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INTERACTION OF 5,5-DIMETHYL-2-PHENACYLPYRROLINE-1-OXIDE - AN EXOCYCLIC β-OXONITRONE - WITH NUCLEOPHILIC REAGENTS

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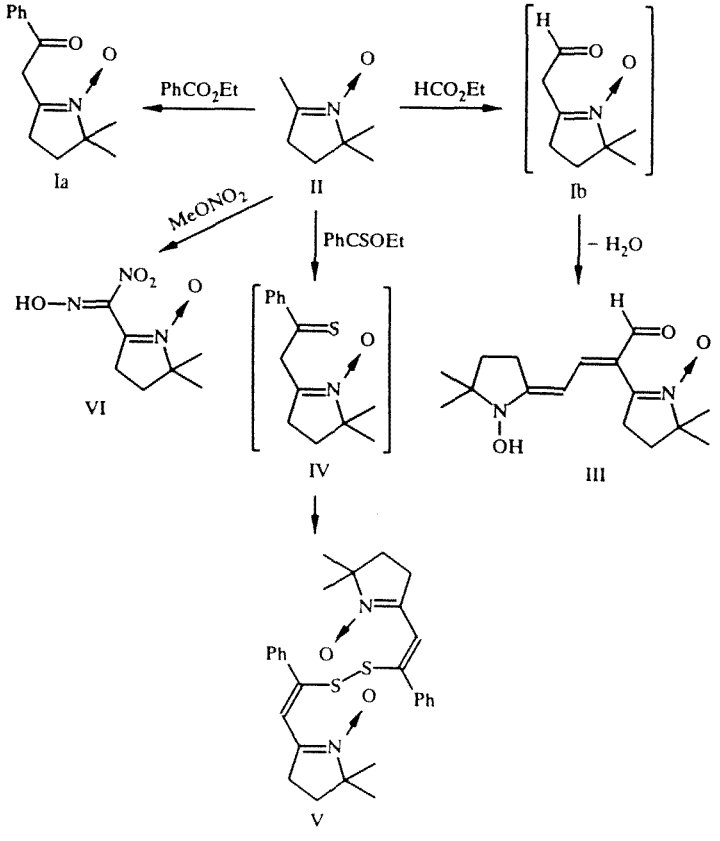
A study has been made of the interaction of 2,5,5-trimethylpyrroline-1-oxide with ethyl formate, ethyl thiobenzoate, and methyl nitrate. It has been shown that the reaction of 5,5-dimethyl-2-phenacylpyrroline-1-oxide with methylmagnesium iodide or phenyllithium proceeds through the nitrone group, while the carbonyl group is preserved; after oxidation, this leads to nitroxyl radicals of the pyrrolidine series. Upon interaction of this same N-oxide with nitrogen-containing binucleophiles, recyclization takes place, forming derivatives of isoxazole and pyrazole.

We had shown previously that β-oxonitrones, the molecules of which have two electrophilic centers, are interesting synthons, in particular for the preparation of staole nitroxyl radicals. In the example of exocyclic β-oxonitrones of the 3-imidazoline-3-oxide series and endocyclic β-oxonitrones that are derivatives of 1-pyrroline-1-oxide, it was shown that the direction of the reaction with nucleophilic regents depends on the topology of the oxonitrone group [1, 2]. The work reported here was aimed at studying the interaction of exocyclic β-oxonitrones - derivatives of 1-pyrroline-1-oxide (I) - with nucleophilic reagents.



