Synthesis of Amphiphilic and Thermoresponsive ABC Miktoarm Star Terpolymer via a Combination of Consecutive Click Reactions and Atom Transfer Radical Polymerization

CHANGHUA LI, ZHISHEN GE, HEWEN LIU, SHIYONG LIU

CAS Key Laboratory of Soft Matter Chemistry, Department of Polymer Science and Engineering, Hefei National Laboratory for Physical Sciences at the Microscale, University of Science and Technology of China, Hefei, Anhui 230026, China

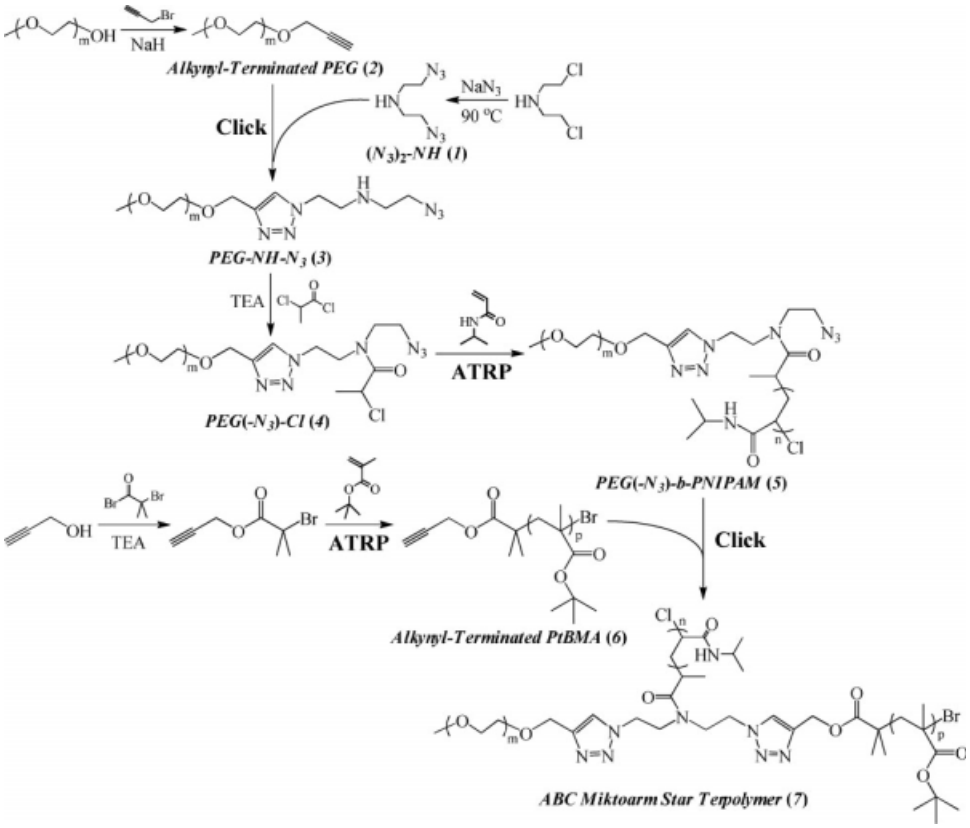
Received 8 March 2009; accepted 7 April 2009
DOI: 10.1002/pola.23461
Published online in Wiley InterScience (www.interscience.wiley.com).

ABSTRACT: Well-defined amphiphilic and thermoresponsive ABC miktoarm star terpolymer consisting of poly(ethylene glycol), poly(*tert*-butyl methacrylate), and poly(*N*-isopropylacrylamide) arms, PEG(-*b*-P*t*BMA)-*b*-PNIPAM, was synthesized via a combination of consecutive click reactions and atom transfer radical polymerization (ATRP). Click reaction of monoalkynyl-terminated PEG with a trifunctional core molecule bis(2-azidoethyl)amine, $(N_3)_2$—*NH*, afforded difunctional PEG possessing an azido and a secondary amine moiety at the chain end, PEG-*NH*—N_3. Next, the amidation of PEG-*NH*—N_3 with 2-chloropropionyl chloride led to PEG-based ATRP macroinitiator, PEG(—N_3)—*Cl*. The subsequent ATRP of *N*-isopropylacrylamide (NIPAM) using PEG(—N_3)—*Cl* as the macroinitiator led to PEG(—N_3)-*b*-PNIPAM bearing an azido moiety at the diblock junction point. Finally, well-defined ABC miktoarm star terpolymer, PEG(-*b*-P*t*BMA)-*b*-PNIPAM, was prepared via the click reaction of PEG(—N_3)-*b*-PNIPAM with monoalkynyl-terminated P*t*BMA. In aqueous solution, the obtained ABC miktoarm star terpolymer self-assembles into micelles consisting of P*t*BMA cores and hybrid PEG/PNIPAM coronas, which are characterized by dynamic and static laser light scattering, and transmission electron microscopy. On heating above the phase transition temperature of PNIPAM in the hybrid corona, micelles initially formed at lower temperatures undergo further structural rearrangement and fuse into much larger aggregates solely stabilized by PEG coronas. © 2009 Wiley Periodicals, Inc. J Polym Sci Part A: Polym Chem 47: 4001–4013, 2009
Keywords: atom transfer radical polymerization (ATRP); block copolymers; supramolecular structures

INTRODUCTION

Compared to AB and ABC linear block copolymers, the unique chain sequence arrangement in ABC miktoarm star polymers endows them with special properties in solution and bulk states.[1–4] The first few examples of the preparation of ABC miktoarm star terpolymers exclusively employed anionic polymerization, relying on the strict control of molar ratios between reactive species.[5–13] With the advent of controlled radical polymerizations, such as nitroxide-mediated radical polymerization (NMP), atom transfer radical polymerization (ATRP), and reversible addition-fragmentation chain transfer (RAFT) polymerization, the once challenging task of synthesizing ABC

Correspondence to: S. Liu (E-mail: sliu@ustc.edu.cn)
Journal of Polymer Science: Part A: Polymer Chemistry, Vol. 47, 4001–4013 (2009)



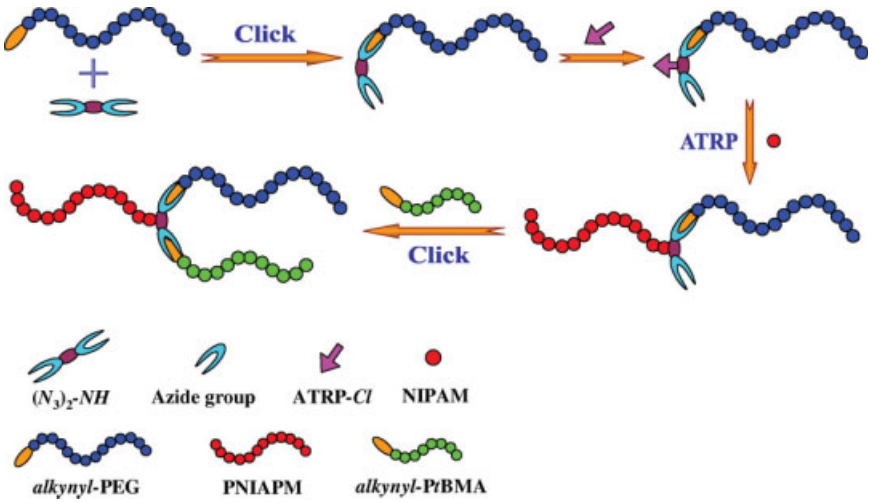
Scheme 1. Synthetic routes employed for the synthesis of well-defined amphiphilic PEG(-*b*-P*t*BMA)-*b*-PNIPAM ABC miktoarm star terpolymer (**7**) via a combination of consecutive click reactions and ATRP.

miktoarm star polymers has been rendered much easier.[14–19]

Feng and Pan[14] successful prepared ABC miktoarm star terpolymers consisting of polystyrene (PS), poly(methyl acrylate) (PMA), and poly(ethylene glycol) (PEG) via successive RAFT polymerization of styrene, maleic anhydride (MAh), and methyl acrylate, followed by the esterification reaction with monohydroxyl-terminated PEG. This strategy takes advantage of MAh's inability to homopolymerize during the RAFT process, and only one MAh unit is incorporated at the diblock junction point. A combination of controlled radical polymerization techniques, ring-opening polymerization (ROP), and Diels-Alder (DA) reaction has also led to the facile preparation of a variety of miktoarm star terpolymers.[15–19]

In the last few years, click reaction has been introduced into the synthesis of novel polymeric materials.[20–30] Tunca and coworkers[22] reported a few excellent works concerning the preparation of ABC miktoarm star terpolymers via a combination of ATRP, NMP, ROP, and click reaction. The introduction of click technique allows the covalent linkage of a well-defined precursor arm into the star terpolymer. They also reported the one-pot synthesis of miktoarm star terpolymers, taking advantage the compatibility of reaction conditions for ATRP, ROP, and click reactions.[20] Trifunctional core molecules are typically employed in the above example.

