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A New Spiro[Indoline-Naphthoxazinic] Spin Trapping Agent

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The synthesis and characterisation of a new spin trapping agent of the spiro[indoline-naphthoxazinic] family is reported. The EPR results of spin trapping experiments are also described, which indicate the ability of this nitrone to react with carbon-, oxygen- and sulphur-centred radicals.

INTRODUCTION

Photochromic compounds, that is compounds capable of undergoing light-induced reversible colour changes, are becoming increasingly important owing to the wide variety of their established and potential applications.[1] One of the major problems encountered in their use is associated with their resistance to fatigue, because all these compounds are sooner or later subject to irreversible degradation.[2,3] Among the photochromic compounds, those belonging to the spiroindolinic family are especially interesting; in particular the spiro[indoline-naphthoxazinic] derivatives[4] have been found to be those characterised by the higher, though not infinite, fatigue resistance, and it has been suggested that their degradation processes may involve radical species, despite the fact that no direct evidence in this direction has been reported.

Although EPR spectroscopy is the technique of choice for the detection and investigation of free radicals, the lifetime of these species under normal experimental conditions is often too short to allow the build up of the steady state concentration necessary for instrumental detection. In order to overcome this impasse the technique of spin trapping has been developed, through which the transient radicals are allowed to react with unsaturated substrates capable of readily undergoing radical addition (the Spin Traps) originating spin-adducts characterised by a greater persistence that can therefore be directly detected without difficulty.[5] Several classes of organic compounds have been exploited as Spin Traps, but the vast majority of these radical scavengers belong to the families of nitroso compounds and of nitrones.[6] Indeed

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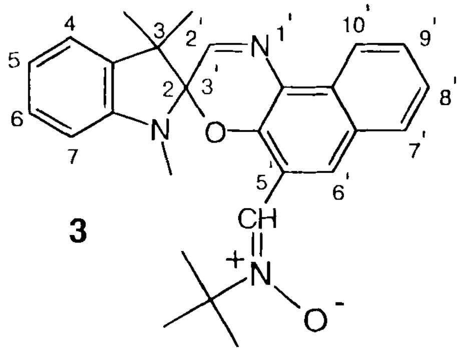
these compounds react with a wide variety of radical species of different nature; thus they easily trap nucleophilic carbon-centred radicals such as alkyls and electrophilic oxygen- or sulphur-centred radicals such as alkoxyls,[7] peroxyls,[8] and thiyls.[9]

Up to recent days a variety of spin traps, light stabilisers as HALS (Hindered Aminic Light Stabilisers) and other conventional antioxidants, have been added to photochromes in polymer matrices to slow down their degradation, the main problem encountered being the different evolution of these additives. Indeed, in order to avoid undesirable screen effects and to maintain the medium as homogeneous as possible the concentration of the antioxidants must be kept very low, often at the expenses of their effectiveness. On this basis, spin trapping agents not affecting the properties of the photochromes would be valuable, and the synthetic procedures of a few nitrones having a spiro[indoline-naphthopyranic] structure have been recently described:[10] we report here the synthesis and the NMR and X-ray diffractometric characterisation of 5′-[2-(*N*-*tert*-butylethanalnitrone)]-1,3,3-trimethyl-spiro[indoline-2,3′-naphtho[2,1-b][1,4]oxazine] **3**, along with the EPR results of several spin trapping experiments.



3

The merocyanine from **3**, i.e. its open form present under the action of light, has a λ_{max} of 597 nm in toluene, a value very close to that of the unsubstituted compound (λ_{max} of 590 nm); thus the presence of **3** even in larger amounts than normally used for the other additives is not bound to substantially affect the photochromic properties of spironaphthoxazinic systems.

Because the radical adducts with **3** or their evolution products have not been isolated in the present study, we are not in a position to say whether or not they maintain the photochromic behaviour of the trap. On the other hand, even if they should not, the fact that the trap itself has properties similar to those of the photochrome(s) makes its use advantageous with respect to that of conventional additives and other spin traps.

