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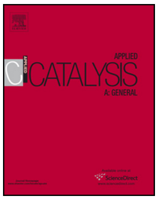

Continuous flow hydrogenation reactions by Pd catalysts onto hybrid ZrO_2/PVA materials

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ABSTRACT

Palladium nanoparticles of 3.2 ± 0.9 nm size were generated within 12–18 mesh pellets of hybrid zirconia/polyvinyl alcohol matrix, to afford a 0.03–0.1% Pd loading (w/w). The material was used in the catalytic, continuous flow hydrogenation reaction of multiple C═C and C≡C bonds and nitrobenzene, showing good selectivity at full conversion and excellent resistance over prolonged time-on-stream under room temperature and 1–2 bar H_2 gas. No metal leaching in solution was detected as well as no additives nor regeneration steps were needed for use in hydrophilic solvents.

1. Introduction

Catalysis under continuous flow is receiving increasing interest for application to selective processes because of the inherent advantages compared to conventional batch operations in terms of purification, safety, waste emission, automation, energy consumption and space-time-yield productivity [1–4]. In particular, the stereo- and chemoselective hydrogenation reaction of functionalized hydrocarbons with multiple C═C and/or C≡C bonds to achieve partial hydrogenation products is a highly desired and challenging process in the pharmaceutical, agrochemical, food and petrochemical industries [5–7], which is usually accomplished in the heterogeneous phase by a range of noble metals catalysts [8–10]. For instance, *cis*-3-hexen-1-ol is a valuable fragrance ingredient (leaf alcohol) [11,12], which is currently manufactured in 400 t/y and ca. 96% selectivity at 99% conversion by the partial hydrogenation of 3-hexyn-1-ol through a batch process using the Lindlar catalyst (5%Pd on $CaCO_3$ doped with 2–3% Pb) [13,14]. 2-Methyl-3-buten-2-ol is an intermediate in the synthesis of vitamins (A, E) and several perfumes [15], which is produced in 95–97% yield by the hydrogenation of 2-methyl-3-butyn-2-ol using the Lindlar and other heterogeneous catalysts under batch conditions [16].

A number of flow systems have been reported for the partial hydrogenation reaction of C-C bonds using immobilized metal nanoparticle (MNP) catalysts, either onto polymeric or inorganic solid supports [17–20]. Organic polymers were much largely employed to this purpose because they provide significant benefits compared to inorganic materials: (i) the sorption and permeability of reagents and products can be driven so as to improve the catalyst performance, (ii) the catalyst efficiency can be increased by incorporation of additives, (iii) the manufacture technology of polymers is much developed, thus allowing for a wider choice of morphologies, mechanical, chemical and thermal properties, affinity for reagents and catalysts [21–25]. Still, issues have to be solved concerning stability, shrinking phenomena, volume and porosity changes with swelling, back pressure evolution, catalyst deactivation, need of regeneration, which adversely affect the efficiency and long-term productivity of the supported catalysts [26–28]. In order to limit these drawbacks, strategies have been developed, including the addition of inorganic materials to the polymer, e.g. raschig rings [29], glass [30], and others [31,32], with clear benefits in terms of catalyst resistance.

In the course of our studies on solid electrolytes for electrochemical applications [33–36], we recently described the synthesis of contactor type, hybrid inorganic (zirconia)/polymeric (PVA, POGE)

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catalytic membranes containing Pd species [37,38], and their use in hydrogenation reactions of various organic substrates in the liquid phase [39] (PVA, polyvinyl alcohol; POGE, polyoxyethylene/polyglyceryl ether). It was shown that the addition of zirconia greatly improves the mechanical and chemical resistance of PVA membranes in hydrophilic solvents, hence, their potential for use under catalytic conditions over prolonged reaction times.

Herein we report on the preparation of PdNP embedded into the parent pellets and their use in catalytic partial hydrogenation reaction of unsaturated C-C bonds, both under batch and continuous flow conditions.

2. Experimental

2.1. General information

All reactions and manipulations were routinely performed under nitrogen atmosphere by using standard Schlenk techniques, unless otherwise stated. The hybrid zirconia/PVA materials containing palladium oxide were prepared as previously described [37,38]. All the other chemicals were reagent grade, commercial products and were used as received without further purification.

2.2. Catalyst preparation

In a typical procedure, the preformed hybrid inorganic/polymeric beads NKZPDB-5 type (1.01 g, 1.7 ± 0.2 mm diameter, composition in weight ratio to 80% saponified PVA normalized to 1: ZrO_2 0.14, PdO 0.21, polyoxyethylene polyglycerol ether 0.19) [37,38] were introduced into a round bottom flask equipped with a lateral stopcock containing nitrogen-degassed water (40 mL). The suspension was cooled to 0 °C and an excess of $NaBH_4$ (365 mg, 9.6 mmol) was added in portions under a stream of nitrogen. The solution was stirred with an orbital-stirrer under nitrogen at 0 °C for 30 min, and then at room temperature for 24 h. After that time, the water solution was removed by decantation, and the pellets were carefully washed with degassed water (3 × 30 mL) and methanol (3 × 30 mL), then dried under a stream of nitrogen overnight. The brow-grey pellets thus obtained (Pd@NKZPDB-5) were stored under nitrogen before being used in catalytic hydrogenation reactions. For the purpose of evaluate the metal loading in Pd@NKZPDB-5, the pellets were dried under vacuum overnight and analyzed by ICP-OES to give a typical bulk 0.10% (w/w) Pd content.

