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Synthesis and characterization of amphiphilic triblock Copolymers with Identical compositions but different block sequences†

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The amphiphilic triblock copolymers poly(acrylic acid)-*b*-poly(styrene)-*b*-poly(acrylic acid) (PAA-*b*-PS-*b*-PAA) and PS-*b*-PAA-*b*-PS with identical compositions but different block sequences were synthesized by a combination of an atom transfer radical polymerization (ATRP) mechanism and a nitroxide radical coupling (NRC) reaction or copper-catalyzed azide/alkyne click (CuAAC) chemistry. Firstly, the diblock copolymers TMS−≡−PS-*b*-P*t*BA-Br were prepared by sequential ATRP of styrene (St) and *tert*-butyl acrylate (*t*BA) monomers from trimethylsilyl propargyl 2-bromoisobutyrate (TMS-PgBiB) initiator. Then, the triblock copolymers PS-*b*-P*t*BA-*b*-PS were prepared by NRC reaction between TMS−≡−PS-*b*-P*t*BA-Br and coupling agent bis[4-(2,2,6,6-tetramethylpiperidine-1-oxyl)] succinate (Bis-TEMPO$_2$). And the triblock copolymers P*t*BA-*b*-PS-*b*-P*t*BA were obtained by CuAAC chemistry between Alkynyl-PS-*b*-P*t*BA-Br and a coupling agent 1,4-diazidobutane (Di-Azide$_2$). The target triblock copolymers PAA-*b*-PS-*b*-PAA and PS-*b*-PAA-*b*-PS were finally derived from the cleavage of the corresponding PS-*b*-P*t*BA-*b*-PS and P*t*BA-*b*-PS-*b*-P*t*BA. The self-assembly behaviour was preliminarily studied by FLS, FESEM and DLS instruments, and the results showed that the PS-*b*-PAA-*b*-PS and PAA-*b*-PS-*b*-PAA could give distinct critical micelle concentration (cmc) values and different sizes of micelles in water.

Introduction

The rapid development of "living"/controlled polymerization mechanisms and efficient coupling techniques in polymer chemistry have greatly accelerated the synthesis of polymers with complicated architectures,[1–7] which further makes it possible to explore the structure–property relationship of polymers. For example, as an important research area, the research on self-assembly behaviour of amphiphilic polymers with complicated architectures has been largely beneficial from the progresses in polymer chemistry and especially focused by numerous scientists, and appreciable improvement has been achieved.

Originally, Eisenberg *et al.* reported that the diblock copolymers, for example of poly(styrene)-*b*-poly(acrylic acid) (PS-*b*-PAA), could form a variety of interesting morphologies like spheres,[8–10] rods,[11,12] lamellas,[13–15] vesicles[8,16,17] and hexagonally packed hollow hoops[18] when the medium was deliberately selected. As the simplest topology of diblock copolymers in various complicated polymers, the effect of topology on self-

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assembly behaviour of polymers might not be reflected in such system. The research model with somewhat complicated topology might be a better choice, for example of PAA-*b*-PS-*b*-PAA, different toroid-shaped and spherical morphologies could be observed in selective solvents.[19] Followed with the pioneer work of Eisenberg's, considerable research progresses have also been made by other researchers. However, most researches were focused on the effect of solvents, compositions, topologies on self-assembly behaviour with multiple independent variables changing at the same time,[14,20–23] and limited works were concentrated on the comparative study of polymers changing a single variable at once (for example, the same compositions but different topologies or conversely the same topologies but different compositions, *etc.*). In our previous work, we had tried to synthesize some triblock copolymer poly(styrene)-poly-(ethylene oxide)-poly(acrylic acid) (PS-*b*-PEO-*b*-PAA) and PEO-*b*-PS-*b*-PAA with different block sequences to investigate and compare their self-assembly behaviours.[20] Although the polymeric segments could be regulated in the different sequences by a certain synthetic procedure, limited in the synthetic methods, the molecular weight of each segment was difficult to control and the obtained results could not be compared in a parallel level. Thus, one could find that the synthesis of polymers with precise compositions and topologies is still a key point and a challenging work.

Typically, for the copolymer with certain compositions and topologies, the "living"/controlled polymerization mechanisms

and efficient coupling techniques must be elaborately combined, rather than a random procedure. Especially, a certain efficient coupling technique always plays an important role in the synthesis of polymers. Copper-catalyzed azide/alkyne click (CuAAC) chemistry, because of its tolerance to solvents and various functional groups, as well as its high efficiency (close to 100%),[24] has been widely applied to the synthesis of multi-block, star-like, hyperbranched, dendrimer-like polymers, *etc.*[25–28] Another coupling reaction developed by our group, nitroxide radical coupling (NRC) reaction, has also been proved to be a rather robust and orthogonal technique with almost 100% efficiency.[29–34] Because of the easily available functional halogen groups from atom transfer radical polymerization (ATRP) mechanism, and nitroxide radicals (such as the 2,2,6,6-tetramethylpiperidine-1-oxyl (TEMPO) group or its derivatives) from anionic polymerization mechanism or further modification, the NRC reaction has become an important candidate of coupling technique in polymer chemistry. By means of this NRC reaction, a library of polymers with complicated architectures has also been smoothly realized.[30–32]

Considering the above researches in self-assembly and the synthetic strategies to complicated polymers, in this contribution, by combination of ATRP mechanism and efficient NRC reaction or CuAAC chemistry, an innovative synthetic process to triblock copolymers PS-*b*-PAA-*b*-PS and PAA-*b*-PS-*b*-PAA with identical compositions but different block sequences was explored. The key precursor of diblock copolymer (TMS-PS-*b*-P*t*BA-Br) with a bromide group and a trimethylsilyl (TMS) protected alkynyl groups was firstly obtained by sequential ATRP mechanism. Then, the NRC reaction and CuAAC chemistry were selectively used to synthesize triblock copolymer PS-*b*-P*t*BA-*b*-PS and P*t*BA-*b*-PS-*b*-P*t*BA, respectively, and PS-*b*-PAA-*b*-PS and PAA-*b*-PS-*b*-PAA were further obtained by cleavage of P*t*BA segment (Scheme 1). In order to study the difference between PS-*b*-PAA-*b*-PS and PAA-*b*-PS-*b*-PAA, the critical micelle concentration (cmc) and the morphologies of copolymers in water were preliminarily investigated and compared.

