Electronic Supporting Information

NMR signal enhancement > 50000 times in Fast Dissolution Dynamic Nuclear Polarization.

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1. Experimental Section

1.1. Materials and Methods

EPR: EPR spectra were recorded on an X-Band Bruker ELEXYS 500 spectrometer equipped with a TE102 microwave cavity, a Bruker variable temperature unit, a field-frequency (F/F) lock system Bruker ER 033 M and built in an NMR Gaussmeter Bruker ER 035 M. Precaution to avoid undesirable spectra distortion and line broadening, such as those arising from microwave power saturation and magnetic field over modulation, were also taken into account. To avoid dipolar line broadening from dissolved oxygen, solutions were always carefully degassed with Argon.

NMR: ¹H, ¹³C and ³¹P-NMR spectra were recorded on a Bruker AVANCE-III 400 at rt. Chemical shifts are expressed in ppm using deuterated-tabulated solvents as a reference¹ ($\delta_{[CDCI3]} = 7.26$, $\delta_{[D20]} = 4.79$, $\delta_{[CD30D]} = 3.31$). The spectra were analyzed using Mestrenova as an informatics tool.

DNP: DNP polarization was performed using a HyperSense^R DNP polarizer (Oxford Instruments, UK) at 3.35 T and 1.4 K. After polarization, all the samples were fast dissolved into hot methanol and automatically transferred to a 600 MHz NMR spectrometer to perform the corresponding ¹³C NMR measurements. The overall transfer time was 6.5 s (5 s of transfer between DNP and NMR instruments, 1 s of sample stabilization and 500 ms of measurement time). The liquid-state signal enhancement (ϵ) was calculated by the acquisition of a conventional 1D ¹³C NMR experiment with 32 scans and using an excitation flip angle $\theta = 90^{\circ}$, for the thermal equilibrium samples and 1 scan and excitation flip angle $\theta = 10^{\circ}$ the hyperpolarized sample, the hyperpolarized sample was maintained 5 minutes outside the magnet to ensure the complete relaxation.

IR: The infrared spectra were recorded in a Perkin Elmer Spectrum One spectrophotometer with ATR (Attenuated Total Reflectance) system. The scan range was 4000 cm⁻¹ to 650 cm⁻¹.

Mass Spectrometry (MS): The mass spectra have been recorded in a MALDI-TOF Bruker Daltonic and in a micro TOF-Q Hewlett-Packard 5989A.

HPLC: Shimadzu SCL-10A VP. Column: TRACER EXCEL 120 ODSA 5µm.

Thin Layer Chromatography (TLC): The TLC were performed over chromatoplates of silica gel with aluminum support (60F, 0.2 mm, Merk).

Column Chromatography: The purification by column chromatography has been carried out with silica gel (Chromatogel 60 Å CC, 230-400 mesh).

Anhydrous Solvents: Anhydrous CH_2Cl_2 has used directly from MBRAUN MB-SPS 800. Anhydrous THF has distilled over metallic sodium and benzophenone under N_2 (g). Anhydrous pentane has distilled over P_2O_5 under N_2 (g). Anhydrous CHCl₃ has distilled over CaH₂ under N_2 (g).

Anhydrous and inert atmosphere reactions, were carried out inside a heat-gun dried schlenk bottom flask under vacuum, introduced the reagents when the schlenk was cooled to rt, and pump field process was done to avoid air and water in the reaction (cycles of argon and vacuum). Finally, the desired solvent was added by syringe to the schlenk.

Reactions with radical envolved, were carried out inside a dark room equipped with red lamps (wavelength 620–750nm) to avoid radical degradation.

1.2. Synthesis

4-Methoxycarbonylmethylidene-2,2,6,6-tetramethyl-1-piperidyloxyl (1)

