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CONSTITUENTS OF JAPANESE PEPPERMINT OIL, I.

ISOLATION AND IDENTIFICATION OF (-) P-MENTHANE-TRANS-2,5-DIOL FROM "RYOKUBI"

Takeshi Hashizume and Isao Sakata*
Department of Agricultural Chemistry,
Kyoto University, Kyoto, Japan

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Despite numerous investigations on the constituents of peppermint oil, only a few monoterpenediols have been isolated. Recently Katsuhara et al.(1) isolated three monoterpenediols from the high-boiling fraction of Mitcham peppermint oil produced in Hokkaido, and identified them as (-) 2-p-menthene-trans-1,4-diol, (-) p-menthane-2,3-diol and (-) (1R:3R:4S)-1-hydroxymenthol, respectively.

The present investigators have first isolated and identified (-) p-menthane-trans-2,5-diol from the natural source, namely the high-boiling fraction of the oil of Mentha arvensis L. var. piperascens H. (34-52) (Japanese name, Ryokubi) which is a new variety produced in Okayama, although Blumann et al.(2) have isolated p-menth-1-ene-3,6-diol from the oil of Eucalyptus dives. This communication deals with the isolation, identification and conformation.

Five kilograms of the oil was fractionally distilled under reduced pressure, and the fraction of boiling point of 115-120°/10 mm Hg (sp. gr. at 17°, 0.906 ; $[\alpha]_D^{21}$, -35.4° ; yield, 179.2 g) was collected. From the fraction 550 mg of crystalline solids were obtained on storing. The solids were fractionated into ethyl acetate-soluble and -insoluble fractions. The ethyl acetate-soluble fraction (449 mg) was placed on the top of a column, 17.5 X 1.7-cm i.d., packed with 25 g of silicic acid (purchased from Mallinckrodt), and eluted successively with chloroform and ethyl acetate at a flow rate of 0.5 ml/min. The ethyl acetate-eluate was collected and evaporated to dryness yielding 237 mg of solid. Upon four recrystallizations from ethyl acetate the new constituent was obtained in the yield of 145 mg. (0.003 % from the oil)

The constituent is colorless needles, m.p. 143-144° (subl. 103-108°), $[\alpha]_D^{16}$ -12.7° (c, 1.025

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* On the leave from The Oriental Menthol Industry Company, Ltd., Okayama

, methanol) and -17.8° (c, 1.065, ethanol), with a molecular formula of $C_{10}H_{20}O_2$. This has been identified as (-) p-menthane-trans-2,5-diol (I) on the basis of the following evidences.

The infrared spectrum (KBr pellet) indicated the presence of hydroxyl group (3260, 1105, 1050 and 1035 cm^{-1}), isopropyl group (1388 and 1375 cm^{-1}) and probably the absence of double bond. The sharp and intense two doublets at 0.93 and 0.99 p.p.m. (6H, J=7 c.p.s.) in the nmr spectrum (FIG.1) are ascribed to an isopropyl group, doublet at 1.27 p.p.m. (3H, J=5 c.p.s.) to a methyl group and 2H signals at 5.8 p.p.m. to two hydroxyl groups which disappeared on shaking with deuterium oxide. Signals at a region of 3.2-3.9 p.p.m. (2H, multiplet) showed the presence of protons attached to carbons bearing hydroxyl groups.

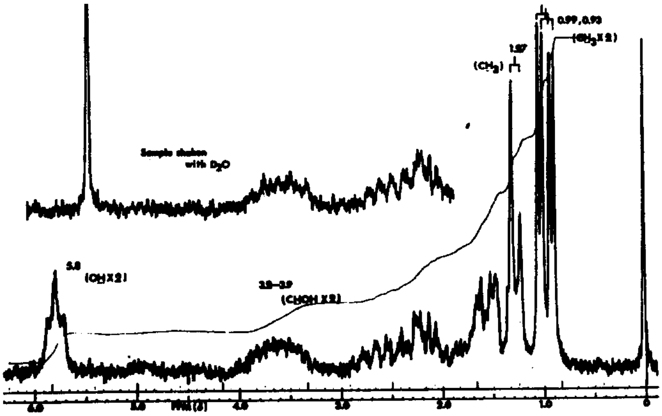


FIG.1 Nmr spectra of I measured in deuterated pyridine

Acetylation of I with pyridine-acetic anhydride yielded a diacetate (II), m.p. 66-67°, $[\alpha]_D^{10}$ +15° (c, 1.00, chloroform). Signals at 1.70 and 1.73 p.p.m. (6H, singlet) in the nmr spectrum (FIG.2) are ascribed to O-acetyl groups and two sextets at 4.53 and 4.78 p.p.m. (2H, J=10 and 5 c.p.s.) to two protons attached to carbons bearing O-acetyl groups.

