

# Synthesis and Colloidal Stability of Poly(*N*-isopropylacrylamide) Microgels with Different Ionic Groups on Their Surfaces

Liusheng Zha,<sup>1,2</sup> Lan Li,<sup>2</sup> Laiyan Bao<sup>1</sup>

<sup>1</sup>State Key Laboratory for Modification of Chemical Fibers and Polymer Materials, Donghua University, Shanghai 200051, People's Republic of China

<sup>2</sup>Research Center for Analysis and Measurement, Donghua University, Shanghai 200051, People's Republic of China

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**ABSTRACT:** Temperature-sensitive poly(*N*-isopropylacrylamide) (PNIPAM) microgels with sulfate, amidino, or carboxylic groups on their surfaces, were synthesized by precipitation polymerization based on ammonium persulfate (APS), 2,2'-azobis(amidinopropane) dihydrochloride (V50), or 4,4'-azobis(4-cyanovaleric acid) (ACVA) as initiator, respectively. Their particle sizes and swelling ratios depended on the reaction pH due to the pH dependence of the ionization degree of the decomposed fragments originating from the initiators and their hydrophilicity-hydrophobicity. The more hydrophobic initiators partitioned into the interior of the PNIPAM microgels under certain pH conditions initiated the crosslinking reaction between the PNIPAM chains, leading to higher crosslink-

ing density of the microgels resulting in their smaller swelling ratio. pH dependence of surface charge density of the microgels with amidino groups or carboxylic acid groups on their surfaces was evidenced by the variation of their  $\zeta$ -potentials as a function of pH. Correspondingly, due to their pH dependence of electrostatic repulsive effect, the colloidal stability of the microgels with amidine groups or carboxylic acid groups on their surfaces was dependent on the pH value of dispersion medium. © 2006 Wiley Periodicals, Inc. *J Appl Polym Sci* 103: 3893–3898, 2007

**Key words:** temperature-sensitive microgels; poly(*N*-isopropyl acrylamide); initiator;  $\zeta$ -potential; colloidal stability

## INTRODUCTION

In the past decade, temperature-sensitive poly(*N*-isopropylacrylamide) (PNIPAM) microgels have attracted increasing attention because of their excellent properties, which make them candidates for many applications.<sup>1–3</sup> A drastic change in the hydrophilic-hydrophobic character of the microgels at a given temperature [the so-called volume phase transition temperature (VPTT)] results in a correspondingly large change in their colloidal properties, such as their particle size, surface charge density, and colloidal stability.<sup>4</sup> Some applications of the microgels, such as colloidal crystal, separation, and immobilization of biologically active molecules, are relative to their surface property. The stability and optical properties of the colloidal crystal made from PNIPAM microgels are dependent on their surface charge property and density.<sup>5</sup> The pH and temperature dependence of charge density of the temperature-sensitive microgels with weak acid groups or

weak basic groups on their surfaces can be used to separate proteins and nucleic acids.<sup>6,7</sup>

The PNIPAM microgels prepared by precipitation polymerization have excellent monodispersity and do not suffer from residual surfactant contamination, which is especially suitable for the application in colloidal crystal and biomedicine. In the polymerization process, *N*-isopropylacrylamide (NIPAM) was used as monomer, *N,N'*-methylene bisacrylamide (MBA) mostly as crosslinker, and potassium persulfate (KPS) [or ammonium persulfate (APS)] and 2,2'-azobis(amidinopropane) dihydrochloride (V50) usually as initiator.<sup>8,9</sup> The effect of reaction temperature and crosslinker agent on the polymerization process (polymerization kinetics, conversion, final particle size, morphology, water-soluble polymer, etc.) have primarily been presented and discussed,<sup>10–12</sup> while there have been few reports on the influence of the initiator on the polymerization process.<sup>13</sup> As expected, the initiator plays an important role in the polymerization process, especially during the nucleation period, and consequently, on the final microgel properties. The role of the initiator in the formation of PNIPAM microgels can be considered as follows: (1) it initiates the polymerization of the monomer and the crosslinker in the water phase leads to the formation of oligomers, which are precipitated to

Correspondence to: L. S. Zha (lszha@dhu.edu.cn).

