THE STRUCTURE OF SEVERINE

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Continuing investigations of alkaloids from the epigeal part of Korolkowia sewerzowii Regel [1], by separating the mother liquor from the combined ether-soluble alkaloids according to basicity and also by chromatography on a column of silica gel we have isolated a base with mp 145-147°C, $[\alpha]_D$ −50.2°, $C_{29}H_{45}NO_6$, and the new alkaloid severine with mp 144-146°C, composition $C_{29}H_{47}NO_4$ (I). The base was also isolated from the combined alkaloids of the epigeal part of this plant collected near Tashkent [2].

Severine is a tertiary base and its IR spectrum shows absorption bands at (cm^{-1}) 3460 (OH), 2947-2860, 1463, 1440 ($-CH_3$; $-CH_2-$), 2770 (trans-quinolizidine), 1734, 1250 (ester C=O). The NMR spectrum of (I) has signals at 0.93 ppm (3 H, 19-CH_3) and 2.00 ppm (3 H, $OCOCH_3$), and poorly resolved doublets from the protons of the secondary methyl groups and a multiplet at 5.07 ppm (H, $\underline{H}C-OCOCH_3$). The mass spectrum of severine contains the main peaks of ions with m/e 98, 111 (100%), 112, 124, 125, 138, 149, 150, 164, 165, 166, 178, 179, 412, 413 $(M-60)^+$, 417, 418, 430 $(M-43)^+$, 431 $(M-42)^+$, 444 $(M-29)^+$, 455 $(M-18)^+$, 458 $(M-15)^+$, 473 (M^+), which are characteristic for C-nor-D-homosteroid alkaloids of the cevine group [2-6].

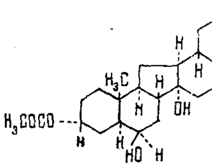
The alkaline hydrolysis of severine gave an amino alcohol with the composition $C_{27}H_{45}NO_3$, mp 240-242°C, identical with korseveriline isolated previously from this plant [2, 3]. Acetic acid was found in the hydrolyzate by paper chromatography. The acetylation of severine gaven an acetyl derivative identical with diacetylkorseveriline which we obtained by the acetylation of korseveriline [2, 3]. The NMR spectrum of the acetate (I) had singlets at (ppm) 0.90 (3 H, 19-CH_3), 1.97 (3 H, $OCOCH_3$), and 2.00 (3 H, $OCOCH_3$), doublets at 0.80 (3 H, 21-CH_3), and 0.80 (3 H, 27-CH_3), and multiplets at 5.05 (H, $HC-OCOCH_3$) and 4.88 (H, $HC-OCOCH_3$). Korseveriline has the structure and configuration of 3α,6β,14α-trihydroxy(27α-methyl)cevanine [3].

The identity of the amino alcohol with korseveriline and also of acetylseverine with diacetylkorseveriline shows that severine is a monoacetyl derivative of korseveriline [3]. The A/B, B/C, C/D, and E/F ring linkages in severine as the same as in korseveriline, and the 21-CH_3 and 27-CH_3 groups are oriented equatorially in the α positions [3, 7-10]. It remains to determine the location of the acetoxy group in the severine molecule.

The acetic acid residue may be present in the amino alcohol severine in one of two possible positions — at C_3 or C_6. In the NMR spectrum of diacetylkorseveriline the multiplet of a proton geminal to an acetoxy group at 5.05 ppm is assigned to $C_3\beta$-H and that at 4.88 ppm to $C_6\alpha$-H.

In severine, the proton geminal to the acetoxy group gives a signal at 5.07 ppm and, consequently, the acetic acid residue in the severine residue can be present only in the C_3 position.

On the basis of the facts presented it may be concluded that severine has the structure of 3α-acetoxy-6β,14α-dihydroxy(27α-methyl)cevanine.



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EXPERIMENTAL

The IR spectra (KBr) were taken on a UR-20 spectrometer, the NMR spectra on a JNM-4H-100/100 MHz instrument ($CDCl_3$ with HMDS as internal standard, values given in the δ scale), and the mass spectra on an MKh-1303 instrument fitted with a glass system for direct introduction into the ion source. For TLC we used Al_2O_3 (activity grade II), the chloroform–methanol (10 : 0.5) system, and the Dragendorff chromogenic reagent.

Isolation of Severine. The material from the mother liquor from the combined ether-soluble alkaloids after the separation of the mixture of crystals [1] (40 g) was dissolved in chloroform and was separated according to basicity into 11 fractions by extraction with 40-ml portions of 1% sulfuric acid. Fractions 6 and 7 were combined (7.39 g) and chromatographed on a column of alumina, the column being washed with chloroform and with chloroform–methanol (10 : 0.3). Fractions with a volume of 30-35 ml were collected. Combined fractions 6-10 (2.19 g) of the chloroform eluate, when treated with acetone, deposited a mixture of crystals (0.23 g).

After the separation of the mixture of crystals, the mother liquor (1.96 g) was chromatographed on a column of silica gel (KSK, 150 mμ) being eluted with chloroform and chloroform–methanol (10 : 0.3 and 10 : 1). The chloroform eluate yielded 0.64 g of a base with mp 145-147°C [acetone–petroleum ether (1 : 5)], $[\alpha]_D$ −50.2° (c 0.777; chloroform). The chloroform–methanol (10 : 0.3) eluate yielded 0.31 g of severine with mp 144-146°C (benzene). $[\alpha]_D$ −20.9° (c 0.43; chloroform), R_f 0.53, M^+ 473.

Saponification of Severine. A solution of 0.1 g of severine in 1 ml of methanol was treated with 5 ml of 5% methanolic caustic potash. The reaction mixture was heated in the water bath for 30 min, and then the methanol was evaporated off in vacuum. The residue was diluted with water and extracted with chloroform. The treatment of the chloroform extract with methanol led to the deposition of crystals with mp 240-242°C (methanol), R_f 0.27, identical with an authentic sample of korseveriline (according to R_f values, mixed melting point, and IR, NMR, and mass spectra). Acetic acid was found in the alkaline mother solution by a method described previously [11].

Acetylation of Severine. A mixture of 0.05 g of severine, 1 ml of pyridine, and 2 ml of acetic anhydride was kept for 2 days at room temperature. Then the solution was evaporated in vacuum, and the residue was dissolved in 5% sulfuric acid. The acid solution was made alkaline with ammonia and the reaction product was extracted with chloroform. This gave amorphous acetylseverine with R_f 0.78, identical and diacetylkorseveriline (according to R_f values and IR, NMR, and mass spectra); M^+ 515.

SUMMARY

1. From the combined ether-soluble alkaloids of the epigeal part of Korolkowia sewerzowii Regel we have isolated a base with mp 145-147°C and the new alkaloid severine.

2. On the basis of the results of a study of its IR, NMR, and mass spectra and its conversion into the known alkaloid korseveriline, the structure of severine has been established as 3α-acetoxy-6β,14α-dihydroxy-(27α-methyl)cevanine.

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