Derivatives of Hydroxyquinol. Part 4.[1] A Synthesis of Di-*O*-methylcitromycin; Electronic Effects in Hydroxyquinol Derivatives

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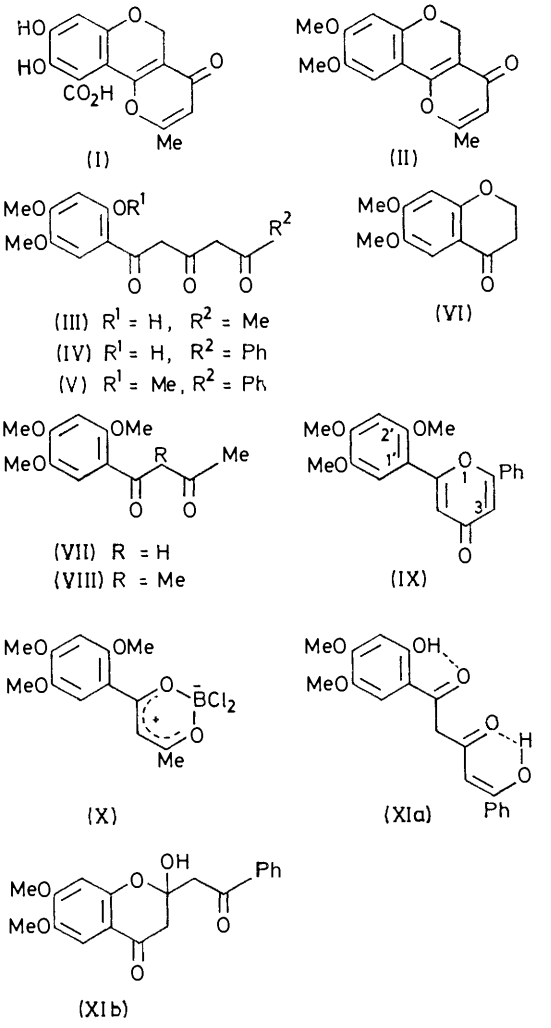
Although the dianion from 1-(2,4,5-trimethoxyphenyl)butane-1,3-dione (VII) reacted with methyl benzoate giving the 1,3,5-triketone (V), the method failed with ethyl acetate and similar reagents. Chromanone and its derivates are converted into their 3-acetyl derivatives by acetic anhydride and boron fluoride as in preparations of compounds (XII), (XIII), and (XXXI). Structures are assigned to the isomeric acetates (XXIV) and (XXV) obtained by treating 3-acetyl-6-methylchroman-4-one (XIII) with acetic anhydride–pyridine, and either acetate is shown to be suitable for transformation by triphenylmethyl-lithium into the crude 6-methyl-3-(3-oxobutanoyl)-chroman-4-one (XXVII). Cyclisation of this in acid gives the pyranopyrone (XXIX). The methoxylated 3-acetylchromanone (XXXI) is much less reactive and gives only the one acetate (XXXIII), but this was converted into the requisite (crude) trione and thence into di-*O*-methylcitromycin (II).

Certain synthetic difficulties with hydroxyquinol derivatives are discussed and attributed to electron release into attached carbonyl groups. The phenomenon also serves to explain the direction and extent of enolization in the various polyketones examined by n.m.r. methods, and also the formation of an arylacetic acid in addition to the benzoic acid derivative expected from the haloform reaction with 2',4',5'-trimethoxyacetophenone.

THE fungal metabolite citromycetin [2] (I) can be transformed into di-*O*-methylcitromycin (II), which contains the same nucleus but offers a simpler synthetic target. In theory, structure (II) should be accessible from the phenolic polyketide (III), but we were unable to obtain this compound notwithstanding a successful synthesis of the model (IV). However, we have synthesised [3] di-*O*-methylcitromycin by building a 4-pyrone ring onto the chromanone derivative (VI), although this process was also more difficult than in a model series. We believe that extensive release of electrons from the hydroxyquinol nucleus into attached carbonyl groups is largely responsible for several such anomalies, including an abnormal iodoform reaction, and also for the control of enolization in triones similar to (III). These and related matters are discussed in a separate section.

A Synthesis of Di-O-methylcitromycin (II).—With sodium sand and ethyl acetate, 2',4',5'-trimethoxyacetophenone gave the diketone (VII), methylation of the sodio-derivative then giving the homologue (VIII). The dianion of (VII) was produced by means of sodium hydride in tetrahydrofuran. With ethyl benzoate it supplied the triketone (V), which was characterized by cyclisation to (IX), a 4-pyrone unexpectedly resistant to hydrolysis by refluxing concentrated sodium hydroxide.

Selective demethylation of the triketone (V) with boron chloride [4] furnished the desired phenol (IV). On the other hand, the reagent did not demethylate the diketone (VII), indicating that the complex (X) is formed in the usual way but then contains no carbonyl group capable of directing the reagent to the adjacent methoxy-group.[4] It seems, therefore, that the triketone (V) must first react with boron chloride at its external β-diketone segment so as to leave the innermost carbonyl group to promote demethylation; in agreement, the chief enolic form of the triketone appears to have structure (XIa),



with the ring tautomer (XIb) as the only other major component of the mixture. This point is discussed further in the later section.

Attempts to apply similar reactions to the synthesis

[1] Part 3, F. M. Dean and D. R. Randell, *J. Chem. Soc.*, 1961, 798.

[2] A. C. Hetherington and H. Raistrick, *Phil. Trans.*, 1931, **B220**, 209; A. Robertson and W. B. Whalley, *J. Chem. Soc.*, 1949, 848; G. G. Badcock, F. M. Dean, A. Robertson, and W. B. Whalley, *ibid.*, 1950, 903.

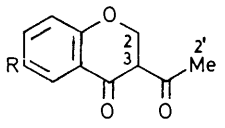
[3] F. M. Dean, S. Murray, and W. Taylor, *J.C.S. Chem. Comm.*, 1974, 440.

[4] F. M. Dean, J. Goodchild, L. E. Houghton, J. A. Martin, R. B. Morton, B. Parton, A. W. Price, and N. Somvichien, *Tetrahedron Letters*, 1966, 4153.

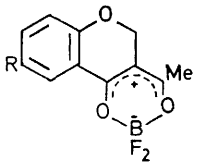
of (III) were not successful. Whether generated by lithium amide in ammonia [5] or by sodium hydride in solvent ethers,[6] the dianion from (VII) appeared not to suffer acylation by ethyl acetate, acetic anhydride, or acetyl chloride, even though the method is satisfactory in the absence of methoxy-groups. When we tried to build up the polycarbonyl chain from the opposite end we readily confirmed that the dianion of pentane-2,4-dione gives the requisite triketone [7] when treated with methyl benzoate, but still failed to induce a reaction with methyl 2,4,5-trimethoxybenzoate.

As the first step in the alternative approach, chromanone was acylated with acetic anhydride and boron fluoride and the resulting 3-acetylchromanone (XII) isolated as its dioxaborin derivative (XIV), a method chosen to secure the pyran ring as far as possible against the ring opening and isomerisations that occur in other, especially basic, conditions.* But since the reagent can also introduce an acetyl group into aromatic nuclei and then acylate that acetyl group,[8] the main product was the polyketone (XVI), isolated as the bis-dioxaborin derivative (XVII). For this reason further work was conducted with 6-methylchroman-4-one, which gave the 3-acetyl derivative (XIII) in high yield.

