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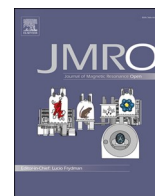
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Research Article

Boosting dissolution-dynamic nuclear polarization by multiple-step dipolar order mediated $^1\text{H} \rightarrow ^{13}\text{C}$ cross-polarization

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ABSTRACT

Dissolution-dynamic nuclear polarization can be boosted by employing multiple-contact cross-polarization techniques to transfer polarization from ^1H to ^{13}C spins. The method is efficient and significantly reduces polarization build-up times, however, it involves high-power radiofrequency pulses in a superfluid helium environment which limit its implementation and applicability and prevent a significant scaling-up of the sample size. We propose to overcome this limitation by a stepwise transfer of polarization using a low-energy and low-peak power radiofrequency pulse sequence where the $^1\text{H} \rightarrow ^{13}\text{C}$ polarization transfer is mediated by a dipolar spin order reservoir. An experimental demonstration is presented for [$1\text{-}^{13}\text{C}$]sodium acetate. A solid-state ^{13}C polarization of $\sim 43.5\%$ was achieved using this method with a build-up time constant of ~ 5.1 minutes, leading to a $\sim 27.5\%$ ^{13}C polarization in the liquid-state after sample dissolution. The low-power multiple-step polarization transfer efficiency achieved with respect to the most advanced and highest-power multiple-contact cross-polarization approach was found to be ~ 0.69 .

1. Introduction

Ordinary magnetic resonance spectroscopy (MRS) and imaging (MRI) methods are often limited by the weak magnetic response from clusters of nuclear spins, even when placed within today's highest field superconducting magnets. The inherent insensitivity of a nuclear spin ensemble is engendered by the small differences in energy between nuclear spin states compared with the energy typically available at room temperature, which results in a rather flat Boltzmann distribution of nuclear spin populations.

To alleviate this issue, dissolution-dynamic nuclear polarization (dDNP) experiments are becoming increasingly employed. The hyperpolarization technique generates strong nuclear magnetic resonance (NMR) signals enhanced by factors approaching 10^4 [1] for a range of nuclear spins in various media, with applications in clinical research [2-4] and metabolomics studies [5], among others [6,7]. For dilute low- γ nuclear spins at low temperatures, the dDNP process [8] suffers from excessively long polarization build-up time constants τ_{DNP}

sometimes exceeding an hour [9].

dDNP methods can be efficiently accelerated (by a factor of up to 40) by the implementation of radiofrequency (*rf*) pulse sequences such as cross-polarization (CP) [10-17], which indirectly transfer electron spin polarization to insensitive nuclear spins (such as ^{13}C) via sensitive nuclear spins (such as ^1H). The acceleration of the DNP process, compared with direct polarization, is attributed to the generally quicker polarization build-up timescales of proton spins at low temperatures when polarized with nitroxide radicals [18]. Multiple applications of intense B_1 -matched (typ. > 15 kHz) simultaneous ^1H and ^{13}C spin-locking *rf*-fields throughout an optimized contact period (typ. > 1 ms) allow the repeated indirect transfer of electron spin polarization, which is accumulated by the insensitive nuclear spins. This multiple-contact CP-DNP approach was implemented in the preparation and transportation of highly polarized metabolites [19].

Such a CP approach under dDNP conditions, and more precisely at or below liquid helium temperatures, is significantly challenging, e.g., necessary high-energy and high-peak power *rf*-pulses can lead to

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detrimental arcing in the superfluid cryogenic bath [20]. As a result, CP is not widely implemented under *dDNP* conditions (typ. $T = 1.0$ - 1.6 K). Such difficulties not only restrict a broader implementation of CP, but also prevent the scaling-up of *dDNP* sample volumes required for human applications or for the parallelization of hyperpolarization [21].

We have recently demonstrated the use in a *DNP* context of an alternative *rf*-pulse sequence to CP which is of low-power, does not require synchronized B_1 -matched spin-locking *rf*-fields and can ultimately overcome all previous limitations [22]. In such cases, the transfer of spin polarization is mediated by an intermediary reservoir of nuclear dipolar spin order [23-33], and even though the exact mechanism underlying the polarization transfer is yet to be fully understood, the *rf*-pulse sequence has consequently been termed dipolar order mediated cross-polarization (*dCP*). It is expected that significant levels of ^{13}C polarization can be accrued if an approach incorporating consecutive *dCP* transfers can be successfully implemented, and that a significant fraction of the resulting solid-state ^{13}C polarization will be preserved upon hyperpolarization by dissolution to the liquid-state.

