Method A. Equimolar amounts of freshly sublimed isoindole Ic, d and N-substituted maleinimide IIa-e were stirred at room temperature in absolute ether (or ethyl acetate), after which the reaction mixture was maintained at the same temperature for several hours. When necessary, the solvent was removed by distillation in vacuo. The precipitated crystals were removed by filtration, and the adduct was purified by crystallization from alcohols (ethanol, isopropyl alcohol) or by column chromatography on silica gel (elution with chloroform).

Method B. A mixture of equimolar amounts of freshly sublimed isoindole and the N-substituted maleinimide was refluxed in isopropyl alcohol. The time required to complete the reaction was determined by means of TLC. The precipitate was removed by filtration and purified by recrystallization from acetonitrile or alcohols (ethanol, isopropyl alcohol).

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STUDY OF THREE-DIMENSIONAL STRUCTURES OF BENZOYLPYRIDINE OXIMES AND THEIR ETHERS BY ^{1}H and ^{13}C NMR SPECTROSCOPY

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The ^{1}H and ^{13}C NMR spectra of the E and Z isomers of 2-, 3-, and 4-benzoylpyridine oximes and their ethers were analyzed thoroughly, and the ^{1}H-^{13}C spin-spin coupling constants (SSCC) were determined. It was established that the magnitude of the γ effect for the quaternary carbon atoms in the E and Z isomers depends on the site of substitution in the pyridine ring. It was assumed that the intermolecular hydrogen bond is stronger in the E form than in the Z form. The existence of the Z isomer of 2-benzoylpyridine oxime in deuterochloroform with an intramolecular hydrogen bond was proved.

It is generally known that spatial isomerism in many cases determines the biological activity of molecules, as well as the strength and degree of its selectivity. The determination of the configurations of various oximes by NMR spectroscopy is widely used in organic chemistry. The chemical shifts of certain carbon atoms (the γ effect) and the ^{13}C-^{13}C and ^{15}N-H spin-spin coupling constants (SSCC) are characteristic criteria for the assignment of E and Z isomers (for example, see [1-3]).

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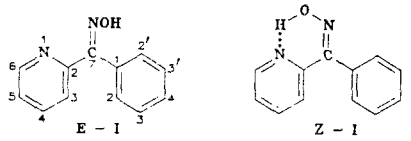
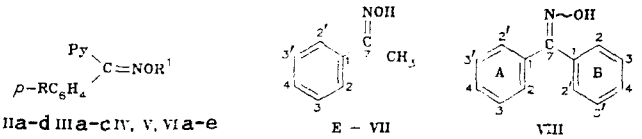
TABLE 1. ^1H Chemical Shifts (δ, ppm) of Benzoylpyridine Oximes and Their Ethers in d_6-DMSO–CCl_4

