

X-RAY STRUCTURAL INVESTIGATION OF THE STEROID ALKALOIDS EDPETILIDININE AND SEVCORIDININE

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The spatial structures of the alkaloids edpetilidinine and sevcoridinine have been determined by x-ray structural analysis and this has permitted a corrected variant to be put forward for the structures of the edpetilinine and sevcorine.

On the basis of the results of IR, PMR, and mass spectroscopy, the same chemical formula and the partial relative configuration (I) were previously proposed for the steroid alkaloid edpetilidinine, which was first isolated from *Petilium eduardii* (Regel) Vved. [1, 2], and sevcoridinine, which was first obtained by the hydrolysis of sevcorine [3] and was later isolated from the epigeal part of *Korolkowia sewerzowii* Regel [4]. It was assumed that edpetilidinine and sevcoridinine were diastereomers at one of the C20 and C22 asymmetric centers [3].

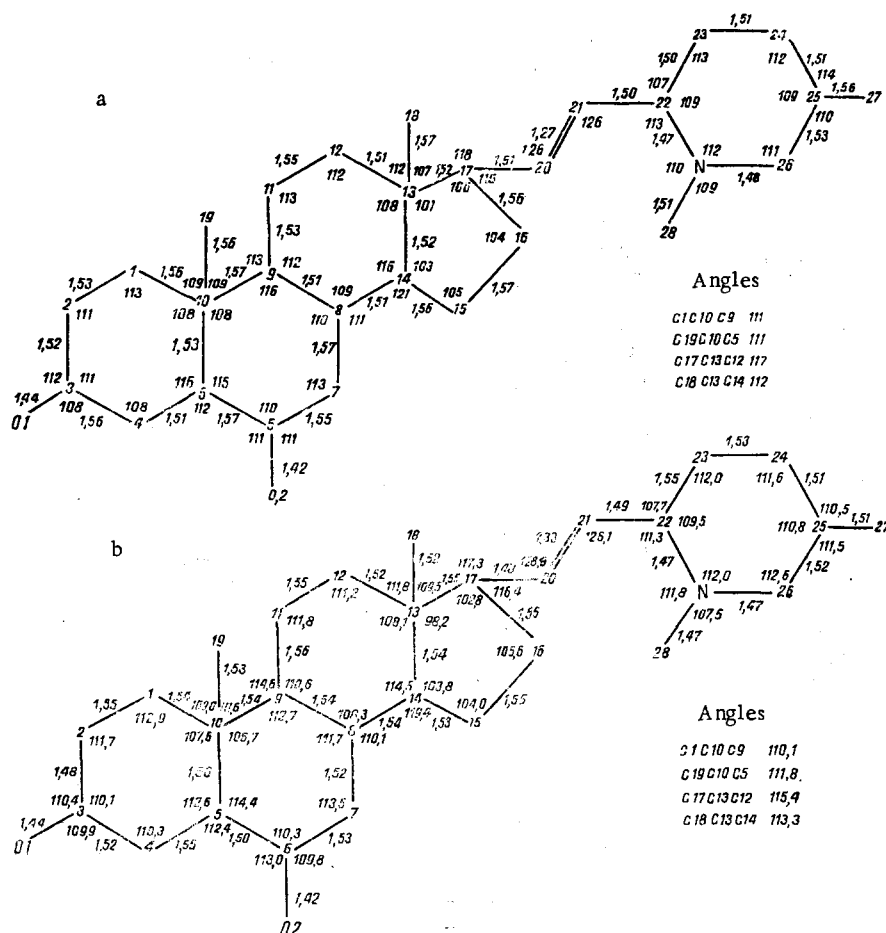
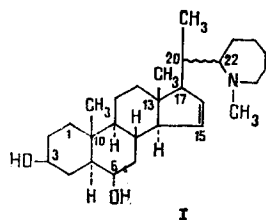


Fig. 1. Geometric parameters of the (Ia) and (Ib) molecules.

