DOI: 10.1002/masy.201150509

Hydration of Temperature-Responsive Polymers Observed by IR Spectroscopy

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Summary: Phase separation of aqueous solutions of temperature-responsive polymers such as poly(*N*-isopropylacrylamide) (PNiPAm) and poly(*N,N*-diethylacrylamide) (PdEA) was investigated. IR spectroscopy was proved to be a quite useful method observing changes in the hydration states of individual chemical groups of the polymers. For example, the analyses of the amide I and II bands provides important information concerning the hydrogen bonding of the C=O group and the N-H group, respectively. Changes in the C−H stretching bands indicate hydration changes of the alkyl groups. In addition, molecular simulations based on quantum chemistry give a strong support to the interpretation on molecular level. Our recent progress on this subject was presented and the relationship between the molecular interactions and the macroscopic phase behaviors was discussed.

Keywords: aqueous solution; density functional theory; IR spectroscopy; phase separation; Raman spectroscopy; temperature-responsive polymer

Introduction

Aqueous solutions of thermosensitive polymers exhibit reversible phase separation above critical temperatures called as lower critical solution temperatures (LCST) or phase transition temperatures (T_p). The systems are clear at low temperature and turbid at high temperature. Microscopic observation shows that small particles appear above the T_p. The transition is often called as coil-globule transition. On molecular level, this phenomenon is related to temperature-dependent changes in the hydration and conformation of the polymer chains. They are hydrated and extended below the T_p and dehydrated and collapsed above T_p. Figure 1 shows structures of typical thermosensitive polymers. They are derivatives of poly(meth)acrylamides, poly(meth)acrylates,[1] and poly(vinyl ether)s.[2] Poly(*N*-isopropylacrylamide) as the most famous thermosensitive polymer has both polar amide group and apolar alkyl groups. The amide groups can form hydrogen bonds with water, and the alkyl groups are unfavorably hydrated through hydrophobic hydration. The balance between hydrophilicity and hydrophobicity is important for the phase transition. Therefore, the value of T_p can be controlled in a wide range by changing the hydrophobicity of the side groups.

There are many kinds of methods such as calorimetry,[3] NMR,[4] fluorescence,[5] light scattering,[6] neutron scattering,[7] Raman spectroscopy,[8] and EPR[9] to study the phenomenon. IR spectroscopy is especially useful to investigate hydration of polymer chains because it is related to molecular vibration, which is sensitive to interaction between molecules. Moreover, IR spectroscopy has extremely high time resolution, because frequencies of molecular vibrations are very high. For example, period of O−H stretching vibration is 10 fs. It is shorter than typical lifetime of H-bonds. We therefore can observe two separate IR bands for free and H-bonding species. This is a reason why IR spectro-

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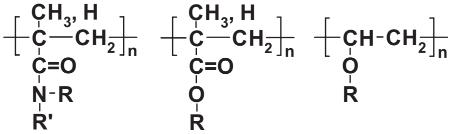

Figure 1.
Structures of typical thermosensitive polymers.

scopy is useful to analyze hydration of molecules.

Methods

IR spectra were measured at a resolution of 2 cm^{-1} by using a Fourier-transform infrared spectrometer (FTS-3000, Digilabo or FTIR-8400, Shimadzu) equipped with a deuterated triglycine sulfate detector. Each polymer solution was placed between two CaF_2 windows directly ($>$ 50 wt%) or with a 10 μm thick spacer ($\leq$ 50 wt%) and its temperature was controlled by using a circulating water bath. IR spectra of the solution were continuously collected (ca. 1 spectrum/min) at different temperatures at a heating or a cooling rate of 0.5 °C/min. DSC measurements were performed using a Micro Calorimetry System (MicroCal Inc.) at a scanning rate of 0.75 °C/min.

