Synthetic Approaches to the Deoxyhumulones; Some New 2,2-Dimethylchromens from Phloroacetophenone

By **W. J. G. Donnelly**, The Research Laboratory, A. Guinness, Son & Co. (Dublin) Ltd
P. V. R. Shannon,* Chemistry Department, University College, Cardiff

Condensation of 3-hydroxy-3-methylbutanal dimethyl acetal with phloroacetophenone (2',4',6'-trihydroxyacetophenone) in the presence of pyridine gave a mixture of 6- and 8-acetyl-2,2-dimethylchromen-5,7-diols (XI) and (XII), respectively, 6,8-diacetyl-2,2-dimethylchromen-5,7-diol (X), and 6-acetyl-2,2,8,8-tetramethyl-2*H*,8*H*-benzo[1,2-*b*,3,4-*b*']dipyran-5-ol (II; R = Me). Also isolated were two complex isomeric products (XIII) and (XIV), resulting from condensation of (II; R = Me) with (XII). In the presence of pyridinium hydrochloride, an increase in the yield of compound (II; R = Me) and the condensation products (XIII) and (XIV) was achieved, with a corresponding decrease in the amounts of compounds (X), (XI), and (XII).

In connection with our studies [1] on hop compounds related to phloroglucinol we were interested in potential synthetic routes to the diprenylated acyl phloroglucinols (deoxyhumulones) of general formula (I). The original synthesis by Riedl,[2] which involved condensation of an acylphloroglucinol with dimethylallyl bromide (prenyl bromide) under basic conditions, results in low yields.

Recently, Birch *et al.*[3] have described the successful ring-opening by metal–ammonia reduction of chromen ring systems to give *o*-prenylphenols; we have applied this procedure to the synthesis of the deoxyhumulones (I) starting with appropriate tricyclic 2,2-dimethylchromens [(II and (III)] in which one or two chromen ring systems might open. Although this approach is not the most direct one,† it seemed attractive because the lupulones ‡ (IV), the biogenetic congeners [4] of both the deoxyhumulones (I) and the more useful humulones (V) in the hop, may be degraded with acid [5] to a mixture of the tricyclic dihydropyrans (VI) and their linear isomers, which are potentially oxidisable [6] to the chromens (II) and (III), respectively.

A number of direct syntheses of 2,2-dimethylchromens are known [7-9] but are not highly efficient. Recently, however, Crombie *et al.*[10] have described the pyridine-catalysed condensation of 3-hydroxy-3-methylbutanal dimethyl acetal (VII) with phenols to give chromens; *e.g.* the phenol (VIII) with (VII) gives isoevodionol (IX) in high yield. This method was chosen as a possible alternative route to the tricyclic dichromens (II; R = Me) or (III; R = Me) in which *two* chromen ring systems would have to be formed involving at least one cyclisation on to a hydroxy-group *ortho* to the acyl side chain. Either of these synthetic objectives [(II or III; R = Me)] would provide model compounds with which to examine the possibility of single or double reductive opening of the chromen ring by Birch's procedure. In this paper we describe the synthesis of the dichromen (II; R = Me) and some by-products of the reaction.[1c]

3-Hydroxy-3-methylbutanal dimethyl acetal (VII) was condensed with phloroacetophenone (2',4',6-'trihydroxyacetophenone) in the presence of pyridine or pyridinium hydrochloride to give the six isolable products (II; R = Me) and (X)—(XIV) whose yields and relative proportions varied with the reaction conditions.

The major product, (II; R = Me), was isolated crystalline by column chromatography. Elemental analysis and the molecular ion (*m/e* 300) in its mass spectrum were consistent with its formulation as a dichromen. The n.m.r. spectrum showed signals typical of acetyl and pyran residues in the ratio of 1 : 2. An alternative structure, that of the linear isomer (III; R = Me), which was not isolated from the mixture, can be excluded because of the existence of a low field n.m.r. signal at τ −4·22, characteristic of a hydrogen-bonded hydroxy-proton *ortho* to a ketonic function. Hydrogenation of the dichromen (II; R = Me) with the uptake of 2 mol. equiv. of hydrogen gave a compound whose u.v. spectrum and m.p. were as reported [11] for 6-acetyl-3,4,9,10-tetrahydro-2,2,8,8-tetramethyl-2*H*,8*H*,-benzo[1,2-*b*,3,4-*b*']dipyran-5-ol (VI; R = Me).

The diacetyl compound (X), M^+ 276, was eluted next in the separation. Its n.m.r. spectrum showed signals corresponding to two acetyl groups and one pyran ring system and the phenolic hydroxy-protons appeared as *two* singlets at τ −5·30 (1H) and −6·31 (1H) in keeping with its structure. Hydrogenation resulted in the

† A more direct synthesis will be described by us in the near future.

‡ No attempt is made to represent the exact tautomeric forms of the non-aromatic compounds which in some cases are still uncertain.

[1] (*a*) D. M. Cahill and P. V. R. Shannon, *J. Chem. Soc.* (*C*), 1969, 938; (*b*) W. J. G. Donnelly and P. V. R. Shannon, *ibid.*, 1970, 524; (*c*) preliminary report, W. J. G. Donnelly and P. V. R. Shannon, *Chem. Comm.*, 1971, 76.

