coprostane skeleton.[12] The observed difference between those (9.02 and 9.15 τ, respectively) of C-14 methyls of valeranone and valerane was 0.13 p.p.m. which indicated valeranone possessing the *cis* ring juncture as shown in stereoformula (VI).

This ring juncture was also supported by the observation that norvaleranone (XIII), $C_{14}H_{24}O$, n_D^{25} 1.481, IR band at 1740 cm^{-1} (cyclopentanone), semicarbazone : $C_{15}H_{27}ON_3$, m.p. 228~230°, 2,4-dinitrophenylhydrazone : m.p. 166.5~167°, prepared according to the method of Govindachari, *et al.*,[7] exhibited a negative Cotton effect ($[\alpha]_{307}^{\text{trough}}$ −1460°, $[\alpha]_{266}^{\text{peak}}$ +2390°).

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Structure of Kanokonol

The sesquiterpenoid keto-alcohol, kanokonol, found mainly as its acetate, has newly been isolated from several kinds of Japanese valerian roots.[1,2] The present communication deals with the evidences of its constitution as shown in formula (I : R=H).

Kanokonyl acetate (I; R=Ac), $C_{17}H_{28}O_3$, d_4^{25} 1.050, n_D^{25} 1.490, $[\alpha]_D$ −54.2°,*1 in its infrared spectrum, exhibited bands (liquid) at 1740, 1227 (acetoxyl), 1702 cm^{-1} (ketonic carbonyl). The nuclear magnetic resonance spectrum showed a doublet (6H) at 9.12 τ (J=5.0) due to the methyl groups of CH_3-CH< type, a singlet (3H) at 8.97 τ due to the methyl group of CH_3-C$\lessdot$ type, a singlet (3H) at 8.08 τ due to the acetoxyl group, and two sets of doublets (2H) in an AB spectrum at 6.12 and 6.30 τ (J=11.2) due to the methylene group of AcO-CH_2-C$\lessdot$ type. On alkaline hydrolysis, I (R=Ac) gave kanokonol (I; R=H), $C_{15}H_{26}O_2$, mol. wt. 238 (mass spec.), m.p. 53~54°, $[\alpha]_D$ −71.0°, semicarbazone: $C_{16}H_{29}O_2N_3$, m.p. 185~186°. I (R=H) had the infrared spectrum which showed bands at 3515 (hydroxyl), 1692 (carbonyl), and 1414 cm^{-1} (methylene adjacent to carbonyl) and the nuclear magnetic resonance spectrum which exhibited a doublet (6H) at 9.16 τ (J=5.0, $C\underline{H}_3$-CH<), a singlet (3H) at 8.99 τ ($C\underline{H}_3$-C$\lessdot$), a singlet (1H) at 7.18 τ ($\underline{H}$O-), and two sets of doublets (2H) in an AB spectrum at 6.62 and 6.76 τ (J=11.0, HO-$C\underline{H}_2$-C$\lessdot$). Reduction of I (R=H) with $LiAlH_4$ afforded the diol (II), $C_{15}H_{28}O_2$, m.p. 152.5~153°, $[\alpha]_D$ +34.8°

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*1 All analytical values are in good agreement with the molecular formulae shown. $[\alpha]_D$s refer to $CHCl_3$ solutions and IR spectra to KBr disks unless otherwise indicated. NMR spectra were measured at 60 Mc. in CCl_4 *vs.* Me_4Si as internal reference. Chemical shifts are given in τ-values and coupling constants (J) in c.p.s.

[1] H. Hikino, Y. Hikino, H. Kato, Y. Takeshita, T. Takemoto : Yakugaku Zasshi, **83**, 219 (1963).

[2] H. Hikino, Y. Hikino, Y. Takeshita, Y. Isurugi, T. Takemoto : *Ibid.*, **83**, 555 (1963).

(EtOH), IR band at 3279 cm^{-1} (hydroxyl).

