Electronic Supplementary Material (ESI) for Physical Chemistry Chemical Physics.

Supporting Information

Hyperpolarized long-lived nuclear spin states in monodeuterated methyl groups

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1. Dissolution-dynamic nuclear polarization methods

Solutions of 0.375 M (N-CH_2D)-2-methylpiperidine in the glass-forming mixture D_2O:glycerol-d_8 (50:50 v/v) were doped with 25 mM TEMPOL (purchased from Sigma-Aldrich). The synthesis of (N-CH_2D)-2-methylpiperidine is reported elsewhere [1]. The solution was sonicated for 2 minutes. Ten frozen pellets of the “DNP mixture” (10 μL volume per pellet) were inserted in the polarizer. The sample polarized at ∼1.3 K and 6.7 T for ∼48 minutes in a home-built polarizer by applying frequency-modulated microwave irradiation at 188.3 GHz frequency and 100 mW power [2, 3]. The microwave modulation frequency and amplitude were 10 kHz and 50 MHz, respectively. The polarized pellets were dissolved with 5 mL CD_3CN solvent (degassed via bubbling with nitrogen gas for 5 minutes) preheated to 410 K at a pressure of 10 bar. The liquid sample was transferred in 10.7 s to a 11.7 T (500 MHz) NMR magnet by pushing with helium gas at 6 bar through a PTFE tube (1.5 mm inner diameter) running inside a magnetic tunnel (0.91 T, 5 m length) [4]. 1 s was taken for sample injection and bubble dissipation. Spectra were recorded by using a 11.7 T Bruker Avance II console and processed with home-written Python software.

2. Solid-state polarization

Zeeman polarization $p_{\mathrm{Z}}^{\mathrm{solid}}$ was accumulated in the solid-state for 0.375 M (N-CH_2D)-2-methylpiperidine in the presence of 25 mM TEMPOL radical and glassy D_2O:glycerol-d_8 matrix in a field of 6.7 T and at a temperature of ∼1.3 K under the action of negative dynamic nuclear polarization (DNP), see the dissolution-dynamic nuclear polarization methods section for more details. A Zeeman polarization of $p_{\mathrm{Z}}^{\mathrm{solid}}$ = -59±5% was achieved in ∼48 minutes, see Fig. S1a. The solid state enhancement $\epsilon_{\mathrm{Z}}^{\mathrm{solid}}$ was approximately -360±20 compared to a spectrum recorded with the microwaves off, see Fig. S1b. The thermal spectrum was acquired after a 1 hour equilibration period at ∼4.2 K.

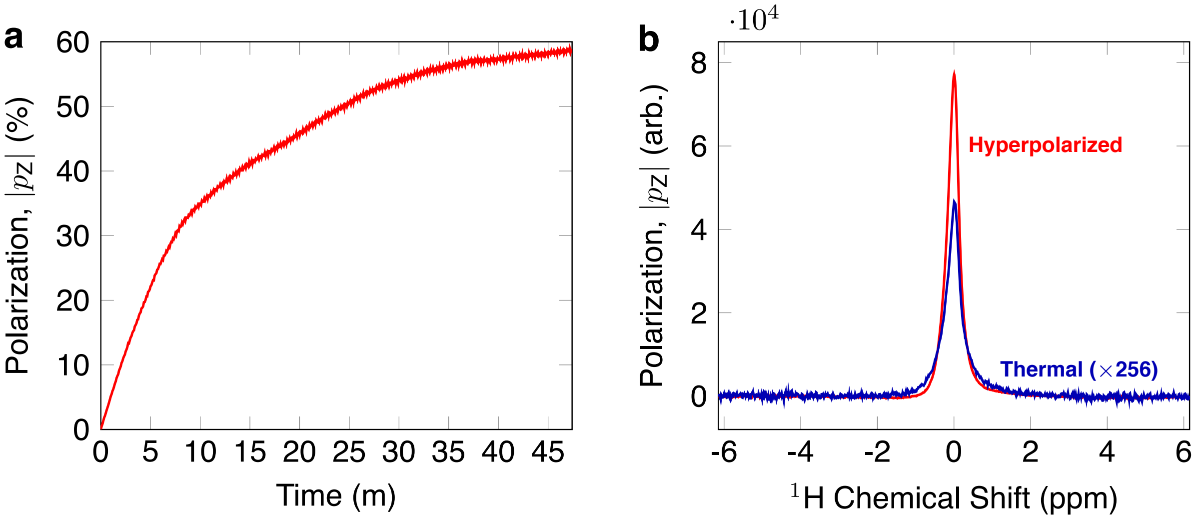

Figure S1: a) Build up of Zeeman polarization $p_{\mathrm{Z}}^{\mathrm{solid}}$ in the solid state for 0.375 M (N-CH_2D)-2-methylpiperidine in the presence of 25 mM TEMPOL radical and glassy D_2O:glycerol-d_8 matrix in a field of 6.7 T and at a temperature of ∼1.3 K. A Zeeman polarization of $p_{\mathrm{Z}}^{\mathrm{solid}}$ = -59±5% was reached after ∼48 minutes. b) Solid state hyperpolarized (red) and thermal (blue) spectra. The enhancement in the solid state is $\epsilon_{\mathrm{Z}}^{\mathrm{solid}} \simeq -360 \pm 20$.

