Polymer Chemistry

Accepted Manuscript

ROYAL SOCIETY OF CHEMISTRY

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Journal Name

RSCPublishing

ARTICLE

Cite this: DOI: 10.1039/x0xx00000x

A new strategy to prepare thermo-responsive multicompartment nanoparticles constructed with two diblock copolymers

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Received 00th January 2012,
Accepted 00th January 2012

DOI: 10.1039/x0xx00000x

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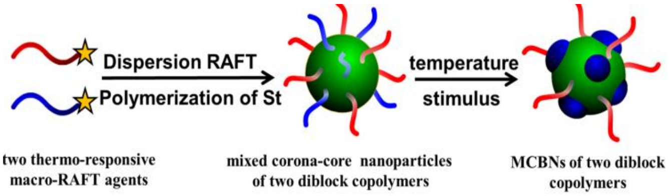
Abstract: Multicompartment block copolymer nanoparticles (MCBNs) constructed with two diblock copolymers of poly[*N*-(4-vinylbenzyl)-*N*,*N*-diethylamine)]-*b*-polystyrene (PVEA-*b*-PS) and poly[2-(dimethylamino) ethyl methacrylate]-*b*-polystyrene (PDMAEMA-*b*-PS) were prepared through the two macro-RAFT agents co-mediated dispersion polymerization. These MCBNs dispersed in water contain a 33 nm solvophobic core of the PS block, 5 nm discrete nodules of the PVEA block and a solvophilic corona of the PDMAEMA block. These MCBNs are thermo-responsive both in water and in methanol. In water, the corona-forming PDMAEMA block exhibits the soluble-to-insoluble phase transition at temperature above the phase-transition temperature (LCST) of 70 ^{0}C to deposit on the PS core of MCBNs. In methanol, the PVEA nodules on the PS core are dissolved at temperature below LCST of the PVEA block at 53 ^{0}C, and when temperature increases above LCST the PVEA block reversibly deposits on the PS core to form discrete PVEA nodules on the PS core. The prepared MCBNs showing thermo-response both in water and in methanol are believed to be useful in nanotechnology.

1 Introduction

Multicompartment block copolymer nanoparticles (MCBNs) containing a solvophilic corona and a solvophobic microphase-separated core have gained considerable attention.[1,3] The special structure of MCBNs affords their potential application in simultaneously entrapping or releasing different hydrophobic ingredients.[1,2] Generally, there are two strategies proposed to prepare MCBNs. The most straightforward method is the self-assembly of linear ABC block terpolymers, ABC miktoarm star terpolymers and multiblock copolymers such as ABCA and ABCBA in the block-selective solvent for the A block, in which A is the solvophilic block and B and C are incompatible solvophobic blocks.[19] The second strategy to prepare MCBNs is through the co-micellization or blending of two or more different block copolymers, such as AB with AC or ABC block terpolymers or ABC miktoarm star terpolymers with AB block copolymers in a suitable block-selective solvent.[20-33] Although two strategies have been proposed, there remains great challenge or inconvenience in synthesis of well-defined MCBNs. For examples, synthesis of linear multiblock copolymers or ABC miktoarm star terpolymers is usually involved in the first strategy,[19] which is a laborious work and therefore its application is somewhat limited. In the second strategy of co-micellization or blending of two or more different block copolymers, besides the targeted MCBNs constructed with two block copolymers, nonergodic micelles constructed with one individual block copolymer are unavoidably formed.[34,35] Furthermore, the two strategies suffer from the same disadvantage that diluted MCBNs with polymer concentration generally below 1% are only prepared.[4-33] Till now, convenient and efficient synthesis of well-defined MCBNs is still a challenge in polymer science.

Recently, the macromolecular RAFT agent (macro-RAFT agent) mediated dispersion polymerization is demonstrated to be an efficient and one-pot synthesis of concentrated block copolymer nano-objects with polymer concentration up to 30%.[36-39] Following this method, a soluble macro-RAFT agent acting as A block, the monomer to form the insoluble B block and initiator are one-pot added, and RAFT polymerization under dispersion condition is performed. Initially, the synthesized AB diblock copolymer is molecularly soluble, since the B block is relatively short. With the proceeding of the RAFT polymerization, the solvophobic B block extends, and onset micellization of the synthesized AB diblock copolymer occurs to form micellar nuclei at a critic polymerization degree (DP) of the solvophobic B block, and ultimately the micellar nuclei grow with extension of the solvophobic B block into diblock copolymer nano-objects.

Thermo-responsive nanoparticles of block copolymers can tune physical properties through the phase transition of the thermo-responsive block at the lower critical solution temperature (LCST) or the upper critical solution temperature (UCST).[40-42] Up to the present, various thermo-responsive block copolymer nanoparticles have been prepared, and the thermo-response has been investigated.[43-51] However, most of thermo-responsive block copolymer nanoparticles make response to the temperature stimulus just in one solvent, *e.g.* in water. In a common organic solvent of alcohol, they make no response to the temperature stimulus at all. This is not a surprise, since most of the thermo-responsive polymers such as poly(*N*-isopropylacrylamide),[51,52] poly[oligo(ethylene glycol) (meth)acrylate],[53] poly(2-alkyl-2-oxazolines),[54] and poly[2-(dimethylamino) ethyl methacrylate],[47,48,55-56] which exhibit soluble-to-insoluble phase transition at LCST in water, are soluble in alcohol. In our previous study,[57] a new family of thermo-responsive polymer based on poly[*N*-(4-vinylbenzyl)-*N*,*N*-diethylamine] (PVEA) which exhibits the LCST-type phase transition in methanol has been reported. Thus, it is reasonable deduced that, block copolymer nanoparticles containing both an alcohol-thermo-responsive PVEA block and an aqueous-thermo-responsive block of poly[2-(dimethylamino) ethyl methacrylate] (PDMAEMA) should give response to the temperature stimulus both in alcohol and in water.



