NMR Signal Amplification by Reversible Exchange (SABRE) in Water

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Summary

Vanderbilt researchers have developed a method to perform the Parahydrogen Induced Polarization (PHIP) based method of Signal Amplification by Reversible Exchange (SABRE) in aqueous media. This allows the resulting hyperpolarized molecules to be used for in vivo applications.

Addressed Need

Hyperpolarization of nuclear spin ensembles has increased NMR and MRI sensitivities >10,000. This has enabled the detection of metabolism in biological tissue through the imaging of injected hyperpolarized biomolecules. The two main hyperpolarization techniques available are Dynamic Nuclear Polarization (DNP) and Parahydrogen Induced Polarization (PHIP). Of these techniques, PHIP requires significantly less instrumentation, is lower in cost, and has a higher throughput. One emerging PHIP technique known as SABRE, allows the hyperpolarization of small molecules using parahydrogen without modification to the contrast agent. The SABRE method uses a catalyst, such as Iridium (Ir) complexes, to enable the exchange of a substrate and parahydrogen in solution. Until this discovery, the SABRE method was only possible in organic solvents, and therefore it precluded in vivo use. This invention allows SABRE hyperpolarization to be performed in aqueous media enabling the use of SABRE hyperpolarized molecules in in vivo applications.

Technology Description

The inventors show multiple approaches for SABRE hyperpolarization in aqueous medium. The first approach uses an Ir-based catalyst which is activated with exposure to hydrogen gas removing a part of the unsaturated protecting moiety via hydrogenation in ethanol solution in the presence of the substrate molecule. The resulting activated (in organic solvent) catalyst is reconstituted to aqueous medium. The second approach achieves a water soluble Ir-based catalyst by tethering the Ir-based complex to a water soluble ligand allowing water solubility without hydrogen-mediated activation.

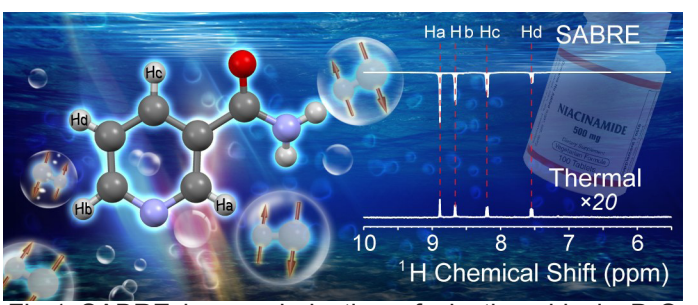

Fig.1 SABRE hyperpolarization of nicotinamide in D_2O yields four enhanced proton peaks (Ha, Hb, Hc, and Hd) with the position of each proton labeled in the structure inset. (upper right) SABRE enhanced proton NMR spectrum acquired at 9.4 T, and (lower right) corresponding thermal reference spectrum magnified by factor of 20, relative to the hyperpolarized SABRE spectrum.

Technology Development Status

- The invention has been demonstrated and proven synthetically
- Hyperpolarization via SABRE in water was achieved for the substrates pyridine and nicotinamide. Nicotinamide is a water-soluble B-group vitamin with broad spectrum of biomedical use. Moreover, other biologically interesting water-soluble molecules can be potentially amenable to this water-soluble SABRE method.

Advantages

- Enables SABRE hyperpolarization in aqueous media
- Expands SABRE to in vivo applications

Intellectual Property Status

A US provisional patent has been filled

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Link to Vanderbilt technologies available for licensing