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Experimental and Theoretical Study of Phase Separation in Aqueous Solutions of Clouding Polymers and Carboxylic Acids

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ABSTRACT: The phase behavior of different carboxylic acids/nonionic polymer/water systems has been studied. The carboxylic acids investigated are acetic acid, propionic acid, and butyric acid. The polymers used are a linear random copolymer of ethylene oxide and propylene oxide (UCON) and ethyl(hydroxyethyl)-cellulose (EHEC). These polymers display a lower critical solution temperature (LCST) in water. The decrease of the polarity in the carboxylic acids as the carbon chain increases causes a decrease of the LCST of the system carboxylic acid/polymer/water. As a consequence of this the two-phase region expands. The experimentally determined phase diagrams can qualitatively be described and compared with a theoretical model, based on Flory–Huggins theory of polymer solubility. The cloud-point temperature of the systems decreases as the difference between the effective interaction of polymer–cosolute and cosolute–water increases.

Introduction

A great deal of research has been done on phase separation in aqueous polymer solutions. Important applications of two-phase aqueous polymer systems are partitioning of biological macromolecules, cell particles, and cells, for separation and purification.[1,2] The ternary system poly(ethylene oxide)/dextran/water is the most common for aqueous two-phase partitioning.[2] Recently phase separation in systems containing one polymer in aqueous solution has been studied.[3,4] The polymer used in these studies was a random copolymer of ethylene oxide and propylene oxide (UCON). This polymer has a lower critical solution temperature (LCST) in water. Below the LCST the solution is a one-phase system. If this one-phase solution is heated until it reaches the critical solution temperature, the solution becomes cloudy. This temperature is called the cloud-point temperature of the system. The point where the concentration and temperature correspond to the lowest cloud point is a critical point. Typical examples of polymers which have a LCST are poly(ethylene oxide),[5] ethyl(hydroxyethyl)cellulose (EHEC),[6] and copolymers of ethylene oxide (EO) and propylene oxide (PO).[3] There are also examples of small molecules which show a LCST in water, e.g., nicotine and triethylamine.[7] However, the phenomenon is more common for large molecules like polymers, since the entropy of mixing, which favors increased solubility with increased temperature, becomes relatively less important when the molecules get larger.

In this work we have studied the phase behavior as a function of temperature and composition of two polymers displaying a LCST in water, a UCON type and an EHEC type. Both polymers have relatively low cloud points in a water solution. The UCON we have used is UCON 50-HB-5100 which has an equal amount of weight of EO and PO. It has a molecular weight of 4000 and a cloud point of 50 °C (323 K) in water. The EHEC which we have used (EHEC CD-101-90) was kindly provided by Berol Nobel AB and has a cloud point of 36 °C (309 K) in water. Its molecular weight is about 50 000. In this work we have studied the effect of adding different substances with increasing hydrophobicity to water solutions of these polymers. As additives we have chosen to work with a homologous series of carboxylic acids, acetic acid, propionic acid, and butyric acid. These acids have a fairly good solubility in water and are easy to analyze. In this study we have compared the experimental phase diagrams with calculated phase diagrams, based on a model of EO-chain solubility in water proposed by one of us.[8]

Theoretical Models

Three different models have been used in the literature in order to explain the phase behavior of these polymers. In the oldest of these models, from Kjellander and Florin,[9] it is proposed that water forms an ordered structure around the ethylene oxide segment at low temperature. This highly ordered structure, which is entropically unfavorable, is destroyed at higher temperature, leading to phase separation. In the second model, by Goldstein,[10] which is based upon Flory–Huggins theory,[11] the decrease in solubility is explained by hydrogen bonds between the EO group and water. The hydrogen bonds are destroyed with increasing temperature. The last model is developed by Karlström[8] and is also based upon Flory–Huggins theory of polymer solubility. The decrease in solubility is explained by conformational changes in the EO chain. At lower temperature the segments of the EO chain are mainly in a polar conformation, which is energetically favored and interacts favorably with water. At higher temperature entropy makes the less polar structures more probable, since they are more numerous. These less polar conformations interact unfavorably with water.

