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Some Novel Liquid Partitioning Systems: Water−Ionic Liquids and Aqueous Biphasic Systems

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Partition coefficients, as values of log *P*, between water and two room-temperature ionic liquids and between water and an aqueous biphasic system have been correlated with Abraham's solute descriptors to yield linear free energy relationships that can be used to predict further values of log *P*, to ascertain the solute properties that lead to increased or decreased log *P* values, and to characterize the partition systems. It is shown that, in all three of the systems, an increase in solute hydrogen-bond basicity leads to a decrease in log *P* and an increase in solute volume leads to an increase in log *P*. For the two ionic liquid systems, an increase in solute hydrogen-bond acidity similarly decreases log *P*, but for the aqueous biphasic system, solute hydrogen-bond acidity has no effect on log *P*. These effects are rather smaller than those observed in traditional water−solvent systems. However, the ionic liquids appear to have an increased affinity for polyaromatic hydrocarbons as compared to traditional organic solvents. Principal component analysis and nonlinear mapping show that the three unconventional partition systems are considerably different from conventional water−organic solvent systems.

Introduction

A major contemporary industrial challenge is to continued manufacturing beneficial chemical products while eliminating or substantially reducing the detrimental environmental consequences of the processes adopted. The Montreal Protocol[1] identified the need to reevaluate chemical processes to take account of their environmental impact, especially with regard to the use of volatile organic solvents. In addition, some 90% of hazardous waste is aqueous in nature,[2] and thus, industry is reliant upon efficient separations from liquid media. To this end, liquid−liquid separations are widely applied in the chemical process industry. Typically, because of their immiscibility with water, volatile organic solvents are often employed in such processes.[3] Taken together, these issues suggest that the elimination of the use of flammable toxic and volatile organic solvents in separations processing represents a significant step in the creation of a sustainable industrial technology.[4]

A number of different approaches to this problem have been identified, including solvent-free synthesis, the use of water as a solvent,[5] the use of supercritical fluids,[6] and the use of ionic liquids. Recently, room-temperature ionic liquids (RTILs) have received worldwide attention[7,8] as replacements for organic solvents in catalysis,[9] synthesis,[10,11] and separations processes.[12,13] Room-temperature ionic liquids, in contrast to conventional ionic liquids such as molten sodium chloride, which are only liquids at temperatures above 800 °C, represent ionic salts that are liquid at room temperature. Many RTILs are liquids over a wide temperature range, and RTILs with melting points as low as −96 °C are known. The constituents of many RTILs (being ionic) are constrained by high Coulombic forces and thus exert practically no vapor pressure above the liquid surface. These ionic liquids offer a highly solvating, yet noncoordinating medium in which a number of organic and inorganic solutes can be dissolved. Many RTILs are nonvolatile and nonflammable and have high thermal stabilities. Importantly, RTILs can be relatively undemanding and inexpensive to manufacture. These properties have been the subject of recent reviews.[14,15] Several studies of the solvatochromic properties of RTILs have also been published.[16−19] More recently, studies have been made of a group of 1-alkyl-3-methylimidazolium ionic liquids, using a linear free energy relationship (LFER) to characterize the solute distribution between water and the RTILs.[20] LFERs have been used to characterize ionic liquids as gas chromatographic (GC) stationary phases, but at 120 °C only,[21−26] and in a recent report,[27] gas−RTIL partition coefficients were determined. It should be noted that physicochemical properties of pure ionic liquids, as determined by

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GC for example, will generally not be the same as those of ionic liquids in water partition systems, because, in the latter case, the ionic liquids are saturated with water.

Aqueous biphasic systems (ABSs) represent a quite different type of alternative solvent system that have mainly been applied to the fractionation of labile biological materials.[28−31] However, recent work shows that they also appear to have some utility for solvent replacement in the extraction of metal ions[32−35] and small organic molecules,[36,37] as a solvent for pharmaceutical compounds,[38] and as a reaction medium.[39,40] Aqueous biphasic systems (ABSs) represent critical phenomena[41] that occur in aqueous solution when two or more polymers, or a polymer and a salt, are added to water above critical concentrations or temperatures.[36,37] Two immiscible liquid phases are formed as a result without the involvement of any organic solvent but still with the potential for use in the differential partition and extraction of a wide variety of solutes. Solutes as varied in molecular size as inorganic ions, small organic molecules, biological macromolecules, colloidal inorganic particles, viruses, and even cells[28−37] can all be successfully partitioned between the phases with the correct choice of ABS.

