The Chemistry of Terpenes. Part XV.[1] Some Oxygenated Derivatives of *p*-Menthane

By **W. Cocker,* K. J. Crowley,** and **K. Srinivasan,** Department of Chemistry, Trinity College, Dublin 2

Reaction of (+)-pin-2-ene (1) or (+)-*trans*-sobrerol (*p*-menth-6-ene-*trans*-2,8-diol) (3) with peroxysuccinic acid gives 6,8-epoxy-*cis*-p-menthane-*trans*-1,*trans*-2-diol (5a) and *trans*-*p*-menthane-*cis*-1,*trans*-2,*trans*-6,8-tetraol (6). Similarly, pinol (6,8-epoxy-*p*-menth-1-ene) (7) yields *endo*-2,*endo*-6-dihydroxycineol (1,8-epoxy-*trans*-*p*-menthane-*trans*-2,*trans*-6-diol) (15a) and *trans*-*p*-menthane-*cis*-1,*trans*-2,*cis*-6,8-tetraol (16). Hydrolysis of pinol *trans*-epoxide (*trans*-1,*trans*-2:6,8-diepoxy-*cis*-*p*-menthane) (12) with water also gives the diol (15a), oxidation of which gives 2,6-dioxocineol (1,8-epoxy-*p*-menthane-2,6-dione) (17) and *endo*-2-hydroxy-6-oxocineol (1,8-epoxy-*trans*-6-hydroxy-*p*-menthan-2-one) (18a). Borohydride reduction of compound (17) affords *exo*-2,*exo*-6-dihydroxycineol (1,8-epoxy-*p*-menthane-*cis*-2,*cis*-6-diol) (19a) and the *endo*-2-hydroxy-isomer (20a); the hydroxy-ketone (18a) similarly yields only compound (15a).

Treatment of compound (15a) with hydrogen bromide in acetic acid gives mainly *trans*-2,*trans*-6-diacetoxy-8-bromo-*trans*-*p*-menthane-*cis*-1-ol (23), which with base affords *p*-menth-4(8)-ene-*trans*-1,*cis*-2,*cis*-6-triol (22). With hydrogen bromide in acetic acid, compound (5a) gives *trans*-2,*cis*-6-diacetoxy-8-bromo-*cis*-*p*-menthane *trans*-1-ol (28) and its 1-epimer (29).

Aqueous mineral acids convert the alcohols (5a) and (16) into *trans*-*p*-menthane-*cis*-1,*trans*-2,*trans*-4-*cis*-6-tetraol (27). The alcohols (6), (15a), and (22) similarly give *trans*-*p*-menthane-*cis*-1,*trans*-2,*trans*-4,*trans*-6-tetraol (24).

Treatment of 2,6-dioxocineol (17) with cold, air-free aqueous sodium hydrogen carbonate gives a mixture of *trans*- and *cis*-2,2,6-trimethyl-5-oxotetrahydropyran-3-acetic acids (30; R^1 = Me; R^2 = H). In air these are converted into a 6-hydroxyperoxide, which with base affords 2,2-dimethyl-5-oxotetrahydrofuran-3-acetic acid (terpenylic acid) (13a).

In the course of investigations of the thermal isomerisations of monoterpenoids we required some oxygenated derivatives of *p*-menthane; these are now described. During this work, another group [2] described some of the compounds we have obtained, though in some instances the methods were different.

Oxidation of (+)-pin-2-ene (1) with peroxysuccinic acid [3] gave [*via* (+)-2α,3α-epoxypinane (2), (+)-*trans*-sobrerol (3), and its epoxide (4)] the diol (5a) and the tetraol (6), both in low yield, and with concurrent loss in optical activity. The major products of this reaction were, however, acidic or highly water-soluble and were not investigated.

The diol, 6,8-epoxy-*cis*-*p*-menthane-*trans*-1,*trans*-2-diol † (5a) has long been known [4a] although its stereochemistry has only recently [2] been defined. The *cis*-configuration of its two hydroxy-groups follows from its formation from 6,8-epoxy-*p*-menth-1-ene (pinol) (7) on treatment either with permanganate,[4a] or with osmium tetraoxide.[2] The *trans*-relationship of the tertiary hydroxy-group and the ether bridge was, however, deduced [2] from the n.m.r. signal of the methine 2-proton, which is part of a multiplet of '$J_{tot.}$ = 15 Hz indicative of an axial rather than an equatorial proton.' While the formation, from pinol (7), of the *trans*-1,*trans*-2-diol (5a) rather than the *cis*-1,*cis*-2-diol (8) is preferred on steric grounds, the n.m.r. evidence given [2] is inconclusive since the 2-H signal overlaps the 6-H signal. Furthermore the alternative diol (8), which from an examination of Dreiding models might be expected to approach the upturned boat conformation shown, would also give a similar splitting pattern for its methine 2-proton.

However, we find that the n.m.r. spectrum of the diol monoacetate (5b) [readily hydrolysed to the diol (5a)] shows the 2-H signal as a quartet [5] centred at τ 4·7 ($J_{ax,ax}$ 11, $J_{ax,eq}$ 7 Hz), well separated from the 6-H signal, which appears as a doublet (J 6 Hz) centred at τ 6·0. The axial character of the 2-H is therefore clear.

Further evidence for the structure (5a) is as follows. (*a*) It is oxidised with chromic acid to 6,8-epoxy-*trans*-1-hydroxy-*cis*-*p*-menthan-2-one (9), whose n.m.r. and mass spectra (see Experimental section) and those of its 3,3-dideuterio-derivative support its structure. Reduction of the keto-alcohol (9) with sodium borohydride

† The configurations of the substituents in the *p*-menthane derivatives are assigned relative to the substituted isopropyl group. In the case of the triol (22), the 1-methyl group is used for this purpose. The configurations of compounds (1)—(3) are absolute.

[1] Part XIV, P. H. Boyle, W. Cocker, and D. H. Grayson, *J. Chem. Soc.* (*C*), 1971, 2136.

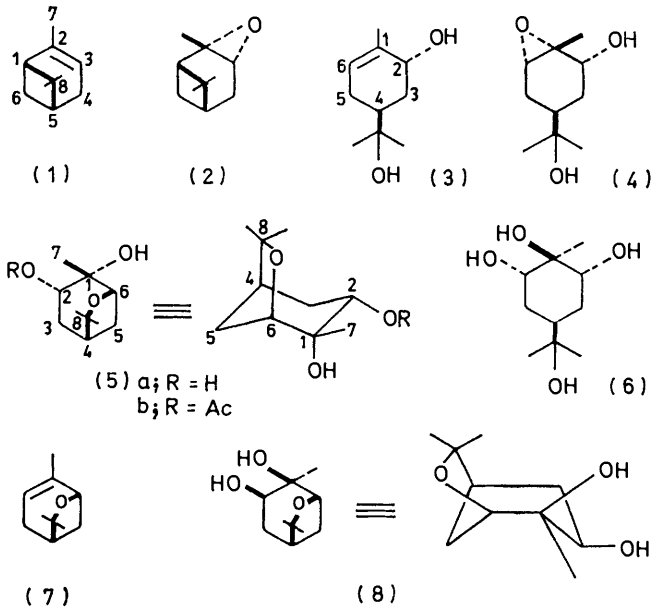
[2] J. Wolinsky, R. O. Hutchins, and J. H. Thorstenson, *Tetrahedron*, 1971, **27**, 753.

[3] R. Lombard and G. Schroeder, *Bull. Soc. chim. France*, 1963, 2800.

[4] (*a*) G. Wagner, *Ber.*, 1894, **28**, 1636; (*b*) G. Wagner and K. Slawinsky, *Ber.*, 1899, **32**, 2064.

[5] R. U. Lemieux and J. W. Lown, *Tetrahedron Letters*, 1963, 1229.

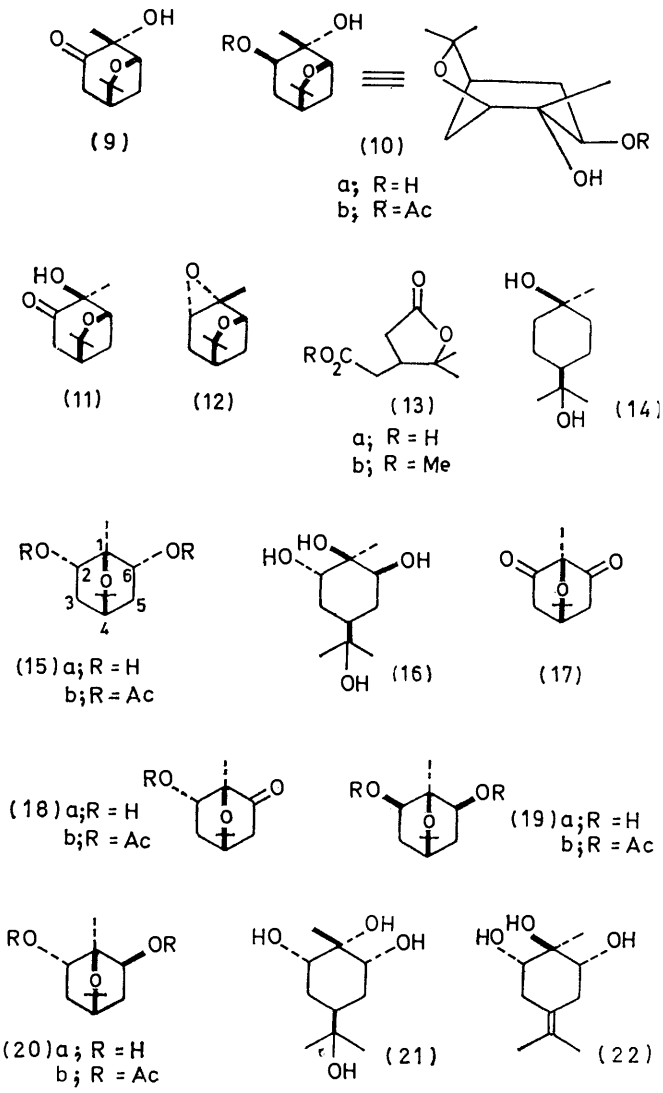
affords a new diol, 6,8-epoxy-*cis*-*p*-menthane-*trans*-1,*cis*-2-diol (10a), as expected from preferential attack on the less hindered side of the molecule, *i.e.* opposite to the ether bridge. If the starting diol were (8), rather than



