

Long-Lasting ^1H -Hyperpolarization in Molecules

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Introduction

Parahydrogen-Induced Polarization (PHIP) yields strong nuclear spin polarization^[1] of protons and heteronuclei including ^{13}C . Using the relatively long T_1 relaxation times of quaternary carbons, ^{13}C -MRI angiography has already been successfully demonstrated in animals^[2]. Following a concept first proposed by Levitt, et al.^[3], we hypothesized that certain nearly-symmetric molecules may experience greatly decreased relaxation rates to thermal equilibrium under conditions of low field (and thus decreased chemical shift anisotropy) and the singlet-like pairing achievable by homogeneous hydrogenation with parahydrogen. We present a demonstration of this effect.

Methods

We prepared approximately 1 ml samples of suitable unsaturated precursors mixed with acetone and various cationic catalysts in NMR tubes. Into each tube, we introduced 2-3 bar of 97% parahydrogen, first at high field (inside the 200 MHz spectrometer), then at low field. The low field cases were further subdivided into samples maintained at low field until immediately before measurement, and those inserted into the spectrometer after a 20 second hydrogenation time. NMR spectra were then acquired with different waiting times, and typical results (for hydrogenation of phenylpropionic ethylester) are displayed in the Figure.

Results and Discussion

We find that in all cases, the relaxation rate to thermal equilibrium is slower for samples maintained at low field. As seen in the Figure, this increase can be very large (from 50 to approximately 200 seconds). When investigating the *a priori* requirements for extending the lifetime of the ^1H -hyperpolarization, we found that the physical properties—for example the shape of the magnetically labelled substance—play a significant role. If the ^1H -hyperpolarization hydrogenation products are almost symmetrical, they exhibit rather long spin-lattice relaxation times, especially when kept after their initial generation at low magnetic fields as long as possible. Systems which satisfy this requirement are for example slightly asymmetric diesters of maleic or fumaric acid, also parahydrogenated asymmetric derivatives of acetylene dicarboxylic acid, or the monoesters of phenylpropionic acid, hydrogenated to the corresponding cinnamic ester. Each of these substances exhibits decreases of between a factor of 2 and 5 in spin-relaxation rate.

Conclusions

We have measured a greatly decreased rate of relaxation to thermal equilibrium of nearly symmetric molecules. This result has several possible applications to hyperpolarization, because time scales of several minutes are much more compatible with both biological processes and hydrogenation rates of several important catalysts, than the sub-minute rates typical of most protonated molecules. For this reason, we expect this result to aid in heteronuclear polarization transfer as well.

References

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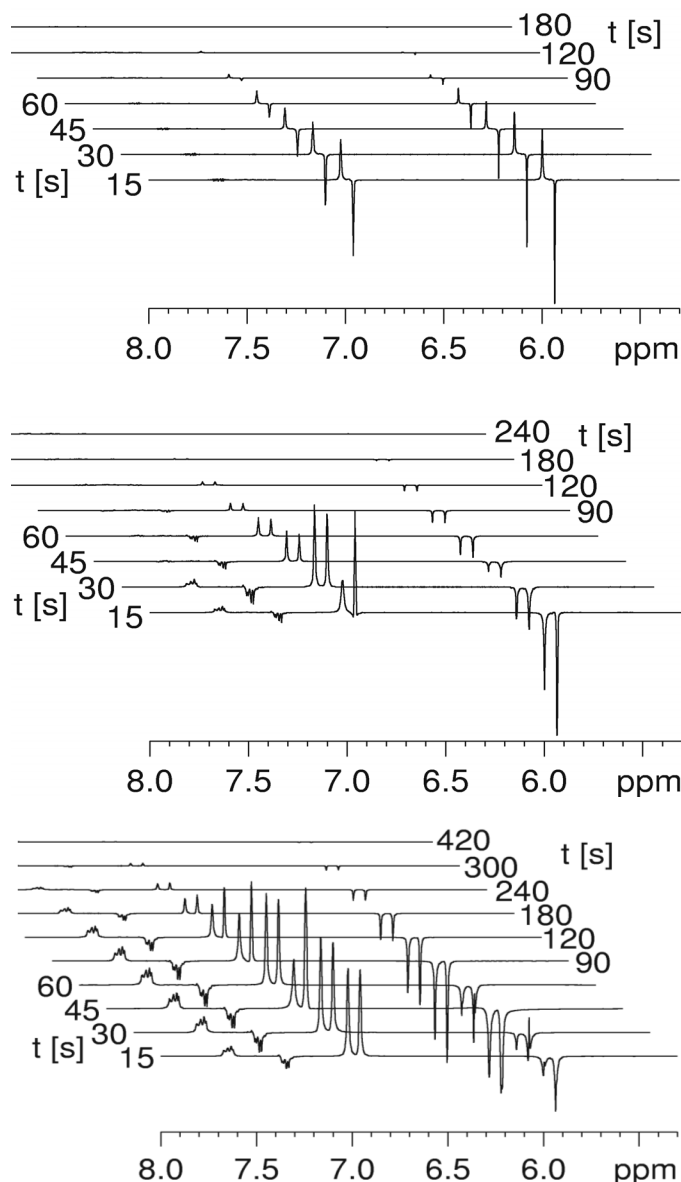


Figure: Aromatic and olefinic region of the ^1H -PHIP NMR spectra recorded during the para-hydrogenation of phenylpropionic ethylester after different delays: Top: Reaction conducted at high field, in situ recording with no delay. Center: Reaction conducted at low field, recording with delay after storage at high field. Bottom: Reaction conducted at low field, recording with delay after storage at low field.