Oxidation of (-)- α -Terpineol to Some Epoxy-Alcohols

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Abstract

 α -Terpineol has been converted by peracid oxidation into a 1,2-epoxy-8-ol (2a) and (2b), a 1,8-epoxy-2-ol (3) and a 2,8-epoxy-1-ol (5). The mechanism for formation and stereochemical assignments for these products are discussed.

As part of an investigation to convert citrus by-product monoterpenoids into novel or more valuable compounds¹ we investigated epoxidation of (-)- α -terpineol (1) with *m*-chloroperbenzoic acid (Scheme 1). The three products identified from the reaction were (-)-*cis*- 2β , 8β -epoxy-*p*-menthan- 1α -ol (5), (-)-*trans*- 1β , 8β -epoxy-*p*-menthan- 2β ol (3) and (-)-1,2-epoxy-*p*-menthan-8-ol (2a) and (2b). Previous workers² had reported that oxidation of α -terpineol with peracetic acid afforded 1,2-epoxide (2a) and *cis*- 2β , 8β -epoxy-*p*-menthan- 1β -ol [the 1β -epimer of (3)] as the only products isolated.

The structure of compound (5) was determined from its spectral data, which suggested the compound contained a tertiary hydroxyl group and a cyclic ether linkage, and from synthesis by a previously reported procedure. Thus, pinol (7) was epoxidized to $cis-1\alpha, 2\alpha$ -epoxydihydropinol (8)^{3,4} which was reduced with lithium aluminium hydride to tertiary alcohol (5).³ This same alcohol (5) was synthesized from pinol (7) by mercuric acetate oxidation, although a long reaction period (6 days reflux) was required to obtain even a 5% yield of (5).⁵ Oxymercuration-demercuration of olefins generally results in hydration from the less-hindered side of the molecule.⁶

The structure $1\beta_{,8}\beta_{-}$ epoxy-*p*-menthan- 2β -ol for compound (3) was assigned on the basis of its spectral data, which suggested that the molecule contained a secondary hydroxyl group and a cyclic ether linkage, its formation from (2a) by treatment with acid, and its chemical transformations. That compound (3) contained one secondary

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- ¹ Wilson, C. W., III, and Shaw, P. E., J. Org. Chem., 1973, 38, 1684.
- ² Piatkowski, K., and Kuczynski, H., Rocz. Chem., 1961, 35, 239.
- ³ Klein, F., and Rojahn, W., Dragoco Rep., Ger. Ed., 1967, 14, 95 (Chem. Abstr., 1967, 67, 116955c).
- ⁴ Cocker, W., Cocker, K. J., Crowley, T. J., and Srinirasan, K., J. Chem. Soc., 1972, 1971.
- ⁵ Brown, H. C., and Geoghegan, P., Jr, J. Amer. Chem. Soc., 1967, 89, 1522.
- ⁶ Brown, H. C., and Hammer, W. J., J. Amer. Chem. Soc., 1967, 89, 1525.

hydroxyl group was shown both by acetylation to a monoacetate (4), and oxidation with N-bromoacetamide to a ketone (9). The high carbonyl frequency of ketone (9) is apparently due to ring strain because a similar high carbonyl frequency had been observed for 1,4-epoxy-p-menthan-2-one.¹ Reduction of (9) with sodium and alcohol afforded the more stable *exo*-alcohol (3), while reduction of (9) with platinum and hydrogen afforded the *endo*-alcohol (10) produced by hydrogenation from the less-hindered side. The presence of a 1,8-epoxide bridge in ketone (9) was shown by Clemmensen reduction⁷ to 1,8-cineole (11).



The structure of the 1,2-epoxide as a mixture of *trans*-1 β ,2 β -epoxy-*p*-menthan-8-ol (2a) and *cis*-1 α ,2 α -epoxy-*p*-menthan-8-ol (2b) was assigned on the basis of its conversion with lithium aluminium hydride into a 4 : 1 mixture of the known 1,8-*cis*-diol (6a) and 1,8-*trans*-diol (6b), and its conversion into (3) as the only product isolated upon treatment with acid. The predominant *trans*-isomer (2a) can rearrange to (3) by acid-catalysed intramolecular 1,2-epoxide opening to a tertiary carbonium ion intermediate followed by 1,8-epoxide formation. Since the less abundant isomer (2b) can theoretically rearrange to (5) by concerted acid-catalysed intramolecular 1,2-epoxide opening and 2,8-epoxide ring formation, the epoxides (2a) and (2b) are possible intermediates in formation of the other two peracid oxidation products, (3) and (5), from α -terpineol.