1.80 ml of lithium diisopropilamide (1.82 mmol, 1.03 eq) was added to a three-necked oven-dried 100 ml round-bottom ask equipped with a magnetic stir-bar containing 14 ml of anfhydrous THF at -78°C under Ar atmosphere. Then, 307 µl of methyl 2-(trimethylsilyl)acetate (1.82 mmol, 1.03 eq) dissolved in 5 ml of dry THF were slowly added. After the addition was completed, the reaction was maintained at -78 °C for 20 minutes before 0.3 g (1.76 mmol, 1 eq) of 2,2,6,6,-tetramethyl-4-oxo-1-piperidinyloxyl in 5 ml of dry THF were slowly added. After 20 minutes, the mixture was warmed to room temperature. Cold HCl 5% was added to attain a pH of 3-4, and the mixture was extracted with pentane/diethyl ether. The organic phase was dried over anhydrous magnesium sulfate, the solvent was removed under vacuum and the organic red oil

obtained was purified by column chromatography on silica gel eluting with pure hexane to hexane/ethyl acetate 4/1. The pure product was isolated as off orange solid (399 mg, 75%). EPR (THF): g: 2.0058, a_N : 15.5 G, Δ Hpp: 0.86 G. MS (MALDI-TOF, positive mode): m/z 226 [M+H]⁺. Calculated: C₁₂H₂₀NO₃: 226. IR-ATR (cm⁻¹): 1720, 1660.

4-Carboxymethylidene-2,2,6,6-tetramethyl-1-piperidyloxyl (2)

To a solution of 1 g (4.42 mmol, 1 eq) of 4-Methoxycarbonylmethylidene-2,2,6,6tetramethyl-1-piperidiyloxyl (1) in 25 ml of methanol a dissolution of 298 mg (5.3 mmol, 1.2 eq) KOH in 2 ml of water were added. The reaction was warmed at 35-38°C of 6 hours. The progress of hydrolysis was monitored by TLC. Once the reaction was completed, the solvent was removed under vacuum. The solid was solved in water and extracted with dichloromethane.

The aqueous phase was then cooled in an ice bath, and the pH was reduced to 3 with HCl 10%. The solution was then extracted with ether, dried over anhydrous magnesium sulfate, the solvent was removed under vacuum to yield the desired product as a red oil, that eventually solidifies (795 mg, 85%). EPR (THF): *g*: 2.0056, a_N : 15.4 G, Δ Hpp: 1.07 G. MS (MALDI-TOF, positive mode): m/z 212 [M+H]⁺. Calculated: C₁₁H₁₈NO₃.: 212. IR-ATR (cm⁻¹): 1708, 1643.

Both radical TEMPOs, **1** and **2**, show the typical EPR spectrum of three sharp lines from the coupling of the electron with the nitrogen nucleus (I=1), and it should be noted that as they are homosubstituted in the 4-position they show a narrower linewidth (Δ Hpp: 0.86 G and 1.07 G, respectively) than a monoradical with an heterosubstitution, as for example 4-amino-TEMPO, Δ Hpp: 1.56 G.

α-H BDPAesterTEMPO (4) and BDPAesterTEMPO radical (5)

To a 10 ml round-bottom fask equipped with a magnetic stir-bar, 57 mg (269 μ mol, 1.2 eq) of 4-carboxymethylidene-2,2,6,6,-tetramethyl-1-piperidyloxyl (2), 33 mg (269 μ mol, 1.2 eq) of dimethylaminopiridine (DMAP), 56 mg (269 μ mol, 1.2 eq) of N,N'-dicyclohexylcarbodiimide (DCC) and 5 ml of dry dichloromethane were added under Ar atmosphere. The solution was stirred for 10 minutes and then, 0.1 g of 4-((9H-fluoren-9-yl)(9H-fluoren-9-ylidene)methyl)phenyl) methanol (3) (224 μ mol, 1 eq) were added. The mixture was stirred at room temperature for 16 hours under Ar atmosphere.

Afterwards, the mixture was diluted in dichloromethane and washed with water. The organic phase was dried over anhydrous MgSO₄, the solvent was removed under vacuum and the organic solid obtained was purified by flash chromatography on silica gel eluting with mixtures of hexane and ethyl acetate. The monoradical **4** was isolated as off orange powder (79 mg, 46%). MS (MALDI-TOF, positive mode): m/z 642.4 [M]⁺. Calculated: C₄₅H₄₀NO₃: 642.3. IR-ATR (v, cm⁻¹): 2922, 2855, 1733, 1688, 1445, 1150. EPR: *g*: 2.0064, *a*_N: 15.4 G. HPLC: 12.60 min. Column: TRACER EXCEL 120 ODSA 5µm. Solvent: 5% of CHCl₃ in CH₃CN with a flow rate 0.5 mL/min and detection at 254 nm.

