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ISOPRENYLATION OF POLYPHENOLS IN AQUEOUS ACID SOLUTIONS

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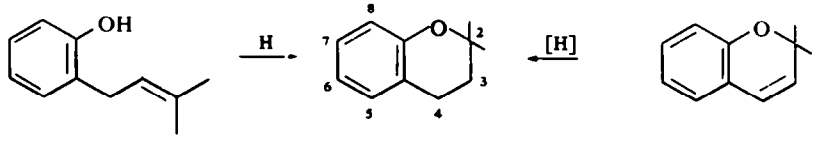
Abstract—Polyphenols condense with 2-methylbut-3-ene-2-ol or γ,γ-dimethylallyl alcohol in 5% aqueous citric acid solution to yield phenolic 2,2-dimethylchromans. These facile condensations provide chemical support for the biogenetic theory of C-isopentenylation of phenols by γ,γ-dimethylallyl pyrophosphate. Iso-psoralidin (**20**) has been synthesized from 7-hydroxy-2,2-dimethylchroman (**12**) by a novel and convenient route.

INTRODUCTION

PHENOLIC natural products bearing isoprenoid substituents exhibit a wide variety of structural types, both with respect to the polyphenolic moiety and the C_5 isoprenyl unit.[1] The most frequently observed types of C_5 substitution in such compounds are the *o*-hydroxy-γ,γ-dimethylallyl (**1**) and 2,2-dimethylchromene (**3**) groupings. In the course of structural elucidation of natural products bearing either of these substitution patterns the compound is almost invariably converted into a derivative having the 2,2-dimethylchroman structure (**2**), either by acid-catalysed cyclization of the γ,γ-dimethylallyl group or by hydrogenation of the chromene double bond. In spite of these facile interconversions the 2,2-dimethylchroman unit occurs very infrequently among phenolic natural products.



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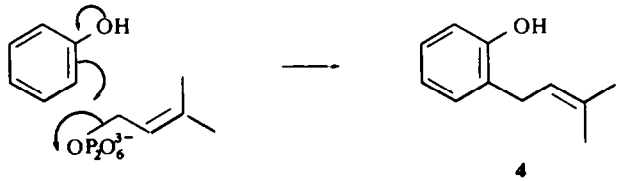
The biosynthesis of C_5 substituted phenolic compounds appears to take place through a combination of the mevalonate and acetate-shikimate pathways. It has been suggested by Birch[2] that the C_5 substituents in phenolic natural products are introduced by way of a C-isopentenylation reaction involving a suitably reactive alkylating agent. Such compounds as isopentenyl pyrophosphate or a γ,γ-dimethylallyl alcohol derivative could alkylate either the previously formed phenol itself or the activated methylene group of the appropriate poly-β-ketonic intermediate.[3,4]

Ollis and Sutherland[1] have proposed mechanisms for the formation of the four

* Employed as a Consultant by the United States Brewers Association.

products which might be expected to arise through S_N2 type of alkylation of a phenol by γ,γ-dimethylallyl pyrophosphate as follows:



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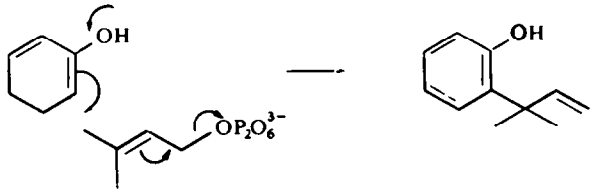

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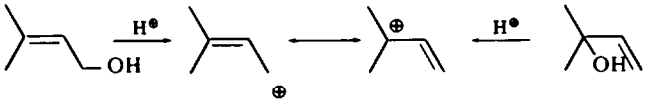
The corresponding O-alkylated products could be formed in a like manner. Of the two C-alkylated isomers (**4** and **5**) the γ,γ-dimethylallyl derivative (**4**) would be the one expected to be formed more readily from a consideration of steric factors.