Compound	Isomer	Pyridine ring					Benzene ring			OH
		2-H	3-H	4-H	5-H	6-H	2,2′-H	3,3′-H	4-H	
I	E	—	7,90	7,76	*	8,46	7,10 ... 7,20			11,60
	Z	—	7,53	7,85	*	8,66	7,10 ... 7,20			11,50
I*1	E	—	7,54	7,66	7,25	8,62	7,30 ... 7,50			9,90
	Z	—	7,33	7,80	*	8,66	7,30 ... 7,50			14,30
IIa	Z	8,48	—	7,70	7,45	8,57	7,30 ... 7,45			11,50
IIb	E	8,61	—	7,73	*	8,52	7,30	7,61	—	10,60
	Z	8,50	—	7,70	7,44	8,58	7,35	7,50	—	10,70
IIb*1	E	8,79	—	7,73	*	8,59	7,30	7,61	—	9,95
	Z	8,68	—	7,76	7,43	8,67	7,32	7,48	—	9,52
IIc	E	8,61	—	7,73	*	8,54	7,35 ... 7,55		—	11,90
	Z	8,52	—	7,70	*	8,58	7,35 ... 7,55		—	11,80
IId	E	8,62	—	7,69	7,25	8,52	7,40	7,15	—	11,70
	Z	8,51	—	7,68	*	8,57	7,44	7,04	—	11,60
IId*1	E	8,80	—	7,73	7,20	8,58	7,20 ... 7,40		—	11,20
	Z	8,69	—	7,77	7,45	8,66	7,20 ... 7,40		—	11,80
IIIa	Z	8,72	7,33	—	7,33	8,72	7,3 ... 7,5			11,80
IIIb	E	8,50	7,34	—	7,34	8,50	7,24	7,61	—	11,90
	Z	8,64	7,25	—	7,25	8,64	7,31	7,47	—	11,70
IIIc*2	E	8,49	7,33	—	7,33	8,49	6,95	7,30	—	11,62
	Z	8,62	7,23	—	7,23	8,62	6,81	7,23	—	11,24
IV	E	—	7,85	7,45	*	8,49	7,30 ... 7,45			—
	Z	—	7,57	7,92	*	8,66	7,30 ... 7,45			—
V	E	8,60	*	7,66	7,38	8,56	7,33	7,63	—	—
	Z	8,57	*	7,76	7,48	8,61	7,37	7,54	—	—
VIa	Z	8,68	7,32	—	7,32	8,68	7,36	7,58	—	—
VIb	E	8,57	7,34	—	7,34	8,57	7,25	7,66	—	—
	Z	8,67	7,30	—	7,30	8,67	7,32	7,57	—	—
VIc	E	8,60	7,35	—	7,35	8,60	7,30	7,70	—	—
	Z	8,70	7,35	—	7,35	8,70	7,30	7,60	—	—
VId*3	E	8,58	7,38	—	7,38	8,58	7,00	7,36	—	—
VIe*4	Z	8,65	7,27	—	7,27	8,65	6,89	7,32	—	—

*Overlapping of the signals.
*1The spectrum was recorded in $CDCl_3$.
*2$Z\ OCH_3$ 3.77 ppm; $\delta_E\ OCH_3$ 3.82 ppm.
*3$\delta_E\ OCH_3$ 3.84 ppm.
*4$\delta_Z\ OCH_3$ 3.62 ppm.

The aim of the present research was an investigation of the three-dimensional structures of 2-, 3-, and 4-benzoylpyridine oximes I, IIa-d, and IIIa-c and the salts of their ethers IV, V, and VIa-e on the basis of data from the ^1H and ^{13}C NMR spectra. The synthesis and study of the pharmacological activity of I, IIa-d, IIIa, b, IV, V, and VIa-c were previously accomplished in [4]. The E isomer (VII) of acetophenone oxime and benzophenone oxime (VIII) were used as model compounds.





II Py=**3-pyridyl** a R=R¹=H; b R=Br, R¹=H; c R=Cl, R¹=H; d R=F, R¹=H. III Py=**4-pyridyl** a R=R¹=H; b R=Br, R¹=H; c R=OCH_3, R¹=H. IV Py=**2-pyridyl** R=H, R¹=$CH_2CH(OH)CH_2NHCH(CH_3)_2$. V Py=**3-pyridyl** R=Br, R¹=$(CH_2)_2N(CH_3)_2$. VI Py=**4-pyridyl** a R=Br, R¹=$(CH_2)_2N(CH_3)_2$; b R=Br, R¹=$CH_2CH(OH)CH_2NH$–$C(CH_3)_3$; c R=Br, R¹=$CH_2CH(OH)CH_2NHCH(CH_3)_2$; d R=$OCH_3$, R¹=$CH_2CH(OH)CH_2NHCH(CH_3)_2$; e R=$OCH_3$, R¹=$CH_2CH(OH)CH_2NHC(CH_3)_3$.
IV — **maleate** V **and** VIa-e — **oxalates**

TABLE 2. ^{13}C Chemical Shifts (δ, ppm) of Benzoylpyridine Oximes and Their Ethers in d_6-DMSO—CCl_4

