Synthesis of Branch-Ring-Branch Tadpole-Shaped [linear-Poly(ε-caprolactone)]-*b*-[cyclic-poly(ethylene oxide)]-*b*-[linear-poly(ε-caprolactone)] by Combination of Glaser Coupling Reaction with Ring-Opening Polymerization

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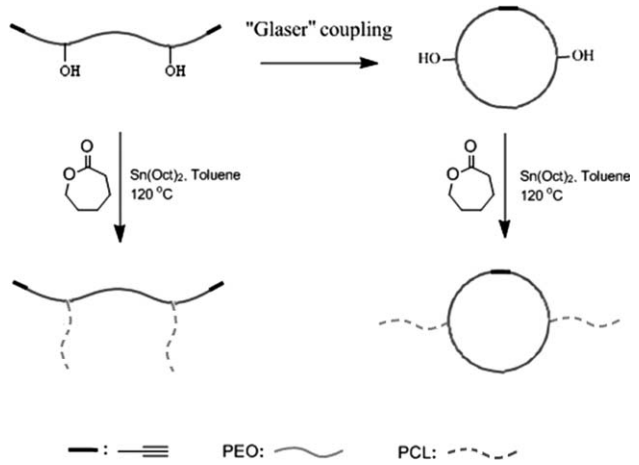
ABSTRACT: A novel amphiphilic branch-ring-branch tadpole-shaped [linear-poly(ε-caprolactone)]-*b*-[cyclic-poly(ethylene oxide)]-*b*-[linear-poly(ε-caprolactone)] [(*l*-PCL)-*b*-(*c*-PEO)-*b*-(*l*-PCL)] was synthesized by combination of glaser coupling reaction with ring-opening polymerization (ROP) mechanism. The self-assembling behaviors of (*l*-PCL)-*b*-(*c*-PEO)-*b*-(*l*-PCL) and their π-shaped analogs of poly(ε-caprolactone)/poly (ethylene oxide)]-*b*-poly(ethylene oxide)-*b*-[poly(ε-caprolactone)/poly(ethylene oxide) with comparable molecular weight in water were preliminarily investigated. The results showed that the micelles formed from the former took a fiber look, however, that formed from the latter took a spherical look. © 2012 Wiley Periodicals, Inc. J Polym Sci Part A: Polym Chem 50: 3095–3103, 2012

KEYWORDS: glaser coupling; macrocycles; poly(ε-caprolactone) (PCL); poly(ethylene oxide) (PEO); ring-opening polymerization; synthesis; tadpole shaped

INTRODUCTION Amphiphilic copolymers can self-assemble into nanosized aggregates of various morphologies in aqueous solution, such as spheres, cylinders, wormlike, helical, bilayers, vesicles, and others.[1,2] These supramolecular assemblies hold great potential applications in drug delivery, tissue engineering, and diagnostic biosensors.[3,4] Over the past few decades, largely owing to the development of various polymerization mechanisms[5–9] and coupling techniques,[10–12] a library of copolymers with complicated structures and compositions emerged, such as comb-shaped, hyperbranched, dendritic, and star shaped.[13] These developments prompted extensive research on the self-assembling behavior of amphiphilic copolymers.[14] It has also been well-established that the topological structures of copolymers may dramatically affect the static and dynamic stability, self-assembling morphology, size and size distribution of assemblies.[15,16] However, micelles formed by amphiphilic cycle-based copolymers were less studied owing to the limited accessibility of the model copolymers.[17]

Using some high-efficient coupling reactions, several pioneer works had opened the doors to cycle-based polymers,[18] and these researches had been comprehensively reviewed in the very recent years.[19] Among them, the tadpole-shaped polymers were regarded as a basic form of a series of "loop and branch" constructions, in which one macrocycle was connected with one tail or more. Considering the synthesis of tadpole-shaped polymers, three typical strategies have been utilized. The first one relied on the synthesis of specially designed linear precursor with two complementary reactive groups located at the chain middle and terminal followed by intramolecular ring-closure reaction under high dilution conditions.[17b,20] The second one employed the intermolecular ring-closure reaction between a functional three-armed star precursor and a complementary reactive reagent.[21] The third one was based on coupling a tail onto a functional macrocycle or directly initiating from a macrocycle.[22] To date, two types of tadpole-shaped polymers have been synthesized via the aforementioned strategies: (1) one macrocycle with one tail, (2) one macrocycle with two tails at the same position. To our knowledge, no examples of tadpole-shaped polymer with two tails at the opposite positions of macrocycle have been reported, especially amphiphilic those.

Glaser coupling reaction was first introduced by our group to synthesize the macrocyclic poly(ethylene oxide) (PEO) and polystyrene (PS), which has been proven to have the same cyclization efficiency as click chemistry between azide and alkyne groups.[23] In this study, the amphiphilic tadpole-shaped copolymers with a novel branch-ring-branch structure, [linear-poly(ε-



SCHEME 1 The synthetical illustration of (*l*-PCL)-*b*-(*c*-PEO)-*b*-(*l*-PCL) and (PEO/PCL)-*b*-PEO-*b*-(PCL/PEO).

