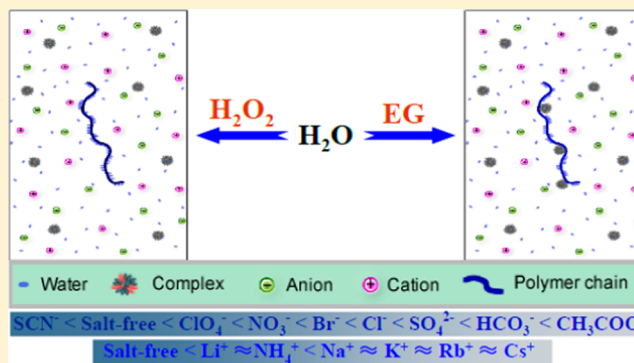


Mechanistic Insights into Amplification of Specific Ion Effect in Water–Nonaqueous Solvent Mixtures

Lvdan Liu,[†] Tao Wang,[†] Chang Liu,[†] Ke Lin,[†] Yanwei Ding,[†] Guangming Liu,^{†,*} and Guangzhao Zhang[‡][†]Department of Chemical Physics, Hefei National Laboratory for Physical Sciences at the Microscale, University of Science and Technology of China, Hefei, P. R. China 230026[‡]Faculty of Materials Science and Engineering, South China University of Technology, Guangzhou, P. R. China 510640

S Supporting Information

ABSTRACT: Ethylene glycol (EG) and hydrogen peroxide (H_2O_2) can act as both hydrogen-bond donors and acceptors in the formation of solvent complexes with water molecules. In the present work, we have systematically investigated the ion-specific lower critical solution temperature (LCST) behavior of poly(*N*-isopropylacrylamide) (PNIPAM) in H_2O –EG and H_2O – H_2O_2 mixtures. The results obtained from turbidity measurements show that the specific anion effect is amplified with the increasing molar fraction of EG (x_{EG}) but is independent of the molar fraction of H_2O_2 ($x_{\text{H}_2\text{O}_2}$). The studies of Raman spectra and differential scanning calorimetry indicate that the discrepancy in amplification of specific anion effect between H_2O –EG and H_2O – H_2O_2 mixtures is due to the difference in the anion–solvent complex interactions rather than the anion–polymer or solvent–polymer interactions. On the other hand, the specific cation effect can also be amplified with the increasing x_{EG} but changes only slightly with the $x_{\text{H}_2\text{O}_2}$. The discrepancy in amplification of specific cation effect between the two types of solvent mixtures is attributed to the difference in the solvent–polymer interactions.



INTRODUCTION

Specific ion effect or the Hofmeister effect is a ubiquitous phenomena in biological and chemical systems.^{1–12} According to the relative ability to precipitate proteins in aqueous solutions, the ordering of ions generally follows the series $\text{SO}_4^{2-} > \text{HCO}_3^- > \text{CH}_3\text{COO}^- > \text{Cl}^- > \text{Br}^- > \text{NO}_3^- > \text{ClO}_4^- > \text{SCN}^-$ for anions and $\text{Li}^+ < \text{Na}^+ < \text{K}^+ < \text{Rb}^+ < \text{Cs}^+ < \text{NH}_4^+$ for cations.¹³ In general, the ions can be categorized as kosmotropes and chaotropes in light of the strength of ionic hydration.^{14–16} Specifically, the highly hydrated ions on the left side of the series are defined as kosmotropes, whereas the weakly hydrated ions on the right side are defined as chaotropes.^{17–20} Recent spectroscopic studies indicate that the ions may primarily affect the hydrogen bonds of water within the hydration shell.^{21–23}

In aqueous solutions, several theoretical models have been proposed to clarify the mechanism of the Hofmeister effect.^{24–26} Collins has proposed a concept of matching water affinities to explain the ion specificity.^{25,27} Ninham et al. have suggested that specific ion effect is due to the polarizability of ions and is manifested through the dispersion forces.²⁴ Kunz et al. have suggested that the nature of surfaces may have significant influences on the specific ion effect.²⁶ In comparison with the extensive studies on the Hofmeister effect in aqueous solutions, little attention has been paid to the specific ion effect

in water–nonaqueous solvent mixtures.²⁴ Our previous study demonstrates that the ordering of ions in water–methanol mixtures is similar to that in water for the ion-specific reentrant behavior of poly(*N*-isopropylacrylamide) (PNIPAM), but the relative strength of specific ion effect is amplified with the addition of methanol.²⁸ However, the mechanism of amplification of specific ion effect still remains unclear.

To deeply understand the mechanism of amplification of specific ion effect in water–nonaqueous solvent mixtures, two types of solvent mixtures, i.e., water–ethylene glycol (H_2O –EG) and water–hydrogen peroxide (H_2O – H_2O_2), have been used as media to study the ion-specific lower critical solution temperature (LCST) behavior of PNIPAM in the present study. In a H_2O_2 molecule, two hydroxyl groups are connected by an oxygen–oxygen bond, while two hydrophobic methylene groups are located between the two hydroxyl groups in an EG molecule. EG and H_2O_2 have some similar properties, for example, each of them can act as both hydrogen-bond donors and acceptors due to the two hydroxyl groups at the end of the molecules. Thus, they can form spatial hydrogen-bond networks in their respective pure liquids.^{29,30} It is reported

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that the molecules mainly form linear hydrogen bonds with a bond energy of ~ 18 kJ/mol in the pure EG liquid, and the molecules primarily form furcated hydrogen bonds with a bond energy of ~ 10 – 14 kJ/mol in the pure H_2O_2 .²⁹ Furthermore, the furcated hydrogen bonds formed in H_2O_2 are similar to that formed in pure water where H_2O molecules may form clusters by themselves via furcated hydrogen bonds, which is an indication of the likeness of the hydrogen-bonded fragments between H_2O and H_2O_2 .^{29,31–33}

In H_2O –EG mixtures, H_2O and EG molecules can form cyclic solvent complexes in which water molecules bridge between the two hydroxyl groups of EG via hydrogen bonds.^{31–33} On the other hand, the most stable conformers of $\text{H}_2\text{O}/\text{H}_2\text{O}_2$ complexes are also the cycle-shaped structures.^{34–37} That is, the solvent complexes formed in the two types of solvent mixtures have similar structures. In the present work, we have systematically investigated the ion-specific LCST behavior of PNIPAM in H_2O –EG and H_2O – H_2O_2 mixtures by using a turbidimeter, Raman spectra, and differential scanning calorimetry (DSC). It is expected that PNIPAM should have similar ion specificities in H_2O –EG and H_2O – H_2O_2 mixtures since EG and H_2O_2 exhibit some similar properties in their respective pure liquids and in the formation of solvent complexes with H_2O . However, our results demonstrate that the specific ion effect is amplified with the addition of EG to water but is independent of the addition of H_2O_2 . We are interested in how the specific ion effect is amplified by the addition of a second water-miscible nonaqueous solvent.

