3. S. L. Zhdanov and A. A. Potekhin, Zh. Org. Khim., 13, 469 (1977).
4. S. I. Yakimovich, K. N. Zelenin, V. N. Nikolaeva, N. V. Koshmina, V. V. Alekseev, and V. A. Khrustalev, Zh. Org. Khim., 19, 1875 (1983).
5. Yu. P. Kitaev and B. I. Buzykin, Hydrazones [in Russian], Nauka, Moscow (1974), p. 48.
6. K. N. Zelenin, I. P. Bezhan, and A. V. Dovgilevich, Zh. Org. Khim., 20, 1977 (1984).
7. K. N. Zelenin, V. V. Pinson, A. A. Potekhin, I. P. Bezhan, V. A. Khrustalev, and P. S. Lobanov, Zh. Org. Khim., 14, 490 (1978).
8. W. Walter and K.-J. Reubke, Chem. Ber., 103, 2197 (1970).
9. J. Godin and A. Le Berre, Bull. Soc. Chim. Fr., No. 10, 4229 (1968).

THREE-DIMENSIONAL STRUCTURES OF 1-ACYL-5-HYDROXYPYRAZOLIDINES

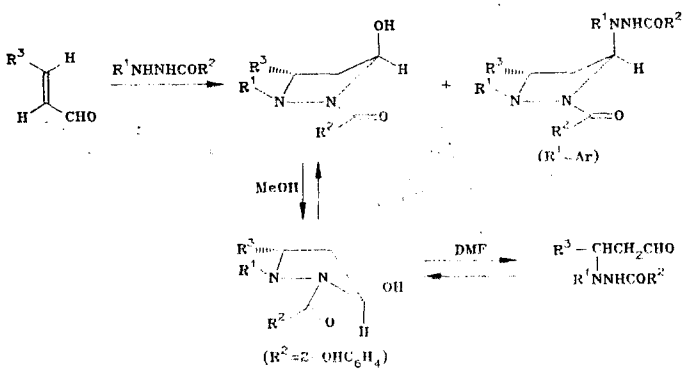
A. V. Dovgilevich, K. N. Zelenin, A. A. Espenbetov, Yu. T. Struchkov, I. P. Bezhan, L. A. Sviridova, G. A. Golubeva, M. Yu. Malov, and Yu. G. Bundel'

UDC 548.737+547.772: 542.953:543.51'422.25

It was shown by x-ray diffraction analysis and PMR spectroscopy that 1-acyl-5-hydroxy- and -5-hydrazinopyrazolidines have a conformation with an axial orientation of the functional group attached to the $C_{(5)}$ atom. The 1-salicylyl derivatives constitute an exception: in methanol solutions they exist in a conformation with an equatorial hydroxy group, whereas in dimethylformamide (DMF) the ring undergoes partial opening to give the corresponding β-hydrazido aldehydes.

We have previously observed that 1-acyl-2-alkyl(aryl)-5-hydroxyprazolidines and 1-acyl-2-aryl-5-(β-acyl-αaryl)hydrazinopyrazolidines are formed in the reactions of 1-acyl-2-alkyl (aryl)-hydrazines with unsaturated aldehydes [1, 2]. Two asymmetric centers develop in the molecules of the resulting pyrazolidines in the reaction of acid hydrazides with β-substituted unsaturated aldehydes (crotonaldehydes and cinnamaldehydes), and this leads to the possibility of the existence of two pairs of diastereomers. We found that the isolated 5-hydroxy- and 5-hydrazinopyrazolidines are represented by only one pair of diastereomers. The chromatographic and spectral characteristics of the compounds obtained constitute evidence in favor of this. It may therefore be asserted that the reaction of hydrazides with unsaturated aldehydes proceeds regio- and stereoselectively.

A combined analysis of the x-ray diffraction data for 1-acetyl-2-phenyl-3-methyl-5-hydroxypyrazolidine (I) and the PMR spectra of the remaining derivatives (see [1]) enabled us to establish a relationship between the spin-spin coupling constants (SSCC) of the protons in the pyrazolidine ring and the orientation of the functional substituents and to ascertain the three-dimensional structures of these compounds.



