polymer

Synthesis of *N*-vinylcaprolactam polymers in water-containing media

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Abstract

Poly(*N*-vinylcaprolactam) (PNVCl) is a polymer possessing a lower critical solution temperature (LCST) in aqueous solutions. To the best of our knowledge, we report the first synthesis of PNVCl in water-containing media, namely in DMSO/water mixtures with as low a DMSO concentration as 10% (v/v) using a pair persulphate/tertiary amine as the redox initiator. The polymerization was carried out in three ways: (i) in homogeneous system at 20°C (below LCST); (ii) as precipitation polymerization at 65°C (above LCST for the given DMSO/water compositions); and (iii) cryogenically at −20°C. The polymer MW distribution and tendency to segregate from solution and form a concentrated polymer phase depended on the solvent composition and polymerization temperature. PNVCl synthesized at 65°C had the largest fraction of high-molecular-weight polymer and the strongest tendency for temperature induced phase separation. Molecular-weight characteristics of the polymers obtained were evaluated with size-exclusion chromatography. Temperature-dependent solution behaviour of the samples was investigated with a thermoturbidimetric technique. Thermodynamic parameters of the temperature-induced phase separation were measured with high-sensitive differential scanning calorimetry. The synthetic methods developed are of interest for the preparation of *N*-vinylcaprolactam copolymers with thermally unstable co-monomers or co-monomers insoluble in organic solvents, as well as for the synthesis of chemically cross-linked PNVCl hydrogels. © 2000 Elsevier Science Ltd. All rights reserved.

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1. Introduction

Poly(*N*-vinylcaprolactam) (PNVCl) is one of the water-soluble polymers that possess a lower critical solution temperature (LCST) in aqueous milieu. Other known examples of similar macromolecular substances are *N*-alkylated poly(acrylamides) [1] (poly(*N*-isopropylacrylamide) is the most well studied among them), methylcellulose [2], poly(methyl vinyl ether) [3] and block co-polymers of ethylene oxide [4]. In recent years these polymers, as well as the hydrogels on their basis, are attracting increasing interest in biotechnological and biomedical areas [5–7]. In this regard, PNVCl exhibits valuable qualities allowing the usage of this polymer for the encapsulation of enzymes and whole cells [5,8].

The initial monomer for the preparation of PNVCl, i.e. *N*-vinylcaprolactam (NVCl), is an organo-soluble amphiphilic substance, which is dissolved in both non-polar and polar organic media, but is a very poor soluble substance in the aqueous ones. Therefore, the solution syntheses of PNVCl are routinely carried out in the solvents like benzene [9,10], isobutanol [11], or isopropanol [12], using the free radical initiation at, as a rule, elevated temperatures. The bulk [13,14] and microemulsion [9] polymerizations of NVCl were also reported. In the latter cases the synthesis was performed at the temperatures higher than the melting point of NVCl (∼35°C), that is, in fact, in the monomer melt. At the same time, the necessity to accomplish PNVCl synthesis in aqueous media exists, especially for the preparation of copolymers of NVCl with organo-insoluble (or poor-soluble) co-monomers or in the case of thermally unstable ones, and also for the formation of chemically cross-linked PNVCl hydrogels, when they are destined for the entrapment-type immobilization of biologically active matter similar to enzymes and even cells. Usually, in similar cases, because of the requirement of moderate or low temperatures, redox initiating systems are routinely used for the generation of primary radicals (more

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exactly, ion-radicals) instead of high-temperature initiators like benzoylperoxide or azoisobutyronitrile, which were implemented for the NVCl polymerization in organic media indicated above. For this reason, in this study we have tried to resolve the problem of the synthesis of *N*-vinylcaprolactam polymers in water-containing solvents and also with the use of a redox initiator, namely, with a well-known pair: inorganic persulphate/tertiary amine.

2. Experimental

2.1. Materials

The following chemicals were used in the work. *N*-vinyl-caprolactam was a generous gift from Gunnar Nord (ISP Norden AB, Sweden). The monomer contained some admixtures (TLC data, "Silufol" plates, Cavalier, Czech Republic); the purification of NVCl was accomplished by dissolution in benzene, refluxing with powdered active charcoal, filtration and crystallization of the target monomer by the addition of hexane. The product thus obtained (gross transparent crystals) had the melting point of 34–35°C (vs. lit. T_m 34.5°C) [13] and showed virtually theoretical results of elemental analysis.

Ammonium persulphate (APS) and L-tryptophan were obtained from Serva (Germany); *N,N,N′,N′*-tetramethyl-ethylenediamine (TMEDA) from Reanal (Hungary) was refined by the distillation in vacuo (29–32°C/10 mm Hg). Blue dextran was from Loba Chemie (Austria). DMSO ("chemically pure" grade, Reakhim, Russia) was additionally purified by the freezing-out. All aqueous solutions were prepared with a deionized water.

2.2. Methods

2.2.1. Synthesis of PNVCl

(i) *In DMSO solution:* Initial monomer solution contained 1 g of NVCl per 20 ml of DMSO, this corresponded to the monomer concentration of 5% ((w/v), and further on throughout the paper for the solutes concentration). The solution was bubbled with an air-free argon for 15 min, then 0.04 ml of TMEDA and 0.04 g of APS were added. The reaction vial was immediately filled with argon, tightly stoppered and immersed in the chamber of ultrathermostat U 10 (MLW, former GDR), where the temperature was already set to either 20 or 65°C. Incubation of the samples was performed for, respectively, 18 or 3 h. Then the reaction solution was cooled till room temperature, put into a cellophane sack (Reakhim, Russia) and dialysed for 72 h against 100-fold excess of deionized water; the water was exchanged every 24 h. The polymer thus purified from the substances with molecular weight less than ca. 30 kDa (the cut-off limit for the cellophane used) was further isolated via freeze-drying and then dried up to a constant weight in a vacuum-dessicator over the water-free $CaCl_2$ granules.

(ii) *In water–DMSO mixed solvents:* The weighed amount of NVCl was initially dissolved in a volume of DMSO, which should correspond to the amount of this solvent in the final water-rich reaction media (either 10 or 20% ((v/v) and further on throughout the paper for the concentration of components of the mixed solvents) of DMSO counting for the total volume of the liquid). The required amount of deionized water was added afterwards. The monomer concentration in the solution thus prepared was 5% (w/v). This value was stipulated by the solubility limit of NVCl in 10% DMSO and therefore was also used for the 20% DMSO medium. In the case of the cryopolymerization procedure, the NVCl + TMEDA solution was, prior to the APS addition, cooled to ~0°C, and just after the initiator introduction the vial was immersed into the liquid coolant (ethanol) in the chamber of precision programmable cryostat FP 45 MH (Julabo, Germany) and kept there for 18 h. The thawing of the frozen sample was conducted in a water bath at 25–30°C. All subsequent manipulations with the samples prepared at positive as well as negative temperatures were accomplished essentially in the same way as described above in (i).

