# Synthesis of Amphiphilic Heteroeight-Shaped Polymer *Cyclic*-[Poly(ethylene oxide)-*b*-polystyrene]₂ via "Click" Chemistry

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ABSTRACT: An amphiphilic heteroeight-shaped polymer *cyclic*-[poly(ethylene oxide)-*b*-polystyrene]₂ ([*c*-(PEO-*b*-PS)]₂) composed of hydrophilic PEO and hydrophobic PS blocks was synthesized by combination of "click" chemistry with anionic ring-opening polymerization (ROP) and atom transfer radical polymerization (ATRP) mechanisms. According to "core-first" strategy, the A₂B₂ star-shaped precursor (PEO-alkyne)₂-(PS-N₃)₂ was obtained by successive ROP of EO monomer, ATRP of St monomer, and modification of functional groups. Under high dilution condition, the intramolecular cyclization of (PEO-alkyne)₂-(PS-N₃)₂ by "click" chemistry produced the amphiphilic heteroeight-shaped polymer [*c*-(PEO-*b*-PS)]₂. The target copolymers and intermediates were well characterized by GPC, MALDI-TOF MS, ¹H NMR, and FT-IR. The self-assembly behavior of [*c*-(PEO-*b*-PS)]₂ and its precursor of (PEO-alkyne)₂-(PS-N₃)₂ were investigated and compared by transmission electron microscopy (TEM) and dynamic light scattering (DLS). In both cases, the spherical micelles were observed, however, the size of formed micelles increased from a star-shaped to a cyclic topology.
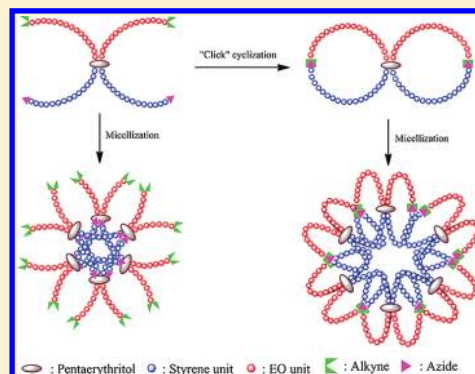
■ INTRODUCTION

Compared with their linear analogues, cyclic polymers exhibit significant different physical properties in both solution and bulk due to their unique topology.[1−6] Most recently, cyclic polymers have attracted increasing interest from polymer chemists, and a wide range of cyclic polymers have been synthesized in good yields including single cyclic polymers[7−11] and complex polymers using cyclic polymers as building block such as sun-shaped,[12−15] tadpole-shaped,[16−19] and eight-shaped.[20−27] These polymers have served as novel models for understanding the relationship between architectures and properties, and unique topologies might endow them special properties and applications.

Among them, the eight-shaped polymer was a kind of complex polymer, in which two cycles as building blocks were connected with one site. Until recently, a few eight-shaped polymers with various compositions have been synthesized.[20−26] Based on their compositions, the eight-shaped polymers could be basically classified into two types: homoeight-shaped polymer (composed of the same blocks) and heteroeight-shaped polymer (composed of the different blocks). For example, Deffieux et al. synthesized homoeight-shaped poly(chloroethyl vinyl ether) (PCEVE) by the reaction between acetal and styrenyl groups.[20] Tezuka et al. synthesized homoeight-shaped poly(tetrahydrofuran) (PTHF) and polystyrene (PS) through the "electrostatic self-assembly and covalent fixation" process.[22,23] Pan et al. synthesized homoeight-shaped PS and heteroeight-shaped polymers composed of PS and poly(ε-caprolactone) (PCL) blocks through the "click" chemistry.[25] Very recently, Wang et al. synthesized homoeight-shaped poly(ethylene oxide) (PEO) by combination of Glaser coupling with anionic ring-opening polymerization (ROP).[26] However, among these polymers reported, most of them belonged

to homoeight-shaped, and the heteroeight-shaped polymers were rather rare due to the synthetic difficulties. Especially, up to now, no amphiphilic heteroeight-shaped polymers have been obtained, such as an amphiphilic one composed of PEO and PS blocks.

Usually, the amphiphilic polymers, those composed of hydrophilic PEO block, have been used as models to study the microphase separation in bulk and self-assembling behavior in solution because of the nonionic and highly crystalline nature of PEO. Various of polymers consisting PEO block have been successfully synthesized, including the linear,[27,28] star-shaped,[29,30] and graft-shaped[31,32] polymers, in which the PEO block was typically introduced by direct and simple ROP of EO monomer or coupling reactions using a monofunctional PEO. Similarly, a library of monocycle PEOs have also been realized.[1,2] However, concerning the selective introduction of a PEO block into a heteroeight-shaped polymer, there was still some difficulties in selecting a functional initiator for ROP of EO monomer as well as screening a heterofunctional PEO for coupling methods. That was, the synthesis of a cyclic polymer contained PEO block was still a challenge work for researchers as well as the study of morphologies of copolymers in solution was also restricted. Until recently, Tezuka et al. opened the door to investigate the effect of topology on self-assembly of amphiphilic cyclic block copolymer and its linear counterpart,[35] in which the copolymers of linear poly(butyl acrylate)-*b*-poly(ethylene oxide)-*b*-poly(butyl acrylate) (*l*-(PBA-*b*-PEO-*b*-PBA)) and cyclized poly(butyl acrylate)-*b*-poly(ethylene oxide) (*c*-(PBA-*b*-PEO))