The solubilizing properties of solutions of polymer molecules in aqueous solution have been used to effect the extraction and fractionation of a wide variety of target solutes. The apparent similarities between many of these aqueous polymeric systems, including cloud-point extraction (CPE), micellar extraction (ME), aqueous biphasic systems (ABSs), and extractions using thermoseparating polymers, have recently been reviewed.[42] Some studies of the solvent properties of some of these systems have been made, including the construction of a number of LFERs. For the most part, these investigations are confined to micellar systems,[43,44] and few comparable studies are available relating to the many polymeric systems showing bulk phase separation. A recent paper illustrates the application of LFERs to poly(ethylene glycol) (PEG)−salt ABSs.[37]

None of the above work related to ionic liquids or ABS systems addresses the important practical problem of how partition in these systems compares with partition in conventional water−solvent systems, and the question of whether RTIL and ABS systems offer any enhanced selectivity, in the partition of particular types of solutes. It is the aim of this work to compare three nonconventional partitioning systems with a number of conventional systems. The RTILs are[20] 1-butyl-3-methylimidazolium hexafluorophosphate ([bmim][PF6]), 1-hexyl-3-methylimidazolium hexafluorophosphate ([hmim][PF6]), and an ABS[37] composed of poly(ethylene glycol), MW 2000 Da, and ammonium sulfate (P2000).

Methodology

We base our analysis on the general LFER of Abraham et al.[45−48]

$$\log P = c + eE + sS + aA + bB + vV \qquad (1)$$

In the dependent variable, P is the partition coefficient for a series of solutes in the same water−solvent system. The independent variables in eq 1 are solute descriptors as follows:[45−48] E is the solute excess molar refractivity in units of mol dm^{-3}/10; S is the solute dipolarity/polarizability; A and B are the overall or summation hydrogen-bond acidity and basicity, respectively; and V is the McGowan characteristic volume in units of (mol dm^{-3})/100. The coefficients in eq 1 are obtained by multiple linear regression analysis and serve to characterize the system under consideration.

Table 1. Coefficients for Water−Solvent Partitioning Systems

solvent	c	e	s	a	b	v
[bmim][PF6]	−0.17	0.45	0.23	−1.76	−1.830	2.150
[hmim][PF6]	−0.13	0.050	0.40	−1.48	−2.110	2.300
P2000	−0.050	0.650	−0.210	0.210	−1.310	1.710
octanol	0.088	0.562	−1.054	0.034	−3.460	3.814
chloroform	0.327	0.157	−0.391	−3.191	−3.437	4.191
cyclohexane	0.159	0.784	−1.678	−3.740	−4.929	4.577
toluene	0.143	0.527	−0.720	−3.010	−4.824	4.525
ether	0.251	0.588	−1.019	−0.238	−4.523	4.043
chlorobenzene	0.040	0.246	−0.462	−3.038	−4.769	4.640
olive oil	−0.035	0.574	−0.798	−1.422	−4.984	4.210
acetone/dry	0.335	0.349	−0.231	−0.411	−4.793	3.963
DMF/dry[a]	0.136	0.305	0.431	0.469	−4.833	3.735
DMSO/dry[a]	−0.250	0.184	0.905	1.921	−4.739	3.509
EG/dry[a]	−0.269	0.586	−0.522	0.712	−2.492	2.708
TFE/dry[a]	0.395	−0.094	−0.594	−1.280	−1.274	3.088

[a] Abbreviations are as follows: DMF, dimethylformamide; DMSO, dimethyl sulfoxide; EG, ethylene glycol; TFE, trifluoroethanol.

However, the coefficients are not simply fitting values but represent the difference in chemical properties between water and the particular solvent in the partitioning system; that is, they can be taken as solvent properties relative to water. The e coefficient gives the tendency of the phase to interact with solutes through polarizability-type interactions, mostly via electron pairs. The s coefficient is a measure of the solvent dipolarity/polarizability. The a coefficient represents the complementary property to solute hydrogen-bond acidity and so is a measure of the phase hydrogen-bond basicity. Likewise, the b coefficient is a measure of the phase hydrogen-bond acidity.

