

MINOR ACIDIC CONSTITUENTS OF VETIVER OIL PART II.(1)

CYCLOCOPACAMPHENIC AND EPICYCLOCOPACAMPHENIC ACIDS

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(Received in Japan 23 June 1969; received in UK for publication 6 July 1969)

Previously we reported the structures of three sesquiterpenic carboxylic acids from vetiver oil: zizanoic acid (the main constituent) (2), epizizanoic and isovalencenic acids (the minor constituents) (1), and now wish to report structures of the additional two minor acids, except the absolute configuration of the carboxyl groups.

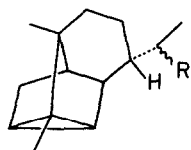
The pure samples of these acids were obtained by mild alkaline hydrolysis of each methyl ester separated by preparative glpc (the major one: 40%, the minor one: 20%) from the lowest boiling fraction (6%, b.p. 112-118°/2 mm through a spinning-band column) of the whole ester mixture (3). The major acid, cyclocopacamphenic acid (I), $C_{15}H_{22}O_2^*$, has the following properties: m.p. 151.5-152.5°, $[\alpha]_D^{19}$ -14.7 (c 1.25, $CHCl_3$), ν^{KBr} 1700, 860, 845 cm^{-1} , $\delta^{CCl_4}^{**}$ 0.77 (3H,s), 1.03 (3H,s), 1.19 (3H,d J=7 Hz) ppm; the minor one, epicyclocopacamphenic acid (II): m.p. 168-168.5°, $[\alpha]_D^{20.5}$ +78.3 (c 3.6, $CHCl_3$), ν^{CHCl_3} 1700, 860 cm^{-1} , δ^{CDCl_3} 0.77 (3H,s), 1.02 (3H,s), 1.17 (3H,d J=6 Hz). Epimeric relationship of the carboxyl groups in these acids was unambiguously confirmed by derivation to the same parent hydrocarbon (III) (see below) from both acids. Spectral and chemical evidence indicated that these acids are saturated tetracyclic compounds possessing one secondary and two tertiary methyl groups; furthermore, the absorption bands at near 3050, 860, and 845 cm^{-1} of ir (4) and at around 0.5-0.9 ppm (m) of nmr in all of the derivatives (described later) suggested the presence of a tricyclene carbon framework.

Treatment of the mixture of these acids with lead tetraacetate-lithium chloride

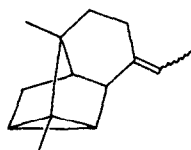
* Satisfactory analytical data were obtained for all new compounds.

** Taken at 60 MHz unless otherwise indicated.

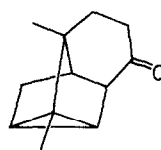
followed by dehydrochlorination of the resulting chloro derivatives (epimers) (IV) gave a mixture of geometrically isomeric olefins (V), $C_{14}H_{20}$. Nmr peak due to the secondary methyl group appeared as two pairs of doublets at 1.41 and 1.53 ppm in IV and at 1.52 and 1.55 ppm in V, respectively; and such chemical shift values clearly showed the existence of the side-chain grouping of $\text{>CH-CH} \begin{matrix} \text{CH}_3 \\ \text{COOH} \end{matrix}$ in the original acids (I,II). The olefins (V) were then converted to a single cyclic ketone (VI), ν^{CHCl_3} 1701, 1420 cm^{-1} (an unstrained ring ketone) through hydroxylation and subsequent glycol-cleavage. The Baeyer-Villiger oxidation of VI afforded an ϵ -lactone (VII), $C_{12}H_{16}O_2$, m.p. 109-111°, ν^{CHCl_3} 1715 cm^{-1} , δ^{CCl_4} 4.10 ppm (1H,br.s), which was subsequently transformed into a keto carboxylic acid (VIII), $C_{12}H_{16}O_3$, m.p. 114-115.5°, by saponification followed by Jones oxidation. The spectral properties of VIII, ν^{CHCl_3} 1743, 1711, 875, 826 cm^{-1} , $\lambda_{\text{max}}^{\text{MeOH}}$ 207 $\text{m}\mu$ (ϵ 3400); and the methyl ester, ν^{CHCl_3} 3050, 1740 (br.), 876, 830 cm^{-1} , $\lambda_{\text{max}}^{\text{MeOH}}$ 204 $\text{m}\mu$ (ϵ 3300), δ^{CCl_4} 0.98 (3H,s), 1.25 (3H,s), 3.62 (3H,s) ppm, distinctly verified the tricyclanone structure (5); thus, it was presumed that the carbon skeleton of the original acids (I,II), including three carbon side-chain moiety, would be exactly same as that of cyclosativene (IX) (6).



