STRUCTURE OF THE NEW DITERPENE ALKALOID ZERACONINE AND ITS N-OXIDE

Z. M. Vaisov and M. S. Yunusov

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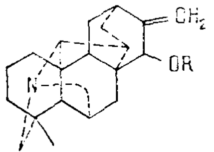
The structures of the new diterpene alkaloid zeraconine and its N-oxide, isolated from *Aconitum zeravschanicum*, have been established on the basis of spectral characteristics and chemical transformations.

We have previously reported the isolation from the plant *Aconitum zeravschanicum* Steinb. of a base with mp 130-131°C [1], which proved to be new, and we have called it zeraconine. The base has the composition $C_{30}H_{40}ON_2$, mol. wt. 444 (mass spectrometrically). Its PMR spectrum contains the following signals (ppm): singlet at 0.90 (3 H), singlet at 2.19 (6 H) strongly broadened singlet at 3.10 (1 H), broadened singlet at 4.38 (2 H), broadened singlet at 5.69 (1 H), and two doublets at 6.68 and 6.95 (2 H each, J = 8.5 Hz) from a pair of equivalent ortho-aromatic protons. The IR spectrum of the base lacks absorption bands due to hydroxy, carbonyl, and ester groups and has bands caused by a para-substituted benzene ring at 810, 830, 1515, 1585, and 1615 cm^{-1}.

According to the facts given above, the six-proton singlet at 2.19 ppm in the PMR spectrum of the base may be due to a N,N-dimethylamino group. The presence in the mass spectrum of the maximum peak with m/z 58 connected with the $CH_2{=}\overset{+}{N}{<}^{CH_3}_{CH_3}$, ions shows that in zeraconine there is a N,N-dimethylaminoethyl group which may be attached to a benzene ring. If this group is deducted from the empirical formula of the alkaloid, a fragment with the composition $C_{20}H_{26}NO$ remains which corresponds to the hetisine type of diterpene alkaloids. The two assumed moities of the alkaloid may be linked by an ether bond.

Thus, structure (I) or (II) can be proposed for zeraconine. The presence in the PMR spectrum of the alkaloid of a signal from one olefinic proton in the form of a broadened singlet at 5.69 ppm, the absence in the 5 ppm region of a signal characteristic for a terminal methylene group, and the absence of a signal from this grouping in the ^{13}C NMR spectrum permit structure (I) to be assigned to zeraconine. Also in harmony with the proposed structure is the presence in the PMR spectrum of a two-proton singlet at 4.38 ppm, which is assigned to the protons of C-17 methylene group.



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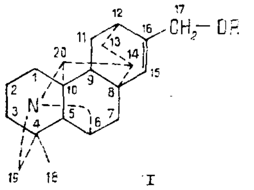

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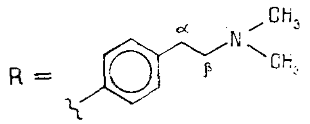

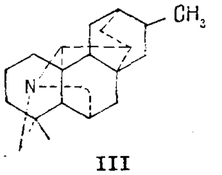

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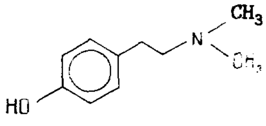

IV

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To confirm the proposed structure we performed the hydrogenolysis of the alkaloid in the presence of Pd. As was to be expected, the reaction gave two products: (III), with the composition $C_{20}H_{29}N$, and (IV), with the composition $C_{10}H_{15}NO$. Mass and PMR spectra showed that product (III) belonged to the hetisine type of alkaloid. Its mass spectrum contained, in addition to the peak of the molecular ion with m/z 283 (100%), the peaks of the $M^+ - 15$, $M^+ - 28$, $M^+ - 29$, and $M^+ - 43$ ions and of ions with m/z 160 and 146.

The nature of the breakdown of the molecular ion coincided with that of the alkaloid nominine (II, R = H) 2, 3 , the spectrum of which contains ions with m/z 297 (M^+), 282, 280, 269, 268, 254, 160 and 146. In the PMR spectrum, signals were observed from a tertiary methyl group at 1.08 ppm (3 H, singlet), from a secondary methyl group at 0.87 ppm (3 H, doublet, J = 7.0 Hz), from H-6 at 3.79 ppm (1 H, broadened singlet, $W_{1/2}$ = 7 Hz), from H-20 at 2.97 ppm (1 H, singlet), from α-H-19 at 3.03 ppm (doublet, J = 12 Hz) and from β-H-19 at 2.73 ppm (doublet, J = 12 Hz).

The second product from the hydrogenolysis of (IV) was a phenol. Its mass spectrum contained in addition to the peak of the molecular ions with m/z 165, a peak with m/z 58 having the maximum intensity and peaks of ions with m/z 121, 120, 107, 91, and 77. Its PMR spectrum contained the following signals: two doublets at 6.65 and 6.93 ppm (2 H each, J = 8.5 Hz) from a pair of equivalent ortho-aromatic protons, a broadened two-proton singlet at 2.86 ppm ($W_{1/2}$ = 8 Hz), a broadened two-proton doublet at 2.62 ppm (J = 3 Hz) and a six-proton singlet at 2.33 ppm. The structure of (IV) was identical with that of hordenine [4]. Because of the small amount of (IV), obtained in the form of a crystallizing mass, it was not separated but was identified by comparison with an authentic sample of hordenine using TLC and mass spectroscopy.