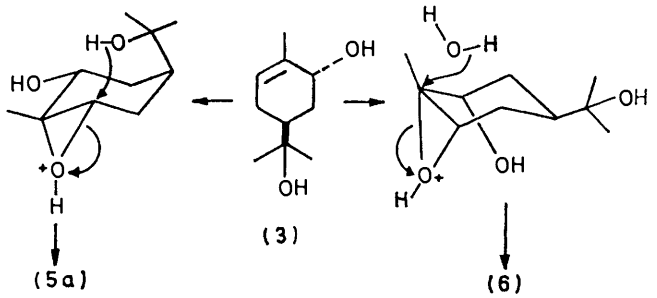
(5a), the former would be regenerated on reduction of the corresponding keto-alcohol (11). The n.m.r. spectrum of the diol (10a) shows incompletely resolved broad multiplets at τ 6·13 and 6·39, but the spectrum of the monoacetate (10b) shows the 6-H signal as a multiplet at τ 6·02 and the 2-H signal as a double doublet at τ 4·9 (J 8 and 5 Hz), which suggests that the molecule is in the upturned boat conformation shown. (*b*) Treatment of (+)-*p*-menth-6-ene-*trans*-2,8-diol [(+)-*trans*-sobrerol] (3), or its racemic form, with aqueous peroxysuccinic acid also gives a mixture of the diol (5a) and the tetraol (6). This reaction, which must involve *trans*-sobrerol epoxide (4), can readily be explained as shown in Scheme 1.

The configuration (2) of (+)-2α,3α-epoxypinane is generally, although not universally [6] accepted. Recent work [7] confirms the configuration (2), and the conversion of this compound (see later) into (+)-*trans*-sobrerol (3), whose configuration is known,[8a,b] supports the assignment. Epoxidation of (+)-*trans*-sobrerol, in accord with the findings of Henbest and Wilson [9] on the directive influence of hydroxy-groups during epoxidation of allylic alcohols, will lead to the configuration (4) for *trans*-sobrerol epoxide. We were unable to prepare this epoxide in a pure state, because of its instability, but reaction of *trans*-sobrerol (3) with buffered perbenzoic acid and immediate treatment of the oily epoxide with cold 1% sulphuric acid gave the tetraol (6). The epoxide as obtained was slowly converted into a mixture of the diol (5a) and its monobenzoate (n.m.r.).

[6] B. A. Arbuzov, V. A. Naumov, and N. V. Alekseer, *Doklady Akad. Nauk S.S.S.R.*, 1964, **155**, 592; D. V. Banthorpe and D. Whittaker, *Chem. Rev.*, 1966, **66**, 643.



The alternative mechanism for the formation of the diol (5a) from *trans*-sobrerol (3), involving initial



SCHEME 1

cyclisation of the latter to pinol (7) followed by epoxidation, is unlikely, since pinol epoxide (12) would have to

[7] R. G. Carlson and J. K. Pierce, *Tetrahedron Letters*, 1968, 6213.

[8] (*a*) H. Schmidt, *Chem. Ber.*, 1953, **86**, 1437; (*b*) S. H. Schroeter and E. L. Eliel, *J. Org. Chem.*, 1965, **30**, 1.

[9] H. B. Henbest and R. A. L. Wilson, *J. Chem. Soc.*, 1957, 1958; H. B. Henbest, *Proc. Chem. Soc.*, 1963, 159.

undergo an abnormal *cis*-opening. In any case the diol (5a) is not the product of hydrolysis of pinol epoxide (see later).

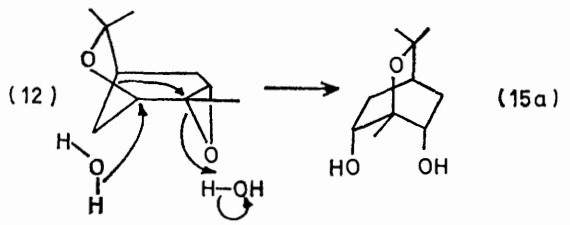
(+)-*trans*-Sobrerol (3) was prepared in 70% yield by hydrolysis with cold aqueous carbonic acid [10] of (+)-2α,-3α-epoxypinane (2). Hydrolysis with boiling water [11] gave a 40% yield of racemic product, whereas cold 1% sulphuric acid or 10% succinic acid gave a 32% yield of largely racemised *trans*-sobrerol.

The tetraol, *trans*-*p*-menthane-*cis*-1,*trans*-2,*trans*-6,8-tetraol (6), m.p. 192—193° (see before), is probably identical with the tetraol of m.p. 193—194° formed by reaction of pin-2-ene with hypochlorous acid followed by alkaline hydrolysis.[4b] Oxidation of the tetraol (6) by Brown and Garg's [12] reagent affords 2,2-dimethyl-5-oxotetrahydrofuran-3-acetic acid (terpenylic acid) (13a), a result which shows that the hydroxy-groups in (6) are at C-1, C-2, C-6, and C-8. The 2- and 6-hydroxy groups were removed by conversion into the bistoluene-*p*-sulphonate followed by reduction with lithium aluminium hydride. The product was *trans*-*p*-menthane-1,8-diol (14) hydrate, thus establishing the *trans*-arrangement of groups at C-1 and C-4. The configurations of the other hydroxy-groups follow from the mechanism suggested in Scheme 1 for the formation of the tetraol (6) from *trans*-sobrerol (3) and from the n.m.r. signals of the 2- and 6-hydroxy-groups (see Table).

Treatment of (±)-pinol (7) with aqueous peroxysuccinic acid affords the recently identified [2] *endo*-2,*endo*-6-dihydroxycineol (1,8-epoxy-*trans*-*p*-menthane-*trans*-2,*trans*-6-diol) (15a) and *trans*-*p*-menthane-*cis*-1,*trans*-2,*cis*-6,8-tetraol (16), m.p. 154—155°. The diol (15a), identical [2] with the compound formerly known as *cis*-pinol glycol,[4a] is also the product of hydrolysis, with water, of pinol *trans*-epoxide (12), although Ginsberg [13] was apparently unable to effect hydrolysis of (12) in this way.

The structure of the diol (15a) is confirmed by reactions detailed later, from the n.m.r. signals of its hydroxy-groups, and from mechanistic considerations.

The formation of the dihydroxycineol (15a) from pinol epoxide (12) by hydrolysis with water can be portrayed

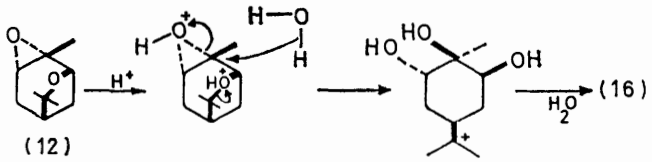


SCHEME 2

as a concerted reaction involving normal *trans*-opening of the 1,2-oxide ring with concurrent migration of the 6,8-oxide bridge and underside attack of water at C-6.

[10] A. J. Durbetaki and S. M. Linder, U.S.P. 2,949,489 (*Chem. Abs.*, 1961, **55**, 608a).
[11] E. A. Klein, U.S.P. 2,815,378 (*Chem. Abs.*, 1958, **52**, 8199e).
[12] H. C. Brown and C. P. Garg, *J. Amer. Chem. Soc.*, 1961, **83**, 2952.

Pinol (7) itself no doubt gives the same epoxide (12) with peroxysuccinic acid, but in presence of the unbuffered stronger acid, an alternative hydrolysis pathway is available, thus giving rise to the tetraol (16). The mechanism suggested in Scheme 3 involves protonation of both oxide bridges, normal opening of the 1,2-epoxide, breakage of the 6,8-bridge with the formation of a tertiary carbonium ion at C-8, and hydration of this ion.



SCHEME 3

Oxidation of dihydroxycineol (15a) with chromium trioxide and sulphuric acid in acetone yielded some 2,6-dioxocineol (1,8-epoxy-*p*-menthane-2,6-dione) (17), but mainly *endo*-2-hydroxy-6-oxocineol (1,8-epoxy-*trans*-6-hydroxy-*p*-menthan-2-one) (18a). This is claimed [2] to be one of the products of reduction of the diketone (17). The ketol (18a) gave a semicarbazone, an acetate (18b), which was readily hydrolysed to the parent alcohol, and a 3,-3-dideuterio-derivative.

