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Preparation of nanospheres with polystyrene shells and cross-linked poly(methacrylamide) cores: a solution approach

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Abstract

Novel narrow distributed nanospheres with polystyrene shells and cross-linked poly(methacrylamide) (polyMMA) cores were fabricated. The cross-linking of the poly(*p*-nitrophenyl methacrylate) (polyNPMA) cores of micelles, formed by the self-assembly of well-defined block copolymer (poly(styrene-*b*-*p*-nitrophenyl methacrylate) (poly(St-*b*-NPMA))) in chloroform, was realized in the solutions directly through the reaction with ethylenediamine instead of in films as in other cases reported [3,8–11]. Further substitution of *p*-nitrophenol units with ammonia produced polyMMA cores. Dynamic light scattering was used to monitor the self-assembly process of poly(St-*b*-NPMA) in chloroform, the effects of the cross-linking and amino-substitution of the polyNPMA cores on the morphologies of the micelles, meanwhile, the changes in the chemical structures were verified by FTIR. © 2002 Elsevier Science Ltd. All rights reserved.

Keywords: Nanospheres; Micelles; Block copolymers

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1. Introduction

Nanospheres have been attracting much attention for their wide applications, such as being used as molecular reactors and templates of reactions [1], for drug delivery [2] and the fabrication of light modulators [3]. The approach via fixing the micelles formed by the self-assembly of block copolymers in selective solvents could produce core–shell nanospheres with small sizes [3–15], which had higher surface areas and could form regular patterns [3]. Fixing the micelles have been realized by cross-linking either the cores [3–11] or shells [12–15], which was necessary because micelles with small radii formed by the self-assembly of block copolymers were unstable.

Core cross-linking is effective to produce stable nanospheres. There were two approaches to fulfill the core cross-linking: one was to polymerize the vinyl groups at the side chains or ends of polymers in the cores initiated by thermal or photo initiators [4–7]; the other is to introduce special cross-linking reagents into the cores to perform the cross-linking reaction [3,8–11]. By the former approach, nanospheres with cross-linked polyvinyl cores/polystyrene shells [4], polydimethylsiloxane capped with cross-linked polyvinyl cores/polyethylene oxide (PEO) shells [5], polylactide capped with polyvinyl cores/PEO shells [6] were prepared. Cores containing vinyl groups were necessary for this approach. The polymerization for the core cross-linking was usually performed in solution. However, by the latter approach, cross-linking reactions were performed in solid films cast from block copolymers to keep micelles stable. Nanospheres with cross-linked poly(vinylpyridine) cores/polystyrene shells [7,8], poly(isoprene) cores/polystyrene shells [9] and poly(methacrylic acid) cores/polystyrene shells [10] were obtained. The drawback of the second approach lies in that well developed phase separated films with spheres of one block dispersed in the matrix of the other blocks are a prerequisite and are needed to be cast elaborately from block copolymers with the content of the sphere forming block to be below around 30% (v/v) [16]. Therefore, it is desirable that the second approach can be realized in solution directly to make the process easier and produce nanospheres with wider compositions.

In this paper, novel nanospheres with polystyrene shells and cross-linked (poly(methacrylamide)) (polyMMA) cores were prepared via the second approach but in solution. Micelles were first formed in chloroform through the self-assembly of block copolymer, poly(styrene-*b*-*p*-nitrophenyl

