

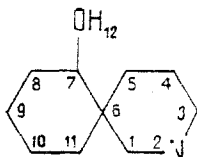
CRYSTAL AND MOLECULAR STRUCTURES OF THE ALKALOIDS
NITRAMINE AND ISONITRAMINE

B. Tashkhodzhaev

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The spatial structures of two alkaloids — nitramine and isonitramine — in the form of crystalline salts have been determined by x-ray structural analysis. It has been established that these alkaloids are conformers differing by the configuration of the C(7) asymmetric center.

It was shown previously [1] as the result of an analysis of ^{13}C NMR spectra, chemical transformations, and preliminary x-radiographic results that the alkaloids nitramine and isonitramine consist of cyclohexanol and piperidine rings forming a spirobicyclic system, i.e., the two alkaloids have the same skeleton. In the present paper we give the results of a complete x-ray radiographic investigation of the compounds nitramine nitrate (I) and isonitramine hydrochloride (II).



The geometries of the nitramine and isonitramine cations projected on the plane passing through the triplet of atoms C(1)C(4)C(6) are shown in Fig. 1a, b. The alkaloids consist of two saturated cyclohexanol and piperidine rings with a common spiro center, C(6). The conformations of the rings can be judged unambiguously from Fig. 1c, in which the torsional angles are given. The cyclohexanol and piperidine rings in (I) and (II) have the chair conformation. In both the alkaloids the hydroxy group is present in the equatorial orientation, as is confirmed by the NMR figures. It follows from the results of a comparative analysis of the torsional angles of (I) and (II) (see Fig. 1c) that the alkaloids nitramine and isonitramine are conformers differing by the configuration of the C(7) asymmetric center (diastereoisomers).

The lengths of the valence bands in (I) and (II) are given in Table 1. Within the limits of experimental error they are close to the corresponding standard values. The mean length of the N—C bonds is 1.50 Å, which is typical for a protonated quaternary nitrogen atom, $\text{N}^+\text{—C}_{\text{sp}^3}$ [2]. The distances of the O...N and Cl...N donor-acceptor interactions (2.87 and 3.09 Å, respectively) also agree with the values found in alkaloid nitrates and hydrochlorides (see, for example [3, 4]). The nitrate group (anion) in (I) is planar and no anomalies are observed in the C...O distances (averaging 1.25 Å) and in the valence angles ($\approx 120^\circ$). The valence angles in the cations, on the whole, are close to the standard values [5]. Slight increases in the C(10)C(11)C(6) angles (114.8° in (I), and 115.1° in (II)) and decreases in the C(7)C(6)C(11) angles (106.5° (I) and 106.7° (II)) are apparently connected with the tendency for the maximum mutual separation of the two rings.

The results of NMR and IR spectroscopy showed the presence of an intramolecular hydrogen bond in each of the bases of (I) and (II), but in the crystalline solvates of the alkaloids no such H bond exists. Thanks to the fixation of the H atom at N(2) in (I) and (II) and also from analysis of Dreiding models it is possible to observe that the direction of the free electron pair of N(2) that has been found does not exclude the formation of an intramolecular H bond of the $\text{N}:\cdots\text{H—O}$ type in the conformers existing in the liquid phase [2].