The coefficients for the water−solvent systems are collected in Table 1. A feature of the two water−RTIL systems and the ABS system is the small s coefficient, which indicates that the RTILs and the less aqueous phase in the ABS system have the same dipolarity/polarizability as water. Systems in which the solvent is only poorly dipolar/polarizable, such as hexane, have very negative s coefficients. The RTIL systems have rather average negative a coefficients, which indicates that the RTILs are less basic than water and about as basic as olive oil, a typical ester. The basicity of the RTILs is probably mainly due to the counteranion. It is known[26] that the basicity of the ionic liquid GC stationary phases depends on the anion—the more the negative charge is dispersed in the anion, the less basic is the ionic salt. The P2000 ABS is different to the extent that, as regards basicity, the system resembles the octanol−water system.

The b coefficients for the RTIL systems lie between those for the ethylene glycol (EG) and 2,2,2-trifluoroethanol (TFE) systems, which shows the strong hydrogen-bond acidity of the RTILs. This is in marked contrast to the ionic liquid GC phases, which have almost zero hydrogen-bond acidity. However, these species are invariably derivatives of quaternary ammonium cations that contain no acidic hydrogen. In contrast, the 1-alkyl-3-methylimidazolinium cation contains three acidic hydrogen atoms, as shown in Figure 1. Thus, the observed acidity of the three RTILs is chemically

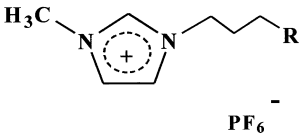

Figure 1. Ionic liquids bmim, R = Me, and hmin, R = Pr.

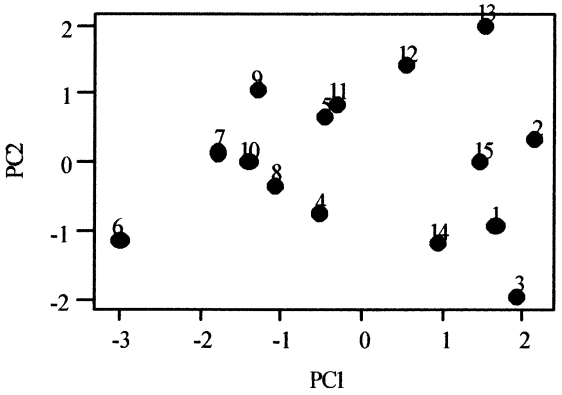

Figure 2. Plot of PC2 vs PC1.

reasonable. A considerable difference between the RTIL and ABS systems and the conventional systems is the small *v* coefficients of the former three systems. In chemical terms, the RTILs are less "hydrophobic", which again makes chemical sense.

Although it is possible to compare LFERs term by term, as above, it would be very helpful to have an overall comparison. A useful method of comparison is to carry out a principal component analysis (PCA) on the coefficients *e*, *s*, *a*, *b*, and *v* for a number of LFERs, the *c* constant being irrelevant in this respect. The procedure is exactly the same as that used for the analysis of HPLC retention data from several systems.[49] The 15 partitioning systems we have used are listed in Table 1. In addition to the three unconventional systems, we include coefficients for seven typical water−solvent systems. To expand the range of the coefficients, we also provide data for five systems, denoted as solvent/dry, where the coefficients refer to hypothetical partition between water and the pure dry solvents. In our PCA, the five columns of coefficients in Table 1, *e*−*v*, are transformed into five principal components (PCs) that contain the same information as the original coefficients. However, the first two PCs account for 72% of the total information, and so, if we restrict our analysis to this 72%, we can reduce a five-component system to two components. A plot of the scores of PC2 vs the scores of PC1 is shown in Figure 2. It is very clear that solvents 14 (ethylene glycol, EG) and 15 (2,2,2-trifluoroethanol, TFE) are closest to the two ionic solvents and the ABS as regards the information content of the coefficients. We can quantify this "nearness" by calculating the distance in the *xy* plane between the point for a standard system, no. 1, and the point for any other system; we denote this distance as *δ*-PCA. We put these distances on a scale such that the distance between the point for the standard system and the point for the water−cyclohexane partition is 10, and we list the distances in Table 2.

