The Conformation of *p*-Menthane-2, 3-diol*

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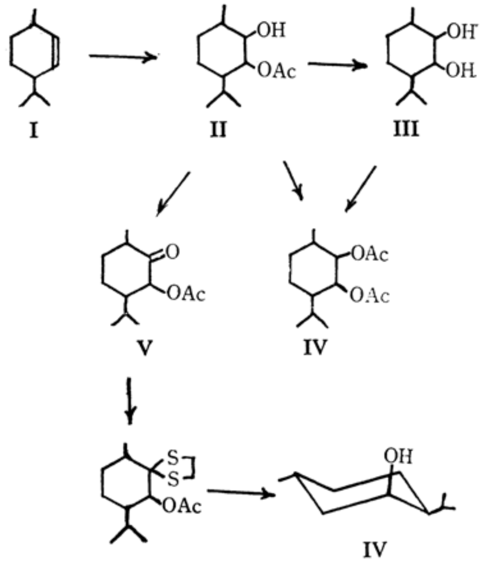
The hydroxylation of (+)-*p*-menth-2-ene (I) with an organic peracid, or the hydrolysis of its epoxide, affords *p*-menthane-2, 3-diol (II), which has its hydroxyls in the trans configuration. Infrared studies[1] have indicated that the diol adopts a conformation in which both the hydroxyls are axial; its spectrum exhibits the absorption (at 3635 cm^{-1}) due to free (non-bonded) hydroxyls only. We have arrived at the same conclusion in the investigation reported here.

(+)-*p*-Menth-2-ene (I), derived from (−)-menthol, after treatment with peracetic acid afforded a viscous liquid b. p. 120—128°C/3mmHg, which deposited crystals of 2-hydroxy-3-acetoxy-*p*-menthane (III), m. p. 114—116°C, $[\alpha]_D = +16.8°$ (methanol), after standing for several days at room temperature. The oily mother liquor, which is apparently a mixture of the diol and its partial acetate, was not separated but was treated with alkali, whereupon it afforded pure *p*-menthane-2, 3-diol (II) b. p. 98—100°C/0.1 mmHg, $[\alpha]_D = +66.4°$ (benzene), identical with that obtained by the hydrolysis of compound III. The diol II and its monoacetate III afforded the same diacetate, m. p. 48—50°C on acetylation. The monoacetate III, which is considered to be an intermediate in the formation of the diol, was used in the following conformational study.

The chromic acid oxidation of the monoacetate III yielded the acetoxy ketone V, m. p. 46—47°C, $[\alpha]_D = +37.1°$ (methanol). The thioketal derived from the ketone V, on desulfurization with Raney nickel, afforded an oil which was identified as (+)-neomenthol by a comparison of their *p*-nitrobenzoates (infrared spectrum and mixed melting point). (+)-Neomenthol has been shown to have the absolute configuration and conformation shown in VI[2]. The acetoxy ketone V is, therefore, 3-acetoxycarvomenthone, which has an axial acetoxyl group, and the conformation of the two oxygenated functions in III and II must be transdiaxial. This finding is in agreement with the ultraviolet spectrum of the monoacetate V, which shows a bathochromic shift of 9 mμ with respect to carvomenthone (see Table I), thus indicating[3] the presence of an axial acetoxyl group at the α-position in V. Consequently, III has axial hydroxyl and acetoxyl groups, and in II both hydroxyls are axial.



The ORD curve of V shows a strong positive Cotton effect in both methanol and in isooctane (see Fig. 1). It has been observed[4] that an α-acetoxyl group makes an irregular contribution to the Cotton effect. In our case the axial acetoxyl group probably does not make much contribution to the effect in both solvents, and the conformational mobility normally

TABLE I

	λ_{max} (mμ)	log ε
V in ethanol	293	1.80
Carvomenthone in ethanol	284[5]	1.35

The bathochromic shifts of the acetoxy ketone V

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* The work was partly reported in a short communication in *Chem. & Ind.*, **1963**, 1119.

[1] P. R. Jefferies and B. Miligan, *J. Chem. Soc.*, **1956**, 2363; A. R. H. Cole and P. R. Jefferies, ibid., **1956**, 4391; T. Matsuura, T. Suge and T. Shishihori, The 16th Annual Meeting of the Chemical Society of Japan, April, Tokyo.

[2] J. L. Simonsen, "The Terpenes," Vol. 1, Cambridge University Press (1953), p. 237.

[3] C. Djerassi, "Optical Rotatory Dispersion," McGraw-Hill, New York (1960), p. 113.

[4] C. Djerassi, O. Halpern, V. Halpern and O. Schindler, *Helv. Chim. Acta*, **41**, 250 (1958).

[5] T. M. Lowry and R. E. Lishmund, *J. Chem. Soc.*, **1935**, 1313.

