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SYNTHESIS OF 2'-HYDROXYCHALCONE EPOXIDES

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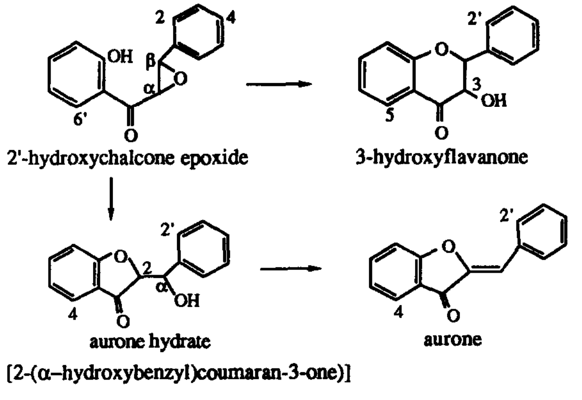
Abstract: Various preparations of some 2'-tetrahydropyran-2-yloxychalcone epoxides and removal of their tetrahydropyranyl (THP) protective groups in slightly aqueous acidic dioxane are described. So synthesised were 2'-hydroxy-6'-isopropoxy- and 2'-hydroxy-6'-methoxychalcone epoxide, as well as the 2-CF_3, 4-Cl and 4-NO_2 analogues of the latter. 2',4'-dihydroxy-6'-methoxychalcone epoxide was similarly prepared. In some other 6'-methoxy cases protective group removal was accompanied by epoxide solvolysis and the corresponding α,β-dihydroxydihydrochalcone was the only isolable product [2-OMe, 4-OMe, 3,4,5-$(OMe)_3$ cases] or a byproduct [4-Me case]. Similarly prepared by THP removal were 2'-hydroxy-4'-methoxychalcone epoxide and 2',4'-dihydroxychalcone epoxide, whereas an attempt to convert 2',6'-ditetrahydropyranyloxychalcone epoxide into 2',6'-dihydroxychalcone epoxide gave the product of cyclisation of the latter, 3,5-dihydroxyflavanone.

Introduction

Because of their potential to cyclise at both α and β positions (Scheme 1), 2'-hydroxychalcone epoxides have long been the subject of conjecture as potential intermediates in the biosynthetic conversion of 2'-hydroxychalcones into flavonoids and aurones,[1] although this has now been ruled out in the case of the former.[2] They have also been proposed as intermediates in the synthesis of 3-hydroxyflavanones and aurones from 2'-hydroxychalcones with alkaline hydrogen peroxide [Algar-Flynn-Oyamada (AFO) reaction] [3,4,5,6] and in other reactions in which aurones are formed from the dibromides (Emilewicz-von Kostanecki reaction)[7] and bromohydrins[8] (Rasoda reaction) of 2'-hydroxychalcones with 6'-substituents. It is remarkable, therefore, that in spite of considerable interest in the chemistry of such epoxides, some of which is outlined in more detail in the introduction to the



Scheme 1

following paper, only one of them is known. This, the parent 2'-hydroxychalcone epoxide itself, was synthesised[9] by direct peracid oxidation. Such epoxidation of the electron-deficient double bond of chalcones has been found, however, to be generally an unsuccessful method for the synthesis of 2'-hydroxychalcone epoxides.[10] The alternative standard reagent for epoxidation of enones, alkaline H_2O_2, requires protection of the 2'-OH group of the chalcone to prevent otherwise rapid cyclisation of any product epoxide: even when only very slightly ionised at neutral pH, for instance, 2'-hydroxychalcone epoxide cyclises with a half-life of 2.5 s. and the rate increases 10-fold per pH unit increase in proportion with the degree of ionisation to the reactive 2'-O- species.[11] Protective-group removal subsequent to epoxidation requires avoidance of alkaline conditions for the same reason, and acid-labile protective groups would only be useful if their cleavage is faster than acid-catalysed ring-opening of the epoxide functions; use of the standard methoxymethyl protective group has been found to be unsuccessful for this reason.[12]

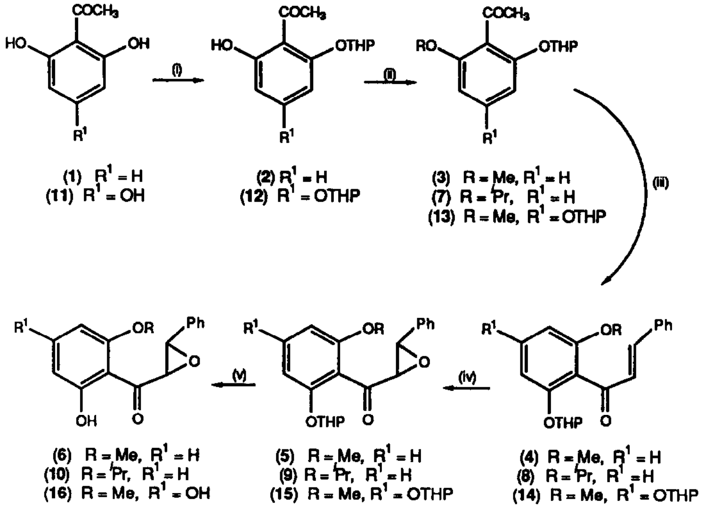
As a basis for the syntheses described in this report, we used u.v. spectroscopy to monitor the removal of the tetrahydropyran-2-yl group from 6'-methoxy-2-*O*-tetrahydropyran-2-ylchalcone epoxide in acidic alcohol solutions. We found that it occurred just sufficiently faster than the competing epoxide ring-opening that the free epoxide should be accessible by quenching the reaction solution after a suitable time. Further tests indicated that slightly aqueous acidic dioxane, a less solvolytic medium, had the advantage that reactions were slowed giving more leeway for successfully timing interruption of the reaction near completion of the deprotection stage. Scaling up to the preparative level was successful in most cases as this report indicates, though not in cases where electron-donating 4-substituents accelerate acid-catalysed cleavage of the epoxide function as will be described.

Our work has been directed to epoxides with 6'-substituents because of our interest in their reactivity: these substituents direct cyclisation under basic conditions to the α rather than the β position[5,7,8] leading to aurone hydrate (Scheme 1), as opposed to the 3-hydroxyflavanone formed[9,11] when the epoxide lacks a 6'-substituent. Details of the cyclisation chemistry will be described in the following paper.

2'-Aminochalcone epoxide, an analogue of the compounds of interest in this study, has recently been reported by Donnelly and Farrell.[13] It can be synthesisied with alkaline H_2O_2 directly from the unprotected aminochalcone and is quite stable to cyclisation which nevertheless is synthetically valuable.

Results and Discussion

Scheme 2 gives the route to 2'-hydroxy-6'-methoxychalcone epoxide (**6**) and the 6'-isopropoxy analogue (**11**). This route was applied successfully also to the 2-trifluoromethyl, 4-chloro, and 4-nitro derivatives of (**6**). Slightly aqueous acidic dioxane was used for the final protective group removal from (**5**); in ethanol and methanol considerable epoxide solvolysis occurred in competition with protective group removal. Even with dioxane, however, epoxide solvolysis was a major limitation in protective group removal from analogues of epoxide (**5**) with electron-donating groups in the 2- or 4- (B-ring) positions. Only the corresponding diols from epoxide solvolysis, the α,β-dihydroxydihydrochalcones, were obtained[14] from the 2-methoxy, 4-methoxy, 3,4,5-trimethoxy and 4-tetrahydropyranyloxy derivatives, indicating that acid-catalysed epoxide solvolysis when activated



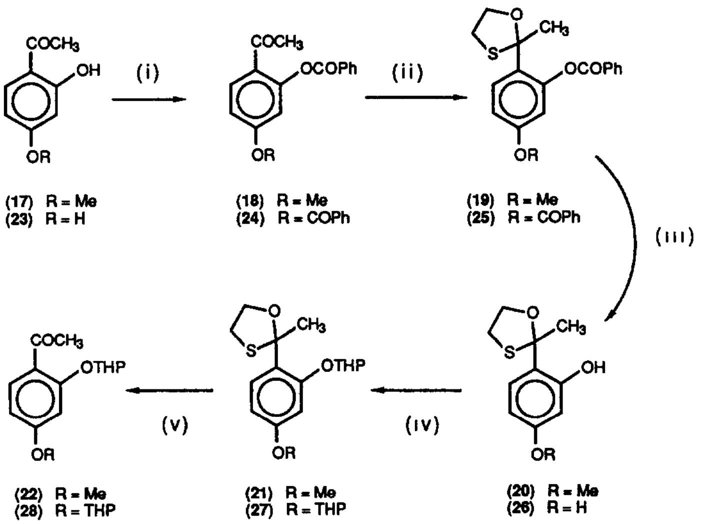
(i) dihydropyran/4-toluenesulphonic acid/dioxane
(ii) MeI/K_2CO_3/acetone
(iii) Benzaldehyde/KOH/MeOH
(iv) H_2O_2/NaOH/MeOH
(v) dioxane/H^+

Scheme 2

by electron-donation from 2- or 4-alkoxy substituents is faster than deprotection of 2'-*O*THP. For the 4-methyl analogue of (**5**) the deprotection and solvolysis rates must be similar as a mixture of the dihydrochalcone diol and the required free epoxide was obtained.

Application of Scheme 2 to the synthesis of 2',4'-dihydroxy-6'-methoxychalcone epoxide (**16**) required the di-OTHP precursor (**12**). Direct tetrahydropyranylation of 2',4',6'-trihydroxyacetophenone gave a mixture of several singly and doubly C- and O-tetrahydropyranylated products from which partially purified (**12**) was obtained by chromatography. Methylation of impure (**12**) gave a product mixture from which pure (**13**) could be separated, and the sequence (**13**→**14**→**15**) followed routinely.

The first step of Scheme 2, in which the 2'-OH is protected as the THP ether, is not possible even with long reaction times if there is just one hydroxy group ortho to the acetyl group, presumably because of intramolecular hydrogen bonding between OH and carbonyl oxygen. In the cases of 2'-hydroxy-4'-methoxy- and 2',4'-dihydroxychalcones, therefore, it was necessary to convert the ketone to a hemithioketal before THP protection. Scheme 3 shows the route to the acetophenones (**22**) and (**28**) required to replace (**3**) in Scheme 2. The hemithioketal was chosen for its ability to withstand the mild acid conditions under which the THP group is attached and for ease of removal (with Ag^+/Ag_2O in acetonitrile) under conditions in which the THP ether is itself stable. Formation of the hemithioketal (**17**→**20**) could not however be achieved in the usual single step using mercaptoethanol and BF_3 because BF_3 reacts alone with (**17**) to give a white crystalline precipitate, whose structure will be reported elsewhere. Conversion of 2'-OH to the benzoate (**18**) allows the hemithioketal function of (**20**), stable also under the alkaline conditions of subsequent removal of the benzoyl group, to be formed. Steps (**20**)→(**21**)→(**22**) follow, the latter being used to synthesise 2'-hydroxy-



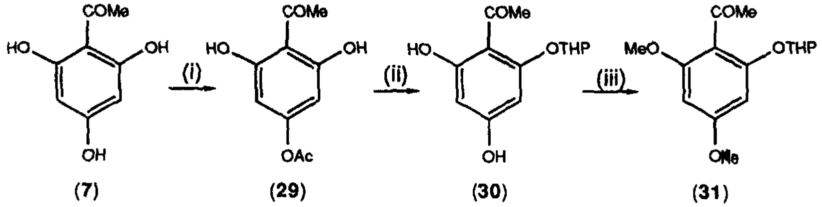
(i) PhCOCl/pyridine
(ii) 2-mercaptoethanol/$BF_3 \cdot Et_2O$/ether
(iii) NaOH/aq.dioxane/methanol
(iv) (a) dihydropyran/4-toluenesulphonic acid/dioxane or (b) dihydropyran/pyridinium 4-toluenesulphonate/dichloromethane
(v) Ag^+/Ag_2O/aqueous acetonitrile

Scheme 3

4'-methoxychalcone epoxide through steps corresponding to the sequence (**3**)→(**6**) in Scheme 2. Later attempts to repeat the steps (**20**)→(**21**) (Scheme 3) using reagents from a different commercial source were unsuccessful, for no apparent reason, even with carefully purified reagents, and the epoxide remains not fully characterised as a result (see experimental). This problem did not arise in the preparation of 2',4'-ditetrahydropyranyloxyacetophenone (**28**; Scheme 3) which provides 2',4'-dihydroxychalcone epoxide by steps equivalent to (**13**)→(**16**) in Scheme 2.

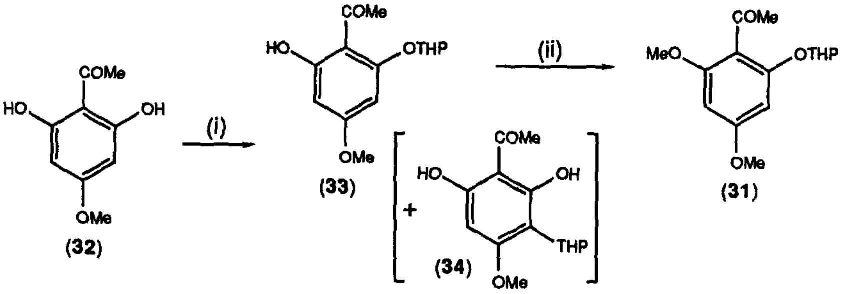
For the synthesis of 2'-hydroxy-4',6'-dimethoxychalcone epoxide, application of the sequence in Scheme 2 required 2',4'-dimethoxy-6'-tetrahydropyranyloxyacetophenone (**31**) which was synthesised by two alternative routes. The first (Scheme 4) involved acetylation of the 4'-OH of 2',4',6'-trihydroxyacetophenone (**7**) to prevent ring tetrahydropyranylation in the subsequent step (**29**→**30**). Conditions were varied to maximise monoacetylation but at best the yield was only 20%. However, di- and tri-acetylated products could be recycled after hydrolysis and the starting compound (**7**) is in any case inexpensive. The alternative route to (**31**) (Scheme 5) involved an initial 2-step synthesis (not shown; see experimental) of 2',6'-dihydroxy-4'-methoxyacetophenone (**32**). The latter, unlike the deactivated 4'-*O*-acetyl analogue (**29**), gave as much *C*-tetrahydropyranylacetophenone (**34**) as required *O*-tetrahydropyranylacetophenone (**33**) in the protection step (Scheme 5). After separation and reaction of (**33**), the overall yield of (**31**) is lower than that from Scheme 4.

Finally, an attempt was made to apply Scheme 2 to the synthesis of 2',6'-dihydroxychalcone epoxide using 2',6'-ditetrahydropyranyloxyacetophenone. Unexpectedly, the latter could be obtained,



(i) acetic anhydride/pyridine
(ii) dihydropyran/4-toluenesulphonic acid/dioxane
(iii) MeI/K_2CO_3/acetone

Scheme 4



(i) dihydropyran/4-toluenesulphonic acid/dioxane
(ii) MeI/K_2CO_3/acetone

Scheme 5

though in only 6% yield, by direct tetrahydropyranylation of 2',6'-dihydroxyacetophenone, which suggests that the 2'-OTHP group of the monoprotected ketone causes the acetyl group to twist out of plane with the ring, weakening the hydrogen bond to the second (6'-) OH sufficiently that it too can be protected. The required di-protected chalcone epoxide was easily prepared but controlled deprotection gave only 2'-hydroxy-6'-tetrahydropyranyloxychalcone epoxide and 3,5-dihydroxyflavanone. The latter is the product of cyclisation of 2',6'-dihydroxychalcone epoxide which clearly, therefore, cyclises much faster than it is formed.