Borohydride reduction of the ketol (18a) yielded only dihydroxycineol (15a), indicative of the absence of *endo*-attack by the reducing agent. This is to be expected as a result of hindrance to *endo*-approach of reagent to the carbonyl group by the axial 2-hydroxy-group and the axial 3- and 5-hydrogen atoms. Similar treatment of the diketone (17), which lacks the bulky axial hydroxy-group, results in both *endo*- and *exo*-attack by borohydride, leading to a mixture of *exo*-2,*exo*-6-dihydroxycineol (19a) (32%) and the *endo*-2-hydroxy-isomer (20a) (41%). Earlier workers [2] reduced 2,6-dioxocineol (17) with lithium aluminium hydride and acetylated the product giving a mixture of the acetates (19b) and (20b). Further reduction of the acetate (20b) gave [2] the alcohol (20a). They also reduced the diketone (17) with the bulkier lithium tri-t-butoxyhydrido-aluminate giving *endo*-2,*exo*-6-dihydroxycineol (20a) and *endo*-2-hydroxy-6-oxocineol (18a), but the characteristics of the latter were not described.

Each of the diols (15a), (19a), and (20a) afforded the diketone (17) on oxidation with excess of Brown and Garg's reagent,[12] and with Jones reagent.[14]

The *gem*-methyl groups of the *endo*,*exo*-diol (20a) give rise to two separate methyl resonances, at τ 8·8 and 8·92, whereas the *endo*,*endo*-diol (15a) shows a six-proton singlet at τ 8·8 and the *exo*,*exo*-diol (19a) shows the corresponding singlet at τ 8·79.

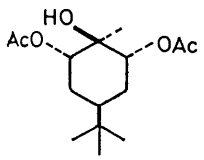
The tetraol (16), which we obtained from pinol (7) by oxidation with aqueous peroxysuccinic acid (see before), is also obtained by the oxidation of (±)-*trans*-sobrerol

[13] A. Ginsberg, *J. Russ. Phys. Chem. Soc.*, 1898, **30**, 681.
[14] K. Bowden, I. M. Heilbron, E. R. H. Jones, and B. C. L. Weedon, *J. Chem. Soc.*, 1946, 39; *cf.* C. Djerassi, R. R. Engle, and A. Bowers, *J. Org. Chem.*, 1956, **21**, 1547.

(3) with potassium permanganate.[15] Thus, if sobrerol gives a normal *cis*-diol with permanganate, the oxidation product will be either (16) or (21). However, the n.m.r. spectrum of the tetraol shows two different doublets at τ 5·65 and 6·07 for the secondary hydroxy-groups, thus excluding structure (21) in which the hydroxy-groups are in similar environments.

Reaction of *endo*-2,*endo*-6-dihydroxycineol (15a) with hydrogen bromide in acetic acid, followed by treatment of the product with alkali, gave the unsaturated triol (22). The presence of the tetrasubstituted double bond in this product was shown by the Raman shift at 1666 cm^{-1} and also by a downfield n.m.r. shift to τ 8·32 of the 9- and 10-methyl signals. Its two secondary hydroxy-groups show a two-proton doublet at τ 5·51, similar to the corresponding two-proton doublet at τ 5·44 for the tetraol (6). Thus the secondary hydroxy-groups of (22) appear to have similar environments to those of (6).

Before treatment with alkali, the product was a



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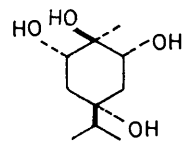

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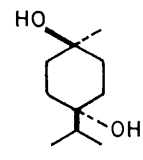

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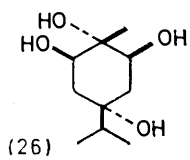

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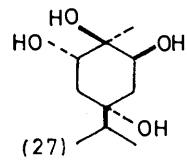

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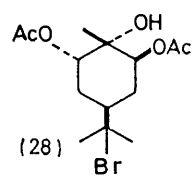

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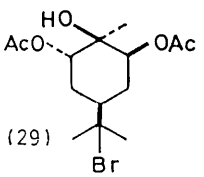

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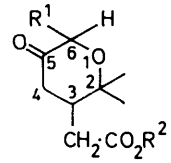
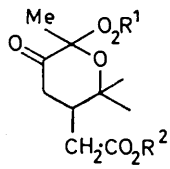
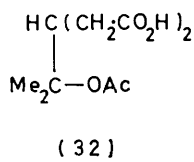


(30)
a; R^1 = *trans*–Me, R^2 = H or Me
b; R^1 = *cis*–Me, R^2 = H or Me

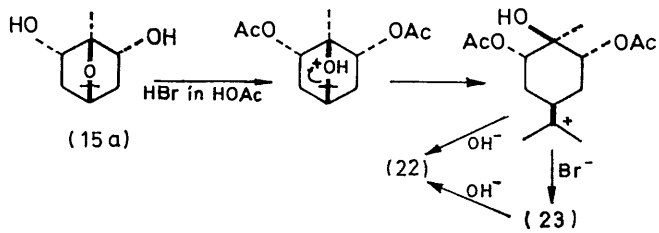


(31)
a; R^1 = R^2 = H
b; R^1 = R^2 = Me



(32)

mixture of acetates and bromo-compounds (n.m.r.), from which the major component, the bromo-hydroxy-diacetate (23) was isolated. The n.m.r. spectrum of this compound showed the presence of a single hydroxy-group (τ 7·47) and two similar secondary acetate groups (τ 7·83). The corresponding methine protons gave rise to a double doublet at τ 5·03 (J 10 and 4·5 Hz). The bromoisopropyl group gave a singlet at τ 8·19 and the 1-methyl group gave a singlet at τ 8·71. The mass spectrum of (23) was also consistent with this structure, which is expected on the basis of the mechanism proposed in Scheme 4.



SCHEME 4

Treatment of compound (23) with 10% aqueous potassium hydroxide gave the unsaturated triol (22), which on hydration with warm dilute sulphuric acid gave a new tetraol, *trans*-*p*-menthane-*cis*-1,*trans*-2,*trans*-4,*trans*-6-tetraol (24). This is also formed by the reaction of *endo*-2,*endo*-6-dihydroxycineol (15a) with aqueous hydrobromic acid and by treatment of the tetraol (6) with warm dilute sulphuric acid or cold aqueous hydrobromic acid. The location of the hydroxy-group at C-4 and the relative configuration at C-1 and C-4 of the new tetraol (24) were deduced by its conversion into *trans*-*p*-menthane-1,4-diol (25); the bis-2,6-toluene-*p*-sulphonate of (24) was reduced with lithium aluminium hydride to compound (25). The secondary hydroxy-groups in the tetraol (24) show a two-proton doublet at τ 5·72. This suggests that these hydroxy-groups are either equatorially oriented as in (26), or, if axial, they are more shielded than the similar secondary hydroxy-groups of the tetraol (6) and triol (22). Normally axial hydroxy-groups resonate further upfield than equatorial hydroxy-groups,[16] but in (6) and (22), the downfield shift comes from strong inter-group hydrogen bonding.[17] However in (24) competitive 2,4-, 2,6-, and 4,6-hydroxy-group hydrogen bonding results in reduced deshielding of the secondary hydroxy-groups, and an upfield shift of their signals takes place relative to those of (6) and (22).

An alternative structure for the tetraol (24) is (26), but this is less likely than (24) on the ground that hydration of the 4,8-double bond in (22) will preferentially afford the more stable *trans*-*p*-menthane. The reactions leading to the formation of (24) are suggested in Scheme 5.

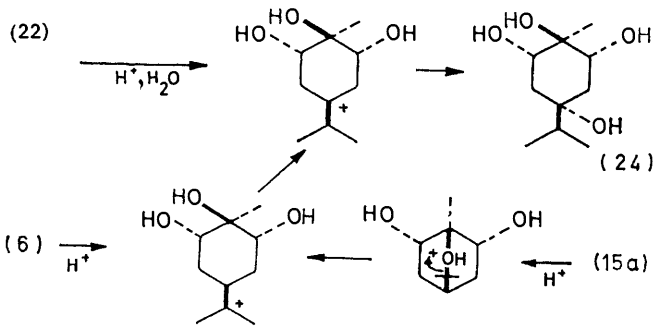
As already mentioned, in the polyhydroxy-compounds (6), (22), and (24), the n.m.r. signals of the axial 2- and 6-secondary hydroxy-groups are shifted downfield [16] by strong hydrogen bonding. A similar downfield shift is also observed in *endo*-2,*endo*-6-dihydroxycineol (15a) relative to its epimers (19a) and (20a), in which the hydroxy-groups are not suitably placed for mutual hydrogen bonding.

Treatment of *trans*-*p*-menthane-*cis*-1,*trans*-2,*cis*-6,8-

[15] A. Ginsberg, *Ber.*, 1896, **29**, 1195.
[16] L. M. Jackman and S. Sternhell, 'Applications of Nuclear Magnetic Resonance Spectroscopy in Organic Chemistry,' Pergamon, Oxford, 2nd edn., 1969, p. 240.
[17] Ref. 16, p. 103.

tetraol (16) with warm dilute sulphuric acid, or 6,8-epoxy-*cis*-*p*-menthane-*trans*-1,*trans*-2-diol (5a) with cold aqueous hydrobromic acid, affords a new tetraol (27), whose structure is assigned by analogy with the similar isomerisation of the tetraol (6).

