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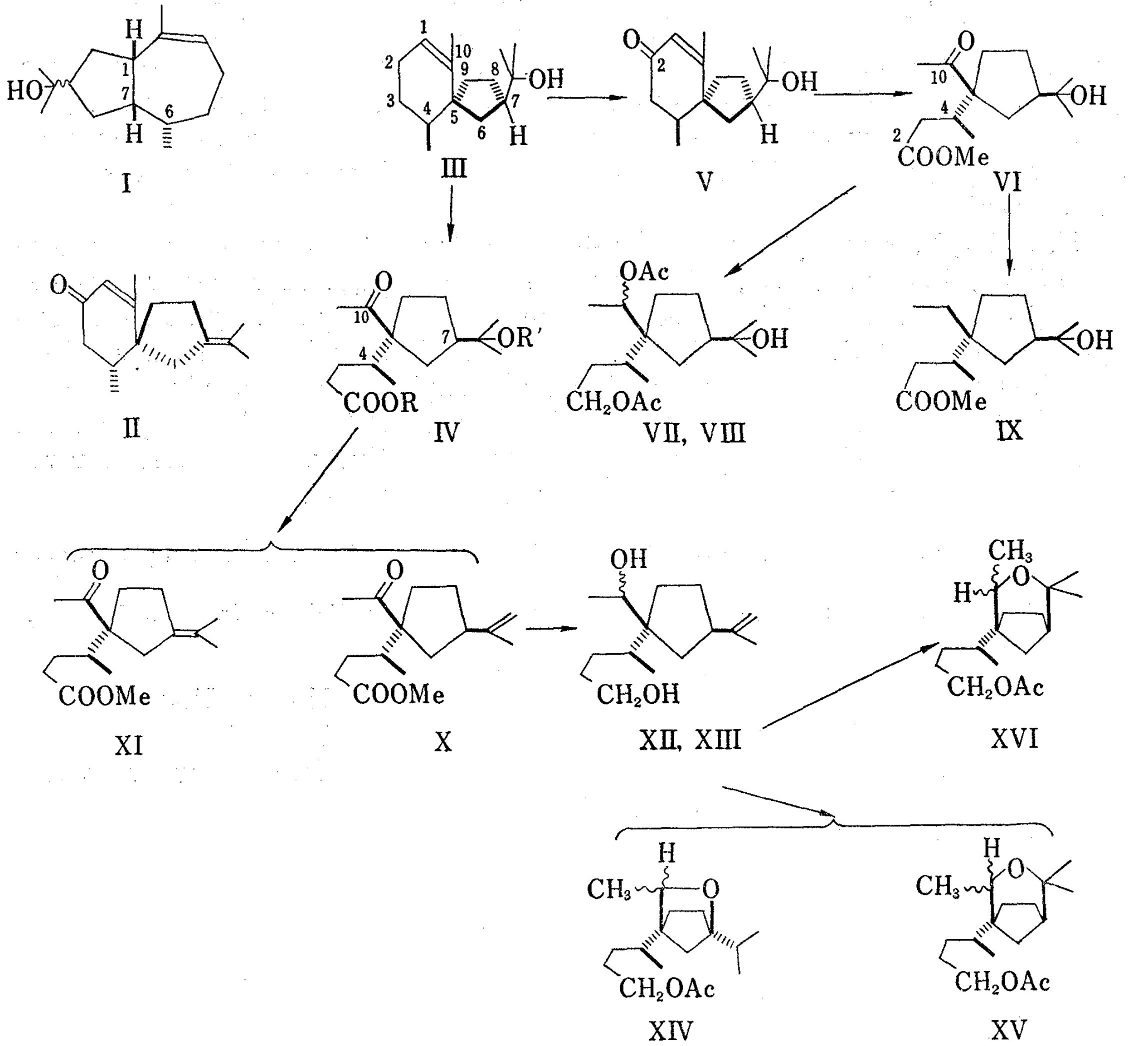
The Structure and Absolute Configuration of Hinesol[1]

In the preceding paper,[2] we reported the experiments of correlation of hinesol, a sesquiterpene alcohol isolated from *Atractylodes lancea* DC.,[3] with the enantiomer of β-vetivone, and proposed its structure as 1(*S*), 6(*S*), 7(*S*)-configuration, expressed by the formula I. But recently J.A. Marshall, *et al.*[4] proposed a revised structure (II) for β-vetivone on the basis of total synthesis, and suggested to revise the structures of some related vetivane sesquiterpenes. Now we wish to report some evidences based on the revised structure of hinesol (III), and determined the absolute configuration of hydroxyisopropyl group.

On treatment with potassium hydroxide or sodium in ethanol, the ketoacid (IV: R=R′ =H), obtained from III on ozonization[5] or Lemieux's oxidation, provided no isomerized product.



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[1] Studies on the constituents of Atractylodes XI.

[2] I. Yosioka and T. Kimura, *Chem. Pharm. Bull.* (Tokyo), **13**, 1430 (1965).

[3] I. Yosioka, S. Takahashi, H. Hikino and Y. Sasaki, *Chem. Pharm. Bull.* (Tokyo), **7**, 319 (1959).

[4] J.A. Marshall, N.H. Andersen and P.C. Johnson, *J. Am. Chem. Soc.*, **89**, 2748 (1967); J.A. Marsh and P.C. Johnson, *ibid.*, 2750 (1967); *Chem. Commun.*, **1968**, 391.

[5] W.Z. Chow, O. Motl and F. Šorm, *Collection Czechoslov. Chem. Communs.*, **27**, 1914 (1962).

