Synthesis of 3-Hydroxy-2,3,4,5-tetrahydro-3-methyl[1]benzoxepins by Ring-closure of Isoprenyl Terminal Epoxides [1]

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Terminal olefins (13), obtained from reactions of tertiary chlorides (10) with triphenylmethyl-lithium, were converted into epoxides (14); base-induced ring-closure of the latter gave 2-hydroxymethyl-2-methylchromans (15) and 3-hydroxy-2,3,4,5-tetrahydro-3-methyl[1]benzoxepins (17). Dehydration of the tetrahydrobenzoxepin (17a) furnished dihydro[1]benzoxepins.

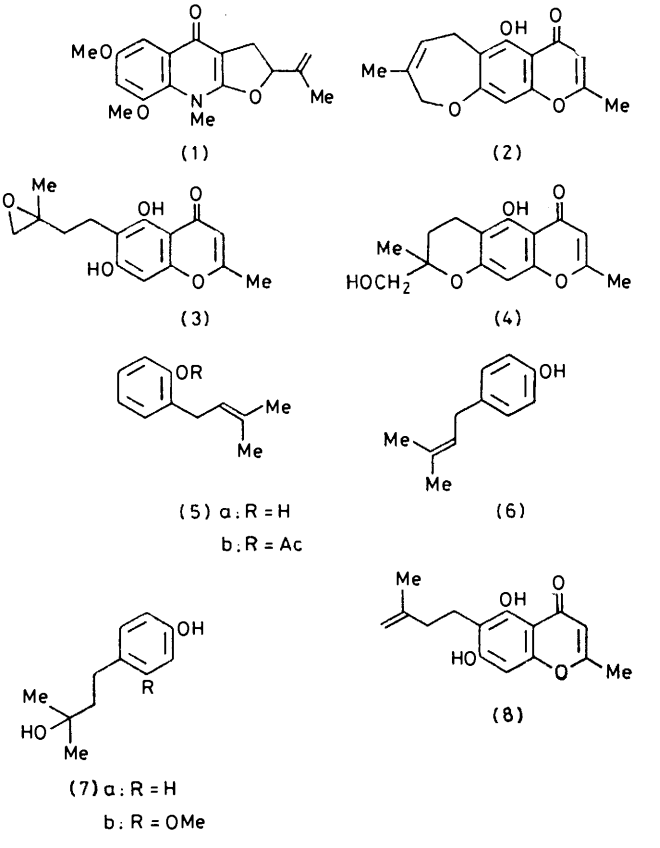
Our interest in aromatic hemiterpenoids containing terminal double bonds and related compounds, *e.g.* the *Ptelea* alkaloid ptelefolone (1) and the natural oxepinochromone, deoxykarenin (2), led us to develop syntheses of the *Ptelea* alkaloids [2] and to study the oxidative cyclisation of isoprenoid terminal olefins.[3] In the latter case, the pyranochromone (4) was the only product isolated from the epoxide (3) and we now report an investigation of this type of ring-closure with simpler systems. Our intention was to prepare oxirans (14) by conversion of the tertiary chlorides (10) into terminal olefins (12), followed by epoxidation and cyclisation (Scheme).

RESULTS AND DISCUSSION

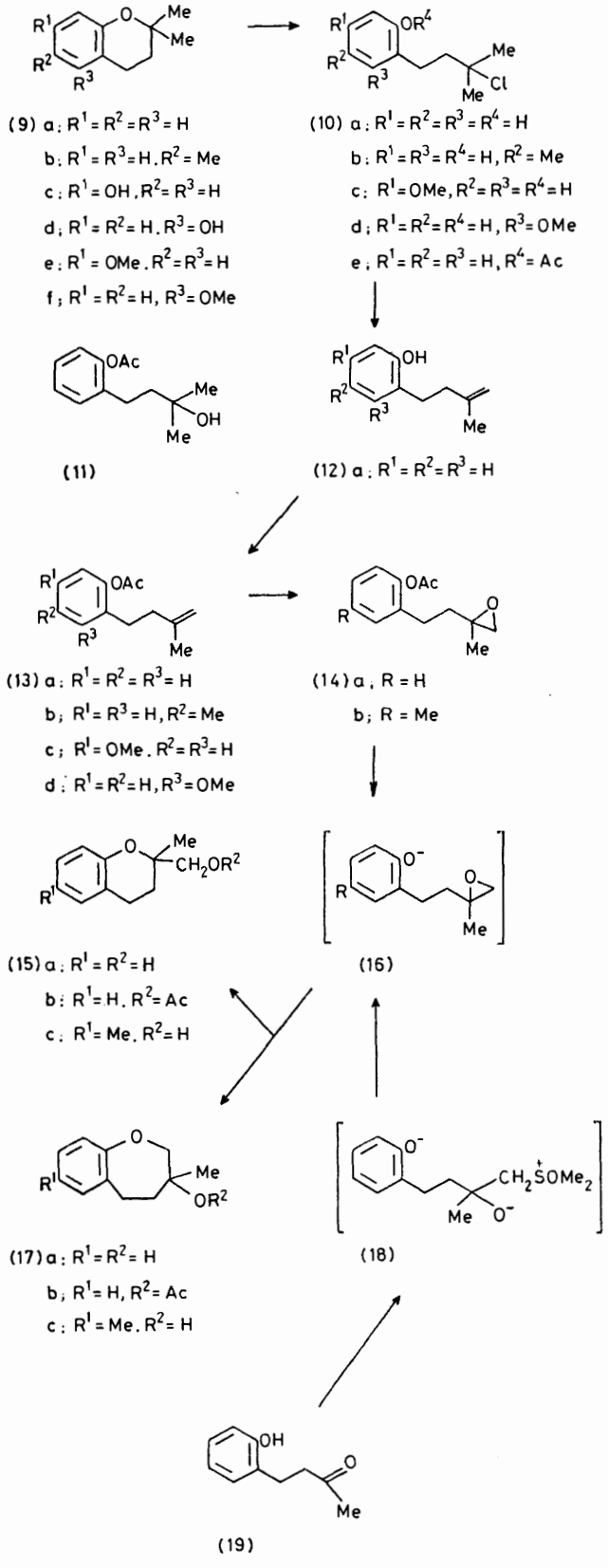
Tertiary Chlorides (10).—Molyneux [4] showed that treatment of 7,8-dimethoxy-2,2-dimethylchroman with boron trichloride resulted in ring-cleavage as well as demethylation to give 2-(3-chloro-3-methylbutyl)-3-hydroxy-4-methoxyphenol, and this reaction seemed promising as a general route to the required tertiary chlorides (10) if the requisite chromans could be obtained readily from phenols. 2,2-Dimethylchroman (9a) can be prepared from phenol by reaction with isoprene,[5] with dimethylallyl pyrophosphate [6] and with butenol derivatives.[7] Substituted 2,2-dimethylchromans were formed in good yield by heating pyrogallol, resorcinol, or phloroglucinol with the readily available 2-methylbut-3-en-2-ol in aqueous citric acid [8] and we decided to apply this reaction to monohydric phenols.