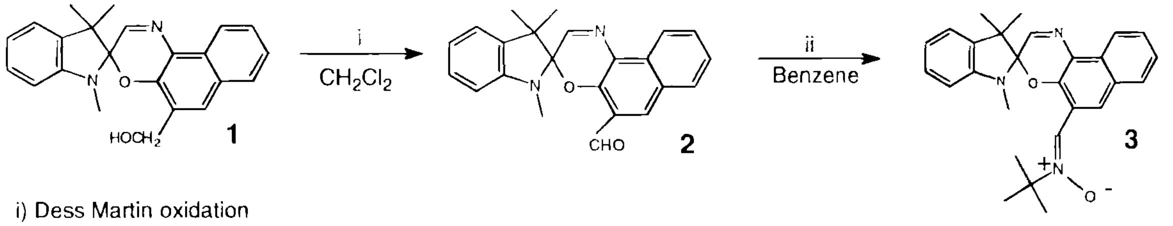
A detailed study of the light-induced degradation of the photochromic nitrone **3** is in progress and the results shall be published elsewhere, along with those concerning the photodegradation of spiro[indoline-naphthoxazinic] photochromes containing variable amounts of **3** as additive.

SYNTHESIS AND X-RAY DIFFRACTOMETRIC CHARACTERISATION

Nitrone **3** was prepared as outlined in Scheme 1 by oxidation of the hydroxymethyl derivative **1** with 1,1,1-tris(acetyloxy)-1,1-dihydro-1.2-benziodoxol 3(1*H*)-one according to the Dess Martin procedure[11] followed by condensation of the resulting aldehyde **2** with *tert*-butylhydroxylamine.

5′-Formyl-1,3,3-trimethylspiro[indoline-2,3′-naphtho[2,1-b][1,4]oxazine]—2

360 mg (0.86 mmol) of 1,1,1-tris(acetyloxy)-1, 1-dihydro-1.2-benziodoxol-3(1*H*)-one (Dess Martin reagent) prepared as described in the literature[11,12] (*CAUTION: Explosive by-products may be formed!*)[13] are added to a solution of 400 mg (1.12 mmol) of **1**[14] in 20 ml of methylene chloride at room temperature. After stirring the mixture for 45 mins the solvent is evaporated and the residue is flash-chromatographed on silica eluting with pentane containing 1% ethyl ether. After evaporation of the solvent pure **2** is obtained as a



i) Dess Martin oxidation
ii) *tert*-Butylhydroxylamine hydrochloride/Pyridine

yellow powder (259 mg, 0.73 mmol) in a 65% yield. ^{1}H-NMR/250 MHz ($CDCl_3$) δ/ppm: 1.31 (6H, s, C-3 methyl groups), 2.70 (3H, s, *N*-methyl group), 6.51 (1H, d, H-7, $J_{7\text{-}6}$ = 7.76 Hz), 6.82 (1H, t, H-5, $J_{5\text{-}4,6}$ = 7.76 Hz), 7.01 (1H, d, H-4, $J_{4\text{-}5}$ = 7.76 Hz), 7.15 (1H, t, H-6, $J_{6\text{-}5,7}$ = 7.76 Hz), 7.41 (1H, t, H-8′, $J_{8'\text{-}7',9'}$ = 8.25 Hz), 7.61 (1H, t, H-9′, $J_{9'\text{-}8',10'}$ = 8.25 Hz), 7.78 (1H, s, H-2′), 7.82 (1H, d, H-7′, $J_{7'\text{-}8'}$ = 8.25 Hz), 8.24 (1H, s, H-6′), 8.48 (1H, d, H-10′, $J_{10'\text{-}9'}$ = 8.25 Hz), 10.26 (1H, s, H-CHO).

5′-[2-(N-tert-butylethanalnitrone)]-1,3,3-trimethylspiro[indoline-2,3′-naphtho[2,1-b][1,4]oxazine]—3

