FULL PAPERS

A Palladium Wall Coated Microcapillary Reactor for Use in Continuous Flow Transfer Hydrogenation

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Abstract: Herein we describe the preparation of a novel continuous flow multi-channel microreactor in which the internal surface has been functionalised with a palladium coating, enabling its use in catalytic heterogeneous liquid-phase reactions. Simple chemical deposition techniques were used to immobilise palladium(0) on the channel wall surface of a polymeric multi-capillary extrudate made from ethylene-vinyl alcohol copolymer. The Pd coating of the microcapillaries has been characterised by mass spectrometry and light and electron microscopy. The functional activity of the catalytic Pd layer was tested in a series of transfer hydrogenation reactions using triethylsilane as the hydrogen source.

Keywords: flow chemistry; hydrogenation; immobilisation; microreactors; palladium; reduction

Introduction

Chemical microreactors are devices containing consistent dimensionally defined, fluidic pathways in the sub-millimetre range. Many designs have a single or multiple parallel channels with diameters between 10 and 1000 μm, where the chemical reaction takes place.[1–5] A major advantage of microreactor technology is the very high surface area to volume ratio of typically 10000 to 50000 m^2/m^3. This contrasts significantly with the specific surface area in conventional reactors which is usually about 100 m^2/m^3 and seldom exceeds 1000 m^2/m^3.[6] Owing to this property, micro-structured reactors with chemically active surfaces offer tangible benefits for use in heterogeneous catalytic processes. Micro- and mesoscale reactor designs for use in catalytic operations include packed bed systems, catalytic wall reactors, flow reactors containing microporous media, such as monolithic structures and other chemically functionalised devices.[6–15]

We have been developing microreactor concepts around multi-channelled polymer devices for use in chemical synthesis and have presented these results in previous publications.[16,17] The design and flexibility of these modular constructs facilitates both development of new synthesis routes within a research laboratory environment and the fast adaptation of these processes for a small production scale by simply increasing the number of reactor units. In this way, the optimisation of reaction conditions can be carried out using a single device with a small number of microcapillaries, whilst the production reactor can be operated using multiple devices with hundreds or even thousands of microcapillaries running in parallel. This so-called 'numbering-up' or 'scale-out' requires neither the redesign of reactors nor extensive optimisation studies which are usually associated with the classical batch scale-up approach.[2] In this new research project, we have developed our microreactor system further to include a catalytic palladium wall coating on the microcapillaries in order to carry out palladium-promoted processes as these are of pivotal importance in modern synthesis projects.

This paper reports a novel process for the preparation of a catalytic wall microreactor through immobilisation of Pd on the walls of polymer channels with a mean capillary diameter of 146 μm using a series of aqueous preparative flow steps. The general procedure was modified from previous protocols for immobilising Pd within monolithic structures or on beads.[11,15,18–20] The reactor system presented herein contrasts traditional polystyrene or silica solid sup-

ports, which have a granular, bead or gel form,[7,20–24] as it consists of multiple capillaries manufactured from ethylene-vinyl alcohol (EVOH). The capillary geometry provides a known flow profile, which can be easily characterised and modelled, and does not suffer from channelling problems that are typically observed in packed bed systems. Due to the small capillary diameters, the microreactor also offers a uniform temperature profile[25] giving a fast thermal response and consequently facile control over its temperature.

Results and Discussion

Preparation of Palladium-Microcapillary Reactors

The disc-shaped microreactors[16] were fabricated from a flat polymer film in which arrays of parallel capillaries are embedded; this structure, termed *microcapillary film* (MCF), is manufactured by a polymer extrusion process, which is described in detail in previous publications.[26,27]

In the MCF manufacturing process, a polymer melt is extruded over an array of injectors that are placed near the exit of a rectangular die.[26] The injectors are connected to an air inlet at ambient conditions and the flow of polymer melt over the injectors causes air to be entrained into the polymer, thus forming an array of continuous, linear capillaries. The extrudate leaving the die passes either through a quench bath or over a set of chilled rollers to solidify the polymer melt. The quenched extrudate is then drawn away from the process by means of a haul-off device. Changing the quench and haul-off conditions enables the capillary diameters and film dimensions to be altered by a significant amount. For the work reported below, MCFs were extruded from ethylene-vinyl alcohol (EVAL F101B, vinyl alcohol content: 68%)[28] at standard extrusion conditions. EVOH is a copolymer containing pendant hydroxy groups which can be used for post-extrusion surface functionalisation (Figure 1).

The selected resin contains a high ethylene content such that it remains resistant to polar solvents, unlike simple polyvinyl alcohol (PVA), which has been used in previous studies.[29] The EVOH capillary structures are stable to water and alcohols and have a good general resistance to many other organic solvents including dichloromethane and tetrahydrofuran. The thickness of the EVOH-MCFs was 0.6 mm, their width was 6.9 mm and they had a mean capillary diameter of 146 μm. For these diameters, and the chosen process flow rates, the flow within each capillary is laminar.[25]

Lengths of MCF were coiled in a double spiral configuration to form reusable reactor cartridges, termed *microcapillary flow discs* (MFDs).[16] These discs had a capillary length of 10 to 15 m with an associated reaction volume of 3.2 to 4.8 mL. They proved suitable to carry out liquid-phase organic synthesis enabling reaction times of between a few minutes and several hours. The double spiral configuration allows for both the inlet and outlet of the reactor to be positioned on the outer edge of the MFD. The reaction mixture enters the disc tangentially at the circumference, progresses concentrically to the centre and subsequently from the centre back to the circumference, where it exits the disc at the outlet. The connection between an MFD and standard microfluidic tubing or pumping devices was achieved using standard microfluidic fittings and tubing and a highly solvent-resistant epoxy resin (Robnor Resins PX439XS), described in more detail in previous work.[17,29]