Scheme 1. Synthetical Route of Amphiphilic Heteroeight-Shaped Polymer [c-(PEO-b-PS)]₂
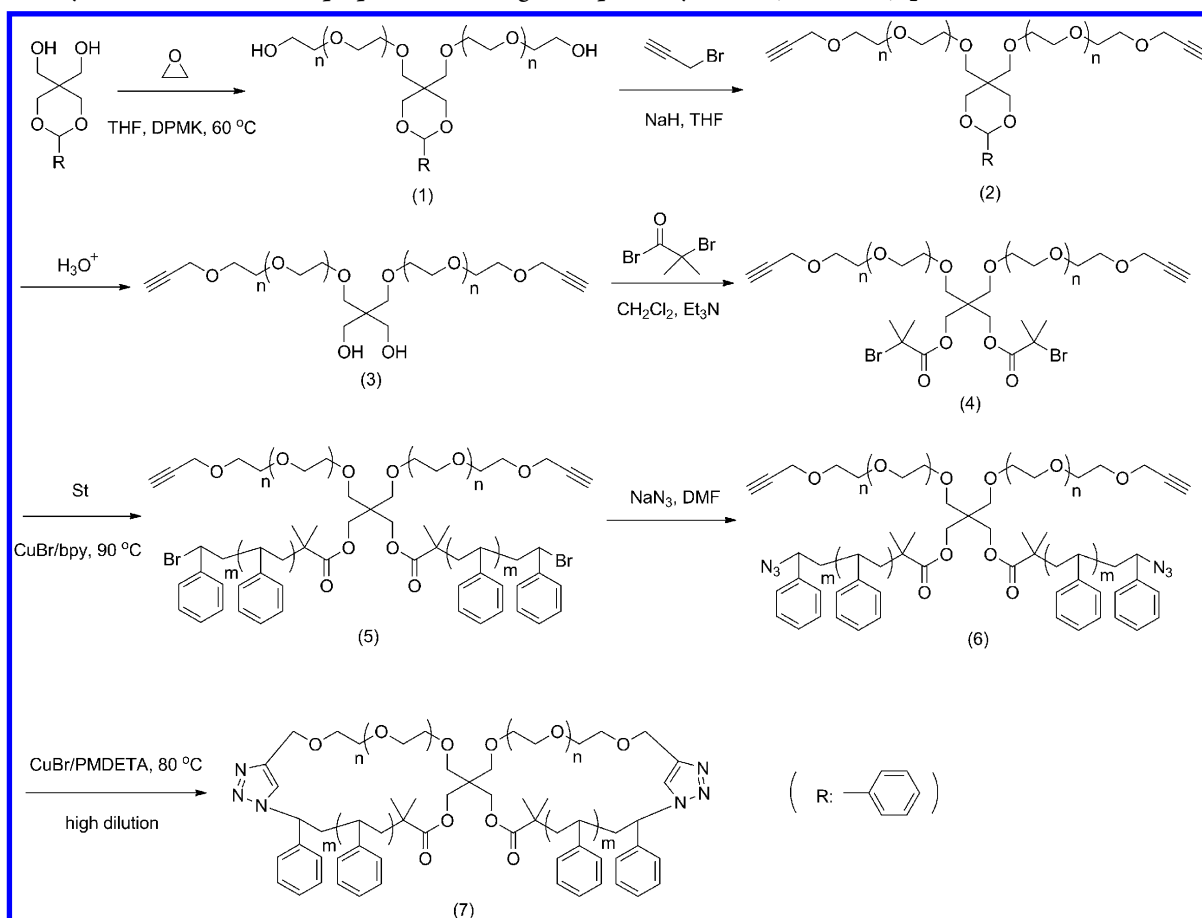
were used as models. Their results showed that the cloud point (T_c) was remarkably elevated by more than 40 °C through the linear-to-cyclic topological conversion of the copolymer.

Herein, from an initiator contained two active and two protected hydroxyl groups, a novel heteroeight-shaped polymer [c-(PEO-b-PS)]₂ was obtained by intramolecular cyclization of "click" chemistry using an amphiphilic A₂B₂ star-shaped polymer (PEO-alkyne)₂-(PS-N₃)₂ as precursor, which was prepared by successive ROP and atom transfer radical polymerization (ATRP) mechanisms (Scheme 1). Moreover, the self-assembly behavior of [c-(PEO-b-PS)]₂ and its precursor of (PEO-alkyne)₂-(PS-N₃)₂ were preliminarily investigated and compared.

■ EXPERIMENTAL SECTION

Materials. Pentaerythritol (98%, Aldrich) was dried at 50 °C under vacuum. Ethylene oxide (EO, 98%, Sinopharm Chemical Reagent Co., Ltd. (SCR)) was dried by calcium hydride (CaH₂) for 48 h and then distilled under N₂ before use. Styrene (St, >99.5%, SCR) was washed with 10% NaOH aqueous solution and water three times successively, then dried over CaH₂, and distilled under reduced pressure. Copper(I) bromide (CuBr, 95%, SCR) was stirred overnight in acetic acid, filtered, washed with ethanol and diethyl ether successively, and dried in vacuum. Sodium hydride (NaH, 60% dispersion in mineral oil, Aldrich), N,N,N′,N″,N″-pentamethyldiethylenetriamine (PMDETA, 99%, Aldrich), N,N-dimethylformamide (DMF, AR, SCR), triethylamine (TEA, AR, SCR), 2-bromoisobutyryl bromide (98%, Aldrich), 2,2′-bipyridine (bpy, 99%, Aldrich), ethylenediaminetetracetic acid disodium salt (EDTA, AR, SCR), and sodium azide (NaN₃, 98%, SCR) were used as received. Propargyl bromide (>99%, Aldrich) was purified by distillation from CaH₂ under reduced pressure. THF

(99%, SCR) was refluxed and distilled from potassium naphthalenide solution. Diphenylmethylpotassium (DPMK) solution with concentration of 0.64 mol/L was prepared according to the literature.[33] 2-Phenyl-5,5-bis(hydroxymethyl)-1,3-dioxane was synthesized according to the literature.[34]

Measurements. Gel permeation chromatographic (GPC) analysis of PEO was performed in 0.1 M NaNO₃ 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 × 10⁴, 5 × 10⁴−8 × 10⁶, and (5−8) × 10⁶ g/mol, respectively) were calibrated with PEO standard samples. GPC analysis of the rest copolymers composed of PEO and PCL blocks were performed in THF at 35 °C with an elution rate of 1.0 mL/min on an Agilent 1100 equipped with 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 × 10⁴ g/mol) and two 5 μm LP gel mixed bed column (molecular range 200−3 × 10⁶ g/mol) were calibrated by PS standard samples. ¹H NMR spectra were recorded on a Bruker (500 MHz) spectrometer in CDCl₃ with tetramethylsilane (TMS) as the internal reference for chemical shifts. The matrix-assisted laser desorption ionization time-of-flight mass spectrometry (MALDI-TOF MS) measurement was performed using a Perspective Biosystem Voyager-DESTRMALDI-TOFMS (PEApplied Biosystems, Framingham, MA). A matrix solution of dithranol (20 mg/mL), polymer (10 mg/mL), and cationizing salt of sodium trifluoroacetate (10 mg/mL) in THF were mixed in the ratio of 10:4:2. Fourier transform infrared (FT-IR) spectra were recorded on a NEXUS 470 FT-IR instrument, and the polymer solution was cast on a NaCl disk to form the film. The size of the micelles was measured by dynamic light scattering (DLS) using an Malvern Zetasizer Nano ZS.

