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Effect of Complexation of Monomer Units on pH- and Temperature-Sensitive Properties of Poly(*N*-vinylcaprolactam-*co*-methacrylic acid)

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ABSTRACT: Laser light scattering and differential scanning calorimetry measurements have been performed for aqueous solutions of thermosensitive linear copolymers of *N*-vinylcaprolactam and methacrylic acid of different composition. It was shown that the copolymers undergo a phase transition upon temperature increase in neutral and basic solutions. The enthalpy of the phase transition sharply decreases with the increase of methacrylic acid fraction, as shown by differential scanning calorimetry. The copolymers demonstrate pH-sensitive properties as well: intermacromolecular aggregation takes place in acidic media. FTIR spectroscopy measurements show that the aggregation is due to formation of insoluble macromolecular complexes. It was found that such complexes are also formed in the mixtures of homopolymers of poly(*N*-vinylcaprolactam) with poly(methacrylic acid). Effect of pH on thermosensitive properties of the copolymers is discussed. In weak acidic media there are narrow pH intervals close to pH of aggregation in which thermosensitive properties of the copolymers diminish considerably and the scattering intensity from the solutions at high temperatures is much less than at basic pH. Also, under these conditions the enthalpy of phase transition decreases significantly. The effect of a similarly charged surfactant (sodium dodecyl sulfate, SDS) on thermosensitive properties of the copolymer containing ~40% of methacrylic acid is studied at pH 3 and 7. SDS solubilizes the copolymer, which is insoluble at pH 3; in the presence of SDS the copolymer is thermosensitive at both pH 3 and pH 7 at studied SDS concentrations; the transition temperature is higher than that of the copolymer in a surfactant-free solution. The enthalpy of the phase transition increases as SDS concentration in solution is increased.

Introduction

In the past few years responsive (sensitive) polymers became an object of intensive study due to the ability of such polymers to change drastically their physical state under small changes of external parameters: temperature, pH, ionic strength, light illumination. These studies appeared to be important both from scientific and technological viewpoints. Recently, chromatographic,^{1,2,3} drug delivery,^{4,5} membrane technology,^{6,7} and kinetic inhibition⁸ applications were reported. Temperature- and pH-sensitive polymers are of the widest use in these studies.

Poly(*N*-isopropylacrylamide)^{9–11} (PNIPA) and poly(*N*-vinylcaprolactam)^{12–14} (PVCL) were intensively investigated due to their thermosensitive properties. These polymers are water soluble at low temperatures. However, they exhibit a lower critical solution temperature (LCST) in water and undergo a coil-to-globule transition and aggregation at higher temperatures. For PNIPA the coil-to-globule transition is around 32 °C.

PVCL is a homologue of poly(*N*-vinylpyrrolidone) (PVP). The latter is a biocompatible polymer widely used in medicine and pharmaceuticals.¹⁵ PVCL combines useful and important properties of PVP and PNIPA. It is a biocompatible polymer with phase transition in the

region of physiological temperature (30–32 °C). This combination of properties allows consideration of PVCL as a prospective material for design of biomedical devices and use in drug delivery systems.

pH-sensitive polymers is another class of responsive polymers. pH-responsive polymers such as poly(propylacrylic acid), poly(ethylacrylic acid), and poly(methacrylic acid) are intensively studied as drug and gene delivery agents.¹⁶ Poly(methacrylic acid) (PMAA) is one of the most widely used pH-responsive polymers. It demonstrates an abrupt conformational change at pH ~5.5–6. At high pH the charge is distributed along the polymer backbone and the electrostatic repulsion of the charged carboxyl groups results in an increase of the hydrodynamic volume of the polymer compared to the uncharged coils existing at low pH. PMAA exhibits thermosensitive properties as well, however, at high polymer concentrations (>5 wt % in water); its LCST is equal to 50 °C.¹⁷

Combination of responses to several stimuli in a single polymer is a task of considerable interest since it allows responsive properties of polymers to vary by changing external parameters. Several groups succeeded in the synthesis of pH–*T*-sensitive systems.

Gan et al.¹⁸ synthesized a novel thermosensitive water-soluble polymer of *N*-acryloyl-*N*-propylpiperazine (PNANP). The LCST of that polymer is highly sensitive to the pH of the medium and varies from 65 °C at pH 6 to 25 °C at pH 10. Copolymers of *N*-isopropylacrylamide and acrylic acid (PNIPA–AA) were reported to demon-

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Table 1. Polymerization Conditions and Resulting Polymer Characteristics

	solvent for synthesis	temp of synthesis	initiator	initial VCL to MAA ratio	MAA content % (titration), only for copolymers	MAA content % (NMR), only for copolymers	M_w (SLS)	R_g
PVCL	benzene	50	AIBN				5.6×10^3	48
PVCL-MAA ₉	DMSO/water, 90 vol % DMSO	50	AIBN	20:1	7	9	4.1×10^3	50
PVCL-MAA ₃₇	DMSO/water, 90 vol % DMSO	50	AIBN	9:1	36	37	3.8×10^3	42
PMAA	water	70	KPS				7.8×10^3	47

strate analogous properties.^{19,20} However, no information on whether these polymers showed conformational changes with pH variation at any constant temperature was presented.

Chi Wu and al.²¹ studied the effect of a surfactant on swelling of pH-*T*-sensitive microgels of poly(*N*-vinylcaprolactam-*co*-sodium acrylate). These microgels showed both pH- and temperature-dependent swelling/deswelling transitions; unlike PNANP and PNIPA-AA, their shrinking temperature was not reported to be sensitive to pH. However, addition of sodium dodecyl sulfate surfactant (SDS) changed drastically pH-sensitive and thermosensitive properties of the microgels. Addition of 0.5 mM SDS led to a sharp increase of the shrinking temperature of the microgel particles from 31 to 45 °C at pH 12. Also the pH of swelling of the microgels at room temperature can be decreased from 8 to 3.5 by adding 2 mM SDS. At an SDS concentration of 0.5 mM, the shrinking temperature was reported to be sensitive to the pH of the medium. These effects were found to be analogous to those produced by introducing the same amount of ionic groups via chemical modification of the microgels.

