

Characterization of the LCST behaviour of aqueous poly(N-isopropylacrylamide) solutions by thermal and cloud point techniques

C. Boutris, E. G. Chatzi and C. Kiparissides*

*Department of Chemical Engineering and Chemical Process Engineering Research Institute, Aristotle University of Thessaloniki, PO Box 472, 54006 Thessaloniki, Greece
(Received 20 November 1996)*

A systematic investigation of the phase separation behaviour of aqueous low molecular weight PNIPA solutions was carried out in order to quantitatively investigate the effect of measurement conditions on the reported phase separation temperatures in relation to three techniques, namely, differential scanning calorimetry, optical cloud point and u.v. turbidimetry. The PNIPA concentration was varied in the range 0.5–22 wt%. All three techniques yielded comparable phase separation temperatures, independently of the transition kinetics, provided that the time scale of the experiments is large enough to ensure close to equilibrium conditions. © 1997 Elsevier Science Ltd.

(Keywords: lower critical solution temperature; poly(N-isopropylacrylamide); phase separation)

Introduction

The nature of interaction between polymeric molecules and solvents, especially for systems showing phase separation upon heating, has been the subject of a large number of experimental and theoretical investigations. The liquid–liquid phase diagram at constant pressure of binary polymer solutions is usually determined by plotting the temperature of incipient phase separation (e.g. cloud point) as a function of the overall polymer concentration, thus obtaining the cloud point curve. The minimum in the cloud-point curve is called the precipitation threshold (or LCST temperature), since it denotes the extreme temperature at which phase separation can occur at all.

Knowledge of the cloud point curve has enabled ingenious applications of thermoreversible phase-separating systems such as aqueous poly(N-isopropylacrylamide) (PNIPA) solutions for controlled drug delivery, enzyme immobilization and separation processes^{1–5}. For instance, membranes consisting of PNIPA or its copolymers were shown to possess thermoselective permeability towards a large range of water-soluble permeants⁶. Also, applications of PNIPA and PNIPA-based copolymers as sun-proofing or shading agents take advantage of their ability to serve as a temperature switch due to the optical changes induced in the polymeric solutions as their temperature exceeds the cloud point^{7,8}.

The phase separation behaviour of PNIPA aqueous solutions has been investigated in the literature by a wide variety of experimental techniques, including i.r. spectroscopy and pH measurements, ¹H n.m.r. spectroscopy, viscometry, light scattering, fluorescence, calorimetry, u.v. turbidimetry and visual observation of macroscopic phase separation. I.r. spectroscopy provides information on the molecular level and on possible inter- and intra-

molecular interactions between functional groups, and has supported the view that the structure of water is different around a PNIPA solute molecule as compared to the bulk aqueous medium^{9,10}. N.m.r. is sensitive to the local structural differences of the polymeric chains and has revealed the existence of a discontinuous transition in the relaxation times at the LCST¹¹. Viscometry detects the hydrodynamic consequences of aggregation, namely a decreasing viscosity with increasing temperature, and has revealed that PNIPA possesses a flexible coil conformation approaching theta state as the temperature is increased towards the LCST^{12,13}. Light scattering has the ability to monitor concentration fluctuations on a spatial scale of approximately 1000 Å and has been used to detect the collapse of single PNIPA chains at a temperature lower than that of macroscopic phase separation^{14,15}. An increased spatial resolution of the measurements has been reported for neutron and X-ray scattering and fluorescence techniques, although the latest requires the use of a probe either in free solution or covalently bound to PNIPA in order to ascertain details of the polymer solution behaviour¹⁶. Solution calorimetry provides thermodynamic parameters that lend insight into the forces responsible for the phase separation and measured transition enthalpies consistent with the loss of approximately one hydrogen bond per PNIPA repeating unit^{14,17}. U.v. turbidimetry can be regarded as the more automated counterpart of the classical visual observation of macroscopic phase separation, although it may suffer complications arising from variations in precipitated aggregate sizes and settling of precipitates¹⁸.