When a mixture of phenol, 2-methylbut-3-en-2-ol, and 5% aqueous citric acid was refluxed, only partial conversion occurred and 2,2-dimethylchroman was not obtained. Two products were isolated from this reaction in *ca.* equal yield and shown by n.m.r. spectroscopy to be (3,3-dimethylallyl)phenols; one, which gave a positive Gibbs test (indicating the absence of a substituent *para* to the phenolic OH group) and was converted by heating into 2,2-dimethylchroman, was the *ortho*-isomer (5a) while the other failed to give a Gibbs test and was apparently the *para*-isomer (6). An acceptable method of preparing 2,2-dimethylchroman (25% yield) involved reaction of phenol and 2-methylbut-3-en-2-ol in 90% orthophosphoric acid at 20 °C; the major product was the *para*-substituted compound (7a), which had been obtained previously from phenol and isoprene.[9] The new procedure was also applied to the synthesis of 2,2,6-trimethylchroman (9b) (85% yield, based on reacted *p*-cresol).

Treatment of *m*-methoxyphenol with 2-methylbut-3-en-2-ol and orthophosphoric acid gave an acidic product (25%), $C_{12}H_{16}O_6$, shown to be the tertiary alcohol (7b) by i.r. and n.m.r. spectroscopy (see Experimental section)



and by its failure to give a positive Gibbs test. Chromatography of the neutral fraction from the reaction furnished two products (24 and 7% yield); the n.m.r. spectra of these compounds were similar and indicated that they were 7- and 5-methoxy-2,2-dimethylchromans, arising from electrophilic substitution at the alternative *ortho*-positions of *m*-methoxyphenol. In order to distinguish between the chromans, we treated resorcinol with 2-methylbut-3-en-2-ol in orthophosphoric acid, a



SCHEME

reaction which is reported to give 7-hydroxy-2,2-dimethylchroman (9c) as the only product.[8] In our hands, the 7-hydroxy-derivative was accompanied by 5-hydroxy-2,2-dimethylchroman (9d) which was distinguished from the 7-isomer by giving a positive Gibbs test. Methylation of the products derived from resorcinol afforded 7-methoxy-2,2-dimethylchroman (9e) and 5-methoxy-2,2-dimethylchroman (9f) (48% and 13%, respectively, based on resorcinol). Comparison with the chromans derived from *m*-methoxyphenol showed that the major product was the 7-methoxy-derivative.

Reaction of the four chromans (9a), (9b), (9e), and (9f) with boron trichloride in methylene chloride at 0 °C, according to the Molyneux procedure,[4] gave the corresponding tertiary chlorides (10; R^4 = H) in excellent yield (88—98%). At ambient temperature, the tertiary chlorides readily evolved hydrogen chloride to form the chroman precursors, and were best stored in ether at 0 °C in the presence of anhydrous potassium carbonate. The tertiary halides were characterised by n.m.r. spectroscopy (see Experimental section) and in the case of 2-(3-chloro-3-methylbutyl)phenol (10a) by acetylation with acetic anhydride and pyridine to give the stable acetate (10e).

Terminal Olefins (13).—Dehydrohalogenation of the tertiary halides, $ArCH_2CH_2C(Cl)Me_2$, promoted by base, normally gives a mixture of olefins, and the ratio is dependent on the steric size of the base.[10] Thus, the use of the hindered base potassium 1,1-diethylpropyl oxide in the chromone series led to a reasonable preparation of the terminal olefin (8), although the separation of the two olefins formed in the reaction was tedious and detracted from the synthesis.[3] We therefore embarked on a study of the dehydrochlorination of the tertiary halide (10a). The compound was refluxed with potassium t-butoxide in t-butyl alcohol, and the mixture of olefins produced was acetylated with acetic anhydride and pyridine in order to prevent cyclisation of the products during isolation. Preparative t.l.c. furnished the isomeric olefins (5b) and (13a), which were characterised by their n.m.r. spectra. The spectrum of the terminal olefin showed a two-proton singlet at τ 5.32 [$-C(Me)=CH_2$], and the trisubstituted olefin showed a two-proton doublet at τ 6.78 ($-CH_2CH=$); these resonances were well separated from other resonances, and their relative intensities were used to determine the composition of mixtures of the acetates (5b) and (13a), and of the phenols (5a) and (12) obtained in elimination reactions. The ratio of the terminal olefin (13a) to the trisubstituted one (5b) formed in the t-butoxide reaction was 1 : 3.7. Reaction of the tertiary chloride with sodium methoxide in boiling methanol and work-up without acetylation gave the olefins (12a) and (5a) in the ratio 1 : 2.7, and with n-butyl-lithium in ether at 20 °C the corresponding ratio was 1 : 1.3. The latter result suggested that treatment of the tertiary chlorides (10) with bulky carbanions in aprotic solvents might furnish a higher proportion of terminal olefins. We accordingly