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produce precursor particles when their critical chain lengths are reached or when the crosslinked chains start to precipitate; (2) its decomposed fragments confer the special charged groups on the surfaces of PNIPAM microgels, which endow the microgels with some applications, such as temperature-sensitive colloidal crystals, separation of bioactive substances, carrier of the reagent for medical test, etc.; (3) the charged groups on the surfaces of PNIPAM microgels electrostatically stabilize these colloidal particles.

In this work, APS, V50, or 4,4'-azobis(4-cyanovaleic acid) (ACVA) were respectively, used to initiate the precipitation polymerization of NIPAM and MBA to form temperature-sensitive microgels. Because the hydrophilic nature of V50 and ACVA is dependent on the degree of dissociation of the carboxylic acid groups and protonation of the amidino groups, respectively, the influence of reaction pH value on the particle sizes, swelling ratios and  $\zeta$ -potentials of PNIPAM microgels was investigated. pH dependence of surface charge density of the microgels with amidino groups or carboxylic acid groups on their surfaces was evidenced by the variation of their  $\zeta$ -potentials as a function of pH, and the pH-dependent colloidal stability of the PNIPAM microgels with different ionizable groups on their surfaces was correspondingly investigated.

## EXPERIMENTAL

### Materials

NIPAM (Acros, New Jersey, USA) and MBA (Aldrich, St. Louis, MO) were purified by repetitive recrystallization in 60/40 pentane/toluene mixture and methanol, respectively. Ammonium persulfate (APS) (Shanghai Shoushi Chemical Co., Shanghai, China), V50 and 4,4'-azobis(4-cyanovaleic acid) (ACVA) (Acros) were used as received. Water was deionized before use by a Millipore apparatus (Direct-Q).

### Preparation and purification of PNIPAM microgels with different ionic groups on their surfaces

The polymerization experiments were performed using a batch polymerization process. The pH of 48 mL aqueous solutions of 1 g NIPAM and 0.1 g MBA was adjusted to a certain value by adding 0.1M HCl or 0.1M NaOH solution. After the solution was stirred for 30 min with a nitrogen purge to remove oxygen, its temperature was raised to 70°C. Initiator (0.05 mmol) (APS, V50, or ACVA) dissolved in water of corresponding pH was added into the reaction solution, which marked the beginning of the polymerization reaction, and a nitrogen atmosphere was maintained throughout the experiment. One or two minutes later, opalescence appeared, and the

reaction was continued for 4 h. All microgel particles were cleaned via repetitive centrifugation and redispersion cycles using deionized water.

## Characterization of the PNIPAM microgels

### Particle size and swelling ratio

The hydrodynamic diameter ( $D_H$ ) of the poly(*N*-isopropylacrylamide) (PNIPAM) microgel particles at 20°C and 50°C were determined in 1mM NaCl aqueous solution at pH 6 by quasielastic light scattering (QELS) (Zetasizer Nano-ZS, Malvern) at a scattering angle of 90°. The mean hydrodynamic diameter was calculated from the diffusion coefficient measurement, which, in the high dilution with negligible particle-particle interactions, is calculated by the Stokes-Einstein equation:<sup>14</sup>

$$D = k_B T / (3\pi\eta D_H) \quad (1)$$

where  $D$  is the diffusion coefficient of the latex particle,  $\eta$  the viscosity of the medium,  $k_B$  the Boltzmann constant, and  $T$  the absolute temperature of the dispersion. The diameter  $D_H$  measured in this manner is usually known as the hydrodynamic diameter.

The swelling ratio (SR) of the PNIPAM microgel particles were calculated as follows:

$$SR = (D_H(25^\circ\text{C})/D_H(50^\circ\text{C}))^3 \quad (2)$$

where  $D_H(25^\circ\text{C})$  and  $D_H(50^\circ\text{C})$  are the hydrodynamic diameter of the microgel particles at 20°C and 50°C, respectively.

### Volume phase transition temperature

The volume phase transition temperature (VPTT) of the temperature-sensitive PNIPAM microgels was determined by measuring the optical density (OD) of a highly diluted microgel dispersion (pH = 6 and [NaCl] = 1 mM) as a function of temperature with an UV/Vis spectrophotometer (Lambda 35, Perkin Elmer) at a 500 nm wavelength. The heating rate was 0.1°C/min and was kept constant during the experiment. The temperature was controlled when heating the dispersion by an internal heating system with an automatic control device. The VPTT was then determined from the inflection point of the OD versus temperature curve.