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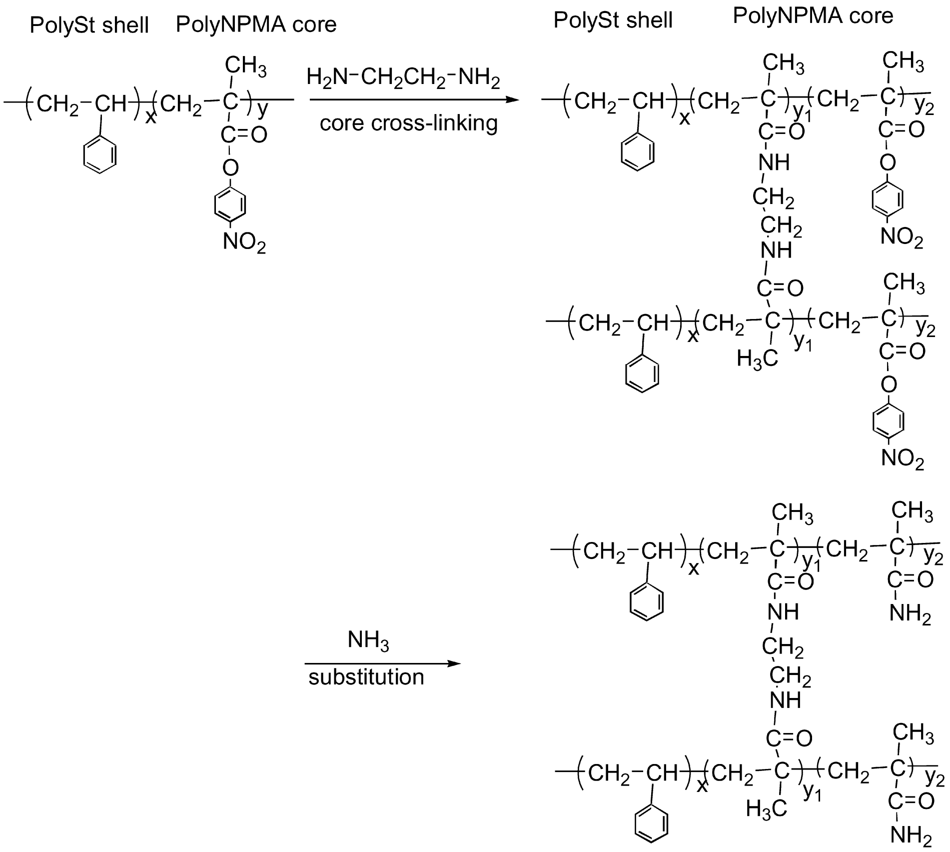

Scheme 1. The cross-linking reaction and the amino-substitution reaction performed in polyNPMA cores.

methacrylate) (St-*b*-NPMA) prepared by atom transfer radical polymerization (ATRP) [17]. Then the cross-linking of polyNPMA cores was realized through the reaction with diamines directly in the solution, further the substitution of the remained *p*-nitrophenol units by ammonia produced polyMMA cores as described in Scheme 1. The chemical feature and particle morphology were characterized by FTIR and dynamic light scattering (DLS), respectively.

2. Experimental section

2.1. Preparation of the core cross-linked nanospheres

Poly(St-*b*-NMPA) ($M_n = 37\,470$, $M_w/M_n = 1.29$, NPMA = 43 mol%) was synthesized by ATRP [17]. Micelles with polyNPMA cores and polySt shells were formed by sonication of the chloroform solution of poly(St-*b*-NPMA) (0.5%, w/v) for 10 min. Then, ethylenediamine (Shanghai No. 1 chemical reagent plant) (NH_2/*p*-nitrophenyl = 1.2:1 in mole) was directly added into the chloroform solutions of micelles, and the reaction was carried out at ambient temperature for 4, 6 and 12 days, respectively. Nanospheres were obtained by precipitating the solutions into methanol followed by filtration and being dried at 50 °C under vacuum.

2.2. Formation of polyMMA cores

The core cross-linked nanospheres were dissolved in THF, then aqueous ammonia (Shanghai chemical reagent plant) or 2-hydroxy ethylamine (Beijing chemical reagent company) (NH_2 or NH_3/*p*-nitrophenyl = 10:1 in mole) was added into the solutions. Afterwards the substitution reaction was performed at ambient temperature and 70 °C for aqueous ammonia and 2-hydroxy ethylamine, respectively. The products were recovered by precipitating the solution into methanol followed by filtration and drying under vacuum.

2.3. Characterization

FTIR spectra were recorded on a Bruker Vector-22 spectrometer using KBr pellets.

