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Reversible Changes in Solution pH Resulting from Changes in Thermoresponsive Polymer Solubility

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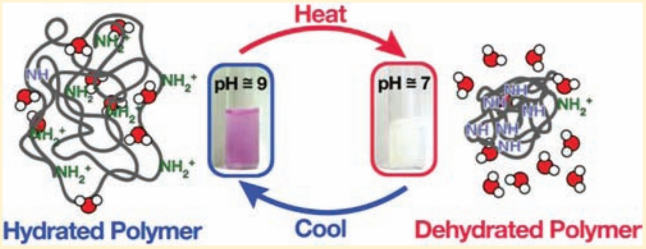
Supporting Information



ABSTRACT: Pendant groups on polymers that have lower-critical solution temperature (LCST) properties experience a water-like environment below the LCST where the polymer is soluble but are less hydrated above the LCST when the polymer phase separates from solution. When these pendant groups are amphoteric groups like carboxylate salts or ammonium salts, the change in solvation that accompanies the polymer precipitation event significantly changes these groups' acidity or basicity. These changes in acidity or basicity can lead to carboxylate salts forming carboxylic acid groups by capturing protons from the bulk solvent or ammonium salts reverting to the neutral amine by release of protons to the bulk solvent, respectively. When polymers like poly(*N*-isopropylacrylamide) that contain a sufficient loading of such comonomers are dissolved in solutions whose pH is near the pK_a of the pendant acid or basic group and undergo an LCST event, the LCST event can change the bulk solution pH. These changes are reversible. These effects were visually followed using common indicators with soluble polymers and or by monitoring solution pH as a function of temperature. LCST events triggered by the addition of a kosmotropic salt lead to similar reversible solution pH changes.

Physical changes in a polymer's properties that affect chemistry are of broad interest.[1] Mechanochemical activation of a catalyst by stressing a polymer would be one example of such chemistry.[2] The design of materials with responsive solubility or permeability useful in biomedical applications is another.[3−5] Responsive polymer properties can also be used to alter surface wettability in response to various stimuli,[6−8] to prepare "smart" and separable catalysts,[9,10] and to design multicomponent systems that phase separate in response to various stimuli.[11] In all of these cases, changes in a polymer's conformational state or solubility affect the chemistry of functional groups on a polymer or affect how a polymer physically interacts with its environment. Here we show that changing a polymer's solubility in a lower-critical solution temperature (LCST) event leads to significant changes in solution pH (a ΔpH). We suggest that the effects we see result from changes in the hydration of polymer-bound acid and base salts. We show that the ΔpH depends on the loading and concentration of the acidic or basic group on the functionalized poly(*N*-isopropylacrylamide) copolymers and that the ionic strength of solutions does not affect the magnitude of these pH changes.

It is well established that the pK_a values of acids or bases change in different solvents or in different solvent environments. Such effects are illustrated by the differences in the acidity and basicity of ammonium and carboxylate groups within biopolymers vis-à-vis similar ammonium and carboxylate groups in water.[12] Indeed, such groups' normal pK_a values of ca. 5 or 9 in bulk water are altered by several pK_a units when the groups are in the active sites of enzymes because of changes in their hydration state. Similar changes in the equilibrium concentrations of conjugate base and acid salts of carboxylic acid and amines should also be seen for such groups bound to synthetic polymers if the solvent environment of carboxylic acid groups or ammonium groups can be changed.

RESULTS AND DISCUSSION

A variety of initial experiments confirmed that solvation environment affects the stability of salts of pendant acids or bases on soluble polymers. First, we prepared a poly(*N*-isopropylacrylamide) (PNIPAM) copolymer containing a low mole percent loading of a pH-sensitive azo dye (Scheme 1). Solutions of this PNIPAM-bound dye are red at pH 1 where the azo dye is protonated (**2a**) and yellow-orange at higher pH values where the dye is not protonated (**2b**). In water at pH 1, **2a** exhibits a clouding curve because of an LCST event like that seen with PNIPAM. Upon being heated from room temperature to ~32 °C, the polymer precipitates (the clouding curve for this polymer is provided as Supporting Information). This precipitation produces a clear solution and a yellow-orange solid. Cooling reverses this process, re-forming the original red solution of **2a**. We ascribe these color changes to the known