The surface functionalisation of MFDs was carried out in four subsequent wet chemical steps under continuous flow conditions. Each of these steps used a simple set-up whereby a premade stock solution was pumped through the MFD *via* an HPLC pump (Knauer Smartline 100), in either a single pass or a recycling loop procedure. In the first of these steps, 1 M sodium hydroxide (NaOH) solution was recycled in a loop for several hours. This was to ensure that the hydroxy groups were fully unmasked and the polymer would reach its maximum functionalistion potential. After this initial conditioning step, the disc was treated with a solution of *N*-trimethoxysilylpropyl-*N,N,N*-trimethylammonium chloride. Here the disc was heated to 40 °C for 3 h using a reactor heater system (Cambridge Disc Microreactor, Lamina Di-
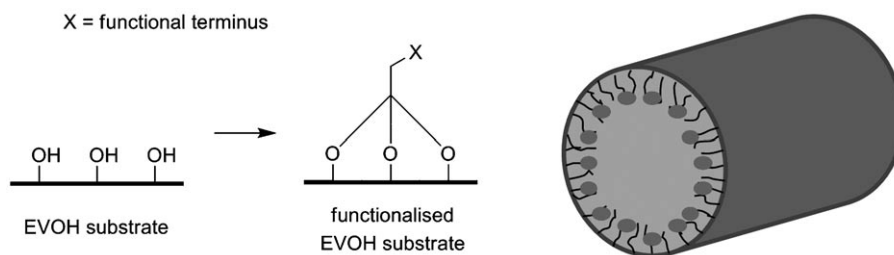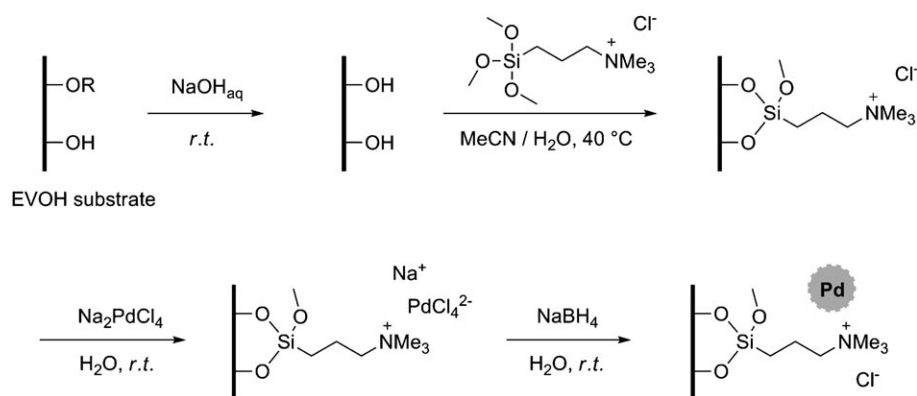

Figure 1. Wall surface functionalisation of microcapillaries inside EVOH-MFDs; *right*: general reaction scheme; *left*: schematic drawing of functionalised capillary.

Scheme 1. Wall surface functionalisation of microcapillaries inside EVOH-MFDs in four preparation steps.

electrics),[30] while the solution was recycled through the disc. Afterwards an aqueous solution of Na_2PdCl_4 was pumped through the disc followed by an aqueous solution of $NaBH_4$, both in a single pass. The Pd(II) salt was trapped onto the polymer surface *via* anion exchange at the silyl linker, and subsequent treatment with $NaBH_4$ reduced it to form a Pd(0) precipitate, which immediately coloured the MFD black. Similar procedures, stabilising Pd particles with quaternary ammonium salts have been reported by Reetz et al.[31,32] All steps except the silylation step were carried out at room temperature and were followed by a short washing protocol. This procedure presents a modification of previous protocols,[11,18] which were used for the immobilisation of Pd on monolithic structures.

Scheme 1 shows the preparation sequence from the untreated EVOH disc to the catalytically active Pd microreactor. Figure 2 shows a microscope image of an MCF cross section, a side view of a typical MCF, an MCF connector and MFDs before and after Pd coating.

Characterisation of Pd-Microcapillary Reactors

A series of analysis methods were used in order to characterise the Pd coating on the channel walls as well as the durability and usability of the polymer disc for continuous flow catalytic processes.

Initially, the amount of Pd per gram or metre of microcapillary film was determined by inductively coupled plasma mass spectroscopy (ICP-MS); these results are shown in Table 1. For this analysis, small strips of MCF were first dissolved in concentrated nitric acid and the solutions obtained were subsequently diluted with water (Milli-Q) prior to the spectroscopy measurements.

The results derived from the three MCF samples prepared under different conditions are interesting. Whilst the first two samples underwent the entire

preparation sequence starting from the conditioning step with NaOH, the third sample was prepared only with Na_2PdCl_4 solution and $NaBH_4$. This comparative experiment was conducted in order to investigate the effect of the silane ion exchange surface capping on the respective capturing of Na_2PdCl_4. As can be seen, the first two samples have a ~9 times higher Pd loading, which leads to the conclusion that the Pd salt is mainly immobilised on the surface *via* the proposed anion exchange mechanism. Control experiments with untreated MCFs established a value of 0.06 µg Pd/g MCF. When comparing the first two samples, which have identical preparation protocols, but differ in the MCF section that was analysed, it can be concluded that the coating shows non-uniformity over the cross section of the MCF. The first sample consisted of a short strip of MCF containing all 19 channels, the second sample was taken from the central section only (middle 11 channels; see Table 1). As the central channels in most MCF extrudates are slightly larger than the outer ones (mean capillary variation 5.6%), they also experience a higher flow rate fraction.[25] Consequently, more Pd is deposited in the central capillaries compared to the outer capillaries, although the difference is small. Based on these results, the total amount of Pd per disc equates to 0.31–0.47 mg.

