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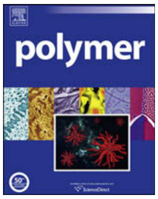

A unique phase behavior of random copolymer of *N*-isopropylacrylamide and *N*,*N*-diethylacrylamide in water

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ABSTRACT

Thermosensitive phase separation of aqueous solutions of the random copolymers of *N*-isopropylacrylamide (iPA) and *N*,*N*-diethylacrylamide (dEA) (PiPA–dEA) and of iPA and *N*-isopropylmethacrylamide(iPMA) (PiPA–iPMA) with different compositions has been investigated by using calorimetry, turbidimetry and infrared spectroscopy. Though the phase transition temperature (T_p) of PiPA–iPMA is a linear function of its composition, a deviation from additivity is observed for that of PiPA–dEA, that is, it has a minimum value at iPA/dEA = 1 (mol/mol). IR spectrum at the amide II mode of the copolymer suggests that part of N–H groups of iPA units form a hydrogen bond with C=O groups of dEA units at $T > T_p$ as well as with those of the iPA units. Effects of methanol on T_p of these copolymers have also been studied.

1. Introduction

Some poly(*N*-alkylacrylamide)s [1], poly(*N*,*N*-dialkylacrylamide)s [2], and poly(*N*-alkylmethacrylamide)s [3] possessing a proper hydrophilicity/hydrophobicity ratio exhibit thermosensitive phase separation above lower critical solution temperatures (LCST) in water. The macroscopic phase separation is accompanied by large changes in both hydration state and conformation of the polymer chains. That is, the alkyl groups are dehydrated on phase separation and an attractive interaction between polymer segments lead extended polymer chains to shrunk and globular conformation. The phenomenon has attracted a keen attention from both basic and technological points of view in the last two decades [4–7]. In particular, the phase transition of poly(*N*-isopropylacrylamide) (PiPA) in water has been extensively studied by using various methods (IR [8], Raman [9], NMR [10], and fluorescence [11] spectroscopy, calorimetry [12], light scattering [13], neutron scattering [14], and so on).

Incorporation of hydrophilic or hydrophobic units into a thermosensitive polymer by random copolymerization reduces or raises the LCST of the parent polymer, respectively. Recently importance of intramolecular hydrogen bonding between comonomer units on the LCST is also suggested [15]. Copolymers which respond to both temperature and other external stimuli such as pH [16] and light [17] have also been prepared by random copolymerization. Block copolymers consisting of thermosensitive and hydrophilic blocks [18,19] and those consist of two different thermosensitive blocks [20,21] form thermally reversible polymer micelles in an appropriate condition.

We are interested in the behaviors of random copolymers consisting of two different thermosensitive units. Differences in the phase behaviors of PiPA and poly(*N*,*N*-diethylacrylamide) (PdEA) aroused our interest. Though both PiPA and PdEA have LCST around 31 °C, their behaviors are different in some aspects [2]. For example, phase separation of PiPA is sharp as shown in DSC thermogram with a width of 1–2 °C [9,22], but that for PdEA is broad (width: ~20 °C) [2]. One of distinctive features of the phase transition of PiPA is co-nonsolvency or reentrant phase separation in methanol/water mixtures [23–25]. Its LCST in the mixtures passes through a minimum at around methanol concentration of 55 (v/v%). On the other hand, the increase of methanol content induces a monotonous increase in the LCST of PdEA. How are the phase behaviors of random copolymers of iPA and dEA? Can we describe them with a linear function of monomer composition of the copolymers? What is the main determinant for their behaviors? These queries are our motivation for the present study. We examined the phase behavior of PiPA–dEA by using IR spectroscopy, turbidimetry and calorimetry. For comparison we also investigated PiPA–iPMA. Distinct differences in the structures of dEA and iPMA as compared with iPA are the absence of the N–H groups as hydrogen bond donor and the presence of additional α-CH_3 groups, respectively. We will discuss about importance of hydrogen bonds between amide groups (N–H···O=C) on their behaviors.

