CHEMISTRY
A EUROPEAN JOURNAL

DOI: 10.1002/chem.201000948

A Brush-Gel/Metal-Nanoparticle Hybrid Film as an Efficient Supported Catalyst in Glass Microreactors

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Abstract: A polymer-brush-based material was applied for the formation and in situ immobilization of silver and palladium nanoparticles, as a catalytic coating on the inner wall of glass microreactors. The brush film was grown directly on the microchannel interior by means of atom-transfer radical polymerization (ATRP), which allows control over the polymer film thickness and therefore permits the tuning of the number of nanoparticles formed on the channel walls. The wide applicability of the catalytic devices is demonstrated for the reduction of 4-nitrophenol and for the Heck reaction.

Keywords: Heck reaction · heterogeneous catalysis · microreactors · nanoparticles · polymerization · reduction

Introduction

Recently, we reported that an organic catalyst can be efficiently immobilized on the microchannel wall of a silicon-glass microreactor by using oxirane-containing polymer brushes,[1] prepared through atom-transfer radical polymerization (ATRP). Polymer brushes offer a wide variety of macromolecular architectures and consequently are a powerful tool for design and preparation of different types of catalytic polymeric materials. In addition, ATRP, being a controlled living radical polymerization, allows one to tune the number of catalytic groups by simply varying the polymerization time. New routes to obtain designer metal nanoparticles (NPs) that exhibit enhanced catalytic activities are among the main achievements of nanotechnology.[2] Metallic NPs, when used as catalysts, are often considered as "semi-heterogeneous" systems, and are at present at the frontiers of scientific interest in catalysis.[2a] Obtaining high turnover rates for product molecules per unit area of the catalytic device over unit time has been a central issue in the development of heterogeneous catalytic systems. When considering catalytic microfluidic devices, which feature NPs in their channels, this requirement would necessitate enhancing NP loading, ensuring molecular access to the catalytic NPs, and removing of the product molecules from the microchannels that function as catalytic beds. We show here that surface-grafted polymer-brush/metal-NP hybrid films obtained by a facile process can fulfil these requirements and can provide highly efficient catalytic microreactors.[3]

The small characteristic dimensions of microfluidic devices—that is, systems composed of flow channels with cross-sectional dimensions in the sub-millimeter range—result in systems with high surface-to-volume ratios. The specific surface areas of microchannel reactors are between 10000 and 50000 $m^2 m^{-3}$, whereas traditional reactors are generally about 100 $m^2 m^{-3}$ and in rare cases reach 1000 $m^2 m^{-3}$. This feature creates suitable environments for heterogeneous catalysis, since a large interfacial area between different phases,

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Supporting information for this article is available on the WWW under http://dx.doi.org/10.1002/chem.201000948.

such as gas–liquid and gas–liquid–solid can be achieved, as well as a high catalyst loading. Moreover, most of the catalytic reactions performed in microreactors are performed under addition of continuous flow. Hence, the product flows continuously out of the channel, minimizing possible side-product accumulation and leaving the catalyst always available to react with fresh reagent solutions. Many examples have been reported on the use of metal catalysts in microreactors.[4] Packed-bed microreactors using palladium powder[5] or functionalized Merrifield resins[6] have been applied for heterogeneous catalysis. However, packed-bed microreactors may cause pressure drops along the channel,[7] and it is difficult to control the exact residence time. To overcome these disadvantages metal catalysts have been immobilized in microchannel walls by anchoring microencapsulated Pd[8] and Au,[9] polysilane with metal oxide,[10] Pd^{2+} bound to organic polymer monoliths[11] or embedded in a catalytic membrane,[12] batchwise synthesized metal nanoparticles,[13] and metal films.[14] One example of in-situ synthesis of gold nanoparticles in a poly(dimethylsiloxane) (PDMS) microfluidic chip was very recently published.[15] Due to the sensitivity of the polymeric material to organic solvents, this chip can only be used for (bio)applications in water. Herein we describe that silver and palladium NPs, prepared in situ and immobilized in a polymer-brush-gel grown on the interior of a glass microreactor, and of which the number can be easily tuned, give rise to considerable reaction rates of metal-catalyzed reactions.

