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Effect of pH on the lower critical solution temperatures of random copolymers of *N*-isopropylacrylamide and acrylic acid

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Abstract

A series of pH and temperature-responsive (*N*-isopropylacrylamide-co-acrylic acid) random copolymers were synthesized by radical copolymerization and their lower critical solution temperatures (LCST) determined by cloud point measurements over a range of pH environments. LCSTs of the copolymers are observed at low pH values and are significantly affected by the variation in pH of the aqueous environment. © 1999 Elsevier Science Ltd. All rights reserved.

1. Introduction

The unique and novel properties of intelligent polymeric materials, which exhibit large property changes in response to small changes in external stimuli such as temperature [1, 2], pH [3, 4], electric fields [5, 6], chemicals [7, 8], offer an unlimited amount of potential applications relevant to industry, the environment and the biomedical field [9–12]. These applications include drug delivery systems [13–15], temperature-sensitive coatings [16]. flocculating agents [17]. smart catalysts [18, 19] and pervaporation membranes [20, 21].

Poly(*N*-isopropylacrylamide) (PNIPAAm) is a temperature-sensitive polymer that has dominated this research area as a result of the reversible macromolecular phase transition from a hydrophilic to a hydrophobic structure, occurring at approximately 32°C [16, 22–24], known as its lower critical solution temperature (LCST). Recently there has been considerable interest in the use of materials that respond to two stimuli, either mutually or independently in specific environments, with particular emphasis on pH/temperature sensitive polymers. Some pH/temperature responsive materials have been prepared by copolymerizing the temperature-sensitive NIPAAm with monomers containing an ionizable group, such as acrylic acid (PAA), to give a pH dependent lower critical solution temperature [25–27].

Earlier studies have concentrated on the comparison between temperature-induced phase transitions of graft and random copolymers of NIPAAm and acrylic acid, over a limited pH range, and others have focused on the effect that polyelectrolytes have on the LCST of random PNIPAAm:PAA copolymers [25–27]. This study focuses on the thermal properties of random copolymers of NIPAAm and acrylic acid over a wider range of pH values, investigating the effect that the pH, and acrylic acid content within the copolymers, have on the LCST of the copolymer. The study also compares these results with the earlier findings.

2. Experimental procedures

All chemicals were acquired from the Aldrich Chemical Company, except 2,2′-azoisobutyronitrile, which was obtained from Akzo Chemical Division, and methanol and toluene, acquired from BDH

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Chemicals. *N*-isopropylacrylamide was recrystallized from *n*-hexane and 2,2′-azoisobutyronitrile (AIBN) was purified by recrystallization from methanol. All other materials were used as supplied. All solvents were either analytical grade or purified by distillation at atmospheric pressure prior to use.

The compositions of the PAA:PNIPAAm copolymers were determined from microanalysis for nitrogen, infra-red spectra of the polymer samples recorded on a Digilab FTS-60 FTIR spectrometer, and from analysis of ^{13}C NMR spectra of the copolymers dissolved in deuterated methanol, recorded on a Bruker AVANCE DRX 400 MHz NMR spectrometer. The temperature/pH-responsive behavior of all the copolymers was determined by studying the turbidity of 5.0 mg/ml polymer solutions, at a range of temperatures and pH values, by measuring the absorbance of light of wavelength 633 nm to give each LCST value or cloud point. The temperature of the polymer solutions was increased from 0°C to 90°C in increments of 5°C every 10 min with continual stirring. The cloud point was determined by calculating the inflection point of the absorbancy versus temperature curves. In the cases where only partial precipitation was observed and there was no inflection point, the LCST is taken as the onset of the maximum increase in absorbance. Differential scanning calorimetry (DSC) was performed on a Perkin Elmer DSC 7 with a TAC 7/DX Thermal Analysis Controller at a scanning rate of 2°C/min, to compare with the results obtained from turbidity experiments.

2.1. Preparation of random copolymers of N-isopropylacrylamide and acrylic acid

A series of random copolymers of acrylic acid and *N*-isopropylacrylamide (PAA:PNIPAAm) were prepared by copolymerization of the two monomers in toluene using AIBN as the initiator. *N*-isopropylacrylamide and acrylic acid were dissolved in toluene and degassed with dry nitrogen for two hours at room temperature. AIBN dissolved in toluene (20 ml), was then added and the polymerization reaction was carried out at 65°C for four hours. The resultant copolymers were twice redissolved in methanol and reprecipitated into *n*-hexane and then dried *in vacuo* for a week at ambient temperature (80–85% conversion). The PNIPAAm homopolymer was synthesized in a similar manner. The details of the feed solutions used in the copolymerizations, as well as the compositions of the resultant copolymers, are shown in Table 1.

