Hydrogen Induced Polarization–Nuclear-Spin Hyperpolarization in Catalytic Hydrogenations without the Enrichment of Para- or Orthohydrogen

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Dedicated to Professor Dr. Joachim Bargon (University of Bonn) on the occasion of his 65th birthday and in recognition of his numerous contributions to chemically induced hyperpolarized NMR.

Abstract: During the last 40 years, Prof. Dr. Joachim Bargon, to whom several articles in this issue are dedicated, has contributed more than 90 scientific publications to the understanding of NMR hyperpolarization phenomena such as chemically induced dynamic nuclear polarization (CIDNP) or parahydrogen induced polarization (PHIP). Both techniques are extremely useful for elucidating the mechanisms and kinetics of chemical reactions involving radicals or catalytic hydrogenations, respectively. To honor Joachim Bargon's scientific achievements, we dedicate to him an additional, newly discovered and somewhat unexpected twist to the PHIP methodology. Accordingly, NMR spectra exhibit the unique, enhanced absorption and emission patterns of PHIP not only if the hydrogen for the catalytic reactions is enriched in one of its nuclear spin states (parahydrogen or orthohydrogen) but also if it is at its thermodynamic equilibrium. Thermally equilibrated gaseous hydrogen is obtained from commercially available hydrogen gas bombs or from electrolytic hydrogen generators. The new finding is explained with the quantum mechanical properties of the small, highly symmetric hydrogen molecule.

Keywords: homogeneous catalysis; hydrogenation; NMR spectroscopy; parahydrogen; spin polarization

Introduction

NMR is a superior tool for investigations with catalytic reactions, because the parameters chemical shift, coupling constant, and relaxation time yield much information about chemical structures, as well as mechanisms and kinetics of the reactions. However, NMR is inherently insensitive when compared with other methods such as infrared (IR) or ultraviolet/visible light (UV/Vis) spectroscopy. The macroscopic magnetization generated by the nuclear spins at thermal equilibrium in the magnetic field of a typical NMR spectrometer is only about 10^{-5} of what it could be if all spins were aligned in parallel. In 1986, it was predicted that molecular hydrogen (H_2) enriched in its nuclear singlet state (parahydrogen) can induce nuclear spin hyperpolarization in the products of hydrogenation reactions, which can lead to largely enhanced NMR signals.[1] The prerequisites for observing the spin hyperpolarization in the NMR spectra of hydrogenation products are:

(a) the two hydrogen atoms must be transferred in pairs,
(b) the nuclear spin relaxation of the transferred hydrogen atoms must be slower than the overall kinetics of the chemical reaction,
(c) the symmetry of the transferred hydrogen atoms must be broken during the reaction.

The conditions (a) and (b) enable the nuclear spin alignment of parahydrogen (p-H_2) to remain – at least partially – intact during the reaction and to be transferred together with the hydrogen atoms to the reaction intermediates and products. Condition (c) is necessary to obtain NMR-observable magnetization from the intermediates or products' hyperpolarization. NMR spectra recorded *in situ* during or shortly after a catalytic hydrogenation with p-H_2 exhibit the largely enhanced signals in unique absorption and emission patterns. The phenomenon was independently termed PASADENA (*parahydrogen and synthesis allow dramatically en-*

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hanced nuclear alignment)[2] and PHIP (*parahydrogen induced polarization*)[3] unfolding an extremely useful method to elucidate mechanisms and kinetics of catalytic hydrogenations. The method is also utilized to identify reactive intermediates that are not seen with other methods. Several reviews with different emphasis on methodical or chemical aspects are available.[4–9]

Similar but inverted signal patterns and somewhat weaker NMR signal enhancements are achieved with H_2 enriched in its nuclear triplet state (i.e., enriched in orthohydrogen).[10] Since the acronym PHIP, however, is commonly used to cover all nuances of hydrogen induced polarization including the effects of orthohydrogen (o-H_2), it might just be interpreted as *"polarized" hydrogen induced polarization*.[11] The acronym PASADENA is nowadays frequently used to characterize an experimental procedure, namely the one in which the hydrogenation and NMR measurement are both carried out in the static magnetic field of an NMR spectrometer. Alternatively, the acronym ALTADENA[12] (*adiabatic longitudinal transport after dissociation engenders net alignment*) is used to describe the procedure in which the hydrogenation is conducted outside of the NMR magnet and the sample is subsequently transported into the magnetic field for the NMR analysis. PHIP patterns vary substantially with the experimental procedure, and PASADENA and ALTADENA are alternately used to optimize PHIP results for the elucidation and analysis of catalytic reactions.

In this article, we report that similar nuclear-spin hyperpolarization effects are obtained even without the enrichment of p-H_2 or o-H_2. Hydrogenation reactions conducted with H_2 at the thermal equilibrium of its nuclear spin states (t-H_2) can likewise lead to PHIP NMR signal patterns in absorption and emission. The new modification (*thermal hydrogen induced polarization*) was observed with both the PASADENA and the ALTADENA experimental procedure.

Quantum-Mechanical Properties of Molecular Hydrogen

The total wave function of the small and highly symmetric molecule H_2 is easily separated into sub wave functions for which the cross products are negligible (e.g., electronic, vibrational, rotational, and nuclear-spin wave function). Since vibrational and electronic modes are not activated in gaseous H_2 at room temperature or below,[13] only the vibrational and electronic ground states are populated and contribute to the partition function of H_2. Consequently, energy transitions in H_2 occur only between rotational and nuclear-spin states.