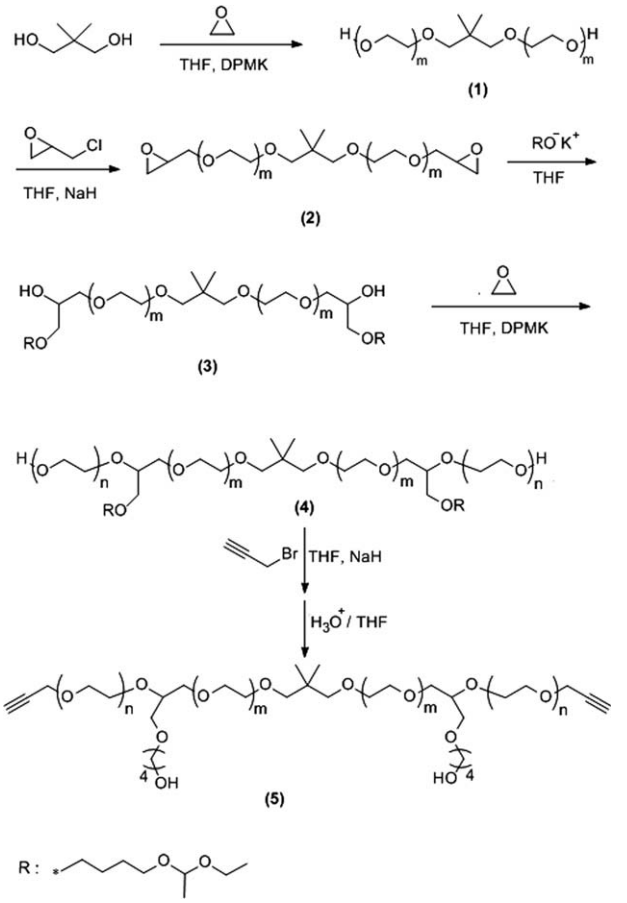
caprolactone)]-*b*-[cyclic-poly(ethylene oxide)]-*b*-[linear-poly(ε-caprolactone)] [(*l*-PCL)-*b*-(*c*-PEO)-*b*-(*l*-PCL)] were synthesized by combination of glaser coupling reaction with ring-opening polymerization (ROP) mechanism (Scheme 1). Moreover, the self-assembling behaviors of (*l*-PCL)-*b*-(*c*-PEO)-*b*-(*l*-PCL) and their π-shaped analogs of poly(ε-caprolactone)/poly(ethylene oxide)]-*b*-poly (ethylene oxide)-*b*-[poly(ε-caprolactone)/poly (ethylene oxide) [(PEO/PCL)-*b*-PEO-*b*-(PCL/PEO)] with comparable molecular weight were investigated and compared.

RESULTS AND DISCUSSION

The target tadpole-shaped copolymers of (*l*-PCL)-*b*-(*c*-PEO)-*b*-(*l*-PCL) were obtained by the following steps: (1) synthesis of linear **PEO(5)** precursor with two terminal alkyne groups and two interior active hydroxyl groups by successive ROP of EO monomers and a series of functional group transformations from **PEO(1)** to **PEO(5)**, (2) synthesis of cyclic **PEO(6)** with two opposite active hydroxyl groups by glaser cyclization in dilute conditions, (3) synthesis of target tadpole-shaped (***l*-PCL)-*b*-(*c*-PEO)-*b*-(*l*-PCL)(7)** by ROP of ε-Cl monomers using **PEO(6)** as macroinitiator (Scheme 2).

Synthesis and Characterization of Linear-Poly(ethylene oxide) with two Terminal Alkyne Groups and two Interior Active Hydroxyl Groups

The **PEO(1)** with different chain lengths were synthesized by ROP of EO monomers using 2,2-dimethyl-1,3-propanediol and diphenylmethyl potassium (DPMK) as coinitiator. The 2,2-dimethyl-1,3-propanediol was chosen as initiator because the methyl groups can be accurately used to calculate the degree of polymerization (DP) and the efficiency of subsequent end functional group modifications. Figure 1(A) showed the gel permeation chromatographic (GPC) trace of **PEO(1a)**, which was a single peak with narrow molecular weight distribution. In a typical ^{1}H NMR spectrum of **PEO(1a)** [Fig. 2(A)], the peaks at 0.88 ppm (a) and that at 3.43–3.64 ppm (c) were assigned to the methyl protons (—OCH$_2$C(C***H***$_3$)$_2$CH$_2$O—) on initiator residual and methylene protons (—C***H***$_2$C***H***$_2$O—) on PEO main chain, respectively. The



SCHEME 2 The synthetical route to linear **PEO(5)** with two terminal alkyne groups and two interior active hydroxyl groups.

DP of PEO main chain (DP_{PEO}) was calculated from the relative integral area ratio by using the Formula 1:

$$DP_{PEO} = \frac{A_c/4}{A_a/6} \quad (1)$$

where A_a and A_c were the integral areas of resonance signals at 0.88 ppm (a) and 3.43–3.64 ppm(c), respectively. The calculated DP_{PEO} for **PEO(1a)** and **PEO(1b)** were 43 and 98.

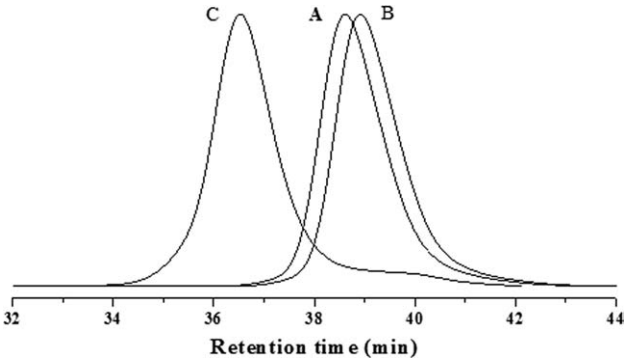


FIGURE 1 GPC traces of **PEO(1a)** (M_n = 2100 g/mol, M_n/M_w = 1.08) (A), **PEO(3a)** (M_n = 1970 g/mol, M_n/M_w =1.07) (B) and **PEO(4a)** (M_n = 5010 g/mol, M_n/M_w = 1.10) (C).

