

Unconventional Pd@sulfonated silica monoliths catalysts for selective partial hydrogenation reactions under continuous flow

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Abstract: Doubly functionalized, hierarchical porosity silica monoliths were synthesized by post-grafting of sulfonic groups and *in-situ* growth of Pd nanoparticles in the order. PdNP of 3.1 nm size located in the mesopores of the material showed to be evenly distributed within 4.6% wt Pd monoliths. The system was explored in the continuous flow, catalytic partial hydrogenation reaction of 3-halogenonitrobenzenes and 3-hexyn-1-ol in the liquid phase, showing remarkable conversion, selectivity and resistance under very mild conditions

Introduction

Continuous flow fine chemical synthesis by mean of supported heterogeneous catalysts is receiving increasing interest in large scale applications, due to the considerable safety, environmental and economic benefits compared to conventional batch operations.^[1] However, the need to overcome the common drawbacks associated with the mesoporous catalysts usually employed to this purpose (including mass transfer limitations, pore clogging, support degradation, active sites accessibility and deactivation, lack of reproducibility) requires a constant effort to develop innovative materials with improved properties.^[2]

Unconventional monoliths^[3] featuring an isotropic, hierarchically porous structure of interconnected flow-through macropores (1 - 30 µm) and diffusive mesopores (6 - 20 nm)^[4] have shown a unique hydrodynamic behavior in the liquid-phase, which is able to address the need of both efficient processing (within small pores) and effective mass transport (by macropores).^[5] Monolithic reactors may also circumvent most problems typical of packed-bed systems, such as pressure drop, low contacting efficiency, broad distribution of residence times. formation of hot-spots, which result in uncontrolled fluid dynamics, hence in low catalyst activity and selectivity.^[6] Polymeric materials were the first to demonstrate the benefits of monolithic supports in the continuous flow, catalytic production of fine-chemicals.^[7] However, polymeric monoliths may be affected by a number of limitations in relation to thermal, mechanical and chemical stability, shrinking phenomena,

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Supporting information for this article can be found under http://dx.doi.org/10.1002/cctc.xxxx volume and porosity changes with swelling, which may result in non-uniform permeability, variation of residence times, back pressure evolution at high flow rates.^[8] In order to avoid these problems, different types of inorganic monoliths have been synthesized featuring better resistance and rigidity.^[9] However, despite the above favorable features, use of hierarchically porous monoliths in catalysis has been scarcely investigated so far. One reason for this is that specific, sometimes troublesome, functionalization of the monolithic support is required for use in catalysis.^[10] Indeed, few inorganic monoliths with grafted functionalities have been described, either based on immobilized noble metal nanoparticles (MNP) for metal-type catalysis (Pd@TiO₂,^[11] Pd@SiO₂,^[12] Ag@SiO₂,^[13]), or acidic/basic functionalities (-SO₃H, -NH₂@SiO₂,^[14] zirconium phosphate^[15]) for organic-type catalysis.

Silica and titania monoliths featured by a hierarchical macroand mesoporosity have proven their highly efficient mass transport properties due to the very good permeability, [5] which have led to successful catalytic application under continuous flow,^[14,15] particularly for selective hydrogenations. ^[11,12] The hydrogenation of cyclohexene, cyclooctadiene and 3-hexyn-1-ol have been performed on such monoliths after immobilization of PdNP through classical impregnation methods.^[11,12a] The catalytic performance of these monoliths have been compared as a single piece or packed-bed (ground monolith 60 - 120 μ m) in continuous flow and in batch arrangements. The better access to the PdNP active sites was clearly demonstrated for the monolith in one piece in comparison to packed-bed and batch reactors, for instance in the hydrogenation of cyclohexene, resulting in TOF values of 1673, 1131 and 932 h⁻¹, and spacetime-yields of 4.02, 0.95 and 0.01 kg L⁻¹ h⁻¹, respectively.^[11] Much lower activity values were observed under continuous flow using PdNP onto conventional mesoporous supports. In the partial hydrogenation reaction of 3-hexyn-1-ol, selectivity using the monolithic SiO₂ reactor was higher both than that of conventional mesoporous silica under continuous flow conditions and the corresponding batch catalyst.^[12a] Irrespective of the support material, the monolithic catalysts could be used for more than 70 hours continuous stream with no significant deactivation and very low pressure drops. Similar favorable comparisons with respect to the corresponding batch and mesoporous catalysts were observed for metal-free transesterification reaction of triacetine using a sulfonated silica monolith.^[14b] All the above demonstrate the advantages in terms of mass transport and reactivity of these kinds of monoliths prepared by spinodal decomposition with respect of conventional

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Scheme 1. Synthetic procedure for Pd-functionalized, sulfonated silica monoliths.



Figure 1. ESEM image (left) and line (red) EDS maps of an equatorial section of Pd@MonoSil-ArSO₃. From the top: Si (K α 1), S (K α 1) Pd (L α 1), (20 keV, 100 points, 43 magnifications).

systems. Since sulfonic resins are known to enable the easy incorporation of metal ions by ion exchange and to stabilize metal particles of small size for use in catalysis through electrostatic stabilization,^[16] we decided to explore the same approach to the immobilization of Pd particles onto hierarchically porous silica monolith, and to examine the influence of these functions on selective hydrogenation reactions.

Herein, we report for the first time the dual functionalization of silica monoliths synthesized by a combination of sol-gel process and spinodal decomposition and featuring bimodal hierarchical porosity (MonoSil, macropore size 5 µm, skeleton thickness of 3 µm, mesopore size 6.6 nm) with both sulfonic groups and supported PdNP, and the engineering of the resulting material into continuous flow, catalytic hydrogenation mesoreactors.^[17] The performance of the catalyst was evaluated in highly significant reactions for the process industry, i.e. the selective, partial hydrogenation of halogeno-nitroarenes and alkynes, particularly 1-chloro-3-nitrobenzene and 3-hexyn-1-ol. The stereo- and chemo-selective hydrogenation of alkynes in the presence of other functional groups is of fundamental importance in the manufacture of several food additives, flavors and fragrances.^[18] Partial hydrogenation reactions are also crucial in the polymerization industry to achieve the complete elimination of alkynes and dienes from alkene feedstocks.^[19] The catalytic hydrogenation of halogeno-substituted nitroarenes to the corresponding amines is a reaction of much practical interest in the polymer and pharmaceutical sectors.^[20]

Results and Discussion

Synthesis and characterization of the catalysts

Hierarchical macro- / mesoporous silica monoliths were first synthesized using the combination of sol-gel process and spinodal decomposition accordingly to our previous works.^[5,12a] The resulting monoliths (MonoSil) were then sulfonated by grafting of 2-(4-phenylsulfonic)ethyl silane (MonoSil-ArSO₃) and 1,3-propylsulfonic (MonoSil-PrSO₃) groups. A sketch of the synthetic procedure is reported in Scheme 1 for MonoSil-ArSO₃. Due to the harmful properties of the pure silylation reagent 2-(4-chlorosulfonylphenyl) ethyltrimethoxy silane (CSPTMS), MonoSil-ArSO₃ was obtained using an alternative method to the literature reported flow protocol.^[14b]

