Electronic Supplementary Material (ESI) for ChemComm.


Supporting Information for

# Blatter-Type Radicals as Polarizing Agents for Electrochemical Overhauser Dynamic Nuclear Polarization

## Experimental procedures

All chemicals were purchased from Sigma-Aldrich, ABCR, Acros Organics, TCI (Tokyo Chemical Industry Co., Ltd.) or Inochem, Ltd. (Frontier Scientific, Inc) and were used as received. The Blatter-type radicals in this study were synthesized following a reported procedure.[1]

**Synthesis of the Blatter-type radical 1.** Nitron (0.99 g, 16 mmol) was dissolved in MeCN (99 mL) under ambient conditions and deionized water (1 mL) was added. The reaction mixture was stirred for 72h at room temperature under air exposure. After evaporation of the solvent, the crude solid was dissolved in a minimum amount of DCM and purified by column chromatography (eluent: DCM:MeOH 98:2). The dark red fractions were combined and the solvent was evaporated to yield a reddish black solid, which was recrystallized in a minimum amount of ethanol (70 °C) to obtain radical **1** (0.73 g, 70%) as reddish black crystals. HRMS (nanochip-ESI/LTQ-Orbitrap) m/z: $[M]^+$ Calcd for $C_{20}H_{15}N_4O^+$ 327.1240; Found 327.1240. Elemental analysis: Calcd for $C_{20}H_{15}N_4O$: C, 73.38; H, 4.62; N, 17.11. Found: C, 73.29; H, 4.63; N, 16.91.

**Synthesis of the Blatter-type radical 2.** Radical **1** (0.39 g, 1.19 mmol) was suspended in a 1M NaOH solution in MeOH:$H_2O$ (1:1, 40 mL) and the reaction mixture was stirred for 72h at room temperature. The solvent was evaporated and the crude solid was dissolved in DCM (50 mL), washed with 1M HCl (1 x 50 mL), sat. NaHCO3 (1x 50 mL) and water (3 x 50 mL). The organic phase was dried over $Na_2SO_4$, filtered and evaporated. The resulting dark green solid was dissolved in a minimum amount of DCM and purified by column chromatography (eluent: DCM:MeOH 98:2). The dark green fractions were combined and the solvent was evaporated to yield radical **2** (0.27 mg, 75%) as a dark green solid. HRMS (ESI/QTOF) m/z: $[M]^+$ Calcd for $C_{19}H_{15}N_4^+$ 299.1291; Found 299.1299. Elemental analysis: Calcd for $C_{19}H_{15}N_4$: C, 76.23; H, 5.05; N, 18.72. Found: C, 75.56; H, 5.07; N, 18.19.

**Electrochemical experiments**. 1 mM of radical was used with 0.1 M tetrabutylammonium perchlorate (TBAP) as a supporting electrolyte in dry acetonitrile (MeCN) for each solution. The experiments were performed in a glove box and recorded against an organic $Ag/Ag^+$ reference electrode, consisting in a Ag wire immersed in 10 mM $AgNO_3$ + 0.2 M TBAP in dry acetonitrile. This inner filling solution was separated from the sample solution by a ceramic frit. 3 mm diameter glassy carbon disc acted as a working electrode and Pt coil as a counter electrode in a one-compartment cell. The potentiostat was Gamry 1010E interface. All the samples were prepared in the glove box and used immediately after preparation. Before each experiment, the glassy carbon working electrode was polished on 0.05 µm alumina, then rinsed and sonicated 5 sec in milli-Q water before drying with $N_2$.

