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Polarization transfer using hyperpolarized, supercritical xenon

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Abstract

Polarization transfer from hyperpolarized gas to ^{1}H, ^{13}C, etc. holds great promise for sensitivity enhancement of solution-state NMR. The route explored here uses hyperpolarized, supercritical xenon as solvent for the organic solute. A method is described for preparation of supercritical xenon solutions with little polarization loss. Detection of Overhauser enhancement of solute proton magnetization by factors of 3 to 7 confirms the intimate contact between ^{129}Xe and ^{1}H. Motivated by more efficient polarization transfer expected in solid solutions, we report survival of non-equilibrium solute polarization upon warming from solid to supercritical fluid. © 2000 Published by Elsevier Science B.V.

1. Introduction

The techniques of optical pumping and spin exchange, together with the availability of intense lasers at the relevant wavelengths, yield remarkably large nuclear spin polarizations in ^{129}Xe and ^{3}He gases [1,2]. These large nuclear spin polarizations are useful for a variety of applications in nuclear magnetic resonance (NMR) [3] and magnetic resonance imaging (MRI). Hyperpolarized gases are ideal for lung-space MRI, as they are chemically inert and can provide the large signals needed for high spatial [4] and temporal [5] resolution, despite the low spin density of gases. Hyperpolarized gases have also been proposed for inspection of materials for pores and cracks [6]. NMR of hyperpolarized xenon has been used both to study adsorbed layers on low surface area materials and polarization transfer to surface spins [7–9]. Direct chemical interest in hyperpolarized gases is limited because the technique is restricted to the inert gases.

The largest application of NMR, however, is in the solution state, both on small organic molecules and biological molecules (for identification and/or structural analysis). If the ^{129}Xe polarization of 20% that has been achieved by some groups [10,11] could be transferred to ^{1}H, sensitivity enhancement of solution-state NMR by a factor of ≈ 4000 would be effected (compared to thermal equilibrium polarization of protons at room temperature and 14 T, the largest commonly available field for NMR today). Larger enhancements would occur for lower frequency nuclei, such as ^{13}C and ^{15}N. The wide applicability of sensitivity enhancement depends critically on an efficient method of transfer of hyperpolariza-

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tion to a variety of organic or biological molecules. We report here progress towards the goal of efficient polarization transfer through the use of supercritical solutions of organic solutes in hyperpolarized xenon. We note that others have studied hyperpolarized ^{129}Xe in the liquid [6,12] and supercritical [13] states as well as polarization transfer in liquid xenon [14].

Any technique for polarization transfer requires intimate contact between the nuclear spins; thus, we have investigated Xe as a solvent. While liquid Xe near the melt is a comparatively poor solvent, the solubilities of organic solutes increase at temperatures and pressures beyond the critical point (58 atm at 290 K) [15–17]. For example, the solubility of naphthalene is 5 mol % in supercritical Xe at 125 atm and 318 K [18]. The increased solubility at supercritical conditions comes at the cost of containing and handling high-pressure samples. Accordingly, a simple technique is presented for producing supercritical xenon solutions with little loss of xenon hyperpolarization. We note that rapid co-condensation of an organic vapor and the polarized xenon gas onto a cryogenic substrate offers a second route to forming intimately-mixed, solid spin systems, following the methods of matrix isolation and trapping [19]. Previous work in solid-state polarization transfer with hyperpolarized ^{129}Xe includes ^{129}Xe–^{131}Xe experiments [20] and exchange from ^{129}Xe to ^{13}C of CO_2 co-solidified in xenon [21]

2. Experimental

The apparatus used in our laboratory for optically pumping xenon is an in-house design. Rubidium vapor at 115°C is optically pumped by a 40 Watt diode laser array and transfers its electron spin polarization to ^{129}Xe nuclear spins [1]. The naturally abundant xenon is carried at 1% concentration in a continuously flowing stream of helium at 7 atm, together with 1% nitrogen buffer gas (to collisionally de-excite the Rb atoms). The flow rate is adjusted to yield a residence time in the polarizing cell of 120 seconds, approximately equal to the spin-exchange time constant. The helium serves to pressure-broaden the Rb absorption to more efficiently use the 2 nm linewidth of the laser. The polarized xenon is then frozen out of the stream in a reservoir immersed in liquid nitrogen in the field of a small permanent magnet (0.2 T). This type of flow apparatus has been described elsewhere [22]. We generally accumulate 2 millimoles of solid xenon at a polarization of approximately 5 to 10 percent in 20 minutes.

