Salting-Out Effect of Ionic Liquids on Poly(propylene glycol) (PPG): Formation of PPG + Ionic Liquid Aqueous Two-Phase Systems

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In the present work, aqueous poly(propylene glycol) (PPG) solution was separated into aqueous two-phase systems (ATPSs) in the presence of ionic liquid 1-allyl-3-methylimidazolium chloride ([Amim]Cl), 1-butyl-3-methylimidazolium acetate ([C_4mim]Ac), or 1-butyl-3-methylimidazolium chloride ([C_4mim]Cl). The top phase was PPG-rich, whereas the bottom phase was ionic liquid (IL)-rich. Liquid−liquid equilibrium data for the ATPSs and the salting-out coefficients of the ILs have been determined at 298.15 K and atmospheric pressure. It was shown that the binodal curves and the tie-lines could be described by a three-parameter equation and the Othmer−Tobias and Bancroft equations, respectively. The salting-out ability of the ILs on PPG was found to follow the order: [Amim]Cl > [C_4mim]Ac > [C_4mim]Cl > [C_4mim][BF_4]. Since PPG is a thermo-sensitive polymer and can be recovered simply by heating, these novel ATPSs are expected to have applications in the recycling and/or enrichment of hydrophilic ILs from aqueous solutions.

Introduction

Aqueous two-phase systems (ATPSs), used first in 1956 by Albertsson,[1] can be formed spontaneously upon mixing two aqueous solutions of structurally different components, such as two polymers or one polymer and one salt, above a certain concentration. In the two phases, the top phase is polymer-rich, and the bottom phase is salt-rich (or the other polymer-rich). Because the bulk of the two phases consists mainly of water and no traditional volatile organic compounds are used, ATPSs are considered to be environmentally friendly and provide a biocompatible environment for biomaterials. Moreover, the separation technique based on the ATPSs is relatively simple and inexpensive, and the equipments traditionally used in the liquid−liquid solvent extraction can be easily adapted for aqueous two-phase extraction.[2,3] As a result, ATPSs have been widely used for the recovery and purification of various biomolecules such as proteins, enzymes, and nucleic acids.[4−6]

In recent years, ionic liquids (ILs) have been used for analytical and separation processes[7,8] owing to their "green" characteristics such as negligible volatility, nonflammability, large liquid range, high thermal and chemical stability, excellent solvation power for organic and inorganic compounds, and a number of possible variations in cation and anion features which allow fine-tuning of the IL properties.[9] In 2003, Rogers and co-workers[10] reported, for the first time, that a hydrophilic IL, 1-butyl-3-methylimidazolium chloride ([C_4mim]Cl), could form ATPSs in the presence of a high concentration of inorganic salt such as K_3PO_4. These ATPSs have many advantages, such as lower viscosity, little emulsion formation, quick phase separation, and gentle biocompatible environment. Since then, IL-based ATPSs have been used to separate testosterone, epitestosterone, opium alkaloids, and bovine serum albumin,[11−13] and their extraction efficiency is usually higher than the classical ATPSs.[14]

Inorganic salts are always used in poly(ethylene glycol) (PEG) + salt and IL + salt ATPSs. It is known from their phase diagrams[10,11,15,16] that the concentration of the salt in the salt-rich phase is quite high. This will produce a great amount of highly salty water in the applications, thus causing environmental problems. In this work, new kinds of APTSs were created from poly(propylene glycol) (PPG) being salted-out by ILs. Here, the thermo-sensitive polymer PPG was used to replace the inorganic salts. This polymer is biodegradable and nontoxic and can be recovered conveniently by heating. To understand the phase behavior of these systems, the liquid−liquid equilibrium data at 298.15 K were determined for the ATPSs of PPG400 + 1-allyl-3-methylimidazolium chloride ([Amim]Cl), PPG400 + 1-butyl-3-methylimidazolium acetate ([C_4mim]Ac), PPG400 + 1-butyl-3-methylimidazolium chloride ([C_4mim]Cl), PPG1000 + [Amim]Cl, and PPG1000 + [C_4mim]Cl. The results have been discussed from the competing interaction of PPG and ILs with water.