A rotation of $(2n+1) \times 180°$ (where n is a positive integer including $n=0$) about an axis perpendicular to the molecular axis of H_2 interchanges its two protons, while a rotation of $2n \times 180°$ brings them back to their original position. Hence, the symmetry of the rotational wave function alternates with the quantum number such that even rotational quantum numbers ($J=0, 2, 4, ...$) correspond to symmetric rotational states and odd numbers ($J=1, 3, 5, ...$) to antisymmetric states. In addition, protons bear a spin quantum number of $I=½$ and, in H_2, couple to a total spin quantum number of either $I=0$ (p-H_2) or $I=1$ (o-H_2). Of these two possibilities, p-H_2 is antisymmetric with respect to the interchange of the two protons, while o-H_2 is symmetric (Fig. 1).

Because protons are fermions, the total wave function of H_2 is antisymmetric, i.e., changes sign when the indistinguishable protons are interchanged (Pauli principle). Consequently, and as a result of the $D_{\infty h}$ symmetry of homonuclear diatomic molecules, the rotational symmetry dictates the symmetry of the nuclear-spin wave function and *vice versa*. While one of the wave functions (rotational or nuclear-spin) is symmetric, the other one must be antisymmetric. Accordingly, p-H_2 with its antisymmetric nuclear-spin wave function occurs exclusively with even rotational quantum numbers, while o-H_2 exclusively occupies energy levels with odd rotational quantum numbers.

The diagram in Figure 2 shows the six lowest rotational energy states of H_2 ($J=0$ to $J=5$) with the relative horizontal location proportional to their energy. The numbers posted above the states represent the numbers of degeneracy, which are calculated from the product of rotational and nuclear-spin degeneracy, $(2I+1) \times (2J+1)$. In the representation of Figure 2, no external magnetic field is assumed for it would lift the threefold nuclear-spin degeneracy of o-H_2. The energy difference between adjacent rotational states, $(J-1) \rightarrow J$, in linear molecules is given by

$$\Delta E_{rot} = hcBJ(J+1) \tag{1}$$

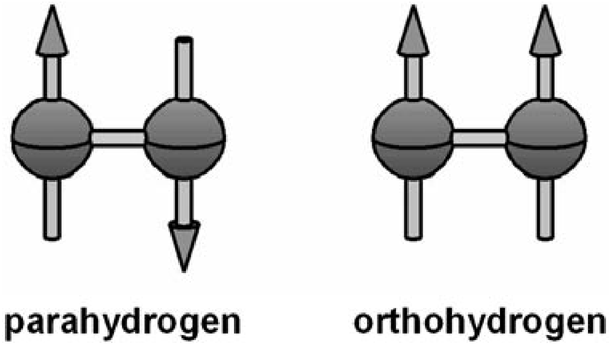


Figure 1. Very much simplified representation of the spin symmetry of p-H_2 and o-H_2. The arrows in the H_2 ball-and-stick models symbolize effective magnetic moments. While this representation is probably a quantum mechanist's nightmare for it particularly violates Heisenberg's uncertainty relation, it still helps visualizing the antisymmetric (p-H_2) and symmetric (o-H_2) nuclear-spin wave function of H_2.

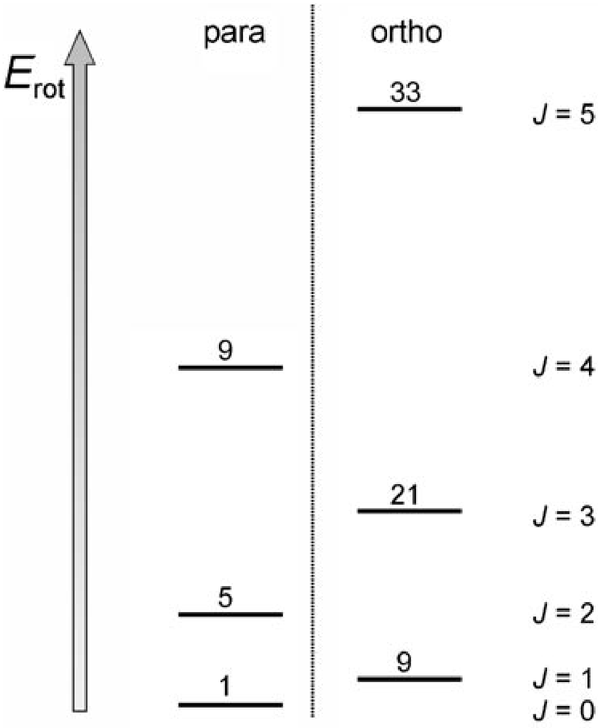


Figure 2. Lower rotational states of H_2 separated into columns of p-H_2 states (left) and o-H_2 states (right). The rotational quantum number (J) of each state is shown to the right of the columns, and the number of degeneracy is posted above each state.

where h is Planck's constant, c is the speed of light in free space, and B is the rotational constant of the molecule. With the rotational constant of H_2 ($B = 60.864\ \mathrm{cm}^{-1}$),[14] the energy difference between the lowest rotational level of p-H_2 ($J = 0$) and the lowest level of o-H_2 ($J = 1$) yields

$$\Delta E_{rot}(J = 0 \rightarrow J = 1) = 1.48\ \mathrm{kJ\ mol}^{-1} = h \times 3.7 \times 10^{12}\ \mathrm{Hz} \tag{2}$$

Thus, the lowest-energy rotational transition in H_2 is quite large exhibiting a transition frequency in the far-infrared spectral range. It is noted, however, that this energy transition is forbidden because of the different rotational and spin symmetries. Because the spacing between rotational states increases with the rotational quantum numbers (Figure 2), the next transition between ($J = 1$) and ($J = 2$) yields the even higher transition frequency

$$\Delta E_{rot}(J = 1 \rightarrow J = 2) = h \times 11.1 \times 10^{12}\ \mathrm{Hz} \tag{3}$$