In the current Paper, we present an *rf*-pulse sequence containing multiple low-power polarization transfer elements in a way that is fully compatible with *dDNP* conditions. The *multi-dCP* *rf*-pulse sequence (see below) yielded a ^{13}C polarization of $\sim 43.5\%$ with a build-up time constant $\tau_{\text{dCP}} = 5.1 \pm 0.2$ minutes (total experiment time > 15 minutes) for a sample of $[1-^{13}\text{C}]$ sodium acetate in the frozen solid-state, which was found to be ~ 0.69 of the efficiency realized by using a most advanced state-of-the-art and fully optimized multiple-contact CP experiment. We additionally investigated the dissolution of $[1-^{13}\text{C}]$ sodium acetate indirectly polarized via this technique, and achieved a liquid-state ^{13}C polarization level of $\sim 27.5\%$.

2. Methods

2.1. Sample preparation

A solution of 3 M $[1-^{13}\text{C}]$ sodium acetate in the glass-forming mixture $\text{H}_2\text{O}:\text{D}_2\text{O}:\text{glycerol-}d_8$ (10%:30%:60% $v/v/v$) was doped with 30 mM TEMPOL radical (all compounds purchased from Sigma Aldrich) and sonicated for ~ 10 minutes. This sample is referred to as I from here onwards. Paramagnetic TEMPOL radicals were chosen to polarize ^1H spins most efficiently under our *dDNP* conditions.

2.2. Sample freezing

100 μL sample volumes were pipetted into a PEEK sample cup and inserted into a 7.05 T prototype Bruker Biospin polarizer equipped with a specialized *dDNP* probe and running TopSpin 3.5 software. The sample temperature was reduced to 1.2 K by submerging the sample in liquid helium and reducing the pressure of the variable temperature insert (VTI) towards ~ 0.7 mbar.

2.3. Dynamic nuclear polarization

Sample I was polarized by applying microwave irradiation at $f_{\mu\text{w}} = 198.128$ GHz (negative lobe of the EPR line) with triangular frequency modulation of amplitude $\Delta f_{\mu\text{w}} = \pm 160$ MHz [34] and rate $f_{\text{mod}} = 0.5$ kHz at a power of ca. $P_{\mu\text{w}} = 125$ mW at the output of the microwave source and ca. $P_{\mu\text{w}} = 30$ mW reaching the *DNP* cavity (evaluated by monitoring the effect of microwave irradiation on the helium path pressure [35]), which were optimized prior to commencing experiments in order to achieve the best possible level of ^1H polarization.

2.4. Multi-dCP RF-pulse sequence

To obtain the highest possible levels of ^{13}C polarization, it is of interest to perform multiple *dCP* *rf*-pulse sequence cycles to incrementally

