

Supporting Information

Nitroxides as building blocks for nanoantioxidants

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The silane nitroxide (8) was synthesized using the procedure already published in literature (ref S1). In a three-neck round-bottom flask 4-carboxy-TEMPO (50 mg, 0.25 mmol) was added to a solution of APTES (58 μ L, 0.25 mmol), EDC-HCl (48 mg, 0.25 mmol), and DMAP (1.2 mg, 0.025 mmol) in dry CH_2Cl_2 (10 mL) at 0°C and the resulting mixture was stirred at room temperature for 48 h. The reaction was monitored by TLC and GC-MS until the starting reagents had disappeared. The reaction mixture was quenched with water and extracted with CH_2Cl_2 (2x50 mL). The organic layers were combined, and the solvent was evaporated by a rotary evaporator. The pale orange oil residue was purified by column chromatography using ethyl acetate as the eluent to give an orange-colored oil (61% yield).

MS (EI, 70 eV) m/z (%): 403 [M⁺], 373 (23), 357 (39), 327 (21), 271 (21), 202 (100), 160 (45), 124 (80), 107 (32), 79 (13). FTIR (KBr): ν = 3320, 2970, 2920, 1650 (C=O), 1550 (NH), 1450 (CH_3), 1380 ($\text{NO}\cdot$), 1325, 1102 (SiO), 1081 cm^{-1} . Elemental analysis calc.d (%) for $\text{C}_{19}\text{H}_{39}\text{N}_2\text{O}_5\text{Si}$ (403.6): C 56.54, H 9.74, N 6.94; found: C 56.79, H 9.85, N 7.05.

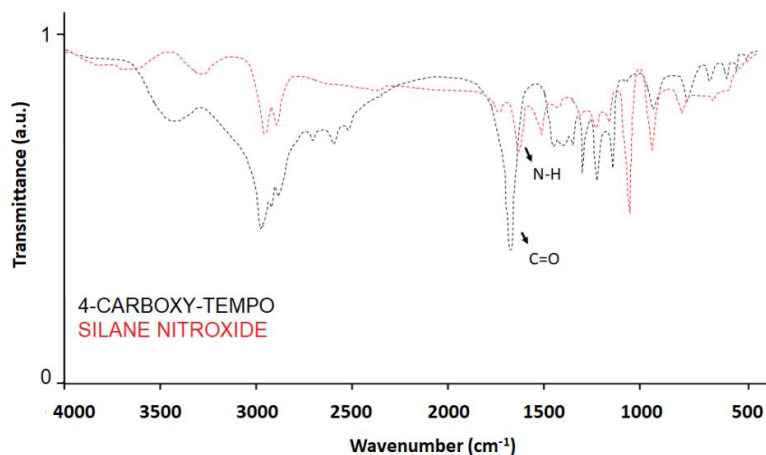


Figure S1. FT-IR spectrum of a KBr pellet of nitroxide **8** (silane nitroxide) and nitroxide **4** (4-carboxy-TEMPO).

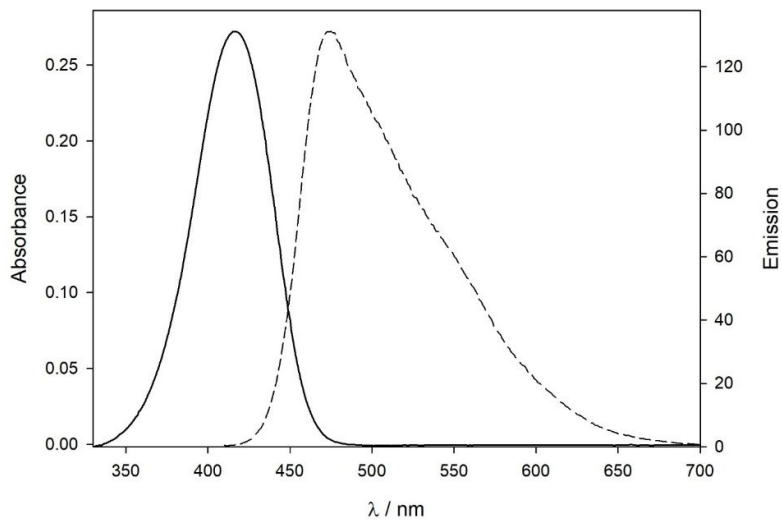


Figure S2. Absorption (continue line) and emission (dashed line, $\lambda_{ex} = 400$ nm) spectra of PluS-NO nanoparticles (2.0×10^{-7} M in H_2O). (Data obtained with a Perkin-Elmer Lambda 45 spectrophotometer and an Edinburgh FLS920 equipped with a photomultiplier Hamamatsu R928P)