Our high-pressure samples are contained in standard-wall, 3 mm OD borosilicate tubes (1.6 mm ID). These tubes have held pressures in excess of 200 atm. They are inexpensive compared to the single-crystal sapphire tubes used by others [13,23], and they require no bulky valve for sealing the sample, being easily closed with a flame. Also, our essentially all-glass system eliminates metal surfaces that can de-polarize the spins. Pre-necking of the tubes aids the sealing. Treatment of the external surface of the glass with aqueous hydrogen fluoride, intended to remove small scratches, appears to reduce the fraction of failing tubes (about 10% at 150 atm). We have witnessed a wide variation of failure pressures; the occasional explosions necessitate wearing eye protection and gloves.

The polarized solid xenon in the accumulation reservoir is carried inside the field of the small permanent magnet to a large, 1 T electromagnet for polarization transfer in the strong fringe field (0.1–0.6 T). This holding field is employed because of its strength and large working volume for sample manipulation (approximately $20 \times 20 \times 20$ cm^3). The relaxation rate due to diffusion through this very inhomogeneous field is negligible here, being estimated as 3×10^{-4} s^{-1} from the expression $T_1^{-1} = DG^2/B^2$. Here D is the diffusivity, G is the field gradient, and B is the mean field strength [24]. The reservoir is attached to a calibrated volume, a vacuum valve, an electronic pressure transducer, and the 3 mm sample tube, all within the fringe field. The tube is pre-loaded with a small quantity ($<$ 2 mol %) of an organic sample (biphenyl or toluene). With the polarized xenon and organic both frozen in liquid N_2 baths, the calibrated volume and sample tube are evacuated. The reservoir is then immersed in tepid water; the xenon evaporates and expands into the calibrated volume. The desired amount of xenon is condensed into the high-pressure sample tube, solid xenon filling the portion of the tube immersed in liquid N_2. Finally, the tube is sealed with a torch. The average xenon density in the tube is determined from the pressure readings before and after condensation and from the tube dimensions (typically 5 cm long). The pressure is obtained from published xenon PVT data [25]; the presence of low-concentration solute makes these pressures slightly inaccurate.

We generally work at room temperature with xenon densities between 0.4 and 0.6 of the solid density (27 mol/L at the triple point) and at pressures between 80 and 180 atm. Under these conditions xenon is a fair solvent for many organics. We have visually observed biphenyl dissolving into supercritical xenon by the disappearance of the white, solid biphenyl. The transition to the fluid state was also observed by the dramatic decrease in the proton NMR linewidth.

Proton and ^{129}Xe NMR data were recorded in a 2.0 T electromagnet with ^{19}F NMR stabilization. The spectrometer is a home-built, superheterodyne design with a maximum of 25W transmitter power. For some measurements a doubly tuned, single-port probe (85.03 and 23.56 MHz for protons and ^{129}Xe, respectively) was used to sequentially inspect both resonances, with the frequency synthesizer switched repetitively. For other measurements a singly tuned probe used a RF coil long enough to cover the 5 cm long sample tube. This allowed inversion of the magnetization in the supercritical state and permitted unbiased comparison of magnetizations in the solid and supercritical states, despite the different densities, because all spins were inside the coil. We note that a long solenoid yields excellent uniformity of sensitivity and RF field. Measurements of ^{129}Xe magnetization inside the solid Xe reservoir were performed in a Hall-effect regulated 1.0 T electromagnet. Small tip angle pulses (1°–2°) were used for hyperpolarized ^{129}Xe, yielding good signals with negligible consumption of longitudinal magnetization (less than 0.1% per pulse).