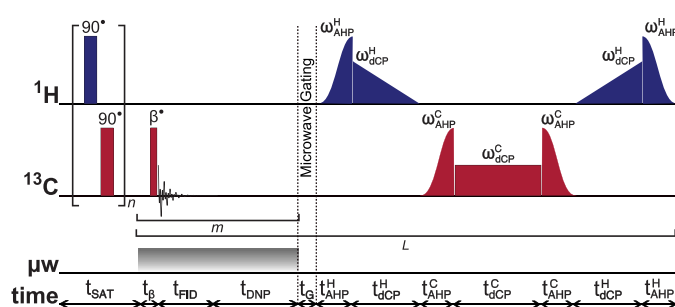


Fig. 1. Schematic representation of the multiple-step dipolar order mediated cross-polarization (*multi-dCP*) *rf*-pulse sequence used for transferring ^1H Zeeman polarization to insensitive ^{13}C nuclear spins in successive steps. The experiments used the following parameters, chosen to maximize $^1\text{H} \rightarrow ^{13}\text{C}$ polarization transfer: $n = 50$; $\beta = 5^\circ$; $\tau_{\text{DNP}} = 30$ s; $m = 7$; $\tau_{\text{G}} = 0.5$ s; $\omega_{\text{AHP}}^{\text{H}}/2\pi = 27.8$ kHz; $t_{\text{AHP}}^{\text{H}} = 175$ μs ; $\omega_{\text{dCP}}^{\text{H}}/2\pi = 16.9$ kHz; $t_{\text{dCP}}^{\text{H}} = 450$ μs ; $\omega_{\text{AHP}}^{\text{C}}/2\pi = 25.8$ kHz; $t_{\text{AHP}}^{\text{C}} = 175$ μs ; $\omega_{\text{dCP}}^{\text{C}}/2\pi = 14.6$ kHz; $t_{\text{dCP}}^{\text{C}} = 49$ ms; $L = 8$. AHP = Adiabatic Half-Passage. AHP sweep width = 100 kHz. All AHP and *dCP* *rf*-pulses have phase x . The $\pi/2$ saturation *rf*-pulses use a thirteen-step phase cycle to remove residual magnetization at the beginning of the experiment: $\{0, \pi/18, 5\pi/18, \pi/2, 4\pi/9, 5\pi/18, 8\pi/9, \pi, 10\pi/9, 13\pi/9, \pi/18, 5\pi/3, 35\pi/18\}$. The resonance offset was placed at the centre of the ^1H and ^{13}C NMR peaks.

transfer ^1H polarization to dilute ^{13}C nuclear spins embedded within the sample. Figure 1 shows such a suitable *rf*-pulse sequence capable of implementing numerous *dCP* *rf*-pulse sequence steps. Consequently, the *rf*-pulse sequence has been termed multiple-step dipolar order mediated cross-polarization (*multi-dCP*).

The *multi-dCP* *rf*-pulse sequence operates as follows:

- (i) A saturation sequence of 90° *rf*-pulses with alternating phases separated by a short delay repeated n times (typ. $n = 50$) kills residual magnetization on both *rf*-channels;
- (ii) The microwave source becomes active;
- (iii) The ^{13}C Zeeman magnetization trajectory is minimally perturbed by the application of a small flip-angle *rf*-pulse (typ. $\beta = 5^\circ$) used for detection, which is then followed by a short acquisition period (typ. $t_{\text{FID}} = 1$ ms);
- (iv) ^1H *DNP* builds-up during a time t_{DNP} (typ. $t_{\text{DNP}} = 30$ s);
- (v) Stages *iii-iv* are cycled m times (typ. $m = 7$) in order to monitor the evolution of the ^{13}C polarization between *dCP* steps;
- (vi) The microwave source is gated, and a delay of duration $t_{\text{G}} = 0.5$ s occurs before the next *dCP* step, thus permitting the electron spins to relax to their highly polarized thermal equilibrium state [36];
- (vii) A ^1H adiabatic half-passage (AHP) *rf*-pulse followed by a linearly decreasing amplitude ramp ^1H *rf*-pulse of amplitude $\omega_{\text{dCP}}^{\text{H}}$ and length $t_{\text{dCP}}^{\text{H}}$ presumably converts ^1H Zeeman polarization into dipolar order [37];
- (viii) A ^{13}C spin-locking *rf*-pulse of amplitude $\omega_{\text{dCP}}^{\text{C}}$ and length $t_{\text{dCP}}^{\text{C}}$ sandwiched between two ^{13}C AHP *rf*-pulses of opposite chronology generates ^{13}C transverse magnetization;
- (ix) Stage *vii* is repeated with reverse chronology;
- (x) Stages *ii-ix* are repeated in L units (typ. $L = 8$) to periodically transfer ^1H Zeeman polarization to ^{13}C spins.

The key element of the *multi-dCP* *rf*-pulse sequence is the loop L which contains a modified *dCP* *rf*-pulse sequence block. Applying the altered *dCP* *rf*-pulse sequence between delays of approximate duration $t_{\text{DNP}} \times L$ transfers ^1H polarization to insensitive ^{13}C heteronuclei in a stepwise manner.

2.5. Microwave gating

The microwave source was gated shortly before and during *dDNP*

transfer elements to allow the electron spin ensemble to return to a highly polarized state, which happens on the timescale of the longitudinal electron relaxation time (typ. $T_{1e} = 100$ ms with $P_e = 99.93\%$ under our experimental *dDNP* conditions) [36]. Microwave gating is key to efficient *dCP* polarization transfer. It provides a way to strongly attenuate paramagnetic relaxation, therefore resulting in a significant increase in the nuclear spin relaxation times in the *rf*-field (or rotating) frame. This allows the application of longer *dCP rf*-pulses, which significantly increases the efficiency of nuclear spin polarization transfer.