EXPERIMENTAL SECTION

Materials. Isopropylacrylamide (NIPAM, Aldrich) was recrystallized three times in a mixture of toluene and hexane (65:35, v/v). 1,4-Dioxane was refluxed over Na and then distilled under vacuum before use. 4,4'-Azobis(isobutyronitrile) (AIBN) was recrystallized three times from ethanol. All salts (AR grade) were purchased from Sinopharm or Aladdin and used as received. 30% H_2O_2 (w/w) in water and EG (99%, AR grade) were purchased from Sinopharm and used as received. The water used was purified by filtration through a Millipore Gradient system after distillation, giving a resistivity of 18.2 M Ω cm. When studying anion specificity, we employed sodium salts so that the influence of cations was constant; similarly, chloride salts were used when investigating cation specificity.

PNIPAM Preparation. Chain transfer agent cyanoisopropyl dithiobenzoate (CPDB) was synthesized following a previous method.³⁸ PNIPAM was synthesized by reversible addition-fragmentation chain transfer (RAFT) polymerization in dioxane at 70 °C for ~ 20 h with CPDB as the chain-transfer agent and AIBN as the initiator. The sample was precipitated three times from tetrahydrofuran (THF) into hexane for purification. The number-average molar mass ($M_n \approx 1.6 \times 10^4$ g/mol) and the polydispersity index ($M_w/M_n \approx 1.3$) of the sample were measured by gel permeation chromatography (Waters 1515) using monodisperse polystyrene as the calibration standard and THF as the eluent with a flow rate of 1.0 mL/min.

Cloud Point Measurements. Cloud points were determined by monitoring the turbidity of solutions heated at a rate of 0.1 °C/min using a UNICO 2802PCS UV–vis spectrophotometer with the wavelength set to 500 nm. The temperature of the cell was controlled using a circulating temperature-controlled bath with an accuracy of ± 0.1 °C and monitored by an electronic thermometer. For measurements below 10 °C,

the cell holder was flushed with nitrogen to prevent moisture condensation on the cell surface. The concentration of PNIPAM in the H_2O –EG and H_2O – H_2O_2 mixtures was fixed at 1.0 mg/mL, and the ionic strength was fixed at 0.5 M. In turbidity studies, we chose to use the temperature at which the transmittance equaled the average of the transmittance values of the high transmittance (low turbidity) and low transmittance (high turbidity) plateaus as the LCST at different molar fractions of EG (x_{EG}) or H_2O_2 ($x_{\text{H}_2\text{O}_2}$) (Figure S1, Supporting Information). Then, we could plot the changes of LCST as a function of x_{EG} or $x_{\text{H}_2\text{O}_2}$ for different ions. The addition of EG or H_2O_2 to water would significantly depress the LCST of PNIPAM, so that the LCST in the presence of some ions (e.g., ClO_4^- and CH_3COO^-) would be lower than the freezing point of the corresponding salt solutions at high x_{EG} or $x_{\text{H}_2\text{O}_2}$. Consequently, it was not possible to determine the LCST for the ions at the high x_{EG} or $x_{\text{H}_2\text{O}_2}$. The maximum x_{EG} and $x_{\text{H}_2\text{O}_2}$ used in the present work were 20% and 16%, respectively.

Raman Spectra Measurements. In the Raman spectra measurements, a CW laser source (Coherent, Verdi-SW, 532 nm), a monochromator with a 600 grooves/mm grating, and a liquid-nitrogen-cooled CCD detector (Acton Research, Triple-Pro) were used to record the spontaneous Raman spectrum.³⁹ Liquid samples in a quartz cell (Spectrocell, 10×10 mm²) were excited by the laser. The Raman scattering photons were collected at 180° geometry relative to the incident laser beam with a pair of $f = 5$ and 20 cm lenses and imaged through a polarization scrambler onto the entrance slit of the monochromator for spectral dispersion. The laser power employed was 0.5 W. The spectral resolution was determined to be ~ 3.0 cm⁻¹. All the Raman spectra were measured at ~ 20 °C.

DSC Measurements. The measurements were conducted on a multicell-DSC (TA Instruments) at a heating rate of 1 °C/min. A reference scan was performed using a blank solution containing all reagents except PNIPAM. The concentration of PNIPAM was fixed at 10.0 mg/mL so that the measurements were sufficient to yield strong signals and had good accuracy. The salt concentration was fixed at 0.5 M. The temperature corresponding to the endothermic peak in the DSC curve was taken as the LCST.

RESULTS AND DISCUSSION

Turbidity Experiments for Anion Specificity. Figure 1 shows the change in LCST of PNIPAM as a function of x_{EG} for

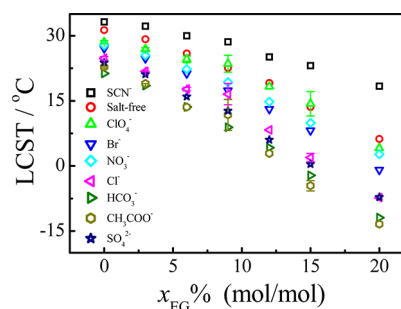


Figure 1. Specific anion effect on the LCST behavior of PNIPAM in the H_2O –EG mixtures as a function of the molar fraction of EG (x_{EG}) with Na^+ as the common cation, where the polymer concentration is fixed at 1.0 mg/mL and the ionic strength is fixed at 0.5 M.