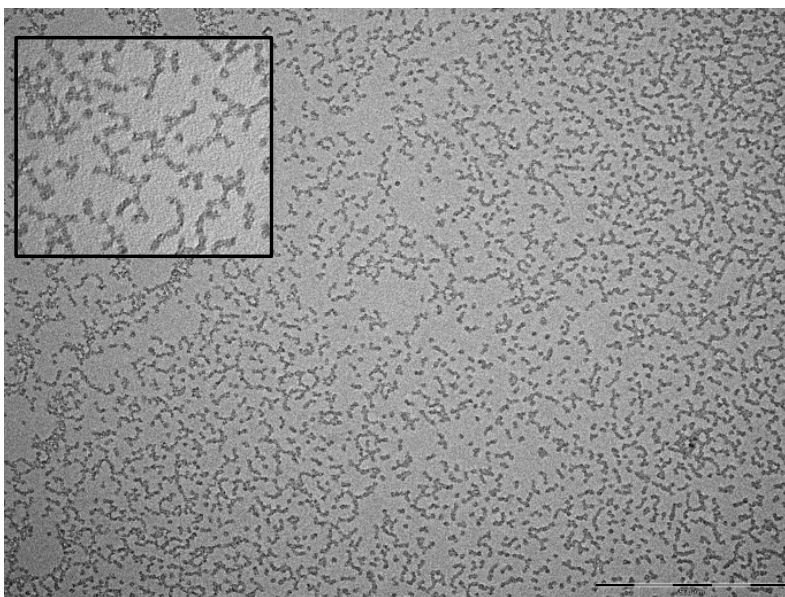


Figure S3. TEM images (magnifications in the inset) of PluS-NO NPs (scale bar 500 nm). Only the dense silica core of diameter = $10 \text{ nm} \pm 1$ can be seen with this technique. (Images taken with a Philips CM 100 TEM operating at 80 kV)