Results and Discussion

Phase Transitions of Aqueous Solutions of poly(*N*-substituted (meth)acrylamide)s

Figure 2a shows IR absorption spectra of PNiPAm measured in D_2O at 25 and 40 °C.[10] To enhance spectral changes occurring upon the phase transition, IR difference spectrum of the two spectra are also shown. Important IR bands are C–H stretching (ν(C–H)), amide I, and amide II bands. The ν(C–H) are observed in the region of 2900 – 3000 cm^{-1}. The amide I band contains contribution from the C=O stretching vibration and appears around 1625 cm^{-1}. The amide II band contains contribution from C–N–D deformation and appears around 1480 cm^{-1} in D_2O. The difference spectrum clearly shows that the ν(C–H), δ(C–H), and amide II band exhibit red shifts and the amide I band exhibit a blue shift on the phase transition. To follow the progress of the phase transition we defined the value of $\Delta\Delta A$ with, $\Delta\Delta A = \Delta A_{pos} - \Delta A_{neg}$, where ΔA_{pos} and ΔA_{neg} indicate differential absorbance at a positive and a negative peak, respectively. The value of $\Delta\Delta A$ for the amide I, amide II, ν(C–H) and δ(C–H) modes are plotted against temperature (Figure 2c). The onset temperatures of these curves are

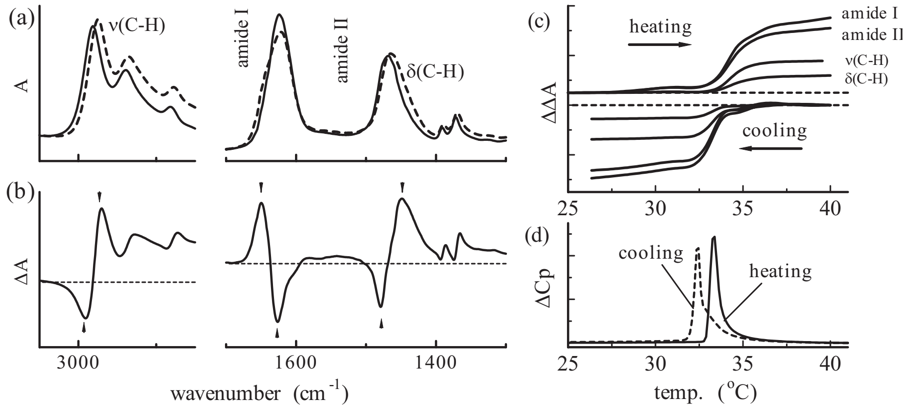

Figure 2.
(a) IR spectra of PNiPAm in D_2O at 25 (solid) and 40 (broken) °C (b) The difference spectrum between the two spectra. (c) The values of $\Delta\Delta A$ of the vibration modes of PNiPAm are plotted against temperature. (d) DSC thermograms of PNiPAm (0.5 wt%) measured in the heating (solid line) and cooling (broken line) processes.

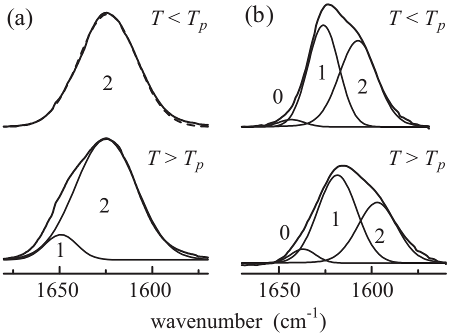

Figure 3.
The amide I band of (a) PNiPAm and (b) PdEA measured below and above T_p.

close to cloud point and the temperature at the endothermic peak in DSC thermogram (Figure 2d). Moreover, the transition temperature range at cooling is slightly lower than that at heating, meaning an existence of a hysteresis. It is known that the hysteresis depends on the tacticity of polymers.[11]

Figure 3a shows the amide I band of PNiPAm measured at different temperatures. The band measured below T_p can be fitted with single component centered at 1625 cm^{-1}. A new component appears at 1650 cm^{-1} above T_p. The amide I bands of poly(*N*-n-propyl acrylamide) and poly(*N*-cyclopropyl acrylamide) also exhibit a similar change during the phase transitions.[12] To assign these components, we underwent vibrational analyses of model compounds using a density functional theory. The 1625-cm^{-1} component can be assigned to H-bonding carbonyl groups to two water molecules (C=O…2HOH) and the 1650-cm^{-1} component is assigned to singly H-bonding carbonyl groups to another amide group or one water molecule (C=O…H−N or C=O…HOH). The amide I band of PdEA, which does not have hydrogen bond donor, contains three components both below and above T_p (Figure 3b).[13] They are assigned to the free and bonding carbonyl groups to one or two water molecules. Area of the two H-bonding species decreases and areas of zero and one H-bonding species increase during the transition.