Earlier we studied thermosensitive properties of copolymers of *N*-vinylcaprolactam and methacrylic acid (PVCL-MAA).²² It was shown that the copolymers containing different amount of MAA monomer units undergo a LCST phase transition in a wide range of neutral and basic pH values, being soluble below critical temperature (T_{cr}). However, under acidic conditions intermolecular aggregation of the macromolecules was observed below T_{cr} as well. So these copolymers appeared to respond also to pH stimuli. The aggregation of the polymer chains below T_{cr} was also observed upon adding an oppositely charged surfactant, cetylpyridinium chloride (CPC). The effect of CPC on the properties of the copolymers was considered from the viewpoint of CPC/copolymer complex formation, which took place due to attractive electrostatic and hydrophobic interactions between the molecules of the surfactant and macromolecular chains. Attractive interactions of CPC hydrophobic tails were supposed to be the cause of surfactant-induced aggregation of the macromolecules.

In the present paper we continue to investigate the properties of PVCL-MAA copolymers. Special attention is paid to the fact that poly(methacrylic acid) is known to interact with the polymers composed of proton-accepting groups. Interaction with poly(ethylene oxide),²³ poly(*N*-vinylpyrrolidone),^{24,25} and poly(ethylene imine)²⁶ was shown to proceed, resulting in polymer complexes that contain an equivalent amount of MAA units and proton-accepting groups. Hydrogen bonding between these groups and PMAA carboxyls is supposed to account for the effect of complex formation.

Thus it appears pertinent to investigate the possibility of macromolecular complex formation in PVCL-MAA copolymers, which may arise from interaction between VCL and MAA monomer units, its supposed role in pH-sensitive properties of the copolymers, and its possible

influence on thermosensitive properties of the copolymers. Effect of fraction of MAA monomer units and anionic surfactant SDS on temperature-sensitive properties of PVCL-MAA is also discussed. Laser light scattering (LLS) and differential scanning calorimetry (DSC) were used to study thermosensitive properties of PVCL-MAA depending on pH, fraction of MAA units, and surfactant concentration. FTIR spectroscopy was used for identification of the interaction between MAA and VCL units. An equilibrium dialysis method was employed to prove formation of SDS/copolymer bound micelles.

Experimental Section

Materials. *N*-Vinylcaprolactam (VCL) (Aldrich) was twice distilled under low pressure ($T = 130$ °C/10 mmHg). Methacrylic acid (MAA) (Merck) was purified on silica gel column. 2,2'-Azobisisobutyronitrile (AIBN) (Merck) was recrystallized from methanol. Sodium dodecyl sulfate (SDS) (Merck) and potassium persulfate (KPS) (Merck) were used without further purification.

Dimethyl sulfoxide, benzene, and diethyl ether (Merck) were analytical purity grade. Water for light scattering and calorimetric experiments was purified by Milli-Q purification system.

Polymer Synthesis. All studied polymers were synthesized by free-radical polymerization in argon atmosphere. Initial monomer solution contained 70 vol % of solvent; initiator concentration was 0.03 wt %

Poly(*N*-vinylcaprolactam). Initial monomer solution in benzene containing AIBN as initiator was incubated in argon atmosphere at 50 °C for 48 h. Then the reaction solution was 5-fold diluted with benzene and poured into diethyl ether. White precipitate was collected, dissolved in deionized water, dialyzed, and freeze-dried.

Poly(*N*-vinylcaprolactam-*co*-methacrylic acid). Initial monomer solution in DMSO/water mixture containing AIBN as initiator was incubated in argon atmosphere at 50 °C for 48 h. Then the reaction solution was 5-fold diluted with ethanol and poured into hot deionized water. White precipitate was collected, dissolved in 0.1 M NaOH, and dialyzed. Before dialysis, pH of the polymer solution was adjusted to 8. After dialysis, polymer solutions were freeze-dried during 20 h.

Poly(methacrylic acid). Initial monomer solution in water containing KPS as initiator was incubated in argon atmosphere at 70 °C for 48 h. Then the reaction solution was 10-fold diluted with deionized water, dialyzed without preliminary isolation, and freeze-dried.

All polymers synthesized were purified by dialysis. Sigma methylcellulose sacks with 15 kDa cutoff limit were used for that purpose. The polymers were dialyzed for 48 h; the water was exchanged every 12 h. The purified polymers were isolated by freeze-drying with a Christ Alpha 1-2LD Instrument.

Polymerization details are described in Table 1.

Equilibrium Dialysis of a PVCL-MAA₃₇ Solution Containing SDS. A solution of polymer containing 0.05 M NaCl and 2 mM SDS was taken as a retentate solution. NaCl solution, 0.05 M, was taken as a permeate solution. Polymer concentration was 1 mg/mL. The presence of NaCl in both solutions allowed no further correction for the Donnan effect since NaCl was taken in 10-fold excess calculated for the total of ionized groups in SDS and PVCL-MAA₃₇. The volume of the permeate solution was 20 times larger than that of the

retentate solution. The equilibrium was found to be attained after 24 h at 25 °C. SDS equilibrium concentrations were determined as follows. Centrifuge tubes were filled with 3 mL of fresh-distilled chloroform, 0.1 mL of solution, containing SDS, and 0.5 mL of 0.01% water solution of methylene blue. The tubes were intensively shaken and centrifuged at 4000 rpm for 20 min. The chloroform phase containing an ion-pair adduct of methylene blue and SDS (methylene blue to SDS ratio in adduct is 1:1) was extracted by syringe. The concentration of the adduct was determined from spectral measurements at 655 nm (Perkin-Elmer Lambda 16 UV/VIS spectrophotometer); the extinction coefficient was found to be $95000 \text{ l} \cdot (\text{mol} \cdot \text{cm})^{-1}$.

Sample Preparation. All samples for light scattering (LS), calorimetric, and phase diagram studies were made by dissolution of the freeze-dried polymers in 0.05 M NaCl aqueous solutions, at room temperature, during 12 h. The polymer concentration used was 1 mg/mL for DLS and calorimetric measurements. An excess of electrolyte (0.05 M NaCl) was used for screening electrostatic interactions between ionized methacrylic acid units. Polymer solutions for LS measurements were clarified by filtration through Millipore GS 0.22 μm pore size filters before use.

Laser Light Scattering Experiments. The laser light scattering experiments were performed with ALV-Instruments ALV/CGS-8F laser goniometer system and ALV-5000 multi- τ digital correlator. The light source was JDS Uniphase helium/neon 22 mW laser operating at $\lambda = 633 \text{ nm}$.

In the dynamic light scattering (DLS) experiments time-intensity correlation functions in the beating mode were measured at a scattering angle of 90° as a function of temperature. Scattering intensity from polymer solutions was also measured at 90°. Temperature ranged from 20 to 60 °C. The correlation functions obtained were analyzed using the CONTIN program.