Among the products from the hydrogenolysis of zeraconine a third substance was detected which, because of its small amount, could not be obtained in sufficiently pure form but was, judging from its mass spectrum, a dihydro derivative of zeraconine.

The structure (I) proposed for zeraconine agrees with its ^{13}C NMR spectrum. Thus, the spectrum contains the signals from a N,N-dimethyl group at 45.5 ppm and from a C-18 methyl group at 28.9 ppm.

Below, we give the chemical shifts of the carbon atoms in the ^{13}C NMR spectra of zeraconine (δ, ppm, $CDCl_3$ 0 — PMS):

$-CH_3$	$>CH_2$	$>CH$ and $-CH=$	$-\overset{\vert}{\underset{\vert}{C}}-$ and $-\overset{\vert}{C}=$
28,9	19,6	31,2	37,4
45,5×2	27,7	48,6	44,9
	29,8	50,1	50,0
	33,2	61,9	132,5
	33,5	65,5	144,2
	34,2×2	74,2	157,4
	61,8	114,8	
	63,1	128,7×2	
	69,0	129,4×2	

The signals of C-17, C-19, and β-CH_2 methylene groups appear at 69.0, 63.1, and 61.8 ppm, respectively, those of the C-20 and C-6 methine groups at 74.2 and 65.5 ppm and that of C-15 at 114.8 ppm, those of two pairs of equivalent aromatic carbon atoms at 128.7 and 129.4 ppm, that of C-16 at 132.5 ppm, the signal of an aromatic carbon atom bearing oxygen at 157.4 ppm and of one bearing an α-CH_2 group at 144.2 ppm. In all, the spectrum contains 26 signals from 30 carbon atoms.

In addition to zeraconine, we isolated from *Aconitum zeravschanicum* a base (V) with mp 94-95°C similar in its spectral characteristics (IR, PMR, mass spectra) to zeraconine and differing from the latter in composition by one oxygen atom, $C_{30}H_{40}O_2N_2$, mol. wt. 460. The PMR spectrum of (V) contained the following signals (ppm); singlet at 0.93 (3 H), singlet at 3.14 (6 H, broadened singlet at 4.42 (2 H), broadened singlet at 5.72 (1 H), and two doublets at 6.73 and 7.03 (2 H each, J = 7.5 Hz). As compared with the PMR spectrum of zeraconine, the six-proton singlet in the spectrum of (V) was shifted downfield by 0.95 ppm, and a broadened ($W_{1/2}$ ~ 6 Hz) two-proton singlet appeared at 3.44 ppm. Otherwise, the PMR spectra of the two bases were practically identical.

The facts given permits us to consider that (V) was seraconine N-oxide at the nitrogen atom of the dimethylamino group. The signal at 3.44 ppm can be assigned to an α-methylene group at a nitrogen oxide atom. The N-oxide structure of (V) was confirmed by its mass spectrum, in which the peak of the molecular ion had an insignificant intensity. Characteristic peaks in the spectrum were those of the ions formed as the result of Cope decomposition with m/z 399 and 61, and also the peaks of ions with m/z 280, 60, and 42. It must be mentioned that the retention of the base (V) in the mass spectrometer led to a change in the spectrum in the direction of a reproduction of the spectrum of zeraconine.

EXPERIMENTAL

Type KSK silica gel was used for column chromatography, and PMR spectra were taken on a JNM-4H-100/100 MHz instrument in CDCl$_3$ (δ, ppm, 0 — HMDS), ^{13}C NMR spectra on a Varian CFT-20 instrument, δ, ppm, 0 — DMS), mass spectra on a MKh-1310 instrument, and IR spectra (KBr) on a UR-20 instrument.

Hydrogenolysis of Zeraconine. A mixture of 0.1 g of the alkaloid, 10 ml of ethanol, and 0.1 g of 10% Pd/C was shaken in an atmosphere of hydrogen for 24 h. The catalyst was separated off, the solvent was evaporated off, and the residue (90 mg) was chromatographed on a column of silica gel (9 g). The reaction products were eluted with chloroform—methanol mixtures: (50:1) — seven fractions; (25:1) — fractions 8-20; (15:1) — fractions 21-30; and (1:1) — fractions 31-40, the volume of each fraction being 5 ml. With the aid of acetone, 10 mg of product (III) with mp 260°C (subl.) was isolated from fractions 13-25. Fractions 35 and 36 were combined and evaporated, and the residue (10 mg) was separated by the usual method into phenolic and nonphenolic parts. The phenolic part consisted of the chromatographically pure substance (IV) (7 mg), while the nonphenolic part (2 mg) was dihydrozeraconine.

SUMMARY

The structure of a new alkaloid of the hetisine type, zeraconine, isolated from the plant *Aconitum zeravschanicum*, has been established. Zeraconine is the first diterpene alkaloid consisting of an ether of a diterpene and of phenethylamine. Zeraconine N-oxide has been found in the same plant.

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