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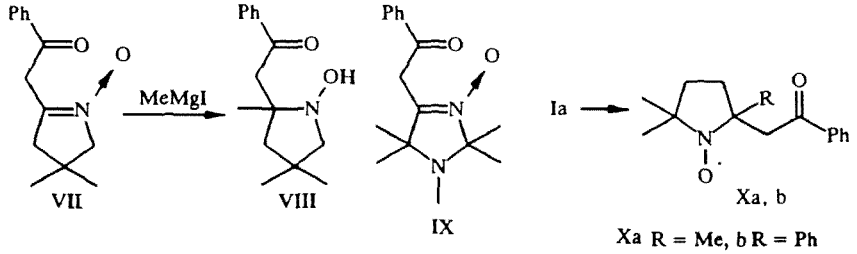
5,5-Dimethyl-2-phenacyl-1-pyrroline-1-oxide (Ia) is obtained by the interaction of trimethylpyrroline oxide (II) with ethyl benzoate in the presence of NaH [3]. We had shown that this reaction also goes forward in the presence of lithium diisopropylamide (LDA), affording the same compound Ia with a yield ~50%. We were unable to effect the interaction of the nitrone II with diethyl carbonate or ethyl N,N-dimethylcarbamate in the presence of LDA or NaH. Upon interaction of compound II with ethyl formate under these conditions, the aldehyde Ib is formed; however, we were unable to isolate it in individual, analytically pure form, since when it is heated or chromatographed on silica gel, it is converted with a high yield to the "dimer" III. Elemental analysis indicates that III is not a product of oxidative dimerization (compare [4]), but is formed as a result of condensation of two molecules of the aldehyde, splitting out a water molecule. On the basis of the ^1H and ^{13}C NMR spectra, compound III was assigned the structure shown in the reaction scheme.

The β-thioxonitrone (IV), formed by the interaction of II with O-ethyl thiobenzoate, is unstable, being converted readily to the disulfide V in the process of isolation (compare [5]).

The only product that we were able to isolate as a result of the reaction of the nitrone II with methyl nitrate in the presence of LDA was the nitroxime VI. The doubled set of signals in the ^{13}C NMR spectrum of VI indicates that this compound exists in the form of a mixture of E and Z isomers.

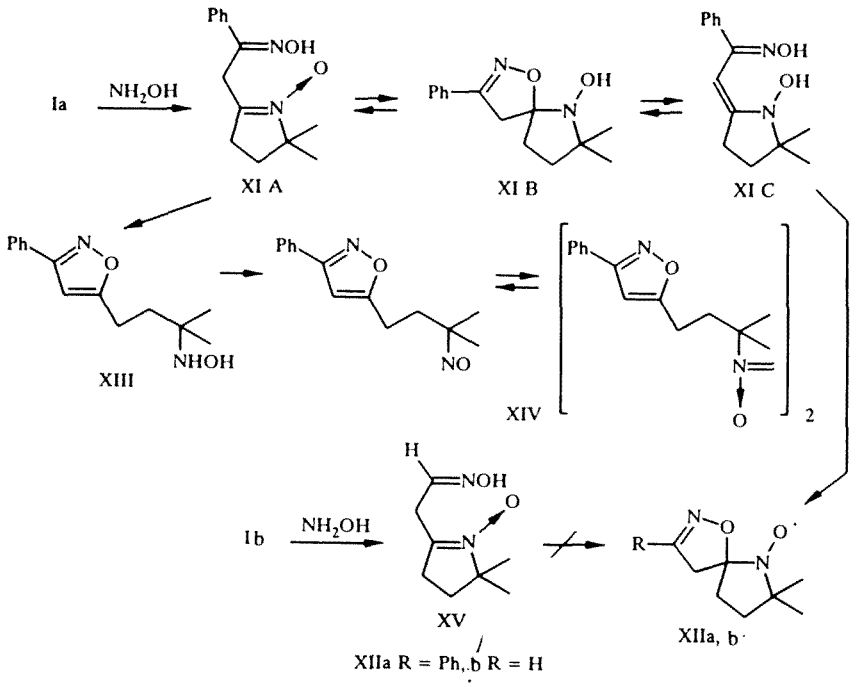
One of the methods for transformation of an endocyclic β-oxonitrone grouping into an oxonitroxyl group is interaction with organomagnesium or organolithium compounds [1]. We had shown previously that when excess methylmagnesium iodide acts on the oxonitrone VII, the addition takes place exclusively at the nitrone group, forming the hydroxylaminoketone VIII; the reaction of the derivative of 3-imidazoline-3-oxide IX with methylmagnesium iodide does not go forward under these conditions. The differences in behavior of the oxonitrones VII and IX can apparently be attributed to steric hindrance of the nitrone group in the molecule of the latter compound [2]. In the work reported here, it was shown that the pyrroline Ia, which has less steric hindrance, reacts slowly with either methylmagnesium iodide or phenyllithium. The reaction proceeds with preservation of the carbonyl group; after oxidation, the respective nitroxyl radicals Xa and Xb were recovered. It is interesting to note that in the IR spectra of compounds Xa,b (solution in CCl_4), two bands of the carbonyl group are observed, one at 1670 and the other at 1680 or 1685 cm^{-1}, respectively. In the IR spectrum of compound Xa in KBr, there is one band of the carbonyl group at 1680 cm^{-1}; the disappearance of the second band is obviously related to the hindrance to rotation around the C–C bond, owing to steric features of the molecule.



