Action of Peracetic Acid on (+)-Sabinol

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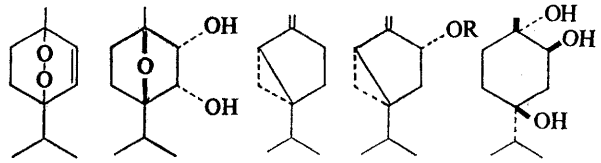
The compound said to have the constitution $C_{10}H_{18}O_3$, obtained by Henderson and Robertson from the action of peracetic acid on (+)-sabinol, has been shown to be *p*-menthane-1α,2β,4β-triol ($C_{10}H_{20}O_3$) by its synthesis from (+)-terpinen-4-ol. The origin of the triol from the sabinol reaction is discussed and it is suggested that it actually arises from terpinen-4-ol, present either as impurity or as a product of the reaction of acetic acid on sabinol. The products of this reaction have been investigated and terpinen-4-ol has been found to be present. (+)-2-*endo*-Hydroxy-1,4-cineole was obtained by acid-catalysed rearrangement of (+)-terpinen-4-ol α-epoxide.

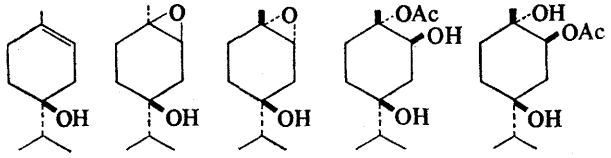
WHEN concerned [1] with the chemistry of ascaridole (I) we noted that Henderson and Robertson [2] had obtained a compound to which they assigned a constitution ($C_{10}H_{18}O_3$) isomeric with that of ascaridole glycol (II). The compound resulted, in dextrorotatory and racemic forms, from the action of peracetic acid (30% aqueous hydrogen peroxide in glacial acetic acid) on both (+)-sabinene (III) and (+)-sabinol (IV; R = H). The genesis of this structure seemed extremely unlikely and the reaction of peracetic acid with a sample of (+)-sabinol (IV; R = H) was re-examined. Recently,



(I) (II) (III) (IV) (V)

Hikino [3] has reported a reinvestigation of the same reaction with (+)-sabinene (III). He obtained the same compounds as Henderson and Robertson and concluded from degradative and physical data that they were (+)-*p*-menthane-1α,2β,4β-triol (V) [(1*S*,2*S*,4*S*)-*p*-menthane-1,2,4-triol] and the corresponding racemate ($C_{10}H_{20}O_3$). We had also concluded [4] that the same products from (+)-sabinol were *p*-menthane-1,2-4-triols. In our experiments only the racemic form of (V), m.p. 171—172·5°, was obtained, in about 3% yield. It gave the correct analysis for $C_{10}H_{20}O_3$ and the n.m.r. spectrum indicated the presence of three exchangeable hydrogens, one C*H*OH (τ 6·58, t, *J* 5 Hz), a tertiary methyl group, and an isopropyl group.

In order to confirm the structure of our product, *p*-menthane-1α,2β,4β-triol was synthesised from a sample of (+)-terpinen-4-ol (VI), $[\alpha]_D$ +21°. The highest rotation quoted [5] for terpinen-4-ol is $[\alpha]_D$ +48·3°, so that used was a partly racemic mixture with an excess of the *dextro*-form, the absolute configuration of which is as depicted in (VI).[6] Oxidation of the terpinen-4-ol with



(VI) (VII) (VIII) (IX) (X)

buffered peracetic acid [7] gave the two epoxides (VII) and (VIII) [6] (7 : 3) which were separated by preparative

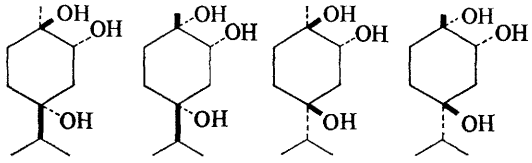
[1] D. Brown, B. T. Davis, T. G. Halsall, and A. R. Hands, *J. Chem. Soc.*, 1962, 4492.
[2] G. G. Henderson and A. Robertson, *J. Chem. Soc.*, 1923, 1849; 1926, 2762.
[3] Y. Hikino, *J. Pharm. Soc. Japan*, 1965, **85**, 477.
[4] P. Garside, D.Phil. Thesis, Oxford, 1964, p. 98.
[5] Y. R. Naves and P. Tullen, *Bull. Soc. chim. France*, 1960, 2123.
[6] G. Ohloff and G. Uhde, *Helv. Chim. Acta*, 1965, **48**, 10.
[7] H. Krimm and H. Schnell, *Chem. Zentr.*, 1958, 12,246.

g.l.c. Oxidation with peroxylauric acid in chloroform gave the two epoxides in the ratio 3 : 2, but oxidation with monoperoxyphthalic acid in ether gave a mixture in which the α-epoxide (VIII) predominated. This suggests that in methylene dichloride and chloroform hydrogen bonding between the hydroxy-group of the (+)-terpinen-4-ol and the peroxy-acid may orient the reagent to bring about formation of the *cis*(β)-epoxide (VII) (*cf.* ref. 8).