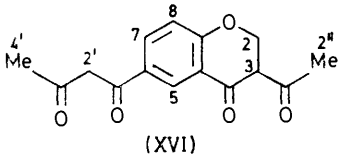
The ketones are readily obtained in enolic forms from their dioxaborin derivatives by means of sodium acetate in warm acetic acid, but prolonged treatment does induce ring opening and ring-substituent interchanges



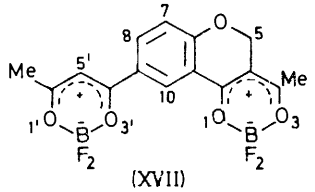
(XII) R = H
(XIII) R = Me



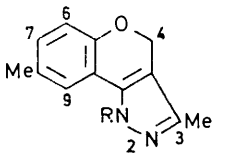
(XIV) R = H
(XV) R = Me



(XVI)

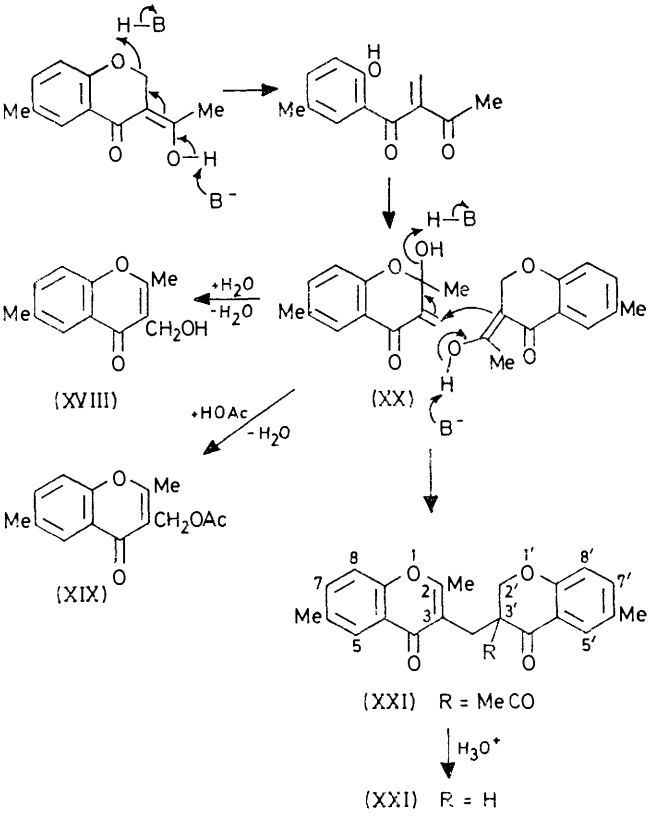


(XVII)



(XXII) R = H
(XXIII) R = Ph

parallel to those described for 3-formylchromanone.[9] Scheme 1 indicates the way in which 3-acetyl-6-methylchroman-4-one is thought to be transformed into the chromones (XVIII), (XIX), and (XXI), but as the



SCHEME 1

discussion would be nearly identical with that in the previous case [9] it is not repeated here. There is one important difference: in this example the acetyl group survives in the dimeric product (XXI; R = Ac), although it is readily removed by acidic hydrolysis, and so offers direct evidence for the coupling reaction shown in (XX). In the previous example hydrolysis had been spontaneous, in agreement with the relatively reactive nature of the formyl group. The structures of the products were confirmed by standard methods, especially n.m.r. spectroscopy; additionally, the structure of the β-diketone (XIII) was checked by formation of the pyrazole derivatives (XXII) and (XXIII) upon treatment with hydrazine and phenylhydrazine, respectively. The orientation of the latter pyrazole was indicated by the large upfield shift in an aromatic proton singlet caused by shielding by the phenyl group.

The acetylchromanone (XIII) is enolic, and upon acetylation furnished both possible acetates (XXIV) and (XXV), which can be distinguished by their u.v. spectra,

* Dioxaborin derivatives have also proved suitable for the isolation and n.m.r. characterization of polyketones that normally exist as mixtures of enols.

[5] S. D. Work and C. R. Hauser, *J. Org. Chem.*, 1963, **28**, 725; A. A. Ravel and N. M. Shah, *ibid.*, 1958, **23**, 748.

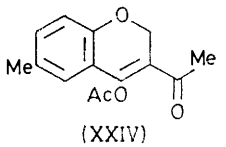
[6] M. L. Miles, T. M. Harris, and C. R. Hauser, *J. Org. Chem.*, 1965, **30**, 1007.

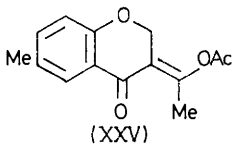
[7] R. J. Light and C. R. Hauser, *J. Org. Chem.*, 1963, **28**, 725.

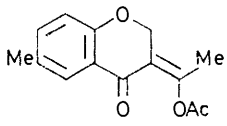
[8] D. Kästner, 'Newer Methods of Preparative Organic Chemistry,' Academic Press, New York, 1948, p. 296; F. M. Dean, A. Robertson, and W. B. Whalley, *J. Chem. Soc.*, 1950, 895; R. M. Manyik, F. C. Frostick, J. J. Sanderson, and C. R. Hauser, *J. Amer. Chem. Soc.*, 1953, **75**, 5030.

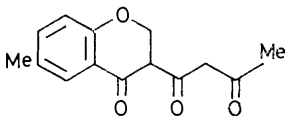
[9] F. M. Dean and S. Murray, *J.C.S. Perkin I*, 1975, 1706.

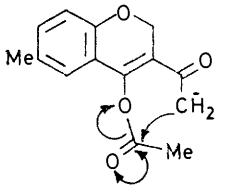
the former having the longer (*i.e.* more extended) chromophore and absorbing at the longer wavelengths. In agreement, the latter exhibits an aromatic proton resonance at very low field, characteristic of deshielding by an adjacent carbonyl group. One isomer (XXV) was relatively stable, but the other deteriorated rapidly, perhaps because the chromene methylene group is subject to radical oxidation as discussed previously.[9] Clearly, removal of a hydrogen atom from the methylene group in (XXIV) would be supported by the development of aromaticity in the heterocycle. Another form of isomerism must also be considered, because the *E*-configuration of (XXV) has a *Z*-counterpart (XXVI). The *Z*-configuration is discounted, however, on the grounds that the methyl proton resonances of (XXV) are at low field, indicative of deshielding by the carbonyl group, and that the *Z*-isomer should equilibrate with (XXIV) and not remain distinct from it at ordinary temperatures.[10]

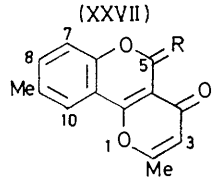

(XXIV)

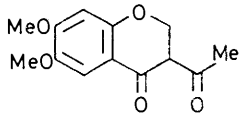

(XXV)

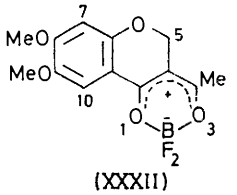

(XXVI)

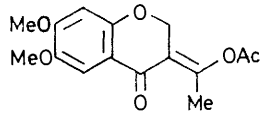

(XXVII)


(XXVIII)

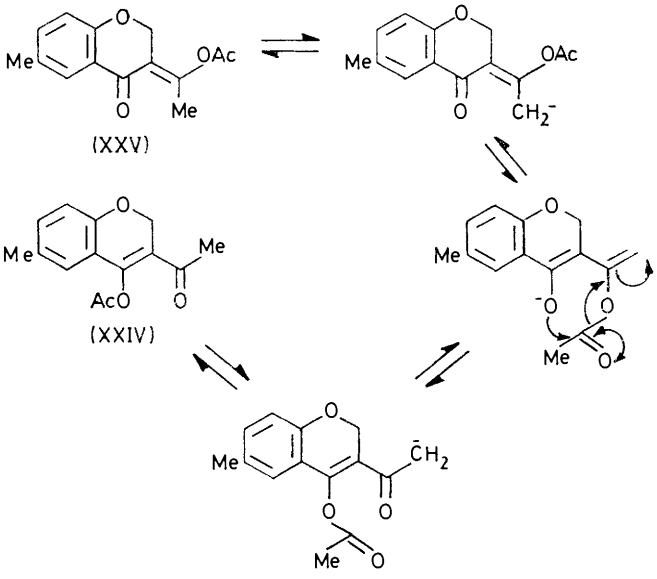

(XXIX) R = H,H
(XXX) R = O


(XXXI)


