Replies to the comments of Anonymous Referee #2.

The authors present PHIP experiments in the gas phase of propyne employing heterogeneous bimetallic catalysts. The study provides useful information for improving HET-PHIP experiments but should be revised with respect to the following specific comments:

1) Line 97: "Pd-Ag/Al_2O_3 catalyst sample contained 2 wt.% of Pd and 6 wt.% of Ag; Pd-In/Al_2O_3 catalyst contained 2 wt.% of Pd and 2 wt.% of In". This result in different dilutions of Pd in the other (less catalytically active) metal. Therefore, the amount of catalytically active Pd_1 sites should be different in the two bimetallic catalysts? How does this impact on the comparability of the results for the Pd-Ag and the Pd-In catalyst?

Authors' response:

There is no doubt that the total number of catalytically active centers (e.g., Pd_1 sites) impacts the performance of a catalyst, and in particular the conversion of reactants into products. The conventional practice in catalysis is the normalization of conversion with respect to the number of e.g., surface metal atoms (or active centers). This normalization yields the turnover frequency (TOF) of a catalyst which characterizes the number of product molecules produced by one catalytic center per unit time.

However, in PHIP experiments we are dealing with an additional factor which is not usually relevant in fundamental and industrial catalysis, namely the selectivity of a catalyst toward pairwise H_2 addition to a substrate. Evaluation of pairwise selectivity and maximizing it by designing an appropriate catalyst is the primary objective of this study. Pairwise selectivity is evaluated from SE value which is the ratio of the polarized and the thermal NMR signals of the product molecule. It is thus already normalized with respect to the amount of product produced (conversion), i.e., is essentially calculated per one active site.

While we fully agree that the overall conversion is highly important in PHIP experiments for achieving the maximum possible NMR signal intensity, our current objective is to find the best catalyst in terms of reaction mechanism which sustains pairwise H_2 addition before attempting to maximize the overall yield of a hyperpolarized product.

2) Very few experimental details are presented in the entire manuscript. Reviewer 1 already asked for more details on the synthesis and analysis of the bimetallic catalysts, which was sufficiently answered by the authors in the revised version of the manuscript. This reviewer is more concerned with the understanding of the NMR experiments and the reaction control of the hydrogenation experiments, which are both not sufficiently described in the experimental section.

Authors' response:

Following reviewer's suggestion, we have added in Section 2.2 of the revised manuscript the detailed description of NMR experiments and the reaction control of the hydrogenation experiments.

The first paragraph of section 2.2 now reads:

"Commercially available hydrogen and propyne gases were used without additional purification. For catalytic tests, propyne was premixed with p-H_2-enriched hydrogen in the molar ratio of 1 : 4. Hydrogen gas was enriched with para-isomer up to 87.0-90.5% using Bruker parahydrogen generator BPHG-90. The catalyst (30 mg, density 0.67 $g \cdot cm^{-3}$) was placed in a stainless steel tubular reactor (1/4'' OD, 4.2 mm ID, 20 cm total length) between two plugs of fiberglass tissue. The bimetallic catalysts (Pd-Ag, Pd-In) as well as monometallic Ag catalyst were reduced in H_2 flow at 550 °C for 1 h before the catalytic tests. Pd/Al_2O_3 catalyst was reduced in H_2 flow at 300 °C for 1 h. The catalyst was cooled down to the desired reaction temperature without H_2 flow termination and the propyne/p-H_2 mixture was introduced to the catalyst. The reactor was positioned outside an NMR magnet and the substrate gas mixture was supplied to the reactor and then the resulting mixture was supplied to the standard screw-cap 10-mm OD NMR tube (Merck, Z271969) placed inside NMR spectrometer for detection (ALTADENA experimental protocol, Pravica and Weitekamp, 1988) though a 1/16'' OD (1/32'' ID) PTFE capillary. In NMR tube the gas mixture was flowing from the bottom to the top and then to the vent through 1/4'' OD (5.8 mm ID) PTFE tubing connected with screw-ending of the NMR tube. All hydrogenation experiments were performed at ambient pressure (ca. 101 kPa). The reactor was heated with a tube furnace and the temperature was varied from 100 to 300 °C (in case of Pd-Ag catalyst) and to 500 °C (Pd-In catalyst) in 100 °C increments (heating rate was 10 °C/min). The temperature was controlled with a K-type thermocouple placed immediately adjacent to the catalyst bed on the external side of the reactor. The reaction was conducted in a continuous flow regime, with the reactor outflow continuously supplied to the probe of an NMR spectrometer and analyzed by ^1H NMR. The gas flow rate was controlled using an Aalborg rotameter and varied stepwise from 1.3 to 3.8 mL/s. The gas flow was periodically interrupted in order to acquire stopped-flow ^1H NMR spectra for evaluating conversion and selectivity. After the introduction of the substrate gas mixture to the catalyst and establishment of the steady-state regime, ^1H NMR spectra were recorded on a 300 MHz Bruker AV NMR spectrometer using a $\pi/2$ rf pulse. A 10-mm BBO 300 MHz Bruker probehead was used."