Xa R = Me, b R = Ph

Interaction of exocyclic β-oxonitrones with nitrogen-containing binucleophiles is another method for converting the nitrone group to nitroxyl [2]. Upon interaction of the oxonitrone Ia with hydroxylamine, the oxime XI is formed. We had shown previously that the corresponding product from the interaction of compound IX with hydroxylamine in DMSO solution exists in the form of a mixture of two tautomeric forms – the nitronoxime form (A) and the spirobicyclic form (B) [2]. According to the NMR spectra, compound XI exists in methanol solution in the unconjugated nitronoxime tautomeric form A. (See scheme on following page.)

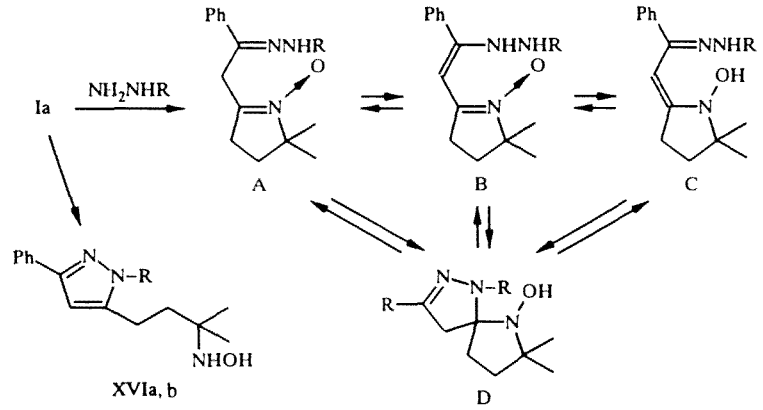
Oxidation of the oxime XI by MnO_2 proceeds smoothly to form the spirobicyclic nitroxyl radical XIIa. Upon attempting to recrystallize the oxime XI from ethanol, it is converted to the product XIII, which, according to the elemental analysis, is an isomer of XI; however, upon oxidation by MnO_2 the nitroxyl radical XII is not formed, but rather a colorless diamagnetic compound XIV, solutions of which are blue, evidently related to the presence of a nitroso group in the molecule. NMR spectroscopic data on compounds XIII and XIV show that they are isoxazole derivatives. It should be noted that the formation of the spirobicyclic radical XIIa by oxidation of the oxime XI, like its recyclization, proceeds with the participation of the spirobicyclic tautomeric form XI-B. Interaction of the aldehyde Ib with hydroxylamine leads to the oxime XV which, according to ^1H and ^{13}C NMR data, exists in an unconjugated tautomeric form of type A, as a mixture of E and Z isomers in a ratio of approximately 1:1. In particular, the PMR spectrum exhibits two triplets of the aldoxime proton at 7.33 and 6.7 ppm; the ^{13}C NMR spectrum exhibits two signals of the oxime carbon atom at 143.94 and 143.26 ppm, as well as two signals of the

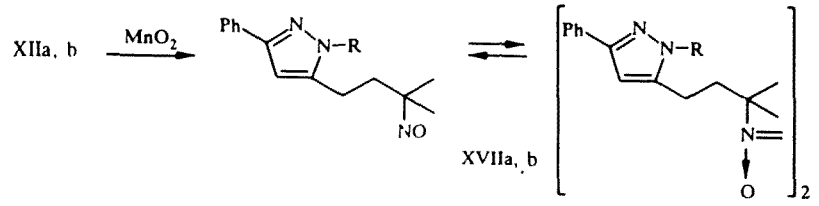


C-5 atom at 72.71 and 72.55 ppm. We were not successful in isolating the corresponding spirobicyclic radical after oxidation of the oxime XV.

