Available online at www.sciencedirect.com
SCIENCE DIRECT®
Polymer 45 (2004) 3055–3061
polymer
www.elsevier.com/locate/polymer

Co-nonsolvency effects in the thermoprecipitation of oligomeric polyacrylamides from hydro-organic solutions

Marilia Panayiotou[a], Frédéric Garret-Flaudy[a], Ruth Freitag[a,b,*]

[a]*Laboratory of Chemical Biotechnology, Faculty of Basic Science, Swiss Federal Institute of Technology, Lausanne, Switzerland*
[b]*Chair for Process Biotechnology, Faculty of Engineering Science, University of Bayreuth, Universitätsstrasse 30, 95447 Bayreuth, Germany*

Received 9 April 2003; received in revised form 6 February 2004; accepted 11 February 2004

Abstract

Co-solutes and co-solvents influence the thermoprecipitation of stimulus-responsive polymers from aqueous solution. Taking the behavior of oligomeric poly-(*N*-isopropylacrylamide) prepared by chain transfer polymerization as reference, the influence of organic solvents (concentration <2 M) on the thermoprecipitation of polyacrylamides with critical solution temperatures (CST) in pure water between 30 and 75 °C is investigated using turbidity and differential scanning calorimetry. Depending on the system, both increase and decrease but also the disappearance of the CST is observed. The strength of the observed effect is related not only to the size but also the structure of the hydrophobic domain of the solvent molecule. Contrary to the effects observed upon the addition of simple salts as additives, the chemistry of the investigated polyacrylamide is of direct consequence for the effect of a given solvent. Certain parallels can hence be drawn to the behavior previously observed for additives such as anionic surfactants and alkylamines.

Keywords: Stimulus-responsive materials; PNIPAM; Thermoprecipitation

1. Introduction

Aqueous solutions of thermoresponsive polymers such as poly-(*N*-isopropylacrylamide), PNIPAM, show abrupt property changes upon stimulation [1]. Thermoresponsive PNIPAM hydrogels will swell and collapse respectively as the critical temperature is passed [2]. Linear PNIPAM molecules precipitate upon stimulation, an effect that is e.g. exploited in affinity precipitation for bioseparation purposes [3]. The effect occurs in systems with negative dissolution enthalpy and negative dissolution entropy. As the critical temperature is surpassed, the free Gibbs energy of dissolution becomes positive and as a consequence precipitation/collapse of the previously solvated polymer chains from solution occurs [4,5]. In addition the strength of the H-bridges, which stabilize the polymer molecules in solution, weakens with increasing temperature. For PNIPAM critical solution temperature (CST)-values between 31 and 34 °C have been reported in pure water [1,6,7].

Any additive to the polymer/water system can be expected to influence the CST. As thermoresponsive materials become candidates for putative applications ranging from drug delivery to artificial muscles and parts for microanalytical systems, the understanding of such complex systems has increased in importance. In principle however, the influence of salts, detergents, and organic solvents on polymer thermoprecipitation from aqueous solution has been studied since the 1960's, albeit mainly for molecules such as poly(ethylene glycol) and polyvinylpyrolidone [8–12]. The interpretation of the observed effects is usually based on the assumption of an interaction of the co-solute with the dissolved polymer or an influence of the co-solute on the solvent water (structure, availability). Simple salts, e.g., are generally assumed to exert their influence by acting on the water structure (salting in/salting out) and the resulting behavior can be interpreted as a consequence of the 'hydrophobic effect' [13,14]. Other co-solutes such as charged surfactants show a more complex influence, where at low concentration a behavior reminiscent of a salting out effect (lowering of the CST) is observed, whereas once a critical co-solute concentration is passed, mixed aggregates of the polymer and the additive start to form [15,16]. As a consequence the CST increases

* Corresponding author. Address: Chair for Bioprocess Engineering, Faculty of Applied Science, University of Bayreuth, Universitätsstrasse 30, 95447 Bayreuth, Germany. Tel.: +49-921-55-7371; fax: +49-921-55-7375.
E-mail address: ruth.freitag@uni-bayreuth.de (R. Freitag).

0032-3861/$ - see front matter © 2004 Elsevier Ltd. All rights reserved.
doi:10.1016/j.polymer.2004.02.046

and often conditions can be found where thermoprecipitation no longer takes place.