different anions. It is known that PNIPAM chains can be solvated by both free solvent molecules and solvent complexes in water–organic solvent mixtures.^{28,40,41} The solvent complexes are generally considered as poorer solvents compared with the free solvent molecules (i.e., cosolvency).^{28,40–42} Thus, the LCST gradually decreases with the increasing x_{EG} for all of the anions, suggesting that the addition of EG makes water become a poorer solvent for the PNIPAM chains due to the increasing concentration of $\text{H}_2\text{O}/\text{EG}$ complexes.^{31–33} In comparison with the LCST in the salt-free solution, SCN^- exhibits a salting-in effect, as indicated by the fact that the value of LCST in the presence of SCN^- is always higher than that in the salt-free solution for the same x_{EG} . In contrast, other anions exhibit a salting-out effect, as reflected by the lower LCST in the presence of the anions than that in the salt-free solution for the same x_{EG} . In an aqueous solution of PNIPAM, the salting-in effect relates to the direct binding of chaotropic anions to polymer surface, and the salting-out effect correlates with the destabilization of hydrogen bonding by kosmotropic anions and the increase of polymer–water interfacial tension by the adsorption of anions.^{43–45} Besides, the influence of anions on water structure may also affect the salting-in/out of PNIPAM.⁴⁶ It is evident that the LCST decreases following the order $\text{SCN}^- > \text{salt-free} > \text{ClO}_4^- > \text{NO}_3^- > \text{Br}^- > \text{Cl}^- > \text{SO}_4^{2-} > \text{HCO}_3^- \approx \text{CH}_3\text{COO}^-$ for the same x_{EG} in either water or H_2O –EG mixtures, which is roughly consistent with the classical Hofmeister series.^{13,17,47–51} This fact indicates that the addition of EG to water will not change the ordering of anions in the Hofmeister series.

Moreover, it is likely that the specific anion effect is gradually amplified with the increasing x_{EG} , which can be seen more clearly in Figure S2 (Supporting Information). In the H_2O –EG mixtures, a dynamic equilibrium exists between the free solvent molecules and the complexes. The shifting of this equilibrium should be influenced by the anion–complex interactions. As reported previously, water and methanol molecules may be able to more easily form complexes in the presence of more kosmotropic anions due to the specific anion–complex interactions.^{52–54} That is, the relative proportion of free solvent molecules decreases as the anions change from chaotropes to kosmotropes in the H_2O –EG mixtures at the same x_{EG} . A lower relative proportion of free solvent molecules would lead to a lower LCST because the free solvent molecules and the solvent complexes are respectively the good and poor solvents for PNIPAM.^{40–42} The increasing concentration of $\text{H}_2\text{O}/\text{EG}$ complexes would enlarge the difference in the interactions between anions and solvent complexes, thereby giving rise to an enhancing difference in PNIPAM solubility between the anions by shifting the equilibrium between the free solvent molecules and the complexes, resulting in a more prominent anion specificity. In other words, the amplification of specific anion effect might be attributed to the enhancing difference in anion–solvent complex interactions with the increasing x_{EG} .

It is expected that the specific anion effect on the LCST behavior of PNIPAM in the H_2O – H_2O_2 mixtures should also be amplified with the addition of H_2O_2 since H_2O_2 exhibits some similar properties with EG and the $\text{H}_2\text{O}/\text{H}_2\text{O}_2$ complexes have similar structures with the $\text{H}_2\text{O}/\text{EG}$ complexes. In Figure 2, the LCST for all anions decreases with the increasing $x_{\text{H}_2\text{O}_2}$ indicating that the addition of H_2O_2 makes water become a poorer solvent due to the increasing concentration of $\text{H}_2\text{O}/$

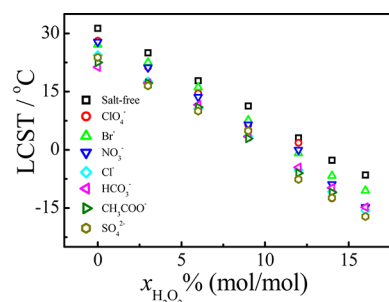


Figure 2. Specific anion effect on the LCST behavior of PNIPAM in the H_2O – H_2O_2 mixtures as a function of the molar fraction of H_2O_2 ($x_{\text{H}_2\text{O}_2}$) with Na^+ as the common cation, where the polymer concentration is fixed at 1.0 mg/mL and the ionic strength is fixed at 0.5 M.

H_2O_2 complexes. Note that SCN^- is not used in the H_2O – H_2O_2 mixtures because of the possible chemical reaction between SCN^- and H_2O_2 .^{55–58} Here, all anions exhibit a salting-out effect, as indicated by the fact that the values of LCST for all the anions are lower than that in the salt-free solution for the same $x_{\text{H}_2\text{O}_2}$. Furthermore, for the same $x_{\text{H}_2\text{O}_2}$, the decrease of LCST roughly follows the order salt-free $> \text{ClO}_4^- > \text{NO}_3^- > \text{Br}^- > \text{Cl}^- > \text{HCO}_3^- \approx \text{CH}_3\text{COO}^- > \text{SO}_4^{2-}$, which is consistent with the classical Hofmeister series.^{13,17,47–51}

Interestingly, the specific anion effect cannot be amplified with the addition of H_2O_2 , which can be more clearly seen in Figure S3 (Supporting Information). This result is obviously inconsistent with that in the H_2O –EG mixtures. What concerns us is why the specific anion effect is amplified in the H_2O –EG mixtures but not in the H_2O – H_2O_2 mixtures. From the discussions above, the amplification of specific anion effect in the H_2O –EG mixtures may be due to the increasing difference in the interactions between anions and solvent complexes with the addition of EG. Therefore, the discrepancy in amplification of anion specificity between H_2O – H_2O_2 and H_2O –EG mixtures might be attributed to the different mechanisms in the formation of solvent complexes via hydrogen bonds between such two types of solvent mixtures. To understand the changes of hydrogen bonds in the formation of solvent complexes with the addition of EG and H_2O_2 , we have measured the Raman spectra of H_2O –EG and H_2O – H_2O_2 mixtures with the x_{EG} and $x_{\text{H}_2\text{O}_2}$ (Figures 3–6).

Raman Spectra Experiments for Anion Specificity.

