Angewandte International Edition Chemie

DOI: 10.1002/anie.201007747

Polymer Capsules

Facile Fabrication of Stimuli-Responsive Polymer Capsules with Gated Pores and Tunable Shell Thickness and Composite**

*Changxu Lin, Wei Zhu, Haowei Yang, Qi An, Cheng-an Tao, Weina Li, Jiecheng Cui, Zilu Li, and Guangtao Li**

In recent years, considerable efforts have been devoted to the synthesis of hollow polymer capsules owing to their potential applications in controlled delivery systems, encapsulation, artificial cells, catalysts, chemical sensors, nanoreactors, and so on.[1] For this class of nanostructured polymer materials, it is well recognized that the control of size, morphology, shell thickness, and composite is critical for their practical applications.[2] For example, the surface characteristics and dispersion behavior of these colloidal capsules in various media are mainly determined by their shell composites. With specific functional groups, the shell molecules can endow the nanocapsules with hydrophilicity, hydrophobicity, amphiphilicity, or even targeting capability.[3] Thus, the fabrication of well-defined polymer capsules with easily tunable composites is highly desirable. Besides the structural parameters mentioned above, the integration of smart pore structure into the polymer shell, which can finely control the permeability of the capsule under desired conditions, is another important issue for the development of the hollow polymer structure. Up to now, various polymer capsules with porous shells have been reported.[2,4] However, polymer capsules with the ability to reversibly switch on/off shell pores or channels without disruption of their original shape, and thus to control the transport of the encapsulated species across the capsule shell, are limited.[2,5] In particular, the effective control of the pore size and thus the rate of release is one of the principal challenges in this field.[6]

Various methods have been developed over the past decade for synthesizing hollow polymer capsules, mostly based on soft and hard templating techniques.[1,2,7] Among the reported methods, the layer-by-layer approach, through sequential deposition of polymer species on sphere substrates mediated by intermolecular interactions and then removal of the core, is the prominent technique towards engineering of structural and property parameters of polymer capsules.[2,8] This powerful assembly process allows tailoring of not only the size, morphology, and shell thickness of capsules, but also their composition, permeability, and surface functionality. Nevertheless, the layer-by-layer method has contradictions: getting full control of capsule fabrication but spending too much time on tedious and delicate manufacturing, especially when many layers, which are necessary for obtaining nanocapsules with enough robustness, are required.[2,9] Additionally, despite its versatility and popularity, this method hits a limit of smaller hollow capsules with sizes below 200 nm, which are desirable for in vivo applications.[9]

Herein, we present a new strategy for efficiently fabricating stimuli-responsive polymer capsules with gated pores and tunable composites as well as controlled size and shell thickness, based on polymerizable mesoporous silica spheres. The key point of this strategy is the application of a special ionic liquid (IL)-based surfactant with a terminal polymerizable unit for the formation of reactive mesoporous silica spheres. Through diffusion-controlled surface polymerization of the resultant spheres followed by the removal of the silica template, hollow capsules with a mesoporous polymer-network shell bearing pendant IL moieties were synthesized. By controlling the diameter of the silica nanospheres and polymerization time, polymer capsules with different shell thicknesses and sizes ranging from tens of nanometers to several micrometers are easily accessible. More importantly, in response to a specific anion the pore size of the shell is reversibly adjustable by simply exchange of counteranions of the pendant IL units. Also, theoretically any functional group with an anion can be introduced into the IL units, and hence a variety of functional moieties, such as targeting ligands and imaging probes, are easy to attach to the surface of the capsule in a noncovalent and modular manner. Moreover, the synthesis is easily scalable to obtain large quantities of the desired polymer capsules. All these virtues can be attributed to the use of a surfactant/monomer/function-anchor "multifunctional molecule", $Py(CH_2)_{12}MIM^+Br^-$ (Py = pyridine, MIM = methylimidazolium; see Figure 1), together with the formed mesoporous structure.