The main objective of this study was to quantitatively investigate the effect of measurement conditions on the reported phase separation temperatures for both the calorimetric and u.v. turbidimetry techniques. Cloud point temperatures are reported for aqueous solutions of PNIPA of a relatively low molecular weight over a wide range of PNIPA concentrations. The results are in good agreement to optical cloud point measurements and

* To whom correspondence should be addressed

reveal a rather significant effect of concentration on the cloud point.

Experimental

Polymerization. N-Isopropylacrylamide (NIPA) monomer (Eastman Kodak Co.) was dried in vacuum for 2 h prior to use. It was free-radically polymerized in a benzene solution (10% w/v) with 1 mol% azoisobutyronitrile (Aldrich Chemicals Co.) as the initiator at 50°C under a nitrogen atmosphere. Subsequently, the solvent was evaporated and the polymer was dissolved in acetone, precipitated in hexane and dried in a vacuum oven. The unfractionated polymer was used for all measurements. A number average molecular weight of $\bar{M}_n = 9000$ was estimated for PNIPA from the intrinsic viscosity of polymer solutions in water at 20°C using the Mark-Houwink-Sakurada equation reported by Fujishige¹⁹:

$$[\eta] = 14.5 \times 10^{-2} \bar{M}_n^{0.50}$$

Preparation of solutions. Samples for thermal analysis and cloud point measurements were prepared either by dissolution of known PNIPA quantities in distilled water in an ice water bath, or by dilution of a 25 wt% stock solution of PNIPA. Since no bactericide was used, the maximum allowable storage time of PNIPA solutions for the present investigation did not exceed one week. The actual PNIPA concentration was determined by using a special sample handling thermogravimetric analysis (t.g.a.) technique yielding the weight fraction of water in the solutions. For those samples prepared by dissolving the weighted amounts of 'dried' PNIPA, a large discrepancy (in some cases as much as 40%) was observed between the nominal and actual solution concentrations, possibly due to the high hydrophilicity of PNIPA under storage conditions.

Thermal analysis (d.s.c.). The phase transition temperatures of the PNIPA solutions were measured by a Perkin Elmer DSC-7 differential scanning calorimeter. The samples were placed in sealed capsules in order to eliminate the possibility of water evaporation, and were scanned at 5°C min⁻¹ over the temperature range of the phase transition against an empty reference pan. The samples were initially heated from 0 to 70°C at a specified heating rate, followed by programmed cooling at the same rate immediately after heating. All the phase separation temperatures were measured as the maximum of the derivative of the heating thermogram. A correction of 1°C was required to the reported characteristic temperatures for the temperature offset associated to the scanning rate of 5°C min⁻¹²⁰. The enthalpies of phase separation were determined as the area under the corresponding endothermic peaks and were independent of the scanning rate.

Cloud point measurements (optical and u.v.). Optical cloud point measurements were carried out by immersing test tubes containing the aqueous PNIPA solutions in a water bath heated at a temperature rate of 0.2°C min⁻¹. The cloud point was determined as the temperature at which the first opaqueness appeared in the solution. The phase transition was also monitored by optical transmittance at 500 nm through a 1 cm sample

cell referenced against distilled water, using a Shimadzu 2100 UV-VIS spectrophotometer. The water-jacketed sample and reference cell holders were coupled with a Julabo HC30 programmable circulating bath adjusted at a heating rate of 0.2°C min⁻¹. A correction of about 0.5°C was required to the reported characteristic temperatures for the offset associated to the heating rate of 0.2°C min⁻¹. Cloud points were defined as the temperature corresponding to a 10% reduction in the original transmittance of the solution.