Organic solvents constitute another type of additive, which is of obvious importance. PNIPAM, for instance, is soluble in a number of organic solvents, provided that they are capable of hydrogen bonding. Examples include acetone, dimethylformamide (DMF), dioxane, ethanol, methanol and tetrahydrofuran (THF). In these solvents, no phase transition is observed and PNIPAM is soluble to the solvent's boiling point. Therefore, it may be assumed that the addition of such an organic solvent to an aqueous PNIPAM-solution should raise the CST and extend the solubility range. However, initial investigations have shown that this is not necessary the case [6,17–21]. Instead, co-nonsolvency (or antagonist solvency) has been observed for hydro-organic mixtures containing methanol, dioxane, or tetrahydrofurane [6,22]. To explain the origin of the co-nonsolvency phenomenon, two theories have been proposed. Schild and Tirrell [6,17] support a model based on the assumption of a preferential interaction of the organic solvent molecules (e.g., methanol) and the polymer chains. The solubilizing effect of the hydrogen bonding between the polymer and the water molecules is much weaker in this case and solubility is reduced. Winnik et al. [18–21] suggest that the driving force for co-nonsolvency is a preferential interaction of the water with the methanol molecules, which limits the number of solvent molecules available to solubilize the polymer.

In this paper a number of thermoresponsive polyacrylamides including PNIPAM is subjected to a systematic investigation of their thermoprecipitation from a wide variety of hydro-organic mixtures with relatively low organic solvent content (≤ 2 M) in order to further investigate the phenomenon.

2. Experimental procedures

2.1. Materials

All chemicals including the solvents were from Sigma, Fluka or Aldrich. The highest available purity was used. Unless indicated otherwise, all substances were used as obtained from the supplier. Salts were dried before use. Solvents such as acetone, diethyl ether, *N*,*N*′-dimethylformamide (DMF), hexane and tetrahydrofuran (THF) were purified and dried by conventional methods in the laboratory. Water was purified with an ELIX 3 water purification system (Millipore). Monomers were purified by recrystallization in hexane and dried in vacuum at room temperature. The radical starter 2,2′-azoisobutyronitrile (AIBN) was recrystallized from diethyl ether prior to use. The chain transfer agent 3-mercaptopropionic acid (MPA) was purified by distillation under reduced pressure.

2.2. Polymerization

Telomerization of the acrylamide monomers was performed in the presence of the chain transfer agent MPA according to the procedure described by Chen and Hoffman [23] and described previously for PNIPAM [14]. In order to obtain oligomers with a narrow molecular mass distribution, fractionation was done using acetone as solvent and *n*-hexane as non-solvent, as suggested by Fujishige [22]. The fractionated polymer was dried in vacuum until constant weight. The living anionic polymerization was carried out according to standard procedures as described previously using BuLi as chain starter [24]. Oligomers were characterized by MALDI-MS (matrix-assisted laser desorption/ionization mass spectrometry, Atheris Laboratories, Geneva, Switzerland), ^{1}H NMR (600 MHz), titration, and FT-IR.

2.3. Sample preparation

For the sample preparation, stock solutions of oligomer (5% w/w) were prepared by allowing the oligomer to dissolve over night in purified water at 4 °C. Aliquots of these solutions were added to water or to the organic solvent stock solutions to give the desired sample concentration and stored over night at 4 °C before measurements. In the case of salt containing systems, the aliquots of the oligomer-containing solutions were added to inorganic salt stock solutions. These solutions were then diluted with purified water to the desired sample concentration and stored over night at 4 °C before measurements. The final sample solution for cloud point and DSC measurements was typically 1% (w/w). Since no bactericide was added, the maximum storage time of stock and sample solutions was less than 1 week.

2.4. Measurement of the critical solution temperature, CST

The CST was determined by cloud point measurements. For this purpose the optical density of the aqueous oligomer solution was monitored as a function of the temperature at 500 nm using a Lambda 20 spectrophotometer (Perkin–Elmer) equipped with a PTP 1 thermostat and a temperature sensor directly inserted in the reference cell. Heating rates were 0.5 °C/min. Pure water was used as a reference. Precipitation occurred rapidly within 1 °C. CSTs were taken at the inflection point in the optical density versus temperature curves (approximated at half height). CST measurements in ternary systems (additive salt or organic solvent) were repeated three times, deviations were < 1 °C. In case of the CST in pure water, measurements were in addition repeated for at least three different batches of each polymer. Batch to batch deviations in the CST were < 2 °C.

2.5. Thermal analysis (DSC)

Differential scanning calorimeter (DSC) data were measured on a high sensitivity differential scanning

calorimeter (Rheometric instruments) at a heating rate of 1 °C/min. The instrument was calibrated with indium. The sample size varied between 10 and 20 μL. Pure water, respectively, the solvent mixture was used as reference.

