	(24)
D (36%)	6.61 (1H, d)	3.76	2.69 (1H, d)	2.30	192	(42)
(*m, m*-)*	6.55–6.40 (3H, m)	3.65	1.98 (1H, d)	2.23	179	(35)
	($J = 3$ Hz)	3.51	($J = -14$ Hz)	1.66	178	(100)
				1.25	—	—
				0.70	(370, 9%)	

*These designations refer to the disposition of the hydrogens in the benzo- and phenyl rings, respectively, of the flavan system.
†Only relative intensities > 20% are indicated.
‡This is an estimated yield, based on n.m.r. spectra of **B** contaminated with varying amounts of **A** and **C**.

groups and five methyl groups, three of which are attached to sp^3 carbon atoms. Assuming from the original mass spectral evidence that a mixture of dimers ($C_{20}H_{24}O_4$) had been formed, then the fourth oxygen present in addition to the three hydroxyl groups must be accounted for by an ether functionality. At this point, the results of related experiments which we had conducted on the rearrangement of **1** in acetic anhydride–sulfuric acid mixtures (1) led us to the conclusion that the products obtained in the present investigation might well be trihydroxyflavans produced by the acid-catalyzed dimerization of the *o*-isopropenylphenols, **4** and **5**, arising from acid-catalyzed ring opening of the cyclopropane ring in **1**. The facility of flavan formation in such cases had been demonstrated earlier by Baker and his collaborators (4). The selectivity of the acid-catalyzed opening of the cyclopropane ring in **1**, apparent in our earlier study (1), is not so evident from the distribution of both "symmetrical" (**A** and **D**) and "mixed" (**B** and **C**) products in Table 1. This may be regarded as supporting evidence for our contention that the reaction leading to the formation of the phenolic diacetates described in ref. 1 is actually initiated by acetylium ions rather than by protons, giving rise to the observed selectivity by virtue of the much greater difficulty of electrophilic attack by a bulky ion at the sterically crowded C-2 carbonyl group site. The mechanism proposed for the formation of the trihydroxyflavans in the present reaction appears in Scheme 1. Further evidence in support of our gross structural assignment arises from the presence of major fragment ions in the mass spectra of **A**, **C**, and **D** at *m/e* 192 and 178. This