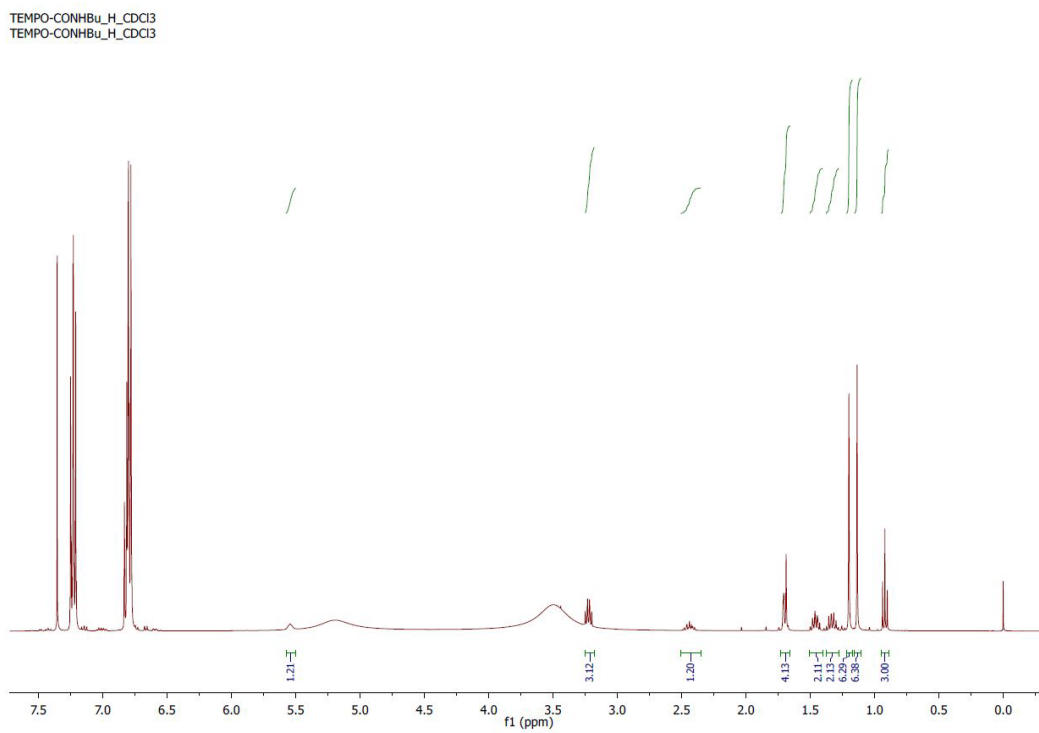


Figure S4. ¹H NMR spectrum of compound **6**

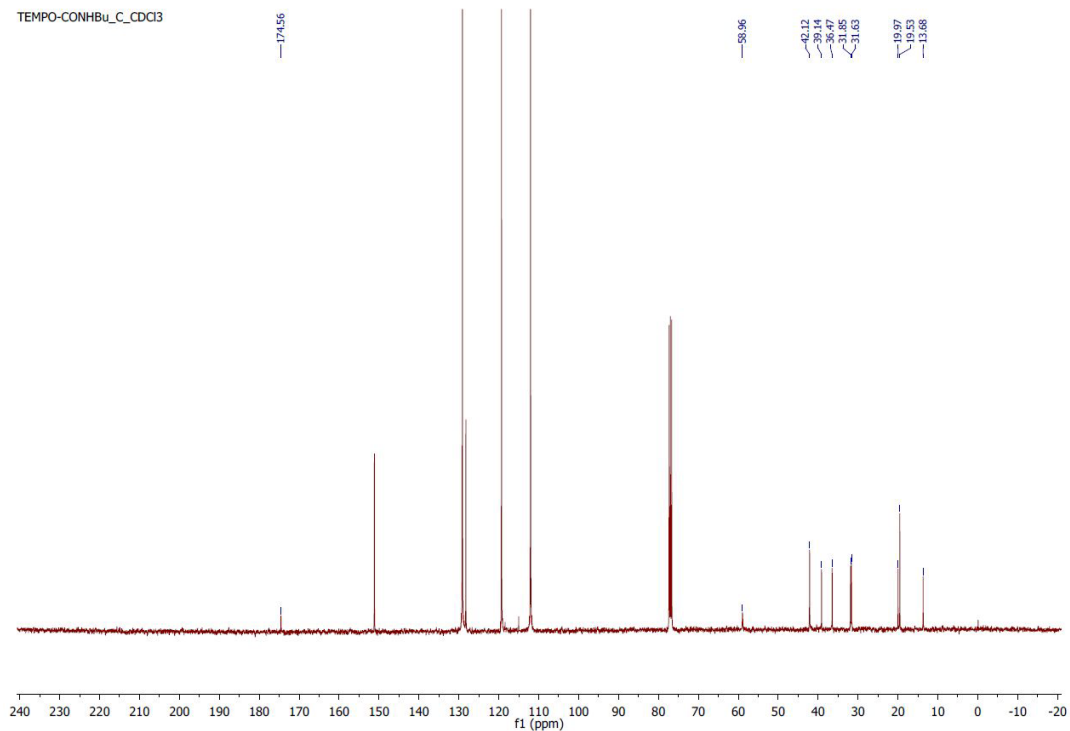


