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QUINONES AND QUINONE-METHIDES—I

CYCLIZATION AND DIMERISATION OF CRYSTALLINE ORTHO-QUINONE METHIDES FROM PHENOL OXIDATION REACTIONS

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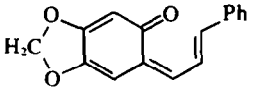
Abstract—Silver oxide or 2,3-dichloro-5,6-dicyanobenzoquinone oxidation of 2-cinnamyl-4,5-methylenedioxyphenol yields a crystalline ortho-quinone methide, which undergoes thermal or acid-catalysed cyclization to 6,7-methylenedioxyflav-3-ene. Oxidation of 2-(4-methoxybenzyl)-4,5-methylenedioxyphenol yields a crystalline ortho-quinone methide which rapidly dimerises in polar solvents. The structure of the colorless dimer, which is of a type not previously reported, suggests that an ionic reaction is involved in its formation.

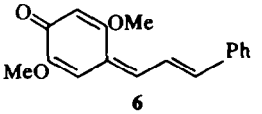
ortho-Quinone methides are suspected to be unstable intermediates in many chemical and biochemical phenol oxidation reactions.[1,2] The oxidative dimerisation and trimerisation of *o*-alkylphenols almost certainly involves these reactive species.[3] It has also been suggested that the oxidative cyclisation of *o*-allylphenols of type **1**, both by enzymic dehydrogenation in biological systems,[4] and by chemical oxidation with one-electron oxidants or by hybride ion abstraction with high potential quinones[5,6] such as 2,3-dichloro-5,6-dicyanobenzoquinone proceeds via intermediate *o*-quinone methides **2** to yield flavenes and the ubiquitous dialkylchromenes of type **3**.

Indirect evidence for *in situ* generation of *o*-quinone methides in these oxidation reactions has resulted from the structural identification of their stable, colorless cyclization or self-condensation products, and from "trapping" by reaction with added dienophiles and nucleophilic reagents.[7,8] Since very few compounds with an *o*-quinone methide structure have actually been detected spectroscopically,[9] isolated, or crystallised,[10-12] direct evidence for their transitory formation has generally been lacking. However, participation of these intermediates has now been unequivocally confirmed by the isolation of crystalline *o*-quinone methides from oxidative cyclisation and dimerisation reactions of 2-cinnamyl-sesamol **4** and 2-(4-methoxybenzyl)-sesamol. Our interest in the chemistry of these particular phenols stems from a recent observation[13] that certain derivatives are highly effective agents for the sterilization of female flies.

Oxidation of **4** with silver oxide gives a quantitative yield of an orange-red crystalline product, m.p. 163°, which is sufficiently stable to be crystallized from acetone and other low boiling solvents without appreciable loss. In accord with an *o*-quinone methide structure **5a** or **5b** it has a molecular weight of 252 (by MS), shows λ_{max} 454 nm in ethanol, has a conjugated "carbonyl" band at 1618 cm^{-1}, and is reduced by sodium borohydride to the original phenol **4**. Its NMR spectrum ($CDCl_3$) shows the presence of a methylenedioxy group (2H, s, δ5.90), two uncoupled quinoidal protons (1H, s, δ5.96; 1H, s, δ6.60), and three highly deshielded olefinic and five phenyl ring protons (8H, m, δ6.97–δ7.65). These chemical shifts correspond well with those reported for the natural *p*-quinone methide, obtusaquinone,[14] and its methyl ether **6**;[15] in **6** the two quinoidal protons appear as singlets at δ5.81 and



5b



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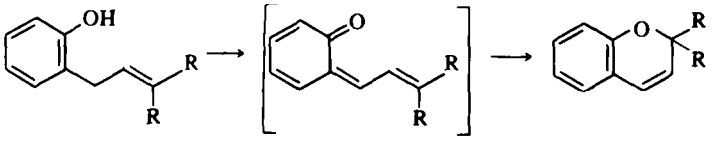
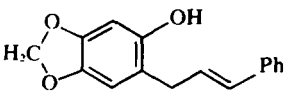


1 **2** **3**

R = H, Alkyl, or Aryl



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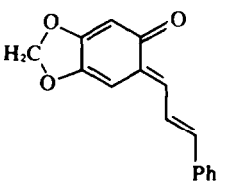
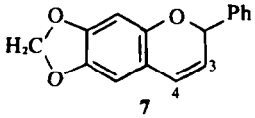


5a

δ6.56, and the three olefinic and five phenyl protons as an 8H multiplet at δ6.95–δ7.55.