**DNP and NMR experiments.** The B magnetic field of 0.295 T was generated with a Varian electromagnet. The microwave irradiation setup was composed of a microwave source Signal Generator Vaunix LMS-123, a 200 Watt traveling wave tube amplifier, a high frequency circulator and a high-power resistance to prevent damage. The EPR resonator was a sapphire tube. The NMR signal was carried out with a home-made setup composed of a pulse generator PulseBlaster Spincore, a PTS 620 frequency synthesizer, a TOMCO RF Pulse Amplifier, a digitizer Gage Applied RazorMax, and a home-made spectrometer. The tuning and matching (T&M) trimmer capacitors (NMTIM120CEK, Municom) were located out of the sample space in an aluminium box. The NMR coil is located into the dielectric resonator. The sample space (EPR resonator and NMR coil) was shielded with a copper cavity. The $^{1}$H relaxation rate of Radical **1**, radical **2** and TEMPOL in MeCN were measured at 12.5 MHz with saturation recovery pulse sequence. The electrochemical cell in the DNP experiments was a 2.41 mm ID glass tube. The radical **1** in 50 mM concentration served as a polarization source in MeCN with 50 mM tetrabutylammonium hexafluorophosphate (TBAHFP) as a supporting electrolyte. A two-electrode configuration was used with Pt coil acted as a working electrode and a Pt mesh as a counter electrode/reference electrode. The radical was oxidized to a diamagnetic form by chronopotentiometry with anodic currents between 100 and 200 μA. To regenerate the radical, cathodic currents with equal magnitudes were employed.

**EPR characterization.** The EPR spectra of radical **1**, radical **2** and TEMPOL in MeCN were measured with a Bruker EMX nano benchtop EPR spectrometer inside a 3 mm inner diameter borosilicate tube.

## Electrochemical characterization

**Assessment of the diffusion limited process.** The peak current of a cyclic voltammogram increases linearly with a square root of scan rate for electrochemically reversible redox species that diffuses freely to the electrode surface. Figure S1 shows peak current densities vs the square root (sqrt) of scan rate for radical **1** (top), radical **2** (middle) and TEMPOL (**3**, bottom). For radicals **1** and **2,** the two graphs show the behavior whether the radical is initially oxidized (left panel) or reduced (right panel). The individual markers represent the experimental data, while the solid lines show the linear fit to the data. $R^2$ values are provided to show the quality of the fit for anodic ($i_P$ Anodic) and cathodic ($i_P$ Cathodic) processes. All results were obtained with a glassy carbon working electrode, 1 mM radical concentration in dry MeCN with 0.1 M TBAP as a supporting electrolyte and against a $Ag/Ag^+$ reference electrode. For the radical **1** all peak currents scale perfectly against the square root of scan rate, whether the radical is oxidized or reduced initially with $R^2$ values of at least 0.9990. For radical **2** the anodic peak currents have an equal linearity, with the cathodic peak currents suffering only slightly worse fit qualities. The lowest quality of the fit was observed for TEMPOL, with initial oxidation peak currents having a fit quality of 0.987 and the following reduction 0.978. Thus, all of the radicals

under study display perfect diffusion limited behavior, or close to it. This is in contrast when compared to the behaviour observed by Grant et. al. where especially the CV for radical **2** reduction showed considerable irreversibility (SI, figure 7) at Pt working electrode. Our results were observed with glassy carbon, which could be an obvious explanation to observed differences in the behaviour.

