Synthesis And Micellization Properties Of Poly(t-Butyl Acrylate) b-Poly(ε-Caprolactone)-b-Poly(t-Butyl Acrylate) Triblock Copolymers

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ABSTRACT

A novel symmetrical triblock copolymer poly (t-butyl acrylate)-b-poly(ε-caprolactone)-b-poly (t-butyl acrylate) (**4**, PBA-b-PCL-b-PBA) was successfully synthesized via ring-open polymerization (ROP) and atom transfer radical polymerization (ATRP) methods. The self-assembly behaviors of the resultant triblock copolymer in trichloromethane/cyclohexane (1:1, v/v) mixture was studied by transmission electron microscopy (TEM). The aggregates were prepared by first dissolving the copolymers in trichloromethane solvent and then adding cyclohexane to induce the segregation of the PCL chains. The elliptical nut-like micelles can be formed in the above mixed solvent. And a possible mechanism for the formation of the aggregates was proposed.   © 2007 Trade Science Inc. - INDIA

INTRODUCTION

Self-assembly is the process by which monomeric molecules recognize each other in solution and form aggregates of complexity ranging from dimers to mesoscopic-size structures[1]. The intermolecular forces that make self-assembly possible are very often dependent on the structure of molecular. For instance, amphophilic block copolymers comprise hydrophobic, water-insoluble blocks that aggregate into micellar cores and hydrophilic, water-soluble blocks that extend into the water phase and prevent

the aggregates from being precipitated[2]. It is well known that the block copolymer precursors could be programmed for multimolecular assembly into complex nanostructures, based on their compositions and structures, which could be controlled during synthesis, using living polymerization techniques and via post-polymerization modifications[3]. Block copolymers containing a minor hydrophobic block generally form spherical starlike micelles, whereas copolymers with major hydrophobic blocks form the so-called crew-cut micelles with various morphologies including spheres, vesicles, rods, bicontinuous structures, lamellae, tubes, large compound vesicles, hexagonally packed hollow hoops, bowl-shaped and ring-shaped structures, and several others[4-9]. The characteristic dimensions of such aggregates, called 'block copolymer micelles', are in the nanometer range. Such nanosized domains dispersed in water have been the focus of much interest, mainly because they can serve as nanoreactors, for example, for the production of colloidally stable(semi)-conducting nanoparticles or as reservoirs for the transport of biologically active molecules such as DNA, enzymes, or drugs[2]. Generally, self-assembly of amphophilic copolymers is then caused by the addition of a critical amount of water, and the final micelles are collected in pure water by gradual elimination of the organic co-solvent by dialysis. This procedure leads to kinetically frozen block copolymer micelles, far from the thermodynamic equilibrium. The synthesis of polymers with amphiphilic architectures is a key problem for self-assembly of polymer science[10]. Recent advancements in controlled radical polymerizations(CRP) alleviate the microstructure designing and synthesis of block copolymers, leading to various fascinating architectures. Atom transfer radical polymerization (ATRP) has proven to be a powerful CRP technique for the synthesis of well-defined polymers(with desired properties). Among the family of amphiphilic block copolymers, interest in the synthesis of poly(ε-caprolactone) (PCL) copolymers has been increasing because of the biodegradable properties of PCL and the potential applications as biomaterials[11].

During the past decade, most studies of self-assembly were made on amphiphilic molecular[12-14]. However, control over the size and shape of self-as-

sembled structures by tuning the chemical details of the molecular building blocks remains a challenging and unresolved issue. We have a long-standing interest in the synthesis and self-assembly of block copolymers and their potential applications. In the present study, poly(t-butylacrylate)-b-poly(ε-caprolactone)-b-poly (t-butyl acrylate) triblock copolymer, (4, PBA-b-PCL-b-PBA), was synthesized by ROP and ATRP methods. Associative behaviors of this triblock copolymer in solution to form stable micelles were studied using TEM.