Static light scattering (SLS) measurements were carried out for M_w determination of the polymers using the Zimm-plot method. The scattering angle was varied from 40 to 140°, polymer concentrations varied from 0.5 to 5 mg/mL. Refractive index increments were measured with Otsuka Photol RM-102 differential refractometer operating at $\lambda = 628 \text{ nm}$.

Calorimetric Measurements. The calorimetric experiments were performed with a SCAL-1 differential scanning microcalorimeter (Scal Co. Ltd, Puschino). All measurements were performed at a heating rate of 1 K/min and excess pressure 3 atm over the temperature range from 4 to 120 °C. A NaCl water solution, 0.05 M, was used as a baseline solution. The thermograms of the polymers studied were analyzed as described elsewhere.²⁷ Transition enthalpies were calculated by integration of the area under the calorimetric peaks.

Polymer Characterization. Polymer characterization details are given in Table 1. Average molecular weights of the synthesized polymers were determined by SLS. The MAA unit fraction in PVCL-MAA copolymers was determined by standard titration and by ^1H NMR.

Potentiometric measurements for titration were carried out with a pH meter (HANNA pH-300) at 25 °C. The solutions of ionized copolymers containing an excess of NaOH were titrated with 0.01 M HCl. The titration details are described elsewhere.²²

The ^1H NMR spectra were recorded with a Bruker Avance DRX 400 MHz spectrometer using deuterated DMSO as solvent. Polymer concentration was 1 wt %. The spectra were collected at 25 °C. Chemical shifts for the proton spectra were referenced to deuterated DMSO at 2.49 ppm.

The FT-IR spectra were recorded with a Bruker IFS 113v FT-IR spectrometer. One hundred scans were single averaged at a resolution of 2 cm^{-1} . The samples for FT-IR measurements were prepared by grinding freeze-dried polymers with KBr powder. The resulting mixtures were pressed into pellets.

Results and Discussion

Reactivity Ratios. Compositions of a copolymer and monomer sequence distribution are mainly dependent

Table 2. Effect of Feed Ratio on the Composition of PVCL-MAA Copolymer

VCL to MAA feed ratio	copolymer composition, VCL to MAA ratio	conversion, %
9:1	1:1	2
2:1	1:1,3	4
2:3	1:2,2	5

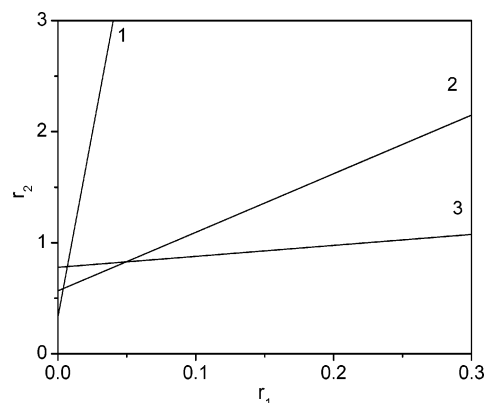


Figure 1. Determination of VCL (r_1) and MAA (r_2) reactivity rates. Initial monomer ratios, VCL to MAA: (1) 9:1; (2) 2:1; (3) 2:3.

on initial concentration of monomers and their reactivity ratios. The data of Table 1 show that the PVCL-MAA₃₇ feed ratio is different from its ultimate composition; therefore it appears important to investigate the reactivity ratios of VCL and MAA.

To analyze the distribution of comonomers in PVCL-MAA chains the copolymerization rates of VCL and MAA in a DMSO/water mixture were studied by the Mayo-Lewis method²⁸ in which composition/conversion data for copolymers are analyzed. In this paper the most traditional variant of the method was used, which requires study of the composition of copolymers at conversion less than 5%. Table 2 shows the feed VCL to MAA ratios and VCL to MAA ratios in the copolymer. Conversion varied from 2% to 5% depending on feed ratio. The composition of the copolymers was determined by standard titration. The values of data points of Figure 1 were calculated by using the Mayo-Lewis equation. The intersection circle showed that $r_1(\text{VCL}) = 0.03 \pm 0.02$ and $r_2(\text{MAA}) = 0.7 \pm 0.2$. Despite that the error is large enough it is possible to state that the reactivity of MAA appears to be much higher than that of VCL.

Macromolecular Complex Formation. Figure 2 (curves 1 and 2) shows the pH dependences of the scattering intensity from the aqueous solutions of PVCL-MAA copolymers with different component fractions at 25 °C. The scattering intensity sharply increases as pH decreases. At low pH PVCL-MAA copolymers undergo intermolecular aggregation, which produces scattering intensity growth. Observed pH sensitivity of PVCL-MAA copolymers is one of their interesting features. It is important to note that both PVCL and PMAA do not aggregate at low pH values (Figure 2, curves 3 and 4), and only the simultaneous presence of VCL and MAA units in a polymer chain results in intermacromolecular aggregation. In that case the pH value at which macromolecular aggregation takes place depends on the fraction of MAA units in copolymers. The increase of the fraction of MAA units leads to an increase in the critical pH value at which intermacromolecular aggregates are formed. In the case of the

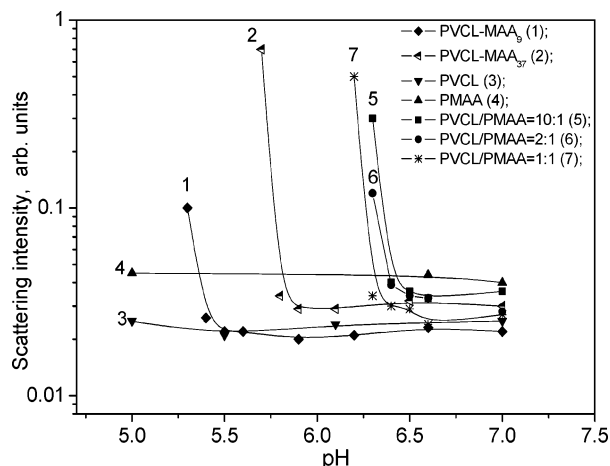


Figure 2. Variation with pH of the total scattering intensity for PVCL-MAA copolymers and PVCL/PMAA mixtures.