3. Results and discussion

The lower critical solution temperature (LCST), or cloud point, of the poly(*N*-isopropylacrylamide) (PNIPAAm) homopolymer was determined by the light absorbance experiments as well as by differential scanning calorimetry (DSC) (Fig. 1) and in both cases was observed at approximately 32°C, which is consistent with literature values [16, 21, 28, 29]. This thermal reversible phase transition in aqueous solutions is a consequence of the macromolecular transition from a hydrophilic to a hydrophobic structure at this temperature. The variation of pH of the aqueous solution of PNIPAAm has no significant effect on the LCST of the homopolymer. The copolymerization of the temperature-responsive NIPAAm with the pH-responsive acrylic acid monomer results in a dual sensitive polymeric material, sensitive to both temperature and pH.

Three random copolymers were prepared by radical polymerization methods to investigate how the LCST of the PAA:PNIPAAm copolymers varies with pH and composition of the copolymers. The lower critical solution temperatures of all three copolymers are significantly affected by the variation in pH of the aqueous environment as the hydrophilic content of the copolymers changes. DSC studies were performed on each of the copolymers at selected pH values to compare with the results obtained from turbidity experiments. The two sets of results were found to be consistent with each other. The DSC trace of the PAA:PNIPAAm (80:20) at approximately pH 2.5 is displayed in Fig. 2

Table 1
Feed compositions used in the preparation of PAA:PNIPAAm copolymers

Feed composition (mol)[a]			
(AA)	(NIPAAm)	(AIBN)	Copolymer composition (mol %)[b] (PAA:PNIPAAm)
0.182	0.061	1.22×10^{-3}	80:20
0.108	0.108	1.08×10^{-3}	54:46
0.049	0.146	9.75×10^{-4}	32:68

[a] 0.5 mol% of monomers.

[b] mol% of repeat units.

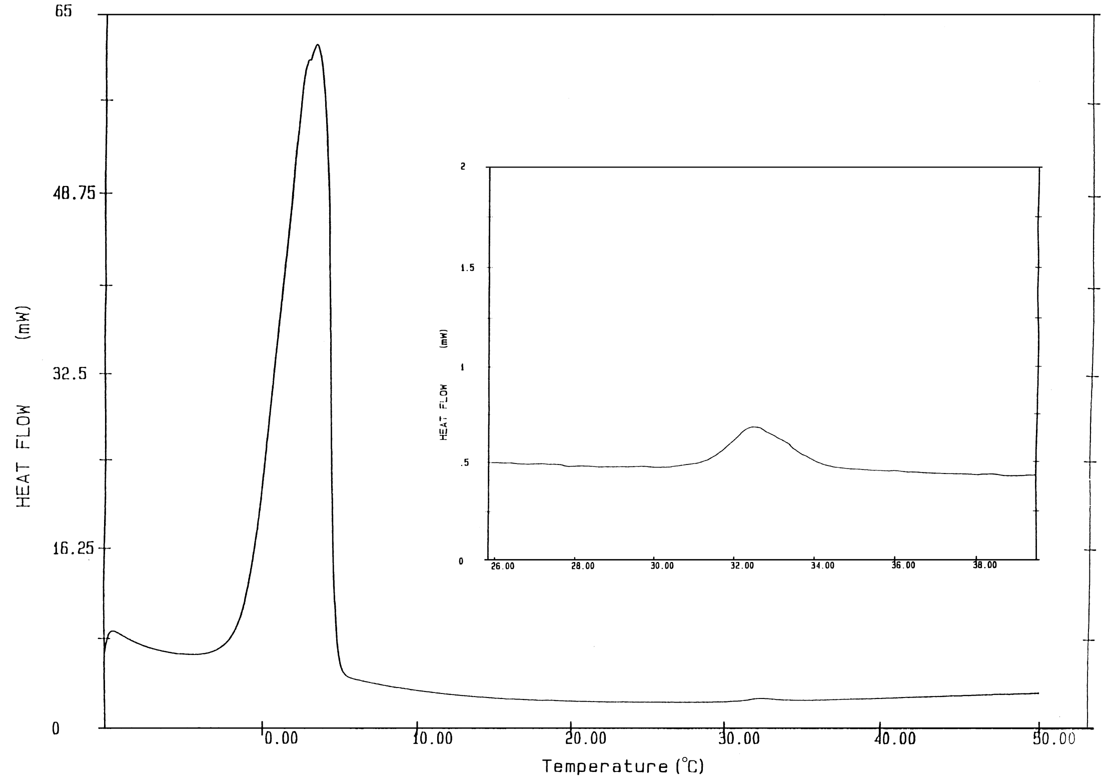

Fig. 1. DSC trace of poly(*N*-isopropylacrylamide (PNIPAAm) homopolymer in aqueous solution.