Leffingwell and Royals [9] have shown that treatment of epoxy-*p*-menthanes with buffered acetic acid gives the *trans*-diaxial diol monoacetates almost exclusively. In agreement with this the epoxides (VII) and (VIII) gave the monoacetates (IX) and (X) which afforded (+)-*p*-menthane-1α,2β,4β-triol (V) on saponification. The structures of the monoacetates (IX) and (X) follow from their n.m.r. spectra; the signals due to the C-2 protons are at τ 6·15 ($W_{\frac{1}{2}}$ 6 Hz) and 5·03 (t, J 4·2 Hz), respectively. The triol (V) was also obtained by the acid-catalysed hydrolysis of the epoxide (VII) and by treatment of (+)-terpinen-4-ol (VI) with hydrogen peroxide in acetic acid. The synthetic triol (V), m.p. 173—174° had a lower rotation, $[\alpha]_D$ +11°, than that ($[\alpha]_D$ +36°) reported by Henderson [2] and Hikino [3] and therefore contained some of the racemic form, in agreement with its synthesis from partly racemic terpinen-4-ol. Further recrystallisation of the triol obtained from the action of hydrogen peroxide in acetic acid raised the rotation to +31°. The i.r. and n.m.r. spectra were identical with those of the triol obtained from the sample of (+)-sabinol and there was no depression of m.p.

Recently the volatile oil of *Zanthoxylum rhetsa* has been examined.[10] The major monoterpenic component was found to be sabinene. In addition a crystalline compound, m.p. 171°, $[\alpha]_D$ ±0°, called mullilam diol was isolated and formulated as $C_{10}H_{18}O_3$. It was shown to be identical with the compound, m.p. 172°, prepared [2] by the action of peracetic acid on sabinene. The original structure and formula ($C_{10}H_{18}O_3$) proposed by Henderson and Robertson [2] were accepted and further evidence in favour of Henderson's structure was adduced. None of the evidence, however, is incompatible with mullilam diol being (±)-*p*-menthane-1α,2β,4β-triol, although the quoted C and H analytical data are not in good agreement with this structure. A (±)-p-menthanetriol, m.p. 169°, has previously been obtained from a volatile oil from *Melaleuca linariifolia* by Jones and Oakes,[11] who suggested it was formed by oxidation in air of terpinen-4-ol. This triol is almost certainly the 1α,2β,4β-triol.

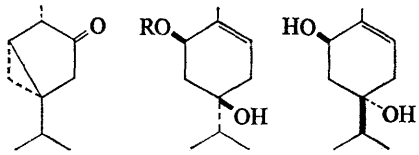
Hikino [3] has explained the formation of the triol from (+)-sabinene (III) in both optically active and racemic forms by proposing that the (+)-sabinene is first hydrated by both concerted and step-wise mechanisms to give both the (+)-optically active and racemic forms of terpinen-4-ol (VI), which is then oxidised to the triol. The formation of (+)- and (±)-*p*-menthane-1α,2β,4β-triol from (+)-sabinol (IV; R = H) [12] is more difficult to explain. A *p*-menthanetriol could arise from sabinol by simple dihydration but none of the four possible triols (XI—XIV) is (+)-*p*-menthane-



(XI) (XII) (XIII) (XIV)

1α,2β,4β-triol (V). One explanation of the formation of (±)-*p*-menthane-1α,2β,4β-triol is the formation of a symmetrical ion, *e.g.* involving acid-catalysed loss of the hydroxy-group of sabinol, although this does not seem likely.

To obtain further information, the action of aqueous acetic acid on two samples of (+)-sabinol (IV; R = H) was studied (see Experimental section). One sample was obtained by hydrolysis of sabinyl acetate (IV; R = Ac) from oil of savin and contained 1·8% terpinen-4-ol (g.l.c. analysis). The other was obtained by preparative g.l.c. and only gave one peak on g.l.c. analysis. No triol (V) was detected in the reaction products, which were distilled to give *p*-cymene and mixtures containing many components from which (+)-isothujone (XV), sabinyl acetate, sabinol, and (+)-terpinen-4-ol (VI) were isolated. Starting from homogeneous (+)-sabinol the yield of (+)-terpinen-4-ol was about 1% by g.lc. analysis. Also isolated were the diol (XVI; R = H) and its acetate (XVI; R = Ac), the structures of which were deduced from their physical data. The diol (XVI; R = H) and its C(4)-epimer (XVII) were also obtained by preparative t.l.c. of the saponified residue of the distillations.



