

The Chemistry of Terpenes. Part XXI.¹ By-products from the Epoxidation of (+)-Car-3-ene with Acetonitrile-Hydrogen Peroxide

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Epoxidation of (+)-car-3-ene (1) with acetonitrile-hydrogen peroxide afforded, besides (+)-3 α ,4 α -epoxycarane (2), minor amounts of (+)-3 α ,4 α -epoxycaran-2-one (3), (-)-3 α ,4 α -epoxycaran-5-one (4), (-)-3 α ,4 α -epoxycaran-2 α -ol (5), and (+)-3 α ,4 α -epoxycaran-5 α -ol (6). Reduction of the epoxy-alcohol (5) with lithium aluminium hydride gave (-)-carane-2 α ,3 α -diol (7), also obtained from (+)-car-2-ene (8) and permanganate. Reduction of the epoxy-ketone (3) with borohydride gave only (-)-3 α ,4 α -epoxycaran-2 β -ol (9), which with lithium aluminium hydride afforded (-)-carane-2 β ,3 α -diol (12). Oxidation of the epoxy-alcohol (6) yielded the epoxy-ketone (4) which, on reduction with borohydride, gave (+)-3 α ,4 α -epoxycaran-5 β -ol (13), isolated as its monohydrate.

IN continuance of our investigations on oxygenated derivatives of (+)-car-3-ene (1), we recently² prepared the epoxide (2) by the peroxyimidic acid method.³ After the product had been distilled, a viscous, high-boiling fraction remained. Examination of this has now provided evidence that allylic oxidation of olefins may take place concurrently with epoxidation by this system.³

Repeated chromatography of the residue on silica gel afforded four main components, identified as (+)-3 α ,4 α -epoxycaran-2-one (3), (-)-3 α ,4 α -epoxycaran-5-one (4), (-)-3 α ,4 α -epoxycaran-2 α -ol (5), and (+)-3 α ,4 α -epoxycaran-5 α -ol (6). The epoxy-ketones (3) and (4), which were eluted together as a mixture, were identified by comparison with authentic specimens.⁴

¹ Part XX, D. A. Baines and W. Cocker, *J.C.S. Perkin I*, 1975, 2232.

² W. Cocker and D. H. Grayson, *J.C.S. Perkin I*, 1975, 1217.

³ G. B. Payne, P. H. Deming, and P. H. Williams, *J. Org. Chem.*, 1961, **26**, 659.

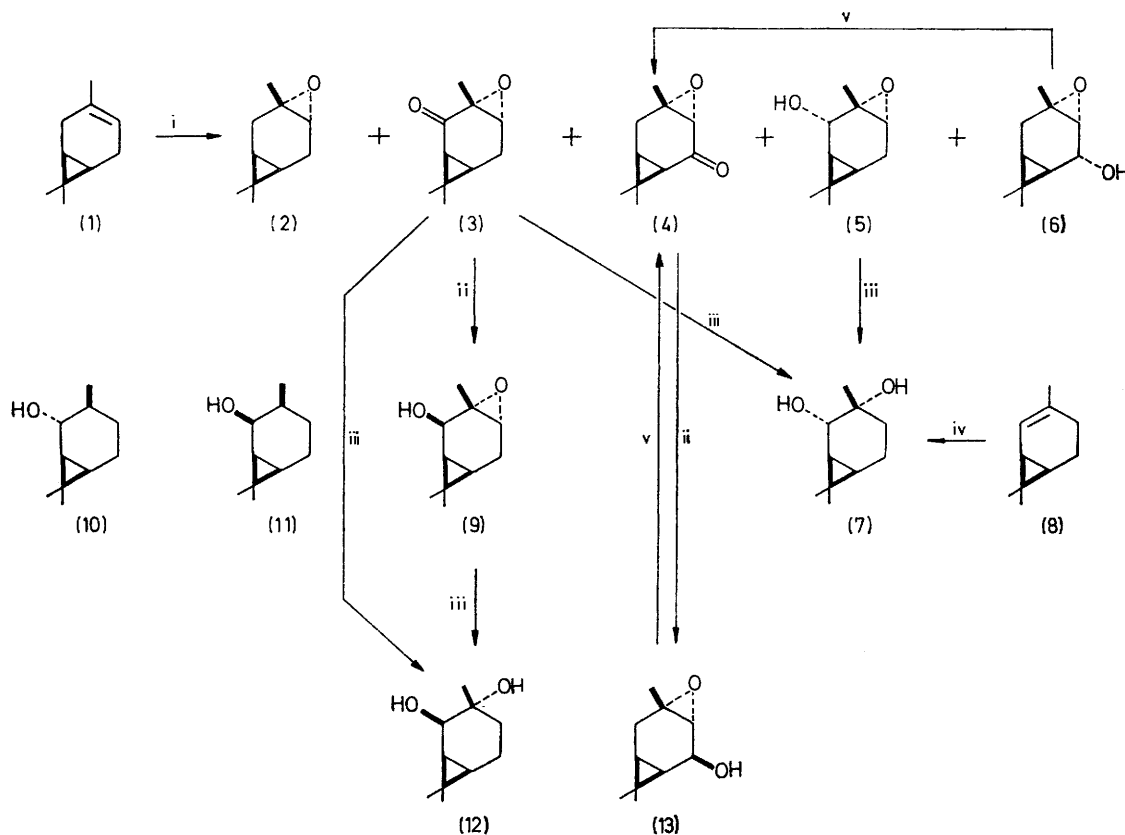
⁴ W. D. P. Burns, M. S. Carson, W. Cocker, and P. V. R. Shannon, *J. Chem. Soc. (C)*, 1968, 3073.