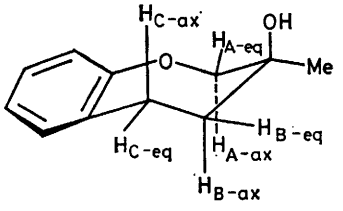
studied the use of triphenylmethyl-lithium, which was generated from triphenylmethane and n-butyl-lithium in tetrahydrofuran–ether. Reaction of this reagent with the tertiary chloride (10a), followed by acetylation, furnished the terminal olefin (13a) in high yield. The trisubstituted olefin (5b) was not formed, but a second product (<5%) was the known tertiary alcohol (11). Application of the elimination reaction to the tertiary chlorides (10b—d) gave as single olefinic products the compounds (13b—d), respectively, which were characterised by n.m.r. spectroscopy. The reaction of tertiary chlorides with triphenylmethyl-lithium is thus a convenient method for the preparation of terminal olefins in this series of compounds.

Ring-closure of the Oxirans (14).—Reaction of the terminal olefin (13a) with *m*-chloroperbenzoic acid in chloroform at 0 °C and separation of the products by preparative t.l.c. gave the epoxide (14a) (89% yield). The structure of the epoxide was indicated by the n.m.r. spectrum, which showed a two-proton singlet at τ 7.54 ($-OCH_2-$) and a three-proton singlet at τ 8.72 [$-C(Me)-O-$]. It was convenient to prepare the epoxide on a larger scale by oxidation of the crude product obtained by reaction of chloride (10a) with triphenylmethyl-lithium, but the epoxide was formed in lower yield and more of the tertiary alcohol (11) was isolated. The 4-methyl-oxiran (14b) was prepared by epoxidation of 4-methyl-2-(3-methylbut-3-enyl)phenyl acetate (13b).

Treatment of the epoxide acetate (14a) with 3M-sodium hydroxide at ambient temperature gave two products, the chroman (15a) (48%) and the [1]benzoxepin (17a) (19%); apparently, hydrolysis of the acetate function resulted in formation and subsequent ring closure of an epoxide anion (16). Under more dilute conditions with sodium hydroxide in aqueous ethanol, the epoxide gave a mixture of chroman and benzo-oxepin, in the ratio of *ca.* 4 : 3. The chroman was characterised as its crystalline toluene-*p*-sulphonate and its structure was established by the n.m.r. spectrum, which showed a finely split doublet at τ 6.50 (CH_2OH) and a three-proton singlet at τ 8.80 (Me). As expected for a primary alcohol, a singlet at τ 5.96 (CH_2OAc) was present in the n.m.r. spectrum of the acetate (15b).

The n.m.r. spectrum of the tetrahydro[1]benzoxepin (17a) was more complex than that of the chroman, and showed multiplets centred at τ 6.34 ($-OCH_2-$), 7.24 ($ArCH_2-$), and 8.25 ($ArCH_2CH_2-$) as well as a singlet at τ 8.86 (Me). A homonuclear INDOR spectrum was recorded for a 300-Hz sweep range, and indicated that the multiplicity was due to long-range coupling between $H_{A\text{-}eq}$ and $H_{B\text{-}eq}$, as well as to vicinal and geminal coupling, *cf.* conformation (20). Monitoring the signals for the protons H_A and for the protons H_B gave the following approximate values for the coupling constants (Hz): $J(H_{A\text{-}eq}–H_{A\text{-}ax})$12, $J(H_{A\text{-}eq}–H_{B\text{-}eq})$2, $J(H_{C\text{-}ax}–H_{C\text{-}eq})$ 15, and the vicinal coupling $J(H_B–H_C)$12 and 3. It is interesting to compare these data with the n.m.r. spectrum of the one tetrahydro[1]benzoxepin [dihydro-(2)] that has been studied previously; [11] in the spectrum of the chromone, the methylene group adjacent to the heterocyclic oxygen function produced one-proton quartets at τ 5.82 and 6.54 with J_{gem} 12 Hz. Reaction of the [1]benzoxepin with acetic anhydride and pyridine furnished the acetate (17b); in accord with this structure, the chemical shift of the low-field signal ($-OCH_2-$) differed little from that in the tertiary alcohol (17a). Dehydration of the hydroxytetrahydro[1]benzoxepin (17a) with thionyl chloride–pyridine gave a mixture of three [1]benzoxepin derivatives, which were shown by g.l.c. analysis to be present in the ratio 73 : 17 : 9. The n.m.r. spectrum of the mixture indicated that the major constituent was the trisubstituted olefin (21), since the most intense signals appeared at τ 4.47 (t, $-CH_2CH=C$), 5.69 (s, $-OCH_2-$), 6.65 (m, $ArCH_2-$), and 8.47 (s, $=C-Me$). The presence of the vinyl ether (22) was shown by the low-field resonance at τ 4.15 ($-O-CH=$); weak signals at τ 5.15 ($=CH_2$) and 6.10 ($-O-CH_2-C=$) suggested that the most minor component was the disubstituted olefin (23).

