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Solution-State Dynamic Nuclear Polarization at High Magnetic Field

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The goal of dynamic nuclear polarization (DNP) is to enhance NMR signals by transferring electron spin polarization to the nuclei. Although mechanisms such as the solid effect and thermal mixing can be used for DNP in the solid state,[1,2] currently, the only practical mechanism in solutions is the Overhauser effect (OE),[3–5] which usually arises due to dipolar relaxation between the electrons and the nuclei. At magnetic fields greater than ~1 T, dipolar relaxation does not result in useful enhancements and therefore the conventional wisdom is that DNP should not work in solutions at high magnetic fields. However, scalar relaxation due to time-dependent scalar couplings has a different magnetic field dependence and can lead to substantial OE enhancements. Here we show that, at room temperature and at a magnetic field of 5 T (211 MHz for protons, 140 GHz for electrons), electron−nuclear scalar relaxation results in NMR signal enhancements in the range of 10−200 for several different nuclear spin species.

In solution-state NMR, dipolar couplings are averaged to zero by the rapid isotropic tumbling of the molecules. Although such couplings are not directly observed in the NMR spectrum, they still play a role in longitudinal relaxation. Couplings will induce relaxation between energy levels if (1) there exists a term in the coupling Hamiltonian connecting the levels and (2) the couplings are modulated on the same time scale as the transition frequency. For dipolar couplings, the source of this modulation is usually rotational and translational diffusion. Figure 1a shows an energy level diagram for a two-spin system; the arrows indicate the transitions induced by the dipolar Hamiltonian. The transition probabilities (W) specify the rate at which the energy levels return to equilibrium with one another; W_I, W_S, W_0, and W_2 correspond to the nuclear single-quantum, electron single-quantum, zero-quantum, and double-quantum transition probabilities.

In a manner similar to that for dipolar couplings, time-dependent scalar couplings that are not directly observed in the NMR spectrum can still influence the relaxation of the spin system. Whereas dipolar couplings are modulated by diffusion, scalar couplings are modulated either by rapid chemical exchange (scalar relaxation of the first kind) or by the rapid relaxation of one of the spins (scalar relaxation of the second kind). The terms in the scalar Hamiltonian induce only zero-quantum transitions. As a result, there is only a single transition, as illustrated in Figure 1b.

If the electron (S) transition is saturated by microwave irradiation, the steady-state enhancement of the nuclear (I) signal is:

$$f_I\{S\} = \frac{\gamma_S}{\gamma_I}\frac{\sigma}{\rho_I}$$

where γ_S and γ_I are the magnetogyric ratios of the electron and the nucleus, respectively. The electron−nuclear cross-relaxation rate (σ) and the nuclear longitudinal relaxation rate (ρ_I) can be written in terms of the transition probabilities:[5]

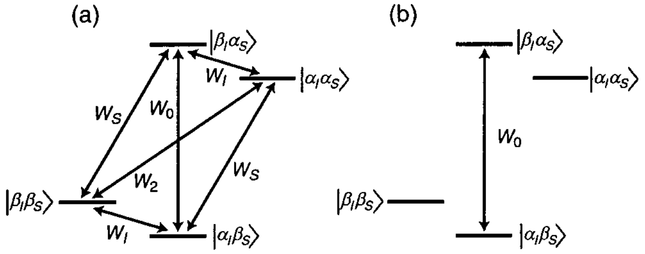

Figure 1. Energy level diagrams and transition probabilities, W, for an electron−nuclear spin system; the nuclear and electron spins are denoted I and S, respectively. The arrows illustrate the transitions that occur due to (a) dipolar relaxation and (b) scalar relaxation. It is assumed that I and S are both spin−$^1/_2$ and that the nuclear spin has a positive magnetogyric ratio (γ); for electrons, $\gamma < 0$, and therefore β corresponds to the lower energy spin state.

