Formation of Colloidally Stable Phase Separated Poly(*N*-vinylcaprolactam) in Water: A Study by Dynamic Light Scattering, Microcalorimetry, and Pressure Perturbation Calorimetry

Antti Laukkanen,[†] **Lauri Valtola,**[†] **Françoise M. Winnik,**[‡] **and Heikki Tenhu***,[†]

Laboratory of Polymer Chemistry, PB 55, University of Helsinki, Helsinki, FIN-00014 HY, Finland, and Department de Chemistry and Faculty of Pharmacy, University of Montreal, CP 6128 succursale Centre-Ville, Montreal, QC, Canada H3C 3J7

Received August 4, 2003; Revised Manuscript Received January 14, 2004

ABSTRACT: The effect of temperature on aqueous solutions of poly(*N*-vinylcaprolactam) (PVCL) samples of molecular weights ranging from 21 000 to 1.5×10^6 g mol^{-1} was monitored by dynamic light scattering (DLS), high-sensitivity microcalorimetry (HS DSC), and pressure perturbation calorimetry (PPC) from 10 to 80 °C. The polymer was soluble in cold water and underwent phase separation at $T_{CP} \sim 31-38$ °C, depending on the molecular weight. The phase transition was endothermic, with an enthalpy change of 4.4 ± 0.4 kJ mol^{-1}. Stable particles of average diameters 80 nm (high molecular weight PVCL) and ~ 180 nm (low molecular weight PVCL) formed above the phase transition temperature. The coefficient of thermal expansion of PVCL in water (α_{pol}), determined by PPC, underwent a sharp decrease at the temperature corresponding to the onset of phase transition, then it passed through a maximum, and decreased continuously with increasing temperature. The stability of the particles formed in PVCL solutions kept at temperatures exceeding T_{CP} suggests that their surfaces possess a hydrophilic character. Results of microcalorimetric measurements carried out with solutions of PVCL in D_2O add further strength to this conclusion. The thermodynamic and volumetric changes associated with the phase transition of aqueous PVCL solutions are compared to those of aqueous solutions of poly(*N*-isopropylacrylamide) (PNIPAM), a polymer that also undergoes a phase transition in water at ~ 31 °C, and of poly(vinylpyrrolidone) (PVP), a polymer structurally related to PVCL, which is soluble in water at all the temperatures investigated here.

Introduction

Poly(*N*-vinylcaprolactam) (PVCL) is one of several nonionic water-soluble polymers that undergo heat-induced phase separation in water. Like poly(*N*-vinylpyrrolidone) (PVP), it has a repeat unit consisting of a cyclic amide, where the amide group nitrogen is directly connected to the hydrophobic polymer backbone (Figure 1). Thus, unlike thermosensitive poly(*N*-alkylacrylamides), it does not produce small amide derivatives upon hydrolysis. This feature, together with its overall low toxicity, high complexing ability, and good film-forming properties, enables its use in many industrial applications, in particular in the biomedical field.[1] Aqueous PVCL gels, as well, have attracted much attention, as they are nonionic, biocompatible, and reversibly thermosensitive near physiological temperature.[2] High-sensitivity microcalorimetry studies have revealed that aqueous PVCL gels undergo two heat-induced transitions: a low-temperature transition at 31.5 °C, attributed to a microsegregation of hydrophobic domains and a higher temperature transition around 37.5 °C, corresponding to the gel volume collapse itself.[3]

The phase transition of aqueous PVCL solutions has been investigated over the entire water/polymer composition domain. Highly concentrated PVCL solutions ($c > 50$ g L^{-1}) obey the "classical" Flory−Huggins miscibility behavior: in water/polymer mixtures the position of the critical point shifts to lower polymer concentration as the molecular weight of the polymer increases.[4] The phase separation of the PVCL solutions in the dilute regime ($c < 5$ g L^{-1}) has been the focus of several studies. Lau and Wu monitored by light scattering techniques the changes with temperature of the hydrodynamic radius (R_h) of high molecular weight PVCL in water in the very dilute regime ($c < 1$ g L^{-1}).[5] They noted that R_h decreases as the solution temperature is increased toward the phase separation temperature, indicating a contraction of the polymer chain. Aggregation of the chains, signaled by an increase in the scattering intensity, occurs at a temperature in the vicinity of 31 °C, which was defined by Lau and Wu as the lower critical solution temperature (LCST) of this polymer in water. Further insight into the water/PVCL interactions in solutions below and above the LCST is given in a recent IR spectroscopy study, in which the changes in hydrogen bonding of the amide groups and the hydration states of the alkyl moieties were scrutinized during the phase transition.[6] Added salts,[6] surfactants,[7,8] or cosolvent[6] all affect the phase transition of aqueous PVCL, either increasing or decreasing the

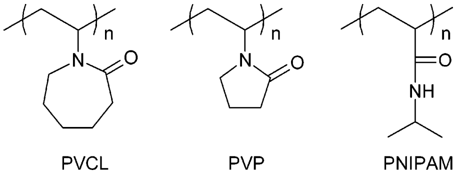

Figure 1. Chemical structure of poly(*N*-vinylcaprolactam), poly(*N*-vinylpyrrolidone), and poly(*N*-isopropylacrylamide).

[†] University of Helsinki.

[‡] University of Montreal.

* Corresponding author: tel +358-9-19150334, fax +358-9-19150330, e-mail heikki.tenhu@helsinki.fi.

