Porous and Nonporous Nanocapsules by H-Bonding Self-Assembly

Shuguang Yang, Yongjun Zhang, Guangcui Yuan, Xiaoli Zhang, and Jian Xu*

State Key Laboratory of Polymer Physics and Chemistry, Institute of Chemistry,
Chinese Academy of Sciences, Beijing 100080, China

Received September 6, 2004; Revised Manuscript Received October 27, 2004

ABSTRACT: On the basis of hydrogen bonding, poly(vinylpyrrolidone) and poly(methacrylic acid) were layer-by-layer deposited on the surface of the AgCl microcrystals or SiO_2 colloidal particles in aqueous solution to construct core−shell structure particles. When the AgCl and SiO_2 cores were removed, the porous and nonporous nanocapsules were obtained, respectively. After the nonporous capsules were incubated in a KSCN and HNO_3 mixture solution for 24 h, the capsules shrank and the pores were formed in the shell of the capsules.

Introduction

The layer-by-layer self-assembly (LBL) technique introduced by Decher et al. was originally developed for fabrication of mutlilayer films on planar substrates,[1] but this technique has an advantage that there is no restriction on the size or shapes of the substrate, which make it extend easily from two-dimensional systems (i.e., planar substrates) to three-dimensional systems (for example, spherical or other nonplanar substrates). Consequently, a large variety of core−shell particles with finely tuned shell thickness and composition have been fabricated,[2] and a series of novel microcapsules have been produced by subsequent removal of the sacrificial core of the resulting core−shell particles.[3] As is well-known, nano- and microscale capsules have attracted considerable attention these years due to their potential applications and fundamental importance. For example, they can be used as a kind of smart material for storage, transport, and release or as special reaction containers for the research of confined chemical reactions and the synthesis of some fine products.[4] So a variety of methods have been developed to fabricate the microcapsules, including nozzle reactor processes, emulsion/phase separation processes, interfacial polymerization, and LBL techniques. However, relatively hashed conditions should be employed in the above-mentioned methods, except the LBL approach. Moreover, using the LBL method, many important parameters of the capsules, such as size, geometry, composition, wall thickness, and uniformity, and diameter-to-wall thickness ratio of the hollow spheres can be easily controlled.[4a]

LBL self-assembly can be divided into several kinds according to its driving force: electrostatic force, hydrogen bonding, covalent bonding, coordination bonding, and charge transform interaction. However, up to now, most works have adopted electrostatic self-assembly (ESA) as the driving force sometimes with small modification. Recently we reported other LBL methods, covalent self-assembly[5] and hydrogen-bonding self-assembly,[6] for the microcapsule fabrication. When these microcapsules were used in controlled encapsulation and release of drugs, enzymes, proteins, and other active materials, the large change of their properties should be brought out by a small environmental spur; i.e., they should be endowed with smart environmental stimulus-responsive capsules. Some polyelectrolyte capsules have been reported responsive to environmental changes,[4b,7] but their stimulus-responsive behavior is not very sensitive, mainly due to their polyelectrolyte complex nature. As a kind of very important secondary interaction, hydrogen bonding plays a crucial role in the basic processes of life such as protein synthesis, recognition, and DNA duplication, and it is endowed with reversible nature and sensitivity to environment, which will open the possibility to design novel and smart stimulus-responsive capsules. So the first hydrogen-bonding capsule was designed and prepared by our group with methanol as solvent, which limit its practical applications.[6] In this paper, the capsules based on hydrogen bonding were fabricated from two kinds of very simple and common water-soluble polymers: poly(vinylpyrrolidone) and poly(methacrylic acid). Porous and nonporous nanocapsules were obtained by using different templates. In addition, this hydrogen-bonding system was reported by Cranick et al. to be pH sensitive; pH = 6.9 is the critical point, and at pH only 0.2 units higher than 6.9 the multilayer structure will dissolve completely.[8] The properties mentioned above provide good basis in their potential application in controlled release.

Experimental Section

Materials. Poly(vinylpyrrolidone) (PVP, 30K) was purchased from the Beijing Chemical Reagent Co. Poly(methacrylic acid) (PMAA, $M_w = 9500$) was obtained from Aldrich. The polymer solutions were prepared with Millipore water (resistivity = 18.2 MΩ cm, Milli Q-plus system). The emulsion contains cubic AgCl microcrystals having an average length of 120 nm, and a narrow size distribution was synthesized according to ref 9. Spherical SiO_2 particles with an average diameter 280 nm were prepared by the method described in the ref 10. Micrographs of two kinds of templates are displayed in Figure 1. Other chemicals are analytical grade and were used as received without further purification.

