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Liquid−Liquid and Solid−Liquid Equilibria of the Poly(ethylene glycol) + Sodium Sulfate + Water System at 298.15 K

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Liquid−liquid and solid−liquid equilibrium data are presented for the PEG 4000 + Na_2SO_4 + water system at 298.15 K. Six equilibrium regions were found. The binodal curve was fitted by means of a three-parameter equation (relative mean deviation 3.95%), and the tie lines compositions were fitted to both the Othmer−Tobias and Bancroft equations. Densities and refractive indices were determined for the solutions in equilibrium. Samples of the solid phase analyzed by X-ray diffraction showed it to consist of anhydrous Na_2SO_4.

Introduction

Aqueous two-phase systems (ATPS) may be formed by water and two polymers or by water, a polymer, and an inorganic salt.[1] In the latter alternative one of the polymers most commonly utilized is poly(ethylene glycol) (PEG), with which are formed two liquid phases which normally contain amounts of water exceeding 80 mol %.[2] This characteristic has permitted the use of these systems for partitioning a large variety of biomaterials and metallic ions;[3−5] several monographs have been prepared on this topic.[2,6−8]

Zaslavsky[2] presented a useful summary of experimental data, including equilibrium phase diagrams for systems, which include PEG, inorganic salts, and water. The principal inorganic salts discussed were ammonium phosphate; ammonium, sodium, and magnesium sulfates; potassium and sodium carbonates; and sodium and potassium hydroxides.

Recent work presented data on phase equilibrium in ATPS formed by PEG and sodium nitrate.[9] Some references exist which present selected data relevant to the biphasic aqueous system presently reported.[10−13] Pathak et al.[10] presented results of research in which they obtained phase diagrams for the biphasic liquid zone for systems containing PEG 4000, salt, and water at 293, 303, and 313 K. The salts studied included sodium sulfate and iron sulfate. It was suggested that these systems were advantageous for the extraction of biomolecules given the low levels of PEG in the saline phase that reduced losses and facilitated later purification and concentration of the biomolecules. Another advantage cited was the improved economy obtained by substitution of a salt for a second polymer, as used in some cases. Ho-Gutierrez et al.[12] presented data on equilibrium of aqueous mixtures of PEG 3350 with Na_2SO_4 at 301 K and NaCl at 333 K. These authors determined the solute concentration using atomic absorption spectrometry and the PEG concentration by the refractive index; they also measured the densities of the solutions. The refractive index is correlated with the salt and PEG concentrations, and it was determined that these were independent of the molecular weight of the polymer. Snyder et al.[11] presented partial information on the phase diagrams of aqueous solutions of PEG with $MgSO_4$, Na_2SO_4, $CaCO_3$, $(NH_4)_2SO_4$, and K_2HPO_4. Binodal curves were obtained from the data for tie lines and are thus of limited accuracy, working only for the liquid−liquid equilibrium zone. Hammer et al.[13] measured the liquid−liquid equilibrium for aqueous solutions of PEG and sodium sulfate. They worked with PEG having molecular weight between 1550 and 6000, pH between 5.2 and 8.1, and temperatures between 293.15 and 313.15 K. They showed that the experimental data were thermodynamically consistent and that both equilibria could be described using an extended osmotic virial equation extended by a Debye−Hückel term.

In general, previous studies (except for that of ref 12) present data for only a small portion of the phase equilibrium diagram, restricted to the liquid−liquid region, without including data on the solid−solid equilibrium.

This study presents complete phase diagrams for the Na_2SO_4 + PEG 4000 + H_2O system at 298.15 K, which permits its use for the design of processes for obtaining anhydrous crystals by the addition of PEG as a cosolvent.

Experimental Section

Materials. Synthesis grade samples of PEG with an average molecular weight of 4000 (3500−4500) and analytical reagent grade +99.5% sodium sulfate were procured from Merck and used without further purification. Milli-Q quality distilled water was used in all experiments. The PEG was dried for 2 weeks at 323 K, after which its water content was determined to be 0.42 mass %. The sodium sulfate was dried for 48 h at 393 K prior to use.

Experimental Procedure. The binodal curve was obtained using a turbidimetric method.[14] Aqueous solutions of sodium sulfate were prepared in 10 mL test tubes thermostated at (298.15 ± 0.05) K monitored with a digital thermometer (Yokogawa Corp., Model #7563). Each point

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on the binodal curve was determined by successive additions of small quantities of PEG-4000 (~0.01 g) until a change in turbidity was detected, characteristic of the emergence of a second liquid phase. The composition at each point on the binodal curve was calculated on the basis of the accumulated masses added up until the moment that turbidity was observed. To complete the binodal curve, the same procedure was carried out using aqueous solutions of PEG and additions of sodium sulfate.