[2] (*a*) W. Riedl and H. Hübner, *Chem. Ber.*, 1957, **90**, 2870; (*b*) G.P. 899,198.

[3] A. J. Birch, M. Maung, and A. Pelter, *Austral. J. Chem.*, 1969, **22**, 1923.

[4] (*a*) W. Riedl and H. Hübner, *Angew. Chem.*, 1958, **70**, 343; (*b*) P. V. Shannon, R. O. V. Lloyd, and D. M. Cahill, *J. Inst. Brewing*, 1969, **75**, 376.

[5] G. A. Howard, J. R. A. Pollock, and A. R. Tatchell, *J. Chem. Soc.*, 1955, 174.

[6] G. Cardillo, R. Cricchio, and L. Merlini, *Tetrahedron*, 1968, **24**, 4825.

[7] (*a*) E. Spath and R. Hillel, *Ber.*, 1939, **72**, 963; (*b*) J. Nickl, *Chem. Ber.*, 1958, **91**, 1372.

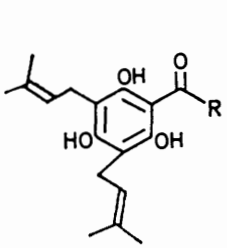
[8] J. R. Beck, R. Kwok, R. N. Booher, A. C. Brown, L. E. Patterson, P. Pranc, B. Rockey, and A. Pohland, *J. Amer. Chem. Soc.*, 1968, 4706.

[9] F. M. Dean, 'Naturally Occurring Oxygen Ring Compounds,' Butterworths, London, 1963, ch. 7.

[10] W. Bandaranayake, L. Crombie, and D. A. Whiting, *Chem. Comm.*, 1969, 970; *J. Chem. Soc.* (*C*), 1971, 811.

uptake of 1 mol. equiv. of hydrogen and afforded 6,8-diacetyl-2,2-dimethylchroman-5,7-diol (XVIII), identical with an authentic specimen (see later).

The formation of the diacetylchromen (X) can be explained by disproportionation of phloroacetophenone



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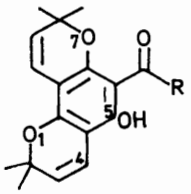

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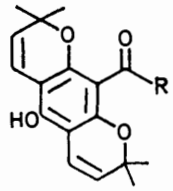

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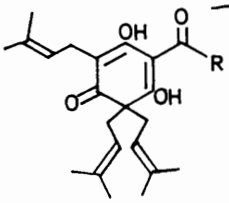

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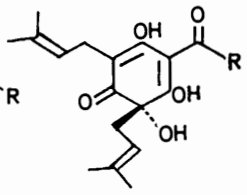

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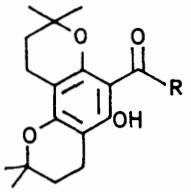

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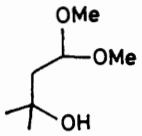

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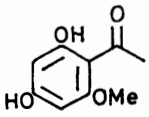

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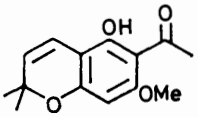

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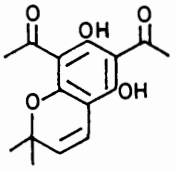

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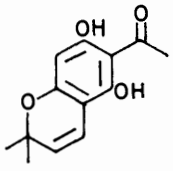

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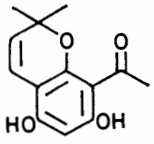

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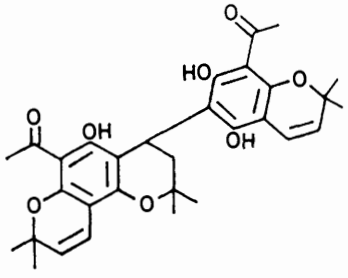

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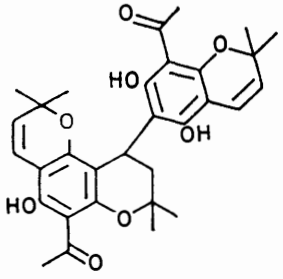
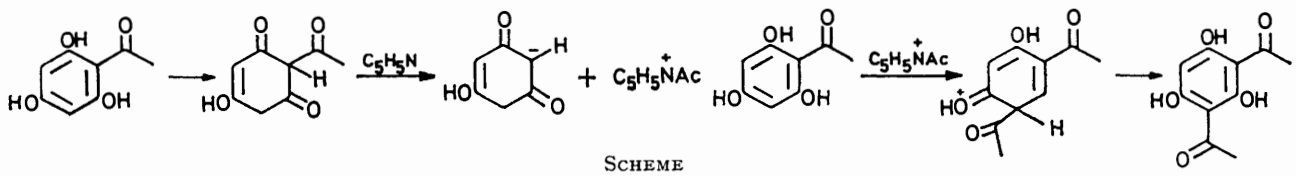


(XIV)

to phloroglucinol and diacetylphloroglucinol (see Scheme) followed by condensation of the latter with the acetal (VII). In fact subjection of phloroacetophenone to the conditions of the reaction, but with the omission of the acetal (VII), led to the formation of both phloroglucinol and diacetylphloroglucinol (t.l.c.), which were subsequently identified by comparison with authentic compounds.