Questions on hydrogenation experiments:

3) In line 110 the authors mention that "propyne was premixed with p-H_2 in the molar ratio of 1:4". What was the overall pressure of the gas mixture before the reaction?

Authors' response:

In order to premix propyne with p-H_2, the gas tank was vacuumed (to ~ 10^{-4} atm) and propyne was introduced up to 1 atm pressure; then p-H_2 gas was added to the gauge pressure of 4 atm. However, the overall pressure in the gas tank is not relevant because, as stated in the manuscript, all hydrogenation experiments were performed at ambient pressure (ca. 101 kPa).

4) The authors performed the hydrogenation experiments at different temperatures, showing how temperature affects the conversion and selectivity of the reaction. It would be also interesting to know how different pressures would affect the reaction. Did the authors

ever tried to perform the hydrogenation with different pressures and can give a hint in which way the hydrogenation is affected by different pressures?

Authors' response:

This is a very interesting and important question, but also a very difficult one to answer at this time, at least in a simple and definite way.

There have been a few studies published in the past that address this very important issue of pressure effects in HET-PHIP. In particular, one study (Barskiy et al., 2017) addressed propene hydrogenation over Rh/TiO_2 catalysts under PASADENA conditions. It showed that the NMR signal enhancement observed for propane depends on both the overall pressure (1-7 bar) of reaction gas mixture (propene + p-H_2) and the propene fraction in the mixture (0-50%). The conversions and the intensity of polarized signals were higher at both higher overall pressures and higher propene fractions. At the same time, polarization levels (or signal enhancements) were decreasing with increasing propene fraction at constant overall pressure, but quickly passed through a pronounced maximum with the increase in the overall pressure at a constant propene fraction. Thus, signal enhancement was efficient only in a narrow range of relatively low propene fractions and total reaction pressures.

Another study (Salnikov et al., 2013) addressed the kinetics of propene hydrogenation over a Pt/Al_2O_3 catalyst. In this case, however, the experiments were performed at a constant overall pressure (1 bar) with He used as a balance gas. As a result, the reaction orders with respect to hydrogen were found to be different for the pairwise and the non-pairwise hydrogen addition and were equal to 0.7 and 0.1, respectively. It implies that while the overall conversion was essentially insensitive to p-H_2 pressure, the polarization level increased almost linearly with increasing p-H_2 pressure. It also implies that the contribution of pairwise addition depends on the fraction of molecular hydrogen in the mixture.

Therefore, the results of any variable pressure studies will largely depend on how exactly the experiment is performed, e.g., i) at constant overall pressure while varying the partial pressures of a substrate and p-H_2; ii) at constant overall pressure in the presence of a balance (inert) gas while changing partial pressures of one or both reactants; iii) with a variable overall pressure at a constant substrate:p-H_2 ratio, etc.

