

MINOR ACIDIC CONSTITUENTS OF VETIVER OIL

Naoki Hanayama, Fusao Kido, Reiko Sakuma, Hisashi Uda,
and Akira Yoshikoshi

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

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Vetiver oil contains some sesquiterpenic carboxylic acids, and recently, the structure (XII) has been suggested for zizanoic acid, the major constituent of the acids, by us (F. K., H. U. and A. Y.)(1). We now report here evidence for the structures (I) and (XIII) assigned to two minor acids, named isovalencenic acid and epizizanoic acid, respectively.

After esterification of a mixture of the whole acids with diazomethane, each carboxylic acid was separated as its methyl ester by careful fractional distillation followed by $\text{AgNO}_3\text{-SiO}_2$ chromatography.

1) Isovalencenic acid (I), $\text{C}_{15}\text{H}_{22}\text{O}_2^*$, m.p. $135\text{-}137^\circ$, λ (MeOH) 225 μ (ϵ 8000), ν (KBr) \sim 2500, 1670, 1622, 844 cm^{-1} , δ (CCl_4) 0.86 (s., 3H), 0.93 (d., J=6, 3H), 1.93 (s., 3H), 5.32 (m., 1H), was obtained in pure state on mild alkaline hydrolysis of methyl isovalencenate (II), $\text{C}_{16}\text{H}_{24}\text{O}_2$, $M^+ = 248$, λ (MeOH) 224 μ (ϵ 9150), ν (liq.) 1720, 1634, 850 cm^{-1} , δ (CCl_4) 0.85 (s., 3H), 0.93 (d., J=6, 3H), 1.87, 3.67 (s., 3H each), 5.31 (m., 1H), $[\alpha]_D^{22} + 136.6^\circ$ (MeOH). Hydrogenation of II on Adams catalyst proceeded to give the dihydro derivative (V), $\text{C}_{16}\text{H}_{26}\text{O}_2$, λ (MeOH) 228 μ (ϵ 8600), ν (liq.) 1713 cm^{-1} , δ (CCl_4) 1.82 (br.s., 3H), in EtOH, and to give an epimer mixture of the tetrahydro derivatives (VII), $M^+ = 252$, ν (liq.) 1725 cm^{-1} , in AcOH.

The mass spectrum of VII showed the peak of m/e 88 [$\text{CH}_3\text{CH}=\text{C}(\text{OCH}_3)\text{OH}^+$] as base peak. On the other hand, ozonization of V afforded the ketone (VIII), $\text{C}_{12}\text{H}_{20}\text{O}$, m.p. $37\text{-}39^\circ$, ν (CCl_4) 1710 cm^{-1} , whose α -positions adjacent to the carbonyl group were shown to be methylenes as indicated by deuterium exchange

* Satisfactory analytical values were obtained for all new compounds.

experiment (M^+ 180 \rightarrow 184). The fragment ions (m/e 122, 109, 82) in the mass spectrum of VIII supported a possible eremophilane structure for isovalencenic acid (2), and the comparison of the i.r. spectrum of VIII with that of the authentic material (IX)(3) showed their identity, except for antipodal feature of their ORD curves.

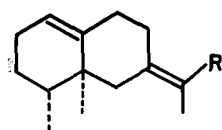
LAH reduction of II gave the alcohol (III), $C_{15}H_{24}O$, m.p. 86-87 $^{\circ}$, ν (KBr) 3250, 1662, 840, 808 cm^{-1} , δ (CCl_4) 0.80 (s., 3H), 0.93 (d., $J=5.5$, 3H), 1.76 (br.s., 3H), 4.07 (s., 2H), 5.27 (br.t., $J=4.5$, 1H), and after treatment of III with $SOCl_2$ at low temperature, the product, without further purification, was allowed to react with LAH giving the hydrocarbon, $C_{15}H_{24}$, ν (liq.) 1668, 848, 812 cm^{-1} , δ (CCl_4) 0.77 (s., 3H), 0.94 (d., $J=5$, 3H), 1.66 (s., 6H), 5.22 (m., 1H), which was identical with one of the dehydration products (IV) of valerianol reported by Šorm et al. (4). This result located the trisubstituted double bond of isovalencenic acid.

In order to examine the geometry of the carboxyl group, dihydroisovalencenic acid (VI) was treated with SeO_2 in boiling AcOH to give the γ -lactone (X), $C_{15}H_{22}O_2$, m.p. 75-76 $^{\circ}$, M^+ = 234, λ (MeOH) 220 $m\mu$ ($\log \epsilon$ 4.08), ν ($CHCl_3$) 1740 cm^{-1} , δ ($CDCl_3$) 1.76 (quint., $J=1$, 3H), 2.40 (br.s., 2H), 5.07 (br.m., 1H). The coupling pattern of the $-\overset{|}{\underset{|}{C}}H-O-$ grouping of X in its n.m.r. spectrum indicated that the lactone formation has taken place at C_B . Recently, Takahashi et al. have obtained the compound (XI) as the hydrogenation product of ligrarenolide (5). However, our lactone (X) was found not to be identical with XI on their physical properties, and it appeared to imply that the former compound is the C_B -epimer of the latter. This assumption was verified by almost identical fragmentation patterns on the mass spectra of both lactones. The conformation for the B ring of this compound will be discussed in a forthcoming paper.