M. V. Lomonosov Moscow State University, Moscow 117234. S. M. Kirov Military Medical Academy, Leningrad 194175. Translated from Khimiya Geterotsiklicheskikh Soedinenii, No. 9, pp. 1242-1247, September, 1985. Original article submitted February 15, 1985.

 0009-3122/85/2109-1034$09.50

TABLE 1. Bond Lengths (d) in the I Molecule

Bond	d, Å	Bond	d, Å	Bond	d, Å
$O_{(2)}$—$C_{(5)}$	1,408(4)	$C_{(1)}$—$O_{(1)}$	1,236(4)	$C_{(7)}$—$C_{(8)}$	1,365(5)
$O_{(2)}$—$H_{(02)}$	0,97(4)	$N_{(2)}$—$C_{(3)}$	1,487(4)	$C_{(7)}$—$C_{(12)}$	1,379(5)
$N_{(1)}$—$C_{(1)}$	1,332(4)	$N_{(2)}$—$C_{(7)}$	1,445(4)	$C_{(8)}$—$C_{(9)}$	1,396(6)
$N_{(1)}$—$N_{(2)}$	1,431(3)	$C_{(3)}$—$C_{(4)}$	1,532(5)	$C_{(9)}$—$C_{(10)}$	1,376(6)
$N_{(1)}$—$C_{(5)}$	1,469(4)	$C_{(3)}$—$C_{(6)}$	1,512(7)	$C_{(10)}$—$C_{(11)}$	1,352(6)
$C_{(1)}$—$C_{(2)}$	1,506(5)	$C_{(4)}$—$C_{(5)}$	1,491(5)	$C_{(11)}$—$C_{(12)}$	1,392(6)

TABLE 2. Bond Angles (ω) in the I Molecule

Angle	ω, deg	Angle	ω, deg	Angle	ω, deg
$C_{(5)}O_{(2)}H_{(02)}$	98(2)	$N_{(1)}C_{(1)}O_{(1)}$	121,4(3)	$N_{(1)}C_{(5)}O_{(2)}$	111,7(3)
$N_{(2)}N_{(1)}C_{(1)}$	121,7(3)	$N_{(1)}C_{(1)}C_{(2)}$	117,9(3)	$N_{(1)}C_{(5)}C_{(4)}$	101,2(3)
$N_{(2)}N_{(1)}C_{(5)}$	109,5(2)	$O_{(1)}C_{(1)}C_{(2)}$	120,7(3)	$O_{(2)}C_{(5)}C_{(4)}$	109,6(3)
$C_{(1)}N_{(1)}C_{(5)}$	124,2(3)	$N_{(2)}C_{(3)}C_{(4)}$	104,5(3)	$N_{(2)}C_{(7)}C_{(8)}$	123,5(3)
$N_{(1)}N_{(2)}C_{(3)}$	106,7(2)	$N_{(2)}C_{(3)}C_{(6)}$	113,7(3)	$N_{(2)}C_{(7)}C_{(12)}$	117,1(3)
$N_{(1)}N_{(2)}C_{(7)}$	113,2(2)	$C_{(4)}C_{(3)}C_{(6)}$	112,6(3)	$CCC_{(Ar)}$	119,1—
$C_{(3)}N_{(2)}C_{(7)}$	115,9(2)	$C_{(3)}C_{(4)}C_{(5)}$	104,5(3)		120,7(4)