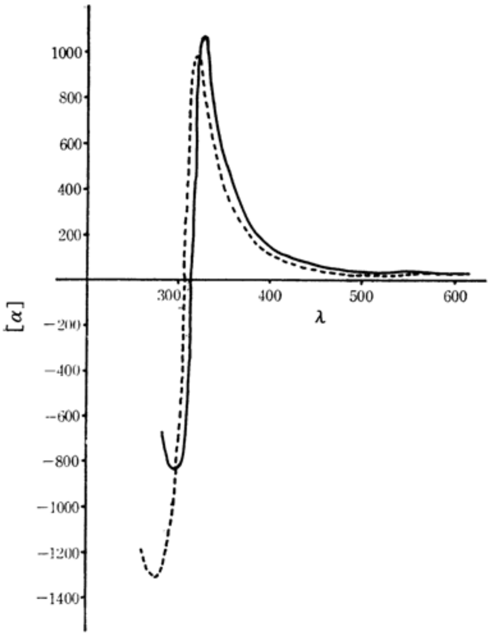

Fig. 1. ORD curves of the acetoxyketone (V).
—— in isooctane
- - - in methanol

dependent on the polarity of the solvents was not observed.

Experimental

The Hydroxylation of *trans-p*-Menth-2-ene (I) with Peracetic Acid. — *trans-p*-Menth-2-ene (I), b. p. 55—56°C/15 mmHg, $d_4^{15}=0.8160$, $[\alpha]_D=+120.46$ (neat), was prepared from 1-menthyl tosylate. I (15 g.) was added drop by drop over a half-hour period to a solution of 30% hydrogen peroxide (25 ml.) in acetic acid (120 ml.) containing a few drops of concentrated sulfuric acid and warmed at 50°C. After the addition of I, the reaction mixture was stirred for another hour. The acetic acid was then removed in vacuo. The residue was dissolved in ether, washed with saturated sodium bisulfite to destroy the excess peracid, and then washed with aqueous sodium carbonate. The evaporation of the dried (sodium sulfate) ether solution yielded a viscous liquid (14.5 g.), b. p. 120—128°C/3 mmHg. On standing at room temperature the liquid gradually deposited crystals of 2-hydroxy-3-acetoxymenthane (III) (1.5 g.); after recrystallization from ligroin, it had an m. p. of 114—116°C, $[\alpha]_D=+16.8°$ (*c* 2.10, methanol) (Found: C, 66.82; H, 10.52. $C_{12}H_{22}O_3$ requires C, 67.25; H, 10.35%). The acetylation of III with acetic anhydride and sodium acetate gave the diacetate IV, m. p. 48—50°C (Found: C, 65.82; H, 9.41. $C_{14}H_{24}O_4$ requires C, 65.59; H, 9.44%).

The filtrate (10 g.) was heated in 20% alcoholic potash (100 ml.) under reflux for an hour. After acidification with hydrochloric acid, the product was isolated by ether extraction to yield *p*-menthane-2,3-diol (II) (8 g.) b. p. 98—100°C/0.1 mmHg, $[\alpha]_D=+66.4°$ (*c* 2.12, benzene)). Diacetate: m. p. and mixed m. p. with acetate IV of III 48—50°C. Di-*p*-nitrobenzoate: m. p. 179—180°C (Found: N, 5.86. $C_{24}H_{26}O_8N_2$ requires N, 5.96%).

The Chromic Acid Oxidation of 2-Hydroxy-3-acetoxymenthane (III).—A solution of 2-hydroxy-3-acetoxymenthane (III) (3 g.) in pyridine (20 ml.) was added drop by drop to a suspension of chromic anhydride (4.5 g.) in pyridine (45 ml.). After the addition of III, the reaction mixture was stirred for five days at room temperature. After acidification with dilute sulfuric acid, the product was isolated by continuous extraction with ether (five days). The evaporation of the ether gave crude 3-acetoxycarvomenthone (V), which, after purification by vacuum sublimation (120°C (bath), 0.03 mmHg), had an m. p. of 46—47°C; yield 2.1 g. (Found: C, 68.04; H, 9.85. $C_{12}H_{20}O_3$ requires C, 67.89; H, 9.50%). 2,4-Dinitrophenylhydrazone: m. p. 157°C (from alcohol) (Found: N, 14.16. $C_{18}H_{24}O_6N_4$ requires N, 14.28%).

The ORD curves were measured in methanol and in isooctane.

In methanol (*c* 0.1025):
$[\alpha]_{318}=+975.6°$ (peak)
$[\alpha]_{280}=-1326.8°$ (trough)
In isooctane (*c* 0.1035):
$[\alpha]_{322}=+1078.4°$ (peak)
$[\alpha]_{308}=-850.3°$ (trough)

The Reduction of 3-Acetoxycarvomenthone (V). —A mixture of 3-acetoxycarvomenthone (V) (2 g.), ethane dithiol (6.5 ml.) and boron trifluoride etherate (6.5 ml.) was allowed to stand for four hours at room temperature. After the addition of water, the product was extracted with ether. The ethereal solution was washed with dilute sodium hydroxide and dried over sodium sulfate. The evaporation of the ether yielded the thioketal of V. Without further purification the thioketal was heated with Raney nickel (from 30 g. of Raney alloy) in dioxane for five hours. After filtration and the removal of the solvent, the residue was treated with *p*-nitrobenzoyl chloride in pyridine at room temperature. The *p*-nitrobenzoate after recrystallization from alcohol showed an m. p. and mixed m. p. with *p*-nitrobenzoate of *d*-neomenthol of 96—99°C. The two *p*-nitrobenzoates showed identical infrared spectra.

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