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Authors: Tatiana Magdesieva, Oleg Levitskiy, Alexey Bogdanov, and Dmitry Eremin

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Twisted diarylnitroxides: an efficient route for radical stabilization

Oleg A. Levitskiy[a], Dmitry B. Eremin[b], Alexey V. Bogdanov[a], and Tatiana V. Magdesieva*[a]

Abstract: New strategy for molecular design of stable diaryl nitroxides was elaborated based on the insertion of a bulky substituent into the ortho-position in the phenyl ring thus disturbing its conjugation with the radical center. A series of new twisted diarylnitroxides with tert-butyl- and trifluoromethyl substituents in different combinations was obtained and fully characterized. ESR and DFT study confirmed that the ortho-substituted phenyl ring is removed out of the conjugation; the O-N-C-C torsion angle was shown to be dependent not only on the bulkiness of the ortho-substituent but it is also influenced by the electron donating or electron withdrawing ability of the substituents in both phenyl rings. Novel nitroxides constitute the first examples of stable diaryl nitroxides with the vacant para-position in the phenyl ring. New approach will allow broadening the scope of available stable diarylnitroxyl radicals which are practically important.

Introduction

Stable N,N-disubstituted NO radicals, nitroxides, are of considerable interest for theoretical research and practical applications. They are widely used as spin and redox traps [1,2], antioxidants [3–6], redox-active electrode materials for energy conversion and storage systems [7–10], regulators in radical polymerization processes [11,12], catalysts [13–17], etc. The most widely investigated are dialkyl nitroxides, foremost, TEMPO (2,2,6,6-tetramethylpiperidine-1-oxyl) and its derivatives [2].

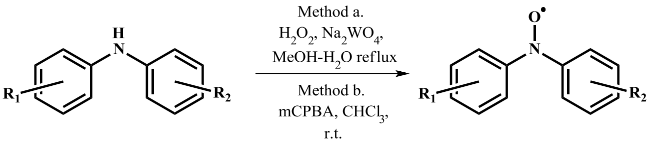
As concerns diarylnitroxides, they are much less investigated. Very limited examples of stable diarylnitroxyls can be found in literature [18–21]. Previously, diarylnitroxyls were not considered as promising candidates for stable radical species since the spin density is delocalized over the *ortho/para* positions of aromatic rings, thus providing additional reaction centers and decreasing stability. It has been shown [22] that the main decay channel for arylnitroxides in solution is radical transformations involving para-position of the phenyl ring leading to quinoid-type structures (see below). In the solid state, bi-, tri- and polyradical species formed from arylnitroxides coupled through the *m*-phenylene units are used as building blocks for organic magnetic materials. [23–26] In all diarylnitroxides which are relatively stable in solution the *para*-positions of the aromatic rings are blocked with the appropriate substituents, to prevent subsequent transformations [22]. This substantially limits the scope of stable radicals available. Meanwhile, diarylnitroxides are more favorable than alkyl derivatives for further functionalization of the molecule aimed at fine tuning of the redox-properties required for the each particular application.

An alternative route to the radical's stabilization might be insertion of a bulky substituent into the *ortho*-position in the phenyl ring thus disturbing its conjugation with the radical center. However, this approach has not been probed yet. In the present paper we demonstrate the possibility of obtaining stable diarylnitroxides with the vacant *para*-position. New *ortho*-substituted diarylnitroxides, devoid of a *para*-substituent, should be nonetheless stable as a result of steric interactions, which force the *ortho*-substituted aryl to be twisted from the N-O plane, with the consequent inhibition of the resonance stabilization.

The first examples of diarylnitroxides containing *ortho*- *tert*-butyl and trifluoromethyl groups in various combinations which are stable in the solid state and in solution are described. Twisted structure of the new compounds was supported by the ESR and DFT study. Stability is a crucial point determining a possibility of practical application of new nitroxides as redox-active electrode materials for energy conversion and storage systems [27]. New approach will allow broadening the scope of available stable diarylnitroxyl radicals which are practically important.

Results and Discussion

Diarylnitroxides can be obtained *via* oxidation of diarylamines using H_2O_2/Na_2WO_4 or *m*-chloroperbenzoic acid [1,2]. A series of new diarylamines (see the accompanying paper [28]) containing *ortho*-*tert*-butyl and trifluoromethyl groups was used as the precursors for the corresponding nitroxides (Scheme 1).



	R_1	R_2	Method	Yield, %
1	p-^{t}Bu	p-^{t}Bu	a	70
2	o-^{t}Bu	p-^{t}Bu	a	45
3	o-^{t}Bu	o-^{t}Bu	b	10
4	p-CF_3	p-^{t}Bu	a	29
5	o-CF_3	p-CF_3	b	25
6	o-CF_3	p-^{t}Bu	b	31
7	o-^{t}Bu	p-CF_3	b	41

Scheme 1. Oxidation of amines to nitroxides

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[a] Dr. O.A. Levitskiy, Dr. A.V. Bogdanov, and Prof., D. Sci.
T.V. Magdesieva
Lomonosov Moscow State University, Chemistry Dept.
Leninskie Gory 1/3, Moscow 119991, Russia
E-mail: tvm@org.chem.msu.ru

[b] D.B. Eremin
Zelinsky Institute of Organic Chemistry Russian Academy of Sciences
Leninsky Prospect, 47, Moscow, Russia

Supporting information: ESI-HRMS spectra, HPLC-MS and ^{1}H NMR data are available free of charge via the Internet at http://onlinelibrary.wiley.com

