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para-Hydrogen-Induced Polarization in Heterogeneous Hydrogenation Reactions

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Abstract: We demonstrate the creation and observation of *para*-hydrogen-induced polarization in heterogeneous hydrogenation reactions. Wilkinson's catalyst, $RhCl(PPh_3)_3$, supported on either modified silica gel or a polymer, is shown to hydrogenate styrene into ethylbenzene and to produce enhanced spin polarizations, observed through NMR, when the reaction was performed with H_2 gas enriched in the para spin isomer. Furthermore, gaseous phase *para*-hydrogenation of propylene to propane with two catalysts, the Wilkinson's catalyst supported on modified silica gel and Rh(cod)(sulfos) (cod = cycloocta-1,5-diene; sulfos = $^{-}O_3S(C_6H_4)CH_2C(CH_2PPh_2)_3$) supported on silica gel, demonstrates heterogeneous catalytic conversion resulting in large spin polarizations. These experiments serve as a direct verification of the mechanism of heterogeneous hydrogenation reactions involving immobilized metal complexes and can be potentially developed into a practical tool for producing catalyst-free fluids with highly polarized nuclear spins for a broad range of hyperpolarized NMR and MRI applications.

Introduction

Molecular hydrogen (H_2) is known to have two spin isomers, *ortho*-H_2 with the total nuclear spin $I = 1$, and *para*-H_2 with $I = 0$. The equilibrium ortho/para ratio is almost 3:1 at room temperature (RT), while at liquid hydrogen temperature (20.4 K) it shifts toward an almost pure *para*-H_2 form. Deviations of nuclear spin alignment from the statistical 3:1 ratio in *para*-enriched mixtures result in enhanced spin polarizations,[1] approaching in some cases 90%.[2] These polarizations are orders of magnitude larger than the thermal polarizations traditionally encountered in NMR. For example, at RT, 100% *para*-hydrogen can, at least theoretically, offer an enhancement of 4×10^4 on a 300 MHz NMR instrument (7 T magnetic field), and even larger enhancements can be expected for instruments with lower field magnets. To detect and utilize this enhancement, however, the equivalence of the two hydrogen atoms has to be broken, for example, by using H_2 in a suitable hydrogenation reaction with the *para*-hydrogen derived protons ending up at magnetically inequivalent sites on the substrate molecule.[3] This phenomenon, termed PASADENA (*para*-hydrogen and synthesis allow dramatic enhancement of nuclear alignment), was first observed and misinterpreted,[4] then predicted theoretically[3] and confirmed experimentally,[5,6] and later developed into a mechanistic tool for studying homogeneous hydrogenation reactions catalyzed by transition metal complexes.[1,7−12] In particular, enormous signal enhancement in the NMR spectra allows one to observe intermediate species and their rearrangements and to monitor reaction kinetics for hydrogenations carried out in the liquid phase.

In the following discussion, it is also useful to distinguish between the experimental schemes termed PASADENA and ALTADENA (adiabatic longitudinal transfer engenders net alignment).[13] The PASADENA effect gives rise to anti-phase

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multiplets in the NMR spectra of reaction products and involves the sudden breaking of magnetic equivalence when hydrogenation is carried out at high magnetic fields. The ALTADENA effect, on the other hand, involves hydrogenation at a low field followed by an adiabatic transfer of the hydrogenated product to the high magnetic field and also results in nonequilibrium population distributions. The exact pattern of the ALTADENA signal depends on the spin system, experimental parameters, and the flip angle of the radio frequency detection pulse, but is generally distinguished by characteristic emission and absorption patterns.[14,15]

The problem of low equilibrium polarization in NMR and MRI has instigated the use of hyperopolarized spin systems. In particular, it has been demonstrated recently that *para*-hydrogen-induced polarization can be used to produce liquid solutions with highly polarized ^{13}C nuclei for high quality, single-shot, sub-second angiography of blood vessels of a guinea pig or a rat.[16−18] However, the fact that the homogeneous catalyst is dissolved in the fluid along with polarized products can be a major obstacle for a much wider practical utilization of the hyperpolarization phenomenon. Catalyst recovery is important in many applications where the toxicity and biocompatibility of the catalyst are of prime concern or whenever the catalyst is expensive and must be recycled. This proves difficult in the case of *para*-hydrogen-induced polarization because the lifetime of nuclear spin polarization in the substrate molecule is of the order of several seconds. Bhattacharya et al. have stated, in their angiographic studies,[18] that it is possible to rapidly remove charged homogeneous catalysts from a polarized solution, yet this approach cannot be applied to all kinds of catalysts. Another viable approach is to use a heterogenized catalyst instead. Such a catalyst can be supported on a porous surface, on a nanocrystal, a microbead, or held between frits. One can then envisage a reaction scheme in which the reactants make sufficient contact with the catalyst and react to form the polarized product, which is then physically transported to the NMR detection (or imaging) coil, while the catalyst remains fixed in position and is easily recoverable, still active for the next batch of reactants.

