Synthesis and properties of monoimines of α-diketones, derivatives of 3-imidazoline nitroxides

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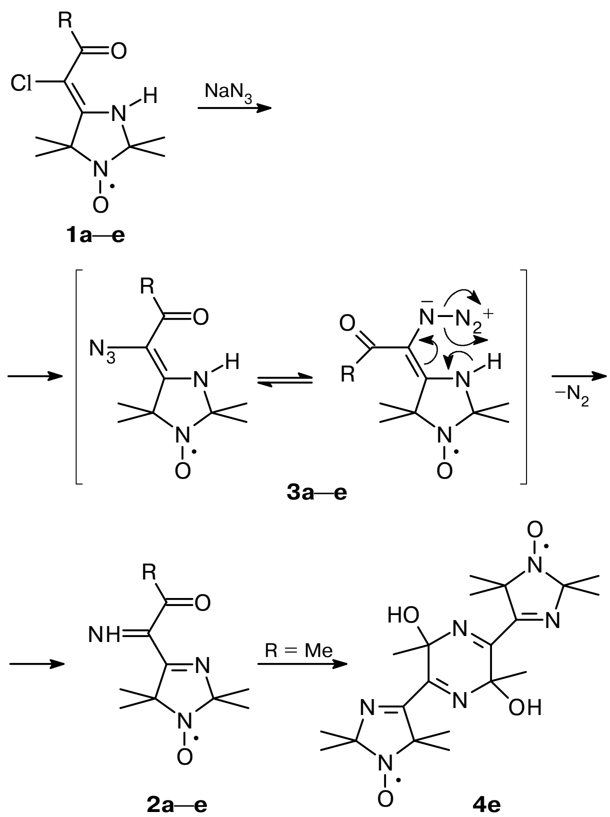
The reaction of 4-(2*R*-1-chloro-2-oxoethylidene)-substituted imidazolidine-1-oxyl with sodium azide gives monoimines of α-diketones, derivatives of 3-imidazoline nitroxides. Reactions of these products with nitrogen binucleophiles were used to prepare various heterocyclic compounds containing an imidazoline nitroxide moiety.

Key words: enamino ketones, azides, monoimines of α-diketones nitroxides, 3-imidazoline, imidazole, quinoxaline, pyrazine, triazine, oxazole.

Previously,[1] we showed that the reaction of chloro-substituted enamino ketones (**1**) with sodium cyanide affords cyano-substituted derivatives. This reaction, which is formally nucleophilic substitution, proceeds in reality *via* the formation of epoxides. The nitriles thus produced can be used as paramagnetic chelating reagents[2] and pH-sensitive spin probes. Probably, azide-substituted enamino ketones would also be of interest as paramagnetic ligands because the azido group, which is geometrically similar to the nitrile group, can be involved in the coordination with a metal. To continue research into the properties of chloro-substituted enamino ketones and to prepare new chelating reagents, in this work, we studied the reactions of chloro-substituted enamino ketones **1a—e** with sodium azide (Scheme 1).

Scheme 1



R = Ph (**a**), EtO (**b**), Pr^n (**c**), 4-pyridyl (**d**), Me (**e**)

Results and Discussion

In view of the previously established possibility of replacement of the chlorine atom in enamino ketones **1** by the cyano group, it could be expected that the reaction with sodium azide will give the corresponding azido derivatives, although according to published data, the substitution of an azide group for chlorine at the C=C bond can proceed only in the presence of an electron-withdrawing substituent in the β-position.[3] However, the reaction of enamino ketone **1a** with NaN_3 in DMSO gave compound **2a** instead of the expected azide (see Scheme 1). The structure of this product as an α-diketone monoimine, a derivative of 3-imidazoline, was confirmed by X-ray diffraction data and by the IR spectrum of this compound, which exhibits absorption bands for the carbonyl group at 1666 cm^{-1}, for C=C and C=N bonds at 1622, 1600, and 1580 cm^{-1}, and an intense band corresponding to NH-bond vibrations at 3219 cm^{-1}.

The molecule of **2a** is generally nonplanar (Fig. 1). The dihedral angle between the imino group and the imidazoline ring is equal to 17.10(8)°, and the angle between the imino group and the benzoyl fragment reaches 89.89(6)°. The PM3 calculations for molecule

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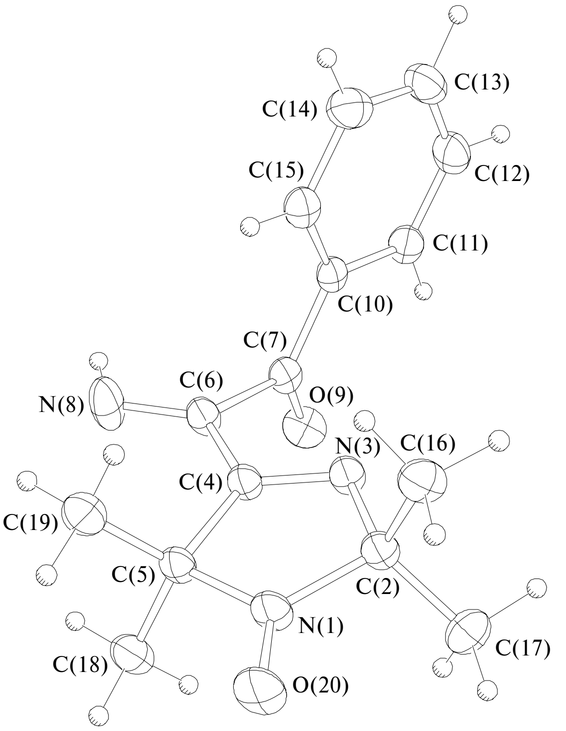


Fig. 1. Structure of molecule **2a** in the crystal.

