12. O. P. Belichenko and O. N. Tolkachev, Khim. Prir. Soedin., 125 (1976).
13. O. P. Belichenko, O. N. Tolkachev, and D. A. Fesenko, Khim. Prir. Soedin., 662 (1977).

X-RAY STRUCTURAL INVESTIGATION OF ALKALOIDS

VI. CRYSTAL STRUCTURE OF THE ALKALOID PARFUMINE

S. M. Nasirov, L. G. Kuz'mina,
Yu. T. Struchkov, I. A. Israilov,
M. S. Yunusov, and S. Yu. Yunusov

UDC 547.944/945 + 536.26

A complete x-ray structural investigation of the alkaloid parfumine has been performed. The lengths of the bonds and the valence angles have the usual values. Benzene rings A and D are planar, B a distorted half-chair $^{C(6)}H_N$, and rings C and E are flattened envelopes, $E_{C(14)}$ and $^{C(19)}E$, respectively.

We have previously determined the crystal structure of the alkaloid sibiricine, which crystallizes in a centrosymmetrical space group [1]. In the present paper we consider the determination of the crystal structure of the related alkaloid parfumine, isolated from Fumaria parviflora in order to confirm the structure proposed previously [2] and to determine the configuration of the spiro center. Parfumine differs from sibiricine by the absence of a hydroxy group in the five-membered ring, and also by the presence of hydroxy and methoxy groups in place of the methylenedioxy group at C(2) and C(3).

The structure of the parfumine molecule is shown in Fig. 1, which also shows the solvate ethanol molecule. The form of the thermal ellipsoids of the carbon atoms of ethanol clearly shows the unorderedness of the ethyl group of this molecule in the crystal. The lengths of the bonds and the valence angles are given in Table 1.

Figure 2 gives a sketch of the parfumine molecule with the torsion angles in the ring. The benzene ring A is somewhat deformed. Thus, the deviations of the atoms of the ring from its mean plane amount to 0.03 Å, and the departure from this plane of the closest atoms of the substituents is −0.07 Å (for C(5), see Table 2, which gives the characteristics of the planes of the fragments of the molecule). The other benzene ring, D, is planar to within 0.01 Å, including the closest atoms of the substituents. The dihedral angle between the planes of benzene rings A and D is 99.6°, i.e., somewhat greater than in the molecules of sibiricine (89.9°) and of other related alkaloids – ochrobirine [3] and ochotensine [4] (about 90°). The six-membered pyridine ring B has a distorted half-chair conformation $^{C(6)}H_N$ in Schwarz's symbols [5], but the nature of the distortion differs from that found in the sibiricine molecule. The five-membered ring C has a flattened envelope conformation $E_{C(14)}$ (the C(14) atom departs from the plane of the C(8) C(17) C(18) C(13) atoms by −0.093 Å), while in the sibiricine molecule this ring has a half-chair conformation.

The difference in the conformations of rings B and C in the parfumine and sibiricine molecules indicates a conformational flexibility of these rings, leading to the realization of different methods of reducing strain in these polycyclic condensed systems.

The other five-membered (dioxolane) ring E also has a flattened envelope conformation $^{C(19)}E$ (as in sibiricine): the C(19) atom departs from the plane of the other atoms of the ring by 0.125 Å.

The nitrogen atom has a pyramidal conformation (sum of the valence angles 334°; the departure of N from the C(6) C(14) C(21) plane amounts to −0.441 Å). All the C–N bond lengths [from 1.45(1) to 1.47(1) Å] are the same and coincide with the standard value for an ordinary C–N bond of 1.472 [6]. The C–C interatomic distances in aromatic rings A and D have a scatter of 1.33(1) to 1.44(1) Å, which exceeds 3σ and is apparently the consequence of the general strain of the skeleton of the molecule or, rather, of the failure to take libration errors into account. All the interatomic distances coincide, within the limits of accuracy, with those found for the sibiricine molecule and are the usual ones for the corresponding types of bonds.

Institute of the Chemistry of Plant Substances, Academy of Sciences of the Uzbek SSR, Tashkent. Institute of Heteroorganic Compounds, Academy of Sciences of the USSR, Moscow. Translated from Khimiya Prirodnykh Soedinenii, No. 1, pp. 66-73, January-February, 1980. Original article submitted October 24, 1979.