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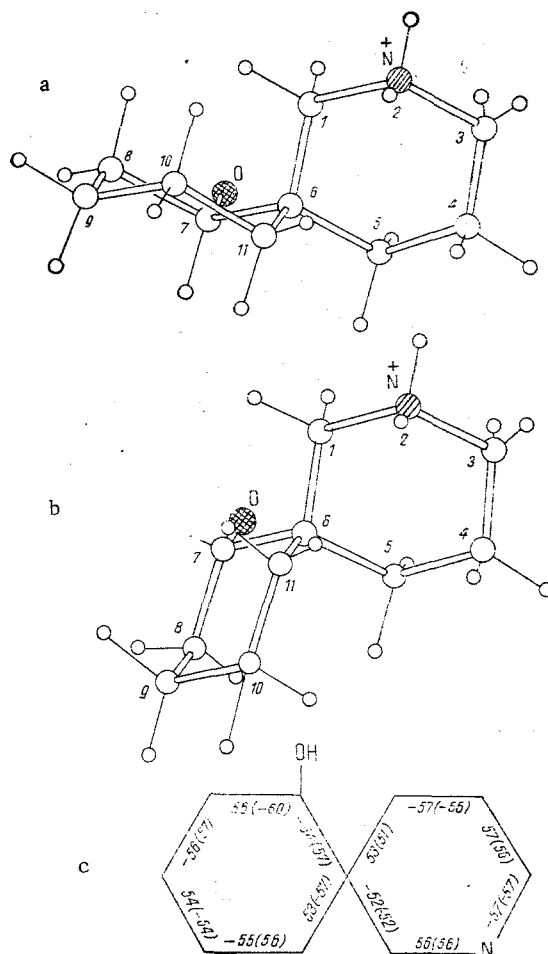


Fig. 1. Geometries of the cations of (I) (a) and (II) (b) (the missing H atoms have been inserted from geometric considerations) and the torsional angles in (I) and (in parentheses) (II) (c).

TABLE 1. Interatomic Distances (R, Å) and Valence Angles (ω , deg)

Distance	R _I	R _{II}	Angle	ω_I	ω_{II}
C (1) —N (2)	1,499 (5)	1,493 (5)	C (5) C (1) N (2)	112,8 (3)	112,7 (4)
N (2) —C (3)	1,505 (6)	1,505 (7)	C (1) N (2) C (3)	113,3 (3)	113,2 (4)
C (3) —C (4)	1,489 (7)	1,498 (8)	N (2) C (3) C (4)	110,7 (4)	109,5 (5)
C (4) —C (5)	1,536 (6)	1,545 (7)	C (3) C (4) C (5)	111,2 (4)	112,2 (5)
C (5) —C (6)	1,536 (5)	1,524 (7)	C (4) C (5) C (6)	112,8 (4)	111,7 (4)
C (6) —C (7)	1,549 (5)	1,551 (7)	C (5) C (6) C (1)	109,8 (3)	110,6 (4)
C (7) —C (8)	1,523 (6)	1,547 (7)	C (5) C (6) C (7)	108,4 (3)	111,7 (4)
C (8) —C (9)	1,530 (6)	1,510 (9)	C (5) C (6) C (11)	110,3 (3)	111,6 (4)
C (9) —C (10)	1,511 (7)	1,540 (9)	C (1) C (6) C (7)	109,6 (3)	106,4 (4)
C (10) —C (11)	1,514 (6)	1,522 (7)	C (1) C (6) C (11)	112,1 (3)	109,6 (4)
C (11) —C (6)	1,554 (5)	1,529 (7)	C (7) C (6) C (11)	106,5 (3)	106,7 (4)
C (7) —O (12)	1,431 (5)	1,435 (6)	C (6) C (7) C (8)	114,3 (3)	111,3 (4)
O (13) —N (16)	1,233 (4)		C (6) C (7) O (12)	107,9 (3)	109,6 (4)
O (14) —N (16)	1,252 (4)		O (12) C (7) C (8)	110,6 (3)	110,7 (5)
O (15) —N (16)	1,244 (5)		C (7) C (8) C (9)	110,6 (4)	110,5 (5)
			C (8) C (9) C (10)	111,2 (4)	111,7 (5)
			C (9) C (10) C (11)	111,1 (4)	109,6 (5)
			C (10) C (11) C (6)	114,8 (4)	115,1 (5)
			O (13) N (16) O (14)	119,5 (4)	
			O (14) N (16) O (15)	120,7 (4)	
			O (13) N (16) O (15)	119,7 (4)	

