J. Chem. Eng. Data **2008,** *53,* 2666–2670

Liquid−Liquid and Liquid−Liquid−Solid Equilibrium of the Poly(ethylene glycol) Dimethyl Ether 2000 + Sodium Sulfate + Water System

Mohammed Taghi Zafarani-Moattar* and Dariush Nikjoo

Physical Chemistry Department, University of Tabriz, Tabriz, Iran

The phase diagram for the poly(ethylene glycol) dimethyl ether (PEGDE) + Na_2SO_4 + H_2O system at 298.15 K using PEGDE with a molar mass of 2000 was determined. Compositions of the liquid−liquid and the liquid−liquid−solid equilibria were determined using calibration curves of refractive index of the solutions, and atomic absorption (AA) and X-ray diffraction analyses were made on the solids. The solid phase in equilibrium with the biphasic region was anhydrous Na_2SO_4. An empirical nonlinear three-parameter expression developed by Merchuk was used for reproducing the experimental binodal data at T = (288.15, 298.15, 308.15, and 318.15) K, and the fitting parameters were obtained for the corresponding temperatures. The effects of temperature on the binodal curve were also studied, and it was observed that the area of the biphasic region increased slightly with an increase in temperature. The experimental tie-line compositions at the aforementioned temperatures were fitted to both the Othmer−Tobias and Bancroft and Setschenow-type equations. Correlation coefficients for all equations are reported.

Introduction

Liquid−liquid extraction utilizing aqueous two-phase systems (ATPSs) has been used to separate and purify biological products from the complex mixtures in which they are produced. ATPSs can be formed by combining either two incompatible polymers or a polymer and a salt in water above a certain critical concentration.[1−3] Poly(ethylene glycol) (PEG), which is a hydrophilic polymer, is often used in aqueous two-phase partitioning studies. In laboratory-scale separations, the most commonly used aqueous systems are comprised of the polymers PEG and dextran, while for large-scale enzyme extraction, aqueous PEG + salt systems are used. The latter systems are more attractive because of their greater selectivity, lower viscosity, lower cost, rapid phase disengagement, and availability of commercial separators, which allow a faster and continuous protein separation. The most common inorganic salts employed by different research groups on the aqueous two-phase extraction technique consist of selective cations (ammonium, potassium, or sodium) and anions (phosphate, sulfate, or carbonate).

Zaslavsky[3] presented a useful summary of experimental liquid−liquid data and equilibrium diagrams for systems formed by PEG, inorganic salts, and water. The principal inorganic salts discussed included ammonium phosphate, ammonium, sodium, and magnesium sulfates, potassium and sodium carbonates, and sodium and potassium hydroxides. Equilibrium diagrams for two-phase systems containing PEG and some organic salts have also been reported, recently. However, there are few data available on the complete phase diagram consisting of liquid−liquid and liquid−solid equilibrium in the literature for aqueous systems containing a polymer and a salt. There are reports on the complete phase diagrams for a few aqueous PEG + salt systems containing Na_2SO_4[4,5] and Ca_2CO_3.[6]

Here, we report liquid−liquid equilibrium data for the new aqueous poly(ethylene glycol) dimethyl ether 2000 ($PEGDE_{2000}$) (1) + Na_2SO_4 (2) + H_2O (3) system at T = (288.15, 298.15, 308.15, and 318.15) K that have not been previously published. The effect of temperature on the binodal curve was studied. In this work, the complete phase diagram of the $PEGDE_{2000}$ (1) + Na_2SO_4 (2) + H_2O (3) system has also been studied at T = 298.15 K. The obtained results are necessary for design and optimization of extraction processes. Further, study of this system permits its use for the design of processes for obtaining anhydrous crystals by the addition of PEGDE as a cosolvent.