Scheme 1. Synthesis of MCBNs through two macro-RAFT agents co-mediated dispersion polymerization.

In this contribution, thermo-responsive MCBNs constructed with two diblock copolymers of poly[*N*-(4-vinylbenzyl)-*N*,*N*-diethylamine)]-*b*-polystyrene (PVEA-*b*-PS) and poly[2-(dimethylamino) ethyl methacrylate]-*b*-polystyrene (PDMAEMA-*b*-PS) were prepared through the two macro-RAFT agents co-mediated dispersion polymerization as shown in Scheme 1. The synthesis includes (1) the two macro-RAFT agents co-mediated dispersion polymerization to prepare mixed corona-core nanoparticles of PVEA-*b*-PS/PDMAEMA-*b*-PS containing a mixed PVEA/PDMAEMA corona and a solvophobic PS core and (2) deposition of the thermo-responsive corona-forming PVEA or PDMAEMA block onto the solvophobic PS core by temperature stimulus to prepare MCBNs constructed with two diblock copolymers of PVEA-*b*-PS/PDMAEMA-*b*-PS. The synthesis shows that well-defined MCBNs containing a core of the PS block, discrete nodules of the PVEA block on the PS core and a solvophilic corona of the PDMAEMA block can be conveniently prepared through the two macro-RAFT agents co-mediated dispersion polymerization, and the thermo-response of the synthesized MCBNs both in methanol and in water is also demonstrated.

2 Experimental

2.1 Materials

The monomer of *N*-(4-vinylbenzyl)-*N*,*N*-diethylamine (VEA) was synthesized by the nucleophilic substitution reaction between 4-chloromethylstyrene (CMS, >97%, Alfa) and diethylamine (DEA, >99%, Tianjin Ruijinte Chemical Reagent) as discussed elsewhere.[58] The monomer of 2-(dimethylamino) ethyl methacrylate (DMAEMA, 98%, Alfa) was dried with CaH_2 overnight and distilled under reduced pressure prior to use. Styrene (St, >98%, Tianjin Chemical Company) was distilled under vacuum and stored at -5 °C prior to use. 2,2'-Azobis(2-methylpropionitrile) (AIBN, >99%, Tianjin Chemical Company) was recrystallized from ethanol before being used. 4-Cyano-4-(dodecylsulfanylthiocarbonyl) sulfanyl pentanoic acid (CDTPA) was synthesized as discussed elsewhere.[59] Other chemical reagents were analytic grade and were used as received. Deionized water was used in the present experiments.

2.2 Synthesis of the macro-RAFT agent of poly[*N*-(4-vinylbenzyl)-*N*,*N*-diethylamine)] trithiocarbonate

The macro-RAFT agent of poly[*N*-(4-vinylbenzyl)-*N*,*N*-diethylamine)] trithiocarbonate (PVEA-TTC) was prepared by solution RAFT polymerization of VEA in 1,4-dioxane at 70 ^{o}C using CDTPA as RAFT agent and AIBN as initiator. Into a 50 mL Schlenk flask with a magnetic bar, VEA (15.00 g, 79.2 mmol), CDTPA (0.229 g, 0.57 mmol), and AIBN (31.0 mg, 0.19 mmol) dissolved in 1,4-dioxane (5.00 g) were added. This flask content was immersed in ice water and was degassed with nitrogen to remove oxygen. Polymerization was performed at 70 ^{o}C for 24 h and then was quenched by rapid cooling upon immersion of the flask in iced water. The monomer conversion, 64.5%, was detected by ^{1}H NMR analysis through comparing the integral area of the characteristic signals at $\delta = 2.53$ ppm and at $\delta = 5.20$ ppm. To collect the PVEA-TTC macro-RAFT agent, the flask content was added dropwise into the ethanol/water mixture (6/5 by weight), washed twice with the ethanol/water mixture, and then the precipitation was collected and dried at room temperature under vacuum to afford pale yellow powder of PVEA-TTC.

2.3 Synthesis of the macro-RAFT agent of poly[2-(dimethylamino) ethyl methacrylate] trithiocarbonate

The macro-RAFT agent of poly[2-(dimethylamino) ethyl methacrylate] trithiocarbonate (PDMAEMA-TTC) was synthesized by solution RAFT polymerization of DMAEMA in 1,4-dioxane using AIBN as initiator and CDTPA as RAFT agent. Into a 50 mL Schlenk flask with a magnetic bar, DMAEMA (10.00 g, 63.7 mmol), CDTPA (0.214 g, 0.53 mmol), and AIBN (10.9 mg, 0.066 mmol) dissolved in 1,4-dioxane (10.00 g) were added. The solution was degassed with nitrogen at 0 ^{o}C, and then the flask content was immersed into a preheated oil bath at 70 ^{o}C for 5 h. The polymerization was quenched by rapid cooling upon immersion of the flask in iced water. The monomer conversion, 66.0%, was detected by ^{1}H NMR analysis through comparing the integral area of the characteristic signals at $\delta = 5.56$ ppm and at $\delta = 4.07$ ppm. To collect the polymer, the flask content was precipitated in *n*-hexane at 0 ^{o}C, and dried under vacuum at room temperature overnight to afford yellow powder of PDMAEMA-TTC.