Treatment of the diol (5a) with hydrogen bromide in acetic acid gave a complex mixture from which two major products were isolated. They gave similar mass spectra, which indicated both to be bromo-hydroxy-diacetates. Their n.m.r. spectra showed 1-methyl signals respectively at τ 8·79 and 8·68, indicative of axial and equatorial methyl groups. On this basis we suggest that the new compounds are respectively *trans*-2,*cis*-6-diacetoxy-8-bromo-*cis*-*p*-menthan-*trans*-1-ol (28) and its 1-epimer (29). In support of these assignments, the n.m.r. spectrum of (28) showed acetoxy-group signals at τ 7·74 and 7·76, and that of (29) at τ 7·82 (6H); the corresponding methine protons gave a complex multiplet, in each case, at τ 4·6—5·3. Both spectra showed a singlet at τ 8·21 [*cf.* the n.m.r. spectrum of (23)], which arises from the $BrCMe_2$ group. The Raman spectra showed the absence of olefinic groups but the presence of the BrC group (535 cm^{-1}). A suggested mechanism for the formation of these compounds is given in Scheme 6, where an unsaturated intermediate is postulated. We were unable to isolate this, but we believe that its formation is likely in view of the formation of the analogous compound (22). However, only carbonium ion intermediates may be involved. Compounds (28) and (29)



SCHEME 5

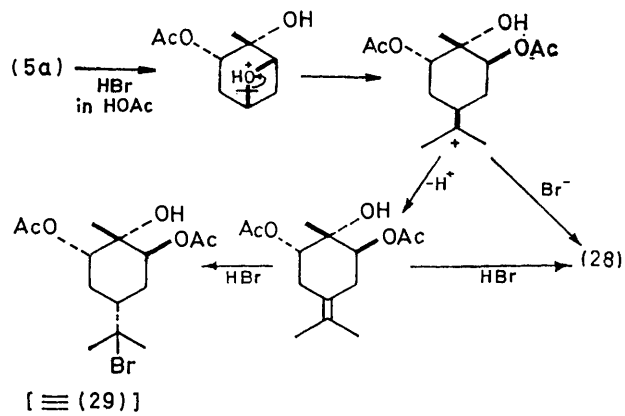
are, in fact, slowly interconvertible (t.l.c.) in the presence of lithium bromide, or hydrogen bromide, in acetic acid. The formation of (29) involves an inversion at C-4.

We now return to the chemistry of 1,8-epoxy-*p*-menthane-2,6-dione (2,6-dioxocineol) (17). At an early stage in our work we found that this diketone dissolves slowly in cold aqueous sodium hydrogen carbonate. Its i.r. spectrum shows two distinct carbonyl stretching bands, characteristic of 1,3-dicarbonyl compounds,[18] and it affords a bis-2,4-dinitrophenylhydrazone. Its n.m.r. spectrum is unusual for such a symmetrical structure, in that it shows a complex five-proton multiplet at τ 6·7—7·9. Its 3,3-dideuterio-derivative, prepared by oxidation

[18] L. J. Bellamy, 'Advances in Infrared Group Frequencies,' Methuen, London, 1968, p. 130.

[19] J. K. M. Saunders and D. H. Williams, *Chem. Comm.*, 1970, 422.

of the 5,5-dideuterio-derivative of *endo*-2-hydroxy-6-oxocineol (18a) shows a similar three-proton multiplet. The complex multiplet is, however, simplified by progressive additions of tris(dipivaloylmethanato)europium-(III),[19] which produce a faster downfield shift of a broadened four-proton AB quartet than of the broad



SCHEME 6

singlet arising from H-4. In the absence of the europium chelate these signals are centred on τ 7·3 and 7·5, respectively. In the AB quartet, J_{AB} is about 20 Hz and $\nu_A - \nu_B = 38$ Hz, and the relative intensities of the inner and outer lines are in agreement with those expected (2 : 5 : 5 : 2) from these figures.

Alkali-catalysed ring opening of cyclohexane-1,3-diones readily takes place, especially when they are 2,2-disubstituted.[20] In fact, the dione (17) dissolved slowly in cold but rapidly in hot aqueous sodium hydrogen carbonate. Methylation of the product obtained after dissolving a test portion of the diketone (17) in alkali, and examination of the ester product by g.l.c. coupled with mass spectrometry, unexpectedly revealed the formation of methyl 2,2-dimethyl-5-oxo-tetrahydrofuran-3-acetate (13b). However, when a solution of sodium hydrogen carbonate made in freshly boiled water was used, an acidic product was formed, which on esterification with diazomethane gave a mixture of esters (30a and b; R^2 = Me), eluted from the g.l.c. column in this order, with slight overlap of the peaks. The mixture of esters showed $\lambda_{max.}$ 293 nm (log ε 1·48) and $\nu_{max.}$ 1730 cm^{-1} (ketone and ester), and its n.m.r. spectra in deuteriochloroform and in [$^2H_5$]-pyridine are in accord with the structures assigned (30a and b; R^2 = Me). The two esters, fed *via* g.l.c. into the mass spectrometer, show virtually identical spectra, including peaks at *m/e* 214 (M^+, 10%), 199 (M^+ — Me), and 182 (M^+ — MeOH); slight differences appeared in the spectra of deuteriated analogues owing to different rates of deuteriation.

The less polar (g.l.c.) ester is tentatively assigned the *trans*-configuration (30a; R^2 = Me) since it was usually

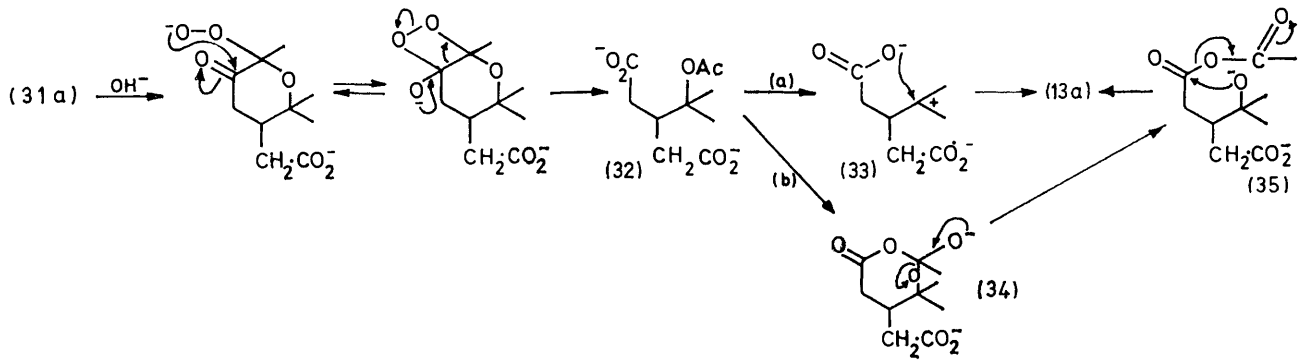
[20] H. Stetter, 'Newer Methods of Preparative Organic Chemistry,' ed. W. Forest, Academic Press, New York, 1963, vol. 2, p. 71.

predominant in a large number of small scale experiments done under varying conditions where equilibration was possible.

When the dione (17) was hydrolysed with sodium hydrogen carbonate in water containing dissolved oxygen and the product was methylated, the mixture of esters (30a and b; R^2 = Me) was obtained along with another product which we believe to be the peroxide (31b). The latter was formed in greater amount when the mixture of esters was left as a thin film on glass and the product then methylated, and in 50% yield (g.l.c.) on passing air through an aqueous methanolic solution of the esters, containing 1% sodium hydroxide, followed by methylation.

The peroxy-ester (31b) showed $\lambda_{max.}$ 295 nm (log ε 1·9) and $\nu_{max.}$ 1730—1740 cm^{-1} (ester and ketone). Its n.m.r. spectrum ([$^2H_5$]pyridine) had signals at τ 6·35 (6H, s, CO_2Me and O_2Me), 7·3—7·6 (4H), 8·12 (3H, s, MeCO), and 8·52 (6H, s, Me_2C). Its mass spectrum gave signals at 245 (M^+ — Me), 229 (M^+ — MeO), and 217 (M^+ — Me_2CH) amongst others. The spectra are in accord with the proposed structure (31b). The enhanced intensity of the keto-group u.v. absorption is similar to that observed for α-ketols.[21]

Ketones with a free α-hydrogen atom are known to be readily autoxidised in presence of base giving α-peroxy-compounds, which are decomposed to form keto-acids or ketones and acids.[22-25] Ethers also undergo autoxidation at the α-carbon atom, though by a free-radical mechanism. The dione (17) has both these features.



SCHEME 7

N.m.r. spectra of alcohols in [$^2H_6$]dimethyl sulphoxide (τ values; coupling constants in Hz)

Compound	1-OH	2-OH	6-OH	2-H	6-H	7-Me	8-OH	Me_2C
(3)		5·51 (d, *J* 6)		6·12(m)	4·5(m)	8·29(m)	6·01(s)	8·95(s)
(6)	5·78(*ax*)(s)	5·44(*ax*) (d, *J* 6)	5·44(*ax*) (d, *J* 6)	6·55(*eq*)(m)	6·55(*eq*)(m)	8·78(*eq*)(s)	6·15(s)	8·99(s)
(14)	6·17(*ax*)(s)					8·92(*eq*)(s)	6·05	8·97(s)
1-Epimer of (14)	5·83(*eq*)(s)					8·94(*ax*)(s)	6·03	8·98(s)
(15a)		5·16(*ax*) (d, *J* 7)	5·16(*ax*) (d, *J* 7)	6·1	6·5	8·85(s)		8·88(s)
(16)	6·39(s)	6·07(*ax*) (d, *J* 4)	5·65(*eq*) (d, *J* 5)	6·55(*eq*)(m)	6·55(*ax*)(m)	8·87(*eq*)(s)	6·16	8·98(s)
(19a)		5·62(*eq*) (d, *J* 5)	5·62(*eq*) (d, *J* 5)	6·3	6·9	9·07(s)		8·79(s)
(20a)		5·77(*ax*) (d, *J* 5)	5·34(*eq*) (d, *J* 6)	6·0	6·7	9·04(s)		8·8(s); 8·92(s)
(22)	5·74(s)	5·51 (d, *J* 4·5)	5·51 (d, *J* 4·5)			8·92(s)		8·32(s)
(24)	5·91(*ax*)(s)	5·72(*ax*) (d, *J* 4·5)	5·72(*ax*) (d, *J* 4·5)	6·65	6·9	9·06(s)	4-OH 5·91(s)	8·94
(27)	5·97(s)	5·79(*ax*) (d, *J* 4)	5·79(*eq*) (d, *J* 4)			9·03(s)	4-OH 5·97(s)	8·96(s)

The methylation of hydroperoxides also readily occurs.[26] The formation of the acid (13a) from the dione (17) can be envisaged as taking place *via* the keto-acids (30a and b; R^2 = H), the hydroperoxide (31a), and the acetate (32). The last can give the acid (13a) by one of the routes shown in Scheme 7.