Experimental

Materials

Styrene [St, 99%, Sinopharm Chemical Reagent Co. (SCR)] was washed with 10% NaOH aqueous solution followed by water three times, dried over anhydrous $MgSO_4$, further dried over CaH_2, and distilled under reduced pressure. *tert*-Butyl acrylate (*t*BA, 99%, SCR) was dried by CaH_2 for 24 h and distilled under reduced pressure before use. Tetrahydrofuran (THF, >99%, SCR) was refluxed and distilled from sodium naphthalenide solution. Copper(I) bromide [Cu(I)Br, 95%, SCR] was stirred overnight in acetic acid, filtered, washed with ethanol and ethyl ether successively, and dried in vacuum. *N*-Phenyl-1-naphthyl-amine (PNA, 97%, Alfa Aesar) was purified by recrystallization in ethanol for three times. Trimethylsilyl propargyl alcohol (99%), 2-bromoisobutyryl bromide (99%), 1,4-dibromobutane (98%), *N*,*N*,*N*′,*N*″,*N*″-pentamethyldiethylenetriamine (PMDETA, 99%) and tetrabutylammonium fluoride hydrate (TBAF, 98%) were purchased from Aldrich and used as received. Tris((*N*,*N*,-dimethylamino)ethyl)amine (Me_6TREN, 99%) was purchased from Alfa Aesar and used as received. Dimethyl sulfoxide (DMSO, 99%), dimethyl formamide (DMF, 99.5%) and sodium azide (NaN_3, 98%) were purchased from SCR and used as received. Trimethylsilyl propargyl-2-bromoisobutyrate (TMS-PgBiB) was synthesized according to literature.[35] 4-Hydroxy-2,2,6,6-tetra-methylpiperidine-1-oxyl (HO-TEMPO) was synthesized according to literature.[36] Bis[4-(2,2,6,6-tetramethylpiperidine-1-oxyl)] succinate (Bis-TEMPO₂) was synthesized according to literature from HO-TEMPO and succinyl dichloride.[37] 1,4-diazidobutane (Di-Azide₂) was synthesized according to literature[38] from 1,4-dibromobutane and NaN_3. All other reagents were all purchased from SCR and used as received except for declaration.

Measurements

Gel permeation chromatographic (GPC) was performed in THF at 35 °C with an elution rate of 1.0 mL min⁻¹ on an Agilent 1100 equipped with a G1310A pump, a G1362A refractive index
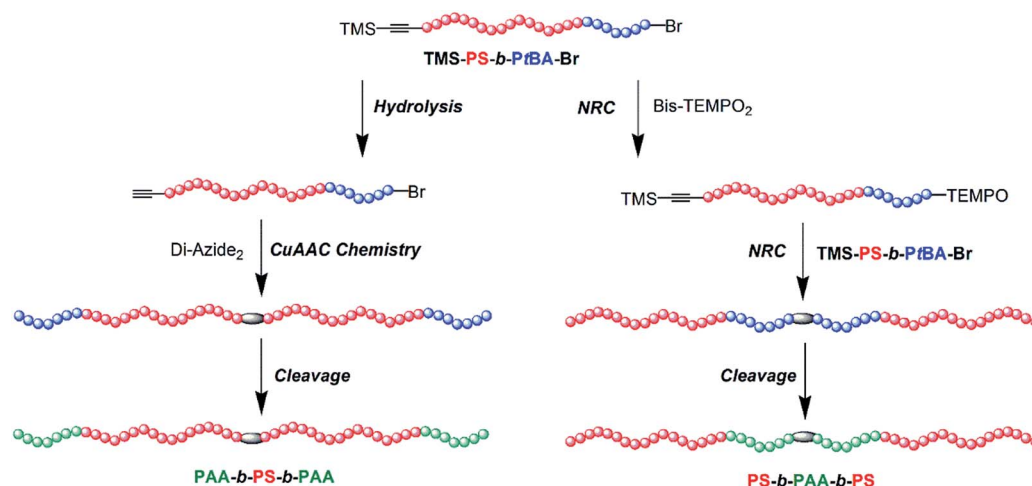
Scheme 1 The synthetic procedure of triblock copolymers PS-*b*-PAA-*b*-PS and PAA-*b*-PS-*b*-PAA.

detector, and a G1314A variable wavelength detector. One 5 μm LP gel column (500 Å, molecular weight range 500–2 × 10^4 g mol^{-1}) and two 5 lm LP gel mixed bed columns (molecular weight range 200–3 × 10^6 g mol^{-1}) were calibrated by PS standard samples. ^{1}H NMR spectra were recorded on a DMX 500 MHz spectrometer in $CDCl_3$ with tetramethylsilane (TMS) as the internal reference, except for the products PS-b-PAA-b-PS and PAA-b-PS-b-PAA, which were measured in DMF-d_7 solvent. Steady-state fluorescent spectra of PNA were measured on a FLS920 spectrometer operating at 25 °C. The emission intensity at 418 nm was recorded to determine the cmc and the λ_{ex} was 340 nm. The size of the micelles was measured by dynamic light scattering (DLS) using a Malvern Zetasizer Nano ZS. Field emission scanning electron microscopy (FESEM) images were obtained by an Ultra 55 field-emission scanning electron microscope operated at 5 kV.

Synthesis of heterofunctional PS with bromide and trimethylsilyl protected alkynyl end groups (TMS–≡–PS-Br). The heterofunctional TMS–≡–PS-Br was obtained by ATRP of St monomers from TMS-PgBiB initiator (Scheme 2). Typically, TMS-PgBiB (0.4610 g, 1.66 mmol), CuBr (0.2450 g, 1.71 mmol), PMDETA (0.35 mL, 1.68 mmol) and St (40 mL, 348 mmol) were introduced into a 100 mL ampule successively. The reaction mixture was degassed by three freeze–pump–thaw cycles and purged with nitrogen, and then immerged into an oil bath at 90 °C for 5.0 h. After the polymerization was stopped by dipping into liquid nitrogen, the crude product was diluted with THF and passed through a column chromatograph filled with neutral alumina to remove the copper complex, and finally precipitated into methanol. The precipitate was collected and dried at 45 °C in vacuum to a constant weight. GPC: $M_{n,GPC}$ = 7500 g mol^{-1}, PDI = 1.06. ^{1}H NMR (CDCl$_3$, δ, ppm, TMS): 0.12–0.22 ((CH$_3$)$_3$Si–), 0.78–0.98 (–C(CH$_3$)$_2$–), 1.17–2.51 (3H, aliphatic main chain –CH$_2$CH– on PS chain), 3.95–4.20 (–C≡C–CH$_2$O–),

4.35–4.55 (BrCHC$_6$H$_5$–), 6.30–7.30 (5H, aromatic –C$_6$H$_5$ on PS chain). $M_{n,NMR}$ = 7400 g mol^{-1}.

