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Stable nitroxyl radicals with triple bonds: 4-acetylenyl-3-imidazoline-3-oxide-1-oxyls

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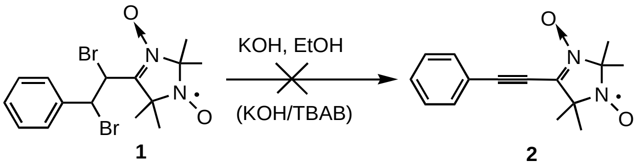
Abstract—Cross-coupling reaction of 1-hydroxy-2,2,5,5-tetramethyl-4-[2-(*p*-iodophenyl)vinyl]-3-imidazoline-3-oxide with copper(I) salts of 1-aryl(hetaryl)alkynes leads to the corresponding 2,2,5,5-tetramethyl-4-[2-(*p*-aryl(hetaryl)ethynylphenyl)vinyl]-3-imidazoline-3-oxide-1-oxyls in high yields.

1. Introduction

A recent extension of the spin-labeling methodology in physicochemical studies consists of the preparation of model systems to gain insight into the phenomenon of spin catalysis,[1] that is, the effect of the 'external' spin on the evolution of a correlated spin system. A reasonable way to accomplish this is the augmentation of a photo- or radiation generated spin-correlated radical pair with a third spin—the spin of a stable radical moiety introduced in the precursor of one of the pair partners. Recently,[2] we have reported the synthesis and physicochemical study of a series of aromatic charge acceptors and luminophores containing a stable 2-imidazoline radical fragment, which under X-irradiation in non-polar solvents, produced biradical ions that are partners in spin-correlated radical ion pairs. An important outcome of this study was the realization that the exchange coupling between the two unpaired spins of the short-lived biradical ion was too strong and must be reduced to allow for more quantitative studies going beyond the mere observation of the effect. In the present paper, we report the synthesis of a series of acetylenic derivatives of 3-imidazoline-1-oxyls. In this way, as opposed to 2-imidazoline radicals, the NO fragment bearing the unpaired electron is isolated from the substituent by single bonds within the radical itself, thus providing the desired attenuation of 'electron spin conductivity' outside the radical moiety of the spin-labeled molecule.

We have already published a preliminary communication devoted to the synthesis of acetylene-containing nitroxides of the 3-imidazoline series.[3] In this work, we will report the synthesis of these compounds and provide additional examples of the preparation of spin-labeled acetylenyl nitroxides as well as their diamagnetic derivatives, in full detail with all spectral and analytical data.

Our attempts to use the classical method for the synthesis of the desired acetylenes,[4] dehydrobromination of the corresponding 1,2-dibromoethane, were unsuccessful. Reaction of **1** with either KOH in boiling EtOH, KOH in the presence of TBAB (tetrabutylammonium bromide), or KOH in DMSO in a wide interval of temperatures (20–100 °C) led to a large number of by-products, from which acetylene **2** could not be isolated (Scheme 1).



Scheme 1. Attempts of dehydrobromination of dibromoethane **1**.

Keywords: Acetylenes; 3-Imidazoline nitroxides; Cross-coupling reaction; Copper acetylides.

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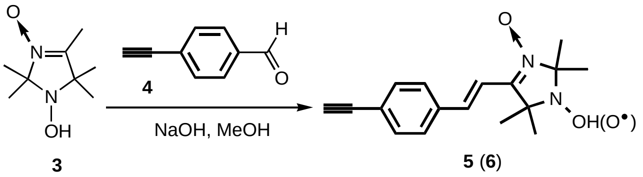
For the preparation of a series of both diamagnetic and paramagnetic acetylenic derivatives of 3-imidazoline-3-oxide-1-oxyl we thought of using the key ethynyl derivatives **5** (**6**). These compounds are obtained by condensation of 1-hydroxy-2,2,4,5,5-pentamethyl-3-imidazoline-3-oxide **3** with *p*-ethynyl benzaldehyde **4** (Scheme 2).

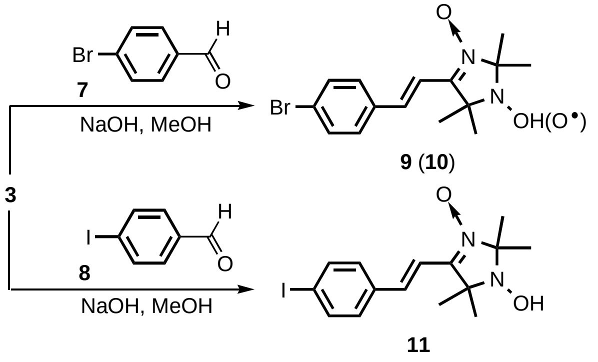


Scheme 2. Condensation of hydroxylamine **3** with the aldehyde **4**.

However, we observed strong polymerization and the mixture of hydroxylamine **5** and nitroxyl **6** was isolated in low yields (2.4 and 3.0%, respectively).

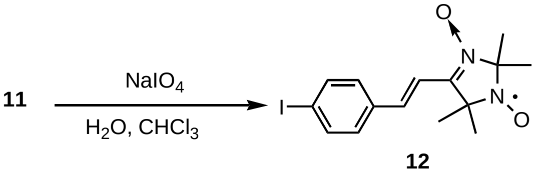
Then we tried another approach to the synthesis of acetylenic derivatives of 3-imidazoline-3-oxide-1-oxyl, based on the Sonogashira cross-coupling reaction[5] of the corresponding iodo(bromo)-imidazolines with acetylenylarenes, a reaction that has been successfully applied to the preparation of a series of acetylenyl derivatives of 2-imidazoline nitroxides.[6]

The starting halogeno-arylimidazolines were synthesized by condensation of 2,2,4,5,5-pentamethyl-imidazoline **3** with *p*-bromobenzaldehyde **7** or *p*-iodobenzaldehyde **8**. In the case of the bromo derivative **7** both para- (**10**, 10%) and diamagnetic (**9**, 36%) (bromophenyl)vinylimidazolines were isolated. On the other hand, only the iodo derivative **11** was isolated in 28% yield in the case of iodoaldehyde **8** (Scheme 3).