To the best of our knowledge, there are no previous reports of observing PASADENA or ALTADENA in a heterogeneous hydrogenation reaction. One study uses the PASADENA effect to probe a solid ZnO surface,[19] but no hydrogenation of a substrate is performed, and the study investigates adsorption dynamics. Another study was published that used colloidal catalyst particles,[20] where it was conjectured that heterogeneous catalysts are not expected to give rise to the PASADENA effect. Indeed, industrial hydrogenation and related manufacturing processes often use heterogeneous catalysts comprising highly dispersed Pt or Pd metal particles supported on an appropriate porous material such as alumina. Hydrogenation on such catalysts is carried out at elevated temperatures and pressures and involves dissociative chemisorption of hydrogen molecules onto the metal particles, migration of hydrogen atoms over the metal particle surface, and spillover onto the support. Under such circumstances, the chances that the quantum correlation of the nuclear spins of the initial *para*-H_2 molecule will be retained and that the two hydrogen atoms of the molecule will end up in the same product molecule are indeed very small.[15] It appeared, therefore, that observation of PASADENA was limited to homogeneous catalysis only.

One of the growing trends in modern catalysis is an attempt to combine advantages of homogeneous catalytic processes with those of heterogeneous catalysis. This can be achieved, for example, by immobilizing a (modified) homogeneous catalyst on an appropriate porous support.[21,22] To date, numerous immobilization strategies have been developed, based on hydrogen bonding, ion pairing, chemical tethering to organic or inorganic supports, etc. Many of these approaches have also been applied to hydrogenation catalysts,[23−28] yielding stable, efficient, and selective catalysts for heterogeneous hydrogenation under mild conditions. The immobilization should, ideally, preserve the chemical characteristics of the catalyst, implying that the reaction mechanism remains unchanged, but a direct proof of this is difficult to furnish. In this paper, we observe, for the first time, PASADENA and ALTADENA spin polarization patterns in hydrogenated product molecules using several heterogenized catalysts, demonstrating that immobilized homogeneous catalysts retain their mechanism of pairwise molecular addition, preserve the original spin correlation between the protons of the *para*-H_2 molecule, and are therefore suitable for producing polarized fluids without the concomitant problems of dissolved homogeneous catalysts.

Experimental Section

Supported Catalysts. In the present study, we used three kinds of catalysts: Wilkinson's catalyst (**1**) supported on styrene-divinylbenzene copolymer (thereafter referred to as **1**/polymer); **1** supported on modified silica gel, $RhCl(PPh_3)_2PPh_2(CH_2)_2{-}SiO_2$ (**1**/SiO_2); and a supported tridentate complex Rh(cod)(sulfos)$-SiO_2$ (**2**/SiO_2; cod = cycloocta-1,5-diene; sulfos = $^{-}O_3S(C_6H_4)CH_2C(CH_2PPh_2)_3$). The **1**/polymer catalyst was obtained from STREM Chemicals Inc. (catalog number: 45-0670, 5 g, maroon beads, 20−60 mesh, 20% cross-linked). The **1**/SiO_2 was synthesized according to the procedure described elsewhere,[29] using commercial Wilkinson's catalyst (Sigma-Aldrich, product # 199982, 1 g) and 2-diphenylphosphinoethyl-functionalized silica gel (Sigma-Aldrich, product # 538019, 5 g, extent of labeling: 0.7 mmol/g loading, 200−400 mesh) as the starting materials. The $RhCl(PPh_3)_3$ catalyst is known to undergo rapid ligand exchange,[30] and therefore the addition of an approximately stoichiometric amount of 2-diphe-

