Supporting Information

Demonstration of Heterogeneous Parahydrogen Induced Polarization Using Hyperpolarized Agent Migration from Dissolved Rh(I) Complex to Gas Phase

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I. Rh(I) complex preparation

Briefly, 1,4-bis[(phenyl-3-propanesulfonate) phosphine] butane disodium salt (0.180 g, 0.32 mmol, 717347, Isotec - Sigma Aldrich, OH, USA) was combined with 10 mL of 99.8% D_2O in a 1 L flask. This solution was then degassed at ambient temperature with a rotary evaporator (model R-215 equipped with V-710 pump, Buchi, New Castle, DE, USA) fitted with an Argon (g) input, by decrementing the onboard pressure slowly to avoid boiling, from 70 to 25 mbar over approximately 10 minutes. The rhodium catalyst, bis(norbornadiene) rhodium (I) tetrafluoroborate (0.10 g, 0.27 mmol, 45-0230, CAS 36620-11-8, Strem Chemicals, MA, USA) was dissolved in 3 mL of acetone and was added drop-wise to the phosphine ligand solution to limit undesirable precipitation. The solution was degassed with the rotary evaporator resulting in solution of **1** containing Rh(I) complex in D_2O with Rh(I) concentration of 26.7 mM with most of acetone being evaporated. A 7 ml aliquot of this solution was used in high-field NMR experiments.

In order to obtain solution of Rh(I) metal complex in an organic solvent, 0.1 g of $[Rh(I)(NBD)_2]^+BF_4^-$ (**2**) was dissolved in the mixture of 5 mL of C_6D_6 and 1.5 mL of CD_3OD. The solution was degassed by passing a stream of Argon gas for ~ 5min.
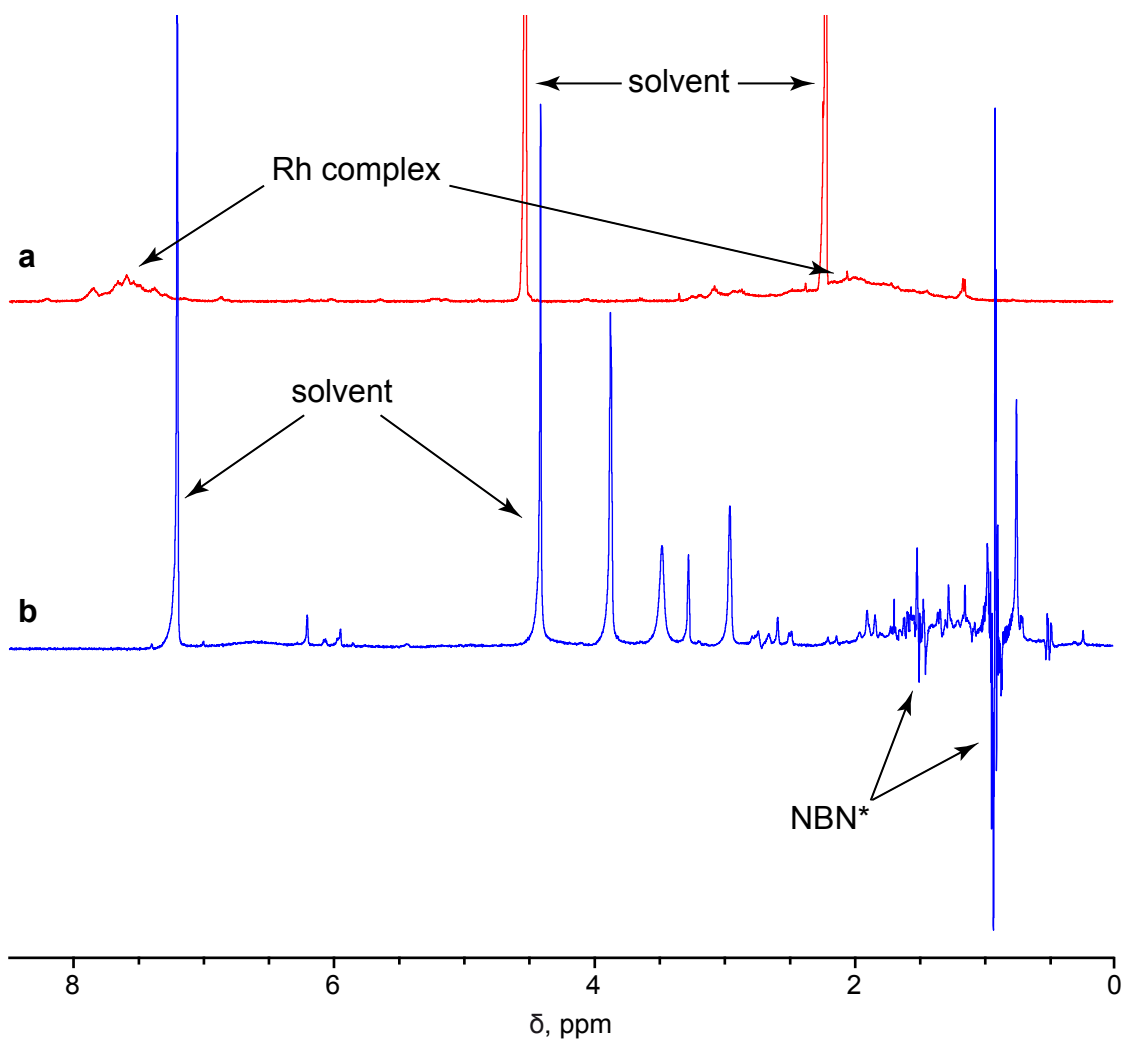
II. NMR experiment at 9.4 T

