

THE STRUCTURE OF CUBENOL AND EPI-CUBENOL

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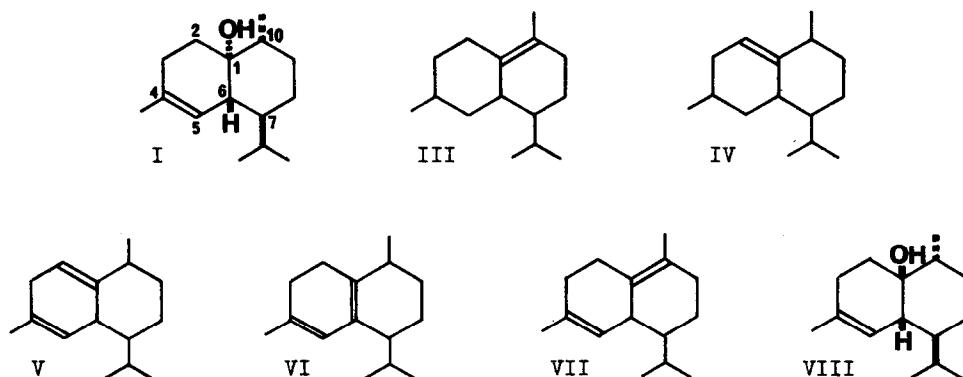
In this paper, we wish to report the structural determination of two new sesquiterpene alcohols, cubenol and epi-cubenol. Commercial cubeb oil was fractionally distilled under reduced pressure and, as reported in a previous paper (1), α -cubebene and β -cubebene had been isolated from the distilled fractions. Both cubenol and epi-cubenol were isolated from the residue by chromatography on a silica gel column.

Cubenol (I), $[\alpha]_D^{26} -24.8^\circ$ (c, 0.93 in CHCl_3), shows the following spectral data, MS: M^+ ion m/e 222 ($\text{C}_{15}\text{H}_{26}\text{O}$) and base peak m/e 161, $\nu_{\text{max}}^{\text{liq}}$ 3500, 1660, 835 and 802cm^{-1} , $\delta_{\text{ppm}}^{\text{CCl}_4}$ 0.72 and 0.92 (6H, two doublets, $J=6.6\text{cps}$), 0.85 (3H, d. $J=4.8\text{cps}$, $\text{CH}_3\text{CH}-$), 1.68 (3H, s. $\text{CH}_3\text{C}=\text{C}-$), 5.35 (1H, broad s. $\text{H}\text{C}=\text{C}-$) and 1.39 (1H, s. $-\text{OH}$), and $\delta_{\text{ppm}}^{\text{d}_6\text{-DMSO}}$ 3.14 (1H, s. tertiary hydroxyl proton). On catalytic hydrogenation with platinum oxide in ethanol, I yielded a saturated dihydro derivative (II), $[\alpha]_D^{21} -7.5^\circ$ (c, 0.53 in CHCl_3), M^+ ion m/e 224 and base peak m/e 181 on electron impact, showing I to be a bicyclic alcohol. Cubenol yielded calamenene together with a small amount of cadalene by dehydrogenation with palladised charcoal at 300° , hence, I has cadinane carbon skeleton.

By dehydration with formic acid at room temperature, II afforded a mixture of two hydrocarbons, III and IV (both $\text{C}_{15}\text{H}_{26}$). The compound III, purified by preparative GLC, shows NMR signals at $\delta_{\text{ppm}}^{\text{CCl}_4}$ 0.79 and 0.94 (6H, two doublets, $J=6.6\text{cps}$, $(\text{CH}_2)_2\text{CH}-$), 0.89 (3H, d. $J=5.7\text{cps}$, $\text{CH}_3\text{CH}-$) and 1.60 (3H, s. $\text{CH}_3\text{C}=\text{C}-$). The structure of IV was deduced from its NMR spectrum (four methyl groups at $\delta_{\text{ppm}}^{\text{CCl}_4}$ 0.71 - 1.06 and one vinyl proton at 5.3). These experiments confirmed the position of the hydroxyl group in II to be at C-1.