The products were visualized using a JEOL 1230 transmission electron microscope (TEM).

Synthesis of Poly(ethylene oxide) with Two Protected Hydroxyl Groups at the Chain Middle (PEO (1)) (Scheme 1). The PEO (**1**) was synthesized by ROP of EO monomer. The typical procedure was as follows: the initiator of 2-phenyl-5,5-bis-(hydroxymethyl)-1,3-dioxane (1.31 g, 5.85 mmol) dried by azeotropic distillation with toluene was dissolved in 140 mL of dried THF, and the solution was introduced into a 250 mL ampule. Then, the solution of DPMK in THF (7.7 mL, 5.85 mmol) was slowly added and the solution took turbid as the alkoxides were formed, and EO (30.0 mL, 0.589 mol) was injected into the ampule under nitrogen. After the reaction was carried out at 55 °C for 48 h, 2.0 mL of methanol was added to terminate the polymerization. Finally, the solution was concentrated and precipitated into an excess of diethyl ether for two times. ^{1}H NMR (CCl$_3$D, δ): 3.43–3.62 ppm (m, $-(CH_2CH_2O)_n-$), 5.40 ppm (s, C_6H_5CH), 7.34–7.46 ppm (m, 5H, C_6H_5). PEO (**1a**): $M_{n,NMR}$ = 3900 g/mol; $M_{n,GPC}$ = 3080 g/mol, PDI = 1.09; PEO (**1b**): $M_{n,NMR}$ = 7640 g/mol; $M_{n,GPC}$ = 6340 g/mol, PDI = 1.08.

Synthesis of α,ω-Dialkyne-poly(ethylene oxide) with Two Hydroxyl Groups at the Chain Middle (PEO (3)) (Scheme 1). For PEO (**3**), the α,ω-dialkyne-poly(ethylene oxide) with two protected hydroxyl groups at the chain middle (PEO (**2**)) was first obtained. The PEO (**1**) (3.51 g, 1.14 mmol) dried by azeotropic distillation with toluene was dissolved in 100 mL of dried THF, and NaH (1.88 g, 22.8 mmol) was added to the solution. After the mixture was stirred for 2 h, propargyl bromide (4.2 mL, 22.8 mmol) was added, and the mixture was stirred at room temperature overnight. The residual NaH was neutralized by adding a few drops of deionized water under rapid stirring. After the mixture was extracted with CH$_2$Cl$_2$, dried with MgSO$_4$, and concentrated under reduced pressure, the products of PEO (**2**) was obtained by precipitating into diethyl ether for three times.

Then, the PEO (**3**) was obtained by removal of the acetal protective groups on PEO (**2**). The PEO (**2**) was dissolved in THF and was adjusted to be acidic by adding 37% HCl (2.5 mL, 30 mmol) and stirred for 2 h at the room temperature. The purification procedure of PEO (**3**) was similar to that of PEO (**2**). ^{1}H NMR (CCl$_3$D, δ): 2.44 ppm (s, $HC{\equiv}CCH_2-$), 3.43–3.62 ppm (m, $-(CH_2CH_2O)_n-$), 4.20 ppm (s, $HC{\equiv}CCH_2-$).

Synthesis of α,ω-Dialkyne–Poly(ethylene oxide) with Two 2-Bromoisobutyryl Groups at the Chain Middle (PEO (4)) (Scheme 1). The macroinitiator PEO (**4**) was obtained by esterification of deprotected hydroxyl groups on PEO (**3**) with 2-bromoisobutyryl bromide. First, PEO (**3**) (1.80 g, 0.462 mmol) dried by azeotropic distillation with toluene was dissolved in 30 mL of dried CH$_2$Cl$_2$, and TEA (1.28 mL, 4.62 mmol) was added. Then, 2-bromoisobutyryl bromide (1.12 mL, 4.62 mmol) was added dropwise over 30 min with vigorous stirring in ice bath, and the mixture was continuously stirred overnight at room temperature. The purification procedure of PEO (**4**) was similar to that of PEO (**2**). ^{1}H NMR (CCl$_3$D, δ): 1.88 ppm (s, $-OCOC(CH_3)_2Br$), 2.44 ppm (s, $HC{\equiv}CCH_2-$), 3.43–3.62 ppm (m, $-(CH_2CH_2O)_n-$), 4.18–4.20 ppm (m, $-CH_2OCO-$, $HC{\equiv}CCH_2-$).

Synthesis of A$_2$B$_2$ Star-Shaped Copolymers (PEO-Alkyne)$_2$-(PS-N$_3$)$_2$ (6) (Scheme 1). For A$_2$B$_2$ star-shaped polymer (PEO-alkyne)$_2$-(PS-N$_3$)$_2$ (**6**), (PEO-alkyne)$_2$-(PS-Br)$_2$ (**5**) was first obtained by ATRP of St monomer from the macroinitiator PEO (**4**). Typically, PEO (**4**) (0.500 g, 0.119 mmol), St (7.0 mL), and Bpy (75.0 mg, 0.476 mmol) were added into a 100 mL ampule and degassed by three freeze–pump–thaw cycles. Then, CuBr (68.5 mg 0.238 mmol) was added into the system under nitrogen as fast as possible, followed by another three freeze–pump–thaw cycles. Sealed under nitrogen, the ampule was immersed into an oil bath preheated to 90 °C for 3.5 h and then dipped into liquid nitrogen to stop the polymerization. The reaction mixture was diluted with a large excess of CH$_2$Cl$_2$ and washed with the aqueous solution of EDTA and water successively. The organic layer was dried with MgSO$_4$, concentrated under reduced pressure, and precipitated into petroleum ether for two times for polymer (PEO-alkyne)$_2$-(PS-Br)$_2$ (**5**).