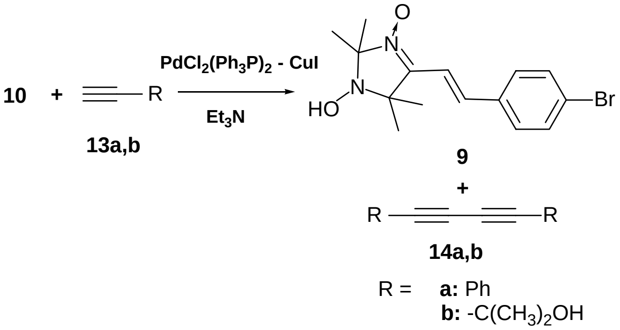
Scheme 3. Condensation of imidazoline **3** with *p*-halogeno benzaldehydes **7** and **8** in the presence of NaOH.

The paramagnetic iodo derivative **12** was synthesized by oxidation of **11** in the presence of $NaIO_4$. It is necessary to emphasize that this is the first successful application of the system $NaIO_4$–H_2O–$CHCl_3$ for preparing 3-imidazoline nitroxyls. The yield of the desired radical **12** was 72% (Scheme 4).



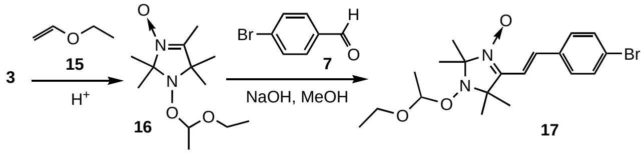
Scheme 4. Oxidation of hydroxylamine **11** into nitroxyl **12** in the presence of $NaIO_4$.

However, we failed to perform cross-coupling of the spin-labeled bromo derivative **10** with both phenylacetylene **13a** and 2-methylbut-3-yn-2-ol **13b**. In both cases the reaction resulted in the obtention of diamagnetic derivatives **9**, accompanied by formation of the homo-coupling product of 1-alkynes—1,4-disubstituted-1,3-diynes **14a**,**b** (Scheme 5). Even the use of the more active, for cross-coupling reactions, iodo compounds **11** or **12**, was unsuccessful.



Scheme 5. Cross-coupling of bromonitroxyl **10** with terminal acetylenes **13a** and **13b**.

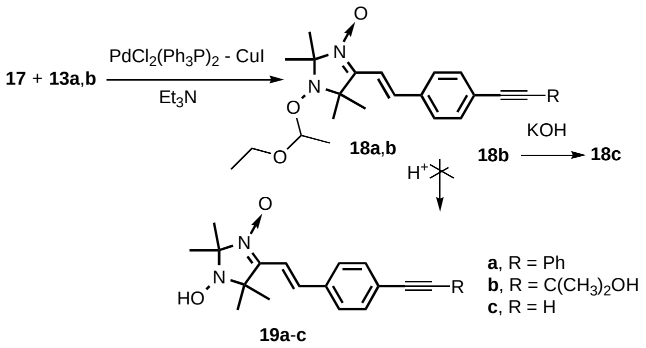
We tried to avoid these complications by protecting the hydroxyl group in the starting halogen derivatives with ethyl vinyl ether **15**.[7] The starting bromide was prepared as shown below (Scheme 6).



Scheme 6. Protection of the hydroxy group in hydroxylamine **3** followed by condensation of **16** with *p*-bromobenzaldehyde **7**.

In case of success, this way could open a route to the synthesis of the diamagnetic acetylenyl-3-imidazolines and the corresponding paramagnetic derivatives. This is important because the study of the phenomenon of spin catalysis requires the determination of quantum yields of luminescence of both dia- and paramagnetic compounds.[8]

Thus protected bromo-imidazoline **17** reacted with terminal acetylenes **13a**,**b** under standard conditions [$Pd(PPh_3)_2Cl_2$–CuI–NEt_3, 55–80 °C] to afford the desired diamagnetic cross-coupling products **18a**,**b** in 60–70% yield (Scheme 7). The mono substituted acetylene derivative **18c** was obtained by alkaline cleavage of **18b**.



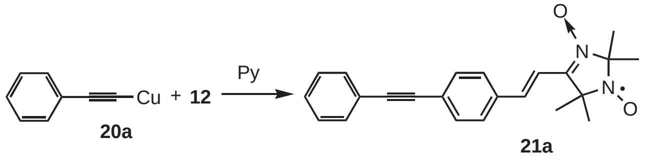
Scheme 7. Cross-coupling of acetal **17** with terminal acetylenes **13a**,**b** followed by attempts to eliminate the protecting group and the cleavage of carbinol **18b**.

Next we tried to remove the protecting group, followed by oxidation of the hydroxyl group. However, deprotection of the acetal group from the acetylenic derivatives in the presence of trace amounts of HCl led only to the formation of a gum.