Experimental Section

Materials. PPG400 (> 99 %), PPG1000 (> 99 %), allyl chloride, and AmberliteIRA-400 (Cl) ion-exchange resin were obtained from Alfa. *N*-Methylimidazole (C. P.) purchased from Linhai Kaile Chem. Co. was distilled before use. All other reagents were of analytical grade, and double-distilled deionized water was used in the experiments. The ILs [C_4mim]Cl (≥ 99.0 %) and 1-butyl-3-methylimidazolium tetrafluoroborate ([C_4mim][BF_4] (≥ 99.0 %) were purchased from Henan Lihua Pharmaceutical Co., Ltd., and dried under vacuum at 60 °C before use. The water content in the ILs determined by Karl Fischer titration was less than 0.002 mass fraction.

Preparation of [C_4mim]Ac and [Amim]Cl. 1-Butyl-3-methylimidazolium acetate was prepared by neutralization:[17] at first,

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the anion exchange resin was transformed from Cl-type into OH-type by passing aqueous NaOH through the resin columns until Cl^- could not be detected with aqueous $AgNO_3$/HNO_3 solution. Excessive NaOH solution was washed out with deionized water. [C_4mim]Cl was transformed into [C_4mim]OH through the OH-type resin. The aqueous [C_4mim]OH solution was then neutralized with equimolar acetic acid. Then, water was evaporated under reduced pressure, and the viscous liquid was obtained through being thoroughly washed with diethyl ether and then dried under vacuum for 48 h at 60 °C.

[Amim]Cl was prepared as described in the literature.[18] Briefly, 1-methylimidazole and allyl chloride were added to a round-bottomed flask fitted with a reflux condenser at a proper mole ratio. The mixture was stirred for 8 h below 60 °C and then distilled under reduced pressure. [Amim]Cl with a slightly amber color was obtained and dried under vacuum for 48 h at 60 °C. The structure of [C_4mim]Ac and [Amim]Cl was confirmed by ^{1}H NMR spectroscopy (AV-400 Bruker spectrometer), and their purity was found to be greater than 0.990 mass fraction.

Methods

The binodal curves were determined by the cloud-point method.[10] Stock aqueous IL solutions were prepared with different mass fractions. A few grams of pure PPG were weighed into a test tube, and a known mass of water was added under stirring. An aqueous IL solution of known mass fraction was added dropwise to the test tube until the mixture became cloudy. Then water was added to get a clear one-phase system again, and the above procedure was repeated. The test tubes were immersed in a jacketed glass vessel, and the temperature of the system was maintained at 298.15 ± 0.05 K by a DC-2006 water thermostat (Shanghai Hengping Instrument Factory). The concentration of the phase components was determined by mass quantification of all of the components added within an uncertainty of $\pm\, 1.0 \cdot 10^{-7}$ kg.

For the determination of tie-lines, a series of ATPSs with different total compositions were prepared in graduated glass tubes which were placed in a thermostatted bath. The system was vigorously stirred for at least 1 h to attain equilibrium. The phase separation occurred quickly after cessation of the stirring. Then, a XYJ-802 centrifuge (Jiangsu Medical Instrument Factory) operated at 2000 rpm was still used for a period of 10 min to ensure a complete phase separation. Then, the systems were placed again into the thermostatted bath. After phase equilibrium, visual estimates of the top and bottom volumes were made. Concentrations of the IL in both the top and the bottom phases were determined by spectrophotometry at 211 nm after dilution. The quantification of water content in the top and bottom phases was determined according to the procedure described in our previous work.[19] A mass balance check was made between the initial mass of each component and the amounts in the top and bottom phases on the basis of equilibrium compositions. Then the concentrations of PPG in the top and bottom phases were calculated by mass balance. The tie-line length (TLL) at different compositions were calculated by using eq 1:[19,20]

$$\mathrm{TLL} = \sqrt{(w_1^{\mathrm{t}} - w_1^{\mathrm{b}})^2 + (w_2^{\mathrm{t}} - w_2^{\mathrm{b}})^2} \qquad (1)$$

where w_1^{t}, w_1^{b}, w_2^{t}, and w_2^{b} represent the equilibrium mass fraction of PPG (1) and ILs (2) in the top and bottom phases, respectively.