Light microscope images were taken of MCF cross sections before and after Pd coating; these are shown in Figure 3.

The image after treatment with Pd (Figure 3, *right*) distinctly shows a dark brown ring originating at the capillary wall and diffusing into the surrounding plastic. At closer inspection, it was confirmed that the intensity of the colouration is at a maximum at the capillary wall and gradually drops with distance. The apparent width of this ring was measured to be 30 to 38 µm. It was observed that the intensity of these rings was not uniform across the 19 capillaries in the cross section, with the central capillaries being stained darker than those situated at the edges (see discussion above).
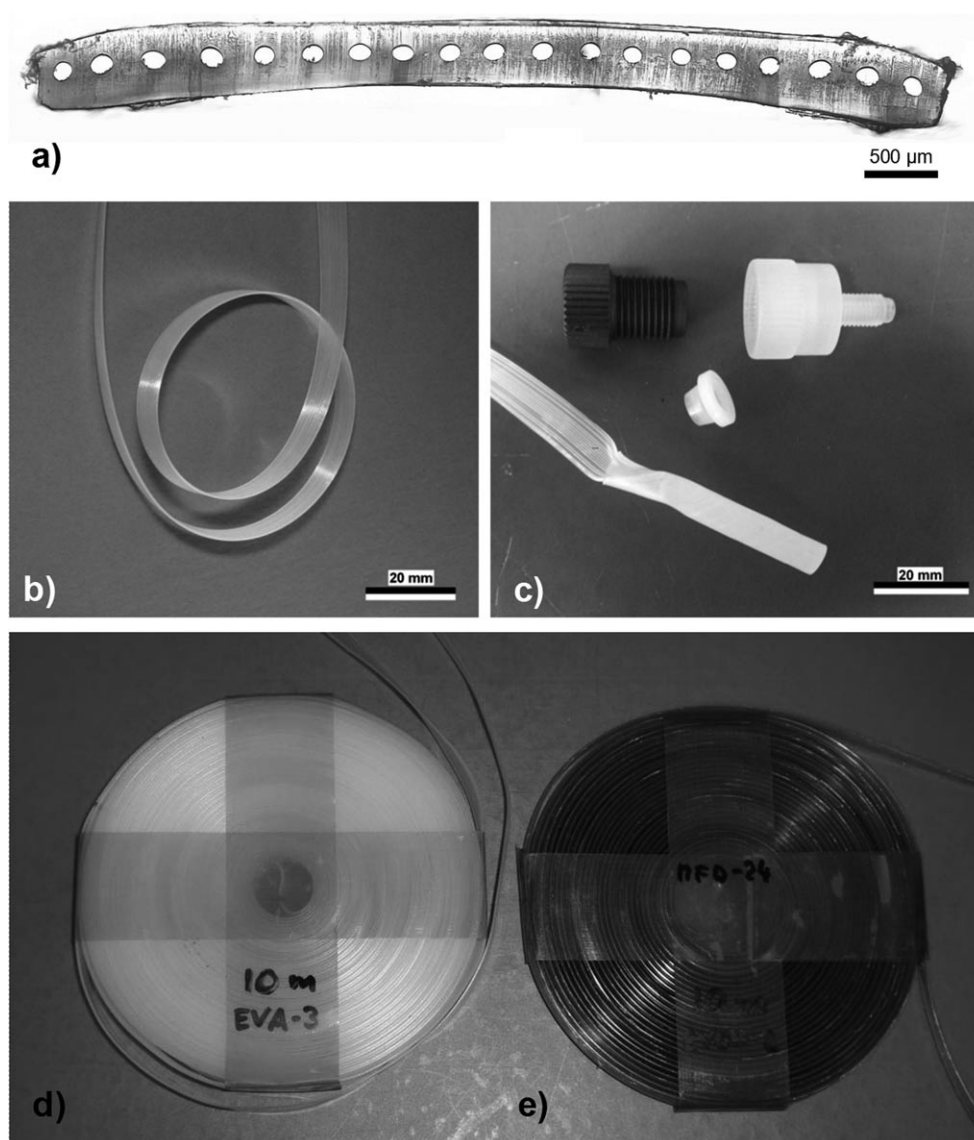
Figure 2. a) Microscope image of an MCF cross section made from EVOH, containing 19 capillaries; **b)** side view of a single length of MCF; **c)** MCF connector components; **d)** EVOH-MFD before and **e)** after functionalisation and reduction to Pd(0).

Table 1. Pd content in MCF extrudate determined by ICP-MS, samples prepared with different protocols.

Sample	NaOH/silane/Pd/NaBH$_4$ *all channels*[a]	NaOH/silane/Pd/NaBH$_4$ *MCF centre*[b]	Pd/NaBH$_4$ *all channels*[a]
µg Pd/g MCF	8.01	8.38	0.91
µg Pd/m MCF	30.89	32.33	3.53

[a] Sample consisted of short MCF strip containing all 19 channels: .

[b] Sample taken from central section of short MCF strip, discarding outer four channels at each side:

 .