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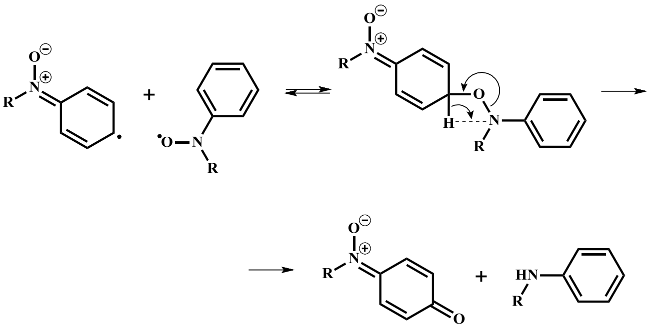
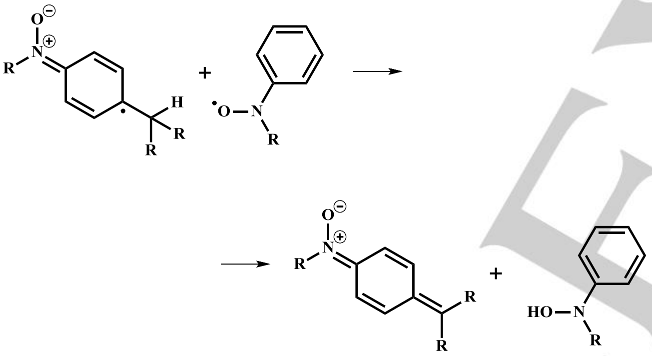
The selection of the starting diarylamines was referred to several reasons. The substituents should be sufficiently bulky, to twist the phenyl ring from the conjugation with the N-O plane and to prevent the possible attack of the radical NO center of the one molecule to the *para*-position of the other molecule keeping a sufficient spin density [22] (Scheme 2).



Scheme 2. Unwanted radical coupling *via para*-position of the arene ring

Only substituents without α-hydrogen atoms are suitable, to suppress the other unwanted reaction channel [22] (Scheme 3)



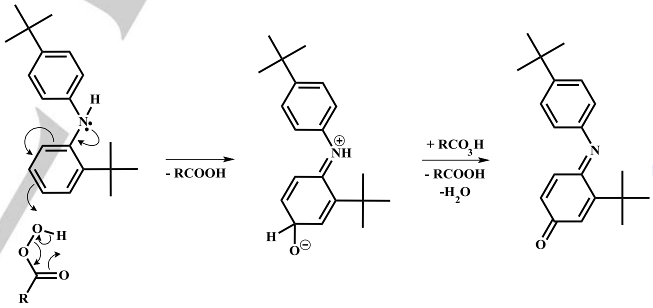
Scheme 3. Main route for decomposition of diarylnitroxides with para-substituents with α-hydrogen atoms

Finally, the chosen substituents exhibit the opposite electronic properties (^{t}Bu is an electron donor whereas CF_3 is an acceptor) allowing estimation of the influence of this parameter on the stability of the nitroxides (e.g., H-atom abstraction ability and other side reactions).

Synthesis of the nitroxides

Oxidation of *4,4'*-bis-(*tert*-butylphenyl)amine was performed with H_2O_2/Na_2WO_4 in boiling methanol, as it has been previously reported [29]. For oxidation of unsymmetrical 2,4'-bis(*tert*-butylphenyl)amine several oxidants were tested. The best results were obtained using H_2O_2 in boiling methanol in the presence of Na_2WO_4 (45% yield). The oxidation with *m*-chloroperbenzoic acid in ether provided the targeted 2,4'-bis-(*tert*-butylphenyl) nitroxide in much lower yield (19%). The oxidation was initially performed at -15°C but 10 min after the temperature was gradually increased and the reaction mixture was stirred for 2 h at room temperature. New unsymmetrical 2,4'-bis-(*tert*-butylphenyl)nitroxyl radical was obtained as red crystals and its identity was proved by ESI-HRMS (see Experimental).

HPLC-MS analysis of the reaction mixture revealed, besides the targeted nitroxide, the presence of a small admixture (ca.10%) corresponding to the compound of the quinoid type. The ^{1}H NMR spectrum of the admixture (Fig. SI-3) exhibits the signals of two non-equivalent tert-butyl groups (1.59 and 1.49 ppm); the signals of the *para*-substituted phenyl ring (AA'BB' spin system signals at 7.56 and 6.91 ppm) and a set of signals corresponding to the substituted 1,4-quinoid ring (two doublets at 7.21 and 6.55 ppm and singlet at 6.73 ppm, Scheme 4). The formation of this by-product (supported also by CI-MS (Fig. SI-2) data) in the course of the amine oxidation is an interesting observation which is in line with the mainstream of our investigation. This is an indication that a certain excess of π electron density is still located at the *para*-position in spite of the presence of the bulky *ortho*-substituent in the close vicinity to the amino group which might influence the conjugation. The increased electron density in the *para*-position provokes an alternative oxidation route via attack of the peroxo-compound at the vacant *para*-position yielding the minor by-product.



Scheme 4. Side reaction in *2,4'*-bis-(*tert*-butylphenyl)amine oxidation with mCPBA

NO group which is more bulky than the NH significantly increases the O-N-C-C torsion angle and the rotation barrier of the *ortho*-substituted ring resulting in a decrease in the conjugation and stabilization of the NO radical due to almost negligible spin density in the *para*-position. This becomes evident from the DFT-optimized structures as well as from the ESR data (see below).

Oxidation of sterically demanding 2,2'-bis-(*tert*-butylphenyl)amine in which the lone pair of the N-atom is shielded by the bulky substituents was performed using *m*-chloroperbenzoic acid which could be expected to provide less sterical hindrance as compared to Na_2WO_4. The reaction was extremely slow, only three days after the starting colorless solution of the amine precursor turned pale red. The solution was evaporated and the excess of the oxidant and *m*-

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chlorobenzoic acid formed was separated by washings with toluene; after subsequent evaporation of the toluene solution the residue was purified by column chromatography. Targeted 2,2'-bis-(*tert*-butylphenyl)nitroxide was isolated (10%) and characterized by HRMS and ESR methods.