Experimental

Reagents were of commercial origin (Aldrich and Sigma). Melting points are uncorrected.

THP stands for the tetrahydropyran-2-yl group. P.l.c. refers to preparative layer chromatography on 2mm layers of silica gel (Merck 60 PF_{254} + 366).

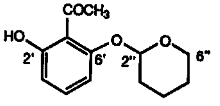
Mass spectra were recorded on a Kratos MS 80 RFM spectrometer at the Ruakura Agricultural Research Centre.

N.m.r. spectra were recorded on a JEOL FX90Q FT spectrometer. The following internal standards were used: for $CDCl_3$ solvent, δ_C 77.06 and δ_H ($CHCl_3$) 7.26; for $(CD_3)_2CO$, δ_C 29.85 and δ_H (CD_3COCD_2H) 2.20. Multiplicities of ^{13}C signals were determined by standard techniques. Signal assignments with paired superscripts x, y, z, or w are interchangeable. Tetrahydropyran-2-yl ring assignments are indicated by double dashes [see structure (2) below] and by triple dashes as well in the cases of di-tetrahydropyranyl derivatives.

Given the standard reaction types of the various steps in the synthetic schemes, the intermediate tetrahydropyran-2-yl compounds, which were oils, were not characterised by elemental analysis if their n.m.r. spectra were unambiguous and indicated the absence of impurity. Elemental analyses were however performed on the final 2'-hydroxychalcone epoxide products.

2',6'-Dihydroxyacetophenone (1).- This compound, prepared by the standard method^{15}, had m.p. 152-154°C (lit.^{15} 151-155°C)].

2'-Hydroxy-6'-tetrahydropyranyloxyacetophenone (2).- 2',6'-Dihydroxyacetophenone (1; 4.9 g, 32.2 mmol) and 3,4-dihydro-2H-pyran (17.2 g, 16 ml, 205 mmol) were dissolved in dioxane (*ca.* 20 ml). To this solution was added a catalytic amount (*ca.* 20 mg in *ca.* 2 ml dioxane) of toluene-4-sulphonic acid. After standing overnight (*ca.* 20 h) the reaction mixture was added to 5 % K_2CO_3 solution (25 ml) and ether (70 ml), and extracted. The ether layer was extracted with 5 % K_2CO_3 solution (2 x 30 ml) and 2 moll^{-1} NaOH (2 x 40 ml) and this alkaline extract added to 5 % K_2CO_3 solution (70 ml). Hydrochloric acid (2 moll^{-1}) was added (slowly) until the pH was *ca.* 8-9 (as judged by pH paper). The aqueous layer was extracted with ether (2 x 50 ml). The ether layer was washed with water (50 ml), dried ($MgSO_4$), and the solvent removed to yield ***2'-hydroxy-6'-tetrahydropyranyloxyacetophenone*** (2) as an oil which crystallised on standing (5.28 g, 69 %); δ_H (89.55 MHz; solvent $CDCl_3$) 13.27 (1H, s, OH), 7.39 [1H, d ($^{4',3'}J$ = 8 Hz) of d ($^{4',5'}J$ = 8 Hz), 4'-H], 6.76 (1H, d, $^{3',4'}J$ = 8 Hz, 3'-H), 6.61 (1H, d, $^{5',4'}J$ = 8 Hz, 5'-H), 5.60 (1H, br s, 2"-H), 3.80 (2H, m, 6"-H), 2.75 (3H, s, $COCH_3$), 1.94 (6H, br m, 3",4",5"-H); δ_C (22.49 MHz; solvent $CDCl_3$) 204.9 (s, $\underline{C}OMe$), 164.3 (s, 2'-C), 159.1 (s, 6'-C), 136.1 (d, 4'-C), 111.7 (s, 1'-C), 111.1 (d, 3'-C), 104.7 (d, 5'-C), 97.3 (d, 2"-C), 62.3 (t, 6"-C), 33.8 (q, $CO\underline{C}H_3$), 30.3 (t, 3"-C), 25.0 (t, 5"-C) 19.2 (t, 4"-C).



(2)

2'-Methoxy-6'-tetrahydropyranyloxyacetophenone (3).- 2'-Hydroxy-6'-tetrahydropyranyloxyacetophenone (2; 5.0 g, 23.3 mmol) and methyl iodide (7 ml) were dissolved in acetone (80 ml) containing a suspension of K_2CO_3 (dry, finely ground, 10 g). The reaction mixture was refluxed until t.l.c. showed no more starting material remained (140 h.). After cooling and filtering, the solvent was removed under vacuum and the residue dissolved in ether (50 ml). The ether solution was extracted with 2 moll^{-1} NaOH (2 x 20 ml), dried ($MgSO_4$), and the ether removed to yield ***2'-methoxy-6'-tetrahydropyranyloxyacetophenone*** (3; 5.49 g, 94 %)) as a colourless oil which could not be crystallised; δ_C (22.49 MHz; solvent $CDCl_3$) 202.2 (s, C=O), 156.3 (s, 2'-C), 153.8 (s, 6'-C), 130.3 (d, 4'-C), 121.4 (s, 1'-C), 107.6 (d, 3'-C), 104.4 (d, 5'-C), 96.2 (d, 2"-C), 61.6 (t, 6"-C), 55.6 (q, OCH_3), 32.1 (q, $COCH_3$), 29.9 (t, 3"-C), 24.9 (t, 5"-C), 18.2 (t, 4"-C).

2'-Methoxy-6'-tetrahydropyranyloxychalcone (4).- 2'-Methoxy-6'-tetrahydropyranyloxyacetophenone (3; 1.0 g, 4.0 mmol) and benzaldehyde (0.64 g, 6.0 mmol) were dissolved in a solution of KOH (5 g), water (5 ml), and methanol (10 ml), and stirred at room temperature for 20 h. Water (20 ml) was added and the suspension extracted with ether (3 x 20 ml). The combined ether extracts were washed with water (2 x 20 ml), dried ($MgSO_4$), and the solvent removed. The remaining yellow oil was chromatographed [p.l.c. using petroleum spirit (b.p. 60-80°C):ether; 3:1] to yield 1.04 g (77 %) of ***2'-methoxy-6'-tetrahydropyranyloxychalcone*** (4) as a pale yellow oil; δ_C (22.49 MHz; solvent $CDCl_3$) 194.5 (s, C=O), 157.4 (s, 2'-C), 154.7 (s, 6'-C), 144.6 (d, β-C), 134.7 (s, 1-C), 130.5 (d, 4'-C), 130.1 (d, 2,6-C)^x, 128.7 (d, 3,4,5-C)^x, 128.0 (d, α-C), 119.5 (s, 1'-C), 107.8 (d, 3'-C), 104.6 (d, 5'-C), 96.2 (d, 2"-C), 61.4 (t, 6"-C), 55.7 (q, OCH_3), 29.8 (t, 3"-C), 24.9 (t, 5"-C), 17.9 (t, 4"-C).

2'-Methoxy-6'-tetrahydropyranyloxychalcone epoxide (**5**).- 2'-Methoxy-6'-tetrahydropyranyloxychalcone (**4**; 0.64 g, 1.89 mmol) was dissolved in a solution of H_2O_2 (100 vols., 2.5 ml), 2 mol*l* $^{-1}$ NaOH (1.0 ml), and methanol (20 ml). The solution was stirred at room temperature for 2 h. Water (20 ml) was added and the resulting suspension extracted with ether (3 x 20 ml). The combined ether extracts were washed with water (1 x 20 ml), dried ($MgSO_4$), and the ether removed to yield 0.62 g (93 %) of ***2'-methoxy-6'-tetrahydropyranyloxychalcone epoxide*** (**5**) as a colourless oil which crystallised on standing, m.p. 77-85°C; δ_C (22.49 MHz; solvent $CDCl_3$) 197.5 (s, C=O), 157.5 and 157.4 (s, 2'-C), 155.1 and 154.7 (s, 6'-C), 135.4 (s, 1-C), 131.7 (d, 4'-C), 128.3 (d, 4-C), 128.1 (d, 2,6-C), 125.3 (d, 3,5-C), 117.1 and 117.0 (s, 1'-C), 107.7 and 107.3 (d, 3'-C), 104.3 and 104.1 (d, 5'-C), 96.7 and 95.7 (d, 6"-C), 63.4 (d, α-C), 61.6 and 61.2 (t, 6"-C), 58.6 (d, β-C), 55.5 (q, OCH_3), 29.6 (t, 3"-C), 24.6 (t, 5"-C), 18.1 and 17.7 (t, 4"-C).

2'-Hydroxy-6'-methoxychalcone epoxide (**6**).- 2'-Methoxy-6'-tetrahydropyranyloxychalcone epoxide (**5**; 270 mg, 0.76 mmol) was dissolved in dioxane (30 ml) and 2 mol*l* $^{-1}$ H_2SO_4 (0.10 ml) was added. After 15 min., water (40 ml) was added and the resulting suspension extracted with CH_2Cl_2 (2 x 30 ml). The combined CH_2Cl_2 extracts were washed with water (2 x 20 ml), dried ($MgSO_4$), and the solvents removed under vacuum to yield 205 mg (100 %) of ***2'-hydroxy-6'-methoxychalcone epoxide*** (**6**) as a pale yellow solid, m.p. 129-132°C; δ_H (89.55 MHz; solvent $CDCl_3$) 12.46 (6H, s, OH), 7.38 (6H, 4',2,3,4,5,6-H), 6.60 (1H, d, $^{3',4'}J$ = 8.4 Hz, 3'-H), 6.34 (1H, d, $^{5',4'}J$ = 8.4 Hz, 5'-H), 4.38 (1H, d, $^{\alpha,\beta}J$ = 2.0 Hz, α-H), 3.98 (1H, d, $^{\beta,\alpha}J$ = 2.0 Hz, β-H), 3.47 (3H, s, OCH_3); δ_C (22.49 MHz; solvent $CDCl_3$) 198.4 (s, C=O), 164.4 (s, 2'-C), 161.5 (s, 6'-C), 137.3 (d, 4'-C), 136.4 (s, 1-C), 128.8 (d, 4-C), 128.6 (d, 2,6-C), 125.7 (d, 3,5-C), 110.9 (d, 3'-C), 110.4 (s, 1'-C), 101.3 (d, 5'-C), 65.1 (d, α-C), 59.5 (d, β-C), 55.8 (q, OCH_3). Found C 70.71, H 5.24; $C_{16}H_{14}O_4$ requires C 71.10, H 5.22 %.

2-Trifluoromethyl-2'-methoxy-6'-tetrahydropyranyloxychalcone.- 2'-Methoxy-6'-tetrahydropyranyloxyacetophenone (550 mg, 2.20 mmol) and 2-trifluoromethylbenzaldehyde (570 mg, 3.30 mmol) were dissolved in a solution of KOH (2.5 g), water (2.5 ml), and methanol (15 ml), and left at room temperature for 24 h. After the usual workup (as for **4**), p.l.c. (hexane:ethyl acetate; 3:1) yielded 762 mg (85 %) of ***2-trifluoromethyl-2'-methoxy-6'-tetrahydropyranyloxychalcone*** as a yellow oil.; δ_C (22.49 MHz; solvent $CDCl_3$) 194.7 (s, C=O), 157.3 (s, 2'-C), 154.8 (s, 6'-C), 140.2 (d, β-C), 133.6 (s, 1-C, q, ^3J = 1.2 Hz), 132.2 (d, 4'-C), 132.0 (br d, 5-C), 130.9 (d, 6-C), 129.5 (d, 4-C), 128.6 (s, 2-C, q, J = 30.1 Hz), 127.8 (d, α-C), 126.0 (d, 3-C, q, ^4J = 5.6 Hz), 123.7 (s, CF_3, q, ^1J = 274.1 Hz), 118.6 (s, 1'-C), 107.7 (d, 3'-C), 104.4 (d, 5'-C), 96.2 (d, 2"-C), 61.4 (t, 6"-C), 55.6 (q, OCH_3), 29.8 (t, 3"-C), 24.9 (t, 5"-C) and 17.9 (t, 6"-C).

2-Trifluoromethyl-2'-methoxy-6'-tetrahydropyranyloxychalcone epoxide.- 2-Trifluoromethyl-2'-methoxy-6'-tetrahydropyranyloxychalcone (200 mg, 0.49 mmol) was dissolved in a solution of 2 mol*l* $^{-1}$ NaOH (0.25 ml), H_2O_2 (100 vols., 0.4 ml), and methanol (3.5 ml), and stirred at room temperature for 2 h. The usual workup (as for **5**) produced ***2-trifluoromethyl-2'-methoxy-6-tetrahydropyranyloxychalcone epoxide*** in *ca.* 90 % yield as a colourless oil; δ_C (22.49 MHz; solvent $CDCl_3$) 197.1 and 196.8 (s, C=O), 157.4 and 157.6 (s, 2'-C), 155.3 and 155.0 (s, 6'-C), 134.5 and 134.4 (s, 1-C), 131.9 (d, 4'-C)^x, 131.6 (d, 5-C)^x, 127.9 (d, 6-C), 127.9 (s, 2-C, q, ^2J = 31.5 Hz), 125.2 (d, 3-C, q, ^3J = 5.4 Hz), 125.1 (d, 4-C), 123.9 (s, CF_3, q, ^1J = 274 Hz), 116.9 and 116.7 (s, 1'-C), 107.7 and 107.3 (d, 3'-C), 104.1 and 103.9 (d, 5'-C), 96.8 and 95.7 (d, 2"-C), 63.1 (d, α-C), 61.5 and 61.0 (t, 6"-C), 55.3 (q, OCH_3), 54.6 (d, β-C, 2 x q (superimposed), J ~ 2.7 Hz), 29.6 and 29.5 (t, 3"-C), 24.7 (t, 5"-C), 17.9 and 17.6 (t, 4"-C).