Scanning electron microscopy (SEM) was used to investigate the surface morphology of the capillary walls and detect the location of Pd deposits. For optimal image quality, a series of MCF samples (before and after Pd loading) were prepared with gold sputter coating; for energy dispersive X-ray spectroscopy
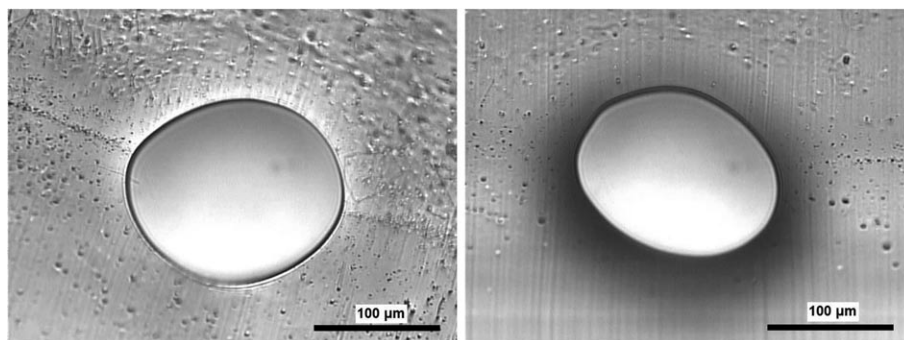
Figure 3. Light microscope images of EVOH-MCF channels before (*left*) and after (*right*) Pd-coating.

(EDS) MCF samples were prepared with a carbon coating. Before the sputter process, both sample sets were prepared by freeze fracturing, which enabled microscope access to the channel walls. Hereby, a small section of MCF was dipped into liquid nitrogen followed by fracturing on a solid metal block while frozen. The aim was to split the sample at a fracture plane with a short angle with respect to the centre line of the channels, such that the electron beam could be focused on the capillary wall. Figure 4 shows a selection of SEM images of the gold coated samples at two different magnifications (*top* and *bottom row*), one before (*left column*) and one after (*right column*) Pd treatment.

The images taken of the untreated sample show a uniformly smooth capillary wall surface (Figure 4 a and c), while the Pd-EVOH sample shows irregularities and a different wall surface morphology (Figure 4 b and d). Larger sections of the capillary wall appear to have undergone a leaching process where parts of the polymer have been either displaced or certain voiding has occurred (Figure 4 b). These areas are believed to have contained amorphous phases which have been attacked by one or several of the stock solutions used during preparation. Interestingly, it was observed that following treatment with NaOH and the silane solution at 40 °C, the MCF became noticeably softer. However, this softening did not noticeably
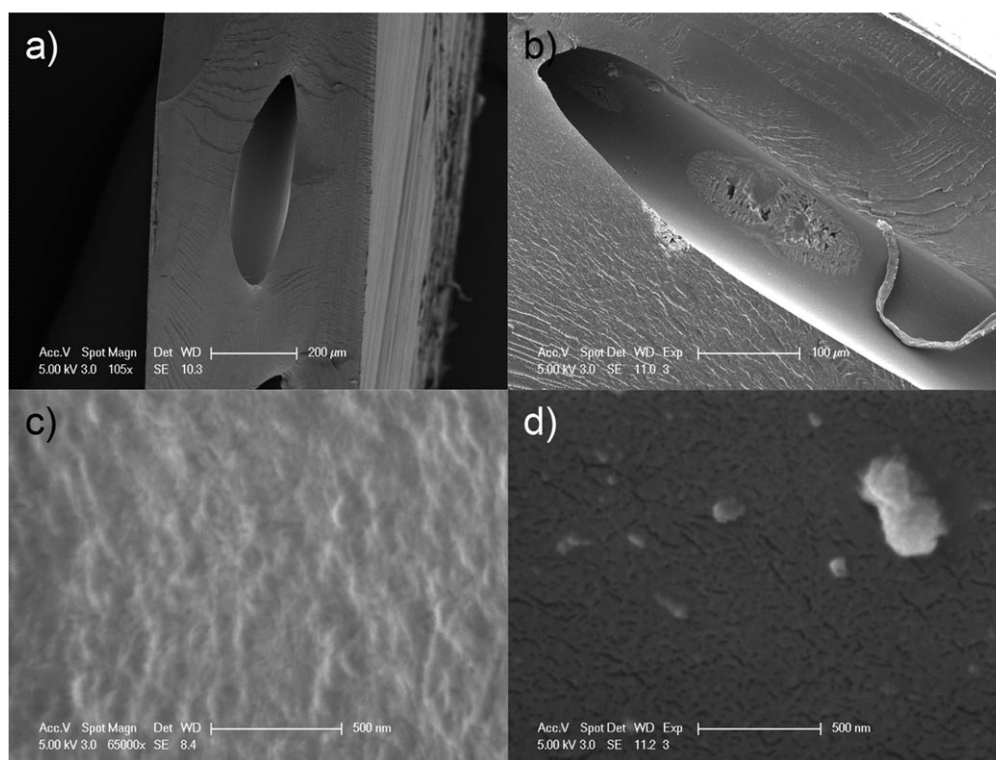
Figure 4. SEM images of EVOH-MCF before (**a** and **c**) and after (**b** and **d**) Pd loading, low magnification (**a** and **b**) and high magnification of channel wall surface (**c** and **d**).

affect the system's overall structural integrity. The images of the channel wall at high magnification show small hairline cracks and deposits on the polymer surface (Figure 4 d) after Pd loading, whilst before, the surface appears regular and homogeneous (Figure 4 c). It would appear that the chemical treatment does change the capillary wall surface and results in small cracks in the nanometre range as well as larger irregular areas. It was not possible to determine the size of Pd particles deposited on the channel walls from these SEM images, however, the relatively uniform channel wall surface after coating and the absence of larger metallic deposits suggests that the particles are in the nanometre range. This agrees with the literature, such as Nikbin et al., 2007 (particle size: 5 to 50 nm)[18] or Mennecke et al., 2008 (particle size: 1 to 10 nm),[15] where similar depositing procedures have been applied. Both these systems are based on polymer monoliths which enabled the observation of the Pd particles using transmission electron microscopy (TEM), which could not be adopted in the same way for our polymer capillary system.

