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Absolute Configuration of Menthenone Oxide

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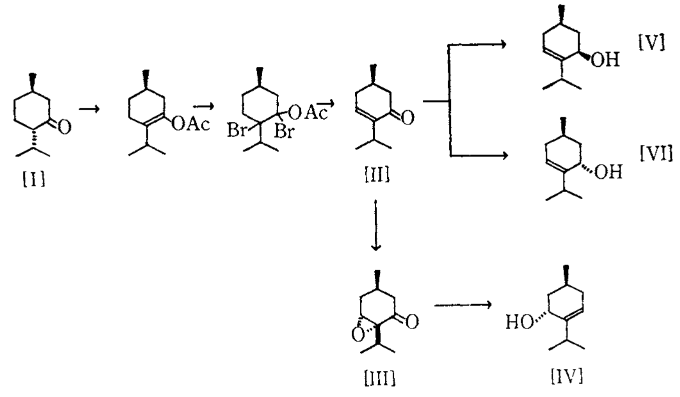
One[1] of the authors (J.K.) has recently discussed the epoxidation mechanism of endocyclic α,β-unsaturated terpene ketones, and, on the basis of orbital-overlap concept,[2] has concluded that the oxirane group is stereoselectively introduced to the double bond so as to sterically enable the most favored transition state conformation to be stabilized by an effective and concomitant orbital-overlap stabilization. When this generalization is applied to (1R)-4-menthene-3-one (II), the exclusive formation of 4-menthen-3-one oxide (III) having the (1R : 4R : 5R)-configuration may be predicted.

We wish in this paper to describe the determination of the absolute configuration of (+)-menthenone oxide (III) by an unequivocal chemical transformation into known derivative (+)-*trans*-menthenol (IV) of the well-defined configuration (1 S : 3 R) by the following scheme.

The results unambiguously demonstrate that the absolute configuration of (+)-menthenone oxide



Scheme 1

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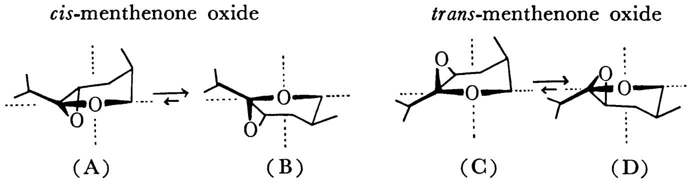
[1] J. Katsuhara, This Bulletin, **42**, 2391 (1969).

[2] H. E. Zimmerman, L. Singer and B. S. Thyagaraja, *J. Amer. Chem. Soc.*, **81**, 108 (1959).


cis-menthenone oxide

trans-menthenone oxide

Scheme 2

(III) is *cis*-(1 R : 4 R : 5 R). This is what was predicted previously.[1]

Octant projection diagrams, when conformational generalization is applied to the present *cis*- and *trans*-menthenone oxide systems, are shown in Scheme 2. It can be seen that, of the four conceivable conformations A, B, C and D, B and D are conformationally more favored than the respective counterpart. The diagrams show that in the ORD-measurement, *cis*-menthenone oxide should exhibit a high positive $[\phi]$ value whereas the *trans*-oxide a low negative $[\phi]$ value. This is also in good agreement[3] with the ORD data found for the (+)-menthenone oxide ($a=+25$), cogently supporting the configuration of *cis*-(+)-III as assigned above.

Experimental

Preparation of Menthenone Oxide (III). (−)-Menthenone (II)[4] 7.0 g, $[\alpha]^{20}_{D}$ −52.2° (*c* 0.6, ethanol), UV; $\lambda_{max}^{methanol}$ 236 mμ (ε, 7240), II-2,4-dinitrophenylhydrazone mp 142°C (lit,[4] mp 143°C), yield 87.0%, derived from (−)-menthone (I), $[\alpha]^{20}_{D}$ −22.1° (*c* 0.6, ethanol) was epoxidized with 26 m*l* of 30% hydrogen peroxide and 3.5 g of sodium in 140 m*l* of methanol for 5 hr at −30°C to menthenone oxide (III). The crude III indicated a single product by VPC analysis. Further purification on a preparative VPC gave pure III, $[\alpha]^{20}_{D}$ +61.5° (*c* 1.0, methanol), UV; $\lambda_{max}^{methanol}$ 299 mμ (ε, 20), 288 mμ (ε, 19), CD; mμ ($[\theta]$) in methanol, 350 (0), 308 (+2035), 245 (0), 205 (+6460), ORD; mμ ($[\phi]$) in methanol, 400 (+392), 355 (+1632), 292 (−849), 250 (+554), 220 (+3589), 210 (+979), yield 63.5%.

Found: C, 71.26; H, 9.65%. Calcd for $C_{10}H_{16}O_2$: C, 71.44; H, 9.60%.

Preperation of (+)-*trans*-Menthenol. By means of the Wharton reaction[5] technique, the oxide III has been converted into crude (+)-*trans*-menthenol (IV), $[\alpha]^{20}_{D}$ +69.1° (*c* 0.6, ethanol), yield 87.0%, IV-*p*-nitrobenzoate mp 54°C (lit,[6] mp 55°C), $[\alpha]^{20}_{D}$ −197° (*c* 0.1, chloroform).

Reduction of Menthenone (II). (−)-Menthenone (II) was reduced with lithium aluminum hydride in ether to give a mixture (yield 80.0%) of (−)-*cis*-menthenol (V), $[\alpha]^{24}_{D}$ −32.0° (*c* 1.0, ethanol), V-*p*-nitrobenzoate mp 38°C, $[\alpha]^{24}_{D}$ −10.4° (*c* 0.1, chloroform), and (−)-*trans*-menthenol (VI), the ratio of formation V : VI was 93 : 7 as determined by VPC analysis. The epimeric (−)-VI was identified to be (+)-IV by comparison of each R_t of VPC.

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6) D. Malcolm and J. Read, *J. Chem. Soc.*, **1939**, 1037.