Natural Occurrence of Humuladienone, Humulenone-II, and α-Corocalene; New Constituents of Hop Oil

Yoko Naya and Munio Kotake

The Institute of Food Chemistry, Dojimanaka, Kita-ku, Osaka

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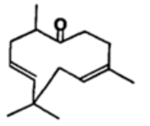
By a combination of fractionation, column chromatography over silica gel and neutral alumina-silver nitrate, and preparative GLC, it has now been possible to isolate the titled sesquiterpenes, (I), (IV), and (V), from the Japanese hop (*Humulus lupulus* L.).

Compound (I), $C_{15}H_{24}O$, $[\alpha]^{24}_{D}$ $+5.0°$ ($c=0.68$, $CHCl_3$) is a colorless oil which exhibited carbonyl absorption (1705 cm^{-1}) in the infrared spectrum. Other peaks of diagnostic value were at 1380, 1363 (gem-dimethyl), and 975 and 840 cm^{-1} (C=C *trans*). Its NMR spectrum[*1] showed a singlet at 1.01 (6H, tertiary methyl) and a doublet at 1.04 (3H, $J=6.8$ cps, secondary methyl); the doublet (3H, $J=1$ cps) at 1.59 is assignable to a methyl on a trisubstituted olefinic linkage; complex multiplets located between 4.80 and 5.25 accounted for three vinyl protons (HC=CH and CH_3C=CH–). Its MS spectrum exhibits the molecular ion peak at *m/e* 220 and the base peak at *m/e* 96, together with quite an abundant peak at *m/e* 138.

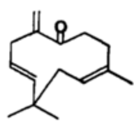
On catalytic hydrogenation over PtO_2 in ethanol, I took up one mole of hydrogen to yield (II), $C_{15}H_{26}O$ (M^+, *m/e* 222). Examination of its IR and NMR spectra revealed that the *trans* C=C bond has been reduced and that CH_3C=CH is still present. On the other hand, the hydrogenation of I by the same catalyst in acetic acid gave the saturated compound (III), $C_{15}H_{28}O$, (M^+, *m/e* 224).

All the above data are compatible with the structure (I) for humuladienone. Such a formulation was also supported by the co-occurrence of humulenone-II (IV), which is identical (IR, NMR) with the ketone derived from humulenol-II by Damodaran and Dev.1) The final conclusion was obtained by the partial hydrogenation of IV over PtO_2 in ethanol-ether, where two products were provided. The main product of the hydrogenation had an IR spectrum completely superimposable on that of I, while the other was found to be identical with that of II.

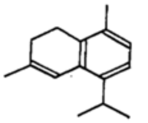
In addition, it may be noted from the solvent effect on the NMR spectra that the methyl group adjacent (α) to a carbonyl function of humuladienone (I) seems to exist in a pseudo-axial nature: ($\Delta=\delta^{\text{obs.}}_{\text{CCl}_4}-\delta]_{\text{C}_6\text{H}_6}=0.1$ ppm). A similar range of up-field shift is also observed for the hydrogenated derivatives, II and III.



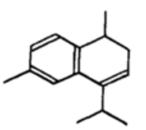
I



IV



V



VI

For compound (V), $C_{15}H_{20}$ (M^+, *m/e* 200), we propose the name α-corocalene. The other ingredient of the same fraction was γ-calacorene (VI), which afforded calamenene on catalytic hydrogenation and which was identical with the compound isolated from *Juniperus rigida* (IR, NMR, MS, UV).2) The infrared spectrum of V showed a characteristic absorption for an aromatic compound (3050, 1875, 1650, 1595, 1480, 860, 815 cm^{-1}). Moreover, the NMR spectrum exhibited a doublet at 1.22 (6H, $J=7.5$ cps) and a singlet at 2.19 (3H) which are assignable to an isopropyl and a methyl on an aromatic ring respectively; a doublet (3H, $J=1$ cps) at 1.94 and a broad singlet at 6.48 (1H) accounting for the group, CH_3C=CH, conjugated to an aromatic ring, and a singlet at 6.86 (2H) and a complex signal located between 2.57 and 3.50 (4H) which are attributable to two aromatic protons and two allylic methylenes respectively. The catalytic hydrogenation of V resulted in the uptake of one mole of hydrogen to give a dihydro-α-corocalene (VII), $C_{15}H_{22}$ (M^+, *m/e* 202). The characteristics mentioned above support the structure of 1,6-dimethyl-4-isopropyl-7,8-dihydronaphthalene for α-corocalene. The IR spectra of V and VII were identical with those of authentic compounds, which were synthesized by Šorm *et al.*3)

[*1] All the NMR spectra were taken in CCl_4 on a JEOL C-60 spectrometer, with TMS as the internal reference. The values are reported in ppm.

1) N. P. Damodaran and Sukh Dev, *Tetrahedron Letters*, **1963**, 1941; *Tetrahedron*, **24**, 4133 (1968).

2) B. Tomita, Y. Hirose and Y. Nakatsuka, "Symposium papers, the 12th Symposium on the Chemistry of Terpenes, Essential Oils, and Aromatics," (Hamamatsu, 1968), p. 144.

3) F. Šorm, K. Vereš and V. Herout, *Coll. Czech. Chem. Commun.*, **18**, 106 (1953).