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NEW MONOTERPENOIDS FROM HOP OIL

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We previously reported the isolation and the characterization of new constituents from Japanese hop "Shinshu-wase" (1)(2). The present paper deals with the investigation of new monoterpene ethers and ketone from the same source, namely hop ether (I), karahana ether (V) and karahanaenone (IX).

By silica gel column chromatography of the fraction, boiling at 50-53°/15 mm Hg, hop ether and karahana ether were eluted successively.

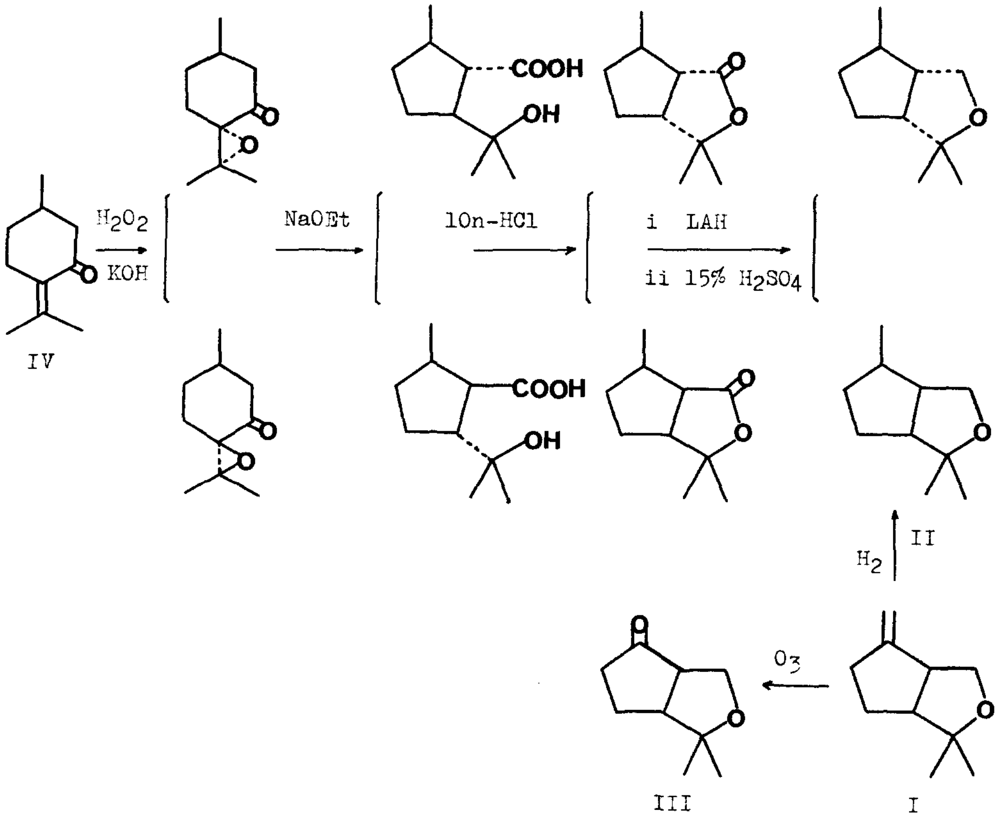
Hop ether (I), $C_{10}H_{16}O$, has following physical properties. ν_{max} 3070, 1650, 880 cm^{-1} (terminal methylene), 1380, 1361 cm^{-1} (gem-dimethyl), 1145, 1125, 1050 cm^{-1} (cyclic ether). $\delta_{ppm}^{CCl_4}$ 1.14 and 1.18 (each 3H, s., $(CH_3)_2\overset{|}{C}-O-$), 1.50-1.80 (2H, m., $-CH_2-$), 2.15-2.60 (3H, m., $-\overset{|}{C}H-$ and $=\overset{|}{C}-CH_2-$), ca. 3.2 (1H, m., $=\overset{|}{C}-\overset{|}{C}H-$), 3.53 (1H, d.d., J=8.2, 4.5 cps) and 4.00 (1H, d.d., J=8.2, 8.2 cps) ($-CH_2-O-$), 4.72 and 4.85 (each 1H, slightly split signals, $=CH_2$). m/e 152 (M^+), 122 (M-30), 107 (M-30-15), 94 (M-58), 79 (base peak).