Thus, the one-pot, batch treatment of MonoSil with a CSPTMS solution in refluxing toluene, followed by hydrolysis of the chlorosulfonyl group, afforded MonoSil-ArSO3 monolith showing features analogous to those of the previously reported material. ICP-OES analysis indicated the bulk sulfur content to be 3.0% wt (corresponding to 0.93 mmol g⁻¹, 1.07 molecule nm⁻², 0.28 mmol mL⁻¹), in line with the literature value (0.95 mmol g⁻¹).^[14b] FT-IR, FT-Raman (reported in the Supporting Information, Figure S8) and TGA (Figure S9) experiments showed all grafted sulfur was in the -SO₃H form. The FT-Raman spectrum of MonoSil-ArSO3 closely resembles that of the model compound 4-toluenesulfonic acid.^[21] In particular, the bands at 1126 and 1176 cm⁻¹ can be attributed to modes involving the -SO3 group.^[22] TGA analysis showed a weight loss (15.9 %) between 410 and 800°C, due to the thermal decomposition of the sulfonic acid group $-(CH_2)_2$ -Ph-SO₃H (desorption peak at 574°C),^[23] whose sulfur loading estimate (0.86 mmol g⁻¹) is consistent with the value obtained from ICP-OES. ESEM analysis (Figure 1) showed the macroscopic structure of the silica monolith was not altered by sulfonation, while EDS line maps, both transversal and longitudinal, demonstrated the sulfonic groups to be evenly distributed within the material. EDS transversal line maps of an equatorial section of Pd@MonoSil-ArSO3 monolith (vide infra), in which silica and sulfur emissions are reported for comparison, are shown in Figure 1. Point-to-point EDS analyses recorded at different monolith depth confirmed this result, while providing sulfur content values comparable to that of ICP-OES within the experimental errors. The mesoporosity of MonoSil-ArSO3 was

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analyzed by nitrogen sorption / desorption isotherms at 77 K (shown in Figure S7). Representative data are reported in Table 1. Compared to the native MonoSil, the phenylsulfonic derivative showed a decrease of surface area (322 vs. 521 m² g^{-1}), pore volume (0.64 vs. 1.07 cm³ g^{-1}) and pore diameter (6.0 vs. 6.6 nm), in accordance with what previously reported and expected for the grafting of molecules inside silica mesopores.^[23b, 24] The covalent functionalization of MonoSil was ascertained by ^{13}C CP and ^{29}Si MAS NMR spectroscopy, after grinding of the sample. The ^{13}C CP-MAS NMR spectrum of MonoSil-ArSO₃ (Supporting Information, Figure S10) showed signals at 13.4 and 29.2 ppm corresponding to methylene CH₂Si and CH₂Ph carbons, respectively. Signals at 128.3, 141.5 and 151.9 ppm are attributed to aromatic CH, C-CH₂ and C-SO₃ nuclei, respectively.^[23b,25] The ²⁹Si MAS NMR spectrum was dominated by a broad resonance centered around -108 ppm, attributable to the overlap of peaks Q4 [(SiO)₄Si] and Q3 [(SiO)₃SiOH] condensed silica network (expected at -110 and -100 ppm, respectively), plus a weak signal at ca. -60 ppm due to functionalized silica species T2 [(SiO)₂Si(OH)-C]^[14b,26] The concentration of Lewis (LAS) and Brønsted (BAS) solid acid sites onto MonoSil-ArSO3 was further investigated by pyridine desorption FT-IR spectroscopy at various temperatures (i.e. rt, 50, 100, 150, 200 and 250°C) (full set of spectra in Figure S11).^[27] Integration of peaks at 1546 and 1446 cm^{-1,[28]} revealed a high concentration of Brønsted acid sites (0.149 mmol g⁻¹ @ 150 °C)^[29] and a negligible quantity of Lewis acid sites (0.002 mmol g⁻¹ @ 150 °C), respectively (Table 2). The bare silica monolith MonoSil showed the almost complete absence of Brønsted and Lewis acidity.

Table 1. Mesoporosity features of monolithic materials. ^[a]								
Material	S [m² g⁻¹]	V [cm ³ g ⁻¹]	D [nm]					
MonoSil	521	1.07	6.6					
MonoSil-ArSO3 ^[b]	322	0.64	6.0					
Pd@MonoSil-ArSO3 ^[C]	322	0.62	6.1					
[a] BET surface area (S), porous volume (V), pore diameter (D). [b] 0.93 meq g^{-1} SO ₃ sites. [c] 4.6 wt % Pd.								

Table 2. Lewis (LAS) and Brønsted (BAS) acid sites concentration on silica monoliths. ^[a]								
Material	LAS [µmol g ⁻¹]	BAS [µmol g ⁻¹]	T _{des} ^[b] [°C]					
MonoSil	0	0	100					
	0	0	150					
MonoSil-ArSO ₃	80	229	100					
	2	149	150					
[a] LAS 1446 cm ⁻¹ , BAS 1546 cm ⁻¹ . [b] Desorption temperature.								



Figure 2. Optical images of cladded a) MonoSil-ArSO_3 and b) Pd@MonoSil-ArSO_3 monoliths.

The propylsulfonic monolithic derivative MonoSil-PrSO₃ was prepared using a two-step, grafting-oxidation procedure using mercaptopropyltrimethoxy silane as anchoring agent and H₂O₂ as oxidant. However, besides a lower sulfur content compared to MonoSil-ArSO₃, ICP-OES, TGA (TGA and DTG in Supporting Information, Figure S3), FT-IR and NMR analyses indicated the partial conversion of -SH groups to -SO₃H and a significant loss of sulfur upon oxidation,^[30] in line with some literature findings.^[31] Therefore, we decided not to investigate further the use of MonoSil-PrSO₃ in catalysis.

After sulfonation of the silica monolith, Pd nanoparticles were grown in-situ onto MonoSil-ArSO₃ by a simple two-steps, onepot flow procedure (Scheme 1). Thus, after allowing a water solution of Pd(NO₃)₂ to flow cyclically through a Teflon-cladded monolith, the Pd(II)-supported material was reduced under concurrent flows of 0.5 mL min⁻¹ methanol and 2 mL min⁻¹ H₂, 1 bar pressure and room temperature. Experimental details are provided in the Supporting Information. The reduction of the metal was evidenced by a color change of the monolith from brownish to black (Figure 2). Selection of palladium nitrate was motivated by the combination of several key factors: i) the need for a cationic palladium precursor, owing to the ion-exchange strategy chosen for the first step of synthesis; ii) high solubility and dissociation in environmentally friendly water solvent; iii) higher reduction potential of "naked" Pd2+ ions,[32] which allows for the quantitative metal reduction by H₂ under milder conditions compared to other precursors, e.g. $\left[Pd(NH_3)_4\right]^{2+}$ or $Pd(CH_3CO_2)_2$ which requires high temperatures or NaBH₄ treatment;^[33,34] iv) lower cost and better stability compared to [Pd(CH₃CN)₄]^{2+.[35]} An analogous ion-exchange / H2 reduction flow procedure, devoid of harsh conditions (1 bar, rt), toxic reagents or elaborate apparatuses, was previously adopted by us for the immobilization of PdNP onto organic-type monolithic resins, taking advantage of the palladium nitrate precursor.^[36]

The as-prepared Pd@MonoSil-ArSO₃ monolith could be directly used in continuous flow catalytic hydrogenation reactions (*vide infra*) without disconnecting from the flow equipment nor any further treatment, or dried under a stream of N₂ before being characterized in the solid state. ICP-OES showed the bulk Pd loading to be 4.6% wt (0.43 mmol g⁻¹), while EDS linear maps, recorded both on radial and longitudinal sections of the monolith, proved the metal to be evenly distributed within the support (Figure 1). These results were possible thanks to the ion-exchange properties of the sulfonated monolith (Scheme 1). Indeed, ICP-OES analyses indicated that all sulfonic sites were replaced with (easily reducible)^[37] Pd²⁺ ions by ion-exchange (molar ratio S / Pd ca. 2). The

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incorporation of Pd did not lead to any significant modification of the macroporous silica skeleton as shown by ESEM analysis (Figure 3, left). Compared to the metal-free monolith (Table 1), nitrogen sorption isotherms showed a slight decrease of the mesoporous volume (0.62 vs. 0.64 cm³ g⁻¹) and a slight increase of mesopore diameter (6.1 vs. 6.0 nm) (Figure 3, right), thus indicating that the PdNP are located within the silica mesopores. Analogous findings were previously observed for Pd onto hierarchically porous titania and silica monoliths^[11,12a] and titanate nanotubes.^[38] Indeed, TEM analysis showed Pd@MonoSil-ArSO₃ to contain spheroidal PdNP of average diameter 3.1 \pm 1.0 nm, with no particles larger than 6.3 nm detected. A typical TEM image and the corresponding PdNP size distribution are reported in Figure 4. The XRD data were in



Figure 3. Pd@MonoSil-ArSO₃ monolith. Left: ESEM image (secondary electrons, 27 keV, 1600 magnifications). Right: BJH mesopore size distribution.



