Structural Studies on Bio-active Compounds. Part 12.[1] Tautomerism and Conformation of Aryl-substituted 1-(2-Hydroxyphenyl)-3-phenylpropane-1,3-diones in the Solid Phase and in Solution

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The tautomerism of a series of aryl-substituted 1-(2-hydroxyphenyl)-3-phenylpropane-1,3-diones has been studied in deuteriochloroform solution by ^{1}H n.m.r. techniques and, in the case of 1-(2-hydroxy-4-methoxyphenyl)-3-phenylpropane-1,3-dione and 1-(2-hydroxy-4,6-dimethoxyphenyl)-3-phenylpropane-1,3-dione, in the solid state by *X*-ray crystallography. Of these compounds, most exist between 80 and 95% in the enolised form in solution and 1-(2-hydroxy-4-methoxyphenyl)-3-phenylpropane-1,3-dione adopts this tautomer in the crystal. However, 1-(2-hydroxy-4,6-dimethoxyphenyl)-3-phenylpropane-1,3-dione is present as the diketone in the solid phase and enolises very slowly in solution. 1-(6-Benzoyloxy-2-hydroxyphenyl)-3-hydroxy-3-phenylprop-2-en-1-one is shown by ^{1}H n.m.r. spectroscopy possibly to adopt a 'coiled' conformation in solution in deuteriochloroform.

During the preparation of a series of flavones as potential enzyme inhibitors, variously substituted 1-(2-hydroxyphenyl)-3-phenylpropane-1,3-diones (**5**) were required as intermediates. The enolisation of 1,3-dicarbonyl compounds and the structure of the enol have been the subject of many studies[2,3] by spectroscopic and other methods. Recently, Bassetti *et al.*[4] have inferred from ^{1}H n.m.r. data on simple 1,3-dialkyl- and 1,3-diaryl-propane-1,3-diones that the six-membered hydrogen-bonded ring system in the enol form of these compounds is best described as 'pseudo-aromatic'. It was therefore of interest to study the extent of tautomerism of the 1,3-diphenylpropane-1,3-diones when a potentially hydrogen-bonding *ortho* phenolic hydroxy group is present on one of the phenyl rings and to study the structure of the enols formed.

The synthesis of the required diones was generally straightforward and is shown in Scheme 1. Appropriately substituted 2-hydroxyacetophenones (**2**) were commercially available or were prepared by a Friedel–Crafts-type acetylation of 3-methoxyphenol (**1a**) or 3,5-dimethoxyphenol (**1b**) using the modification described by Piccolo *et al.*[5] using boron trichloride as a catalyst. In this procedure, an initial complex or borate ester is formed between the phenolic oxygen and the Lewis acid in dichloromethane solution at −10 °C. Addition of acetyl chloride leads to complexation of its carbonyl oxygen to the boron, ensuring that acylation takes place exclusively at the carbon *ortho* to the phenolic hydroxy group. The results presented here show that there is no interference caused by the potentially complexing methoxy group to the regioselectivity of the acylation. This process obviates the need for the harsh conditions of the classical *ortho* acylation of phenol by esterification and subsequent Fries rearrangement at elevated temperature in the presence of aluminium chloride. Phenols (**2**) were then acylated with a benzoyl chloride (**3**) in pyridine with or without catalysis by 4-(dimethylamino)pyridine to give the esters (**4**). Migration of the acyl group from oxygen to carbon was then achieved under base catalysis either by the method of Furniss *et al.*[6] with powdered potassium hydroxide in pyridine or, in the cases of the more labile or recalcitrant esters, under anhydrous and non-nucleophilic conditions using lithium hexamethyldisilazide as the base.

The 400 MHz ^{1}H n.m.r. spectrum of the prototype unsubstituted 1-(2-hydroxyphenyl)-3-phenylpropane-1,3-dione (**5c**) shows the presence of both keto and enol tautomers (Scheme 2) in solution in deuteriochloroform at ambient temperature in the ratio 7:93 respectively. The methylene protons of the keto form resonate as a singlet at δ 4.63; the corresponding vinylic proton of the enol appears as a singlet at δ 6.84. The resonances arising from the OH protons were observed in the downfield portion of the spectrum, as expected for hydroxy groups in strongly hydrogen-bonded environments. Sharp singlets were observed at δ 11.93, 12.19, and 15.94, corresponding to the phenolic OH of the keto and enol tautomers and to the 'enol' respectively. It has been reported by Burdett and Rogers[3] that 1,3-diphenylpropane-1,3-dione is fully enolised in solution in carbon tetrachloride, whereas Bassetti *et al.*[4] observed both keto and enol forms in deuteriochloroform. In the solid state, Weast[7] records the existence of crystals of each tautomer.

The majority of the 1-(2-hydroxyphenyl)-3-phenylpropane-1,3-diones (**5a, c–k**) showed greater than 80% enolisation in deuteriochloroform as revealed by their ^{1}H n.m.r. spectra. The dimethoxy compound (**5b**), however, was shown to exist initially as the keto tautomer in solution in this solvent. Progressive enolisation was observed on increasing the temperature from 295 to 325 K in steps of 5 K. This was not reversed on cooling and the final solution contained 38% enol and 62% keto forms of (**5b**). To investigate whether the enolisation of (**5**) was an effect of dissolution or, alternatively, the enol form was present in the solid state, a determination of the crystal structure of an example of a 1-(2-hydroxyaryl)-3-arylpropane-1,3-dione was carried out by *X*-ray diffraction techniques. Similarly, the solid state structure of the anomalous (**5b**), which is very slowly enolised in solution, was investigated. The monomethoxy analogue (**5a**) was selected as a typical 'enolisable' propane-1,3-dione on two grounds. Firstly, ^{1}H n.m.r. spectroscopy of its deuteriochloroform solution showed it to be *ca.* 92% enolised. Secondly, whereas careful recrystallisation of (**5c–k**) from a variety of solvents furnished only powders, (**5a**) formed large transparent brown crystals from

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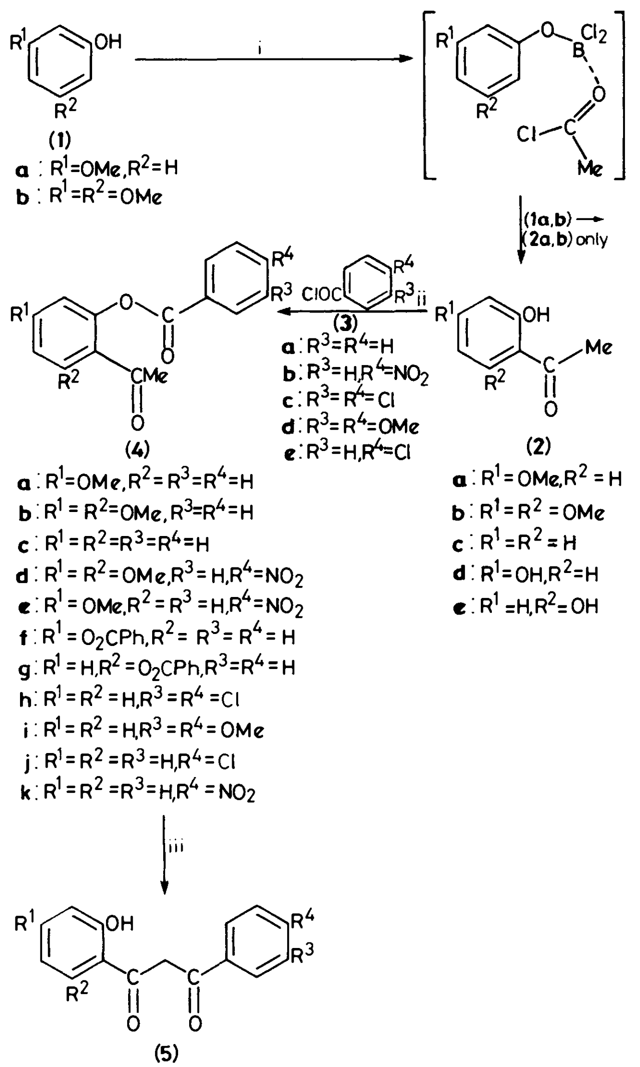
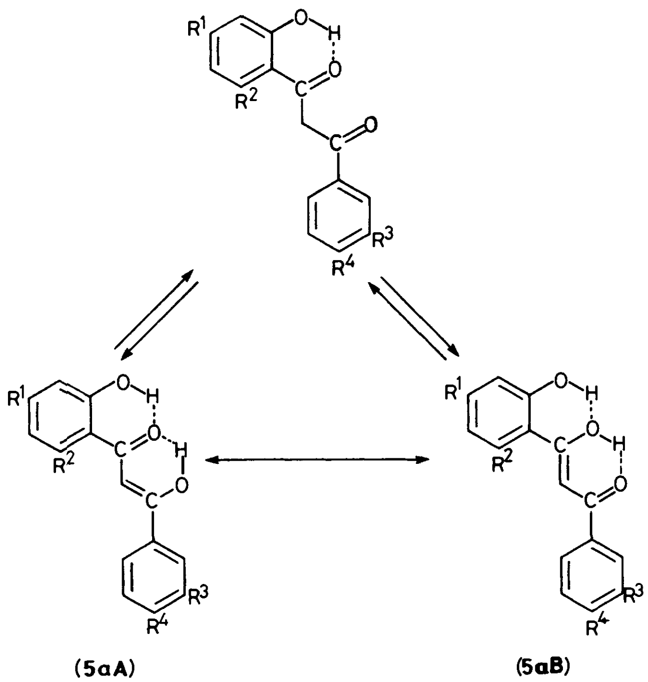


Scheme 1. Synthesis of 1,3-Diarylpropane-1,3-diones (**5**). *Reagents:* i, BCl_3–AcCl–CH_2Cl_2; ii, pyridine ±4-(dimethylamino)pyridine; iii, KOH–pyridine or $Li^+ \ ^-N(SiMe_3)_2$.



Scheme 2. Keto–enol tautomerism of (**5**) (R^1,R^2,R^3,R^4 as Scheme 1); (**5aA**) and (**5bB**) are limiting structures of the enol of (**5a**) (R^1 = OMe, R^2 = R^3 = R^4 = H).

