Synthesis of Stimuli-Responsive Star-Like Copolymer H20-PNIPAm-*r*-PEGMA via the ATRP Copolymerization Technique and its Micellization in Aqueous Solution

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ABSTRACT: A series of novel star-like copolymers H20-poly(*N*-isopropylacrylamide)-random-poly(poly(ethylene glycol) methyl ether methacrylate) (H20-PNIPAm-*r*-PEGMA), which could respond to both temperature and ionic strength stimuli in aqueous solution were synthesized by atom transfer radical polymerization. Stimuli-response of these copolymers in aqueous solution was characterized by dynamic laser scattering (DLS), ^{1}H-NMR and turbidity. In aqueous solution, these star-like copolymers exhibited response to temperature and ionic strength with tunable low-critical solution temperature (LCST) from 32 to 100°C. The LCST values of copolymers increased with increasing PEGMA contents, while decreased with increasing ionic strength. An interesting phenomenon, which should be a unique character of star-like copolymer, was observed by the turbidity test of copolymer 1160. The addition of sodium chloride and increase of concentration can let copolymer 1160 behave normally, which was further confirmed by atomic force microscopy and DLS. © 2009 Wiley Periodicals, Inc. J Appl Polym Sci 115: 1831–1840, 2010

Key words: ATRP; star-like copolymer; stimuli-response

INTRODUCTION

Dendrimers are highly branched macromolecules with a big amount of "tunable" surface groups and an interior.[1] Their star-like structure and thus unique properties are useful in many fields, including drug delivery, catalysis, gene therapy, chemical sensors, etc.[2–6] The incorporation of stimuli-responsive character into dendrimers can significantly expand the scope of these molecules in application.[7,8] Recent efforts in the fields of stimuli-response materials have been focusing on the design of structures that respond to various stimuli.[9–12] As one of most extensively studied thermosensitive polymers, poly(*N*-isopropylacrylamide) (PNIPAm) shows a low-critical solution temperature (LCST) at around 32°C in aqueous solutions.[13–16] This distinctive property of PNIPAm is attributed to its unique rapid alternation in hydrophilicity and hydrophobicity around LCST. The LCST of PNIPAm can be tuned to a desired temperature range by copolymerizing a more hydrophilic comonomer (which raises the LCST) or a more hydrophobic comonomer (which lowers the LCST).[17–19]

The thermoresponsive PNIPAm segment brings interesting properties to the block and graft copolymers containing it. Among all these thermoresponsive copolymers, PNIPAm-*g*-PEO and PEO-*b*-PNIPAm are of particular interest. Previous studies of the copolymers of PNIPAm with poly(ethylene glycol) (PEO) have shown that the blocks formed polymeric micelles with a core of collapsed PNIPAm stabilized by a corona of PEO above the LCST.[20,21] Wu and coworkers investigated the folding and unfolding of the individual PNIPAm-*g*-PEO chains during the heating and cooling process.[22] Annaka and coworkers synthesized three relatively narrowly distributed block copolymers with different block lengths and investigated the self-assembly of these block copolymers in detail, where they obtained the binary phase diagram of these block copolymers in solution.[23] Bruno and coworkers studied the influence of macromolecular architecture on the thermal response rate of PEO-modified thermoresponsive PNIPAm copolymers in solution.[24] In the field of stimuli-response, it should be noted that most of the published works focused on the linear copolymers. Few have studied the behavior of star-like copolymers such as PNIPAm-*g*-PEO or PEO-*b*-PNIPAm. Thus, it would be interesting to explore the properties of star-like copolymer of PNIPAm with PEO.

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In this work, PEGMA and NIPAm copolymer compositions with different PEGMA contents were synthesized using atom transfer radical polymerization (ATRP) to get controlled and narrow molecular weight distributions. According to a previous report,[25] both the molecular weight and its polydispersity of PNIPAm influence the LCST. The dual temperature and ionic strength responses have been characterized, and their sharp, tunable phase transitions around neutral pH may be exploitable in drug delivery, molecular switching, and responsive hydrogel applications.

EXPERIMENTAL SECTION

Materials

N-Isopropylacrylamide (NIPAm) (Shanghai Wu Jing Co., 99%) was purified by crystallization from hexane before use. *N*,*N*-Dimethylformamide (DMF) (Sinopharm Chemical Reagent Co., 99.5%), 1,1,4,7,7-pentamethyldiethylenetriamine (PMDETA) (Alfa Aesar, 98%), hyperbranched polymer Boltorn H20 (Perstorp Specialty Chemicals AB, Sweden, M_n = 1747, M_w = 2100), 2-bromoisobutyryl bromide (BIB) (Alfa Aesar, 97%), poly(ethylene glycol) methyl ether methacrylate (PEGMA) (Aldrich, $M_n \sim 1100$), CuBr (Sinopharm Chemical Reagent Co., 97%), and all other reagents were used as supplied.

Preparation of the ATRP initiator H20-Br

H20 (2.0 g, 0.625 mmol) was added to a three-neck round-bottom flask and dissolved in 20 mL DMF. The H20 solution was cooled to 0°C under a nitrogen atmosphere by an ice bath. BIB (5.0 mL, 40 mmol) was dissolved in DMF (10 mL) and then cooled to 0°C. Under continuous stirring, the BIB solution was added dropwise to the H20 solution using a pressure-equalizer funnel over 30 min. The reaction temperature was maintained at 0°C for 2 h and then allowed to rise slowly to ambient temperature after which the reaction continued for 18 h. The syrup was poured into 20-fold cold deionized water to produce white viscous liquid. The product was washed by cold deionized water for three times and then dried in a vacuum oven at 80°C (see Scheme 1).