There are additional factors that would further complicate any such study and its interpretation. i) The reaction is highly exothermic, so an increased conversion (e.g., as a result of an increase in the overall pressure) will lead to the catalyst temperature rise, changing the rates of all kinetic stages of the reaction and possibly altering the catalyst structure. ii) If a catalyst is tested under the ALTADENA protocol, the decrease in the volume flow rate upon an increase in the gas pressure will increase the contact time between the reactants and the catalyst and can also increase the gas delivery time to the NMR, altering the reaction progress and boosting relaxation losses during gas transfer. iii) In both ALTADENA and PASADENA protocols, the situation is further exuberated by the T_1 relaxation time dependence on the overall gas pressure and gas mixture composition.

The effects of the reaction pressure on the catalyst activity in pairwise addition are the subject of our ongoing studies. Here in this work we studied catalytic behavior of different Pd-based bimetallic catalysts in hydrogenation with parahydrogen under the identical reaction conditions, while the complex issue of pressure effects is definitely outside the scope of this work.

5) In table 1 the authors provide conversion rates and selectivity values for different flow rates of the gas mixture and state in line 124-125 that “Slightly higher selectivity values at high gas mixture flow rates is explained by the lower catalyst contact times”. However, any information on the design of the tubular reactor for the hydrogenation reaction is missing (i.e. inner diameter and length of the reactor, length of fixed bed containing solid catalyst) that would allow the reader to estimate contact times of the gas stream with the catalyst bed from the provided flow rates.

Authors’ response:

Regarding the design of the tubular reactor, a stainless steel tube with 1/4’’ OD, 4.2 mm ID and 20 cm total length equipped with the stainless steel nuts and ferrules was used as the reactor. The catalyst was placed in the middle of the tube between two plugs of fiberglass tissue.

The catalyst loading (m_{cat}) used in the work is 30 mg, the apparent density of the granular catalyst bed (ρ) is 0.67 g·cm^{-3}, so the length of the catalyst bed can be evaluated as follows:

$$l = \frac{4m_{cat}}{\rho \cdot \pi \cdot d^2} = 3.2\,mm.$$

To a first approximation it can be assumed that the reaction proceeds in an ideal plug-flow reactor, so the contact time (τ) can be crudely estimated as follows:

$$\tau = \frac{V_{cat}}{u_0} = \frac{m_{cat}}{\rho \cdot u_0},$$

where u_0 is the volume flow rate of the substrate/p-H_2 mixture. For 1.3 mL/s flow rate the contact time equals 34 ms; for 3.8 mL/s τ =12 ms.

However, it should be noted that the values presented above are, without doubt, underestimated since hydrocarbons are known to adsorb strongly on the surface of porous catalysts. For instance, direct observation of the adsorbed hyperpolarized products in HET-PHIP studies by MAS NMR have been reported previously (Henning et al., 2013). The pool of adsorbed reactants and products is constantly exchanging with the flowing gas, resulting in a significant increase in the effective contact time. The later will depend on the amount of adsorbed hydrocarbons, which in turn depends on pressure, gas mixture composition, catalyst temperature, etc.

It is thus essentially impossible to estimate a realistic value of the contact time.

However, there can be no doubt that an increase in the gas flow rate inevitably reduces the contact time between the gas and the catalyst bed. The direct consequence of this is the reduced reaction conversion at higher flow rates, the effect which is clearly observed experimentally. As a crude approximation, the contact time should change in the inverse proportion to the gas flow rate. However, strictly speaking this is valid only if the exchange between the gas and the adsorbed pool of molecules is rapid and complete, an assumption which in itself is difficult to ascertain.

Based on the arguments outlined above, we therefore believe that providing any estimates of the contact times in the manuscript would be misleading and inappropriate.

