

Synthesis of Novel Magnetic Polymer Microspheres with Amphiphilic Structure

Xue-Yong Liu,^{1,2} Xiao-Bin Ding,¹ Zhao-Hui Zheng,¹ Yu-Xing Peng,¹ Xin-Ping Long,² Xiao-Chuan Wang,² Albert S. C. Chan,³ C. W. Yip³

¹Chengdu Institute of Organic Chemistry, Chinese Academy of Sciences, Chengdu 610041, People's Republic of China

²Institute of Chemical Materials, China Academy of Engineering Physics, Shichuan Mianyang 919-311, 621900, People's Republic of China

³Open Laboratory of Chirotechnology and Department of Applied Biology and Chemical Technology, The Hong Kong Polytechnic University, Hong Kong, People's Republic of China

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ABSTRACT: Novel magnetic polymer microspheres with amphiphilic structure ranging in diameter from 5 to 80 μm were prepared by dispersion copolymerization of styrene and poly(ethylene oxide) acrylamide macromonomer (MPEO) in the presence of Fe_3O_4 magnetic fluid. The effects of various polymerization parameters on the average particle size were systematically investigated. The average particle size was found to increase with increasing initiator

concentration. It also increased with decreasing stabilizer concentration and MPEO concentration. The content of the amino groups localized in the microspheres ranged from 0.01 to 0.25 mmol/g. © 2003 Wiley Periodicals, Inc. *J Appl Polym Sci* 90: 1879–1884, 2003

Key words: amphiphilic; magnetic; microsphere

INTRODUCTION

In the past twenty years magnetic polymer microspheres have been widely used in many fields, such as cell separation, magnetic target drug, enzyme immunoassay, magnetic field assisted radionuclide therapy, etc., because of their relatively rapid and easy magnetic separation and specific surface.^{1–3}

With the development of solid-phase synthesis, especially combinatorial synthesis, amphiphilic polymer microspheres have become the focus of greater attention due to their special chemical and physical qualities. As a novel material of functional polymers, amphiphilic polymer microspheres have been applied in many fields such as solid-phase organic synthesis, organic catalysis, biomedicine and analytic chemistry, etc.^{4,5} For example, as support for catalysts, amphiphilic polymer microspheres exhibit a homogeneous catalysis property, which causes the catalysts immobilized on amphiphilic polymer microspheres to have similar reactivity and enantioselectivity compared with catalyst itself.

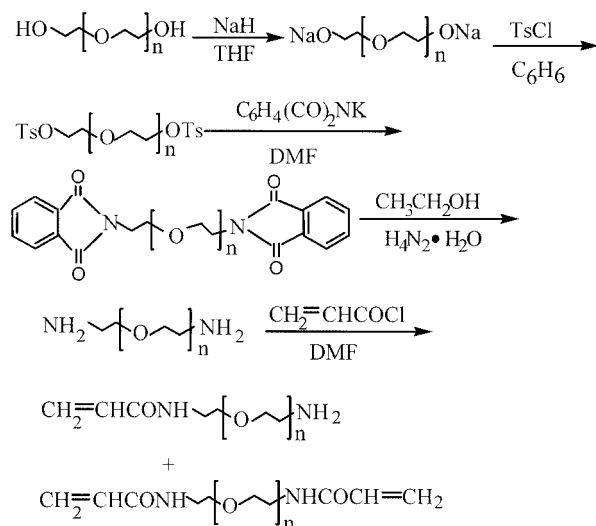
Recently, polymer-supported catalysts have attracted much interest due to the recyclability of the catalysts. Different kinds of inorganic and organic polymers, including soluble and insoluble types, have been devised as support for catalysts. A soluble polymer such as poly(ethylene oxide) supported catalysts exhibits excellent reactivity and selectivity, but the separation of the polymers from the solution requires special treatments such as adding a nonsolvent, which is time-consuming and energy-consuming.^{6,7} As for an insoluble polymeric membrane or microspheres (e.g., crosslinked polystyrene) used as support, though it is better than a soluble polymer for recycling of catalysts, it also needs centrifugation or filtration. Furthermore, it causes a decrease of reaction yield and enantioselectivities.^{8,9} In order to overcome such problems, magnetic polymer microspheres with amphiphilic structure, combined with the merits of homogeneous catalysis with easy separation property, were designed and prepared by us.