On the basis of the NMR spectra of compound XVIa, which is formed by the interaction of Ia with phenylhydrazine, we were able to assume that this compound exists in the conjugated enhydrazinonitrone (B) or enhydroxylaminohydrazone (C) tautomeric form; this is contradictory to the UV spectrum of this compound, in which absorption is observed at λ_{max} 266 nm (log ε = 4.03), whereas the original oxonitrone Ia, which also exists primarily in the enolized form, absorbs at considerably longer wavelengths [3].

Compound XVIb, formed by the interaction of Ia with hydrazine, has analogous spectral characteristics. Upon oxidation of XVI, colorless diamagnetic compounds XVII are formed. A solution of XVIIa in chloroform is green, XVIIb blue. According to TLC data, compounds XVII consist of two components, one colored and the other colorless. Bidirectional chromatography shows that these components exist in an equilibrium that is established in the course of chromatographing. These data show that the compounds XVII are nitroso compounds, dimeric in the crystalline state, but existing in solution in the form of a mixture of monomer and dimer. According to PMR spectroscopic data, the content of monomer in $CHCl_3$ solution is about 15%. On the basis of the ^1H and ^{13}C NMR spectra, the pyrazole structure has been assigned to the compounds XVII. The NMR and UV spectra of compounds XVI and XVII are similar; and on this basis, the compounds XVI are also classed as pyrazole derivatives.





XVIIa R = Ph, b R = H

In conclusion, let us note that in the reaction we had detected previously, the recyclization of enaminoketones – derivatives of imidazoline and β-oxonitrones of the 3-imidazoline-3-oxide series – to form pyrrolines, the driving force is the hydrolytic lability of the imidazoline heterocycle, owing to the presence of two nitrogen atoms located on the same carbon atom in this heterocycle [2, 6, 7, 8]. The reaction results in the formation of a heterocycle with one nitrogen atom that is more resistant to hydrolysis. The apparent reason why the recyclization reaction of pyrroline derivatives that has been found in the present work can be realized is that as a result of the reaction, aromatic heterocyclic systems are formed – isoxazole and pyrazole.

EXPERIMENTAL

IR spectra were recorded in a Specord M-80 spectrometer in KBr tablets (concentration 0.25%) and in CCl_4 and $CHCl_3$ solutions (concentration 5%). UV spectra were measured in a Specord UV-Vis spectrometer in ethanol, ^1H and ^{13}C NMR spectra in a Bruker AC-200 instrument at 300 K (solution concentration 5%). The chemical shifts were determined relative to the signal of the solvent. The characteristics of the synthesized compounds are listed in Table 1, and the NMR spectroscopic data are listed in Tables 2-4.

2-(5,5-Dimethylpyrroline-1-oxide-2-yl)-4-(1-hydroxy-5,5-dimethylpyrrolidin-2-ylidene)-2-butenal (III). To a mixture of 3 mg of NaH (80% suspension in silicone oil, 0.1 mmole) and 5.7 g (70 mmoles) of ethyl formate in 50 ml of absolute ether, 3 g (23.6 mmoles) of the pyrroline II and 10 ml of ether were added dropwise with stirring over the course of 30 min, while heating the solution to boiling. The reaction was performed in an argon atmosphere. Stirring was continued for 3 h with refluxing, and then another 10 h at 20°C. The excess NaH was decomposed with 5 ml of methanol, 40 ml of water was added, the aqueous layer was removed, and the ether solution was extracted with 2×10 ml of 3% NaOH. The combined aqueous solution was washed with ether (3×30 ml), acidified to pH 6 with 5% HCl, saturated with NaCl, and extracted with $CHCl_3$ (5×25 ml). The extract was dried with $MgSO_4$, the solution was evaporated down, the residue was crystallized by triturating with hexane, and the precipitate of 5,5-dimethyl-2-(2-oxoethyl)pyrroline-1-oxide Ib was filtered off, weight 1.8 g. Upon chromatographing compound Ib on silica gel (eluent a 30:1 mixture of $CHCl_3$ and methanol), compound III was recovered.