### Zeta potential

The  $\zeta$ -potentials ( $\xi$ ) of the latex microgel particles were measured with a  $\zeta$ -potential meter (ZetaSizer 3000HS, Malvern) as a function of pH ([NaCl] = 1 mM) at 20°C or 50°C. Each point was obtained by taking

**TABLE I**  
Hydrodynamic Diameter ( $D_H$ ) and Swelling Ratio (SR) of PNIPAM Microgels Prepared Using Different Initiators Under Various Reaction pH<sup>a</sup>

Samples	Initiators	pH values of reaction medium	$D_H$ (nm)		SR
			25°C	50°C	
APS-3	APS	3.0	703	452	3.75
APS-5	APS	5.0	670	395	4.85
APS-8	APS	8.0	647	375	5.13
V50-3	V50	3.0	635	386	4.42
V50-5	V50	5.0	673	406	4.56
V50-7	V50	7.0	743	516	2.98
ACVA-9	ACVA	9.0	640	416	3.62
ACVA-10	ACVA	10.0	544	343	3.98
ACVA-11	ACVA	11.0	518	315	4.42

<sup>a</sup> Measured at pH = 6 and [NaCl] = 1 mM.

the average of at least three measurements. The  $\zeta$ -potentials used in this work was calculated from electrophoretic mobility,  $\mu$ , using the Helmholtz–Smoluchowski equation:<sup>14</sup>

$$\xi = \mu\eta/\varepsilon \quad (3)$$

where  $\varepsilon$  is the dielectric constant of the medium,  $\eta$  the viscosity of the medium.

#### Colloidal stability

The colloidal stability of the PNIPAM microgel lattices was evaluated by their  $n$  value change as a function of NaCl concentration, where  $n$  values were determined from the wavelength ( $\lambda$ ) dependence of the turbidity ( $\tau$ ):<sup>15</sup>

$$n = -(d \log \tau / d \log \lambda) \quad (4)$$

The measurement of  $n$  values was carried out using dispersions of 0.1% (wt/vol) the PNIPAM microgel particles, containing various concentrations of NaCl under different pH conditions. The samples were placed in a water bath at 25°C and allowed to stand for 24 h. The turbidity variation versus the wavelength at 25°C was obtained over the wavelength range 400–625 nm using an UV/Vis spectrophotometer (Lambda 35, PerkinElmer).

## RESULTS AND DISCUSSION

### The effect of pH value of reaction medium on the particle size and the swelling ratio of PNIPAM microgels

APS, V50, and ACVA are three different initiators, being an inorganic salt, organic base and organic acid, respectively. APS is soluble in both acidic and basic aqueous solutions, but V50 is soluble in acidic

or neutral solutions and ACVA is only soluble in basic solutions. In the precipitation polymerization process for preparing PNIPAM microgels, an upper reaction pH limit for V50 was 7.0 and a lower reaction pH limit for ACVA was 9.0, while the reaction pH range for APS was from 2 to 12, otherwise the microgel lattices were found to be partially or totally flocculated beyond the pH limit or the pH range. This shows that the pH value of the polymerization medium had an effect on the nucleation step and the microgel stability.