We suppose that the successful application of cross-coupling in the 2-imidazoline series and the negative result of the same reaction for 3-imidazolines is related to stronger oxidative properties of the nitroxide group in 3-imidazoline-3-oxide-1-oxyls as compared with 2-imidazoline-3-oxide-1-oxyl derivatives.[9] On the other hand, this result is connected also with the low reactivity of the bromine atom in the aryl moiety due to +M-effect of the *N*-oxide fragment.[10] This effect of the N–O group for 3-imidazolines is confirmed by the data from ^{13}C NMR spectra.[11]

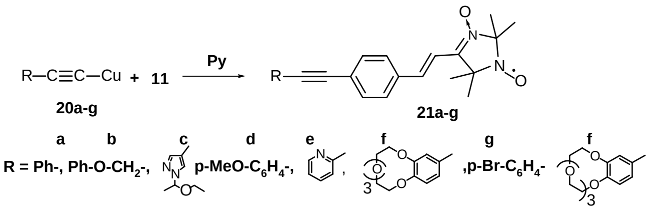
For this reason, and taking into account the difference in the mechanisms of Cu- and Pd-catalyzed cross-coupling reaction of alk-1-ynes,[12] we supposed that the described difficulties could be overcome by using the acetylide synthesis to obtain the desired products.

As a model, the copper salt of phenylacetylene **20a** was allowed to react with paramagnetic iodo-imidazoline **12** in boiling pyridine to afford product **21a** in 83% yield (Scheme 8).



Scheme 8. Cross-coupling of paramagnetic iodo-imidazoline **12** with the copper salt of phenylacetylene **20a**.

It is important to note that the diamagnetic analogue, the iodo-imidazoline **11** was also successfully used in the cross-coupling reaction affording the radical **21a**. The transformation of the reaction products directly into radicals **21a–g** probably takes place during the work-up of the reaction mixture (Scheme 9). We observed similar transformations in the condensation of 1-hydroxy-2,2,4,5,5-pentamethyl-3-imidazoline-3-oxide **3** with *p*-bromo-benzaldehyde **7**.



Scheme 9. Cross-coupling of diamagnetic iodo-imidazoline **11** with the copper salt of phenylacetylenes **20a**–**g**.

The series of acetylenic nitroxides **21a–e**, were obtained in good yields (90–95%), and even in the worst case of low reactive crown ether **20f** or the bromo derivative **20g** the yields of **21f**,**g** were 50 and 60%.

Thus, new methods for the acetylide synthesis of aryl(hetaryl)ethynylphenyl-3-imidazoline nitroxides have been developed.

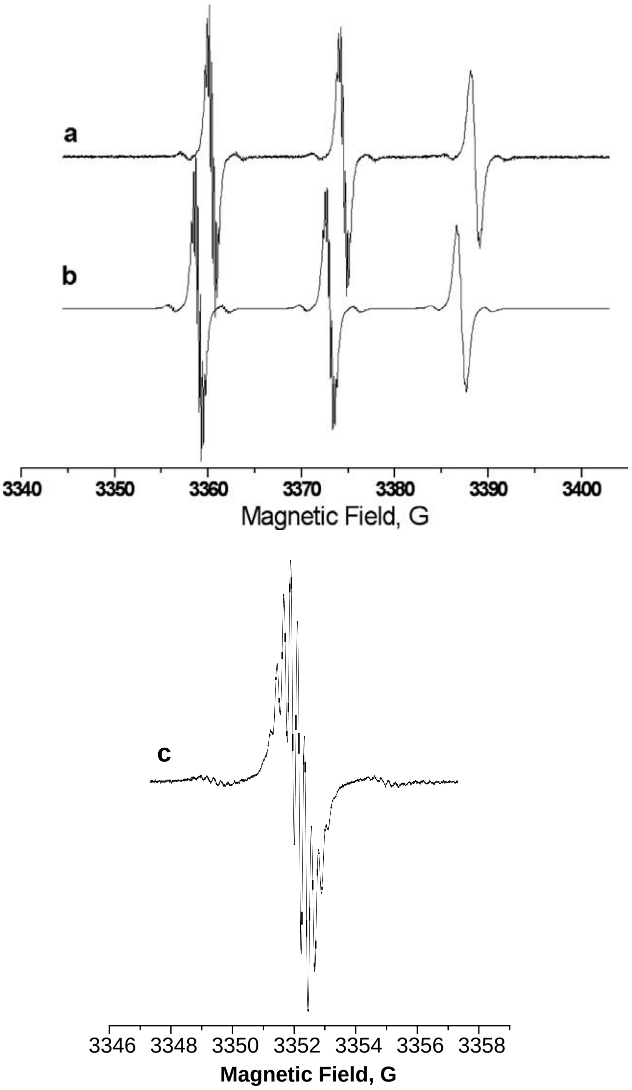


Figure 1. (a) X-band CW ESR spectrum of 10^{-5} M **21d** in degassed toluene, room temperature, microwave power 2 mW, modulation 0.1 G 100 kHz, single scan of 40 min; (b) simulation (shifted), $A_N = 4.09$ G, $A(^{13}C)_{(CH_3)} = 5.71$ G, $A_{H(CH_3)}(12H) = 0.23$ G; (c) expanded view of the low-field line. The structure from minor coupling with 12 methyl hydrogens is clearly seen both for the main line and for the ^{13}C satellites.

ESR spectra of the nitroxides are typical for 3-imidazoline radicals with spin density localized mostly at the NO fragment (Fig. 1). All spectra show a dominant triplet at N atom in the first position with splitting of about 14.1 G (in toluene) and weaker satellites from ^{13}C nuclei of the four methyl groups in natural abundance (splitting about 5.7 G). Minor splittings of 0.23 G from 12 nearly equivalent methyl protons are also neatly resolved (Fig. 1c).

