SYNTHESIS AND STRUCTURE OF 5-HYDRAZINO- AND 5-HYDROXYAMINO-3-ARYL-2-PYRAZOLINES AND -2-ISOXAZOLINES

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It was established by the methods of ^{1}H and ^{13}C NMR spectroscopy that the oximohydrazones and bis(hydrazones) of aroylacetic aldehydes exist in the form of the corresponding 5-hydrazino- and 5-hydroxyamino-3-aryl-2-pyrazolines and -2-isoxazolines. The features of the aromatization of these compounds to the corresponding pyrazoles and isoxazoles were studied. Data on the mass-spectral study of the 5-hydroxyamino-2-pyrazoline-5-hydrazino-2-isoxazoline tautomerism in the gas phase are presented.

We previously found that the products of the condensation of aliphatic 1,3-dioxo compounds with hydrazides in the 1:2 ratio are 5-hydrazino-2-pyrazolines [1, 2] and the "oximohydrazones" of acetylacetone – 5-hydrazino-2-isoxazolines [3]. The tautomerism of the two 5-hydrazino-2-pyrazoline rings [4] or 5-hydroxyamino-2-pyrazoline – 5-hydrazino-2-isoxazoline [5] – was observed for some of them.

There was no information on the structure of the bis(hydrazones) and oximohydrazones of the aromatic 1,3-dicarbonyl compounds. Of these, only the isomeric aldo- and ketooximosemicarbazones of benzoylacetic aldehyde were known [6].

The present communication is dedicated to the investigation of the reaction of hydrazides and hydroxylamine with aromatic 1,3-dioxo compounds (dibenzoylmethane benzoylacetone, aroylacetic aldehydes).

It was shown that the reaction of acetyl- and benzoylhydrazine with (dibenzoylethane and benxoylacetone is limited by the formation of the monosubstitution product – the corresponding 3,5-disubstituted 5-hydroxy-1-acyl-2-pyrazoline [7-9]. The change of the conditions (heating, acid catalysis, variation of the solvent) did not lead to the disubstitution products, but only to the corresponding 3,5-disubstituted pyrazoles and the 1,2-diacylhydrazines. The action of the same hydrazides on the oximes of dibenzoylmethane and benzoylacetone likewise did not give the desired result.

In contrast, benzoylacetic aldehyde readily gives 1-acyl-5-hydrazino-3-phenyl-2-pyrazolines (IIIa) and (IIIc) with acet- and benzhydrazide.

The monohydrazones, semicarbazone, and oximes of aroylacetic aldehydes (Ia-j) also react with the hydrazides (IIa-c), the semicarbazide (IId), and the hydroxylamine (IIe) with the formation of the compounds (IIIa-o) (Table 1); they include the isomeric pairs (IIIℓ)-(IIIn), (IIIm)-(IIIo) and the derivative (IIId) with different acyl substituents. It should be noted that if the reaction between the compounds (Ic) and (IIa) is performed even with insignificant heating, the products of "symmetrization" (IIIa) and (IIIc) start to accumulate besides the compound (IIId) both in DMSO and in ethanol.

The difference in the reactivity of benzoylacetic aldehyde and its derivatives from the aromatic diketones is evidently associated with the varying structure of their monohydrazones and monooximes. The corresponding derivatives of dibenzoylmethane and benzoyllacetone occur virtually completely in the 5-hydroxy-2-pyrazoline or -2-isoxazoline form [7-9], whereas the same derivatives of benzoylacetic aldehyde show the tendency to exist in the form of

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TABLE 1. Characteristics of the Synthesized Compounds (IIIa-ℓ), (IIIn)

