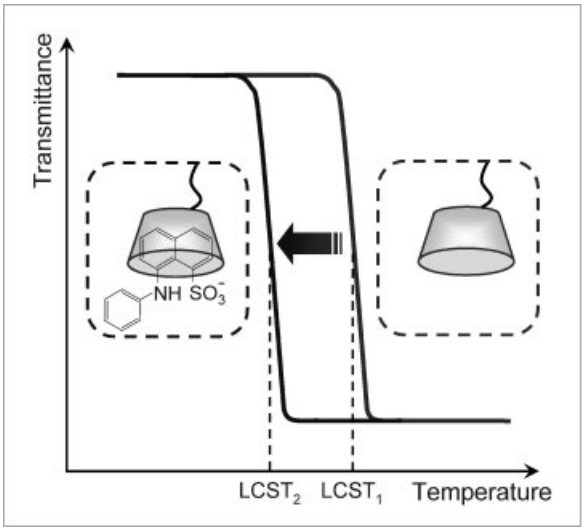
Molecular-Recognition-Induced Phase Transitions of Two Thermo-Responsive Polymers with Pendent β-Cyclodextrin Groups

Mei Yang, Liang-Yin Chu,* Rui Xie, Chun Wang

PNIPAM-based thermo-responsive polymers with pendent β-cyclodextrin groups were synthesized and the molecular-recognition-induced phase-transition behavior of fabricated polymers was investigated. The results showed that the thermo-sensitive PNG-ECD and PNG-HCD polymers could significantly recognize the guest ANS molecules, and their LCSTs in ANS aqueous solutions were lower than those in blank aqueous solution. The more ANS could be recognized by the polymer, the lower was the LCST of the polymer. The guest NS molecules had an opposite influence on the LCSTs of the PNG-ECD and PNG-HCD polymers, because the complexation between CD and NS slightly enlarged the hydrophilic moiety of the polymers.



Introduction

During the past decade, smart materials have received increasing attention because of their great scientific and technological significance. These materials are supposed to be able to respond to environmental changes such as temperature,[1–7] pH,[8–10] light,[11] electric field,[12] magnetic field,[13,14] and chemical or biological species[15–19] at the most optimum conditions and manifest their own functions according to the changes.

Of the thermo-sensitive smart polymers, poly(*N*-isopropylacrylamide) (PNIPAM) has been receiving much attention due to its sharp phase-transition behavior and well-defined lower critical solution temperature (LCST) in water of around 32 °C.[20,21] When the environmental temperature is below the LCST, PNIPAM is in the swollen and hydrophilic state in water; while it is in the shrunken and hydrophobic state when the environmental temperature is above the LCST. Furthermore, by means of introducing functional groups to the polymeric network of PNIPAM, it is an effective approach to obtain multi-stimuli-sensitive or multifunctional polymers that have many potential applications in many attractive fields.[15,22–27]

β-Cyclodextrin (β-CD), which is composed of cyclic α-1,4-oligoglucopyranosides, possesses a hydrophobic cavity and a hydrophilic external surface. Through a series of weak intermolecular forces, such as hydrophobic, electrostatic, and hydrogen-bonding interactions, β-CD is a well-known host molecule capable of selectively associating with guest molecules with a similar size to its cavity;

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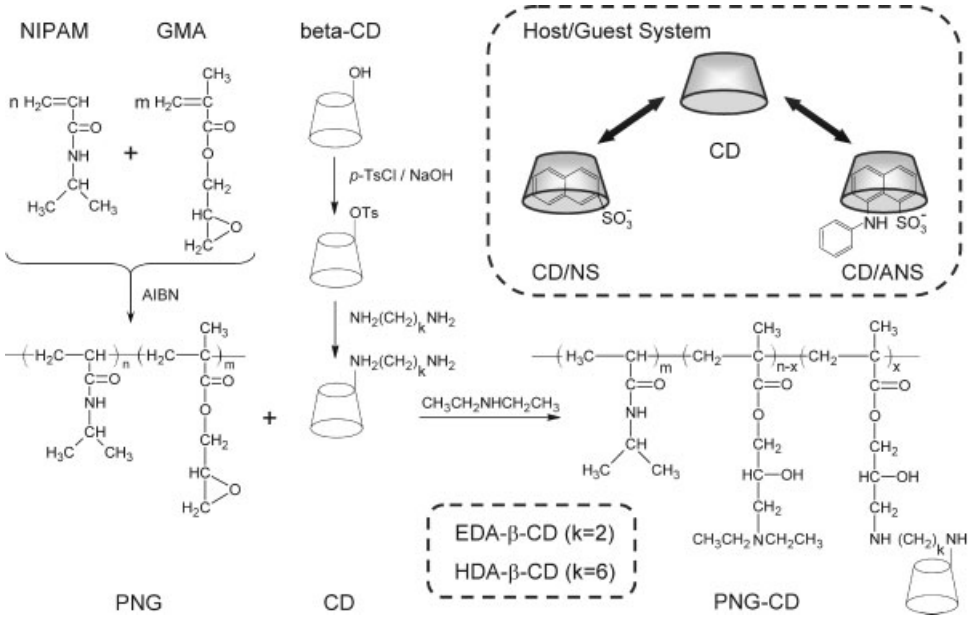

