Electronic Supplementary Material (ESI) for RSC Advances

Electronic Supplementary Information

The efficiency of DPPH as a polarising agent for DNP-NMR spectroscopy

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I. W-band ESR spectra of BDPA, DPPH, and 4-oxo-TEMPO at 100 K

As mentioned in the main text, the ESR properties of the free radicals are crucial elements to the DNP process.[1] As such, we have measured the ESR spectra of the free radicals discussed in this work. Fig. S1 displays the W-band ESR spectra of (a) 1,3-bisdiphenylene-2-phenylallyl (BDPA; 20 mM in 1:1 v/v sulfolane:DMSO) , (b) 2,2-diphenyl-1-pycrylhydrazyl (DPPH; 20 mM in 1:1 v/v sulfolane:DMSO), and (c) 4-oxo-2,2,6,6-tetramethylpiperidine-1-oxyl (4-oxo-TEMPO; 15 mM in 1:1 glycerol:water) measured at 100 K. It is evident that the DPPH base to base linewidth *D* (290 MHz) is intermediate between that of BDPA (62 MHz) and 4-oxo-TEMPO (465 MHz). The ESR spectra of the N-centered DPPH and the nitroxide-based 4-oxo-TEMPO show similar features due to the hyperfine interaction of the paramagnetic electron with the quadrupolar ^{14}N nuclei. These data at 100 K should reflect the same features of the ESR spectra at DNP conditions (1.4 K).

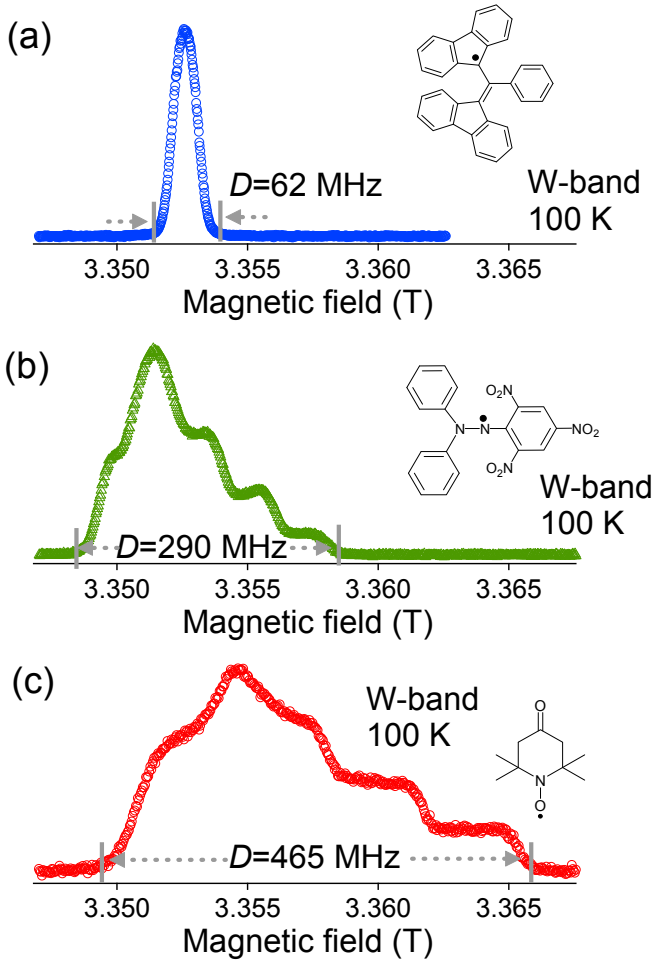

Fig. S1 W-band ESR spectra of (a) BDPA (20 mM in 1:1 v/v sulfolane:DMSO), (b) DPPH (20 mM in 1:1 v/v sulfolane:DMSO), and (c) 4-oxo-TEMPO (15 mM in 1:1 v/v glycerol:water) measured at 100 K. The insets are the corresponding structures of the free radicals.

