Tetrahedron Letters No.3, pp. 231-234, 1970. Pergamon Press. Printed in Great Britain.

MINOR SESQUITERPENE ALCOHOLS OF VETIVER OIL

Akiko Homma (in part), Michiharu Kato, Ming-Der Wu, and Akira Yoshikoshi

Chemical Research Institute of Non-Aqueous Solutions, Tohoku University,
Sendai, Japan

(Received in Japan 29 November 1969; received in UK for publication 18 December 1969)

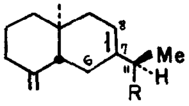
The constituents of the essential oil of vetiver (<u>Vetiveria zizanoides</u> Stapf) has been extensively studied, and some sesquiterpene alcohols have been reported so far (1-6).

We have also studied on the fraction of the sesquiterpene alcohol of the oil, and isolated four new alcohols, vetiselinenol, zizanol, cyclocopacamphenol and epicyclocopacamphenol, beside khusimol (major component), valerianol (kusunol) (7), β-eudesmol and elemol.

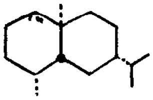
1) Vetiselinenol (I), $C_{15}H_{24}O$ (M^+=220), $[\alpha]_D^{18}$ -18.1°($CHCl_3$), ν (neat) 3300, 3060, 1645, 1030, 885, 810 cm^{-1}, δ ($CDCl_3$) 0.70 (s., 3H), 1.03 (d., J=6.6, 3H), 3.45, 3.57 (br.s., 1H each), 4.57, 4.78 (s., 1H each), 5.44 (br.t., 1H), is a bicyclic sesquiterpene alcohol, and upon hydrogenation on Pd, gave ultimately the tetrahydro derivative, $C_{15}H_{28}O$. The nmr spectrum of I in benzene showed a clear AB-pattern of ABX-system at 3.35 and 3.55 ppm (J_{AB} =10.8, J_{AX} =7.2 and J_{BX} = 6.7), indicating a β,β-disubstituted ethanol moiety. In the nmdr (100 mHz) experiment of I, irradiation at near 2.2 ppm (methine proton) collapsed the doublet due to the secondary methyl to a sharp singlet, as well as the signals of the AB-pattern mentioned above changed to an AB-quartet (J=10.8). This indicated the grouping -CHMe-CH_2OH. The Jones oxidation product of I was esterified with CH_2N_2 to give the methyl ester (II), $C_{16}H_{24}O_2$, ν (neat) 1725 cm^{-1}, δ ($CDCl_3$) 1.27 (d., J=7, 3H), 3.10 (br.q., J=7, 1H). The signals at 3.10 ppm of II may be assigned to the α-methine proton of β,γ-unsaturated ester, and nmdr indicated that the methine proton couples with both secondary methyl protons and the vinyl proton of the trisubstituted double bond. Thus, this result expanded the partial structure of I to $\rangle CH{=}\overset{|}{C}\text{-}CHMe\text{-}CH_2OH$.

LAH reduction of the tosylate of I afforded the diene (III), $C_{15}H_{24}$, ν (neat) 3070, 1645, 890, 810 cm^{-1}; δ($CDCl_3$) 0.64 (s., 3H), 1.14 (d., J=6.5, 6H), 4.52, 4.70 (br.s., 1H each), 5.24 (br.s., 1H), and hydrogenation of the latter gave a mixture of two saturated hydrocarbons, from which the major product (IV), $C_{15}H_{26}$, $[\alpha]_D^{20}$-18.9° ($CHCl_3$), was separated by glc. IV was shown to be identical with that of (+)-selinane (8) by a comparison of the ir, nmr and mass spectra, except the signs of optical rotation. Thus the gross structure of I should be expressed with Va or Vb.

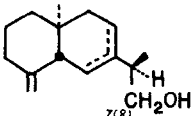
On treatment with equimolar perphthalic acid in ether, the trisubstituted double bond of I was selectively oxidized to yield the monoepoxide (VI), $C_{15}H_{24}O$, mp. 144-145°, ν 1645, 890 cm^{-1}. The coupling pattern at 3.01 ppm (J=3.9 and 2.1) of VI suggested that there must be a methylene protons adjacent to the oxirane methine proton. The dihydro derivative (VII), $C_{15}H_{26}O$, δ($CDCl_3$) 5.31 (br.t., 1 H), obtained on hydrogenation of I using $(Ph_3P)_3RhCl$ as a catalyst, was converted to the olefin (VIII), $C_{15}H_{26}$, <u>via</u> a tosylate. Then VIII was submitted to hydroboration-oxidation giving the ketone (IX), $C_{15}H_{26}O$, ν(neat) 1710, 1410 cm^{-1}, ord $[\alpha]_{310}$+1130°, $[\alpha]_{273}$-1370°. IX was stable for the treatment with NaOMe, and gave a trideutero compound (M^+=225) by base-catalyzed deuteration. These results