Figure 4. Left: TEM image of Pd@MonoSil-ArSO₃. Right: PdNP size histogram. Statistical nanoparticle size distribution analysis was carried out on 300-400 particles at 120 keV.



Figure 5. XPS spectrum of Pd@MonoSil-ArSO3 in the Pd 3d region.

line with those of TEM, within the experimental errors. A surface/bulk palladium atoms ratio of 36% could be estimated from TEM data [39] XPS measurements were carried out to analyze the oxidation state of the supported Pd particles. Figure 5 shows the XPS spectrum in the Pd 3d region where the usual palladium doublet is observed. The Pd 3d peaks were deconvoluted into two oxidation states, namely metallic Pd(0) at lower binding energy (Pd 3d_{5/2} 335.0 ± 0.1 eV) and Pd(II) at higher BE (Pd 3d_{5/2} 337.1 ± 0.1 eV) with the latest likely due to PdO.^[40] No other palladium species were detected. The calculated abundance of the two species was 86.7% for Pd(0) and 13.3% for Pd(II). As it was previously reported,^[41] the presence of PdO can be safely attributed to a layer covering the core of metallic palladium particles due to sample manipulation in air prior of measurements, since the percentage of Pd(0) was increased up to 91.1% after sputtering with Ar, a procedure that removes the most superficial atoms of the nanoparticle.[42] Pyridine desorption experiments showed Pd@MonoSil-ArSO₃ to have a higher density of Lewis acid sites (0.017 mmol g⁻¹ @ 150 °C) and a lower density of Brønsted sites (0.037 mmol g⁻¹ @ 150 °C), compared to the metal free MonoSil-ArSO₃ monolith. These findings are in line with those previously reported for other solid-supported Pd⁰ materials, and attributed to the residual Lewis acid contribution of PdNP^[43] and to the partial recovery of sulfonic acid sites after H₂ reduction of palladium under mild conditions, [44] respectively. Quantitative restoration of acidic sites may require rinsing with strong mineral acid solution, in that case.^[45]

The immobilization of PdNP onto inorganic oxide monoliths (SiO₂, TiO₂) has been previously described in the literature through impregnation / (calcination) reduction procedures, either using $Pd(NH_3)_4(NO_3)_2$, $Pd(NO_3)_2$ or Na_2PdCl_4 precursors. Particularly, Pd particles of 6.5 ± 1.0 nm size were obtained by impregnation of unsulfonated silica monoliths usina Pd(NH₃)₄(NO₃)₂, followed by treatment under harsh, batch conditions (280 °C).^[12a] The amount of Pd incorporated showed to be strongly pH-dependent in that case, with a 1.3% wt maximum loading achieved at pH 10. Reaction of the silica surface with a strong base was required to increase the negative charge of the silica support, that can be justified by the point of zero charge of silica below pH 7.5.^[46] PdNP onto unfunctionalized SiO₂ monoliths were also obtained by incipient wetness impregnation using Na_2PdCl_4 and 340 °C H₂ reduction, resulting in Pd particles of 2 -10 nm size.^[12b] To further ascertain the efficacy of the synthetic protocol herein described, we performed a countercheck immobilization experiment using the unsulfonated MonoSil monolith and the same experimental conditions adopted for the preparation of Pd@MonoSil-ArSO3, i.e. Pd nitrate precursor, room temperature, H₂ 1 bar flow reduction. This protocol resulted in ca. 0.3% wt Pd loading and 4.7 ± 2.1 nm PdNP (see Supporting Information). This clearly indicates that the synthetic strategy devised in the present work for the immobilization of PdNP onto silica monolith, involving ion-exchange of sulfonated materials, provides multiple benefits over previously reported methods: i) milder reactions conditions and more friendly procedure, ii) easier access to high Pd loading, iii) better control and higher dispersion of PdNP since, irrespective of the precursor, size was twice smaller than in silica monoliths without sulfonation of the support, whereas the monoliths feature analogous textural properties (mesopore size, surface area, mesoporous volume).

The above findings can be attributed to the atomic level dispersion of the Pd ions within MonoSil-ArSO₃, as a consequence

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Scheme 2. Common reaction pathways for the hydrogenation reactions of 1-chloro-3-nitrobenzene (1) and 3-hexyn-1-ol (2).



Figure 6. Continuous flow hydrogenation of 1 to 1a over Pd@MonoSil-ArSO₃ catalyst (4.6% wt Pd, rt, methanol 0.01 M, reactor volume 141 µL). Left: conversion and selectivity as a function of residence time τ and solution flow rate under fixed H₂:1 molar ratio 4.3. Centre: conversion and selectivity as a function of H₂:1 molar ratio and H₂ flow rate under fixed residence time τ as (solution flow rate 0.30 mL min⁻¹). Right: selectivity / conversion diagram at: • fixed H₂:1 ratio = 4.3 and residence time 21 - 42 s, O fixed residence time 28 s and H₂:1 ratio rang 2.8 - 7.3 (H₂ flow rate 0.2 - 0.5 mL min⁻¹).

of the ion-exchange procedure,^[47] and to the smooth reduction conditions available, thanks to the use of $Pd(NO_3)_2$ precursor. The present synthetic approach has been widely used for the immobilization of metals onto organic polymers,^[16] and it was successfully applied here for the first time to the incorporation of MNP onto inorganic monoliths.

Continuous flow catalytic reactions

Owing to the peculiar hydrodynamic properties of the hierarchically porous monolithic support and to the high Pd loading, Pd@MonoSil-ArSO3 was specifically designed for application to continuous flow processes requiring an efficient interaction, but a short contact time, with a dispersed metal active phase to achieve the best selectivity at the highest conversions.^[48] Suitable examples to this regard are partial hydrogenation reactions.^[49] We thus investigated the catalytic performance of Pd@MonoSil-ArSO3 in the selective hydrogenation of 1-chloro-3-nitrobenzene and 3hexyn-1-ol under continuous flow conditions, as test reactions (Scheme 2). Catalytic experiments were carried out by connecting the cladded monolith to a home-made reactor system allowing for the controlled, concurrent flows of substrate solution and H₂ gas (sketch of reactor equipment in Supporting Information, Scheme S1). The reaction start time was taken as the attainment of steady state conditions, ca. 1h. Hydrogen gas was released at

atmospheric pressure at the outlet of the reactor. Reactions were typically monitored for conversion, selectivity and metal leaching over 8 h continuous time-on-stream, followed by overnight switchoffs and restart the day after under the same conditions. Benchmark reaction conditions were room temperature and methanol solvent.

Both processes were investigated under a wide range of H_2 and substrate solution flows and the combinations thereof. As expected for similar systems, conversion and selectivity showed to be dependent from the reactants flow rates. As a common trend, under a fixed solution flow rate (i.e. for the same residence time τ), an increase of the H_2 flow (i.e. of the H_2 :substrate molar ratio) resulted in higher conversions (up to 100 %) and in lower selectivities, Under a fixed H_2 :substrate molar ratio, a decrease of the solution flow rate (i.e. an increase of residence time τ) resulted in higher conversions and in a selectivity decrease.