2. Conclusions

A synthetic approach to acetylenic derivatives of 3-imidazoline nitronyl nitroxide radicals (NNR) has been found. Unlike nitronyl nitroxides of the 2-imidazoline series, Sonogashira cross-coupling reaction is unsuitable for the synthesis of 3-imidazoline nitroxides. It was found that coupling reaction of Cu(I)-salts of 1-alkynes with the corresponding iodo-containing 3-imidazolines leads to disubstituted spin-labeled acetylenes in good yield. We have investigated the cross-coupling of copper acetylides with both spin-labeled **12** and diamagnetic **11** iodo-imidazolines. In both cases cross-coupling leads to paramagnetic derivatives **21a–g** in 50–90% yields. ESR-spectra of the prepared compounds are typical for 3-imidazoline radicals with spin density localized mostly at the nitroxyl fragment.

3. Experimental

3.1. General

Melting points were determined with a hot-stage microscope. Column chromatography was performed on Al_2O_3. The R_f values were measured on aluminium backed TLC plates of silica gel 60 F254 (Merck, 0.2 mm) with the indicated eluent. ^{1}H NMR spectra were recorded on a Bruker DRX 400 (9.4 T, 200.13 MHz) spectrometer. Chemical shifts (δ in parts per million) are given from internal $CHCl_3$ (7.24). Coupling constants (J in Hertz) were accurate to ±0.2 Hz for ^{1}H. Mass spectra (HRMS) were measured on a Finnigan SSQ-710 at 70 eV using electron impact modes. The IR-spectra were recorded on a Bruker IFS 66 spectrometer (potassium bromide). CW ESR spectra were taken in degassed solutions on a Bruker EMX CW ESR spectrometer, all hyperfine coupling constants and field offsets from standard DPPH line are given in Gauss with accuracy ±0.02 G, except for the couplings with methyl carbon-13 for which the accuracy is ± 0.1 G, concentration of radicals 10^{-5}–10^{-4} M in the indicated solvent. Compounds **1**,[13] **3**,[9] **4**[6] and **7**[8] were prepared by previously reported methods. Copper(I) acetylides (**20a–g**) were prepared according to the published procedure[12] from the corresponding acetylenes. Commercial ethoxyethene **15** was used freshly distilled over sodium and pyridine over NaOH; phenylacetylene was used freshly distilled. Compound **16** and $PdCl_2(PPh_3)_2$ were used without additional purification.

3.1.1. 4-[2-(*p*-Iodophenyl)vinyl]-2,2,5,5-tetramethyl-3-imidazoline-3-oxide-1-oxyl (12). A mixture of **11** (0.11 g, 0.28 mmol) and $NaIO_4$ (0.09 g, 4.2 mmol) in chloroform (7 mL) and water (7 mL), was stirred at room temperature for 2–2.5 h till absence of **11** (TLC-control). The organic layer was separated and dried over K_2CO_3 and evaporated to dryness under reduced pressure. Purification of the crude product by column chromatography on Al_2O_3 (elution with chloroform) and following recrystallization gave 80 mg (72%) compounds **12**, mp 180.5–182.0 °C (from mixture of hexane–benzene). IR, cm^{-1}: ν_{max} = 1306 (N → O), 1362 (N–$^{\cdot}$O). HRMS, m/z (%): 384.8 [M]$^+$ (16.84), 337.8 (73.54), 295.0 (19.22), 240.8 (21.97), 170.0 (99.63), 155.9 (57.73), 141.0 (69.80), 129.0 (50.06), 115.0 (49.39). Found: m/z 385.03914 [M]$^+$. $C_{15}H_{18}IN_2O_2$. Calcd: M = 385.04148. ESR, G: g_{iso} = 2.0060 (ΔH_{DPPH} = 4.05 G), A_N = 14.10 $A_{H(CH_3)}$(12H) = 0.23, $A(^{13}C)$ = 5.78. Solvent: toluene.

3.1.2. 1-(*O*-Ethoxyethyl)-2,2,4,5,5-pentamethyl-3-imidazoline-3-oxide (16). A solution of imidazoline **3** (6.1 g, 35.3 mmol) and freshly distilled ethoxyethene **15** (5.1 mL, 52.9 mmol) in benzene (7 mL) was stirred at 45–50 °C in the presence of traces of HCl for 3.5–4 h till absence of **3** (TLC-control). The reaction mixture was neutralized and dried over K_2CO_3, filtered through $A1_2O_3$, and concentrated under reduced pressure. The final yellowish oil was purified by vacuum distillation to give 8.2 g (95%) of the title compound as a colorless oil, bp 110–111 °C/0.5 Torr, n_D^{17} = 1.4750. ^{1}H NMR ($CDCl_3$) δ 1.09–1.53 (m, 18H, –CH–CH_3, –OCH_2–CH_3, 2,2,5,5-CH_3), 1.90 (s, 3H, 4-CH_3), 3.52–3.75 (two q, 2H, –OCH_2–CH_3, J = 5 Hz), 4.77 (q, 1H, –CH–CH_3, J = 9 Hz). Anal. Calcd for $C_{12}H_{24}N_2O_3$: C, 58.98; H, 9.86; N,11.46. Found: C, 58.35; H, 9.48; N, 10.97.