Results and discussion

The demixing/mixing behaviour of PNIPA solutions, as detected by d.s.c., was found to be a completely reversible process with an observed cooling hysteresis attributed to the restricted mobility of the phase separated polymer chains. The d.s.c. demixing curves were measured for a series of samples at different PNIPA concentrations. The measured peak heights and areas (expressed in Watts and Joules, respectively, per unit weight of solution) were found to increase with PNIPA concentration, whereas the transition width ($\Delta T_{1/2}$) remained almost constant (i.e. approximately 7°C). A half-width larger than 4°C was also reported by Schild and Tirrell¹⁷ for a low molecular weight PNIPA solution. As shown in Figure 1, the heat of demixing, expressed per unit weight of PNIPA in the solution, is independent of the polymer concentration. According to Privalov²¹ and Mabrey and Sturtevant²², this indicates a constant size of ca. 750 monomer repeating units for the cooperative chain segment associated with the phase separation of PNIPA solutions over the range of polymer concentrations investigated. A cooperative chain segment of this magnitude indicates that the process detected by d.s.c. involves the entire length of the PNIPA chain, in agreement to the observations of Schild and Tirrell¹⁷ for PNIPA of a comparable molecular weight. The endothermic heat of demixing of the aqueous PNIPA solutions was found to be ca. 32 J g⁻¹ of polymer, corresponding to 0.86 kcal mol⁻¹ of repeating unit. This transition enthalpy is in good agreement to the one reported by Fujishige *et al.*¹⁴ (i.e. 1.1 kcal mol⁻¹ of repeating unit). Schild and Tirrell¹⁷, on the other hand, calculated transition enthalpies of ca. 1.5 kcal mol⁻¹ of repeating unit for PNIPA having a wide range of molecular weights, but reported a quite low value of 0.3 kcal mol⁻¹ of repeating unit for PNIPA having a molecular weight comparable to the one used in the present investigation. The transition enthalpy calculated

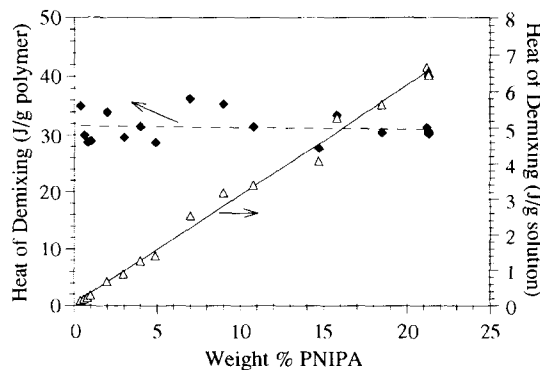


Figure 1 Heat of demixing of aqueous PNIPA solutions plotted as a function of polymer concentration

in the present study is consistent with a loss of 1 or less hydrogen bonds per repeating unit upon phase separation¹⁷. This is in agreement with the model of coil-globule transition followed by subsequent aggregation, of Heskins and Guillet¹² and Fujishige *et al.*¹⁴. Thus, as the temperature approaches the phase transition point, an abrupt conformational change occurs from a state of well-solvated random coils to a state of tightly packed globular particles. The relatively strong hydrogen bonds, formed between water molecules and N-H or C=O groups of PNIPA in dilute solutions, become weaker and break as the temperature is raised, resulting in an endothermic heat of phase separation. This initial stage is followed by the formation of polymer aggregates through interpolymeric hydrogen bonding.

In the literature, the characteristic phase separation temperatures have been defined either as the onset of the transition endotherm (i.e., the intersection of the baseline and the leading edge of the endotherm²³, or as the temperature at the peak of the thermogram¹⁷). However, the peak maximum is strongly affected by the weight of the sample placed in the sample pan, shifting to higher temperatures with increasing sample mass. The effect of the sample weight on the onset temperature is negligible. However, it should be pointed out that the onset temperature is very sensitive to the polydispersity of the polymer and especially, to the presence of a high molecular weight fraction. These problems can be overcome by defining the characteristic transition temperature as the temperature corresponding to the maximum of the first derivative of the observed thermogram. At equilibrium conditions (i.e., scanning rate equal to zero) this characteristic temperature is about 0.5°C higher than the onset temperature and 2°C lower than the temperature at the maximum of the phase separation endotherm.