Table 1. Binodal Data for the $PEGDE_{2000}$ (1) + Na_2SO_4 (2) + H_2O (3) System at T = (288.15, 298.15, 308.15, and 318.15) K

T = 288.15 K		T = 298.15 K		T = 308.15 K		T = 318.15 K	
100 w_1	100 w_2	100 w_1	100 w_2	100 w_1	100 w_2	100 w_1	100 w_2
0.26	0.62	0.35	58.52	0.49	57.77	0.49	57.43
0.67	0.54	0.64	52.36	0.99	47.20	1.08	45.43
0.92	0.48	0.89	48.03	1.56	40.64	1.95	35.59
1.43	0.40	1.28	43.26	2.28	34.10	3.25	27.29
2.01	0.35	1.54	40.41	3.18	28.28	4.77	19.86
3.14	0.28	2.26	34.28	4.16	23.34	6.35	13.72
4.43	0.22	2.63	31.62	5.54	17.80	7.51	9.70
6.03	0.17	3.80	25.13	6.79	13.53	8.32	7.06
7.37	0.13	5.14	19.63	8.08	9.52	9.00	5.22
8.43	0.10	6.63	14.67	9.17	6.46		
	7.93	10.83					
	9.06	7.76					
	9.74	6.04					
	10.34	4.65					

Experimental Section

Materials. Poly(ethylene glycol) dimethyl ether, of molar mass 2000, and sodium sulfate with purity of min. 99 % by mass were supplied from Merck. The polymer and salt were used without further purification, and double distilled deionized water was used. The number average molar mass and polydispersity of the polymer were determined to be 2305 $g \cdot mol^{-1}$ and 1.0579, respectively, using gel permission chromatography (GPC, Agilent).

---

* Corresponding author. Fax: +98 411 3340191. E-mail: zafarani47@yahoo.com.

10.1021/je8005858 CCC: $40.75

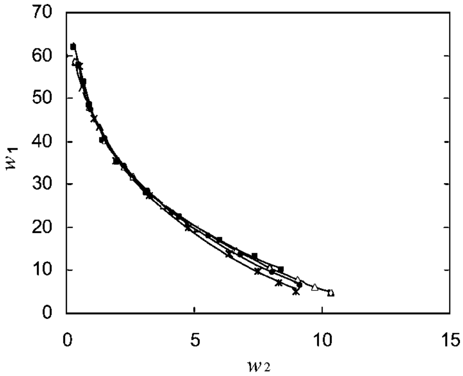

Figure 1. Binodal curves for the $PEGDE_{2000}$ (1) + sodium sulfate (2) + H_2O (3) two-phase system at different temperatures: ■, 288.15 K; △, 298.15 K; ●, 308.15 K; *, 318.15 K; —, calculated from eq 2.

Table 2. Experimental Phase Equilibrium Compositions for the $PEGDE_{2000}$ (1) + Na_2SO_4 (2) + H_2O (3) System at T = (288.15, 298.15, 308.15, and 318.15) K

top phase: polymer-rich phase		bottom phase: salt-rich phase	
$100\ w_1$	$100\ w_2$	$100\ w_1$	$100\ w_2$
	T = 288.15 K		
29.16	2.80	2.74	14.44
32.51	2.49	2.11	15.67
34.51	1.98	1.80	17.05
37.73	1.67	1.82	18.37
40.60	1.39	1.70	19.41
42.92	1.33	1.55	20.58
	T = 298.15 K		
32.95	2.34	2.10	14.72
36.28	1.89	1.81	16.37
40.85	1.48	1.59	18.43
42.72	1.21	1.33	19.94
45.38	1.08	1.08	21.40
	T = 308.15 K		
33.10	2.24	1.75	12.61
35.30	2.08	1.04	14.76
38.02	1.69	1.00	16.09
40.74	1.36	0.97	17.35
43.13	1.23	0.74	18.63
45.22	1.05	0.66	20.10
	T = 318.15 K		
32.61	2.36	2.35	12.33
37.63	1.81	1.24	14.08
40.29	1.42	0.83	15.48
43.55	1.08	0.54	16.96
45.04	1.05	0.39	18.36
46.81	0.93	0.40	19.69

Table 3. Values of Parameters of Equation 2 for $PEGDE_{2000}$ (1) + Sodium Sulfate (2) + H_2O (3) at T = (288.15, 298.15, 308.15, and 318.15) K

T/K	a	b	c	sd[a]
288.15	0.8618	−6.1776	548.8927	0.79
298.15	0.8291	−5.8030	860.8625	0.24
308.15	0.8909	−6.2711	866.7698	0.26
318.15	0.8927	−6.4036	1139.3000	0.39

[a] sd = $(\sum_{i=1}^{N}[(w_1^{\mathrm{cal}} - w_1^{\mathrm{exp}})^2/N])^{0.5}$, where N is the number of binodal data.