Figure S5. ¹³C NMR spectrum of compound **6**

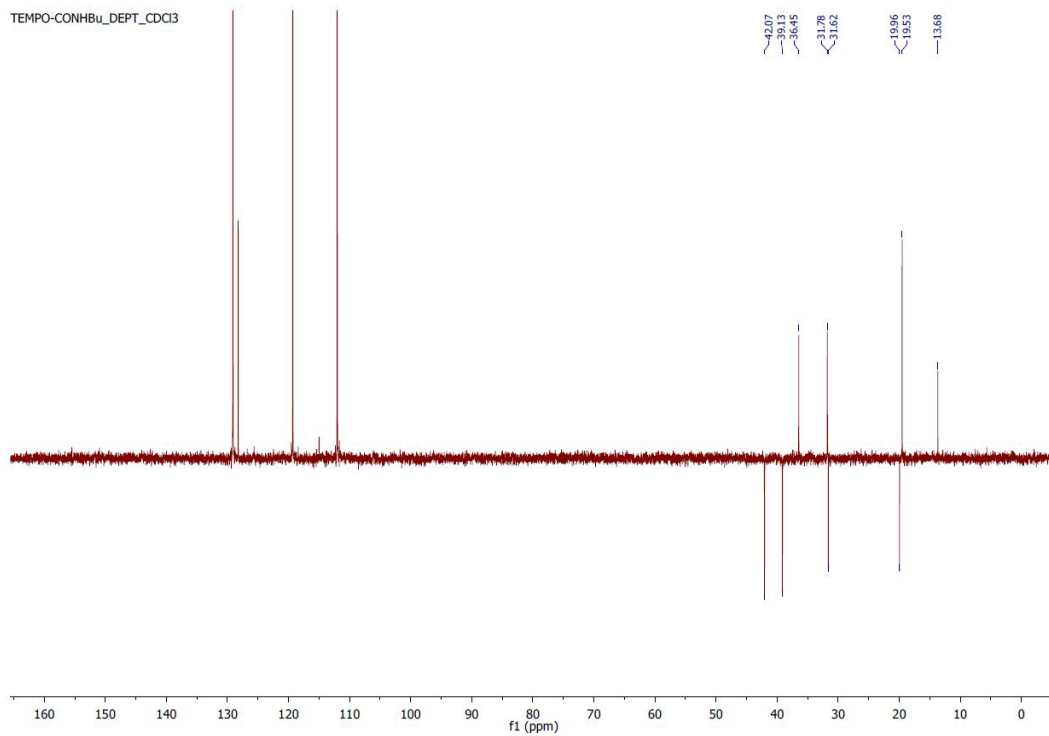


Figure S6. DEPT 135 spectrum of compound 6

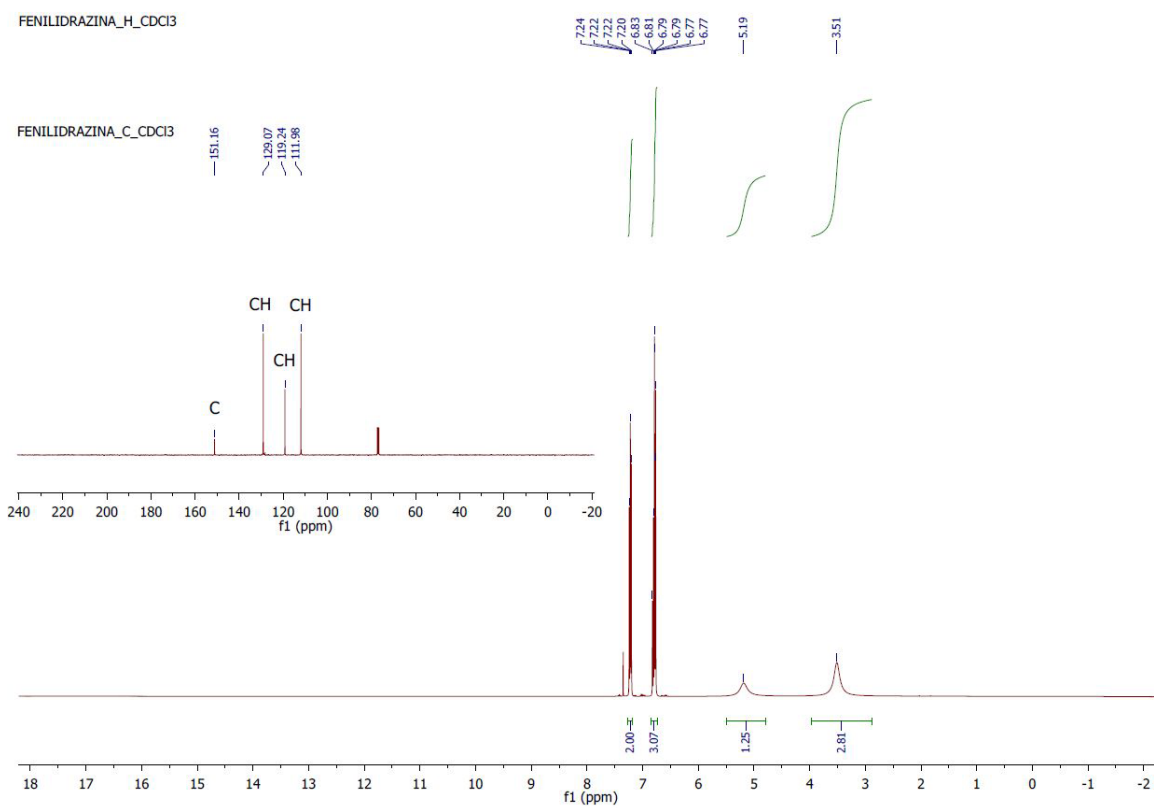