Multilayer Films on Planar Substrates. The self-assembled films were fabricated on quartz or silicon slides. Both slides were first treated in boiling H_2SO_4/H_2O_2 mixture (7:3 v/v) for 30 min, then rinsed with deionized water thoroughly, and finally blown dry with a stream of N_2. The assembly process was controlled with an automated device (North Tianfu Ltd. Beijing, China). The concentrations of PMAA and PVP solution are both 1.0 mg/mL. PMAA solution was adjusted to pH = 3, and PVP solution and rinse solutions were adjusted to pH = 5 with HCl solution. Deposition time was 4 min per layer with 3 × 60 s rinses in acid water between layers.

Fabrication of Nanocapsules. *AgCl Microcrystals as Templates*. 2.0 g of AgCl emulsion was first dissolved in 30

---

* Corresponding author. E-mail: jxu@iccas.ac.cn.

10.1021/ma048182v CCC: $27.50

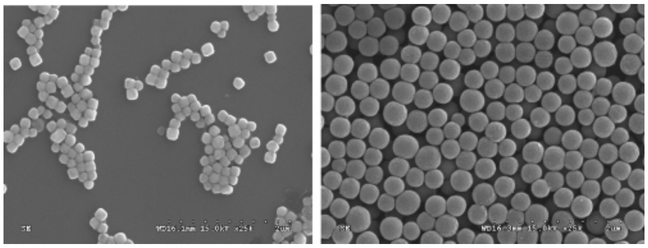

Figure 1. SEM micrographs of the templates of the assembly: cubic AgCl microcrystals (left); spherical SiO_2 particles (right).

mL of hot water and centrifuge to discard the supernatant, and this process was repeated five times to remove gelatin completely. The volume of the suspension was kept at 30 mL, and the solid content of the AgCl was 0.5%. Then 1 mL of 1 mg/mL PMAA (pH = 3) was added. After the solution was allowed to stand for 10 min for sufficient adsorption, excess PMAA was removed by three repeated centrifugation/washing/redispersion cycles (washing and redispersion water is acidic, pH = 5). After that, 1 mL of 1 mg/mL PVP was added, and after 10 min adsorption the excess PVP was removed by the above centrifugation/washing/redispersion cycles, too. The PVP was added again for the deposition of another layer of PVP, and then PMAA was added. The process was repeated, and in this way the core−shell particle was built up. The core−shell particles were annealing in the KSCN (0.1 M) and HNO_3 (0.01 M) mixture solution for 2 h to remove the AgCl core. The resulting solution was dialyzed against water to purify the capsules. Finally, several drops of HCl aqueous solution were added to adjust the solution to pH = 5 so as to ionize the outer layer PMAA somewhat, which will enable the capsule more stable.

SiO_2 Colloidal Particles as Templates. The solid content of SiO_2 was also adjusted to 0.5%. Compared with AgCl microcrystals as templates, the operations were same except that PVP was assembled first. The SiO_2 core was dissolved by the 10% HF solution. The resulting capsules were dialyzed and finally preserved in solution at pH = 5, too.

Characterization. A UV-1601 PC spectrometer (Shimadzu, Japan) was applied to monitor assembly process on the planar template. FTIR spectra were measured on a Bruke Equinox 55 FT-IR/FAR 106 spectrophotometer equipped with a variable temperature cell (P/N 21525 series, SPECAC Inc.). TEM observations were carried out on a JEM-100CX electron microscope (Japan Electronic Co.), and the samples were prepared by dripping a drop of the capsules suspension onto the Formvar-coated copper grids. SEM images were obtained from a S-4300F electron microscope (Hitachi, Japan). Dynamic laser light scattering (DLS) was carried out at 20 °C on a commercial light scattering spectrometer (ALV/SP-125, Langen in Hessen, Germany) equipped with an ALV-5000 multi-τ digital time correlator and an He−Ne laser light source (632.8 nm), and ALV Correlator Software version 3.0 was used to evaluated the dynamic light scattering data.

