

Electronic Supplementary Information

Toward Production of Pure ^{13}C Hyperpolarized Metabolites Using Heterogeneous Parahydrogen-Induced Polarization of Ethyl [1- ^{13}C]acetate

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Catalyst preparation

Rh/TiO₂ catalysts with 1 wt% and 23.2 wt% metal loadings were prepared using wet impregnation technique. For the preparation of Rh/TiO₂ catalyst with 1 wt% metal loading the acidic solution of Rh(NO₃)₃ (C_{Rh} = 38 mg/mL) was used. The 1.06 mL of Rh(NO₃)₃ solution was evaporated to dryness and after that was diluted with water to a total volume of 1.6 mL. The 2 g of TiO₂ powder (Hombifine N, S_{BET} = 107 m²/g) was initially calcined at 500 °C for 2 h and then was impregnated with aqueous solution of Rh(NO₃)₃ for 1 h at room temperature. Then the solvent excess was evaporated and catalyst was dried in air at 120 °C for 4 h. Next, calcination of the obtained sample at 400 °C in air for 3 h and the subsequent reduction in H₂ flow at 330 °C for 3 h were carried out.

For the preparation of Rh/TiO₂ catalyst with 23.2 wt% metal loading, a slightly different procedure was used. The acidic solution of Rh(NO₃)₃ (C_{Rh} = 88 mg/mL) was utilized. The 5.68 mL of Rh(NO₃)₃ solution was evaporated to dryness and after that was diluted with water to a total volume of 2 mL and then approximately 5 drops of 25 wt% tetramethylammonium hydroxide aqueous solution (Acros, CAS:75-59-2) was added. The 2 g of TiO₂ was impregnated with obtained rhodium solution for 2.5 h at room temperature. Then the solvent excess was evaporated and formed catalyst was dried in air at 120 °C for 4 h. The subsequent calcination of the sample at 400 °C in air for 3 h and reduction in H₂ flow at 330 °C for 3 h resulted in the formation of 23.2 wt% Rh/TiO₂.

Heterogeneous hydrogenation of propene

Heterogeneous gas phase hydrogenation of propene to propane was carried out in the standard 5 mm NMR tube. For that 30 mg of each catalyst (1 wt% and 23.2 wt% Rh/TiO₂) was placed at the bottom of the NMR tube and the reactant mixture (propene + parahydrogen) flowed through the capillary extended to the bottom of NMR tube. NMR tube was placed inside the NMR spectrometer, meaning that PASADENA type of experiment was performed. The resultant ¹H NMR spectra are shown in Fig. S1.

