

Tweezers for Parahydrogen: A Metal-Free Probe of Nonequilibrium Nuclear Spin States of H₂ Molecules

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Supporting Information

ABSTRACT: To date, only metal-containing hydrogenation catalysts have been utilized for producing substantial NMR signal enhancements by means of parahydrogen-induced polarization (PHIP). Herein, we show that metal-free compounds known as molecular tweezers are useful in this respect. It is shown that *ansa*-aminoborane tweezers QCAT provided (20–30)-fold signal enhancements of parahydrogen-originating hydrogens in ¹H NMR spectra. Nuclear polarization transfer from the polarized hydrogens to ¹¹B nuclei leads to a 10-fold enhancement in the ¹¹B NMR spectrum. Moreover, our results indicate that dihydrogen activation by QCAT and CAT tweezers is carried out in a pairwise manner, and PHIP can be used for understanding the activation mechanism in metal-free catalytic systems in general.

The observation of large NMR signal enhancements produced by parahydrogen-induced polarization (PHIP)¹ requires breaking the high symmetry of H₂ molecules. Since the first experiments, this has been accomplished chemically using metal-containing compounds and catalysts.² As a result, PHIP has been successfully utilized for mechanistic studies and NMR/MRI sensitivity boosting in homogeneous³ and heterogeneous⁴ processes that involve H₂ activation mediated by metal complexes and nanoparticles. Recently, pairs of various sterically separated ('frustrated') Lewis acids and Lewis bases (FLPs) were reported to split dihydrogen heterolytically.⁵ Molecular tweezers⁶ are unimolecular FLPs containing functional centers connected by a chelating molecular link. Dihydrogen molecules captured by the tweezers and other FLPs can be transferred to other organic substrates providing metal-free catalytic hydrogenation.^{6,7} Despite progress in FLPs chemistry and applications, a detailed mechanism of H₂ splitting by FLPs is still debated.⁸ In particular, previous studies of the reaction between CAT tweezers and isotope-labeled H-D molecule could not clarify whether hydrogen was split via pairwise (CAT + HD) or termolecular pathway (CAT + HD + CAT).^{7a} PHIP experiments can shed light on this problem and can generally serve as a useful tool for studies of

FLP-H₂ reactivity and catalysis such as detection of unstable intermediates,⁹ dynamics of the diionic FLP-H₂ adducts in solution, etc. In NMR, molecular tweezers could serve as perfect model systems for studying quadrupolar relaxation influence on PHIP as H₂ is commonly captured by heteroatomic domains containing quadrupolar nuclei in their structure. Moreover, the tweezers preserve their chemical structure throughout the entire H₂ activation process and thus constitute a well-defined molecular unit which can be utilized as a label. Since parahydrogen (pH₂) has the most long-lived nuclear spin order known to date (up to months), its introduction into an examined medium would serve as an excellent technique for monitoring the distribution of the tweezers-labeled species. Combining PHIP produced in this way with double-quantum filtering (DQF) or 'only parahydrogen spectroscopy' (OPSY)¹⁰ techniques would enable the observation of PHIP signals only, instead of a crowded spectrum, providing a unique type of contrast which is only sensitive to the labeled species.

In this study, we demonstrate the basic idea of employing molecular tweezers in revealing nonequilibrium nuclear spin states of H₂, and observation of PHIP. The experiments were performed using 1-{2-[bis(pentafluorophenyl)boryl]benzyl}-2,2,4,7-tetramethyl-1,2,3,4-tetrahydroquinoline, the so-called QCAT tweezers,^{6b} which can reversibly capture and release H₂ under mild conditions. As the adduct of H₂ to QCAT (QCAT-H₂) is an air- and moisture-stable^{6b} solid compound, it was used in these proof-of-principle experiments.

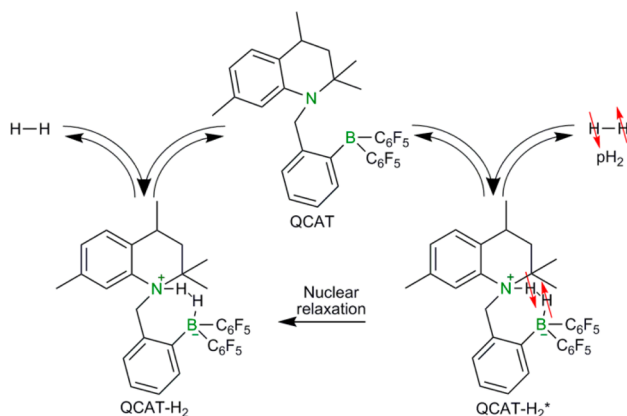
At elevated temperatures, there is a dynamic chemical equilibrium between QCAT-H₂, QCAT, and H₂ in solution which could lead to a continuous exchange between H₂-derived hydrogens in the adduct and free H₂. Therefore, PHIP effects should be observed after every bubbling of pH₂ through the QCAT-H₂ solution as soon as the hydrogens with correlated nuclear spins become inequivalent in QCAT-H₂* upon the chemical interaction, see Scheme 1.