Figure S7. ^1H NMR and ^{13}C NMR spectrum of phenylhydrazine

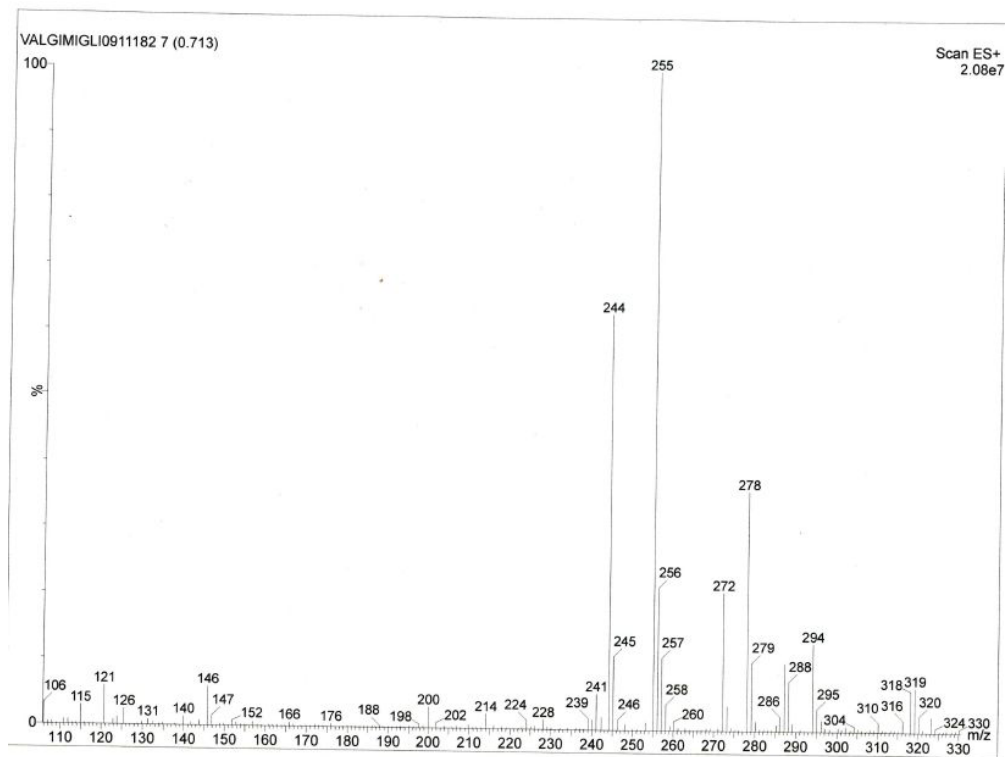
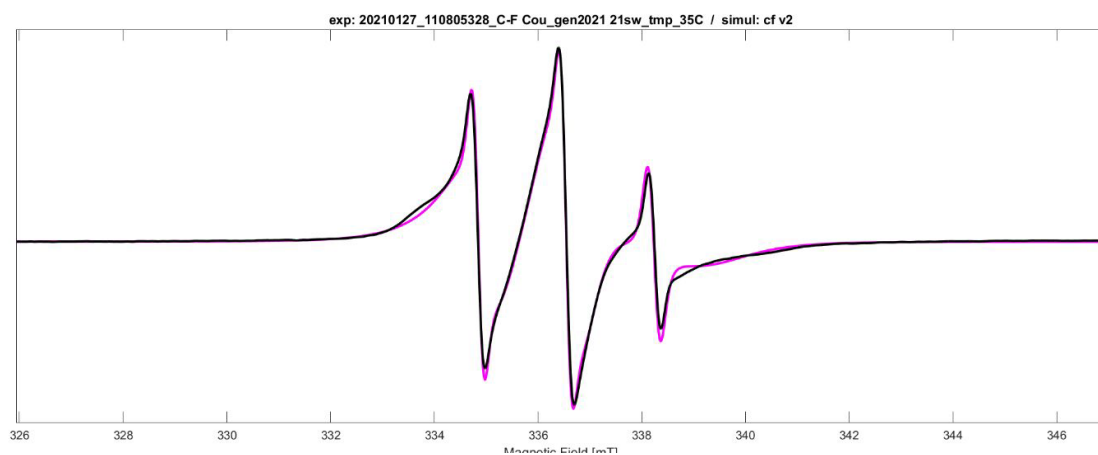