3. Results

The DNP build-up time constant of ^1H polarization for sample I at 1.2 K was measured to be: $\tau_{\text{DNP}} = 225 \pm 1$ s (for the positive lobe of the DNP microwave spectrum). Consequently, the period between *dCP* and CP polarization transfer steps was chosen to be: $t_{\text{DNP}} = 210$ s, corresponding to $m = 7$, see Fig. 1.

The ^{13}C nuclear spin polarization level achieved by the *multi-dCP rf*-pulse sequence is $\sim 32.2\%$ after 7 minutes (2 transfer steps) and ultimately reaches $\sim 43.5\%$ with a build-up time constant $\tau_{\text{dCP}} = 5.1 \pm 0.2$ minutes, see Fig. 2 (grey curve). The very first $^1\text{H} \rightarrow ^{13}\text{C}$ nuclear polarization transfer step alone achieves a ^{13}C polarization of $\sim 21.2\%$ after only 3.5 minutes. A multiple-step CP *rf*-pulse sequence (see the Supporting Information (SI) for more details) obtains a maximum ^{13}C polarization level of $\sim 63.3\%$ under the same experimental conditions (black curve). ^{13}C polarizations were determined according to the procedure detailed in [8]. The overall performance of the *multi-dCP rf*-pulse sequence compared with a sophisticated and high-power multiple-contact CP *rf*-pulse sequence is ~ 0.69 , which is determined from the integrals of the multiple-contact CP and *multi-dCP* ^{13}C NMR signal maxima. The grey curve in Fig. 2 also shows a small decrease in ^{13}C polarization following each transfer step. ^{13}C NMR spectra acquired around these regions are shown in the SI. It is also interesting to note that the decay of the ^{13}C NMR signal at each plateau for the *multi-dCP* experiment appears to be slower than in the case of the *multi-CP* experiment.

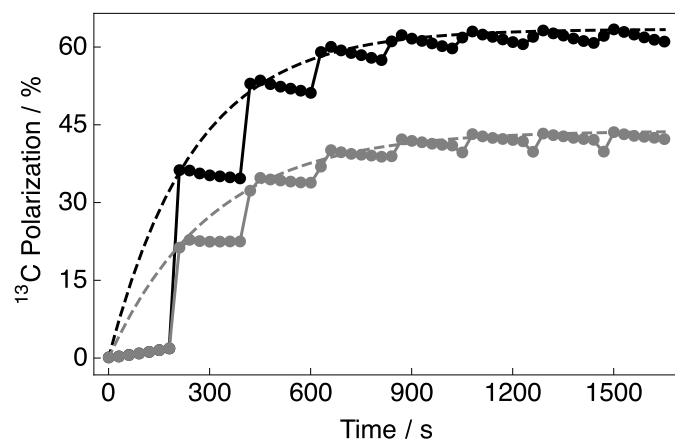


Fig. 2. Experimental ^{13}C polarization build-up curves for a sample of I acquired at 7.05 T (^1H nuclear Larmor frequency = 300.13 MHz, ^{13}C nuclear Larmor frequency = 75.47 MHz) and 1.2 K with a single scan per data point. The build-up of ^{13}C polarization was measured by using: Black curve: A state-of-the-art and high-power CP *rf*-pulse sequence described in the Supporting Information (SI); and Grey curve: The low-power *multi-dCP rf*-pulse sequence described in Fig. 1. The traces have the same overall form, and plateau over a period of ~ 1500 s. The *dCP* and CP build-up curves were fitted with a mono-exponential build-up function $A(1 - \exp\{-t/\tau\})$ using the build-up time constants $\tau = \tau_{\text{CP}}$ and $\tau = \tau_{\text{dCP}}$, respectively. Build-up time constants: Black dashed curve (CP): $\tau_{\text{CP}} = 4.2 \pm 0.2$ minutes; Grey dashed curve (*dCP*): $\tau_{\text{dCP}} = 5.1 \pm 0.2$ minutes.