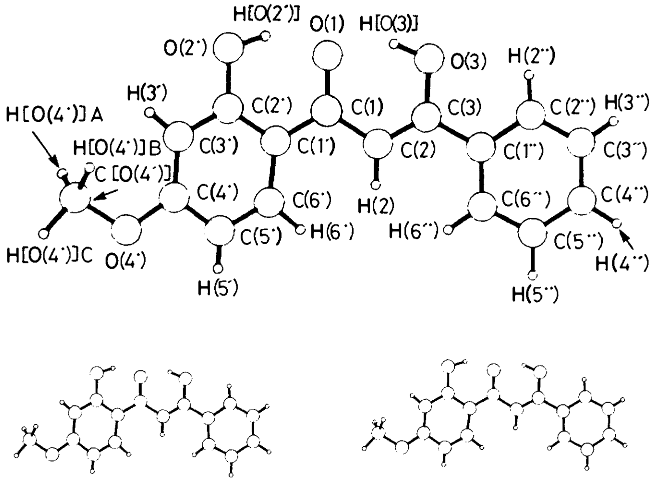


Figure 1. (*a*) Numbering scheme for atoms in (**5a**). (*b*) Stereo plots of (**5a**).

methanol. Similarly, the dimethoxy compound (**5b**) formed elegant hexagonal plates from the same solvent.

Crystal Structure of 1-(2-*Hydroxy*-4-*methoxyphenyl*)-3-*phenylpropane*-1,3-*dione* (**5a**).—The numbering scheme used in the crystallographic determination is shown in Figure 1(*a*).

Crystal data. 1-(2-*Hydroxy*-4-*methoxyphenyl*)-3-*phenylpropane*-1,3-*dione* (**5a**).—$C_{16}H_{14}O_4$, M = 270.3. Monoclinic, a = 10.622(2), b = 12.795(5), c = 10.748(3) Å, β = 111.77(1)°, V = 1 356.6(6) Å^3 (by least-squares refinement on diffractometer angles for 25 automatically centred reflections λ = 0.710 69 Å), space group $P2_1/a$, Z = 4, D_x = 1.321 g cm^{-3}, crystal dimensions = 0.6 × 0.55 × 0.325 mm, μ(Mo-K_α) = 0.57 cm^{-1}.

Crystal Structure of 1-(2-*Hydroxy*-4,6-*dimethoxyphenyl*)-3-*phenylpropane*-1,3-*dione* (**5b**).—The numbering scheme used in the crystallographic determination is shown in Figure 2(*a*).

Crystal data. 1-(4,6-*Dimethoxyphenyl*-2-*hydroxy*)-3-*phenylpropane*-1,3-*dione* (**5b**).—$C_{17}H_{16}O_5$, M = 300.3. Monoclinic, a = 9.503(2), b = 9.924(2), c = 16.125(3) Å, β = 102.22(2)°, V = 1 486.3 Å^3 (by least-squares refinement on diffractometer angles for 25 automatically centred reflections, λ = 0.710 69 Å), space group $P2_1/c$, Z = 4, D_x = 1.439 g cm^{-3}. Crystal dimensions = 0.80 × 0.48 × 0.64 mm, μ(Mo-K_α) = 0.64 cm^{-1}.

Collection and Processing of Data.—Enraf-Nonius CAD4 diffractometer, ω–2θ mode with scan width = 1.0 + 0.35 tan θ, scan speed 0.9–3.3° min^{-1}, graphite monochromated Mo-K_α radiation; for compound (**5a**) 2 671 unique reflections (merging R = 0.093) were measured between 2° ⩽ θ < 26° for $+h$, $\pm k$, $\pm l$ giving 1 939 with $|F_0| > 3\sigma(F_0)$; for compound (**5b**), 2 970 unique reflections (merging R = 0.025) were measured between 2° ⩽ θ < 26° giving 2 442 with $|F_0| > 3\sigma(F_0)$. No decomposition or movement of the crystal was detected during data collection and refinement. No correction was made for absorption or extinction.

Analysis and Refinement of Structures.—The structure of

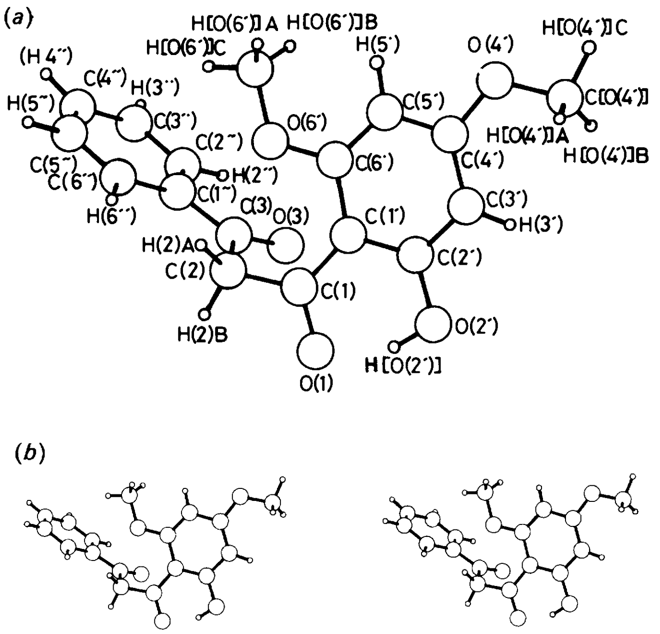


Figure 2. (*a*) Numbering scheme for atoms in (**5b**). (*b*) Stereo plots of (**5b**).

Table 1. Positional parameters (fractional co-ordinates × 10^4) for (**5a**) with estimated standard deviation (esd) in parentheses.

Atom	*x*	*y*	*z*
C(1)	2 766(3)	1 296(2)	3 899(3)
C(2)	2 278(3)	1 960(2)	2 747(3)
C(3)	2 902(3)	2 027(2)	1 862(3)
C(1″)	2 424(3)	2 654(2)	621(3)
C(2″)	2 981(4)	2 483(3)	−353(3)
C(3″)	2 516(4)	3 033(3)	−1 536(4)
C(4″)	1 533(4)	3 765(3)	−1 761(4)
C(5″)	1 001(4)	3 965(3)	−796(4)
C(6″)	1 443(3)	3 411(3)	388(3)
C(1′)	2 050(3)	1 199(2)	4 821(3)
C(2′)	2 440(3)	445(2)	5 853(3)
C(3′)	1 743(4)	340(3)	6 704(3)
C(4′)	660(4)	958(3)	6 567(3)
C[O(4′)]	311(6)	184(5)	8 437(5)
C(5′)	255(4)	1 713(3)	5 573(4)
C(6′)	937(4)	1 824(3)	4 727(3)
O(1)	3 831(2)	756(2)	4 114(2)
O(3)	4 048(2)	1 499(2)	2 035(2)
O(2′)	3 498(2)	−206(2)	6 049(2)
O(4′)	96(2)	912(2)	7 350(2)
H(2″)	3 614(28)	1 945(21)	−186(26)
H(3″)	2 813(39)	2 858(28)	−2 192(38)
H(4″)	1 057(35)	4 129(26)	−2 623(36)
H(5″)	212(35)	4 422(27)	950(35)
H(6″)	1 065(28)	3 574(21)	1 028(28)
H(2)	1 423(30)	2 261(21)	2 595(26)
H[O(3)]	4 209(35)	1 068(26)	2 803(35)
H(6′)	669(46)	2 481(33)	4 045(42)
H(5′)	−437(40)	2 081(29)	5 472(39)
H(3′)	2 112(32)	−98(24)	7 348(32)
H[O(2′)]	3 959(42)	73(32)	5 427(40)
H[O(4′)]A	1 250(40)	404(26)	8 983(35)
H[O(4′)]B	−501(44)	231(31)	8 849(40)
H[O(4′)]C	342(51)	−581(40)	8 067(48)

1-(2-hydroxy-4-methoxyphenyl)-3-phenylpropane-1,3-dione (**5a**) was solved by the use of SHELX.[8] All hydrogen atoms were located by difference electron density synthesis. Final full-matrix least-squares refinement of co-ordinates and anisotropic

Table 2. Bond distances of (**5a**) with esds in parentheses.

Bond	Distance/Å
C(1)–C(2)	1.431(4)
C(1)–C(1′)	1.461(4)
C(1)–O(1)	1.272(3)
C(2)–C(3)	1.349(4)
C(3)–C(1″)	1.476(4)
C(3)–O(3)	1.343(3)
C(1′)–C(2″)	1.399(4)
C(1″)–C(6″)	1.375(4)
C(2″)–C(3″)	1.374(5)
C(3″)–C(4″)	1.356(5)
C(4″)–C(5″)	1.377(5)
C(5″)–C(6″)	1.378(4)
C(1′)–C(2′)	1.411(4)
C(1′)–C(6′)	1.400(4)
C(2′)–O(2)	1.351(3)
C(2′)–C(3′)	1.380(4)
C(3′)–C(4′)	1.359(4)
C(4′)–O(4′)	1.362(3)
O(4′)–C[O(4′)]	1.430(5)
C(4′)–C(5′)	1.386(5)
C(5′)–C(6′)	1.364(4)
C(2)–H(2)	0.94(3)
C(2″)–H(2″)	0.93(3)
C(3″)–H(3″)	0.90(4)
C(4″)–H(4″)	0.99(4)
C(5″)–H(5″)	0.98(3)
C(6″)–H(6″)	0.94(3)
C(3′)–H(3′)	0.86(3)
C[O(4′)]–H[O(4′)]A	0.99(4)
C[O(4′)]–H[O(4′)]B	1.11(4)
C[O(4′)]–H[O(4′)]C	1.06(5)
C(5′)–H(5′)	0.85(4)
C(6′)–H(6′)	1.08(4)
O(3)–H[O(3)]	0.95(4)
O(2′)–H[O(2′)]	1.03(4)

Table 3. Interatomic angles for (**5a**) with esds in parentheses.