In boiling benzene solutions the colored oxidation product cyclizes to the colorless flav-3-ene **7**, in which protons on carbons 2, 3 and 4 of the heterocyclic ring appear as characteristic[16] double doublets at δ5.85, δ5.72, and δ6.46 respectively, with $J_{2,3} = 3.5$ Hz, $J_{2,4} = 1.5$ Hz, $J_{3,4} = 9.0$ Hz. The flav-3-ene structure of the cyclization product was confirmed by its catalytic reduction to the flavan **8**, and by its oxidation with perchloric acid to the flavylium salt **9**.



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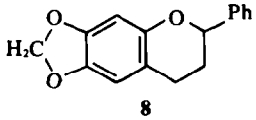

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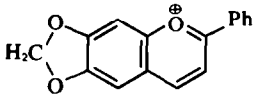

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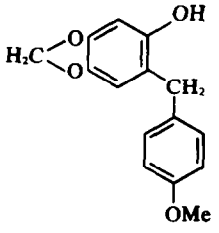
The unusual stability of this *o*-quinone methide is due to the extended conjugation of the quinoid nucleus with the cinnamylidene group. Although the stereochemistry of this group has not been established with certainty, an *o*-quinone methide with the configuration shown in **5b** would be expected to cyclize with extreme ease, perhaps even spontaneously in solution. Since thermal cyclisation in boiling benzene occurs relatively slowly, the isomeric structure **5a** is probable.

The *o*-quinone methide **5a** is also formed by dehydrogenation of **4** with 2,3-dichloro-5,6-dicyanobenzoquinone in acetone or ether solutions. In this case, however, the crystalline quinonemethide is contaminated with 2,3-dichloro-5, 6-dicyanohydroquinone and it cannot be purified by recrystallization, since the hydroquinone catalyses the rapid cyclization of **5a** to the flavene **7**. Thus, when cooled solutions of **4** and 2,3-dichloro-5,6-dicyanobenzoquinone in acetone are mixed, crystallisation of the red *o*-quinone methide and the hydroquinone begins almost at once. All attempts to purify the product gave only **7**; however, the identity of the oxidation product as **5a** was unambiguously established by silicic acid TLC in a number of solvent systems, and by comparison of its NMR spectrum in cold acetone solution. The catalytic effect of 2,3-dichloro-5,6-dicyanohydroquinone in promoting rapid cyclisation of *o*-quinone methides was confirmed by briefly warming pure **5a** (from the silver oxide oxidation) with acetone containing a small quantity of the hydroquinone. Under these conditions **5a** was rapidly converted to **7**, although, as previously indicated, in acetone alone **5a** is quite stable. The catalytic effect of 2,3-dichloro-5,6-dicyanohydroquinone is due, presumably, to its acidity, and in support of this it has been observed that the cyclisation of **5a** to **7** also occurs rapidly in acetic acid solutions.

Because of the stability of the *p*-methoxybenzyl cation in aqueous acid media, *p*-methoxybenzyl-phenols can be synthesised readily by adaptation of a procedure developed for the synthesis of natural cinnamylphenols.[17] Thus, *p*-methoxybenzyl alcohol condenses with sesamol in aqueous citric acid solution to give almost quantitative yields of 2-(4-methoxybenzyl)-4, 5-methylenedioxyphenol **10**.

Oxidation of **10** with silver oxide yields two crystalline products, viz an orange colored compound, $C_{15}H_{12}O_4$, m.p. 143°, and a colorless dimer, $C_{30}H_{24}O_8$, m.p. 203–204°. The colored product, λ_{max} 433 nm, is readily reduced by sodium borohydride to the phenol **10**, and has a CO band at 1615 cm^{-1} in the IR spectrum. The NMR spectrum ($CDCl_3$) shows two singlets at δ5.97 and 6.70 from two uncoupled quinoidal protons, and a singlet at low field, δ7.88, due to a highly deshielded olefinic proton. The methoxyl and methylenedioxy groups appear as singlets at δ3.36 (3H) and δ5.88 (2H), and the four aromatic protons of the p-methoxyphenol ring as an A_2B_2 system (2H, d, J = 8 Hz, δ6.95; 2H, d, J = 8 Hz, δ7.49). On the basis of these spectral data the colored product is the *o*-quinone methide **11a** (or **11b**), a conclusion confirmed by its reaction with ethyl vinyl ether[7] to yield the colorless chroman **12**, and by its facile dimerization. The *o*-quinone methide dimerizes rapidly in methanol, and more slowly in benzene, to a colorless product identical with the crystalline dimer isolated from the oxidation reaction. Since molecular models indicate less steric hindrance to planarity in structure **11a** compared to the geometric isomer **11b**, the *o*-quinone methide is probably the former isomer.

