Thermosensitive Reentrant Swelling Behavior of *N*-(Alkoxyalkyl)acrylamide Gels in Water

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ABSTRACT: The swelling equilibria of four different *N*-(alkoxyalkyl)acrylamide gels in water were measured at various temperatures. The *N*-3-(methoxypropyl)acrylamide (NMPA) gel hardly changed its volume upon heating. Three gels (*N*-(2-ethoxyethyl)acrylamide (NEEA), *N*-(3-ethoxypropyl)acrylamide (NEPA), and *N*-(tetrahydrofurfuryl)acrylamide (NTFA) gels) exhibited reentrant type swelling curves of a swollen–shrunken–swollen cycle in water in response to a change in temperature. The gradual shrinking of the NEEA, NEPA, and NTFA gels upon heating within the temperature range 25–35 °C was considered to be due to the weak hydrophobic interaction based on the alkoxyalkyl groups, while the subsequent swelling at higher temperatures was due to the thermal mixing which dominated the hydrophobic interaction. These discussions were supported by preliminary calculations introducing the temperature dependence of hydrophobic interaction into the ΔF term of Tanaka's equation.

I. Introduction

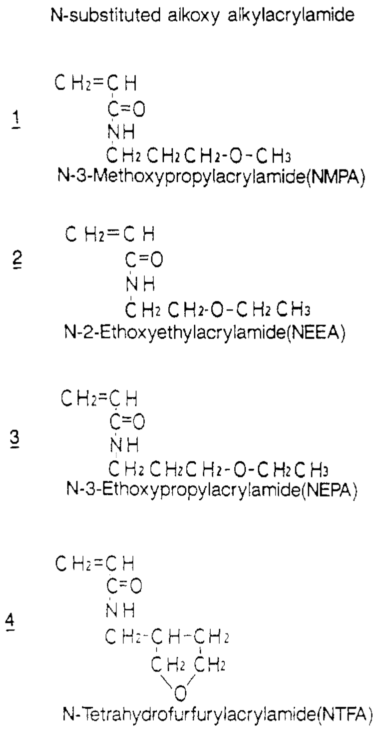
Hydrogels sometimes undergo reversible, discontinuous large volume changes in response to a continuous change in environmental conditions such as solvent composition, pH, ionic composition, and temperature.[1-3] This kind of phase transition has been observed universally in various natural and synthetic gels. *N*-isopropylacrylamide (abbreviated as NIPA) gel has been known to exhibit a collapse transition in water at about 34 °C, in response to an increase in temperature.[4,5] This temperature-induced collapse (so-called "thermoshrinking") transition could be observed for the hydrogels containing hydrophobic groups. Recently, many researchers have produced a variety of experimental results demonstrating that in the thermoshrinking type of transition, hydrophobic interaction plays an important role.[5-7]

In light of these findings, hydrogels whose monomers contain hydrophobic groups can be expected to undergo a thermoshrinking phase transition in water. A previous communication revealed that a gel of *N*-cyclopropylacrylamide (NCPA) showed a continuous thermoshrinking type swelling curve and an *N*-*n*-propylacrylamide (NNPA) gel exhibited a volume phase transition at 24 °C, 10 K lower than that of the NIPA gel.[8] These swelling behaviors result from the difference in the strength of the hydrophobic interaction acting in NIPA, NNPA, and NCPA gels, in short, the difference in the N substituent groups. The previous results thus indicated the importance of hydrophobic interaction in thermoshrinking swelling behavior. However, the magnitude of hydrophobic interaction of the N substituent depends on various factors and its relationship with the swelling behavior of a gel has yet to be elucidated.

The present paper substantiates the major points of the discussion above. We prepared four different *N*-(alkoxyalkyl)acrylamide gels and investigated the relationship between the swelling behaviors and the monomer structures of these gels. As for aqueous solutions of poly[*N*-(alkoxyalkyl)acrylamide], their cloud point temperatures were recently reported by Ito.[9] However, the swelling behavior of these gels has not been reported.