Figure 5 shows a typical spectrum taken from SEM-EDS experiments with carbon coated samples.

This spectrum shown in Figure 5 was taken at the capillary wall surface and indicates the presence of Pd and chloride next to strong carbon and oxygen signals, which result from the EVOH polymer. The signal intensity varied between the channels with maximum values of up to 5 wt% for Pd and 8 wt% for chloride. The chloride residues remain from the synthesis of the Pd-MFDs introduced from the silane and Na_2PdCl_4. In some spectra, an additional signal for low levels of sodium (Na) could also be detected. A total of 49 spectra at different positions over several channels were taken and in 70% of them Pd was detected, while control samples before functionalistion did not show any Pd signals.

In summary, the results obtained from SEM-EDS, ICP-MS and light microscopy indicate that Pd is deposited on the microcapillary wall surface 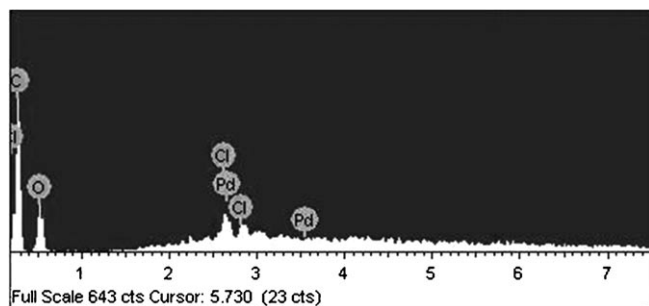and also penetrates to some extent into the surrounding polymer matrix. This can be rationalised through the diffusive nature of the polymer composite that allows the priming solutions of activators and then palladium to permeate to a certain extent into the resin structure. Furthermore, it would appear that the coating process results in some non-uniformity along the length of the capillaries as well as the cross section of the MCF capillaries. This can also be explained in terms of the effective residence time and resulting exposure of each section of the capillary to the reacting solutions.

Melting point experiments of untreated EVOH-MCF on a Perkin–Elmer Pyres-1 differential scanning calorimeter (DSC) were carried out in order to investigate the stability of the polymer, EVAL F101B at elevated temperatures (Figure 6). This information was important as initial flow experiments at 80 to 100 °C resulted in softening of the polymer and bursting of the capillaries (see Experimental Section).

The graph in Figure 6 shows the heating (*upper*) and cooling (*lower*) curves for an untreated EVOH-MCF sample between 50 and 250 °C. It can be observed that the main melting region lies in the area of 187 °C, which agrees well with the manufacturer information of 183 °C.[28] However, a small peak can also be observed around 125 °C, which could correspond to a secondary melting region. This behaviour can be explained by the copolymeric nature of EVOH, which is polymerised from two different monomers: ethylene and vinyl alcohol. Previous experiments with polyethylene MFDs (LLDPE NG5056E), which have a melting region around 120 °C (similar to the observed secondary melting region of EVOH), have shown softening at relatively low temperatures of 60 to 70 °C when in contact with organic solvents. A small irregularity in the heating curve of EVOH at
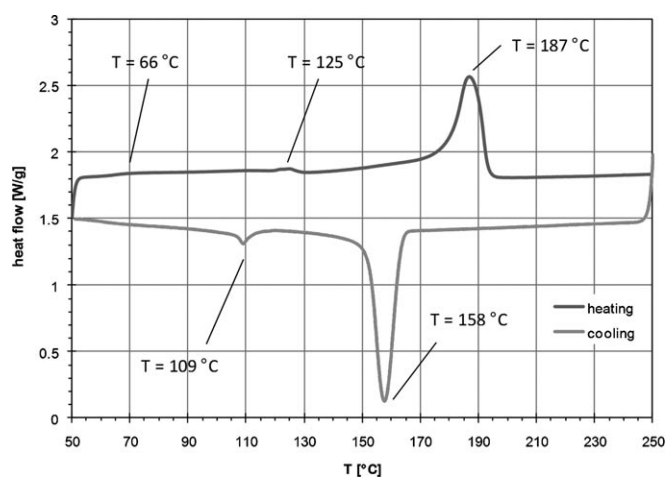

Figure 5. SEM-EDS spectrum of the capillary wall surface in a Pd-coated EVOH-MCF.

Figure 6. Differential scanning calorimetry results of untreated EVOH-MCF showing main (187 °C) and secondary (125 °C) melting regent.

66°C can also be seen. These observations lead to the conclusion that the ethylene content of EVOH results in a softening of the polymer around 60 to 70°C, which is significantly lower than the melting point of 183°C, and was not expected initially. Consequently, reaction systems at lower temperatures were investigated.