The epoxy-alcohol (5), only obtainable in *ca.* 90% purity, had i.r. maxima at 3 350 and 860 cm^{-1} and its n.m.r. spectrum (CDCl_3) had signals at τ 6.71 (2-H), 6.92 (4-H), and 8.59, 8.94, and 9.23 (methyl groups). Its structure and configuration were established by reduction with lithium aluminium hydride to (–)-carane-2 α ,3 α -diol (7), an authentic specimen of which was obtained by oxidation of (+)-car-2-ene (8) with alkaline potassium permanganate.⁵

For comparative purposes, the readily available ⁴ (+)-3 α ,4 α -epoxycaran-2-one (3) was reduced with potassium borohydride to give, as the sole product, (–)-3 α ,4 α -epoxycaran-2 β -ol (9), ν_{max} 3 400 and 840 cm^{-1} . In its n.m.r. spectrum, the 2-H signal appeared at τ 5.61

diols (7) and (12) reflect their environments in n.m.r. signals at τ 6.78 and 5.87, respectively.

(+)-3 α ,4 α -Epoxy-caran-5 α -ol (6) was obtained as an oil of *ca.* 95% purity, ν_{max} 3 380 and 856 cm^{-1} , τ 6.05 (5-H), 6.61 (OH), 6.94 (4-H), and 8.68, 8.91, and 9.23 (methyl groups). On careful oxidation it gave mainly the epoxy-ketone (4), thus establishing the α -orientation of the oxiran ring. Reduction of the epoxy-ketone (4) with potassium borohydride afforded (+)-3 α ,4 α -epoxycaran-5 β -ol (13), obtained as its crystalline monohydrate, ν_{max} 3 440 and 3 245 (OH) and 850 cm^{-1} , τ 5.42 (d, *J* 7.8 Hz, 5-H), 7.06 (4-H), 8.10 (3 H, exch. D_2O , OH and H_2O), and 8.65, 8.89, and 8.93 (methyl groups). Oxidation regenerated (4) in good yield.



Reagents: i, H_2O_2 -MeCN; ii, KBH_4 ; iii, LiAlH_4 ; iv, KMnO_4 ; v, $\text{Na}_2\text{Cr}_2\text{O}_7$ - H_2SO_4

[*cf.* τ 6.71 for the corresponding proton in the epimeric alcohol (5)]. The shielding effect of the cyclopropyl system is also reflected in the spectra of the caran-2 α - and -2 β -ols (10) and (11) in which the 2-H signals appear at τ (CCl_4) 7.06 and 5.68, respectively.⁶

Reduction of the epoxy-alcohol (9) with lithium aluminium hydride at room temperature gave (–)-carane-2 β ,3 α -diol (12).⁵ This was also obtained directly from (+)-3 α ,4 α -epoxycaran-2-one (3) with the same reagent, a little (–)-carane-2 α ,3 α -diol (7) being formed concurrently. Like those of the alcohols (5) and (9), the 2-protons of the

The mechanism by which these by-products are formed from (+)-car-3-ene (1) is not clear. Initial allylic oxidation at C-2 and C-5, followed by epoxidation of the olefinic bond, could lead to hydroperoxides from which the ketones (3) and (4) could arise by loss of water. Reduction of the hydroperoxides by exchange with solvent would give the epoxy-alcohols (5) and (6). That allylic oxidation of (1) is the first step is suggested by the inertness of (+)-3 α ,4 α -epoxycaran-2-one (3) to oxidation under similar reaction conditions.

⁵ B. A. Arbuzov, V. V. Ratner, Z. G. Isaeva, and N. Kh. Abaeva, *Izvest. Akad. Nauk S.S.S.R., Ser. khim.*, 1974, 2762 (*Chem. Abs.*, 1975, 82, 17,1212t).