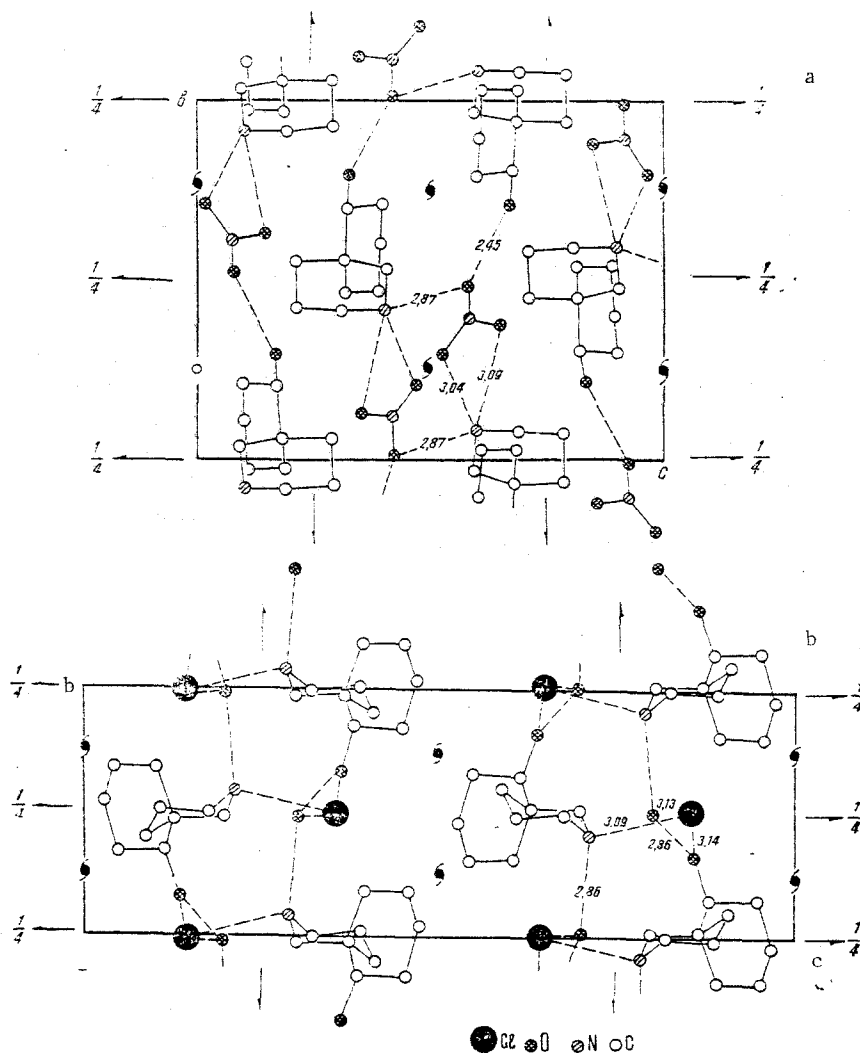


Fig. 2. Packing of the molecules of (I) (a) and (II) (b).

Thus, it is possible to assume that, on solvation the intramolecular H bond in nitramine and that in isonitramine cleaved, and the conformations described above are realized in the molecules. This fact suggests that the conformations of the alkaloids (I) and (II) are best studied by the method of x-ray structural analysis in the form of the bases. The packing of the molecules in the crystal is shown in Fig. 2.

An analysis of intermolecular contacts shows the possibility of intermolecular H bonds of the O-H...O and N-H...O types. The distances between the atoms concerned are as follows: O(14)...O(12) 2.95 Å; N(2)...O(13) 3.04 Å; and (2)...O(15) 3.09 Å. The O(14) atom approaches the N(2) atom from the side of the free electron pair and possibly forms a donor-acceptor bond.

Packing of the Molecules of (II). It has been found that the H atom at N(2) forms a H bond with a molecule of water of crystallization N(2)...O(13) 2.86 Å and the H atom of an HCl molecule is attached to the free electron pair of N(2), forming an ionic bond. The proton of a water molecule also participates in H bonds with O atoms O(13)...O(12) 2.86 Å. In their turn, the H atom from the OH group and another proton from a water molecule are attracted to the Cl⁻ anion (Cl...O(12) and Cl...O(13) distances 3.13 and 3.14 Å, respectively). Thus, the isonitramine molecules, linked by screw axes of symmetry through the anion and water molecule are joined into infinite chains directed parallel to the crystallographic b axis.