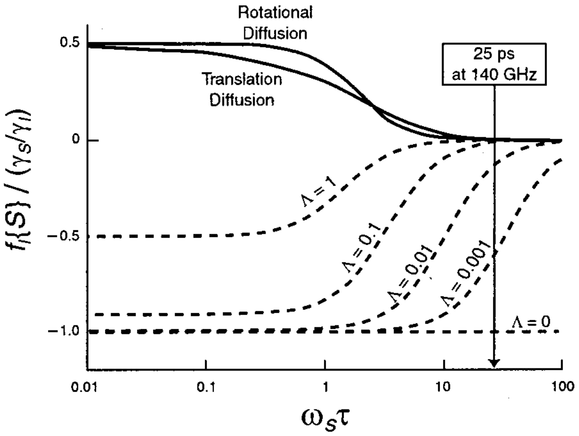

Figure 2. The Overhauser effect (OE) enhancement due to dipolar cross-relaxation depends on the correlation function for translational and rotational diffusion (solid lines). Note the ω_S is the electron Larmor frequency. At 140 GHz, even molecules with short correlation times ($\tau \sim 25$ ps) have only a small OE enhancement due to dipolar relaxation. Depending on the amount of leakage (Λ) from competing relaxation pathways, scalar relaxation can result in appreciable OE enhancements (dashed lines) even at high magnetic fields and/or long correlation times.

$$\sigma = W_2 - W_0 \quad \text{and} \quad \rho_I = W_2 + 2W_I + W_0$$

In the case of dipolar relaxation, the zero, single, and double quantum terms for σ and ρ_I are all present. For electron−nuclear dipolar relaxation at high magnetic fields (1 T and above), W_I is much larger than both W_2 and W_0 for correlation times (τ) that correspond to rotational and translational diffusion in regular solution-state NMR samples. Therefore, ρ_I is much greater than σ and the OE enhancement due to dipolar relaxation approaches zero (Figure 2, solid lines).

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Table 1. BDPA Concentrations, Nuclear Longitudinal Relaxation Times ($1/\rho_I$) and Steady-State Enhancements ($f_I\{S\}$) for the Samples Investigated

sample (nucleus observed)	[BDPA] (mM)	$1/\rho_I$ (in s)	$f_I\{S\}$
triphenylphosphine (^{31}P)	17(±2)	4.1(±0.2)	180(±5)
carbon tetrachloride (^{13}C)	40(±5)	11(±0.5)	40(±2)
aniline (^{15}N)	20(±2)	27(±1)	−36(±2)
hexafluorobenzene (^{19}F)	20(±3)	1.7(±0.1)	8.4(±0.4)

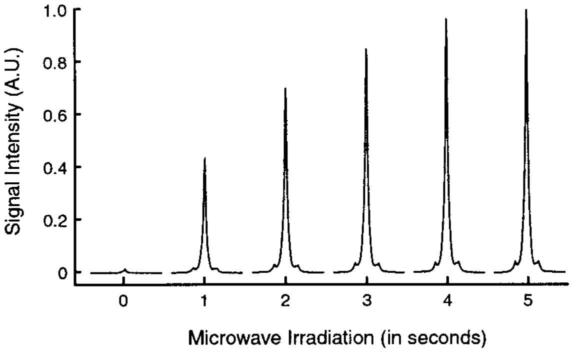

Figure 3. ^{31}P spectra of triphenylphosphine in deuterated benzene with BDPA as a function of the length of microwave irradiation prior to the acquisition of the NMR signal. The line width at half-height is 1.6 Hz.

In the case of scalar relaxation, only the zero quantum terms are present in σ and ρ_I. However, it is more realistic to include the effect of competing relaxation mechanisms that reduce the OE enhancement. The competing mechanisms will affect the single quantum transition probability and, consequently,

$$\sigma = -W_0 \quad \text{and} \quad \rho_I = W_0 + \Lambda W_I$$

where Λ indicates the contribution of the competing relaxation mechanisms to the nuclear longitudinal relaxation rate. If ΛW_I is smaller than W_0, the OE enhancement due to scalar relaxation is appreciable, even at high magnetic fields (Figure 2, dashed lines).

Although electron−nuclear dipolar relaxation will occur in any NMR sample containing a radical, scalar relaxation is relatively rare because it requires a time-dependent scalar coupling. For scalar relaxation of the first kind, this means that there must be an orbital at the nucleus in question that has *s*-character and that is accessible to the radical electron. OE enhancements due to scalar relaxation have been observed at low magnetic fields for a large number of systems;[6−8] here we show that, for several of these systems, there is still an appreciable enhancement at a high magnetic field due to scalar relaxation of the first kind.