Figure 3 shows the area-normalized Raman spectra of the H_2O –EG mixtures as a function of x_{EG} . It is known that the

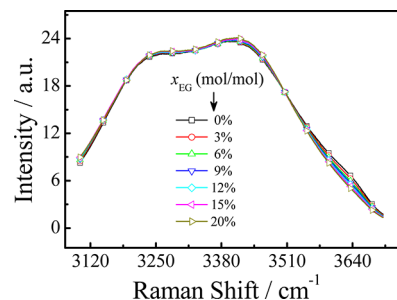


Figure 3. Area-normalized Raman spectra of the H_2O –EG mixtures as a function of the molar fraction of EG (x_{EG}).

high frequency band ($\sim 3635\text{ cm}^{-1}$) and the low frequency bands ($\sim 3200\text{--}3400\text{ cm}^{-1}$) are ascribed, respectively, to the free hydroxyl groups and the hydroxyl groups in a strong hydrogen-bond network in the H_2O –EG mixtures.^{29,30} The Raman spectra for the low frequency bands and the high frequency band are magnified in Figure 4a and b, respectively,

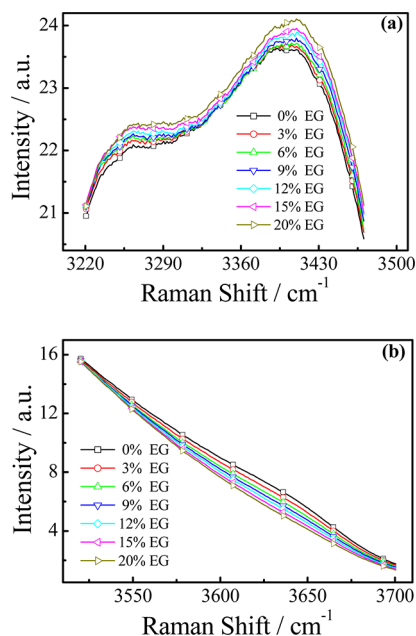


Figure 4. Magnification of the corresponding parts of the Raman spectra (Figure 3). (a) The low frequency bands and (b) the high frequency band.

so that the change in intensity of the spectra can be seen more clearly. It can be seen that the intensity of the low frequency bands gradually increases with the increasing x_{EG} , whereas the intensity of the high frequency band gradually decreases with the increase of x_{EG} . This fact indicates that some free hydroxyl groups in water transform into the hydroxyl groups in the strong hydrogen-bond network with the addition of EG. In other words, the formation of H_2O /EG complexes via the strong hydrogen bonds would consume some free hydroxyl groups in water. Moreover, the concentration of H_2O /EG complexes increases with the x_{EG} , as reflected by the increasing intensity of the low frequency bands with the addition of EG. Consequently, the increasing concentration of H_2O /EG complexes with the x_{EG} leads to an enhancing difference in the interactions between anions and solvent complexes by shifting the equilibrium between the free solvent molecules and the complexes, thereby resulting in the amplification of specific anion effect.

Figure 5 shows the area-normalized Raman spectra of the H_2O – H_2O_2 mixtures as a function of $x_{\text{H}_2\text{O}_2}$. It is reported that the high frequency band ($\sim 3635\text{ cm}^{-1}$), the middle frequency band ($\sim 3520\text{ cm}^{-1}$), and the low frequency bands ($\sim 3200\text{--}3400\text{ cm}^{-1}$) are ascribed, respectively, to the free hydroxyl groups, the hydroxyl groups in a weak hydrogen-bond network, and the hydroxyl groups in a strong hydrogen-bond network.^{29,30} In general, the hydroxyl groups primarily form furcated and linear hydrogen bonds in the weak and strong hydrogen-bond networks, respectively.^{29,30,59}

The corresponding magnifications of the Raman spectra for the low, middle, and high frequency bands are shown in Figure

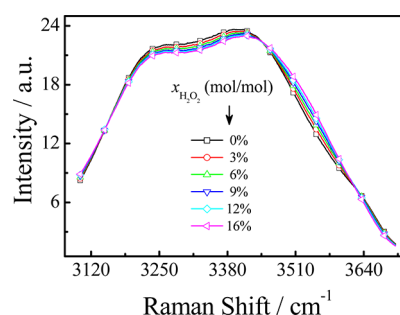


Figure 5. Area-normalized Raman spectra of the H_2O – H_2O_2 mixtures as a function of the molar fraction of H_2O_2 ($x_{\text{H}_2\text{O}_2}$).

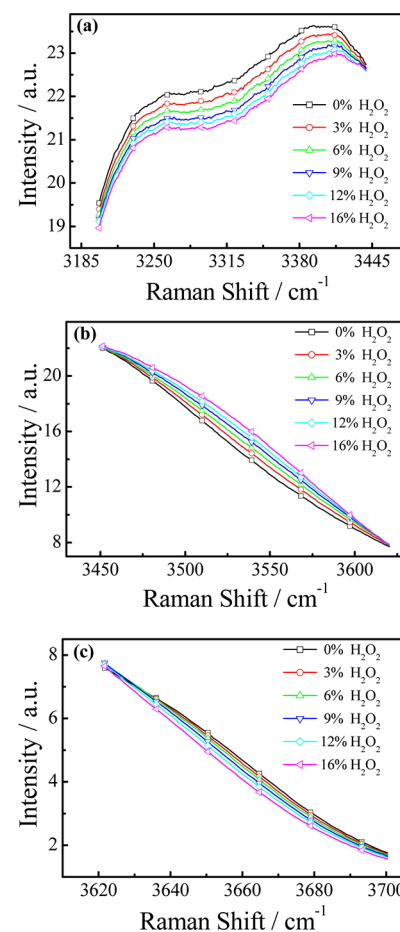


Figure 6. Magnification of the corresponding parts of the Raman spectra (Figure 5). (a) The low frequency bands, (b) the middle frequency band, and (c) the high frequency band.