2.2.2. Size-exclusion chromatographic (SEC) analysis of PNVCl samples

This was carried out using the column (15×450 mm) filled with CL-Sepharose 6B resin (Pharmacia Fine Chemicals, Sweden). Recording of the elution curves was performed at 220 nm with the flow-through UV/VIS-Spectrophotometer Model 260-10 (Hitachi, Japan). Preliminary experiments showed that pure water was not appropriate as an eluent liquid at room temperature, since certain non-specific interactions between the polysaccharide resin and PNVCl observed thus interfering the analysis. The introduction of 0.2 mol of NaCl per 1 l of water eliminated such a non-specificity. Therefore, in the subsequent experiments the 0.2 M NaCl solution was used as an eluent, and the rate of its pumping through the column was 18 ml/h. The samples of the polymers to be analysed were dissolved in 0.2 M NaCl solution at a concentration of 0.2% (w/v). Calibration of the column was accomplished with a series of fractions of gelatin with known molecular weights. Gelatin samples with MW of 1400; 350; 240, 190, 135 and 45 kDa were, in their turn, fractionated by alcohol precipitation from the water solution of commercial gelatin of "Foto" brand (Reakhim, Russia) and then characterized with SEC and viscometry as described elsewhere [15]. Blue dextran (MW ca. 2,000 kDa) was used for the determination of a void volume of the column, and tryptophan (MW 0.204 kDa) for the determination of the total volume of the column.

2.2.3. Thermoturbidimetric measurements (TTM)

The studies were performed with the Specol VIS-spectrophotometer (Carl Zeiss Jena, former GDR) equipped with the turbidimetric attachment of Ti model connected with ultrathermostat U 4 (MLW, former GDR). In turn, the
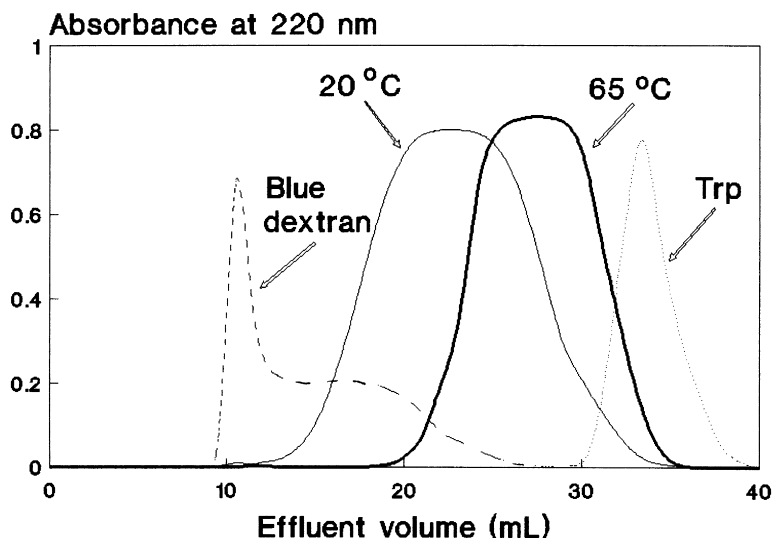
Absorbance at 220 nm

Fig. 1. SEC profiles of PNVCl samples prepared in the medium of neat DMSO at 20 and 65°C.

attachment was supplied with the vacuum photocell F3MO-19 and additional photomultiplier Pho M3/19. The measurements of turbidity of the 0.1% (w/v) PNVCl water solutions were conducted at a wavelength of 500 nm under the angle of 90° and then expressed as a percentage of to the turbidity (relative units) of a polymer-free solvent used. The rate of the rise in temperature in the course of similar experiments was maintained at about 1°C/min.

2.2.4. Calorimetric measurements

The experiments were performed using the high-sensitive DSC method (HS-DSC) in accordance with the described procedure earlier [16], using a DASM-4 differential scanning microcalorimeter (Biopribor, Russia) at a heating rate of 1 K/min and the excess pressure of 2.5 atm over a temperature range of 10–70°C. Aqueous solutions of the polymers with concentration about 0.2% (w/v) were used in the calorimetric measurements. As a rule, two subsequent scans were performed for each sample. The first scan was required to eliminate a prehistory of the sample, and the results of the second scan were assumed to characterize the thermodynamic properties of the system under study. Apparent specific partial heat capacity functions of the polymers were calculated, assuming their specific partial volume to be equal to 0.01 dl/g. They were converted into specific excess heat capacity functions using the spline approximation of the transition base line. Since in all the cases studied the calorimetrically detected transition was caused by demixing of the system upon heating, the first point of the excess heat capacity function deviating from zero was assumed to be the transition point with the transition temperature T_t. Evidently, this point corresponded to the point of the binodal of the system at a given concentration of the polymer. Specific transition enthalpies were determined by integration of the excess heat capacity

functions. By definition such a transition enthalpy is equal to the specific enthalpy of transfer of the polymer from the initial dilute solution to the concentrated phase formed as a result of demixing. In doing so, there were two main contributions to the transfer enthalpy. These were the dehydration and co-operative polymer–polymer interactions. The first contribution was positive and the second was negative. Obviously, the dehydration contribution prevails for the systems with low solution critical temperature (LCST) like the PNVCl–water system. However, intensive polymer–polymer interactions in the concentrated phase could significantly decrease the transfer enthalpy.

3. Results and discussion

3.1. PNVCl synthesized in the medium of neat DMSO

3.1.1. Preparation of the polymers

The following key problem has been considered by the authors at the beginning of the study: what are the aqueous media (suitable for the synthesis of PNVCl) containing the minimum possible amount of organic solvents as additives? Such a reaction media should, on the one hand, supply sufficient solubility of the initial monomer (i.e. NVCl), and, on the other, not suppress the hydrophobic interactions of lactam pendant residues completely in the polymers formed (the characteristic feature routinely exhibited by PNVCl in water). This latter requirement of the water–organic mixed solvents will be discussed in more detail later.