It is noteworthy that the above examples mainly focused on the synthetic aspect. Our research interests involve the controlled synthesis of responsive block copolymers and their supramolecular self-assembly in aqueous solution.[31–34] In this work, we synthesized a novel ABC miktoarm star terpolymer consisting of hydrophilic PEG, hydrophobic poly(*tert*-butyl methacrylate) (P*t*BMA), and thermoresponsive poly(*N*-isopropylacrylamide) (PNIPAM) arms via a combination of consecutive click reactions and ATRP, starting from bis(2-azidoethyl)amine, $(N_3)_2$—*NH*, which contains two azide groups and one secondary amine moiety (Schemes 1 and 2). We then investigated the supramolecular self-assembly behavior



Scheme 2. Schematic illustration of the synthesis of PEG_{113}(-*b*-P*t*BMA_{58})-*b*-$PNIPAM_{70}$ ABC miktoarm star terpolymer (**7**) via a combination of consecutive click reactions and ATRP.

of PEG(-*b*-P*t*BMA)-*b*-PNIPAM miktoarm star terpolymer in aqueous solution. The thermoresponsive rearrangement of P*t*BMA-core micelles stabilized with PEG/PNIPAM hybrid coronas was characterized by dynamic and static laser light scattering (LLS) and transmission electron microscopy (TEM).

EXPERIMENTAL

Materials

N-Isopropylacrylamide (NIPAM, 97%, Tokyo Kasei Kagyo Co.) was purified by recrystallization from a mixture of benzene and *n*-hexane (1/3, v/v). Poly(ethylene glycol) monomethyl ether (PEG_{113}-OH, M_n = 5000, M_w/M_n = 1.06, mean degree of polymerization, DP, is 113) and 2-chloropropionyl chloride (97%) were purchased from Aldrich and used as received. *tert*-Butyl methacrylate (*t*BMA, 98%, TCI) was vacuum-distilled over CaH_2. Tris(2-aminoethyl)amine (TREN), copper(I) chloride (CuCl, 99.99%), copper(I) bromide (CuBr, 99.99%), 2-bromoisobutyryl bromide (97%), and *N,N,N′,N″,N″*-pentamethyldiethylenetriamine (PMDETA) were purchased from Fluka and used as received. Sodium azide (NaN_3, 99%), propargyl alcohol, and propargyl bromide (80% in toluene) were purchased from Alfa Aesar and used without further purification. Merrifield Resin was purchased from GL Biochem (Shanghai) Ltd. and used as received. Triethylamine (TEA) and toluene were distilled over CaH_2. 2-Propanol, *N,N*-dimethylformamide (DMF), and all other chemicals were purchased from Sinopharm Chemical Reagent Co. Ltd. and used as received. Tris(2-(dimethylamino)ethyl)amine (Me_6TREN) and azido-functionalized Merrifield resin were prepared according to literature procedures.[35,36]

Synthetic schemes employed for the synthesis of PEG(-*b*-P*t*BMA)-*b*-PNIPAM ABC miktoarm star terpolymer were shown in Schemes 1 and 2.

Synthesis of $(N_3)_2$—NH (1)

To a stirred solution of sodium azide (14.6 g, 0.225 mol) in 150 mL water was added bis(2-chloroethyl)amine hydrochloride (20.0 g, 0.112 mol). After stirring for 2 h at 90 °C, another potion of sodium azide (14.6 g) was added, and the reaction mixture was stirred for 48 h at 90 °C. After cooling to room temperature, the solution pH was adjusted to 10 with aqueous NaOH (10 mol/L). The aqueous solution was extracted with ethyl ether (5 mL × 50 mL). The combined organic layers were dried over anhydrous Na_2SO_4, and the solvent was removed using a rotary evaporator. After distillation at reduced pressure, a colorless liquid was obtained (11.85 g, yield: 68.2%). (Caution: special care should be taken when heating the azide compound above 80–85 °C because it becomes shock-sensitive at elevated temperatures; this compound is stable and not shock-sensitive at 25 °C) ^{1}H NMR ($CDCl_3$, δ, ppm, TMS): 3.42 (4H, N_3CH_2—), 2.79 (4H, —CH_2NHCH_2—), and 1.38 (1H, —N*H*—).

Synthesis of Monoalkynyl-Terminated PEG (2)

Typical procedures employed for the preparation of **2** was as follows. PEG_{113}-OH (15.0 g, 3.0 mmol) was dissolved in toluene (180 mL) at 60 °C. After azeotropic distillation of 30–40 mL of toluene at reduced pressure to remove traces of water, sodium hydride (0.216 g, 9.0 mmol, three times molar excess to hydroxyl groups) was added to the solution under stirring. After H_2 evolution for about 15 min, propargyl bromide (1.33 mL, 15 mmol, five times molar excess to hydroxyl groups) in 20 mL of dry toluene was added dropwise. The reaction was then stirred at 60 °C for 18 h. After filtration of insoluble salts, the filtrate was evaporated to dryness. The obtained solid was dissolved in 100 mL CH_2Cl_2. After extraction with aqueous solution of saturated $NaHCO_3$ (3 mL × 30 mL), the organic phase was dried over anhydrous Na_2SO_4 and treated with activated charcoal. After filtration, the solution was precipitated into *n*-hexane. The above dissolution-precipitation cycle was repeated for three times. After drying in a vacuum oven overnight at room temperature, **2** was obtained as a white solid (12.24 g, yield: 81%; $M_{n,GPC}$ = 4.7 kDa, M_w/M_n = 1.06). ^{1}H NMR (D_2O, δ, ppm): 4.13 (2H, —OC*H*$_2$C=CH), 3.69–3.43 (450H, —OC*H*$_2$C*H*$_2$— of PEG main chain), 3.26 (3H,C*H*$_3$O—), and 2.77 (1H, —OCH$_2$C=C*H*).

Synthesis of PEG-NH—N$_3$ (3)

To a Schlenk tube equipped with a magnetic stirring bar, monoalkynyl-terminated PEG (2) (4.03 g, 0.8 mmol), (N_3)$_2$—*NH* (6.2 g, 40.0 mmol, 50 times molar excess to alkynyl groups), and 45 mL DMF were added. After one brief freeze-thaw cycle, CuBr (58 mg, 0.4 mmol) was introduced under protection of N_2 flow. The reaction tube was carefully degassed by three freeze-pump-thaw cycles, sealed under vacuum, and placed in an oil bath held at 30 °C. After stirring for 20 h, the polymer solution was exposed to air, diluted with THF, and passed through a basic alumina column to remove copper catalysts. After removing the solvent, the residue was dissolved in THF and precipitated into an excess of cold ethyl ether. The above dissolution-precipitation cycle was repeated for three times. After drying in a vacuum oven overnight at room temperature, **3** was obtained as a white solid (4.1 g, yield: 99%; $M_{n,GPC}$ = 4.8 kDa, M_w/M_n = 1.06). ^{1}H NMR (D_2O, δ, ppm): 7.94 (1H, C*H in triazole*), 4.58 (2H, —OC*H*$_2$—triazole), 4.46 (2H, triazole—C*H*$_2$—CH$_2$—NH—), 3.69–3.43 (450H, —OC*H*$_2$C*H*$_2$— of PEG main chain), 3.26 (3H,C*H*$_3$O—), 3.03 (triazole—CH$_2$—C*H*$_2$—NH), 2.65 (NH—C*H*$_2$—CH$_2$—N$_3$).