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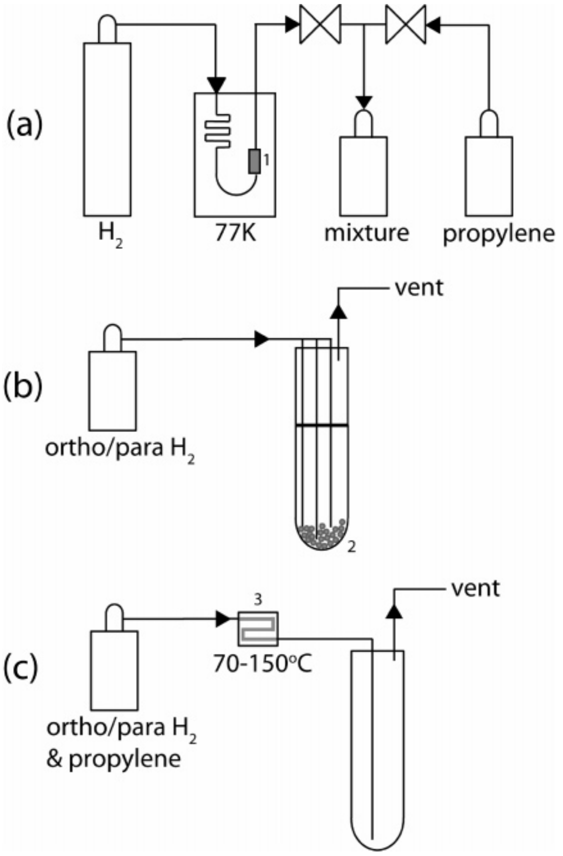
Scheme 1. Schematic Diagram of the Experimental Setup[a]



[a] (a) Production of *para*-enriched H_2 and preparation of a mixture of gaseous reactants. Normal H_2 (25% *para*-H_2) is passed through an ortho/para conversion catalyst (FeO(OH), labeled as 1) held at 77 K, producing a stream of 50% *para*-H_2. For gas-phase experiments, *para*-enriched H_2 is stored in a small cylinder (up to 100 psi), to which propylene gas is then added. (b) Liquid-phase hydrogenation experiment. The solution is bubbled with *para*-H_2 through an arrangement of 345 μm OD capillaries. The bottom of the 10 mm NMR tube contains one of the supported catalysts (labeled 2), and the solution contains approximately 0.1 M styrene in deuterated benzene. (c) Gas-phase hydrogenation experiment. The mixture of *para*-H_2 and propylene gas flows through a small reactor (labeled 3) consisting of copper tubing packed with a supported catalyst and held at 70−150 °C. The resulting mixture of propane gas with the unreacted propylene and H_2 flows into the NMR tube residing in the probe of the NMR spectrometer.

nylphosphinoethyl-functionalized silica gel to a toluene solution of Wilkinson's catalyst leads to formation of the required catalyst.[29] To ensure full replacement of ligands, the mixture was stirred overnight at RT. The supported catalyst was then removed from the solution by filtering, washed three times with toluene, and dried under vacuum at RT. To prevent oxidation of the catalyst, all manipulations were carried out under nitrogen atmosphere.[26] The catalyst **2**/SiO_2 (0.54 wt % Rh) was obtained from P. Barbaro and colleagues.[31]

***para*-Hydrogen Production.** Approximately 5 g of FeO(OH) (Sigma-Aldrich, 30−50 mesh, used as received) was placed in the straight section of a heat exchanger, which was then immersed in a liquid nitrogen dewar (Scheme 1a). Ultrahigh purity H_2 was first passed through the coiled section of the exchanger and, only thereafter, came in contact with the catalyst. This produces a constant flow of approximately 50% *para*-H_2. We verify this using porous alumina (γ-Al_2O_3) that had been dried for 1 h at 250 °C under vacuum. Either normal or *para*-enriched H_2 gas was freely flowing through the cell filled with alumina beads while NMR spectra were acquired. A 2-pulse spin echo sequence with 1 ms echo time was used to diminish the contribution of the residual water to the detected NMR signal. The background signal was measured after purging alumina with nitrogen gas and was later subtracted from the signal intensity measured in the presence of H_2. The decrease in signal relative to the normal H_2 gives a quantitative measure of the conversion to *para*-H_2. We observed that we could achieve the desired 1:1 para/ortho ratio at flow rates up to 150 standard $cm^3\ min^{-1}$ (sccm).