Dimers and trimers, produced from a wide variety of substituted *o*-alkylphenols and *o*-alkylnaphthols in oxida-



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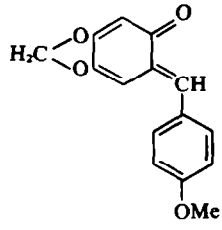
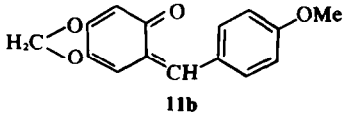
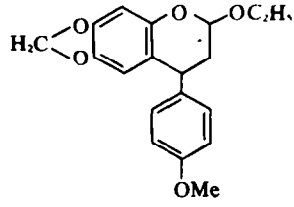


11a



11b



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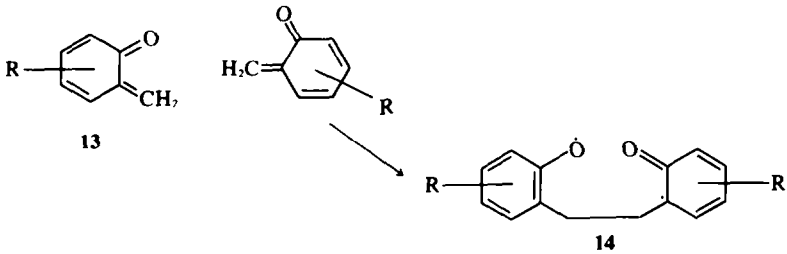
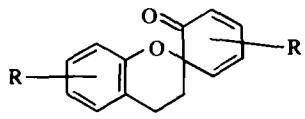
tion, pyrolytic, and elimination reactions, have proven in all cases to be spiro-compounds of type **15**. These dimers are formed by a non-ionic process involving a Diels–Alder addition of two molecules of an *o*-quinone methide **13** to give an intermediate diradical **14**.[1,2] The dimerization of 10-benzylidene-9-phenanthrone **16**, which is similar to the *p*-methoxybenzylidene compound **11a**, yields dimer **17**.[11] On the basis of precedent, therefore, the dimer formed from **11a** would be expected to be **18**. This structural assignment, however, is incompatible with the spectral properties of the dimer and its derivatives. An alternate structure **19** is now proposed, indicating that the dimerization of this particular *o*-quinone methide **11a**, in contrast to earlier observations, can be rationalized by an ionic reaction mechanism.

The IR spectrum of the dimer has a strong CO band at



13 **14**



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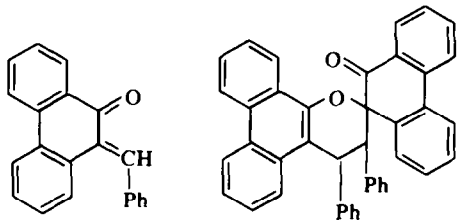
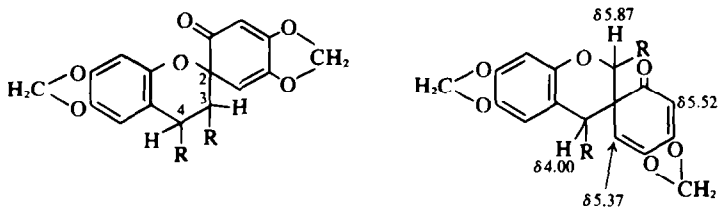
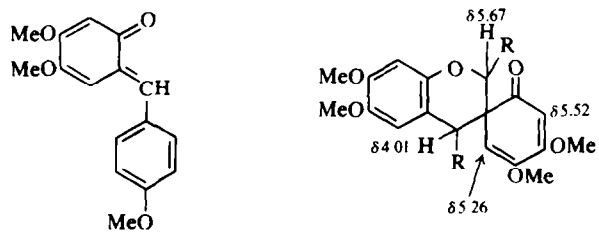