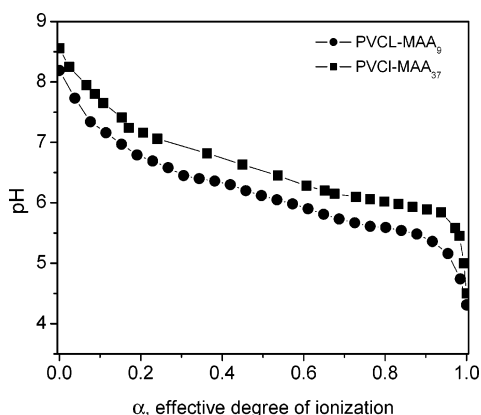


Figure 3. Titration curves of PVCL-MAA₉ and PVCL-MAA₃₇.

copolymer containing 9% MAA units, this critical pH value is close to 5.3, and for the copolymer with 37% MAA units, it is 5.7.

It should be also noted that the aggregation of the copolymers starts when the effective degree of ionization becomes very low. Figure 3 shows titration curves of the copolymers of different composition at 25 °C. The ionized copolymer solutions containing excessive amount of NaOH are titrated with HCl until the pH changes rapidly. This pH region practically coincides with the pH of aggregation of the copolymer solutions (cf. Figure 2 (curves 1,2), Figure 3). The effective degree of ionization of both copolymers at the start of the aggregation is approximately 0.05.

To understand the physics of the pH-sensitive behavior of PVCL-MAA copolymers, the aqueous solutions of PVCL/PMAA homopolymer mixtures with different composition of PVCL and PMAA were studied at different pHs. The scattering intensity sharply increases as pH decreases to 6.2 (Figure 2, curves 5–7), indicating intermacromolecular aggregation. In contrast to PVCL-MAA copolymers, the pH of aggregation does not depend on the PVCL to PMAA ratio, and the corresponding critical value is about 6.2. The difference in the pH-dependent behavior between the copolymer solutions and solutions of homopolymer mixtures may be ascribed to the differences in pK_a of PMAA and PVCL-MAA copolymers.

The effect of aggregation of PVCL-MAA copolymers and PVCL/PMAA mixtures may be connected with macromolecular complex formation.

Poly(methacrylic acid) is well-known for its complexation properties when protonated. Several complexes with macromolecular compounds such as poly(ethylene oxide),²³ poly(*N*-vinylpyrrolidone),^{24,25} and poly(ethylene imine)²⁶ have been observed due to hydrogen bonding of carboxyl groups of PMAA and negatively charged groups of macromolecules acting as proton acceptors. In particular, PMAA/PVP complexes are formed because of H-bonding between amide and carboxyl groups; the carboxyl group is a proton donor; the C=O fragment of the amide group is a proton acceptor. *N*-vinylcaprolactam is a homologue of *N*-vinylpyrrolidone and complexation of the same nature between VCL and MAA units in PVCL-MAA copolymers and PVCL/PMAA mixtures can be expected.

One of the practical methods to identify molecular complexes formed by H-bonding is the IR method. Broadening, low frequencies shift, and intensity increase of OH stretching absorption bands indicate the presence of H-bonds. However, investigation of OH absorption bands is mainly applicable for systems with a single type of proton acceptor. If hydrogen bonds are formed in systems with several types of proton acceptors, the changes in OH-band parameters are not always sufficient to define which groups are involved in H-bonding. In that case investigation of proton acceptor bands is actual. As the macromolecular complexes in PVCL/PMAA mixtures and PVCL-MAA copolymers are supposed to be formed due to the coordination of amide and carboxyl groups, it is appropriate to study stretching vibrations of amide C=O fragments as proton acceptors. If a C=O bond is involved in hydrogen bond formation, its peak shifts to lower frequencies by 1–6%.²⁹ Also there is a possibility of splitting of proton acceptor bands as reported in refs 30–32, including splitting of C=O bands in complexes of *N*-methylacetamide and phenol.³²

We will first compare IR spectra of fully ionized PVCL-MAA₃₇ and PVCL-MAA₃₇ aggregated at low pH. Ionization of PVCL-MAA₃₇ closes out the possibility of H-bonding between amide and carboxyl groups; the copolymer aggregated at low pH contains protonated COOH groups and the formation of macromolecular complexes due to H-bonding is suspected for that sample. Ionized PVCL-MAA₃₇ is used as a control because there are technical difficulties in obtaining a sample of nonprotonated PVCL-MAA₃₇ that should not be disturbed by H-bonding between MAA and VCL units.

Figure 4a,b shows the IR spectra of PVCL-MAA₃₇ in the ionized (a) and aggregated (b) state. In spectrum (a) only an amide band at 1637 cm⁻¹ is observed, spectrum (b) shows both amide (1623 cm⁻¹) and carboxyl (1716 cm⁻¹) C=O absorption bands. In spectrum (b) the amide band exhibits a low-frequency shift (14 cm⁻¹) compared to spectrum (a). This indicates that the amide C=O bond is involved in H-bonding with a proton donor, supposedly carboxyl groups of MAA units. The changes of C=O or OH bands of MAA are not possible to detect since sample (a) is not protonated. For that purpose it is appropriate to compare two mixtures of PVCL and PMAA. This makes it possible to compare C=O and OH absorption bands of the COOH groups that might bind the amide groups with those that do not exhibit binding.

The first mixture should be prepared by mechanical mixing of the two components; the second one should be prepared by acid-induced aggregation of the components in aqueous medium. The ratio of MAA to VCL

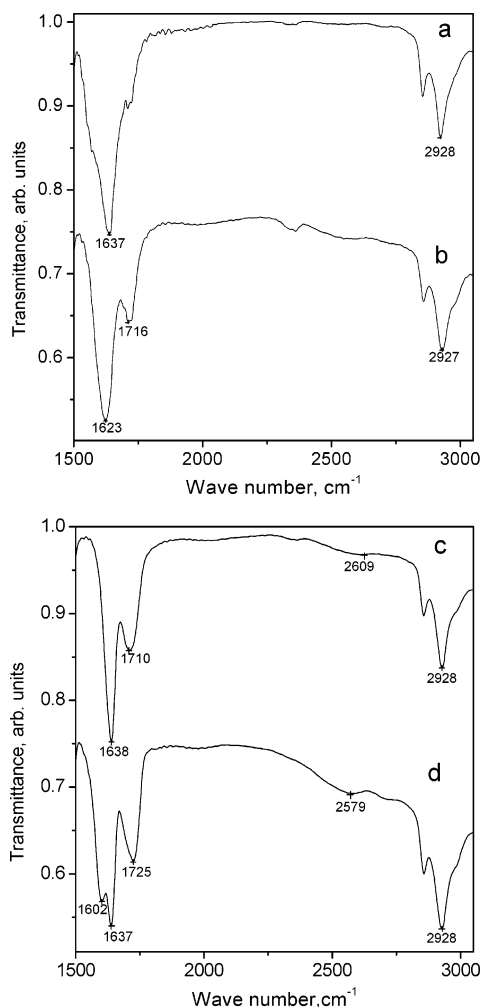


Figure 4. IR-spectra of ionized PVCL-MAA₃₇ (a), PVCL-MAA₃₇ aggregates (b), PVCL/PMAA 1:1 mechanical mixture (c), and PVCL/PMAA 1:1 aggregates (d).