II. Experiment

Preparation of Samples. Monomers of *N*-(3-methoxypropyl)acrylamide (NMPA, 1), *N*-(2-ethoxyethyl)acrylamide (NEEA, 2), *N*-(3-ethoxypropyl)acrylamide (NEPA, 3), and *N*-(tetrahydrofurfuryl)acrylamide (NTFA, 4) were prepared from the corresponding amines and acryloyl chlorides via the following reaction, in accordance with Ito:[9]



$$CH_2{=}CHCOCl + NH_2R + (C_2H_5)_3N \xrightarrow{0-10\,°C} CH_2{=}CHCONH{-}R + (C_2H_5)_3NHCl$$

reaction solvent: toluene

R: alkoxyalkyl group

The synthesized monomers were purified via vacuum distillation under a nitrogen atmosphere. The boiling points of the monomers were as follows:

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NMPA: 98 °C/2 mmHg

NEEA: 85 °C/1 mmHg

NEPA: 85 °C/1 mmHg

NTFA: 115 °C/1 mmHg

The identification of monomers was performed via ^{1}H NMR (240 MHz, $CDCl_3$).

Gel samples were prepared via radical polymerization in water at 0 °C. The reagents (*N,N'*-methylenebis[acrylamide] (BIS); cross-linker; and *N,N,N',N'*-tetramethylethylenediamine (TEMED); accelerator) were all special grade products made by Tokyo Kasei Kogyo Co., Ltd. They were used without further purification. Potassium persulfate (KPS) was used as an initiator after recrystallization from an aqueous solution.

Monomers composed of the main constituent of the gels (NMPA, NEEA, NEPA, NTFA) were dissolved along with BIS in distilled and degassed water. KPS was dissolved in a separate container of distilled and degassed water. The two solutions were then cooled to 0 °C and mixed. The accelerator (TEMED) was then added to the mixture. The concentrations of monomer, BIS, KPS, and TEMED were adjusted to about 700, 7, 30, and 0.012 mM, respectively. This pregel solution was transferred into a vial containing glass tubes with an inner diameter of 1.65 mm. After the gelation was completed (elapsed time over 1 h), gels of 1.65 mm in diameter were taken out of the tubes and immersed in an excess amount of water. This was to wash away any residual chemicals. The process took about a few days. These gels were then cut into 1.6–1.7-mm length rods.

Swelling Equilibrium Measurements. The gel rods were immersed in an excess amount of pure water until swelling equilibrium was attained. The diameter of the gels, d, was measured via calibrated scale photography. The swelling ratios of the gels were calculated from the ratio of the equilibrium gel diameter to the diameter at preparation d_0, as follows:

$$\text{swelling ratio } V/V_0 = (d/d_0)^3 \qquad (1)$$

where d_0 is 1.65 mm.

III. Experimental Results

Figure 1 shows the temperature dependence of the equilibrium swelling ratios of the four gels (NMPA, NEEA, NEPA, and NTFA). The swelling of the gels in water is strongly dependent on the structure of the monomer comprising the gels. All four of these gels underwent continuous volume change within the temperature range studied.

The volume of the NMPA gel did not change significantly within the temperature range studied. It is known that alkoxy groups have a hydrophilic property due to their oxygen atom possessing an electron lone pair. For this reason, they form hydrogen bonds with water molecules. This might be the reason why the NMPA gel swelled in water even at higher temperatures. The NEEA, NEPA, and NTFA gels all initially decreased in volume and then swelled with an increase in temperature. In other words, these gels exhibited a reentrant type swelling behavior of a swollen–shrunken–swollen cycle in water in response to a change in temperature. To our knowledge, there has been no nonionic gel reported to have undergone thermosensitive reentrant type swelling in water. One explanation why the NEEA, NEPA, and NTFA gels undergo reentrant type swelling in water is this: since the ethoxy and tetrahydrofurfuryl groups are less hydrophilic than the methoxy group, the hydrophobic and hydrophilic properties of these three gels may be comparable. For this reason, water behaves as a good or poor solvent for these hydrogels dependent upon temperature. Consequently, the NEEA, NEPA and NTFA gels collapsed with an increase in temperature, due to hydrophobic interaction in the temperature range 25–35 °C. Moreover, further increases in temperature make the gels swell in water due to thermal mixing.