In view of the successful synthesis of naturally occurring C-cinnamyl phenols by condensation of simple phenols with cinnamyl alcohol under mildly acidic conditions in aqueous solution[5,6] it seemed appropriate to attempt to prepare C-isopentenyl phenols by an analogous method. Since the protonated C_5 alcohol would be expected to be similar in reactivity to γ,γ-dimethylallyl pyrophosphate, the formation of C-alkylated phenols under such mild conditions could be regarded as a chemical equivalent of the proposed biosynthetic pathway to such compounds.

The mesomeric cation (**6**), required to carry out the above condensation, could be generated by protonation of either γ,γ-dimethylallyl alcohol (**7**) or 2-methylbut-3-ene-2-ol (**8**):



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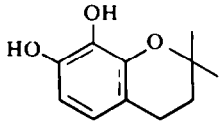
As will be shown later, the use of either of these alcohols gives rise to identical products in the same yield on condensation with a given phenol, indicating that the reaction involves an S_N1 type of mechanism. In contrast, Ollis *et al.* found that the acid-catalysed reaction of phenols with cinnamyl alcohol and 1-phenylallyl alcohol involved a mechanism having some S_N2 character since the products obtained excluded the intermediacy of the same 1-phenylallyl cation in both cases.[6]

2-Methylbut-3-ene-2-ol (**8**) is readily available from commercial sources, and therefore this alcohol was used, rather than γ,γ-dimethylallyl alcohol (**7**), for the acid-

catalysed condensation with simple phenols. Thus, when pyrogallol was warmed with 2-methylbut-3-ene-2-ol (**8**) in 5% aqueous citric acid solution containing a small amount of ascorbic acid to suppress oxidation of the phenol, it gave a brown oil which separated from the reaction mixture. Distillation of the oil under vacuum gave two easily separable major fractions. The first fraction was a colorless oil, b.p. 110–115°/0·1 mm which solidified on standing and crystallized from 30–60° light petroleum as white needles, m.p. 99–100°. The NMR spectrum of the compound showed the absence of a γ,γ-dimethylallyl grouping but indicated the presence of a 2,2-dimethylchroman grouping (**2**) which must therefore have been formed by acid-catalysed cyclization of an *o*-hydroxy-γ,γ-dimethylallyl group (**1**). The *gem*-dimethyl groups occurred as a singlet at δ 1·31 and the 3- and 4-methylene groups of the chroman ring as distinctive triplets at δ 1·74 and 2·66, respectively. The structure of the compound was established by NMR of its crystalline acetate, m.p. 66·5–7·5°, which showed two acetoxy groups at δ 2·25 and two ortho-coupled aromatic protons as doublets at δ 6·60 and 6·91 (J = 8 Hz). Thus the condensation product is 7,8-dihydroxy-2,2-dimethylchroman (**9**).

The second fraction was obtained as a pale yellow oil, b.p. 160–170°/0·2 mm which could not be crystallized. NMR indicated that the material was either a mixture of the chroman (**9**) and its uncyclized precursor or, more likely in view of the higher b.p., the di-alkylated partially cyclized compound (**10**). On warming the oil in ethanolic hydrochloric acid under reflux a crystalline product, m.p. 139–140°, was obtained showing no vinylic Me group signals in its NMR spectrum. The NMR of its crystalline acetate showed a single acetoxyl group at δ 2·26 and a single aromatic proton at δ 6·60, together with signals characteristic of the 2,2-dimethylchroman ring. The cyclized product is therefore the dichroman (**11**), and the second condensation product must be 6-(γ,γ-dimethylallyl)-7,8-dihydroxy-2,2-dimethylchroman (**10**), presumably derived from the chroman (**9**) by further isoprenylation.