Conversion of 1-chloro-3-nitrobenzene (1) to 3chloroaniline (1a): The hydrogenation of 1 was examined in the H_2 flow range 0.2 - 0.5 mL min⁻¹ (H_2 :1 molar ratio = 2.8 - 7.3) and in the solution flow range 0.4 - 0.2 mL min⁻¹ (τ = 21 - 42 s). Under these conditions, the hydrogen pressure measured at the reactor inlet was 1.1 - 1.2 bar, hence the pressure drop generated by monolithic reactor was lower than 0.2 bar in any case. The H₂ pressure at the reactor inlet was not significantly affected by moderate changes in the H₂ flow rate, that can be attributed to the scarce flow resistance of the monolithic support owing the open-cell macroporous structure. Figure 6 left shows the conversion and selectivity change upon variation of the residence time under fixed H₂:substrate ratio 4.3. The conversion increased from 79.5% to 95.9% and the selectivity to 1a decreased from 82.6% to 70.1%, on passing from 0.4 to 0.2 mL min⁻¹ solution flow. A conversion enhancement from 88.3% to 98.0% and a selectivity drop from 78.4% to 64.1% was observed on passing from 0.2 to 0.5 mL min⁻¹ H₂ flow at fixed 28 s residence time (Figure 6 center). A reproducible selectivity / conversion diagram could be obtained on these bases, as reported in Figure 6 right. A more complete picture of 1a yield as a function of τ and H₂ : substrate ratio is shown in the diagram of Figure 7. The reaction conditions (τ 28 s, H₂:1 ratio = 4.3) resulting in the best compromise results between conversion (95%) and selectivity (76%), corresponding to a 1a yield of 72%, are reported in Table 3, in which productivities are express both as mol_{prod} g_{Pd}⁻¹ h⁻¹ and space-time-yield (STY, kg_{prod} L_{reactor}⁻¹ h⁻¹ ¹).^[50] Irrespective of the reaction conditions, the only by-product

Table 3. Selected data for continuous flow hydrogenation reactions by Pd@MonoSil-ArSO3 monolithic catalyst [a]									
	Reaction conditions								
Substrate	Solution		H ₂		11. (1.	Conv. ^[e]	Selectivity ^[f]	Productivity ^[g,h]	STY ^[h]
oubside	Flow rate [mL min ⁻¹]	τ ^[b] [S]	Flow rate [mL min ⁻¹]	Pressure ^[c] [bar]	H ₂ / sub. Ratio ^[d]	[%]	[%]	$[mol g_{Pd}^{-1} h^{-1}]$	[kg L ⁻¹ h ⁻¹]
1-chloro-3-nitrobenzene (1)[1]	0.30	28	0.30	1.07	4.3	95 ± 2	76 ± 1 (1a)	0.07 (1a)	0.12 (1a)
3-hexyn-1-ol (2) ^[]	0.48	28	1.25	1.15	1.2	94 ± 1	91 ± 1 (2a+2b)	0.80 (2a)	1.09 (2a+2b)
							94 ± 1 (2a)		

[a] Best compromise results in terms of conversion and selectivity to the partial hydrogenation product indicated. Reaction conditions: methanol 0.1 M, room temperature, 4.6% wt Pd. Start time attainment of steady state conditions 1h. [b] Residence time (τ). [c] Pressure at the reactor inlet. [d] Hydrogen to substrate molar ratio at the reactor inlet. [e] Conversion average value over 8 h time-on-stream. [f] Selectivity to the product indicated in brackets. Average value over 8 h time-on-stream. Selectivity **2a+2b** = (**2a+2b**)/(**2a+2b+2c+2d**). Selectivity to *cis* isomer **2a** = **2a**/(**2a+2b**). [g] Calculated on bulk Pd content. [h] Calculated on the products indicated. [i] Solution 0.01 M, reactor volume 141 μ L. [i] Reactor volume 226 μ L.



Figure 7. Contour plot of **1a** yield in the hydrogenation of **1** by Pd@MonoSilArSO₃ catalyst under continuous flow conditions (4.6% wt Pd, rt, methanol 0.01 M, reactor volume 141 μ L). Residence time (τ) range 21 - 42 s, H₂ : **1** molar ratio range 2.8 - 7.3



Figure 8. Conversion and selectivity vs. time on stream in the continuous flow hydrogenation of 1 over Pd@MonoSil-ArSO₃ catalyst (4.6% wt Pd, rt, methanol 0.01 M, reactor volume 141 μ L, solution 0.30 mL min⁻¹, H₂ 0.30 mL min⁻¹). Start time: attainment of steady state conditions, ca. 1 h. Filled symbols, conversion; empty symbols, selectivity to 1a.

observed was aniline (1c). No traces of nitrobenzene (1b), benzene (1d) or condensation products (e.g. 3,3'-dichlorohydrazobenzene) were detected by GC-Ms analysis. The catalyst showed a minor activity decay over 7 h time-on-stream (ca. 4%), whereas conversion stabilized with $\pm 2\%$ fluctuation for longer reaction periods (Figure 8). Selectivity was pretty constant with a mean 76 $\pm 1\%$ value over 8 h time-on-stream. Productivities of 0.07 mol_{1a} g_{Pd}⁻¹ h⁻¹ and 0.12 kg_{1a} L⁻¹ h⁻¹ STY could be calculated on these bases.^[51] The catalyst could be reused with no significant efficiency decay, provided it was stored under nitrogen or hydrogen overnight. Conversions and selectivities values were within the specified ranges after 3 days catalyst reuse. In no case the amount of palladium leached in solution was above the detection limit of ICP-OES, nor catalytic activity was shown by the recovered reaction solution, thus ruling out the loss of active species during catalysis.^[52] At the same time, the sulfur content in the recovered catalyst was the same as in the starting material (ICP-OES), thus indicating the stability of the grafted phenylsulfonic groups under the conditions of catalysis.^[53] The dimension of PdNP did not change significantly after use of Pd@MonoSil-ArSO₃ in catalytic experiments (for the statistical distribution and data, see Figure S13), which confirms the effective stabilization of metal particles by the grafted sulfonic groups.^[37]

3-Chloroaniline is an intermediate for the manufacture of agricultural chemicals, pigments, pharmaceuticals and polymers.^[54] Current production methods base on the batch hydrogenation of 1 by noble metal catalysts. Several monometallic heterogeneous catalysts have been described for the lab-scale batch hydrogenation of 1 to 1a with selectivity > 78% and conversion > 95%, however with catalyst deactivation as common drawback. Representative data are reported in Supporting Information, Table S2. Activity decay of chloronitrobenzene hydrogenation catalysts was previously attributed to catalyst leaching,^[55] poisoning^[56] or MNP aggregation.^[57] Deposition of carbonaceous materials was also observed at medium temperatures and low $H_2{:}substrate\ ratios.^{[\,58\,]}$ Few examples have been reported in the liquid phase for the continuous flow hydrogenation reaction of 1 by supported metal catalysts. A reason for this may reside in the fact that, among the chloro-nitrobenzene isomers, the meta one is the most recalcitrant to (selective) hydrogenation.[59] The continuous hydrogenation of 1 to 1a, in 99% conversion and 98% selectivity, was described using 1.9% $Au@\gamma\text{-}Al_2O_3$ packed catalysts in toluene at 80 °C, 10 bar H₂ pressure and very high H₂:1 ratio (107).^[60] However, the catalyst deactivated rapidly, since ca. 20% of its starting activity was lost after 2 h continuous stream.