Table 1. Binodal Data for PPG400 (1) + ILs (2) + H_2O (3) Systems at T = 298.15 K

PPG400 + [Amim]Cl		PPG400 + [C_4mim]Ac		PPG400 + [C_4mim]Cl	
w_1	w_2	w_1	w_2	w_1	w_2
0.0934	0.4159	0.1323	0.4401	0.2110	0.5268
0.1040	0.3704	0.1405	0.3998	0.2229	0.4927
0.1196	0.3214	0.1542	0.3467	0.2329	0.4686
0.1435	0.2725	0.1685	0.3060	0.2398	0.4429
0.1559	0.2513	0.1854	0.2653	0.2521	0.4096
0.1611	0.2366	0.2037	0.2289	0.2679	0.3763
0.1745	0.2150	0.2297	0.1937	0.2796	0.3523
0.1975	0.1851	0.2453	0.1460	0.2944	0.3201
0.2167	0.1616	0.2742	0.1335	0.3145	0.2925
0.2340	0.1449	0.2960	0.1057	0.3359	0.2664
0.2552	0.1249	0.3262	0.0939	0.3575	0.2387
0.2833	0.1021	0.3600	0.0742	0.3781	0.2151
0.3027	0.0887	0.3968	0.0564	0.4000	0.1954
0.3221	0.0768	0.4422	0.0526	0.4228	0.1798
0.3416	0.0659	0.4910	0.0317	0.445	0.1662
0.3588	0.0571			0.4677	0.1509
				0.5112	0.1326

Table 2. Binodal Data for PPG1000 (1) + ILs (2) + H_2O (3) Systems at T = 298.15 K

PPG1000 + [Amim]Cl		PPG1000 + [C_4mim]Cl	
w_1	w_2	w_1	w_2
0.0465	0.0392	0.0414	0.0827
0.0408	0.0619	0.0334	0.1146
0.0360	0.0748	0.0302	0.1239
0.0322	0.0868	0.0271	0.1387
0.0281	0.0995	0.0242	0.1513
0.0247	0.1110	0.0210	0.1668
0.0214	0.1261	0.0190	0.1776
0.0192	0.1368	0.0173	0.1883
0.0174	0.1468	0.0160	0.1973
0.0159	0.1514	0.0148	0.2044
0.0141	0.1627	0.0132	0.2145
0.0130	0.1701	0.0120	0.2236
0.0121	0.1759	0.0109	0.2325
0.0113	0.1811	0.0100	0.2389
0.0104	0.1875	0.0094	0.2452
0.0097	0.1934	0.0085	0.2524
0.0088	0.1999	0.0079	0.2603
0.0082	0.2068		
0.0076	0.2110		
0.0063	0.2409		

Results and Discussion

Binodal Curves. The binodal data determined at 298.15 K for PPG400 + ILs ([Amim]Cl, [C_4mim]Ac, or [C_4mim]Cl) + H_2O and PPG1000 + ILs ([Amim]Cl or [C_4mim]Cl) + H_2O systems are reported in Tables 1 and 2. For the sake of easy understanding of the phase behavior, the binodal curves are plotted in Figures 1 and 2. These curves provide information about the concentration of phase-forming components required to form two phases. The closer the binodal curve is to the origin, the lower the IL concentration required for the formation of two phases. It can be seen from Figure 1 that the IL concentration required for the formation of two phases increases in the order: [Amim]Cl < [C_4mim]Ac < [C_4mim]Cl. Therefore, the ability of these ILs for the phase separation follows the order: [Amim]Cl > [C_4mim]Ac > [C_4mim]Cl. However, it was found that phase separation cannot be observed in the presence of [C_4mim][BF_4] IL. This order follows the Hofmeister series for the strength of the water structure-making anions. Considering the fact that [C_4mim]Ac, [C_4mim]Cl, and [C_4mim][BF_4] share a common imidazolium cation but contain different anions, it is easy to see that the anion with a higher salting-out ability has a more negative value of Gibbs energy of hydration (ΔG_{hyd}):[21] $CH_3CO_2^-$ ($\Delta G_{\mathrm{hyd}} = -365\ \mathrm{kJ \cdot mol^{-1}}$) > Cl^- ($\Delta G_{\mathrm{hyd}} = -340\ \mathrm{kJ \cdot mol^{-1}}$) > BF_4^- ($\Delta G_{\mathrm{hyd}} = -190\ \mathrm{kJ \cdot mol^{-1}}$). The hydration