Oxidation of CF_3-containing amines is impeded due to the presence of the electron-withdrawing group. Oxidation of 4-*tert*-butyl-4′-trifluoromethyl-diphenylamine was performed with H_2O_2/Na_2WO_4 in boiling methanol, after 15 h of heating the corresponding nitroxide was obtained in 29% yield. The oxidation of the isomeric 4-*tert*-butyl-2′-trifluoromethyl-diphenylamine using the same oxidant was not successful: no radical was obtained after three days of reflux. Therefore, the stronger oxidant (mCPBA) was used for obtaining the nitroxide radical from *4-,2′-bis-(*trifluoromethylphenyl)amine. The reaction mixture containing the amine and mCPBA in chloroform solution was heated for 5 h at 40°C. The corresponding *4-,2′-bis-(*trifluoromethylphenyl) nitroxide was isolated in 25% yield.

All radicals were characterized by HRMS and ESR methods (see Experimental and SI).

The purity of the isolated radical species was proved by the ESR method via spin counting on the nitroxide samples, to determine their spin concentration.

ESR characterization

Experimental and DFT-simulated spectra for all nitroxides under discussion were obtained. Computed and experimental data are in good agreement; with the mean square deviation of 0.05 G. Based on the previously reported data [30] which demonstrated that for nitroxides application of B1LYP functional is preferential over B3LYP providing reasonable agreement of computed and experimental constants, the B1LYP functional with cc-pVDZ basis set was selected. Commonly used for ESR computation PWP functional with EPR-II basis set gave huge difference in a_N values; the accuracy for the a_H values were in the same range as we previously obtained using B1LYP (see SI).

Comparative ESR investigation of isomeric 2,4′-, 2,2′- and 4,4′-bis-(*tert*-butylphenyl)nitroxides was performed revealing the influence of the sterical bulkiness on the hyperfine constants values. A series of unsymmetrical ^{t}Bu and CF_3-substituted nitroxides demonstrates the additional influence of the electronic effects. The ESR spectra obtained are given in Fig.1.

The ESR spectra of all nitroxides exhibit a triplet signal due to the spin splitting on the N atom. Besides, an additional splitting of the each triplet component is observed which is dependent on the type of the substituent and its position. Experimental and simulated ESR spectra are in good agreement.

For three isomeric bis-(*tert*-butylphenyl) nitroxides, additional splitting on the aromatic protons is observed. Digital simulation showed that the spectral pattern observed for 2,4'-bis-(*tert*-butylphenyl) nitroxide is consistent with the spin splitting on the N atom as well as on two pairs of equivalent protons. This means that the spin density in this radical is delocalized over only one phenyl ring giving rise to the spin coupling on two *ortho*- and two *meta*-protons (a_N = 10.34 G, a_H = 2.65 G and 0.88 respectively, see Table 1). Hence, the other phenyl ring (containing the *ortho*-*tert*-butyl group) is removed from the conjugation plane with the nitroxyl radical center. The decrease in the conjugation chain (one ring in conjugation instead of two) is the reason for the observed increase in the spin splitting constants as compared to that for *4,4′*-bis-(*tert*-butylphenyl) nitroxyl radical (see Table 1 and previously reported data, a_N = 9.9 G, a_H = 1.86 G (*ortho*) and 0.9 G (*meta*) [29]). The maximal *hfcc* value with the ^{14}N nucleus is observed in the case of 2,2'-bis-(*tert*-butylphenyl) nitroxide (Table 1) indicating poor delocalization of the spin density over both phenyl rings.

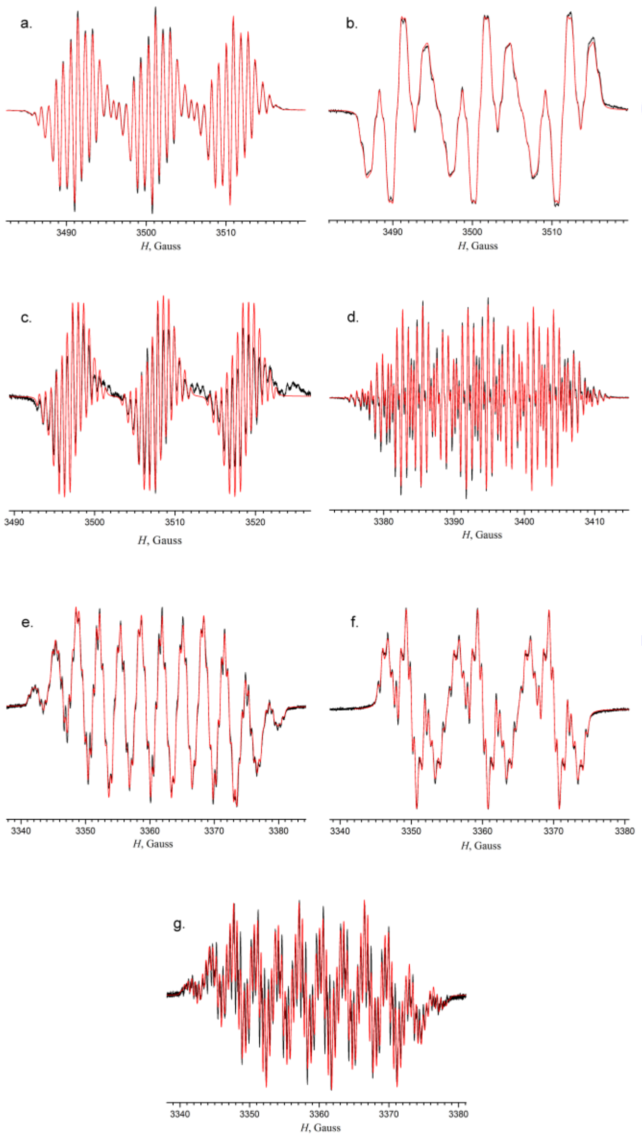

Figure 1. Experimental (black line) and simulated (red line) ESR spectra for 4,4'-bis-(*tert*-butylphenyl)nitroxide (a); 2,4'-bis-(*tert*-butylphenyl)nitroxide (b); 2,2'-bis(*tert*-butylphenyl)nitroxide (c); 4-(trifluoromethylphenyl)-4'-(tert-butylphenyl)nitroxide (d); 4-(trifluoromethylphenyl)-2'-(tert-butylphenyl)nitroxide (e); 2-(trifluoromethylphenyl)-4'-(tert-butylphenyl)nitroxide (f); 2,4'-bis(trifluoromethylphenyl)nitroxide (g).