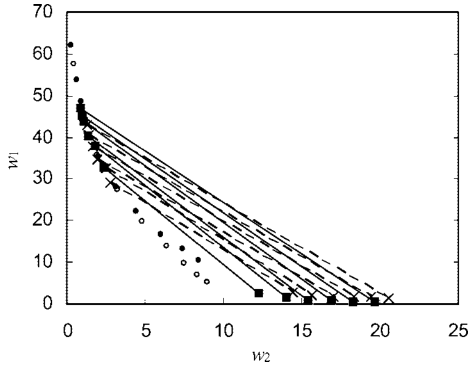

Figure 2. Effect of temperature on the equilibrium phase compositions for the $PEGDE_{2000}$ (1) + sodium sulfate (2) + H_2O (3) system: ●, experimental binodal at 288.15 K; ○, experimental binodal at 318.15 K; --- × ---, tie-lines at 288.15 K; —■—, tie-lines at 318.15 K. These tie-lines were obtained by connecting the experimental equilibrium phase composition data.

Table 4. Values of Parameters from Least-Squares Linear Fits to Setschenow-Type Equation (Equation 3) for $PEGDE_{2000}$ (1) + Sodium Sulfate (2) + H_2O (3) at T = (288.15, 298.15, 308.15, and 318.15) K

T	k_S			
K	$(\mathrm{kg \cdot mol^{-1}})$	intercept	R^2	dev[a]
288.15	1.3179	1.4597	0.952	0.08
298.15	1.3341	1.6829	0.996	0.01
308.15	1.5479	2.1220	0.956	0.10
318.15	2.7910	0.9987	0.956	0.11

[a] dev = $(\sum_p \sum_l \sum_j (wp,l,j^{\mathrm{cal}} - wp,l,j^{\mathrm{exp}})^2\ /6N)$, where $w_{p,l,j}$ is the mass fraction of the component j (i.e., polymer, salt, or water) in the phase p for the lth tie-line and the superscripts "cal" and "exp" refer to the calculated and experimental values, respectively. N is the number of tie-line data.

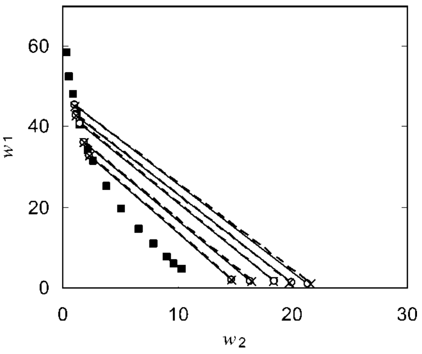

Figure 3. Phase diagram of the $PEGDE_{2000}$ (1) + sodium sulfate (2) + H_2O (3) two-phase system at 298.15 K: ■, experimental binodal; —○—, experimental tie-lines; -- × ---, calculated tie-lines using eq 3.

Table 5. Values of Parameters of Equation 4a and Equation 4b for PEGDE (1) + Sodium Sulfate (2) + H_2O (3) at T = (288.15, 298.15, 308.15, and 318.15) K

T/K	k	n	R^2	k_1	r	R^2	dev[a]
288.15	0.20996	1.37424	0.993	3.11892	0.72213	0.993	0.09
298.15	0.26288	1.16324	0.996	3.15749	0.86493	0.996	0.04
308.15	0.34239	0.93085	0.979	3.24114	1.05648	0.981	0.21
318.15	0.22730	1.11413	0.984	3.84542	0.87857	0.980	0.25

[a] Definition is given in Table 4.

Apparatus and Procedure. The experimental apparatus employed is essentially similar to the one used previously.[7,8] A glass vessel, volume 50 cm^3, was used to carry out the phase equilibrium determinations. The glass vessel was provided with an external jacket in which water at constant temperature was circulated using a thermostat. The temperature was controlled to within ± 0.05 K. The binodal curves were determined by a titration method. A salt solution of known concentration was titrated with the polymer solution or vice versa, until the solution turned turbid, which indicated the formation of two liquid phases. In accordance with the amount of titrant added until turbidity was observed, the composition of the mixture for each point on the binodal curve was calculated by mass using an analytical balance (Shimatzu, 321-34553, Shimatzu Co., Japan) with a precision of $\pm 1 \cdot 10^{-7}$ kg. The maximum uncertainty