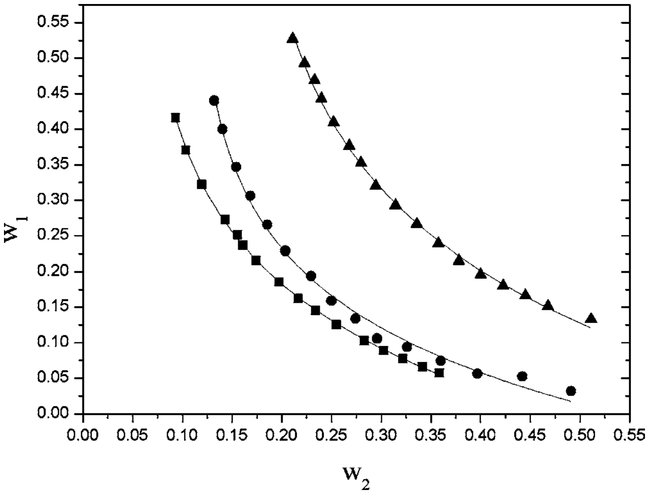

Figure 1. Binodal curves for PPG400 (1) + IL (2) ATPSs at 298.15 K: ■, [Amim]Cl; ●, [C_4mim]Ac; ▲, [C_4mim]Cl.

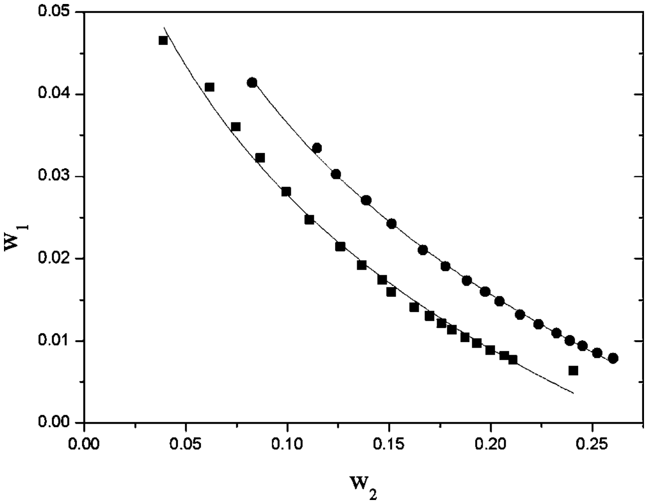

Figure 2. Binodal curves for PPG1000 (1) + IL (2) ATPSs at 298.15 K: ■, [Amim]Cl; ●, [C_4mim]Cl.