A solution of pyridine (80 mg, 1.06 mmol) in benzene (10 ml) is added dropwise under argon to a refluxing solution of *N*-(*tert*-butyl)hydroxylamine hydrochloride (130 mg, 1.06 mmol) in benzene (10 ml). After refluxing the mixture for 10 mins, a solution of **2** (200 mg, 0.56 mmol) in benzene (10 ml) is added dropwise, and the resulting mixture is refluxed for 2 hours. After evaporation of the solvent the residue is flash-chromatographed on silica with pentane: ethyl ether (with a gradient from 0 to 30% Et_2O). After evaporation of the solvent 150 mg (0.35mmol) of pure **3** are obtained as a white powder (yield, 62%). Crystals of **3** can be obtained by saturating with pentane a solution obtained by dissolving a small amount of the compound in as little methylene chloride as possible, and allowing a very slow evaporation of the solvent (mp 128°C). ^{1}H-NMR/250 MHz ($CDCl_3$) δ/ppm: 1.16 (3H, s. C-3 methyl group), 1.22 (3H, s, C-3 methyl group), 1.24 (9H, s, *tert*-butyl), 2.50 (3H, s, *N*-methyl group), 6.37 (1H, d, H-7, $J_{7\text{-}6}$ = 7.68 Hz), 6.71 (1H, t, H-5, $J_{5\text{-}4,6}$ = 7.55–7.68 Hz), 6.82 (1H, d, H-4, $J_{4\text{-}5}$ = 7.55 Hz), 7.02 (1H, t, H-6, $J_{6\text{-}5,7}$ = 7.68 Hz), 7.22 (1H, t, H-8′, $J_{8'\text{-}7',9'}$ = 8.30 Hz), 7.41 (1H, t, H-9′, $J_{9'\text{-}8',10'}$ = 8.30 Hz), 7.63 (1H, s, H-2′), 7.64 (1H, s, H-6′), 7.66 (1H, d, H-7′, $J_{7'\text{-}8'}$ = 8.30 Hz), 8.32 (1H, d, H-10′, $J_{10'\text{-}9'}$ = 8.30 Hz), 9.67 (1H, s, CH bound to C-5′).

The structure of **3** was also confirmed by X-ray diffractometric studies and an *ORTEP*II[15] view of the molecule is shown in Figure 1, while the relevant crystallographic data are collected in Table I.

It is worth noting that the angle between the two mean planes C_{19}-N_{22}-C_{23}-C_{24}-C_{25}-C_{29}-C_{30}-C_{31}-C_{32} and C_1-C_{10}-C_9-C_8-O_{18}-C_{19}-C_{20}-N_{21}-C_7-C_6 is 109.5°. This value may be taken as the consequence of steric repulsion between the methyl groups C_{26} and C_{27} and carbon C_{20} which also results in a widening of the angle C_{25}-C_{19}-C_{20} (117.7°). It should also be noted the remarkable dissimmetry of the bond lengths corresponding to the atom O_{18}. Indeed the fact that the C_{19}-O_{18} bond length is 1.475 Å and that of the C_8-O_{18} is 1.358 Å is indicative of the weakness of the spiro bond responsible for the photochromic properties of the compound.

EPR STUDIES

Nitrogen purged benzene or *tert*-butylbenzene solutions of nitrone **3** were EPR silent. On the other hand, when nitrone **3** was allowed to react with a variety of radicals generated *in situ* at room temperature, the EPR spectra of the resulting spin adducts were recorded. In particular, the spin adducts between **3** and methyl, ethyl, ben-