Information concerning hydration of alkyl groups can be obtained from the ν(C−H) region. These bands exhibit red shifts on the phase separation and an increase in polymer concentration. Figure 4 show dependences of the ν(C−H) wavenumbers of poly(*N*-ethoxyethyacrylamide) (PEoEA) on temperature and polymer concentration.[14] They critically start to decrease at T_p of 36 °C at heating and decrease with increasing polymer concentration with a bending point at $W_p \approx 0.5$ (Figure 4d), which may correspond to hydration number (7 water molecules/monomer unit). Because the

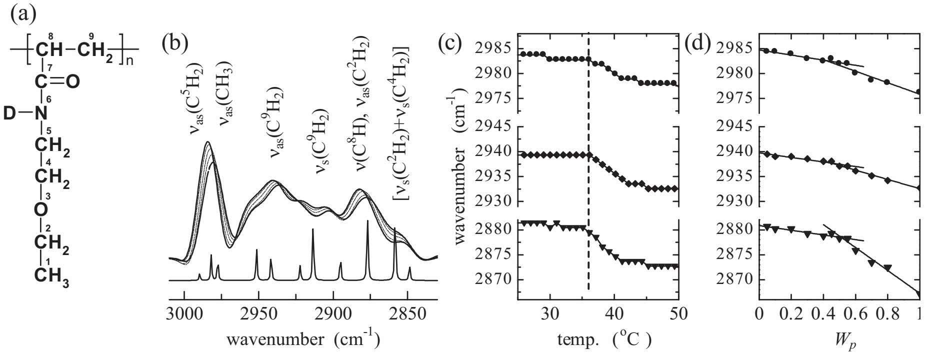

Figure 4.
(a) The structure and (b) the ν(C−H) spectra of PEoEA measured at different temperatures. The ν(C−H) frequencies are plotted against (c) temperature and (d) polymer concentration.

number of water molecules per one monomer unit is smaller than the hydration number at $W_p > 0.5$, they directly associate the polymer chain and the effect on the ν(C–H) frequencies is significant. At $W_p < 0.5$, additional water molecules exist as bulk water and have a smaller effect. Moreover, the amplitudes of total shifts are different from one peak to another. The 2880-cm^{-1} band due to the methylene groups nearby ether oxygen exhibits the largest shift. Interaction between the alkyl groups and water can be divided into two. A direct interaction between the C–H group and water results in a decrease in the C–H bond length and a blue shift of the ν(C–H) bands.[15] H-bonding to neighboring hydrophilic sites, especially to ether oxygen, also affects the frequency of the ν(C–H) bands. This is related to hyperconjugation between lone pair electron of the ether oxygen and antibonding π^* orbital of the C–H bond. H-bonding to the oxygen reduces the lone pair electron density and the extent of the hyperconjugation, which raises the strength of the C–H bond and the of the ν(C–H) frequencies. In practice, DFT calculation shows that H-bonding to the ether oxygen result in a relatively large blue shift of the ν(C–H) bands of the neighboring alkyl groups.

Effects of Additives on Phase Behavior

Effects of additives such as salts and organic cosolvents on the phase behaviors are also interesting. Polymer-additive and water-additive interactions exist as well as polymer-water interaction in these three components systems. IR spectroscopy is useful to determine which interaction is important for the behavior. The effect of salts is simple. The values of T_p linearly decrease with an increase of the salt concentration. T_p linearly decreases also with an increase in ΔB of the anions which is an indicator of strength of salt-water interaction (Figure 5a). Moreover, the profiles of IR spectra measured in the absence and presence of these salts are the same in spite of deference in T_p. These results suggest that direct interaction between polymer and ions is not important. It is probable that strong interaction between water and ions induces dehydration of polymer chain and decreases of T_p. However, we can observe polymer-ion interactions in the cases of organic ions such as tetraalkylammonium halides, which raise T_p.[16]