16 **17**

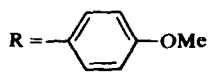


18 **19**



20 **21**

22 **23**



1635 cm^{-1}, and its 100 MHz NMR spectrum ($CDCl_3$) shows signals expected from two OMe groups, two methylenedioxy groups, two aromatic protons (1 H singlets at δ6.32 and δ6.57), and the eight aromatic protons of the two *p*-methoxyphenyl rings. The spectrum also shows four sharp 1H singlets at δ4.00, δ5.87, δ5.37 and δ5.52. The singlets at δ5.87 and δ4.00 may be assigned to the methine protons at positions 2 and 4 respectively of the chroman ring in **19**, and the singlets at δ5.37 and δ5.52 may be assigned to the olefinic methine protons of the cyclohexadienone ring. These assignments are complicated by the fact that the two protons of one methylenedioxy group appear as 1H singlets δ5.89, δ5.92, and the two protons of the other methylenedioxy group as 1H singlets at δ5.70, δ5.76. This complexity was resolved by the synthesis (in small yield) of the analogous *o*-quinone methide **20** and its dimer **21** from 2-(4-methoxyphenyl)-4,5-dimethoxyphenol. The NMR spectrum is similar (1H singlets at δ4.01, 5.67, 5.26, 5.52) to that of **19** except that the confusing, overlapping signals from methylenedioxy groups are absent. The C_2 methine proton of 2-phenylchromans (flavans) of type **22** and the C_3 methine proton of 3-phenylchromans (isoflavans) of type **23** have chemical shifts of about δ5.0–δ5.50 and δ2.8–δ3.1 respectively.[18] Thus, both the chemical shifts and the absence of coupling of the two protons of the chroman ring of these dimers are in complete accord with the proposed flavan structures **19** and **21**. These data are inconsistent, however, with alternate isoflavan structures of type **18**, in which the two methine protons at positions 3 and 4 should be coupled and appear as doublets at about δ3.0 and 4.0 respectively.

On catalytic hydrogenation the dimer **19** yields a small quantity of the phenol **10**, and is also partially reduced to a non-phenolic, dihydroderivative in which the γ, δ double bond of the original cyclohexadienone ring is now saturated. In agreement with structure **24** the IR spectrum of the dihydro derivative shows a strong CO band with a characteristic double peak at 1640, 1650 cm^{-1} (O=C–CH=C–); in the model, O-ethyl-dimedone, the CO absorbs at 1640, 1655 cm^{-1}. In its NMR spectrum a methine proton of the cyclohexenone ring appears as a double doublet (J = 12, 6 Hz) at δ4.90, coupled to the two protons of a methylene group (1H, dd, J = 12, 6 Hz, δ2.52; 1H, dd, J = 12, 12 Hz, δ2.17), and the olefinic methine proton appears as a singlet at δ5.54. As with the original dimer, the protons of the chroman ring of the dihydro compound appear as sharp singlets at δ5.74, 4.19. The protons of the aromatic methylenedioxy group do not shift (1H singlets at δ5.89, δ5.91), while the protons of the methylenedioxy group attached to the cyclohexenone ring undergo a large upfield shift to δ5.33 (1H) and δ5.27 (1H).

Reduction of the dimer **19** or its dihydro-derivative **24** with sodium borohydride results in the loss of a methylenedioxy group and formation of a spirocyclohexanediol **25a** or **26a**. On benzoylation the diol yields a monobenzoate, suggesting that one OH group is hindered. In accord with structure **25b** or **26b** the NMR spectrum ($CDCl_3$) of the monobenzoate shows a 7H multiplet at δ1.2–δ2.2 (three methylene groups, one OH group), a methine proton as a multiplet at δ3.22 (>CH*OH), and a methine proton as a multiplet at δ5.54 (>CH*OR_1). The proton at position 4 of the chroman ring appears at δ4.38 (1H, s), while the proton at position 2 and the two protons of the methylenedioxy group appear as three overlapping 1H singlets at δ5.83, 5.84 and 5.85.

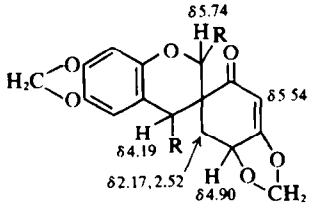
Although the formation of previously isolated dimers **15** and **17** can be accounted for on the basis of diradical intermediates,[1,2] the structure of the dimer **19** clearly indicates that the *o*-quinone methide **11a** is highly polarisable, and that its dimerisation may involve an ionic reaction. The observation that the dimerisation is much more rapid in polar solvents such as methanol than in benzene supports this suggestion. Furthermore, the *p*-methoxyphenyl substituent would be expected to permit extensive charge delocalisation and, consequently, enhance the stability and ease of formation of an intermediate ionic species.[8]

EXPERIMENTAL

All m.ps are uncorrected. NMR spectra, unless stated otherwise, were determined in $CDCl_3$ with a TMS internal standard on a modified Varian HA-100 instrument. IR data were obtained in mineral oil on a Perkin-Elmer model 237 B grating infrared spectrophotometer.