SCHEME 1

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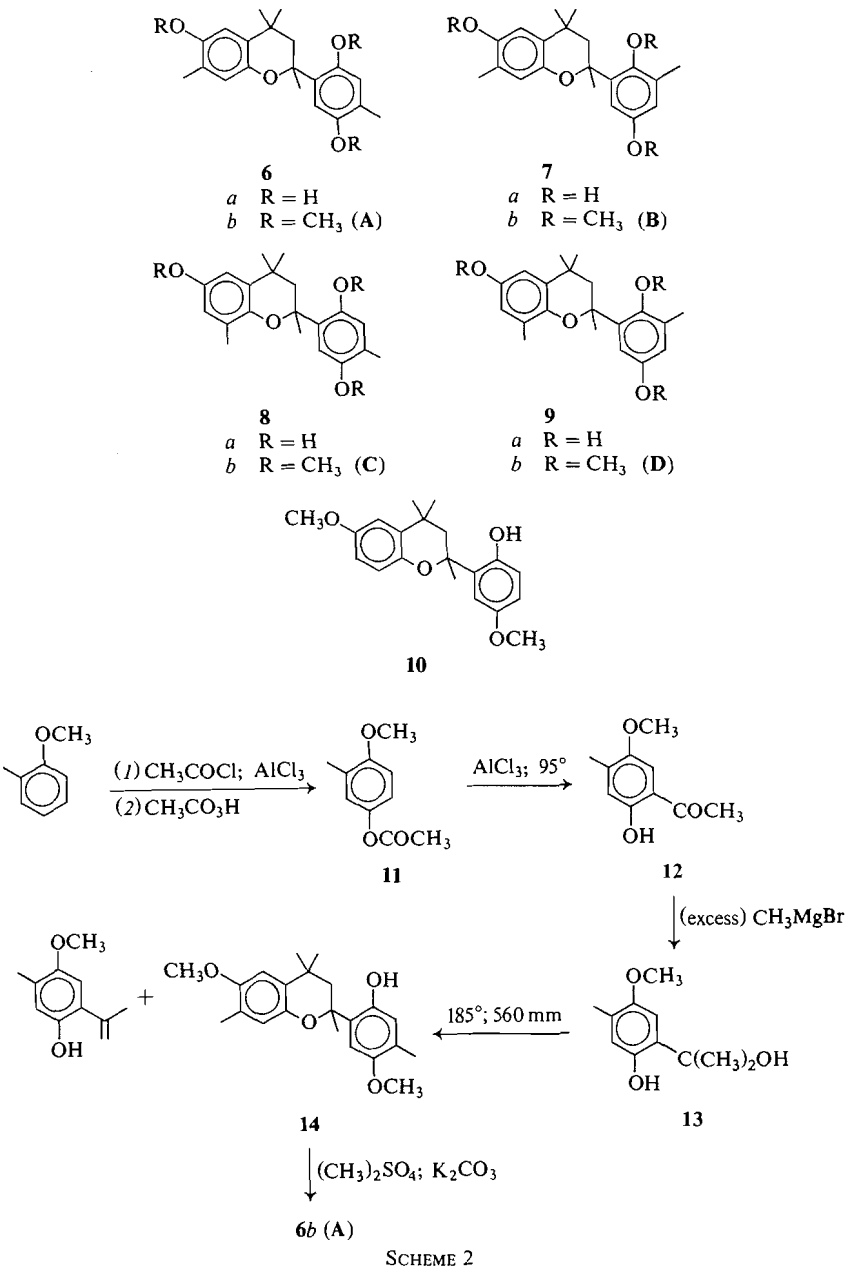

SCHEME 2

is indicative of a *retro*-Diels–Alder type of disintegration, observed previously (5–7) as being characteristic of flavan derivatives.

The individual assignments of structures **6***b*–**9***b* to the methylated products **A**–**D** respectively, and hence of structures **6***a*–**9***a* to the original phenolic products, were made largely on the basis of the n.m.r. spectra and in particular from an inspection of the aromatic region. The spectrum of methylated dimer **A** revealed four singlets of equal intensity between δ 6.48 and 6.83 p.p.m. and thus the *p*,*p*-relationship of the hydrogens in each aromatic ring, as represented in structure **6** was assigned. On the

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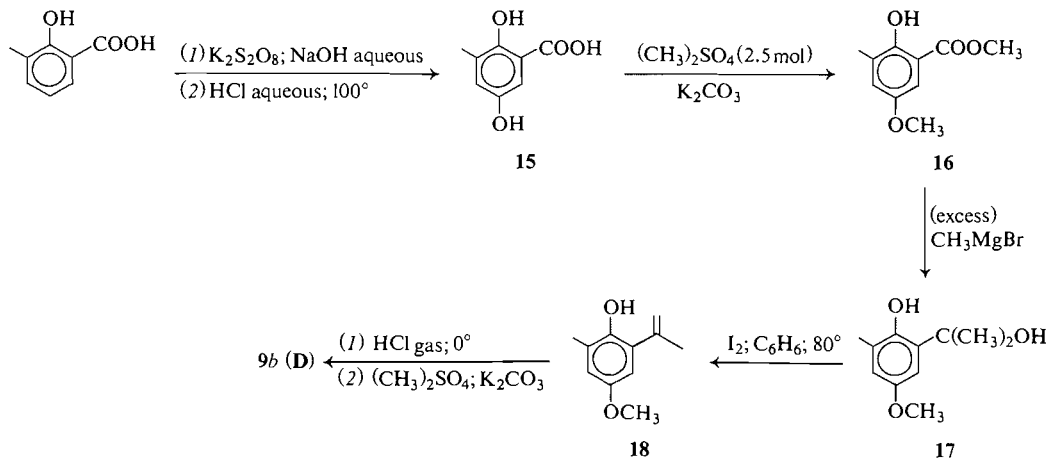

SCHEME 3

other hand, the dimer **D** was assigned structure **9** because its spectrum possessed the most complex aromatic region, δ 6.40–6.55 (m, 3H) and 6.61 (1H, d, $J = 3$ Hz), in accord with expectation for the *m*-orientation of the hydrogens in both aromatic rings. The structural assignments for both **A** and **D** have been confirmed by unambiguous syntheses (see Schemes 2 and 3).