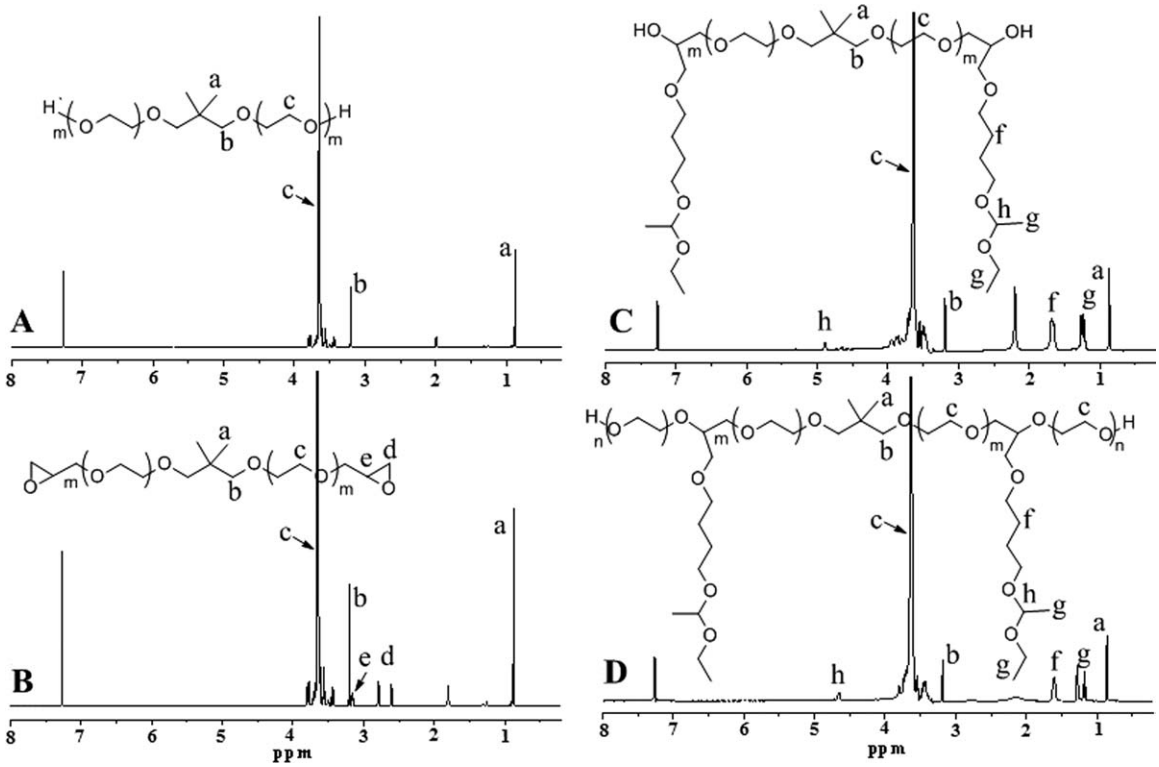


FIGURE 2 ^{1}H NMR spectra of **PEO(1a)** (A), **PEO(2a)** (B), **PEO(3a)** (C), and **PEO(4a)** (D) in $CDCl_3$.

The **PEO(2)** was prepared by nucleophilic reaction of **PEO(1)** with epichlorohydrin in the presence of NaH. Figure 2(B) showed the ^{1}H NMR spectrum of **PEO(2a)**. The peaks at 2.59 and 2.78 ppm (d) and that at 3.15 ppm (e) assigned to the protons (—C***H***OC***H***$_2$—) on epoxide end groups were observed clearly. Moreover, the relative integral area ratio of the peaks (a) to (d) was nearly 3:2, indicating that epoxidation was complete.

The **PEO(3)** with an active hydroxyl group and a protected hydroxyl group at each end was obtained by ring-opening reaction of **PEO(2)** with potassium 1-ethoxyethyl 1,4-butylene glycoxide. To avoid the formation of multiblocked PEO, two measures were taken: (1) the solution of **PEO(2)** was slowly added dropwise into the solution of potassium 1-ethoxyethyl-1,4-butylene glycoxide, (2) the potassium 1-ethoxyethyl 1,4-butylene glycoxide was used in large excess (40 equiv of the epoxide groups). The GPC trace of **PEO(3a)** also showed a monomodal peak, confirming that the multiblocked PEO did not exist actually [Fig. 1(B)]. Figure 2(C) showed the ^{1}H NMR spectrum of **PEO(3a)**, compared with the spectrum of Figure 2(B), the characteristic resonance signals of epoxide groups disappeared thoroughly, indicating that the ring-opening reaction was complete. The new peaks at 1.68 ppm (f), 1.25 ppm (g) and that at 4.90 ppm (h) were assigned to the methyl, methylene, and methine protons (C***H***$_3$C***H***$_2$OC***H***(C***H***$_3$)O(C***H***$_2$)$_4$—) on 1-ethoxyethyl-1,4-butylene glycol, respectively.

The **PEO(4)** with two terminal active hydroxyl groups and two interior protected hydroxyl groups was obtained by ROP of EO monomers employing **PEO(3a)**, as macroinitiator. The DP_{PEO} of **PEO(4)** can also be calculated from the relative integral area ratio of peaks at 0.88 ppm (a) to that at 3.43–3.64 ppm (c) by using the Formula 1. The obtained DP_{PEO} for **PEO(4a)** and **PEO(4b)** were 108 and 191. Compared with the GPC trace of **PEO(1a)**, that of **PEO(4a)** clearly shifted to the higher molecular weight region [Fig. 1(C)].

The **PEO(5)** were prepared by the functional group transformation of **PEO(4)** with propargyl bromide and the subsequent cleavage of the acetal protective group. Figure 3(A) showed the ^{1}H NMR spectrum of **PEO(5a)**. The peaks at 2.44 ppm (i) and that at 4.20 ppm (j) were attributed to alkynyl proton (—CH_2—C≡C***H***) and methylene protons (—C***H***$_2$—C≡CH) on propargyl groups, respectively. The relative integral area ratio of peaks (j) to that of peaks (a) was about 2:3, indicating that the efficiency of propargylation was almost 100%. Meanwhile, the characteristic resonance signals at 4.90 ppm (g) and 1.25 ppm (h) attributed to protons (C***H***$_3$CH$_2$OC***H***(C***H***$_3$)O—) on the protective group could not be observed anymore, demonstrating the hydrolysis was also complete.

Synthesis and Characterization of Branch-Ring-Branch Tadpole-Shaped (*l*-PCL)-*b*-(*c*-PEO)-*b*-(*l*-PCL)

The cyclic **PEO(6)** with two active hydroxyl groups at opposite positions was prepared by glaser cyclization using **PEO(5)** as precursor, which was carried out using CuBr/$CuBr_2$ as catalyst in pyridine at 50°C under high dilute conditions (Scheme 3). The column technique was a