units should be 1:1 since PMAA is known to form equimolar complexes with macromolecular proton acceptors.²³

Figure 4c,d shows the IR spectra of these PVCL/PMAA mixtures. In the spectrum of the mechanical mixture (c) one can observe two strong peaks of amide (1636 cm⁻¹) and carboxyl (1710 cm⁻¹) C=O bonds. In PMAA the frequency of C=O bonds may be affected by intra- and interchain H-bonding between carboxyls. In the spectrum of the PVCL/PMAA aggregates (d) the positions of the amide and carboxyl C=O absorption bands change. The carboxyl CO peak shifts to higher frequencies (1725 cm⁻¹). The amide band splits into a doublet (1636 and 1606 cm⁻¹). The amide low-frequency splitting is likely to be caused by the formation of the new hydrogen bonds between carboxyl O-H groups and amide C=O groups. The high-frequency shift of the carboxyl C=O band is due to the destruction of the H-bonds that exist between PMAA carboxyl groups leading to the release of free C=O bonds.

Figure 4c,d shows also the OH absorption bands of PMAA in the mechanical mixture (2609 cm⁻¹) and in the precipitated mixture (2579 cm⁻¹). Both bands are very broad. This fact confirms that in both cases the carboxyl groups are involved in H-bonding. In the spectrum of the PVCL/PMAA precipitate the OH band is, however, shifted by 30 cm⁻¹ to low frequencies, implying a change of the nature of H-bonding. This fact

eventually confirms the formation of H-bonds between amide and carboxyl groups.

Some attention should be also paid to the fact that the amide absorption band of PVCL-MAA₃₇ undergoes a low-frequency shift whereas that of PVCL/PMAA shows splitting, the additional mode being of lower frequency. Both these phenomena may be considered as characteristic of H-bond formation judging by the literature data. However, it is difficult to establish the causes of such distinctions in very closely related systems. Possibly, the band of PVCL-MAA₃₇ also would split but for some reasons the resulting peaks are not resolved, giving a single peak.

The effect of complexation between VCL and MAA units due to hydrogen bonding leads to the change in the hydrophilic-hydrophobic balance of macromolecules. Hydrophobic interactions are increased since interacting hydrophilic groups of macromolecules are partially expelled from the water surrounding. This leads to intermacromolecular aggregation. The effect of the hydrophilic-hydrophobic balance changes due to complex formation was studied by using interaction of PVCL with organic acids. We tested the behavior of PVCL in dilute (0.01 M) water solutions of various low molecular weight carboxylic acids which have a different balance of hydrophobic and hydrophilic groups. Hydrophobicity of the acids used increases as acetic < acrylic < crotonic < methacrylic < 6-hexenoic. The interaction of PVCL with methacrylic acid and 6-hexenoic acids results in the formation of insoluble aggregates. In the case of acetic, acrylic and crotonic acids, no formation of aggregates was observed. The general tendency of the effect is that the aggregation is observed only in the presence of the acids of higher hydrophobicity. This confirms the hypothesis that hydrophobic interactions should be responsible for insolubility of the complexes.

Effect of pH on Temperature Sensitive Properties. It is known that in aqueous solutions PVCL undergoes a phase transition when the temperature is raised to about 30–32 °C. The complexation between VCL and MAA units may somehow affect the thermosensitive properties of PVCL and PVCL-MAA copolymers, since it changes the hydrophilic-hydrophobic balance of macromolecular groups, which are responsible for these properties. One of the simplest and informative methods to find out how the macrocharacteristics of polymers would change due to complexation is to investigate temperature dependencies of the scattering intensity from the solutions at different pH values. Complex formation is strongly pH-dependent, as follows from Figure 2. This means that the pH of the solution is one of the major factors that can regulate the thermosensitive properties of the systems studied.

The thermosensitive behavior of PVCL-MAA₃₇, PVCL/PMAA 1:1 mixture, and PVCL homopolymer as a function of pH and temperature was studied. Poly(methacrylic acid) is temperature insensitive at the working concentrations. The temperature dependencies of the scattering intensity from PVCL-MAA₃₇, PVCL/PMAA 1:1, and PVCL solutions at different pH-values are presented in Figure 5.

Figure 5a shows that the scattering intensity from solutions of PVCL is practically independent of pH. The cloud-point temperature of PVCL is around 30 °C and depends slightly on pH, which may be connected with differences in the effect of ions in acidic and neutral solutions on the hydrophobic interactions of VCL units.

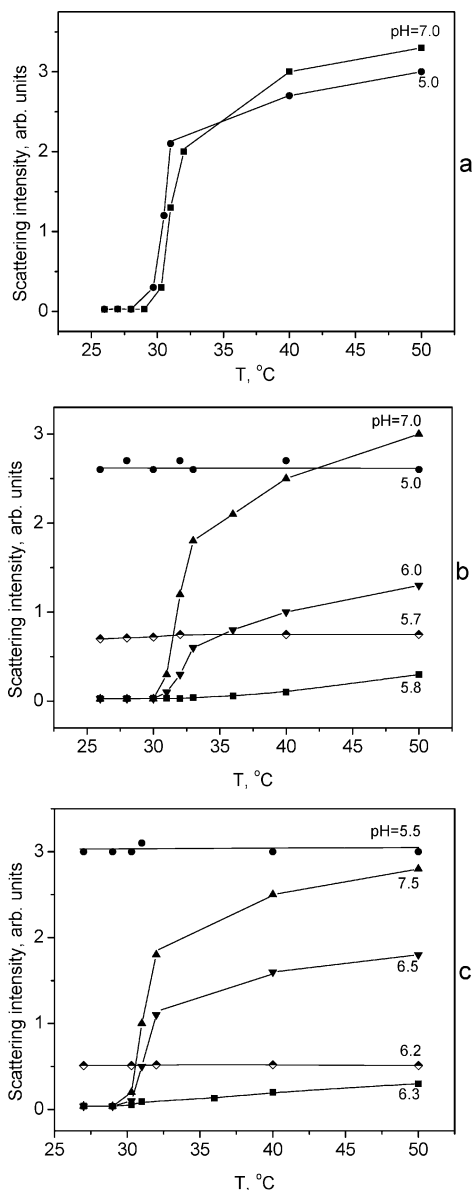


Figure 5. Temperature dependencies of scattering intensity from polymer solutions at different pH values. (a) PVCL; (b) PVCL-MAA₃₇; (c) PVCL/PMAA 1:1 mixture.