6a, b, and c, respectively. The intensity of the low frequency bands decreases as the $x_{\text{H}_2\text{O}_2}$ increases. In contrast, the intensity of the middle frequency band increases with the increasing $x_{\text{H}_2\text{O}_2}$. Besides, the intensity of the high frequency band also has a slight decrease with the addition of H_2O_2 . These facts suggest that some hydroxyl groups in the strong hydrogen-bond network and a few free hydroxyl groups are consumed to form the H_2O / H_2O_2 complexes via the furcated hydrogen bonds with the addition of H_2O_2 . Because the strength of furcated

hydrogen bonds in the $\text{H}_2\text{O}/\text{H}_2\text{O}_2$ complexes may be similar to that of the furcated hydrogen bonds formed in the H_2O clusters in pure water,^{34,60,61} the anions should have similar influences on the structure of $\text{H}_2\text{O}/\text{H}_2\text{O}_2$ complexes and H_2O clusters. That is, the difference in the interactions between anions and solvent complexes is expected to be constant with the increasing $x_{\text{H}_2\text{O}_2}$. Consequently, the specific anion effect cannot be amplified with the addition of H_2O_2 even though the concentration of $\text{H}_2\text{O}/\text{H}_2\text{O}_2$ complexes increases with the $x_{\text{H}_2\text{O}_2}$.

Now, we know that the solvent complexes formed by the strong hydrogen bonds in the H_2O –EG mixtures may more effectively differentiate the interactions between anions and solvent complexes than the H_2O clusters formed in pure water. Therefore, the increasing concentration of $\text{H}_2\text{O}/\text{EG}$ complexes with the x_{EG} will amplify the specific anion effect by shifting the equilibrium between the solvent complexes and the free solvent molecules. On the other hand, the solvent complexes formed by the weak furcated hydrogen bonds in the H_2O – H_2O_2 mixtures may have a similar effectiveness to differentiate the interactions between anions and solvent complexes with the H_2O clusters formed in the pure water. Hence, the anion specificity cannot be amplified with the addition of H_2O_2 . Regarding the amplification of specific anion effect in the H_2O –EG mixtures, it is also possible that the aqueous environment that kosmotropes favor is broken with the addition of EG, so the anions may migrate more toward the PNIPAM–water interface, leading to an increase of local concentration of anions near the PNIPAM–water interface. This would cause an increasing salting-out effect by either the destabilization of hydrogen bonding between PNIPAM and water molecules or the increase in PNIPAM–water interfacial tension.⁴³ Meanwhile, this would also lead to an amplification of the specific anion effect because the increase of anion concentration can amplify the ion specificity (Supplementary Figure S4).⁴³ Obviously, the conclusion is the same as that from the model of forming solvent complexes mentioned above, but the exact mechanism still needs further investigations.

Modeling Changes in LCST for Anion Specificity. It is reported that the specific anion effect on the LCST behavior of PNIPAM in aqueous solutions is correlated with (i) salting-out effects by the destabilization of hydrogen bonding between polymer and water molecules by kosmotropic anions, (ii) salting-out effects by an increase in polymer–water interfacial tension by both chaotropic and kosmotropic anions, and (iii) salting-in effects by direct binding of chaotropic anions to the polymer surface.⁴³ Furthermore, the salt concentration dependence of LCST can be modeled by the following equation:⁴³

$$T = T_0 + c[M] + \frac{B_{\max}K_A[M]}{1 + K_A[M]} \quad (1)$$

where T_0 is the LCST of PNIPAM in the salt-free solution, and $[M]$ is the molar concentration of salt. The constant c has units of temperature divided by molar concentration, which is correlated with the salting-out effects by the anions.⁴³ K_A is the binding constant of chaotropic anion to the polymer surface, and B_{\max} represents the maximum increase in LCST caused by the direct anion binding, which are related to the salting-in effects by chaotropic anions.⁴³ Actually, the salt concentration dependence of LCST of PNIPAM in the H_2O –EG and H_2O – H_2O_2 mixtures can also be fit by eq 1 (Figure S4, Tables S1 and S2 in Supporting Information). Here, c should relate to the

destabilization of hydrogen bonding polarized by the anions and the change of interfacial tension of the polymer–solvent interface modulated by the anions. That is, c should be correlated with the interactions between anions and solvent complexes. B_{\max} and K_A are related to the direct interactions between chaotropic anions and polymer surface.

ClO_4^- is a typical chaotropic anion, whereas CH_3COO^- is a typical kosmotropic anion.²⁵ Cl^- locates between chaotropes and kosmotropes in the Hofmeister series.²⁵ We have chosen to use these three typical anions to study how the difference in c (Δc) between the anions is influenced by the addition of EG or H_2O_2 to water. Note that we will not compare the values of B_{\max} and K_A between the anions because they can be obtained only for the strong chaotropic anions. In Figure 7, the

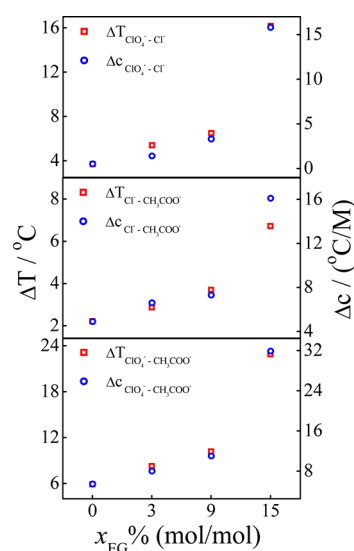


Figure 7. Dependence of the difference in LCST (ΔT) and in c (Δc) on the molar fraction of EG (x_{EG}) for ClO_4^- , Cl^- , and CH_3COO^- with Na^+ as the common cation, where the polymer concentration is fixed at 1.0 mg/mL.

difference in LCST (ΔT) between the anions obtained from Figure 1 increases with the x_{EG} , indicating the amplification of specific anion effect with the addition of EG. On the other hand, the Δc between the anions also increases with the x_{EG} , implying that the difference in the interactions between anions and solvent complexes is enlarged with the addition of EG. More interestingly, the trends between the changes in Δc and ΔT with the x_{EG} are overlapped well, suggesting that the amplification of specific anion effect is induced by the enhancing difference in the interactions between anions and solvent complexes with the addition of EG. This result agrees with that from the Raman spectra measurements. In the H_2O – H_2O_2 mixtures, the values of Δc between the anions only slightly change with the increasing $x_{\text{H}_2\text{O}_2}$ (Figure 8), indicating that the difference in the interactions between anions and solvent complexes remains almost constant with the addition of H_2O_2 . This is why the specific anion effect cannot be amplified with the addition of H_2O_2 .

