Electronic Supplementary Information for

# Green production of polymer-supported Pd NPs: application to the environmentally benign catalyzed synthesis of cis-3-hexen-1-ol under flow conditions

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## General information

All reactions and manipulations were routinely performed under nitrogen atmosphere by using standard Schlenk techniques, unless otherwise stated. Diethyl ether and dichloromethane were distilled over Na-benzophenone and $CaH_2$, respectively. DOWEX® 50WX2 - 100 ($H^+$ form, 2% cross-linked, gel-type, 50-100 mesh [150-300 µm] bead size, 4.8 meq/g exchange capacity), DOWEX® 50WX2 - 400 ($H^+$ form, 2% cross-linked, gel-type, 200-400 mesh [38-75 µm] bead size, 4.8 meq/g exchange capacity) strong cation-exchange resins were obtained from Aldrich. Tetrakis(acetonitrile)palladium(II) tetrafluoroborate was obtained from Aldrich. All the other chemicals were reagent grade commercial products and were used as received without further purification. ESEM (Environmental Scanning Electron Microscopy) measurements were performed on a FEI Quanta 200 microscope operating at 25 KeV accelerating voltage in the low-vacuum mode (1 torr) and equipped with an EDAX Energy Dispersive X-ray Spectrometer (EDS). X-ray maps were acquired on the same instrument using a 512x400 matrix, 25 KeV accelerating voltage and 350 µm horizontal full width. Samples for EDS maps were prepared by inclusion of the resin beads into Struers EpoFix® epoxy resin, followed by lapping. TEM (Transmission Electron Microscopy) analyses were performed using a Leo 922 transmission electron microscope operating at 200 kV accelerating voltage, equipped with a built-in omega filter for electron energy loss spectroscopy (EELS). The sample preparation was carried out by dispersing the grinded resin into about 1 ml of ethanol and treating the solution in an ultrasonic bath for 30min. Successively, a drop of the solution was deposited onto a carbon coated Cu TEM grid and the solvent left to evaporate. Reactions under a controlled pressure of hydrogen of 1 bar were performed in a flask using a $H_2$ generator (Paker H2PEM-260). GC analyses were performed on a Shimadzu GC-2010 gas chromatograph equipped with a flame ionization detector and a 30 m (0.25 mm ID, 0.25 µm FT) Varian VF-WAXms capillary column and SPB-1 capillary column. GC-Ms analyses were performed on a Shimadzu QP2010S spectrometer equipped with identical capillary columns. The metal content in the resin-supported catalysts was determined by Atomic Absorption Spectrometry (AAS) using a AANALYST200 spectrometer. Each sample (50-100 mg) was treated in a microwave-heated digestion bomb (Milestone, MLS-200, 20 min.@ 220 °C) with concentrated $HNO_3$ (1.5 mL), 98% $H_2SO_4$ (2 mL), and 0.5 mL of $H_2O_2$ 30%. After filtration, the solutions were analyzed. The content of metal leached in the recovered solutions after catalysis was determined by Inductively Coupled Plasma Atomic Emission Spectroscopy (ICP-OES) with a Varian 720ES instrument at a sensitivity of 500 ppb. The solutions were analyzed directly after 1:5 dilution in 0.1 M hydrochloric acid.

## Preparation of the resins

The following operations were performed in air atmosphere. The commercial resins were washed prior of use to remove incidental impurities. 20 g of cation exchange resin were washed with refluxing deionised water for 2 h and with refluxing methanol for 1 h using a Soxhlet apparatus. After cooling down to room temperature, the resin was washed sequentially with dichloromethane (3 x 100 ml), methanol (3 x 100 ml) and diethyl ether (3 x 100 ml). Then, it was dried in a stream of nitrogen and stored under nitrogen.

## Preparation of the resin-supported Pd species

Palladium was immobilized onto the resin in two different states; i) $R\text{-}SO_3^-H^+$: commercial resin previously washed as abovementioned, ii) $R\text{-}SO_3^-Li^+$: commercial resin previously washed as abovementioned and subsequently treated with lithium hydroxide. Henceforth, palladation and reduction steps follow the same procedure.