Compound*	Empirical formula	R	X	Y	mp, °C (from pyridine)**	Yield, %***
IIIa	$C_{13}H_{16}N_4O_2$	H	$NCOCH_3$	$NCOCH_3$	167...168	70 (50)
IIIb	$C_{15}H_{14}N_6O_2$	H	$NCOCH_2CN$	$NCOCH_2CN$	192...193	80
IIIc	$C_{23}H_{20}N_4O_2$	H	$NCOC_6H_5$	$NCOC_6H_5$	204...205	95 (60)
IIId	$C_{18}H_{18}N_4O_2$	H	$NCOC_6H_5$	$NCOCH_3$	190...191	25
IIIe	$C_{24}H_{22}N_4O_2$	*p*-CH_3	$NCOC_6H_5$	$NCOC_6H_5$	175...176	85
IIIf	$C_{23}H_{19}BrN_4O_2$	*p*-Br	$NCOC_6H_5$	$NCOC_6H_5$	205...207	90
IIIg	$C_{23}H_{19}N_5O_6$	*p*-NO_2	$NCOC_6H_5$	$NCOC_6H_5$	190...192	90
IIIh	$C_{23}H_{19}N_5O_6$	*m*-NO_2	$NCOC_6H_6$	$NCOC_6H_6$	192...194	90
IIIi	$C_{24}H_{22}N_4O_3$	*p*-OCH_3	$NCOC_6H_5$	$NCOC_6H_5$	188...191	90
IIIj	$C_{11}H_{13}N_3O_2$	H	O	$NCOCH_3$	139...141	65
IIIk	$C_{12}H_{12}N_4O_2$	H	O	$NCOCH_2CN$	154...155	60
IIIℓ	$C_{16}H_{15}N_3O_2$	H	O	$NCOC_6H_5$	130...131	70
IIIn	$C_{16}H_{15}N_3O_2$	H	$NCOC_6H_5$	O	180...183	75

*For (IIIm), R = H, X = O, and Y = $NCONH_2$; for (IIIo), R = H, X = $NCONH_2$, and Y = O.

**The compounds were recrystallized as follows: (IIIa,j) from methanol, (IIId) from the 1:1 mixture of acetonitrile–pyridine, (IIIk) from acetonitrile, and (IIIℓ) from the 1:1 mixture of benzene–hexane.

***The yield of the reaction of the hydrazide with benzoylacetic aldehyde is presented in brackets.

TABLE 2. PMR Spectra of the Compounds (IIIa-o)

Compound	δ, ppm (SSCC J, Hz) in DMF-D7*			
	4-H (2H)	5-H (1H)	NH (OH) (1H+1H)	other signals **
IIIa***	3,50 & 3,30, ABX-system (18,5; 9,3; 4,2)	5,55 (2,5)	5,80 d.d (6,0; 2,5); 9,29 d (6,0)	1,70 (3H, s, CH_3); 2,20 (3H, s, CH_3)
IIIb	3,85 & 3,55, ABX-system (19,0; 9,7; 3,8)	5,88	Not localized 9,35 broad s	3,76 (2H, s, CH_2); 4,30 (2H, s, CH_2)
IIIc	3,56 d (6,5)	5,92 t.d (6,5; 2,5)	6,25 d.d (6,0; 2,5); 9,75 d (6,0)	—
IIId	3,56 d (6,5)	5,69 t.d (6,5; 2,5)	6,15 d.d (6,0; 2,5); 10,0 d (6,0)	2,20 (3H, s, CH_3)
IIIe	3,60 d (6,5)	5,92 t.d (6,5; 2,5)	6,41 d.d (5,0; 2,5); 10,03 (5,0)	2,27 (3H, s, CH_3)
IIIf	3,62 d (6,5)	5,92 t.d (6,5; 2,0)	6,41 d.d (5,5; 2,0); 10,0 d (5,5)	—
IIIg	3,71 d (6,5)	6,03 t.d (6,5; 2,5)	6,48 d.d (6,0; 2,5); 10,05 d (6,0)	—
IIIh	3,70 d (6,5)	5,96 t.d (6,5; 2,5)	6,40 d.d (6,0; 2,5); 10,06 d (6,0)	—
IIIi	3,59 d (6,5)	5,91 t.d (6,5; 2,5)	6,40 d.d (5,5; 2,5); 10,01 d	3,76 (3H, s, CH_3)
IIIj	3,22 & 3,51, ABX-system (18,0; 10,0; 5,0)	5,47 (1,0)	6,25 d.d (3,0; 1,0); 6,76 d (3,0)	2,03 (3H, s, CH_3)
IIIk	3,29 & 3,40, ABX-system (18,0; 10,0; 5,0)	5,56	6,23 broad s; not localized	4,25 (2H, s, CH_2)
IIIℓ	3,23 & 3,59, ABX-system (18,5, 10,0; 4,5)	5,71	6,34 broad s; not localized	—
IIIm	3,25 & 3,62, ABX-system (16,0; 9,0; 5,0)	5,37	6,17 broad, s; not localized	6,60 (2H, s, NH_2)
IIIn	3,19 & 3,47, ABX-system (18,0; 8,0, 4,0)	5,62	4,90 d (6,0); 7,91 d (6,0)	—
IIIo	3,05 & 3,48, ABX-system (17,0; 9,0, 6,0)	5,45	5,89 d (6,0); 7,13 d (6,0)	6,0 (2H, s, NH_2)

*The PMR spectra were taken at 26°C and at 140°C for (IIIb), and −40°C for (IIIj); the solvent was DMSO-D_6 for (IIIb,ℓ,o) $(CD_3)_2CO$ for (IIIj), and $CDCl_3$ for (IIIn).