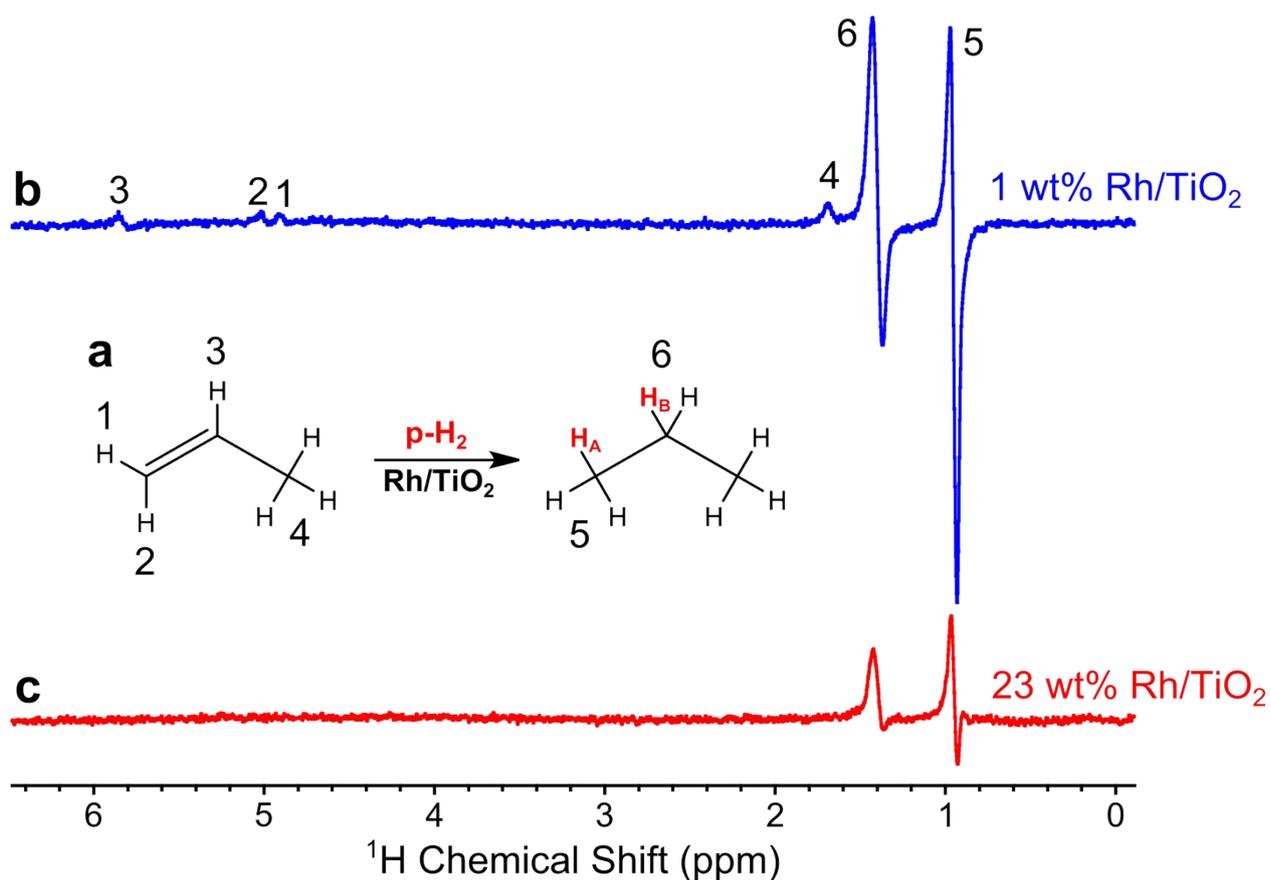


Fig. S1. The reaction scheme (a) and ¹H NMR spectra for gas phase heterogeneous hydrogenation of propene to propane over 1 wt% Rh/TiO₂ (b) and 23.2 wt% Rh/TiO₂ (c) with parahydrogen.

Sample preparation for heterogeneous hydrogenation of ^{13}C labeled and unlabeled vinyl acetate

For the liquid phase heterogeneous hydrogenation of vinyl acetate, 10 mL of benzene- d_6 , methanol- d_4 or DMSO- d_6 was premixed with 68.8 mg of vinyl acetate. The resulting 80 mM solution (0.5 mL) was placed in a medium-wall 5 mm NMR tube with 30 mg of 1 wt% or 23.2 wt% Rh/TiO₂ catalyst placed at the bottom. The total number of samples was 18: 4 samples in benzene- d_6 were tested in PASADENA type hydrogenations at 1 atm (2 samples) and 7 atm (2 samples) (Fig. S2), and 2 samples were used ALTADENA experiments at 7 atm. The samples prepared in methanol- d_4 and DMSO- d_6 solutions were tested analogously.

