REACTION OF β-OXONITRONES — IMIDAZOLINE AND PYRROLINE DERIVATIVES — WITH NUCLEOPHILIC REAGENTS

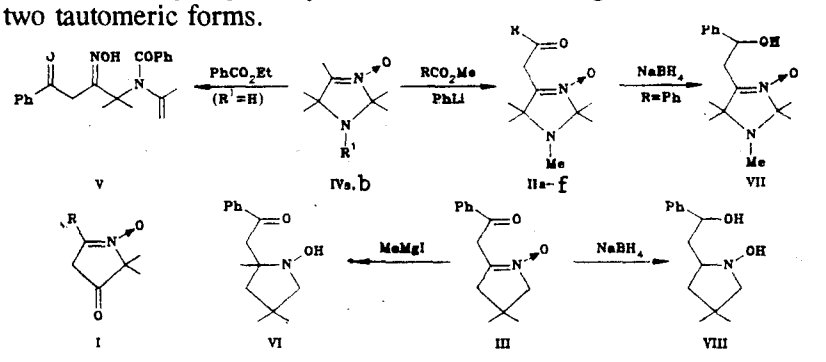
V. A. Reznikov and L. B. Volodarskii

UDC 547.781.3:541.515

The reaction of β-oxonitrones — imidazoline derivatives — with hydroxylamine, phenylhydrazine, and semicarbazide takes place at the carbonyl group with retention of the nitrone group. Stable nitroxyl radicals — spiroimidazoisoxazole derivatives — are formed in the oxidation of β-hydroximinonitrones. The recyclization of the β-oxonitrones, which takes place in an acidic medium, as well as by the action of hydrazine and thiosemicarbazide, leads, respectively, to pyrroline and pyrazole derivatives.

In a previous study of the properties of 2-substituted 5,5-dimethyl-4-oxo-1-pyrroline 1-oxides I — cyclic β-oxonitrones — it was shown that their reaction with nucleophilic reagents may take place either at the nitrone group or at the carbonyl group [1]. In the present research we examined the reaction of β-oxo nitrones, in which the oxonitrone group is included in part in the composition of the imidazoline (II) and pyrroline (III) heterorings, with nucleophilic reagents.

Compounds II were obtained by condensation of imidazoline IVa with esters in the presence of phenyllithium [2]. It should be noted that, under similar conditions, the reaction of imidazoline IVb with ethyl benzoate leads to opening of the imidazoline heteroring to give acyclic V, which, according to the PMR data, exists in solution in the form of a mixture of two tautomeric forms.



II a R=H, b R=CH_3, c R=C_6H_5, d R=α nitrone e R=CF_3, f R=$C(CH_3)_3$; IV a R¹=CH_3, b R¹=H

In contrast to the reaction of β-oxonitrones of the pyrroline I series, the reaction of β-oxonitrones II with methylmagnesium iodide and methyllithium, which was studied in the case of IIc, does not lead to the formation of addition products. At the same time, the reaction of pyrroline III with methylmagnesium iodide leads to addition at the nitrone group to give VI. The reaction of imidazoline IIc with $NaBH_4$ leads to alcohol VII, while pyrroline III under similar conditions undergoes reduction at both the carbonyl and nitrone groups to give VIII. It should be noted that compounds of the VII type can be obtained by condensation of imidazoline IVa with aldehydes in the presence of phenyllithium [2]. The fact that the nitrone group in the composition of the imidazoline IIc molecule does not react with $NaBH_4$ and methylmagnesium iodide is evidently associated with its greater steric shielding as compared with the nitrone group in the composition of the pyrroline III heteroring [3].

Oximes IXa-c,g and X, respectively, are formed in the reaction of imidazolines IIa-c, as well as imidazoline IIg, obtained by the method in [2], and pyrroline III with hydroxylamine (see Tables 1 and 2). The reaction of imidazoline IId with hydroxylamine also leads to oxime IXd, attempts to isolate which in the individual analytically pure form were unsuccessful. On the basis of the ^{13}C NMR spectra of the compounds obtained it was established that oximes IX exist in several isomeric and tautomeric forms.

Novosibirsk Institute of Organic Chemistry, Siberian Branch, Academy of Sciences of the USSR, Novosibirsk 630090. Translated from Khimiya Geterotsiklicheskikh Soedinenii, No. 7, pp. 912-919, July, 1991. Original article submitted December 15, 1988; revision submitted June 20, 1990.