On oxidation with H_2CrO_4, I (R=H) gave the keto-acid (III), $C_{15}H_{24}O_3$, m.p. 152~153°, $[\alpha]_D$ −40.6°, IR bands at 3400~3050, 2800~2400, 1709, 1242, 936 (carboxyl), 1694 cm^{-1} (carbonyl). Reduction of III with $LiAlH_4$ yielded the hydroxy-acid (IV), $C_{15}H_{26}O_3$, m.p. 183~184°, $[\alpha]_D$ +58.5° (EtOH), IR bands at 3205 (hydroxyl), 2800~2300, 1675, 1247, 950 cm^{-1} (chelated carboxyl), which by boiling with Ac_2O afforded the lactone (V), $C_{15}H_{24}O_2$, m.p. 64~66°, $[\alpha]_D$ +45.8°, IR band at 1767 cm^{-1} (γ-lactone). Thus the relative situation of the carbonyl group and the hydroxy-methylene group in I was established.

That I had the valeranone skeleton was very probable from the following facts: 1) The nuclear magnetic resonance spectra of I (R=H, Ac) were closely resembled to that of valeranone except the differences caused by replacement of the methyl group by the hydroxy- or acetoxy-methylene system. 2) The rotatory dispersion curve of I (R=H) showed a negative Cotton effect ($[\alpha]^{\text{trough}}_{313}$ −2660°, $[\alpha]^{\text{peak}}_{268}$ +3600° (MeOH)) and was almost superimposable with that of valeranone ($[\alpha]^{\text{trough}}_{316}$ −2760°, $[\alpha]^{\text{peak}}_{274}$ +3610° (MeOH)). 3) On the quantitative replacement reaction of activated hydrogen for deuterium, I (R=H) gave the dideutero-derivative, mol. wt. 240 (mass spec.), IR $\nu^{\text{Nujol}}_{\text{max}}$ cm^{-1}: 2212 (C-D stretching), 3436 (hydroxyl), 1690 (carbonyl).

Further chemical evidence on the skeleton was obtained from the subsequent series of reactions: On tosylation followed by reduction with $LiAlH_4$, I (R=H) did not give the expected deoxy-compound but the oxide (VI), $C_{15}H_{26}O$, n^{25}_{D} 1.497, $[\alpha]_D$ +62.1°, together with small amount of II, m.p. 150~151°. VI was confirmed by the infrared spectrum which exhibited a band (liquid) at 1022 cm^{-1} assigned to ether function and by the nuclear magnetic resonance spectrum which showed a doublet (6H) at 9.09 τ (J=5.4, $C\underline{H}_3$-CH<), a singlet (3H) at 8.95 τ ($C\underline{H}_3$-C$\leqslant$), and eight lines (3H) in the 6.32~6.68 τ region (>C$\underline{H}$-O-C$\underline{H}_2$-). Thence, I (R=H) was converted with ethylene glycol-benzene-TsOH mixture at reflux to the ethylene ketal (VII), $C_{17}H_{30}O_3$, n^{25}_{D} 1.512, $[\alpha]_D$ +11.7°, IR $\nu^{CCl_4}_{\text{max}}$ cm^{-1}: 3663, 3527 (hydroxyl), 1190, 1073 (ketal), which afforded by treatment with TsCl in pyridine the tosylate (VIII), $C_{24}H_{36}O_5S$, m.p. 88°, IR bands at 1600, 1350, 1174 cm^{-1} (tosylate). While reduced with $LiAlH_4$ VIII reverted to VII, then transformed by treatment with $PhCH_2$-