DSC Experiments for Anion Specificity. From the discussions above, the amplification of specific anion effect is determined by the anion–solvent complex interactions. Previous studies demonstrate that calorimetry measurements can provide useful information on the anion–polymer and solvent–polymer interactions.^{28,62,63} To gain deeper insights

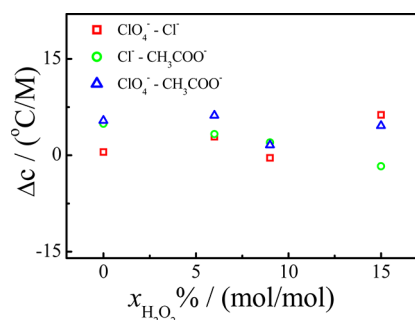


Figure 8. Dependence of the difference in c (Δc) on the molar fraction of H_2O_2 ($x_{\text{H}_2\text{O}_2}$) for ClO_4^- , Cl^- , and CH_3COO^- with Na^+ as the common cation, where the polymer concentration is fixed at 1.0 mg/mL.

into the mechanism of specific anion effect in the mixed solvents, we have also investigated the LCST behavior of PNIPAM in the H_2O –EG and H_2O – H_2O_2 mixtures in the presence of ClO_4^- , Cl^- , and CH_3COO^- by using DSC. The changes of LCST in the DSC measurements show that the specific anion effect is amplified with the addition of EG but cannot be amplified with the addition of H_2O_2 (Figures S5 and S6, Supporting Information), which is consistent with the result from the turbidity measurements (Figures 1 and 2). The temperature dependence of heat flow as a function of x_{EG} or $x_{\text{H}_2\text{O}_2}$ is shown in Supplementary Figures S7 and S8.

It is known that the width of endothermic peak reflects the cooperativity in the desolvation and collapse of PNIPAM chains.⁶² More specifically, a sharp endothermic peak indicates an abrupt phase transition due to the cooperative desolvation and collapse of PNIPAM chains, whereas a broad endothermic peak reflects a weak cooperativity in chain desolvation and collapse.⁶² Figure 9 shows the change in full width at half-maximum (fwhm) of the endothermic peaks as a function of x_{EG} in the presence of ClO_4^- , Cl^- , and CH_3COO^- . Clearly, the

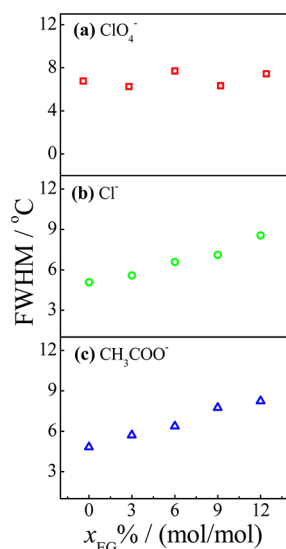


Figure 9. Change in the full width at half-maximum (fwhm) of the endothermic peaks as a function of the molar fraction of EG (x_{EG}) for ClO_4^- , Cl^- , and CH_3COO^- with Na^+ as the common cation, where the polymer concentration is fixed at 10.0 mg/mL and the ionic strength is fixed at 0.5 M. (a) ClO_4^- , (b) Cl^- , and (c) CH_3COO^- .

fwhm of ClO_4^- remains almost constant with the x_{EG} , while the fwhm of Cl^- and CH_3COO^- gradually increases with the addition of EG. In the aqueous solution, PNIPAM chains are solely and cooperatively solvated by water molecules. As x_{EG} increases, more H_2O /EG complexes are formed and involved in chain solvation, resulting in a reduction in the degree of cooperative solvation.⁶⁴ A weaker cooperativity in the chain solvation will cause a weaker cooperativity in the desolvation and collapse of PNIPAM chains upon heating, leading to a broader endothermic peak. This is why the fwhm of Cl^- and CH_3COO^- gradually increases with the addition of EG. On the other hand, a previous study shows that the binding of chaotropic anions to PNIPAM chain surface is an entropy-driven endothermic process due to the disturbance of solvation shell.⁶² Consequently, the binding of ClO_4^- would reduce the cooperativity of chain solvation by increasing the heterogeneity in distribution of solvent molecules within the solvation shell, thereby causing weakly cooperative desolvation and collapse of PNIPAM chains during the heating process. Therefore, it is difficult to observe the weakening of cooperativity induced by the addition of EG because the cooperativity is already poor in water due to the binding of ClO_4^- . This is why the fwhm of ClO_4^- remains almost constant with the x_{EG} .

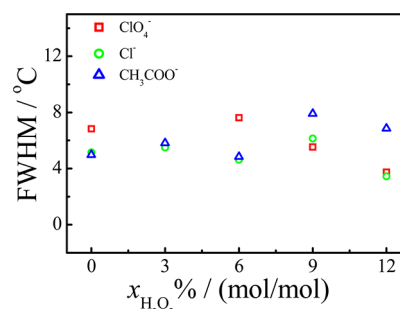


Figure 10. Change in the full width at half-maximum (fwhm) of the endothermic peaks as a function of the molar fraction of H_2O_2 ($x_{\text{H}_2\text{O}_2}$) for ClO_4^- , Cl^- , and CH_3COO^- with Na^+ as the common cation, where the polymer concentration is fixed at 10.0 mg/mL and the ionic strength is fixed at 0.5 M.

In Figure 10, the values of fwhm of ClO_4^- , Cl^- , and CH_3COO^- only slightly change with the increasing $x_{\text{H}_2\text{O}_2}$, implying that the formation of H_2O /EG complexes will not significantly influence the cooperativity of chain solvation. The possible explanation is that the H_2O_2 and H_2O molecules primarily form furcated hydrogen bonds in the H_2O /EG complexes and the solvent complexes may have few hydrogen-bond sites to interact with the PNIPAM chains.⁶¹ Considering the competition of hydrogen bonding between PNIPAM/ H_2O and PNIPAM/ H_2O /EG complex, the PNIPAM chains might be mainly solvated by the free water molecules in the H_2O – H_2O_2 mixtures. This suggestion is supported by the fact that the H_2O /EG complexes act as poorer solvents than the H_2O /EG complexes because the addition of H_2O_2 to water can more significantly depress the LCST than that of EG at the same value of x_{EG} and $x_{\text{H}_2\text{O}_2}$ (Figures 1 and 2). As a result, the cooperativity in solvation and desolvation of PNIPAM chains is only slightly influenced by the addition of H_2O_2 .

