Nadeln vom Schmp. 160~161° (Zers.). IR ν_{max}^{KBr} cm^{-1} : 3145, 3125 (CH, Furan); 2220 (-C≡C-); 1675 (C=O); 1610 (NH_2). $C_7H_4O_4N_2$—Ber. : C, 46.67; H, 2.24; N, 15.55. Gef. : C, 46.93; H, 2,18; N, 15.54.).

IX und X zeigten höhere Aktivitäten gegen Bakterien und Fadenpilze als das 3-(5-Nitro-2-furyl)acrylsäuremethylester und -amid. Darüber wir in einem anderen Bericht veröffentlichen.

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Structure of Valeranone

The sesquiterpenoid ketone, valeranone, was first isolated from the root of an european valerian by Stoll, *et al.*[1] It has since been encountered in a number of valerianaceous species : *e.g.* an Indian nard,[2] a Russian valerian,[3] and several kinds of Japanese valerians.[4,5] The structural investigations of it were initiated by Govindachari, *et al.*[2] followed by Křepinský, *et al.*[6] who advanced two alternative formulae (I) and (II). Shortly afterwards, the Indian workers[7] proposed structure (III) and, on the basis of this skeleton, Djerassi, *et al.*[8] suggested its absolute configuration as shown in formula (IV). Recently the Czechoslovakian workers[9] re-investigated the main series of reactions which led the Indian workers[7] to structure (III), pointed out that the dehydrobromination product of monobromo-jatamansic anhydride did not give (—)-carvomenthone, and proposed the gross structural formula (I) for valeranone, but left its stereochemistry unsettled. Quite recently the authors have isolated the new sesquiterpenoid ketol, kanokonol, from several kinds of Japanese valerians[4,5] and established that kanokonol is 15-hydroxy-valeranone.[10] In this communication, the evidences on the constitution and the absolute configuration of valearnone, as shown in formula (VI), is described.

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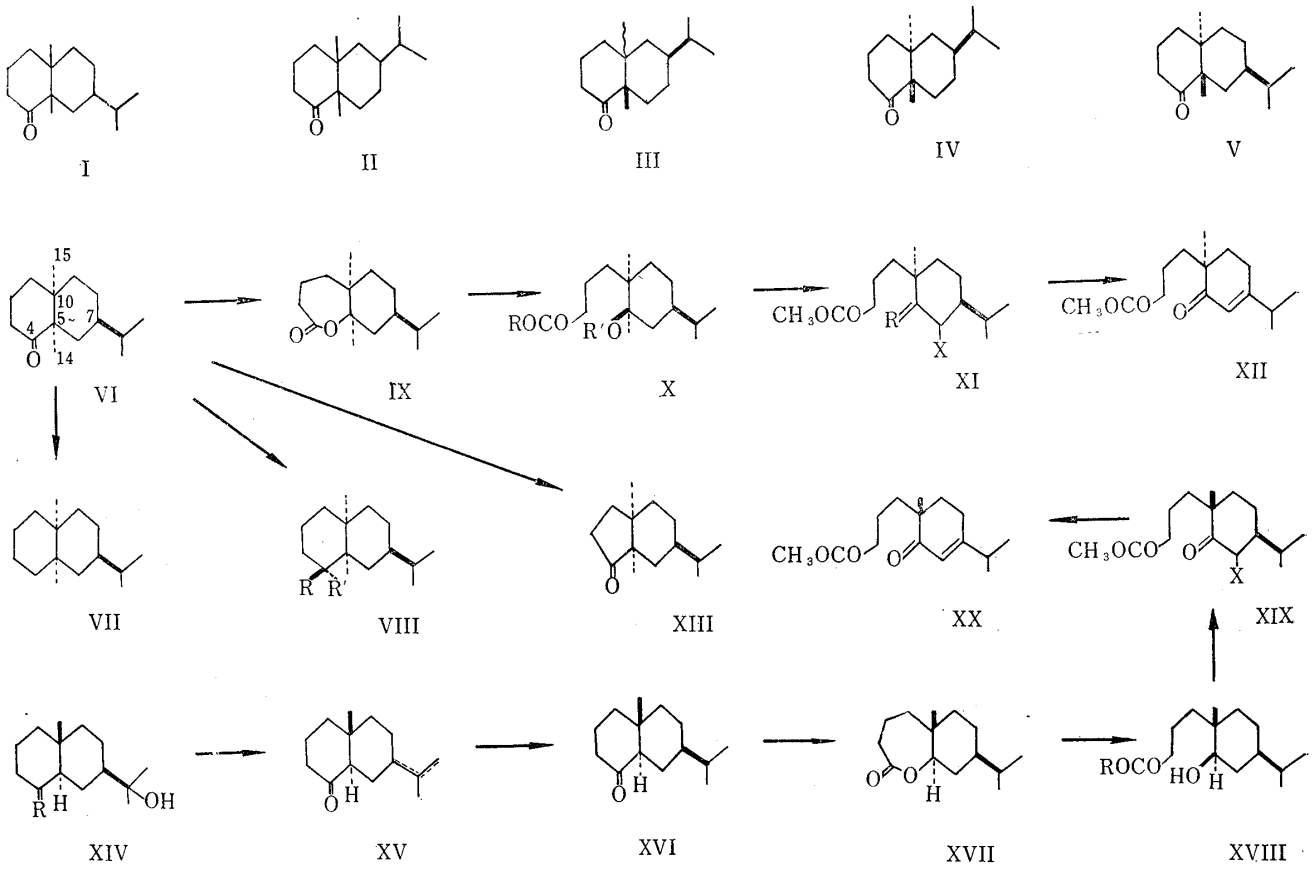

Chart 1.