We performed a series of studies aimed at comparing the performance of: i) the bimodal macro/mesoporous monolithic catalyst *versus* conventional mesoporous catalysts, and ii) continuous flow *versus* batch setups. To this purpose, the continuous flow hydrogenation of **1** was carried out using commercial 5% wt Pd onto mesoporous silica under reaction

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Table 4. Continuous flow hydrogenation of 1-chloro-3-nitrobenzene (1) by supported Pd catalysts. ^[a]								
Entry	Catalyst	Conv. [%]	Sel. 1a [%]	Productivity 1a ^[b] [mol $g_{Pd}^{-1} h^{-1}$]				
1	4.6% Pd@MonoSil-ArSO3	95 ^[c]	76	0.07				
2	5% Pd@SiO ₂	93 ^[d]	8	0				
3	5% Pd@C	99 ^[e, f]	0	0				
4	4.6% Pd@MonoSil_ArSO. ^[9]	98	0	0				

[a] Reaction conditions: solution 0.01 M, room temperature, $\tau 28 \text{ s}$, $H_2:1$ ratio = 4.3, weight amount of catalyst corresponding to 0.022 mmol Pd. Solution flow rate 0.3 mL min⁻¹, H_2 flow rate 0.3 mL min⁻¹. [b] Calculated on bulk Pd content. [c] Pressure drop 0.07 bar. [d] Pressure drop 0.57 bar. [e] $H_2:1$ ratio = 7.4 [f] Pressure drop 0.84 bar. [g] Batch conditions, 1 bar H_2 , 60-120 μ m sieved fraction, 500 rpm.



Figure 9. Continuous flow hydrogenation of 1 to 1a over 4.6% Pd@MonoSil-ArSO₃ (•) and 5% Pd@SiO₂ (**O**) catalyst (0.022 mmol Pd, rt, methanol 0.01 M). Left: selectivity / conversion diagram at fixed residence time 28 s and H₂:1 ratio range 2.1 - 7.3 (H₂ flow rate 0.1 - 0.5 mL min⁻¹). Right: pressure drops observed as a function of the H₂ linear flow rate (τ 28 s).

conditions analogous to those adopted for Pd@MonoSil-ArSO3. [30] Using the conditions of optimized yield found for Pd@MonoSil-ArSO₃ (τ 28 s, H₂:1 ratio = 4.3), the packed Pd@SiO₂ catalyst showed a lower substrate conversion (93%) and only 8% selectivity to 1a, since the major product observed was the over-hydrogenated aniline 1c, while the pressure drop generated was one order magnitude higher compared to the monolithic catalysts (0.57 vs. 0.07 bar) (Table 4, entry 2). The reaction using Pd@SiO₂ was investigated under a range of reactants flow rates and selectivity / conversion diagrams were obtained, as e.g. the one reported in Figure 9, left for fixed residence time 28 s and H₂:1 ratio 2.1 - 7.3 (H₂ flow 0.1 - 0.5 mL min⁻¹). The superior performance of the monolithic catalyst was observed in any case. The back pressure generated to the mesoporous catalyst was higher than that of Pd@MonoSil-ArSO₃ irrespective of the flow rates. Figure 9 right shows the pressure drop divided by the length of the reactor as a function of the H₂ linear flow rate, from which the Darcy permeability coefficient of the porous materials can be calculated $^{\left[5b\right] }$ It is worth also noticing that, compared to the conventional mesoporous support, the monolithic reactor shows much shorter equilibration times: slight increases of back pressure with timeon-stream were observed in the former case due to increasingly close packing of the material. The above findings can be attributed to the specific texture of the hierarchically porous monolith, which ensures efficient mass transport and fast desorption of the intermediate hydrogenation product from the metal site, thus enhancing selectivity, in contrast to purely mesoporous materials.^[11,12a] Similar results were obtained using commercial 5% Pd onto carbon (Table 4, entry 3). In line with previous findings,^[10a,11,14b] the monolithic Pd@MonoSil-ArSO₃ catalyst showed to be more efficient under flow rather than under batch setup (crushed 60–120 μ m fraction), the latter providing similar conversion (98%) but complete overhydrogenation to **1c** under analogous conditions (Table 4, entry 4). High stirring rates were adopted to ensure minimization of mass transfer limitations.^[14b]

Conversion of 3-hexyn-1-ol (2) to cis-3-hexen-1-ol (2a): The hydrogenation of 2 by Pd@MonoSil-ArSO₃ was carried out analogously to that of 1 using similar ranges of H₂ and substrate solution flows. The changes in conversion and selectivity observed at different residence time, under a fixed H₂:substrate ratio of 1.2, are graphically reported in Figure 10 left, while the corresponding selectivity / conversion diagram is shown in Figure 10 right. The best compromise between conversion and selectivity, resulting in the highest yield of the semihydrogenation alkene product 2a, was obtained for 0.48 (τ 28 s) and 1.25 mL min⁻¹ (H₂ : 2 ratio = 1.2) solution and H₂ flows, respectively. Under these conditions, 3-hexen-1-ol (2a+2b) was obtained with a 91 ± 1% selectivity, whose 94 ± 1% was the cis isomer 2a, at 94 ± 1% conversion over 8h time-on-stream (Table 3). Neither significant catalyst efficiency decay nor Pd leaching in solution was observed over that time, as well as upon 3 days catalyst reuse. For comparative purposes, the continuous flow hydrogenation of 2 was also carried out using commercial 5% Pd@SiO₂ mesoporous silica catalyst under analogous reaction conditions, showing much lower optimal 2a yield (54% selectivity 84% conversion, Table 5, entry 2) and much higher H₂ pressure drop (2.06 versus 0.15 bar). Compared to Pd@MonoSil-ArSO₃, yields of 2a were lower and pressure drops were higher in the entire range of flow rates examined. A complete selectivity / conversion diagram for 5% Pd@SiO₂ is reported in Supporting Information, Figure S19.



Figure 10. Continuous flow hydrogenation of **2** over Pd@MonoSil-ArSO₃ catalyst (4.6% wt Pd, rt, methanol 0.1 M, reactor volume 226 μ L). Left: conversion and selectivity to **2a+2b** as a function of residence time τ and solution flow rate under fixed H₂:**2** molar ratio 1.2. Right: selectivity/conversion diagram at fixed H₂:**2** ratio = 1.2 and residence time 26 - 30 s.

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Table 5. Continuous flow catalytic hydrogenations of 3-hexyn-1-ol (2). ^[a]								
F .(1)	Catalyst	Conversion [%]	Selectivity [%]		Yield 2a ^[d]	Productivity 2a	STY ^[e]	Def
Entry			ene ^[b]	Z/E ^[c]	[%]	$[mol g_{Pd}^{-1} h^{-1}]$	[kg L ⁻¹ h ⁻¹]	Ret.
1	4.6% Pd@MonoSil-ArSO ₃	94	91	94	80	0.8	1.09	This work
2	5% Pd@SiO ₂	85	54	70	32	0.3	0.52	This work
3	5% Pd@C	94	22	81	17	0.9	0.20	64
4	5% Pd(Pb)@CaCO ₃	99	64	62	39	0.2	0.16	65
5	1.2% Pd@Dowex-Li	75	80	89	53	2.3	0.82	66
6	1.2% Pd@SiO ₂	40	87	93	32	7.1	1.54	64
7	0.73% Pd@TiO ₂	84	80	85	57	19.2	0.23	64
8	0.50% Pd@TiNT	88	94	93	77	40.6	4.57	64
9	1.3% Pd@MonoSil	85	80	80	54	0.5	0.22	12a
10	0.2% Pd@TiO ₂ monolith	61	63	87	33	1.8	0.59	11
11	0.7% Pd@MonoBor	99	94	93	86	6.8	0.80	65
8 9 10 11	0.50% Pd@ IIN I 1.3% Pd@MonoSil 0.2% Pd@TiO ₂ monolith 0.7% Pd@MonoBor	88 85 61 99	94 80 63 94	93 80 87 93	77 54 33 86	40.6 0.5 1.8 6.8	4.57 0.22 0.59 0.80	64 ▼ 12a 11 65

[a] Best compromise results in terms of 2a yield, i.e. between conversion and selectivity. Reaction conditions: methanol solution, room temperature. [b] Selectivity to the alkene product 2a+2b = (2a+2b)/(2a+2b+2c+2d). [c] Selectivity to the *Z*-alkene product 2a = 2a/(2a+2b). [d] Yield of 2a is calculated as Conv. $Sel_{ene} \cdot Sel_{ZE} = 2a/(2+2a+2b+2c+2d)$, where 2 is the concentration at the reactor outlet. Data from GC analysis. [e] Calculated on the *ene* product 2a+2b.