to illustrate the decrease in LCST value at one pH value. Table 2 and Figs 3–5, graphs of absorbance versus temperature at a range of pH values, show the LCST variations with temperature and pH for each of the copolymers for the results obtained from cloud point experiments.

However, the cloud point, resulting from the turbidity of the polymer solutions, is only observed at low pH values and no cloud points are observed for any of the three copolymers at values above pH 4.0. At pH 1.0, each of the polymer solutions is partially cloudy at 0°C, due to the insoluble aggregates beginning to form and the phase separation taking place. As the temperature is slowly increased, the copolymer rapidly precipitates, and this is seen as a rapid increase in the light absorbance on each of the graphs in Figs. 3–5. As the pH is increased, the LCST also gradually increases until the pH reaches a critical value, dependant on the structure and composition of the copolymer. At this critical pH value, the polymers only partially precipi-

Table 2
LCST values of PAA:PNIPAAm copolymers determined by cloud point experiments with 0.5 wt% polymer solutions

	PAA:PNIPAAm (80:20)	PAA:PNIPAAm (54:46)	PAA:PNIPAAm (32:68)
LCST at pH = 1.0	< 0°C	< 0°C	< 0°C
LCST at pH = 1.5	3°C	10°C	11°C
LCST at pH = 2.0	16°C	15°C	14°C
LCST at pH = 2.5	26°C	26°C	18°C
LCST at pH = 3.0	[a]51°C	*45°C	22°C
LCST at pH = 3.5	not observed	not observed	28°C
LCST at pH = 4.0	not observed	not observed	*43°C
LCST at pH > 4.0	not observed	not observed	not observed

[a] Only partial precipitation observed.
Uncertainty limits ±1.0°C.