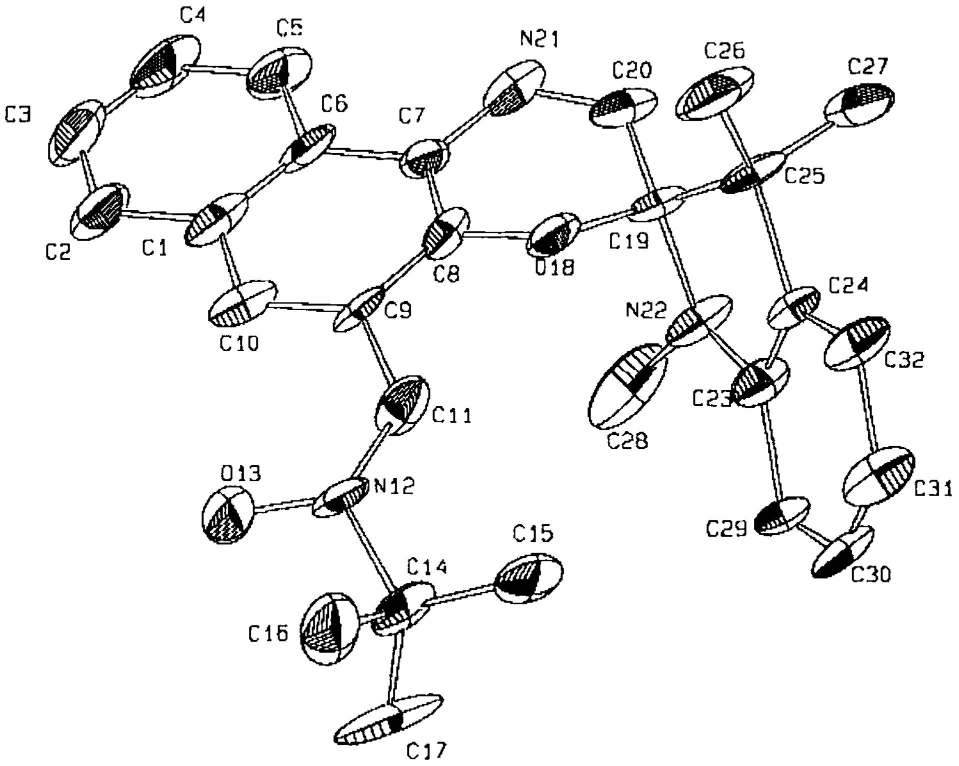


FIGURE 1 *ORTEP*II drawing of nitrone **3** with displacement ellipsoids at 50% probability.

TABLE I Diffractometric data of compound **3**

Crystal data		Data collection
$C_{27}H_{29}N_3O_2$	Mo Kα radiation	Enraf-Nonius CAD-4 diffractometer[17]
$M_r = 427.55$	l = 0.709	
Monoclinic	Cell parameters from 25 reflections	scans
$P2_1/c$		Absorption correction: none
$a = 8.580(2)$ Å	∂ = 15–32˚	
$b = 13.901(3)$ Å	$\mu = 1.78\ \mathrm{mm}^{-1}$	4834 measured reflections
$c = 19.977(6)$ Å	$T = 293\mathrm{K}$	4732 independent reflections
$\beta = 98.57(3)˚$	Hexagonal prism	2652 observed reflections $[I > 3\sigma(I)]$
$V = 2356.1(6)$ Å^3	0.5×0.2×0.3 mm	
$Z = 4$	Colourless	$\partial_{max} = 32°$
$D_c = 1.21\ \mathrm{Mg\ m}^{-3}$	Crystal resolution	Data reduction
	SHELXS86[16]	Datared[18]
Refinement		
SHELX93[19]	$(\Delta/\sigma)_{max} = 0.20$	
Refinement on F	$\Delta\rho_{max} = 0.25$ eÅ^{-3}	
$R = 0.0472$	$\Delta\rho_{min} = -0.23$ eÅ^{-3}	
$wR = 0.0465$	Atomic scattering factors from *International Tables for X-ray Crystallography* (1974, Vol. IV, table 2.2B)	
$S = 0.73$		
2382 reflections		
376 parameters		
H-atoms fixed at 0.9 Å		
Unit weights applied		

zyl, cyanomethyl, 2-cyanoprop-2-yl, *tert*-butoxyl, superoxide anion, methylthiyl, *tert*-butylthiyl, phenylthiyl, and methylcarboxyl radicals were characterised and their spectral parameters are collected in Table II.

$$\mathbf{3} + \cdot X \longrightarrow \cdot\mathbf{3}^{-}X$$

From an examination of the EPR data it emerges that the adducts of carbon centred radicals are characterised by hyperfine nitrogen splittings in the range 13.2 to 13.9 G, while those of oxygen and sulphur centred radicals have slightly greater nitrogen splittings, ranging from 13.9 to 14.7 G.

One or more radical adducts were observed at a time, depending on the conditions under which the transient radicals were generated. Thus photolysis of solutions of **3** containing dimethyl-, diethyl-, or dibenzylmercury led to the corresponding alkyl adducts, while when the methyl radical was generated via decomposition of iodosobenzene diacetate (IBDA), the spectrum of the methyl adduct was superimposed to a second signal which we attribute to the methylcarboxyl adduct (see Fig. 2). In the absence of UV irradiation of the sample IBDA decomposes very slowly and the spectrum is weak, while direct irradiation of the sample leads to the detection of much stronger signals. It would also appear that UV irradiation facilitates the decarboxylation process (reaction 3), as under this condition the intensity of the spectrum due to the methylcarboxyl adduct becomes vanishingly small. Prolongued irradiation also results in the detection of an additional, three-line spectrum with nitrogen splitting (ca. 7.4 G) and g-factor (2.0068$_9$) typical of an acyl nitroxide.[20]