⁷ Martin, E. L., Org. React., 1942, 1, 155.

Experimental

Instrumentation

Infrared spectra were obtained from thin liquid films with a Perkin Elmer Infracord. Nuclear magnetic resonance spectra were obtained with a Varian A-60 spectrometer from samples dissolved in $CDCl_3$ containing tetramethylsilane as internal standard. Optical rotations were determined on absolute ethanol solutions with a Rudolf 62 polarimeter. Low-resolution mass spectra were determined at 70 eV with a Bendix 3012 time-of-flight mass spectrometer. High-resolution mass spectra were determined with a Du Pont 21-492 mass spectrometer at 70 eV. Melting points are uncorrected and were determined between glass plates on a Nalge block type melting point apparatus.

Gas chromatographic separations were performed on an F&M 700 gas chromatograph equipped with 0.20 in. by 20 ft stainless steel columns packed with 40% Carbowax 20M on 60/80 mesh Gas-Chrom P using a thermal conductivity detector. Temperature programming was from 100 to 220° at 1°/min at a helium flow rate of 100 ml/min and an injection port temperature of 245°. Reaction product percentages were determined by integrating the g.l.c. curve (peak height times width at half height) for the crude reaction mixture.

Epoxidation of *a*-Terpineol

To $15 \cdot 0$ g (0.97 mol) of (-)- α -terpineol (Lilacin, Fisher Scientific Co., Fairlawn, New Jersey), $[\alpha]_{D}^{29} - 31 \cdot 8^{\circ}$ (c, 1.19), in 200 ml of tetrahydrofuran cooled in an ice bath, were added 16.5 g (0.96 mol) of *m*-chloroperbenzoic acid (Eastman Chemical Co., Rochester, New York). The reaction mixture was kept in the ice bath and stirred for 4 h, the solvent removed at 40° and 28 in. Hg, and the residue dissolved in 200 ml of methylene chloride. The methylene chloride solution was washed with 5×50 ml of saturated sodium carbonate and then concentrated to small volume. Separation by g.l.c. afforded 4% starting material (1); 37% of a 4 : 1 mixture (see LiAlH₄ reduction below) of (-)-*trans*-and (-)-*cis*-1,2-epoxy-*p*-menthan-8-ol (2a) and (2b) { $[\alpha]_{D}^{27}$ -48.0° (*c*, 2.70); i.r. (oil film) v_{max} 3600, 1150 cm⁻¹; mass spectrum *m*/e 170 (M⁺), 43, 71, 41, 59}; 37% (-)-1,8-epoxy-*p*-menthan-2-ol (3) {m.p. 63.5-65.0, $[\alpha]_{D}^{27}$ -24.2° (*c*, 1.63); i.r. (oil film) v_{max} 3500, 1040–1068 cm⁻¹; ¹H n.m.r. δ 3.78 (m, 1H, CHOR), 2.82 (m, 1H, COH), 1.47 and 1.38 (s, 3H, (CH₃)₂CO), 1.12 (s, 3H, CH₃CO); mass spectrum *m*/e 170 (M⁺) 43, 41, 71, 126}; and 18% (-)-2,8-epoxy-*p*-menthan-1-ol (5) { $[\alpha]_{D}^{27}$ 29.1° (*c*, 1.99); i.r. (oil film) v_{max} 3500, 1098, 1065 cm⁻¹; ¹H n.m.r. δ 3.59 (m, 1H, HCOR), 3.05 (m, 1H, COH), 1.79 (s, 6H, (CH₃)₂C); mass spectrum *m*/e 170 (M⁺), 43, 71, 26}.

(-)-1,8-Epoxy-p-menthan-2-yl Acetate (4)

This compound, prepared from (3) with acetic anhydride and pyridine, showed: $[\alpha]_D^{28} - 34 \cdot 2^{\circ}$ (c, 2 · 33); i.r. (oil film) v_{max} 1750, 1240 cm⁻¹; mass spectrum m/e 212 (M⁺), 43, 126, 41, high resolution m/e 212 · 1446 (calc. for C₁₂H₂₀O, 212 · 1412).