Preparation of the graft copolymer H20-PNIPAm-*r*-PEGMA

H20-PNIPAm-*r*-PEGMA was synthesized by ATRP of NIPAm and PEGMA using H20-Br as the initiator and CuBr as the catalyst. PMDETA was used as the ligand in this system. The detailed procedure was as follows: 0.0359 g CuBr and 0.0434 g PMDETA were added into the reaction flask and 10 mL DMF was then added. The sample was first stirred and then degassed under nitrogen purge. Subsequently, 0.0639 g H20-Br, 2.829 g NIPAm, and different weight of PEGMA were added into the flask and degassed by purging with nitrogen under protection of liquid nitrogen. The $[H20\text{-}Br]_0$: $[NIPAm]_0$ was maintained at 1 : 1600 (mole basis) whereas the $[H20\text{-}Br]_0$: $[PEGMA]_0$ ratio was varied to prepare random polymers with a range of compositions. Polymerization was performed at 40°C for 2 h. The block copolymer was purified by passing through an Al_2O_3 column to remove the copper catalyst and then was precipitated in ether to produce a white precipitate. The precipitate was then recrystallized for three times. Finally, the precipitate was filtered and dried in a vacuum oven at 40°C. Monomer conversions of these polymers were about 30%. The synthetic procedure for H20-PNIPAm-*r*-PEGMA by ATRP is illustrated in Scheme 1.

Characterization

Gel permeation chromatography

Molecular weights (M_n) and molecular weight distributions (M_w/M_n) were determined by a PE Series 200 gel permeation chromatography (GPC). The *N*,*N*-dimethylformamide (DMF) was used as the eluent at a flow rate of 1.0 mL/min and polystyrene as the calibration standard.

Nuclear magnetic resonance spectroscopy

^{1}H-NMR measurements were carried out on a Varian Mercury Plus spectrometer operating at 400 MHz for protons equipped with a temperature control unit. Solvent for nuclear magnetic resonance (NMR) spectroscopy were $CDCl_3$ (TMS internal standard) and D_2O (HOD internal standard).

Dynamic light scattering

Dynamic light scattering (DLS) studies of the copolymers at concentrations of 1.00/L were conducted using a Malvern Instruments Zetasizer Nano ZS instrument equipped with a 4 mW He-Ne laser (λ = 633 nm) at an angle of 173°, an avalanche photodiode detector with high-quantum efficiency, and an ALV/LSE-5003 multiple τ digital correlator electronics system. The CONTIN analysis method was used.

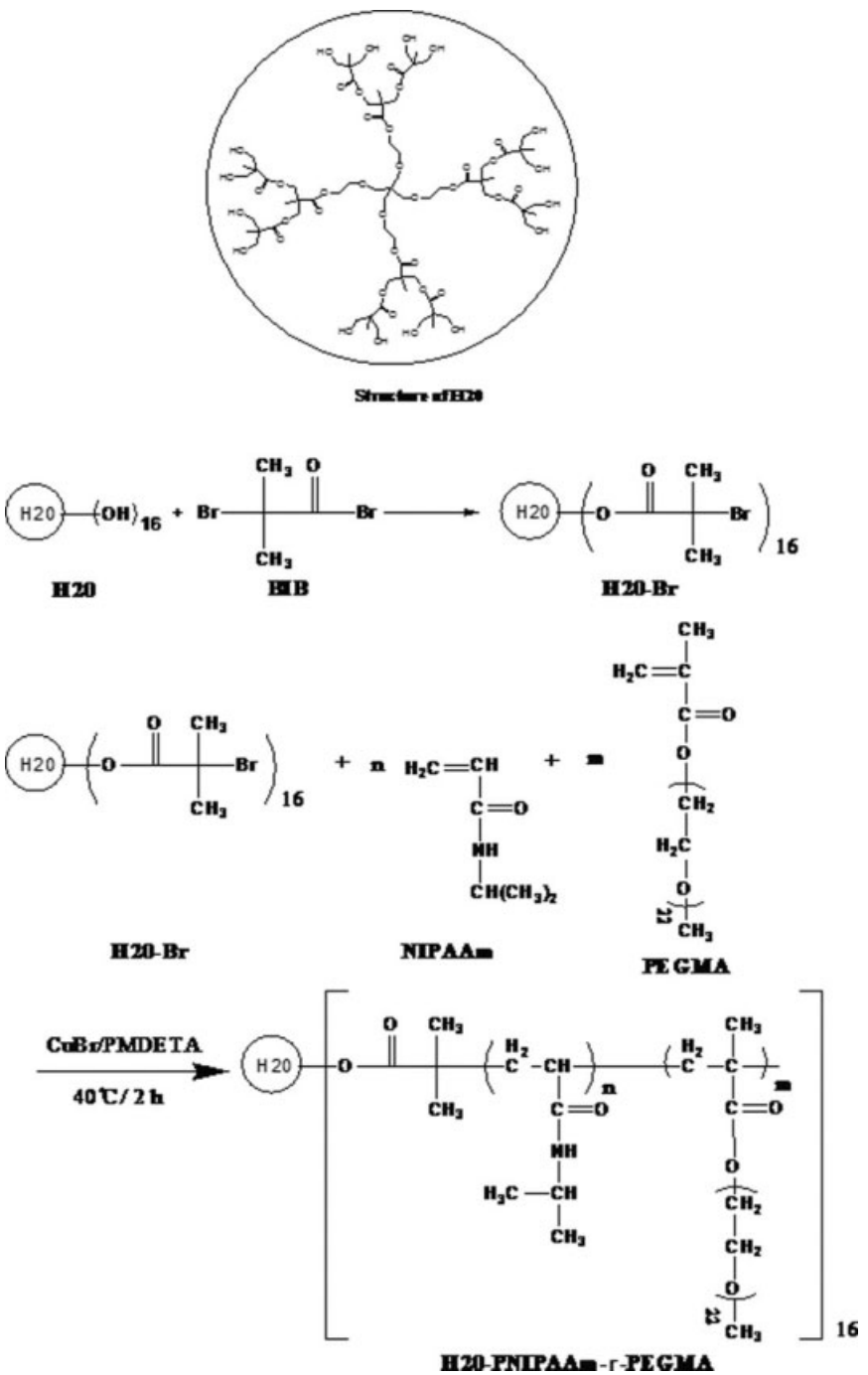
Elemental analysis

Elemental analysis (EA) was conducted on an Elmentar Varioel apparatus. Ratio of (PEGMA/NIPAm) in the copolymers were calculated using the following equation.