Reaction of the 4-methyl-epoxide (14b) with base gave the chroman (15c) and the [1]benzoxepin (17c) in a ratio of *ca.* 2 : 1. The isomers were separated by repeated preparative t.l.c.; although insufficient quantities were available for full characterisation, the structures of the compounds were supported by the n.m.r. spectra (see Experimental section). After the completion of this work a high-yield synthesis of 3-hydroxy-2,3,4,5-tetrahydro[1]benzoxepins was reported,[12] involving reaction of dimethyloxosulphonium methylide with 2-(*o*-hydroxyphenyl)alkyl ketones, *cf.* (19), in tetrahydrofuran or in dimethyl sulphoxide; chromans were only minor products of the reactions.



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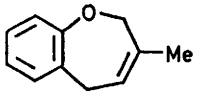

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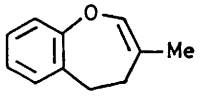

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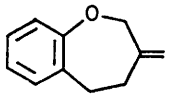

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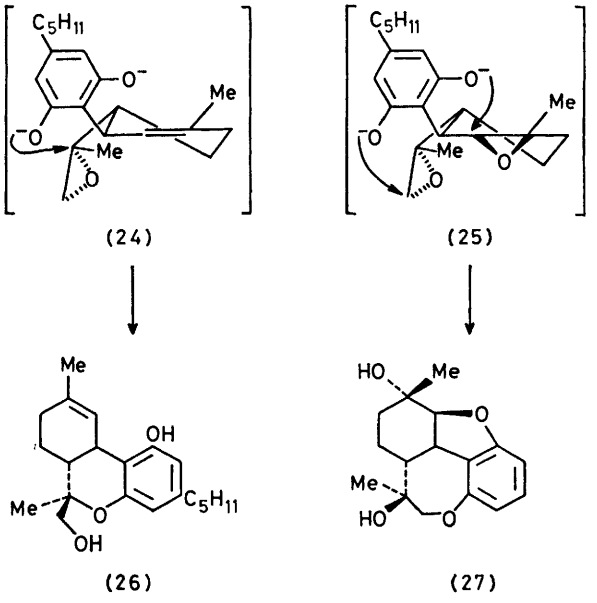
In considering stereo-electronic control of the ring-closure of the epoxy-anions (16), the work of Ulisz *et al.*[13] is particularly significant. These authors showed that the epoxide (24) gave the chroman derivative (26) by nucleophilic attack of phenoxide ion at the more substituted carbon of the epoxide ring. The diepoxide (25), however, was converted into the [1]benzoxepin derivative (27); it was suggested that in this case prior formation of the dihydrofuran ring produced sufficient steric constraint to promote subsequent reaction at the

less substituted carbon of the second epoxide ring. Such steric control is not apparent in the epoxide (16), and 6-*endo*- or 7-*exo*-ring-closure to give a mixture of the chroman (15) and the [1]benzoxepin (17) is to be expected.[14] The ratio of products is likely to be sensitive to medium effects and the high proportion of benzoxepins obtained in the dimethyloxosulphoxonium methylide reaction, which may also involve the epoxide



(24) (25)

(26) (27)

(16), could be due to the use of aprotic solvents; the [1]benzoxepins may also be formed by direct cyclisation of intermediate (18), as proposed previously.[12]

EXPERIMENTAL

N.m.r. spectra were determined with Perkin-Elmer R12A (60 MHz) or R32 (90 MHz) spectrometers ($SiMe_4$ as internal standard), mass spectra with an A.E.I. MS902 instrument, and i.r. spectra with a Perkin-Elmer 457 spectrometer. T.l.c. was carried out with fluorescent silica gel type 7741 with ether–light petroleum (b.p. 40—60 °C) in a ratio of 1 : 9 (system A), 3 : 7 (system B), 1 : 19 (system C), 3 : 17 (system D), 1 : 4 (system E), or 1 : 1 (system F), unless stated otherwise.

Reaction of Phenols with 2-Methylbut-3-en-2-ol.—(a) *Phenol.* 2-Methylbut-3-en-2-ol (44 g) was added during 30 min to a vigorously stirred mixture of phenol (50 g) and orthophosphoric acid (75 ml, 90%) and the mixture was stirred for 12 h at 20 °C. After addition of water (200 ml), the products were obtained by extraction with ether as an oil (82 g), which deposited crystals. Filtration gave 4-(4-hydroxyphenyl)-2-methylbutan-2-ol (7a), m.p. 127—129 °C (needles from chloroform) (lit.,[9] m.p. 130—131 °C); τ [$(CD_3)_2CO$] 2.89—3.32 (4 H, m, Ar-H), 7.34—7.52 (2 H, m, $ArCH_2-$), 8.28—8.44 (2 H, m, $ArCH_2CH_2-$), and 8.76 (6 H, s, CMe_2) (Found: C, 73.1; H, 8.8. Calc. for $C_{11}H_{16}O_2$: C, 73.25; H, 8.9%). Chromatography of the filtrate on alumina and elution with light petroleum (b.p. 40—60°) gave 2,2-dimethylchroman as an oil (2.5 g, 25%), R_F 0.9 (system A, but alumina not silica); τ (CCl_4) 2.50—2.90 (4 H, m, Ar-H), 7.33 (2 H, t, $ArCH_2-$), 8.32 (2 H, t, $ArCH_2CH_2-$), and 8.74 (6 H, s, CMe_2). Further elution gave the tertiary alcohol (7a) (total 64 g, 74%).