In previous work, a sort of magnetic amphiphilic polymer microsphere was synthesized by copolymerization of a styrene and poly(ethylene oxide) vinylbenzyl (PEO-VB) macromonomer.^{10,11} The catalysts can be immobilized on the magnetic microspheres containing hydroxyl groups in the form of ester or ether. In the following organic catalysis experiments, however, we find the ester or ether bond between catalysts and magnetic polymer microspheres is not stable in reaction media. Because the amide bond is more stable than the ester or ether bond, in this study we first

Correspondence to: Y.-X. Peng (xyliu73@hotmail.com).

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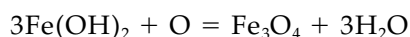
Scheme 1 The reaction procedure of MPEO.

prepared a poly(ethylene oxide) acrylamide ($\text{NH}_2\text{-PEO-AA}$) macromonomer (MPEO); then novel magnetic amphiphilic polymer microspheres containing amino groups were synthesized by copolymerization of styrene and MPEO in the presence of magnetic fluid; and the influences of several key polymerization parameters on particle diameter, including initiator concentration, stabilizer concentration, and monomer concentration, were described.

EXPERIMENTAL

Materials

Styrene (St) was distilled under reduced pressure to remove the inhibitor. Tetrahydrofuran (THF, analytical reagent (AR)), *N,N*-dimethylformamide (DMF, A.R.), and methylene chloride (CH_2Cl_2 , AR) were purified by distillation. Poly(ethylene oxide) (PEG, $M_w = 4000$, $M_w = 2000$) was dried under vacuum at 90°C at least 12 h. Acryloyl chloride (stabilized with 0.1% phenothiazine, Acros), potassium persulfate (KPS, A.R.), and ethanol (A.R.) were used without further purification. Triethylamine was refluxed with sodium to remove water. Water was distilled twice. Fe_3O_4 magnetic fluid with average diameter of 50 nm was prepared by the precipitation-oxidation method as mentioned in our previous work.¹²



Synthesis of MPEO

The schematic reaction procedure of MPEO is represented in Scheme 1. First, diamino poly(ethylene ox-

ide) ($\text{NH}_2\text{-PEO-NH}_2$) was prepared from PEG ($\bar{M}_w = 2000$) by the Gabriel-S method.¹³ Then MPEO was synthesized as follows: 2 g $\text{NH}_2\text{-PEO-NH}_2$ was dissolved in 80 mL DMF, 0.2 mL triethylamine was added to the mixture, and the mixture stirred for 2 h at 10°C under a nitrogen atmosphere. Then 0.1 mL acryloyl chloride was slowly added to the reaction mixture at 10°C and stirred for another 10 h. The products were precipitated from the filtrate by adding ethyl ether and then dissolved in DMF to remove insoluble impurities by filtration. Solid products were obtained by adding cold ethyl ether in the mother liquid. Pure products were obtained by drying under vacuum at 40°C .

Preparation of magnetic amphiphilic polymer microspheres

Magnetic amphiphilic polymer microspheres were prepared by dispersion copolymerization of St and PEO acrylamide macromonomer in the presence of Fe_3O_4 magnetic fluid in ethanol/water. KPS and PEG ($M_w = 4000$) were used as initiator and stabilizer, respectively, in the polymerization. The required ingredients were added into a 250 mL four-necked flask and the mixture was stirred for 10 h at 70°C under a nitrogen atmosphere. The resulted microspheres were purified with distilled water and separated under a magnetic field, respectively. This procedure was repeated after the microspheres were immersed in a 1 mol/L HCl solution for 48 h to remove the Fe_3O_4 powder nonencapsulated by the polymer. The typical recipe used in this study is given in Table I.

Characterization

The structure of MPEO was confirmed by $^1\text{H-NMR}$ (nuclear magnetic resonance) spectra (AC-P, 300 MHz; Bruker Instruments) in CDCl_3 with tetramethylsilane as an internal standard.

