

Experimental Measurements of Octanol-Water Partition Coefficients of Ionic Liquids

Montalbán MG¹, Collado-González M², Trigo R¹, Díaz Baños FG² and Villora G^{1*}

¹Department of Chemical Engineering, University of Murcia, Murcia, Spain

²Department of Physical Chemistry, University of Murcia, Murcia, Spain

Abstract

Interest in ionic liquids (ILs) has increased due to their promising use as “green solvents” because of their negligible vapor pressure. However, their solubility in water could lead to their dispersion into the environment through liquid effluents, generating an important toxicological effect in soils and seawater. One of the most relevant parameters related to the assessment of environmental risk is the octanol-water partition coefficient (K_{ow}). With this parameter is possible to estimate some ecosystem risk factors such as bioaccumulation, sorption to soils and sediments and toxicity in fish by the usage of experimental correlations. Shake-flask and slow-stirring methods are the most currently used methods for determining the K_{ow} of a chemical compound. The former has the disadvantage that equilibrium might not be reached quickly, while the slow-stirring method is not always suitable for ILs, since some of them may decompose after continuous contact with water. We have developed a combined version of both methods. Here, we present measurements of the K_{ow} of twenty-four ILs at 30°C, using the three experimental methods. The types of anion and alkyl chain length of the cation are among the parameters studied. The K_{ow} of ILs used in this study range between 0.0017 and 3.6567 at 30°C. The K_{ow} of ILs studied is lower than in commonly used industrial solvents.

Keywords: Ionic liquids; Octanol-water partition coefficient; Hydrophobicity; Hydrophilicity; Ecosystem risk factor

Introduction

Ionic liquids (ILs) are low melting point organic salts, most of which are liquids at room temperature. In the past decade they have generated a huge interest in research and industrial fields for their capacity to serve as chemical and biochemical reaction media. In addition, ILs are of interest because they constitute a new group of polar and non-aqueous solvents, whose most important advantage is their negligible vapor pressure [1]. It is mainly for this reason that they are considered “green solvents” compared to conventional volatile organic compounds (VOCs). Due to their high chemical and thermal stability, ILs can resist high temperatures. However, for their potential applications, ILs are mainly valued because of the possibility of modulating their physical and chemical properties, such as melting point, viscosity, density, hydrophobicity and polarity by selecting the anion, the cation or substituent present in their specific structure. The number of different combinations of anions and cations that can be used to form potential ILs is enormous.

Due to the non-volatile character of ILs, they do not contribute to atmospheric pollution [2]. However, despite their significant degree of solubility in water, their effect in this respect has not been studied in depth [3-5]. Moreover, because of their high stability, ILs could represent serious pollutants in aqueous waste streams or accidental spills. For this reason, it is very important to quantify this effect by means of toxicological parameters such as the octanol-water partition coefficient (K_{ow}) that we study in this work. The K_{ow} is known to be one of the quantitative physical properties that best correlate with biological activity because the water-saturated octanol system is considered a reasonable model of the physico-chemical environment in living organisms [6,7]. K_{ow} classifies ILs according to their hydrophobicity or hydrophilicity, the latter characteristic being closely linked to the lipophilicity of a chemical compound and this parameter constitutes an essential physicochemical property in medicinal chemistry. For instance, it plays a crucial role in the absorption, distribution, metabolism and excretion (ADME) characteristics of drugs [8]. In fact, K_{ow} is used to model blood/lipid partition in toxicology to understand

the tendency of a compound to cross biological membranes [9]. Therefore, K_{ow} is the key parameter for use in experimental correlations to estimate some parameters related to bioconcentration [10-13] and toxicity in fish [14,15], as well as sorption to soils [16-18].

Octanol and lipids have similar molecular structures containing both polar and hydrophilic oxygen at the end of a long hydrophobic alkyl chain and also similar physical properties. For this reason, correlations between natural ecosystems and K_{ow} are highly useful [19]. A high number of empirical correlations have been developed to estimate bioconcentration (BCF) and bioaccumulation (BAF) factors, soil sorption coefficients (K_{oc}), and toxicity. Bioconcentration is the process that causes an increased chemical concentration in an aquatic organism compared to that observed in water, due to the absorption of chemicals by different metabolic routes. The bioconcentration factor, BCF, is the equilibrium ratio of the chemical's concentration in the organism, in $\mu\text{g}/\text{kg}$ lipid, to the concentration in the water, in $\mu\text{g}/\text{L}$, when exposure is only to the chemical in the water [20]. Pollutants also enter the biota through the food chain, which is referred to as biomagnification. The sum of bioconcentration and biomagnification is referred to as bioaccumulation [21]. The soil sorption coefficient, K_{oc} , describes soil-water partitioning. The K_{oc} is the ratio of the mass of a chemical adsorbed per unit weight of organic carbon in a soil to the concentration of the chemical in a liquid phase. Toxicity is typically reported in terms of mortality to various species quantified by the