TABLE 3. Some Torsion Angles (τ) in the I Molecule

Angle	τ, deg	Angle	τ, deg	Angle	τ, deg
$O_{(1)}C_{(1)}N_{(1)}N_{(2)}$	−172,1(5)	$N_{(1)}N_{(2)}C_{(7)}C_{(12)}$	179,1(5)	$C_{(3)}C_{(4)}C_{(5)}O_{(2)}$	82,2(4)
$O_{(1)}C_{(1)}N_{(1)}C_{(5)}$	−18,6(4)	$C_{(3)}N_{(2)}C_{(7)}C_{(8)}$	126,1(6)	$C_{(3)}C_{(4)}C_{(5)}N_{(1)}$	−35,9(4)*,
$C_{(2)}C_{(1)}N_{(1)}N_{(2)}$	9,6(5)	$C_{(3)}N_{(2)}C_{(7)}C_{(12)}$	−57,1(5)		−40†
$C_{(2)}C_{(1)}N_{(1)}C_{(5)}$	163,1(6)	$N_{(1)}N_{(2)}C_{(3)}C_{(4)}$	−5,5(4)*,	$C_{(4)}C_{(5)}O_{(2)}H_{(02)}$	−174(5)
$C_{(1)}N_{(1)}N_{(2)}C_{(3)}$	138,9(5)		0†	$N_{(1)}C_{(5)}O_{(2)}H_{(02)}$	−63(5)
$C_{(1)}N_{(1)}N_{(2)}C_{(7)}$	−92,4(5)	$N_{(1)}N_{(2)}C_{(3)}C_{(6)}$	−128,6(6)	$O_{(2)}C_{(5)}N_{(1)}N_{(2)}$	−82,5(4)
$C_{(5)}N_{(1)}N_{(2)}C_{(3)}$	−18,0(4)*,	$C_{(7)}N_{(2)}C_{(3)}C_{(4)}$	−132,6(5)	$O_{(2)}C_{(5)}N_{(1)}C_{(1)}$	121,3(5)
	−25†	$C_{(7)}N_{(2)}C_{(3)}C_{(6)}$	104,3(6)	$C_{(4)}C_{(5)}N_{(1)}N_{(2)}$	34,1(4)*, 40†
$C_{(5)}N_{(1)}N_{(2)}C_{(7)}$	110,7(4)	$N_{(2)}C_{(3)}C_{(4)}C_{(5)}$	26,2(4)*,	$C_{(4)}C_{(5)}N_{(1)}C_{(1)}$	−122,2(6)
$N_{(1)}N_{(2)}C_{(7)}C_{(8)}$	2,4(4)		25†		
		$C_{(6)}C_{(3)}C_{(4)}C_{(5)}$	150,0(6)		

*Torsion angles in the ring of the I molecule.
†Calculation by the mechanical model method (MMM) for cyclopentane [3].

The structure of the I molecule according to the x-ray diffraction data is shown in Fig. 1. The bond lengths, the bond angles, and some torsion angles are presented in Tables 1-3, respectively. The pyrazolidine ring is a slightly distorted flattened envelope [Table 3; in addition to the endocyclic torsion angles in the I molecule, the values calculated by the mechanical model method (MMM) for cyclopentane in the ideal envelope conformation [3] are presented]. The deviation of the $C(_5)$ atom from the $N(_1)N(_2)C(_3)C(_4)$ plane[plane P_1; the deviations of the $N(_1)$, $N(_2)$, $N(_3)$, and $C(_4)$ atoms from the root-mean-square (rms) plane calculated from it are, respectively, −0.014(3), 0.021(3), −0.040(4), and 0.029(4) Å] is −0.520(3) Å; the angle between the $N(_1)C(_4)C(_5)$ and P_1 planes is 34.1°. In accordance with the nomenclature in [3], the $O(_2)$ and $C(_1)$ atoms occupy axial positions and the $C(_6)$ and $C(_7)$ atoms occupy isoclinic positions [the $C(_5)$—$O(_2)$, $N(_1)$—$C(_1)$, $N(_2)$—$C(_7)$, and $C(_3)$—$C(_6)$ bonds form angles of −87.8°, 35.3°, −42.7°, and 46.1° with the P_1 plane].

The adjacent substituents in the 1, 2, 3, and 5 positions have a relative trans orientation, which is responsible for the minimal steric interactions between them, and the axial orientation of the hydroxy and hydrazino groups is possibly due to the most favorable electronic interactions [4, 5].