Lithium Aluminium Hydride Reduction of 1,2-Epoxides (2a) and (2b) to 1,8-Diols (6a) and (6b)

To 100 mg of (2) in 1 ml of tetrahydrofuran was added 100 mg of lithium aluminium hydride and the mixture allowed to stand overnight. The reaction was quenched with 100 μ l distilled water, filtered and concentrated in a rotary evaporator. The reduction products were isolated by g.l.c. in a 4:1 ratio and identified as *trans-p*-menthan-1,8-diol (6a) and *cis-p*-menthan-1,8-diol (6b) by comparison of their i.r. spectra with those of authentic samples.⁸

Rearrangement of 1,2-Epoxide (2) to 1,8-Epoxide (3)

A solution of 50 μ l of (2), 1 ml of tetrahydrofuran and 0.5 ml of aqueous 0.1N H₂SO₄ was allowed to stand 24 h at room temperature. The crude reaction mixture was separated by g.l.c. to afford (3) as the only significant peak, and was identified by comparison of its g.l.c. retention time and i.r. spectrum to those for (3) isolated above.

⁸ Mitzner, B. M., Mancini, V. J., Lemberg, S., and Theimer, E. T., Appl. Spectrosc., 1968, 22(1), 44.

Oxidation of (3) to 1,8-Epoxy-p-menthan-2-one (9)

To 100 mg of (3) was added 1 ml of a solution prepared from 200 mg of N-bromoacetamide, 3 ml of acetone and 0.7 ml of water.⁹ The reaction mixture was kept 18 h in the dark at 5° and then portions of it were separated by g.l.c. to afford (9). I.r. (oil film) ν_{max} 3050, 1755 cm⁻¹; mass spectrum m/e 168 (M⁺), 43, 41, 82.

Reduction of 1,8-Epoxy-p-menthan-2-one (9)

(A) With sodium in alcohol.²—Following the procedure of Gandini,² 50 mg of (9) was reduced with 75 mg of sodium in absolute ethanol to give an alcohol having the same i.r. spectrum and g.l.c. retention time as those of (3) isolated above.

(B) With PtO₂ and hydrogen in acetic acid.—Reduction of 50 mg of (9) in 0.5 ml of acetic acid containing 200 mg of PtO₂ with hydrogen at 55 p.s.i. for 24 h in a Parr hydrogenation apparatus afforded, by g.l.c. separation, $1\beta_{,8}\beta_{-}$ epoxy-*p*-menthan- 2α -ol (10).² I.r. (oil film) ν_{max} 3600, 1170, 1130, 1090 cm⁻¹; mass spectrum m/e 170 (M⁺), 43, 71, 126.

Clemmensen Reduction of Ketone (9) to 1,8-Cineole (11)

Ketone (9) (50 mg) was reduced with zinc amalgam to 1,8-cineole.⁷ G.l.c. separation afforded 10 mg (20%) of cineole (11) which had an infrared spectra identical with that of an authentic sample.

Lithium Aluminium Hydride Reduction of 1,2-Epoxydihydropinol (8) to (5)

1,2-Epoxide (8) (100 mg), prepared by epoxidation of pinol (7) as previously described, in 1 ml of tetrahydrofuran was reduced with lithium aluminium hydride as described above. Separation by g.l.c. afforded 25 mg (25%) of a product that was identical by i.r. and mass spectral comparison to (5) isolated from the peracid oxidation of α -terpineol described above.

Oxidation of Pinol (7) to $(5)^5$

To 10 g (0.012 mol) of pinol was added 5.0 g (0.012 mol) of mercuric acetate in 30 ml of tetrahydrofuran. The reaction mixture was refluxed 6 days before the yellow colour disappeared, then 30 ml of 3N NaOH, followed by 30 ml of 0.5M NaBH₄ in 3N NaOH were added. The lower aqueous layer was withdrawn and the tetrahydrofuran removed under vacuum at 40° and 28 in. Hg. The crude mixture was separated by g.l.c. to afford, in a 19:1 ratio, starting material (8) and 2,8-epoxy-*p*menthan-1-ol (3), having the same i.r. spectrum as that of (3) isolated above.

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⁹ Herzug, H. L., Jevnik, M. A., Perlman, P. L., Nobile, A., and Hershberg, E. B., *J. Amer. Chem. Soc.*, 1953, **75**, 266.