***Corresponding author:** Villora G, Faculty of Chemistry, Regional Campus of International Excellence “Campus Mare Nostrum”, University of Murcia, P.O. Box 4021, Campus of Espinardo, E-30071, Murcia, Spain, Tel: +34-868-887-363; E-mail: gvillora@um.es

Received August 02, 2015; **Accepted** September 03, 2015; **Published** September 12, 2015

Citation: Montalbán MG, Collado-González M, Trigo R, Díaz Baños FG, Villora G (2015) Experimental Measurements of Octanol-Water Partition Coefficients of Ionic Liquids. J Adv Chem Eng 5: 133. doi:10.4172/2090-4568.1000133

Copyright: © 2015 Montalbán MG, et al. This is an open-access article distributed under the terms of the Creative Commons Attribution License, which permits unrestricted use, distribution, and reproduction in any medium, provided the original author and source are credited.

LC_{50} in $\mu\text{mol/L}$, which is the concentration lethal to half of the species population [22]. Examples of equations based on experimental data relating K_{ow} with BCF, K_{OC} and LC_{50} are shown in Table 1 [23,24].

The activity of a compound, a_i , in the water-rich phase and the octanol rich-phase will be, by definition, the same ($a_i^{(w)} = a_i^{(o)}$) when the equilibrium is reached. Because $a_i = \gamma_i x_i$, where γ_i is the activity coefficient and x_i is the mole fraction in the water rich (w) and octanol rich (o) phases, respectively, the following expression can be deduced:

$$\frac{x_i^o}{x_i^w} = \frac{\gamma_i^w}{\gamma_i^o} \quad (1)$$

If the test compound solution is very dilute and pressure and temperature are constant, concentrations and mole fractions will be proportional. In addition, if the compound is extremely dilute in both phases, so-called “infinite dilution”, activity coefficients can be considered not to change with small variations in the concentrations. As a result, the Nernst distribution law is followed:

$$K_{ow} = \frac{C_i^o}{C_i^w} \quad (2)$$

where K_{ow} is the octanol-water partition coefficient and C_i are sufficiently dilute concentrations in both phases [3,6].

Ideally, concentrations of the same solute species are measured in the two liquid phases when determining K_{ow} values. This may be difficult for species such as acids or salts, in which the solute tends to dissociate more in the aqueous phase than in the octanol-rich phase. As shown in Figure 1, ILs [$M_{v+} X_{v-}$] tend to have a greater tendency to dissociate in the water-rich phase [3].

When solute dissociation is expected, the K_{ow} is calculated as the ratio between the concentration of the undissociated and dissociated species of the salt in the octanol-rich phase and in the water-rich phase. For this work, concentrations were measured in each phase using UV-Vis spectroscopy, which detects the imidazolium, pyridinium and ammonium group on the cation (whether dissociated or undissociated). Therefore, the K_{ow} values reported are given by Eq.3:

$$K_{ow} = \frac{[M_{v+} X_{v-}]^{octanol} + [M^{Z+}]^{octanol}}{[M_{v+} X_{v-}]^{water} + [M^{Z+}]^{water}} \quad (3)$$

It is important to recognize that octanol and water are not completely immiscible. At 25°C, the solubility of water in octanol is approximately 0.275 mole fractions, but the solubility of octanol in water is 7.45×10^{-5} mole fraction [25]. Since the solubility of water in octanol is high, the K_{ow} cannot be represented simply as the ratio of saturation concentrations of a solute dissolved in separate solutions of octanol and water. The mutually saturated octanol and water phases affect the partitioning of the solute between the two solvents.