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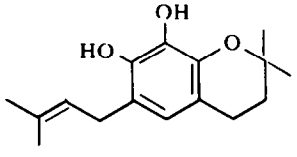

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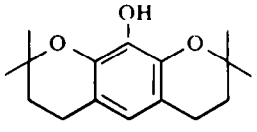

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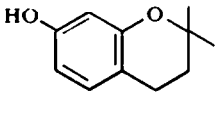
Condensation of pyrogallol with γ,γ-dimethylallyl alcohol (**7**) under the same mildly acidic conditions gave two major fractions on distillation of the product, identical in all respects with the two products obtained from the pyrogallol- -2-methylbut-3-ene-2-ol condensation. The yields of the first and second fractions were 25% and 15% respectively, closely comparable with the yields of 21% and 12% obtained in the first experiment.

Resorcinol, on condensation with 2-methylbut-3-ene-2-ol in aqueous citric acid solution gave a single product, obtained as a colorless oil, b.p. 145–150°/0·1 mm. Crystallization from 30–60° light petroleum gave white needles, identical with 7-hydroxy-2,2-dimethylchroman (**12**), m.p. 72°, b.p. 140–143°/0·1 mm, previously obtained by Robertson *et al.* by Clemmensen reduction of 7-hydroxy-2,2-dimethyl-

chromanone (**13**).[7] NMR of the product confirmed its identity as the chroman (**12**), the *gem*-dimethyl groups occurring at δ 1·30, the methylene groups as triplets at δ 1·74 and 2·66, and the aromatic protons exhibiting signals at δ 6·30–6·90 characteristic of a 1,2,4-trisubstituted benzene ring. Acetylation with acetic anhydride-pyridine gave an uncrystallizable mono-acetate, whereas *p*-nitrobenzoyl chloride in pyridine gave 7-(*p*-nitrobenzoyloxy)-2,2-dimethylchroman, identical with the derivative obtained by Robertson *et al.*[7]



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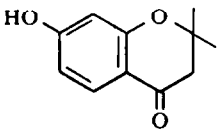

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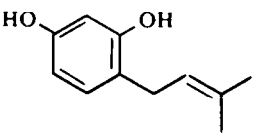

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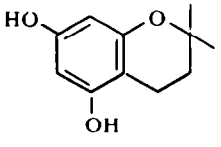
Kakhniashvili and Chikhladze[8] have reported that 2-methylbut-3-ene-2-ol condenses with resorcinol in the presence of 85% phosphoric acid to yield 4-(γ,γ-dimethylallyl)-resorcinol (**14**). Since the latter compound is a possible product from the condensation of the same reactants in citric acid, as well as the cyclized product (**12**), the phosphoric acid catalysed reaction was repeated under the conditions described,[8] for comparative purposes. However, the only product obtained was 7-hydroxy-2,2-dimethylchroman (**12**).

The oily product obtained on condensation of phloroglucinol with 2-methylbut-3-ene-2-ol in 5% aqueous citric acid afforded a single major fraction, b.p. 155–170°/0·2 mm. The NMR spectrum of this material indicated that it was not homogeneous, but rather an approximately 50:50 mixture of the monochroman (**15**) and a dichroman which could have either the linear (**16**) or angular structure (**17**). Fractional crystallization gave the dichroman as white needles, m.p. 161–162·5°, the single aromatic proton occurring at δ 5·92 in the NMR spectrum and the *gem*-dimethyl groups at δ 1·28. A positive Gibbs test for an unsubstituted position para to the —OH group established the structure as the linear dichroman (**16**).

Further crystallization from the mother liquors gave 5,7-dihydroxy-2,2-dimethylchroman (**15**), identical in all respects with the product obtained on Clemmensen reduction of 5,7-dihydroxy-2,2-dimethylchromanone.[10] No trace of the angular dichroman (**17**) was observed, TLC of the reaction product indicating the presence of only two compounds.