II. DPPH electronic magnetisation recovery fitting curves

Fig. S2 shows the W-band electronic magnetisation recovery curves for 20 mM DPPH at (a) 100 K and (b) 5 K. These relaxation data were fitted to different exponential recovery equations to extract the electron spin-lattice relaxation time T_{1e}: (i) Single exponential equation $M_z(t)=M_0[1-\exp(-t/T_{1e})]$, (ii) stretched exponential equation $M_z(t)=M_0[1-\exp(-(t/T_{1e})^{\beta})]$ where the exponent β is the "stretching" parameter, and (iii) double exponential equation $M_z(t)=M_0[1-\exp(-t/T_{1e})-\exp(-t/T_{cr})]$ where the longer relaxation component gives the T_{1e} value and the shorter component T_{cr} is ascribed to cross relaxation effects.[2] At 100 K, the stretched (T_{1e}=0.7783 ms with β=0.64) and double (T_{1e}=1.87 ms with T_{cr}=0.31 ms) exponential recovery equations give excellent fits with the data in Fig. S2a whereas the single exponential equation gave a sufficiently good fit with T_{1e}=1.13 ms. However at 5 K, it is evident that a single exponential equation is incompatible with the data. The stretched exponential equations yielded a good fit with the 5 K data which T_{1e}=21 ms but the stretching parameter dropped from 0.64 to 0.24. The double exponential equation gave the best fit to the 5 K data with T_{1e}=30.1 ms and T_{cr}=0.43 ms. This type of relaxation behaviour (bi-exponential electronic magnetisation recovery curve) was also observed in TEMPO (40 mM) at high fields where cross relaxation effects become evident at such relatively high concentration of free radicals.[2]

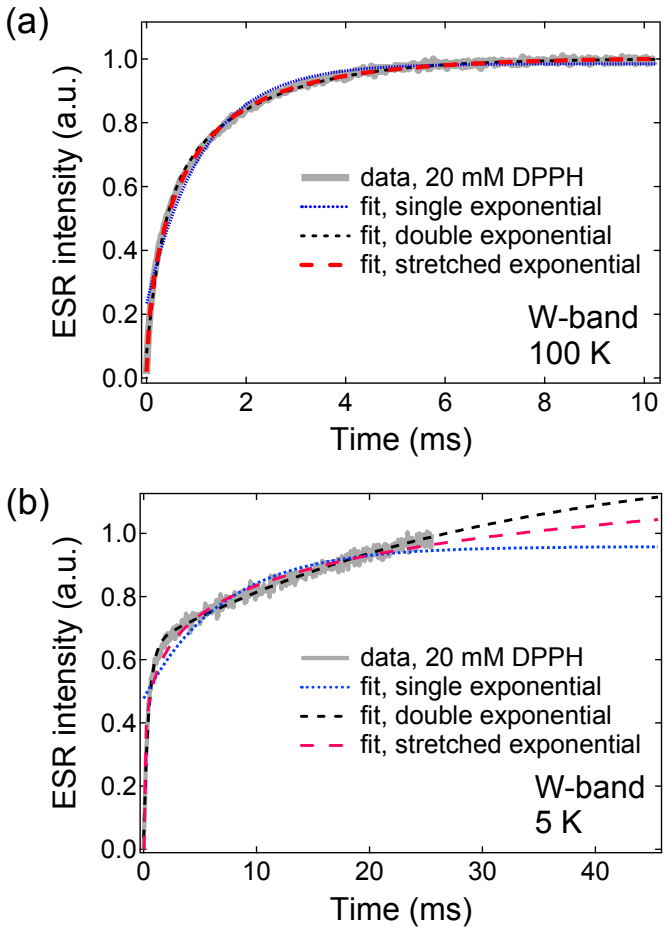

Fig S2 Recovery curve of the electron magnetisation of 20 mM DPPH in 1:1 sulfolane:DMSO taken at W-band and 5 K. The dashed lines are fits to the data.