 0009-3122/91/2707-0722$12.50

TABLE 1. Characteristics of the Synthesized Compounds

Compound	Structure-formula	T_{pl}, °C*	IR spectra (KBr) ν, см⁻¹	UV spectra (ethanol), λ_{max}, nm (lg ε)	Yield, %
IIb	$C_{11}H_{20}N_2O_2$	90...91	1590...1660 (O=C—C=C—N)**	233 (4,13), 320 (4,02)	50
IIg	$C_{20}H_{24}N_2O_2$	103...105	1580...1650 (O=C—C=C—N)**	217 (4,71), 343 (4,11)	70
IIf	$C_{14}H_{26}N_2O_2$	82...84	1590...1690 (O=C—C=C—N)**	233 (3,81), 317 (3,69)	60
V	$C_{22}H_{24}N_2O_3$	178...179	1560...1615 (C=N, C=O)**	—	30
VI	$C_{15}H_{21}NO_2$	None	1690 (C=O), 3580 (OH)***	242 (3,53)	80
VIII	$C_{14}H_{21}NO_2$	76...77	3580 (OH)***	—	80
IXa	$C_{10}H_{19}N_3O_2$	129...131	1610, 1645 (C=N)	238 (4,09)	~100
IXb	$C_{11}H_{21}N_3O_2$	143...145	1600, 1660 (C=N)	236 (4,11)	80
IXc	$C_{16}H_{23}N_3O_2$	151...153	1510, 1615 (C=N), 3580 (OH)***	243 (4,21)	90
IXh	$C_{17}H_{25}N_3O_2$	155...157	1610 (C=N)	238 (4,11)	80
X	$C_{14}H_{18}N_2O_2$	104...106	1600, 1620 (C=N)	247 (4,16)	70
XIc	$C_{16}H_{22}N_3O_2$	136...138	1560, 1605 (C=C, C=N)	256 (4,16)	90
XIg	$C_{20}H_{24}N_3O_2$	130...132	1515, 1600 (C=C, C=N)	224 (4,63), 305 (4,0)	90
XIh	$C_{17}H_{24}N_3O_2$	97...99	1610 (C=N)	250 (4,13)	95
XII	$C_{23}H_{27}N_3O_3$	173...175	1760 (O—CO), 1605 (C=N)	220 (4,23), 234 (4,28), 263 (4,16)	90
XV	$C_{14}H_{16}N_2O_2$	88...90	1600, 1585 (C=N), 3110 (=CH—)	243 (4,25)	50
XVI	$C_{14}H_{16}N_2O_3$	223...224	1700 (C=O), 1600, 1560 (C=C, C=N)	261 (4,32)	20
XVIIa	$C_{17}H_{25}N_5O_2$	163...165	1710 (C=O), 1600 (C=C, C=N), 3160, 3220, 3330, 3470 (NH_2)	222 (4,32), 237 (4,20), 286 (4,20)	~100
XVIIb	$C_{22}H_{28}N_4O$	142...145	1575, 1590, 1610 (C=N, C=C), 3170 (NH)	236 (4,40), 303 (4,03), 347 (4,28)	~100
XVIII	$C_{17}H_{24}N_5O_2$	147...149	1705 (C=O), 1595 (C=N), 1620 (C=C), 3490, 3300, 3230, 3160 (NH_2)	288 (4,23)	50
XIXa	$C_{13}H_{16}N_3 \cdot HCl$	225...226	1580, 1595, 1615 (C=C, C=N), 2700...3000 ($^+$NH), 3200 (NH)	256 (4,30)	~100
XIXb	$C_{14}H_{18}N_4S \cdot HCl \cdot H_2O$	206...207	1530, 1550, 1600 (C=C, C=N), 2700...3000 ($^+$NH), 3190, 3300, 3415 (NH_2)	232 (4,32), 320 (4,40)	~100
XXc	$C_{13}H_{16}N_2O \cdot HCl \cdot H_2O$	171...173	1650, 1610, 1595, 1580 (C=C, C=N), 2700...3000 ($^+$NH)	264 (4,20)	30
XXf	$C_{11}H_{20}N_2O \cdot HCl$	238...239	1590 (C=C, C=N), 2700...3000 ($^+$NH)	217 (3,90)	20
XXI	$C_{13}H_{15}NO$	79...81	1700 (C=O), 1600 (C=C)	233 (4,18), 337 (3,88)	50
XXIIg	$C_{17}H_{18}N_2O$	247...249	1560, 1590, 1665 (C=C, C=N)	224 (4,90), 294 (4,18), 313 (4,19)	50
XXIId	$C_8H_{11}F_3N_2O$	125...126	1660, 1590 (C=N)	329 (4,08)	30

*The compounds were purified by recrystallization: IIb, f, XXI, and XXIIe from hexane, V, IXa, b, XVI, and XXc from ethyl acetate, VIII and XII from cyclohexane, IXc, X, XId, g, and XV from hexane—ethyl acetate (3:1), IXg from cyclohexane—ethyl acetate (1:1), XVIIa and XXIId from isopropyl acetate, XIXa from $CHCl_3$—isopropyl alcohol (1:1), XXf from ethanol—ethyl acetate (2:1). Compounds IId, VI, XIc, XVIIb, and XVIII were purified by chromatography.

