Generating 1H- and 13C-Hyperpolarized Molecular Probes of Variable Size from Parahydrogen to Explore the Lung via MRI

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Introduction

Simple alkanes like cyclopropane qualify as inhalation narcotics. In principle, the Parahydrogen-Induced Polarization (PHIP)[1] phenomenon is qualified to hyperpolarize a variety of target molecules and nuclei, however, cyclopropane itself is very difficult to ^{1}H-hyperpolarize, because of a lack of a suitable precursor. However, its methyl-substituted derivative, methylcyclopropane, can be both ^{1}H- and ^{13}C-hyperpolarized from methylenecyclopropropane via PHIP. The same holds for the homologous series of the larger methylenecycloalkanes even past methylenecyclohexane. Their increasing size renders them attractive as molecular probes to explore and measure the size of cavities within the lung using PHIP-MRI. Also, ^{1}H- and ^{13}C-hyperpolarized ethylene or ethane can be obtained via PHIP from acetylene or ethylene, respectively.[2]

Results

This system yields strong proton polarization when following the reaction scheme outlined in Figure 1. From the samllest member of this homologous series, methylenecyclopropane, however, some straight-chain side products result (due to ring opening) in addition to the wanted methylcyclopropane. These side products can be suppressed using a different catalyst. The higher methylenecycloalkanes are better behaved. This is evident in Figure 2, showing the ^{1}H-PHIP spectra obtained when conducting the reactions at low or high magnetic fields, respectively, namely the parahydrogenation of methylenecyclopentane in a 6 : 1 mixture of D_2O and $CDCl_3$. In this case, methylcyclopentane is formed as the only hydrogenation product.

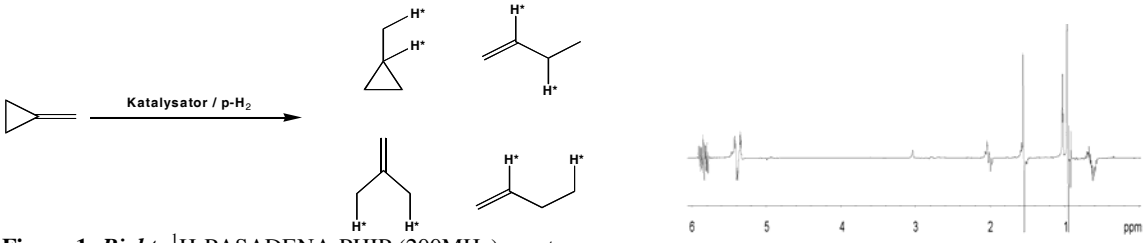

Figure 1: ***Right:*** ^{1}H-PASADENA-PHIP (200MHz) spectrum obtained during the hydrogenation of methylenecyclopropane (MC) to methylcyclopropane with a cationic catalyst.
Left: Reaction scheme outlining the parahydrogenation of MC .

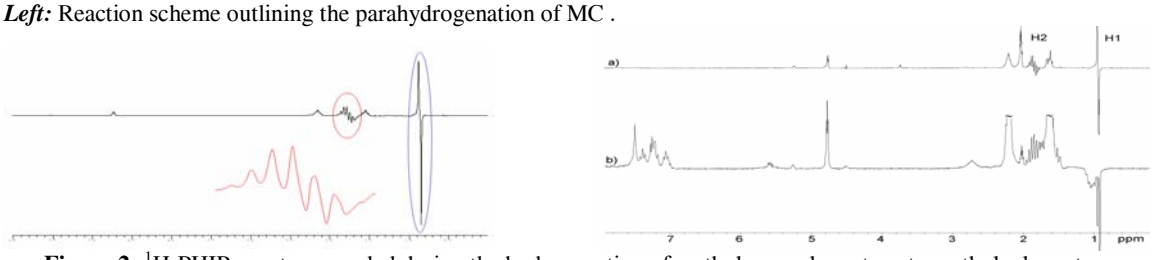

Figure 2: ^{1}H-PHIP-spectra recorded during the hydrogenation of methylenecyclopentane to methylcylopentane (200 MHz, 5 bar, room temperature) a) PASADENA, b) ALTADENA conditions

Discussion and Conclusions

^{1}H- and ^{13}C-hyperpolarized molecular probes can conveniently be obtained via parahydrogenation of the homologous series of methylenecycloalkanes. Their staggered sizes allows to determine the shape and the dimensions of cvities in a variety of environments, including those within the lung.

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2.) S. Aime, R. Gobetto, F. Reineri, D. Canet, J. Chem. Phys. **2003**, 119, 8890-8896