III. W-band electronic relaxation of BDPA

The W-band electronic magnetisation recovery curves of BDPA (20 mM in 1:1 v/v sulfolane:DMSO), shown in Fig. S3, were traced by saturation recovery technique. Similar to the fitting procedure used for DPPH, a single exponential recovery equation did not yield an appropriate fit especially at low temperatures; a double exponential recovery equation was found to be more appropriate where the longer component gives the T_{1e} value as discussed before. Since the concentration and glassing conditions were the same for both BDPA and DPPH ESR samples, a direct comparison can be made. BDPA has longer electronic T_{1e}'s than DPPH, with T_{1e}=21.8 ms at 100 K and T_{1e}=176 ms at 5 K as shown in Fig. S3; DPPH T_{1e}=1.87 ms at 100 K and T_{1e}=30.1 ms at 5 K as illustrated in Fig. S2. This can be qualitatively ascribed to the less g-anisotropy and hyperfine interaction relaxation contribution in BDPA than DPPH.

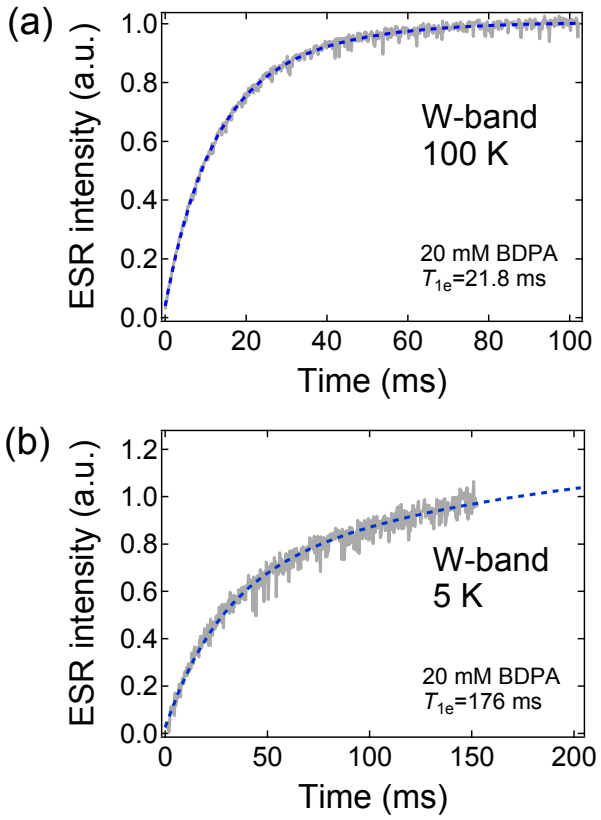

Fig. S3 W-band electronic magnetisation recovery curves of 20 mM BDPA in 1:1 v/v sulfolane:DMSO measured at (a) 100 K and (b) 5 K. The dashed lines are fits to a double exponential recovery equation where the longer component as described previously.

IV. Optimisation of DPPH concentration for DNP

Fig. S4a shows the representative ^{13}C polarisation buildup curves of 1:1 [1-^{13}C]ethyl pyruvate:sulfolane doped with the optimum DPPH concentration (20 mM or 40 mM) for DNP at 3.35 T and 1.4 K. A maximum polarisation of ~5 % was achieved for the optimum DPPH-doped sample, whereas the same sample doped with BDPA yielded a ^{13}C polarisation of 11 %. As mentioned in the main text, the higher polarisation achieved with BDPA is a consequence of its small ESR linewidth *D*, which implies that a lower spin temperature of the electron dipolar system can be achieved with DNP via thermal mixing, thus resulting in "colder" spin temperature (higher polarisation) of the nuclear Zeeman system.[1,3] Fig. S4b displays the plot of the dependence of the ^{13}C polarisation with DPPH concentration where it can be seen that the polarisation is maximum in the concentration range 20-40 mM.