EXPERIMENTAL

Materials

Toluene was dried by refluxing over sodium and distilled under nitrogen prior to use. The ε-caprolactone(99%; Acros) and tert-butyl methacrylate(98%; Acros) were dried over CaH_2, distilled under reduced pressure, and stored under a nitrogen atmosphere. The 2,2′-bis(hydroxymethyl) propionic acid and 2-bromoisobutyryl bromide(97%; Acros) were obtained from Acros and used without further purification. Cu(I)Br (98%; Acros) was purified by stirring overnight in acetic acid. After filtration, it was washed with ethanol and then dried *in vacuo*. Other reagents were purchased from Shanghai Chemical Reagent Co. and used as received.

Synthetic Part

1. Synthesis of benzyl 2,2′-bis(hydroxymethyl) propionate (1)

Benzyl 2,2′-bis(hydroxymethyl) propionate, **(1)**, was synthesized according to the previous method[15] from the reaction of benzyl bromide and 2,2′-bis (hydroxymethyl) propionic acid in the presence of KOH as the acceptors of HBr. ^{1}HNMR($CDCl_3$, ppm): δ 1.08(s, 3H, -CH_3), 3.74(d, 2H, -CH_2OH), 3.95(d, 2H, -CH_2OH), 5.22(s, 2H, -CH_2Ar), 7.36(m, 5H, ArH).

2. Synthesis of poly(2-caprolactone) (2, PCL) by ring-open polymerization (ROP)

Polymerization of ε-caprolactone was initiated with benzyl 2,2′-bis(hydroxymethyl) propionate using a catalytic amount of $Sn(Oct)_2$. The polymerization was carried out at 120°C(18h) using toluene as

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solvent. The resultant polymer was then dissolved in THF and precipitated in cold methanol[16]. ^{1}HNMR (CDCl$_3$, ppm): δ 1.25(s, 3H, -CH$_3$), 1.29-1.45(br, -CH$_2$-), 1.55-1.72(br, -CH$_2$-), 2.24-2.36(br, -CH$_2$-), 3.65(t, -CH$_2$OH), 4.00-4.10(br, -CH$_2$-O), 4.20-4.25(s, -CH$_2$-O), 5.15-5.17(s, -CH$_2$-Ar), 7.30-7.37(m, ArH).

3. Synthesis of macroinitiator (3, PCL-Br)

PCL20 (2.60 g, 1.1 mmol of OH group) 20 was the targeted degree of polymerization of PCL was dissolved in 20 mL of dry THF. To this solution was added 1 mL of triethylamine. Then, 2-bromoisobutyryl bromide(0.5mL, 4.0mmol) in 10mL of THF was added dropwise to the solution at 0°C. The reaction mixture was stirred at room temperature for 24h. The precipitated by product was removed by filtration, and the solution was evaporated to dryness. The crude product was dissolved in 100mL of methylene chloride, and then the organic phase was washed successively with 100mL of water, 1M HCl, and a 1M NaOH aqueous solution and finally dried over MgSO$_4$. The concentrated solution was poured into methanol to precipitate the product. The resulting white solid was dried at 40°C for 24h *in vacuo*. ^{1}HNMR (CDCl$_3$, ppm): δ 1.25(s, 3H, -CH$_3$), 1.29-1.45(br, -CH$_2$-), 1.55-1.72(br, -CH$_2$-), 1.90-2.00(m, -C-(CH$_3$)$_2$-Br), 2.24-2.36(br, -CH$_2$-), 3.65(t, -CH$_2$OH), 4.00-4.10(br, -CH$_2$-O), 4.20-4.25(s, -C-CH$_2$-O), 5.15-5.17(s, -CH$_2$-Ar), 7.30-7.37(m, ArH).