Synthesis of PEG(—N$_3$)—Cl Macroinitiator (4)

To a 250 mL three-neck flask, PEG-*NH*—N_3 (3.01 g, 0.58 mmol) and 80 mL toluene were added. After azeotropic distillation of 20–30 mL toluene at reduced pressure to remove traces of water, triethylamine (165 μL, 1.16 mmol) was added and the solution was cooled to 0 °C. 2-Chloropropionyl chloride (115 μL, 1.16 mmol) in 5 mL dry toluene was then added dropwise via a syringe. After stirring at 0 °C for 2 h, the reaction mixture was continued to stir overnight at room temperature. After filtration of insoluble salts, the filtrate was evaporated to dryness. The obtained solid was dissolved in 100 mL CH_2Cl_2. After extraction with aqueous solution of saturated $NaHCO_3$ (3 mL × 30 mL), the organic phase was dried over anhydrous Na_2SO_4 and treated with activated charcoal. After filtration, the solution was precipitated into *n*-hexane. The above dissolution-precipitation cycle was repeated for three times. After drying in a vacuum oven overnight at room temperature, **2** was obtained as a white solid (2.64 g, yield: 86%; $M_{n,GPC}$ = 4.8 kDa, M_w/M_n = 1.05). ^{1}H NMR (D_2O, δ, ppm): 7.94 (1H, C*H in triazole*), 3.69–3.43 (450H, —OC*H*$_2$C*H*$_2$— of PEG main chain), 3.26 (3H,C*H*$_3$O—), 1.45 (3H, —ClCH(C*H*$_3$)—).

Synthesis of PEG(—N$_3$)-b-PNIPAM (5)

Typical procedures employed for the synthesis of **5** was as follows. PEG(—N_3)—*Cl* macroinitiator (0.845 g, 0.16 mmol), NIPAM (1.45 g, 12.8 mmol), Me_6TREN (74 mg, 0.32 mmol), 2-propanol (4 mL), and DMF (1 mL) were added into a reaction flask. The solution mixture was degassed by two freeze-pump-thaw cycles. After thermostating at 40 °C in an oil bath, CuCl (32 mg, 0.32 mmol) was introduced under the protection of N_2 flow to start the polymerization. The solution turned dark green and apparently more viscous as polymerization proceeded. After 8 h, the monomer conversion was determined to be 88% as judged by ^{1}H NMR. The polymerization was quenched with $CuCl_2$, diluted with 20 mL THF, and then exposed to air. The reaction mixture was passed through a silica gel column to remove the copper catalysts. After removing the solvent by a rotary evaporator, the residue was dissolved in THF and precipitated

into an excess of ethyl ether. The above dissolution-precipitation cycle was repeated twice. The final product was dried in a vacuum oven, yielding a white solid (2.05 g, yield: 89%; $M_{n,GPC}$ = 11.2 kDa, M_w/M_n = 1.15). The actual DP of PNIPAM block was determined to be 70 by ^{1}H NMR analysis in D_2O. Thus, the polymer was denoted as $PEG_{113}(—N_3)$-*b*-$PNIPAM_{70}$.

Synthesis of Propargyl 2-Bromoisobutyrate

The ATRP initiator, propargyl 2-bromoisobutyrate (PBIB), was prepared by the esterification reaction of propargyl alcohol with 2-bromoisobutyryl bromide. A 250 mL round-bottom flask was charged with propargyl alcohol (11.21 g, 0.2 mol), TEA (20.2 g, 0.2 mol), and dry CH_2Cl_2 (100 mL).[37,38] The mixture was cooled to 0 °C in an ice-water bath, 2-bromoisobutyryl bromide (25.2 mL, 0.2 mol) in CH_2Cl_2 (20 mL) was then added dropwise over 1.5 h. After the addition was completed, the reaction mixture was stirred at 0 °C for another 1 h and then at room temperature for 12 h. After removing the insoluble salts by suction filtration, the filtrate was concentrated and then further purified by silica gel column chromatography using petroleum ether/ethyl acetate (1:1 v/v) as the eluent. After removing the solvent by a rotary evaporator, the obtained residue was distilled under reduced pressure (bp: 30 °C/0.5 Torr). A colorless liquid was obtained (30.76 g, yield: 75%). ^{1}H NMR ($CDCl_3$, δ, ppm, TMS): 4.7 (2H, —CH_2O), 2.5 (1H, CH=C—), and 1.9 (6H, —C(CH_3)$_2$Br).

*Synthesis of Alkynyl-Terminated P*t*BMA (6)*

Monoalkynyl-terminated P*t*BMA was obtained by ATRP of *t*BMA monomer using PBIB as initiator. In a typical experiment, PBIB (0.287 g, 1.4 mmol), *t*BMA (9.95 g, 70 mmol), PMDETA (0.243 g, 1.4 mmol), and 2-propanol (10 mL) were added into a reaction flask. The solution mixture was degassed by two freeze-pump-thaw cycles. After the flask was held at 40 °C, CuCl (0.2 g, 1.4 mmol) was introduced under the protection of N_2 flow to start the polymerization. The reaction solution became dark green and more viscous as polymerization proceeded. After 5 h, the monomer conversion was determined to be ~95% by ^{1}H NMR analysis. The reaction mixture was diluted with 20 mL THF and then exposed to air. After passing through a silica gel column and removing the solvent on a rotary evaporator, the residue was dissolved in THF and precipitated into an excess of water/methanol (1:1 v/v) mixture. The final product was dried in a vacuum oven overnight at room temperature, yielding a white solid (8.8 g, yield: 86%; $M_{n,GPC}$ = 5.9 kDa, M_w/M_n = 1.12). The actual DP of PNIPAM block was determined to be 58 by ^{1}H NMR analysis in $CDCl_3$. Thus, the polymer was denoted as *alkynyl*-P*t*BMA_{58}.

Synthesis of the ABC Miktoarm Star Terpolymer (7)

The synthesis of the PEG(-*b*-P*t*BMA)-*b*-PNIPAM miktoarm star terpolymer was accomplished by click reaction of PEG(—N_3)-*b*-PNIPAM (**5**) with an excess of monoalkynyl-terminated P*t*BMA. A typical procedure was as follows. *alkynyl*-P*t*BMA_{58} (0.76 g, 0.09 mmol) was dissolved in 40 mL DMF. To this solution was added $PEG_{113}(—N_3)$-*b*-$PNIPAM_{70}$ (0.79 g, 0.06 mmol). After one brief freeze-thaw cycle, CuBr (9 mg, 0.06 mmol) was introduced under the protection of N_2 flow. The reaction tube was carefully degassed by three freeze-pump-thaw cycles, and placed in an oil bath held at 80 °C. After stirring for 24 h, azide-functionalized Merrifield resin (0.188 g, 0.15 mmol azide moiety) was then added. The suspension was kept stirring for another 8 h at 80 °C. After suction filtration, the filtrate was diluted with THF, and passed through a basic alumina column to remove the copper catalyst. After removing the solvent at reduced pressure, the residue was dissolved in THF and precipitated into an excess of *n*-hexane. The final product was dried in a vacuum oven overnight at room temperature, yielding a white solid (1.2 g, yield: 93%; $M_{n,GPC}$ = 12.7 kDa, M_w/M_n = 1.18). Molecular parameters of all the intermediate and final products are summarized in Table 1.

Preparation of Micellar Solutions

Ten milligrams of PEG(-*b*-P*t*BMA)-*b*-PNIPAM ABC miktoarm star terpolymer was dissolved in 1 mL of DMF. Under vigorous stirring, 9 mL of deionized water was added via syringe pump at a flow rate of 0.2 mL/min. After the addition is completed, the dispersion was left stirring for another 5 h. DMF was then removed by dialysis (MW cut-off, 14,000 Da) against deionized water for 24 h. Fresh deionized water was replaced approximately every 6 h. Micellar solutions with a characteristic bluish tinge were typically obtained. The micellar solution exhibited no macroscopic phase separation upon standing at room

Table 1. Summary of Structural Parameters of Polymers Synthesized in This Work

Samples	$M_{n,NMR}$ (kDa)[a]	$M_{n,GPC}$ (kDa)[b]	M_w/M_n[b]
alkynyl-PEG_{113}	5.0	4.7	1.06
PEG_{113}-*NH*—N_3	5.2	4.8	1.06
PEG_{113}(—N_3)—*Cl*	5.3	4.8	1.05
PEG_{113}(-N_3)-*b*-$PNIPAM_{70}$	13.2	11.2	1.15
alkynyl-P*t*BMA_{58}	8.4	5.9	1.12
PEG_{113}(-*b*-P*t*BMA_{58})-*b*-$PNIPAM_{70}$	21.6	12.7	1.18

[a] Determined by ^{1}H NMR analysis in $CDCl_3$.
[b] Molecular weights (M_n) and molecular weight distributions (M_w/M_n) were determined by GPC using DMF as the eluent.

temperature for more than 3 months, suggesting the formation of stable aggregates.