(XV) (XVI) (XVII)

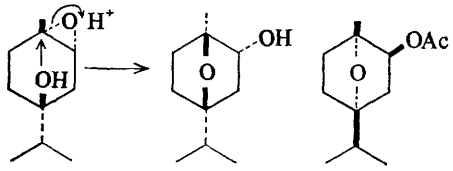
The n.m.r. spectrum of the acetate (XVI; R = Ac) showed an isopropyl doublet, a low field methyl singlet (τ 8·54), and an acetate methyl signal. The low-field region showed an olefinic proton as a triplet at τ 4·45 and another one-proton triplet at τ 4·74. Saponification of the acetate gave the diol, in the spectrum of which the two low-field protons had shifted to τ 4·62 and 6·13. The i.r. spectrum of the diol showed evidence of intramolecular hydrogen bonding. The diol (XVII) showed

[8] H. B. Henbest, *Proc. Chem. Soc.*, 1963, 159.
[9] J. C. Leffingwell and E. E. Royals, *Tetrahedron Letters*, 1965, 3829.
[10] R. K. Mathur, S. K. Ramaswamy, A. S. Rao, and S. C. Bhattacharyya, *Tetrahedron*, 1967, **23**, 2495.
[11] T. G. H. Jones and H. C. Oakes, *Univ. Queensland Papers, Dep. Chem.*, 1940, no. 18, 3 (*Chem. Abs.*, 1942, **36**, 4967).
[12] G. Ohloff, G. Uhde, A. F. Thomas, and E. Sz. Kovats, *Tetrahedron*, 1966, **22**, 309.

evidence of no such hydrogen bonding, although its n.m.r. spectrum was very similar, with the low-field protons at τ 4·55 and 5·67. The mass spectra of the two diols had molecular ions at *m/e* 170; water is lost most readily from the molecular ion of the diol (XVI; R = H), which suggests [13] that the C(2)-hydroxy-group is axial, in agreement with the assigned structures. The two diols are the expected products of the hydration of (+)-sabinol. One of them was originally obtained by Wallach [14] when sabinol was treated with sulphuric acid.

The presence of (+)-terpinen-4-ol in samples of oil of savin is already established [15] but the presence of terpinen-4-ol in the products of the action of aqueous acetic acid on pure (+)-sabinol and the presence of about 3·5% in the products of the sample containing 1·8% (*i.e.* about double the original amount) is less expected. The formation of terpinen-4-ol from sabinol is formally a reduction and may result from a disproportionation reaction. The formation of terpinen-4-ol indicates that the *p*-menthane-1α,2β,4β-triol (V) which is formed by the action of peracetic acid on sabinol really arises from terpinen-4-ol present either as an impurity or formed as an intermediate from sabinol. The yield (3·5%) of triol is greater than can be accounted for entirely by the presence of terpinen-4-ol as an impurity. Treatment of (+)-terpinen-4-ol with 30% hydrogen peroxide in acetic acid afforded the triol (V) in 31% yield.

Treatment of (+)-terpinen-4-ol (VI) with hydrogen peroxide in formic acid afforded (+)-2-*endo*-hydroxy-1,4-cineole (XVIII). Its structure was deduced as follows. It had the correct analysis for $C_{10}H_{18}O_2$. Its n.m.r. spectrum indicated the presence of one methyl, one isopropyl, and one hydroxy-group. The hydroxy-group was secondary and the C(2)-proton (τ 6·23) on the carbon carrying the hydroxy-group gave rise to a quartet with further coupling of 0·8 Hz similar to that reported for the C(2)-*exo*-proton in 2-*endo*-substituted bornanes.[16] No evidence for intramolecular hydrogen bonding was found in the i.r. spectrum. The cineole is probably formed *via* the epoxide (VIII) with the C(4)-hydroxy-



(VIII) (XVIII) (XIX)

group functioning as a nucleophile on acid-catalysed opening of the epoxide ring. A (−)-form of (XVIII) was obtained as its acetate (XIX) by chromatography of the mixed acetates obtained from the acid-hydrolysis products of the mixed epoxides (VII) and (VIII). Saponification of the aceteate gave the laevo form of 2-*endo*-hydroxy-1,4-cineole. It is probably formed by acid-catalysed dehydration of the acetate (X) or the corresponding triol with formation of a carbonium ion at C-4 and nucleophilic attack by the hydroxy-group at C-1.

[13] A. F. Thomas and B. Willhalm, *J. Chem. Soc.* (*B*), 1966, 219.
[14] O. Wallach, *Annalen*, 1908, **360**, 99; 1917, **414**, 203.
[15] E. von Rudloff, *Canad. J. Chem.*, 1963, **41**, 2876.

EXPERIMENTAL

M.p.s were determined with a Kofler hot-stage apparatus. Optical rotations were determined at 20° for solutions in chloroform. Hydroxy-stretching frequencies were determined with a Perkin-Elmer 521 spectrometer for solutions in carbon tetrachloride. N.m.r. spectra were determined at 60 MHz. Mass spectra were measured with an MS9 spectrometer. T.l.c. was carried out on baked or unbaked silica gel G or H plates. G.l.c. was carried out with a Pye Argon Aerograph [15% Carbowax 6000 on Embacel (60—100 mesh) at 125° unless otherwise stated]. Preparative g.l.c. was carried out on a column (16 ft. × 7 in.) of Carbowax on Embacel by use of the F and M model 770.