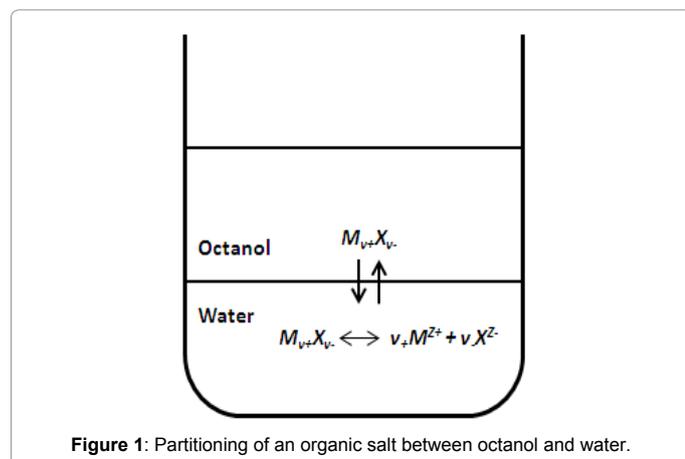
Many different experimental methods (direct and indirect) exist for determining K_{ow} of a chemical compound, but two methods are the most commonly used: shake-flask and slow-stirring, both direct methods. In the traditional shake-flask method, octanol and water are mutually saturated for three days. A sufficiently dilute solution of the test compound and water-saturated octanol is brought into contact with the same quantity of saturated water and shaken for about five minutes to achieve equilibrium. Next, both phases are separated by centrifugation and the test chemical concentrations are measured in each phase. This method has speed as an advantage and the disadvantages of the possible formation of microdroplets after centrifugation and the fact that equilibrium is not guaranteed, then the evaluation of partition equilibrium can be done by monitoring the

absorbance after the phase separation [3,26-28]. Slow-stirring method is similar to the previous method. However, instead of rigorously shaking both phases, they are stirred slowly for an extended period of time (45 days, approximately). After that, each phase is analyzed in the same way as in the shake-flask method. The main advantage of this method is to avoid the emulsification due to the reduction of the stagnant diffusion layer between the two phases. Nevertheless, care must be taken with the length of time that the phases are in contact since some ILs may decompose after continuous contact with water [3,29].

Our research group is especially interested in working with ILs hence this paper is focused on the determination of the K_{ow} for a group of ILs. Information about the toxicological risk of ILs is limited in the literature. Our research group has already measured several K_{ow} values for some imidazolium-based ILs using our own method, which will be explained below [30]. Other authors, for example, Ropel et al. [3], Deng et al. [7,31] and Ventura et al. [32] used the slow-stirring method to measure K_{ow} for imidazolium, pyridinium, ammonium and pyrrolidinium-based ILs. Others like Kaar et al. [33], Zhao et al. [34] and Lee and Lee [9] determined K_{ow} values for imidazolium and pyrrolidinium-based ILs using the shake-flask method. The results reported by these publications for ILs have been inconsistent due to different experimental methods and range of IL concentrations established in the experiments. However, some tendencies can be extracted. For instance, it is clear that more hydrophobic anions such as $[\text{NTf}_2^-]$ lead to higher K_{ow} values and, K_{ow} values increase with alkyl chain length in ILs with the same anion. Some studies have developed an indirect way to determine K_{ow} from the ratio of IL solubility in water and in octanol but this value does not exactly correspond with the definition of K_{ow} [35,36]. Other authors have preferred to use computational simulations [37,38] or DFT calculations (LFER parameters) [39] to determine K_{ow} for ILs. Recently, a robust and automated method for measurement of K_{ow} has been established. It consists of a syringe pump with a selection valve, a holding column, a silica capillary flow-cell and an in-line spectrophotometer. Distribution of the drug between the aqueous and octanol phases occurs by the oscillation movement of the syringe pump piston. The system has been applied to the determination of the K_{ow} of some common drugs, achieving high precision with only one-phase measurement [40]. Other new experimental methodology to obtain K_{ow} has been developed by the use of a bubble column set-up in combination with headspace concentration measurement [41]. Finally, a K_{ow} prediction method based on the lipophilicity estimation of ILs by chromatographic methods was used by Stepnowski et al. [42], Ranke et al. [43] and Studzińska et al. [44]. Due to the quantity of ionic ILs synthesized and the lack of information data about their toxicological

Correlation	Reference
$\text{Log}(\text{BCF})=0.85\text{log}(K_{ow})-0.70$	[23]
$\text{Log}(\text{BCF})=0.79\text{log}(K_{ow})-0.40$	[24]
$\text{Log}(\text{BCF})=\text{log}(K_{ow})-1.32$	[10]
For $\text{Log}(K_{ow}) < 5$; $\text{Log}(\text{BCF})=0.5$	[13]
$\text{Log}(\text{BCF})=0.791\text{log}(K_{ow})-0.729$	[15]
$\text{Log}(K_{oc})=0.544\text{log}(K_{ow})+1.377$	[16]
$\text{Log}(K_{oc})=0.989\text{log}(K_{ow})-0.364$	[17]
$\text{Log}(K_{oc})=0.679\text{log}(K_{ow})+0.663$	[18]
$\text{Log}(1/LC_{50})=0.854\text{log}(K_{ow})-1.74^a$	[15]
$\text{Log}(1/LC_{50})=0.629\text{log}(K_{ow})-0.489^a$	[15]
$\text{Log}(1/LC_{50})=0.89(\pm 0.03)\text{log}(K_{ow})-1.75(\pm 0.05)^b$	[14]

Table 1: Correlations of K_{ow} with ecosystem risk parameters. ^aFor guppies, fathead minnow, rainbow trout and medaka. ^bfor guppies, fathead minnow and rainbow trout.



risk, more studies are required to ensure the safe and environmental friendly use of ILs by researchers and industries.