PVCL/PMAA 1:1 mixture and PVCL-MAA₃₇ behave in a different way (Figure 5b,c). In this case the strong pH dependence of thermosensitive behavior of studied systems is observed. From the obtained data one can see that three characteristic pH regions can be distinguished for the phase behavior of these polymer systems.

First, at $\text{pH} > 6.5$ (for PVCL/PMAA 1:1) and $\text{pH} > 6.0$ (for PVCL-MAA₃₇) we observe a phase transition from a soluble to an insoluble state when the temperature is raised to 30–32 °C. The phase behavior in this region of pH is similar to that of PVCL. The cloud point temperature of PVCL-MAA₃₇ shows a slight increase (31 °C) compared to PVCL (30 °C).

Second, at weakly acidic pH values, the thermosensitive behavior of the polymer systems containing MAA units changes. The distinctive feature of PVCL-MAA₃₇ as well as of the PVCL/PMAA 1:1 mixture is the thermosensitive behavior in the pH region 5.5–6.5. When the pH is close to 6.5 in the case of the PVCL/PMAA 1:1 mixture and 6.0 in the case of PVCL-MAA₃₇,

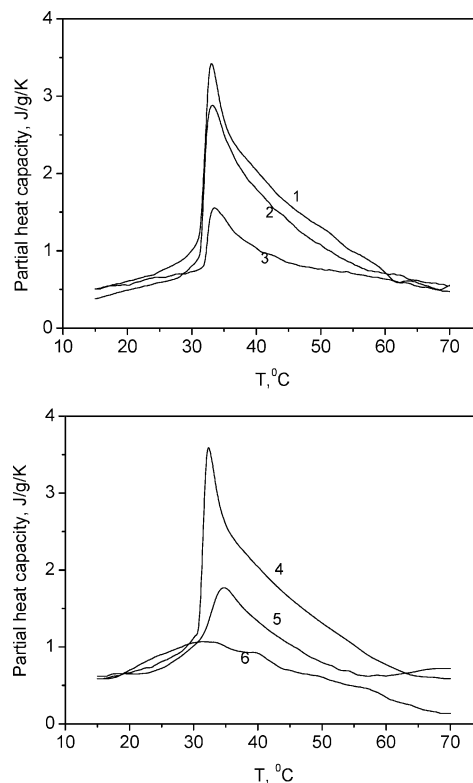


Figure 6. Effect of MAA fraction on the form of calorimetric peaks of PVCL and PVCL-MAA copolymers at various pH values. (1) PVCL, $\text{pH} = 7$; (2) PVCL-MAA₉, $\text{pH} = 7$; (3) PVCL-MAA₃₇, $\text{pH} = 7$; (4) PVCL, $\text{pH} = 5.3$; (5) PVCL-MAA₉, $\text{pH} = 5.5$; (6) PVCL-MAA₃₇, $\text{pH} = 5.8$.

heating these solutions up to 50 °C produces less scattering intensity compared to the solutions at higher pH values. A more profound decrease of scattering intensity is observed at pH 5.8 and 6.3 for PVCL-MAA₃₇ and PVCL/PMAA 1:1, respectively. Besides that, the cloud-point temperature of PVCL-MAA₃₇ is larger by 2 °C at pH 5.8 than at higher pH values. The effective ionization degree of PVCL-MAA₃₇ and PMAA at these pH values is about 0.1.

Third, when the pH of the solutions is further decreased, the scattering intensity grows and it becomes insensitive to the temperature regime. As was shown above, this behavior is due to the formation of insoluble macromolecular complexes at low pH values.

Thus, in the case of PVCL-MAA₃₇ and PVCL-MAA mixtures, there exists a pH interval in which a very slight aggregation is observed in a wide range of temperatures. In that pH interval a minimum of scattering intensity is observed at high temperatures compared to the scattering intensity for all other pH values. At higher pH values the scattering intensity increases as temperature is increased due to the temperature-induced aggregation of the polymers. At lower pH values the level of the scattering intensity is high and constant due to pH-induced macromolecular complex formation.

For quantitative characterization of the phase transitions of PVCL-MAA copolymers, calorimetric studies of their aqueous solutions at various pH values have been performed.

Figure 6 shows the DSC thermograms of PVCL and PVCL-MAA copolymers of different composition at various pH values. The thermograms were measured first at pH 7, where the effective degree of ionization of the copolymers is high ($\alpha = 0.9$). Then the thermograms

Table 3. Phase Transition Parameters of PVCL and PVCL-MAA Copolymers at pH 7

polymer	T_{cp}	T_{tr}	ΔH_{tr} , J/g	relative enthalpy decrease	MAA mole fraction
PVCL	30	33	22	0	0
PVCL-MAA ₉	30	33	16	0.27	0.09
PVCL-MAA ₃₇	31	33	4	0.82	0.37

at weakly acidic pH values were obtained. For PVCL, the pH of the solution has no effect on the properties of the polymer; the pH value for the calorimetric study was the same as in the scattering intensity study (Figure 5a). For PVCL-MAA₉ and PVCL-MAA₃₇ we have chosen pH values at which the least possible aggregation at high temperature is observed and which are close to the pH value where the complex formation in these systems starts, but slightly higher than this value (Figures 2 and 5b,c).

All the polymers studied show a phase transition peak at pH 7 (Figure 6, curves 2,3). The thermograms obtained during heating of the copolymers show a single broad and asymmetric peak of heat capacity, observed within the temperature range 10–80 °C. These results demonstrate that all studied polymers undergo a cooperative transition which is accompanied by a considerable endothermic heat effect. The observed phase transition is reversible since the thermograms during the second and subsequent heatings at the same heating rate were reproduced. The start of peak shoulders is usually identified with the cloud-point temperature of polymer solutions. The maximum of the peak will be called below a transition temperature (T_{tr}) according to ref 14.