A mixture of phenol (5 g), 2-methylbut-3-en-2-ol (4.7 g) and 5% aqueous citric acid (200 ml) was refluxed for 30 min, and extracted with ether. The ether solution was washed with water and saturated sodium chloride solution and evaporated to give an oil (6.8 g). Preparative t.l.c. of a portion (system B) gave 2-(3,3-dimethylallyl)phenol (5a) as an oil (16%), n_D^{19} 1.539 0 (lit.,[9] n_D^{20} 1.539 5); τ ($CDCl_3$) 2.81—3.43 (4 H, m, Ar-H), 4.63 (1 H, t, $-CH{=}CMe_2$), 6.67 (2 H, d, $-CH_2CH{=}$), and 8.25 (6 H, s, CMe_2), giving a positive Gibb's test and converted (by heating at 200 °C for 2 h) into 2,2-dimethylchroman. A fraction of R_F 0.57—0.28 was also obtained, and on further t.l.c. furnished phenol (47%) and 4-(3,3-dimethylallyl)phenol (6) (15%), n_D^{19} 1.539 5 (lit.,[9] n_D^{20} 1.540 0); τ ($CDCl_3$) 2.85—3.31 (4 H, m, Ar-H), 4.68 (1 H, t, $-CH{=}CMe_2$), 6.70 (2 H, d, $-CH_2CH{=}$), and 8.24 (6 H, s, CMe_2) giving a negative Gibb's test.

(b) p-*Cresol.* Reaction of *p*-cresol (5.5 g) with 2-methylbut-3-en-2-ol and orthophosphoric acid as described in (a), and chromatography of the products on alumina afforded 2,2,6-trimethylchroman (9b) [15] as an oil (2.45 g, 27%); τ (CCl_4) 3.25—3.65 (3 H, m, Ar-H), 7.37 (2 H, t, $ArCH_2-$), 7.77 (3 H, s, Ar*Me*), 8.25 (2 H, t, $ArCH_2CH_2-$), and 8.70 (6 H, s, CMe_2) (Found: C, 81.9; H, 9.4. Calc. for $C_{12}H_{16}O$: C, 81.8; H, 9.15%). Further elution gave *p*-cresol (3.7 g, 67% recovery).

(c) m-*Methoxyphenol.* Reaction of *m*-methoxyphenol (33 g) with 2-methylbut-3-en-2-ol and orthophosphoric acid as described in (a), extraction of the ether solution with 1N-sodium hydroxide, and chromatography of the non-acidic fraction on alumina, gave 5-methoxy-2,2-dimethylchroman (9f) as an oil (3.4 g, 7%), n_D^{25} 1.535 2 (lit.,[16] n_D^{20} 1.534 0), R_F 0.77 (system C); τ (CCl_4) 3.05—3.69 (3 H, m, Ar-H), 6.30 (3 H, s, OMe), 7.44 (2 H, t, $ArCH_2-$), 8.34 (2 H, t, $ArCH_2CH_2-$), and 8.75 (6 H, s, CMe_2). Further elution furnished 7-methoxy-2,2-dimethylchroman (9e) as an oil (12.4 g, 24%), n_D^{25} 1.524 7 (lit.,[17] n_D^{25} 1.525 0), R_F 0.69 (system C); τ (CCl_4) 3.14—3.80 (3 H, m, Ar-H), 6.33 (3 H, s, OMe), 7.36 (2 H, t, $ArCH_2-$), 8.30 (2 H, t, $ArCH_2CH_2-$), and 8.72 (6 H, s, CMe_2).

Acidification of the sodium hydroxide solution and extraction with ether gave 4-(4-*hydroxy*-2-*methoxyphenyl*)-2-*methylbutan*-2-*ol* (7b) (12.5 g, 25%), m.p. 127—128 °C (needles from chloroform), R_F 0.2 (system C); $\nu_{max.}$ (KBr) 3 458 and 3 225 cm^{-1}; τ [$(CD_3)_2CO$] 3.00—3.73 (3 H, m, Ar-H), 6.26 (3 H, s, OMe), 7.27—7.53 (2 H, m, $ArCH_2-$), 8.20—8.37 (2 H, m, $ArCH_2CH_2-$), and 8.78 (6 H, s, CMe_2) (Found: C, 68.2; H, 8.5. $C_{12}H_{18}O_3$ requires C, 68.55; H, 8.65%). The compound gave a negative Gibb's test.

(d) *Resorcinol.* Reaction of resorcinol (27 g) with 2-methylbut-3-en-2-ol and orthophosphoric acid as described in (a) gave an oil (34.5 g), shown by t.l.c. to contain two compounds; neither was olefinic (n.m.r.). A portion on alumina was eluted with light petroleum (b.p. 40—60 °C), to furnish 5-hydroxy-2,2-dimethylchroman (9d) m.p. 120—121 °C (prisms from dichloromethane) (lit.,[18] m.p. 122 °C); τ ($CDCl_3$) 3.11—3.72 (3 H, m, Ar-H), 7.38 (2 H, t, $ArCH_2-$), 8.31 (2 H, t, $ArCH_2CH_2-$), and 8.72 (6 H, s, CMe_2) (Found: C, 74.3; H, 7.9. Calc. for $C_{11}H_{14}O_2$: C, 74.15; H, 7.9%), giving a positive Gibb's test. Further elution yielded 7-hydroxy-2,2-dimethylchroman (9c), m.p. 68—69 °C [needles from light petroleum (b.p. 40—60 °C)] (lit.,[17] m.p. 73 °C); τ ($CDCl_3$) 3.05—3.78 (3 H, m, Ar-H), 7.35 (2 H, t, $ArCH_2-$), 8.22 (2 H, t, $ArCH_2CH_2-$), and 8.69 (6 H, s, CMe_2) (Found:

C, 74.0; H, 8.0. Calc. for $C_{11}H_{14}O_2$: C, 74.15; H, 7.9%), giving a negative Gibb's test.