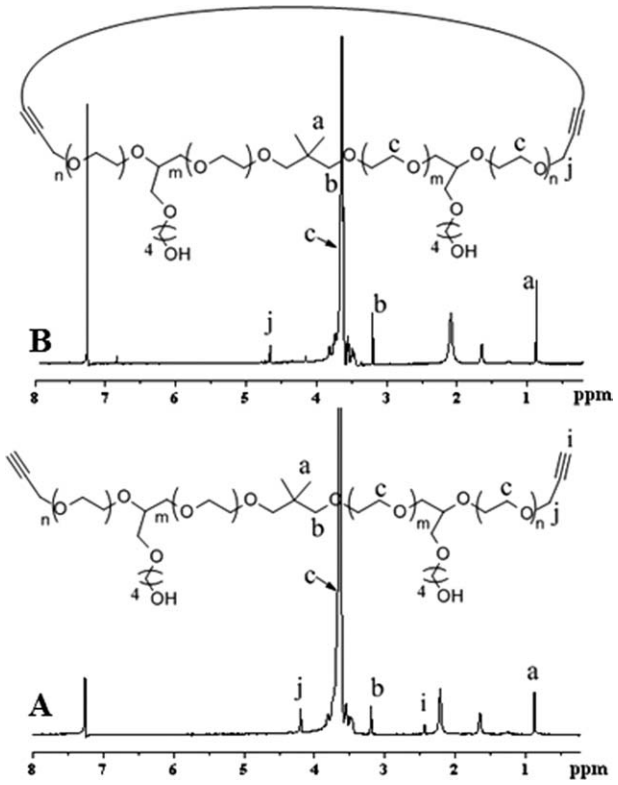
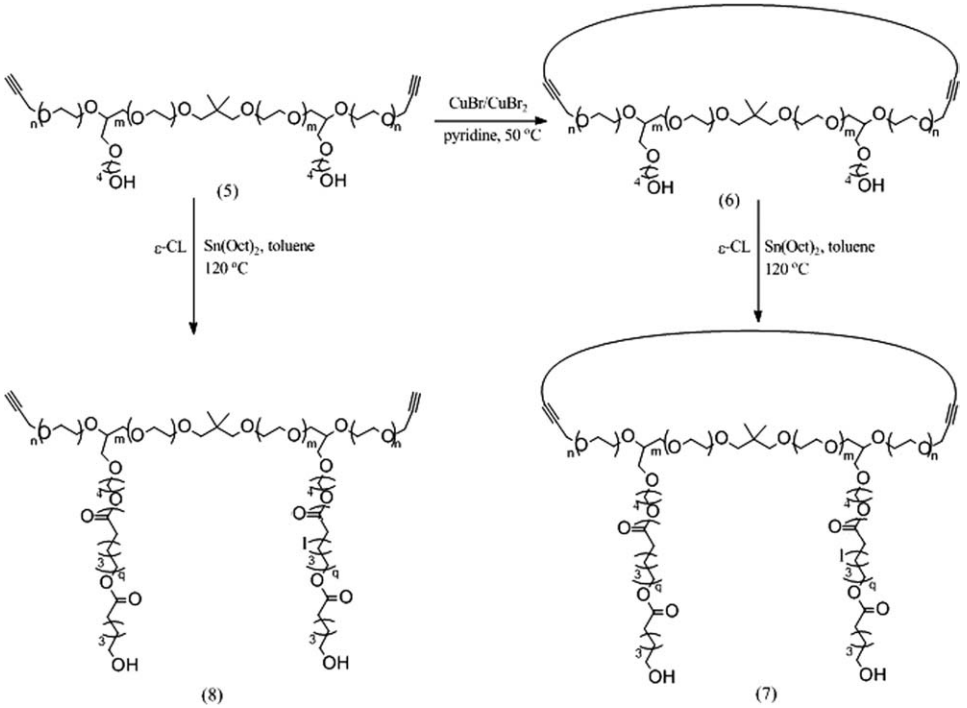


FIGURE 3 ^{1}H NMR spectra of **PEO(5a)** (A) and **PEO(6a)** (B).

conventional method to remove the copper complex, but the yield was rather low (<43%) owing to the strong interaction of PEO chain with the substrate.[23] Here, the copper salts were removed by reacting with Na_2S to form the deposits Cu_2S/CuS and the yield was significantly enhanced (>70%).

Figure 3(B) showed the ^{1}H NMR spectrum of cyclic **PEO(6a)**; it can be seen that the peak at 2.44 ppm (i) assigned to the alkynyl proton (—CH_2—C≡C***H***) on propargyl groups disappeared completely after cyclization. As shown in Figure 4, it can be seen that the GPC trace of **PEO(6a)** clearly shifted toward the lower molecular weight region, which can be attributed to its lower hydrodynamic volume compared to that of linear precursor **PEO(5a)**. Meanwhile, the <G> values, the ratio of the apparent peak molar masses of cyclic **PEO(6a)** to that of linear **PEO(5a)**, were about 0.89 and 0.91 (Table 1), which were coincident with the reported values.[24] The success of glaser cyclization was further verified by MALDI-TOF MS technique. As shown in Figure 5, the molecular weight of cyclic product **PEO(6a)** and the linear precursor **PEO(5a)** were rather close. Clearly, there was a decrease of about $m/z = 2.0$ from **PEO(5a)** to **PEO(6a)**, which corresponded to the weight of two hydrogen atoms. Based on these results, it can also be concluded that the cyclization was successful.

The target tadpole-shaped (***l*-PCL)-*b*-(*c*-PEO)-*b*-(*l*-PCL)(7)** was obtained by ROP of ε-CL monomers by using **PEO(6)** as macroinitiator. In Figure 4(C), the GPC trace of (***l*-PCL)-*b*-(*c*-PEO)-*b*-(*l*-PCL)(7a)** showed a monomodal peak in the higher molecular weight region, which confirmed the successful synthesis of the copolymers of (***l*-PCL)-*b*-(*c*-PEO)-*b*-(*l*-PCL)**. Figure 6 showed the ^{1}H NMR spectrum of copolymer (***l*-PCL)-*b*-(*c*-PEO)-*b*-(*l*-PCL)(7a)**, and the characteristic peaks at 4.06 ppm (r), 2.32 ppm (k), 1.40 ppm and 1.65



SCHEME 3 The synthetical route to (*l*-PCL)-*b*-(*c*-PEO)-*b*-(*l*-PCL) and (PEO/PCL)-*b*-PEO-*b*-(PCL/PEO).