In the present paper, we measured the K_{ow} of dilute samples of several imidazolium, pyridinium and ammonium-based ILs. The K_{ow} values previously reported for some ILs have shown huge discrepancies, as can be seen below. For this reason, we have used three different experimental methods and compared the results obtained, which has not been done before now. Furthermore, the effect of the anion and cation alkyl chain length on the K_{ow} values is discussed.

Experimental

Experimental method

The K_{ow} values of ILs were measured using three different methods, two of them explained in the previous section (the shake-flask and slow-stirring methods) and the other one a combined version of the same which our research group developed in a previous paper [30]. Before to carry out each experiment, both water and octanol were mutually saturated by stirring for three days or more. The experimental setup for the slow-stirring method and the combined method is very similar, both consisting of a 22 mL glass vial with an open-top screw cap sealed with a silicone/Teflon septum. In the slow-stirring method and our combined method, approximately 10 mL of distilled, deionised water, presaturated with octanol was added to the glass vial. A 12-gauge Teflon tube was introduced into the vial, reaching just below the water surface. Approximately 10 ml of octanol-IL “stock” solution, consisting of octanol presaturated with water and containing a known concentration of IL (1 mM), was added to the vial. In the combined method, the vial was shaken vigorously for 5 minutes and then maintained at $30 \pm 0.5^\circ\text{C}$ in a thermostatic bath without stirring for 13 days. In the slow-stirring method, the vial was not shaken intensely, but was maintained in the same bath at $30 \pm 0.5^\circ\text{C}$ with a 1 cm Teflon coated magnetic stir bar which provided slow-stirring for 45 days. In both methods, samples were taken from the octanol-rich phase by penetrating the silicone septum with a stainless-steel needle fitted with a glass syringe. Samples were withdrawn from the water-rich phase by inserting the needle through the Teflon tubing directly into the aqueous phase to prevent octanol contamination. In both cases, samples of each phase were taken from the vials until three measurements coincided confirming that the concentrations in both phases had stabilized.

In the shake-flask method, the apparatus consists of a 12 mL centrifuge tube with cap. Approximately 5 mL of distilled, deionised water, presaturated with octanol and 5 mL of octanol-IL “stock” solution, consisting of octanol presaturated with water and containing

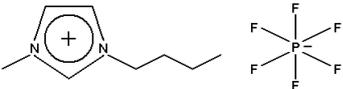
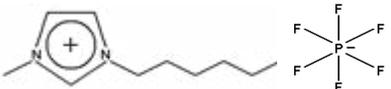
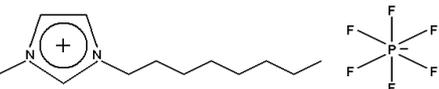
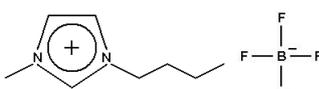
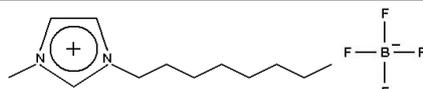
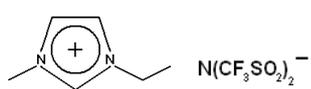
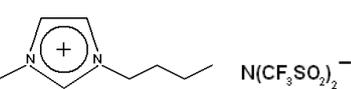
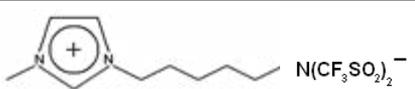
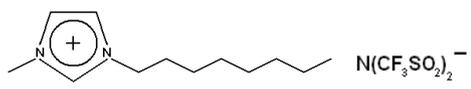
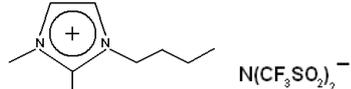
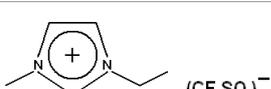
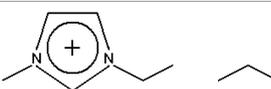
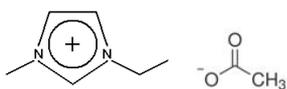
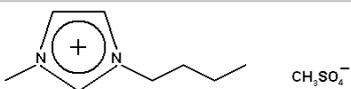
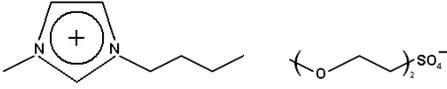
a known concentration of IL (1 mM) was added to the centrifuge tube. The tube was shaken vigorously for about five minutes and then the octanol and water phases were separated by centrifugation. Samples were taken from the octanol-rich phase and the water-rich phase with a glass syringe and analyzed directly.

