

Preparation and Self-Assembly of Poly(diglycidyl maleate-*co*-stearyl methacrylate)

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Received 21 December 2005; accepted 30 January 2007

DOI 10.1002/app.26264

Published online 10 April 2007 in Wiley InterScience (www.interscience.wiley.com).

ABSTRACT: Poly(diglycidyl maleate-*co*-stearyl methacrylate) (P(DGMA-*co*-SMA)) with reactive epoxy groups was synthesized by reaction of poly(maleic anhydride-*co*-stearyl methacrylate) (P(MA-*co*-SMA)) and epichlorohydrin. The effect of precipitant on self-assembly behaviors of the resultant copolymer was investigated. It was found that vesicles and nanotubule liked aggregates can be obtained through self-assembly of P(DGMA-*co*-SMA) in THF solu-

tion using CH₃CH₂OH (EtOH) as precipitant while spherical aggregates can be obtained using H₂O as precipitant. The mechanism of the self-assembly behavior was discussed. © 2007 Wiley Periodicals, Inc. *J Appl Polym Sci* 105: 1156–1161, 2007

Key words: self-assembly; aggregate; epoxy; copolymer; morphology

INTRODUCTION

Amphiphilic polymers have received considerable attention because of their special self-assembly ability to form nanoscale or micrometer-scale aggregates.^{1–4} Researchers have obtained aggregates with various morphologies, including vesicles,^{5,6} capsules,⁷ spheres,^{8,9} tubules,¹⁰ films,¹¹ and fibers,¹² by using copolymers with different structures or changing the self-assembly conditions such as concentration,^{13–15} solvents,¹⁶ temperature and pH.^{17,18} The resultant aggregates have potential applications in the fields such as microreactors, microcapsules, and drug delivery systems.^{19–22} The stabilization of aggregates is of great importance in most applications. Core or shell crosslinking is a favorable way to obtain stable aggregates. Many efforts have been made to synthesize copolymers with reactive groups for self-assembly.^{23–25} Cao et al. synthesized poly(isoprene-*b*-ferrocenylphenylphosphine) by sequential living anionic polymerizations, and the polyisoprene segment can be crosslinked under UV irradiation in the presence of radical initiator after self-assembly process.²⁶ Pilon et al. prepared shell crosslinked micelles of a new thermoresponsive triblock copolymer,²⁰ and they found that the diameters of the

micelles could be adjusted by simply varying the temperature at which shell crosslinking was carried out. Du and Armes prepared pH-responsive vesicles based on a hydrolytically self-*cross*-linkable copolymer by the crosslinking of 3-(trimethoxysilyl) propyl methacrylate groups.²⁷

Compounds with epoxy groups have been applied in many fields, including proteins and enzymes immobilization,^{28,29} biological tissue fixation and biomolecule binding,^{30,31} for their easily transformable epoxy groups. The self-assembly of copolymers with epoxy groups can provide aggregates with reactive shells or cores and the resultant aggregates can be crosslinked or introduce guest molecules or other functional segments to the aggregates by reaction with the epoxy group. Cañamero et al. synthesized poly(glycidyl methacrylate)-*b*-poly(butyl acrylate) through atom transfer radical polymerization (ATRP).³² However, it is hard to control the number of epoxy group in each segment by this method. The structure of copolymers may have significant effect on their self-assembly behavior and the distribution of the epoxy group will greatly affect the crosslinking properties.

We have synthesized P(MA-*co*-SMA) and investigated its self-assembly behavior in our previous work.³³ In this article, we report the synthesis of poly(diglycidyl maleate-*co*-stearyl methacrylate) (P(DGMA-*co*-SMA)) through grafting epichlorohydrin to P(MA-*co*-SMA). The self-assembly behavior of the resultant copolymer was investigated in THF solution using EtOH and H₂O as precipitants and the mechanism of self-assembly behaviors was discussed.

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Contract grant sponsor: The Science and Technology Commission of Zhejiang Province; contract grant number: 2004C34005.