During the transformation of terminal bromide groups into azide groups, the (PEO-alkyne)$_2$-(PS-Br)$_2$ dissolved in DMF, NaN$_3$ (0.30 g, 4.62 mmol) was added into a 250 mL round-bottom flask and the reaction was carried out at 50 °C for 24 h. The reaction mixture was diluted with CH$_2$Cl$_2$ and washed with water for two times to remove DMF and the excessive NaN$_3$. The polymer (PEO-alkyne)$_2$-(PS-N$_3$)$_2$ (**6**) was obtained by precipitating into petroleum ether for two times. ^{1}H NMR (CCl$_3$D, δ): 1.25–2.11 ppm (m, $-CH_2CH(C_6H_5)-$, $-OCOC(CH_3)_2-$), 2.44 ppm (s, $HC{\equiv}CCH_2-$), 3.43–3.62 ppm (m, $-(CH_2CH_2O)_n-$), 4.20 ppm (s, $HC{\equiv}CCH_2-$), 6.27–7.27 ppm (m, $-CH_2CH(C_6H_5)-$).

Synthesis of Amphiphilic Heteroeight-Shaped Copolymers [c-(PEO-b-PS)]$_2$ (7) (Scheme 1). Typically, DMF (300 mL), Cu(I)Br (0.300 g, 2.10 mmol), and PMDETA (0.44 mL, 2.10 mmol) was added into a 500 mL round-bottom flask and degassed with 99.99% nitrogen flow for 0.5 h. In a separate 100 mL round-bottom flask, the polymer (PEO-alkyne)$_2$-(PS-N$_3$)$_2$ (**6**) (0.25 g, 0.0210 mmol) dissolved in 80.0 mL of DMF was degassed by a similar way above. Under vigorous stirring and protection of nitrogen flow, the solution of (PEO-alkyne)$_2$-(PS-N$_3$)$_2$ (**6**) was slowly added into that of CuBr/PMDETA (heated to 90 °C) by a peristaltic pump at a rate of 2 drop/min. After the addition was finished, the reaction mixture was stirred for another 4 h, and the DMF was removed under reduced pressure. And the purification procedure of [c-(PEO-b-PS)]$_2$ (**7**) was similar to that of (PEO-alkyne)$_2$-(PS-Br)$_2$ (**5**). ^{1}H NMR (CCl$_3$D, δ): 1.25–2.11 ppm (m, $-CH_2CH(C_6H_5)-$, $-OCOC(CH_3)_2-$), 3.43–3.62 ppm (m, $-(CH_2CH_2O)_n-$), 6.27–7.27 ppm (m, $-CH_2CH(C_6H_5)-$), 7.52 ppm (s, triazole ring proton).

Self-assembly Behavior of Copolymers [c-(PEO-b-PS)]$_2$ and (PEO-Alkyne)$_2$-(PS-N$_3$)$_2$. The micelles were prepared by adding the solution of the copolymers in good solvent slowly into the selective solvent. In a typical procedure, 2.0 mg of [c-(PEO-b-PS)]$_2$ or (PEO-alkyne)$_2$-(PS-N$_3$)$_2$ copolymers was dissolved in 2.0 mL of THF, and then the solution was added into 20.0 mL of deionized water slowly via a microsyringe under rapid stirring. Then the THF was evaporated under reduced pressure, and the final concentration of the aggregate suspension was 1.0 mg/mL. The formed micelles were observed by a JEOL 1230 transmission electron microscope (TEM).

RESULTS AND DISCUSSION

The synthetic procedure for amphiphilic heteroeight-shaped polymer composed of PEO and PS blocks was presented in Scheme 1: (1) synthesis of macroinitiator PEO (**4**) with two 2-bromoisobutyryl groups at the chain middle and two alkyne groups at the chain terminal by ROP mechanism and transformation of functional groups from the initiator with two active and two protected hydroxyl groups, (2) synthesis of A$_2$B$_2$ star-shaped (PEO-alkyne)$_2$-(PS-N$_3$)$_2$ by ATRP mechanism and azidation of bromide groups, and (3) synthesis of [c-(PEO-b-PS)]$_2$ by intramolecular cyclization of "click" chemistry.