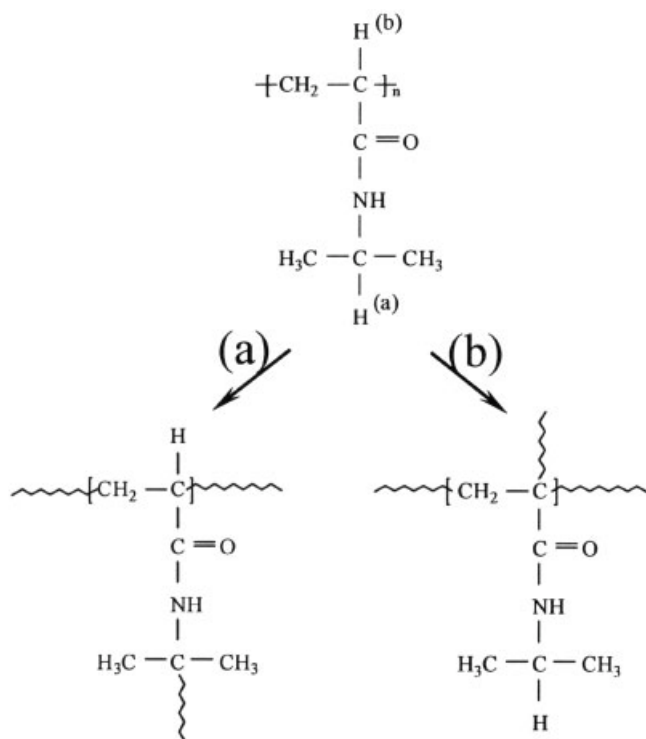
The effect of the reaction pH value on the particle size of PNIPAM microgels based on APS, V50, or ACVA as initiator was examined keeping constant the mole concentration of initiators, as shown in Table I. The increase in reaction pH value lowered the particle size of PNIPAM microgels based on APS or ACVA as initiator, but enhanced the one based on V50 as initiator. This is due to the fact that the dissociation degree of the sulfate acid groups or carboxylic acid groups resulting from the decomposed fragments of APS or ACVA, respectively, increased with the reaction pH value, while the protonation degree of amidino groups derived from the decomposed fragments of V50 decreased with the increase of the reaction pH value. More charged groups enhanced the formation of more precursor particles and increased the colloidal stabilization of the nucleated particles through an electrostatic mechanism, thus lowering the final particle size of PNIPAM microgels. This argument can be further evidenced by the variation of the  $\zeta$ -potentials of the PNIPAM microgel lattices against the reaction pH value, as exhibited in Table II.

The particle size measured by QELS at 20°C was that of water-swollen PNIPAM microgel, whereas the size at 50°C corresponded to the microgel in a collapsed state. We defined the swelling ratio as the ratio of the particle volume determined by QELS at 20°C to that at 50°C. The swelling ratio could be

**TABLE II**  
Zeta Potentials of PNIPAM Microgels Using Different Initiators Under Various Reaction pH Conditions<sup>a</sup>

Samples	Initiators	pH values of reaction medium	Zeta potentials (mv)	
			25°C	50°C
APS-3	APS	3.0	-4.4	-46.1
APS-5	APS	5.0	-6.4	-49.3
APS-8	APS	8.0	-8.5	-48.7
V50-3	V50	3.0	11.9	37.5
V50-5	V50	5.0	8.9	34.3
V50-7	V50	7.0	2.9	24.9
ACVA-9	ACVA	9.0	-2.9	-23.6
ACVA-10	ACVA	10.0	-6.5	-30.8
ACVA-11	ACVA	11.0	-8.3	-35.5

<sup>a</sup> Measured at pH = 6 and [NaCl] = 1 mM.



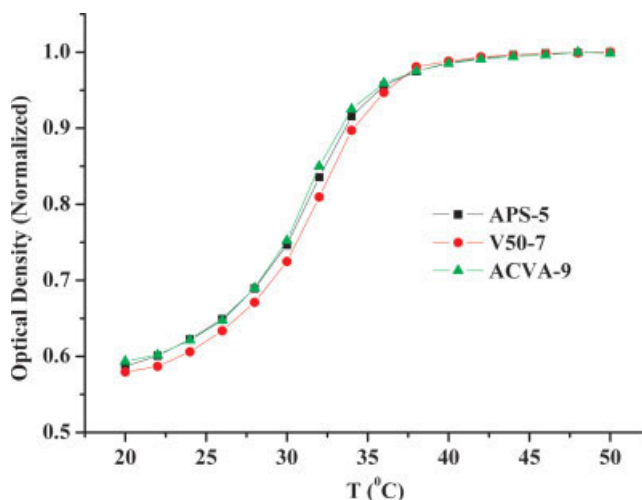
**Figure 1** Possible sites on a PNIPAM chain for formation of *tert*-carbon free radicals and resultant crosslinking points.

used to evaluate the crosslinking density of the PNIPAM microgel. The effect of reaction pH values on the swelling ratios of PNIPAM microgels based on APS, V50, or ACVA as initiator was examined, as shown in the last column of Table I. Under constant concentration of the crosslinker (MBA) used in the polymerization recipe, increasing the reaction pH value led to a decrease in the swelling ratio of the PNIPAM microgels based on V50 as initiator, but an increase for the PNIPAM microgels based on APS or ACVA as initiator. The decrease in swelling ratio was attributed to a more crosslinked structure of the microgels, which may be formed by the decomposition and crosslinking reaction of the initiator partitioned into the microgel particles. Because the hydrophobic nature of the initiators can be adjusted by changing the pH, the more hydrophobic the initiator at the reaction pH, the more the amount of the initiator partitioned into the microgel particles due to the hydrophobicity of PNIPAM chains at the reaction temperature. The initiators partitioned into the interior of the PNIPAM microgels initiated the crosslinking reaction between the PNIPAM chains, leading to higher crosslinking density of the microgels. As enlightened by the Ref. 16, Figure 1 shows the two most probable sites of PNIPAM chains for the crosslinking reaction: (a) the hydrogen atom on the *tert*-carbon of the pendent isopropyl group and (b) the hydrogen atom on the *tert*-carbon of the main