Atoms	Bond angle/°
C(1′)–C(1)–C(2)	121.7(3)
O(1)–C(1)–C(2)	119.5(2)
O(1)–C(1)–C(1′)	118.8(2)
C(3)–C(2)–C(1′)	122.2(3)
C(1″)–C(3)–C(2)	125.3(3)
O(3)–C(3)–C(2)	121.8(3)
O(3)–C(3)–C(1″)	112.9(2)
C(2″)–C(1″)–C(3)	119.5(3)
C(6″)–C(1″)–C(3)	122.1(2)
C(6″)–C(1″)–C(2″)	118.4(3)
C(3″)–C(2″)–C(1″)	120.4(3)
C(4″)–C(3″)–C(2″)	120.5(3)
C(5″)–C(4″)–C(3″)	119.9(3)
C(6″)–C(5″)–C(4″)	120.3(4)
C(5″)–C(6″)–C(1″)	120.4(3)
C(2′)–C(1′)–C(1)	121.1(3)
C(6′)–C(1′)–C(1)	122.7(3)
C(6′)–C(1′)–C(2′)	116.2(2)
C(3′)–C(2′)–C(1′)	120.9(3)
O(2′)–C(2′)–C(1′)	121.9(2)
O(2′)–C(2′)–C(3′)	117.2(3)
C(4′)–C(3′)–C(2′)	120.9(3)
C(5′)–C(4′)–C(3′)	119.8(3)
O(4′)–C(4′)–C(3′)	125.3(3)
O(4′)–C(4′)–C(5′)	114.9(3)
C(6′)–C(5′)–C(4′)	119.8(3)
C(5′)–C(6′)–C(1′)	122.4(3)
C[O(4′)]–O(4′)–C(4′)	117.7(3)

Table 4. Selected torsion angles for (**5a**).

Atoms	Angle/°
C(1′)–C(1)–C(2)–C(3)	−177.5
O(1)–C(1)–C(2)–C(3)	0.8
C(2)–C(1)–C(1′)–C(2′)	171.8
C(2)–C(1)–C(1′)–C(6′)	−7.1
O(1)–C(1)–C(1′)–C(2′)	−6.5
O(1)–C(1)–C(1′)–C(6′)	174.6
C(1)–C(2)–C(3)–C(1″)	176.9
C(1)–C(2)–C(3)–O(3)	−2.2
C(2)–C(3)–C(1″)–C(2″)	−165.9
C(2)–C(3)–C(1″)–C(6″)	14.4
O(3)–C(3)–C(1″)–C(2″)	13.4
O(3)–C(3)–C(1″)–C(6″)	−166.4
C(3)–C(1″)–C(2″)–C(3″)	177.7
C(6″)–C(1″)–C(2″)–C(3″)	−2.5
C(3)–C(1″)–C(6″)–C(5″)	−178.5
C(2″)–C(1″)–C(6″)–C(5″)	1.7
C(1″)–C(2″)–C(3″)–C(4″)	1.5
C(2″)–C(3″)–C(4″)–C(5″)	0.4
C(3″)–C(4″)–C(5″)–C(6″)	−1.2
C(4″)–C(5″)–C(6″)–C(1″)	0.1
C(1)–C(1′)–C(2′)–C(3′)	−178.6
C(1)–C(1′)–C(2′)–O(2′)	1.1
C(6′)–C(1′)–C(2′)–C(3′)	0.4
C(6′)–C(1′)–C(2′)–O(2′)	−180.0
C(1)–C(1′)–C(6′)–C(5′)	178.5
C(2′)–C(1′)–C(6′)–C(5′)	−0.4
O(2′)–C(2′)–C(3′)–C(4′)	−179.4
C(2′)–C(3′)–C(4′)–C(5′)	−0.8
C(2′)–C(3′)–C(4′)–O(4′)	179.7
C(3′)–C(4′)–C(5′)–C(6′)	0.8
O(4′)–C(4′)–C(5′)–C(6′)	−179.7
C(3′)–C(4′)–O(4′)–C[O(4′)]	2.5
C(5′)–C(4′)–O(4′)–C[O(4′)]	−176.9
C(4′)–C(5′)–C(6′)–C(1′)	−0.1

Table 5. Positional parameters (fractional co-ordinates $\times 10^4$) of (**5b**) with esds in parentheses.

Atom	*x*	*y*	*z*
C(6′)	5 031(2)	2 921(1)	5 792(1)
C(5′)	4 117(2)	2 418(2)	6 266(1)
C(4′)	3 137(2)	1 411(1)	5 934(1)
C(3)′	3 047(2)	912(2)	5 127(1)
C(2′)	3 978(2)	1 424(1)	4 649(1)
C(1′)	5 003(2)	2 442(1)	4 953(1)
C(1)	5 964(2)	2 902(2)	4 420(1)
C(2)	7 085(2)	3 977(2)	4 690(1)
C(3)	8 313(2)	3 508(2)	5 386(1)
C(1″)	9 195(2)	4 514(1)	5 957(1)
C(2″)	10 356(2)	4 064(2)	6 566(1)
C(3″)	11 148(2)	4 966(2)	7 135(1)
C(4″)	10 789(2)	6 307(2)	7 100(1)
C(5″)	9 657(2)	6 763(2)	6 498(1)
C(6″)	8 870(2)	5 884(2)	5 922(1)
O(6′)	5 984(1)	3 923(1)	6 075(1)
C[O(6′)]	6 081(3)	4 428(2)	6 917(1)
O(4′)	2 306(1)	996(1)	6 472(1)
C[O(4′)]	1 224(2)	5(2)	6 185(1)
O(2′)	3 587(1)	902(1)	3 866(1)
O(1)	5 878(1)	2 414(1)	3 697(1)
O(3)	8 587(1)	2 314(1)	5 461(1)
H(5′)	4 161(17)	2 728(16)	6 810(11)
H(3′)	2 402(19)	237(17)	4 880(11)
H[O(6′)]A	5 152(24)	4 790(19)	6 973(13)
H[O(6′)]B	6 400(21)	3 667(19)	7 332(12)
H[O(6′)]C	6 808(20)	5 101(18)	6 987(11)
H[O(4′)]A	478(23)	382(20)	5 747(14)
H[O(4′)]B	1 646(22)	−802(21)	6 040(13)
H[O(4′)]C	771(25)	−139(21)	6 713(16)
H(2)A	6 641(17)	4 785(16)	4 844(10)
H(2)B	7 487(18)	4 193(16)	4 207(11)
H[O(2′)]	4 545(27)	1 358(23)	3 659(14)
H(2″)	10 587(20)	3 118(18)	6 591(11)
H(3″)	11 898(22)	4 629(18)	7 530(13)
H(4″)	11 323(22)	6 922(20)	7 536(14)
H(5″)	9 385(22)	7 736(21)	6 470(12)
H(6″)	8 095(20)	6 228(18)	5 474(11)

thermal parameters for non-hydrogen atoms, and co-ordinates and isotropic temperature factors for hydrogen atoms reduced $R = \Sigma||F_0| - |Fc||/\Sigma|F_0|$ and $R_w = \Sigma w^{\frac{1}{2}}||F_0| - |Fc||/\Sigma|w^{\frac{1}{2}}|F_0|$ to 0.056 and 0.057 respectively. In the final stages of refinement, reflections were weighted according to $W = k/\sigma^2(F_0)$ where k converged at 2.3867 and $\sigma(F_0)$ was obtained from counting statistics and an allowance for the instability of the instrument. Refinement was terminated when no positional parameter shifted by more than 0.006 esd, at which point a difference electron density map showed no feature greater than ± 0.19 e Å^{-3}.

The structure of 1-(2-hydroxy-4,6-dimethoxyphenyl)-3-phenylpropane-1,3-dione (**5b**) was solved by the use of the MULTAN78 direct methods package[9] and subsequently refined using SHELX.[8] Again, all hydrogen atoms were located by difference electron density synthesis. Final full-matrix least-squares refinement, as for (**5a**), reduced R and R_w to 0.042 and 0.041 respectively and reflections in the final stages were weighted according to $w = k/\sigma^2(F_0)$ where k converged at 3.195. The refinement was terminated when no positional parameter shifted by more than 0.002 esd, at which point a difference electron density map showed no feature greater than ± 0.27 e A^{-3}.

Positional parameters for the structure of (**5a**) are shown in Table 1, with bond lengths in Table 2, bond angles in Table 3, and selected torsion angles in Table 4. The corresponding data for the dimethoxy analogue (**5b**) are reported in Tables 5–8 respectively.*

The crystal structures confirm that (**5a**) exists in the enol form in the solid state and that (**5b**) exists in the keto form. As expected, the enol system in (**5a**) is planar. However, unlike the situation for enols of simple 1,3-diarylpropane-1,3-diones,[3] this six-membered hydrogen-bonded ring is not symmetrical in terms of bond lengths and thus the enol can be described as tending towards either structure (**5aA**) or structure (**5aB**) (Scheme 2). The distinction between these two limiting structures is revealed by the differences between the lengths of the two carbon–oxygen bonds, with C(1)–O(1) being 1.273 Å and C(3)–O(3) being 1.343 Å. The former is slightly longer than expected for a ketonic carbonyl group;[10] this may be attributable to a reduction in bond order through hydrogen-bonding both from the phenolic and the enolic OH. The length of C(3)–O(3) is comparable to that of a shortened C–O single bond (*e.g.* in a carboxylic acid) (*ca.* 1.36 Å).[10] That the solid state structure of the enol of (**5a**) tends to the limit (**5aA**) is confirmed by comparison of the lengths of C(1)–C(2) (1.431 Å) and C(2)–C(3) (1.349 Å), indicating *approach* to single and double bond character respectively. Indeed, the phenyl–carbonyl bond [C(1′)–C(1)] also has bond order slightly higher than unity with length 1.461 Å compared with the normal alkane C–C bond length of *ca.* 1.541 Å.[10] The shortening of C(1′)–C(1) and C(1)–C(2) reflects

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* *Supplementary data:* (see section 5.6.3 of Instructions for Authors, in the January issue). Full lists of bond lengths and angles and of thermal parameters have been deposited at the Cambridge Crystallographic Data Centre.

Table 6. Bond distances of (**5b**) with esds in parentheses.