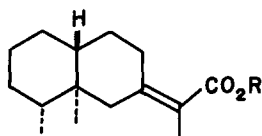
2) Epizizanoic acid (XIII), $C_{15}H_{22}O_2$, m.p. 109-110.5 $^{\circ}$, ν (KBr) \sim 2500, 1700, 1640, 898 cm^{-1} , δ (CCl_4) 1.05, 1.09 (s., 3H each), 4.57, 4.77 (t., $J=1.5$, 1H each), was also obtained from methyl epizizanoate (XIV), $C_{16}H_{24}O_2$, M^+ = 248, b.p. 128-132 $^{\circ}$ /1 mm, ν (liq.) 3090, 1735, 1640, 1380, 1365, 895 cm^{-1} , δ (CCl_4) 1.06, 1.08, (s., 3H each), 2.78 (m., 1H), 3.62 (s., 3H), 4.59, 4.77 (t., $J=1.4$,

1H each), $[\alpha]_D^{22} - 28.4^\circ$ (MeOH), on hydrolysis with alkali under mild condition. The physical data mentioned above indicated the presence of an exo methylene group and two tert. methyl groups in XIII.

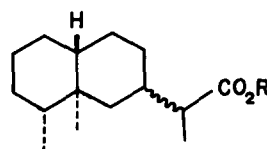
Catalytic hydrogenation of XIV afforded a saturated compound, methyl dihydroepizizanoate (XVI), $C_{16}H_{26}O_2$, m.p. 79° , ν (CCl_4) 1730 cm^{-1} , δ (CCl_4) 0.80 (d., $J=8$, 3H), 0.82, 0.87, 3.62 (s., 3H each). Oxidation of the exo methylene group of XIV with OsO_4 followed by $Pb(OAc)_4$ resulted in the formation of the ketoester (XVIII), $C_{15}H_{22}O_3$, m.p. $77.5-78.5^\circ$, ν (KBr) $1737, 1713\text{ cm}^{-1}$, δ (CCl_4) 1.00, 1.18, 3.62 (s., 3H each), $ORD[\phi]_{314} + 8670^\circ, [\phi]_{272} - 10680^\circ$ (a + 193). The conversion of the carbomethoxyl group of XIV into a methyl group, according to the reaction sequence $CO_2Me \rightarrow CH_2OH \rightarrow CH_2OTs \rightarrow Me$, gave an olefin, epizizaene (XV), $C_{15}H_{24}$, $M^+ = 204$, ν (liq.) $3080, 1638, 890\text{ cm}^{-1}$, δ (CCl_4) 0.87 (d., $J=6$, 3H), 1.08 (s., 6H), 4.53, 4.73 (t., $J=1.6$, 1H each).



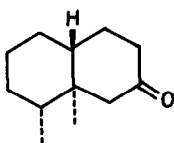
I; R=CO₂H
II; R=CO₂Me
III; R=CH₂OH
IV; R=Me



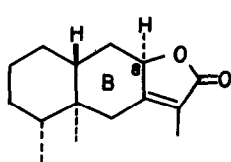
V; R=Me
VI; R=H



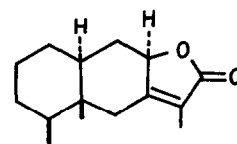
VII



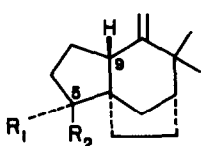
VIII
IX; enantiomer



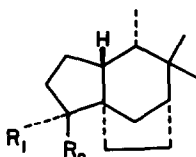
X



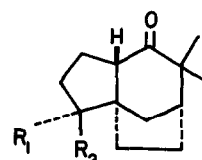
XI



XII; R₁=H, R₂=CO₂H
XIII; R₁=CO₂H, R₂=H
XIV; R₁=CO₂Me, R₂=H
XV; R₁=Me, R₂=H



XVI; R₁=CO₂Me, R₂=H
XVII; R₁, R₂=O



XVIII; R₁=CO₂Me, R₂=H
XIX; R₁=H, R₂=CO₂Me

The mass spectra of XIV, XV and XVIII showed the fragmentation patterns almost identical with the corresponding derivatives of zizanoic acid (XII) except for slight differences in the relative intensity of some peaks, thus indicating that epizizanoic acid may be an epimer of zizanoic acid. However, both XVIII and its C₉-epimer, which were obtained as a mixture by treatment of the former with NaOMe under mild condition, were not identical with the known ketoester (XIX)(1). XVI was derived to a norketone by the same degradation sequence as reported earlier for zizanoic acid (1), and the identity of the final product with XVII, including optical rotation, was confirmed. Thus, epizizanoic acid was shown to be the C₅-epimer of zizanoic acid. By treatment with NaOMe in boiling MeOH, methyl zizanoate (methyl ester of XII) slowly epimerized into a 2:1 equilibrium mixture, from which methyl epizizanoate (XIV) could be separated by preparative VPC.

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