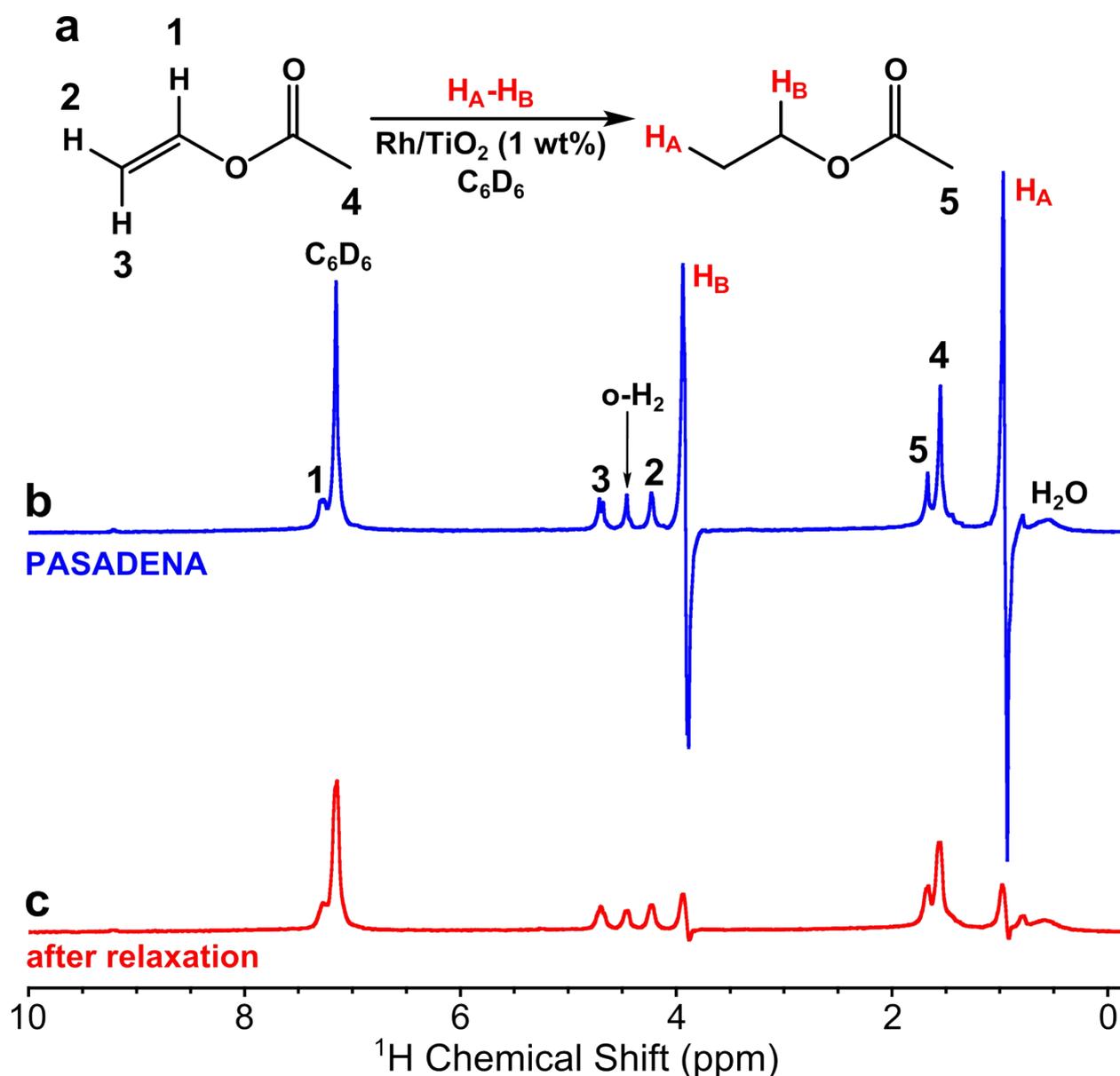


Fig. S2. Reaction scheme (a) and ^1H NMR spectrum for heterogeneous hydrogenation of vinyl acetate to ethyl acetate with parahydrogen over 1 wt% Rh/TiO₂ catalyst in benzene- d_6 (PASADENA-type experiment) (b). ^1H NMR spectrum (c) of relaxed

reaction mixture after experiment (b); weak polarization for nascent protons of parahydrogen is still visible due to the presence of dissolved parahydrogen in the solution.

For the liquid phase heterogeneous hydrogenation of vinyl [$1\text{-}^{13}\text{C}$]acetate over Rh/TiO₂ catalysts the same sample preparation as described above for unlabeled vinyl acetate was used, with the exception of DMSO-d₆ utilization because the activity of the catalysts in this solvent was negligibly low. The total number of samples was 12.

For the polarization transfer experiments, the field cycling approach with magnetic shield was used. The detailed information about the setup, polarization transfer procedure and magnetic field strength are given in references 1 and 2.