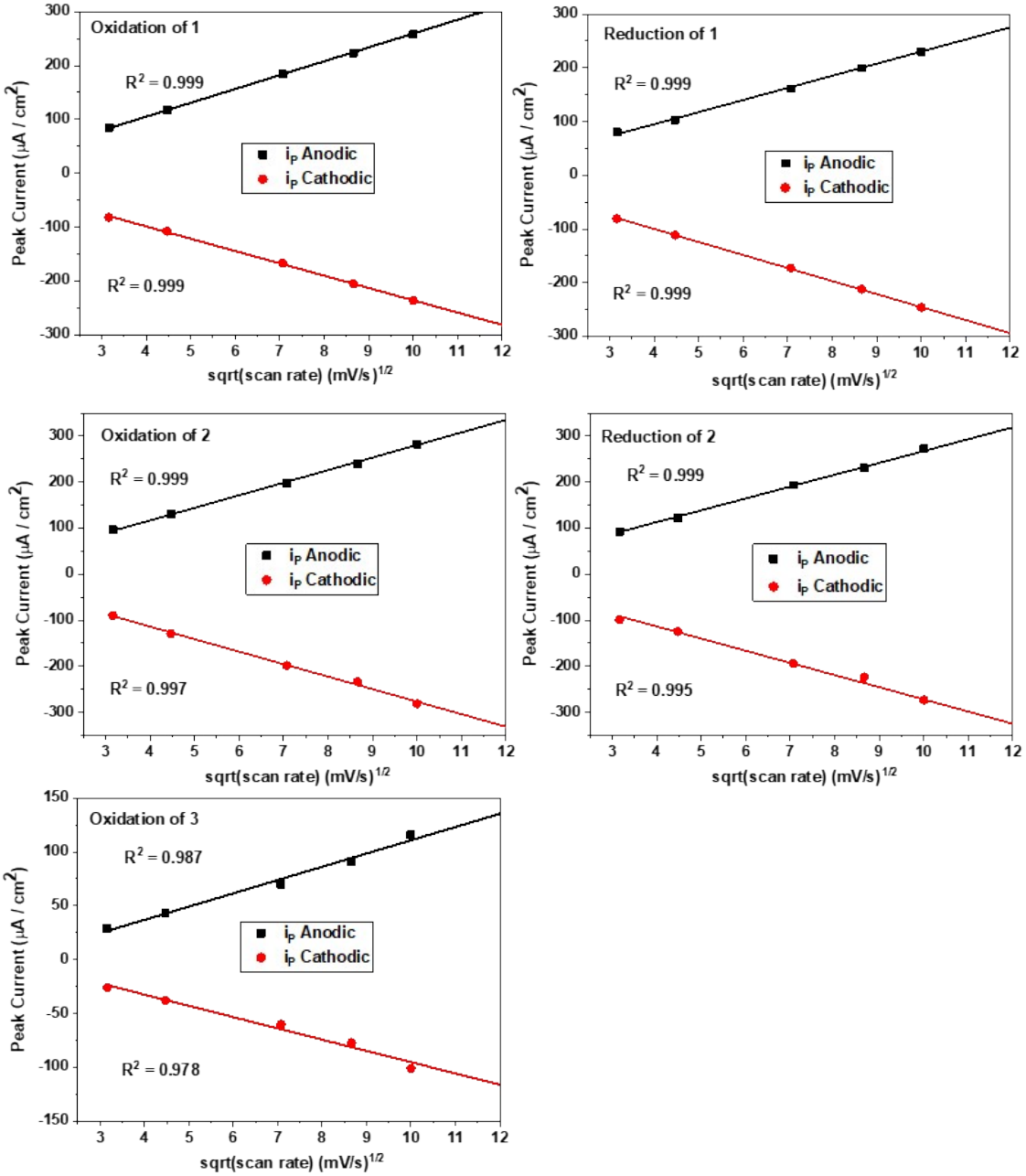


**Figure S1:** Peak anodic and cathodic currents vs square root of scan rate for radical **1** (top row), radical **2** (middle row) and TEMPOL (**3**, bottom). The left-hand side shows the results when the radical is initially oxidized, and the right-hand side when it is reduced. Circles and squares represent the experimental data and the solid lines show the quality of the linear fits.