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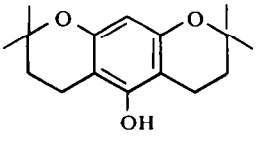

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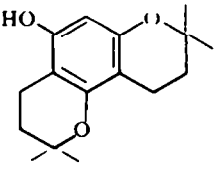

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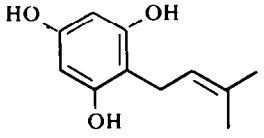
The formation of 2,2-dimethylchromans in the condensation of the above phenols with 2-methylbut-3-ene-2-ol is somewhat surprising in view of the very mild acidic

conditions used to effect reaction. The *o*-hydroxy-γ,γ-dimethylallyl grouping, in which subsequent cyclization has not taken place, was observed only in the isopentenylchroman (**10**); no significant amounts of uncyclized products being obtained from any of the other condensations which were studied. Similar results have been observed by Nilsson *et al.*[10] who obtained various Me substituted 6-hydroxy-2,2-dimethylchromans, analogs of the tocols, on condensation of a number of methylhydroquinones with γ,γ-dimethylallyl alcohol in refluxing formic acid. However, the conditions used for these syntheses were strongly acidic, so that the isopentenyl phenols would not be expected to remain uncyclized.

The conditions used to bring about cyclization of *o*-hydroxy-γ,γ-dimethylallyl groupings are normally quite vigorous, usually involving treatment with strong acids such as hydrogen bromide in acetic acid, ethanolic sulfuric acid or ethanolic hydrochloric acid under reflux. The formation of 2,2-dimethylchromans in 5% aqueous citric acid indicates that the drastic conditions formerly used may not be necessary in most cases. The use of aqueous citric acid may thus provide a convenient method for the cyclization of isopentenyl compounds which contain additional acid-labile substituents. In fact, 2-(γ,γ-dimethylallyl)-phloroglucinol (**18**), prepared by deacetylation of 3-(γ,γ-dimethylallyl)-phloroacetophenone (**19**) according to the method of Mitteldorf and Riedl,[11] gave a quantitative yield of 5,7-dihydroxy-2,2-dimethylchroman (**15**) when warmed overnight in 5% aqueous citric acid solution.



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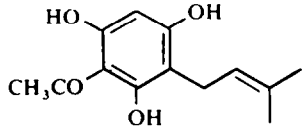

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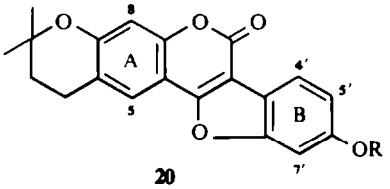
The condensation of simple phenols with 2-methylbut-3-ene-2-ol under the above conditions provides a much more facile synthetic route to 2,2-dimethylchromans than previously available. In the past such chromans have been prepared by Clemmensen reduction of 2,2-dimethylchromanones or by treatment of dihydrocoumarins with methyl magnesium iodide. However, the appropriate chromanone or dihydrocoumarin is often difficult to prepare and yields are variable. The simple 2,2-dimethylchromans are of great utility as an aid to structural elucidation since they are necessary starting materials for the synthesis of the more complex chromans derived from naturally occurring polyphenols containing *o*-hydroxy-γ,γ-dimethylallyl or 2,2-dimethylchromen groupings. Moreover, the recent discovery by Cardillo, Cricchio and Merlini[12] that chromans can be dehydrogenated to chromens by DDQ, provides a convenient method for the synthesis of the many natural products containing the latter grouping which have been difficult to prepare by the methods previously available.

As an example of the utility of the 2,2-dimethylchromans for synthesis, isopsoralidin (**20**, R = H) derived from the natural product psoralidin (**21**) by acid catalysed cyclization, has been prepared by a novel route which is more facile than the conventional methods.[13–14] Thus, a Hoesch reaction between 7-hydroxy-2,2-dimethylchroman (**12**) and methoxyacetonitrile gave a 60% yield of the ω-methoxyacetophenone

(**22**, R = H), the phenolic OH group of which was protected by formation of the benzyl ether (**22**, R = $C_6H_5CH_2$—). Condensation of the latter with 2,4-dihydroxybenzaldehyde in ether solution saturated with gaseous HCl gave the flavylium salt (**23**, R = $C_6H_5CH_2$—) which was readily debenzylated by warming with a mixture of glacial acetic acid and concentrated HCl to yield the phenolic flavylium salt (**23**, R = H).