Four different spin adducts were simultaneously observed when reacting the nitrone **3** with *tert*-butoxyl radical generated either by photolysis of di-*tert*-butyl peroxide or by thermal decomposition of *tert*-butyl hyponitrite. The relative amounts of the different species were different in the two cases, and besides depended markedly on temperature and on the initial concentration of the starting nitrone. Two of the adducts were identified with the *tert*-butoxyl- and the methyl-adduct, the latter identification following the generation of the authentic adduct through the alternative way outlined in reactions (2–6):

$$\mathrm{PhI(O_2CCH_3)_2} \xrightarrow{h\nu} \mathrm{PhI} + 2\,\mathrm{CH_3CO_2}\cdot \qquad (2)$$

$$\mathrm{CH_3CO_2}\cdot \longrightarrow \cdot\mathrm{CH_3} + \mathrm{CO_2} \qquad (3)$$

TABLE II EPR spectral parameters for the spin adducts between nitrone **3** and radicals ***X***.[a]

X	X source	a_N	a_H	a_{other}	g	T/K
CH_3	MeHgMe/hv IBDA/hv	13.60	3.42		2.0060$_2$	298
CH_3CH_2	EtHgEt/hv	13.67	3.29		2.0062$_2$	298
$C_6H_5CH_2$	$PhCH_2HgPhCH_2$/hv	13.95	2.65	0.4 (9H)	2.0061$_9$	298
$NC(CH_3)_2C$	AIBN/hv	13.67	1.74		2.0063$_1$	298
$NCCH_2$	IBDA/$NCCH_2COOH$/hv	13.24	1.28		2.0063$_3$	298
$(CH_3)_3CO$	^{t}BuON=NO^{t}Bu ^{t}BuO-O^{t}Bu/hv	14.40	2.35		2.0062$_1$	328 298
$O_2^{\cdot -}$	KO_2/18-C-6 ether	14.51	2.00		2.0062$_4$	298
$CH_3C(O)O$	IBDA/hv	13.30	1.71		2.0061$_5$	298
CH_3S	MeS-SMe/hv	14.11	2.28	0.4 (9H)	2.0066$_0$	298
$(CH_3)_3CS$	^{t}BuS-S^{t}Bu/hv	14.31	2.64	0.3 (9H)	2.0064$_5$	298
C_6H_5S	PhS-SPh/hv	13.91	1.92	0.4 (9H)	2.0065$_9$	298
	Radical adduct					
$RC(O)N(O\cdot)C(CH_3)_3$		7.40			2.0068$_9$	298
$RCXYN(O\cdot)C(CH_3)_3$		13.6			2.0061$_3$	298

[a] Coupling constants in Gauss = 10^{-4} mT

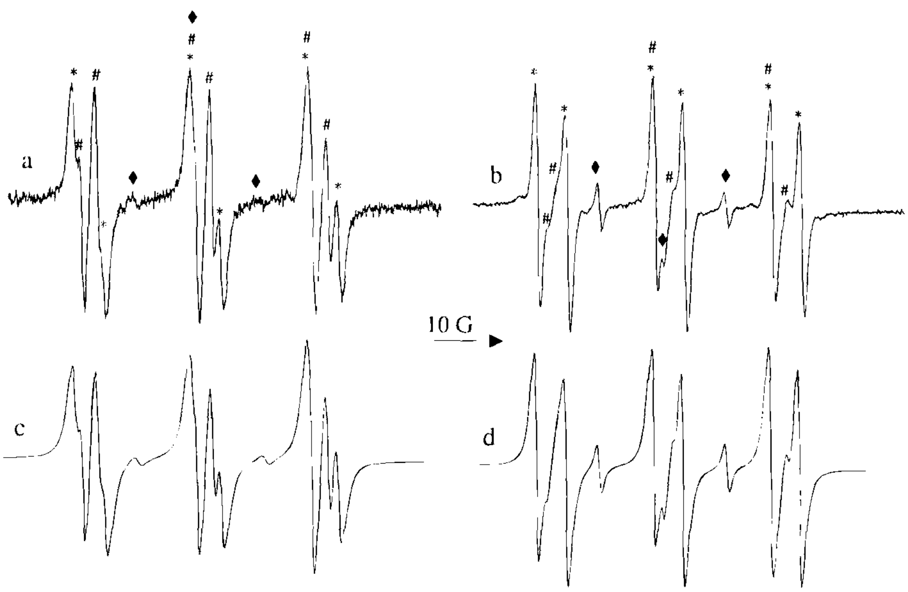


FIGURE 2 Experimental and simulated spectra observed upon reaction of **3** with iodosobenzene diacetate in absence (a, c) and in presence (b, d) of UV irradiation. The lines marked * are due to the methyl adduct, those marked # to the methylcarboxyl adduct, and those marked ◆ to an acyl nitroxide.