Pd-Catalysed Transfer Hydrogenation

Transfer hydrogenations are commonly used in organic synthesis[33] as well as in industrial processes, where the use of gaseous hydrogen (H$_2$) is undesirable either because of inconvenience, safety or cost. A large-scale example is coal liquefaction using hydrogen donor solvents such as tetralin.[34] In this paper, a transfer hydrogenation using triethylsilane as the hydrogen donor was chosen, as this can be carried out at room temperature. This case study was based on work by Mandal and McMurray, who used a palladium on charcoal catalyst in suspension in batch reduction reactions.[35]

A simple experimental configuration was used to perform this reaction at room temperature, whereby a solution of 0.5 to 2 mmol substrate (**1**) and 10 equivalents of triethylsilane (**2**) in methanol (MeOH) was pumped *via* an HPLC pump through the reactor at 0.1 mL min^{-1} in a single pass (see Figure 7). Upon first entry of substrate into the microcapillaries, formation of small gas bubbles was noticed, which increased over time to a fully developed gas-liquid slug flow at steady-state conditions. The formation of gaseous H$_2$ during the reaction, resulting in a two phase flow, was believed to be beneficial for mixing inside the capillaries, thus ensuring that the reaction mixture was in good contact with the catalytic wall. With this procedure, a series of reduction reactions was successfully carried out, including the reduction of carbonyl groups to alcohols, imines and nitro-groups to amines, as well as carbon-carbon double and triple bonds. Figure 7 shows the experimental set-up and the general reaction scheme using the example of a carbonyl reduction, while Table 2 lists several reaction examples together with the corresponding conversions.

Products **3a** to **3d** were obtained with high conversions of greater than 95%. Substrate **1f**, which contained both a carbon-carbon double bond and a carbonyl group, resulted in a mixture of two products, namely the fully reduced alcohol **3g** and the partially reduced aldehyde **3f**. Using pure MeOH as solvent, the double-bond reduction had a conversion of 93% and the carbonyl reduction 75%. No partially reduced alcohol was detected and the remaining 7% were returned as unreacted starting material. Substrate **1e** showed a poor solubility in pure MeOH, and thus solvent mixtures with isopropyl alcohol (*i*-PrOH) or toluene were used in higher dilutions than the other substrates. The observed lower conversions are believed to be a result of the solvent mixture rather than the inherent activity of the substrate. The range of different substrates shows the versatility of the reactor system and its efficiency for heterogeneous catalytic reactions. Leaching of Pd during reaction was minimal as any amount of catalyst in the product was below the detection limit for the investigated reaction scale (0.5 to 2 mmol of substrate). Furthermore, the reactor discs could be used several times without a noticeable loss of catalytic activity. The reduction of **1e** after ten repeated reactions in the same disc showed similar conversion (~3% less) when compared to a fresh disc.

A detailed description of the reaction protocol is given in the Experimental Section for one example, namely the reduction of acetophenone (**1a**) to 1-phenylethanol (**3a**).
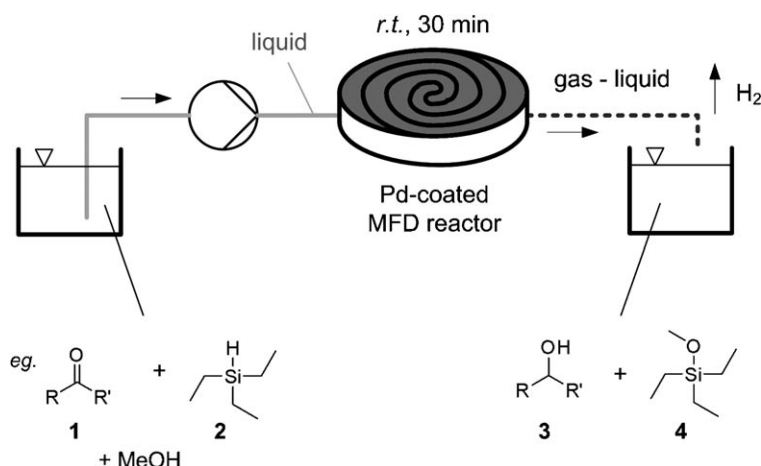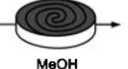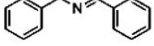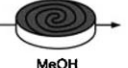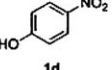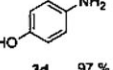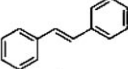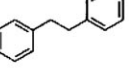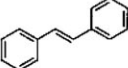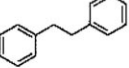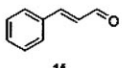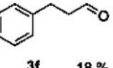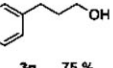

Figure 7. Flow diagram and reaction scheme of transfer hydrogenation reactions in Pd-MFDs, using an HPLC pump.

Table 2. Transfer hydrogenation in Pd-MFDs using triethyl-silane.[a]

Substrate	Solvent	Product
1a	MeOH	3a 95 %
1b	MeOH	3b 98 %
1c	MeOH	3c 96 %
1d	MeOH	3d 97 %
1e	MeOH / iPrOH 5 : 3	3e 42 %
1e	MeOH / toluene 1 : 1	3e 83 %
1f	MeOH	3f 18 % + 3g 75 %
1f	MeOH / iPrOH 1 : 1	3f 24 % + 3g 27 %

[a] Conversions measured by ^{1}H NMR.

Conclusions

This paper reports the preparation and evaluation of novel plastic continuous flow microreactors for heterogeneous catalysis reactions at temperatures typically below 60 °C. By performing a transfer hydrogenation wit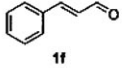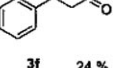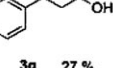h Pd(0) immobilised on the capillary walls of the disc-shaped microreactor, we demonstrated that coated *microcapillary flow discs* (MFDs) can be used as reusable reactors. Each MFD was composed of 19 parallel channels with a mean diameter of 146 µm and a length of between 10 and 15 m. The discs were manufactured from ethylene-vinyl alcohol (EVOH) and functionalised by a series of four wet chemical steps, resulting in a catalytic Pd coating at the channel wall surface. The Pd coating was characterised by light and electron microscopy and its con-

tent quantified to be 31 µg Pd/m MCF by ICP-MS. It would appear that this value is higher than the theoretical estimation for a Pd monolayer on the surface. Coated EVOH also appears to have nano-cracks and there is some evidence pointing towards Pd penetrating into the polymer support.