The H₂ gas enriched in parahydrogen (pH₂; in our experiments the ortho:para ratio was 1:1, see Supporting

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Scheme 1. Expected Dynamic Chemical Equilibrium between QCAT, QCAT-H₂, QCAT-H₂^{*}, H₂, and pH₂



Information [SI]) was bubbled through a 0.02 M solution of QCAT-H₂ residing in a 7 T NMR magnet at 90 °C. The ¹H NMR spectrum of the reaction mixture obtained immediately after bubbling is shown in Figure 1a. Note the presence of

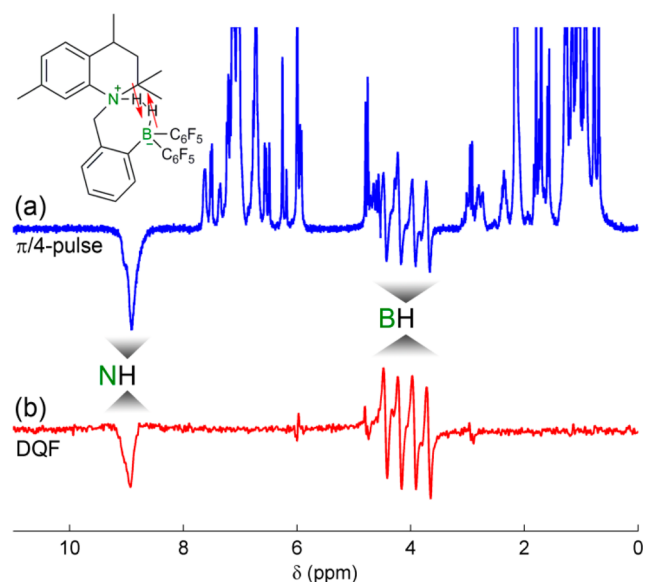


Figure 1. ¹H NMR spectra measured after pH₂ bubbling through QCAT-H₂ solution (0.02 M) in toluene-*d*₈ at 90 °C. (a) Single shot spectrum acquired with a $\pi/4$ -pulse. (b) DQF OPSY spectrum. The high-intensity signals corresponding to thermally polarized QCAT-H₂, QCAT-H₂^{*}, QCAT, and toluene-*d*₈ protons are off-scale and are cut in (a) for a better visibility of PHIP.

PHIP signals¹¹ observed for pH₂-originating hydrogens of the NH and BH groups in QCAT-H₂^{*} molecule. In order to highlight PHIP, the signals of thermal (Boltzmann) polarization were eliminated by double-quantum filtering using OPSY NMR.¹⁰ The corresponding spectrum is shown in Figure 1b. We note that at 25 °C no visible PHIP effects were observed, implying significant dependence of the dynamic equilibrium on temperature. The H₂ exchange becomes faster as temperature increases, leading to the larger concentration of QCAT-H₂^{*}.

Because of the splitting induced by the spin-3/2 ¹¹B nucleus, the polarized ¹H NMR signal of the BH group appears as a set of four antiphase doublets instead of a single doublet as would be expected for an AX spin system of spin-1/2 nuclei in a

PASADENA experiment.¹¹ One could expect to see a corresponding set of antiphase doublets for the NH group due to coupling to the spin-1 ¹⁴N nucleus, but instead, a broad signal showing negative net polarization is observed. Such an interesting observation is likely a result of an interplay between nuclear spin coupling and longitudinal relaxation having a strong influence in the case of QCAT-H₂^{*}, since both ¹⁴N and ¹¹B, the most abundant isotopes of N and B present in the adduct, are quadrupolar. The evidence that relaxation can convert the original antiphase polarization to the net one is reported in the literature.¹² Another consequence of the relaxation is that it destroys PHIP in QCAT-H₂^{*} molecule quite rapidly and results in thermal polarization signals, which are hardly detectable for NH and BH groups under the same experimental conditions (see SI).

Transverse nuclear relaxation has a harmful effect on the detected antiphase signals, since the resulting line broadening leads to a substantial degree of cancellation of the multiplet components with the opposite phases. It should be most pronounced in the case of NH signals, since the line width is ~40 Hz, which is notably larger than the typical proton scalar coupling splittings. To diminish this effect, we performed the experiments similar to the one shown in Figure 1a, but using either ¹⁴N or ¹¹B decoupling during the signal acquisition; see spectra a and b, respectively, in Figure 2.