Figure 1 displays the overall production strategy. A special methylimidazolium-based surfactant containing a terminal pyrrole moiety is used to construct mesoporous silica spheres. Since pyrrole is an excellent compound to form polymer under oxidative chemical or electrochemical conditions, this surfactant can serve simultaneously both as structure-directing agent and monomer.[10] During the formation of the spherical mesoporous silica framework, the pyrrole moieties could be densely packed in a controlled

---

[*] C. Lin, W. Zhu, H. Yang, Q. An, C. Tao, W. Li, J. Cui, Z. Li,
Prof. Dr. G. Li
Key Lab of Organic Optoelectronics & Molecular Engineering
Department of Chemistry, Tsinghua University
Beijing 100084 (China)
Fax: (+86) 10-6279-2905
E-mail: lgt@mail.tsinghua.edu.cn

[**] We gratefully acknowledge the financial support from the NSF China (20533050, 50873051, 21025311, and 50673048), MOST (2007AA03Z07), and the transregional project (TR61). We are also grateful for the BET measurement by the Administration Key Laboratory of Thermo Science and Power Engineering, Tsinghua University.

Supporting information for this article is available on the WWW under http://dx.doi.org/10.1002/anie.201007747.

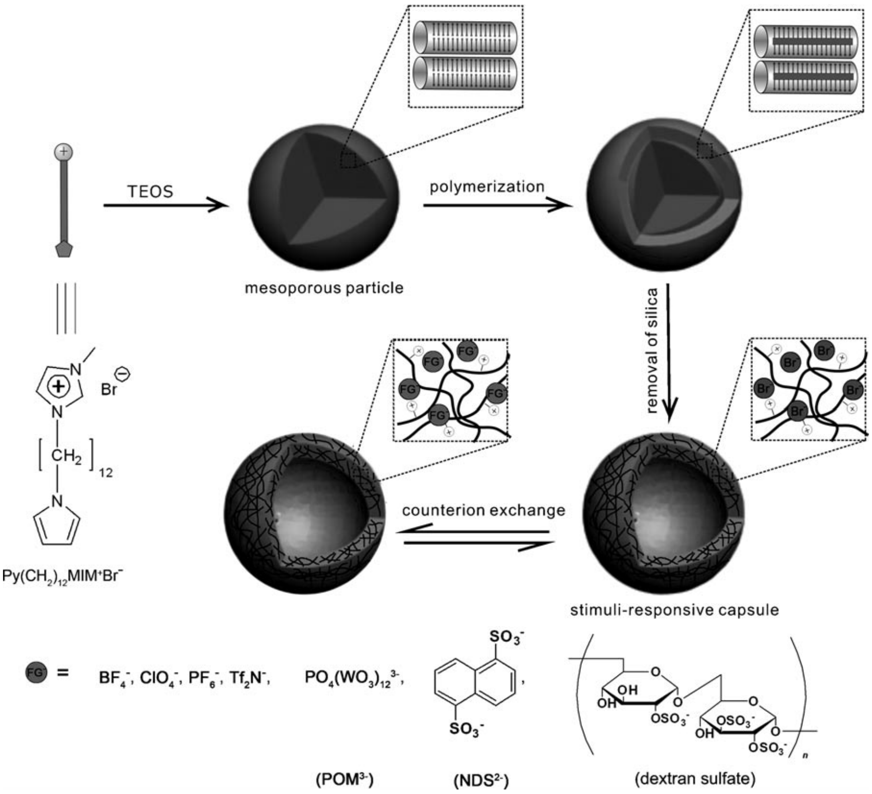

Figure 1. Preparation of stimuli-responsive polymer capsules with gated pores and tunable shell thickness and composites. TEOS = tetraethoxysilane, FG = functional group, Tf = trifluoromethanesulfonyl, POM = polyoxometalate, NDS = naphthalene-1,5-disulfonic acid.

fashion within silica mesochannels, which provided the prerequisite for producing well-defined polymer chains in a confined space. Polymerization of the organized pyrrole moieties in mesopores was performed using $FeCl_3$ as oxidant. After diffusion-controlled surface polymerization followed by dissolution of the silica template, the reactive spheres were individually transferred into hollow capsules with a mesostructured polymer network shell and pendant imidazolium IL units. Clearly, this three-step procedure provides a controllable rational route for producing large-scale well-defined polymer capsules with tunable size and shell thickness.