TABLE 2. Coordinates and Anisotropic Temperature Parameters ($\times 10^4$) of the O, C, and N Atoms and of the H Atoms ($\times 10^3$) of the Molecule of (I)

Atom	x/a	y/b	z/c	b ₁₁	b ₂₂	b ₃₃	b ₁₂	b ₁₃	b ₂₃
C (1)	3033 (5)	4565 (4)	9134 (3)	79	63	40	-12	9	3
N (2)	4017 (4)	5762 (3)	9060 (3)	98	57	56	9	-3	0
C (3)	5002 (6)	5795 (5)	8114 (4)	97	93	64	-27	-20	-4
C (4)	4037 (6)	5635 (4)	7178 (4)	123	94	36	-43	39	-6
C (5)	3045 (5)	4417 (5)	7226 (3)	123	82	59	-24	-36	-29
C (6)	2040 (5)	4353 (4)	8192 (3)	73	49	42	7	3	2
C (7)	1280 (5)	2989 (4)	8244 (3)	102	59	48	-9	27	-11
C (8)	81 (5)	2845 (4)	9087 (3)	100	73	57	-28	31	13
C (9)	-1179 (6)	3876 (5)	8974 (4)	91	106	79	-4	-30	-1
C (10)	-504 (5)	5233 (5)	8951 (4)	89	74	74	-4	39	8
C (11)	705 (5)	5357 (4)	8121 (3)	102	67	45	32	33	-7
O (12)	2479 (4)	2044 (3)	8364 (3)	111	59	85	15	50	11
O (13)	1666 (5)	7745 (3)	9803 (3)	191	73	80	5	-24	-11
O (14)	1137 (4)	9682 (3)	9291 (3)	147	73	67	-22	35	-10
O (15)	2987 (4)	8582 (4)	8584 (3)	150	137	76	32	-68	18
N (16)	1940 (4)	8672 (3)	9230 (3)	100	71	50	-1	21	25
H (1)	376	377	919						
H (1)'	247	441	672						
H (2)	348	625	720						
H (4)	338	644	905						
H (5)	382	358	724						
H (5)'	257	459	978						
H (7)	85	285	760						
H (8)	67	301	973						
H (8)'	-67	209	898						
H (9)	-172	379	856						
H (9)'	-204	397	952						
H (10)	-9	550	970						
H (10)'	-145	600	866						
H (11)	112	624	824						
H (11)'	25	504	744						

EXPERIMENTAL

The crystals of (I) and (II), grown from chloroform solution, had the form of elongated prisms. The space groups and parameters of the elementary cells were determined from rotation and Weissenberg x-ray photographs refined on a Syntex P2₁ diffractometer using Cu K α radiation. For compound (I): $a = 8.682(5)$; $b = 10.260(5)$; $c = 13.069(8)$ Å; $d_{\text{calc}} = 1.251$ g/cm³. For compound (II): $a = 8.031(5)$; $b = 7.122(3)$; $c = 20.810(11)$; $d_{\text{calc}} = 1.254$ g/cm³. Space groups P2₁2₁2₁, $z = 4$. A three-dimensional set of intensities was obtained on the diffractometer mentioned with $0 \leq 57.5^\circ$. About 1000 independent nonzero reflections were measured. In the calculations 894 (I) and 874 (II) structural factors exceeding 2σ were used.