Figure S1. a) ^{1}H NMR spectrum of solution of **1** in D_2O recorded at 9.4 T after bubbling para-H_2. Left peak at ~4.7 ppm corresponds to HDO and/or H_2O; the other main resonance on the right corresponds to acetone leftovers of the preparation procedure. b) ^{1}H NMR spectrum of solution of **2** in C_6D_6/CD_3OD (5/1.5) recorded at 9.4 T after bubbling para-H_2. Antiphase multiplets clearly indicate PASADENA-type PHIP in spectrum (b) but not in spectrum (a).
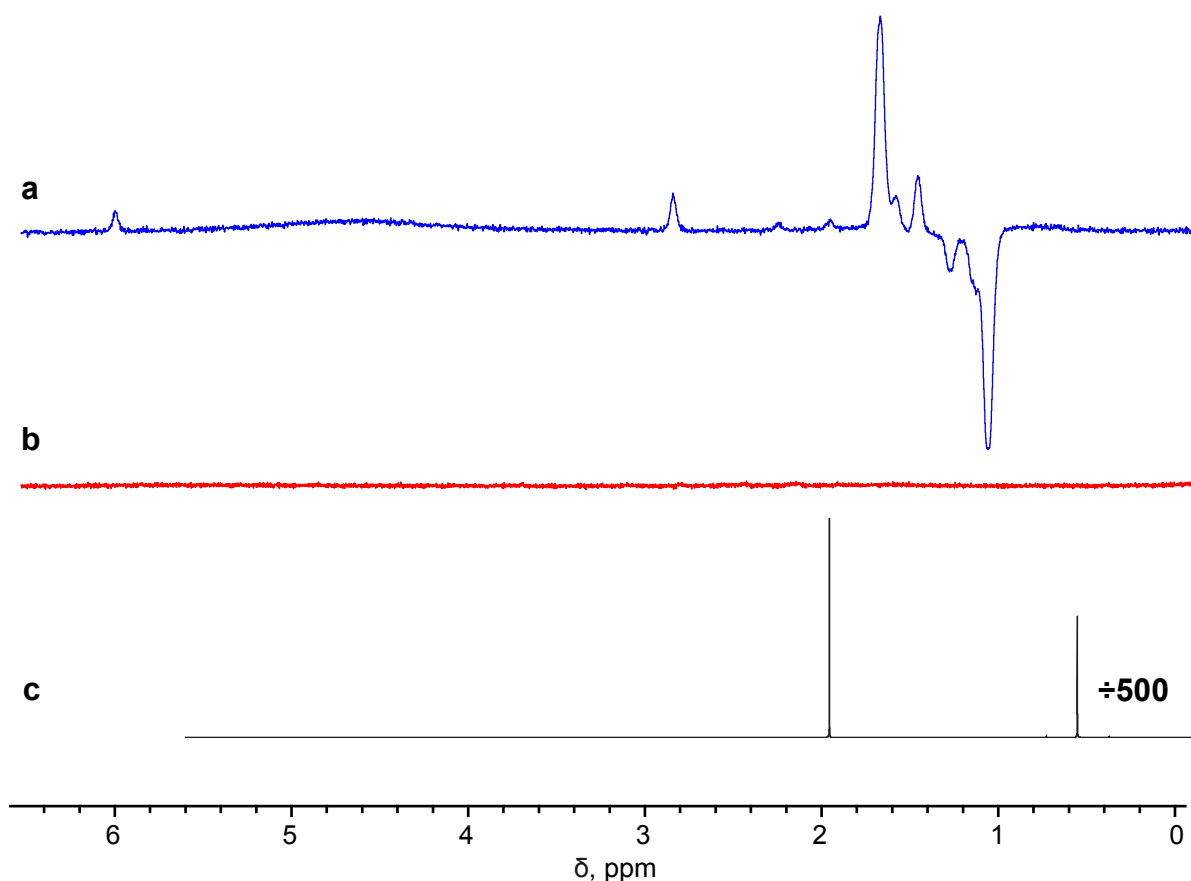
Figure S2. a) ALTADENA ^{1}H NMR spectrum of the gaseous stream during bubbling of para-H_2 through D_2O solution of $[Rh(I)(NBD)L]^+BF_4^-$ at 70-80 °C using the setup shown in Fig. 2c. The spectrum was acquired with 4 averages; b) ^{1}H NMR spectrum acquired with 1 signal average after flow termination; c) ^{1}H NMR spectrum of the reference sample containing 56 mM solution of CH_3OD in D_2O for signal enhancement calculation. All spectra are acquired at 9.4 T.