6-Cinnamylidene-3,4-methylenedioxy-cyclohexa-2,4-dienone **5a**

(a) A soln of **4**[19] (10.0 g) in dry ether (100 ml) was stirred with silver oxide (20.0 g) at room temp. for 20 hr. Orange colored crystals separated from the soln. The reaction was filtered and the solid was extracted with boiling acetone (3 X250 ml). The acetone



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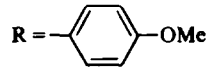
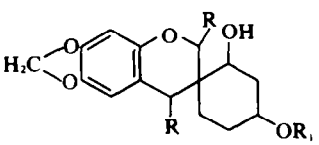
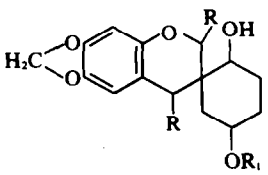




25a: R_1 = H
25b: R_1 = COPh



26a: R_1 = H
26b: R_1 = COPh

soln was concentrated to 40 ml and cooled, whereupon the product crystallized (9.4 g; m.p. 162–163°). Recrystallized from acetone *6-cinnamylidene-3, 4-methylenedioxy-cyclohexa-2,4-dienone* **5a** separated as glistening, orange–red plates m.p. 164°. (Found: C, 76.2; H, 4.89. Calc. for $C_{16}H_{12}O_3$; C, 76.2; H, 4.80%), λ_{max}^{EtOH} 454 (4.08), 396 (4.10), 376 (4.12), 355 (4.10), 227 (3.97) nm (log ε); NMR spectrum in acetone-D_6: 1H, s, δ5.78; 2H, s, δ6.04; 1H, s, δ6.92; 8H, m, δ7.14-δ7.80; NMR in $CDCl_3$, see text.

Reduction of **5a** with $NaBH_4$ in MeOH gave an oily product, the major constituent of which was identical (TLC) with **4**. Acetylation of the reduced product gave a crystalline acetate, identical (m.m.p., NMR) with **4** *acetate*, colorless needdles *ex* MeOH, m.p. 81–82°. (Found: C, 72.9; H, 5.38. Calc. for $C_{16}H_{16}O_4$: C, 73.0; H, 5.44%); NMR spectrum: 3H, s, δ2.26; 2H, d, J = 6.0 Hz, δ3.35; 2H, s, δ5.94; 1H, m. δ6.04–δ6.32; 1H, d, J = 16.0 Hz, δ6.42; 1H, s, δ6.58; 1H, s, δ6.72; 5H, m, δ7.18–δ7.40.

(b) 2,3-Dichloro-5,6-dicyanobenzoquinone (1.14 g) was added to a cooled (5°) solution of **4** (1.27 g) in acetone (10 ml). Within 1 min bright red needles began to separate. After 1 hr the product was collected (1.0 g). TLC on silicic acid showed two components with R_F values (in benzene–ethanol, 9:1 v/v; ether-Skellysolve F, 2:1 v/v; ethylacetate-Skellysolve F, 1:4 v/v) identical with **5a** and 2,3-dichloro-5,6-dicyanohydroquinone; NMR spectrum in acetone was identical with that of **5a**.

6,7-Methylenedioxyflav-3-ene **7**

(a) The *o*-quinone methide **5a** (3.0 g) was heated under reflux in benzene soln (150 ml) for 2 hr. TLC then showed complete conversion to the flavene. The soln was evaporated and the residue was extracted with boiling Skellysolve F. On concentration and cooling the Skellysolve F soln deposited the crystalline flavene. Recrystallized from Skellysolve F *6,7-methylenedioxyflav-3-ene* **7** separated as colorless plates, m.p. 73° (2.3 g). (Found: C, 76.1; H, 4.90. Calc. for $C_{16}H_{12}O_3$: C, 76.2; H, 4.80%). λ_{max}^{EtOH} 330 (4.04), 233 (4.51), 218 (4.51), nm (log ε); NMR spectrum: 1H, dd, J = 9.0, 3.5 Hz, δ5.72; 1H, dd, J = 3.5, 1.5 Hz, δ5.85; 2H, s, δ5.89; 1H, s, δ6.43; 1H, dd, J = 9.0, 1.5 Hz, δ6.46; 1H, s, δ6.54; 5H, m, δ7.30–δ7.64.