The remaining dimers **B** and **C** resulting from "mixed" coupling of the carbonium ion precursors **2** and **3** with the isopropenylphenols **4** and **5** were more difficult to differentiate. Methylated dimer **C** was assigned structure **8** on the following grounds. Mechanistic analogy to the result obtained in the acetic anhydride – sulfuric acid system (1) and the observed preponderance of **D** over **A** (see Table 1) suggests that formation of carbonium ion **2** would be preferred and thus one might reasonably expect that the *m,p*-mixed dimer would be formed in greater amount than the *p*-, *m*-mixed dimer. The methylated dimer **B** could never be obtained free of contamination with **A** and **C**, and thus analytical, n.m.r., and mass spectral data are not reported for this isomer. The general similarity of its i.r., u.v., and n.m.r. spectra, to those of **A**, **C**, and **D**, however, as well as very similar elution properties lead us very tentatively to assign the remaining mechanistically probable structure **7** to this isomer. One remaining feature of interest in the n.m.r. spectra of **A**, **C**, and **D** is the relatively large chemical shift difference (0.71–0.94 p.p.m.) observed for the two methylene protons in the heterocyclic rings of the flavans. Bowman *et al.* (8) have observed a similar difference (0.70 p.p.m.) and an identical coupling constant ($J = -14$ Hz) for the two methylene protons in the closely related structure **10**.

The synthetic routes to the methylated dimers **A** and **D** from *o*-methylanisole and 2-hydroxy-3-methylbenzoic acid (*o*-cresotic acid), respectively, are illustrated in Schemes 2 and 3, and were generally straightforward, with satisfactory yields being obtained in all steps. In Scheme 2, dehydration of **13** proceeded almost quantitatively, producing a mixture of the monomeric and dimeric dehydration products in a ratio of 1:4. In Scheme 3, the crucial hydroxylation step to produce the dihydroxybenzoic acid derivative **15** with the desired substitution pattern proceeded in 43% yield (9). The iodine-catalyzed dehydration of the tertiary alcohol **17** produced the monomeric *o*-isopropenylphenol **18** almost quantitatively and strong acid catalysis was required to produce dimerization. The presumed intermediate monohydroxy-dimethoxyflavan was not isolated and the synthesis of **9***b* was completed by methylation. The synthetic routes provide additional, indirect support for the mechanistic scheme already described in Scheme 1, in that an *o*-isopropenylphenol derivative is a presumed intermediate in each case.

Experimental

General

The i.r. spectra (cm^{-1}) in CCl_4 solution or as otherwise specified were recorded on a Perkin–Elmer 337 grating spectrophotometer and the u.v. spectra (in methanol) on a

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Unicam SP 800 recording instrument. The n.m.r. spectra (δ) were obtained on Varian A-60 and HA-100 instruments in the solvents specified, using tetramethylsilane as the internal standard. Mass spectra were recorded on a Bell and Howell 21-490 spectrometer and the elemental analyses were performed by A. B. Gygli, 329 St. George Street, Toronto and by the Scandinavian Microanalytical Laboratory, Herlev, Denmark. Column chromatography was performed using silica gel (Davison Chemical, Grade 923, 100–200 mesh) or neutral alumina (Fisher Grade I, 80–200 mesh) and Fisher A.C.S. grade solvents. All melting points and boiling points are uncorrected.

*3-Carene-2,5-dione (**1**)*

This compound was synthesized and purified by a previously published procedure (10).