III. Additional experimental details relevant to experimental setup of Fig. 2c

7 ml of solution of Rh(I) complex **1** was added to the reactor, Fig. 2c. The reactor utilized had an inner volume of 56 mL and was made of polysulfone. Filling the reactor with polypropylene hollow balls reduced the effective volume to 30 mL. ^{1}H NMR ALTADENA spectra were recorded in the gas phase using the setup shown in Fig. 2c while para-H_2 was bubbled through the reactor. Once started, the para-H_2 gas flow rate was held constant at 5.3 mL/s until the end of

the reaction, which was detected by NMR spectra. The reaction was completed after acquisition of forty spectra (4 signal averages per spectrum) corresponding to 228 seconds.

IV.   *In situ* NMR experiment at 47.5 mT

Because NBN is insoluble in water under these conditions, as confirmed by high-field NMR studies, the obtained low-field NMR signal corresponds to polarized NBN in the gas phase only. Because the 0.5 L RF coil covers the 56 mL reactor completely, it is possible to calibrate the hyperpolarized NMR signal to the NMR signal of an external reference sample of water with the goal of polarization enhancement quantification.

3.6 mL of 10 mM aqueous solution of catalyst (Rh(I) complex **1** in 99.8% D_2O) was preheated at 60°C for 20 seconds, and then injected into an atmosphere of >90%[1] parahydrogen gas at 35 °C (56 mL, 7 bar). The foamed solution was allowed 3 seconds for the hydrogenation reaction time, and then spectra were acquired with 45° excitation RF pulses (42 μs at 10 W). The RF probe used in these studies was similar to that described by Coffey and co-workers[2] with minor modifications to the coil windings inside a 90 mm gradient coil (Magritek, Wellington, New Zealand). The magnet was shimmed using an automated shimming routine provided by the manufacturer. The signal enhancement was calculated as described previously[3] although accounting for the number of averages, because the spectrometer detector was in averaging mode. The signal integral from polarized NBN (Fig. 3a) was 11.9-fold less than that from water (Fig. 3c), when adjusted for the number of scans. There were 86400 times more water molecules in the reference sample than the number of injected NBD molecules. The calculated enhancement factor of 10300 is the lower estimate, because it assumes no polarization losses during the 3-second reaction time and a complete (100%) chemical conversion of NBD to NBN. We also note that the resulting anti-phase signal would likely suffer intensity loss from partial collapse, because the spin-spin coupling is ~6-10 Hz in similar spin systems, the chemical shift of the two nascent parahydrogen protons differs by < 2 Hz, and the FWHH was ~40 Hz for a water reference sample.

