Poly(*N*-isopropylacrylamide) Grafted to a Strongly Charged Backbone: Thermoresponsive Behavior in Aqueous Solution

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Received 31 July 2003; accepted 2 October 2003

ABSTRACT: The thermoresponsive properties in aqueous solution of the graft copolymer poly(acrylic acid-*co*-2-acrylamido-2-methyl propane sulfonic acid)-*g*-poly(*N*-isopropylacrylamide) [P(AA-*co*-AMPSA)-*g*-PNIPAM] were studied and compared to the corresponding behavior of the poly(acrylic acid)-*g*-poly(*N*-isopropylacrylamide) (PAA-*g*-PNIPAM) graft product. Both products contain about 40% (w/w) of PNIPAM, whereas the backbone, P(AA-*co*-AMPSA), of the first copolymer contains about 40% of AMPSA mole units. The strongly charged P(AA-*co*-AMPSA)-*g*-PNIPAM graft copolymer was water soluble over the whole pH range, whereas the PAA-*g*-PNIPAM copolymer precipitated out from water at pH < 4. As a result, the first product exhibited a temperature-sensitive behavior in a wide pH range, extended in the acidic region, whereas in semidilute aqueous solutions, an important thermothickening behavior was observed, even at low pH (pH $= 3.0$). © 2004 Wiley Periodicals, Inc. J Appl Polym Sci 92: 3466–3470, 2004

Key words: water-soluble polymers; graft copolymers; solution properties; association; stimuli-sensitive polymers

INTRODUCTION

Poly(*N*-isopropylacrylamide) (PNIPAM) is a widely studied water-soluble polymer, mainly because of its lower critical solution temperature (LCST) behavior in water (i.e., its inverse solubility behavior), as it precipitates out from water upon heating at $T \sim 33$°C.[1,2] Among other applications, this temperature-induced phase separation has been exploited for the synthesis of the so-called thermoassociative polymers, that is, polymers that tend to associate in aqueous solution upon heating. A familiar and well-studied example of such systems offers the graft copolymer PAA-*g*-PNIPAM, consisting of PNIPAM side chains grafted onto a neutralized poly(acrylic acid) (PAA) backbone.[3–6] In aqueous solutions of this graft copolymer, thanks to the highly hydrophilic neutralized PAA backbone, the LCST-type phase separation of the thermosensitive PNIPAM side chains is confined at a local scale. In semidilute solutions, the hydrophobic aggregates, formed upon heating over the LCST of PNIPAM, crosslink reversibly the polymer chains, resulting in a significant viscosity increase and a thermothickening behavior is exhibited.

It is known that PNIPAM forms compact hydrogen-bonding interpolymer complexes with PAA,[7,8] precipitating out from aqueous solutions, even at pH values as high as 4.[9–12] This behavior restricts the application of the PAA-*g*-PNIPAM copolymers in the alkaline and neutral pH region. To avoid this inconvenience, backbones other than PAA have been used, as for instance polyacrylamide, a nonionic water-soluble polymer,[13] or carboxymethylcellulose, a water-soluble cellulose derivative.[14] Alternatively, we propose here the use as a backbone of a copolymer of acrylic acid (AA) and of a strongly anionic monomer, the 2-acrylamido-2-methylpropane sulfonic acid (AMPSA). The chemical structure of the final graft copolymer synthesized, P(AA-*co*-AMPSA)-*g*-PNIPAM, is presented in Scheme I. The large fraction of AMPSA units in the backbone ensures the high hydrophilicity of the graft copolymer even at very low pH because it does not allow the formation of intrachain hydrogen-bonding complexes between the remaining AA units and the PNIPAM side chains.

The dilute solution properties of P(AA-*co*-AMPSA)-*g*-PNIPAM were studied as a function of pH and temperature by viscometry and fluorescence probing and were related to the thermothickening behavior observed in semidilute solution. Moreover, they were compared to the properties of the corresponding PAA-*g*-PNIPAM graft copolymer.

