Thermosensitivity of Aqueous Solutions of Poly(*N*,*N*-diethylacrylamide)

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ABSTRACT: The thermally induced phase separation of aqueous poly(*N*,*N*-diethylacrylamide) (PDEA) was studied by means of differential scanning calorimetry and UV−visible spectrophotometry. The polymer was shown to have a well-defined lower critical solution temperature (LCST) of 33 °C. The addition of sodium chloride to the polymer solution resulted in a linear decrease of the LCST. Sodium dodecyl sulfate, at concentrations up to its critical micelle concentration, caused a gradual increase in the LCST of PDEA.

Introduction

Water-soluble polymers with thermosensitivity are of great scientific and technological importance. These polymers are extensively used as additives by pharmaceutical, cosmetic, food, and paint industries. They serve to modify rheology and viscosity and to encapsulate active compounds, and they are increasingly instrumental in controlled drug delivery systems.[1−3] Their behavior in aqueous solution continues to be the subject of many scientific investigations. Polymers of this type undergo a thermally induced, reversible phase transition. The temperature at which this occurs is commonly referred to as the lower critical solution temperature (LCST). Below the LCST the polymer molecules exist in solution as extended coils, surrounded by ordered water molecules. This shell of hydration causes a decrease in the entropy of the system. Thus, the free energy of solution is lowered by the formation of hydrogen bonds but is raised by the loss of entropy. At temperatures above the LCST the entropy term dominates, and the polymer precipitates out of solution.

Several N-substituted poly(acrylamides) exhibit this kind of behavior in aqueous solution. The homopolymers of *N*,*N*-diethylacrylamide, *N*-cyclopropylacrylamide, *N*-isopropylacrylamide, and *N*-ethylacrylamide have been reported to have LCSTs of 25, 32, 58, and 74 °C, respectively.[4] Research, however, has almost exclusively been focused on one member of this class of polymers, poly(*N*-isopropylacrylamide) (PNIPA).[5−16] The fact that PNIPA solutions undergo a sharp phase transition, conveniently at 32 °C, facilitates experimental procedures. This possibly has made it the preferred temperature-sensitive polymer to study.[5]

Our research led to the discovery that poly(*N*,*N*-diethylacrylamide) (PDEA) has an LCST of ca. 33 °C, higher than 25 °C as reported by Taylor and Cerankowski.[4] Intrigued by the similarity of the LCST of PNIPA and that of PDEA, we conducted a survey of the literature but found little information on the phase transition of PDEA aqueous solutions. We report here the results of a study of the LCST of aqueous PDEA solutions and of the changes in transition temperature caused by an added salt or a surfactant. Differential scanning calorimetry (DSC) and UV−visible spectrophotometry were used to measure the phase transitions. The conditions of measurement were varied in order to quantitatively evaluate their effect on the LCST.

Experimental Section

Materials. Acryloyl chloride, diethylamine, sodium dodecyl sulfate (SDS), and sodium chloride were purchased from Aldrich Chemical Co. and used as received. 2,2′-Azobis(isobutyronitrile) (AIBN) was obtained from Eastman Kodak and recrystallized from methanol prior to use. Dichloromethane was dried and distilled over calcium hydride. Reagent grade methanol, acetone, and hexane were purchased from ACP Chemical Co. and used as received.

Polymer Synthesis. A solution of acryloyl chloride (46.7 mL, 0.574 mol) in dichloromethane (30 mL) was added to diethylamine (208 mL, 2.0 mol) previously dissolved in dichloromethane (450 mL) at 0 °C under N_2 atmosphere. The reaction mixture was stirred for 4 h, filtered, and washed with water. After drying over magnesium sulfate, the solvent was removed under reduced pressure. The crude product was distilled in the presence of hydroquinone at 53 °C under vacuum at 1 mmHg, to yield a colorless oil (58.3 g, 80%). ^{1}H NMR ($CDCl_3$): δ 6.5 (dd, 1 H, $J = 10.3$, 17.3 Hz), 6.3 (dd, 1 H, $J = 17.3$, 2.2 Hz), 5.6 (dd, $J = 10.3$, 2.2 Hz), 3.4 (q, 4 H, $J = 7.2$ Hz), 1.1 (t, 6 H, $J = 7.2$ Hz) ppm.