Synthesis and Characterization of Macroinitiator PEO (4) with Two 2-Bromoisobutyryl Groups at the Chain Middle and Two Alkyne Groups at the Chain Terminal. First, by changing the molar ratio of EO monomers to initiator, two well-defined α,ω-dihydroxyl-poly(ethylene oxide) with two protected hydroxyl groups at the chain middle (PEO (**1**)) were synthesized by ROP of EO monomers using 2-phenyl-5,5-bis(hydroxymethyl)-1,3-dioxane as initiator and DPMK as co-initiator. In a typical ^{1}H NMR spectrum for PEO (**1a**) (Figure 1A), the resonance signals at 7.34 and 7.49 ppm (a) were assigned to phenyl-ring protons (C_6H_5CH-$(OCH_2-)_2$) and that at 5.40 ppm (b) was assigned to methine proton ($C_6H_5CH(OCH_2-)_2$) of protective group, and the signals at 3.43–3.64 ppm (c) were assigned to methylene protons ($-CH_2CH_2O-$) of EO units. The molecular weights of PEO (**1**) ($M_{n,NMR,PEO(1)}$) were derived by ^{1}H NMR spectra according to formula 1:
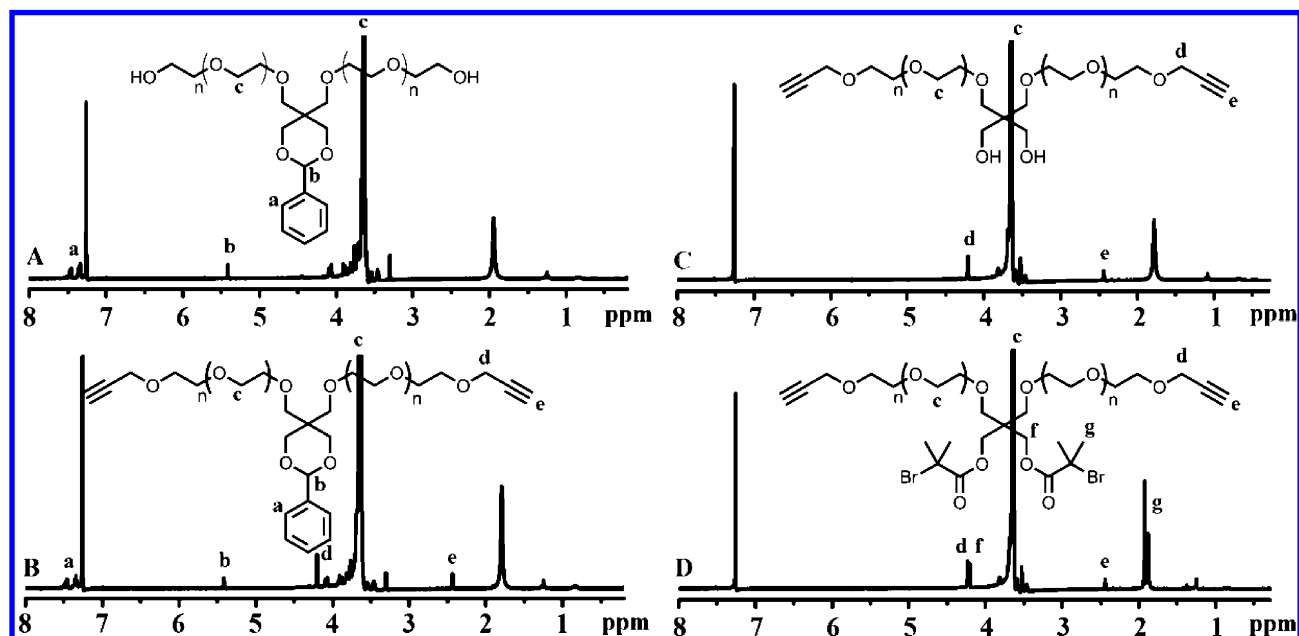
Figure 1. ¹H NMR spectra of PEO (**1a**) (A), PEO (**2a**) (B), PEO (**3a**) (C), and PEO (**4a**) (D) in CDCl₃.
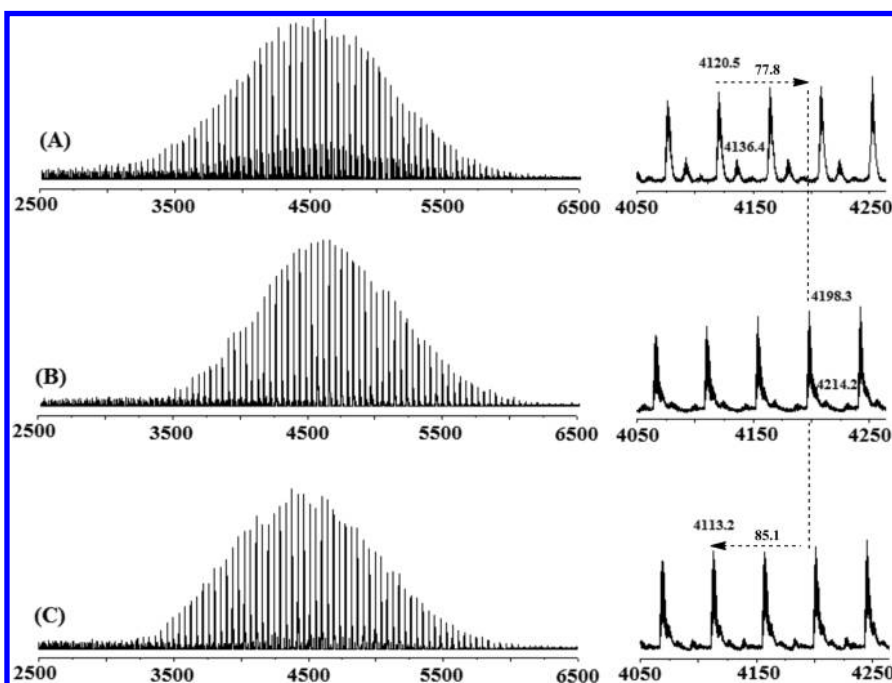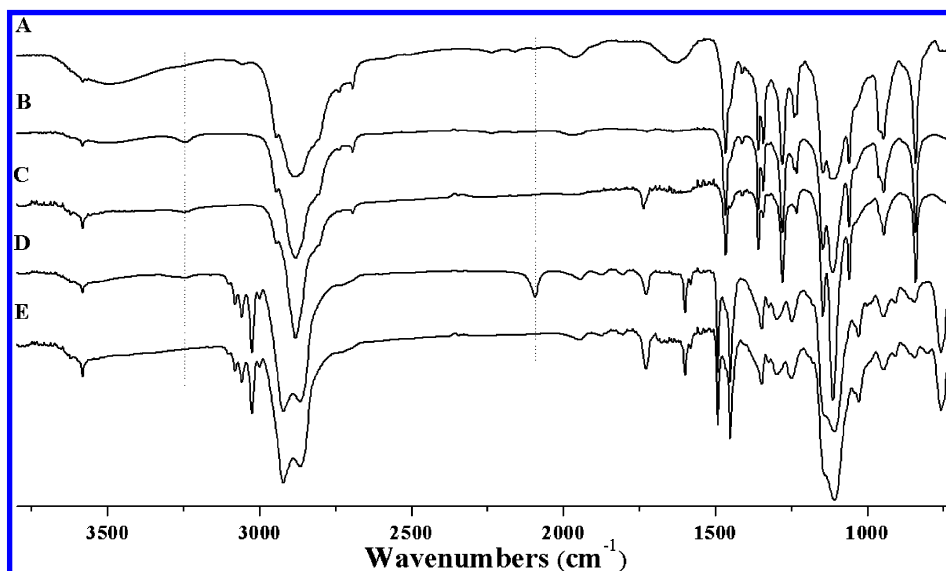

Figure 2. MALDI-TOF mass spectra of PEO (**1a**) (A), PEO (**2a**) (B), and PEO (**3a**) (C) with dithranol as matrix and sodium trifluoroacetate as cationizing salt.

$$M_{n,\text{NMR,PEO}(1)} = \frac{A_c/4}{A_b} \times 44 + 222 \tag{1}$$

where A_c and A_b were the integral areas of signals at 3.43–3.64 ppm and that at 5.40 ppm, respectively. The values of 44 and 222 were the molecular weight of EO unit and the residual of initiator $(C(OCH_2-)_2((OCH_2-)_2CHC_6H_5))$, respectively.