In the nuclear magnetic resonance spectrum of valerane (Ⅶ), $C_{15}H_{28}$, n_D^{25} 1.483, $[\alpha]_D$ +76.0°,*1 obtained by Huang-Minlon reduction of valeranone, two tertiary methyl groups appeared as a singlet (6H) at 9.15 τ. Reduction of valeranone with Na-EtOH afforded 4-*epi*-valeranol[9] (Ⅷ; R=OH, R′=H), $C_{15}H_{28}O$, m.p. 85~86.5°, $[\alpha]_D$ +62.5°, IR : ν_{max}^{KBr} 3356 (hydroxyl) cm^{-1}. The nuclear magnetic resonance spectrum exhibited a singlet (3H) at 9.15 τ (C-15 methyl), a singlet (3H) at 9.00 τ (C-14 methyl), and a broadened peak (1H) at 6.41 τ (C-4 methine). These facts showed that the secondary hydroxyl group was equatorially disposed. On the other hand, $LiAlH_4$ reduction of valeranone gave valeranol[2,9] (Ⅷ; R=H, R′=OH), $C_{15}H_{28}O$, m.p. 56.5~57°, $[\alpha]_D$ +51.6°, IR : ν_{KBr}^{max} 3448 (hydroxyl) cm^{-1}, 3,5-dinitrobenzoate : $C_{22}H_{30}O_6N_2$, m.p. 128~128.5°. The nuclear magnetic resonance spectrum displayed an unresolved doubled (1H) at 6.75 τ (C-4 methine) indicating the axial orientation of the hydroxyl. The C-14 methyl signal appeared at 8.99 τ as in Ⅷ (R=OH, R′=H) but the C-15 methyl signal at 8.98 τ which was suffered from the down-field shift by 0.17 p.p.m. than that (9.15 τ) of Ⅶ or Ⅷ (R=OH, R′=H) and moved up-field by 0.14 p.p.m. on acetylation. This observation revealed the spatial close relation,[11] *viz.* 1,3-diaxial position, of the C-15 angular methyl group to the C-4 axially oriented hydroxyl in Ⅷ (R=H, R′=OH).

In the sequence of degradative reactions of valeranone, Czech workers[9] obtained the key compounds Ⅺ (R=O, X=H) and Ⅻ, of which physical constants, however, were

*1 All analytical values are in good accord with the molecular formulae shown. $[\alpha]_D$s refer to $CHCl_3$ solutions and IR spectra to liquid films unless otherwise stated. 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.

11) Y. Kawazoe, Y. Sato, M. Natsume, H. Hasegawa, T. Okamoto, K. Tsuda : This Bulletin, **10**, 338 (1962).

not recorded. Then the sequence was traced. Valeranone by peracid oxidation followed by hydrolysis and methylation gave the hydroxy-ester (X; R=CH_3, R'=H), $C_{16}H_{30}O_3$, n_D^{25} 1.477, $[\alpha]_D$ +22.0°, IR bands at 3560 (hydroxyl), 1736 cm^{-1} (ester), which was acetylated to afford the acetoxy-ester (X; R=CH_3, R'=$COCH_3$), $C_{18}H_{32}O_4$, n_D^{25} 1.468, $[\alpha]_D$ −12.0°, IR bands at 1740 (ester), 1730, 1247 cm^{-1} ((acetoxyl). Pyrolysis of X (R=CH_3, R'=$COCH_3$) formed the unsaturated ester (XI; R=CH_2, X=H), $C_{16}H_{28}O_2$, n_D^{25} 1.470, $[\alpha]_D$ +34.6°, IR bands at 3090, 1634, 888 (vinylidene), 1740 cm^{-1} (ester), which on ozonolysis yielded the keto-ester (XI; R=O, X=H), $C_{15}H_{26}O_3$, n_D^{25} 1.466, $[\alpha]_D$ +83.5°, IR $\nu_{max}^{CCl_4}$ 1743 cm^{-1} (ester), 1706 (cyclohexanone), NMR : doublet (6H) at 9.10 τ (J=5.2, $(CH_3)_2CH$-), singlet (3H) at 9.06 τ (CH_3-C<CO-), singlet (3H) at 6.40 τ (CH_3-O-CO-). By bromination and subsequent dehydrobromination, XI (R=O, X=H) gave the α,β-unsaturated ketonic ester (XII), $C_{15}H_{24}O_3$, n_D^{25} 1.487, $[\alpha]_D$ +5.5°, IR $\nu_{max}^{CCl_4}$ cm^{-1} : 1740 (ester), 1669, 1630 (cyclohexenone), UV : λ_{max}^{EtOH} 237 mμ (log ε 4.18), NMR : singlet (3H) at 9.00 τ (CH_3-C<CO-), doublet (6H) at 8.89 τ (J=6.8, $(CH_3)_2CH$-C=C), singlet (3H) at 6.42 τ (CH_3-O-CO-), unresolved band (1H) at 4.38 τ (-CO-CH=C<).