Figure 1. The synthesis route of poly(NIPAM-*co*-GMA) with pendent CD groups (PNG-CD). Insert top right: complexation between CD and two guest molecules.

therefore, β-CD and its derivatives have been used widely in molecular-recognition systems.[28–30]

Due to the interesting integration of the molecular-recognition ability of β-CD and the thermo-sensitivity of PNIPAM, certain attention has been drawn to hydrogels and polymers with a combination of NIPAM and β-CD.[22–26,31–35] Previous studies have investigated the temperature dependence of β-CD-modified PNIPAM, and found that a PNIPAM chain attached to the side arm of β-CD had considerable influence on the association constant of β-CD towards guest molecules, which was ascribed to the steric hindrance that was caused by the PNIPAM chains.[22–24] Other studies on β-CD-containing PNIPAM hydrogels mainly dealt with the controlled drug release and/or the temperature/pH sensitivity of the hydrogel.[31–35] Yamaguchi et al.[25] developed a novel polymer system based on β-CD-modified PNIPAM that exhibits a coordination of molecular recognition and actuation functionalities within itself. It was found that both these components affect each other. That is, the complexation between CD and the guest molecule induces a phase transition in the NIPAM chain; meanwhile, the phase transition in the NIPAM chain affects the association between CD and guest molecule. However, to the best of our knowledge, no systematic researches have been made on the molecular-recognition-induced phase transitions of thermo-responsive polymers with pendent β-cyclodextrin groups, to date.

In this study, we synthesized two novel, thermo-responsive polymers that exhibited a coordination behavior, with a molecular-recognition ability based on β-CD, and temperature sensitivity based on PNIPAM. As shown in Figure 1, the copolymer of PNIPAM and glycidyl methacrylate (GMA) was prepared first, and then the modified β-CD, which could form a complex with 8-anilino-1-naphthalenesulfonic acid ammonium salt (ANS) or 2-naphthalenesulfonic acid (NS), was attached to the polymer chains. Investigations were carried out on the phase-transition behaviors of the synthesized, molecular-recognizable, thermo-sensitive polymers. The results showed that the association between β-CD and the guest molecule could considerably affect the LCSTs of the synthesized polymers, and the polymers could be used for engineering molecular-recognition sensors and switches, and also molecular separation systems.

Experimental Part

Materials

The monomer *N*-isopropylacrylamide (NIPAM) was kindly provided by Kohjin Co., Ltd., Japan, and was used after being purified by recrystallization in hexane and acetone, and then drying under vacuum at room temperature. Glycidyl methacrylate (GMA) with a purity of 97% was obtained from Acros. β-CD was purchased from the Tianjin Bodi Chemicals Co., Ltd., China, and purified by recrystallization in water and then dried at 110 °C for 12 h before use. ANS was obtained from Aldrich Chemical Co., Inc. NS was purchased from Alfa Aesar China Co., Ltd. All of the other chemicals, including *p*-toluenesulfonyl chloride (*p*-TsCl), ethylenediamine (EDA), 1,6-hexanediamine (HDA), diethylamine (DEA), *N*,*N*-dimethylformamide (DMF), 2,2′-azoisobutyronitrile (AIBN), tetrahydrofuran (THF), 1,4-dioxane, acetonitrile, acetone, methanol,

and ethanol, were of analytical grade and used as received, without further purification. The water used in the experiments was well deionized.

Synthesis of Mono-6-OTs-β-CD[36]

100.0 g of β-CD was suspended in 833 mL of water, and 33 mL of water containing 10.95 g of NaOH was added drop-wise over 10 min. The suspension became homogeneous and slightly yellow before the addition was complete. 16.82 g of *p*-TsCl in 50 mL of acetonitrile was added drop-wise over 75 min, causing an immediate white precipitate to form. After 2.5 h of vigorous stirring at 25 °C, a 1 mol · L^{-1} HCl aqueous solution was added to modulate the pH value to 8 at the end of the reaction. The suspension was then refrigerated overnight at 4 °C. The resulting white precipitate was recovered by suction filtration and then immersed in ethyl ether for 48 h to remove the residual *p*-TsCl. After washing twice by hot water and drying under vacuum at 70 °C overnight, 12.63 g of a pure white mono-6-OTs-β-CD was obtained.

^{1}H NMR (300 MHz, DMSO-d_6): $\delta = 7.75$ (d, H^2), 7.43 (d, H^2), 5.87–5.65 (m, H^{14}), 4.84–4.77 (d, H^6), 2.43 (s, H^3).