(+)-*Sabinol* (IV; R = H).—Sabinyl acetate (58 g.), b.p. 48—50°/0·1 mm., n_D^{20} 1·471, $[\alpha]_D^{25}$ +63°, obtained from oil of savin (Schimmel and Co., Miltitz, Leipzig), was hydrolysed with 10% ethanolic potassium hydroxide (150 ml.) at 50° for 24 hr. to give (+)-sabinol (purified by fractional distillation) as an oil, b.p. 46—48°/0·1 mm., n_D^{20} 1·4836, $[\alpha]_D^{25}$ +20·5°, $\nu_{max.}$ (film) 3350, 1655, and 895 cm.$^{-1}$ (Found: C, 79·05; H, 10·7. Calc. for $C_{10}H_{16}O$: C, 78·9; H, 10·6%), containining 2% impurity (g.l.c.). Preparative g.l.c. gave two compounds: (i) (+)-terpinen-4-ol which was bulb-distilled to give an oil, $[\alpha]_D$ +21° (*c* 1·3), n_D^{25} 1·4771 (lit.,[5] $[\alpha]_D$ +48°, n_D^{20} 1·4778), i.r. spectrum was identical with that of the sample of (+)-terpinen-4-ol used for preparative work and described below, and (ii) (+)-sabinol $[\alpha]_D$ +23° (*c* 2·4), n_D^{25} 1·4856 (lit.,[12] $[\alpha]_D$ +8·3°, n_D^{25} 1·4850), homogeneous on g.l.c.[17]

The Action of Peracetic Acid on (+)-*Sabinol*.—Sabinol (37 g.), $[\alpha]_D$ +20·5° (98% purity by g.l.c.), in glacial acetic acid (150 ml.) was treated with hydrogen peroxide (30%; 58 g.) as described by Henderson and Robertson.[2] The mixture, maintained at 50°, started to darken after 4 hr. and was yellow after 12 hr., but did not darken subsequently. The mixture was cooled, diluted with water (1 l.), neutralised with potassium carbonate, and exhaustively extracted with ether to give a yellow oil which deposited fine crystals (0·5 g.) when cooled. Two recrystallisations from ether gave (±)-*p*-menthane-1α,2β,4β-triol as needles, m.p. 171—172·5°, $\nu_{max.}$ (Nujol) 3280 cm.$^{-1}$ (OH with hydrogen bonding), τ (Me_2SO) 9·15 (d, *J* 6 Hz, Me_2CH), 8·85 (s, $MeCR_3$), 6·58 (t, *J* 5 Hz, $CH{\cdot}OH$), and three bands due to low-field protons which were lost by addition of deuterium oxide (Found: C, 63·8, 63·8, 63·6; H, 10·65, 10·5, 10·5; O, 25·65. $C_{10}H_{20}O_3$ requires C, 63·8; H, 10·7; O, 25·5%). There was no peak of mass number 188 (corresponding with the molecular weight) in the mass spectrum, but the compound was shown, in an independent experiment, to be dehydrated rapidly below 200° (the inlet temperature of the MS9 spectrometer).

A portion of the oil (4·5 g.) remaining after removal of the crystals was chromatographed on silica gel (100 g.).

[16] T. J. Flautt and W. F. Erman, *J. Amer. Chem. Soc.*, 1963, **85**, 3212.
[17] T. Norin, *Acta Chem. Scand.*, 1962, **16**, 640.

Benzene and ether eluted mixtures of oils which were shown to be hydroxy-esters ($\nu_{max.}$ 3500, 1740—1700, and 1240 cm.$^{-1}$). Ethyl acetate eluted an oil which deposited crystals; these gave p-*menthane*-1α,2β,4β-*triol* 2β-*monoperacetate* as plates, m.p. 191—192·5: (from chloroform), $\nu_{max.}$ (Nujol) 3450 (OH) and 1720 and 1245 (ester) cm.$^{-1}$, τ (Me_2SO) 9·18 (6H, d, *J* 6 Hz, $CHMe_2$), 8·89 (s, tertiary Me), 8·05 (s, CH_3·CO·O·), and 5·28 (1H, t, *J* 3 Hz, CH·O·OAc) (Found: C, 58·75; 58·7; H, 8·85, 8·9; O, 32·65. $C_{12}H_{22}O_5$ requires C, 58·5; H, 9·0; O, 32·5%). The crystals liberated iodine from acidified potassium iodide.

A portion (20 g.) of the ethereal extract from the initial reaction product was hydrolysed with 10% ethanolic potassium hydroxide (100 ml.) at 50° for 12 hr. The mixture became black almost immediately. Removal of the ethanol under reduced pressure left a brown tar which was shaken with water and saturated with carbon dioxide. Ether extractions gave a dark brown oil which deposited crystals (0·6 g.); these gave needles, m.p. 171—172° (from ether), identical (mixed m.p. 171—172°) with (±)-*p*-menthane-1α,2β,4β-triol obtained directly from the initial reaction product. The hydrolysate continued to deposit small quantities of the crude crystals for several days.

