Polymeric Monolithic Media: Synthesis, Pore Size Selective Functionalization and Applications

M. R. Buchmeiser,[*1,2] *R. Bandari,*[1] *A. Prager-Duschke,*[1] *A. Löber,*[1] *W. Knolle*[1]

Summary: This contribution will briefly summarize the latest developments in ring-opening metathesis polymerization (ROMP) and electron beam-triggered free radical polymerization derived monolithic supports. Issues relevant to separation science and heterogeneous catalysis will be addressed.

Keywords: electron beam triggered free radical polymerization; heterogeneous catalysis; monoliths; ring opening metathesis polymerization (ROMP); separation science; surface functionalization

Introduction

Introduced into separation science some 20 years ago, monolithic supports nowadays hold a strong position in separation science.[1] Monolithic materials may be prepared via various polymerization techniques including free radical and controlled free radical polymerization, polyaddition and polycondensation.[1] During the last years, we have developed alternative techniques based on ring-opening metathesis polymerization (ROMP) and electron beam (EB) triggered free radical polymerization. Taking advantage of the living nature of the ROMP-based polymerization protocol, polymer microglobule diameters, pore size distribution and specific surface areas could successfully be varied in a highly reproducible way. In addition, functionalization can be accomplished *in situ*. Complete removal of the initiator as well as of unreacted monomers, necessary for any subsequent application, may be realized by special capping sequences.[2–4] Alternatively to the ROMP-derived monoliths, an electron-beam (EB) triggered free radical polymerization based protocol for both the synthesis and functionalization of these materials has been elaborated.[5] This novel approach allows for realizing monolithic devices up to 5 L in volume as well as microdevices, e.g. applicable to chip technology and coupling to mass spectroscopy. Furthermore, combinations of the ROMP-based and free radical polymerization based synthetic protocol allow for an unprecedented variability in the dimension as well as functionalization of monolithic supports.[6] This allows for applying the thus prepared monolithic materials in membrane technology as well as to bioseparations including *ds*-DNA, protein and peptide analysis.[7-11] Selected examples for the use of monolithic media in these areas are illustrated.[12–14]

Results and Discussion

Issues Related to Synthesis and Microstructure

Polymeric monolithic materials may prepared within the confines of choice in a one-step procedure using appropriate amounts of monomer(s), crosslinker(s) and porogenic solvents. The latter are usually based on a good and a bad solvent for the corresponding polymer, thus serving as microporogen and macroporogen, respectively. The entire process needs to be designed in way that phase separation is

[1] Leibniz-Institut für Oberflächenmodifizierung, Permoserstr. 15, Leipzig 04318, Germany
E-mail: michael.buchmeiser@iom-leipzig.de
[2] Institut für Technische Chemie, Universität Leipzig, Linnéstr. 3, Leipzig 04103, Germany

faster than gelation. According to the Flory-Huggins theory,[15–17] the enthalpy term in equation (1) needs to be largely positive in order to provide a value for ΔG that is also positive, a requirement for phase separation to occur. Hence the interaction parameter Ξ needs to be large and both the monomers, crosslinkes and solvents have to be chosen accordingly.

$$\Delta G \sim RT[(\Phi_1/P_1)\ln\Phi_1 + (\Phi_2/P_2)\ln\Phi_2 + \Xi_{12}\Phi_1\Phi_2] \quad (1)$$

($\Phi_i (0 < \Phi_i < 1)$..... volume fraction of component i
P_i..... degree of polymerization of component *i*
Ξ_{12}..... interaction parameter).

The use of appropriate amounts of monomer(s), crosslinker(s) and porogenic solvents, however, allows for designing monolithic supports in terms of porosity, pore size distribution, pore volume and specific surface area. This is necessary in order to meet the requirements for any support to be used in separation science or heterogeneous catalysis. While both areas of application ask for large interconnected pores that finally allow for high flow rates through the support (usually up to 20 column volumes per minute!), particularly the use of monolithic supports in the separation of proteins requires materials with low or even no micro- and mesoporosity.

Recent Applications in Separation Science

ROMP-derived monolithic capillary columns have recently been reported as excellent devices for the quantification of insulin and insulin analogues from interstitial liquid.[9] 200 and 100 μm I.D. capillary columns prepared from norborn-2-ene, 1,4,4a,5,8,8a-hexahydro-1,4,5,8-*exo*, *endo*-dimethanonaphthalene (DMN-H6), toluene (microporogen) and 2-propanol (macroporogen) under the action of the 1st-generation Grubbs initiator $RuCl_2(PCy_3)_2$-(CHPh) (Cy = cyclohexyl) were found suitable for the separation of insulin at the from other biogenic proteins. The total amount injected was 100 femtomol (Figure 1). It is also worth mentioning that the column also allows for the separation of insulin from artificial insulin analogues such insulin *lispro*. The difference between both types of insulin is the order of the last two amino acids, which are switched in position (!).

ROMP was also used for the synthesis of monolithic 200 μm I.D. capillary columns. The resulting polymeric monoliths were characterized by inverse size-exclusion chromatography (ISEC).[18,19] Surface functionalization was carried out *in situ* using 2-(N,N-dimethylaminoethyl)norborn-5-ene-2-ylcarboxylic amide (**1**). The resulting functionalized monoliths were successfully used in anion-exchange chromatography of oligodeoxynucleotides (Figure 2).