The effects of organic solvents such as alcohols are diverse. Winnik et al. found that T_p of PNiPAm once decreased to minima and then increased with increasing

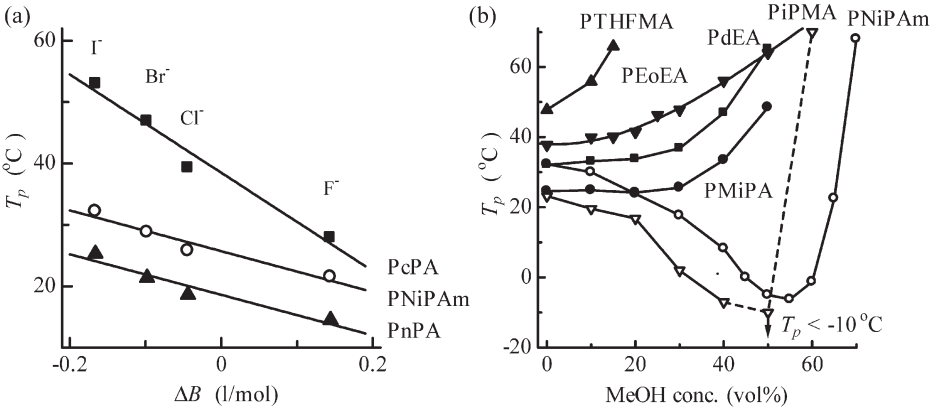

Figure 5.
(a) T_p of PnPA (▲), PNiPAm (•) and PcPA (■) in aqueous KF, KCl, KBr and KI solutions (0.5 mol/l-solv.) is plotted against ΔB of anions. (b) MeOH concentration dependence of T_p of PNiPAm (○), PiPMA (▽), PdEA (■), PMiPA (•), PEoEA (▼), and PTHFMA (▲) in MeOH/H_2O mixtures.

concentration of methanol.[17] This phenomenon is called as cononsolvency or reentrant phase separation. Other poly(mono-alkyl acrylamide)s also exhibit similar behaviors, whereas T_p of di-alkyl polymers such as PdEA and poly(*N*-methyl-*N*-isopropylacrylamide) (PMiPA) monotonically increases with increasing concentration of methanol (Figure 5b). On the other side, both poly(mono- and di- alkoxy acrylamide)s such as PEoPA and poly(*N*-tetrahydrofurfurylmethacrylamide) (PTHFMA) do not exhibit the cononsolvency. Hydrophobicity of alcohols is also important. Poly(*N*,*N*-dialkylacrylamide)s exhibit cononsolvency in propanol/water. In a similar way, poly(mono- and di- alkoxy acrylamide)s exhibit the cononsolvency in propanol/water.

In these systems, polymer-alcohol interactions exist as well as polymer-water and water-alcohol interactions. IR spectroscopy provides important information to answer which interaction is more important. Figure 6 shows profiles of the amide I bands of PNiPAm, PdEA, and PTHFMA [18] in methanol/water mixtures of different composition. The bands consist of three components due to the carbonyl groups forming two, one, and zero H-bonds. By using a curve fitting method we can estimate relative intensities of these components. Figure 6d shows MeOH concentration dependence of the relative intensities of the two, one and zero H-bonding carbonyl species of PTHFMA. The ratio of doubly H-bonding carbonyls decreases and those of singly and no H-binding carbonyls increase with increasing concentration of methanol. We can say that the average number of H-bonds to one carbonyl group decreased with increasing methanol concentration. The number of H-bonds of other polymers similarly decreases with methanol concentration despite of their different behaviors. This result shows that a qualitative change of the solvation to the amide carbonyls is the same in the three polymers. However, the number of H-bonds is the highest for PNiPAm among the three polymers. As for the amide II band of the polymer, it shifts toward lower wavenumbers with increasing methanol concentration indicating that the number of the H-bonds to the amide N-H also decreases.