*Reaction of **1** with Concentrated HCl*

3-Carene-2,5-dione (2.0 g) was finely powdered and added rapidly to concentrated HCl (50 ml) with stirring at 25 °C. After 2–3 min a pale brown precipitate appeared and the acid solution was poured into iced water (100 ml). The precipitate was filtered off, washed thoroughly with ice-cold water, 5% sodium hydrogen carbonate solution, and finally again with ice-cold water before drying in a vacuum desiccator for 2 days. The crude product (1.55 g, 77%) was recrystallized from a variety of mixed solvents such as ether–hexane, methylene chloride–petroleum ether (30–60°) but no purified sample with a range of melting of less than 5° could be obtained. (The melting points varied from 160–190° depending on the solvent system used.)

The mass spectrum of this product showed an apparent molecular ion at *m/e* 328, while the n.m.r. spectrum (acetone-d_6) looked exceedingly complex. The i.r. spectrum showed a broad OH band at 3600–3100 and prominent peaks at 1600 and 1485 indicative of aromatic character. The u.v. spectrum showed a prominent maximum at 295 nm (ε, 7000).

Methylation of Mixture of Dimers

The product (1.05 g) obtained as described above was methylated under standard conditions with an excess of methyl sulfate in acetone in the presence of anhydrous potassium carbonate. Examination of the i.r. spectrum of the viscous yellow oil (1.13 g) so obtained revealed almost no residual OH absorption bands. Chromatography of the crude methylation product on alumina (850 g) and examination of the fractions by following changes in the intensity of the 295 nm band in the u.v. led to the isolation of four main fractions designated **A**, **B**, **C**, and **D** in the order of their elution. The product **A** began to elute with 12% ether–hexane and the last traces of **D** were eluted with ether. The four isomers accounted for essentially all of the substrate chromatographed. The i.r. spectra of **A**–**D** showed general similarities with no hydroxyl or carbonyl absorption and peaks characteristic of $-OCH_3$ at 2830, as well as the aromatic bands at 1600 and 1490. The details of the n.m.r. and mass spectra of **A**, **C**, and **D**, as well as the relative yields of the methylated dimers, appear in Table 1.

Methylated dimer **A**, **6***b* was recrystallized from methanol, m.p. 115–116°.

Anal. Calcd. for $C_{23}H_{30}O_4$: C, 74.56, H; 8.16. Found: C, 74.72, H; 8.09.

Methylated dimer **C**, **8***b* was recrystallized from 60% aqueous ethyl alcohol, m.p. 96.5–97.5°.

Anal. Calcd. for $C_{23}H_{30}O_4$: C, 74.56; H, 8.16. Found: C, 74.71; H, 8.13.

Methylated dimer **D**, **9***b* was recrystallized from 50% aqueous ethyl alcohol, m.p. 94–94.5°.

Anal. Calcd. for $C_{23}H_{30}O_4$: C, 74.56; H, 8.16. Found: C, 74.82; H, 7.96.

*4-Methoxy-3-methylphenyl Acetate (**11**)*

4-Methoxy-3-methylacetophenone (11) was converted to 4-methoxy-3-methylphenyl acetate by the procedure of Bowman *et al.*, (8). The product was obtained as a pale yellow oil (19.2 g, 51%), b.p. 136–138°/20 mm; i.r. 2835, 1770, 1503, 1210; n.m.r. ($CHCl_3$-d_1) 2.24 (3H, s), 2.29 (3H, s), 3.80 (3H, s), and 6.85 (3H, m) p.p.m. The mass spectrum showed the expected molecular ion at *m/e* 180 (17) and major fragment ions at *m/e* 138 (100) and 123 (68).

Anal. Calcd. for $C_{10}H_{12}O_3$: C, 66.65; H, 6.71. Found: C, 66.42; H, 6.73.