**A broad band as a consequence of rapid intrachelate exchange between the tautomeric forms [2].

***The spectrum was obtained from a solution in CCl_4.

TABLE 2. PMR Spectra of 3-Imidazoline 3-Oxide Derivatives in d_6-DMSO

Compound	Chemical shifts, δ, ppm (SSCC, J Hz)				
	2-$(CH_3)_2$	5-$(CH_3)_2$	N—CH_3	—CH_2—	
IXa	1,28	1,13	2,30	3,30 (d J=5,0)	6,67 (1H, t, 5,0); 11,1 (1H, s NOH)
IXb*	1,27	1,12	2,29	3,22, 3,26 (br.s) 4,20	1,69 (3H, s, CH_3); 10,6 (1H, s, NOH); 10,4 (1H, s NOH)
IXc**	1,33	1,10	2,25		7,1...7,9 (5H, m, C_6H_5)
IXc***	0,98, 1,08, 1,13, 1,20		2,18	3,29 (form. A); 3,97 (form. B)	7,3...7,7 (5H, m, C_6H_5); 11,8 (1H, NOH)
IXh	0,58 (3H), 1,08 ((6H), 1,18 (3H)		2,12	3,80 (1H, q, J=7,0, $CHCH_3$)	1,18 (3H, d, J=7,0, $CHCH_3$); 7,1 (5H, m, C_6H_5); 10,55 (1H, s, NOH)
XII**	1,18 (3H), 1,30 (6H), 1,39 (3H)		2,32	3,14	7,2...8,1 (10H, m, $(C_6H_5)_2$)
XVIIa	1,20	0,96	2,21	3,80	6,4 (2H, br.s, NH_2); 7,3...8,0 (5H, m, C_6H_5); 10,2 (1H, br.s, NHCO)

*Mixture of E and Z isomers.
**The spectrum was recorded from a solution in $CDCl_3$.
***The spectrum was recorded from a solution in CCl_4.

TABLE 3. ^{13}C NMR Spectra of Imidazoline IX Derivatives in d_6-DMSO]

Compound	Form	Yield	Chemical shifts, δ, ppm							
			2,5-$(CH_3)_2$	N—CH_3	$C_{(2)}$	$C_{(4)}$	$C_{(5)}$	$C_{(6)}$	$C_{(7)}$	
IXa	A_E	85	23,2; 23,9	26,9	88,8	141,7	63,2	20,6	142,9	—
	A_Z	15	23,5; 24,6	—	—	—	—	—	143,2	—
IX b	A_E	60	23,9; 23,5	26,8	88,8	141,3	63,4	29,8	151,7	13,3 (CH_3C=NOH)
	A_Z	40	23,2	26,9	—	141,4	—	18,9	150,2	22,8 (CH_3C=NOH)
IX c	A	60	23,1; 23,4	26,3	88,6	141,6	63,4	19,3	152,0	125,5, 128,1, 128,9, 135,0 (C_6H_5)
	B	40	20,4; 20,7; 24,4; 24,6	27,0	78,0	108,4	61,0	35,9	154,5	125,9, 128,5, 129,3, 130,2 (C_6H_5)
IX d*	A	100	23,2; 23,5	26,4	89,3	146,0	64,1	19,9	152,4	125,9, 128,1, 129,0, 134,8 (C_6H_5)
IX h	A	100	22,5; 23,1; 23,8; 23,9	26,8	88,3	144,3	63,5	36,0	155,0	127,2, 127,5, 128,0, 135,5 (C_6H_5), 12,0 ($CHCH_3$)

*The spectrum was recorded from a solution in $CDCl_3$.

