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Green semi-hydrogenation of alkynes by Pd@borate monolith catalysts under continuous flow

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ABSTRACT

Palladium nanoparticles were immobilized onto an unconventional polymeric borate macroporous monolith and the resulting mesoreactor (i.d. 3 mm, length 25 mm) used in liquid-phase catalytic semi-hydrogenation reaction of substituted alkynes under continuous flow. The catalytic system showed excellent efficiency, both in terms of activity and selectivity, and long-term stability under mild reaction conditions (methanol, room temperature, 1.5 bar H_2 max), with no need of additives. Particularly, the leaf alcohol *cis*-3-hexen-1-ol was for the first time obtained with selectivity comparable to that of the industrial batch process. The performance of the catalyst is discussed and compared with those of the analogous batch and industrial processes.

1. Introduction

Fine-chemicals production *via* continuous flow of a liquid-phase over-structured heterogeneous catalysts is receiving increasing interest due to the need of greener technologies [1,2] in an industrial sector blemished by the highest E-factors [3–5], while contributing to most of the EU chemicals trade market [6]. Indeed, compared to conventional batch systems, catalysis under continuous flow provides considerable benefits in terms of efficiency, purification, safety, waste emission, automation, space and energy consumption [7–10]. Particularly, monolithic reactors may be extremely useful in the synthesis of fine-chemicals because of the improved mass and heat transfer, lower pressure drop, uniform residence times distribution, with respect to packed-bed setups [11,12]. To this purpose, *true monoliths* [13], either from inorganic [14–18] and organic materials [19–24], featured by uniformly distributed meso and/or macropores, and not to be confused with conventional foams or honeycombs with millimeter size cavities [25,26], have been used to support catalytically active species. Due to the simpler synthetic procedures compared to the parent inorganic materials, these unconventional polymer-based monoliths were the first to demonstrate the utility of monoliths in the fine-chemicals production [27,28]. However, issues have still to be solved concerning chemical stability, shrinking phenomena and back pressure evolution at high flow rate due to limited porosity, which adversely affect the performance of polymeric monoliths as catalysts support [29,30].

Among organic polymers, ion-exchange resins are particularly suited to engineer single-site heterogeneous catalysts [31], either immobilized metal nanoparticles (MNPs) [32,33] or molecular complexes [34,35], due to several favorable features [36]:

- low manufacture costs,
- possibility to be obtained with diverse functionalities, porosities and morphologies,
- ease of handling,
- satisfactory chemical, mechanical, and thermal resistance,
- ability to stabilize MNPs due to the dual effect of charged functional groups (electrostatic stabilization) [37] and porosity (steric stabilization) [38,39],
- effective and easy catalyst anchoring *via* non-covalent linkage [40,41],
- versatility in terms of accessible reactions.

Despite the above advantages, very few polymeric ion-exchange monoliths were described so far, and mostly limited to chromatographic applications. Examples include sulfonated resins obtained either by removal of water from water-in-oil styrene-DVB emulsions followed by post functionalization [42], or by sulfonation of preformed poly(styrene-*co*-DVB) and poly(GMA-*co*-EDMA) monoliths in capillary silica columns [43–45], and quaternary

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Abbreviations: DVB, divinylbenzene; GMA, glycidyl methacrylate; EDMA, ethylene glycol dimethacrylate; PEGDA, polyethylene glycol diacrylate.

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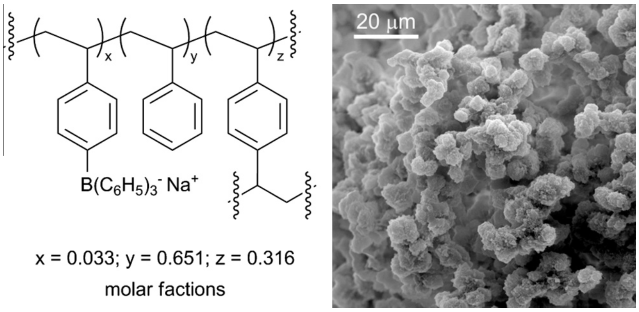

Fig. 1. Sketch of composition (left) and representative SEM image (1600 magnifications, right) of MonoBor.

ammonium polymers prepared by amine treatment [46] or by copolymerization of 2-(acryloyloxy)ethyl trimethylammonium chloride and PEGDA [47].

We recently reported the synthesis and characterization of a macroporous polymeric monolith, hereinafter called MonoBor (Fig. 1), in which cation-exchange tetraphenylborate anions are incorporated in a highly cross-linked styrene–divinylbenzene matrix [48]. A striking feature of this material is its reproducible, isotropic microstructure based on a 'rigid' skeleton of ca. 6 μm thickness forming a narrow size distribution of interconnected flow-through pores of 10 μm size, corresponding to a BET surface area of 9.72 $m^2\,g^{-1}$, which guarantees a very low flow resistance and a high mechanical stability. The chemical and thermal resistance of the polymer was demonstrated up to 350 °C. The monolith was easily obtained *in situ* within the walls of a commercial glass column resistant up to 1200 psi pressure, so as to provide a monolithic mesoreactor (i.d. 3 mm, length 25 mm) perfectly suited for use in synthetic applications under continuous flow [49]. The exchange ability of the monolith was demonstrated and the anchoring of cationic metal complexes was successfully achieved to give a uniform metal distribution within the solid support.