In an analogous procedure, the hybrid inorganic/polymeric beads NKZPDB-1 type, featuring a ca. 0.8 mm diameter ZrO_2 core covered with a film of ca. 300 μm hybrid material (1.2 ± 0.2 mm diameter, composition in weight ratio to 80% saponified PVA normalized to 1: ZrO_2 0.10, PdO 0.21, polyoxythylene polyglycerol ether 0.19), was treated as above to give the same Pd content in the film (EDS) and a bulk 0.03% (w/w) Pd loading (ICP-OES).

2.3. Catalyst characterization

Environmental Scanning Electron Microscopy measurements (ESEM) 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). Samples for Transmission Electron Microscopy (TEM) analyses were prepared by inclusion of the membranes into Struers EpoFix® epoxy resin, followed by lapping. The samples were then cut with a RMC MT-XL ultramicrotome to give a film thickness of 60 nm. TEM measurements were carried out using a CM12 PHILIPS instrument at 120 keV accelerating voltage. Statistical nanoparticle size distribution analysis was typically carried out on 300–400 particles. X-ray diffraction (XRD) spectra were recorded with a PANanalytical XPERT PRO powder diffractometer, employing CuKα radiation ($\lambda = 1.54187$ Å), a parabolic MPD-mirror and a solid state detector (PIXcel). The samples were subjected to measurement without grinding and prepared on a silicon wafer (zero background) that was rotating (0.5 rotations per second) during spectra acquisition. All XRD spectra were acquired at room temperature in a 2θ range from 4 to 95°, applying a step size of 0.0263° and a counting time of 77.5 s.

2.4. Hydrogenation reactions

Reactions under a controlled pressure of hydrogen were performed using a non-metallic Büchi Miniclave® (50 mL internal volume) equipped with a pressure controller and an orbital stirrer set at 150 rpm rate and a H_2 generator Parker H2PEM-260. Catalytic flow hydrogenations were carried out using a homemade continuous-flow reactor system constructed at Istituto di Chimica dei Composti Organo Metallici, Firenze (Italy). The system was designed to allow for a simultaneous flow of substrate solution and hydrogen gas 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 packed into a commercial 3 mm inner diameter Omnifit® glass column, equipped with 10 μm 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.

2.4.1. Hydrogenation reactions by Pd@NKZPDB pellets under batch conditions

In a typical experiment, Pd@NKZPDB -1 pellets (440 mg, 0.03 wt% Pd, 1.1×10^{-3} mmol Pd), were placed under nitrogen into a metal-free autoclave. A degassed solution of substrate in methanol (0.05 M, 21.0 mL) was transferred under nitrogen via a Teflon tube into the autoclave. Nitrogen was replaced by hydrogen with three cycles pressurization/depressurization. The autoclave was finally charged with the desired pressure of hydrogen and stirred at 150 rpm using a orbital stirrer. After the desired time, the reactor was depressurized and the solution was completely removed under a stream of hydrogen using a gas-tight syringe. A sample of this solution was analyzed by GC and GC-MS for product identification and determination and by ICP-OES for metal leaching. For recycling experiments, a fresh solution of the substrate was then transferred under hydrogen via a gas-tight syringe into the reactor containing the catalyst recovered. The autoclave was again charged with hydrogen, stirred at 150 rpm 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 × 10 mL) and diethyl ether (3 × 10 mL), dried in a stream of nitrogen. The reaction products were unequivocally identified by the GC retention times and mass spectra of those of authentic specimens.

2.4.2. Hydrogenation reactions by Pd@NKZPDB pellets under continuous flow conditions

Reactions under continuous flow were carried out using the flow reactor system described above. In a typical experiment, Pd@NKZPDB-1 (440 mg, 0.03 wt% Pd, 1.1×10^{-3} mmol Pd) was packed into a commercial glass tube (3 mm diameter × 25 mm length). The system was degassed with N_2 at 3 mL min^{-1} flow rate for 15 min, then the N_2 flow was stopped and a degassed solution of the substrate in methanol (0.05 M) was allowed to flow through the catalytic bed at a constant 0.05 mL min^{-1} rate until the catalyst was completely wet. Molecular hydrogen was then allowed to flow through the catalyst at a constant H_2 flow of 1.2 mL min^{-1} at room temperature, together with the substrate solution. Attainment of steady state conditions, ca. 1 h, was then taken as the reaction start time. The product solution was periodically analysed for conversion by GC, while aliquots were continuously sampled for Pd leaching analysis by ICP-OES. At the outlet of the reactor the excess of the hydrogen gas released to the atmospheric pressure. The reaction was monitored for 8 h time-on-stream, followed by overnight switch off while maintaining an H_2 atmosphere in the reactor, and restart the day after for an analogous period. The reaction products were unequivocally identified by the GC retention times and mass spectra of those of authentic specimens.

