A New Strategy for the Preparation of Polyamide-6 Microspheres with Designed Morphology

Aihua Pei,[†,‡] Andong Liu,[†,‡] Tingxiu Xie,[§] and Guisheng Yang*[,†,§]

Beijing National Laboratory for Molecular Sciences, Key Laboratory of Engineering Plastic, Joint Laboratory of Polymer Science and Technology, Institute of Chemistry, Chinese Academy of Sciences, Beijing 100080, China; Graduate School of the Chinese Academy of Sciences, Beijing 100080, China; and Shanghai Genius Advanced Materials Co., Ltd., Shanghai 201109, China

Received August 18, 2006
Revised Manuscript Received September 21, 2006

1. Introduction. Protein (enzyme, antibody) immobilization has wide applications in many areas, such as solid-phase diagnostics, biosensors, biocatalysts, extracorporeal therapy, and bioseparation.[1−5] Polymer microspheres with functional groups including hydroxyl, amine, carboxyl, and aldehyde groups are often used as supports for protein covalent immobilization.[6−11] Containing amine and carboxyl group, polyamide-6 (nylon-6) microsphere is an attractive carrier and thus has great potential in bioengineering involving protein (or enzyme) immobilization because of the same functional bond namely amide in their main chains. Furthermore, nylon-6 microspheres are of particular interest for their direct and potential applications in fields of industrial materials for rotational molding, sintering, powder coating, etc. However, facile methods for preparation of micron-sized nylon-6 spheres with narrow size distribution were scarcely reported.

Nylon-6 can be synthesized either via anionic ring-opening polymerization that being carried out at rather low temperature of 150 °C in the presence of an activator or via hydrolytic polycondensation reaction at much higher temperature of 250 °C. Compared with hydrolytic polycondensation, nylon-6 made via anionic polymerization possesses more predominance due to the faster polymerization rate and higher molecules weight. Nylon-6 powders with diameters of 250−500 μm have been obtained by the ϵ-caprolactam (CL) precipitation polymerization via anionic route in solution.[12−14] Ricco et al. synthesized powdered nylon-6 via suspension polymerization of ϵ-caprolactam taking advantage of the "activated anionic mechanism", and micron-sized particles with average diameter from 53 to 479 μm were obtained.[15] Crespy and Landfester synthesized nylon-6 nanoparticles by anionic polymerization of ϵ-caprolactam in heterophase using the miniemulsion process.[16] However, all these processes are limited to quite complex technics and/or give comparatively low efficiency and thus are difficult for commercialization. Furthermore, most of the obtained nylon-6 particles are irregular powder with wide size polydispersity or a mixture of spherical shaped and irregularly shaped multiparticle microaggregates and thus would make big difficulties for the potential applications. Additionally, the pollution to environment given by the suspension[15] and miniemulsion[16] processes would also exercise a great influence for the potential applications. Therefore, exploring an alternative method for preparation of nylon-6 particles with regularly spherical shape and controllable size should be of great interests to biologists, chemists, and materials scientists and shows attractive commercial promise.

In this communication, we report a new method for synthesis of nylon-6 microspheres with tunable diameters according to the method presented in our patent.[17] It is highly important that the diameter range of the nylon-6 microspheres synthesized were among several to several dozen micrometers, and the size distribution was rather narrow. The key strategy is to adjust the phase inversion morphology generated in the PS (polystyrene)/nylon-6 blends to prepare size controllable nylon-6 microspheres via a successively in-situ polymerization method. Interestingly, the phase inversion occurs at an extremely low PS content (15 wt %), and it is impossible for the polymer pairs via the traditional melt mixing.[18,19] Another novel characteristic is that the desired diameters of the nylon-6 microspheres can be obtained by only changing the PS content in the nylon-6/PS blends.