⁶ W. Cocker, P. V. R. Shannon, and P. A. Staniland, *J. Chem. Soc. (C)*, 1967, 485, and unpublished data from this laboratory; *cf.* S. P. Acharya and H. C. Brown, *J. Amer. Chem. Soc.*, 1967, 89, 1925.

Initial formation of allylic hydroperoxides without migration of the double bond is a characteristic of reaction with triplet oxygen,^{7,8} but introduction of gaseous oxygen into the reaction mixture did not increase the yield of oxidation products. An alternative, oxidation of the hydrogen peroxide by peroxyimide anion (*cf.* ref. 3), might be expected to lead to the singlet species.⁹ Rapid allylic rearrangement¹⁰ of the derived hydroperoxides would then be necessary to give the observed products.

The exact nature of the oxidant of this reactive¹¹ olefin therefore remains in doubt, but thermal decomposition of the peroxyimide acid to give free radical intermediates (*cf.* ref. 12) cannot be excluded.

EXPERIMENTAL

The general experimental conditions were those defined earlier.¹ Unless otherwise stated, n.m.r. spectra were obtained at 60 MHz for solutions in deuteriochloroform, *i.e.* spectra were recorded for Nujol mulls (N) or neat liquids (L),* and optical rotations were measured for ethanolic solutions with a Perkin-Elmer 141 automatic polarimeter.

Chromatography of By-products from the Oxidation of (+)-Car-3-ene (1) with Hydrogen Peroxide-Acetonitrile.—The residue (8 g) obtained by removing (+)-3 α ,4 α -epoxycarane from an oxidation of (+)-car-3-ene (136 g) as previously described² was chromatographed on silica gel (300 g) in a gradient of ether in light petroleum. Three main fractions were obtained. The first (2 g) was a mixture of (+)-3 α ,4 α -epoxycaran-2-one (3) and (–)-3 α ,4 α -epoxycaran-5-one (4) in the ratio 20 : 80 (g.l.c.). The second fraction (0.6 g) was rechromatographed to give (–)-3 α ,4 α -epoxycaran-2 α -ol (5)* as an oil of *ca.* 90% purity, $[\alpha]_D^{21} - 1^\circ$ (*c* 0.5). It could not be further purified. The third fraction (3 g) was also rechromatographed, giving (+)-3 α ,4 α -epoxycaran-5 α -ol (6)* as an oil of *ca.* 95% purity, $[\alpha]_D^{20} + 32^\circ$ (*c* 0.2).

Oxidation of (–)-3 α ,4 α -Epoxycaran-2 α -ol (5) with Lithium Aluminium Hydride.—The epoxide (100 mg), in ether (10 ml), was stirred for 6 h at room temperature with an excess of lithium aluminium hydride. Saturated aqueous ammonium chloride was added and the product was isolated from the organic layer in the usual way as a waxy solid (92 mg), which was recrystallised from light petroleum to give (–)-carane-2 α ,3 α -diol (7)^{5*} as needles, m.p. 58–59° (*lit.*,⁵ 55–56°), $[\alpha]_D^{20} - 27^\circ$ (*c* 0.2), ν_{\max} (N) 3340 and 1068 cm⁻¹, τ 6.78br (1 H, s, 2-H), 7.73 (2 H, *exch.* D₂O, OH), and 8.74, 8.91, and 9.01 (9 H, 3s, 3 Me) (Found: C, 70.3; H, 10.5. Calc. for C₁₀H₁₈O₂: C, 70.5; H, 10.7%).

Oxidation of (+)-Car-2-ene (8) with Permanganate.—The olefin (3 g) $\{[\alpha]_D^{19} + 86^\circ$ (*c* 0.2) $\}$ was treated with potassium permanganate as described earlier² for (+)-car-3-ene (1). The crude product (3.2 g), recrystallised from light petroleum, gave (–)-carane-2 α ,3 α -diol (7)⁵ (2.9 g), identical with the material obtained as described above.

Reduction of (+)-3 α ,4 α -Epoxycaran-2-one (3) with Borohydride.—The epoxy-ketone (3)⁴ (2 g) $\{[\alpha]_D^{20} + 19^\circ$ (*c* 0.2) $\}$ in methanol (30 ml) was treated at 0 °C with potassium borohydride (1 g) in sodium hydroxide solution (0.1M; 10 ml). After 1.5 h at 0 °C, the excess of borohydride was

carefully decomposed with acetic acid and the product was collected in ether. Recrystallisation from light petroleum afforded (–)-3 α ,4 α -epoxycaran-2 β -ol (9)* as needles (1.8 g), m.p. 79–80°, $[\alpha]_D^{21} - 73^\circ$ (*c* 0.2), τ 5.61 (1 H, d, *J* 8.0 Hz, 2-H), 6.97 (1 H, m, 4-H), 8.31br (1 H, *exch.* D₂O, OH), and 8.59, 8.88, and 8.92 (9 H, 3s, 3 Me) (Found: C, 71.1; H, 9.5. C₁₀H₁₆O₂ requires C, 71.4; H, 9.6%).