Compositions of the liquid−liquid equilibrium mixture were determined according to previously described procedures.[9] Solutions were prepared containing different concentrations of PEG and sodium sulfate using an analytical balance with a precision of $\pm 10^{-4}$ g. About 50 g of each solution was deposited individually into 50 mL graduated, capped Pyrex flasks.

Samples were placed in a Haake Fisions Co. # DC3 rotary bath, thermostatically controlled at 298.15 K, and agitated for 48 h. These were then allowed to settle for 24 h at 298.15 K. Longer stirring and settling periods did not result in any sensible change in the phase compositions.

After equilibrium was achieved, the volume of each equilibrium phase was measured to ± 0.5 cm^3, and composition, density, and index of refraction were determined on each separated phase. Refractive index was measured using a Mettler Toledo model # RE50 refractometer ($\pm 0.0001 n_D$). Density was measured using a Mettler Toledo model # DE50 ($\pm 5 \times 10^{-5}$ g/mL). To obtain concentrations of the solutions, samples of the top phase were diluted by a factor of 2, and samples of the bottom phase were diluted by a factor of 10, with all samplings carried out in triplicate. The concentration of sodium sulfate was obtained by determination of sodium using atomic absorption spectrometry in a Varian SpectrAA model # 220 with λ of 589 nm. The PEG concentration was obtained using eq 1, which related the refractive index to the concentrations of sodium sulfate and PEG at 298.15 K,[12] where w_1 represented the mass fraction of Na_2SO_4, w_3 the mass fraction of PEG, and 1.3325 the value of the refractive index of pure water at 298.15 K.

$$n = 1.3325 + 0.1158 w_1 + 0.1443 w_3 \tag{1}$$

Equation 1 was verified by determining the refractive indexes of aqueous solutions containing different concentrations of Na_2SO_4 and PEG 4000. Good representation of the equation was obtained (relative deviations less than 0.1%) initially employing PEG 3350. It was observed that the refractive index for dilute solutions was independent of the molecular weight of the PEG.

Once the concentrations of sodium sulfate and PEG were determined, the water content was given by difference.

Various series of solutions of the three components were prepared in order to delimit the three-phase region from the two-phase region. Two liquids and one solid-phase coexist in equilibrium in this zone. Once the equilibrium was obtained, the samples of both liquid phases (top and bottom) were analyzed for density, refractive index, and composition. The solid phase (salt) was dried and analyzed by X-ray diffraction using an automatic, computerized X-ray diffractometer (Siemens Co., model D5000), which showed the salt to be anhydrous sodium sulfate.

Results and Discussion

Experimental data for the binodal curve are presented in Table 1 and those for tie lines in Table 2. Data are plotted in Figure 1.

Table 1. Binodal Curve Data of the Sulfate Sodium (1) + Water (2) + PEG (3) System at 298.15 K as Mass Fraction w

$100w_1$	$100w_3$	$100w_1$	$100w_3$	$100w_1$	$100w_3$
23.84	0.29	8.35	6.25	1.39	40.98
21.89	0.38	7.09	10.04	1.29	41.74
17.95	0.38	6.83	10.83	1.28	42.53
14.93	0.55	5.08	17.71	1.18	42.98
11.92	0.68	4.73	18.40	1.11	44.91
11.25	1.15	3.39	24.79	0.82	49.31
9.62	3.99	2.91	28.01	0.72	50.16
8.78	5.16	1.68	38.00		

Observation of the binodal curve shown in Figure 1 shows that the addition of PEG decreased the solubility of sodium sulfate and that a concentration of PEG as low as 0.63% made possible the emergence of two liquid phases, one of which was a mixture enriched with sodium sulfate.

The binodal curve was fitted using the following nonlinear expression,[15] where w_1 represented the mass fraction of Na_2SO_4 and w_3 the mass fraction of PEG.

$$\ln w_3 = a + b {w_1}^{0.5} + c {w_1}^{3.0} \tag{2}$$

The parameters of the fit were $a = 4.495$, $b = -0.663$, and $c = -0.001$; obtained by the method of minimum squares. The relative mean deviation between experimental and calculated values using eq 2 was ±3.96%.

The tie line compositions are given in Table 2, and the phase concentrations are also plotted in a phase diagram in Figure 2.

In Table 2 it is observed that the density of the top phase was between 1072.3 and 1093.7 kg m^{-3}, while the density of the bottom phase varied between 1117.2 and 1266.2 kg m^{-3} and the density difference between the phases increased with the tie line length.

A mass balance was obtained for each component, comparing the initial mass with the amounts in the bottom and top phases. The mass of each component was calculated from volume, density, and equilibrium composition measurements. The average relative error for the mass balance was less than 1%.