Bis[2-(5-dimethylpyrroline-1-oxide-2-yl)-1-phenylethene-1-yl] disulfide (V) was obtained by the interaction of the pyrroline II with ethyl thiobenzoate under conditions described in [3]. From the aqueous solution, the thione IV was extracted at pH 7 by chloroform that had been presaturated with an NaCl solution. The extract was evaporated down, and the residue was dissolved in 40 ml of ether and extracted with a 2% solution of NaOH in water. The alkaline extract was washed with ether, neutralized with 5% HCl, and extracted with ether. The ether extract was dried with $MgSO_4$, and the solution was evaporated down; in the residue was the thioketone IV in the form of a readily oxidized red oil. Compound IV was dissolved in 30 ml of $CHCl_3$ and stirred with 5 g of MnO_2 for 20 min at 20°C. The excess oxidizing agent was filtered off, the solution was evaporated down, and the disulfide V was isolated by chromatography in a column with silica gel, eluent a 30:1 mixture of $CHCl_3$ and methanol.

5,5-Dimethyl-(2-oximinonitromethyl)pyrroline-1-oxide (VI). To a solution of PhLi prepared from 4.5 ml (42.5 mmoles) of bromobenzene and 0.6 g (85 mmoles) of lithium in 30 ml of ether, 5 ml (35.5 mmoles) of diisopropylamine was added dropwise with stirring. The reaction was performed in an argon atmosphere. Stirring was continued for 15 min at 20°C, the reaction mixture was chilled to −10°C, and a solution of 2.3 ml (35.5 mmoles) of methyl nitrate in 5 ml of ether was added in a single batch. Stirring was continued for 30 min without cooling, 15 ml of water was added, and the aqueous solution was separated off, washed with 10 ml of ether, and neutralized with 5% HCl. Upon shaking the aqueous solution with 15 ml of $CHCl_3$, compound VI precipitated; this was filtered off after holding the mixture for 2 h at 0°C; the VI was washed with $CHCl_3$ and dried.

TABLE 1. Characteristics of Synthesized Compounds

Compound	Empirical formula	found % / calculated %			mp, °C, and solvent	IR spectrum (KBr), ν, cm^{-1}	UV spectra, λ_{max}, nm (log ε)	Yield, %
		C	H	N				
1	2	3	4	5	6	7	8	9
Ib	$C_8H_{13}NO_2$					1550, 1600 (O–C–C–C–N)	233 (3,76), 297 (4,08)	50
III	$C_{16}H_{24}N_2O_3$	66.0 65,8	8.4 8,2	9.6 9,6	140...142, heptane/ethyl acetate	1550, 1630 (O–C–C–C–N)	258 (3,62), 339 (4,50)	50*
V	$C_{28}H_{32}N_2O_2S_2$ †	68.0 68,3	6.7 6,5	5.7 5,7	134...136, ethyl acetate	1480, 1495 (C–C–S)	248 (4,19), 343 (4,40)	20*
VI	$C_7H_{11}N_3O_4$	41.8 41,8	5.7 5,5	20.9 20,9	116...117, ethanol	1550, 1565 (C–N)	276 (3,72)	30
X a	$C_{15}H_{20}NO_2$	73.0 73,2	8.4 8,1	5.7 5,7	72...74, hexane	1680 (C–O)	244 (4,15)	30
Xb	$C_{20}H_{22}NO_2$	77.6 77,9	6.9 7,1	4.5 4,5	Oil	1670, 1685 (C–O) ‡	246 (4,06)	40
XI	$C_{14}H_{18}N_2O_2$	68.6 68,4	7.1 7,3	11.1 11,4	123...125••	1610, 1630 (C–C, C–N)	240 (2,40)	90
XII a	$C_{14}H_{17}N_2O_2$	68.3 68,6	6.9 6,9	11.2 11,4	109...111, hexane		247 (4,10)	85

TABLE 1 (Continued)