A portion of the crude product (15.2 g) in acetone was refluxed with methyl iodide in the presence of anhydrous *potassium* carbonate; chromatography of the methylated product on alumina and elution with light petroleum (b.p. 40—60 °C) gave 5-methoxy-2,2-dimethylchroman (2.7 g, 13% based on resorcinol) and 7-methoxy-2,2-dimethylchroman (10.2 g, 48% based on resorcinol).

2-(3-*Chloro*-3-*methylbutyl*)*phenols* (10).—The 2-(3-chloro-3-methylbutyl)phenols were prepared from the corresponding 2,2-dimethylchromans by the method illustrated below for compound (10a).

Boron trichloride (4 g) was added in one portion to a solution of 2,2-dimethylchroman (1.78 g) in methylene chloride (50 ml), stirred at 0 °C. After 2 h, the temperature was allowed to rise to 20 °C, water was added slowly, the mixture was filtered, and the methylene chloride solution on evaporation gave 2-(3-chloro-3-methylbutyl)phenol as an oil (2.0 g, 98%), R_F 0.2 (system C); τ (CCl_4) 2.85—3.50 (4 H, m, Ar-H), 4.85 (1 H, br s, OH), 7.23 (2 H, t, $ArCH_2$–), 8.05 (2 H, t, $ArCH_2CH_2$–), and 8.40 (6 H, s, CMe_2). The compound, which decomposed at ambient temperature with loss of hydrogen chloride and formation of the chroman (9a), was stored in ether solution at 0 °C over anhydrous potassium carbonate.

The following were also prepared and characterised by n.m.r. spectroscopy and by t.l.c. (system C): 2-(3-chloro-3-methylbutyl)-4-methylphenol (10b) (88%), R_F 0.2, τ (CCl_4) 3.17—3.59 (3 H, m, Ar-H), 5.03 (1 H, br s, OH), 7.30 (2 H, t, $ArCH_2$–), 7.80 (3 H, s, ArMe), 8.17 (2 H, t, $ArCH_2CH_2$–), and 8.42 (6 H, s, CMe_2); 2-(3-chloro-3-methylbutyl)-3-methoxyphenol (10d) (88%), R_F 0.25; τ (CCl_4) 3.00—3.76 (3 H, m, Ar-H), 4.30 (1 H, br s, OH), 6.47 (3 H, s, OMe), 7.40 (2 H, t, $ArCH_2$–), 8.25 (2 H, t, $ArCH_2CH_2$–), and 8.42 (6 H, s, CMe_2); 2-(3-chloro-3-methylbutyl)-5-methoxyphenol (10c) (88%), R_F 0.15; τ (CCl_4) 3.12—3.90 (3 H, m, Ar-H), 4.27 (1 H, br s, OH), 6.50 (3 H, s, OMe), 7.44 (2 H, t, $ArCH_2$–), 8.27 (2 H, t, $ArCH_2CH_2$–), and 8.42 (6 H, s, CMe_2).

2-(3-*Chloro*-3-*methylbutyl*)*phenyl Acetate* (10e).—2-(3-Chloro-3-methylbutyl)phenol (4.3 g), pyridine (40 ml), and acetic anhydride (20 ml) were kept at ambient temperature for 24 h, and the mixture was evaporated. The residue in ether was washed with aqueous hydrochloric acid, and then evaporated to give the *acetate* as an oil (3.3 g, 64%); τ (CCl_4) 2.57—3.47 (4 H, m, Ar-H), 7.38 (2 H, t, $ArCH_2$–), 7.89 (3 H, s, OAc), 8.27 (2 H, t, $ArCH_2CH_2$–), and 8.52 (6 H, s, CMe_2) (Found: C, 65.3; H, 7.25. $C_{15}H_{17}ClO_2$ requires C, 64.9; H, 7.05%).

2-(3-*Methylbut*-3-*enyl*)*phenyl Acetate* (13a).—A solution of n-butyl-lithium in hexane (14.3 ml, 2.1M) was added during 5 min to a solution of triphenylmethane (4.98 g) in ether (33 ml) and tetrahydrofuran (2 ml) under nitrogen.[19] A solution of 2-(3-chloro-3-methylbutyl)phenol (1.3 g) in ether (10 ml), which had been passed through a cotton-wool plug containing anhydrous potassium carbonate, was then added, and the mixture was stirred for 1 h and evaporated. Acetylation of the residue with acetic anhydride (6 ml) and pyridine (12 ml), dilution with water (500 ml), and extraction with ether gave compound (13a) (1.1 g), shown by n.m.r. spectroscopy to contain 5% of 2-(3-hydroxy-3-methylbutyl)phenyl acetate (11). Preparative t.l.c. (system A) of a sample gave 2-(3-*methylbut*-3-*enyl*)*phenyl acetate* as an oil, R_F 0.42; τ (CCl_4) 2.81—3.20 (4 H, m, Ar-H), 5.32 [2 H, s, $-C(Me)=CH_2$], 7.38 (2 H, t, $ArCH_2$–), 7.84 (2 H, t, $ArCH_2CH_2$–), 7.81 (3 H, s, Ac), and 8.27 [3 H, s, $-C(Me)=CH_2$] (Found: C, 76.4; H, 8.2. $C_{13}H_{16}O_2$ requires C, 76.4; H, 7.85%): and compound (11) as an oil, R_F 0.5, n_D^{18} 1.504 3 (lit.,[20] n_D^{20} 1.505 0); τ (CCl_4) 2.67—3.25 (4 H, m, Ar-H), 7.46 (2 H, t, $ArCH_2$–), 7.82 (3 H, s, Ac), 8.38 (2 H, t, $ArCH_2CH_2$–), and 8.81 (6 H, s, CMe_2).