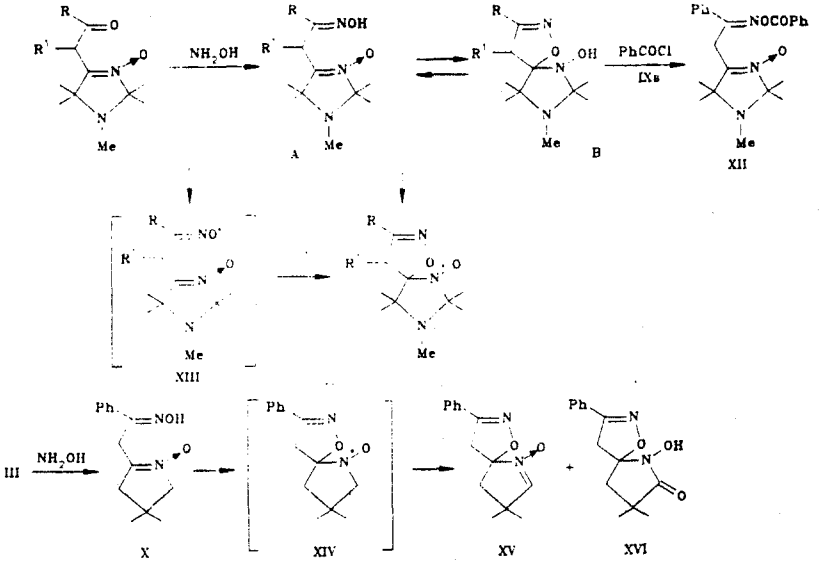
TABLE 4. PMR Spectra of Pyrrolidone Derivatives XX-XII in d_6-DMSO

Compound	Chemical shifts, δ, ppm *			
	5-$(CH_3)_2$	N—CH_3	3-H	Other protons
XX c	1,94	2,50	7,16	7,6 (5H, m, C_6H_5)
XXf	1,62	2,35	6,35	1,25 (9H, s $C(CH_3)_3$)
XXI	1,32	2,97	5,24	7,3...8,2 (5H, m, C_6H_5)
XXIIg	1,36	2,38	5,95	7,8 (7H, m, α), 9 55 (1H, s, NOH)
XXIId	1,27	2,82	5,80	9,83 (1H, s, NOH)

*The spectrum of XXI was recorded in solution in $CDCl_3$, while the spectrum of XXIIe was recorded in CCl_4.

Judging from the set of signals in the ^{13}C NMR spectra, IXa, b (see Table 3) consist of mixtures of E and Z isomers with respect to the oxime group, as evidenced by the presence in the spectra of two signals of $C_{(2)}$ and $C_{(5)}$ atoms vis-à-vis the absence of the signal at 100-120 ppm that is characteristic for the carbon atom of the $C_{(4)}$ spiro node in tautomeric form B. Signals of carbon atoms of only tautomeric form A are observed in the ^{13}C NMR spectrum of IXc in solution in $CDCl_3$, while signals that can be assigned to bicyclic tautomeric form B, as, for example, the signal at 108.4 ppm, which corresponds to the carbon atom of the $C_{(4)}$ spiro node, as well as four signals of carbon atoms of methyl groups, appear on passing to a solution in DMSO. There is also a substantial shift of the signal of the methylene group. In accordance with these data, the observed signals are related not to a mixture of E and Z isomers with respect to the oxime group but rather to a mixture of tautomeric forms A and B, the ratio of which in solution in DMSO is 3:2. Signals of only one isomer of tautomeric form A are observed in the ^{13}C NMR spectrum of IXg, obtained by oximation of imidazoline IIg. (See scheme, top of the next page.)

Stable nitroxyl radicals are formed in the oxidation of oximes IXc, d, g; the existence of these radicals is confirmed by the EPR spectroscopic data. Thus the EPR spectrum of radical XIc consists of a triplet with hyperfine coupling constant α_N = 14.08 G, which is somewhat smaller than the constants of tetraalkyl-substituted nitroxyl radicals and considerably smaller the constants of iminoxyl radicals [4]; this excludes structure XIII. The decrease in the hyperfine coupling constants may be associated with the presence of a heteroatom attached to the α-carbon atom of the nitroxyl group. The reduction of XIc by zinc in methanol in the presence of NH_4Cl leads to the



formation of starting oxime IXc; this excludes the possibility of the oxidation of the methylamino group in the composition of the heteroring to a nitroxyl group. Benzoyl derivative XII, obtained from oxime IXc, does not react with MnO_2. These data constituted evidence that nitroxyl radical XIc has a spiroimidazoisoxazole structure. The production of radical XIc can be conceived of as either the formation of, initially, iminoxyl radical XIII with subsequent cyclization at the nitrone group or as the existence of ring-chain tautomerism with subsequent oxidation of tautomer B to the corresponding nitroxyl radical.