Compound	Isomer	Pyridine ring					Benzene ring				$C_{(7)}$
		$C_{(2)}$	$C_{(3)}$	$C_{(4)}$	$C_{(5)}$	$C_{(6)}$	$C_{(1)}$	$C_{(2,2')}$	$C_{(3,3')}$	$C_{(4)}$	
I	E	155,17	121,47	136,03	123,00	148,37	132,76	129,43	127,24	127,91	155,19
	Z	152,54	125,21	135,87	128,40	149,05	135,80	126,84	127,86	127,70	154,31
IIa	Z	149,36	129,20	136,49	123,02	149,01	136,19	126,88	128,15	128,78	152,31
IIb	E	148,03	132,35	134,01	122,69	149,12	131,34	131,08	131,03	122,38	151,50
	Z	149,55	128,66	136,48	122,73	149,02	135,47	128,66	131,00	122,70	151,33
IIc	E	147,79	132,28	134,29	123,32	149,35	131,05	130,86	128,43	133,67	151,99
	Z	149,55	128,84	136,63	123,32	149,32	134,90	128,32	128,49	134,03	151,75
IId	E	148,06	132,77	134,31	122,94	149,18	128,48	131,36	115,03	162,23	152,43
	Z	149,51	129,15	136,67	123,01	149,06	132,64	128,98	115,12	162,80	151,79
IIIa	Z	149,71	123,62	141,35	123,62	149,71	135,21	126,67	128,50	129,18	153,26
IIIb	E	149,33	121,14	143,75	121,14	149,33	130,96	130,96	131,10	122,46	152,18
	Z	149,42	123,65	140,79	123,65	149,42	134,55	128,55	131,22	122,80	151,98
IIIc*1	E	149,54	121,48	144,55	121,48	149,54	123,89	130,60	113,59	159,51	153,05
	Z	149,54	123,59	141,64	123,59	149,54	127,76	128,08	113,88	160,11	152,85
IV	E	153,84	122,13	136,53	123,69	148,81	132,13	129,18	127,57	129,49	156,73
	Z	151,74	123,91	136,38	124,77	149,36	134,51	127,09	128,21	128,54	156,16
V	E	148,10	131,01	133,99	123,50	150,44	130,73	131,45	131,01	122,90	154,57
	Z	149,99	128,12	136,58	123,50	148,90	134,94	129,33	131,57	123,65	154,29
VIa	Z	149,84	123,12	139,90	123,12	149,84	133,18	129,05	131,50	123,72	154,35
VIb	E	149,90	121,27	142,29	121,27	149,90	130,42	130,92	131,35	123,44	153,66
	Z	149,78	123,19	140,02	123,19	149,78	133,33	128,88	131,55	122,74	153,52
VIc*2	E	149,79	121,34	142,34	121,34	149,78	130,35	130,94	131,38	123,56	153,87
	Z	149,75	123,21	139,75	123,21	149,75	133,34	128,95	131,38	122,88	153,73
VId*3	E	149,57	121,85	143,52	121,85	149,57	123,18	130,75	113,61	159,92	154,44
VIe*4	Z	149,62	123,14	140,89	123,14	149,62	126,36	128,49	113,62	160,70	154,52
VII (A)*5	E	—	—	—	—	—	137,34	125,68	128,19	128,39	153,08
VIII (A)	—	—	—	—	—	—	133,57	128,91	127,93	128,20	154,99
VIII (B)	—	—	—	—	—	—	136,85	126,99	127,93	128,08	

*1 $\delta_{E,Z}^{OCH_3}$ 55.11 ppm.

*2 The assignment of the signals was made in analogy with IIIb.

*3 $\delta_{E}^{OCH_3}$ 55.12 ppm.

*4 $\delta_{Z}^{OCH_3}$ 56.18 ppm.

*5 $\delta_{E}^{CH_3}$ 11 ppm.