Synthesis of Mono-6-Deoxy-6-Ethylene Diamino-β-CD (EDA-β-CD, ECD)[32]

5.0 g of mono-6-OTs-β-CD was reacted with 30 mL of EDA at 75 °C for 6 h. After evaporation of EDA, the reaction mixture was allowed to cool to room temperature, and was poured into 250 mL of cold acetone. The precipitate was filtered. The precipitate was repeatedly dissolved in 80 mL of a water/methanol (3:1, v/v) solution mixture, and poured into 250 mL of acetone for the removal of unreacted EDA. After filtration, the precipitate was dried under vacuum at 50 °C for 3 d, and 4.2 g of ECD was obtained. The structure of ECD was characterized by Fourier-transform IR spectroscopy (FT-IR, Nicolet 560, P-E Com., US) and ^{1}H NMR spectroscopy.

IR (KBr): 3 381 (s, OH), 2 927 (m, CH_2), 1 030 cm^{-1} (s, C–OH).

^{1}H NMR (300 MHz, D_2O): $\delta = 5.01$ (s, H^7), 3.99–3.88 (m, H^{28}), 3.67–3.45 (m, H^{14}), 2.83–2.78 (m, H^2).

Synthesis of Mono-6-Deoxy-6-Hexane Diamino-β-CD (HDA-β-CD, HCD)[32]

10.0 g of HDA was suspended in 20 mL of DMF, and 5.0 g of mono-6-OTs-β-CD was then added at 75 °C. After 8 h, the reaction mixture was allowed to cool to room temperature, and was poured into 250 mL of cold acetone and the precipitate was filtered. The precipitate was repeatedly dissolved in 80 mL of water/methanol (3:1, v/v) solution mixture, and poured into 250 mL of acetone. After filtration, the precipitate was dried under vacuum at 50 °C for 3 d, and 4.3 g of HCD were obtained.

^{1}H NMR (300 MHz, D_2O): $\delta = 5.00$ (s, H^7, C(1)–H), 2.83 (s, H^2, –CH_2NH–β-CD).

Synthesis of Poly(NIPAM-*co*-GMA) (PNG) and PNIPAM

PNG was synthesized by free-radical polymerization. NIPAM and GMA (10:1, mol/mol) were dissolved in THF with bubbling of nitrogen for 30 min. AIBN (1 wt.-% of monomers) was added when the mixture reached 60 °C. After 5 h, the reaction mixture was allowed to cool to room temperature, and an excess of ethyl ether was added to the solution to precipitate the copolymer. The copolymer was purified twice by reprecipitation with ethyl ether from THF and dried under vacuum at 50 °C for 2 d. The PNIPAM homopolymer, which served as a reference, was also prepared and purified using the protocol described above, except that GMA was not present.

The weight- and number-average molecular weights ($\overline{M}_w$ and $\overline{M}_n$) of the PNG and PNIPAM obtained were measured by gel-permeation chromatography (GPC) (Agilent 1100, USA) calibrated with polystyrene standards, using THF as solvent and applying a flow rate of 1 mL · min^{-1}. The $\overline{M}_n$ and $\overline{M}_w/\overline{M}_n$ values of PNG were 2.51×10^3 and 1.56, and the $\overline{M}_n$ and $\overline{M}_w/\overline{M}_n$ values of PNIPAM were 1.87×10^3 and 1.29, respectively. The structure of PNG was characterized by FT-IR spectroscopy and ^{1}H NMR spectroscopy.

IR (KBr): 1 720 (w, C=O), 1 650 (s, C=O), 1 550 cm^{-1} (s, N–H).

^{1}H NMR (400 MHz, $CDCl_3$): $\delta = 4.46$ and 3.85 (br, $2 \times H^1$, –O–CH_2–CH–Epox), 4.02 (br, H^1, –NH–C*H*–Me_2), 3.33 (br, H^1, –O–CH_2–C*H*–Epox).

Synthesis of PNG-ECD and PNG-HCD

PNG-ECD and PNG-HCD were synthesized by the reaction of PNG with ECD or HCD in DMF. The mixture was stirred under certain conditions at 50 °C. After 48 h, 4 mL of DEA was added, and the mixture was stirred continuously to eliminate the unreacted epoxy groups. Later, the resulting polymer was purified by precipitation in hot water and acetone, and dried under vacuum at 50 °C for 3 d.

IR (KBr): 3 400 (s, OH), 2 927 (m, CH_2), 1 650 (s, C=O), 1 550 (s, N–H), 1 030 cm^{-1} (s, C–OH).

For PNG-ECD:

^{1}H NMR (400 MHz, D_2O): $\delta = 4.91$ (s, H^7, C(1)–H), 2.86 (m, H^2, –CH_2–NH–β-CD), 2.70 (m, H^2, –NH–CH_2–CH_2–NH–β-CD), 1.04–1.00 (s, H^6, –CH_3 for DEA).

For PNG-HCD:

^{1}H NMR (400 MHz, D_2O): $\delta = 4.93$ (s, H^7, C(1)–H), 2.86 (m, H^2, –CH_2–NH–β-CD), 2.70 (m, H^2, –NH–CH_2–CH_2–NH–β-CD), 1.08–0.99 (s, H^6, –CH_3 for DEA).