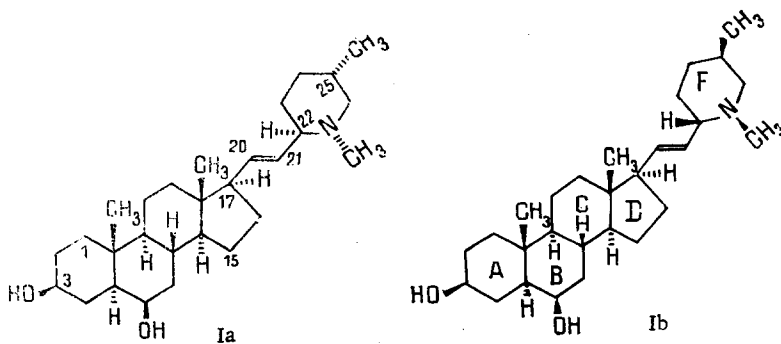
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TABLE 1. Coordinates of the Atoms ($\times 10^4$) of the Edpetilidinine and Sevcoridinine Molecules

Atom	Edpetilidinine			Sevcoridinine		
	x/a	y/b	z/c	x/a	y/b	z/c
O1	-4199 (7)	-1544 (29)	11561 (5)	6950 (9)	-2616 (2)	6547 (3)
O2	-3781 (8)	-5344 (28)	8559 (7)	9491 (8)	-1515 (2)	3863 (3)
N	3594 (7)	690 (20)	7075 (6)	5718 (7)	2868 (2)	2910 (3)
C1	-1897 (10)	-1100 (35)	10357 (7)	5702 (12)	-1089 (2)	6025 (4)
C2	-2464 (9)	-2578 (36)	11098 (7)	5414 (12)	-1725 (3)	6247 (4)
C3	-3566 (11)	-1091 (31)	10871 (8)	7264 (11)	-2025 (2)	6343 (3)
C4	-3955 (10)	-2527 (33)	10109 (8)	8426 (10)	-1979 (2)	5547 (4)
C5	-3291 (10)	-2026 (28)	9393 (7)	8781 (9)	-1345 (2)	5327 (4)
C6	-3751 (10)	-2989 (37)	8545 (9)	10167 (9)	-1275 (3)	4620 (5)
C7	-3137 (10)	-2142 (33)	7839 (8)	10637 (9)	-0643 (2)	4491 (4)
C8	-1970 (9)	-2540 (29)	7943 (7)	8871 (8)	-0267 (2)	4417 (3)
C9	-1596 (9)	-1585 (28)	8778 (7)	7456 (8)	-0370 (2)	5139 (3)
C10	-2157 (9)	-2418 (28)	9556 (8)	6886 (8)	-1002 (2)	5228 (3)
C11	-0444 (10)	-1722 (33)	8892 (8)	5732 (10)	53 (2)	5085 (4)
C12	108 (9)	-0674 (34)	8157 (8)	6407 (11)	681 (2)	5071 (4)
C13	-0255 (9)	-1636 (29)	7323 (7)	7772 (9)	789 (2)	4352 (4)
C14	-1404 (10)	-1445 (29)	7255 (7)	9458 (8)	368 (2)	4427 (4)
C15	-1659 (11)	-2032 (4)	6323 (8)	10907 (10)	585 (3)	3791 (5)
C16	-0747 (10)	-1100 (48)	5838 (9)	10637 (10)	1240 (3)	3803 (5)
C17	31 (10)	-0372 (33)	6545 (8)	8935 (10)	1352 (2)	4404 (4)
C18	116 (14)	-4087 (37)	7218 (14)	6752 (9)	758 (2)	3517 (4)
C19	-1925 (11)	-4935 (29)	9701 (10)	5716 (9)	-1207 (2)	4482 (4)
C20	1124 (11)	-0415 (35)	6312 (8)	7877 (11)	1891 (2)	4282 (4)
C21	1805 (9)	936 (32)	6579 (7)	8013 (10)	2263 (2)	3664 (4)
C22	2891 (10)	920 (30)	6347 (8)	7043 (10)	2830 (2)	3621 (4)
C23	3092 (11)	3087 (35)	5919 (8)	8623 (11)	3292 (2)	3535 (4)
C24	4191 (11)	3322 (39)	5687 (8)	7776 (11)	3889 (2)	3431 (4)
C25	4910 (10)	2939 (31)	6429 (8)	6312 (10)	3907 (2)	2737 (3)
C26	4660 (10)	728 (30)	6840 (10)	4837 (11)	3437 (2)	2843 (4)
C27	6048 (11)	2965 (36)	6206 (9)	5375 (17)	4488 (3)	2696 (4)
C28	3397 (12)	-1458 (35)	7528 (10)	4160 (12)	2451 (3)	2974 (5)