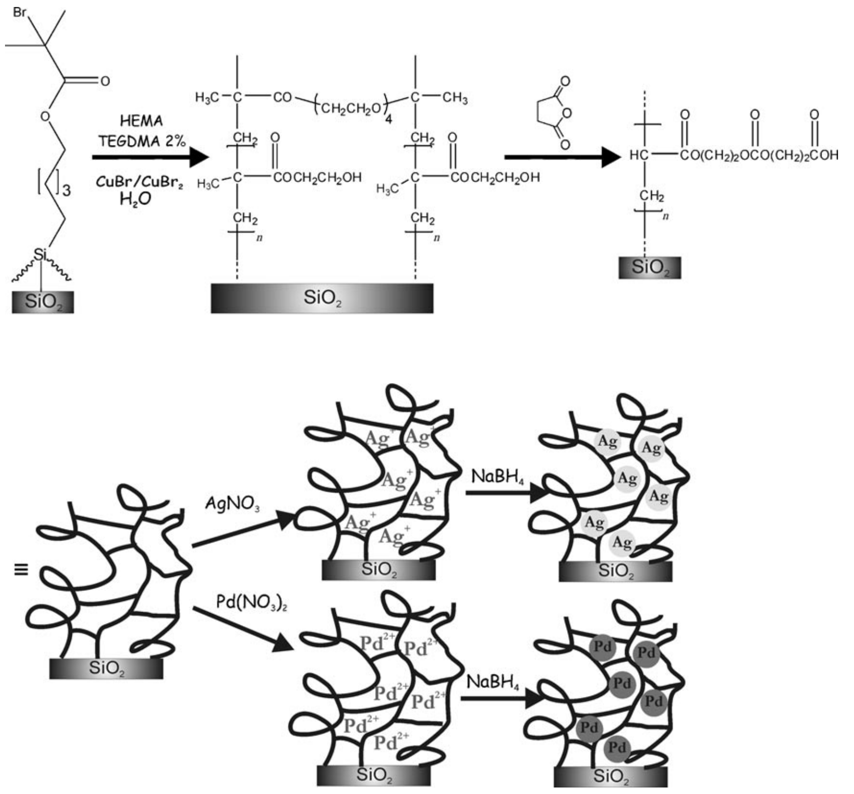
Results and Discussion

To study the conditions to immobilize the catalytic nanoparticles on the microreactor interior as well as their characteristics, the brush/NP hybrid film was also fabricated on silicon oxide surfaces following the procedure that we recently developed for gold substrates[16] (Scheme 1).

First a monolayer of ATRP initiator was grown on silicon oxide substrates.[17] Subsequently, a solution of 2-hydroxyethyl methacrylate (HEMA) with 2% tetraethylene glycol dimethacrylate (TEGDMA) in water in the presence of 2-2′-bipyridyl, CuBr, and $CuBr_2$, was used to grow the brush-gel (PHEMA-PEG) by means of ATRP. To introduce carboxylic groups, the PHEMA-PEG layers were reacted with a 0.1 M solution of succinic anhydride in dry pyridine for 24 h. Subsequent incubation of the substrate in a 0.05 M solution of silver nitrate in water or palladium nitrate in DMSO/water (3:1), overnight, led to the formation of the carboxylate–silver/palladium complexes. Then, the material was treated with a 1.3 mM solution of sodium borohydride ($NaBH_4$) in water for 10 s or 3 min, to give the Ag and Pd NPs, respectively.[18] The results of each step were characterized by atomic force microscopy (AFM), ellipsometry, and FT-IR (see the Supporting Information).

From AFM analysis of the brush/NP hybrid layers obtained after 10 min polymerization time, the average size and the size distribution of the NPs were determined. An average diameter of 20 ± 5 and 30 ± 3 nm was found for Ag and Pd NPs, respectively, at the given amount of cross-linking agent[16] (see the Supporting Information). The nanoparticles were not shown to aggregate or detach following immersion in a suitable solvent for the brush matrix. This is presumably due to stabilization by oxygen atoms present both on the TEGDMA and on the HEMA functions, and by steric stabilization which is gained in the brush structure. Electrostatic interactions between the NPs and the brush are supposed to be slightly repulsive in basic solutions. In this case the carboxylic acid functions would be partially negatively charged and they would repel the outer surface of NPs, because of the presence of adsorbed negative borohydride ions.[19]

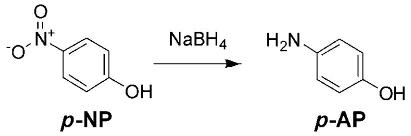
The same procedure used for the silicon oxide substrates was followed to fabricate brush/NP hybrid layers on the



Scheme 1. General scheme for initiator immobilization, surface initiated polymerization of HEMA-TEGDMA, and in situ formation of Ag and Pd NPs.

channel interior of a glass microreactor with typical dimensions of 110 μm in width, 50 μm in depth, and 300 mm in length (see the Supporting Information). The brush/NP hybrid film was grown on the microchannel interior in a stop-flow mode, varying the polymerization time between 1.5–20 min in order to obtain different polymer layer thicknesses, and consequently a different number of functional groups. PHEMA-PEG was then reacted with a solution of succinic anhydride in the continuous-flow (0.1 $\mu L\,min^{-1}$) mode. Afterwards an aqueous solution of silver nitrate was allowed to flow through the microchannels overnight (0.1 $\mu L\,min^{-1}$). Upon salt reduction within the polymer matrix, the microchannel turned yellow indicating the formation of Ag NPs.