| | **Radical 1** | | | | | |
|---|---|---|---|---|---|---|
| | **Oxidation** | | | | | |
| | sqrt rate $(mV/s)^{1/2}$ | iP Anodic (uA) | iP Cathodic (uA) | Ratio iPs | dEp (mV) | E0' vs Ag/Ag+ (V) |
| | 3.16 | 84.87 | -82.04 | 1.03 | 73.00 | 0.029 |
| | 4.47 | 117.40 | -107.50 | 1.09 | 70.00 | 0.030 |
| | 7.07 | 183.88 | -166.90 | 1.10 | 68.00 | 0.029 |
| | 8.66 | 223.48 | -205.09 | 1.09 | 69.00 | 0.029 |
| | 10.00 | 257.43 | -236.21 | 1.09 | 67.00 | 0.030 |
| AVG | | | | 1.08 | 69.40 | 0.029 |
| STD(sample) | | | | 0.03 | 2.30 | 0.001 |
| | | | | | | |
| | **Reduction** | | | | | |
| | sqrt rate $(mV/s)^{1/2}$ | iP Anodic (uA) | iP Cathodic (uA) | Ratio iPs | dEp (mV) | E0' vs Ag/Ag+ (V) |
| | 3.16 | -80.62 | 80.62 | 1.00 | 73.00 | -0.934 |
| | 4.47 | -111.74 | 103.25 | 0.92 | 70.00 | -0.934 |
| | 7.07 | -172.56 | 161.24 | 0.93 | 70.00 | -0.933 |
| | 8.66 | -212.16 | 199.43 | 0.94 | 68.00 | -0.932 |
| | 10.00 | -246.11 | 230.55 | 0.94 | 69.00 | -0.933 |
| AVG | | | | 0.95 | 70.00 | -0.933 |
| STD(sample) | | | | 0.03 | 1.87 | 0.001 |
| | | | | | | |
| | **Radical 2** | | | | | |
| | **Oxidation** | | | | | |
| | sqrt rate $(mV/s)^{1/2}$ | iP Anodic (uA) | iP Cathodic (uA) | Ratio iPs | dEp (mV) | E0' vs Ag/Ag+ (V) |
| | 3.16 | 96.89 | -89.67 | 1.08 | 77.00 | -0.122 |
| | 4.47 | 130.69 | -129.28 | 1.01 | 73.00 | -0.122 |
| | 7.07 | 198.02 | -198.02 | 1.00 | 70.00 | -0.118 |
| | 8.66 | 239.04 | -233.38 | 1.02 | 72.00 | -0.118 |
| | 10.00 | 282.89 | -281.47 | 1.01 | 68.00 | -0.114 |
| AVG | | | | 1.02 | 72.00 | -0.119 |
| STD(sample) | | | | 0.03 | 3.39 | 0.003 |
| | | | | | | |
| | **Reduction** | | | | | |
| | sqrt rate $(mV/s)^{1/2}$ | iP Anodic (uA) | iP Cathodic (uA) | Ratio iPs | dEp (mV) | E0' vs Ag/Ag+ (V) |
| | 3.16 | -99.01 | 91.94 | 0.93 | 79.00 | -1.032 |
| | 4.47 | -124.47 | 123.06 | 0.99 | 73.00 | -1.028 |
| | 7.07 | -193.78 | 193.78 | 1.00 | 74.00 | -1.024 |
| | 8.66 | -223.48 | 230.55 | 1.03 | 75.00 | -1.020 |
| | 10.00 | -272.98 | 272.98 | 1.00 | 70.00 | -1.021 |
| | | | | 0.99 | 74.20 | -1.025 |
| | | | | 0.04 | 3.27 | 0.005 |
| | **TEMPOL** | | | | | |
| | **Oxidation** | | | | | |
| | sqrt rate $(mV/s)^{1/2}$ | iP Anodic (uA) | iP Cathodic (uA) | Ratio iPs | dEp (mV) | E0' vs Ag/Ag+ (V) |
| | 3.16 | 29.00 | -26.00 | 1.12 | 82.00 | |
| | 4.47 | 43.00 | -38.00 | 1.13 | 76.00 | 0.470 |
| | 7.07 | 70.00 | -60.00 | 1.17 | 73.00 | 0.475 |
| | 8.66 | 91.00 | -77.00 | 1.18 | 74.00 | 0.479 |
| | 10.00 | 116.00 | -101.00 | 1.15 | 73.00 | 0.489 |
| AVG | | | | 1.15 | 75.60 | 0.478 |
| STD(sample) | | | | 0.03 | 3.78 | 0.008 |