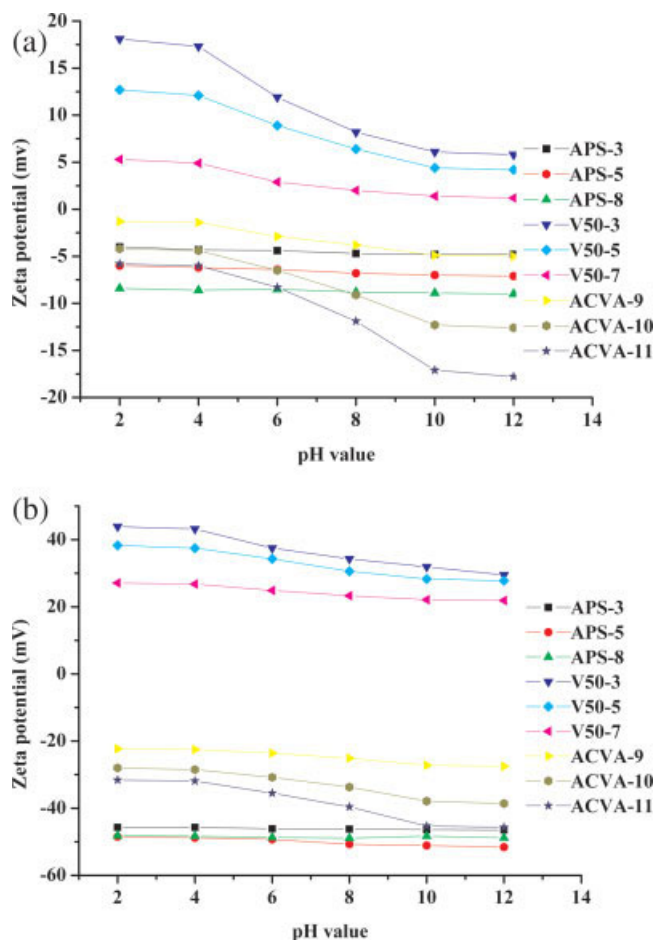
chain backbone. These hydrogen atoms are both active and are likely to be attacked by free radicals derived from the decomposition of the initiators, forming *tert*-carbon free radicals that are stabilized by conjugating with adjacent groups. In either case, the *tert*-carbon free radical may react further with another *tert*-carbon active hydrogen on an adjacent PNIPAM chain to produce crosslinking points.

### The effect of initiator species on the volume phase transition temperature of the PNIPAM microgels

Volume phase transition temperature (VPTT) is the most important property parameter of temperature-sensitive microgels. To examine the effect of initiator species and the crosslinking points resulting from the partitioned initiators on the VPTTs of the PNIPAM microgels, the OD of the highly diluted PNIPAM microgel dispersion as a function of temperature was measured. The curves of the OD variation as a function of temperature obtained for all PNIPAM microgel were reported in normalized form, as illustrated in Figure 2. From the inflection points of the curves, it can be pointed out that there is no significant effect of the initiator species and the crosslinking points resulting from the partitioned initiators on the VPTTs of the PNIPAM microgels. This could be explained by the phenomena that the content of decomposed fragments of initiators in the microgel particles was very low and they were mostly located on the surface of the particles, and the self-crosslinking of PNIPAM chains did not change the hydrophilic–hydrophobic nature of the whole polymer network.



**Figure 2** The curve of the absorbency variation of highly diluted PNIPAM microgel dispersion versus temperature (pH = 6, [NaCl] = 1 mM).



**Figure 3** Variation of the  $\zeta$ -potentials of PNIPAM microgels against pH value at 25°C (a) and 50°C (b) ([NaCl] = 1mM).