**Synthesis of diblock copolymer with bromide and trimethylsilyl protected alkynyl end groups (TMS–≡–PS-b-PtBA-Br).** The diblock copolymer TMS–≡–PS-b-PtBA-Br was obtained by ATRP of tBA monomers initiated from TMS-PS-Br macro-initiator (Scheme 2). First, TMS–≡–PS-Br (3.00 g, 0.40 mmol), CuBr (0.0630 g, 0.44 mmol), PMDETA (0.10 mL, 0.48 mmol), tBA (20 mL, 138 mmol) and toluene (12 mL) were sequentially introduced into a 100 mL ampule. The reaction mixture was degassed by three freeze–pump–thaw cycles and purged with nitrogen, and immerged into an oil bath at 80 °C for 5.0 h. After the polymerization was stopped by dipping into liquid nitrogen, the crude product was diluted with THF and passed through a column chromatograph filled with neutral alumina to remove the copper complex, and precipitated into the mixed solvents of methanol and water ($V_{methanol}/V_{water}$ = 1 : 1). The precipitate was collected and dried at 45 °C in vacuum to a constant weight. GPC: $M_{n,GPC}$ = 9000 g mol^{-1}, PDI = 1.10. ^{1}H NMR (CDCl$_3$, δ, ppm, TMS): 0.12–0.22 ((CH$_3$)$_3$Si–), 0.78–0.98 (–C(CH$_3$)$_2$–), 1.13–2.48 (15H, aliphatic main chain –CH$_2$CH– on PS chain, aliphatic main chain –CH$_2$CH– on PtBA chain and tert-butyl group protons –C(CH$_3$)$_3$), 3.70–3.90 (BrCHCOO–), 3.95–4.20 (–C≡C–CH$_2$O–), 6.30–7.30 (5H, aromatic –C$_6$H$_5$ on PS chain). $M_{n,NMR}$ = 10 300 g mol^{-1}.

Synthesis of triblock copolymer PS-b-PtBA-b-PS. Firstly, the diblock copolymer with a TEMPO and a trimethylsilyl protected alkynyl end groups (TMS–≡–PS-b-PtBA-TEMPO) was achieved by NRC reaction between TMS–≡–PS-b-PtBA-Br and Bis-TEMPO$_2$ (Scheme 3). Into a 100 mL ampule, the TMS-PS-b-PtBA-Br (0.1540 g, 0.017 mmol), Bis-TEMPO$_2$ (0.5090 g, 0.8 mmol), Cu (0.0480 g, 0.75 mmol), CuBr (0.0881 g, 0.60 mmol), Me$_6$TREN (0.2740 g, 1.19 mmol), DMSO (1.5 mL) and toluene (1.5 mL) were introduced successively. The reaction mixture was degassed by three freeze–pump–thaw cycles and purged with nitrogen, and then immerged into an oil bath at 50 °C for 36 h. After the copper powder was removed by centrifugation, the product was purified according to that of TMS–≡–PS-b-PtBA-Br, and dried at 45 °C in vacuum to a constant weight.

Then, the triblock copolymer PS-b-PtBA-b-PS was obtained by a second NRC reaction between TMS–≡–PS-b-PtBA-TEMPO and TMS–≡–PS-b-PtBA-Br. The sample TMS–≡–PS-b-PtBA-TEMPO (0.1511 g, 0.017 mmol), TMS–≡–PS-b-PtBA (0.1870 g, 0.02 mmol), Cu(0) (0.0100 g, 0.16 mmol), CuBr (0.0321 g, 0.22 mmol), Me$_6$TREN (0.079 g, 0.34 mmol), DMSO (1.0 mL) and toluene (1.0 mL) were introduced into a 100 mL ampule successively. The reaction mixture was degassed by three freeze–pump–thaw cycles and purged with nitrogen, and then immerged into an oil bath at 50 °C for 36 h. The subsequent purification procedure was also similar to that of TMS–≡–PS-b-PtBA-Br. In order to remove the uncoupled diblock copolymers, the product was further purified by fractional precipitation from THF/H$_2$O system, and the obtained product was dried at 45 °C in vacuum to a constant weight. GPC: $M_{n,GPC}$ = 19 800 g mol^{-1}, PDI = 1.13. ^{1}H NMR (CDCl$_3$, δ, ppm, TMS): 2.10–2.48 (–CH$_2$CH– on PtBA chain), 6.30–7.30 (5H, aromatic –C$_6$H$_5$ on PS chain).
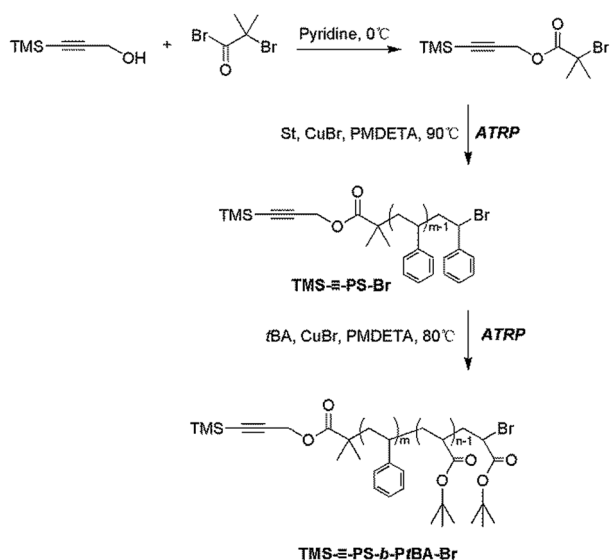
Scheme 2 The synthetic procedure of diblock copolymer TMS–≡–PS-b-PtBA-Br.
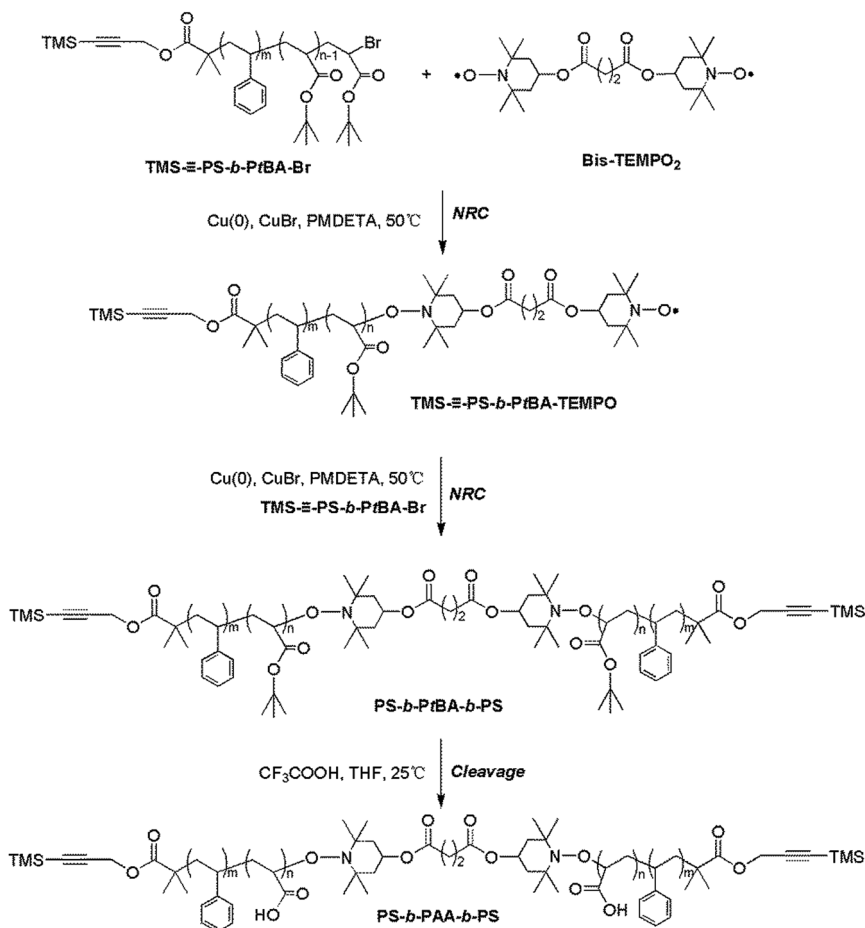
Scheme 3 The synthetic procedure of ABA type triblock copolymer PS-*b*-PAA-*b*-PS.