Typical optical density curves are shown in *Figure 2* for a 9 wt% PNIPA solution as a function of the heating rate. The reduction of u.v. transmittance observed upon heating is a rather abrupt phenomenon, while the accompanying redissolution upon cooling at the same rate was observed to be a considerably slower process. Furthermore, the final % u.v. transmittance reached upon cooling was higher than the values measured for fresh PNIPA solutions, indicating that the system does not reach complete redissolution within the time frame of the u.v. turbidimetry experiments in the absence of mechanical stirring in the u.v. sample cell. As depicted in *Figure 2*, an increase of the heating rate from 0.02 to

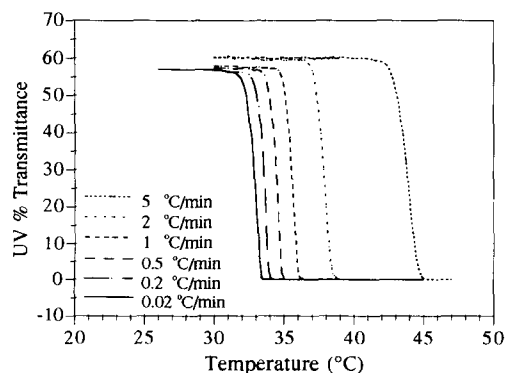


Figure 2 Effect of the scanning rate on the u.v. light transmittance curves of a 9 wt% aqueous PNIPA solution

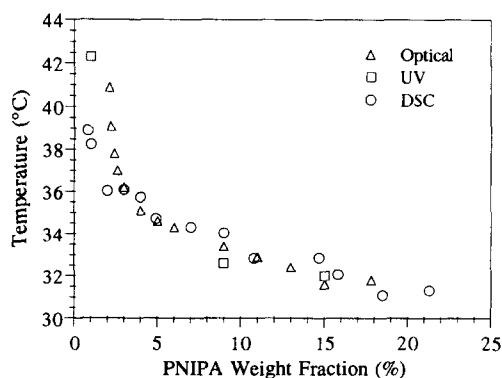


Figure 3 Phase separation temperatures obtained by d.s.c., u.v. and optical methods, plotted as a function of concentration of the aqueous PNIPA solutions

5°C min⁻¹ results in a shift of approximately 11°C of the u.v. transmittance curve. For the heating rate used in this study (i.e. 0.2°C min⁻¹) a temperature offset of 0.5°C was calculated based on the limiting equilibrium temperature. Usually, a sample is completely transparent when its transmittance, (I/I_0), is greater than 95% [i.e. (I/I_0) > 0.95], it becomes dim at (I/I_0) < 0.90, and finally becomes totally opaque when (I/I_0) < 0.75²⁴. In the present work, the temperature corresponding to a 10% reduction in transmittance was used as a measure of the cloud point. This characteristic value marks the onset of deviation from complete transparency (which would imply that the size of the polymeric moieties are much smaller than the wavelength of light used), i.e. the onset of deviation from homogeneity of the aqueous PNIPA solution.

Finally, in *Figure 3* the phase separation temperatures obtained by d.s.c., u.v. and optical methods are compared at close to equilibrium conditions. The reported u.v. and d.s.c. characteristic temperatures have not been corrected for the heating rate, since no similar correction could be applied to the optical cloud point data. It can be observed that if the time scale of the experiments is large enough to ensure close to equilibrium conditions, all three techniques yield comparable phase separation temperatures, independently of the transition kinetics over the investigated PNIPA concentration range. The characteristic temperatures obtained by d.s.c. at low PNIPA concentrations are slightly lower than those obtained by the cloud point measurement techniques (i.e., optical and u.v.). This might be attributed to the fact that the calorimetric technique detects the hydrogen bond disruption phenomena, which is actually the first stage of the phase separation process upon heating, whereas the cloud point techniques are sensitive only to the macroscopic phase separation phenomena (i.e., the formation of polymer aggregates), which is a much slower process at very low PNIPA concentrations²⁵.