TABLE 3. Spin-Spin Coupling Constants* $^{n}J_{CH}$ (Hz) of Benzoylpyridine Oximes in d_6-DMSO–CCl_4

Compound	Isomer	Pyridine ring														Benzene ring							
		$C_{(2)}$			$C_{(3)}$[2]			$C_{(4)}$[3]			$C_{(5)}$[4]		$C_{(6)}$				$C_{(1)}$[5]	$C_{(2,2')}$[6]		$C_{(3,3')}$		$C_{(4)}$		
		$^{1}J_{23}$	$^{4}J_{24}$	$^{3}J_{26}$	$^{1}J_{33}$	$^{2}J_{32}$	$^{3}J_{35}$	$^{1}J_{44}$	$^{3}J_{42}$	$^{3}J_{46}$	$^{1}J_{5,5}$	$^{2}J_{5,6}$	$^{1}J_{66}$	$^{2}J_{65}$	$^{3}J_{62}$	$^{3}J_{64}$	^{3}J	^{1}J	^{3}J	^{1}J	^{3}J	^{1}J	^{2}J	^{3}J
I	E	—	8,5	12,0	165,7	—	6,6	164,0	—	6,2	164,2	7,3	178,8	3,3	—	6,8	6,5	161,2	7,0	160,5	5,6	160,3	—	—
	Z	—	8,5	11,0	165,3	—	5,2	165,0	—	6,2	160,7	7,8	178,8	3,0	—	6,8	6,2	161,0	7,2	160,0	5,5	160,0	—	—
IIa	Z	188,7	6,0	12,1	—	—	—	166,2	5,5	6,5	166,7	8,9	188,0	3,7	11,1	6,9	7,6	162,0	6,0	161,0	8,5	160,7	0,6	7,5
IIb	E	180,5	5,7	11,3	—	—	—	162,8	5,4	6,9	160,0	8,2	179,0	3,0	11,5	6,9	7,7	166,6	7,0	169,0	—	—	3,2	11,0
	Z	180,7	6,1	10,7	—	7,0	7,0	166,6	5,0	6,4	167,8	8,2	179,0	3,0	11,1	6,9	7,4	163,0	6,6	164,0	—	—	2,9	10,8
IIc	E	180,1	6,3	11,6	—	7,0	7,0	162,7	6,0	6,0	165,3	8,5	180,0	*	*	*	7,7	164,3	7,5	163,0	—	—	3,1	10,8
	Z	180,0	—	—	—	7,3	7,3	165,6	5,9	5,9	165,3	8,5	180,0	*	*	*	6,9	163,0	—	163,0	—	—	3,0	9,3
IId[1]*	E	180,4	5,7	11,3	—	—	—	163,3	6,0	6,0	161,6	7,3	180,0	*	*	*	7,8	163,2	7,9	163,0	4,0	—	4,8	10,9
	Z	180,7	6,0	11,3	—	7,1	7,1	166,1	5,9	5,9	167,3	7,3	180,0	*	*	*	7,6	161,4	7,9	163,0	4,2	—	4,9	10,9
IIIa	Z	180,1	—	11,5	165,2	6,0	6,5	—	6,7	6,7	165,2	6,0	180,1	—	11,5	—	6,3	160,0		161,5	6,3	160,8	1,5	6,5
IIIb	E	181,3	—	10,1	160,0	*	6,0	—	6,4	6,4	160,0	6,0	181,3	—	10,1	—	7,8	166,0	—	166,0	—	—	—	—
	Z	181,3	—	10,1	160,0	*	6,0	—	6,4	6,4	160,0	6,0	181,3	—	10,1	—	7,5	165,7	6,8	166,7	—	—	3,0	9,5
IIIc	E	179,0	—	10,9	—	*	*	—	7,0	7,0	*	*	179,0	—	10,9	—	6,6	163,0	7,3	162,6	4,7	—	—	—
	Z	179,0	—	10,9	—	*	*	—	6,6	6,6	*	*	179,0	—	10,9	—	7,6	159,0	7,3	164,0	4,6	—	—	—

*The asterisks denote the impossibility of measuring the constants because of overlapping of the signals or insufficient resolution.

1* $^{1}J_{CF}$ = 248.2 and 249.0 Hz; $^{2}J_{CF}$ = 21.7 and 21.9 Hz; $^{3}J_{CF}$ = 7.9 and 8.0 Hz; $^{4}J_{CF}$ = 3.4 and 3.5 Hz for the E and Z isomers, respectively.

2* $^{4}J_{3,6}$ for IIb^{Z}, $IIc^{E,Z}$, IId^{Z}, and IIa^{Z} are 1.3, 1.5, 1.7, and 1.7 Hz, respectively.

