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THE STEREOCHEMISTRY OF ZIZANOIC ACID

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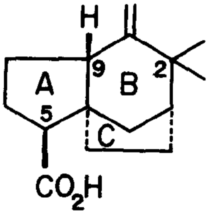
In an earlier communication (1) we have proposed the structure (II) for zizanoic acid, one of the sesquiterpenoids of vetiver oil. We now wish to report additional evidence for II and to suggest the stereostructure (I) for zizanoic acid.



I

The monomethyl ester (VI)(1) was chlorodecarboxylated by treatment with lead tetraacetate and lithium chloride (2) to give the chloroketoester (VII), $C_{14}H_{21}O_3Cl$, ν^{liq} 1732, 1406 cm^{-1}, whose NMR spectrum (1.55 ppm, s., 6H) shows the presence of the Me_2CCl- group in VII.

On the other hand, the ketoester (III)(1), upon irradiation with UV light followed by Jones' oxidation, afforded the unsaturated carboxylic acid (VIII), $C_{15}H_{22}O_4$, ν^{chl} 1727, 1705, 1647, 893 cm^{-1}; δ^{CCl_4} 1.69 (br.s., 3H), 4.65 (br.s., 2H), a product containing an isopropenyl group.

These results confirm the presence of a gem-dimethyl group on C_2 of zizanoic acid.

The carboxylic acid corresponding to III was chlorodecarboxylated with lead tetraacetate and lithium chloride (2) to give the chloroketone (IV), ν^{liq} 1710 cm^{-1}, as a mixture of epimers. The chloroalcohol (V), ν^{liq} 3510 cm^{-1}, a mixture of epimers, was obtained by $NaBH_4$ reduction of IV. Treatment of the chloroalcohol (V) with tert. BuOK in DMSO afforded the unsaturated alcohlol(IX), ν^{liq} 3460, 3050, 718 cm^{-1}, which was converted into the triol (X), $C_{13}H_{22}O_3$, mp 190-192°, ν (KBr) 3400 cm^{-1}; δ (pyridine) 1.02 (s., 3H), 1.23 (s., 3H) 3.63 (d., J=3.5, 1H), 3.98 (d., J=5, 1H), 4.68 ppm (d.d., J=5 and 8, 1H), by OsO_4 oxidation. The coupling constants of the signals at 3.98 and 4.68 ppm in X are not acceptable for the alternative structure (XI) containing an exo-α-glycol moiety in the C-ring. This reaffirms the location of the carboxyl group on C_5 for zizanoic acid (c.f. Ref. 1).

Stereochemistry

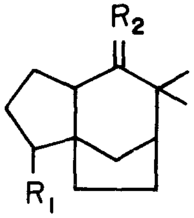
The ketone (XII) reported in the previous communication (1) exhibited strong negative Cotton effect ($[\phi]_{312}$ -5200°, $[\phi]_{278}$ +5200°; a -104), thus suggesting the absolute configuration as shown by the formula (XII) and trans juncture for the A/B ring on the basis of the ORD data of androstan-17-one ($[\phi]_{318}$ +7500°, $[\phi]_{279}$ -6500°; a +140)(3) and 14β-androstan-17-one-3β-ol acetate ($[\phi]_{301}$ +330°, $[\phi]_{267.5}$ -100°; a +34)(3).

The ketoester (III) showed a strong positive Cotton effect ($[\phi]_{312.5}$ +7200°, $[\phi]_{273.5}$ -6100°; a +133). The octant rule predicts that the Cotton effect of III should be strongly positive or strongly negative, depending on whether the A/B ring juncture is trans or cis, respectively. The values recorded also support the trans-fused A/B ring.

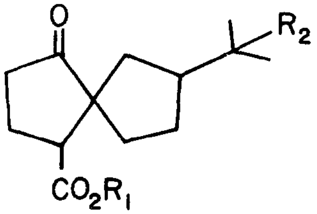
The carboxylic acid obtained from the diolester (XIII)(1) was treated with dicyclohexylcarbodiimide to give the γ-lactone (XIV), $C_{14}H_{20}O_3$, mp 83°, ν^{chl} 3554, 1783 cm^{-1}; δ^{CCl_4} 1.08 (s., 3H), 1.12 (s., 3H), 3.62 (s., 1H), thus suggesting β-orientation of the carboxyl group in view of the known preferential exo attack of a reagent (OsO_4 in this case) on the bicyclo[3,2,1]oct-2-ene system (4).

The stereostructure (I) is agreeable with these results.

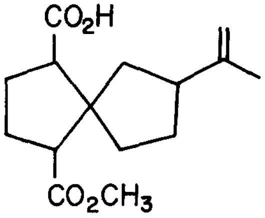
Previously we have proposed for zizanoic acid a possible biogenetic pathway (1) which involves the cationic precursor (XV) common to both zizanoic acid and cedrene, however elucidation of the stereochemistry shows that



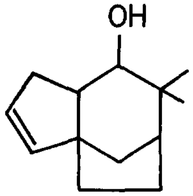
II ; R_1=COOH, R_2=CH_2
III; R_1=COOMe, R_2=O
IV ; R_1=Cl, R_2=O
V ; R_1=Cl, R_2=OH,H



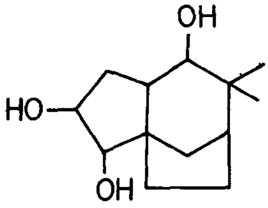
VI ; R_1=CH_3, R_2=COOH
VII; R_1=CH_3, R_2=Cl



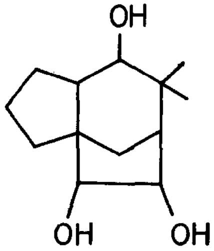
VIII



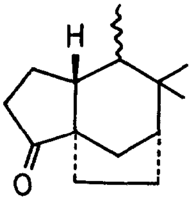
IX



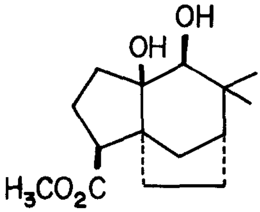
X



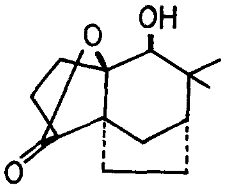
XI



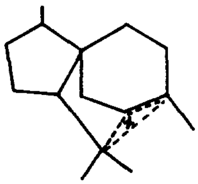
XII



XIII



XIV



XV

zizanoic acid belongs to a new series of biogenetic cyclization products of farnesyl pyrophosphate.

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4) See, for example, R. R. Saiers, H. M. How and H. Feilich, Tetrahedron, **21**, 983 (1965).