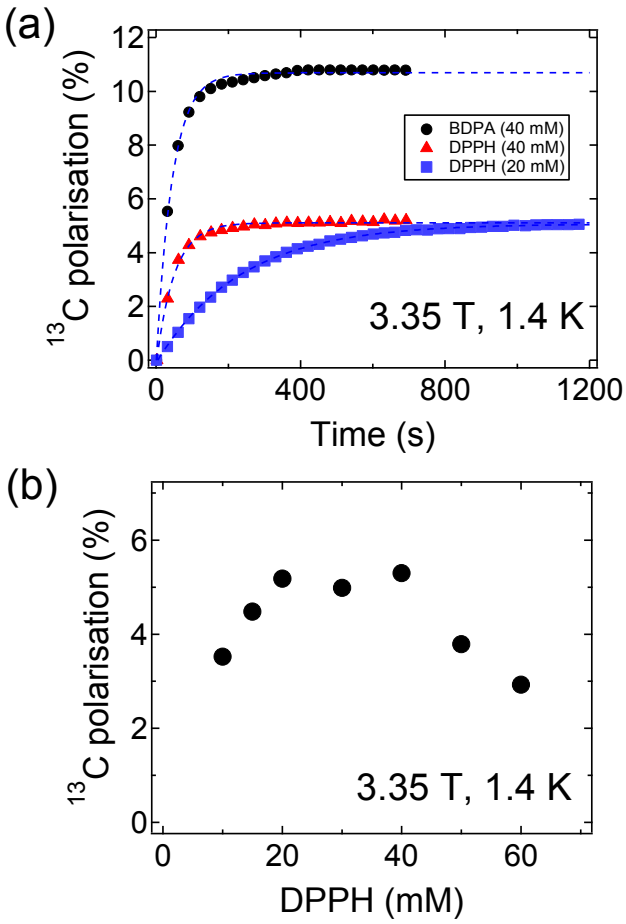

Fig. S4 (a) Polarisation buildup curves of 1:1 [1-^{13}C]ethyl acetate:sulfolane doped with the optimum concentrations of DPPH (20 mM or 40 mM) and BDPA (40 mM). (b) Summary of the dependence of ^{13}C polarisation with DPPH concentration. These data were taken at 3.35 T and 1.4 K.

V. ^{13}C microwave DNP spectra of samples doped with DPPH and DPPH-derivative

Fig. S5 shows the microwave DNP spectra of 1:1 v/v [1-^{13}C]ethyl acetate:sulfolane doped with a) 20 mM 2,2-diphenyl-1-picrylhydrazyl (DPPH) and b) 20 mM of a DPPH derivative, 2,2-di(4-tert-octylphenyl)-1-picrylhydrazyl. These data were taken in the HyperSense at 3.35 T and 1.4 K with a 100 mW microwave source. The features of the ^{13}C DNP spectra are nearly identical for both free radicals; a slight shift up in frequency (downfield shift) was observed for the DPPH-derivative due to the chemical modifications made in the phenyl groups.

