CRYSTAL AND MOLECULAR STRUCTURE OF ANHYDROPERFORINE

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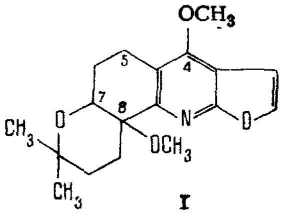
A complete x-ray structural investigation has been made of the alkaloid anhydroperforine. The crystals are rhombic: a = 17.425(5) Å, b = 8.166 Å, c = 11.284(5) Å, z = 4, space group $P2_12_12_1$ (diffractometer, 1000 reflections, MLS in the anisotropic approximation, R = 0.11). The investigation has unambiguously demonstrated the conformation of the anhydroperforine molecule and has confirmed its structure. The lengths of the bonds and the values of the valence angles are the usual ones. The conformations of rings B and C are planar, ring D has a chair, and ring A, a distorted half-chair conformation.

Anhydroperforine forms a cyclic isomer of haplophyllidine and belongs to the type of 5,6,7,8-tetrahydrofuranoquinoline derivatives which are found only in the plant Haplophyllum perforatum [1, 2].



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Anhydroperforine was investigated by the NMR method and structure (I) was suggested for it [3].

In order to unambiguously determine the spatial structure of anhydroperforine, we have investigated it by the method of x-ray structural analysis.

The anhydroperforine molecule in projection on the XY plane is shown in Fig. 1. The basis of the anhydroperforine molecule consists of rings A, B, C, and D. Table 1 gives the equations of the planes and the deviations of the atoms from these planes. It can be seen from Table 1 that the furan ring is planar and the pyridine ring B with the C(8) and C(5) atoms attached to it also has a planar configuration. The tetrahydropyran ring has the chair conformation. The deviations of the O(14) and C(17) atoms in different directions from the plane determined by the atoms C(7), C(8), C(15), C(16) amount to 0.61 and −0.62 Å. The cyclohexene ring A has a distorted half-chair conformation. The linkage of rings A/D is cis and the angle between the mean-square planes of rings A and D amounts to 103°.

The methoxy group at C_4 of ring B has the pseudoequatorial orientation in relation to the mean-square plane of the pyridine ring, and the methoxy group at C_8 of ring A has the pseudoaxial orientation in relation to the mean-square cyclohexene plane. The methyl groups (C_{23} and C_{22}) are located pseudoaxially and pseudoequatorially, respectively, in relation to the mean-square plane of the tetrahydropyran ring.

The bond lengths and valence angles are given in Tables 2 and 3. Their values agree with those reported in the literature [4-6]. However, appreciable deviations in the bond lengths are observed in the molecule; for example, for the C_4—OCH_3 bond (1.325 Å) and the C_8—OCH_3 bond (1.473 Å) the deviation amounts to 0.15 Å. This scatter is apparently due to the (sp^2) state of the carbon atom in the pyridine ring. The N=C_{10} double bond has a length of 1.284 Å, which agrees with information obtained from the covalent radii in the sp^2-hybridized state of the carbon atom, and the other double bonds of the pyridine ring are

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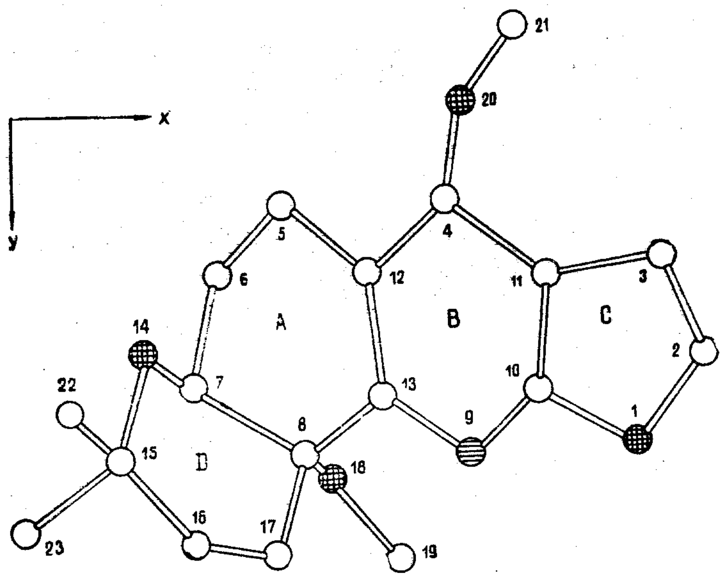

Fig. 1. Conformation of the anhydroperforine molecule on the XY plane.