Oxidation of (+)-*Terpinen*-4-*ol* (VI) *with* 40% *Peracetic Acid*.—Peracetic acid solution was prepared by adding acetic anhydride (8·0 ml., 0·085 mole) to an ice-cooled mixture of methylene chloride (30 ml.) and hydrogen peroxide (87%; 2·2 ml., 0·08 mole). Methyl cyanide was added to form a homogeneous solution.

The peroxy-acid solution was added during 1 hr. to a stirred mixture of (+)-terpinen-4-ol, $[\alpha]_D$ +21° (*c* 1·0), n_D^{25} 1·4782 (11·5 g., 0·075 moles), and anhydrous sodium acetate (9 g.) in methylene chloride (50 ml.). The mixture was kept at 25—30° for 3 hr. and then diluted with methylene chloride (100 ml.) and washed with 2N-sodium hydroxide solution (100 ml. portions) until it gave a negative starch–iodide test. Work-up of the methylene dichloride solution in the usual manner then afforded an oil (10·85 g.) which was filtered through deactivated alumina (200 g.) in benzene solution. The first 200 ml. of eluate gave an oil (9·67 g., 76%) which was separated into the following fractions by preparative g.l.c.: (i) (+)-terpinen-4-ol (1·2 g., 10%), $[\alpha]_D$ +21°, n_D^{25} 1·4745, identified by its g.l.c. retention time and i.r. spectrum; (ii) (+)-1β,2β-epoxy-*p*-menthan-4β-ol (1·18 g., 9%) (VII), $[\alpha]_D$ +22° (*c* 0·4), n_D^{25} 1·4594 (lit.[6] for enantiomer, $[\alpha]_D$ −26°, n_D^{20} 1·4641) (Found: C, 70·2; H, 10·85. Calc. for $C_{10}H_{18}O_2$: C, 70·5, H, 10·65%), $\nu_{max.}$ (film) 3480, 829, 759, and 730 cm.$^{-1}$, τ (CCl_4) 9·14 (d, *J* 6 Hz, isopropyl), 8·66 (s, Me), and 6·90 (t, epoxide proton), *m/e* 170 (M^+); (iii) crystals (possibly 2-*exo*-hydroxy-1,4-cineole) (0·023 g., 0·2%), m.p. 67—71°, $[\alpha]_D$ +0·1° (*c* 0·7), τ (CCl_4) 9·05 (d, *J* 6·5 Hz, isopropyl), 8·61 (s, Me), 8·2br (OH), and 6·28 (q, *J* 6 and 2 Hz), *m/e* 170 (M^+), 98% pure by g.l.c.; (iv) unresolved material (0·031 g., 0·3%); and (v) (+)-1α,2α-epoxy-*p*-menthan-4β-ol (0·55 g., 4%) (VIII), $[\alpha]_D$ +3·2° (*c* 0·2), n_D^{25} 1·4665 (lit.[12] for enantiomer, $[\alpha]_D$ −3·3°, n_D^{20} 1·4725), $\nu_{max.}$ (film) 3440, 836, 775, and 716 cm.$^{-1}$, τ (CCl_4) as for the β-epoxide [fraction (ii)] except for the epoxide proton at τ 7·17 (q, *J* 3·0 and 2·4 Hz), *m/e* 170 (M^+).

Oxidation of (+)-*Terpinen*-4-*ol with Peroxylauric Acid*.—Peroxylauric acid was prepared as described by Silbert, Siegel, and Swern.[18] The reaction was carried out in chloroform solution for 12 hr. at room temperature to give mixed epoxides (86%) shown by g.l.c. to consist of 1β,2β- and 1α,2α-epoxides [(VII) and (VIII)] in a 3 : 2 ratio.

Oxidation of (+)-*Terpinen*-4-*ol with Monoperoxyphthalic Acid*.—A solution of (+)-terpinen-4-ol (10·44 g.) in dry ether (40 ml.) was treated with monoperoxyphthalic acid solution[19] (24·7 g., 2 equiv., in 252 ml.). The solution was kept at 20° for 24 hr. The mixture was washed with 5% sodium carbonate solution (50 ml. portions) until no iodine was liberated from 10% potassium iodide solution and then afforded an oil (2·8 g.), which was dissolved in benzene and chromatographed on silica gel (100 g.). Benzene–ether (2 : 1) (800 ml.) eluted a mixture of 1β,2β- and 1α,2α-epoxy-*p*-menthan-4β-ols [(VII) and (VIII)] (1·65 g.), n_D^{25} 1·4728, $\nu_{max.}$ (film) 838, 780, and 719 cm.$^{-1}$, τ (CCl_4) 9·16 (d, *J* 5·5 Hz, isopropyl), 8·73 (s, Me), 7·19 [t, $W_{\frac{1}{2}}$ 3 Hz, 82% of (A)], and 6·92 [t, $W_{\frac{1}{2}}$ 2 Hz, 18% of (B).