The two isomeric chromens (XI) and (XII) were obtained as a mixture which decomposed on attempted chromatographic separations. On hydrogenation the mixture gave two compounds which were indistinguishable (t.l.c. and g.l.c. of their trimethylsilyl ethers) from authentic samples of 6-acetyl-2,2-dimethylchroman-5,7-diol (XVI) and its 8-acetyl isomer (XVII) (see later). The major isomer was (XVII). Separation of the mixture of (XVI) and (XVII) derived by hydrogenation gave small amounts of the individual compounds which showed u.v. spectra identical with those of the authentic specimens.



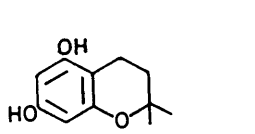
SCHEME

When the chroman (XV) [12] was acylated with acetic anhydride in boron trifluoride–ether, the isomers (XVI) and (XVII) were obtained in equal proportions, but they

[11] P. M. Brown, J. S. Burton, and R. Stevens, *Tetrahedron Letters*, 1963, 289.

[12] E. Byrne and P. V. R. Shannon, *J. Chem. Soc.* (*C*), 1969, 1540.

were formed in the ratio 3 : 1 when the previously reported [13] acetyl chloride–aluminium chloride procedure was employed. The earlier authors reported [13] the isolation only of the isomer (XVI). In our hands both acylation reactions afforded a small amount of a third crystalline product (XVIII). This (M^+ 278) showed $\lambda_{max.}$ 274 nm, typical of a diacylphloroglucinol, and its n.m.r. spectrum was consistent with the structure shown. In particular, a pair of low field singlets (τ −5·50 and −6·50) was in keeping with two hydrogen-bonded phenolic protons.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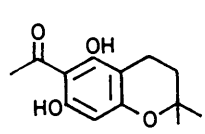
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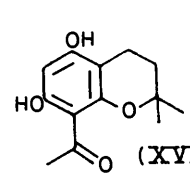
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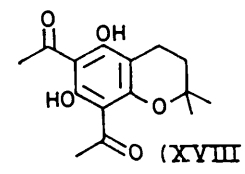
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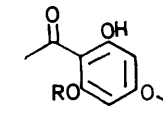
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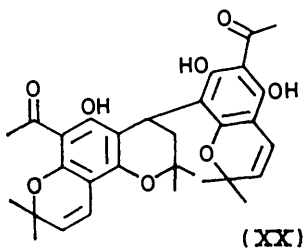
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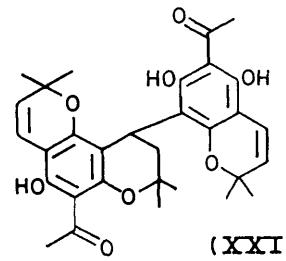
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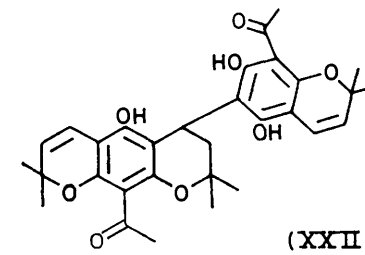
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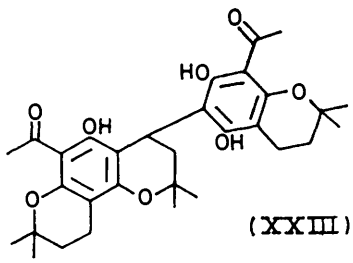
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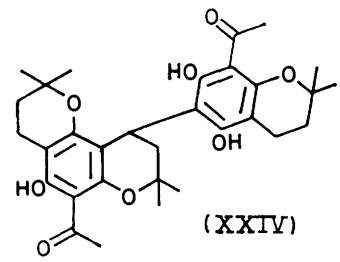
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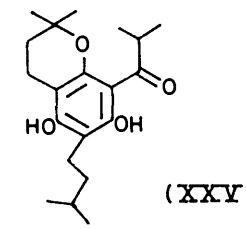
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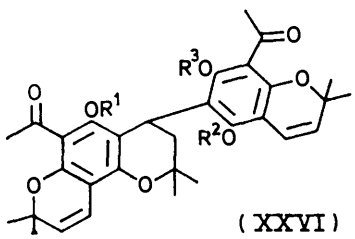
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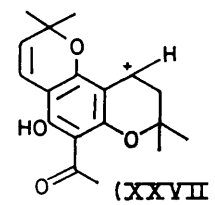
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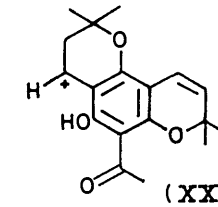

(XXVIII)

The two condensation products (XIII) and (XIV) were ultimately isolated in small quantities by column chromatography and fractional crystallisation. Their structures were assigned by spectral and chemical evidence.