In all three methods, the IL concentration in each phase was analysed by UV-VIS spectrophotometry as described in the section Analytical Method. Determinations were made at least in triplicate to ensure repeatability of the tests and the mean values are reported. The samples were diluted until the absorbance was less than 1. The initial concentration of IL in the octanol phase was less than 1.2×10^{-2} mol/L, but enough to ensure that the IL could be measured accurately. The final concentrations of IL in the octanol phase were between 1.77×10^{-5} mol/L and 3.92×10^{-3} mol/L and in the water phase between 2.75×10^{-5} and 8.38×10^{-3} mol/L. IL concentrations were kept at the dilution limit so that K_{ow} values would be independent of concentration.

In the present paper, we have studied twenty-four ILs based on imidazolium, pyridinium and ammonium salts with different substituents: 1-butyl-3-methylimidazolium hexafluorophosphate ([bmim⁺][PF₆⁻]), 1-hexyl-3-methylimidazolium hexafluorophosphate ([hmim⁺][PF₆⁻]), 1-methyl-3-octylimidazolium hexafluorophosphate ([omim⁺][PF₆⁻]), 1-butyl-3-methylimidazolium tetrafluoroborate ([bmim⁺][BF₄⁻]), 1-methyl-3-octylimidazolium tetrafluoroborate ([omim⁺][BF₄⁻]), 1-ethyl-3-methylimidazolium bis(trifluoromethylsulfonyl)imide ([emim⁺][NTf₂⁻]), 1-butyl-3-methylimidazolium bis(trifluoromethylsulfonyl)imide ([bmim⁺][NTf₂⁻]), 1-hexyl-3-methylimidazolium bis(trifluoromethylsulfonyl)imide ([hmim⁺][NTf₂⁻]), 1-methyl-3-octylimidazolium bis(trifluoromethylsulfonyl)imide ([omim⁺][NTf₂⁻]), 1-butyl-2,3-dimethylimidazolium bis(trifluoromethylsulfonyl)imide ([bdmim⁺][NTf₂⁻]), 1-ethyl-3-methylimidazolium triflate ([emim⁺][TfO⁻]), 1-ethyl-3-methylimidazolium ethylsulphate ([emim⁺][EtSO₄⁻]), 1-ethyl-3-methylimidazolium acetate ([emim⁺][CH₃COO⁻]), 1-butyl-3-methylimidazolium methylsulphate ([bmim⁺][MeSO₄⁻]), 1-butyl-3-methylimidazolium 2-(2-methoxyethoxy) ethylsulphate ([bmim⁺][MDEGSO₄⁻]), 1-methylimidazolium chloride ([mim⁺][Cl⁻]), 1-ethyl-3-methylimidazolium chloride ([emim⁺][Cl⁻]), 1-(2-hydroxy-ethyl)-3-methylimidazolium chloride ([hemim⁺][Cl⁻]), 1,2-dimethylimidazolium chloride ([dmim⁺][Cl⁻]), 1-ethylimidazolium chloride ([eim⁺][Cl⁻]), 1-hexyl-3-methylimidazolium chloride ([hmim⁺][Cl⁻]), 1-ethyl-3-methylpyridinium ethylsulphate ([empy⁺][EtSO₄⁻]), 1-butyl-3-methylpyridinium tetrafluoroborate ([bmpy⁺][BF₄⁻]) and ethylammonium nitrate (ETAN).