#### The effect of pH value of dispersion medium on the zeta potentials of PNIPAM microgels

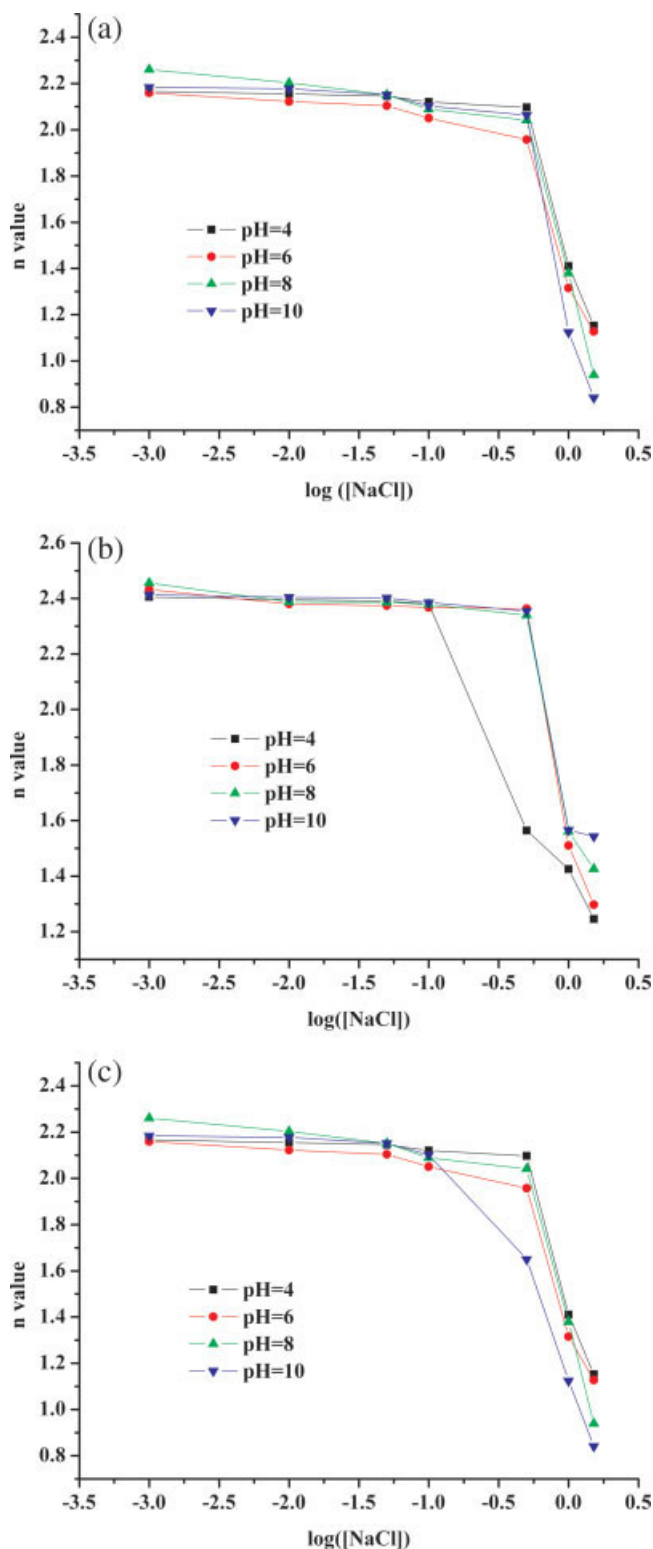
The surface charge density of the temperature sensitive microgels with ionisable groups resulting from the initiators used in the polymerization recipe can be determined by zeta potentiometry. The investigation of  $\zeta$ -potentials versus pH can be considered as a key point for the analysis of surface charge density variation. Since amidino groups and carboxylic acid groups are weakly basic groups and weakly acidic groups, respectively, their degree of ionization should rely on the pH value of the media. Correspondingly, the surface charge density of the microgels with amidino groups or carboxylic acid groups on their surfaces may depend on the pH value of the media. Because the surface charge density of colloidal particles is proportional to their  $\zeta$ -potential, we measured the  $\zeta$ -potential variation of PNIPAM microgel lattices against the pH value of the media at temperatures both below (20°C) and above (50°C) their VPTT to evaluate the effect of pH on their surface charge density, as shown in Figure 3. The PNIPAM microgels based on V50 as the initiator in the