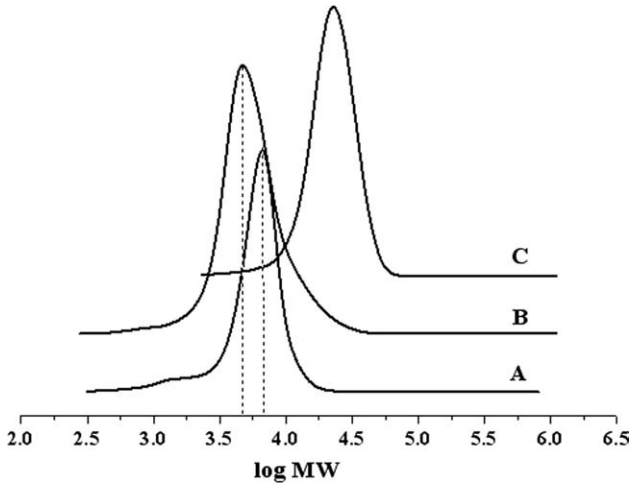


FIGURE 4 GPC traces of **PEO(5a)** (M_n = 4410 g/mol, M_w/M_n = 1.12) (A), **PEO(6a)** (M_n = 4180 g/mol, M_w/M_n =1.16) (B) and (***l*-PCL)-*b*-(*c*-PEO)-*b*-(*l*-PCL)(7a)** ($M_n = 1.59 \times 10^4$ g/mol, M_w/M_n = 1.21) (C).

ppm (l) attributed to protons on PCL segments can be discriminated clearly. Based on the relative integral area ratio of peaks at 4.06 ppm (r) to that at 0.88 ppm (a), assigned to the methylene protons (—COOC$\boldsymbol{H}_2$) on PCL main chain and methyl protons (—OCH$_2$C(C$\boldsymbol{H}_3$)$_2$CH$_2$O—) on initiator residual, respectively, the DP of PCL segments could be calculated by using the Formula 2:

$$\mathrm{DP_{PCL}} = \frac{A_r/2}{A_a/6} \quad (2)$$

where A_a and A_c were the integral areas of resonance signals at 0.88 ppm (a) and 4.06 ppm (r), respectively. The obtained DP_{PCL} for **(*l*-PCL)-*b*-(*c*-PEO)-*b*-(*l*-PCL)(7a)** and **(*l*-PCL)-*b*-(*c*-PEO)-*b*-(*l*-PCL)(7a)** were 80 and 124.

Self-Assembly of the Tadpole-Shaped (*l*-PCL)-*b*-(*c*-PEO)-*b*-(*l*-PCL) and π-shaped Analogs of (PEO/PCL)-*b*-PEO-*b*-(PCL/PEO)

As many other topological copolymers consisting of PEO hydrophilic segment and PCL hydrophobic segment, the amphiphilic branch-ring-branch tadpole-shaped copolymers of **(*l*-PCL)-*b*-(*c*-PEO)-*b*-(*l*-PCL)** should also be able to self-assemble to form the micelles in water. Figure 7(A,B) showed atomic force microscope (AFM) tapping mode height images of the micelles from **(*l*-PCL)-*b*-(*c*-PEO)-*b*-(*l*-PCL)**. The formed micelles were intertwined fibrils and the size of the fibrils increased with the increasing of PEO length. For comparison, the π-shaped copolymers of **(PEO/PCL)-*b*-PEO-*b*-(PEO/PCL)** with comparable molecular weight were synthesized from **PEO(5)** (Table 2) and the self-assembling behavior was also investigated. Figure 7(C,D) showed the images of the micelles from the π-shaped copolymers, which took a usual spherical look. The results indicated that the cyclic conformation might exhibit some effects on the self-assembly of **(*l*-PCL)-*b*-(*c*-PEO)-*b*-(*l*-PCL)**.

EXPERIMENTAL

Materials

2,2-Dimethyl-1,3-propanediol (Aldrich, 98%) was recrystallized from acetone/H_2O (v/v = 1:1) and dried at 50°C under vacuum. Ethylene oxide (EO, 98%, Sinopharm Chemical Reagent (SCR)) was dried by calcium hydride (CaH_2) for 48 h and then distilled under N_2 before use. Cuprous bromide (CuBr, 95%) was stirred overnight in acetic acid, filtered, washed with ethanol, and diethyl ether successively, and dried under vacuum. Cupric bromide (CuBr, >98.5, SCR), Sodium hydride (NaH, 60% dispersion in mineral oil, Aldrich) and *N,N,N′,N,"N"*-pentamethyldiethylenetriamine (99%, Aldrich) were used as received. Propargyl bromide (>99%), epichlorohydrin (99%, Aldrich), and ε-caprolactone (99%, Aldrich) were purified by distillation from CaH_2 under reduced pressure. Tetrahydrofuran (THF, 99%, SCR) was refluxed and distilled from potassium naphthalenide solution. Tin (II) *bis*(2-ethylhexanoate) ($Sn(Oct)_2$, 95%, Sigma) was dissolved in dried toluene (10 mg/mL). DPMK solution with concentration of 0.64 mol/L was prepared according to the literature.[25] 1-Ethoxyethyl-1,4-butylene glycol was synthesized from1,4-butylene glycol and ethyl vinyl ether according to the literature.[26]

Measurements

GPC analysis of PEO was performed in 0.1M $NaNO_3$ aqueous solution at 40°C with an elution rate of 0.5 mL/min on an Agilent 1100 equipped with a G1310A pump, a G1362A refractive index detector, and a G1315A diode-array detector. Three TSK-gel PW columns in series (bead size: 6, 13, and 13 μm; pore size: 200, >1000, and <100–1000 Å; molecular range: (0–5) × 10^4, 5 × 10^4–8 × 10^6, and (5–8) × 10^6 g/mol, respectively) were calibrated with PEO standard samples. GPC analysis of the rest of copolymers containing PEO and PCL segments was performed in THF at 35°C with an elution rate of 1.0 mL/min on an Agilent 1100 equipped with

TABLE 1 The Data of **PEO(5)** and **PEO(6)**

	PEO(5)				PEO(6)				
Entry	$M_{n,NMR}$ (g/mol)	$M_{n,GPC}$[a] (g/mol)	PDI[a]	Mp[a] (g/mol)	$M_{n,NMR}$ (g/mol)	$M_{n,GPC}$[a] (g/mol)	PDI[a]	M_p[a] (g/mol)	$<G>$[b]
A	4,690	4,410	1.12	5,340	4,720	4,180	1.16	4,730	0.89
B	8,380	7,820	1.07	8,680	8,450	6,400	1.13	7,890	0.91

[a] Determined by GPC using PEO as standard and 0.1 M aqueous $NaNO_3$ as eluent.
[b] The ratio of the apparent peak molar masses (M_p) derived from the GPC of cyclic **PEO(6)** to that of their linear precursors **PEO(5)**.