A nor ketoacid methyl ester (VI), $C_{15}H_{26}O_4$,[6] mp 61°, $[\alpha]_D^{15}$ $-21.1°$ ($CHCl_3$, $c=1.14$), IR cm^{-1}: 3510, 1739, 1701, NMR τ: 9.11 (3H, d. $J=6$ cps), 8.83 (3H, s.), 8.81 (3H, s.), 7.81 (3H, s.), 6.33 (3H, s.), was obtained by oxidative cleavage with ozone and hydrogen peroxide followed by methylation with diazomethane, from 2-oxohinesol (V).[2] This ketoester (VI) was treated with lithium aluminum hydride in ether, followed by acetylation, and two triol diacetates VII, $C_{18}H_{32}O_5$, colorless oil, $[\alpha]_D^{12}$ $-22.6°$ ($CHCl_3$, $c=2.21$), IR cm^{-1}: 3400, 1741, 1240, and VIII, $C_{18}H_{32}O_5$, colorless oil, $[\alpha]_D^{12}$ $-2.5°$ ($CHCl_3$, $c=1.19$), IR cm^{-1}: 3550, 1740, 1240, were obtained. In nuclear magnetic resonance (NMR), VII and VIII showed the signal peaks of quartet corresponding to $C_{(10)}$–H, at τ: 4.95 and 6.12 (1H, $J=7$ cps) respectively. The above two observations are consistent with the formula III but not by I.

The infrared spectrum of ester VI showed absorption of intramolecular hydrogen bond at 3530 cm^{-1}, nevertheless that of deoxo–compound (IX), $C_{15}H_{28}O_3$, colorless oil, $[\alpha]_D^{11}$ $-6.4°$ ($CHCl_3$, $c=0.47$), IR cm^{-1}: 3625, 3500, 1738, NMR τ: 9.18 (3H, t. $J=5$ cps), 9.11 (3H, d. 5.5 cps), 8.83 (6H, s.), 6.34 (3H, s.), obtained from VI on Huang–Minlon reduction, showed no absorption in this region in dilution of 10^{-3} mole. These facts suggested the existence of intramolecular hydrogen bond between the hydroxyl group and the carbonyl group of $C_{(10)}$-ketone, and not of $C_{(2)}$-ester, in VI. Therefore, the hydroxyisopropyl group must be *cis* configuration to the acetyl group. This presumption was confirmed by the following experiments.

On pyrolysis of ketoacid methyl ester benzoate (IV: $R=CH_3$, $R'=COC_6H_5$), $C_{23}H_{32}O_5$, colorless oil, $[\alpha]_D^{12}$ $-54.5°$ ($CHCl_3$, $c=2.24$), IR cm^{-1}: 1741, 1710, 1285, 1170, provided from IV ($R=R'=H$) on esterification with diazomethane and benzoylchloride in pyridine, two dehydroxy compounds X, $C_{16}H_{26}O_3$, colorless oil, $[\alpha]_D^{12}$ $-55.9°$ ($CHCl_3$, $c=1.02$), IR cm^{-1}: 1740, 1703, 1644, 1172, 890, NMR τ: 9.21 (3H, d. $J=7$ cps), 8.29 (3H, br.s.), 7.86 (3H, s.), 6.32 (3H, s.), 5.32 (2H, ABq. $J=1$ cps), and XI, $C_{16}H_{26}O_3$, colorless oil, $[\alpha]_D^{12}$ $+35.0°$ ($CHCl_3$, $c=2.26$), IR cm^{-1}: 1741, 1701, 1170, NMR τ: 9.11 (3H, d. $J=6$ cps), 8.39 (3H, br.s.), 8.34 (3H, br.s.), 7.87 (3H, s.), 6.35 (3H, s.), were obtained. The isopropenyl isomer (X), on reduction with lithium aluminum hydride in ether, produced two diol XII, colorless oil, IR cm^{-1}: 3330, 1642, 888, and XIII, colorless oil, IR cm^{-1}: 3360, 1642, 888. On treatment with boron trifluoride in ether, followed by acetylation, XII produced a colorless oil which was supposed with gas chromatography and NMR to be a mixture of two bridged ether acetates XIV and XV, GLC: peak area ratio, 2.1:1, NMR τ: 9.18 (d. $J=6$ cps), 9.06 (d. $J=7$ cps at both of 60 and 100 Mc), 8.98 (d. $J=6$ cps), 8.71 (s.), 8.69 (s.), 6.36 (2H, t. $J=5$ cps), 6.16 (1H, q. $J=6$ cps), and XIII produced another ether acetate XVI, $C_{17}H_{30}O_3$, colorless oil, $[\alpha]_D^{15}$ $-50.0°$ ($CHCl_3$, $c=0.58$), IR cm^{-1}: 1741, 1236, NMR τ: 9.06 (3H, d. $J=6$ cps), 9.01 (3H, d. $J=6$ cps), 8.85 (3H, s.), 8.78 (3H, s.), 7.95 (3H, s.), 6.12 (1H, q. $J=6$ cps), 5.93 (2H, t. $J=6$ cps).

All of the above observations are satisfied by the formula III for hinesol. Biogenetical consideration, related with β-eudesmol, which had been obtained from the same original plant, also approve this absolute configuration.

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[6] All the compounds given with the chemical formulae gave satisfactory analytical values. IR spectra were taken in CCl_4 solution. NMR spectra were measured at 60 Mc in $CDCl_3$ solution with tetramethylsilane as an internal standard.