DLS was carried out at 25 °C using a modified commercial light-scattering spectrometer (ALV/SP-125) equipped with an ALV-5000 digital time correlator and a solid-state laser (ADLAS DPY 425 II, output power ca. 400 mW at $\lambda = 532$ nm). In DLS [18], the Laplace inversion (the CONTIN procedure) of each measured intensity–intensity time correlation function $G^{(2)}(q,t)$ in the self-beating mode can be related to a line-width distribution $G(\Gamma)$. For a diffusive relaxation, Γ is related to the translation diffusion coefficient D by $(\Gamma/q^2)_{C\to 0,q\to 0} \to D$, so that $G(\Gamma)$ can be converted into a transitional diffusion coefficient distribution $G(D)$ or a hydrodynamic radius distribution $P(R_h)$ via the Stokes–Einstein equation, $R_h = (k_BT/6\pi\eta)D^{-1}$, where k_B, T, and η are the Boltzmann constant, the absolute temperature, and the solvent viscosity, respectively. The cumulant analysis of $G^{(2)}(t)$ of a narrowly distributed sample can result in an accurate average line-width ($\langle\Gamma\rangle$), and the relative distribution width ($\mu_2/\langle\Gamma\rangle^2$) was used as a polydispersity index (PDI) to indicate the degree of the dispersity of the polymer micelles or particles.

3. Results and discussion

3.1. Fabrication of core cross-linked nanospheres

Micelles of block copolymers are preferably formed by dispersing their solutions in good solvents into selective solvents of one of the blocks. But no good solvent of poly(St-*b*-NPMA) could be found, so micelles with polystyrene shells and polyNPMA cores were formed directly by sonication of the chloroform solution of poly(St-*b*-NPMA) at a concentration of 0.5% (w/v). Fig. 1 shows the distribution of hydrodynamic radius (R_h) of the formed micelles measured by DLS and reflects that micelles with $R_h = 30$ nm and a narrow polydispersity factor (PDI = 0.02) were obtained. Theoretically phase separated films with a lamella morphology would be formed from poly(St-*b*-NPMA) with the content of NMPA to be 40 mol%. Therefore, no core–shell micelles could be obtained by fixing the structures of the self-assembled solid films of this block copolymer. In the NMR spectrum of poly(St-*b*-NPMA) in *d*-chloroform, the peaks attributed to polyNPMA disappeared and those ascribed to polystyrene remained [17]. Therefore, the micelles consisted of polyNPMA cores and polystyrene shells.

p-Nitrophenol groups in polyNPMA blocks could be substituted easily by amino group, so polyNPMA cores could be cross-linked by using diamine [19,20]. Here, the core cross-linking was performed in the solution directly instead of in solid films as reported [3,8–11]. First, hexanediamine was used but no distinct reaction was observed after 6 days of illumination by no apparent changes in FTIR spectra, which should be attributed to the difficult diffusion of haxanediamine into dense polyNPMA cores across polystyrene shells. However, the solution turned to yellow just after ethylenediamine was added, indicating the release of *p*-nitrophenol from polyNPMA after being substituted by amino groups. Ethylenediamine with a molar ratio of NH_2/*p*-nitrophenyl to be 1.2:1 was used to avoid the collapse of the micelles and render a suitable cross-linking rate and degree. The cross-linking reaction in the cores was monitored by using a FTIR spectrometer and the results are shown in Fig. 2. As shown in Fig. 2, the characteristic peaks of amide groups at 1666 cm^{-1} appeared and the intensity of the peak at 1750 cm^{-1} of the ester carbonyl groups of polyNPMA decreased. The cross-linking degree (CRD) could be calculated according to Eq. (1)

$$\mathrm{CRD} = 1 - (I_{1750}/I_{759})_t/(I_{1750}/I_{759})_0 \quad (1)$$

where I_{1750} and I_{759} stand for the peak intensities of carbonyl groups in polyNPMA segment and the benzene groups in polystyrene segment, and t and 0 for the reaction time and the original, respectively. The cross-linking reaction had no effects on the content of the phenyl groups in the micelles so I_{759} was used as an internal standard. The results are tabulated in Table 1 and reflected CRD increased when the reaction time extended. The effect of cross-linking reaction on the micelle morphology was investigated by DLS and the results are listed in Table 1. It was clear that the core cross-linking had little effects on the sizes of nanospheres but increased the values of PDI. Even precipitation occurred when CRD reached 42% after the cross-linking reaction was performed for 12 days. These indicated that micelle fusion happened during the cross-linking process as reported by Saito et al. [21,22] and Liu et al. [23] for the existence of the kinetically unfrozen or