Mass spectrometry showed the compounds to be isomers of formula $C_{31}H_{34}O_8$. The general similarity of their spectral properties suggested closely related structures. A dominant peak at *m/e* 301 in both mass spectra [base peak in (XIII)] suggested the union of a tricyclic system, *e.g.* (II; R = Me), with a bicyclic portion such as (XI) or (XII), the dominant fragmentation being due to fission of the bond linking the two units. Also, in the n.m.r. spectra of (XIII) and (XIV) the absence of an aromatic proton signal indicated a direct linkage between the free nuclear position of the bicyclic unit and a vinylic carbon atom α or β to the aromatic ring in the tricyclic system; the triplet at τ 5·40 (1H) in the spectrum of (XIII) [or τ 5·37 for (XIV)] pointed strongly to an α carbon atom as the linkage position. The low-field hydroxy-region of the spectrum showed a broad singlet at τ −4·06 in (XIII) [two singlets at τ −3·80 and −3·93 for (XIV)], thus requiring the partial structure (XIX). (In similar systems, signals for phenolic hydroxy-groups in other environments are sometimes not visible.[14]) The other resonances in the spectra confirmed the presence of the chromen and dihydropyran *gem*-dimethyl groups, the acetyl groups,

[13] T. Backhouse and A. Robertson, *J. Chem. Soc.*, 1939, 1257.
[14] W. J. G. Donnelly, Ph.D. Thesis, University of Dublin, 1970.

and the α (2H) and β vinylic protons of the two remaining chromen ring systems. These facts allow five possible structures for the condensation products *i.e.*, (XIII), (XIV), (XX), (XXI), and (XXII).

Hydrogenation of the condensation products gave tetrahydro-derivatives whose spectroscopic properties were consistent only with the structures (XXIII) and (XXIV). Thus the u.v. spectra of compounds (XXIII) and (XXIV) would be expected to be qualitatively similar to the sum of the main bands of the spectra of compounds (XXV) [15] and (VI; R = Pr^i) [15] as is found (see Table).

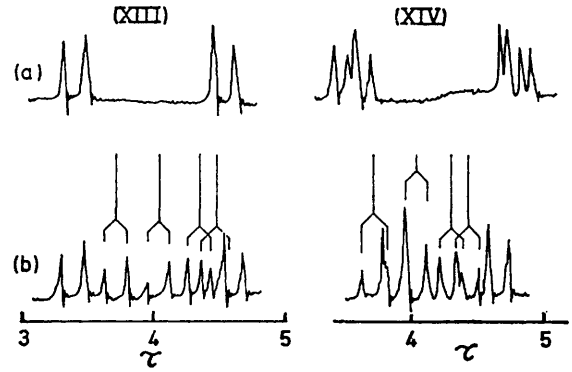
	$\lambda_{max.}$ (EtOH)/nm		
Compound	In acid	In alkali	
(XXV)	296		338
(VI; R = Pr^i	298	298	
(XXIII)	297 (ε 26,700)	310sh (ε 19,400)	337 (24,700)
(XXIV)	298	309	337

The tetrahydro-derivatives of (XX) and (XXI) do not have a free hydroxy-group *para* to the acyl substituent and would therefore not be expected to display the large bathochromic u.v. shift in alkali observed for the intense band, *i.e.* from 296—298 to 337—338 nm. The tetrahydro-derivative of (XXII) could be excluded because the n.m.r. spectrum of (XXIII) showed a broad singlet at τ 4·15 and a pair of singlets at τ −4·49 and −4·61 (each 1H) in accord with one *para* and two *ortho* hydrogen-bonded hydroxy-protons which would not fit the pattern of hydroxy-gr oups in structure (XXII). For similar reasons the low-field n.m.r. pattern, previously mentioned for compound (XIV), ruled out the possibility of the hydrogenation product being the tetrahydro-derivative of structure (XXII).

A specific distinction between the two remaining isomeric structures for compounds (XIII) and (XIV) was in principle possible using the chemical shift correlations of Arnone *et al.*[16] who showed that acetylation of 5-hydroxychromens induced a shielding ($\tau_{OAc} - \tau_{OH}$ = 0·3—0·4) of the chromen 4-proton and a small deshielding ($\tau_{OAc} - \tau_{OH}$ = −0·1) of the chromen 3-proton. Acetylation of 7-hydroxychromens did not produce these shifts.

Acetylation of the product (XIII) should produce a shift for two of the four vinyl protons. By contrast, all four vinyl protons of the isomer (XIV) should shift accordingly. The isomer (XIV), on acetylation, gave a product, formulated as the triacetate, which showed the expected shifts of both sets of α and β chromen proton doublets from their positions in (XIV),* thus establishing its structure. Hence by elimination, the second condensation product was assigned structure (XIII). This was confirmed by its acetylation to a product which was apparently pure (t.l.c.) but which gave a positive iron(III) chloride test and which showed two separated low-field hydroxy-resonances in its n.m.r. spectrum (see Experimental section). It was considered to be a mixture of the two diacetates (XXVI; $R^2 = R^3$ = Ac, R^1 = H) and (XXVI; $R^1 = R^2$ = Ac, R^3 = H). The mixture showed one set of α- and β-chromen vinyl proton resonances which was unaffected by the acetylation and one set which was shifted from the original positions in the expected manner.† The results of acetylation of the condensation products (XIII) and (XIV) are shown in the Figure. The apparent difference in ease of acetylation between compounds (XIII) and (XIV) may be due to the greater steric hindrance associated with triacetylation of the former.