3. Results

3.1. Preparation of the oligomeric acrylamides

Previous experiments regarding co-nonsolvency effects have almost exclusively been carried out with poly-(*N*-isopropylacrylamide), PNIPAM, as thermoresponsive polymer. While these experiments have certainly elucidated some aspects of the phenomenon, the generic validity of the results remains to be discussed. We have in the past been able to show that the chemistry and even the tacticity of a polymer can have drastic consequences for the precipitation behavior [24]. In order to investigate the thermoprecipitation of a variety of polymer chemistries, the oligomers compiled in Table 1 were synthesized. With the exception of PNIPAM all polyacrylamides were produced by telomerization (chain transfer polymerization) and anionic polymerization. The presence of a carboxylic acid end group in all telomers was verified by titration. The mass average of the molar mass of all oligomers was below 5000 g/mol with polydispersities <1.5 as verified by MALDI-MS measurements.

As noted previously [24,25], the CST of the predominately isotactic poly-(*N*,*N*-diethylacrylamide), PDEAM, prepared by anionic polymerization was several degrees higher than that of the corresponding PDEAM prepared by telomerization. An effect of the terminal carboxylic acid group of the telomer on the CST could be ruled out in this context. First of all it is the anionic PDEAM (butyl end group) that shows the deviation from the typical PDEAM CST of 32 °C [7]. Secondly it could be shown that the coupling of the terminal carboxylic acid group of the PDEAM telomer with a variety of charged and uncharged ligands does not change the CST to a measurable extent. Different CSTs were also observed in case of the two poly-(pyrrolidinoacrylamides), PPAM, although in this case the telomer had the higher CST. The two poly-(*N*-ethyl,*N*-methyl acrylamides) PEMAM, showed hardly any difference in their respective CSTs. However, the values, which were measured with minor variation (±2 °C) for several batches of these polymers are well above the literature values for the corresponding polymeric PEMAM, namely 56 °C [1,7].

Table 1
Polyacrylamides prepared for the investigations and their CST in pure water

Polymer	Abbreviation	Polymerization	CST (°C)
Poly-(*N*-ethyl-*N*-methyl-acrylamide)	PEMAM	Chain transfer	72
Poly-(*N*-ethyl-*N*-methyl-acrylamide)	PEMAM	Anionic	75
Poly-(pyrrolidinoacrylamide)	PPAM	Chain transfer	72
Poly-(pyrrolidinoacrylamide)	PPAM	Anionic	58
Poly-(*N*,*N*-diethylacrylamide	PDEAM	Chain transfer	32
Poly (*N*,*N*-diethylacrylamide	PDEAM	Anionic	40
Poly (*N*-isopropylacrylamide)	PNIPAM	Chain transfer	34

3.2. Salt effects on the solubility

Previous experiments with PNIPAM and PDEAM oligomers [14,16,26] had shown that two classes of additives can be differentiated. While simple salts exert their effect in a characteristic way and independent on the chemical nature and tacticity of the dissolved polymer, anionic surfactants and alkylamines influence the CST also as a function of the polymer chemistry. In order to extend this investigation to PEMAM and PPAM oligomers, the effect of a series of potassium salts on the CST was investigated, Fig. 1. As expected—save for small amounts of KI, which is known to have a salting in effect [14]—the CST dropped in a linear fashion with increasing salt concentration. The drop in the CST values upon the addition of a certain quantity of a given salt is very similar in all cases. This is also visible in Fig. 2, which shows the CST of the four PEMAM and PPAM species as a function of the ammonium sulfate concentration. Moreover, the observed

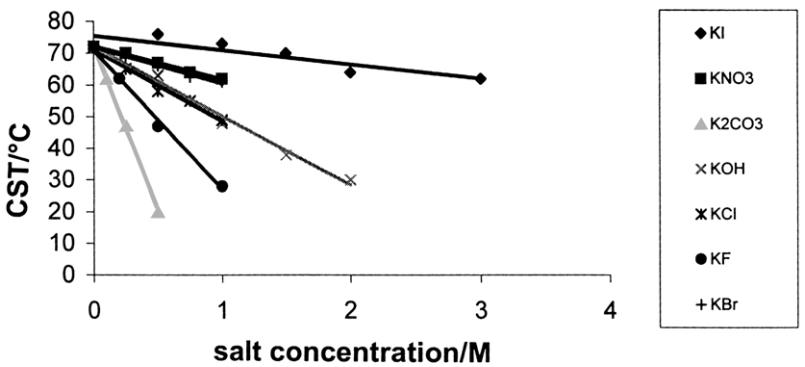

Fig. 1. Influence of various potassium salts on the CST of a 1% (w/w) aqueous solution of PEMAM prepared by chain transfer polymerization.

