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STRUCTURE OF THE STEROID ALKALOID RADPETINE FROM Petilium raddeana

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A new base with the composition $C_{29}H_{45}NO_3$ has been isolated from the plant Petilium raddeana and has been called radpetine. Its structure has been established as 3β-hydroxy-23,28-epoxy-23-ethyl-$\Delta^{22(N)}$-22,26-iminocholestan-y-one- by the x-ray structural method (diffractometer, CuK_α, 1046 reflections, direct method, MLS in the anisotropic approximation, R = 0.118). Radpetine belongs to a new type of steroid alkaloids with a spiro-methyloxirane grouping at C-23 in the azomethine ring F.

From the plant Petilium raddeana we have isolated a new base with the composition $C_{29}H_{45}NO_3$ (M^+ 455 in the high-resolution mass spectrum), which has been called radpetine (I). The structure of (I) has been studied by IR-, PMR-, and mass-spectral methods, and this has enabled it to be assigned to the steroid alkaloids containing one ketone and one hydroxy group. However, because of the small amount of substance isolated and the unusual spectral characteristics of the nitrogen-containing part of the molecule of (I) it was impossible to establish its structure completely. In order to determine the structure and stereochemistry of radpetine unambiguously we have made an x-ray structural investigation of its hydrochloride.

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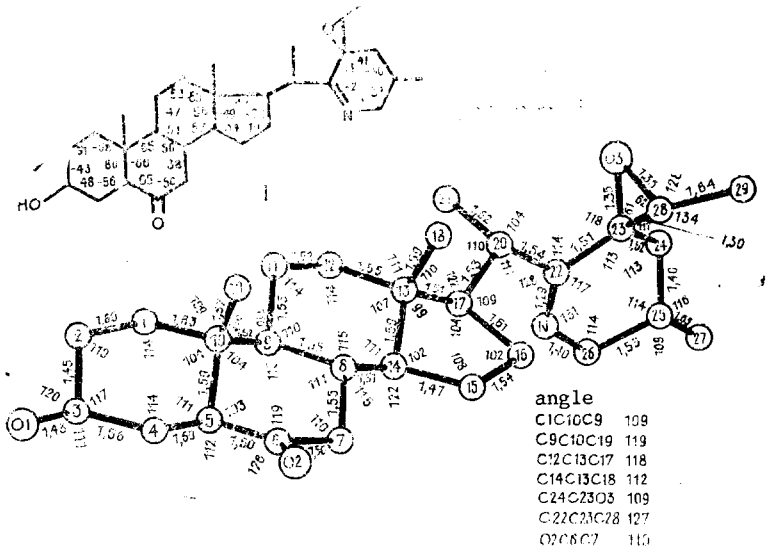

Fig. 1. Structure of the (I) molecule protonated at the N atom with bond lengths (Å) and valence and torsional angles (degrees).

Because of the high degrees of error in the determination of the bond lengths and valence angles (see the Experimental part), in determining the position of the epoxide group and the C=N in the azomethine ring F, in the initial stage of the x-ray structural analysis we made use of the results of mass and PMR spectroscopies.

The spatial structure of (I) is shown in Fig. 1 in a projection giving the smallest degree of overlapping of the atoms.

As can be seen from the chemical formula given in Fig. 1, radpetine is a natural derivative of the alkaloid petiline [1, 2] differing from the latter by the presence of a spiro-methyloxirane group in ring F. At the same time, the configurations of the asymmetric centers in the steroid part of the molecule of (I) are identical with those observed in petiline and also in other related alkaloids – edpetilidinine and sevcoridinine [3]: the methyl groups at C10 and C13, the hydroxy group at C3, and the C17–C20 bond are β-oriented; the A/B, B/C, and C/D ring linkages are trans. The spiro-methyloxirane group in the C23 position adjoins the heterocycle F, having the α orientation of the C23–O3 bond and the β orientation of the C23–C28 bond. The methyl groups at C25 and C28 are α-oriented. Thus, radpetine corresponds to the structure and stereochemistry of 3α-hydroxy-23,28-epoxy-23-ethyl-$\Delta^{22(N)}$-22,26-imino-cholestan-6-one. Analysis of the literature has shown that radpetine is the sole representative of a steroid alkaloid with a spiro-oxirane group at C23 in the azomethine ring F.

