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Synthesis and self-assembly of reactive H-shaped block copolymers

Abstract The H-shaped block copolymers (PTMSPMA)$_2$-PEG(PMPSTMSPMA)$_2$, with two compositions, (EG)$_{91-}b$-(TMSPMA)$_{92}$ and (EG)$_{455-}b$-(TMSPMA)$_{176}$ have been successfully synthesized by atom transfer radical polymerization (ATRP) of tri(methoxysilyl)propyl methacrylate (TMSPMA) at room temperature in methanol. The initiation system applied was composed of 2,2-bis(methylene a-bromoisobutyrate)propionyl terminated poly(ethylene glycol) (Br$_2$PEGBr$_2$) with $M_n = 4000$ or 20000, CuBr and 2,2′-bipyridine. The macroinitiator, Br$_2$PEGBr$_2$, was prepared by the reaction of two hydroxyl groups terminated PEG with 2,2-bis(methylene a-bromoisobutyrate)propionyl chloride. The NMR spectroscopy and GPC measurements were used to characterize the structure and molecular weight and molecular weight distribution of the resultant copolymers. The H-shaped block copolymers Sam 1 and Sam 2 were self-assembled in DMF/water mixtures and then the trimethoxysilyl groups in PTMSPMA were cross-linked by condensation reaction in the presence of triethylamine. Stable large-compound vesicles with 10 nm diameter of cavities were formed for Sam 1 which contains a short PEG chain. However, the self-assembling of the Sam 2 in the selective solvents resulted in big vesicles aggregates. These two different morphologies of aggregates are attributed to their relative chain length of water soluble PEG. The vesicles formed from Sam 1 with short PEG chains have big surface energy which will lead them to self-assemble further, forming large-compound vesicles.

Keywords aggregates, atom transfer radical polymerization, macroinitiator, vesicle, self-assembly

1 Introduction

In the past decade, self-assembly of linear block copolymers has attracted much attention [1–4] due to their potential applications in controlled drug delivery and release, catalysis and microelectronics [5–7]. However, researches on the self-assembly of nonlinear block copolymers are still limited [8,9]. In comparison with the linear ones, nonlinear copolymers could exhibit more architecture, such as combination of different solvophilic and solvophobic segments and the various joint modes between them. These complex structures lead to more confined conditions in phase separation and intricate thermodynamic stable structures. Therefore, research about self-assembly of nonlinear block copolymer is a necessary work.

With the recent development of controlled radical polymerization, especially the broad applications of ATRP and RAFT polymerization, it becomes easier to synthesize many nonlinear block copolymers with complicated architecture [10,11]. One type of nonlinear polymers, the H-shaped block copolymers B2AB2, can be considered as two side-arms attached to difunctional living macromolecular chains [12] which have been prepared by controlled radical polymerization in previous reports. However, their self-assembly is, as yet, little known [13,14]. Herein, we report the synthesis and self-assembly of a new type of reactive H-shaped block copolymer.

2 Experiment

2.1 Materials

Methanol was dried over anhydrous magnesium sulfate. THF and petroleum ether (30°C–60°C) were distilled from a purple sodium ketyl solution. The 3-(trimethoxysilyl)propyl methacrylate (TMSPMA) was dried with CaH$_2$ overnight and distilled under reduced pressure. Triethylamine was refluxed with CaH$_2$ for 4 h and then distilled. Poly(ethylene glycol) (PEG, $M_n = 4000$ or
20000 g/mol) was freed of water by azeotropic distillation in the presence of benzene. All the other reagents were analytical grade and used as received. The 2,2-bis(methylene \( \alpha \)-bromoisobutyrate)propionyl chloride (BBIBPC) was synthesized by reaction of \( \alpha \)-bromoisobutyl bromide with 2,2-bis(hydroxymethyl)propionic acid under a yield of 63% according to the method described in reference 11. 1H-NMR (300 MHz, CDCl\(_3\), \( \delta \), TMS) 1.5 (3H, CH\(_3\)), 1.92 (12H, C(Br)(CH\(_3\))\(_2\)), 4.4 (4H, COOCH\(_3\)).

### 2.2 Synthesis of H-shaped PEG macroinitiator (Br\(_2\)PEGBr\(_2\))

In a typical experiment, water-free PEG (\( M_n = 4000 \) g/mol, 8 g, 2 mmol) and freshly distilled triethylamine (1.21 g, 12 mmol) were dissolved in 30 mL of anhydrous benzene in a 100 mL flask under stirring. After cooling to 0°C, BMBIBPC (5.4 g, 12 mmol) was added drop-wise to the reaction mixture. Then, the reaction was carried out at room temperature for 24 h. After filtering off the salt formed in reaction, benzene was removed under reduced pressure. Then the crude product was dissolved in CH\(_2\)Cl\(_2\), and washed with water for 3 times. After precipitation in diethyl ether for 3 times, the product was dried under vacuum to obtain white macroinitiator in 80% yield.