Herein we describe the immobilization of palladium nanoparticles onto MonoBor and the use of the corresponding monolithic reactor (Pd@MonoBor) in the catalytic partial hydrogenation reaction of alkynes under continuous flow. Choice of palladium NPs was motivated by their known versatility as catalysts, so as to be often used to investigate the effect of the support on the catalyst efficiency [50], and by the method we recently developed for the effective and environmentally friendly immobilization of PdNPs onto monolithic supports [15]. The hydrogenation reaction of substituted alkynes was selected because of its high significance as probe of catalyst chemo-, stereo- and regio-selectivity, and because it is the technology currently adopted for the large-scale production of several important fine-chemicals, including pharmaceuticals, fragrances and food ingredients [51].

2. Experimental section

2.1. 1. Materials and methods

All reaction and manipulations were performed under nitrogen by using standard Schlenk techniques, unless otherwise stated. Tetrahydrofurane was distilled from sodium-benzophenone prior of use. The MonoBor monolith was prepared as previously described into a commercial Omnifit Labware Glass Column (3.0 i.d. × 25 length mm) equipped with 0.2 μm PE frit to ensure an optimum flow distribution [48]. All the other reagents were commercial products and were used as received without further purification. Palladium on activated charcoal (5 wt.%) was obtained from Aldrich. 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 512 × 400 matrix, 100 μs dwell time and 25 keV accelerating voltage. TEM (Transmission Electron Microscopy) analyses were performed using a CM12 PHILIPS instrument at 120 keV accelerating voltage. 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 30 min. Successively, a drop of solution was deposited onto a carbon coated Cu TEM grid and the solvent left to evaporate. XRD (X-ray Diffraction) patterns 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 prepared on a silicon wafer (zero background) that was rotating (0.5 rotations per second) during acquisition. All XRD patterns were acquired at room temperature in a 2θ range from 30° to 55°, applying a step size of 0.0263° and a counting time of 295.29 s. TGA analyses were performed with a Seiko EXSTAR TG/DTA 7200 thermogravimetric analyzer. The metal content in the supported catalysts was determined by Atomic Absorption Spectrometry (AAS) using a ANALYST200 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 solutions recovered 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. GC-analyses were performed on a Shimadzu GC 2010 gas chromatograph equipped with flame ionization detector and a 30 m (0.25 mm ID., 0.25 μm FT) SPB-1 Supelco or a 30 m (0.25 mm ID, 0.25 μm FT) VF-WAXms fused silica capillary column. GC–MS analyses were performed on a Shimadzu QP5000 apparatus equipped with a SPB-1 Supelco fused silica capillary column or on a Shimadzu GC–MS 2010 apparatus equipped with a 30.0 m (0.32 mm ID) WCOT-Fused silica CP-Wax 52 CB capillary column. Reactions under a controlled pressure of hydrogen were performed using a H_2 generator Parker H2PEM-260. Reactions under continuous flow were carried out using a reactor system constructed at Istituto di Chimica dei Composti OrganoMetallici, Sesto Fiorentino (Italy). The system was designed to allow for a simultaneous flow of substrate solution and hydrogen gas (up to 40 bar pressure). The reactor was completely inert, as all wet parts were made of PEEK, PFA or PFTE. A constant flow of substrate solution was regulated by an Alltech® model 426 HPLC pump in PEEK. A constant flow of hydrogen gas was adjusted, and its pressure monitored, by a BRONKHORST flow controller and pressure meter, respectively. 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 switching valve in PEEK. The system was equipped with a temperature controller. 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. The reaction products were unequivocally identified by the GC retention times, mass and NMR spectra of those of authentic specimens.

2.2. Synthesis of Pd@MonoBor

A solution of $Pd(NO_3)_2$ in THF (0.025 M) was flowed through a MonoBor monolithic column (3.0 i.d. × 25 length mm, ca. 30 mg dry material) at 0.5 mL min^{-1} for 3 h using an HPLC pump and an endless loop system. The brownish monolith obtained was then washed with THF and methanol (0.5 mL min^{-1} for 1 h, for each solvent). After connection to the flow reactor system described above, H_2 (2 mL min^{-1}, typical pressure measured at the reactor inlet 2 bar) and methanol (0.5 mL min^{-1}) were allowed to flow simultaneously through the impregnated monolith for 3 h at r.t. The as-obtained gray material was then washed with methanol (0.5 mL min^{-1} for 15 min) under nitrogen, before being directly used as catalyst in hydrogenation reactions, or dried under a N_2 stream (0.2 mL min^{-1} for 12 h) before being analyzed by ICP–EOS and EDS to give a typical Pd loading of 0.67% (w/w). EDS spot spectra recorded on radial and longitudinal sections of the monolithic catalyst showed the metal to be evenly distributed within the support. Twenty spectra were typically recorder both for longitudinal and radial sections at different monolith depth showing the same Pd content within ±0.04%.

2.3. Catalytic reactions under continuous flow

In a typical experiment, a deaereated solution of alkyne in methanol (0.1 M) was allowed to flow through the Pd@MonoBor column catalyst (29 mg, reactor volume 176 μL) at 0.2 mL min^{-1} together with a H_2 flow of 1.3 mL min^{-1} at r.t. This resulted in a H_2 pressure at the reactor inlet of ca. 1.2 bar (corresponding to a H_2/alkyne molar ratio of ca. 2.8), while the hydrogen gas was released at atmospheric pressure at the outlet of the reactor. Therefore, the pressure drop generated by monolithic reactor was ca. 0.2 bar. The attainment of the steady-state conditions (ca. 1 h) was taken as the reaction start time. The reaction was typically monitored for 14 h time-on-stream by periodically analyzing the product solution for conversion and selectivity by GC, while 5.0 mL aliquots were sampled at 1 h intervals for Pd leaching determination by ICP-OES. The amount of Pd in solution was below the detection limit in each sample (0.006 ppm).

