MOLECULAR AND CRYSTAL STRUCTURE OF ISOSOPHORIDINE

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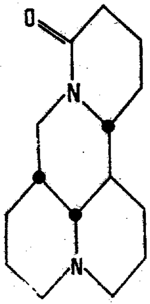
Isosophoridine, $C_{15}H_{24}N_2O$, was first obtained by F. Rulko [1] by isomerizing sophoridine with PtO_2 (Adams catalyst) in acetic acid at 70-80°C. Two possible configurational formulas were proposed for it [1].



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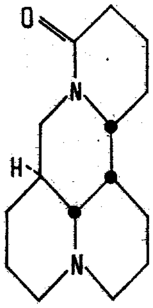

II

Chemical transformations of isosophoridine and isosophoridane that have been performed [2-4] permit the assumption that the most probable configuration for isosophoridine is that in which rings A/B and A/C are cis-linked and B/C and C/D are trans-linked (I). However, it is difficult to give a definitive answer to the question of the conformation and configuration of isosophoridine by chemical methods. The study of its three-dimensional structure by the x-ray method may introduce clarity into this problem.

Single crystals of isosophoridine obtained by crystallization from petroleum ether are unstable in the air. To determine the parameters of the elementary cell and the space group of this compound in a precession camera and for further recording on a syntex-$P2_1$ autodiffractometer we used a single crystal of isosophoridine sealed into a thin-walled glass capillary.

The crystallographic parameters of isosophoridine measured in the precession camera and refined in the difrractometer mentioned were as follows: $a = 9.696(1)$, $b = 10.844(2)$, $c = 12.837(2)$ Å, $v = 1350.28$ Å^3, $M = 248$, $\rho_{calc} = 1.22$ g/cm^3, $Z = 4$, space group $P2_12_12_1$. The intensities of 1392 reflections were measured by $\theta/2\theta$ scanning in CuK_α radiation (graphite monochromator) up to $2\theta \leq 120°$ in the syntex $P2_1$ diffractometer, and the 1141 reflections with $I \geq 2\sigma$ were used in the calculations.

We found a model of the structure by using the "Rentgen-75" system of programs [5] and it was refined by the method of least squares by means of the "Kristall" group of programs [6]. The usual geometric considerations were brought in for finding the hydrogen atoms. The final R factor was 0.065.

The geometry of the isosophoridine molecule established as the result of the x-ray study is shown in Fig. 1. The stereoisomers of matrine are subdivided according to linkage of rings A and B into representatives of the trans and cis series. We have previously studied the structures of representatives of the trans series — matrine [7], sophoridine [8], and allomatrine [9] — by the x-ray method. Isosophoridine is the first member of the cis series that has been investigated by x-ray structural analysis.

Rings A, B, and C have the chair form, and the form of D is close to that of a half-chair. The A/B and A/C ring linkages are cis and the B/C and C/D linkages are trans, which

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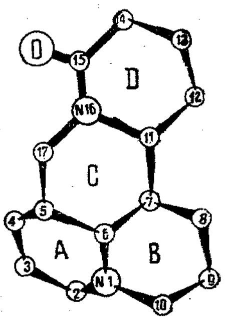

Fig. 1

confirms the first of the two possible configurational formulas [1]. The C(5)—C(17) and C(7)—C(11) bonds occupy the equatorial positions relative to rings A and B, respectively. Because of the peculiar condensation of the six-membered rings in this tetracyclic compound, the conformations of the rings differ from the ideal cyclohexane chair conformation. In the latter, the deviation of the "corner" atoms is ±0.73 Å [10]. The corresponding deviations for the C(2) and C(5) of ring A are smaller, at 0.64 and 0.65 Å, respectively.

In ring B, the departures of the C(7) and C(10) atoms from the plane of the other atoms of the ring are more asymmetric and amount to 0.70 and 0.62 Å, while for the C(6) and C(16) atoms the corresponding departures are 0.67 and 0.63 Å. Because the conjugation in the lactam fragment of the molecule, ring D is flattened and its form is close to that of a half-chair: the C(12) and C(13) atoms depart from the plane of the C(11), N(16), N(15), and C(14) atoms on opposite sides by 0.15 and 0.52 Å, respectively.