In contrast with the large rotational energy splitting in H_2, the energy difference between the spin couplings in p-H_2 and o-H_2 is only

$$\Delta E_{spin} = E_{spin}(I = 1) - E_{spin}(I = 0) = 1.1 \times 10^{-7}\ J\ mol^{-1} = h \times 276\ \mathrm{Hz} \tag{4}$$

where $E_{spin}(I = 0)$ is the nuclear-spin energy of the antisymmetric coupling in p-H_2, which is smaller than $E_{spin}(I = 1)$, the energy of the symmetric coupling in o-H_2.[15] The frequency difference of 276 Hz [Eq. (4)] is known as the ^1J(H,H) coupling constant of H_2 and is independent of external magnetic fields. A comparison of ^1J(H,H) with the smallest rotational transition frequency [Eq. (2)] shows that the partition function of p-H_2 and o-H_2 at thermal equilibrium is solely governed by the occupation of rotational states. The o-H_2/p-H_2 ratio at thermal equilibrium is calculated from the energies of the rotational states and their numbers of degeneracy according to the Boltzmann distribution:

$$\frac{N_{ortho}}{N_{para}} = \frac{3 \sum\limits_{J=1,3,5,\dots} (2J+1) e^{-\left(\frac{\Delta E_J}{kT}\right)}}{\sum\limits_{J=0,2,4,\dots} (2J+1) e^{-\left(\frac{\Delta E_J}{kT}\right)}} \tag{5}$$

where k is Boltzmann's constant, T is the absolute temperature, and ΔE_J is the energy difference between the rotational levels $E_{J=0}$ and E_J. At about room temperature ($T = 295$ K), Eq. (5) yields 25.09% p-H_2 and 74.91% o-H_2. Thus, H_2 at its thermal equilibrium of 295 K (*thermal hydrogen* or t-H_2) consists of 99.88% non-polarized H_2 (3 : 1 mixture reflecting the threefold spin degeneracy of o-H_2) and 0.12% spin-polarized p-H_2. Hence, t-H_2 carries a 1.2×10^{-3} excess of p-H_2 or, put another way, has a thermal spin polarization of 1.2×10^{-3} compared with the equal population of all energy levels achieved only at infinite temperature.

In standard PHIP experiments, p-H_2 is typically enriched up to the ratio of its thermal equilibrium at liquid-nitrogen temperature ($T = 77$ K) yielding 52% p-H_2 and 48% o-H_2. This enrichment still consists of 64% non-polarized H_2 (o-H_2/p-H_2 ratio of 3 : 1) but leads to 36% spin-polarized p-H_2. Figure 3 shows histograms of the thermally equilibrated partition between H_2 rotational states at liquid-nitrogen temperature ($T = 77$ K) and at room temperature ($T = 295$ K).

In the static magnetic field of an NMR spectrometer, the nuclear-spin states of o-H_2 loose their degeneracy and split into three states that are equidistant in energy, each with the rotational-state degeneracy of ($2J + 1$) remaining. The different nuclear spin states are now labeled T_{+1}, T_0, T_{-1} reflecting the triplet symmetry. The energy spacing between o-H_2 spin states depends on the external magnetic field (B_0) and is calculated with the magnetogyric ratio (γ) according to

$$\Delta E_{B_0} = \hbar \gamma B_0 \tag{6}$$

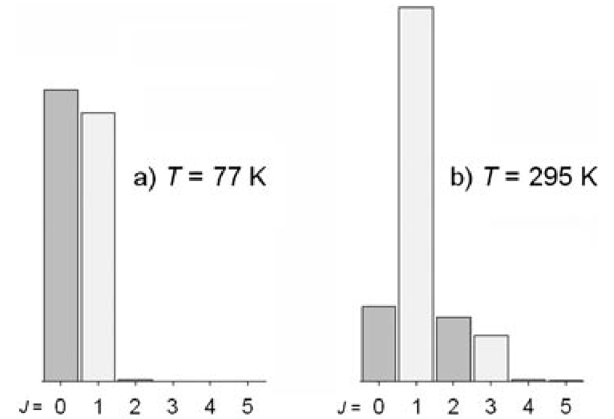


Figure 3. Partition histograms for the six lowest rotational states of H_2 at thermal equilibrium of (a) $T = 77$ K and (b) $T = 295$ K. Dark grey bars represent states of p-H_2, while light grey bars refer to the states of o-H_2. At 77 K, only the lowest two states (ground states for p-H_2 and o-H_2) and, at 295 K, only the lowest four rotational states are substantially populated.[16]

where $\hbar = h/2\pi$. The p-H_2 levels ($I = 0$, $J = 0, 2, 4, ...$) are usually labeled S (or S_0) to reflect the singlet symmetry, but they remain unaffected by an external magnetic field. The single line that is observed in the NMR spectrum of H_2 originates from transitions between the o-H_2 levels only, whereas p-H_2 is NMR inactive. Even in the field of the strongest NMR magnets currently available commercially ($B_0 = 21$ T, resonance frequency of 900 MHz $= 9 \times 10^8$ Hz), the splitting of the o-H_2 spin levels is three to four orders of magnitude below the energy difference between the rotational states; thus, NMR magnetic fields do not influence the H_2 partition function.

For the hydrogenation experiments described below, we used a 200 MHz Bruker Avance DRX NMR spectrometer ($B_0 = 4.7$ T). In this field, the population difference, ΔN, between a lower and upper resonant level of ^{1}H NMR (α and β, respectively) is calculated from the Boltzmann distribution at 295 K using Eq. (6) and the proton's magnetogyric ratio ($\gamma = 26.752 \times 10^7$ rad s^{-1} T^{-1}):[17]

$$\frac{\Delta N}{N} = \frac{N_\alpha - N_\beta}{N_\alpha + N_\beta} = \frac{1 - e^{-\frac{\Delta E_{B_0}}{kT}}}{1 + e^{-\frac{\Delta E_{B_0}}{kT}}} = 1.63 \times 10^{-5} \tag{7}$$

where N_α and N_β are the populations of the levels α and β, respectively.

