RECYCLIZATION OF α-HYDROXIMINO-β-OXO-3-IMIDAZOLINE AND 3-IMIDAZOLINE-3-OXIDE DERIVATIVES TO PYRROLINES

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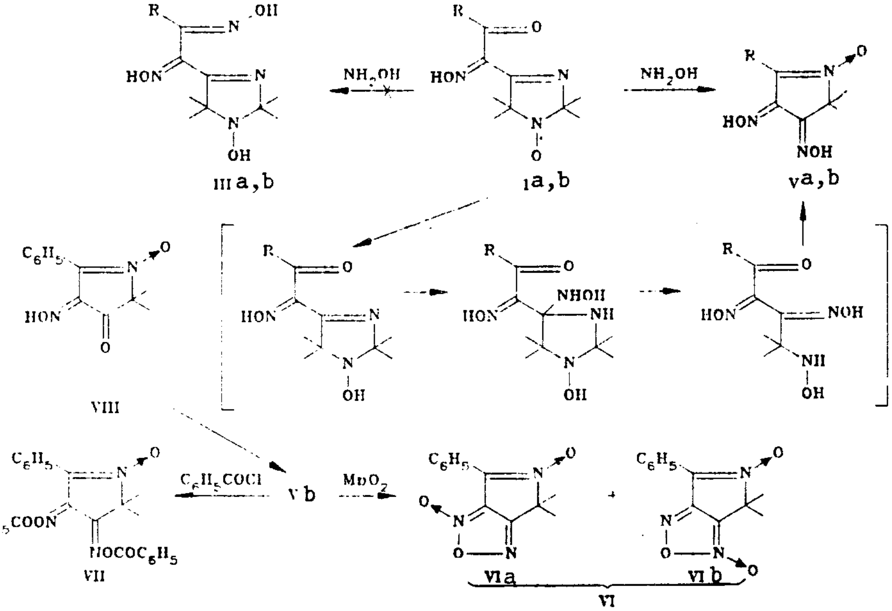
Reaction of α-hydroximino-β-oxo-3-imidazoline and 3-imidazoline-3-oxide derivatives with hydroxylamine results in recyclization leading to the formation of pyrroline derivatives, namely dioximes or nitrosooximes. Oxidation of dioximinopyrroline gives a pyrrolofuroxane.

As part of our continuing study of the properties of enaminoketones in the 3-imidazoline series, and of β-oxonitrones in the 3-imidazoline-3-oxide series [1, 2], we have examined the reactions of α-hydroximino-β-oxoimidazoline derivatives I and 3-imidazoline-3-oxide derivatives II with hydroxylamine. We believed that these reactions would lead to the corresponding dioximes III and IV, which might be of interest in the synthesis of paramagnetic chelate-forming reagents. Upon reaction of compound Ib with hydroxylamine hydrochloride or free hydroxylamine in methanol only reduction of the nitroxyl radical site takes place to give a hydroxylamino group, and dioxime III is not formed. Upon refluxing compound Ib with hydroxylamine hydrochloride in pyridine, however, compound Vb was formed unexpectedly; the latter was oxidized upon treatment with MnO_2 not to a nitroxyl radical, but rather to diamagnetic compounds VIa, b.



I, III, V a R = CH_3, b R = C_6H_5

The PMR spectra of compounds Vb and VIa, b exhibit signals due to the two methyl groups and the phenyl group protons. Apparently, compound Vb is formed via cleavage of the imidazoline heterocycle and loss of an acetone molecule or its oxime. The ^{13}C-NMR spectrum of compound Vb displays three signals for sp^2-hybridized carbon atoms (at 135.51, 141.86, and 148.83 ppm), corresponding to the nitrone group (cf. [3]) and two oxime group carbon atoms. Reaction of compound Vb with benzoyl chloride gave the dibenzoyl derivative VII, which confirms the presence of two oxime groups in the molecular composition of Vb. Based on these data, we have assigned compound Vb a recyclization product structure, namely dioximinopyrroline-1-oxide. The structure of compound Vb was verified by independent synthesis from monooxime VIII [4].

