

First step to ^{19}F Hyperpolarization of Biocompatible Substrates Generated via Parahydrogen-Transfer

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Introduction

A complete lack of natural background signal in body tissues and advantageous MR characteristics like a 100% natural abundance and 84% MR sensitivity in comparison to ^1H qualify fluorinated substrates as preminent reporter molecules for MRI- and MRS-investigations. Even the simultaneous detection of multiple signals from separate molecules in MRS investigations is facilitated by a wide chemical shift range. However, an effective signal enhancement is advantageous for a successful application of such agents as a diagnostic tool as their concentration usually is limited *in vivo*. PHIP hyperpolarization (ParaHydrogen Induced Polarization¹) is a promising strategy towards MR-based molecular imaging and first images of a ^{19}F hyperpolarized substrate as a model compound could be obtained². A prerequisite for an implementation of this method in living systems is the biocompatibility of these contrast agents. Many pharmaceuticals contain a fluorine atom allowing detection of pharmacokinetics and their metabolism. Even passive substrates like perfluorinated alkanes can be used to investigate anatomical properties such as lung volume. In this contribution we chose a semi-fluorinated alkane as an exemplary, physiologically compatible target molecule. The characteristics of semi-fluorinated alkanes are similar to perfluorinated alkanes. They show an enhanced solubility for oxygen and are nontoxic. Thus they could be used as passive contrast agents. In analogy to perfluorinated alkanes they might also be applied for *in vivo* monitoring of inflammatory processes³.

Method and Results

^1H -hyperpolarization based on the PHIP-effect can be transferred to hetero nuclei such as ^{13}C , ^{31}P , or ^{19}F . The applicability of ^{13}C hyperpolarized substrates for MRI investigations is already proved⁴. So far the successful hyperpolarization transfer to ^{19}F is only documented for a class of closely related aromatic systems⁵. Initial experiments showed that Imaging of hyperpolarized ^{19}F nuclei, using one of those systems, is also feasible². In order to extend this method to biocompatible substrates we chose (perfluoro-n-hexyl)acetylene parahydrogen transfer to this unsaturated compound (fig. 1) using a Rh-catalyst for homogeneous hydrogenation generates the ^1H hyperpolarized substrate. We selected the mentioned substrate because in reactions of this kind high conversion rates for triple bond systems can be expected. Under low field conditions hyperpolarization is transferred to the ^{19}F nuclei of the corresponding reaction product. Figure 2 shows two magnitude spectra, obtained during the hydrogenation of (perfluoro-n-hexyl)acetylene yielding (perfluoro-n-hexyl)ethylene, detected using a 4.7 T small animal scanner. From the spectra in fig. 2 it can be seen that the initial hyperpolarization is transferred to all ^{19}F nuclei in the molecule. For clarity reasons three signals are pointed out. In fig. 1 the related nuclei are marked. For these moieties of the substrate a signal enhancement of 14 for a 23 for b and 45 for c (fig. 1, 2) could be determined.

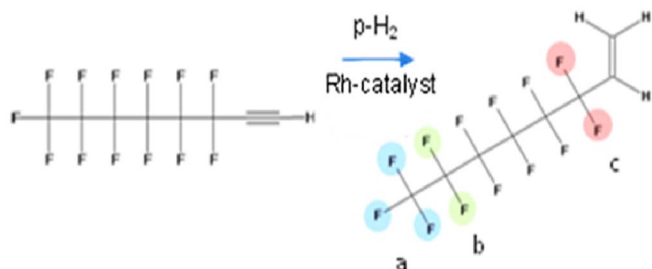


Figure 1: Illustration of the parahydrogen transfer

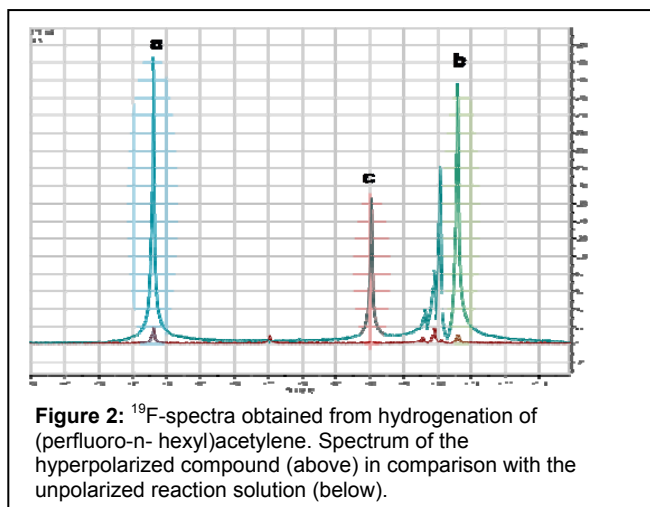


Figure 2: ^{19}F -spectra obtained from hydrogenation of (perfluoro-n-hexyl)acetylene. Spectrum of the hyperpolarized compound (above) in comparison with the unpolarized reaction solution (below).

Discussion and Conclusions

The spectra presented in fig.1 clearly show that a transfer of hyperpolarization to ^{19}F nuclei for this kind of molecules is feasible. This leads to a signal enhancement even for the terminal moiety of the molecule. The next step in this hydrogenation procedure (fig. 1) will provide the corresponding semi-fluorinated alkane which is physiologically compatible. Further optimization of reaction conditions and the application of adequate INEPT-sequences for example can even allow for a selective transfer of hyperpolarization to selected moieties.

References

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