



High resolution para-hydrogen induced polarization in inhomogeneous magnetic fields

L. Buljubasich^a, I. Prina^a, M.B. Franzoni^b, K. Münnemann^b, H.W. Spiess^b, R.H. Acosta^{a,*}

^aFAMAF Universidad Nacional de Córdoba, IFEG CONICET, X5016LAE Córdoba, Argentina

^bMax Planck Institute for Polymer Research, Ackermannweg 10, 55128 Mainz, Germany

ARTICLE INFO

Article history:

Received 27 December 2012

Revised 28 January 2013

Available online 21 February 2013

Keywords:

Parahydrogen

Hyperpolarization

Enhanced NMR

PHIP

PASADENA

J-spectrum

Inhomogeneous Fields

CPMG

ABSTRACT

The application of parahydrogen for the generation of hyperpolarization has increased continuously during the last years. When the chemical reaction is carried out at the same field as the NMR experiment (PASADENA protocol) an antiphase signal is obtained, with a separation of the resonance lines of a few Hz. This imposes a stringent limit to the homogeneity of the magnetic field in order to avoid signal cancellation. In this work we detect the signal arising from hyperpolarized Hexene by means of a CPMG pulse train. After Fourier transformation the obtained *J*-spectra not only presents an enhanced spectral resolution but also avoids partial peak cancellation.

© 2013 Elsevier Inc. All rights reserved.

1. Introduction

Nuclear Magnetic Resonance (NMR) has become a very powerful technique than can be applied in different fields encompassing physics, chemistry, biology and medicine among others. Despite its widely recognized advantages, NMR suffers from extremely low sensitivity due to the low polarization achieved by thermal equilibrium with an external magnetic field. Several methods have been implemented to obtain metastable states with polarization levels that can be orders of magnitude higher than thermal. Among these so called hyperpolarization methods, the hydrogenation of substrates with parahydrogen has grown significantly in the last years. Para-Hydrogen Induced Polarization (PHIP), involves a chemical reaction in which molecules of hydrogen gas enriched in the para-state (*p*-H₂) are deposited into an unsaturated precursor, prior to the NMR signal acquisition [1,2].

PHIP experiments have found different applications within the NMR community [3], including the study of kinetics of inorganic reactions [4–6], research of heterogeneous reactions [7] and the introduction of new MRI contrast agents [8–12]. Additionally, hyperpolarization transfer via special pulse sequences [13,14], by diabatic field cycling [15] or by transport through level avoiding

crossing have been implemented [16–18] along with the study of long lived states originated from *p*-H₂ [19–22].

The set of PHIP experiments is split into two subsets depending on the experimental protocol used. When the hydrogenation reaction and the NMR experiment are performed at the same magnetic field the process is referred to as PASADENA [1] (PArahydrogen and Synthesis Allow Dramatically Enhanced Nuclear Alignment). On the other hand, if the chemical reaction is performed at low magnetic field, followed by an adiabatic transport of the sample to a high magnetic field for signal detection, the process is called ALTA-DENA [2] (Adiabatic Longitudinal Transport After Dissociation Engenders Net Alignment). Polarization can be enhanced typically by several orders of magnitude with both methods.

Signals arising from PHIP hyperpolarization differ not only by the signal from those obtained from samples at thermal equilibrium at the same magnetic field. Consider, for instance, that both hydrogen nuclei that originally belong to the *p*-H₂ molecule (labelled 1 and 2) occupy chemically inequivalent sites in the target molecule, after a pairwise hydrogenation process has taken place. If their chemical shift difference, $\Delta\nu$, is much larger than the coupling constant J_{12} and we neglect coupling to other nuclei in the molecule, an isolated AX spin system is created. In PASADENA conditions, the resulting spectrum presents two anti-phase doublets with splitting equal to their coupling constant, whereas at thermal equilibrium two in-phase doublets are present. The anti-phase doublet in PASADENA is associated with the presence of a

* Corresponding author. Fax: +54 3514334054.

E-mail addresses: racosta@famaf.unc.edu.ar, rodolfoacosta@gmail.com (R.H. Acosta).

longitudinal two-spin order term in the density operator, of the form $I_1^z I_2^z$ [23,24].

The difference between anti- and in-phase doublets is crucial when the magnetic field homogeneity is limited. As the homonuclear coupling constants are of the order of few Hz in liquid samples, even relatively high homogeneous magnetic fields can produce partial signal cancellation in PASADENA experiments, thus diminishing the method's applicability. It is worth noticing that linebroadening not only refers to the homogeneity of the external magnetic field, but also to susceptibility changes introduced either by the sample itself or by the experimental setup.

The straightforward solution to overcome this drawback consists in performing the NMR experiments in extremely homogeneous magnetic fields, combined with sample setups that avoid susceptibility disturbances. This last condition imposes severe limitations in the variety of experiments that can be carried out in PASADENA conditions, such as MRI experiments with heterogeneous samples or the dilution of p-H₂ enriched gas via hollow-fiber membranes for instance [25].