EXPERIMENTAL

Materials

Maleic anhydride (MA), stearyl methacrylate (SMA), and di-*tert*-butyl peroxide (DTBP) were purchased from Shanghai No.1 Chemical reagent factory. Epichlorohydrin obtained from Wulian Chemical Plant in Shanghai is an analytical reagent and was used as received. Tetrabutyl ammonium bromide (TBAB) were purchased from Sinopharm Chemical Reagent. THF, NaOH, and EtOH were purchased from East of China Chemical. MA was recrystallized in chloroform before use. SMA was purified as described in reference.³⁴ DTBP was treated according to the literature method.³⁵ THF was purified by fluxing over a K—Na alloy under nitrogen. Other reagents were used as received.

Preparation of P(DGMA-co-SMA)

P(MA-co-SMA) was synthesized according to the reference.³⁶ P(DGMA-co-SMA) was synthesized through the reaction between P(MA-co-SMA) and epichlorohydrin. The typical process is as following: 0.8171 g of P(MA-co-SMA), 4.8 mL of Epichlorohydrin, 0.0102 g of TBAB, and 0.15 mL of H₂O were mixed in a 25 mL three-necked flask with a magnetic stirrer and a reflux condenser and reacted for 2.5 h in a 120°C oil bath. Then the excessive epichlorohydrin was removed under vacuum. The product was dissolved in 10 mL of THF at room temperature, and then 0.51 mL of 30 wt % NaOH solution was added dropwise in 15 min. The reaction was continued for another 2 h with magnetic stirring. Then the product was purified by precipitation in 200 mL of deionized water twice and dehydrated under vacuum at room temperature.

Preparation of self-assembly system

EtOH or H₂O, precipitants for P(DGMA-co-SMA), were added dropwise to the THF solution of P(DGMA-co-SMA) at 25°C with a volume ratio 1 : 9, respectively. Samples for TEM observation were prepared by dropping 10 μL of dilute aggregates solution onto 200-mesh gilder copper TEM grids and air-dried at room temperature.

Characterization

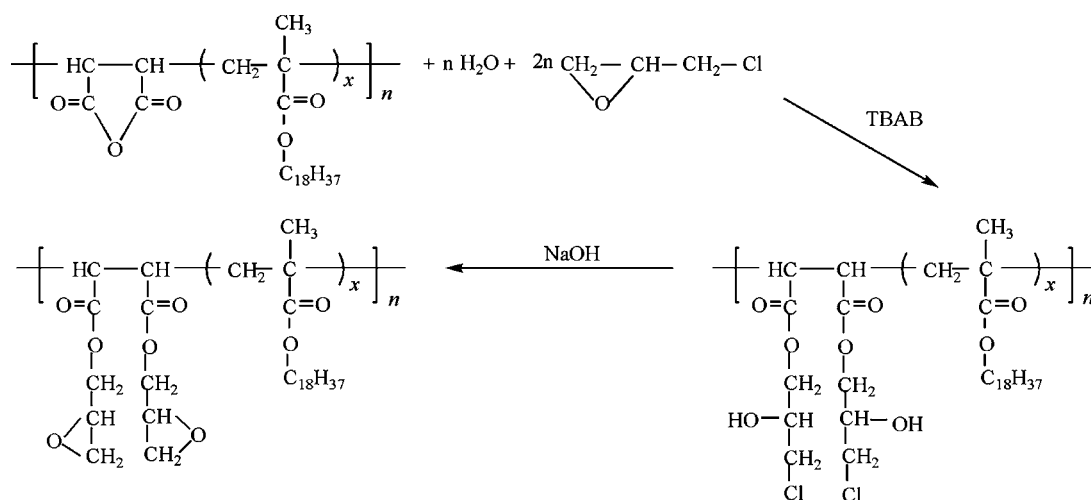
¹H-NMR spectra of polymers in CDCl₃ were recorded on a 500 MHz AVANCE NMR spectrometer (Model DMX500), using TMS as a standard. TEM images were obtained on a JEOL model 1200EX instrument operated at an accelerating voltage at 160 kV. The gel permeation chromatography (GPC) measurements were carried out on a Waters 201 with a μ-styragel column and THF as an eluent, and the molecular weight was calibrated with standard polystyrene (PS).