TABLE 1. Equations of the Planes, $Ax + By + Cz - D = 0$, and Deviations of the Atoms from the Corresponding Planes, δ (Å)

Ring	Atom	*A*	*B*	*C*	*D*	δ
A	C (5)	10,100	70,184	—9,191	0.762	0,07
	C (6)					—0,06
	C (8)					0,05
	C (12)					—0,02
	C (13)					—0,03
	C (7)*					0,70
B	C (4)	—8,251	0,457	9,919	0,028	—0,02
	N (9)					—0,01
	C (10)					0,02
	C (11)					—0,00
	C (12)					0,03
	C (13)					—0,01
C	O (1)	—8,129	0,492	9,958	0,101	—0,02
	C (2)					—0,02
	C (3)					—0,01
	C (10)					0,02
	C (11)					0,01
D	C (7)	—7,859	5,693	6,288	0,839	—0,01
	C (8)					0,01
	C (15)					0,01
	C (16)					—0,01
	O (14)*					0,61
	C (17)*					—0,62

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

averaged with the ordinary bonds, i.e., there is a redistribution of the double-bondedness (Table 2). A similar phenomenon has been described elsewhere [7]. In the cyclohexane ring, the mean length of the $C_{(sp^3)}$—$C_{(sp^2)}$ bonds is 1.480 Å, and in the tetrahydropyran ring the mean length of the C—O bond is 1.445 Å, which are close to the standard values [4].

Figure 2 shows, in a projection on the XY plane, the mutual positions of the molecules in the elementary cell of the anhydroperforine crystal. All the molecular contacts are in harmony with the scheme of Van der Waals radii. No anomalously short intermolecular contacts are observed.

TABLE 2. Lengths of the Bonds r (Å) in the Structure of Anhydroperforine

Bond	r	Bond	r
O (1)—C (2)	1.376 (11)	C (8)—C (13)	1.500 (11)
O (1)—C (10)	1.435 (11)	C (8)—C (17)	1.572 (13)
C (2)—C (3)	1.350 (14)	C (8)—O (18)	1.473 (10)
C (3)—C (11)	1.493 (11)	N (9)—C (10)	1.284 (11)
C (10)—C (11)	1.397 (13)	N (9)—C (13)	1.350 (10)
C (4)—C (11)	1.425 (11)	C (16)—C (17)	1.527 (13)
C (4)—C (12)	1.418 (11)	C (16)—C (20)	1.506 (13)
C (4)—O (20)	1.325 (11)	C (20)—O (14)	1.496 (11)
C (5)—C (12)	1.461 (11)	C (20)—C (22)	1.511 (14)
C (5)—C (6)	1.554 (13)	C (20)—C (23)	1.558 (13)
C (7)—C (6)	1.436 (12)	O (18)—C (19)	1.410 (11)
C (7)—C (8)	1.578 (12)	O (20)—C (21)	1.440 (13)
C (7)—O (14)	1.395 (9)	C (12)—C (13)	1.419 (12)