Additional ^1H and ^{13}C NMR spectra

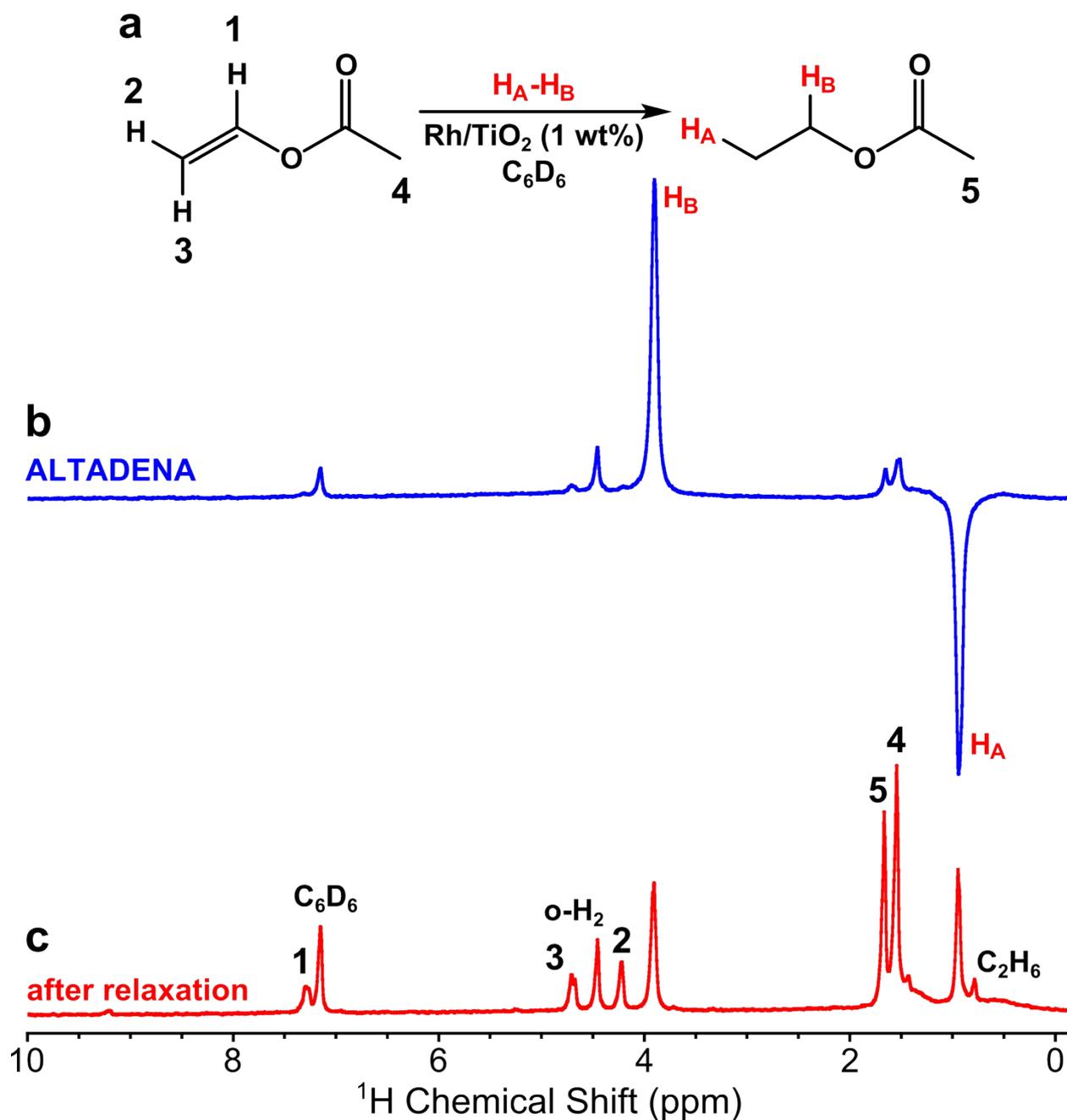


Fig. S3. Reaction scheme (a) and ^1H NMR spectrum for heterogeneous hydrogenation of vinyl acetate to ethyl acetate with parahydrogen over 1 wt% Rh/TiO_2 catalyst in benzene- d_6 solution in the Earth's magnetic field (ALTADENA-type experiment) (b). ^1H NMR spectrum (c) of fully relaxed reaction mixture obtained after experiment (b). Signal enhancement – 3.377; polarization – 0.022%.