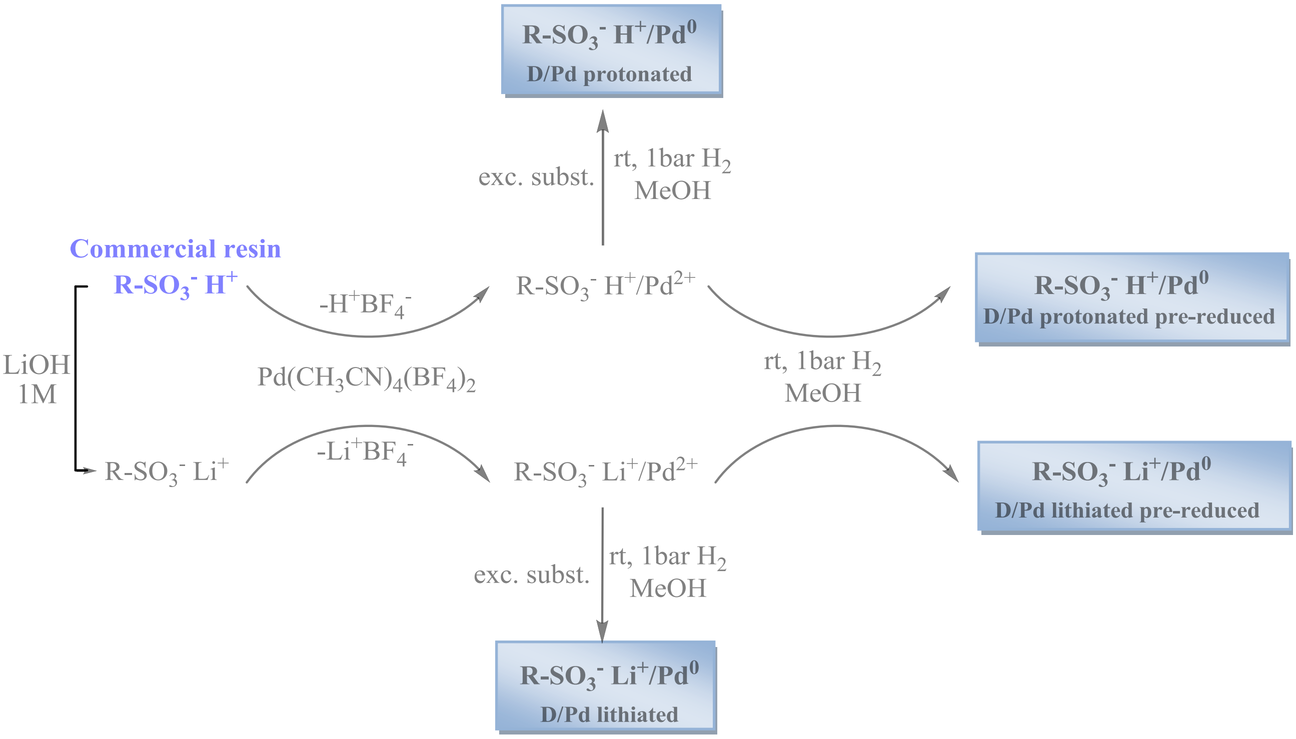


**Fig. S1** Scheme of the synthetic procedure for the preparation of D/Pd protonated, protonated pre-reduced, lithiated and lithiated pre-reduced respectively.

Lithiation of strong cation-exchange resin $R\text{-}SO_3^-H^+$: 5 g of the protonated form of the commercial resin purified as above were added to a 1M solution of lithium hydroxide (150 ml) in air atmosphere. The mixture was stirred at 150 rpm at room temperature for 24 h using an orbital stirrer. The resin obtained was placed in a glass filter and washed repeatedly with deionised water (3 x 100 ml) until neutral pH of the washings. Then, it was washed with methanol (3 x 100 ml) and diethyl ether (3 x 100 ml) and dried in a stream of nitrogen. The lithiated resin $R\text{-}SO_3^-Li^+$ obtained as white beads was stored under nitrogen.

a) Resin-Palladium (II) species: In a typical procedure, 1 g of dry cation-exchange resin ($R\text{-}SO_3^-H^+$ or $R\text{-}SO_3^-Li^+$) was added into a flask containing a degassed solution of tetrakis(acetonitrile)palladium(II) tetrafluoroborate (64 mg, 0.145 mmol, ratio Pd/sulfonic groups = 1/33) in deionised water (55 ml). The mixture was stirred at room temperature for 24 h using an orbital stirrer. The resin obtained was transferred into a glass filter via a Teflon tube under nitrogen and washed sequentially with deionised water (3 x 50 ml), methanol (3 x 50 ml) and diethyl ether (3 x 50 ml) before being dried in a stream of nitrogen overnight. The palladiated resins obtained as orange ($R\text{-}SO_3^-Li^+/Pd^{2+}$) *and* brownish ($R\text{-}SO_3^-H^+/Pd^{2+}$) beads were stored under nitrogen in the dark. AAS analysis showed the resins to contain 1.25% (w/w) of Pd, which indicates 89% of palladium used was deposited onto the resin.