Atoms	Distances
C(5′)–C(6′)	1.368(2)
C(1′)–C(6′)	1.429(2)
C(6′)–O(6′)	1.358(2)
C(4′)–C(5′)	1.393(2)
C(3′)–C(4′)	1.378(2)
O(3′)–C(3′)	1.355(2)
C(2′)–C(3′)	1.387(2)
C(1′)–C(2′)	1.417(2)
C(2′)–O(2′)	1.348(2)
C(1′)–C(1)	1.453(2)
C(1)–C(2)	1.506(2)
C(1)–O(1)	1.249(2)
C(2)–C(3)	1.510(2)
C(3)–C(1″)	1.490(2)
C(3)–O(3)	1.213(2)
C(1″)–C(2″)	1.386(2)
C(1″)–C(6″)	1.393(2)
C(2″)–C(3″)	1.386(2)
C(3″)–C(4″)	1.373(3)
C(4″)–C(5″)	1.365(3)
C(5″)–C(6″)	1.374(3)
C[O(6′)]–O(6′)	1.432(2)
C[O(4′)]–O(4′)	1.427(2)
C(5′)–H(5′)	0.92(2)
C(3′)–H(3′)	0.94(2)
C(2)–H(2)A	0.90(2)
C(2)–H(2)B	0.96(2)
C(2″)–H(2″)	0.96(2)
C(3″)–H(3″)	0.91(2)
C(4″)–H(4″)	0.99(2)
C(5″)–H(5″)	1.00(2)
C(6″)–H(6″)	0.98(2)
C[O(6′)]–H[O(6′)]A	0.98(2)
C[O(6′)]–H[O(6′)]B	1.00(2)
C[O(6′)]–H[O(6′)]C	0.95(2)
C[O(4′)]–H[O(4′)]A	0.96(2)
C[O(4′)]–H[O(4′)]B	0.95(2)
C[O(4′)]–H[O(4′)]C	1.04(3)
O(2′)–H[O(2′)]	0.92(3)

Table 7. Interatomic angles for (**5b**) with esds in parentheses.

Atoms	Bond angle/°
C(1′)–C(6′)–C(5′)	121.5(1)
O(6′)–C(6′)–C(5′)	122.4(1)
O(6′)–C(6′)–C(1′)	116.1(1)
C(4′)–C(5′)–C(6′)	119.9(1)
C(4′)–C(3′)–C(2′)	121.6(1)
O(4′)–C(4′)–C(5′)	113.9(1)
O(4′)–C(4′)–C(3′)	124.5(1)
C(2′)–C(3′)–C(4′)	118.3(2)
C(1′)–C(2′)–C(3′)	122.9(1)
O(2′)–C(2′)–C(3′)	116.2(1)
O(1′)–C(2′)–C(1′)	120.9(1)
C(2′)–C(1′)–C(6′)	115.9(1)
C(1)–C(1′)–C(6)	124.6(1)
C(1)–C(1′)–C(2)	119.5(1)
C(2)–C(1)–C(1′)	123.1(1)
O(1)–C(1)–C(1′)	120.3(1)
O(1)–C(1)–C(2)	116.6(1)
O(3)–C(2)–C(1)	112.1(1)
C(1″)–C(3)–C(2)	119.9(1)
O(3)–C(3)–C(2)	119.4(1)
O(3)–C(3)–C(1″)	120.8(1)
C(2″)–C(1″)–C(3)	118.8(1)
C(6″)–C(1″)–C(3)	122.6(1)
C(6″)–C(1″)–C(2″)	118.6(2)
C(3″)–C(2″)–C(1″)	120.1(2)
C(4″)–C(3″)–C(2″)	120.2(2)
C(5″)–C(4″)–C(3″)	120.2(2)
C(6″)–C(5″)–C(4″)	120.2(2)
C(5″)–C(6″)–C(1″)	120.6(2)
C[O(6′)]–O(6′)–C(6′)	118.7(1)
C[O(4′)]–O(4′)–C(4′)	118.6(1)

the extensive conjugation in this system resulting in co-planarity of the phenyl ring bearing the OH substituent and the enol system. It is interesting to note, however, that the phenyl ring attached to C(3) is not co-planar with the enol system but is at an angle of 14°. While it might initially be thought that there would be further conjugation of the π-bonds of the enol system with the π system of the phenyl ring, consideration of the interatomic distance between the vinyl proton and the aromatic proton *ortho* to the enol system explains this effect. Even at an angle of 14°, the contact distance between H(2) (the vinyl proton) and H(6″) (one of the *ortho* protons) is 2.308 Å. If the phenyl ring were co-planar with the enol system, then these protons would virtually be in contact.

In contrast to the enol system seen in (**5a**), the crystal structure of (**5b**) shows no such tautomerism, although the carbonyl oxygen [O(1)] is hydrogen-bonded to the *ortho* phenolic OH. The C–C single bond lengths of the propane-1,3-dione system are similar to the single bonds in (**5a**), although they are not identical (Tables 2 and 6).

The ^1H n.m.r. spectrum of (**5b**) showed a marked difference in chemical shift of the two *O*-methyl groups. This $\Delta\delta$ is surprising when compared with the corresponding value for the precursor benzoate ester (**4b**) (Table 9). It appears that one of the *O*-methyl groups is being unusually shielded. Consideration of the crystal structure and data supplies a reasonable explanation for this effect. Since this compound exists as the diketone, the molecule is not constrained to planarity about the propane-1,3-dione system. In the crystal, the *O*-methyl group in the 6′-position lies very close to the phenyl ring attached to C(3) of the propane-1,3-dione. If this structure were maintained in solution, there would be a contact distance of *ca.* 2.97 Å between one of the protons of the *O*-methyl group [HO(6′)] and C(6″), placing this methyl group within the anisotropic shielding region of the phenyl ring. The shielding is also notable in the ^1H n.m.r. spectrum of the 4″-nitro analogue (**5d**) (keto form) with resonances for the methoxy groups at δ 3.53 and 3.82.

A trend is notable in the chemical shifts of the phenolic OH in the enol forms of (**5a**, **c**–**k**) as shown in Table 10. The enols of compounds (**5c**, **h**–**k**) with no substituent in the phenolic ring give $\delta_{\text{Phenol-OH}}$ in the range 11.92–12.10, whereas (**5a**, **e**, **f**) with one electron-donating oxygen substituent give resonances for this proton in the range δ 12.36–12.50 and the dimethoxy compound (**5d**) shows δ_{OH} 13.33. The chemical shift of the enol OH proton varied from δ 15.20 to 15.85 with 4″-electron-withdrawing substituents causing the upfield shift and *vice versa*. Introduction of a 4′-methoxy substituent also resulted in a slight upfield shift of this proton. In contrast, the reported[4] chemical shift for this proton in 3-hydroxy-1,3-diphenylprop-2-en-1-one is δ 16.80. Little variation is seen in the chemical shifts of the vinyl proton in the enol forms of (**5a**, **c**, **e**, **f**, **h**–**k**) in that they lie in the range δ 6.62–6.90, consistent with the corresponding value (δ 6.82)[3] for 3-hydroxy-1,3-diphenylprop-2-en-1-one. The exceptions are (**5b**, **d**), with $\delta_{\text{Vinyl-H}}$ 7.32 and 7.41, respectively, resulting from the electronic or steric effects of the introduction of the 6′-methoxy function.

In an attempt to prepare 5-hydroxyflavone, 2-acetylbenzene-1,3-diol (**2d**) was benzoylated to give the diester (**4g**) which was rearranged to furnish the propane-1,3-dione (**5g**). No hydrolysis of the remaining benzoate ester was evident under the conditions of the rearrangement (hot potassium hydroxide–pyridine). The chemical shifts of the ArH protons of the enol

Table 8. Selected torsion angles for (**5b**).

Atoms	Angle/°
C(1′)–C(6′)–C(5′)–C(4′)	0.4
C(6′)–C(6′)–C(5′)–C(4′)	178.4
C(2′)–C(1′)–C(6′)–C(5′)	0.0
C(1)–C(1′)–C(6′)–C(5′)	−178.3
O(6′)–C(6′)–C(1′)–C(2′)	−178.2
O(6′)–C(6′)–C(1′)–C(1)	3.5
C(5′)–C(6′)–C(6′)–C[O(6′)]	3.0
C(1′)–C(6′)–O(6′)–C[O(6′)]	−178.9
C(3′)–C(4′)–C(5′)–C(6′)	−0.9
C(6′)–C(5′)–C(4′)–O(4′)	179.5
C(2′)–C(3′)–C(4′)–C(5′)	1.0
C(2′)–C(3′)–C(4′)–O(4′)	−179.4
C(5′)–C(4′)–C(4′)–C[O(4′)]	177.6
C(3′)–C(4′)–O(4′)–C[O(4′)]	−2.1
C(4′)–C(3′)–C(2′)–C(1′)	−0.6
C(4′)–C(3′)–C(2′)–O(2′)	179.7
C(6′)–C(1′)–C(2′)–C(3′)	0.2
C(1)–C(1′)–C(2′)–C(3′)	178.5
O(2′)–C(2′)–C(1′)–C(1)	−179.9
C(2′)–C(1′)–C(1)–O(1)	0.8
C(1′)–C(1)–C(2)–C(3)	70.1
O(1)–C(1)–C(2)–C(3)	−110.5
O(2)–C(2)–C(3)–C(1″)	−156.4
C(1)–C(2)–C(3)–O(3)	25.3
C(2)–C(3)–C(1″)–C(2″)	−177.1
C(2)–C(3)–C(1″)–C(6″)	5.1
O(3)–C(3)–C(1″)–C(2″)	1.2
O(3)–C(3)–C(1″)–C(6″)	−176.5
C(3)–C(1″)–C(2″)–C(3″)	−176.5
C(6″)–C(1″)–C(2″)–C(3″)	1.3
C(3)–C(1″)–C(6″)–C(5″)	175.6
C(2″)–C(1″)–C(6″)–C(5″)	−2.1
C(1″)–C(2″)–C(3″)–C(4″)	0.0
C(2″)–C(3″)–C(4″)–C(5″)	−0.6
C(3″)–C(4″)–C(5″)–C(6″)	0.1
C(4″)–C(5″)–C(6″)–C(1″)	1.5