A technique that allows all of the information content in the coefficients to be used is that of nonlinear mapping (NLM),[50] as applied by Valko et al.[51,52] Two components are obtained from the five coefficients, and a nonlinear map of the two components is shown in Figure 3. We calculate the distance in the *xy* plane between the point for a given system and the point for system no. 1 as before. This distance, *δ*-NLM, is also scaled as before, and values of the scaled distance are given in Table 2.

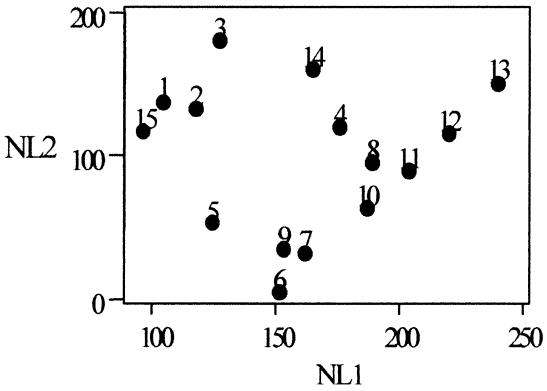

Figure 3. Plot of NL2 vs NL1.

Table 2. Nearness Parameters for the Water−Solvent Partition Systems

solvent	no.	*δ*-PCA	*δ*-NLM
[bmim][PF6]	1	0.0	0.0
[hmim][PF6]	2	2.9	1.0
P2000	3	2.3	3.4
octanol	4	4.7	5.2
chloroform	5	5.6	6.2
cyclohexane	6	10.0	10.0
toluene	7	7.7	8.5
ether	8	6.0	6.6
chlorobenzene	9	7.6	8.0
olive oil	10	6.8	7.8
acetone/dry	11	5.6	7.8
DMF/dry	12	5.5	8.3
DMSO/dry	13	6.2	9.6
EG/dry	14	1.6	4.5
TFE/dry	15	2.0	1.6

Table 3. Descriptors for Some Solutes

solute	*E*	*S*	*A*	*B*	*V*
iodomethane	0.676	0.43	0.00	0.13	0.5077
4-chloroaniline	1.060	1.13	0.30	0.31	0.9390
benzoic acid	0.730	0.90	0.59	0.40	0.9317
4-hydroxybenzoic acid	0.930	0.90	0.81	0.56	0.9904
benzamide	0.990	1.50	0.49	0.67	0.9728
1,2,4-trichlorobenzene	0.980	0.81	0.00	0.00	1.0836
bromohexane	0.349	0.40	0.00	0.12	1.1290
fluoranthene	2.377	1.55	0.00	0.24	1.5846
bromooctane	0.339	0.40	0.00	0.12	1.4108

According to both the PCA and NLM methods, the hypothetical water−solvent systems with solvents TFE and EG are the closest to the standard ionic liquid system, no. 1. This is largely due to the rather small numerical values for the *b* and *v* coefficients in the five solvent group including nos. 1, 2, 3, 14, and 15. In chemical terms, all five solvents are nearer water in hydrogen-bond acidity, because a numerically small *b* coefficient corresponds to a high solvent acidity. The *v* coefficient in water−solvent systems can be thought of as a measure of solvent hydrophobicity with respect to water as the standard. The small *v* coefficients in the two RTIL systems are probably due to the small intrinsic hydrophobicity of the ionic liquids themselves, together with the fact that the organic layer will contain a substantial amount of water. In the case of the ABS system, both phases are aqueous, and so the *v* coefficient is almost bound to be rather small. For systems 14 and 15, the small *v* coefficient is entirely due to the small intrinsic hydrophobicity of organic solvent.