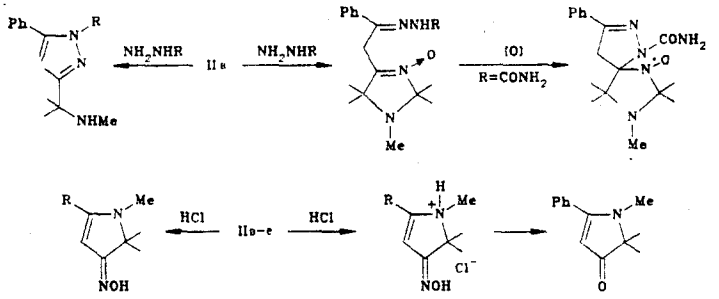
Fig. 1. EPR spectrum of nitroxyl radical XVIII.

In the case of the oxidation of oxime X the nitroxyl radical is unstable, and only products of its further oxidation — aldonitrone XV and hydroxamic acid XVI — can be isolated from the reaction mixture.

To study the range of application of the observed oxidative cyclization of the oxonitrone derivatives of imidazoline to give nitroxyl radicals — spiroimidazoisoxazole derivatives — in the case of imidazoline IIc we studied their reaction with other nitrogen nucleophiles. Compound IIc was selected in connection with the fact that the nitroxyl radicals formed in the oxidation of oximes IXa, b are unstable, while oxonitrones IIe, f undergo decomposition under the influence of nucleophilic reagents.

Semicarbazone XVIIa and phenylhydrazone XVIIb, respectively, are formed in the reaction of IIc with semicarbazide and phenylhydrazine. The oxidation of XVIIa leads to nitroxyl radical XVII, in the EPR spectrum of which one observes splitting into three nonequivalent nitrogen atoms (see Fig. 1), which constitutes evidence for the formation of a spiro node with the nitrogen atom attached to the α-carbon atom of the nitroxyl group.

The reaction of oxonitrone IIc with hydrazine and thiosemicarbazide leads to opening of the imidazoline heteroring with subsequent recyclization to pyrazole derivatives XIXa, b [5], which were isolated in the form of the hydrochlorides.



XVII a R=$CONH_2$, b R=C_6H_5; XIX a R=H, b R=$CSNH_2$; XX c R=C_6H_5, e R=$=C(CH_3)_3$, XXII g R=α nitrone, d R=CF_3

Thus the oxidative cyclization of oxonitrone derivatives — oximes and semicarbazone — makes it possible to obtain nitroxyl radicals with a spiro node that contains a heteroatom in the α position relative to the nitroxyl group.

We have previously shown that enamino ketones — imidazolidine derivatives — in an acidic medium undergo recyclization leading to pyrrolines I [5]. Under similar conditions β-oxonitrones — imidazoline derivatives — also undergo recyclization. Thus maintaining IIc, f in 5% HCl solution gives pyrrolines XXc, f, which, as evidenced by the broad band at 2700-3000 cm^{-1} in the IR spectra, which is characteristic for ammonium compounds, are enamino oxime hydrochlorides. Iminium salts are usually formed in the protonation of enamines [6]; however, the IR spectrum of XXc does not contain an absorption band of a $C=N^+$ band at 1680 cm^{-1} [7], and one observes a band at 1650 cm^{-1}, which can be assigned to vibrations of a C=C bond. The proposed structure is confirmed by the UV spectral data for XXc (λ_{max} 264 nm), as well as the data from the PMR spectrum (see Table 4), in which there are signals of methyl groups at 1.94 (6H) and 2.50 ppm (3H and signals of a proton attached to a double bond. Protonation of the oxime group seems unlikely, since its basicity is substantially lower than the basicity of the enamine fragment. Maintaining XXc in HCl solution gives derivative XXI, which has, according to the spectral data, enamino ketone groupings in its molecule [8], on the basis of which a pyrrolinone structure was assigned to it. Under similar conditions imidazolines IId, e undergo recyclization to enamino oximes XXIId, e, which were isolated in the free form.

EXPERIMENTAL

The IR spectra of KBr pellets (0.25% concentrations) and solutions (5%) in CCl_4 were recorded with a UR-20 spectrometer. The UV spectra of solutions in ethanol were recorded with a Specord UV-vis spectrophotometer. The PMR spectra of solutions in d_6-DMSO, $CDCl_3$, and CCl_4 (c 7-10%) were obtained with a Varian A-56-60A spectrometer with hexamethyldisiloxane (HMDS) as the internal standard. The ^{13}C NMR spectra were obtained with

a Bruker WP 200 SY spectrometer at 300°K under pulse conditions. For the measurements we used 10-15% solutions in $CDCl_3$ and DMSO with the addition of 10% d_6-DMSO. The chemical shifts were measured relative to the signal of the solvent.