Results and Discussion

PVP and PMAA were used as proton acceptor and proton donor, respectively. PVP and PMAA form interpolymer complexby hydrogen bonding,[11] and the work of erasable multilayer film from PVP and PMAA based on hydrogen bonding was reported recently.[8] To get straightforward understanding of the assembly nature of the PVP and PMAA, the LBL film was first constructed on the planar film of quartz and assembly process was monitored by the UV−vis spectrometer. The absorbance at 197 nm, which was contributed by the $\pi-\pi$ transition of PVP, increases linearly as a function of assembly cycle, indicating assembly process is successful. Convinced by the successful assembly on the planar template, PVP and PMAA were assembled on the cubic AgCl microcrystals and spherical SiO_2 particles. As shown in Figure 2, when the AgCl microcrystals were used as templates, the clear core−shell structure can be observed with SEM because the AgCl microcrystals were sensitive to electron beam that make the core−shell boundary manifest. In the case of the SiO_2 particles, the core−shell structure is not clear.

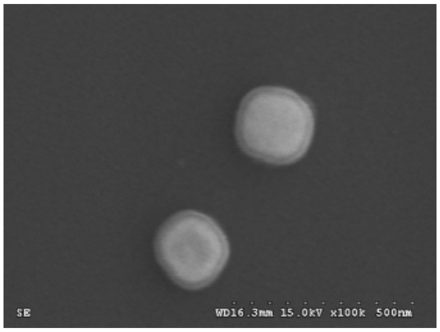

Figure 2. SEM micrographs of core−shell particles. Core: AgCl. Shell: $(PVP/PMAA)_5$.

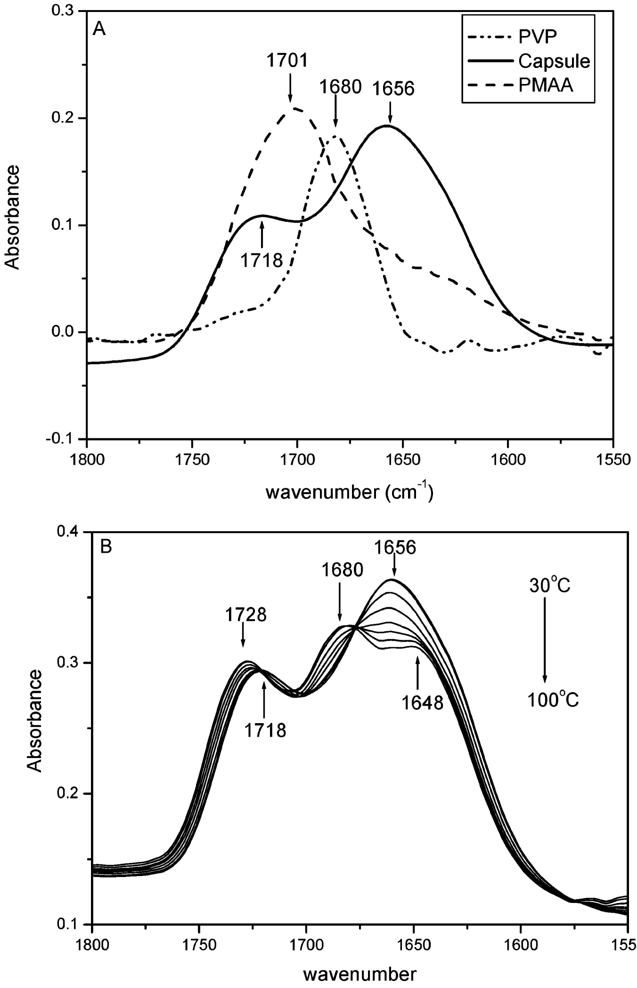

Figure 3. (A) FTIR spectra of PMAA, PVP, and $(PVP/PMAA)_5$ capsules. (B) Effect of temperature on the FTIR spectra for the capsules.