2.5. Analysis

GC analyses were performed on a Shimadzu GC-2010 gas chromatograph equipped with a flame ionization detector and 30 m (0.25 mm i.d., 0.25 μm film thickness) VF-WAXms column or a 30 m (0.25 mm i.d., 0.25 μm f.t.) SPB-1 column. GC-MS analyses were performed on a Shimadzu QP2010S spectrometer equipped with identical capillary columns. The metal content in the supported catalytic was determined by EDS analysis and by Inductively Coupled Plasma Atomic Emission Spectroscopy (ICP-OES) with a Varian 720ES instrument at a sensitivity of 500 ppb. Each sample (ca. 100 mg) was treated in a microwave-heated digestion bomb (Milestone, ETHOS LabStation with Easy Wave Software, 20 min at 220 °C) with 8 mL aqua regia and 0.5 mL of H_2O_2 30%. The content of metal leached in the catalytic reaction solutions was determined by ICP-OES. Palladium detection limit was 0.006 ppm. The solutions were analyzed directly after 1:2 dilution in 1% HNO_3.

3. Results and discussion

3.1. Catalyst preparation and characterization

We have previously reported the manufacture of the hybrid Pd(II)/ZrO_2/PVA/POGE material in large amounts at competitive costs by straightforward procedure [39]. The material is catalytically inactive prior of palladium reduction. However, catalytically active PdNP can be easily generated within the solid matrix by a conventional method, using water as solvent and sodium borohydride as palladium reducing agent. In the present work, we adopted the above protocol to immobilize PdNP onto the corresponding hybrid pellets support (NKZPDB) (Fig. 1).

The as-prepared catalysts (abbreviated Pd@NKZPDB) showed no significant physical or morphological changes with respect to the native pellets by ESEM analysis, and could be handled easily, provided that it was stored under nitrogen for long periods. For the purpose of the hydrogenation reaction tests, two main types of catalytic pellets were prepared: the first (Pd@NKZPDB-1) features a core of ZrO_2 of ca. 0.8 mm diameter covered with a film of ca. 300 μm hybrid material, the second (Pd@NKZPDB-5) devoid of zirconia core. Accordingly, while the palladium content in the hybrid material was the same (EDS), the overall Pd loading in the pellets was of 0.03% (w/w) and 0.10% (w/w) for Pd@NKZPDB-1 and Pd@NKZPDB-5, respectively (ICP-EOS). Irrespective of the bead type, TEM analysis showed Pd@NKZPDB hybrid material to contain a narrow size distribution of evenly dispersed, spheroidal PdNPs with a mean diameter of 3.2 ± 0.9 nm. A representative TEM image and the measured Pd particles size distribution are reported in Fig. 2. X-ray diffraction data were in line with those obtained from TEM. The size of the supported PdNPs was significantly lower than that reported for PVA-stabilized palladium colloids (8–50 nm) [40], that can be safely attributed to the steric stabilization of the porous solid material [41,42]. A summary of the catalysts' characteristics are reported in Table 1.

Fig. 1. Sketch of the synthesis of the hybrid catalytic materials with abbreviations adopted (top). Images of NKZPDB-1 beads (bottom), before (left) and after (right) palladium reduction.

3.2. Selective hydrogenation reactions by Pd@NKZPDB catalysts

3.2.1. Catalysis under batch conditions

In order to achieve a preliminary estimate of the reaction conditions and catalyst performance, the hybrid catalytic pellets Pd@NKZPDB were tested in the batch hydrogenation reaction of various substrates bearing multiple unsaturations and/or functionalities. The substrates examined are sketched in Fig. 3, together with the products obtained, while representative results are summarized in Table 2. Due to the presence of the zirconia core, that ensures a better mechanical stability under stirring, the Pd@NKZPDB-1 material was first investigated to this purpose. Catalyst productivities are reported in terms of both turnover frequency ($TOF = mol_{product}/mol_{Pd} \times h$) and space-time-yield ($STY = kg_{product}/litre_{reactor\ volume} \times h$).

The catalyst showed to be active under smooth reaction conditions (room temperature, 1 bar H_2 pressure) for all substrates examined, providing the partial hydrogenation products with high conversions within reasonable time. Typical TOFs were in the range of 130–250 h^{-1} at ca. 90% conversion. Catalyst selectivity was good (67% **4a**) to excellent (93–100% **1a**, **2a**) at this conversion level. Hydrogenation of nitrobenzene **6** gave aniline **6a** as the sole product. Catalyst reuse was possible by simple decantation, showing

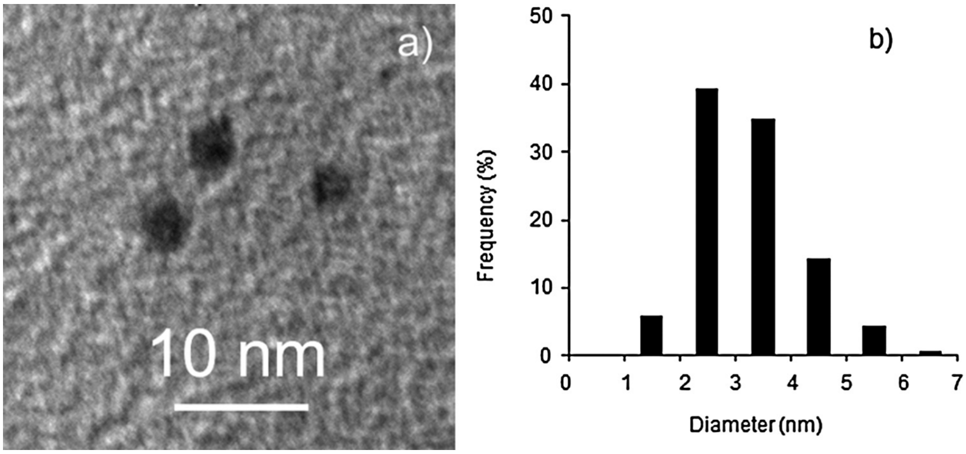

Fig. 2. 'TEM image of Pd@NKZPDB-5 (a) and relevant size distribution of PdNPs (b).