Measurement of the LCST of PNIPAM, PNG, PNG-ECD and PNG-HCD

To investigate the LCST of polymers, the transmittance of PNIPAM, PNG, PNG-ECD, and PNG-HCD aqueous solutions (the concentrations of PNIPAM and PNG were both 1 wt.-%; the concentrations of PNG-ECD and PNG-HCD were both 2 wt.-%) with different contents of ANS or NS was observed by a UV-visible (UV-vis) spectrophotometer (752UV, China) using visible light at a wavelength of 650 nm. Pure water was used as a reference. The temperature at

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which the transmittance decreased to half the initial value was recorded as the LCST.

Observation of Phase-Transition Behavior of PNG-ECD and PNG-HCD in ANS Solution

As the change of absorbance is more sensitive than that of transmittance, especially for polymers in the shrunken state, the absorbance change of PNG-ECD and PNG-HCD aqueous solution with different ANS content, in response to a "sharp temperature jump", was also observed by a UV-visible spectrophotometer using visible light at a wavelength of 650 nm. The "sharp temperature jump" referred to a range of temperature that from T_1 (below the LCST of the polymer in solution) to T_2 (above the LCST of the polymer in the same solution).

Results and Discussion

Componential Characterization of PNG, PNG-ECD and PNG-HCD

The successful synthesis of PNG, PNG-ECD and PNG-HCD was determined using FT-IR and ^{1}H NMR spectroscopy.

Figure 2 shows the IR spectra of PNG, PNG-ECD and PNG-HCD. For all of the three IR absorption curves, it is obvious that there are strong C=O stretching vibration at around 1 650 cm^{-1}, and an N–H deformation vibration at around 1 550 cm^{-1} from the PNIPAM component. However, in comparison with IR characteristic absorptions of PNG, PNG-ECD and PNG-HCD, it is clearly observed from the IR absorption curves of the PNG-ECD and PNG-HCD that there is a strong C–O–C characteristic stretching vibration at around 1 030 cm^{-1} from the ECD or HCD units. The results demonstrated that ECD or HCD was successfully conjugated into the PNG backbone chains.

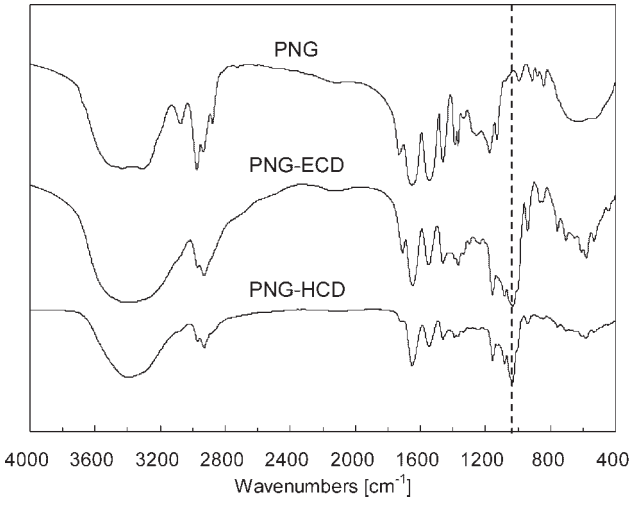

Figure 2. IR spectra of PNG, PNG-ECD and PNG-HCD.

Table 1. Molar composition of PNG, PNG-ECD and PNG-HCD polymers. The results were determined by ^{1}H NMR spectroscopy; The molar ratios "*m*", "*n*", and "*x*" are the same as those shown in Figure 1.

Sample	NIPAM molar ratio (*m*)	GMA molar ratio (*n*)	CD molar ratio (*x*)
	mol-%	mol-%	mol-%
PNG	91.60	8.40	0
PNG-ECD	91.60	8.40	1.45
PNG-HCD	91.60	8.40	1.18

The molar composition of the PNG, PNG-ECD and PNG-HCD was obtained from ^{1}H NMR spectra. The peak area of the 1H atoms of –NH–C*H*–Me$_2$ in the NIPAM moiety (occurring at around 4.02 ppm), the peak area of the 1H atom of –O–CH$_2$–C*H*–Epox in the GMA moiety (occurring at 3.33 ppm), the peak area of 6H atom of the methyl group in the DEA moiety (occurring at 1.04–1.00 ppm), and the peak area of the 7H$_1$ groups of the CD (occurring at 4.91 ppm) were used to determine their molar ratio in PNG, PNG-ECD and PNG-HCD. The composition of each polymer is listed in Table 1.

The LCST of PNIPAM, PNG, PNG-ECD and PNG-HCD

All of the polymers were water-soluble at or below room temperature. The LCST of the polymer in aqueous solution was determined by turbidity experiments. When a polymer is in the hydrophobic and shrunken state, the polymer aggregates and scatters visible light. On the other hand, when a polymer is in the hydrophilic and swollen state, the polymer is homogeneously dispersed in solution and visible light can penetrate. Therefore, the LCST of a polymer can be determined from the temperature where the absorption of visible light exhibits a sharp change.