To confirm the hydrogen-bonding nature of the assembly, FTIR spectra were measured. As shown in Figure 3, PMAA exhibits a strong absorption band at 1701 cm^{-1} which is associated with the stretching of the uncharged dimerized or associated form of carboxylic groups,[8,12] while the bands with frequencies much higher than 1701 cm^{-1} are usually observed for an

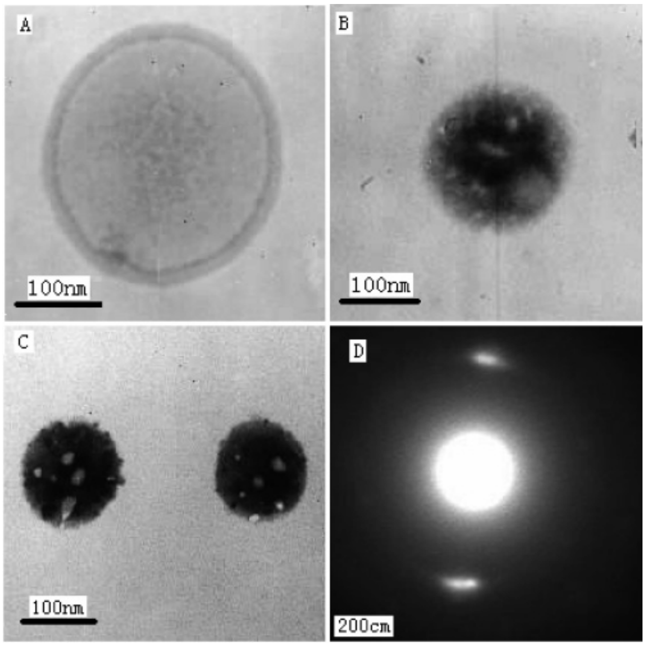

Figure 4. TEM image of five-bilayer capsules: (A) SiO_2 colloid particles as templates. (B) SiO_2 colloid particles as templates but incubated in the mixed solution of 0.1 M KSCN and 0.01 M HNO_3 for 24 h. (C) AgCl microcrystals as templates. (D) ED of the five-bilayer AgCl-templated capsules.

uncharged monomeric form of the carboxylic group.[13] The shape of the 1701 cm^{-1} band is clearly asymmetric with a noticeable spectral broadening at the lower frequencies. The peak broadening might be rooted in short-range interactions of carbonyl dipoles (higher probability of antiparallel arrangement of the dipoles)[14] or hydrogen bonding between more than two carboxylic groups.[12b] PVP exhibits a strong absorption band at 1680 cm^{-1}. As a comparison, the IR spectrum of the PVP/PMAA capsules shows two main strong absorption bands centered at 1718 and 1656 cm^{-1}. The 1718 cm^{-1} band was assigned to the carboxylic groups of PMAA, which shifts to higher frequencies compared with pure PMAA, indicating the hydrogen bonds among the carboxylic groups of PMAA were partly detached and intermolecular hydrogen bonds were formed between PMAA and PVP. The 1656 cm^{-1} band was assigned to C=O of the PVP, which shifts 24 cm^{-1} to the lower frequency and shows a broadening at the lower frequency side due to the hydrogen bonds formation between the carbonyl group of PVP and the carboxylic hydroxyl group of PMMA. The hydrogen bonding between PMAA and PVP was further confirmed by temperature-increased FTIR (Figure 3B). As the temperature increased, the peaks at 1718 cm^{-1} moved to 1728 cm^{-1} gradually because more intramolecular hydrogen bonding among PMAA carboxylic hydroxyl groups were detached at high temperature. At the same time, the peak at 1656 cm^{-1} disappeared, and a new peak at 1680 cm^{-1} which could be assigned to the free C=O of PVP appeared, clearly indicating the breakage of hydrogen bonding between PVP and PMAA at high temperature. The peak at 1680 cm^{-1} of PVP shifts to low frequencies on being assembled with PMAA and returns to 1680 cm^{-1} on temperature increasing further, demonstrating the hydrogen-bonding nature of the capsule.

The morphologies of the capsules were examined using TEM. Figure 4A shows a representative TEM image of the capsules using SiO_2 colloidal particles as templates, which presents a clear contrast between the center and the shell, indicating the presence of a hollow morphology. The capsules are round in shape just like the SiO_2 templates, and their average diameter is 300 nm, which is in accord with the average size of the templates. The capsule wall is continuous and smooth similar to that of the hydrogen-bonding capsules from PVP and phenolic resin,[6] but its analogues based on electrostatic force assembly usually show folds and creases.[3]

The capsules using cubic AgCl microcrystals as template exhibit a quite different morphology (Figure 4C). They have a highly rough surface. Because of the high roughness, there is no contrast between the center and the shell. In addition, some holes with a diameter of about 15 nm were found on the capsules wall. The average diameter of the capsules is about 120 nm, which corresponds to the size of the AgCl template. The capsules are round, indicating that the mutlilayer shells assembled on essentially cubic AgCl microcrystals undergo a morphology change from cubic to spherical upon dissolution of the AgCl cores. The result of electronic diffraction (ED) in the TEM shows that there remain silver particles on the capsule wall, which is a result of the photolysis of AgCl during the buildup of the assembled film and dissolution of the AgCl cores. The presence of silver particles is another reason for the absence of contrast between the center and the shell.