10.1021/ma035124l CCC: $27.50

Table 1. Summary of the Reaction Conditions and Molecular Characteristics of the Product Polymers

sample	solvent	[VCL] (mol/L)	[initiator] (mmol/L)	temp (°C)	reaction time (h)	M_w (g/mol)	PDI
PVCL-1500	water[a]	1.08	7.28	70	20	1500 000	2.3
PVCL-1300	benzene[b]	1.08	7.03	35	68	1300 000	1.8
PVCL-330	benzene[b]	1.08	2.56	70	20	330 000	1.6
PVCL-30	toluene[b]	1.08	2.56	70	20	30 000	1.4
PVCL-21	2-propanol[b]	1.08	2.56	70	20	21 000	1.7

[a] Initiator VA-086. [b] Initiator AIBN.

LCST. Interestingly, it was observed in most cases that the effect of additives was opposite to their influence on the phase transition temperature of aqueous solutions of poly(*N*-isopropylacrylamide) (PNIPAM) (Figure 1), another nonionic water-soluble polymer with a cloud point of 31−32 °C in water.[9] For example, whereas addition of methanol (MeOH) to aqueous PNIPAM triggers a decrease of the LCST when MeOH < 55 vol %, followed by a sharp increase of the LCST for 55 vol % < MeOH < 65%,[10] it hardly affects the LCST of PVCL aqueous solutions up to a 40% volume content.[6] Such strikingly different macroscopic effects result from profound differences in the hydration state of PNIPAM and PVCL.

There are only a few techniques sensitive to solute hydration in dilute aqueous solutions. High-precision compressibility measurements by acoustic techniques give access to solute volumetric parameters, as demonstrated in studies of protein and amino acid aqueous solutions.[11] Kujuwa and Winnik reported recently that the volumetric properties of dilute PNIPAM solutions can be derived easily from pressure perturbation calorimetry (PPC) results, a technique which measures the heat absorbed or released by a solution due to a sudden pressure change at constant temperature.[12] This heat can be used to calculate the coefficient of thermal expansion of the solute and its temperature dependence.[13] The technique has been exploited to obtain the changes in the volume of the solvation layer around proteins before and after unfolding[14] and to monitor the volume changes accompanying the pretransition and transition of phospholipid bilayers.[15]

We present here the results of a study by PPC of the phase transition of aqueous solutions of PVCL samples of varying molecular weights. Measurements were carried out with solutions of PVCL in H_2O and in D_2O to assess the relative importance of solvent/polymer hydrogen bonds and polymer/polymer hydrophobic interactions. The two solvents are chemically identical, yet their physical properties differ significantly.[16] The differences between H_2O and D_2O are believed to stem from differential energetics of intermolecular hydrogen bonds. The lengths of hydrogen bonds in the two liquids are about the same, but a “hydrogen” bond in D_2O is about 5% stronger than a hydrogen bond in H_2O. Overall, D_2O is a “more structured” liquid than light water.

The same PVCL samples were analyzed also by standard microcalorimetry, which yields the temperature and the enthalpy of the phase transition, and by temperature-dependent dynamic light scattering (DLS), which measures the changes in the size of a polymer chain and of the polymer aggregates formed upon heating. Taken together, the results of the PPC, DLS, and microcalorimetry experiments suggest a description of the PVCL/water interactions which will be compared to the currently accepted view of the phenomena at play in aqueous PNIPAM solutions.

Experimental Section

Materials. *N*-Vinylcaprolactam (VCL, Aldrich Chemicals) was purified by recrystallization from benzene. 2,2′-Azobis(isobutyronitrile) (AIBN, Aldrich Chemicals) was purified by recrystallization from methanol. 2,2′-Azobis[2-methyl-*N*-(2-hydroxyethyl)propionamide] (VA-086, Wako Chemicals) was used as received. Poly(*N*-vinylpyrrolidone) (Aldrich Chemicals) had a molecular weight of 1.3×10^6 g mol^{-1}, as determined by static light scattering. Deionized water was obtained from a Elgastat UHQ-PS water purification system. Deuterium oxide (99.9%) was purchased from Euriso-top. Tetrahydrofuran (THF, HPLC grade, Rathburn), hexane (HPLC grade, Rathburn), benzene (99.7%, Reidel-de-Haen), toluene (99%, JT Baker), and 2-propanol (HPLC grade, Lab Scan) were used without further purification.

Polymerizations. Poly(*N*-isopropylacrylamide) (PNIPAM, M_v 300 000) was prepared as previously described.[17] Poly(*N*-vinylcaprolactam) samples were prepared by the following procedure. A solution of VCL in the selected solvent (see Table 1) was degassed with nitrogen for 30 min. It was heated to 70 °C, unless otherwise indicated. As soon as the polymerization temperature was reached, a solution of the initiator was injected into the solution. At the end of the polymerization, the mixture was cooled to room temperature, and the polymer was isolated by precipitation in hexane. The polymer was purified further by two reprecipitations from THF into hexane. In the case of PVCL-1500 it was necessary to dry the polymer in vacuo prior to reprecipitation. All polymers were purified further by extensive dialysis against water (7 days) and isolated by freeze-drying. The exact reaction conditions of the polymers are given in Table 1. The structure and purity of the polymers were ascertained by ^{1}H NMR spectroscopy with a 200 MHz Varian Gemini 2000 spectrometer: δ, (ppm, $CDCl_3$): 4.4 (1 H), 2.4 (2H), 2.4 (2 H), 1.2−2.0 (8H). The molecular weights of the polymers were determined by static light scattering. The molecular weight distributions of the polymers were determined by size exclusion chromatography using a Waters liquid chromatography system equipped with a Waters 2410 differential refractometer and three Styragel columms (HR2, HR4, HR6) kept at 30 °C and eluted with chloroform with a 0.8 mL min^{-1} flow rate. The molar mass data were determined using polystyrene molecular weight standards (Polymer Laboratories). The physical characteristics of the polymers are given in Table 1.