EXPERIMENTAL

Chemicals

The monomers acrylic acid (AA) and 2-acrylamido-2-methylpropane sulfonic acid (AMPSA) were pur-

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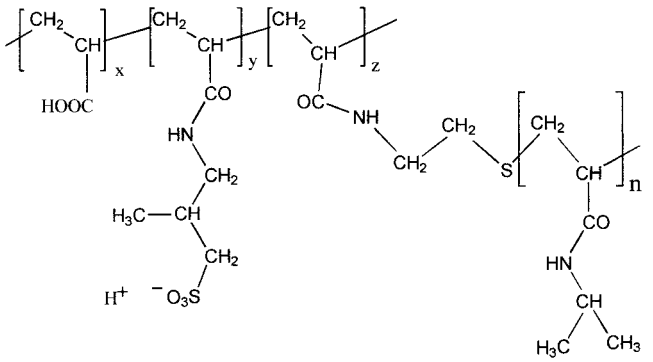
Journal of Applied Polymer Science, Vol. 92, 3466–3470 (2004)



Scheme 1

chased from Polysciences, (Warrington, PA), whereas the monomer *N*-isopropylacrylamide (NIPAM) was a product of Aldrich (Milwaukee, WI) Ammonium persulfate (APS; Serva, Heidelberg, Germany), potassium metabisulfite (KBS; Aldrich), 2-aminoethanethiol hydrochloride (AET; Aldrich) and 1-(3-(dimethylamino)propyl)-3-ethyl-carbodiimide hydrochloride (EDC; Aldrich) were used for the synthesis of the graft copolymers.

For the synthesis of the graft copolymer PAA-*g*-PNIPAM, poly(acrylic acid) (PAA, nominal molar mass of 250,000 daltons; Polysciences) was used.

For the preparation of the buffer solutions NaCl, citric acid (CA) and Na_2HPO_4 from Merck (Darmstadt, Germany) were used.

Water was purified by means of a Seralpur Pro 90C apparatus (Seral, Rotkreuz, Switzerland) combined with a USF Elga laboratory unit (Vivendi Water Systems, Bucks, UK).

Polymer synthesis

Amine-terminated PNIPAM was synthesized by free-radical polymerization of NIPAM in water at 28°C for 6 h using the redox couple APS and AET as initiator and chain transfer agent, respectively. The polymer was purified by dialysis against water through a membrane (cutoff ~ 12 kDa) and freeze dried.

The copolymer of AA and AMPSA, P(AA-*co*-AMPSA), was prepared by free-radical copolymerization of the two monomers in water, in a 65 : 35 mole ratio, after a partial neutralization (80–85 mole %) with NaOH at pH ~ 6–7, at 30°C for 6 h using the redox couple APS/KBS. The product obtained was then fully neutralized (pH = 11) with NaOH, purified by dialysis, and freeze dried.

The graft copolymer P(AA-*co*-AMPSA)-*g*-PNIPAM was synthesized by a coupling reaction between P(AA-*co*-AMPSA) and amine-terminated PNIPAM. The two polymers were dissolved in water at a 2 : 1 weight ratio. Then, an excess of the coupling agent EDC was added and the solution was stirred for 6 h at room temperature. Addition of EDC was repeated for a second time. The reaction mixture was purified with a Pellicon system equipped with a tangential flow filter membrane (cutoff = 100 kDa; Millipore, Milford, MA) and freeze dried.

The graft copolymer PAA-*g*-PNIPAM was synthesized by a similar coupling reaction between PAA and amine-terminated PNIPAM. The experimental procedure was identical to the procedure followed for the synthesis of the graft copolymer P(AA-*co*-AMPSA)-*g*-PNIPAM.

Characterization

To confirm the completion of the grafting reactions, the products were analyzed by SEC. The number-average molecular weight of the amine-terminated PNIPAM chains was determined to be 23,000 from the potentiometric titration of the end groups with HCl, whereas the weight-average molecular weight was 45,000 from the determination of its intrinsic viscosity in 0.5 $LiNO_3$ aqueous solution at 20°C.[15] The composition of the backbone and the two graft copolymers was assessed from the potentiometric titration of the acrylate content of the three products. It was found that the backbone, P(AA-*co*-AMPSA), contains 41 mol % AMPSA units, whereas the PNIPAM content of the two graft copolymers, P(AA-*co*-AMPSA)-*g*-PNIPAM and PAA-*g*-PNIPAM, was 37 and 39 wt %, respectively. The intrinsic viscosity of the sodium salt form of PAA and P(AA-*co*-AMPSA) in 0.5*M* NaBr at 25°C was 193 and 168 $cm^3\ g^{-1}$, respectively.