Figure 3 shows the thermo-sensitive phase transitions of the PNIPAM and PNG polymers. It was evident that the two polymers underwent an abrupt change in turbidity when the temperature reached the LCST of the corresponding polymer. Furthermore, the introduction of the hydrophobic GMA units resulted in a slight decrease in the LCST of the polymer. The LCST of PNIPAM in aqueous solution was found to be approximately 32.0 °C, and the LCST of the PNG in aqueous solution decreased to 29.3 °C.

PNIPAM exhibits an LCST due to the presence of both hydrophilic amide groups and hydrophobic isopropyl groups in the side chains of the polymer. When the environmental temperature was below the LCST, the polymer is hydrophilic and soluble due to the formation of hydrogen bonds between the water molecules and the isopropyl groups. Conversely, at a temperature above the

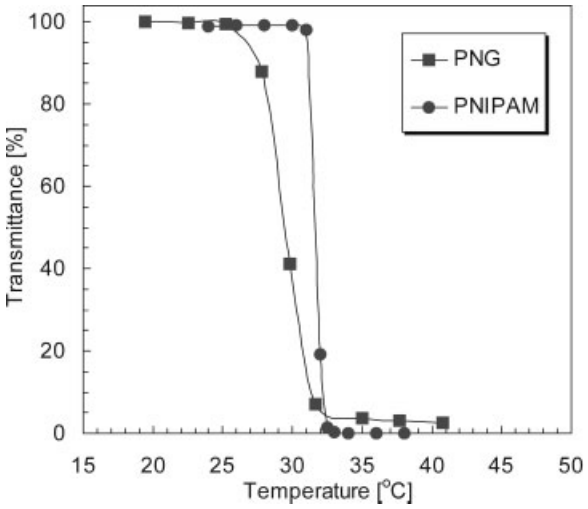

Figure 3. Thermo-sensitive phase transitions of PNIPAM and PNG polymers in aqueous solutions.

LCST, the hydrogen bonds are broken, causing a reversible phase transition from a hydrophilic to a hydrophobic structure, and precipitation of the polymer.[20,21] This phase-transition phenomenon was still significantly evident even when PNIPAM polymer chains were introduced with GMA units; however, the LCST value was lower than that of the PNIPAM. Incorporation of GMA would cause an increase of hydrophobic moieties in the polymer and change the balance between the hydrophilic and hydrophobic interactions in the polymer. Consequently, the hydrogen bonds would be broken and the phase transition of polymer would occur at a lower temperature.

Figure 4 shows the thermo-sensitive phase transitions of PNG-ECD and PNG-HCD in aqueous solutions with different concentrations of ANS. The LCSTs of PNG-ECD and PNG-HCD in aqueous solutions without ANS were both higher than that of PNG (around 29.3 °C), which was due to the incorporation of the hydrophilic CD moieties. Interestingly, the LCSTs of PNG-ECD and PNG-HCD were both decreased by the addition of ANS, and the shift of the LCST was larger for higher ANS concentrations. The molecular structure of PNG-CD/ANS was shown in Figure 1 above. When the CD moiety recognizes the guest ANS molecule, the CD/ANS complex leaves a hydrophobic phenyl group out of the CD cavity, which enlarges the hydrophobic moiety of the polymer. Therefore, the higher the concentration of ANS, the more CD/ANS complexes formed, and therefore the more hydrophobic moieties in the polymer chains. As a result, the more the ANS was recognized, the lower the LCST of the polymer became.

Figure 5 shows the molecular-recognition-induced LCST shifts for PNG-ECD and PNG-HCD in aqueous solutions with different concentrations of ANS. The LCSTs of PNG-ECD with different concentrations of ANS (0.0, 0.1, 0.4, 1.0, and 2.0×10^{-3} M) were 43.8, 38.9, 37.6, 32.8, and