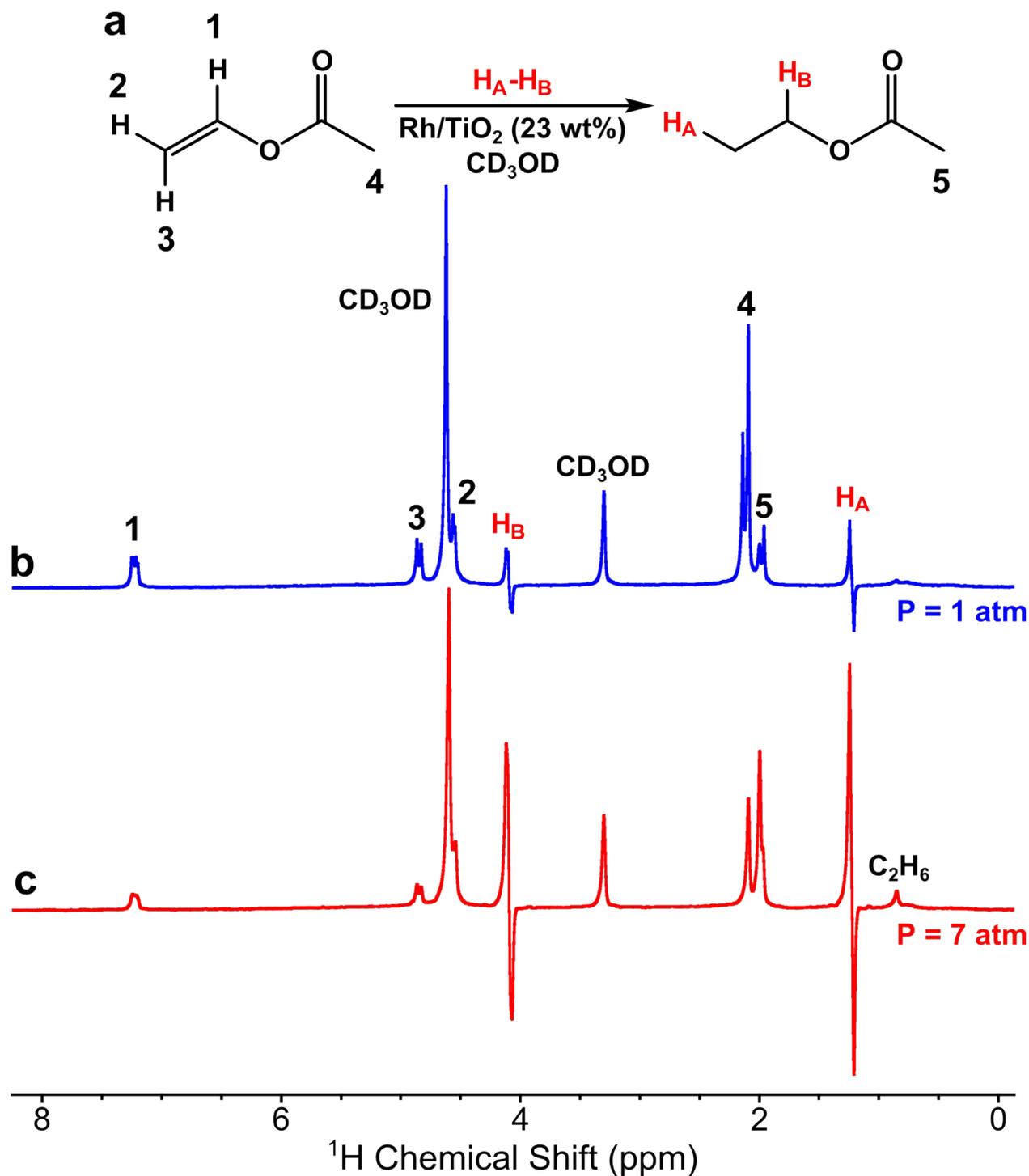


Fig. S4. Reaction scheme (a) and ^1H NMR spectrum for heterogeneous hydrogenation of vinyl acetate to ethyl acetate with parahydrogen over 23.2% Rh/TiO₂ catalyst in methanol-d₄ solution (PASADENA-type experiment) at 1 atm of hydrogen pressure (b) and 7 atm of hydrogen pressure (c).

