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Synthesis and self-assembly of poly(ethylene oxide)-*b*-poly (2-hydroxyethyl methacrylate)

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Abstract: Poly(ethylene oxide)-*b*-poly(2-hydroxyethyl methacrylate) (PEO-*b*-PHEMA) was synthesized by successive atom transfer radical polymerization (ATRP) of 2-hydroxyethyl methacrylate (HEMA) monomer using PEO-Br macroinitiator as initiator, CuBr/$CuBr_2$ and 2,2'-bipyridyl (bpy) as catalyst and ligand. IR, ^1H NMR, and GPC analysis indicate that PEO-*b*-PHEMA block copolymer with low polydispersity index ($M_w/M_n \approx 1.1$) has been formed. Self-assembly of this double hydrophilic block copolymer in the selective solvent and water was also studied. Owing to the high hydrophilic nature of the PEO and PHEMA blocks, this double hydrophilic block copolymer cannot disperse well in water. So block copolymer was modified by part esterification of PEO-*b*-PHEMA with acetic anhydride, which increased the hydrophobic group of the PHEMA block. The TEM results show that this block copolymer spontaneously form well-defined micelles in water.

Introduction

Double hydrophilic block copolymers (DHBCs) are water-soluble macromolecular compounds which consist of two water-soluble blocks of different chemical nature [1]. Poly(ethylene oxide) (PEO) and poly(2-hydroxyethyl methacrylate) (PHEMA) are two of the most frequently investigated classes of hydrophilic polymers. PHEMA, which is currently used in contact lenses [2], biocompatibilization, and drug delivery [3], is an important hydrophilic polymer. The recent development of controlled/'living' radical polymerizations, especially atom transfer radical polymerization (ATRP), has opened a new route to synthesize functional and architectural polymers with well-defined structures [4]. In particular, HEMA can be successfully polymerized with the molecular weight distributions ranging from 1.1 to 1.5 in both silyl-protected [5] and unprotected forms [6-10]. PEO-Br macroinitiator has been widely used in atom transfer radical polymerization [11-13]. Thus PEO-*b*-PHEMA double hydrophilic block copolymer can be synthesized using this method.

DHBCs can spontaneously form well-defined micelle aggregates in a selective solvent and water [14-17]. According to previous works, many factors may affect the final morphologies of the aggregates. Among these factors, the most important are the nature of the core-forming block and the shell-forming block, the composition of the copolymer, the nature of the common solvent and the precipitant, and the presence and nature of any additives [18]. The self-assemble behaviors of DHBCs in water have attracted much interest recently due to its two water-soluble blocks [19]. A recent overview on the synthetic routes toward DHBCs and some of their prominent applications was presented by Colfen [1]. Armes [20] found that copolymerizations of HEMA with other comonomers allowed the cloud point behavior to be manipulated. A range of novel HEMA-based block copolymers were synthesized in which the HEMA block was either thermo-responsive or permanently hydrophilic, depending on its degree of polymerization (DP_n) and the nature of the second block. Thus, diblock copolymer micelles with either hydroxylated cores or coronas could be prepared in water. Water-soluble polymers with hydrophobic substituents have also been extensively studied from the theoretical and experimental points of view due to their important role as thickeners and viscosity modifiers in a variety of water-borne technologies including paints, inks and cosmetics [21].

In this paper, PEO-*b*-PHEMA copolymer with well-controlled molecular weight and narrow molecular weight distribution was synthesized using ATRP. First, a macroinitiator (PEO-Br) for atom transfer radical polymerization was synthesized by reacting PEO with 2-bromoisobutyryl bromide. Then polymerizing of HEMA was conducted with PEO-Br as macroinitiator, CuBr/$CuBr_2$, 2,2'-bipyridyl (bpy) as catalyst and ligand, respectively. PEO-*b*-PHEMA copolymer in THF can form the aggregates with compact cores of insoluble blocks surrounded by a soluble shell composed of soluble blocks as THF is a good solvent for PEO block, but it is not a good solvent for PHEMA block. PEO-*b*-PHEMA copolymer behavior in water is just like usual neutral hydrophilic polymers, which has no intense tendency towards aggregation for water is the common solvent of PEO and PHEMA. Thus the PEO-*b*-PHEMA copolymer was part esterified with acetic anhydride in order to increase the hydrophobic group of the PHEMA block. Micellization ensues via assembly of the newly formed hydrophobic blocks in water.