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Table 1
Characteristics of the used polymers.

	x	M_w	M_w/M_n
PiPA	–	23,000	2.5
PdEA	–	31,000	2.6
PiPMA	–	25,000	3.0
$PiPA_{0.9}$–dEA	0.91	33,000	3.0
$PiPA_{0.8}$–dEA	0.82	29,000	2.6
$PiPA_{0.7}$–dEA	0.69	22,000	2.2
$PiPA_{0.6}$–dEA	0.62	25,000	2.8
$PiPA_{0.5}$–dEA	0.51	39,000	2.7
$PiPA_{0.4}$–dEA	0.40	26,000	2.6
$PiPA_{0.3}$–dEA	0.28	34,000	3.0
$PiPA_{0.2}$–dEA	0.21	43,000	3.1
$PiPA_{0.1}$–dEA	0.10	29,000	2.5
$PiPA_{0.9}$–iPMA	0.92	35,000	2.9
$PiPA_{0.7}$–iPMA	0.69	41,000	3.1
$PiPA_{0.5}$–iPMA	0.52	31,000	2.3
$PiPA_{0.3}$–iPMA	0.29	19,000	2.5
$PiPA_{0.1}$–iPMA	0.11	29,000	2.6

2. Experiments

2.1. Materials

N-isopropylacrylamide (iPA) and *N,N*-diethylacrylamide (dEA) were kindly donated by Kohjin (Tokyo, Japan). *N*-isopropylmethacrylamide was synthesized via coupling of methacryloyl chloride with isopropylamine in benzene and purified by recrystallization in benzene/hexane. Polymers were synthesized with radical polymerization in methanol at 70 °C for 7 h using 2,2′-azobis(isobutyronitrile) as an initiator (0.5 mol% to the monomers). Polymers obtained were purified by dialysis (Visking tube) for a week against water (changed three times a day) at temperatures below T_p and recovered by freeze-drying. Mole fractions of the iPA unit (x) in these copolymers were evaluated by using ^{1}H NMR (LA-500, JEOL). $PiPA_{0.5}$–dEA indicates PiPA–dEA copolymer with $x = 0.5$ in the fed monomers. The copolymer compositions of both PiPA–dEA and PiPA–iPMA were confirmed to be close to the feed compositions. The weight-average molecular weights (M_w) and polydispersity (M_w/M_n) estimated by size exclusion chromatography (column; Toso GMH_{HR}-M (30 cm), mobile phase; chloroform at 40 °C (0.5 ml min^{-1})) in poly(oxyethylene) standards were shown in Table 1.

2.2. Measurements

IR, DSC, and turbidity measurements were performed by using a FTS-3000 FTIR spectrometer (Varian), a Micro Calorimetry System (MicroCal Inc.), and a UV–vis spectrophotometer (UV200-100, Hitachi). Details of the measurements were described in our previous paper [1–3]. In brief, a polymer solution was placed between two CaF_2 windows with a spacer (10-μm thick) and IR spectra were collected at a resolution of 2 cm^{-1} during a continuous heating at a rate of 1 °C/min. DSC measurements were performed with 0.5 wt% polymer solutions at a scanning rate of 0.75 °C min.

2.3. Vibration analysis

Theoretical calculations based on density functional theory (DFT) were performed using Gaussian 98 at the B3LYP level with the 6-31G(d) basis set. The structures of dimer models of iPA–iPA and iPA–dEA units with racemo configuration were optimized and the vibrational frequencies and intensities were calculated.

3. Results

3.1. DSC measurements

First, we measured DSC thermograms of aqueous solutions of PiPA–dEA and PiPA–iPMA with various copolymer compositions (Fig. 1). The temperature at the maximum of an endothermic peak (T_p) is plotted against the mole fraction of the iPA units (x) (Fig. 2a). We also measured cloud point (T_{cp}) and conformed that T_{cp} of each solution is slightly lower than T_p. It is clear that T_{cp} and T_p of PiPA–dEA are not a linear function of x, but they have minimum values at $x = 0.5$, meaning that the copolymers have lower T_p than both of the homopolymers. On the other hand, T_p of PiPA–iPMA linearly decreases with x.