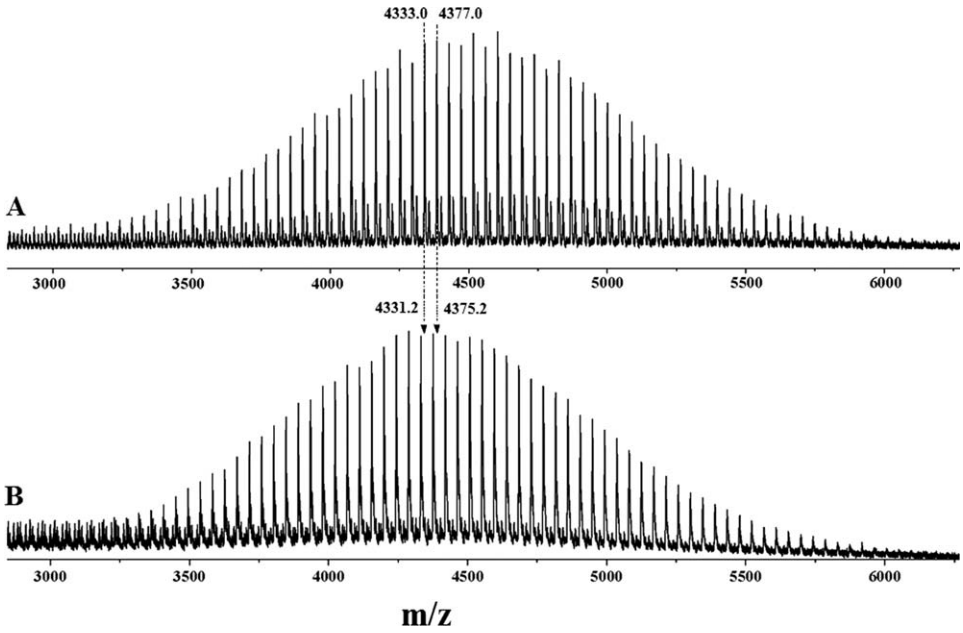


FIGURE 5 MALDI-TOF mass spectra of **PEO(5a)** (A) and **PEO(6a)** (B) with dithranol as matrix and sodium trifluoroacetate as cationizing salt.

a G1310A pump, a G1362A refractive index detector, and a G1314A variable wavelength detector. One 5 LP gel column (500 Å, molecular range 500–2 $\times$ 10^4 g/mol) and two 5-μm LP gel mixed bed column (molecular range, 200–3 $\times$ 10^6 g/mol) were calibrated by PS standard samples. ^{1}H NMR spectra were recorded on a Bruker (500 MHz) spectrometer in $CDCl_3$ with tetramethylsilane as the internal reference for chemical shifts. The AFM images were acquired in tapping mode by using a Nanoscope IV from Digital Instruments. For AFM observations, the samples were prepared by casting and drying the solution on freshly cleaved mica at room temperature. The matrix-assisted laser desorption ionization time-of-flight mass spectrometry (MALDI-TOF MS) measurement was performed using a Perspective Biosystem Voyager-DESTRMALDI-TOF MS (PEApplied Biosystems, Framingham, MA). Matrix solution of dithranol (20 mg/mL), polymer (10 mg/mL), and cationizing salt of sodium trifluoroacetate (10 mg/mL) in THF was mixed in the ratio of 10:4:2.

Synthesis of α,ω-Dihydroxy-PEO(1)

The **PEO(1)** was synthesized by ROP of EO monomers in THF using 2,2-dimethyl-1,3-propanediol and DPMK as coinitiator. The typical procedure was as follows: 2,2-dimethyl-1,3-propanediol (1.15 g, 10.8 mmol) dried by azeoptropic distillation with toluene was dissolved in 140 mL dried THF, then the solution was introduced into a 250-mL ampoule. The solution of DPMK in THF (10.1 mL, 6.48 mmol) was slowly added and the solution took turbid as the alkoxides were formed. Then, the monomers of EO (30.0 mL, 0.589 mol) were injected into the ampoule under N_2 atmosphere, and the reaction was carried out at 55°C for 48.0 h. After the reaction was terminated by acid methanol, the solution was concentrated and precipitated into an excess of diethyl ether for two times, and the product was under vacuum at 40°C to a constant weight for **PEO(1)**. (**PEO(1a)**: $M_{n,GPC}$ = 2100 g/mol, M_w/M_n = 1.08; $M_{n,NMR}$ = 1940 g/mol. **PEO(1b)**: $M_{n,GPC}$ = 4380 g/mol, M_w/M_n = 1.11; $M_{n,NMR}$ = 4200 g/mol).

Synthesis of α,ω-Diepoxy-PEO (2)

For the **PEO(2),** the typical procedure was as follows: **PEO(1)** (15.0 g, 7.73 mmol) dried by azeotropic distillation with toluene was dissolved in 120 mL dried THF, and NaH (3.10 g, 77.3 mmol) was added into the solution. The mixture was stirred at room temperature for 2.0 h. Then, epichlorohydrin (6.1 mL, 77.3 mmol) was added and the

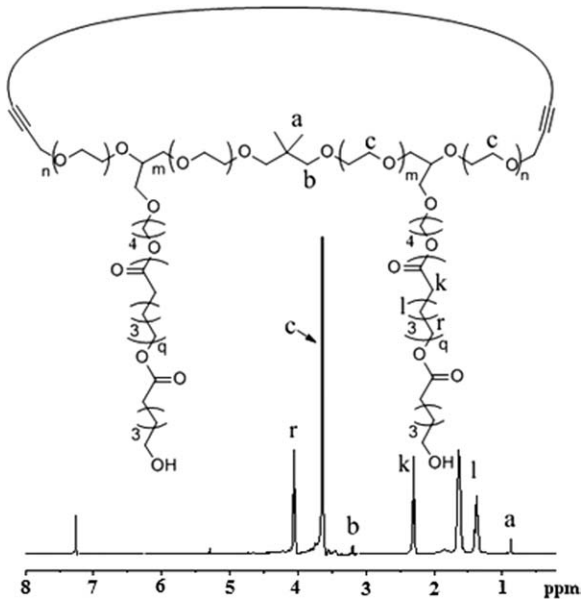


FIGURE 6 ^{1}H NMR spectrum of (*l*-PCL)-*b*-(*c*-PEO)-*b*-(*l*-PCL)(7a).