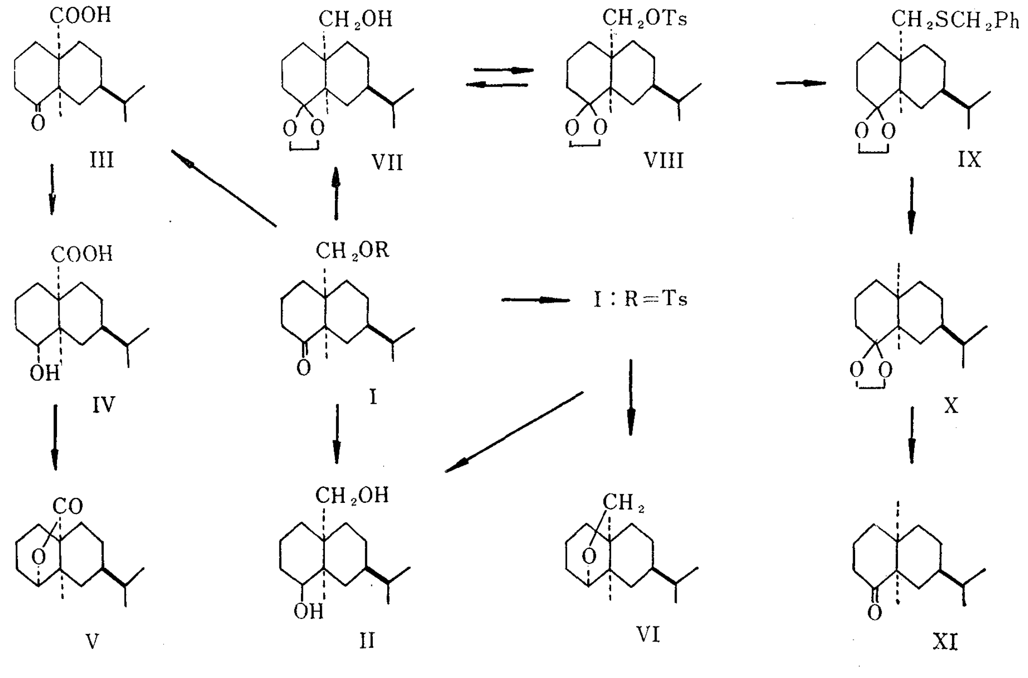

Chart 1.

SNa3) in refluxing diglyme to the benzylthioether (IX), IR $\nu_{\max}^{\text{liquid}}$ cm^{-1} : 3070, 3040, 1603, 1495, 699 (phenyl), 2674, 1418 cm^{-1} (methylene adjacent to sulfur), which on desulfurization with Raney nickel yielded the ketal (X), $C_{17}H_{30}O_2$, n_D^{25} 1.497, $[\alpha]_D$ +23.2°, IR $\nu_{\max}^{\text{liquid}}$ cm^{-1}: 1198, 1078 (ketal). Acid-catalyzed hydrolysis of X produced the corresponding ketone (XI), $C_{15}H_{26}O$, d_4^{25} 0.963, n_D^{25} 1.491, $[\alpha]_D$ −49.0°, IR $\nu_{\max}^{\text{liquid}}$ 1702 cm^{-1} (carbonyl), NMR : singlet (3H) at 9.21 τ ($C\underline{H}_3$-C<), doublet (6H) at 9.13 τ (J=7.1, $C\underline{H}_3$-CH<>), singlet (3H) at 9.02 τ ($\underline{C}H_3$-C<CO-), which was identified with authentic valeranone by means of gas chromatogram, infrared spectrum, and 2,4-dinitrophenylhydrazone, $C_{21}H_{30}O_4N_4$, m.p. 101.5~102°.

The stereochemistry of valeranone as shown in formula (XI) has been rigorously established by the authors.4) Whereupon it follows that kanokonol is correctly presented as 15-hydroxyvaleranone.

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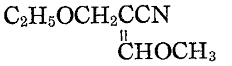
Isolation of *cis*- and *trans*-2-Methoxymethylene-3-ethoxypropionitrile

As had been reported previously,1) infrared spectrum of 2-methoxymethylene-3-ethoxypropionitrile (I) which was used as a starting material for pyrimidine derivatives has suggested that I is a mixture of its geometrical isomers. However, the determination of the *cis*- and *trans*-isomers has not yet been made completely.



$$\begin{array}{l} C_2H_5OCH_2CCN \\ \qquad\qquad\quad \| \\ \qquad\qquad\quad CHOCH_3 \end{array}$$

I

The product prepared from 3-ethoxypropionitrile as cited in the previous paper1) gives two peaks at the retention times of 9.6 and 11.7 minutes by a gas chromatographic analysis.*1a Further, the nuclear magnetic resonance (NMR) spectrum*2 of this product

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*1 Gas chromatography was carried out under the following conditions : Apparatus, Shimadzu GC-1B. *a*) Column, 4 mm. × 1.5 m.; 0.75% N.G.S. on Anackrom A; column temp., 106°; N_2 23 ml./min. *b*) Column, 6 mm. × 3 m.; 5% KF-54 on Chromosorb W; column temp. 120.5°; H_2 100 ml./min.

*2 The NMR spectra were taken with a Varian A-60 analytical spectraometer system on about 10% solutions in carbon tetrachloride containing about 1% tetramethylsilane as an internal reference. Chemical shifts are expressed in τ-units and coupling constants are in c.p.s. Accuracy limits are about ±0.02 τ and ±0.3 c.p.s.

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