**The H_{arom} signals lie in the region of 7.0...8.3 ppm.

***The mixture of the stereoisomers is on account of the restricted rotation about the N–CO bond in the exocyclic acetamide grouping; the content of the minor form E does not exceed 8% (1.98; 2.31, s, CH_3).

TABLE 3. ^{13}C NMR Spectra of the Compounds (IIIc, j, ℓ, m, o)

Compound	δ, ppm (in DMSO-D_6)*			
	$C_{(3)}$, s	$C_{(4)}$, t	$C_{(5)}$, d	C=O, s
IIIc	155,6	29,5	72,5	166,3; 166,6
IIIj	154,4	35,7	73,7	168,9
IIIℓ	155,5	35,0	75,1	166,2
IIIm	151,3	35,9	74,1	155,8
IIIo	156,4	36,7	92,8	160,5

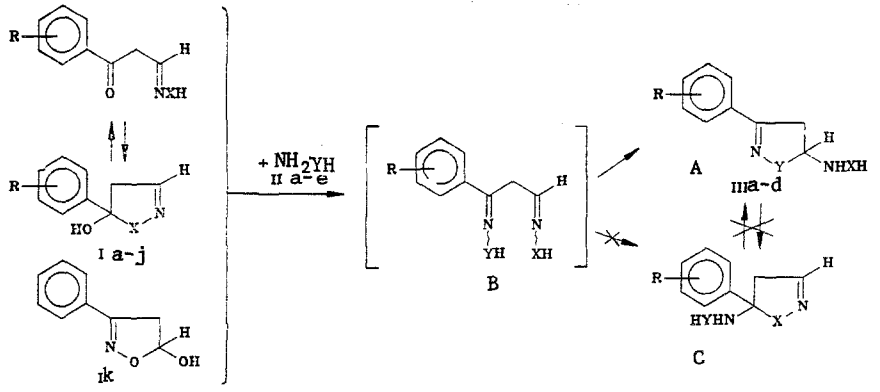
*The C_{arom} signals of the compounds (IIIc,ℓ-o) lie in the range of 125...134 ppm. The quartet of the methyl group of the compound (IIIj) occurs at 21.7 ppm.

TABLE 4. Mass Spectra of the Compounds (IIIa, c, d, j, ℓ, n) and (IVa-f)

Compound	m/z (I_{rel}, %)*
IIIc	**260** (1), 188 (6), 187 (53), 146 (19), 145 (100), 144 (11), 118 (14), 104 (5), 91 (8), 77 (13), 42 (30)
IIIc	249 (9), 149 (11), 105 (100), 97 (7), 85 (8), 78 (14), 77 (43), 71 (10), 60 (10), 42 (22)
IIId	**322** (1), 249 (3), 187 (45), 186 (3), 145 (100), 144 (18), 136 (4), 118 (8), 105 (42), 77 (30), 42 (13)
IIIj	**219** (7), 187 (19), 161 (3), 159 (6), 145 (100), 144 (6), 118 (5), 104 (4), 91 (4), 71 (10), 43 (19)
IIIℓ	281 (13), 265 (5), 249 (28), 248 (4), 223 (3), 146 (6), 144 (4), 105 (100), 77 (33), 51 (6), 43 (6)
IIIn	**281** (0,9), 147 (11), 146 (89), 136 (30), 118 (18), 117 (3), 105 (100), 91 (8), 78 (8), 77 (64), 51 (15)
IVa	**233** (0,1), 201 (3), 161 (4), 136 (16), 106 (11), 105 (93), 98 (100), 77 (51), 56 (67), 43 (33), 42 (12)
IVb	**278** (0,2), 246 (10), 181 (13), 150 (44), 134 (4), 120 (8), 104 (18), 98 (100), 76 (14), 56 (78), 43 (49)
IVc	139 (43), 138 (31), 137 (21), 123 (100), 82 (12), 56 (28), 55 (17), 51 (16), 42 (43), 41 (38)
IVd	**185** (1), 153 (33), 152 (46), 151 (9), 137 (100), 123 (14), 109 (65), 96 (10), 68 (15), 42 (43), 41 (36)
IVe	167 (12), 126 (75), 101 (29), 86 (65), 85 (60), 84 (100), 83 (65), 82 (57), 71 (73), 43 (50)
IVf	214 (21), 213 (15), 199 (13), 126 (18), 91 (100), 77 (40), 84 (51), 57 (32), 55 (42), 43 (62)

*The 10 most intense peaks are presented; the m/z values of the molecular ions are distinguished by the semi-fat type.

linear tautomers [8, 10, 11]. It is probable that the formation of the bis-derivatives (III) is preferably achieved due to the reaction of the hydrazides with the carbonyl group of the last, and not by the substitution of the hydroxyl group in their cyclic isomers.