Results and Discussion

Signal Enhancement

If pure p-H_2 (spin polarization of $\Delta N/N = 1$) is used for catalytic hydrogenations, and spin relaxation is negligible during the catalytic cycles, only those energy levels are populated in the intermediates and products of the reactions, which share – at least partially – the singlet symmetry of p-H_2. For simplicity, we assume at first that hydrogenation products are formed in which the transferred hydrogen atoms couple only with each other but not with other nuclei. However, the concept exemplified here is used similarly for hydrogenation products with more complex coupling patterns. Furthermore, it is supposed that the chemical-shift difference between the transferred hydrogen atoms in the product is large compared with the coupling constant. Then, the high-field approximation for a loosely coupled spin system applies (AX spin system) leading to four spin states (Figure 4) two of which are mixed states of 50% singlet and 50% triplet symmetry ($|\alpha\beta>$ and $|\beta\alpha>$), while the others are pure triplet states ($|\alpha\alpha>$ and $|\beta\beta>$). If the hydrogenation reaction occurs instantaneously (i.e., fast with respect to the spin-spin relaxation of the transferred hydrogen atoms) and within the NMR magnetic field (PASADENA procedure), the two mixed states, $|\alpha\beta>$ and $|\beta\alpha>$, are exclusively and equally populated because of their singlet character (Figure 4a). Accordingly, a hyperpolarization of all NMR transitions (1–4 in Figure 4) is achieved in the product, each carrying $\Delta N/N = 0.5$. This hyperpolarization leads to both the large signal enhancement of PHIP and the distinct absorption and emission pattern schematically shown in the NMR spectrum of Figure 4a. If, however, the catalytic hydrogenation is conducted outside of the spectrometer's magnetic field (ALTADENA procedure), only the state that, in a magnetic field, converts to $|\beta\alpha>$ shares the singlet symmetry of p-H_2 and, thus, is the only one populated (Figure 4b).[12] Accordingly, transitions 1 and 4 are the only ones seen in the spectrum. However, since only one state is populated, the hyperpolarization is $\Delta N/N = 1$, and the transitions occur with twice the intensity of the PASADENA signals. After relaxation of the hyperpolarization, the remaining thermal polarization leads to the standard thermal spectrum (Figure 4c).

The theoretical (i.e., maximum) enhancement factor (ς) is calculated from the ratio of the product's PHIP hyperpolarization to the thermal polarization. Accordingly, with pure p-H_2 and our 200 MHz NMR spectrometer ($B_0 = 4.7$ T), the theoretical enhancement factor is [cf. Eq. (7)]

$$\varsigma = \frac{(\Delta N/N)_{PASADENA}}{(\Delta N/N)_{thermal}} = \frac{0.5}{1.63 \times 10^{-5}} = 3.07 \times 10^4 \tag{8}$$

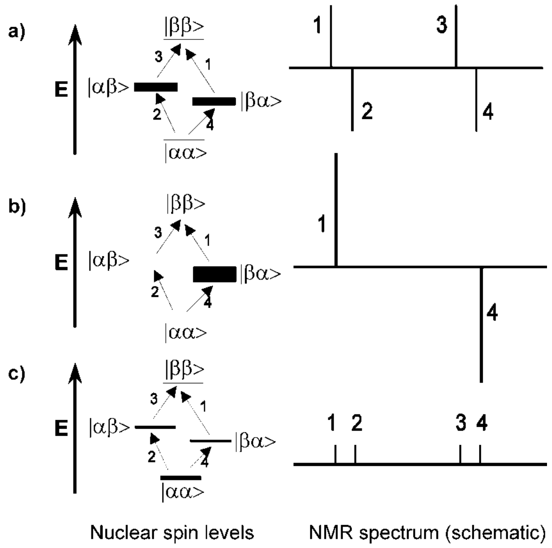


Figure 4. Spin-state diagram of hydrogen nuclei in an AX spin system (left). The populations are depicted by the line width of the states and yield the NMR spectra schematically shown on the right; (a) population and spectrum expected for PASADENA hydrogenation with pure p-H_2, (b) population and spectrum expected for ALTADENA hydrogenation with pure p-H_2, (c) population and spectrum expected after relaxation to thermal equilibrium.

for the PASADENA procedure and

$$\varsigma = \frac{(\Delta N/N)_{ALTADENA}}{(\Delta N/N)_{thermal}} = \frac{1}{1.63\times10^{-5}} = 6.13\times10^{4} \qquad (9)$$

for the ALTADENA procedure. In contrast, p-H_2 spin polarization is only 36% (*vide supra*) in a H_2 gas sample that was enriched to its thermal equilibrium at liquid-nitrogen temperature (77 K). The maximum hyperpolarization achieved with 36% spin-polarized p-H_2 in an AX hydrogenation product is therefore $\Delta N/N = 0.36$ for ALTADENA (leading to $\varsigma = 2.20 \times 10^4$) and $\Delta N/N = 0.18$ for PASADENA ($\varsigma = 1.10 \times 10^4$).

Because thermal polarization of spin states depends on the B_0 field [Eqs. (6) and (7)], enhancement factors also depend on B_0. An increased magnetic field leads to an increased thermal NMR signal, which, in turn, decreases the enhancement factors [Eqs. (8) and (9)]. In the temperature range that is suitable for catalytic reactions, the hyperpolarization with p-H_2, however, is independent of the B_0 field. This makes the enhancement factor a relative measure. For example, the factor is reduced to about half the value of Eqs. (8) or (9), if the magnetic field is increased to 9.4 T (400 MHz ^{1}H resonance frequency). However, a B_0 field of 1.6×10^5 T is needed to reduce the enhancement factor of PASADENA experiments to $\varsigma = 1$. Put another way, only a field of $B_0 = 1.6 \times 10^5$ T leads to a thermal polarization that is as high as the hyperpolarization achievable with p-H_2 in a PASADENA experiment. To match ALTADENA hyperpolarization, the field must even approach infinity. Enhancement factors also depend on the temperature. An increased temperature generally decreases the thermal polarization [Eq. (7)] and, thus, increases the enhancement factor.