Similar steps were adopted to synthesize the macroinitiator of Br\(_2\)PEGBr\(_2\) (PEG, \( M_n = 20000 \) g/mol).

### 2.3 Synthesis of H-shaped block copolymer (PTMSMPA\(_2\)PEGPTMSMPA\(_2\))

In a typical experiment for Sam1 (PEG\(_{4000}\)) in Table 1, macroinitiator, Br\(_2\)PEGBr (0.48 g, 0.1 mmol), TMSMPA monomer (2.5 g, 10 mmol) and methanol (2 mL) were added into a 20 mL flask with a stirring bar. After purging with nitrogen gas, CuBr (58 mg, 0.4 mmol) and bipyridine (bPy, 188 mg, 1.2 mmol) were added into the mixture while stirring. After the reaction was carried out for 4 h, the flask was immersed in liquid nitrogen to stop the polymerization and diluted with anhydrous THF and then the diluted polymer solution was passed through a short column of silica for removal of the melt salt. Then, the crude product was dissolved in CH\(_2\)Cl\(_2\), and washed with water for 3 times. After precipitation in diethyl ether for 3 times, the product was dried under vacuum to obtain white macroinitiator in 80% yield.

### 2.4 Self-assembly of H-shaped block copolymer

4 mg of H-shaped block copolymer was dissolved in 2 mL of dimethyl formamide and then 3 mL of water was added at a rate of 1 drop every 10 seconds using a syringe under vigorous stirring. Turbidity was typically occurred when the content of water reached 5 vol%, indicating the formation of aggregates. After stirring for five hours, 20 mg of triethylamine was added to cross-link the aggregates. The solution was stirred at room temperature for 3 days for further measurements.

### 2.5 Instrumentation

1H-NMR spectra were recorded on a Bruker DMX-300 nuclear magnetic resonance (NMR) instrument with CDCl\(_3\) as solvent and tetramethylsilane (TMS) as internal standard. The molecular weight and molecular weight distribution of the polymers were measured on a Waters 150C gel permeation chromatography (GPC). Molecular weights were calibrated against polystyrene standards of narrow molecular weight distribution. THF was used as eluent at a flow rate of 1.0 mL/min. The size measurement and morphology of the resultant aggregates were performed on a JEM100-SX transmission electron microscopy (TEM) operating at an acceleration voltage of 200 kV. The samples used in the measurements were prepared by depositing polymer solutions onto copper grids which had been coated with a thin film of Formvar and then coated with carbon.

### 3 Results and discussion

#### 3.1 Synthesis of H-shaped block copolymers

Two steps were applied for synthesis of H-shaped block copolymer, synthesis of macroinitiator and ATRP of TMSMPA monomer. Macroinitiators, Br\(_2\)PEGBr\(_2\), were synthesized by esterification reaction of hydroxyl-terminated PEG (\( M_n = 4000, 20000 \) g/mol) with BBIBPC. Their structures are shown in Fig. 1. To complete the reaction, excess BBIBPC was added which can be moved off by washing with water and precipitation. 1H-NMR spectra of two kinds of macroinitiators are shown in Fig. 1. Peaks at \( \delta = 4.2–4.4 \) (a'), \( \delta = 1.8–2.0 \) (c) and \( \delta = 1.3–1.4 \) (d) are attributed to BBIBPC, and peak b is attributed to PEG. The signal of ester methylene protons formed from the reaction of BBIBPC with HO-PEG-OH is overlapped at \( \delta = 4.2–4.4 \) (a). The integration ratio of signals (a+a') to c and d, \( I_{a+b}/I_{c+d} \) is 12:24:6, which is consistent with their proton ratio and indicates that all PEG hydroxyl groups were transformed to ester groups. We also can measure the integration ratio of \( I_{a+b} \) and \( I_{c+d} \) to calculate the reaction efficiency which is higher than 95%, signifying the nearly complete esterification of hydroxyl groups to form Br\(_2\)PEGBr\(_2\).

These two kinds of Br\(_2\)PEGBr\(_2\) were used as macroinitiators in ATRP of TMSMPA monomer in methanol at room temperature to prepare the targeted products, Sam 1 and Sam 2. The polymerization condition and