In order to solve this basic problem, we first of all synthesized PNVCl in the medium of DMSO, since it dissolves both NVCl monomer and APS/TMEDA initiating mixture well. Then the temperature-dependent solution behaviour of the resultant PNVCl in the aqueous media of various DMSO
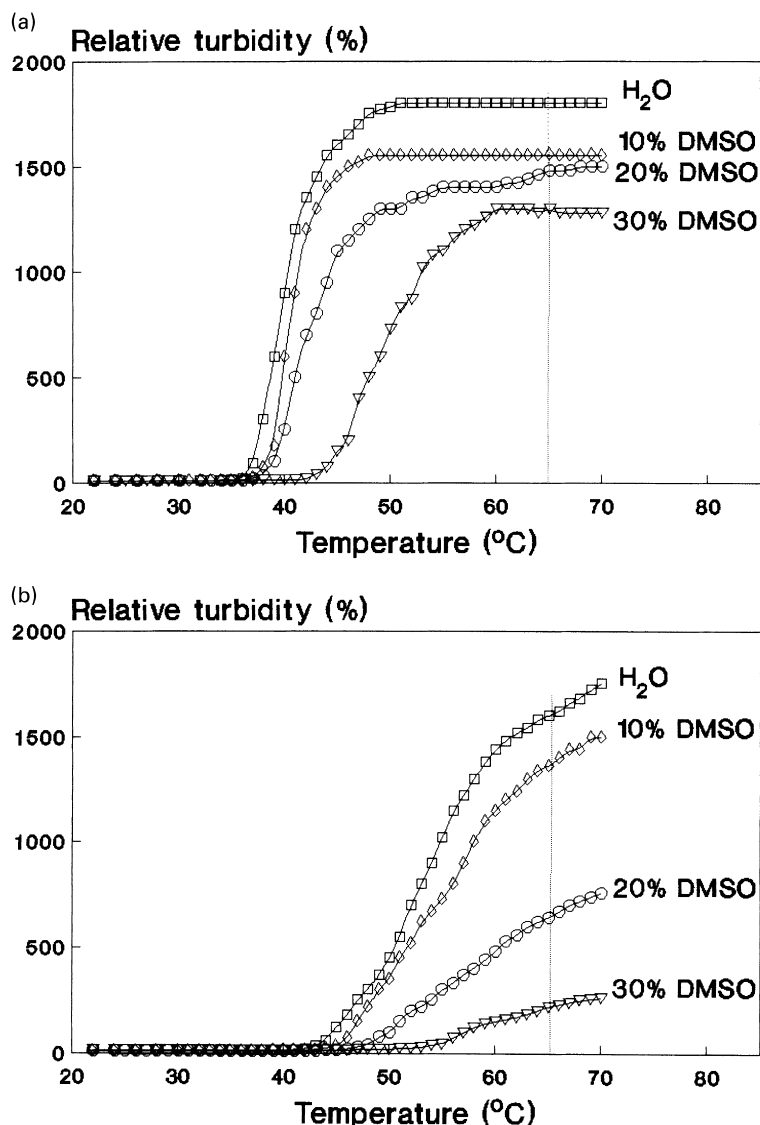
Fig. 2. Heating-induced variation of the relative turbidity of 0.1% (w/v) solutions of PNVCl samples prepared in the medium of neat DMSO at (a) 20 and (b) 65°C (composition of the solvents used is indicated near the curves).

content was investigated. The results of these studies allowed us to choose DMSO concentrations in the aqueous reaction systems, which were afterwards used for the preparation of PNVCl in mixed water–organic solvents. The molecular-weight characteristics of the polymer products fabricated in pure organic solvent, as well as in the medium of aqueous DMSO solutions, were evaluated with the SEC in aqueous medium under the conditions described in Section 2.2. The temperature-dependent solution behaviour of the corresponding PNVCl samples was examined with the TTM. The thermodynamic characteristics of the heating-induced phase separation of PNVCl water solutions were studied by the HS-DSC.

Synthesis of PNVCl in the neat DMSO was conducted at two temperatures: 65 and 20°C. Preliminary studies have demonstrated that in this case at 65°C the 3 h duration of the process was enough for the completion of

polymerization, as no further change in polymer yield was observed. At 20°C around 15 h was required for the completion of the reaction. The results of the analyses of PNVCl samples obtained are presented in Figs. 1–3.

3.1.2. SEC data

It was found that chromatographic profiles for these two polymeric products represented virtually symmetric, rather broad peaks, which differed in their effluent volumes (V_e, their values are further presented in the order of fraction elution from SEC column). These V_e corresponded to molecular weights in the vicinity of 800–500 kDa for the PNVCl synthesized at room temperature and of 600–350 kDa for the macromolecular product formed at an elevated temperature (Fig. 1). Besides, a practically identical SEC profile was observed for the polymer prepared at 50°C, the case not shown in Fig. 1. However, to demonstrate better the
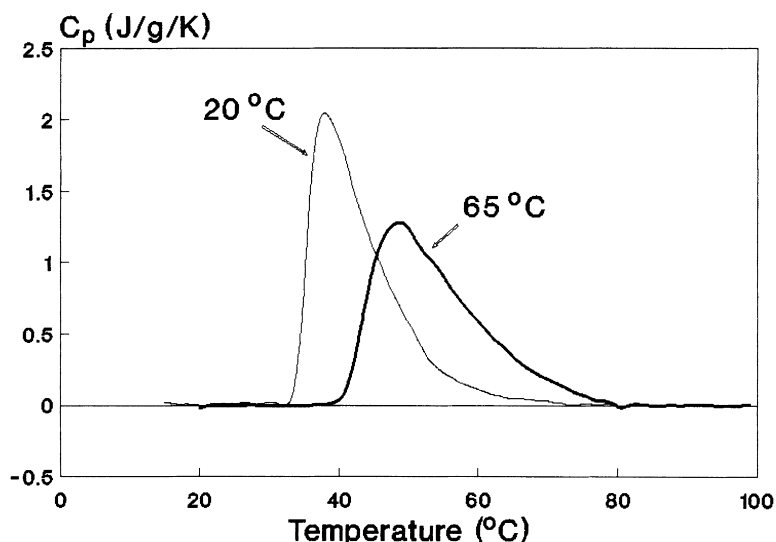
Fig. 3. Excess heat capacity functions in aqueous solutions of the PNVCl samples prepared in the medium of neat DMSO at 20 and 65°C. Heating rate is 1 K/min. Polymer concentration is 0.2% (w/v).

working volumes of the chromatographic column employed, the elution curves of two molecular-weight probes: blue dextran (MW of the major fraction of about 2,000 kDa) and tryptophan (MW 0.2 kDa) are depicted in Fig. 1 as well. The SEC data testified that the decrease in temperature of the redox-initiated polymerization of NVCl in the medium of a neat DMSO gave rise to the formation of the higher-molecular-weight products. Such a result agreed with the common knowledge concerning the influence of reaction temperature on the molecular weight of macromolecules produced via a free radical polymerization in a solution [17]. In the case under discussion the molecular weight of PNVCl prepared at 20°C turned out to be 1.5–2 times greater than for the macromolecular products prepared at 50 or 65°C.