Microreactors bearing Ag NPs formed in situ were used for the reduction of 4-nitrophenol[20] (***p*-NP**) to 4-aminophenol (***p*-AP**) in the presence of $NaBH_4$ at room temperature, in water (Scheme 2).



Scheme 2. Reduction of 4-nitrophenol (***p*-NP**) to 4-aminophenol (***p*-AP**) in water at room temperature.

The brush/NP hybrid layer turned out to be very efficient in the catalysis. In all experiments performed in the presence of the catalytic coating, the reaction was complete within a few seconds. No reaction was observed when the reagents flowed through microreactors only coated with PHEMA-PEG, proving that the Ag NPs were the catalytically active species. The reaction times were varied by changing the flow rates from 20 to 0.1 $\mu L\,min^{-1}$ and the formation of the product was monitored using UV/Vis detection, measuring the extinction of the solution at 400 nm. For these experiments the microreactor was placed in a custom-built chip holder designed for fitting fused silica fibres into the inlet/outlet reservoirs.

A kinetic analysis of the reduction of ***p*-NP** was carried out by using an excess of $NaBH_4$. Measurements at different concentrations of ***p*-NP** ($4–8\times10^{-5}$ M) were carried out in microreactors with a coating of 47 nm obtained after 10 min polymerization time, keeping the excess concentration of $NaBH_4$ constant (Figure 1).

The experimental data were fitted to a first-order rate equation. The values of the rate constant of $(34\pm2)\times10^{-3}\,s^{-1}$ for the conversion of ***p*-NP** were the same, within experimental error, for different initial concentrations of ***p*-NP**, as expected for first-order conditions. The $NaBH_4$ concentration was varied in the range $2.5–5\times10^{-3}$ M. The pseudo-first-order rate constants were proportional to the concentration of $NaBH_4$, indicating a first-order dependence of $NaBH_4$. The resulting second-order rate constant is $13\pm1\,s^{-1}M^{-1}$.

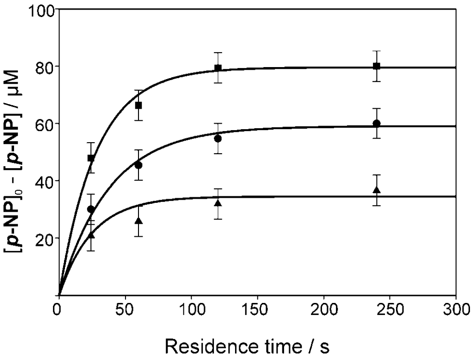


Figure 1. Conversion of ***p*-NP** catalyzed by Ag-NPs in a microreactor at different initial concentrations of 4-nitrophenol ([***p*-NP**]$_0$): (■) = 8×10^{-5} M, (●) = 6×10^{-5} M, (▲) = 4×10^{-5} M ([$NaBH_4$] = 2.5×10^{-3} M), hydrogel thickness 47 nm.

The thickness of the brush/NP hybrid layers grown on the microchannel interior was measured by high-resolution scanning electron microscopy (HR-SEM) and found to be 47 ± 5.5 and 100 ± 13 nm after 10 and 20 min polymerization time, respectively[21] (Figure 2). This analysis was performed after cleaving the devices (see Supporting Information).

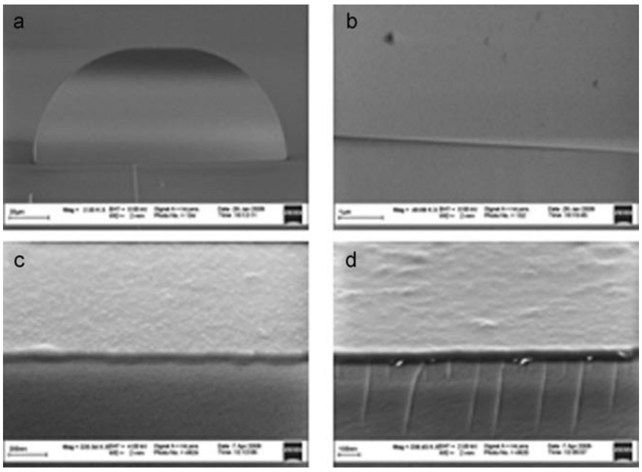


Figure 2. High-resolution scanning electron microscopy (HR-SEM) of a) microchannel cross section without polymer; b) zoom of microchannel cross section without polymer; c) zoom microchannel cross section of polymer film with silver nanoparticles (10 min polymerization time, thickness 47 nm); d) zoom microchannel cross section of polymer film with palladium nanoparticles (20 min polymerization time, thickness 100 nm).