Experimental Setup. Our experiments were performed on a 300 MHz Bruker Avance DRX spectrometer equipped with a 10 mm BBO (broad-band observe) probe. A variable-temperature unit was used to keep the samples at 65 or 80 °C to increase the rate of the reactions. All spectra were acquired using 45° rf pulses to obtain maximum signal[3] from the PASADENA experiments. Our flow setup comprises five fused silica capillaries (345 μm OD, Polymicro Inc.) that extend to the bottom of the 10 mm NMR tube to provide the inflow of gas and a 1/16" tube at the top to vent the gas to a hood (Scheme 1b). These are attached to a Teflon insert that seals the tube to prevent oxygen from entering and deactivating the catalyst. A pinch valve is located just above the magnet to close both the input and the output lines to allow very quick initiation and termination of the gas flow. Both the pinch valve and the selection of gas are controlled from the spectrometer via TTL lines.

Heterogeneous Hydrogenation in Solution. The samples comprising 4 mL of C_6D_6 and 50 μL of styrene were deoxygenated for several minutes by bubbling N_2 through the solution before adding the supported catalyst. The N_2 flow was left on while assembling the flow setup to purge any oxygen in the NMR tube or other tubing. The prepared sample was placed inside the NMR magnet, and an initial delay of 15 min was used to allow the reaction mixture to equilibrate at 65 °C. The reaction was initiated by bubbling *para*-enriched H_2 through the solution for some duration of time (ranging from 5 s to 5 min) at a flow rate of 100 sccm. After the pinch valve was closed, a delay of 5 s was used to allow the supported catalyst particles to settle out of the RF-sensitive region before acquisition, protecting against susceptibility-induced broadening in the PASADENA spectra. ALTADENA spectra were obtained by bubbling *para*-enriched H_2 through the sample while holding it outside the magnet, and then quickly placing it in the magnet bore. The H_2 used in these experiments came directly from the conversion setup described above, thus being nominally 50% *para*-H_2.

Heterogeneous Hydrogenation in Gas Phase. Each sample was prepared by purging the NMR tube with N_2 before adding the supported catalyst and leaving the flow of N_2 on while assembling the flow setup. For the PASADENA experiments, the sample was placed inside the NMR magnet, and an initial delay of 10 min was used for the sample to reach 80 °C. The gaseous reactant mixture was prepared by purging an aluminum cylinder (by alternately filling it with ultrahigh purity N_2 and evacuating with a pump) and then filling it with 50 psi H_2 from the conversion setup already described. This cylinder was then filled with an additional 50 psi of propylene, yielding a mixture of 50% propylene, 25% *para*-H_2, and 25% *ortho*-H_2 (Scheme 1a). PASADENA experiments were performed by completely opening the needle valve regulating the gas flow, and driving the gas at full pressure (20−100 psig) to maximize stirring of the catalyst in the NMR tube. The spectrum was acquired while the gas was still flowing through the NMR tube. For the gas-phase ALTADENA experiment, we made a small S-shaped reaction cell from a short (6") length of 1/8" copper tubing (Scheme 1c). About 0.1 g of the catalyst was packed between plugs of glass wool. The cell was held at 70−150 °C while the mixture of propylene and H_2 flowed through the cell and then into the bore of the magnet to the NMR tube. Typical flow rates ranged between 50 and 225 sccm.

Results

Heterogeneous Hydrogenation in Solution. Both **1**/SiO_2 and **1**/polymer supported catalysts hydrogenate styrene when H_2 is bubbled through the sample tube containing the solution of

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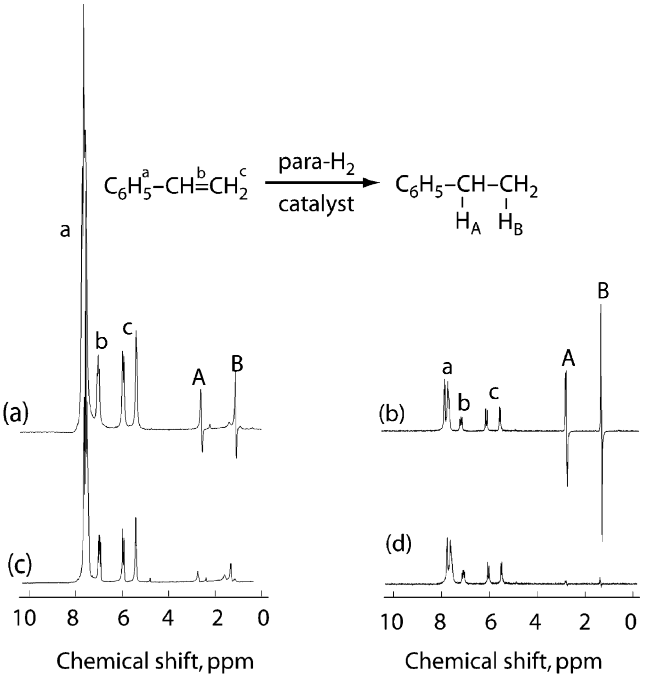