The obtained monoradical **4** was treated with 100 µL of 1,8-Diazabicyclo[5.4.0]undec-7-ene (DBU) (672 µmol, 3 eq) in 5 mL of dichlorometane during 1 hour to generate the anion. Then, 448 µL of a 1M solution of AgNO₃ in CH₃CN (448 µmol, 2 eq) was added. The reaction was followed up by UV-Vis. Once the anion was fully converted into radical, the reaction mixture was filtered and the solvent was removed under vacuum. The product was purified by flash chromatography on silica gel with mixtures of hexane and ethyl acetate. HPLC: Peak 1: 12.64 min. (area %: 29.5 monoradical 4); peak 2: 13.64 min. (area %: 70.5 % biradical 5). Column: TRACER EXCEL 120 ODSA 5µm. Solvent: 5% of CHCl₃ in CH₃CN with a flow rate 0.5 mL/min and detection at 254 nm. MS (MALDI-TOF, positive mode): m/z 641.2 [M]⁺. Calculated: C₄₅H₃₉NO₃: 641.3. EPR: g = 2.0041, aH (4H) = 1.0 G, aH (4H) = 0.92 G, aH (4H) = 0.36 G, aH (4H) = 0.23 G, aN = 7.82 G. We realized that after being stored in the freezer for 6 months the EPR intensity signal of sample 5 decreases in 15 %. 2. EPR spectra (Figs. S1 and S2)



Fig. S1. EPR spectra of monoradical precursor 4, monoradical BDPA derived from 3 and sample 5.



Fig. S2. EPR spectrum of the BDPAesterTEMPO sample in black (71 % biradical **5** with 29 % monoradical **4**, marked by asterisks) and the simulation of the biradical species in red.





Fig. S3. HPLC chromatogram of monoradical TEMPO precursor 4. Peak at 12.60 min. A TRACER EXCEL 120 ODSA 5 μ m column was used for the analysis using 5% of CHCl₃ in CH₃CN with a flow rate 0.5 mL/min and detection at 254 nm.

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Fig. S4. HPLC chromatogram of BDPA-ester-TEMPO. Peak 1: 12.64 min. (area %: 29.5 monoradical 4); peak 2: 13.64 min. (area %: 70.5 % biradical 5). A TRACER

EXCEL 120 ODSA 5 μ m column was used for the analysis using 5% of CHCl₃ in CH₃CN with a flow rate 0.5 mL/min and detection at 254 nm.

When we added an amount of monoradical **4** to the sample of biradical **5**, we observed an increase of the peak at 12.62 min. corresponding to the monoradical **4**.



Fig. S5. a) HPLC chromatogram of a mixture of sample 5 with an addition of monoradical TEMPO 4. b) UV/Visible absorption spectra obtained from peaks I and II. A TRACER EXCEL 120 ODSA 5 μ m column was used for the analysis using 5% of CHCl₃ in CH₃CN with a flow rate 0.5 mL/min and detection at 254 nm.

4. EPR integration (Fig. S6)



Fig. S6. EPR signal integration of sample 5 spectrum.

The first isolated peak between 3330-3340 G, which is attributed to the monoradical impurity, is integrated and given the arbitrary value 1.00. The rest of the middle portion, which contains most of the biradical signal and two-thirds of the impurity signal, integrates to 16.66. The smaller integral represents one-third of the impurity's signal because it represents one of the three peaks of the triplet.

Monoradical area: 3

Biradical area: 16.66-2 = 14.66. Each biradical has two spins and therefore gives twice the signal compared to the monoradical impurity. Therefore, to compare on a molar basis the biradical's signal must be divided by 2, giving 7.33.

% Monoradical: 3/3+7.33 * 100 = 29 %

% Biradical: 7.33/3+7.33 * 100 = 71 %

5. Half-field EPR spectrum of biradical 5



Fig. S7. Half-field EPR spectrum of sample BDPAesterTEMPO biradical **5** in dichloromethane:toluene (1:1) at 130 K.

6. ¹³C microwave spectrum and build-up time constants



Fig. S8. ¹³C microwave spectrum of 100 μl sulfolane:[2-¹³C]acetone 1:1 doped with 18 mM of BDPAesterTEMPO (**5**) at 3.35 T and 1.4 K.



Fig. S9. Build-up time constants versus concentration of DPAester-TEMPO biradical 5.

¹ Fulmer, G. R.; Miller, A. J. M.; Sherden, N. H.; Gottlieb, H. E.; Nudelman, A.; Stoltz, B. M.; Bercaw, J. E.; Goldberg, K. I. *Organometallics.*, **2010**, 29, 2176-2179.