$$\cdot CH_3 + \mathbf{3} \longrightarrow \cdot\mathbf{3}^{-}CH_3 \qquad (4)$$

$$CH_3CO_2\cdot + \mathbf{3} \longrightarrow \cdot\mathbf{3}^{-}O_2CCH_3 \qquad (5)$$

The formation of methyl radicals in the evolution of *tert*-butoxyl radical (reaction 6) is a well known process, and in some instances only methyl radicals have been trapped by reacting ${}^{t}BuO\cdot$ radicals with hindered nitrones.[21]

$$(CH_3)_3CO\cdot \longrightarrow \cdot CH_3 + (CH_3)_2CO \qquad (6)$$

While a third adduct was identified as an acylnitroxide similar to that observed by prolongued photolysis of **3** in the presence of IBDA, we identify the fourth species, whose spectrum is a simple 1:1:1 triplet (a_N = 13.6 G), as a nitroxide bearing no hydrogens bound at the carbon α to the nitrogen atom. Although one might hypotesize that such species is formed through disproportionation of either the methyl or the butoxyl adduct, followed by further radical addition to the newly formed nitrone, no definite evidence in this direction is available.

The fact that the same spectra were observed independently of the conditions under which the *tert*-butoxyl radicals were generated, that is either by thermal decomposition of *tert*-butylhyponitrite in the dark or by photodecomposition of di-*tert*-butyl peroxide, may deserve a short comment. Indeed it is known that under the action of visible or UV light spiro[indoline-naphthoxazinic] compounds undergo opening of the oxazinic ring to give the corresponding coloured merocyanines.[1–4] The most plausible explanation of the similarity of the spectra observed under dark and light conditions is that the nitroxidic function is far from the bond that undergoes reversible cleavage in the photochromic process: indeed **3** can be seen as a substituted naphthyl *tert*-butyl nitrone independent of whether the oxazinic ring is closed or open. It seems on the contrary rather unlikely that only the closed form of **3** undergoes radical addition.

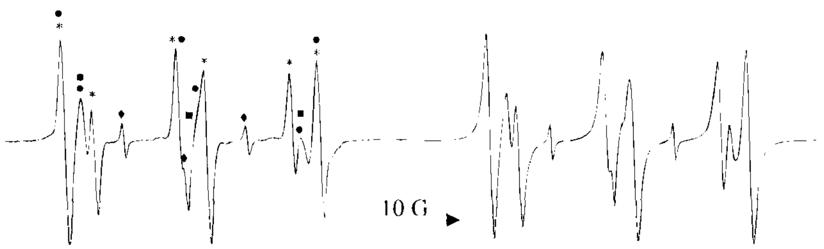


FIGURE 3 Experimental (left) and simulated spectra observed when heating at 328 K a benzene solution of **3** containing some *tert*-butylhyponitrite. The observed spectrum results from the overimposition of four signals due to the methyl adduct (*, 58%), the *t*-butoxy adduct (●, 32%), an acyl nitroxide (◆, 2%), and di-*tert*-alkylnitroxide (■, 8%).

The spectrum of the adduct of **3** with the superoxide radical anion was observed by adding to a benzene solution of the nitrone and the 18-crown-6 ether a small amount of potassium superoxide.[22] In the presence of atmospheric oxygen the signal is weak and poorly resolved, but the spectral parameters are in line with an oxygen centred radicals. Prolongued argon-purging of the solution results in a substantial improvement of the quality of the spectrum, the signal being more intense and resolved than that of the similarly generated superoxide adduct to PBN. The ability of **3** to trap $O_2^{\bullet-}$ is interesting and let foresee a possible use of **3** in biological studies with the obvious restriction to lipophilic systems, the structure of this nitrone making it insoluble in aqueous media.

Acknowledgements

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