The enthalpy change (ΔH) during the phase transition can be obtained from the integration of endothermic peaks. It is suggested that the endotherm in the heating process is due to the heat required to break PNIPAM-solvent hydrogen bonds.⁶⁵ Hence, the ΔH gradually decreases with the increasing x_{EG} for ClO_4^- , Cl^- , and CH_3COO^- (Figure 11), indicating that the

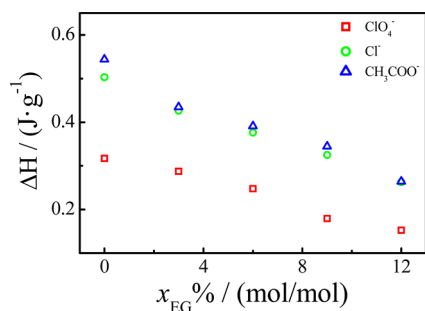


Figure 11. Dependence of change in calorimetric enthalpy (ΔH) on the molar fraction of EG (x_{EG}) in the presence of ClO_4^- , Cl^- , and CH_3COO^- with Na^+ as the common cation, where the polymer concentration is fixed at 10.0 mg/mL and the ionic strength is fixed at 0.5 M.

addition of EG reduces the number of PNIPAM-solvent hydrogen bonds. This is understandable because the $\text{H}_2\text{O}/\text{EG}$ complexes have a lower number of accessible hydrogen bonds per unit volume than the free solvent molecules.^{28,40} Besides, the weakening of cooperativity in chain solvation with the addition of EG may also reduce the number of PNIPAM-solvent hydrogen bonds.^{64,66,67} Additionally, the ΔH of ClO_4^- is smaller than that of Cl^- and CH_3COO^- for the same x_{EG} , which is because ClO_4^- can bind to PNIPAM chain surface and in so doing break some PNIPAM-solvent hydrogen bonds.

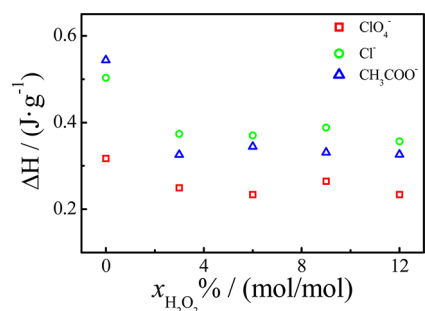


Figure 12. Dependence of change in calorimetric enthalpy (ΔH) on the molar fraction of H_2O_2 ($x_{\text{H}_2\text{O}_2}$) in the presence of ClO_4^- , Cl^- , and CH_3COO^- with Na^+ as the common cation, where the polymer concentration is fixed at 10.0 mg/mL and the ionic strength is fixed at 0.5 M.

In Figure 12, the values of ΔH for ClO_4^- , Cl^- and CH_3COO^- decrease with the increasing $x_{\text{H}_2\text{O}_2}$ from 0% to 3%, and then they remain almost constant with the further increase of $x_{\text{H}_2\text{O}_2}$. This observation is quite different from that in Figure 11. The decrease of ΔH with the increasing $x_{\text{H}_2\text{O}_2}$ from 0% to 3% implies that a few $\text{H}_2\text{O}/\text{H}_2\text{O}_2$ complexes may bind to the PNIPAM chain surface through hydrogen bonds with the initial addition of H_2O_2 , resulting in a reduction in the number of

PNIPAM-solvent hydrogen bonds due to the relatively low number of accessible hydrogen bonds per unit volume of the $\text{H}_2\text{O}/\text{H}_2\text{O}_2$ complexes. The values of ΔH only slightly change with the increasing $x_{\text{H}_2\text{O}_2}$ from 3% to 12%, indicating that no more $\text{H}_2\text{O}/\text{H}_2\text{O}_2$ complexes can bind to the chain surface with the further addition of H_2O_2 . That is, the PNIPAM chains are mainly solvated by the water molecules in $\text{H}_2\text{O}-\text{H}_2\text{O}_2$ mixtures. Again, the relatively low value of ΔH for ClO_4^- compared with that of Cl^- and CH_3COO^- for the same $x_{\text{H}_2\text{O}_2}$ is attributed to the breaking of PNIPAM-solvent hydrogen bonds induced by the binding of ClO_4^- to the chain surface. From the DSC measurements, it can be concluded that the discrepancy in amplification of specific anion effect between $\text{H}_2\text{O}-\text{H}_2\text{O}_2$ and $\text{H}_2\text{O}-\text{EG}$ mixtures cannot be attributed to the anion-polymer and solvent-polymer interactions.

Cation Specificity. It is generally accepted that the specific cation effect on the LCST behavior of PNIPAM can be neglected.^{46,68} However, Figure 13a shows that the specific

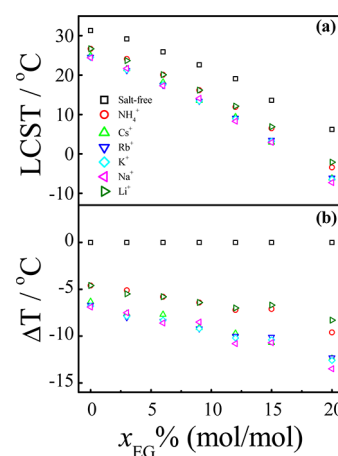


Figure 13. Specific cation effect on the LCST behavior of PNIPAM in the $\text{H}_2\text{O}-\text{EG}$ mixtures with Cl^- as the common anion, where the polymer concentration is fixed at 1.0 mg/mL and the ionic strength is fixed at 0.5 M. (a) Dependence of LCST on the molar fraction of EG (x_{EG}) for the cations and (b) dependence of the difference in LCST (ΔT) on the molar fraction of EG (x_{EG}) for the cations.