3.1.3. TTM data

The curves in Fig. 2 show the variation of relative

Table 1
Data of the thermoturbidimetric examination of 0.1% (w/v) solutions of PNVCl samples prepared in the medium of neat DMSO at 20 and 65°C

Temperature at the PNVCl synthesis (°C)	Solvent used during the turbidimetric tests	T_{cp} (°C)	The slope of the linear section of the turbidimetric curve[a]
20	H$_2$O	35.5–36.0	6.11
65		40.5–41.5	2.20
20	10% DMSO	36.0–37.0	6.05
65		42.5–43.5	1.62
20	20% DMSO	37.0–38.0	3.41
65		44.5–45.5	0.75
20	30% DMSO	42.5–43.5	2.28
65		46.0–47.0	0.43

[a] The tangent of the sharp angle between the abscissa axis and a linear region of the respective curve in Fig. 2.

turbidity of 0.1% (w/v) polymer-containing systems upon their gradual heating. The temperatures at which the turbidity reached the values as high as 10% of its initial level at 22°C, were, in accordance with the approach of Boutris et al. [18], identified with cloud points (T_{cp}) for every particular composition of the liquid medium examined. The slope of the linear section of these curves may be considered as an indicator, characterizing the intensity of the temperature-induced phase separation in the given systems. As a rule, for the thermo-responsible polymers similar to PNVCl, the temperature of such a phase separation depends on the polymer concentration, as well as on the method and equipment employed for the determination of this parameter. Therefore, the values of T_{cp} could differ somewhat from those measured by other techniques. The magnitudes of T_{cp} determined with TTM and the slope of the respective lines in Fig. 2 are listed in Table 1.

PNVCl, formed in DMSO at room temperature and then dissolved in pure water, had T_{cp} in the vicinity of 35.5–36°C (Fig. 2a, Table 1). The polymer prepared at 65°C possessed a cloud point at around 40.5–41.5°C (Fig. 2b, Table 1). That is, the phase separation for the former polymer started earlier with the increase in temperature, and the "steepness" of the ascending branch of its turbidity curve was higher comparing that for the PNVCl prepared at 65°C. This clearly pointed to the differences in the temperature-dependent solution behaviour of these two PNVCl samples. Such a non-identity, was, apparently, associated with the above-indicated distinctions in the MW of these polymeric products (Fig. 1). Note that similar observations on the higher cloud point temperatures for the PNVCls of lower MW was earlier made by Tager et al. [19,20] for the polymers synthesized in the medium of isopropanol.

Thermoturbidimetric studies of these two PNVCl samples, which revealed not only the non-equal T_{cp} values,

Table 2

Calorimetric data for the PNVCl samples synthesized at different conditions (T_{cp} is the cloud point temperature; T_t the incipient phase separation temperature according to the HS-DSC data; $\Delta_t H$ the specific enthalpy of the phase separation. Solvent—water; polymer concentration—0.2% (w/v))

Solvent used at the PNVCl synthesis	Temperature at the PNVCl synthesis (°C)	T_t (°C)	$\Delta_t H$ (J/g)
100% DMSO	20	33 ± 1	24 ± 2
	65	39 ± 1	22 ± 2
20% DMSO	−20	30 ± 1	26 ± 2
	20	31 ± 1	15 ± 1
	65	28 ± 1	15 ± 1
10% DMSO	−20	32 ± 1	20 ± 2
	20	31 ± 1	23 ± 5
	50	30 ± 1	26 ± 3
	65	29 ± 1	23 ± 1

but also various slopes of the linear sections of respective curves (Fig. 2, Table 1), naturally testified to the higher ability of the polymer synthesized at room temperature compared to the thermally induced phase segregation in the water milieu. Confirmation of such a conclusion was also obtained from the data of DSC investigations.

3.1.4. HS-DSC data

Fig. 3 shows excess heat capacity functions of these samples in 0.2% (w/v) aqueous solutions (such a concentration has been chosen because of the sensitivity requirements of the instrument used). Both functions had a pulse-like profile that could be expected in the case of demixing of a polymer solution upon heating. Parameters of these functions are collected in Table 2. The transition temperature of the sample prepared at 20°C was lower than that of the sample prepared at 65°C, although the transition enthalpies of both samples practically coincided with each other. In addition, the samples differed markedly in the apparent width of the transition. The transition of the sample prepared at 20°C seemed to be a more co-operative one.

The transition temperatures T_t determined by the HS-DSC were, in general, close to the cloud point temperatures (T_{cp} values in Table 1), although they were a little bit lower then the latter ones. These small deviations were, apparently, connected to the fact that calorimetric measurements were done at higher polymer concentration (0.2%) than during the turbidimetric studies. Actually, both intrinsic temperatures belonged to the points of binodal in the phase diagram of the system, but at different polymer concentrations. The difference in the transition temperatures of the samples considered was likely to arise from the difference in their molecular weights.

According to the theory of Grosberg and Kuznetsov [21], the thermodynamics of polymer solutions can be adequately described in terms of the reduced temperature

$$t \sim \tau M^{0.5}$$

where $\tau = (\theta - T)/\theta$ is the case of a system with LCST, θ the θ-temperature, T the temperature and M the molecular weight of a polymer. At a given polymer concentration the solutions of polymer homologues are demixed at the same reduced temperature t_t which belongs to the binodal. Evidently, the higher the molecular weight of the polymer, the lower the temperature corresponding to t_t, i.e. the transition temperature T_t.

Another interesting feature of the excess heat capacity functions of PNVCl species under study was their extraordinary large width. In fact, from these functions it followed that, in the course of heating, the phase separation was apparently completed only after the temperature was raised to about 40°C above LCST. For comparison, note that for practically any binodal the theoretical width of the demixing transition in a closed system should be less than one degree Celsius. The following reasons can in principle lead to an abnormal peak broadening: (i) instrumental broadening due to a limited time response of the calorimeter [22]; (ii) molecular heterogeneity of the samples; and (iii) slow secondary processes in the concentrated phase resulting in the formation of its equilibrium structure.

The DASM-4 microcalorimeter [23] used in this study stands out among modern HS-DSC instruments in having the smallest time constant of the order of 20 s. Hence, it would hardly be expected that introduction of the corresponding correction for the instrumental broadening would significantly change the profiles of the peaks, especially of their descending branches. The molecular heterogeneity was also unlikely to be an important factor in the case under consideration, as the sample prepared at 20°C, which gave the more narrow peak of the excess heat capacity, displayed a larger apparent heterogeneity (a broader molecular-weight distribution) in the SEC pattern (Fig. 1). Therefore, it seemed that the most probable reason for the heat capacity peak broadening was a slow equilibration process in the separated phase with high polymer concentration. Certainly, the hypothesis that slow phase equilibration is the main motive for the heat capacity peak broadening needs to be further supported by a study of the effect of heating rate on HS-DSC results for PNVCl solutions.