2a predict a similar nonplanar structure. A search through the Cambridge Structural Database[4] for a N=C—C(=N)—C=O fragment not incorporated in cyclic systems resulted in three nonplanar structures. However, the ketoimine fragment in these three compounds is planar, unlike that in molecule **2a**. The bond lengths in **2a** are close to the statistical mean values[5] and to those in 4-(1-methoxyiminoethyl)-2,2,5,5-tetramethyl-3-imidazoline 1-oxide.[6]

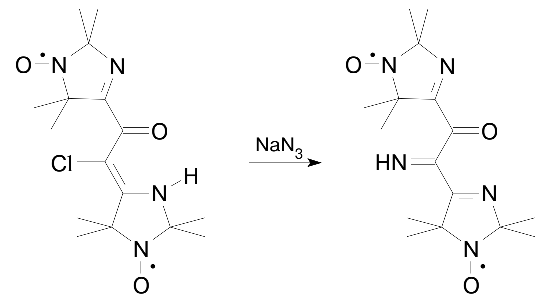
Bond	*d*/Å	Bond	*d*/Å
N(1)—O(20)	1.267(2)	C(6)—C(7)	1.522(2)
N(3)—C(4)	1.279(2)	C(7)—O(9)	1.215(2)
C(4)—C(6)	1.480(2)	C(7)—C(10)	1.473(2)
C(6)—N(8)	1.263(2)		

Attention is attracted by the length of the C(6)—C(7) bond (1.522(2) Å) between the carbonyl and imino groups, which is longer than the statistical mean value for the nonconjugated C=C—C=O fragment (1.484(17) Å)[5] and than, for example, the length of this bond in (*E*,*E*)-hexane-2,3,4,5-tetraone 3,4-dioxime, which is 1.494 Å.[7] The length of this bond found by PM3 calculations is 1.52 Å. In the crystal, the molecules of **2a** are connected in chains stretched along the *a* axis through N—H...O type interactions.

Interaction	*d*/Å	Angle	ω/deg
N(8)—H	0.96(3)	N(8)—H...O(20)	171(2)
H...O(20)	2.32(3)		
N(8)...O(20)	3.270(2)		

Enamino ketones **1b—e** react with NaN_3 in a similar way (see Scheme 1). It should be noted that the reaction of enamino ester **1b** with NaN_3 gives, apart from imine **2b**, intermediate azide **3b**, which is easily converted into imine **2b** on recrystallization. Conversely, in the case of ketone **1e**, the corresponding imine cannot be isolated, dimer **4** being produced as the reaction product. The dimeric structure of **4** is confirmed by the double molecular mass found by ebullioscopy and by the ESR spectrum, which is a quintet with the HFC constant a_N = 14.3 Gs ($CHCl_3$). The transformation of chloro-substituted enamino ketones into imino ketones is apparently a fairly general process. In particular, biradical **5** is converted into imine **6** under similar conditions (Scheme 2).

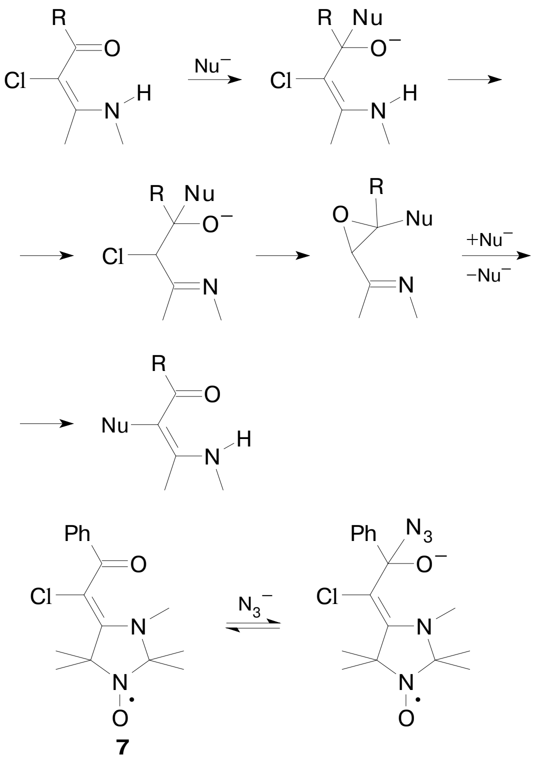
Scheme 2



5 **6**

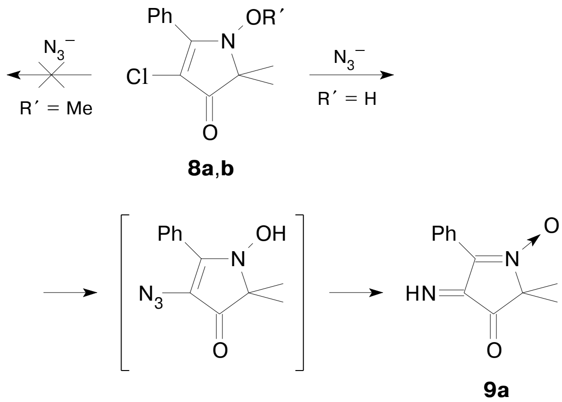
It is known that imines can be formed on treatment of azides with strong acids. Under these conditions, the azido group is protonated and a nitrogen molecule is cleaved. Since the reaction of chloro-substituted enamino ketones **1** with NaN_3 was carried out in a nearly alkaline medium, the instability of azides **3** could be explained by migration of a proton from the ring heteroatom to the azido group. The ease of this migration might be due to the fact that it occurs as an intramolecular process. Yet another possibility is deprotonation of the ring nitrogen atom induced by the azide ion followed by elimination of a nitrogen molecule and protonation of the resulting imine anion (*cf.* Ref. 8). In order to verify the possibility of participation of the hydrogen atom in position 3 of the heterocycle in the formation of imines, enamino ketone **7**, whose molecule contains no N—H bond, was involved in the reaction with NaN_3. However, it was found that this compound does not react with NaN_3 under similar conditions (~20 °C), and only slow reduction of the nitroxide group to the hydroxylamine group takes place on heating (70 °C). This reaction route seems unusual if one recalls that DMSO is an oxidant. However, the absence of nucleophilic substitution in this case confirms the substitution mechanism proposed in our previous study,[1] according to which nucleophilic addition at the carbonyl carbon atom is the first step. This step is evidently followed by migration of the double bond into the ring, stimulated by the absence of conjugation. As a result, the chlorine atom becomes attached to an sp^3 carbon atom, which ensures the possibility of intramolecular nucleophilic substitution to give an epoxide. The subsequent opening of the epoxide ring induced by a second equivalent of the nucleophile furnishes the reaction product (Scheme 3).