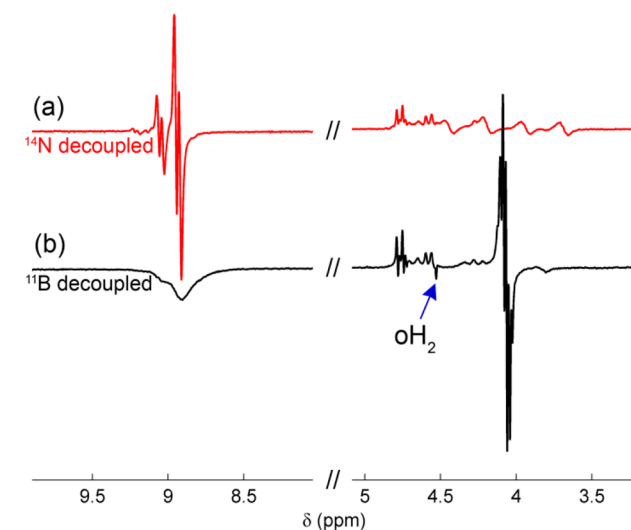


Figure 2. (a) ¹⁴N- and (b) ¹¹B-decoupled ¹H NMR spectra measured under similar conditions as those in Figure 1. The N–H and B–H signal regions are presented in the figure.

The use of decoupling led to a dramatic increase in PHIP signal intensities and altered signal shapes, and it also revealed some fine details. Acquisition of the ¹⁴N-decoupled spectrum (Figure 2a) allows one to observe the antiphase character of the NH signal, which was totally buried by transverse relaxation in Figure 1a. One can also notice that this signal can be separated into two sets of similar-shaped antiphase multiplets of different intensities belonging to two diastereomers of QCAT-H₂^{*} molecule.^{6b} The presence of the diastereomers is also visible in Figure 1 as the asymmetry of the broad NH signal. In contrast, the BH signal does not reveal any pronounced asymmetry as can be seen in ¹¹B-decoupled spectrum in Figure 2b, which means that this signal position is essentially the same for different diastereomers. The coincidence of the BH signals of

different diastereomers was shown independently using 2D ^1H NOESY spectra, see SI. The ^{11}B -decoupled spectrum exposes some splittings caused by the spin coupling network contributing to the BH signal in QCAT- H_2^* molecule.

Since our experiments were performed in the relatively high magnetic field (7 T), the presence of PHIP signals (Figures 1 and 2) itself serves as an evidence of nonzero nuclear spin–spin scalar coupling between pH_2 -originating hydrogens in QCAT- H_2^* .^{3a,11} As the direct covalent bond between the hydrogens in the molecular tweezers is absent, one could expect that the J coupling is induced indirectly through the $-\text{N}-\text{CH}_2-\text{C}-\text{C}-\text{B}-$ molecular chain of QCAT- H_2^* . The typical expected values for a long-range 6J constant are lower than 1 Hz,¹³ which is much less than that observed experimentally (2.9 Hz). Therefore, the J -coupling is likely direct in nature and is induced by the orbital through-space interactions¹⁴ or by hydrogen bonding between pH_2 -originating hydrogens captured by the tweezers. The latter interpretation is in a good agreement with the structure of crystallized QCAT- H_2 and other similar *ansa*-ammonium borates.^{6,7,15}

The polarization effects were observed also for orthohydrogen (oH_2) molecule, since the inversion of its signal was detected in some experiments after pH_2 bubbling through QCAT- H_2 solution, see Figure 2b. Such an observation reveals further details of the proposed dynamic polarization scheme shown in Scheme 1. It implies that during the time the H_2 molecule remains captured by molecular tweezers, the singlet–triplet conversion followed by the release of H_2 leads to polarization within the oH_2 nuclear states manifold. Such polarization is most likely induced by nuclear relaxation, similar to the observations reported for Ru complexes.^{12b}

In addition to the signals of NH and BH groups as well as oH_2 , a low-intensity PHIP was observed for many other groups in QCAT- H_2^* molecule, see SI. This observation shows that there is a polarization transfer induced by an incoherent mechanism, which likely takes place due to the influence of direct dipolar magnetic interactions.¹⁶ In fact, polarization transfer to other spins, especially to low-abundance heteronuclei, significantly extends the range of PHIP applications in general, but the transfer should be efficient to use it in practice. Herein we show that ^{11}B nuclei of the molecular tweezers can be polarized by the transfer of nuclear order from pH_2 . In the experiments we tested pulse sequences of the INEPT family adapted for PHIP,^{16,17} and found that PH-INEPT($+\pi/4$) provided the best results, see Figure 3. In this case, the polarization transfer resulted in an antiphase multiplet, and provides additional means for understanding polarization patterns of NH and BH groups depicted in Figures 1 and 2, which will be considered in the future works. We also observed a significant, about 10-fold enhancement of ^{11}B signals, see thermally polarized signals in Figure 3b for comparison. To the best of our knowledge, this is the first time that PHIP is used for ^{11}B NMR sensitivity boosting.