Figure S8. ESI⁺ mass spectrum of compound 6

Numerical fitting of experimental X-band EPR spectra by Simlabel software

- 1) Results of the numerical simulation of the experimental spectrum of Plus-NO (black).
The simulated spectrum contains two components. The first one has a low correlation time and an abundance of 92.6%, and was identified as the bound nitroxide. The second one has a higher correlation time, an abundance of 7.4 %, and was interpreted as a trace of unreacted nitroxide adsorbed on the surface.



To Next

component 1 Include Visible Hidden

weight = 0.12575 (92.6%)

g

2.01123	←	→
2.00104	←	→
2.00340	←	→

Axial $g_{iso} = 2.00522$

A_1

1	0.74 mT	←	→
Axial	0.06 mT	←	→
Axial	3.98 mT	←	→

A_1_iso = 1.59 mT

A_2

↓	←	→
Axial	←	→

A_2_iso = mT

Correlation Time

1.66e-09 s	←	→
5.59e-09 s	←	→
4.64e-09 s	←	→

Aniso. Axial $t_{corr_iso} = 3.96e-09$ s

Broadening

Gaussian: 0.03 mT ← →

Lorentzian: 0.05 mT ← →

To Next

component 2 Include Visible Hidden

weight = 0.009996 (7.4%)