All experiments were conducted at room temperature on a 5 T (211 MHz for ^{1}H, 140 GHz for e$^-$) NMR spectrometer. The pulse sequence used consisted of a period of microwave irradiation followed by a single ($\pi/2$) radio frequency pulse and observation of the NMR signal. The 140 GHz microwave irradiation (~0.5 W) was generated using a cyclotron resonance maser (gyrotron).[9] The molecules studied were triphenylphosphine (Ph$_3$P), carbon tetrachloride (^{13}CCl$_4$), aniline ($C_6H_5{}^{15}NH_2$), and hexafluorobenzene (C_6F_6). These were dissolved along with the stable radical α,γ-bisdiphenylene-β-phenylallyl (BPDA) in deuterated benzene; the BDPA concentrations are given in Table 1. All samples were degassed using an oxygen scavenger (triphenylphosphine); this reduced the competing relaxation mechanism of dipolar relaxation due to dissolved molecular oxygen.

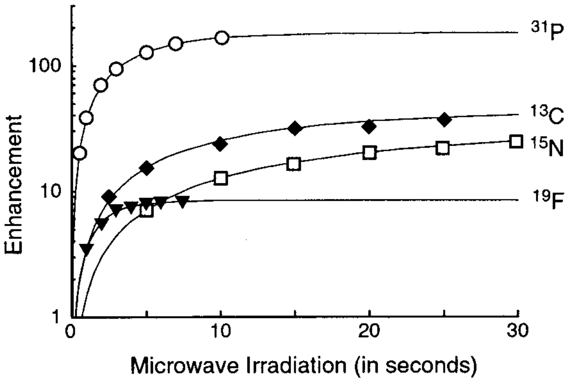

Figure 4. The NMR signal enhancement as a function of the length of microwave irradiation prior to signal acquisition for the triphenylphosphine (^{31}P, open circles), carbon tetrachloride (^{13}C, solid diamonds), aniline (^{15}N, open squares), and hexafluorobenzene (^{19}F, solid triangles) samples described in the text. The solid lines are derived by fitting the experimental data to the Solomon equations;[5] the fitting results are given in Table 1. For the ^{15}N data the absolute value of the enhancement is shown; the enhancement is negative because $\gamma < 0$ for ^{15}N.

The signal intensity of the ^{31}P spectrum of the Ph$_3$P sample as a function of the length of microwave irradiation is shown in Figure 3. The positive signal enhancement is indicative of scalar relaxation; dipolar relaxation would result in a negative enhancement. Although the presence of the BDPA radical in the system reduces the transverse relaxation time (T_2) for the nuclear spin, this does not result in a noticeable change in the NMR spectrum because the ^{31}P T_2 is still long enough (>2 s) that the line shape is primarily due to magnetic field inhomogeneities.

In addition to Ph$_3$P, we have also examined the ^{13}C, ^{15}N, and ^{19}F spectra of ^{13}CCl$_4$, $C_6H_5{}^{15}NH_2$, and C_6F_6 and obtained enhancements of 42, −36, and 8 for ^{13}C, ^{15}N, and ^{19}F, respectively. The enhancement as a function of the microwave irradiation time for all the systems investigated is shown in Figure 4; the relaxation times and the steady-state OE enhancements derived from these data are summarized in Table 1.

For ^{1}H, a small negative OE enhancement due to electron−nuclear dipolar relaxation is observed. This enhancement, which is ~−0.5, *reduces* the NMR signal and, consequently, is of no use for DNP at magnetic fields of 5 T and higher.

Electron−nuclear scalar cross-relaxation results in large signal enhancements, even at fields of 5 T, and is therefore of interest for the purpose of enhancing the signal in high-resolution NMR spectrometers. Currently, we are exploring the applicability of the scalar OE at 9 T (380 MHz for ^{1}H) as well as to other molecules and nuclei. Ultimately, we hope to extend this work to aqueous samples since it would then be possible to enhance signals in biological samples.

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