Figure 1. Proton NMR spectra for in situ (PASADENA) *para*-hydrogenation of styrene in C_6D_6 at 65 °C. The spectra in (a) and (c) are from **1**/SiO_2, and those in (b) and (d) are from **1**/polymer. Antiphase peaks from the polarized protons in the ethylbenzene product labeled A and B appear at $\delta = 2.6$ and 1.2 ppm. Spectrum (a) was acquired after *para*-hydrogenation for 8 s inside the magnet. Spectrum (b) was acquired after *para*-hydrogenation for 15 s. Spectra (c) and (d) were acquired after bubbling *para*-H_2 gas through the supernatant solutions after removing the catalysts; (c) was acquired after 15 min of bubbling, no PASADENA or product formation is observed. The spectrum in (d), acquired after 15 s of bubbling, shows a very small anti-phase pattern. The spectra [(a) and (c)] [(b) and (d)] are plotted to the same vertical scale.

styrene and the catalyst. More importantly, both catalysts produce clear PASADENA signals as *para*-enriched H_2 is bubbled through the sample at high field. The catalysts also produce ALTADENA signals when *para*-enriched H_2 is bubbled outside the magnet. We also observed that the polymer-supported Wilkinson's catalyst beads appear to be very sensitive to conditions allowing efficient diffusion of the reactants and products into and out of the beads. Long activation times, sometimes greater than 1 h at elevated temperatures, were needed before the catalyst became active, presumably allowing the beads to swell and expose their catalytic centers.[32] Furthermore, having high flow rates of gas that produced good stirring of the beads and long bubbling times (more than 1 min) to ensure saturation of the solution with H_2 were critical to consistently observe polarization with this catalyst. The **1**/SiO_2 catalyst, on the other hand, becomes active as soon as the temperature is raised above RT and produces large polarization even for bubbling times as short as a few seconds. The results from the high-field *para*-enriched hydrogenation (PASADENA) employing these catalysts are shown in Figure 1a and b, and the ALTADENA spectrum for the **1**/SiO_2 catalyst is shown in Figure 2.

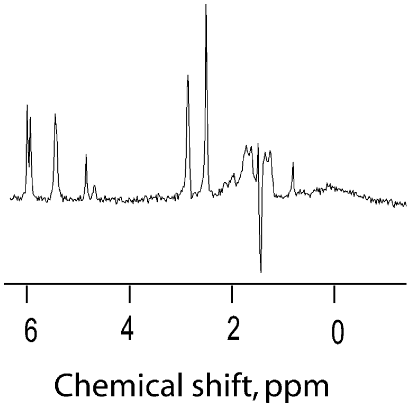

Figure 2. Proton NMR spectra from ex situ (ALTADENA) *para*-hydrogenation of styrene in C_6D_6 in the presence of the **1**/SiO_2 catalyst. The ALTADENA peaks appear as emission and absorption signals at $\delta =$ 1.2 and 2.6 ppm, respectively. The spectrum was acquired with a 45° flip angle pulse, after bubbling *para*-H_2 for 10 s and subsequent transfer to the high field magnet for detection.