*2-Hydroxy-5-methoxy-4-methylacetophenone (**12**)*

Fries rearrangement of **11** (18.4 g) was carried out by adding aluminum chloride (15 g) to the ice-cold acetate. A vigorous reaction occurred as the flask warmed up to room temperature. The reaction mixture was then stirred at 90° for 16 h before cooling and adding 2 *N* HCl (80 ml). The resulting yellow solid was extracted with ether and the combined extracts in turn extracted thoroughly with cold 2 *N* NaOH solution. The alkaline solution was strongly acidified with concentrated HCl and the product steam-distilled (a total of 1100 ml was collected). Extraction of the phenol with ether gave, on evaporation of the dried extract, a yellow solid (7.8 g). Recrystallization from aqueous ethyl alcohol afforded **12** as small yellow needles (5.9 g, 38%), m.p. 108–109°. (Some unreacted starting material was recovered from the neutral fraction in the original ethereal extract.) The i.r. 2850, 2830, 1650, 1630 (sh), 1585, 1495; n.m.r. ($CHCl_3$-d_1) 2.22 (3H, s), 2.57 (3H, s), 3.82 (3H, s), 6.78 (1H, s), and 6.99 (1H, s); u.v. λ_{max} 230 (ε, 16 100), 265 (ε, 9900), 352 nm (ε, 5100). The mass spectrum showed the expected molecular ion at *m/e* 180 (63) and further peaks at 165 (100), 147 (11), and 137 (10).

Anal. Calcd. for $C_{10}H_{12}O_3$: C, 66.65; H, 6.71. Found: C, 66.64; H, 6.70.

*2-(2-Hydroxy-5-methoxy-4-methylphenyl)-2-propanol (**13**)*

The substituted acetophenone, **12** (2.83 g, 0.016 mol) in ether (15 ml) was added to a refluxing ethereal solution of methylmagnesium bromide, prepared from magnesium (1.13 g, 0.047 g-atom) and excess methyl bromide. After refluxing the reaction mixture for 1 h under N_2, saturated ammonium chloride solution (10 ml) was added dropwise until a clear supernatant ethereal layer was obtained. Separation and drying of the ethereal layer gave on evaporation a white solid. Recrystallization from petroleum ether (b.p. 60–70°) with the aid of charcoal gave the expected tertiary alcohol (2.53 g, 82%); m.p. 70–71°; i.r. 3640, 3420, 2815, 1495; n.m.r. ($CHCl_3$-d_1) 1.63 (6H, s), 2.14 (3H, s), 3.74 (3H, s), 5.13 (1H, s), 6.57 (1H, s), 6.67 (1H, s). (The phenolic proton was not detected.) The mass spectrum showed a molecular ion at *m/e* 196 (20) and major fragment ions at 178 (100) and 163 (76).

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Anal. Calcd. for $C_{11}H_{16}O_3$: C, 67.32; H, 8.22. Found: C, 67.12; H, 8.11.

Dehydration of ***13****: Formation of 2-(2-Hydroxy-5-methoxy-4-methylphenyl)-6-methoxy-2,4,4,7-tetramethylchroman (****14****)*

The tertiary alcohol **13** (2.75 g) was heated at 185°/580 mm for 1 h and a product (0.37 g, 18%), b.p. 174–176°/11 mm, was collected. This was shown to be the expected *o*-isopropenylphenol derivative (see Scheme 2) arising from simple dehydration; i.r. 3530, 2830, 1620, 1500, and 911; n.m.r. ($CHCl_3$-d_1) 2.11 (3H, s), 2.17 (3H, s), 3.76 (3H, s), 5.13 (1H, bs), 5.31 (1H, bs), 5.52 (1H, bs), 6.60 (1H, s), and 6.70 (1H, s).

The glassy residue in the distilling flask was extracted with hot benzene and the solvent evaporated. Trituration with petrol afforded white crystals of **14**, (2.06 g, 81%) which were recrystallized from petroleum ether (b.p. 60–70°, m.p. 106–107°; i.r. 3420, 2830, 1500; n.m.r. ($CHCl_3$-d_1) 1.13, 1.39, 1.70, 2.12, 2.18, 3.70, 3.77 (each 3H, s) 2.0 (1H, d), and 2.67 (1H, d)($J = -14$ Hz), 6.69 (4H, m), and 7.56 (1H, s). The mass spectrum showed the expected molecular ion at *m/e* 356 (42) and major fragment ions at *m/e* 180 (13), 179 (96), 178 (100), and 163 (16).