2. Experimental Section. a. Materials. CL was obtained from Nanjing Oriental Chemical Co. (Commercial Grade, China). Azodiisobutyronitrile (AIBN), sodium caprolactamate (NaCL), and 2,4-toluene diisocyanate (TDI) (analysis purity) used in this study were all purchased from Shanghai Chemical Reagents Co. and used without further treatment. Styrene was freshly distilled at 40 °C under vacuum before use.

b. Polymerization of Styrene in ϵ-Caprolactam. Freshly distilled styrene was dispersed in melted ϵ-caprolactam monomer at 80 °C with the weigh ratio of 40/60, and a homogeneous transparent mixture was observed. Then 0.2 wt % AIBN was added and kept stirred for 24 h at 80 °C for the polymerization of styrene. After it, a clear and viscous mixture was obtained.

c. Preparation of Nylon-6/PS Blends. A certain amount of the obtained PS/CL mixture was taken out and mixed with ϵ-caprolactam to desired PS concentration. Then the mixture was vacuumed at 150 °C for 20 min to remove residual styrene monomer and the trace amount of the water. After this, 4 wt % NaCL was added under stirring for 5 min, and then 0.4 wt % TDI was added with stirring. The mixture was then immediately poured into a mold preheated to 180 °C and polymerized in oven at 180 °C for 20 min. The blends obtained were denoted as S15 (PS 15 wt %), S20 (PS 20 wt %), S25 (PS 25 wt %), S30 (PS 30 wt %), S35 (PS 35 wt %), and S40 (PS 40 wt %).

d. Preparation of Nylon-6 Microspheres. The obtained nylon-6/PS blends with different composition were shattered and then immersed into tetrahydrofuran (THF) for 2 h to allow the dissolving of the PS. The nylon-6 microspheres were separated by centrifugation.

e. Characterization. Gel permeation chromatography (GPC) was used to evaluate the weight-average molecular weight (M_w) of PS and nylon-6 microspheres and their polydispersity (M_w/M_n) by calibration with a PS and PA6 standard, respectively. The measurements were carried out in polymeric solution at 35 °C. A JSM LV-5600 (JEOL) transmission electron microscope was performed at an acceleration voltage 10 kV. A MASTERSIZER 2000 (MALVERN) laser diffraction size analyzer was used to determine the number-average (D_n) and volume-average (D_v) diameters of the nylon-6 microspheres. The size distribution was calculated from D_v/D_n.

3. Results and Discussion. The nylon-6/PS blends were prepared via successive in-situ polymerization of the styrene

---

[†] Chinese Academy of Sciences.
[‡] Graduate School of the Chinese Academy of Sciences.
[§] Shanghai Genius Advanced Materials Co., Ltd.
***** Correspondence author: E-mail ygs@geniuscn.com.