g

2.00611	←	→
2.00746	←	→
2.00244	←	→

Axial $g_{iso} = 2.00533$

A_1

1	0.60 mT	←	→
Axial	0.60 mT	←	→
Axial	3.90 mT	←	→

A_1_iso = 1.70 mT

A_2

↓	←	→
Axial	←	→

A_2_iso = mT

Correlation Time

2.22e-10 s	←	→
←	→	
←	→	

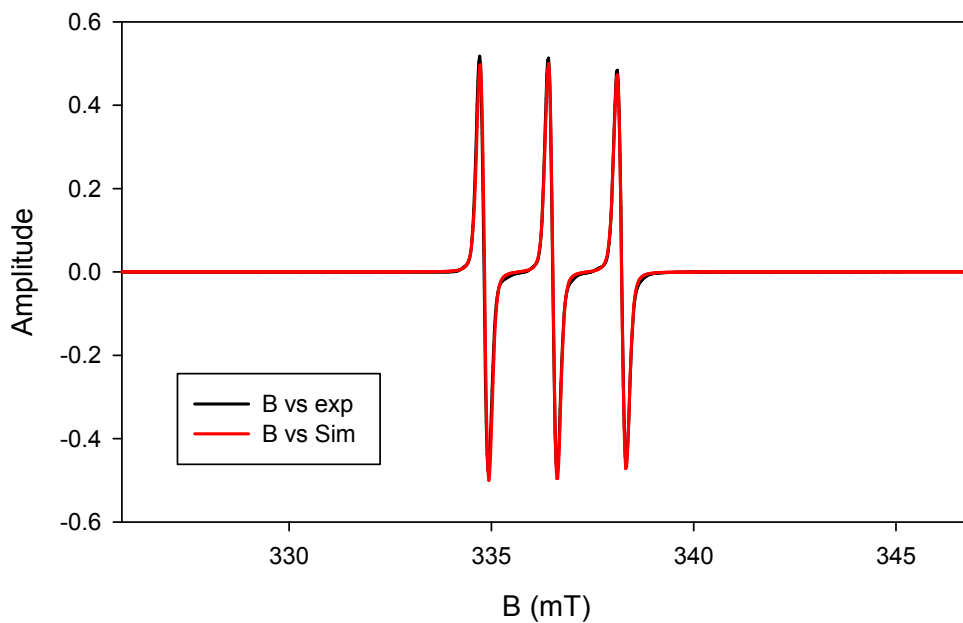
Aniso. Axial $t_{corr_iso} =$ s

Broadening

Gaussian: 0.22 mT ← →

Lorentzian: 0.08 mT ← →

- 2) Results of the numerical simulation of the experimental spectrum of nitroxide **6**. The low correlation time is consistent with a dissolved nitroxide.



Software control panel for the simulation, showing parameters for component 1.

Component 1: Include, Visible, Hidden

Correlation Time: 2.28e-11 s

Broadening: Gaussian: 0.22 mT, Lorentzian: 0.08 mT

g: 2.01121, 2.00262, 2.00238. Axial, $g_{iso} = 2.00540$

A_1: 1, 0.61 mT, 0.61 mT, Axial, 3.88 mT. $A_{1,iso} = 1.70$ mT

A_2: Axial, $A_{2,iso} =$ mT

Numerical simulation of autoxidation of THF inhibited by nitroxides

Table S1. Reaction scheme and rate constants. R• = alkyl radicals, ROO• = peroxy radicals, RH = THF, NO• = nitroxide; NO_x = oxoammonium cation, NOH = hydroxylamine.

Reaction	Rate constant	note
Initiator → R•	$R_i = 1.6e-9 \text{ Ms}^{-1}$	Experimentally determined
$R\bullet + O_2 \rightarrow ROO\bullet$	$k = 4e9 \text{ M}^{-1}\text{s}^{-1}$	Ref S2
$ROO\bullet + RH \rightarrow ROO + R\bullet$	$k = 4.8 \text{ M}^{-1}\text{s}^{-1}$	Ref S3
$ROO\bullet + ROO\bullet \rightarrow \text{Inactive Products}$	$k = 3.3e7 \text{ M}^{-1}\text{s}^{-1}$	Ref S3
$NO\bullet + R\bullet \rightarrow NOR$	<i>fitted</i>	
$NO\bullet + ROO\bullet \rightarrow NO_x + ROOH$	<i>Fitted</i>	
$NO_x + RH \rightarrow NOH + RHox$	<i>Fitted</i>	
$NOH + ROO\bullet \rightarrow NO\bullet + ROOH$	<i>fitted</i>	

Table S2. Results of numerical simulations.