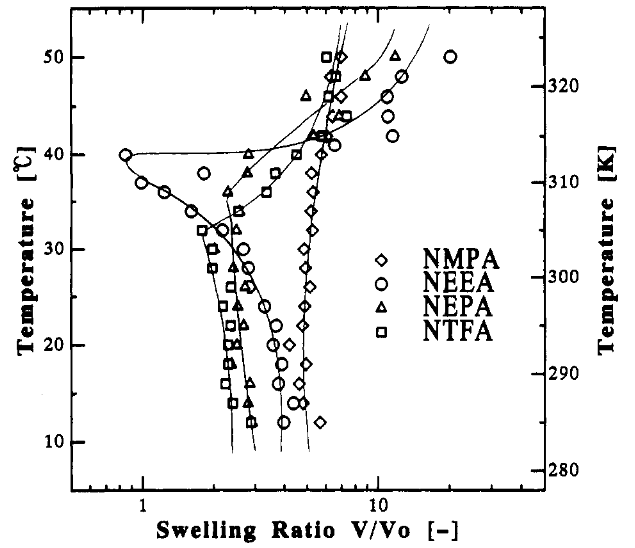

Figure 1. Swelling equilibria of *N*-(alkoxyalkyl)acrylamide gels: (△) *N*-(3-methoxypropyl)acrylamide (NMPA) gel; (□) *N*-(2-ethoxyethyl)acrylamide (NEEA) gel; (◇) *N*-(3-ethoxypropyl)acrylamide (NEPA) gel; (○) *N*-(tetrahydrofurfuryl)acrylamide (NTFA) gel.

For aqueous solutions of poly[*N*-(alkoxyalkyl)acrylamide] showing a LCST type of phase separation, Ito reported their cloud point temperatures.[9] In the report, Ito pointed out that the cloud point temperature was strongly dependent on the alkyl chain length of the alkoxyalkyl group, in other words, the hydrophobicity of the alkoxyalkyl group. In the present study, the volume phase transition of the gel was not observed. Therefore, we could not directly compare our results with those obtained by Ito. However, both results seem to suggest that hydrophobicity of the N substituent group plays an important role in shrinking behavior. Recently, Ito and Yada[10] suggested that the cloud point of poly-NTFA aqueous solutions depended on its molecular weight while that of poly(*N*-alkylacrylamide) (e.g. NIPA) was not affected. Considering this suggestion, it could be inferred that the polydispersity of molecular weight between the cross-linking points of the gels was also an important factor in creating the continuous swelling curves of the NEEA, NEPA, and NTFA gels.

IV. Discussion

A gel's swelling curve is calculated using the criterion that the osmotic pressure differences between the inside and outside of the gel must be zero in its swelling equilibrium. To interpret the reentrant swelling behavior noted in the previous section, we used Tanaka's qualitative formula[11] for the osmotic pressure of a gel.

$$P = -\frac{NkT}{v}\left[\phi + \ln(1-\phi) + \frac{\Delta F}{2kT}\phi^2\right] + \nu kT\left[\frac{\phi}{2\phi_0} - \left(\frac{\phi}{\phi_0}\right)^{1/3} + \nu f kT\left(\frac{\phi}{\phi_0}\right)\right] \qquad (2)$$

where N is Avogadro's number, k is the Boltzmann constant, T is the temperature, v is the molar volume of the solvent, ϕ is the volume fraction of the gel network, and ΔF denotes the difference between the free energies of polymer segment–segment and polymer–solvent interactions. This equation, based on Flory's lattice model, is known to be able to represent the thermoswelling behaviors of gels.[12,13] Recently, Erman and Flory,[14] and Hirotsu[15] showed that eq 2 was applicable to various swelling behaviors of gels by introducing the concentration dependence or temperature dependence into ΔF.

As mentioned in section III, it seems that the temperature dependence of hydrophobic interaction was very important in reentrant swelling behavior. Therefore we introduced the hydrophobic interaction into the ΔF term in order to calculate the reentrant swelling equilibria. Hence, we have revised the term so that it now includes the mixing enthalpy and the contribution of hydrophobic interaction.

$$\Delta F = \Delta H_{\text{mix}} + \Delta F_{\text{HI}} = \Delta H_{\text{mix}} + (\Delta H_{\text{HI}} - T\Delta S_{\text{HI}}) \quad (3)$$

As stated at the outset, the purpose of this section is to produce a preliminary qualitative calculation for the experimental results. Because our aim is not quantitative understanding, we assume that ΔF can be represented by ΔF_{HI}. For convenience, ΔH_{mix} is intentionally neglected.

$$\Delta F \doteqdot \Delta F_{\text{HI}} = \Delta H_{\text{HI}} - T\Delta S_{\text{HI}} \quad (4)$$