Rheology

Reduced viscosity studies, as well as intrinsic viscosity determination, were carried out with an automated viscosity measuring system (Schott-Gerate AVS 300, Schott Gerate GmbH, Mainz, Germany) equipped with a Ubbelohde-type viscometer (Cannon–Ubbelohde, State College, PA).

Steady-state shear viscosity measurements of semidilute aqueous polymer mixtures were performed on a Rheometrics (Piscataway, NJ) SR-200 controlled-stress rheometer, using a cone-plate geometry (diameter = 25 mm, angle = 2°).

Fluorescence probing

Steady-state fluorescence spectra of pyrene were recorded on a Perkin–Elmer LS50B luminescence spectrometer (Perkin Elmer Cetus Instruments, Norwalk, CT), equipped with a circulating water bath. A stock ethanolic solution, containing 1×10^{-3} *M* pyrene, was used. The final concentration of the probe was 6×10^{-7} *M* and the excitation wavelength was 334 nm. The intensity ratio (I_1/I_3) of the first (I_1) over the third (I_3) vibronic band of the emission spectrum of pyrene, at 373 and 384 nm, respectively, was used to detect the formation of hydrophobic microdomains.

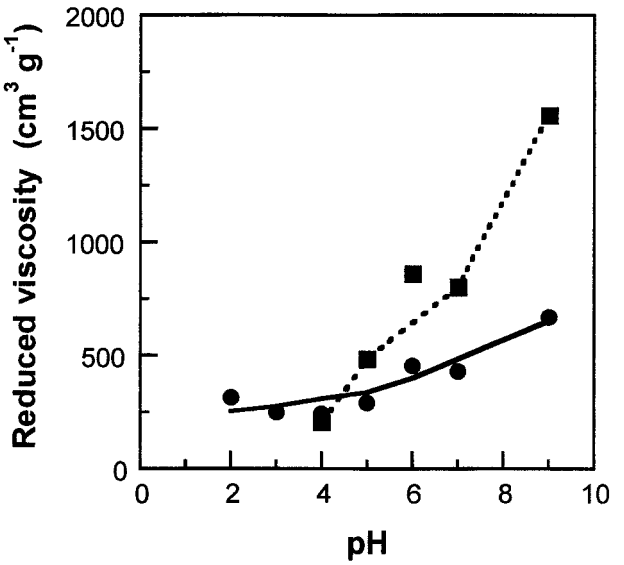


Figure 1 pH dependency of aqueous solutions of PAA-*g*-PNIPAM (■) and P(AA-*co*-AMPSA)-*g*-PNIPAM (●) at 25°C. The polymer concentration is 2.5×10^{-3} g cm^{-3}.

Sample preparation

For the physicochemical studies in dilute solution, pH adjustment was achieved by appropriately mixing 0.05*M* CA with 0.05*M* Na_2HPO_4 solutions, whereas the polymer concentration was 2.5×10^{-3} g cm^{-3}. For the rheological studies in semidilute solution, pH adjustment was achieved by appropriately mixing 0.15*M* CA with 0.15*M* Na_2HPO_4 solutions and the polymer concentration was 5×10^{-2} g cm^{-3}.

RESULTS AND DISCUSSION

pH dependency at $T = 25$°C

To clarify the importance of introducing the strongly charged AMPSA units in the polymer backbone we conducted viscometric and fluorescence probing studies of the two graft copolymers in dilute solution as a function of pH at constant temperature, $T = 25$°C, lower than the LCST of PNIPAM.

In Figure 1 the reduced viscosity of the two graft copolymers is presented as a function of the pH of the solution. The reduced viscosity of PAA-*g*-PNIPAM increases continuously and significantly as the pH of the solution increases from 4 to 9. Obviously, this increase in viscosity is related to the increasing charge density of the graft copolymer backbone. As the pH increases, the fraction of the negatively charged carboxylate groups increases and the polymer backbone expands because of the electrostatic repulsions. On the other hand, the value pH = 4 is the limit for polymer solubility; at pH values lower than 4, phase separation takes place, apparently attributable to hydrogen-bonding association between the PNIPAM side chains and the PAA backbone.