V. Signal enhancement factor calculation using ALTADENA, setup 1, Fig. 2c.

An external reference sample was also used to estimate signal enhancements (Fig. S2c). Note that continuous production of NBN by bubbling para-H_2 through solution of **1** eventually leads to a complete depletion of NBD, because the reaction is irreversible. Therefore, the total amount of polarized NBN may be estimated by comparing peak production (Fig. S3c) to an external reference (Fig. S2c), assuming that all produced NBN migrates to the gas phase and is transported to the NMR tube. Since the melting point of NBN is > 40 °C and a fraction of NBN can deposit on the walls of the 1/32" I.D. 3-m long PTFE tubing between the reactor and the NMR tube in the bore of the magnet, Fig. 2c, this second estimate of enhancement factor of 11 is expected to be lower than $\varepsilon = 164$ obtained with the former quantification method described in the main text. Nevertheless, the two numbers are in a qualitative agreement assuming that delivery-associated losses of NBN are significant. The details are provided below.

40 spectra (recorded using 4 signal averages each) were acquired during 228 seconds after the start of para-H_2 bubbling. The same region from 1.5 - 1.8 ppm corresponding to one of the aliphatic NBN protons was integrated after baseline correction. All integral values were normalized to the reference integral value (external reference used), Fig. S3c. A reference sample for polarization enhancement ε calculation was prepared by following procedure. 50 μL of CH_3OD was mixed with 1 mL of 99.8% D_2O. Then 50 μL of this solution was mixed with 1 mL of 99.8% D_2O again. This resulted in 56 mM solution of CH_3OD in D_2O. The concentration of protons in the reference sample, therefore, was 167 mmol/L.

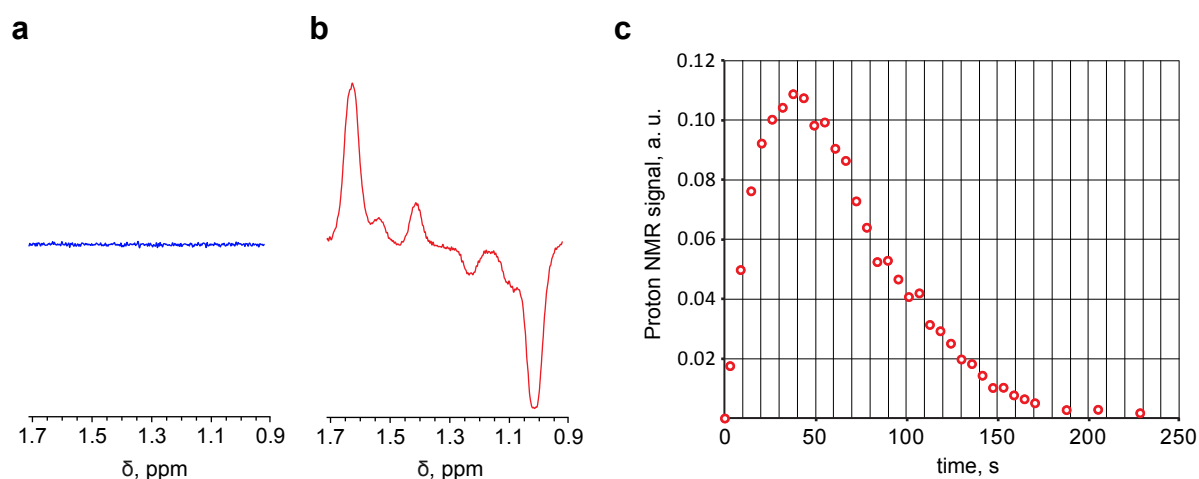**Figure S3.** a) Comparative representation of the NBN aliphatic protons region (0.9 – 1.7 ppm) for ^{1}H NMR spectra of gaseous streams when C_6D_6/CD_3OD (a) and D_2O (b) were used as solvents for the Rh(I) complex. c) The dependence of aliphatic NBN proton signal integral (1.5 - 1.8 ppm) on reaction time. The parahydrogen flow rate was constant at 5.3 mL/s. All spectra were acquired at 9.4 T.