Characterization

Nuclear Magnetic Resonance Spectroscopy

All nuclear magnetic resonance spectroscopy (NMR) spectra were recorded on a Bruker AV300 NMR spectrometer (resonance frequency of 300 MHz for ^{1}H) operated in the Fourier transform mode. $CDCl_3$ and D_2O were used as the solvent.

Fourier Transform Infrared Spectroscopy

Fourier transform infrared (FTIR) spectra were recorded on a Bruker VECTOR-22 IR spectrometer. The spectra were collected at 64 scans with a spectral resolution of 4 cm^{-1}.

Gel Permeation Chromatography

Molecular weights and molecular weight distributions were determined by gel permeation chromatography (GPC) equipped with Waters 1515 pump and Waters 2414 differential refractive index detector (set at 30 °C). It used a series of three linear Styragel columns HT2, HT4, and HT5 at an oven temperature of 45 °C. The eluent was DMF at a flow rate of 1.0 mL/min. A series of low polydispersity polystryene (PS) standards were employed for the GPC calibration.

Laser Light Scattering

A commercial spectrometer (ALV/DLS/SLS-5022F) equipped with a multi-tau digital time correlator (ALV5000) and a cylindrical 22 mW UNIPHASE He-Ne laser (λ_0 = 632 nm) as the light source was employed for dynamic and static laser light scattering (LLS) measurements. Scattered light was collected at a fixed angle of 90° for duration of ~10 min. Distribution averages and particle size distributions were computed using cumulants analysis and CONTIN routines. All data were averaged over three measurements.

Transmission Electron Microscopy

TEM observations were conducted on a Hitachi H-800 electron microscope at an acceleration voltage of 200 kV. The sample for TEM observations was prepared by placing 10 μL of micellar solution on copper grids coated with thin films of Formvar and carbon successively.

RESULTS AND DISCUSSION

Synthesis of ABC Miktoarm Star Terpolymer

The synthetic route employed for the preparation of PEG(-*b*-P*t*BMA)-*b*-PNIPAM ABC miktoarm star terpolymer (**7**) was shown in Scheme 1. Click reaction of monoalkynyl-terminated PEG with a trifunctional core molecule bis(2-azidoethyl)-amine, $(N_3)_2$—*NH*, afforded difunctional PEG possessing an azido and a secondary amine moiety at the chain end, PEG-*NH*—N_3. After amidation of PEG-*NH*—N_3 (**3**) with 2-chloropropionyl chloride, the obtained difunctional PEG(—N_3)—*Cl* (**4**) was used as the macroinitiator for the ATRP of NIPAM monomer. The subsequent click reaction of PEG(—N_3)-*b*-PNIPAM (**5**) with monoalkynyl-terminated P*t*BMA (**6**) led to well-defined amphiphilic and thermoresponsive miktoarm star terpolymer, PEG(-*b*-P*t*BMA)-*b*-PNIPAM (**7**). Table 1 summarizes structural parameters of all the intermediate polymers and the final product synthesized in this work.

The reaction of PEG_{113}-OH with propargyl bromide was conducted in the presence of NaH. To ensure complete end group transformation, an excess amount of propargyl bromide was used. It should be noted that quantitative end group transformation is pivotal for the successful preparation of miktoarm star polymers. ^{1}H NMR spectrum of **2** was shown in Figure 1(a). The signal at 3.6 ppm (peak *b*) can be ascribed to the methylene protons of PEG main chain, whereas signals at 4.1 ppm (peak *c*) and 2.8 ppm (peak *d*) were attributed to methylene and alkynyl protons of

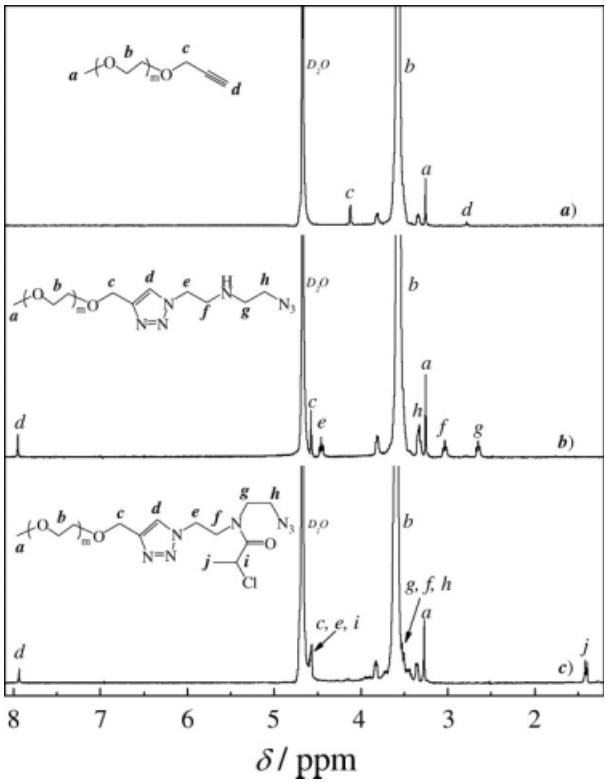


Figure 1. ^{1}H NMR spectra of recorded in D_2O for (a) monoalkynyl-terminated PEG_{113}, (b) PEG_{113}—*NH*—N_3 (**3**), and (c) PEG_{113}(—N_3)—*Cl* (**4**).

the terminal propargyl group, respectively. By comparing integral ratios of peaks *d* and *c* to that of peak *b*, the degree of end group functionalization was calculated to be 100%, that is, a quantitative end group transformation was achieved. Thus, the obtained polymer was denoted as *alkynyl*-PEG_{113}.

PEG-*NH*—N_3 (**3**) was obtained by the click reaction of **2** with an excess of $(N_3)_2$—*NH*. This step is quite crucial for the preparation of well-defined target miktoarm star polymer due to the possible click coupling of **2** by $(N_3)_2$—*NH*. The presence of coupling product, PEG-*NH*-PEG, will lead to the formation of Y-shaped AB_2 product, PNIPAM-*b*-$(PEG)_2$. In designing the reaction, the molar ratio of $(N_3)_2$—*NH* to alkynyl moieties of **2** was fixed at 50:1. A large excess of $(N_3)_2$—*NH* end can theoretically ensure that only one azide group participate in the click reaction. In Monteiro's work,[21] a large excess of TPA was also used to prevent the possible click coupling of azide-terminated polymers by TPA. However, we find this reaction is quite tricky to tackle. Initial click reaction was conducted at a polymer concentration of 10 g/L and 80 °C, from the GPC trace of the click product [Fig. 2(a)], we can clearly discern a shoulder peak, which was resulted from the coupling reaction of **2** by $(N_3)_2$—*NH*. To optimize the reaction conditions, the reaction was then conducted at a polymer concentration of 100 g/L and 80 °C, and a decreasing dimer shoulder peak was observed [Fig. 2(b)]. Finally, we conducted the click reaction at 30 °C and a concentration of 100 g/L. In this case, we obtained a clean GPC trace for the click product [Fig. 2(c)], indicating the absence of any click coupling of **2**. Although the optimization of reaction condition (100 g/L, 30 °C) lacks the support of theoretical considerations, we did obtain well-defined difunctional precursor, PEG-*NH*—N_3 (**3**). Figure 1(b) shows the ^{1}H NMR spectrum of **3**, and all signals can be well-assigned according to its chemical structure. Besides the characteristic peaks of PEG main chain, newly appeared peaks *g* (2.7 ppm, $NHCH_2CH_2N_3$), *f* (3.0 ppm, triazole-CH_2CH_2NH), and *e* (4.5 ppm, triazole—CH_2CH_2NH—), as well as the presence of signals at 7.9 ppm characteristic of 1,2,3-triazole proton all supported the successful preparation of PEG-*NH*—N_3 (**3**).

On the other hand, peak *c* (4.1 ppm) in the ^{1}H NMR spectrum of **2** completely shifted to 4.6 ppm in that of **3** due to the formation of triazole ring. Moreover, the presence of coupling product, PEG-*NH*-PEG, can be expected to increase the integral areas of peaks *f* and *e* relative to that of peak *g*.