3.1.3. 1-Hydroxy-4-[2-(*p*-ethynylphenyl)vinyl]-2,2,5,5-tetramethyl-3-imidazoline-3-oxide (5) and 4-[2-(*p*-ethynylphenyl)vinyl]-2,2,5,5-tetramethyl-3-imidazoline-3-oxide-1-oxyl (6). A solution of NaOH (440 mg, 11 mmol), imidazoline derivative **3** (1.72 g, 10 mmol), and aldehyde **4** (1.3 g, 10 mmol) in MeOH (7 mL) was stirred at 45–50 °C in argon atmosphere for 3.5–4 h till absence of aldehyde (TLC-control). $CHCl_3$ (30 mL) and water (40 mL) were then added. The organic layer was separated and dried over K_2CO_3 and evaporated to dryness under reduced pressure. Purification of the mixture of **5** and **6** (420 mg, 15%) by column chromatography on Al_2O_3 (elution with chloroform) followed by recrystallization gave the corresponding compounds **5** and **6**.

For **5** the yield was 68 mg (2.4%), mp 169.0–171.0 °C (from mixture of benzene–hexane). IR, cm^{-1}: ν_{max} = 1295 (N → O), 2105 (–C≡C–), 3251 (C≡C–H), 3441 (br, OH). ^{1}H NMR ($CDCl_3$) δ, 1.48 (s, 6H, 2,2-CH_3), 1.59 (s, 6H, 5,5-CH_3), 3.15 (s, 1H, H–C≡C), 4.77 (s br, 1H, OH), 6.65 (d, –CH=CH-Ar, J = 16 Hz), 7.49 (s, 4H, H_{Ar}), 8.38 (d, –CH=CH-Ar, J = 16 Hz). Anal. Calcd for $C_{17}H_{20}N_2O_2$: C, 71.81; H, 7.09; N, 9.85. Found: C, 71.65; H, 6.96; N, 9.98.

For **6** the yield was 85 mg (3%), mp 182.0–184.0 °C (from mixture of benzene–hexane). IR, cm^{-1}: ν_{max} = 1275 (N → O), 1355 (N–$^{\cdot}$O), 2104 (–C≡C–); 3250 (≡C–H). Anal. Calcd for $C_{17}H_{19}N_2O_2$: C, 72.06; H, 6.76; N, 9.89. Found: C, 72.25; H, 6.55; N, 9.86. ESR, G: g_{iso} = 2.0058 A_N = 13.81 $A_{H(CH_3)}$(12H) = 0.24, $A(^{13}C)$ = 5.74. Solvent: n-hexane.

3.1.4. 1-Hydroxy-4-[2-(*p*-bromophenyl)vinyl]-2,2,5,5-tetramethyl-3-imidazoline-3-oxide (9) and 4-[2-(*p*-bromophenyl)vinyl]-2,2,5,5-tetramethyl-3-imidazoline-3-

oxide-1-oxyl (10). For **9** the yield was 1.67 g (49%), mp 153.0–154.0 °C (from mixture of hexane–benzene). IR, cm^{-1}: $\nu_{max}=1320$ (N→O), 3241 (br, OH). ^1H NMR ($CDCl_3$) δ, 1.44 (s, 6H, 2,2-CH_3), 1.58 (s, 6H, 5,5-CH_3), 5.29 (s br, 1H, *OH*), 6.61–6.65 (d, 1H, –*CH*=CH-Ar, $J=16$ Hz), 7.35–7.49 (d, d, 4H, H_{Ar}), 8.30–8.34 (d, 1H, –CH=*CH*-Ar, $J=16$ Hz). HRMS, *m/z* (%): 338.0 $[M]^+$ (7.90), 265.0 (8.19), 237.0 (8.97), 236.0 (8.40), 157.0 (15.24), 156.0 (100.0), 141.1 (30.46), 115.1 (9.83), 74.1 (10.60). Found: *m/z* 338.06344 $[M]^+$. $C_{15}H_{19}BrN_2O_2$. Calcd: $M=338.06299$.

For **10** the yield was 480 mg (14%), mp 189.5–192.0 °C (from mixture of benzene–hexane). IR, cm^{-1}: $\nu_{max}=1279$ (N→O), 1363 (N–$^{\cdot}$O). HRMS, *m/z* (%): 337.0 $[M]^+$ (6.14), 291.8 (51.08), 290.0 (25.81), 247.9 (14.43), 236.9 (2.73), 170.1 (100.0), 156.0 (56.52), 141.1 (58.93), 115.1 (32.81), 102.1 (26.81). Found: *m/z* 337.05547 $[M]^+$. $C_{15}H_{18}BrN_2O_2$. Calcd: $M=337.05521$. ESR: $g_{iso}=2.0059$ ($\Delta H_{DPPH}=3.97$ G), $A_N=13.86$ G, $A_{H(CH_3)}(12H)=0.22$ G, $A(^{13}C)=5.62$ G. Solvent: toluene.

3.1.5. 1-Hydroxy-4-[2-(*p*-iodophenyl)vinyl]-2,2,5,5-tetramethyl-3-imidazoline-3-oxide (11). The yield of compound **11** was 2.15 g (28%), mp 175 (decomp.) °C (from ethylacetate). IR, cm^{-1}: $\nu_{max}=1310$ (N→O), 3233 (br, OH). ^1H NMR ($CDCl_3$) δ, 1.44 (s, 6H, 2,2-CH_3), 1.55 (s, 6H, 5,5,-CH_3), 5.46 (s br, 1H, *OH*), 6.64 (d, 1H, –*CH*=CH-Ar, $J=8$ Hz), 7.22 (d, 2H, 2,6-H_{Ar}, $J=4$ Hz), 7.65 (d, 2H, 3,5-H_{Ar}, $J=4$ Hz), 8.27 (d, –CH=*CH*-Ar, $J=8$ Hz). Anal. Calcd for $C_{15}H_{19}IN_2O_2$: C, 46.65; H, 4.96; N, 7.25; I, 32.86. Found: C, 47.00; H, 5.40; N, 6.92; I, 32.39.