At pH 7 the form of the calorimetric peaks of both copolymers is similar to that of PVCL. The transition temperature of PVCL and PVCL-MAA copolymers is about 33 °C. T_{tr} is almost independent of the MAA fraction in the copolymers. The cloud-point temperatures determined from the thermograms are also close to each other (Table 3). This appears to be an unexpected result, since for NIPA-based copolymers it is well-known that the introduction of hydrophilic units into the PNIPA backbone results in an increase of the cloud-point temperature.^{33,34} The starting temperature of the peaks is close to the cloud-point values determined in LLS experiments, so the cloud point-values obtained by LLS and DSC methods are in good agreement.

Transition enthalpy (ΔH_{tr}) of the copolymers was found to decrease abruptly with an increase in the fraction of MAA units (Table 3). ΔH_{tr} of PVCL is 22 J/g/K. The introduction of 9% of MAA units decreases the transition enthalpy by 30% (PVCL-MAA₉). PVCL-MAA₃₇ has a transition enthalpy 6 times lower than that of PVCL. It may be supposed that this effect can be ascribed to a different VCL mole fraction of the copolymers. In that case the relative enthalpy decrease should be equal to the MAA mole fraction. The data of Table 3 do not confirm this assumption. Nevertheless, the reasons that account for this effect are tightly connected with the presence of MAA units.

Coil-to-globule transitions of polymers such as PNIPA and PVCL are usually explained by the intensification of hydrophobic interactions, which occurs at higher temperatures due to the destruction of so-called water "cages" surrounding hydrophobic groups.³⁵ The endothermic effect of the transition is supposed to be caused by "melting" of the water "cages". In PVCL-MAA copolymers, charged MAA units disturb water sur-

Table 4. Hydrodynamic Radius of PVCL-MAA₃₇ Particles as a Function of pH and Temperature

temp, °C	hydrodynamic radius, nm, pH = 7	hydrodynamic radius, nm, pH = 5.8
25	25	34
27	26	
29	24	35
30	26	33
31	200	34
32	300	35

rounding PVCL hydrophobic fragments, violating the compactness and continuity of the water cages. This leads to a decrease of cooperativity of the phase transition and consequently of its enthalpy.

The effect of pH on the shape of the thermograms is one of the important points in understanding the main driving forces which affect the thermosensitive behavior of macromolecules.

For the low pH polymer solutions the results of the calorimetric studies are different from those at high pH (Figure 6, curves 4–6). The thermogram of PVCL shows no changes compared to the study at pH 7. For PVCL-MAA₉ one can observe a peak which starts at 25 °C. The cloud-point temperature of the PVCL-MAA₉ solution at pH 5.5 is 33 °C. This peak is broader than that obtained at pH 7. The transition enthalpy has decreased from 16 to 6 J/g. In other words, at pH 5.5 PVCL-MAA₉ shows a partial loss of thermosensitivity, which manifests in a decrease of cooperativity and enthalpy of the transition.

As for PVCL-MAA₃₇, the thermogram obtained at pH 5.8 shows a very broad peak that starts at 20 °C, its maximum being equal to 31 °C. This peak cannot be considered as characteristic of any change of physical state of the copolymer. This presumption was confirmed by DLS measurements (Table 4). The data of Table 4 show that there is no variation of hydrodynamic radius of PVCL-MAA₃₇ macromolecules between 20 and 32 °C at pH 5.8. This indicates that no conformational changes of PVCL-MAA₃₇ occur in that temperature region. As was shown in Figure 5b slight temperature-induced aggregation of PVCL-MAA₃₇ starts only at 33 °C. If any conformational changes occurred between 20 and 32 °C, they would be detected by DLS as well. Thus, most probably the calorimetric effect of the phase transition of PVCL-MAA₃₇ at pH 5.8 is too weak to be detected by DSC.

Thus the calorimetric and DLS measurements confirm the data of LLS experiments. PVCL-MAA copolymers exhibit a loss of thermosensitivity at pH values which by 0.1–0.2 units exceed the pH values of the complex formation in these systems. The scattering intensity from the polymer solutions, enthalpy, and cooperativity of the transition are decreased under these conditions. The mechanism of this effect remains unclear. Probably it can be associated with the peculiarities of macromolecular complex formation in these systems. This problem will be further considered in subsequent publications.

Effect of a Similarly Charged Surfactant. It is necessary to stress that the temperature-sensitive properties of PVCL-MAA copolymers should be considered from the point of view of the hydrophobic-hydrophilic balance of macromolecular groups. pH-sensitive properties of the copolymers were shown to be due to complex formation between VCL and MAA units. However, the insolubility of these complexes is a

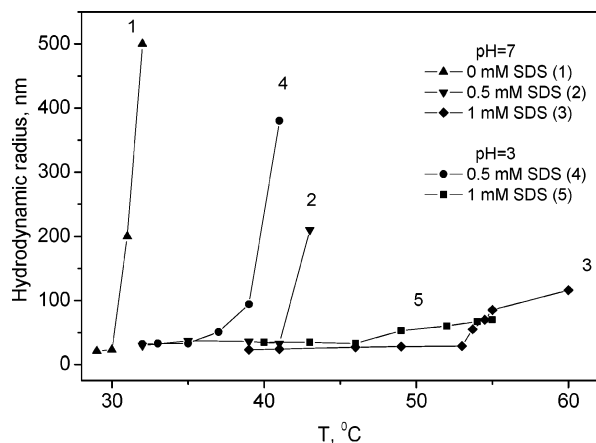


Figure 7. Temperature dependencies of hydrodynamic radius of PVCL-MAA₃₇ particles in the presence of SDS at pH = 3 and 7.

consequence of their hydrophobicity. Thus both pH-sensitivity and thermosensitivity can be influenced by hydrophobic-hydrophilic balance changes. One of the possible ways for changing the balance is addition of surfactants to solution. The effect of an oppositely (positively) charged surfactant (CPC) was discussed earlier.²² In this work the effect of a similarly (negatively) charged surfactant (SDS) is studied. Ionic surfactants are known for their ability to adsorb on polymer chains due to hydrophobic interactions, producing polymer-bound micelles at concentrations lower than the cmc.³⁶ So it appears challenging to observe the competition of two processes: formation of hydrophobic macromolecular complexes by interaction of MAA and VCL units and formation of polymer-bound micelles of SDS.