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For comparison, the ESR data previously obtained for the unsubstituted diphenylnitroxide are also inserted in Table 1. As can be expected, g-factor and a_N and a_H hfcc are very close to our results obtained for planar *4,4'*-bis-(*tert*-butylphenyl) nitroxide radical.

The ESR spectra for trifluoromethylated diarylnitroxides are more complicated due to additional splitting on the fluorine atoms. The a(F) constants are sensitive to the location of the CF_3 group. In case of the *ortho*-CF_3 group, the phenyl ring is partially removed from the conjugation with the NO radical center and the *hfcc* with the F nucleus are much lower than that for the *para*-CF_3-substituent (0.16 G and 3.43 G, respectively, see Table 1).

The *hfcc* values are also influenced by the electronic properties of the substituents in the phenyl rings. Thus, the a(N) values for 2,4'-bis- (t-Bu phenyl)nitroxide and for 2-t-Bu,4'-CF_3-diphenylnirtoxide are sufficiently different (10.34 G and 9.7 G, respectively) though the sterical bulkiness for both compounds attributed to the same *ortho*-t-Bu group might be expected to be similar.

Table 1. g-Values and hyperfine spin coupling constants with ^{14}N, ^{1}H and ^{19}F nucleus for isomeric bis(tert-butylphenyl)nitroxides

Radical	g-value	a(N), G	DFT-calculated a(N), G	a(H), G	DFT-calculated a(H), G	a(F), G	DFT-calculated a(F), G
4,4'- ^{t}Bu	2.00586	9.74	9.53	1.81 (2H) 0.91 (2H)	2.01 ($2H_{ortho}$) 1.08 ($2H_{meta}$)	-	
2,4'- ^{t}Bu	2.00580	10.34	10.55	2.65 (2H) 0.88 (2H) 0.66 (1H) 0.50 (1H) 0.43 (1H)	2.81 ($2H_{ortho}$) 1.30 ($2H_{meta}$) 0.56 ($1H_{meta}$) 0.47 ($1H_{ortho}$) 0.36 ($1H_{para}$) 0.47 ($1H_{meta}$)	-	
2,2'- ^{t}Bu	2.00621	10.59	11.59	1.40 (2H) 1.21 (2H) 0.82 (2H) 0.67 (2H)	1.27 ($2H_{ortho}$) 0.90 ($2H_{meta}$) 1.36 ($2H_{para}$) 0.89 ($2H_{meta}$)	-	
4-^{t}Bu-4'-CF_3	2.00595	9.29	9.26	2.86 (2H) 0.88 (2H) 0.82 (2H) 0.74 (2H)	2.30 ($2H_{meta\ vs.\ CF3}$) 1.80 ($2H_{meta\ vs.\ tBu}$) 1.18 ($2H_{ortho\ vs.\ CF3}$) 1.01 ($2H_{ortho\ vs.\ tBu}$)	2.86 (3F)	3.18 (3F)
2-^{t}Bu-4'-CF_3	2.00611	9.70	10.01	2.61 (2H) 0.92 (2H) 0.63 (1H) 0.48 (1H) 0.43 (1H) 0.24 (1H)	2.91 ($2H_{ortho}$) 1.37 ($2H_{meta}$) 0.51 ($1H_{meta}$) 0.43 ($1H_{meta}$) 0.40 ($1H_{ortho}$) 0.28 ($1H_{para}$)	3.74 (3F)	3.87 (3F)
4-^{t}Bu-2'-CF_3	2.00607	10.02	9.69	2.52 (2H) 0.85 (2H) 0.4 (1H)	2.56 ($2H_{ortho}$) 1.23 ($2H_{meta}$) 0.97 ($1H_{ortho}$) 0.95 ($1H_{para}$) 0.72 ($1H_{meta}$) 0.70 ($1H_{meta}$)	0.63 (3F)	0.33 (3F)
4-CF_3-2'-CF_3	2.00610	9.39	9.12	2.57 (2H) 1.05 (2H) 0.51 (1H) 0.40 (1H) 0.44 (1H) 0.49 (1H)	2.69 ($2H_{ortho}$) 1.29 ($2H_{meta}$) 0.23 ($1H_{ortho}$) 0.20 ($1H_{meta}$) 0.19 ($1H_{meta}$) 0.19 ($1H_{para}$)	3.43 (3F) 0.16 (3F)	3.60 (3F) 0.36 (3F)
H,H*	2.0055	9.66		1.83 0.79 1.83			
H,H**	2.0055	9.77		1.86 0.87			

* in xylene, see ref. [18]

** imbedded in a benzophenone single crystal, see ref. [31]

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Table 2. DFT calculated O-N-C-C torsion angles in the series of the twisted nitroxides $(R_1C_6H_4)(R_2C_6H_4)NO$ and standard Gibbs free energies for the unwanted dimerization via phenyl ring (Scheme 2)

Compound number	Substituents in the phenyl rings		C-C-N-O torsion angle, degrees
	R_1	R_2	
2	o-^{t}Bu	p-^{t}Bu	67.4
3	o-^{t}Bu	o-^{t}Bu	45.3
5	o-CF_3	p-CF_3	59.9
6	o-CF_3	p-^{t}Bu	52.2
7	o-^{t}Bu	p-CF_3	69.8

The comparison of the a(F) values for the *ortho*-CF_3 group in 2,4'-bis-(trifluoromethylphenyl)nitroxide and 2-CF_3,4'-t-Bu diphenylnitoxide shows that the values are significantly different (0.16 G and 0.63 G) in spite of the similar bulkiness, thus indicating the influence of the electronic effects. Combined influence of the electronic effects and sterical bulkiness in the series of the twisted nitroxides can be deduced from the comparison of the torsion angle values between the phenyl ring and the N-O plane which are given in Table 2.