2-Trifluoromethyl-2'-hydroxy-6'-methoxychalcone epoxide.- 2'-Methoxy-6'-tetrahydropyranyloxy-2-trifluoromethylchalcone epoxide (150 mg, 0.36 mmol) was dissolved in dioxane (30 ml). 2 mol*l* $^{-1}$ H_2SO_4 (0.10 ml) was added and the solution left for 20 min. The usual workup (as for **6**) produced ***2-trifluoromethyl-2'-hydroxy-6'-methoxychalcone epoxide*** in *ca.* 90 % yield, as a white solid, m.p. 151-156°C; δ_H (89.55 MHz; solvent $CDCl_3$) 12.50 (1H, s, OH), 7.59 (5H, m, 4',3,4,5,6-H), 6.60 (1H, d, $^{3',4'}J$ = 8.4 Hz, 3'-H), 6.34 (1H, d, $^{5',4'}J$ = 8.4 Hz, 5'-H), 4.35 (2H, br s, α-H, β-H), 3.48 (3H, s, OCH_3); δ_C (22.49 MHz; solvent $CDCl_3$) 197.4 (s, C=O), 164.6 (s, 2'-C), 161.4 (s, 6'-C), 137.5 (d, 4'-C), 135.1 (s, 1-C), 132.5 (d, br, 5-C), 128.5 (s, 2-C, q, J = 31.7 Hz), 128.4 (d, 4-C), 125.7 (d, 3-C, q, J = 5.5 Hz), 125.3 (d, 6-C), 124.1 (s, CF_3, q, J = 274 Hz), 110.8 (d, 3'-C), 110.3 (s, 1'-C), 101.2 (d, 5'-C), 64.8 (d, α-C), 55.9 (d, β-C, q, J = 3.4 Hz), 55.6 (q, OCH_3). Found C 60.15, H 3.86; $C_{17}H_{13}O_4F_3$ requires C 60.36, H 3.87 %.

4-Chloro-2'-methoxy-6'-tetrahydropyranyloxychalcone.- 2'-Methoxy-6'-tetrahydropyranyloxyacetophenone (0.50 g, 2.0 mmol) and 4-chlorobenzaldehyde (0.42 g, 3.0 mmol) were dissolved in a solution of KOH (2.5 g) in water (2.5 ml) and methanol (10 ml), and stirred at room temperature for 24 h. After the usual workup (as for **4**) p.l.c. [petroleum spirit (b.p. 60-80°C): ether; 3:1] yielded 0.66 g (89 %) of ***4-chloro-2'-methoxy-6'-tetrahydropyranyloxychalcone*** as a yellow oil.; δ_C (22.49 MHz; solvent $CDCl_3$) 194.4 (s, C=O), 157.4 (s, 2'-C), 154.8 (s, 6'-C), 143.1 (d, β-C), 136.0 (s, 1-C), 133.3 (s, 4-C), 130.8 (d, 4'-C), 129.3 (d, 3,5-C)^x, 129.0 (d, α-C)^x, 129.0 (d, 2,6-C)^x, 119.2 (s, 1'-C), 107.7 (d, 3'-C), 104.6 (d, 5'-C), 96.2 (d, 2"-C), 61.6 (t, 6"-C), 55.8 (q, OCH_3), 29.9 (t, 3"-C), 25.0 (t, 5"-C), 18.0 (t, 4"-C).

4-Chloro-2'-methoxy-6'-tetrahydropyranyloxychalcone epoxide.- 4-Chloro-2'-methoxy-6-tetrahydropyranyloxychalcone (0.66 g, 1.77 mmol) was dissolved in a solution of 2 mol*l*$^{-1}$ (0.5 ml), H_2O_2 (100 vols., 0.5 ml), and methanol (5.0 ml). The usual workup (as for **5**) yielded 0.69 g (100 %) of 4-chloro-2'-methoxy-6'-tetrahydropyranyloxychalcone epoxide as a colourless oil; δ_C (22.49 MHz; solvent $CDCl_3$) 197.6 (s, C=O), 157.9 and 157.8 (s, 2'-C), 155.6 and 155.2 (s, 6'-C), 134.5 (s, 1-C)^x, 134.5 (s, 4-C)^x, 132.1 (d, 4'-C), 128.7 (d, 3,5-C), 127.0 (d, 2,6-C), 117.3 and 117.2 (s, 1'-C), 108.1 and 107.6 (d, 3'-C), 104.7 and 104.5 (d, 5'-C), 97.2 and 96.1 (d, 2"-C), 63.6 (d, α-C), 62.0 and 61.7 (t, 6"-C), 58.3 (d, β-C), 55.9 (q, OCH_3), 30.0 (t, 3"-C), 25.0 (t, 5"-C), 18.5 and 18.1 (t, 4"-C).

4-Chloro-2'-hydroxy-6'-methoxychalcone epoxide.- 4-Chloro-2'-methoxy-6'-tetrahydropyranyloxychalcone epoxide (200 mg, 0.51 mmol) was dissolved in dioxane (40 ml). 2 mol*l*$^{-1}$ H_2SO_4 (0.10 ml) was added and the solution left for 30 min. The usual workup (as for **6**) produced ***4-chloro-2'-hydroxy-6'-methoxychalcone epoxide*** in *ca.* 90 % yield, as a white solid, m.p. 111-115°C; δ_H (89.55 MHz; solvent $CDCl_3$) 12.39 (1H, s, OH), 7.33 (5H, s superimposed on 4'-H signal, 4',2,3,5,6-H), 6.55 (1H, d, $^{3',4'}J$ = 8.4 Hz, 3'-H), 6.32 (1H, d, $^{5',4'}J$ = 8.4 Hz, 5'-H), 4.31 (1H, d, $^{\alpha,\beta}J$ = 2.0 Hz, α-H), 3.94 (1H, d, $^{\beta,\alpha}J$ = 2.0 Hz, β-H), 3.49 (3H, s, OCH_3); δ_C (22.49 MHz; solvent $CDCl_3$) 197.7 (s, C=O), 164.0 (s, 2'-C), 161.2 (s, 6'-C), 137.2 (d, 4'-C), 134.7 (s, 4-C)^x, 134.4 (s, 1-C)^x, 128.6 (d, 2,6-C), 126.9 (d, 3,5-C), 110.6 (d, 3'-C), 110.0 (s, 1'-C), 101.2 (d, 5'-C), 64.7 (d, α-C), 58.5 (d, β-C), 55.7 (q, OCH_3). Found C 62.95, H 4.31; $C_{16}H_{13}O_4Cl$ requires C 63.06, H 4.30 %.

2'-Methoxy-4-nitro-6'-tetrahydropyranyloxychalcone.- 2'-Methoxy-6'-tetrahydropyranyloxyacetophenone (305 mg, 1.22 mmol) and 4-nitrobenzaldehyde (280 mg, 1.85 mmol) were dissolved in methanol (10 ml), and the temperature lowered to -20°C. A solution of KOH (0.7 g) in water (0.7 ml) was added dropwise over 10 min. The solution was then stirred at room temperature for 24 h. After the usual workup (as for **4**), p.l.c. (hexane:ethyl acetate; 5:2) yielded 161 mg (34 %) of ***2'-methoxy-4-nitro-6'-tetrahydropyranyloxychalcone*** as a yellow oil; δ_C (22.49 MHz; solvent $CDCl_3$) 193.5 (s, C=O), 157.3 (s, 2'-C), 154.7 (s, 6'-C), 18.1 (s, 4-C), 140.9 (s, 1-C), 140.7 (d, β–C), 131.9 (d, 4'-C), 131.0 (d, α-C), 128.5 (d, 3,5-C), 123.8 (d, 2,6-C), 118.7 (s, 1'-C), 107.6 (d, 3'-C), 104.5 (d, 5'-C), 96.2 (d, 2"-C), 61.5 (t, 6"-C), 55.6 (q, OCH_3), 29.7 (t, 3"-C), 24.8 (t, 5"-C), 18.0 (t, 4"-C).

2'-Methoxy-4-nitro-6'-tetrahydropyranyloxychalcone epoxide.- 2'-Methoxy-4-nitro-6'-tetrahydropyranyloxychalcone (161 mg, 0.42 mmol) was dissolved in a solution of 2 moll^{-1} NaOH (0.4 ml), H_2O_2 (100 vols., 0.4 ml), and methanol (10 ml) and stirred at room temperature for 1.5 h. After the usual workup (as for **5**) p.l.c. [petroleum spirit (b.p. 60-80°C): ether; 3:1] yielded 144 mg (86 %) of ***2'-methoxy-4-nitro-6'-tetrahydropyranyloxychalcone epoxide*** as a pale yellow oil.; δ_C (22.49 MHz; solvent $CDCl_3$) 196.7 (s, C=O), 157.9 and 157.8 (s, 2'-C), 155.6 and 155.3 (s, 6'-C), 148.0 (s, 4-C), 143.3 (s, 1-C), 132.3 (d, 4'-C), 126.5 (d, 2,6-C), 123.7 (d, 3,5-C), 117.0 and 116.9 (s, 1'-C), 108.2 and 107.7 (d, 3'-C), 104.7 and 104.4 (d, 5'-C), 97.2 and 96.2 (d, 2"-C), 63.7 (d, α-C), 62.1 and 61.8 (t, 6"-C), 57.6 (d, β-C), 55.9 (q, OCH_3), 30.0 (t, 3"-C), 24.9 (t, 5"-C), 18.6 and 18.2 (t, 4"-C).

2'-Hydroxy-6'-methoxy-4-nitrochalcone epoxide.- 2'-Methoxy-4-nitro-6'-tetrahydropyranyloxychalcone epoxide (100 mg, 0.25 mmol) was dissolved in dioxane (30 ml). 2 moll^{-1} H_2SO_4 (0.10 ml) was added and the solution left for 25 min. The usual workup (as for **6**) produced ***2'-hydroxy-6'-methoxy-4-nitrochalcone epoxide*** in *ca.* 90 % yield, as a pale yellow solid, m.p. 111-115°C; δ_H (89.55 MHz; solvent $CDCl_3$) 12.35 (1H, s, OH), 8.29 (2H, d, $^{3,5\text{-}2,6}J$ = 8.8 Hz, 3,5-H), 7.57 (2H, d, $^{2,6\text{-}3,5}J$ = 8.8 Hz, 2,6-H), 7.42 (1H, t, $^{4'\text{-}3',5'}J$ = 8.4 Hz, 4'-H), 6.63 (1H, d, $^{3',4'}J$ = 8.4 Hz, 3'-H), 6.36 (1H, d, $^{5',4'}J$ = 8.4 Hz, 5'-H), 4.37 (1H, d, $^{\alpha,\beta}J$ =1.5 Hz, α-H), 4.10 (1H, d, $^{\beta,\alpha}J$ = 1.5 Hz, β-H), 3.52 (3H, OCH_3); δ_C (22.49 MHz; solvent $CDCl_3$) 197.2 (s, C=O), 164.6 (*s*, 2'-C), 161.3 (s, 6'-C), 143.8 (s, 4-C), 137.7 (d, 4'-C), 126.6 (d, 2,6-C), 124.0 (d, 3,5-C), 111.3 (d, 3'-C), 110.3 (s, 1'-C), 101.4 (d, 5'-C), 65.0 (d, α-C), 58.2 (d, β-C), 56.0 (q, OCH_3). Found C 60.47, H 4.23, N 4.40; $C_{16}H_{13}O_6N$ requires C 60.95, H 4.16, N 4.44 %.

2'-Methoxy-4-methyl-6'-tetrahydropyranyloxychalcone.- 2'-methoxy-6'-tetrahydropyranyloxyacetophenone (400 mg, 1.6 mmol) and 4-methylbenzaldehyde (290 mg, 2.4 mmol) were dissolved in a solution of KOH (2.5 g) in water (2.5 ml), and methanol (15 ml), and stirred at room temperature for 24 h. After the usual workup (as for **4**) p.l.c. [petroleum spirit (b.p. 60-80°C):ether; 3:1] yielded 479 mg (85 %) of 2'-methoxy-4-methyl-6'-tetrahydropyranyloxychalcone as a yellow oil; δ_C (22.49 MHz; solvent $CDCl_3$) 195.0 (s, C=O), 157.4 (s, 2'-C), 154.8 (s, 6'-C), 145.1 (d, β-C), 140.8 (s, 1-C), 132.1 (s, 4-C), 130.6 (d, 4'-C), 129.6 (d, 2,6-C), 128.2 (d, 3,5-C), 127.9 (d, α-C), 119.5 (s, 1'-C), 107.7 (d, 3'-C), 104.6 (d, 5'-C), 96.2 (d, 2"-C), 61.6 (t, 6"-C), 55.9 (q, OCH_3), 30.0 (t, 3"-C), 25.1 (t, 5"-C), 21.4 (q, CH_3), 18.0 (t, 4"-C).

2'-Methoxy-4-methyl-6'-tetrahydropyranyloxychalcone epoxide.- 2'-Methoxy-4-methyl-6'-tetrahydropyranyloxychalcone (429 mg, 1.22 mmol) was dissolved in a solution of 2 moll^{-1} NaOH (0.7 ml), H_2O_2 (100 vols; 0.7 ml), and methanol (15 ml), and stirred at room temperature for 1.5 h. The usual workup (as for **5**) yielded 411 mg (92 %) of ***2'-methoxy-4-methyl-6'-tetrahydropyranyloxychalcone epoxide.***; δ_C (22.49 MHz; solvent $CDCl_3$) 198.0 (s, C=O), 157.7 and 157.6 (s, 2'-C), 155.3 and 154.9 (s, 6'-C), 138.4 (s, 1-C), 132.7 (s, 4-C), 131.7 (d, 4'-C), 129.0 (d, 2,6-C), 125.5 (d, 3,5-C), 117.5 and 117.4 (s, 1'-C), 108.0 and 107.5 (d, 3'-C), 104.5 and 104.3 (d, 5'-C), 96.9 and 95.9 (d, 2"-C), 63.6 (d, α-C), 61.7 and 61.4 (t, 6"-C), 58.9 (d, β-C), 55.7 (q, OCH_3), 29.8 (t, 3"-C), 24.9 (t, 5"-C), 20.9 (q, CH_3), and, 18.3 and 17.9 (t, 4"-C).

