J|A|C|S
COMMUNICATIONS

Nanostructure Based on Polymer Brushes for Efficient Heterogeneous Catalysis in Microreactors

Francesca Costantini,† Wojciech P. Bula,‡ Riccardo Salvio,§ Jurriaan Huskens,†
Han J. G. E. Gardeniers,‡ David N. Reinhoudt,†,§ and Willem Verboom*,†

Molecular Nanofabrication (MnF), Mesoscale Chemical Systems (MCS), and Supramolecular Chemistry and Technology (SMCT), University of Twente, MESA+ Institute for Nanotechnology, P.0. Box 217, 7500 AE Enschede, The Netherlands

Received September 25, 2008; E-mail: w.verboom@utwente.nl

The advantages of using microreactors to enhance the efficiency of chemical reactions have been described in several reviews.[1−3] The improved performance is due to faster heat and mass transfer as a result of the enormously increased surface-to-volume ratio, when compared with conventional laboratory equipment.[4] This aspect is particularly interesting for heterogeneous catalysis,[5] in addition to the use of continuous flow.

In literature, several methods to incorporate organic catalysts in microreactors have been reported, for example, "packed-bed" microreactors[6] in which the catalysts are attached to polymeric particles entrapped in the microchannel. Despite the good conversion obtained, the main drawback is the swelling of many polymeric materials. This may cause pressure drop along the microchannel, resulting in variations in the residence time for pressure-driven microreactors. This problem can be overcome using electroosmotic flow,[7] but this is limited to polar solvents.

Although immobilization of metal catalysts[8] and enzymes[9,10] to microreactor channel walls has been described, to the best of our knowledge there is only one example where an organic catalyst was anchored onto the microchannel interior.[11]

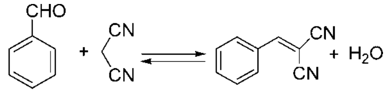
In this communication we report the use of polyglycidylmethacrylate (PGMA) polymer brushes as a new method to form a polymeric nanostructure to covalently attach an organic catalyst to the inner wall of a silicon−glass microreactor.

PGMA brushes[12] contain a large number of epoxy groups that can be used for linkage of an organic catalyst via nucleophilic attack. Polymer brushes are prepared via atom transfer radical polymerization (ATRP).[13] By varying the polymerization time and consequently the nanostructure thickness, the amount of catalyst can be easily tuned.

To study our approach, 1,5,7-triazabicyclo[4.4.0]dec-5-ene (TBD)[14] was attached to the PGMA polymer brushes. The Knoevenagel condensation reaction between benzaldehyde (**1**) and malononitrile (**2**) to give 2-benzylidene malononitrile (**3**) (Scheme 1) was chosen as a model reaction to study the performance of these catalytic devices.

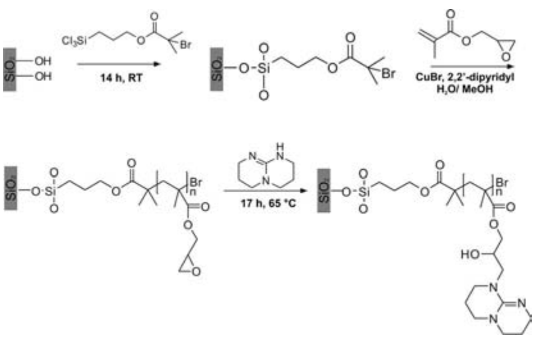
An initial experiment was carried out using a microreactor in which the inner surface was coated with a monolayer of TBD. The formation of the product (**3**) was followed in real time, by using in-line UV−vis detection, to give a second-order rate constant of $(2.0 \pm 0.2) \times 10^{-3}\ s^{-1}\ M^{-1}$. The monolayer contains 0.7 μg of TBD as measured by X-ray photoelectron spectroscopy (XPS).

Scheme 1. Knoevenagel Condensation Reaction between Benzaldehyde (**1**) and Malononitrile (**2**) in Acetonitrile at 65 °C



The fabrication of the catalytic nanostructure based on polymer brushes was first studied on a flat silicon oxide surface. PGMA polymer brushes[12] were synthesized according to the procedure summarized in Scheme 2. Subsequently, the polymer coated surfaces were reacted in a 0.1 M solution of TBD in ethanol at 65 °C for 17 h (Scheme 2). Upon reaction of the oxirane groups of the polymer with TBD, the thickness of the layer increased from 180 nm (obtained after 2 h of polymerization) to about 230 nm as measured by ellipsometry and atomic force microscopy (AFM) (see Supporting Information). This thickness increase suggests that the reaction between the oxirane groups and the TBD occurred.