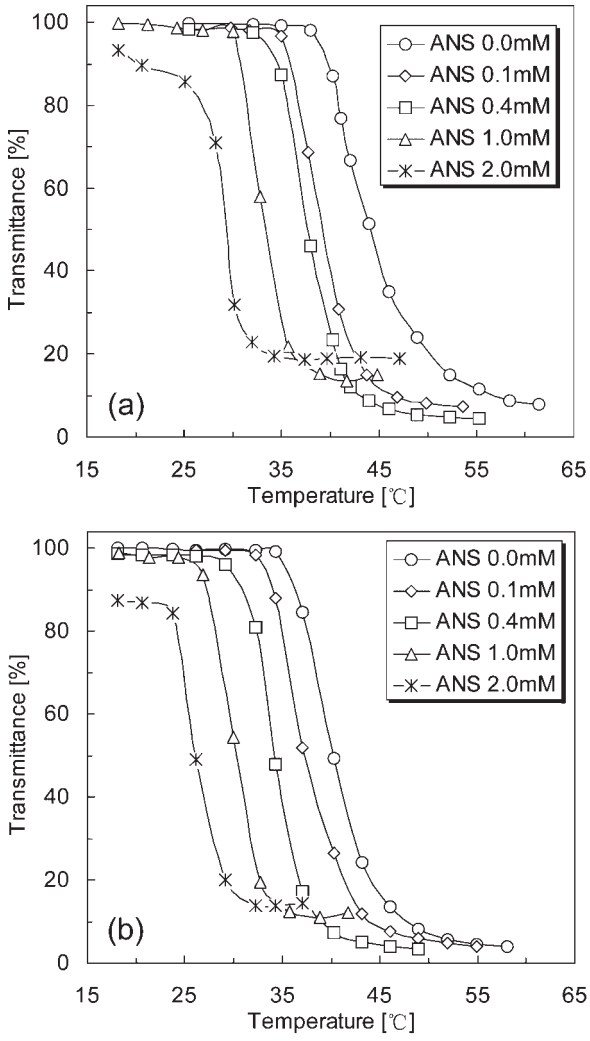

Figure 4. Thermo-sensitive phase transitions of (a) PNG-ECD and (b) PNG-HCD in aqueous solutions with different concentrations of ANS.

29.0 °C, and the LCSTs of PNG-HCD with different concentrations of ANS (0.0, 0.1, 0.4, 1.0, 2.0×10^{-3} M) were 39.9, 37.2, 34.1, 30.3, and 26.0 °C, respectively. That is, the LCST of polymer decreased with an increase in the concentration of ANS in the aqueous solution. The results also indicated that with the same concentration of ANS, the PNG-HCD was more hydrophobic than PNG-ECD, due to the extra four methylene groups (Figure 1). In summary, all the phenomena described above can be ascribed to the change of the balance between hydrophilic and hydrophobic interactions in the polymer.

Figure 6 shows the thermo-sensitive phase transitions of PNG polymers in aqueous solutions with different concentrations of ANS. It was found that ANS had almost no influence on the LCST of PNG, no matter how the ANS concentration changed. The results of this control study verified that the negative shifts in the LCSTs of PNG-ECD

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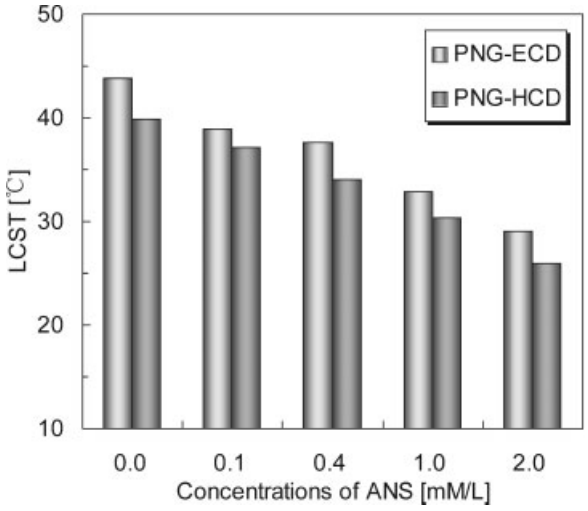

Figure 5. Molecular-recognition-induced LCST shifts of PNG-ECD and PNG-HCD in aqueous solutions with different concentrations of ANS.

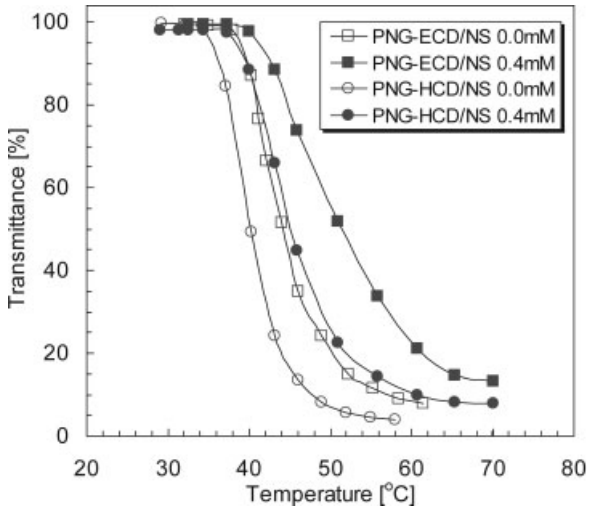

Figure 7. Thermo-sensitive phase transitions of PNG-ECD and PNG-HCD in aqueous solutions with different concentrations of NS.

and PNG-HCD (shown in Figure 4) were solely triggered by the CD/ANS host-guest recognition and not by any polymer-guest interactions.