The conformations of the rings are characterized by the endocyclic torsional angles given in Fig. 1. In the steroid moiety, the conformations of the rings coincide completely with those observed in the alkaloids edpetilidinine and sevcoridinine (although (I) differs from them by the existenc eof a C_{sp^2} hybridized C6 atom): rings A, B, and C have chair conformations and the five-membered ring D the half-chair conformation (with deviations of the C13 and C14 atoms by 0.54 and −0.25 Å, respectively). Ring F, contains the endocyclic C=N double bond has the half-chair conformation, but the ring is considerably flattened: the deviations of the C24 and C25 atoms from the plane of the other four atoms amount to −0.41 and 0.18 Å, respectively.

The geometric parameters of the molecule of (I) are given in Fig. 1, the errors and the determination of the bond lengths and valence angles not exceeding 0.05 Å and 3°, respectively. In spite of the high values of the errors, a comparison of the corresponding bond lengths and valence angles of (I) with those observed in related alkaloids [2] revealed no anomalous discrepancies and showed their agreement with the standard values to within the 3σ limits [4].

The packing structure of (I) is shown in Fig. 2. The presence of O1–H...Cl and N–H... Cl hydrogen bonds (3.24 and 3.08 Å, respectively) is obvious. Thanks to the above-mentioned

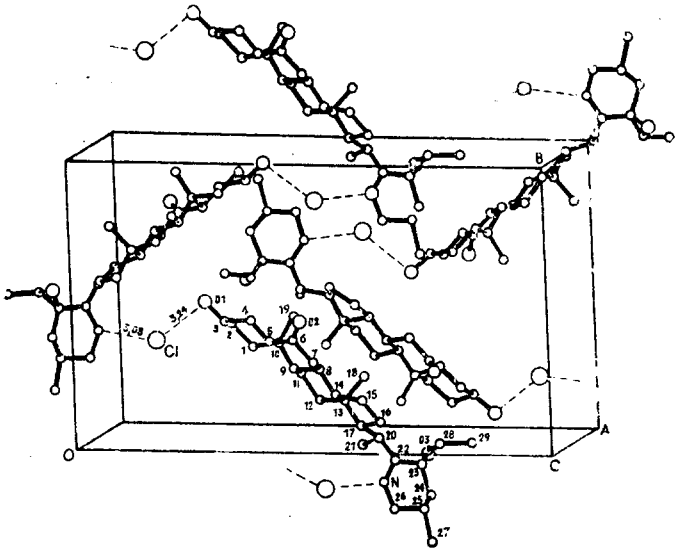

Fig. 2. Crystal structure of radpetine hydrochloride. Hydrogen bonds are shown by dashed lines (in the top molecule a C–C bond in ring F has been omitted).

bonds, the protonated radpetine molecules, transformed by a $2_1[0, y, 1/4]$ screw axis are cross-linked through the Cl anions and form an infinite helix along the b axis.

EXPERIMENTAL

IR spectra (KBr) were taken on a UR-20 instrument, PMR spectra on a JNM-4H-100/100 MHz instrument (in $CDCl_3$ with HMDS as standard), and mass spectra on a MKh-1310 instrument.

Radpetine. The epigeal part of the Petilium raddeana (34 kg) gathered in Khazardag mountains, Turkmen SSR, yielded a total of 0.81% of alkaloids by chloroform extraction. The ether-soluble alkaloids (85 g) were separated according to basicity by nitrate-phosphate buffer solutions (pH 8-2.2; pH interval 1). This gave 36 fractions. By chromatography on a column of alumina with elution by benzene–chloroform, fractions 32 and 33 yielded 0.76 g of radpetine having mp 229-231°C (acetone–petroleum ether (3:1)).