Experimentally, enhancement factors are determined from the ratio of PHIP signal intensities to the intensities of the corresponding signals at thermal equilibrium (thermal signals). Mainly because of relaxation phenomena and *J*-couplings to further protons in the product molecules, however, experimentally derived enhancement factors are typically smaller than their theoretical values [Eq. (8) or (9)].

Because of the exclusive occupation of, and the large energy difference between, the rotational states in H_2 (*vide supra*), t-H_2 already carries a spin polarization of 1.2×10^{-3} [cf. Eq. (3)]. This value is about two orders of magnitude larger than the thermal polarization in a typical hydrogenation product [1.63×10^{-5}, Eq. (5)]. Accordingly but initially much to our surprise, a p-H_2 PHIP pattern with an enhancement factor of

$$\varsigma = \frac{0.5\times1.2\times10^{-3}}{1.63\times10^{-5}} = 36.8 \qquad (10)$$

is still expected for t-H_2 PASADENA hydrogenations, and

$$\varsigma = \frac{1.2\times10^{-3}}{1.63\times10^{-5}} = 73.6 \qquad (11)$$

is expected for t-H_2 ALTADENA. Because t-H_2 is directly obtained from standard gas bombs or electrolytic H_2 generators, the result of Eqs. (10) and (11) means that everyone with access to standard laboratory equipment and an NMR spectrometer should be able to observe PHIP signals from appropriate and efficient catalytic hydrogenations without going through a procedure of p-H_2 or o-H_2 enrichment.

In situ NMR of Homogeneously Catalyzed Hydrogenations

To observe PHIP hyperpolarization in NMR spectra, the hydrogen atoms of H_2 must be transferred in pairs to the product. This particular mechanism is most likely with homogeneous hydrogenations using organometallic complexes as the catalyst. Because the reaction must break the singlet symmetry of the transferred hydrogen atoms [condition (c), *vide supra*], an asymmetrically substituted acetylene, i.e., ethyl propiolate (propiolic acid ethyl ester, H-C≡C-COOEt), was chosen as the substrate. It is noted, however, that reactions with symmetrically substituted olefins and acetylenes also exhibit PHIP signals, namely if the transferred hydrogen atoms in the product are chemically equivalent but magnetically different (e.g., hydrogenation into an AA′BB′ system).[8] Even if the hydrogen atoms are transferred into chemically *and* magnetically equivalent positions, naturally abundant ^{13}C breaks the symmetry in 1.1% of the product for every carbon atom that exhibits a measurable $^1H/^{13}C$ *J*-coupling to the transferred hydrogen atoms.[18]

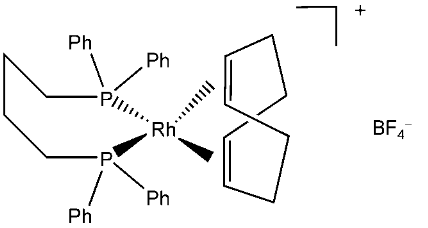
Still, for optimum results, we picked a catalytic reaction with hydrogen transfer into chemically different positions and selected appropriate reaction conditions according to:

(a) The hydrogenation must be fast, so that much spin-polarized product is formed in a given time span.
(b) None of the substances in the solution should carry nuclear quadrupole moments that increase nuclear-spin relaxation. For example, palladium with its strong quadrupole moment was not selected, although its reactivity is very high and palladium-organic catalysts are still known to generate PHIP hyperpolarization in the products of hydrogenation reactions.

Among the many reactions that comply with the above-mentioned conditions, we selected [Rh(DPPB)(COD)] BF_4 (Scheme 1), where DPPB = 1,4-bis(diphenylphosphino)butane, and COD = 1,5-cyclooctadiene, as a simple but efficient, commercially available catalyst precursor for the hydrogenation of the electron-deficient substrate ethyl propiolate to form ethyl acrylate (acrylic acid ethyl ester).

To determine the efficiency of generating hyperpolarization in the chosen hydrogenation, we compared experimental enhancement factors of PHIP spectra with the corresponding theoretical factors (ALTADENA: $\varsigma = 2.20 \times 10^4$, PASADENA: $\varsigma = 1.10 \times 10^4$, *vide supra*). The PHIP spectra were recorded *in situ* during catalytic hydrogenations with H_2 enriched in p-H_2 up to the thermal equilibrium at liquid-nitrogen temperature. Details of the reactions and the p-H_2 enrichment procedure are given in the experimental section.

It is noted that PHIP signal intensities depend differently on NMR pulse widths than regular, thermal signal intensities.[12] In first approximation and for loosely coupled spin systems, maximum PHIP intensities are observed with the 45° pulses of standard NMR signals rather than with 90° pulses. Actually, most PHIP intensities vanish at the 90° pulse of the standard intensities. Furthermore, at 135°, PHIP signals show another intensity maximum but with inverted signal patterns. Accordingly, the periodicity of PHIP intensities as a function of pulse width (or pulse intensity) is twice the periodicity of regular NMR signals. Thus, it is possible to observe PHIP signals while suppressing thermal signals with a difference spectroscopy of a 45° and a 135° pulse experiment, which efficiently co-adds PHIP intensities but cancels thermal signal intensities. Alternatively, the addition of a 45° and a 225° pulse experiment leads to the same result.



Scheme 1. [1,4-Bis(diphenylphosphino)butane](1,5-cyclooctadiene)rhodium(I) tetrafluoroborate.