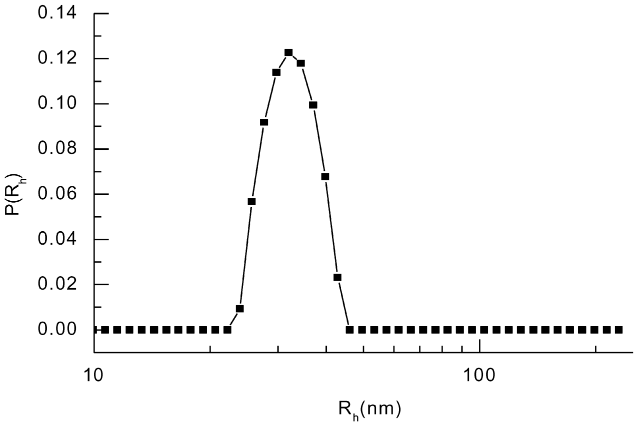

Fig. 1. Distribution of R_h of the micelles formed from the self-assembly of poly(St-*b*-NPMA) in chloroform analyzed by DLS.

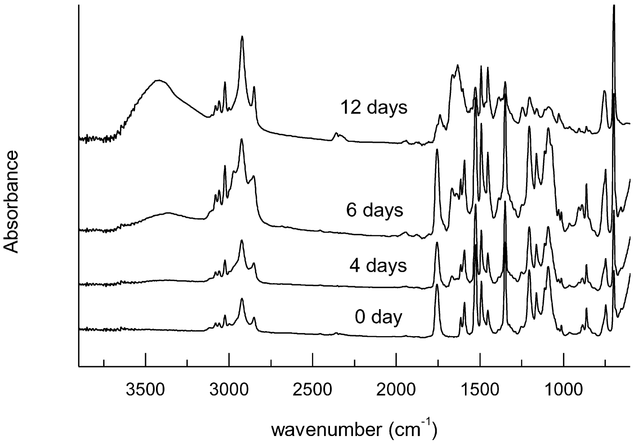

Fig. 2. Change in FTIR spectra of polymer micelles as a function of the cross-linking reaction time.

Table 1
Conditions and results of the core cross-linking of the micelles

Sample	Solvent	Time (days)[a]	CRD (%)[b]	R_h (nm)[c]	PDI[c]
1	$CHCl_3$	0	0	30	0.02
2	$CHCl_3$	4	19	35	0.08
3	$CHCl_3$	6	23	28	0.10
3[d]	THF	6	23	35	0.14
4	$CHCl_3$	12	42	–	–

Core cross-linking reactions were performed at ambient temperature by using ethylenediamine as a cross-linking agent with a molar ratio of NH_2/NPMA = 1.2:1.

[a] Reaction time.

[b] CRD obtained from FTIR spectra.

[c] Determined by DLS at a scattering angle of 90°.

[d] Obtained by dispersion of the sample 3 in THF.

openly associated micelles. External cross-linking among the micelles led to increased PDI values and even precipitation.

The stability of nanospheres after the core cross-linking was confirmed by the existence of nanospheres in THF, in which no micelles were formed from poly(St-*b*-NPMA). The morphologies of nanospheres in THF at a concentration of 0.5% (w/v) were characterized by using a DLS spectrometer. The typical distribution of R_h of the micelles is shown in Fig. 3, and the results are listed in Table 1. R_h in THF was larger than that in chloroform for the same sample, which resulted from the swollen of the cores in THF, a solvent for polyNPMA segments.

