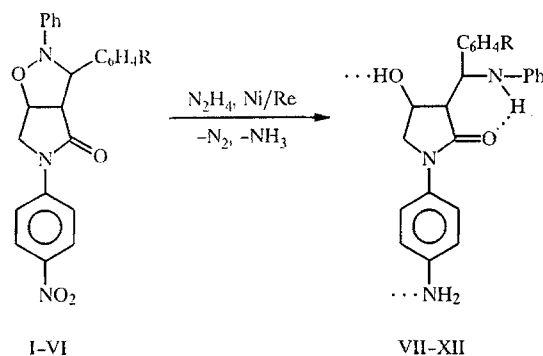


## REDUCTION OF 2-OXA-3,7-DIAZABICYCLO[3.3.0]OCTANES

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*The reduction of 2-oxa-6-oxo-3-phenyl-4-(R-phenyl)-7-(4-nitrophenyl)-3,7-diazabicyclo[3.3.0]octanes with hydrazine hydrate in the presence of Raney nickel gave the corresponding amino alcohols. X-ray diffraction analysis established the stereochemistry of the molecule in the crystal of 1-(4-anilino)-3-[anilino(phenyl)-methyl]-4-hydroxypyrrolidone-2.*

The N—O bond in isoxazolidines is ruptured by different reducing agents, including hydrazine hydrate in the presence of Raney nickel [1] with the formation of the corresponding amino alcohols. We have reduced the N—O bond in the previously synthesized 2-oxa-6-oxo-3-phenyl-4-(R-phenyl)-7-(4-nitrophenyl)-3,7-diazabicyclo[3.3.0]octanes I-VI with hydrazine hydrate in the presence of Raney nickel [2].



I, VII R=H; II R=3-NO<sub>2</sub>; VIII R=3-NH<sub>2</sub>; III, IX R=4-Br; IV, X R=4-Me; V, IX R=4-OMe;  
VI, XII R=4-NMe<sub>2</sub>

The IR spectra of the obtained amino alcohols VII-XII (Table 1) show absorption bands, which are characteristic for the carbonyl group and the aromatic ring, present in the corresponding isoxazolidines I-VII [2]; new broad bands appear in the region 3300-3450 cm<sup>-1</sup>, caused by the vibrations of the associated NH and OH groups [3].

In the UV spectra of compounds VII-XII the absorption maximum is shifted strongly to the low-frequency zone as compared to I-VI; this indicates not only the opening of the isoxazolidine ring, but also the reduction of the nitro groups in the nitrophenyl fragments. The PMR spectra of the compounds also support the proposed structure. Thus, the spectrum of compound VII in DMSO contains signals at 5.0 (NH<sub>2</sub>), 6.72 (NH), 5.43 (OH), 2.88 (2-H), 3.83 (3-H), 4.70 (11-H), and 6.52-7.58 ppm (H<sub>arom</sub>).

Nevertheless, the PMR spectrum provided little information, since the spin-spin interaction is absent of the protons H<sub>4a</sub> and H<sub>4e</sub>; H<sub>4e</sub> and H<sub>3</sub>; H<sub>3</sub> and H<sub>02</sub>. Besides this, the signal of the hydroxyl group splits into a doublet.

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TABLE 1. Characteristics of the Synthesized Compounds

Compound	Empirical formula	mp, °C	IR spectrum, cm <sup>-1</sup>		UV spectrum (in ethanol), λ <sub>max</sub> , nm (log ε)	Yield, %
			C=O	OH, NH		
VII	C <sub>23</sub> H <sub>23</sub> N <sub>3</sub> O <sub>2</sub>	193...195	1690	3220, 3340, 3410	211 (4,48), 252 (4,38)	62
VIII	C <sub>23</sub> H <sub>24</sub> N <sub>4</sub> O <sub>2</sub>	194...196	1685	3220, 3330, 3420	210 (4,41), 248 (4,21)	56
IX	C <sub>23</sub> H <sub>22</sub> N <sub>3</sub> O <sub>2</sub> Br	183...185	1670	3200, 3340, 3430	210 (4,66), 254 (4,47)	54
X	C <sub>24</sub> H <sub>25</sub> N <sub>3</sub> O <sub>2</sub>	85...87	1690	3230, 3350, 3440	214 (4,28), 252 (4,38)	74
XI	C <sub>24</sub> H <sub>25</sub> N <sub>3</sub> O <sub>3</sub>	90...92	1685	3220, 3350, 3440	212 (4,26), 241 (4,23)	70
XII	C <sub>25</sub> H <sub>28</sub> N <sub>4</sub> O <sub>2</sub>	101...103	1665	3210, 3350	210 (4,40), 263 (4,27)	51