A short mathematical description for the last model will be given here first for a simple system containing only one polymer and water. See also ref 8. The change in free energy when the polymer is mixed with water is

$$\Delta G_{\text{mix}} = \Delta H_{\text{mix}} - T\Delta S_{\text{mix}} \qquad (1)$$

Since ΔV_{mix} is almost zero, we have $\Delta H_{\text{mix}} = \Delta U_{\text{mix}}$. Then we have

$$\Delta G_{\text{mix}} = \Delta U_{\text{mix}} - T\Delta S_{\text{mix}} \qquad (2)$$

The total internal energy of the system is described as in the Flory–Huggins theory with the dimensionless interaction parameter χ, which can be defined as $\chi_{nk} = w_{nk}/RT$, where w_{nk} is the pairwise interaction parameter for components n and k, expressed in J/mol. We then get

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$$U^{\mathrm{T}} = n^{\mathrm{T}}RT[\Phi_1\Phi_2(P\chi_{1\mathrm{p}} + (1-P)\chi_{1\mathrm{u}}) + \Phi_2^{\,2}(P(1-P)\chi_{\mathrm{pu}} + (1-P)^2\chi_{\mathrm{uu}}/2)] \quad (3)$$

The entropy is

$$S^{\mathrm{T}} = -n^{\mathrm{T}}R[\Phi_1 \ln \Phi_1 + (\Phi_2/M_2) \ln \Phi_2 + \Phi_2(P \ln P + (1-P) \ln((1-P)/f))] \quad (4)$$

The superscript T refers to the total system. P is the probability of a polar conformation. Φ_1 and Φ_2 are the molar fractions of water and monomer in the solution. M_2 is the number of monomer units in the polymer chain. n^{T} is the total amount of moles in the system. Subscripts u and p refer to the nonpolar and polar conformations of the polymer. The parameter f is the ratio between the number of possible nonpolar conformations and the number of possible polar conformations of the polymer segment. This value[8] is chosen to be 8. Formally there should also be χ_{pp} and χ_{11} in eq 3, but these two can be put equal to zero without loss of generality. The χ_{uu} parameter must be retained in eq 3 in order to describe the equilibrium between the high- and low-temperature states of the polymer. In a three-component system eqs 3 and 4 change to:

$$U^{\mathrm{T}} = n^{\mathrm{T}}RT[\Phi_1\Phi_2(P\chi_{1\mathrm{p}} + (1-P)\chi_{1\mathrm{u}}) + \Phi_2^{\,2}(P(1-P)\chi_{\mathrm{pu}} + (1-P)^2\chi_{\mathrm{uu}}/2) + \Phi_1\Phi_3\chi_{13} + \Phi_2\Phi_3(\chi_{\mathrm{p3}}P + \chi_{\mathrm{u3}}(1-P))] \quad (5)$$

$$S^{\mathrm{T}} = -n^{\mathrm{T}}R[\Phi_1 \ln \Phi_1 + (\Phi_2/M_2) \ln \Phi_2 + \Phi_2(P \ln P + (1-P) \ln((1-P)/f)) + (\Phi_3/M_3) \ln \Phi_3] \quad (6)$$

The subscript 3 refers to the third component. M_3 is the number of monomer units in the third-component molecule. In our calculations $M_3 = 1$. If n is the amount of moles and superscript i refers to the phase i and subscript k refers to the component k, then the total amount of moles in phase i is

$$n^{\mathrm{t},i} = \sum_k n_k^{\,i} \quad (7)$$

The molar fraction of component k in phase i is

$$\Phi_k^{\,i} = n_k^{\,i}/n^{\mathrm{t},i} \quad (8)$$

The molar fraction of component k in the system is

$$\Phi_k = \sum_i n_k^{\,i}/n^{\mathrm{T}} \quad (9)$$

The total free energy is the sum of the free energy of the different phases, i.e.

$$G^{\mathrm{T}} = \sum G^i(n^{\mathrm{t},i},P^i,\Phi_1^{\,i},\Phi_2^{\,i},\Phi_3^{\,i}) \quad (10)$$

By minimizing the total free energy G^{T} with respect to $(n^{\mathrm{t},i}, P^i, \Phi_1^{\,i}, \Phi_2^{\,i}, \Phi_3^{\,i})$ for fixed Φ_k and n^{T}, one may construct a phase diagram for the system. Equation 10 was minimized by using a Monte Carlo procedure, where random amounts of the components were moved between the phases, keeping the total amounts of the components fixed.