Calculation of signal enhancement factor from the above data. By multiplying the gas volume flow rate U $[mL/s]$ by the experiment time t $[s]$, and dividing by the total number of NMR acquisitions (N – number of spectra, n – number of averaging scans/spectrum used to record one NMR spectrum in signal accumulation mode), it is possible to calculate the volume of gas passing through the detector RF coil during one NMR acquisition:

$$V = \frac{U \cdot t}{N \cdot n} = \frac{5.3[mL/s] \cdot 228[s]}{40 \cdot 4} = 7.55[mL]$$

The gas volume $V_{\text{RF coil}}$ contributing to the NMR signal after RF pulse excitation equals the volume of RF coil, which is approximately 0.3 mL. This means that most of the NBN gas passes through the RF coil without being detected. To account for this "dark" volume, a correction factor F_V can be used, with $F_V = 7.55/0.3 = 25$. The sum of all normalized integrals, Fig. S3c, was calculated, and was equal to 1.6 [normalized units]. If it would be possible to collect all polarized NBN gas without any detection losses associated with the small volume of RF coil, the

corrected sum of all normalized integrals would then be approximately equal to 1.6*25 = 40 [n.u.]. The signal enhancement factor, ε, may be calculated using the integrals of the signals of hyperpolarized NBN (I_{HP}) and thermally polarized reference sample (I_{REF}):

$$\varepsilon = \frac{I_{HP}/n_{HP}}{I_{REF}/n_{REF}}$$

$n_{HP} = number\ of\ NBN\ molecules\ (=$

$number\ of\ protons\ contributing\ to\ the\ integral) = 187$ µmoles

$n_{REF} = number\ of\ protons\ in\ reference\ sample = 167$ mmol/L $* 0.3$ mL $= 50$ µmoles

Because the reference signal of NBN had a very low intensity, we used this method based on the maximum quantity of detected NBN and NMR of the reference to calculate ε:

$$\varepsilon = 40\frac{50}{187} \approx 11$$

This means that the signal of polarized NBN gas was more than 11 times greater than Boltzmann polarization at a 9.4 T magnetic field strength, because the above calculation doesn't take into account the gas phase NBN transfer losses, which are likely due to condensation on the walls of the Teflon capillaries along the path to the NMR spectrometer RF coil. Comparison of the two spectra in Fig. 2 shows that the actual enhancement factor is indeed larger than 11, as otherwise the NBN signals would be observable in the spectrum of Fig. 2b. The concentration of NBN in the gas phase can be roughly estimated as 187 µmoles /(5.3 mL/s * 228 s) = 0.15 mM, which is below the vapor pressure level for NBN (32 hPa at 65 °C, or ca. 1 mM; data from http://www.merckmillipore.com/).