**Table S1:** Electrochemical data for each redox mediator and for each process used to construct Table 1.

**Diffusion coefficients.** From a steady state current equation $i_{ss} = 4nFaDC$ where *n* is the number of electrons transferred, *F* is a Faraday constant, *a* is the radius of the disc, *C* the concentration of the redox mediator the diffusion coefficient *D* can be determined. The diffusion coefficients were $1.7\times10^{-5}$ $cm^2s^{-1}$ and $7.3\times10^{-6}$ $cm^2s^{-1}$ for **1** and **3**, respectively. A small pre-peak was observed for **1**, indicated by the arrow in Figure S1. The origin of this pre-peak could be due to a reduction of an impurity, or adsorption of the impurity/mediator to the Pt surface at the onset of the reduction.

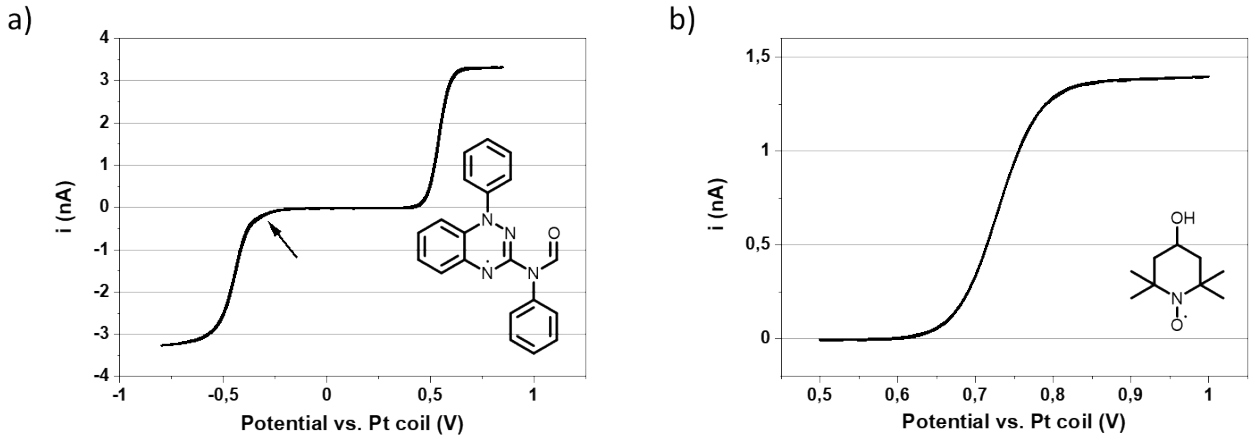


**Figure S2:** Steady state currents for a) Blatter radical **1** and b) TEMPOL (**3**). The steady state currents were measured at a 10 µm diameter Pt disc for 1 mM mediator concentration in dry acetonitrile with 0.1 M TBAP as a supporting electrolyte. A Pt coil served as a reference electrode. The steady state currents were observed to be 3.3 nA and 1.4 nA for **1** and **3**, respectively. The arrow indicates a pre-peak.