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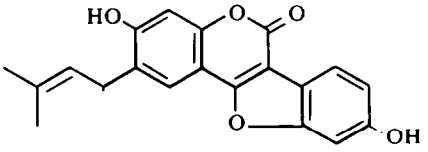

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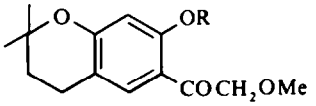

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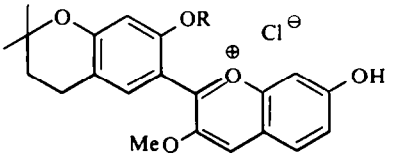

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Oxidation of the flavylium salt (**23**, R = H) with 30% aqueous hydrogen peroxide according to the method previously developed for the synthesis of coumestrol[15] resulted in ring contraction to the furan (**24**) which on acidification rapidly lactonized

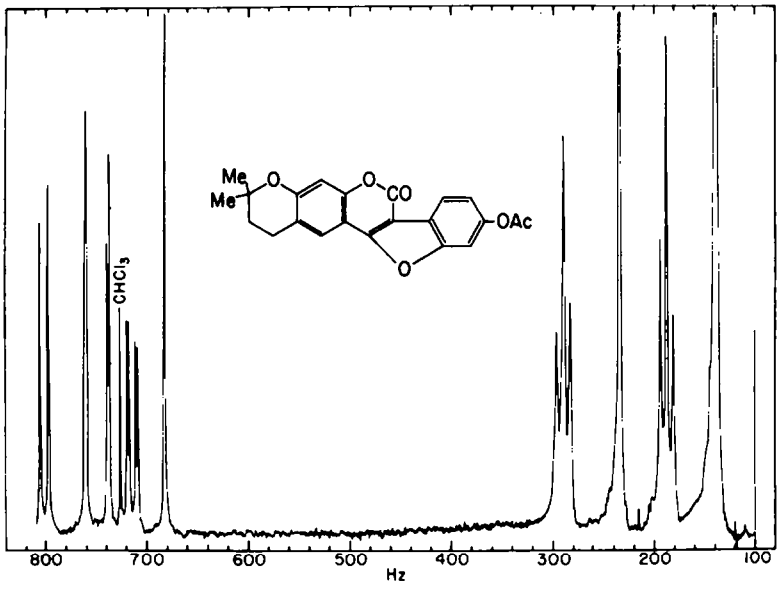
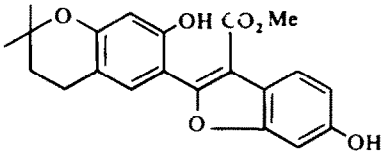


FIG 1. 100 MHz NMR spectrum of isopsoralidin acetate (**20**, R = $COCH_3$) in $CDCl_3$; TMS as internal reference.

to isopsoralidin (**20**, R = H). The properties of this product closely agreed with those described[13,14] for isopsoralidin and its structure was confirmed by the 100 MHz



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NMR spectrum of its acetate (**20**, R = —$COCH_3$), (Fig. 1). The acetoxy group occurred as a singlet at δ 2·35, the *gem*-dimethyl groups as a singlet at δ 1·39 and the methylene groups of the chroman ring as triplets at δ 1·88 and 2·90. The 5 and 8 protons of the A ring occurred as singlets at δ 6·83 and 7·61 while the B ring protons occurred as an ortho-coupled doublet at δ 8·02, J = 8·5 Hz (4′ proton), a meta-coupled doublet at δ 7·39, J = 2 Hz (7′ proton) and a quartet at δ 7·15, J = 2 and 8·5 Hz showing both ortho- and meta-coupling (5′ proton).

The condensation of phenols with appropriate allylic alcohols under mildly acidic conditions as demonstrated above thus appears to be a valid model for the C-alkylation step in the biosynthesis of natural products. Moreover it suggests that a convenient route to 2,2-dimethylchromenes might be via direct condensation of phenols with the corresponding acetylenic alcohol under the same conditions.

