Hyperpolarization storage at different magnetic field on perdeuterated parahydrogenated molecules for MRI application

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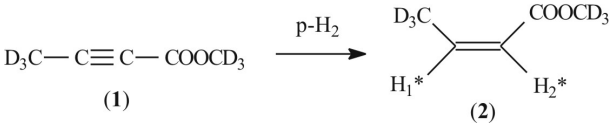
Introduction

The application of hyperpolarized molecules as MRI contrast agents is gathering increasing attention. Two methods are used to achieve hyperpolarization, namely DNP and ParaHydrogen Induced Polarization. The application of both is strongly limited by polarization decay rate, which tends to restore the equilibrium population of spin levels in times dictated by the relaxation time constant T_1. The most common way to slow down polarization decay on parahydrogenated molecules is the use of deuterated substrates. Recently [1] another more efficient method has been introduced to store polarization for times longer than T_1: it is based on the fact that transitions from singlet states are not allowed by selection rules.
Here we report the effect of both deuteration and singlet state maintenance on polarization decay rate of parahydrogenated but-2-enoic acid methyl ester (**2**). The application of this molecule as MRI contrast agent has already been explained [2]. In order to assess the effect of singlet state maintenance on polarization decay rate, the relaxation rates at earth magnetic field (50 μT) is compared with those at high field (14 T, NMR spectrometer) and zero field (0.1 μT).



(**1**) (**2**)

Materials and methods

The relaxation rate of **2** at earth magnetic field was measured as follows:
1) the parahydrogenation (p-H_2=50%) of **1** was carried out in a 5 mm NMR tube provided with Teflon Young valve by vigorous shaking (10 s) at earth magnetic field (50 μT);
2) the NMR tube was quickly opened to release the non reacted hydrogen and then kept for a time delay (τ) at 50 μT;
3) the sample was placed into the spectrometer (600 MHz) and a ^{1}H NMR spectrum was acquired.
The whole process was repeated varying the time τ from 60 to 420s: the resulting ^{1}H-NMR spectra are reported in figure 1.
Polarization decay rates were derived by reporting the mean intensities of the polarized signals as a function of the exposure time at each magnetic field.
The polarization decay at 0.1 μT was measured using the same procedure, keeping the parahydrogenated sample inside a μ-metal cylinder (figure 1, right).
The relaxation time constant T_1 inside the spectrometer was measured using the inversion recovery sequence.

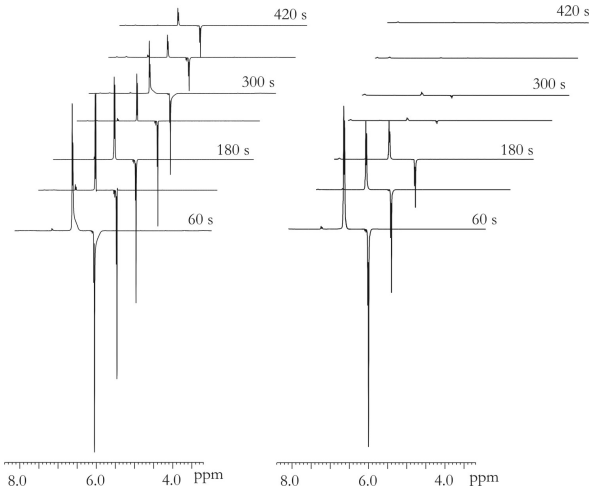


Figure 1: ^{1}H polarized signals of **2** at increasing time delays for samples kept at 50 μT (left) and at 0.1 μT inside the magnetic field shield (right).

Results and discussion

In the parahydrogenation of **1** the two protons are added in chemically different environments and parahydrogen symmetry is lost. However, when the sample is kept at low magnetic field (earth field 50 μT) the two protons resonance is the same, therefore the singlet state is maintained. In fact the T_1 for hyperpolarized protons at 50 μT was 100 s, considerably longer than the relaxation time measured at high magnetic field inside the spectrometer (21 s).
Unexpectedly, when the magnetic field strength is decreased to 0.1 μT, T_1 diminishes to 42 s. This is due to isotropic mixing between protons and deuterium nuclei which takes place at zero field.

Conclusions

Deuteration and singlet state allows obtain an exceptionally long relaxation time. However, when deuterium nuclei are scalarly coupled with parahydrogen protons, magnetic field strength must be carefully chosen in order to avoid isotropic mixing between ^{1}H and ^{2}H.

[1] M.Carravetta, O.G.Johannessen and M.H.Levitt *Phys. Rev. Lett.* **92**, 153003 (2004)
[2] W. Dastrù, A.Viale, D.Santelia, F.Reineri, R.Napolitano, R.Gobetto, S.Aime, ISMRM 16th Scientific Meeting, 2008, Poster presentation