The synthesis of the surfactant $(Py(CH_2)_{12}MIM^+Br^-)$-$(CH_2)_{12}$ was described in our previous work.[11] In a typical preparation, $Py(CH_2)_{12}MIM^+Br^-$ (0.3 g) was dissolved in HCl aqueous solution (5.0 g, pH 3). After 30 min of stirring, tetraethoxysilane (TEOS, 0.6 g) was added dropwise under vigorous stirring, and a $TEOS/Py(CH_2)_{12}MIM^+Br^-/H_2O$ molar ratio of 1:0.12:100 was established in the reaction mixture. After two hours of further stirring at room temperature, the solution was left standing at 80 °C for 48 h in an autoclave. A white powder was collected by centrifugation, washed with Millipore water, and dried in air. Figure 2 A shows a typical TEM image of the resultant silica particles, which exhibit a uniform spherical morphology and have a diameter of 380 nm. High-resolution TEM (HRTEM; inset in Figure 2 A) reveals a disordered wormlike mesoporous structure throughout the whole nanosphere with a smooth surface. In agreement with this result, the XRD pattern shows only one broad Bragg diffraction peak located at $2\theta = 2.8°$ with d spacing of 3.4 nm. In our work, through altering the preparation parameters, the synthesis of large-scale discrete and monodisperse mesoporous silica particles with sizes ranging from 80 nm to 1 μm is achieved (see Figure S1 in the Supporting Information).

As-synthesized mesoporous spheres were redispersed in dried CH_2Cl_2 containing $FeCl_3$ for the polymerization of the preorganized pyrrole units inside the silica channels. Interestingly, it is found that, because of the physically constrained diffusion of $FeCl_3$ within the pores, the polymerization reaction is a diffusion-controlled process in our case and thus spatially controllable. $FeCl_3$ oxidant first diffuses into the pores to reach the pyrrole moieties and induces polymerization. With increased penetration of oxidant into the interiors of the prepared spheres, more pyrrole units in nanochannels are converted into polymer. Remarkably, it is observed that the slow diffusion of the oxidant from the exterior of mesoporous spheres to their interior is uniform and nearly simultaneous.

Upon exposure of the spheres to CH_2Cl_2 containing $FeCl_3$, dark rings appeared immediately in their outermost layers, which indicated that polypyrrole (PPy) had formed at the openings of mesochannels. With time the ring became clearer and the thickness and darkness of the ring increased. For example, ring thicknesses of 50 and 80 nm, corresponding to the extent of polymerization, were achieved after 24 and 48 h of reaction time, respectively (see Figure S2 in the Supporting Information). When the time was prolonged, complete polymerization of pyrroles throughout the whole mesoporous particles was realizable. In previous works, similar diffusion-controlled reactions or phenomena were also reported and exploited to locate the multiple molecular functionalities in different spatial regions of mesoporous particles.[12] In our case, the finding described actually provides an effective and convenient means to tune the thickness of the formed polymer capsules.

After diffusion-controlled polymerization with the synthesized mesoporous spheres, dilute HF aqueous solution (5%) was used to remove the silica template. Indeed, after the removal of the template, capsules with different shell thickness were obtained (Figure 2 A–E). X-ray photoelectron survey spectra of the particles before and after removal of silica are provided in Figure S3 in the Supporting Information, which confirmed the removal of silica. Clearly, in addition to a hollow interior, massive resulting capsules with a uniform thickness inherited the fine spherical shape and good monodispersity of the silica templates. It should be noted that, compared to the template used, the obtained