Reaction of 2-(3-chloro-3-methylbutyl)phenol with potassium t-butoxide in refluxing t-butyl alcohol, followed by acetylation and separation of the products by preparative t.l.c. (system A) gave a mixture of compound (13a) and 2-(3-methylbut-2-enyl)phenyl acetate (5b) as an oil, R_F 0.52, n_D^{25} 1.511 7 (lit.,[20] n_D^{20} 1.512 0); τ (CCl_4) 2.73—3.15 (4 H, m, Ar-H), 4.73 (1 H, t, $-CH=CMe_2$), 6.78 (2 H, d, $-CH_2-CH=$), 7.87 (3 H, s, Ac), and 8.29 (6 H, s, CMe_2). Compounds (13a) and (5b) were shown by n.m.r. spectroscopy to be formed in the ratio 1 : 3.7.

The corresponding phenols (12a) [τ (CCl_4) 5.33 (2 H, s, $=CH_2$)] and (5a) [τ 6.67 (2 H, d, $ArCH_2$–)] were obtained in the ratio 1 : 1.3 when the elimination reaction was carried out with n-butyl-lithium in ether at 20 °C and work-up the reaction without acetylation; with sodium methoxide in refluxing methanol the ratio was 1 : 2.7 (n.m.r.).

2-(2-*Methyloxiran*-2-*yl*)*ethylphenyl Acetate* (14a).—(*a*) A solution of 2-(3-methylbut-3-enyl)phenyl acetate (13a) (68 mg) and *m*-chloroperbenzoic acid (88 mg) in chloroform (5 ml) at 0 °C was stirred for 3 h and evaporated. Preparative t.l.c. (system D) gave the *epoxide* as an oil (65 mg, 89%), R_F 0.3; τ (CCl_4) 2.53—3.0 (4 H, m, Ar-H), 7.44 (2 H, t, $ArCH_2$–), 7.54 (2 H, s, $-OCH_2$–), 7.78 (3 H, s, Ac), 8.30 (2 H, t, $ArCH_2CH_2$–), and 8.72 [3 H, s, $-C(Me)-O-$] (Found: C, 71.25; H, 7.4. $C_{13}H_{16}O_3$ requires C, 70.9; H, 7.3%).

(*b*) A mixture of 2-(3-methylbut-3-enyl)phenyl acetate and triphenylmethane [obtained from 2-(3-chloro-3-methylbutyl)phenol (4.65 g) as described above] was epoxidised as in (*a*). Chromatography of the product on silica and elution with light petroleum (b.p. 60—80 °C) gave triphenylmethane; elution with ether–light petroleum (1 : 4) gave 2-(3-hydroxy-3-methylbutyl)phenyl acetate (11) (2.1 g, 49%) and then epoxide (14a) (1.85 g, 44%).

4-*Methyl*-2-(2-*methyloxiran*-2-*yl*)*ethylphenyl Acetate* (14b).—Reaction of 4-methyl-2-(3-methylbutyl)phenol (10b) (2.6 g) with triphenylmethyl-lithium as described for compound (10a) gave 4-methyl-2-(3-methylbut-2-enyl)phenyl acetate (13b) as an oil; τ (CCl_4) 3.17—3.54 (3 H, m, Ar-H), 5.28 [2 H, s, $-C(Me)=CH_2$], 7.44 (2 H, t, $ArCH_2$–), 7.76 (3 H, s, Ar*Me*), 7.84 (3 H, s, Ac), 8.16 (2 H, t, $ArCH_2CH_2$–), and 8.46 [3 H, s, $-C(Me)=CH_2$]. Reaction of the terminal olefin with *m*-chloroperbenzoic acid in the usual way and preparative t.l.c. (system E) of the product furnished *epoxide* (14b) as an oil, R_F 0.17; τ (CCl_4) 3.05—3.28 (3 H, m, Ar-H), 7.50 (2 H, t, $ArCH_2$–), 7.55 (2 H, s, $-CH_2-O-$), 7.70 (3 H, s, Ar*Me*), 7.77 (3 H, s, Ac), 8.22 (2 H, t, $ArCH_2CH_2$–), and 8.70 [3 H, s, $-C(Me)-O-$] (Found: C, 72.3; H, 7.5. $C_{14}H_{18}O_3$ requires C, 71.8; H, 7.7%).

Reaction of 2-(3-*Chloro*-3-*methylbutyl*)*methoxyphenols with Triphenylmethyl-lithium*.—Reaction of 2-(3-chloro-3-methylbutyl)-3-methoxyphenol (10d) (1 g) as described for compound (10a) gave 2-(3-methylbut-3-enyl)-3-methoxyphenyl acetate (13d) as an oil (0.8 g, 85%); τ (CCl_4) 2.90—3.61 (3 H, m, Ar-H), 5.37 [2 H, s, $-C(Me)=CH_2$], 6.35 (3 H, s, OMe), 7.22—7.49 (2 H, m, $ArCH_2$–), 7.70—8.04 (2 H, m, $ArCH_2CH_2$–), and 8.30 [3 H, s, $-C(Me)=CH_2$].

2-(3-Chloro-3-methylbutyl)-5-methoxyphenol (10c) (1.05 g) similarly gave 2-(3-methylbut-3-enyl)-5-methoxyphenyl acetate (13c) as an oil (0.16 g, 19%); τ (CCl_4) 2.74—3.73

(3 H, m, Ar-H), 5.30 [2 H, s, $-C(Me)=CH_2$], 6.38 (3 H, s, OMe), 7.37 (2 H, t, $ArCH_2-$), 7.84 (2 H, t, $ArCH_2CH_2-$) and 8.29 [3 H, s, $-C(Me)=CH_2$].