3.1.5. Temperature-dependent solution behaviour in the mixed water-DMSO media of the PNVCl samples prepared in DMSO

Curves 2–4 in Fig. 2a and b show a marked shift of T_{cp} values as compared to the TTM curves recorded for the same polymers in water. After purification and drying, they were re-dissolved for the thermoturbidimetric experiments in 10-, or 20-, or 30%-DMSO–water solutions. The position of the curves was shifted towards higher temperatures, and the slopes of linear regions of the curves for the PNVCl samples decreased. The numerical values of the cloud point temperatures in these mixed solvents and corresponding slopes are also collected in Table 1. Such a shift
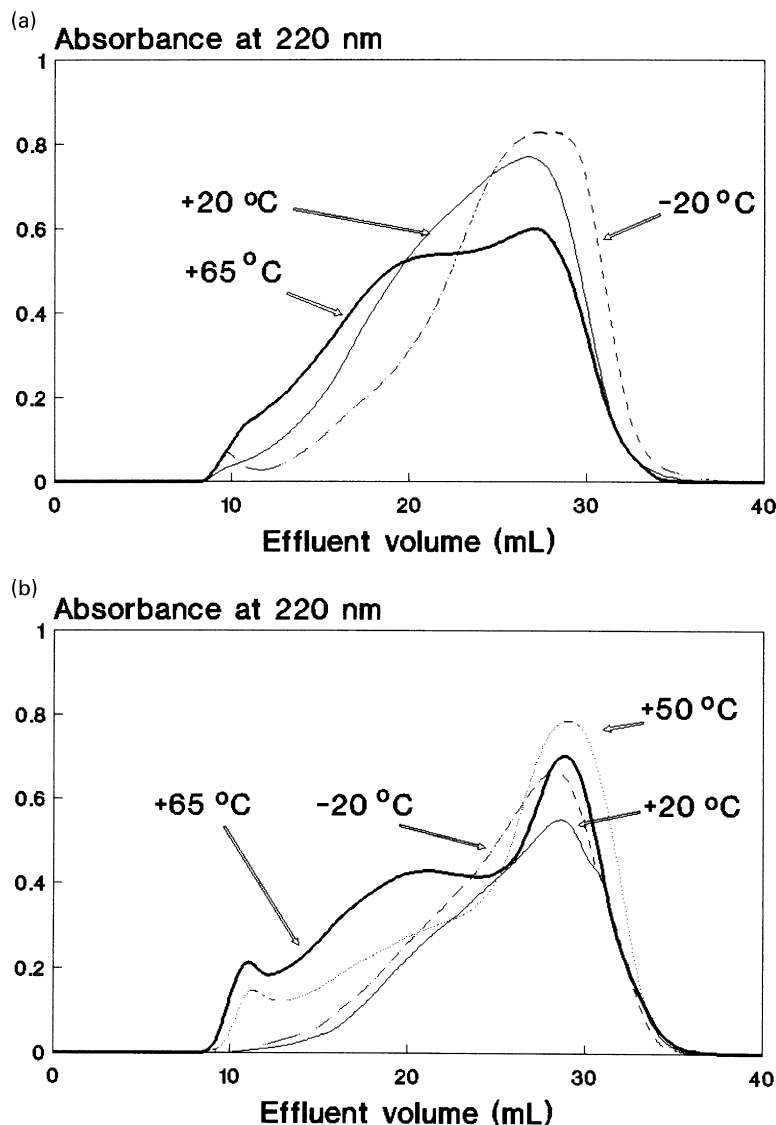
(a)

Absorbance at 220 nm

Effluent volume (mL)

(b)

Absorbance at 220 nm

Effluent volume (mL)

Fig. 4. SEC profiles of PNVCl samples prepared in the media of (a) 20% or (b) 10% DMSO–water solutions at various temperatures.

was undoubtedly caused by the partial inhibition (by the DMSO additives) of hydrophobic interactions. They are well known [5,24] to be mainly responsible, along with the formation of specific H-bonded cyclic structures [1], for the occurrence of temperature-induced "coil-globule" transition in the thermoresponsible polymers and, as a consequence, for the drastic reduction of their solubility in water. On the one hand, the experimental data obtained evidently testified that in PNVCl at the temperatures as high as T_{cp} similar transition was not inhibited completely in the water–DMSO mixtures, at least until the 30% content of the given organic solvent. On the other hand, this gave us the information on the temperatures at which either PNVCl, being formed in such mixed solvents, could be in a soluble state (the temperatures below the respective cloud points), or the reacting system could undergo the phase separation ($> T_{cp}$). This latter case was of particular interest, while it represented the instance of a "precipitation polymerization",

when the polymer, arising in the course of the chain growth, was capable of forming a segregated polymer-rich phase. The hydrophobicity of such a phase separated from the liquid bulk should be higher as compared to the external water-rich solution. Therefore, the matter of this segregated phase should act as an extraction medium with respect to the poor-water-soluble NVCl molecules.