4X-TEMPO	$k(NO\bullet+ROO\bullet) \text{ M}^{-1}\text{s}^{-1}$	$k(NO\bullet+R\bullet) \text{ M}^{-1}\text{s}^{-1}$	$k(NO_x+RH) \text{ M}^{-1}\text{s}^{-1}$	$k(NOH+ROO\bullet) \text{ M}^{-1}\text{s}^{-1}$
H (1)	5.1e6	2.0e11	2e-3	3.8e6
OH (2)	1.1e6	2.7e10	0.01	2.5e6
NH ₂ (3)	5.4e5	1.5e10	0.02	1.0e6
COOH (4)	3.7e5	4.0e10	6e-4	4.3e6
NHCOCH ₃ (5)	1.1e5	2.6e10	0.01	2.3e6
CONHBut (6)	1.9e5	2.7e10	5e-4	4.5e6
=O (7)	5.6e4	1.9e10	3.6e-3	2.0e6
PLUS-NO	1.5e5	1.8e10	2.4e-4	1.2e6

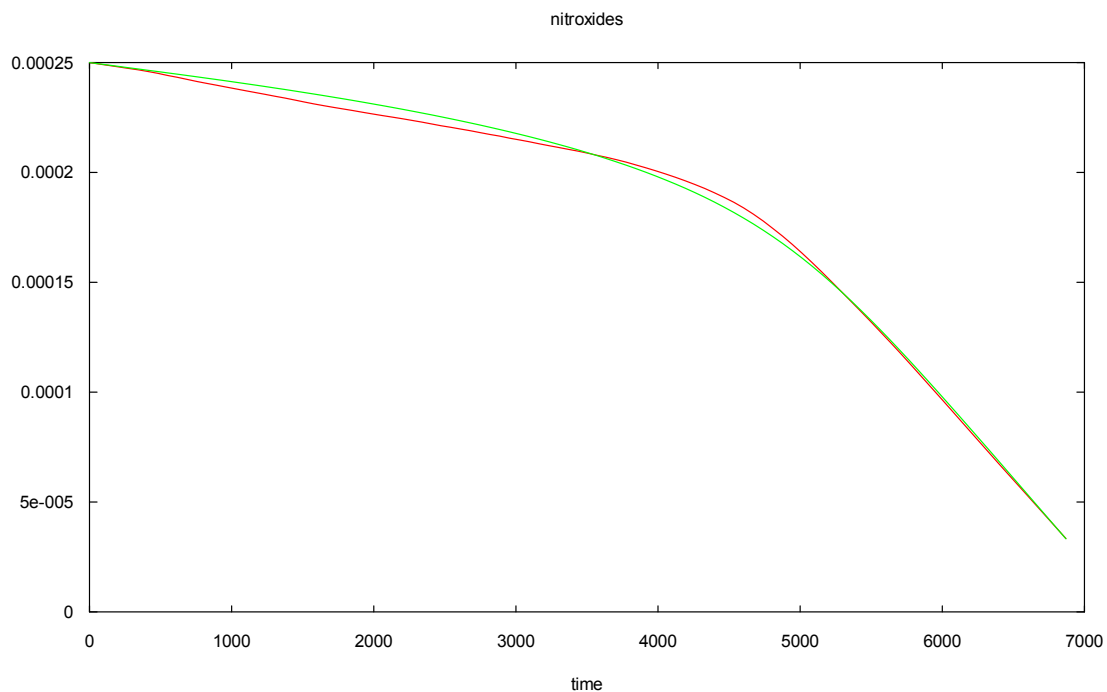


Figure S9. Example of result obtained by the numerical simulation. Autoxidation of THF inhibited by hydroxyl TEMPO (**2**), experimental trace (red) and simulated trace (green). Y-axis: $[O_2]$.

References

- S1 Cicco S. R.; Vona D.; De Giglio E.; Cometa S.; Mattioli-Belmonte M.; Palumbo F.; Ragni R.; Farinola G. M. Chemically Modified Diatoms Biosilica for Bone Cell Growth with Combined Drug-Delivery and Antioxidant Properties. *Chem. Plus. Chem* **2015**, *80*, 1104 –1112.
- S2 Maillard B.; Ingold K. U.; Scaiano J. C. Rate constants for the reactions of free radicals with oxygen in solution. *J. Am. Chem. Soc.* **1983**, *105*, 5095-5099
- S3 Amorati R.; Baschieri A.; Morroni G.; Gambino R.; Valgimigli L. Peroxyl Radical Reactions in Water Solution: A Gym for Proton-Coupled Electron-Transfer Theories. *Chem. Eur. J.* **2016**, *22*, 7924 – 7934