Cis-3-hexen-1-ol (**2a**) is an important ingredient in the fragrance industry (leaf alcohol).^[61] It is currently manufactured from **2** in 400 t/y and ca. 96 % selectivity at 99 % conversion by a batch process using the Lindlar catalyst (5 % Pd on CaCO₃ doped with 2-3 % Pb)^[62] which, however, shows serious drawbacks in terms of recovery, deactivation, presence of toxic lead, need of excess of amine modifier.^[63]

In the recent years, a number of catalysts have been reported for the synthesis of 2a under continuous flow conditions (Table 5). These include packed-bed systems based onto commercial (Pd@C,^[64] Lindlar,^[65] entries 3, 4) and laboratory catalysts (Pd@ion-exchange resins,[66] Pd@SiO₂,TiO₂ mesoporous xerogels,^[64] Pd@titanate nanotubes,^[64] entries 5-8), as well as monolithic systems (Pd@MonoSil,^[12a] Pd@TiO2 monolith,^[11] Pd@MonoBor,^[65] entries 9-11). In terms of product yield, the Pd@MonoSil-ArSO3 system ranks just below the best catalyst so far reported for this reaction (Pd@MonoBor organic monolith, entry 11) and whose selectivity is the only one comparable to that of the industrial batch process. It must be underlined that Pd@MonoSil-ArSO3 was more efficient than the parent, unsulfonated Pd@MonoSil catalyst (entry 1 vs. 8). Particularly, while the selectivity was 91% at 94% conversion using Pd@MonoSil-ArSO₃ (80% 2a yield), selectivity was 80% at 85% conversion (yield 2a 54%) and 40% at 94% conversion (yield 2a 30%) using Pd@MonoSil.^[12a] Given the same textural properties the two catalysts, this finding can be ascribed to the combination of multiple factors: a) the smaller size of PdNP in the sulfonated monolith, since a positive effect of an higher percentage of surface atoms on the selectivity of 3-hexyn-1-ol hydrogenation by solid-supported Pd catalysts was highlighted in the past, ^[37,67,68] b) the "proton-acceleration" effect on the metal hydrogenation activity due to the Brønsted acid sites from the support, as invoked for other solid acid-supported MNP catalysts,^[69] c) a negative influence of the excess surface silanol groups on the metal sites in Pd@MonoSil, as previously suggested [12a] The Pd@MonoSil-ArSO3 catalyst performed better than Pd@MonoSil even in term of mass productivity (0.8 vs. 0.5 mol g_{Pd}^{-1} h⁻¹, entries 1, 9), that can be attributed to the smaller PdNP size. Noteworthy, Pd@MonoSil-ArSO3 was more productive than the analogous hierarchically porous silica and titania monolith catalysts in term of STY (1.09 vs. 0.22 and 0.59 kg L⁻¹ h⁻¹, entries 1, 9 and 10) that can be safely ascribed to higher Pd loading per unit reactor volume. The productivity of Pd@MonoSil-ArSO3 was somewhat lower than the best ever reported for the hydrogenation of 2, namely Pd@TiNT (entry 8), and that was attributed to the scarce flow resistance of the tubular titanate material, which allows for high substrate flow rates.[65] Overall, Pd@MonoSil-ArSO₃ provides a aood compromise between selectivity and productivity for the catalytic hydrogenation of 2 under continuous flow, with clear operational advantages over packed-bed reactors.

The above results point out to hydrogenation pathways involving a fast interaction of the substrate with easily available Pd sites onto the solid catalyst. As previously reported for comparable heterogeneous systems,^[64,65] the high substrate flow rates and the short residence times allowed by the monolithic catalyst may result in a fast interaction of the active sites with the intermediate semi-hydrogenation products, that quickly leave the metal after formation with no possibility to react further, thus to be beneficial in terms of both selectivity and productivity of partial hydrogenation. If the substrate would have a prolonged adsorption with the metal sites inside the pores, the intermediate formed cannot diffuse away fast enough and it is hydrogenated before leaving the catalyst, resulting in a lower selectivity at the same conversion level. In the case of the batch partial hydrogenation reaction of alkynes, a short contact time of the intermediate alkene has been invoked for the high selectivity observed by 3-D egg-shell Pd@TiS catalysts.[67]



Scheme 3. Continuous flow hydrogenations by Pd@MonoSil-ArsO₃ catalyst. Substrates investigated and main reaction products with labelling.

Table 6. Continuous flow hydrogenations by Pd@MonoSil-ArSO3 catalyst							
Entry	Substrate	Conv. ^[b] [%]	Selectivity ^[c] [%]	STY ^[d] [kg L ⁻¹ h ⁻¹]			
1	2-methyl-3-butyn-2-ol (3)	78 ± 2	56 ± 1 (3a)	0.70 (3a)			
2	2-butyn-1,4-diol (4) ^[e]	72 ± 2	91 ± 1 (4a+4b)	0.43 (4a)			
			> 99 (4a)				
3	1-fluoro-3-nitrobenzene (5) ^[f]	99 ± 1	> 99 (5a)	0.08 (5a)			
4	1-chloro-2-nitrobenze (6) ^[f]	90 ± 1	73 ± 1 (6a)	0.29 (6a)			
5	1,5-cyclooctadiene (7)	94 ± 1	87 ± 1 (7a) ^[9]	0.50 (7a)			
			85 ± 1 (7a) ^[h]				

[a] Best compromise results in terms of yield, i.e. between conversion and selectivity, to the partial hydrogenation product indicated. Reaction conditions: methanol 0.1 M, room temperature. H₂ pressure 1.09 - 1.18 bar. Start time attainment of steady state conditions 1h. [b] Conversion average value over 8 h time-on-stream. [c] Selectivity to the product indicated in brackets. Average value over 8 h time-on-stream. Selectivity **4a**+4b = mol (**4a**+4b)/(mol substrate converted). Selectivity to *cis* isomer **4a** = **4a**/(**4a**+4b). [d] Calculated on the product indicated. [e] Solution 0.025 M. [f] Solution 0.01 M. [g] Hydrogenation selectivity = **7a** / (**7a** + **7c**). [h] Overall selectivity = **7a** / (**7a** + **7b** + **7c**).

Catalyst and substrate scope. Having investigated in detail the catalytic performance of Pd@MonoSil-ArSO₃ in the liquid phase continuous flow partial hydrogenation reaction of probe substrates, including comparison with conventional systems, we examined the hydrogenation of other alkynes and nitro arene substrates of *industrial interest*, under a broad range of solution and H₂ flow rates and benchmark reaction conditions (Scheme 3). Best compromise results between conversion and selectivity are reported in Table 6, together with the corresponding STY values of the desired partial hydrogenation products. Complete experimental data and selectivity/conversion diagrams for all substrates investigated are reported in the Supporting Information (Table S3, Figures S20-S25).