EXPERIMENTAL

Condensation of 2-methylbut-3-ene-2-ol with pyrogallol. A soln of pyrogallol (90 g) and 2-methylbut-3-ene-2-ol (45 g) in 5% aqueous citric acid (1500 ml) containing ascorbic acid (7·5 g) was heated on a steam-bath overnight. The resulting mixture was cooled to 0° and the oily ppt separated and taken up in ether. The ether soln was washed with water, dried and the solvent evaporated. The residue was distilled under vacuum to give a colorless oil, b.p. 110–115°/0·1 mm which gave **9** as white needles, m.p. 99–100° on crystallization from Et_2O—30–60° light petroleum, (20·5 g, 21%). (Found: C, 68·3; H, 7·41. Calc. for $C_{11}H_{14}O_3$: C, 68·0; H, 7·27%); 100 MHz NMR spectrum in $CDCl_3$: 6H, δ 1·31, s; 2H, δ 1·74, t, J = 7Hz; 2H, δ 2·66, t, J = 7Hz; 2H, δ 5·66, s, broad; 2H, δ 6·45, s. The diacetate of the chroman **9**, prepared by treatment with Ac_2O and pyridine, crystallized from 30–60° light petroleum as white needles, m.p. 66·5–67·5°. (Found: C, 64·9; H, 6·62. Calc. for $C_{15}H_{18}O_5$: C, 64·7; H, 6·52%); 100 MHz NMR spectrum in $CDCl_3$: 6H, δ 1·29, s; 2H, δ 1·76, t, J = 7 Hz; 3H, δ 2·25, s; 2H, δ 2·75, t, J = 7 Hz; 1H, δ 6·60, d, J = 8 Hz; 1H, δ 6·91, d, J = 8 Hz.

Further distillation gave an orange colored oil, b.p. 160–170°/0·2 mm which could not be crystallized. The oil was dissolved in EtOH (250 ml), conc HCl (25 ml) added and the soln heated under reflux for 2 hr. The mixture was poured into water (1250 ml) and the aqueous soln extracted with Et_2O. The Et_2O extract was washed with water, dried and evaporated to give a brown oil which solidified on standing. Crystallization from 30–60° light petroleum gave **11** as white needles, m.p. 138–140° (17 g, 12%). (Found: C, 73·6; H, 8·45. Calc. for $C_{16}H_{22}O_3$: C, 73·3; H, 8·45%); 100 MHz NMR in $CDCl_3$: 12H, δ 1·37, s; 4H, δ 1·77, t, J = 7 Hz; 4H, δ 2·68, t, J = 7 Hz; 1H, δ 5·34, s; 1H, δ 6·31, s. The dipyran **11** gave a mono-acetate as colorless cubes, m.p. 91–93° (30–60° light petroleum) on treatment with Ac_2O in pyridine. (Found: C, 70·9; H, 7·89. Calc. for $C_{18}H_{24}O_4$: C, 71·0; H, 7·90%); 100 MHz NMR in $CDCl_3$: 12H, δ 1·27, s; 4H, δ 1·73, t, J = 7 Hz; 3H, δ 2·26, s; 4H, δ 2·66, t, J = 7 Hz; 1H, δ 6·60, s.

Condensation of γ,γ-dimethylallyl alcohol with pyrogallol. Pyrogallol (24 g) was condensed with γ,γ-dimethylallyl alcohol (12 g) in 5% aqueous citric acid (400 ml) in the same manner as described for the

reaction with 2-methylbut-3-ene-2-ol. The product was distilled under vacuum to give a colorless oil, b.p. 112–115°/0·1 mm which gave **9** on crystallization from 30–60° light petroleum (6·5 g, 25%).

A second fraction, b.p. 160–180°/0·2 mm, was obtained as a yellow oil which could not be crystallized Treatment with ethanolic HCl gave **11** on crystallization from 30–60° light petroleum (5·5 g, 15%).