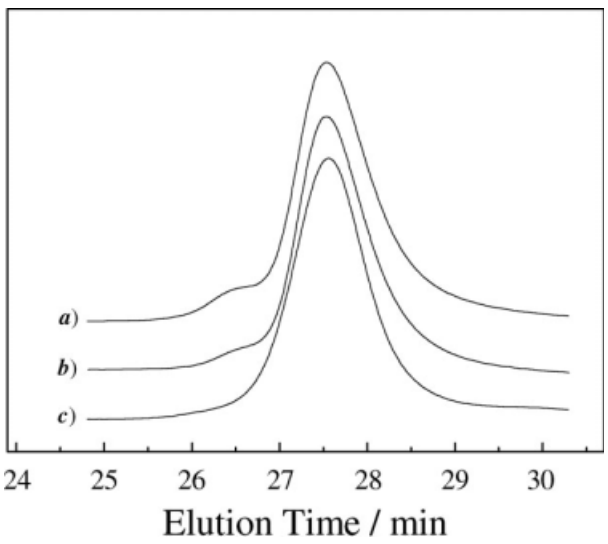


Figure 2. DMF GPC traces recorded for PEG_{113}—*NH*—N_3 prepared from the click reaction of monoalkynyl-terminated PEG_{113} (**2**) with $(N_3)_2$—*NH* (**1**) at different conditions: (a) 10 g/L of **2**, 80 °C; (b) 100 g/L of **2**, 80 °C; (c) 100 g/L of **2**, 30 °C. The molar ratios of $(N_3)_2$—*NH* to that of **2** were fixed at 50:1.

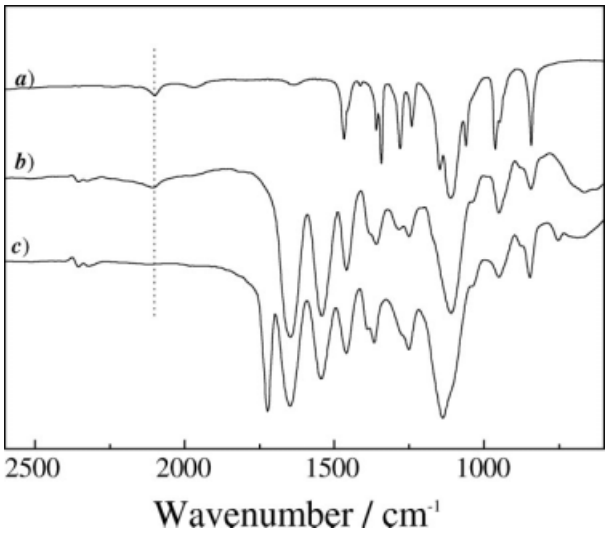


Figure 3. FTIR spectra recorded for (a) PEG_{113}—*NH*—N_3 (***3***), (b) PEG_{113}(—N_3)-*b*-$PNIPAM_{70}$ (***5***), and (c) PEG_{113}(-*b*-P*t*BMA_{58})-*b*-$PNIPAM_{70}$ ABC miktoarm star terpolymer (**7**).

Thus, the "clean" formation of **3** can also be judged from Figure 1(b), as the integral ratio between peaks *e*, *f*, and *g* was determined to be close to unity. The presence of a residual azide group in **3** can also be evidenced by the presence of characteristic azide absorbance peak at ~2100 cm^{-1} in its FTIR spectrum [Fig. 3(a)]. It should be noted that the click reaction was conducted in DMF under ligand-free conditions. It has been established previously that the click reaction can be quite efficient even in the absence of any ligands if the solvent can facilitate sufficient solubility for copper catalyst.[39]

Next, PEG-*NH*—N_3 (**3**) was transformed into PEG(—N_3)—*Cl* (**4**) by amidation with 2-chloropropionyl chloride. Figure 1(c) shows the ^{1}H NMR spectrum of **4**. It was interesting to note that the amidation reaction led to severe overlapping of signal peaks. However, compared to that of **3**, we can clearly see the complete disappearance of peaks *g* (2.7 ppm, NH—CH_2—CH_2—N_3), *f* (3.0 ppm, triazole—CH_2—CH_2—NH—) and the appearance of signal at 1.4 ppm in the ^{1}H NMR spectrum of **4**; moreover, the integral ratio between peaks *j* (1.4 ppm, 3H, —ClCH(CH_3)—) and *d* (7.9 ppm, 1H, C*H* in triazole) in **4** is close to 3:1. These results confirmed the quantitative transformation of **3** to **4**. PEG(—N_3)-*b*-PNIPAM (**5**) was prepared by the ATRP of NIPAM monomer in 2-propanol/DMF mixture (4:1 v/v), using PEG_{113}(—N_3)—Cl (**4**) as the macroinitiator and CuCl/Me_6TREN as the catalysts. Typical GPC trace of **5** was shown in Figure 4(c), exhibiting a monomodal and quite symmetric elution peak. When compared with the GPC trace of PEG(—N_3)—*Cl* macroinitiator [**4**, Fig. 5(b)], the GPC trace of **5** showed a clear shift to the higher molecular weight region, indicating that well-defined AB diblock copolymer with an azide moiety at the junction point was obtained. GPC analysis revealed an M_n of 11.2 kDa and an M_w/M_n of 1.15 for **5**.

^{1}H NMR spectrum of **5** was shown in Figure 5(a), and all signals characteristic of PEG and PNIPAM segments can be clearly observed. Although we can not discern the signal of methylene protons neighboring to the azide group from the ^{1}H NMR spectrum of **5** due to peak overlapping [Fig. 5(a)], FTIR spectrum of **5** revealed the presence of azide group at the diblock junction point [Fig. 3(b)]. The actual DP of PNIPAM block in **5** was calculated to be 70 by comparing integration areas of peaks *b* and *f* [Fig. 5(a)]. Thus, the obtained polymer was denoted as PEG_{113}(—N_3)-*b*-$PNIPAM_{70}$.

Finally, the synthesis of ABC miktoarm star polymer, PEG(-*b*-P*t*BMA)-*b*-PNIPAM (**7**), was accomplished by the click reaction between PEG_{113}(—N_3)-*b*-$PNIPAM_{70}$ (**5**) and monoalkynyl-terminated P*t*BMA (**6**) (Scheme 1). Tunca and coworkers[22] reported the synthesis of ABC miktoarm terpolymer by using click reaction. The

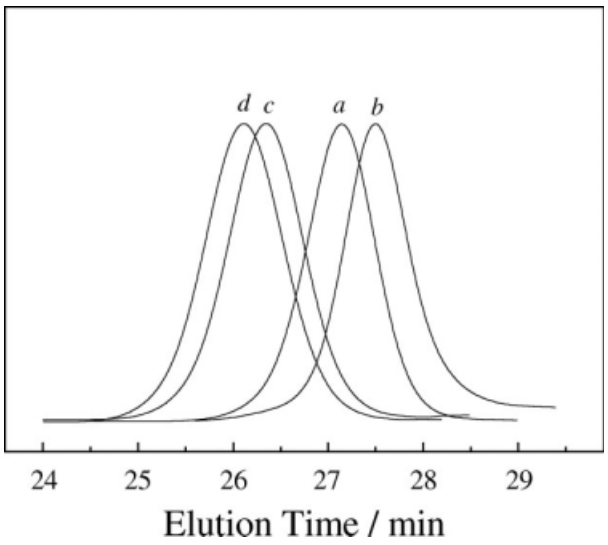


Figure 4. DMF GPC traces recorded for (a) monoalkynyl-terminated P*t*BMA_{58} (**6**), (b) PEG_{113}(—N_3)—*Cl* (**4**), (c) PEG_{113}(—N_3)-*b*-$PNIPAM_{70}$ (**5**), and (d) PEG_{113}(-*b*-P*t*BMA_{58})-*b*-$PNIPAM_{70}$ ABC miktoarm star terpolymer (**7**).