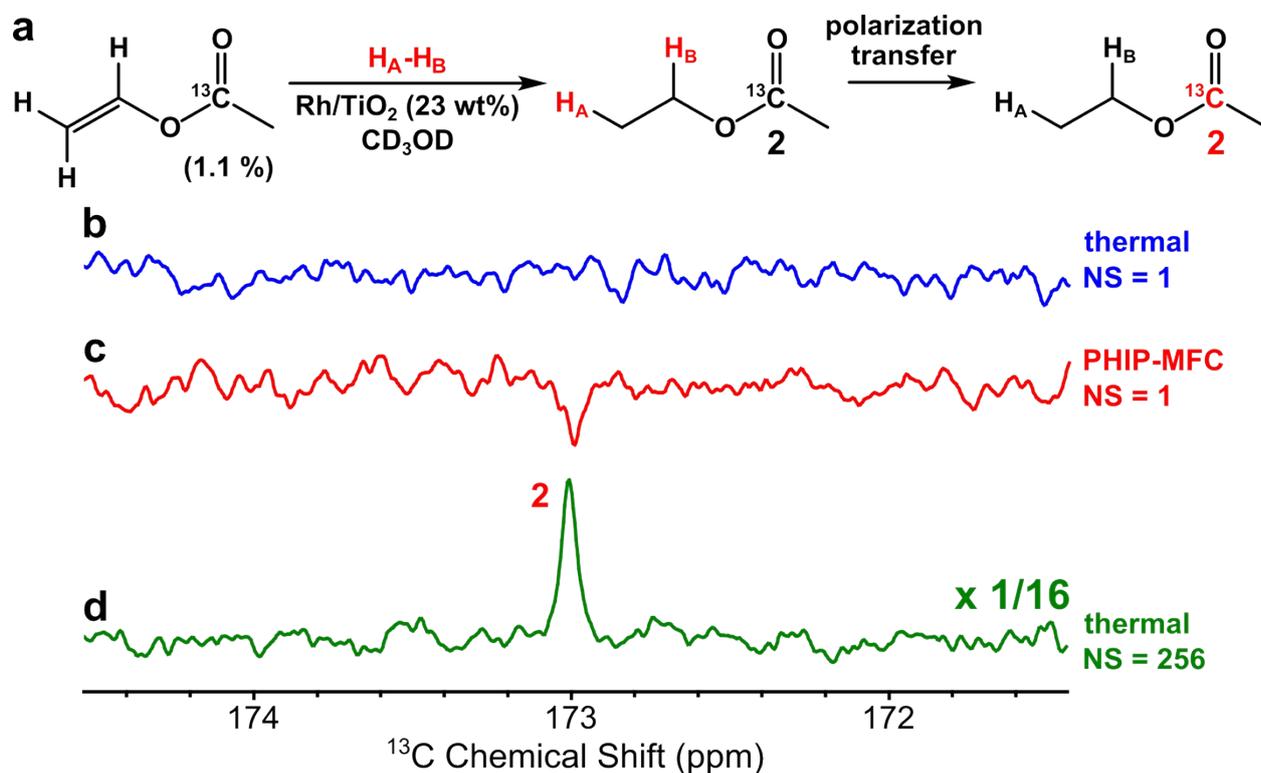


Fig. S5. Reaction scheme (a) of unlabeled vinyl acetate (1.1% natural abundance of ^{13}C nuclei) heterogeneous hydrogenation by parahydrogen over 23.2 wt% Rh/TiO₂ catalyst in methanol-d₄ solution. ^{13}C NMR spectrum of thermally polarized ethyl acetate obtained with single acquisition (b). ^{13}C NMR spectrum of polarized ethyl acetate via polarization transfer from protons to carbon obtained with single acquisition (c). ^{13}C NMR spectrum of fully relaxed reaction mixture after experiment (c) obtained with 256 acquisitions (total experimental time 768 min). Integrals (a. u.): c – -1, d – 42.92, polarization – 0.005%.