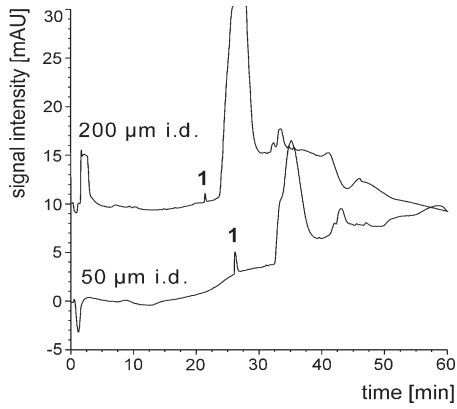


Figure 1.
Analysis of a human insulin in interstitial fluids using capillary monoliths of (a) 200 μm I.D. and (b) 50 μm I.D. Interstitial fluid samples diluted (a) 1:10 and (b) 1:160 and spiked with (1) human insulin (100 fmol/μl), injection volume 1 μl. The length of monoliths was 8 cm throughout. Chromatographic conditions: mobile phase: (A) 95% water, 5% acetonitrile, 0.05% TFA, (B) 20% water, 80% acetonitrile, 0.04% TFA; gradient: 0–30 min 0–60% B; 50–90% B within 5 min; flow (a) 1.5 μl/min, (b) 0.5 μl/min; 25°C; UV (190 nm).

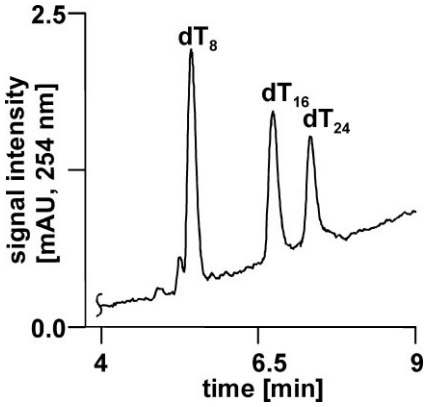
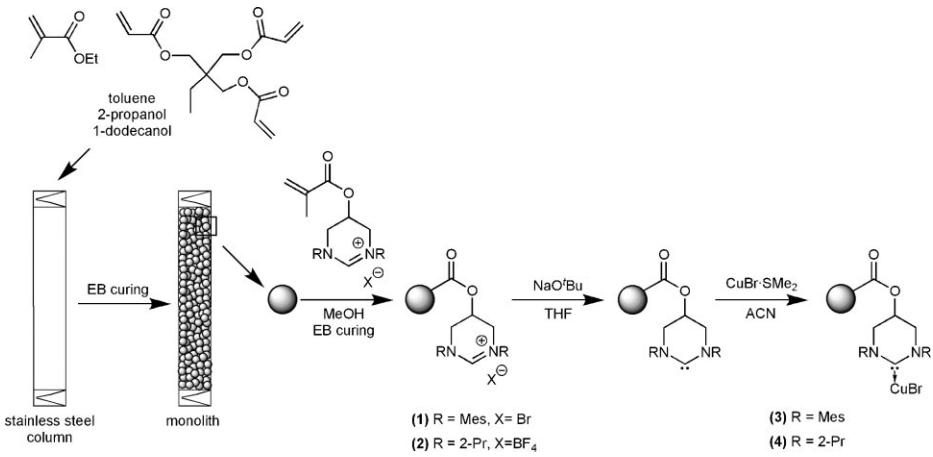


Figure 2.
Separation of dT_8, dT_{16} and dT_{24} (2 ng each) on a monolithic capillary column (57 × 0.2 mm). Mobile phase: 20 mM ammonium acetate, pH = 5.0, 80% water, 20% acetonitrile, linear gradient 0–1.0 M NaCl within 10 minutes, flow = 3.1 μL/min, 25 °C; detection, UV (254 nm).

Though resolution was lower compared to octamethylferrocene-derivatized silica columns prepared *via* 1-alkyne graft polymerization,[20] sufficient separation efficiency was achieved allowing for the base line separation of these analytes (Figure 2). Peak half widths were in the range of 8.4–11.4 s, peak resolution was 4.59 and 2.14, respectively. As can also be deduced from Figure 2, separation was achieved within less than 8 minutes. Elution of the oligodeoxynucleotides was accomplished with a gradient of 0–1.0 M NaCl, and potential solvophobic interactions of the analytes with the NBE/DMN-H6 backbone were efficiently suppressed by the addition of 20% acetonitrile to the eluent. A pH of 5 guaranteed for the formation of the quaternary ammonium sites necessary for anion-exchange chromatography. The comparably strong retention of the anionic analytes to the functionalized surface is indicative for substantial amounts of grafted **3** present at the surface of the monolith.