Experimental Section

Materials. UCON 50-HB-5100 was obtained from Union Carbide, New York. It is a random copolymer of an equal amount of weight of ethylene oxide and propylene oxide. The molecular weight is 4000. The UCON was used without further purification. Ethyl(hydroxyethyl)cellulose (EHEC CD-101-90) was supplied by Berol Nobel AB, Stenungsund, Sweden. The average degrees of substitution of ethyl and ethylene oxide groups per anhydroglucose unit are 1.7 and 0.7, respectively. The molecular weight is about 50 000. EHEC was filtered with an ultrafiltration unit (Filtron Corp., Clinton, MA) to remove the small amount of NaCl in the product. Millipore water was used in all water solutions. CH_3COOH and CH_3CH_2COOH was purchased from Merck, Darmstadt, Germany. $CH_3CH_2CH_2COOH$ was purchased from Fluka AG, Buchs, Switzerland. All of the carboxylic acids were of analytical grade.

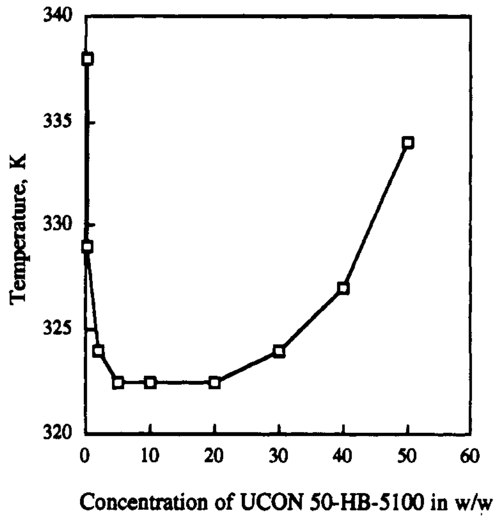

Figure 1. Cloud-point diagram for the binary system UCON 50-HB-5100/water. The molecular weight of the polymer is 4000. The two-phase region is above the binodal curve.

Methods. The limits of the two-phase regions were obtained through cloud-point measurements. Cloud-point determination was made by weighing the components in a glass tube and stirring the solution in a water bath. The total weight of each solution was 15 g. The glass tubes were of flat-bottomed type. The stirring was achieved with a magnetic stirrer. The temperature was given by a mercury thermometer in the solution. The cloud point was taken as the temperature when the first visual sign of turbidity appeared on heating. The samples were retained in the water bath during the visual observation. The heating rate was about 1 °C/min.

Phase separation in systems containing UCON was performed in glass tubes in a water bath. Phase separation in systems containing EHEC was made by centrifugating the samples (3700 revolutions/min, 3 h) in an incubator at 35 °C. Tie lines were determined by analyzing the top and bottom phases. The acid content was determined by titration. The UCON content was not determined, but the tie lines could be fitted into the phase diagram, since the acid concentration was determined and the volume ratio of top/bottom phases was known. The EHEC content was determined by evaporating water and acid at 120 °C for 2 h and weighing the residue.

Results and Discussion

Two-Component Systems. In Figure 1 a temperature–concentration phase diagram is shown for the system UCON 50-HB-5100 in water. The two-phase region is above the binodal curve. A large change in cloud point is observed below 2% UCON. In a region from 5 to 20% UCON the cloud-point temperature hardly changes, and above 20% the cloud-point temperature increases moderately. The critical point of the system is 323 K at a UCON concentration between 10 and 20%. The upper critical solution temperature is calculated to be above 550 K (see Figure 2) and was not experimentally determined. In Figure 2 a theoretical phase diagram for the UCON/water system is shown with different degrees of polymerization (N) of the polymer. The points in the diagram have been evaluated by use of eq 2–4, 9, and 10. The interaction parameters $\chi_{1\mathrm{p}}$, $\chi_{1\mathrm{u}}$, χ_{pu}, and χ_{uu} are listed in Table I and have been taken from the literature[8] and scaled in order to get a lower critical point of the system at 323

