Metal-free catalysis driving nuclear spin hyperpolarization

Vladimir V. Zhivonitko[1]*

1 NMR Research Unit, University of Oulu, P, Oulu, Finland

**Corresponding author: vladimir.zhivonitko@oulu.fi*

Highlights

- Metal-free catalysts are applied to obtain molecules with hyperpolarized nuclear spins.
- Frustrated Lewis pairs and biradicaloids are investigated as platforms for H_2 activation.
- Mechanistic pathways of parahydrogen activation are analyzed in detail.
- NMR signal enhancements are demonstrated for ^1H, ^{11}B, ^{15}N, and ^{31}P nuclei.

1. Introduction

Catalysis has numerous applications primarily directed toward the production of valuable chemical compounds. At the same time, catalytic processes are also essential in less conventional contexts, where their role is not immediately associated with synthetic output. In particular, chemical activation of dihydrogen is a key step in the preparation of molecules with hyperpolarized nuclear spins using parahydrogen, the spin-0 nuclear spin isomer of H_2, as a chemical precursor. The resulting hyperpolarized species manifest themselves in nuclear magnetic resonance (NMR) spectra through strongly amplified signal intensities. The ability to generate enhanced signals, in turn, has enabled a steadily expanding range of advanced NMR applications with unprecedented sensitivity, including reaction monitoring, mechanistic investigations, biomedical imaging, and mixture analysis.[1,2]

In these applications, homogeneous transition-metal complexes are employed almost exclusively as catalysts to mediate activation of parahydrogen and to generate hyperpolarized species.[1] Nevertheless, metal-free systems capable of activating parahydrogen have also been reported.[3-10] In a broader context, metal-free catalysis involving dihydrogen activation remains uncommon as well.

In this communication, we provide an overview of recent progress in metal-free parahydrogen-induced polarization (MF-PHIP) and signal amplification by reversible exchange (MF-SABRE) based on such metal-free catalytic systems. Particular emphasis is placed on elucidation of the mechanistic aspects of the underlying catalytic processes and on identifying the fundamental differences between metal-based and metal-free systems.

2. Methods

Metal-free catalysts based on *ansa*-aminoboranes and pnictogen biradicaloids were synthesized according to original synthetic procedures, affording analytically pure compounds soluble in common organic solvents.[3-10] For hyperpolarization experiments, NMR samples were prepared by dissolving the respective catalyst in the desired solvent directly in 5 mm gas-tight NMR tubes, followed by addition of the unsaturated substrate under inert atmosphere. The sealed tubes were subsequently charged with parahydrogen-enriched H_2 gas (92%) to a pressure of 6 bar by controlled bubbling inside the 400 MHz NMR spectrometer. Where required, minor procedural modifications were introduced depending on the specific experimental protocol.

3. Results and discussion

We demonstrate that unimolecular pairs of sterically separated ("frustrated") Lewis acids and bases (FLPs) act as efficient metal-free activators of parahydrogen and enable hyperpolarization of both protons and heteronuclei (^{15}N, ^{11}B, ^{31}P) in the corresponding FLP-H_2 adducts as well as in the free FLP species.[3-6] Furthermore, ansa-aminoborane-based FLPs are found to catalyze hydrogenation of alkynes and imines under parahydrogen atmosphere, resulting in signal enhancements of several orders of magnitude at 9.4 T for the corresponding alkene and amine products, respectively.[7,8] Figure 1 illustrates the proposed catalytic cycle for alkyne hydrogenation mediated by parahydrogen, highlighting the key elementary steps that lead to formation of a strongly polarized alkene product.

In addition to FLPs, pnictogen biradicaloids constitute a distinct class of metal-free activators for molecular hydrogen and have been shown to produce substantial hyperpolarization effects in parahydrogen activations, leading to the formation of highly hyperpolarized adducts.[9,10] Furthermore, the photochemical properties of five-membered phosphorus biradicaloids enable light-controlled modulation of parahydrogen activation, providing precise external control over the reaction and the resulting hyperpolarization process.[9]

Overall, we examine the role of non-pairwise H_2 addition mechanisms characteristic of our metal-free catalysts, which directly influence the hyperpolarization patterns observed in NMR spectra. These mechanistic distinctions result in hyperpolarization features that differ substantially from those obtained with conventional metal-based catalysts.

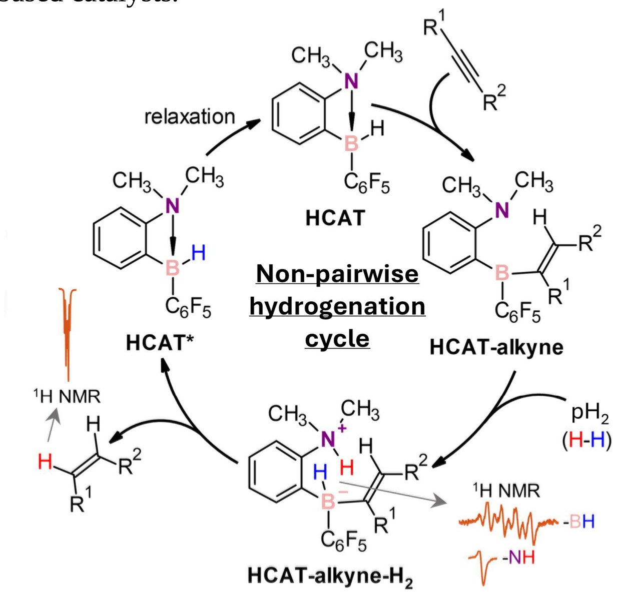

Figure 1. Mechanism of alkyne semi-hydrogenation catalyzed by the metal-free HCAT FLP-type catalyst. The catalytic process involves parahydrogen (pH_2) and results in amplified ^{1}H NMR resonances for the resulting alkene products.

4. Conclusions

Our results demonstrate that, although metal-free catalysts are uncommon, they efficiently activate parahydrogen, enable hyperpolarization of multiple nuclei, and catalyze hydrogenation reactions, highlighting their potential as a versatile and conceptually distinct alternative to conventional metal-based systems.

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