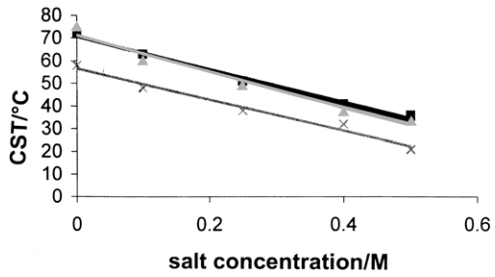

Fig. 2. Influence of increasing amount of ammonium sulfate on the CST of 1% (w/w) aqueous solutions of PEMAM (chain transfer polymerization, ◆), PEMAM (anionic polymerization, ▲), PPAM (chain transfer polymerization, ■), and PPAM (anionic polymerization, ✕).

absolute changes in the CST correspond in magnitude to those previously observed for PNIPAM and PDEAM [14]. The assumption that salts exert their effect independent of the polymer species is hence corroborated by these findings.

3.3. Solvent effects of the solubility of PNIPAM

Our investigation of possible co-nonsolvency effects started with a study of the thermoprecipitation of PNIPAM telomers from mixtures containing certain alcohols. At room temperature, oligomeric PNIPAM is well soluble in alcohols such as pure methanol, ethanol, propanol, and butanol. However, when even small amounts of any of these alcohols are added to water, the solubility of the oligomer in that particular solvent mixture is reduced, as evidenced by a lowered CST, Fig. 3. In such cases the CST appears to decrease almost linearly with the alcohol concentration for the investigated range (< 2 M alcohol). The extent of the variation of the CST for a given 'co-solvent' depends in a characteristic manner on the length of the alcohol's alkyl chain. If the effects of methanol, ethanol, 1-propanol and 1-butanol are compared, the effects on the CST become more pronounced as the chain length of the alcohol increases and slopes of − 1.4, − 2.8, − 8.5 and − 27 °C/mol are measured respectively.

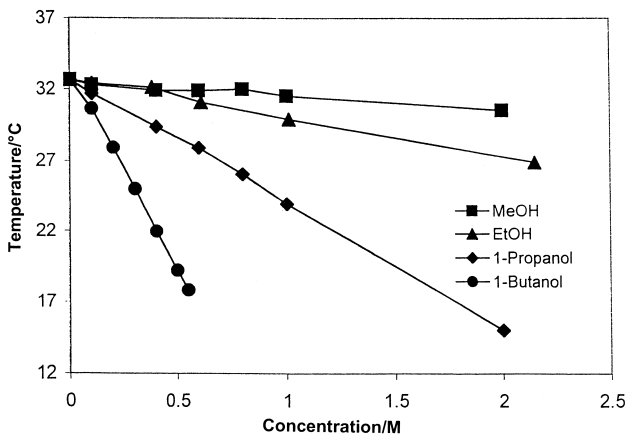

Fig. 3. Influence of the alkyl chain length of various alcohols as co-solvent on the CST of a 1% (w/w) aqueous PNIPAM solution.

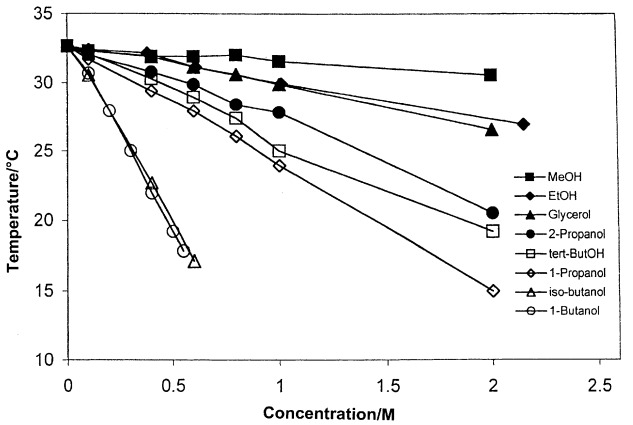

Fig. 4. Influence of the structure of the co-solvent's alkyl chain on the CST of 1% (w/w) aqueous PNIPAM solutions.

In addition to the length, the structure of the alkyl chain also exerts a strong influence on the magnitude of the observed effect, Fig. 4. While the effect of *iso*-butanol on the CST of the oligomer solutions is almost indistinguishable from that of 1-butanol (slope values of − 27 and − 26 °C/mol, respectively), solutions containing *tert*-butanol show a significantly different behavior. With a slope of − 6 °C/mol, the more compact *tert*-butanol is four times less efficient in decreasing the CST the either 1- or *iso*-butanol. In fact even 1-propanol shows a more pronounced effect than *tert*-butanol in such cases. The CST trend is also influenced by the position of the alcoholic group on the alkyl chain. As the comparison of 1- and 2-propanol demonstrates, the effect of an alcoholic group in the *n*-terminal position (1-propanol) on the CST is much stronger than that of one located closer to the center of the molecule (i.e., 2-propanol).