The partition coefficient for the salt in the biphasic zone, defined for Na_2SO_4 as w_{1b}/w_{1t}, gave values between 4 and 40. Thus, the percentage of salt recovered for the tie line most distant from the water vertex was 97.56%.

The Othmer−Tobias correlation (eq 3) and the Bancroft potential equation (eq 4) satisfactorily reproduce the equilibrium concentrations for both phases.

$$\left(\frac{1 - w_{3t}}{w_{3t}}\right) = k\left(\frac{1 - w_{1b}}{w_{1b}}\right)^n \tag{3}$$

$$\left(\frac{w_{2b}}{w_{1b}}\right) = k_1\left(\frac{w_{2t}}{w_{3t}}\right)^r \tag{4}$$

w_{3t} is the mass fraction of PEG in the top phase, w_{1b} is the mass fraction of Na_2SO_4 in the bottom fraction, w_{2b} and w_{2t} are the fractions of the water mass in the bottom and top phases, respectively, and k, n, k_1, and r are the parameters to be determined. A linear dependency of both plots using the $\log\{(1 - w_{3t})/w_{3t}\}$ versus $\log\{(1 - w_{1b})/w_{1b}\}$ and $\log(w_{2b}/w_{1b})$ versus $\log(w_{2t}/w_{3t})$ plots indicated acceptable consistency of the results. Values for the parameters are given in Table 3. The best fit was obtained using the Bancroft potential equation.

The compositions of the plait points obtained using eqs 2 and 3 were 13.88 mass % PEG and 6.10 mass % Na_2SO_4.

Table 2. Tie Lines for the Sodium Sulfate (1) + Water (2) + PEG (3) System at 298.15 K at Various Initial Mass Fractions w

initial comp		top phase				bottom phase			
$100w_1$	$100w_3$	$100w_1$	$100w_3$	ρ/kg·m^{-3}	n	$100w_1$	$100w_3$	ρ/kg·m^{-3}	n
14.1	27.46	0.6859	50.1480	1093.7	1.3690	29.7986	0.6203	1266.2	1.3362
9.84	29.23	0.8865	46.0444	1089.2	1.3665	24.6045	0.6118	1229.3	1.3357
9.40	27.10	1.1757	42.5577	1085.3	1.3641	20.9990	0.5881	1204.2	1.3353
8.84	23.80	1.4228	39.0811	1081.6	1.3618	18.7505	0.5603	1176.2	1.3350
8.17	19.40	2.0508	33.3775	1076.4	1.3580	15.4734	0.4728	1143.6	1.3346
7.68	15.38	2.9660	26.7123	1072.3	1.3540	12.8113	0.3481	1117.2	1.3342

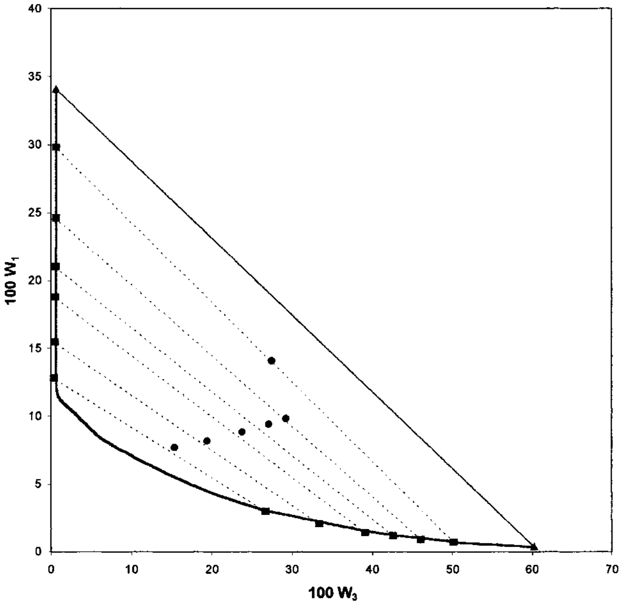

Figure 1. Binodal curve and tie lines for Na_2SO_4 (1) + H_2O (2) + PEG 4000 (3) at 298.15 K: —, binodal at 25 °C; ▲, eutectic points; ■, tie lines; ●, total composition.