In contrast to the results reported by Fujishige *et al.*¹⁴, the phase behaviour analysis of aqueous PNIPA solutions over the relatively wide concentration range from 0.5 to 22 wt%, has revealed a rather significant effect of concentration on the cloud point. Notice that the only complete experimental phase diagram reported in the literature for PNIPA is that obtained by Heskins and Guillet¹² using a composite of cloud point and centrifugation results. Their measurements were based

on one unfractionated polymer sample with $\bar{M}_w = 1\,000\,000$ and a polydispersity ratio of 3.5. The experimentally measured phase diagram¹² showed a rounded cloud point behaviour with a minimum at about 15 wt% PNIPA. The low concentration branch of the phase diagram depicted in *Figure 3* tends to reach a plateau at PNIPA concentrations in the range of 15–20 wt% and shows a significant concentration dependence especially at low PNIPA concentrations, i.e. smaller than 5 wt%.

Acknowledgement

We gratefully acknowledge the European Union for supporting this research under the BRITE/EURAM project BE 3287/89.

References

- Hoffman, A. S. and Dong, L. C., *Am. Chem. Soc. Symp. Ser.*, 1987, **350**, 236.
- Priest, J. H., Murrey, S. L., Nelson, R. J. and Hoffman, A. S., *Am. Chem. Soc. Symp. Ser.*, 1987, **350**, 255.
- Japanese Patent 149,691 (July 20, 1984), assigned to Lion Corp.
- European Patent Application DE-636904 (November 10, 1986), assigned to Henkel Corp.
- U.S. Patent 4,762,637 (August 9, 1988), assigned to M. Aronson, M. Lock, and E. Santos.
- Taylor, L. D. and Cerankowski, L. D., *J. Polym. Sci., Polym. Chem. Edn*, 1975, **13**, 2551.
- Irie, M., *Adv. Polym. Sci.*, 1990, **94**, 27.
- Gundlach, D. P. and Burdett, K. A., *J. Appl. Polym. Sci.*, 1994, **51**, 731.
- Snyder, W. D. and Klotz, I. M., *J. Am. Chem. Soc.*, 1967, **97**, 4999.
- Scarpa, J. S., Mueller, D. D. and Klotz, I. M., *J. Am. Chem. Soc.*, 1967, **89**, 6024.
- Ohta, H., Ando, I., Fujishige, S. and Kubota, K., *J. Polym. Sci., Part B, Polym. Phys.*, 1991, **29**, 963.
- Heskins, M. and Guillet, J. E., *J. Macromol. Sci. Chem.*, 1968, **A2(8)**, 1441.
- Kubota, K., Fujishige, S. and Ando, I., *Polymer J.*, 1990, **22**, 15.
- Fujishige, S., Kubota, K. and Ando, I., *J. Phys. Chem.*, 1989, **93**, 3311.
- Kubota, K., Fujishige, S. and Ando, I., *J. Phys. Chem.*, 1990, **94**, 5154.
- Winnik, F. M., *Macromolecules*, 1990, **23**, 233.
- Schild, H. G. and Tirrell, D. A., *J. Phys. Chem.*, 1990, **94**, 4352.
- Cole, C., Schreiner, S. M., Priest, J. H., Monji, N. and Hoffman, A. S., *Am. Chem. Soc. Symp. Ser.*, 1987, **350**, 245.
- Fujishige, S., *Polymer*, 1987, **19**, 297.
- Strella, S. and Erhardt, P. F., *J. Appl. Polym. Sci.*, 1969, **13**, 1373.
- Privalov, P., *Pure Appl. Chem.*, 1976, **52**, 479.
- Mabrey, S. and Sturtevant, J. M., *Methods Membrane Biol.*, 1978, **9**, 237.
- Otake, K., Inomata, H., Konno, M. and Saito, S., *Macromolecules*, 1990, **23**, 283.
- Xiao, H., Jiang, M. and Yu, T., *Polymer*, 1994, **35**, 5523.
- Schild, H. G., Muthukumar, M. and Tirrell, D. A., *Macromolecules*, 1991, **24**, 948.