Methods: High-Sensitivity Differential Scanning Calorimetry (HS DSC). HS DSC measurements were performed on a VP-DSC microcalorimeter (MicroCal Inc) at an external pressure of ca. 180 kPa. The cell volume was 0.507 mL. The instrument response time was set at 5.6 s. Scans were performed from 10 to 100 °C at heating rates of 10, 20, 30, 60, and 90 °C h^{-1}. Prior to each scan, the sample was kept at 10 °C for 15 min. Data were corrected for instrument response time and analyzed using the software supplied by the manufacturer. The polymer concentration was 1.0 g L^{-1}, unless otherwise specified.

Pressure Perturbation Calorimetry (PPC). PPC measurements were performed on a VP-DSC microcalorimeter equipped with a pressure perturbation accessory (MicroCal Inc). The reference cell and sample cell volumes were identical (0.507 mL). The polymer concentration was 5.0 g L^{-1}. Control experiments were performed, namely water (sample cell) vs water (reference cell), H_2O vs D_2O, and D_2O vs D_2O. The PPC accessory of the VP-DSC instrument has been described in detail elsewhere.[13] It measures the volumetric properties of dilute polymer solutions through calorimetric heat changes caused by a sudden small pressure change above the polymer solution. Briefly, it applies a pressure of 500 kPa, then a pressure release to ambient pressure, to the sample which is kept at constant temperature. The temperature of the cell is kept constant by compensation of the heat change caused by the pressure jump. After equilibration, an upward pressure jump is performed. The heat peaks caused by the compression and decompression are opposite in sign but agree in absolute value. A large number of compression/decompression cycles are performed at different temperatures.

The coefficient of thermal expansion of a polymer solute in a solvent is obtained from eq 1

$$\alpha_{\mathrm{pol}} = \alpha_{\mathrm{solv}} - \frac{\Delta Q_{\mathrm{rev}}}{T \Delta P m_{\mathrm{pol}} \bar{V}_{\mathrm{pol}}} \qquad (1)$$

where α_{pol} and α_{solv} are the thermal expansion coefficients of the polymer and the solvent, respectively, ΔQ_{rev} corresponds to the heat consumed or released upon the small pressure changes, ΔP is the change in pressure, T is the temperature, $\bar{V}_{\mathrm{pol}}$ is the partial specific volume of the polymer, and m_{pol} is the mass of polymer in solution.[12,13]

The coefficient of thermal expansion, α_{pol}, of the polymer reflects the changes in the partial specific volume of the polymer and not simply the expansion of the intrinsic volume of the polymer chain. The partial specific volumes of the polymers were determined by an increment method based on the group contribution theory developed to estimate $\bar{V}$ of aqueous systems and estimated to be accurate within 2%.[18] Thus, for PVCL, $\bar{V} = 0.834$ cm^3 g^{-1}, and for PNIPAM, $\bar{V} = 0.894$ cm^3 g^{-1}. The same values were used for the corresponding monomers.

The change in volume of the solvation layer of the polymer (ΔV) during a phase transition is obtained by integration of the curve of the changes in the coefficient of thermal expansion with temperature (eq 2), assuming that ΔV is small compared to V, the intrinsic volume of the polymer.

$$\frac{\Delta V}{\bar{V}} = \int \alpha \, \mathrm{d}T \qquad (2)$$

Laser Light Scattering. A commercial light scattering system was employed to perform static light scattering (SLS) and dynamic light scattering (DLS) measurements. It consisted of a Brookhaven Instruments BI-200SM goniometer, a BI-9000AT digital correlator, and a LEXEL 85, 1 W laser operating at a 514.5 nm wavelength in the power range of 15–100 mW. DLS measurements were performed with a scattering angle of 90°. The temperature of the cell was controlled by a Lauda RC 6C thermostat. The time correlation functions were analyzed by the Laplace inversion program (CONTIN) and with the cumulants method. The cumulant analysis was used to estimate the polydispersity, μ_2/Γ^2, of the particles at 50 °C. The SLS data were treated using the Zimm's double extrapolation method. The specific refractive index increment (dn/dc) was measured with a Abbe 60/ED high-precision refractometer (Bellingham and Stanley, Ltd.) at a wavelength of 514.5 nm.

SLS measurements were carried out at 20 °C with solutions of PVCL-1200, PVCL-930, and PVCL-230 in THF and of PVCL-30 and PVCL-21 in methanol. Methanol and THF were selected to carry out the measurements since they are good solvents of the respective polymers. DLS measurements were carried out with aqueous polymer solutions at 50 °C. All solutions were kept at room temperature for 24 h prior to measurements. They were filtered through 0.45 μm filters (Millex, PVDF for aqueous solutions and Millex PTFE for solutions in organic solvents). For the kinetic measurements, polymer aggregation was induced by heating filtered solutions (2 mL, 0.10 g L^{-1}) placed in the light scattering cell to 50 °C and keeping the samples at 50 °C for 1 h prior to measurement.

Cloud Point Determinations. The cloud points of the polymer solutions were obtained by spectrophotometric detection (Shimadzu UV-1601PC spectrophotometer) of the changes in turbidity at the wavelength of 514.5 nm for polymer solutions (1 g L^{-1}) heated at a constant rate (30 °C h^{-1}) in the UV cell compartment. The cloud point temperature, T_{Cp}, was taken as the temperature of the onset of turbidity of the sample.

Table 2. Summary of DSC Results for PVCL with Various Molar Mass and PNIPAM in Water and in D$_2$O

sample	solvent	T_{CP}[b] (°C)	T_{onset} (°C)	T_{max} (°C)	ΔH (kJ mol^{-1})[c]
PVCL-1500	H_2O	31.0	30.9	33.1	4.4
PVCL-1300	H_2O	30.8	30.8	33.5	4.4
PVCL-330	H_2O	31.8	31.7	35.0	4.4
PVCL-330	D_2O	31.2	30.8	34.3	4.8
PVCL-30	H_2O	35.7	36.1	40.0	4.2
PVCL-21	H_2O	37.5	38.0	43.6	4.2
PNIPAM[a]	H_2O	31.8		33.7	5.9
PNIPAM[a]	D_2O	33.7		34.3	6.3

[a] Data from ref 12. [b] Cloud point temperature by turbidometry. [c] The unit is given in kilojoules per moles of monomer units.