3. Results and discussion

3.1. Synthesis and characterization of the catalyst

The Pd@MonoBor catalyst was prepared following the approach previously adopted for the synthesis of Pd@TiO_2 monoliths [15]. The method is based on the use of $Pd(NO_3)_2$ being a cheap, commercial Pd precursor that can be easily anchored by ion-exchange, then smoothly reduced *in situ* by H_2 (1 bar, r.t.) [52], thus to avoid any excess of hazardous reductant (borohydrides, hydrazine), harsh conditions, time-consuming steps, toxic stabilizers or elaborate devices, thereby satisfying most Principles of Greener Nanomaterial Production [53]. Thus, the catalyst was generated in one-pot by flowing a THF solution of $Pd(NO_3)_2$ through a preformed MonoBor monolith (3 h @ 0.5 mL min^{-1}), followed by reduction under a stream of H_2 (1 bar, 2 mL min^{-1}, r.t., 3 h) (Fig. 2). Use of THF was motivated by the appropriate swelling and stability of the polymer in the solvent, while avoiding the erratic co-precipitation of PdNPs if methanol is used [54]. The as-prepared monolithic catalyst could be directly used in subsequent hydrogenation reactions under continuous flow, with no need of removal from the column nor any further treatment.

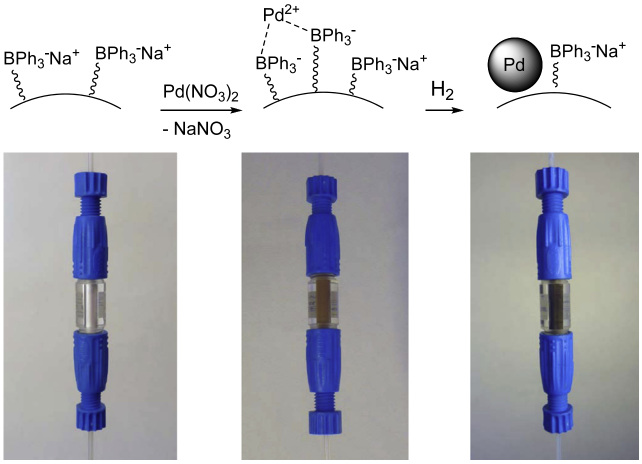

Fig. 2. Scheme of the synthetic procedure (top) and images of MonoBor (left), $Pd(NO_3)_2$ impregnated MonoBor (center) and Pd@MonoBor (right) monolithic columns (i.d. 3 mm, length 25 mm).

The catalyst was characterized in the solid state by a combination of ICP-OES, EDS, ESEM, TEM, XRD and TGA analysis, after careful drying and extraction from the glass column to obtain ca. 2.5 × 20 mm (diameter × length) and 30 mg rods. ICP-OES measurements indicated a typical 0.67% (w/w) Pd loading. EDS microanalysis was in line with this figure, while X-ray emission maps recorded on radial and longitudinal sections of the monolith proved the metal to be evenly distributed within the material. Palladium, carbon, and sodium maps are reported in Fig. 3 for comparison. ESEM inspection revealed no significant change in the monolith microstructure after exposure to palladium immobilization. TEM and XRD analyses showed the above synthetic procedure to provide well-dispersed, spheroidal PdNPs of uniform size embedded in the polymeric matrix. Mean diameter values were consistent within the experimental errors affording 2.5 ± 0.8 nm by TEM (Fig. 4) and 3.8 ± 0.8 nm by XRD. After use in catalysis (see below), Pd@MonoBor showed a significant increase in PdNPs diameter and size distribution resulting in 5.3 ± 1.6 nm by TEM (6.2 ± 1.2 nm by XRD). TGA experiments under nitrogen/air were carried out to evaluate the thermal stability of the catalyst. A representative TGA plot for Pd@MonoBor under air is reported in Fig. S2, while significant thermogravimetric data and the residue yields % are summarized in Table 1. Compared to the metal-free monolith, Pd@MonoBor showed a better thermal stability (T_{max} 426 °C) and a higher residue at 700 °C, consistently with the presence of Pd. The loading of Pd estimated from the R_{900} value was in agreement with that obtained from ICP-OES analyses, within the experimental errors.

3.2. Continuous-flow hydrogenations

The catalytic semi-hydrogenation of alkynes using H_2 to selectively obtain (*Z*)-alkenes is a reaction of central relevance in the production of several important building blocks for the fine-chemicals industry, including bioactive molecules, natural products, and flavors [55,56]. It is also crucial in the bulk polymerization industry to achieve the complete elimination of alkynes from alkene feedstocks [57]. The conventional Pd-based heterogeneous catalysts used to this purpose are generally problematic because of selectivity issues, overhydrogenation to alkanes, isomerization, scarce resistance of other functional (e.g. carbonyl) groups [58,59].

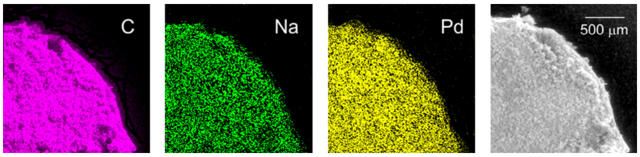

Fig. 3. ESEM image (25 keV, 70 magnifications) and EDS maps of a quadrant of a radial section of Pd@MonoBor monolith. From the left: C map (C Kα1); Na map (Na Kα1); Pd map (Pd Lα1); secondary electrons image.