The formation of these condensation products (XIII) and (XIV) can be explained by the protonation of the



N.m.r. spectra of chromen vinylic protons of (a) dimers (XIII) and (XIV) and (b) their products of acetylation

dichromen (II; R = Me) to give the carbonium ions (XXVII) and (XXVIII), which then attack the unsubstituted position of the chromen (XII). Reactivity of this type has previously been reported [9] for 2,2-dimethylchromens although the products have been little examined and, in theory, any of the chromens which have been isolated from the condensation reaction could undergo this kind of reaction. Indeed t.l.c. examination of the crude product from the condensation reaction showed traces of other compounds which were not isolated but whose structures might be predicted on the above basis.

The influence of acid on the chromenylation reaction was demonstrated by the addition of pyridine hydrochloride to the reaction medium. A substantial increase (200—300%) in the yield of the main product (II; R = Me) was effected. The addition also resulted in a significant increase in the formation of the condensation products (XIII) and (XIV), as would be expected, whilst a reduction in the yield of the chromens (XI) and (XII) was observed, presumably due to the increased conversion into (II; R = Me) (XIII) and (XIV).

* For one set a splitting is evident which may be due to the existence of two conformations of the triacetate arising from steric hindrance to rotation of the bicyclic system.

† The duplication in the resonances of one set of chromen protons might alternatively be explained by the existence of two conformers of one diacetate [either (XXVI; $R^2 = R^3$ = Ac, R^1 = H) or (XXVI, $R^1 = R^2$ = Ac, R^3 = H)]. However, the evidence for the structure of (XIII) would not be altered by this possibility.

[15] E. Byrne, D. M. Cahill, and P. V. R. Shannon, *J. Chem. Soc.* (*C*), 1970, 1637.

[16] A. Arnone, G. Cardillo, L. Merlini, and R. Mondelli, *Tetrahedron Letters*, 1967, **43**, 4201.

Disproportionation of phloroacetophenone leading to the diacylchromen (X) was almost entirely suppressed.

EXPERIMENTAL

M.p.s are corrected. Unless stated otherwise i.r. spectra were measured for chloroform solutions with a Unicam SP 200 spectrophotometer, u.v. spectra with a Beckman DB spectrophotometer, and n.m.r. spectra with a Perkin-Elmer R10 spectrometer at 60 MHz with tetramethylsilane as internal standard. G.l.c. was carried out as described previously.[1a] Silica gel for t.l.c. was Merck Kieselgel G and column chromatography was carried out on Mallinckrodt silicic acid (100 mesh). Light petroleum refers to the fraction b.p. 40—60°.

Condensation of 3-Hydroxy-3-methylbutanal Dimethyl Acetal with Phloroacetophenone.—Phloroacetophenone (4 g) and dry pyridine (1·9 g) were preheated to 160° under nitrogen. The acetal (VII) (4·05 ml) was added dropwise during 45 min. More acetal (12·1 ml) was added similarly during the next 6 h and heating was continued for an additional 4 h. The pyridine was removed under reduced pressure and the residue was taken up in ethyl acetate, washed with water (× 3), and dried. The aqueous washings after re-extraction with ether and drying gave unchanged acetal (5 ml), b.p. 64—68° at 10 mmHg.

The ethyl acetate was distilled off and the residual brown oil was chromatographed on silicic acid. Elution with ether–light petroleum (4 : 1) gave an oil (1·5 g, portion A) which showed six components on t.l.c., all of higher R_F value than the starting material. The remaining material (2·2 g, portion B) was eluted in ether–methanol (1 : 1) as a brown resinous oil which showed no definite spots on t.l.c., but g.l.c. of the trimethylsilylated material showed the presence of unchanged phloroacetophenone. Rechromatography of portion B effected no further purification.

Portion A was rechromatographed as above. Elution with ether–light petroleum (1 : 9) gave 6-*acetyl*-2,2,8,8-*tetramethyl*-2H,8H-*benzo*[1,2-b,3,4-b′]*dipyran*-5-*ol* (II; R = Me) (295 mg), yellow needles, m.p. 87—90° (from hexane), $\lambda_{max.}$ (EtOH) 295sh, 280sh, 269 (ε 27,000), and 243sh nm $\lambda_{max.}$ (alkaline EtOH) 297sh and 278 (ε 23,450) nm, τ ($CDCl_3$) 8·58 (6H, s, CMe_2), 8·53 (6H, s, CMe_2), 7·36 (3H, s, COMe), 4·58 (1H, d, *J* 10 Hz, ArCH=C*H*), 4·56 (1H, d, *J* 10 Hz, ArCH=C*H*), 3·41 (1H, d, *J* 10 Hz, ArCH=), 3·34 (1H, d, *J* 10 Hz, ArCH=), and −4·22 (1H, s, hydrogen-bonded OH), *m/e* 300 (16%, M^+) and 285 (100, $M^+ - CH_3$). (Found: C, 72·0; H, 6·8. $C_{18}H_{20}O_4$ requires C, 72·0; H, 6·7%).