The solvation of the alkyl groups also changes concomitantly. Figure 7 shows effect of methanol on the ν(C–H) frequencies of PTHFMA. The ν(C–H) bands gradually shift toward lower wavenumbers with increasing concentration of methanol indicating that interaction between the alkyl groups of the polymer and methanol exists. Propanol has a similar but slightly stronger effect than methanol. After all, the added alcohols interact with the polymers at both the amide and the alkyl groups. Because the amide-alcohol complexes are more hydrophobic than the amide-water complexes as a whole they destabilize the polymer in the solution and reduce T_p. The effect is significant for hydrophobic alcohols. The interaction between the alkyl

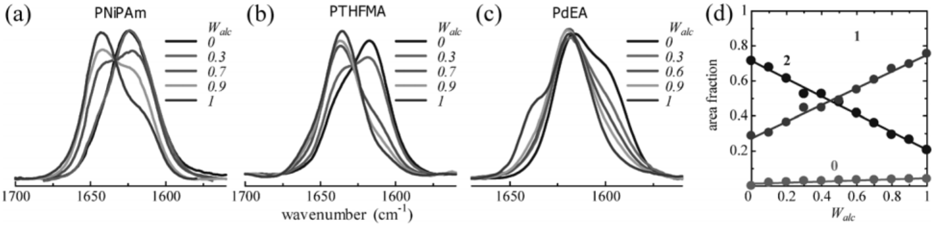

Figure 6.
The amide I bands of (a) PNiPAm, (b) PTHFMA, and (c) PdEA measured in methanol-d_4/ D_2O mixtures of different W_{alc} (weight fraction of methanol-d_4 in the solvents). (d) The dependences of the relative intensities of the two, one, and zero H-bonding carbonyl species of PTHFMA on W_{alc}.

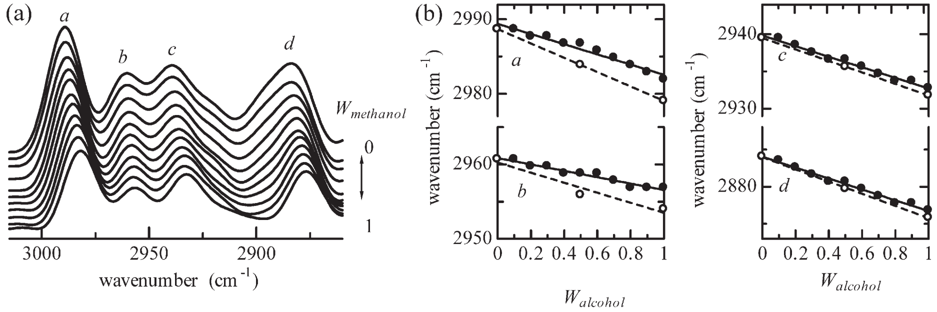

Figure 7.
(a) The ν(C–H) spectra of PTHFMA in MeOH-d_4/D_2O of different compositions (weight fraction of the alcohol; $W_{alc} = 0 - 1$) at 25 °C. (b) Wavenumbers of the peaks *a* - *d* measured in MeOH-d_4/D_2O (●) and 2PrOH-d_8/D_2O (○) at 25 °C are plotted against W_{alc}.

groups of the polymers and alcohols reduces unfavorable alkyl-water interaction and raises T_p. After all, the balance between the two opposite effects finally determines whether T_p will increase or decrease in alcohol/water mixtures at low alcohol contents.

Application of IR Spectroscopy to Thermosensitive Block Copolymers and Microgels

Many types of block copolymers and graft copolymers with thermosensitive units have been prepared up to now. They exhibit temperature-responsive micellization[19] and gelation and have been desired medical and industrial applications such as controlled drug delivery systems, nano containers and nano reactors. Especially, block copolymers consisting of a LCST block and a UCST block exhibit a unique behavior, that is, double temperature-responsiveness, in which they form reversible polymer micelles. For example, block copolymers of polysulfobetaine (poly(3-dimethyl-(methacryloyloxyethyl) ammonium propane sulfonate), PdMMAEAPS) and PdEA form PdMMAEAPS-core micelles below the UCST and PdEA-core micelles above the LCST (Figure 8).[20] The polymers exist as unimers at temperatures between the UCST and the LCST. Figure 8c shows IR spectra of the block copolymer. The ester band and ν(S=O) bands are specific to the PdMMAEAPS block and the amide I band is specific to the PdEA block. Figure 8e indicates that the PdMMAEAPS block solely changes on UCST transition and PdEA block solely change on LCST transition.