b) Resin-Palladium (0) species: For the reduction step in the absence of substrate (*D/Pd protonated pre-reduced* or *D/Pd lithiated pre-reduced*), 50mg of resin supported palladium (II) were swollen in 12ml of methanol in a flask, then a flow of 1bar $H_2$ was bubbled at room temperature for 1 h under orbital stirring at 160 rpm. The resin became black (ca. 10 min.). After MeOH removal and without isolation, the substrate solution was added in the same flask to perform the hydrogenation reaction. On the other hand, when resin-Palladium (0) species were formed *in situ*, in the presence of excess of substrate (*D/Pd protonated* or *D/Pd lithiated*), 50mg of resin supported palladium (II) were swollen in a 0.17M substrate solution contained into a flask, then a flow of 1bar $H_2$ was bubbled at room temperature for 1 h under orbital stirring at 160 rpm. The resin became slowly black (ca. 20 min.).

## Hydrogenation reactions in batch mode, catalysts recycle.

All the hydrogenation reactions have been performed in a 100ml flask using very mild conditions at 1bar of $H_2$ and room temperature. The experimental procedure shows slight differences depending on the catalytic specie used.

a) Resin-Palladium (0) formed in excess of substrate: In a typical experiment, the resin supported palladium (II) (50 mg, ca. 1.25% Pd w/w, ca. 0.006 mmol of palladium) was added into a flask containing a degassed solution of the substrate (2.08 mmol) in methanol (12 ml). A flow of hydrogen gas was bubbled at 1 bar and 15 mL/min at room temperature, using an orbital stirrer at 160 rpm. This was taken as the start time of the reaction. The resin-Palladium(II) became slowly black (ca. 20 min.). After the desired time, the methanol solution was completely removed under a stream of hydrogen using a gas-tight syringe. A sample of this solution (0.5 μl) was used for GC (product yield), GC-MS (product identification) and ICP-OES analysis (Pd leaching), while the remaining aliquot was used for the Maitlis test (catalyst leaching test, see below). A fresh solution of the substrate (2.08 mmol) in methanol (12 ml) was then transferred under hydrogen via a gas-tight syringe into the flask containing the recovered supported catalyst. The mixture was stirred at 160 rpm and room temperature under hydrogen flow and, after the desired time, the mixture was treated as described above. The same recycling procedure was used in the subsequent hydrogenation cycles. After use in catalysis, the solid catalyst was washed with methanol (3 x 10 ml) and diethyl ether (3 x 10 ml), dried in a stream of nitrogen overnight and stored under nitrogen for later characterization. Catalyst leaching test: an additional portion of the substrate (2.08 mmol) was added under hydrogen to the clear solution recovered after the first and subsequent cycles, hydrogen was then bubbled through the solution at room temperature for 1h and the mixture analyzed by GC for conversion measurement.

b) Resin-Palladium (0) formed in absense of substrate: In a typical experiment, resin-palladium (II) (50 mg, ca. 1.25% Pd w/w, ca. 0.006 mmol of palladium) was added into a flask containing a degassed solution of methanol (12ml). A flow of hydrogen gas was bubbled at 1 bar and 15 mL/min at room temperature for 1h under orbital stirrer at 160 rpm. The resin became black (ca. 10 min.) After 1h, the methanol was completely removed under a stream of hydrogen using a gas-tight syringe. A solution of the substrate (2.08 mmol) in methanol (12 ml) was then transferred under hydrogen via a gas-tight syringe into the flask containing the supported catalyst. This was taken as the start time of the reaction. After the desired time, the methanol solution was completely removed under a stream of hydrogen using a gas-tight syringe. From here on, it proceed as abovementioned.

## Hydrogenation of Isophorone

The main by-product in the hydrogenation of isophorone in methanol is the formation of acetals what affects the selectivity to unsaturated ketone.