Condensation of resorcinol with 2-methylbut-3-ene-2-ol. Resorcinol (90 g) and 2-methylbut-3-ene-2-ol (45 g) were condensed in 5% citric acid soln (1500 ml) in the usual manner. Distillation of the product gave a single fraction, b.p. 145–150°/0·1 mm which crystallized with difficulty from 30–60° light petroleum, giving **12** as white needles, m.p. 71–72° (51·5 g, 55%); 100 MHz NMR in $CDCl_3$: 6H, δ 1·30, s; 2H, δ 1·74, *t*, J = 7 Hz; 2H, δ 2·66, t, J = 7 Hz; 1H, δ 6·30, d, J = 2·5 Hz; 1H, δ 6·35, q, J = 2·5 and 8 Hz; 1H, δ 6·88, d, J = 8 Hz.

Condensation of resorcinol (18 g) with 2-methylbut-3-ene-2-ol (22 g) in 85% phosphoric acid (20 ml), according to the method of Kakhniashvili and Chikhladze[8] gave a colorless oil, b.p. 142–145°/0·1 mm (12·5 g, 43%) shown to be **12** by NMR.

On treatment with *p*-nitrobenzoyl chloride in pyridine **12** gave 7-(*p*-nitrobenzoyloxy)-2,2-dimethylchroman as pale yellow plates, m.p. 122–124° from MeOH (lit. m.p. 126°).[7] (Found: C, 65·8; H, 5·15. Calc. for $C_{18}H_{17}NO_5$: C, 66·05; H, 5·24%).

Condensation of phloroglucinol with 2-methylbut-3-ene-2-ol. Phloroglucinol (90 g) and the alcohol (45 g) were condensed in 5% citric acid soln (1500 ml) in the usual manner. The product was distilled to give a pale yellow oil, b.p. 155–170°/0·2 mm shown by TLC to be a mixture of two compounds. Crystallization from 30–60° light petroleum gave **16** as white needles, m.p. 161–162·5° (18 g, 13%). (Found: C, 73·4; H, 8·38. Calc. for $C_{16}H_{22}O_3$: C, 73·3; H, 8·45%); 100 MHz NMR in $CDCl_3$: 12H, δ 1·29, s; 4H, δ 1·77, t, J = 7 Hz; 4H, δ 2·55, t, J = 7 Hz; 1H, δ *ca* 4·50, broad; 1H, δ 5·92, s.

Further crystallization of the mother liquors from the same solvent gave **15**, m.p. 163–164° (18·8 g, 18·5%); 100 MHz NMR in $CDCl_3$: 6H, δ 1·32, s; 2H, δ 1·32, s; 2H, δ 1·80, t, J = 7 Hz; 2H, δ 2·58, t, J = 7 Hz; 2H, δ 5·92, s; 2H, δ 7·27, s.

Cyclization of 2-(γ,γ-dimethylallyl) phloroglucinol (**18**) *to 5,7-dihydroxy-2,2-dimethylchroman* (**15**). 2-(γ,γ-Dimethylallyl)-phloroglucinol (0·5 g), prepared according to the method of Mitteldorf and Riedl,[11] was dissolved in 5% aqueous citric acid (25 ml) and warmed at 100° on a steam-bath overnight. The soln was cooled, extracted with Et_2O and the solvent evaporated to give a colorless oil which yielded **15** as white needles, m.p. 163–164°, on crystallization from $CHCl_3$ (0·47 g, 94%).

2,2-Dimethyl-6-(ω-methoxyacetyl)-7-hydroxychroman (**22**, R = H). 2,2-Dimethyl-7-hydroxychroman (10 g), ω-methoxyacetonitrile (4·4 g) and anhyd $ZnCl_2$ (5 g) in Et_2O (100 ml) were cooled in an ice-bath and the soln saturated with HCl gas. The mixture was kept at 0° overnight and the solvent decanted from the crystalline ketimine which was dissolved in H_2O (200 ml) and heated on a steam-bath for 30 min. On cooling a yellow oil was obtained which was separated and crystallized from Et_2O—30–60° light petroleum to give 2,2-dimethyl-6-(ω-methoxyacetyl)-7-hydroxychroman (6·7 g, 48%) as colorless prisms, m.p. 111°. The compound gave a red brown color with alcoholic $FeCl_3$. (Found: C, 67·4; H, 7·17. Calc. for $C_{14}H_{18}O_4$: C, 67·2; H, 7·25%); 100 MHz NMR in $CDCl_3$: 6H, δ 1·32, s; 2H, δ 1·77, t, J = 6·5 Hz; 2H, δ 2·69, t, J = 6·5 Hz; 3H, δ 3·46, s; 2H, δ 4·58, s; 1H, δ 6·27, s; 1H, δ 7·37, s.