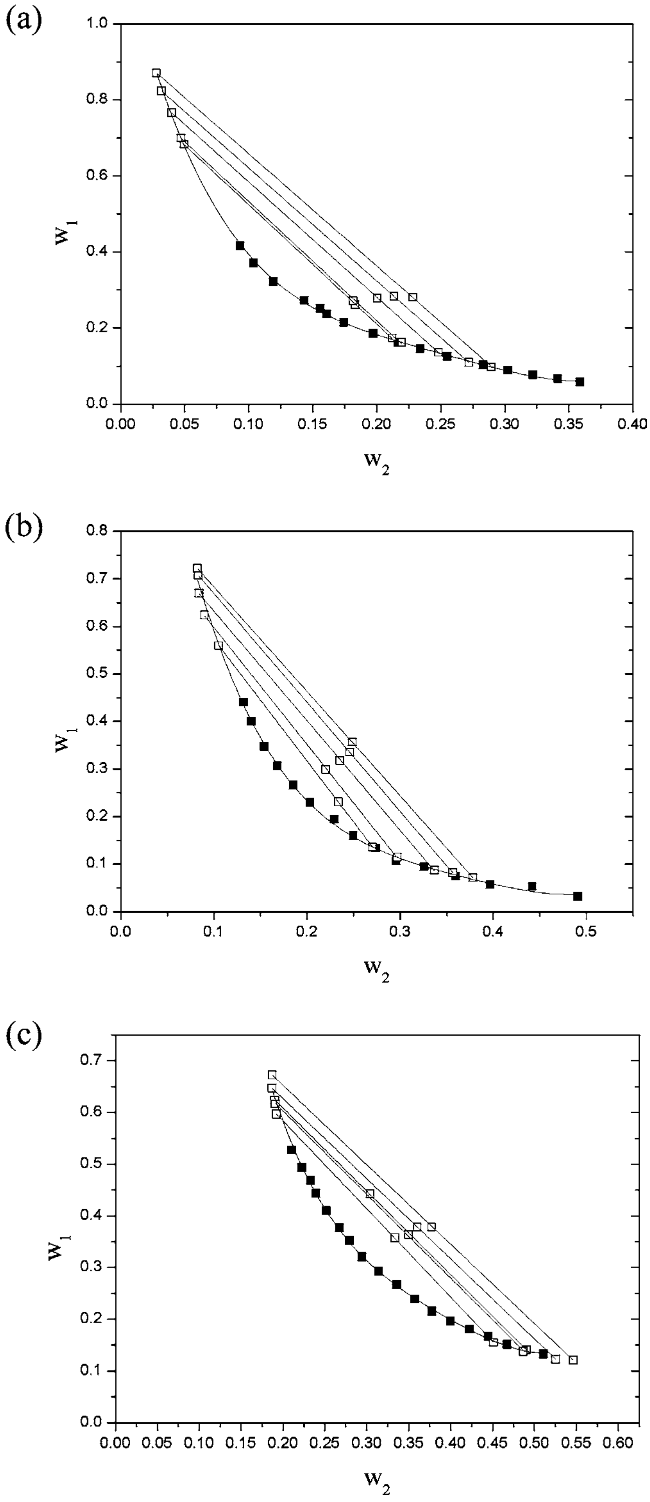

Figure 3. Phase diagram for the PPG400 (1) + ILs (2) ATPSs at 298.15 K: ■, binodal curve; □, tie line; (a) [Amim]Cl; (b) [C_4mim]Ac; (c) [C_4mim]Cl.

of BF_4^- is not strong enough to induce the formation of ATPSs. On the other hand, [Amim]Cl and [C_4mim]Cl have the same anion but different cations. Their binodal data can be used to compare the phase separation ability of the cations. It is obvious from Figures 1 and 2 that the salting-out ability of the cations decreases in the order [Amim]$^+$ > [C_4mim]$^+$. The possible reason is that, compared with [C_4mim]$^+$, the shorter alkyl chain length and the plain configuration of double bond in the alkyl chain make [Amim]$^+$ to have stronger interaction with water. Compared with IL + salt and PEG + salt ATPSs, the novel ATPSs developed in the present work are much more environmentally friendly due to the use of thermo-sensitive PPG which can be recovered simply by heating.

In fact, the formation of ATPSs is the result of competing hydration of the two phase-forming components such as the polymer and IL. In the two phase-forming components, one is water structure-making, while another one is water structure-breaking in nature. In the traditional polymer + salt ATPSs, polymer was salted-out by salt; here the salt is a water structure-making component because of its stronger hydration ability compared with the polymer.[22,23] Similarly, in IL + salt ATPSs, the IL was salted-out by inorganic salts,[11,19,24] and the salt is also a water structure-making component, while IL is a water structure-breaking component. However, in the present work, PPG was salted-out by the ILs due to their stronger hydration ability than PPG. Therefore, in ILs + PPG ATPSs, ILs are water structure-making components, while PPG is the water structure-breaking component. This can be understood from the content of water in the two phases. It was known that for the IL + salts systems, the content of water in the top IL-rich phase was lower than that in the bottom salt-rich phase.[19] On the contrary, it can be seen from Table 4 that the content of water in the bottom IL-rich phase was higher than that in the top PPG-rich phase