Scheme 3



When there is no proton at the enamine nitrogen atom, as in compound **7**, the double bond migration is impossible and no substitution takes place. Similarly, the reaction of pyrroline **8a** with sodium azide gives rise to imine **9**, while the methoxy derivative **8b** does not react under these conditions (Scheme 4).

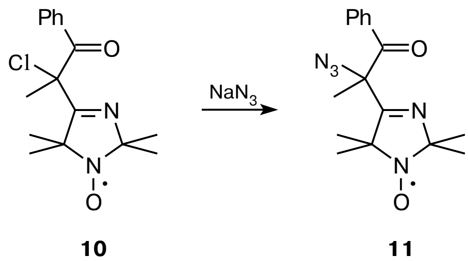
Scheme 4



R′ = H (**a**), Me (**b**)

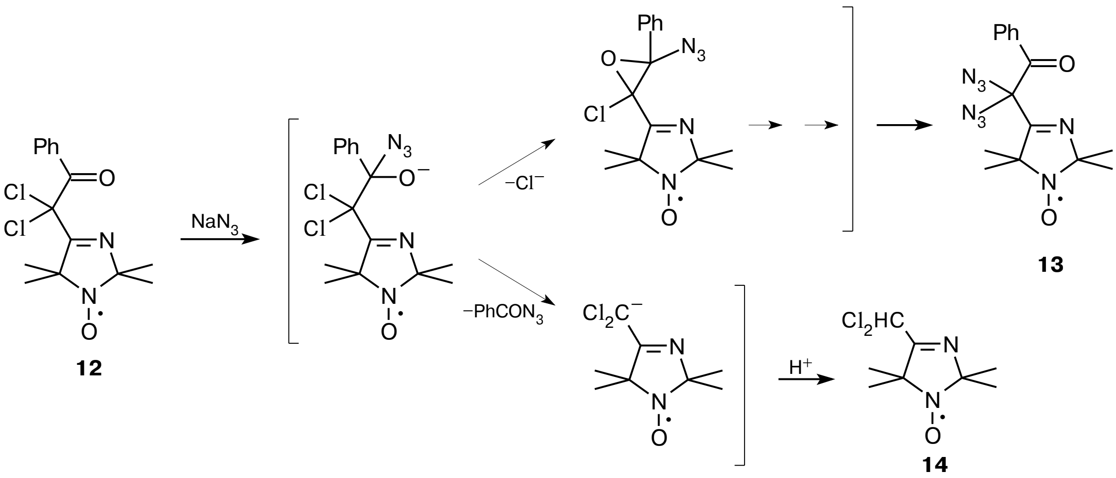
An indirect piece of evidence for the involvement of the N—H-bond proton in the decomposition of azides is the reaction of compound **10** with NaN_3, giving rise to stable azide **11** as the only product (Scheme 5).

Scheme 5



The reaction of dichloro derivative **12** with NaN_3 follows a more complicated route. In addition to the expected diazide **13**, it affords dichloro 3-imidazoline **14** and benzoyl azide. This composition of the reaction products is consistent with the assumption that the reaction of chloro-substituted enamino ketones with

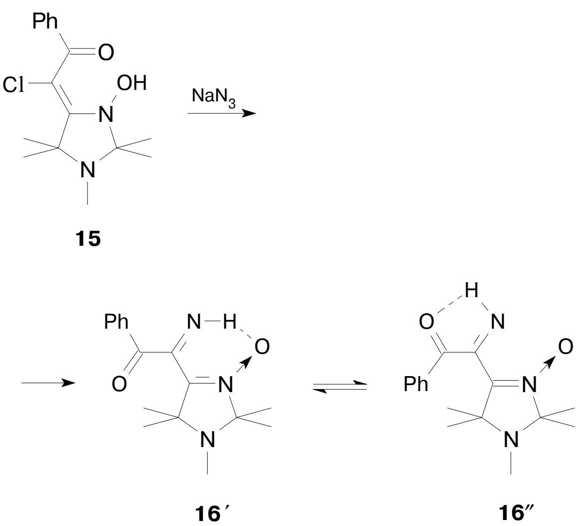
Scheme 6



nucleophiles starts with the addition to the carbonyl group (*cf.* Ref. 1) (Scheme 6).

As was to be expected, the reaction of the chlorinated β-oxo nitrone **15** with NaN_3 follows a similar route and yields imine **16**. Apparently, the nitroxide group does not influence the reaction pathway (Scheme 7).

Scheme 7



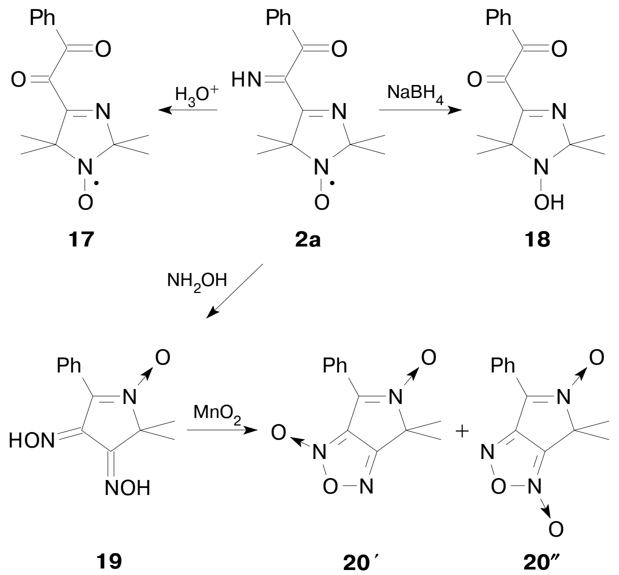
An interesting feature of compound **16** is the double set of signals in the NMR spectra in $CDCl_3$, which can be indicative of the existence of two isomers (**16′** and **16″**), differing in the position of the intramolecular hydrogen bond. The presence of an intramolecular hydrogen bond in both forms is indicated by the fact that the NH-proton signals are located in a very low field, at 10.4 and 13.5 ppm for isomers **16′** and **16″**, respectively. The signals were assigned proceeding from the position of a more intense low-field signal corresponding to C(4) in form **16′** in the ^{13}C NMR spectrum (*cf.* Ref. 9). According to NMR data, in DMSO, the compound exists almost exclusively as isomer **16′**.