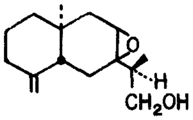
I; R=CH_2OH
II; R=CO_2Me
III;R=Me



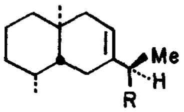
IV



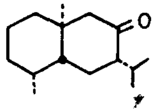
Va; $\Delta^{7(8)}$
Vb; $\Delta^{6(7)}$



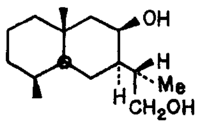
VI



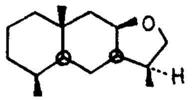
VII; R=CH_2OH
VIII;R=Me



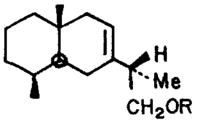
IX



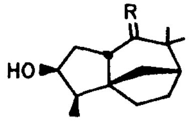
X



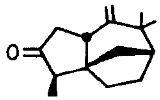
XI



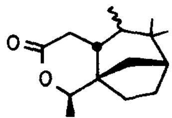
XII; R=Ac
XIII;R=H



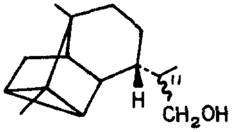
XIV; R=CH_2
XV; R=O
XVI; R=Me, H
XVII;R=CH_2OH, OH



XVIII



XIX



XXa
XXb; C_{11}-epimer

located the trisubstituted double bond as seen in Va.

The absolute configuration at C_{11} of I was determined as follows. The diol (X), $C_{15}H_{28}O_2$, mp. 108-110°, obtained from tetrahydroalantolactone (9) by LAH reduction, was dehydrated to yield the cyclic ether (XI), $C_{15}H_{26}O$, ν 1040 cm^{-1}, δ ($CDCl_3$) 3.3-4.1 (m., 3H). The reaction of XI with pyridine hydrochloride in Ac_2O resulted in formation of the unsaturated acetate (XII), $C_{17}H_{28}O_2$, ν (neat) 1740 cm^{-1}, δ ($CDCl_3$) 2.0 (s., 3H), 4.01 (br.d., J=5.0), 5.4 (br.s., 1H), in good yield, and XII was reduced with LAH to the alcohol (XIII). The ir, nmr and mass spectra of XIII were superimposable with those of VII, whereas the ord curves of both alcohols were absolutely antipodal.

Hence, vetiselinenol is represented by the stereoformula I (10).

2) Zizanol (XIV), $C_{15}H_{24}O$ (M^+=220), $[\alpha]_D^{18}$+10.4°, ν (neat) 3350, 3070, 1645, 1045, 890 cm^{-1}, δ ($CDCl_3$) 1.05 (d., J=7.0, 3H), 1.06 (s., 6H), 3.84 (sextet, J=7.2 and 3.3, 1H; $-CH_2CHOH-CH$), 4.58, 4.78 (t., J=1.7, 1H each), upon hydrogenation on Pd, gave dihydro derivative (XVI), $C_{15}H_{26}O$, δ ($CDCl_3$) 0.75 (d., J=7.5, 3H), 0.77, 0.85 (s., 3H each), 0.96 (d., J=7.0, 3H), 3.79 (m., 1H), thus indicating it to be tricyclic. The crystalline triol (XVII), $C_{15}H_{26}O_3$, mp. 94-95°, was obtained from XIV by OsO_4 oxidation, and XVII furnished the ketoalcohol (XV), $C_{14}H_{22}O_2$, by $Pb(OAc)_4$ oxidation. Jones oxidation of XIV, on the other hand, afforded the five-membered ketone (XVIII), $C_{15}H_{22}O$, mp. 51-52.5°, ν 1735, 1402 cm^{-1}, from which XIV was regenerated in a high yield by LAH or Na-liq. NH_3 reduction. Base-catalyzed deuteration of XVIII allowed introduction of three deuterium atoms (M^+=221), and the doublet signal due to the secondary methyl of XVIII collapsed to the singlet after deuteration. Hydrogenation of XVIII followed by perbenzoic acid oxidation gave the δ-lactone (XIX), $C_{15}H_{24}O_2$, mp. 118-119°, ν 1700 cm^{-1}, 1.37 (d., J=7.5, 3H), 4.23 (q., J=7.5, 1H), whose coupling pattern of the signal at 4.23 ppm indicated that there is no proton coupled with the δ-proton other than methyl protons.

