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NIGRANOIC ACID, A NEW A-SECO-CYCLOARTENE TRITERPENOID

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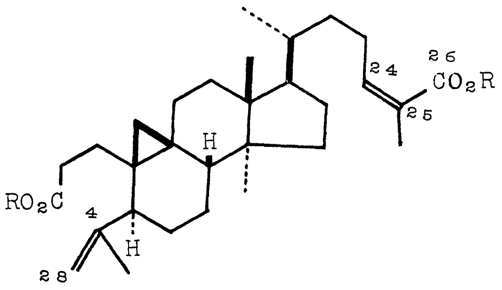
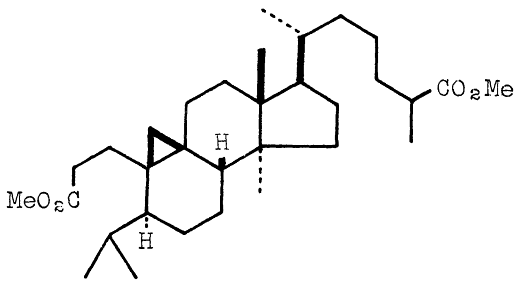
Nigranoic acid, a new seco-triterpenoid, was isolated from Schizandra nigra and proved to be 3,4-seco-9,19-cyclo-9β-lanosta-4(28),24-dien-3,26-dioic acid (I).

Nigranoic acid (I) is a 3,4-seco-cycloartene triterpene obtained from the stems of Schizandra nigra (Japanese name; Matsubusa). The ether extracts of the stems were extracted with aq. Na_2CO_3, and the acidic constituents[†] obtained were treated with diazomethane. The product was chromatographed on silica gel to afford oily methyl nigranoate (II), $C_{32}H_{50}O_4$ (M^+, m/e 498), $[\alpha]_D$ +47.0° (c 0.26 in MeOH), ν (neat) 3060, 3040, 1740, 1720, 1640, and 885 cm^{-1}, δ (CCl_4) 0.39 and 0.72 (d, J 4.5 Hz each, cyclopropane methylene), 0.91 (d, J 5 Hz, sec. Me), 0.92 and 0.95 (s each, tert. Me), 1.68 and 1.88 (s each, olefinic Me), 3.60 and 3.71 (s each, OMe), 4.74 and 4.83 (br s each, $>C=CH_2$), and 5.91 (br t, $>C=CH-$). The stereochemistry of the trisubstituted double bond in conjugation with one of the ester groups was assigned as shown in (II) by the fact that the chemical shift value of the trisubstituted olefin proton was closer to that reported for methyl angelate (5.97 ppm) than methyl tiglate (6.72 ppm)[1] and that the nuclear Overhauser effect was observed between the olefinic methyl at 1.88 ppm and the trisubstituted olefin proton.

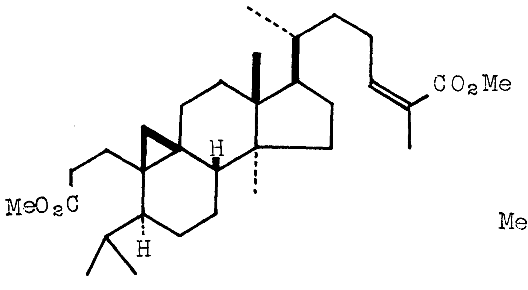
Upon hydrolysis of (II) with NaOH in DMSO at room temperature, nigranoic acid (I), $[\alpha]_D$ +55.8° (c 2.45 in MeOH), ν (KBr) -2600, 1700,