In the crystalline state the I molecules form centrosymmetric dimers due to the development of an intermolecular hydrogen bond between the hydroxy group and the carbonyl $O(_1)$ atom. The parameters of the hydrogen bond are as follows: $O(_2)$—$H(O_2)$ 0.97(4) Å, $O(_2)$ ...$O(_1)$ 2.735(3) Å, $H(O_2)$...$O(_1)$ 1.77(4)Å, and angle $O(_2)H(O_2)O(_1)$171(4)°. A structure with an intramolecular hydrogen bond and, consequently, with an equatorial orientation of the hydroxy group

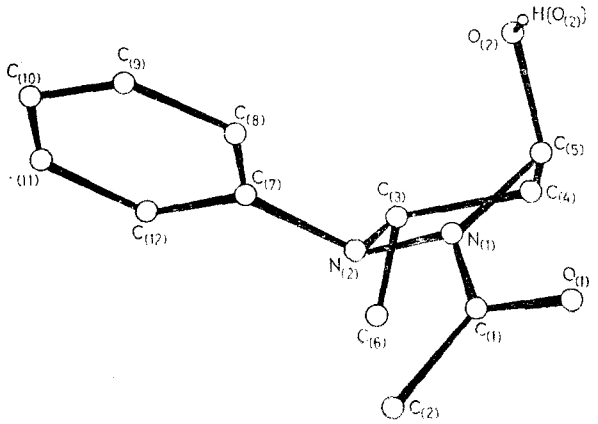


Fig. 1. Structure of 1-acetyl-2-phenyl-3-methyl-5-hydroxypyrazolidine (I).

is not realized, apparently because of the development in this conformation of destabilizing steric repulsion between the $O(_1)$ and $O(_2)$ atoms.

On turning to an examination of the conformational peculiarities of 5-hydroxypyrazolidines in solutions, one must take into account possible changes as compared with the crystalline state. These changes may be due to both different intermolecular interactions and to different solvation effects. It seems to us that the possible changes in the conformation are accompanied by inversion at the nitrogen atom, since any ring conversions should include this process [6, 7].

In aprotic solvents with different polarities all of the previously described 1-acyl-2-alkyl(aryl)-5-hydroxy- and 5-hydrazinopyrazolidines [1, 2] exist, as indicated above in a single stereo form with an axial orientation of the functional substituent attached to the $C(_5)$ atom. The close values of the chemical shifts of the monotypic protons of the pyrazolidine ring and the constants of spin-spin coupling (SSC) between them for the series of compounds I make it possible to assert that they all have the same three-dimensional structure. The J_{45} SSCC, which correspond to an axial orientation of the hydroxy group in 1-acyl-5-hydroxypyrazolidines, are, respectively, J_{ee} = 4.0-5.7 Hz and J_{ae} = 5.5-7.0 Hz. As in the case of the crystals, the dimeric structure is retained in these solvents; this is confirmed in the case of 1-acetyl-2-isopropyl-3-methyl-5-hydroxypyrazolidine [1] by cryoscopic determination of the molecular mass in benzene.

Dimers evidently do not exist in polar protic solvents (D_2O, CD_3OD), since the molecular mass determined by cryoscopy corresponds to the monomeric form; however, a three-dimensional structure with an axial orientation of the substituent attached to the $C(_5)$ atom is retained for virtually all of the 1-acyl-5-hydroxy- and 1-acyl-5-hydrazinopyrazolidines (the SSCC have the values indicated above, and the chemical shifts of the protons of the pyrazolidine ring vary over a range of no more than 0.1 ppm).

The constancy of the chemical shifts and SSCC of the ring protons of 1-acetyl-2-phenyl-3-methyl-5-hydroxypyrazolidine over the temperature range from −100°C to +100°C in solvents with different chemical natures and polarities constitutes evidence that the observed pattern of the PMR spectra is not averaged as a consequence of fast processes involving conversion of the pyrazolidine ring.