(XXXII)


(XXXIII)

The use of Harris–Hauser methods for extending the β-dicarbonyl system of the acetylchromanone (XIII) into the tricarbonyl system of (XXVII) would rely on the formation of dianions in the presence of strong bases, and seemed precluded here because of the danger of ring opening of the heterocyclic system. This danger was minimised by using the acetate (XXIV) to generate its carbanion (XXVIII), thus allowing an internal acylation as shown which is reminiscent of the Baker–Venkataraman rearrangement in flavone chemistry [11] and leaves the heterocycle at risk only after the triketonic system has been formed. In practice, Baker–Venkataraman reagents had little effect upon the acetate, nor did the ' proton sponge ' (1,8-bisdimethylaminonaphthalene [12]) in refluxing 1,2-dimethoxyethane or in bis-(2-methoxyethyl) ether. Some reaction was induced by carbanions, however, and after preliminary work the relatively non-nucleophilic triphenylmethyl-lithium was chosen. Two equivalents of base transformed the acetate (XXIV) into the desired triketone (XXVII) as a mixture of enols that could not be separated. Consequently, the mixture was cyclised as such with hydrochloric acid giving the pyranopyran (XXIX) in 24% yield. Fortunately, the synthesis does not depend upon selection of the correct acetate; the isomer (XXV) gives exactly the same results. It may be that the acetates are interconvertible under the conditions of the experiment (their carbanions would be particularly labile as suggested by Scheme 2) or that inter- are as feasible as intra-molecular acylations.


SCHEME 2

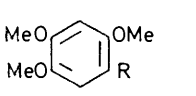
The pyranopyran derivative (XXIX) had the appropriate spectroscopic properties and the sensitivity to oxidation characteristic of chromens, chromic acid converting it into the citromycinone analogue (XXX) that has already been synthesised in other ways.[13,14] For the

[10] A. Mannschreck and H. Dvorak, *Tetrahedron Letters*, 1973, 547.
[11] W. Baker, *J. Chem. Soc.*, 1933, 1381; H. S. Mahal and K. Venkataraman, *ibid.*, 1934, 1767; J. E. Gowan and T. S. Wheeler, *ibid.*, 1950; 1925.
[12] R. W. Alder, P. S. Bowman, W. R. S. Steele, and D. R. Winterman, *Chem. Comm.*, 1968, 723.
[13] F. M. Dean, J. Goodchild, and A. W. Hill, *J.C.S. Perkin I*, 1973, 1022.
[14] S. A. Ali, J. W. Powell, and W. B. Whalley, *J.C.S. Perkin I*, 1973, 173.

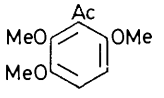
citromycinone series itself, the acetylchromanone (XXXI) was obtained from (V) *via* the dioxaborin derivative (XXXII) and gave an acetate (XXXIII). The alternative ester was not detected. Triphenylmethyl-lithium converted the acetate into a complex mixture of enols, and cyclisation by hydrochloric acid then gave the pyrone (II), identical with di-*O*-methylcitromycin from natural sources.

Electronic Character of the Hydroxyquinol Nucleus.— During the above work it became evident that the hydroxyquinol nucleus could control the behaviour of the carbonyl compounds containing it, and that this control was probably exerted through exceptional π-electron availability at the 5-position. Since this view also serves to correlate a variety of additional observations, we offer here a preliminary qualitative discussion pending results from quantitative work.

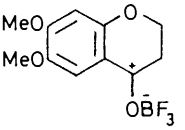
In accord with a relatively high electron availability at the 5-position, hydroxyquinol and its ethers are easily



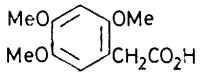
(XXXIV) R = H
(XXXV) R = Ac
(XXXVI) R = OMe



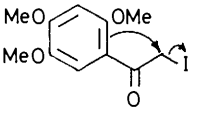
(XXXVII)



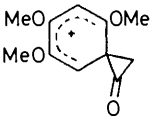
(XXXVIII)



(XXXIX)



(XL)



(XLI)

attacked by electrophiles at that point; we have already recorded [15] an internal Hoesch reaction [16] that proceeds nearly quantitatively with no catalyst other than hydrogen chloride. It is also reported that under very mild conditions, acetic acid and polyphosphoric acid convert 1,2,4-trimethoxybenzene (XXXIV) into the ketone (XXXV), and that if the isomeric ketone (XXXVII) is subjected to the same conditions it merely changes into (XXXV). In accord with the hypothesis, therefore, it is this ketone that is favoured both kinetically and thermodynamically. Even more striking is the formation of the same ketone (XXXV) when 1,2,4,5-tetramethoxybenzene (XXXVI) is attacked by the reagent, a methoxy-group being extruded in an unusual fashion.[17]

The acylation of the dimethoxychromanone (VI) by acetic anhydride and boron fluoride requires more vigorous conditions (heat) than that of chromanone itself, suggesting that the ion (XXXVIII) is stabilized by the substituents. Again, electron release into the carbonyl group explains the inability of the dicarbanion from pentane-2,4-dione to attack methyl 2,4,5-trimethoxybenzoate. A related effect was observed during a preparation of this ester. An attempt to obtain the requisite benzoic acid from the ketone (XXXV) by means of the standard iodoform reaction [18] led to a mixture of the acid with its homologue (XXXIX) so that permanganate oxidations had to be used for preparative work. In haloform reactions, the slower, rate-determining steps are those introducing the first halogen atom,[19] and we believe that the internal displacement shown in (XL) is able to compete with the faster, later substitutions thus leading *via* the cyclopropane intermediate (XLI) to the arylacetic acid observed. In the absence of methoxy-groups halogeno-ketones do not undergo reactions indicative of cyclopropane intermediates or transition states.[20] Whatever the reason, the formation of an unexpected homologue is clearly a previously unrecognised hazard in the use of haloform reactions for structural determination.[18]

Release of electrons into more remote carbonyl groups should be possible, and would account for the stability of the trimethoxyphenyl-4-pyrone (IX) towards sodium hydroxide, but on general grounds it would be expected that the effect would be greater for a directly attached carbonyl group. This would explain why the 3-acetylchromanone (XIII) is extensively enolized in solution whereas the dimethoxy-analogue (XXXI) is not and, furthermore, is relatively difficult to transform into an enol acetate. And it accounts for the fact that when methoxy-groups are present the only enol acetate formed has structure (XXXIII), with the carbonyl group directly attached to the hydroxyquinol nucleus.

The modes of enolization in more complex polyketones can also be rationalized along the same lines. N.m.r. methods have proved very suitable for determining the extent and sometimes the direction of enolization in polyketones,[21] and results for the β-diketone (VII) and benzoylacetone [22] are compared in the Table. It is again clear that methoxy-groups suppress enolization, and the same effect appears in the triketone (IX) where the benzoyl end of the molecule is much more highly enolized than the trimethoxybenzoyl end. It is reasonable to suppose that this fact underlies the success of the selective demethylation by boron chloride; had the enolization been mainly in the reverse direction the complex first

[15] F. M. Dean and K. B. Hindley, *Tetrahedron Letters*, 1972, 1445.
[16] W. A. Ruske, in ' Friedel–Crafts and Related Reactions,' ed. G. A. Olah, vol. 3, part 1, Interscience, New York, 1964, pp. 383 *et seq.*
[17] W. Schafer, I. Geyer, and R. Leute, *Chem. Ber.*, 1967, **100**, 930.
[18] K. W. Bentley, in ' The Elucidation of Organic Structures by Physical and Chemical Methods,' ed. K. W. Bentley and G. W. Kirby, Wiley, New York, 1973, part II, p. 194 *et seq.*
[19] *Cf.* W. Hückel, ' Theoretical Principles of Organic Chemistry,' Elsevier, Amsterdam, 1955, vol. 1, p. 303, and references cited therein.
[20] C. L. Stevens, W. Malik, and R. Pratt, *J. Amer. Chem. Soc.*, 1950, **72**, 4758.
[21] S. Forsen and M. Nilsson, in ' The Chemistry of the Carbonyl Group,' ed. S. Patai, Wiley, London, 1970, p. 157; L. W. Reeves, *Canad. J. Chem.*, 1957, **35**, 1351; J. L. Burdett and M. Y. Rogers, *J. Amer. Chem. Soc.*, 1964, **86**, 2105; *Canad. J. Chem.*, 1965, **43**, 1516.
[22] G. A. Allen and R. A. Dwek, *J. Chem. Soc.* (*B*), 1966, 161.