Results and discussion

Synthesis of macroinitiator and PEO-b-PHEMA copolymer

Fig. 1 reveals the representative FT-IR spectra of PEO, PEO–Br and the PEO-*b*-PHEMA block copolymers. The absorption occurs at 1109 cm^{-1} which are attributed to the ether group of the copolymers and PEO precursor. After acetylation reaction, carbonyl absorption occurs at 1734 cm^{-1} correspondingly in the spectrum of PEO–Br macroinitiator (Fig. 1b). An increasing absorption at 1734 cm^{-1} is due to the ester group of the PHEMA chain (Fig. 1c). These data illustrate the presence of both PEO and PHEMA blocks in the polymer chain.

PEO-Br macroinitiator was prepared according to previous work [17, 18]. ^1H NMR study in $CDCl_3$ indicated that the hydroxyl end group of the PEO was fully esterified (data not shown). HEMA was polymerized in methanol using PEO-Br as the macroinitiator, CuBr/ bpy as the catalyst and ligand. The part esterified PEO-*b*-PHEMA copolymer was obtained using purification of PEO-*b*-PHEMA reacted with acetic anhydride. ^1H NMR spectrum of PEO-*b*-PHEMA and the part esterified polymer are shown in Fig. 2 and Fig. 3. The peak d at δ= 4.04 ppm is characteristic of the α hydrogens of the ester group in HEMA. The peak e at δ=3.74 ppm is characteristic of the ethyl hydrogens in HEMA, and the peaks c+c', b at δ=0.80-2.10 ppm are backbone hydrogens.

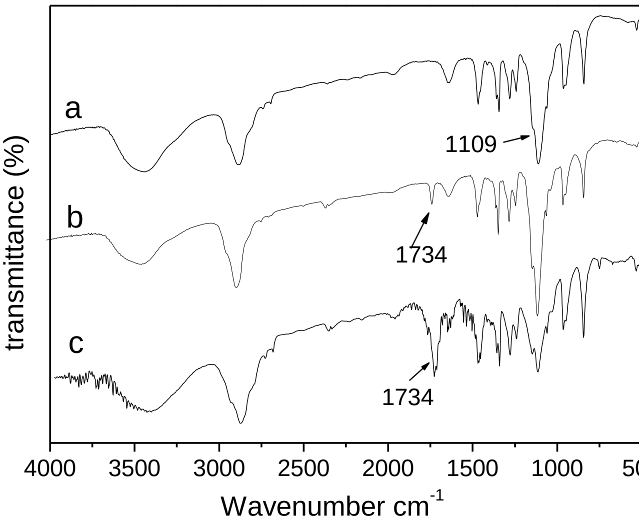


Fig. 1. FT-IR spectra of (a) PEO, (b) PEO–Br and (c) PEO-*b*-PHEMA.

Careful analysis of Fig. 2, reveal that the residual species of PEO-Br stand at both end of PHEMA chain. The peak f at δ=3.4 ppm are corresponding to methyl protons of PEO-Br. On comparing Fig. 2 and Fig. 3, the peak e in Fig. 2 divide into peak e and e' in Fig. 3. These results indicated that the hydroxyl in HEMA has been part esterified. The appearance of peak g at δ=2.10 ppm also confirm the results of part esterification. Thus the degree of esterification can be calculated using ^{1}H NMR according to following equation:

$$E\% = \frac{I_{e'}}{I_{e'}+I_{e}} \times 100\,\% \tag{1}$$

I_e and $I_{e'}$ are integral values of peak e and peak e' respectively in Fig. 3. The calculated results showed that about 25% hydroxyl groups in copolymer (PEO-*b*-PHEMA-4, Table 1) have been esterified.

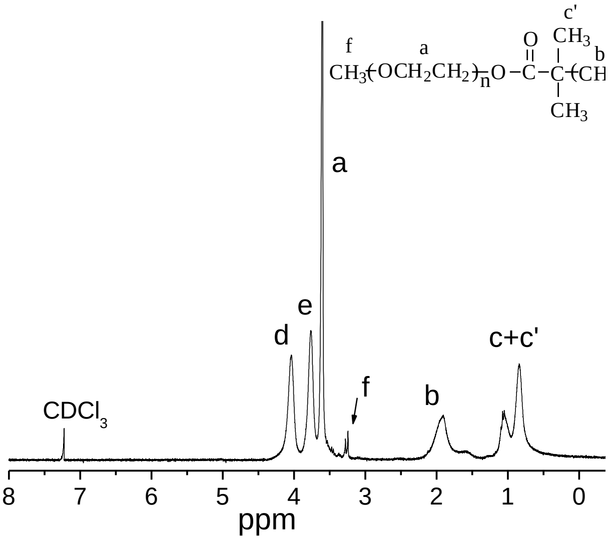


Fig. 2. ^{1}H NMR spectra of PEO-*b*-PHEMA.