The significant difference in morphology between the capsules from SiO_2 template and AgCl template could be attributed to the different methods of removing the cores. To remove the AgCl cores, a mixture solution of KSCN (0.1 M) and HNO_3 (0.01 M) was used. Our preliminary experiment indicated that the annealing LBL films based on hydrogen bonding in aqueous solution with high ionic strength resulted in significant change of morphology. After annealing, the film became rougher, and holes formed on the films. To confirm this hypothesis, the capsules from SiO_2 template were annealed in the same mixture solution of KSCN and $HNNO_3$. After 24 h, the solution was dialyzed against the water to remove the excess KSCN, and the pH of the solution was adjusted to 5. The resultant capsules were examined using TEM. As shown in Figure 4B, the morphology of the capsules changed significantly. The capsule wall was no longer smooth but was as rough as those using AgCl microcrystals as template. In addition, similar holes were also found on the shell of these capsules. The average diameter of the capsules is about 200 nm much less than that before annealing, indicating during annealing the capsules underwent not only a morphological change but also shrinkage.

TEM only provided information about the dried samples. To reveal the change of the capsules in situ, dynamic laser light scattering was employed. As shown in Figure 5, before the KSCN annealing, the R_h distribution displays three peaks. The main peak is at 143.2 nm and is attributed to single capsules. The peak at 5.7 nm indicates that there still are PVP/PMAA complexes in the solution. Our previous work of DLS study of nanocapsule based on electrostatic assembly showed that R_h has a peak at this position, too.[15] In the washing process of the preparation of the capsules, the polymers applied to assemble cannot be removed completely. The remained trace in the solution tends to form polymer complex. This polymer complex was so small that it cannot be separated by filtration in the sample prepara-

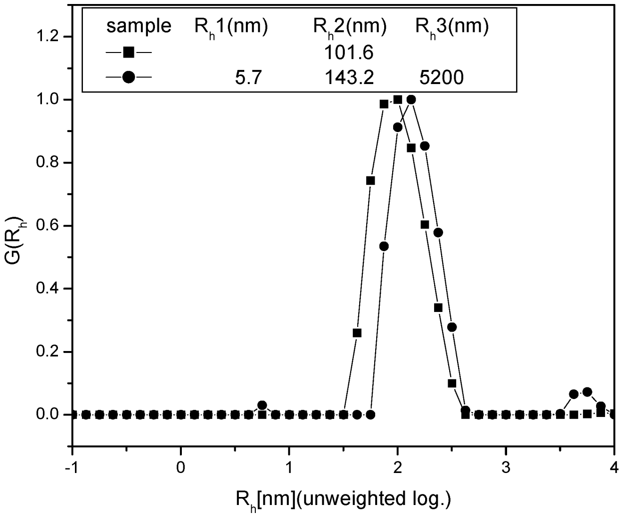

Figure 5. Distributions of hydrodynamic radius of the nanocapsules from SiO_2 template: (●) before KSCN annealing; (■) after KSCN annealing.

tion of DLS, so the peak at 5.7 nm appeared. The peak at 5200 nm is assigned to capsule aggregates. The outer layer of the resultant capsule is PMAA, and only part of the carboxylic groups of PMAA ionizes at pH = 5, which provides an opportunity to integrate with other capsules. After KSCN annealing, the R_h distribution exhibits only a peak at 101.6 nm. The change of R_h indicates that KSCN probably causes the rearrangement among the polymer chain in the capsule, which is the main reason for the capsules shrinking and forming pores on their shells.

In conclusion, we have successfully prepared the porous and nonporous nanocapsules based on hydrogen bonding in the aqueous solution. Inorganic ions can make the nonporous capsule shrink and form pores, which is probably very useful in the application of drug release.

Acknowledgment. This work was supported by National Natural Science Foundation of China (No. 20204017) and 2004 Outstanding Young Foundation of NSFC rewarded for J. Xu.