Synthesis of triblock copolymer P*t*BA-*b*-PS-*b*-P*t*BA. Firstly, the Alkynyl-PS-*b*-P*t*BA-Br was obtained by removal of TMS group from diblock copolymer TMS–≡–PS-*b*-P*t*BA-Br (Scheme 4). Typically, the sample TMS–≡–PS-*b*-P*t*BA-Br (0.7801 g, 0.060 mmol) was dissolved in THF (30 mL) and TBAF (0.29 g, 0.92 mmol) was introduced. After the mixture was immerged into an oil bath at 25 °C for 24 h, the product was precipitated into a mixed solvent of methanol and water ($V_{methanol}/V_{water}$ = 1 : 1). The precipitate was collected and dried at 45 °C in vacuum to a constant weight.

Subsequently, the triblock copolymer P*t*BA-*b*-PS-*b*-P*t*BA was obtained by CuAAC chemistry between Di-Azide$_2$ and Alkynyl-PS-*b*-P*t*BA. Alkynyl-PS-*b*-P*t*BA (0.2900 g, 0.023 mmol), CuBr (0.0851 g, 0.060 mmol), PMDETA (1.2 mL, 5.76 mmol) and DMF (1.5 mL) were introduced into a 100 mL ampule successively. After the reaction mixture was degassed by three freeze–pump–thaw cycles and purged with nitrogen, the ampule was immerged into an oil bath at 80 °C and Di-Azide$_2$ (0.0231 g, 0.118 mmol) was added into the ampule dropwise by syringe in 12 h. After another 24 h, the crude polymers were recovered by the similar procedure for TMS–≡–PS-*b*-P*t*BA-Br. The uncoupled diblock copolymers were also removed by fractional precipitation from THF/H$_2$O system, and the obtained product was dried at 45 °C in vacuum to a constant weight. GPC: $M_{n,GPC}$ = 20 000 g mol^{-1}, PDI

= 1.10. ^{1}H NMR (CDCl$_3$, δ, ppm, TMS): 2.10–2.48 (–CH$_2$CH– on P*t*BA chain), 6.30–7.30 (5H, aromatic –C_6H_5 on PS chain).

Synthesis of ABA type PS-*b*-PAA-*b*-PS and BAB type PAA-*b*-PS-*b*-PAA triblock copolymer. The triblock copolymers PS-*b*-PAA-*b*-PS and PAA-*b*-PS-*b*-PAA were prepared by cleavage of the P*t*BA segment on corresponding triblock copolymer PS-*b*-P*t*BA-*b*-PS and P*t*BA-*b*-PS-*b*-P*t*BA. Taking the cleavage of the P*t*BA segment on PS-*b*-P*t*BA-*b*-PS as example, PS-*b*-P*t*BA-*b*-PS (0.0201 g, 8 × 10^{-4} mmol), THF (5.0 mL) and CF$_3$COOH (1.0 mL) were introduced into a 50 mL round-bottom flask. After 24 h, the reaction mixture was evaporated by a rotary evaporator to remove the solvent. The crude product was dissolved by DMF and precipitated into water. The solvent was removed by centrifugation and the achieved product was dried at 45 °C in vacuum to a constant weight. ^{1}H NMR (CDCl$_3$, δ, ppm, TMS): 2.10–2.48 (–CH$_2$CH– on PAA chain), 6.30–7.30 (5H, aromatic –C_6H_5 on PS chain). Similarly, the PAA-*b*-PS-*b*-PAA was obtained by cleavage of the P*t*BA segment on triblock copolymer P*t*BA-*b*-PS-*b*-P*t*BA.

Determination of critical micelle concentration (cmc) of amphiphilic ABA type PS-*b*-PAA-*b*-PS and BAB type PAA-*b*-PS-*b*-PAA triblock copolymers. According to literature,[39] the PNA was used as fluorescence probe to measure the cmc values of triblock copolymer PS-*b*-PAA-*b*-PS or PAA-*b*-PS-*b*-PAA in water. First, the acetone solution of PNA (0.001 mol L^{-1}) was added
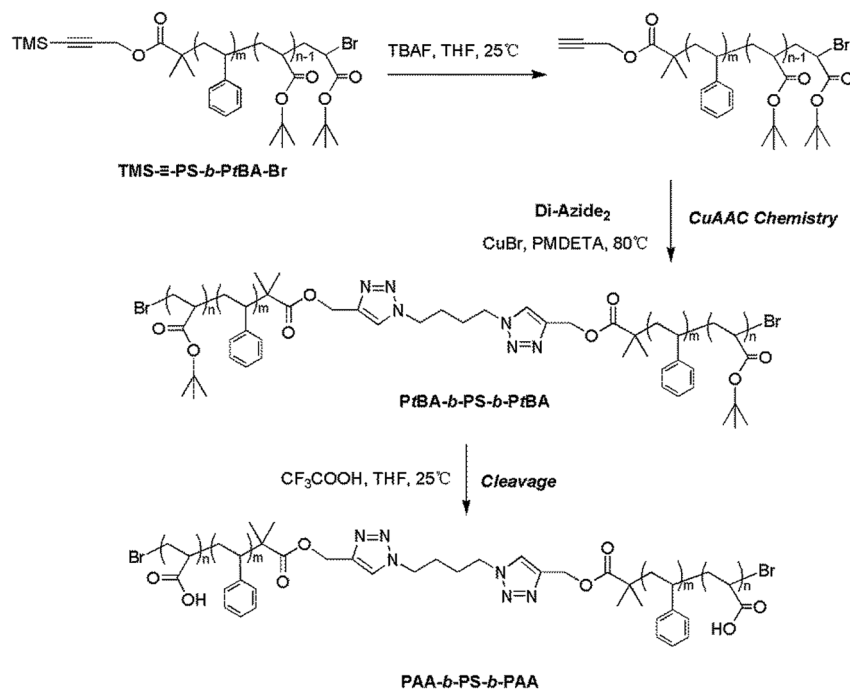
Scheme 4 The synthetic procedure of BAB type triblock copolymer PAA-*b*-PS-*b*-PAA.