Reaction of 2-(2-Methyloxiran-2-yl)ethylphenyl Acetate (14a) *with Sodium Hydroxide.*—A mixture of the epoxide (14a) (187 mg) and 3M-sodium hydroxide (10 ml) was stirred for 3 h, and the products were obtained with ether. Preparative t.l.c. (system F) gave *2-hydroxymethyl-2-methylchroman* (15a) as an oil (73 mg, 48%), R_F 0.25; τ ($CDCl_3$) 2.73—3.27 (4 H, m, Ar-H), 6.50 (2 H, d, *J* 1 Hz, $-CH_2OH$), 7.20 (2 H, t, $ArCH_2-$), 7.92—8.42 (2 H, m, $ArCH_2CH_2-$), and 8.80 (3 H, s, Me); *m/e* 178.099 2 (M^+, 35%; $C_{11}H_{14}O_2$ requires *M* 178.099 4), 147 ($M^+ - CH_2OH$, 100), and 107 ($M^+ - C_4H_7O$, 27) (satisfactory elemental analysis was not obtained): and *3-hydroxy-2,3,4,5-tetrahydro-3-methyl*[1]*benzoxepin* (17a) as an oil (28 mg, 19%), R_F 0.35; τ (CCl_4) 2.9—3.3 (4 H, m, Ar-H), 6.1—6.58 (2 H, m, $-OCH_2-$), 6.83—7.65 (2 H, m, $ArCH_2$), 8.05—8.56 (2 H, m, $ArCH_2CH_2-$), and 8.86 (3 H, s, Me); *m/e* 178.099 0 (M^+, 100%; $C_{11}H_{14}O_2$ requires *M*, 178.099 4), 147(26), 145(26), 121(99), 107(63), and 106(50).

The *toluene*-p-*sulphonate* of the chroman (15a) separated from ethanol as prisms, m.p. 76—77 °C; *m/e* 332.108 1 (M^+, 20%; $C_{18}H_{20}O_4S$ requires *M* 332.108 2) and 147 ($M^+ - C_8H_9O_3S$, 100). A satisfactory elemental analysis was not obtained. Reaction of chroman (15a) with methyl-lithium and acetyl chloride in hexane furnished the *acetate* (15c) as an oil; τ (CCl_4) 2.89—3.39 (4 H, m, Ar-H), 5.96 (2 H, s, $-CH_2O-$), 7.26 (2 H, t, $ArCH_2-$), 7.98 (3 H, s, Ac), 7.98—8.34 (2 H, m, $ArCH_2CH_2-$), and 8.73 (3 H, s, Me) (Found: C, 71.3; H, 7.3. $C_{13}H_{16}O_3$ requires C, 70.9; H, 7.25%).

A small sample of the benzoxepin (17a) was refluxed with acetic anhydride–pyridine for 6 h; preparative t.l.c. (system B) of the product gave an oil, R_F 0.5; τ (CCl_4) 2.29—3.30 (4 H, m, Ar-H), 5.9—6.4 (2 H, m, $-OCH_2-$), 6.90—7.30 (2 H, m, $ArCH_2-$), 7.40—7.86 (2 H, m, $ArCH_2CH_2-$), 8.0 (3 H, s, Ac), and 8.87 (3 H, s, Me), believed to be the acetate (17b).

Slow addition of epoxide (14a) (110 mg) in ethanol (20 ml) to 1M-sodium hydroxide–ethanol (1 : 1, 100 ml) yielded a mixture of the chroman (15a) and the benzoxepin (17a) (70 mg, 79%), in the ratio of *ca.* 4 : 3 (n.m.r.).

Reaction of 4-Methyl-2-(2-methyloxiran-2-yl)ethylphenyl Acetate (14b) *with Sodium Hydroxide.*—Slow addition of epoxide (14b) to aqueous ethanolic sodium hydroxide, as described for epoxide (14a), and preparative t.l.c. (system F) of the products (four times) furnished the chroman (15c), R_F 0.3; τ ($CDCl_3$) 2.77—3.41 (3 H, m, Ar-H), 6.38 (2 H, br s, $-CH_2OH$), 7.21 (2 H, t, $ArCH_2-$), 7.88 (3 H, s, $ArMe$), 7.95—8.44 (2 H, m, $ArCH_2CH_2-$), and 8.76 (3 H, s, Me): and the benzoxepin (17c), R_F 0.29; τ ($CDCl_3$) 2.70—3.06 (m, Ar-H), 5.90—6.50 (m, $-OCH_2-$), 7.27 (t, $ArCH_2-$), 7.84 (s, $ArMe$), 8.10—8.50 (m, $ArCH_2CH_2-$), and 8.80 (s, Me) in the ratio of *ca.* 2 : 1 (n.m.r.).

Dehydration of the Hydroxytetrahydro[1]*benzoxepin* (17a).—An excess of thionyl chloride was added to a solution of the tetrahydrobenzo-oxepin (17a) (186 mg) in pyridine (10 ml). After 1 h, the mixture was evaporated and the residue in ether was washed with aqueous hydrochloric acid and with water, and the solution was evaporated to give an oil (119 mg). The products were examined by g.l.c. using an SE301 (2-m column and had the following retention times (%); 450(9), 571(73), and 905 (17), shown (n.m.r. of the mixture; see text) to be compounds (23), (21), and (22), respectively.

[9/1553 *Received*, 1*st October*, 1979]

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