3. Results and discussion

Dilute solutions of biphenyl or toluene (< 2 mol %) in hyperpolarized, supercritical xenon were prepared in 3 mm OD glass tubes. The ^{129}Xe longitudinal relaxation time T_1 was measured from the amplitudes of free-induction decays following small tip-angle pulses and ranged from 5 to 10 minutes, regardless of the presence of solute. These T_1 values are in accord with a previous estimate for neat supercritical xenon in a 0.8 mm ID borosilicate glass tube [13]. The T_1 values of solid xenon at 77 K and liquid xenon near the melt (165 K) are reported to be 142 min. and 31 min., respectively, with both values depending weakly on the strength of the magnetic field (for fields above 200 Gauss) and the liquid phase value depending also on surface characteristics [12,20]. Thus, negligible loss of magnetization should occur during sample manipulation, because the manipulations can be performed in times much shorter than T_1. Experimentally, we consistently find 66% of the original xenon polarization remaining after 1 cycle of freezing to solid at 77 K and returning to room temperature gas at 1 atm. The 34% loss is larger than expected from T_1 of the individual phases, suggesting that some of this loss is due to enhanced relaxation *at* the phase transition (as proposed by an anonymous reviewer). For the process of transferring the xenon from 77 K solid in the accumulation reservoir to supercritical fluid at room temperature in the 3 mm OD glass tube, the efficiency is about 50% (which involves thawing in the reservoir, freezing in the 3 mm tubing, and heating to supercritical conditions).

Proton and ^{129}Xe polarizations are reported in Fig. 1 for a biphenyl solution in supercritical xenon at room temperature. The xenon data were obtained

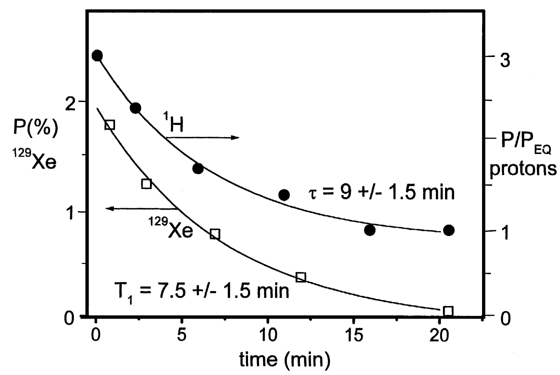

Fig. 1. ^{129}Xe and proton polarizations as functions of time for a dilute solution of biphenyl in highly polarized, supercritical xenon, sealed in a small glass tube. The vertical scale at left is absolute xenon polarization (open squares); the scale at right is the ratio of proton polarization to the thermal equilibrium value of 6.8×10^{-6} (filled circles). The time constants of the fitted, exponential decay curves are listed and are approximately equal.

every 3 minutes with a 2° RF pulse, which negligibly perturbed the remaining longitudinal magnetization. Proton signals were enhanced by the nuclear Overhauser effect with the polarized xenon [3]; proton signals were acquired with 90° pulses every ≈ 3 minutes, interleaved between xenon acquisitions. The initial xenon signal amplitude corresponds to an absolute polarization of 2.0 ± 0.5%, as determined by comparison with the proton signal of H_2O in the same apparatus at the same frequency (i.e., lower field strength). The xenon polarization decays with a time constant $T_1 = 7.5 \pm 1.5$ minutes, presumably decaying to the thermal equilibrium polarization of 1.8×10^{-6}, too small to be evident in Fig. 1. The maximum proton enhancement in this figure is a factor of 3. The proton signal decays to the equilibrium value with essentially the same time constant as the xenon signal, as expected.