Recent Applications in Heterogeneous Catalysis

Porous polymeric monoliths were prepared via electron beam-triggered free radical polymerization of (meth-)acrylates and used as supports in contiuous flow catalysis. Post-synthesis functionalization of these supports was accomplished via electron beam initiated free radical graft polymerization of methacryloyl-substituted N-heterocyclic carbene precursors. The grafted precursors were converted into the corresponding copper complexes (Scheme 1). These supported catalysts were



Scheme 1.
Synthesis of monolith-immobilized Cu(I)-NHC complexes **3** and **4**.

used in selected C=O hydrosilylation and cyanosilylation reactions.[14]

The catalytic activity of the supported catalysts **3** and **4** in the cyanosilylation of *p*-fluorobenzaldehyde and *p*-chlorobenzaldehyde reached a maximum after 2 hours. Important too, in the cyanosilylations of both *p*-chlorobenzaldeyde and benzil with trimethylsilyl cyanide, the activity of **4** remained constant over at least 6 days. The corresponding TONs were 9500 and 1060, respectively. Cu contamination was <1 and 10 ppm, respectively.

Compared to cyanosilylation reactions, the catalytic activity was high from the very beginning in the hydrosilylation of *p*-chlorobenzaldehyde with trimethylsilane. Due to the use of 0.3 molequiv. of K-*tert*.-butylate, *tert*.-butyl-4-chlorobenzoate was observed as a byproduct. In fact, the activity of **3** remained constant for at least 3 days in the hydrosilylation of *p*-chlorobenzaldeyde and benzophenone, respectively, without any observable loss in activity. The corresponding TONs were 900 and 830, respectively. The copper contamination of the products collected after 2 hours was low (7 and 13 ppm, respectively).

Conclusion

The area of monolithic supports has become a mature one. With an armor of polymerization and functionalization techniques in hand, both small-volume as well as large-volume applications are currently being explored. Significant contributions to materials science have already been made and many more are to be expected in the near future.

Acknowledgements: This work was supported by the *Deutsche Forschungsgemeinschaft DFG* (BU-2174/1-1 and BU2174/1-2), the *Federal Government of Germany* and the *State of Saxony*.

[1] M. R. Buchmeiser, *Polymer* **2007**, *48*, 2187–2198.
[2] F. Sinner, M. R. Buchmeiser, *Angew. Chem.* **2000**, *112*, 1491–1494; *Angew. Chem. Int. Ed.* **2000**, *39*, 1433–1436.
[3] F. Sinner, M. R. Buchmeiser, *Macromolecules* **2000**, *33*, 5777–5786.
[4] R. Bandari, A. Prager-Duschke, C. Kühnel, U. Decker, B. Schlemmer, M. R. Buchmeiser, *Macromolecules* **2006**, *39*, 5222–5229.
[5] R. Bandari, W. Knolle, A. Prager-Duschke, M. R. Buchmeiser, *Macromol. Chem. Phys.* **2007**, *208*, 1428–1436.
[6] R. Bandari, W. Knolle, M. R. Buchmeiser, *Macromol. Rapid Commun.* **2007**, *28*, 2090–2094.
[7] B. Mayr, R. Tessadri, E. Post, M. R. Buchmeiser, *Anal. Chem.* **2001**, *73*, 4071–4078.
[8] R. Bandari, C. Elsner, W. Knolle, C. Kühnel, U. Decker, M. R. Buchmeiser, *J. Sep. Sci.* **2007**, *30*, 2821–2827.
[9] F. M. Sinner, C. Gatschelhofer, A. Mautner, C. Magnes, M. R. Buchmeiser, T. R. Pieber, *J. Chromatogr. A.* **2008**, *1191*, 274–281.
[10] R. Bandari, W. Knolle, M. R. Buchmeiser, *J. Chromatogr. A.* **2008**, *1191*, 268–273.
[11] M. R. Buchmeiser, *J. Sep. Sci.* **2008**, *31*, 1907–1922.
[12] M. Mayr, B. Mayr, M. R. Buchmeiser, *Angew. Chem.* **2001**, *113*, 3957–3960; *Angew. Chem. Int. Ed.* **2001**, *40*, 3839–3842.
[13] M. Mayr, D. Wang, R. Kröll, N. Schuler, S. Prühs, A. Fürstner, M. R. Buchmeiser, *Adv. Synth. Catal.* **2005**, *347*, 484–492.
[14] M. J. Beier, W. Knolle, A. Prager-Duschke, M. R. Buchmeiser, *Macromol. Rapid Commun.* **2008**, *29*, 904–908.
[15] M. L. Huggins, *J. Phys. Chem.* **1942**, *46*, 151–158.
[16] P. J. Flory, *J. Chem. Phys.* **1942**, *10*, 51–61.
[17] M. L. Huggins, *J. Am. Chem. Soc.* **1942**, *64*, 1712–1719.
[18] I. Halász, K. Martin, *Ber. Bunsenges. Phys. Chem.* **1975**, *79*, 731–732.
[19] I. Halász, K. Martin, *Angew. Chem.* **1978**, *90*, 954–961; *Angew. Chem. Int. Ed.* **1978**, *17*, 901–909.
[20] K. Eder, E. Reichel, H. Schottenberger, C. G. Huber, M. R. Buchmeiser, *Macromolecules* **2001**, *34*, 4334–4341.