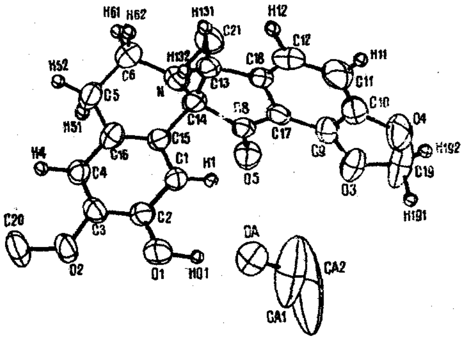

Fig. 1

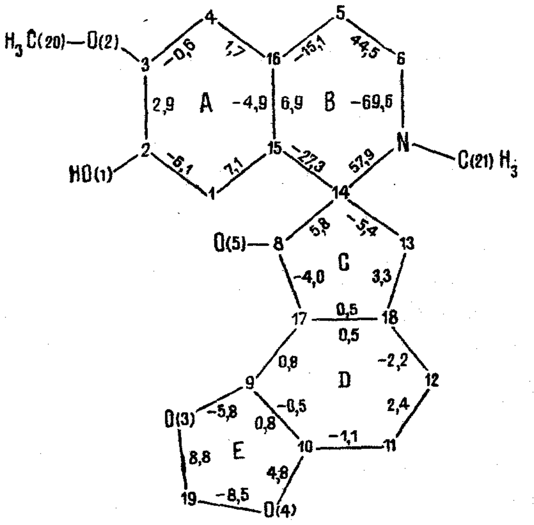

Fig. 2

Fig. 1. Contents of the independent part of the elementary cell with parfumine and ethanol molecules (ellipsoids of the thermal vibrations with p = 0.5).

Fig. 2. Torsion angles in the rings.

The parfumine and ethanol molecules each have one "active" hydrogen atom which, in the crystal, participates in the form of hydrogen bonds. The hydroxy group of parfumine plays the role of donor in a O(1)−H···O(A hydrogen bond with the hydroxy group of ethanol, the O(1)···O(A) distance being 2.65(1) Å, the O(1)−H(01) distance 1.06 Å, and the H(01)···O(A) distance 1.62 Å, and the angle at the H(01) hydrogen atom is 164°, i.e., this bond of medium strength is close to linear. The hydrogen atom of the hydroxy group of ethanol participates in a H bond with the nitrogen atom of the parfumine molecule obtained from a basis translation *a*. The O(A)···N distance is 2.84(1) Å, this hydrogen bond also, apparently, being close to linear (the hydrogen atom at O(A) could not be objectively localized), since the angles between the O(A)···N vector and the nitrogen-atom bonds N−C(14), N−C(6), and N−C(21) are 123.7(5), 102.9(5), and 94.5(5)°, respectively, i.e., they do not greatly differ from one another and from the tetrahedral angle. Thus, the hydrogen bonds with the participation of the ethanol molecule join the parfumine (II) molecules into endless chains along the *a* axis: $\ldots\underset{\substack{|\\ \text{Et}}}{\text{O}}(\text{A})\text{—H}\ldots\text{N}(11)\ \text{O}(1)\text{—H}\ldots$

EXPERIMENTAL

The parfumine crystals obtained from solutions in ethanol and subjected to x-ray structural investigation proved to be the monoethanol solvate $C_{20}H_{19}NO_5 \cdot C_2H_5OH$. The crystals were monoclinic; at 20°C, a = 7.936(1), b = 17.861(4), c = 7.7623(8) Å, β = 110.262(9)°, V = 1032.3(3) Å^3, d_{calc} = 1.14 g/cm^3 for Z = 2, space group $P2_1$.

The parameters of the elementary cell and the intensities of 1834 reflections with $I > 2\sigma$ were measured in a Hilger-Watts four-circle automatic diffractometer (λ CuK_α, graphite monochromator, $\theta/2\theta$ scanning, $2° \leq 2\theta \leq 120°$). The structure was interpreted by the direct method using the "MULTAN" program. An E-synthesis was constructed from the best variant of the signs which enabled almost the whole of the skeleton of the molecule to be determined. In the following two F-synthesis all the atoms of the parfumine molecule were localized and the solvate molecule of ethanol was detected.