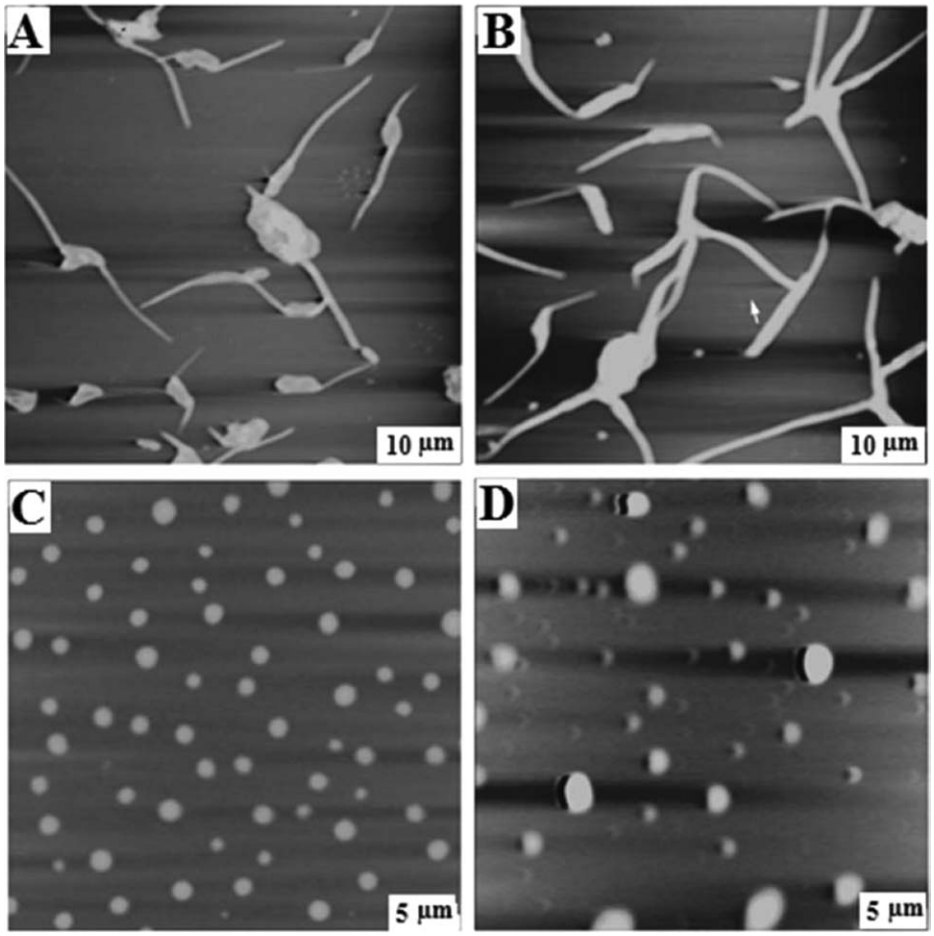


FIGURE 7 AFM images of tadpole-shaped **(*l*-PCL)-*b*-(*c*-PEO)-*b*-(*l*-PCL)(7a)** (A), **(*l*-PCL)-*b*-(*c*-PEO)-*b*-(*l*-PCL)(7b)** (B) and their π-shaped analogs with comparable molecular **(PEO/PCL)-*b*-PEO-*b*-(PCL/PEO)(8a)** (C), **(PEO/PCL)-*b*-PEO-*b*-(PCL/PEO)(8b)** (D) on the surface of mica.

mixture was stirred for additional 6.0 h. The residual NaH was neutralized by adding a few drops of deionized water under rapidly stirring. After removing the THF solvent under reduced pressure, the residual was dissolved again with CH_2Cl_2 and washed with water. The organic layer was dried with $MgSO_4$, filtered, concentrated, and precipitated in diethyl ether for three times, and the product was dried under vacuum at 40°C to a constant weight for **PEO(2)**.

Synthesis of α, α'-(1-Ethoxyethoxy *n*-butyl), hydroxy-ω,ω'-(1-ethoxyethoxy *n*-butyl), hydroxyl-PEO(3)

For the **PEO(3),** the typical procedure was as follows: 1-ethoxyethyl-1,4-butylene glycol (47.5 g, 0.293 mol) was dissolved in 100 mL dried THF, then potassium metal (2.86 g, 73.3 mmol) with fresh surface was added. Under N_2 atmosphere, the reaction mixture was stirred overnight at 50°C to obtain potassium 1-ethoxyethyl-1,4-butylene glycoxide. The solution of **PEO(2)** (7.51 g, 3.66 mmol) in 60 mL dried THF was added dropwise to the above system over 6.0 h, then the reaction was continued for another 24.0 h. After the alkoxides were deactivated by adding deionized water, the THF solvent was evaporated, and the residual was extracted with CH_2Cl_2. The organic layer was dried with $MgSO_4$, filtered, concentrated, and precipitated into diethyl ether for three times, and the product was dried under vacuum at 40°C to a constant weight for **PEO(3)**.

Synthesis of α,ω-Dihydroxy-PEO with two Interior Protected Hydroxyl Groups [PEO (4)]

The **PEO(4)** was synthesized by using the active hydroxyl groups on **PEO(3)** to initiate the ROP of EO monomers. The typical procedure was as follows: **PEO(3)** (4.70 g, 1.98 mmol) dried by azeoptropic distillation with toluene was dissolved in 80 mL dried THF. After the solution was introduced into an ampoule, DPMK (6.0 mL, 3.60 mmol) and EO

TABLE 2 The Data of **(*l*-PCL)-*b*-(*c*-PEO)-*b*-(*l*-PCL)(7)** and Their π-Shaped Analogs of **(PEO/PCL)-*b*-PEO-*b*-(PCL/PEO)(8)**

	^{1}H NMR[a]	GPC[b]	
Samples	M_n (g/mol)	M_n (g/mol)	M_n/M_w
7a	13,800	15,900	1.21
7b	22,600	25,100	1.40
8a	12,400	14,500	1.32
8b	19,600	21,000	1.21

[a] Determined by ^{1}H NMR.
[b] Determined by GPC using PS as standard and THF as eluent.

(6.0 mL, 0.118 mmol) were injected into the ampoule under N_2 atomsphere successively. The reaction lasted for 48.0 h at 55°C and was terminated by acid methanol. The solution was concentrated and precipitated into an excess of diethyl ether for two times, and the product was dried under vacuum at 40°C to a constant weight for **PEO(4)**. (**PEO(4a)**: $M_{n,GPC}$ = 5010 g/mol, M_w/M_n = 1.10; $M_{n,NMR}$ = 4800 g/mol. **PEO(4b)**: $M_{n,GPC}$ = 9190 g/mol, M_w/M_n = 1.05; $M_{n,NMR}$ = 8460 g/mol).