neither significant activity nor selectivity drop over five consecutive runs or 6 h overall use. Representative results are reported in graphical format in Fig. 4 for the hydrogenation reaction of cyclohexene **1**. Palladium leaching in solution was below the ICP-EOS detection limit in each run, while the absence of catalytic activity of the recovered reaction solutions indicated the catalyst to be truly heterogeneous, ruling out the contribution of homogeneous species to the catalytic conversion [43]. The above findings are in line with those previously reported for the parent membrane-supported PdNP [39], and indicate the strong palladium anchoring and the high resistance of the support under the conditions of catalysis. Deactivation of polymer-supported PdNP hydrogenation catalysts was previously attributed to the dissolution of Pd crystallites, to unfavourable interactions with the support and to the chemical degradation of the polymer under catalytic conditions [44–46], that can be reasonably ruled out in our case.

3.2.2. *Catalysis under continuous flow conditions*

Prompted by the above favourable results, we decided to investigate the viability of the catalyst under concurrent, continuous flows

Table 1
Main features of the catalysts used.

Catalyst	Bead size[a] (mm)	ZrO_2 core (mm)	Composition[b]	Bulk Pd loading (%)	PdNPs size (nm)
Pd@NKZPDB-1	1.2 ± 0.2	0.8	PVA 1, ZrO_2 0.10, PdO 0.21, POGE 0.19	0.03	3.1 ± 0.9
Pd@NKZPDB-5	1.7 ± 0.2	–	PVA 1, ZrO_2 0.14, PdO 0.21, POGE 0.19	0.10	3.2 ± 0.9

[a] Diameter.
[b] Weight composition of the hybrid material normalized to 80% saponified PVA. [c]From ICP-OES, w/w%.

Table 2
Catalytic hydrogenation reactions using Pd@NKZPDB-1 beads.[a]

Substrate	Batch reactor [b]		Flow reactor [c]	
1	Reaction conditions	4 h, 1 bar H_2	Reaction conditions	solution 0.05 mL/min, H_2 1.2 mL/min, 2.8 bar H_2
	Conversion (%)	92.7	Conversion (%)	89 ± 2.0
	TOF (h^{-1})	249	TOF (h^{-1})	120
	STY (kg L^{-1} h^{-1})	0.00046	STY (kg L^{-1} h^{-1})	0.062
	Sel. to 1a (%)	100	Sel. to 1a (%)	100
2	Reaction conditions	6 h, 1 bar H_2	Reaction conditions	solution 0.05 mL/min, H_2 1.2 mL/min, 4.3 bar H_2
	Conversion (%)	85.3	Conversion (%)	81 ± 3.0
	TOF (h^{-1})	134	TOF (h^{-1})	108
	STY (kg L^{-1} h^{-1})	0.00032	STY (kg L^{-1} h^{-1})	0.074
	Sel. to 2a (%)	92.9	Sel. to 2a (%)	73
4	Reaction conditions [d]	3.5 h, 1 bar H_2	Reaction conditions [d]	solution 0.16 mL/min, H_2 1.2 mL/min, 4 bar H_2
	Conversion (%)	91.6	Conversion (%)	89 ± 2.4
	TOF (h^{-1})	202	TOF (h^{-1})	230
	STY (kg L^{-1} h^{-1})	0.00044	STY (kg L^{-1} h^{-1})	0.14
	Sel. to 4a + 4b (%)	53.2 (67% 4a)	Sel. to 4a + 4b (%)	71 (85% 4a)
6	Reaction conditions [e]	3 h, 1 bar H_2	Reaction conditions [e]	solution 0.04 mL/min, H_2 1.4 mL/min, 2.3 bar H_2
	Conversion (%)	89.2	Conversion (%)	87 ± 3.1
	TOF (h^{-1})	129	TOF (h^{-1})	38
	STY (kg L^{-1} h^{-1})	0.00035	STY (kg L^{-1} h^{-1})	0.028
	Sel. to **6a** (%)	100	Sel. to **6a** (%)	100

[a] Reaction conditions: methanol 0.05 M, room temperature. Catalyst 440 mg, Pd 0.03% (w/w). Selectivity e.g.: 2a = 2a/(2a + 2b).
[b] Reactor volume 50 mL.
[c] H_2 pressure measured at the reactor inlet. Start time: attainment of steady state conditions, ca. 1 h. Reactor volume 176 μL. Conversions: average value over 8 h time-on-stream. Productivities calculated from conversion average value.
[d] Substrate 0.03 M.
[e] Substrate 0.02 M.