into a large amount of water to give the concentration of PNA of 2×10^{-9} mol mL^{-1}. Then, different amounts of micellar solution of PS-*b*-PAA-*b*-PS or PAA-*b*-PS-*b*-PAA were added into water containing PNA ([PNA] = 2×10^{-9} mol mL^{-1}), and the concentration of triblock copolymer PS-*b*-PAA-*b*-PS or PAA-*b*-PS-*b*-PAA were modulated from 2.0×10^{-8} to 0.1 g mL^{-1} for FLS measurement.

Self-assembly behaviour of amphiphilic ABA type PS-*b*-PAA-*b*-PS and BAB type PAA-*b*-PS-*b*-PAA triblock copolymers. Typically, the triblock copolymer PS-*b*-PAA-*b*-PS or PAA-*b*-PS-*b*-PAA (6.0 mg) was dissolved in DMF (2.0 mL), and the deionized water (8 mL) was added dropwise using syringe pump under vigorous stirring within 3.0 h. After stirring for another 24 h, the suspension system was dialyzed against deionized water for three days using a dialysis bag with a 3 kDa cutoff molecular weight. The obtained micelle solution was diluted to 5×10^{-4} g mL^{-1} and characterized by FESEM instrument. The samples were freeze in liquid nitrogen and dried in a freeze drier before observation.

Results and discussion

Synthesis and characterization of diblock copolymer TMS–≡–PS-*b*-P*t*BA-Br

The diblock copolymer TMS–≡–PS-*b*-P*t*BA-Br with a bromide group and a protected alkynyl end group was prepared by ATRP of *t*BA monomers from TMS–≡–PS-Br macro-initiator, which was synthesized by ATRP of St monomers from TMS-PgBiB initiator. Fig. 1A and 1B showed the GPC traces of TMS–≡–PS-Br and TMS–≡–PS-*b*-P*t*BA-Br, respectively, the monomodal peaks, low PDIs and the clear shift from TMS–≡–PS-Br curve to

TMS–≡–PS-*b*-P*t*BA-Br curve confirmed that both ATRP procedures were successful.

In Fig. 2A for the ^{1}H NMR of TMS–≡–PS-Br, except for the characteristic resonance signals for aromatic protons ($-C_6H_5$) on PS chain at 6.30–7.30 ppm (e), the ^{1}H NMR spectrum also exhibited the characteristic resonance signals due to methine group proton (BrCHC_6H_5–) at 4.35–4.55 ppm (d′), propargyl group protons ($-C\equiv C-CH_2O-$) at 3.95–4.20 ppm (a) and methyl group protons ($-C(CH_3)_2-$) at 0.78–0.98 ppm (b), which further proved the successful preparation of TMS–≡–PS-Br. According to ^{1}H NMR spectrum, the $M_{n,NMR}$ of TMS–≡–PS-Br was calculated by Formula (1):

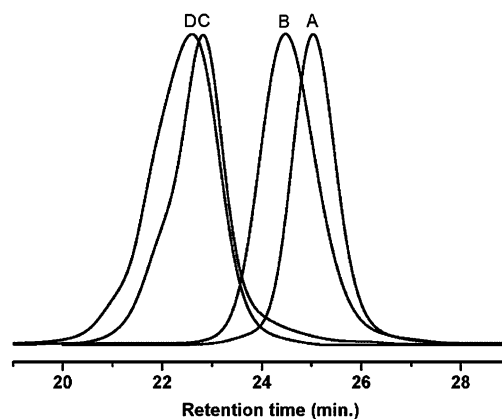**Fig. 1** The GPC traces of TMS–≡–PS-Br (A) (M_n = 7500 g mol^{-1}, PDI = 1.06), TMS–≡–PS-*b*-P*t*BA-Br (B) (M_n = 9000 g mol^{-1}, PDI = 1.10), PS-*b*-P*t*BA-*b*-PS (C) (M_n = 19 800 g mol^{-1}, PDI = 1.13) and P*t*BA-*b*-PS-*b*-P*t*BA (D) (M_n = 20 000 g mol^{-1}, PDI = 1.10).
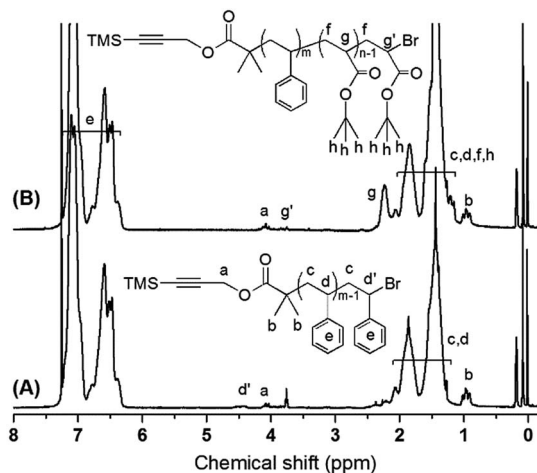
Fig. 2 The ^{1}H NMR spectra of TMS−≡−PS-Br (A) and TMS−≡−PS-b-PtBA-Br (B) (in CDCl$_3$ solvent).

$$M_{n,NMR} = \frac{A_{6.30-6.90}/2}{A_{3.95-4.20}/2} \times 104 + 277 \tag{1}$$

where $A_{6.30-6.90}$ was the integral area of partial aromatic protons on PS chain, and $A_{3.94-4.20}$ was the integral area of propargyl group protons (−C≡C−CH_2O−) at 3.95–4.20 ppm. The values of 104 and 277 were the molecular weight of St unit and that of initiator residue, respectively. The obtained $M_{n,NMR}$ was 7400 g mol^{-1}, which approximated to that obtained from above GPC measurement (7500 g mol^{-1}). The amount of St unit on each macromolecule was also estimated as 68, and the detailed data was listed in Table 1.