Some properties of the monoimines synthesized were studied taking compound **2a** as an example. Thus imine **2a** is hydrolyzed in dilute HCl to give α-diketone **17**, while the reaction of the same imine with an equivalent amount of $NaBH_4$ reduces the nitroxide group and is accompanied by hydrolysis of the imino group giving rise to diamagnetic diketone **18** (Scheme 8).

The nitroxide group is usually stable against $NaBH_4$. The reduction of the nitroxide group in this particular case is due to a multistep process that includes preliminary hydrolysis of the imino group, its reduction with sodium borohydride, and subsequent reduction of the nitroxide group by the intermediate hydroxy ketone, which affords diamagnetic diketone **18** (*cf.* Ref. 10).

The reaction of imine **2** with hydroxylamine is also accompanied by reduction of the nitroxide group; this results in the hydrolytic cleavage of the 3-imidazoline ring. The subsequent recyclization and oximation give rise to dioxime derived from pyrroline oxide **19** (*cf.* Ref. 11). It should be noted that the properties of compound **19**, in particular, the melting point and NMR chemical shifts, differ markedly from published data, although they do not contradict the structure ascribed. The data of elemental analysis also correspond to structure **19**.

Scheme 8

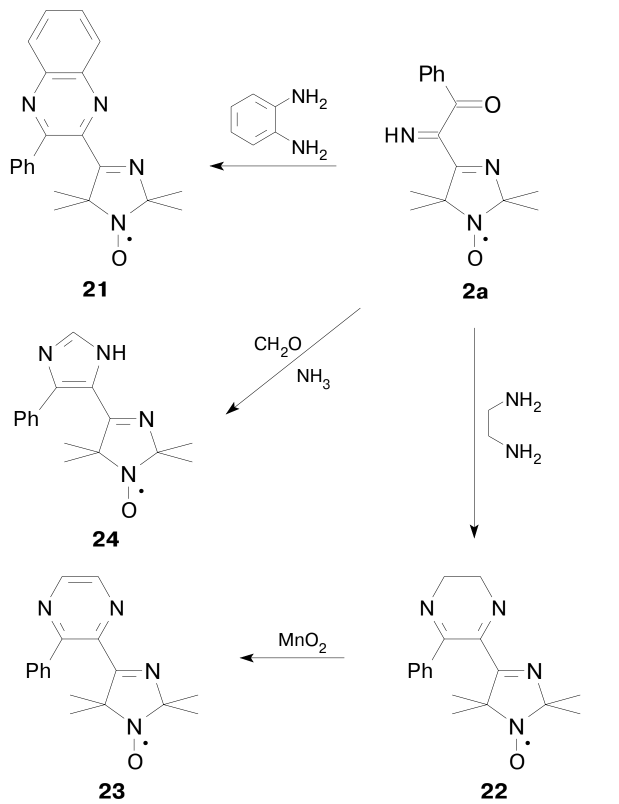


According to published data, dioxime **19** is oxidized by MnO_2 to give furoxan derivative **20**; judging by NMR spectra, this product is mainly formed as one of the two possible isomers, namely, **20′**.[11] Oxidation of compound **19** under similar conditions also produces two isomeric furoxans **20** but these are formed in approximately equal amounts, their ratio changing with time toward isomer **20′**. According to ^1H NMR, the **20′** : **20″** ratio after 2 h at 20 °C in a $CDCl_3$ solution is 1.5 : 1.

The foregoing facts indicate that compound **19** is actually a dioxime but it differs from the compound reported in the literature in the configuration of the oxime groups. The different positions of signals in the NMR spectra suggest that in compound **19**, the oxime group in position 4 has a *Z*-configuration relative to the methyl groups, whereas the compound described in the literature is the *E*-isomer. This is quite consistent with the fact that the conditions for the synthesis of dioxime **19** described in the literature,[11] are much more rigorous (refluxing in pyridine for 6 h) than those used in this study.

The ease of formation of the heterocyclic system of dihydropyrazine **4** from monoimine **2e** stimulated us to attempt to synthesize heterocyclic compounds from the α-diketone monoimines prepared in this work. When compound **2a** is made to react with *o*-phenylenedi-

Scheme 9



amine, quinoxaline derivative **21** is formed; the reaction with ethylenediamine affords dihydropyrazine derivative **22**, which readily undergoes aromatization on treatment with MnO_2 to give pyrazine **23**. The reaction of imine **2a** with formaldehyde and ammonia affords imidazole **24** (Scheme 9).

Quite unexpectedly, the reaction of α-diketone monoimine **2a** with benzamidine gives rise to two compounds. According to elemental analysis and spectral characteristics, one product can be identified as oxazole derivative **25** and the other product is triazine derivative **26**. However, it cannot be ruled out that these compounds are derivatives of compounds **25′** and **26′**, respectively, with a different arrangement of heteroatoms. The formation of oxazole **25** cannot be explained without the step of reduction, while the formation of triazine **26** cannot be interpreted without oxidation. Apparently, the first step of the reaction is the nucleophilic addition of the benzamidine amino group to either the imino or the carbonyl group of the substrate **2a** to give the corresponding intermediates, and at the second step, these intermediates are reduced and oxidized giving rise to the final products (Scheme 10).