Table 3. Parameters Obtained by Equation 2 for the Binodal Curves of the PPG + ILs ATPSs at $T = 298.15$ K

system	*a*	*b*	*c*	σ^a	R^2
PPG400-[Amim]Cl	−0.1729	−0.1521	−0.0558	0.002	0.9995
PPG400-[C$_4$mim]Ac	−0.1458	−0.1247	−0.1126	0.011	0.9916
PPG400-[C$_4$mim]Cl	−0.2105	−0.1012	−0.1627	0.006	0.9976
PPG1000-[Amim]Cl	−0.1076	−0.2772	0.0027	0.004	0.9948
PPG1000-[C$_4$mim]Cl	−0.1619	−0.3979	0.0095	0.001	0.9996

[a] σ, standard deviation.

for the PPG + ILs systems studied here. As a result, ILs are water structure-breaking components in IL + inorganic salts ATPSs, but they are water structure-making components in IL + PPG ATPSs. Therefore, ILs can be either water structure-making or water structure-breaking components in the formation of ATPSs, depending on their relative hydration ability to the other phase-forming component.

The binodal data for the PPG + ILs ATPSs can be fitted by the equation:[12]

$$w_1 = a \ln(w_2 + c) + b \tag{2}$$

which relates the mass fraction of PPG (w_1) to the mass fraction of the ILs (w_2). The parameters *a*, *b*, and *c* were obtained by nonlinear regression as described in our previous work,[19] and the result was given in Table 3.

Tie Lines. The phase compositions determined for the PPG400 + ILs + water systems are collected in Table 4 and illustrated in Figure 3, parts a, b, and c. The tie lines for PPG1000 + ILs + water systems were very difficult to be determined because of the low solubility of PPG1000. Therefore, no reliable data have been reported in the present paper. Generally, in traditional PEG + salt + water systems, the top and bottom phases mainly consist of water, and the top polymer-rich phase contains a small quantity of salt and the bottom salt-rich phase a small quantity of polymer. However, in the PPG400 + ILs ATPSs studied here, the top PPG400-rich phase contains about (10 to 40) % water, and the bottom IL-rich phase contains (7 to 17) % PPG400. These unusual results can be explained by the two following reasons: (i) PPG is more hydrophobic than PEG due to methyl group of the side chain;[25] (ii) the imidazolium cation can form hydrogen bonds with oxygen atom of PPG through H atoms of the imidazolium ring,[26] so the imidazolium-based ILs can dissolve PPG400.

Table 5. Parameter Values for Equations 3 and 4 at $T = 298.15$ K

system	*k*	*n*	σ^a	k_1	*r*	σ^a
PPG400-[Amim]Cl	0.0148	2.6617	0.009	3.6458	0.2622	0.004
PPG400-[C$_4$mim]Ac	0.1796	1.4550	0.003	2.8820	0.5031	0.002
PPG400-[C$_4$mim]Cl	0.5847	0.8434	0.101	1.7072	0.6714	0.010

[a] σ, standard deviation.

The empirical equations proposed by Othmer−Tobias[27] (eq 3) and Bancroft[20] (eq 4):

$$\left(\frac{1 - w_1^{\,\mathrm{t}}}{w_1^{\,\mathrm{t}}}\right) = k\left(\frac{1 - w_2^{\,\mathrm{b}}}{w_2^{\,\mathrm{b}}}\right)^n \tag{3}$$

$$\left(\frac{w_3^{\,\mathrm{b}}}{w_2^{\,\mathrm{b}}}\right) = k_1\left(\frac{w_3^{\,\mathrm{t}}}{w_1^{\,\mathrm{t}}}\right)^r \tag{4}$$

for the assessment and correlation of the tie-lines for PEG + salt ATPSs[27−31] have been used to correlate the tie-line data determined in the present work. In these equations, w_1^{t} and w_3^{t} represent the mass fraction of PPG and water in the top phase, while w_2^{b} and w_3^{b} stand for the mass fraction of ILs and water in the bottom phase, respectively. The *k*, *n*, k_1, and *r* represent the fitting parameters which can be calculated by linear least-squares regression.[19] The TLL values and the parameters calculated by eqs 3 and 4 were given in Tables 4 and 5, respectively.