I a R=H, X=NCOCH$_3$; b R=H, X=NCOCH$_2$CN; c R=H, X=NCOC$_6$H$_5$; d R=H, X=NHCONH$_2$; e R=H, X=O; f R=*p*-CH$_3$, X=NCOC$_6$H$_5$; g R=*p*-Br, X=NCOC$_6$H$_5$; h R=*p*-NO$_2$, X=NCOC$_6$H$_5$; i R=*m*-NO$_2$, X=NCOC$_6$H$_5$; j R=*p*-OCH$_3$, X=NCOC$_6$H$_5$; II a Y=NCOCH$_3$; b Y=NCOCH$_2$CN; c Y=NCOC$_6$H$_5$; d Y=NCONH$_2$; e Y=O

TABLE 5. Intensity of the Characteristic Ions and the Tautomeric Composition in the Mass Spectra of the Compounds (IIIa, c, d, j, ℓ, n) and (IVa-f) (%Σ_{40})

Compound	W_M	Intensity of the peaks							Tautomeric form, %*		
		Φ_1 (Φ_1 – $-CH_2CO$)**	Φ_2	Φ_3 (Φ_3')	Φ_4 (Φ_4')***	Φ_5	Φ_7	Φ_8 (Φ_8')	A	B	C
IIIa	0,3	16,8 (31,9)	0,6	0,5	—	—	—	9,8	100	—	—
IIIc	—	2,3	0,9	1,0	—	—	—	25,0	100	—	—
IIId	0,3	13,1 (29,4)	1,0	1,0	—	0,7	0,1	16,0	95	—	5
IIIj	3,2	7,4 (83,4)	0,5	—	0,9	0,5	—	7,4	85	10	5
IIIℓ	4,8	9,4	1,3	—	1,0	0,5	1,6	33,5	78	7	15
IIIn	0,3	22,0	0,5	—	2,8 (0,1)		—	24,7	89	11	—
IVa	<0,1	0,7	—	(3,5)	0,8	21,1	0,6	19,8	3	3	94
IVb	<0,1	2,1	—	(2,8)	0,9 (1,8)	21,4	0,8	9,4	8	10	82
IVc	—	9,3	6,8	—	—	—	—	—	100	—	—
IVd	0,2	7,0	9,8	—	—	0,3	0,6	—	95	—	5
IVe	—	1,2	—	—	0,2 (0,3)	7,5	0,4	5,3	13	5	82
IVf	—	—	3.0	0.7	0.3	2.6	—	14.4	51	5	44

*$A = \frac{\Phi_1+\Phi_2+\Phi_3}{\Sigma\Phi_i}\cdot 100\%$; $B = \frac{\Phi_4+\Phi_5}{\Sigma\Phi_i}\cdot 100\%$; $C = \frac{\Phi_6+\Phi_7}{\Sigma\Phi_i}\cdot 100\%$.

**Moreover, the (Φ_1 – CH_3) and (Φ_2 – CH_3) ions are observed for the compounds (IVc, d); Σ = 24.8% for (IVc), and Σ = 23.4% for (IVd).

***The (M – C_2H_2NOH) ion for the compound (IVf).

TABLE 6. Chemical Ionization Mass Spectra (i-C_4H_{10}) of the Compounds (IIIa, c, j) and (Va-c, f)

Compound	m/z (I_{rel}, %)
IIIa*	278 (16) $(M+NH_4)^+$, 261 (35) MH^+, 204 (4), 187 (100)
IIIc*	385 (35) MH^+, 249 (100), 105 (16), 77 (3)
IIIj	220 (16) MH^+, 202 (4), 187 (100), 160 (7), 145 (75)
IVa	234 (24) MH^+, 201 (24), 98 (100)
IVb	279 (21) MH^+, 241 (21), 182 (5), 98 (100)
IVc	172 (20) MH^+, 139 (100), 138 (22), 83 (8)
IVf	248 (67) MH^+, 215 (100), 214 (38), 147 (5), 126 (14), 123 (8), 83 (14)