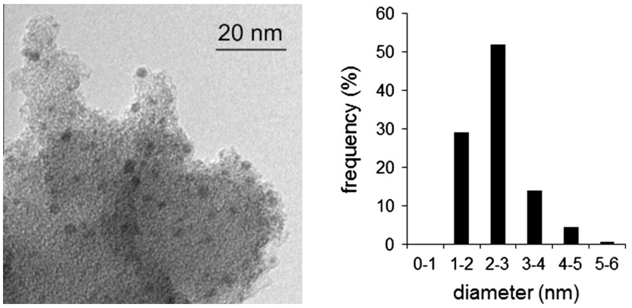

Fig. 4. TEM image of Pd@MonoBor sample (left) and PdNPs size distribution (right) before use in catalysis.

Table 1
TGA (nitrogen, air) data of the monoliths.

Sample	Nitrogen			Air
	$T_{5\%}$ (°C)	T_{max} (°C)[b]	R_{700} (%)	R_{900} (%)
MonoBor[a]	352	429	8.8	3.9
Pd@MonoBor	389	426	11.6	2.3

[a] Data from Ref. [48].
[b] Temperature of the maximum degradation rate.

Strategies were developed to enhance the selectivity of these systems by addition of variable, often large, amounts of contaminants, either organic bases (quinoline, triphenylphosphine), carbon monoxide, sulfides, dimethyl sulfoxide or metal ions (Cu, Pb), whose purpose is invariably to poison the hyperactivity of the metal [60–63]. On the industrial scale, the hydrogenation process is usually carried out using the Lindlar catalyst (5% Pd on $CaCO_3$ doped with 2–3% Pb) that, however, shows serious drawbacks in terms of reuse, deactivation, presence of toxic lead, need of excess of amine modifier [64–67], and whose catalytically active sites still remain unknown. Several efficient homogeneous catalysts were also reported for this reaction [68–70], although heterogeneous catalysts are clearly preferred by industry to address sustainability criteria. The development of well-defined, effective and environmentally friendly catalysts for the partial hydrogenation reaction of alkynes is thus of utmost importance [71].

The Pd@MonoBor monolithic catalyst was employed in the liquid-phase continuous-flow hydrogenation reactions of alkynes, by direct connection to a home-made reactor system based on concurrent flows of substrate solution and H_2 gas reactant (Fig. S1). Various substrates were chosen to test the efficiency of the catalyst for productivity and selectivity in semi-hydrogenation, including terminal and internal alkynols, diols, alkyn-esters, unsubstituted alkynes (Fig. 5). All reactions were monitored for conversion, selectivity and metal leaching in solution with time. Various