Questions on NMR experiments and relaxation issues

6) Line 111: Were the NMR experiments conducted as continuous flow experiments (i.e. on the flowing gas) (if so, please provide the mean velocity of the flowing sample) or in a stopped flow fashion? Was the used probehead a standard probehead for 5mm NMR tubes? How does the sample container in the NMR probehead looked like? Was it just a tube passed through the NMR coil (if so, please provide the inner diameter of the tube) or a flow cell with a more sophisticated geometry (if so, please provide a description of the geometry)? These points are important for a better understanding of the NMR experiments, as all points have an impact on the SNR of the spectra (i.e. filling factor, outflow effects and line broadening in continuous flow NMR).

Authors' response:

The Materials and Methods section now contains the following information:

The reaction was conducted in a continuous flow regime with the reactor outflow continuously supplied to the probe of an NMR spectrometer and analyzed by ^{1}H NMR. The PHIP spectra were acquired while the gas mixture was flowing. In order to evaluate the conversion and selectivity for each data point, the gas flow was periodically interrupted in order to acquire stopped-flow ^{1}H NMR spectra under thermal equilibrium conditions. After the introduction of the reactant gas mixture to the catalyst and after each change in the gas flow rate, we waited to ensure that the steady-state regime was established.

The reaction mixture from the reactor was supplied to the bottom of a standard screw-cap 10-mm NMR tube (Merck, Z271969) positioned in a 10-mm BBO 300 MHz Bruker probehead though a 1/32'' ID (1/16'' OD) PTFE capillary. The gas mixture was supplied via the capillary to the bottom of the NMR tube and was then flowing from the bottom to the top and on to the vent though 1/4'' OD (5.8 mm ID) PTFE tubing connected with screw-ending of the NMR tube.

Further comments:

Because the number of molecules in the gas phase decreases in the hydrogenation reaction (*propyne* + H_2 → *propene*), the gas volume flow rate after the reactor (the flow rate that determines the transport time of hydrogenation products and an unreacted substrate to the NMR tube) depends on the conversion:

$$u = u_0 \cdot \frac{5 - X}{5},$$

where X is conversion value (between zero and one), u_0 is the inlet gas flow rate.

So, for example, for Pd catalyst tested at 200 °C and 3.8 mL/s flow rate, the conversion was 92 %, so the gas in the NMR tube is flowing with the following rate: $u = 3.8 \cdot \frac{5-0.92}{5} = 3.10$ mL/s. The volume of the sensitive region of rf coil is ~ 2 mL, so the residence time is ~0.65 s. This shortens an FID and leads to line broadening of NMR signals. As it was shown earlier (Barskiy et al., 2017), this situation is especially unfavorable in case of a PADADENA experiment, since antiphase multiplets will collapse significantly with line broadening – the flow rate of about 4 mL/s reduces PASADENA signals for hyperpolarized propane by a factor of ~2. Line broadening is much less critical for propene hyperpolarized in ALTADENA experiment since the chemical shifts for CH and CH_2-groups differ by ~ 0.8 ppm so that line broadening does not reduce the integrals of the polarized lines.

7) The distance between the tubular reactor and the RF coil of the NMR spectrometer should also be mentioned in the experimental section or even better the transport time (for the two different flow rates) of the hyperpolarized gas from the reactor to the detection site. These times together with the T1 relaxation time of propene (which should also be provided) would help the reader to estimate how severe hyperpolarization loss due to T1 relaxation was. This could also explain the very different SE values for the experiments conducted with 1.3 and 3.8 ml/s flow rates. The authors started a discussion on hyperpolarization losses due to T1 relaxation in chapter 3.3 (line 194-211), but do not provide enough information to understand if the hyperpolarization losses due to T_1 relaxation were dramatic (e.g. on the order of 60% of the initial signal enhancement) or minor (e.g. on the order of 10% of the initial signal enhancement).