3* $^{2}J_{4,5}$ for IIa^{Z}, IIb^{E}, and IIc^{E} are 1.0, 1.3, and 1.5 Hz, respectively.

4* $^{3}J_{5,3}$ for I^{EZ} are 7.3 and 7.8 Hz, respectively.

5* ^{4}J for IIa^{Z} is 4.4 Hz.

6* ^{3}J for IIa^{Z} and $I^{E,Z}$ are 7.0 Hz and 7.0 and 7.2 Hz, respectively.

TABLE 4. Difference in the Chemical Shifts δ_{E-Z} (ppm) of the Quaternary Carbon Atoms of the E and Z Isomers of Benzoylpyridine Oximes and Their Ethers in d_6-DMSO—CCl_4

Compound	Benzene ring	Pyridine ring			$C_{(7)}$
	$C_{(1)}$	$C_{(2)}$	$C_{(3)}$	$C_{(4)}$	
I	−3,04	2,62	—	—	0,88
IIb	−4,13	—	3,69	—	0,17
IIc	−3,85	—	3,44	—	0,24
IId	−4,16	—	3,62	—	0,64
IIIb	−3,59	—	—	2,96	0,20
IIIc	−3,87	—	—	2,91	0,20
IV	−2,38	2,10	—	—	0,57
V	−4,21	—	2,89	—	0,32
VIb	−2,91	—	—	2,27	0,14
VIc	−3,00	—	—	2,37	0,14

The parameters of the ^1H NMR spectra of the investigated compounds are presented in Table 1. The assignment of the signals of the pyridine region of oximes I and IIa-d was made taking into account the results of double-resonance experiments and the literature data on the chemical shifts and SSCC* of 2- and 3-substituted pyridines in d_6-DMSO [5]. The signals of the protons of the pyridine ring in oximes IIIa-c were identified on the basis of an analysis of their AA'XX' spectra. The assignment of the signals of the protons of the benzene ring in IIb-d and IIIb, c was made by means of an additive scheme [6]. Satisfactory agreement between the calculated and experimental values of the chemical shifts was obtained. In a number of cases, when the chemical shifts of the isomeric protons were close, the separation of the signals of the isomers was achieved by analysis of their integral intensities.

It should be noted (see Table 1) that the SSCC of the protons of the pyridine ring, as well as their chemical shifts, are virtually independent of the type of substituent in the benzene ring and the solvent ($CDCl_3$, d_6-DMSO—CCl_4, d_6-acetone). The dependence of the chemical shifts of the protons of the hydroxy groups of the E and Z isomers on the character of the solvent seems of interest. In deuterochloroform the signals of the hydroxy groups of oxime I are located at 14.3 and 9.9 ppm. The weak-field signal evidently corresponds to the Z isomer, since the formation of a sufficiently stable six-membered quasi-ring with an intramolecular hydrogen bond is possible only in this case. Raising the temperature does not cause a substantial shift of this signal to strong field. However, in solution in d_6-DMSO—CCl_4 the intramolecular hydrogen bond in I is destroyed, as evidenced by drawing together of the signals of the hydroxy groups. For all of the oximes in d_6-DMSO—CCl_4 the signals of the OH groups of the E isomer are shifted ~0.1 ppm to weaker field than in the case of the Z isomer; only IIb constitutes an exception. A similar regularity is observed in solutions in $CDCl_3$ for all of the oximes, but the difference in the chemical shifts of the protons of the OH groups of the E and Z isomers increases to 0.4 ppm.

Proceeding from the information set forth above one may make the preliminary assumption that a stronger intermolecular bond is formed in the E isomers, because in the case of the Z isomers, with the exception of the above-mentioned Z-oxime I, an intramolecular hydrogen bond cannot develop because of steric reasons.

The ^1H NMR spectra of the E and Z isomers of ethers IV-VI in the region of the signals of the protons of the pyridine and benzene rings are virtually the same as the spectra of the corresponding oximes.