Figure 7 shows the thermo-sensitive phase transitions of PNG-ECD and PNG-HCD polymers in aqueous solutions with different concentrations of NS. Compared with the result from ANS, the NS had an opposite influence on the LCSTs of PNG-ECD and PNG-HCD. On adding NS molecules to the aqueous solutions, both the LCSTs of PNG-ECD and PNG-HCD increased by a certain degree. The complexation between CD and the guest molecules (NS and ANS) was illustrated in Figure 1 above (the insert top right). When the CD moiety recognizes the guest molecules, the CD/ANS complex has a hydrophobic phenyl group out of the CD cavity; on the other hand, the CD/NS complex has no side group out of the CD cavity. However, the complexation between CD and NS could enlarge the hydrophilic moiety of polymers due to the dissociation of NS in the water. The results of such parallel controls proved that it was just the hydrophobic phenyl group of ANS that resulted in the negative shift of the LCST of PNG-ECD and PNG-HCD polymers.

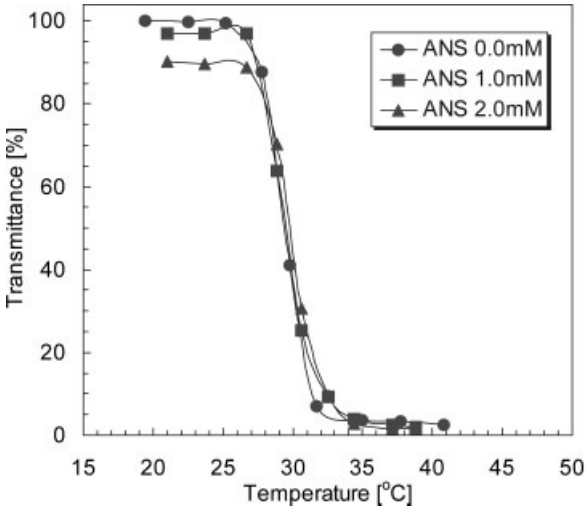

Figure 6. Thermo-sensitive phase transitions of PNG in aqueous solutions with different concentrations of ANS.

Phase-Transition Behaviors of PNG-ECD and PNG-HCD in ANS Solutions

The phase transition behaviors of PNG-ECD and PNG-HCD in aqueous ANS solutions in response to the "sharp temperature jump" (ANS concentrations ranged from 0.0 to 2.0×10^{-3} M) were observed according to the change in light absorbance.

Figure 8 shows the thermo-sensitive absorbance variations of PNG-ECD and PNG-HCD in aqueous solutions with different concentrations of ANS in response to the sharp temperature jump. As shown in Figure 8a and 8b, the variation trends of absorbance of PNG-ECD and PNG-HCD solutions were almost the same within the "sharp temperature jump" of 10 °C. For those polymer solutions with $[ANS] < 2.0 \times 10^{-3}$ M, a mild change in absorbance was observed within the first two minutes. However, when the temperature reached the LCST of the polymer, a sharp rise in absorbance occurred and the absorbance value was almost unchanged after the temperature was steady. On increasing the ANS concentration in polymer solution, the rise in absorbance during the sharp temperature jump also increased.

When the environmental temperature was lower than the LCST of the polymer, the polymer chains were

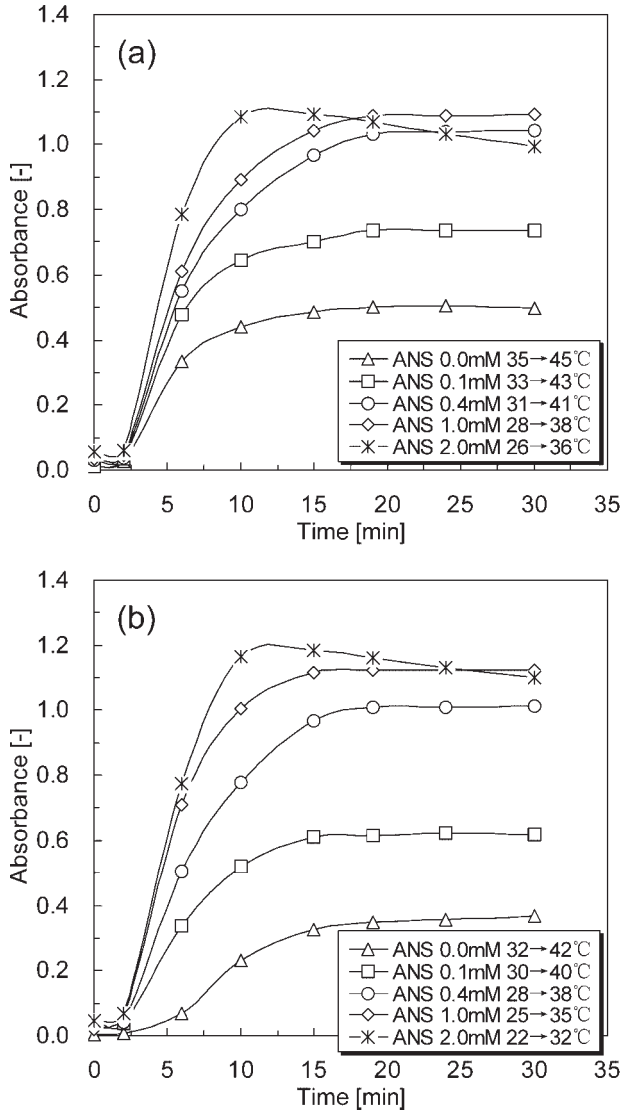

Figure 8. Thermo-sensitive absorbance variations of (a) PNG-ECD and (b) PNG-HCD aqueous solutions with different concentrations of ANS, in response to the sharp temperature jump.