TABLE 3. Values of the Valence Angles in the Structure of Anhydroperforine

Angle	Degrees	Angle	Degrees
C (10) O (1) C (2)	106.7 (7)	C (6) C (5) C (12)	113.1 (7)
O (1) C (2) C (3)	114.0 (8)	C (5) C (6) C (7)	110.0 (7)
C (2) C (3) C (11)	103.7 (8)	C (6) C (7) C (8)	109.4 (7)
C (3) C (11) C (4)	138.2 (8)	C (6) C (7) O (14)	110.8 (7)
C (3) C (11) C (10)	108.4 (8)	C (8) C (7) O (14)	110.5 (6)
C (4) C (11) C (10)	113.3 (7)	C (7) C (8) C (13)	112.0 (7)
O (1) C (10) N (9)	120.6 (8)	C (7) C (8) O (18)	104.5 (6)
O (1) C (10) C (11)	106.9 (7)	C (13) C (8) O (18)	112.7 (7)
N (9) C (10) C (11)	132.3 (8)	C (7) C (8) C (17)	108.7 (7)
C (13) N (9) C (10)	112.4 (8)	C (13) C (8) C (17)	110.5 (7)
C (11) C (4) O (12)	119.3 (8)	C (17) C (8) C (18)	108.3 (7)
C (11) C (4) O (20)	125.4 (7)	C (8) C (17) C (16)	111.3 (7)
C (12) C (4) O (20)	115.2 (7)	C (17) C (16) C (20)	114.5 (8)
C (4) C (12) C (5)	118.6 (8)	C (16) C (15) O (14)	108.6 (7)
C (4) C (12) C (13)	116.4 (7)	C (16) C (15) C (23)	110.6 (8)
C (5) C (12) C (13)	125.0 (7)	C (16) C (15) C (22)	112.2 (8)
N (9) C (13) C (12)	115.2 (7)	O (14) C (15) C (22)	103.3 (8)
N (9) C (13) C (8)	116.3 (7)	O (14) C (15) C (23)	110.8 (8)
C (8) C (13) C (12)	117.6 (7)	C (22) C (15) C (23)	111.0 (8)
C (4) O (20) C (21)	119.3 (7)	C (7) O (14) C (20)	116.5 (6)
C (8) O (18) C (19)	116.1 (7)		

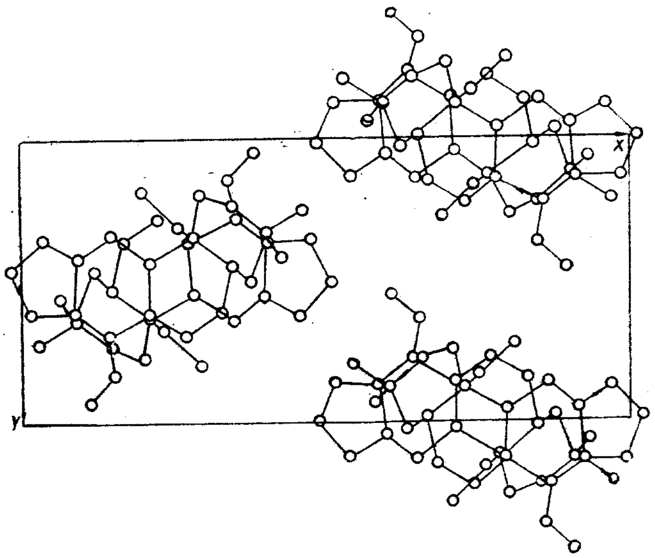

Fig. 2. Packing of the molecules in the elementary cell.

TABLE 4. Coordinates of the Atoms and Their Anisotropic Thermal Factors in the Structure of Anhydroperforine, $\times 10^4$