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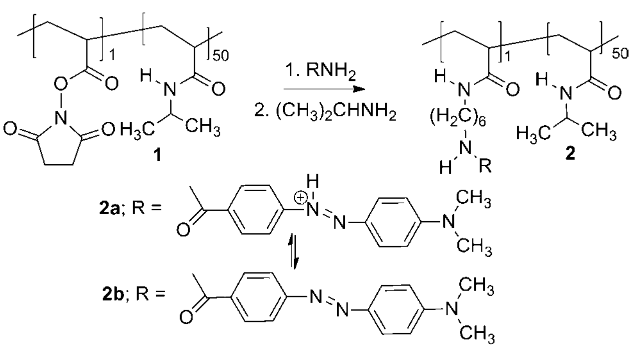
Scheme 1. Synthesis of a Thermoresponsively Soluble Amphoteric Polymer-Bound Azo Dye and the Acid−Base Forms of This Azo Dye That Are Present below and above 2's LCST[a]



[a] **2a** is the most stable conjugate acid of the azo dye present below **2**'s LCST, and **2b** is the neutral form of this dye and the predominant form of the dye present after the precipitation.

entropy-favored loss of solvent water that accompanies the precipitation of this thermally responsively soluble PNIPAM copolymer.[13,14]

In solution, the cationic conjugate acid salt of the dye is stabilized by solvent water. However, after the LCST event and formation of a solid, the less hydrated protonated form of *p*-methyl red azo dye[15] is less stable and reverts to its unprotonated form. These changes in protonation state for **2** are analogous to the behavior of charged groups at enzyme active sites where the acidity of ammonium groups or the basicity of carboxylate groups differ significantly from values in a dilute aqueous solution.[12] Similar solvation-dependent behavior is exhibited by other polymer-bound conjugate acids that undergo a phase change as shown in the experiments described below.

We next examined the acid−base behavior of phase-selectively soluble polymers in nonpolar/polar solvent mixtures to see if phase switching a polymer from a polar to nonpolar environment would lead to similar behavior (Figure 1).[11] A dansyl-labeled poly(4-*tert*-butylstyrene) **3** was prepared from a linear copolymer of 4-*tert*-butylstyrene and 4-chloromethylstyrene[16] and dissolved in a miscible mixture of equal volumes of 95% aqueous ethanol and heptane. Addition of CH_3SO_3H initially quenched **3**'s fluorescence. However, as more acid was added, the additional acid perturbs this solvent mixture, forming two phases: a heptane-rich phase and an ethanol-rich phase. At this point, the nonpolar dansyl-labeled 4-(*tert*-butylstyrene) partitions to the heptane phase where 95% of the original dansyl fluorescence reappears. In this case, the transfer of the fluorophore to a nonpolar heptane-rich solution after phase separation leads to a deprotonation of the protonated dansyl species because the protonated dansyl species is less stable in a nonpolar medium.

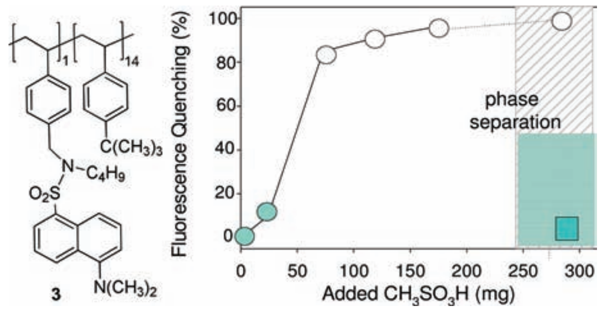
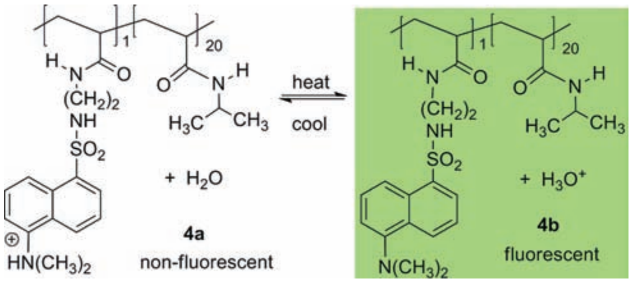


Figure 1. Fluorescence quenching of **3** in 10 mL of a miscible equivolume heptane/95% aqueous ethanol solution (green circles to white circles) due to the addition of increasing amounts of CH_3SO_3H to this ethanol/heptane mixture. Addition of 290 mg of CH_3SO_3H makes this solvent mixture biphasic with virtually no **3** and no fluorescence in the ethanol-rich phase (○) and significant fluorescence for unprotonated **3** in the heptane-rich phase (green square).