2'-Hydroxy-6'-methoxy-4-methylchalcone epoxide.- 2'-Methoxy-4-methyl-6'-tetrahydropyranyloxychalcone epoxide (150 mg) was dissolved in dioxane (30 ml). 2 Moll^{-1} H_2SO_4 (0.075 ml) was added and the solution left for 30 min. After the usual workup (as for **6**) ^{13}C-n.m.r. (see below) indicated the presence of three major compounds; unreacted 2'-methoxy-4-methyl-6'-tetrahydropyranyloxychalcone epoxide, 2'-hydroxy-6'-methoxy-4-methylchalcone epoxide, and the diol α,β,2'-trihydroxy-6'-methoxy-4-methyldihydrochalcone (*ca.* 2:4:1). Repetition of this reaction using a 45 min. reaction time gave after chromatography [p.l.c. using petroleum spirit (b.p. 60-80°C)

/ ether; 3:1] two major separable fractions. The more mobile one was extracted and rechromatographed (same conditions) in an attempt to get pure 2'-hydroxy-6'-methoxy-4-methylchalcone epoxide, but after extraction the product (39 mg) was found to be contaminated with α,β,2'-trihydroxy-6'-methoxy-4-methyldihydrochalcone (the less mobile fraction in the original separation) which must be formed from the epoxide after development of the plate because the two compounds are clearly separable by chromatography. A completely pure sample of the epoxide could not therefore be obtained, but n.m.r. data for it and for the diol were as follows: ***2'-hydroxy-6'-methoxy-4-methylchalcone epoxide:*** δ_H (89.55 MHz; solvent CDCl$_3$) 12.47 (1H, s, OH), 7.23 (5-H, s, 4',2,3,5,6-H), 6.60 (1H, d, $^{3',5'}J$ = 8.4 Hz, 3'-H), 6.35 (1H, d, $^{5',3'}J$ = 8.4 Hz, 5'-H), 4.38 (1H, d, $^{\alpha,\beta}J$ = 1.8 Hz, α-H), 3.93 (1H, d, $^{\beta,\alpha}J$ = 1.8 Hz, β-H), 3.49 (3H, s, OCH$_3$), and 2.38 (3H, s, CH$_3$); δ_C (22.49 MHz; solvent CDCl$_3$) 198.6 (s, C=O), 164.3 (s, 2'-C), 161.5 (s, 6'-C), 138.7 (s, 1-C), 137.2 (d, 4'-C), 133.2 (s, 4-C), 129.3 (d, 2,6-C), 125.7 (d, 3,5-C), 110.8 (d, 3'-C), 110.4 (s, 1'-C), 101.3 (d, 5'-C), 64.9 (d, α-C), 59.6 (d, β–C), 55.8 (q, OCH$_3$), and 21.2 (q, CH$_3$). ***α,β,2'-trihydroxy-6'-methoxy-4-methyldihydrochalcone*** : δ_C (22.49 MHz; solvent CDCl$_3$) 204.5 (s, C=O), 164.9 (s, 2'-C), 160.7 (s, 6'-C), 138.7 (s, 1-C), 137.2 (s, 4-C), 137.2 (d, 4'-C), 128.9 (d, 2,6-C), 126.1 (d, 3,5-C), 111.3 (d, 3'-C), 108.7 (s, 1'-C), 101.5 (d, 5'-C), 79.1 (d, α-C), 73.5 (d, β-C), 55.7 (q, OCH$_3$), 21.0 (q, CH$_3$).

2'-Isopropoxy-6'-tetrahydropyranyloxyacetophenone (**7**).- 2'-Hydroxy-6'-tetrahydropyranyloxyacetophenone (**2**; 3.6 g, 15.3 mmol) and 2-bromopropane (3.89 g, 23.0 mmol) were refluxed in acetone (50 ml) containing a suspension of K$_2$CO$_3$ (3 g) for 48 h. The usual workup (as for **3**) yielded 1.53 g (36 %) of ***2'-isopropoxy-6'-tetrahydropyranyloxyacetophenone*** (**7**) as an oil; δ_C (22.49 MHz; solvent CDCl$_3$) 201.5 (s, $\underline{C}$OMe), 154.6 (s, 2'-C), 153.6 (s, 6'-C), 129.7 (d, 4'-C), 122.8 (s,1'-C), 107.3 (d, 3'-C)^x, 106.7 (d, 5'-C)^x, 96.1 and 93.9 (d, 2"-C), 70.5 [d, O$\underline{C}$H(Me)$_2$], 62.2 and 61.3 (t, 6"-C), 31.8 (q, CO$\underline{C}$H$_3$), 30.3 and 29.7 (t, 3"-C), 25.1 and 24.8 (t, 5"-C), 21.6 [q, OCH($\underline{C}$H$_3$)$_2$], 19.3 and 18.0 (t, 4"-C).

2'-Isopropoxy-6'-tetrahydropyranyloxychalcone (**8**).- 2'-Isopropoxy-6'-tetrahydropyranyloxyacetophenone (**7**; 1.17 g, 4.21 mmol) and benzaldehyde (0.67 g, 6.3 mmol) were dissolved in a solution of KOH (6.0 g) in water (6 ml) and methanol (20 ml), and stirred at room temperature for 24 h. After the usual workup (as for **4**), p.l.c. [petroleum spirit (60-80°C):ethyl acetate; 5:1] yielded 0.98 g (63 %) of ***2'-isopropoxy-6'-tetrahydropyranyloxychalcone*** (**8**) as a yellow oil; δ_C (22.49 MHz; solvent CDCl$_3$) 194.9 (s, C=O), 155.9 (s, 2'-C), 154.9 (s, 6'-C), 144.6 (d, β-C), 134.9 (s, 1-C), 130.4 (d, 4'-C)^x, 130.1 (d, α-C)^x, 128.9 (d, 4-C), 128.8 (d, 3,5-C), 128.1 (d, 2,6-C), 120.8 (s, 1'-C), 107.5 (d, 3'-C)^y, 107.3 (d, 5'-C)^y, 96.2 (d, 2"-C), 71.0 [d, O$\underline{C}$H(Me)$_2$], 61.9 (t, 6"-C), 29.9 (t, 3"-C), 25.1 (t, 5"-C), 22.0 [q, OCH($\underline{C}$H$_3$)$_2$], 18.0 (t, 4"-C).

2'-Isopropoxy-6'-tetrahydropyranyloxychalcone epoxide (**9**).- 2'-Isopropoxy-6'-tetrahydropyranyloxychalcone (**8**; 0.90 g, 2.4 mmol) was dissolved in a solution of 2 mol*l*$^{-1}$ NaOH (1.0 ml) and H$_2$O$_2$ (100 vols., 1.0 ml) in methanol (25 ml), and stirred at room temperature for 1.5 h. The usual workup (as for **5**) yielded 0.89 g (97 %) of ***2'-isopropoxy-6'-tetrahydropyranyloxychalcone epoxide*** (**9**) as an oil; δ_C (22.49 MHz; solvent CDCl$_3$) 197.9 (s, C=O), 156.1 and 156.0 (s, 2'-C), 155.3 and 154.9 (s, 6'-C), 135.7 (s, 1-C), 131.5 (d, 4'-C), 128.5 (d, 4-C), 128.3 (d, 2,6-C), 125.6 (d, 3,5-C), 118.7 and 118.5 (s, 1'-C), 107.7 and 107.1 (d, 3'-C)^x, 106.6 and 106.4 (d, 5'-C)^x, 96.9 and 95.8 (d, 2"-C), 70.7 [d, O$\underline{C}$H(CH$_3$)$_2$], 63.5 (d, α–C), 61.7 and 61.4 (t, 6"-C), 58.8 (d, β-C), 29.8 (t, 3"-C), 24.9 (t, 5"-C), 21.8 [q, OCH($\underline{C}$H$_3$)$_2$], 21.6 [q, OCH($\underline{C}$H$_3$)$_2$], 18.3 and 17.9 (t, 4"-C).

2'-Hydroxy-6'-isopropoxychalcone epoxide (**10**).- 2'-Isopropoxy-6'-tetrahydropyranyloxychalcone epoxide (**9**; 200 mg, 0.52 mmol) was dissolved in dioxane (40 ml). 2 mol*l*$^{-1}$ H$_2$SO$_4$ (0.10

ml) was added and the solution left for 20 min. The usual workup (as for **6**) produced ***2'-hydroxy-6'-isopropoxychalcone epoxide*** (**10**) in *ca.* 90 % yield, as a white solid, m.p. 127-130°C; δ_H (89.55 MHz; solvent CDCl$_3$) 12.65 (1H, s, OH), 7.35 (6H, s superimposed on 4'-H signal, 4',2,3,4,5,6-H), 6.52 (1H, d, $^{3',4'}J$ = 8.2 Hz, 3'-H), 6.32 (1H, d, $^{5',4'}J$ = 8.4 Hz, 5'-H), 4.50 (1H, d, $^{\alpha,\beta}J$ = 1.7 Hz, α-H), 3.95 (1H, d, $^{\beta,\alpha}J$ = 1.7 Hz, β-H), 0.87 [3H, d, J = 2.5 Hz, OCH(CH$_3$)$_2$], 0.80 [3H, d, J = 2.5 Hz, OCH(CH$_3$)$_2$]; δ_C (22.49 MHz; solvent CDCl$_3$) 198.3 (s, C=O), 164.5 (s, 2'-C), 159.7 (s, 6'-C), 137.0 (d, 4'-C), 136.1 (s, 1-C), 128.7 (d, 4-C), 128.4 (d, 3,5-C), 125.6 (d, 2,6-C), 111.0 (s, 1'-C), 109.9 (d, 3'-C), 102.6 (d, 5'-C), 70.9 [d, OCH(Me)$_2$], 64.4 (d, α-C), 59.7 (d, β-C), 21.1 [q, OCH(CH$_3$)$_2$], 20.7 [q, OCH(CH$_3$)$_2$]. Found C 72.30, H 6.19; $C_{18}H_{18}O_4$ requires C 72.46, H 6.08 %.

Preparation of 2'-hydroxy-4',6'-ditetrahydropyranyloxyacetophenone (**12**).- 2',4',6'-Trihydroxyacetophenone (**11**; 2.0 g, 3.2 mmol) and 3,4-dihydro-2H-pyran (12 ml) were dissolved in dioxane (30 ml). *p*-Toluenesulphonic acid (20 mg) was added and the solution left at room temperature for 24 h. Saturated NaHCO$_3$ solution (100 ml) was added and the resulting suspension extracted with ether (3 x 30 ml). The combined ether extracts were washed with water (4 x 20 ml), dried (MgSO$_4$), and solvent removed to yield 2.52 g of a multi-component mixture which was separated by p.l.c. [petroleum spirit (b.p. 60-80°C):ethyl acetate; 4:1, 2 developments] into six major fractions (*a-f*, in order of decreasing Rf). Incomplete separation was observed for bands *c*, *e* and *f*. The n.m.r. data for the product from band (*a*) [37 mg], is consistent with 2',4',6'-trihydroxy-3',5'-ditetrahydropyranylacetophenone (*ca.* 1%). Band (*b*) [312 mg] is 2',4'-dihydroxy-3'-tetrahydropyranyl-6'-tetrahydropyranyloxyacetophenone (*ca.* 8%), m.p. 118-121°C. Band (*c*) [403 mg] is a mixture of three compounds, the major one being 2'-hydroxy-4',6'-ditetrahydropyranyloxyacetophenone [**12**; *ca.* 65 % of the mixture (by n.m.r.); overall *ca.* 6.5 %)]. Band (*d*) [423 mg] is 2',4',6'-trihydroxy-3'-tetrahydropyranylacetophenone (14 %). Band (*e*) [648 mg] is mainly 2',6'-dihydroxy-4'-tetrahydropyranyloxyacetophenone [*ca.* 66 % of the mixture (by n.m.r.); overall *ca.* 14 %)], along with some 2',4',6'-trihydroxy-3'-tetrahydropyranylacetophenone [*ca.* 33 % of the mixture (by n.m.r.); overall *ca.* 7 %)]. Band (*f*) [483 mg] is mainly 2',4'-dihydroxy-6'-tetrahydropyranyloxyacetophenone [*ca.* 60 % of the mixture (by n.m.r.); overall *ca.* 10 %], along with some 2',6'-dihydroxy-4'-tetrahydropyranyloxyacetophenone [*ca.* 40 % of the mixture (by n.m.r.); overall *ca.* 6 %)]. N.m.r. data on which assignments were made are as follows. ***2',4',6'-Trihydroxy-3',5'-ditetrahydropyranylacetophenone:*** δ_H (89.55 MHz; solvent CDCl$_3$) 14.31 (1H, br s, OH), 9.85 (1H, s, OH), 9.79 (1H, s, OH), 5.00 (2H, m, 2",2'''-H), 4.37, 4.18 and 3.68 (4H, m, 6",6'''-H), 2.69 (3H, s, COCH$_3$), and 1.75 (12H, m, 3",3''',4",4''',5",5'''-H); δ_C (22.49 MHz; solvent CDCl$_3$) 203.8 (s, COMe), 161.0 (br s, 2',6'-C)^x, 158.94 and 158.89 (s, 4'-C)^x, 105.3 and 105.2 (s, 3',5'-C), 104.7 (s, 1'-C), 76.3 (d, 2",2'''-C), 69.5 (t, 6",6'''-C), 32.72 (q, COCH$_3$), 31.2 and 31.1 (t, 2",2'''-C), 25.8 (t, 5",5'''-C), and 23.1 (t, 4",4'''-C). ***2',4'-Dihydroxy-3'-tetrahydropyranyl-6'-tetrahydropyranyloxyacetophenone:*** δ_H (89.55 MHz; solvent CDCl$_3$) 14.48 (1H, s, OH), 9.62 (1H, br s, OH), 6.33 (1H, br s, 5'-H), 5.56 (1H, br s, 2"-H), 4.99 (1H, m, 2'''-H), 4.39, 4.13 and 3.79 (4H, m, 6",6'''-H), 2.71 (3H, s, COCH$_3$), and 1.80 (12H, m, 3",3''',4",4''',5",5'''-H); δ_C (22.49 MHz; solvent CDCl$_3$) 202.8 (s, COMe), 162.9 (s, 2'-C)^x, 162.3 (s, 4'-C)^x, 159.6 and 159.5 (s, 6'-C), 107.0 (s, 1'-C), 104.8 (s, 3'-C), 96.9 and 96.7 (d, 2"-C), 94.5 and 94.3 (d, 5'-C), 76.2 and 76.0 (d, 2'''-C), 69.2 (t, 6'''-C), 61.94 and 61.86 (t, 6"-C), 31.5 (q, COCH$_3$), 30.8 (t, 3'''-C), 30.0 (t, 3"-C), 25.5 (t, 5'''-C), 24.4 (t, 5"-C), 22.8 (t, 4'''-C) and 18.7 (t, 4"-C). ***2'-Hydroxy-4',6'-ditetrahydropyranyloxyacetophenone*** (**12**): δ_H (89.55 MHz; solvent CDCl$_3$) 13.66 (1H, s, OH), 6.34 (1H, s, 3'-H), 6.23 (1H, s, 5'-H), 5.45 (2H, br s, 2",2'''-H), 3.73 (4H, m, 6",6'''-H), 2.64 (3H, s, COCH$_3$), 1.82 and 1.63 (12H, m, 3",3''',4",4''',5",5'''-H); δ_C (22.49 MHz; solvent CDCl$_3$) 202.9 (s, COCH$_3$), 166.6 and 166.5 (s, 2'-C)^x, 163.6 and 163.5 (s, 4'-C)^x, 160.4 and 160.3 (s, 6'-C), 106.7 (s, 1'-C), 97.27 and 96.13 (d, 2",2'''-C), 96.2 and 95.9 (d, 3'-C), 94.9 and 94.6 (d, 5'-C), 62.1 (t, 6",6'''-C), 33.1 (*q*, COCH$_3$), 30.2 and 29.9 (*t*, 3",3'''-C), 24.9 (*t*, 5",5'''-C), and 19.0 and 18.5 (t, 4",4'''-C). ***2',4',6'-Trihydroxy-3'-tetrahydropyranyloxyacetophenone:*** δ_H (89.55 MHz; solvent CDCl$_3$) 12.46 (1H, v br s, OH), 9.1 (1H, v br s, OH), 5.86 (1H, s, 5'-H), 4.92 (1H, m, 2"-H), 4.19 (1H, br d, 6"-H), 3.63 (1H, br m, 6"-H), 2.65 (3H, s, $COCH_3$), and 1.64 (6H, m, 3",4",5"-H); δ_C (22.49 MHz; solvent $CDCl_3$) 204.2 (s, $\underline{C}$OMe), 162.03, (s, 2'-C)^x, 161.95 (s, 4'-C)^x, 161.7 (s, 6'-C)^x, 106.0 (s, 3'-C)^y, 104.9 (s, 1'-C)^y, 95.4 (d, 5'-C), 76.5 (d, 2"-C), 69.7 (t, 6"-C), 32.6 (q, $CO\underline{C}H_3$), 31.1 (t, 3"-C), 25.9 (t, 5"-C), and 23.2 (t, 4"-C). ***2',6'-Dihydroxy-4'-tetrahydropyranyloxyacetophenone:*** δ_H (89.55 MHz; solvent $CDCl_3$) 11.13 (1H, br s, OH), 6.04 (2H, s, 3',5'-H), 5.35 (1H, br s, 2"-H), 2.63 (3H, s, $COCH_3$), 1.77 and 1.57 (6H, m, 3",4",5"-H). ***2',4'-Dihydroxy-6'-tetrahydropyranyloxyacetophenone:*** δ_H (89.55 MHz; solvent $CDCl_3$) 13.83 (1H, s, OH), 6.19 (1H, s, 5'-H), 5.96 (1H, s, 3'-H), 5.38 (1H, br s, 2"-H), 2.61 (3H, s, $COCH_3$), and 1.81 and 1.61 (6H, m, 3",4",5"-H).