Not only alcohols give rise to co-nonsolvency effects. In Fig. 5 the results obtained with various other organic co-solvents are compiled. For the concentration range considered here, only DMF was capable of elevating the CST to some extent (slope: + 1 °C/mol). For all other organic co-solvents investigated, a linear drop of the CST of

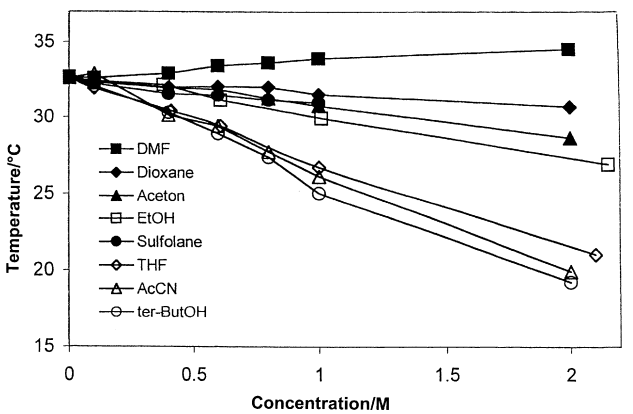

Fig. 5. Influence of various organic solvents on the CST of a 1% (w/w) aqueous PNIPAM solution.

PNIPAM is observed with increasing concentration of the organic solvent.

In order to investigate the phase transition further, differential scanning calorimetry (DSC) was used to obtain microcalorimetric data for the temperature induced phase transition of PNIPAM in some of the hydro-organic oligomer solutions, Table 2. In general the calorimetric enthalpy of the phase transition decreases as the concentration of the organic solvent increases. This is the case for the solubility decreasing additives, but also for DMF, a solvent that was found to consistently increase the CST. This suggests that in all cases the organic solvent reduces either the frequency or the strength of the oligomer–water contacts. The drop in the transition enthalpy (16.7 J/g in pure water) is more pronounced for solvents such as *tert*-butanol (down to 4.2 J/g for a 1 M alcohol solution) compared to that observed, e.g., in the case of DMF (still 15.9 J/g for a 1 M solution). Moreover, the effect of butanol on the phase transition enthalpy seems to be in the same order of magnitude as previously observed for butylamine [26].

3.4. Solvent effects of the solubility of the other acrylamides

Up to now the co-solvent effect is very reminiscent of the salt effect, where after all some salting in could be observed in the case of KI, while most other salts exert a salting out effect. However, the simple analogy breaks down when other acrylamides besides PNIPAM are included in the investigation. Other than in the case of salts as co-solutes, the effect of a given co-solvent depends strongly on the chemistry of the oligomer. In the case of PDEAM prepared by anionic and chain transfer polymerization, Fig. 6, all investigated solvents save for propanol and butanol increased the CST. The tacticity of the molecule may also

Table 2
Phase transition enthalpies measured by DSC for PNIPAM solutions (1% w/w) containing the indicated amounts of the organic solvent

Additive	ΔH^a (J g^{-1})
None	16.7
DMF (0.5 M)	15.9
DMF (1 M)	15.9
DMF (1.5 M)	6.3
DMF (2 M)	2.5
Acetone (0.5 M)	14.2
Acetone (1 M)	12.5
Acetone (1.5 M)	5
Acetone (2 M)	1.2
Ethanol (0.5 M)	14.6
Ethanol (1 M)	11.7
Ethanol (1.5 M)	2.9
Ethanol (2 M)	2
tert-Butanol (0.5 M)	9.6
tert-Butanol (1 M)	4.2
tert-Butanol (1.5 M)	1.7
tert-Butanol (2 M)	0

[a] Calorimetric enthalpy calculated from the DSC endotherm.

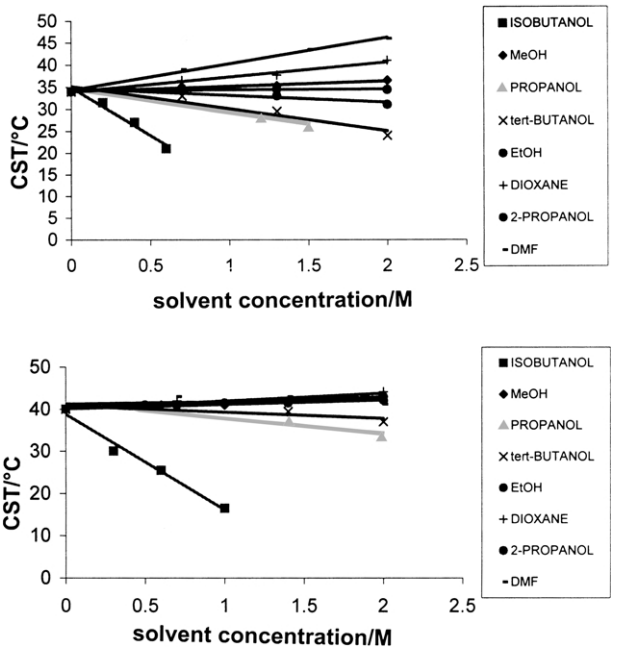

Fig. 6. Influence of various organic solvents on the CST of a 1% (w/w) aqueous solution of PDEAM prepared by (a) chain transfer and (b) anionic polymerization.