Hydrogenation of I in ethanol with platinum oxide yielded the dihydro hop ether, $C_{10}H_{18}O$ (II). In the NMR spectrum of II, in addition to gem-dimethyl signals at 1.10 and 1.12 ppm, a doublet (J=6.7 cps) was observed at 0.97 ppm instead of the terminal methylene signals of I. Signals of ordinary methine and methylene protons (7H) and a doublet at 3.58 ppm (2H, J=6.7 cps, $-CH_2-O-$) were also observed. In the MS spectrum of II, besides M^+ ion (m/e 154) and base peak (m/e 43), the following ions are remarkable, m/e 139 (M-15), 96 (M-58) and (M-58-15). In the comparison of the MS spectra of I and II, the ions, M-58, were observed in the both, whereas a pair of characteristic peaks in the former, M-30 and M-30-15, was negligible in the latter. On the basis of the above spectral data (IR, NMR and MS spectra), hop ether must have the partial structure of

$CH_2{=}\overset{|}{C}{-}\underset{|}{\overset{|}{C}}{-}CH_2{-}O{-}\overset{|}{C}(CH_3)_2$.

Ozonolysis of I at -70° in ethyl acetate afforded a ketone (III), $C_9H_{14}O_2$, m/e 154 (M^+), 43 (base peak). ν_{max} 1740 cm^{-1} (five-membered cyclic ketone), 1410 cm^{-1} (active methylene). $\delta^{CCl_4}_{ppm}$ 1.20 and 1.27 (each 3H, s., $-O-\overset{|}{C}(CH_3)_2$), 1.70-2.50 (3H, m., $-\overset{|}{C}H-$ and $-CH_2-$), 2.70-3.00 (2H, m., $-CO-CH_2-$), 3.46 (1H, m., $-CO-\overset{|}{C}H-$), 3.90 and 3.94 (each 1H, d., J=4.0 and 8.0 cps, respectively, $-O-CH_2-$).

From the above observation, hop ether was inferred to have the structure I. In addition, the identity of dihydro hop ether (II) with an authentic sample derived from pulegone (IV) <u>via</u> pulegone lactone (3)(4), as shown in the following scheme, was proved by the comparison of their IR, NMR and [illegible] spectra.



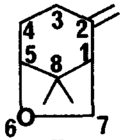
Karahana ether (V), $C_{10}H_{16}O$, m/e 152 (M^+), 107 (M-30-15, base peak), 122 (M-30). ν_{max} 3060, 1640, 880 cm^{-1} (terminal methylene), 1385, 1365 cm^{-1} (gem-dimethyl), 1065 cm^{-1} (cyclic ether). $\delta_{ppm}^{CCl_4}$ 0.92 and 1.04 (each 3H, s., $-\overset{|}{C}(CH_3)_2$), 1.45-1.76 (2H, m., C_4-methylene), 2.07-2.28 (3H, m., $=\overset{|}{C}-CH_2-$ and $=\overset{|}{C}-CH-$: C_1-methine at the allylic position (2.24 ppm) couples with C_7-H_b, d., J=4.5 cps), 3.63 (1H, unresolved peak, C_5-H), 3.66 (1H, d., J=7.5 cps, C_7-H_a), 3.93 (1H, d.d., J=7.5, 4.5 cps, C_7-H_b), 4.50 and 4.55 (each 1H, slightly split signals, $-\overset{|}{C}=CH_2$).

The compound V was hydrogenated with platinum oxide in ethanol to give the dihydro derivative (VI), $C_{10}H_{18}O$, m/e 154 (M^+), 69 (base peak). $\delta_{ppm}^{CCl_4}$ 0.97 and 1.18 (each 3H, s., $-\overset{|}{C}(CH_3)_2$), 1.12 (3H, d., J=7.0 cps, $-\overset{|}{C}H-C\underline{H}_3$), 1.50-2.10 (6H, m., $-\overset{|}{C}H-$ and $-CH_2-$), 3.55 (1H, unresolved peak, C_5-H), 3.50 (1H, d., J=7.5 cps, C_7-H_a), 3.92 (1H, d.d., J=7.5, 4.5 cps, C_7-H_b).

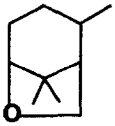
Ozonolysis of V at -70° in ethyl acetate gave a ketone (VII), $C_9H_{14}O_2$, m/e 154 (M^+), 85 (base peak). ν_{max} 1720 cm^{-1} (six-membered cyclic ketone), 1410 cm^{-1} (active methylene). $\delta_{ppm}^{CCl_4}$ 1.05 and 1.17 (each 3H, s., $-\overset{|}{C}(CH_3)_2$), 2.03 (2H, m., $-CH_2-$), 2.30-2.55 (3H, m., $-\overset{|}{C}\underline{H}-CO-C\underline{H}_2$), 4.01 (3H, broad signal, C_5-H and C_7-H_2).