Materials

The structures of the ILs used in this study are listed in Table 2. The ILs [bmim⁺][PF₆⁻] (purity>99%), [hmim⁺][PF₆⁻] (purity>99%), [omim⁺][PF₆⁻] (purity>99%), [bmim⁺][BF₄⁻] (purity>99%), [emim⁺][NTf₂⁻] (purity>99%), [bmim⁺][NTf₂⁻] (purity>99%), [hmim⁺][NTf₂⁻] (purity>99%), [omim⁺][NTf₂⁻] (purity>99%), [bdmim⁺][NTf₂⁻] (purity>99%), [emim⁺][TfO⁻] (purity>99%), [emim⁺][EtSO₄⁻] (purity>99%), [emim⁺][CH₃COO⁻] (purity>95%), [mim⁺][Cl⁻] (purity>98%), [emim⁺][Cl⁻] (purity>98%), [hemim⁺][Cl⁻] (purity>99%), [dmim⁺][Cl⁻] (purity>98%), [eim⁺][Cl⁻] (purity>98%), [hmim⁺][Cl⁻] (purity>98%) and ETAN (purity>97%) were purchased from Iolitec (Germany). The ILs [omim⁺][BF₄⁻] (purity>99%), [bmim⁺][MeSO₄⁻] (purity>99%), [bmim⁺][MDEGSO₄⁻] (purity>98%), [empy⁺][EtSO₄⁻] (purity>99%) and [bmpy⁺][BF₄⁻] (purity>99%) were purchased from Solvent Innovation GmbH (Cologne, Germany). The reagent octanol was purchased from Merck Eurolab (Germany).

Abbreviation	Molecular weight (g mol ⁻¹)	Structure
[bmim ⁺][PF ₆ ⁻]	284.18	
[hmim ⁺][PF ₆ ⁻]	312.08	
[omim ⁺][PF ₆ ⁻]	340.29	
[bmim ⁺][BF ₄ ⁻]	226.02	
[omim ⁺][BF ₄ ⁻]	282.13	
[emim ⁺][NTf ₂ ⁻]	391.31	
[bmim ⁺][NTf ₂ ⁻]	419.37	
[hmim ⁺][NTf ₂ ⁻]	447.42	
[omim ⁺][NTf ₂ ⁻]	475.47	
[bdmim ⁺][NTf ₂ ⁻]	433.39	
[emim ⁺][TfO ⁻]	260.24	
[emim ⁺][EtSO ₄ ⁻]	236.29	
[emim ⁺][CH ₃ COO ⁻]	170.21	
[bmim ⁺][MeSO ₄ ⁻]	250.32	
[bmim ⁺][MDEGSO ₄ ⁻]	338.43	

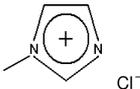
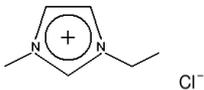
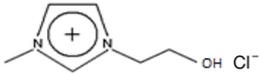
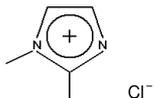
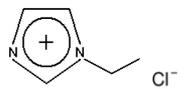
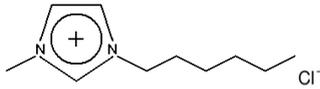
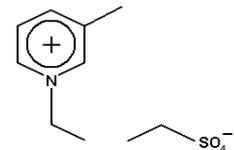
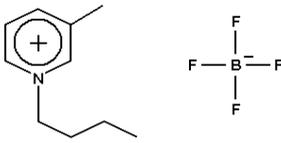
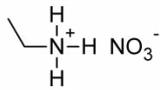
[mim ⁺][Cl ⁻]	118.57	
[emim ⁺][Cl ⁻]	146.02	
[hemim ⁺][Cl ⁻]	162.62	
[dmim ⁺][Cl ⁻]	131.58	
[eim ⁺][Cl ⁻]	131.58	
[hmim ⁺][Cl ⁻]	202.72	
[empy ⁺][EtSO ₄ ⁻]	247.32	
[bmpy ⁺][BF ₄ ⁻]	237.05	
ETAN	108.1	

Table 2: Abbreviations and structures of the studied ILs.

Analytical method

The concentration of the ILs in octanol and water was measured by UV-VIS spectrophotometry using a ThermoSpectronic UV-VIS recording spectrophotometer (Helios α), which has a sensitivity of ± 0.001 . A calibration curve was prepared for the different ILs at their maximum absorbance wavelength: 212 nm for imidazolium, 216 nm for pyridinium and 210 nm for ammonium-based ILs. The calibration curves were made in duplicate and mean values of the extinction coefficients are reported (Table 3). Samples were diluted if their concentration exceeded the calibration range.

Results and Discussion

Experimental technique evaluation

The combined experimental technique developed by our group was validated in a previous work [30] with benzaldehyde, which has a well-known $\log(K_{ow})=1.48$. Benzaldehyde shows two characteristic

peaks at 250 and 200 nm in water, and at 245 and 207 nm in octanol. The wavelengths at 250 nm and 245 nm were selected for absorbance measurements in water and octanol, respectively. The extinction coefficient in water and octanol is shown in Table 3. $\log(K_{ow})$ of benzaldehyde obtained was 1.43, which is very close to the value given in the literature (1.48), confirming the validity of the proposed method [30].