The value of ε might also be estimated directly from the spectra based on the SNR of the two spectra: (i) obtained in the gas phase during para-H_2 flow through the chamber, Fig. S2a, and (ii) after flow termination, Fig. S2b. By using exponential line broadening of 20 Hz, the SNR in the spectrum of Fig. 2a was evaluated as 82 ± 13. The noise level in the spectrum of Fig. S2b is the same. Therefore, given that the NBN signals in Fig. S2b are below the noise level and accounting for the proton quantity difference by a factor of 2 in a) and b), it was concluded that ε

was no less than 164. We note that this is the lower limit for the enhancement factor, which is likely limited by the poor SNR of spectrum in Fig. S2b and relaxation-associated polarization losses during NBN transport into the RF coil of the 9.4 T high-field NMR spectrometer.
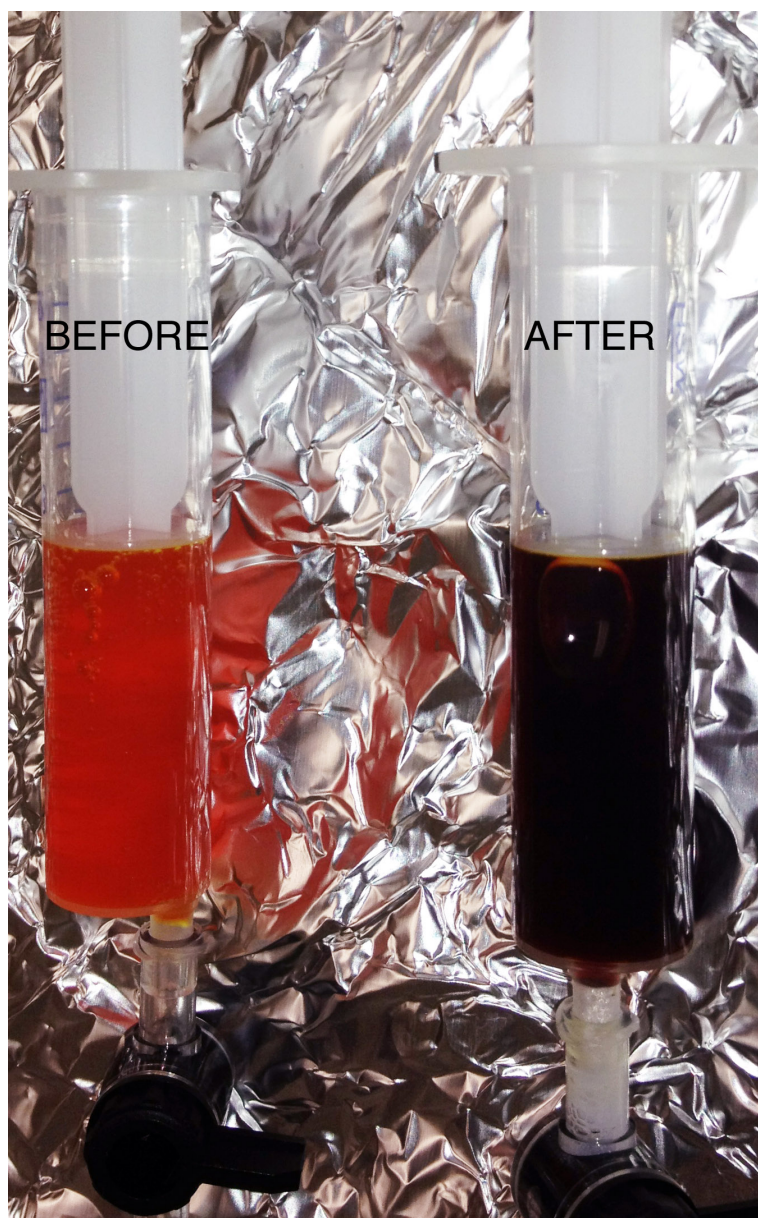

Figure S4. Photographs of Rh(I) complex solution in D_2O before and after the hydrogenation reaction.

References cited in Supporting Information

(1) Feng, B.; Coffey, A. M.; Colon, R. D.; Chekmenev, E. Y.; Waddell, K. W. *J. Magn. Reson.* **2012**, *214*, 258-262.
(2) Coffey, A. M.; Shchepin, R. V.; Wilkens, K.; Waddell, K. W.; Chekmenev, E. Y. *J. Magn. Reson.* **2012**, *220*, 94–101.

(3) Waddell, K. W.; Coffey, A. M.; Chekmenev, E. Y. *J. Am. Chem. Soc.* **2011**, *133*, 97-101.