Changes in the fluorescence of a protonated dansyl group bound to PNIPAM further confirmed that the phase change associated with an LCST process can induce a deprotonation event for a polymer-bound conjugate acid salt. When the dansyl-labeled PNIPAM **4** was dissolved in water at pH 1, it exhibits no fluorescence because protonation of the -$N(CH_3)_2$ group of dansyl quenches dansyl's fluorescence. When this solution of **4a** was heated above its LCST (24 °C), the precipitate that formed fluoresced brightly. This process was as thermally reversible as the deprotonation or protonation event for **2a** or **2b**, respectively. This change in fluorescence parallels the change in fluorescence described above for a protonated dansyl group that phase switched from a polar solution to a nonpolar heptane-rich solution.

Fluorescence has previously been used to study LCST events with PNIPAM polymers. For example, a PNIPAM-bound hydrocarbon pyrene fluorophore whose fluorescence was quenched in solution fluoresced after an LCST event.[17] However, the appearance of fluorescence seen in those studies as a result of an LCST event was due to physical separation of the PNIPAM-bound pyrene from the external quenching agent by formation of the PNIPAM precipitate. In the studies of **4** shown in Scheme 2, the appearance of fluorescence is due to a chemical reaction, phase change-induced deprotonation of the dimethylamino group of the PNIPAM-bound dansyl group.

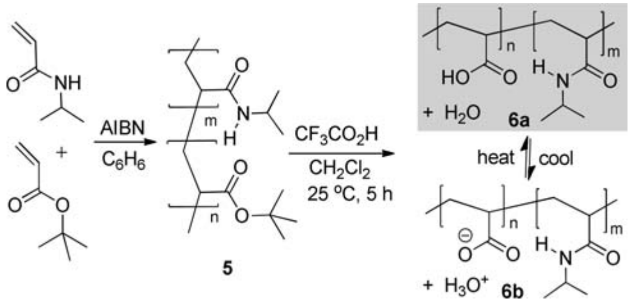
Scheme 2. Temperature and pH-Sensitive Fluorescence of Dansyl-Labeled PNIPAM Copolymer 4



These studies of polymer-bound dyes show that phase separation of a soluble polymer affects the solvation environment and stability of charged pendant groups and suggested that reversible protonation and deprotonation of a more highly loaded PNIPAM copolymer could affect solution pH. To probe this, we prepared polymer **5** by a radical copolymerization using *N*-isopropylacrylamide and various amounts of *tert*-butyl acrylate. The resulting copolymers **5** were analyzed by ^1H NMR spectroscopy and had 9:1, 6:1, and 4:1 ratios of *N*-isopropyl acrylamide to *tert*-butyl acrylate groups. These polymers were characterized by GPC and had M_w values of 255, 76, and 75 kDa, respectively, with PDIs that varied from 2.2 to 3.9 (see the Supporting Information for details). The ester groups in each of these polymers were converted to carboxylic acid groups of **5** by acidolysis using CF_3CO_2H at 25 °C for 5 h in CH_2Cl_2.

Our initial experiments with **6** used a solution of 20 mg/mL polymer **6** with 10 mol % -CO_2H groups. This room-temperature solution was adjusted to pH 4 by addition of HCl. Heating to 40 °C was sufficient to induce precipitation of polymer **6** (Scheme 3). This change in solubility of **6** led to a reversible change in solution pH. This change was easily seen by adding an indicator to the solution. When the indicator bromocresol green was added to the solution, the solution was a bright yellow-green color. Heating this solution to 40 °C produced a precipitate and a more basic solution as indicated by a change in the color of the solution from yellow-green to blue. This process was reversible, and redissolution of the polymer upon cooling re-formed the original yellow-green solution. These color changes and the observed LCST behavior were reversible through more than 100 cycles of heating and cooling.