(b) A soln of **5a** (0.5 g) and 2,3-dichloro-5,6-dicyanohydroquinone (0.1 g) in acetone (10 ml) was warmed for 1 min and evaporated. The residue was extracted with boiling Skellysolve F and the soln was filtered through a short column of silicic acid. Concentration of the filtrate gave 6,7-methylenedioxyflav-3-ene as colorless plates, m.p. and m.m.p. 73° (0.31 g). A soln of **5a** (1.0 g) in glacial AcOH (5 ml), warmed for 1 min, gave **7**, m.p. and m.m.p. 73° (0.45 g).

6,7-Methylenedioxyflavan **8**

Compound **7** (0.3 g) was hydrogenated in THF (20 ml) at room temp and pressure with 5% PdC catalyst. Evaporation of the soln gave *6,7-methylenedioxy-flavan* **8** as colorless needles (*ex* Skellysolve F), m.p. 81° (0.22 g). (Found: C, 75.9; H, 5.60. Calc. for $C_{16}H_{14}O_3$; C, 75.6; H, 5.55%); NMR spectrum: 2H, m, δ2.08; 2H, m, δ2.78; 1H, dd, J = 9.0, 4.0 Hz, δ4.99; 2H, s, δ5.86; 1H, s, δ6.47; 1H, s, δ6.52; 5H, m, δ7.38.

6,7-Methylenedioxyflavylium perchlorate **9**

Compound **7** (0.5 g) was heated on a steam-bath with 35% aqueous perchloric acid for 1 hr. The mixture was diluted with water (10 ml) and ether (20 ml), cooled, and filtered. The crystalline flavylium salt was recrystallized from MeOH-aqueous perchloric acid to yield *6,7-methylenedioxyflavylium perchlorate* **9** as yellow needles, m.p. 305–306° (dec) (0.28 g) (Found: C, 55.5; H, 3.35. Calc. for $C_{16}H_{11}O_7Cl$: C, 55.0; H, 3.16%).

2-(4-Methoxybenzyl)-4,5-methylenedioxyphenol **10**

A suspension of sesamol (26.8 g) and 4-methoxybenzyl alcohol (27.6 g) in 2% aqueous citric acid (500 ml) containing ascorbic acid (5.0 g) was heated under reflux for 17 hr. On cooling, the oily product crystallized (50.2 g). Recrystallized from benzene (*2-(4-methoxybenzyl)-4,5-methylenedioxy-phenol* separated as colorless prisms, m.p. 110° (42.0 g). (Found: C, 70.0; H, 5.64. Calc. for $C_{15}H_{14}O_4$: C, 69.8; H, 5.46%); NMR spectrum: 3H, s, δ3.77; 2H, s, δ3.82; 1H (OH), s, δ4.68; 2H, s, δ5.85; 1H, s, δ6.37; 1H, s, δ6.56; 2H, d, J = 9.0 Hz, δ6.81; 2H, d, J = 9.0 Hz, δ7.12.

With Ac_2O and a drop of pyridine **10** formed a *monoacetate*, colorless glistening needles, m.p. 80° (*ex* MeOH). (Found: C, 68.3; H, 5.54. Calc. for $C_{17}H_{16}O_5$: C, 68.0; H, 5.37%); NMR spectrum: 3H, s, δ2.20; 2H, s, δ3.71; 3H, s, δ3.76; 2H, s, δ5.89; 2H, s, δ6.55; 2H, d, J = 8.5 Hz, δ6.79; 2H, d, J = 8.5 Hz, δ7.05.

Oxidation of **10**

A soln of 2-(4-methoxybenzyl)-4,5-methylenedioxyphenol (2.0 g) in ether (150 ml) was heated under reflux with silver oxide (6.0 g) for 3.5 hr, and filtered. Orange colored crystals separated from the filtrate. The soln was concentrated to 70 ml, cooled, and the colored product was collected (0.76 g; m.p. 143°). The ether filtrate was diluted to 100 ml and treated once again with silver oxide (3.0 g) for 2 hr to give an additional quantity of the orange colored product (0.20 g). Recrystallized from benzene-Skellysolve F.