10.1021/ma061905l CCC: $33.50

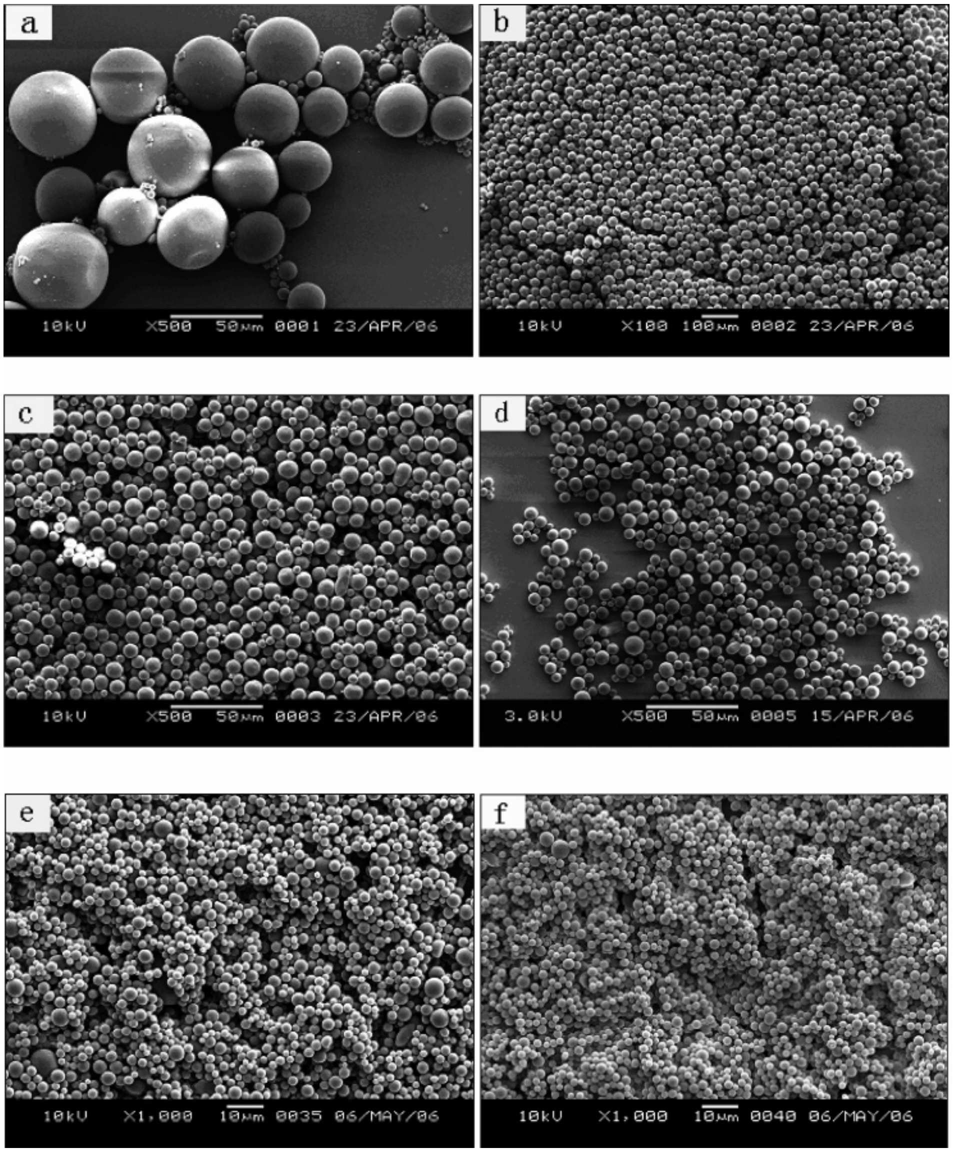

Figure 1. SEM images of the nylon-6 microspheres prepared after the dissolution of the PS phase from the nylon-6/PS blend: (a) S15, (b) S20, (c) S25, (d) S30, (e) S35, and (f) S40.

(free radical polymerization) and ϵ-caprolactam monomers (anionic ring-opening polymerization) in one reactor. During the in-situ compounding process, the free radical polymerization of styrene was first performed using ϵ-caprolactam as solvent, and second, the anionic ring-opening of ϵ-caprolactam was initiated in situ in the in-situ prepared PS component. The morphologies of the blends show great differences with the variation of the PS content (see the Supporting Information for SEM images of the in-situ prepared blends). Once the PS content is higher than 15 wt %, phase inversion starts up, and the phase morphology of the nylon-6/PS blends gradually changes from the PS dispersed/nylon-6 matrix to nylon-6 dispersed/PS matrix system. As PS content is between 15 and 35 wt %, the nylon-6 phase is spherical, and the PS component exists mainly in the gap of nylon-6 spheres, though the PS might not entirely enwrap the nylon-6 particles. As PS content is up to 40 wt %, phase inversion completes, and the nylon-6 particles are completely isolated by the PS matrix. By etching the PS matrix with solvent, the nylon-6 spheres were easily obtained. For the phase inversion blends, as soon as the PS continuous phase was removed by THF, the systems collapsed completely, and therefore nylon-6 microspheres will be obtained. The morphology of the nylon-6 microspheres will be described in detail in the next paragraph.