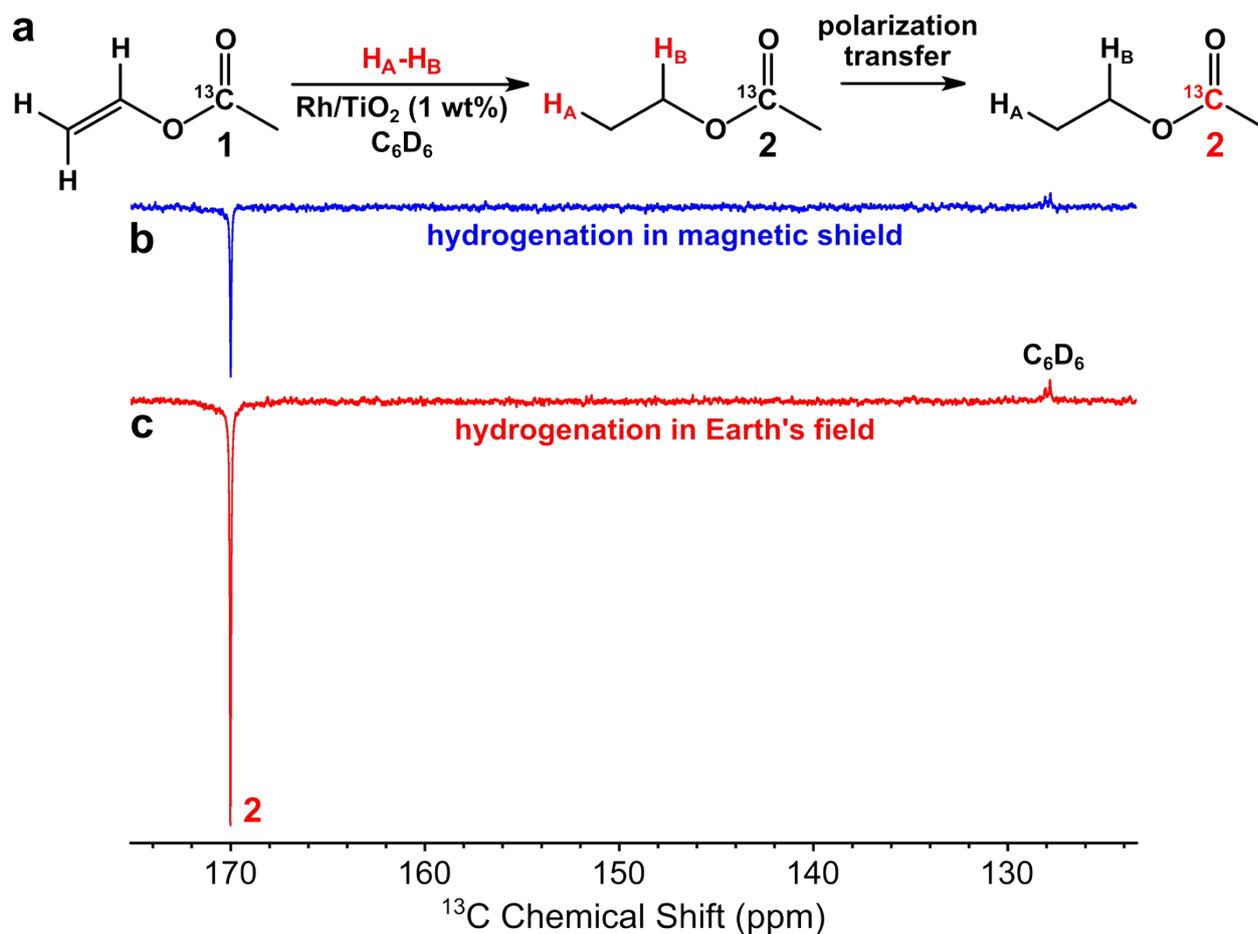


Fig. S6. Reaction scheme (a) and (b-c) ^{13}C NMR spectra for heterogeneous hydrogenation of vinyl [1- ^{13}C]acetate to ethyl [1- ^{13}C]acetate with parahydrogen over 1 wt% Rh/TiO_2 catalyst in benzene- d_6 solution. Hydrogenation was carried out in the magnetic shield *in situ* (b) or in Earth's magnetic field with subsequent transfer to the magnetic shield for 2 s for polarization transfer (c). Integrals (a. u.): b – 1, c – 2.96.