The IR spectrum of (I) showed absorption bands at (cm^{-1}) 3380 (OH), 1712 (ketonic C=O), and 1645 (C=N). The PMR spectrum of (I) contained the following proton signals (ppm): singlets at 0.65 (3H, 18-CH_3), 0.71 (3H, 19-CH_3); doublets at 0.95 (3H, J = 6 Hz, 27-CH_3), 1.01 (3H, J = 6 Hz, 21-CH_3) and 1.29 ppm. (3H, J = 6 Hz, CH_3–CH–O–); multiplet with its center at 3.52 ppm. (1H, H–C–OH). Mass spectrum, m/z: 112, 152, 167 (100%), 178, 192, 206, 384, 398, 412, 424, 437 $(M-18)^+$, 440 $(M-15)^+$, 455 M^+.

Radpetine Monoacetate. White crystalline substance, mp 100-103°C. IR spectrum, cm^{-1}: 1740, 1250 (C=O and C–O of an acetate group); 1715 (ketonic C=O); 1655 (C=N). The PMR spectrum contained a signal at 1.98 ppm (3H, CH–C$\diagdown\!\!\diagup^{O}$) and the signal of a gem-acyl proton in the form of a multiplet at 4.60 ppm. (1H, $W_{1/2}$ = 27 Hz, HC–C$\diagdown\!\!\diagup^{O}_{CH_3}$).

X-Ray Structural Analysis. Single crystals suitable for the investigation were obtained (after numerous unsuccessful variations in the conditions of crystallizing the base (I)) from the hydrochloride of (I) in the form of thin plates. The space group and parameters of the unit cell were determined from precession photographs and were refined in a SYNTEX $P2_1$ diffractometer using CuK_α radiation: a = 7.829(3), b = 14.394(4), c = 25.108(7) Å; d_{calc} = 1.159 g/cm³; space group $P2_12_12_1$; Z = 4.

The intensities of 1958 reflections with $\theta < 58°$ were measured on the above-mentioned diffractometer ($\theta/2\theta$ scanning). The calculations made use of 1046 reflections with $|F|^2 > 1.5\sigma(|F|^2)$. The large number of practically zero reflections was connected with the unsatisfactory quality and small dimensions of the crystal.

TABLE 1. Coordinates of the Atoms ($\times 10^3$) in the Structure of (I)

Atom	x	y	z	Atom	x	y	z
C1	−144(4)	718(3)	710(2)	C18	−034(4)	826(2)	485(1)
C2	−126(6)	640(3)	755(1)	C19	016(5)	629(2)	634(1)
C3	039(7)	647(3)	781(1)	C20	−140(4)	1024(2)	450(1)
C4	198(4)	663(3)	744(2)	C21	−335(3)	1035(2)	469(1)
C5	176(2)	740(3)	704(1)	C22	−093(4)	1120(2)	427(2)
C6	320(6)	744(4)	665(2)	C23	−110(6)	1126(3)	367(2)
C7	325(5)	821(2)	626(2)	C24	−131(5)	1232(4)	347(1)
C8	151(5)	830(2)	597(1)	C25	−023(5)	1294(3)	374(1)
C9	−000(5)	811(2)	635(1)	C26	−031(5)	1286(2)	434(1)
C10	014(4)	722(3)	668(1)	C27	−040(5)	1403(2)	357(1)
C11	−171(4)	812(3)	604(1)	C28	−060(8)	1065(2)	333(1)
C12	−191(4)	895(3)	567(2)	C29	034(7)	1070(3)	275(1)
C13	−040(5)	909(3)	527(1)	O1	081(3)	586(3)	824(1)
C14	129(4)	915(3)	562(1)	O2	448(3)	691(2)	664(1)
C15	256(4)	941(2)	521(1)	O3	−228(5)	1072(3)	343(1)
C16	170(4)	1008(3)	482(1)	N	−060(4)	1196(2)	452(1)
C17	−028(5)	1000(2)	499(1)	Cl	045(1)	723(7)	926(3)

The structure was determined by the direct method using the SHELXS-86 program [5] and was refined in the full-matrix isotropic-anisotropic approximation using the SHELXS-76 program [6] (MS DOS version). The H atoms in the structure of (I) were located geometrically and their positions were refined isotropically. The final value of the divergence factor R was 0.118 (R_w = 0.098). The coordinates of the nonhydrogen atoms are given in Table 1.

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