Polarized samples of I were dissolved with 5 mL of D_2O solvent prepressurized at 6 bar, and subsequently heated to 180°C (and a pressure of 9 bar). The liquid sample was transferred in 10 s to a *Bruker Biospin* prototype *dDNP* injector placed in the bore of a 1.88 T (^1H nuclear Larmor frequency = 80.05 MHz, ^{13}C nuclear Larmor frequency = 20.13 MHz) permanent magnet *Bruker Biospin Fourier 80* benchtop NMR system by pushing with helium gas at 6 bar through a PTFE tube (1.6 mm inner diameter) running inside a series of solenoid coils (2 A power source) producing a minimum magnetic field of 4 mT along the sample transfer path between the bore exit/entry of the two magnets (~ 2.8 m length), see Fig. 3a [38]. Experimental liquid-state ^1H and ^{13}C NMR data were recorded and processed using *TopSpin 4.0*

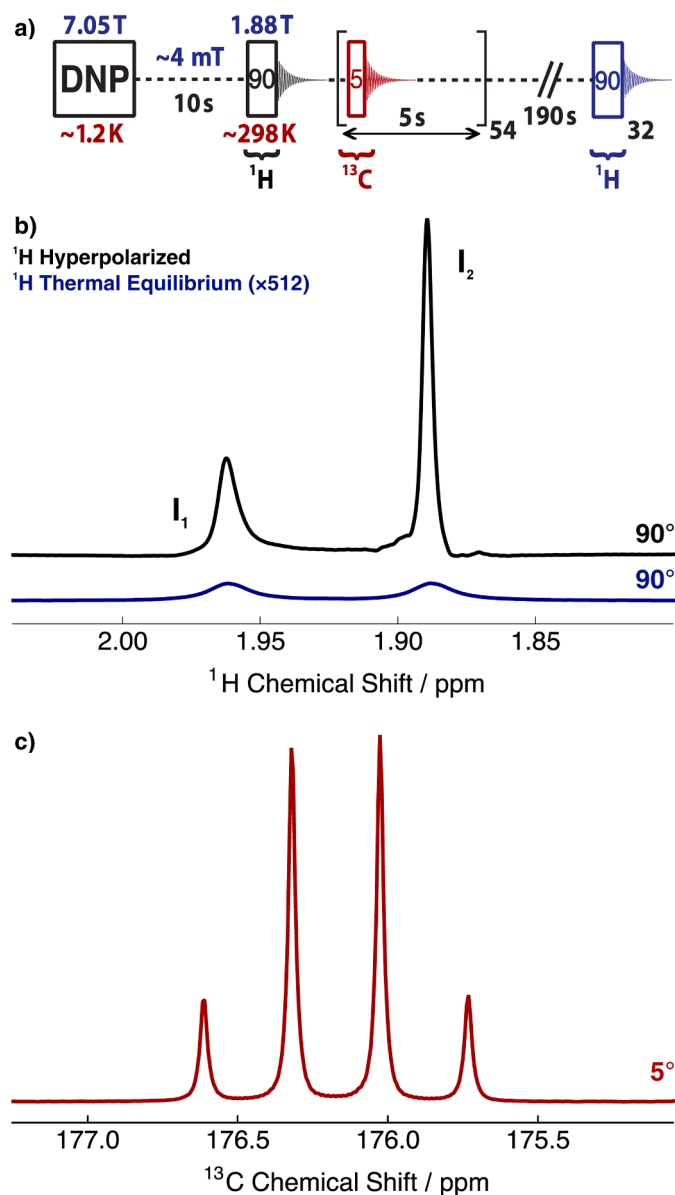


Fig. 3. (a) Events and timings for DNP, sample dissolution and acquisition of liquid-state NMR spectra. Relevant portions of the experimental b) ^1H and c) ^{13}C NMR spectra belonging to the methyl (CH_3) group and ^{13}C -labelled carbonyl site, respectively, of sample I in approximately 0.6 mL of D_2O solution acquired at 1.88 T (^1H nuclear Larmor frequency = 80.05 MHz, ^{13}C nuclear Larmor frequency = 20.13 MHz) and 298.15 K. The experimental NMR spectra were acquired in accordance with the events and timings depicted in a). I_1 and I_2 refer to the ^1H NMR signal integrals of the multiplet lineshape components. The first experimental ^{13}C NMR spectrum of the small flip-angle *rf*-pulse and acquire train in a) is shown in c).

software.