Poly(*N*,*N*-diethylacrylamide) was prepared by free radical polymerization. *N*,*N*-diethylacrylamide (1.27 g, 10 mmol) in methanol (1.5 mL) was stirred with AIBN (8 mg, 0.05 mmol) under N_2 at 60 °C. Stirring stopped after 30 min. Heating was continued for 6 h. The polymer was cooled to room temperature and then dissolved in acetone (4 mL) and precipitated from hexane (80 mL). The yield was 1.02 g (80%). Size exclusion chromatography of a 0.25 wt % solution of the polymer in tetrahydrofuran (THF) on styrogel columns with polystyrene standards and THF as eluent gave an M_n of 20 370 and M_w/M_n of 3.13.

LCST Measurements. Samples for cloud point and calorimetric measurements were prepared by dissolving appropriate amounts of PDEA in distilled water in an ice−water bath.

Calorimetric measurements were done using a differential scanning calorimeter (TA Instruments DSC 2910). The PDEA solutions, ranging in concentration from 0.5 to 20 wt %, were placed and sealed in DSC cells and were scanned against an empty reference cell from 0 to 80 °C at heating rates varying from 5 to 20 °C min^{-1}.

The cloud points were measured optically, using a CARY 1 BIO UV−visible spectrophotometer, coupled to a temperature controller. A 1 cm sample cell, containing approximately 3 mL of PDEA solution, was used against distilled water as reference. The heating rates ranged from 0.06 to 5 °C min^{-1} and the polymer concentrations from 0.1 to 4 wt %. The polymer

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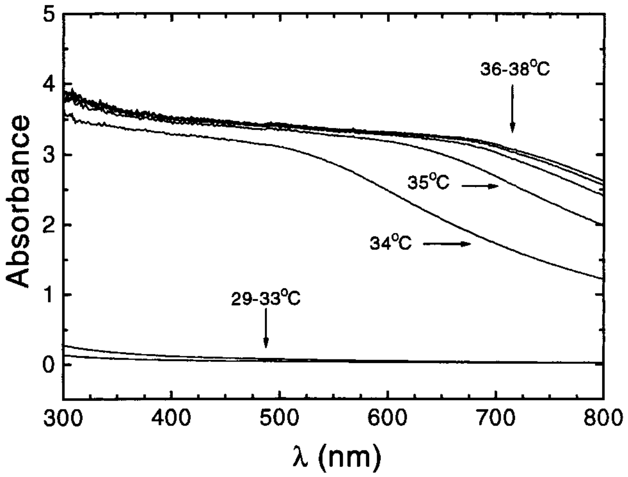

Figure 1. UV−visible absorbance spectra of a 0.5 wt % aqueous PDEA solution, recorded at various temperatures below and above the LCST of the sample.

solutions were heated from 15 to 50 °C. All measurements were taken at a wavelength of 500 nm, unless specified otherwise.

Cosolutes. Solutions of 0−1.7 M NaCl containing 0.5 wt % PDEA in distilled water were prepared. The same NaCl concentrations were used for the reference solutions. The heating rates were 0.25 and 5 °C $\min^{-1}$ for the UV−visible spectrophotometric and DSC measurements, respectively. The SDS concentrations ranged from 0 to 9 mM; the other parameters were the same as for the NaCl measurements.

Results and Discussion

UV−visible spectrophotometry was used to optically measure the cloud point of the PDEA solutions, while DSC provided insight into the thermodynamic parameters of phase separation. The concentrations of the solutions and the heating rates were varied in order to evaluate their effect on the LCST measurements.

The LCST, determined by UV−visible spectrophotometry, is here defined as the temperature at which the differential of transmittance with respect to the temperature at a certain wavelength is maximal. We consider this a more accurate and reproducible way of measurement than taking the temperature corresponding to a 10% reduction of the initial transmittance, as proposed by Boutris et al.[6]

To establish the optimal wavelength for LCST determination, we varied the scanning wavelength as we heated the PDEA solution through its LCST. Figure 1 depicts UV−visible light absorbance measurements of a 0.5 wt % PDEA solution at temperatures ranging from 29 to 38 °C. Below 34 °C no absorbance was recorded; the solution was optically transparent. Above this temperature absorbance was observed, starting at a wavelength of 500 nm. A stepwise increase of the temperature to 38 °C resulted in greater absorbance at progressively higher wavelengths. We therefore chose 500 nm as the wavelength for optimal measurement of the LCST of PDEA. As the spectrophotometer can only detect particles larger than the scanning wavelength, these measurements also give an indication of the influence of temperature on the size of the polymer aggregates.

As shown in Figure 2, the rate at which the PDEA solutions are heated affects the optical LCST measurement to the extent that an increase in heating rate from 0.06 to 5 °C $\min^{-1}$ results in a shift from 33 to 39 °C. A similar experiment performed by Boutris et al. involving PNIPA resulted in LCST values ranging from 32 to 43 °C.[4] For practical reasons we mostly used a heating rate of 1 °C $\min^{-1}$ for further UV−visible spectrophotometric measurements.