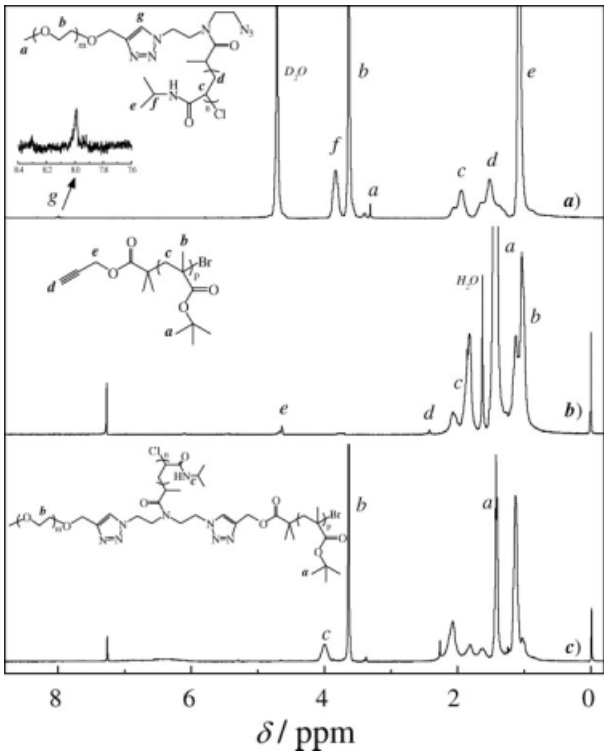


Figure 5. ^{1}H NMR spectra of (a) PEG$_{113}$(—N_3)-*b*-PNIPAM$_{70}$ (**5**) in D_2O, (b) monoalkynyl-terminated P*t*BMA$_{58}$ (**6**) in $CDCl_3$, and (c) PEG$_{113}$(-*b*-P*t*BMA$_{58}$)-*b*-PNIPAM$_{70}$ (**7**) ABC miktoarm star terpolymer in $CDCl_3$.

click reaction of azido group located at the junction of AB diblock with monoalkynyl-terminated polymer led to the formation of ABC miktoarm star terpolymer. In this study, an excess of **6** was used to ensure complete consumption of azide moieties in **5**, and the reaction was conducted at 80 °C for 24 h. The removal of excess **6** was facilely achieved by clicking onto azido-functionalized Merrifield resin and the subsequent simple filtration step.[36] Figure 3 shows the FTIR spectra of the final purified product. Compared to that of **5**, the IR spectrum of **7** revealed the complete disappearance of characteristic azide absorbance peak at 2100 cm^{-1}. This indicates that all azide groups were consumed and participated in the click reaction with terminal alkynyl group of P*t*BMA.

GPC analysis further supported the successful preparation of ABC miktoarm star terpolymer. GPC trace of **7** was again monomodal and quite symmetric. Compared to the diblock precursor (**5**) and monoalkynyl-terminated P*t*BMA (**6**), the elution peak of 7 clearly shifted to the higher MW side (Fig. 4). GPC analysis revealed an M_n of 12.7 and an M_w/M_n of 1.15. The relatively small elution peak shift of **7** relative to that of **5** can be explained by the star topology of **7**, which tends to give smaller hydrodynamic volume when compared with linear triblock copolymers with comparable molecular weights. This phenomenon was also observed in previous works reported by other research groups.[16,22] From ^{1}H NMR of **7** [Fig. 5(c)], we can discern all characteristic signals of PEG, PNIPAM, and P*t*BMA blocks, and the peak integral ratios between these peaks agreed quite well with the relative segment lengths between these three arms. Based on the above results, we concluded that well-defined miktoarm star terpolymer, PEG$_{113}$(-*b*-P*t*BMA$_{58}$)-*b*-PNIPAM$_{70}$, has been reliably obtained via a combination of consecutive click reactions and ATRP.

Micellization Properties of PEG$_{113}$(-*b*-PtBMA$_{58}$)-*b*-PNIPAM$_{70}$ Miktoarm Star Terpolymer

The obtained miktoarm star terpolymer contains a hydrophobic P*t*BMA block, a permanently hydrophilic PEG block, and a thermoresponsive PNIPAM block (Schemes 1 and 2). Using a cosolvent approach, stable aggregates were obtained in aqueous solution. Based on chemical intuition, the formed aggregates should possess P*t*BMA cores and PEG/PNIPAM hybrid coronas. Employing a combination of LLS and TEM, we further characterized the self-assembled micelles and their thermoresponsive aggregation in aqueous solution. It is worthy of noting that Armes and coworkers[40–42] have originally reported several excellent works concerning the synthesis of Y-shaped AB$_2$ miktoarm star copolymers and their stimuli-responsive aggregation in aqueous solution. In previous works, we have reported the synthesis and stimuli-responsive micellization behavior of a variety of nonlinear block copolymers including A$_2$BA$_2$ and A$_4$BA$_4$ dumbbell-shaped,[32] AB$_4$[33] and AB$_2$ Y-shaped[31,34] star polymers.

It is well-known that PNIPAM homopolymer undergoes a coil-to-globule phase transition in dilute aqueous solution above the lower critical solution temperature (LCST) at ~32 °C.[43–48] At temperatures below the LCST, PNIPAM chains adopt a randomly coiled conformation due to the predominantly intermolecular hydrogen bonding interaction between PNIPAM chain segments and water molecules. At temperatures above the LCST, predominant intramolecular hydrogen-bonding interactions reduce the water-solubility, accompanied by the collapse and aggregation of

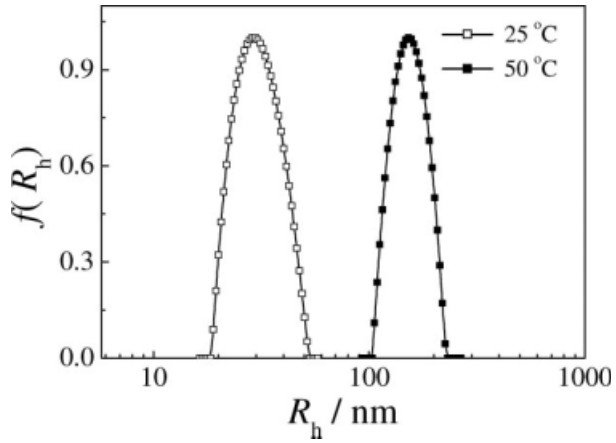


Figure 6. Temperature-dependent hydrodynamic radius distributions, $f(R_h)$, obtained for 0.5 g/L aqueous solution of P*t*BMA-core micelles stabilized by PEG/PNIPAM hybrid coronas self-assembled from PEG_{113}(-*b*-P*t*BMA_{58})-*b*-$PNIPAM_{70}$ miktoarm star terpolymer (**7**). Scattered light was collected at a fixed angle of 90° for duration of ~10 min and the heating rate was 0.2 °C/min.

PNIPAM chains. The LCST of PNIPAM in solution also depends on the molecular weights[49,50] and type of end groups.[51–53] The phase transition of PNIPAM coronas or cores in micelles self-assembled from amphiphilic or double hydrophilic block or star copolymers have also been investigated.[33,54–61] To the best of our knowledge, the phase transition of micelles containing mixed coronas of thermoresponsive PNIPAM and hydrophilic chain sequences has not been reported yet. The close neighboring between PNIPAM and PEG chains will surely affect the phase transition behavior. Because of thermoresponsive solubility changes of PNIPAM within the self-assembled aggregates, two micellar states existed in aqueous solution depending on the solution temperatures.

Figure 6 shows typical plots of the hydrodynamic radius distribution, $f(R_h)$, obtained for 0.5 g/L aqueous solution of PEG_{113}(-*b*-P*t*BMA_{58})-*b*-$PNIPAM_{70}$ miktoarm star terpolymer at varying temperatures. At 25 °C, P*t*BMA-core micelles with mixed PEG/PNIPAM coronas exhibited an intensity-average hydrodynamic radius, $\langle R_h \rangle$, of about 30 ± 2 nm. Upon heating to 50 °C at a rate of 0.2 °C/min, dynamic LLS revealed a $\langle R_h \rangle$ of about 110 ± 5 nm, clearing indicating the further growth of micelles. At elevated temperatures, PNIPAM segments within micelles are getting insoluble, and this breaks the hydrophilic/hydrophobic balances of originally formed micelles at lower temperatures; thus they tend to undergo further structural rearrangement and form micelles with mixed P*t*BMA/PNIPAM cores stabilized solely by hydrophilic PEG segments. Both types of aggregates formed at 25 and 50 °C were relatively monodisperse, and the polydispersity indexes of the size distributions (μ_2/Γ^2) were typically small, being 0.09 and 0.13 at 25 °C and 50 °C, respectively.