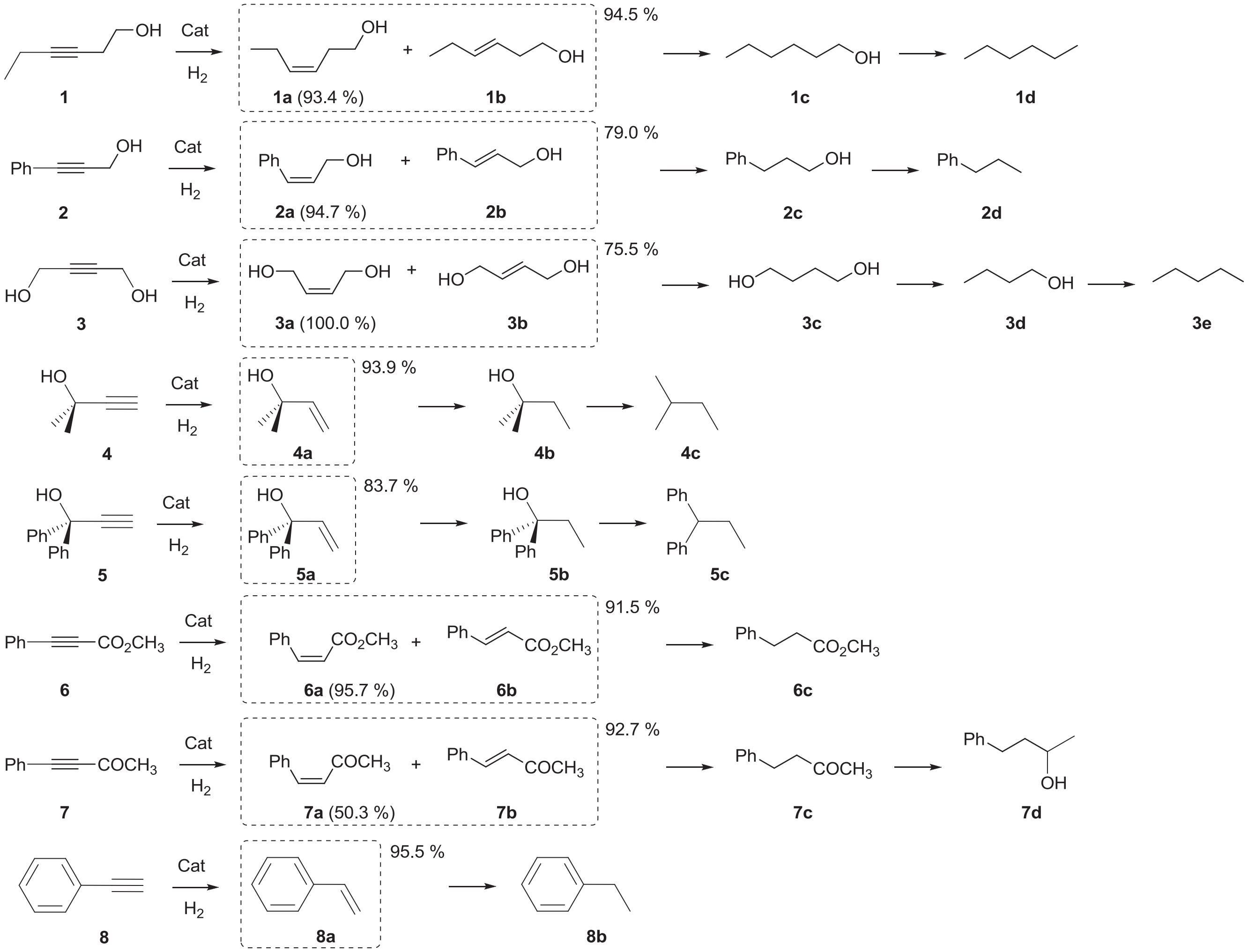

Fig. 5. Sketch of the substrates investigated and potential hydrogenation products, with labeling scheme adopted. Values in percentages refer to representative selectivity data obtained using Pd@MonoBor catalyst under continuous flow (values in brackets refer to Z/E selectivity).

combination of H_2 and solution flow rates were used to examine the effect of the *residence time* and of the *H_2: substrate ratio* on the process output [72].

Representative results are summarized in Table 2 in which productivity, both turnover frequency (TOF = mol product/mol Pd × h) and space-to-time yield (STY = kg product/liter reactor volume × h) [73], selectivity to alkene and Z/E ratio are reported [74]. To the purpose of comparison, TOFs at ca. 90% conversion are indicated. Irrespective of the substrate, under a fixed solution flow rate (i.e. for the same residence time), an increase in the H_2 flow resulted in higher conversions (up to 100%) and in lower selectivities. On the other hand, as expected, the opposite effect was observed on increasing the solution flow rate while keeping constant the H_2/substrate molar ratio. The best compromise results between conversion and selectivity were obtained for residence times in the range 20–100 s and for 0.3–2.5 mL min^{-1} H_2 flows (corresponding to 1.2–2.0 bar H_2 inlet pressure). In any experiment, the pressure drop measured was lower than 1.0 bar.

The hydrogenation reaction of 3-hexyn-1-ol (**1**) was investigated in detail since the *cis*-partial hydrogenation product leaf alcohol **1a** is an important ingredient in the fragrance industry [75,76], currently manufactured in 400 t/y and ca. 96% selectivity @ 99% conversion by a batch process using the Lindlar catalyst [77,78]. The Pd@MonoBor catalyst provided the desired product with 94.5% alkene selectivity (93.4% of which the *cis* product) at 99.5% conversion, corresponding to an overall TOF and STY of 829 h^{-1} and 0.85 kg L^{-1} h^{-1}, respectively, under very mild flow conditions (methanol, r.t., 1.35 mL min^{-1} H_2). The only by-products observed were hexan-1-ol (**1c**), due to overhydrogenation, and traces of isomerization products 4- and 2-hexen-1-ol. The reaction was monitored for 14-h time-on-stream, showing no appreciable decay of conversion nor selectivity (Fig. 6, left). An overall TON of 11,600 after 14 h can be estimated under these conditions. The catalyst could be reused several times with no significant activity drop, just by switching off the reactor system and restart it, provided it was stored under nitrogen or hydrogen meantime. Experiments were carried out to investigate the selectivity/conversion dependence showing slight selectivity changes up to 99.5% conversion. This is graphically shown in Fig 6 right, in which the conversions and the selectivities obtained by varying the residence time, while keeping constant the H_2/substrate ratio are reported (see also Table S2). In no case palladium was detected in solution by ICP-OES, nor catalytic activity was shown by the recovered solution, thus ruling out the leach of active species during the reaction [79].

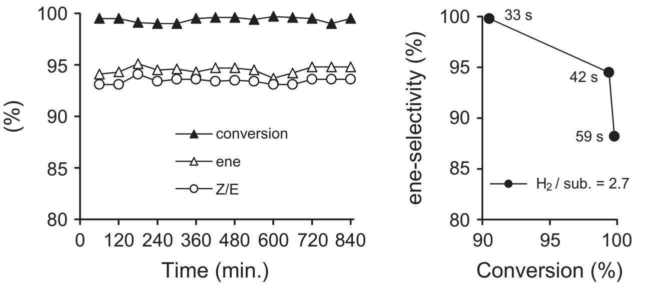

Fig. 6. Continuous-flow hydrogenation of **1** over Pd@MonoBor catalyst (29 mg, 0.67% w/w Pd, methanol solution 0.25 mL min^{-1}, H_2 1.35 mL min^{-1}, 2.5 bar, r.t.). Left: conversion and selectivity vs. time-on-stream. Right: selectivity/conversion diagram at fixed H_2/substrate molar ratio = 2.7 and residence time range 33–59 s (solution 0.18–0.32 mL min^{-1}, H_2 1.0–1.7 mL min^{-1}).

The above findings show that, while the Pd@MonoBor system here described is only slightly less selective than the industrial catalyst, it provides clear advantages in terms lower noble metal loading, productivity, safety, environmental impact, no contamination by toxic Pb nor by other additives [80]. To the best of our knowledge, this is *the first example of flow process for the production of cis-3-hexen-1-ol with selectivity comparable to that of the industrial process.* Previous examples reported for the catalytic hydrogenation of 3-hexyn-1-ol under continuous flow invariably showed lower productivity and selectivity at the same conversion level. These systems include Pd-doped silica and titania inorganic monoliths (Table 3, entry 2 and 3) and packed-bed reactors based on gel-type, ion-exchange sulfonated resins in which PdNPs are embedded (Table 3, entry 4). The latter catalyst is the most similar to Pd@MonoBor. However, it is much less efficient showing worse selectivity (80%) at lower conversion (75%) and overall activity (TOF 352 vs. 829 h^{-1}) [81]. Limited productivity was attributed in that case to the strong interaction between the sulfonate groups from the polymer and the metal center which hampers the effective replacement of reactants around the active site [82,83]. The commercial catalysts 5% Pd/C and 5% Pd (Pb doped)/$CaCO_3$ (Lindlar) were also tested under comparable flow conditions

Table 2
Representative continuous-flow liquid-phase hydrogenation of alkynes by Pd@MonoBor monolithic catalyst.

