apparatus. This gave 560 g of combined alkaloids or 0.8% of the air-dry weight of the raw material.

The combined alkaloids (560 g) were dissolved in 3 liters of acetone, and the solution was left for 12 h. The precipitate of technical heliotrine that deposited was filtered off, washed with acetone, and dried (515 g). To obtain heliotrine satisfying the demands of the TU, the technical heliotrine was recrystallized from acetone. The yield was 470 g on 0.67% of the air-dry raw material.

SUMMARY

A method has been developed for obtaining heliotrine by aqueous ethanolic extraction with a yield of 75% of the amount in the raw material.

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X-RAY STRUCTURAL INVESTIGATION OF A DERIVATIVE OF THE ALKALOID KESSELRINGINE

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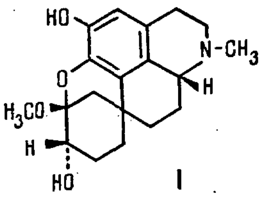
The molecular and crystal structures of 2,6-dimethyl-12-demethylkesselringine methosulfate have been determined by x-ray structural analysis. The relative configurations of the chiral centers in the R, S nomenclature have been established.

Structure (I) has been established for the homoproaporphine alkaloid kesselringine isolated from the Central Asian species of autumn crocus Colchicum kesselringii Regel [1] on the basis of IR, PMR, and mass spectroscopy and chemical transformations [2, 3].



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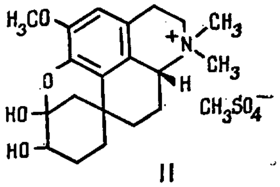

II

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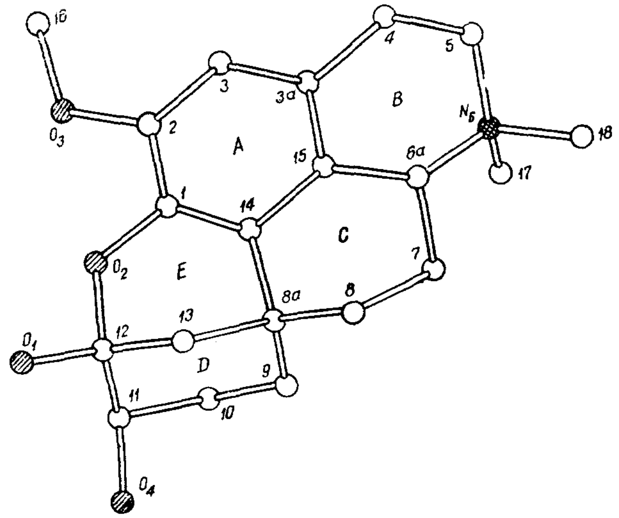

Fig. 1. Conformation of the cation in the structure of 2,6-dimethyl-12-demethylkesselringine methosulfate.

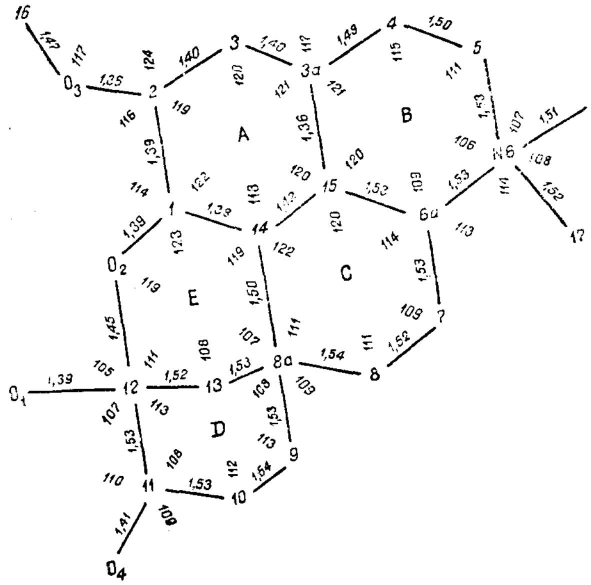

Fig. 2. Bond lengths and valence angles of the cation in the structure of 2,6-dimethyl-12-demethylkesselringine methosulfate.