The findings mentioned above was suggesting zizanol to be 6-hydroxyzizaene (10). An olefin, which was obtained from the tosylate of XIV by LAH reduction or from the ethylenethioacetal of XVIII, $C_{17}H_{26}S_2$, mp. 44-45°, by desulfurization, was identical in every respects with the authentic specimen of zizaene (11).

The coupling pattern (a doublet of triplets) due to the proton on C_6 seems to be indicative a β-hydroxy group for zizanol. Application of the "Benzoate Rule" to zizanol ($[M]_D^{benzoate}-[M]_D^{zizanol}=+39.7°$) also supported β-orientation (12).

Thus, zizanol (XIV) is 6β-hydroxyzizaene.

3) Cyclocopacamphenol (XXa) and epicyclocopacamphenol (XXb) were isolated as an inseparable mixture. The mixture indicated the following character: $C_{15}H_{24}O$ ($M^+=220$), ν(neat) 3350, 3040, 1030 cm^{-1}, δ($CDCl_3$) 0.75 (s., 3H), ca. 1.0 (d., 3H) and 1.02 (s., 3H), 3.42, 3.78 (AB-pattern of ABX system; J=10.5, 5.5 and 3.0, 2H). Jones oxidation of the above mixture provided a mixture of carboxylic acids, from which two carboxylic acids were separated by fractional crystallization. These carboxylic acids were identified to be cyclocopacamphenic acid and epicyclocopacamphenic acid (13), respectively.

The authors acknowledge Professor N. H. Andersen for his helpful discussion. We also thank Dr. H. Minato and Mr. Y. Ueno for supplying alantolactone and vetiver oil, respectively. We were indebted Drs. J. W. Rowe and H. Hikino for identification of β-eudesmol and valerianol, respectively.

References

1) (Khusimol) F. Kido, H. Uda and A. Yoshikoshi, Tetra. Lett., 2815 (1967); D.C. Umarani, K.G. Gore and K.K. Chakravarti, ibid., 1255 (1967).
2) (Khusol) S.N. Dhingra, D.R. Dhingra and S.C. Bhattacharyya, Perf. Essen. Oil Rec., 47, 350 (1960); P.S. Kalsi, K.K. Chakravarti and S.C. Bhattacharyya, Tetrahedron, 19, 233 (1963).
3) (Khusinol) A.A. Rao, K.L. Surve, K.K. Chakravarti and S.C. Bhattacharyya, ibid., 19, 233 (1963).
4) (Junenol) S.C. Bhattacharyya, A.S. Rao and A.M. Shalingram, Chem. Ind. (London), 469 (1960).
5) (Laevo-junenol) R. Seshadri, P.S. Kalsi, K.K. Chakravarti and S.C. Bhattacharyya, Tetrahedron, 23, 1269 (1967).
6) (A bicyclic primary alcohol) S. Takahashi, Chem. Pharm. Bull. (Japan), 16, 2447 (1968).
7) G. Jommi, J. Křepinský, V. Herout and F. Šorm, Tetra. Lett., 677 (1967); H. Hikino, N. Suzuki and T. Takemoto, Chem. Pharm. Bull. (Japan), 16, 832 (1968)
8) V. Benešová, V. Herout and F. Šorm, Coll. Czech. Chem. Comm., 47, 2365 (1959)
9) W. Cocker and M.A. Nibet, J. Chem. Soc., 559 (1963).
10) Professor N.H. Andersen has also isolated from Haiti oil, and assigned the same structure. Private communication.
11) R. Sakuma and A. Yoshikoshi, Chem. Comm., 41 (1968).
12) The C_6-epimer of zizanol, $C_{15}H_{24}O$, mp. 60°, was prepared by treatment of the tosylate of XIV with H_2O in DMF, followed by alkaline hydrolysis. $[M]_D^{benzoate}-[M]_D^{epialcohol}$ was $-28.7°$.
13) F. Kido, R. Sakuma, H. Uda and A. Yoshikoshi, Tetra. Lett., 3169 (1969).