Atoms	x/a	y/b	Z/c	B(11)	B (22)	B (33)	B (12)	B (23)	B (13)
O (1)	4664 (3)	6314 (6)	3619 (5)	26	162	86	−55	5	−14
C (2)	5137 (5)	5087 (12)	4025 (9)	22	145	98	−25	−10	34
C (3)	4847 (5)	3567 (15)	3889 (9)	28	201	78	20	− 6	−29
C (4)	3480 (5)	2903 (11)	2813 (7)	34	101	68	50	35	−31
C (5)	2268 (5)	2710 (12)	1688 (9)	35	123	101	33	−54	−88
C (6)	1700 (5)	3720 (11)	909 (8)	33	150	66	−39	9	− 6
C (7)	1509 (5)	5228 (10)	1493 (7)	33	114	62	−26	25	− 3
C (8)	2250 (5)	6328 (12)	1601 (7)	29	100	67	− 7	− 4	8
N (9)	3468 (3)	6374 (9)	2633 (7)	20	104	102	43	1	−14
C (10)	4013 (5)	5530 (13)	3087 (8)	23	197	73	− 3	−37	27
C (11)	4102 (4)	3848 (10)	3267 (6)	13	123	56	−24	6	−16
C (12)	2871 (4)	3705 (10)	2214 (6)	10	75	57	0	− 3	−37
C (13)	2896 (4)	5442 (11)	2202 (7)	12	110	84	− 2	11	−75
O (14)	1195 (3)	4928 (7)	2610 (4)	28	87	60	21	12	−35
C (15)	934 (5)	6393 (14)	3300 (9)	20	183	101	12	5	−38
C (16)	1612 (5)	7531 (13)	3449 (9)	33	150	97	19	−21	33
C (17)	2038 (5)	7929 (11)	2302 (8)	37	67	83	57	4	−23
O (18)	2433 (3)	6787 (9)	371 (5)	39	184	63	−19	8	−44
C (19)	3004 (6)	7994 (13)	227 (11)	44	127	143	−60	−15	−26
C (20)	3434 (3)	1284 (7)	2840 (6)	35	103	106	37	−42	−30
C (21)	3879 (6)	389 (12)	3700 (10)	30	123	143	8	−27	4
C (22)	678 (8)	5671 (17)	4465 (9)	69	227	76	23	−28	89
C (23)	266 (5)	7282 (15)	2659 (11)	18	219	160	79	−16	24

EXPERIMENTAL

Crystals of anhydroperforine were grown from ethanol solution in the form of plates with dimensions of 0.2 × 0.4 × 0.8 mm. The parameters of the elementary cell and the space group were determined from precession x-ray diagrams. The parameters of the elementary cell were refined on an "Enraf-Nonius" semiautomatic diffractometer (using CuK_α radiation):

$a = 17.425\ (5)$ Å
$b = 8.166\ (4)$ Å
$c = 11.284\ (5)$ Å
$Z = 4$
$V = 1605.63$ Å^3
$M = 317.2$
$\rho_{\mathrm{calc}} = 1.31\ \mathrm{g/cm^3}$
sp. gr. $P2_12_12_1$

A three-dimensional set of intensities was obtained on the same diffractometer. A total of 1200 reflections was recorded. The formation of the working group was carried out by means of V. V. Borisov's program (Institute of Crystallography of the Academy of Sciences of the USSR), reflections the intensities of which were less than 3σ being discarded from the group. The final set of the working group amounted to 1000 independent and nonzero reflections. No correction was applied for absorption.

The structure was interpreted by means of the "Rentgen-75" program [8] on a BÉSM-6 computer (Computing Center of the Institute of Crystallography, Academy of Sciences of the Uzbek SSR). After the standardization of the structural amplitudes by means of the program, 330 E-normalized amplitudes were selected for phase determination. An attempt at interpretation in the automatic regime, i.e., by screening 1024 variants and investigating the 15 E-syntheses with the best S-estimates characterizing the quality of the given phase system, was unsuccessful. Then to calculate the variants we selected 250 normalized amplitudes with $E \geqslant 1.2$ and estimated a series of E-syntheses from the set of phases obtained. In the E synthesis best with respect to the R factor but not the best with respect to the S estimate we found the solution, and out of the 23 atoms of the molecule we isolated 18. The subsequent F-synthesis calculated with respect to the coordinates of the 18 atoms enabled us to find all the nonhydrogen atoms of the molecule, the R factor being 0.30. The structure was refined in the isotropic, and then in the anisotropic approximation to an R factor of 0.11.

The coordinates of the atoms and the anisotropic thermal factors are given in Table 4.