With the aid of objectively establishing the difference in their spatial structures, we have performed an x-ray structural investigation, the results of this work also permit a reliable determination of the structures of the natural gluco derivatives of the alkaloids: edpetilidinine and sevcoridinine [3, 5, 6]. The desirability of this investigation was also justified by the absence from the world literature of information of steroid alkaloids with a questionable seven-membered heterocycle (hexamethylenemethylamine moiety). The x-ray structural analysis had enabled the structures of the alkaloids proposed previously to be refined in the form of (Ia) (edpetilidinine) and (Ib) (sevcoridinine) in which, in the first



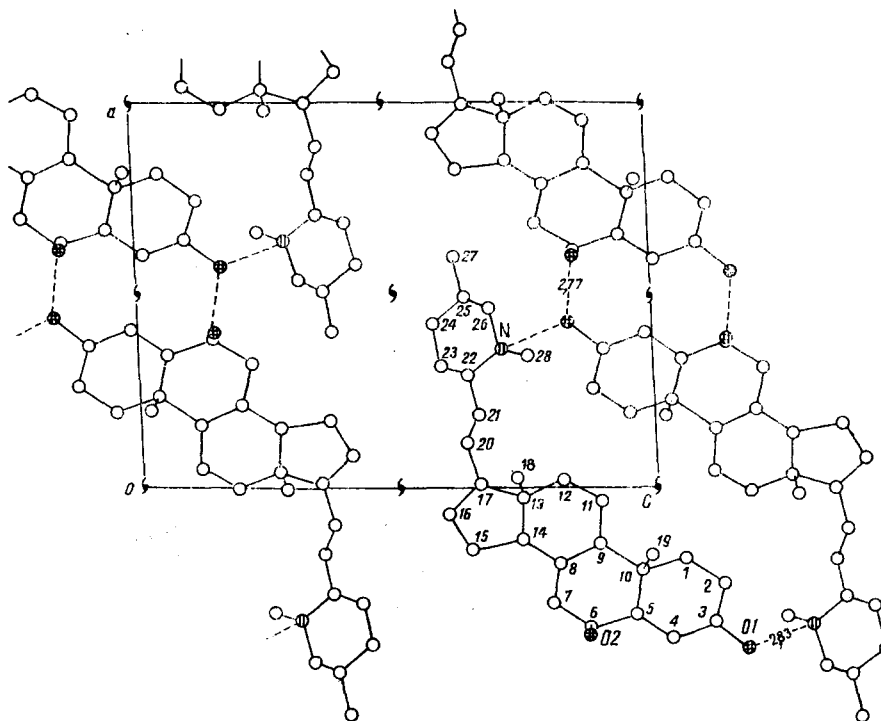


Fig. 2. Packing of the molecules of (Ia).

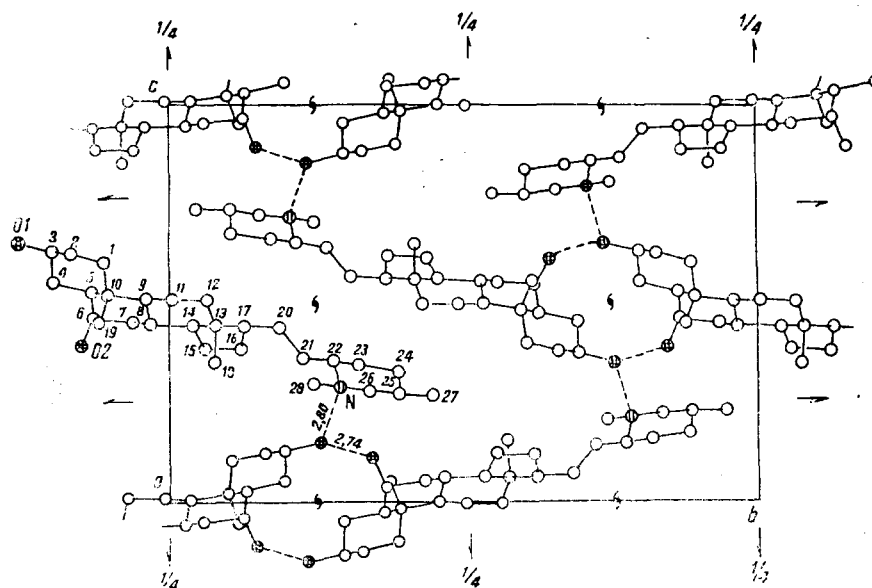


Fig. 3. Packing of the molecules of (Ib).