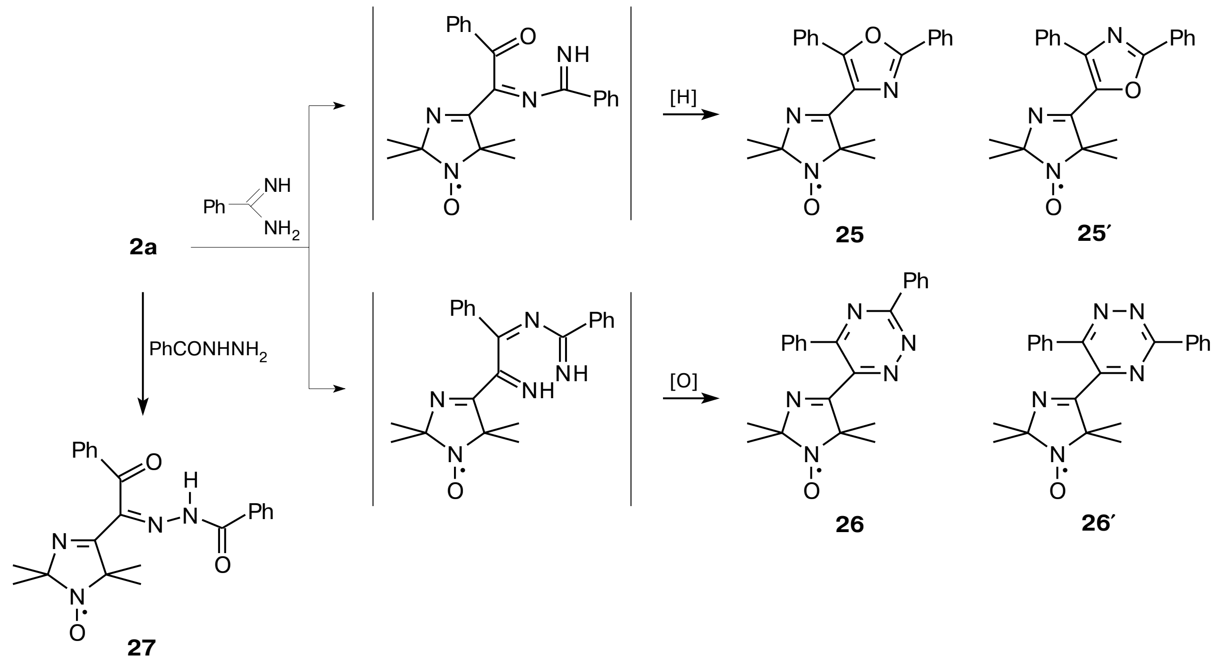
The reaction of **2a** with benzoylhydrazine, which was performed in order to synthesize **26** *via* an alternative route yielded benzoylhydrazone **27**, resulting from nucleophilic attack at the imino group.

Thus, it was demonstrated that imines **2** are useful starting compounds in the synthesis of heterocyclic compounds containing an imidazoline nitroxide-containing fragment as a substituent and presenting interest as paramagnetic chelate-forming compounds.[12]

Experimental

IR spectra were recorded on a Bruker IFS 66 spectrometer as KBr pellets (concentration 0.25%, thickness of a pellet

Scheme 10



1 mm). UV spectra were measured on a Specord M-40 spectrophotometer in EtOH. ^{1}H and ^{13}C NMR spectra were run on a Bruker WP 200SY spectrometer for a 5% solution in $CDCl_3$ using HMDS as the internal standard. High-resolution mass spectra were recorded on a Finnigan MAT 8200 mass spectrometer with direct sample injection. The chloro-substituted enamino ketones **1** were prepared by a procedure described previously;[1] dichloro derivative **12** was synthesized by a known procedure;[13] and oxonitrone **15** and pyrroline **8a** were prepared by a known procedure.[14] Commercial-grade $CHCl_3$ and CCl_4

Table 1. Characteristics of the compounds synthesized

Compound[a]	Yield (%)	M.p. /°C	IR (KBr), ν/cm^{-1}	UV (EtOH), λ_{max}/nm (logε)	Found/Calculated (%) C	H	N	Molecular formula
2a	95	148—150	1666 (C=O); 1622, 1600, 1580 (C=C, C=N), 3219 (NH)	253 (4.28)	66.43	6.79	15.65	$C_{15}H_{18}N_3O_2$
					66.16	6.66	15.43	
2b	65	73—75	1743 (C=O), 1626, 1605 (C=N), 3198 (NH)	—	55.01	7.52	17.42	$C_{11}H_{18}N_3O_3$
					55.99	7.55	17.59	
2c	75	63—65	1710 (C=O), 1602 (C=N), 3216 (NH)	—	60.33	8.80	17.34	$C_{12}H_{20}N_3O_2$
					60.48	8.46	17.63	
2d	75	147—148	1696 (C=O), 1621, 1600 (C=N), 3140 (NH)	—	61.24	6.22	20.12	$C_{14}H_{17}N_4O_2$
					61.52	6.27	20.50	
2e	—	—	1720 (C=O), 1624, 1603 (C=N), 3184 (NH)	—	—	—	—	—
4	50	177—179	1636, 1608 (C=N); 3273, 3405 (OH)	—	57.11	7.82	19.83	$C_{20}H_{32}N_6O_4$
					57.12	7.67	19.99	
6	60	172—173	1628, 1607 (C=N); 3261 (NH)	335 (3.09)	57.34	7.71	20.54	$C_{16}H_{25}N_5O_3$
					57.30	7.51	20.88	
7	90	153—155	1620, 1597, 1576, 1530 (C=C—C=O)	249 (4.16), 372 (4.0)	62.03	6.51	8.94	$C_{16}H_{20}ClN_2O_2$
					62.43	6.55	9.10	
9	60	101—104	1766 (C=O), 1616 (C=N), 3224 (NH)	244 (3.57), 296.4 (3.82), 334.4 (3.37)	66.72	5.51	13.04	$C_{12}H_{12}N_2O_2$
					66.65	5.59	12.96	
10	60	108—110	1697 (C=O), 1611, 1597, 1582 (C=N, C=C)	252 (4.07)	62.05	6.55	8.83	$C_{16}H_{20}ClN_2O_2$
					62.43	6.55	9.10	
11	80	45—48	1697 (C=O), 1626, 1598, 1579 (C=N, C=C), 2109 (N_3)[b]	250 (4.10)	60.01	6.51	22.91	$C_{16}H_{20}N_5O_2$
					61.13	6.41	23.28	
13	25	79—81	1697 (C=O), 1622, 1598, 1582 (C=N, C=C), 2131 (N_3)	256 (4.15)	52.82	5.14	33.10	$C_{15}H_{17}N_8O_2$
					52.79	5.02	32.82	
16	~100	120—122	1675 (C=O), 1599, 1580, 1548 (C=C, C=N), 3253 (NH)	253 (4.08), 289 (3.91)	66.92	7.31	14.63	$C_{16}H_{21}N_3O_2$
					66.88	7.37	14.62	
17	80	135—136	1704, 1675 (C=O), 1638, 1597, 1581 (C=C, C=N)	251 (4.08)	65.73	6.23	10.13	$C_{15}H_{17}N_2O_3$
					65.92	6.27	10.25	
18	60	128—130	1701, 1673 (C=O), 1626, 1596 (C=C, C=N), 3240 (OH); 3586 (OH)[c]	252 (4.02)	65.43	6.60	10.30	$C_{15}H_{18}N_2O_3$
					65.68	6.61	10.21	
19	70	178—180	1650, 1607 (C=NOH), 1545 (C=N), 3220, 3145 (OH)	235 (4.27), 297 (3.82)	57.93	5.01	17.00	$C_{12}H_{13}N_3O_3$
					58.29	5.30	17.00	
21	50	146—148	1634 (C=N)	246 (4.66), 333 (3.92)	73.15	6.14	16.18	$C_{21}H_{21}N_4O$
					73.02	6.13	16.22	
22	60	152—154	1621 (C=N)	262 (3.88), 283 (3.96)	68.42	6.96	18.81	$C_{17}H_{21}N_4O$
					68.66	7.12	18.84	
23	90	98—100	1617 (C=N)	232 (4.09), 281 (3.92)	69.13	6.38	19.03	$C_{17}H_{19}N_4O$
					69.13	6.48	18.97	
24	50	185—187	1608 (C=N), 3230 (NH)	281 (3.83)	67.54	6.81	19.54	$C_{16}H_{19}N_4O$
					67.82	6.76	19.77	
25[d]	20	146—148	1615, 1600, 1580 (C=N, C=C)	233 (4.11), 286 (4.15)	—	—	—	$C_{22}H_{22}N_3O_2$
26	20	188—190	1621, 1661 (C=C, C=N)	273 (4.48)	70.54	5.89	18.69	$C_{22}H_{22}N_5O$
					70.95	5.95	18.80	
27	25	160—163	1682, 1664 (C=O), 1603, 1581 (C=N), 3436 (NH)	258 (4.32)	67.12	5.78	14.47	$C_{22}H_{23}N_4O_3$
					67.50	5.92	14.31	

