Monocyclic biradicals in the imidazolidine series

V. A. Reznikov,^a L. B. Volodarskii,^{a*} A. P. Spoyalov,^b and S. A. Dikanov^b

^a Novosibirsk Institute of Organic Chemistry, Siberian Branch of the Russian Academy of Sciences, 9 prosp. Akad. Lavrent'eva, 630090 Novosibirsk, Russian Federation. Fax: +7 (383) 235 4752

^b Institute of Chemical Kinetics and Combustion, Siberian Branch of the Russian Academy of Sciences, 3 ul. Institutskaya, 630090 Novosibirsk, Russian Federation.

Fax: +7 (383) 235 2350

The reaction of 1-hydroxy-3-imidazoline 3-oxides with alkyl- or phenyllithium followed by oxidation gives stable biradicals with two nitroxyl groups in the imidazolidine ring. Anisotropic ESR spectra of these biradicals are discussed.

Key words: imidazolidine; 3-imidazoline 3-oxide; nitroxyl radicals and biradicals; nitrone; ESR spectrum.

In recent years great attention has been paid to investigating nitroxyl bi- and polyradicals that are potentially useful for creating new organic ferromagnetic materials.^{1,2} Particulary interesting in this respect are the nitroxyl biradicals which exhibit strong exchange interaction that has a ferromagnetic character;² the strongest exchange interaction has been observed³ for compound 1 (Scheme 1). This structure is practically the only representative of stable nitroxyl biradicals with two nitroxyl groups in one heterocycle. The reaction of sterically hindered nitrones with organometallic reagents followed by oxidation is one of the routine methods for the generation of a nitroxyl group.⁴ Taking this into account one can assume that the derivatives of 3-imidazoline 3-oxide (2) can be used as precursors of various monocyclic biradicals of the imidazolidine series. It is also known that the interaction of the derivatives of 2 with organomagnesium compounds leads to opening of the imidazoline ring to give α -hydroxyamino oximes.⁵ Assuming that the derivatives of 2 would react similarly with organolithium compounds,⁶ we attempted to employ other 1-substituted 3-imidazoline 3-oxides instead of the 1-hydroxy derivatives of 1 as the precursors of nitroxyl radicals. The use of 1-methyl-substituted 3-imidazoline-3-oxides or their tetrahydropyranyl analogs made it possible to obtain dihydroxy compounds 3a and 3b, but we failed to oxidize them to the corresponding biradicals 4a and 4b. Only the monoradicals, tentatively formulated as 5, could be obtained in low yields (see Scheme 1). Therefore, it was concluded⁶ that the indispensable condition of stability of isocyclic biradicals was the spiro-junction in position 2 of the imidazolidine ring (cf. ref. 3).

To verify this assumption we studied the reaction of phenyllithium with imidazoline 3-oxide 6. Subsequent

Scheme 1 8 óн ò 2a,c-g 9 R²Li PhLi Rź OH MnO ÒН òн ċ٠ 3a-e,h,k 5 1,4a-c,k [0] =NOH + =0 1: $R = R^2 = R^3 = Me$, 2 $R^1 = (CH_2)_5$ **a**: $R = R^2 = Ph$, $R^1 = R^3 = Me$ **b**: R = Ph, $R^1 = R^2 = R^3 = Me$ c: $R = R^2 = Ph$, 2 $R^1 = (CH_2)_5$, $R^3 = Me$ **d**: $R = R^2 = Ph, R^1 = OEt, R^3 = Me$ e: $R = R^2 = Ph$, 2 $R^1 = OCH_2CH_2O$, $R^3 = Me$ $f: R = R^1 = R^2 = R^3 = Me$ **g**: $R + R^3 = (CH_2)_4$, $R^1 = Me$ h: $R = R^1 = R^2 = Ph, R^3 = Me$ k: R = Ph, $R^2 = n$ -Bu, $R^1 = R^3 = Me$

oxidation of the product afforded monoradical 7 (see Scheme 1). To synthesize the corresponding biradical **4c**, a sequence of transformations was attempted which included the acylation of the hydroxyamino derivative **8**, oxidation, deprotection, and mild oxidation (*cf.* ref. 3). However, upon the oxidation of the NMe group to a nitroxyl group in the H_2O_2/Na_2WO_4 system the fragmentation of the heterocycle took place (*cf.* ref. 6) and benzophenone was formed as the only product.