Results

Preparation and Characterization of the Polymers. To prepare PVCL samples of varying molecular weights, N-vinylcaprolactam was polymerized in solvents of different chain transfer capacity with different initial molar ratios of monomer and initiator. The neutral initiator AIBN was employed in polymerizations carried out in organic solvents, whereas a water-soluble initiator was used in the polymerization of VCL carried out in water to obtain a sample of high molecular weight (Table 1). The molecular weights were determined by static light scattering and the molecular weight distributions were obtained from SEC measurements (Table 1). The Zimm plots are available in the Supporting Information.

Phase Transition of the Polymer in Water. Turbidity and Light Scattering Measurements. The fastest method to determine the cloud point of a polymer solution consists of measuring the changes in turbidity as the solution is heated at a constant rate. The temperature of turbidity onset, defined here as the cloud point temperature, T_{CP}, decreased with increasing PVCL molecular weight. The cloud point temperature of a PVCL-330 solution (1.0 g L^{-1}) was determined in light and heavy water: it was lower by ~0.5 °C in D_2O compared to H_2O (Table 2).

To assess the long-term stability of PVCL particles above the solution cloud point, we carried a series of DLS measurements of solutions preequilibrated at 50 °C. The apparent hydrodynamic radii, for samples kept at 50 °C for 1 h, ranged from 180 to 80 nm, the largest radius corresponding to the PVCL sample of low molecular weight. In all cases the size of the particle was far larger than the size of a single polymer chain in water at 20 °C. For instance, the polymers in Figure 2, PVCL-1300, PVCL-330, and PVCL-30, were measured in water at 20 °C, and the apparent mean R_{h} were 24, 15, and 4 nm, respectively (CONTIN analysis). Thus, the particles result from the aggregation of several collapsed polymer chains. The size distributions of the particles are rather narrow, especially in the case of particles formed by higher molecular weight polymers: μ_2/Γ^2 is 0.023, 0.048, and 0.067 for PVCL-1300, PVCL-330, and PVCL-30, respectively. The size distributions were monomodal in all cases. For additional information on correlation functions, see Figures S-1 and S-2 in the Supporting Information.

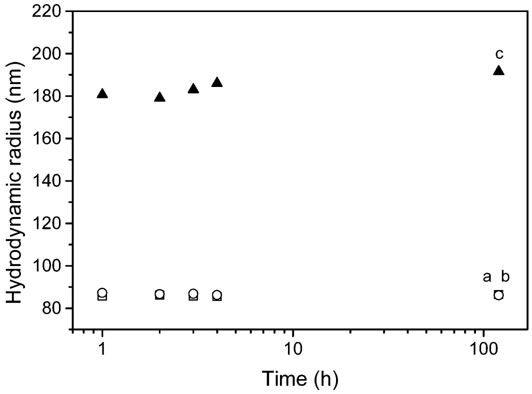

Figure 2. Time dependence of the hydrodynamic radius (R_h) for PVCL solutions kept at 50 °C: (a) PVCL-1300, (b) PVCL-330, (c) PVCL-30; polymer concentration: 0.1 g L^{-1}.

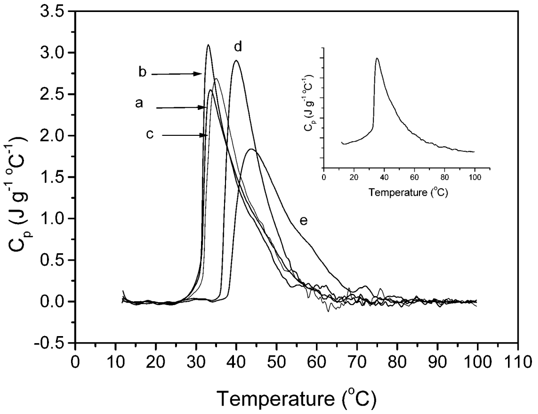

Figure 3. Microcalorimetric endotherms for aqueous solutions of PVCL samples: PVCL-1500 (a), PVCL-1300 (b), PVCL-330 (c), PVCL-30 (d), and PVCL-21 (e). Heating rate: 60 °C h^{-1}. The endotherm without baseline subtraction is shown for PVCL-330 in the inset. The negative change in C_p between temperatures 25 and 90 °C is -0.5 J g^{-1} °C^{-1}.

Once the particle is formed and the solution is kept at 50 °C for 1 h, the size remains constant. We did not observe any interparticle flocculation when the particles were monitored with DLS for several days (Figure 2). The colloidal stability of the aggregates formed upon heating of thermosensitive nonionic polymer solutions in water was observed also for dilute PNIPAM solutions.[19,20] However, the PNIPAM samples investigated were obtained by free radical polymerization initiated with a persulfate initiator. Thus, each PNIPAM chain carried a negative charge, which can account in part for the stabilization of individual globules.[19] A neutral initiator was used to prepare the PVCL samples monitored in our DLS study; therefore, electrostatic repulsion among polymer aggregates cannot account for their colloidal stability. Their stability may result from a balance between the interglobule van der Waals attraction, their size, according to Hamaker theory, which states that the attractive potential between two spheres scales with size,[21] and the steric stabilization provided by hydrophilic chains present on the outer surface of the particles.