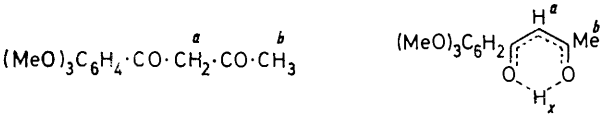
formed would have been similar to (X) and no demethylation would have ensued.

^{1}H N.m.r. spectral analysis * of keto–enol equilibria

(1) 1-Phenylbutane-1,3-dione †

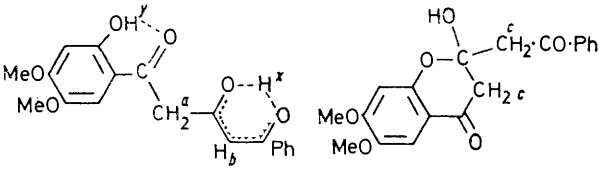
a 6.09 *b* 7.82 *a* 3.95 *b* 7.94 *x* −6.09
% 10 % 90

(2) 1-(2,4,5-Trimethoxyphenyl)butane-1,3-dione (VII)



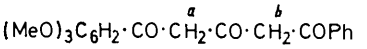
a 5.98 *b* 7.77 *a* 3.50 *b* 7.85 *x* −6.71
% 39 % 61

(3) 1-(2-Hydroxy-4,5-dimethoxyphenyl)-5-phenylpentane-1,3,5-trione (IV)

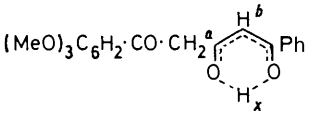


a 6.01 *b* 3.67 *x* *y* −2.16 *c* 7.05
% 75 % 25

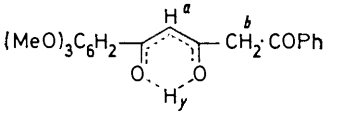
(4) 1-Phenyl-5-(2,4,6-trimethoxyphenyl)pentane-1,3,5-trione ‡ (V)



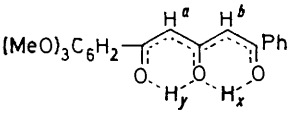
% *a* 5.73 *b* 5.90 13



a 5.85 *b* 3.72 *x* −4.62 43



a 3.26 *b* 6.14 *y* −4.72 27



a 3.42 *b* 3.97 *x*, *y* −5.21 17

* At 60 MHz; τ scale. Spectra were repeatedly determined on 10% solutions in $CDCl_3$ at 36 °C until a steady state was reached. The values given are means from three runs. † Allen and Dwek [22] give somewhat different values for a solution in tetrachloromethane. ‡ Also at 220 MHz.

EXPERIMENTAL

U.v. spectra were determined on *ca.* 10^{-3}M-solutions in ethanol. ^{1}H N.m.r. spectra (100 MHz) were determined for solutions in $CDCl_3$. Coupling constants are quoted (Hz), but relative intensities, all of which were in agreement with the assignments, are given only where necessary for clarity. Light petroleum refers to the fraction b.p. 60—80 °C. Molecular weights were obtained from mass spectra. Molecular weights of dioxaborin derivatives are given only for the major isotope (^{11}B) of boron.

1-(2,4,5-*Trimethoxyphenyl*)*butane*-1,3-*dione* (VII).—A mixture of 2′,4′,5′-trimethoxyacetophenone (30 g), sodium sand (30 g), and ethyl acetate (600 ml) was warmed gently until a vigorous reaction set in. When this had subsided the mixture was heated under reflux for 2 h and then cooled and treated with methanol (60 ml), added in small portions to destroy residual sodium. The mixture was then diluted with water (1 l), adjusted to pH 4, and extracted with ether (3 × 250 ml). Removal of the ether left an oil that was dried *in vacuo* and then crystallised from light petroleum giving the *dione* as pale yellow plates (27.5 g), m.p. 89°, $\nu_{max.}$ (Nujol) (mainly enolic forms) 1 615, 1 265, 1 215, 1 034, and 837 cm^{-1}, $\nu_{max.}$ (warm film) (mainly ketonic form) 1 737, 1 617, 1 266, 1 214, 1 034, and 832 cm^{-1}, $\nu_{max.}$ ($CHCl_3$) 1 716, 1 695, 1 605, 1 573, 1 463, 1 270, 1 196, and 1 024 cm^{-1} (Found: C, 61.9; H, 6.5%; *M*, 252. $C_{13}H_{16}O_5$ requires C, 61.9; H, 6.4%; *M*, 252).

2-*Methyl*-1-(2,4,5-*trimethoxyphenyl*)*butane*-1,3-*dione* (VIII).—The foregoing dione (10 g) in tetrahydrofuran (25 ml) was gradually added to sodium hydride [50% dispersion (8 g) in oil with the oil washed out by tetrahydrofuran] stirred in tetrahydrofuran (25 ml). When the effervescence had finished the mixture was kept at 50 °C for a short time and then concentrated under reduced pressure to about 20 ml. The sodium salt of the *dione* separated as buff crystals (9 g), m.p. 201° (decomp.). This salt (5.5 g) was warmed with iodomethane (40 ml) for 4 h, after which the filtrate was concentrated to give the *dione* as yellow plates (from ethanol) (4.1 g), m.p. 114.5°, $\nu_{max.}$ (mull) 1 704, 1 653, 1 609, 1 586, 1 272, 1 029, and 837 cm^{-1}, τ 8.67 (d, *J* 7, CH·C*H*$_3$), 7.82 (s, COMe), 6.15, 6.12, and 6.07 (each s, OMe), 5.54 (q, *J* 7, C*H*·CH$_3$), 3.50 (s, 3′-H), and 2.58 (s, 6′-H) (Found: C, 62.9; H, 6.9%; *M*, 266. $C_{14}H_{18}O_5$ requires C, 63.1; H, 6.8%; *M*, 266).

1-(2,4,5-*Trimethoxyphenyl*)-5-*phenylpentane*-1,3,5-*trione* (V).—The dione (VII) (0.8 g) in tetrahydrofuran (10 ml) was added to sodium hydride [50% dispersion in oil (1.2 g) with the oil washed out by tetrahydrofuran] also in tetrahydrofuran (10 ml), and the mixture was warmed until it refluxed gently. After 45 min, methyl benzoate (1.2 g) in tetrahydrofuran (10 ml) was added dropwise during 15 min, the vessel being protected from oxygen and moisture. After 6 h under reflux the mixture was evaporated under reduced pressure, and ether (40 ml) was added, followed (cautiously) by water (20 ml). The ether layer was washed with water (2 × 50 ml) and the water solutions were combined, acidified (hydrochloric acid), and extracted with ether. The extract gave a crude paste which crystallised from ethanol giving the *trione* as orange-brown prisms (0.98 g), m.p. 133°, $\nu_{max.}$ (mull) 1 596, 1 566, 1 267, 1 216, 1 155, and 839 cm^{-1} (Found:* C, 67.75; H, 6.2%; *M*, 356. $C_{20}H_{20}O_6$ requires C, 67.4; H, 5.8%; *M*, 356).