$$\begin{cases} \mathrm{N}\% = \dfrac{\sum M_n(\mathrm{N})}{M_n(\mathrm{H20-PNIPAm-}r\mathrm{-PEGMA})} = \dfrac{14 \times n \times 16}{1475 + 16 \times (86 + 113 \times n + 1067 \times m)} \\ \mathrm{C}\% = \dfrac{\sum M_n(\mathrm{C})}{M_n(\mathrm{H20-PNIPAm-}r\mathrm{-PEGMA})} = \dfrac{828 + 16 \times (48 + 72 \times n + 588 \times m)}{1475 + 16 \times (86 + 113 \times n + 1067 \times m)} \\ \mathrm{H}\% = \dfrac{\sum M_n(\mathrm{H})}{M_n(\mathrm{H20-PNIPAm-}r\mathrm{-PEGMA})} = \dfrac{116 + 16 \times (6 + 11n + 96m)}{1475 + 16 \times (86 + 113 \times n + 1067 \times m)} \end{cases}$$

Ratio of (PEGMA/NIPAm) $= \frac{m}{n}$

where n and m were illustrated in Scheme 1.



Scheme 1 Process for synthesis of star-like copolymer H20-PNIPAm-*r*-PEGMA by ATRP.

TABLE I
Preparation of H_2O-PNIPAm-*r*-PEGMA Using ATRP

Polymer[a]	Monomer (in feed)[b] [PEGMA]/[I]	[NIPAm]/[I]	Ratio ([PEGMA]/[NIPAm])	Ratio ([PEGMA]/[NIPAm]) (in products)[c]	% conv.[d]	M_n (expt)	M_w/M_n
1000 (PNIPAm)		100		0	31	5.69×10^4	1.28
1160 (H20-PNIPAm-*r*-PEGMA)	0.625	100	1/160	0.014	29	6.01×10^4	1.31
1020 (H20-PNIPAm-*r*-PEGMA)	5	100	1/20	0.158	32	6.94×10^4	1.32
1010 (H20-PNIPAm-*r*-PEGMA)	10	100	1/10	0.241	33	7.59×10^4	1.30
1005 (H20-PNIPAm-*r*-PEGMA)	20	100	1/5	0.476	31	7.90×10^4	1.38

[a] Copolymerization was carried out at 40°C for 2 h, H20-Br as initiator, CuBr as catalyst, PMDETA as ligand, and DMF as solvent.
[b] [I], [PEGMA], and [NIPAAm] represent mole fraction of ATRP initiator H20-Br, PEGMA, and NIPAAm, respectively.
[c] Component of copolymers was determined by EA.
[d] Determined by ^{1}H-NMR.

Atomic force microscopy

The deposition of H20-PNIPAm-*r*-PEGMA self-assemblies from the solution was carried out on mica sheet. The surface morphologies of samples were acquired in contacting mode on atomic force microscopy (AFM; NanoscopeIII, Digital instruments, USA).

LCST measurement (turbidity)

The LCSTs of the polymer solutions were measured on a GBC Cintra 10e UV–visible spectrophotometer by monitoring the turbidity of the polymer solutions as a function of temperature at 500 nm and under the heating rate of 1°C/min. The temperature at 90% light transmittance of the polymer solution was defined as the LCST. The concentration of polymer used for LCST determination was 1 mg/mL, which was given at caption to figures. Other concentrations of polymer, such as 4 mg/mL, 7 mg/mL, and 10 mg/mL, were also used to study the influence of concentration to LCST of polymer.

RESULTS AND DISCUSSION

Synthesis of H20-PNIPAm-*r*-PEGMA

Following the idea that the LCST of PNIPAm can be tuned to a desired temperature range by copolymerizing a more hydrophilic comonomer (which raises the LCST), five H20-PNIPAm-*r*-PEGMA copolymers with different PEGMA contents were prepared according to Scheme 1, and their conditions and results are summarized in Table I. The ATRP copolymerization proceeds in a controlled way with a [I]/[CuBr]/[PMDETA] ratio of 1/1/1, yielding polymers with relatively low M_w/M_n values (~1.3). The composition of the obtained H20-PNIPAm-*r*-PEGMA were determined by ^{1}H-NMR and EA, and shown in Table I.

Temperature response of copolymers

The LCST behaviors of H20-PNIPAm-*r*-PEGMA copolymer solutions were characterized by measuring their cloud points. Figure 1 shows typical transmittance versus temperature curves for copolymers with rationally varied compositions. The copolymerization of NIPAm with PEGMA is able to adjust LCST of PNIPAm at a range from 32 to 100°C.