Synthesis of α,ω-Dialkyne-PEO with two Interior Active Hydroxyl Groups [PEO(5)]

For the **PEO(5),** the typical procedure was as follows: **PEO(4)** (7.26 g, 1.51 mmol) dried by azeotropic distillation with toluene was dissolved in 100 mL dried THF. After NaH (1.20 g, 30.0 mmol) was added to the solution, the mixture was stirred at room temperature for 2.0 h. Then, propargyl bromide (2.7 mL, 30.0 mmol) was added and the mixture was stirred for another 6.0 h. After the residual NaH was neutralized by adding a few drops of deionized water under rapidly stirring, the solution was adjusted to be acidic by adding the hydrochloric solution to remove the acetal protective groups. After 3.0 h, the solvent was removed under reduced pressure, and the residual was dissolved with water and extracted with CH_2Cl_2. The organic layer was dried with $MgSO_4$, filtered, concentrated, and precipitated into diethyl ether for three times for **PEO(5)**. (**PEO(5a)**: $M_{n,GPC}$ = 4410 g/mol, M_w/M_n = 1.12; $M_{n,NMR}$ = 4690 g/mol; **PEO(5b)**: $M_{n,GPC}$ = 7820 g/mol, M_w/M_n = 1.07; $M_{n,NMR}$ = 8380 g/mol).

Synthesis of Cyclic PEO with two Active Hydroxyl Groups at Opposite Positions [PEO(6)]

For the **PEO(5)**, the typical procedure was as follows: to a 1.0-L round-bottomed flask was added pyridine (700 mL), CuBr (1.39 g, 9.71 mmol), and $CuBr_2$ (0.443 g, 1.98 mmol). In a separate 150-mL flask, **PEO(5)** (0.410 g, 8.54 × 10–5 mol) was dissolved in 100 mL pyridine. Under vigorous stirring, the solution of **PEO(5)** was slowly added into the 1.0-L flask (heated to 50°C) via a peristaltic pump at a rate of 1.4 mL/h. After the addition was finished, the reaction mixture was allowed to stir for another 6.0 h. The solvent was evaporated under reduced pressure and the residual was dissolved with water. To remove the copper complex, Na_2S was added to form the Cu_2S/CuS precipitate. After centrifugation, the solution was extracted with CH_2Cl_2 (2 × 200 mL). The organic layer was dried with $MgSO_4$, filtered, concentrated, and precipitated in diethyl ether for two times, and the product was dried under vacuum at 40°C to a constant weight for **PEO(6)**. (**PEO(6a)**: $M_{n,GPC}$ = 4180 g/mol, M_w/M_n = 1.16; $M_{n,NMR}$ = 4720 g/mol. **PEO(6b)**: $M_{n,GPC}$ = 6400 g/mol, M_w/M_n = 1.13; $M_{n,NMR}$ = 8450 g/mol).

Synthesis of Tadpole-shaped (*l*-PCL)-*b*-(*c*-PEO)-*b*-(*l*-PCL)(7) and π-Shaped (PEO/PCL)-*b*-PEO-*b*-(PCL/PEO)(8)

For the (***l*-PCL)-*b*-(*c*-PEO)-*b*-(*l*-PCL)(7)**, in a typical procedure, dried **PEO(6)** (0.300 g, 6.25 × 10^{-5} mol), freshly distilled ε-CL monomers (0.340 g, 2.98 mmol), and the $Sn(Oct)_2$ solution in toluene (2.5 mL, 6.25 × 10^{-5} mol) were added into 100-mL ampoule. The polymerization was performed at 110°C for 12.0 h. The product was precipitated into petroleum ether and dried under vacuum 40°C to a constant weight. ((***l*-PCL)-*b*-(*c*-PEO)-*b*-(*l*-PCL)(7a)**: $M_{n,GPC}$ = 15,900 g/mol, M_w/M_n = 1.21; $M_{n,NMR}$ = 13,800 g/mol. (***l*-PCL)-*b*-(*c*-PEO)-*b*-(*l*-PCL)(7b)**: $M_{n,GPC}$ = 25,100 g/mol, M_w/M_n = 1.40; $M_{n,NMR}$ = 22,600 g/mol).

For the π-shaped **(PEO/PCL)-*b*-PEO-*b*-(PCL/PEO)(8)**, the procedure was in a similar way using **PEO(5)** as macrointiators. **(PEO/PCL)-*b*-PEO-*b*-(PCL/PEO)(8a)**: $M_{n,GPC}$ = 14,500 g/mol, M_w/M_n = 1.32; $M_{n,NMR}$ = 12,400 g/mol. **(PEO/PCL)-*b*-PEO-*b*-(PCL/PEO)(8b)**: $M_{n,GPC}$ = 21,000 g/mol, M_w/M_n = 1.21; $M_{n,NMR}$ = 19,600 g/mol).

Self-Assembly of the Copolymers (*l*-PCL)-*b*-(*c*-PEO)-*b*-(*l*-PCL)(7) and (PEO/PCL)-*b*-PEO-*b*-(PCL/PEO)(8)

Using (***l*-PCL)-*b*-(*c*-PEO)-*b*-(*l*-PCL)(7a)** as a typical example: 25.0 mg of the polymer was dissolved in 10 mL DMF, and 10 mL deionized water was slowly added to the DMF solution at a rate of one drop every 15 s via a microsyringe under rapid stirring. Then, the solution was dialyzed against deionized water using a dialysis bag (M_w cutoff, 14 kDa). After 2 days, the micelle solution was transferred into a 25-mL flask, and deionized water was added to make the concentration to be 1.0 mg/mL.

CONCLUSIONS

A novel amphiphilic branch-ring-branch tadpole-shaped (*l*-PCL)-*b*-(*c*-PEO)-*b*-(*l*-PCL) was synthesized by combination of glaser coupling reaction with ROP mechanism. The self-assembling behaviors of (*l*-PCL)-*b*-(*c*-PEO)-*b*-(*l*-PCL) in water were investigated and compared with that of π-shaped analogs (PEO/PCL)-*b*-PEO-*b*-(PCL/PEO) with comparable molecular weight. The results preliminarily showed that the topology might exert some effect on the properties of copolymers.

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