The results of elementary analysis of the synthesized compounds were in agreement with the calculated values.

Compounds IIa, c, e, g were obtained by the method in [2], III was obtained by the method in [9], and IVa, b were obtained by the method in [10].

4-Acetonyl-1,2,2,5,5-pentamethyl-3-imidazoline(IIb)4-[2-oxo-(1-naphthyl)ethyl]-1,2,2,2,5,5-pentamethyl-3-imidazoline 3-oxide (IId), and 4-(3,3-dimethyl-2-oxobutyl)-1,2,2,5,5-pentamethyl-3-imidazoline 3-oxide (IIf) were obtained by the method in [2] by the action on imidazoline IVa of, respectively, ethyl acetate and methyl α-naphthoic and trimethylacetic acids in the presence of phenyllithium.

N-(3-Hydroximino-2-methyl-5-oxo-5-phenyl-2-pentyl)-N-2-propenylbenzamide (V). This compound was similarly obtained by the action of ethyl benzoate on imidazoline IVb in the presence of phenyllithium. PMR spectrum ($CDCl_3$): 1.60 (3H, s, CH_3), 1.68 (3H, s, CH_3), 2.08 (3H, s, CH_3), 3.07 (1H, s, CH_2=), 3.12 (1H, s, CH_2=), 7.1-7.9 [10H, m, $(C_6H_5)_2$], 11.8 (1H, broad s, NOH), 4.14 (2H, s, CH_2), 5.65 ppm (1H, s, —CH=).

1-Hydroxy-2-(2-oxo-2-phenyl-1-propyl)-2,4,4-trimethylpyrrolidine (VI). A solution of 0.4 g (2 mmole) of pyrroline III was added dropwise with stirring to a solution of methylmagnesium iodide, prepared from 0.24 g (10 mmole) of magnesium and 0.9 ml (14 mmole) of methyl iodide in 20 ml of dry ether, after which stirring was continued for 3 h at 20°C, 5 ml of water was then added, and the organic layer was separated. The aqueous layer was extracted with ether (5 × 10 ml), and the combined extract was dried with $MgSO_4$, the solution was evaporated, and VI was isolated by chromatography with a column packed with silica gel (100 ml) by elution with ether—hexane (1:1).

4-(2-Hydroxy-2-phenylethyl)-1,2,2,5,5-pentamethyl-3-imidazoline 3-Oxide (VII). A suspension of 0.3 g (1.1 mmole) of imidazoline IIc and 0.3 g (8.5 mmole) of $NaBH_4$ in 20 ml of ethanol was stirred for 12 h at 20°C, after which the residue was diluted with 10 ml of water, and the aqueous mixture was extracted with $CHCl_3$. The extract was dried with $MgSO_4$, the solution was evaporated, and the residue was chromatographed with a column packed with silica gel (50 ml). Elution with ethyl acetate gave 90.2 g of VII with mp 112-114°C [2].

1-Hydroxy-2-(2-hydroxy-2-phenylethyl)-4,4-dimethylpyrrolidine (VIII). This compound was obtained by a similar method by the reduction of pyrroline III.

4-(2-Hydroximino-2-phenylethyl)-1,2,2,5,5-pentamethyl-3-imidazoline 3-Oxide (IXc). A solution 0.83 (15 mmole) CH_3ONa in 20 ml of methanol was added to a solution of 1.75 g (25 mmole) of hydroxylamine hydrochloride in 20 ml of methanol, after which the precipitated NaCl was removed by filtration, 1.1 g (4 mmole) of imidazoline IIc was added to the solution, and the mixture was maintained at 20°C for 24 h. The solution was evaporated, the residue was diluted with 10 ml of a saturated solution of NaCl in water, and the resulting aqueous mixture was extracted with ethyl acetate (3 × 20 ml). The extract was dried with $MgSO_4$, the solution was evaporated, the residue was washed with hexane, and the precipitated oxime IXc was removed by filtration.

4-(2-Hydroxyiminoethyl)- (IXa), 4-(2-Hydroxyiminopropyl)- IXb), 4-(2-Hydroxyimino-2-[1-naphthyl)ethyl)-(IXd),and4-(3-Hydroxyimino-3-phenyl-2-propyl)-1,2,2,5,5-pentamethyl-3-imidazoline3-Oxide (IXg). These compounds were obtained under similar conditions by the action of hydroxylamine on imidazolines IIa, b, d, g. Compound IXd could not be isolated in analytically pure form; however, it could be used without further purification for oxidation to the corresponding nitroxyl radical XId.