Extinction coefficients

To determine the concentrations of IL in each phase and the resulting K_{ow} values, the IL extinction coefficients (ϵ) in octanol and water were obtained at the wavelength of maximum absorption of the imidazolium ($\lambda_{max} = 212$ nm), pyridinium ($\lambda_{max} = 216$ nm) and ammonium ($\lambda_{max} = 210$ nm) groups (Table 3).

The extinction coefficients of all the ILs have values of between 3000 and 6000 L mol⁻¹ cm⁻¹ except [hmim⁺][NTf₂⁻] in water and in octanol and [bmpy⁺][BF₄⁻] in octanol which were greater. The ones of [hmim⁺][NTf₂⁻] in water and in octanol and [bmpy⁺][BF₄⁻] and ETAN in octanol

Compound	ε in water/L mol ⁻¹ cm ⁻¹	ε in octanol/L mol ⁻¹ cm ⁻¹
Benzaldehyde	1363.7	1303.6
[bmim ⁺][PF ₆ ⁻]	4472.5	3455.7
[hmim ⁺][PF ₆ ⁻]	2977.6	5719.0
[omim ⁺][PF ₆ ⁻]	3828.4	5100.0
[bmim ⁺][BF ₄ ⁻]	4212.3	4639.6
[omim ⁺][BF ₄ ⁻]	4207.1	4787.0
[emim ⁺][NTf ₂ ⁻]	4397.7	3996.4
[bmim ⁺][NTf ₂ ⁻]	3367.6	4904.1
[hmim ⁺][NTf ₂ ⁻]	6817.3	9380.8
[omim ⁺][NTf ₂ ⁻]	3103.3	4483.1
[bdmim ⁺][NTf ₂ ⁻]	3067.3	5168.7
[emim ⁺][TfO ⁻]	4326.7	4977.2
[emim ⁺][EtSO ₄ ⁻]	3604.8	4190.8
[emim ⁺][CH ₃ COO ⁻]	5481.9	4617.4
[bmim ⁺][MeSO ₄ ⁻]	3999.5	4777.0
[bmim ⁺][MDEGSO ₄ ⁻]	5372.7	4776.9
[mim ⁺][Cl ⁻]	4197.7	5136.6
[emim ⁺][Cl ⁻]	4477.8	4513.2
[hemim ⁺][Cl ⁻]	3741.3	4703.9
[dmim ⁺][Cl ⁻]	5808.9	5803.6
[eim ⁺][Cl ⁻]	3988.6	4562.5
[hmim ⁺][Cl ⁻]	4671.8	4368.0
[empy ⁺][EtSO ₄ ⁻]	4062.2	4961.0
[bmpy ⁺][BF ₄ ⁻]	4346.1	9246.3
ETAN	5254.5	12865

Table 3: Extinction coefficients of Benzaldehyde and ILs in water and Octanol.

are bigger than the others, perhaps as a result of different interactions with the solvents.

K_{ow} Values

The values of K_{ow} measured for each ionic liquid and obtained with the three methods indicated in Experimental Method Section are shown in Table 4. The K_{ow} values found in literature for some of the ILs have been added to compare the results, distinguishing between the K_{ow} values obtained by the shake-flask or slow-stirring method. The uncertainties reported are standard deviations of multiple tests, as detailed in the Experimental section.

The K_{ow} of a given chemical structure can also be estimated. Most methods divide the molecule into fragments or groups of atoms, each with its corresponding empirical constant and structural factor. Using experimental data, a database of the different contributing fragments and structure factors possible can be computed. We used two of these approaches to estimate the K_{ow} values of ILs, both using SMILES notation (Simplified Molecular Input Line Entry System): web page molinspiration.com [45] and Bio-Loom Software [46]. The estimated values are also shown in Table 4 [47-49].

Discussion

The ILs studied here based on imidazolium, pyridinium and ammonium, are fairly hydrophilic so their K_{ow} were expected to be low. Indeed, the experimental values shown in Table 4 are lower than those in commonly used industrial solvents (i.e., $K_{ow(ethanol)}=0.479$ [50]; $K_{ow(n-heptane)}=31623$ [51]).

On the other hand, the three methods used here to determine the K_{ow} of ILs have their advantages and drawbacks.