Also, the ^{1}H NMR spectrum of TMS−≡−PS-b-PtBA-Br was shown in Fig. 2B, compared with that of TMS−≡−PS-Br, the new resonance signal at 3.70–3.90 ppm (g') for methine group proton (BrCHCOO−) and the resonance signal at 2.10–2.48 ppm (g) for methine group proton (−CH_2CH) confirmed the successful ATRP of tBA monomers from TMS−≡−PS-Br macro-initiator. According to ^{1}H NMR spectrum, the $M_{n,NMR}$ of TMS−≡−PS-b-PtBA-Br could be derived from Formula (2):

$$M_{n,NMR} = \left(\frac{A_{2.10-2.48}}{A_{6.30-6.90}/2} \times \frac{128}{104} + 1 \right) \times M_{n,NMR,(TMS-≡-PS-Br)} \tag{2}$$

where $A_{2.10-2.48}$ was the integral area of the methine group proton (−CH_2CH) at 2.10–2.48 ppm. The value of 128 was the molecular weight of tBA unit. And others were the same as defined before. The obtained $M_{n,NMR}$ was 10 300 g mol^{-1}, and the amount of PtBA units introduced on each macromolecule was calculated as 23.

Synthesis and characterization of ABA type triblock copolymer PS-b-PAA-b-PS

For the target ABA type triblock copolymer PS-b-PAA-b-PS, the atom transfer radical coupling (ATRC)[40] was initially adopted to synthesize PS-b-PtBA-b-PS. However, almost no coupling product was discriminated from GPC measurement, which can be ascribed to the disproportionation termination on terminal PtBA-Br.[41-43] Especially, the higher molecular weight of precursor would bring a larger hindrance, and further led to a lower coupling efficiency. Alternatively, the NRC reaction was considered to synthesize PS-b-PAA-b-PS. Firstly, its precursor PS-b-PtBA-b-PS was obtained by NRC reaction between TMS−≡−PS-b-PtBA-Br and TMS−≡−PS-b-PtBA-TEMPO, and the latter was first prepared by NRC reaction between TMS−≡−PS-b-PtBA-Br and the coupling agent Bis-TEMPO$_2$.

In order to obtain a high coupling efficiency, the feed procedure was well analyzed and balanced. In the first case, an attempt was made to couple the TMS−≡−PS-b-PtBA-Br and Bis-TEMPO$_2$ directly to get the target PS-b-PtBA-b-PS. That was, the TMS−≡−PS-b-PtBA-Br and Bis-TEMPO$_2$ were simultaneously added and sealed in the system. However, the inevitable equivalent deviation between the macromolecule TMS−≡−PS-b-PtBA-Br and small molecular weight compound Bis-TEMPO$_2$ always produced amount of uncoupled precursors. Alternatively, the equivalent deviation between macromolecules and Bis-TEMPO$_2$ might be solved by a dropwise addition procedure. Thus, in the second case, the macromolecule TMS−≡−PS-b-PtBA-Br was first added and the compound Bis-TEMPO$_2$ was added dropwise by syringe. However, the trace oxygen might be introduced by syringe, which would have a vital effect on the NRC reaction. Also, the instantaneous low concentration of TEMPO groups in system would not guarantee the sufficient NRC reaction and the side reaction (such as the disproportionation termination) of generated carbon radicals might be enhanced. Conversely, in the third case, the compound Bis-TEMPO$_2$ was first added and the macromolecule TMS−≡−PS-b-PtBA-Br in toluene was then added dropwise. Similarly, except for the introduction of trace oxygen, the viscous TMS−≡−PS-b-

Table 1 The data of the target copolymers and the intermediates

Entry	$M_{n,GPC}{}^a$ (g mol^{-1})	PDI^a	$M_{n,NMR}$ (g mol^{-1})	$N_{St}{}^d$	$N_{tBA}{}^e$
TMS−≡−PS-Br	7500	1.06	7400^b	68	
TMS−≡−PS-b-PtBA-Br	9000	1.10	10 300^c	68	32
PS-b-PtBA-b-PS	19 800	1.13	20 600	136	64
PtBA-b-PS-b-PtBA	20 000	1.10	20 600	136	64

^{a} Determined by GPC performed in THF solvent using PS as standard. ^{b} The molecular weight was calculated according to Formula (1). ^{c} The molecular weight was calculated according to Formula (2). ^{d} The number of St unit was calculated using Formula: $N_{St} = M_{n,NMR,(TMS-≡-PS-Br)}/104$, where the value of 104 corresponded to the molecular weight of St unit. ^{e} The number of tBA unit was calculated using Formula: $N_{tBA} = (M_{n,NMR,(TMS-≡-PS-b-PtBA-Br)} - M_{n,NMR,(TMS-≡-PS-Br)})/128$, where the value of 128 corresponded to the molecular weight of tBA unit.
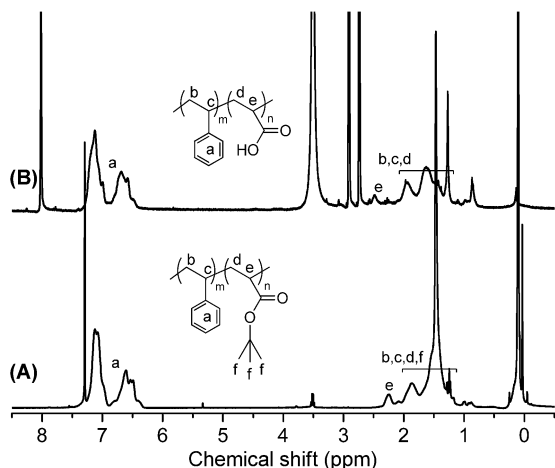
Fig. 3 The ^{1}H NMR spectra of PS-*b*-P*t*BA-*b*-PS (A) (in CDCl$_3$ solvent) and PS-*b*-PAA-*b*-PS (B) (in DMF-d$_7$ solvent).

P*t*BA-Br solution also increased the trouble of feeding procedure. Thus, in order to avoid the equivalent deviation from calculation and the introduction of trace oxygen, as well as reduce the side reaction of formed carbon radical in system and simplify the operation, a fourth route in this work was designed and adopted. That was, the precursor TMS–≡–PS-*b*-P*t*BA-TEMPO was first formed by NRC reaction between TMS–≡–PS-*b*-P*t*BA-Br and excess coupling agent Bis-TEMPO$_2$, and the purified TMS–≡–PS-*b*-P*t*BA-TEMPO (see Fig. S1 in ESI†) could then couple with the precursor TMS–≡–PS-*b*-P*t*BA-Br.