3.1.6. 1-(*O*-Ethoxyethyl)-4-[2-(*p*-bromophenyl)vinyl]-2,2,5,5-tetramethyl-3-imidazoline-3-oxide (17). The yield of compound **17** was 1.50 g (36%, viscous liquid). IR, cm^{-1}: $\nu_{max}=1298$ (N→O). ^1H NMR ($CDCl_3$) δ, 1.15–1.54 (m, 18H, 2,2,5,5-CH_3, –OCH_2–CH_3, –CH–CH_3), 3.54–3.85 (m, 2H, –CH_2–CH_3), 4.79 (q, 1H, –*CH*–CH_3, $J=9$ Hz), 6.39–6.47 (d, 1H, –*CH*=CH-Ar, $J=16$ Hz), 7.31–7.43 (q, 4H, H_{ar}), 8.30–8.38 (d, 1H, –CH=*CH*-Ar, $J=16$ Hz). HRMS, *m/z* (%): 409.9 $[M]^+$ (12.41), 339.8 (63.51), 337.8 (64.89), 156.0 (58.47), 140.9 (40.75), 98.0 (41.37), 73.0 (100.0), 56.0 (35.40), 45.0 (89.33). Found: *m/z* 410.12611 $[M]^+$. $C_{19}H_{27}BrN_2O_3$. Calcd: $M=410.12054$.

3.1.7. 1-(*O*-Ethoxyethyl)-2,2,5,5-tetramethyl-4-{2-[4-(*p*-phenylethynyl)phenyl)vinyl}-3-imidazoline-3-oxide (18a). A mixture of the halogen compound **17** (171 mg, 0.4 mmol), alkyne **13a** (43 mg, 0.43 mmol), $PdCl_2(PPh_3)_2$ (40 mg) and CuI (20 mg) and Et_3N or piperidine (10 mL) was stirred under argon stream at 80 °C for 3 h. The solvent was removed with an oil pump (0.1 Torr) at 20 °C, the residue was dissolved in benzene, the solution was filtered through a thin-layer of Al_2O_3 and evaporated to dryness under reduced pressure. The crude product was purified by column chromatography on Al_2O_3, and the solvent was distilled off. Purification of the crude product by column chromatography on Al_2O_3 (elution with chloroform) and following crystallization gave the corresponding compound **18a**. The yield of compound **18a** was 125 mg (72%), mp 138–140 °C (from hexane). IR, cm^{-1}: $\nu_{max}=1325$ (N→O), 2220 (–C≡C–). ^1H NMR ($CDCl_3$) δ, 1.12–1.16 (m, 6H, –CH–CH_3, –OCH_2–CH_3), 1.26–1.43 (m, 12H, 2,2,5,5-CH_3), 3.45–3.75 (m, 2H, –OCH_2–CH_3), 4.74 (q, 1H, –*CH*–CH_3), 6.41–6.49 (d, –*CH*=CH-Ar, $J=16$ Hz), 7.21–7.41 (m, 9H, H_{ar}), 8.31 (d, 1H, –CH=*CH*-Ar, $J=16$ Hz). Anal. Calcd for $C_{27}H_{32}N_2O_3$: C, 74.97; H, 7.46; N, 6.48. Found: C, 74.83; H, 7.28; N, 6.30.

3.1.8. 1-(*O*-Ethoxyethyl)-2,2,5,5-tetramethyl-4-{2-[*p*-(3-methyl-3-hydroxybutyn-1-yl)phenyl]vinyl}-3-imidazoline-3-oxide (18b). The yield of compound **18b** was 580 mg (48%) obtained from 1.23 g (3.0 mmol) of **17**, mp 104.0–106.0 °C (from hexane). IR, cm^{-1}: $\nu_{max}=1278$ (N→O), 2220 (–C≡C–), 3406 (br, OH). ^1H NMR ($CDCl_3$) δ, 1.18 (t, 3H, –OCH_2–CH_3, $J=6$ Hz), 1.21 (d, 3H, –CH–CH_3, $J=7$ Hz), 1.31–1.65 (m, 18H, 2,2,5,5-CH_3, –C(CH_3)OH), 2.035 (s br, –C(CH_3)*OH*), 3.51–3.91 (two q, 2H, –OCH_2–CH_3, $J=6$ Hz), 4.80–4.91 (q, 1H, –*CH*–CH_3, $J=7$ Hz), 6.54–6.65 (d, –*CH*=CH-Ar, $J=16$ Hz), 7.32–7.47 (dd, 4H, H_{ar}), 8.37–8.48 (d, –CH=*CH*-Ar, $J=16$ Hz). HRMS, *m/z* (%): 414.1 $[M]^+$ (10.04), 343.0 (25.46), 342.1 (77.46), 295.2 (14.03), 239.0 (17.93), 98.0 (19.81), 73.0 (100.0), 56.1 (13.72), 45.1 (82.62). Found: *m/z* 414.25148 $[M]^+$. $C_{24}H_{34}N_2O_4$. Calcd: $M=414.25184$.