High-Sensitivity Differential Calorimetry. The changes with temperature of the partial excess heat capacity C_p of aqueous solutions of several PVCL samples (1 g L^{-1}) are presented in Figure 3. The thermograms are endothermic, broad, and markedly asymmetric, with a sharp increase in heat capacity on the low-temperature side (onset of the transition, T_{onset}) and a gradual decrease of the heat capacity for temperatures higher than a maximum temperature $T_{\max}$. In the inset of Figure 3, a calorimetric trace is presented for PVCL-330. In this trace, the baseline was not subtracted. A negative change in heat capacity due to the transition can be detected. For all polymers the value of ΔC_p was -70 ± 20 J mol^{-1} °C^{-1}. A similar observation was also detected for cooling scans from 100 to 10 °C, although the sign of ΔC_p was opposite. A similar negative change in C_p has been observed also for PNIPAM (ΔC_p -63 J mol^{-1} K^{-1})[12] as well as for the phase transitions of various pluronic-type block copolymers.[22] Such a negative heat capacity change during the phase transition may be taken as an indication of diminished interaction between water molecules and polymer chains. Thermograms of similar shape were reported previously in studies of aqueous solutions (5 g L^{-1}) of PVCL samples of M_w 13 000 and 150 000 g mol^{-1} [6] and in a study of PVCL gels.[2] Note that the thermograms recorded for PVCL gels suspensions presented a shoulder on the low-temperature side,[3] which could not be detected in the PVCL solutions thermograms. Changing the concentration of the solution from 0.1 to 10 g L^{-1} did not affect the shape or position of the signal, except that the value of T_{onset} was higher in the thermogram of the most dilute sample (33.4 ± 0.1 °C vs 31.7 ± 0.1 °C, PVCL-330). A similar increase in the transition onset temperature was observed in a previous study of PVCL in the very dilute regime.[5] Varying the scanning rate from 10 to 90 °C/h had no effect on the shape of the thermograms. Therefore, the characteristic times of the transitions are shorter than those of the thermal equilibration of the cells. The reproducibility of the thermograms was demonstrated during the second and third heating at the same heating rate. Thus, the transition observed is completely reversible.

From the plots of the partial heat capacity of PVCL solutions vs temperature, one can extract three thermodynamic parameters: T_{onset}, $T_{\max}$, and ΔH, the enthalpy of the transition (Table 3). The values of T_{onset} and $T_{\max}$ follow the same trends as the values of T_{CP}: they decrease with increasing polymer molecular weights, and for a given polymer, they are slightly lower in D_2O compared to H_2O. We note, however, that thermograms recorded for polymer solutions in D_2O exhibit the same skewed shape as the thermograms of polymer solutions in H_2O, as exemplified in Figure 4 (top), where we show the HS DSC scans for solution of PVCL-330 in heavy and light water. The enthalpy of the transition was the same for all polymers. It was significantly higher than the value reported in the case of PVCL gels (2.2 kJ mol^{-1}).[3,23] The enthalpy of the transition was ~10% larger for solutions of PVCL in D_2O compared to H_2O.

Pressure Pertubation Calorimetry. PPC scans were carried out next with solutions of PVCL in H_2O and in D_2O, yielding the changes with temperature of the thermal expansion coefficient α_{pol} shown in Figure 4 (bottom), in the case of PVCL-330 in H_2O. The plot can be divided in four temperature ranges. Below T_{onset}, for 10 °C $< T <$ 31.7 °C, α_{pol} remains constant. It undergoes a sharp decrease, reaches a minimum for $T_{\mathrm{peak}} = 32.9$ °C, then increases abruptly with increasing temperature to reach a maximum value for $T \sim 45$ °C, and gradually decreases as the temperature further increases. PPC scans recorded with solutions of the same polymer in D_2O presented the same features, with

Table 3. Summary of PPC Measurements

sample	solvent	T_{peak} (°C)	$\Delta V/V_1$ (%)	$\Delta V/V_2$ (%)	$\alpha_{pol\ 10}$ (K^{-1})	$\alpha_{pol\ 30}$ (K^{-1})	$\Delta\alpha_{pol\ trans}{}^b$ (K^{-1})	$\alpha_{pol\ 80}$ (K^{-1})
PVCL-330	H_2O	32.9	−0.10	+0.50	0.94×10^{-3}	0.92×10^{-3}	0.15×10^{-3}	0.99×10^{-3}
PVCL-330	D_2O	32.0	−0.10	+0.57	1.02×10^{-3}	0.92×10^{-3}	0.10×10^{-3}	0.95×10^{-3}
PNIPAM[a]	H_2O	33.7	+1.01		0.72×10^{-3}	0.96×10^{-3}	0.52×10^{-3}	1.37×10^{-3}
PNIPAM[a]	D_2O	34.3	+1.32		1.56×10^{-3}	1.30×10^{-3}	-0.12×10^{-3}	1.16×10^{-3}
VCL	H_2O				1.37×10^{-3}	1.22×10^{-3}		1.31×10^{-3}
NIPAM	H_2O				0.53×10^{-3}	0.80×10^{-3}		1.20×10^{-3}

[a] Data from ref 12. [b] For PVCL $\Delta\alpha_{pol\ trans} = \alpha_{pol\ 60} - \alpha_{pol\ 15}$, and for PNIPAM $\Delta\alpha_{pol\ trans} = \alpha_{pol\ 50} - \alpha_{pol\ 15}$.