The structure was refined by the method of least squares in the full-matrix − first isotropic and then anisotropic − approximations. After this, the positions of the hydrogen atoms were calculated geometrically, except for the atoms of the methyl and hydroxy groups of the ethanol. Further refinement was carried out by taking into account the H atoms with fixed temperature (B_{iso} = 6 Å^2) and position parameters. As a result of the refinement, the values of the parameters B_{ij} of the anisotropic temperature factor of the carbon atoms of the ethanol molecule proved to be very high (Table 3). This indicated the lack of orderedness of the ethanol molecules in the crystal. Consequently, guided by the shape of the thermal ellipsoids of the C(A1) and C(A2) atoms (Fig. 1) and the known geometric parameters of the EtOH molecule, we calculated two possible orientations [C(A1), C(A2), and C(A1'), C(A2')] of the ethyl groups. Then we carried out a refinement of the multi-

TABLE 1. Bond Lengths d (Å) and Valence Angles ω (degrees)

Bond	d	Bond	d	Bond	d	Bond	d
O (1) — C (2)	1,38 (1)	O (A) — C (A1)	1,38 (3)	C (15) — C (1)	1,44 (1)	C (9) — C (10)	1,37 (1)
O (2) — C (3)	1,39 (1)	N — C (14)	1,45 (1)	C (16) — C (5)	1,53 (1)	C (10) — C (11)	1,39 (2)
O (2) — C (20)	1,46 (2)	N — C (6)	1,47 (1)	C (5) — C (6)	1,55 (1)	C (11) — C (12)	1,41 (2)
O (3) — C (9)	1,35 (1)	N — C (21)	1,47 (1)	C (14) — C (15)	1,53 (1)	C (12) — C (18)	1,34 (1)
O (3) — C (19)	1,43 (2)	C (1) — C (2)	1,40 (1)	C (8) — C (14)	1,55 (1)	C (17) — C (9)	1,41 (1)
O (4) — C (10)	1,37 (1)	C (2) — C (3)	1,36 (1)	C (14) — C (13)	1,53 (1)	C (A1) — C (A2)	1,52 (9)
O (4) — C (19)	1,39 (2)	C (3) — C (4)	1,39 (1)	C (13) — C (18)	1,55 (1)	C (A1′) — C (A2′)	1,33 (7)
O (5) — C (8)	1,24 (1)	C (4) — C (16)	1,40 (1)	C (18) — C (17)	1,44 (1)		
O (A) — C (A1)	1,45 (4)	C (16) — C (15)	1,33 (1)	C (17) — C (8)	1,41 (1)		
Angle	ω	Angle	ω	Angle	ω	Angle	ω
C (3) O (2) C (20)	115,4 (8)	C (2) C (3) C (4)	120,1 (9)	C (9) C (10) C (11)	124 (1)	C (14) C (15) C (16)	122,5 (8)
C (9) O (3) C (19)	103,7 (9)	C (3) C (4) C (16)	119,9 (9)	C(10)C(11) C (12)	116 (1)	C (4) C (6) C (5)	116,2 (8)
C (10) O (4) C (19)	106 (1)	C (6) C (5) C (16)	109,5 (8)	C (11) C (12) C (18)	121,4 (9)	C (4) C (18) C (15)	121,1 (8)
C (6) NC (14)	110,3 (6)	NC (6) C (5)	109,9 (7)	C (14) C (13) C (18)	107,5 (7)	C (5) C (16) C (15)	122,5 (8)
C (6) NC (21)	115,0 (6)	O (5) C (8) C (14)	121,9 (7)	NC (14) C (8)	108,7 (7)	C (8) C (17) C (9)	132,2 (8)
C (14) NC (21)	108,7 (6)	O (5) C (8) C (17)	128,9 (8)	NC (14) C (13)	116,4 (7)	C (8) C (17) C (18)	112,7 (7)
C(2)C(1)C (15)	118,9 (8)	C (14) C (8) C (17)	109,2 (7)	NC (14) C (15)	108,5 (7)	C (9)C (17) C (18)	115,1 (7)
O (1) C (2) C (1)	12[illegible],2 (8)	O (3) C (9) C (10)	111,8 (8)	C (8) C (14) C (13)	103,8 (7)	C (12) C (18) C (13)	130,0 (8)
O (1) C (2) C (3)	119,2 (8)	O (3) C (9) C (17)	127,9(8)	C (8) C (14) C (15)	108,0 (7)	C (12) C (18) C (17)	123,1 (8)
C (1) C (2) C (3)	120,4 (8)	C (10) C (9) C (17)	120,3 (8)	C (13) C (14) C (15)	111,0 (7)	C (13) C (18) C (17)	106,7 (7)
O (2) C (3) C (2)	114,8 (8)	O (4) C (10) C (9)	108,1 (9)	C (1) C (5) C (14)	118,1 (7)	O (3) C (19) O (4)	110 (1)
O (2) C (3) C (4)	125,1 (8)	O (4) C (10) C (11)	128 (1)	C (1) C (15) C (16)	119,2 (8)	O (A) C (A1) C (A2)	108 (4)
						O (A) C (A1′) C (A2′)	115 (3)