Table 4. Calculated Values of log *P* for Solutes in Water−Solvent Partitioning Systems[a]

solute	octanol (4)	cyclohexane (6)	$CHCl_3$ (5)	[bmim][PF6] (1)	[hmim][PF6] (2)	P2000 (3)
iodomethane	1.50	1.65	1.95	1.09	0.97	0.99
	(1.51)		(2.13)	(0.93)	(0.97)	(0.75)
4-chloroaniline	1.87	0.74	2.01	1.48	1.41	1.61
	(1.88)	(0.69)	(2.09)	(1.25)	(1.31)	(1.44)
benzoic acid	1.74	−0.69	0.74	0.60	0.69	1.43
	(1.87)	(−0.85)	(0.71)	(0.57)	(0.85)	(1.45)
4-hydroxybenzoic acid	1.53	−1.88	−0.24	0.14	0.17	1.49
	(1.58)	(−1.77)	(−0.50)	(0.06)	(−0.04)	(1.63)
benzamide	0.47	−2.26	0.11	0.63	0.62	1.16
	(0.64)	(−1.92)	(0.11)	(0.66)	(0.66)	(1.24)
1,2,4-trichlorobenzene	3.92	4.53	4.71	2.79	2.73	2.26
	(4.02)			(2.97)	(2.74)	(2.14)
bromohexane	3.75	4.34	4.55	2.29	2.39	1.87
	(3.80)					
fluoranthene	5.00	5.44	5.91	4.22	3.75	3.57
	(5.16)					
bromooctane	4.82	5.62	5.72	2.89	3.04	2.34
	(4.89)					

[a] Experimental values are in parentheses.

It is not obvious how the coefficients dictate the partitioning behavior of solutes, because any two solutes will usually differ in several descriptors, not just one. Furthermore, the analysis is made more difficult in that the small *v* coefficient for the RTIL and ABS systems means that the actual range of observed log *P* values is considerably condensed. This might be an advantage, because log *P* values in the RTIL and ABS systems could be determined in cases where log *P* values in conventional water−solvent systems might be out of practical range. Descriptors for some typical solutes are listed in Table 3; these solutes were chosen because they cover a range of properties and also because a number of experimental partition coefficients are available for these particular solutes.

In Table 4, we present 36 pairs of calculated and experimental log *P* values, covering a range of 7.08 log units in the experimental values. For these 36 pairs, the average deviation in the log *P* values, defined as $[\Sigma(\text{calc} - \text{exp})]/36$, is −0.01 log units; the average absolute deviation, defined as $[\Sigma|(\text{calc} - \text{exp})|]/36$, is 0.11 log units; and the standard deviation, defined as $\sqrt{\{[\Sigma(\text{calc} - \text{exp})^2]/35\}}$, is 0.14 log units. We are therefore reasonably certain that we can use calculated values of log *P* in cases where there are no available experimental values in the following discussion.

Iodomethane and the two bromoalkanes were chosen to show the effect of solute size, the other descriptors being almost the same. On the other hand, the solutes from 4-chloroaniline to benzamide have very similar *V* descriptors but differ markedly in other properties. The pairs of solutes 1,2,4-trichlorobenzene−bromohexane and fluoranthene−bromooctane were included to examine any effect of the RTIL systems on aromatic solutes. A comparison of the three haloalkanes shows very clearly that an increase in the solute volume results in much larger increases in log *P* for the three conventional systems than for the two RTIL systems and the ABS system. If we take bromohexane as a standard "nonpolar" solute, then a polar hydrogen-bond base such as 4-chloroaniline has very much smaller log *P* values in the three conventional systems, smaller values in the two RTIL systems, but a nearly unchanged one in the ABS system (−0.26 log units). However, polar hydrogen-bond acids are very difficult to extract into cyclohexane or chloroform, moderately extractable into octanol and the two RTILs, but easily extracted into the ABS system. An examination of the final two pairs of solutes shows that the three unconventional systems have a slight extra affinity for 1,2,4-trichlorobenzene and a substantial affinity for the polyaromatic hydrocarbon fluoranthene. None of the conventional systems would separate fluoranthene from bromooctane, but there are considerable differences in the log *P* values in the three unconventional systems.

Although the above analysis has been carried out on log *P* values that were calculated from the solvation equation and solute descriptors, a comparison of the observed and experimental log *P* values in Table 4 indicates that the method has considerable predictive value.

Conclusion

The use of our general LFER in an analysis of water−solvent partitioning systems enables RTIL and ABS systems to be compared with conventional systems in general chemical terms. In addition, possible separations can be investigated theoretically, and partition coefficients can be predicted through the LFERs and compound descriptors. A comparison of predicted log *P* values for two or more solutes then provides a method of predicting possible separations and of choosing a particular solvent system for these separations. At the moment, descriptors are available for over 3000 compounds,[34] and so a huge number of partitions and separations can be predicted.

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