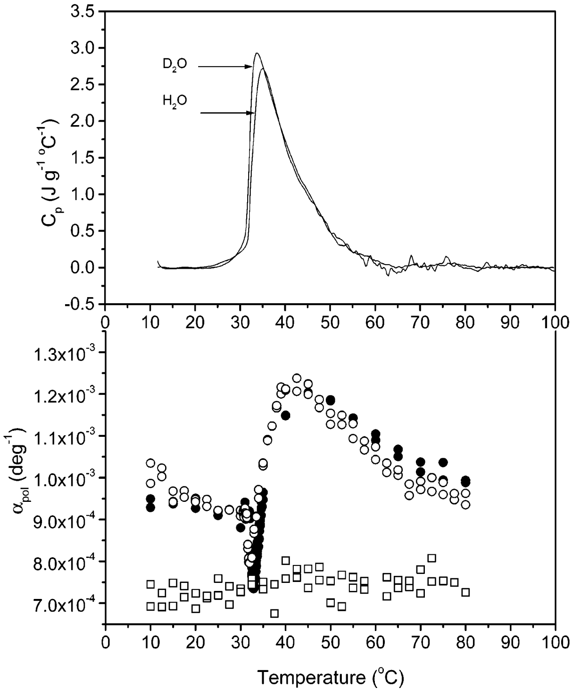

Figure 4. (top) Microcalorimetric endotherms for a solution of PVCL-330 in H_2O and in D_2O. Polymer concentration 1 g L^{-1}. (bottom) Temperature dependence of the coefficient of thermal expansion (α_{pol}) of PVCL-330 in H_2O (full circle) and in D_2O (open circle) and PVP in H_2O (open square); polymer concentration: 5 g L^{-1}.

slight differences in the temperatures of the minimum and maximum of α_{pol}, which correspond to the slight shifts of T_{onset} and T_{max} already noted in the DSC scan. Also presented in Figure 4 (bottom) is the PPC trace recorded for a solution in H_2O of poly(vinylpyrrolidone) (PVP, Figure 1), a polymer with a repeat unit similar in structure to that of PVCL but which does not undergo phase separation in water below 170 °C.[24] The coefficient of thermal expansion of this polymer remains constant from 10 to 80 °C. Values of α_{pol} of PVCL in H_2O and D_2O at 10, 30, and 80 °C, as well as $\Delta\alpha_{pol}$(trans), the difference of the polymer coefficient of thermal expansion before and after the transition, are listed in Table 3. The observed changes in α_{pol} of PVCL support the conclusion from the IR spectroscopic studies by Maeda et al. that the phase separation of a PVCL solution is accompanied by changes in the hydration states and/or conformation of the polymer chain.[6]

The changes in volume of the solvation layer of the polymer (ΔV) corresponding to the collapse of the chain and chain aggregation during the phase transition can be extracted from PPC scans, by integration of the changes in α_{pol} as a function of temperature, assuming that the intrinsic volume occupied by a polymer chain remains constant. The volume change, expressed as $\Delta V/\bar{V}$ in percent of the partial volume of the polymer (eq 2), is taken usually as the area defined by the peak of the PPC scan and a progress baseline drawn from projections of the baselines in the pretransition and posttransition regions.[13] Applying this method to a PPC scan of PVCL in water (Figure 4) yields a value of $\Delta V/\bar{V} = -0.10\%$ for the sharp negative transition at 32.9 °C. However, the PPC trace recorded for PVCL solutions may be viewed as consisting of two parts: the sharp signal ($\Delta V/\bar{V} = -0.10\%$) and a broader signal ($\Delta V/\bar{V} = +0.50\%$) in the low- and high-temperature ranges of the transition, respectively. This data analysis is supported by the asymmetry of the DSC trace (Figure 4, top), which may be interpreted as the overlap of two phenomena—first the collapse of the chains, then aggregation of collapsed chains, each phenomenon characterized by a change in the polymer hydration volume. This two-step phase transition mechanism was considered also by Kirsh et al. in their viscometry and fluorescence study of PVCL aqueous solutions.[25] The shoulder detected on the low-temperature side of the endotherm of PVCL gels DSC scans gives further support to our analysis of the PPC data.[2]

On the basis of the changes in the water/polymer interactions taking place as a PVCL solution is heated from 15 to 80 °C, we propose the following interpretation of the PPC data. Below the phase transition temperature, the PVCL chains are solvated to the greatest extent, implying a large number of contacts between polymer groups and water molecules, a fact confirmed by IR spectroscopy studies of cold (5 °C) PVCL solutions.[26] Other weak forces also occur in the water/PVCL system, namely dipole/dipole interactions between the polar amide groups, dispersion forces between the methylene groups of the caprolactam rings in the chair conformation. The hydration of the hydrophobic methylene groups is expected to weaken mildly, as the temperature increases within this range.[27,28] Several events take place at the phase transition. Contacts between water molecules and the hydrophobic groups of the polymer become thermodynamically less favorable than contacts between the hydrophobic groups themselves. As a result, the polymer chains tend to collapse into a conformation in which methylene groups are mostly shielded by hydrophilic polar groups of the polymer, resulting in a decrease of the solvent accessible surface area (ASA) and, consequently, of the hydration volume, detected in the PPC experiment as a small negative signal. Because of topological constraints, all the hydrophobic groups cannot be shielded from surrounding water molecules, and eventually, with further increase of the temperature, collapsed chains tend to aggregate, releasing bound water molecules, a mechanism responsible for the positive volume change detected by PPC.