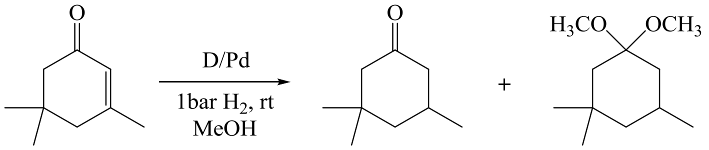
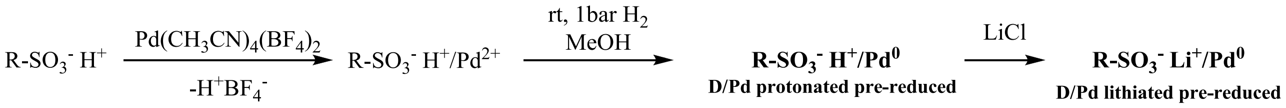


**Fig. S2** Hydrogenation of **5** isophorone in methanol.

The presence of acetals can be significantly reduced by treating the catalyst with lithium chloride prior to use.



$$R\text{-}SO_3^-\,H^+ \xrightarrow[-H^+BF_4^-]{Pd(CH_3CN)_4(BF_4)_2} R\text{-}SO_3^-\,H^+/Pd^{2+} \xrightarrow{\text{rt, 1bar } H_2,\ \text{MeOH}} \underset{\textbf{D/Pd protonated pre-reduced}}{\mathbf{R\text{-}SO_3^-\,H^+/Pd^0}} \xrightarrow{LiCl} \underset{\textbf{D/Pd lithiated pre-reduced}}{\mathbf{R\text{-}SO_3^-\,Li^+/Pd^0}}$$

**Fig. S3** Scheme of the synthetic procedure for the preparation of D/Pd lithiated pre-reduced and treated with LiCl.

**Table S1** Hydrogenation of **5** isophorone in methanol

| Catalyst | t(min) | Isophorone (%) | Unsaturated ketone (%) | Acetal (%) |
|---|---|---|---|---|
| D/Pd lithiated | 15 | 83.9 | 8.8 | 6.0 |
| | 30 | 43.7 | 32.9 | 26.9 |
| | 45 | 0.1 | 58.1 | 38.8 |
| D/Pd lithiated pre-reduced (LiCl treatment) | 15 | 79.1 | 18.5 | 1.7 |
| | 30 | 58.1 | 35.2 | 5.5 |
| | 45 | 41.5 | 47.0 | 10.0 |
| | 60 | 23.4 | 56.8 | 14.7 |
| | 75 | 15.4 | 63.3 | 19.0 |
| | 90 | 7.4 | 67.7 | 22.5 |

Reaction conditions: $H_2$ pressure 1 bar, r.t., substrate : Pd = 175 : 1 molar ratio, substrate concentration 0.17 M.

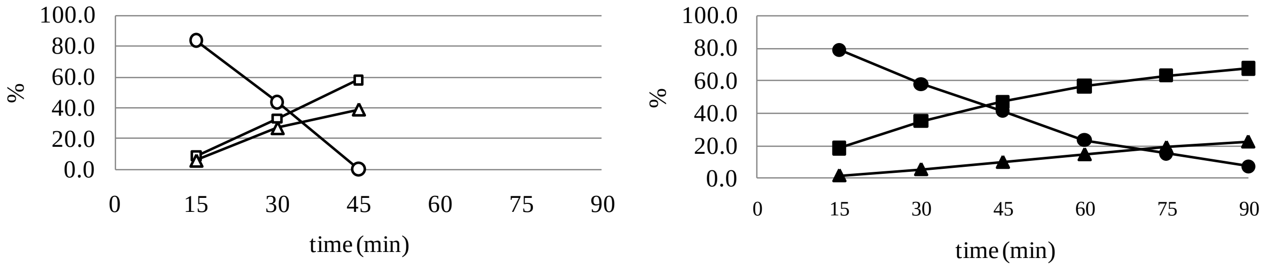


**Fig. S4** Hydrogenation of **5** isophorone. Left: D/Pd lithiated catalyst. Right: D/Pd lithiated pre-reduced and trated with LiCl catalyst. (circle) isophorone (square) unsaturated ketone (triangle) acetal

As previously stated, in terms of efficiency there is a clear benefit when active catalytic species are formed *in situ* (complete reaction at 45min for D/Pd lithiated *versus* 90min for D/Pd lithiated pre-reduced). However, in the case of isophorone is more convenient the use of pre-reduced species since a post-reduction treatment with LiCl decreases acetal formation up to 1.7 times.

## Hydrogenation reactions in continuous flow mode.

Catalytic flow hydrogenations were carried out using the continuous-flow reactor system constructed at Istituto di Chimica dei Composti Organo Metallici, Firenze (Italy) shown in Fig S5.