Crystals sublimed from the crude epoxide oils over a period of several months. These were identified, after recrystallisation from ether, as *p*-menthane-1α,2β,4β-triol by m.p. and mixed m.p. 172°, and by their i.r. spectrum.

(A) (B)

(+)-1α-*Acetoxy*-p-*menthane*-2β,4β-*diol* (IX).—The β-epoxide (400 mg.) was treated with acetic acid (2·5 ml.) and anhydrous sodium acetate (400 mg.), and the mixture was kept at 50—60° for 5 hr. Work-up in the usual way gave an oil (480 mg.), which was dissolved in benzene and chromatographed on alumina (5% deactivated; 40 g.). Benzene–ether (4 : 1) (200 ml.) eluted (+)-1α-*acetoxy*-p-*menthane*-2β,4β-*diol* as an oil (375 mg., 70%), homogenous by t.l.c., which gave needles, m.p. 45—60° (from ether), $[\alpha]_D$ +1·7° (*c* 1·5) (Found: C, 63·1; H, 9·8. $C_{12}H_{22}O_4$ requires C, 62·6; H, 9·6%), τ (CCl_4) 9·14 (d, *J* 7 Hz, isopropyl), 8·52 (s, Me), 8·08 (s, O·COMe), 6·15 (m, *H*COH), 6·10 [C(4)-OH], and 5·03 [d, *J* 8 Hz, C(2)-OH].

Further elution with ether (100 ml.) gave crystalline material (12 mg.) which gave *p*-menthane-1α,2β,4β-triol as needles, m.p. and mixed m.p. 169—170° (from ether).

The acetate was saponified with 3% methanolic potassium hydroxide solution. Work-up with ethyl acetate in the usual way gave *p*-menthane-1α,2β,4β-triol, which gave needles, m.p. and mixed m.p. 171—173° (from ether).

(+)-2β-*Acetoxy*-p-*menthane*-1α,4β-*diol* (X).—The α-epoxide (75 mg.) and anhydrous sodium acetate (70 mg.) in acetic acid (0·6 ml.) were kept at 50° for 6 hr. The usual work-up gave 2β-acetoxy-*p*-menthane-1α,4β-diol as a gum, τ 9·02 (d, *J* 7 Hz, isopropyl), 8·72 (s, Me), 7·84 (s, O·COMe), and 5·03 (t, *J* 4·2 Hz, *H*C·OAc).

Saponification as above gave *p*-menthane-1α,2β,4β-triol, which gave needles, m.p. and mixed m.p. 171—172° (from ether).

(+)-p-*Menthane*-1α,2β,4β-*triol* (V).—The β-epoxide (115 mg.) (VII) was dissolved in tetrahydrofuran (5 ml.) and treated with 0·1N-sulphuric acid (2 ml.). The solution was kept at 40—50° for 4 hr. and then poured into saturated sodium hydrogen carbonate solution (30 ml.). Work-up

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[19] S. Linholten and P. Sorensen, *Acta Chem. Scand.*, 1958, **12**, 1331.

in the usual way gave a solid (95 mg.), which gave (+)-*p*-menthane-1α,2β,4β-triol as needles, m.p. 173—174° (from ether), $[\alpha]_D$ +11° (*c* 0·5 in ethanol) [Found (sample sublimed at 0·5 mm.): C, 63·7; H, 10·7. Calc. for $C_{10}H_{20}O_3$: C, 63·8; H, 10·7%], *m/e* 188 (M^+), τ (pyridine) 8·97 (d, *J* 7 Hz, isopropyl), 8·40 (s, Me), 5·92 (t, $W_{\frac{1}{2}}$ 8 Hz, *HC*·OH), and 4·3 (m, OH), identical with the triol obtained from sabinol (mixed m.p. and i.r. and n.m.r. spectra); mono-*p*-nitrobenzoate, m.p. 172—173°, $[\alpha]_D$ +4° (*c* 0·8), identical with a sample prepared from the triol from sabinol.

The α-epoxide was recovered unchanged after a similar reaction.

Reaction of (+)-*Sabinol with Acetic Acid.*—(i) (+)-Sabinol (98% pure by g.l.c.; 11·05 g.) was dissolved in acetic acid (50 ml.) and water (20 ml.), and the mixture was kept in the dark at 20° for 4 weeks. It was then poured into water (200 ml.) and neutralised with sodium carbonate solution. Extraction with ether afforded an oil (9·95 g.), which was distilled at 20 mm. to give fractions (*a*), b.p. 95° (0·35 g., 3%); (*b*), b.p. 95—150° (4·32 g., 39%); (*c*), b.p. 150—165° (3·29 g., 30%); and (d), residue (2 g.).

(ii) Sabinol (pure; 4·74 g.) was dissolved in acetic acid (25 ml.) and water (10 ml.), and the mixture was kept at 45—50° for 4 days. Work-up as above gave a yellow oil (3·55 g.), which was distilled at 140° (20 mm.) to give a distillate (2·13 g.) and a residue (1·42 g.).