4. Synthesis of poly(t-butyl acrylate)-b-poly(2-caprolactone)-b-poly(t-butyl acrylate)(4, PBA-b-PCL-b-PBA) triblock copolymer by atom transfer radical polymerization (ATRP)

A typical polymerization procedure was as follows: 2,2′-bipyridy(bipy), Cu(I)Br, PCL-Br(2:1:1 in molar ratio) and t-butyl acrylate with a certain molar ratio were added to a dry tube. The tube was cycled between vacuum and nitrogen more than 10 times to remove the oxygen. Then, the tube was sealed and placed in a preheated, thermally regulated oil bath at certain temperature. After a certain period of polymerization, the tube was removed from the oil bath and allowed to cool for a few minutes. Then, several milliliter of chloroform(CHCl$_3$) was added to the tube, and the mixture was placed for a period of time at room temperature to complete the disso-

lution of the polymer. The resulting solution was passed through a short column containing basic aluminum oxide to remove most of the Cu complex. The excess CHCl$_3$ was removed under reduced pressure and the product was precipitated from a large amount of methanol, filtered, and dried under vacuum to constant weight. ^{1}HNMR(CDCl$_3$, ppm): δ 1.25(s, 3H, -CH$_3$), 1.29-1.45(br, -CH$_2$-), 1.28-1.34(br, -C-(CH$_3$)$_3$), 1.55-1.72(br, -CH$_2$-), 1.80-1.90(br, -CH-), 2.18-2.25(br, -CH$_2$-CH-), 2.24-2.36(br, -CH$_2$-), 3.65(t, -CH$_2$OH), 4.00-4.10(br, -CH$_2$-O), 4.20-4.25(s, -C-CH$_2$-O), 5.15-5.17(s, -CH$_2$-Ar), 7.30-7.37(m, ArH).

Measurements

^{1}H-NMR spectra were recorded with an AVANCE DMX-500 NMR spectrometer by using tetramethylsilane(TMS) as internal standard at room temperature. 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). Infrared spectra were recorded on Jasco IR-700 infrared spectrophotometer. Differential scanning calorimetry(DSC) was carried out on a DS822 with a heating rate of 10°C/min from 30 to 200°C under nitrogen atmosphere, relative to indium standards. Transmission electron micrographs were obtained on a JEOL model 1200EX instrument operated at an accelerating voltage at 160kV.

RESULTS AND DISCUSSION

Polymerization and characterization

Benzyl 2,2′-bis(hydroxymethyl) propionate, **(1)**, was synthesized according to the previous method[15]. Polymerization of ε-caprolactone was initiated with benzyl 2,2'-bis(hydroxymethyl) propionate using a catalytic amount of Sn(Oct)$_2$ 120°C. Then, 2-bromo-isobutyryl bromide was reacted with poly(ε-caprolactone)**(2)**, PCL to synthesize a macroinitiator **(3)**, PCL-Br). The use of mixed halide systems to better control ATRP polymerizations of t-butyl acrylate was carried out, while Cu(I)Br as catalyst and bipy as ligand.