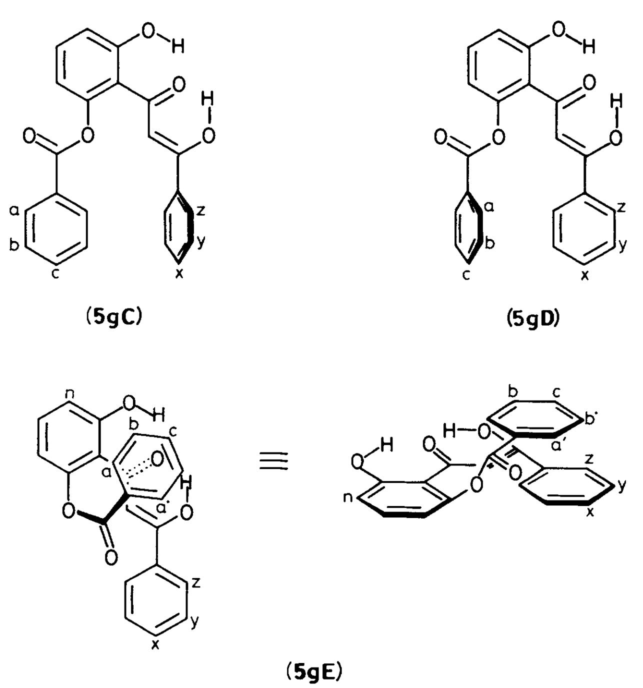
Table 9. Chemical shifts of methoxy groups in compounds (**4b**), (**5b**), and (**5d**).

Compound	δ_H of OMe groups	
(**4b**)	3.73	3.75
(**5b**)	3.43	3.79
(**5d**) (keto)	3.53	3.82

Table 10. Chemical shifts of phenol OH, vinyl H, and enol OH of enol forms of compounds (**5a**, **c**–**k**).

Compound	Substituents	$\delta_{\text{phenol OH}}$	$\delta_{\text{vinyl H}}$	$\delta_{\text{enol OH}}$
(**5a**)	4′-OMe	12.50	6.62	15.40
(**5c**)	unsubstituted	12.10	6.84	15.54
(**5d**)	4′,6′-(OMe)$_2$, 4″-NO$_2$	13.33	7.41	15.26
(**5e**)	4′-OMe, 4″-NO$_2$	12.44	6.78	15.20
(**5f**)	4′-O$_2$CPh	12.36	6.80	15.45
(**5g**)	6′-O$_2$CPh	11.91	6.87	15.73
(**5h**)	3″,4″-Cl$_2$	11.95	6.78	15.43
(**5i**)	3″,4″-(OMe)$_2$	12.09	6.75	15.85
(**5j**)	4″-Cl	11.95	6.70	15.5
(**5k**)	4″NO$_2$	11.92	6.90	15.30

form of (**5g**) were anomalous in the ^{1}H n.m.r. spectrum, with resonances of the 'benzoyl' groups spread over the range δ 7.16–8.26. Despite the apparent similarity of environment of these two phenyl rings, the chemical shifts of the two pairs of *ortho* protons were widely different at δ 7.40 and 8.26. A two-dimensional technique (COSY 45) grouped the former with the *meta* proton resonances at δ 7.16 and the *para* proton resonance at δ 7.37. Similarly, the signals at δ 7.52 and 7.68 were shown to arise from the same phenyl ring as downfield *ortho* proton resonances. The chemical shift of the 'downfield' set of signals is unremarkable but that of the 'upfield' set is unusual. The orientation of the phenyl rings in the molecule should explain the shielding of one of the rings seen in the spectrum. There are a number of potential orientations of the two phenyl rings and these are shown in Figure 3.



(**5gC**) (**5gD**)

(**5gE**)

Figure 3. Possible conformations of (**5g**).

The first conformation (**5gC**) shows the *x*,*y*,*y*′,*z*,*z*′ ring to be at a steep angle to the enol system and so the *z*,*z*′ protons may be shielded by loss of conjugation. The second orientation (**5gD**) shows the *a*,*a*′,*b*,*b*′,*c* phenyl ring at a steep angle to the carbonyl group, shielding the *a*,*a*′ protons. The third possible orientation (**5gE**) shows the benzoate ester to be positioned so that the phenyl ring lies over the enol system in a 'coiled' molecular conformation. In this last orientation, the *a*,*a*′ protons would be shielded by interaction with the π-orbitals of the enol system.

In order to verify which, if any, of these possibilities is correct, a number of n.m.r. experiments were performed. If the *z*,*z*′ phenyl ring is in plane with the enol system [as in (**5gD**)], then the *z*,*z*′ protons would be expected to experience a nuclear Overhauser effect (n.O.e.) from the vinylic proton. Irradiation of the proton at δ 6.87 did indeed produce an n.O.e., however both sets of protons *ortho* to the carbonyl groups showed an enhancement, although there was a fivefold enhancement of the resonances at δ 7.4 compared with that at δ 8.3. This suggests that the protons generating the upfield signal are closer in space to the vinyl protons than the protons generating the downfield signal, although these protons are also close enough to the vinyl proton to experience some small n.O.e. This experiment rules out one of the potential orientations of the phenyl rings (**5gD**). If the *a*,*a*′ phenyl ring were normal to the carboxylate system then no n.O.e. would be experienced by the *a*,*a*′ protons when the vinyl proton was irradiated.

If the *z*,*z*′ phenyl ring were at right angles to the carbonyl system [as in (**5gC**)], then no n.O.e. would be expected. If, however, this phenyl ring were co-planar with the enol system then a large n.O.e. should be seen but this does not explain why these protons would be shielded. Consideration of the crystal structure of 1-(2-hydroxy-4-methoxyphenyl)-3-phenylpropane-1,3-dione shows that the phenyl ring attached to the 3-carbon in (**5a**) is out of plane by 14°, so this may explain why an n.O.e. is seen at both the *z,z′* and the *a,a′* protons.

To determine if the *a,b,c* phenyl ring is orientated in such a way that it lies over the top of the enol system [as in (**5gE**)], another n.O.e. difference experiment was carried out. This time the enolic OH, at δ 15.5, was irradiated. This, too, produced an ambiguous result, in that saturation transfer to the phenolic OH caused enhancement of the resonance due to the *ortho* proton. However, by far the largest n.O.e. enhancement observed was again at the *ortho* doublet of the upfield set of protons, although the downfield *ortho* protons also appeared to be stimulated but to a much smaller extent. Although none of these spectroscopic data are completely conclusive, the balance of evidence would tend to support the 'coiled' conformation (**5gE**) as representing the structure of the enol form of (**5g**).

The results of the spectroscopic experiments described above show that extensive enolisation of the majority of the substituted 1-(2-hydroxyphenyl)-3-phenylpropane-1,3-diones (**5**) is facile in solution in deuteriochloroform. Crystallographic evidence on (**5a, b**) illustrates that, depending on substitution patterns, these compounds can crystallise either in the keto or enol form.

Experimental

I.r. spectra were recorded on a Perkin-Elmer 1310 spectrometer. ^{1}H N.m.r. spectra were recorded at 60 MHz using a Varian EM360A instrument, at 300 MHz using a Bruker AC300 instrument, and at 400 MHz with a Bruker WH400 spectrometer; samples were dissolved in $CDCl_3$ and tetramethylsilane was used as an internal standard. Mass spectra were obtained using a VG Micromass 12B single focussing mass spectrometer in the electron-impact mode. Light petroleum refers to the fraction b.p. 60–80 °C.

1-*Acetyl*-4,6-*dimethoxy*-2-*hydroxybenzene* (**2b**).—3,5-Dimethoxyphenol (**1b**) (7.7 g, 50 mmol) in dichloromethane (50 cm^3) was added to boron trichloride in dichloromethane (1 mol dm^{-3}; 50 cm^3) under nitrogen at −10 °C. The mixture was stirred for 5 min and acetyl chloride (3.9 g, 50 mmol) was added. The reaction mixture was then heated to reflux for 3 h before being carefully quenched by addition of an excess of hydrochloric acid (1 mol dm^{-3}). After 1 h at ambient temperature, the organic phase was separated and the solvent was evaporated under reduced pressure. The residue, in dichloromethane (50 cm^3), was filtered through a silica plug. Removal of the solvent from the filtrate under reduced pressure afforded 1-acetyl-2-hydroxy-4,6-dimethoxybenzene (7.7 g, 78%) as a white solid, m.p. 82 °C (lit.,[11] 82–83 °C); δ_H(60 MHz) 2.56 (3 H, s, COMe), 3.78 (3 H, s, OMe), 3.80 (3 H, s, OMe), 5.85 (1 H, d, *J* 2 Hz, ArH), 6.00 (1 H, d, *J* 2 Hz, ArH), 6.00 (1 H, d, *J* 2 Hz, ArH), and 13.9 (1 H, s, OH).

1-*Acetyl*-2-*hydroxy*-4-*methoxybenzene* (**2a**).—3-Methoxyphenol (**1a**) was treated with boron trichloride and acetyl chloride, as for the preparation of (**2b**) above, to afford 1-acetyl-2-hydroxy-4-methoxybenzene (78%) as white crystals, m.p. 50 °C (lit.,[12] 48 °C); δ_H(60 MHz) 2.50 (3 H, s, COMe), 3.75 (3 H, s, OMe), 6.30 (1 H, d, *J* 2 Hz, 6-H), 6.37 (1 H, dd, *J* 9, 2 Hz, 4-H), 7.54 (1 H, d, *J* 9 Hz, 3-H), and 12.72 (1 H, s, OH).