	Substrate	Reaction conditions[a]					Conversion (%)	TOF[d] (h^{-1})	STY[d] (kg L^{-1} h^{-1})	Selectivity	
		Solution		H_2		H_2/sub. ratio[c]				ene[e] (%)	Z/E[f] (%)
		Flow rate (mL min^{-1})	Residence time (s)	Flow rate (mL min^{-1})	Inlet pressure (bar)[b]						
1	3-Hexyn-1-ol	0.25	42	1.35	1.26	2.7	99.5	829	0.85	94.5	93.4
2	3-Phenyl-2-propyn-1-ol[h]	0.15	70	0.67	1.50	10.8	96.2	120	0.16	79.0	94.7
3	2-Butyne-1,4-diol[h]	0.60	18	2.50	1.76	11.8	93.3	466	0.42	75.5	100.0
4	2-Methyl-3-butyn-2-ol	0.60	18	1.30	1.40	1.2	92.0	1840	1.62	93.9	–
5	1,1-Diphenyl-2-propyn-1-ol[h]	0.16	66	0.30	1.26	3.8	85.2	114	0.24	83.7	–
6	Methyl phenylpropiolate[i]	0.50	21	1.20	1.67	3.2	90.4	754	1.25	91.5	95.7
7	4-Phenyl-3-butyn-2-one[l]	0.20	53	0.85	1.20	5.1	91.9	245	0.37	92.7	50.3
8	Phenylacetylene	0.10	106	1.60	1.27	8.2	98.1	327	0.34	95.5	–

[a] Methanol solution 0.1 M, room temperature. Dry catalyst 29 mg, 0.67% (w/w) Pd. Reactor volume 176 μL. Data from GC analysis. Start time: attainment of steady-state conditions, ca. 1 h.
[b] Pressure measured at the reactor inlet.
[c] Hydrogen to substrate molar ratio.
[d] Calculated on overall conversion.
[e] Percentage of $C{\equiv}C$ semi-hydrogenation compounds in the reaction products, e.g. (**1a** + **1b**)/(**1a** + **1b**+**1c** + **1d**).
[f] Selectivity to Z isomer, e.g. **1a**/(**1a** + **1b**).
[h] 0.025 M.
[i] 0.05 M.
[l] 0.04 M.

resulting in moderate selectivity at very low conversion, and lower selectivity at the same conversion, respectively, however (Table 3, entry 5 and 6) [84]. The hydrogenation of **1** by Pd@MonoBor under flow was examined using various solvents in which the monolith is chemically and mechanically resistant. Representative results are reported in Table 4 for methanol and THF, showing best selectivity at comparable conversions for methanol. This finding can be attributed to the higher swelling of the polymeric monolith in solvents other than methanol (13.1 and 3.2 mL g^{-1} in THF and in methanol, respectively). Indeed, swelling propensity has two important consequences on the catalytic performance of the system: (i) a higher swelling volume may lead to some pore blockage and in a significant contribution to back-pressure [48], resulting in lower selectivity (Table 4, entry 1 and 2), (ii) a better swelling allows for the solvent to diffuse thoroughly the support thus producing a larger number of substrate–catalyst interactions, which equally results in significant overhydrogenation and lower alkene selectivity. Selectivity enhancement at egg-shell catalyst, where the intermediate alkene quickly leaves the active metal after formation with no possibility to react further, was recently proposed for Pd/TiS supported systems [85]. This may also stand for Pd@MonoBor for which scarce swelling in methanol limits the site accessibility only to the sites on the surface of the solid catalyst.

The efficiency and durability of Pd@MonoBor is attributable to the strategic combination of innocent (non-coordinating) and chemically inert borate functional groups in the polymer [86,87], with the rigid, homogeneous macroporous structure of the monolith. This results in the formation of small-size MNPs, not leached from the support under the conditions of catalysis and not affected by poisoning from the matrix, as well as in a flat flow profile and in a scarce flow resistance over prolonged reaction times. These features allow for the hydrogenation reactions to be carried out efficiently under mild conditions and short residence times, with very low pressure drops, which guarantees for the high selectivity of the process. Deactivation of ion-exchange resins-supported MNP catalysts was previously attributed to the loss of the active species, to unfavorable interactions with the functional groups, and to the chemical degradation of the polymer under catalytic conditions [88], that can be reasonably ruled out in our case. Agglomeration of PdNPs under the conditions of catalysis (see “Characterization of the catalyst” above) may be responsible for minor activity drop [89], as previously pointed out for similar systems [52].

Having established a very efficient catalytic flow system for the semi-hydrogenation of **1**, we examined the other alkyne substrates under analogous conditions. Compared to **1**, the internal (di)alcohols **2** and **3** were hydrogenated with lower selectivity at similar conversions. Thus, cinnamyl alcohol **2a** + **2b** was obtained in 79.0% selectivity, 94.7% of which the *Z* isomer **2a**, at 96% conversion, with formation of 21% overhydrogenation product **2c**. In this case, the catalyst efficiency showed to be quite sensitive to the experimental conditions, as graphically shown in Fig. 7 in which selectivity vs. conversion are reported for various H_2 flows and fixed residence times. The highest selectivity reported so far in the heterogeneous-phase catalytic hydrogenation of **2** was recently observed using dendron-stabilized PdNPs and quinoline additives under batch mode (97% ene, 98% *Z*) [90].