We can estimate the sharpness of the phase transition by the value of C_p(peak)/ΔH, where C_p(peak) and ΔH indicate heat capacity at maximum and heat of transition given by the area of the peak, respectively. The phase transition of PiPA–dEA became sharper with an increase of x, whereas that of PiPA–iPMA is almost independent of x as shown in Fig. 2b.

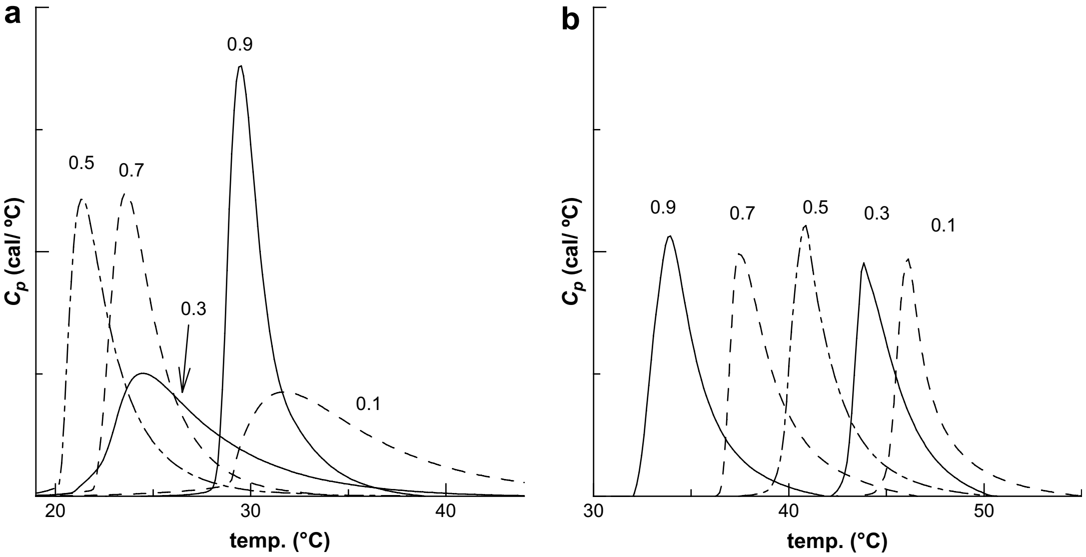

Fig. 1. DSC thermograms of (a) PiPA–dEA and (b) PiPA–iPMA (0.5 wt%) of various compositions. Inlet numbers indicate iPA mole fraction (x).