Scheme 3. Synthesis of PNIPAM−PAA Copolymer 6 Whose Thermoresponsive Solubility Increases the Bulk Solution pH upon Being Heated above Its LCST



This qualitative visual study of the reversibility of these changes in bulk solution pH was verified by studying the pH at 25 and 40 °C using a pH meter. These studies are shown in Figure 2.

The effects of changing the temperature on the pH for a solution of 20 mg/mL **6** (14 mol % -CO_2H) were studied in detail as a function of the starting pH (Figure 3). These studies show that the ΔpH averaged 1.2 pH units. These solutions have an average ΔpH of 0.004 pH unit/°C below the transition temperature, an average ΔpH of 0.68 pH unit/°C during the transition, and an average ΔpH of 0.04 pH unit/°C above the transition temperature.

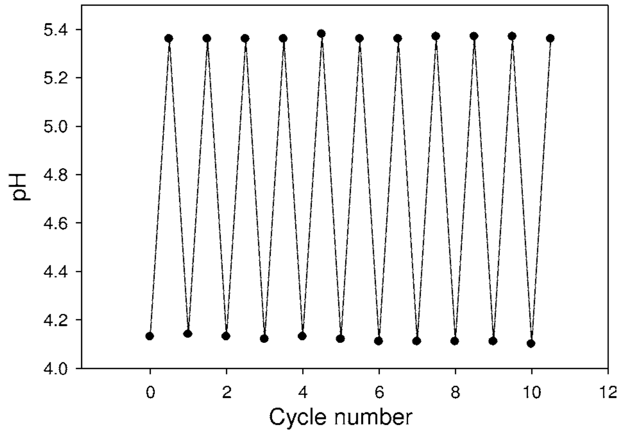


Figure 2. Reversibility of the pH changes for heating to 45 °C and cooling to 25 °C for a 20 mg/mL solution of **6** (this sample of **6** contained ~10 mol % -CO_2H groups).

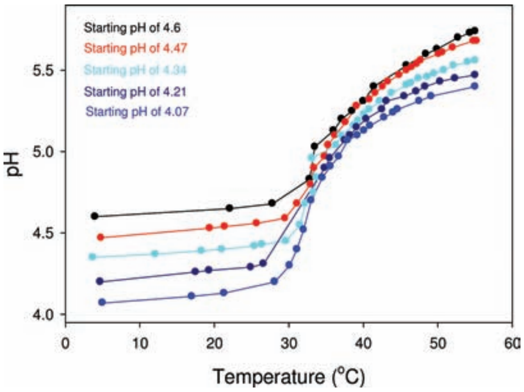


Figure 3. Change in pH on heating an aqueous solution of polymer **6** (14 mol % -CO_2H group loading) starting at initial pH values of 4.1−4.6.

The effect of carboxylic acid group loading in **6** and the concentration of polymer **6** in changing the bulk solution pH as a function of temperature was tested using the three different loadings of **6** (Table 1). Results of control experiments that aimed to examine the changes in solution pH with temperature using solutions of propanoic acid, an unfunctionalized PNIPAM, and a polyacrylamide [poly(*N*,*N*-dimethylacrylamide)] that does not have an LCST are also listed in Table 1. The change in the pH of the bulk solution depends on the -CO_2H group loading in **6** and on the concentration of **6**.

Table 1. Changes in pH with Temperature for Various Samples of 6 and for Solutions That Contain Various Concentrations of 6 over a Temperature Range of 5−55 °C[a]

-CO_2H loading in **6** (mol %)	[**6**] (mg/mL)	initial pH	final pH	ΔpH
20	40	3.95	5.10	1.15
14	40	3.95	5.25	1.30
10	40	4.19	5.71	1.52
10	20	4.17	5.68	1.51
10	10	4.05	5.32	1.27
10	5	4.13	5.10	0.97
10	1	4.23	4.69	0.46
10[b]	20	4.04	5.14	1.10
10[c]	10	4.06	5.23	1.17
10[d]	20	4.05	5.13	1.08
10	20	2.27	2.19	−0.08
10	20	6.81	6.84	−0.03
N-isopropylacrylamide[e]	20	4.23	4.07	−0.16
N,*N*-dimethylacrylamide[f]	20	4.28	4.11	−0.17
propanoic acid[g]	3.1	3.96	3.95	−0.01
propanoic acid[h]	3.1	3.21	3.24	0.03