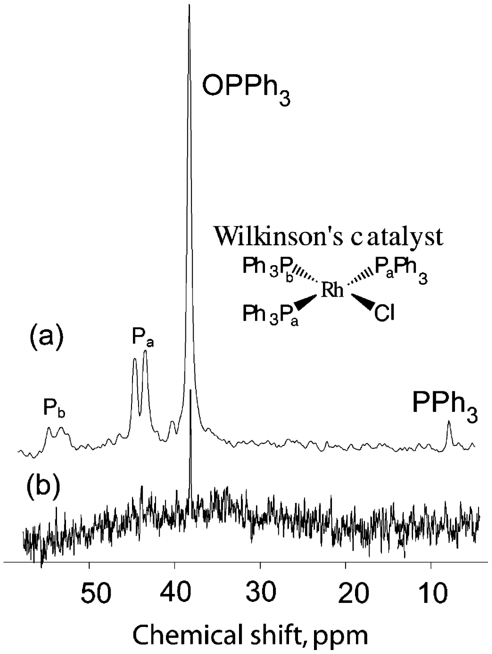

Figure 3. ^{31}P NMR spectrum of (a) homogeneous Wilkinson's catalyst dissolved in C_6D_6 and (b) supernatant solution, recovered after *para*-hydrogenation of styrene with **1**/polymer. The sharp peak around $\delta =$ 38 ppm is assigned to $OPPh_3$. In (a), the multiplets at shifts $\delta = 44$ and 54 are from the metal-bound phosphoruses; in (b), neither of these peaks are observed, whereas the broad hump in spectrum (b) indicates the likely presence of very fine heterogeneous polymer particles in solution accounting for the small PASADENA signal in Figure 1d. The two spectra were detected using identical experimental parameters except the number of accumulations, which was 512 for spectrum (a) and 4096 for (b).

To exclude the possibility that polarization is produced in a homogeneous hydrogenation reaction due to metal complex leaching off the support, the following test was performed. After hydrogenation, the solution was separated from the supported catalyst, and *para*-enriched H_2 was bubbled through the supernatant liquids. The resulting spectra are shown in Figure 1c and d and demonstrate that the contribution of the homogeneous process is negligible. Additionally, a ^{31}P spectrum detected for this solution is shown in Figure 3 (see discussion below).

Heterogeneous Hydrogenation in Gas Phase. As a further demonstration that the supported catalysts produce PASADENA signals heterogeneously and not via a homogeneous reaction mechanism, we used **1**/SiO_2 and **2**/SiO_2 to *para*-hydrogenate propylene gas. In the gas phase, there is no possibility for

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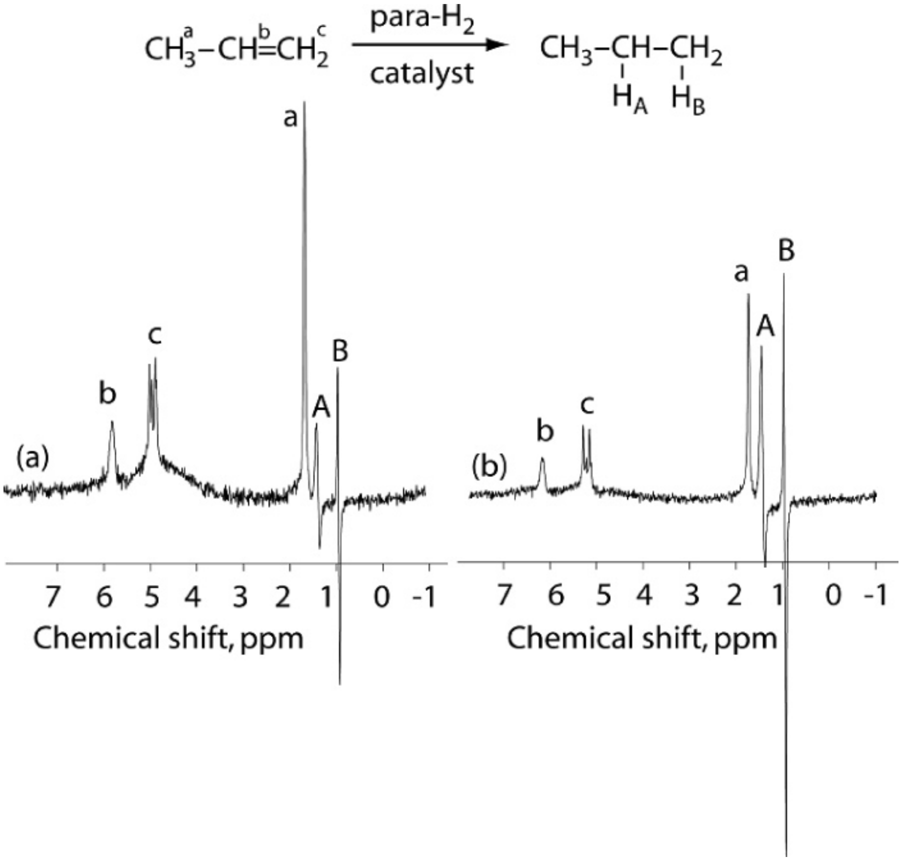

Figure 4. Proton NMR spectrum from the in situ hydrogenation of propylene with 50% *para*-hydrogen. Spectrum (a) shows the result obtained using the **1**/SiO_2 catalyst, and (b) is from the **2**/SiO_2 catalyst. The sample temperature was 80 °C. The peaks from the polarized spins in the propane product appear at $\delta = 1.4$ and 0.96 ppm and are labeled as A and B in the spectra. The remaining peaks are from the unreacted propane, and the hump between $\delta = 4$ and 5 ppm is from *ortho*-H_2. Because of the absence of a lock reference, the chemical shift scale is internally calibrated with respect to the propylene CH_3 peak.