RESULTS AND DISCUSSION

Synthesis and characterization of P(DGMA-co-SMA)

The synthesis process of P(DGMA-co-SMA) is shown in Scheme 1. The MA segment was hydrolyzed and reacted with epichlorohydrin using TBAB as catalyst. Followed by ring-closing, P(DGMA-co-SMA) was obtained.

The structure of P(MA-co-SMA) was characterized by ¹H-NMR and the peaks was assigned as following:^{34,37} 0.88 ppm (3H, in CH₃(CH₂)₁₅—), 0.86 and 0.90 ppm (3H, in CH₃C—), 1.20 ~ 1.40 ppm (30H, in —(CH₂)₁₅CH₃), 1.58 ~ 1.78 ppm (2H, in



Scheme 1 Synthesis process of P(DGMA-co-SMA).

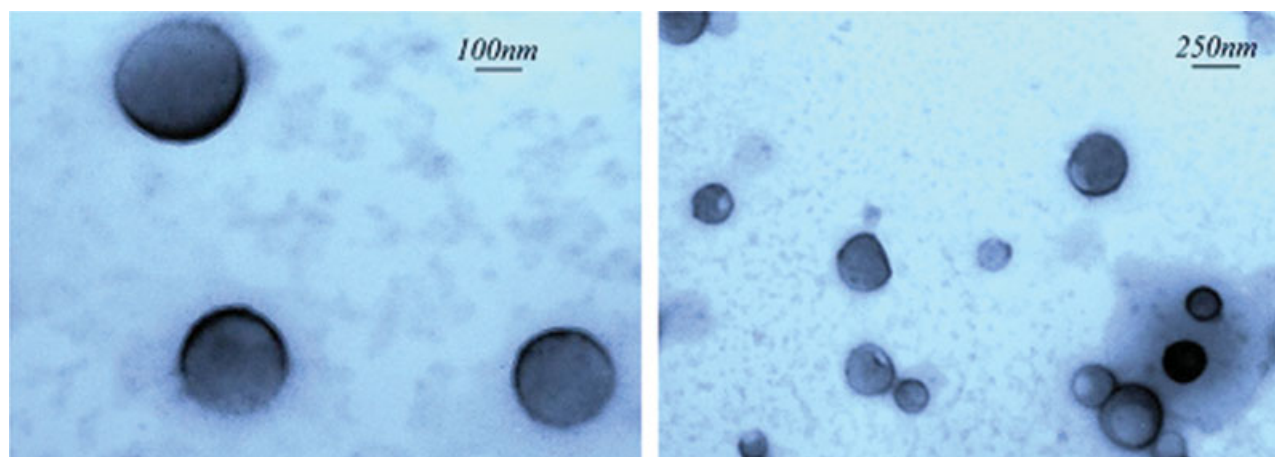


Figure 1 TEM images with different magnifications of spherical aggregates of P(DGMA-*co*-SMA) from the solution of P(DGMA-*co*-SMA) in THF/H₂O mixed solvent (THF/H₂O = 9/1, v/v) with a polymer concentration of 0.1 wt % at 25 °C. [Color figure can be viewed in the online issue, which is available at www.interscience.wiley.com.]

—CH₂(CH₂)₁₅CH₃, 2H, in —CH₂C—), 2.2 ~ 3.8 ppm (2H, in —CHCH—), 4.13 (2H, in —OCH₂—). ¹H-NMR spectrum indicated that P(MA-*co*-SMA) has been successfully synthesized. The molecular weight

of PMA₅-*b*-PSMA₈ was $M_n \approx 3400$, and its polydispersity index is 1.73. The MA segment content of the copolymer was 15.34 wt %. Mole ratio of MA segment and SMA segment = 5 : 8.