The sequence of events given in Fig. 3a detail how the experimental NMR spectra were acquired. After DNP and sample dissolution and transfer, a 90° *rf*-pulse is used to record a hyperpolarized ¹H NMR spectrum (black). Subsequently, *i.e.*, after the ca. 4 s used for ¹H signal acquisition, a train of 5° *rf*-pulses separated by 5 s is used to record the hyperpolarized ¹³C NMR spectra (red). The sample is allowed to rest in the 1.88 T magnet for an additional 190 s to achieve thermal equilibrium, and a proton NMR signal is acquired using a 90° *rf*-pulse (blue). [1-¹³C]sodium acetate was chosen for sample dissolution because the carbonyl site displays a suitably lengthy longitudinal relaxation time constant *T*₁ in regions of low magnetic field since it is not efficiently relaxed by nearby ¹H nuclei.

The black spectrum in Fig. 3b shows the relevant region of the experimental ¹H NMR spectrum of sample I acquired immediately after sample dissolution and transfer. The sample was initially hyperpolarized in the solid-state by using the *multi-dCP rf*-pulse sequence. The methyl (CH₃) group resonance located at ~1.93 ppm is split into two peaks due to a scalar coupling with the ¹³C-labelled carbonyl site (scalar coupling constant: |²*J*_{HC}| ≈ 5.8 Hz).

The proton NMR lineshape in Fig. 3b is highly asymmetric and indicates that the scalar coupled ¹³C nuclear spins within the sample are significantly hyperpolarized. The degree of multiplet asymmetry can be used to infer the ¹³C polarization of the sample upon arrival inside the receiving magnet, a methodology known as SPY-MR [39]. The ¹³C polarization level *P*(¹³C) is given by the following expression:

$$P(^{13}\text{C}) = \frac{I_1 - I_2}{I_1 + I_2} \times 100\% \quad (1)$$

where *I*₁ ≈ 0.637 and *I*₂ ≈ 0.363 are the ¹³C NMR signal integrals of the most and least intense multiplet peaks, respectively. In the case of the ¹H NMR spectrum presented in Fig. 3b, by using Eq. (1) it can be deduced that the ¹³C polarization *P*(¹³C) is ~27.5%. The hyperpolarized ¹³C NMR spectrum (Fig. 3c) was also compared indirectly to the thermal equilibrium ¹H NMR spectrum of sample I (Fig. 3b, blue spectrum), with a 0.8% agreement on the final ¹³C polarization.

The ¹³C NMR spectrum acquired immediately after sample dissolution and transfer is shown in Fig. 3c. The ¹³C carbonyl resonance of sample I is positioned at ~176.2 ppm and displays an approximate 1:3:3:1 quartet structure due to the |²*J*_{HC}| scalar coupling with the 3 methyl group protons. The small asymmetry in the observed ¹³C NMR multiplet intensities is likely due to a non-zero ¹H polarization (ca. <5%) which is present after the application of the *multi-dCP rf*-pulse sequence, dissolution and sample transfer. The signal-to-noise ratio (SNR) of the NMR peak belonging to the ¹³C-labelled site was determined to be ~1905.

The longitudinal relaxation time constant *T*₁ of the ¹³C-labelled carbonyl site in sample I was measured by applying a small flip-angle *rf*-pulse (5°) followed directly by ¹³C NMR signal detection (acquisition time = 3 s) every 5 s, see Fig. 3a (red section). The resulting curve was found to have a single exponential relaxation behaviour (data not shown) and is well fitted with a mono-exponential decay function using a sole relaxation time constant *T*₁. Mono-exponential decay function: *A*exp{-*t*/*T*₁}. The value of *T*₁ was determined to be: 99.0 ± 0.7 s, considering the influence of the small flip-angle *rf*-pulse train.

The relevant portion of the experimental ¹H NMR spectrum belonging to the methyl (CH₃) group protons of sample I acquired under thermal equilibrium conditions is also shown in Fig. 3b (blue spectrum). This spectrum allows an estimate of the resulting liquid-state sample concentration for sample I after dissolution and transfer by comparing the ¹H NMR signal integral to that from a sample of I at a known concentration. The solution-state sample concentration of I was consequently found to be: ~14.7 mM. Given the initial ¹³C sample concentration of 3 M, and a dilution factor of 50, the liquid-state sample concentration is a factor of ~4 less than the target concentration of 60 mM.