References and Notes

(1) (a) Decher, G.; Hong, J. D. *Makromol. Chem. Macromol. Symp.* **1991**, *46*, 321. (b) Decher, G.; HONG, J. D. *Phys. Chem. Chem. Phys.* **1991**, *95*, 1430. (c) Decher, G.; Hong, J. D.; Schmitt, J. *Thin Solid Films* **1992**, *210*, 831.

(2) Donath, E.; Walther, D.; Shilov, V. N.; Knippel, E.; Budde, A.; Lowack, K.; Helm, C. A.; Mohwald, H. *Langmuir* **1997**, *13*, 5294.

(3) (a) Donath, E.; Sukhorukov, G. B.; Caruso, F.; Davis, S. A.; Mohwald, H. *Angew. Chem., Int. Ed.* **1998**, *37*, 2202. (b) Sukhorukov, G. B.; Donath, E.; Davis, S.; Lichtenfeld, H.; Caruso, F.; Popov, V. I.; Mohwald, H. *Polym. Adv. Technol.* **1998**, *9*, 759. (c) Caruso, F.; Caruso, R. A.; Mohwald, H. *Science* **1998**, *282*, 111. (d) Berth, G.; Voigt, A.; Dantzenberg, H.; Donath, E.; Mohwald, H. *Biomacromolecules* **2003**, *3*, 579.

(4) (a) Caruso, F. *Chem.—Eur. J.* **2000**, *6*, 413. (b) Ibarz, G.; Dahne, L.; Donath, E.; Mohwald, H. *Adv. Mater.* **2001**, *13*, 1324. (c) Dahne, L.; Lepotratti, S.; Donath, E.; Mohwald, H. *J. Am. Chem. Soc.* **2001**, *123*, 5431.

(5) Zhang, Y.; Yang, S.; Guan, Y.; Cao, W.; Xu, J. *Macromolecules* **2003**, *36*, 4238.

(6) Zhang, Y.; Guan, Y.; Yang, S.; Xu, J.; Han, C. C. *Adv. Mater.* **2003**, *15*, 832.

(7) (a) Ibarz, G.; Dahne, L.; Donath, E.; Mohwald, H. *Chem. Mater.* **2002**, *14*, 4059. (b) Lulevich, V. V.; Radtchenko, I. L.; Sukhorukov, G. B.; Vinogradova, O. I. *J. Phys. Chem. B* **2003**, *107*, 2735. (c) Lulevich, V. V.; Radtchenko, I. L.; Sukhorukov, G. B.; Vinogradova, O. I. *Macromolecules* **2003**, *36*, 2832. (d) Sukhorukov, G. B.; Brumen, M.; Donath, E.; Mohwald, H. *J. Phys. Chem. B* **1999**, *103*, 6434. (e) Petrov, A. I.; Garvyushkin, A. V.; Sukhorukov, G. B. *J. Phys. Chem. B* **2003**, *107*, 868. (f) Gao, C.; Leporatti, S.; Moya, S.; Donath, E.; Mohwald, H. *Chem.—Eur. J.* **2003**, *9*, 915.

(8) Sukhishvili, S. A.; Cranick, S. *Macromolecules* **2002**, *35*, 301.

(9) Sugimoto, T.; Shiba, F.; Sekiguchi, T.; Itoh, H. *Colloids Surf. A* **2000**, *164*, 183.

(10) Stober, W.; Fink, A.; Bohn, E. *J. Colloid Interface Sci.* **1968**, *26*, 62.

(11) Yan, S.; Chen, Z.; Song, Z.; Pao, Q. *Water Soluble Polymer: Poly (methacrylic acid) and Poly (acrylic acid)*, in Chinese; Chemical Industry Press: Beijing, 1988.

(12) (a) Lu, X.; Weiss, R. A. *Macromolecules* **1995**, *28*, 3022. (b) Dong, J.; Ozaki, Y.; Nakashima, K. *Macromolecules* **1997**, *30*, 1111.

(13) Lee, J. Y.; Painter, P. C.; Coleman, M. M. *Macromolecules* **1988**, *21*, 346.

(14) Painter, P. C.; Pehlert, G. J.; Hu, Y. H.; Coleman, M. M. *Macromolecules* **1999**, *32*, 2055.

(15) Zhang, Y.; Guan, Y.; Yang, S.; Xu, J.; Miao, Y.; Cao, W. *Chin. J. Polym. Sci.* **2004**, *22*, 111.

MA048182V