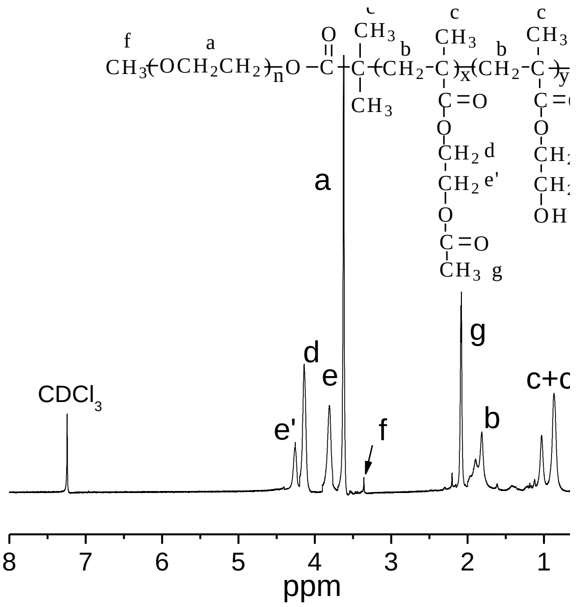


Fig. 3. ^{1}H NMR spectra of part esterified PEO-b-PHEMA.

The representative GPC curves of the PEO-*b*-PHEMA shown in Fig. 4 are symmetrical and the polydispersity of the PEO-*b*-PHEMA is low (M_w/M_n ≈1.1, see Table 1), indicating excellent control over the polymerization. The polydispersity of the PEO-*b*-PHEMA remained quite low throughout the esterification reaction (M_w/M_n = 1.14, see Table 1).

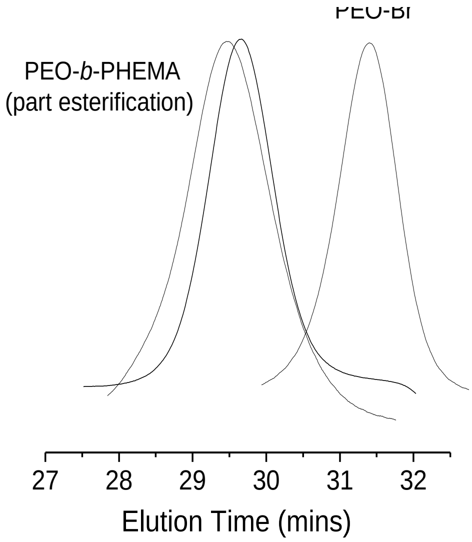


Fig. 4. GPC curves of PEO, PEO-*b*-PHEMA and part esterified PEO-*b*-PHEMA.

The molecular weights of the resulting PHEMA increased linearly with conversion as shown in Table 1, therefore the molecular weight can be controlled by the initial feed ratio of HEMA to PEO-Br and conversion. After the fast polymerization, the polymerization slowed down and the PDI slightly increases. Other researches and our previous work also found the same phenomena. Probable reasons may be due to too much irresistible termination reactions between primary and chain radicals. Another reason may be the decrease of the concentration of HEMA [7, 12, 22]. All these facts indicate that the polymerization of HEMA with PEO-Br/CuBr/bpy as initiation system is of “living” nature. The PEO-*b*-PHEMA copolymer and part esterified PEO-*b*-PHEMA copolymer have been successfully synthesized. The results are listed in Table 1.