In fact, SDS is capable of forming polymer-bound micelles with PVCL-MAA₃₇ at pH 7. The adsorption of SDS molecules to copolymer chains should result in the fact that if a solution containing the copolymer and SDS is dialyzed as a retentate solution, at equilibrium, the concentration of SDS in the retentate should be higher than in the permeate.

After the 24-h dialysis of a PVCL-MAA₃₇ solution in the presence of 2 mM SDS at 25 °C, the concentration of SDS in the permeate solution was 0.11 mM, while in the retentate solution it was 0.23 mM, which is almost 2 times larger. Thus it is possible to state that despite being having charges of the same sign SDS molecules adsorb on copolymer chains at pH 7 where more than 90% of carboxyl groups are ionized. The calculations show that the degree of adsorption is 5 mM SDS per gram of the copolymer; SDS to VCL units molar ratio in the initial solution is 0.6.

Figure 7 shows the temperature dependencies of the hydrodynamic radius of PVCL-MAA₃₇ particles at acidic and neutral pHs at different SDS concentrations. At both at pH 3 and 7 a sharp increase of the scattering intensity with temperature growth and an increase of hydrodynamic radius of the copolymer particles are observed. So PVCL-MAA₃₇ is thermosensitive under these experimental conditions. Note that PVCL-MAA₃₇ does not separate from the solution below T_{tr} at pH 3. In that case polymer-bound SDS molecules create a negative charge on polymer chains and the resulting repulsive electrostatic interactions prevent formation of hydrophobic macromolecular complexes. Thus addition of a small amount of SDS renders the copolymer pH insensitive.

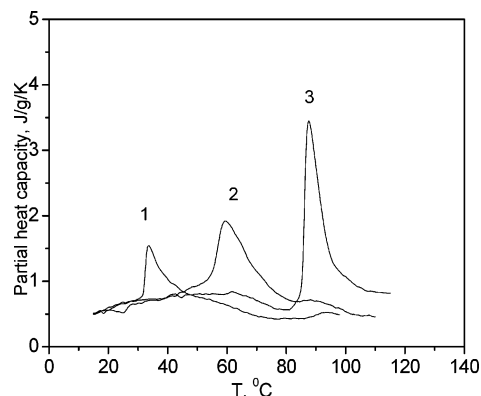


Figure 8. Effect of SDS on the form and position of calorimetric peaks of PVCL-MAA₃₇, pH = 7. (1) no SDS; (2) 1 mM SDS; (3) 4 mM SDS.

At both at pH 3 and 7, the phase transition temperature increases sharply with the increase of SDS content in the solution. The effect of such a shift is also connected with formation of polymer-bound micelles. The collapse of the copolymer chains at higher temperatures is caused by an increase of attractive hydrophobic interactions of VCL units. The higher the temperature is, the stronger the attraction is. The repulsive electrostatic interactions produced by adsorbed SDS molecules compete with the attractive forces. Thus to overcome the repulsive interactions and create a new phase larger temperature is needed.

At pH 3 repulsive electrostatic interactions exist only between surfactant molecules which are attached to the copolymer chains, since most MAA units of the copolymer are not ionized. However, at pH 7 the effective degree of ionization of MAA units is considerable ($\alpha = 0.9$) and their interaction with surfactant molecules produces additional repulsive forces between the segments of the copolymer chains. So at pH 7 larger attraction (compared to pH 3) is needed to overcome additional repulsion forces between ionized MAA units and SDS molecules, consequently the collapse takes place at higher temperatures.

It is necessary to note that the behavior of the PVCL homopolymer in the presence of SDS was previously reported to be different.³⁷ If SDS is present in aqueous solution of PVCL, it suppresses intermacromolecular aggregation of the polymer when the temperature is raised. However, intramacromolecular aggregation is conserved in that case, as shown by the decrease of the hydrodynamic radius of macromolecules.

To estimate the enthalpy of the phase transition of PVCL-MAA₃₇ in the presence of SDS, a calorimetric study was performed. Figure 8 shows the thermograms of PVCL-MAA₃₇ in the presence of SDS. Besides the effect of SDS on the transition temperature, one may also observe changes in the ΔH_{tr} and the form of the calorimetric peaks. First, at a 1 mM SDS concentration the peak is broader as compared to the surfactant-free study. On the other hand, at 4 mM SDS it contracts significantly. Second, ΔH_{tr} of the copolymer in the presence of SDS increases sharply. The parameters of the peaks are presented in Table 5.

One can expect a decrease of ΔH_{tr} with an increase in SDS concentration, because if the surfactant adsorbs to thermosensitive PVCL-MAA₃₇ copolymer chains, it would decrease the cooperativity of the phase transition behaving similarly to MAA monomer units. Indeed, in

Table 5. Dependence of PVCL–MAA₃₇ Phase Transition Parameters on SDS Concentration in Solution

SDS concn, mM	ΔH_{tr} , J/g	peak half-width, °C
0	4	3
1	11	6
4	18	3

ref 38 for thermosensitive nonionized triblock copolymers of poly(ethylene oxide) and poly(propylene oxide) (a somewhat similar system to that studied here) an abrupt decrease of the transition enthalpy was observed when SDS was added to the solution. In our case, however, the effect is opposite. The reasons for this are presently unclear.

Conclusion

Using IR techniques we have proved that poly(*N*-vinylcaprolactam-*co*-methacrylic acid) as well as mixtures of PMAA and PVCL form insoluble macromolecular complexes at low pH in water by cooperative H-bonding between VCL and MAA units. Macromolecular complex formation appears to be the cause of the pH-sensitive properties of PVCL–MAA copolymers. With the technique of laser light scattering and differential scanning calorimetry, the effect of pH on thermosensitive properties of poly(*N*-vinylcaprolactam-*co*-methacrylic acid) was studied. Our results show that there exists a pH interval where the effective degree of ionization of the copolymers is low and the thermosensitive properties of PVCL–MAA copolymers are less pronounced than at higher degrees of ionization.

Addition of SDS to PVCL–MAA₃₇ aggregates at low pH values leads to their solubilization. Decay of the complexes takes place due to formation of charged polymer-bound micelles. In the presence of SDS the copolymer is temperature sensitive both at low and high pH; however, the transition temperature increases as compared to the surfactant-free study. The increase of the transition temperature is connected with the repulsive electrostatic interactions of adsorbed SDS molecules. An increase of the transition enthalpy is observed with an increase of SDS concentration at pH 7.

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