At this point, a very important distinction between signal cancellation due to magnetic field inhomogeneities and initial absence of signal after a radiofrequency pulse must be made. Due to the structure of the PASADENA operator, the initial free induction decay (FID) is zero, and builds up due to evolution with J -couplings. If a waiting period, or J -coupling delay, is introduced after the excitation pulse the anti-phase doublet will evolve to an in-phase doublet. In other words, the intensity of the signal in the time domain will increase [24,26]. The introduction of a spin-echo, with a proper echo time, will refocus magnetic field inhomogeneities, therefore mitigating the attenuation of the top of the echo. Spin echoes in combination with J -coupling delays have been successfully implemented for instance in PHIP-MRI for monitoring chemical reactions [11], as contrast agents [12], in time domain NMR at low fields [27], to study relaxation time of hyperpolarized states [28] or in combination with selective frequency pulses for COSY experiments [29] among others. Nevertheless, no gain in spectral resolution can be achieved with these methods.

In the present work we apply the well-known J -Spectrum technique proposed by Freeman et al. in 1971 [30] to PHIP signals in PASADENA condition. The technique consists in the application of an echo train, where only the top of the echoes are acquired. By introducing suitable digital filters we show that not only partial signal cancelling is achieved, but also a significant enhancement of the spectral resolution for each individual multiplet in hyperpolarized samples can be obtained.

2. Theoretical background

Initially we consider an AX system subject to the application of a CPMG pulse train. By properly selecting the pulse repetition rate, as discussed below, the nonsecular part of the J -coupling Hamiltonian can be neglected and the secular part is unaffected by 180° pulses, thus the magnetization decay will appear modulated [24,31]. If the top of the successive echoes are recorded and Fourier transformed a J -spectrum is obtained, where the linewidth is proportional to $(\pi T_2)^{-1}$, essentially independent of magnetic field inhomogeneities. In the particular case of two isolated spins, the J -spectrum will consist of a doublet centred at zero frequency with a splitting equal to the J -coupling constant, because both doublets from the AX spin system collapse at the same frequency. In larger spin systems, detailed information of coupling constants can be obtained through a J -spectrum. For example, the determination of long range J -coupling constants of simple esters as methyl acetate, ethyl acetate, isopropyl acetate among others, were obtained with high accuracy [32].

In order to get pure J -spectra, with the resonance lines only related to the coupling constant, several conditions must be fulfilled: (i) the magnetic field must be strong enough to ensure first order approximation for the couplings, i.e. weak coupling limit, (ii) the pulse repetition rate must be small compared to the smallest chemical shift difference, (iii) the 180° pulses must be carefully adjusted, and (iv) any other possible source of modulation, e.g. chemical exchange, must be absent [30].

Violation of the conditions listed above lead to different consequences. For instance, if the spin system is strongly coupled, new frequencies will be present in the echo-train envelope. If the echo time is too long the resonance positions are shifted, whereas if the repetition rate is too high all J -modulations vanish. If the pulses are not set with enough accuracy, new resonances at frequencies related to the chemical shifts show up. In any of these cases the spectrum of the echo-train envelope can be classified as *spin-echo spectrum* instead of a J -spectrum [30]. The method is of course not restricted to simple AX systems, in fact, closed formulas for AB, A₂B, A₃B [33] and A_qBX_x spin systems [34] have been reported.

In the present work we restrict ourselves to the study of J -spectra. Even in this case, the response of multispin systems can become quite complex, nevertheless an elegant alternative was suggested by Freeman and Hill in 1971 [30]. In their work, they proposed to split the J -spectrum in subspectra by filtering the undesired frequency components during the acquisition of the echo maxima. The method consists in the application of hard 180° pulses centered at the resonance frequency of the desired multiplet, with digital filtered acquisition of the echo train. The authors have suggested to refer to this filtered data as *partial J-Spectra*.

3. Results and discussions

3.1. Partial J -spectra in inhomogeneous magnetic fields.

The setup performance was tested in ethanol, due to the simplicity of its NMR spectrum. The experiments were carried out with the excitation pulse set to 45° followed by an train of 180° pulses in order to reproduce the measurement conditions with p-H₂ hyperpolarized samples. The phases of the refocusing pulses were alternated in blocks of two as (yyyy). Possible artifacts in the spectra due to the use of the initial 45° instead the usual 90° pulse were tested by simulations, where off-resonance effects were incorporated to the pulses.

Fig. 1A displays a simulated NMR spectrum with high resolution, along with the partial J -spectra of the methylene and methyl group respectively. The partial J -spectra were simulated by evolving the density operator with the Hamiltonian $\mathcal{H} = \mathcal{H}^{CS} + \mathcal{H}^d$ where only the secular part of the J -coupling Hamiltonian was retained.

Experimental results are summarized in Fig. 1B–D, where the inhomogeneity of the magnetic field is systematically increased by gradually introducing a field gradient via the Z-coil of the shimm system. Horizontal lines in Fig. 1B indicate the center of irradiation and the 1 kHz digital bandwidth used for each multiplet. The expected increase of the spectral resolution in the partial J -spectra is evident. The agreement between the simulated and experimental J -spectra are independent of the field inhomogeneity as expected. Small artifacts due to off resonance effects in the 180° can be observed in the simulations as well as in the experimental data. For all experiments the echo time was set to $t_e = 8$ ms, resulting in a frequency window of 125 Hz, to ensure that the majority of artifacts due to pulse errors lie far from the region of interest.

3.2. Partial J -spectra in PHIP

We now turn our attention to the acquisition of partial J -spectra in PHIP hyperpolarized samples, in particular for the PASADENA

Download English Version:

<https://daneshyari.com/en/article/5405702>

Download Persian Version:

<https://daneshyari.com/article/5405702>

[Daneshyari.com](https://daneshyari.com)