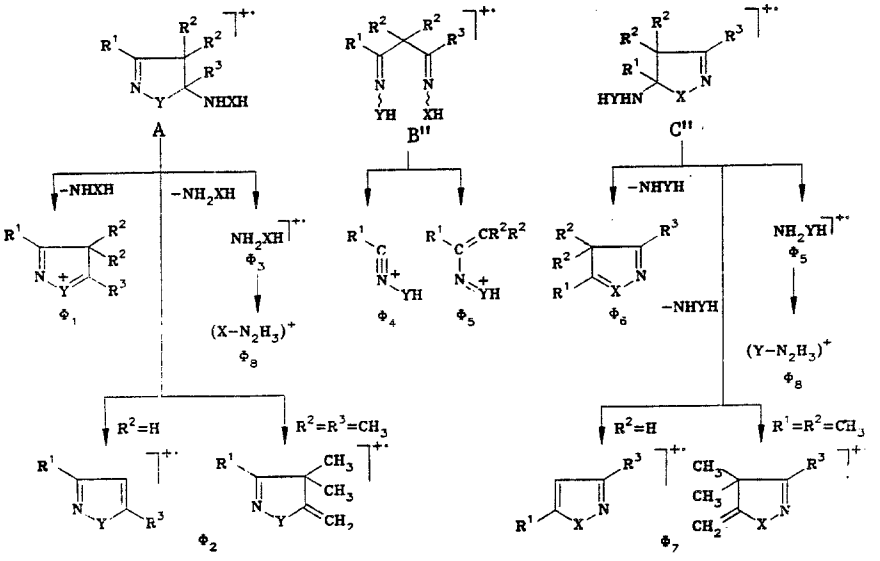
*Gas reagent ammonia.

The compounds (IIIa-o) exist in the single cyclic form A in different solvents (DMF-D_7, DMSO-D_6, pyridine-D_5, CD_3OD, acetone-D_6, $CDCl_3$), and do not exhibit the tendency for the transition to the linear (the hydrazone B or the enehydrazine) or other cyclic isomer C in the temperature range of –40...140°C.

The form in which the compounds (IIIa-o) occur does not depend on the nature of the initial hydrazides and the carbonyl component or the mutual disposition of the oxime and hydrazone groups in the compounds (IIIℓ-o), but is determined by steric factors. Only the isomer in which the aryl substituent occurs in the position 3 of the heterocycle occurs.

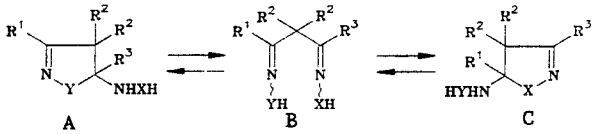
The cyclic structure A for all the compounds (IIIa-o) obtained follows unambiguously from the NMR spectral data: the characteristic CS and the doublet character of the sp^3-hydridized $C(_5)$ atom in the ^{13}C NMR spectra, the low-field CS of 5-H and the nature of its splitting, particularly the presence of the SSCC between 5-H and NH (it could only be found at a decreased temperature in some cases), in the PMR spectra, the existence of the ABX-system for the compounds (IIIa, b, j-o), and other details (Tables 2 and 3).

The analysis of the mass spectra of the compounds (IIIa, c, d, j, ℓ, n) (Tables 4 and 5) shows that good conformity between their tautomeric forms predominating in the solutions and in the gas phase is observed. The decomposition of the molecular ions of these compounds* proceeds selectively, whereby the ions characterizing the primary fragmentation of each of the three possible tautomeric forms of the M^+ ion are frequently present in the spectra. Thus, the Φ_1, Φ_2, and Φ_3 ions are associated with the decomposition of the tautomeric form A, whereas the formation of the Φ_4 and Φ_5 ions is specific for the fragmentation of the form B. Finally, the Φ_3, Φ_6, and Φ_7 ions give the best match for the characteristics of the tautomeric form C of the molecular ion.