We anticipate that, with similar experimental protocols, it should be possible to immobilise other catalytically active transition metals such as gold, nickel or copper onto MFD microcapillary walls. The upper temperature limit of EVOH of around 60 to 70 °C however, confines the range of applications of discs made from this particular polymer. So far, MCFs have been extruded from a wide range of different thermoplastic polymers, including highly solvent- and temperature-resistant fluorinated polymers.[17,30] These extrudates easily withstand temperatures of 150 °C but cannot be functionalised in the same way as EVOH. Future work will be dedicated to finding a melt-extrudable polymer, which combines both the ability to immobilise catalytic materials or other functional groups and high thermal stability.

From the proof of principle reactions carried out inside Pd-MFDs, using triethylsilane in MeOH as the hydrogen source, it can be concluded that the catalytic Pd layer inside the microchannels is active enough to yield excellent conversions at a reaction time of 30 min at room temperature. The gaseous hydrogen produced during the reaction results in a two phase gas-liquid flow inside the reactor, which is believed to be beneficial for mixing inside the capillaries, thus ensuring that the reaction mixture is in good contact with the catalytic wall.

Compared to polymeric monolith structures or packed bed columns using polymer beads, microchannels with catalytic wall coatings have well defined flow geometries, which simplifies model predictions of fluid mechanics and heat and mass transfer processes inside the reactor and additionally results in a potentially lower pressure drop along the channel, depending on its diameter. We believe that microscale catalytic wall reactors that offer a high enough catalytic activity combined with a practical channel diameter, where diffusion lengths are minimal and convective mass transport through the channel is fast and unhindered, such as coated MFDs, can provide a superior reaction environment for many heterogeneous catalytic reactions.

Experimental Section

General Remarks

Initially we attempted to perform cross-coupling reactions at elevated temperatures inside the Pd microcapillary reactors as proof of principle. First a Sonogashira-type coupling

using benzoyl chloride and phenylacetylene at 100°C and then a Suzuki–Miyaura coupling using 4-(methoxycarbonyl)-phenylboronic acid and benzylbromide at 80°C were investigated. Unfortunately, both reactions failed owing to insufficient stability of the polymer, as channels started to buckle and burst at the bespoke temperatures. These findings were unexpected as the polymer used (EVAL F101B), has a defined literature melting point of 183°C,[28] and so we had initially estimated the discs to be stable up to at least 100 or 120°C. Consequently, melting point experiments of EVOH-MCFs on a differential scanning calorimeter (DSC) were carried out (see Figure 6). These experiments enabled us to develop a better feel for stable reaction conditions using this polymer.

Surface Functionalisation of EVOH-MFDs

Firstly 50 mL of 1 M aqueous NaOH solution were recycled through the disc in a loop for 4 to 12 h at room temperature and a flow rate of 0.5 mL min^{-1}, followed by a wash with water at 0.5 mL min^{-1} for 30 min. Then, a solution of 1029 mg N-trimethoxysilylpropyl-N,N,N-trimethylammonium chloride in 30 mL acetonitrile (MeCN) and 10 mL water at a pH between 1 and 2 was recycled through the MFD in a loop at 0.5 mL min^{-1} and 40°C for 3 h, followed by a wash with MeCN at room temperature and 0.5 mL min^{-1} for 20 min and a wash with water at room temperature and 0.5 mL min^{-1} for 30 min. Afterwards, an aqueous solution of 147 mg Na$_2$PdCl$_4$ in 25 mL of water was pumped through the disc in a single pass at room temperature and 0.3 mL min^{-1}, followed by a wash with water at 0.5 mL min^{-1} for 30 min. The Pd salt was reduced by pumping a solution of 322 mg of NaBH$_4$ in 25 mL water through the disc in a single pass at 0.3 mL min^{-1}. Finally, the disc was washed with copious amounts of water, then 20 mL of 1 M aqueous HCl solution and 20 mL of MeOH.

Transfer Hydrogenation of Acetophenone (1a)

Starting materials, reagents, and solvents were obtained from commercial suppliers and were used without further purification. A substrate solution of 0.5 mmol (60 mg) acetophenone and 5 mmol (581 mg) triethylsilane in 1 mL methanol was prepared. The reactor was flushed for ~20 min with methanol at 0.5 mL min^{-1} before the substrate solution was pumped through the reactor at 0.1 mL min^{-1} in a single pass. Upon first entry of substrates into the microcapillaries, the formation of gas was observed. After the substrate solution had passed through the reactor, it was flushed with methanol until no gas bubbles could be observed anymore inside the capillaries. The collected product solution was first filtered through a short plug of quartz sand before solvent removal and subsequent analysis. ^{1}H NMR spectra were recorded on a Bruker Avance DPX-400 or Bruker DPX-600 spectrometer with residual chloroform as the internal reference ($\delta = 7.26$ ppm).

1-Phenylethanol (3a): Conversion: 95.4%, ^{1}H NMR (400 MHz, CDCl$_3$): $\delta = 7.36$ (4 H, m), 7.28 (1 H, t, $J = 6.1$ Hz), 4.91 (1 H, q, $J = 6.3$ Hz), 1.51 (3 H, d, $J = 6.4$ Hz).