The additionally synthesized 1-salicylyl-2-alkyl-5-hydroxypyrazolidines II-IV constituted exceptions. According to the PMR spectra (see Table 4), these substances undergo a change in the configuration at the $C(_5)$ atom upon dissolving in CD_3OD – the hydroxy group in this case occupies an equatorial position. This follows from the significant strong-field shift of all of the protons of the pyrazolidine ring, primarily that of the 5-H proton ($\Delta\delta \simeq 1.3$ ppm) and the change in the J_{45} SSCC (J_{aa} = 5.0-5.5 Hz; J_{ea} = 3.0-5.0 Hz). The detection of long-range SSCC J_{35} = 2.0 Hz, which was not noted in a single case in the alternative ring conformation with an axial hydroxy group, serves as an additional indication of a change in the configuration of the $C(_5)$ atom. The observed effect is possibly due to stabilization of the conformation with an equatorial hydroxy group due to the probable formation of a hydrogen bond with participation of the salicylyl residue.

TABLE 4. Signals of the Protons of the Pyrazolidine Ring in the PMR Spectra of II-IV

Compound	PMR spectrum, δ, ppm (J, Hz)			Solvent
	3-H	4-H	5-H	
II	3,0—4,0, m	2,1—2,5, m	5,96, dd (J_{ee}=5,0, J_{ae}=6,0)	$CDCl_3$
	2,8—3,0, m	1,6—2,0, m	4,65, dd ($J_{aa}=J_{ee}$=5,0)	CD_3OD
	3,0—3,5, m	2,0—2,4, m	5,92, dd (J_{ee}=5,0, J_{ae}=6,0)	d7-DMF*
III	3,0—3,6, m	2,0—2,5, m	6,02, dd (J_{ee}=5,0, J_{ae}=6,5)	$CDCl_3$
	2,8—3,4, m	1,6—1,9, m	4,62, dd J_{aa}=5,5, J_{ea}=3,0, J_{35}=2,0)	CD_3OD
	3,0—3,6, m	2,0—2,6, m	5,97, ddd (J_{ee}=4,0, J_{ae}=6,5)	d_7-DMF*
IV	3,72, ddq ($J_1=J_2$=7,0, J_3=1,0)	1,88, ddd (13,0, 1,0, 6,0)	6,07, dd (J_{ee}=5,0, J_{ae}=6,0)	$CDCl_3$
	3,0—3,6, m	1,6—2,0, m	4,60, br	CD_3OD†
	3,6—3,9, m	1,8—2,2, m	6,02, dd (J_{ee}=5,0, J_{ae}=6,0)	d7-DMF*

*The signals of the cyclic form are presented.
†The sample decomposes when the solution is allowed to stand.

It is noteworthy that the presence of a salicylyl substituent attached to the $N_{(1)}$ atom promotes ring opening in polar aprotic solvents (DMF, DMSO) and the development in the mixture of the corresponding linear tautomer, viz., the β-hydrazino aldehyde (see the scheme), in analogy with the previously noted case of ring-chain tautomerism of 1-benzoyl-2-benzyl-5-hydroxypyrazolidine [8]. Additional triplet signals of the protons of the aldehyde group (II, 9.80 ppm, 1.5 Hz; III, 9.80 ppm, 1.4 Hz; IV, 9.40 ppm, 1.5 Hz) and broadened singlet signals of the NH protons (II, 9.80 ppm; III, 9.40 ppm; IV, 9.80 ppm) appear in the PMR spectra (d_7-DMF) in this case. Bands of vibrations of an aldehyde carbonyl group at ~1700 cm^{-1} are observed in the IR spectra (solutions in DMSO). According to the PMR spectral data, the percentage of the linear form in the tautomeric mixtures does not exceed 20%.

Thus the results that we obtained regarding the relationship between the SSCC and chemical shifts of the protons of the pyrazolidine ring can be used to determine the structures and three-dimensional structures of functionally substituted pyrazolidines and similarly constructed compounds.