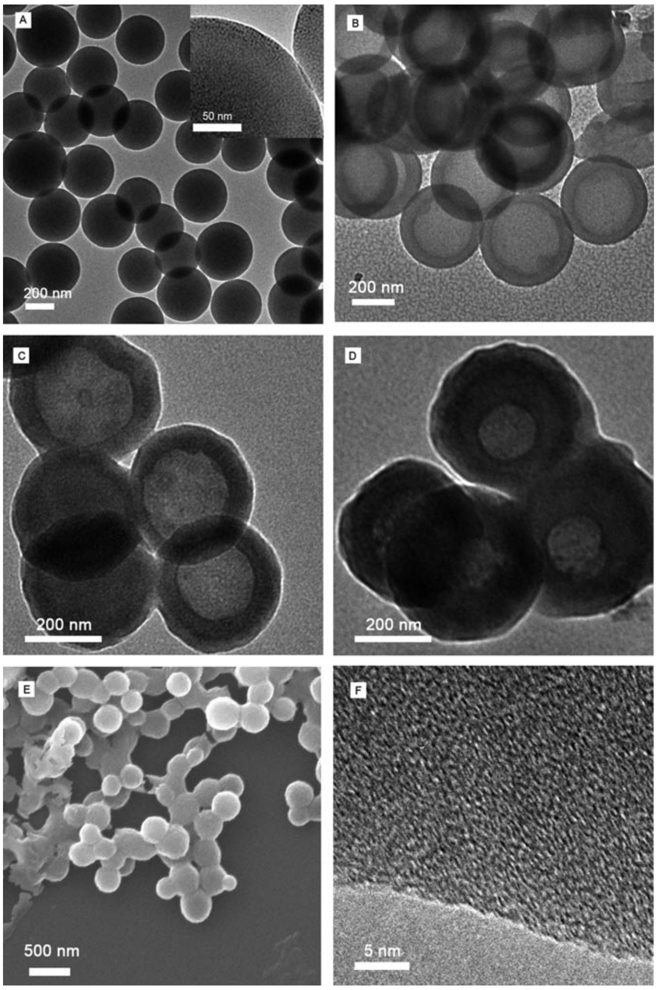

Figure 2. TEM images of A) as-synthesized silica spheres (inset: HRTEM image) and B–D) the resulting polymer capsules after polymerization for B) 24, C) 48, and D) 72 h. E) SEM image of the fabricated polymer capsules. F) HRTEM image of the shell film of the capsules.

capsules usually have a relatively larger size, probably because of the swelling or elasticity of the organic polymer. Under high magnification, a mesoporous structure descending from the silica templates in the shell is clearly observed (Figure 2F).

In addition, Brunauer–Emmett–Teller (BET) experiments were carried out on the mesoporous silica spheres and the resulting capsules. The results verified the mesoporosity of the capsules. Compared to the silica spheres with filled surfactants in channels (pore volume: 0.067 $cm^3 g^{-1}$; average pore diameter: 3.1 nm), however, both pore diameter and pore volume decreased with the fabrication of the capsules (pore volume: 0.0072 $cm^3 g^{-1}$; average pore diameter: 1.8 nm). The phenomenon is probably due to the collapse of the polymer capsule shell under the BET experimental conditions (in the dried state) with the loss of the rigid mesoporous silica frame.

Figure S4 in the Supporting Information displays FTIR spectra of $Py(CH_2)_{12}MIM^+Br^-$ and the formed polymer capsules. Instead of IR bands of pyrrole monomer, at 1500, 1458, and 723 cm^{-1} (see Figure S4A in the Supporting Information), new IR bands at 1572 and 1463 cm^{-1}, the typical set of bands characteristic of PPy,[13] appeared in the spectrum after polymerization (see Figure S4B in the Supporting Information). The absorbance at 723 cm^{-1} (see Figure S4A in the Supporting Information), attributed to the α-(C–H) bending mode of the pyrrole ring, is absent in the polymer, thus indicating that α–α coupling of the pyrrole units occurred and PPy was really formed in the channels. Additionally, the capsules show the signals from IL units at about 1550, 2800, and 3300 cm^{-1}.[14]

A hollow interior surrounded by a three-dimensional (3D) mesoporous polymer network bearing pendant IL moieties presents the main structural feature of the synthesized capsules. The presence of IL units in the polymer shell should endow the capsule with anion-triggered stimuli responsiveness. Indeed, when the shell film was mounted on a platinum electrode and water-soluble and neutral 1,1′-ferrocenedimethanol was used as redox probe molecule, we found that the permeability of the capsule shell is controllable by counteranions. The original shell film (Br^- as anion) allows electron exchange of the probe molecule with the underlying electrode, and shows a couple of well-defined redox peaks of 1,1′-ferrocenedimethanol (Figure 3). However, the redox activity of the probe molecule was gradually suppressed by shell films bearing other anions, in the following order: $Tf_2N^- > PF_6^- > ClO_4^- > BF_4^-$ (Figure 3). In the case of Tf_2N^- as counteranion, for instance, the permeation of the probe molecule in the shell film was nearly blocked. Since the current intensity is proportional to the molecular flux through the porous film,[15] these results clearly indicate that the pore size and thus the permeability of the capsule shell are definitely determined by a given counteranion. Of particular interest, such an anion-directed gating system is reversible; when the blocked shell was exposed to an acetone solution of LiBr (0.1 M), the molecular transport across the shell film was recovered (inset in Figure 3).