The hydrolysis of the tertiary acetate (32) may take place by a $B_{AL}1$ mechanism (sequence a) requiring

[21] R. C. Cookson and S. H. Dandegaonker, *J. Chem. Soc.*, 1955, 352.
[22] W. Pritzkow, *Chem. Ber.*, 1955, **88**, 572.
[23] F. G. Bordwell and A. C. Knipe, *J. Amer. Chem. Soc.*, 1971, **93**, 3416.
[24] E. P. Kohler and R. B. Thompson, *J. Amer. Chem. Soc.*, 1937, **59**, 887.
[25] E. J. Bailey, D. H. R. Barton, J. Elks, and J. F. Templeton, *J. Chem. Soc.*, 1962, 1578.
[26] A. Rieche, *Ber.*, 1929, **62**, 218.

neutral or mildly basic conditions,[27] such as are present in cold sodium hydrogen carbonate, giving the ion (**33**). The tetrahydrofuran-3-acetate may then be formed directly by attack of carboxylate on this carbonium ion. Alternatively and more likely, as in sequence (b), attack of carboxylate on the acetoxy-group can lead *via* the intermediate (**34**) (*cf.* ref. 28), to the mixed anhydride (**35**), which on ring closure will yield tetrahydrofuran-acetate, or on hydrolysis and acidification will yield the corresponding acid (**13a**).

In the Table we give a list of n.m.r. signals for a series of *p*-menthane alcohols.

EXPERIMENTAL

I.r. spectra were measured for liquid films (L) or Nujol mulls (N). N.m.r. and u.v. spectra were measured for solutions in [^{2}H]chloroform and ethanol, respectively, unless otherwise stated. Hydroxy-proton assignments for compounds in water-immiscible solvents were invariably checked by deuterium oxide exchange. Mass spectra were measured on a Hitachi–Perkin-Elmer R.M.S. 4 instrument with a Perkin-Elmer F11 g.l.c. attachment equipped with a Carbowax (15 : 85) 20M column. Detailed mass and i.r. spectral data are given in Supplementary Publication No. SUP 20425 (24 pp., 1 microfiche).*

(+)-2α,3α-*Epoxypinane* (2).—A mixture of (+)-pin-2-ene (1) {*ca.* 99% pure by g.l.c., $[\alpha]_D^{20}$ +17·03° (*c* 0·28 in $CHCl_3$)} (80 g), peracetic acid [acetic anhydride (100 g); hydrogen peroxide (30%; 100 ml)], and sodium acetate (100 g) was kept at 5° for 38 h. Excess of acetic anhydride was decomposed by stirring with 10% sodium hydroxide at 50—55°. The epoxide (2) was fractionated in a spinning-band column and collected as an oil (47·6 g), b.p. 69·5—73° at 12 mmHg, $[\alpha]_D^{20}$ +46·24° (*c* 0·19 in $CHCl_3$).

(+)-trans-*Sobrerol* (p-*Menth*-6-*ene*-trans-2,8-*diol*) (3).—(+)-2α,3α-Epoxypinane (2) (54 g) was stirred for 1 h with water (200 ml) containing solid carbon dioxide (12 g).[10] The solid product was collected and dried at 20° and 12 mmHg giving (+)-*trans*-sobrerol (3) (42·8 g), m.p. 136—141°, $[\alpha]_D^{20}$ +94° (*c* 0·44 in $CHCl_3$) (lit.,[8a] m.p. 149°, $[\alpha]_D$ +150°), τ 4·46 (1H, m, HC=C), 6·0 (1H, m, C*H*·OH), 7·91 (2H, s, OH), 8·23br (3H, s, MeC=C), 8·85 (6H, d, *J ca.* 2 Hz, Me_2C), τ [$(CD_3)_2SO$] 4·5 (1H, m, HC=C), 5·51 (1H, d, *J* 6 Hz, CH·O*H*), 6·01 (1H, s, Me_2C·OH), 6·12 (1H, m, C*H*·OH), 8·29 (3H, m, MeC=C), and 8·95 (6H, s, Me_2C), *m/e* 152 (M^+ — H_2O, 14%), 137 (16), and 123 (2). Hydrolysis of the epoxide by refluxing with distilled or deionised[11] water gave (±)-sobrerol (40%), m.p. 130—131° (lit.,[8a] 136°). Hydrolysis with cold 1% sulphuric or aqueous 10% succinic acid afforded sobrerol of low optical purity ($[\alpha]_D^{20}$ +13·2° [*c* 0·29 in $CHCl_3$]) in 32% yield.

(±)-*Pinol* (6,8-*Epoxy*-p-*menth*-1-*ene*) (7).—(±)-Sobrerol (1 g) was heated and vigorously stirred at 60—65° for 1 h with 1% sulphuric acid (25 ml). The product was collected in light petroleum, giving pinol (0·66 g) (95% pure by g.l.c.), τ 4·83 (1H, m, HC=C), 6·05br (1H, d, HCO), 8·32 3H, d, MeC=C), 8·71 and 8·81 (6H, 2s, Me_2CO), *m/e* 152 (M^+, 13%), 137 (M^+ — Me, 22), and 94 (30).

(±)-*Pinol* trans-*Epoxide* (trans-1,trans-2:6,8-*Diepoxy*-cis-p-*menthane*) (12).—A mixture of pinol (7) (1·1 g), perbenzoic acid [from benzoyl peroxide[29] (5 g)] in chloroform (30 ml), and sodium benzoate (2·4 g) was stirred at 0° for 3 h and at 15° for 12 h. The epoxide (99% pure by g.l.c.) obtained by work-up in the usual way, had b.p. 81° at 13 mmHg (lit.,[4] 92—93° at 16 mmHg; lit.,[30] 61° at 1·5 mmHg), τ 5·86br (1H, d, HCO), 7·12 (1H, m, CH·C·O), and 8·66, 8·74, and 8·84 (9H, 3s, Me_2C and MeC), *m/e* 168 (M^+, 10%), 153 (M^+ — Me, 13), and 140 (4).

6,8-*Epoxy*-cis-p-*menthane*-trans-1,trans-2-*diol* (5a) *and* trans-p-*Menthane*-cis-1,trans-2,trans-6,8-*tetraol* (6).—(*a*) Freshly distilled (+)-pin-2-ene (23·8 g) was added dropwise to a vigorously stirred solution of peroxysuccinic acid[3] [from succinyl monoperoxide (50 g)] in water (150 ml) kept at 50—55° during 3 h. The mixture was basified with solid sodium carbonate, left for 15 h, then extracted continuously † for 6 days with ethyl acetate. The semi-solid product was crystallised from ethyl acetate and further separated by hand picking. The diol (5a) consisted of cubes (1·08 g), m.p. 125—126° (lit.,[2,4] 127—129°), τ 6·08 (2H, m, HCOR superimposed on C*H*·OH), 7·24 (2H, d on s, OH), 8·66 (3H, s, MeCO), and 8·73 and 8·81 (6H, 2s, Me_2CO), *m/e* 186 (M^+, 2%), 171 (M^+ — Me, 1·2), and 168 (M^+ — H_2O, 10) (Found: C, 64·4; H, 9·9. Calc. for $C_{10}H_{18}O_3$: C, 64·5; H, 9·7%). This diol (5a) was also obtained in 53% yield when pinol was oxidised with potassium permanganate, and, after the reported[2] work-up, the product was extracted with ethyl acetate. The low yield (3·3%) previously reported[2] is presumably a result of the low solubility of the diol in hexane used for its extraction. The *acetate* (5b), made in benzene with acetyl chloride and pyridine was obtained as plates (from light petroleum–ether), m.p. 96—97°, τ (C_6D_6) 4·7 (1H, q, $J_{ax,ax}$ 11, $J_{ax,eq}$ 7 Hz, C*H*·OAc), 6·0 (1H, d, *J* 6 Hz, HCO), 8·03br (1H, s, OH), 8·29 (3H, s, $MeCO_2$), and 8·61, 8·78, and 8·95 (9H, 3s, 3Me), *m/e* 228 (M^+, 0·75%), 168 (M^+ — AcOH, 34), and 153 [M^+ — (Me + AcOH), 4·5] (Found: C, 63·1; H, 8·75. $C_{12}H_{20}O_4$ requires C, 63·1; H, 8·8%). Hydrolysis of the acetate with aqueous methanolic 10% potassium hydroxide yielded the diol (5a) (mixed m.p., i.r. spectrum).