Experiments carried out on microreactors with different brush/NP hybrid layer thicknesses showed a correlation with the catalytic activity (Figure 3a). A linear dependence was found between the polymerization time and the pseudo-first-order rate constants k_{obs} (Figure 3b). This result indicates that, since PHEMA-PEG is completely swollen at pH 9,[16] that is the pH of the reaction mixture, the entire brush structure is involved in the catalysis, and consequently

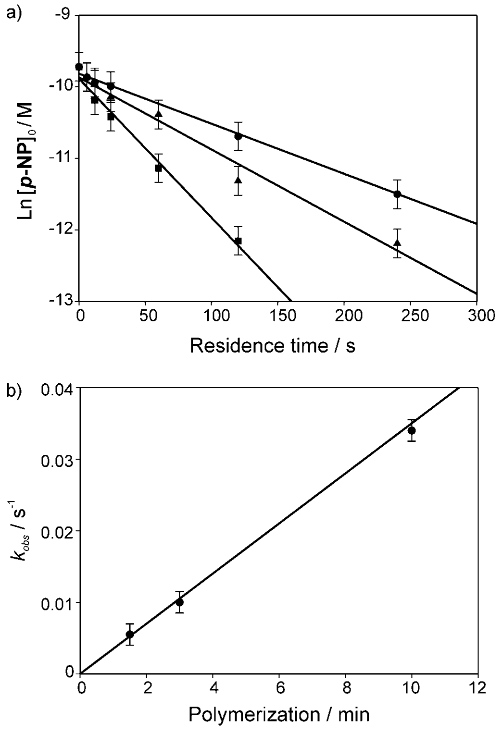


Figure 3. a) Conversion of ***p*-NP** in microreactors catalyzed by a polymer/Ag NP layer created with different polymerization times: (■) = 10 min, (▲) = 3.5 min, (●) = 1.5 min, ([NaBH$_4$] = 2.5×10^{-3} M, [*p*-**NP**]$_0$ = 6×10^{-5} M). b) Dependence of observed pseudo first-order rate constant k_{obs} as a function of polymerization time, for the reduction of ***p*-NP** catalyzed by Ag NPs.

that the nanoparticles are formed within the whole polymer matrix.

As a second example, Pd NPs were formed inside the brush-gel structure following the same procedure. Upon reduction of the palladium ions (Scheme 1) the microchannel turned black, indicating the formation of the Pd NPs. Microreactors with immobilized Pd NPs were used for carrying out the reduction[18] of ***p*-NP** to ***p*-AP**, using the same conditions as applied with the Ag NPs. Kinetic analysis performed with catalytic microreactors with a 47 nm coating gave k_{obs} of $(33\pm3)\times10^{-3}$ s^{-1}. The second-order rate constant is 6.6 ± 0.7 s^{-1}M^{-1}. Microreactors with different concentrations of Pd NPs also exhibited a linear dependence of the k_{obs} and the polymerization time (Figure 4).

To compare the catalytic activity of the Ag and Pd NPs, the second-order rate constants obtained for ***p*-NP** reduction catalyzed by Ag (k_{Ag}) and Pd NPs (k_{Pd}) were normalized to the whole nanoparticle surface contained in the system (see the Supporting Information). In line with the literature data,[18] Pd NPs showed a higher catalytic activity than Ag NPs, being $k_{Ag}=0.20\times$ s^{-1}M^{-1}m^{-2}L and $k_{Pd}=0.36\times$ s^{-1}M^{-1}m^{-2}L.

The silver and palladium catalytic devices exhibited no leaching and could be re-used for at least four months, without showing a decrease of catalytic activity, when stored under nitrogen.

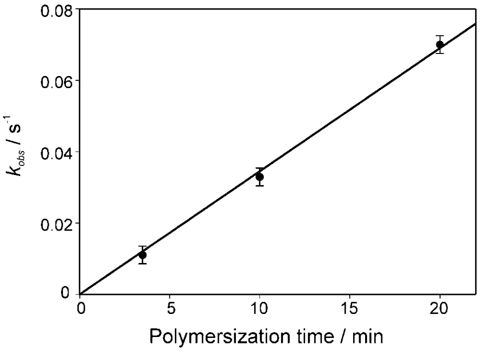
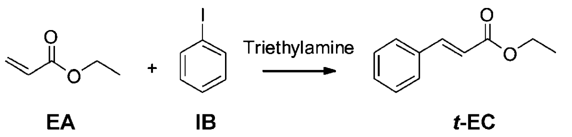


Figure 4. Dependence of observed pseudo first-order rate constant k_{obs} as a function of polymerization time, for the reduction of ***p*-NP** catalyzed by Pd NPs.