[a] The initial pH was adjusted to ~4.1 for each experiment. [b] This sample of **6** contained 0.4 M LiBr. [c] This sample of **6** contained 0.2 M LiBr. [d] This sample of **6** contained 0.4 M LiCl. [e] This sample of unfunctionalized PNIPAM that had an LCST of 32.6 °C. [f] This was a sample of unfunctionalized polyacrylamide [poly(*N*,*N*-dimethylacrylamide)] that does not have an LCST under these conditions. [g] This was a sample containing propanoic acid (0.38 mM) where the starting pH was adjusted to 3.96. [h] The pH of this 0.38 mM sample for initial pH was calculated to be 3.15 and was not adjusted to ~4.

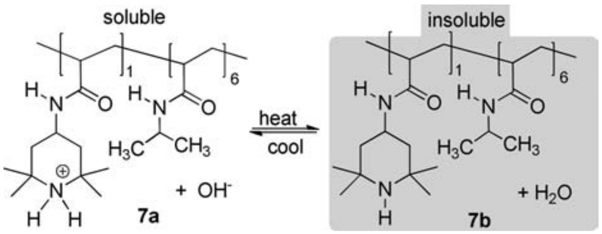
These changes in solution pH were not seen if the starting solution pH differed significantly from the pK_a of a carboxylic acid group. When **6** with -CO_2H loadings of 10 mol % was dissolved in a solution at either pH 2.3 or 6.8 and heated from 5 to 55 °C, a <0.1 ΔpH was observed. This small change in the solution pH was smaller than the ΔpH change seen in all other experiments with **6** containing a 10 mol % -CO_2H group loading even when the concentration of **6** was only 1 mg/mL. Studies with solutions containing added salts (LiCl or LiBr) show that the solution ionic strength does not significantly affect the ΔpH, though the clouding curve's onset changes. Control experiments showed that a solution containing propanoic acid, PNIPAM, or poly(*N*,*N*-dimethylacrylamide) (PDMAM) exhibits pH changes of <0.004 pH unit/°C upon being heated from 5 to ∼55 °C. The minimal change in pH we measured for solutions with polymers like PNIPAM containing no acidic group or PDMAM[18] that does not have an observable LCST and the lack of a ΔpH for propanoic acid are in accord with others' work that has shown little background change in the pH for acidic solutions using pH meters and a glass electrode.[19−21] These control experiments show no ΔpH in the presence of unfunctionalized polyacrylamides regardless of whether they exhibit LCST behavior.

Solutions of **6** studied in Table 1 and in Figures 2 and 3 generally have pH-sensitive cloud points that range from 26 to 30 °C for pH 4.1 solutions (clouding curves are shown as Supporting Information). The very dilute 1 mg/mL solution of **6** and the pH 6.8 solution of **6** do not have a detectable cloud point. Visually, the cloud point of these solutions is at the point where major changes in pH begin to occur (Figure 3). The cloud point curve is most narrow with **6** containing a 10 mol % loading of -CO_2H groups. This sharper cloud point led to the largest ΔpH of ∼1.5. The clouding curves also are broader for lower concentrations of **6**. Samples of **6** with a higher loading of -CO_2H groups had slightly lower ΔpH values that might be related to the extent to which the phase-separated polymers aggregate to form larger particles. Similar effects on aggregate particle size have been reported by others, though those studies often use polymer concentrations that are orders of magnitude lower than those used in this work.[22,23] PNIPAM homopolymers have a very sharp clouding curve and form flocculated solid suspensions in water upon being heated between 32 and 33 °C. However, other poly(*N*-alkylacrylamide)s and poly(*N*-alkylacrylamide) copolymers have both a different onset of clouding and often broader clouding curves. The varied sharpness of the clouding curve and differences in flocculation of the initially phase-separated poly(*N*-alkylacrylamide) polymers can depend on the polymer concentration, polymer structure, pH, and other solution components. There are detailed studies of the effect of morphology, polymer functionality, and solution composition on the swelling and deswelling of thermally responsive cross-linked PNIPAM gels.[24] While there are some similar studies with PNIPAM[25] and while such studies might be possible with the various phase-separated PNIPAM copolymer colloidal globules formed in this work, the details of the morphology of these initially formed precipitates and how these precipitates flocculate to form larger solid particles over the concentration ranges we use here are outside the scope of this study.