TABLE 1. Main Planar Fragments of the Cation and Deviations of the Atoms (Δ, Å) from the Planes

Ring *A*		Ring *B*		Ring *C*		Ring *E*		Ring *D*	
Atom	Δ	Atom	Δ	Atom	Δ	Atom	Δ	Atom	Δ
C (1)	−0,01	C (3*a*)	0,06	C (6*a*)	0,02	C (1)	−0,002	C (8*a*)	−0,004
C (2)	0,02	C (4)	−0,01	C (15)	−0,05	O(2)	0,001	C (9)	0,004
C (3)	−0,01	C (5)	0,02	C (14)	0,05	C(12)*	0,08	C (10)*	−0 64
C (3*a*)	−0,01	N (6)*	−0,68	C (8*a*)	0,02	C(13)*	−0,78	C (11)	−0,004
C (15)	0 03	C (6*a*)	−0,03	C (8)*	0,43	C (8*a*)	−0,001	C (12)	0,004
C (14)	−0,02	C (15)	−0,05	C (7)*	−0,33	C (14)	0,002	C (13)*	0,74

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*Atoms not included in the calculation of the equations of the planes.

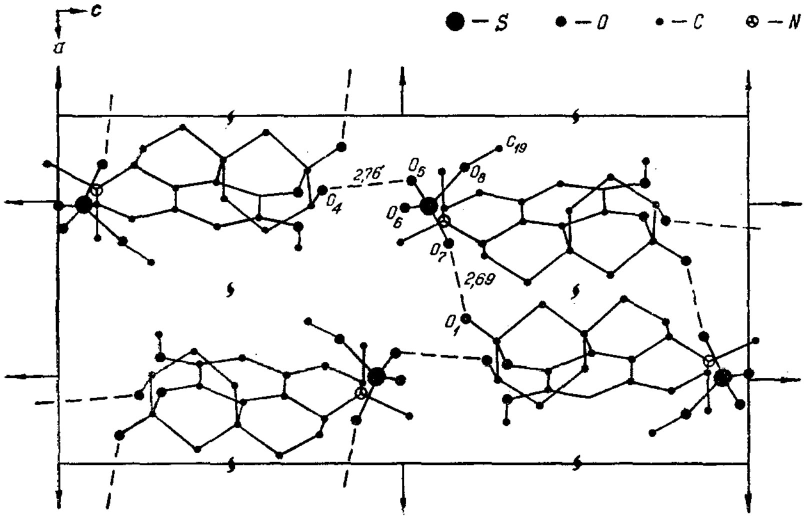

Fig. 3. Packing of the molecules in the crystal structure of 2,6-dimethyl-12-demethylkesselringine methosulfate.

TABLE 2. Coordinates of the Atoms

Atom	x	y	z	Atom	x	y	z
C (1)	0,2792	−0,0003	0,7930	C (13)	0,4627	0.1915	0.8084
C (2)	0,2178	−0,1206	0,7922	C (14)	0,3195	0,0578	0,7380
C (3)	0,1976	−0,1779	0,7308	C (15)	0,3053	0,0052	0,6773
C (3a)	0,2402	−0,1171	0,6750	C (16)	0,1353	0,2988	0,8499
C (4)	0,2102	- 0,1805	0,6114	C (17)	0,1513	0,0722	0,5586
C (5)	0,2834	−0,1278	0,5550	C (18)	0,3619	0 0586	0,4957
N (6)	0,2896	0,0165	0,5571	O (1)	0,4232	0,1645	0·9228
C (6a)	0,3753	0,0492	0.6163	O (2)	0,2928	0,0505	0,8550
C (7)	0,4134	0,1848	0,6210	O (3)	0,1901	−0,1713	0,8501
C (8)	0,4823	0,2119	0,6862	O (4)	0,3080	0,3875	0,8795
C (8a)	0,3837	0,1885	0,7430	S	0,2531	0,4748	0,5423
C (9)	0.2743	0,2878	0,7434	O (5)	0,1855	0,5798	0,5123
C (10)	0,1731	0,2755	0,8013	O (6)	0,2585	0,3637	0.5048
C (11)	0,2479	0,2708	0,8677	O (7)	0,3725	0,4961	0.5763
C (12)	0,3604	0,1689	0,8629	O (8)	0,1392	0,4167	0.5947
				C (19)	0,0897	0,5022	0.6398

In spite of advances in the determination of the structure and the synthesis of analogs [4], the configurations of the majority of the asymmetric centers in kesselringine have not been established sufficiently clearly. This relates particularly to the spirocyclohexane part of the molecule.