3. T_{00} filter and singlet to magnetization pulse sequence

In the current study, we use the combination of a T_{00} filter and the S2M (singlet-to-magnetization) pulse sequence to retrieve singlet order generated directly from DNP. The T_{00} filter and S2M pulse sequence are shown in Fig. S2.

The singlet state is a magnetically silent arrangement of nuclear spin configurations and is unperturned by the T_{00} filter, which employs the optimized parameters shown in Table S1 to remove signals deriving from residual magnetization. Details of the T_{00} filter are also given in Refs [1, 5].

The S2M pulse sequence converts hyperpolarized singlet order into hyperpolarized transverse magnetization. The S2M pulse sequence consists of two spin-echo trains generated by a recurring sequence of a composite 180° pulse (90°_0-180°_{90}-90°_0) sandwiched between two evolution periods τ_J of duration $\frac{1}{4J}$, where J is the in pair scalar coupling (11.7 Hz). The first and second spin-echo trains are repeated n_2 and n_1 times, respectively, with $n_1 \sim n_2/2$. An additional τ_J-90°_0 module is inserted between the two echo trains [6, 7]. The parameters of the S2M pulse sequence were as follows: $\tau_\mathrm{J} = 21.4\,\mathrm{ms}$, $n_1 = 3$ and $n_2 = 1$.

In order to determine the efficiency of the S2M sequence η_{S2M} we converted the magnetization of a thermally polarized sample to singlet order by using the M2S (magnetization "to" singlet) pulse sequence. The M2S pulse sequence is the time-reversal of the S2M pulse sequence including an initial 90°_{90}-τ_J segment. The M2S pulse sequence employs the same parameters as the S2M pulse sequence. Any remaining magnetization was quenched by using a T_{00} filter and the singlet order was back-converted to magnetization using the S2M pulse sequence. The signal was recorded and compared to a separate signal which was acquired following an excitation with a 90°_0 pulse. The ratio of the two signals was found to be 0.4. The efficiency of the S2M pulse sequence is therefore: $\eta_{\mathrm{S2M}} = 0.4^{1/2} = 0.63 \pm 0.02$, which is close to the theoretical maximum of $\sqrt{2/3}$ [8]. The experiment was carried out on a sample of $5\,\mu$L "DNP mixture" in 0.5 mL $\mathrm{CD_3CN}$ solvent.

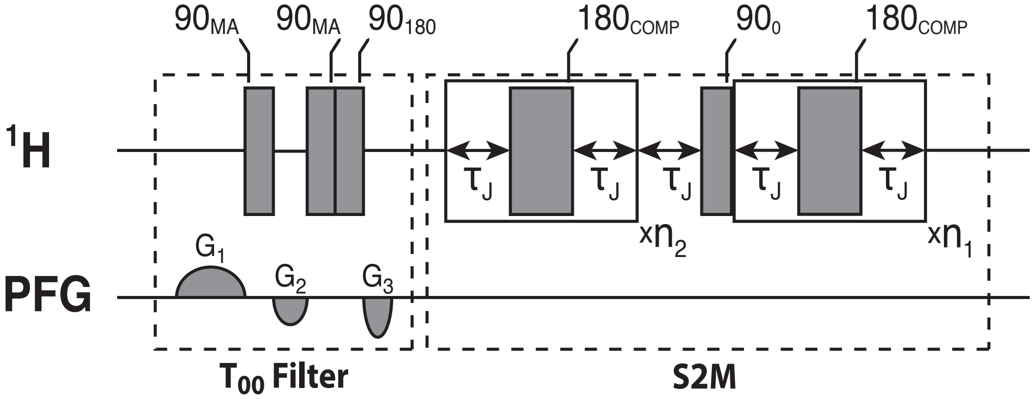

Figure S2: The T_{00} filter and S2M (singlet-to-magnetization) pulse sequence. MA denotes the magic angle (54.7°). COMP denotes a composite 180° pulse: 90°_0-180°_{90}-90°_0.

Table S1: Optimized parameters for the T_{00} filter. The T_{00} filter is implemented to suppress all signals not originating from the singlet state. NMR signals passing through spherical tensors of rank 1 or 2 are destroyed.