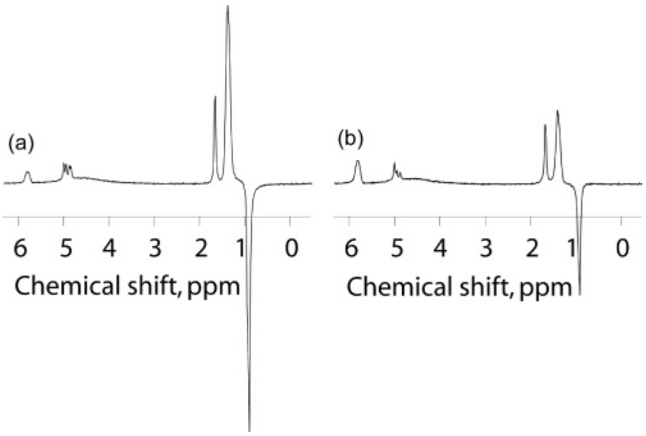

Figure 5. Proton NMR spectrum from the ALTADENA experiments, hydrogenating propylene in the presence of (a) **1**/SiO_2 and (b) **2**/SiO_2 catalysts, packed in a catalytic cell, at 150 °C and subsequently flowing the gaseous mixture into the high field of the magnet, at flow rates of 100 and 225 sccm, respectively. The ALTADENA peaks from the *para*-hydrogen derived protons appear as significantly enhanced absorption and emission signal peaks at $\delta = 1.4$ and 0.96 ppm.

catalyst leaching, and any observation of polarization must stem from a heterogeneous catalytic reaction. Both catalysts were very active in the gas phase and produced exceedingly strong antiphase multiplets and fast product formation, the results of which are shown in Figure 4. Because of the increased catalytic activity observed with these complexes, we found it important to acquire background spectra with the catalyst removed from the NMR tube before and after each experiment, to ensure the absence of catalytic contaminants from prior hydrogenations as even small amounts can produce enhanced polarizations. We also observed large signal enhancements from ALTADENA experiments with both the **1**/SiO_2 and the **2**/SiO_2 catalysts, the spectra being shown in Figure 5.

Discussion and Conclusions

Our results constitute the first direct confirmation of the mechanism of the hydrogenation reaction utilizing immobilized metal complexes. The clear PASADENA and ALTADENA spectral patterns confirm the preservation of the longitudinal spin order between the protons derived from the same *para*-hydrogen molecule, proving that the addition is, indeed, pairwise. Moreover, there can be no a priori certainty that an immobilized complex will produce polarization even if the chemical mechanism of the reaction remains essentially the same as in homogeneous solution. Indeed, the transfer of both hydrogen atoms of an H_2 molecule to the same product molecule is a necessary condition for the observation of PASADENA or ALTADENA, but is not a sufficient one. In the transient dihydride complex formed upon interaction of H_2 with the catalyst, the equivalence of the two H atoms is lost, and the initial coherence of nuclear spins starts to decay due to spin

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relaxation processes.[34] Therefore, significant polarization in the product can be expected only if the lifetime of the intermediate dihydride complex is not much longer than its spin−lattice relaxation time. Because the mobility of the dihydride complex is expected to change substantially upon immobilization, this could lead to a significant enhancement of nuclear relaxation processes and to a complete loss of spin coherence. Furthermore, for homogeneous hydrogenation with transition metal complexes, it is well known that subtle modifications of the catalyst and its environment, for example, slight variation of the ligand structure, can have a pronounced effect on the reaction efficiency, and in particular on the lifetime of the dihydride complex. A more stable dihydride intermediate may still yield hydrogenation product, but could be detrimental for the observation of *para*-hydrogen-induced polarization. The results presented above demonstrate that there are systems where this does not happen.