EXPERIMENTAL

The PMR spectra were recorded with a Tesla BS-497 spectrometer (100 MHz), and ^{13}C NMR spectra were recorded with a CFT-20 spectrometer with hexamethyldisiloxane (HMDS) as the internal standard. The IR spectra of solutions in $CHCl_3$ and DMSO were obtained with a Specord 75-IR spectrometer. Monitoring of the purity of the compounds obtained and the course of the reactions was accomplished on Silufol plates in chloroform—methanol (20:1) and benzene—ethyl acetate (2:3) systems (development by means of iodine vapors).

The salicyclic acid hydrazides were obtained by the method in [9] by refluxing equimolar amounts of methyl- and isopropylhydrazine with methyl salicylate.

1-Salicylyl-2-alkyl-5-hydroxypyrazolidines. A 30-mmole sample of the alkenal was added to a solution of 10 mmole of the corresponding hydrazide in 10 ml of ether, and the mixture was stirred at room temperature for 10 min. The ether and excess alkenal were removed *in vacuo*, and the residue was washed repeatedly with heptane and dissolved in 30 ml of ether. The solution was cooled to −70°C, and the liberated crystals were removed by filtration. The compounds were obtained in 80-90% yields.

1-Salicylyl-2-methyl-5-hydroxypyrazolidine (II). This compound had mp 70°C (decomp.). Found: C 59.6; H 6.5; N 12.5%. $C_{11}H_{14}N_2O_3$. Calculated: 59.5; H 6.4; N 12.6%.

1-Salicylyl-2-isopropyl-5-hydroxypyrazolidine (III). This compound had mp 84°C (dec.). Found: C 62.6; H 7.4; N 11.0%. $C_{13}H_{18}N_2O_3$. Calculated: 62.4%; H 7.3; N 11.2%. ^{13}C NMR

TABLE 5. Coordinates of the Atoms ($\cdot 10^4$; $\cdot 10^3$ for the H Atoms) and Their Equivalent Isotropic (Isotropic for the H Atoms) Temperature Factors $B_{iso}^{eq} = \frac{1}{3}\Sigma\Sigma B_{ij} a_i^* a_j^* (\vec{a}_i \vec{a}_j)$

Atom	x	y	z	B_{iso}^{eq} or B_{iso}, A^2
$O_{(1)}$	2744(4)	4907(3)	−568(2)	4,49(7)
$O_{(2)}$	−901(4)	5008(3)	2857(3)	4,43(7)
$N_{(1)}$	2239(4)	3749(3)	1485(3)	3,37(7)
$N_{(2)}$	2880(4)	2553(3)	2377(3)	3,38(7)
$C_{(1)}$	3136(5)	3803(3)	160(3)	3,59(9)
$C_{(2)}$	4605(7)	2457(5)	−439(5)	4,90(1)
$C_{(3)}$	2944(5)	3198(4)	3714(4)	3,81(9)
$C_{(4)}$	2505(6)	4859(4)	3450(4)	4,0(1)
$C_{(5)}$	1251(5)	5045(3)	2310(4)	3,72(9)
$C_{(6)}$	5011(8)	2698(5)	4230(6)	6,0(2)
$C_{(7)}$	1631(5)	1394(3)	2452(3)	3,34(8)
$C_{(8)}$	52(6)	1409(4)	1707(4)	4,8(1)
$C_{(9)}$	−1048(6)	228(4)	1819(5)	5,6(1)
$C_{(10)}$	−556(6)	−957(4)	2671(5)	5,2(1)
$C_{(11)}$	1026(7)	−971(4)	3394(5)	5,4(1)
$C_{(12)}$	2160(7)	187(4)	3274(4)	4,9(1)
$H_{(02)}$	−141(6)	503(4)	199(5)	6,0(9)
$H_{(2.1)}$	476(7)	253(5)	−134(6)	8(1)
$H_{(2.2)}$	399(9)	158(7)	0(5)	10(1)
$H_{(2.3)}$	563(9)	234(6)	10(6)	9(2)
$H_{(3)}$	187(5)	295(3)	437(3)	3,7(7)
$H_{(4.1)}$	166(5)	539(4)	430(4)	4,4(7)
$H_{(4.2)}$	393(5)	520(4)	313(3)	4,4(7)
$H_{(5)}$	138(4)	588(3)	167(3)	3,0(6)
$H_{(6.1)}$	496(8)	3321(6)	525(6)	9(1)
$H_{(6.2)}$	613(8)	300(5)	352(5)	8(1)
$H_{(6.3)}$	530(8)	170(7)	454(6)	10(1)