Figure 2 shows LCST of copolymers with different PEGMA contents. The LCST values of H20-PNIPAm-*r*-PEGMA copolymers increase with increasing PEGMA contents indicating its well tunability of LCST. The LCST of thermoresponsive polymers is attributed to a change in the hydrophilic/hydrophobic balance of the polymers with respect to the

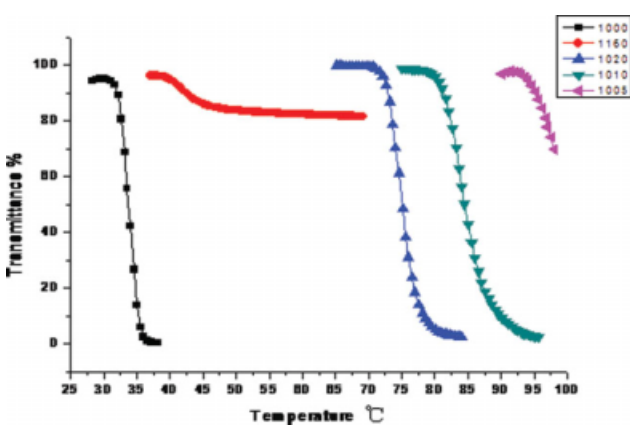


Figure 1 Phase transitions of H_2O-PNIPAm-*r*-PEGMA copolymers aqueous solutions (1 mg/mL) measured by the cloud point method. [Color figure can be viewed in the online issue, which is available at www.interscience.wiley.com.]

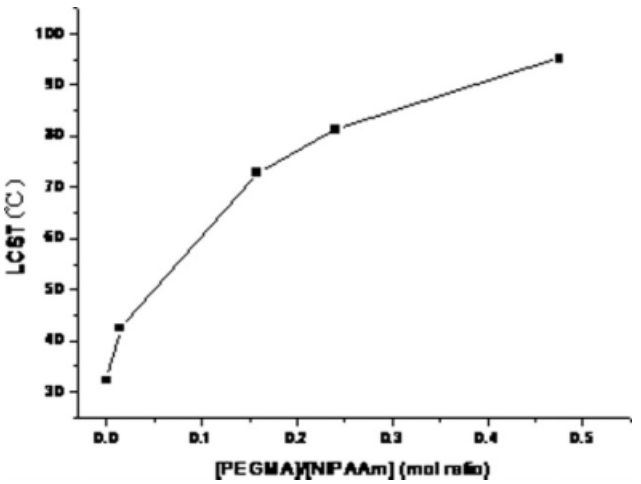


Figure 2 Relationship between LCST and PEGMA content of copolymers. Component of copolymers was determined by EA.

hydrophobic and H-bond interactions of water molecules with the polymer chain. At low temperature, strong H-bonding interactions between polar groups and water lead to good solubility of the polymer, which is opposed by the hydration of apolar groups. The water surrounding the apolar groups is in a low-entropy state relative to free water, leading to an entropic penalty. As the apolar surface area of the polymer increases, this entropic penalty will increase and the LCST will decrease. In this work, the increasing PEGMA contents, which were hydrophilic, of H20-PNIPAm-*r*-PEGMA made the apolar surface area of the copolymers decrease, leading to the decrease of entropic penalty and the increase of the LCST of the copolymers.

PNIPAm homopolymer is hydrophilic and exists as individual random coil chains in water when the temperature is lower than the LCST, while PNIPAm becomes hydrophobic and collapses into individual single-chain globules or stable multichain aggregates, depending on the solution condition, at higher temperatures. Figure 3 shows temperature dependence of the average hydrodynamic radius (Z-Ave) of copolymer 1000 in pure water. The figure shows a clear tendency that the change of Z-Ave of the copolymers can be divided into three stages[26]: (1) when temperature is below LCST, water progressively becomes a poor solvent for the PNIPAm backbone chain with increasing temperature, resulting in a slight decrease of Z-Ave. (2) When temperature is around LCST, with increasing temperature, the formation of the star-like copolymer H20-PNIPAm-*r*-PEGMA nanoparticles actually involves three simultaneous processes: the PNIPAm backbone chains of the star-like copolymer undergo the intermolecular aggregation which is dominant and quick, the intramolecular multichain aggregation and intrachain "coil-to-globule" transition, so that Z-Ave increases rapidly and then decreases slowly. (3) When temperature is far above LCST, the PNIPAm backbone chains are already in its fully collapsed state so that a further increase of temperature has little effect on Z-Ave.

Effect of ionic strength and concentration on LCST

Figure 4 shows the influence of the ionic strength on the LCSTs of the copolymers solutions and on the sensitivity of thermoresponse. The influence of salts on the thermal behavior of the polymers is indeed an important parameter for biomedical applications. The salt effects on the water solubility of nonionic compounds have been of interest since the pioneering study of Hofmeister[27] and have been discussed extensively recently.[28,29] Solubility of organic compounds in water can be adjusted by adding inorganic salts. Most of the salts decrease water solubility of organic solutes (salting-out phenomenon), whereas some of them (NaI, $NaClO_4$, NaSCN) have the opposite effect (salting-in). Figure 4(A) shows cloud points recorded for the five copolymers solutions in the presence of increasing amount of sodium chloride. The typical salting-out effect was observed. The presence of sodium chloride makes the macromolecules partially dehydrated and consequently leads to a decrease of the LCST. Figure 4(B) shows the transmittance versus temperature curves for copolymer 1010 solution with different ionic strength. It should be noted that the copolymer respond more sharply to temperature in the solution with a higher ionic strength. The reason is supposed to be that the increasing of ionic strength is able to speed up the dehydration of the macromolecules.

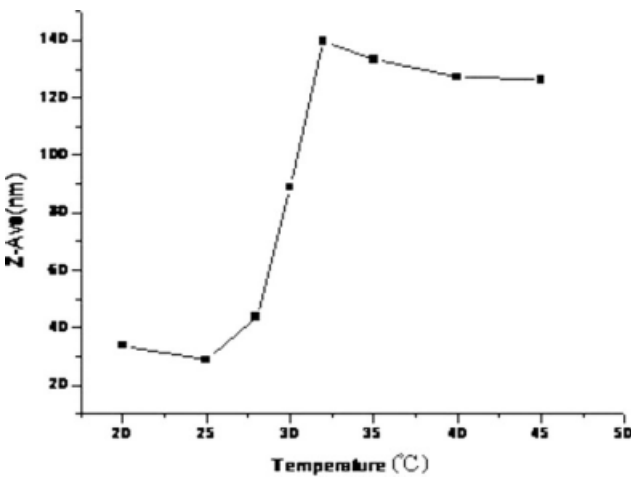


Figure 3 Temperature dependence of the average hydrodynamic radius (Z-Ave) of copolymer 1000 in pure water (1 mg/mL).

