19F-MRI using Hyperpolarized Substrates Generated via Parahydrogen-Transfer

U. Bommerich1, S. Mulla-Osman2, J. Bargon3, and J. Bernarding2

1Leibniz Institute for Neurobiology, Magdeburg, Germany, 2IBMI, University of Magdeburg, Magdeburg, Germany, 3Institute for Physical Chemistry, University of Bonn, Bonn, Germany

Introduction

19F attracts increasingly more attention for MRI and MRS investigations due to its interesting MR characteristics that include a 100% natural abundance and 84% sensitivity in comparison to 1H. Although 19F has a wide chemical shift range (~ 300 ppm?) the essentially complete lack of a natural background signal in body tissues qualify fluorinated substrates as excellent reporter molecules. They allow the simultaneous detection of multiple signals from separate molecules in MRS investigations, or the direct pharmacokinetic analysis of anatomical and functional sites in the living system due to the high sensitivity to changes in the microenvironment. Many pharmaceuticals contain a fluorine atom allowing detection of pharmacokinetics and their metabolism. Even passive substrates like perfluorocarbons can be used to investigate anatomical properties such as lung volume. Although the sensitivity of 19F is rather high, the concentration of 19F-containing reporter molecules is usually limited in vivo and the signal remains very weak. Enhancement of the 19F signal is therefore essential for using high-sensitivity reporter molecules. We have therefore applied an effective signal enhancement provided by the PHIP hyperpolarization method (ParaHydrogen Induced Polarization) as a new promising strategy towards MR-based molecular imaging.

Method and Results

1H-hyperpolarization based on the PHIP-effect can be transferred to hetero nuclei such as 13C, 31P, or 19F. The applicability of 13C hyperpolarized substrates for MRI investigations was already proved. So far the successful hyperpolarization transfer to 19F is only documented for a class of closely related aromatic systems. In order to show the feasibility of 19F-MR imaging we selected one of those substrates to which a considerable signal enhancement has been attested. In situ parahydrogenation of the unsaturated compound as detailed in Fig. 2 to its corresponding saturated derivative using an appropriate homogeneous hydrogenation catalyst does introduce the required hyperpolarization into the hydrogenation product. Figure 1 shows two magnitude spectra detected using a 4.7 T small animal scanner obtained during the hydrogenation of 3-fluorophenylacetylene yielding 3-fluorostyrene.

Discussion and Conclusions

The system outlined in Fig. 2 simply serves as a characteristic example for different kinds of potential reporter molecules. The images could be detected using a simple FLASH sequence (for parameters see fig. 3). From this promising result we conclude that the application of hyperpolarized fluorine for molecular imaging purposes is feasible. Further optimization of imaging sequences, hyperpolarization procedure as well as thorough selection of substrates and reaction conditions can lead to a wide spread implementation of this new reporter molecules which could establish completely new options for MRI investigations.

References