2.4 Synthesis of MCBNs through the two macro-RAFT agents co-mediated dispersion polymerization

The two macro-RAFT agents co-mediated dispersion polymerization of styrene was performed in the 95/5 ethanol/water mixture at 70 ^{o}C under $[St]_0:[PVEA\text{-}TTC]_0:[PDMAEMA\text{-}TTC]_0:[AIBN]_0 = 1200:2:2:1$ with the fed styrene monomer to the solvent at 20 wt%. Into a Schlenk flask with a magnetic bar, PVEA-TTC (0.280 g, 0.016 mmol), PDMAEMA-TTC (0.206 g, 0.016 mmol), St (1.00 g, 9.62 mmol) and AIBN (1.32 mg, 0.0080 mmol) dissolved in the 95/5 ethanol/water mixture (5.00 g) were added. The solution was degassed with nitrogen at 0 ^{o}C, and then the polymerization was performed at 70 ^{o}C under vigorous stirring. After 32 h of polymerization at 75.0% monomer conversion, the polymerization was quenched by rapid cooling upon immersion of the flask in iced water to afford the colloidal dispersion of PVEA-*b*-PS/PDMAEMA-*b*-PS with polymer concentration at 19 wt%. The conversion of the styrene monomer was detected by UV-vis analysis at 245 nm as discussed elsewhere.[60]

The resultant colloidal dispersion was dialyzed against methanol at room temperature (20-25 ^{0}C) for three days (molecular weight cutoff: 7000 Da) to remove the residual St monomer to afford the block copolymer nanoparticles of PVEA-*b*-PS/PDMAEMA-*b*-PS dispersed in methanol. To obtain the aqueous colloidal dispersion, part of the methanol dispersion of the PVEA-*b*-PS/PDMAEMA-*b*-PS nanoparticles was further dialyzed against water at room temperature for three days (molecular weight cutoff: 7000 Da) to remove the methanol solvent, and the aqueous dispersion of the PVEA-*b*-PS/PDMAEMA-*b*-PS nanoparticles was kept at room temperature for next use.

To collect the mixture of PVEA-*b*-PS/PDMAEMA-*b*-PS, part of the methanol dispersion of the PVEA-*b*-PS/PDMAEMA-*b*-PS nanoparticles was concentrated by rotary evaporation under reduced pressure, and dried under vacuum at room temperature overnight to afford pale yellow powder of the PVEA-*b*-PS/PDMAEMA-*b*-PS mixture.

2.5 Separation of the PVEA-*b*-PS/PDMAEMA-*b*-PS mixture

To separate PVEA-*b*-PS or PDMAEMA-*b*-PS from the PVEA-*b*-PS/PDMAEMA-*b*-PS mixture, the PVEA-*b*-PS/PDMAEMA-*b*-PS mixture (0.5 g) was dispersed in acetone (2 mL) at room temperature, magnetically stirred for 1 h, and then separated by centrifugation (12500 r/min, 30 min). The supernatant solution was collected, and the solvent of acetone was removed by rotary evaporation under reduced pressure to afford the PDMAEMA-*b*-PS diblock copolymer. The precipitate was collected, dispersed in acetone (10 mL), magnetically stirred for 1 h, and then separated by centrifugation (12500 r/min, 30 min). The supernatant solution was discarded and the precipitate was collected. The collected precipitate was washed with acetone (5 mL × 4) and then dried under vacuum at room temperature to afford the PVEA-*b*-PS diblock copolymer. The success separation of the PDMAEMA-*b*-PS/PVEA-*b*-PS diblock copolymer mixture was judged by ^{1}H NMR analysis of the separated PDMAEMA-*b*-PS or PVEA-*b*-PS diblock copolymer.

2.6 Characterization

The ^{1}H NMR analysis was performed on a Bruker Avance III 400 MHz NMR spectrometer using $CDCl_3$ as solvent. The molecular weight and the polydispersity index (PDI, PDI = M_w/M_n) of the synthesized polymers were determined by gel permeation chromatography (GPC) equipped with a Waters 600E GPC system, where THF was used as eluent and the narrow-polydispersity polystyrene was used as calibration standard. The transmission electron microscope (TEM) observation was performed using a Tecnai G^2 F20 electron microscope at an acceleration of 200 kV, in which a small drop of the diluted dispersion was deposited onto a piece of copper grid, dried at room temperature, stained initially by phosphotungstic acid at room temperature and then by RuO_4 vapour at 50 ℃ for 30 min, and lastly observed by TEM. The phase-transition temperature or LCST of the thermo-responsive polymers were determined by turbidity analysis at 500 nm on a Varian 100 UV-vis spectrophotometer equipped with a thermo-regulator (± 0.1 ^{o}C) with the heating rate at 1 ^{o}C/min. The LCST values were determined as the middle point of the transmittance change. The dynamic light scattering (DLS) analysis was performed on a Nano-ZS90 (Malvern) laser light scattering spectrometer with He-Ne laser at the wavelength of 633 nm at 90^o angle, in which the hydrodynamic diameter of MCBNs with the diluted polymer concentration (~0.01 wt%) was determined by intensity following the CONTIN method.

3 Results and discussion

3.1 Synthesis and thermo-response of PVEA-TTC and PDMAEMA-TTC

The PVEA-TTC macro-RAFT agent was synthesized via RAFT polymerization of VEA in 1,4-dioxane under $[VEA]_0:[CDTPA]_0:[AIBN]_0$ = 420:3:1. The solution RAFT polymerization of VEA was quenched at 64.5% monomer conversion. The theoretical number-average molecular weight ($M_{n,th}$) of PVEA-TTC is 17.5 kg/mol. The THF based GPC analysis gives the polymer molecular weight $M_{n,GPC}$ = 9.8 kg/mol, which is much lower than $M_{n,th}$, and the PDI value is 1.24 (Figure 1). The underestimated $M_{n,GPC}$ of PVEA-TTC is possibly ascribed to the interaction between the tertiary amine groups in the PVEA backbone and the GPC columns. Besides, the GPC analysis is based on the calibration with the non-polar polystyrene standards, which also contributes to the underestimation in the molecular weight of the polar PVEA-TTC. The ^{1}H NMR spectrum of PVEA-TTC is shown in Figure 2A, from which the characteristic chemical shifts corresponding to the polymer backbone are clearly discerned. However, the chemical shift corresponding to the RAFT terminal δ = 1.26 ppm is partly overlapped with those of the polymer backbone. By assuming the signal at δ = 1.26 ppm being symmetrical, the polymer molecular weight $M_{n,NMR}$ of PVEA-TTC, 9.3 kg/mol, corresponding to DP = 47 can be determined following eqn S1 (seeing detail in Figure S1). It is found that $M_{n,NMR}$ is very close to $M_{n,GPC}$ determined by GPC analysis. In the next discussion, PVEA-TTC is labelled as $PVEA_{50}$-TTC, in which the DP is determined by $M_{n,GPC}$.