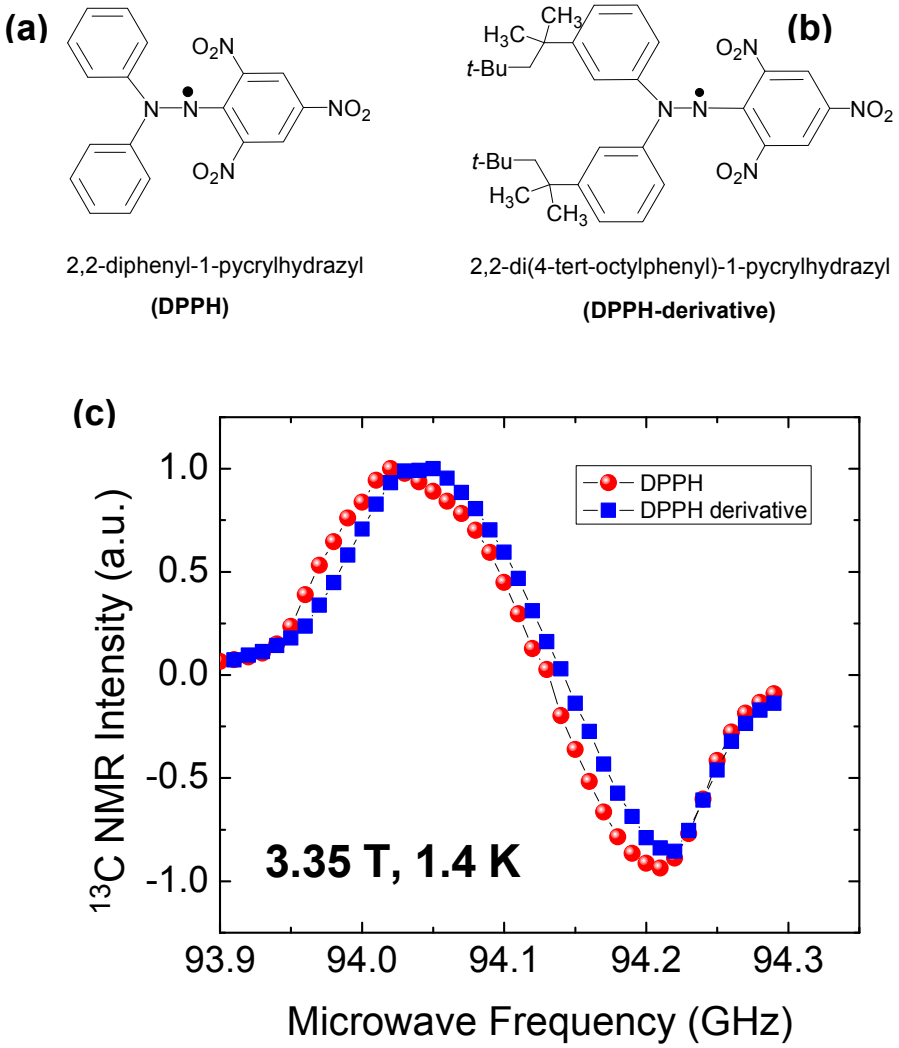

Fig. S5 Structures of (a) 2,2-diphenyl-1-picrylhydrazyl (DPPH) and (b) a DPPH derivative 2,2-di(4-tert-octylphenyl)-1-picrylhydrazyl . (c) ^{13}C microwave DNP spectra of 1:1 v/v [1-^{13}C]ethyl acetate:sulfolane doped with DPPH (20 mM) and a DPPH derivative (20 mM; see structure in Figure 1b). These data were taken at 3.35 T and 1.4 K with a 100 mW microwave source.

VI. ^{15}N T_1 decay curves of hyperpolarised pentaerythrityl tetraazide

In fast dissolution DNP-NMR, long spin-lattice relaxation time T_1 translates to long lifetime of the hyperpolarised state. Fig. S6 shows the decay of the hyperpolarised ^{15}N NMR signals emanating from the CH_2-linked, central, and terminal ^{15}N (natural abundance) nuclei of pentaerythrityl tetraazide in methanol solution. These data were collected at 9.4 T and 298 K. The decay of the hyperpolarised signal was monitored by applying a small rf detection pulse with flip angle $\theta_{flip}=5^0$ every time interval TR=10 s. To extract the T_1 values, the data were fitted to the equation:[4]

$$M_z(t)=M_0 \sin\theta_{flip}(\cos\theta_{flip})^{t/TR}\exp(-t/T_1)$$

where M_0 is the original magnetisation prior to rf pulsing. This equation accounts for the loss of magnetisation due to rf excitation and T_1 relaxation.