The proton T_1 of the biphenyl solution was measured to be ≈ 20 s, using the traditional saturation-recovery-inspection method after the xenon polarization had fully decayed. The 3-minute delay between 90° proton pulses in Fig. 1 allows essentially full recovery of the proton polarization to its Overhauser-enhanced value, as sketched in Fig. 2. We note that the proton T_1 is much smaller than the Xe T_1. Further, the rate of xenon-proton cross-relaxation is negligible compared to the proton self-relaxation rate, as demonstrated by the small polarization transfer efficiency (see below). Fig. 2 also presents proton polarization enhancement data for a dilute solution of toluene in highly polarized, supercritical xenon at room temperature. Here the maximum enhancement is a factor of 7 compared to the equilibrium polarization in the 1.0 T field. The T_1 of the methyl protons in toluene was measured to be 7 s, while the ring protons had T_1 equal to 33 s. As expected, the longer T_1 results in preferential enhancement for the ring protons ($\times 9$ for ring, $\times 4$ for CH_3) [14,26,27]. Compared to liquid solutions, T_1 at supercritical conditions is generally longer because of the decreased viscosity and smaller rotational correlation times [28]. The appearance of xenon-proton Overhauser enhancements confirms the intimate contact between the spins in these supercritical samples. We note that larger enhancements of proton polarization, up to $\times 45$, have been reported in *liquid* xenon [14]. The larger enhancement in the liquid results from a larger initial ^{129}Xe polarization, isotopic enrichment to 71%, and no doubt more favorable correlation times. A factor of 70 enhancement for ^{13}C signal from CS_2 partly reflects the very weak self-relaxation in this single-spin molecule [14].

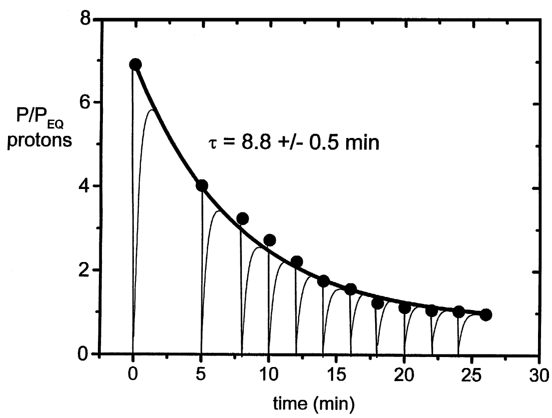

Fig. 2. Proton polarization enhancement for a dilute solution of toluene in highly polarized, supercritical xenon. The data (solid circles) are fitted to an exponential decay (heavy curve), with the time constant τ shown. The light curve is a conceptual sketch of the proton polarization, which is driven to zero by each 90° inspection pulse and recovers to the heavy curve with a time constant T_1 (taken here as 20 s).

An important result of the data in Fig. 1 is the polarization transfer efficiency. The specific level of enhancement achieved is of less interest, because it is proportional to the initial xenon polarization (our 2% is relatively low). We define the transfer efficiency η to be $\Delta I/\Delta S$, where ΔI and ΔS are the changes in absolute polarizations from their thermal equilibrium values for proton and ^{129}Xe, respectively. For the data presented in Fig. 1, η is $1.4 \times 10^{-5}/2 \times 10^{-2} = 0.7 \times 10^{-3}$. In terms of the Solomon-derived equation for steady-state Overhauser effect, one has

$$\frac{I_z - I_o}{I_o} = -\frac{\gamma_S}{\gamma_I}\frac{S(S+1)}{I(I+1)}\frac{\sigma_{IS}}{\rho_I}\frac{(S_z - S_o)}{S_o}. \tag{1}$$

Here I_o and S_o are proton and xenon equilibrium polarizations, respectively, σ_{IS} is the cross-relaxation rate, and ρ_I is the proton auto-relaxation rate [29]. The small transfer efficiency obtained in supercritical xenon solutions implies a small ratio σ_{IS}/ρ_I, that is, very little of the solute relaxation is due to solvent spins. While improvements in the initial xenon hyperpolarization will yield larger solute polarizations, the small transfer efficiency sets a substantial, fundamental limitation on the attainable results.