Scheme 2. General Scheme for Initiator Immobilization, Surface-Initiated Polymerization of GMA, and Reaction with TBD



Analysis of the surfaces by transmission FTIR spectroscopy, before and after the reaction with TBD, showed the complete disappearance of the epoxide stretching band at 910 cm^{-1} indicating that all oxirane units reacted with TBD[15] (see Supporting Information).

The inner walls of several microreactors (100 μm width and depth, 103 cm length), see Figure 1, were coated with PGMA polymer brushes by filling the channel with a solution of glycidyl methacrylate (GMA) monomer in MeOH:H_2O 4:1 in the presence of CuBr and 2-2′-bipyridyl and leaving the solution inside for 20−120 min. To obtain different polymer thicknesses and consequently different numbers of catalytic units, we varied the reaction time. Afterward, a 0.1 M solution of TBD in EtOH was flowed through the channel at 65 °C for 17 h. The Knoevenagel condensation reaction between **1** and **2** in acetonitrile was carried out in these catalytic microreactors at 65 °C, in continuous flow. The formation of the condensation product **3** was monitored in real time by in-line UV−vis detection (see Supporting Information).

---

† Molecular Nanofabrication.
‡ Mesoscale Chemical Systems.
§ Supramolecular Chemistry and Technology.

10.1021/ja807616z CCC: $40.75

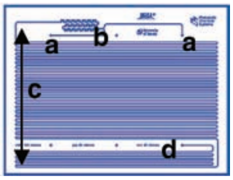


Figure 1. Silicon-glass microreactor (a) inlets, (b) mixing zone, (c) reaction zone, and (d) outlet.

The reaction times were varied by changing the flow rates from 20 to 0.2 μL/min. 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.

To perform a kinetic analysis of the Knoevenagel condensation reaction, an excess of malononitrile **2** was used to achieve pseudo-first-order conditions. The polymeric coating turned out to be highly effective in the catalysis. In all experiments carried out in the presence of the catalytic coating the reaction was complete in a few minutes. No reaction was observed when the reagents were flowed into a microreactor coated with unmodified PGMA brushes for 2 h. This proved that TBD is the catalytically active species. The experimental data were fitted to a first-order rate equation. Measurements at different concentrations of **1** were carried out in a microreactor with a layer thickness of 150 nm, keeping constant the concentration of **2** (Figure 2a); hourly output at 75 μM of **1** is 1.2 mM of **3**. The values of the rate constants at different benzaldehyde **1** concentrations were the same, within experimental error. The value of the pseudo-first-order rate constant is $(1.3 \pm 0.1) \times 10^{-2}$ s^{-1} ([**2**] = 125 mM).

Also the malononitrile **2** concentrations were varied in the range 31−125 mM. The rate constants are proportional to the concentration of **2**, as expected for a pseudo-first-order reaction. The second-order rate constant is 0.10 ± 0.01 s^{-1} M^{-1}. After each experiment the catalytic nanostructure was regenerated by flushing a 0.1 M solution of triethylamine through the microchannel. The PGMA-TBD coated devices showed no decreasing of the catalytic activity or leaching after being used for 25 times. With the catalytic device, stored under nitrogen, the results of the experiments were reproducible also when repeated, after 30 days.

Experiments carried out with microreactors bearing coatings with different thicknesses showed a relation with the catalytic activity. The thicknesses (θ) of the polymeric coatings were measured by high resolution scanning electron microscopy (HR-SEM). These analyses were carried out on the channel cross section after breaking the device (see Supporting Information).

A linear dependence was found between θ and the pseudo-first-order rate constant k_{obs} (Figure 2b). For PGMA-TBD thicknesses of 50 and 400 nm, the k_{obs} values are $(6.9 \pm 0.7) \times 10^{-3}$ and $(3.7 \pm 0.4) \times 10^{-2}$ s^{-1}, respectively ([**2**] = 125 mM; [**1**] = 50 μM). On the basis of this result, we conclude that the whole nanostructure is involved in the catalysis and that reaction does not occur only at the interface, but the reagents diffuse throughout the coating to reach all catalytic units. This also proves the complete swelling of the PGMA polymer brushes in acetonitrile. Other solvents have not been studied here, since the rate of the Knoevenagel condensation reaction is solvent dependent.[16] Although batch reactions appeared to be faster in DMF and EtOH (data not shown), acetonitrile constitutes a good compromise as PGMA brushes are known to swell in this solvent.[17] In addition, changing the solvent will also influence the swelling of the PGMA polymer brushes, resulting in less accessible catalytic sites. This makes a comparison of the effect of different solvents very complicated.