After the purification of crude product, Fig. 1C showed the GPC trace of PS-*b*-P*t*BA-*b*-PS. The monomodal peak, low PDI (1.13) and the significantly increased $M_{n,GPC}$ (19 800 g mol^{-1}) compared with that of TMS–≡–PS-*b*-P*t*BA-Br confirmed that the NRC was successful. In Fig. 3A, except for the characteristic resonance signals for aromatic protons (–C_6H_5) on PS chain at 6.30–7.30 ppm (a), the ^{1}H NMR spectrum of PS-*b*-P*t*BA-*b*-PS also exhibited the characteristic resonance signal due to methine group proton (–CH_2CH–) at 2.10–2.48 ppm (e). Finally, the ABA type triblock copolymer PS-*b*-PAA-*b*-PS was further prepared by cleavage of P*t*BA segment on PS-*b*-P*t*BA-*b*-PS in THF solvent in the presence of CF$_3$COOH. Fig. 3B showed the ^{1}H NMR spectrum of PS-*b*-PAA-*b*-PS in DMF-d$_7$. Compared with the spectrum of PS-*b*-P*t*BA-*b*-PS, the resonance signal at 1.13–2.48 ppm in the spectrum of PS-*b*-PAA-*b*-PS was obviously weakened, which showed that the *tert*-butyl groups on P*t*BA segment were removed. Thus, all the above information clearly confirmed that the ABA type triblock copolymer PS-*b*-PAA-*b*-PS was obtained.

Synthesis and characterization of BAB type triblock copolymer PAA-*b*-PS-*b*-PAA

Also, in order to get the target BAB type triblock copolymer PAA-*b*-PS-*b*-PAA, its precursor P*t*BA-*b*-PS-*b*-P*t*BA was prepared by CuAAC chemistry between Alkynyl-PS-*b*-P*t*BA-Br (see Fig. S2 in ESI†) and the coupling agent Di-Azide$_2$, and the former was derived from the cleavage of protected group TMS–≡–PS-*b*-P*t*BA-Br in the presence of TBAF. Unlike the NRC reaction, because the CuAAC chemistry tolerates a certain content of

oxygen, the dropwise addition procedure could be considered in this system. That was, the Alkynyl-PS-*b*-P*t*BA-Br was firstly added and Di-Azide$_2$ was then added dropwise, which could largely exclude the equivalent deviation between macromolecules Alkynyl-PS-*b*-P*t*BA-Br and small molecular weight compound Di-Azide$_2$ and further ensure the high coupling efficiency. As mentioned in the above section, the terminal P*t*BA-Br tended to the disproportionation termination[43] and the products formed from ATRC reaction can be neglected. Thus, under this CuAAC chemistry condition, the interruption of ATRC reaction can be excluded and the aimed product P*t*BA-*b*-PS-*b*-P*t*BA was achieved.

Fig. 1D showed the GPC trace of purified P*t*BA-*b*-PS-*b*-P*t*BA. The monomodal peak, low PDI (1.10), as well as the increased $M_{n,GPC}$ (20 000 g mol^{-1}) confirmed that the CuAAC chemistry was successful. The ^{1}H NMR spectra of P*t*BA-*b*-PS-*b*-P*t*BA and PAA-*b*-PS-*b*-PAA showed similar results to those of the above PS-*b*-P*t*BA-*b*-PS and PS-*b*-PAA-*b*-PS (see Fig. S3 in ESI†), which further meant that these two series of triblock copolymers actually had the identical compositions but different block sequences.

Self-assembly behaviour of amphiphilic ABA type PS-*b*-PAA-*b*-PS and BAB type PAA-*b*-PS-*b*-PAA triblock copolymer

The amphiphilic nature of triblock copolymer PS-*b*-PAA-*b*-PS or PAA-*b*-PS-*b*-PAA, consisting of hydrophobic PS chain and hydrophilic PAA chain, provided an opportunity to form micelles in a selective solvent (such as water). The cmc of
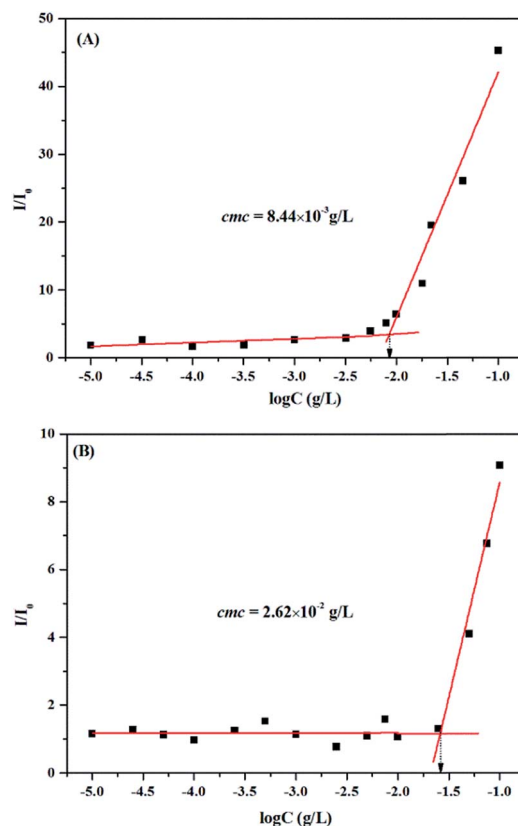

Fig. 4 Dependence of fluorescence intensity ratio I/I_0 of PNA fluorescence emission spectra on the concentration of PS-*b*-PAA-*b*-PS (A) or PAA-*b*-PS-*b*-PAA (B) triblock copolymer (λ_{ex} = 340 nm).
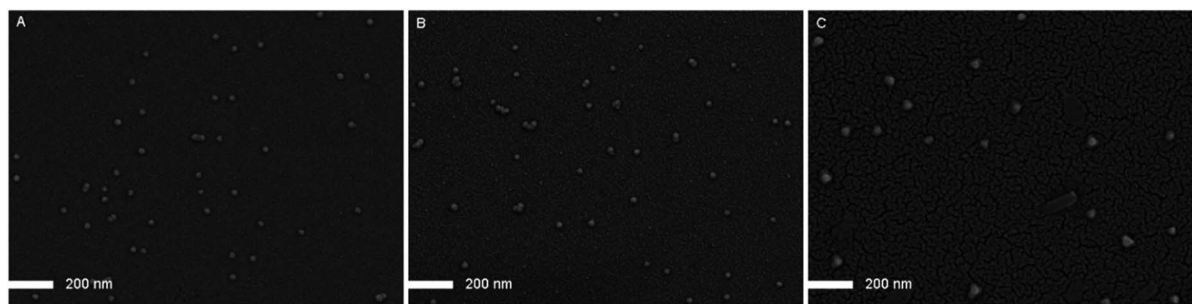
Fig. 5 FESEM images of micelles formed by PS-*b*-PAA (A), PS-*b*-PAA-*b*-PS (B) and PAA-*b*-PS-*b*-PAA (C) in water.