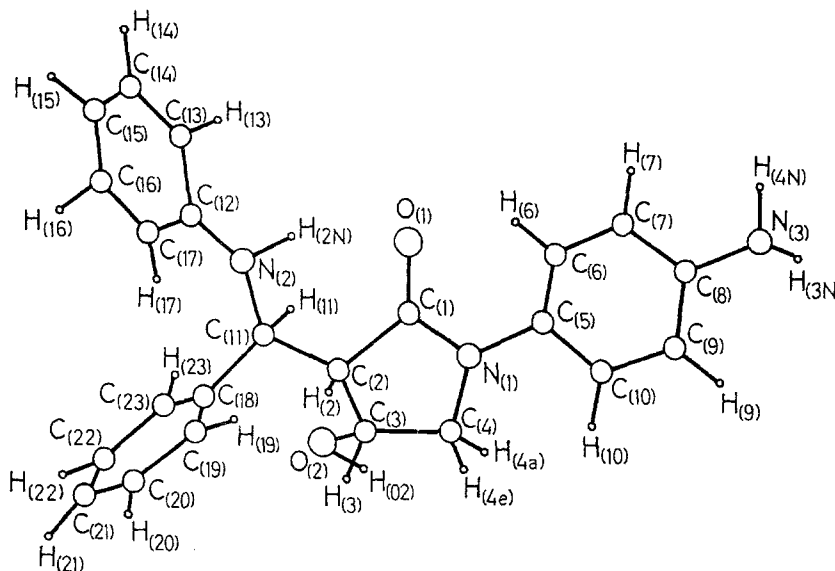


Fig. 1. X-ray diffraction pattern of the molecule of compound VII in the crystal form.

An x-ray structural analysis of compound VII was carried out in order to establish the structure of the amino alcohols formed (Fig. 1). The bond lengths, the valence angles, and the coordinates of the atoms are presented in Tables 2-4.

The geometry of the phenyl fragments is the usual one [4]. Unusual in the structure of compound VII is the nonplanarity of the pyrrolidine ring, which is strongly distorted and is not described by the usual "convert" (due to the presence in the ring of three carbon atoms in the sp<sup>3</sup> hybrid state, related to polar and bulky groups). If we take as the basis the plane passing through the atom C<sub>(1)</sub> (sp<sup>2</sup> hybridization and sum of valence angles 359.9), N<sub>(1)</sub> and C<sub>(2)</sub>, the atom C<sub>(4)</sub> lies by 1.3° below and the atom C<sub>(3)</sub> by 18.8° above the plane.

The angle  $\tau$  between the phenyl ring and the plane, passing through the atoms C<sub>(1)</sub>C<sub>(2)</sub>N<sub>(1)</sub> in the pyrrolidine ring, is approximately equal to 40°. Such an unfolding is the result of a competition between the electron n(N)– $\pi^*$ (Ph) and the steric factors. The first is at a maximum at  $\tau = 0^\circ$ , the second is at a minimum at  $\tau = 90^\circ$ . At  $\tau = 40^\circ$  evidently the minimum permissible interaction between the atoms O<sub>(1)</sub> and C<sub>(6)</sub>, 2.947 Å, takes place (sum of van der Waals radii for O–C is 3.0 Å [5]).

It was noticed that the length of the bond N<sub>(1)</sub>–C<sub>(1)</sub> of 1.360 Å decreased by 0.015–0.020 Å in comparison with the N-alkylamides [6]; it can also be stated that it became shorter by 0.011 Å than the corresponding bond in the unreduced molecule I. Besides this, the length of the N<sub>(1)</sub>–C<sub>(5)</sub> bond of 1.429 Å increased by 0.05 Å.

All this indicates a large contribution of the unshared electron pair of the N<sub>(1)</sub> atom to the conjugation with the carbonyl group, i.e., the effect of n(N)– $\pi^*$ (C=O) interaction is stronger than n(N)– $\pi^*$ (Ph) interaction.