spectrum ($CDCl_3$), ppm: 19.8 [$(CH_3)_2CH$], 31.2 [$C_{(4)}$], 48.9 [$CH(CH_3)_2$], 56.7 [$C_{(3)}$], 83.1 [$C_{(5)}$], 120-157 (Ar), and 188.3 (C=O). Test results showed that the preparation displays moderate anti-inflammatory activity (Department of Pharmacology, Leningrad Institute of Pharmaceutical Chemistry).

1-Salicylyl-2-isopropyl-3-methyl-5-hydrozypyrazolidine (IV). This compound was obtained in the form of an oil. Found: C 63.8; H 7.9; N 10.4%. $C_{14}H_{20}N_2O_3$. Calculated: C 63.6; H 7.6; N 10.6%.

1-Acetyl-2-phenyl-3-methyl-5-hydroxypyrazolidine (I). This compound was obtained in the form of triclinic crystals with the following unit cell parameters at 20°C: a = 6.4936(5), b = 9.2607(4), c = 9.8671(4) Å, α = 87.029(3), β = 79.390(5), γ = 79.978(5)°, V = 574.2(1) Å^3, d_{calc} = 1.274 g/cm^3, Z = 2, space group P_1.

The cell parameters and intensities of 1565 independent reflections with $F^2 \geq 3\sigma$ were measured with a Hilger-Watts four-circle automatic diffractometer (λ Cu K_α, graphite monochromator, θ/2θ scanning, θ ≤ 66°).

The structure was decoded by the direct method by means of the MULTAN program and was refined by the total-matrix method of least squares, initially within the isotropic approximation and then within the anisotropic approximation. The hydrogen atoms were ascertained objectively in differential synthesis and were included in the refinement within the isotropic approximation [except for the hydrogen atoms of the benzene ring, which were placed in the geometrically calculated positions and included in the refinement with fixed positional and temperature (B_{iso} = 6.0 Å^2) parameters]. The final R factor was 0.068 (P_ω = 0.087). All of the calculations were made with an Eclipse S/200 computer by means of the INEXTL program [10]. The coordinates of the atoms and their temperature factors are presented in Table 5.

LITERATURE CITED

1. K. N. Zelenin, A. V. Dovgilevich, I. P. Bezhan, G. A. Golubeva, L. A. Sviridova, L. V. Pastushenkov, E. G. Gromova, T. A. Gatchina, and S. V. Pomogaibo, Khim. Geterotsikl. Soedin., No. 5, 659 (1984).
2. I. P. Bezhan, K. N. Zelenin, and V. V. Pinson, Zh. Org. Khim., 27, 493 (1982).
3. B. Fuchs, "Conformations of five-membered rings," in: Topics in Stereochemistry, E. L. Eliel and N. L. Allinger, eds., Vol. 10, Wiley, New York (1978), p. 1.