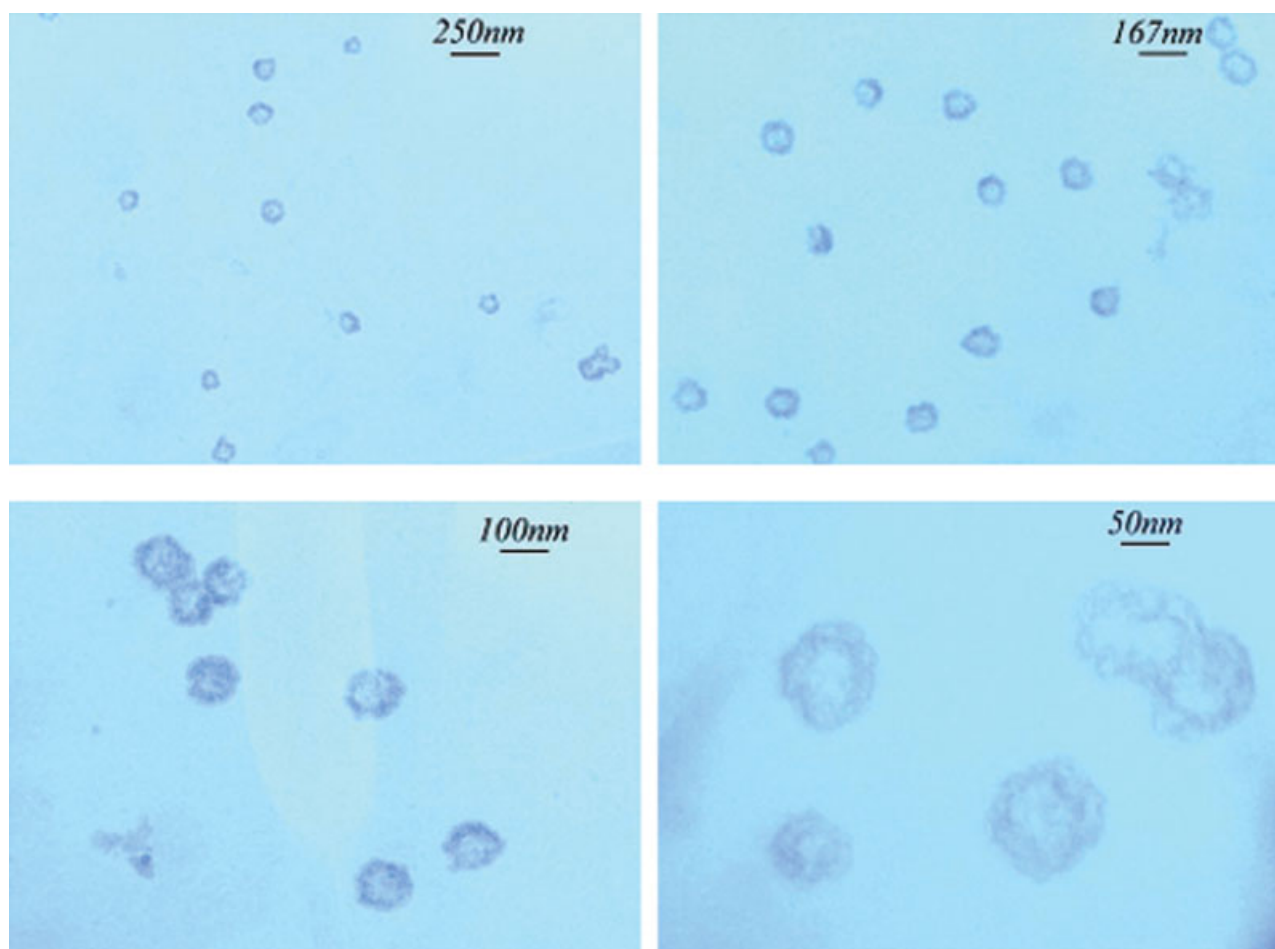


Figure 2 TEM images with different magnifications of spherical vesicles of P(DGMA-*co*-SMA) from the solution of P(DGMA-*co*-SMA) in THF/EtOH mixed solvent (THF/EtOH = 9/1, v/v) with a polymer concentration of 0.1 wt % at 25 °C. [Color figure can be viewed in the online issue, which is available at www.interscience.wiley.com.]