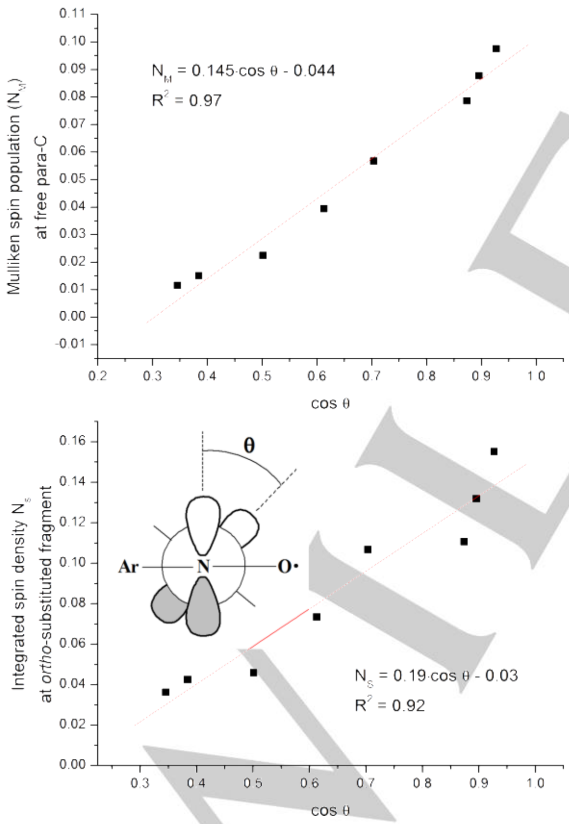

Figure 2. The Mulliken spin population at the carbon atoms in para-position of the twisted ring vs. cos θ linear fit (a) and the integrated spin density over the whole ortho-substituted ring vs. cos θ linear fit (b). The Newman projection given in the inset illustrates the π-π overlap between the NO and the twisted aryl moiety. Points for two 4,4'-substituted nitroxides **1** and **4** are also included.

Calculated torsion angle values nicely correlate with the spin density at the carbon atoms taken from the ORCA output. The linear plots between the cos θ and the Mulliken spin population at the carbon atoms in the *para*-position of the twisted ring as well as of the integrated spin density over the whole *ortho*-substituted ring are given in Fig.2. The Newman projection given in the inset illustrates the π-π overlap between the NO and the twisted aryl moiety controlling spin delocalization over the *ortho*-substituted ring.

UV-Vis

UV–vis spectra for two sets of new isomeric diarylnitroxides are shown in Fig. 3. The wavelengths (λ_{max}) and the molar extinction coefficients (*ε*) are summarized in Table SI-8. All the samples exhibit intensive peak at 200 nm, a broad intensive peak around 300 nm and a set of much less intensive peaks in 430-530 nm region. The most interesting is the weak absorption peak in the visible region since it is mainly associated with free radical electrons located on the SOMOs. The λ_{max} for the absorption in visible region for diarylnitroxides (430–530 nm) is red-shifted as compared to *λ*max for alkyl derivatives (428–468 nm) [32]*;* the *ε* values are significantly higher for aromatic than for aliphatic (*ε* 4–10) compounds due to spin delocalization. The minimal extinction among the set of compounds given in Fig. 3 is observed for the *ortho*-*t*-Bu, *para*-CF_3 derivative which exhibits the maximal dihedral O-N-C-C angle (see Table 2). The interpretation of the wavelengths values observed within the series of nitroxides given in Table 2 is not trivial since the SOMO energy is influenced by the different trends including the bulkiness of the molecule and electron effects of the substituents The latter are dependent not only on the nature of the addends but on the conjugation degree as well.

Stability tests

The idea that removing the aryl moiety from the conjugation plane with the nitroxyl radical center (thus preventing spin density delocalization over the phenyl ring) will drastically increase the stability of the radical was supported by the ESR data.

The radicals are highly stable. In a crystal form, they stay for months in an open air without any noticeable destruction. For quantitative estimation of the radicals' life time, spin counting method was applied. Thus, the sample of 2-^{t}Bu,4'-CF_3-diphenyl nitroxide stayed for more than two weeks in benzene solution in an open air at room temperature without protection of light and exhibited the amount of radical species which was 100% of the starting value. The isomeric 2-CF_3,4'-^{t}Bu diphenyl nitroxide is relatively less stable: after 7 days of staying in toluene solution in an open air at room temperature the sample exhibited the amount of radical species which was 85 % of the starting value. A decrease in stability might be attributed to more significant spin delocalization over the phenyl ring, as follows from the comparison of the calculated torsion O-N-C-C angle and the a(N) hfcc values for these two isomers (see Tables 1 and 2 below). Interestingly, new nitroxides are relatively stable even in