It was found that, in contrast to organomagnesium reagents, ring opening did not take place in the reaction of 3-imidazoline 3-oxide 2a-e with organolithium reagents. The imidazolidine derivatives 3a-e, and 3k were formed as a result of the addition of the organolithium compound to the nitrone group. It should be noted that the addition of butyllithium or phenyllithium proceeds under mild conditions, and in high yields. In contrast to this, the reaction between 2a and methyllithium proceeds slowly and is not completed even if a tenfold excess of the reagent is used. The dihydroxy imidazolidine derivative 3h can be obtained by the reaction of 4H-imidazole 1,3-dioxide (9) with phenyllithium. 4-Alkyl substituted derivatives of 3-imidazoline 3-oxide 2f and 2g do not form adducts with organometallic reagents, probably due to metallation of the alkylnitrone group (cf. refs. 7, 8).

The stability of dihydroxyimidazolidines 3 depends markedly on the nature of the substituents at positions 2 and 4 of the heterocycle, in particular, their size and the presence of a spiro-junction at C-2. Thus, imidazolidines **3a-c** and **3k** were stable in the solid state as well as in solution under an inert atmosphere, whereas 3d, 3e, and 3h decomposed with elimination of nitrogen oxides both in the solid state and on crystallization to give a complex mixture of products. 1-Phenyl-2,2-dimethylstyrene, benzophenone oxime, benzophenone, and dinitrophenylmethane were isolated from the product mixture and identified by comparison with authentic samples. Similar mixtures of products were formed when these dihydroxyimidazolidines were oxidized with MnO_2 . In the course of oxidation of dihydroxy derivatives 3a, 3b, and 3k with MnO₂ in ether, complex mixtures containing monoradicals 5a, 5b, and 5k, respectively, were formed (TLC data). This fact can be explained by assuming that the biradicals 4 could not survive under the chromatography conditions. By decreasing the exposure of 3 and the reaction products in solution to the oxidant we succeeded in preparing 4a and 4k as individual substances. Biradicals 4a and 4k are bright red crystals stable at 0 °C for a long time but unstable in solution; they totally decompose at 20 °C in 2-3 h. Because the biradical 4b is less stable than 4a and 4k we failed to obtain it in the individual state. When the analogous oxidation of 3c was carried out the characteristic brightly red color was observed, but upon evaporation or standing for several minutes biradical 4c decomposed; nitrogen oxides and a complex mixture containing benzophenone were formed.

The ESR spectra of biradicals 4a, 4b, and 4k in dilute solutions were singlets with $\Delta H_{1/2} = 10 \div 15$ mT. To confirm the structures of 4, the ESR spectra of frozen glassy solutions in toluene were measured. The first derivatives of the ESR spectra of 4b and 4k in frozen toluene appeared as chaotically oriented triplets with S = 1 and an axial tensor of fine splitting¹³ (Fig. 1). The spectra represented two doublets of lines with low and high amplitudes located symmetrically relative to the resonance field $H_0 = h\nu/(g\beta)$. These lines were assigned to the allowed transitions $\Delta M_c = \pm 1$ with parallel and perpendicular orientations of the external magnetic field in relation to the fine splitting tensor axis. Moreover, a forbidden transition line with $\Delta M_s = \pm 2$ in the range $\Delta H_0/2$ was also observable. In all of the spectra lines attributed to monoradical species located near H_0 were also present.

One of the tensor parameters which characterizes the fine dipole-dipole interactions of unpaired electrons (D) can be easily determined from the position of the $\Delta M_s = \pm 1$ transition lines. Splitting between the outer peaks is equal to 2D (see Fig. 1). The second parameter (E) cannot be determined from the spectra, so the only possible conclusion is that $|E| \le |D|$.

