STRUCTURE OF VERAMILINE, AN ALKALOID FROM *Veratrum album* SUBSP. *Lobelianum* (BERNH.) SUESSENGUTH*

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The structure of veramiline (*I*), a minor alkaloid isolated from the aerial part of *Veratrum album* subsp. *Lobelianum*, was deduced on the basis of spectral evidence and comparison of its dihydro derivative with the authentic specimen. The semisystematic name of the alkaloid *I* is (22*S*, 25*S*)-22,26-epiminocholest-5-en-3β-ol.

The isolation of veramiline, $C_{27}H_{45}NO$, was described in the preceding paper[1]; it is the first base isolated from *Veratrum album* having an epiminocholestane skeleton with a saturated heterocyclic ring. Alkaloids of this type reported so far in the literature possess an azomethine double bond in the heterocyclic moiety of the molecule[2-4]. Veramiline belongs to genuine steroids with a 3β-OH group, since it gave a positive digitonine test.

The mass spectrum of *I* revealed peaks at *m/e* 398 (M−1), 384 (M−15), 382 and 98 (base peak) diagnostic of the presence of piperidine substituted with a methyl group[5]. Since substances of this structural feature do not exhibit a well pronounced peak of molecular radical ion, we determined its molecular formula from the high resolution measurement of its N,O-diacetyl derivative. The ^{1}H-NMR spectrum (on the δ scale in ppm) showed two singlets of tert-methyl groups at 0·68 ($C_{(18)}$) and 1·00 ($C_{(19)}$), the position of which coincided with that given by Zürcher[6] for the particular groups on a genuine steroid skeleton with a Δ^5 double bond, two doublets of sec-methyl groups at 1·03 ($C_{(27)}$, J = 7·5 Hz) and 0·86 ($C_{(21)}$, J = 7 Hz), an AB doublet at 5·3 (a vinylic proton at $C_{(6)}$) and a multiplet at 3·5 (H adjacent to OH). The IR spectrum displayed an absorption band at 1045 and 3350 cm^{-1} (OH).

Acetylation of veramiline with acetic anhydride in pyridine afforded N,O-diacetyl derivative *II*. Its mass spectrum revealed a peak of the molecular radical ion at *m/e*

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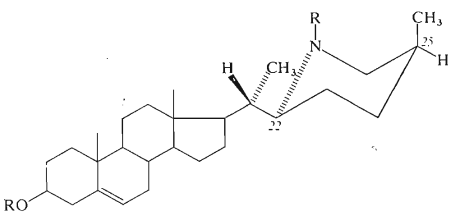
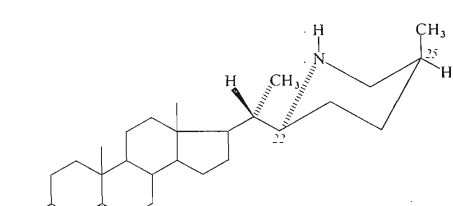
483·37256 (for $C_{31}H_{49}NO_3$ calculated: 483·37122) in addition to other peaks at *m/e* 468 (M−15), 440 (M−43), 423 (M−60), 140 (base peak) and 98. The ^{1}H-NMR spectrum took further two singlets at 2·00 and 2·05 (6 protons of acetyl groups) and the multiplet was shifted to 4·6 (H adjacent to an acetyl). The IR spectrum showed adsorption bands indicative of a 3β-acetyl group (1035, 1250 and 1725) and an amide (1615 cm^{-1}).



I, R = H
II, R = CH_3CO



III

Hydrogenation of veramiline in acetic acid over Adams catalyst gave dihydroveramiline *III* the mass spectrum of which displayed peaks at *m/e* 400 (M−1), 386 (M−15) and 98 (base peak). In the ^{1}H-NMR spectrum of *III* the signal of the $C_{(19)}$-methyl group was shifted upfield to 0·8, whereas the signal of the vinylic proton at 5·3 disappeared.

The negative difference between molecular rotations of veramiline and its dihydro derivative $[\phi]_D$ (*I*) − $[\phi]_D$ (*III*) = −195° −32° = −227° agreed with the data[7] given for saturation of a $C_{(5)}$ double bond of a steroid backbone.

On the basis of arguments presented herein, veramiline is 22,26-epimino-cholest--5-en-3β-ol. To specify the configuration at $C_{(22)}$ and $C_{(25)}$ we contrasted the dihydro derivative *III* with the synthetic[2] (22*S*, 25*S*) and (22*R*, 25*S*)-22,26-epimino-5α-cholestan-3β-ols (tetrahydroverazines A and B). Since dihydroveramiline is identical (the

mass and ^{1}H-NMR spectra, optical rotation, mixed m.p.) with the former, veramiline is assigned the structure of (22*S*, 25*S*)-22,26-epiminocholest-5-en-3β-ol.

EXPERIMENTAL

Melting points were determined on a Kofler micro hot-stage, optical rotation of ethanol solutions with a Perkin-Elmer model 141 polarimeter. The IR spectra of chloroform solutions were measured with a Perkin-Elmer model 457 spectrophotometer, mass spectra with a JMS-D 100 instrument and ^{1}H-NMR spectra with a Tesla 487-B spectrometer in deuteriochloroform with tetramethylsilane as internal reference substance. Developing systems for thin-layer chromatography on neutral alumina Woelm (TLC) activated at room temperature for 24 h S_1 benzene–ethanol 19 : 1 and S_2 benzene–ethanol 17 : 3.

Veramiline (*I*)

This alkaloid was isolated from a benzene extract of dried aerial part of *V. album* subsp. *Lobelianum*[1]; m.p. 198–200°C (acetone), $[\alpha]_D^{22}$ −49° (*c* 0·79), R_F 0·4 (S_1).

N,O-Diacetylveramiline (*II*)

A solution of veramiline (30 mg) in pyridine (1·5 ml) and acetic anhydride (1 ml) was allowed to stand at room temperature for 24 h. The solvent was distilled off under diminished pressure and the residue (37 mg) was chromatographed over neutral alumina (2·4 g) Reanal, activity grade II. Elution with benzene–ethanol (99 : 1) afforded the product; m.p. 156–157° (ether), $[\alpha]_D^{22}$ −21° (*c* 0·72), R_F 0·77 (S_1).

Dihydroveramiline (*III*)

Veramiline (18 mg) in acetic acid (7 ml) was hydrogenated in the presence of Adams catalyst (10 mg) at room temperature for 20 h. The mixture was worked up and extracted with chloroform (5 × 10 ml). The yield (16 mg) was purified on a column with basic alumina (1·5 g) Woelm, activity grade III. Elution with benzene–ether (95 : 5) gave the product; m.p. 179–182°C (methanol), $[\alpha]_D^{22}$ +8° (*c* 0·4), R_F 0·70 (S_2). (22*S*, 25*S*)-Tetrahydroverazine A (*III*, ref.[2]): m.p. 180 to 184°C, $[\alpha]_D^{22}$ +9·4° (*c* 0·5), R_F 0·70 (S_2). Mixed m.p. 179–183°C.

All spectra were taken in the department of analytical chemistry, Institute of Chemistry, Slovak Academy of Sciences.

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