The n.m.r. spectrum of fraction (*a*) from experiment (i) was identical with that of *p*-cymene:[17] τ 8·78 (d, *J* 7 Hz, isopropyl), 7·71 (s, Me), 7·13 (quintet, C*H*Me_2), and 2·95 (4-H, s, aromatic).

The distillate from reaction (ii) and fraction (*b*) from reaction (i) were examined by g.l.c. The similar results are compared in the Table. Peaks 4, 9, 10, 11, 19, and 21 were separated by preparative g.l.c.:

Peak 4: (+)-isothujone, $[\alpha]_D$ +65° (*c* 1·3), n_D^{25} 1·4605 [lit.,[21] $[\alpha]_D$ +86° (*c* 1·9), n_D^{25} 1·4492], $\lambda_{max.}$ 245 (ε 530) and 212 (ε 560) nm. $\nu_{max.}$ (film) 3040, 1742, and 1011 cm.$^{-1}$, n.m.r. spectrum (CCl_4) identical with Norin's spectrum:[20] τ 10·07 and 9·44 (2H, m, cyclopropane protons) and 9·13, 9·06, and 8·97 (methyl signals).

Peak 9: (+)-terpinen-4-ol, $[\alpha]_D$ +19·5° (*c* 1·1), g.l.c. retention time and i.r. spectrum identical with those of authentic material.

Peak 10: (+)-sabinyl acetate, $[\alpha]_D$ +68° (*c* 1·5), n_D^{25} 1·4784, g.l.c. retention time and i.r. spectrum identical with those of authentic material.

Peak 11: (+)-sabinol, $[\alpha]_D$ +24° (*c* 1·6), n_D^{25} 1·4795, g.l.c. retention time and i.r. spectrum identical wth those of authentic material.

Peak 19: 6β-*acetoxy*-p-*menth*-1-*en*-4β-*ol* (XVI; R = Ac), $[\alpha]_D$ +13° (*c* 0·8), $\nu_{max.}$ (CCl_4) 3610, 1730, and 1230 cm.$^{-1}$, *m/e* 212 (M^+), τ (CCl_4) 9·10 (q, isopropyl), 8·54 (s, Me), 7·97 (s, O·COMe), 7·4 (m, OH), 4·74 (t, *HC*·OAc), and 4·45 (t, olefinic proton); saponification gave material identical to that from peak 21.

Peak 21: p-*menth*-1-*ene*-4β,6β-*diol* (XVI; R = H), $\nu_{max.}$ (CCl_4) 3625 and 3540 cm.$^{-1}$, *m/e* 170 (M^+), τ (CCl_4) 9·10 (q, isopropyl), 8·20 (s, Me), 6·64 (2H, m, 2OH), 6·13 (t, *HC*·OH), and 4·62 (t, olefinic proton).

Residue products. The residual oils from each reaction and the distillate from the reaction (ii) were each saponified with 2% potassium hydroxide in methanol. The product from reaction (i) residue was chromatographed but little separation of the components was achieved. None of the products showed any sign of *p*-menthane-1α,2β,4β-triol on careful t.l.c.

Preparative t.l.c. on reaction (i) residue product gave two compounds (R_F 0·52 and 0·42). The less polar was identified as *p*-menth-1-en-4β,6β-diol (peak 21 above) (t.l.c. and i.r. and n.m.r. spectra). The more polar (R_F 0·42) was *p-menth*-1-*en*-4α,6β-*diol* (XVII), $[\alpha]_D$ +2·4°

Peak:	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	19	20	21
Fraction (*b*) from reaction (i):																					
R	0·14	0·18	0·23	0·32	0·35	0·45			0·64	0·82	1·0	[flat peak]			1·67	1·85	2·02	2·22	4·5	5·9	8·18
%	19	†	†	6	†	†			9	18	21				2	3	4	1	8	7	7
Distillate from reaction (ii):																					
R	0·18	0·19		0·32		0·44	0·51	0·56	0·63	0·83	1·0	1·22		1·41	1·68	1·87	2·04	2·58	4·6	5·9	
%	3	1		12		1	1	†	2	17	5	†		†	11	3	2	†	31	7	

R values are relative retention times. Figures quoted are % based on peak areas.

† Trace. The g.l.c. running temperature was 125° for sample (i).

(*c* 0·3) $\nu_{max.}$ (CCl_4) 3630, 3615, and 3605 cm.$^{-1}$, *m/e* 170 (M^+), τ (CCl_4) 9·05 (q, isopropyl), 8·18 (s, Me), 8·2br (OH), 5·67 (m, *HC*·OH), and 4·58 (t, olefinic proton).