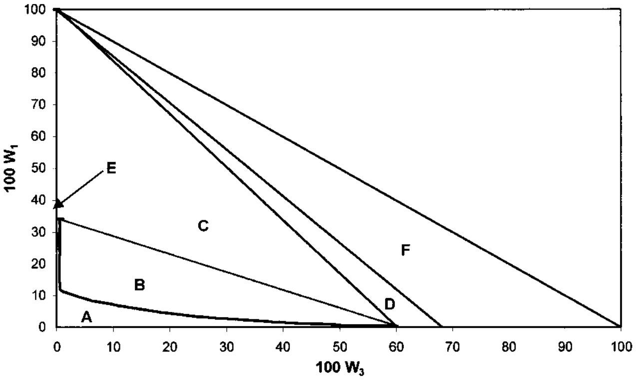

Figure 2. Phase diagram for Na_2SO_4 (1) + H_2O (2) + PEG 4000 (3) at 298.15 K: (A) liquid phase; (B) two-liquid phase; (C) a solid phase (Na_2SO_4) and two-liquid phase; (D) crystals and liquid saturated; (E) a solid phase (Na_2SO_4) and a liquid phase; (F) two-solid phase (Na_2SO_4 and PEG) and a liquid phase.

Table 3. Values of the Parameters of Eq 3 and Eq 4[a]

k	n	R^{reg}	k_1	r	R^{reg}
0.332	1.075	0.993	2.798	0.956	0.994

[a] reg = linear regression index.

The complete phase diagram is presented in Figure 2. A simple liquid-phase exists in region A.

Region B includes two liquid phases in equilibrium, the bottom phase rich in Na_2SO_4 and poor in PEG and the top phase rich in PEG and poor in salt. In this zone, any addition of sodium sulfate would alter the compositions of the two immiscible phases. The two-liquid envelope occupies a small portion of the total phase diagram.

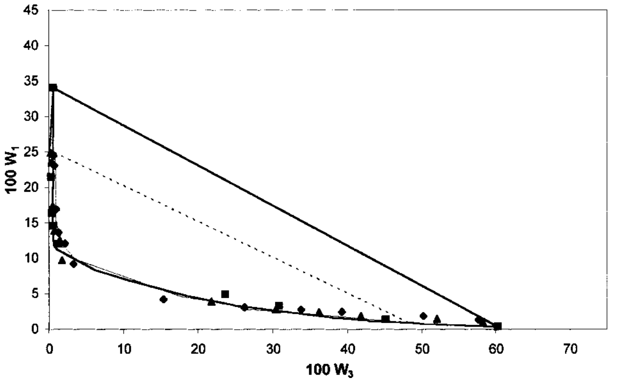

Figure 3. Comparison of the data for different authors in the biphasic region: —, binodal at 25 °C, PEG 4000, this work; ■, limit region 3 phases, PEG 4000; - - -, binodal at 28 °C, PEG 3350, Ho-Gutierrez et al.; ···, limit region 3 phases, PEG 3350; —, solubility at 25 °C, PEG 4000; ●, data at 25 °C, PEG 3350, Snyder et al.; ◆, data at 20 °C, PEG 4000, Pathak et al.; ▲, data at 30 °C, PEG 4000, Pathak et al.

In region C exist two immiscible liquid phases in equilibrium with a solid phase. In this case the system is saturated with salt and the composition of each liquid phase will remain constant even though the relative amount of the two liquids will change, as predicted by the phase rule.

In region D there exists equilibrium between crystals (Na_2SO_4) and a saturated liquid. The eutectic points were 60.25 mass % PEG with 0.37 mass % Na_2SO_4 (top phase) and 0.63 mass % PEG with 34.08 mass % Na_2SO_4 (bottom phase).

In region E, which is delimited by region A only by the solubility of the Na_2SO_4 at 298.15 K (30.1 g Na_2SO_4/100 g H_2O), a solid (Na_2SO_4) and a liquid phase coexist. The solubility of sodium sulfate in water is increased in mass from 23% to 34% (corresponding to a eutectic point with 0.63 mass % PEG). For concentrations of PEG above 0.63 mass %, the solubility of sodium sulfate decreases, following the line that separates regions B and C (this region is insignificant).

In region F exist two solid phases (Na_2SO_4 and PEG) and a liquid phase.

It was experimentally determined that the solubility of PEG 4000 in water at 298.15 K was 68.2 mass %, which produces the appearance of regions D and F as a consequence.

In Figure 3, where part of the results is compared to those of three other authors,[11,12] who worked with the same systems with similar ranges of variables, it was observed that the binodal curve showed practically no change, although data were presented for PEG 3350 and 4000.

There was, however, a major difference between results obtained in the present research when compared with those of Ho-Gutierrez et al.,[12] who did not consider the solubility of PEG in water and in contrast suggested that the region near the PEG vertex was formed by a solid phase and a liquid. This is inconsistent with the affirmation made by these authors that most of the phase diagram consists of a solid−liquid−liquid region (correctly presented) and a solid−solid−liquid region (nonexistent in the diagram proposed by these authors). In accord with data presented in the present study, the major regions occurred in zone C, in which coexisted crystals of sodium sulfate and two immiscible liquids, and zone F, in which coexisted the salt and solid PEG with a PEG-saturated solution.

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