To demonstrate the wider applicability of our system, microreactors with Pd NPs were used to perform the Heck reaction[22] between ethyl acrylate (**EA**) and iodobenzene (**IB**), in the presence of triethylamine, to give *trans*-ethyl cinnamate (***t*-EC**) in DMSO at 80 °C (Scheme 3).



Scheme 3. Heck reaction between ethyl acrylate (**EA**) and (**IB**) to give *trans*-ethyl cinnamate (***t*-EC**) in DMSO at 80 °C.

The formation of the product, ***t*-EC**, was monitored in real-time by measuring the increase of the absorption peak at 290 nm.[1] A 50 μL sample of the reaction product was also analyzed by ^{1}H NMR spectroscopy showing the exclusive formation of ***t*-EC**; no side products could be detected.

When the reaction was performed in the catalytic device only coated with PHEMA-PEG no product was formed. The reaction time was varied by changing the flow rate between 0.2–0.06 μL min^{-1}; after 26 min **IB** was fully converted into ***t*-EC** (Figure 5).

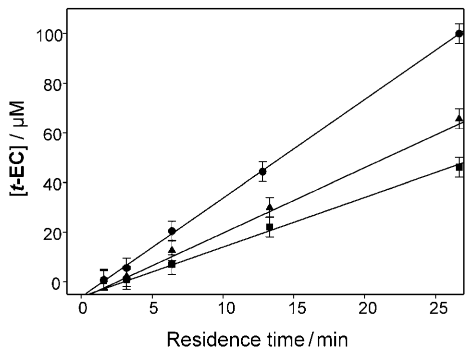


Figure 5. Formation of ***t*-EC** catalyzed by Pd NPs in a microreactor at different initial concentrations of [**IB**], (■) = 4.5×10^{-5} M, (▲) = 6.5×10^{-5} M, (●) = 10^{-4} M, **EA** = 0.01-0.02 M, in DMSO at 80 °C, hydrogel thickness 100 nm.

We also conducted a kinetic study using an excess of **EA**. Data obtained carrying out experiments using different concentrations of **EA** (0.01–0.02 M) and **IB** ($50–100\times10^{-6}$ M) showed a short induction period,[22a] and they fitted a zero-order rate equation. The rate constant of $(6.6\pm0.3)\times10^{-4}\,\text{s}^{-1}$ (Figure 5) was the same for each concentration, as expected for zero-order conditions. Nevertheless, the rate constants depend on the concentration of **IB**, being $(6.7\pm0.3)\times10^{-8}$, $(4.3\pm0.2)\times10^{-8}$, and $(3.3\pm0.16)\times10^{-8}\,\text{M}\,\text{s}^{-1}$ for **IB** concentrations of 10^{-4}, 6.5×10^{-5}, and 4.5×10^{-5} M, respectively (Figure 5).

This can be attributed to a leaching phenomenon. Inherent to the mechanism of the Heck reaction, Pd^{2+} ions are generated when using Pd^0 NPs, for which **IB** acts as the oxidant.[23] As a consequence leaching of catalyst will take place.[24] Inductively coupled plasma-mass spectrometry (ICP-MS) analysis of one of the reaction samples showed the presence of 8 ppm of Pd. There was no leaching when only DMSO was flowed through the channel at 80 °C, and in the observed induction period. Thus, the leached palladium is the active catalyst and is dependent on the initial concentration of **IB** and on the residence time applied.

Devices with a 100 nm polymer-hydrogel layer could be re-used for about 40 h before showing decrease of activity. On the other hand, devices prepared with 10 and 3.5 min polymerization time, exhibited diminished catalytic activity after being employed for about 17 and 7 h, respectively.

Conclusion

In conclusion, we have demonstrated that an easily tuneable brush-gel/metal-nanoparticle hybrid system in a microchannel is very efficient in heterogeneously catalyzed reactions in microreactors. The metal nanoparticles are stable during reduction of 4-nitrophenol, and the number of nanoparticles can simply be tuned by varying the polymerization time. In the case of the Heck reaction, the hybrid nanostructure acts as a reservoir, releasing Pd catalytic active species into solution. This shows that our approach is versatile and can be efficiently used for conducting a variety of metal-catalyzed chemical reactions in microreactors.