6-(4-methoxybenzylidene)-3,4-methylenedioxy-cyclohexa-2,4-dienone **11a** was obtained as orange colored needles, m.p. 143–144°. (Found: C, 70.5; H, 4.75. Calc. for $C_{15}H_{12}O_4$: C, 70.3; H, 4.72%); $\lambda_{max}^{CHCl_3}$ 433, 362, 301 nm (accurate extinction coefficients not obtained because of dimerization). Reduced with $NaBH_4$ in MeOH **11a** gave colorless needles identical (NMR, m.p. and m.m.p. 110°) with **10**.

The ether reaction filtrate after removal of **11a** was evaporated to a gum which was dissolved in warm benzene (2 ml). On standing colorless crystals separated (0.41 g). Recrystallized from acetone the *dimer* **19** separated as colorless, glistening prisms, m.p. 203–204° (to an orange liquid with the same R_F as the quinone methide **11a**). (Found: C, 70.4; H, 4.85. Calc. For $C_{30}H_{24}O_8$: C, 70.3; H, 4.72%); NMR spectrum: 3H, s, δ3.75; 3H, s, δ3.79; 1H, s, δ4.00; 1H, s, δ5.37; 1H, s, δ5.52; 1H, s, δ5.70; 1H, s, δ5.79; 1H, s, δ5.87; 1H, s, δ5.89; 1H, s, δ5.92; 1H, s, δ6.32; 1H, s, δ6.57; 2H, d, J = 9 Hz, δ6.74; 2H, d, J = 9 Hz, δ6.77; 2H, d, J = 9 Hz, δ6.91; 2H, d, J = 9 Hz, δ7.24.

A soln of **11a** (0.20 g) in benzene (2.0 ml) was heated for 10 min and kept at room temp. for 48 hr. The dimer **19** separated as colorless needles, m.p. and m.m.p. 203–204° (0.13 g). A soln of **11a** in warm MeOH was decolorized at once and the dimer **19** crystallized from the warm soln.

Catalytic hydrogenation of **19**

A soln of **19** (1.0 g) in THF (100 ml) was hydrogenated at room temp. and 30 p.s.i. in the presence of 5% PdC for 1 hr. The filtered soln was concentrated, diluted with MeOH and reconcentrated until colorless needles began to separate (0.51 g). Recrystallized from acetone-methanol the **24** separated as colorless needles, m.p. 269–270°. (Found: C, 70.1; H, 5.21. Calc. for $C_{30}H_{26}O_8$: C, 70.0; H, 5.09%); NMR spectrum: 1H, dd, J = 12, 12 Hz, δ2.17; 1H, dd, J = 12, 6 Hz, δ2.52; 6H, s, δ3.78; 1H, s, δ4.19; 1H, dd, J = 12, 6 Hz, δ4.91; 1H, s, δ5.27; 1H, s, δ5.33; 1H, s, δ5.54; 1H, s, δ5.74; 1H, s, δ5.89; 1H, s, δ5.91; 1H, s, δ6.38; 1H, s, δ6.57; 6H, m, δ6.70–δ6.95; 2H, d, J = 9.0 Hz, δ7.33.

After removal of **24** the THF–MeOH reaction filtrate was evaporated and the residue was dissolved in benzene. On cooling **10** separated as colorless needles, m.p. and m.m.p. 110° (0.15 g).

Sodium borohydride reduction of **19** and **24**

A soln of **24** (0.20 g) in warm THF (10 ml) was diluted with MeOH (20 ml) and treated with $NaBH_4$ (0.40 g). After 30 min the soln was concentrated and diluted with water. The solid product crystallized from acetone–MeOH to yield the diol **25a** or **26a** as colorless needles, m.p. 172–173° (0.15 g) (Found: C, 70.8; H, 6.11. Calc. for $C_{29}H_{30}O_7$: C, 71.0; H, 6.16). Reduction of **19** under the same conditions gave the diol, m.p. and m.m.p. 172–173°. With benzoyl chloride and pyridine the diol formed a monobenzoate **25b** or **26b**, colorless needles *ex* acetone-MeOH, m.p. 257° (Found: C, 73.0; H, 5.80. Calc. for $C_{36}H_{34}O_8$: C, 72.7; H, 5.576%); NMR spectrum: 7H, m, δ1.20–δ2.20; 1H, m, δ3.22; 3H, s, δ3.82; 3H, s, δ3.85; 1H, s, δ4.38; 1H, m, δ5.54; 1H, s, δ5.83; 1H, s, δ5.84; 1H, s, δ5.85; 1H, s, δ6.34; 1H, s, δ6.49; 2H, d, J = 9.0 Hz, δ6.92; 2H, d, J = 9.0 Hz, δ6.94; 7H, m, δ7.22–δ7.60; 2H, d, J = 9.0 Hz, δ7.96.