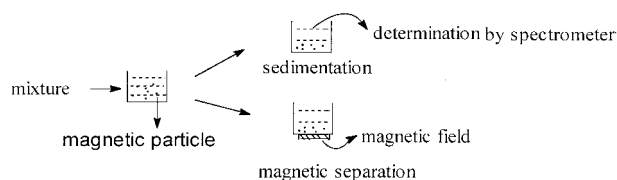
The structure of copolymer was confirmed by infrared spectroscopy (Nicolet 200SXV) using KBr pellets.

The average size and size distribution of magnetic microspheres were obtained by means of a scanning

TABLE I
Typical Recipe for Dispersion Copolymerization^a

Materials	Weight (g)
Styrene	15.0
MPEO	1.2
PEG	4.0
Magnetic fluid	10.0
Ethanol	52.0
Water	40.0
KPS	0.45

^a 70°C , 10 h.



Scheme 2 Method for determining the magnetic responsiveness.

electron microscope (AMRAY-1000, Amray, USA). The data analysis was conducted for more than 800 microspheres by computer. For SEM studies, the samples were coated under vacuum with a thin layer of gold.

The content of amino groups localized in the microspheres were determined by the Gisin test.¹⁴The whole procedure of the Gisin test is as follows: The amine-containing polymer is treated with a solution of picric acid to form a salt with the polymer-bound amino groups. After thorough washing to remove the excess of picric acid, the polymer is treated with an excess of a strong base, which quantitatively releases the picrate from the polymer into solution. The concentration of picrate in this solution is determined spectrophotometrically and reflects the amino groups content of the polymer.

The magnetic responsiveness of the microspheres was investigated as follows: 0.5 g microspheres were suspended in 20 mL water and then the transmittance of the suspension was determined with a spectrometer (721) at 580 nm at a predetermined time under an additional 0.42T magnetic field or under sedimentation condition. The shorter the time required for transmittance to reach 98%, the better the magnetic responsiveness indicated. The whole process is shown in Scheme 2.

RESULT AND DISCUSSION

Synthesis of MPEO

Figure 1 shows the ¹H-NMR of MPEO (PEG, $M_w=2000$) used in our experiment. The ratio of bifunctional PEO macromonomer (AA-PEO-AA) can be determined by probability analysis, according to the following equation¹⁵:

$$AA-PEO-AA = P^2$$

where P is the probability of the hydroxyl group to be substituted.

Obviously, the resulted microspheres are crosslinked polymer. The crosslinked structure is very essential for magnetic microspheres, which can avoid encapsulated magnetic powder detaching from microspheres. By analyzing the squares of different peaks, the composition of the PEO macromonomer can be calculated as follows: $NH_2-PEO-AA:AA-PEO-AA:NH_2-PEO-NH_2 = 0.48:0.34:0.18$.

Synthesis of magnetic amphiphilic microspheres

In this study, the influences of various polymerization parameters, including initiator concentration, monomer concentration, and stabilizer concentration, were investigated systematically. In all these studies, the basic recipe given in Table I was used, while one parameter was varied as specified, keeping the others the same as given in the recipe.

Effect of MPEO concentration

Table II shows the effect of the concentration of macromonomer MPEO on the particle size. The particle size decreased gradually with an increase of MPEO

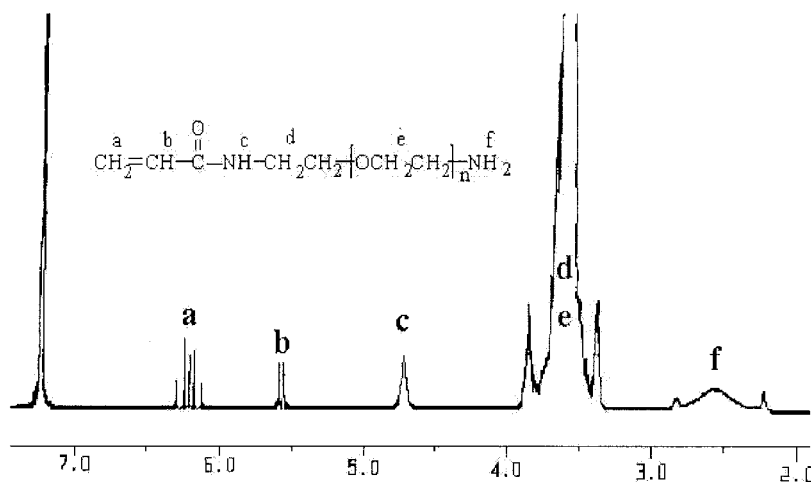


Figure 1 ¹H-NMR spectra of PEO macromonomer in CDCl₃.