A final experiment showed that an LCST event induced by a kosmotropic salt also produces a solution pH change. In this case, 20 mg of Na_2SO_4 was added to 1 mL of an acidic yellow-green solution of **6** containing bromocresol green (20 mg/mL **6**, 10 mol % -CO_2H group loading). After centrifugation, a blue supernatant solution formed. The precipitated **6** that formed as a result of the Na_2SO_4-induced LCST event could then be redissolved in distilled water containing bromocresol green to re-form the original yellow-green solution of **6**. In this case, polymer **6** precipitated because Na_2SO_4 changed **6**'s LCST to below room temperature because of the Hofmeister effect.[26]

The premise that an LCST event and the resulting solvation changes affect the environment of a charged amphoteric group that in turn changes the solution pH was further tested by preparing a second PNIPAM copolymer containing a piperidyl amine group that could affect the solution pH because of the solvation-dependent stability of the ammonium form of a PNIPAM-bound piperidyl base. The thermoresponsive polymer **7** used in these experiments was prepared either from copolymer **1** by reaction of **1** with 4-amino-2,2,6,6-tetramethylpiperidine[27] or by copolymerization of *N*-isopropylacrylamide with *N*-4-acrylamido-2,2,6,6-tetramethylpiperidine. We tested the hypothesis that **7** could affect the solution pH using several examples of polymer **7** that contained various loadings of the pendant 2,2,6,6-tetramethylpiperidyl group. In these materials, the tetramethylpiperidyl group bound to **7** at pH 9−11 would be in equilibrium with its ammonium salt (Scheme 4). We expected that this equilibrium would be affected by an LCST event that places the ammonium groups in a less polar environment if the polymer phase separates because of an LCST event. This proved to be the case, and heating a solution of **7** that had a sufficient loading of the ammonium salt did alter the pH of the bulk solution.

Scheme 4. Reversible Protonation of a Poly(*N*-isopropylacrylamide)-*c*-Poly(4-*N*-2,2,6,6-tetramethylpiperidylacrylamide) 7 on Heating and Cooling



Our initial experiments used copolymer **7** with a 6:1 ratio of *N*-isopropyl to 4-*N*-2,2,6,6-tetramethylpiperidyl groups that was prepared from copolymer **1**. This sample of **7** had an M_w of 179 kDa and a PDI of 1.75. Heating a 4 wt %, pH 9.0 solution of this sample of **7** from 25 to 50 °C precipitated **4** and changed the solution pH to 7.4. The change in pH for the bulk solution was reversible upon cooling, as is shown by analysis of this solution with a pH meter. The reversibility of these heating and cooling-induced pH changes through hundreds of cycles was visually confirmed by examining a solution of **7** containing phenolphthalein. These heating−cooling cycles led alternately to a colorless white suspension above **7**'s LCST and a clear fuchsia solution below **7**'s LCST.

The measured pH change in these basic solutions of **7** changes reversibly, and the observed pH changes we see, like those for **7**, are greatest in the 30−40 °C temperature range where polymer **7** phase separates from solution. Changes in pH for 20 mg/mL solutions of **7** that had a 6, 9, 13, or 24 mol % loading of amine averaged 1.4 pH units when the starting pH was in the range of 10−11. Starting with polymer concentrations of 10, 5, and 1 mg/mL with 9 mol % piperidine loading, we produced ΔpH values of 1.2, 1.0, and 0.4, respectively. These ΔpH changes were corrected for pH changes due to effects of temperature on K_a and the effects of temperature changes on the pH measurements in alkaline solutions.[19−21] This correction involved comparison of the pH changes seen for **7** with the linear change in pH/°C seen for an aqueous solution that contains an equivalent concentration of the monomer *N*-4-acrylamido-2,2,6,6-tetramethylpiperidine over this same temperature range.