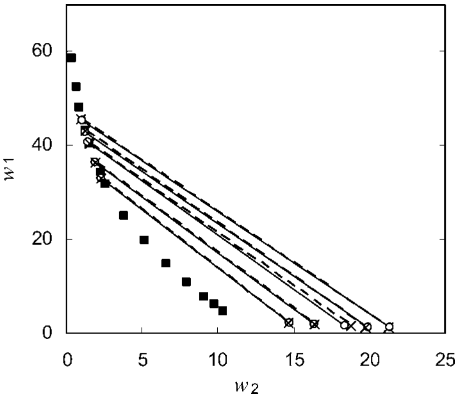

Figure 4. Phase diagram of the PEGDE$_{2000}$ (1) + sodium sulfate (2) + H_2O (3) two-phase system at 298.15 K: ■, experimental binodal; —○—, experimental tie-lines; --- × ---, calculated tie-lines using eqs 4a and 4b.

was found to be 0.002 in determining the mass fraction of both polymer and salt by the titration method used. For the determination of the tie-lines, feed samples (about $2 \cdot 10^{-5}$ m^3) were prepared by mixing appropriate amounts of polymer, salt, and water in the vessel. The thermostat was set at a desired temperature, and the samples were stirred for 1 h. Then the samples were placed in thermostat and allowed to settle for at least 72 h to separate into two clear phases. After separation of the two phases, the concentrations of sodium sulfate in the top and bottom phases were determined by flame photometry. The concentration of PEGDE in both phases was determined by refractive index measurements performed at 298.15 K using a refractometer (ATAGO DR-A1, Japan) with a precision of ± 0.0001. The uncertainty in refractive index measurement is ± 0.0002. For dilute aqueous solutions containing a polymer and a salt, the relation between the refractive index, n_D, and the mass fractions of polymer, w_1, and salt, w_2 is given by[9]

$$n_D = n_0 + a_1 w_1 + a_2 w_2 \tag{1}$$

Here n_0 is the refractive index of pure water which is set to 1.3325 at 298.15 K. The values of coefficients a_1 and a_2 for the applied system were obtained at 298.15 K as 0.1354 and 0.1450, respectively. However, it should be noted that this equation is only valid for dilute solutions ($w_1 \leq 0.1$ and $w_2 \leq 0.05$) for which linear calibration plots of the refractive index of ternary solutions with a fixed mass fraction of salt or polymer against polymer or salt are obtained. Therefore, before refractive index measurements, it was necessary to dilute the samples to the above mass fraction range. The uncertainty of the mass fraction of PEGDE achieved using eq 1 was better than 0.002.

Various series of solutions of the three components were prepared 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 refractive index and composition. The solid phase was dried and analyzed by X-ray diffraction using an automatic, computerized X-ray diffractometer (Siemens Co., model D5000), which showed the solid phase to be anhydrous sodium sulfate.

Results and Discussion

Correlation and Phase Diagrams. For the PEGDE$_{2000}$ (1) + sodium sulfate (2) + water (3) system, the binodal data and the tie-line compositions determined experimentally at T = (288.15, 298.15, 308.15, and 318.15) K are given in Tables 1 and 2, respectively.

For the studied system, the experimental binodal data were fitted by the least-squares regression method to the following empirical nonlinear expression developed by Merchuk[10]

$$w_1 = a \exp(b w_2^{0.5} - c w_2^3) \tag{2}$$

where a, b, and c represent fit parameters. Recently, the above equation has been successfully used for the correlation of binodal data of some aqueous polymer + salt systems.[11,12] Using eq 2, the fitting parameters a, b, and c obtained from the correlation of experimental binodal data along with the corresponding standard deviations are given in Table 3. The binodals reproduced from eq 2 at different temperatures are also shown in Figure 1. On the basis of the obtained standard deviations, we conclude that eq 2 can be satisfactorily used to reproduce the binodal curves of the investigated system.

The effect of temperature on the phase-forming ability for the studied system is also illustrated in Figure 1. The locus for the experimental binodals shown in Figure 1 demonstrates that the two-phase area is expanded with an increase in temperature which is attributed to the decrease in solubility or increase in phase-forming ability in the studied system. Additionally, to show the effect of temperature on the equilibrium phase compositions for the investigated system, the experimental tie-lines are compared in Figure 2, for the temperatures (288.15 and 318.15) K, as an example. As shown in Figure 2, the slope and the length of the tie-lines increase with an increase in temperature, similar to the one observed in our previous work[13] for the aqueous PEG + trisodium citrate system.