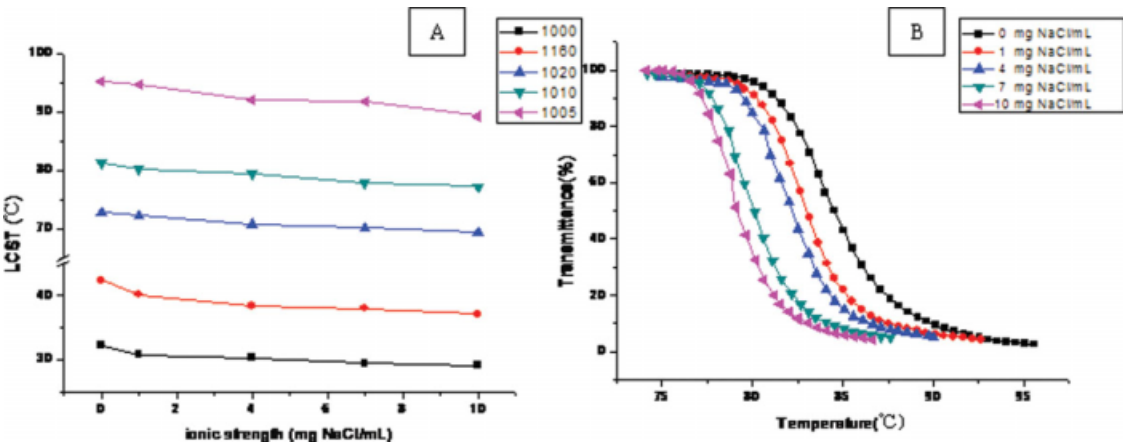


Figure 4 A: The LCSTs of H_2O-PNIPAm-*r*-PEGMA copolymers aqueous solutions (1 mg/mL) with different ionic strength. B: Transmittance versus temperature curves for copolymer 1010 aqueous solution (1 mg/mL) with different ionic strength. [Color figure can be viewed in the online issue, which is available at www.interscience.wiley.com.]

Figure 5 shows the influence of the solution concentration to the LCSTs of the copolymers solutions and to the sensitivity of thermoresponse. It can be found from Figure 5(A) that the LCSTs of copolymers solutions increase a few degrees with dilution in the studied range of concentration (1–10 mg/mL). The dilution of copolymers solutions decrease the opportunity of intermolecular aggregation, which leads to the increase of LCST. Figure 5(B) shows transmittance versus temperature curves for copolymer 1020 solutions with different concentration. The phase transition of copolymer 1020 solutions was found to be relatively independent of their concentration, which becomes a bit sharper with the increasing of the concentration.

Mechanism for copolymer's phase transition in aqueous solution

Figure 6 shows the ^{1}H-NMR spectra recorded for H20-PNIPAm-*r*-PEGMA in D_2O at different temperatures. At 25°C, the copolymer is molecularly dissolved and all the signals due to both segments (PNIPAm and PEGMA) are visible. When the temperature was 60°C, all of the signals attributed to both segments are greatly suppressed, indicating that both segments of PNIPAm and PEGMA are no longer soluble in water.

Based on the above results, together with the findings about PNIPAm and PEO-*co*-PNIPAm in literatures,[30] Scheme 2 gives a possible mechanism for the aggregation behavior of star-like copolymer

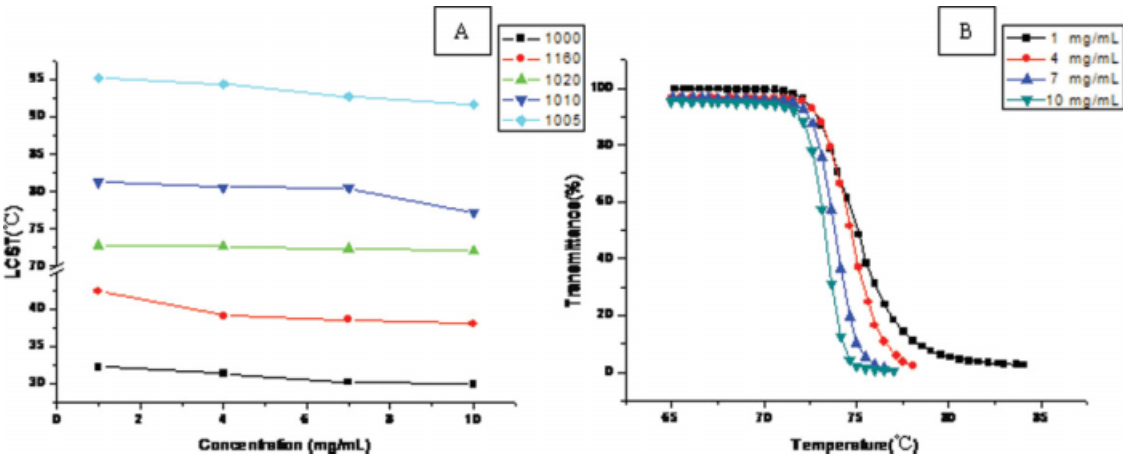


Figure 5 A: The LCSTs of H_2O-PNIPAm-*r*-PEGMA copolymers pure water solutions with different concentration. B: Transmittance versus temperature curves for copolymer 1020 pure water solutions with different concentration. [Color figure can be viewed in the online issue, which is available at www.interscience.wiley.com.]