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References

[1] K. Jähnisch, V. Hessel, H. Löwe, M. Baerns, *Angew. Chem.* **2004**, *116*, 410–451; *Angew. Chem. Int. Ed.* **2004**, *43*, 406–446.

[2] V. Hessel, S. Hardt, H. Löwe, *Chemical Micro Process Engineering (1), Fundamentals, Modelling and Reactions*, Wiley-VCH, Weinheim, **2004**.

[3] S. V. Ley, I. R. Baxendale, *Chimia* **2008**, *62*, 162–168.

[4] K. F. Jensen, *Chem. Eng. Sci.* **2001**, ##56-56##65, 293–303.

[5] S. V. Ley, I. R. Baxendale, in: *Proceedings of Bosen Symposium, Systems Chemistry*, May 26–30, **2008**, 65–85.

[6] L. Kiwi-Minsker, A. Renken, *Catal. Today* **2005**, *110*, 2–14.

[7] S. V. Ley, I. R. Baxendale, R. N. Bream, P. S. Jackson, A. G. Leach, D. A. Longbottom, M. Nesi, J. S. Scott, R. I. Storer, S. J. Taylor, *J. Chem. Soc. Perkin Trans. 1* **2000**, 3815–4195.

[8] P. L. Mills, D. J. Quiram, J. F. Ryley, *Chem. Eng. Sci.* **2007**, *62*, 6992–7010.

[9] G. Kolb, V. Hessel, *Chem. Eng. J.* **2004**, *98*, 1–38.

[10] A. Kirschning, W. Solodenko, K. Mennecke, *Chem. Eur. J.* **2006**, *12*, 5972–5990.

[11] U. Kunz. A. Kirschning, H.-L. Wen, W. Solodenko, R. Cecilia, C. O. Kappe, T. Turek, *Catal. Today* **2005**, *105*, 318–324.

[12] J. Kobayashi, Y. Mori, S. Kobayashi, *Chem. Commun.* **2005**, 2567–2568.

[13] I. R. Baxendale, J. J. Hayward, S. Lanners, S. V. Ley, C. D. Smith, in: *Microreactors in Organic Synthesis and Catalysis*, (Ed.: T. Wirth), Wiley-VCH, Weinheim, **2008**, pp 84–122.

[14] J. Sedelmeier, S. V. Ley, H. Lange, I. R. Baxendale, *Eur. J. Org. Chem.* **2009**, 4412–4420.

[15] K. Mennecke, R. Cecilia, T. N. Glasnov, S. Gruhl, C. Vogt, A. Feldhoff, M. A. Larrubia Vargas, C. O. Kappe, U. Kunz, A. Kirschning, *Adv. Synth. Catal.* **2008**, *350*, 717–730.

[16] C. H. Hornung, M. R. Mackley, I. R. Baxendale, S. V. Ley, *Org. Process Res. Dev.* **2007**, *11*, 399–405.

[17] C. H. Hornung, B. Hallmark, M. Baumann, I. R. Baxendale, S. V. Ley, P. Hester, P. Clayton, M. R. Mackley, *Ind. Eng. Chem. Res.* **2010**, *49*, 4576–4582.

[18] N. Nikbin, M. Ladlow, S. V. Ley, *Org. Process Res. Dev.* **2007**, *11*, 458–462.

[19] W. Solodenko, H. Wen, S. Leue, F. Stuhlmann, G. Sourkouni-Argirusi, G. Jas, H. Schönfeld, U. Kunz, A Kirschning, *Eur. J. Org. Chem.* **2004**, 3601–3610.

[20] T. Matsumoto, M. Ueno, N. Wang, S. Kobayashi, *Chem. Asian J.* **2008**, *3*, 196–214.

[21] R. Akiyama, S. Kobayashi, *Chem. Rev.* **2009**, *109*, 594–642.

[22] S. Kobayashi, R. Akiyama, *Chem. Commun.* **2003**, 449–460.

[23] S. Kobayashi, *Curr. Opin. Chem. Biol.* **2000**, *4*, 338–345.

[24] P. K. Jal, S. Patel, B. K. Mishra, *Talanta* **2004**, *62*, 1005–1028.

[25] C. H. Hornung, B. Hallmark, R. P. Hesketh, M. R. Mackley, *J. Micromech. Microeng.* **2006**, *16*, 434–447.

[26] B. Hallmark, M. R. Mackley, F. Gadala-Maria, *Adv. Eng. Mater.* **2005**, *7*, 545–547.

[27] B. Hallmark, F. Gadala-Maria, M. R. Mackley, *J. Non-Newtonian Fluid Mech.* **2005**, *128*, 83–98.

[28] EVAL Europe, http://www.eval.be/.

[29] C. H. Hornung, *PhD thesis*, University of Cambridge, UK, **2007**.

[30] Lamina Dielectrics Ltd., http://www.laminadielectrics. com/.

[31] M. T. Reetz, M. Winter, B. Tesche, *Chem. Commun.* **1997**, 147–148.

[32] U. Kolb, S. A. Quaiser, M. Winter, M. T. Reetz, *Chemistry of Materials* **1996**, *8*, 1889–1894.

[33] J. Sedelmeier, S. V. Ley, I. R. Baxendale, *Green Chem.* **2009**, *11*, 683–685.

[34] J. G. Speight, *The Chemistry and Technology of Coal*, Marcel Dekker, New York, **1983**, pp 226 ff.

[35] P. K. Mandal, J. S. McMurray, *J. Org. Chem.* **2007**, *72*, 6599–6601.