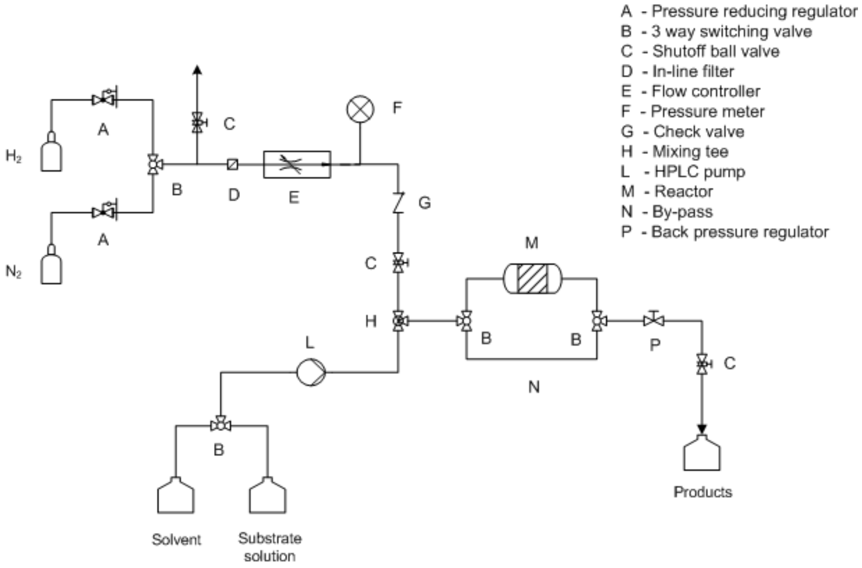


Fig **S5**. Schematic view of the continuous-flow, high-pressure reactor system used.

The system was designed to allow for a simultaneous flow of substrate solution and hydrogen gas (up to 40 bar pressure) through a reactor tube containing the heterogeneous catalyst. The reactor was completely inert, as all wet parts were made of PEEK, PFA or PFTE. The flow of the substrate solution was regulated by an Alltech® model 426 HPLC pump in PEEK. A constant flow of hydrogen gas was adjusted by a flow controller BRONKHORST HI-TEC model F200CV-002-RGD-11-V-MFC. The hydrogen pressure in the reactor was monitored by a BRONKHORST HI-TEC P502C-AGD-11-V-6K0R-EPC meter. The concurrent flows of gas and liquid were driven through a T-shaped PEEK mixer to ensure efficient gas dispersion. The mixed hydrogen-substrate solution stream was introduced in the reactor through a 6-port Rheodyne mod. 9060 switching valve in PEEK. The solid catalyst was pre-packed into a commercial 3 mm inner diameter Omnifit® glass column, equipped with 10μm PE frits at the entrance of the catalyst bed to ensure an optimum flow distribution. At the outlet of the reactor, the product solution was collected for GC analysis and the excess amount of the hydrogen gas released to the atmospheric pressure. Commercially available $H_2$ (99.995%) was used as received.

Catalytic reactions in continuous flow mode

In a typical experiment, a degassed solution of substrate in methanol (0.2M) was allowed to flow through the catalyst beads (45 mg, 1.25 % Pd w/w) packed into the commercial tubular glass microreactor (3 mm diameter x 25 mm length) at a constant 0.2 mL min$^{-1}$ rate, together with a constant $H_2$ flow of 0.8 mL min$^{-1}$ at RT. This resulted in a $H_2$ pressure at the reactor inlet of ca. 2.5 bar (corresponding to a $H_2$:substrate molar ratio of ca. 2.3), while the hydrogen gas was released at atmospheric pressure at the outlet of the reactor. Therefore, the pressure drop generated by the packed bed reactor was ca. 1.5 bar. The attainment of the steady state conditions (ca. 1 h) was taken as the reaction start time. The product solution was periodically analyzed for conversion by GC, while 12 mL $h^{-1}$ aliquots were continuously sampled for subsequent Pd leaching analysis by ICP-OES. Under these experimental conditions, the hydrogenation of **3** cyclooctadiene gave cyclooctene with ca. 97% selectivity@87% conversion, that corresponds to a productivity of 395 $h^{-1}$ (TOF) and 1.30 kg $l^{-1}$ $h^{-1}$ (STY), and to an overall TON of 1700 after 4.7 h. In the hydrogenation of **4** 3-hexyn-1-ol, the leaf alcohol *cis*-3-hexen-1-ol was obtained with 89% selectivity@75% conversion (cis+trans selectivity 80%), corresponding to a productivity of 352 h-1 (TOF) and 1.02 kg l-1 h-1 (STY), and to an overall TON of 1650 after 4.7 h. The amount of Pd leached in the recovered solutions was below the detection limit in each sample (ICP-OES).