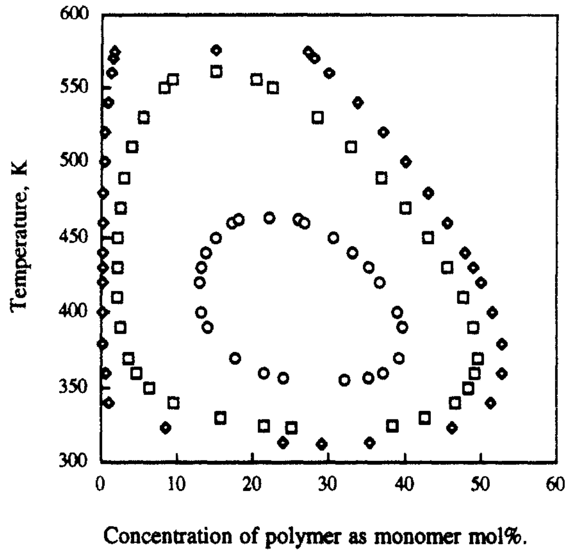

Figure 2. Calculated phase diagram for the polymer UCON in water with different degrees of polymerization (N). The interaction parameters χ_{1p}, χ_{1u}, χ_{pu}, and χ_{uu} are listed in Table I. The numbers of monomers N in the polymer are N = 39 (○), N = 78 (□), and N = 156 (◇).

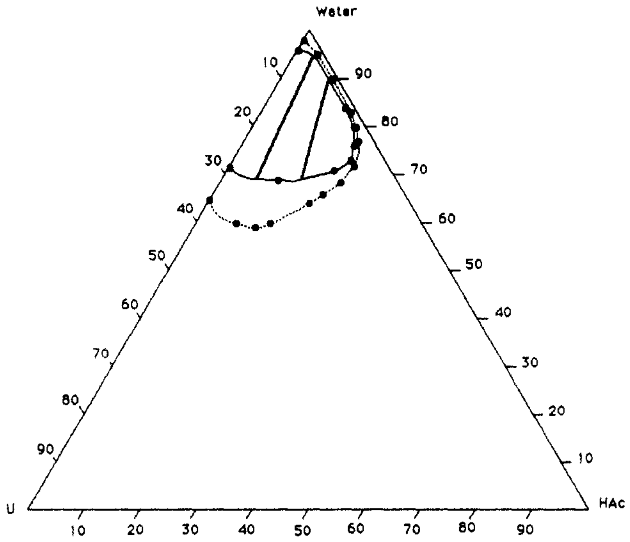

Figure 3. Experimental phase diagram for the system UCON 50-HB-5100/water/acetic acid. Concentrations in w/w %. Isotherms: (—) 323 K; (- - -) 325 K. HAc = acetic acid. U = UCON 50-HB-5100.

K. The original parameters were fitted for a poly(ethylene glycol) molecule.[8] With a polymerization degree of 78 (i.e., the number of monomers of the UCON 50-HB-5100 molecule), the calculated cloud-point temperature of the system was 398 K. In order to get a system with a cloud-point temperature of 323 K, the parameters had to be multiplied with 323/398. Further minor changes of the parameters were done in order to get a higher concentration of the polymer in the polymer-enriched phase above the cloud point. The effect of polymer molecular weight is observed as a slight increase in the two-phase region when N is doubled from 78 to 156. In contrast, a large reduction of the two-phase region is obtained when N is reduced from 78 to 39. The lower left part of the diagram for N = 78 resembles the experimental diagram in Figure 1. The system has three critical points and two of them are shown in Figure 2. The third critical point for N = 78 is calculated to be at 78.3 K and 9 mol % polymer. The solubility of the polymer decreases below this temperature.

Three-Component Systems. Figure 3 presents the ternary UCON/water/acetic acid system at 323 and 325 K. Acetic acid causes a small decrease of the critical temperature (about 2 K) compared to the UCON/water system. The two-phase region expands as the temperature is increased by 2 K. The effect is observed mainly in the polymer-rich area of the diagram. The tie lines indicate that acetic acid is slightly more partitioned in the polymer-rich phase. These results imply that acetic acid is a better solvent for UCON than water. The ternary system EHEC/water/acetic acid is shown in Figure 4. The two-phase region is shown at 301 and 308 K. The tie line, which was determined at 308 K is parallel to the EHEC/water line. The reason why acetic acid decreases the cloud-point temperature in this system, without an increase of the concentration of acetic acid in one of the two phases, is not fully understood. One explanation could be that the degree of protonation of the acetic acid is different in the different phases. In this case the free energy of the system could be minimized, if the acetic acid is less protonated in the water-rich phase and more protonated in the polymer-rich phase.