The conformation of the central part of the molecule is stabilized by the intramolecular hydrogen bond N<sub>(2)</sub>–H<sub>(2N)</sub>...O<sub>(1)</sub> with 2.039 Å. We assume that the "loose" hydrogen bond C<sub>(6)</sub>–H<sub>(6)</sub>...O<sub>(1)</sub> with 2.450 Å also exists; it is, however, very weak, since it is smaller by only 0.02 Å than the van der Waals radii H–O of 2.47 Å. In the crystal the molecules are also bound by the relatively strong intermolecular bond O<sub>(2)</sub>–H<sub>(02)</sub>...N<sub>(3)</sub> with 2.009 Å.

TABLE 2. Valence Angles ( $\omega$ ,  $^\circ$ ) in the Structure of VII

Angle	$\omega^\circ$	Angle	$\omega^\circ$
C(1)N(1)C(4)	112,8(5)	C(8)C(9)C(10)	120,4(5)
C(1)N(1)C(5)	124,6(6)	C(5)C(10)C(9)	120,2(5)
C(4)N(1)C(5)	122,2(5)	N(2)C(11)C(2)	109,5(4)
C(11)N(2)C(12)	118,3(4)	N(2)C(11)C(18)	110,7(4)
C(1)C(1)N(1)	125,8(5)	N(2)C(11)C(18)	109,4(4)
C(1)C(1)C(2)	126,6(5)	N(2)C(12)C(13)	119,2(5)
N(1)C(1)C(2)	107,5(5)	N(2)C(12)C(17)	123,3(6)
C(1)C(2)C(3)	103,0(4)	C(13)C(12)C(17)	117,5(5)
C(1)C(2)C(11)	117,1(3)	C(12)C(13)C(14)	120,7(5)
C(3)C(2)C(11)	114,3(4)	C(13)C(14)C(15)	120,8(6)
O(2)C(3)C(2)	107,2(5)	C(14)C(15)C(16)	119,3(6)
O(2)C(3)C(4)	110,4(5)	C(15)C(16)C(17)	120,5(5)
C(2)C(3)C(14)	103,0(5)	C(12)C(17)C(16)	121,2(5)
N(1)C(4)C(3)	102,9(5)	C(11)C(18)C(19)	120,3(4)
N(1)C(5)C(6)	120,7(4)	C(11)C(18)C(25)	121,4(4)
N(1)C(5)C(8)	120,0(4)	C(19)C(18)O(23)	118,2(4)
C(6)C(5)C(10)	119,3(4)	C(18)C(19)C(20)	121,4(4)
C(5)C(6)C(7)	120,1(4)	C(19)C(20)C(21)	119,1(5)
C(6)C(7)C(8)	121,2(5)	C(20)C(21)C(22)	120,2(5)
N(3)C(8)C(7)	120,2(4)	C(21)C(22)C(23)	120,3(5)
N(3)C(8)C(9)	121,1(4)	C(18)C(23)C(22)	120,7(4)
C(7)C(8)C(9)	118,7(4)		

TABLE 3. Bond Length  $d$ ,  $\text{\AA}$ , in the Structure of VII

Bond	$d$ , $\text{\AA}$	Bond	$d$ , $\text{\AA}$
O(1)—C(1)	1,229(8)	C(8)—C(9)	1,374(7)
O(2)—C(3)	1,427(7)	C(9)—C(10)	1,396(8)
N(1)—C(1)	1,360(8)	C(11)—C(18)	1,523(6)
N(1)—C(4)	1,474(10)	C(12)—C(13)	1,396(8)
N(1)—C(5)	1,429(7)	C(12)—C(17)	1,388(8)
N(2)—C(11)	1,466(6)	C(13)—C(14)	1,384(8)
N(2)—C(12)	1,412(7)	C(14)—C(15)	1,370(10)
N(3)—C(8)	1,425(6)	C(15)—C(15)	1,369(10)
C(1)—C(2)	1,529(6)	C(6)—C(17)	1,387(8)
C(2)—C(3)	1,543(8)	C(18)—C(19)	1,376(6)
C(2)—C(11)	1,537(6)	C(18)—C(23)	1,390(6)
C(3)—C(4)	1,516(9)	C(19)—C(20)	1,396(7)
C(5)—C(6)	1,372(5)	C(20)—C(21)	1,379(7)
C(5)—C(10)	1,387(7)	C(21)—C(22)	1,369(8)
C(6)—C(7)	1,387(6)	C(22)—C(23)	1,384(7)
C(7)—C(8)	1,383(7)		