Discussion

As noted in the Introduction, aqueous solutions of the two nonionic polymers PVCL and PNIPAM exhibit a

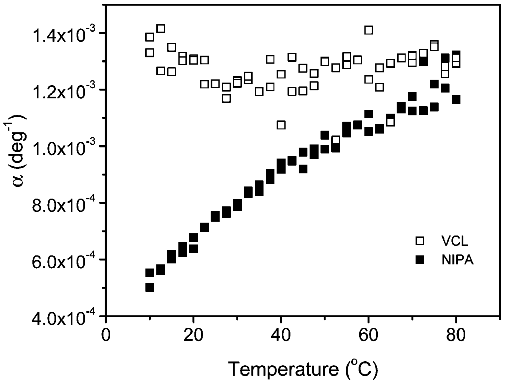

Figure 5. Temperature dependence of the coefficient of thermal expansion (α) of vinylcaprolactam (VCL) in H_2O (open square) and of *N*-isopropylacrylamide (NIPAM) in H_2O (full square).

phase transition at a temperature of ~31 °C. This similarity between the LCST of solutions of the two polymers masks, in fact, significant differences in the thermodynamic and molecular mechanisms underlying the phase transition. A systematic comparative study of the solutions of the two polymers is beyond the scope of this report; nonetheless, we contrast here aspects of the transition mechanisms that can be derived from the DSC and PPC results reported here and in a previous study of PNIPAM solutions.[12]

The existence of an LCST is evidence of catastrophic changes, with solution temperature, of the hydration of the polymer chains. The partial volume of a solute is highly sensitive to temperature-induced changes in the organization of water molecules around the solute and permits one to differentiate hydrophobic groups, which act to increase the amount of ordered structure in water and hydrophilic groups which tend to decrease the ordered structure of water.[29] Thus, to gain more insight into the state of hydration of PVCL and PNIPAM, we determined the temperature dependence of α for each monomer (Figure 5). The value of α is positive for both NIPAM and VCL in water, but while α_{VCL} remains nearly constant from 10 to 80 °C, α_{NIPAM} values increase with temperature to reach values similar to α_{VCL} for $T > 70$ °C. The fact that α_{NIPAM} becomes progressively more positive as temperature increases reflects the release of ordered water molecules to bulk water. Similar trends were reported for the changes with temperature of α values of amino acid with hydrophobic side chains, such as alanine or valine.[13] In contrast, α values of hydrophilic amino acids, such as asparagine, are large and positive at low temperature and decrease with increasing temperature, a pattern characteristic of structure breakers. The α values of amino acids carrying aromatic groups, such as tryptophan and phenylalanine, are positive at all temperatures, remaining nearly constant with temperature, in agreement with the fact that aromatic groups are poor water structure makers compared to alkyl groups.[30] Since α values of VCL are nearly constant with temperature (Figure 5), it must be concluded that this solute is a rather poor structure maker, at least compared to NIPAM.

How are the difference in the "philicities" of NIPAM and VCL reflected in the volumetric properties of their respective polymers? The DSC and PPC scans recorded for PNIPAM and PVCL solutions in H_2O are presented in Figure 6, and important volumetric and thermodynamic parameters of PNIPAM are listed in Table 3 (solutions in light and heavy water). We note that the endotherm relating the phase transition of a PNIPAM solution is sharp, with a width at half-peak of 2.0 °C and the transition temperature for a solution in D_2O is shifted to *higher* temperature by about 0.5 °C compared to its value in H_2O (Table 3). As noted earlier, in the case of PVCL solutions, the transition occurs at a slightly *lower* temperature for solutions in D_2O compared to H_2O. The exact magnitude of the shift is not as easily determined than for PNIPAM solutions, given the breadth of the PVCL endotherm. Turning to the PPC scans recorded for PVCL and PNIPAM (Figure 6, bottom), we observe that the magnitude of the changes in α_{pol} values, and consequently of $\Delta V/\bar{V}$, are significantly larger for solutions of PNIPAM compared to PVCL. Also, the "dip" in the α_{pol} vs temperature plot noticed in the PVCL PPC traces near T_{onset} does not appear in the trace corresponding to the PNIPAM solution. The large volume change that accompanies the phase transition of PNIPAM in water reflects the expulsion of polymer bound water molecules into bulk water. The fact that this volume change is significantly larger for PNIPAM solutions (1.01%) compared to PVCL solutions (0.50% for the positive peak) can be taken as a consequence of the poorer water structuring properties of VCL, compared to NIPAM, signaled by the differences between the PPC scans of the two monomers (Figure 5).

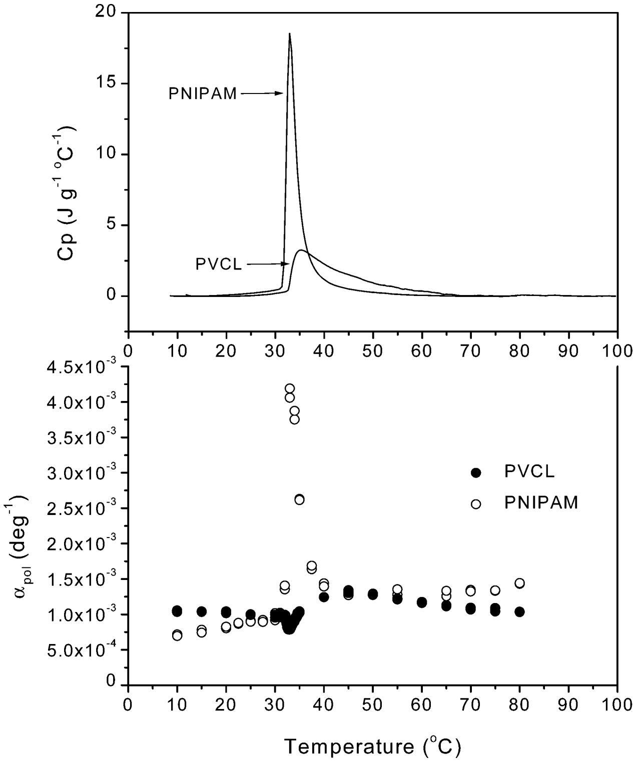

Figure 6. (top) Microcalorimetric endotherms for solution of PVCL-330 and PNIPAM in H_2O; polymer concentration: 1 g L^{-1}. (bottom) Temperature dependence of the coefficient of thermal expansion (α_{pol}) of PVCL-330 (full circle) and PNIPAM (open circle) in water; polymer concentration: 5 g L^{-1}.