For the correlation of LLE data of polymer + salt + water systems, several models have been developed. However, in this work we decided to use a relatively simple two-parameter equation, which can be derived from the binodal theory.[14] The equation used has the following form

$$\ln\left(\frac{C_p^{top}}{C_p^{bot}}\right) = k_p(C_p^{bot} - C_p^{top}) + k_s(C_s^{bot} - C_s^{top}) \tag{3}$$

in which k_s is the salting-out coefficient and k_p is the constant related to the activity coefficient. Superscript "top" and "bot" stand for the polymer-rich phase and salt-rich phase, respectively. Recently, we successfully used eq 3 for the correlation of tie-line data for the aqueous poly(propylene glycol) + potassium citrate two-phase system.[12] The fitting parameters of eq 3 along with the corresponding standard deviations are presented in Table 4 for the investigated system. On the basis of standard deviations reported in Table 4, it is interesting to note that eq 3 with only two parameters represents the experimental LLE data with good accuracy for the studied system at different temperatures. To show the reliability of eq 3, comparison between the experimental and correlated tie-lines is shown in Figure 3 for the PEGDE$_{2000}$ (1) + sodium sulfate (2) + water (3) system at 298.15 K, as an example.

The correlation equations[15] given by Othmer–Tabias (eq 4a) and Bancroft (eq 4b) have also been used to correlate the tie-line compositions.

$$\left(\frac{1 - w_1^{top}}{w_1^{top}}\right) = k\left(\frac{1 - w_2^{bot}}{w_2^{bot}}\right)^n \tag{4a}$$

$$\left(\frac{w_3^{bot}}{w_2^{bot}}\right) = k_1\left(\frac{w_3^{top}}{w_1^{top}}\right)^r \tag{4b}$$

where k, n, k_1, and r represent fit parameters. These equations have also been used to assess the reliability of LLE data. A

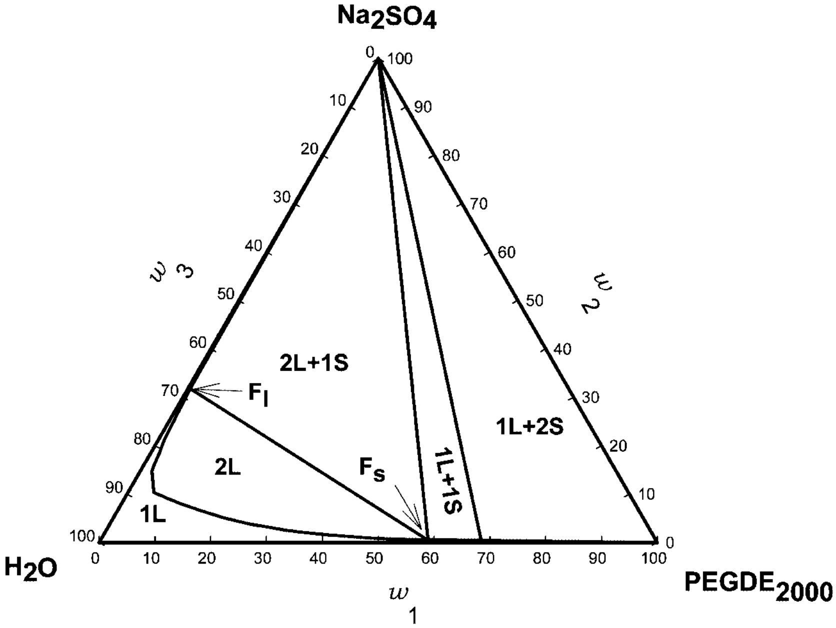

Figure 5. Complete phase diagram of the $PEGDE_{2000}$ (1) + sodium sulfate (2) + H_2O (3) two-phase system at 298.15 K in triangular coordinates: (1L), liquid phase; (2L), two-liquid phase; (2L + 1S), a solid phase (Na_2SO_4) and two-liquid phase; (1L + 1S) solid phase (Na_2SO_4) and liquid saturated; (1L + 2S) two-solid phase (Na_2SO_4 and PEGDE) and a liquid phase; (F_I) and (F_S) are eutectic points in the bottom and top phases, respectively.