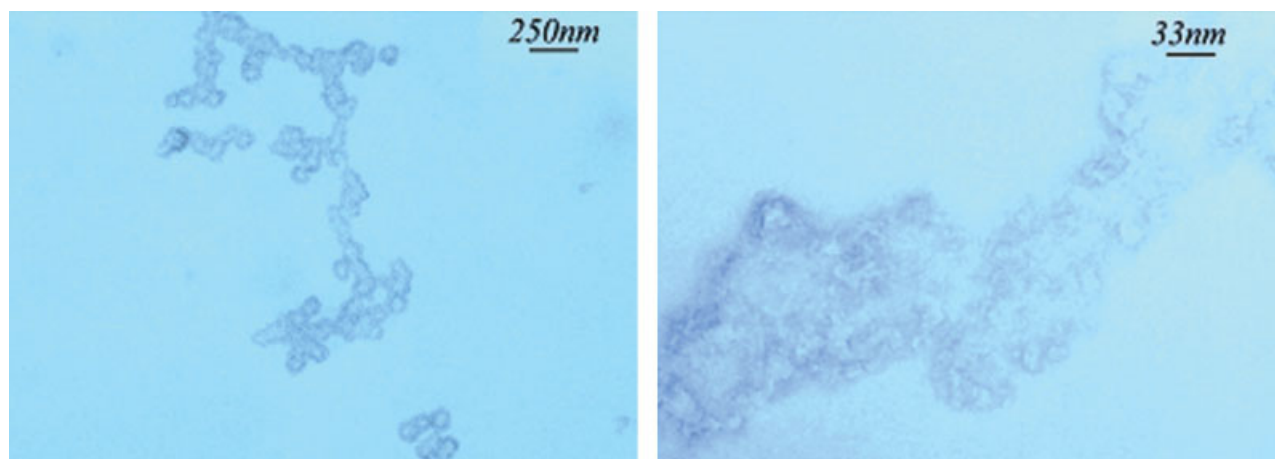


Figure 3 TEM images of nanotubule like aggregates of P(DGMA-co-SMA) from the solution of P(DGMA-co-SMA) in THF/EtOH mixed solvent (THF/EtOH = 9/1, v/v) with a polymer concentration of 0.1 wt % at 25 °C. B is magnified part of A. [Color figure can be viewed in the online issue, which is available at www.interscience.wiley.com.]

$^1\text{H-NMR}$ spectrum of P(DGMA-co-SMA) showed following shifts:³⁸ 0.88 ppm (3H, in $\text{CH}_3(\text{CH}_2)_{15}-$), 0.86 and 0.90 ppm (3H, in $\text{CH}_3\text{C}-$), 1.20 ~ 1.40 ppm (30H, in $-(\text{CH}_2)_{15}\text{CH}_3$), 1.58 ~ 1.78 ppm (2H, in $-\text{CH}_2(\text{CH}_2)_{15}\text{CH}_3$, 2H, in $-\text{CH}_2\text{C}-$), 2.2 ~ 3.8 ppm (2H, in $-\text{CHCH}-$), 2.61 and 2.81 ppm (4H, in $-\text{CHCH}_2\text{O}-$), 3.17 ~ 3.27 ppm (2H, in $-\text{OCH}<$), 3.36 and 3.86 ppm (4H, in $-\text{OCH}_2\text{CH}<$), 4.13 ppm (2H, in $-\text{OCH}_2-$). Compared with the $^1\text{H-NMR}$ spectrum of P(MA-co-SMA), new peaks of the oxirane ring in glycidyl ester appeared at 2.61, 2.81, and 3.17 ~ 3.27 ppm, which indicates that epichlorohydrin has been grafted onto P(MA-co-SMA).