However, the ESR spectrum of biradical 4a revealed splitting of the weak lines with parallel orientation of the



Fig. 1. ESR spectrum of biradical 4k in frozen toluene solution at 77 K.



Fig. 2. ESR spectrum of biradical 4a in frozen toluene solution at 77 K.

compounds 3k, 4a, 4k, 6, and 7

$2D (\pm 0.3)/mT$	<i>R</i> /Å	
160.2	3.26	
160.8 (1) 149.6 (11)	3.26 3.34	
161.6	3.25	
160.6	3.26	
	2D (±0.3)/m1 160.2 160.8 (1) 149.6 (11) 161.6 160.6	2D (±0.3)/m1 R/A 160.2 3.26 160.8 (1) 3.26 149.6 (11) 3.34 161.6 3.25 160.6 3.26

Table 1. The D parameters of the tensor of biradical structures and the distances (R) between unpaired electrons

* Literature data. 3.

triplet (ca. 5 mT) (Fig. 2). Splitting of the intense lines with perpendicular orientation (which is about twice as weak) was observed in the second derivative spectrum. The two-quanta transition line in the spectrum of 4a was also split into two components; therefore two states of the biradical with different D existed.

The *D* parameters for all of the biradicals obtained are presented in Table 1. They are close to the value 2D = 160.6 mT found for biradical 1 in which the nitroxyl fragments are separated by two C—N bonds (*cf.* ref. 3).

The distance between the uncoupled electrons in the biradicals can be estimated from the value of parameter D by using the approximation of point dipoles

$$R = [5.56 \cdot 10^4 / (2D)]^{1/3}.$$
 (1)

Distances between uncoupled electrons in the biradicals calculated by means of eqn. (1), are presented in Table 1. They are in accordance with the distances between the middle points of the N-O bonds calculated from the structural parameters of 3-imidazoline 3-oxide.³

Taking into account the results obtained, the occurence of the two types of states of **4a** can be explained by the existence of two conformations having different deviation angles between the plane of the cycle and the N—'O fragments. These deviation angles were approximated as $\alpha_1 = 38^\circ$ and $\alpha_2 = 25^\circ$ for the first and the second conformation, respectively. It was shown¹⁴ that the line shape for $M_s = \pm 2$ is sensitive to the orientation of the fine interaction tensor in relation to the g tensor of the triplet, and the line can be split under some orientations. Various values of D and the orientations of the fine splitting tensor in relation to the g factor for these conformations determine the complex shape of the two-quants transition line.

Experimental

IR spectra were recorded with a Specord M-80 spectrometer in KBr pellets (0.25 % conc.) and in CCl₄ solutions (5 % conc.). UV spectra were obtained with a Specord UV VIS spectrometer in ethanol solutions. ¹H NMR spectra were measured with a Bruker WP-200 SY instrument in pulsed mode at 300 K in CDCl₃ solutions (5 % conc.); chemical shifts were measured in relation to the residual signal of CDCl₃. ESR

Com- pound	Yield (%)	B.p. ∕°C	Found Calculated (%)		1 ^(%)	Molecular formula	
			C	Н	N		
3k	75	128-131	<u>69.9</u> 69.1	<u>9.8</u> 9.6	<u>9.5</u> 9.6	$C_{17}H_{28}N_2O_2$	
4 a	80	88—90	<u>73.3</u> 73.6	<u>7.4</u> 7.1	<u>8.8</u> 9.0	$C_{19}H_{22}N_2O_2$	
4k	80	65—66	<u>70.6</u> 70.4	<u>9.2</u> 9.0	<u>9.7</u> 9.7	$C_{17}H_{26}N_2O_2$	
6	75	50-52	<u>74.7</u> 74.9	. <u>8.6</u> 8.8	<u>10.4</u> 10.3	$C_{17}H_{24}N_2O$	
7	90	154—156	<u>78.9</u> 79.2	<u>8.3</u> 8.3	<u>8.2</u> 8.0	C ₂₃ H ₂₉ N ₂ O	

Table 2. Yields, melting points, and elemental analysis data of

spectra were measured with a Bruker ESR-300 in the 3-cm range at 77K. Yields, m.p., and elemental analysis data of some of the synthesized compounds are presented in Table 2.