Reaction of (+)-*Terpinen*-4-*ol with Hydrogen Peroxide in Acetic Acid.*—A solution of (+)-terpinen-4-ol (10 g.) in acetic acid (40 ml.) was treated with hydrogen peroxide (100 vols.; 15 ml.) at 20°. The mixture was kept at about 50° for 4 days. 5N-Sodium hydroxide (*ca.* 140 ml.) was added slowly and with cooling until the solution was just alkaline (litmus). The aqueous mixture was worked up with ethyl acetate in the usual way to give a gum (9·1 g.). This gave crystals (2·9 g.) from ether. Saponification of the mother liquors and crystallisation from ether gave more crystals (0·85 g., total 31%), m.p. 167—169°, $[\alpha]_D$ +16° (*c* 1·5 in ethanol). Recrystallisation from ether gave (+)-*p*-menthane-1α,2β,4β-triol as needles, m.p. and mixed m.p. 171—172°, $[\alpha]_D$ +31° (*c* 1·3 in ethanol) (lit.,[3] m.p. 174°, $[\alpha]_D$ +36°), i.r. spectrum identical with that of the triol obtained *via* epoxidation.

The yield was not improved by carrying out the reaction in more dilute solution and/or at 40°.

Oxidation of (+)-*Terpinen*-4-*ol with Performic Acid.*—(+)-Terpinen-4-ol (3·34 g.) in 90% formic acid (8·5 ml.) was treated with hydrogen peroxide (100 vols., 2·8 ml.) with stirring during 0·5 hr. The mixture was maintained at 60° for 10 hr., and then at 20° for 12 hr. It was then steam-distilled; distillate (400 ml.) was collected and extracted with ether (4 × 80 ml.). The extracts were washed with 5% sodium hydrogen carbonate solution (60 ml. portions), until no iodine was liberated from N-potassium iodide, and water (50 ml.), and dried. Removal of solvent left a yellow oil (1·7 g.), which was heated under reflux

[20] M. S. Bergqvist and T. Norin, *Arkiv Kemi*, 1963, **22**, 137.

with 1% methanolic potassium hydroxide solution (30 ml.) for 1 hr. The mixture was concentrated and then worked up as usual to give a brown oil (0·95 g.), $\nu_{max.}$ (film) 3400 and 1705 cm.$^{-1}$. The oil was dissolved in benzene and chromatographed on silica gel (70 g.). Elution with the solvents indicated gave the following fractions: (1) benzene–ether (4 : 1) (400 ml.), 0·18 g.; (2) benzene–ether (4 : 1 (200 ml.), 0·38 g.; (3) benzene–ether (2 : 1), (200 ml.), 0·19 g.; (4) benzene–ether (1 : 1) (200 ml.), 0·14 g.; and (5) ether (300 ml.), 0·18 g. Fraction (2) showed one peak (retention time 3·45 relative to terpinen-4-ol) on g.l.c. (15% GEO), and all other fractions were mixtures. These were not further investigated.

Fraction (2) was distilled at 130° (17 mm.) to give (+)-2-endo-*hydroxy*-1,4-*cineole* (XVIII) as an oil (0·24 g.), $[\alpha]_D$ +5° (*c* 0·5), n_D^{25} 1·4660 (Found: C, 68·1; H, 10·8. $C_{10}H_{18}O_2$ requires C, 70·5; H, 10·7%), *m/e* 170 (M^+), τ (CCl_4) 9·12 (d, *J* 6 Hz., isopropyl), 8·70 (s, Me), 6·62 (m, OH), and 6·24 (q, *J* 10 and 4 Hz, *H*C·OH).

(−)-2-endo-*Acetoxy*-1,4-*cineole* (XIX).—The mixed 1β,2β- and 1α,2α-epoxy-*p*-menthan-4β-ols (1·0 g.) were dissolved in tetrahydrofuran (20 ml.) and warmed with 0·1N-sulphuric acid (20 ml.) for 4 hr. at 50—60°. After neutralisation of the acid with barium hydroxide solution an oil (1·0 g.) was obtained, which showed two components on t.l.c. The oil was acetylated and the resulting yellow oil (0·6 g.) was dissolved in benzene and chromatographed on silica gel (40 g.). Benzene–ether (4 : 1) (50 ml.) eluted an oil (0·21 g.). Further elution with graded solvents gave intractable mixtures.

The oil was bulb-distilled at 130° (20 mm.) to give (−)-2-endo-*acetoxy*-1,4-*cineole* $[\alpha]_D$ −26° (*c* 0·6), n_D^{20} 1·4515 (Found: C, 68·1; H, 9·7. $C_{12}H_{20}O_3$ requires C, 67·9; H, 9·5%), *m/e* 212 (M^+), $\nu_{max.}$ (film) 1730 and 1240 cm.$^{-1}$, τ (CCl_4) 9·08 (d, *J* 6·5 Hz, isopropyl), 8·61 (s, Me), 7·94 (s, O·COMe), and 5·33 (q, *J* 10·8 and 3·6 Hz, *H*C·OAc).

Saponification of the acetate with 2% methanolic potassium hydroxide solution and the usual work-up gave (−)-2-*endo*-hydroxy-1,4-cineole, $[\alpha]_D$ −8°, which had the same g.l.c. behaviour as the (+)-compound described above.

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