Cis-2-butene-1,4-diol **3a** is an important pharmaceutical and agrochemical intermediate (endosulfan, vitamin B6) [91]. It is industrially produced in ca. 5000 t/y by the batch hydrogenation of **3** in the liquid phase (water) under elevated pressures and/or temperatures, using Pd/Al_2O_3 catalysts doped with Cd, Zn, Bi or Te [92]. On the laboratory scale, it was obtained with high selectivity (70–99% @ 80–90% conversion) by the same route, using various supports and additives (including Zn, NH_3, pyridine, KOH) [93–96]. A rather systematic study was carried out on the catalytic hydrogenation of **3** using 0.5–2 wt.% Pd onto carboxylate

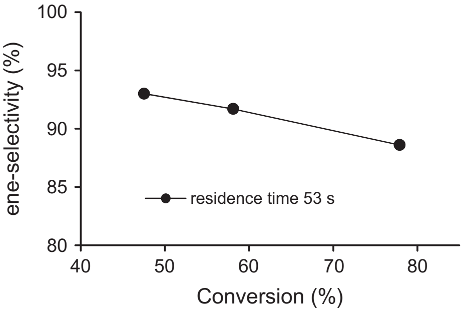

Fig. 7. Continuous-flow hydrogenation of **2** over Pd@MonoBor catalyst. Selectivity/conversion diagram at fixed residence time = 53 s and different H_2/substrate molar ratios 3.6–10.8 (solution 0.20 mL min^{-1}, H_2 0.33–1.0 mL min^{-1}, r.t., 29 mg, 0.67% w/w Pd, methanol).

Table 3
Continuous-flow catalytic hydrogenation of 3-hexyn-1-ol (**1**).[a]

No.	Catalyst	Conversion (%)	TOF (h^{-1})	Selectivity		Refs.
				ene (%)	*Z*/*E* (%)	
1	Pd@MonoBor	99.5	829	94	93	This work
2	Pd@SiO_2 monolith	85.0	80	80	80	[14]
3	Pd@TiO_2 monolith	61.4	350	63	87	[15]
4	D/Pd	75.0	352	80	89	[81]
5	Pd/C	20.0	102	83	92	This work
6	Pd (Pb)/$CaCO_3$	99.2	44	64	62	This work

[a] Methanol, room temperature.

Table 4
Continuous-flow hydrogenations of **1** by Pd@MonoBor using various solvents.[a]

Solvent	Solution flow (mL min^{-1})	H_2		H_2/sub. ratio	Conv. (%)	Sel. ene (%)
		Flow (mL min^{-1})	Press. (bar)			
Methanol	0.25	1.35	1.26	2.7	99.5	94.5
THF	0.25	1.35	1.60	3.5	99.1	11.8
THF	0.25	1.10	1.50	2.7	97.6	4.5

[a] 3-Hexyn-1-ol 0.1 M, room temperature.

Table 5
Continuous-flow catalytic hydrogenation of 2-butyne-1,4-diol (**3**).

No.	Catalyst	Reactor type	Conversion (%)	TOF (h^{-1})	ene[a](%)	Refs.
1	Pd@MonoBor	Monolithic[b]	93.3	466	75.5	This work
2	Pd/Al_2O_3	Honeycomb[c]	90.0	71	99.0	[98]
3	Pd/Al_2O_3	Packed-bed[c]	90.1	125	93.9	[98]
4	Pt/$CaCO_3$	Packed-bed[d]	78	10	27	[99]
5	Pd/C	Packed-bed[e]	92	n.d.	97.4	[100]
6	Pd/Al_2O_3	Capillary[f]	90	n.d.	90	[101]

[a] Selectivity to **3a** + **3b**. *Z*/*E* selectivity 100% in any case.
[b] Room temperature, 1.8 bar H_2.
[c] At 55 °C, 2.0 bar H_2.
[d] At 100 °C, 20 bar H_2.
[e] At 50 °C, 10 bar H_2, with KOH 0.2 g L^{-1}.
[f] At 50 °C.

ion-exchange resins having various cross-linking degrees [97]. Selectivity to alkene near to 98% was observed at 90% conversion, but no *Z*/*E* selectivity was specified. The suppression of alkane formation was ascribed to the steric hindrance of the polymer around the Pd centers, in that case. Pd@MonoBor provided **3a** + **3b** in 75.5% selectivity, 100% of which the *Z* isomer, at ca. full conversion under continuous flow, with the formation of butyraldehyde by-products, in addition to the saturated alcohols **3c** and **3d**, as commonly reported in the literature. Few catalytic flow systems were previously described for the semi-hydrogenation reaction of **3** (Table 5). Compared to conventional honeycomb or packed-bed systems (entry 2–5), Pd@MonoBor was generally less selective, although much more productive under friendlier conditions, showing higher TOF and up to two order magnitudes higher STY.