**Non-reversibility of TEMPOL reduction.**

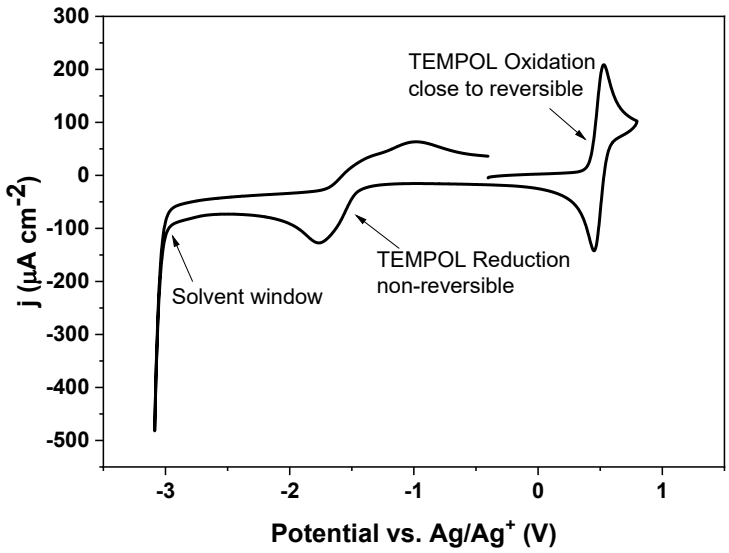


**Figure S3:** CV behavior for TEMPOL (**3**) for the oxidation and reduction of the radical. The CV was recorded in a glove box with a glassy carbon working electrode (vs. $Ag/Ag^{+}$) using a solution of the TEMPOL (**3**, 2 mM) in dry MeCN, with 0.1 M TBAP as supporting electrolyte and a scan rate of 50 mV/s.