Experimental Section

Materials and equipment: All commercial reagents were purchased from Aldrich Chemicals. All chemicals were used without purification unless specified. 3-(5′-Trichlorosilylpentyl) 2-bromo-2-methylpropionate was synthesized following a literature procedure.[25] CuBr (99.999 %) was stored in a vacuum desiccator. Methanol and ethanol (VWR, analytical reagent grade) were used without further purification. Toluene (VWR, analytical reagent grade) was distilled over sodium. Pyridine was distilled over calcium hydride prior to use. Water was purified with the Milli-Q pluse (MILLIPORE, $R=18.2\,\text{M}\Omega\,\text{cm}$) ultra pure water system. Ellipsometry measurements were performed with a plasmon ellipsometer at a fixed angle of 70° ($\lambda=632.8$ nm) assuming a refractive index of 1.5 for the polymer. The sample morphology and step-height of the brush films were measured by using an atomic force microscope (AFM) Nanoscope III (Veeco digital instrument, USA) in the tapping mode, equipped with a Si_3N_4 tip with a J scanner at a scan rate of 0.6 Hz. FT-IR spectra were recorded using a BioRad FTS-60 A spectrometer. Spectra of polymer films were taken in transmission mode with a bare silicon wafer as background. Polymer films in microreactors were analyzed by high-resolution scanning electron microscopy (HR-SEM), breaking the device and measuring the thickness at the channel cross section (see Supporting Information). All SEM images were taken with a HR-LEO 1550 FEF SEM instrument. The UV measurements to follow the reduction of 4-nitrophenol were performed with a standard Varian Cary 300 spectrophotometer. ^{1}H NMR spectra were recorded on a Varian Unity INOVA (300 MHz). ICP-MS was performed by MiPlaza Materials Analysis of Philips Research Europe at Eindhoven (The Netherlands).

Microreactor fabrication: The microfluidic devices used in this work were made of borosilicate glass (Borofloat 33, Schott Technical Glasses, Germany). Borosilicate glass substrates (100 mm diameter, thickness 1.1 mm) were ultrasonically cleaned in isopropanol (15 min) and fuming 100 % nitric acid (15 min), followed by quick-dump rinsing in de-mineralized water and dry spinning. Subsequently, the topside of the substrates was sputter-coated with a gold–chromium layer (200 nm Au, 15 nm Cr). This metal thin-film was patterned by using photoresist (standard UV-lithography), Au and Cr etchant, and the stack of photoresist/Au/Cr acted as a mask-layer during isotropic etching of the serpentine-shaped microchannels (depth 50 μm, width 110 μm, length 300 mm) with 25 % hydrofluoric acid. After etching, the substrates were ultrasonically rinsed with flushing DI-water (5 min), followed by removal of the photoresist layer and the Au/Cr thin-film. A photosensitive foil was attached to the topside of other substrates. In this foil access holes were defined using lithography, and powderblasting was used to make access holes through the substrates. After removal of the foil, ultrasonic cleaning with demineralized water and rinsing with 100 % nitric acid, substrates with microchannels and substrates with access holes were aligned and prebonded[26] with the following procedure: after cleaning both glass substrates, the wafers are aligned to each other and contacted. This results in a bond with a rather low bond strength, which is commonly referred to as a prebond. A prebonded waferstack becomes a very robust bond after an annealing step at high temperature (here 1 h at 600 °C). This results in a stack of which the two individual glass wafers cannot be discriminated anymore, and with a very strong bond. The waferstacks were diced obtaining individual chips of 20 × 10 mm.

Setup of the microfluidic device: In all experiments sample solutions were mobilized by means of a PHD 22/2000 series syringe pump (Harvard Apparatus, United Kingdom) equipped with 250 μL flat tip syringes (Hamilton). Syringes were connected to fused silica capillaries (100 μm i.d.) by means of Upchurch NanoportTM assembly parts (i.e., NanoTightTM unions and fittings, Upchurch Scientific Inc. USA). During the experiments the microreactor was placed in a home-built chip holder designed for fitting fused silica fibers into the inlet/outlet chip reservoirs by means of commercially available Upchurch NanoportTM assembly parts. The temperature in the microreactor was controlled by interfacing a thermoelectric module with a heat sink to the microreactor. The temperature variation on the glass surface of the microreactor measured with a thermocouple was less then ± 0.1 °C.

On-line UV/Vis detection: The formation of *trans*-ethyl cinnamate (***t*-EC**) was followed using a micro HPLC flow-through cell (ZEUTEC opto-eletronik, Germany), with a spectral UV/VIS/NIR range of 250–2500 nm, an optical path length of 5 mm, and an internal volume of 1 μL. The flow cell is connected by means of two optical fibers (SR 600 nm, Ocean optics Inc., The Netherlands) to a miniature deuterium halogen light source (DT-Mini-2-GS, Mikropack GmbH, Germany) and to a high-resolution miniature fiber optic spectrometer (HR4000, Ocean optics Inc., The Netherlands).

Synthesis of the catalytic polymer coating: Trichlorosilane initiator immobilization and the polymer brushes synthesis on the silicon oxide surface were carried out following a published procedure.[16] Microchannels and silicon wafers were first cleaned with a Piranha solution (H_2SO_4:H_2O_2 3:1) and then copiously rinsed with water and dried with a stream of nitrogen. (Caution: Piranha solution is a very strong oxidant and reacts violently with many organic materials). The cleaned silicon wafers were soaked in a solution of 3-(5′-trichlorosilylpentyl) 2-bromo-2-methylpropionate (20 μL) in dry toluene (10 mL) for 14 h under argon. For the synthesis in the device the same solution was flowed for 14 h at a flow rate of 0.1 μL min^{-1}. Silicon wafers and microchannel were rinsed with dry toluene, ethanol, and acetone and dried with a stream of nitrogen.