Thus, we believe that successful polarization transfer schemes will ultimately be performed in the solid state. For example, in the limiting case of dilute protons in a sea of ^{129}Xe spins, the polarization transfer efficiency of the Hartmann–Hahn technique can approach 100% [30]. Crucially, transfer in the solid state requires the solute to be dispersed in the xenon host (i.e., a solid solution). Rapid freezing of a supercritical fluid solution is one route, though the required rate of cooling is not known. While polarization transfer is likely to be much more efficient in the solid state, there is a multitude of reasons to choose the fluid state for NMR detection of the solute spins [31]. Many of the reasons result from the extremely narrow resonances in the fluid state, including the clean separation of multiple resonances (high resolution), the simplicity of spectral interpretation, and the increased signal-to-noise attendant upon a narrow bandwidth. There are also many well-developed multi-dimensional NMR techniques for the fluid state. Hence, we imagine experiments in which polarization is transferred in the solid, the sample is warmed to supercritical fluid conditions, and then the solute NMR signal is recorded.

A key issue is whether enhanced solute polarization would survive the transition from the solid to the supercritical fluid. This was tested by using a biphenyl-in-xenon sample with both proton and xenon magnetizations originally at thermal equilibrium. If we consider the magnetization m to be 1 for the protons at room temperature, then $m = -4$ was created by reducing the sample temperature by a factor of 4 (to 77 K), waiting many T_1's, and applying a π-pulse to protons with the sample in a coil longer than the sample (6 cm). In a separate experiment we confirmed that the inversion factor was between -0.9 and -1.0. The sample was then heated to become supercritical fluid by immersion of the tube in Fluorinert FC-77 at 320 K for approximately 15 s; the use of this fully fluorinated liquid avoids proton NMR signals from the fluid film remaining on the outside of the tube. Then, the magnetization was inspected by a $\pi/2$-pulse. The magnetization m was approximately equal to -0.2, implying a substantial fraction of the non-equilibrium solute magnetization remained in the supercritical fluid state. During the warm-up, the magnetization relaxed from its initial value of -4 towards an equilibrium value between $+4$ and $+1$, depending on the temperature at which the relaxation occurred. Thus the observed $m = -0.2$ represents between 52.5% and 24% of the initial non-equilibrium magnetization. Relaxation in the supercritical fluid accounts for much of the lost magnetization, since the proton T_1 was approximately 20 seconds for this sample. In any case, a significant amount of non-equilibrium proton magnetization survived the transition from solid to supercritical fluid.

4. Conclusions

We report here techniques and experimental results using hyperpolarized, supercritical xenon solvent for polarization transfer to an organic solute. Supercritical xenon solutions can be prepared reliably, safely, and easily by condensing the organic and the xenon into a glass tube, flame sealing, and then warming to room temperature, all in the fringe field of a magnet. A high fraction of xenon polarization survives the process. Nuclear Overhauser enhancements of the solute proton magnetization by factors of 3–7 are observed in room temperature solutions of biphenyl or toluene in hyperpolarized xenon (with polarizations of 2–5%), confirming the intimate contact between ^{129}Xe and ^{1}H spins. Because very little of the solute relaxation comes from cross-relaxation with the solvent, the polarization transfer efficiency is only about 10^{-3}.

Polarization transfer in the solid state is expected to be much more efficient; in the limit of dilute solute spins, the Hartmann–Hahn technique could ideally transfer 100% of the solvent polarization. Solution-state spectroscopy, however, yields excellent resolution and allows the arsenal of highly-developed, multi-dimensional solution-state NMR techniques to be employed. Thus, we address whether enhanced solid solute polarization would survive the transition to the supercritical fluid state. In experiments starting with thermal equilibrium solute polarization in the solid, the polarization was inverted and the sample warmed rapidly into the supercritical state, where an appreciable fraction of the non-equilibrium polarization was detected. Thus, the strategy of polarization transfer in the solid state and signal collection in the fluid state will be practical, especially with technical improvements to make the phase transition more rapid. This will be even more important with large solute molecules, owing to their longer rotational correlation times and correspondingly smaller T_1 values.

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