3.1.9. 1-(*O*-Ethoxyethyl)-2,2,5,5-tetramethyl-4-[2-(*p*-ethynylphenyl)vinyl]-3-imidazoline-3-oxide (18c). A mixture of **18b** (150 mg, 0.36 mmol) and KOH (130 mg, 0.33 mmol) in 10 mL of toluene was stirred at 80–85 °C for 14 h till absence of alcohol (TLC-control). The reaction mixture was filtered off through Al_2O_3 (elution with chloroform), and evaporated to dryness under reduced pressure. The crude product was purified by column chromatography on Al_2O_3 (elution with chloroform) and following recrystallization gave 74 mg (62%) of compound **18c**, mp 93.0–94.5 °C (from mixture of hexane–benzene). IR, cm^{-1}: $\nu_{max}=1325$ (N→O), 2099 (–C≡C–), 3221 (C≡C–H), ^1H NMR ($CDCl_3$) δ, 1.18–1.25 (t, 3H, –OCH_2–CH_3, $J=4$ Hz), 1.31–1.34 (d, 3H, –CH–CH_3, $J=3$ Hz), 1.43–1.65 (m, 12H, 2,2,5,5-CH_3), 3.13 (s, 1H, C≡C–*H*), 3.50–3.92 (two q, 2H, –OCH_2–CH_3, $J=4$ Hz), 4.80–4.92 (q, 1H, –*CH*–CH_3, $J=3$ Hz), 6.55–6.63 (d, –*CH*=CH-Ar, $J=16$ Hz), 7.43–7.45 (s br, 4H, H_{ar}), 8.42–8.53 (d, –CH=*CH*-Ar, $J=16$ Hz). HRMS, *m/z* (%): 356.0 $[M]^+$ (1.07), 355.9 (3.78), 283.8 (58.09), 268.8 (4.17), 236.8 (9.31), 180.8 (11.41), 164.8 (15.12), 72.9 (100.0), 45.1 (86.33). Found: *m/z* 356.20998 $[M]^+$. $C_{21}H_{28}N_2O_3$. Calcd: $M=356.20999$.

3.1.10. 2,2,5,5-Tetramethyl-4-{2-[4-(*p*-phenylethynyl)phenyl]vinyl}-3-imidazoline-3-oxide-1-oxyl (21a). A mixture of copper(I) salt of acetylenes **20a** (60 mg, 0.36 mmol) and diamagnetic (**11**) or spin-labeled iodide (**12**) (130 mg, 0.33 mmol) in 10 mL of pyridine was stirred at 80–85 °C in argon atmosphere for 3.5–4 h till absence of iodide (TLC-control). Then $CHCl_3$ (30 ml) and water (40 mL) were added. The organic layer was separated, the water layer was extracted with $CHCl_3$ (2×25 mL), and the combined organic layers were washed with 25% NH_{3aq} (2×15 mL), dried over K_2CO_3, filtered off and evaporated to dryness under reduced pressure. The crude product was purified by column chromatography on Al_2O_3 (elution with chloroform) and following recrystallization gave 100 mg (85%) of nitroxide **21a**, mp 197.5–198.5 °C (from benzene). IR, cm^{-1}: $\nu_{max}=1315$ (N→O), 1364 (N–$^{\cdot}$O), 2216 (C≡C). Anal. Calcd for $C_{23}H_{23}N_2O_2$: C, 76.85; H, 6.45; N, 7.79.

Found: C, 76.63 H, 6.51 N, 7.87 ESR: $g_{iso}=2.0058$ ($\Delta H_{\mathrm{DPPH}}=3.79$ G), $A_{\mathrm{N}}=14.05$ G, $A_{\mathrm{H(CH_3)}}(12\mathrm{H})=0.23$ G, $A(^{13}\mathrm{C})=5.66$ G. Solvent: toluene.

From spin-labeled iodide **12**: the yield of compound **21a** was 50 mg (85%) obtained from 65 mg (0.165 mmol) of **12**, mp 197.5–198.5 °C (from benzene).

3.1.11. 2,2,5,5-Tetramethyl-4-{2-[4-(3-phenoxyprop-1-ynyl)phenyl]vinyl}-3-imidazoline-3-oxide-1-oxyl (21b). The yield of compound **21b** was 120 mg (92%), mp 161.5–163.5 °C (from mixture of benzene–hexane). IR, cm^{-1}: $\nu_{\max}=1318$ (N→O), 1360 (N–$^{\cdot}$O), 2225 (C≡C). HRMS, *m/z* (%): 389.0 [M^+] (24.15), 222.0 (27.09), 221.0 (15.41), 207.9 (11.70), 194.9 (39.90), 94.0 (11.80), 73.1 (43.77), 72.0 (63.66), 67.0 (14.59). Found: *m/z* 389.18652 [M^+]. $\mathrm{C_{24}H_{25}N_2O_3}$. Calcd: $M=389.18650$. ESR: $g_{iso}=2.0059$ ($\Delta H_{\mathrm{DPPH}}=4.00$ G), $A_{\mathrm{N}}=14.13$ G, $A_{\mathrm{H(CH_3)}}(12\mathrm{H})=0.23$ G, $A(^{13}\mathrm{C})=5.81$ G. Solvent: toluene.