The *tetraol* (6) was obtained as an amorphous solid (0·15 g), m.p. 192—193°, τ (Me_2SO) 5·44 (2H, d, *J* 6 Hz, OH), 5·78br (1H, s, OH), 6·15br (1H, s, OH), *ca.* 6·55 (2H, m, C*H*·OH), 8·78 (3H, s, MeCO), and 8·99 (6H, s, Me_2C), *m/e* 186 (M^+ — H_2O, 3%), 168 (M^+ — $2H_2O$, 1), and 109 (32) (Found: C, 59·0; H, 10·3. $C_{10}H_{20}O_4$ requires C, 58·8; H, 9·9%).

(*b*) A solution of sobrerol (0·57 g) in chloroform (5 ml) was added dropwise to a stirred mixture of perbenzoic acid [from benzoyl peroxide (5 g)] and sodium benzoate (2·4 g) in chloroform (30 ml) kept at 0°. The epoxide was recovered in the usual way and stirred for 1 h at 20° with 1% sulphuric acid (25 ml). The mixture was continuously extracted for 5 days with ethyl acetate, giving the tetraol (6), m.p. and mixed m.p. 192—193°.

(*c*) Oxidation of sobrerol (7 g) at 40—45° with a solution of peroxysuccinic acid [from succinoyl monoperoxide (18 g)] in water (50 ml) gave a mixture of diol (5a) (3·97 g) and tetraol (6) (1·31 g).

* For details of Supplementary Publications see Notice to Authors No. 7 in *J. Chem. Soc.* (*A*), 1970, Issue No. 20.

† The tetraols were sparingly soluble in most organic solvents. Boiling ethyl acetate was the best solvent.

[27] C. K. Ingold, 'Structure and Mechanism in Organic Chemistry,' Bell, London, 1969, p. 1138.

[28] M. L. Bender, *Chem. Rev.*, 1960, **60**, 53 (the authors thank a referee for notifying them of this reference).

[29] G. Braun, *Org. Synth.*, 1941, Coll. Vol. I, p. 431.

[30] K. Piatkowski and H. Kuczynski, *Roczniki Chem.*, 1961, **35**, 239, 1579 (*Chem. Abs.*, 1962, **57**, 2259c).

Conversion of the Tetraol (6) *into* trans-p-*Menthane*-1,8-*diol* (14) *Hydrate*.—A mixture of the tetraol (6) (0·2 g), toluene-*p*-sulphonyl chloride (0·42 g), and pyridine (3 ml) was set aside for 5 days. Pyridine was removed under reduced pressure, water (5 ml) was added, and the product was extracted with ethyl acetate. The extract was washed with water (3 × 5 ml), dried, and evaporated under reduced pressure. The residual gum (0·43 g), in ether (15 ml), was refluxed for 2 h with lithium aluminium hydride (0·2 g). After the usual work-up, the product was crystallised from ethyl acetate–light petroleum giving the diol (14) hydrate identical with an authentic specimen.

6,8-*Epoxy*-trans-1-*hydroxy*-cis-p-*menthan*-2-*one* (9).—A solution of sodium dichromate dihydrate (0·6 g) in sulphuric acid (0·5 ml) was diluted to 3 ml,[12] and added at 0° to a stirred solution of the diol (5a) (0·55 g) in ether (5 ml). Stirring was continued at 15° for 48 h; the ether layer was separated, washed with 5% sodium hydrogen carbonate and water, dried, and evaporated. This left a semi-solid (0·22 g) which was chromatographed on silica and eluted with light petroleum–ether (3 : 1). The *ketol* (9) (0·15 g), crystallised from ethyl acetate, had m.p. 72°, τ 5·96 (1H, m, HCO), 7·41 (2H, m, CH_2·CO), 7·45 (1H, s, OH), 8·66 (3H, s, MeC), and 8·77 and 8·83 (6H, 2s, Me_2C), *m/e* 184 (M^+, 12%), 166 ($M^+ - H_2O$, 1), and 141 ($M^+ - Me_2CH$, 1) (Found: C, 65·2; H, 9·0. $C_{10}H_{16}O_3$ requires C, 65·2; H, 8·75%). Its 3,3-dideuterio-derivative was prepared by shaking a solution of the ketol (9) in [$^2H_4$]methanol with a drop of sodium deuterioxide in deuterium oxide for 0·5 h. The product lacked the n.m.r. signal at τ 7·41 shown by (9); it showed *m/e* 186 (M^+, 4%), 168 ($M^+ - H_2O$, 0·7), and 143 ($M^+ - Me_2CH$, 0·6).

6,8-*Epoxy*-cis-p-*menthane*-trans-1,cis-2-*diol* (10a).—A solution of the ketol (9) (64 mg) and sodium borohydride (10 mg) in methanol (1 ml) was kept for 2 h and worked up in the usual way. The *diol* (10a) was obtained as fine needles (from ethyl acetate–light petroleum), m.p. 96·5°, τ 6·13 (1H, m, HCO), 6·39 (1H, m, C*H*·OH), 7·39 (1H, d, *J* 9 Hz, CH·O*H*), 7·84br (1H, s, C·O*H*), 8·53 and 8·76 (6H, 2s, Me_2C), and 8·68 (3H, s, *Me*C·OH), *m/e* 186 (M^+, 1·2%), 171 ($M^+ - Me$, 1·4), and 168 ($M^+ - H_2O$, 22) (Found: C, 64·2; H, 9·9. $C_{10}H_{18}O_3$ requires C, 64·5; H, 9·7%). Its *monoacetate* (10b), prepared in benzene with acetyl chloride and pyridine, and purified by chromatography on silica gel, was a gum, τ (C_6D_6) 4·90 (1H, q, *J* 8 and 5 Hz, C*H*·OAc), 6·02 (1H, m, HCO), 7·95br (1H, s OH), 8·26 (3H, s, $MeCO_2$), and 8·66, 8·71, and 8·88 (9H, 3s, 3Me) (Found: C, 62·8; H, 9·0. $C_{12}H_{20}O_4$ requires C, 63·1; H, 8·8%). Hydrolysis of the acetate with aqueous methanolic 10% potassium hydroxide yielded the starting diol (10a).

Oxidation of the Tetraol (6).—The tetraol (0·25 g), suspended in ether (20 ml), was stirred with an excess of Brown's reagent,[12] and the acidic product (0·11 g) was treated with diazomethane. The ester was sublimed at 12 mmHg and crystallised from light petroleum giving methyl 2,2-dimethyl-5-oxotetrahydrofuran-3-acetate (13b) as needles (0·06 g), m.p. 55·5—56·5° (ref. 31 describes the ester as a liquid), τ 6·3 (3H, s, CO_2Me), 6·95—8·05 (5H), and 8·54 and 8·73 (6H, 2s, Me_2C), *m/e* 171 ($M^+ - Me$, 48%), 155 (18), and 140 (8) (Found: C, 57·8; H, 7·4. Calc. for $C_9H_{14}O_4$: C, 58·05; H, 7·6%).

endo-2,endo-6-*Dihydroxycineol* (1,8-*Epoxy*-trans-p-*menthane*-trans-2,trans-6-*diol*) (15a) *and* trans-p-*Menthane*-cis-1,trans-2,cis-6,8-*tetraol* (16).—(*a*) Pinol, freshly prepared from sobrerol (6 g), was added dropwise to a stirred solution of peroxysuccinic acid [from succinoyl monoperoxide (15 g)] in water (45 ml) at 45—50°. After stirring for 3 h, the mixture was basified with solid sodium carbonate and extracted with ethyl acetate. The product, crystallised from ethyl acetate–light petroleum, was the diol (15a) (3·2 g), obtained as needles, m.p. 120° (lit.,[32] 125°; lit.,[2] 122—124°), τ 6·18 (2H, q, $J_{exo,exo}$ 10, $J_{exo,endo}$ 3·5 Hz, C*H*·OH), 6·47 (2H, s, OH), 8·68 (3H, s, MeCO), and 8·81 (6H, s, Me_2CO), τ (C_5D_5N) 4·18br (2H, s, OH), 5·93 (2H, q, $J_{exo,exo}$ 10, $J_{exo,endo}$ 3·5 Hz, C*H*·OH), 8·4 (3H, s, MeCO), and 8·79 (6H, s, Me_2CO), *m/e* 186 (M^+, 12%), 168 ($M^+ - H_2O$, 2), and 142 (5) (Found: C, 64·9; H, 9·8. Calc. for $C_{10}H_{18}O_3$: C, 64·5; H, 9·7%). Its diacetate (15b), prepared in benzene with acetyl chloride and pyridine, consisted of fine needles (light petroleum), m.p. 89—89·5° (lit.,[32] 91°; lit.,[2] 90—92°), τ 5·14 (2H, q, $J_{exo,exo}$ 9·5, $J_{exo,endo}$ 5 Hz, C*H*·OAc), 7·93 (3H, s, $MeCO_2$), 8·72 (6H, s, 2Me), and 8·89 (3H, s, Me), *m/e* 270 (M^+, 0·75%), 255 (M^+ — Me, 0·5), and 229 (8) (Found: C, 62·1; H, 8·5. Calc. for $C_{14}H_{22}O_5$: C, 62·2; H, 8·2%). Hydrolysis of the diacetate with aqueous methanolic 10%potassium hydroxide afforded the diol (15a).