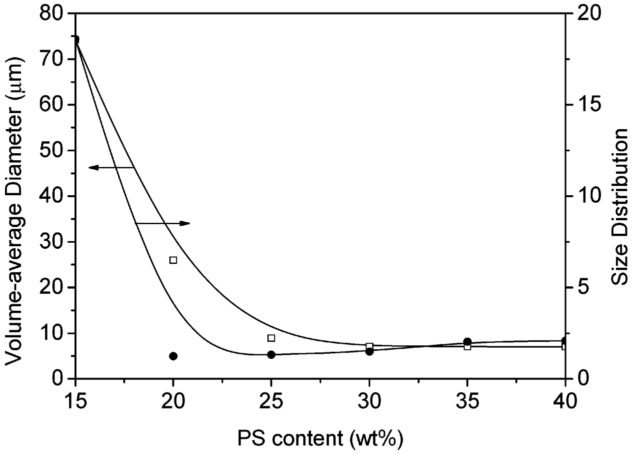

Figure 2. Volume-average diameter (D_v) and size distribution of the nylon-6 microspheres as a function of the PS content in nylon-6/PS blends.

Attractively, the phase inversion of the nylon-6/PS blends occurs at very low PS content, providing a convenient way to remove the PS. The solvent for the PS dissolving can be recycled, and the PS dissolved can be reclaimed for utilization. Therefore,

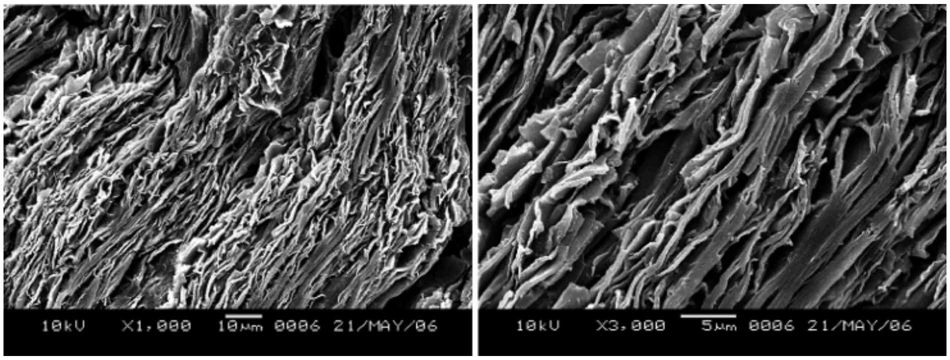

Figure 3. SEM images of the PS/CL mixture with PS content of 40 wt %.

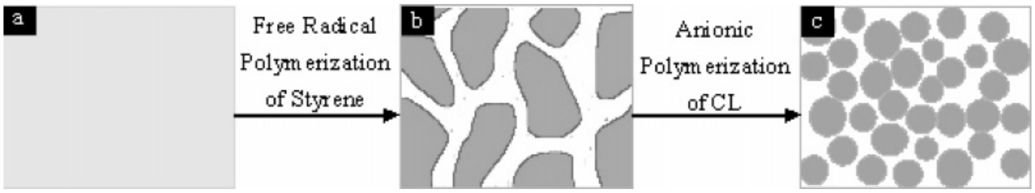

Figure 4. Schematic diagram for preparation of nylon-6 microspheres: (a) mixture of styrene and CL; (b) mixture of PS and CL; (c) blend of nylon-6/PS. The gray part in (b) and (c) is CL and nylon-6 particles, respectively. The white part in (b) and (c) is PS phase.

the present method used for the preparation of nylon-6 microspheres shows the advantage for commercialization.

The diameter of the nylon-6 microspheres changes with the composition of the blends, as verified by the scanning electron microscope (SEM) displayed in Figure 1 and laser diffraction size analyzer (Figure 2). In the case of the S15 system, the volume mean diameter of nylon-6 spheres is 74.2 μm, and the size is poorly uniform. While for the S20 system, the nylon-6 spheres become much smaller (26.0 μm in diameter) and more uniform. With the PS content further increasing to 25 wt %, the size of the nylon-6 spheres decreases and the volume-average diameter is 8.9 μm. For the systems of S30, S35, and S40 systems, the nylon-6 diameter decreases slightly, though the trend is not so obvious (Figure 2). The curious phenomenon is that the particle size distribution of the S15 is the broadest, while S20 is the narrowest. For the other blending systems with higher PS content, the size distribution again gets a little bit broader, but the uptrend is neglectable. The above series of experiments demonstrate that, by varying the PS content in the blends, nylon-6 microspheres with controllable size can be conveniently prepared.