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TABLE 1. Physical Characteristics of Compounds IV, Va, b, VI, VII, IX, XII, and XIII

Compound	Molecular formula	mp . C°*	IR spectrum (KBr) ν, cm^{-1}		UV spectrum (ethanol), λ_{max}, nm (log ε)	Yield, %
			C=O	C=N		
IV	$C_{16}H_{22}N_4O_3$	205 . . . 207	—	1570	250 (4,18), 284 (3,99)	50
Va	$C_7H_{11}N_3O_3$	261 . . . 263	—	1500, 1545, 1580	263 (3,97), 286 (4,04)	60
Vb	$C_{12}H_{13}N_3O_3$	248 . . . 250	—	1580	233 (4,23), 305 (4,08)	90
VI**	$C_{12}H_{11}N_3O_3 \cdot \cdot H_2O$	131 . . . 133	—	1690	227 (4,12), 312 (4,15), 246 (4,09)	90
VII	$C_{26}H_{21}N_3O_5$	185 . . . 186	1750	1530, 1590	232 (4,25), 243 (4,23)	80
IX	$C_{13}H_{15}N_3O_2$	135 . . . 137	—	1590, 1620	269 (4,01), 370 (3,25)	35
XII	$C_{14}H_{16}N_2O_3$	229 . . . 230	1690	1585	250 (4,24), 293 (4,04)	60
XIII	$C_{14}H_{17}N_3O_3$	232 . . . 233	—	1500, 1600	250 (3,90), 292 (3,73)	35

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*Compounds Va, b and XIII were recrystallized from alcohol, VI from hexane, VII from a 1:3 mixture of ethyl acetate–hexane, IV from a 1:3 mixture of ethanol–ethyl acetate, IX from ethyl acetate, and XII from a 1:1 mixture of $CHCl_3$–ethanol.

**Mixture of isomers VIa and VIb.

TABLE 2. PMR Spectra of Compounds IV-VI, IX, XII, XIII

Compound	Chemical shifts, δ, ppm (in DMSO-D_6)*
IV	1,26 (6H, 5-$(CH_3)_2$); 1,49 (6H, 2-$(CH_3)_2$); 2,32 (3H, N—CH_3); 7,5 (5H, m., C_6H_5); 11,8 (1H, NOH); 12,1 (1H, NOH)
Va	1,52 (6H, $C(CH_3)_2$); 1,99 (3H, 2-CH_3); 12,1 (1H, NOH); 12,2 (1H, NOH)
Vb	1,58 (6H, $C(CH_3)_2$); 7,3 . . . 8,1 (5H, m, C_6H_5); 12,4 (2H, br.s , NOH)
VI**	1,68 (6H, $C(CH_3)_2$); 7,2 . . . 8,3 (5H, m C_6H_5)
IX***	1,61 (6H, $C(CH_3)_2$); 3,27 (3H, N—CH_3); 7,54 (5H, m C_6H_5); 11,64 (1H, NOH)
XII	1,15 (6H, $C(CH_3)_2$); 2,75 (2H, br.s , 3-CH_2); 3,14 (2H, br.s , 5-CH_3); 8,0 (5H, m, C_6H_5); 12,1 (1H, NOH)
XIII	1,11 (6H, $C(CH_3)_2$); 2,75 (2H, 3-CH_2); 3,63 (2H, 5-CH_2); 7,4 (5H, m , C_6H_5); 11,2 (1H, NOH); 11,8 (1H, NOH)

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*Singlet, if not specified otherwise.

**Mixture of isomers VIa and VIb.

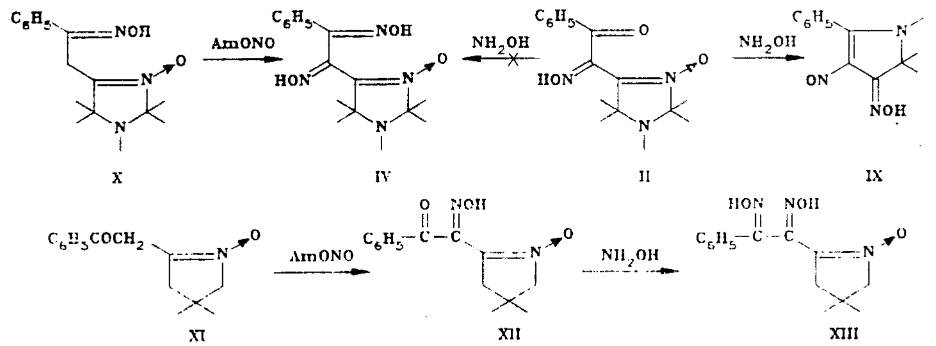
***The spectrum was recorded in $CDCl_3$ solution.

The reaction scheme for the formation of compound Vb involves initial reduction of the nitroxyl group, followed by cleavage of the imidazoline heterocyclic ring as a result of nucleophilic attack by hydroxylamine, and subsequent recyclization involving the newly formed hydroxylamino group at the carbonyl group. Enaminoketone derivatives of imidazolidine and 3-imidazoline-3-oxide β-oxonitrones undergo an analogous recyclization reaction in aqueous acidic solutions (cf. [5, 6]).