Elution with ether–light petroleum (3 : 17) gave 6,8-*diacetyl*-2,2-*dimethylchromen*-5,7-*diol* (X) (120 mg), needles, m.p. 138—139° (from hexane), $\lambda_{max.}$ (EtOH) 366 (ε 3150) and 270 (36,420) nm, $\lambda_{max.}$ (alkaline EtOH) 286 (ε 23,130) nm, τ ($CDCl_3$) 8·49 (6H, s, CMe_2), 7·33 (3H, s, COMe), 7·31 (3H, s, COMe), 4·55 (1H, d, *J* 10 Hz, ArCH=C*H*), 3·36 (1H, d, *J* 10 Hz, ArCH=), −5·30 (1H, s, hydrogen-bonded OH), and −6·31 (1H, s, hydrogen-bonded OH), *m/e* 276 (24%, M^+), 261 (100, $M^+ - CH_3$), and 243 [41, $M^+ - (CH_3 + H_2O)$] (Found: C, 65·3; H, 5·8. $C_{15}H_{16}O_5$ requires C, 65·1; H, 5·8%).

Elution with ether–light petroleum (1 : 1) gave a mixture of the acylchromens (XI) and (XII), (155 mg). Repeated chromatography failed to separate the isomers, and caused extensive decomposition. A small amount of the mixture obtained in this way showed $\lambda_{max.}$ (EtOH) 275 nm, τ [$(CD_3)_2CO$] 8·50 (s, CMe_2), 7·37 (s, MeCO), 4·4 (d, *J* 10 Hz, ArCH=C*H*), 4·04 (s, ArH), 3·39 (d, *J* 10 Hz, ArCH=CH), and −3·83 (s, OH). The first, fourth, and fifth signals were barely separated duplicated resonances. G.l.c. of the trimethylsilylated derivative gave two peaks in the ratio 2 : 1.

The Isomeric Condensation Products (XIII) *and* (XIV).—Elution of the products of the condensation reactions of the acetal (VII) in light petroleum–ether (4 : 1) gave a mixture of two compounds (280 mg) from which a yellow crystalline compound (102 mg), m.p. 175—190°, was obtained by fractional crystallisation from hexane. Recrystallisation afforded the *product* (XIII) m.p. 200·5—202°, $\lambda_{max.}$ (EtOH) 349 (ε 4958), 288 (25,930), and 275infl. nm, $\lambda_{max.}$ (alkaline EtOH) 340 (ε 14,880) and 293 (25,900) nm, τ [$(CD_3)_2CO$] 8·70 (s) and 8·52br (s) (18H, C*Me*$_2$·CH_2 and 2 × C*Me*$_2$·C=), 8·0 (m, obscured CMe_2·C*H*$_2$), 7·43 (3H, s, COMe), 7·40 (3H, s, COMe), 5·40 (1H, t, *J* 8 Hz, ArC*H*CH_2), 4·53 (1H, d, *J* 9 Hz, ArCH=C*H*), 4·52 (1H, d, *J* 9 Hz, ArCH=C*H*), 3·40 (2H, d, *J* 9 Hz, 2 × ArCH=), and −4·06br (2H, s, hydrogen-bonded OH), *m/e* 534 (6%, M^+), 301 (100), 300 (14), 286 (20), 285 (58), 267 (11), 219 (30), and 201 (16) (Found: M^+, 534·2253. $C_{31}H_{34}O_8$ requires *M*, 534·2254).

The mother liquors, after crystallisation contained a second compound of lower R_F value. Preparative t.l.c. gave a yellow oil which crystallised from ether–light petroleum to give the *product* (XIV) m.p. 190—192°, $\lambda_{max.}$ (EtOH) 355 (ε 3708), 297sh, 278 (38,930), and 270sh nm, $\lambda_{max.}$ (alkaline EtOH) 346sh and 281 (ε 34,850) nm, τ ($CDCl_3$) 8·78 (s) and 8·55 (m) (18H, C*Me*$_2$C*H*$_2$ and 2 × C*Me*$_2$C=), 8·02 (m, CMe_2C*H*$_2$), 7·42 (3H, s, COMe), 7·39 (3H, s, COMe), 5·37 (1H, t, *J* 8 Hz, ArC*H*CH_2), 4·81 (1H, d, *J* 9 Hz, ArCH=C*H*), 4·75 (1H, d, *J* 9 Hz, ArCH=C*H*), 3·63 (1H, d, *J* 9 Hz, ArC*H*=CH), 3·51 (1H, d, *J* 9 Hz, ArC*H*=CH), and −3·80 and −3·93 (2H, each s, hydrogen-bonded OH) (Found: M^+, 534·2251).

Alternative Conditions for Condensation Reaction.—The reaction was repeated with the following alterations: the reaction temperature was 140°; the acetal (VII) (10 ml) was added dropwise, with stirring, in two equal portions at zero reaction time and after 6 h; and pyridine hydrochloride (200 mg) was added at the beginning of the reaction and a further quantity (200 mg) was added after 6 h. Heating was continued after the final addition for 5 h. Work-up and column chromatography, as before, gave (II; R = Me) (700 mg), (X) (10 mg) (XI and XII) (30 mg), and (XIII and XIV) (426 mg). The addition of small amounts of pyridine to facilitate dissolution of the phloroacetophenone did not affect the yield appreciably.