Typical PHIP spectra recorded *in situ* from PASADENA and ALTADENA experiments of our catalytic model hydrogenation are shown in Figures 5a and 6a, respectively. The PHIP patterns at 6.3–5.8 ppm are easily assigned to the vinyl moiety of the product ethyl acrylate, which was formed by the reaction. In the ALTADENA spectrum, PHIP signals are also observed at 2.4 ppm and 0.8 ppm originating from the subsequent hydrogenation of ethyl acrylate forming ethyl propionate (propionic acid ethyl ester). The experimental enhancement factors for the signals of the vinyl moiety are $\varsigma = 1.8 \times 10^3$ (PASADENA) and $\varsigma = 1.2 \times 10^4$ (ALTADENA) compared with thermal signal intensities recorded from the same samples but after the hyperpolarization has completely relaxed. Compared to the theoretical maximum, the experimental PHIP signals are diminished by a factor of 6.1 for PASADENA and 1.8 for ALTADENA. The diminishment is caused by the acetylenic proton of the propiolic acid ester, which, in the product, couples to both of the transferred hydrogen atoms. In the high-field approximation, the additional *J*-couplings split each of the nuclear spin states of Figure 4 into two equally populated states, thus, reducing the hyperpolarization of each transition to $\Delta N/N = 0.25$ for PASADENA and $\Delta N/N = 0.5$ for ALTADENA. Thermal polarization, however, is largely independent of additional *J*-couplings. In the PASADENA experiment, relaxation of the hyperpolarization or an incomplete reaction at the time of recording the spectra accounts for further diminishment. In PASADENA experiments, we sometimes observed increasing PHIP intensities in a spectrum recorded several seconds after the first spectrum. This indicates that the reaction was still incomplete at the time of the first spectrum. Since it takes substantially longer to transport the sample tube into the magnetic field of the NMR spectrometer, we did not observe this effect with ALTADENA. In summary, the experimental enhancement factors show that the reaction we selected works very efficiently for the transfer of hyperpolarization *via* p-H_2 and that an exclusive reaction mechanism of pairwise transfer of hydrogen atoms is most likely.

For the quantitative determination of the enhancement factors, integrated signal intensities of both the PHIP hyperpolarization signals and the signals recorded after the population of nuclear-spin states has completely relaxed were calibrated with the solvent's signal intensity. This calibration is advisable because the receiver gain setting of the NMR spectrometer must inevitably be changed when switching from recording largely enhanced PHIP signals to recording thermal signals that are up to four orders of magnitude smaller.

The same experiments (PASADENA and ALTADENA) were repeated with t-H_2 taken directly from an H_2 gas bomb. To ensure that the gas bomb's H_2 did not accidentally carry spin hyperpolarization, the measurements were repeated with H_2 obtained from an H_2 generator that electrolyzes water. By electrolyzing water, H_2 is always generated at the current temperature's thermal equilibrium. For the reproducibility of the hydrogenation experiments with H_2 from the electrolytic generator, however, it is important that the H_2 gas is carefully dried (i.e., over silica gel) before it is used in the catalytic reaction. Still, no differences were detected in the NMR spectra from the experiments with H_2 from the electrolytic generator compared with the experiments with H_2 from the gas bomb.

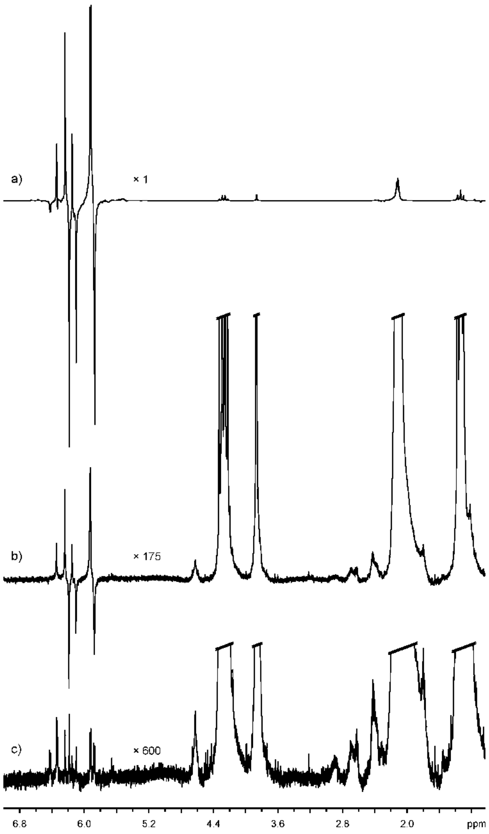


Figure 5. 200 MHz ^{1}H PASADENA NMR spectra recorded *in situ* from the catalytic hydrogenation of ethyl propiolate to form ethyl acrylate (a) during the reaction with 36% spin-polarized p-H_2, (b) during the reaction with t-H_2, and (c) after the reaction with t-H_2 and complete relaxation of the hyperpolarization. The vertical scales of (b) and (c) are enlarged *versus* (a) by the factors posted. NMR signals are assigned as follows: 4.2 ppm, acetylene proton of ethyl propiolate; 3.8 and 1.2 ppm, ester group of ethyl propiolate; 6.5–5.8 ppm, vinyl moiety of ethyl acrylate; 4.6 and 2.4 ppm, ester group of the product ethyl acrylate; 2.0 ppm residual protons of the solvent acetone-d_6.