Data from the ^{13}C NMR spectra of oximes I-III and their ethers IV-VI, as well as model compounds VII and VIII, are presented in Tables 2 and 3. The signals of the carbon atoms of the benzene rings were assigned on the basis of a comparison of their chemical shifts with the corresponding values for model oximes VII and VIII in the region of the A and B rings, in which the γ effect of the quaternary carbon atoms was traced distinctly. We also took into account literature data on monosubstituted benzenes [5-7]. The assignment of the sig-

*The SSCC of the compounds that we studied do not exceed the limits of the standard values and therefore are not presented in our paper.

nals of the carbon atoms of the pyridine rings was fraught with difficulties in a number of cases primarily because of the closeness of the chemical shifts of the isomers, although strictly the identification of the isomeric substances did not present any difficulty owing to the existence of the γ effect of the quaternary carbon atoms of the pyridine ring (Δδ 2.0-3.5) (Table 4). The difficulties in the assignment of each individual signal of a carbon atom of the pyridine ring were overcome by joint analysis of the ^1H-^{13}C SSCC (see Table 3), by comparison of them with the literature data [5], and in some cases by means of experiments involving 2DHC-correlation spectroscopy, since there were no doubts about the assignment of the signals of the corresponding protons. The chemical shift of the $C_{(7)}$ atom has a certain correlation dependence on the E,Z configuration of oximes I-III. Thus, the signal of the indicated atom for the E isomer is located at weaker field. In addition, in the case of oximes I-III the signals of the $C_{(7)}$ atoms are shifted to strong field in the order I > III > II. This effect is insignificant for ethers IV-VI.

Let us note that the spectral characteristics of benzoylpyridine oxime ethers IV-VI are almost identical to the corresponding values for oximes I-III. The observed (by us) tendency for a decrease in the difference in the chemical shifts of some carbon atoms of the pyridine and benzene rings in the E and Z isomers of the oximes and their ethers on passing from the 3-pyridyl-substituted to the 4- and 2-pyridyl-substituted compounds is noteworthy (see Table 4); as a rule, the difference $\Delta\delta_{E-Z}$ for the oxime is greater than for the corresponding ether. In the case of the Z and E isomers of the oximes and their ethers for the $C_{(1)}$ atom of the benzene ring we were able to find a simple relationship between the chemical shifts of the isomers: $\delta C_{(1)}^{E} = 1.04\ \delta C_{(1)}^{Z} = 8.69$ ($r = 0.967$, $s = 0.67$).

EXPERIMENTAL

The ^1H NMR spectra of 5-10% solutions of the compounds in d_6-DMSO/CCl_4, $CDCl_3$, and $(CD_3)_2CO$ were recorded with Bruker T-60, HA-100, and AC-250 spectrometers with tetramethylsilane (TMS) as the internal standard. The ^{13}C and two-dimensional $^1H/^{13}C$ NMR spectra of 20-25% solutions in d_6-DMSO/CCl_4 were obtained with an AC-250 spectrometer with TMS as the internal standard. The POWGATE, GATEHET, and XHCORR automatic programs, respectively, which enter into the standard packet of Bruker microprograms, were used for recording the ^{13}C resonance signals in the experiments with complete spin-spin decoupling of the protons, the high-resolution experiments, and in the two-dimensional spectra.

The results of elementary analysis of the synthesized compounds for C, H, and N were in agreement with the calculated values.

4-(4-Methoxybenzoyl)pyridine Oxime (IIIc, $C_{13}H_{12}N_2O_2$). A solution of 5.2 g (0.075 mole) of hydroxylamine hydrochloride in 6 ml of water was added to a solution of 5.3 g (0.025 mole) of 4-(4-methoxybenzoyl)pyridine in 50 ml of alcohol, after which a solution of 2.5 g (0.0625 mole) of NaOH in 3.5 ml of water was added dropwise, and the mixture was refluxed for 4 h. The reaction mass was evaporated, the residue was treated with water, and the precipitate was removed by filtration to give 5.5 g (96%) of oxime IIIc with mp 139-140°C (from alcohol).