Hydrogenation of Compound (II; R = Me).—The dichromen (II; R = Me) (100 mg) in methanol (20 ml) was hydrogenated over palladium-charcoal. Two mol. equiv. of hydrogen were rapidly taken up. The product obtained after filtration and removal of solvent was crystallised from hexane to give 6-acetyl-3,4,9,10-tetrahydro-2,2,8,8-tetramethyl-2*H*,8*H*,benzo[1,2-*b*,3,4-*b*′]dipyran-5-ol (VI; R = Me) (85 mg), m.p. 118—119° (lit.,[11] 117—118°) $\lambda_{max.}$ (EtOH and alkaline EtOH) 340 (ε 3192) and 297·5 (18,690) nm, τ ($CDCl_3$) 8·64 (12H, s, 2 × C*Me*$_2$), 8·25 (4H, t, *J* 7 Hz, 2 × CH_2C*Me*$_2$), 7·49 (4H, partially obscured t, ArC*H*$_2$), 7·40 (3H, s, COMe), and −4·36 (1H, s, hydrogen-bonded OH) (Found: C, 70·8; H, 7·9. Calc. for $C_{18}H_{24}O_4$: C, 71·0; H, 7·9%).

Disproportionation of Phloroacetophenone.—Phloro-

acetophenone (150 mg) and dry pyridine (125 mg) were heated at 160°. T.l.c. after 1 h showed the appearance of two new products. After a further 4 h heating, work-up and silicic acid chromatography gave phloroacetophenone (94 mg), phloroglucinol (16 mg), m.p. 117° (from water), identical (g.l.c. and i.r.) with an authentic specimen, and diacetylphloroglucinol (25 mg), m.p. 168° (from light petroleum), identical (mixed m.p., u.v., and i.r. spectra) with an authentic specimen.[17]

Hydrogenation of the Chromen (X).—The chromen (X) (10 mg) in methanol (2 ml) was hydrogenated over palladium–charcoal. Uptake of hydrogen ceased after 1 mol. equiv. had been consumed. Filtration followed by distillation of solvent gave a product, m.p. 131—132° (from light petroleum), identical (m.p., mixed m.p., and spectra) with 6,8-diacetyl-2,2-dimethylchroman-5,7-diol (XVIII) (see below).

Acetylation of 2,2-Dimethylchroman-5,7-diol (XV).— (*a*) The chroman (XV) [12] (3·4 g) in boron trifluoride–ether (redistilled; 32 ml) was treated, with stirring, with acetic anhydride (1·8 ml), and the solution was kept at 20° for 48 h. After removal of the boron trifluoride–ether the crude product was taken up in ether, washed with water (×4), and dried (Na_2SO_4). Careful chromatography on silicic acid and elution with ether–light petroleum (1 : 1) gave 6-acetyl-2,2-dimethylchroman-5,7-diol (XVI) as a yellow solid (0·5 g), m.p. 222—225°, and elution with ether–light petroleum (3 : 2) gave 8-acetyl-2,2-dimethylchroman-5,7-diol (XVII) (0·5 g) as a yellow solid, m.p. 138—145°. Starting material (200 mg) was also recovered. Recrystallisation of the chroman (XVI) from ethyl acetate–chloroform gave a sample, m.p. 230° (lit.,[13] 230°), $\lambda_{max.}$ (EtOH) 293 (ε 16,780) and 231 (18,070) nm, $\lambda_{max.}$ (alkaline EtOH) 302·5 (ε 16,000) and 242·5sh nm, τ [$(CD_3)_2CO$] 8·70 (6H, s, CMe_2), 8·22 (2H, t, *J* 6 Hz, CMe_2CH_2), 7·46 (partially obscured t, *J* 6 Hz, $ArCH_2$), 7·40 (3H, s, COMe), and 4·16 (1H, s, ArH) (Found: C, 65·8; H, 6·7. Calc. for $C_{13}H_{16}O_4$: C, 66·1; H, 6·8%). The *diacetate*, formed by treatment with acetic anhydride in pyridine, had m.p. 83—85° (Found: C, 63·5; H, 6·2. $C_{17}H_{20}O_6$ requires C, 63·7; H, 6·3%). Recrystallisation of the chroman (XVII) from chloroform–light petroleum gave a sample, m.p. 150° (lit.,[13] 150°), $\lambda_{max.}$ (EtOH) 293 (ε 14,960) nm, $\lambda_{max.}$ (alkaline EtOH) 326 (ε 23,600) and 245 (4720) nm, τ ($CDCl_3$) 8·62 (6H, s, CMe_2), 8·17 (2H, t, *J* 6 Hz, CMe_2CH_2), 7·40 (partially obscured t, *J* 6 Hz, $ArCH_2$), 7·39 (3H, s, COMe), 4·09 (1H, s, ArH), 3·41br (1H, s, non-hydrogen-bonded OH), and −3·78 (1H, s, hydrogen-bonded OH) (Found: C, 65·8; H, 6·9. Calc. for $C_{13}H_{16}O_4$: C, 66·1; H, 6·8%).

Elution with ether–light petroleum (1 : 9) gave 6,8-*diacetyl-2,2-dimethylchroman-5,7-diol* (XVIII) (720 mg), m.p. 131—132·5° (from light petroleum), $\lambda_{max.}$ (EtOH) 340 (ε 3850) and 274 (31,230) nm, $\lambda_{max.}$ (alkaline EtOH) 329 (ε 14,810) and 291·5 (17,750) nm, τ ($CDCl_3$) 8·59 (6H, s, CMe_2), 8·20 (2H, t, *J* 7 Hz, CMe_2CH_2), 7·39 (2H, partially obscured t, *J* 7 Hz, $ArCH_2$), 7·38 (3H, s, COMe), 7·31 (3H, s, COMe), −5·50 (1H, s, hydrogen-bonded OH), and −6·50 (1H, s, hydrogen-bonded OH) (Found: C, 64·5; H, 6·5. $C_{15}H_{18}O_5$ requires C, 64·8; H, 6·5%).