TABLE II
Effect of MPEO Concentration on Particle Size

Sample	MPEO concentration ^a (%)	\bar{D} (μm) ^b	Standard deviation (μm) ^c
S1	2	14.6	3.26
S2	4	12.9	4.78
S3	6	11.8	2.27
S4	8	11.0	2.16
S5	11	10.5	3.71

^a MPEO concentration relative to total monomers (w/w).

^b $\bar{D} = \sum_{i=1}^n D_i/n$; \bar{D} is average diameter.

^c Standard deviation = $\sqrt{\sum_{i=1}^n (D_i - \bar{D})^2/n - 1}$.

concentration. In our polymerization systems, the macromonomer acts not only as a comonomer, but also as a costabilizer to prevent the particles from coalescing during the growth stage due to the hydrophilic PEO chains.

Effect of initiator concentration

As seen in Table III, it can be found that the particle size increased with increasing KPS concentration. This may due to the fact that increasing the initiator concentration causes the increase in the instantaneous concentration of the oligomeric radicals, which in turn increases the rate of association of the oligomers and the coagulation rate of the unstable nuclei to form larger permanent particle nuclei, resulting in larger final particle size.

Effect of stabilizer concentration

From Table IV it can be found that the particle size decreased with increasing concentration of PEG ($M_w = 4000$) stabilizer. Increasing the PEG concentration increases the rate of adsorption of stabilizer and the viscosity of the continuous phase, as well as the rate of anchoring adsorption of the grafted stabilizer, since the amount of grafted stabilizer increases. All these would reduce the extent of aggregation of the nuclei and reduce the particle size.

TABLE III
Effect of Initiator Concentration on Particle Size

Sample	Initiator concentration ^a (%)	\bar{D} (μm)	Standard deviation (μm)
S6	1	8.1	2.55
S7	2	10.2	2.71
S8	3	11.7	3.42
S9	4	12.8	4.57
S10	5	13.5	3.79

^a Initiator concentration relative to monomers (w/w).

TABLE IV
Effect of Stabilizer Concentration on Particle Size

Sample	PEG concentration ^a (%)	\bar{D} (μm)	Standard deviation (μm)
S11	2	15.2	4.42
S12	4	11.5	3.35
S13	6	9.0	2.41
S14	8	8.3	5.12
S15	10	7.8	2.23

^a Stabilizer concentration relative to total mixture.

In our study, magnetic amphiphilic microspheres ranging in diameter from 5 to 80 μm were prepared by changing the polymerization condition.

Characterization of magnetic amphiphilic microspheres

The average size and size distribution of magnetic amphiphilic microspheres were measured by means of a scanning electron microscope. Figure 2 and Figure 3 show the photograph and size histogram of the magnetic microspheres, respectively. The size distribution shows that the microspheres are polydispersity, and in accordance with a Gaussian distribution. The average diameter of the microspheres is about 11 μm .

Figure 4 shows the infrared (IR) spectrum of magnetic microspheres. The bands in the regions 3100–3000 cm^{-1} and 2000–1668 cm^{-1} are the characteristic peaks of C—H of benzene ring. The four adsorption peaks are observed at 1601, 1583, 1493, and 1450 cm^{-1} due to the vibration of C—C of the benzene ring. The double peaks at 760 and 690 cm^{-1} are the typical absorption of single-substituted benzene. These results confirm the existence of polystyrene in the mag-