2-*Acetyl*-3,5-*dimethoxyphenyl Benzoate* (**4b**).—2-Acetyl-3,5-dimethoxyphenol (**2b**) (2.94 g, 15 mmol) was treated with benzoyl chloride (**3a**) (2.8 g, 20 mmol), and 4-(dimethylamino)pyridine (366 mg, 3 mmol) in pyridine (15 cm^3) at ambient temperature for 10 min. The mixture was poured onto an excess of hydrochloric acid (1 mol dm^{-3}) and crushed ice. The solid was collected by filtration and recrystallised from chloroform–light petroleum to furnish 2-*acetyl*-3,5-*dimethoxyphenyl benzoate* (3.16 g, 70%) as white crystals, m.p. 92–93 °C (Found C, 67.7; H, 5.4. $C_{17}H_{16}O_5$ requires C, 68.0; H, 5.35%); ν_{max}(Nujol) 1 735 and 1 680 cm^{-1}; δ_H(60 MHz) 2.41 (3 H, s, COMe), 3.73 (3 H, s, OMe), 3.75 (3 H, s, OMe), 6.32 (2 H, s, 4,6-H), 7.3–7.7 (3 H, m, 3′,4′,5′-H), and 8.05 (2 H, dd, *J* 7, 2 Hz, 2′,6′-H); *m*/*z* 300 (M^+), 285, 105 (100%), and 77.

2-*Acetylphenyl Benzoate* (**4c**).—2-Acetylphenol (**2c**) was treated with benzoyl chloride (**3a**) as for the preparation of (**4b**) above, except that the dimethylaminopyridine was omitted and the solvent for recrystallisation was methanol, to afford 2-acetylphenyl benzoate (78%) as a white solid, m.p. 89–90 °C (lit.,[6] 87–88 °C); δ_H(60 MHz) 2.4 (3 H, s, COMe), 7.0–7.6 (6 H, m, 3′,4,4′,5,5′,6-H), 7.70 (1 H, dd, *J* 8, 2 Hz, 3-H), and 8.15 (2 H, dd, *J* 6, 2 Hz, 2′,6′-H).

2-*Acetyl*-5-*methoxyphenyl Benzoate* (**4a**).—1-Acetyl-2-hydroxy-4-methoxybenzene (**2a**) was treated with benzoyl chloride (**3a**) as for the preparation of (**4b**) above, with the exception of recrystallisation, to give 2-*acetyl*-5-*methoxyphenyl benzoate* (84%) as a pale yellow oil; ν_{max} (liquid film) 1 735 and 1 680 cm^{-1}; δ_H(60 MHz) 2.45 (3 H, s, COMe), 3.78 (3 H, s, Me), 6.70 (1 H, d, *J* 2 Hz, 6-H), 6.75 (1 H, dd, *J* 8, 2 Hz, 4-H), 7.53 (3 H, m, 3′,4′,5′-H), 7.81 (1 H, d *J* 8 Hz, 3-H), and 8.15 (2 H, dd, *J* 9, 2 Hz, 2′,6′-H); *m*/*z* 270.0891 (M^+) ($C_{16}H_{14}O_4$ requires 270.0892), 105 (100%), and 77.

2-*Acetyl*-3,5-*dimethoxyphenyl* 4-*Nitrobenzoate* (**4d**).—1-Acetyl-4,6-dimethoxy-2-hydroxybenzene (**2b**) was treated with 4-nitrobenzoyl chloride (**3b**) as for the preparation of (**4b**) above, except that ethyl acetate–light petroleum was used as the solvent for recrystallisation, to give 2-*acetyl*-3,5-*dimethoxyphenyl* 4-*nitrobenzoate* (67%) as pale yellow crystals, m.p. 159–160 °C (Found C, 59.15; H, 4.35; N, 4.05. $C_{17}H_{15}NO_7$ requires C, 59.15; H, 4.35; N, 4.05%); δ_H(60 MHz) 2.45 (3 H, s, COMe), 3.80 (3 H, s, OMe), 3.86 (3 H, s, OMe), 6.31 (1 H, d, *J* 2 Hz, 6-H), 6.38 (1 H, d, *J* 2 Hz, 4-H), and 8.26 (4 H, s, 2′,3′,5′,6′-H); *m*/*z* 345 (M^+), 330 (100%), 314, 286, 256, 150, 137, 104, and 76.

2-*Acetyl*-5-*methoxyphenyl* 4-*Nitrobenzoate* (**4e**).—2-Acetyl-1-hydroxy-5-methoxybenzene (**2a**) was treated with 4-nitrobenzoyl chloride (**3b**) as for the preparation of (**4b**) above to afford 2-acetyl-5-methoxyphenyl 4-nitrobenzoate (68%) as a pale yellow solid, m.p. 141 °C (lit.,[13] 135–137 °C); δ_H(60 MHz) 2.45 (3 H, s, COMe), 3.83 (3 H, s, OMe), 6.66 (1 H, d, *J* 2 Hz, 6-H), 6.76 (1 H, dd, *J* 9, 2 Hz, 4-H), 7.80 (1 H, d, *J* 9 Hz, 3-H), and 8.28 (4 H, s, 2′,3′,5′,6′-H).

1-*Acetyl*-2,4-*bis*(*benzoyloxy*)*benzene* (**4f**).—1-Acetylbenzene-2,4-diol (**2d**) (7.6 g, 50 mmol) was treated with benzoyl chloride (**3a**) (16.8 g, 120 mmol) in pyridine (20 cm^3) for 1 h and the mixture was poured onto an excess of hydrochloric acid (1 mol dm^{-3}) and ice. The solid was collected by filtration and recrystallised from methanol to furnish 1-*acetyl*-2,4-*bis*(*benzoyloxy*)*benzene* (14.94 g, 83%) as a white solid, m.p. 85 °C (Found: C, 73.25; H, 4.45. $C_{22}H_{16}O_5$ requires C, 73.3; H, 4.45%); δ_H(60 MHz) 2.53 (3 H, s, COMe), 7.18 (1 H, d, *J* 2 Hz, 6-H), 7.37 (1 H, dd, *J* 8, 2 Hz, 4-H), 7.40–7.63 (6 H, m, 3′,4′,5′,3″,4″,5″-H), 7.90 (1 H, d, *J* 8 Hz, 3-H), and 8.06–8.26 (4 H, m, 2′,6′,2″,6″-H); *m*/*z* 360 (M^+), 105 (100%), 77, 52, and 43.

2-*Acetyl*-1,3-*bis*(*benzoyloxy*)*benzene* (**4g**).—2-Acetylbenzene-1,3-diol (**2e**) was treated with benzoyl chloride (**3a**) as for the preparation of (**4e**) above to afford 2-*acetyl*-1,3-*bis*(*benzoyloxy*)-

benzene (63%) as a white solid, m.p. 108 °C (Found: C, 73.3; H, 4.6. $C_{22}H_{16}O_5$ requires C, 73.3; H, 4.45%); δ_H(60 MHz) 2.45 (3 H, s, COMe), 7.1–7.7 (9 H, m, 4,5,6,3′,4′,5′,3″,4″,5″-H), and 8.14 (4 H, m, 2′,2″, 6′,6″-H); *m*/*z* 360 (M^+), 105 (100%), 77, 52, and 43.

2-*Acetylphenyl* 3,4-*Dichlorobenzoate* (**4h**).—2-Acetylphenol (**2c**) was treated with 3,4-dichlorobenzoyl chloride (**3c**) as for the preparation of (**4e**) above to afford 2-*acetylphenyl* 3,4-*dichlorobenzoate* (78%) as a white solid, m.p. 84 °C (Found: C, 58.1; H, 3.25. $C_{15}H_{10}Cl_2O_3$ requires C, 58.25; H, 3.25%); δ_H(60 MHz) 2.52 (3 H, s, COMe), 7.15 (1 H, dd, *J* 8, 2 Hz, 6′-H), 7.30–7.50 (2 H, m, 4,5-H), 7.56 (1 H, d, *J* 8 Hz, 5′-H), 7.83 (1 H, dd, *J* 8, 2 Hz, 3-H), 7.92 (1 H, dd, *J* 8, 2 Hz, 6′-H), and 8.26 (1 H, d, *J* 2 Hz, 2′-H); *m*/*z* 308/310/312 (M^+), 173/175/177 (100%), 145/145/149, and 75.

2-*Acetylphenyl* 3,4-*Dimethoxybenzoate* (**4i**).—2-Acetylphenol (**2c**) was treated with 3,4-dimethoxybenzoyl chloride (**3d**) as for the preparation of (**4e**) above to afford 2-acetylphenyl 3,4-dimethoxybenzoate (84%) as a white solid, m.p. 126–127 °C (lit.,[14] 129 °C) (Found: C, 68.0; H, 5.4. $C_{17}H_{16}O_5$ requires C, 68.0; H, 5.35%); δ_H(60 MHz) 2.5 (3 H, s, COMe), 3.92 (6 H, s, 2 × OMe), and 6.8–7.9 (7 H, m, ArH).

2-*Acetylphenyl* 4-*Chlorobenzoate* (**4j**).—2-Acetylphenol (**2c**) was treated with 4-chlorobenzoyl chloride (**3e**) as for the preparation of (**4e**) above to yield 2-acetylphenyl 4-chlorobenzoate (75%) as a white solid, m.p. 94 °C (lit.,[15] 92–93 °C) (Found: C, 65.65; H, 4.2. $C_{15}H_{11}ClO_3$ requires C, 65.6; H, 4.05%); δ_H(60 MHz) 2.50 (1 H, s, COMe), 7.1–7.4 (3 H, m, 4,5,6-H), 7.42 (2 H, d, *J* 8 Hz, 3′,5′-H), 7.80 (1 H, dd, *J* 7 and 1.5 Hz, 3-H), and 8.08 (2 H, d, *J* 8 Hz, 2′,6′-H).

2-*Acetylphenyl* 4-*Nitrobenzoate* (**4k**).—2-Acetylphenol (**2c**) was treated with 4-nitrobenzoyl chloride (**4b**) as for the preparation of (**4e**) above to yield 2-acetylphenyl 4-nitrobenzoate (65%) as a pale yellow solid, m.p. 90 °C (lit.,[16] 99–100 °C); δ_H(60 MHz) 2.50 (3 H, s, COMe), 7.10–7.67 (3 H, m, 4,5,6-H), 7.88 (1 H, dd, *J* 6, 2 Hz, 3-H), and 8.36 (4 H, s, 2′,3′,5′,6′-H).

