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VERATRUM ALKALOIDS XXII [x]

VERACINTINE - A NOVEL TYPE OF VERATRUM ALKALOID WITH A PYRROLINE RING

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Dedicated to the 60th anniversary of Professor M. Pailer

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The structure of veracintine the novel alkaloid isolated from the aboveground part of Veratrum album subsp. lobelianum (Bernh.) has been inferred basing upon the study of n.m.r., i.r., u.v. and mass spectra of its and its derivatives. Veracintine, 20-(2-methyl-1-pyrrolin-5-yl)-pregn-5-ene-3β-ol, is shown to be a novel structural type of a biogenetically interesting veratrum alkaloid.

Veracintine (I), m.p. 196-201°, $[\alpha]_D^{25}$+7.5° (chloroform) shows in its mass spectrum a molecular ion peak at m/e 383 and species at m/e 110, 91, 83, 82, 69, 67, 55 and 41. The base peak at m/e 82 could be formed as a result of the C-20 C-22 bond fission similarly as described with the sex-membered side chain ring detachment from 22,26-epiminocholestane (1). High resolution mass spectrometry reading for the molecular ion peak of veracintine 383.3186 ± 0.0019 is in accordance with the calculated value 383.3188 for $C_{26}H_{41}NO$.

The alkaloid reveals in its infrared spectrum bands at 1058 and 3636 cm^{-1} due to a hydroxy group; further band of medium intensity at 1655 cm^{-1} is characteristic of a C=N double bond.

The n.m.r. spectrum displays two singlets (3 protons each) at δ 0.99 and 0.69 ppm indicative of a C-18 and C-19 angular methyl groups of a normal steroid ring system with a Δ^5 double bond (2), one doublet centered at δ 0.69 ppm (J=6.5 cps)

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[x] For part XXI, see Chem. zvesti 25, 69 (1971)

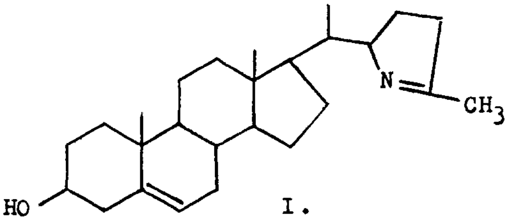
corresponding to a secondary methyl group at C-20, signal (doublets) of a C-6 vinyl proton at δ 5.36 ppm and one C-22 proton as an unresolved multiplet centered at δ 4.09 ppm. Another proton (multiplet centered at δ 3.50 ppm) is associated with a hydrogen adjacent to a hydroxyl at C-3. The singlet (3 protons) at δ 2.1 ppm belongs to a C-26 methyl group in the neighbourhood of a double bond.

Partial catalytic hydrogenation of veracintine in ethanol over platinum oxide afforded dihydroveracintine (II), m.p. 103-5°, $[\alpha]_D$ -27° ($CHCl_3$). The band at 1665 cm^{-1} is no more present in the infrared spectrum of this substance what evidences the C=N double bond to be hydrogenated. The molecular ion peak in the mass spectrum of this substance was raised by two mass units to m/e 385. The base peak at m/e 84 proves that the hydrogenation took place in the heterocyclic part of the alkaloid. In the n.m.r. spectrum of dihydroderivative II the position of the vinyl proton signal at C-6 and also those of methyl groups at C-18, C-19 and C-21 remained practically unaffected only the singlet of the C-26 methyl group was shifted to a doublet centered at δ 1.19 ppm (J=6 cps).

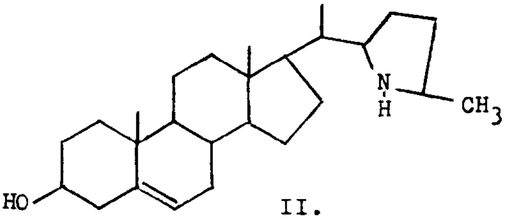
Hydrogenation of veracintine in acetic acid using platinum oxide as catalyst led to the tetrahydroderivative III (M^+ m/e 387), m.p. 247-250°, $[\alpha]_D$ +10.7° (ethanol). The upfield shift of the C-19 angular methyl group signal by 0.80 ppm undoubtlessly indicate that the hydrogenation of the second double bond occured in the Δ^5 position. This fact is in full agreement with the negative value of the molecular optical rotation difference between the dihydro and tetrahydroderivatives (3) $M_D(II) - M_D(III)$ -105°-42° = -147°.

The amorphous N,O-diacetylderivative IV $[\alpha]_D^{25}$-98° (ethanol) was isolated when reacting veracintine with acetic anhydride in pyridine. This compound reveals strong bands at 1748 and 1250 cm^{-1} (carbonyl and acetate band) and 1035 cm^{-1} (3β-acetyl group) (4) in its infrared spectrum. The band of the same intensity appearing at 1680 cm^{-1} is characteristic of the amide group and that at 1657 cm^{-1} indicates the presence of a double bond in a $CH_3-CO-\underset{|}{N}-\underset{|}{C}=CH$ grouping (5) in the structure of this substance.

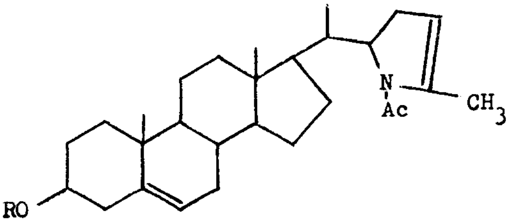
The absorption at 244 nm (log ε 3.89) in the ultraviolet spectrum, as well as the above-mentioned band in the infrared spectrum evidence that the double bond izomerized during acetylation .



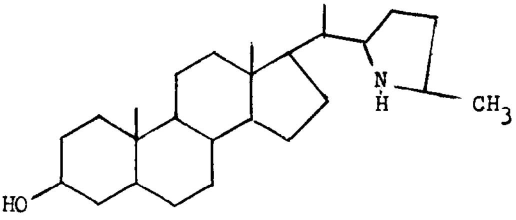
I.



II.



IV R = Ac
V R = H



III.

In the n.m.r. spectrum of substance IV a multiplet at δ 4.9 ppm **ascribable** to a further vinyl proton at C-24 could be observed. Upon saponification with methanolic potassium hydroxide N,O-diacetylveracintine furnishes N-acetylveracintine V in the infrared spectrum of which bands corresponding to an amide group remained unaffected,whereas those characteristic of an ester group disappeared. Respecting the biogenetic scheme and with regard to analogy with other veratrum alkaloids we assume the point of attachment of the pyrroline ring to be C-17.

As it follows from results presented,veracintine, 20-(2-methyl-1-pyrrolin-5-yl)-pregn-5-ene-3β-ol, is the first representative of a new type of veratrum alkaloids possessing a 5-membered heterocycle in the side chain of the steroidal skeleton. This alkaloid is being synthesized in order to verify the structure proposed.

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