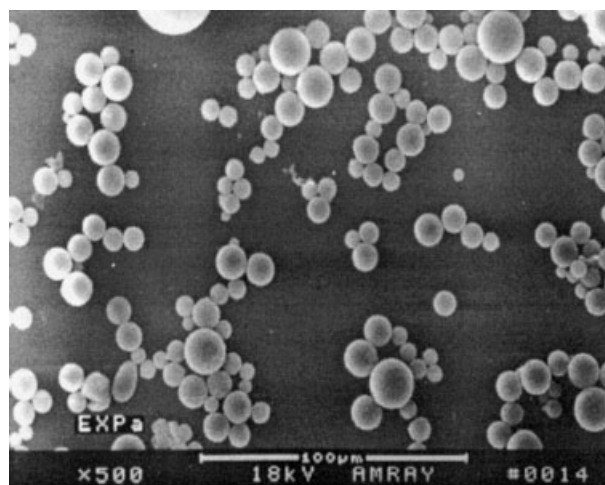


Figure 2 SEM photograph of magnetic amphiphilic microspheres. Polymerization conditions: 4.0 g PEG, 15.0 g St, 0.45 g KPS, 40.0 g H₂O, 10.0 g magnetic fluid, 52.0 g ethanol, 1.2 g MPEO.

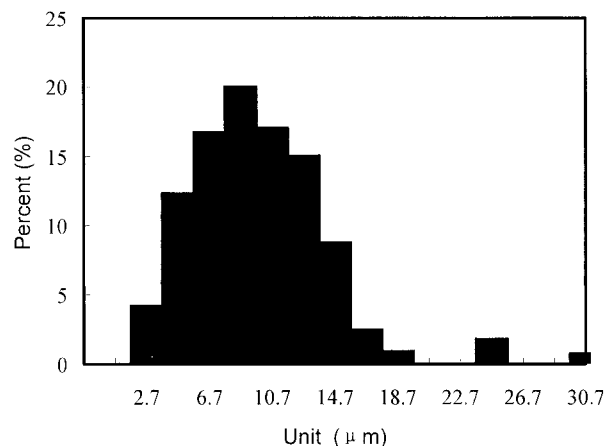


Figure 3 Histogram of magnetic amphiphilic microspheres. Polymerization conditions: 4.0 g PEG, 15.0 g St, 0.45 g KPS, 40.0 g H₂O, 10.0 g magnetic fluid, 52.0 g ethanol, 1.2 g MPEO.

netic microspheres. The peaks at 1090 and 1652 cm⁻¹, which attribute to the band of C—O of the PEO chain and the band of C=O of amide, respectively, indicate the existence of MPEO in the microspheres.

As magnetic microspheres could be used for supporting catalysts, the content of functional groups is one of the essential factors. The content of amino groups (—NH₂) localized in the magnetic microspheres was determined by virtue of the Gisin test. The results show that the amino content increased with the increase of the ratio of MPEO to styrene, as shown in Figure 5. Our experimental results show that amphiphilic magnetic microspheres containing 0.01–0.25 mmol/g amino groups could be prepared by changing MPEO concentration in the copolymerization.

Magnetic responsiveness is an important property of magnetic microspheres. Using this property, we can realize fast separation and purification. The magnetic responsiveness of magnetic amphiphilic polymer microspheres is showed in Figure 6. From Figure 6 we

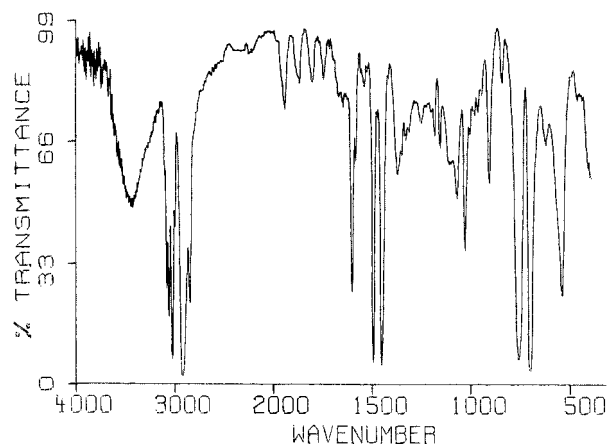


Figure 4 IR spectrum of magnetic microspheres.