Conclusions

High-sensitivity differential calorimetric studies of aqueous solutions of PVCL indicate that in the dilute regime the phase transition temperature increases with decreasing PVCL molecular weight while the enthalpy of the transition does not depend on molar mass. The endotherm corresponding to the phase transition has an asymmetric shape, characterized by a sharp increase in heat capacity at the onset of the transition with a more gradual decrease in heat capacity for temperatures higher than T_{max}. Colloidally stable PVCL particles, detected by dynamic light scattering measurements, are formed above the solution cloud point temperature. The changes in the polymer hydration layer during the phase transition were monitored by pressure perturbation calorimetry. Polymer-bound water molecules are released to the bulk solvent as the polymer chains collapse, generating particles stabilized against further aggregation via hydrophilic surfaces, in agreement with the negative slope of the changes in the thermal expansion coefficient of PVCL with increasing temperature.

Acknowledgment. The work was supported by the Academy of Finland and INTAS project (INTAS-01-607). We thank Dr. P. Kujawa (Université de Montréal) for helpful comments on the interpretation of PPC data.

Supporting Information Available: Correlation functions of the phase separated PVCL aggregates and Zimm plots of the polymers in THF. This material is available free of charge via the Internet at http://pubs.acs.org.

References and Notes

(1) Kirsch, Y. E. *Prog. Polym. Sci.* **1993**, *18*, 519.
(2) Makhaeva, E. E.; Thanh, L. T. M.; Starodubtzev, S. G.; Khokhlov, A. R. *Macromol. Chem. Phys.* **1996**, *197*, 1973.
(3) Mikheeva, L. M.; Grinberg, N. V.; Mashkevich, A. Y.; Grinberg, V. Y.; Thanh, L. T. M.; Makhaeva, E. E.; Khokhlov, A. R. *Macromolecules* **1997**, *30*, 2693.
(4) Meeussen, F.; Nies, E.; Berghmans, H.; Verbrugghe, S.; Goethals, E.; Du Prez, F. *Polymer* **2000**, *41*, 8597.
(5) Lau, A. C. W.; Wu, C. *Macromolecules* **1999**, *32*, 581.
(6) Maeda, Y.; Nakamura, T.; Ikeda, I. *Macromolecules* **2002**, *35*, 217.
(7) Makhaeva, E. E.; Tenhu, H.; Kohkhlov, A. R. *Macromolecules* **1998**, *31*, 6112.
(8) Qiu, Q.; Somasundaran, P.; Pethica, B. A. *Langmuir* **2002**, *18*, 3482.
(9) Heskins, M.; Guillet, J. E. *J. Macromol. Sci., Chem. A2* **1968**, 1441.
(10) Winnik, F. M.; Ringsdorf, H.; Venzmer, J. *Macromolecules* **1990**, *23*, 2415.
(11) See for example: Likhodi, O.; Chalikian, T. V. *J. Am. Chem. Soc.* **1999**, *121*, 1156 and references therein.
(12) Kujawa, P.; Winnik, F. *Macromolecules* **2001**, *34*, 4130.
(13) Lin, L.-N.; Brandts, J. F.; Brandts, M.; Plotnikov, V. *Anal. Biochem.* **2002**, *302*, 144.
(14) Ravindra, R.; Winter, R. *Chem. Phys. Chem.* **2003**, *4*, 359.
(15) Heerklotz, H.; Seelig, J. *Biophys. J.* **2002**, *82*, 1445.
(16) Nemethy, G.; Sheraga, H. A. *J. Chem. Phys.* **1964**, *41*, 680.
(17) Ringsdorf, H.; Venzmer, J.; Winnik, F. M. *Macromolecules* **1991**, *24*, 1678.
(18) Zana, R. J. *J. Polym. Sci., Polym. Phys. Ed.* **1980**, *18*, 121.
(19) Chan, K.; Pelton, R.; Zhang, J. *Langmuir* **1999**, 4018.
(20) Gorelov, A. V.; Du Chesne, A.; Dawson, K. A. *Physica* **1997**, *A240*, 443.
(21) Adamson, A. W.; Gast, A. P. In *Physical Chemistry of Surfaces*, 6th ed.; John Wiley & Sons: New York, 1997; Chapter 6.
(22) Beezer**,** A. E.; Loh, W.; Mitchell, J. C.; Royall, P. G.; Smith, D. O.; Tute, M. S.; Armstrong, J. K.; Chowdhry, B. Z.; Leharne, S. A.; Eagland, D.; Crowtherg, N. J. *Langmuir* **1994**, *10*, 4001.
(23) This discrepancy may be attributed to difficulties in assigning a baseline to perform the integration of the endotherm (see Figure 1 in ref 2) or may reflect uncertainties in the exact determination of the PVCL gel concentration.
(24) Kirsh, Y. E. In *Water Soluble Poly-N-Vinylamides*; John Wiley & Sons: Chichester, 1998; Chapter 3.
(25) Kirsh, Y. E.; Sus', T. A.; Karaputadze, T. M.; Kobyakov, V. V.; Sinitzina, L. A.; Ostrovskii, S. A. *Vysokomol. Soedin.* **1979**, *21A*, 2734.
(26) Kirsh, Y. E.; Yanul, N. A.; Kalninsh, K. K. *Eur. Polym. J.* **1999**, *35*, 305.
(27) Ben-Naim, A. In *Hydrophobic Interactions*; Plenum Press: New York, 1980.
(28) Tanford, C. In *The Hydrophobic Effect: Formation of Micelles and Biological Membranes*; Wiley: New York, 1973.
(29) Hepler, L. G. *Can. J. Chem.* **1969**, *47*, 4613.
(30) Kauzmann, W. *Adv. Protein Chem.* **1959**, *14*, 1.

MA035124L