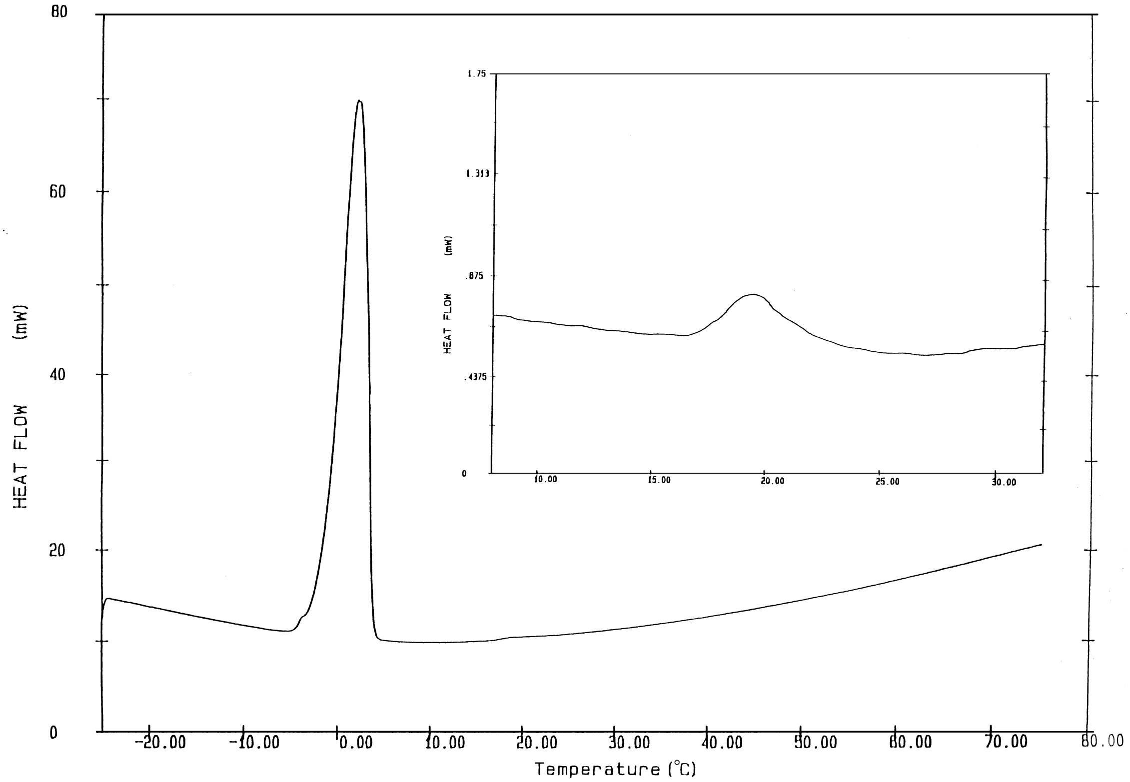

Fig. 2. DSC trace of PAA:PNIPAAm (80:20) random copolymer in aqueous solution at pH 2.5.

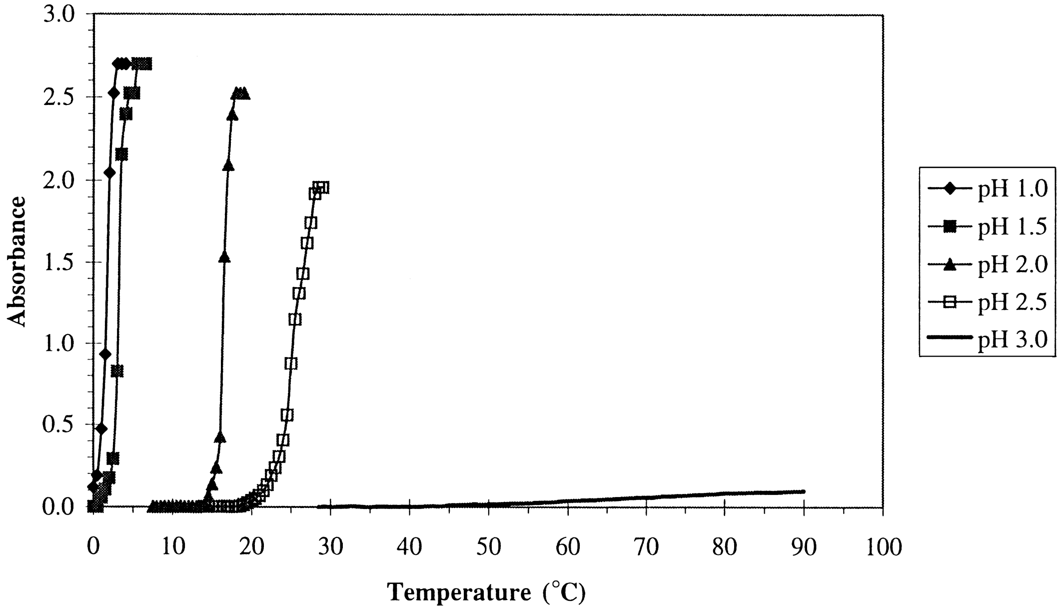

Fig. 3. Absorbance of 0.5% solutions of PAA:PNIPAAm (80:20) random copolymers versus temperature at differing pH.