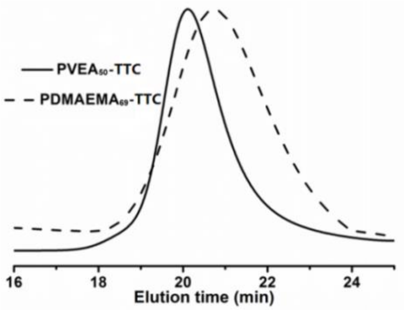


Figure 1. GPC traces of the $PVEA_{50}$-TTC and the $PDMAEMA_{69}$-TTC macro-RAFT agents.

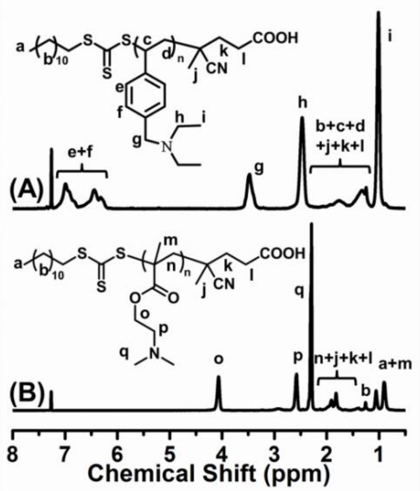


Figure 2. ^{1}H NMR spectra of $PVEA_{50}$-TTC (A) and $PDMAEMA_{69}$-TTC (B).

The PDMAEMA-TTC macro-RAFT agent was synthesized by RAFT polymerization of DMAEMA in 1,4-dioxane under $[DMAEMA]_0:[CDTPA]_0:[AIBN]_0$ = 960:8:1. The RAFT polymerization was quenched at 66.0% monomer conversion to ensure the narrowly dispersed molecular weight of the synthesized PDMAEMA-TTC. The theoretical number-average molecular weight ($M_{n,th}$) of PDMAEMA-TTC is 12.8 kg/mol. The THF based GPC analysis gives the polymer molecular weight $M_{n,GPC}$ = 7.2 kg/mol, which is lower than $M_{n,th}$, and the PDI value is 1.29 (Figure 1). The ^{1}H NMR spectrum of PDMAEMA is shown in Figure 2B. Based on the characteristic chemical shift at δ = 4.07 ppm [$C\boldsymbol{H}_2CH_2N(CH_3)_2$ in the PDMAEMA backbone] and the chemical shift at δ = 1.26 ppm [$CH_3(CH_2)_{10}CH_2S$ in the terminal group originated from the RAFT agent of CDTPA], the polymer molecular weight $M_{n,NMR}$ of the synthesized PDMAEMA-TTC at 11.2 kg/mol corresponding to DP = 69 is calculated, which is close to $M_{n,th}$. In the subsequent discussion, the synthesized PDMAEMA-TTC is labelled as PDMAEMA$_{69}$-TTC, in which the DP is determined by $M_{n,NMR}$.

The solubility of PVEA$_{50}$-TTC and PDMAEMA$_{69}$-TTC in methanol and in water is investigated. It is found that, PVEA$_{50}$-TTC is insoluble in water, and is soluble in methanol at temperature below the LCST of 52 ^{o}C (Figure S2), and becomes insoluble in methanol at temperature above LCST. PDMAEMA$_{69}$-TTC is soluble in methanol, and is soluble in water at temperature below LCST at 43 ^{o}C, and becomes insoluble in water at temperature above LCST. The LCST of PDMAEMA$_{69}$-TTC matches well with those reported elsewhere.[61] Besides the thermo-response, both PVEA and PDMAEMA are also pH-responsive due to the tethered amine group.[55-57] However, in the present study, just the thermo-response of MCBNs is investigated. To eliminate the pH effect on the thermo-response of MCBNs, neutral water or methanol was employed in the present study.

3.2 Synthesis of MCBNs through the two macro-RAFT agents co-mediated dispersion polymerization

The two macro-RAFT agents co-mediated dispersion polymerization of styrene was performed in the 95/5 ethanol/water mixture under $[St]_0:[PVEA\text{-}TTC]_0:[PDMAEMA\text{-}TTC]_0:[AIBN]_0$ = 1200:2:2:1. The 95/5 ethanol/water mixture is chosen as the polymerization medium, since it is a solvent for the fed monomer of St and the two macro-RAFT agents while the non-solvent for the PS block at the polymerization temperature, which is essential for the polymerization induced self-assembly for the *in situ* synthesized block copolymers of PVEA-*b*-PS and PDMAEMA-*b*-PS. Similarly with the individual macro-RAFT agent mediated dispersion polymerization, an initial homogeneous polymerization before 6 h and a subsequent heterogeneous polymerization were included in the present two macro-RAFT agents co-mediated dispersion polymerization. After 32 h of polymerization at 75.0% monomer conversion, the polymerization was quenched, and the *in situ* synthesized colloids were transferred into water at room temperature by dialysis and then checked by TEM. From the TEM image shown in Figure 3A, formation of uniform nanoparticles with the average diameter at 39 nm is concluded. To clarify whether the nanoparticles being constructed with the two diblock copolymers of PVEA-*b*-PS and PDMAEMA-*b*-PS or being constructed with one individual block copolymer, the individual macro-RAFT agent meditated dispersion polymerization under similar conditions with $[St]_0:[PVEA_{50}\text{-}TTC]_0:[AIBN]_0$ = 1200:4:1 or $[St]_0:[PDMAEMA_{69}\text{-}TTC]_0:[AIBN]_0$ = 1200:4:1 was performed and the nano-objects constructed with one individual block copolymer were checked by TEM. As shown in Figure S3, the PVEA$_{50}$-*b*-PS$_{390}$ nano-objects, which are the mixture of 94 nm vesicles and 41 nm nanoparticles, and the PDMAEMA$_{69}$-*b*-PS$_{162}$ nano-objects of 27 nm nanoparticles were formed at the two cases of the individual macro-RAFT agent meditated dispersion polymerization. It is found that, the present 39 nm nanoparticles prepared through the two macro-RAFT agents co-mediated dispersion polymerization are different from the PVEA$_{50}$-*b*-PS$_{390}$ nano-objects and the PDMAEMA$_{69}$-*b*-PS$_{162}$ nanoparticles, although the composition of the diblock copolymers in the PVEA$_{50}$-*b*-PS$_{390}$ nano-objects and in the PDMAEMA$_{69}$-*b*-PS$_{162}$ nanoparticles is similar as those in the present mixed nanoparticles. Note: see Figures S4-S5 for the characterization of the diblock copolymers in the nano-objects constructed with one individual diblock copolymer. This result suggests that the present 39 nm nanoparticles should be constructed with the two block copolymers of PVEA-*b*-PS and PDMAEMA-PS.