The trione (1 g) in acetic acid (100 ml) was kept with concentrated hydrochloric acid (2 ml) at 90 °C for 6 h, and the product was precipitated with water. Purified from ethanol, the solid supplied 2-*phenyl*-6-(2,4,5-*trimethoxy*-

* Attempts to remove traces of solvent induced decomposition.

phenyl)pyran-4-one (IX) as pale yellow needles (0.91 g), m.p. 157°, $\nu_{max.}$ (mull) 1 642, 1 587, 1 573, 1 278, 1 220, 1 040, and 794 cm^{-1}, τ 6.07, 6.04, and 5.99 (each s, OMe), 3.34 (s, 3′-H), 3.20 and 2.87 (d, *J* 2, 3- and 5-H), 2.36 (s, 6′-H), and 2.7—2.0 (mm, other ArH) (Found: C, 70.6; H, 5.4%; *M*, 338.11580. $C_{20}H_{18}O_5$ requires C, 71.0; H, 5.4%; *M*, 338.11541).

1-(2-*Hydroxy*-4,5-*dimethoxyphenyl*)-5-*phenylpentane*-1,3,5-*trione* (XIa,b).—The foregoing trione (0.2 g) was stirred in dichloromethane (50 ml) with boron chloride (1.5 ml) for 30 min, during which time the colour changed from a fluorescent lime green to blood red. The mixture was stirred into aqueous sodium acetate (10%; 50 ml) and the product extracted into dichloromethane and chromatographed on silica from light petroleum–trichloromethane (1 : 1). The main band supplied the enolic *hydroxy-trione* (XI) as a crystalline mass, m.p. 52°, $\nu_{max.}$ (film) 1 693, 1 646, 1 609, 1 521, 1 489, 1 442, and 771 cm^{-1}, that could not be recrystallised without inducing unwanted changes (Found: *M*, 342.10868. $C_{19}H_{18}O_6$ requires *M*, 342.11033).

2,4,5-*Trimethoxybenzoic Acid*.—(i) *Iodoform reaction*. 2′,4′,5′-Trimethoxyacetophenone (0.20 g) in water (5 ml) and dioxan (2 ml) was warmed gently and aqueous 5% potassium hydroxide (4 ml) was added followed by aqueous I_2 (10%) in KI (20%) until the colour of I_2 persisted. The colour was cleared with a few drops of sodium hydroxide solution and the mixture diluted with an equal volume of water. After 10 min, the iodoform (0.22 g) was collected and the filtrate extracted with ether to remove unchanged trimethoxyacetophenone. Acidification then liberated the acid products which were isolated by means of ether and crystallised from water as prisms (0.16 g). T.l.c. showed that two very similar compounds were present, but efforts to obtain either in a pure state were not successful. The mass spectrum showed two parallel series of fragmentations: (*a*) *m/e* 212, 197(212 − Me), 169(197 − CO), *etc.* and (*b*) *m/e* 226, 211(226 − Me), 183(211 − CO) *etc.* The n.m.r. spectrum of the mixture contained a band at τ 5.5 appropriate to the methylene group in (XXXIX), and integration showed this and the desired acid to be present in the ratio 2 : 3. The reaction was varied with respect to time, concentrations of base and of iodine, and order of addition of reagents, without any marked effect upon this ratio.

(ii) *Permanganate oxidation*. This method was adopted for preparative purposes. A mixture of 2′,4′,5′-trimethoxyacetophenone (30 g), water (1 l), and potassium hydroxide (30 g) was kept at 60 °C during the addition over 2 h of potassium permanganate (110 g) in water (400 ml). The mixture was then heated to boiling for 4 h and filtered. The filtrate was adjusted to pH 4 and the product collected ether–ethyl acetate (1 : 1; 3 × 500 ml) and re-extracted into aqueous 2N-sodium hydroxide (2 × 200 ml). This solution was treated with aqueous hydrogen peroxide (100 vol.; 10 ml), and the resulting acid recovered in the usual way and purified from hot water giving 2,4,5-trimethoxybenzoic acid as fine needles (26 g), m.p. 145° (lit.,[23] 144—145°). Obtained by heating the acid with iodomethane and potassium carbonate in acetone, the methyl ester separated from light petroleum as prisms, m.p. 90° (lit.,[23] 97.5°) identified spectroscopically. The acid chloride was obtained by use of oxalyl chloride in benzene at room temperature for about 2 h, and when volatile materials were removed it formed a crystalline mass, m.p. 56°, $\nu_{max.}$ (mull) 1 757 and 1 716 (acid chloride doublet), 1 615, 1 296, 1 141, 1 031, and 804 cm^{-1}, not further characterised.

6-*Acetoacetyl*-3-*acetylchroman*-4-*one* (XVI).—Acetic acid (25 g) was saturated with boron fluoride at 0 °C and chroman-4-one (1 g) in acetic anhydride (20 g) was added dropwise, also at 0 °C. The mixture was left at room temperature for 19 h and then poured into trichloromethane (200 ml) and washed twice with saturated aqueous sodium hydrogen carbonate. The solution was then shaken with a mixture of sodium sulphate and sodium hydrogen carbonate, filtered, and evaporated leaving a yellow solid that separated from light petroleum–acetone giving the *bis-dioxaborin* (XVII) as tiny yellow needles (0.69 g), m.p. 230° (decomp.), $\nu_{max.}$ 1 623, 1 594, 1 540, 1 523, 1 178, 1 155, 1 101, and 1 060 cm^{-1}, τ 7.55 (s, 4-Me), 7.51 (s, 6′-Me), 4.59 (s, CH_2), 2.88 (s, 5′-H), 2.86 (d, *J* 8.5, 7-H), 1.73 (d, *J* 8.5 and 2.5, 8-H), and 1.46 (s, *J* 2.5, 10-H) (Found: C, 49.0; H, 3.4%; *M*, 370. $C_{15}H_{12}B_2F_4O_5$ requires C, 48.7; H, 3.3%; *M* 370). More (0.44 g) of this compound was obtained from the mother liquors but had to be purified by chromatography on silica, first from light petroleum, then from ether–light petroleum, and finally from trichloromethane.

The material eluted by ether–light petroleum supplied the *dioxaborin* (XIV), which crystallised from hexane–ethyl acetate as bright yellow needles (0.42 g), m.p. 196—197° (decomp.), $\nu_{max.}$ 1 616, 1 596, 1 570, 1 540, 1 490, 1 360, 1 280, 1 235, 1 157, 1 094, 1 058, 846, 800, and 778 cm^{-1}, τ 7.65 (s, Me), 4.95 (s, CH_2), and 3.2—2.0 (mm, ArH) (Found: C, 55.5; H, 3.9%; *M*, 238. $C_{11}H_9BF_2O_3$ requires C, 55.5; H, 3.8%; *M*, 238).

The bisdioxaborin (XVII) (0.25 g) was heated in refluxing acetic acid (25 ml) with sodium acetate (2.5 g) and water (25 ml) for 10 min. The solution was poured into water (200 ml) and the product collected into trichloromethane and purified by chromatography on silica from ether–light petroleum (1 : 9). Crystallised from ethanol, the product gave the *acetoacetylchromanone* (XVI) in a doubly enolic form as light yellow needles (0.13 g), m.p. 118—119°, $\lambda_{max.}$ 230sh, 253, and 314 nm (log ε 3.95, 4.08, and 4.41), $\nu_{max.}$ 1 614vbr, 1 324, 1 198, 1 148, 1 106, 1 012, 931, 856, and 792 cm^{-1}, τ 7.87 (s, 2″-H_3), 7.84 (s, 4′-H_3), 4.98 (s, 2-H_2), 3.88 (s, 2′-H), 3.12 (d, *J* 8.5, 8-H), 2.08 (dd, *J* 8.5 and 2.5, 7-H), 1.73 (d, *J* 2.5, 5-H), −5.55br (OH·O), and −5.94br (OH·O) giving an intense brown colour in ethanolic iron(III) chloride (Found: C, 65.55; H, 5.2%; *M*, 274, $C_{15}H_{14}O_5$ requires C, 65.7; H, 5.15%; *M*, 274).