4-(4-Methoxybenzoyl)pyridine Oxime 2-Hydroxy-3-isopropylaminopropyl Ether oxalate (VId, $C_{19}H_{25}N_3O_3 \cdot 2C_2H_2O_4$). A solution of 2.28 g (0.01 mole of oxime IIIc in 8 ml of DMF was added to a suspension of 0.7 g (0.02 mole) of 80% sodium hydride in 2 ml of dry DMF, after which the mixture was stirred for 30 min. A 6.3-g (0.063 mole) sample of epichlorohydrin was then added, and the mixture was stirred for 4 h (~20°C). The reaction mass was diluted with water, and the aqueous mixture was extracted with ether. The extract was dried over $MgSO_4$ and evaporated, and the residue (2 g of an oil) was dissolved in 10 ml of alcohol. A 2.07-g (0.035 mole) sample of isopropylamine was added, and the mixture was refluxed for 23 h. It was then diluted with water, the aqueous solution was decanted, and the oily residue was dissolved in 10% HCl. Activated charcoal was added to the acidic solution, the mixture was filtered, and the filtrate was made alkaline with 10% NaOH solution. The alkaline solution was extracted with benzene, and the extract was dried and evaporated to give 1.66 g of VId with mp 156-157°C (from alcohol).

4-(4-Methoxybenzoyl)pyridine Oxime 2-Hydroxy-2-tert-butylaminopropyl Ether oxalate (VIe, $C_{20}H_{27}N_3 \cdot 0.5C_2H_2O_4$). This compound, with mp 148-149°C (from alcohol), was obtained by a method similar to that used to prepare oxalate VId.

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CHARACTERISTICS OF HETEROCYCLIZATION OF TRIKETONES OF THE 2-(3-OXOPROPYL)CYCLOHEXANE-1,3-DIONE SERIES WITH HYDROXYLAMINE HYDROCHLORIDE

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A rearrangement that leads to the formation of mixtures of 2,4- and 2,3-diaryl-substituted 5-oxotetrahydroquinoline oximes was observed in the heterocyclization of oxo 1,5-diketones of the 2-(3-oxopropyl)cyclohexane-1,3-dione series, as well as in the recyclization of 5-oxotetrahydro-4H-chromenes, in the presence of excess hydroxylamine hydrochloride. It was established that the rearrangement proceeds only when electron-donor groups are present in the starting compounds.

According to the literature data [1], 2-(1,3-diphenyl-3-oxopropyl)cyclohexane-1,3-dione (Ia) on reaction with excess hydroxylamine hydrochloride is converted to 2,4-diphenyl-5-oxo-5,6,7,8-tetrahydroquinoline oxime (IIIa), which under acid-hydrolysis conditions (25% sulfuric acid) forms two tautomeric 5-oxotetrahydroquinolines. However, the character of the tautomerism was not ascertained.

We have reproduced this reaction in accordance with [1]. It was established that 2,3-diphenyl-5-oxo-5,6,7,8-tetrahydroquinoline oxime (IVa) [2] is formed along with the expected 2,4-diphenyl-5-oxo-5,6,7,8-tetrahydroquinoline oxime (IIIa). The acidic hydrolysis of oxime IVa gave 2,3-diphenyl-5-oxo-5,6,7,8-tetrahydroquinoline (VIa), which in [1] was erroneously assumed to be a tautomer of ketone Va. Thus, we have observed the previously unknown rearrangement of triketone Ia during its reaction with excess hydroxylamine hydrochloride.

In order to ascertain the general character of the observed rearrangement, as well as its possible mechanism, we made a systematic study of the reactions of oxo 1,5-diketones Ia-h and 5-oxotetrahydro-4H-chromenes IIa, c, h with hydroxylamine hydrochloride in absolute ethanol (see top of following page).

We found that the reaction of oxo 1,5-diketones Ia-g with a threefold molar excess of hydroxylamine hydrochloride is accompanied by heterocyclization with simultaneous oximation of the third carbonyl group. In each case oxo 1,5-diketones Ia-g react with hydroxylamine to give mixtures of two isomeric oximes – 2,4-diaryl- (IIIa, g) and 2,3-diaryl-5-oxo-5,6,7,8-tetrahydroquinolines (IVa-g).

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