Reduction of (–)-3 α ,4 α -Epoxycaran-2 β -ol (9) with Lithium Aluminium Hydride.—The epoxide (1.3 g) in ether (50 ml) was stirred with an excess of lithium aluminium hydride for 5 h at 20 °C. Chromatography of the oily product (1 g) on silica gel gave starting material (9) (0.3 g) and (–)-carane-2 β ,3 α -diol (12)* (0.5 g), b.p. 78–80° at 0.2 mm Hg, m.p. 30–31° (*lit.*,⁵ 30–32°), $[\alpha]_D^{19} - 66^\circ$ (*c* 0.1), ν_{\max} (L) 3400 and 1042 cm⁻¹, τ 5.87 (1 H, d, *J* 9.0 Hz, 2-H), 8.19br (2 H, *exch.* D₂O, 2 OH), and 8.68, 8.73, and 8.90 (9 H, 3s, 3 Me) (Found: C, 70.5; H, 10.8. Calc. for C₁₀H₁₈O₂: C, 70.5; H, 10.7%).

Reduction of (+)-3 α ,4 α -Epoxycaran-2-one (3) with Lithium Aluminium Hydride.—The epoxy-ketone (3)⁴ (2 g) in dry ether (50 ml) was stirred with an excess of lithium aluminium hydride for 4 h at 20 °C. The product, a viscous oil, was chromatographed on silica gel giving (–)-carane-2 α ,3 α -diol (7) (0.4 g) and (–)-carane-2 β ,3 α -diol (12) (1.2 g), identical with specimens obtained as described above.

Oxidation of (+)-3 α ,4 α -Epoxycaran-5 α -ol (6).—The alcohol (0.2 g) in ether (10 ml) was stirred for 1 h at 0 °C with a solution of sodium dichromate dihydrate (0.14 g) in sulphuric acid (0.1 ml) and water (2 ml). The neutral product (0.15 g) consisted substantially of (–)-3 α ,4 α -epoxycaran-5-one (4) (g.l.c., *i.r.*). Of the other substances present in minor amounts, the most abundant was unchanged alcohol (6).

Reduction of (–)-3 α ,4 α -Epoxycaran-5-one (4) with Borohydride.—The epoxy-ketone (4)⁴ (2 g) was reduced with potassium borohydride as described for the isomeric ketone (3). The crude product (1.7 g) was chromatographed on silica gel giving a solid (1.3 g), which crystallised from pentane at –20 °C to give (+)-3 α ,4 α -epoxycaran-5 β -ol monohydrate (13)* as needles, m.p. 43–44°: $[\alpha]_D^{20} + 51^\circ$ (*c* 0.3) (Found: C, 64.7; H, 9.3. C₁₀H₁₈O₃ requires C, 64.5; H, 9.7%).

Oxidation of (+)-3 α ,4 α -Epoxycaran-5 β -ol Monohydrate.—The epoxy-alcohol (13) (0.5 g) in ether (10 ml) was stirred for 0.5 h at 0 °C with a solution of sodium dichromate dihydrate (0.4 g) and sulphuric acid (0.25 ml) in water (5 ml). The neutral product (0.4 g) consisted of the epoxy-ketone (4).

Epoxidation of (+)-Car-3-ene (1) in the Presence of Gaseous Oxygen.—The reaction was carried out as previously described² except that oxygen was passed into the reaction mixture at *ca.* 250 ml min⁻¹. After work-up, the residue (8.4 g) contained the same mixture of compounds as was obtained without oxygen, and the yield of (+)-3 α ,4 α -epoxycarane (2) (72 g) did not differ significantly from that realised earlier.²

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⁸ D. Swern, 'Organic Peroxides,' Wiley, New York, 1971, vol. 2, p. 22.

⁹ K. Akiba and O. Simamura, *Tetrahedron*, 1970, **26**, 2527.

¹⁰ Ref. 8, p. 14.

¹¹ G. Widmark and S-G. Blohm, *Acta Chem. Scand.*, 1957, **11**, 392.

¹² M. Gruselle, J. Fossey, and D. Lefort, *Tetrahedron Letters*, 1970, 2069.

* *I.r.* data for compounds marked with an asterisk are available as Supplementary Publication No. SUP 21674 (6 pp.). For details of Supplementary Publications, see Notice to Authors No. 7 in *J.C.S. Perkin I*, 1975, Index issue.

⁷ K. Gollnick, S. Schroeter, G. Ohloff, G. Schade, and G. O. Schenck, *Annalen*, 1965, **687**, 14.