To explore the formation mechanism of nylon-6 microspheres, the morphology of the PS/CL mixture with 40 wt % PS was also investigated by SEM Figure 3 to show how the molecules of PS and the CL coexist. For a clear observation, the CL in the mixture was carefully extracted by methanol, and then the interpenetrating characteristic of the cocontinuous morphology was found, in which the PS disperses as platelet or lamellar with CL exists in the interlayers. Though the structure might suffer slight distortion, it still could reflect the original framework of the PS/CL mixture. The PS/CL mixture with 20 wt % PS was also studied by SEM, but the attempt failed due to the fragile structure contributed to the large quantity of CL. On the basis of the results, we derived the schematic diagram for the formation of the nylon-6 spheres (Figure 4). When the mixture of 40 wt % PS/CL was diluted with CL, the CL molecules would penetrate into the framework of PS to form a swelled cocontinuous system. In the case of the mixture with sufficient low PS concentration (10 wt % or lower), PS molecules could not exist in the continuous form anymore, and it would be fully surrounded by CL. So in blends of S10, the PS was dispersed phase and the nylon-6 was the matrix. While for the mixture with 15 wt % PS or higher, the PS phase was still continuous, even after dilution with CL. After in-situ rapid anionic polymerization of the CL existed among the PS phase, the original structure was maintained. Therefore, the blends of S15−S40 gave a morphology in which nylon-6 was dispersed in the continuous PS matrix.

Furthermore, hydrolytic polycondensation instead of anionic polymerization was also utilized to polymerization the CL in the presence of PS compound for preparation of nylon-6/PS blends with 20 wt % PS; the other conditions were exactly the same. Unfortunately, the SEM of the blends synthesized showed that the PS was dispersed as minor phase in the PA6 matrix, and it could not be separated in THF, which further proved that the PS was not the continuous phase. These phenomena show obvious difference from that PS/MCPA6 blend with same PS content synthesized from in-situ anionic ring-opening polymerization of CL. As a result, we can speculate that the in-situ anionic ring-opening of ϵ-caprolactam developed here plays a pivotal role in determining the morphology development of the nylon-6/PS blends. The greatest interest of the ϵ-caprolactam anionic polymerization resides in that it is a fast material generation process, and it is well-known that ϵ-caprolactam anionic polymerization occurs at a significantly faster rate (total conversion within only a few minutes) compared to the classical hydrolytic polymerization process which takes about several hours depending on the conditions used. Another predominance of anionic polymerization is that it can be operated in a comparatively low temperature lower than the melt point of nylon-6 while higher than the T_g of PS. As a result, the solid-state PA6 that resulted from faster polymerization of CL contracted into spheres and was dispersed among the softened PS once the PS content was high enough to envelop the nylon-6.

The weight-average molecular weight (M_w) and number-average molecular weight (M_n) of the PS and nylon-6 were determined by gel permeation chromatography (GPC). M_n of the PS in the systems mentioned above is 5.6×10^4 g mol^{-1}, and M_w is 11.1×10^4 g mol^{-1}. The polydispersity (M_w/M_n) is 1.98. M_n of the nylon-6 microspheres is $(1.4-1.7) \times 10^4$ g mol^{-1}, and M_w is $(2.4-3.5) \times 10^4$ g mol^{-1}. Because the activator and catalyst were consistent in all systems for the anionic ring-opening polymerization, the value of molecular weight was varied according to the nylon-6 contents, and it decreased with decreasing of the nylon-6.

During the experiment, it can be found that the onset of the phase inversion changes with the molecular weight of PS. The larger the PS molecular size, the lower the PS content at which the phase inversion was generated. In general, the higher the molecular weight, the higher the viscosity of PS. It seems that the viscosities of the PS play a pivotal role in the dispersion of PS in CL, and as a result, the morphology of the nylon-6/PS blends evidently changed. The mechanism is still under study.