PFG	Shape	Strength ($\mathrm{G\,cm^{-1}}$)	Duration (ms)
G1	SINE.100	5.0	4.4
G2	SINE.100	-5.0	2.4
G3	SINE.100	-7.5	2.0

4. Singlet-filtered saturation recovery experiment

The pulse sequence for measuring the ^{1}H T_1 of the CH_2D peak obscured by the suspected water impurity is shown in Fig. S3. The scheme commences with a "saturation comb" (90°_0 - delay)$_{100}$ which crushes all observable magnetization. The delay between 90°_0 pulses was 5 ms. After an evolution period τ_{EV}, ordinary magnetization is accrued and converted into singlet order by the M2S (magnetization to singlet) pulse sequence [6, 7]. The T_{00} filter destroys all signals not orgininating from the proton singlet order [1, 5], which is subsequently back-converted into observable magnetization by the S2M pulse sequence. The S2M applies the same transformations as the M2S but in reverse chronological order. The triplet-singlet-triplet conversion has an efficiency of 40%, see the main text for more details. NMR spectra were acquired as a function of τ_{EV} and the CH_2D T_1 of 5.9 ± 0.7 s was determined from the integrals of the resulting singlet resonances.

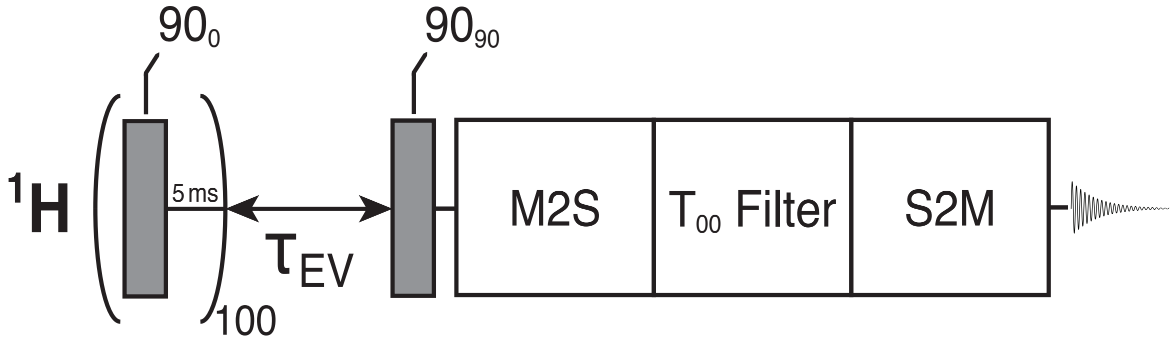

Figure S3: Pulse sequence for estimating the longitudinal relaxation time of the obscured CH_2D resonance. The "T_{00} filter" and the S2M pulse sequence are described in more detail in section 3, the main text and Refs [1-4].

5. Impurity

The resonance position of the impurity, thought to be residual water [9], was found to be dependent on the volume of DNP mixture ((N-CH_2D)-2-methylpiperidine, glass-forming D_2O:glycerol-d_8 (50:50 v/v) and TEMPOL) dissolved in CD_3CN solvent, see table S2. At higher concentrations of "DNP mixture", the water impurity was shifted sufficiently far downfield such that the CH_2D resonance was unobscured in the proton NMR spectrum. At a 10 μL volume of "DNP mixture" dissolved in CD_3CN solvent, the CH_2D peak was observed at 2.19 ppm. For "DNP mixture" concentrations $<2\,\mu$L, such as those achieved after dissolution, the CH_2D peak was obscured by a more intense water resonance. The resonance shift of the water impurity as a function of "DNP mixture" volume is approximately linear, but is not currently understood. A plausible mechanism would be an exchange interaction between the -OH protons of the TEMPOL radical with those of the residual protonated water belonging to the glassy matrix. Such an exchange interaction could simultanesouly lead to a downfield peak shift for water and broader NMR lines. We are not aware of previous reports of similar phenomena.

Table S2: Resonance position of the suspected water impurity for different volumes of (N-CH_2D)-2-methylpiperidine, glass-forming D_2O:glycerol-d_8 (50:50 v/v) and TEMPOL mixture dissolved in 0.5 mL degassed CD_3CN solvent at 11.7 T (500 MHz) and 25°C. Chemical shifts were referenced with respect to the CD_3CN solvent peak.

Volume (μL)	Position (ppm)
2	2.217
5	2.297
10	2.389

6. Video of hyperpolarized long-lived state experiment

Please see the online, electronic Supporting Information (SI) for the video of our hyperpolarized long-lived state experiment.

7. References

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