We verified that *ansa*-aminoboranes other than QCAT are also capable of producing PHIP upon interaction with pH_2 , implying that the suggested “metal-free” approach is not limited to some particular cases. It is found that bubbling of pH_2 through toluene- d_8 solution of CAT molecular tweezers (1-{2-[bis(pentafluorophenyl)boryl]benzyl}-2,2,6,6-tetramethylpiperidine),⁶ leads to PHIP signals corresponding to produced CAT- H_2^* molecules, see SI. However, the polarization was observed only after the first bubbling, most likely because of the strong binding of the H_2 molecule by CAT tweezers.

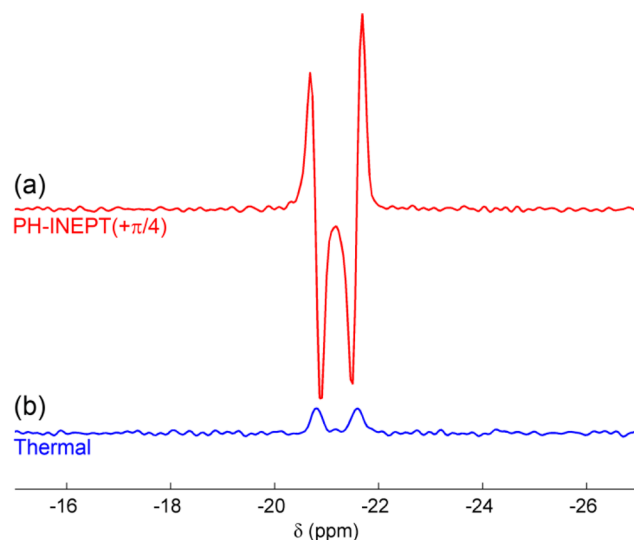


Figure 3. ^{11}B NMR spectra acquired for (a) the hyperpolarized QCAT- H_2^* and (b) the thermally polarized QCAT- H_2 molecules after pH_2 bubbling and subsequent relaxation, respectively. For spectrum (a), the PH-INEPT($+\pi/4$) NMR pulse sequence was used to transfer polarization from pH_2 -originating protons to ^{11}B nuclei.

In conclusion, we have shown that metal-free compounds are capable of allowing PHIP to be observed just by bubbling pH_2 through solution, thus enabling detection of nonequilibrium nuclear spin states in H_2 molecules. Moreover, our results constitute an example of PHIP observation when dihydrogen molecule undergoes heterolytic splitting upon its activation. The PHIP observation indicates also that the activation proceeds via a pairwise hydrogen addition process, i.e., hydrogens of the same H_2 molecule end up in the same tweezers molecule, which presents an unambiguous experimental justification for considering QCAT molecule as tiny tweezers capturing other molecules. The latter result clearly confirms the presence of the proposed dynamic chemical equilibrium shown in Scheme 1. The substantial ^1H NMR signal enhancements obtained for BH and NH signals (30- and 20-fold, respectively) as well as the demonstration of polarization transfer to ^{11}B nuclei, which led to a 10-fold enhancement of ^{11}B NMR signal, are encouraging for using metal-free catalysts in boosting the sensitivity of NMR and for investigating reaction mechanisms in metal-free catalysis with similar compounds by means of PHIP. Meanwhile, we would stress the uniqueness of QCAT tweezers which demonstrate a facile and reversible H_2 addition, and thus allow the fast dynamic equilibrium shown in Scheme 1 to take place. As it is demonstrated, CAT molecular tweezers, which bind H_2 rather irreversibly compared to QCAT, provided PHIP observation only at the first moments after pH_2 bubbling through its solution, as fresh portions of pH_2 could not enter CAT molecule on the subsequent bubbling rounds. We also believe that further application of PHIP NMR opens a new route in studying hydrogen activation and transfer by frustrated Lewis pairs and other metal-free catalytic systems.

■ ASSOCIATED CONTENT

📄 Supporting Information

Description of experimental procedure, additional NMR spectra illustrating results of the work. This material is available free of charge via the Internet at <http://pubs.acs.org>.

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Notes

The authors declare no competing financial interest.

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