In contrast, the reduced viscosity of the graft copolymer P(AA-*co*-AMPSA)-*g*-PNIPAM changes only slightly with the pH of the solution. For pH $\leq$ 4 the reduced viscosity is rather constant, whereas for higher pH values a very smooth increase is observed. Moreover, no phase separation is observed in this case, even for pH values as low as 2. These results indicate that the strongly charged AMPSA units now dominate the behavior of the polymer, imposing an extended conformation of the polymer backbone and an increased reduced viscosity of the graft copolymer. Any further extension of the backbone, resulting from the increasing fraction of the negatively charged carboxylate groups as the pH increases, is rather slight. Besides, the negatively charged AMPSA groups do not allow hydrogen-bonding complexation between the PNIPAM side chains and the AA backbone units, even if they are all in the acid form of carboxylic groups (at low pH). In fact, this is not unexpected. As a general rule, charged units are very effective structural defects and inhibit hydrogen-bonding association between polyacids and nonionic polybases, even if their fraction is low. For example, introduction of 10 mol % of charged groups in the polyacid chain suffices to inhibit the hydrogen-bonding association between polyethylene glycol (PEG) and PAA.[16–18] Although PNIPAM forms stronger hydrogen-bonding interpolymer complexes with PAA than with PEG, this could hardly compensate for the large fraction (41 mol %) of AMPSA units, contained in the backbone of the graft copolymer P(AA-*co*-AMPSA)-*g*-PNIPAM.

With respect to hydrogen-bonding association, additional confirmation of the above conclusions was obtained from the fluorescence probing studies presented in Figure 2. The hydrogen-bonding association between PNIPAM and PAA is accompanied by an increased hydrophobicity, which can be detected by using adequate fluorescence probes, like pyrene.[19,20] As known, the intensity ratio (I_1/I_3) of the first over the third vibronic band of the emission spectrum of pyrene is sensitive to the polarity of the microenvironment sensed by the probe.[21,22] As we see in Figure 2, the value of the ratio I_1/I_3 is around 1.7 for the graft copolymer P(AA-*co*-AMPSA)-*g*-PNIPAM, regardless of pH, as well as for the graft copolymer PAA-*g*-PNIPAM for pH $\geq$ 5. This means that pyrene in these polymer solutions essentially senses a hydrophilic environment (in pure water, $I_1/I_3 \sim 1.8$) and it does not detect the formation of any hydrophobic microdomains. On the contrary, for the graft copolymer PAA-*g*-PNIPAM at pH = 4, where a strong intrapolymer hydrogen-bonding association between the PAA backbone and the PNIPAM side chains is expected to take place, the ratio I_1/I_3 takes a substantially lower value ($\sim$ 1.4), indicative of a much more hydrophobic mi-

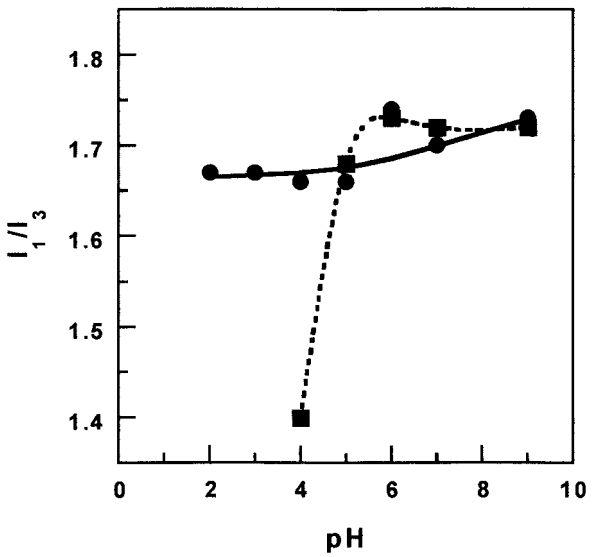


Figure 2 Variation of the ratio I_1/I_3 with pH of aqueous solutions of PAA-*g*-PNIPAM (■) and P(AA-*co*-AMPSA)-*g*-PNIPAM (●) at 25°C. The polymer concentration is 2.5×10^{-3} g cm^{-3}.