For PEO (**2**), the propargylation of PEO (**1**) was carried out by reacting with propargyl bromide in the presence of NaH. Compared the ¹H NMR spectrum for PEO (**2a**) (Figure 1B) with that for PEO (**1a**) (Figure 1A), the new resonance signals at 4.20 ppm (d) and 2.44 ppm (e) could be assigned to methylene protons and alkynyl protons on propargyl groups.

The propargylation procedure was verified by MALDI-TOF mass spectra. From Figure 2A,B, we could observe an increase of 2 × 38.9 Da from peak (224.3 ($C_{12}H_{16}O_4$) + 44.0 (EO) × n + 23.0 (Na⁺) = 4120.5 Da) of PEO (**1a**) to peak (224.3 ($C_{12}H_{16}O_4$) + 44.0 (EO) × n + 39.1 (C_3H_3) × 2 + 23.0 (Na⁺) = 4198.3 Da) of PEO (**2a**), which corresponded to the molecular weight of two propargyl groups. Moreover, the trace of PEO (**1a**) was not detected in Figure 2B, indicating the propargylation was performed completely. The propargylation was further verified by FT-IR analysis. Compared the spectrum for PEO (**2a**) with that for PEO (**1a**), the characteristic signal of alkyne groups at 3325 cm⁻¹ in spectrum for PEO (**2a**) was discriminated clearly (Figure 3B).

Figure 3. FT-IR spectra of PEO (**1a**) (A), PEO (**2a**) (B), PEO (**4a**) (C), (PEO-alkyne)$_2$-(PS-N$_3$)$_2$ (**6a**) (D), and the eight-shaped polymer [c-(PEO-b-PS)]$_2$ (**7a**) (E).

For PEO (**3**), the protective group on PEO (**2**) was cleaved under mild acidic conditions and monitored by ^{1}H NMR and MALDI-TOF mass spectra. In the ^{1}H NMR spectrum for PEO (**3a**) (Figure 1C), the resonance signals at 7.34 and 7.49 ppm (a) for phenyl-ring protons and that at 5.40 ppm (b) for methine proton could not be seen again, which confirmed that the hydrolysis was complete. Compared with the MALDI-TOF mass spectrum for PEO (**2a**) (Figure 2C), the peaks in spectrum for PEO (**3a**) (Figure 2B) decreased 85.1 Da (nearly the molecular weight of a protective group). The disappearance of trace for PEO (**2a**) in spectrum for PEO (**3a**) also confirmed that the hydrolysis was complete.

Finally, the macroinitiator PEO (**4**) was obtained by esterification of hydroxyl groups on PEO (**3**) by reacting with 2-bromoisobutyryl bromide. To ensure the complete esterification, a 10-fold excess of 2-bromoisobutyral bromide was used. In Figure 1D, the new resonance signals at 4.18 ppm (f) and 1.88 ppm (g) were attributed to methylene protons (−CH_2OCO−) and methyl protons (−OCOC(CH_3)$_2$Br), respectively. The efficiency of esterification could be calculated according to formula 2:

$$\text{EF}_{\text{esterification}} = \frac{A_{\text{d+f}} - 2A_{\text{e}}}{2A_{\text{e}}} \times 100\% \qquad (2)$$

where $A_{\text{d+f}}$ was the total integral area of the methylene protons at 4.20 ppm (d) on propargyl groups and the methylene protons at 4.18 ppm (f) connecting to ester bonds, and A_{e} was the integral area of methine protons on propargyl groups. The value of EF$_{\text{esterification}}$ was nearly 100%, indicating the esterification was performed completely. From FT-IR spectrum of PEO (**4a**) (Figure 3C), the absorption of ester bond at 1736 cm^{-1} could be observed clearly when compared with that for PEO (**2a**).

Synthesis and Characterization of A$_2$B$_2$ Star-Shaped Copolymers (PEO-Alkyne)$_2$-(PS-N$_3$)$_2$ (6). Using PEO (**4**) as macroinitiator, the ATRP of St monomer was performed for A$_2$B$_2$ star-shaped copolymers (PEO-Alkyne)$_2$-(PS-Br)$_2$ (**5**). The length of PS blocks could be controlled by tuning the polymerization time, and the high degree of bromide-end functionality could be realized by keeping a relatively lower monomer conversation (<30%).[35,36] From Figure 4, it could be
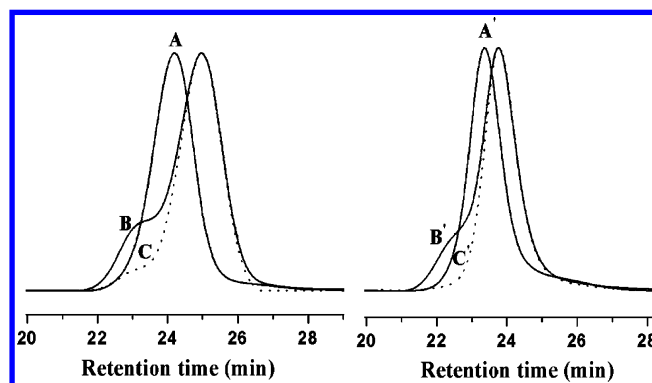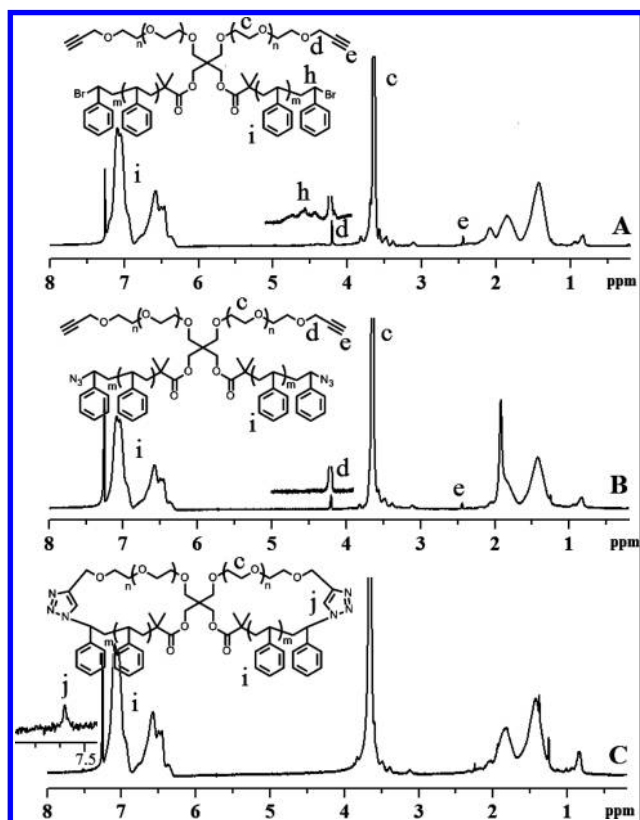