Compounds 2a,c,f, and 2g were obtained as reported in ref. 9, 2d and 2e were prepared as in ref. 10, and 4H-imidazole 9 as in ref. 11. The compounds synthesized were identified using TLC, melting points, and IR and ¹H NMR spectra.

Dihydroxyimidazolidines (3): general synthetic procedure. 3-Imidazoline 3-oxide 2 (5 mmol) or 4H-imidazole 9 (10 mmol) was added to a stirred solution of an organolithium compound prepared from phenyl bromide, methyl iodide, or butyl bromide (30 mmol) and lithium (60 mmol) in 40 mL of anhydrous ether. The reaction was carried out under Ar. In the case of 2c 10 mL of anhydrous THF was added dropwise. The reaction mixture was stirred for 2 h at 20 °C then treated with 20 mL of water. The organic layer was separated, and the aqueous layer was extracted with ether. Combined extracts were dried over MgSO, and evaporated, the residue was mixed with a small portion of hexane, and the precipitates of imidazolidines 3a,d,e,h,k were separated by filtration. Yields of imidazolidines obtained were 75-90 %. In the case of 3b and 3c, after the addition of water to the reaction mixture the precipitates of unreacted 2a and 2c respectively, were filtered off (60-70 % recovery), and 3b and 3c were separated as described above. As a result of instability, imidazolidines 3c,d,e, and 3h could not be isolated in pure form.

The absorbance band of the C=N group $(1500-1650 \text{ cm}^{-1})$ was absent from the spectrum of **3**, while two OH group absorption bands in the 3300-3400 and 3400-3500 cm⁻¹ regions were present. Compounds **3** have no UV absorption at λ >200 nm. ¹H NMR of **3k**, δ : 0.69 (s, 3 H); 1.21 (s, 3 H); 1.38 (s, 3 H); 1.50 (s, 3 H, 2,5-(CH₃)₂); 0.8-2.2 (m, 9H, C₄H₉); 4.19 (br.s, 1 H, OH); 5.36 (br.s, 1 H, OH); 7.4 (m, 5 H, Ph).

4-Substituted 2,2,5,5-tetramethyl-4-phenyl-1,3-dioxyls (4a,b,k). A suspension of imidazolidines 3a, b or 3k (0.2 g) and MnO₂ (2 g) in 10 mL of a mixture of pentane and ether (1:2) was stirred for 30 s, the supernatant was removed by decantation, then 10 mL of the solvent mixture was added and the treatment was repeated. Fresh portions of the solvent were added untill the decantate became colorless. The obtained portions of the solution were evaporated immediately and compound 4a, b, or 4k was obtained.

1,2,2-Trimethyl-2-spirocyclohexyl-4-phenyl-3-imidazoline 3-oxide (6) was obtained by alkylating 2,2-dimethyl-2-spirocyclohexyl-4-phenyl-3-imidazoline 3-oxide with formaldehyde and HCOOH.¹² Compound 6 was purified by column chromatography on Al₂O₃ using AcOEt—hexane (1:5) as the eluent. IR (KBr), v/cm⁻¹: 1545, 1570 (C=C, C=N); 2800 (N-CH₃); 3050 (C-H in Ph). UV (EtOH), $\lambda_{max}/nm: 284$ (loge = 3.93). ¹H NMR, δ : 1.39 (s, 6H, 5-(CH₃)₂); 1.64 (m, 2 H); 1.93 (m, 6 H, (CH₂)₅); 2.37 (s, 3 H, N-CH₃); 7.4 (m, 3 H); 8.0 (m, 2 H, Ph).