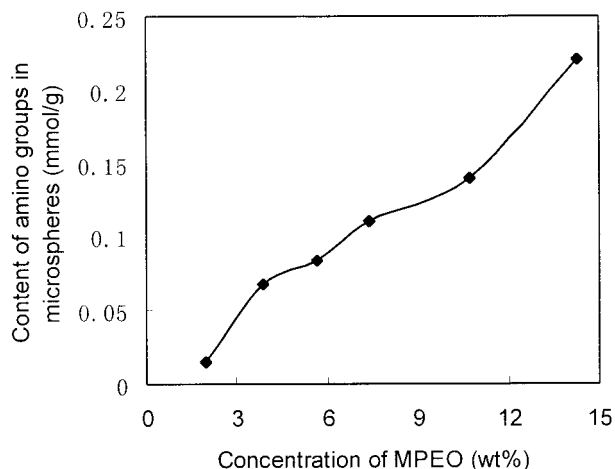


Figure 5 Content of amino groups localized in magnetic microspheres prepared using different MPEO concentrations. Polymerization conditions: 4.0 g PEG, 15.0 g St, 0.45 g KPS, 40.0 g H₂O, 10.0 g magnetic fluid, 52.0 g ethanol. MPEO concentration is relative to monomers.

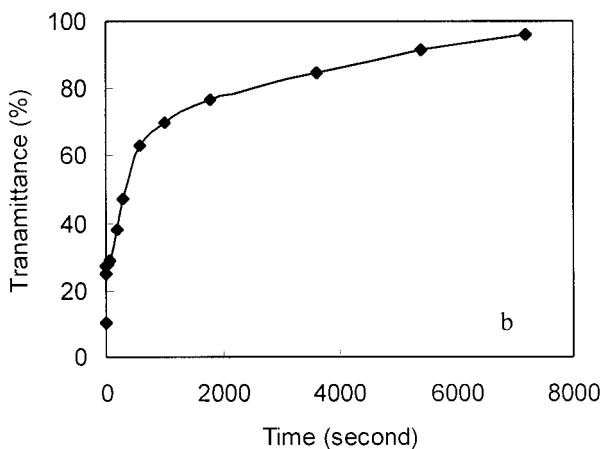
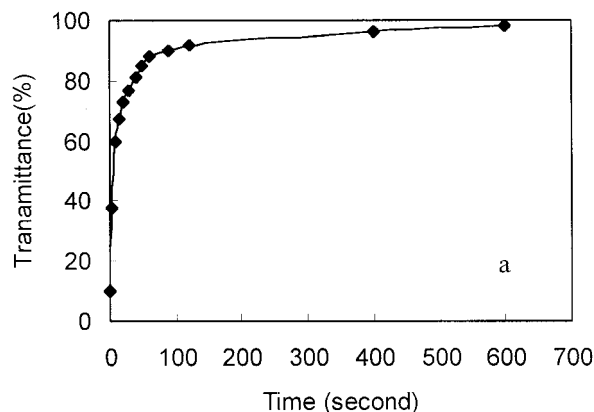


Figure 6 Transmittance of suspension of magnetic microspheres after being separated by an additional magnetic field (0.42T) for a certain time. (a) Magnetic separation; (b) sedimentation.

find that it took about 2 h under sedimentation for the transmittance to reach 98%, under a 0.42T magnetic field; however, it only needed about 10 min. The experimental results show that the magnetic separation using magnetic microspheres is rapid and easy.

CONCLUSION

Novel magnetic polymer microspheres with amphiphilic structure ranging in diameter from 5 to 80 μm were prepared by dispersion copolymerization of styrene and poly(ethylene oxide) acrylamide (NH_2 -PEO-AA) macromonomer (MPEO) in the presence of Fe_3O_4 magnetic fluid in ethanol/water.

The average size of the resulting magnetic microspheres increased with increasing initiator concentration. It also increased with decreasing stabilizer concentration and MPEO concentration.

The magnetic microspheres containing 0.01–0.25 mmol/g amino groups could be prepared by changing MPEO concentration.

The magnetic microspheres have excellent magnetic responsiveness. The magnetic separation using the magnetic microspheres is rapid and easy.

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