The latter plane is inclined relative to the plane of ring C by 46°. The planes of rints B and C are almost parallel, the angle between them being 4°, while rings A and C are more strongly inclined with respect to one another, the angle of inclination being 55°. The angle between the planes A and B in matrine [7] and allomatrine [9] is close to zero. The corresponding angle in isosophoridine is 51°. With such an inclination of the rings the atoms of rings A and B prove to be close, and considerable steric stresses arise which increase the equilibrium energy of the molecule as a whole. The shortened lengths of the nonbond contacts of the isosophoridine molecule, which are given below, confirm this (R_i and R_j are the van der Waals radii of atoms i and j, respectively; δ is the overlapping of the van der Waals spheres that is acceptable for a normal contact):

Contact	Length of the contact, Å	$2\sqrt{R_iR_j}$, Å	$2\sqrt{R_iR_j}-\delta$, Å
C (2) — C (7)	3,12	3,42	3,27
C (2) — C (9)	3.13	3,42	3.27
C (4) — C (7)	3,14	3.42	3,27
H_a (2) — H_a (9)	1,95	2,31	2,01
H_a (4) — H_a (7)	1,95	2,31	2,01
O — C (17)	2,70	2,97	2,82
C (8) — C (12)	3.15	3,42	3 27

The equilibrium values of the lengths of the nonbond contacts have been taken from a paper [11] in which contacts having a length less than $2\sqrt{R_iR_j} - \delta$ are considered to be shortened. The 1st to 5th shortened interatomic distances are determined by the specific conformational state of the molecule, and the lengths of the 6th and 7th contacts are found with some variations in all the stereoisomers of the matrine series. Because of the strain of the molecule, the valence angles of rings A and B are somewhat increased and values of up to 113-114° are found. The lengths of the bonds are normal (in comparison with the other stereoisomers studied) with the exception of a somewhat decreased C(12)-C(13) distance of 1.47 Å. The C(15)—O interatomic distance is 1.22 Å.

No special features of packing are observed in the crystal structure of isosophoridine; all the intermolecular contacts are normal from the point of view of intermolecular radii [11].

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STRUCTURE OF TETRAHYDRONEOSOPHORAMINE

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Tetrahydroneosophoramine is a new stereoisomer of matrine in which the linkages of rings A/B and B/C are cis and of A/C trans. It is obtained by the hydrogenation of neosophoramine over platinum oxide in ethanolic solution [1]. Stereoisomerism of the matrine alkaloids has been discussed by Japanese workers [2] and exactly the same configuration is given for darvasamine [3]. However, the physicochemical constants of tetrahydroneosophoramine and darvasamine differ sharply.

In view of this, to elucidate the stereochemistry of these alkaloids we have studied the three-dimensional structure of tetrahydroneosophoramine by x-ray structural analysis. Tetrahydroneosophoramine is the second, after isosophoridine [4], of the cis isomers of matrine that has been studied by this method.

The crystallographic parameters of tetrahydroneosophoramine measured in a precession camera and refined in a syntex-$P2_1$ diffractometer are as follows:

$a = 8{,}211\,(1)\,\text{Å}$ $M = 248$
$b = 14{,}021\,(2)\,\text{Å}$ $\rho_{\text{calc}} = 1{,}24\ \text{g/cm}^3$
$c = 6{,}002\,(1)\,\text{Å}$ $Z = 2$
$\gamma = 105{,}9°$ Space group $P2_1$
$V = 664{,}63\,\text{Å}^3$

The intensities of 1283 reflections were measured by $\theta/2\theta$ scanning in CuK_α radiation (graphite monochromator) to $2\theta \leq 120°$ on the diffractometer mentioned, and 1072 reflections with $I \geqslant 2\sigma$ were used in the calculations.

The model of the structure was found by the multivariant tangent method using the programs of the "Rentgen-75" group [5] and was refined by the method of least squares by the programs of the "Kristall" group [6]. The hydrogen atoms were located geometrically. The final value of the R factor was 0.062.

The conformation of the tetrahydroneosophoramine molecule is shown on Fig. 1. Rings A, B, and C have the chair form, and the form of D is close to the half-chair. The linkages of rings A/B and B/C are cis and of A/C and C/D trans. Such a configuration can be obtained from the configuration of isosophoridine [4] by changing the positions of rings A and B rela-

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