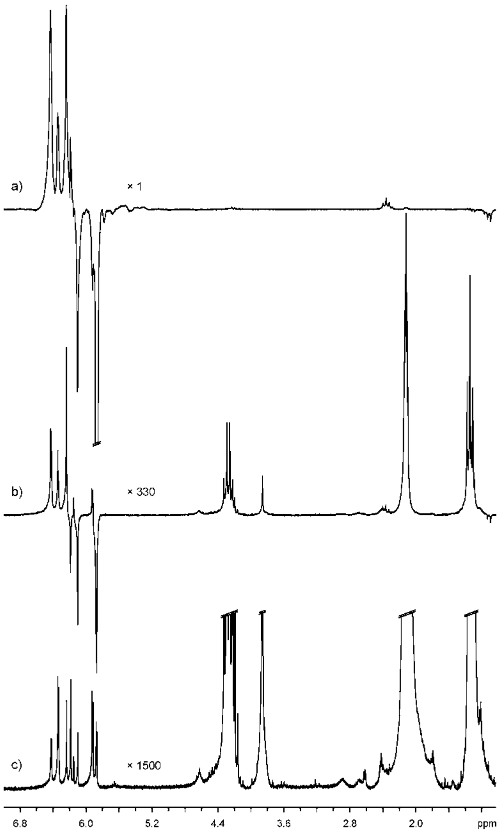


Figure 6. 200 MHz ^{1}H ALTADENA NMR spectra recorded from the catalytic hydrogenation of ethyl propiolate to form ethyl acrylate (a) during the reaction with 36% spin-polarized p-H_2, (b) during the reaction with t-H_2, and (c) after the reaction with t-H_2 and complete relaxation of the hyperpolarization. The vertical scales of (b) and (c) are enlarged *versus* (a) by the factors posted. NMR signals are assigned as explained in the legend to Figure 5. In addition, however, PHIP signals from the subsequent hydrogenation of ethyl acrylate to form ethyl propionate are observed in (a) and (b) at 2.4 ppm and 0.8 ppm for the methylene and methyl group of the propionate, respectively.

Spectra recorded *in situ* during the catalytic hydrogenations with t-H_2 are shown is Figures 5b and 6b, respectively. They exhibit the same qualitative information (the same signal pattern) as observed from the hydrogenations with p-H_2 enriched gas samples. However, the enhancement factors of the t-H_2 PHIP signals are only $\varsigma = 6$ for PASADENA and $\varsigma = 29$ for ALTADENA compared with the thermal signals that were recorded after complete relaxation (Figures 5c and 6c, respectively).

Table 1 summarizes the theoretical and experimental NMR enhancement factors of the hydrogenations conducted with (a) H_2 thermally equilibrated at room temperature (t-H_2), (b) H_2 enriched in p-H_2 to the thermal equilibrium at liquid-nitrogen temperature (77 K, i.e., 36% p-H_2), and (c) with 100% (i.e., pure) p-H_2.

The ratio between the theoretical enhancement factors of 36% p-H_2 and t-H_2 is 299 (Table 1d). This ratio is most accurately reproduced experimentally by the PASADENA experiments. In the ALTADENA experiment, a ratio of 410 was determined, which is far more than expected from the theory. However, unlike PASADENA, where the experimental conditions are highly reproducible (cf. experimental section), ALTADENA is prone to many experimental uncertainties such as the time frame of hydrogen insertion and sample-tube shaking, and the transport from the earth magnetic field under which the reaction is conducted into the NMR main magnetic field.

Conclusion

PHIP investigations are an established NMR technique for the elucidation of hydrogenation reactions. If largely enhanced PHIP patterns are recorded in the NMR spectra of catalytic hydrogenations, much information is directly revealed about the reaction under investigation. For example, the reaction mechanism is, at least for the part that generates the hyperpolarization, such that the hydrogen atoms are transferred in pairs from the same H_2 molecule. The positions of the transferred hydrogen atoms in the product molecules are often identified easily from the signal patterns of PHIP, although, it is sometimes advisable to run a computer simulation for back up of the spectrum analysis.

To record PHIP spectra from a catalytic hydrogenation, gaseous H_2 is usually enriched in p-H_2 up to the thermal equilibrium at liquid-nitrogen temperature. However, we found that even thermal H_2 taken as is from a gas bomb or obtained from an electrolytic H_2 generator carries a spin polarization about three orders of magnitude higher than the thermal polarization in most reaction products. This spin polarization results in similar PHIP signal patterns, although, with much smaller signal enhancements.

An investigator who wishes to analyze catalytic hydrogenations with respect to the pairwise mechanism, its kinetics, and the positions into which the hydrogen atoms are transferred, or who tries to identify intermediates in the catalytic cycle, will always strive to use the largest NMR signal enhancement achievable at a reasonable expense. Since it is neither expensive nor much time-consuming to enrich p-H_2 up to the thermal equilibrium at liquid-nitrogen temperature (cf. experimental section), the 36% spin-polarized p-H_2 provided by this procedure is usually a good compromise even for investigators that do not use the technique on a daily basis. However, for preliminary experiments and demonstrations, *in situ* NMR spectra from catalytic hydrogenations with the H_2 taken as is from a standard gas bomb may already be sufficient to reveal the desired results, as shown in this article. The ALTADENA procedure is usually preferred over the PASADENA procedure for such preliminary experiments, because it is easily conducted outside of the NMR magnet, intrinsically shows stronger enhancement factors, and is conducted with slightly enhanced H_2 pressure (up to 3 bar), if needed, in a simple NMR tube with a septum screw cap.