[a] The compounds were recrystallized from a hexane—AcOEt mixture (**2a**,**d**, **4**, **16**, **18**, **26**, **27**), hexane (**2b**,**c**, **9**, **10**, **13**, **25**), CCl_4 (**7**), AcOEt (**6**, **21**, **22**, **23**), aqueous EtOH (**11**), or EtOH (**19**).

[b] The IR spectrum was recorded in CCl_4.

[c] The IR spectrum was recorded in $CHCl_3$.

[d] Found, *m/z*: 360.17045. $C_{22}H_{22}N_3O_2$. Calculated: M = 360.17119.

were dried over $CaCl_2$ and distilled, DMSO was dried with NaOH and distilled *in vacuo* over NaOH, and "pure" grade hexane and rectified EtOH were used as received; *N*-chlorosuccinimide (NCS, Fluka) was used for chlorination. Manganese(IV) oxide for catalysis (TU 6-09-01-718-87) was used as the oxidant. Chromatographic purification of the synthesized compounds was performed using KSK silica gel ground at the pilot chemical plant of the Novosibirsk Institute of Organic Chemistry of the Siberian Branch of the RAS and activated by heating at 110—120 °C for 6 h and neutral Al_2O_3 with Brockman activity II. In all cases, evaporation was carried out in the vacuum of a water aspirator pump. The yields and characteristics of the compounds synthesized are presented in Table 1.

4-(1-Imino-2-oxo-2-phenylethyl)-2,2,5,5-tetramethyl-3-imidazoline-1-oxyl (2a). Enamino ketone **1a** (1.47 g, 5 mmol) was added in portions with stirring to a solution of NaN_3 (0.65 g, 10 mmol) in 25 mL of anhydrous DMSO. The reaction mixture was stirred for 2 h at 20 °C, cooled to 0 °C, and diluted with 40 mL of ice-cooled brine. The resulting precipitate of imine **2a** was filtered off, washed with brine and water and dried. The precipitate was dissolved in 10 mL of $CHCl_3$ and the solution was filtered through a silica gel layer (10 cm) and eluted with $CHCl_3$. The solution was concentrated to give imine **2a**.

Similar procedures were used to prepare imines **2b—d** and **6** from enamino ketones **1b—d** and **5**, imine **9** from pyrroline **8a**, and imine **16** from oxo nitrone **15**. The ^{1}H NMR spectrum of compound **16** (DMSO-d_6), δ: 1.28 (s, 6 H); 1.54 (s, 6 H, 2,5-Me_2); 2.37 (s, 3 H, N—Me); 7.70 (m, 5 H, C_6H_5); 11.81 (s, 1 H, NH). ^{13}C NMR (DMSO-d_6), δ: 23.4 (2,5-Me_2); 26.1 (N—Me); 62.4 (C(5)); 89.5 (C(2)); 127.8, 128.4, 133.1, 134.0 (C_6H_5); 140.8 (C(4)); 166.7 (<u>C</u>=NH); 190.1 (<u>C</u>=O). ^{1}H NMR ($CDCl_3$), δ: 1.35 (s, 6 H); 1.59 (s, 6 H, 2,5-Me_2, **16´**); 1.30 (s, 6 H); 1.49 (s, 6 H, 2,5-Me_2, **16″**); 2.31 (s, 3 H, N—Me, **16´**); 2.39 (s, 3 H, N—Me, **16″**); 7.70 (m, 5 H, C_6H_5, **16´+16″**); 10.41 (s, 1 H, NH, **16´**); 13.50 (s, 1 H, NH, **16″**). Ratio of the isomers **16´** : **16″** = 4 : 1. ^{13}C NMR ($CDCl_3$), δ: 23.9 (2,5-Me_2, **16´**); 24.2 (2,5-Me_2, **16″**); 26.3 (N—Me, **16″**); 26.6 (N—Me, **16´**); 63.2 (C(5), **16´**); 90.3 (C(2), **16´**); 91.3 (C(2), **16″**); 128.4, 128.5, 130.3, 133.4, 133.8, 134.0 (C_6H_5, **16´+16″**); 141.8 (C(4), **16´**); 138.0 (C(4), **16″**); 162.9 (C=NH, **16″**); 168.8 (C=NH, **16´**), 190.7 (C=O).