polymerization recipe had positive  $\zeta$ -potentials due to the protonation of amidino groups originating from V50 on their surfaces, and they decreased markedly as the medium pH values increased from 4 to 10, reflecting the lowering of the degree of protonation of the amidino groups. Comparatively, the PNIPAM microgels based on ACVA as the initiator have negative  $\zeta$ -potentials due to the dissociation of the carboxylic acid groups deriving from ACVA on their surfaces, and the absolute value of their  $\zeta$ -potentials was raised significantly as the medium pH value increased from 4 to 10, representing the enhancement of the dissociation of the carboxylic acid groups. Because the sulfate group is a strong acid group, the  $\zeta$ -potentials of the PNIPAM microgels based on APS as the initiator are slightly dependent on the medium pH value. Comparing Figures 2(a) and 2(b), the measured absolute values of  $\zeta$ -potentials as a function of pH above the VPTT was found to be higher than that below the VPTT for all the PNIPAM microgels, irrespective of the nature of the surface charge. This observed behavior can be explained by an increase in the surface charge density induced by the reduction in particle size due to the temperature-sensitivity of these microgels.

#### Colloidal stability of PNIPAM microgels with different ionic groups on their surfaces

Turbidity–wavelength measurement is a sensitive method for detecting aggregation in dispersions, and Daly and Saunders<sup>17</sup> have shown that the method is applicable to poly(NIPAM) microgel latex. Poly(NIPAM) microgel latex was colloidally stable when their  $n$  value remained constant, and aggregated when the  $n$  value decreased abruptly. In this work, the colloidal stability of the PNIPAM microgels with different ionic groups on their surfaces was investigated as their  $n$  values versus NaCl concentrations under different pH conditions. The  $n$  values measured for APS-5, ACVA-11, and V50-3 are shown in Figures 4(a)–4(c), respectively, they remain constant in the low NaCl concentrations and decrease at certain high NaCl concentration. The lower the NaCl concentration at which the  $n$  value started to decrease abruptly, the poorer the colloidal stability of the PNIPAM microgel dispersion. The sulfate groups, carboxylic acid groups and amidine groups were linked to the surfaces of APS-5, ACVA-11, and V50-3, respectively. The effect of pH value of the dispersion media on the colloidal stability of three kinds of the PNIPAM microgels was different, and the colloidal stability of the microgels with amidine groups or carboxylic acid groups on their surfaces was dependent on the pH value. In the pH range from 4 to 10, no dependence of the colloidal stability of the PNIPAM microgels with sulfate groups on





**Figure 4** Variation of  $n$  values of highly diluted PNIPAM microgel dispersion [(a): APS-5; (b): ACVA-11; (c): V50-3] against NaCl concentrations at different pH conditions ( $T = 25^{\circ}\text{C}$ ).

their surface on the pH value of the dispersion medium was observed, and the colloidal stability of the microgels with carboxylic acid groups was lowered

at pH 4, whereas the colloidal stability of the microgels with amidine groups was decreased at pH 10. These behaviors can be explained by the just reported relationship between the  $\zeta$ -potentials of the PNIPAM microgels and the pH value of the dispersion medium. The higher the  $\zeta$ -potential of the PNIPAM microgel dispersion under certain pH condition, the stronger the electrostatic repulsive force between the microgels, and the better the colloidal stability of the dispersion.

## CONCLUSIONS

Three different initiators, ammonium persulfate (APS), 2,2'-azobis(amidinopropane) dihydrochloride (V50), and 4,4'-azobis(4-cyanovaleric acid) (ACVA), were used to prepare temperature-sensitive PNIPAM microgels by precipitation polymerization. Their particle sizes and swelling ratios were dependent on the reaction pH due to the pH dependence of the ionization degree of their decomposed fragments and their hydrophilicity-hydrophobicity. The more hydrophobic initiators partitioned into the interior of the PNIPAM microgels under certain pH conditions initiated the crosslinking reaction between the PNIPAM chains, leading to higher crosslinking density of the microgels. The PNIPAM microgels with amidino groups or carboxylic acid groups based on V50 or ACVA as initiator, respectively, have sharp pH dependence of surface charge density. Correspondingly, the colloidal stability of the microgels with amidine groups or carboxylic acid groups on their surfaces was dependent on the pH value of the dispersion medium.

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