1-(2-*Hydroxy*-4,6-*dimethoxyphenyl*)-3-*phenylpropane*-1,3-*dione* (**5b**).—Butyl-lithium (1.44 mol dm^{-3} in hexane; 14 cm^3, 20 mmol) was added to hexamethyldisilazane (2.82 g, 20 mmol) in anhydrous tetrahydrofuran (30 cm^3) at −78 °C under nitrogen. 2-Acetyl-3,5-dimethoxyphenyl benzoate (**4b**) (2.25 g, 10 mmol) in anhydrous tetrahydrofuran (20 cm^3) was then added during 15 min. The mixture was allowed to warm to 20 °C and was quenched with an excess of hydrochloric acid (1 mol dm^{-3}). The solid was collected by filtration and washed with water before being recrystallised from methanol to yield 1-(2-*hydroxy*-4,6-*dimethoxyphenyl*)-3-*phenylpropane*-1,3-*dione* (1.42 g, 63%) as a yellow solid, m.p. 151 °C (Found: C, 67.95; H, 5.30. $C_{17}H_{16}O_5$ requires C, 68.0; H, 5.35%); ν_{max}(Nujol) 2 700 br and 1 600 cm^{-1}; δ_H(300 MHz) 3.43 (3 H, s, OMe), 3.78 (3 H, s, OMe), 4.51 (2 H, s, $COCH_2CO$), 5.78 (1 H, d, *J* 2 Hz, 3′-H), 6.02 (1 H, d, *J* 2 Hz, 5′-H), 7.4–7.6 (3 H, m, 3″,4″,5″-H), 7.8–8.0 (2 H, m, 2″,6″-H), and 13.67 (1 H, s, OH); *m*/*z* 300 (M^+), 283, 269, 181, 105 (100%), and 77.

1-(2-*Hydroxy*-4-*methoxyphenyl*)-3-(4-*nitrophenyl*)*propane*-1,3-*dione* (**5e**).—2-Acetyl-5-methoxyphenyl 4-nitrobenzoate (**4e**) was treated with lithium hexamethyldisilazide as for the synthesis of (**5b**) above to give 1-(2-*hydroxy*-4-*methoxyphenyl*)-3-(4-*nitrophenyl*)*propane*-1,3-*dione* (48%) as yellow hexagonal crystals, m.p. 200 °C (Found: C, 60.7; H, 4.15; N, 4.45. $C_{16}H_{13}NO_6$ requires C, 60.95; H, 4.15; N, 4.45%); δ_H(300 MHz) 3.81 (3 H, s, OCH_3), 4.61 (0.16 H, s, $COCH_2CO$), 6.48 (1 H, d, *J* 2.4 Hz, 3′-H), 6.51 (1 H, dd, *J* 8.9, 2.4 Hz, 5′-H), 6.78 (0.92 H, s, vinyl-H), 7.70 (1 H, d, *J* 8.9 Hz, 6′-H), 8.08 (2 H, d, *J* 8.8 Hz, 2″,6″-H), 8.33 (2 H, d, *J* 8.8 Hz, 3″,5″-H), 12.20 [0.08 H, s, phenolic OH (keto form)], 12.44 [0.92 H, s, phenolic OH (enol form)], and 15.20 (0.92 H, s, enol OH); *m*/*z* 315 (M^+), 298, 285, 193, 150 (100%), 104, and 76.

1-(2-*Hydroxy*-4-*methoxyphenyl*)-3-*phenylpropane*-1,3-*dione* (**5a**).—2-Acetyl-5-methoxyphenyl benzoate (**4a**) was treated with lithium hexamethyldisilazide as for the synthesis of (**5b**) above to give 1-(2-*hydroxy*-4-*methoxyphenyl*)-3-*phenylpropane*-1,3-*dione* (37%) as brown transparent crystals, m.p. 138 °C (Found: C, 71.1; H, 4.95. $C_{16}H_{14}O_4$ requires C, 71.1; H, 5.2%); ν_{max}(Nujol) 2 700 br, 1 680, and 1 580 cm^{-1}; δ_H(300 MHz) 3.76 (3 H, s, OMe), 4.5 (0.16 H, brs, $COCH_2CO$), 6.42 (2 H, dd, *J* 9, 2 Hz, 5′-H), 6.53 (1 H, d, *J* 2 Hz, 3′-H), 6.62 (0.88 H, s, vinyl-H), 7.4–7.6 (3 H, m, 3″,4″,5″-H), 7.60 (1 H, d, *J* 9 Hz, 6-H), 7.7–7.9 (2 H, m, 2″,6″-H), 12.50 (1 H, s, phenolic OH), and 15.40 (0.88 H, s, enol OH); *m*/*z* 300 (M^+), 283, 269, 181, 105 (100%), and 77.

1-(2-*Hydroxy*-4,6-*dimethoxyphenyl*)-3-(4-*nitrophenyl*)-*propane*-1,3-*dione* (**5d**).—2-Acetyl-3,5-dimethoxyphenyl 4-nitrobenzoate (**4d**) was treated with lithium hexamethyldisilazide as for the synthesis of (**5b**) above to give 1-(2-*hydroxy*-4,6-*dimethoxyphenyl*)-3-(4-*nitrophenyl*)*propane*-1,3-*dione* (53%) as a bright yellow solid, m.p. 192 °C (Found: C, 59.05; H, 4.4; N, 3.85. $C_{17}H_{15}NO_7$ requires C, 59.15; H, 4.35; N, 4.05%); ν_{max}(Nujol) 2 700–3 100 br, 1 575, 1 515, and 1 340 cm^{-1}; δ_H(300 MHz) 3.53 [0.6 H, s, OMe (keto)], 3.82 [0.6 H, s, OMe (keto)], 3.85 [2.4 H, s, OMe (enol)], 3.94 [2.4 H, s, OMe (enol)], 4.59 (0.4 H, s, $COCH_2CO$), 5.87 [0.2 H, d, *J* 2.4 Hz, 5′-H (keto)], 6.06 [0.8 H, d, *J*, 2.4 Hz, 5′-H (enol)], 6.11 [0.2 H, d, *J* 2.4 Hz, 3′-H (keto)], 6.13 [0.8 H, d, *J* 2.4 Hz, 3′-H (enol)], 7.41 (0.8 H, s, vinyl-H), 8.03 [1.6 H, d, *J* 8.9 Hz, 2″,6″-H (enol)], 8.13 [0.4 H, d, *J* 8.9 Hz, 2″,6″-H (keto)], 8.32 [1.6 H, d, *J* 8.9 Hz, 3″,5″-H (enol)], 8.36 [0.4 H, H, d, *J* 8.9 Hz, 3″,5″-H (keto)], 13.33 [0.8 H, s, phenolic OH (enol)], 13.55 [0.2 H, s, phenolic OH (keto)], and 15.26 (0.8 H, s, enol OH).

1-(2-*Hydroxyphenyl*)-3-*phenylpropane*-1,3-*dione* (**5c**).—Finely powdered potassium hydroxide (1.7 g, 30 mmol) was added to 2-acetylphenyl benzoate (**4c**) (4.8 g, 20 mmol) in pyridine (50 cm^3) at 50 °C. The mixture was stirred for 20 min before being poured into a slight excess of hydrochloric acid (1 mol dm^{-3}). The solid was collected by filtration and was recrystallised from methanol to give 1-(2-hydroxyphenyl)-3-phenylpropane-1,3-dione (1.07 g, 63%) as a yellow solid, m.p. 124 °C (lit.,[17] 117–120 °C); δ_H(400 MHz) 4.63 (0.13 H, s, $COCH_2CO$), 6.84 (0.94 H, s, vinyl-H), 6.92 (1 H, ddd, *J* 8.0, 7.0, 1.1 Hz, 5′-H), 7.00 (1 H, dd, *J* 8.3, 1.1 Hz, 3′-H), 7.46 (1 H, ddd, *J* 8.3, 7.0, 1.1 Hz, 4′-H), 7.48 (2 H, dd, *J* 8.0, 7.3 Hz, 3″,5″-H), 7.56 (1 H, tt, *J* 7.3, 1.6 Hz, 4″-H), 7.79 (1 H, dd, *J* 8.0, 1.6 Hz, 6′-H), 7.94 (2 H, dd, *J* 8.0, 1.6 Hz, 2″,6″-H), 11.93 [0.06 H, s, phenolic OH (keto)], 12.10 [0.94 H, s, phenolic OH (enol)], and 15.54 (0.94 H, s, enol OH).

1-(4-*Benzoyloxy*-2-*hydroxyphenyl*)-3-*phenylpropane*-1,3-*dione* (**5f**).—1-Acetyl-2,4-bis(benzoyloxy)benzene (**4f**) was treated with potassium hydroxide in pyridine as for the preparation of (**5c**) above to give 1-(4-benzoyloxy-2-hydroxyphenyl)-3-phenylpropane-1,3-dione (52%) as yellow crystals, m.p. 171 °C (lit.,[18] 167 °C); δ_H(400 MHz) 4.63 (0.2 H, s, $COCH_2CO$), 6.80 (0.9 H, s, vinyl-H), 6.84 (1 H, dd, *J* 8.9, 2.3 Hz, 5′-H), 6.89 (1 H, d, *J* 2.3 Hz, 3′-H), 7.5 [5 H, m, 3″,3‴, (4″-H or 4‴-H), 5″,5‴-H], 7.66 (1 H, tt, *J* 7.4, 1.3 Hz, 4″-H or 4‴-H), 7.85 (1 H, d, *J* 8.9 Hz, 6′-H), 7.94 [2 H, dd, *J* 8.4, 1.3 Hz, (2″,6″-H) or (2‴,6‴-H)], 8.19 [2 H, dd, *J* 8.4, 1.2 Hz, (2″,6″-

H) or (2‴,6‴-H)], 12.16 [0.1 H, s, phenolic OH (keto)], 12.36 [0.9 H, s, phenolic OH (enol)] and 15.45 (0.9 H, s, enol OH).