be of consequence, since 2-propanol increased the CST in the case of the predominately isotactic PDEAM prepared by anionic polymerization, whereas the CST of the heterotactic PDEAM prepared by chain transfer polymerization was lowered by this solvent under otherwise similar circumstances.

The effect of a variety of alcohols on the CST of PEMAM and PPAM is summarized in Table 3 and Fig. 7.

Table 3
Influence of alcohols on the CST of 1% (w/w) solutions of the indicated oligomers

Polymer	Methanol	*iso*-Butanol	*iso*-Propanol
PPAM, chain transfer	No CST	0.000 M 72 °C 0.125 M 67 °C 0.250 M 64 °C 0.375 M 60 °C 0.500 M 58 °C	No CST
PPAM, anionic	0.0 M 58 °C 0.5 M 64 °C 1.0 M 62.5 °C 1.5 M 62.5 °C 2.0 M 67 °C	0.000 M 58 °C 0.125 M 54.5 °C 0.250 M 53 °C 0.375 M 51 °C 0.500 M 48 °C	0.0 M 58 °C 0.5 M 58 °C 1.0 M 58 °C 1.5 M 57 °C 2.0 M 54 °C
PEMAM, chain transfer	0.0 M 72 °C 0.5 M 65 °C 1.0 M 63 °C 1.5 M 61 °C	0.000 M 72 °C 0.125 M 67 °C 0.250 M 63 °C 0.375 M 59 °C 0.500 M 57 °C	0.0 M 72 °C 0.5 M 70 °C 1.0 M 67 °C 1.5 M 63.5 °C 2.0 M 62.5 °C
PEMAM, anionic	0.0 M 75 °C 0.5 M 64 °C 1.0 M 63 °C 1.5 M 62 °C	0.00 M 75 °C 0.25 M 62 °C 0.50 M 48 °C	No CST

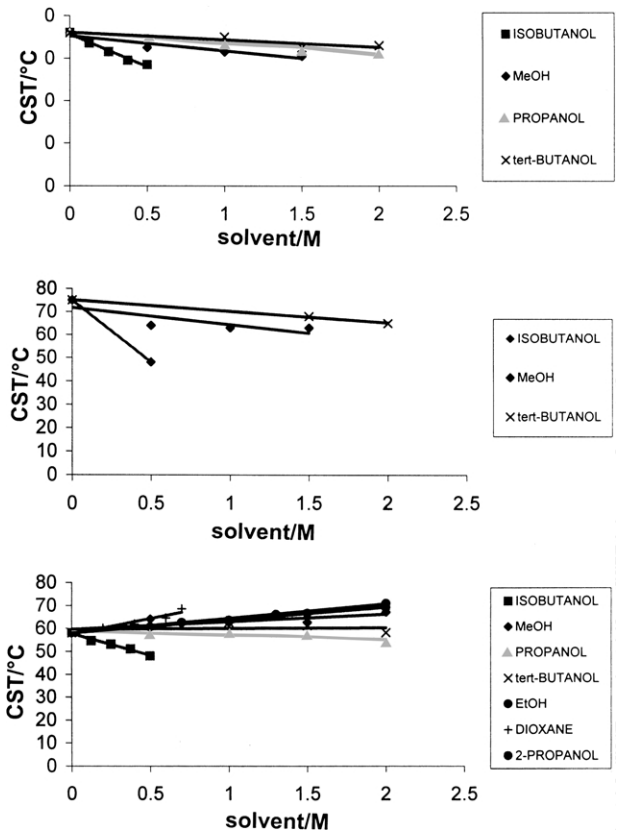

Fig. 7. Influence of various organic solvents on the CST of a 1% (w/w) aqueous solution of (a) PEMAM prepared by chain transfer polymerization, (b) PEMAM prepared by anionic polymerization, and (c) PPAM prepared by anionic polymerization. PPAM prepared by chain transfer polymerization is not presented since this oligomer failed to show a CST save in hydro-organic mixtures containing *iso*-butanol.