4. Conclusions. In conclusion, we have demonstrated a facile approach to prepare nylon-6 microspheres by adjusting phase inversion morphology generated in the nylon-6/PS blends at very low PS contents. The process consisted of first radical polymerization of styrene in CL and second in-situ anionic ring-opening polymerization of CL in the presence of in-situ prepared PS component. The fast anionic polymerization of CL favors the formation of the phase inversion morphology in nylon-6/PS blends at an extremely low PS content. The nylon-6 microspheres with a diameter ranging from 7 to 80 μm are easily obtained by adjusting the PS content of the nylon-6/PS blends. The M_w of the nylon-6 in this system is varied from 2.4×10^4 to 3.5×10^4 g mol^{-1}. The nylon-6 microspheres obtained possibly find extensive use especially for protein immobilization due to its intrinsic functional group and morphology characteristics.

Acknowledgment. This work was supported by the 973 Program (No. 2003CB6156002).

Supporting Information Available: SEM images of nylon-6/PS blends S15, S20, S25, S30, S35, and S40 and SEM micrograph of 80PA6/20PS blend. This material is available free of charge via the Internet at http://pubs.acs.org.

References and Notes

(1) Zhao, X. W.; Liu, Z. B.; Yang, H.; Nagai, K.; Zhao, Y. H.; Gu, Z. Z. *Chem. Mater.* **2006**, *18*, 2443−2449.
(2) Ma , Z. Y.; Guan, Y. P.; Liu, X. Q.; Liu, H. Z. *Polym. Adv. Technol.* **2005**, *16*, 554−558.
(3) Bousalem, S.; Benabderrahmane, S.; Sang, Y. Y. C.; Mangeney, C.; Chehimi, M. M. *J. Mater. Chem.* **2005**, *30*, 3109−3116.
(4) Phadtare, S.; Kumar, A.; Vinod, V. P.; Dash, C.; Palaskar, D. V.; Rao, M.; Shukla, P. G.; Sivaram, S.; Sastry, M. *Chem. Mater.* **2003**, *15*, 1944−1949.
(5) Jia, H. F.; Zhu, G. Y.; Wang, P. *Biotechnol. Bioeng.* **2003**, *84*, 406−414.
(6) Godjevargova, T.; Nenkova, R.; Dimova, N. *Macromol. Biosci.* **2005**, *5*, 760−766.
(7) Darkow, R.; Groth, T.; Albrecht, W.; Lützow, K.; Paul, D. *Biomaterials* **1999**, *20*, 1277−1283.
(8) Yalçin, G.; Elmas, B.; Tuncel, M.; Tuncel, A. *J. Appl. Polym. Sci.* **2006**, *101*, 818−824.
(9) Hu, J.; Li, S. J.; Liu, B. L. *Biotechnol. J.* **2006**, *1*, 75−79.
(10) Wu, C. W.; Lee, J. G.; Lee, W. C. *Biotechnol. Appl. Biochem.* **1998**, *27*, 225−230.
(11) Bahar, T.; Tuncel, A. *React. Funct. Polym.* **2000**, *44*, 71−78.
(12) Vasiliu-Oprea, C.; Dan, F. *J. Appl. Polym. Sci.* **1996**, *62*, 1517−1527.
(13) Vasiliu-Oprea, C.; Dan, F. *J. Appl. Polym. Sci.* **1997**, *64*, 2575−2583.
(14) Dan, F.; Vasiliu-Oprea, C. *J. Appl. Polym. Sci.* **1998**, *67*, 231−243.
(15) Ricco, L.; Monticelli, O.; Russo, S.; Paglianti, A.; Mariani**,** A. *Macromol. Chem. Phys.* **2002**, *203*, 1436−1444.
(16) Crespy, D.; Landfester, K. *Macromolecules* **2005**, *38*, 6882−6887.
(17) Pei, A. H.; Xie, T. X.; Yang, G. S. Application No. 2006100268059 (China Patent).
(18) Omonov, T. S.; Harrats, C.; Groeninckx, G. *Polymer* **2005**, *46*, 12322−12336.
(19) Li, J. M.; Ma, P. L.; Favis, B. D. *Macromolecules* **2002**, *35*, 2005−2016.

MA061905L