A solution of 2-hydroxyethyl methacrylate (HEMA; 5 mL, 5.36 g, 41 mmol) with 2 % tetraethylene glycol dimethacrylate (TEGDMA) in water (4 mL) was degassed using the freeze–pump–thaw method (in a sealed Schlenk vessel). [The solution was frozen by immersion in liquid nitrogen. When the solvent was completely frozen the flask is kept under high vacuum for 5 min, with the flask still immersed in the liquid nitrogen. The flask was then closed and warmed until the solvent has completely melted. This process was repeated three times and after the last cycle the flask was filled with argon.] CuBr (53 mg, 0.37 mmol), $CuBr_2$ (6 mg, 0.02 mmol), and 2,2′-bipyridyl (0.350 g, 2.24 mmol) were added to this solution. To dissolve all solids, the mixture was stirred for 30 min under a continuous flow of argon. Afterwards an initiator coated silicon wafer was placed in a Schlenk tube and the flask sealed with a septum. The tube was filled with argon and the monomer solution syringed inside. For the polymerization in the device, the same solution was syringed through the microchannel till the device was completely filled. The solution was kept in contact with the silicon wafer and with the microchannel for 1.5–20 min. After the polymerization, the silicon wafer and the microchannel were rinsed with methanol and water, and dried with a stream of nitrogen. In the next step the silicon wafers were soaked in a 0.1 M solution of succinic anhydride for 24 h. The same solution was flowed with a flow rate of 0.1 μL min^{-1} through the microreactor. After 24 h they were rinsed with methanol and water and subsequently dried with a stream of nitrogen. For the preparation of brush-film/silver and palladium nanoparticle hybrid layers, all samples were first incubated overnight in a 0.5 M aqueous solution of $AgNO_3$ and $Pd(NO_3)_2$ in DMSO/water (3:1), respectively. The same solutions were flowed at a flow rate of 0.1 μL min^{-1} through the microrecator. Subsequently, the silicon wafer and microchannel were rinsed with milliQ water. Then the material was treated with a 1.3 mM solution of sodium borohydride ($NaBH_4$) for 10 s for the formation of silver nanoparticles, and with a 10 mM solution of sodium borohydride ($NaBH_4$) for 3 min for the formation of palladium nanoparticles.

Data analysis: The error bars in Figures 1 and 3–5 represent the standard deviation calculated over nine measurements for each point: three different measurements with three different catalytic microreactors. The standard deviation of the height of the brush/NP layers determined with HR-SEM was calculated over six measurements, namely three different points in two microreactors with a polymer grown for 10 and 20 min, respectively. The nanoparticles size distribution was determined by measuring the size of at least 50 metallic nanoparticles with HR AFM from micrographs recorded in different regions of three samples obtained after a polymerization time of 10 min.

Acknowledgements

We thank NanoNed, a nanotechnology program of the Dutch ministry of Economic Affairs (F.C.) and the Biopolysurf Marie Curie research network of the EU (E.M.B.) for the financial support. We thank also Clemens Padberg, Janet Acigkoz, and XiaoFeng Sui for the precious technical support.

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[1] F. Costantini, W. P. Bula, R. Salvio, J. Huskens, H. Gardeniers, D. N. Reinhoudt, W. Verboom, *J. Am. Chem. Soc.* **2009**, *131*, 1650.

[2] a) D. Astruc, F. Lu, J. R. Aranzaes, *Angew. Chem.* **2005**, *117*, 8062; *Angew. Chem. Int. Ed.* **2005**, *44*, 7852; b) J. Grunes, J. Zhu, G. A. Somorjai, *Chem. Commun.* **2003**, 2257.

[3] For loading of brushes with nanoparticles in general, see for example: a) I. Tokarev, I. Tokareva, V. Gopishetty, E. Katz, S. Minko, *Adv. Mater.* **2010**, *22*, 1412; b) M. Schrinner, M. Ballauf, Y. Talmon, Y. Kauffmann, J. Thun, M. Möller, J. Breu, *Science* **2009**, *323*, 617; c) Q. Ye, X. Wang, H. Hu, D. Wang, S. Li, F. Zhou, *J. Phys. Chem. C* **2009**, *113*, 7677; d) I. Tokarev, I. Tokareva, S. Minko, *Adv. Mater.* **2008**, *20*, 2730; e) S. Gupta, P. Uhlmann, M. Agrawal, S. Chapuis, U. Oertel, M. Stamm, *Macromolecules* **2008**, *41*, 2874.