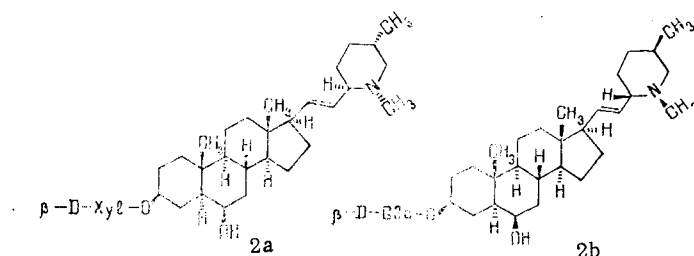
place, the double bond is not endocyclic but is present in the C20-C21 position and, in the second place, the hexamethylenemethylamine moiety contains a six-membered heterocycle and not a seven-membered one as was previously assumed.

As can be seen from their structural formulas, (Ia) and (Ib) are in fact diastereoisomers and differ by the configurations of the C22, C25, and N asymmetric centers. The configurations of the asymmetric centers in the steroid moieties of the (Ia) and (Ib) molecules found by the method of x-ray structural analysis confirm what was previously assumed [3]: the OH groups at C3 and C6 and the methyl groups at C10 and C13 are β -oriented, and the A/B, B/C, and C/D ring linkages are trans. In both alkaloids, the exo C17-C20 bond in ring D has the β -orientation. The six-membered rings A, B, and C and the heterocycle F each have the chair conformation, and the five-membered ring D the half-chair conformation.

The geometric parameters of the (Ia) and (Ib) molecules are given in Fig. 1. A comparison of the corresponding bond lengths and valence angles reveals no anomalous discrepancies and shows their good agreement with the corresponding standard values [7]. In both molecules, a tendency to an increase in the values of the angles of the C20 and C21 trigonal atoms (to 128.9°) is observed, which is apparently connected with the mutual repulsion of the heterocycle from the steroid part of the molecule. The error in the determination of the bond lengths in (Ia) was not worse than 0.02 Å, and in (Ib) 0.01 Å, the corresponding values for the valence angles being 1.3° (Ia) and 0.6° (Ib).

The packing of the molecules of (Ia) and (Ib) is shown in Figs. 2 and 3. Analysis of the crystal structures of (Ia) and (Ib) reveals the presence of hydrogen bonds of the O—H...O and O—H...N types. In the crystal structure of (Ia), O1—H...N hydrogen bonds (2.83 Å) are formed between molecules linked by a screw axis [0, y, 0] and also O2—H...O1 bonds (2.77 Å) between molecules connected by a 2_1 axis [0, y, 1/2]. Thus, the molecules are united by H-bonds into layers parallel to the xy0 plane. In the structure of (Ib), H bonds of the O1—H...N type (2.80 Å) form a infinite helix of molecules about a 2_1 axis [1/4 and 1/2, z]. These helices are linked by H-bonds of the O2—H...O type (2.74 Å) along a 2_1 screw axis [x, 1/4, 1/2].

It must be mentioned that the results of the present investigation permit the following structures to be suggested for glucoalkaloids of this series (edpetilinine (2a) and sevcorine (2b)):



EXPERIMENTAL

Crystals of the alkaloids (Ia) and (Ib) were obtained from solution in ethanol-acetone (20:1). The space groups and the parameters of the elementary cells were determined from precession photographs and were refined on a Syntex P1 diffractometer (All-Union Scientific-Research Institute of Antibiotics) using Mo K_α radiation:

Ia	Ib
$a=13.240(3) \text{ \AA}$	$a=6.977(2) \text{ \AA}$
$b=6.026(2)$	$b=23.456(5)$
$c=16.918(4)$	$c=16.094(3)$
$\beta=92.63(9)^\circ$	
$d=1.12 \text{ g/cm}^3$	$d=1.09 \text{ g/cm}^3$
Space group $P2_1, z=2$	$P2_12_1, z=4$