For the hydrophobic interaction, Neméthy and Scheraga quantitatively investigated its temperature dependence and presented the following equations for the temperature range 0–70 °C.[16–18]

$$\Delta F_{\text{HI}} = a + bT + cT^2$$
$$\Delta H_{\text{HI}} = a - cT^2$$
$$\Delta S_{\text{HI}} = -b - 2cT \quad (5)$$

where a, b, and c are system-dependent constants whose values were proposed by Neméthy and Scherage as amino acid substitutes.[18]

Regarding the parameters of the above equations, v is the molar volume of water and ϕ_0 is estimated to be 0.07, given the experimental conditions. For ν, we adopted the value for the NIPA gel (1.0×10^{22} L^{-1}), in consideration of the synthesis condition. We then calculated the swelling equilibria with the values a, b, and c for the isopropyl group[18] (valine–valine, a = 5480 cal/mol, b = 36.2 (cal/mol)/K, c = 0.0495 (cal/mol)/K^2). The calculated results, shown as a solid line in Figure 2, indicate a thermoshrinking curve that could not be obtained by eq 2 where there is a constant value for ΔF. In accordance with the notion that the hydrophobic interaction of (alkoxyalkyl)acrylamide is less than that of alkylacrylamide, we carried out a test calculation by reducing the values of the temperature-dependent terms (b and c). The dashed line in Figure 2 shows the results (where b = −34.5 and c = 0.0470). These figures are slightly smaller (ca. 5%) than those for the isopropyl group. The calculation represents a reentrant type of swelling curve which was observed in the experiments. It may be noted from these calculations that the reentrant type of swelling curves are strongly related to the temperature dependence of the hydrophobic interaction of the gels, despite the assumption neglecting the mixing enthalpy.

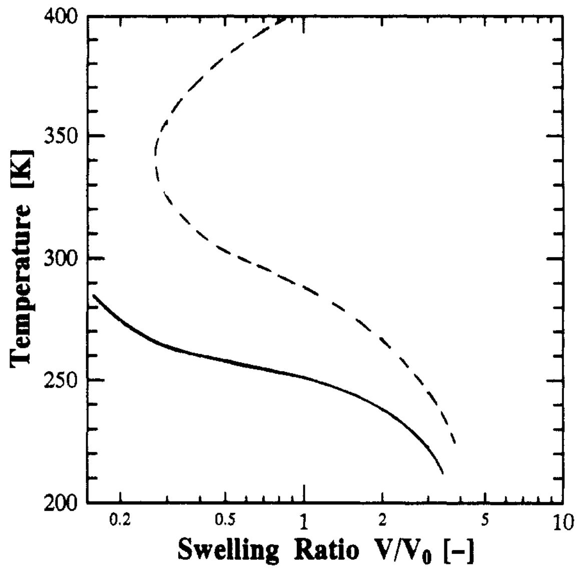

Figure 2. Swelling curves calculated with Tanaka's equation (eq 2), ΔF of which was expressed in terms of the temperature dependence of hydrophobic interaction proposed by Neméthy and Sheraga (eq 5). The solid line (—) denotes calculated values with a = 5480 cal·mol^{-1}, b = −36.2 cal·mol^{-1}·K^{-1}, and c = 0.0495 cal·mol^{-1}·K^{-2}, while the dashed line (- - -) denotes calculated values with a = 5480 cal·mol, b = −34.5 cal·mol·K^{-1}, and c = 0.0470 cal·mol^{-1}·K^{-2}.

V. Conclusions

The present work has revealed that the N-(3-methoxypropyl)acrylamide (NMPA) gel hardly changed its volume upon heating. It also demonstrated that three gels (N-(2-ethoxyethyl)acrylamide (NEEA), N-(3-ethoxypropyl)acrylamide (NEPA), and N-(tetrahydrofurfuryl)acrylamide (NTFA) gels) exhibited swelling curves of the reentrant type. The gradual shrinking of the NEEA, NEPA, and NTFA gels upon being heated within the temperature range 25–35 °C was considered to be due to the weak hydrophobic interaction based on the alkoxyalkyl groups. The subsequent swelling was believed due to the thermal mixing which dominated the hydrophobic interaction. These discussions were supported by preliminary calculations introducing the temperature dependence of the hydrophobic interaction, provided by Neméthy and Scheraga, into the ΔF term of Tanaka's equation. In addition, it was inferred that the polydispersity of molecular weight between the cross-linking points was an important factor in understanding N-(alkoxyalkyl)acrylamide gels.

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