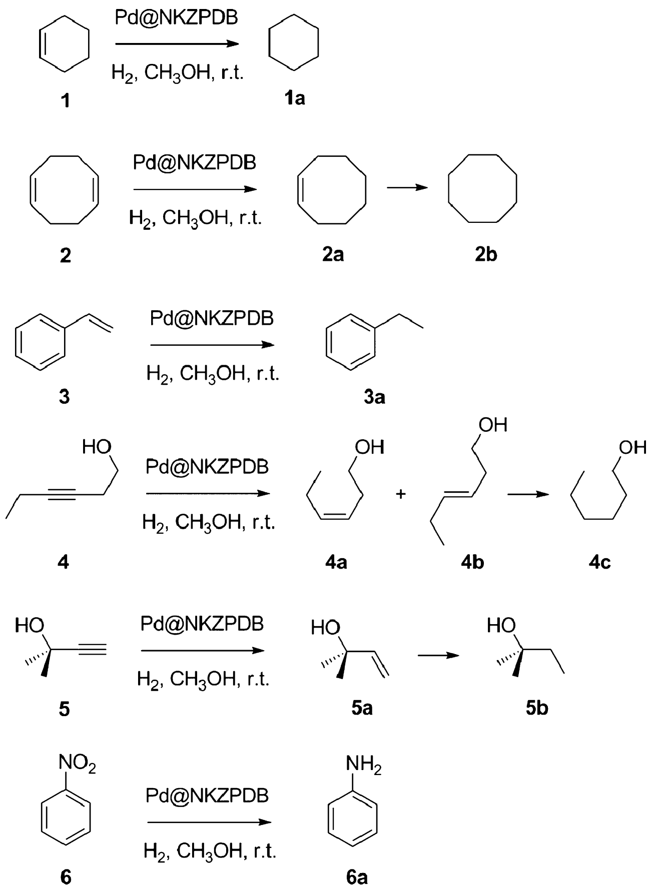

Fig. 3. Sketch of substrates investigated and products detected with labelling scheme.

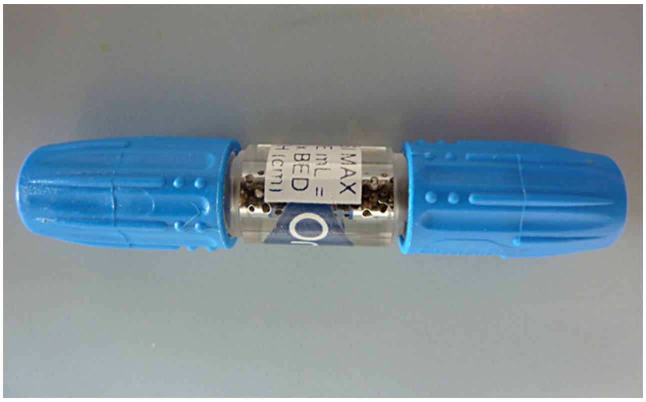

Fig. 5. Image of the packed bead Pd@NKZPDB-5 flow reactor.

of solution and hydrogen gas after packing the catalyst into a commercial glass tube (Fig. 5). The conversion and the selectivity of the hydrogenation processes were examined under various combination of H_2 and solution flow rates. Experimental conditions as similar as possible to those of batch operations were employed for comparative purpose. As general trend, conversions could be easily adjusted to 100%, either by decreasing the solution flow rate (i.e. by increasing the residence time) or by increasing the hydrogen flow rate (i.e. by increasing the H_2/substrate molar ratio), with slight selectivity decrease upon increasing conversion, as expected for similar systems. Selected, best compromise results between conversion and selectivity are reported in Table 2. Irrespective of the substrate, all reactions were achieved under very mild conditions and, in any case, comparable to those of batch operations. Productivities were similar to the batch processes, if normalized to the palladium content, whereas they were 10^2–10^3 times higher if STY was considered. Similar selectivity was also observed, albeit 3-hexen-1-ol isomers (**4a** + **4b**) was obtained with higher purity (71% selectivity, of which 85% the *cis* isomer **4a**, at 90% conversion), that can be justified by the quick detachment of the intermediate alkene from palladium surface after formation, with no possibility of further reaction, as recently proposed for similar Pd/TiS supported systems [47]. All flow processes were monitored for 8 h continuous time-on-stream, followed by overnight switch-off, and restart for an analogous period. Most importantly, neither significant activity nor selectivity decrease were detected over that time. Data for the continuous flow partial hydrogenation reaction of **1** and 1,5-cyclooctadiene **2** are graphically reported in Fig. 6, as representative examples.

We then turned our attention to the Pd@NKZPDB-5 catalyst, whose lack of zirconia core provides an higher number of active Pd sites for the same weight amount of solid catalyst, compared to Pd@NKZPDB-1. Indeed, better productivities were found in this case, both in terms of TOF and STY (up to 4 times higher), under room temperature and 1–2 bar H_2 pressure. Noteworthy, selectivities were also better at higher conversions. Selected, best compromise data are reported in Table 3.