3.2. PNVCl synthesized in the medium of DMSO–water mixed solvents

3.2.1. Preparation of the polymers

Taking into account all the results and speculations described above, we have selected the thermal regimes for the synthesis of PNVCl species in the water–DMSO mixed solvents. These were the same two temperatures of 20 and 65°C the dotted vertical lines in Fig. 2 show the latter region). As it was supposed, these temperatures should
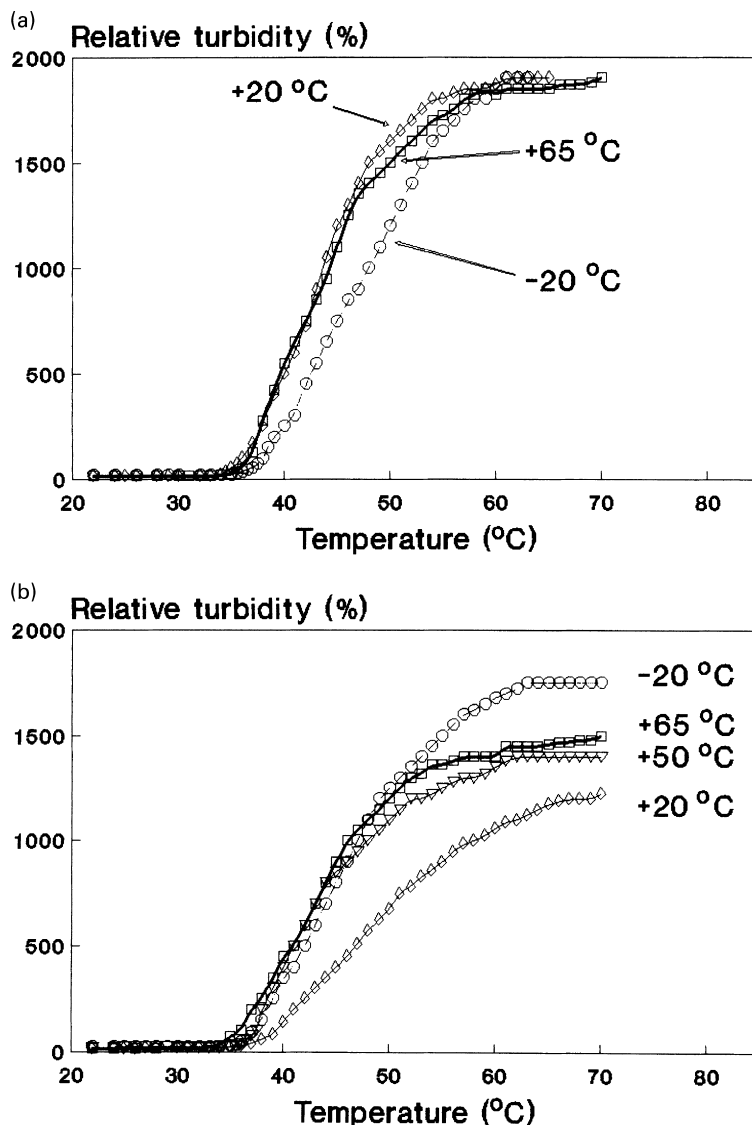
(a)

Relative turbidity (%)

(b)

Relative turbidity (%)

Fig. 5. Heating-induced variation of the relative turbidity of 0.1% (w/v) solutions of PNVCl samples prepared in the media of (a) 20% or (b) 10% DMSO–water solutions at various temperatures.

provide the conditions of homophase and heterophase reaction systems, correspondingly. Therefore, the compositions of the mixed aqueous solvents throughout respective experiments were 10%- and 20%-DMSO, but not 30%-DMSO, since in the latter medium a high enough temperature was required in order to cause the phase separation (curve "30% DMSO" in Fig. 2a). We have also tried to accomplish the polymerization of NVCl in the moderately frozen water–DMSO solutions for the demonstration of the possibility of the preparation of this particular polymer by means of the cryochemical process [25,26]. Similar to other cryochemical reactions of various low-molecular reagents in the non-deeply frozen solutions, similar cryopolymerization occurs in the liquid-like inclusions (the so-called 'unfrozen liquid microphase') [27–29] of the macroscopically frozen reaction bulk. In other words, such cryopolymerization process should proceed in the heterophase system consisting of the

solid crystals of frozen solvent and the aforementioned unfrozen liquid microphase, where solutes are concentrated.

It was observed that carrying out the NVCl polymerization in both 10%- and 20%-DMSO at 65°C caused a very fast (1–2 min) production of a turbidity of the initially transparent reaction solution. At the elapse of the third hour the system looked like a white milk; its viscosity was low. After chilling till room temperature this milky system transformed into a transparent liquid. Virtually the same appearance was inherent in the reaction bulk at 50°C (solvent 10% DMSO), but the turbidity arose somewhat slower compared to the case at 65°C. At the same time, upon the NVCl polymerization in the same solvents at 20°C, the system remained as a transparent fluid throughout all the reaction time, i.e. for 18 h. In the case of the cryopolymerization process, the reaction bulk was stored frozen for the same 18-h-period, and after thawing the system
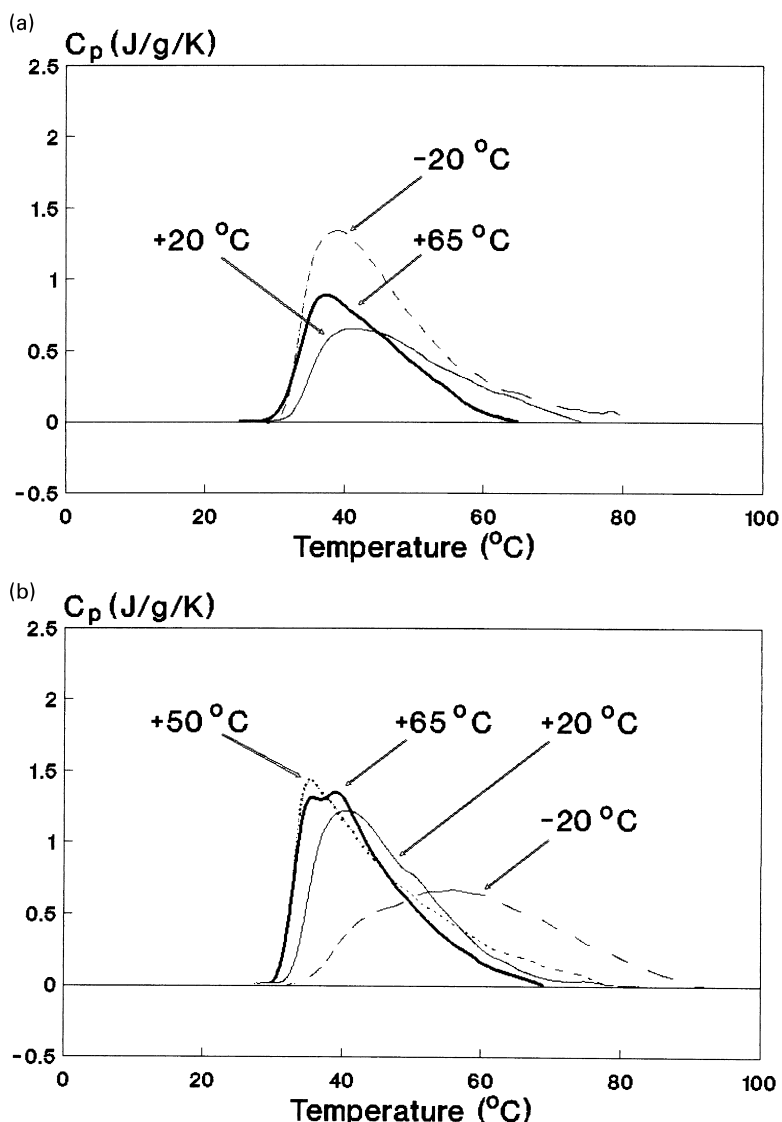
Fig. 6. Excess heat capacity functions in aqueous solutions of the PNVCl samples prepared in a media of (a) 20% or (b) 10% water–DMSO solutions at various temperatures. Heating rate is 1 K/min. Polymer concentration is 0.2% (w/v).

obtained looked like a transparent fluid at room temperature. The temperature of 50°C was tested for the sake of comparison, since this temperature region was slightly above the vicinity of a cloud point for PNVCl dissolved in 10%-DMSO. In other words, at around 50°C a "boundary (transition) zone" between the homogeneous solution and the heterogeneous dispersion was located. The results of the examination of PNVCls formed in the mixed solvents (10 and 20% of DMSO) under the conditions of homogeneous solutions (20°C), heterogeneous dispersion (50–65°C) and freeze-solidified (−20°C) reaction bulk are summarized in Figs. 4–6. For the cryopolymerization case, its temperature was chosen from the water–DMSO "liquid–solid" phase diagram [30], showing that at this temperature both compositions of the mixed solvent should freeze.