Figure 4. GPC traces of A$_2$B$_2$ star-shaped polymer (PEO-alkyne)$_2$-(PS-Br)$_2$ (**5a**) (A) (PEO-alkyne)$_2$-(PS-Br)$_2$ (**5b**) (A′)), the eight-shaped polymer [c-(PEO-b-PS)]$_2$ (**7a**) before (B) and after purification (C), [c-(PEO-b-PS)]$_2$ (**7b**) before (B′) and after purification (C′)) using THF as elution.

seen that the GPC traces of obtained A$_2$B$_2$ star-shaped copolymers were monodal peaks with narrow molecular distribution, revealing that the polymerization was successful. The ^{1}H NMR spectrum of (PEO-alkyne)$_2$-(PS-Br)$_2$ (**5a**) was shown in Figure 5A, in which the resonance signals of PS block could be discriminated clearly. Based on ^{1}H NMR, the molecular weight of (PEO-alkyne)$_2$-(PS-Br)$_2$ (**5**) was derived from formula 3:

$$M_{\text{n,NMR,(PEO-alkyne)}_2-(\text{PS-Br})_2}$$

$$= \frac{A_i/5}{A_c / \left(\frac{M_{\text{n,NMR,PEO}}}{44}\right) \times 4} \times 104 + M_{\text{n,NMR,PEO}} \qquad (3)$$

where A_i and A_c were the integral areas of aromatic signals at 6.27−7.27 ppm on PS arms and that of methylene protons at 3.43−3.64 ppm on PEO arms, respectively. The value of 104 was the molecular weight of St unit. The others were the same as defined before and the data are listed in Table 1.

The terminal bromine groups on (PEO-alkyne)$_2$-(PS-Br)$_2$ (**5**) could be easily transformed into azide groups in quantitative yields under mild conditions. Figure 5B showed

Figure 5. ^{1}H NMR spectra of (A) (PEO-alkyne)$_2$-(PS-Br)$_2$ (**5a**), (B) (PEO-alkyne)$_2$-(PS-N$_3$)$_2$ (**6a**), and (C) the purified eight-shaped polymer $[c$-(PEO-b-PS)$]_2$ (**7a**) in CDCl$_3$.

Table 1. Data of the $[c$-(PEO-b-PS)$]_2$ and Their Precursor of A$_2$B$_2$ Star-Shaped Polymers (PEO-Alkyne)$_2$-(PS-Br)$_2$

		^{1}H NMR	GPC^b			
entry	samples	$M_n{}^a$ (g/mol)	M_n (g/mol)	$M_p{}^c$ (g/mol)	PDI	$\langle G \rangle^d$
I	**5a**	11 900	10 780	10 830	1.12	
	7a		8 280	8 100	1.16	0.75
II	**5b**	19 040	17 790	19 770	1.11	
	7b		15 240	15 020	1.10	0.76

^{a}Calculated by formula 3. ^{b}Performed by GPC with THF as elution and PS as standard. ^{c}The peak value of the molecular weight measured by GPC. ^{d}The ratio of $M_{p,c}$ to $M_{p,s}$.

a typical ^{1}H NMR spectrum of (PEO-alkyne)$_2$-(PS-N$_3$)$_2$ (**6**). Compared with Figure 5A, the resonance signals at 4.50 ppm (h) assigned to methine protons neighboring to terminal bromide groups disappeared in Figure 5B. In FT-IR spectrum of (PEO-alkyne)$_2$-(PS-N$_3$)$_2$ (**6a**) (Figure 3D), the characteristic peak of azide groups at 2093 cm^{-1} could also be observed clearly, which further confirmed the successful introduction of azide groups.

Synthesis and Characterization of Heteroeight-Shaped Copolymers $[c$-(PEO-b-PS)$]_2$ (7). The intramolecular cyclization of "click" chemistry was carried out by slowly and continuously adding the solution of copolymers (PEO-alkyne)$_2$-(PS-N$_3$)$_2$ (**6**) into the catalyst solution to suppress the intermolecular reaction. The GPC traces of the resulting products revealed there was about 15% double molecular weight byproducts (shoulder peaks at shorter retention time) existed (Figures 4B and 4B′). The heteroeight-shaped copolymers were purified by fractional precipitation in

petroleum ether. The yields of the purified copolymers $[c$-(PEO-b-PS)$]_2$ (**7a**) and $[c$-(PEO-b-PS)$]_2$ (**7b**) were 47% and 58%, respectively.

The purified copolymers were characterized by ^{1}H NMR, GPC, and FT-IR, respectively. A typical ^{1}H NMR spectrum of heteroeight-shaped polymer c-$[$(PEO-b-PS)$]_2$ (**7a**) was shown in Figure 5C. Compared with that of its precursor (Figure 5B), the resonance signals (d) and (e) belonging to propargyl groups disappeared completely and the new signal at 7.52 ppm (j) was assigned to proton on triazole ring formed from the alkyne and azide groups. Experiments have proved that a cyclic polymer had lower hydrodynamic volume than its linear precursor, and this feature could be described by using $\langle G \rangle$, the ratio of the peak value of the molecular weight of the cyclic polymer ($M_{p,c}$) to that of the linear precursor ($M_{p,l}$) measure by GPC.[7−26] As seen in Figure 4, the GPC traces of cyclic copolymers clearly shifted to the longer retention time, and the $\langle G \rangle$ values were about 0.75 and 0.76, respectively (shown in Table 1). Theoretically, the homopolymers with high MWs (MW > 20K) indicated an expected value in the order of 0.70. Herein, the resultant values were somewhat greater than the theory. This difference might be contributed to the compositional and topological complexity in this particular case. From the FT-IR spectrum (Figure 3E), it could be observed that the characteristic absorption of azide at 2093 cm^{-1} disappeared after cyclization. From the results above, it could be concluded that the amphiphilic heteroeight-shaped copolymers were synthesized successfully.