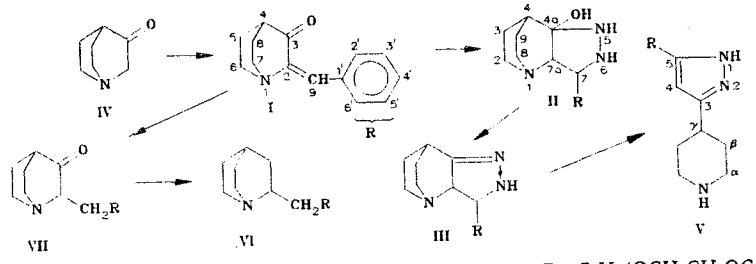
4. N. S. Zefirov and N. M. Shekhtman, Usp. Khim., 40, 593 (1971).
5. A. J. Kirby, The Anomeric Effects and Related Stereoelectronic Effects at Oxygen, Springer-Verlag, Berlin (1983), p. 149.
6. S. F. Nelson and J. M. Buschek, J. Am. Chem. Soc., 96, 6982 (1974).
7. S. F. Nelson and J. M. Buschek, J. Am. Chem. Soc., 96, 6987 (1974).
8. K. N. Zelenin, A. V. Dovgilevich, and I. P. Bezhan, Khim. Geterotsikl. Soedin., No. 10, 1422 (1983).
9. M. C. E. Carron, A. F. Jullien, M. Peron, and N. Y. M. H. Letterob, French Patent No. 1,336,069; Chem. Abstr., 60, 2865d (1964).
10 R. G. Gerr, A. I. Yanovskii, and Yu. T. Struchkov, Kristallografiya, 28, 1029 (1983).

SYNTHESIS, STRUCTURE, AND PROPERTIES OF PYRAZOLO[4,3-b]QUINUCLIDINE DERIVATIVES

K. F. Turchin, A. D. Yanina, T. Ya. Filipenko,
E. E. Mikhlina, Yu. N. Sheinker, and L. N. Yakhontov UDC 547.834.4'771.2:543.422.25

It was shown by means of ^{1}H and ^{13}C NMR spectroscopy that the reaction of 2-arylmethylene-3-oxoquinuclidines with hydrazine hydrate gives 4a-hydroxy-7-aryl-4a,5,7,7a-tetrahydropyrazolo[4,3-b]quinuclidines, which are stable in the crystalline state but undergo dehydration to the corresponding 7-aryl-6H-7,7a-dihydropyrazolo[4,3-b]quinuclidines in solutions. The latter undergo cleavage to 3-(4-piperidyl)-5-arylpyrazoles when they are heated in an alkaline medium.

We have previously shown that the reactions of 2-arylmethylene-3-oxoquinuclidines with hydrazine hydrate lead to 7-aryl-6H-7,7a-di-hydropyrazolo[4,3-b]quinuclidines [1]. In expanding our research in this direction we have accomplished the synthesis of new 2-arylmethylene-3-oxoquinuclidines (I), have studied their reaction with hydrazine hydrate under various conditions, and have established the structure of the resulting compounds, viz., 4a-hydroxy-7-aryl-4a,5,7,7a-tetrahydropyrazolo[4,3-b]quinuclidines (II), the products of the transformation of which are 7-aryl-6H-7,7a-dihydropyrazolo[4,3-b]-quinuclidines (III). We also investigated the properties of these substances.



I, II, V, VI, VII a R=$C_6H_3(OCH_3)_2$-3,4, b R=$C_6H_4OCH_3$-4, c R=$C_6H_4(OCH_2CH_2OC_6H_5)$-4, d R=$C_{10}H_7$-1; I, II, III e R=C_6H_4Cl-2; III c R=$C_6H_4(OCH_2CH_2OC_6H_5)$-4; VI f R=$C_6H_3(OH)_2$-3,4, g R=C_6H_4OH-4

Unsaturated ketones Ia-e were synthesized by condensation of 3-oxoquinuclidine (IV) with the corresponding aromatic aldehydes in the presence of sodium hydroxide [2, 3]. The structures of ketones I — individual geometrical isomers Ia-c,e and a mixture of Id isomers — were confirmed by data from the ^{1}H and ^{13}C NMR spectra (Table 1). The configurations of ketones Ia-c,e were established on the basis of the spectra recorded in aqueous acetone

S. Ordzhonikidze All-Union Scientific-Research Institute of Pharmaceutical Chemistry, Moscow 119021. Translated from Khimiya Geterotsiklicheskikh Soedinenii, No. 9, pp. 1248-1256, September, 1985. Original article submitted October 1, 1984.