2 - Ethoxy - 4 - (4 - methoxyphenyl) - 6,7 - methylenedioxy - chroman **12**

A soln of **11a** (0.5 g) in ethyl vinyl ether (50 ml) was kept at room temp. for 5 hr, filtered, and evaporated. The residue crystallized from Skellysolve F and from MeOH to yield **12** as colorless needles, m.p. 116–117° (0.43 g). (Found: C, 69.5; H, 6.14. Calc. for $C_{21}H_{24}O_6$: C, 69.5; H, 6.14%); NMR spectrum: 2H, m, δ2.23; 1H, m, δ3.64; 3H, s, δ3.81; 2H, m, δ4.05; 1H, dd, J = 8.0, 3.0 Hz, δ5.18; 2H, s, δ5.83; 1H, s, δ6.17; 1H, s, δ6.42; 2H, d, J = 8.5 Hz, δ6.85; 2H, d, J = 8.5 Hz, δ7.12.

2-(4-Methoxybenzyl)-4,5-dimethoxyphenol.

A mixture of 3,4-dimethoxyphenol (15.4 g), 4-methoxybenzyl alcohol (13.8 g), ascorbic acid (5 g) and 2% aqueous citric acid (500 ml) was heated under reflux for 18 hr and cooled. the crystalline product (29 g) was recrystallized from aqueous MeOH and from benzene-Skellysolve F to give 2-(4-methoxybenzyl)-4,5-dimethoxyphenol as colorless needles, m.p.: 66–67°, resolidify and melt again at 99–100° (Found: C, 69.6; H, 6.63. Calc. for $C_{16}H_{18}O_4$: C, 70.0; H, 6.61%); NMR spectrum: 9H, s, δ3.80; 2H, s, δ3.87; 1H, s, δ4.76 (OH); 1H, s, δ6.43; 1H, s, δ6.63; 2H, d, J = 8.0 Hz, δ6.82; 2H, d, J = 8.0 Hz, δ7.12. With Ac_2O and pyridine the phenol forms an *acetate*, colorless needles *ex* MeOH, m.p. 72–73°. (Found: C, 68.3; H, 6.37. Calc. for $C_{18}H_{20}O_5$: C, 68.3; H, 6.37%); NMR spectrum: 3H, s, δ2.22; 9H, s, δ3.78; 2H, s, δ3.84; 1H, s, δ6.59; 1H, s, δ6.62; 2H, d, J = 8.0 Hz, δ6.80; 2H, d, J = 8.0 Hz, δ7.07.

Oxidation of 2-(4-methoxybenzyl)-4,5-dimethoxyphenol

A mixture of the phenol (2.5 g), silver oxide (8.0 g) and ether (150 ml) was heated under reflux for 3 hr and filtered. The ether filtrate was concentrated to 15 ml. On scratching orange crystals separated. These were recrystallized from benzene-Skellysolve F to give *6-(4-methoxybenzylidene)-cyclohexa-2,4-dienone* **20** as orange-red needles, m.p. 151–152° (0.21 g) (Found: C, 70.4; H, 6.11. Calc. for $C_{16}H_{16}O_4$: C, 70.6; H, 5.32%); NMR spectrum 3H, s, δ3.82; 6H, s, δ3.87; 1H, s, δ5.85; 1H, s, δ6.52; 2H, d, J = 9.0 Hz, δ6.97; 2H, d, J = 9.0 Hz, δ7.53; 1H, s, δ7.83.

The ether filtrate from which **20** crystallized was evaporated and the residue dissolved in warm MeOH. On standing clusters of colorless needles separated (0.32 g). Recrystallized from acetone-MeOH the dimer **21** separated as colorless needles, m.p. 183–184° (to an orange liquid). (Found: C, 70.7; H, 6.04. Calc. for $C_{32}H_{32}O_8$: C, 70.6; H, 5.92%); NMR spectrum: 3H, s, δ3.66; 3H, s, δ3.69; 6H, s δ3.76; 3H, s, δ3.80; 3H, s, δ3.90; 1H, s, δ4.01; 1H, s, δ5.26; 1H, s, δ5.52; 1H, s, δ5.67; 1H, s, δ6.35; 1H, s, δ6.63; 2H, d, J = 9.0 Hz, δ6.74; 2H, d, J = 9.0 Hz, δ6.79; 2H, d, J = 9.0 Hz, δ6.91; 2H, d, J = 9.0 Hz, δ7.28.

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