Finally, the self-assembly behavior of $[c$-(PEO-b-PS)$]_2$ and (PEO-alkyne)$_2$-(PS-N$_3$)$_2$ copolymers were investigated and compared. Usually, except the quantity of the solvent, the morphology and size of the self-assembled micelles were also affected by characteristics of macromolecules, including the compositions, the length of the blocks, and the architecture or topology of copolymers. After the cyclization of (PEO-alkyne)$_2$-(PS-N$_3$)$_2$ copolymers, the derivation of the architectures from star-shaped to cycle might affect the micellization of $[c$-(PEO-b-PS)$]_2$ copolymers. From Figure 6, it can be seen
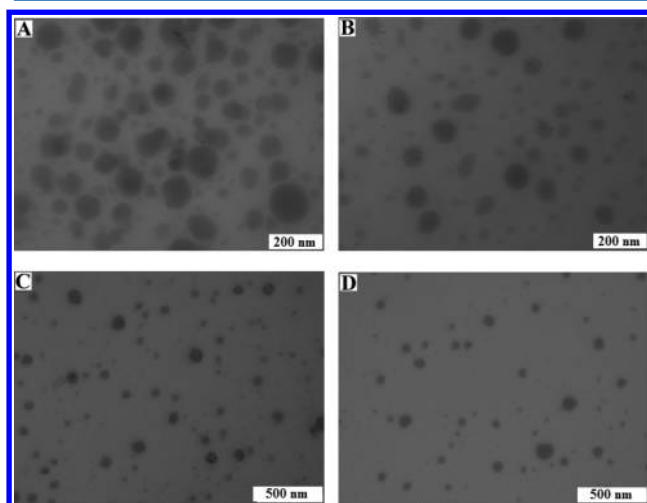
Figure 6. TEM images of the formed micelles by $[c$-(PEO-b-PS)$]_2$ (**7a**) (A), **7b** (B), and (PEO-alkyne)$_2$-(PS-N$_3$)$_2$ (**6a**) (C), (**6b**) (D) in aqueous solution (1.0 mg/mL).

that both of heteroeight-shaped $[c$-(PEO-b-PS)$]_2$ and star-shaped (PEO-alkyne)$_2$-(PS-N$_3$)$_2$ copolymers self-assembled into spherical micelles, however, there were significant differences
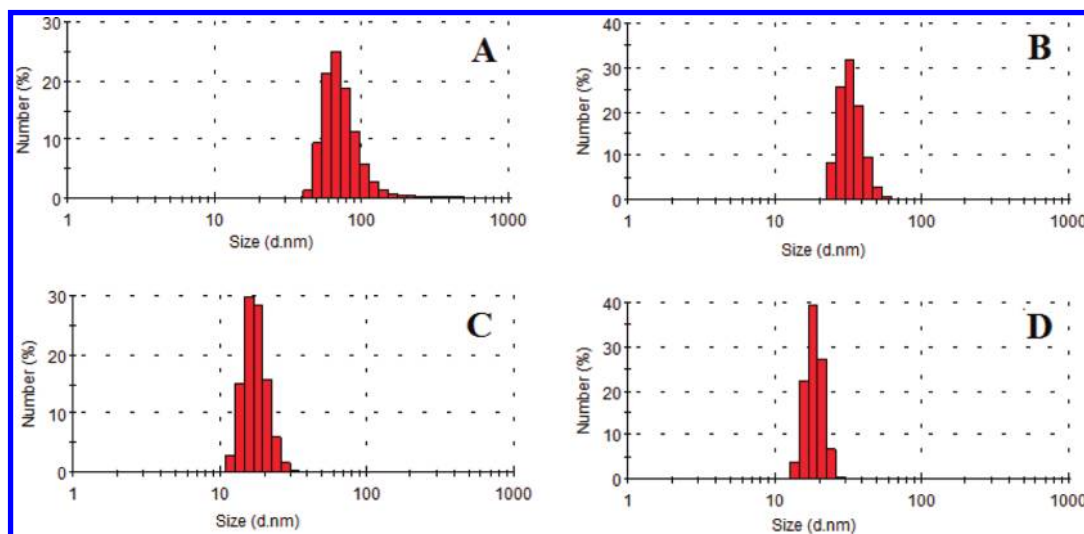
Figure 7. Size distribution of the formed micelles by $[c\text{-}(PEO\text{-}b\text{-}PS)]_2$ (**7a**) (A), **7b** (B), and $(PEO\text{-}alkyne)_2\text{-}(PS\text{-}N_3)_2$ (**6a**) (C), (**6b**) (D).

in the size. That was, the size of micelles formed by $[c\text{-}(PEO\text{-}b\text{-}PS)]_2$ were much bigger than that of $(PEO\text{-}alkyne)_2\text{-}(PS\text{-}N_3)_2$. Figure 7 showed the size distribution of the formed micelles (75 nm for **7a**, 42 nm for **7b**, 20 nm for **6a**, 18 nm for **6b**), these results were coincident with that of the TEM. The increase in size of the formed micelles was likely attributed to the fact that the complex dicyclic topology formed after cyclization, which restricted the stretching of the blocks during the self-assembly and the micelles with more loose core were formed.

CONCLUSION

Well-defined amphiphilic heteroeight-shaped polymers consisting of PEO and PS segments were successfully synthesized by combination of "click" chemistry with ROP and ATRP mechanisms. This versatile synthetical method might be used to synthesize a series of eight-shaped copolymers with different compositions. The self-assembly behavior of copolymers with the same compositions and different topologies were investigated and compared, and the preliminary results revealed that the size of formed micelles increased from a star-shaped to a cyclic topology.

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Notes
The authors declare no competing financial interest.

ACKNOWLEDGMENTS

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