Figure 1 shows the ^{1}H-NMR spectra of poly(ε-caprolactone) (**2**, PCL), macroinitiator (**3**, PCL-Br)
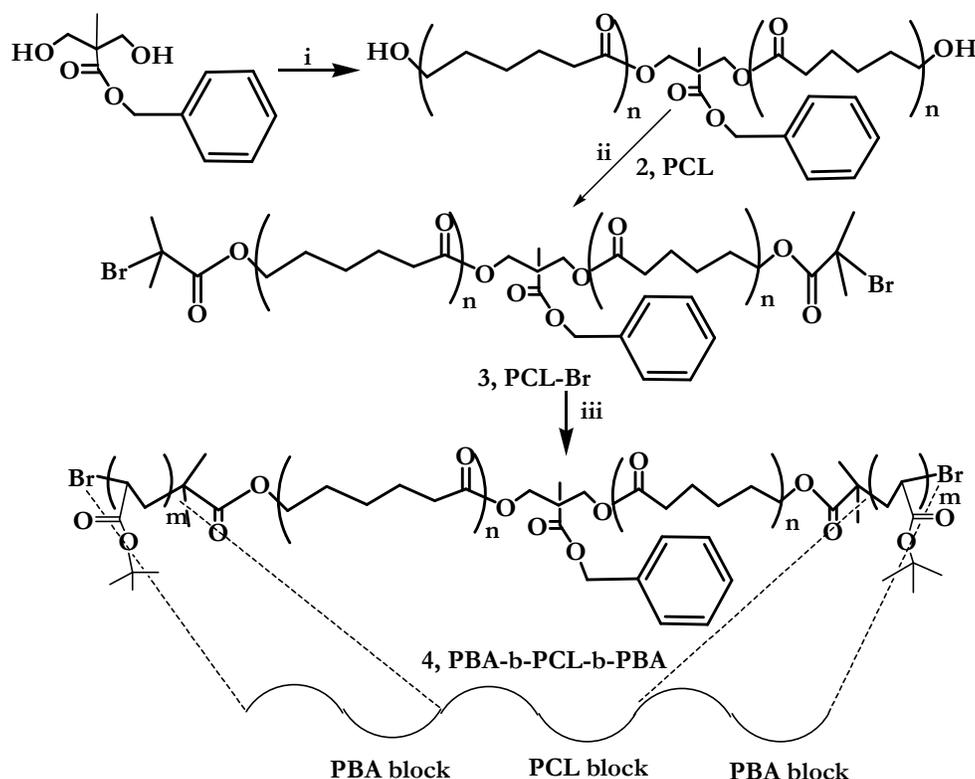
SCHEME 1: Synthetic route of triblock polymers by ring-open polymerization (ROP) and atom transfer radical polymerization (ATRP). Reaction conductions: i) ε-caprolactone, Sn(Oct)$_2$, 120°C,18h, toluene; ii) 2-bromoisobutyryl bromide, 0°C, 24h, THF; iii) 2,2′-bipyridy (bipy), Cu(I)Br, PCL-Br (2:1:1 in molar ratio) and t-butyl acrylate, 100°C, 24h

and poly(t-butyl acrylate)-b-poly(ε-caprolactone)-b-poly (t-butyl acrylate) (**4**, PBA-b-PCL-b-PBA) triblock copolymer. The peaks at 1.90-2.00 ppm for PCL-Br ^{1}H-NMR data correspond to the methyl protons from bromo-isobutyl segment which indicates the introduction of halide initiator systems. The ^{1}HNMR spectrum of PBA-b-PCL-b-PBA) show the characteristic at 1.40ppm for isobutyl groups in PBA. Clearly by this technique, the desired product is obtained.

The samples were dried and analyzed by infrared spectroscopy. As shown in figure 2, the characteristic carbonyl band of the polymers at 1730cm^{-1} was observed in all cases[18]. After polymerization of PCL with t-butyl acrylate, the intensity of 1730cm^{-1} band increased by around 50% in the triblock copolymer. This provides some evidences for obtaining the desired product.

Assuming that each chain is end-capped by an hydroxyl group at one end and a carboxylic acid function at the other end. In the case of **(2)**, a molar mass of 4900 g·mol^{-1} can be calculated by ^{1}HNMR

spectroscopy from the relative intensity of the methylene protons of the main chain at 2.30 ppm (-O-(CH$_2$)$_4$-CH$_2$-COO-) and the phenyl protons at 7.30-7.37 ppm (ArH-CH$_2$-O-). Similarly, an molar mass of **(4)** can also be calculated by ^{1}HNMR 10193g·mol^{-1} by comparison the signal intensity of the methyl protons of butyl groups in PBA at 1.28-1.34 ppm(-C(CH$_3$)$_3$), the methylene protons of the main chain at 2.30ppm(-O-(CH$_2$)4-CH$_2$-COO-) and the phenyl protons at 7.30-7.37 ppm(ArH-CH$_2$-O-). These data are close to the molecular weights that measured by GPC can calculate the molar masses(Mn) of 5371 and 10491 g·mol^{-1}, respectively. As evidenced by GPC, the molar mass distribution is monomodal and narrow(PD=Mw/Mn=1.32 and 1.35 for **(2)** and **(4)**, respectively (As showed in TABLE 1).