Compound	Empirical formula	found % / calculated %			mp, °C, and solvent	IR spectrum (KBr), ν, cm^{-1}	UV spectra, λ_{max}, nm (log ε)	Yield, %
		C	H	N				
1	2	3	4	5	6	7	8	9
XIII	$C_{14}H_{18}N_2O_2$	68.4 68,4	7.4 7,3	11.6 11,4	127...128, ethanol	1575, 1600 (C=C, C=N)	244 (4,17)	75
XIV	$C_{14}H_{16}N_2O_2$	68.6 68,8	6.3 6,5	11.4 11,4	82...84, methanol	1575, 1600 (C=C, C=N)	242 (4,17)	75
XV	$C_8H_{14}N_2O_2$	56.3 56,4	8.2 8,2	16.2 16,5	131...133, ethyl acetate	1655 (C=N)	237 (4,02)	70
XVI a	$C_{20}H_{23}N_3O$	74.7 74,8	7.2 7,2	13.0 13,1	134...136, ethanol	1500, 1550, 1600 (C=C, C=N)	262 (4,03)	90
XVI b	$C_{14}H_{19}N_3O$	68.7 68,6	7.6 7,8	17.0 17,2	116...117, $CHCl_3$	1560 (C=C, C=N)	252 (4,16)	90
XVII a	$C_{20}H_{21}N_3O$	75.4 75,2	6.8 6,6	13.2 13,2	120...122, heptane/ethyl acetate	1540, 1595 (C=C, C=N)	263 (4,23)	80
XVII b	$C_{14}H_{17}N_3O$	69.0 69,2	7.2 7,0	17.3 17,3	120...121, ethyl acetate	1565, 1580 (C=C, C=N), 3290 (NH)	254 (4,31)	75

*Calculated on pyrroline 2.

†%found/% calculated (S) 13.2/13.0; molecular weight (osmometric, in $CHCl_3$) 485/492.

‡In CCl_4 solution.

**Chromatographic purification.

TABLE 2. NMR Spectra of Pyrroline Derivatives

Compound	^{13}C					^{1}H			Solvent
	C-2	C-3, C-4	C-5	$(CH_3)_2$	R-2	$(CH_3)_2$	$-CH_2CH_2-$	R-2	
III	141,10, 152,63	24,46, 27,94, 32,02, 33,38	71,30, 72,97	24,97, 25,07	103,73 (C-CH), 111,02 (C-CH), 133,06 (CH-CN), 172,56 (CH-O)	1,27 (6H, s), 1,31 (6H, s)	1,90 (2H, t, J = 6,5 Hz), 2,00 (2H, t, J =6,5 Hz), 2,59 (2H, t, J = 7,5 Hz), 2,88 (2H, t, J = 7,5 Hz)	6,51, 6,58 (2H, CH=CH, J_{AB} = =16 Hz), 7,87(1H, s, CH=O), 14,0 (1H, br. s,. OH)	$CDCl_3$
V	139,30, 139,50	26,17, 27,11, 32,55, 32,78	72,49, 72,73	25,19, 25,31	127,82...129,70 (m, Ph), 142,28, 143,39 (C-C-S), 128,17 (CH-CS)	1,26 (6H, s), 1,29 (6H, s)	1,7...3,0 (8H, m)	7,0...7,6 (12H, Ph_2, CH=)	$CDCl_3$
VI	126,35, 126,72	24,23, 24,93, 31,50, 32,70	74,43, 76,56	24,53, 24,78	146,40	1,31 (6H, s)	2,2 (2H, m), 2,9 (2H, m)	13,21 (1H, br. s, OH)	DMSO-D_6
XI	148,46	25,88, 28,53	75,39	25,69	32,98 (CH_2), 153,01 (C=N), 129,21, 129,62, 130,140 (Ph)	1,36 (6H, s)	1,97 (2H, t, J = 7,5 Hz), 2,54 (2H, t, J = 7,5Hz)	3,92 (2H, br. s, 7,3...7,7 (5H, m, Ph)	CD_3OD
XV	138,55	23,79, 26,79, 27,31, 31,61	72,55, 72,71	25,00	31,61 (CH_2), 143,26, 143,94 (CH=N)	1,21 (6H, s)	1,9 (2H, m), ,5 (2H, m)	6,74 (1H, t, J = =5 Hz), 7,34 (1H, t, J = 5,5 Hz), 11,7 (1H, br. s, OH), 3,19 (2H, d, J = =5,5 Hz), 3,29 (2H, d, J = 5Hz)	DMSO-D_6