As shown in Figure 4, the clouding behavior of these polymers varies depending on the amine loading of the polymer and on the conditions of the experiment. PNIPAM itself has a clouding curve with an onset of clouding at 32.6 °C. When polymer **7** with a 6, 9, 13, and 24 mol % loading of amine was dissolved in deionized water at a concentration of 20 mg/mL, the onset of clouding (5% arbitrary scattering) occurred at 30.8, 33.4, 34.6, and 35.7 °C, respectively. However, unlike PNIPAM that phase separates into a solid white opaque suspension within 1 or 2 °C, these highly loaded amine-containing PNIPAM copolymer solutions form a cloudy solution with broader clouding curves. Similar variations in clouding behavior for copolymers **6** are discussed above and were noted by Franks for PNIPAM copolymers containing carboxylate or quaternary ammonium salts.[21,22] Addition of salts to this solution led to formation a more distinct PNIPAM-like clouding curve, though the onset of clouding that is typically used to define the LCST occurs at a lower temperature.[27]

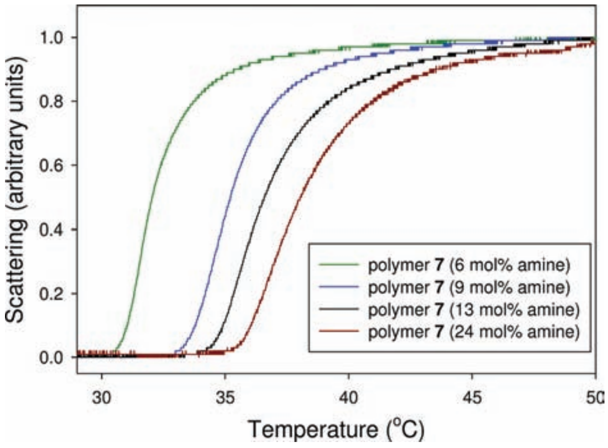


Figure 4. Clouding curve samples of **7** with 6, 9, 13, and 24 mol % 2,2,6,6-tetramethylpiperidyl groups (20 mg/mL solutions heated at a rate of 0.2 °C/min using an OptiMelt apparatus).

A visible spectroscopy study of the changes in concentration of the phenolphthalein dianion (λ_{max} = 553 nm) with temperature examined the effect of temperature on pH (Figure 5). The initial fuchsia color of these solutions at pH ~9 does not change significantly below 30 °C.[29] However, between 30 and 40 °C, a significant change in color occurs. We generally use a melting point apparatus to measure cloud points in place of transmittance studies with UV−visible spectrometers to determine LCSTs.[28] However, in this case, analysis of the absorbance at 553 nm (the λ_{max} for phenolphthalein in our experiments) was enlightening. When we examined the absorbance changes at the cloud point, a detectable inflection occurred that mirrored the visual observation that the bright fuchsia solution of **7** was changing before a cloudy white suspension formed. While this color change is evident in a visible spectrum (a set of visible spectra as a function of temperature are provided as Supporting Information), there is also a subtle change that is seen as an inflection in absorbance at 553 nm just before the absorbance increases significantly at the cloud point from scattering due to formation of precipitated **7** and an opaque suspension. This detectable but small change in absorbance seen at the cloud point is consistent with our other observations and with the notion that phase separation of the polymer is associated with an onset of a change in solution pH.

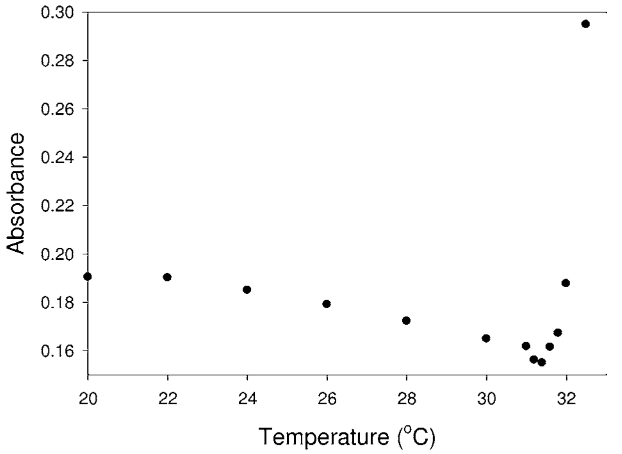
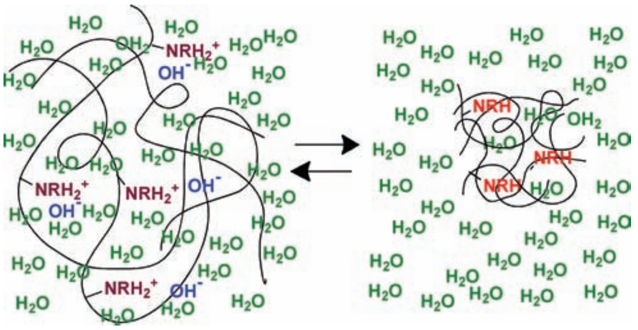


Figure 5. Absorbance at 553 nm for a 5 mg/mL solution of **7** (6 mol % loading of 2,2,6,6-tetramethylpiperidyl groups in **7**) in water containing ~0.25 M NaCl as a function of temperature.