swollen and soluble. With time, the temperature increased gradually to reach and cross the LCST; thus the polymer transformed from a hydrophilic to a hydrophobic structure and precipitated from the solution. Once the transition was in equilibrium, the absorbance value was maximal and there was no further variation. Furthermore, the amount of polymer in the insoluble state was increased with the increase of the ANS concentration at the same temperature, because the LCST shift was larger for higher ANS concentrations. Consequently, the absorbance value increased on increasing the ANS concentration in the polymer solutions.

Another interesting phenomenon was observed in Figure 8a and 8b for the polymer solution with [ANS] = 2.0×10^{-3} M: there was a moderate decrease in absorbance following the sharp rise. As shown in Figure 9, visible precipitation of PNG-ECD/ANS complexes in the cell bottom was observed in response to the sharp temperature jump. The precipitation of PNG-ECD/ANS complexes should be the reason for the decrease of the absorbance value, because such precipitation did not occur when the ANS concentration in polymer solution was less than 2.0×10^{-3} M, as mentioned above. Elemental analysis results (Table 2) showed that the carbon, nitrogen, and sulfur compositions of the precipitates were in the range between the compositions of ANS and PNG-CD; that is, the precipitate was verified to be the PNG-ECD/ANS complexes. This phenomenon could be useful in some separations of particular molecules, such as enantiomers, proteins, hormones, as long as the CD moieties in the synthesized polymers can recognize the target molecules.

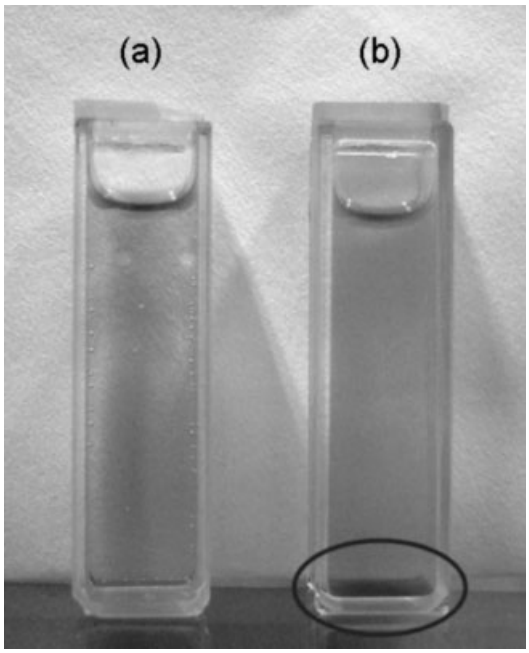

Figure 9. Precipitation of PNG-ECD/ANS complexes in the cell bottom, in response to the sharp temperature jump (corresponding to the curve of [ANS] = 2.0×10^{-3} M in Figure 8a). (a) Before heating; (b) after heating.

Table 2. Elemental-analysis results of the precipitate from the ANS solution. The ANS concentration was 2.0×10^{-3} M.

Sample	C	N	S
	%	%	%
Precipitate	50.73	6.54	0.5
PNG-ECD	47.80	2.94	0
ANS	60.76	8.86	10.13

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Conclusion

In the present study, PNIPAM-based thermo-responsive polymers with pendent β-CD groups were successfully synthesized, and the molecular-recognition-induced phase-transition behaviors of the fabricated polymers were investigated. The experimental results showed that the synthesized thermo-sensitive PNG-ECD and PNG-HCD polymers could significantly recognize the guest ANS molecules, and their LCSTs in the ANS aqueous solutions were lower than those in blank aqueous solution, because of the hydrophobic phenyl group of the ANS being out of the cavity, after CD/ANS complexation. The more ANS in the environmental solution there was, the lower the LCSTs of the two polymers were. When the temperature was increased to pass through the LCST, the absorbance of polymer aqueous solution with ANS $\leq 1.0 \times 10^{-3}$ M increased suddenly due to the phase transition, first, and then remained almost unchanged. When the ANS concentration in the polymer aqueous solution was as large as 2.0×10^{-3} M, the absorbance decreased slightly when the temperature was higher than the LCST due to the precipitation of PNG-ECD/ANS or PNG-HCD/ANS complexes. On the other hand, the guest NS molecules had an opposite influence on the LCSTs of PNG-ECD and PNG-HCD polymers, because the complexation between CD and NS slightly enlarged the hydrophilic moiety of polymers, due to the dissociation of NS molecules in the water. The synthesized copolymers in this study were able to simultaneously respond to temperature and recognize guest molecules, and could be used for engineering molecular-recognition sensors and switches, and also in molecular-separation systems

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