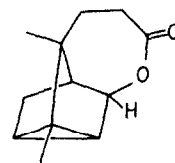
- I: R=COOH (major)
 II: R=COOH (minor)
 III: R=CH₃
 IV: R=Cl (epimers)
 X: R=CH₂OH (epimers)
 XI: R=OAc (epimers)



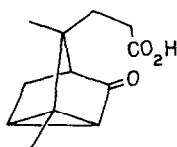
V: geometrical isomers



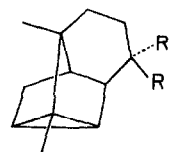
VI



VII



VIII



IX: R=CH $\begin{matrix} \text{CH}_3 \\ \text{CH}_3 \end{matrix}$

R'=H
 XII: R=H

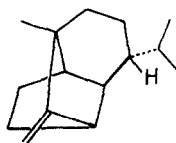
R'=COCH₃

XIII: R=COCH₃

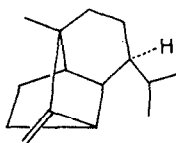
R'=H

XIV: R=C(CH₂)₂-CH₃

R'=H



XV



XVI

Either methyl ester of these acids (I,II) gave the same parent hydrocarbon, cyclocopacamphene (III)(7), $C_{15}H_{24}$, $[\alpha]_D^{19.5} +35.0$ (c 1.6, $CHCl_3$), $M^+ 204$, according to the reaction sequence: $-CO_2CH_3 \rightarrow -CH_2OH$ (X)(8) $\rightarrow -CH_2OTs \rightarrow -CH_3$. Although the values of the main absorption bands, 3050, 860, 845 cm^{-1} (ir, neat) and 0.62, 0.67, 0.75 (3H,s), 0.88 and 0.91 (each 3H,d J=6.5 Hz), 1.02 (3H,s), ppm (100 MHz nmr, CCl_4), of this hydrocarbon are in good agreement with those of cyclosativene (IX), the whole spectra are not identical. The most probable structure, formulated as III, for this parent hydrocarbon would be the stereoisomer of cyclosativene (IX) with respect to configuration of the isopropyl group.

This supposition was eventually confirmed by conversion of I and II to cyclosativene (IX) through the following reaction sequence: (i) decarboxylative acetoxylation of the mixture of I and II to XI with lead tetraacetate; (ii) hydrolysis with ethanolic potassium hydroxide followed by Jones oxidation to give a single acetyl derivative (XII), $C_{14}H_{20}O$, ν^{neat} 3050, 1705, 860, 843 cm^{-1} , δ^{CCl_4} 0.75 (3H,s), 1.02 (3H,s), 2.03 (3H,s), 2.55 (1H,m) ppm; (iii) epimerization to the isomer (XIII)(94% pure, determined on glpc), ν^{neat} 3050, 1705, 860, 846 cm^{-1} , δ^{CCl_4} 0.78 (3H,s), 1.02 (3H,s), 2.05 (3H,s), 2.51 (1H,m) ppm, with sodium methoxide; (iv) Wittig reaction with methylenetriphenylphosphorane followed by catalytic hydrogenation of the resulting isopropenyl derivative (XIV), $C_{15}H_{22}$, ν^{neat} 3050, 1642, 885, 860, 846 cm^{-1} , δ^{CCl_4} 0.80 (3H,s), 0.98 (3H,s), 1.83 (3H,br.t), 4.63 (2H,br.s) ppm, using tris(triphenylphosphine)-rhodium chloride as a catalyst. The hydrocarbon thus obtained, $C_{15}H_{24}$, $[\alpha]_D^{20} +67.8$ (c 1.15, $CHCl_3$), $M^+ 204$, isomeric to the parent one (III), was spectroscopically (ir, 100 MHz nmr) completely identical with (+)-cyclosativene (IX), $[\alpha]_D +94.1$ (6); this experimental fact leads the structures of two natural carboxylic acids to be I and II. The names of cyclocopacamphenic acid (major) and epicyclocopacamphenic acid (minor) are based on the name of the parent hydrocarbon, cyclocopacamphene (III), relating to copacamphene (XV)(9) by analogy with the relation between cyclosativene (IX) and sativene (ylangocamphene)(XVI)(8,10).

On the basis of the absolute stereochemistry of (+)-sativene (XVI)(10), the

absolute stereostructure of (+)-cyclosativene would be represented as IX (11); consequently, cyclocopacamphenic acid as I and so on, by applying the analogous structural correlation between (+)-longifolene and (+)-longicyclene (12). Sign of the Cotton effect (strongly positive) in the optically rotatory dispersion of the ketone (VI) would also support the absolute stereostructure of the carbon skeleton of VI, in consistent with the sign predicted from its octant diagram. At present the absolute configuration of the carboxyl group in I or II, including conformation of the six-membered ring, has not yet been determined.

Acknowledgement: We are greatly indebted to Mr. Yasuhiko Ueno (Ogawa Perfumery Co.) for supplying vetiver oil, and to Dr. E. Zavarin (University of California, Berkeley, Forest Products Laboratory) for providing the copies of ir and nmr spectra of cyclosativene.

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- 12) U. R. Nayak and S. Dev, Tetrahedron Letters, 243 (1963).