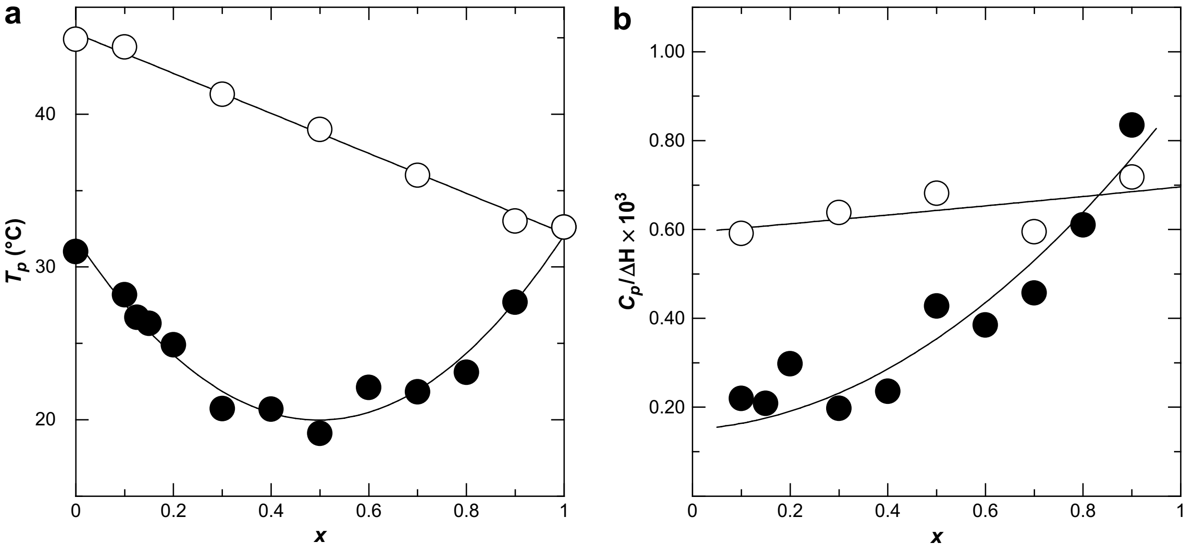

Fig. 2. The values of (a) T_p and (b) C_p(peak)/ΔH of PiPA–dEA (●, 0.5 wt%) and PiPA–iPMA (○, 0.5 wt%) measured in water are plotted against iPA mole fraction (x).

There is a possibility that the copolymers have composition distributions, that is, the copolymer composition is different from one chain to another. Though we could not estimate the distribution precisely, we can say that the composition of each polymer chain is important to the phenomenon from the following experiment. The equimolar mixture of PiPA and PdEA and the equimolar mixture of $PiPA_{0.2}$–dEA and $PiPA_{0.8}$–dEA, for example, have average values of $x = 0.5$ but did not have lower T_p than those of the parent polymers. This observation indicates that the important determinant is not the average composition but the composition of each polymer chain.

3.2. IR measurements

Fig. 3a shows IR absorbance spectra of PiPA, PdEA, and $PiPA_{0.5}$–dEA measured in H_2O and in D_2O at the temperatures below (solid lines) and above (broken lines) T_p of each solution. Fig. 3b shows IR difference spectra of these polymers resulted from a subtraction of a spectrum measured below T_p from that measured above T_p. Prominent IR bands of these polymers are the C–H stretching bands, the amide I and II bands, and the C–H bending (δ(C–H)) bands.

We recognize hydrogen bonding of the amide C=O groups from the positions of the amide I bands. We analyzed the bands in D_2O instead of H_2O because the O–H bending band of H_2O overlaps them. As shown in our previous paper [8], the amide I band of PiPA homopolymer consists of two components centered at 1625 cm^{-1} and 1650 cm^{-1}, which can be assigned to the C=O groups bound to water and those bound to the amide N–H group through a hydrogen bond (C=O···H–O and C=O···H–N), respectively. The 1650-cm^{-1} band appears only above T_p, meaning that part of the amide groups form the intramolecular hydrogen bonds in the globule state of PiPA. On the other hand, the amide I band of PdEA consists of three components centered at 1638 cm^{-1}, 1619 cm^{-1} and 1599 cm^{-1}, which can be assigned to the C=O groups that associate with 0, 1, and 2 water molecules through hydrogen bonds, respectively [2]. The profiles of the amide I band of $PiPA_{0.5}$–dEA are close to those obtained by summing up the bands for PiPA and PdEA.

The amide II band of PiPA shows a deuterium isotope shift and appears at 1561 cm^{-1} and 1470 cm^{-1} (referred to as amide II′ band) in H_2O and D_2O, respectively, because the band contains contribution from the bending vibration of the N–H (N–D in D_2O) groups. The 1561-cm^{-1} band observed in H_2O is used to analyze hydrogen bonding of the N–H groups of the iPA units because the amide II′ band overlaps with the δ(C–H) bands of the polymer. The