3.2.2. SEC data

The above-indicated differences in the aggregate status of the polymerizing systems, as well as in the temperature of the reaction, gave rise to the considerable distinctions of properties of the resultant polymeric products. Thus, for the PNVCl formed in the medium of 20% DMSO a complex polymodal molecular-weight distribution was observed (Fig. 4a). The major fraction of the lowest MW equal to 150–100 kDa was registered for the cryogenically synthesized polymer, although a certain small peak in the vicinity of very high molecular weights ($V_e \sim 10$ ml, MW $\sim$ 2000–1000 kDa) was also recorded. At room temperature the polymer with MW of the major fraction around 300–200 kDa was produced, and the "shoulder" in the vicinity of V_e values of about 20 ml also pointed to the presence of the higher-molecular fractions (700–600 kDa) in this PNVCl sample. The increase in the reaction temperature up to

65°C, resulting in the phase separation (or collapse of individual coils, when the polymer concentration was still low enough), gave rise to the fabrication of the larger amount of polymeric fractions of the significantly higher MW (shoulders at $V_e \sim 10$ ml, MW ~ 2000–1000 kDa and V_e around 18–20 ml, MW ~ 900–600 kDa). At the same time, the relative amount of the lower-molecular fraction (V_e around 28–29 ml, MW ~ 100–60 kDa) decreased. The results obtained for the cases of these three thermal regimes have pointed, first of all, to the possibility of preparing NVCl polymers in aqueous media. Secondly, the final products of similar redox-initiated polymerization of the monomer in 20% DMSO at elevated temperatures in the heterogeneous dispersion were shown to be enriched with the higher molecular fractions as compared to PNVCl samples formed in the neat DMSO under analogous thermal conditions. In other words, in this aqueous medium a certain inversion of dependences of the PNVCls MW on the synthesis temperature was obtained, thus showing the significance of the aggregate state of this polymerizing system for the propagation of growing chains.

More "interesting" pattern was observed when the polymerization was carried out in the medium with a smaller content of organic solvent, namely, in 10% DMSO (Fig. 4b). It turned out that the differences between the MW characteristics of PNVCl samples formed above and below the T_{cp} were in this case more markedly manifested than in the previous case, i.e. in 20% DMSO mixed solvent. The SEC profiles of the samples prepared in homogeneous solution at 20°C in the medium of these two mixed solvents had the peaks of the major fraction, which, in fact, was eluted from the column in the identical volume. This showed a rather slight influence of the solvent composition (in the range examined) on MW characteristics of final products. At the same time, the accomplishment of NVCl polymerization in the medium of 10% DMSO, but in the heterogeneous system (arising at 65°C due to the phase separation), resulted in the more pronounced enrichment of the final product with the higher-molecular fractions (especially in the region of effluent volumes of ~ 10 ml), than for the medium of 20% DMSO (cf. curves 65°C in Fig. 4a and b). One may see that in a "less hydrophobic" liquid the relative amount of high-molecular-weight fractions increased. And, lastly, the polymer synthesized at 50°C possessed "intermediate" molecular-weight characteristics between the PNVCl samples prepared at lower and higher temperatures (curve 50°C in Fig. 4b), thus demonstrating the promotion influence on MW of both the rise in temperature and phase separation.

Similar effects of the increase in MW of polymers with temperature are, in principle, well known for the precipitation polymerization of various unsaturated monomers in the medium of organic solvents [16]. But in this latter case it is meaningless to speculate on the hydrophilicity/hydrophobicity of the phases separated. At the same time, in the case under consideration in the present study, the significant differences in hydrophilicity of discrete (polymer-rich) and continuous (monomer solution) phases could act as an additional factor determining the properties of the polymer products formed. One of the probable mechanisms could be, as was indicated above, the extracting action of the "hydrophobic" polymer-rich phase with respect to the poor-water-soluble NVCl molecules.

As for the cryopolymerization of NVCl initially dissolved in 10% DMSO, we observed a certain decrease in the amount of low-molecular polymeric products ($V_e \geq 32$ ml) in comparison with those in the PNVCl samples formed after the freeze–thaw-treatment of the reaction ingredients initially dissolved in 20% DMSO. One of the possible reasons for such a result could be the higher extent of cryoconcentrating of solutes in the unfrozen liquid microphase of the former system. According to the phase diagram [30], the concentration of DMSO in a liquid microphase of the 10–20% DMSO solutions frozen at -20°C is close to 28% (in the presence of solutes, apparently, this fraction is somewhat smaller due to the solvate liquid bearing by these substances). Similar temperature and DMSO concentration correspond to the region above the glass transition ($T_g \leq -40$°C), therefore such frozen systems should be considered as two-phase systems, consisting of a solid ice and $\sim 28\%$ DMSO water solution. However, in order to reach this concentration originating from the initially 10% solution of DMSO a larger amount of water is required to be frozen-out than originating from the 20% solution. Hence, providing the initial solute concentration in both cases was identical, the final concentration of the reactants in an unfrozen liquid microphase should be higher for the system with the initially higher concentration of water. While the monomer concentration increases, the amount of low-molecular polymer products can decrease.

3.2.3. TTM data

The polymers formed at 65 and 20°C in 20% DMSO showed very similar TTM curves (Fig. 5a), their T_{cp} values and slopes of linear portions of the curves were close, as well (Table 3). These data could mean that for the given PNVCl samples possessing a very broad molecular-weight distribution (Fig. 4a) there was no significant influence of the temperature of polymer synthesis on the heating-induced phase separation. PNVCl prepared in the same initial solvent, but using the cryopolymerization procedure, exhibited higher cloud point, while the intensity of increase in turbidity with the rise of temperature was lower as compared to the former two polymers. One may suggest that this was due to the lower MW of the major fraction of this "cryogenically produced" polymer.