2-Methyl-3-buten-2-ol (3a) is an important intermediate for the synthesis of vitamins (A, E) and perfumes, that is currently obtained via conventional Lindlar hydrogenation of 3, however with fast catalyst deactivation.^[70,71] Cis-2-buten-1,4-diol (4a) is used in the manufacture of antibiotics, vitamins A and B6, insecticides and pharmaceuticals. It is industrially produced from 4 in 5000 t/y using 0.5% Pd@Al₂O₃ batch catalysts, doped with Cd, Zn, Bi or Te, under elevated pressures / temperatures.^[72,73] Use of Pd@MonoSil-ArSO3 catalyst provided 3a in good yields with no conversion decay over 10 h continuous reaction (56% selectivity, 78% conversion), Table 6, entry 1). Better performance was observed in the reduction of 4, wherein the partial hydrogenation product 4a+4b was obtained in 91% selectivity, whose 99% the cis isomer 4a, at 72% conversion, under very mild conditions (Table 6, entry 2). Despite higher product purity has been reported on the lab scale for the continuous hydrogenation of 3 and 4 in the liquid phase using 1% Pd₂₅Zn₇₅@TiO₂ (capillary reactor)^[74] and 0.5% Pd@Al₂O₃ (honeycomb reactor)^[75] catalysts, respectively, it is worth noticing that STY for the pure 3a and 4a partial hydrogenation products was ca. one order magnitude higher using Pd@MonoSil-ArSO₃. This finding can be safely attributed to both the textural properties of the monolithic support, which allows for very fast reactants' flow rates at low back pressures, and to the high Pd content per unit reactor volume. Indeed, the hydrogenation of alkynes substrates over Pd@MonoSil-ArSO3 was carried out at remarkable weight hourly space velocities, ranging from 1.8 to 4.3 h^{-1} (WHSV = $g_{substrate} / g_{catalyst}^{-1} h^{-1}$). The partial hydrogenation reaction of short chain internal alkynes over unmodified Pd⁰ catalysts is usually achieved, at comparable conversion level, with higher selectivity compared to terminal alkynes,^[76] as indeed observed for 2 and 4 versus 3. This substrate effect was tentatively justified on the basis of the so-called thermodynamic selectivity concept, i.e. the higher stability of the Pd-adsorbed intermediate terminal alkene, which favors further reaction with H-species, thereby reducing selectivity.^[77]

The liquid phase hydrogenation of 1-fluoro-3-nitrobenzene (5) over Pd@MonoSil-ArSO3 was accomplished in excellent yields (> 99% selectivity to 5a at 99% conversion, STY 0.08 kg L⁻¹ h⁻¹) under very undemanding reaction conditions, i.e. room temperature, residence time 85 s, H₂ pressure 1.15 bar (Table 6, entry 3). To the best of our knowledge, no catalyst has been previously reported for the partial hydrogenation of 5 under continuous flow. Under experimental conditions comparable to that of Table 6, the selective hydrogenation of 5 to 5a was described using batch reactors and silica gel supported palladium^[78] or platinum^[79] catalysts, with an estimated STY of 0.01 and 0.02 kg L⁻¹ h⁻¹ respectively. Compared to the chlorine analogue 1, the nitrobenzene 5 was more resistant to hydrogenation using Pd@MonoSil-ArSO3 catalyst. In fact, under the same flow conditions, a conversion of 45% was observed for 5, against 95% of **1**, resulting in a productivity of 0.04 mol g_{Pd}^{-1} h⁻¹ for **5a** and 0.07 mol g_{Pd}^{-1} h⁻¹ for **1a**, respectively (Supporting Information, Table S3).

Similarly, Pd@MonoSil-ArSO₃ catalyst was less active in the hydrogenation of 1-chloro-2-nitrobenze (6) than in the hydrogenation of the *meta* isomer 1. Under the same reactants' flow rates, **6a** was obtained in ca. 30% lower conversion (62%)

and productivity (0.04 mol g_{Pd}^{-1} h⁻¹) compared to **1** (Table S3). The catalyst activity showed to decrease in the series 1 > 6 > 5, that can be attributed to deactivating effect of the substituents on the benzene ring. Nonetheless, the reaction conditions could be optimized (r 17 s, H2:6 ratio 9) so as to achieve a 73% 6a selectivity at 90% 6 conversion, with a remarkable 6a STY of 0.29 kg L^{-1} h⁻¹ (Table 6, entry 4). As above described for 1, the liquid phase continuous flow hydrogenation of 6 was previously reported in 99% conversion and 99% selectivity using 1.9% Au@y-Al₂O₃ packed catalysts, however under harsher conditions compared to Pd@MonoSil-ArSO3 catalyst (80 °C, 10 bar H2, H₂:6 ratio 107, catalyst regeneration at 400 °C required).^[60] The batch hydrogenation of 6 by Pd catalysts was previously reported using Pd@SiliaCat^[79] and 5% Pd@C in scCO2, [80] however with complete and significant (16%) de-chlorination, respectively.

Finally, the catalytic hydrogenation of the unfunctionalized olefin 1,5-cyclooctadiene (7) was investigated, owing the challenging selectivity issues and the available literature data using comparable monolithic flow reactors. The reaction produces cyclooctene (7a), an important monomer for the manufacture of a variety of polymeric materials.^[81] During the process, besides over hydrogenation to cyclooctane (7c), competitive hydro-isomerization to 1,4-cyclooctadiene (7b) is known to occur over supported PdNP systems, particularly at low H₂ pressures (Scheme 3).^[82] Under the optimized condition for **7a** yield (τ 85 s, H₂:**7** ratio 1.6, H₂ pressure 1.08 bar) use of Pd@MonoSil-ArSO₃ provided the desired partial hydrogenation product 7a with 85% overall selectivity [7a / (7a + 7b + 7c)] and 87% selectivity in hydrogenation reaction [7a / (7a + 7c)] at 94% conversion, corresponding to a 80% 7a yield (Table 6, entry 5). Analogously to the other substrates examined, a reproducible selectivity / conversion diagram could be obtained by varying either the H₂:substrate ratio or the residence time. A representative example is shown in Figure 11, left for fixed H₂:7 ratio 1.6. A typical composition of the reaction mixture under different residence times (23 - 85 s) and the same H₂:7 ratio is reported in Figure 11, right, showing the decrease of 7 and 7b, and the increase of **7a** and **7c**, upon increasing τ . As expected, the amount of isomerization product 7b obtained is lower for higher H₂ pressures (Supporting Information, Figure S26). Compared to the previously reported Pd@MonoSil^[12a] and Pd@TiO₂ monolith^[11] catalysts, under analogous flow conditions Pd@MonoSil-ArSO3 provided 7a with similar or better yields (85, 68 and 80%, respectively) and higher STY (0.07, 0.40 and 0.50 kg L⁻¹ h⁻¹, respectively) at remarkably lower H₂:7 ratio (4.0, 4.8 and 1.6) (Table S4). The continuous flow partial hydrogenation of 7 was previously accomplished in ca. 95% 7a yield, but in much lower STY (ca. 0.1 kg L⁻¹ h⁻¹), using a pore-through-flow Pd@Al₂O₃ catalytic membrane reactor under 50 °C and 10 bar H₂, however with periodic regeneration at 250°C under H₂ required.[83]

Importantly, irrespective of the substrate, all above processes could be achieved with full conversion by selection of appropriate, very mild flow conditions (τ 21 - 100 s, H₂ 1.07 - 1.16 bar, room temperature), showing no significant change of activity and selectivity *over one week* continuous reaction time. Palladium leaching in solution was below the ICP-OES detection limit, in any case.



Figure 11. Continuous flow hydrogenation of 7 over Pd@MonoSil-ArSO₃ catalyst (rt, methanol 0.1 M). Left: selectivity/conversion diagram at fixed H₂:7 ratio = 1.6 and residence time in the range 23 - 85 s. Right: reaction mixture composition (mol %) under these conditions.