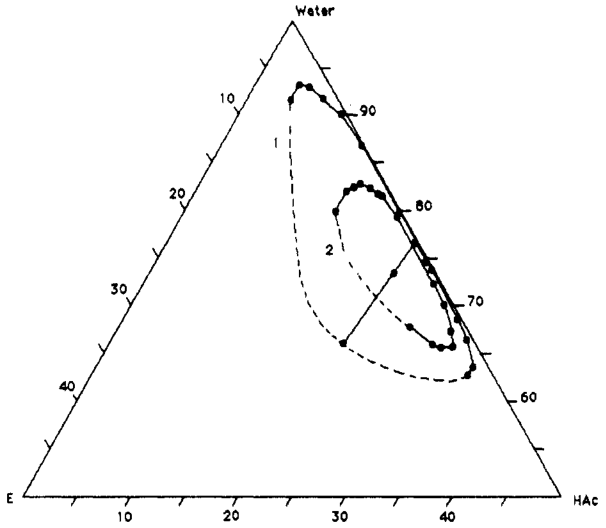

Figure 4. Experimental phase diagram for the system EHEC/water/acetic acid. Concentrations in w/w %. Isotherm 1: 308 K. Isotherm 2: 301 K. The dashed lines are estimations of the two-phase boundary. E = EHEC CD-101-90. HAc = acetic acid.

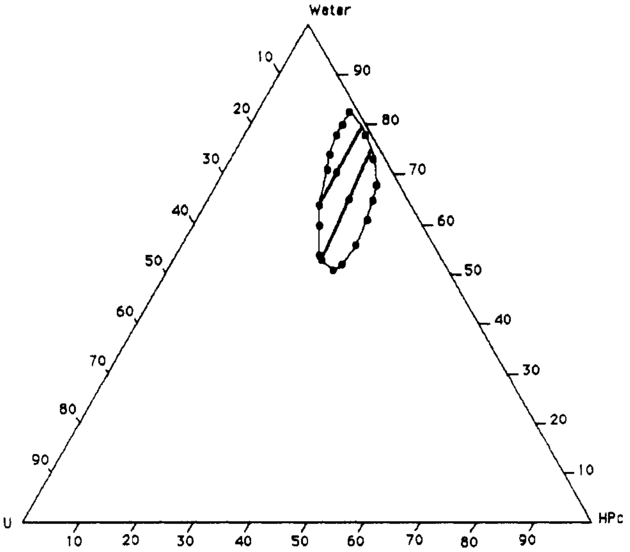

Figure 5. Experimental phase diagram for the system UCON 50-HB-5100/water/propionic acid. Concentrations in w/w %. Temperature: 295 K. U = UCON. HPc = propionic acid.

The increase of the carbon chain of the cosolute leads to a substantial decrease of the polymer solubility (Figures 5 and 6). At room temperature both of the acids, propionic acid and butyric acid, form two-phase regions together with UCON and water. The two-phase region of the

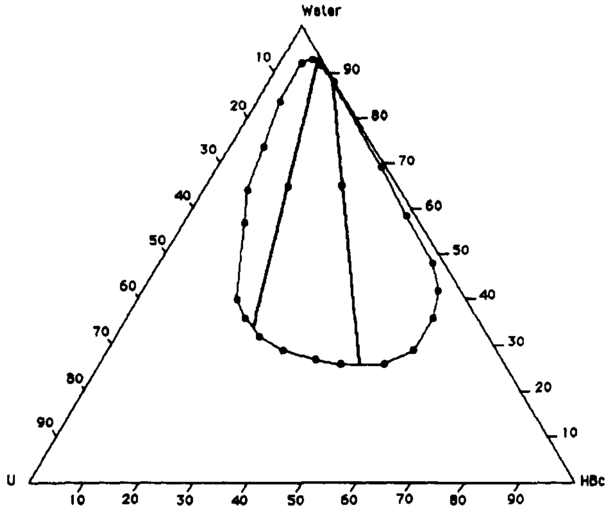

Figure 6. Experimental phase diagram for the system UCON 50-HB-5100/water/butyric acid. Concentrations in w/w %. Temperature: 295 K. U = UCON. HBc = butyric acid.