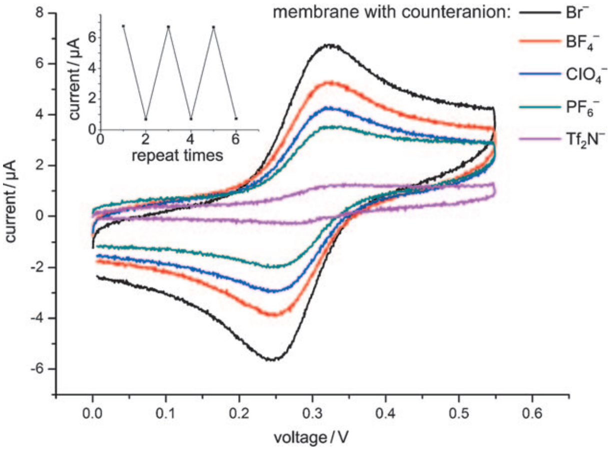

Figure 3. Cyclic voltammograms of the capsule-membrane-coated electrode with different counteranions; inset: the reversibility of the gated pores in the shell.

In response to a special anion the prepared capsule shell has the capability of controlling pore size, which is in agreement with the results obtained with nanoporous poly(ionic liquid) materials.[16,17] On the other hand, the degree of hydrophilicity of the pore channels is also correspondingly adjusted by the attached anions, thus generating a different osmotic pressure. Both the physical size change and osmotic-driven processes, we believe, are responsible for the observed molecule gating switch.

Besides the novel pore-gating function, the integration of IL units in the polymer shell also makes the composite of the prepared capsule tunable to a wide extent in a noncovalent and modular manner. Based on the concept of "task-specific" ILs,[18] a variety of functional groups as anions can be facilely introduced into the pendant IL units simply by an ion-exchange reaction, thereby leading to hollow polymer capsules with desired composites and decorated function. As demonstrations, redox-active polyoxometalate (POM), fluorophore, and sugar cluster anions (Figure 1) were incorporated into the capsule shell, and as a result, polymer capsules with electrochemical activity, fluorescence emission, or targeting ligand, respectively, were achieved (Figure 4 A,B and Figure S4C,D in the Supporting Information). Confocal fluorescence microscopy was employed to investigate whether the fluorescent compound penetrated into the capsule shell. The results confirmed that the fluorescent compound did not stick to the outside, but penetrated into the shells of the capsules (see Figure S5 in the Supporting Information). In fact, as one of the distinct properties, the counteranion-exchange capability of ILs offers virtually unlimited tunability.[19] Through rational modulation of the combination of cations and anions, the synthesized capsule provides tremendous opportunities for the design of new capsule-based chemical systems.