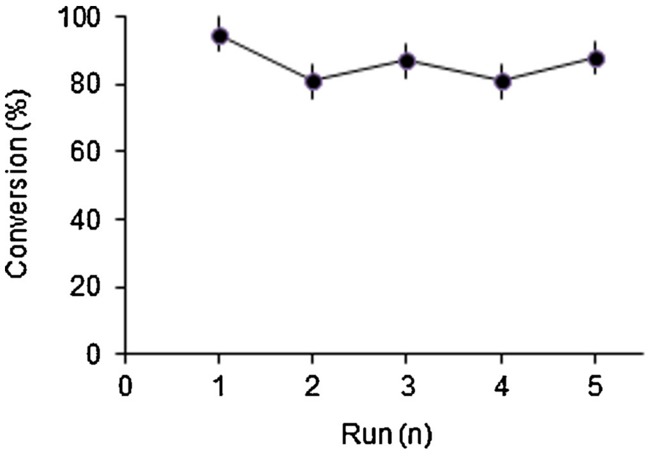

Fig. 4. Reuse of Pd@NKZPDB-1 catalyst in the batch hydrogenation reaction of **1**. Experimental conditions: methanolic solution 0.05 M, room temperature, 1 bar H_2, substrate: catalyst ratio 294, catalyst Pd 0.03% (w/w), run time 1 h.

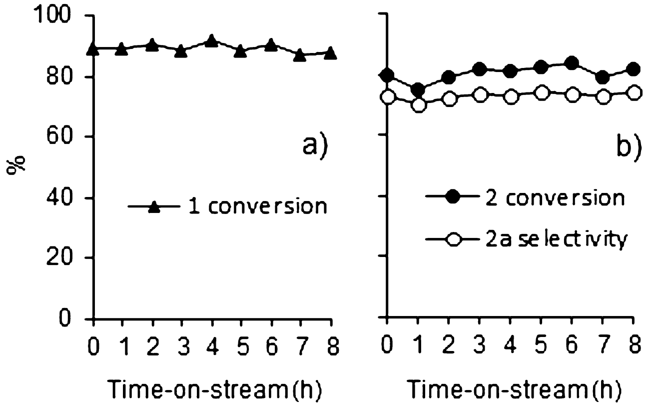

Fig. 6. Continuous flow partial hydrogenation reactions over of Pd@NKZPDB-1 catalyst: substrate **1** (a) and substrate **2** (b). Experimental conditions: substrates in methanolic solution 0.05 M, room temperature, solution 0.05 mL/min, H_2 1.2 mL/min. Reactor volume 176 μL. Dry catalyst 440 mg, Pd 0.03% (w/w). Start time: attainment of steady state conditions, ca. 1 h.

Table 3
Continuous flow hydrogenation reactions catalysed by Pd@NKZPDB-5 beads.[a]

Substrate	Reaction conditions	Conversion (%)	TOF (h^{-1})	STY ($kg\,L^{-1}\,h^{-1}$)	Selectivity (%)
2	solution 0.10 mL/min, H_2 0.7 mL/min, 1.2 bar H_2	91 ± 2.0	282	0.10	**2a** 88
3	solution 0.07 mL/min, H_2 1.2 mL/min, 1.6 bar H_2	98 ± 2.0	213	0.07	**3a** 100
4	solution 0.62 mL/min, H_2 3.4 mL/min, 1.5 bar H_2	99 ± 1.0	1761	0.62	**4a** + **4b** 83 (**4a** 83)
5[b]	solution 0.20 mL/min, H_2 3.8 mL/min, 2.1 bar H_2	99 ± 0.9	1033	0.29	**5a** 60
6[c]	solution 0.02 mL/min, H_2 0.4 mL/min, 1.1 bar H_2	99 ± 0.8	21	0.08	**6a** 100

[a] Reaction conditions: substrates in methanolic solution 0.03 M, room temperature. Dry catalyst 61 mg, Pd 0.10% (w/w). H_2 pressure measured at the reactor inlet. Reactor volume 176 μL. Start time: attainment of steady state conditions, ca. 1 h. Data from GC analysis. Conversions: average value over 8 h time-on-stream. Productivities calculated from conversion average value. Selectivity, for example, **2a** = **2a**/(**2a** + **2b**).

[b] Substrate 0.05 M.

[c] Substrate 0.01 M.

Thus, the partial hydrogenation reaction of **2** could be achieved with 88% selectivity to cyclooctene **2a** at 91% conversion (1.2 bar H_2, TOF 282 h^{-1}, STY 0.10 $kg\,L^{-1}\,h^{-1}$). The only other by-product detected was cyclooctane **2b**, with no formation of the isomerization products 1,3- or 1,4-cyclooctadiene. Selectivity to **2a** was slightly dependent from conversion upon change of the H_2/substrate ratio or (less significantly) the residence time, while keeping constant the other parameter, as shown in Fig. 7. Use of the parent membrane catalyst required higher H_2 pressure (5 bar) to give 78% selectivity at 88% conversion and lower productivity (78 h^{-1}) [39]. The continuous flow, partial hydrogenation reaction of **2** has been previously described using supported PdNP catalysts, both onto purely polymeric and inorganic materials. PdNP onto commercial ion-exchange resin beads provided comparable results at slightly higher pressures (97% sel. at 87% conv., 2.5 bar H_2) [48], whereas unconventional silica and titania monoliths resulted in better (90% sel. at 95% conv., 2.6 bar H_2) [49] and worse (91% sel. at 75% conv., 2.3 bar H_2) [50] efficiency, respectively. Use of Pd onto membrane supports has also been reported. PdNPs onto PVA membranes (5% w/w Pd) gave **2a** in 82% selectivity at 50% conversion [51], while pore-through-flow catalytic membranes based either on polyacrylic acid [52,53] or alumina [54] provided **2a** in ca. 95% selectivity at >90% conversion, at 50 °C and 10–40 bar H_2, however.