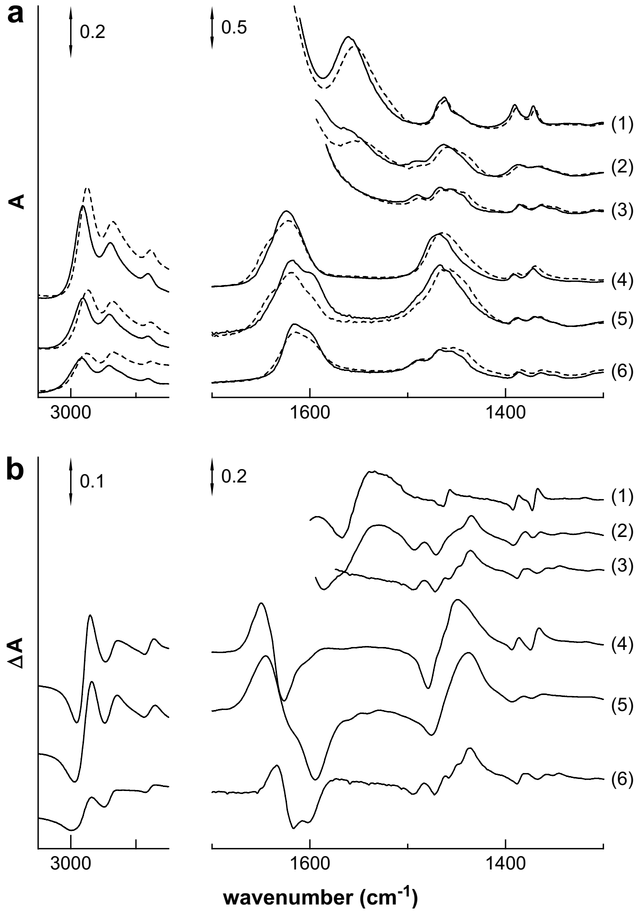

Fig. 3. (a) IR absorption and (b) difference spectra of (1) PiPA, (2) $PiPA_{0.5}$–dEA and (3) PdEA in H_2O and (4) PiPA, (5) $PiPA_{0.5}$–dEA and (6) PdEA in D_2O. Solid and broken lines in (a) indicate spectra measured below and above T_p, respectively.

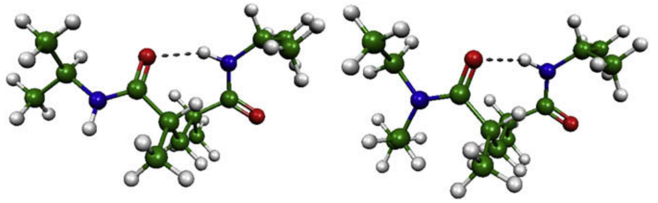

Fig. 4. The optimized structures of dimer models of iPA–iPA (left) and iPA–dEA (right) of a racemo configuration. Broken lines indicate the N–H···O=C hydrogen bonding.

amide II band for PiPA homopolymer consists of two components centered at 1559 cm^{-1} and 1535 cm^{-1}, which can be assigned to the N–H···OH$_2$ and N–H···O=C hydrogen bonds, respectively [8]. The amide II band of PiPA$_{0.5}$–dEA appears at a slightly lower wave number as compared with that of PiPA homopolymer at $T > T_p$, suggesting that another type of hydrogen bond exists in the N–H groups of the copolymer with shrunk conformation.

We performed DFT calculation using iPA–iPA and iPA–dEA dimmer models in racemo configuration (Fig. 4) to estimate the frequency of the amide II mode of the iPA unit. The frequency of the amide II mode is 1561 and 1557 cm^{-1} for N–H(iPA)···O=C(iPA) and N–H(iPA)···O=C(dEA), respectively. Therefore, the lower-wave number component expected in the amide II band of PiPA$_{0.5}$–dEA can be assigned to the N–H(iPA)···O=C(dEA) hydrogen bond. It means that the N–H group of the iPA unit associates with the C=O group of both iPA and dEA units in its globular conformation.

3.3. Effects of methanol on phase separation temperature

Next, we investigated effects of methanol on phase transition of PiPA–dEA and PiPA–iPMA in aqueous solutions. Endothermic peak in the DSC thermograms of these copolymers became smaller with increasing concentration of MeOH and were too small to determine T_p at MeOH concentrations above 40 v/v%. However, turbidity of the solutions critically changes at T_{cp} even at high MeOH concentrations. Fig. 5a and b show the values of T_{cp} of PiPA–dEA and PiPA–iPMA plotted against methanol concentration. T_{cp} of both PiPA and PiPMA homopolymers once decreases to the minima and then increases with increasing concentration of methanol. It is known that poly(*N*-n-propylacrylamide) and poly(*N*-n-propylmethacrylamide) also exhibit such reentrant phase behavior. On the other hand, T_p of PdEA monotonously increases. Poly(*N*-methyl-*N*-isopropylacrylamide) also shows a similar behavior.