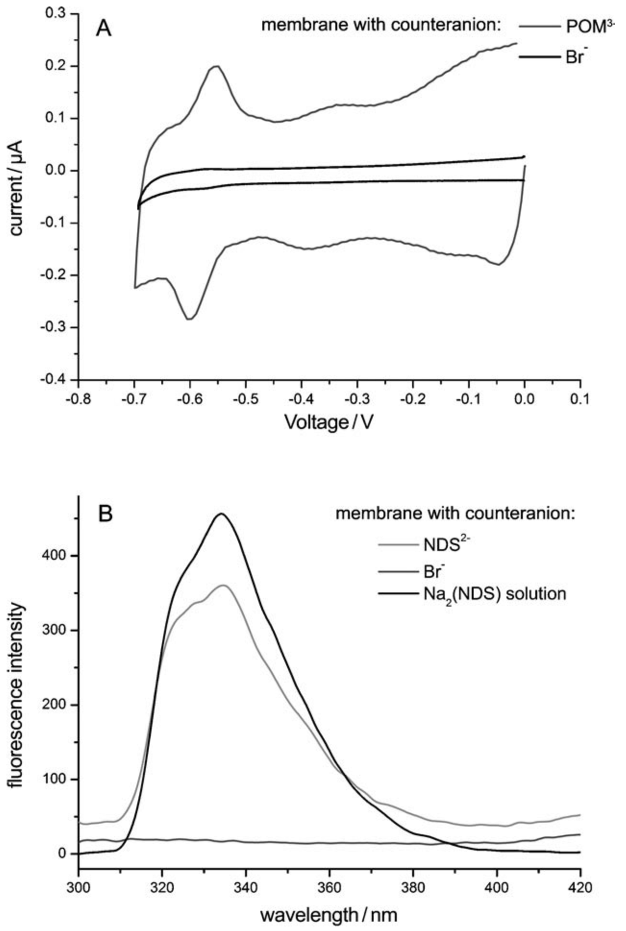

Figure 4. A) Cyclic voltammograms of the as-synthesized capsules before and after exchange with the POM^{3-} anion. B) Fluorescence spectra of the as-synthesized capsules before and after exchange with the fluorophore anion (NDS^{2-}) as well as of the fluorophore molecule in water.

In summary, by using an imidazolium-based surfactant bearing a terminal pyrrole unit as structure-directing agent, monomer, and function anchor (multifunctional molecule), polymerizable mesoporous silica spheres with high monodispersity and tunable sizes have been successfully synthesized. Interestingly, it was found that the slow and continuous diffusion of oxidant from the exterior of the mesoporous spheres to their interior controlled the polymerization process of the preorganized pyrrole units in channels, thus providing an efficient and scalable method to produce well-defined hollow capsules with a 3D mesoporous polymer-network shell and pendant IL moieties after the removal of the silica template. Depending on the preparation parameters, the size and shell thickness of the capsules are controllable in a wide range. More importantly, the pore size of the capsule shell is adjustable in response to a special anion, and thus the fine control of molecular transport across the shell film is realizable. Moreover, the integration of IL moieties into the mesoporous shell also endows the resultant polymer capsules with unprecedented composite tunability, and various functional groups can be easily introduced into the capsules in a modular manner. Although an imidazolium-based and pyrrole-containing surfactant is used for the present study, the results are expected to be universal for other types of IL molecules and polymerizable units. Thus, we believe our findings may open up a new route with great extendibility to obtain a new class of stimuli-responsive polymer capsules with gated pores and tunable composite and shell thickness, which could find a wide range of applications.

Received: December 9, 2010

Keywords: core–shell materials · ionic liquids · mesoporous materials · polymers · template synthesis

---

[1] a) W. Meier, *Chem. Soc. Rev.* **2000**, *29*, 295; b) C. S. Peyratout, L. Daehne, *Angew. Chem.* **2004**, *116*, 3850; *Angew. Chem. Int. Ed.* **2004**, *43*, 3762; c) B. G. De Geest, N. N. Sanders, G. B. Sukhorukov, J. Demeester, S. C. D. Smedt, *Chem. Soc. Rev.* **2007**, *36*, 636.
[2] S. F. M. van Dongen, H. M. De Hoog, R. J. R. W. Peters, M. Nallani, R. J. M. Nolte, J. C. M. van Hest, *Chem. Rev.* **2009**, *109*, 6212.
[3] a) E. Kim, D. Kim, H. Jung, J. Lee, S. Paul, N. Selvapalam, Y. Yang, N. Lim, C. G. Park, K. Kim, *Angew. Chem.* **2010**, *122*, 4507; *Angew. Chem. Int. Ed.* **2010**, *49*, 4405; b) D. Ni, L. Wang, Y. Sun,

Z. Guan, S. Yang, K. Zhou, *Angew. Chem.* **2010**, *122*, 4319; *Angew. Chem. Int. Ed.* **2010**, *49*, 4223.

[4] J. C. M. van Hest, *Macromol. Biosci.* **2010**, *10*, 463.

[5] a) E. Kim, J. Lee, D. Kim, K. E. Lee, S. S. Han, N. Lim, J. Kang, C. G. Park, K. Kim, *Chem. Commun.* **2009**, 1472; b) J. Kim, E. Lee, Y. Lim, M. Lee, *Angew. Chem.* **2008**, *120*, 4740; *Angew. Chem. Int. Ed.* **2008**, *47*, 4662.