cation effect in the $\text{H}_2\text{O}-\text{EG}$ mixtures can be observed, though it is weaker than that of anions in Figure 1. The LCST in the presence of cations decreases following the order salt-free > $\text{NH}_4^+ \approx \text{Li}^+ > \text{Cs}^+ \approx \text{Rb}^+ \approx \text{K}^+ \approx \text{Na}^+$ for the same x_{EG} . Here, the lower values of LCST in the presence of cations compared to the salt-free solution are attributed to the counterion Cl^- , since it can significantly decrease the LCST. The cation specificity observed here may be attributed to the specific interactions between cations and PNIPAM chains because cations only have weak effects on the structure of solvent complexes.^{28,69–71} Li^+ is expected to have stronger interactions with the oxygen atom of carbonyl group on the PNIPAM chains than other cations due to its smaller ionic size and larger ionic surface charge density, resulting in a stronger salting-in effect.⁷² In the case of NH_4^+ , in addition to the electrostatic charge-dipole attraction with the oxygen atom, the hydrogen atoms can form hydrogen bonds with the oxygen and nitrogen atoms on the PNIPAM chains, which can also lead to the salting-in effect. This is why NH_4^+ and Li^+ exhibit a higher LCST than other cations for the same x_{EG} .

Figure 13b shows the difference in LCST (ΔT) for the cations obtained by taking the LCST of salt-free solution as the reference for the same x_{EG} . Here, the cations can be classified into two groups, namely, NH_4^+ and Li^+ are in one group, and other cations are in the other group. It can be seen that the difference in ΔT between such two groups increases with the x_{EG} , implying that the specific cation effect is amplified with the addition of EG. It is suggested that water/organic solvent complexes are poor solvents for the bare PNIPAM chains but are somewhat better solvents for the cation-bound PNIPAM chains.²⁸ Because NH_4^+ and Li^+ adsorb onto the chain surface more strongly than other cations, the coverage of NH_4^+ and Li^+ on the chain surface is expected to be higher than that of other cations. Therefore, as x_{EG} increases, the increasing concentration of H_2O/EG complexes will amplify the difference in solubility of PNIPAM chains between the two cationic groups, giving rise to an enlargement of the difference in ΔT . This is why the specific cation effect can be amplified with the increasing x_{EG} in the H_2O-EG mixtures.

In Figure 14a, the weak cation specificity can also be observed in the $H_2O-H_2O_2$ mixtures. The lower LCST of the

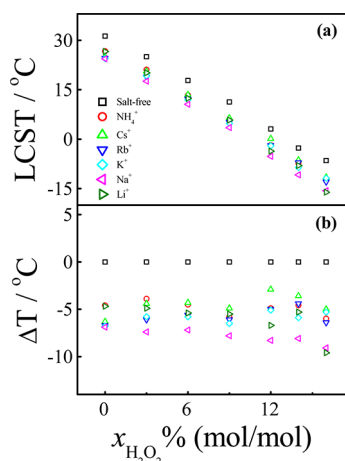


Figure 14. Specific cation effect on the LCST behavior of PNIPAM in the $H_2O-H_2O_2$ mixtures with Cl^- as the common anion, where the polymer concentration is fixed at 1.0 mg/mL and the ionic strength is fixed at 0.5 M. (a) Dependence of LCST on the molar fraction of H_2O_2 ($x_{H_2O_2}$) for the cations and (b) dependence of the difference in LCST (ΔT) on the molar fraction of H_2O_2 ($x_{H_2O_2}$) for the cations.

cations compared with the salt-free solution for the same $x_{H_2O_2}$ is also attributed to the presence of counterion Cl^- . The difference in LCST (ΔT) for the cations can be obtained by taking the LCST of salt-free solution as the reference for the same $x_{H_2O_2}$ (Figure 14b). Clearly, the difference in ΔT between the cations only slightly changes with the $x_{H_2O_2}$, suggesting that the specific cation effect cannot be amplified with the addition of H_2O_2 . As discussed above, the EG molecules prefer to form strong linear hydrogen bonds with water molecules in the H_2O/EG complexes, so that the solvent complexes have some accessible hydrogen bonds to interact with the PNIPAM chains even though the complexes are poorer solvents for the chains than the free water molecules.⁴⁰ However, H_2O_2 and H_2O molecules primarily form weak furcated hydrogen bonds in the H_2O/H_2O_2 complexes; thus the solvent complexes may have few hydrogen-bond sites to interact with the PNIPAM chains.⁶¹ As a result, the PNIPAM chains may be mainly solvated by the

free water molecules in the $H_2O-H_2O_2$ mixtures. Thus, the difference in the cation bound PNIPAM-solvent interactions between the cations only slightly changes with the addition of H_2O_2 . In other words, the difference in solubility of PNIPAM chains between the cations remains almost constant with the increasing $x_{H_2O_2}$. This is why the specific cation effect cannot be amplified with the addition of H_2O_2 .

CONCLUSION

In the present work, we have systematically investigated the ion-specific LCST behavior of PNIPAM in the H_2O-EG and $H_2O-H_2O_2$ mixtures. Our studies demonstrate that the specific anion effect is amplified with the increasing x_{EG} but is independent of the $x_{H_2O_2}$. The results from Raman spectra and DSC measurements reveal that the discrepancy in amplification of specific anion effect between the two types of solvent mixtures is due to the difference in the anion-solvent complex interactions rather than the anion-polymer or solvent-polymer interactions. On the other hand, the specific cation effect can also be amplified with the addition of EG but only slightly changes with the addition of H_2O_2 . The discrepancy in amplification of specific cation effect between the two types of solvent mixtures is attributed to the difference in the solvent-polymer interactions.

ASSOCIATED CONTENT

Supporting Information

Data of the temperature dependence of transmittance, the difference in LCST for the anions, the curve fit of LCST, and the ion specificity and temperature dependence of heat flow in DSC measurements. This material is available free of charge via the Internet at <http://pubs.acs.org>.

AUTHOR INFORMATION

Corresponding Author

*E-mail: gml@ustc.edu.cn.

Notes

The authors declare no competing financial interest.

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