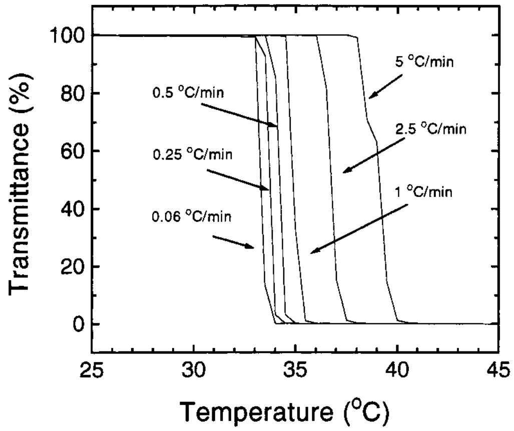

Figure 2. Transmittance curves of a 0.5 wt % aqueous PDEA solution at a wavelength λ of 500 nm, showing the effect of the heating rate.

The concentration of the PDEA solutions was also found to have an effect on the optical LCST measurement. At concentrations below 0.5 wt % the polymer particles fail or are slow to aggregate to a size that can be detected by the spectrophotometer. This effect is particularly pronounced for a high heating rate of a dilute solution. A heating rate of 5 °C $\min^{-1}$ of a 0.2 wt % PDEA solution raises the LCST measurement to 41 °C, which is 8 °C higher than for the same concentration heated at 0.06 °C $\min^{-1}$. These results can be explained in analogy to the transition mechanism of aqueous PNIPA solutions described by Fujishige et al.[7] At the molecular level the phase transition of temperature-sensitive polymers is a change from hydrated random coil to hydrophobic globule. The first step of the phase separation is the breaking up of the ordered water structure around the polymer coil, followed by the collapse of the polymer molecule into a hydrophobic globule. Polymer−polymer interactions are responsible for the aggregation and the subsequent precipitation of the polymer out of solution. This process requires a certain amount of time. Raising the temperature of the solution too quickly results in the recording of a less sharp transition and a too high cloud point. Transition kinetics therefore must be taken into account for accurate LCST determination by optical means.

Variation of the polymer concentration over a range of 0.5−20 wt % did not significantly affect the LCST measurements that were obtained by DSC (Figure 3A). What is measured by this latter method is the heat required for the breaking of the hydrogen bonds around the polymer. The transition temperatures are then calculated as the maximum of the endothermic peak of the heating thermogram. Contrary to LCST determination by optical means, particle size does not influence LCST values measured by DSC. Figure 3A also shows that optical LCST values obtained at low heating rates are comparable to those measured by DSC.

Figure 3B illustrates that the heating rate has some effect on the LCST values obtained by DSC, but the effect is not as pronounced as for the optical measurements. The kinetics of phase transition are not of the same importance for DSC as for UV−visible measure-

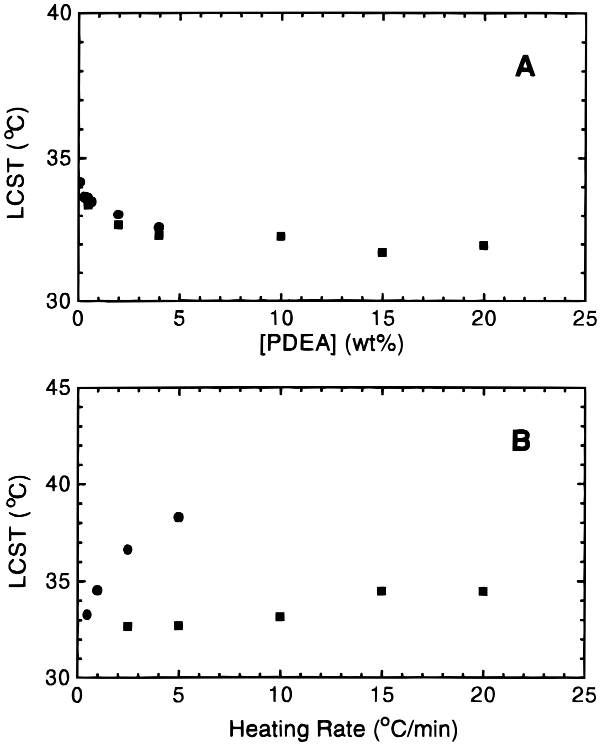

Figure 3. (A) Concentration effect on the LCST of aqueous PDEA measured by DSC (squares) at a heating rate of 5 °C min^{-1} and by UV−visible spectrophotometry (circles) at 0.25 °C min^{-1} ($\lambda = 500$ nm). (B) Effect of heating rate on the LCST of a 2 wt % PDEA solution measured by DSC (squares) and UV−visible spectrophotometry ($\lambda = 500$ nm).

ments. Furthermore, the DSC sample size is very small, and thus the efficiency of heat transfer is superior, avoiding a delay in response.