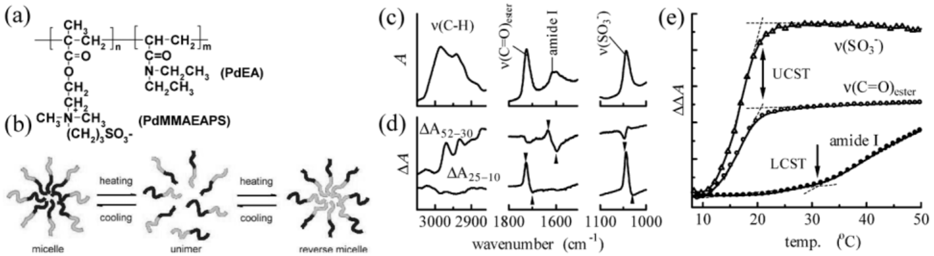

Figure 8.
(a) Structure of PdMMAEAPS-*b*-PdEA. (b) Schematic drawing of the micellization. (c) IR absorption spectrum and (d) difference spectra during the UCST (top) and LCST (bottom) transitions. (e) The values of ΔΔA for the $\nu(SO_3^-)$, $\nu(C{=}O)_{ester}$, and amide I modes are plotted against temperature.

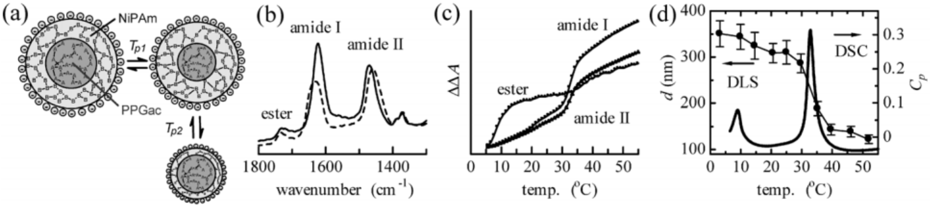

Figure 9.
(a) Schematic drawing of the two-step VPT of PPGac-core-NiPAm-shell microgel. (b) IR absorption spectra of the microgel. (c) Temperature dependences of the values of ΔΔA, (d) hydrodynamic diameter, and heat capacity of the microgel.

Thermosensitive gels expel water and reduce their sizes above the LCST of the corresponding linear polymers. The phenomenon is called volume phase transition (VPT) and has been attracted considerable attention because it can be applied to controlled capture or release of useful materials or wastes in water. Thermosensitive microgel particles with sizes of several hundred nm also exhibit the same behavior.[21] Many types microgels including fluorescent, core-shell, photo-responsive, oscillating microgels have been prepared and investigated up to now. Figure 9 shows structure and properties of double thermosensitive core-shell microgels. The core and shell consist of polypropyleneglycol methacrylate (PPGac) and NiPAm, respectively. The PPGac core has a specific IR absorption at ester carbonyl which exhibits critical change around 10 °C. The amide bands of the NiPAm shell exhibit a change around 30 °C. During the dehydration of the core and the shell, the diameter of the gels is reduced in two steps and two endothermic peaks are observed in DSC thermogram.

Conclusion

In the present study we have applied IR spectroscopy to investigate phase transitions of temperature-responsive polymeric systems including coil-globule transitions of linear polymers, micellizations of block copolymers, and volume phase transitions of microgels. IR spectroscopy was proved to be a quite useful method observing changes in the hydration states of individual chemical groups of the polymers. Molecular simulations based on quantum chemistry further enhance the usefulness of the methods by giving a molecular-level interpretation to the experimental results.

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