It follows form the data in Table 5 that the most intense peaks in the mass spectra of the compounds (IIIa, c, d, j, ℓ, n) are those of the Φ_1† and Φ_2 ions in almost all cases; this indicates the preferential (exclusive) existence of their molecular ions in the form A. However, the high sensitivity of the method of mass spectrometry evidently also permits the detection of the compounds (IIIj) and (IIIℓ) in the second cyclic tautomeric form of the molecular ion C in the gas phase. Moreover, insignificant amounts of the molecules with the linear structure B are also present in the vapors of the compounds (IIIj, ℓ, n). We performed the quantitative evaluation of the ratios of the tautomeric forms in the gas phase starting from the assumptions that the intensities of the peaks of the characteristic Φ_1–Φ_7 ions are proportional to the shares of the corresponding forms of the molecular ions in the mass spectrum. It should be noted that the ratio of the A and C forms only changed from 95:5 to 94:6 when the energy of the ionizing electrons decreased from 70 to 18 eV in the case of the compound (IIId); this excludes the possibility of the processes of tautomeric conversions in the molecular ions which have already been formed.

Therefore, the mass spectral data indicate that the most stable form of the compounds (III) in the gas phase, as well as in their condensed state, is the tautomeric form A, which contains the aryl residue in the position 3 of the hetero ring.



IV a-f $R^1=R^3=CH_3$; a,b $R^2=H$, c-f $R^2=CH_3$; a-f X=O; a Y=$NCOC_6H_5$, b Y=$NCOC_6H_4$—*p*-NO_2, c Y=NCH_3, d Y=NC_2H_5, e Y=$NCH(CH_3)_2$, f Y=$NCH_2C_6H_5$

*The stability of the molecular ions of the 5-hydroxyamino-2-pyrazolines (IIIj, ℓ) is appreciably higher than that of the 5-hydrazino-2-pyrazolines (IIIa, c, d).

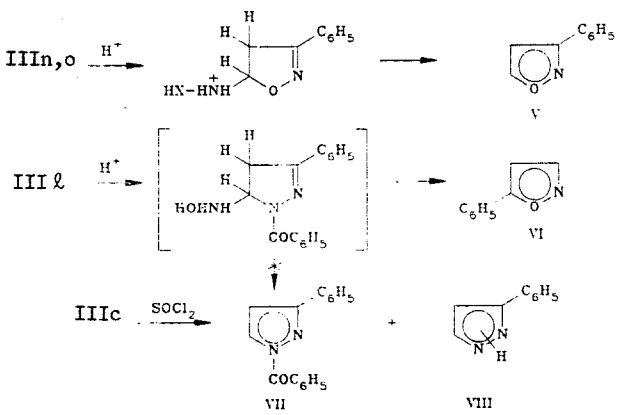
†In the chemical ionization mass spectra of the compounds (IIIa, c) (Table 6), the peak of the Φ_1 ion is maximal; this indicates in favor of the protonation of the molecule exclusively at the exocyclic nitrogen atom in the gas phase.

The comparison of these data with the results of the mass spectral investigation obtained analogously, and previously described [3, 5], for the oximo-N-acyl(alkyl)hydrazones of acetylacetone (IVa, b) and dimethylacetylacetone (IVc-f) indicates that the first two of them exist mainly in the isoxazoline form C in the gas phase and in solution. The same form predominates in the vapors of the partly sterically hindered monoisopropylhyrazone of the monooxime of 3,3-dimethyl-2,4-pentane-dione (IVe), whereas the pyrazoline structures A of the molecular ion are more stable for the N-methyl- (Vc), N-ethyl- (IVd), and N-benzyl- (IVf) hydrazones of the same monooxime.

The scheme of the decomposition of the compounds (III) and (IV), which we presented, was confirmed by the analysis of the mass spectra of the deutero-labeled compounds (IIj, ℓ) and (IVa), the high-resolution mass spectra of (IVa), as well as the DADI mass spectra of the compounds (IIIj) and (IVc).

As can be seen from Table 4, the molecular ions in the electron-impact mass spectra of the compounds (IVa-f) are not registered, or their peaks have very low intensity; this is evidently associated with their low stability. The mass spectra of the compounds (IVa-c,f) under the conditions of chemical ionization (reagent gas isobutane) were obtained to confirm the presence of the molecules of these compounds in the gas phase of the mass spectrometer (Table 6). In all cases, we observed the intense peaks of the protonated molecular ions; this excluded any thermal conversions of the compounds which we investigated when they were vaporized in the ionization chamber of the mass spectrometer. It is important to emphasize that the same form of the molecular ion with the electron impact is identified under the conditions of such "mild ionization" in the gas phase. In the case of the compounds (IVa) and (IVb), it is mainly the isoxazoline form C (C:A = 5:1), and in the case of the compounds (IVc) and (IVf), it is mainly the pyrazoline form A [100% of (IVc), and 88% of (IVf)]. On the basis of the analysis of chemical-ionization mass spectra, we come to the conclusion that the exocyclic nitrogen atom is mainly protonated in the MH^+ ion [as in the case of the compounds (IIIa, c)] since the MH^+ ion eliminates the corresponding acylhydrazine in the case of the compounds (IVa, b), and hydroxylamine is eliminated in the case of the compounds (IVc, f). Therefore, the molecular ions formed by electron impact or chemical ionization in the ionization chamber of the mass spectrometer have mainly the same tautomeric form as occurs in the crystalline form or in the solutions of non-polar solvents, i.e., the state of the ring-chain tautomeric equilibrium of the nitrogen derivatives of 1,3-dicarbonyl compounds in non-polar solvents may be predicted on the basis of the analysis of their mass spectra.