The sample of imine **2b** prepared under the indicated conditions contained, according to IR, an impurity of azide **3b**, which disappeared upon recrystallization.

In the case of reaction with enamino ketone **1e**, the precipitate formed was a mixture of imine **2e** and dimer **4**; on washing with hexane, imine **2e** was dissolved and was converted into dimer **4** upon recrystallization.

2,2,5,5-Tetramethyl-4-[2-oxo-2-(2,2,5,5-tetramethyl-1-oxyl-3-imidazolin-4-yl)-1-chloroethylidene]imidazolidine-1-oxyl (5). *N*-Chlorosuccinimide (0.27 g, 2 mmol) was added in portions over a period of 10 min to a stirred solution of 2,2,5,5-tetramethyl-4-[2-oxo-2-(2,2,5,5-tetramethyl-1-oxyl-3-imidazolin-4-yl)ethylidene]imidazolidin-1-oxyl (0.59 g, 1.8 mmol), prepared by a known procedure,[15] in 20 mL of $CHCl_3$. The mixture was stirred for 10 min at 20 °C and concentrated, the residue was washed with hexane, and the precipitate of compound **5** containing a succinimide impurity was filtered off, washed with hexane, and used in the reaction with NaN_3 without purification.

2,2,3,5,5-Pentamethyl-4-(2-oxo-2-phenyl-1-chloroethylidene)imidazolidine-1-oxyl (7). *N*-Chlorosuccinimide (0.27 g, 2 mmol) was added to a solution of 2,2,3,5,5-pentamethyl-4-phenacylideneimidazolidin-1-oxyl (0.55 g, 2 mmol), prepared by a known procedure,[16] in CCl_4, and the mixture was stirred for 15 min at 20 °C. The succinimide precipitate was filtered off and washed with CCl_4 until the filtrates were colorless. The solution was concentrated, the residue was washed with hexane, and the precipitate of compound **7** was filtered off and also washed with hexane.

2,2,5,5-Tetramethyl-4-(2-oxo-2-phenyl-1-chloroprop-1-yl)-3-imidazoline-1-oxyl (10). A solution of 2,2,5,5-tetramethyl-4-(1-methyl-2-oxo-2-phenylethylidene)imidazolidin-1-oxyl (0.41 g, 1.5 mmol), prepared by a previously reported procedure,[17] and NCS 0.22 g (1.7 mmol) in $CHCl_3$ was kept for 30 min at 20 °C and concentrated. Compound **10** was isolated by chromatography on a column with silica gel using $CHCl_3$ as the eluent.

4-(2-Azido-3-oxo-3-phenylprop-2-yl)-2,2,5,5-tetramethyl-3-imidazoline-1-oxyl (11). Compound **10** (0.24 g, 0.8 mmol) was added to a solution of NaN_3 (0.1 g, 1.6 mmol) in 10 mL of anhydrous DMSO. The reaction mixture was stirred for 3 h at 20 °C, cooled to 0 °C, and diluted with 20 mL of ice-cooled brine. The solution was extracted with $CHCl_3$ (3×15 mL), and the extract was washed with brine (3×15 mL) and water, dried with $MgSO_4$, and concentrated to give azide **11**.

Reaction of enamino ketone 7 with NaN_3. A suspension of compound **5** (0.5 g, 1.6 mmol) and NaN_3 (0.21 g, 3.3 mmol) in 10 mL of anhydrous DMSO was heated for 30 h at 70 °C, cooled to 0 °C, and worked-up as described for azide **11**. The mixture obtained after the workup was chromatographed on a column with silica gel using $CHCl_3$ as the eluent; this gave successively the starting enamino ketone **7** (0.1 g) and 1-hydroxy-2,2,3,5,5-pentamethyl-4-(2-oxo-2-phenyl-1-chloroethylidene)imidazolidine (0.1 g), whose structure was confirmed by oxidation by MnO_2 in enamino ketone **7**. For this purpose, a solution of 1-hydroxy-2,2,3,5,5-pentamethyl-4-(2-oxo-2-phenyl-1-chloroethylidene)imidazolidine (0.1 g) in 10 mL of $CHCl_3$ was stirred with MnO_2 (1 g) for 15 min, filtered, and concentrated. The residue was enamino ketone **7**, whose structure was established by comparison of the IR spectrum with the spectrum of an authentic sample.

Reaction of dichloro derivative 12 with NaN_3. Dichloro derivative **12** (0.8 g, 2.4 mmol) was added with stirring to a solution of NaN_3 (0.47 g, 7.2 mmol) in 25 mL of anhydrous DMSO. The mixture was stirred for an additional 2.5 h at 20 °C and worked-up as indicated for azide **11**. The resulting product mixture was chromatographed on a column with silica gel (using a hexane—AcOEt mixture, 10 : 1, as the eluent); this gave successively benzoyl azide (0.1 g), diazide **13** (0.2 g), and dichloro derivative **14** (0.12 g)[18].

2,2,5,5-Tetramethyl-4-(1,2-dioxo-2-phenylethyl)-3-imidazoline-1-oxyl (15). A 5% solution of HCl was added dropwise to a stirred suspension of imine **2a** (0.1 g) in 3 mL of MeOH to pH 1. The mixture was stirred for an additional 10 min and the precipitate of diketone **17** was filtered off, washed with water, and dried.