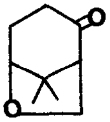
According to the above spectroscopic studies and the chemical evidences, it is apparent that karahana ether is a bicyclic fused ring skeleton which consists of a five-membered cyclic ether and a cyclohexane ring with a terminal methylene. In the comparison of the MS spectra of V and VI, only the former has a pair of characteristic peaks, the same as in hop ether, M-30 and M-30-15, which indicats that karahana ether has the partial structure of $CH_2=\overset{|}{C}-\underset{|}{\overset{|}{C}}-CH_2-O-$. On the other hand, a peak, M-58, was negligible in the both spectra of V and VI. This accounts for nonexistence of gem-dimethyl group on the carbon bonded to the oxide linkage, and therefore, C_4or C_8 remains for the carbon linked to a gem-dimethyl group.

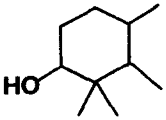
When the dihydro ether VI reacted with $LiAlH_4$ in the presence of $AlCl_3$ as catalyst, the ether linkage was cleavaged to form a small amount of secondary alcohol preferentially along with the recovered starting materials. The resulting alcohol showed molecular ion peak at m/e 156 ($C_{10}H_{20}O$) and base peak at m/e 57 and the fragments at mass 70 and 97 are well accounted for the structure, 2,2,3,4-tetramethyl-cyclohexanol (VIII). On the other hand, synthetic 2,2,4,5-tetramethyl-cyclohexanol showed molecular ion peak at m/e 156 and intense peaks at m/e 83 (base peak) and m/e 71. These results revealed that thus, karahana ether is shown as structure V.



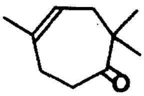
V


VI


VII



VIII

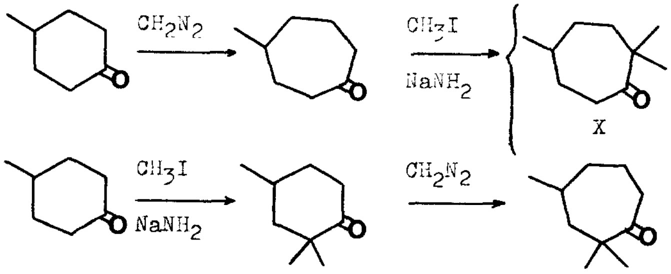

IX

Karahanaenone (IX), $C_{10}H_{16}O$, was isolated as a minor constituent from the fraction, boiling at 55-63°/15 mm Hg, by silica gel column chromatography and preparative gas chromatography. The infrared spectrum exhibited bands at 1695 (C=O), 1640 (C=C) and 1375, 1355 $(-\overset{|}{C}(CH_3)_2)$ cm^{-1}. The NMR spectrum showed peaks at $\delta^{CCl_4}_{ppm}$ 1.05 (6H, s., $(CH_3)_2\overset{|}{C}-CO-$), 1.70 (3H, slightly split signals, $CH_3-\overset{|}{C}=\overset{|}{C}-$), between 2.05-2.40 (4H, m., $-CH_2-\overset{|}{C}=\overset{|}{C}-CH_2-$) and between 2.60-2.85 (2H, m., $-CH_2-CO-$). The MS spectrum of IX showed the intense peaks at m/e 152 (M^+), 109 (M-43), 95, 81, 67 and 41 (base peak).

For the determination of the number of hydrogen atoms attached to a carbon alpha to a corbonyl group, IX was treated with D_2O and K_2CO_3 in CH_3OD (5). The resulting dideuterokarahanaenone showed molecular ion peak at m/e 154 and remarkable peaks at m/e 95, 83 and 41 (base peak).

Hydrogenation of IX in ethanol with platinum oxide gave the dihydro derivative (X), $C_{10}H_{18}O$, m/e 154 (M^+), 69 (base peak). In the NMR spectrum of X, in addition to a singlet for gem-dimethyl group at 1.05 ppm, a doublet (J=6.0 cps) was observed at 0.95 ppm instead of the signal of methyl gorup attached to a double bond. Signals of ordinary methine and methylene protons (7H) and multiplet between 2.05-2.72 ppm (2H, $-CH_2-CO-$) were also observed.

Dihydro compound (X) was identical in all respects (GLC analysis, IR, NMR and MS spectra) with an authentic sample which was prepared as follows.



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