4. Discussion

In the solid-state, the multiple-contact CP *rf*-pulse sequence is clearly superior in terms of ¹H→¹³C polarization transfer and achieves a higher final ¹³C polarization before sample dissolution. A suspected reason for the lower efficiency of *dCP* polarization transfer could be the quantity of ¹H polarization depleted to complete the *dCP* transfer step compared with the CP *rf*-pulse sequence. Proton NMR spectra showing this effect are given in the SI. It was found that a CP contact retains ~82.9% of the initial ¹H polarization, whereas the *dCP rf*-pulse sequence retains only ~19.8%, *i.e.*, there is less ¹H polarization initially available after each polarization transfer step. However, a sufficiently long time (~*τ*_{DNP}) separates the polarization transfer elements such that a considerable proportion of the ¹H polarization is replenished by DNP.

It has been shown that the *dCP rf*-pulse sequence is ultimately less efficient in transferring ¹H polarization to ¹³C spins than the CP *rf*-pulse sequence under our experimental *dDNP* conditions [22]. This effect was investigated and despite recent optimization of the *dCP rf*-pulse sequence a discrepancy remains [37] and is particularly evident upon inspection of the data points in Fig. 2 which correspond to the first polarization transfer step. The ratio of the ¹³C polarizations achieved by using the *dCP* and CP *rf*-pulses sequences in this case is ~0.59, which is rather striking since the ¹H polarization available for transfer is the same at this point in both *rf*-pulse sequences. This very likely inhibits the efficiency of the individual polarization transfer stages in the *multi-dCP rf*-pulse sequence. Liquid-state ¹³C polarizations on the order of ~40% have previously been demonstrated for [1-¹³C]sodium acetate by using a multiple-contact CP *rf*-pulse sequence prior to sample dissolution [40, 41]. Nevertheless, a liquid-state ¹³C polarization of ~27.5% is encouraging given the initial solid-state ¹³C polarization of ~43.5%.

SPY-MR polarimetry [39] in liquid-state NMR works in the case that the nuclear spins involved: (i) are not participating in strong coupling at the moment of detection (which cannot be the case for heteronuclear spins at sufficiently high magnetic fields); and (ii) have not experienced relaxation at ultralow magnetic fields, *i.e.*, where the spin system would enter the regime of strong coupling. As a result, the SPY-MR approach was implemented to infer the level of ¹³C polarization from the hyperpolarized ¹H NMR spectrum in the liquid-state after dissolution. This is a feasible approach since the lower sensitivity of our benchtop magnet, with respect to higher magnetic field superconducting instruments, requires very long (on the order of days) accumulations of ¹³C thermal equilibrium spectra to obtain an NMR signal with a sufficient SNR.

There is evidentially a discrepancy between solid-state and liquid-state ¹³C polarizations. Given the long *T*₁ of sample I at low magnetic field, it is unlikely that solely ¹³C nuclear spin relaxation is responsible for the difference in results. Another possibility is that higher-order multiple-spin terms are generated and survive the dissolution process and are not eradicated by changing magnetic field gradients during the sample transfer step to the detection magnet. The presence of such higher-order multiple-spin terms would limit the applicability of the SPY-MR approach [39]. The excessive losses in ¹³C polarization are not accounted for at present and are largely thought to be related to the sample dissolution and transfer processes but also could be attributable to zero or double quantum coherences created in regions of low magnetic field and incoherent cross-relaxation phenomena [42].

5. Conclusions

An *rf*-pulse sequence which employs low-power *rf*-pulses for the stepwise transfer of ¹H polarization to ¹³C nuclear spins under *dDNP* conditions was demonstrated. The *multi-dCP rf*-sequence achieves a ¹³C polarization level of ~43.5% in the solid-state after ~25 minutes (7 polarization transfer steps). The overall *dCP* polarization transfer efficiency was found to be ~0.69 with respect to a sophisticated and high-power multiple-contact CP experiment. After dissolution with a hot solvent, hyperpolarized liquid-state NMR signals were detected and a

^{13}C polarization of $\sim 27.5\%$ was observed in a separate permanent magnet benchtop NMR system. These results are promising for future applications of indirect hyperpolarization techniques and dissolution of insensitive nuclear spins. The low-power nature of the *multi-dCP* approach may allow polarization transfer techniques to be implemented in larger sample volumes, paving the way to the use of indirect $^1\text{H} \rightarrow ^{13}\text{C}$ polarization transfer schemes in (pre)clinical settings.

Declaration of Competing Interest

None.

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Supplementary materials

Supplementary material associated with this article can be found, in the online version, at doi:10.1016/j.jmro.2021.100018.

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