Here, the ease of diffusion of ethylenediamine into the cores to react with polyNPMA combined with the little effect of adding ethylenediamine on the micelle morphology made it possible to perform the core cross-linking reaction directly in the micelle solution to render stable nanospheres.

3.2. Formation of polyMMA cores

PolyMMA cores could be produced by the substitution of the remained *p*-nitrophenol groups by amino compounds. At first, 2-hydroxy ethylamine was adopted to perform the substitution in the THF solution of nanospheres. The processes were monitored by using a FTIR spectrometer and the results are shown in Fig. 4. After 1 day at 70 °C, the intensity of the characteristic peaks of the carbonyl group of NPMA at 1750 cm^{-1} decreased and of the amide group at 1666 cm^{-1} increased as shown in Fig. 4(a). The substitution degree (SD) of *p*-nitrophenol group can be calculated by Eq. (1), where 0 and *t* indicate the original and the substitution reaction time, respectively. The results are listed in Table 2. The amino-substitution could be realized in the cross-linked cores, but precipitation occurred when the total substitution of all the *p*-nitrophenol units were obtained (demonstrated by FTIR spectra) after the reaction was carried out at 70 °C for 2 days. The precipitation probably resulted from the damage of the cross-linking by the exchange between the amide groups of ethylenediamine and that of 2-hydroxy ethylamine when the reaction was performed at 70 °C.

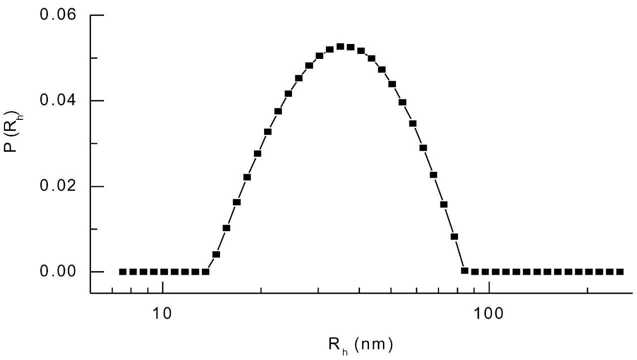

Fig. 3. Typical distribution of R_h of the core cross-linked nanospheres (sample 3 in Table 1) in THF determined by DLS.

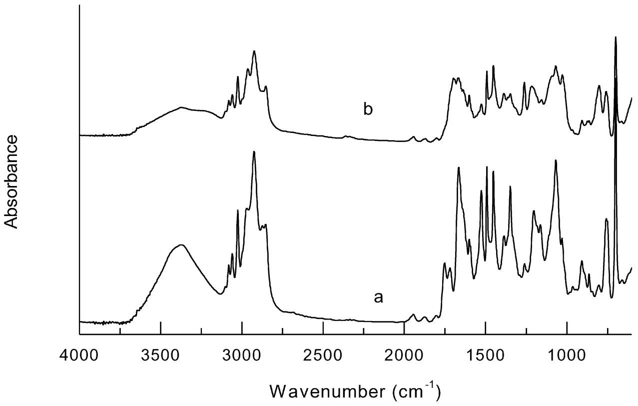

Fig. 4. Comparison of FTIR spectra of the core cross-linked nanospheres substituted (a) by 2-hydroxy ethylamine at 70 °C and (b) by aqueous ammonia at ambient temperature, respectively, for 1 day.

In order to realize the full substitution of the remained *p*-nitrophenol units, aqueous ammonia solution was used for the smaller molecular sizes of ammonia, and the reactions were carried out at ambient temperature to avoid the collapse of nanospheres. After 24 h, the total substitution of *p*-nitrophenol units was verified by the complete disappearance of the characteristic peak of *p*-nitrophenyl ester group at 1750 cm^{-1} and the intensified peaks of amide