The thermal behaviors of the copolymers were evaluated by DSC measurements. As showed in figure 3, poly(ε-caprolactone) (**2**, PCL) has a melting temperature (Tm) around 49°C which attributed to the meltings of the crystalline phases[19]. In the case of
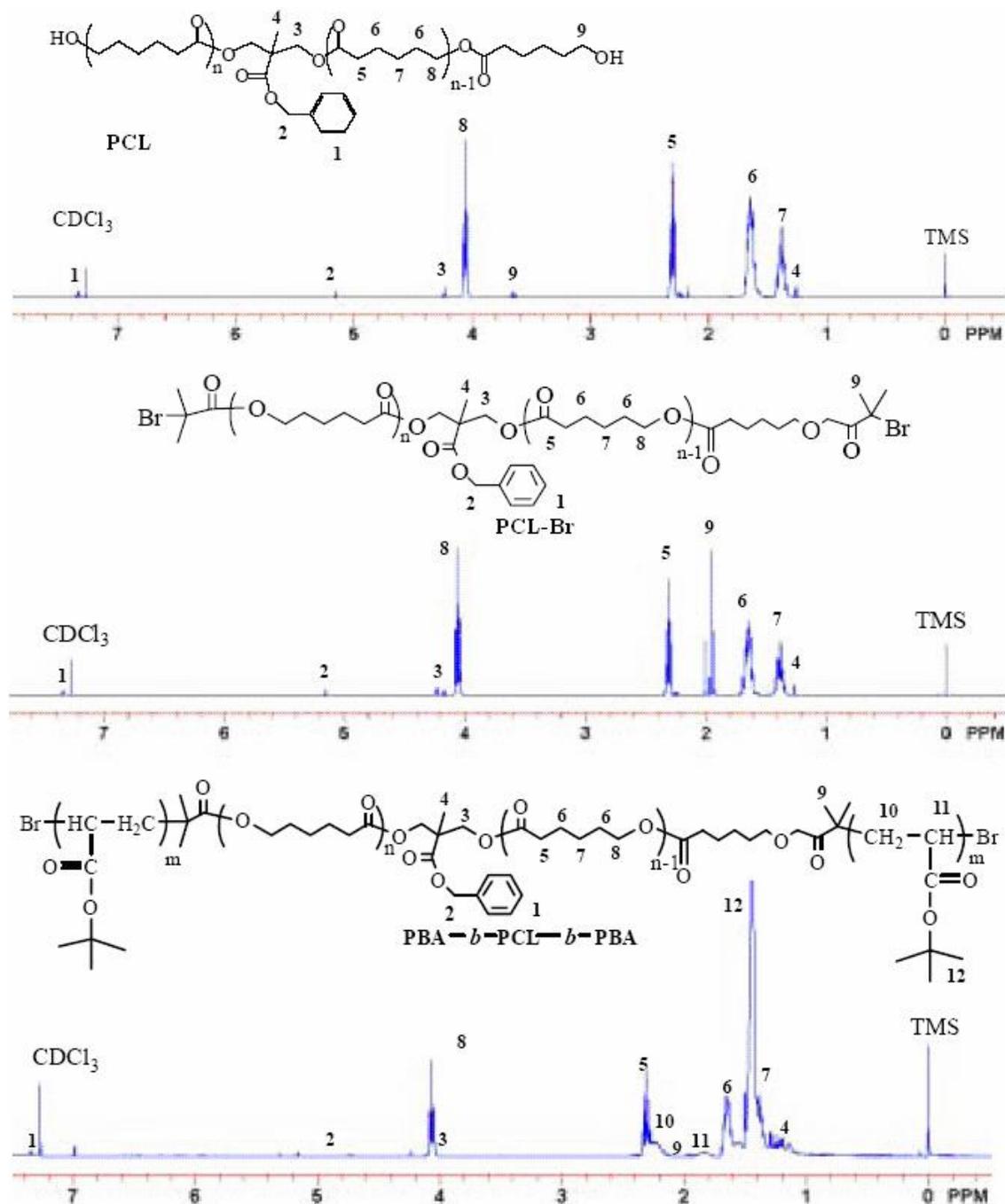
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Figure 1: ^{1}H-NMR spectra of poly(ε-caprolactone) (2, PCL), macroinitiator (3, PCL-Br) and poly(t-butyl acrylate)-b-poly(ε-caprolactone)-b-poly(t-butyl acrylate) (4, PBA-b-PCL-b-PBA) triblock copolymer

the triblock copolymers, PBA-b-PCL-b-PBA, showed two glass temperatures (Tg) and one Tm. The Tm attributed to the meltings of PCL, and the two Tg in the PBA-b-PCL-b-PBA triblock copolymers may be attributed to the meltings of the metastable and the stable domains of poly(t-butyl acrylate), respectively.