Anal. Calcd. for $C_{22}H_{28}O_4$: C, 74.13; H, 7.92. Found: C, 74.15; H, 7.89.

*2-(2,5-Dimethoxy-4-methylphenyl)-6-methoxy-2,4,4,7-tetramethylchroman (****6b****)*

Methylation of **14** (0.95 g) using methyl sulfate and anhydrous potassium carbonate in acetone under standard conditions afforded the expected methyl ether, ***6b*** (0.87 g, 88%), m.p. 114–115° on recrystallization from aqueous ethyl alcohol, undepressed on admixture with a pure sample of methylated dimer, **A**. The i.r., n.m.r., and mass spectra of the synthetic sample were identical with those of dimer **A**.

*2,5-Dihydroxy-3-methylbenzoic Acid (****15****)*

A solution of 2-hydroxy-3-methylbenzoic acid (Eastman Kodak) (10 g, 0.067 mol) in 10% NaOH solution (125 ml), was cooled to 10° and a saturated aqueous solution of potassium perdisulfate ($K_2S_2O_8$) (18 g in 350 ml, 0.067 mol) was added with stirring, over a period of 5 h. During this period, the temperature was never allowed to rise above 15°. The reaction was then stirred overnight at 25° before acidifying first with solid CO_2 and then to p*H* 4 with 2 *N* HCl. Extraction with ether and washing the ethereal extract (water, saturated brine) afforded on drying ($MgSO_4$) and evaporation some unreacted starting material (4.6 g); i.r. (Nujol) 3250–2300, 1670, 1605; m.p. 166–167°, undepressed on admixture with 2-hydroxy-3-methylbenzoic acid.

The p*H* of the residual aqueous solution was readjusted to about p*H* 8 with (solid) $NaHCO_3$, and the solution evaporated to dryness at 60°, under vacuum. The brown solid residue was extracted thoroughly on the steam bath with three portions of 90% aqueous ethyl alcohol (500 ml in total) according to the modified procedure of Baker and Brown (9). The residue (6.5 g) obtained on evaporation was then hydrolyzed on the steam bath with 2 *N* HCl for 1 h, in the presence of a layer of ether. Removal of the ethereal layer, washing (brine), and drying ($MgSO_4$) gave the crude dihydroxybenzoic acid derivative (3.9 g) which afforded the expected product (2.65 g, 43%) on recrystallization from 20% aqueous ethyl alcohol; m.p. 222–223° (dec.) (lit (12) m.p. 215° (dec.)); i.r. (Nujol) 3290–2400, 1660, 1605; n.m.r. (DMSO-d_6) 2.18 (3H, s), 6.97 (1H, d, $J = 3.2$ Hz), and 7.14 (1H, d, $J = 3.2$ Hz) p.p.m. (The acidic protons were unobservable.) The mass spectrum showed the expected molecular ion at *m/e* 168 (46) and major fragment ions at 150 (100) and 121 (74).

Anal. Calcd. for $C_8H_8O_4$: C, 57.14; H, 4.80. Found: C, 56.76; H, 4.86.

*Methyl 2-Hydroxy-5-methoxy-3-methylbenzoate (****16****)*

Esterification of the acid **15** was accompanied by concomitant methylation of the unhindered phenolic group when carried out by treating **15** (2.37 g, 14.5 mmol) with methyl sulfate (4.5 g, 36 mmol) and anhydrous potassium carbonate (5.0 g) in anhydrous acetone (20 ml). After refluxing for 2 h and stirring at room temperature overnight, the product was isolated as a semi-solid material (3.5 g). Chromatography on silica gel (80 g) and elution with 10% ether–benzene led to the recovery of pure **16** (1.71 g, 62%), m.p. 78–79° on recrystallization from petroleum ether (b.p. 60–70°); i.r. 3200, 2835, 1685, 1615; n.m.r. (CCl_4) 2.22 (3H, s), 3.68 (3H, s), 3.89 (3H, s), 6.83 and 6.97 (each 1H, d, $J = 3.2$ Hz), 10.44 (1H, s) p.p.m. The mass spectrum showed the expected molecular ion at *m/e* 196 (41), with major fragment ions at 164 (100), 136 (23), and 121 (14).