Authors' response:

The difference in SE values observed at different flow rates is without doubt determined by the relaxation losses while the gas is flowing from the reactor to the NMR tube; this is an established fact.

1/32'' ID PTFE capillary was connected with the outflow end of the reactor; the other end of the capillary was inserted in the NMR tube all the way down to the bottom. The capillary length is ~ 240 cm. So, the capillary volume is $V_{capillary} = \frac{\pi \cdot d^2}{4} \cdot l = 1.19$ cm^3. The catalyst (3.2 mm length) was placed in the middle of a stainless steel tube (20 cm length, 4.2 mm ID), so the tube volume that the hyperpolarized products need to pass after contacting the catalyst is $V_{tube} = \frac{l \cdot \pi d^2}{4} = 1.38$ cm^3. The time-of-flight (ToF) of hydrogenation products depends on the conversion, $ToF = \frac{V_{capillary}+V_{tube}}{u} = \frac{V_{capillary}+V_{tube}}{u_0 \cdot \frac{5-X}{5}}$. For example, for Pd catalyst tested at 200 °C and 3.8 mL/s flow rate, ToF equals $\frac{1.19+1.38}{3.8 \cdot \frac{5-0.92}{5}} = 0.83$ s. This value is already comparable to the T_1 value of propene at the spectrometer field (ca. 0.6 s) (Skovpin et al., 2013). At the flow rate of 1.3 ml/s, ToF is ca. 2.47 s, and thus the relaxation losses should be dramatic.

These numbers provide the general picture of the overall situation, but a more or less accurate estimation of the relaxation losses from ToF values is not possible. The T_1 time of propene depends on pressure, gas mixture composition, temperature, etc. It also depends on the magnetic field in a non-trivial way (for instance, at low fields the long-lived spin states may be involved (Kovtunov et al., 2014)), and the gas experiences magnetic field with a varying amplitude while in transit.

Some useful information on polarization losses during the transfer of HP products can be found in some of our precious publications in which the "true" pairwise H_2 addition percentages were evaluated by taking into account relaxation losses and non-adiabaticity caused by fast gas inflow. Those studies demonstrated that the apparent signal enhancement factors can be significantly reduced due to the abovementioned causes – by one order of magnitude or possibly even more (Barskiy et al., 2015; Burueva et al., 2018).

We did not directly measure the polarization losses due to the transfer of HP products in this study because it is not essential for comparing different catalysts. The comparison is valid if the gas flow rate is the same in the experiments that are being compared, which ensures that relaxation losses are similar and thus the observed difference in polarizations is brought about solely by the use of different catalysts.

We have added the discussion of hyperpolarization losses evaluation in section 3.3. This part now reads:

"Hence, the apparent signal enhancements evaluated for Pd-based catalysts presented in Table 2 and Table 3 are lower estimates of the actual values of initial enhancements, underestimated (and possibly significantly) because hyperpolarization relaxation dramatically reduces the intensities of enhanced ^{1}H NMR signals of propene during the transfer. The accurate analysis of processes leading to polarization losses in the ALTADENA experiment (non-adiabaticity of magnetic field change during the transfer of hyperpolarized product from the Earth's magnetic field, the relaxation losses in both high and low magnetic fields, etc.) performed previously (Barskiy et al., 2015; Burueva et al., 2018) indicates that the apparent signal enhancement factors are significantly reduced due to the abovementioned causes – by one order of magnitude or possibly more. ….. At the same time, while minimization of relaxation losses is very important for applications of HET-PHIP, the primary objective of this work is the exploration of how the nature of a catalyst affects its selectivity toward pairwise H_2 addition to a substrate."

Technical comments:
Line 199: please correct the wrong spelling of "experimental"

Authors' response:
This typo has been corrected.

Line 265: add "in" before "order"

Authors' response:
The typo has been corrected. The document was proofread and the text was corrected where required.

References

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