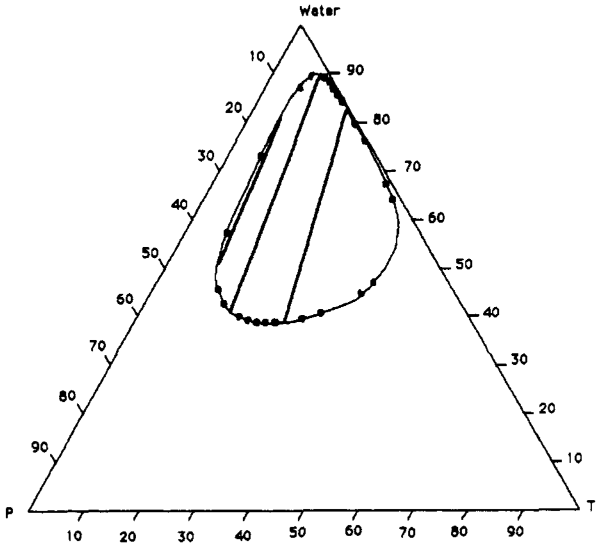

Figure 7. Calculated phase diagram for the polymer UCON 50-HB-5100 and a cosolute in water. Temperature: 270 K. P = a UCON-like polymer. T = low molecular, hydrophobic cosolute. Concentrations in mol %. The interaction parameters are listed in Table I. The number of monomers N of the polymer is 78.

butyric acid/UCON/water system is much larger than the two-phase region in the corresponding system with propionic acid. The butyric acid is more partitioned in the UCON-rich phase than propionic acid. This is clearly seen from the tie lines in Figures 5 and 6. The tie lines for the propionic acid system (Figure 5) are almost parallel to the UCON/water line. This is probably due to the fact that the temperature is close to the critical point of the system. Acetic acid, propionic acid, and butyric acid are all completely miscible with water. If we assume that the interaction between water and carboxylic acid is roughly the same for the three carboxylic acids, then the phase behavior described above would indicate a stronger attractive interaction between the polymer and the larger carboxylic acid (butyric acid), compared with the smaller carboxylic acids (acetic and propionic acid).

Model Calculations of Three-Component Systems. Calculations of the phase behavior with changing temperature in polymer/cosolute/water systems have been made using the described theoretical model. The results are shown in Figures 7–9. The components in the system are water, a UCON-like polymer (i.e., a polymer which has the same LCST (323 K) and degree of polymerization (N = 78) as UCON 50-HB-5100), and a hydrophobic

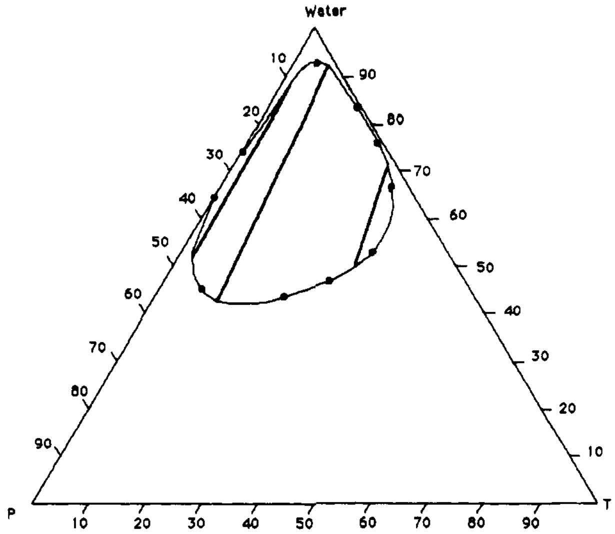

Figure 8. Calculated phase diagram for the polymer UCON 50-HB-5100 and a cosolute in water. Temperature: 323 K. P = a UCON-like polymer. T = low molecular, hydrophobic cosolute. Concentrations in mol %. The interaction parameters are listed in Table I. The number of monomers N of the polymer is 78.