The dioxaborin (XIV) (0.2 g) was also warmed with aqueous sodium acetate in acetic acid and supplied an oil that, when purified by chromatography on silica from ether–light petroleum and then by crystallisation from light petroleum, afforded the enolic 3-*acetylchroman*-4-*one* (XII) as yellow plates (0.14 g), m.p. 72.5—73.5°, $\lambda_{max.}$ 220, 255, 306, and 351 nm (log ε 3.97, 3.73, 3.88, and 3.88), $\nu_{max.}$ (mull) 1 603vbr, 1 490, 1 290, 1 146, 1 094 1 040, 878, 843, and 775 cm^{-1}, τ 7.88 (s, Me), 5.04 (s, CH_2), 3.2—2.5 (mm, ArH), 2.15 (dd, 5-H), and −5.72 (OH · · · O), imparting an intense brown colour to ethanolic iron(III) chloride (Found: C, 69.8; H, 5.35%; *M*, 190. $C_{11}H_{10}O_3$ requires C, 69.5; H, 5.3%; *M*, 190).

3-*Acetyl*-6-*methylchroman*-4-*one* (XIII).—Acetic acid (25 g) was saturated with boron fluoride at 0 °C and to it was gradually added 6-methylchroman-4-one (4 g) in acetic anhydride (25 g). The mixture was re-saturated with

[23] *Cf.* 'Asarylic Acid,' in ' Dictionary of Organic Compounds,' ed. Sir I. Heilbron and H. M. Bunbury, Eyre and Spottiswoode, London, 1953.

boron fluoride and left over night at room temperature. It was then diluted with trichloromethane (200 ml), freed from acid with sodium hydrogen carbonate in water, dried (Na_2SO_4), and concentrated leaving a dark solid. This crystallised from ethyl acetate giving the *dioxaborin* (XV) as bright yellow rhombs (5.6 g), m.p. 198°, $\nu_{max.}$ (mull) 1 627, 1 593, 1 579, 1 542br, 1 461, 1 348, 1 220, 1 149, 1 060, 843, 794, and 782 cm^{-1}, τ 7.67 (s, 2 × Me), 4.98 (s, CH_2), 3.17 (d, *J* 8.5, 8-H), 2.64 (dd, *J* 8.5 and 2.5, 7-H), and 2.27 (d, *J* 2.5, 5-H) (Found: C, 57.1; H, 4.6%; *M*, 252. $C_{12}H_{11}BF_2O_3$ requires C, 57.2; H, 4.4%; *M*, 252).

Liberated by treating the dioxaborin (1 g) with aqueous sodium acetate in acetic acid at reflux temperature, the boron-free product was chromatographed on silica from ether–light petroleum and crystallised from benzene–light petroleum giving the *acetylchromanone* in an enolic form as light yellow needles (0.73 g), m.p. 99—100°, $\lambda_{max.}$ 225, 258, 310, and 362 nm (log ε 4.09, 3.75, 3.92, and 3.88), $\nu_{max.}$ (mull) 1 623vbr, 1 470, 1 386, 1 302, 1 227, 1 140, 858, 841, 762, and 734 cm^{-1}, τ 7.88 (s, 2′-H_3), 7.70 (s, 6-H_3), 5.10 (s, CH_2), 3.26 (d, *J* 8.5, 8-H), 2.83 (dd, *J* 8.5 and 2, 7-H), and 2.42 (d, *J* 2, 5-H), imparting an intense brown colour to ethanolic iron(III) chloride (Found: C, 70.8; H, 5.9%; *M*, 204. $C_{12}H_{12}O_3$ requires C, 70.6; H, 5.9%; *M*, 204).

The acetylchromanone (0.15 g) was treated with hydrazine dihydrochloride (0.15 g) in 95% ethanol (20 ml), water being added in drops, with warming, until dissolution was complete. The mixture was then left for 20 h. It was poured into water and the product was isolated with ether and purified from either benzene–light petroleum or trichloromethane–light petroleum giving 1,4-*dihydro*-3,8-*dimethyl*-[1]*benzopyrano*[4,3-c]*pyrazole* (XXII) as needles (0.12 g), m.p. 180.5—181°, $\nu_{max.}$ 3 080, 1 518, 1 518, 1 490, 1 301, 1 225, 1 096, 1 008, 842, 830, and 821 cm^{-1}, τ 7.78 (s, 2 × Me), 4.85 (s, CH_2), 3.18 (d, *J* 8, 6-H), 3.02 (dd, *J* 8 and 2, 7-H), 2.56 (d, *J* 2, 9-H), and −0.03 (NH). [Found: C, 71.9; H, 6.1; N, 14.1%; *m/e* 200 and 199 (*M* − H). $C_{12}H_{12}N_2O$ requires C, 72.0; H, 6.0; N, 14.0%; *M*, 200].

A similar reaction between the acetylchromanone (0.15 g) and phenylhydrazine hydrochloride (0.21 g) gave 1,4-*dihydro*-3,8-*dimethyl*-1-*phenyl*[1]*benzopyrano*[4,3-c]*pyrazole* (XXIII) as rhombs (from light petroleum) (0.12 g), m.p. 118.5—120°, $\nu_{max.}$ 1 622, 1 597, 1 529, 1 511, and 1 493 cm^{-1}, τ 7.97 (s, 8-Me), 7.75 (s, 3-Me), 4.85 (s, CH_2), 3.13 (mm, 6- and 7-H), and 3.41 (d, *J* 2, 9-H) [Found: C, 78.3; H, 5.9; N, 10.0%; *m/e* 276 and 275 (*M* − H). $C_{18}H_{16}N_2O$ requires C, 78.2; H, 5.8; N, 10.0%; *M*, 276].

2,6-*Dimethyl*-3-(3-*acetyl*-6-*methyl*-4-*oxochroman*-3-*ylmethyl*)*chromone* (XXI; R = Ac).—(i) *From* 3-*acetyl*-6-*methylchroman*-4-*one*. The chromanone (XIII) (1 g) was treated with sodium acetate (2.5 g) in a refluxing mixture of water (40 ml) and acetic acid (10 ml) for 12 h. The organic products were isolated by dilution with water and collection into trichloromethane. Chromatography on silica (60 g) from ether–petroleum (1 : 9) retrieved some 3-acetyl-6-methylchromanone (0.04 g). Further elution (solvent ratio 3 : 19) then gave fractions containing the *acetyloxochroman*-3-*ylmethylchromone*, which separated from ether as needles (0.45 g), m.p. 79°, containing ether of solvation; the solvent-free compound was obtained by removing the ether *in vacuo* over refluxing hexane (48 h) and had m.p. 133° $\lambda_{max.}$ 231, 153, 310, and 335 nm (log ε 4.44, 4.25, 3.90, and 3.50), $\nu_{max.}$ 1 708 (acetyl C:O), 1 675 (chromanone C:O), 1 638 and 1 623 (chromone bands), 1 584, 1 500, and 1 460 cm^{-1}, τ 7.71 (s, 6′-Me), 7.66 (s, COMe), 7.58 (s, 2- and 6-Me), 6.97 (d) and 6.53 (d) (*J* 14, AB system from C·CH_2·C), 5.70 (d) and 5.02 (d) (*J* 12, AB system from C·CH_2·O), and 3.4—2.0 (mm, ArH) (Found: C, 73.9; H, 5.5%; *M*, 390. $C_{24}H_{22}O_5$ requires C, 73.8; H, 5.7%; *M*, 390).