Anal. Calcd. for $C_{10}H_{12}O_4$: C, 61.21; H, 6.17. Found: C, 61.54; H, 6.44.

*2-(2-Hydroxy-5-methoxy-3-methylphenyl)-2-propanol (****17****)*

The ester **16** (1.5 g, 7.5 mmol) in ether (35 ml) was added to a refluxing solution of methylmagnesium bromide, prepared from magnesium (0.65 g, 0.0265 g-atom) and excess methyl bromide in ether (15 ml) over 0.75 h and the reaction mixture refluxed for a further 2 h. Addition of saturated ammonium chloride solution (15 ml), extraction with ether, and evaporation afforded a pale brown solid (1.46 g) which gave a white solid (0.99 g, 66%) on recrystallization from petroleum ether (b.p. 60–70°), m.p. 99–100°; i.r. (Nujol) 3415, 3165, 2850, and 1605; n.m.r. ($CHCl_3$-d_1) 1.60 (6H, s), 2.21 (3H, s), 3.70 (3H, s), 4.73 (1H, s), 6.52 and 6.66 (each 1H, d, $J = 3.0$ Hz) p.p.m. The mass spectrum showed the expected molecular ion at *m/e* 196 (23), and major fragment ions at *m/e* 179 (21), 178 (100), 163 (37), 135 (11), 131 (31), and 119 (14).

Anal. Calcd. for $C_{11}H_{16}O_3$: C, 67.32; H, 8.22. Found: C, 67.08; H, 8.02.

*2-(2-Hydroxy-5-methoxy-3-methylphenyl)propene (****18****)*

The tertiary alcohol **17** (490 mg) was refluxed for 5 h in anhydrous benzene (10 ml) containing iodine (5 mg). The cooled reaction mixture was washed successively with 5% sodium hydrogen sulfite solution, water, and saturated brine. Drying ($MgSO_4$) and evaporation afforded a mobile colorless oil (412 mg, 93%). The i.r. spectrum (liquid film) showed peaks at 3520, 2835, 1605, and 910, and the n.m.r. spectrum (CCl_4) 2.05, 2.18, 3.66 (each 3H, s), 5.08 (1H, bs), 5.16 (1H, s), 5.31 (1H, bs), 6.36 (1H, d, $J = 3.2$ Hz), and 6.50 (1H, d, $J = 3.2$ Hz) p.p.m. were in accord with expectation for the simple dehydration product **18**.

*2-(2,5-Dimethoxy-3-methylphenyl)-6-methoxy-2,4,4,8-tetramethylchroman (****9b****)*

Anhydrous hydrogen chloride was bubbled through the

o-isopropenylphenol derivative **18** (380 mg) for 15 min at $-10°$ (*cf.* Baker *et al.* (4)) and the reaction mixture allowed to warm to 25° (1 h). Excess iced water (100 ml) was added and the product extracted with ether. Washing the ethereal extracts (water, $NaHCO_3$ solution, water, and saturated brine), drying ($MgSO_4$), and evaporation afforded a very viscous pale yellow gum (355 mg) which did not crystallize on standing or cooling. Further purification was not attempted and the viscous oil was dissolved in anhydrous acetone (10 ml) containing methyl sulfate (200 mg) and anhydrous potassium carbonate (250 mg). After refluxing the mixture for 2 h and stirring overnight at 25°, the methylation product was isolated as a yellow gum (375 mg). Chromatography on silica gel (80 g) gave, on elution with 7% ether in benzene, a fraction (179 mg) which partly crystallized on standing. Isolation of the solid product (65 mg), m.p. 93–95°, was achieved by adding ice-cold pentane and thorough washing with the same solvent. The melting point of the product on admixture with pure methylated dimer "**D**" was undepressed (91–94°), and the identity of the two materials was further confirmed by comparison of the i.r., n.m.r., and mass spectra.

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