As for the copolymers, T_{cp} of PiPA–dEA at $x < 0.2$ is almost independent of methanol concentration up to 30%. T_{cp} of PiPA–dEA with high iPA contents decreases with methanol concentration up to 30%. Because T_{cp} of both of the parent polymers (PiPA and PiPMA) decreases with increasing concentration of methanol up to 40%, T_{cp} of each PiPA–iPMA copolymer also decreases with increasing concentration of methanol. Moreover, the higher the iPMA contents in PiPA–iPMA, the higher the value of T_{cp} at the same methanol concentration.

4. Discussion

We set up a simple model for the phase separation to explain the dependence of T_p of the copolymers on monomer composition. To the Gibbs free energy of mixing (ΔG) of aqueous PiPA solution we assume contribution of the C=O···H–N hydrogen bonding between amide groups. ΔG for PiPA solution is, therefore,

$$\Delta G(\text{PiPA}) = \Delta G_{\text{H-b}}(\text{iPA—iPA}) + \Delta G_{\text{other}}(\text{iPA}) \tag{1}$$

where $\Delta G_{\text{other}}(\text{iPA})$ contains any other contributions concerning such as polymer–water, water–water, and polymer–polymer interactions except for the hydrogen bonding. The solution exhibits phase separation at $\Delta G(\text{PiPA}) > 0$. Because PdEA does not form intermolecular hydrogen bond, ΔG for PdEA solution is

$$\Delta G(\text{PdEA}) = \Delta G_{\text{other}}(\text{dEA}) \tag{2}$$

In the copolymers of iPA and dEA, the N–H groups of the iPA units can form hydrogen bond with the C=O groups of both iPA and dEA units. For the copolymer with iPA fraction of x, the probabilities of iPA–iPA and iPA–dEA diads are x^2 and $2x(1-x)$, respectively. Therefore, we write

$$\begin{aligned}\Delta G(\text{PiPA—dEA}) = {}& x\Delta G_{\text{other}}(\text{iPA}) + (1-x)\Delta G_{\text{other}}(\text{dEA}) \\ & + x^2\Delta G_{\text{H-b}}(\text{iPA—iPA}) \\ & + 2x(1-x)\Delta G_{\text{H-b}}(\text{iPA—dEA})\end{aligned} \tag{3}$$