Further elution of the column (solvent ratio 1 : 4) gave 2,6-*dimethyl*-4-*oxochromen*-3-*ylmethyl acetate* (XIX), which crystallised from benzene–light petroleum as needles (0.12 g), m.p. 100.5°, $\lambda_{max.}$ 233 and 304 nm (log ε 4.28 and 3.80), $\nu_{max.}$ 1 731 (ester), 1 646 and 1 615 (chromone bands), 1 582, and 1 492 cm^{-1}, τ 7.97 (s, COMe), 7.58 (s, 6-Me), 7.52 (s, 2-Me), 4.90 (s, CH_2·OAc), 2.78 (d, *J* 9, 8-H), 2.57 (dd, *J* 9 and 2, 7-H), and 2.07 (d, *J* 2, 5-H) (Found: C, 68.0; H, 5.8%; *M*, 246. $C_{14}H_{14}O_4$ requires C, 68.3; H, 5.7%; *M*, 246).

Final elution with ether alone gave 3-*hydroxymethyl*-2,6-*dimethylchromone* (XVIII), which formed silvery plates (from benzene–light petroleum) (0.28 g), m.p. 117.5°, $\lambda_{max.}$ 237, 268sh, and 305 nm (log ε 4.09, 3.69, and 3.81), $\nu_{max.}$ (mull) 3 300 and 3 400 (OH), 1 642 and 1 628 (chromone bands), 1 605, 1 578, and 1 492 cm^{-1}, $\nu_{max.}$ ($CHCl_3$) 3 470 (OH), 1 634, 1 615 (chromone bands), 1 615, 1 583, 1 493, 1 450, and 1 403 cm^{-1}, τ 7.59 (s, 6-Me), 7.55 (s, 2-Me), 6.65br (OH), 5.39 (s, CH_2·OH), 2.74 (d, *J* 9, 8-H), 2.57 (dd, *J* 9.2, 7-H), and 2.07 (d, *J* 2, 5-H) (Found: C, 70.6; H, 6.1%; *M*, 204. $C_{12}H_{12}O_3$ requires C, 70.6; H, 5.9%; *M*, 204).

A similar experiment, but with the acetylchromanone (XIII) (1 g), acetic acid (50 ml), water (50 ml), and sodium acetate (5 g), gave unchanged acetylchromanone (0.051 g), the chromanonylmethylchromone (0.070 g), the acetoxymethylchromone (0.39 g), and the hydroxymethylchromone (0.37 g).

(ii) *From the dioxaborin* (XV). The dioxaborin (2.5 g) and sodium acetate (2.5 g) were added to boiling water (100 ml). After 40 min sodium acetate (5 g) and acetic acid (30 ml) were added, and heating was continued for 4 h. The products were isolated with ether, freed from acetic acid with aqueous sodium hydrogen carbonate, and then separated as in (i) giving unchanged acetylchromanone (0.36 g), the chromanonylmethylchromone (0.76 g), and the hydroxymethylchromone (0.22 g). The acetoxymethylchromone was not found.

2,6-*Dimethyl*-3-(6-*methyl*-4-*oxochroman*-3-*ylmethyl*)*chromone* (XXI; R = H).—The acetyl compound (XXI; R = Ac) (250 mg) was hydrolysed by concentrated hydrochloric acid (75 ml) and ethanol (75 ml) under reflux for 6 h. After dilution with water, the product was collected into ether and isolated in the usual way giving a gum that, crystallised from methanol, supplied the *chromone* as needles (173 mg), m.p. 155—156°, $\lambda_{max.}$ 234, 251, 312, and 335 nm (log ε 4.36, 4.23, 3.93, and 3.53), $\nu_{max.}$ (mull) 1 678 (chromanone C:O), 1 618 (chromone band), 1 580, and 1 503 cm^{-1} (aromatic), τ 7.71 (s, 6′-Me), 7.57 (s) and 7.60 (s) (2- and 6-Me), 7.4—6.8 (3 H, mm, CH·CH·CH_2·O), 5.8—5.3 (2 H, mm, CH·CH_2·O), and 3.2—2.0 (mm, ArH) (Found: C, 75.6; H, 5.8; *M*, 348. $C_{22}H_{20}O_4$ requires C, 75.8; H, 5.8; *M*, 348).

Acetylation of 3-*Acetyl*-6-*methylchroman*-4-*one*.—The chromanone (2 g) was kept with acetic anhydride (25 g) and pyridine (2.5 g) in a closed vessel for 7 days, and then poured into ice–water (200 ml) containing sodium hydrogen carbonate (50 g) under a layer of ether (100 ml). After being stirred for 10 min, the layers were separated and the aqueous one repeatedly extracted with ether. The combined ether solutions were washed with water, dried (Na_2SO_4), filtered, and concentrated to an orange oil which was chromatographed on silica (200 g). Elution with ether–

light petroleum (1 : 9) removed 3-acetyl-6-methylchromanone (40 mg) and then supplied (*E*)-3-(1-*acetoxyethylidene*)-6-*methylchroman*-4-*one* (XXV), crystallising from petroleum as needles (1 g), m.p. 73°, $\lambda_{max.}$ 226, 274, and 354 nm (log ε 4.16, 4.18, and 3.62), $\nu_{max.}$ 1 748 (ester), 1 681 (chromanone C:O), 1 623, 1 582, and 1 500 cm^{-1}, τ 7.78 (s, COMe), 7.71 (s, ArMe), 7.75 (t, *J* 1.5, vinyl Me), 5.16 (t, *J* 1.5, CH_2), 3.19 (d, *J* 8, 8-H), 2.76 (dd, *J* 8 and 2, 7-H), and 2.26 (d, *J* 2, 5-H) (Found: C, 68.2; H, 5.8%; *M*, 246. $C_{14}H_{14}O_4$ requires C, 68.3; H, 5.7%; *M*, 246).

Continued elution (solvent ratio 1 : 3) removed more 3-acetyl-6-methylchromanone (80 mg); and final elution (solvent ratio 1 : 1) gave fractions containing 4-*acetoxy*-3-*acetyl*-6-*methyl*-2H-1-*benzopyran* (XXIV), which separated from ether–light petroleum chilled in ice as light yellow needles m.p. 60°, $\lambda_{max.}$ 227, 245, 291, and 367 nm (log ε 4.08, 4.04, 4.00, and 3.69), $\nu_{max.}$ 1 755 (ester), 1 651 (acetyl C:O), 1 633. 1 580, and 1 496 cm^{-1}, τ 7.74 (2 × Me) and 7.63 (1 × Me), 5.01 (s, CH_2), 3.22 (d, *J* 8, 8-H), and 3.1—2.8 (nm, ArH) (Found: C, 68.2; H, 5.8%; *M*, 246. $C_{14}H_{14}O_4$ requires C, 68.3; H, 5.7%; *M*, 246).