2'-Methoxy-4',6'-ditetrahydropyranyloxyacetophenone (**13**).- A crude sample of 2'-hydroxy-4',6'-ditetrahydropyranyloxyacetophenone (**12**; *ca.* 310 mg, 0.92 mmol) from the tetrahydropyranylation of 2',4',6'-trihydroxyacetophenone was refluxed with methyl iodide (2 ml) and K_2CO_3 (1 g) in acetone (30 ml) for 20 h. After workup (as for **3**), p.l.c. [petroleum spirit (b.p. 60-80°C): ethyl acetate; 4:1, 3 developments] yielded 304 mg (*ca.* 94 %) of ***2'-methoxy-4',6'-ditetrahydropyranyloxyacetophenone*** (**13**) as a colourless oil: δ_C (22.49 MHz; solvent $CDCl_3$) 200.3 (s, $\underline{C}$OMe), 159.1 and 158.9 (s, 4'-C), 157.3 (s, 2'-C), 154.8 and 154.6 (s, 6'-C), 115.1 and 115.0 (s, 1'-C), 96.4, 96.4, 95.9, and 95.6 (d, 5'-C, 2",2"'-C), 93.4 and 93.3 (d, 3'-C), 61.2 (t, 6",6"'-C), 55.1 (q, OCH_3), 31.8 (q, $CO\underline{C}H_3$), 29.63 and 29.55 (t, 3",3"'-C), 24.6 (t, 5",5"'-C), and 18.0 (t, 4",4"'-C).

2'-Methoxy-4',6'-ditetrahydropyranyloxychalcone (**14**).- 2'-Methoxy-4',6'-ditetrahydropyranyloxyacetophenone (**13**; 304 mg, 0.87 mmol) and benzaldehyde (138 mg, 1.3 mmol) were dissolved in a solution of KOH (2 g), water (2 ml), and methanol (10 ml), and stirred at room temperature for 12 h. After the usual workup (as for **4**), p.l.c. [petroleum spirit (b.p. 60-80°C): ether; 3:1] yielded 309 mg (81 %) of ***2'-methoxy-4',6'-ditetrahydropyranyloxychalcone*** (**14**) as a yellow oil; δ_C (22.49 MHz; solvent $CDCl_3$) 193.7 (s, C=O), 159.6 and 159.4 (s, 4'-C), 158.2 (s, 2'-C), 155.7 and 155.5 (s, 6'-C), 142.6 (d, β-C), 134.7 (s, 1-C), 129.8 (d, α-C), 128.8 (d, 4-C), 128.5 (d, 2,6-C), 127.8 (d, 3,5-C), 113.1 and 113.0 (s, 1'-C), 96.5 (d, 5'-C), 96.2 and 95.8 (d, 2",2"'-C), 93.7 (d, 3'-C), 61.6 and 61.2 (t, 6",6"'-C), 55.5 (q, OCH_3), 29.9 and 29.6 (t, 3",3"'-C), 24.8 (t, 5",5"'-C), and 18.28 and 17.71 (t, 4",4"'-C).

2'-Methoxy-4',6'-ditetrahydropyranyloxychalcone epoxide (**15**).- 2'-Methoxy-4',6'-ditetrahydropyranyloxychalcone (**14**; 309 mg, 0.71 mmol) was dissolved in a mixture of H_2O_2 (100 vols., 1.0 ml), 2 mol*l* $^{-1}$ NaOH (1.0 ml) and methanol (10 ml), and stirred for 2 h. After the usual workup (as for **5**) p.l.c. [petroleum spirit (b.p. 60-80°C): ether; 2:1] yielded 260 mg (81 %) of ***2'-methoxy-4',6'-ditetrahydropyranyloxychalcone epoxide*** (**15**) as a colourless oil; δ_C (22.49 MHz; solvent $CDCl_3$) 196.1 and 196.0 (s, C=O), 160.9 and 160.7 (s, 4'-C), 159.2, 159.1, and 159.0 (s, 2'-C), 157.1, 157.9, 156.7, and 156.5 (s, 6'-C), 136.1 and 136.0 (s, 1-C), 128.4 (d, 4-C), 128.3 (d, 2,6-C), 125.5 (d, 3,5-C), 111.4 and 111.2 (s, 1'-C), 97.27, 96.94, 96.89, 96.51, 96.35, 96.21, 95.91 (d, 5'-C, 2",2"'-C), 93.75, 93.66, 93.61, and 93.42 (d, 3'-C), 63.7 (d, α-C), 61.6 (t, 6",6"'-C), 59.0 (d, β-C), 55.7 (q, OCH_3), 29.82 and 29.77 (t, 3",3"'-C), 24.8 (t, 5",5"'-C), 18.2 and 17.9 (t, 4",4"'-C).

2',4'-dihydroxy-6'-methoxychalcone epoxide (**16**).- 2'-Methoxy-4',6'-ditetrahydropyranyloxychalcone epoxide (**15**; 130 mg, 0.29 mmol) was dissolved in 25 ml of dioxane. 2 Mol*l* $^{-1}$ H_2SO_4 (0.075 ml) was added and the reaction left for 45 min. After the usual workup (as for **6**) p.l.c. [petroleum spirit (b.p. 60-80°C):ether:acetone; 4:1:1] yielded 72 mg (88 %) of ***2',4'-dihydroxy-6'-methoxychalcone epoxide*** (**16**) as a white solid, m.p. 145-150°C; δ_H (89.55 MHz; solvent d^6-acetone) 13.16 (1H, s, OH), 7.40 (5H, s, 2,3,4,5,6-H), 5.96 (2H, s, 3',5'-H), 4.38 (1H, d, $^{\alpha,\beta}J$ = 1.8 Hz, α-H), 3.93 (1H, d, $^{\beta,\alpha}J$ = 1.8 Hz, β-H), and 3.44 (3H, s, OCH_3); δ_C (22.49 MHz; solvent d^6-acetone) 197.0 (s, C=O), 167.8 (s, 4'-C)^x, 166.9 (s, 2'-C)^x, 164.7 (s, 6'-C), 138.0 (s, 1-C), 129.3

(d, 2,4,6-C), 126.7 (d, 3,5-C), 105.0 (s, 1'-C), 98.9 (d, 3'-C), 92.1 (d, 5'-C), 65.1 (d, α-C), 59.4 (d, β-C), and 56.3 (q, OCH_3). Found C 66.78, H 4.63; $C_{16}H_{14}O_5$ requires C 67.12, H 4.93 %.

2'-Hydroxy-4'-methoxyacetophenone **(17)**.- 2',4'-Dihydroxyacetophenone (**23**; 15 g, 99 mmol) and a large excess of methyl iodide (10 ml) were refluxed in acetone (70 ml) containing a suspension of K_2CO_3 (15 g, finely ground and oven dried) for 2 h. After filtering, the solvent was removed and the residue dissolved in ether (80 ml) and filtered again. The ether solution was extracted with 2 mol*l* $^{-1}$ NaOH (3 x 40 ml), washed with water (1 x 40 ml), dried ($MgSO_4$), and the ether removed to yield 11.9 g (73 %) of ***2'-hydroxy-4'-methoxyacetophenone*** **(17)** as a white solid, m.p. 49-50°C (lit.[16] 48-50°C); δ_C (22.49 MHz; solvent $CDCl_3$) 202.4 (s, COMe), 166.0 (s, 4'-C)^{x}, 165.1 (s, 2'-C)^{x}, 132.2 (d, 6'-C), 113.8 (s, 1'-C), 107.3 (d, 5'-C)^{y}, 100.7 (d, 3'-C)^{y}, 55.3 (q, OCH_3), and 25.8 (q, $CO\underline{C}H_3$).

2'-Benzoyloxy-4'-methoxyacetophenone **(18)**.- 2'-Hydroxy-4'-methoxyacetophenone (**136**; 9.3 g, 56.0 mmol) and benzoyl chloride (9.1 g, 67 mmol) were dissolved in pyridine (20 ml) and left to stand at room temperature for 6 h. Ether (50 ml) was added and the solution extracted with 2 mol*l* $^{-1}$ HCl (6 x 20 ml), water (2 x 20 ml) and saturated $NaHCO_3$ solution (2 x 20 ml). The solution was dried ($MgSO_4$) and the ether removed to yield an oil. P.l.c. [petroleum spirit (b.p. 60-80°C):ether; 5:1] gave 15.1 g (100 %) of ***2'-benzoyloxy-4'-methoxyacetophenone*** **(18)** as a colourless oil; δ_C (22.49 MHz; solvent $CDCl_3$) 195.4 (s, COMe), 164.9 (s, OCOPh)^{x}, 163.6 (s, 4'-C)^{x}, 151.5 (s, 2'-C), 133.6 (d, 4-C)^{y}, 132.3 (d, 6'-C)^{y}, 130.1 (d, 2,6-C), 128.5 (d, 3,5-C), 129.2 (s, 1-C), 123.4 (s, 2'-C), 111.7 (d, 5'-C), 109.2 (d, 3'-C), 55.6 (q, OCH_3), and 29.2 (q, $CO\underline{C}H_3$).

2'-Benzoyloxy-4'-methoxyacetophenone ethylene hemithioketal **(19)**.- 2'-Benzoyloxy-4'-methoxyacetophenone (**18**; 10.0 g, 37.0 mmol) and 2-mercaptoethanol (3.47 g, 44.4 mmol) were refluxed in ether (60 ml). $BF_3{\cdot}Et_2O$ (6.30 g, 44.4 mmol, freshly distilled) was added dropwise over a period of 1 h. Further $BF_3{\cdot}Et_2O$ (6.30 g, 44.4 mmol) was added over a period of 8 h. Chloroform (30 ml) was added and the solution washed with saturated $NaHCO_3$ solution (5 x 25 ml) and water (2 x 25 ml), dried ($MgSO_4$), and solvent removed. Ether (35 ml) was added and ***2'-benzoyloxy-4'-methoxyacetophenone ethylene hemithioketal*** **(19)**, which crystallised from solution, was collected by filtration as a white solid, 10.3 g (85 %), m.p. 104-106°C; δ_C (22.49 MHz; solvent $CDCl_3$) 164.6 (s, OCOPh), 159.3 (s, 4'-C), 147.9 (s, 2'-C), 133.5 (d, 4-C), 130.3 (d, 2,6-C), 130.2 (s, 1-C)^{x}, 129.5 (s, 1'-C)^{x}, 128.6 (d, 3,5-C), 125.7 (d, 6'-C), 111.3 (d, 5'-C), 109.7 (d, 3'-C), 92.6 (s, Ar-$\underline{C}$Me), 70.6 (t, OCH_2), 55.4 (q, OCH_3), 33.8 (t, SCH_2), 31.5 (q, Ar-$C\underline{C}H_3$).

2'-Hydroxy-4'-methoxyacetophenone ethylene hemithioketal **(20)**.- 2'-Benzoyloxy-4'-methoxyacetophenone ethylene hemithioketal (**19**, 1.0g, 3.0 mmol) was dissolved in methanol (30 ml) and dioxane (10 ml). 2 Mol*l* $^{-1}$ NaOH (10 ml) was added and the reaction mixture stirred at room temperature for 12 h. Careful adjustment to pH *ca.* 8 with 2 mol*l* $^{-1}$ HCl was followed by extraction with ether (3 x 20 ml). The combined ether extracts were washed with water (2 x 20 ml), dried ($MgSO_4$), and solvent removed to yield 0.58 g (86 %) of ***2'-hydroxy-4'-methoxyacetophenone ethylene hemithioketal*** **(158)** as a colourless oil; δ_C (22.49 MHz; solvent $CDCl_3$) 160.5 (s, 4'-C), 154.4 (s, 2'-C), 128.9 (d, 6'-C), 121.2 (s, 1'-C), 105.8 (d, 5'-C), 102.1 (d, 3'-C), 97.4 (s, Ar-$\underline{C}$Me), 70.2 (t, OCH_2), 55.0 (q, OCH_3), 33.1 (t, SCH_2), 30.5 (q, Ar-$C\underline{C}H_3$). This compound can also be prepared from the 2'-acetoxy instead of the 2'-benzoyloxy precursor, but the yield is similar. The compound should be stored at $0^{o}C$ to reduce decomposition which gives it a purple colour.

4'-Methoxy-2'-tetrahydropyranyloxyacetophenone ethylene hemithioketal **(21)**.- 2'-Hydroxy-4'-methoxyacetophenone ethylene hemithioketal (**20**; 103 mg, 0.46 mmol) and 3,4-dihydro-2H-pyran (0.35 ml) were dissolved in dioxane (10 ml). Toluene-4-sulphonic acid (*ca.* 1 mg) was added and the solution left to stand at room temperature for 6 h. Water (40 ml) was added and the resulting suspension extracted with ether (2 x 30 ml). The combined ether extracts were extracted with 2 moll^{-1} NaOH (2 x 10 ml), washed with water (1 x 10 ml), dried (MgSO$_4$), and the solvent removed. Chromatography [p.l.c. petroleum spirit (b.p. 60-80°C):ether; 6:1] yielded 60 mg (42 %) of ***4-methoxy-2'-tetrahydropyranyloxyacetophenone ethylene hemithioketal*** (21) as a pale yellow oil; δ_C (22.49 MHz; solvent CDCl$_3$) 159.8 and 159.7 (s, 4'-C), 154.6 and 153.9 (s, 2'-C), 127.6 and 127.3 (s, 1'-C), 123.4 and 123.2 (d, 6'-C), 105.0 and 104.5 (d, 5'-C), 101.9 and 101.2 (d, 3'-C), 97.2, 95.1 and 94.34 (d, 2"-C), 92.61 and 92.55 (s, Ar-$\underline{C}$Me), 70.7 (t, OCH$_2$), 62.6 and 61.6 (t, 6"-C), 55.1 (q, OCH$_3$), 33.4 and 33.2 (t, SCH$_2$), 31.3 and 31.0 (q, Ar-C$\underline{C}$H$_3$), 30.5 and 30.1 (t, 3"-C), 25.3 and 25.2 (t, 5"-C), 19.6, 18.6 and 17.9 (t, 4"-C). A second attempt produced a 23 % yield. Several later attempts to prepare this product with reagents from a different commercial source failed completely for no apparent reason. The use of pyridinium p-toluenesulphonate as an alternative catalyst [step iv(b); Scheme 5] was not successful.