TABLE 2. Equations Ax + By + Cz − D = 0 of the Planes of the Individual Fragments of the Molecule and the Departures of the Atoms from Their Planes

Plane	Atoms and their departures from the plane			*A*	*B*	*C*	*D*
A	C (1) 0,033 (8) C (4) 0,007 (9) O (1)* 0,023 (7) C (5)* —0,071 (10)	O (2) −0,019 (9) C (6) 0,009 (9) O (2)* —0.026 (8)	C (3) −0.002 (9) C (15) —0,029 (8) C (14)* —0,001 (9)	0,398	0,630	0,667	—7,280
B	C (14) 0,013 (8) C (5) —0,013 (10)	C (15) —0,029 (8) C (6)* 0,255 (10)	C (16) 0,029 (9) N* —0,520 (5)	0,375	0,637	—0,674	—7,375
C	C (8) 0,002 (8) C (13) —0,001 (9) C (12)* 0,023 (10)	C (17) −0,003 (8) C (14)* —0,093 (9)	C (18) 0,002 (8) C (9)* 0,004 (9)	−0,740	−0,378	—0,556	6,423
D	C (9) 0,007 (9) C (12) 0,013 (10) O (3)* −0,017 (7) C (13)* -0,014 (9)	C (10) 0.000 (10) C (8) —0,006 (8) O (4)* —0,012 (9)	C (11) -0,001 (12) C (17) —0,004 (8) C (8)* 0,000 (8)	−0,740	—0,383	—0,553	6,486
E	0 (3) —0,003 (7) 0 (4) 0,003 (9) C (11)* —0,031 (12)	C (9) 0,004 (9) C (19)* 0,125 (18)	C (10) −0,004 (10) C (17)* —0.250 (8)	—0,736	—0,396	—0,549	6,709

plicities of these atoms, which proved to be approximately equal (0.44 and 0.56 for the two orientations of the Et group), and after this of their position and isotropic temperature parameters. In the subsequent difference synthesis only the peak corresponding to the hydrogen atom of the hydroxy group of parfumine appeared. After this a correction was made for the anomalous scattering of the x rays by the O and N atoms and a final isotropic refinement was carried out (the C atoms of the ethanol were refined isotropically and the H atoms with fixed parameters), both of the structure found and of the inverted structure, to $R_1 = 0.0788$ ($R_2 = 0.128$) and $R_1 = 0.0788$ ($R_2 = 0\ .0128$), respectively. The coincidence of the R factors did not enable us to determine the absolute configuration of the molecule which (as also the fairly high R factor and the errors of the bond length) is due to the unorderedness of the ethanol molecule. All the calculations were performed on an Eclipse S/200 mini-computer by means of the Syntex-EXTL program. The coordinates of the atoms and the B_{ij} parameters of the anisotropic temperature factor are given in Table 3.

SUMMARY

The complete x-ray structural investigation of the alkaloid parfumine in the form of the solvate with ethanol has been performed. The structure put forward previously has been confirmed. Bond lengths and valence angles have the usual values.

TABLE 3. Coordinates of the Atoms (× 10^4) and the Parameters B_{ij} (× 10) of the Anisotropic Temperature Factor in the Form $T = \exp[-1/4(B_{11}a^{*2}h^2 + B_{22}b^{*2}k^2 + \ldots + 2B_{23}b^*c^*kl)]$