2,9-*Dimethyl*-4H,5H-*pyrano*[3,2-c][1]*benzopyran*-4-*one* (XXIX).—A solution of triphenylmethyl-lithium was prepared from triphenyl methane (2.25 g) in 1,2-dimethoxyethane (18.75 ml) under nitrogen by addition of methyllithium in ether (*ca.* 2M; 3.75 ml) and 3 h stirring at room temperature. A solution of 4-acetoxy-3-acetyl-6-methyl-2*H*-1-benzopyran (500 mg) in 1,2-dimethoxyethane (30 ml) was flushed with oxygen-free nitrogen for 45 min, and then treated with triphenylmethyl-lithium solution (10 ml; *ca.* 2 equiv.) added by syringe. The deep red colour of the reagent faded and the mixture turned yellow and then green-black. After 10 min the reaction was quenched with acetic acid in dimethoxyethane and it became red and deposited a fluffy white solid. The mixture was diluted with ether and washed repeatedly with water. The water washings were re-extracted with trichloromethane, and the organic solutions were combined, dried (Na_2SO_4), and filtered. The solvents were removed *in vacuo* leaving a solid that t.l.c. indicated to contain triphenylmethane, 3-acetyl-6-methylchromanone, and a new substance. Chromatography on silica removed the triphenylmethane without separating the other two constituents, which formed one fraction. This was dissolved in acetic acid (25 ml) and warmed with concentrated hydrochloric acid (0.5 ml) for 20 min, and the products were isolated by dilution with water and extraction into ether. After removal of acetic acid by sodium hydrogen carbonate solution, evaporation of the ether left a viscous red oil that was chromatographed on neutral alumina (grade III, 6% water; 30 g) from benzene. The major fraction gave the *pyranopyranone*, which crystallised from ethanol as cream-coloured needles (109 mg), m.p. 212—213°, $\lambda_{max.}$ 232, 268, 279, 289, and 346 nm (log ε 4.09, 3.99, 4.11, 4.07, and 3.86), $\nu_{max.}$ 1 664 (pyrone), 1 626, 1 604, 1 577, and 1 500 cm^{-1}, τ 7.69 (s) and 7.66 (s) (2 × Me), 4.48 (s, CH_2), 3.86br (3-H), 3.20 (d, *J* 8, 7-H), 2.86 (dd, *J* 8 and 2, 8-H), and 2.61 (d, *J* 2, 10-H) (Found: C, 73.4; H, 5.3%; *M*, 228. $C_{14}H_{12}O_3$ requires C, 73.7; H, 5.3%; *M*, 228).

The result was identical when the acetoxyethylidene isomer (XXV) was used instead of the 4-acetoxypyran (XXIV).

2,9-*Dimethyl*-4H,5H-*pyrano*[3,2-c][1]*benzopyran*-4,5-*dione* (XXX).—The foregoing pyranopyranone (67 mg) and chromium(VI) oxide (100 mg) were dissolved in acetic acid (5 ml) and heated on a steam-bath for 15 min. The green solution was poured into water and the product isolated with trichloromethane in the usual way, though emulsification was unusually pronounced and led to considerable mechanical losses of material. When purified from ethanol, the product furnished the dione as tiny needles (38 mg), m.p. 220° (decomp.) (not depressed by an authentic sample), $\nu_{max.}$ 1 750 (2-pyrone), 1 659 (4-pyrone), 1 623, 1 598, 1 565, and 1 506 cm^{-1}, *M*, 242. The compound was not distinguishable from an authentic sample by t.l.c. or spectroscopic methods.[14]

3-*Acetyl*-6,7-*dimethoxychroman*-4-*one* (XXXI).—6,7-Dimethoxychroman-4-one (0.3 g) was treated in acetic anhydride (10 ml) with boron fluoride–ether complex (1 ml) added in one portion, and the dark brown mixture was kept at 60 °C for 35 min and then left at room temperature overnight. The yellow mass that had formed was collected and washed with ether and then crystallised from ether–trichloromethane to give the *dioxaborin* (XXXII) as yellow plates (0.3 g), m.p. 232°, $\nu_{max.}$ 1 625, 1 575, and 1 530 cm^{-1}, τ 7.78 (s, 4-Me), 6.16 (s) and 6.11 (s) (2 × OMe), 5.02 (s, CH_2), 3.13 (s, 7-H), and 2.76 (s, 10-H) (Found: C, 52.4; H, 4.65; *M*, 298. $C_{13}H_{13}BF_2O_5$ requires C, 52.4; H, 4.4%; *M*, 298).

The boron complex (1 g) was heated for 45 min in refluxing acetic acid (50 ml) and water (50 ml) containing sodium acetate (5 g) and ethanol (25 ml), and the products were collected into trichloromethane (4 × 50 ml), washed with water, and recovered as an oil. This was dissolved in methanol (5 ml) and vigorously stirred with aqueous copper(II) acetate (12%; 10 ml). The precipitate was washed with water by decantation and then suspended in water and treated with concentrated hydrochloric acid (3 ml). After being left overnight, the solid was collected and crystallised from methanol to give the *acetylchromanone* (0.66 g), m.p. 116—118°, $\nu_{max.}$ 1 705 (acetyl C:O), 1 670 (chromanone C:O), 1 610, 1 595, and 1 530 cm^{-1}, τ 7.62 (s, COMe), 6.13 (s) and 6.10 (s) (2 × OMe), 6.29 (3-H), 5.44 (2-H), and 5.20 (2-H) (ABX system, *J ca.* 5, 7.5, and 12), 3.54 (s, 8-H), 2.70 (s, 5-H), and −5.72 (faint, OH · · · O) (Found: C, 62.4; H, 5.5%; *M*, 250. $C_{13}H_{14}O_5$ requires C, 62.4; H, 5.6%; *M*, 250).

The compound was difficult to acetylate. A variety of methods were examined, with acid or with basic catalysts, but the conditions had to be somewhat forced, no yields better than 50% were obtained, and several coloured impurities also resulted. For preparative work acetyldimethoxychromanone (0.25 g) was treated with acetic anhydride (10 ml) and pyridine (5 drops) at 60 °C for 4 days. Ice–water (50 ml) was added and next day the solid was collected and crystallised from benzene–light petroleum giving 3-(1-*acetoxyethylidene*)-6,7-*dimethoxychroman*-4-*one* (XXXIII) (0.14 g), m.p. 131°, $\nu_{max.}$ 1 750 (ester), 1 685 (chromanone C:O), 1 630sh, 1 615, 1 590, and 1 520 cm^{-1}, τ 7.76 (s, COMe), 7.54 (t, *J* 1, vinyl Me), 6.15 (s) and 6.13 (s) (2 × OMe), 5.15br (CH_2), 3.61 (s, 8-H), and 2.62 (s, 5-H) (Found: C, 61.3; H, 5.5%; *M*, 292. $C_{15}H_{16}O_6$ requires C, 61.6; H, 5.5%; *M*, 292).

8,9-*Dimethoxy*-2-*methyl*-4H,5H-*pyrano*[3,2-c]*benzopyran*-4-*one* (II) (*Di*-O-*methylcitromycin*).—The acetoxyethylidenechromanone (XXXIII) (1.0 g) in 1,2-dimethoxyethane (40 ml) under nitrogen was cooled to −15 °C and injected with the triphenylmethyl-lithium solution (20 ml; see above). The mixture became yellow and then red. After 1 h it was allowed to reach 0 °C and after another 15 min it was quenched with acetic acid (2 ml) in dimethoxyethane (30 ml).

Water (50 ml) was added, and the mixture extracted with trichloromethane (4 × 25 ml). The extracts were washed with water, dried (Na_2SO_4), and concentrated to a red oil which was chromatographed on silica from ether–light petroleum. Fractions imparting an intense colour to ethanolic iron(III) chloride were combined (total 120 mg) and dissolved in acetic acid (10 ml) containing concentrated hydrochloric acid (0.2 ml). The solution was heated on a steam-bath for 1 h, and the initial yellow colour changed to deep red. The products were recovered by dilution with water and collection into trichloromethane, and purified by chromatography on silica from benzene–trichloromethane (1 : 1). Several fractions resulted. One crystallised readily and when recrystallised from ethanol gave the *pyranopyranone* (12 mg), m.p. 225—227°, unchanged by admixture with authentic di-*O*-methylcitromycin (Found: *M*, 274.08469. $C_{15}H_{14}O_5$ requires *M*, 273.0847.) The two materials were further identified by their identical i.r. and n.m.r. spectra.

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