Tab. 1. ATRP of HEMA initiated with PEO-Br/CuBr/ bpy [a]

No.	time (h)	conversion(%)	$M_{n,\,\mathrm{th}}$ [b]	M_n (GPC)	M_w/M_n (GPC)
PEO-Br	—	—	2150	2050	1.06
PEO-*b*-PHEMA-1	0.5	22	5160	5200	1.08
PEO-*b*-PHEMA-2	1.0	46	6280	6570	1.08
PEO-*b*-PHEMA-3	1.5	64	10620	10980	1.06
PEO-*b*-PHEMA-4	2.0	85	13350	14600	1.09
PEO-*b*-PHEMA-4 [c] (part esterification)	—	—	—	15450	1.14

[a] Polymerization conditions: HEMA/PEO-Br/CuBr/bpy=100/1/1/2 (molar ratio); Temperature: 25 ^{0}C; Solvent:methanol.

[b] $M_{n,\,\mathrm{th}} = (M_m \times \mathrm{conversion} \times [M]/[I]) + M_i$, where M_m and M_i are the molar masses of monomers and macroinitiator, respectively, [M] and [I] are the concentration of monomer and macroinitiator, respectively.

[c] Esterification conditions: PEO-*b*-PHEMA-4/ acetic anhydride = 5/1 (w/w); Solvent: chloroform.

Self-assembly of PEO-b-PHEMA copolymer in selective solvent

The self-assembly of the double hydrophilic block copolymer in selective solvent has attracted much interest recently [15]. As for PEO-*b*-PHEMA copolymer, THF is a good solvent for PEO block [23, 24], but it is not a good solvent for PHEMA block, leading to the formation of aggregates with compact cores of insoluble blocks surrounded by a soluble shell composed of soluble blocks.

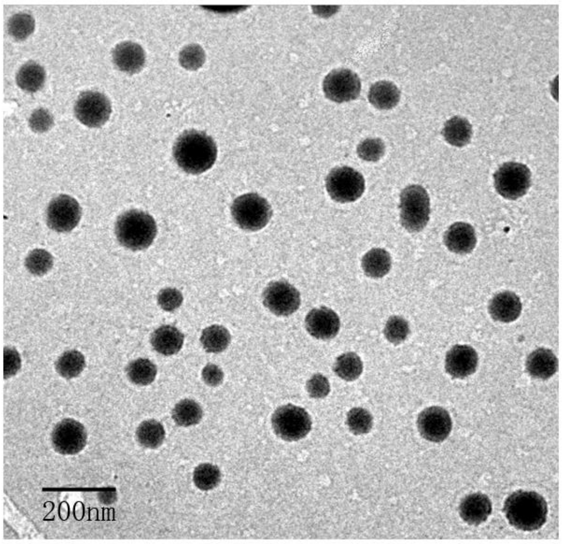


Fig. 5. TEM micrograph of PEO-*b*-PHEMA specimen cast from methanol/THF (1/10, v/v) solution.

The size and shapes of the resulting polymer micelles were studied by transmission electron microscopy. The morphology formed from PEO-*b*–PHEMA-4 block copolymer can be observed in methanol/THF (1/10, v/v) solvent. The PHEMA block formed the core and PEO block formed the shell, which was proven by the TEM results. Fig. 5 shows these micelles are spheres, which have an average diameter of 80-100 nm. The hydrophilic PEO chains adjusting their conformation stretch outside to stabilize the micelles. The double layer core-shell structure can be observed clearly from the TEM picture. Solvents play an important role in the aggregation process in general. The common solvent (methanol) mainly modifies the degree of the stretching of the core-forming block in the core. The formation of multilayer structures may be due to the rapid change in solvent composition upon addition of the poor solvent. Some observed objects are much bigger than length of two stretched macromolecules and contain above 10 thousands of chains. This suggests that these particles are thermodynamically stable. We also tried to change the solvent composition by diffusing the poor solvent into the polymer solution. However, it took a very long time and the change in solvent composition gave unreliable results.

Self-assembly of PEO-b-PHEMA copolymer in water

DHBCs self-assemble behaviors in water have attracted much interest recently. As for PEO-*b*-PHEMA copolymer, although PEO and PHEMA are water soluble blocks, HEMA homopolymers with DPn's higher than 50 were actually partially soluble [20]. So PEO-*b*–PHEMA-4 was selected to investigate its self-assembly in water. The micelles formed from PEO-*b*–PHEMA-4 block copolymer in water can be observed in Fig. 6a.