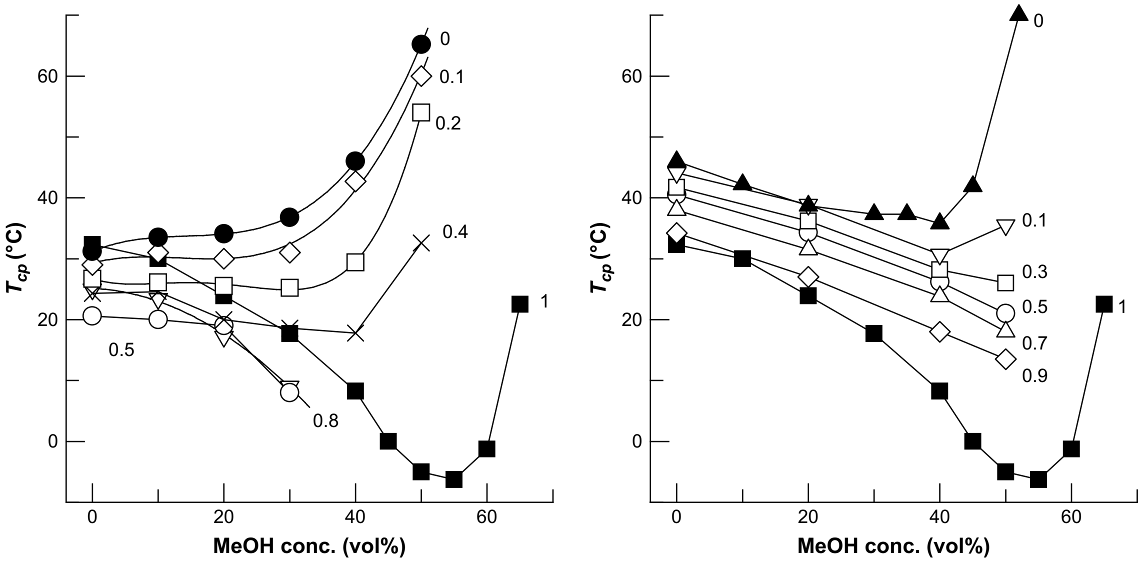

Fig. 5. The values of T_{cp} of PiPA–dEA and PiPA–iPMA (0.5 wt%) with different monomer composition (x) measured in methanol/water mixtures are plotted against methanol concentration.

Because the DFT calculation indicates that the energy for the C=O···H–N hydrogen bonding of the iPA–dEA diad is close to that of the iPA–iPA diad, we can assume $\Delta G_{\text{H-b}}(\text{iPA–iPA}) = \Delta G_{\text{H-b}}(\text{iPA–dEA})$ $(\equiv \Delta G_{\text{H-b}})$. Then ΔG for the copolymer is written as

$$\Delta G(\text{PiPA—dEA}) = x\Delta G_{\text{other}}(\text{iPA}) + (1-x)\Delta G_{\text{other}}(\text{dEA}) + \left(2x - x^2\right)\Delta G_{\text{H-b}} \tag{4}$$

Differentiation of Eq. (4) with respect to x gives

$$\mathrm{d}\Delta G(\text{PiPA–dEA})/\mathrm{d}x = \Delta G_{\text{other}}(\text{iPA}) - \Delta G_{\text{other}}(\text{dEA}) - 2(1-x)\Delta G_{\text{H-b}} \tag{5}$$

Therefore, T_p is a quadratic function of x and has minimum value at $x = (\Delta G_{\text{other}}(\text{iPA}) - \Delta G_{\text{other}}(\text{dEA}) + 2\Delta G_{\text{H-b}})/2\Delta G_{\text{H-b}}$. Because PiPA and PdEA have almost the same T_p (31 °C), at the temperature

$$\Delta G_{\text{other}}(\text{iPA}) + \Delta G_{\text{H-b}} = \Delta G_{\text{other}}(\text{dEA}) \tag{6}$$

We conclude that T_p has minimum value at $x = 1/2$.

As for the copolymers of iPA and iPMA, the iPMA units act as a proton donor as well as the iPA units. If we assume that $\Delta G_{\text{H-b}}(\text{iPA–iPA}) = \Delta G_{\text{H-b}}(\text{iPA–iPMA}) = \Delta G_{\text{H-b}}(\text{iPMA–iPMA})$ $(\equiv \Delta G_{\text{H-b}})$, ΔG for the copolymer is written as

$$\Delta G = x\Delta G_{\text{other}}(\text{iPA}) + (1-x)\Delta G_{\text{other}}(\text{iPMA}) + \Delta G_{\text{H-b}} \tag{7}$$

Because transition temperature of PiPMA is higher than that of PiPA, $\Delta G_{\text{other}}(\text{iPA}) > \Delta G_{\text{other}}(\text{iPMA})$. Therefore, T_p linearly decreases with an increase of x. This simple mathematical model can explain the dependence of T_p on x.

Sharpness of the phase transition may also closely relate to the formation of the intrachain hydrogen bonds. PiPA and PiPMA homopolymers and PiPA–iPMA have the N–H groups as hydrogen donors and exhibit sharp transitions. Intrachain hydrogen bonds may have so-called zipper effects and enhance cooperativity of the conformational changes in the polymer chains. On the other hand, because PdEA have no hydrogen donors, such effects cannot be expected. Therefore, the phase transition of PiPA–dEA becomes narrower with an increase in the iPA content.