Self-assembly behaviors of P(DGMA-co-SMA)

In this study, we introduced EtOH and H_2O into the THF solution of P(DGMA-co-SMA) to study the influence of different precipitants on its self-assembly behavior. As for P(DGMA-co-SMA), THF is a good solvent for both pendant group, while EtOH is nonsolvent for the stearyl pendant group but solvent for epoxy pendant group, and H_2O is the nonsolvent for both pendant group but more hydrophilic to epoxy group for the oxide atom of oxirane ring may form hydrogen bonds with H_2O molecule. To induce the self-assembly of P(DGMA-co-SMA), the copolymer was dissolved in THF with a concentration of 0.1 wt % and EtOH or H_2O , as precipitants, were added dropwise to the solution, respectively. Figure 1 shows TEM images of spherical aggregates formed in the THF solution of P(DGMA-co-SMA) using H_2O as precipitant (THF/ H_2O = 9/1, v/v). Figure 2 shows TEM images of spherical vesicles of P(DGMA-co-SMA) formed in the THF solution of P(DGMA-co-SMA) using EtOH as precipitant (THF/EtOH = 9/1, v/v). The vesicles obtained in THF/EtOH system

had a diameter of about 100 nm. We can see that the cavum of vesicles was about 50 nm and the wall thickness of the vesicles was about 25 nm. Comparing Figure 2 with Figure 1, we can see that the property of precipitant had great effect on the morphology of the resultant aggregates for the attractive and repulsive forces balance among the segments and the solvents.³³ The attractive force between the epoxy group and the EtOH lead to the formation of vesicle structure of the resultant aggregates.

Nanotubule-like aggregates were also obtained in the self-assembly system of P(DGMA-co-SMA)/THF solution with EtOH as precipitant as shown in Figure 3. Figure 3(A) shows the image of a whole nanotubule-like aggregates and Figure 3(B) is the magnified part of Figure 3(A). We can see that the diameter of the nanotubule-like aggregate was about 100 nm and the wall thickness was about 30 nm, which were similar with those of the spherical vesicles.

Mechanism of the formation of nanovesicles and nanotubules

Figure 4 shows the possible mechanism of the self-assembly process of P(DGMA-co-SMA). Figure 4(A) is the extended chain of P(DGMA-co-SMA) in the THF solution because THF is a good solvent for both segments. When precipitant was added dropwise to the polymer solution, the polymer chain coiled and the epoxy groups were extended to the precipitant interface for the interactions such as hydrogen bonding between them while the segments with stearyl pendant were shrinked [as shown in Fig. 4(B)]. The addition of H_2O induced the polymer to aggregate and formed spherical aggregates as shown in Figure 4(C). With the addition of EtOH, the coiled polymer aggregated and the EtOH dissolvable segment