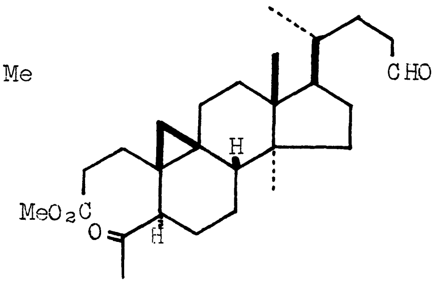
I R = H
II R = Me



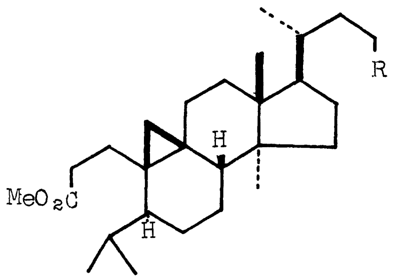
III



IV



V



VI R = CHO
VII R = CH=CMe$_2$

and 1640 cm^{-1}, δ (CCl$_4$) 0.40 (br d), 1.57 and 1.90 (s each), 4.75 and 4.83 (br s each), 6.07 (br t), and 12.00 (br s), was obtained as an amorphous solid. Hydrogenation of (II) over Pt in EtOH yielded the tetrahydro derivative (III), an oil, $C_{32}H_{54}O_4$ (M^+, m/e 502), ν (neat) 1740 cm^{-1}, demonstrating nigranoic acid to be a tetracyclic triterpene.

On the other hand, hydrogenation of (II) in benzene containing tris(triphenylphosphine)chlororhodium as the catalyst proceeded stepwise to give the dihydro derivative (IV), an oil, $C_{32}H_{52}O_4$, ν (neat) 1740, 1720, and 1640 cm^{-1}. The latter hydrogenation was accompanied by the partial isomerization of the trisubstituted double bond as shown by a newly appeared triplet signal at 6.65 ppm in the NMR spectrum of the product, and the chemical shift value indicated that the olefin proton should be assigned to a tiglate-type one. Methyl nigranoate (II) was ozonized, and the ozonide was hydrogenated over Pd-C in EtOH. The product was submitted to steam distillation, and methyl pyruvate was isolated from the distillate as the 2,4-dinitrophenylhydrazone. OsO_4-HIO_4 oxidation of (II) gave oily ketoaldehyde (V), ν (CCl_4) 2700, 1730, 1725, and 1710 cm^{-1}, δ (CCl_4) 2.08 (s, acetyl), 3.61 (s, OMe), and 9.67 (t, J 1.5 Hz, CHO).

The above results implied that nigranoic acid may be a derivative of 3,4-seco-cycloartene. (IV) was oxidized with OsO_4-HIO_4 to give aldehyde (VI), an oil, $[\alpha]_D$ +38° (c 0.26 in MeOH), ν(neat) 2700, 1735, and 1717 cm^{-1}, δ(CCl_4) 0.36 and 0.58 (d each, J 5 Hz), 0.82 (3H, d, J 6 Hz), 0.90, 0.97 (3H, s each), 3.64 (3H, s), and 9.85 (1H, t, J 2 Hz). The same aldehyde was derived from cycloartenone[2] as follows: irradiation of cycloartenone in MeOH yielded (VII), an oil, ν(neat) 3040 and 1730 cm^{-1}, δ (CCl_4) 0.35 and 0.58 (d, J 4.5 Hz each), 0.81 (d, J 5 Hz), 1.59 and 1.67 (br s each), 3.58 (s), and 5.05 (br t), in 55% yield. OsO_4-HIO_4 oxidation of (VII) gave an aldehyde, whose IR and NMR spectra were identical with those of the aldehyde (VI). The ORD of both the aldehydes also proved the identity of their absolute stereochemistry.

Nigranoic acid was thus proved to be 3,4-seco-9,19-cyclo-9β-lanosta-4(28),24-dien-3,26-dioic acid (I).

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References

The IR and NMR spectra of a total mixture of the acids showed neither absorptions due to ester group nor signals due to methoxyl group

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2) D.H.R. Barton, J. Chem. Soc., 1444 (1951); D.S. Irvin, J.A. Henry, and F.S. Spring, ibid., 1316 (1955).

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