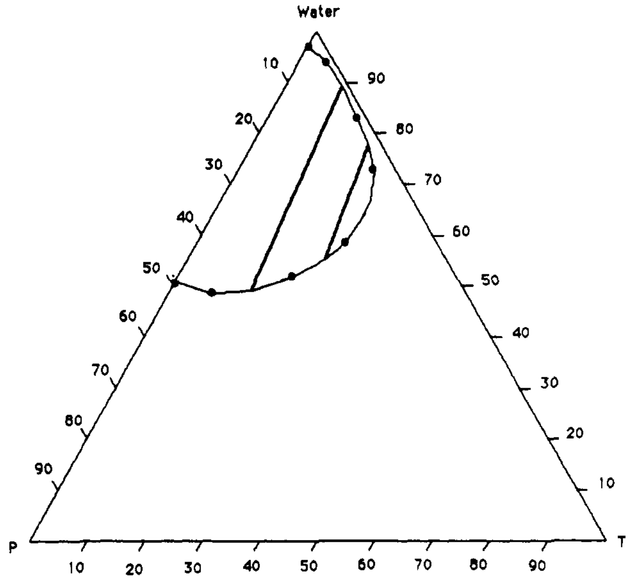

Figure 9. Calculated two-phase diagram of the polymer UCON 50-HB-5100 and a cosolute in water. Temperature: 387 K. P = a UCON-like polymer. T = low molecular, hydrophobic cosolute. Concentrations in mol %. The interaction parameters are listed in Table I. The number of monomers N of the polymer is 78.

Table I. Interaction Parameters at T = 323 K, Used for the Theoretical Calculations in Figures 2 and 7–9

χ_{1p}	0.152	χ_{u3}	0.012
χ_{1u}	3.333	χ_{pu}	1.868
χ_{13}	0.500	χ_{uu}	3.024
χ_{p3}	−1.500		

cosolute. The interaction parameters used for the calculations are listed in Table I. The interaction parameter χ_{p3} is −1.5, which indicates a strong attractive interaction between the polymer and cosolute. The interaction parameter χ_{13} is 0.5, which means that the cosolute is completely miscible with water. Figure 7 presents the system at 270 K. This phase diagram resembles the UCON/butyric acid/water phase diagram in Figure 6. As the temperature is increased, the two-phase boundary extends to the UCON/water line (Figures 8 and 9). A notable reduction of the two-phase region takes place at the cosolute-rich area of the diagram as the temperature increases. If we study the line P/T (cosolute) in Figures 7–9, we see that the pure polymer and the pure cosolute

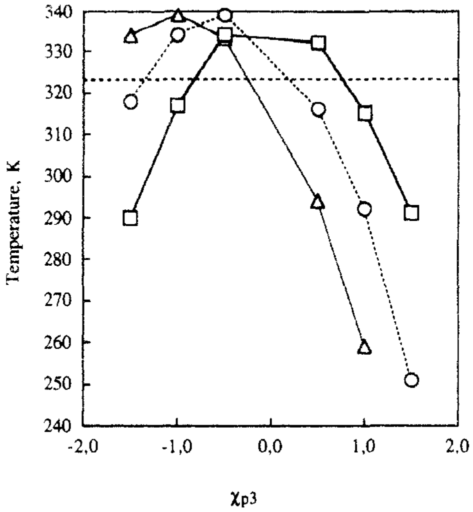

Figure 10. Cloud-point temperature in a three-component system as a function of the interaction parameters χ_{p3} and χ_{13}. Parameter values: $\chi_{13} = -0.5$ (△); $\chi_{13} = 0.0$ (○); $\chi_{13} = +0.5$ (□). The composition of the system is water 72%, polymer 24%, and cosolute 4%. Concentrations in mol %. The cloud-point temperature for the binary UCON (24%)/water system is 323 K (- - -).

are completely miscible with each other at all temperatures studied. The free energy of mixing of the polymer and the cosolute becomes more negative with higher temperature. The same happens to the free energy of mixing of the cosolute and water. The solubility is *favored* with increased temperature in these two cases. In contrast, the solubility of the polymer in water *decreases* with increasing temperature (see Figure 2 and the P/water line in Figures 7–9). This is explained in our model by the increasing dominance of the nonpolar polymer conformations at higher temperatures. Therefore, the two-phase region moves to the polymer/water line in the phase diagram with increasing temperature.