The enthalpy of phase separation of PDEA solutions was calculated from the DSC thermogram. This is a quantitative measure of the strength of hydrogen bonding of the PDEA−water system. This information, combined with the LCST, provides insight into the enthalpy−entropy balance of phase transition. For aqueous PDEA the enthalpy of separation was 22.9 J g^{-1} of polymer, corresponding to 0.70 kcal (2.9 kJ) mol^{-1} of repeating unit of the polymer. This value is lower than the 1.1 and 1.5 kcal mol^{-1} for PNIPA, reported by Fujishige et al. and Schild and Tirrell, respectively.[7,8] Considering that amide groups of PNIPA can be a proton donor as well as a proton acceptor, while the amide groups of PDEA can only be an acceptor, this is reasonable. Thus, as the LCST of PDEA is comparable to that of PNIPA, the smaller enthalpy change of PDEA must be offset by a lesser change in entropy upon solution.

Cosolute Effect. Aqueous solutions containing polymers and surfactants have a variety of biological and industrial applications.[13−16] In addition, the study of such systems can provide valuable insight into the nature of polymer−surfactant interactions and the possibility of polymer-mediated surfactant micelle formation.[15−19] The changes in LCST caused by the addition of a surfactant to a polymer solution are an indication of the strength and nature of these interactions.[20] A rise in transition temperature indicates the formation of surfactant micelles along the polymer chain,[16,18,19] causing an increase in hydrophilicity and a delayed collapse to the hydrophobic conformation.

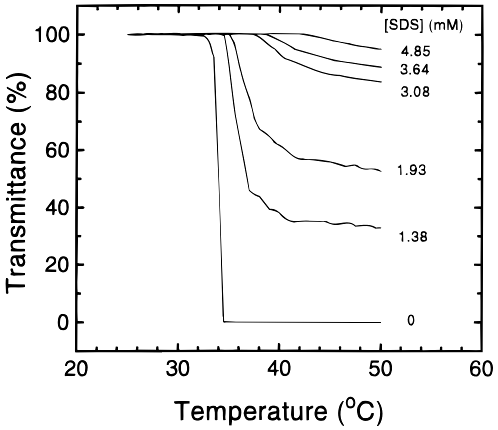

Figure 4. Effect of various SDS concentrations on the transmittance curves ($\lambda = 500$ nm) of 0.5 wt % PDEA solutions with increasing temperatures. The heating rate was 1 °C min^{-1}.

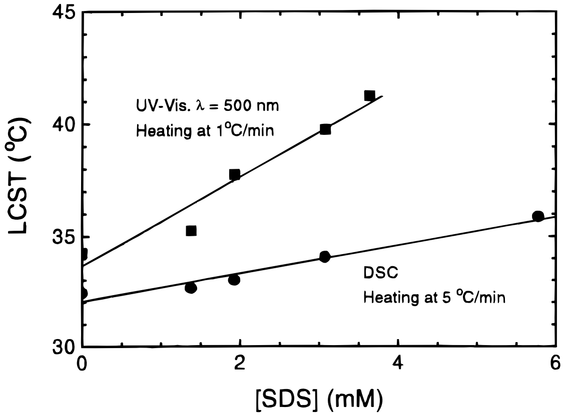

Figure 5. DSC and UV−visible ($\lambda = 500$ nm) measurements of the LCST of a 0.5 wt % PDEA solution in the presence of increasing amounts of SDS. Heating rates were 5 and 1 °C min^{-1} for DSC (circles) and UV−visible (squares) measurements, respectively.