SUMMARY

The spatial configuration of anhydroperforine has been established unambiguously by x-ray structural analysis and its structure has been confirmed.

LITERATURE CITED

1. Z. Sh. Faizutdinova, I. A. Bessonova, and S. Yu. Yunusov, Khim. Prir. Soedin., 360 (1968); I. A. Bessonova, Z. Sh. Faizutdinova, Ya. V. Rashkes, and S. Yu. Yunusov, Khim. Prir. Soedin., 273 (1969).
2. I. A. Bessonova, M. R. Yagudaev, and S. Yu. Yunusov, Khim. Prir. Soedin., 597 (1978).
3. I. A. Bessonova, Kh. A. Abdullaeva, and S. Yu. Yunusov, Khim. Prir. Soedin., 682 (1974).
4. Tables of Interatomic Distances and Configuration in Molecules and Ions, Chemical Society, London (1955).
5. S.-M. Nasirov, V. G. Andrianov, Yu. T. Struchkov, and S. Yu. Yunusov, Khim. Prir. Soedin., 395 (1975).
6. S.-M. Nasirov, V. G. Andrianov, Yu. T. Struchkov, and S. Yu. Yunusov, Khim. Prir. Soedin., 197 (1976).
7. A. T. McPhail and G. A. Sim, J. Chem. Soc., B, 923 (1968).
8. V. I. Andrianov, Z. Sh. Safina, and B. L. Tarnopol'skii, Zh. Strukt. Khim., 15, 911 (1974).

ALKALOIDS OF Haplophyllum dubium

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From the epigeal part of Haplophyllum dubium we have isolated dubamine, γ-fagarine, skimmianine, graveoline, haplopine, the new alkaloid norgraveoline, and the steroid β-sitosterol. This is the first time that γ-fagarine has been found in this plant. On the basis of the results of a study of spectral characteristics and also passage to the known alkaloid graveoline, it has been established that norgraveoline has the structure of 2-piperonyl-4-quinolone.

The alkaloid composition of the plant Haplophyllum dubium Eug. Kor. (family Rutaceae) has been studied previously [1]. We have investigated this plant from a different growth site, since the qualitative and quantitative compositions of the alkaloids change according to the conditions of growth of the plant. The epigeal part, collected in the flowering phase by S. A. Khamidkhodzhaev in the southern part of the Babatag range in the region of Kara-Kuz, Tadzhik SSR, was extracted with methanol and the extract was separated into basic, acidic, and neutral fractions. Chromatography of the basic fraction led to the isolation of dubamine, γ-fagarine, skimmianine, graveoline, and base (I) with mp 288-290°C (decomp.), while the neutral fraction yielded β-sitosterol, and the acid fraction haplopine.

The known alkaloids and the β-sitosterol were identified by direct comparison in TLC and by mixed melting points with authentic samples.

The amount of alkaloids in the epigeal part of H. dubium in the flowering period was 0.3% (on the air-dry weight of the raw material). Base (I) had the composition $C_{16}H_{11}NO_3$, mol. wt. 265 (mass spectrometrically). $\lambda_{\max}^{C_2H_5OH}$ 213.5, 243.5, 276, 324 nm (log ε 4.46, 4.46, 4.13, 4.30). The long-wave absorption maximum in the UV spectrum of (I) underwent a hypsochromic shift on alkalinification and was observed at 301 nm, which is characteristic of 4-quinolones containing no alkyl group on the nitrogen atom [2]. The IR spectrum of (I) had absorption maxima in the 3260-2840 cm^{-1} region, which are characteristic for associated NH groups, and at 1635, 1600, 1555, and 1505 cm^{-1} (4-quinolone system). The NMR spectrum of (I) showed the signals of seven aromatic protons and singlets of the protons of a methylenedioxy group and of H_3 of a quinolone nucleus, indicating that (I) belongs to the class of 2-phenyl-4-quinolone alkaloids. Analysis of the splitting of the signals of the aromatic protons showed that the methylenedioxy group was present in the aryl part of the molecule.

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