Similarly, styrene **3** was selectively hydrogenated to ethylbenzene **3a** at >98% conversion using Pd@NKZPDB-5 under 1.6 bar H_2. The same reaction was recently achieved using a commercial H-Cube® packed bed flow reactor equipped with 10% Pd/C catalyst to provide **3a** in 80% conversion under 30 °C and 80 bar [55].

The hydrogenation of 3-hexyn-1-ol **4** over Pd@NKZPDB-5 gave the ene product **4a** + **4b** with remarkable productivity (1761 h^{-1} TOF, 0.62 $kg\,L^{-1}\,h^{-1}$ STY) and 83% selectivity, whose 83% is the leaf alcohol *cis* isomer **4a**, at 99% conversion under 1.5 bar H_2. Almost constant conversion and selectivity were observed over 8 h time-on-stream, as graphically shown in Fig. 8. Importantly, no catalyst regeneration nor additives were required, as usually reported for this reaction using solid-supported Pd catalysts [56–59]. The results obtained compare favourably with most examples described for the catalytic hydrogenation of **4** under continuous flow, including Pd-doped silica and titania inorganic monoliths [49,50], Pd onto ion-exchange resins [48], and commercial 5% Pd/C and Lindlar catalysts [60], which invariably showed lower productivity and selectivity at the same conversion level. The only superior flow catalyst reported was Pd@MonoBor (PdNP onto monolithic ion-exchange borate resin, 94.5% sel.@ 99.5% conv.) [60].

The terminal alkynol 2-methyl-3-butyn-2-ol **5** was also reduced under continuous flow, showing excellent productivity (1033 h^{-1} TOF), but only moderate selectivity to the mono hydrogenate alkene product **5a** (60%). Conventional, heterogeneous batch systems for the catalytic hydrogenation of **5** often suffer from fast deactivation due to degradation of the support, sintering of metal nanoparticles [61,62] or poisoning by dimers and other by-products adsorption on the catalyst surface [63,64]. Few reports exist on the partial hydrogenation of **5** under continuous flow. Best performances in terms of selectivity were observed using Pd@MonoBor (93.9% at 92.0% conversion) [60] or a capillary microreactor coated with $Pd_{25}Zn_{75}/TiO_2$ catalyst (90% at 99.9% conversion), that could be further improved by addition of pyridine [65].

Finally, the selective, catalytic hydrogenation of nitroarenes in the liquid phase is a reaction of much practical interest in the polymer and pharmaceutical sectors, which has been extensively

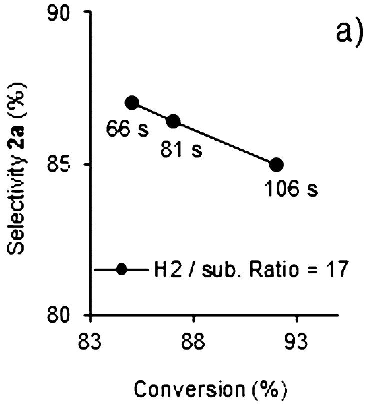

Fig. 7. Selectivity/conversion diagram for the continuous-flow hydrogenations of **2** over Pd@NKZPDB-5 catalyst (61 mg, Pd 0.10%, w/w, methanolic solution 0.03 M, room temperature. Reactor volume 176 μL. Data from GC analysis): ● at fixed H_2/substrate ratio = 17 and residence time range 66–106 s (a, left), ○ at fixed residence time 106 s and H_2/substrate ratio range 5–17 (H_2 flow rate 0.3–0.8 $mL\,min^{-1}$) (b, right).

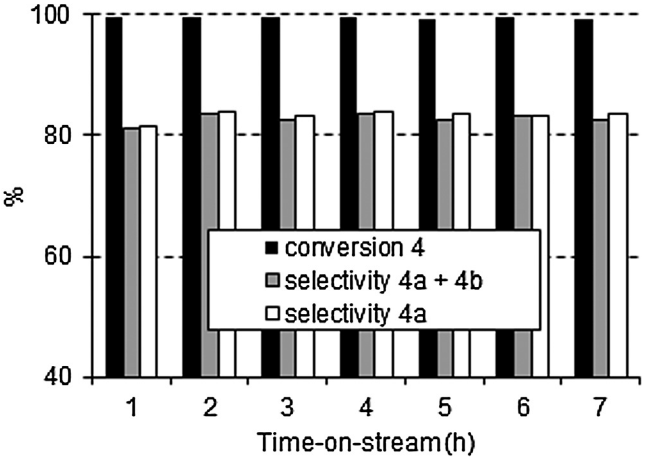

Fig. 8. Continuous flow partial hydrogenation of **4** over of Pd@NKZPDB-5 catalyst. Reaction conditions: methanolic solution 0.03 M, 0.62 mL/min, H_2 3.4 mL/min, 1.5 bar H_2, room temperature. Catalyst 61 mg, Pd 0.10% (w/w). Reactor volume 176 μL. Start time: attainment of steady state conditions, ca. 1 h. Data from GC analysis. Selectivity **4a** + **4b** = (**4a** + **4b**)/(**4a** + **4b** + **4c**). Selectivity **4a** = (**4a**)/(**4a** + **4b**).