Experimental Section

PASADENA Hydrogenation of Ethyl Propiolate with [Rh(DPPB)(COD)]BF_4

In a standard 5-mm NMR sample tube, 2.17 mg (3 μmol) of [Rh(DPPB)(COD)]BF_4 were dissolved in 500 μl of acetone-d_6. Thereafter, 15.2 μL of ethyl propiolate (14.7 mg, 150 μmol, SCR = 50) were added to the solution, the sample tube temporarily sealed, and the solution thoroughly mixed by shaking. The 5-mm sample tube with the freshly made solution was positioned in an NMR spinner and hooked up, at its open end, to a 5-mm glass extension tube by a tightly fitting rubber hose connection. The assembly with the extension tube was lowered into the NMR magnet, whereby the spinner ensures an optimum positioning in the sweet spot of the magnetic field. The length of the extension tube was chosen to reach slightly above the upper end of the magnet bore. A long glass capillary tube was lowered through the extension tube into the sample tube reaching just above the reactive solution. Thereafter, the capillary was hooked up to a magnetic drive by a rope mechanism. The magnetic drive was positioned

Table 1. Calculated and experimentally derived PHIP enhancement factors.

	Calculation		Experiment	
	PASADENA	ALTADENA	PASADENA	ALTADENA
(a) t-H_2	36.8	73.6	6	29
(b) 36% p-H_2	1.10×10^4	2.20×10^4	1.8×10^3	1.2×10^4
(c) 100% p-H_2	3.07×10^4	6.13×10^4	–	–
(d) Ratio t-H_2/36% p-H_2	299	299	300	410

further away from the NMR magnet to avoid interference of its magnetic field with the NMR field but enabled the capillary tube to be lowered into the solution for hydrogen addition and to be removed from the solution for the NMR measurements. The insertion of the capillary into, and its removal from, the solution was controlled by the spectrometer console *via* a special TTL gate line.

The hydrogen gas for the reaction was either enriched in p-H_2 up to its thermal equilibrium at liquid-nitrogen temperature (77 K, 36% spin-polarized p-H_2), taken as is from a standard H_2 gas bomb, or generated with an electrolytic H_2 generator. For 3 s, it was bubbled at a pressure of minimally more than 1 bar through the capillary glass tube into the reactive solution. Thereafter, the capillary was raised and a waiting period of 2 s was passed to allow excess hydrogen bubbles to part from the solution before the NMR spectrum was recorded.

In the homogeneous hydrogenations with the catalyst precursor [Rh(DPPB)(COD)]BF_4, the COD must be hydrogenated first and removed from the catalyst before the hydrogenation of the designated reagent ethyl propiolate can occur. Therefore, hydrogen was bubbled several times in 3 s intervals into the reaction solution before PHIP signals of the desired product were recorded. Sometimes, however, some ethyl acrylate had already formed before COD was completely removed from the catalyst precursor. If the amount of acrylate was significant and seen in the NMR spectra even before a measurement of PHIP hyperpolarization was conducted, we used the difference between the integrated intensities of the acrylate's thermal signals before the reaction and after complete relaxation of the hyperpolarization to quantify the thermal signal intensity of acrylate formed during the 3 s of hydrogen injection.

ALTADENA Hydrogenation of Ethyl Propiolate with [Rh(DPPB)(COD)]BF_4

Similar to the PASADENA experiments, a reaction solution was prepared by dissolving 3 μmol of [Rh(DPPB)(COD)]BF_4 and, subsequently, 150 μmol of ethyl propiolate in 500 μL of acetone-d_6. A 5-mm NMR tube with a septum screw cap was used as the sample container and pressurized with H_2 gas up to 3 bar through a needle that was forced through the septum. The H_2 gas was either taken directly from an H_2 gas bomb, from an electrolytic H_2 generator, or after it had been enriched in p-H_2 to its thermal equilibrium at 77 K. The reaction was initiated outside of the NMR magnet by intense shaking of the sample tube. Thereafter, the sample tube was transported into the field of the NMR magnet by the standard pneumatic lift. A spectrum was recorded immediately after the deuterium lock of the spectrometer was stabilized.

Enrichment of p-H_2

Enrichment of p-H_2 up to its thermal equilibrium at liquid-nitrogen temperature (77 K) was achieved by flowing H_2 gas through a U-shaped brass tube reactor that was immersed into a liquid-nitrogen bath. The reactor was filled up to 2/3 of its height with activated coarse-grained charcoal and topped off with glass wool to constrain the filling. At 77 K, activated charcoal not only adsorbs H_2 but also catalyzes the conversion between o-H_2 and p-H_2, which is otherwise forbidden. About half an hour after initially flushing the charcoal reactor with H_2 from a standard gas bomb, a continuous flow of room-temperature H_2 gas enriched to 36% spin-polarized p-H_2 was obtained from one leg of the U-shaped reactor up to 100 mL/min. The flow was controlled by adding fresh H_2 from the gas bomb into the other leg of the reactor.

Acknowledgements

The idea to obtain PHIP NMR signals without the enrichment of para- or orthohydrogen (i.e., from reactions with hydrogen gas at its room-temperature thermal equilibrium) was sparked in 1993 by a discussion that one of the authors (K. W.) had with Prof. Simon B. Duckett (University of York, UK). Several years later (1997), Dr. Johannes Natterer and Dr. Ralph Giernoth (University of Cologne, Germany) were Ph.D. students of Prof. Dr. Joachim Bargon (University of Bonn). J. Natterer suggested to K. W. that thermal hydrogen should yield PHIP patterns; however, this was based upon density-matrix calculations in the product-operator formalism. R. Giernoth succeeded to obtain small PHIP signals during catalytic reactions with hydrogen from a standard hydrogen gas bomb. However, he was unable to decide whether the effect was real or due to parahydrogen enriched residues in the supply lines. The contributions and preliminary work of S. B. Duckett, J. Natterer, and R. Giernoth are greatly acknowledged. Finally, on a more amusing note, the motivational slogan "PHIP, PHIP, hurray!" introduced to Prof. Bargon's group for successful PHIP measurements by Dr. Stefan Klages is recognized. With this article, however, the slogan may return to its original version "HIP, HIP, hurray!" for the term "parahydrogen" or "polarized" in the acronym PHIP (parahydrogen induced polarization or polarized hydrogen induced polarization) is no longer needed.

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