It is well known that the ionization is accomplished by the bombardment of the target by ions of heavy atoms with high energy in the taking of the secondary-ion mass spectra (SIMS), whereby the molecules of the sample being analyzed pass into the gas phase without heating, simultaneously (or subsequently) being ionized [12]. We investigated the mass spectrometric behavior of compound (IVc), for which a shift of the tautomeric equilibrium in favor of the more polar pyrazoline form A is observed in the DMSO solutions, using the method of SIMS. When the polar matrix of thioglycerol was utilized, we observed the appearance of the ion at m/z 126, which is formed from the MH^+ ion as the result of the elimination of a molecule of methylhydrazine and indicates the presence of the molecular ion less polar than the isoxazoline form C in the gas phase (according to our evaluation, its share reached 14-15%), besides the protonated molecular ions and the Φ_1 ions characterizing their pyrazoline tautomeric form. The taking of the mass spectra by the method of SIMS thereby allows the prediction of the character of the shift of the tautomeric equilibrium of the investigated system in polar solvents.



The possibilities of the utilization of the substances (III) for the synthesis of pyrazoles and isoxazoles were investigated taking the typical examples of the compounds (IIIc, ℓ, n, o). The behavior of these derivatives was studied in the solutions of CF_3COOH. Under these conditions, the protonation proceeds at the α-exocyclic nitrogen atom of the form A; this is indicated by the low-field CS of the 5-H signal in the PMR spectrum by comparison with the spectrum of the free base ($\Delta\delta \sim 0.2$-0.5 ppm) and the data of the mass spectral investigations. Further, the cations of the 5-hydrazino-2-isoxazolines (IIIn, o) undergo aromatization to one and the same 3-phenylisoxazole (V), the structure of which was shown by the PMR and ^{13}C NMR spectra (Experimental). This conforms with the data [6] on the aromatization of the derivative (IIIo).

At first sight, the conversion of 1-benzoyl-5-hydroxylamino-3-phenyl-2pyrazoline (IIIℓ) completely to the previously described [6] 5-phenylisoxazole (VI) in the acid medium appeared unexpectedly; this should correspond with the aromatization of the form C. However, this is readily explained if the principal possibility of the ring-ring tautomerism A ⇄ C [4] is taken into account; this is also indicated by the mass spectral data presented above.

As a result of the aromatization of the form A by the action of $SOCl_2$, 5-hyrazino-2-pyrazoline (IIIc) was converted to 1-benzoyl-3-phenylpyrazole (VII) with the yield of 40%; (VII) was obtained by direct synthesis (Experimental). The 3(5)-phenylpyrazole (VIII) accompanied it. The tendency of the acyl-pyrazoles to lose the acyl group is known [13]. Therefore, it is not surprising that only the formation of the pyrazole (VIII) was observed in the experiments on the aromatization of the derivative (IIIc) and other 5-hydrazino-2-pyrazolines by the action of CF_3COOH.

The results obtained on the aromatization should be considered in regard to the reaction of hydrazines and hydroxylamine with 1,3-dioxo compounds, in which the possibility of the intermediate formation of the bis derivatives was not previously taken into account.

EXPERIMENTAL

The PMR spectra were obtained on a Tesla BS-497 spectrometer (100 MHz) for the 5% solutions of the substances; the external and internal standard was HMDS. The ^{13}C NMR spectra were taken on the CFT-20 (20 MHz) and Tesla BS-497 (20.41 MHz) instruments for the 25% solutions of the substances under conditions of the complete suppression of the spin-spin interaction of the protons with the carbon atoms, and without the uncoupling from the protons.