Self-assembly of triblock copolymer

Different morphologies of self-assembly systems are basically related to the chemical composition of the copolymer and to the relative volume ratio of the two blocks[20-22]. In order to estimate the aggregation behaviors of **(4)** in solution, the triblock copolymer solutions with $CHCl_3$ and cyclohexane as solvents are prepared and the concentration of polymer fixed at 5mg/mL in the mixed solvent. Then the
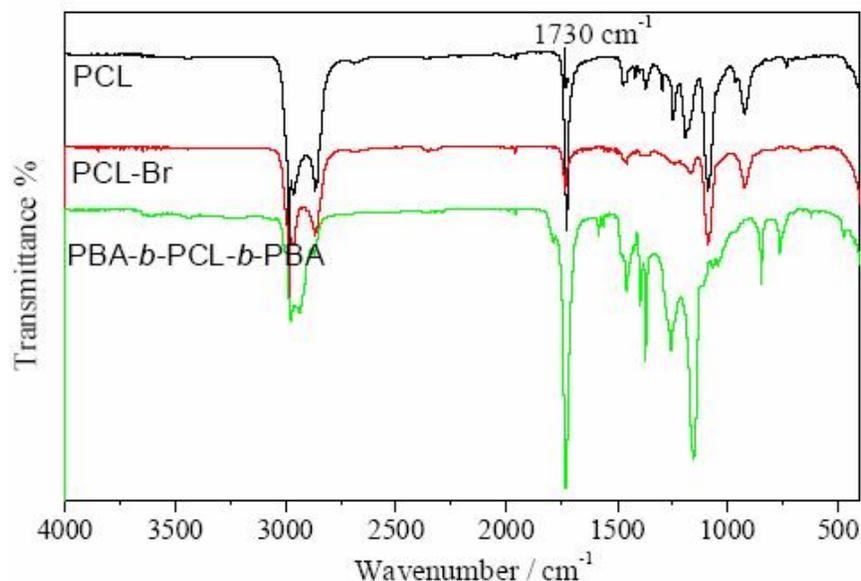
Figure 2: FT-IR spectra of poly(ε-caprolactone) (2, PCL), macroinitiator (3, PCL-Br) and poly(t-butyl acrylate)-b-poly(ε-caprolactone)-b-poly(t-butyl acrylate) (4, PBA-b-PCL-b-PBA) triblock copolymer

TABLE 1: Molecular characteristics of PCL and PBA-b-PCL-b-PBA

Sample	M_n^a (g mol^{-1})	PD^b	M_n^c (g mol^{-1})	Tm/°C	Tg/°C
2, PCL	5371	1.32	4913	49	-
4, PBA-b-PCL-PBA	10490	1.35	10193	49	65/124

[a] The molecular weights were measured by GPC with polystyrenes as standards and tetrahydrofuran as eluent. [b] PD=Mw/Mn in GPC experiment. [c] Obtained by H-NMR spectroscopy data
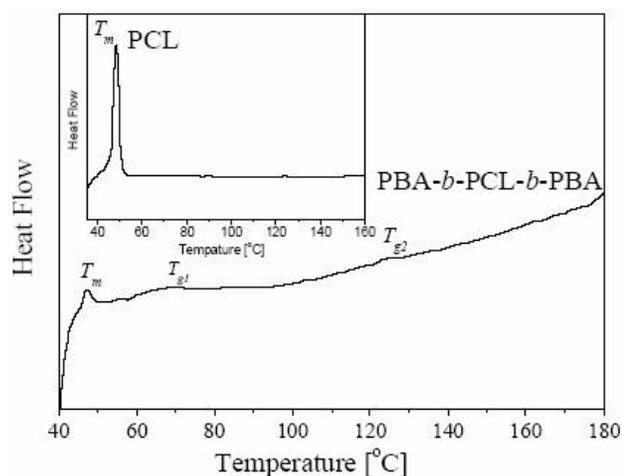