With reactions catalyzed by supported complexes, there is always a question of whether the formation of the product and/or polarization is indeed due to heterogeneous catalysis and not catalyzed by rhodium complexes that leach off the surface and are present in solution. To establish a control for this potential problem, we separated the solutions from the catalyst after the hydrogenation experiment and bubbled *para*-enriched H_2 through the supernatant liquids. The resulting spectra shown in Figure 1c and d demonstrate that the solution from the polymer-supported Wilkinson's catalyst beads gave a very small polarization (with an absolute integrated intensity that is approximately 3% of the PASADENA signal with the catalyst). Such a dramatic decrease of polarization efficiency rules out the possibility of seeing polarization due solely to catalyst leaching into solution and acting homogenously. Furthermore, a ^{31}P spectrum of this solution, shown in Figure 3, contains no peaks from free Wilkinson's catalyst, but only a sharp peak from the oxidized form of the PPh_3 ligand, which dissociates from the Rh precatalyst.[33] Additionally, a very broad peak is also evident, which is consistent with small polymer particles dispersed through the solution. Both the distribution of polymer chain lengths (and thus ^{31}P content) as well as the rigid polymer that the ^{31}P nuclei are attached to would contribute to a very broad ^{31}P peak. Most likely, the small polarization observed in the decanted solution is due to such small polymer particles, some of which have the bound catalyst and give rise to the small PASADENA signal patterns in Figure 1d. When testing **1**/SiO_2, we avoided the potential problem of very fine particles dispersed in solution by filtering the solution through a Hirsch funnel (4−5.5 μm pore size). We then bubbled *para*-H_2 through this solution for 15 min and observed no detectable PASADENA signal or product buildup, as demonstrated with the spectrum shown in Figure 1c. The solution was recombined with the catalyst, and PASADENA signal was again observed (data not shown), demonstrating that the reaction is being catalyzed solely by the heterogenized catalyst. While such tests cannot rule out the presence of traces of the metal catalyst in solution, they do prove that spin polarization is almost exclusively produced by the immobilized catalyst.

Numerous NMR and MRI applications, in particular those carried out in low and ultralow magnetic field environments,[35,36] could immensely benefit from the ability to produce polarized media (both liquid and gas phase), free of dissolved catalyst.[37] For low field measurements, the thermal polarization is exceedingly small, and it is, therefore, very attractive to utilize *para*-hydrogen-induced polarization for increased sensitivity. Our gas-phase ALTADENA experiments demonstrate that it is also possible to hyperpolarize a continuously flowing stream of a fluid by passing it through a catalytic reactor packed with an active heterogenized catalyst. This mechanism can become a promising candidate for replacing the costly ^3He or ^{129}Xe gases that are currently used for void-space MRI. Previously demonstrated applications include hyperpolarized lung imaging,[38−40] or measuring profiles of fluid flow in porous media[41] or microchannels.[42,43] Heterogenized catalysts can also contribute to the rapidly advancing area of studying catalyzed reactions with NMR microfluidic technology.[44,45] For example, a porous silicon layer supporting the catalyst and etched in the form of a microchannel can simulate a catalytic microreactor,[46] allowing the possibility of investigating multiphase reactions in the silicon chip. It should also be mentioned that heterogeneously catalyzed *para*-hydrogenations can, just as their homogeneous counterparts, lead to enhanced signals on other nuclei. For example, the ALTADENA and field cycling methods can efficiently transfer polarization to ^{13}C nuclei, which are especially attractive for their slow longitudinal relaxation rates. It is straightforward to implement these methods using immobilized catalysts and, therefore, to achieve long-lived, polarized nuclear spin states opening up possibilities for enhanced signal-to-noise imaging and spectroscopy.[14,16−18]

Last, we would like to stress that conditions of hydrogenation and sample transfer used in this work were not optimized, and yet hydrogenation at a reasonable temperature and atmospheric pressure has yielded pronounced nuclear spin polarization. This gives us confidence that this first observation of *para*-hydrogen-induced polarization in a heterogeneous reaction can be developed into a useful practical tool for sensitivity-enhanced NMR and MRI.

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(37) We note that the procedures outlined above are not suitable for an immediate use in in vivo applications. Such applications would require the use of different solvents and substrates, and a careful measurement of the residual quantities of the metal in solutions after the reaction. While our tests indicate that supernatant solutions are inactive in hydrogenating the substrates and in producing polarization, they cannot exclude the presence of residual amounts of metal in its inactive form.

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