Cloud-Point Temperature as a Function of Interaction Parameters. Figure 10 shows calculated cloud-point temperatures for the system polymer/cosolute/water as a function of the interaction parameters χ_{p3} and χ_{13}. The more negative χ_{p3} is, the stronger is the attraction between the cosolute and the polymer. The more negative χ_{13} is, the stronger is the attraction between the cosolute and water. All points in the diagram represent a fixed point in a three-component diagram. When the χ_{p3} parameter changes, χ_{u3} also changes according to:

$$\chi_{u3} = \chi_{p3} + 0.5\chi_{uu} \tag{11}$$

Generally the effective interaction is

$$\chi^{\mathrm{eff}}_{ab} = \chi_{ab} - 0.5(\chi_{aa} + \chi_{bb}) \tag{12}$$

The superscript eff indicates an effective interaction parameter. To simplify the calculations, we have chosen

$$\chi^{\mathrm{eff}}_{u3} = \chi^{\mathrm{eff}}_{p3} \tag{13}$$

Since χ_{33} and χ_{pp} are zero in this model, eq 11 is obtained by applying eqs 12 and 13. The term $0.5\chi_{uu}$ models the intrinsic energy difference between the nonpolar and the polar forms of the polymer. It determines the equilibrium between the two forms of the polymer. The interaction parameters χ_{1p}, χ_{1u}, χ_{pu}, and χ_{uu} are the same as in Table I. By changing the parameters χ_{p3} and χ_{13}, the chemical character of the cosolute is changed. A point with a high positive value of χ_{p3} and a negative value of χ_{13} corresponds to a strongly polar substance, for instance, a salt. A point with a negative value of χ_{p3} and a positive value of χ_{13} corresponds to a moderately hydrophobic substance, for instance, butyric acid. The results in Figure 10 show that the cloud-point temperature decreases, compared with pure water as a solvent, when the absolute value of the difference ($\chi_{13} - \chi_{p3}$) is high. All systems in Figure 10 have a cloud-point temperature less than 323 K, which is the cloud-point temperature of the binary system of UCON/water, when the absolute value of ($\chi_{13} - \chi_{p3}$) is 1.5 or higher.

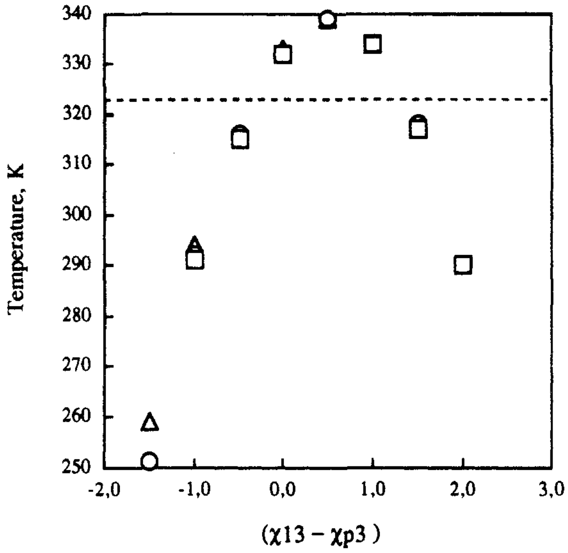

Figure 11. Cloud-point temperature in a three-component system as a function of the difference of the interaction parameters $\chi_{p3} - \chi_{13}$. Parameter values: $\chi_{13} = -0.5$ (△); $\chi_{13} = 0.0$ (○); $\chi_{13} = +0.5$ (□). The composition of the system is water 72%, polymer 24%, and cosolute 4%. Concentrations in mol %. The cloud-point temperature for the binary UCON (24%)/water system is 323 K (- - -).

In Figure 11 the cloud-point temperature of the same model system as in Figure 10 is plotted as a function of the difference of the interaction parameters $\chi_{13} - \chi_{p3}$. From the diagram it follows that the cloud-point temperature of the system is increased if the following condition is fulfilled:

$$-0.5 < \chi_{13} - \chi_{p3} < 1.5 \tag{14}$$

This result is also obtained in a model system containing an infinitely long polymer and an infinitely dilute concentration of polymer and cosolute.[12] The diagram is not symmetrically centered around the zero value for $\chi_{13} - \chi_{p3}$ since there is a difference in mixing entropy if the cosolute is mixed with the solvent or with the polymer.

Conclusions

The conclusion from the model calculations, presented in Figures 10 and 11, is that widely differing substances can induce phase separation in a UCON/water solution. We have shown that hydrophobic molecules can decrease the cloud-point temperature of a UCON/water system. It has previously been shown that sugars[13] and salts[14] can decrease the cloud-point temperature in systems containing poly(ethylene oxide). The increase of the cloud-point temperature in systems containing ionic surfactants and EHEC has also been reported.[6] These experimental findings can be understood as the interplay of the interaction parameters according to Figures 10 and 11.

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