Atom	x	y	z	B_{11}	B_{22}	B_{33}	B_{12}	B_{13}	B_{23}
N	−2919 (9)	−7561 (0)	−2679 (8)	39 (3)	36 (3)	31 (3)	−2 (2)	12 (2)	−2 (2)
O (1)	4964 (7)	−6978 (5)	1652 (8)	29 (2)	54 (3)	49 (3)	1 (2)	3 (2)	−7 (2)
O (2)	3738 (8)	−5892 (5)	3142 (9)	37 (3)	52 (3)	60 (3)	−3 (2)	1 (2)	−30 (3)
O (3)	1542 (9)	−9888 (5)	−3011 (9)	54 (3)	33 (2)	68 (3)	4 (2)	25 (3)	2 (2)
O (4)	2511 (10)	−[illegible] (6)	−5471 (11)	66 (4)	67 (4)	70 (4)	14 (3)	33 (3)	−21 (3)
O (5)	−607 (8)	−8803 (5)	−1155 (8)	56 (3)	39 (2)	37 (2)	2 (2)	24 (2)	9 (2)
O (A)†	−6089 (9)	−3150 (15)	−255 (11)	50 (3)	54 (3)	76 (4)	−9 (3)	24 (3)	3 (3)
C (1)	2006 (10)	−7161 (5)	−478 (10)	27 (3)	33 (3)	34 (3)	4 (2)	3 (2)	−2 (2)
C (2)	3155 (10)	−6845 (6)	999 (10)	30 (3)	35 (3)	34 (3)	1 (2)	7 (2)	1 (2)
C (3)	2473 (11)	−6270 (6)	1708 (11)	39 (3)	34 (3)	35 (3)	−4 (3)	10 (3)	−5 (3)
C (4)	651 (11)	−6110 (6)	1027 (12)	38 (4)	31 (3)	50 (4)	1 (3)	7 (3)	−7 (3)
C (5)	−2507 (12)	−6355 (6)	−991 (14)	35 (4)	30 (3)	66 (5)	6 (3)	7 (4)	−8 (3)
C (6)	−3550 (11)	−6781 (6)	−2787 (12)	35 (3)	41 (4)	46 (4)	7 (3)	13 (3)	−4 (3)
C (8)	−425 (10)	−8410 (5)	−2392 (10)	34 (3)	29 (3)	32 (3)	0 (2)	−1 (2)	−2 (2)
C (9)	1135 (11)	−9262 (5)	−4060 (11)	36 (3)	30 (3)	42 (3)	−6 (3)	−14 (3)	4 (3)
C (10)	1712 (12)	−9309 (6)	−5528 (14)	30 (3)	53 (4)	56 (4)	0 (3)	10 (3)	−14 (4)
C (11)	1512 (15)	−8742 (8)	−6807 (13)	60 (5)	82 (6)	35 (4)	12 (5)	22 (4)	−6 (4)
C (12)	626 (12)	−8093 (7)	−6544 (11)	38 (4)	61 (5)	35 (3)	−2 (3)	0 (3)	7 (3)
C (13)	−876 (11)	−7367 (5)	−4515 (10)	45 (4)	30 (3)	31 (3)	1 (3)	3 ([illegible])	5 (2)
C (14)	−1103 (11)	−7588 (5)	−2698 (11)	39 (4)	25 (3)	37 (3)	1 (3)	−1 (3)	2 (3)
C (15)	110 (9)	−7116 (5)	−1111 (9)	28 (3)	30 (3)	29 (3)	5 (2)	7 (2)	3 (2)
C (16)	−505 (10)	−6540 (5)	−411 (12)	33 (3)	33 (3)	47 (4)	4 (3)	17 (3)	3 (3)
C (17)	288 (10)	−8607 (5)	−3760 (9)	32 (3)	32 (3)	27 (3)	−3 (2)	3 (2)	0 (2)
C (18)	77 (10)	−8024 (5)	−5099 (9)	27 (3)	44 (3)	24 (3)	1 (2)	4 (2)	1 (2)
C (19)	2269 (20)	−1038 (7)	−4022 (28)	84 (8)	38 (4)	152 (13)	6 (5)	74 (9)	−9 (6)
C (20)	3010 (15)	−5359 (8)	4125 (17)	55 (5)	71 (6)	65 (6)	0 (4)	19 (4)	−40 (5)
C (21)	−4242 (13)	−8003 (6)	−4087 (12)	44 (4)	50 (4)	41 (4)	−8 (3)	8 (3)	−1 (3)
C (A1)	−0,5767 (36)	−0,3912 (17)	−0,0015 (39)	[7,1(5)]‡ 160 (18)	61 (8)	322 (34)	−11 (10)	163 (22)	−48 (15)
C (A1′)	−0,6405 (47)	−0,3850 (22)	−0,1277 (53)	[7,5(7)]‡					
C (A2)	−0,6212 (89)	−0,4305 (38)	−0,1560 (79)	[14,7(1,5)]‡ 589 (72)	148 (24)	391 (47)	−62 (36)	396 (56)	−124 (26)
C (A2′)	−0,4947 (98)	−0,4395 (48)	−0,0224 (99)	[18,1(2,4)]‡					
H (01)	5316	2500	1234						
H (1)	2553	−7670	−1143						
H (4)	125	−5649	1610						
H (51)	−2996	−6538	94						
H (52)	−2707	−5758	−1161						
H (61)	−4962	−6745	−2997						
H (62)	−3303	−6484	−3905						
H (11)	1941	−8817	−7990						
H (12)	427	−7612	−7505						
H (131)	−2187	−7265	−5546						
H (132)	−99	−6853	−4336						
H (191)	3628	−10563	−3103						
H (192)	1461	−10853	−4476						