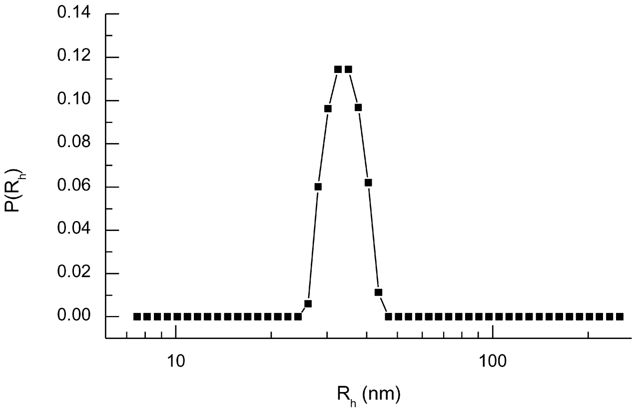

Fig. 5. Distribution of R_h of nanospheres with polySt shells and polyMMA cores (sample 7 in Table 2) in THF analyzed by DLS.

Table 2
Conditions and results of the amino-substitution of the remained *p*-nitrophenol units in the cores

No.	Original micelle[a]	Solvent	Agent	Temperature (°C)	Time (days)	SD[b]	R_h (nm)[c]	PDI[c]
5	2	THF	HEA[d]	70	1	78	32	0.1
6	2	THF	HEA[d]	70	2	100	–[e]	–[e]
7	3	THF	NH_3	Ambient	1	100	36	0.06

[a] The same samples as in Table 1.
[b] SD obtained from FTIR spectra.
[c] Determined by DLS at a scattering angle of 90°.
[d] 2-Hydroxy ethylamine.
[e] Precipitation occurred.

group at 1666 cm^{-1} in the FTIR spectrum as shown in Fig. 4(b). After the total amino-substitution, DLS results reflected that R_h was almost kept the same and PDI became narrower as shown in Fig. 5 and Table 2.

Angle-trace DLS measurements could be used to depict the shapes of the micelles [14,24]. Here, DLS were carried out at detection angles of 30, 45, 60, 75, 90, 105, 120, and 135°, respectively. The sphere morphology of the nanospheres was clearly illuminated by the independence of R_h on the scattering angle as shown in Fig. 6.

4. Conclusions

Narrow distributed micelles with polySt shells and polyNPMA cores were formed from the self-assembly of block copolymers, poly(St-*b*-NPMA), in chloroform. The core cross-linking reaction could be realized directly in the micelle solution by using a suitable reagent, which made it possible to fabricate nanospheres with wide compositions in an easy way. Ethylenediamine was an effective reagent for the cross-linking of polyNPMA cores to produce stable nanospheres with almost the same R_hs and higher PDIs as compared to the original micelles when the CRD was kept below 42%. The total substitution of the remained *p*-nitrophenol units in the cores by ammonia rendered nanospheres with polySt shells and cross-linked polyMMA cores. However, total substitution of *p*-nitrophenol groups by larger 2-hydroxy ethylamine could not be realized without damaging the nanospheres.

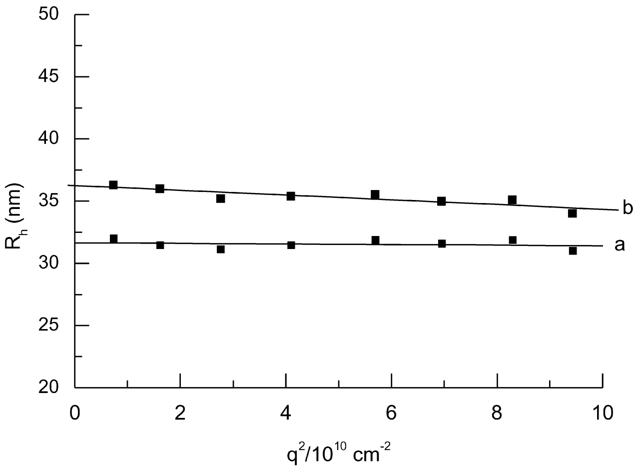

Fig. 6. Dependence of R_h of nanospheres with polySt shells and polyMMA cores ((a) sample 5 and (b) sample 7 in Table 2) on the scattering vector q^2 ($q = (4\pi n_s/\lambda)\sin(\theta/2)$), where n_s is the refractive index, λ the laser wavelength, and θ the detection angle.

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