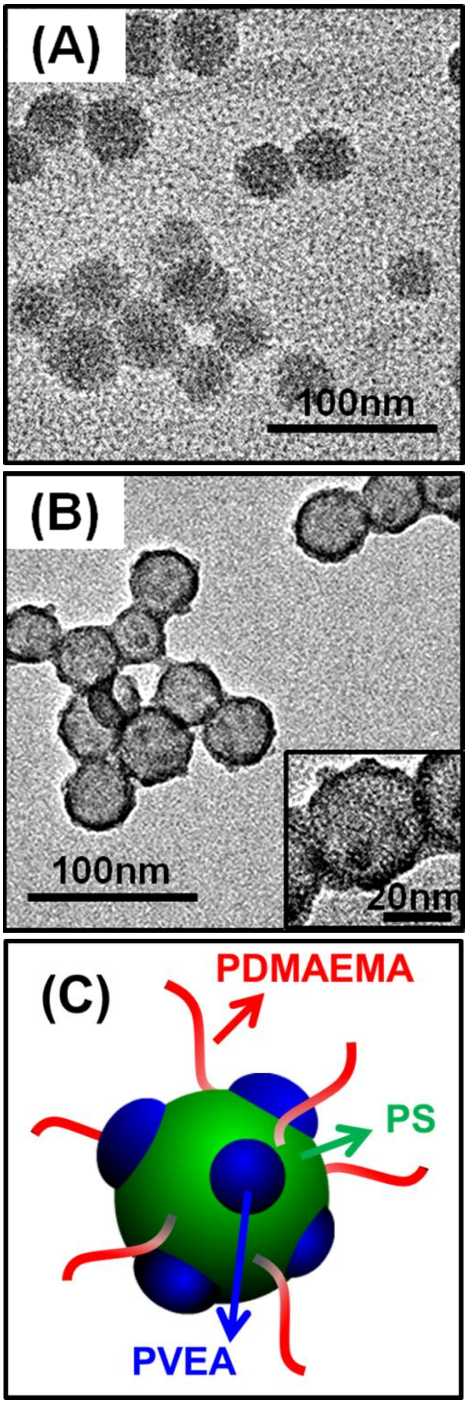


Figure 3. TEM images of the MCBNs of PVEA$_{50}$-*b*-PS$_{373}$/PDMAEMA$_{69}$-*b*-PS$_{186}$ dispersed in water (A, B) and the schematic structure of MCBNs (C).

To further confirm the structure of the nanoparticles prepared through the two macro-RAFT agents co-mediated dispersion polymerization, the nanoparticles distributed in water were stained jointly with phosphotungstic acid and RuO_4 vapour as discussed elsewhere,[62,63] and then checked by TEM. This jointed staining initially with phosphotungstic acid and then with RuO_4 helps to discern the solvophobic PVEA in the block copolymer nanoparticles. Figure 3B show the TEM images of such stained nanoparticles, in which the light gray region is ascribed to the PS core and the dark domains is due to the RuO_4-stained PVEA phase, and whereas the solvophilic corona of the PDMAEMA block is not visible (note: PS and PVEA are insoluble in water and PDMAEMA is soluble in water at room temperature). Therefore, formation of MCBNs constructed with PVEA-*b*-PS/PDMAEMA-*b*-PS containing a PS core with the average diameter at 33 nm, 5 nm discrete PVEA nodules on the PS core and a PDMAEMA corona as schematically shown in Figure 3C is sufficiently concluded. Note: due to the small size and the slight dark difference between the PVEA and PS domains, approximate estimation of the size of the PVEA nodules is made.

The formation of the discrete PVEA nodules on the PS core is partly ascribed to the PVEA block being immiscible with PS as discussed previously.[64.] Besides, the formation of discrete PVEA nodules but not an uninterrupted shell on the PS core is due to the PVEA chains being segregated by the neighboring PDMAEMA chains during the PVEA chains depositing on the PS core of mixed corona-core nanoparticles as shown in Scheme 1.

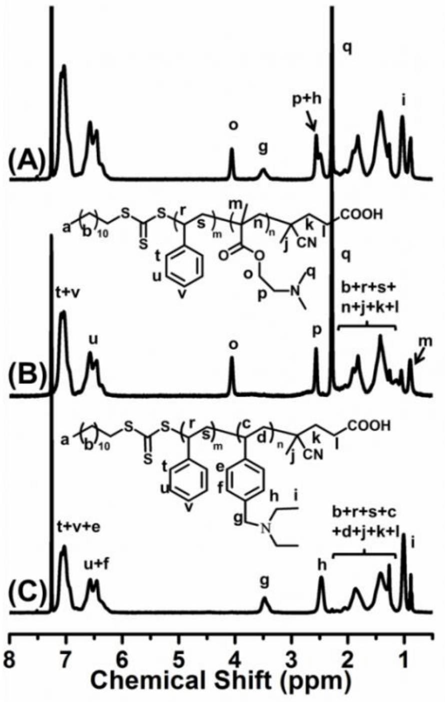


Figure 4. ^{1}H NMR spectra of the $PVEA_{50}$-*b*-PS_{373}/$PDMAEMA_{69}$-*b*-PS_{186} mixture in MCBNs (A), the separated $PDMAEMA_{69}$-*b*-PS_{186} diblock copolymer (B) and the separated $PVEA_{50}$-*b*-PS_{373} diblock copolymer (C).