---

†O(A), C(A1), C(A1′), C(A2), and C(A2′) are the atoms of the solvate molecule of ethanol.

‡B_{iso}, Å^2.

LITERATURE CITED

1. S. M. Nasirov, I. A. Israilov, L. G. Kuz'mina, M. S. Yunusov, Yu. T. Struchkov, and S. Yu. Yunusov, Khim. Prir. Soedin., 752 (1978).
2. I. A. Israilov, M. S. Yunusov, and S. Yu. Yunusov, Dokl. Akad. Nauk SSSR, 189, 1262 (1969).
3. M. Mathew and G. J. Palenik, Acta Crystallogr., B31, 2899 (1975).
4. A. C. Macdonald and J. Trotter, J. Chem. Soc., B, 929 (1966).
5. J. C. P. Schwartz, Chem. Commun., 505 (1973).
6. L. E. Sutton, Tables of Interatomic Distances and Configuration in Molecules and Ions, The Chemical Society, London, Special Publication No. 18 (1965).

A STUDY OF THE VENOM OF RENARD'S VIPER

Vipera ursini renardi

II. CHEMICAL AND BIOLOGICAL CHARACTERIZATION OF THE FRACTIONS

G. E. Lyubimtseva and L. Ya. Yukel'son

UDC 591.145:598.126

Of the five fractions obtained as the result of the fractionation of the venom of Renard's viper on Sephadex G-75, the first two possessed a high proteolytic and coagulating activity and had a hemorrhagic and lethal action, and the third fraction has been identified as phospholipase A_2.

The separation of the venom of Renard's viper *Vipera ursini renardi* Ch. into its individual components and the comparative investigation of their chemical and biological properties is the most rational approach to the solution of problems connected with the elucidation of the mechanism of the action of the venom and its use in scientific and medical practice. Information has been published previously [1] on the chemical composition and biological action of the whole viper venom. The present paper gives the results of fractionation of the viper venom on Sephadex and of a study of the chemical properties and biological effects of the fractions obtained in comparison with those of the whole venom.

When the whole viper venom was passed through Sephadex G-75 gel, it was separated into five fractions (Fig. 1). Proteolytic activity was detected mainly in fractions I and II, which left the dextran gel column in a volume of eluent of 150 ml. In view of the fact that fractions I and II begin to emerge immediately after the passage of the free volume of the column (130 ml), in accordance with the theory of gel filtration [2] it may be assumed that the proteolytic activity of the venom is connected with components having molecular weights of 15,000-25,000 dalton. Phospholipase A_2 was separated from the proteolytic enzymes and appeared in fraction III, containing substances with molecular weights of 15,000 and below. These three fractions compose the bulk of the whole viper venom and are characterized by a predominantly protein composition:

	Fraction				
	I	*II*	*III*	*IV*	*V*
Yield, %	29,2	23,2	22.1	5,1	18.1
Protein according to Lowry 83	92,0	93.0	98.0	37,0	37,0

The yields of fractions IV and V were only 5.1 and 18.1%, respectively, and their content of protein substances was extremely low. It may be assumed these fractions contained low-molecular weight components (peptides of different sizes, free amino acids, catecholamines) similar to those obtained from the venom of the Bulgarian viper [3]. On the whole, the results of gel filtration show that the viper venom that we are investigating differs fundamentally in the ratio of high- and low-molecular-weight components from the venoms of the *Elapidae* [4, 5] and, according to the chemical classification of snake venoms [6], it can be assigned to the high-molecular-weight group.

Institute of Biochemistry, Academy of Sciences of the Uzbek SSR, Tashkent. Translated from Khimiya Prirodnykh Soedinenii, No. 1, pp. 73-76, January-February, 1980. Original article submitted September 21, 1979.