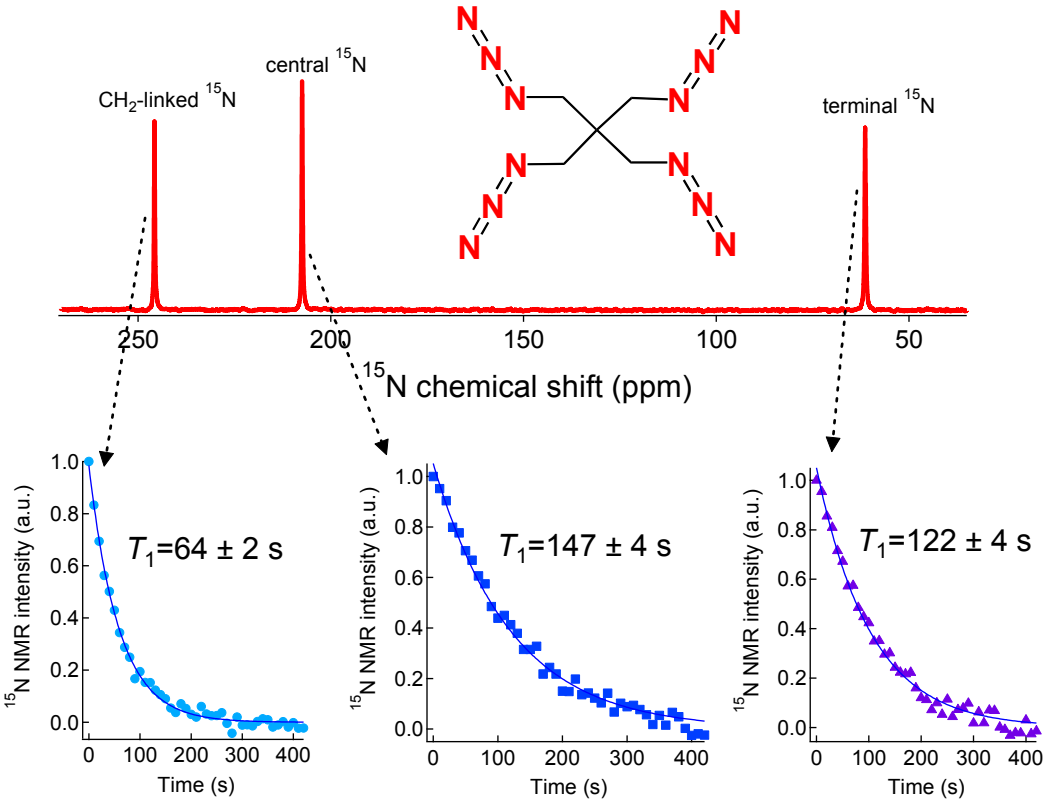

Fig. S6 Decay of the hyperpolarised ^{15}N NMR signals from the CH_2-linked, central, and terminal ^{15}N (natural abundance) nuclei of pentaerythrityl tetraazide (31 mM in methanol). These measurements were taken at 9.4 T and 298 K. The decay of the hyperpolarised signal was monitored by applying a 5-degree detection pulse every 10 s.

VII. UV/Vis spectroscopy of filtered and unfiltered DPPH solutions

Similar to the fast dissolution DNP of BDPA-doped samples,[3] the hydrophobic DPPH free radical can be easily removed from aqueous dissolution liquids by a simple mechanical filtration process. Fig. S7 shows the UV/Vis spectra of varying DPPH concentration in methanol solution and the filtered aqueous dissolution liquid showing the absence of DPPH after filtration using a 0.2-micron syringe filter. The preparation of radical-free hyperpolarised solution is an important attribute for future *in vivo* magnetic resonance spectroscopy or imaging experiments.

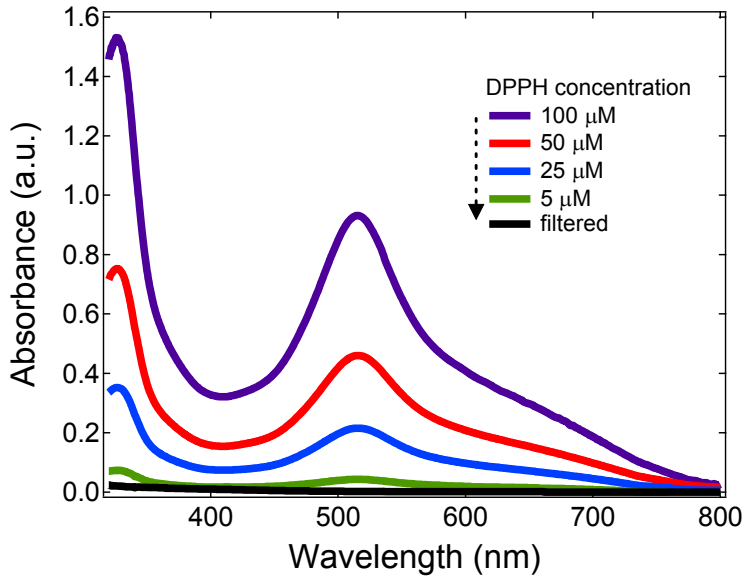

Fig. S7 UV/Vis spectra of varying DPPH concentration in methanol solution and the filtered aqueous dissolution liquid.

VIII. References

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[2] C. T. Farrar, D. A. Hall, G. J. Gerfen, S. J. Inati and R. G. Griffin, *J. Chem. Phys.*, 2001, **114**, 4922.

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