## Mass spectra

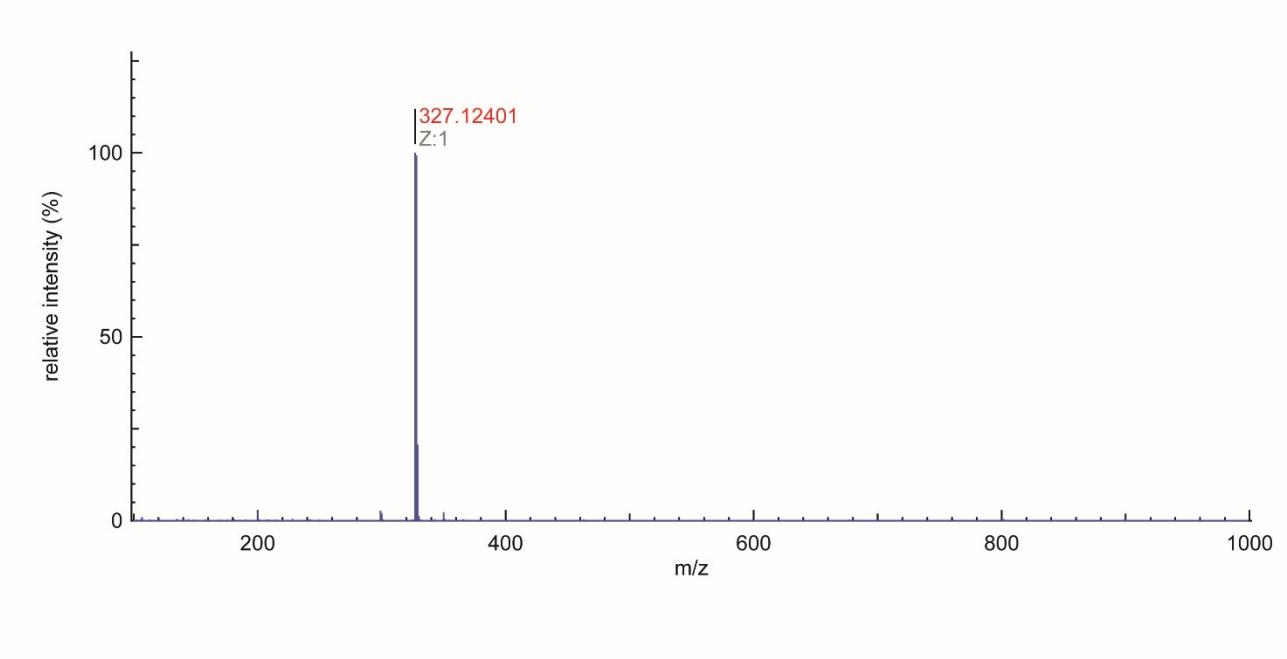


**Figure S4:** Mass spectrum of radical **1**.

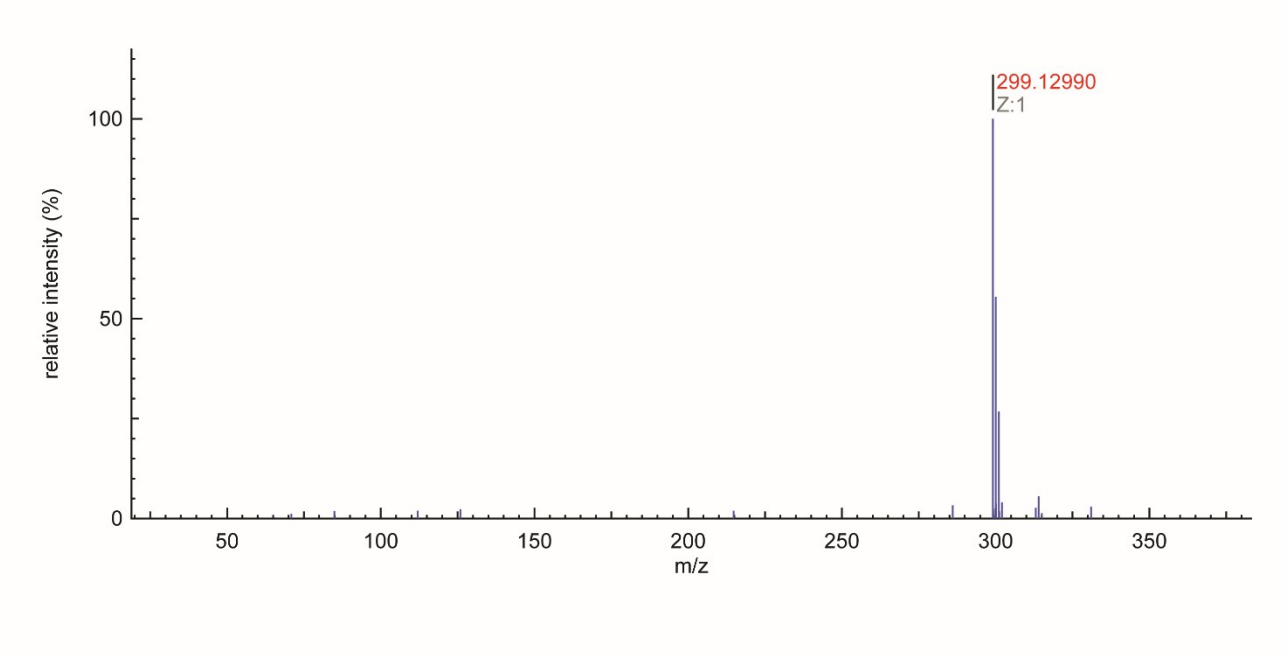


**Figure S5:** Mass spectrum of radical **2**.

## EPR spectra

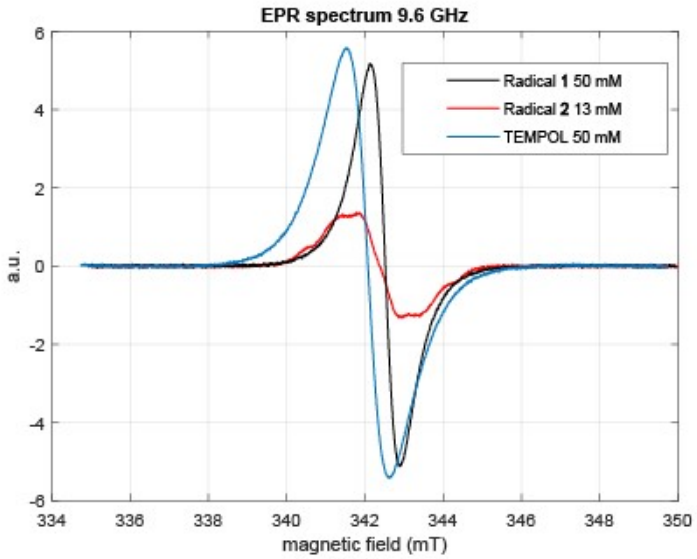


**Figure S6:** EPR spectra of Radical **1** (50 mM), Radical **2** (13 mM) and TEMPOL (**3**, 50 mM) in dry MeCN, respectively.