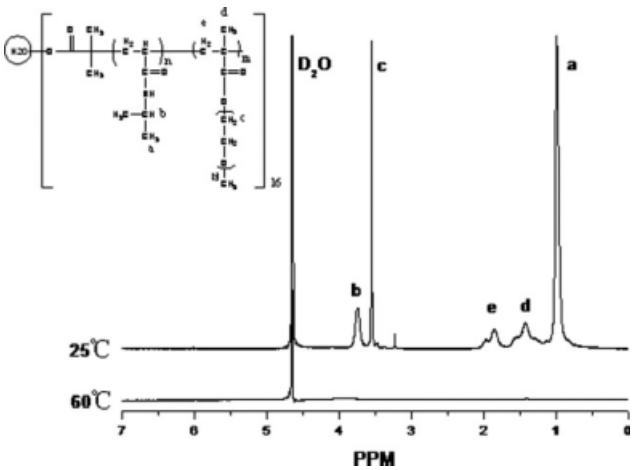


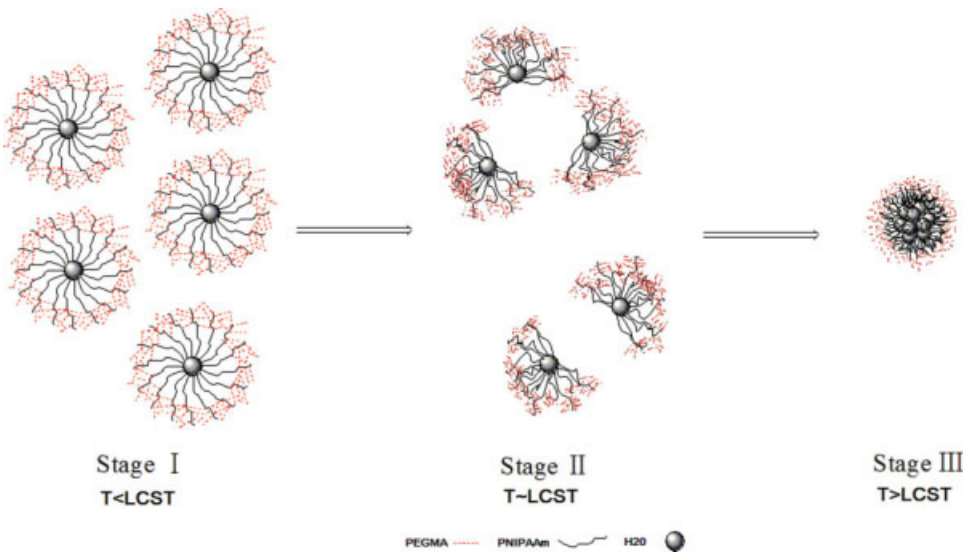
Figure 6 ^{1}H-NMR spectra obtained for copolymer 1160 in D_2O (8 mg/mL) at different temperatures.

H20-PNIPAm-*r*-PEGMA during the heating process. It was easy to understand that the steric hindrance of PEGMA is much stronger than the steric hindrance of NIPAm, especially at the forepart of copolymerization. Therefore, the PEGMA chains tend to locate at the terminal of the PNIPAm backbone. At temperatures below the LCST of PNIPAm (Stage I), water was a good solvent for both PEGMA and PNIPAm. Sixteen arms consist of PNIPAm backbones are in a random coil conformation with a core of H20. On further increasing of the temperature, water slowly become a less selective solvent for PNIPAm chains (Stage II) and thus PNIPAm chains started to shrink and tended to aggregate. Also, because of the solubility of PEGMA, free chains with a core of H20 still widely existed in this stage. Most star-like macromolecule contains a PNIPAm-rich domain and a PEGMA rich domain at temperature above the LCST of PNIPAm. And only relatively loose aggregates, containing a larger PNIPAm-rich domain, were formed. Such aggregates were believed to have acted as precursors for micelle formation. At temperatures above the LCST of copolymer (Stage III), PNIPAm segment collapsed and the solubility force of PEGMA was relatively not important any more. Similar to linear copolymer of PNIPAm with PEGMA, the primary micelles, with PNIPAm being the core and PEGMA being the corona, were formed, and the number of unimers quickly diminished.

Unique phase transition behavior for copolymer 1160

There is something interesting which can be seen in Figure 1 that the transmittance curve of copolymer 1160 pure water solution just reached 80% and did not go down over a wide temperature range. Such phenomenon of star-like copolymers of PNIPAm with PEGMA should be a special character of star-like copolymer of PNIPAm with PEGMA. To understand this special behavior of copolymer 1160, further experiments were carried out.

Figure 7 shows transmittance versus temperature curves for copolymer 1160 solution with different ionic strength and with different concentration. It is clear that both the presence of sodium chloride and the increase of concentration could sharpen the phase separation of copolymer 1160 solution. The increase of concentration gave more opportunities to



Scheme 2 Illustration of the three distinct stages of the star-like copolymer H20-PNIPAAm-*g*-PEGMA in aqueous solution during a heating process. [Color figure can be viewed in the online issue, which is available at www.interscience.wiley.com.]