3.1.12. 4-{2-[*p*-(*N*-Ethoxyethyl-1*H*-pyrazol-4-ylethynyl)-phenyl]vinyl}-2,2,5,5-tetramethyl-3-imidazoline-3-oxide-1-oxyl (21c). The yield of compound **21c** was 111 mg (80%), mp 169.0–170.0 °C (from benzene). IR, cm^{-1}: $\nu_{\max}=1310$ (N→O), 1351 (N–$^{\cdot}$O), 2214 (C≡C). Anal. Calcd for $\mathrm{C_{24}H_{29}N_4O_3}$: C, 68.39; H, 6.93; N, 11.39. Found: C, 66.35; H, 7.07; N, 12.09. ESR: $g_{iso}=2.0060$ ($\Delta H_{\mathrm{DPPH}}=4.10$ G), $A_{\mathrm{N}}=14.11$ G, $A_{\mathrm{H(CH_3)}}(12\mathrm{H})=0.23$ G, $A(^{13}\mathrm{C})=5.93$ G. Solvent: toluene.

3.1.13. 2,2,5,5-Tetramethyl-4-{2-[4-(*p*-methoxyphenyl ethynyl)phenyl]vinyl}-3-imidazoline-3-oxide-1-oxyl (21d). The yield of compound **21d** was 120 mg (92%), mp 172.0–173.0 °C (from mixture of benzene–hexane). IR, cm^{-1}: $\nu_{\max}=1295$ (N→O), 1343 (N–$^{\cdot}$O), 2212 (C≡C). Anal. Calcd for $\mathrm{C_{24}H_{25}N_2O_3}$: C, 74.01; H, 6.47; N, 7.19. Found: C, 74.15; H, 6.58; N, 7.12. ESR: $g_{iso}=2.0058$ ($\Delta H_{\mathrm{DPPH}}=3.71$ G), $A_{\mathrm{N}}=14.09$ G, $A_{\mathrm{H(CH_3)}}(12\mathrm{H})=0.23$ G, $A(^{13}\mathrm{C})=5.71$ G. Solvent: toluene.

3.1.14. 2,2,5,5-Tetramethyl-4-{2-[*p*-(2-pyridinylethynyl) phenyl]vinyl}-3-imidazoline-3-oxide-1-oxyl (21e). The yield of compound **21e** was 84 mg (90%) obtained from 100 mg (0.239 mmol) of **11**, mp 179.5–180.0 °C (from mixture of benzene–hexane). IR, cm^{-1}: $\nu_{\max}=1283$ (N→O), 1365 (N–$^{\cdot}$O), 2221 (C≡C). Anal. Calcd for $\mathrm{C_{22}H_{22}N_3O_2}$: C, 73.31; H, 6.15; N, 11.66. Found: C, 73.33; H, 6.60; N, 11.20. ESR: $g_{iso}=2.0059$ ($\Delta H_{\mathrm{DPPH}}=4.05$ G), $A_{\mathrm{N}}=13.81$ G, $A_{\mathrm{H(CH_3)}}(12\mathrm{H})=0.23$ G, $A(^{13}\mathrm{C})=5.60$ G. Solvent: toluene.

3.1.15. 2,2,5,5-Tetramethyl-4-{2-[*p*-(2,3,5,6,8,9,11,12-octahydro-1,4,7,10,13-pentaoxabenzocyclopentadecen-15-yl-ethynyl)phenyl]vinyl}-3-imidazoline-3-oxide-1-oxyl (21f). The yield of compound **21f** was 90 mg (50%), mp 178.5–180.0 °C (from mixture of benzene–hexane). IR, cm^{-1}: $\nu_{\max}=1253$ (N→O), 1363 (N–$^{\cdot}$O), 2205 (C≡C). HRMS, *m/z* (%): 549.2 $[\mathrm{M}]^+$ (15.31), 534.1 (31.71), 504.1 (24.31), 502.2 (45.38), 448.3 (12.07), 447.3 (35.54), 343.1 (11.61), 295.2 (18.03), 189.2 (6.38), 180.1 (23.58), 163.1 (33.76), 98.2 (28.67). Found: *m/z* 549.25942 $[\mathrm{M}]^+\mathrm{C_{31}H_{37}N_2O_7}$. Calcd: $M=549.26006$. ESR: $g_{iso}=2.0059$ ($\Delta H_{\mathrm{DPPH}}=4.10$ G), $A_{\mathrm{N}}=3.74$ G, $A_{\mathrm{H(CH_3)}}(12\mathrm{H})=0.22$ G, $A(^{13}\mathrm{C})=5.57$ G. Solvent: toluene.

3.1.16. 2,2,5,5-Tetramethyl-4-{2-[4-(*p*-bromophenyl-ethynyl)phenyl]vinyl}-3-imidazoline-3-oxide-1-oxyl (21g). The yield of compound **21g** was 100 mg (69%), mp 192.5–193.5 °C (from benzene). IR, cm^{-1}: $\nu_{\max}=1314$ (N→O), 1361 (N–$^{\cdot}$O), 2212 (C≡C). HRMS, *m/z* (%): 437.0 $[\mathrm{M}]^+$ (6.34), 410.1 (7.24), 407.0 (35.07), 394.0 (39.32), 391.9 (100.00), 350.9 (37.18), 349.9 (45.67), 294.9 (37.56), 257.1 (9.18), 239.1 (50.58), 176.0 (23.43), 150.0 (11.40), 135.1 (30.55), 98.1 (24.57). Found: *m/z* 437.08795 $\mathrm{C_{23}H_{22}N_2O_2Br}$. Calcd: $M=437.08651$. ESR: $g_{iso}=2.0057$ ($\Delta H_{\mathrm{DPPH}}=3.6$ G), $A_{\mathrm{N}}=14.09$ G, $A_{\mathrm{H(CH_3)}}(12\mathrm{H})=0.23$ G, $A(^{13}\mathrm{C})=5.72$ G. Solvent: toluene.

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