Continuous extraction for 72 h of the aqueous mother liquor, after removal of compound (15a), gave a gum (2·3 g) which slowly solidified. Two crystallisations from large volumes of ethyl acetate gave the tetraol (16) (90 mg), m.p. 154—155° (lit.,[15] 155—156°), τ [$(CD_3)_2SO$] 5·65 (1H, d, *J* 5 Hz, OH), 6·07 (1H, d, *J ca.* 4 Hz, OH), 6·16 (1H, s, OH), 6·39 (1H, s, OH), 6·55 (2H, m, C*H*·OH), 8·87 (3H, s, Me), and 8·98 (6H, 2s, 2Me), *m/e* 186 ($M^+ - H_2O$, 5%), 171 (4), and 168 (2).

(*b*) This tetraol (16) was also obtained (26% yield) by permanganate oxidation of sobrerol under the conditions used for the oxidation of pinol.[2]

(*c*) A mixture of pinol epoxide (12) (65 mg) and deionised water (0·39 g) was refluxed and stirred for 1·5 h. The clear solution was extracted with ethyl acetate giving the diol (15a) (60 mg, 84%), m.p. and mixed m.p. 120°.

endo-2-*Hydroxy*-6-*oxocineol* (1,8-*Epoxy*-trans-6-*hydroxy*-p-*methan*-2-*one*) (18a).—A solution of chromium trioxide (1·5 g) in 45% sulphuric acid [14] (5·6 ml) was added dropwise to a stirred solution of the diol (15a) (2·64 g) in acetone (50 ml). Stirring was continued for 5 min; the mixture was diluted with water (100 ml) and extracted several times with ethyl acetate. The extract was washed with water, dried, and evaporated. The semi-solid residue (2·18 g) was chromatographed on silica gel (65 g) and eluted with light petroleum–ether (4 : 1), giving 2,6-dioxocineol (17) (0·27 g) (see later). Further elution of the column, with light petroleum–ether (11 : 7), gave endo-2-*hydroxy*-6-*oxocineol* (18a) (1·01 g), which crystallised from light petroleum–ether as rods, m.p. 93—94°, τ 4·98 (1H, q, $J_{exo,exo}$ 8·5, $J_{exo,endo}$ 4 Hz, C*H*·OH), 7—8·6 (5H, complex m), 7·9 (1H, s, OH), 8·67 (3H, s, MeCO), and 8·76 (6H, s, Me_2CO), *m/e* 184 (M^+, 57%), 167 (2), and 166 ($M^+ - H_2O$, 5) (Found: C, 65·8; H, 8·9. $C_{10}H_{16}O_3$ requires C, 65·2; H, 8·75%). Its *semicarbazone* had m.p. 223—225° (decomp.) (from methanol), $\lambda_{max.}$ 231 nm (log ε 4·12) (Found: C, 51·1; H, 8·05; N, 16·1. $C_{11}H_{19}N_3O_3,H_2O$ requires C, 50·95; H, 8·2; N, 16·2%). Its *acetate* (18b), made in benzene with acetyl chloride and pyridine, crystallised from light petroleum–ether as rods, m.p. 72·5°, τ 8·0 (3H, s, $MeCO_2$), 8·64 (3H, s,

[31] P. Barbier and R. Locquin, *Bull. Soc. chim. France*, 1912, [4], **13**, 232.
[32] O. Wallach, *Annalen*, 1890, **259**, 309.

Me), 8·74 (3H, s, Me), 8·86 (3H, s, Me), and 5·0 (1H, q, $J_{exo,exo}$ 8·5, $J_{exo,endo}$ 4·0 Hz, C*H*·OAc), *m/e* 226 (M^+, 10%), 198 (4), and 184 (38) (Found: C, 63·9; H, 8·05. $C_{12}H_{18}O_4$ requires C, 63·7; H, 8·0%). Hydrolysis of this acetate with aqueous methanolic 10% potassium hydroxide gave the ketol (18a). 5,5-*Dideuterio*-endo-2-*hydroxy*-6-*oxocineol*, prepared by treating the ketol (18a) in dioxan–deuterium oxide with sodium, showed the expected n.m.r. spectrum and *m/e* 186 (M^+, 16%).

2,6-*Dioxocineol* (1,8-*Epoxy*-p-*menthane*-2,6-*dione*) (17).—Jones reagent [14] (2 ml) was added to *endo*-2-hydroxy-6-oxocineol (18a) (1·98 g) in acetone (20 ml) kept at 15°. After 5 min, the product was isolated and separated into acidic and neutral fractions with saturated aqueous sodium hydrogen carbonate. Crystallisation of the neutral product from light petroleum–ether gave 2,6-dioxocineol (17) (1·03 g) as long rods, and the starting material (18a) (0·37 g). 2,6-Dioxocineol had m.p. 120—121·5° (lit.,[2] 125—128°), τ ($CDCl_3$) as reported,[2] τ (C_5D_5N) 6·7—8·1 (5H, complex m), 8·6 (3H, s, MeCO), and 8·72 (6H, s, Me_2CO), *m/e* 182 (M^+, 20%), 167 (1), and 154 (1) (Found: C, 65·6; H, 7·7. Calc. for $C_{10}H_{14}O_3$: C, 65·9; H, 7·7%). Its *bis*-2,4-*dinitrophenylhydrazone* (yellow leaflets from chloroform–methanol) had m.p. 271—272° (decomp.), $\lambda_{max.}$ ($CHCl_3$) 363 nm (log ε 4·57) (Found: C, 48·7; H, 4·2; N, 20·2. $C_{22}H_{22}N_8O_9$ requires C, 48·7; H, 4·1; N, 20·7%).

Oxidation of 5,5-dideuterio-*endo*-2-hydroxy-6-oxocineol (73 mg) in hexadeuterioacetone by the method described for the oxidation of (18a) gave 3,3-dideuterio-2,6-dioxocineol (43 mg; >95% purity by mass spectroscopy). Its n.m.r. spectrum showed a complex multiplet (τ 6·7—8·1, 3H) similar to that of its analogue (17).

Acidification of the sodium hydrogen carbonate extract (see before) gave a gum (0·31 g) which reacted with diazomethane giving methyl 2,2-dimethyl-5-oxotetrahydrofuran-3-acetate (13b), identical with an authentic specimen.

Reduction of endo-2-*Hydroxy*-6-*oxocineol* (18a) *with Sodium Borohydride*.—The ketol (18a) (37 mg) and sodium borohydride (15 mg) in methanol (1 ml) were kept for 2 h and then worked up in the usual way to give *endo*-2,*endo*-6-dihydroxycineol (15a) (27 mg), identical with a sample prepared as above.

Reduction of 2,6-*Dioxocineol* (17) *with Sodium Borohydride*.—A solution of the diketone (17) (0·53 g) and sodium borohydride (90 mg) in methanol (10 ml) was kept at 15° for 1 h and then acidified with acetic acid. The solution was concentrated under reduced pressure; the residue was dissolved in 4% sodium carbonate solution (5 ml) and extracted continuously with ethyl acetate for 15 h. The solid product, fractionally crystallised from ethyl acetate, gave *exo*-2,*exo*-6-dihydroxycineol (19a) (0·17 g) and *endo*-2,*exo*-6-dihydroxycineol (20a) (0·22 g). Each was sublimed under atmospheric pressure [at 225—230° for (19a) and 155—160° for (20a)] then crystallised, respectively, from ethyl acetate and benzene. exo-2,exo-6-*Dihydroxycineol* (19a) was obtained as shining rhombs, m.p. 229—230°, τ [$(CD_3)_2SO$] 5·62 (2H, d, *J* 5 Hz, OH), 8·85 (3H, s, MeCO), and 8·88 (6H, s, Me_2CO), *m/e* 186 (M^+, 20%), 168 ($M^+ - H_2O$, 1), and 150 ($M^+ - 2H_2O$, 2) (Found: C, 64·7; H, 9·6. $C_{10}H_{18}O_3$ requires C, 64·5; H, 9·7%). Its diacetate (19b) crystallised from light petroleum–ether as fine needles, m.p. 80—81·5° (lit.,[2] 82—85°), *m/e* 270 (M^+, 0·75%), 255 (M^+ – Me, 1), and 229 (7) (Found: C, 62·4; H, 8·3. Calc. for $C_{14}H_{22}O_5$: C, 62·2; H, 8·2%). *endo*-2,*exo*-6-Dihydroxycineol (20a), an amorphous solid (from benzene), had m.p. 156—156·5° (lit., 162·5—164°), τ [$(CD_3)_2SO$] 5·34 (1H, d, *J* 5 Hz, OH), 5·77 (1H, d, *J* 6 Hz, OH), 8·8 and 8·92 (6H, 2s, Me_2CO), and 9·04 (3H, s, MeCO), *m/e* 186 (M^+, 18%), 168 ($M^+ - H_2O$, 4), and 150 ($M^+ - 2H_2O$, 4) (Found: C, 65·2; H, 9·5. Calc. for $C_{10}H_{18}O_3$: C, 64·5; H, 9·7%).