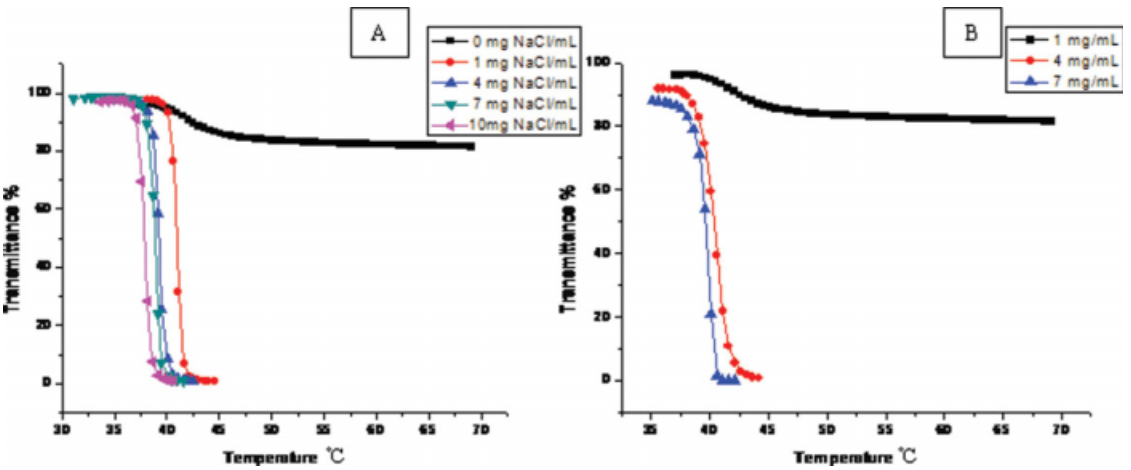


Figure 7 A: Transmittance versus temperature curves for copolymer 1160 aqueous solution (1 mg/mL) with different ionic strength. B: Transmittance versus temperature curves for copolymer 1160 pure water solution with different concentration. [Color figure can be viewed in the online issue, which is available at www.interscience.wiley.com.]

intermolecular aggregation, which leads to a sharp phase separation.

To confirm the influence of ionic strength on the special behavior of copolymer 1160, both copolymer 1160 solutions with and without sodium chloride were checked by AFM and DLS measurements, which are shown in Figures 8 and 9, respectively. It can be clearly seen from Figure 8(A) that most of the

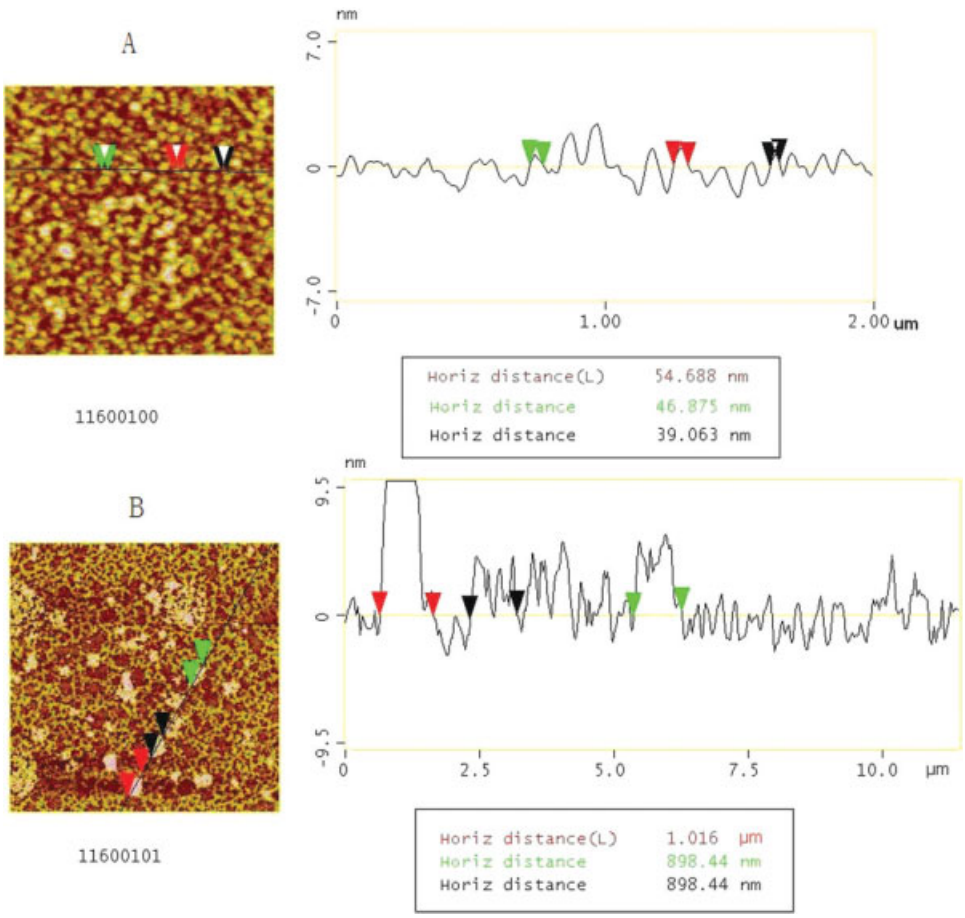


Figure 8 AFM images of copolymer 1160: (A) in pure water solution and (B) in aqueous solution with addition of sodium chloride (0.1 mg NaCl/mL). Concentration of both solutions was 0.05 mg/mL. [Color figure can be viewed in the online issue, which is available at www.interscience.wiley.com.]