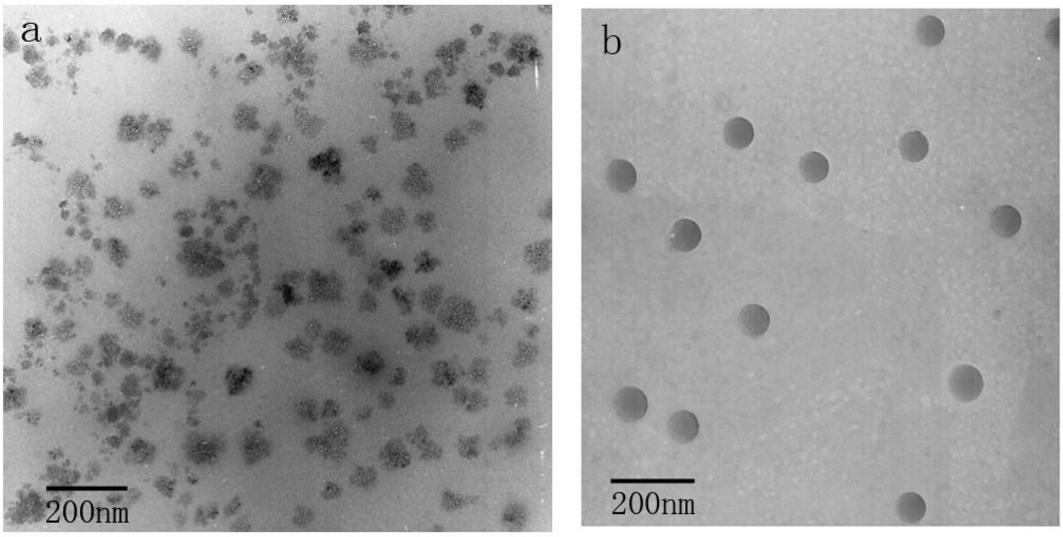


Fig. 6. TEM micrograph of (a) PEO-*b*-PHEMA and (b) part esterified PEO-*b*-PHEMA specimens in water.

Conclusions

The ATRP of HEMA with PEO-Br has been successfully carried out. The living nature of the polymerization is evidenced by linear evolution of molecular weight with conversion. The copolymer has low polydispersity indexes. Then the part esterification PEO-*b*-PHEMA copolymer was synthesized by using PEO-*b*-PHEMA reacted with acetic anhydride to increase the hydrophobic group of the PHEMA block. The self-assembly behaviors of PEO-*b*-PHEMA in methanol/THF and water were studied. The TEM results showed that the part esterified PEO-*b*-PHEMA can form spherical micelles with good dispersivity.

Experimental section

Materials.

2-Hydroxyethyl methacrylate (HEMA, 99%, Aldrich) was distilled under vacuum prior to use. 2-Bromoisobutyryl bromide (98%, Aldrich) was freshly distilled at room temperature under vacuum. Triethylamine (TEA) was refluxed with p-toluenesulfonyl chloride and then distilled. Bpy, $CuBr_2$ and acetic anhydride (First Shanghai Chemical Reagent Company, Shanghai, China) were used without further purification. CuBr (First Shanghai Chemical Reagent Company, Shanghai, China) was purified by stirring in acetic acid, washing with ethanol, and then drying under vacuum. PEO (M_n=2000, Fluka, monomethyl ether) was dried by azeotropic distillation with toluene before use.