Benzoylation of I with 3,5-dinitrobenzoyl chloride afforded a bis-(3,5-dinitrobenzoyl) derivative (III), m.p. >300°, with a molecular formula of $C_{24}H_{24}O_{12}N_4$.

Oxidation of I with Jones reagent$^{(3)}$ yielded a dione (IV), m.p. 56-57°. The ultraviolet absorption maximum ($\lambda_{max}^{ethanol}$, 285 mμ ; $\mathcal{E}$, 45) of this compound resulted in no bathochromic shift in alkaline alcohol solution indicating the absence of conjugated carbonyl group.$^{(4a)}$ The infrared spectrum indicated only the presence of ketones. (1720 cm^{-1} in carbon tetrachloride)$^{(5,6,7)}$

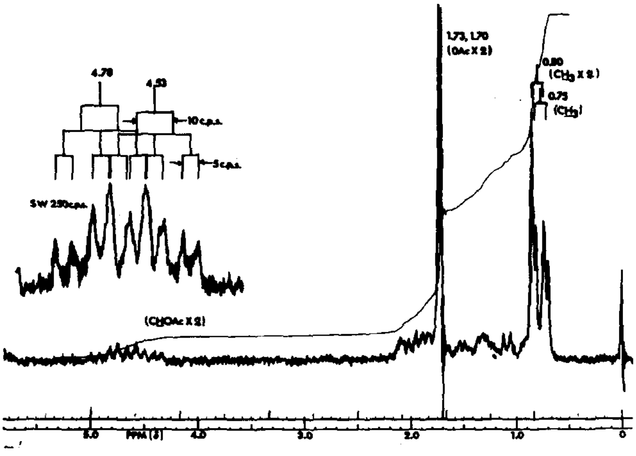


FIG.2 Nmr spectra of II measured in benzene

The ultraviolet spectra of bis-(2,4-dinitrophenylhydrazone) derivatives (Va and Vb) provide further evidence for that the compound is saturated diketone, since the absorption maximum exists in 365 mμ (ε, 5.5 X 10^4, chloroform) and the molar extinction equals to the sum of those of 2,4-dinitrophenylhydrazones of menthone and carvomenthone.(4b,8)

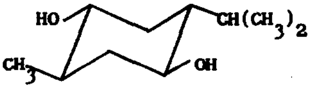
The compound I showed negative periodate-benzidine reaction(9) and the ultraviolet spectrum of III showed $\lambda_{max}^{dioxane}$ at 231 mμ. From the above observations, the compound IV was inferred to be γ-diketone.

The compound IV, by using the thin-layer chromatography (tlc), was identified with the authentic p-menthane-2,5-dione (VI) which was prepared by the Jones oxidation of p-menthane-cis-2,5-diol (VII).(10) In addition, the identity of the compound Va with the authentic bis-(2,4-dinitrophenylhydrazone) derivative (VIIIa) derived from VI, and the compound Vb with VIIIb was proved respectively by the tlc, the infrared spectra and the melting point upon admixing. Therefore, this new constituent must be p-menthane-2,5-diol.

It is noteworthy that the bis-(2,4-dinitrophenylhydrazone) derivative of IV was resolved into two components, Va and Vb, by the tlc. Similarly, the bis-(2,4-dinitrophenylhydrazone) derivative of the authentic 2,5-diketone VI was resolved into VIIIa and VIIIb. Pairs of these derivatives Va and Vb, VIIIa and VIIIb are assumed to exist in the syn and anti forms from the results of tlc,(11,12) ultraviolet and infrared spectra.(13,14)

Sixteen conformers are theoretically possible for p-menthane-2,5-diol. Comparing the retention time of the diol with that of the authentic sample of VII, slight difference between both retention times was observed, The fact that the position of the signals to H-C-OH is in 3.2-3.9 p.p.m.(15) as shown in FIG.1 suggests that two hydroxyl groups attached to the p-menthane ring are equatorial. This can also be confirmed from the chemical shifts of the acetyl protons (2.02 and 2.05 p.p.m.) and H-C-OAc (4.25-4.90 p.p.m.) in deuterated chloroform solution, which indicates that two acetoxy groups are equatorial and two H-C-OAc are axial.(16) The nmr spectrum (FIG.2) of II in benzene solution showed two sextets clearly which are due to two axial protons attached to carbons bearing O-acetyl groups.(17) Two diaxial splittings of 10 c.p.s. and axial-equatorial splitting of 5 c.p.s. are operative in forming the pattern.

Therefore, the conformation I is given to the diol which was newly isolated.



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