On treatment with thionyl chloride in pyridine at 0°, I yielded a mixture of three hydrocarbons (V, VI and VII). Each one of these hydrocarbons purified by preparative GLC shows M^+ ion m/e 204 ($C_{15}H_{24}$) in its mass spectrum. Hydrocarbon V shows NMR signals at $\delta_{ppm}^{CCl_4}$ 0.84 and 0.89 (6H, two doublets, $J=6.6$ cps, $(CH_3)_2CH-$), 1.00 (3H, d. $J=6.9$ cps, CH_3CH-), 1.69 (3H, s. $CH_3C=C-$), 5.22 (1H, broad s. $H=C-C-$) and 5.43 (1H, broad s. $H=C-C-$). Its UV spectrum shows the absence of conjugated double bond system. One of the double bonds, induced by the dehydration of C-1 hydroxyl group, is trisubstituted and should, therefore, be located between C-2 and C-1. The position of another double bond which was present in I is located between C-4 and C-5 as V yielded carvomenthone on ozonolysis. Hydrocarbon VI, NMR: $\delta_{ppm}^{CCl_4}$ 0.73 and 0.94 (6H, two doublets, $J=6.5$ cps, $(CH_3)_2CH-$), 0.98 (3H, d. $J=7.1$ cps, CH_3CH-), 1.85 (3H, broad s. $CH_3C=C-$) and 5.84 (1H, broad s. $-C=C-CH=C-$), UV: λ_{max} 266m μ (ϵ , 7,225) and 273m μ (ϵ , 6,800) (homo annular conjugation of two double bonds), and hydrocarbon VII, NMR: $\delta_{ppm}^{CCl_4}$ 0.76 and 0.92 (6H, two doublets, $J=6.5$ cps, $(CH_3)_2CH-$), 1.57 (6H, s. two olefin methyl groups), 5.29 (1H, broad s. $H=C-C-$), UV: no absorption maximum in the longer wave-length region than 210m μ , are compatible with the structures VI and VII, respectively.

epi-Cubenol (VIII), $[\alpha]_D^{26}$ -95.7° (c, 0.86 in $CHCl_3$), MS: M^+ ion m/e 222 ($C_{15}H_{26}O$) and base peak m/e 119, is also an alcohol having a trisubstituted double bond, ν_{max}^{liq} 3520, 1667 and 855 cm^{-1} ; $\delta_{ppm}^{CCl_4}$ 0.80 and 0.87 (6H, two doublets, $J=6.7$ cps), 0.91 (3H, d. $J=6.3$ cps, CH_3CH-), 1.68 (3H, s. $CH_3C=C-$), 5.4 (1H, m. $H=C-C-$) and 1.58 (1H, $-OH$). The tertiary nature of the hydroxyl group indicated by NMR spectrum was supported by inertness of the group toward the acetylation with acetic anhydride in pyridine. The carbon skeleton of VIII is also a cadinane type, as, on dehydrogenation, it afforded calamenene and cadalene. VIII resisted to catalytic reduction with platinum oxide in ethanol. It was partially reduced with the same catalyzer in acetic acid and gave a saturated dihydro derivative ($[\alpha]_D^{21}$ -5.2° (c, 0.29 in $CHCl_3$), M^+ ion m/e 224 and base peak m/e 163 on electron impact). The double bond in VIII was deduced to be at C 4-5 by converting it into 5-methyl cadalene (IX) through following stepwise reactions, i.e., hydroboration, chromic acid oxidation into ketoalcohol, methylation with CH_3MgI and dehydrogenation with palladium charcoal, and IX showed the identical IR spec-



trum with the one reported by Sukh Dev (2). On dehydration with thionyl chloride in pyridine at 0° , VIII yielded V as a sole product. Consequently, the position of the hydroxyl group should be at C-1 and VIII is epimeric with I.

Stereochemistry of I and VIII was deduced from the following evidences. Exhaustive reduction of both alcohols, via the hydrocarbon V, yielded mixtures of four saturated hydrocarbons and one of which was identical with (-)-cadinane. The fact that I gives three hydrocarbons V, VI and VII on dehydration with thionyl chloride in pyridine (trans elimination of water molecule (3)) indicates that each one hydrogen on C-2 β , C-6 and C-10 is trans to the α -hydroxyl group at C-1. On the other hand, β -configuration of the hydroxyl group of VIII is evident from the fact that it yielded only one product V under the same condition. In this case, only a hydrogen on C-2 α is trans and the others on C-6 and C-10 are cis to the hydroxyl group.

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