(*b*) The chroman (XV) (3·4 g) dissolved in boron trifluoride–ether (redistilled; 32 ml) was cooled to 0°, and acetic anhydride (1·6 ml) was added dropwise with stirring. The solution was allowed to warm slowly to 20° and then kept at 20° for 48 h. Work-up as before gave, after chromatography, compounds (XVI) (810 mg), (XVII) (840 mg), and (XVIII) (170 mg) with a small amount (50 mg) of starting material.

(*c*) The chroman (XV) (3·4 g), mixed with anhydrous aluminium chloride, (7·0 g) was dissolved in nitrobenzene (54 ml). Acetyl chloride (redistilled; 1·57 g) was added dropwise to the stirred solution at 0° and the mixture was kept at 20° for 96 h. After work-up the crude products (2·5 g) were chromatographed on silicic acid to give compounds (XVI) (1·32 g) (XVII) (476 mg), and (XVIII) (107 mg).

Hydrogenation of Condensation Product (XIII).—Compound (XIII) (100 mg) in methanol (20 ml) was hydrogenated over palladium–charcoal. Two mol. equiv. of hydrogen were rapidly consumed. Work-up in the usual way and chromatography gave the *tetrahydro-derivative* (XXIII) (96 mg), m.p. 225—228° (from chloroform–light petroleum); for u.v. spectrum see Discussion; τ ($CDCl_3$) 8·65 (18H, m, 3 × CMe_2), 8·27 (2H, t, *J* 6·5 Hz, CMe_2CH_2), 8·23 (2H, t, *J* 6·5 Hz, CMe_2CH_2), 8·0 (2H, m, CMe_2CH_2), 7·53 (4H, partially obscured t, *J* 7 Hz, 2 × $ArCH_2$), 7·42 (3H, s, COMe), 7·39 (3H, s, COMe), 5·34 (1H, t, *J* 9 Hz, ArCH), 4·15br (1H, s, non-hydrogen-bonded OH), −4·49 (1H, s, hydrogen-bonded OH), and −4·61 (1H, s, hydrogen-bonded OH) (Found: C, 68·9; H, 6·9. $C_{31}H_{38}O_8$ requires C, 69·1; H, 7·1%).

Hydrogenation of Product (XIV).—Compound (XIV) (5 mg) was hydrogenated as for (XIII) to give a product (XXIV); for u.v. spectrum see Discussion section.

Acetylation of Compound (XIII).—Compound (XIII) (100 mg) in dry pyridine (1 ml) was treated with acetic anhydride (117 mg). The solution was kept at 20° for 48 h. Work-up, followed by column chromatography, gave an oil (85 mg) which showed a single spot on t.l.c. and gave a blue coloration with iron(III) chloride. The oil, considered to be a mixture of the diacetates (XXVI; $R^2 = R^3 = Ac$, $R^1 = H$) and (XXVI; $R^1 = R^2 = Ac$, $R^3 = H$), showed $\lambda_{max.}$ (EtOH) 283 and 260 nm, τ [$(CD_3)_2CO$] 8·74 and 8·47 (6H, 2s, CMe_2CH_2), 8·54br (12H, s, $CMe_2{\cdot}C=$), 8·29 and 8·11 (3H, 2s, OCOMe), 8·0 (m, partially obscured, CH_2CMe_2), 7·74 and 7·64 (3H, 2s, OCOMe), 7·59 and 7·46 (3H, 2s, CCOMe), 7·43 (3H, s, CCOMe), 5·83 and 5·76 (2t, *J* 9 Hz, ArCH), 4·51 (1H, d, *J* 10 Hz, ArCH=CH), 4·32 and 4·21 (1H, 2d, each *J* 10 Hz, ArCH=CH), 3·91 and 3·61 (1H, 2d, *J* 10 Hz, ArCH=), 3·41 (1H, d, *J* 10 Hz, ArCH=), −4·13 and −4·11 (1H, 2s, hydrogen-bonded OH).

Acetylation of Compound (XIV).—Compound (XIV) (100 mg) was acetylated as described for (XIII). Column chromatography of the reaction mixture gave the triacetate (70 mg) as a semi-solid, $\lambda_{max.}$ (EtOH) 252 nm, τ ($CDCl_3$) 9·2, 8·72, 8·65, 8·6 (s, CMe_2CH_2 and $CMe_2CH=$), 8·19 and 8·08 (3H, 2s, OCOMe), 7·80 (3H, s, OCOMe), 7·75 and 7·60 (3H, 2s, OCOMe), 7·6 and 7·48 (3H, 2s, CCOMe), 7·54 (3H, s, CCOMe), 6·0 (m, ArCH), 4·65 (1H, d, *J* 10 Hz, ArCH=CH), 4·45 and 4·33 (2d, *J* 10 Hz, ArCH=CH), 4·06 and 3·73 (2d, *J* 10 Hz, ArCH=), and 3·88 (1H, d, *J* 10 Hz, ArCH=).

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