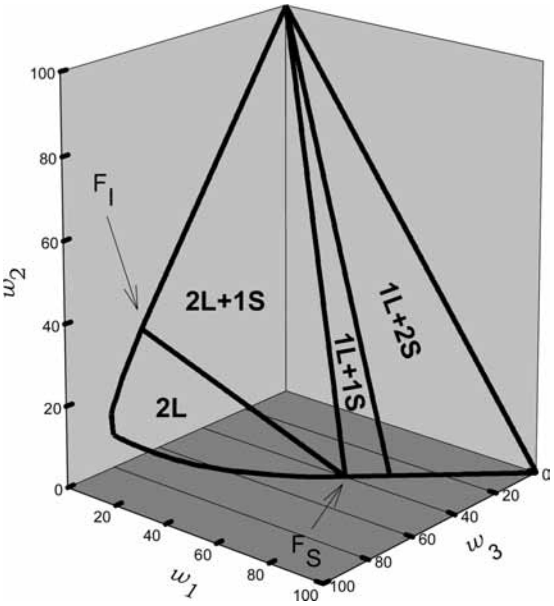

Figure 6. Three-dimensional complete phase diagram of the $PEGDE_{2000}$ (1) + sodium sulfate (2) + H_2O (3) two-phase system at 298.15 K. (2L), two-liquid phase; (2L + 1S), a solid phase (Na_2SO_4) and two-liquid phase; (1L + 1S) solid phase (Na_2SO_4) and liquid saturated; (1L + 2S) two-solid phase (Na_2SO_4 and PEGDE) and a liquid phase; (F_I) and (F_S) are eutectic points in the bottom and top phases, respectively.

linear dependency of the plots $\log(1 - w_1^{top}/w_1^{top})$ against $\log(1 - w_2^{bot}/w_2^{bot})$ and $\log(w_3^{bot}/w_2^{bot})$ against $\log(w_3^{top}/w_1^{top})$ indicated an acceptable consistency of the results. The corresponding correlation coefficient values, R, and the values of the fitted parameters are given in Table 5. On the basis of the obtained standard deviations given in Table 5, we conclude that eqs 4a and 4b can also be satisfactorily used to correlate the tie-line data of the investigated systems. To show the reliability of eq 4a and 4b, comparison between the experimental and correlated tie-lines is shown in Figure 4 at 298.15 K, as an example.

Figure 5 shows the complete phase diagram for the studied system plotted on triangular coordinates. The corresponding three-dimensional complete phase diagram is shown in Figure 6. The letters L and S denote liquid and solid phases, respectively. Most of the phase diagram consists of either a solid−liquid−liquid or solid−solid−liquid region.

In Figure 5 or 6, region 1L represents unsaturated solutions. The biphasic zone is labeled 2L. The two liquid regions occupy a small portion of the total phase diagram, although the coexisting phases are generally quite different in composition. There are two single liquid−liquid regions, one with a liquid rich in water and another with a liquid rich in PEGDE. Any addition of sodium sulfate would alter the compositions of the two immiscible phases.

The 2L + 1S region represents 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.

The 1L + 1S region contains the anhydrous salt in equilibrium with PEGDE saturated solutions. Finally, the 1L + 2S region consists of two solid phases (Na_2SO_4 and PEGDE) and a liquid phase.

It was experimentally determined that the solubility of $PEGDE_{2000}$ in water at 298.15 K was 68.6 mass %, which produces the appearance of regions 1S + 1L and 2S + 1L as a consequence. The eutectic points F_I and F_S were 0.5 % (PEGDE) and 31.9 % (salt) in the bottom phase and 58.7 % (PEGDE) and 0.4 % (salt) in the top phase. There exists a zone of insignificant size, which is not visible in the diagram, as it is practically superimposed by the ordinate. This corresponds to crystals in equilibrium with a saturated sodium sulfate solution which varies between the solubility of the salt in water (30.1 g of Na_2SO_4/100 g of H_2O), to the invariant F_I (0.5 % PEGDE and 31.8 % salt). These observations are very similar to those obtained for the phase diagram of the PEG + Na_2SO_4 + H_2O system, given by Ho-Gutierrez et al.[4] and Taboada et al.[5]

Conclusions

Liquid−liquid equilibrium data for the $PEGDE_{2000}$ (1) + sodium sulfate (2) + H_2O (3) system were obtained at $T =$

(288.15, 298.15, 308.15, and 318.15) K. The experimental binodal data were satisfactorily correlated with the Merchuk equation. The effect of temperature on the phase-forming ability for the studied system was also studied, and it was observed that the area of the biphasic region increased slightly with increase of temperature. Additionally, the tie-line data for the investigated system can be successfully represented by the Setschenow-type and Othmer−Tobias equations. Also, liquid−liquid−solid equilibria were determined for this system and observed that the solid phase in equilibrium with the biphasic region was anhydrous Na_2SO_4. Furthermore, the complete phase diagram was determined for the PEGDE (1) + Na_2SO_4 (2) + H_2O (3) system at 298.15 K.