2-(2-Hydroximino-2-phenylethyl)-4,4-dimethyl-1-pyrroline 1-Oxide (X). This compound was obtained under similar conditions by the action of hydroxylamine on pyrroline III. PMR spectrum (d_6-DMSO): 1.09 [6H, s, 4-$(CH_3)_2$], 1.94 (2H, broad s, 3-CH_2), 2.80 (1H, broad s, 5-CH_2), 2.86 (1H, broad s, 5-CH_2), 3.30 (2H, s, CH_2), 7.4 ppm (5H, m, C_6H_5).

1-Oxyl-2,2,3,4,4-pentamethyl-1,2,3,4-tetrahydroimidazole-5-spiro(3′-phenyl-4′,5′-dihydro)-5′-isoxazole (XIc). A solution of 0.2 g of oxime IXc in 10 ml of chloroform was stirred with 1 g of MnO_2 for 30 min at 20°C, after which the excess oxidizing agent was removed by filtration, and the solution was evaporated. Compound XIc was isolated by chromatography with a column packed with silica gel (50 ml) with elution by chloroform.

1-Oxyl-2,2,3,4,4-pentamethyl-1,2,3,4-tetrahydroimidazo-5-spiro-[3′-(1′-naphthyl)-4′,5′-dihydro]-5′-isoxazole(XId)and1-Oxyl-2,2,3,4,4-pentamethyl-1,2,3,4-tetrahydroimidazo-5-spiro-(4′-methyl-3′-phenyl-4′,5′-isoxazole (XIe). These compounds were similarly obtained by the oxidation of, respectively, unpurified oxime IXd and oxime IXg.

4,4-Dimethyl-2,3-dihydro-4H-pyrrolo-2-spiro(3′-phenyl-4′,5′-dihydro)-5′-isoxazole Oxide (XV) and 1-Hydroxy-4,4-dimethyl-5-oxa-2,3,4,5-tetrahydropyrrolo-2-spiro)3′-phenyl-4′,5′-dihydro)-5′-isoxazole (XVI). These compounds were obtained by the oxidation of oxime X in the form of a mixture, which was separated chromatography with a column packed with silica gel (100 ml) by elution with chloroform. PMR spectrum of XV (CCl_4): 1.13 [6H, s, 3-$(CH_3)_2$], 2.92 (4H, broad s, 4-CH_2, 4′-CH_2), 6.5 (1H, s, —CH=), 7.6 ppm (5H, m,

C_6H_5). PMR spectrum of XVI (d_6-DMSO): 1.17 (3H, s, 3-CH_3), 1.05 (3H, s, 3-CH_3), 2.28 (2H, a, CH_2), 3.57 (2H, s, CH_2), 7.5 ppm (5H, m, C_6H_5).

4-(benzoyloximino-2-phenylethyl)-1,2,2,5,5-pentamethyl-3-imidazoline 3-Oxide (XII). A solution of 0.2 ml (1.8 mmole) of benzoyl chloride in 5 ml of $CHCl_3$ was added dropwise with stirring to la solution of 0.4 g (1.38 mmole) of oxime IXc and 0.38 ml (2.77 mmole) of triethylamine in 30 ml of chloroform, after which the reaction mixture was washed with water (2 × 20 ml) and dried with $MgSO_4$. The mixture was then evaporated, the residue was washed with hexane, and the precipitated XII was removed by filtration.

4-(2-Oxo-2-phenylethyl)-1,2,2,5,5-pentamethyl-3-imidazoline Oxide (XVIIa). A solution of 0.55 g (2 mmole) of imidazoline IIc, 0.45 g (4 mmole) of semicarbazide hydrochloride, and 0.17 g (3 mmole) of CH_3ONa in 20 ml of methanol was refluxed for 2.5 h, after which it was evaporated. The residue was diluted with 10 ml of water, and the precipitated semicarbazone XVIIIa was removed by filtration.

4-(2-Oxo-2-phenylethyl)-1,2,2,5,5-pentamethyl-3-imidazoline 3-Oxide Phenylhydrazone (XVIIb). A mixture of 0.7 ml (6 mmole) of phenylhydrazine and 8 ml of water was acidified to pH 4 with 50% CH_3COOH, after which 0.55 g (2 mmole) of imidazoline IIc and 15 ml of ethanol were added, and the mixture was heated until all solid materials had dissolved, and the solution was allowed to stand for 24 h at 20°C. The alcohol was evaporated, the aqueous solution was extracted with $CHCl_3$, and the extract was dried with $MgSO_4$. The solution was evaporated, the residue was diluted with a small amount of hexane, and the precipitated phenylhydrazone XVIIb was removed by filtration.