In the present paper we give the results of an x-ray structural analysis of a derivative of this alkaloid – 2,6-dimethyl-12-demethylkesselringine methosulfate (II), $C_{20}H_{28}O_4N^+ \cdot CH_3SO_4^-$, which permit an unambiguous conclusion on the relative configurations of all the asymmetric centers and also the deduction of some features of the structure of the initial base kesselringine.

It can be seen from the structural formula of kesselringine (I) that an oxygen bridge links the C(1) and C(2) atoms of rings A and D, respectively. The linkage of rings D and E takes place through C(8a) and C(12) diaxial bonds. The hydroxy group at C(12) is equatorial and that at C(11) is axial in ring D. These facts were confirmed by the results of the x-ray structural analysis (Fig. 1). Starting from the sign of the specific rotation, by analogy with other homoproaporphine and proaporphine compounds and the CD spectrum in [3] for kesselringine, the R configuration at the C(6a) center has been proposed. The results that we have obtained permit the relative configuration of compound (II) to be expressed as 6aR, 8aR, 11R, 12R, which differs from that given in [3].

As can be seen from Table 1, in the aromatic ring A (Fig. 1), which is planar, the deviations of the atoms from the mean-square plane do not exceed 0.03 Å. Ring B of the isoquinoline A/B fragment has the sofa configuration in which the N(6) atom departs from the plane of the other atoms by 0.68 Å. Ring C has the half-chair conformation: the C(7) and C(8) atoms depart from the plane of the other four atoms on opposite sides by 0.33 and 0.43 Å, respectively. The fourth ring of the base E also has a conformation close to the sofa type: the deviation of the C(13) atom from the plane of the C(2), C(1), C(14), C(8a) atoms amounts to 0.78 Å. The spirocyclohexane ring D has the ${}_{10}C^{13}$ chair conformation.

The mean length of a C—C bond in ring A is 1.39 Å, and that of the C—N$^+$ (sp^3) bond in ring B is 1.52 Å. The ordinary C_{sp^3}—C_{sp^3} bonds are likewise close, on average, to the standard value of 1.54 Å (Fig. 2). No anomalies are observed in the values of the valence angles which are close to the standard values, on the whole [5]. The mean square errors in the determination of the lengths of the valence bonds and angles do not exceed 0.01 Å and 0.6°, respectively.

The packing of the molecules of (II) in the crystal is shown in Fig. 3 in the form of a projection on the plane of the crystallographic axes *a* and c. The hydroxy groups at the C(11) and C(12) atoms form hydrogen bonds with the O(5) and O(7) oxygen atoms of the sulfate groups with lengths of 2.76 and 2.69 Å, respectively, and being linked by H bonds, the cations and anions form helices around screw axes parallel to the *a* axis.

EXPERIMENTAL

The parameters of the elementary cell of the crystals investigated were determined in a precession camera and were refined on a Syntex P2$_1$ automatic four-circle diffractometer: $a = 9.858(2)$ Å, $b = 10.726(3)$ Å, $c = 20.605(7)$ Å; sp. gr. $P2_12_12_1$; $z = 4$.

The integral intensities were measured on the same instrument by the θ/2θ-scanning method in CuK$_\alpha$ radiation using a graphite monochromator. After the polarization and Lorentz factors had been taken into account and weak reflections with $|f|^2 \leq 2\sigma$ had been eliminated, the working group amounted to 1663 reflections. The structure was deciphered by the direct method with the aid of the Rentgen-75 group of programs [6]. Preliminary refinement was performed by the programs of the same group. Further refinement of the structure was carried out with programs of the Kristall group [7], taking the anisotropy of the thermal vibrations of the atoms into account, to give R = 0.082. The final values of the coordinates of the atoms are given in Table 2.

SUMMARY

The molecular and crystal structures of 2,6-dimethyl-12-demethylkesselringine methosulfate have been determined by x-ray structural analysis.

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