Table 4
Continuous flow catalytic hydrogenations of nitrobenzene (**6**) to aniline (**6a**).

Catalyst	H-source	Conversion (%)	Selectivity (%)	Reactor type	Reaction conditions	Ref.
Pd@NKZPDB-5	H_2	99	100	Packed bed	r.t., 1 bar	this work
Pt@TiO$_2$	H_2	100	92 [a]	Microreactor	40 °C	[69]
3Au–40Co@SBA15	H_2	98.9	100	Fixed bed down flow	200 °C, solventless	[70]
5.5% Pd@Al$_2$O$_3$	H_2	97	94	Falling-film	60 °C, 6 bar	[71]
5% Pd@Deloxan	H_2	100	100	Supercritical CO_2	150 °C, 80 bar	[72]
Pd@PSi–Al$_2$O$_3$	H_2	100	100	Packed	70 °C	[73]
Pd@anion exchange	Cyclohexene	95	100	Glass/polymer composite	100 °C	[74]
10% Pd@C	Cyclohexene	84	100	Inductive heating	70 °C	[75]

[a] 6% yield nitrosobenzene.

studied in the past [66–68]. Particularly, the conversion of **6** to **6a** under continuous flow was reported using various heterogeneous catalysts and hydrogen sources, as summarized in Table 4. Pd@NKZPDB-5 provided **6a** in 100% selectivity at full conversion under room temperature and ca. 1 bar H_2, with good productivity, which is among the best results obtained for this reaction, both in terms of efficiency an energy requirements.

The results obtained indicate that the Pd@NKZPDB catalysts are featured by a remarkable mechanical and chemical resistance, which allow for their use both under batch and continuous flow hydrogenation conditions for prolonged reaction times. Particularly, Pd@NKZPDB-5 type material, having a Pd loading as low as 0.1%, couples resistance with efficiency so as to provide partial hydrogenation products of multiple $C{=}C$ or $C{\equiv}C$ bonds, with high selectivity at nearly full conversion in most cases, and with good productivities under very mild flow reaction conditions, i.e. room temperature and 1–2 bar H_2. Noteworthily, the performance offered by Pd@NKZPDB-5 in the continuous flow hydrogenation reaction of **2**, **4** and **6** compares favourably with that obtained using commercial supported-Pd catalysts, either polymeric (resins, carbon) or inorganic (Lindlar), in terms of milder reaction conditions, lower pressure drop, catalyst deactivation, selectivity at full conversion.

PVA-stabilized PdNP heterogeneous catalysts have a number of precedents. PdNP onto polyvinyl alcohol films were used as catalyst for the Suzuki–Miyaura reaction of *p*-iodonitrobenzene with phenylboronic acid. However, catalyst reuse was limited by the leaching of palladium species, as consequence of the action of oxygen in the presence of iodide ions [76]. The catalytic reduction of hexavalent chromium to Cr(III) was reported using PdNP onto polyethyleneimine/PVA nanofibers [77]. Crosslinked polyvinyl alcohol/polyacrylamide particles embedding PdNP were fabricated for use as catalyst in Heck-type reactions. The catalyst was not truly heterogeneous in this case, since an homogeneous mechanism involving the participation of dissolved Pd atoms was highlighted [78]. The superior performance of the hybrid Pd@NKZPDB catalysts can be attributed to the favourable combination of several factors, including the lack of strong coordination interaction between functional groups from the polymer and the metal centre, hampering the effective replacement of reactants around the active site [79], the steric stabilization of PdNP by the porous polymer network [41], the mechanical strengthening and SMSI effect of ZrO_2 [80] and the good swelling propensity of PVA.

4. Conclusions

We have shown that 3.2 nm size palladium nanoparticles can be easily grown within a hybrid zirconia/PVA matrix, to afford catalytic beads readily suitable for application to continuous flow, partial hydrogenation reactions in the liquid phase under mild conditions. A Pd content of 0.03–0.10% weight allowed for the complete hydrogenation of $C{=}C$ and $C{\equiv}C$ bonds and nitrobenzene within reasonable timeframes and satisfactory selectivity, and with no significant loss of catalytic performance over prolonged time-on-stream. Compared to known similar systems, the supported catalyst devised offers multiple advantages in terms of cost and availability, activity under mild reaction conditions, negligible Pd leaching, high durability, possibility of use in hydrophilic solvents, no need of regeneration nor additives [81]. The results obtained are of relevance to development of green methods for the long-term, sustainable production of fine-chemicals and, particularly, to the engineering of new reactors and applications requiring continuous processing conditions [82]. Despite the higher selectivity of the industrial process, the catalyst described in the present work provides clear advantages in terms of environmental impact due to no contamination by toxic Pb nor other additives and lower noble metal loading.

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