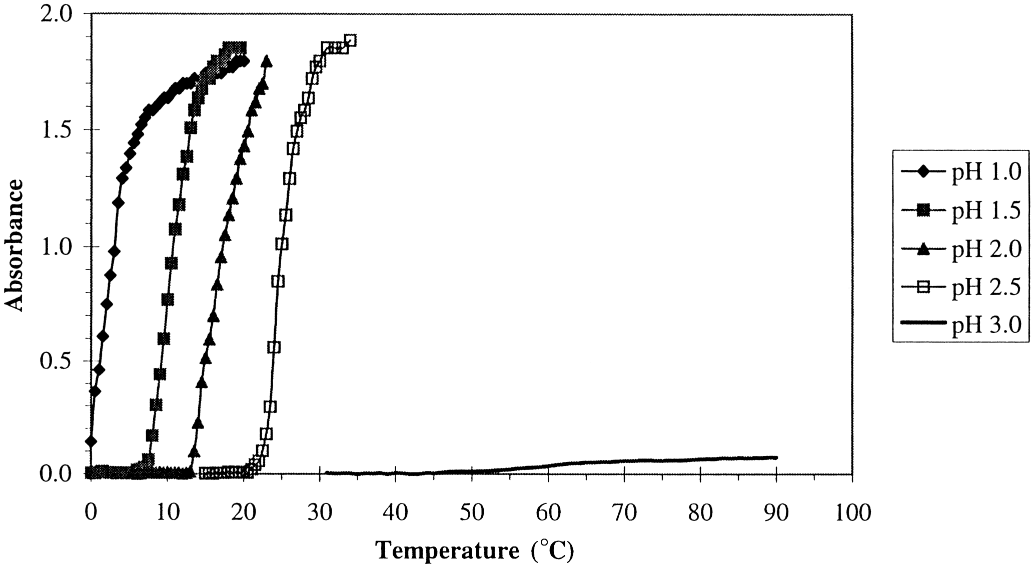

Fig. 4. Absorbance of 0.5% solutions of PAA:PNIPAAm (54:46) random copolymers versus temperature at differing pH.

tate and this is observed as a very small increase in light absorbance.

Below pH 1.0, each of the copolymers precipitates and coagulates as the hydrophobic groups within the solution form insoluble aggregates. Generally, it appears that the lowest LCST values are obtained with higher acrylic acid content with LCSTs of 3°C being achieved at low pH. However, any slight increase in pH results in a rapid increase in the cloud point.

The observation of the cloud points at low pH is believed to result from the formation of inter- and intra-molecular hydrogen bonding complexes between the acid moieties of the carboxylic acid and the amide groups of the PNIPAAm (Fig. 6). This subsequently hinders the water–NIPAAm interactions and increases the hydrophobicity of the copolymer environment. This theory was initially proposed by Chen and Hoffman, who have previously investigated the thermal properties of PNIPAAm oligomeric side-chains grafted onto the pH-sensitive poly(acrylic acid) backbone to create copolymers that exhibit temperature induced phase transitions over a wide pH range [25,26]. They observed phase transitions as low as 16°C due to the increase in hydrophobic interactions within the copoly-

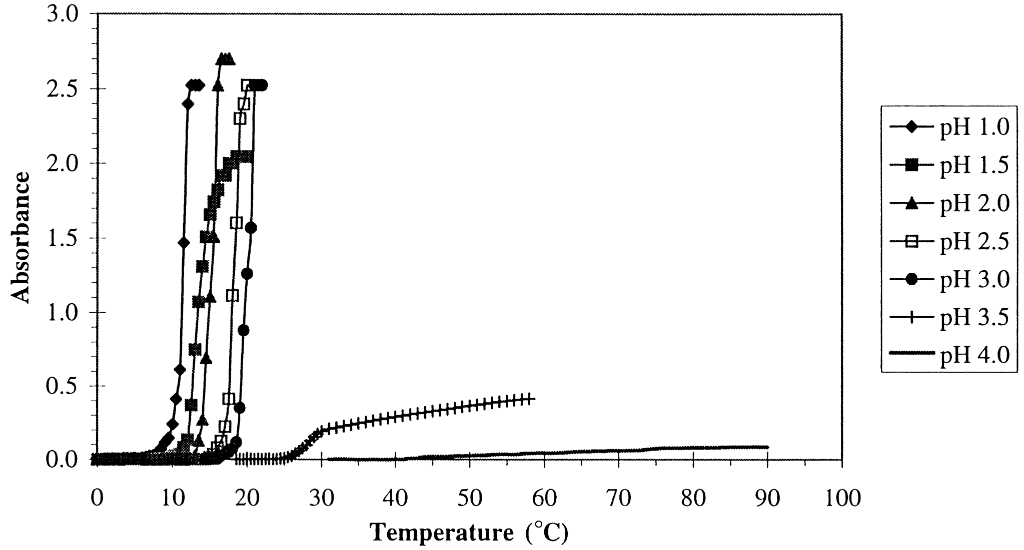

Fig. 5. Absorbance of 0.5% solutions of PAA:PNIPAAm (32:68) random copolymers versus temperature at differing pH.

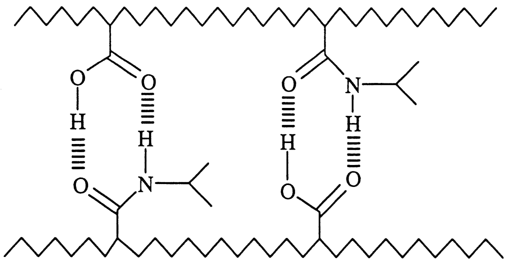

Fig. 6. Intermolecular hydrogen bonding between the acrylic acid and NIPAAm units.