Literature Cited

(1) Albertsson, P. A. *Partitioning of cell particles and macromolecules*, 3rd ed.; Wiley: New York, 1986.

(2) Walter, H.; Brooks, D. E.; Fisher, D. *Partitioning in aqueous two-phase systems*; Academic Press: New York, 1985.

(3) Zaslavsky, B. Y. *Aqueous two-phase partitioning, physical chemistry and bioanalytical applications*; Marcel Dekker: New York, 1995.

(4) Ho-Gutierrez, I. V.; Cheluget, E. L.; Vera, J. H.; Weber, M. E. Liquid-liquid equilibrium of aqueous mixture of poly (ethylene glycol) with Na_2SO_4 or NaCl. *J. Chem. Eng. Data* **1994**, *39*, 245–248.

(5) Taboada, M. E.; Rocha, O. A.; Graber, T. A. Liquid-liquid and solid-liquid equilibria of the poly(ethylene glycol) + sodium sulfate + water system at 298. 15 K. *J. Chem. Eng. Data* **2001**, *46*, 308–311.

(6) Taboada, M. E.; Asenjo, J. A.; Andrews, B. A. Liquid-liquid and liquid-liquid-solid equilibrium in Na_2CO_3-PEG-H_2O. *Fluid Phase Equilib.* **2001**, *180*, 273–280.

(7) Ting, A. M.; Lynn, S.; Prausnitz, J. M. Liquid−liquid equilibria for aqueous systems containing N,N-diethylmethylamine and sodium chloride or sodium sulfate. *J. Chem. Eng. Data* **1992**, *37*, 252–259.

(8) Zafarani-Moattar, M. T.; Sadeghi, R. Liquid-liquid equilibria of aqueous two-phase systems containing polyethylene glycol and sodium dihydrogen phosphate or disodium hydrogen phosphate. Experiment and correlation. *Fluid Phase Equilib.* **2001**, *181*, 95–112.

(9) Cheluget, E. L.; Gelinas, S.; Vera, J. H.; Weber, M. E. Liquid-liquid equilibrium of aqueous mixtures poly (propylene glycol) with NaCl. *J. Chem. Eng. Data* **1994**, *39*, 127–130.

(10) Merchuk, J. C.; Andrews, B. A.; Asenjo, J. A. Aqueous two-phase systems for protein separation: Studies on phase inversion. *J. Chromatogr. B* **1998**, *711*, 285–293.

(11) Zafarani-Moattar, M. T.; Hamzehzadeh, S.; Hosseinzadeh, S. Phase diagrams for liquid-liquid equilibrium of ternary poly(ethylene glycol) + di-sodium tartrate aqueous system and vapor-liquid equilibrium of constituting binary aqueous systems at T = (298.15, 308.15 and 318.15) K experiment and correlation. *Fluid Phase Equilib.* **2008**, *268*, 142–152.

(12) Zafarani-Moattar, M. T.; Emamian, S.; Hamzehzadeh, S. Effect of temperature on the phase equilibrium of the aqueous two-phase poly(propylene glycol) + tripotassium citrate system. *J. Chem. Eng. Data* **2008**, *53*, 456–461.

(13) Zafarani-Moattar, M. T.; Sadeghi, R.; Hamidi, A. A. Liquid-liquid equilibria of an aqueous two-phase system containing polyethylene glycol and sodium citrate: experiment and correlation. *Fluid Phase Equilib.* **2004**, *219*, 149–155.

(14) Hey, M. J.; Jackson, D. P.; Yan, H. The salting-out effect and phase separation in aqueous solutions of electrolytes and poly(ethylene glycol). *Polymer* **2005**, *46*, 2567–2572.

(15) Othmer, D. F.; Tobias, P. E. Liquid-liquid extraction data-toluene and acetaldehyde systems. *Ind. Eng. Chem.* **1942**, *34*, 690–692.

Received for review July 29, 2008. Accepted October 6, 2008.

JE8005858