Transfer of Parahydrogen-Induced Polarization to 19F:

J. Bargon[1], U. Bommerich[2], L. T. Kuhn[3], R. R. Rizi[4]

[1]Institute of Physical Chemistry, University of Bonn, Bonn, Germany, [2]Leibniz-Institute for Neurobiology, University of Magdeburg, Magdeburg, Germany, [3]Physical and Theoretical Chemistry Laboratory, Oxford University, Oxford, United Kingdom, [4]University of Pennsylvania Medical Center, Philadelphia, PA, United States

Introduction

Parahydrogen-Induced Polarization (PHIP)[1] leads to strong signal enhancement in ^{1}H-NMR if unsaturated substrates are hydrogenated with parahydrogen (p-H_2) applying an appropriate catalyst. As shown before, this polarization can be transferred to heteronuclei such as ^{13}C.[2] For imaging the lung, a ^{19}F-hyperpolarized contrast agent should be available, if possible for inhalation. Normally, this demands aerosols; however, fluorinated gases[3] may also qualify.

Experimental

To explore the feasibility of this concept, we have chosen 1,1,1,2,2-H-perfluorohexane (I) as an exploratory target molecule. This product, which is structurally similar to components of artificial blood such as 1-bromoper-fluorooctane. I has been generated from an olefin with a perfluorinated alkyl chain, namely from 1,1,2-H-perfluoro-1-hexene (II).

Results

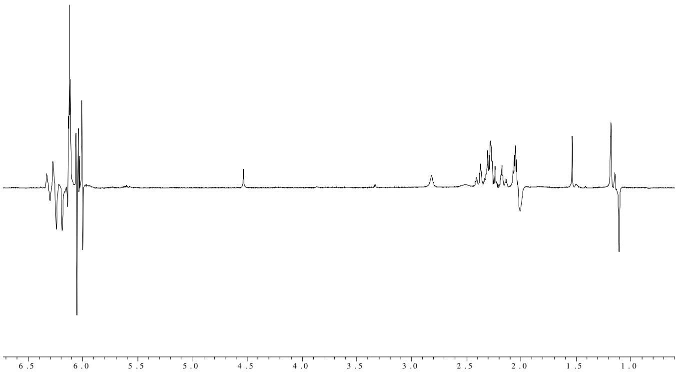

Figure: ^{1}H-PHIP NMR spectrum (200 MHz) recorded *in situ* upon hydrogenating 1,1,2-H-perfluoro-1-hexene.

The figure shows the ^{1}H-PHIP NMR spectrum recorded while hydrogenating II with 97% parahydrogen within the 4.7 T magnetic field of the 200 MHz ^{1}H-NMR spectrometer. Since the hydrogenation has been conducted at high field, the ^{1}H PHIP spectrum exhibits antiphase resonance lines.To qualify for MRI purposes, this reaction has to be carried out at low or zero field to obtain net polarization (i.e., all the resonance lines of one and the same multiplet have to appear exhibiting only emission or enhanced absorption).

Discussion and Conclusions

Already the high-field hydrogenation results confirm that it is indeed possible to obtain ^{1}H-polarization; therefore, - at least in principle, - the transfer of polarization to the ^{19}F nuclei in I should be straightforward. We have found, however, that this characteristically depends on the distribution of the ^{19}F and initially polarized ^{1}H in the hydrogenation product, rendering structural isomers suitable for the purpose to a different degree, due to different molecular shapes and associated dipolar coupling. ^{19}F-hyperpolarized contrast reagents for inhalation should have both a high initial degree of polarization and sufficiently long relaxation times (T_1). For hydrocarbons in the gas phase, this is typically not the case. However, for certain fluorinated compounds Kating and coworkers have demonstrated that under appropriate conditions the T_1 of perfluorocarbons (PFC) are sufficiently long to render even NMR investigations in the gas phase feasible.(3) PFC aerosols could allow administering the ^{19}F-hyperpolarized agent and enable simultaneous analysis of the lung structure and of pulmonary oxygenation patterns. Techniques to nebulize and administer neat liquid PFCs have been developed and tested successfully in an experimental rat model.[4] Pneumatic aerosol generators were configured to produce a neat liquid PFC perfluorotributylamine (FC-43) aerosol, and the PFC aerosol delivery into the rat lung was documented through ^{19}F-MRI in correlation with high-resolution anatomic proton MR images. Potentially, hyperpolarized PFCs might perhaps be administered as liquids. Partial liquid ventilation[5], namely, using PFCs is an innovative treatment of acute respiratory distress syndrome. The aim thereof is to investigate the distribution of oxygen partial pressure within the PFC-filled lung (ppO_2). Or preliminary findings suggest that in principle generating ^{19}F-hyperpolarized contrast agents for inhalation to image the lung using ^{19}F MRI is feasible.

References

[1] Natterer J et al. Parahydrogen induced polarization. Prog Nucl Mag Res 1997; 31: 293-315.
[2] Golman K et al. Parahydrogen-induced polarization in imaging: Subsecond C-13 angiography. Mag Res Med 2001; 46:1-5.
[3] Laukemper-Ostendorf S et al. ^{19}F-MRI of perflubron for measurement of oxygen partial pressure in porcine lungs during partial liquid ventilation. Magn Reson Med 2002; 47: 82-89.