Now, we intend to detect the detailed composition of MCBNs, including the molar ratio of PVEA-*b*-PS/PDMAEMA-*b*-PS in MCBNs and the chemical composition of the PVEA-*b*-PS and PDMAEMA-*b*-PS diblock copolymers. To achieve this goal, separation of the individual diblock copolymers from the PVEA-*b*-PS/PDMAEMA-*b*-PS mixture is performed. Since the synthesized PDMAEMA-*b*-PS is soluble in acetone at room temperature whereas PVEA-*b*-PS is insoluble in acetone, separation following the procedures introduced in the Experimental section was made. The diblock copolymers before separation and after separation were characterized by ^{1}H NMR analysis (Figure 4) and GPC analysis (Figure 5). By checking the characteristic chemical shift at $\delta = 4.07$ ppm [$CH_2CH_2N(CH_3)_2$ in the PDMAEMA block] and $\delta = 3.48$ ppm [$PhCH_2N(CH_2CH_3)_2$ in the PVEA block] in the ^{1}H NMR spectra of the diblock copolymers before and after separation shown in Figure 4, it is concluded that successful separation is achieved. From the ^{1}H NMR spectra of the PVEA-*b*-PS/PDMAEMA-*b*-PS mixture (Figure 4A), the molar ratio of PVEA-*b*-PS/PDMAEMA-*b*-PS in MCBNs, 1.07, is determined by the integration areas of the signal at $\delta = 3.48$ ppm and at $\delta = 4.07$ ppm and the DP of the two macro-RAFT agents following eqn S2. It is found that, the molar ratio of PVEA-*b*-PS/PDMAEMA-*b*-PS in MCBNs is very close to that of the feeding macro-RAFT agents of $PVEA_{50}$-TTC/$PDMAEMA_{69}$-TTC (1.07 *vs* 1), suggesting almost all of the two macro-RAFT agents are block-extended to form the corresponding diblock copolymers in MCBNs. From the ^{1}H NMR spectra of the separated diblock copolymers of PDMAEMA-*b*-PS (Figure 4B) and PVEA-*b*-PS (Figure 4C), the molecular weight $M_{n,NMR}$ of PDMAEMA-*b*-PS at 41.0 kg/mol and $M_{n,NMR}$ of PVEA-*b*-PS at 51.3 kg/mol are calculated. From the GPC traces of the diblock copolymers before and after separation, the molecular weight $M_{n,GPC}$ of the PVEA-*b*-PS/PDMAEMA-*b*-PS mixture and the separated PVEA-*b*-PS and PDMAEMA-*b*-PS diblock copolymers and their PDI values are obtained and are indicated out by the insets in Figure 5. It is found that, the $M_{n,GPC}$ of PDMAEMA-*b*-PS is slightly lower than the average value of the PVEA-*b*-PS/PDMAEMA-*b*-PS mixture, and the $M_{n,GPC}$ of PVEA-*b*-PS is larger than the average value of the PVEA-*b*-PS/PDMAEMA-*b*-PS mixture, respectively. The reason of the different $M_{n,GPC}$ of PDMAEMA-*b*-PS and PVEA-*b*-PS but the monomodal GPC traces of the PVEA-*b*-PS/PDMAEMA-*b*-PS mixture is not very clear, and possibly the different interaction between the N-containing polymers of PVEA-*b*-PS and PDMAEMA-*b*-PS with the GPC columns is involved.

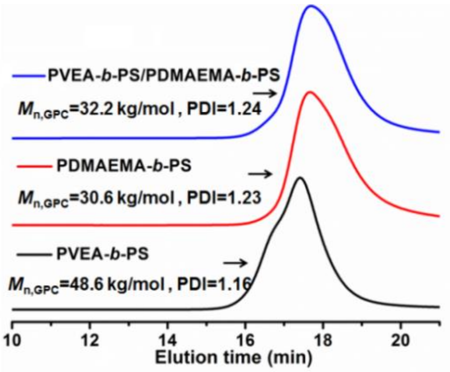


Figure 5. GPC traces of the $PVEA_{50}$-*b*-PS_{373}/$PDMAEMA_{69}$-*b*-PS_{186} mixture in MCBNs (A), the separated $PDMAEMA_{69}$-*b*-PS_{186} diblock copolymer (B) and the separated $PVEA_{50}$-*b*-PS_{373} diblock copolymer (C).

3.3 Thermo-response of MCBNs

The prepared MCBNs constructed with PVEA-*b*-PS/PDMAEMA-*b*-PS contain two thermo-responsive blocks of PVEA and PDMAEMA, in which PDMAEMA shows the soluble-to-insoluble phase at LCST in water and PVEA shows the soluble-to-insoluble phase at LCST in methanol, respectively, and therefore their temperature-sensitive response both in methanol and in water is expected.