4'-Methoxy-2'-tetrahydropyranyloxyacetophenone (22)- 4'-Methoxy-2'-tetrahydropyranyloxyacetophenone ethylene hemithioketal (21; 279 mg, 0.90 mmol) was dissolved in a solution of acetonitrile (8 ml) and water (2 ml), and cooled to 0°C. AgNO$_3$ (310 mg, 1.8 mmol) and Ag$_2$O (830 mg, 3.6 mmol) were added and the solution stirred for 8 min. After filtration, ether (30 ml) was added and the resulting solution extracted with 2 moll^{-1} NaOH (3 x 10 ml). [This step has a twofold purpose: it extracts any 2'-hydroxy-4'-methoxyacetophenone (23) produced, and secondly, prevents further deprotection of the tetrahydropyranyl group, presumably by removing any acidic impurities. When the reaction was first carried out, water was used instead of 2 moll^{-1} NaOH, and the recovered tetrahydropyranyloxyacetophenone (22) was unstable toward loss of the protective group. Adding the base extraction step eliminated this problem.] The ether extract was then washed with water (1 x 10 ml), dried (MgSO$_4$), and solvents removed to yield 117 mg (52 %) of ***4'-methoxy-2'-tetrahydropyranyloxyacetophenone*** (22) as a pure (t.l.c.) colourless oil; δ_C (22.49 MHz; solvent CDCl$_3$) 197.5 (s, $\underline{C}$OMe), 164.3 (s, 4'-C), 158.6 (s, 2'-C), 132.1 (d, 6'-C), 121.4 (s, 1'-C), 107.4 (d, 5'-C), 100.8 (d, 3'-C), 96.9 (d, 2"-C), 61.9 (t, 6"-C), 55.4 (q, OCH$_3$), 31.9 (q, CO$\underline{C}$H$_3$), 30.2 (t, 3"-C), 24.9 (t, 5"-C), 18.8 (t, 4"-C).

4'-Methoxy-2'-tetrahydropyranyloxychalcone.- 4'-Methoxy-2'-tetrahydropyranyloxyacetophenone (22; 117 mg, 0.47 mmol) and benzaldehyde (74 mg, 0.70 mmol) were dissolved in a solution of KOH (1 g) in water (1 ml) and methanol (5 ml), and the solution stirred at room temperature for 20 h. After the usual workup (as for 4), chromatography [p.l.c. petroleum spirit (b.p. 60-80°C): ethyl acetate; 3:1] yielded 94 mg (59 %) of ***4'-methoxy-2'-tetrahydropyranyloxychalcone*** as a yellow oil; δ_H (89.55 MHz; solvent CDCl$_3$) 7.77 (1H, d, ${}^{6',5'}J$ = 8.8 Hz, 6'-H), 6.75 (1H, d, ${}^{3',5'}J$ = 2.4 Hz, 3'-H), 6.51 (1H, dd, ${}^{5',6'}J$ = 8.8 Hz, ${}^{5',3'}J$ = 2.4 Hz, 5'-H), 5.49 (1H, s, 2"-H), 3.78 [5H, s (OCH$_3$) superimposed on 6"-H resonances], 2.60 (3H, s, COCH$_3$), and 1.87-1.66 (6H, m, 2",3",4"-H); δ_C (22.49 MHz; solvent CDCl$_3$) 190.2 (s, C=O), 163.8 (s, 4'-C), 157.6 (s, 2'-C), 141.2 (d, β-C), 135.1 (s, 1-C), 132.1 (d, 6'-C), 129.6 (d, 4-C), 128.5 (d, 3,5-C), 127.8 (d, 2,6-C), 127.2 (d, α-C), 122.5 (s, 1'-C), 106.8 (d, 5'-C), 101.3 (d, 3'-C), 96.7 (d, 2"-C), 61.7 (t, 6"-C), 55.1 (q, OCH$_3$), 30.0 (t, 3"-C), 24.7 (t, 5"-C), and 18.1 (t, 4"-C).

4'-Methoxy-2'-tetrahydropyranyloxychalcone epoxide.- 4'-Methoxy-2'-tetrahydropyranyloxychalcone (94 mg, 0.28 mmol) was dissolved in a solution of 2 moll^{-1} NaOH (0.5 ml), H$_2$O$_2$ (100 vols., 0.5 ml), and methanol (5 ml), and stirred at room temperature for 1.5 h. The usual workup (as for 5) yielded 97 mg (99 %) of ***4'-methoxy-2'-tetrahydropyranyloxychalcone epoxide*** as a colourless oil; δ_C (22.49 MHz; solvent CDCl$_3$) 192.9 and 192.2 (s, C=O), 165.1 and 165.0 (s, 4'-C), 159.2 and 158.9 (s, 2'-C), 136.3 (s, 1-C), 132.4 and 132.2 (d, 6'-C), 128.4 (d, 4-C), 128.2 (d, 3,5-C), 125.6 and 125.5 (d, 2,6-C), 119.8 and 119.4 (s, 1'-C), 107.2 and 107.1 (d, 5'-C), 101.0 and 100.9 (d, 3'-C), 97.3 and 97.2 (d, 2"-C), 63.1 and 62.9 (d, α-C), 62.1 and 62.0 (t, 6"-C), 59.5 (d, β-C), 55.3 (q, OCH$_3$), 29.6 and 29.3 (t, 3"-C), 24.4 (t, 5"-C), and 18.4 and 18.0 (t, 4"-C).

2'-Hydroxy-4'-methoxychalcone epoxide.- 4'-Methoxy-2'-tetrahydropyranyloxychalcone epoxide (97 mg, 0.27 mmol) was dissolved in dioxane (30 ml). 2 moll^{-1} H_2SO_4 (0.075 ml) was added and the solution left for 2 h. The usual workup (as for **6**) yielded 67 mg (91 %) of ***2'-hydroxy-4'-methoxychalcone epoxide*** as a white solid; δ_H (89.55 MHz; solvent $CDCl_3$) 12.42 (1H, s, OH), 7.72 (1H, d, J = 9.5 Hz ,6'-H), 7.37 (5H, s, 2-6-H), 7.37 (2H, s, 3',5'-H), 4.22 (1H, d, $^{\alpha,\beta}J$ = 1.8 Hz, α-H), 4.11 (1H, d, $^{\beta,\alpha}J$ = 1.8 Hz, β-H), 3.83 (3H, s, OCH_3); δ_C (22.49 MHz; solvent $CDCl_3$) 195.1 (s, C=O), 166.9 (s, 2'-C)^x, 165.8 (s, 4'-C)^x, 135.4 (s, 1-C), 131.0 (d, 6'-C), 129.1 (d, 4-C), 128.8 (d, 3,5-C), 125.8 (d, 2,6-C), 113.1 (s, 1'-C), 108.4 (d, 5'-C), 101.3 (d, 3'-C), 59.7 (d, α-C), 59.5 (d, β-C), 55.6 (q, OCH_3). This compound has not been fully characterised because the first sample was used in reactivity studies before it was found that the synthesis of the precursor ethylene hemithioketal (**21**) could not be repeated (see above).

2',4'-Dibenzoyloxyacetophenone (**24**).- 2',4'-Dihydroxyacetophenone (**23**; 10.0 g, 65.8 mmol) was dissolved in pyridine (40 ml). Benzoyl chloride (20.0 g, 142 mmol) was added and the reaction left for 6 h. Ether (60 ml) was added and the ether extract solution washed with 2 moll^{-1} HCl (4 x 25 ml), water (25 ml), 5 % $NaHCO_3$ solution (2 x 25 ml), dried ($MgSO_4$), and the solvent removed. Recrystallisation from ether yielded 14.7 g (62 %) of ***2',4'-dibenzoyloxyacetophenone*** (**24**) as a white solid, m.p. 76-78°C; δ_C (22.49 MHz; solvent $CDCl_3$) 196.1 (s, $\underline{C}$OMe), 164.7 (s, O$\underline{C}$OPh)^w, 164.1 (s, O$\underline{C}$OPh)^w, 154.2 (s, 4'-C), 150.3 (s, 2'-C), 133.94 (d, 4''-C)^x, 133.86 (d, 4'''-C)^x, 131.3 (d, 6'-C), 130.3 (d, 2'',6''-C)^y, 130.2 (d, 2''',6'''-C)^y, 128.9 (s, 1''-C)^z, 128.7 (s, 1'''-C)^z, 128.7 (d, 3'',3''',5'',5'''-C), 119.4 (d, 5'-C), 117.6 (d, 3'-C), and 29.7 (q, CO$\underline{C}H_3$).

2',4'-Dibenzoyloxyacetophenone ethylene hemithioketal (**25**).- 2',4'-Dibenzoyloxyacetophenone (**24**; 14.7 g, 40.8 mmol) and 2-mercaptoethanol (6.2 g, 80 mmol) were refluxed in 5:3 ether:chloroform (80 ml). $BF_3 \cdot Et_2O$ (freshly distilled, 17.0 g, 120 mmol) was added over 6 h. After a further 4 h. the reaction solution was washed with 5 % $NaHCO_3$ solution (5 x 20 ml), water (20 ml), dried ($MgSO_4$), and the solvents removed. Recrystallisation (ether) yielded 15.8 g (92 %) of ***2',4'-dibenzoyloxyacetophenone ethylene hemithioketal*** (**25**) as a white solid, m.p. 126-129°C; δ_C (22.49 MHz; solvent $CDCl_3$) 164.7 (s, OCOPh)^w, 164.5 (s, OCOPh)^w, 150.1 (s, 4'-C), 147.5 (s, 2'-C), 135.8 (s, 1'-C), 133.8 (d, 4''-C)^x, 133.7 (d, 4'''-C)^x, 130.4 (d, 2'',6''-C)^y, 130.2 (d, 2''',6'''-C)^y, 129.3 (s, 1'',1'''-C), 128.7 (d, 3'',5''-C)^z, 128.6 (d, 3''',5'''-C)^z, 125.4 (d, 6'-C), 118.8 (d, 5'-C), 117.7 (d, 3'-C), 92.3 (s, Ar-$\underline{C}$Me), 70.8 (t, OCH_2), 33.9 (t, SCH_2), and 31.4 (q, Ar-C$\underline{C}H_3$).

2',4'-Dihydroxyacetophenone ethylene hemithioketal (**26**).- To a solution of 2',4'-dibenzoyloxyacetophenone ethylene hemithioketal (**25**; 5.0 g, 11.9 mmol) in dioxane (50 ml) was added 2 moll^{-1} NaOH solution (20 ml). After stirring at room temperature for 36 h, saturated $NaHCO_3$ solution (100 ml) was added. The resulting suspension was extracted with ether (3 x 30 ml). The combined ether extracts were washed with water (3 x 25 ml), dried ($MgSO_4$), and the solvents removed to yield 2.27 g (90 %), of ***2',4'-dihydroxyacetophenone ethylene hemithioketal*** (**26**) as a colourless oil; δ_C (22.49 MHz; d^6-acetone) 158.4 (s, 2'-C)^x, 155.4 (s, 4'-C)^x, 125.8 (d, 6'-C), 124.0 (s, 1'-C), 107.0 (d, 5'-C)^y, 104.2 (d, 3'-C)^y, 95.3 (s, Ar-$\underline{C}$Me), 71.2 (t, OCH_2), 33.7 (t, SCH_2), 31.1 (q, Ar-C$\underline{C}H_3$). This compound, like 2'-hydroxy-4'-methoxyacetophenone ethylene hemithioketal (**20**), gradually turns purple on standing. This process is slowed by storing at 0^{o}C.

2',4'-Ditetrahydropyranyloxyacetophenone ethylene hemithioketal (**27**).-
(i) Using *p*-toluenesulphonic acid [step iv(a) in Scheme 4].- 2',4'-Dihydroxyacetophenone ethylene hemithioketal (**26**; 338 mg, 1.6 mmol) and 3,4-dihydro-2H-pyran (*ca.* 2 ml) were dissolved in dioxane (10 ml). *p*-Toluenesulphonic acid (*ca.* 5 mg) was added and the reaction left for 6 h. Ether (40 ml) was added and this solution extracted with 2 moll^{-1} NaOH solution (3 x 10 ml), dried ($MgSO_4$), and the solvent removed. P.l.c. [petroleum spirit (b.p. 60-80°C):ether, 3:1] yielded *ca.* 55

mg (9 %) of ***2',4'-ditetrahydropyranyloxyacetophenone ethylene hemithioketal*** (27) as a colourless oil (n.m.r data below)

(ii) Using pyridinium *p*-toluenesulphonate (PPTS) [step iv(b) Scheme 4].- 2',4'-Dihydroxyacetophenone ethylene hemithioketal (26; 700 mg, 3.3 mmol) and 3,4-dihydro-2H-pyran (3 ml) were dissolved in CH_2Cl_2 (25 ml). PPTS (50 mg) was added and the reaction left until t.l.c. showed no starting material remained (*ca.* 4 h). The solution was extracted with 2 moll^{-1} NaOH (2 x 10 ml), dried ($MgSO_4$), and the solvent removed. P.l.c. [petroleum spirit (b.p. 60-80°C):ether, 3:1] yielded 392 mg (31 %) of ***2',4'-ditetra-hydropyranyloxyacetophenone ethylene hemithioketal*** (27) as a colourless oil; δ_C (22.49 MHz; solvent $CDCl_3$) 157.1, 157.0, and 156.9 (s, 4'-C), 154.3, 154.2, 153.6, and 153.4 (s, 2'-C), 128.2, 128.1, 128.0, and 127.8 (s, 1'-C), 123.1 and 122.9 (d, 6'-C), 107.7, 107.4, 107.2, and 107.0 (d, 5'-C), 104.1, 103.7, 103.4, and 102.8 (d, 3'-C), 97.1, 96.9, 96.2, 96.1, 95.9, 95.8, 94.9, and 94.7 (d, 2",2'''-C), 92.4 and 92.3 (s, Ar-$\underline{C}$Me), 70.5 (t, OCH_2), 61.5 and 61.4 (t, 6",6'''-C), 33.2 and 33.0 (t, SCH_2), 31.1 and 30.7 (q, Ar-C$\underline{C}H_3$), 30.0 and 29.9 (t, 3",3'''-C), 24.9 (t, 5",5'''-C), and 18.4 (t, 4",4'''-C).