The stability of the Pd@MonoSil-ArSO₃ catalyst can be ascribed to both the stabilization of embedded PdNP, thanks to the combined effect of mesoporosity (steric stabilization)^[84] and sulfonated groups (electrostatic stabilization),^[85] and to the mild operating conditions attained, thanks to the efficiency of the monolithic catalyst. As a matter of fact, neither leaching of metal in solution (ICP-OES) nor sintering of PdNP (TEM) has been observed upon use in catalysis. Minimization of active site inhibition by non-accumulation of adsorbed by-products, e.g. dimers in the case of alkyne hydrogenation,^[86] may be also of relevance under the conditions of continuous flow.^[87]

Conclusion

A facile method was described for the synthesis of PdNP- doped hierarchical porosity silica monoliths, based onto an ionexchange / reduction sequence of post-functionalized sulfonated materials. The procedure afforded PdNP of small size evenly distributed within the monolith and resulting in a 4.6% wt bulk metal loading. Compared to known synthetic methods, the actual strategy provides significant advantages in terms of higher metal content and smoother, environmentally friendlier, procedure.[88] The as-prepared material was scrutinized as catalysts for the continuous flow, partial hydrogenation reaction of various substrates, showing remarkable versatility and efficiency under very mild conditions. Very good activity and selectivity was achieved in the hydrogenation of halogenonitrobenzenes. Particularly, no significant de-halogenation was observed at full conversion in the hydrogenation of 1-fluoro-3nitrobenzene. The hydrogenation of alkynols showed to be significantly substrate-dependent in terms of chemoselectivity to the alkene product. Better results were obtained for internal alkynes, and particularly for 3-hexyn-1-ol, whose corresponding leaf alcohol product was obtained with yield comparable to the best ever reported for a continuous flow catalytic system. Irrespective of the substrate, compared to similar hierarchically porous materials (and also most of the conventional systems), the monolithic catalyst showed better performance in terms of STY of desired product at comparable conversion levels. This can be attributed to the high Pd loading per unit volume catalyst and to the high permeability of the support material. Highly reproducible flow processes with very short equilibration times and low pressure drops were achieved in any case. The catalyst showed pretty nice constant efficiency over prolonged time on stream, with no regeneration treatments required.

Selectivity enhancement in catalytic, partial hydrogenation reactions is a critical goal for industrial applications, which is often problematic because of over hydrogenation reactions, isomerization, limited resistance of other functional groups. Strategies have been developed in order to enhance the selectivity of these systems, e.g. in the case of alkynes hydrogenation, by addition of variable, often large, amounts of (toxic) modifiers.^[89] Compared to the known catalysts for the flow processes herein examined, if any, the reported catalysts provide a good compromise solution between product purity and productivity, with no need of additives to achieve satisfactory selectivity.

Experimental Section

General information

Unfunctionalized, dual porosity silica monoliths (MonoSil) of 6 mm diameter, featuring a skeleton thickness of 3 μ m, a macropore size of 5 μ m and a macroporous volume of 1.8 cm³ g⁻¹ (SEM, mercury porosimetry) , were prepared as previously described.^[5a] The BET surface area was 521 \pm 6 m² g⁻¹, the BJH desorption cumulative pore volume and desorption average pore width was 1.07 cm3 g-1 and 6.6 nm, respectively. 5% Pd@SiO₂ (Escat™ 1351, 40 µm grain size, surface area 400 m² g⁻¹) and 5% Pd@C were obtained from Strem Chemicals and Aldrich, respectively. Reactions under continuous flow were carried out using a home-made reactor system constructed at ICCOM-CNR (Scheme S1). The system was designed to allow for a concurrent flow of substrate solution and hydrogen gas through the monolithic catalyst. The reactor was completely inert since 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 while the hydrogen pressure in the reactor was monitored by a pressure meter. The concurrent flows of gas and liquid were driven through a T-shaped PEEK mixer equipped with a 2 µm PE filter to ensure efficient gas dispersion. The monolithic catalyst was cladded into a heat-shrinkable 1/4" Deray-KY175 PTFE tube together with two glass tubes (4 mm inner diameter) at each end, and connected in a top-down arrangement to the system by PFA Swagelok fittings, Chemraz® O-rings and 1/16" PEEK tubing. At the outlet of the reactor, the reaction solution was collected for GC, GC-Ms and ICP-OES analysis and the excess amount of the hydrogen gas released to the atmospheric pressure. Commercially available H₂ (99.995%) was used as received. The reaction products were unequivocally identified by the GC retention times and mass spectra of those of authentic specimens. Quantitative analysis of the reaction products was carried out via GC based on calibration curves of the pure compounds

Synthesis of sulfonated silica monolith MonoSil-ArSO₃

Prior of functionalization, the bare silica monolith (0.424 g, 7.07 mmol) was activated under vacuum at 100 °C for 18h then at 150°C for further 18h. After cooling to rt under nitrogen, the monolith was transferred under nitrogen into a two-necked, round-bottomed flask equipped with a refrigerator. Dry toluene (13 mL) was added under nitrogen by a gas-tight syringe and the mixture was degassed by three cycles vacuum/nitrogen. A 50% wt solution of CSPTMS in dichloromethane (0.442 mL corresponding to 0.297 g, 0.91 mmol of CSPTMS) was added dropwise under nitrogen. The mixture was refluxed for 48h without stirring then cooled to rt. The monolith was decanted, washed sequentially with

toluene, ethanol, methanol : H_2O = 50 : 50, acetone and dried under high vacuum at rt for 1h, then at 75°C for 3 days.

Synthesis of the Pd catalysts Pd@MonoSil-ArSO₃

In a typical procedure, the cladded MonoSil-ArSO₃ monolith (6 mm diameter, 1 cm length, 81.8 mg, 0.08 meq sulfonic sites) was connected through PFA Swagelok fittings and Teflon tubing to a diaphragm metering pump. The system was conditioned by flowing deionized-water 0.3 mL min⁻¹ for 30 min. A solution of Pd(NO₃)₂·2H₂O in H₂O (0.025 M, 15.0 mL, 0.375 mmol) was allowed to cyclically flow through the cladded monolith at 0.5 mL min⁻¹ for 3h. The brownish monolith obtained was then thoroughly washed with H₂O (0.5 mL min⁻¹ for 1h) and methanol (0.5 mL min⁻¹ for 30 min).

After connection to the flow reactor system described above, H₂ (2 mL min⁻¹, pressure at the reactor inlet 2 bar) and methanol (0.5 mL min⁻¹) were flowed simultaneously through the monolith for 3h at rt. The asprepared black-monolith was directly used in catalytic hydrogenation reactions without disconnecting from the system or dried under a stream of N₂ (2 mL min⁻¹ for 12 h at rt) before being characterized.

Catalytic reactions in continuous flow mode

In a typical experiment, a deaereated solution of substrate in methanol (0.1 M) was allowed to flow through the cladded Pd@MonoSil-ArSO₃ monolith (6 mm diameter, 1 cm length, 81.8 mg, 0.283 cm³, 4.6% wt Pd) at 0.48 mL min⁻¹ rate, together with a H₂ flow of 1.25 mL min⁻¹ under rt. This resulted in a H₂ pressure at the reactor inlet of ca. 1.15 bar (corresponding to a H₂ : substrate molar ratio of ca. 1.2), 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 monitored periodically by analyzing the product solution for conversion and selectivity by GC. Aliquots were sampled at 1 h intervals for Pd leaching determination by ICP-OES.

Catalytic reactions in batch mode

Reaction conditions analogous with those used for the continuous flow experiments were adopted. Particularly, in order to establish a proper comparison, the catalytic reactions were performed by contacting the same amount of substrate per unit catalyst and time as in the flow mode. Thus, in a typical procedure, the Pd@MonoSil-ArSO3 monolith was crushed in an agate mortar and sieved to collect a 60-120 um fraction using a glove-box. The ground catalyst (53 mg, 4.6% wt Pd) was placed under nitrogen into a glass non-metallic Büchi Miniclave® and a solution of 1-chloro-3-nitrobenzene (1) in methanol (18 mL, 0.01 M,) was added via a Teflon capillary under nitrogen. Nitrogen was then replaced by hydrogen with three cycles pressurization (1 bar) / depressurization. The autoclave was finally charged with a constant H₂ pressure of 1 bar. The mixture was stirred under room temperature at 500 rpm, in order to avoid mass transfer limitations.^[14b] After 1 h, the reactor was depressurized and the solution analyzed via GC to yield a 98 %, conversion and a 100% selectivity to aniline 1c.

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