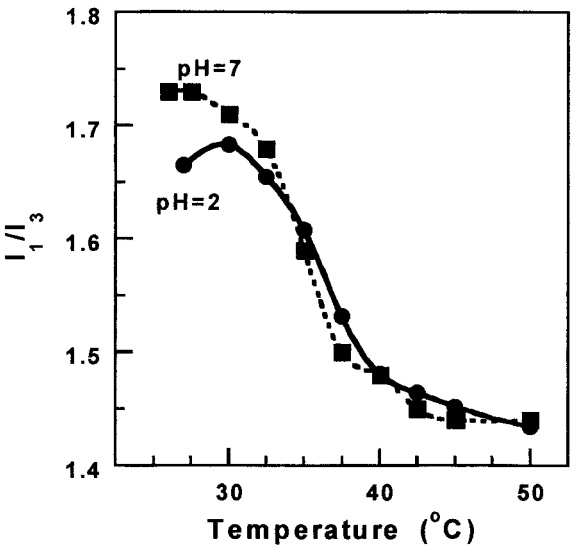


Figure 4 Variation of the ratio I_1/I_3 of aqueous solutions of P(AA-*co*-AMPSA)-*g*-PNIPAM with temperature at pH = 2 (●) and pH = 7 (■). The polymer concentration is 2.5×10^{-3} g cm^{-3}.

croenvironment as a result of a compact complex formation between PNIPAM, bearing the hydrophobic isopropyl side groups, and PAA.[19]

Thermoresponsive properties of the P(AA-*co*-AMPSA)-*g*-PNIPAM

The reduced viscosity of a dilute aqueous solution of the graft copolymer P(AA-*co*-AMPSA)-*g*-PNIPAM at pH values of 2 and 7 is presented in Figure 3, as a function of temperature. The reduced viscosity values at pH = 7 are generally higher than those at pH = 2, attributed to the additional extension of the backbone, resulting from the neutralization of the AA units at the higher pH, although the behavior is similar: regardless of pH, the reduced viscosity is rather constant or slightly decreasing with increasing temperature up to about 34°C. As temperature increases further, the reduced viscosity increases rather sharply to reach a plateau value at about 42°C. Such an increase of the reduced viscosity, when temperature exceeds the LCST of PNIPAM, has also been observed with similar graft copolymers.[14,23] Under these conditions the hydrophobic PNIPAM aggregates interconnect smoothly in the system, even if they do not yet allow the formation of a physical gel because the polymer concentration is rather low.

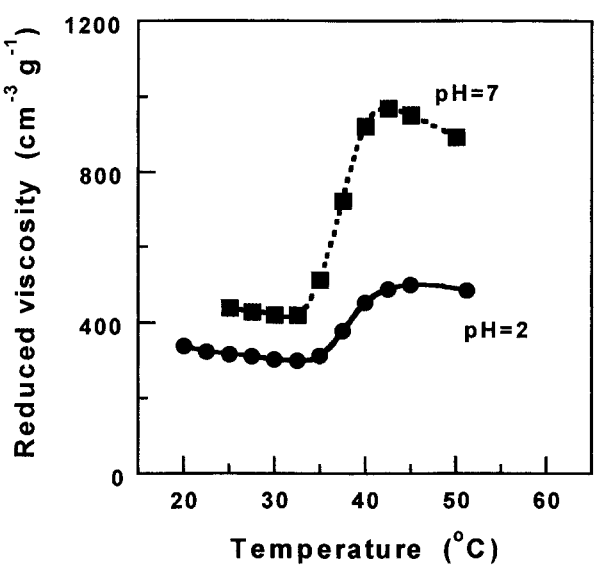


Figure 3 Variation of the reduced viscosity of aqueous solutions of P(AA-*co*-AMPSA)-*g*-PNIPAM with temperature at pH = 2 (●) and pH = 7 (■). The polymer concentration is 2.5×10^{-3} g cm^{-3}.