Figure 7(a) shows the temperature dependence of $\langle R_h \rangle$ of micellar nanoparticles self-assembled from **7** in aqueous solutions. $\langle R_h \rangle$ remained constant at about 30 nm below 40 °C. Above that micelle sizes started to increase, and $\langle R_h \rangle$ stabilizes at ~110 nm above ~47 °C. This indicated the formation of another type of stable aggregates. To further verify this, static LLS measurements were employed. Because of the miktoarm star topology of PEG_{113}(-*b*-P*t*BMA_{58})-*b*-$PNIPAM_{70}$, PEG and PNIPAM chains from the same star molecule were grafted from a single point at the surface of micellar cores. Compared to that of free PNIPAM chains of comparable MW, the relatively high transition temperature (39 °C) for P*t*BMA-core micelles should be ascribed to the close neighboring between PEG and PNIPAM segments within micellar coronas. The presence of hydrophilic PEG chain sequences seemed to be able to hinder the collapse and aggregation of PNIPAM. Additional work to investigate this phenomenon is currently underway.

Figure 7(b) shows the temperature dependence of apparent molecular weight, $M_{w,app}$, of the self-assembled micelles. $M_{w,app}$ remains almost

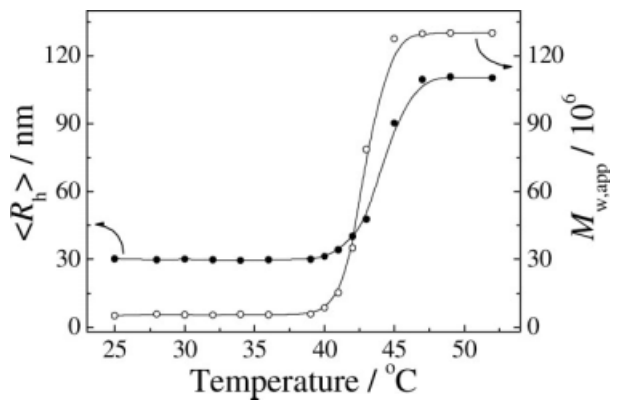


Figure 7. Temperature dependence of intensity-average hydrodynamic radius, $\langle R_h \rangle$, (●) and apparent molecular weights, $M_{w,app}$, (○) obtained for 0.5 g/L micellar solution of PEG_{113}(-*b*-P*t*BMA_{58})-*b*-$PNIPAM_{70}$ miktoarm star terpolymer (**7**). A thermostatically controlled couvette was employed and the heating rate was 0.2 °C min^{-1}.

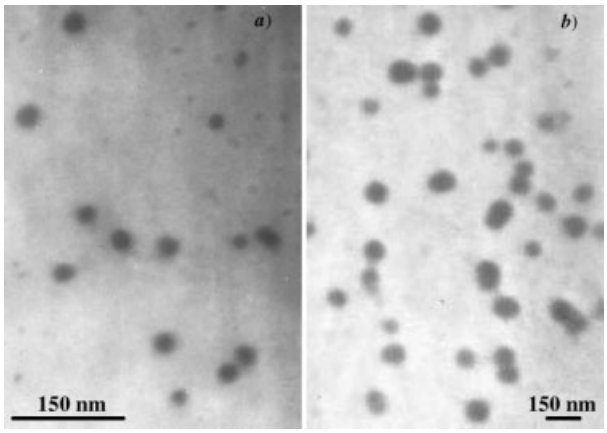


Figure 8. Typical TEM images obtained by drying 0.5 g/L micellar solution of PEG_{113}(-*b*-P*t*BMA_{58})-*b*-$PNIPAM_{70}$ at (a) 25 °C and (b) 50 °C.

constant at about 5.3×10^6 in the temperature range of 25–40 °C. Above 40 °C, the micelles undergo aggregation, as evidenced by the dramatic increase of $M_{w,app}$. The weight-average molecular weight of PEG_{113}(-*b*-P*t*BMA_{58})-*b*-$PNIPAM_{70}$ was estimated to be 24,900 g/mol, and the average aggregation number, N_{agg}, of PtBMA-core micelles below 40 °C was then calculated to be about 210. When the temperature was increased to above 47 °C, $M_{w,app}$ and N_{agg} of aggregated micelles increased to $\sim 1.3 \times 10^8$ g/mol and ~5200, respectively. This indicated that at elevated temperatures, the newly formed core-shell aggregates consist of ~24 P*t*BMA-core micelles originally formed at lower temperatures. The average micelle density calculated for aggregates at 25 and 50 °C were 0.078 and 0.0039 g/mL, respectively. The relatively low overall density for the aggregates formed at elevated temperatures reflected that these aggregates were formed by the loose connection of originally formed micelles.

Transmission electron microscopy (TEM) observations were performed to examine the actual morphologies of micellar aggregates formed from 0.5 g/L aqueous solution of PEG_{113}(-*b*-P*t*BMA_{58})-*b*-$PNIPAM_{70}$ at 25 °C and 50 °C (heating rate: 0.2 °C/min). Both images clearly revealed the presence of spherical nanoparticles of around 25 ± 10 (averaged from 110 particles) and 125 ± 20 nm (averaged from 75 particles) in diameter for micelles at 25 °C and 50 °C, respectively, (Fig. 8). The results were in reasonable agreement with those determined by LLS (Figs. 6 and 7). It is well-known that TEM determines micelle dimensions in the dry state, whereas dynamic LLS report the intensity-average dimensions in solution, which contains the dominant contribution of well-solvated coronas. Moreover, micellar nanoparticles at the surface of copper grids tend to collapse to some extent, leading to larger apparent sizes as determined by TEM. Overall, it is quite reasonable that micelle sizes determined by TEM were systematically smaller than those by LLS.

CONCLUSIONS

A novel method for the synthesis of ABC miktoarm star terpolymer via a combination of consecutive click reactions and ATRP was developed. The amidation reaction of PEG-*NH*—N_3 with 2-chloropropionyl chloride afforded PEG-based difunctional initiator bearing an azide moiety and a chloro functionality at the chain terminal. The subsequent coupling of ATRP and click reactions led to the formation of well-defined PEG(-*b*-P*t*BMA)-*b*- PNIPAM miktoarm star terpolymer. The possible coupling reaction of monoalkynyl-terminated PEG chains by $(N_3)_2$—*NH* has been be efficiently eliminated by optimize the click conditions. All the intermediate and final products were characterized by FTIR, GPC, and ^{1}H NMR. In aqueous solution, PEG(-*b*-P*t*BMA)-*b*-PNIPAM self-assembled into P*t*BMA-core micelles with mixed hydrophilic PEG and thermoresponsive PNIPAM coronas. Dynamic and static LLS revealed that $\langle R_h \rangle$ and $M_{w,app}$ remained constant below 40 °C. Above that, $\langle R_h \rangle$ and $M_{w,app}$ started to increase, indicating the fusion of P*t*BMA-core micelles. The close neighboring of PEG and PNIPAM chains within micellar coronas endowed them with novel phase transition behavior, when compared with those of free PNIPAM chains in solution.

The financial supports of National Natural Scientific Foundation of China (NNSFC) Projects (20534020, 20674079, 20874092, and 50425310), Specialized Research Fund for the Doctoral Program of Higher Education (SRFDP), and the Program for Changjiang Scholars and Innovative Research Team in University (PCSIRT) are gratefully acknowledged.

REFERENCES AND NOTES

1. Yamauchi, K.; Takahashi, K.; Hasegawa, H.; Iatrou, H.; Hadjichristidis, N.; Kaneko, T.; Nishikawa, Y.; Jinnai, H.; Matsui, T.; Nishioka, H.; Shimizu, M.; Fukukawa, H. Macromolecules 2003, 36, 6962–6966.