2,2-Dimethyl-6-(ω-methoxyacetyl)-7-benzyloxychroman (**22**, R = $-CH_2C_6H_5$). A mixture of **22** (R = —H; 2·0 g), benzyl chloride (4·0 ml), KI (1·0 g), K_2CO_3 (6·0 g) and dry acetone (50 ml) was heated under reflux for 3 hr. The mixture was filtered and the filtrate evaporated to give an oil which crystallized from ether–light petroleum to give **22**, (R = $-CH_2C_6H_5$) as glistening prisms, m.p. 113–114° (1·75 g, 65%), which did not give a color with alcoholic $FeCl_3$. (Found: C, 73·9; H, 7·16. Calc. for $C_{21}H_{24}O_4$: C, 74·1; H, 7·11%).

7-Hydroxy-3-methoxy-2-(7-hydroxy-2,2-dimethylchroman-6-yl)-benzopyrylium chloride (**23**, R = H). A soln of 2,4-dihydroxybenzaldehyde (0·81 g) and **22** (R = $CH_2C_6H_5$; 2·0 g), in EtOAc (10 ml) and ether (30 ml) was cooled in an ice-bath, saturated with HCl gas and allowed to stand overnight. Ether (25 ml) was added to precipitate the flavylium salt as a gum, which solidifed as an orange powder on scratching.

The above product (2·51 g) was debenzylated by heating on a steam-bath with glacial AcOH (10 ml) and conc HCl (10 ml) for 1 hr, 10% HCl aq (25 ml) and benzene (10 ml) were added and, after cooling, the crystalline product collected. The flavylium salt was purified by digestion with MeOH (30 ml) containing 10% HCl aq (5 ml) and recrystallization from glacial AcOH—10% HCl aq. The flavylium chloride (**23**, R = H) separated as orange-red needles which darkened but did not melt below 320°. (Found: C, 65·0; H, 5·44. Calc. for $C_{21}H_{21}ClO_5$: C, 64·8; H, 5·45%); λ_{max} (EtOH containing 5% aqueous HCl): 271, 313, 367 and 517 mμ.

Isopsoralidin (**20**, R = H). Aqueous H_2O_2 (30%; 1·0 ml) was added to a soln of **23** (R = H; 0·60 g) in

MeOH (10 ml) and H_2O (5 ml) at 50%. After 10 min conc H_2SO_4 (1·0 ml) was added, the soln was heated on a steam-bath for 30 min and concentrated until crystals began to separate. Isopsoralidin (**20**, R = H) crystallized from aqueous MeOH as needles, m.p. 282° (lit.[13] m.p. 284–287°) (0·10 g, 19%). (Found: C, 71·1; H, 4·84. Calc. for $C_{20}H_{16}O_5$: C, 71·4; H, 4·80%); λ_{max}^{EtOH}: 249, 310 and 352 mμ λ_{max}^{NaOEt}: 274 and 319 mμ.

The *acetate* (**20**, R = —$COCH_3$) crystallized from acetone–MeOH as cream-colored, glistening prisms, m.p. 218–220° (lit.[13] m.p. 220°). The acetate showed an intense blue fluorescence in dil alcoholic solns. (Found: C, 69·5; H, 4·72. Calc. for $C_{22}H_{18}O_6$: C, 69·8; H, 4·80%); λ_{max}^{EtOH}: 243, 305, 343 and 360 mμ; 100 MHz NMR spectrum in $CDCl_3$: Fig 1.

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