A final experiment showed that an LCST event induced by a kosmotropic salt also produces a solution pH change. When 20 mg of Na_2SO_4 was added to a 40 mg/mL solution of **7** (14 mol % loading of amine) at pH 9.5, polymer **7** precipitated because Na_2SO_4 changed **7**'s LCST to below room temperature because of the Hofmeister effect.[26] When this experiment was conducted in the presence of phenolphthalein, the original fuchsia solution became a water white suspension after precipitation of **7**. Decantation of the supernatant and dissolving this precipitated polymer regenerated a basic solution as evidenced by the characteristic fuchsia color of the added phenolphthalein indicator. In the absence of **7**, addition of sodium sulfate did not produce a color change.

Our proposed explanation for the solution pH changes and the underlying change in the protonation state for PNIPAM containing a carboxylate or ammonium salt is illustrated in an exaggerated form in Scheme 5. In this scheme, the polymer below the LCST exists as a fully hydrated random coil where the pendant ammonium groups would be stabilized by solvent water. Above the LCST, the polymer loses waters of hydration because of entropy effects and the less solvated polymer precipitates. The charged groups (in this scheme the ammonium groups) of the phase-separated PNIPAM copolymer both in the initially formed globules and in the flocculated solid precipitate that forms are now less hydrated and therefore less stabilized by solvent water. The end result is a situation that is analogous to that seen by ammonium groups in an enzyme active site.[12] This lower stability of the ammonium group makes the ammonium group a stronger acid, leading to loss of protons to solvent to form a more neutral amino group. This leads to formation of water, and concomitant consumption of hydroxide anions as a result of an LCST event. This

Scheme 5. Effect of Polymer Desolvation on the Protonation State of a Pendant Ammonium Group in a PNIPAM Copolymer after an LCST Event



explanation is consistent both with the significant change in bulk pH seen due to temperature changes and with isothermal experiments involving addition of a kosmotropic salt.

CONCLUSION

In summary, the relative concentration of a conjugate base of a weak acid and its acid or the conjugate acid of a weak base and a base incorporated into a poly(*N*-isopropylacrylamide) copolymer that exhibits inverse temperature-dependent solubility can be affected by an LCST event. The changes in the stability and the relative concentration of the acid and base forms of these pH-sensitive groups during an LCST event are most significant at pH values that are near the pK_a of the polymer-bound acid or base. Using 10−40 mg/mL solutions of a carboxylic acid-containing copolymer in deionized water, precipitation and the decrease in the level of solvation of carboxylate groups during an LCST event consume protons from bulk solution, changing the bulk solution pH by 1−2 pH units with the majority of this change occurring during the polymer's LCST event. This behavior is fully reversible, and the extent of the pH change varies with the loading of the acid group in the product copolymer. When similar solutions of a PNIPAM copolymer containing an amine group are prepared, the ammonium groups of this copolymer form neutral amine groups after a precipitation induced by heating. This behavior is also reversible and leads to bulk solution pH changes of ∼1.5 pH units, with the majority of this change again occurring over a few degrees during the LCST event. These pH changes can also be induced without heating by addition of a kosmotropic salt like Na_2SO_4 and are not significantly affected by the solution ionic strength. Control experiments show that the polyacrylamide homopolymers alone do not produce such changes in solution pH. Studies with phase-selectively soluble polymer-bound dyes whose phase behavior is changed with temperature or additives support the notion that these pH changes are a result of a change in the solvation of the amphoteric group.

ASSOCIATED CONTENT

Ⓢ Supporting Information

Experimental procedures for the synthesis of copolymer, a description of the fluorescence experiments, clouding curves, and photos of the pH changes seen using indicator dyes. This material is available free of charge via the Internet at http://pubs.acs.org.

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Notes

The authors declare no competing financial interest.

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