On the other hand, the keto-esters, (XIX: X=H) and (XX), were prepared by the subsequent way : β-eudesmol (XIV; R=CH_2) on ozonolysis followed by dehydration with $POCl_3$-pyridine gave the mixture of two isomeric unsaturated ketones (XV), the isopropenyl and the isopropylidene derivatives, $[\alpha]_D$ +50.8°, IR bands at 1712 (cyclohexanone), 3096, 1643, 886 cm^{-1} (vinylidene), in which the latter isomer crystallized, $C_{14}H_{22}O$, m.p. 82~83°, $[\alpha]_D$ +66.7°, IR : ν_{max}^{KBr} 1710 cm^{-1} (cyclohexanone), NMR : singlet (3H) at 9.17 τ (CH_3-C<), singlet (6H) at 8.37 τ ($(CH_3)_2C$=C<). This mixture was hydrogenated to yield noreudesmone (XVI), $C_{14}H_{24}O$, n_D^{25} 1.486, $[\alpha]_D$ +15.6°, IR band at 1710 cm^{-1} (cyclohexanone), NMR : singlet (3H) at 9.25 τ (CH_3-C<), doublet (6H) at 9.09 τ (J=5.7, $(CH_3)_2CH$-), semicarbazone : $C_{15}H_{27}ON_3$, m.p. 221~223°, 2,4-dinitrophenylhydrazone : $C_{20}H_{28}O_4N_4$, m.p. 141~142°. On peracid oxidation, XVI afforded the ε-lactone (XVII), hydrolyzed and successively methylated to the hydroxyester (XVIII; R=CH_3), $C_{15}H_{28}O_3$, n_D^{25} 1.475, $[\alpha]_D$ +27.7°, IR bands at 3500 (hydroxyl), 1730 cm^{-1} (ester), and further oxidized with H_2CrO_4 to the keto-ester (XIX; X=H), $C_{15}H_{26}O_3$, n_D^{25} 1.474, $[\alpha]_D$ +45.7°, IR $\nu_{max}^{CCl_4}$ cm^{-1} : 1739 (ester), 1706 (cyclohexanone), NMR : doublet (6H) at 9.17 τ (J=5.7, $(CH_3)_2CH$-), singlet (3H) at 9,00 τ (CH_3-C<CO-), singlet (3H) at 6.43 τ (CH_3-O-CO-), which was not identical with XI (X=H) by comparisons of gas chromatograms, infrared spectra, and nuclear magnetic resonance spectra. Bromination and following dehydrobromination of XIX (X=H) furnished the α,β-unsaturated ketonic ester (XX), $C_{15}H_{24}O_3$, n_D^{25} 1.487, $[\alpha]_D$ −4.6°, IR $\nu_{max}^{CCl_4}$ cm^{-1} : 1740 (ester), 1669, 1630 (cyclohexenone), UV : λ_{max}^{EtOH} 236 mμ (log ε 4.19), NMR : singlet (3H) at 9.00 τ (CH_3-C<CO-), doublet (6H) at 8.89 τ (J=6.8, $(CH_3)_2CH$-C=C), singlet (3H) at 6.42 τ (CH_3-O-CO-), unresolved band (1H) at 4.38 τ (-CO-CH=C<).

The properties of XX agreed in all respects with those of XII prepared from valeranone except for the rotation values, which were equal in magnitude, but opposite in sign. It is clear that XII is the enantiomer of the corresponding XX from natural eudesmane series. These results thus established not only the location of the isopropyl group at C-7, but also the absolute configurations of the isopropyl being β-oriented and the C-15 methyl group α-oriented. Then the only question remaining was the choice between the two possibilities, V and VI, for valeranone.

The C-14 methyl groups in V and VI stereochemically corresponded to the C-19 methyls in cholestan-1-one and coprostan-1-one, respectively. In the nuclear magnetic resonance, the differences between the C-19 methyl signals of 1-oxo- and 1-deoxo-derivatives were found to be 0.360~0.384 p.p.m. in cholestane skeleton and 0.212 p.p.m. in

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 ($[\alpha]_{307}^{rough}$ −1460°, $[\alpha]_{266}^{peak}$ +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< 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< 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, $\underline{CH_3}$-CH<), a singlet (3H) at 8.99 τ ($\underline{CH_3}$-C<), a singlet (1H) at 7.18 τ ($\underline{HO}$-), and two sets of doublets (2H) in an AB spectrum at 6.62 and 6.76 τ (J=11.0, HO-$\underline{CH_2}$-C<). 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°

*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.

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