## NMR relaxation

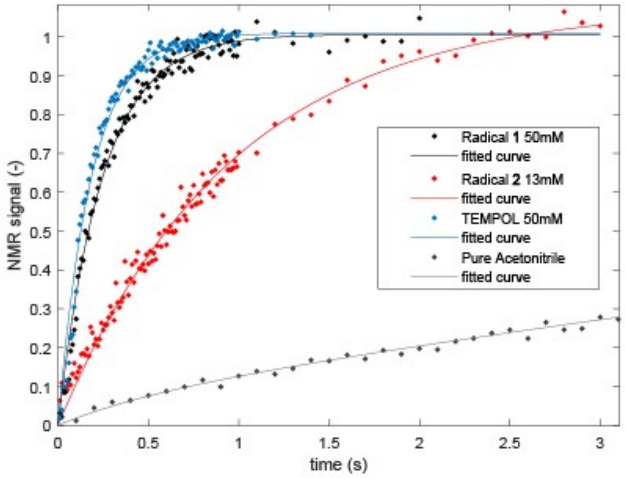


**Figure S7:** Saturation recovery of Radical **1** (50 mM), Radical **2** (13 mM), TEMPOL (**3**, 50 mM) in dry MeCN and pure, dry MeCN, respectively.

| | Radical **1** (50 mM) | Radical **2** (13 mM) | TEMPOL (50 mM) | MeCN |
|---|---|---|---|---|
| $T_1$ | 0.25 ± 0.01 | 0.96 ± 0.04 | 0.18 ± 0.01 | 11.90 ± 0.39 |
| Leakage factor | 0.98 ± 0.07 | 0.92 ± 0.07 | 0.99 ± 0.07 | - |

**Table S2:** $T_1$ values for each radical and MeCN and leakage factor values.for each radical. The $T_1$ values were extracted from fitting the saturation recovery (Figure S7) and the leakage factor values were calculated using a reported method.[2]

## Saturation power

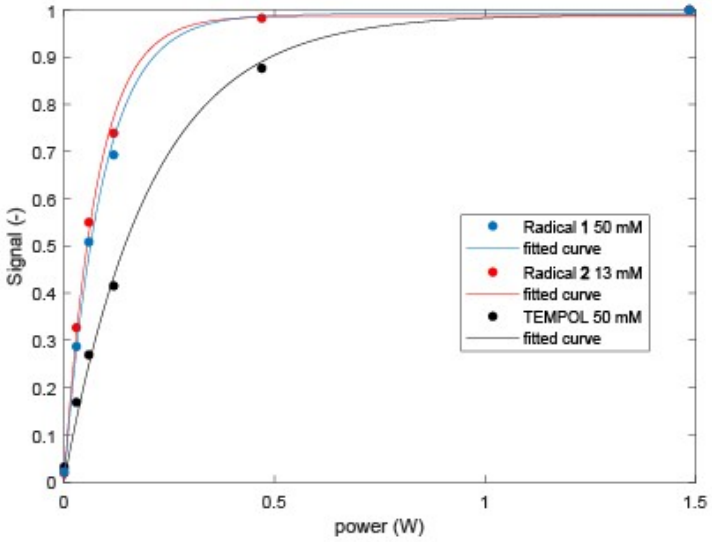


**Figure S8:** Saturation behaviour of Radical **1** (50 mM), Radical **2** (13 mM) and TEMPOL (**3**, 50 mM) in dry MeCN, respectively.

## Supplementary references

1. J. A. Grant, Z. Lu, D. E. Tucker, B. M. Hockin, D. S. Yufit, M. A. Fox, R. Kataky, V. Chechik and A. C. O'Donoghue, *Nat. Commun.*, 2017, **8**, 15088.

2. Ravera, C. Luchinat and G. Parigi, *J. Magn. Reson.*, 2016, **264**, 78–87.