According to mass spectral data, the molecular formula of the oxidation products derived from dioximinopyrroline Vb, namely compounds VIa, b, differs from the molecular formula of the starting material by the presence of two hydrogen atoms. It was therefore hypothesized that compounds VI had pyrrolofuroxane structures. The ^{13}C-NMR spectrum of compounds VIa, b exhibited a doubling of the number of signals in a 10:1 ratio, due to the presence of two isomers, VIa and VIb, which differ from one another in the position of the N-oxide oxygen atom in the furoxane ring. The $C_{(4)}$ atom signal is found higher upfield, but occurs in series with the $C{=}N{\rightarrow}O$ fragment in the furoxane ring (cf. [7]); we assume, therefore, that the less-intense signals in the spectrum correspond to structure VIb. Reaction of compound Ia with hydroxylamine under analogous conditions gave pyrroline Va.

It was also found that the appropriate dioxime IV was not formed upon reaction of the 3-imidazoline-3-oxide derivative II with free hydroxylamine in aqueous chloroform; recyclization takes place, leading to pyrroline IX. The structure of compound IX was established based on its ^{13}C-NMR spectrum, which contained, in addition to the phenyl group signals, three signals due to sp^2-hybridized carbon atoms, at 176.0, 151.6, and 149.2 ppm. In addition, signals for the three methyl-group carbon atoms and the $C_{(5)}$ were also observed (cf. [6]). Pyrroline IX was also formed in low yield upon refluxing compound II with hydroxylamine hydrochloride in methanol; dioxime IV was not formed. The latter can be prepared by nitrosation of β-oximinonitrone X.

In contrast to the behavior of the imidazoline oxooximes I and II, the pyrroline derivative XII, prepared via nitrosation of oxonitrone XI, did react with hydroxylamine to form the corresponding dioxime XIII in limited yield.



EXPERIMENTAL

Infra-red spectra were recorded on a UR-20 spectrophotometer using KBr (c = 0.25%). Ultra-violet spectra were measured on a Specord UV-vis spectrophotometer using alcohol solutions. PMR spectra were obtained on a Varian A-56-60A spectrometer using solutions in DMSO-D_6 and $CDCl_3$ (c = 7-10%), versus HMDS as internal standard. ^{13}C-NMR spectra were recorded on a Bruker WP200SY spectrometer at 300 K under pulsed conditions. The measurements were made using solutions in $CDCl_3$ and DMSO with 10% DMSO-D_6 added (c = 15%). Chemical shifts were measured relative to the solvent signal.

The physical characteristics of the newly synthesized compounds are summarized in Tables 1 and 2. The results of C, H, N elemental analysis for these compounds agreed with calculations.

Compounds Ia, b were prepared according to [1], II according to [2], XI based on [8].

3,4-Dihydroximino-5,5-dimethyl-2-phenyl-1-pyrroline-1-oxide (Vb). A solution of 1.8 g (7.1 mmoles) compound Ib and 4.5 g (71 mmoles) hydroxylamine hydrochloride in 25 ml pyridine was refluxed 6 h, then evaporated. The residue was diluted with 20 ml water, and the resulting precipitate of compound Vb was removed by filtration, washed with water, and dried. Mass spectrometric data, M 247.0943, $C_{12}H_{13}N_3O_3$, calculated M 247.0956. ^{13}C-NMR spectrum (DMSO): 19.89 [5-$(CH_3)_2$]; 72.67 ($C_{(5)}$); 125.56, 126.46, 128.19, 128.67 (C_6H_5); 131.51 ($C_{(2)}$); 141.86, 148.83 ppm ($C_{(3)}$, $C_{(4)}$).

3,4-Dihydroximino-2,5,5-trimethyl-1-pyrroline-1-oxide (Va) was prepared in an analogous manner from compound Ia.

3,4-Dibenzoyloximino-5,5-dimethyl-2-phenyl-1-pyrroline-1-oxide (VII). To a solution of 0.2 g (0.8 mmoles) pyrroline Vb in 3 ml of 5% NaOH solution in water was added dropwise with stirring 0.2 ml (1.7 mmoles) benzoyl chloride. The mixture was stirred for 15 min, diluted with 10 ml ether, and the precipitate of compound VII was removed by filtration and washed with ether.