1-Hydroxy-2,2,5,5-tetramethyl-4-(1,2-dioxo-2-phenylethyl)-3-imidazoline (18). A mixture of imine **2a** (0.3 g, 1.1 mmol) and $NaBH_4$ (0.013 g, 0.33 mmol) in 10 mL of EtOH was stirred for 1 h at 20 °C, then an additional $NaBH_4$ (0.013 g, 0.33 mmol) was added, and stirring was continued for an additional 2 h. The solution was concentrated, water (5 mL) was added to the residue, and the product was extracted with $CHCl_3$. The extract was dried with $MgSO_4$, the solution was concentrated, and compound **18** was isolated by preparative TLC on silica gel using a 30 : 1 $CHCl_3$—MeOH mixture as the eluent.

3,4-Dihydroximino-5,5-dimethyl-2-phenylpyrroline 1-oxide (19). Sodium methoxide (0.53 g, 10 mmol) and then imine **2a**

(0.67 g, 2.5 mmol) were added to a solution of $NH_2OH \cdot HCl$ (1.05 g, 15 mmol). The resulting mixture was kept for 24 h at 20 °C and concentrated. Water (5 mL) was added to the residue, the precipitate of dioxime **19** was filtered off, washed with water, and dried. ^{1}H NMR (DMSO-d$_6$), δ: 1.53 (s, 6 H, 5,5-Me$_2$); 7.50 (m, 5 H, C_6H_5); 12.14 (s, 2 H, NOH). ^{13}C NMR (DMSO-d$_6$), δ: 24.8 (5,5-Me$_2$); 72.3 (C(5)); 127.0, 128.8, 129.2, 129.9 (C_6H_5); 136.6 (C(2)); 140.85, 147.9 (C=N). Dioxime **19** was oxidized to give a mixture of furoxans **20** by treatment of **19** (0.2 g, 0.9 mmol) with MnO_2 (1 g, 11.4 mmol) in $CHCl_3$ (stirring for 1 h at 20 °C). The reaction mixture was filtered through a silica gel layer (10 cm) and the solution was concentrated. The ^{13}C NMR spectrum ($CDCl_3$) corresponds to published data.[11] ^{1}H NMR ($CDCl_3$), δ: 1.76 (s, 6 H, Me$_2$, **20′**); 1.82 (s, 6 H, Me$_2$, **20″**); 7.50 (m, 3 H, C_6H_5, **20′**+**20″**); 8.40 (m, 2 H, C_6H_5, **20″**); 8.60 (m, 2 H, C_6H_5, **20′**); the ratio **20′** : **20″** = 1.5 : 1.

2-(2,2,5,5-Tetramethyl-1-oxyl-3-imidazolin-4-yl)-3-phenylquinoxaline (21). A solution of imine **2a** (0.3 g, 1 mmol), *o*-phenylenediamine (0.12 g, 1 mmol), and a small amount of $TsOH \cdot H_2O$ (~10 mg) in 5 mL of EtOH was refluxed for 2 h and concentrated. Compound **21** was isolated by chromatography on a column with Al_2O_3 using $CHCl_3$ as the eluent.

The reaction of **2a** with ethylenediamine under similar conditions gave dihydropyrazine **22**, which was purified by chromatography on a column with silica gel using $CHCl_3$ as the eluent.

2-(2,2,5,5-Tetramethyl-1-oxyl-3-imidazolin-4-yl)-3-phenylpyrazine (23) was prepared by oxidation of dihydropyrazine **22** by MnO_2 (10 mmol of the oxidant per mmol of the substrate) in $CHCl_3$ for 10 min and purified by chromatography on a column with silica gel using $CHCl_3$ as the eluent.

5-(2,2,5,5-Tetramethyl-1-oxyl-3-imidazolin-4-yl)-4-phenylimidazole (24). A solution of imine **2a** (0.1 g) and 0.2 mL of formalin in 5 mL of MeOH saturated with ammonia at 20 °C was refluxed for 2 h and concentrated. Water (1 mL) and a 1 : 3 ether—hexane mixture were added to the residue. On trituration, imidazole **24** crystallized and the precipitate was filtered off.

4-(2,2,5,5-Tetramethyl-1-oxyl-3-imidazolin-4-yl)-2,5-diphenyloxazole (25) and 6-(2,2,5,5-tetramethyl-1-oxyl-3-imidazoline-4-yl)-3,5-diphenyl-1,2,4-triazine (26). A solution of benzamidine hydrochloride (0.16 g, 1 mmol) in 5 mL of MeOH was made alkaline to pH 11 by sodium methoxide, imine **2a** (0.3 g, 1 mmol) was added, and the resulting mixture was refluxed for 2 h. The solution was concentrated and the residue was chromatographed on a column with silica gel using $CHCl_3$ as the eluent; this gave successively oxazole **25** and triazine **26**.

2,2,5,5-Tetramethyl-4-(1-benzoylhydrazono-2-oxo-2-phenylethyl)-3-imidazoline-1-oxyl (27). A mixture of imine **2a** (0.5 g, 1.8 mmol) and benzoylhydrazine (0.24 g, 1.8 mmol) in 10 mL of EtOH was heated until the compounds dissolved and the solution was kept for 30 h at 20 °C and concentrated. Compound **27** was isolated by chromatography on a column with silica gel using a 1 : 1 ether—hexane mixture as the eluent.

X-ray diffraction analysis of compound 2a was performed on a Bruker P4 diffractometer with a graphite monochromator (Mo-Kα radiation). The crystals of compound **2a** are monoclinic: a = 8.6964(8), b = 15.423(2), c = 11.621(1) Å, β = 109.862(6)°, V = 1465.9(3) Å^3, space group $P2_1/s$, $C_{15}H_{18}N_3O_2$, Z = 4, d_{calc} = 1.234 g cm^{-3}, μ = 0.084 mm^{-1}, sample dimensions 0.22×0.25×0.88 mm. The intensities of 2488 independent reflections were measured using θ/2θ scan mode in the region of 2θ < 50°. The absorption corrections were applied over crystal faceting (transmission 0.97—0.99). The structure was solved by the direct method using the SHELXS-86 program and refined using the SHELXL-97 program by the least-squares method in the full-matrix anisotropic or isotropic (for H atoms) approximation to wR_2 = 0.0994, S = 1.042 for all reflections (R = 0.0352 for 1975 $F_0 > 4\sigma$).

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