PPAM prepared by chain transfer polymerization shows the most extreme behavior. For this molecules no CST is observed in most solvent mixtures save for those that contain *iso*-butanol. In the other cases we see a similar behavior as for PDEAM, i.e. solvents with large hydrophobic domains such as *iso*-butanol lower the CST; in solvent mixtures that contain organic solvents with small hydrophobic domains a CST is still observed but at a higher value than in pure water.

4. Discussion

The behavior of a polymer in solution is determined by the interactions taking place between its segments and the surrounding solvent molecules. The salt effect observed for oligomeric PNIPAM and PDEAM had previously been described by the effect of the salt on the water structure and mainly on the surface tension increment (salting out/salting in effects) [14]. In the case of the addition of anionic surfactants we also ascribed the lowering of the CST observed at low additive concentration to a salting out effect, whereas the increase (or disappearance) of the CST at higher concentrations could be shown to coincide with the formation of mixed micelles [15]. In the case of non-charged alkylamines as additives, a similar behavior was observed, i.e. a lowering of the CST at low concentration for all investigated additives of this kind. In addition however, alkylamines large enough for self aggregation ($C \geq 3$) and therefore, able to form mixed aggregates were able to increase the CST of a given oligomer solution, once the critical association concentration was surpassed [26]. In this context we observed not only the similar trends as for the organic solvents in respect to their effects on the CST as a function of the size (C2, C3, C4, C5, C6) but also the structure (*n*- versus *iso*- and *tert*-butylamine) of the additive.

Interestingly anionic PDEAM showed some deviations in its behavior, which could be important to the interpretation of the co-solvent effect. The oligomer was apparently able to promote hydrophobic interactions, as in the case of anionic PDEAM the critical alkylamine concentration for the formation of mixed aggregates was significantly below that of the critical self-association concentration. This was not the case for telomeric PDEAM or PNIPAM oligomers. Concomitantly alkylamines such as propyl- and butylamine increased the CST of anionic PDEAM even at very small concentration, whereas the CST of PNIPAM (PDEAM telomers) was lowered. Only pentylamine below a concentration of ca. 1 M lowered the CST of anionic PDEAM (CST-minimum: 0.4 M).

In the case of the organic solvents considered here, the generally observed decrease in the CST upon the addition of the organic solvent could also simply be linked to the solvent's effect on the water structure. The viscosity *B* coefficient has been proposed as a qualitative measure of the effect of additives on the water structure [27]. A positive viscosity *B* value implies positive hydration of the solute molecules and a strengthening of the water structure. Hydrophobic interactions are promoted under these conditions. In the cases considered here, this would lead to the collapse and subsequent aggregation/precipitation of the acrylamide molecules, especially when their concentration is high compared to that of the additive. In the case of the alcohols for example, with values of 0.087 L/mol (methanol), 0.17 L/mol (ethanol), 0.25 L/mol (*n*-propanol) and 0.3 L/mol (*n*-butanol) [10], the viscosity *B* coefficient seems to correlate well with an alcohol's ability to suppress the CST of PNIPAM and most of the other investigated oligomers.

However, local contacts between the oligomers and the organic solvent molecules are also possible and have been demonstrated by Durand and Hourdet [28] for the formation of hydrophobic aggregates between hexanol and PNIPAM side chains in an aqueous solution containing less than 0.5 M of hexanol. In the case of alkylamines as additives, and there especially in the case of molecules $C \geq 4$ the formation of mixed aggregates was important enough to overcome the salting out effect and increase the CST. However, such a CST minimum as a function of the additive

concentration was not observed in the concentration range investigated here. Given that the tendency for formation of mixed aggregates increases with increasing size of the hydrophobic domain, the formation of mixed aggregates can also not explain the steady increase of the CST observed, e.g. when methanol was added to the PDEAM-solutions. A similar inexplicable increase in CST had previously been observed in the case of anionic PDEAM and certain alkylamines. Clearly the simple water structuring argument is not sufficient to explain all observed effects.

The results of the DCS-measurements, Table 2, show that the calorimetric enthalpy of the phase transition decreases as the concentration of the organic solvent increases. This is the case for substances such as *tert*-butanol that decreases the CST, but also for DMF, i.e. a solvent that was found to consistently increase the CST. In general, this suggests that in all cases the organic solvent reduces either the frequency or the strength of the oligomer–water contacts. However, the effect is much larger in the case of CST-depressing than of CST-increasing additives. Preferential adsorption/interaction of the non-aqueous solvent on the oligomers would result in a decrease of the transition enthalpy, since the strength of the hydrogen bonding between the dissolved acrylamide and the organic solvent molecules is likely to be lower in this case than for water as solvent [17,29].