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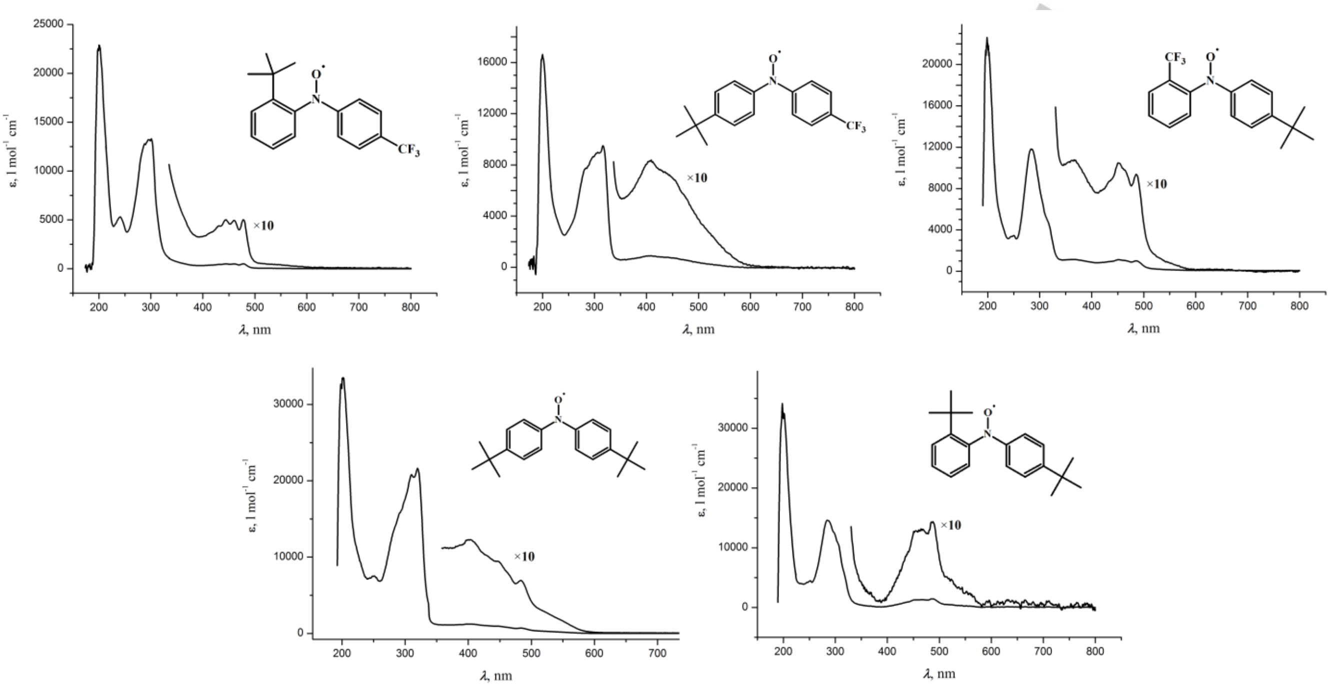

Figure 3. UV–vis spectra for two sets of new isomeric diarylnitroxides

halogenated solvents (such as e.g., $CHCl_3$). Thus, the NMR sample of 2,4’ bis-(tert-butylphenyl)nitroxide in $CDCl_3$ stayed unchanged for more than 30 h without light protection. For comparison, previously reported [33] relatively stable bridged diarylnitroxides decomposed in $CHCl_3$ solution under solar irradiation in 12 min.

To quantify stability of the radicals and to demonstrate the role of twisting in their stabilization, kinetic measurements in toluene were performed. The experiments in toluene are important sincethey allow estimation the inherent stability of the radicals toward decomposition contrary to the experiments in chloroform. The latter is known to produce the radicals which can initiate secondary radical transformations, whereas the H-donor abilities of both solvents are similar. Since the radicals are stable in solution under solar irradiation, harsher irradiation (laser light, wavelength 405 nm, intensity $5{\cdot}10^{-9}$ Einstein/s per sample) were applied to get reliable quantitative data. ESR spectra of two isomeric 2,4’- and 4,4’- bis-(tert-butylphenyl)nitroxides were recorded in the course of irradiation and quantum yields of photochemical decomposition were determined.

The following kinetic model of photochemical radical decomposition was used:

$$\frac{dN}{dt} = I_0\left(1 - 10^{-A(t)}\right)\varphi$$

where N is the number of radical molecules, I_0 is light intensity, φ is the quantum yield of the reaction, $A(t)$ is absorbance of the solution at the irradiation wavelength (calculated by Bouguer-Lambert-Beer’s law $A(t) = \frac{\varepsilon_{405} l}{V} \cdot N(t)$ where ε_{405} is extinction coefficient on the irradiation wavelength, l is the optical path length of irradiating light, and V is the sample volume).

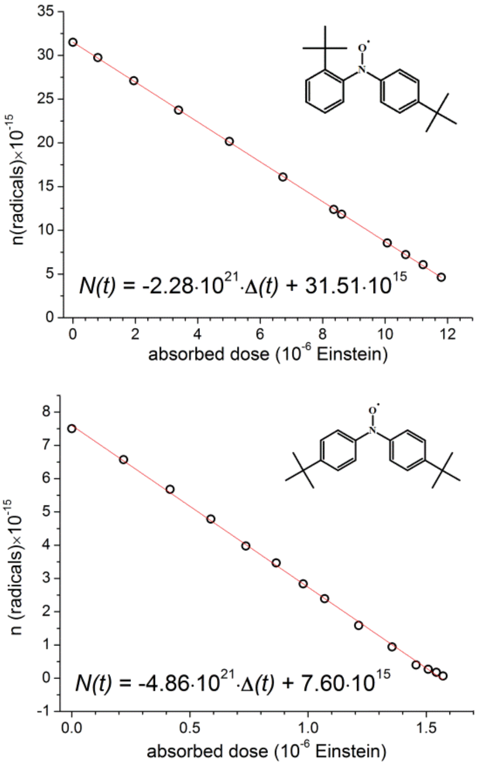

Figure 4. Stability tests under laser irradiation.

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In equation given above the value $I_0\left(1-10^{-A(t)}\right)$ is the number of photons absorbed by radical molecules per unit time, and the expression $\Delta(t)=\int_0^t I_0\left(1-10^{-A(\tau)}\right)d\,\tau$ represents the absorbed irradiation dose. According to equation, the slope of the $N(t)$ vs. $\Delta(t)$ linear dependences gives the quantum yield of photochemical decomposition of the radicals. The results obtained for isomeric 2,4'- and 4,4'- bis-(tert-butylphenyl)nitroxides are given in Fig. 4. The quantum yields of photochemical decomposition measured as described are $(8\pm2)\cdot10^{-3}$ for 4,4'-substituted radical and $(4\pm1)\cdot10^{-3}$ for the 2,4'-isomer. The results obtained clearly indicate the increased stability of the twisted isomer as compared to the planar one.