However, a similar correlation between the MW characteristics of PNVCl samples and the behaviour of their temperature-dependent solutions behaviour was not observed in all the cases of polymeric products synthesized in the more hydrophilic solvent, namely, in 10% DMSO (Fig. 5b). First of all, this concerned the cryogenically

Table 3
Data of the thermoturbidimetric examination of 0.1% (w/v) solutions of PNVCl samples prepared in the medium of 10 or 20% water–DMSO solutions at various temperatures

Solvent used at the PNVCl synthesis	Temperature at the PNVCl synthesis (°C)	T_{cp} (°C)	The slope of the linear section of the turbidimetric curve[a]
20% DMSO	−20	36–37	1.95
	20	34.5–35	2.46
	65	35.5–36	2.17
10% DMSO	−20	34–35	1.63
	20	37–38	1.00
	50	36.5–37.5	1.50
	65	35.5–36	1.88

[a] The tangent of the sharp angle between the abscissa axis and a linear region of the respective curve in Fig. 5.

produced polymer, which contained a significantly lower amount of high molecular-weight fractions compared to the polymers obtained at 65 or 50°C (Fig. 4b), but exhibited a higher ability to the heating-induced phase segregation (lower T_{cp} and higher slope, Table 3).

At the same time, the comparison of the TTM curves for the samples formed in homogeneous medium at 20°C and those prepared under the conditions of precipitation polymerization at 65 and 50°C showed the same tendency as in the above-discussed case of 20% DMSO solvent: the higher the relative amount of high-molecular fractions in the polydisperse PNVCl specimens, the higher their capability of separating into the polymer-rich phase with increase in temperature. Unfortunately, the reason for the anomalous solution behaviour of the polymer synthesized in frozen reaction bulk is not still clear.

3.2.4. HS-DSC data

Fig. 6 represents HS-DSC data for PNVCls produced at different temperatures in 20% (a) and 10% (b) DMSO. In the first case, the change in the temperature of the synthesis did not practically affect the transition temperature of aqueous solutions of the polymers. However, as the temperature changed, drastic changes in the transition enthalpies were observed. While the transition enthalpy for the sample synthesized at −20°C was close to the transition enthalpies of the samples prepared in the neat DMSO (of about 20 J/g), the enthalpies of the samples prepared at 20 and 65°C were significantly lower (15 ± 1 J/g). Since the chemical compositions of the first and both other samples were likely to be identical, it could be assumed that in all these cases the hydration contributions into the transition enthalpy should be similar. For this reason, the effect of the synthesis temperature on the transition enthalpy may apparently be ascribed to a change in polymer–polymer interaction energetics, which, defining a negative contribution into the transition enthalpy, should be connected with a local ordering of the polymer chain via the co-operative

effects in polymer–polymer interactions. Thus, it could be proposed that the samples synthesized at 20 and 65°C were evidently different with respect to a local ordering, for example, due to the different degree of stereoregularity.

In accordance with the data of Kirsh et al. [12], the macromolecules of PNVCl synthesized in organic solvents have dominantly syndiotactic configuration of their chains due to rather bulky pendant seven-number rings, which induces mainly transoidal orientation of lactam residues of the neighbouring monomer units during chain propagation in the course of polymerization. But this is the case for the formation of PNVCl in the medium of a good solvent, where no phase separation occurs and, hence, no gradients of hydrophobicity/hydrophilicity exist. In contrast to this, in the case of polymer synthesis in heterogeneous media, especially at the temperatures as high as LCST, when a new polymer-rich phase appears, the conditions for the pronounced hydrophobic interactions between the neighbouring lactam cycles do arise. This can, in principle, facilitate the formation of isotactic regions in the growing chain. Therefore, one may suppose that the resultant polymer will possess the structure of a block-copolymer, where the blocks are the long enough chain fragments of the non-identical tacticity. In this case different blocks may exhibit different thermochemical behaviour giving rise to the multi-peak DSC thermograms.

In the case of PNVCl formed in 10% DMSO (Fig. 6b) there were no significant differences in the transition parameters for the samples synthesized at different temperatures. On average, the transition temperature and enthalpy were about 30°C and 20 J/g, respectively. Alternatively, profiles of the transition for the samples differed rather significantly. Besides, the transition became more co-operative when the synthesis temperature increased. In this case there was no apparent correlation with the SEC data (Fig. 4b). For instance, the sample prepared at −20°C, which displayed the lowest transition cooperativity, seemed to be more homogeneous in the molecular weight than the other samples prepared in 10% DMSO. It was also noted that the excess heat capacity function of the sample produced at 65°C showed some bimodality. This testified to some overlapping of at least two nearly located transitions. The possible reasons for this could be both the most pronounced polymodality of the molecular weight distribution (SEC data in Fig. 4b) and the above-discussed changes in the chain configuration in the case of precipitation-mode polymerization. At the same time, the polymer formed at 50°C, i.e. under the conditions of a "boundary" temperature region (see above), exerted monomodal DSC peak. This obviously meant that, for the pronounced influence of the features of NVCl precipitation polymerization on the properties of the resultant macromolecular products, the completed phase separation was required.

The heat capacity functions of all the samples formed in the water–DMSO mixtures were also very diffuse. The transitions were completed only within the temperature range of

about 30–60°C. As mentioned above, such a large broadening of the transitions is very likely to be associated with the secondary processes of structure formation in the concentrated polymer phase of the system.

4. Conclusions

The preparation of the *N*-vinylcaprolactam polymers in aqueous media by means of a free radical polymerization was accomplished through the use of mixed water–DMSO solvents and redox initiation. The molecular weight of the final macromolecular products, their molecular-weight distribution, their temperature-dependent solution behaviour and the thermodynamic parameters of the phase segregation process were dependent on the amount of organic moiety in the mixed solvent system employed, as well as on the aggregate status of the reaction bulk (homogeneous solution, heterophase moderately frozen solution or heating-induced dispersion). Although, more clear understanding is needed of some of the experimental findings, it was evidently demonstrated that polymers enriched at a highest extent with the high-molecular fractions were mainly formed upon the precipitation polymerization. The studies performed open new opportunities for the preparation of *N*-vinylcaprolactam homo- and co-polymers in aqueous milieu and over a wide range of temperatures. We can preliminarily report also on successive experiments for the production of the co-polymers of *N*-vinylcaprolactam and acrylamide. These polymeric products, similar to the NVCl homopolymers, were capable of heating-induced phase separation, i.e. they behaved as typical temperature-responsible polymers. The studies of these macromolecular compounds are now in progress and will be reported elsewhere.

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