Both diols (19a) and (20a) were oxidised with Brown's reagent to 2,6-dioxocineol (17).

p-*Menth*-4(8)-*ene*-trans-1,cis-2,cis-6-*triol* (22) *and* trans-2,trans-6-*Diacetoxy*-8-*bromo*-trans-p-*menthan*-cis-1-*ol* (23).—A solution of the diol (15a) (0·23 g) in 45% hydrogen bromide in acetic acid (5 ml) was left at 15° for 15 h, neutralised with sodium carbonate solution, evaporated to dryness, and extracted with ethyl acetate. The product was left overnight with aqueous 10% potassium hydroxide (2 ml), neutralised, evaporated to dryness, and extracted with ethyl acetate. Crystallisation from ethyl acetate gave the *triol* (22) (28 mg) as shining plates, m.p. 205—208°, Raman shift 1666 cm^{-1} (intense), τ [$(CD_3)_2SO$] 5·51 (2H, d, *J* 4·5 Hz, CH·O*H*), 5·74 (1H, s, C·OH), 8·32 (6H, s, Me_2C=C), and 8·93 (3H, s, MeC), *m/e* 186 (M^+, 8%), 168 ($M^+ - H_2O$, 7), and 150 (10) (Found: C, 63·9; H, 9·9. $C_{10}H_{18}O_3$ requires C, 64·5; H, 9·7%). The diol (15a) (0·1 g) was similarly treated with hydrogen bromide (1 ml); the product was neutralised with a saturated solution of sodium hydrogen carbonate and extracted with ethyl acetate, giving a thick gum (0·19 g). It showed several spots on t.l.c. Chromatography on silica and elution with ether–light petroleum (4 : 1) gave the *bromo-diacetate* (23) as cubes (53 mg), m.p. 123—124°, *m/e* 310 and 308 (2%), 250 and 248 (3), and 228 (7·5) (Found: C, 48·3; H, 6·6; Br, 22·8. $C_{14}H_{23}BrO_5$ requires C, 47·9; H, 6·6; Br, 22·8%).

Similar treatment of the diacetate (15b) (0·7 g) with hydrogen bromide in acetic acid (5 ml) gave the same bromo-compound (23) (0·42 g) as the major product.

When the diacetate (23) (14 mg) was set aside overnight with aqueous 10% potassium hydroxide (2 ml), the usual work-up then gave the unsaturated triol (22) (4 mg).

trans-p-*Menthane*-cis-1,trans-2,trans-4,trans-6-*tetraol* (24).—(*a*) The tetraol (6) (0·15 g) was stirred with M-sulphuric acid (6 ml) at 70—72° for 8 h. The mixture was neutralised with sodium carbonate and evaporated to dryness, and the solid residue was extracted with ethyl acetate (10 × 4 ml). The *tetraol* (24) (93 mg) was obtained as shining plates, m.p. 163—164°, τ [$(CD_3)_2SO$] 5·72 (2H, d, *J* 4·5 Hz, CH·O*H*), 5·91 (2H, s, C·O*H*), *ca.* 6·75 (2H, m, C*H*·OH), 8·94 (6H, s, Me_2C), and 9·06 (3H, s, MeCO), *m/e* 186 ($M^+ - H_2O$, 1·5%), 171 (5), and 168 ($M^+ - 2H_2O$, 1·5) (Found: C, 59·2; H, 9·9. $C_{10}H_{20}O_4$ requires C, 58·8; H, 9·9%).

(*b*) The same product (24) was obtained when the tetraol (6) was left overnight at room temperature with aqueous 48% hydrobromic acid.

(*c*) The unsaturated triol (22) (25 mg) was stirred with M-sulphuric acid (6 ml) at 75—80° for 8 h and the product was worked up as in (*a*), giving the tetraol (24) (12 mg), identical with the product obtained before.

Conversion of the Tetraol (24) *into* trans-p-*Menthane*-1,4-*diol* (25).—The tetraol (24) (41 mg) was converted into its bis-2,6-toluene-*p*-sulphonate (105 mg), obtained as an oil, under the conditions described for the tosylation of (6). The oil was refluxed in ether (15 ml) with lithium aluminium hydride (50 mg), and the product was worked up in the usual way. The diol (25) (9 mg), m.p. 134—137° (lit.,[33]

[33] O. Wallach, *Annalen*, 1907, **357**, 64; see G. Ohloff and G. Uhde, *Helv. Chim. Acta*, 1965, **48**, 10 for other refs.

137—138°) was similar in i.r. spectrum to an authentic specimen (spectrum supplied by G. Ohloff).

trans-p-*Methane*-cis-1,trans-2,trans-4,cis-6-*tetraol* (27).—The tetraol (16) (0·15 g) was stirred with M-sulphuric acid (6 ml) at 60—65° for 24 h and the product (65 mg) was isolated as for (24). Crystallisation from ethyl acetate yielded the *tetraol* (27), m.p. 148—149°, τ [$(CD_3)_2SO$] 5·79 (2H, d, *J* 4 Hz, CH·O*H*), 5·97 (2H, s, C·OH), 6·2—6·7 (2H, m, C*H*·OH), 8·96 (6H, s, Me_2C), and 9·03 (3H, s, MeC), *m/e* 189 (M^+ — Me, 1%), 186 ($M^+ - H_2O$, 6), and 171 (2) (Found: C, 58·6; H, 9·9. $C_{10}H_{20}O_4$ requires C, 58·8; H, 9·9%). This tetraol (27) (58 mg) was also obtained when the diol (5a) (0·37 g) was stirred at 15° for 15 h with aqueous 48% hydrobromic acid (5 ml).

Reaction of 6,8-*Epoxy*-cis-p-*menthane*-trans-1,trans-2-*diol* (5a) *with Hydrogen Bromide in Acetic Acid.* trans-2,cis-6-*Diacetoxy*-8-*bromo*-cis-p-*menthane*-trans-1-*ol* (28) *and its* 1-*Epimer* (29).—The diol (5a) (0·15 g) was treated with 45% hydrogen bromide in acetic acid (2 ml) for 15 h; the mixture was neutralised with a saturated solution of sodium hydrogen carbonate and extracted with ethyl acetate. The product (0·32 g), a thick gum which showed two major and three minor spots on t.l.c., was chromatographed on silica and eluted with ether–light petroleum (4 : 1). The trans-1-*ol* (28) (41 mg) was eluted first; m.p. 121—122°, *m/e* 350 and 352 (M^+, 0·1%), 335 and 333 (0·1), and 310 and 308 (6) (Found: C, 47·7; H, 6·4; Br, 22·7. $C_{14}H_{23}BrO_5$ requires C, 47·9; H, 6·6; Br, 22·8%). The cis-1-*ol* (29) (75 mg) was eluted next; m.p. 93—93·5°, *m/e* 352 and 350 (M^+, 0·7%), 335 and 333 (0·8), and 310 and 308 (6), 55 (11), 43 (100), and 41 (26) (Found: C, 48·2; H, 6·4; Br, 22·85%).

Reaction of 2,6-*Dioxocineol* (17) *with Base. Methyl* 2,2,trans-6-*Trimethyl*-5-*oxotetrahydropyran*-3-*acetate* (30a; R^2 = Me) *and its* cis-*Isomer* (30b; R^2 = Me).—The diketone (17) (94 mg) was heated for 2 min at 100° with 2·5% sodium hydrogen carbonate solution (10 ml) made up in freshly boiled water. The cooled solution was washed with ethyl acetate (2 × 6 ml), acidified with acetic acid (0·3 ml), and extracted with ethyl acetate (2 × 5 ml). Part of the extract (8·5 ml) was washed with water, dried, and treated with excess of ethereal diazomethane. A mixture of esters (98 mg) was obtained as a yellow oil, consisting of methyl 2,2,*trans*-6-trimethyl-5-oxotetrahydropyran-3-acetate (30a; R^2 = Me) and its *cis*-isomer (30b; R^2 = Me) in this order of polarity (g.l.c.); $\lambda_{max.}$ (Et_2O) 293 nm (ε 50), ε_{225} 500, τ (CCl_4) 5·95 (1H, m, MeC*H*·O), 6·37 (3H, s, CO_2Me), 7·0—8·1 (5H, m), and 8·65—8·95 (9H, complex m with five main signals, MeC and Me_2C). On g.l.c.–mass spectroscopy both esters showed the same peaks, including *m/e* 214 (M^+, 10%), 199 (M^+ — Me, 1), 183 (M^+ — MeO, 2), and 182 (M^+ — MeOH, 3).

Methyl 2,2,6-*Trimethyl*-6-*methylperoxy*-5-*oxotetrahydropyran*-3-*acetate* (31b).—(*a*) The reaction of the diketone (17) (already described) with deoxygenated sodium hydrogen carbonate solution was repeated with base made up in unboiled water. Alternatively, air was passed through a cold solution of the diketone in aqueous methanolic 1% sodium hydroxide. The product, worked up as before, was treated with ethereal diazomethane, giving the peroxide (31b) as an oil (50% yield under the latter conditions), together with a smaller amount of the tetrahydrofuran ester (13b), both identified by g.l.c.–mass spectroscopy.

(*b*) The acidic fraction (0·31 g) obtained in the formation of 2,6-dioxocineol (17) from *endo*-2-hydroxy-6-oxocineol (18a) and Jones reagent, was treated with excess of diazomethane in ether. Ethyl acetate (10 ml) was added and the solution was shaken for 5 min with aqueous 3% sodium hydroxide (10 ml) to remove the tetrahydrofuran ester. The organic layer was dried and evaporated giving the peroxy-ester (31b) (0·12 g) as an oil (72% pure by g.l.c.), contaminated with 18% of an unidentified compound and 9% of the starting ketol (18a). In addition to the characteristics given in the Discussion section the mass spectrum showed *m/e* 259 (M^+ — 1, 0·02%), 245 (0·03), and 229 (0·04).

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