General procedure for polymerization from macroinitiator

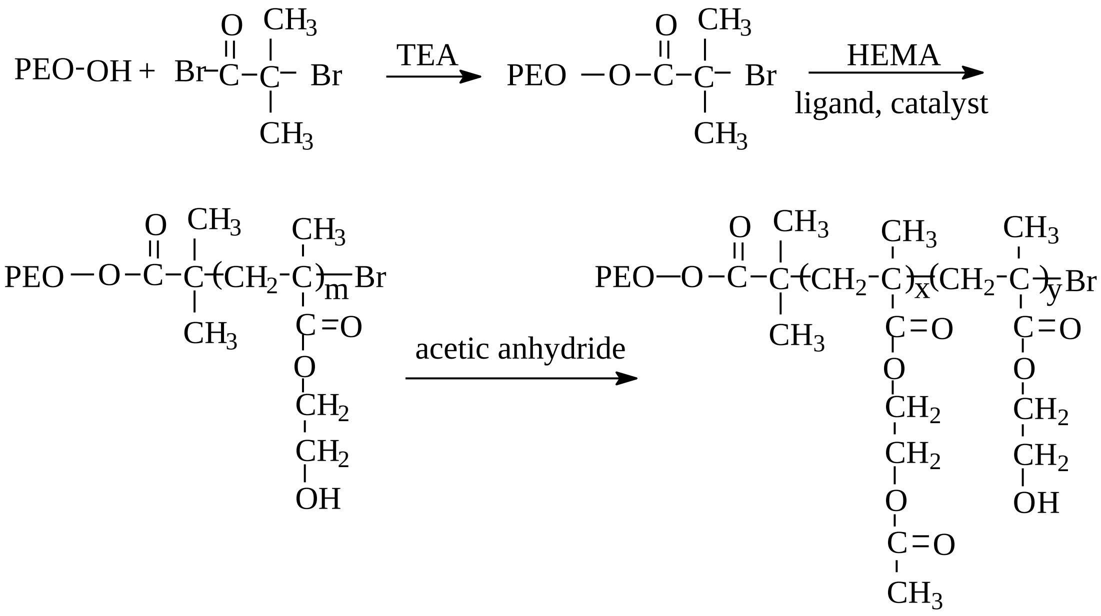
PEO-Br macroinitiator was prepared according to literature [17, 18]. 0.55 g PEO-Br macroinitiator (0.26 mmol), 3.2 mL of HEMA (3.4 g, 0.026 mol), 2 mL of methanol, 0.0832 g of bpy (0.53 mmol) and 0.0059 g of $CuBr_2$ (0.026 mmol) were placed into a dried glass tube with a magnetic bar and degassed three times with freeze-pump-thaw cycle. Then 0.0372 g of CuBr (0.26 mmol) was introduced into the solution mixture. The mixture was degassed by three freeze-pump-thaw cycles again. The polymerization started immediately at room temperature (25 °C). Samples were taken after certain time intervals with a syringe, then diluted with methanol and subsequently analyzed by ^1H NMR spectroscopy, from which the polymerization conversion was obtained. The residual reaction mixture was diluted with methanol and passed through a neutral Al_2O_3 column to remove copper ions. Precipitation in diethyl ether and drying at 40 °C under vacuum produced a white powder polymer.

Esterification of PEO-b-PHEMA with acetic anhydride

PEO-b-PHEMA copolymer (0.5 g) dissolved in 10 mL of chloroform was mixed with 0.1 g of acetic anhydride, and the solution was refluxed for 2 h. Most of the unreacted acetic anhydride was removed by precipitating the products in diethyl ether, then drying at 40 °C under vacuum. The synthesis route is displayed in Scheme 1.

Characterization

^1H NMR spectra were performed in an AV-300 NMR spectrometer, using $CDCl_3$ as solvents and tetramethylsilane (TMS) as internal reference. The IR spectra were recorded in solid state using KBr pellet. A MAGNA-IR 750 (Nicolet Instrument Co. U.S.A) was used to record the spectra in the range of 400–4000 cm^{-1}. Molecular weights and molecular weight distributions were determined by gel permeation chromatography (GPC) equipped with a Waters 1515 pump and Waters 2414 differential refractive index detector (set at 30 °C). It used a series of three linear Styragel columns HT2, HT4, and HT5 at an oven temperature of 35 °C. The eluent was DMF at a flow rate of 1.0 mL/min. A series of low polydispersity polystyrene (PS) standards were employed for the GPC calibration.



Scheme 1. Formation of PEO-*b*-PHEMA and the part esterification of PEO-*b*-PHEMA.

Transmission electron microscopy

The morphologies of the copolymer films were studied by transmission electron microscopy (TEM) performed on a JEOL – 2010 (JEOL, Japan). The PEO-*b*-PHEMA copolymers were first dissolved in methanol, a common solvent for both PEO and PHEMA blocks, to give a stock solution. Subsequently, THF was added dropwise to the polymer solution with stirring (methanol/THF=1/10, v/v). PEO-*b*-PHEMA and the part esterified PEO-*b*-PHEMA copolymer were directly dissolved in water in order to study the morphologies of them. To prepare TEM samples for the study of the size and the morphology of the self-assembly, a drop of PEO-*b*-PHEMA dilute solution (about 2.0 mg/ml) was deposited onto a copper EM grid, which had been precoated with a thin film of Formvar and then coated with carbon. Two minutes after the deposition, the solution was allowed to dry in air for a few hours. When taking photos, the polymer films were stained with phosphotungstic acid solution (0.3%).

Acknowledgements

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