1-Hydroxy-2,2,3,4,4-pentamethyl-1,2,3,4-tetrahydro-5H-imidazo-5-spiro(1′-carbamoyl-3′-phenyl-4′,5′-dihydro)-5′-pyrazole (XVIII). This compound was obtained by oxidation of semicarbazone XVIIa.

3-(2-(Methylamino-2-propyl)-5-phenylpyrazole Hydrochloride (XIXa). A solution of 0.55 g (2 mmole) of imidazoline IIc, 0.7 g (10 mmole) of hydrazine hydrochloride, and 0.33g (6 mmole) of CH_3ONa in methanol was maintained for 24 h at 20°C, after which the mixture was evaporated. The residue was diluted with 10 ml of a saturated solution of NaCL in water, and the resulting mixture was extracted with $CHCl_3$. The extract was dried with $MgSO_4$, the solution was evaporated, and the residue was washed with ether. The precipitated XIXa was removed by filtration. PMR spectrum (d_6-DMSO): 1.67 [6H, s, $(CH_3)_2$], 2.33 (3H, s, N—CH_3), 6.95 (1H, s, —CH=), 7.4-7.8 ppm (5H, m, C_6H_5).

5-(2-Methylamino-2-propyl)-1-thiocarbamoyl)-5-phenylpyrazole Hydrochloride (XIXb). A solution of 0.55 g (2 mmole) of imidazoline IIc, 0.36 g (4 mmole) of thiosemicarbazide, and 0.2 ml of concentrated HCl in methanol was refluxed for 1 h, after which it was evaporated. The residue was diluted with 5 ml of water, the aqueous mixture was neutralized with 10% NaOH, and the precipitated XIXb was removed by filtration.

4-Hydroximino-1,5,5-trimethyl-2-phenyl-2-pyrrolineHydrochloride(XXc)and4-Oxo-1,5,5-trimethyl-2-phenyl-2-pyrroline (XXI). A solution of 0.5 g of imidazoline IIc in 10 ml of 5% HCl was refluxed for 1 h, after which it was extracted with $CHCl_3$. The extract was dried with $MgSO_4$, the solution was evaporated, and XXc and XXI were isolated by chromatography with a column packed with silica gel (50 ml). Compound XXI was eluted with $CHCl_3$—methanol (50:1), while hydrochloride XXc was eluted with $CHCl_3$—methanol (15:1).

Under similar conditions, from imidazoline IIf we obtained **4-hydroximino-1,5,5-trimethyl-2-tert-butyl-2-pyrroline (XXf)** , from imidazoline IId we obtained **4-hydroximino-1,5,5-trimethyl-2-(1-naphthyl)-2-pyrroline (XXIId),** and from imidazoline IIe we obtained **4-hydroximino-1,5,5-trimethyl-2-trifluoromethyl-2-pyrroline (XXIIe).**

LITERATURE CITED

1. V. A. Reznikov and L. B. Volodarskii, *Izv. Akad. Nauk SSSR, Ser. Khim.*, No. 2, 390 (1990).
2. V. V. Martin and L. B. Volodarskii, *Izv. Akad. Nauk SSSR, Ser. Khim.*, NO. 6, 1336 (1980).
3. D. St. C. Black, V. M. Clark, R. S. Thakur, and A. Todd, *J. Chem. Soc., Perkin 1*, No. 18, 1951 (1976).
4. I. A. Grigor'ev and S. A. Dicanov, *Imidazoline Nitroxides* [in Russian], Vol. 1, edited by L. B. Volodarskii (Volodarsky), CRC Press, Inc., Boca Raton, Florida (1988), p. 101.
5. V. A. Reznikov and L. B. Volodarskii, *Khim. Geterotsikl. Soedin.*, No. 7, 921 (1990).
6. A. G. Cook (ed.), *Enamines: Synthesis, Structure, and Reactions*, Marcel Dekker, New York—London (1969), p. 117.
7. L. B. Volodarskii, V. A. Reznikov, and V. S. Korbin, *Zh. Org. Khim.*, **15**, 415 (1979).
8. Ya. F. Freimanis, *The Chemistry of Enamino Ketones, enamino Imines, and Enamino Thiones*, Zinatne, Riga (1974), p. 80.
9. D. St. C. Black, V. M. Clark, B. G. Odell, and A. Todd, *J. Chem. Soc., Perkin 1*, No. 18 (1944), 1976).
10. V. V. Martin and L. B. Volodarskii, *Khim. Geterotsikl. Soedin.*, No. 1, 103 (1979).