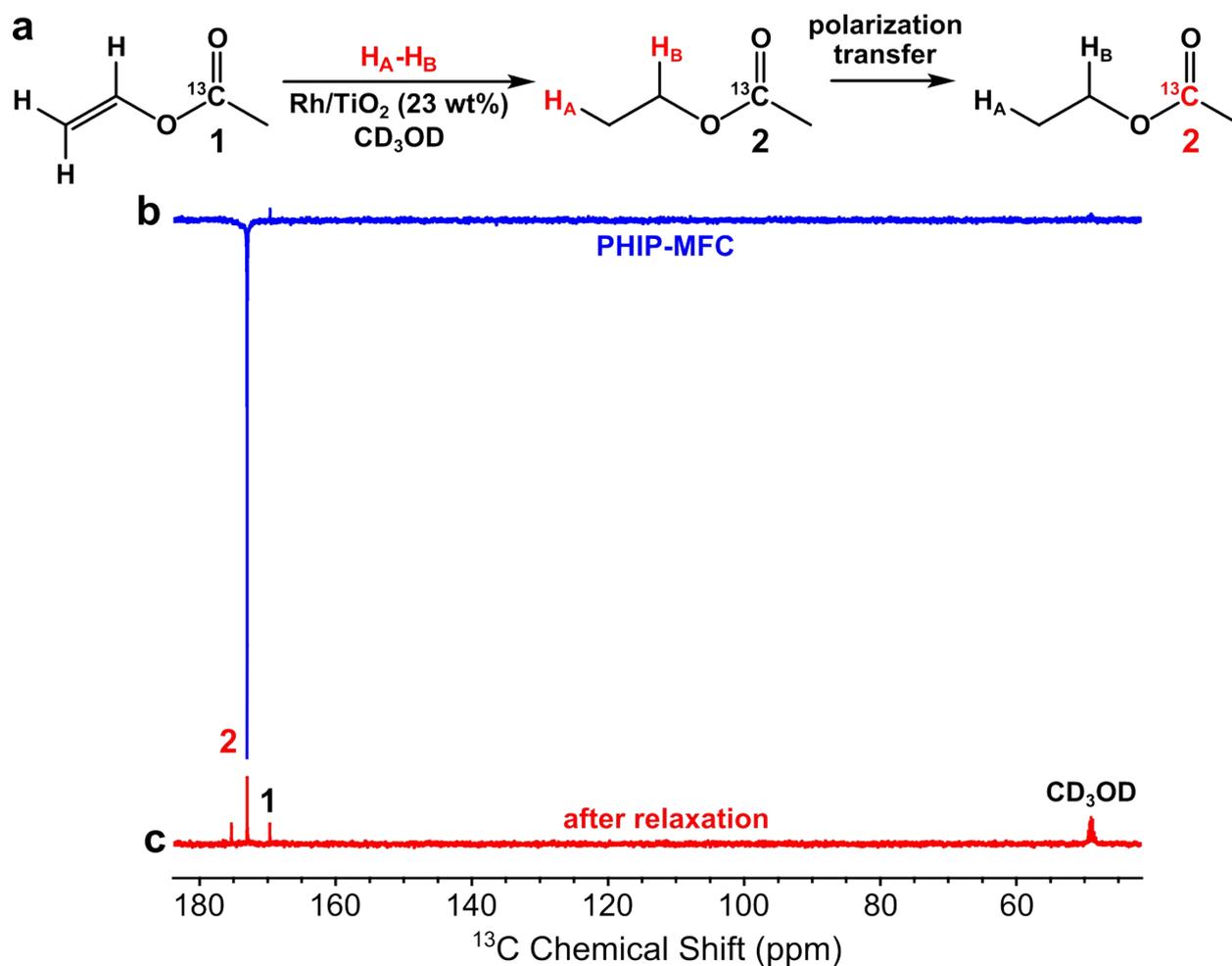


Fig. S7. Reaction scheme (a) of vinyl $[1-^{13}\text{C}]$ acetate heterogeneous hydrogenation with parahydrogen over 23.2 wt% Rh/TiO_2 catalyst in methanol- d_4 solution with subsequent polarization transfer from protons to carbon, and ^{13}C NMR spectra of hyperpolarized (b) and thermally polarized (c) products. Integrals (from left to right): b – -177.55; 1; c – 4.90; 17.73; 4.05. Polarization: 0.008%.

References

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2. R. V. Shchepin, D. A. Barskiy, A. M. Coffey, I. V. M. Esteve and E. Y. Chekmenev, *Angew. Chem., Int. Ed.*, 2016, **55**, DOI: 10.1002/anie.201600521.