4,4-Dimethyl-6-phenyl-2H-pyrrolo[3,4-c]furazan-3,5-dioxide (VI). A solution of 1 g (4.2 mmoles) dioxime Vb in 50 ml ethanol was stirred with 3 g MnO_2 for 48 h at 20°C; excess oxidant was filtered off, and the solvent was evaporated. The mixture of compounds VIa, b was isolated by column chromatography on silica gel (100 ml) with $CHCl_3$ eluent; it was not possible to separate compounds VIa and VIb. According to mass spectrometry, M (found): 245.0079, $C_{12}H_{11}N_3O_3$; calculated M: 245.0080. ^{13}C-NMR spectrum (DMSO): 20.03 (VIa), 21.61 (VIb) [$C(CH_3)_2$]; 73.22 (VIb), 73.62 (VIa) [$C(CH_3)_2$]; 110.60 ($C{=}N \rightarrow O$); 124.84, 125.68, 128.14 (VIa) (C_6H_5); 126.70, 127.68 (VIb) (C_6H_5); 130.05 (VIb) (C_6H_5–$C{=}N \rightarrow O$); 130.60 (VIa) (C_6H_5–$C{=}N \rightarrow O$); 154.69 ppm (VIa) ($C{=}N$–O).

4-(1,2-Dihydroximino-2-phenylethyl)-1,2,2,5,5-pentamethyl-3-imidazoline-3-oxide (IV). A solution of 0.29 g (1 mmole) oxime II, 0.27 g (5 mmoles) CH_3ONa, and 0.4 g (3 mmoles) amyl nitrite in 20 ml methanol was mixed at 20°C for 24 h, then evaporated. The residue was diluted with 10 ml water and washed with ether (2 × 15 ml). The aqueous solution was neutralized with 5% HCl, saturated with NaCl, and extracted with ethyl acetate (5 × 20 ml). The extract was dried over $MgSO_4$, the solution evaporated, and the residue washed with hexane; the precipitate of dioxime IV was removed by filtration.

Nitrosation of pyrroline XI under analogous conditions gave **2-(1-hydroximino-2-oxo-2-phenylethyl)-4,4-dimethyl-1-pyrroline-1-oxide (XII).**

4-Hydroximino-3-nitroso-1,5,5-trimethyl-2-phenyl-2-pyrroline (IX). To a solution of 1.5 g (19.5 mmoles) hydroxylamine hydrochloride and 0.8 g (20 mmoles) NaOH in 10 ml water was added 1 g (3.6 mmoles) of compound II and 50 ml chloroform. The mixture was refluxed for 100 h, and the chloroform solution was separated while the aqueous solution was extracted with 2 × 20 ml chloroform. The combined chloroform extract was dried over $MgSO_4$, the solution evaporated, and compound IX isolated by column chromatography on silica gel (100 ml) with $CHCl_3$ eluent. ^{13}C-NMR spectrum ($CDCl_3$): 25.7 [$C(CH_3)_2$],; 32.4 ($N-CH_3$); 72.6 [$C(CH_3)_2$]; 127.8, 129.3, 130.8, 132.8 (C_6H_5); 149.6, 151.6 (C=C); 176.0 ppm (C=N).

2-(1,2-Dihydroximino-2-phenylethyl)-4,4-dimethyl-1-pyrroline-1-oxide (XIII). A solution of 0.52 g (2 mmoles) oxime XII and 1.4 g (20 mmoles) hydroxylamine hydrochloride in 20 ml ethanol was refluxed for 10 h, and evaporated. The residue was diluted with 10 ml water, neutralized with 10% Na_2CO_3, saturated with NaCl, and shaken with 10 ml $CHCl_3$. The resulting precipitate of dioxime XIII was removed by filtration, washed with ether, and dried.

LITERATURE CITED

1. V. A. Reznikov, T. I. Reznikova, and L. B. Volodarskii, *Izv. Sib. Otd. Akad. Nauk SSSR, Ser. Khim. Nauk,* No. 5, 128 (1982).
2. V. V. Martin and L. B. Volodarskii, *Izv. Akad. Nauk SSSR, Ser. Khim.*, No. 6, 1336 (1980).
3. I. A. Grigor'ev, G. I. Shchukin, V. V. Martin, and V. I. Mamatyuk, *Khim. Geterotsikl. Soedin.*, No. 2, 252 (1985).
4. V. A. Reznikov, L. A. Vishnivetskaya, and L. B. Volodarskii, *Izv. Akad. Nauk SSSR, Ser. Khim.* (in press).
5. V. A. Reznikov and L. B. Volodarskii, *Khim. Geterotsikl. Soedin.*, No. 7, 921 (1990).
6. V. A. Reznikov and L. B. Volodarskii, *Khim. Geterotsikl. Soedin.* (1990) (in press).
7. L. I. Khmel'nitskii, S.S. Novikov, and T. I. Godovikova, *The Chemistry of Furoxanes. Structure and Synthesis* [in Russian], Nauka, Moscow (1981), p. 56.
8. D. St. C. Black, V. M. Clark, B. G. Odell, and Todd, *J. Chem. Soc.*, Perkin Trans. I, No. 18, 1944 (1976).