HRMS analysis of the solutions obtained after irradiation of the radicals was performed. It revealed formation of corresponding amines and a certain amount of O-arylated diarylnitroxides. The analog of the latter product (O-alkylated nitroxide) was also detected among the products of photochemical destruction of stable di-tert-butyl nitroxide [34]. The detailed analysis of the possible photochemical decay channels for all new diarylnitroxides is in progress now and will be the subject of the forthcoming paper.

Conclusions

The main problem decreasing stability of diaryl nitroxides as compared to the aliphatic analogs is spin density delocalization over the phenyl ring which provokes various radical transformations. New strategy for the molecular design of stable diaryl nirtoxides was elaborated based on the insertion of a bulky substituent into the *ortho*-position in the phenyl ring thus disturbing its conjugation with the radical center. A series of new twisted diarylnitroxides with tert-butyl- and trifluoromethyl substituents in different combinations was obtained and fully characterized with HRMS, ESR and UV-Vis methods. The compounds are stable in the solid state and in solution. Novel nitroxides constitute the first examples of stable diaryl nitroxides with the vacant para-position in the phenyl ring. ESR and DFT study confirmed that the *ortho*-substituted phenyl ring is removed out of the conjugation with the NO radical center. Comparative ESR investigation of the isomeric 4,4'-, 2,4'- and 2,2'- bis(tert-butylphenyl)nitroxides indicated significant difference in the spin splitting constants. The maximal *hfcc* value with the ^{14}N nucleus is observed in the case of 2,2'-isomer indicating poor delocalization of the spin density over both phenyl rings.

It was shown that O-N-C-C torsion angle is dependent not only on the bulkiness of the *ortho*-substituent but it is also influenced by the electron donating or electron withdrawing ability of the substituents in the both phenyl rings. The presence of the strong electron-withdrawing group in the one phenyl ring facilitates delocalization of the nitrogen lone pair over the ring; thus, the necessity for the conjugation of the NO moiety with the other ring is decreased and the *ortho*-substituted ring is more prone to be twisted out of the plane according to the sterical demands of the *ortho*- group.

New approach will allow broadening the scope of available stable diarylnitroxyl radicals which are practically important.

Experimental Section

General information

Mass spectra were measured with high-resolution time-of-flight instrument using electrospray ionization (ESI-MS)^{20}**.** Measurements were performed in positive ion mode, interface capillary voltage at 4.5 kV, effective scan range at *m/z* 100 – 1200, external calibration (0.016 M sodium formate in MeCN-water 1 : 1 mixture or ESI-L Low Concentration Tuning Mix, Agilent Technologies), direct syringe injection at flow rate of 3 µL/min, nitrogen as dry gas at 4 L/min, interface temperature at 180 °C.

ESR spectra were recorded for solutions in toluene deaerated using standard freeze-pump-thaw technique containing appr. $5\cdot10^{15}$ radical molecules.

UV-vis spectra were recorded for $5\cdot10^{-5}$ – $1\cdot10^{-4}$ M solutions of the nitroxides in dry acetonitrile.

^{1}H (400.0) MHz) *NMR spectra* were recorded in $CDCl_3$. Chemical shifts were referenced to a residual non-deuterated solvent.

Computational details

Stationary point structure search for all the radicals as well as vibrational analysis for the structures obtained was performed in PRIRODA quantum-chemistry program [35,36]. The gradient-corrected exchange-correlation Perdew, Burke, and Ernzerhof (PBE) functional [37] and basis sets L1 were used for calculations [38]. The 10^{-6} threshold on the molecular gradient at the geometry optimization procedure was employed. Integration of spin density over ortho-substituted aromatic moiety basin was performed in Multiwfn program [39]. The region of integration was defined as the combination of Bader's atomic basins of C and H atoms of the ortho-substituted ring and all atoms of the ortho-substituent.

ESR spectra were calculated in ORCA 3.0 quantum chemistry program [40] for gas phase optimized geometries at B1LYP/cc-pVDZ level with SMD solvation model [41]. RIJCOSX [42] approximation was employed.

Oxidation to nitroxides.

2,4'-bis(tert-butylphenyl)nitroxide (method a). A solution of 281 mg (1.0 mmol) of unsymmetrical 2,4'-bis-(*tert*-butylphenyl)amine in 5 ml of methanol was heated to the boiling point. Afterwards, 340 µl (3.0 mmol) of 30% hydrogen peroxide and a solution of 33 mg (0.1 mmol) of $Na_2WO_4\cdot2H_2O$ in 70 µl of water were successively added and the mixture was heated under reflux for 12 hours. New portions of hydrogen peroxide (340 µl) were added every 3 hours. The consumption of diarylamine was monitored by TLC (eluent — toluene/hexane 1:10). After all starting material was consumed, the reaction mixture was cooled, diluted with water and extracted with ether. Organic fractions were washed with water dried over sodium sulfate and purified by column chromatography on silicagel (eluent — toluene, R_f = 0.44). Nitroxide was obtained as reddish-orange oil (133 mg, 45% yield). ESI-HRMS: m/z 296.2012 (M^+, 296.2009 calculated for $C_{20}H_{26}NO$), 297.2078 ($M+H^+$, 297.2087 calculated for $C_{20}H_{27}NO$). λ_{max}, nm: 538 (sh), 487, 465, 302 (sh), 285, 251, 200

2,4'-Bis(tert-butylphenyl)nitroxide (method b). To a solution of 50 mg (0.18 mmol) of unsymmetrical 2,4'-bis(*tert*-butylphenyl)amine in 1.5 ml of ether cooled to −15 °C, a solution of 46 mg (0.29 mmol) of *m*CPBA in

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1 ml of ether was added. The mixture was hold at −15 °C for 10 min and, afterwards, at room temperature for 2 hours. The color of solution gradually changed to dark red. The mixture was quenched with water, washed with saturated aqueous $NaHCO_3$, dried over Na_2SO_4, evaporated and purified by column chromatography on silicagel using toluene as an eluent; 10 mg (19%) of the nitroxide was obtained.