The electron-impact mass spectra were obtained on a Varian MAT-212 instrument at the energy of 70 eV with the introduction of the substance at the ion source. The chemical ionization mass spectra were taken on the AEI MS-30 instrument at the energy of 100 eV. The mass spectra of the metastable ions were taken on the Varian MAT-311A instrument by the DADI method. The high-resolution mass spectra were obtained on the same instrument. The secondary-ion mass spectra were taken on the Hitachi M-80A instrument utilizing a beam of the Xe^+ bombarding ions with the energies of 5-10 keV in a matrix of glycerol or thioglycerol.*

The compounds (Ia-c, f-j) were obtained by the methods of [8, 10]; (Id, e) were obtained according to [6]. The data of the elemental analysis of the previously undescribed compounds correspond with the calculated values.

1-Acyl-5-hydrazino-3-aryl-2-pyrazolines (IIIa-i). The mixture of 10 mmole of the monohydrazone of the aroylacetic aldehyde (Ia-c, f-j) and 10 mmole of the hydrazide (Ia-c) in 5 ml of DMSO with several drops of CF_3COOH was kept for 1 day. The mixture was poured into 50 ml of water, and the precipitated residue was filtered off, washed with water, dried, and recrystallized. In the case of the compounds (IIIa, d), the reaction was performed in abs. ethanol, and the product was precipitated in the residue. The compounds (IIIa, c) were also obtained by the reaction of 10 mmole of benzoylacetic aldehyde with the two-fold amount of the hydrazide (IIa) in methanol.

1-Acyl-5-hydroxyamino-3-phenyl-2-pyrazolines (IIIj, k, ℓ). The equimolar amounts (50 mmole) of the compounds (Ie) and (IIa, c) were boiled in 200 ml of benzene until the release of water ceased. The solvent was removed, and the residue was crystallized. The compound (IIIℓ) separated out in the form of a residue on maintaining the solution of the substance (Ie) and (IIb) in 200 ml of methanol with a catalytic amount of acid in the course of a week.

*We express thanks to the collaborator of the VASKhNIL, V. L. Sadovskaya, for the taking of the SIMS.

The compounds (IIIm, o) were obtained according to the method of [6]. The derivative (IIIn) was isolated in the reaction of 5-hydroxy-3-phenyl-2-isoxazoline [14] with benzhydrazide by analogy with the synthesis of the 5-hydrazino-2-pyrazolines (IIIb-i).

3- and 5-Phenylisoxazoles (V) and (VI) [6]. The solution of 5 mmole of the compound (IIIℓ, n, o) in the mixture of 10 ml of chloroform and 1 ml of CF_3COOH was kept for 1 day; the volatile components were removed, and the residue was extracted with CCl_4.

Compound (V). An oil with the R_f 0.53 (benzene/Silufol). The PMR spectrum (acetone-D_6) was as follows: 6.91 ppm (1H, d, J = 2.0 Hz, 4-H), 7.3-8.0 ppm (5H, m, H_{arom}), and 8.72 ppm (1H, d, J = 2.0 Hz, 5-H). The ^{13}C NMR spectrum (acetone-D_6) was as follows: 102.6 ppm (d, C(4)), 160.0 ppm (s, C(3)), and 130-140 ppm (C_{arom} and C(5) – 5 signals).

Compound (VI). An oil with the R_f 0.43 (benzene/Silufol). The PMR spectrum (acetone-D_6) was as follows: 6.85 ppm (1H, d, J = 2.0 Hz, 4-H), 7.3-8.0 ppm (5H, m, H_{arom}), and 8.45 ppm (1D, d, J = 2.0 Hz, 3-H).

1-Benzoyl-3-phenylpyrazole (VII). A. To the solution of 10 mmole of 3(5)-phenylpyrazole in 25 ml of pyridine were added, in the course of 15 min, 10 mmole of benzoyl chloride; the mixture was stirred for 1 h, and was poured into 100 ml of a 10% solution of HCl. The mixture was extracted with ether, and the extract was dried over Na_2SO_4. After the removal of the solvent, the residue was recrystallized. The yield was 60%. The mp was 84-85°C. The PMR spectrum ($CDCl_3$) was as follows: 6.85 and 8.47 ppm (2H, d, J = 3.0 Hz, 4-H and 5-H) and 7.3-8.3 ppm (10H, m, H_{arom}).

B. To the suspension of 10 mmole of the compound (IIIc) in 30 ml of benzene was added, in the course of 20 min, the solution of 20 mmole of thionyl chloride in 20 ml of benzene, and the mixture was stirred for 1 h. The volatile components were removed in vacuo; the residue was extracted with ether, and the solvent was removed. The pure product (VII) was isolated after the fourfold recrystallization from hexane.

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