Structures were interpreted by the direct method using the Rentgen-75 program [6] in the automatic regime: from 147 (I) and 128 (II) values of $E \geq 1.30$ (I) and 1.40 (II) 2250 (I) and 1950 (II) ternary derivatives were composed, and the space groups consisted of eight reflections. From the best variant E series were constructed [R factors 0.22 (I) and 0.32 (II)] in which almost all the nonhydrogen atoms of the molecule were found, apart from the C(9) and C(11) atoms in compound (II). For a more accurate localization of the atoms and in order to find the missing atoms, several $\rho(x, y, z)$ indices were calculated. In this way the presence of a molecule of water of crystallization in the crystal of (II) was detected. Then the structures were refined by the method of least squares (MLS) in the isotropic approximation to $R = 0.185$ (I) and 0.106 (II). In the following stage, the positional parameters of all the atoms were refined in the block-diagonal anisotropic approximation to $R = 0.105$ (I) and 0.084 (II). In the final stage, difference electron density (ED) syntheses were calculated by MLS in order to find the coordinates of the hydrogen atoms.

In the molecule of (II) it was possible to determine the coordinates of almost all the H atoms. To reveal the H atoms in the molecule of the water of crystallization and those attached to the N and Cl heteroatoms, the packing of the molecules was also considered; those peaks for H atoms which favor complex-formation were taken. The following were not found: one of the H atoms in the water molecule and the H of the OH group of the molecule of (II).

TABLE 3. Coordinates and Anisotropic Temperatures Parameters ($\times 10^4$) of the Cl, O, C, and N Atoms and of the H Atoms ($\times 10^3$) of the Molecule of (II)

Atom	x/a	y/b	z/c	b ₁₁	b ₂₂	b ₃₃	b ₁₂	b ₁₃	b ₂₃
C (1)	3743 (6)	178 (8)	7013 (2)	122	187	16	-90	3	15
N (2)	2172 (6)	-849 (6)	7166 (2)	146	127	24	12	18	3
C (3)	678 (7)	-79 (9)	6818 (3)	141	206	29	-43	23	-11
C (4)	996 (6)	-108 (9)	6108 (3)	120	264	28	-14	-8	3
C (5)	2600 (7)	968 (8)	5927 (2)	113	161	20	-14	-9	9
C (6)	4107 (6)	241 (7)	6295 (2)	89	127	18	-20	-9	-12
C (7)	5641 (6)	1540 (8)	6209 (2)	107	175	20	11	15	-7
C (8)	6247 (7)	1552 (9)	5504 (3)	151	231	21	-53	31	5
C (9)	6722 (8)	-405 (9)	5293 (3)	158	263	24	-42	51	-37
C (10)	5270 (8)	-1796 (9)	5376 (3)	167	232	23	-73	19	-36
C (11)	4630 (7)	-1710 (8)	6064 (2)	156	154	18	-16	17	-23
O (12)	5230 (5)	3404 (5)	6417 (2)	145	165	31	-52	24	-24
O (13)	2434 (5)	-4838 (6)	7024 (2)	171	184	30	-43	7	-21
Cl	1151 (2)	87 (2)	8562 (1)	134	250	21	99	11	-11
H (1)	489	-35	730						
H (1)'	362	149	726						
N (2)	198	11	761						
N (2)'	243	-211	707						
H (3)	64	135	698						
H (3)'	17	-100	698						
H (4)	-70	20	578						
H (4)'	120	-154	594						
H (5)	303	730	541						
H (5)'	235	249	602						
H (7)	678	740	643						
H (8)	536	237	529						
H (8)'	735	250	553						
H (9)	793	-106	566						
H (9)'	723	-58	476						
H (10)	416	-114	510						
H (10)'	578	-315	523						
H (11)	377	-270	624						
H (11)'	554	-215	641						
H (13)	331	499	176						

However, in the molecule of (I) a total of 15 H atoms out of 20 was found; the H atom in the hydroxy group, that from the nitric acid, and also those in some methylene fragments were not revealed.

The final values of the R factors after refinement by MLS taking the coordinates of the H atom into account were 0.073 (I) and 0.066 (II). The coordinates of the nonhydrogen atoms and the anisotropic temperature corrections and the coordinates of the H atoms found from a difference ED synthesis are given in Tables 2 and 3.

CONCLUSION

The spatial structures of two alkaloids - nitramine and isonitramine - in the form of crystalline solvates have been determined by x-ray structural analysis. It has been established that these alkaloids are conformers differing by the configuration of the C(7) asymmetric center (diastereoisomers).

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