TABLE 3. ^{13}C NMR Spectra of Pyrazole and Isoxazole Derivatives

Compound	C-3	C-4	C-5	3-Ph	$(CH_2)_2$	$(CH_3)_2$	$C(CH_3)_2$	Solvent
XIII	161,66	98,75	174,91	126,41, 128,93, 129,85	21,23, 35,64	24,16	55,69	DMSO-D_6
XIV*	163,95	100,32	174,98	127,74, 130,01, 131,14	22,39, 35,65	20,97	99,29	CD_3OD
XVIa	151,42	102,68	144,93	139,82, 133,22, 125,42...128,98	21,03, 37,41	23,98	56,83	$CDCl_3$
XVIb	—	99,91	—	124,86, 127,05, 128,45	37,90	24,17	56,93	DMSO-D_6
XVIIa	151,51	102,79, 98,20	143,96, 143,66	139,63, 133,14, 125,3...129,07	23,82, 24,02, 36,23, 36,65	20,68, 21,35	79,02	$CDCl_3$

*Monomer-dimer ratio 1:9.

TABLE 4. PMR Spectra of Pyrazole and Isoxazole Derivatives

Compound	CH-	CH_2CH_2	$(CH_3)_2$	3-Ph	Solvent
XIII	6,75 (1H, s)	1,75 (2H, m), 2,8 (2H, m),	1,02 (6H, s),	7,4...7,8 (5H, m)	DMSO-D_6
XIV*	6,61 (1H, s)	2,5 (2H, m), 2,7 (2H, m),	1,21 (6H, s), 1,68 (6H, s),	7,4...7,8 (5H, m)	CD_3OD
XVIa	6,54 (1H, s)	1,76 (2H, m), 2,63 (2H, m),	1,02 (6H, s),	7,3...7,9 (10H, m)†	$CDCl_3$
XVIb	6,43 (1H, s)	1,72 (2H, m), 2,60 (2H, m),	1,03 (6H, s),	7,3...7,8 (5H, m)‡	DMSO-D_6
XVIIa	6,53 (1H, s) 6,59 (1H, s)	2,35 (2H, m), 2,53 (2H, m),	1,10 (6H, s), 1,46 (6H, s),	7,4...7,9 (5H, m)	$CDCl_3$
XVIIb	6,47 (1H, s)	2,4 (4H, m),	1,16 (6H, s), 1,59 (6H, s),	7,3...7,8 (5H, m)‡	DMSO-D_6

*Monomer-dimer ratio 1:9.

†1,3-Ph_2.

‡12.4 (1H, br.s, NH), XVIb; 12.65 (1H, br.s, NH), XVIIb.

2,5,5-Trimethyl-2-phenacylpyrrolidine-1-oxide (Xa). To a solution of methylmagnesium iodide, prepared from 0.36 g (15 mmoles) of magnesium and 1.1 ml (10 mmoles) of methyl iodide in 20 ml of ether, a solution of 0.7 g (3 mmoles) of the pyrroline Ia in 10 ml of THF was added dropwise with stirring. The stirring was continued for 72 h at 20°C, an aqueous solution of NH_4Cl was added until a solution had been formed, the organic layer was separated off, and the aqueous layer was extracted with ether. The combined extract was dried with $MgSO_4$, the drying agent was filtered off, 0.3 g of MnO_2 was added to the solution, and the mixture was stirred for 30 min at 20°C. The excess oxidizing agent was filtered off, the solution was evaporated down, and compound Xa was recovered by chromatographing in a column with silica gel, eluent $CHCl_3$.

5,5-Dimethyl-2-phenacyl-2-phenylpyrrolidine-1-oxide (Xb). To a solution of phenyllithium, prepared from 0.34 g (48 mmoles) of lithium and 2.5 ml (24 mmoles) of bromobenzene in 20 ml of ether, a solution of 0.7 g (3 mmoles) of the pyrroline Ia in THF was added dropwise with stirring. The reaction was performed in an argon atmosphere. Stirring was continued for 2 h at 20°C; then 10 ml of water was added, the organic layer was separated off, and the aqueous layer was extracted with ether. Compound Xb was recovered under the conditions indicated above, with the eluent in the chromatography a 10:1 mixture of hexane and ethyl acetate.