2. Li, Z. B.; Kesselman, E.; Talmon, Y.; Hillmyer, M. A.; Lodge, T. P. Science 2004, 306, 98–101.
3. Hadjichristidis, N.; Pitsikalis, M.; Pispas, S.; Iatrou, H. Chem Rev 2001, 101, 3747–3792.
4. He, X. H.; Huang, L.; Liang, H. J.; Pan, C. Y. J Chem Phys 2003, 118, 9861–9863.
5. Iatrou, H.; Hadjichristidis, N. Macromolecules 1992, 25, 4649–4651.
6. Sioula, S.; Tselikas, Y.; Hadjichristidis, N. Macromolecules 1997, 30, 1518–1520.
7. Fujimoto, T.; Zhang, H. M.; Kazama, T.; Isono, Y.; Hasegawa, H.; Hashimoto, T. Polymer 1992, 33, 2208–2213.
8. Huckstadt, H.; Abetz, V.; Stadler, R. Macromol Rapid Commun 1996, 17, 599–606.
9. Huckstadt, H.; Gopfert, A.; Abetz, V. Macromol Chem Phys 2000, 201, 296–307.
10. Lu, Z. J.; Chen, S.; Huang, J. L. Macromol Rapid Commun 1999, 20, 394–400.
11. Lambert, O.; Dumas, P.; Hurtrez, G.; Riess, G. Macromol Rapid Commun 1997, 18, 343–351.
12. Quirk, R. P.; Yoo, T.; Lee, B. J. J Macromol Sci Pure Appl Chem 1994, A31, 911–926.
13. Lambert, O.; Reutenauer, S.; Hurtrez, G.; Riess, G.; Dumas, P. Polym Bull 1998, 40, 143–149.
14. Feng, X. S.; Pan, C. Y. Macromolecules 2002, 35, 4888–4893.
15. Feng, X. S.; Pan, C. Y. Macromolecules 2002, 35, 2084–2089.
16. He, T.; Li, D. J.; Sheng, X.; Zhao, B. Macromolecules 2004, 37, 3128–3135.
17. Durmaz, H.; Karatas, F.; Tunca, U.; Hizal, G. J Polym Sci Part A: Polym Chem 2006, 44, 499–509.
18. Shi, P. H.; Li, Y. G.; Pan, C. Y. Eur Polym J 2004, 40, 1283–1290.
19. Li, Y. G.; Wang, Y. M.; Pan, C. Y. J Polym Sci Part A: Polym Chem 2003, 41, 1243–1250.
20. Altintas, O.; Yankul, B.; Hizal, G.; Tunca, U. J Polym Sci Part A: Polym Chem 2007, 45, 3588–3598.
21. Whittaker, M. R.; Urbani, C. N.; Monteiro, M. J. J Am Chem Soc 2006, 128, 11360–11361.
22. Altintas, O.; Hizal, G.; Tunca, U. J Polym Sci Part A: Polym Chem 2006, 44, 5699–5707.
23. Billiet, L.; Fournier, D.; Du Prez, F. J Polym Sci Part A: Polym Chem 2008, 46, 6552–6564.
24. Jiang, X. Z.; Zhang, J. Y.; Zhou, Y. M.; Xu, J.; Liu, S. Y. J Polym Sci Part A: Polym Chem 2008, 46, 860–871.
25. Liu, Y.; Diaz, D. D.; Accurso, A. A.; Sharpless, K. B.; Fokin, V. V.; Finn, M. G. J Polym Sci Part A: Polym Chem 2007, 45, 5182–5189.
26. Mespouille, L.; Coulembier, O.; Paneva, D.; Degee, P.; Rashkov, I.; Dubois, P. J Polym Sci Part A: Polym Chem 2008, 46, 4997–5013.
27. Takizawa, K.; Nulwala, H.; Thibault, R. J.; Lowenhielm, P.; Yoshinaga, K.; Wooley, K. L.; Hawker, C. J. J Polym Sci Part A: Polym Chem 2008, 46, 2897–2912.
28. Vestberg, R.; Malkoch, M.; Kade, M.; Wu, P.; Fokin, V. V.; Sharpless, K. B.; Drockenmuller, E.; Hawker, C. J. J Polym Sci Part A: Polym Chem 2007, 45, 2835–2846.
29. Yang, L. P.; Dong, X. H.; Pan, C. Y. J Polym Sci Part A: Polym Chem 2008, 46, 7757–7772.
30. Yang, L. P.; Zhou, H. X.; Shi, G. Y.; Wang, Y.; Pan, C. Y. J Polym Sci Part A: Polym Chem 2008, 46, 6641–6653.
31. Liu, H.; Xu, J.; Jiang, J. L.; Yin, J.; Narain, R.; Cai, Y. L.; Liu, S. Y. J Polym Sci Part A: Polym Chem 2007, 45, 1446–1462.
32. Xu, J.; Ge, Z. S.; Zhu, Z. Y.; Luo, S. Z.; Liu, H. W.; Liu, S. Y. Macromolecules 2006, 39, 8178–8185.
33. Ge, Z. S.; Cai, Y. L.; Yin, J.; Zhu, Z. Y.; Rao, J. Y.; Liu, S. Y. Langmuir 2007, 23, 1114–1122.
34. Rao, J. Y.; Zhang, Y. F.; Zhang, J. Y.; Liu, S. Y. Biomacromolecules 2008, 9, 2586–2593.
35. Ciampolini, M.; Nardi, N. Inorg Chem 1966, 5, 41–44.
36. Chen, G. J.; Tao, L.; Mantovani, G.; Ladmiral, V.; Burt, D. P.; Macpherson, J. V.; Haddleton, D. M. Soft Matter 2007, 3, 732–739.
37. Laurent, B. A.; Grayson, S. M. J Am Chem Soc 2006, 128, 4238–4239.
38. Tsarevsky, N. V.; Sumerlin, B. S.; Matyjaszewski, K. Macromolecules 2005, 38, 3558–3561.
39. Sumerlin, B. S.; Tsarevsky, N. V.; Louche, G.; Lee, R. Y.; Matyjaszewski, K. Macromolecules 2005, 38, 7540–7545.
40. Cai, Y. L.; Tang, Y. Q.; Armes, S. P. Macromolecules 2004, 37, 9728–9737.
41. Cai, Y. L.; Armes, S. P. Macromolecules 2005, 38, 271–279.
42. Cai, Y. L.; Burguiere, C.; Armes, S. P. Chem Commun 2004, 802–803.
43. Heskin, M.; Guillet, J. E. J Macromol Sci Pure Appl Chem 1968, A2, 1441–1455.
44. Schild, H. G. Prog Polym Sci 1992, 17, 163–249.
45. Okada, Y.; Tanaka, F. Macromolecules 2005, 38, 4465–4471.
46. Wu, C.; Zhou, S. Q. Macromolecules 1995, 28, 8381–8387.
47. Wu, C.; Zhou, S. Q. Macromolecules 1995, 28, 5388–5390.
48. Ono, Y.; Shikata, T. J Am Chem Soc 2006, 128, 10030–10031.
49. Xia, Y.; Yin, X. C.; Burke, N. A. D.; Stover, H. D. H. Macromolecules 2005, 38, 5937–5943.
50. Tong, Z.; Zeng, F.; Zheng, X.; Sato, T. Macromolecules 1999, 32, 4488–4490.
51. Xia, Y.; Burke, N. A. D.; Stover, H. D. H. Macromolecules 2006, 39, 2275–2283.
52. Chung, J. E.; Yokoyama, M.; Aoyagi, T.; Sakurai, Y.; Okano, T. J Control Release 1998, 53, 119–130.

53. Narumi, A.; Fuchise, K.; Kakuchi, R.; Toda, A.; Satoh, T.; Kawaguchi, S.; Sugiyama, K.; Hirao, A.; Kakuchi, T. Macromol Rapid Commun 2008, 29, 1126–1133.
54. Deng, Y. L.; Pelton, R. Macromolecules 1995, 28, 4617–4621.
55. Yan, J. J.; Ji, W. X.; Chen, E. Q.; Li, Z. C.; Liang, D. H. Macromolecules 2008, 41, 4908–4913.
56. Chen, H. W.; Li, J. F.; Ding, Y. W.; Zhang, G. Z.; Zhang, Q. J.; Wu, C. Macromolecules 2005, 38, 4403–4408.
57. Qiu, X. P.; Wu, C. Macromolecules 1997, 30, 7921–7926.
58. Virtanen, J.; Tenhu, H. Macromolecules 2000, 33, 5970–5975.
59. Zhang, J. Y.; Zhou, Y. M.; Zhu, Z. Y.; Ge, Z. S.; Liu, S. Y. Macromolecules 2008, 41, 1444–1454.
60. Couet, J.; Biesalski, M. Macromolecules 2006, 39, 7258–7268.
61. Iijima, M.; Nagasaki, Y. J Polym Sci Part A: Polym Chem 2006, 44, 1457–1469.