mers, as a result of the grafted PNIPAAm side-chains forming hydrogen bonds with the poly(acrylic acid) backbone. Hoffman has also studied random copolymers of acrylic acid and NIPAAm over a limited pH range of 4.0 to 7.4, which give significantly different phase transitions to those of the graft copolymers. At pH 7.4, where the carboxylic acid groups are completely ionized, no LCST was observed for any PAA:PNIPAAm copolymer with greater than 10 mol% acrylic acid content. At pH 4.0, the critical acrylic acid content appears to be 40 mol%, above which the temperature sensitivity is lost. Our findings extend this work to low pH values where the stronger acidic environments can tolerate a larger acrylic acid content within the copolymer. This phenomenon has been explained by the exothermic water interaction of the carboxylic acid group competing with the entropic driving force of the phase separation of the PNIPAAm homopolymer, as a result of hydrophobically-bound water. The results of our research suggest that the critical pH value appears to lie between pH 3.5 and pH 4.5 as we have observed no LCST behavior above pH 4.0 for any of the copolymers. This agrees well with the recently published work of Yoo et al. who observed significant absorbance changes around pH 4.2, the pK_a value of the poly(acrylic acid) homopolymer [27]. Both our results and those of Yoo can be explained in terms of electrostatic interactions occurring between the carboxylic groups. Above its pK_a value the PAA is completely ionized and the carboxylic acid groups electrostatically repel each other. Below the pK_a value the LCST of the copolymers decreases with pH as more non-ionized acid groups are present, which enables them to participate in hydrogen bonding. Fig. 7 illustrates the changes in cloud point with pH for each of the copolymers.

Therefore, it is believed that as the pH is lowered further, there is an increase in the ratio of the non-ionized CO_2H groups to the ionized acid groups (CO_2^-). This increases the likelihood of the formation of inter- and intra-molecular hydrogen bonds and a decrease in the hydrophilic nature of the copolymers. As the temperature is increased, the CO_2H:CO_2^- ratio decreases as more of the acid groups become ionized, therefore this would reduce the amount of hydrogen bonds present and subsequently increase the hydrophilicity of the PAA:PNIPAAm copolymers. Other researchers have found comparable results with other polymeric systems, which can be explained in similar terms [30–32].

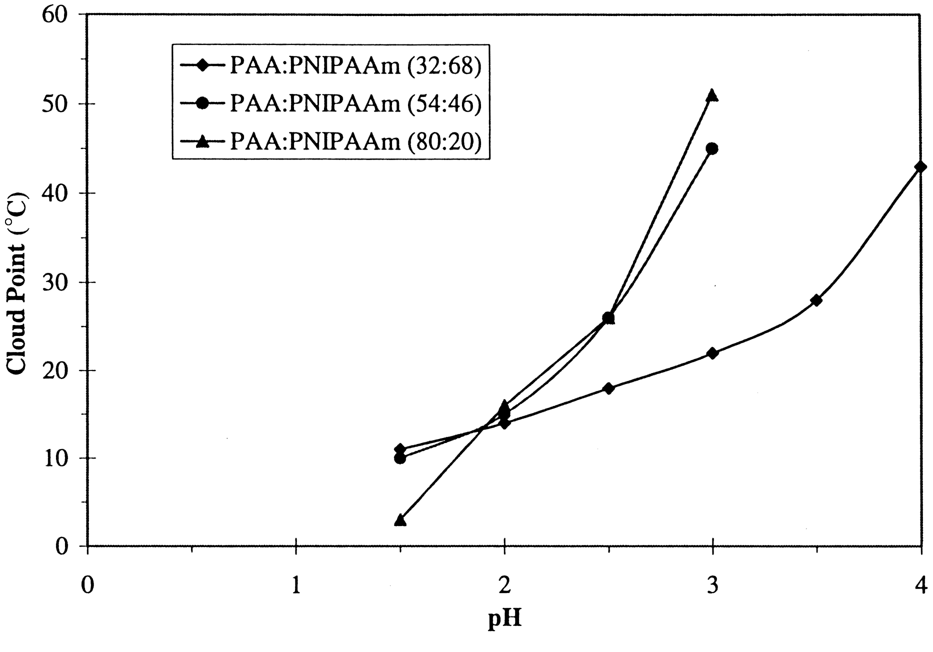

Fig. 7. Cloud point (°C) versus pH for random (PAA:PNIPAAm) copolymers.

4. Conclusions

This work has shown that the lower critical solution temperatures of PAA:PNIPAAm copolymers can be significantly altered by slight modifications of the copolymer composition or changes in pH of the aqueous environment.

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