Figure 3: DSC curves of poly(e-caprolactone) (2, PCL) and poly(t-butyl acrylate)-b-poly(ε- caprolactone)-b-poly(t-butyl acrylate) (4, PBA-b- PCL-b-PBA) triblock copolymer
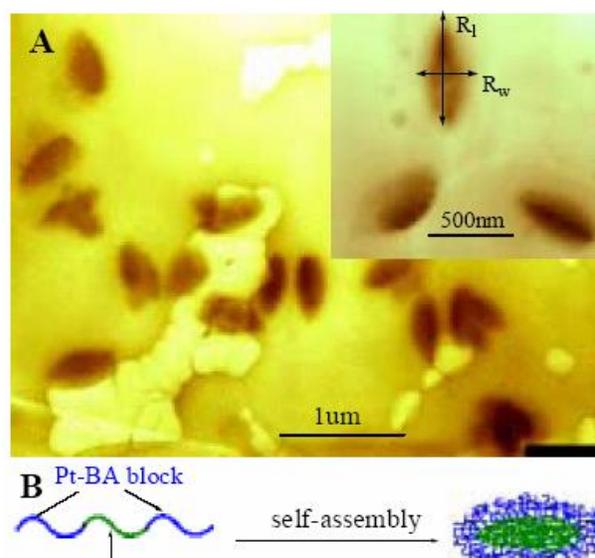

Figure 4: TEM images of the micelles formed by poly(t-butyl acrylate)-b-poly(ε-caprolactone)-b-poly(t-butyl acrylate) (4, PBA-b-PCL-b-PBA) triblock copolymer in the mixed solvent (CHCl$_3$/cyclohexane=1:1, v/v)

by aerosol spraying a dilute micellar solution(ca. 50μL, ca. 5.0mg/mL) onto 200-mesh gilder copper TEM grids.

The formation of micelles during the self-assembling process was confirmed by the TEM study. As showed in figure 4A, elliptical nut-like micelles can been formed by PBA-b-PCL-b-PBA) triblock copolymer in the mixed solvent (trichloromethane/cyclo-

mixture was shaken for 30s and deposited for 24h before measurement. Samples for TEM were prepared

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hexane =1:1, v/v). The micelles have shell-core structure with 600~700 nm in length and 200~300 nm in width, as showed in the magnification TEM images(inset in figure 4). The possible reasons are the PCL segments have a fairly strong steric effect between the phenyl groups which will encounter strong repulsive forces when trying to accommodate the elliptical core. Because the triblock copolymers **(4)** consist of two segments: PCL and PBA segments, because both two segments can be dissolving in trichloromethane. However, cyclohexane is a good precipitator for PCL segment. Therefore, it is assumed that the excess PBA chains are encapsulated in the aggregates and PCL cores are hidden in the center of the micelles(as showed in figure 4B).

CONCLUSION

A triblock copolymer poly(t-butyl acrylate)-b-poly(ε-caprolactone)-b-poly (t-butyl acrylate) **(4)**, PBA-b-PCL-b-PBA) was successfully synthesized via ring-open polymerization (ROP) and atom transfer radical polymerization (ATRP) methods. The resultant polymers were characterized by ^{1}H-NMR, FT-IR, DSC and GPC. The self-assembly behavior of the resulting triblock copolymer in trichloromethane and cyclohexane(1:1, v/v) mixture was studied by transmission electron microscopy(TEM). The elliptical nut-like micelles can be formed by PBA-b-PCL-b-PBA triblock copolymer in the mixed solvent. The resultant micelles have shell-core structure with 600~700 nm in length and 200~300 nm in width.

ACKNOWLEDGMENT

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