2',4'-Ditetrahydropyranyloxyacetophenone (28).- 2',4'-Ditetrahydropyranyloxyacetophenone ethylene hemithioketal (27; 392 mg, 1.0 mmol) was dissolved in acetonitrile (8 ml) and water (2 ml). $AgNO_3$ (340 mg, 2.0 mmol) and Ag_2O (928 mg, 4.0 mmol) were added and the reaction stirred at 0°C for 5 min. Ether (30 ml) was added and the suspension removed by filtration. The ether solution was extracted with 2 moll^{-1} NaOH solution (3 x 15 ml), dried ($MgSO_4$), and the solvent removed to yield 128 mg (40 %) of ***2',4'-ditetrahydropyranyloxyacetophenone*** (28) as a colourless oil; δ_H (89.55 MHz; solvent $CDCl_3$) 7.78 (1H, d, $^{6',5'}J$ = 8.8 Hz, 6'-H), 6.92 (1H, d, $^{5',6'}J$ = 8.8 Hz, 5'-H), 6.71 (1H, br s, 3'-H), 5.51 (2H, br s, 2",2'''-H), 3.73 (4H, br m, 6",6'''-H), 2.63 (3H, s, $COCH_3$), 1.88 and 1.67 (12H, br m, 3",3",4",4'''.5",5'''-H); δ_C (22.49 MHz; solvent $CDCl_3$) 197.6 (s, $\underline{C}$OMe), 161.8 and 161.7 (s, 4'-C), 158.4 and 158.3 (s, 2'-C), 131.9 (d, 6'-C), 122.1 and 122.0 (s, 1'-C), 109.1 and 108.8 (d, 5'-C), 103.4 and 103.0 (d, 3'-C), 96.9 and 96.7 (d, 2"-C), 96.2 and 95.9 (d, 2'''-C), 62.0 (t, 3",3'''-C), 31.9 (q, CO$\underline{C}H_3$), 30.2 and 30.0 (t, 3",3'''-C), 24.9 (t, 5",5'''-C), and, 18.8 and 18.4 (t, 4",4'''-C).

2',4'-Ditetrahydropyranyloxychalcone.- 2',4'-Ditetrahydropyranyloxyacetophenone (128 mg, 0.40 mmol) and benzaldehyde (64 mg, 0.60 mmol) were dissolved in a solution of KOH (0.6 g), water (0.6 ml), and methanol (5 ml), and stirred at room temperature for 20 h. After the usual workup (as fot 4) p.l.c. [petroleum spirit (b.p. 60-80°C):ether, 3:1] yielded 129 mg (79 %) of ***2',4'-ditetrahydropyranyloxychalcone*** as an yellow oil; δ_C (22.49 MHz; solvent $CDCl_3$) 190.6 (s, C=O), 161.4 and 161.2 (s, 4'-C), 157.5 and 157.4 (s, 2'-C), 141.4 (d, β-C), 135.2 (s, 1-C), 131.9 (d, 6'-C), 129.7 (d, 4-C), 128.6 (d, 3,5-C), 127.9 (d, 2,6-C), 127.3 (d, α-C), 123.3 and 123.2 (s, 1'-C), 109.3 and 109.1 (d, 5'-C), 103.8 and 103.4 (d, 3'-C), 96.8 and 96.6 (d, 2"-C), 96.2 and 95.9 (d, 2"-C), 61.8 (t, 6",6'''-C), 30.0 and 29.9 (t, 3",3'''-C), 24.8 (t, 5",5'''-C), and 18.36, 18.28, 18.23 and 18.15 (t, 4",4'''-C).

2',4'-Ditetrahydropyranyloxychalcone epoxide.- 2',4'-Ditetrahydropyranyloxychalcone (90 mg, 0.22 mmol) was dissolved in a solution of H_2O_2 (100 vols., 0.2 ml), 2 moll^{-1} NaOH solution (0.2 ml), and methanol (5 ml), and the solution stirred at room temperature for 1.5 h. The usual workup (as for 5) yielded 85 mg (91 %) of ***2',4'-ditetrahydropyranyloxychalcone epoxide*** as a colourless oil; δ_C (22.49 MHz; solvent $CDCl_3$) 193.10, 193.03, 192.53, and 192.48 (s, C=O), 162.68, 162.60, and 162.41 (s, 4'-C), 159.08, 159.00, 158.84, and 158.73 (s, 2'-C), 136.3 (s, 1-C), 132.18 and 132.07 (d, 6'-C), 128.47 (d, 4-C), 128.3 (d, 3,5-C), 125.65 and 125.57 (d, 2,6-C), and 109.27 (d, 5'-C), 103.44 and 103.01 (d, 3'-C), 97.43, 97.38, 97.29, and 97.19 (d, 2"-C), 96.18, 96.13, and 95.91 (d, 2'''-C), 63.16 and 62.94 (d, α-C), 62.30 and 61.94 (t, 6"-C), 61.84 (t, 6'''-C), 59.51 (d, β-C), 29.79, 29.60, and 29.41 (t, 3",3'''-C), 24.78 and 24.48 (t, 5",5'''-C), and, 18.52 and 18.23 (t, 4",4'''-C).

2',4'-Dihydroxychalcone epoxide.- 2',4'-Ditetrahydropyranyloxychalcone epoxide (85 mg, 0.20 mmol) was dissolved in dioxane (25 ml). 2 Mol*l* $^{-1}$ H_2SO_4 (0.075 ml) was added and the solution left for 2 h. The usual workup yielded 49 mg (95 %) of ***2',4'-dihydroxychalcone epoxide*** as a pale yellow oil; δ_H (89.55 MHz; solvent $CDCl_3$) 12.28 (1H, s, 2'-OH), 8.61 (1H, br s, 4'-OH), 7.65 (1H, d, $^{6',5'}J$ = 9.2 Hz, 6'-H), 7.35 (5H, s, 2,3,4,5,6-H), 6.37 (2H, br s, 3',5'-H), 4.23 (1H, s, α-H), and 4.07 (1H, s, β-H); δ_C (22.49 MHz; solvent $CDCl_3$) 194.8 (s, C=O), 165.4 (s, 4'-C)^x, 164.8 (s, 2'-C)^x, 135.1 (s, 1-C), 131.6 (d, 6'-C), 128.9 (d, 4-C), 128.6 (d, 3,5-C), 125.6 (d, 2,6-C), 112.7 (s, 1'-C), 108.7 (d, 5'-C), 103.3 (d, 3'-C), 59.5 (d, α-C)^y, and 59.3 (d, β–C)^y.

4'-Acetoxy-2',6'-dihydroxyacetophenone* (29)**.- 2',4',6'-Trihydroxyacetophenone (**7**; 2.0 g, 11.9 mmol) and (0.71 g, 0.66 ml, 7.0 mmol) of acetic anhydride were dissolved in pyridine (15 ml) and left to stand at room temperature for 1 h. Ether (50 ml) was added and the ether extract solution washed with 2 mol*l* $^{-1}$ HCl (5 x 20 ml), water (2 x 20 ml), and 5 % $NaHCO_3$ solution (2 x 20 ml), dried ($MgSO_4$) and the ether removed to yield a mixture (1.96 g) of three products (t.l.c.). Chromatography [p.l.c. petroleum spirit (b.p 60-80°C): ether; 3:1] yielded as the middle band 497 mg (20 %) of the required ***4'-Acetoxy-2',6'-dihydroxyacetophenone* (29)** as a white solid: δ_C (22.49 MHz; solvent d^6-acetone) 205.3 (s, $\underline{C}$OMe), 168.8 (s, O$\underline{C}$OMe), 164.2 (s, 2',6'-C), 157.7 (s, 4'-C), 108.9 (s, 1'-C), 102.0 (d, 3',5'-C), 33.0 (q, CO$\underline{C}H_3$), 21.0 (q, OCO$\underline{C}H_3$). Also obtained as a white solid from the band of highest R*f* was 217 mg (7 %) of ***2',4'-Diacetoxy-6'-hydroxyacetophenone: δ_C (22.49 MHz; solvent $CDCl_3$) 203.7 (s, $\underline{C}$OMe), 169.1 (s, O$\underline{C}$OMe)^x, 168.7 (s, O$\underline{C}$OMe)^x,164.9 (s, 6'-C), 156.5 (s, 4'-C), 153.2 (s, 2'-C), 113.6 (s, 1'-C), 109.5 (d, 3'-C)^y, 109.2 (d, 5'-C)^y, 32.3 (q, CO$\underline{C}H_3$), 21.4 (q, OCO$\underline{C}H_3$)^z, 21.0 (q, OCO$\underline{C}H_3$)^z. The slowest moving band appeared from n.m.r. to be a mixture of 2',4',6'-trihydroxyacetophenone and 2',4',6'-triacetoxyacetophenone.

2',4'-Dihydroxy-6'-tetrahydropyranyloxyacetophenone* (30)**.- 4'-Acetoxy-2',6'-dihydroxyacetophenone (**29**; 595 mg, 2.8 mmol) and 3,4-dihydro-2H-pyran (4 ml) were dissolved in dioxane (25 ml). A small amount of toluene-4-sulphonic acid (*ca.* 3 mg) was added and the solution left for 18 h. The usual workup (as for **2**) yielded 360 mg of a two component mixture (t.l.c.). P.l.c. [petroleum spirit (60-80°C):ethyl acetate; 4:1, several developments] yielded 228 mg (32 %) of the desired 2',4'-dihydroxy-6'-tetrahydropyranyloxyacetophenone (**30**) as a white solid (lower Rf), and 55 mg (8 %) of 2',6'-dihydroxy-4'-tetrahydropyranyloxyacetophenone as a white solid (higher Rf). When repeated, yields of 49 % [2',4'-dihydroxy-6'-tetrahydropyranyloxyacetophenone (**30**)] and 11 % [2',6'-dihydroxy-4'-tetrahydropyran-yloxyacetophenone] were obtained. For ***2',4'-Dihydroxy-6'-tetrahydropyranyloxyacetophenone* (30)**: δ_C (22.49 MHz; solvent d^6-acetone) 203.3 (s, $\underline{C}$OMe), 167.7 (s, 4'-C), 165.5 (s, 2'-C), 162.0 (s, 6'-C), 106.2 (s, 1'-C), 98.0 (d, 3'-C), 97.2 (d, 2"-C), 94.8 (d, 5'-C), 62.5 (t, 6"-C), 33.2 (q, CO$\underline{C}H_3$), 30.6 (t, 3"-C), 25.6 (t, 5"-C), 19.6 (t, 4"-C). For ***2',6'-dihydroxy-4'-tetrahydropyranyloxyacetophenone: δ_C (22.49 MHz; solvent $CDCl_3$) 204.1 (s, $\underline{C}$OMe), 164.9 (s, 2',6'-C), 164.3 (s, 4'-C), 106.3 (s, 1'-C), 96.7 (d, 2"-C), 96.2 (d, 3',5'-C), 62.5 (t, 6"-C), 32.9 (q, CO$\underline{C}H_3$), 30.6 (t, 3"-C), 25.7 (t, 5"-C), 19.3 (t, 4"-C).

***2',4'-Dimethoxy-6'-tetrahydropyranyloxyacetophenone* (31)** as in Scheme 3.- 2',4'-Dihydroxy-6'-tetrahydropyranyloxyacetophenone (**30**; 100 mg, 0.42 mmol) and methyl iodide (*ca.* 0.1 ml) were dissolved in dry acetone containing a suspension of K_2CO_3 (*ca.* 1 g, finely ground, oven dried) in dry acetone (25 ml), and refluxed, with stirring, until t.l.c. showed no starting material remained (*ca.* 42 h.). The reaction mixture was then filtered, solvent removed under vacuum, and the residue redissolved in ether (40 ml), filtered again, extracted with 2 mol*l* $^{-1}$ NaOH (2 x 15 ml), washed with water (1 x 15 ml), dried ($MgSO_4$) and the ether removed to yield 103 mg (94 %) of ***2',4'-dimethoxy-6'-tetrahydropyranyloxyacetophenone* (31)** as a colourless oil; δ_H (89.55 MHz; solvent $CDCl_3$) 6.52 (1H, d, $^{5',3'}J$ = 2.4 Hz, 5'-H), 6.28 (1H, d, $^{3',5'}J$ = 2.4 Hz, 3'-H), 5.54 (1H, br s, 2"-H), 3.83 (6H, s, OCH_3), 3.73 (1H, br m, 6"-H), 2.52 (3H, s, $COCH_3$), 1.83 (6H, br m, 3",4",5"-H); δ_C (22.49 MHz; solvent $CDCl_3$) 200.8 (s, COMe), 161.8 (s, 4'-C), 157.6 (s, 2'-C), 155.3 (s, 6'-C), 114.4 (s, 1'-C), 96.4 (d, 2"-C), 93.5 (s, 5'-C), 91.6 (s, 3'-C), 61.5 (t, 6"-C), 55.4 (q, OCH_3), 55.0 (q, OCH_3), 32.2 (q, $COCH_3$), 29.8 (t, 3"-C), 24.8 (t, 5"-C), 17.6 (t, 4"-C). This compound was also prepared as in Scheme 4 as described below.

2',4'-Dimethoxy-6'-tetrahydropyranyloxychalcone.- 2',4'-Dimethoxy-6'-tetrahydropyranyloxyacetophenone (**31**; 103 mg, 0.36 mmol) and benzaldehyde (58 mg, 0.55 mmol) were dissolved in a solution of KOH (0.5 g), water (0.5 ml) and methanol (2 ml), and stirred at room temperature for 18 h. The usual workup (as for **4**) produced 145 mg of a crude yellow oil. P.l.c. [petroleum spirit (b.p. 60-80°C):ether; 3:1] yielded 107 mg (81 %) of ***2',4'-dimethoxy-6'-tetrahydropyranyloxychalcone*** as a yellow oil; δ_C (22.49 MHz; solvent $CDCl_3$) 193.5 (s, C=O), 162.0 (s, 4'-C), 158.3 (s, 2'-C), 155.8 (s, 6'-C), 143.5 (d, β-C), 134.6 (s, 1-C), 129.8 (d, α-C), 128.8 (d, 4-C), 128.5 (d, 3,5-C), 127.8 (d, 2,6-C), 112.3 (s, 1'-C), 96.1 (d, 2"-C), 93.3 (d, 5'-C), 91.7 (d, 3'-C), 61.2 (t, 6"-C), 55.5 (q, OCH_3), 55.0 (q, OCH_3), 29.6 (t, 3"-C), 24.7 (t, 5"-C), 17.6 (t, 4"-C).