The existence of the N–H groups may also have a great importance on methanol concentration dependence of T_p. T_p of PiPA and PiPMA homopolymers and PiPA–iPMA copolymers once decreases with increasing concentration of methanol, whereas that of PdEA homopolymer continuously increases. The N–H groups of iPA and iPMA can form hydrogen bond with both water and methanol as solvents as well as the C=O groups. Replacement of water molecules bound to the C=O and the N–H groups by methanol molecules may destabilize the polymer and reduce T_p in water-rich media. On the other hand, replacement of water molecules surrounding hydrophobic alkyl groups of the polymers by methanol molecules may stabilize the polymer and raise T_p. Balance between the opposite effects finally determines whether the value of T_p increases or decreases.

In conclusion, the two types of random copolymers, PiPA–dEA and PiPA–iPMA, exhibit quite different phase behaviors in water. (1) Though T_p of PiPA–iPMA is a linear function of its composition, that of PiPA–dEA has a minimum value at iPA/dEA = 1. (2) Though the sharpness of the phase transition of PiPA–iPMA is almost independent of the composition, the phase transition of PiPA–dEA becomes broad with increasing contents of the dEA units. (3) Though PiPA–iPMA at any composition exhibits the reentrant phase behavior in methanol/water mixtures, the behavior of PiPA–dEA changes from a reentrant one to a monotonous one with increasing contents of the dEA units. The presence or absence of the amide N–H groups is suggested to be important in these differences. However, further theoretical study is necessary to know the precise mechanism of the phenomena.

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References

[1] Maeda Y, Nakamura T, Ikeda I. Macromolecules 2001;34:1391.
[2] Maeda Y, Nakamura T, Ikeda I. Macromolecules 2002;35:10172.
[3] Maeda Y, Nakamura T, Ikeda I. Macromolecules 2001;34:8246.
[4] Hoare TR, Kohane DS. Polymer 2008;49:1993.
[5] You YZ, Kalebaila KK, Brock SL, Oupický D. Chem Mater 2008;20:3354.
[6] Castellanos A, DuPont SJ, Heim II AJ, Matthews G, Stroot PG, Moreno W, et al. Langmuir 2007;23:6391.
[7] Rzaev ZMO, Dincer S, Pis-kin E. Prog Polym Sci 2007;32:534.
[8] Maeda Y, Higuchi T, Ikeda I. Langmuir 2000;16:7503.
[9] Maeda Y, Yamamoto H, Ikeda I. Macromolecules 2003;35:5055.
[10] Starovoytova L, Spěváček J. Polymer 2006;47:7329.
[11] Shirota H, Kuwabara N, Ohkawa K, Horie K. Macromolecules 1999;103:10400.
[12] Tiktopulo EI, Uversky VN, Lushchik VB, Klenin SI, Bychkova VE, Ptitsyn OB. Macromolecules 1995;28:7519.
[13] Wang X, Qiu X, Wu C. Macromolecules 1998;31:2972.
[14] Lee LT, Cabane B. Macromolecules 1997;30:6559.
[15] Francis R, Jijil CP, Prabhu CA, Suresh CH. Polymer 2007;48:6707.
[16] Maeda Y, Yamamoto H, Ikeda I. Langmuir 2001;17:6855.
[17] Sumaru K, Kameda M, Kanamori T, Shinbo T. Macromolecules 2004;37:4949.
[18] Topp MDC, Leunen IH, Dijkstra PJ, Tauer K, Schellenberg C, Feijen J. Macromolecules 2000;33:4986.
[19] Maeda Y, Taniguchi N, Ikeda I. Macromol Rapid Commun 2001;22:1390.
[20] Arotçaréna M, Heise B, Ishaya S, Laschewsky A. J Am Chem Soc 2002;124:3787.
[21] Maeda Y, Mochiduki H, Ikeda I. Macromol. Rapid Commun 2004;25:1330.
[22] Okada Y, Tanaka F. Macromolecules 2005;38:4465.
[23] Winnik FM, Ringsdorf H, Venzmer J. Macromolecules 1990;23:2415.
[24] Schild HG, Muthkumar M, Tirrell DA. Macromolecules 1991;24:948.
[25] Tao CT, Young TH. Polymer 2005;46:10077.