Based on these observations one could come to the conclusion that organic solvents with a strong water structuring ability (e.g., *n*-butanol) lower the CST of all thermoresponsive acrylamides due to the enforcement of the hydrophobic interactions. The effect is related to the size and shape of the hydrophobic domain of the solvent and *n*-butanol shows a very similar effect as, e.g., *n*-butylamine. The importance of the oligomer–water contacts is strongly decreased under these conditions. Solvents that disturb the water structure (e.g., DMF) increase the CST. Number and frequency of the oligomer–water contacts are slightly decreased under these circumstances, but presumably replaced by equally solvating oligomer-DMF contacts. Solvents such as methanol play an intermediate role. They are (weak) water structure enforcers and—as one would have predicted—(slightly) lower the CST of PNIPAM and PEMAM. The CST of PPAM and PDEAM, on the other hand, is increased by the addition of methanol to the aqueous solution. The basis for such differences in the solubilizing ability of solvents such as methanol is currently under investigation in our laboratory.

5. Conclusions

Previous papers on the co-solvent effect [6,17–21] have focussed on PNIPAM and the fact that certain commonly used solvents lowered the CST of this molecule in aqueous solution. In this paper we demonstrated that not all solvents lower the CST of PNIPAM and that the situation becomes even more complex as other thermoresponsive acrylamides are included in the investigation. We propose that the influence of the co-solvent on the water structure as characterized by the viscosity *B* coefficient is a major determinant in the observed co-nonsolvency effects. At the same time some local preferential interaction between the solvent molecules and the oligomers may occur, which could presumably equilibrate or even overcome the co-nonsolvency effect.

Acknowledgements

We gratefully acknowledge support from the Swiss National Science Foundation (grants No 21-49276.96 and 20-55643.98 to RF). The technical assistance of Veronique de Figueiredo was extremely valuable to us throughout this work.

References

[1] Galaev IY, Mattiasson B. Enzyme Microb Technol 1993;15:354–66.
[2] Bae YH, Okano T, Kim SW. J Polym Sci B, Polym Phys 1990;28:923–36.
[3] Hilbrig F, Freitag R. J Chromatogr A 2003;790:79–90.
[4] Kubota K, Fujishihe S, Ando I. J Phys Chem 1990;94:5154–8.
[5] Schild HG, Tirrell DA. J Phys Chem 1990;94:4352–6.
[6] Schild HG. Prog Polym Sci 1992;17:163–249.
[7] Ito S, Mizogushi K, Suda Y. Bull Res Inst Polym Text 1984;144:7.
[8] Eliassef J. J Appl Polym Sci 1978;22:873.
[9] Florin E, Kjellander R, Eriksson C. J Chem Soc Faraday Trans 1984;80:2889–910.
[10] Ataman M, Boucher E. J Polym Sci Phys 1982;20:1585–92.
[11] Saito S, Yukawa M. J Colloid Interface Sci 1969;30:211.
[12] Von Hippel PH, Wong K. Science 1964;145:577.
[13] Tanford C. The hydrophobic effect. New York: Wiley; 1980.
[14] Freitag R, Garret-Flaudy F. Langmuir 2002;18(9):3434–40.
[15] Schild HG, Tirrell DA. Langmuir 1991;7:665–71.
[16] Garret-Flaudy F, Freitag R. Langmuir 2001;17(16):4711–6.
[17] Schild HG, Muthukumar M, Tirrell DA. Macromolecules 1991;24:948–52.
[18] Winnik FM, Ringsdorf H, Venzmer J. Macromolecules 1990;23:2415–6.
[19] Winnik FM, Ottaviani MF, Bossmann SH, Garcia-Garibay M, Turro NJ. Macromolecules 1992;25:6007–17.
[20] Winnik FM, Ottaviani MF, Bossmann SH, Pan W, Garcia-Garibay M, Turro NJ. Macromolecules 1993;26:4577–85.
[21] Asano M, Winnik FM, Yamashita T, Horie K. Macromolecules 1995;28:5861–6.
[22] Fujishige S. Polym J 1987;19:297–300.
[23] Chen GH, Hoffman AS. Polym Prepr 1992;33:468.
[24] Baltes T, Garret-Flaudy F, Freitag R. J Polym Sci A 1999;37:2977–89.
[25] Freitag R, Baltes T, Eggert M. J Polym Sci A 1994;32:3019–30.
[26] Garret-Flaudy F, Freitag R. J Polym Sci A 2000;38:4218–29.
[27] Jones G, Doles M. J Am Chem Soc 1929;51:2950.
[28] Durand A, Hourdet D. Polymer 2000;41:545–57.
[29] Franks F. Water: a comprehensive treatise. New York: Plenum Press; 1973.