From the transmittance curves (Figure 4) of a 0.5 wt % aqueous PDEA solution in the presence of various amounts of SDS, it appears that the addition of increasing amounts of SDS leads to phase transitions at increasingly higher temperatures. Obviously, the ionic surfactant molecules make the polymer more soluble due to binding of the surfactants with the polymer through hydrophobic interactions, as observed for PNIPA.[17] The results of the DSC measurements over the same SDS concentration range (Figure 5) show that SDS has a smaller effect on the LCST. At a SDS concentration of 4 mM the calculated optical and calorimetric values diverge by 6 °C, while at 6 mM the LCST becomes difficult to measure by UV−visible spectrophotometry at a wavelength of 500 nm (Figure 4). Seemingly, the results obtained by calorimetric and optical means are not in agreement. However, the elevated LCST from the optical measurements at low SDS concentration can be explained if we consider that SDS binds to the polymer after the phase transition. Micelles around the hydrophobic particles can prevent, by ionic repulsion, the aggregation of the precipitating polymer, leaving the particles too small to be spectroscopically detected at 500 nm. The formation of small colloidal particles of PNIPA in the presence of surfactant molecules (SDS) was observed with small-angle neutron scattering by Lee and Cabane.[19] Thus, as the SDS

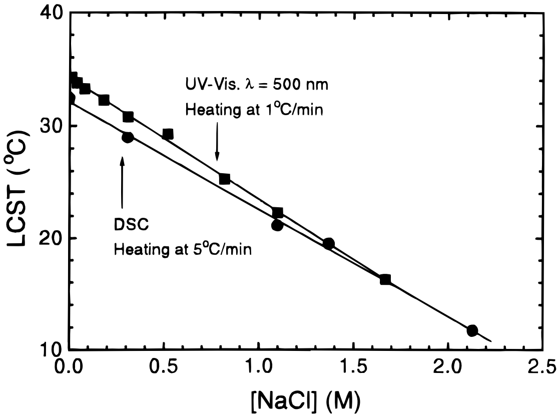

Figure 6. Effect of sodium chloride on the LCST of a 0.5 wt % aqueous PDEA solution, measured by DSC and UV−visible spectrophotometry ($\lambda = 500$ nm). Heating rates were 5 and 1 °C min^{-1} for DSC (circles) and UV−visible (squares) measurements, respectively.

concentration is raised, the polymer−water system remains optically transparent when it is heated through the LCST. However, when the scanning wavelength was decreased from 500 to 350 nm, we observed a sharp drop in transmittance at a temperature more in agreement with the LCST value determined by DSC. Schild and Tirrell report a similar observation concerning the lack of aggregation of PNIPA particles in solutions containing SDS.[15] When the PDEA solution was sufficiently concentrated (2.5 wt %), the LCST could still be optically measured at 350 nm in the presence of SDS, up to a SDS concentration of 8.4 mM (slightly above its critical micelle concentration of 8.2 mM[21]). At a SDS concentration of 9 mM the LCST could no longer be optically observed. For PNIPA, Lee and Cabane observed the solubilization of the polymer at higher surfactant concentrations by the formation of necklace-like micelles.[19]

The sensitivity of the LCST to ionic species is of practical and theoretical importance.[16,22] The extent of perturbation of the system's balance by salt deserves to be accurately assessed. As expected, the addition of NaCl to the PDEA solution resulted in a lowering of the LCST. Salt ions disrupt hydrogen bonding, break up the ordered water structure, and promote hydrophobic polymer−polymer interactions. A linear relationship was observed between the LCST and the NaCl concentration (Figure 6). The optically measured LCST values are in agreement with the DSC measurements when a slower heating rate was used for the UV−visible spectrophotometric measurements. Zhang et al. has shown that the addition of surfactants can alter the dependence of LCST of PNIPA on the salt concentration,[16] making the polymer less sensitive to the presence of salts.

Conclusion

The optical measurement of the LCST of PDEA is influenced by the heating rate and the concentration. The LCST determined by DSC is less dependent on these factors. Except for very dilute PDEA solutions, the results obtained by the two methods are in good agreement as long as the heating rate is low enough to allow sufficient time for equilibration of the system. When interpreting the UV−visible spectrophotometry results, it must be kept in mind, however, that the polymer particles should be of sufficient size in order to be detected at the selected wavelength setting. Lack of or delayed aggregation of the particles results in an artificially high LCST reading. This is particularly important for the determination of the LCST in the presence of additives. The UV−visible spectrophotometer remains nevertheless a practical and convenient tool for LCST measurements, especially in view of its sensitivity to less concentrated samples.

The values that we observed for the enthalpy of the PDEA phase transition are lower than those reported for PNIPA.[6] This points to a difference between the two polymers with regard to the water structure immediately surrounding the polymers and to the polymer conformations. PDEA, containing *N*,*N*-dialkyl-substituted amides, is expected to be more lipophilic than the *N*-monoalkyl-substituted PNIPA. The physical properties of PDEA should make it a useful alternative to PNIPA where a polymer with an LCST close to physiological temperature is needed.

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