Salting-Out Coefficients. The salting-out ability of the ILs for the PPG400 in aqueous solutions could be expressed quantitatively by the salting-out coefficient k_{s} calculated from the following equation:[32,33]

$$\ln\left(\frac{c_{\mathrm{p}}^{\,\mathrm{t}}}{c_{\mathrm{p}}^{\,\mathrm{b}}}\right) = k_{\mathrm{p}}(c_{\mathrm{p}}^{\,\mathrm{b}} - c_{\mathrm{p}}^{\,\mathrm{t}}) + k_{\mathrm{s}}(c_{s}^{\,\mathrm{b}} - c_{\mathrm{s}}^{\,\mathrm{t}}) \tag{5}$$

where k_{p} is a constant relating the activity coefficient of PPG to its concentrations, k_{s} represents the salting-out coefficient of

Table 4. Tie-Line Compositions (in Mass Fraction) Determined for the Feed, Top, and Bottom Phases and the Corresponding Tie-Line Length at $T = 298.15$ K

feed composition		top phase		bottom phase		
IL	PPG400	IL	PPG400	IL	PPG400	TLL
			PPG400-[Amim]Cl			
0.1832	0.2606	0.0498	0.6821	0.2123	0.1734	0.5340
0.1816	0.2711	0.0474	0.6991	0.2196	0.1619	0.5641
0.2006	0.2784	0.0399	0.7665	0.2484	0.1354	0.6646
0.2285	0.2803	0.0282	0.8701	0.2896	0.0973	0.8158
0.2136	0.2829	0.0321	0.8229	0.2721	0.1089	0.7532
			PPG400-[C$_4$mim]Ac			
0.2340	0.2304	0.1054	0.5593	0.2708	0.1350	0.4554
0.2206	0.2981	0.0911	0.6191	0.2973	0.1143	0.5452
0.2357	0.317	0.0856	0.6755	0.3303	0.0869	0.6374
0.2462	0.3347	0.0836	0.7065	0.3569	0.0811	0.6825
0.2489	0.3562	0.0827	0.7212	0.3786	0.0706	0.7147
			PPG400-[C$_4$mim]Cl			
0.3045	0.4422	0.1905	0.6231	0.4906	0.1401	0.5686
0.3777	0.3785	0.1876	0.6721	0.5466	0.1208	0.6579
0.3339	0.3574	0.1924	0.5963	0.4514	0.1546	0.5120
0.3501	0.3632	0.1911	0.6162	0.4871	0.1373	0.5630
0.3604	0.3774	0.1875	0.6467	0.5258	0.1225	0.6239

Table 6. k_s Values Calculated by Equation 5 at $T = 298.15$ K

system	k_s kg·mol^{-1}	R^2
PPG400-[Amim]Cl	8.28	0.9985
PPG400-[C$_4$mim]Ac	7.00	0.9856
PPG400-[C$_4$mim]Cl	3.75	0.9903

ILs, c_p and c_s stand for the molality of PPG400 and the ILs, and superscripts "t" and "b" refer to the top polymer-rich phase and the bottom IL-rich phase, respectively. The values of salting-out coefficients of the ILs were included in Table 6. It can be seen that k_s values of the three ILs decrease in the order: [Amim]Cl > [C$_4$mim]Ac > [C$_4$mim]Cl. This order is in agreement with that determined from the binodal curves.

Conclusions

In the present work, new kinds of ATPSs were reported. These ATPSs were formed from PPG which was salted-out by ILs. The phase-forming ability of the studied ILs follows the order: [Amim]Cl > [C$_4$mim]Ac > [C$_4$mim]Cl > [C$_4$mim]BF$_4$, and the salting-out ability of [C$_4$mim]BF$_4$ is not strong enough to form ATPSs. This order is consistent with the Gibbs energy of hydration for anions of the ILs. The binodal curves for the PPG + ILs ATPSs can be fitted to the three-parameter equation, and the tie lines can be described by the Othmer−Tobias and Bancroft equations. Considering the fact that PPG is a thermosensitive polymer and can be recovered simply by heating, it is expected that the new ATPSs are useful for the recycling and/or enrichment of hydrophilic ILs from aqueous solutions.

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