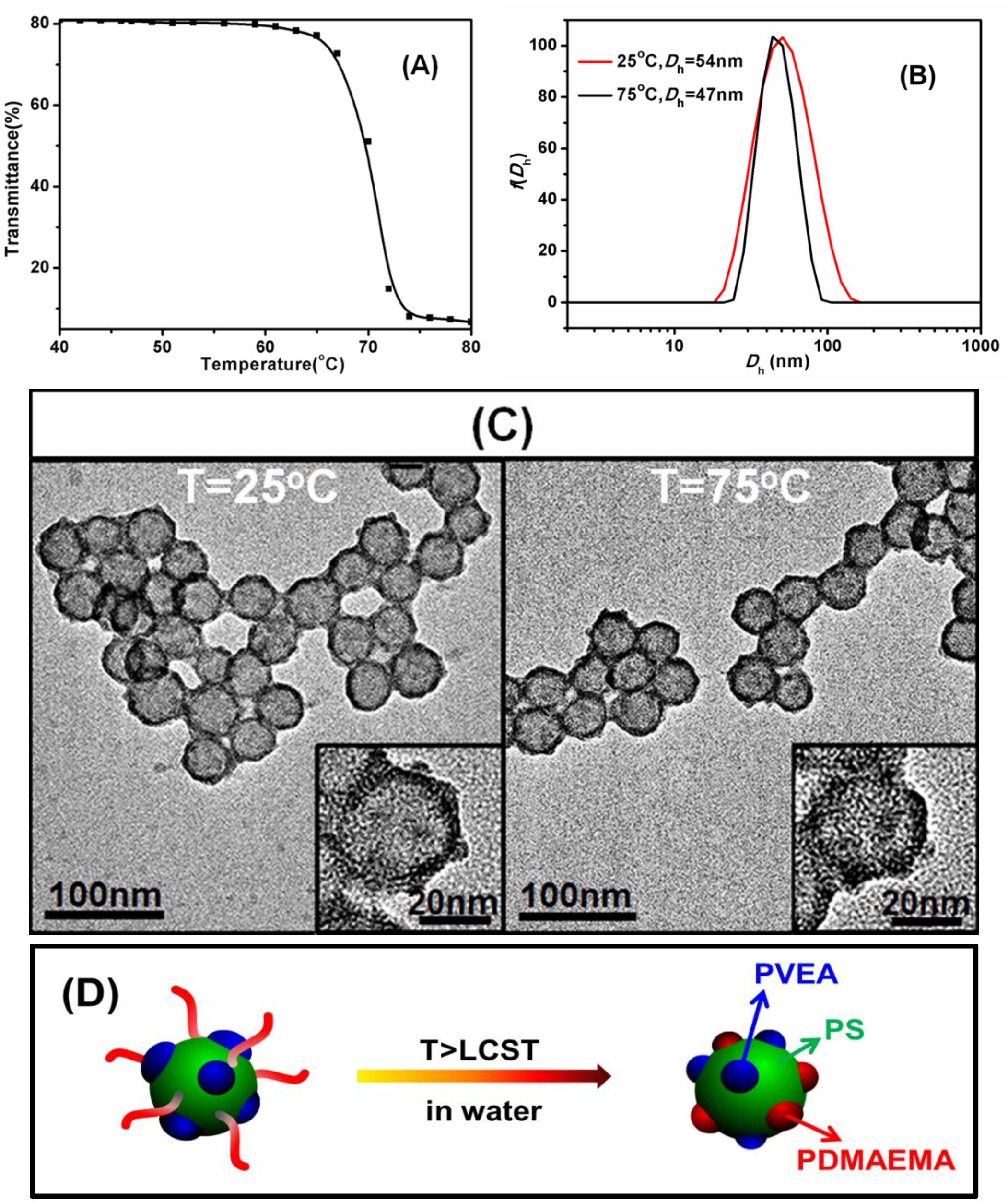


Figure 6. Temperature dependent transmittance of the 0.1 wt% aqueous solution of MCBNs (A), the hydrodynamic diameter distribution (B) and the TEM images (C) of MCBNs at temperature below and above LCST, and the schematic thermo-response of MCBNs in water (D).

Figure 6A shows the temperature dependent transmittance of the aqueous dispersion of MCBNs, from which the phase transition temperature of the PDMAEMA block on the PS core of MCBNs at 70 ^{o}C is obtained. Compared with the LCST of the reference PDMAEMA$_{69}$-TTC at 43 ^{o}C (Figure S2), the LCST of the PDMAEMA block on MCBNs is much higher, and the reason is possibly due to the steric repulsion among the crowded PDMAEMA chains tethered on the PS core of MCBNs, which retards the soluble-to-insoluble transition of the PDMAEMA chains as discussed elsewhere.[48] DLS analysis of the diluted aqueous dispersion of MCBNs shows that the average hydrodynamic diameter D_h of MCBNs decreases from 54 to 47 nm when the temperature increases from 25 ^{o}C (below LCST) to 75 ^{o}C (above LCST) (Figure 6B), confirming the soluble-to-insoluble transition of the tethered PDMAEMA chains on the PS core of MCBNs. The soluble-to-insoluble transition of the tethered PDMAEMA chains on the PS core of MCBNs is expected to form new PDMAEMA nodules on the PS core, since PDMAEMA is immiscible with PS as discussed elsewhere.[48] To confirm this hypothesis, MCBNs dispersed in water at 25 ^{0}C below LCST and at 75 ^{o}C above LCST are checked by TEM, respectively. As shown in Figure 6C, two MCBNs containing a PS core with the average diameter at 33 nm and 5-7 nm discrete nodules are observed at the two cases of temperature. The nodules on MCBNs dispersed in water at 25 ^{0}C below LCST is ascribed to the PVEA chains as discussed above, and the nodules on MCBNs dispersed in water at 75 ^{0}C above LCST should be ascribed to the PVEA and PDMAEMA chains. However, due to the very similar size of the PVEA and PDMAEMA nodules, they can not be identified from each other by TEM. Despite this, the thermo-response of MCBNs in water as shown in Figure 6D is expected.