triblock copolymer in water was determined by fluorescence technique using PNA as probe, which is a more suitable fluorescent probe than pyrene in terms of reproducibility because it displays higher fluorescence activity in nonpolar environments and can also be very easily quenched by polar solvents (such as water).[39] The relationship of the fluorescence intensity ratio (I/I_0) of PNA as a function of the concentration of PS-*b*-PAA-*b*-PS was plotted in Fig. 4A. It was found that I/I_0 increased sharply when the concentration exceeded a certain value, which demonstrated that the PNA probe began to be incorporated into the hydrophobic region of micelles. Thus, the intersection of two straight lines with a value of 8.44×10^{-3} g L^{-1} was determined as the cmc of PS-*b*-PAA-*b*-PS. Similarly, the cmc of PAA-*b*-PS-*b*-PAA was also determined as 2.62×10^{-2} g L^{-1} according to Fig. 4B. Obviously, the cmc value of PS-*b*-PAA-*b*-PS was about 32 times higher than that of PAA-*b*-PS-*b*-PAA. In a parallel level, with the identical compositions but different block sequences, these two copolymers show distinct cmc values. This result could give the information that the block sequence (connection style of segment) actually has effect on the self-assembly behaviour of amphiphilic triblock copolymers.

To further investigate the differences of solution behaviour between the triblock copolymer PS-*b*-PAA-*b*-PS and PAA-*b*-PS-*b*-PAA, the micelle morphology was observed by FESEM instrument. As a reference, the micelle morphology of PS-*b*-PAA was also observed simultaneously. The diblock copolymer PS-*b*-PAA was obtained by the typical cleavage of PtBA segment on TMS–≡–PS-*b*-P*t*BA-Br by CF$_3$COOH. Fig. 5A–C showed the micelle morphologies of PS-*b*-PAA, PS-*b*-PAA-*b*-PS and PAA-*b*-PS-*b*-PAA in water, respectively. Small particles could be found scattered in all the three FESEM images, which meant that the micelles were formed by all the three copolymers. Differently, it was found that the size of micelles from triblock copolymer PS-*b*-PAA-*b*-PS was similar to the that of micelles from diblock copolymer PS-*b*-PAA, while the size of micelles from triblock copolymer PAA-*b*-PS-*b*-PAA were somewhat lager. That was, the average diameter of PS-*b*-PAA micelles or PS-*b*-PAA-*b*-PS micelles was around 30 nm, and the average diameter of PAA-*b*-PS-*b*-PAA micelles was around 47 nm. Also, by DLS measurement, the sizes of micelles formed by PS-*b*-PAA, PS-*b*-PAA-*b*-PS and PAA-*b*-PS-*b*-PAA copolymers were obtained as 17 nm, 18 nm and 44 nm, respectively (Fig. S4†), which were well agreed with those by FESEM instrument.

From Fig. 5A–C, all these amphiphilic copolymers showed the classical spherical morphologies in water. As has been well

investigated, the spherical morphologies were the simplest morphologies of micelles, in which the hydrophobic segments tend to form a core inside the micelle while the hydrophilic segments tend to form a shell outside the micelle (Scheme 5).[44] Based on the result that the size of PS-*b*-PAA-*b*-PS micelles was similar to PS-*b*-PAA micelles, while the PAA-*b*-PS-*b*-PAA micelles were somewhat larger, we might figure that the block sequence of the copolymers played a very important role in the formation of micelles. For triblock copolymer PS-*b*-PAA-*b*-PS, because both ends of PAA segment were seriously restricted by PS segments, the outer PAA shell in micelle could not be well solubilized in water. Differently, for triblock copolymer PAA-*b*-PS-*b*-PAA, only one end of PAA segment was connected on PS segment, and the outer PAA segments in micelle could wind into water freely. This fact could also explain why the size of PAA-*b*-PS-*b*-PAA micelles were larger than that of PS-*b*-PAA-*b*-PS micelles.

As described in Introduction section, although plenty of works had focused on the self-assembly behaviour of amphiphilic polymers, rare of them had aimed to study the effect of solvents, compositions, topologies on their properties changing a single variable at once. In this contribution, based on the precisely designed synthetic route, the ABA type triblock copolymer PS-*b*-PAA-*b*-PS and BAB type triblock copolymer PAA-*b*-PS-*b*-PAA were both synthesized from the same precursor of TMS–≡–PS-*b*-P*t*BA-Br, which made the two triblock copolymers
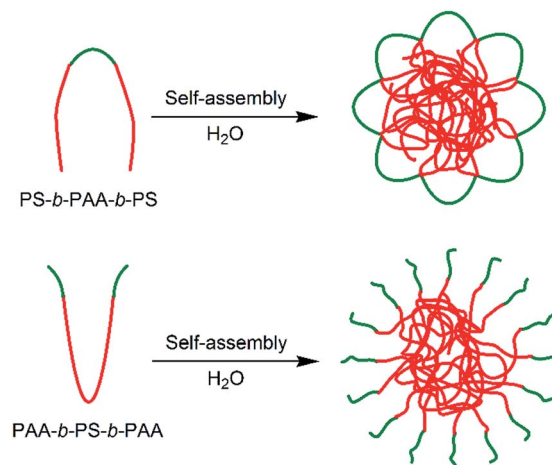
Scheme 5 The proposed mechanism for the formation of micelles of triblock copolymer PS-*b*-PAA-*b*-PS and PAA-*b*-PS-*b*-PAA with identical compositions but different block sequences in selective solvent.

share the identical compositions but different block sequences. The different self-assembly behaviour of these copolymers in water might be an important result to enrich the structure–property relationship. Also, this difference might be evidence that the triblock copolymers with identical compositions but different block sequences were actually synthesized.

Conclusions

In conclusion, the amphiphilic ABA type PS-b-PAA-b-PS and BAB type PAA-b-PS-b-PAA triblock copolymers with identical compositions but different block sequences were successfully synthesized by combination of ATRP mechanism and NRC or CuAAC chemistry. This versatile synthetic route might be used to derive series of copolymers with varied compositions. The self-assembly behaviour of copolymers was preliminarily studied and compared, and the results showed that the PS-b-PAA-b-PS and PAA-b-PS-b-PAA could give distinct cmc values and different sizes of micelles in selective solvent, which further enriches the related theory of structure–property relationship.

Acknowledgements

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