5,5-Diphenyl-3,4,4-trimethyl-2-spiro-cyclohexylimidazolidine-1-oxyl (7). A solution of imidazoline 6 (1g, 3.68 mmol) was added dropwise under Ar to a stirred solution of phenyllithium prepared from phenyl bromide (2.3 mL, 22.1 mmol) and Li (0.31 g, 44.2 mmol) in 30 mL of anhydrous ether. The mixture was stirred for 1 h, then treated with 10 mL of water. The organic layer was separated, and the aqueous layer was extracted with ether. The combined extracts were dried over MgSO₄ and evaporated to give 1.25 g of imidazolidine 8. Product 8 was dissolved in 20 mL of hexane and stirred with MnO₂ (5 g) for 20 min at 20 °C. The excess oxidant was removed by filtration, the solution was concentrated in vacuo. and product 7 was purified by column chromatography on SiO, using hexane as the eluent. The IR spectrum of 7 did not contain characteristic absorption bands of the C=N and OH groups; only the absorption of the nitroxyl group was observed in the UV spectrum.

References

- 1. L. Dulog and J. S. Kim, Angew Chem., 1990, 102, 403.
- 2. A. Rassat, Pure Appl. Chem., 1990, 62, 233.
- 3. J. F. W. Keana, R. S. Norton, M. Morello, D. Van Engen,

and J. Clardy, J. Am. Chem. Soc., 1978, 100, 934.

- 4. J. F. W. Keana, in *Spin Labeling in Pharmacology*, Ed. J. L. Holzmann, Acad. Press., Orlando (Fla), 1984, **102**, 1.
- L. B. Volodarskii, V. V. Martin, and V. S. Kobrin, *Zh. Org. Khim.*, 1976, **12** 2267 [*J. Org. Chem. USSR*, 1976, **12** (Engl. Transl.)].
- 6. V. V. Martin, L. B. Volodarskii, and L. A. Vishnivetskaya, *Izv. Akad. Nauk SSSR, Ser. Khim.*, 1981, 94 [Bull. Acad. Sci. USSR, Div. Chem. Sci., 1981, 30, No 1 (Engl. Transl.)].
- V. V. Martin and L. B. Volodarskii, *Izv. Akad. Nauk SSSR,* Ser. Khim., 1980, 1336 [Bull. Acad. Sci. USSR, Div. Chem. Sci., 1980, 29, 956 (Engl. Transl.)].
- 8. V. A. Reznikov and L. B. Volodarskii, *Khim. Geterotsikl.* Soed., 1991, 912 [Chem. Heterocycl. Comp., 1991 (Engl. Transl.)].
- L. B. Volodarskii, I. A. Grigor'ev, S. A. Dikanov, V. A. Reznikov, and G. I. Schukin, *Imidazolidinovye Nitroksil'nye* Radikaly [Nitroxyl Radicals of the Imidazolidine Series], Nauka, Sib. Div., 1988, 216 (in Russian).
- I. A. Grigor'ev, V. F. Starichenko, I. A. Kiriliuk, and L. B.Volodarskii, *Izv. Akad. Nauk SSSR, Ser. Khim.*, 1989, 1624 [*Bull. Acad. Sci. USSR, Div. Chem. Sci.*, 1989, 1488 (Engl. Transl.)].
- I. A. Grigor'ev, I. A. Kiriliuk, and L. B. Volodarskii, *Khim. Geterotsikl. Soed.*, 1988, 1640 [*Chem. Heterocycl. Comp.*, 1988 (Engl. Transl.)].
- V. V. Martin and L. B. Volodarskii, *Khim. Geterotsikl.* Soed., 1979, 103 [Chem. Heterocycl. Comp., 1979 (Engl. Transl.)].
- 13. A. Carrington and A. D. McLachlan in Introduction to Magnetic Resonance with Applications to Chemistry and Chemical Physics, Mir, Moscow, 1984, 24 (Russ. Transl.).
- 14. R. S. Stevenson, J. Magn. Reson., 1984, 57, 24.

Received June 9, 1992