[6] a) A. P. R. Johnston, G. K. Such, F. Caruso, *Angew. Chem.* **2010**, *122*, 2723; *Angew. Chem. Int. Ed.* **2010**, *49*, 2664; b) Y. Wang, V. Bansal, A. N. Zelikin, F. Caruso, *Nano Lett.* **2008**, *8*, 1741.

[7] a) K. Breitenkamp, T. Emrick, *J. Am. Chem. Soc.* **2003**, *125*, 12070; b) H. Huang, E. E. Rmsen, T. Kowalewski, K. L. Wooley, *J. Am. Chem. Soc.* **1999**, *121*, 3805.

[8] F. Caruso, R. A. Caruso, H. Moehwald, *Science* **1998**, *282*, 1111.

[9] a) X. W. Lou, L. A. Archer, Z. Yang, *Adv. Mater.* **2008**, *20*, 3987; b) L. J. De Cock, S. De Koker, B. G. De Geest, J. Grooten, C. Vervaet, J. P. Remon, G. B. Sukhorukov, M. N. Antipina, *Angew. Chem.* **2010**, *122*, 7108; *Angew. Chem. Int. Ed.* **2010**, *49*, 6954.

[10] a) G. T. Li, S. Bhosale, T. Y. Wang, H. S. Zhu, J. H. Fuhrhop, *Angew. Chem.* **2003**, *115*, 3948; *Angew. Chem. Int. Ed.* **2003**, *42*, 3818; b) G. T. Li, S. Bhosale, S. Bhosale, F. T. Li, Y. H. Zhang, R. R. Guo, H. Zhu, J. H. Fuhrhop, *Chem. Commun.* **2004**, 1760; c) M. Ikegame, K. Tajima, T. Aida, *Angew. Chem.* **2003**, *115*, 2204; *Angew. Chem. Int. Ed.* **2003**, *42*, 2154.

[11] W. X. Zhang, J. C. Cui, C. X. Lin, Y. G. Wu, L. Ma, Y. Q. Wen, G. T. Li, *J. Mater. Chem.* **2009**, *19*, 3962.

[12] a) V. Cauda, A. Schlossbauer, J. Kecht, A. Zuerner, T. Bein, *J. Am. Chem. Soc.* **2009**, *131*, 11361; b) A. Schlossbauer, S. Warncke, P. M. E. Gramlich, J. Kecht, A. Manetto, T. Carell, T. Bein, *Angew. Chem.* **2010**, *122*, 4842; *Angew. Chem. Int. Ed.* **2010**, *49*, 4734; c) K. Cheng, C. C. Landry, *J. Am. Chem. Soc.* **2007**, *129*, 9674.

[13] K. G. Neoh, T. C. Tan, E. T. Kang, *Polymer* **1988**, *29*, 553.

[14] R. Marcilla, M. Sanchez-Paniagua, B. Lopez-Ruiz, E. Lopz-Cabarcos, E. Ochoteco, H. Grande, D. Mecerreyes, *J. Polym. Sci. Part A* **2006**, *44*, 3958.

[15] O. Schepelina, I. Zharov, *Langmuir* **2006**, *22*, 10523.

[16] a) J. Lu, F. Yan, J. Texter, *Prog. Polym. Sci.* **2009**, *34*, 431; b) F. Yan, J. Texter, *Angew. Chem.* **2007**, *119*, 2492; *Angew. Chem. Int. Ed.* **2007**, *46*, 2440.

[17] J. Huang, C. Tao, Q. An, W. Zhang, Y. Wu, X. Li, D. Shen, G. Li, *Chem. Commun.* **2010**, *46*, 967.

[18] a) S. G. Lee, *Chem. Commun.* **2006**, 1049; b) Z. Fei, T. J. Geldbach, D. Zhao, P. J. Dyson, *Chem. Eur. J.* **2006**, *12*, 2122.

[19] a) T. P. Lodge, *Science* **2008**, *321*, 50; b) M. Antonietti, D. Kuang, B. Smarsly, Y. Zhou, *Angew. Chem.* **2004**, *116*, 5096; *Angew. Chem. Int. Ed.* **2004**, *43*, 4988.