2',4'-Dimethoxy-6'-tetrahydropyranyloxychalcone epoxide.- 2',4'-Dimethoxy-6'-tetrahydropyranyloxychalcone (107 mg, 0.29 mmol) was dissolved in a solution of 2 moll^{-1} NaOH (0.15 ml) and H_2O_2 (100 vols., 0.15 ml) in methanol (2.5 ml), and stirred at room temperature for 100 min. The usual workup (as for **5**) yielded 79 mg (71 %) of ***2',4'-dimethoxy-6'-tetrahydropyranyloxychalcone epoxide*** as a white solid; δ_C (22.49 MHz; solvent $CDCl_3$) 195.8 (s, C=O), 163.3 (s, 4'-C), 159.3 and 159.2 (s, 2'-C), 157.2 and 156.9 (s, 6'-C), 136.0 and 135.9 (s, 1-C), 128.3 (d, 4-C), 128.2 (d, 3,5-C), 125.4 (d, 2,6-C), 110.6 and 110.5 (s, 1'-C), 97.1 and 96.1 (d, 2"-C), 93.9 and 93.4 (d, 5'-C), 91.7 and 91.5 (d, 3'-C), 63.6 (d, α-C), 61.6 and 61.5 (t, 6"-C), 58.9 (d, β-C), 55.6 (q, OCH_3), 55.1 (q, OCH_3), 29.6 (t, 3"-C), 24.8 (t, 5"-C), 18.1 and 17.8 (t, 4"-C).

2'-Hydroxy-4',6'-dimethoxychalcone epoxide.- 2',4'-Dimethoxy-6'-tetrahydropyranyloxychalcone epoxide (79 mg, 0.21 mmol) was dissolved in dioxane (20 ml). 2 Moll^{-1} H_2SO_4 (0.10 ml) was added and the solution left for 15 min. The usual workup (as for **6**) produced 58 mg (92 %) of ***2'-hydroxy-4',6'-dimethoxychalcone epoxide*** as a white solid, m.p. 100-104°C; δ_H (89.55 MHz; solvent $CDCl_3$) 13.17 (1H, s, OH), 7.35 (5H, s, 2-6-H), 6.05 (1H, d, $^{3',5'}J$ = 2.4 Hz, 5'-H), 5.85 (1H, d, $^{5',3'}J$ = 2.4 Hz, 3'-H), 4.31 (1H, d, $^{\alpha,\beta}J$ = 2.2 Hz, α-H), 3.93 (1H, d, $^{\beta,\alpha}J$ = 2.2 Hz, β-C), and 3.40 [3H, s, OCH_3(6'-C)]; δ_C (22.49 MHz; solvent $CDCl_3$) 195.8 (s, C=O), 167.0 (s, 2'-C)^x, 166.9 (s, 4'-C)^x, 162.6 (s, 6'-C), 136.2 (s, 1-C), 128.4 (d, 4-C), 128.3 (d, 2,6-C), 125.5 (d, 3,5-C), 104.7 (s, 1'-C), 93.5 (d, 3'-C), 90.6 (d, 5'-C), 64.3 (d, α-C), 59.0 (d, β–C), and 55.4 (q, 2 x OCH_3). Found: C 67.39, H 5.41; $C_{17}H_{16}O_5$ requires C 68.00, H 5.37.

2',6'-Dihydroxy-4'-methoxyacetophenone (**32**).- 1,3-Dihydroxy-5-methoxybenzene, prepared essentially by the method described[17] by Effenberger and Schonwalder, as an oil [δ_C (22.49 MHz; solvent d^6-acetone) 162.4 (s, 5-C), 159.7 (s, 1,3-C), 96.5 (d, 2-C), 94.0 (d, 4,6-C), 55.3 (q, OCH_3)] was reacted *via* 2,2,2-trichloroacetophenone intermediates as described[18] by Whalley to form 2',6'-dihydroxy-4'-methoxyacetophenone, m.p. 134-136°C (lit[18] 136°C); δ_H (89.55 MHz; solvent d^6-acetone) 11.73 (1H, s, OH), 5.98 (2H, s, 3',5'-H), 3.78 (3H, s, OCH_3), 2.63 (3H, s, $COCH_3$). δ_C (22.49 MHz; solvent d^6-acetone) 204.0 (s, COMe), 167.0 (s, 4'-C), 165.2 (s, 2',6'-C), 105.9 (s, 1'-C), 94.2 (d, 3',5'-C), 55.8 (q, OCH_3), 32.8 (q, $COCH_3$).

2'-Hydroxy-4'-methoxy-6'-tetrahydropyranyloxyacetophenone (**33**).- 2',6'-Dihydroxy-4'-methoxyacetophenone (**32**; 139 mg, 0.76 mmol) and 3,4-dihydro-2H-pyran (1 ml) were dissolved in dioxane (15 ml) and cooled to 0°C. Toluene-4-sulphonic acid (*ca.* 2 mg) was added and the solution left at room temperature for 18 h. The usual workup produced 148 mg of a mixture of two compounds (as judged by ^1H n.m.r. and t.l.c.). P.l.c. [petroleum spirit (b.p. 60-80°C):ether; 5:1, 4 developments] yielded 59 mg (29 %) of ***2',6'-dihydroxy-4'-methoxy-3'-tetrahydropyranylacetophenone*** (**34**; highest R*f*) as a white solid, m.p. 71-76°C; δ_H (89.55 MHz; solvent CDCl$_3$) 13.77 [1H, s, OH(internal H bond)], 9.89 (1H, s, OH), 5.91 (1H, s, 5'-H), 4.83 (1H, m, 2"-H), 3.72 [s (OCH$_3$) superimposed on 6"-H], 2.61 (3H, s, COCH$_3$), 1.66 (6H, m, 3",4",5"-H); δ_C (22.49 MHz; solvent CDCl$_3$) 203.8 (s, $\underline{C}$OMe), 165.8 (s, 4'-C), 161.6 (s, 2'-C)^x, 159.9 (s, 6'-C)^x, 105.9 (s, 1'-C), 105.8 (s, 3'-C), 91.3 (d, 5'-C), 76.1 (d, 2"-C), 69.6 (t, 6"-H), 55.6 (q, OCH$_3$), 32.8 (q, CO$\underline{C}$H$_3$), 31.2 (t, 3"-C), 25.8 (t, 5"-C), 23.2 (t, 4"-C). Also formed was 58 mg (29 %) of the desired product, ***2'-hydroxy-4'-methoxy-6'-tetrahydropyranyloxyacetophenone*** (**33**), as a white solid, m.p. 88-92°C; δ_H (89.55 MHz; solvent CDCl$_3$) 13.81 (1H, s, OH), 6.20 (1H, d, $^{3',5'}J$ = 2.4 Hz, 3'-H), 5.98 (1H, d, $^{5',3'}J$ = 2.4 Hz, 5'-H), 5.40 (1H, br s, 2"-H), 3.72 (3H, s, OCH$_3$), 3.65 (1H, br s, 6"-H), 2.60 (3H, s, COCH$_3$), 1.82 and 1.62 (6H, br m, 3",4",5"-H); δ_C (22.49 MHz; solvent CDCl$_3$) 202.7 (s,$\underline{C}$OMe), 166.9 (s, 2'-C)^x, 165.9 (s, 4'-C)^x, 160.3 (s, 6'-C), 106.1 (s, 1'-C), 97.1 (d, 2"-C), 94.2 (d, 3'-C)^y, 93.5 (d, 5'-C)^y, 62.0 (t, 6"-C), 55.3 (q, OCH$_3$), 33.0 (q, CO$\underline{C}$H$_3$), 30.0 (t, 3"-C), 24.8 (t, 5"-C), 18.9 (t, 4"-C).

2',4'-dimethoxy-6'-tetrahydropyranyloxyacetophenone (**31**) as in Scheme 4.- 2'-Hydroxy-4'-methoxy-6'-tetrahydropyranyloxyacetophenone (**33**; 50 mg, 0.19 mmol) and an excess of methyl iodide (*ca.* 0.2 ml) were refluxed in acetone (30 ml) containing a suspension of K$_2$CO$_3$ (*ca.* 0.5 g) for 10 h. After filtering, the acetone was removed, then ether (30 ml) was added and the solution filtered again. It was then washed with NaOH solution (2 mol*l* $^{-1}$, 2 x 10 ml) and water (1 x 10 ml), dried (MgSO$_4$), and the solvent was removed to yield 50 mg (94 %) of 2',4'-dimethoxy-6'-tetrahydropyranyloxyacetophenone (**31**) as a colourless oil [n.m.r. data identical to that above for (**31**) prepared by the method of Scheme 3]

2',6'-Ditetrahydropyranyloxyacetophenone.- 2',6'-Dihydroxyacetophenone (2 g, 4.0 mmol) and 3,4-dihydro-2H-pyran (10 ml, 100 mmol) were dissolved in dioxane (15 ml). Toluene-4-sulphonic acid (ca. 2 mg) was added and the mixture left 5 days. The same workup as for 2'-hydroxy-6'-tetrahydropyranyloxyacetophenone was used except that the ether fraction, after base extraction, was retained. After this fraction was washed with water (3 x 15 ml), dried (MgSO$_4$), and the solvent removed, p.l.c. [petroleum spirit (b.p. 60-80°C): ether; 6:1] yielded three major bands. The band of lowest R$_f$ (0.64; pale yellow under u.v. light of wavelength 356 nm) was ***2',6'-ditetrahydropyranyloxyacetophenone*** (270 mg, 6 %). δ_C (22.49 MHz; solvent CDCl$_3$) 201.0 (s, $\underline{C}$OMe), 153.3 (s, 2',6'-C), 129.7 (d, 4'-C), 122.4 and 122.2 (s, 1'-C), 108.1 and 108.0 (d, 3',5'-C), 96.1 and 95.9 (d, 2"-C), 61.2 (t, 6"-C), 31.7 (q, CO$\underline{C}$H$_3$), 29.6 (t, 3"-C), 24.7 (t, 5"-C), 18.0 (t, 4"-C). The two other compounds were combinations of three linked 3,4-dihydro-2H-pyran monomer units as judged from ^{13}C n.m.r.

2',6'-Ditetrahydropyranyloxychalcone.- 2',6'-Ditetrahydropyranyloxyacetophenone (1.1 g, 3.4 mmol) and benzaldehyde (0.44 g, 4.13 mmol) were dissolved in a solution of KOH (5 g), water (5 ml), and methanol (10 ml), and stirred at room temperature for 24 h. After the usual workup (as for 4), p.l.c. [petroleum spirit (b.p. 40-60°C): ethyl acetate; 7:2] yielded 1.09 g (77 %) of ***2',6'-ditetrahydropyranyloxychalcone*** as a yellow oil; δ_C (22.49 MHz; solvent CDCl$_3$) 194.5 and 194.4 (s, C=O), 154.6 and 154.5 (s, 2',6'-C), 144.7 and 144.6 (d, β-C), 134.6 (s, 1-C), 130.4 and 130.1 (d, 4-C), 128.7 (d, α-C)^x, 128.7 (d, 3,5-C)^z, 128.0 (d, 2,6-C), 120.2 and 120.1 (s, 1'-C), 108.4 and 108.2 (d, 3',5'-C), 96.2 and 95.9 (d, 2"-C), 61.4 (t, 6"-C), 29.8 (t, 3"-C), 24.9 (t, 5"-C), 17.9 (t, 4"-C).

2',6'-Ditetrahydropyranyloxychalcone epoxide.- 2',6'-Ditetrahydropyranyloxychalcone (210 mg, 0.51 mmol) was dissolved in a solution of 2 mol*l* $^{-1}$ NaOH (0.2 ml), H$_2$O$_2$ (100 vols., 0.2 ml), and methanol (4 ml) and stirred at room temperature for 2 h. The usual workup (as for 5) produced ***2',6'-ditetrahydropyranyloxychalcone epoxide*** in *ca.* 90 % yield; δ_C (22.49 MHz; solvent CDCl$_3$)

198.1 (s, C=O), 155.23, 155.13, 154.83 and 154.77 (s, 2',6'-C), 135.8 (s, 1-C), 131.7 (d, 4'-C), 128.7 (d, 4-C), 128.4 (d, 2,6-C), 125.7 (d, 3,5-C), 118.5 and 118.4 (s, 1'-C), 108.7, 108.4, 108.2 and 108.1 (d, 3',5'-C), 97.0 and 96.0 (d, 2"-C), 63.5 (d, α-C), 61.9 and 61.6 (t, 6"-C), 58.8 (d, β-C), 29.9 (t, 3"-C), 25.0 (t, 5"-C), 18.4 and 18.1 (t, 4"-C).

Deprotection of 2',6'-ditetrahydropyranyloxychalcone epoxide (in dry ethanol).- In three parallel experiments[(i)-(iii)], 2',6'-Ditetrahydropyranyloxychalcone epoxide (100 mg, 0.24 mmol) was dissolved in dry ethanol (20 ml), 2 moll^{-1} H_2SO_4 (0.10 ml) was added and the solutions left for (i) 20, (ii) 32, and (iii) 40 min. The usual workup and separation [p.l.c. using petroleum spirit (b.p. 60-80°C):ethyl acetate; 4:1] gave (i) [20 min. reaction time] unreacted 2',6'-ditetrahydropyranyloxychalcone epoxide (*ca.* 60 % by n.m.r.) and ***2'-hydroxy-6'-tetrahydropyranyloxychalcone epoxide*** (*ca.* 40 %); δ_C (22.49 MHz; solvent $CDCl_3$) 198.4 (s, C=O), 164.3 and 163.9 (s, 2'-C), 159.1 and 158.8 (s, 6'-C), 137.3 and 137.1 (d, 4'-C), 136.1 and 136.0 (s, 1-C), 128.8 (d, 4-C), 128.5 (d, 2,6-C), 125.8 and 125.7 (d, 3,5-C), 111.4 and 111.3 (d, 3'-C), 111.3 and 111.0 (s, 1'-C), 105.0 and 104.9 (d, 5'-C), 97.9 and 97.8 (d, 2"-C), 63.6 and 63.3 (d, α–C), 62.8 and 62.7 (t, 6"-C), 60.2 and 60.1 (d, β-C), 29.7 and 29.3 (t, 3"-C), 24.5 (t, 5"-C), and 19.2 and 18.5 (t, 4"-C); (ii) [32 min. reaction time] 2'-hydroxy-6'-tetrahydropyranyloxychalcone epoxide (*ca.* 70 %) and ***3,5-dihydroxyflavanone*** (*ca.* 30 %): δ_H (89.55 MHz; solvent $CDCl_3$) 10.96 (1H, s, OH), 7.48 (6H, m, 2',3',4',5',6'-H, 7-H), 6.59 (1H, d, $^{6,8}J$ ~ 8 Hz, 6-H), 6.51 (1H, d, $^{8,6}J$ ~ 8 Hz, 8-H), 5.15 (1H, d, $^{2,3}J$ = 12.1 Hz, 2-H), and 4.61 (1H, d, $^{3,2}J$ = 12.1 Hz, 3-H); δ_C (22.49 MHz; solvent $CDCl_3$) 198.4 (s, C=O), 161.7 (s, 9-C)^{x}, 161.5 (s, 5-C)^{x}, 139.2 (d, 7-C), 136.0 (s, 1'-C), 129.4 (d, 4'-C), 128.7 (d, 2',6'-C), 127.5 (d, 3',5'-C), 109.8 (d, 9-C)^{y}, 107.9 (d, 5-C)^{y}, 106.1 (s,10-C), 83.3 (d, 2-C), and 73.0 (d, 3-C); (iii) [40 min. reaction time] 2'-hydroxy-6'-tetrahydropyranyloxychalcone epoxide (*ca* 40 %) and 3,5-dihydroxyflavanone (*ca.* 60 %).

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