2,2'-Bis(tert-butylphenyl)nitroxide. A solution of 28 mg (117 µmol) of *m*-chloroperbenzoic acid in 3 ml of diethyl ether was added to a solution of 30 mg of 2,2'-bis(tert-butylphenyl)amine in 6 ml of diethyl ether. The mixture was kept in the dark for 5 days at room temperature. Resulting pale red solution was evaporated, the residue washed with toluene on glass filter. The toluene solution was concentrated and purified by column chromatography on silicagel using toluene as an eluent. 2,2'-bis(*tert*-butylphenyl)nitroxide was isolated in 10% yield as a red solid. ESI-HRMS: m/z 296.2010 (M^+, 296.2009 calculated for $C_{20}H_{26}NO$), 297.2081 ($M+H^+$, 297.2087 calculated for $C_{20}H_{27}NO$).

4-(trifluoromethylphenyl)-4'-(tert-butylphenyl)nitroxide. A solution of 200 mg (0.68 mmol) of 4-(trifluromethyl)-4'-tert-butyldiphenylamine in 5 ml of methanol was heated to the boiling point. Afterwards, 230 µl (2.2 mmol) of 30% hydrogen peroxide and a solution of 22 mg (0.07 mmol) of $Na_2WO_4{\cdot}2H_2O$ in minimal volume of water were successively added. The mixture was heated under reflux for 12 hours. New portions of hydrogen peroxide (230 µl in 1.3 ml of MeOH) were added every 5 hours. After 15 h of refluxing the reaction mixture was diluted with CH_2Cl_2 (20 ml), washed with water, dried over Na_2SO_4 and evaporated under reduced pressure. The residue was purified by column chromatography on silicagel using toluene/hexane 1:1 mixture as an eluent eluent. After evaporation of the colored fraction, 30 mg of the targeted nitroxide was obtained. 100 mg of the starting amine was also recovered from the preceding colorless fraction. ESI-HRMS: m/z 308.1262 (M^+, 308.1262 calculated for $C_{17}H_{17}F_3NO$); λ_{max}, nm: 518 (sh), 450 (sh), 408, 316, 306, 295, 281, 199

2-(trifluoromethylphenyl)-4'-(tert-butylphenyl)nitroxide. 100 mg (0.34 mmol) of 2-tert-butyl-4'-(trifluromethyl)diphenylamine was dissolved in 2 ml of $CHCl_3$. A solution of 140 mg (0.57 mmol) of 70% mCPBA in 2 ml of $CHCl_3$ was added. The reaction mixture was kept at room temperature for 3 hours, diluted with $CHCl_3$ (10 ml), washed with Na_2CO_3 solution, dried over Na_2SO_4 and evaporated under reduced pressure. The residue was purified by column chromatography on silicagel (with CH_2Cl_2/hexane 1:1 as an eluent). The second colored fraction was collected and evaporated yielding 33 mg (31%) of the targeted nitroxide as a brownish-yellow oil. ESI-HRMS: m/z 308.1262 (M^+, 308.1262 calculated for $C_{17}H_{17}F_3NO$); λ_{max}, nm: 534 (sh), 485, 463 (sh), 452, 434 (sh), 366, 314 (sh), 284, 247, 199

4-(trifluoromethylphenyl)-2'-(tert-butylphenyl)nitroxide. 100 mg (0.34 mmol) of 2-tert-butyl-4'-(trifluromethyl)diphenylamine was dissolved in 2 ml of $CHCl_3$. A solution of 140 mg (0.57 mmol) of 70% mCPBA in 2 ml of $CHCl_3$ was added. The resulting solution was kept at room temperature for 3 hours, diluted with $CHCl_3$ (10 ml), washed with Na_2CO_3 solution, dried over Na_2SO_4 and evaporated under reduced pressure. The residue was purified by column chromatography on silicagel (with CH_2Cl_2/hexane 1:2 as an eluent). The first colored fraction was collected and evaporated yielding 43 mg (41%) of the targeted nitroxide as a brownish-orange oil. ESI-HRMS: m/z 308.1260 (M^+, 308.1262 calculated for $C_{17}H_{17}F_3NO$), ESI-HRMS: m/z 309.1339 ($M+H^+$, 309.1335 calculated for $C_{17}H_{18}F_3NO$); λ_{max}, nm: 531 (sh), 477, 460, 443, 430, 413 (sh), 301, 295, 288, 240, 200

2,4'-Bis(trifluoromethylphenyl)nitroxide. 150 mg (0.49 mmol) of 2,4'-bis(trifluromethyl)diphenylamine was dissolved in 5 ml of $CHCl_3$. A solution of 140 mg (0.57 mmol) of 70% mCPBA in 5 ml of $CHCl_3$ was added. The resulting solution was heated to 40°C, kept at this temperature for 5 hours and left overnight at room temperature. The resulting solution was diluted with $CHCl_3$ (10 ml), washed with Na_2CO_3 solution, dried over Na_2SO_4 and evaporated under reduced pressure. The residue was purified by column chromatography on silicagel (with hexane/ethylacetate 8:1 as an eluent). The second colored fraction was collected and evaporated yielding 39 mg (25%) of the targeted nitroxide as a brownish-orange oil. ESI-HRMS: m/z 320.0504 (M^+, 320.0510 calculated for $C_{14}H_8F_6NO$).

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Keywords: stable radical • nitroxides • ESR • conjugation • steric effects

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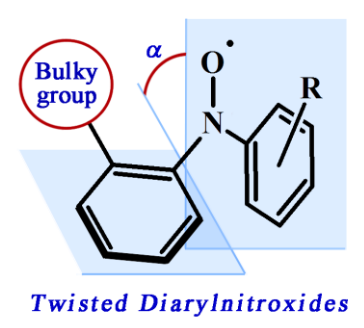

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