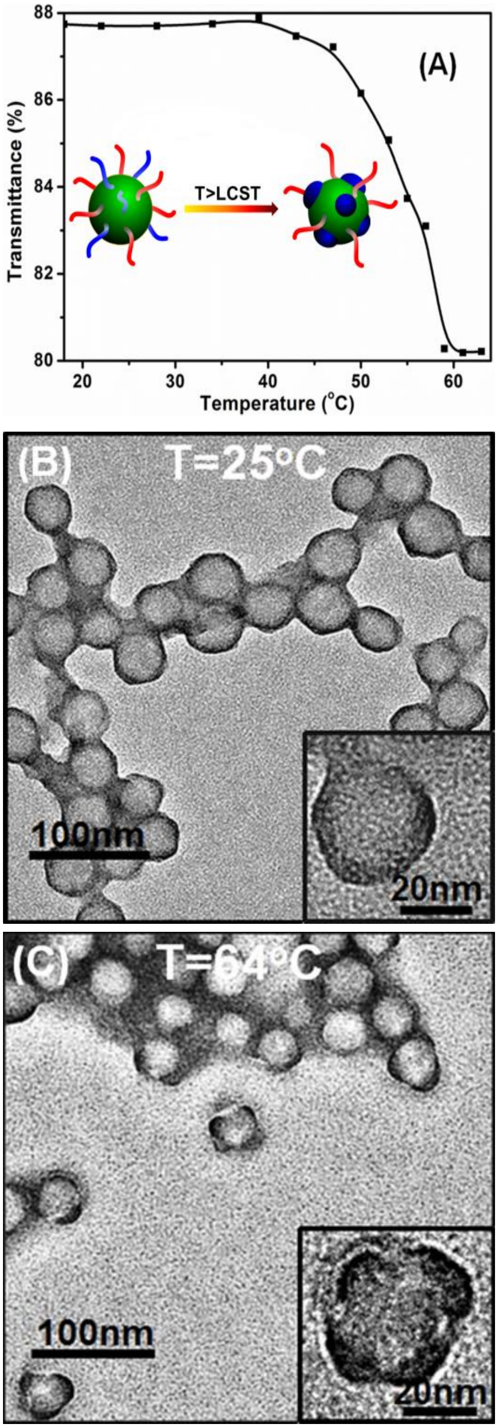


Figure 7. Temperature dependent transmittance of the 0.1 wt% methanol solution of MCBNs (A), the TEM images of MCBNs formed in methanol at 25 ^{o}C (B) and at 64 ^{o}C (C).

Lastly, the thermo-response of MCBNs in methanol is investigated. From the temperature dependent transmittance of the methanol dispersion of MCBNs shown in Figure 7A, the thermo-response of MCBNs in methanol is concluded. The LCST of the MCBNs in methanol is 53 ^{o}C, which is slightly higher than that of PVEA$_{50}$-TTC at 52 ^{o}C. In methanol at temperature below LCST, both the PVEA and PDMAEMA chains are soluble, and therefore the nanoparticles should have corona-core structure, in which the PVEA and PDMAEMA chains form the mixed corona and the PS chains form the core; in methanol at temperature above LCST, MCBNs containing a solvophobic PS core, discrete PVEA nodules on the PS core and a solvophilic PDMAEMA corona are expected to form as shown by the insets in Figure 7A. The TEM images showed in Figure 7B and 7C, in which 36 nm corona-core nanoparticles and MCBNs containing a 33 nm PS core and 9 nm PVEA nodules on the PS core are observed, respectively, confirm the speculation. Note: the soluble corona of PVEA/PDMAEMA in the corona-core nanoparticles and the soluble PDMAEMA corona in MCBNs are invisible in the TEM images. Interestingly, the size of the PVEA nodules on the MCBNs dispersed in methanol at 64 ^{o}C is much larger than those of the PVEA nodules on the MCBNs dispersed in water 25 ^{o}C (5 nm vs 9 nm), although the two MCBNs have a PS core with the similar size at 33 nm. This result shows that, more PVEA chains are aggregated together in methanol at temperature above LCST than those in water to form the discrete PVEA nodules on the PS core, and it suggests that the size of the nodules on MCBNs may be tuned by the deposition procedures such as the solvent character. Also, it is approximately calculated that the number of the PVEA nodules on the PS core of MCBNs in methanol is just 20% ($5^3/9^3 \approx 20\%$) of those of MCBNs in water.

Conclusions

MCBNs constructed with two diblock copolymers of PVEA-*b*-PS and PDMAEMA-*b*-PS were prepared through the two macro-RAFT agents co-mediated dispersion polymerization. The synthesis includes the initial two macro-RAFT agents co-mediated dispersion polymerization of styrene in the 95/5 ethanol/water mixture to prepare mixed corona-core nanoparticles of PVEA-*b*-PS/PDMAEMA-*b*-PS containing a solvophilic corona of the PVEA/PDMAEMA blocks and a solvophobic core of the PS block and the subsequent deposition of the corona-forming PVEA block onto the solvophobic PS core to prepare MCBNs dispersed in water. The synthesis results show that well-defined MCBNs containing a 33 nm PS core, 5 nm discrete PVEA nodules on the PS core and a PDMAEMA corona with polymer concentration at 20% can be conveniently prepared. These MCBNs are thermo-responsive both in water and in methanol. In water, the corona-forming PDMAEMA block exhibits the soluble-to-insoluble phase transition at temperature above LCST of 70 ^{0}C and deposits on the PS core of MCBNs. In methanol at temperature below LCST of the PVEA block at 25 ^{0}C, both the PVEA and PDMAEMA chains are soluble, and the block copolymer nanoparticles are composed of a mixed PVEA/PDMAEMA corona and a PS core. When temperature increases above LCST, the mixed corona-core nanoparticles convert into MCBNs with 9 nm PVEA nodules on the PS core. The proposed two macro-RAFT agents co-mediated dispersion polymerization is believed to be a valid way to prepared block copolymer nanoparticles constructed with two or more diblock copolymers, and the prepared MCBNs showing thermo-response both in water and in methanol are believed to be useful in nanotechnology.

Acknowledgements

The financial support by National Science Foundation of China (№ 21274066 and 21474054) and PCSIRT (IRT1257) is gratefully acknowledged.

Notes and references

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Electronic Supplementary Information (ESI) available: See DOI: 10.1039/b000000x/

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