1-(6-*Benzoyloxy*-2-*hydroxyphenyl*)-3-*phenylpropane*-1,3-*dione* (**5g**).—2-Acetyl-1,3-bis(benzoyloxy)benzene (**4g**) was treated with potassium hydroxide in pyridine as for the preparation of (**5c**) above to give 1-(6-*benzoyloxy*-2-*hydroxyphenyl*)-3-*phenylpropane*-1,3-*dione* (64%) as yellow crystals, m.p. 184 °C (Found: C, 73.4; H, 4.5. $C_{22}H_{16}O_5$ requires C, 73.3; H, 4.45%); δ_H(400 MHz) 6.75 (1 H, dd, *J* 7.8, 0.9 Hz, 3′-H or 5′-H), 6.87 (1 H, s, vinyl-H), 6.95 (1 H, dd, *J* 8.5, 0.9 Hz, 3′-H or 5′-H), 7.16 (2 H, dd, *J* 8.1, 7.6 Hz, 3‴,5‴-H), 7.37 (1 H, tt, *J* 7.3, 1.2 Hz, 4‴-H), 7.40 (2 H, dd, *J* 7.3, 1.2 Hz, 2‴,6‴-H), 7.45 (1 H, t, *J* 8.2 Hz, 4′-H), 7.52 (2 H, dd, *J* 7.9, 7.6 Hz, 3″,5″-H), 7.68 (1 H, tt, *J* 7.4, 1.2 Hz, 4″-H), 8.26 (2 H, dd, *J* 8.3, 1.2 Hz, 2″,6″-H), 11.91 (1 H, s, phenolic OH), and 15.73 (1 H, s, enol OH); *m*/*z* 260 (M^+), 238, 105 (100%), and 77.

1-(3,4-*Dichlorophenyl*)-3-(2-*hydroxyphenyl*)*propane*-1,3-*dione* (**5h**).—2-Acetylphenyl 3,4-dichlorobenzoate (**4h**) was treated with potassium hydroxide in pyridine as for the preparation of (**5c**) above to give 1-(3,4-*dichlorophenyl*)-3-(2-*hydroxyphenyl*)*propane*-1,3-*dione* (47%) as a yellow solid, m.p. 155–157 °C (Found: C, 58.1; H, 3.2. $C_{15}H_{10}Cl_2O_3$ requires C, 58.25; H, 3.25%); δ_H(400 MHz) 4.59 (0.14 H, s, $COCH_2CO$), 6.78 (0.93 H, s, vinyl-H), 6.93 (1 H, ddd, *J* 8.16, 7.1, 1.0 Hz, 5′-H), 7.00 (1 H, dd, *J* 8.4, 1.0 Hz, 3′-H), 7.48 (1 H, ddd, *J* 8.4, 7.0, 1.5 Hz, 4′-H), 7.56 (1 H, d, *J* 8.5 Hz, 5″-H), 7.75 (1 H, dd, *J* 8.5, 2.1 Hz, 6″-H), 7.77 (1 H, dd, *J* 8.2, 1.5 Hz, 6′-H), 8.00 (1 H, d, *J* 2.1 Hz, 2″-H), 11.80 [0.07 H, s, phenolic OH (keto)], 11.95 [0.93 H, s, phenolic OH (enol)], and 15.43 (0.93 H, s, enol OH); *m*/*z* 308/310/312 (M^+), 173/175/177 (100%), and 121.

1-(3,4-*Dimethoxyphenyl*)-3-(2-*hydroxyphenyl*)*propane*-1,3-*dione* (**5i**).—2-Acetylphenyl 3,4-dimethoxybenzoate (**4i**) was treated with potassium hydroxide in pyridine as for the preparation of (**5c**) above to give 1-(3,4-dimethoxyphenyl)-3-(2-hydroxyphenyl)propane-1,3-dione (62%) as a yellow solid, m.p. 115 °C (lit.,[19] 115 °C); δ_H(400 MHz) 3.90 [0.63 H, s, OMe (keto)], 3.94 [0.63 H, s, OMe (keto)], 3.95 [2.37 H, s, OMe (enol)], 3.96 [2.37 H, s, OMe (enol)], 4.58 (0.42 H, s, $COCH_2CO$), 6.75 (0.79 H, s, vinyl-H), 6.90 [0.79 H, ddd, *J* 8.1, 7.0, 1.0 Hz, 5′-H (enol)], 6.91 [0.21 H, ddd, *J* 8.0, 7.0, 1.0 Hz, 5′-H (keto)], 6.91 [0.21 H, d, *J* 8.5 Hz, 5″-H (keto)], 6.92 [0.79 H, d, *J* 8.5 Hz, 5-H (enol)], 6.97 (0.21 H, dd, *J* 8.6, 1.0 Hz, 3′-H (keto)], 6.98 (0.79 H, dd, *J* 8.4, 1.0 Hz, 3′-H (enol)], 7.43 (0.79 H, ddd, *J* 8.4, 7.0, 1.5 Hz, 4′-H (enol)], 7.44 (1 H, d, *J* 2.1 Hz, 2″-H), 7.47 (0.21 H, ddd, *J* 8.6, 7.0, 1.6 Hz, 4′-H (keto)], 7.56 [0.79 H, dd, *J* 8.5, 2.1 Hz, 6″-H (enol)], 7.63 [0.21 H, dd, *J* 8.3, 2.0 Hz, 6″-H (keto)], 7.75 [0.79 H, dd, *J* 8.1, 1.5 Hz, 6′-H (enol)], 7.80 [0.21 H, dd, *J* 8.0, 1.6 Hz, 6′-H (keto)], 11.96 [0.21 H, s, phenolic OH (keto)], 12.09 [0.79 H, s, phenolic OH (enol)], and 15.85 (0.79 H, s, enol OH).

1-(4-*Chlorophenyl*)-3-(2-*hydroxyphenyl*)*propane*-1,3-*dione* (**5j**).—2-Acetylphenyl 4-chlorobenzoate (**4j**) was treated with potassium hydroxide in pyridine as for the preparation of (**5c**) above to give 1-(2-hydroxyphenyl)-3-(4-chlorophenyl)propane-1,3-dione (43%) as yellow crystals, m.p. 120 °C (lit.,[15] 122.4 °C); δ_H(60 MHz) 6.70 (1 H, s, vinyl-H), 6.80–7.40 (3 H, m, 3′,4′,5′-H), 7.37 (2 H, d, *J* 8 Hz, 3″-H), 7.66 (1 H, dd, *J* 7, 1 Hz, 6′-H), 7.79 (2 H, d, *J* 8 Hz, 2″-H), 11.95 (1 H, s, phenolic OH), and 15.5 (1 H, brs, enol OH).

1-(2-*Hydroxyphenyl*)-3-(4-*nitrophenyl*)*propane*-1,3-*dione* (**5k**).—2-Acetylphenyl 4-nitrobenzoate (**4k**) was treated with potassium hydroxide in pyridine as for the preparation of (**5c**) above to give 1-(2-hydroxyphenyl)-3-(4-nitrophenyl)propane-1,3-dione (58%) as a yellow solid, m.p. 195 °C (lit.,[16] 198–201 °C); δ_H(400 MHz) 6.90 (1 H, s, vinyl-H), 6.95 (1 H, ddd, *J* 8.1, 7.1, 1.0 Hz, 5′-H), 7.03 (1 H, dd, *J* 8.5, 1.0 Hz, 3′-H), 7.51 (1 H, ddd, *J* 8.5, 7.1, 1.6 Hz, 4′-H), 7.79 (1 H, dd, *J* 8.1, 1.6 Hz, 6′-H), 8.09 (2 H, d, *J* 8.9 Hz, 2″,6″-H), 8.33 (2 H, d, *J* 8.9 Hz, 3″,5″-H), 11.92 (1 H, s, phenolic OH), and 15.30 (1 H, s, enol OH).

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References

1 Part 11. S. J. B. Tendler, C. H. Schwalbe, M. D. Threadgill, M. J. Tisdale, and L. Schirch, *J. Chem. Soc., Perkin Trans. 2*, 1989, 431.
2 N. N. Shapet'ko, *Org. Magn. Reson.*, 1975, **7**, 237.
3 J. L. Burdett and M. T. Rogers, *J. Am. Chem. Soc.*, 1964, **86**, 2105.
4 M. Bassetti, G. Cerichelli, and B. Floris, *Gazz. Chim. Ital.*, 1986, **116**, 579.
5 O. Piccolo, L. Filippini, L. Tinucci, E. Valoti, and A. Citterio, *Tetrahedron*, 1986, **42**, 885.
6 B. S. Furniss, A. J. Hannaford, V. Rogers, P. W. G. Smith, and A. R. Tatchell, 'Vogel's Textbook of Practical Organic Chemistry,' Longman's, London, 1978.
7 'CRC Handbook of Chemistry and Physics,' ed. R. C. Weast, CRC Press, Cleveland, Ohio, U.S.A., 1979, 58th edn., p. C-451.
8 G. M. Sheldrick, SHELX-76, Program for Crystal Structure Determination, University of Cambridge, 1976.
9 P. Main, S. E. Hull, L. Lessinger, G. Germain, J. P. Declercq, and M. M. Woolfson, 'A System of Computer Programs for the Automatic Solution of Crystal Structures from *X*-ray Diffraction Data,' Universities of York and Louvain-La-Neuve, 1977.
10 International Tables for *X*-ray Crystallography, IV, Kynoch Press, Birmingham, p. 275.
11 V. D. Nageswara Sastri and T. R. Seshadri, *Proc. Indian Acad. Sci., Sect. A*, 1946, **23**, 262.
12 H. Garcia and J. Primo, *Synthesis*, 1985, 901.
13 P. N. Wadodkar and M. G. Marathey, *Indian J. Chem.*, 1972, **10**, 145.
14 W. Baker and F. Glocking, *J. Chem. Soc.*, 1950, 2759.
15 W. Baker, J. Harborne, and W. D. Ollis, *J. Chem. Soc.*, 1952, 1294.
16 V. V. Virkar, *J. Univ. Bombay*, 1942, **11**, 136.
17 T. S. Wheeler, *Org. Synth.*, 1963, Coll. Vol. 4, 478.
18 A. C. Jain, S. K. Mathur, and T. R. Seshadri, *J. Sci. Ind. Res.*, 1962, **21**, 214.
19 F. M. Dean, A. McGookin, and B. M. Marshall, *J. Chem. Soc.*, 1954, 4573.

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