[4] a) M. Brivio, W. Verboom, D. N. Reinhoudt, *Lab Chip* **2006**, *6*, 329; b) J. Kobayashi, Y. Mori, S. Kobayashi, *Chem. Asian J.* **2006**, *1*, 22; c) P. Watts, C. Wiles, *Chem. Commun.* **2007**, 443.

[5] P. He, S. J. Haswell, P. D. I. Fletcher, *Lab Chip* **2004**, *4*, 38.

[6] S. J. Haswell, B. O'Sullivan, P. Styring, *Lab Chip* **2001**, *1*, 164.

[7] B. P. Mason, K. E. Price, J. L. Steinbacher, A. R. Bogdan, D. T. McQuade, *Chem. Rev.* **2007**, *107*, 2300.

[8] J. Kobayashi, Y. Mori, K. Okamoto, R. Akiyama, M. Ueno, T. Kitamori, S. Kobayashi, *Science* **2004**, *304*, 1305.

[9] N. Wang, T. Matsumoto, M. Ueno, H. Miyamura, S. Kobayashi, *Angew. Chem.* **2009**, *121*, 4838; *Angew. Chem. Int. Ed.* **2009**, *48*, 4744.

[10] M. Ueno, T. Suzuki, T. Naito, H. Oyamada, S. Kobayashi, *Chem. Commun.* **2008**, 1647.

[11] A. Gömann, J. A. Deverell, K. F. Munting, R. C. Jones, T. Rodemann, A. J. Canty, J. A. Smith, R. M. Guijt, *Tetrahedron* **2009**, *65*, 1450.

[12] Y. M. A. Yamada, T. Watanabe, K. Torii, Y. Uozomi, *Chem. Commun.* **2009**, 5594.

[13] a) E. V. Rebrov, A. Berenguer-Murcia, H. E. Skelton, B. F. G. Johnson, A. E. H. Wheatley, J. C. Schouten, *Lab Chip* **2009**, *9*, 503; b) E. V. Rebrov, A. E. Klinger, A. Berenguer-Murcia, E. Sulman, J. C. Schouten, *Org. Process Res. Dev.* **2009**, *13*, 991.

[14] G. Shore, S. Morin, M. G. Organ, *Angew. Chem.* **2006**, *118*, 2827; *Angew. Chem. Int. Ed.* **2006**, *45*, 2761.

[15] Q. Zhang, J. J. Xu, Y. Liu, H. Y. Chen, *Lab Chip* **2008**, *8*, 352.

[16] E. M. Benetti, X. F. Sui, S. Zapotoczny, G. J. Vancso, *Adv. Funct. Mater.* **2010**, *20*, 939.

[17] S. Edmondson, W. T. S. Huck, *J. Mater. Chem.* **2004**, *14*, 730.

[18] Y. Mei, Y. Lu, F. Polzer, M. Ballauff, M. Drechsler, *Chem. Mater.* **2007**, *19*, 1062.

[19] a) S. Behrens, J. Wu, W. Habicht, E. Unger, *Chem. Mater.* **2004**, *16*, 3085; b) D. L. Van Hyning, C. F. Zukoski, *Langmuir* **1998**, *14*, 7034.

[20] K. Esumi, R. Isono, T. Yoshimura, *Langmuir* **2004**, *20*, 237.

[21] Devices with a brush-gel thickness obtained with a polymerization time <3.5 min, could not be accurately measured by HR-SEM. Glass is a non-conductive material (i.e., electrically not conductive), due to which surface charging occurs, leading to limitations in the SEM resolution. This effect becomes an issue for features <5 nm.

[22] a) K. Okamoto, R. Akiyama, H. Yoshida, T. Yoshida, S. Kobayashi, *J. Am. Chem. Soc.* **2005**, *127*, 2125; b) H. Bönnemann, W. Brijoux, A. Schulze Tilling, K. Siepen, *Top. Catal.* **1997**, *4*, 217.

[23] A. Biffis, M. Zecca, M. Basato, *Eur. J. Inorg. Chem.* **2001**, 1131.

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

[25] M. Husseman, E. E. Malmström, M. McNamara, M. Mate, D. Mecerreyes, D. G. Benoit, J. L. Hedrick, P. Mansky, E. Huang, T. P. Russell, C. J. Hawker, *Macromolecules* **1999**, *32*, 1424.

[26] R. M. Tiggelaar, F. Benito-Lopez, D. C. Hermes, H. Rathgen, R. J. M. Egberink, F. G. Mugele, D. N. Reinhoudt, A. van den Berg, W. Verboom, H. Gardeniers, *Chem. Eng. J.* **2007**, *131*, 163.

Received: April 14, 2010