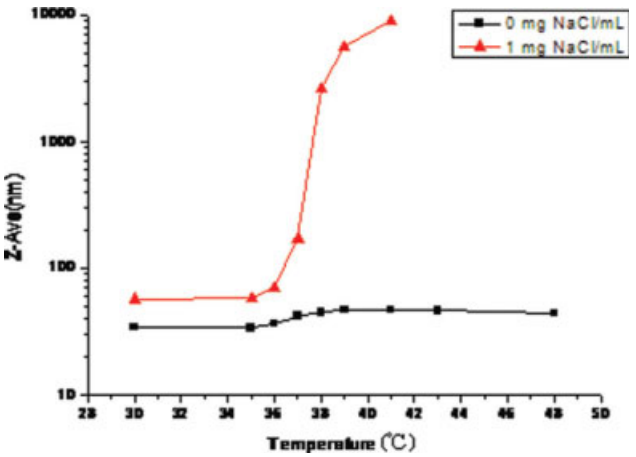
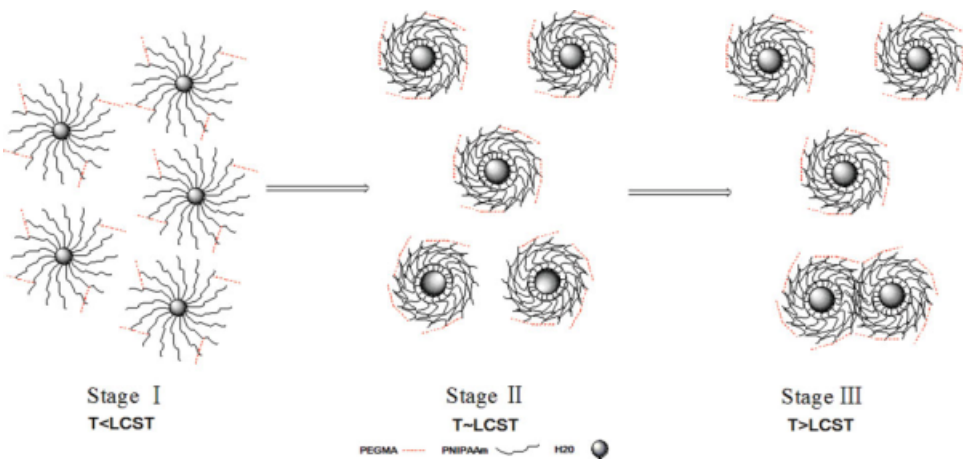


Figure 9 Temperature dependence of the average hydrodynamic radius (Z-Ave) of copolymer 1160 solutions (1 mg/mL) with different ionic strength. [Color figure can be viewed in the online issue, which is available at www.interscience.wiley.com.]

copolymer 1160, in pure water solution without sodium chloride, kept individual like a ball instead of forming large aggregates, when the temperature of the solution was above the LCST of copolymer 1160. In contrast, with the addition of sodium chloride, many enormous aggregations could be seen in the AFM image [Fig. 8(B)], when the temperature of the solution was above the LCST of copolymer 1160. Figure 9 clearly shows that temperature has little influence on the size of copolymer 1160 in pure water solution. The particle size was uniform around 40 nm which was corresponding to the AFM image [Fig. 8(A)], indicating that few aggregations formed. The addition of sodium chloride made the size of copolymer 1160 in aqueous solution increase extremely with the increasing of temperature, which implied that aggregations formed and became more and more enormous on increase of the temperature. The presence of ionized sodium chloride in copolymer 1160 aqueous solution broke ionic stabilization, which might increase the intermolecular aggregation into large aggregates. However, the fundamental mechanisms of salts' influence on micellization and phase separation remain elusive.[28,29]

On the basis of these results, we could draw a conclusion that intermolecular aggregation is the keystone of the phase separation of these copolymers, and rapid intermolecular aggregation into large aggregates leads to sharp phase separation.

By comparing copolymer 1160 with the other copolymers in this work and with the copolymers of PNIPAm with PEO in literatures, it can be found that very small amount of PEGMA content and the star-like structure should be the reasons of such special phenomenon. Different from the other copolymers in this work, the PEGMA content of copolymer 1160 was too small to cover each PNIPAm backbones. On the basis of the aforementioned results, we give a possible explanation to the special phenomenon of copolymer 1160. As schematically shown in Scheme 3, copolymer 1160 also underwent three stages of transformation with increasing temperature. At Stage I, water was a good solvent for both PEGMA and PNIPAm. Sixteen arms consisted of PNIPAm backbones were in a random coil conformation with a core of H20. At Stage II, water slowly became selective solvent for PNIPAm chains and thus PNIPAm chains started to shrink and tended to aggregate. Each star-like macromolecule contained a PNIPAm-rich domain, whereas no PEGMA rich domain was formed because of the exceeding small content of PEGMA, while linear macromolecules could hardly keep such a structure. At Stage III, PNIPAm segment collapsed and tended to aggregate



Scheme 3 Illustration of the three distinct stages of the star-like copolymer 1160 in pure water solution with low concentration (~1 mg/mL) during heating process. [Color figure can be viewed in the online issue, which is available at www.interscience.wiley.com.]

to form micelles. However, the relatively long PEGMA chains outside the PNIPAm-rich domain of copolymer shielded the PNIPAm segment against intermolecular aggregation. The star-like structure of the copolymer made it imaginable to prevent the intermolecular aggregation in all exposures, whereas linear copolymers could hardly achieve it. There were few copolymer 1160 macromolecules aggregated by the PNIPAm-rich domains without PEGMA chains. The abnormal phenomenon of copolymer 1160 should attribute to the few intermolecular aggregations to a great extent.

CONCLUSIONS

We have prepared a series of novel star-like copolymers of H20-PNIPAm-*r*-PEGMA using ATRP technique. These copolymers respond sharply to temperature and ionic strength. The LCST value of the copolymers increases with increasing PEGMA contents and decreases a few with increasing concentration. An abnormal phenomenon, which should be a unique character of star-like copolymer, was found by turbidity test of copolymer 1160. The aggregation process of these copolymers in aqueous solutions was studied by AFM and DLS techniques, indicating that intermolecular aggregation is the key of the phase separation of this series of copolymers. The rapid intermolecular aggregation into large aggregates leads to sharp phase separation. The concept may be applied to other star-like copolymers that can respond to stimuli such as changes in pH, temperature, ionic strength, and presence of bioactive species. The high sensitivity of this series of star-like copolymers to small changes in temperature and ionic strength suggests that they could be useful in biotechnology, drug delivery, and stimuli-response smart switch.

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