The complete set of experimental results was obtained on the diffractometer mentioned. The calculations made use of 1379 (Ia) and 1958 (Ib) reflections with $I \geq 2\sigma$. The structures were determined by the direct method by means of the Rentgen-75 program [8] in the automatic regime. For the more accurate localization of the atoms, several $\rho(xyz)$ syntheses were calculated. The structures were refined by the method of least squares in the full-matrix anisotropic approximation to R factors of 0.117 (Ia) and 0.074 (Ib). An electron-density difference synthesis did not permit all the H atoms to be determined [28 (Ia) and 38 (Ib) out of the 47 H atoms in each case were localized]. The coordinates of the basis atoms are given in Table 1.

SUMMARY

The spatial structures of the two steroid alkaloid edpetilidinine and sevcoridinine have been determined by the method of x-ray structural analysis. It has been established that they are diastereomers and differ by the configurations of the C22, C25, and N centers. Corrected variants have been proposed for the structure of the glucoalkaloids edpetilidinins and sevcordinine.

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14-METHYLISOTALATISIDINE - A NEW ALKALOID FROM *Delphinium confusum*

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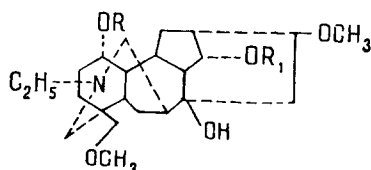
The known alkaloids isotalatisidine, nevadensine, delcosine, delsoline, and isobaldine have been isolated from the epigeal part of *Delphinium confusum* M. Pop., collected in the flowering period, and also a new alkaloid with the composition $C_{24}H_{39}NO_5$, mp 136-137°C (acetone), for which the structure of 14-methylisotalatisidine has been established on the basis of spectral characteristics and of passages from condelphine and isotalatisidine. This is the first time that the alkaloids nevadensine, delcosine, delsoline, isobaldine, and 14-methylisotalatisidine have been isolated from this plant.

From the epigeal part of *Delphinium confusum* M. Pop., collected in the flowering period in the upper reaches of the R. Talas, in addition to the condelphine, virescenine, 14-acetyl-virescenine, and 14-acetylkarakoline isolated previously [1], we have isolated isotalatisidine [2], nevadensine [3], delcosine [4], delsoline [5], and isobaldine [6], and a new base (V) with the composition $C_{24}H_{39}NO_5$, M^+ 421, mp 136-137° (acetone).

Its IR spectrum contained absorption bands of hydroxy groups at 3210 and 3560 cm^{-1} and of ester bonds at 1120 cm^{-1} . According to its PMR spectrum, the alkaloid contained an N-ethyl group (three-proton triplet with $J = 7$ Hz at 1.06 ppm) and three methoxy groups (singlets at 3.28, 3.30, and 3.36 ppm, 3 H each). Its mass spectrum contained, in addition to the peak of the molecular ion, the peaks of ions with m/z $M^+ - 15$ (30%), $M^+ - 17$ (100%), $M^+ - 56$ (2.5%), and $M^+ - 87$ (15%).

The mass spectrum of the alkaloid was characteristic for C_{19} diterpene alkaloids and had as its maximum peak that of the $M^+ - 17$ ion, which showed the presence of an α -hydroxy group at C-1 [7]. This was confirmed by the presence in the mass spectrum of a peak due to the $M^+ - 56$ ion [8]. The medium intensity of the peak of the $M^+ - 87$ ion was due to the presence of a methoxymethyl group at C-4 [8].

In the mass spectrum of the alkaloid, the peak of the $M^+ - 15$ ion amounted to 30% of the maximum peak, which is characteristic for α -1,8-dihydroxy C_{19} diterpene alkaloids [8]. A two-proton signal at 3.68 ppm was probably due to H-14 α and H-1 β atoms, geminal to methoxy



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|------|-------|---------------------------------|
| I. | R=H; | R ₁ =Ac |
| II. | R=Ac; | R ₁ =Ac |
| III. | R=Ac; | R ₁ =H |
| IV. | R=Ac; | R ₁ =CH ₃ |
| V. | R=H; | R ₁ =CH ₃ |
| VI. | R=H; | R ₁ =H |

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