5,5-Dimethyl-2-(2-oximino-2-phenylethyl)pyrroline-1-oxide (XI). A solution of 0.5 g (2.2 mmoles) of the ketone Ia, 0.76 g (11 moles) of hydroxylamine hydrochloride, and 0.36 g (6.5 mmoles) of CH_3ONa in 15 ml of methanol was held for 5 h at 20°C and then evaporated down. The residue was treated with 10 ml of a saturated aqueous NaCl solution; the precip-

itate, consisting of the oxime XI, was filtered off, washed with water and then hexane, and dried. The oxime XI can be purified by chromatography in a column with silica gel, eluent a 20:1 mixture of $CHCl_3$ and methanol.

Nitroxyl radical XIIa: Obtained by oxidation of 0.2 g of the oxime XI by 1 g of MnO_2 in 10 ml of $CHCl_3$, for 10 min.

Upon dissolving the oxime XI in boiling ethanol, with subsequent cooling, a precipitate is formed, consisting of 5-(3-hydroxylamino-3-methylbutyl)-3-phenylisoxazole (XIII). Compound XIII is also formed in a small amount in the chromatography of XI on silica gel.

2-(2-Oximinoethyl)-5,5-dimethylpyrroline-1-oxide (XV). To a solution of hydroxylamine, prepared from 1.3 g (19 mmoles) of hydroxylamine hydrochloride and 0.6 g (11.4 mmoles) of CH_3ONa in 20 ml of methanol, 0.6 g (3.8 mmoles) of the aldehyde Ib was added, and the mixture was held for 1 h at 20°C. The solution was evaporated down, 10 ml of saturated aqueous NaCl solution was added to the residue, and the mixture was then extracted with $CHCl_3$ (6×15 ml). The extract was dried with $MgSO_4$, the solution was evaporated down, the residue was crystallized by triturating with a small quantity of a 3:1 mixture of hexane and ethyl acetate, and the precipitate of the oxime XV was filtered off.

5-(3-Hydroxylamino-3-methylbutyl)-1,3-diphenylpyrazole (XVIa). To a solution of 0.5 g (2.2 mmoles) of the ketone Ia in methanol, a solution was 0.32 ml (3.3 mmoles) of phenylhydrazine in a mixture of 2 ml of methanol and 2 ml of water was added; this solution was neutralized with CH_3COOH (pH 7), and the mixture was left was 72 h at 20°C and then evaporated down. A 5-ml quantity of water was added to the residue, and the mixture was extracted with $CHCl_3$ (2×20 ml). The extract was dried, the solution was evaporated down, and compound XVIa was recovered by chromatographing in a column with silica gel, eluent a 30:1 mixture of $CHCl_3$ and methanol.

5-(3-Hydroxylamino-3-methylbutyl)-3-phenylpyrazole (XVIb). A solution of 0.5 g (2.2 mmoles) of the ketone Ia and 1 ml of hydrazine in 10 ml of methanol was held for 12 h at 20°C and then evaporated down. A 10-ml quantity of saturated aqueous NaCl solution was added to the residue, and the mixture was extracted with $CHCl_3$ (4×15 ml). Upon standing in the cold, the pyrazole XVIb precipitated from the extract; this was filtered off and washed with hexane.

5-(3-Nitroso-3-methylbutyl)-1,3-diphenylpyrazole (XVIIa). A solution of 0.2 g of the pyrazole XVIa in $CHCl_3$ was stirred with 2 g of MnO_2 for 30 min; the excess oxidizing agent was filtered off, and the solution was evaporated down. The nitroso compound XVIIa was purified by chromatography in a column with silica gel, eluent a 30:1 mixture of $CHCl_3$ and methanol.

Under analogous conditions, by the oxidation of compounds XIII and XVIb, the nitroso compounds XIV and XVIIb were obtained, and by oxidation of the oxime XI the nitroxyl radical XIIa.

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