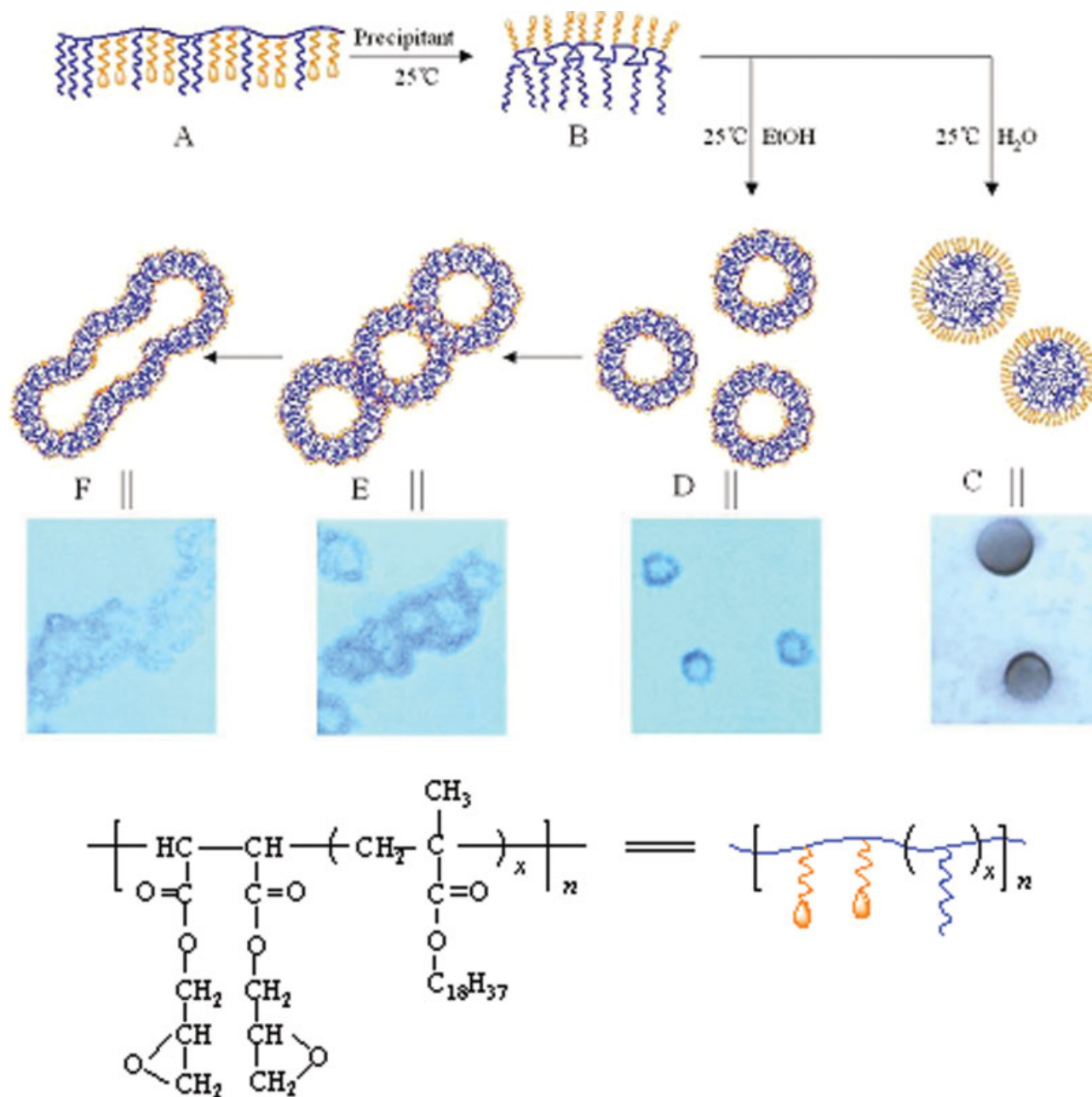


Figure 4 Mechanism of self-assembly behavior of P(DGMA-*co*-SMA). [Color figure can be viewed in the online issue, which is available at www.interscience.wiley.com.]

migrated to the surface to form bilayer formation of the vesicles as Figure 4(D) shows. Then the vesicles with epoxy corona [Fig. 4(D)] collided with each other during the Brownian motion, and connected together for the same composition of the periphery as Figure 4(E) shows. The segments with epoxy pendant at the interface between the connected aggregates migrated to the surface under the tensile force of the solvent and result in the amalgamation of the vesicles to form nanotubules as shown in Figure 4(F). For the copolymer has epoxy group, which is in the surface of the vesicles during self-assembly, the shape of the obtained vesicles and nanotubules

can be fixed and stable in different conditions through the crosslinking of the epoxy group. These kinds of vesicles and nanotubules have potential applications in the fields such as drug delivery, microreactors, nanodevices, and microcapsules.

CONCLUSIONS

P(DGMA-*co*-SMA) with reactive epoxy groups was synthesized by reaction between P(MA-*co*-SMA) and epichlorohydrin. Different aggregates were obtained through self-assembly of P(DGMA-*co*-SMA) in THF

solution using EtOH or H₂O as precipitants, respectively. The mechanism of the self-assembly behavior was discussed. Because the resultant aggregates have epoxy groups, the morphology of the resultant can be fixed by crosslinking of the epoxy groups, and guest molecules and other functional segments also can be introduced to the micelles by reaction with the epoxy group. The obtained vesicles and nanotubules have promising applications in the fields such as drug delivery, microreactors, and microcapsules.

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