In fact, the formation of hydrophobic aggregates with increasing temperature can be monitored using pyrene fluorescence probing. The ratio I_1/I_3 for P(AA-*co*-AMPSA)-*g*-PNIPAM at the same conditions as those described above is presented in Figure 4, as a function of temperature. At low temperature, the ratio I_1/I_3 is around 1.65–1.7, indicative of a hydrophilic environment. For $T > 33$°C, I_1/I_3 decreases significantly with temperature and it reaches a value of about 1.45 at $T > 40$°C. This value coincides well with the values observed[20,24] for the PNIPAM homopolymer in water at temperatures higher than its LCST. Here, the pyrene molecules sense a hydrophobic environment as they are preferentially dissolved in the hydrophobic PNIPAM aggregates formed at $T >$ LCST. In the case of the homopolymers, this transition from a hydrophilic chain at $T < 33$°C to hydro-

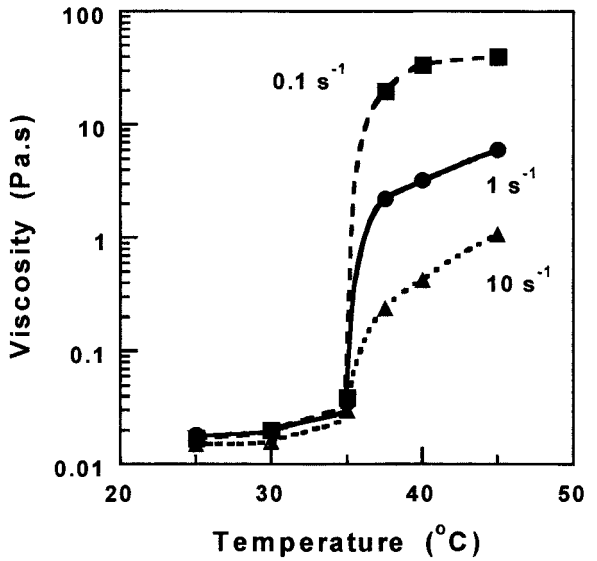


Figure 5 Temperature dependency of the shear viscosity of aqueous solutions of P(AA-*co*-AMPSA)-*g*-PNIPAM with temperature at pH = 3. The shear rate is 0.1 s^{-1} (■), 1 s^{-1} (●), and 10 s^{-1} (▲), and the polymer concentration is 5 $\times 10^{-2}$ g cm^{-3}.

phobic aggregates at higher temperatures is accompanied by phase separation. In the case of the graft copolymers, macroscopic phase separation is prevented as a result of the attachment of the PNIPAM chains onto the charged backbone. For the copolymer P(AA-*co*-AMPSA)-*g*-PNIPAM, the backbone is strongly charged, regardless of the pH of the solution. As a result, we observe a very similar temperature dependency of the ratio I_1/I_3, not only at the high pH region (pH = 7), as is the case for the copolymer PAA-*g*-PNIPAM, but also under acidic conditions (pH = 2).

When more concentrated solutions are used, a significant thermothickening behavior is observed upon heating. The viscosity at shear rates 0.1, 1, and 10 s^{-1} of a P(AA-*co*-AMPSA)-*g*-PNIPAM semidilute aqueous solution at pH = 3 is presented in Figure 5 as a function of temperature. The viscosity of the backbone P(AA-*co*-AMPSA), under the same conditions, is low and decreases smoothly with increasing temperature (results not shown). This is also the case for the graft copolymer when the temperature is lower than 33°C, that is, the LCST of the PNIPAM side chains under these conditions. On the contrary, as temperature increases above 33°C, a viscosity enhancement of about four orders of magnitude (at 0.1 s^{-1}) is observed within a temperature range of about 10°C. Furthermore, the system is strongly shear thinning, so that the viscosity enhancement with temperature decreases to about 2 and 1 orders of magnitude when the shear rate is 1 and 10 s^{-1}, respectively. A similar viscosity profile has also been observed at higher pH values. This thermally induced thickening behavior and the strong shear thinning behavior are in agreement with the formation of hydrophobic PNIPAM aggregates at temperatures higher than the LCST of the PNIPAM side chains and it has been observed using similar graft copolymers.[3,4,5,14,23]

CONCLUSIONS

Because of the strong electrolyte character of the AMPSA units, the graft copolymer P(AA-*co*-AMPSA)-*g*-PNIPAM is very hydrophilic, whereas the formation of hydrogen-bonding complexes between the PNIPAM side chains and the AA units of its backbone is not allowed, even at very low pH. For this reason, P(AA-*co*-AMPSA)-*g*-PNIPAM is water soluble in the acidic pH region, contrary to the behavior of the corresponding PAA-*g*-PNIPAM graft copolymer. As a result, the thermally induced aggregation of the PNIPAM side chains and the respective thermothickening behavior in semidilute aqueous solutions are observed, even at the low pH region (pH = 3).

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