## EXPERIMENTAL

The UV spectra were recorded on a Specord spectrophotometer in ethanol, the IR spectra on a UR-20 spectrometer. The  $^1\text{H}$  NMR spectra were recorded on a Bruker WM-250 (250 MHz) instrument in DMSO- $D_6$  (with HMDS as the internal standard). TLC was carried out on Silufol-254 sheets, using a mixture of acetone— $\text{CCl}_4$ —petroleum ether (4:2:1) as the eluent. The spots were revealed with 2,4-dinitrophenylhydrazine hydrochloride and an alkaline  $\text{KMnO}_4$  solution. The x-ray diffraction analysis of compound VII was carried out on a P-I Syntex automatic diffractometer ( $\lambda\text{MoK}_\alpha$  radiation, graphite monochromator,  $\theta/2\theta$  sweep to  $2\theta_{\text{max}} = 45^\circ$ ). For the transparent  $\text{C}_{23}\text{H}_{23}\text{N}_3\text{O}_2$  monoclinic crystals a total of 1119 images was obtained with  $J > 3\sigma(J)$ . The unit-cell parameters are:  $a = 14.276(3)$ ,  $b = 14.971(3)$ ,  $c = 9.112(2)$   $\text{\AA}$ ;  $V = 1936.8(6)$   $\text{\AA}^3$ ;  $\gamma = 96.03(2)^\circ$ , the space group P is  $2_{1a}$ ,  $Z = 4$ . The structure was resolved by the direct method by using the SHELXTL program package [7] on a NOVA-3 computer; the precision was improved in the anisotropic (isotropic for hydrogen atoms) approximation to the divergence factors  $R = 0.032$ ;  $R_w = 0.034$ .

TABLE 4. Coordinates of Atoms ( $\times 10^4$ ) in the Structure of VII

Atom	x	y	z	Atom	x	y	z
O(1)	2097(4)	1331(4)	6199(7)	C(10)	385(4)	-842(4)	8673(7)
O(2)	2262(2)	2261(2)	10362(3)	C(11)	3386(4)	2736(3)	7933(6)
N(1)	1826(4)	656(4)	8455(7)	C(12)	3515(4)	3678(4)	5701(8)
N(2)	3524(2)	2820(2)	6343(3)	C(13)	3439(2)	3749(3)	4180(4)
N(3)	-1213(4)	-1896(4)	6927(7)	C(14)	3434(4)	4579(5)	3515(7)
C(1)	2289(4)	1247(3)	7503(6)	C(15)	3500(4)	5351(4)	4334(8)
C(2)	3117(2)	1745(2)	8331(4)	C(16)	3571(4)	5295(4)	5828(7)
C(3)	2843(5)	1582(4)	9953(8)	C(17)	3583(4)	4468(3)	6509(6)
C(4)	2270(5)	670(4)	9917(8)	C(18)	4280(2)	3085(2)	8751(4)
C(5)	1056(3)	32(2)	8067(4)	C(19)	4228(3)	3565(3)	1003(6)
C(6)	363(3)	238(3)	7136(5)	C(20)	5038(4)	3942(3)	10750(6)
C(7)	-372(4)	-399(4)	6747(7)	C(21)	5908(4)	3822(3)	10169(6)
C(8)	-436(2)	-1261(2)	7310(4)	C(22)	5973(4)	3319(3)	8925(6)
C(9)	236(4)	-1476(4)	829(7)	C(23)	5166(3)	2957(3)	8209(5)

**Amino Alcohols VII-XII.** A solution of the initial isoxazolidine I-VI (1.5 mmole) in 80 ml ethanol was treated with 15-20% of the mass of the initial substance of the catalyst Raney nickel, activated by the method given in [8]. The solution was heated to the boiling point, 3 g (60 mmole) of hydrazine hydrate was added in small portions and the mixture refluxed until the evolution of gas ceased. The solvent was then stripped off to 2/3 of the original volume and the residue treated with water and NaCl. The crystals precipitated were filtered off, dried in air, and purified from hot benzene.

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