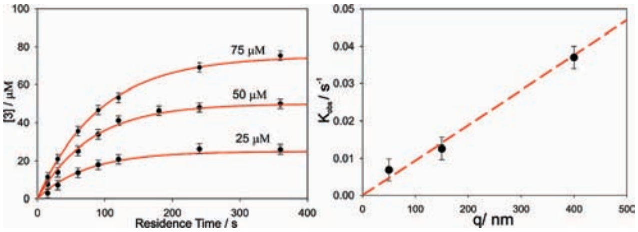


Figure 2. (a) Formation of **3** catalyzed by the polymeric coating (150 nm) in the microreactor at different concentrations of **1** ([**2**] = 125 mM, 65 °C); (b) rate constants for reaction of **1** with **2** in microreactors with different polymer coating thicknesses.

The second-order rate constant of 0.30 ± 0.03 s^{-1} M^{-1}, calculated for the device having a layer of 400 nm PGMA-TBD, shows that the reaction proceeds up to 150 times faster than in the case of a monolayer coating of TBD.

To estimate the number of TBD units in the polymer, we applied Gisin's acid−base titration procedure.[18] The amount of catalyst is 2, 4, and 9 μg of TBD for the devices with thicknesses of 50, 150, and 400 nm, respectively (see Supporting Information).

In conclusion, we report the fabrication and application of a catalytic nanostructure based on polymer brushes as support for the catalytic coating of the inner wall of microreactors. We also show that the amount of catalyst can be tuned by variation of the polymerization times. An advantage of PGMA polymer brushes is the versatility offered by the oxirane groups for the anchoring of a variety of catalysts via a nucleophilic substitution reaction.

Acknowledgment. We thank NanoNed, a nanotechnology programme of the Dutch ministry of Economic Affairs, for the financial support.

Supporting Information Available: Experimental, microreactor fabrication, UV−vis in-line detection, PGMA-TBD layer characterization on silicon oxide, HR-SEM pictures. This material is available free of charge via the Internet at http://pubs.acs.org.

References

(1) Ahmed-Omer, B.; Brandt, J. C.; Wirth, T *Org. Biomol. Chem.* **2007**, *5*, 733–740.
(2) Brivio, M.; Verboom, W.; Reinhoudt, D. N. *Lab Chip* **2006**, *6*, 329–344.
(3) Watts, P.; Wiles, C. *Chem. Commun.* **2007**, 443–467.
(4) Jahnisch, K.; Hessel, V.; Lowe, H.; Baerns, M. *Angew. Chem., Int. Ed.* **2004**, *43*, 406–446.
(5) Kobayashi, J.; Mori, Y.; Kobayashi, S. *Chem. Asian. J.* **2006**, *1*, 22–35.
(6) Bogdan, A. R.; Mason, B. P.; Sylvester, K. T.; McQuade, D. T. *Angew. Chem., Int. Ed.* **2007**, *46*, 1698–1701.
(7) Wiles, C.; Watts, P.; Haswell, S. J. *Lab Chip* **2007**, *7*, 322–330.
(8) Kobayashi, J.; Mori, Y.; Okamoto, K.; Akiyama, R.; Ueno, M.; Kitamori, T.; Kobayashi, S. *Science* **2004**, *304*, 1305–1308.
(9) Honda, T.; Miyazaki, M.; Yamaguchi, Y.; Nakamura, H.; Maeda, H. *Lab Chip* **2007**, *7*, 366–372.
(10) Miyazaki, M.; Maeda, H. *Trends Biotechnol.* **2006**, *24*, 463–470.
(11) Jackson, T.; Clark, J. H.; Macquarrie, D. J.; Brophy, J. H. *Green Chem.* **2004**, *6*, 193–195.
(12) Edmondson, S.; Huck, W. T. S. *J. Mater. Chem.* **2004**, *14*, 730–734.
(13) Edmondson, S.; Osborne, V. L.; Huck, W. T. S. *Chem. Soc. Rev.* **2004**, *33*, 14–22.
(14) Rao, Y. V. S.; De Vos, D. E.; Jacobs, P. A. *Angew. Chem., Int. Ed. Engl.* **1997**, *36*, 2661–2663.
(15) No changes in the FT-IR spectra were observed when PGMA polymer brushes, grown on a silicon oxidized surface, were kept in ethanol at 60 °C for 17 h.
(16) Corma, A.; Iborra, S.; Rodriguez, I.; Sanchez, F. *J. Catal.* **2002**, *211*, 208–215.
(17) Fukuda, T.; Kohara, N.; Onogi, Y.; Inagaki, H. J. *Appl. Poly. Sci.* **1991**, *43*, 2201–2205.
(18) Gisin, B. F. *Anal. Chim. Acta* **1972**, *58*, 248.

JA807616Z