The terminal alkynols **4** and **5** were also hydrogenated using Pd@MonoBor, both showing high ene selectivity and durability of the catalyst at nearly complete conversion. Indeed, **4a** was obtained in 93.9% selectivity @ 92% conversion, and **5a** in 83.7% @ 85.2%, respectively. The conversion/selectivity diagram vs. time-on-stream for the hydrogenation reaction of **5** is reported in Fig. 8. No significant catalyst efficiency decay over a 8-h reaction period was detected. No evidence for Pd leaching in solution was given by ICP-OES throughout the reactions. A small activity loss can be attributed to poisoning by dimers and other by-products adsorption on the catalyst surface [102]. 2-methyl-3-butyn-2-ol (**4**) is among the most studied alkyne substrates in semi-hydrogenation reactions. It has also been used as probe for optimal catalyst design through the so-called "integrated multilevel approach" [103]. A reason for this is that the alkene **4a** is an important intermediate in the synthesis of vitamins (A, E) and several perfumes [104]. It is manufactured in 95–97% yield using the Lindlar and other heterogeneous catalysts under batch conditions which, however, often suffer from fast deactivation due to degradation of the support or sintering of Pd nanoparticles [105–107]. Few reports exist on the partial hydrogenation of **4** under continuous flow. Best performances in terms of selectivity (90% @ 99.9% conversion) were observed using a capillary microreactor coated with Pd$_{25}$-Zn$_{75}$/TiO$_2$ catalyst, that could be further improved by addition of pyridine [108]. The partial hydrogenation of **5** to **5a** was previously reported in 82–90% yield (no *cis* selectivity specified) using phosphinated polymer incarcerated palladium catalysts under batch conditions [109].

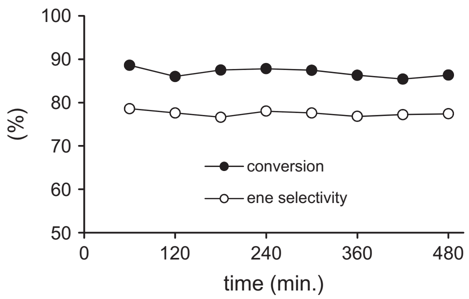

Fig. 8. Conversion and selectivity vs. time-on-stream for the continuous-flow hydrogenation of **5** over Pd@MonoBor catalyst (29 mg, 0.67% w/w Pd, methanol solution 0.16 mL min^{-1}, H_2 1.00 mL min^{-1}/1.29 bar, r.t.).

In order to test the catalyst tolerance and selectivity in the presence of other functional groups other than alcohols, the carbonyl substrates **6** and **7** were examined. Methyl phenylpropiolate (**6**) was hydrogenated with >91% ene selectivity (95.7% of which the *Z* isomer) at ca. 90% conversion, whereas 4-phenyl-3-butyn-2-one (**7**) gave ca. 93% ene selectivity at 92% conversion, albeit with negligible stereoselectivity, under continuous flow (Table 2). In both cases, the only by-products observed were the $C{\equiv}C$ full-hydrogenation compounds **6c** and **7c**, respectively. No previous examples for the continuous catalytic semi-hydrogenation of **6** and **7** were reported. The best selectivity observed in the hydrogenation of **6** (ca. 90% @ 90% conversion) was obtained using conventional heterogeneous Pd batch catalysts, either Lindlar's-type [110] or pumice-supported [111], in the presence of 2.5–30% amine additives [112]. Comparable results were obtained using analogous systems in the semi-hydrogenation reaction of **7** [113].

Finally, the performance of Pd@MonoBor catalyst toward unsubstituted alkynes was evaluated using phenyacetylene (**8**) as probe. High selectivity to styrene (95.5%) was obtained at >98% conversion under very mild conditions (r.t., ca.0.3 bar H_2 pressure drop), corresponding to 0.34 kg L^{-1} h^{-1} STY productivity and 327 h^{-1} TOF. Despite the liquid-phase partial hydrogenation of **8** was successfully achieved in the past using batch catalysts [114–116], few experimental works were described under continuous mode and none with better results compared to Pd@MonoBor. Styrene was obtained in 95% selectivity @ ca. 30% conversion using a capillary reactor (diameter of 250 μL) internally coated with Pd-doped mesoporous titania film [117], while 80% selectivity @ ca. 90% conversion was achieved over amorphous Pd$_{81}$Si$_{19}$ alloy catalyst in supercritical CO_2 [118].

4. Conclusions

The catalytic, selective partial hydrogenation of substituted alkynes is a reaction of high current interest because of the central relevance in the production of several fine-chemical intermediates. It is usually accomplished on the industrial scale in the liquid phase using Lindlar's type catalysts, with serious drawbacks in terms of environmental impact, process economy and catalyst deactivation, however. Herein we described a novel type of heterogeneous catalyst for this reaction based on PdNPs embedded onto an unconventional, macroporous polymeric borate monolith. The catalyst was successfully used in the reduction of various alkyne substrates *under continuous flow*, *mild reaction conditions* and *without additives*, showing excellent performance in terms of space-to-time yield productivity, selectivity and catalyst durability. Particularly, 2-methyl-3-buten-2-ol and 3-hexen-1-ol were obtained with selectivities comparable to those of the batch industrial processes, retaining >99% of the starting catalyst activity for long-term time-on-stream with no need of reactivation treatments. Therefore, the present system couples the inherent advantages of flow chemistry with an excellent efficiency in the absence of toxic contaminants, thus representing a significant contribution to the development of greener industrial manufacture processes [119]. The performance and stability of the catalyst is attributed to the strategic combination of non-coordinating and chemically inert borate functional groups in the polymer with the rigid, homogeneous macroporous structure of the monolith. Not least, the catalyst was obtained through a simple design and environmentally friendly method, which adds further benefits to the overall procedure.

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Appendix A. Supplementary material

Supplementary data associated with this article can be found, in the online version, at http://dx.doi.org/10.1016/j.jcat.2013.11.027.

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