The shake-flask method is a classical method to measure the K_{ow} that

has been widely used in recent decades; however, several parameters need to be taken into account for the measurement to be valid. For example, pre-saturation of the two solvents with each other is essential to obtain accurate numbers for the volume of each phase. Shaking has to be carried out manually or mechanically for a sufficiently long time to homogenize the solution and, since octanol and water form an emulsion, the two phases have to be separated. This problem may be overcome by centrifugation, but, even so, micro droplets might still remain in each phase, which can introduce large errors in the final measurements, especially in the case of hydrophobic ionic compounds. The K_{ow} values obtained by the shake-flask method are generally the lowest, probable because the equilibrium had not been achieved.

The slow stirring method can avoid the measurement errors introduced by the emulsion between octanol and water, especially for hydrophobic compounds. This method is generally considered a better representation of ecological conditions, whereby oil and water are equilibrated and the IL is present in very dilute amounts. Nevertheless, it is not appropriate for all ILs, since some may decompose after continuous contact with water for a long period of time. The values obtained by the slow stirring method are generally much higher than those obtained by the other methods.

The combined version of both methods seeks to avoid the disadvantages of each of the conventional methods. As can be seen in Table 4, the values obtained with the combined method are generally intermediate with respect to the other two procedures. However, depending on the IL, different situations can be found. For some ILs the combined method provides results very similar to those obtained with the shake-flask method and, for others they are similar to the slow-stirring results. This may be due to the different rates of degradation in water and/or the different tendencies to form microemulsions, and demonstrates the difficulty involving in using the technique.

However, while the three methods deliver different results, some trends can be identified. The K_{ow} values increase with increasing alkyl chain length of the cation (Figure 2), which is consistent with the findings of other authors [3,5,7,30,37,39,52]. The ILs with a bis(trifluoromethylsulfonyl)imide anion have higher K_{ow} values and the ILs with an ammonium cation have the lowest values.

Keeping the imidazolium cation constant, it is possible to see the effect by changing the anion. The hydrophilic order for the ILs which are not completely soluble with water are [BF₄⁻] > [PF₆⁻] > [NTf₂⁻]. These results can be explained by the greater symmetry and consequent greater hydrophobic character of [PF₆⁻] compared with [BF₄⁻] and of [NTf₂⁻] compared with [PF₆⁻], due to the inclusion of two carbon atoms in the [NTf₂⁻] skeleton. At the other extreme, the hydrophilic order for the ILs completely soluble in water is [CH₃COO⁻] > [Cl⁻]. For the same cation, the ILs with the anions [MDEGSO₄⁻], [MeSO₄⁻], [TfO⁻] and [EtSO₄⁻] have an intermediate hydrophilicity between the two groups of anions mentioned above (Figure 3).

The insertion of a hydroxy group reduces the lipophilicity of an imidazolium chloride IL, as can be observed when [hemim⁺][Cl⁻] is compared with [emim⁺][Cl⁻].

There are some differences between the K_{ow} values calculated by the two molecular simulation methods, but the trends observed are similar and agree with the experimental results.

Conclusions

The K_{ow} of ILs is an important parameter because describes the lipophilicity of ILs and can be used to determine properties such as

Compound	K_{ow} shake-flask method	K_{ow} combined method	K_{ow} slow-stirring method	Literature values		K_{ow} estimated
				shake-flask method	slow-stirring method	
[bmim ⁺][PF ₆ ⁻]	0.0200 ± 0.0062	0.0323 ± 0.0001 [30]	0.2539 ± 0.0443	0.0200 [47], 0.0041 [33], 0.0035 [9], 0.0191 [48].	0.0219 [3] 0.0037 [32]	0.0091[45], 0.0054 [46]
[hmim ⁺][PF ₆ ⁻]	0.0230 ± 0.0072	0.1120 ± 0.0023	0.3130 ± 0.0019	0.0631 [48]	0.1202-0.338 [49] , 0.1380 [32]	0.0931[45], 0.0617[46]
[omim ⁺][PF ₆ ⁻]	0.4663 ± 0.0338	0.2388 ± 0.0279 [30]	0.9196 ± 0.0338	0.4467 [48]	1.2106 [49], 0.4009 [32],	0.9500[45], 0.7079[46]
[bmim ⁺][BF ₄ ⁻]	0.0094 ± 0.0003	0.0054 ± 0.0005 [30]	0.1303 ± 0.0186	0.0031 [34]	0.0030 [3],	0.0091[45], 0.0054[46]
[omim ⁺][BF ₄ ⁻]	0.0152 ± 0.0009	0.0537 ± 0.0011 [30]	0.0746 ± 0.0085	0.2089 [48], 0.0457 [34]	0.5754-1.2190 [49],	0.9500[45], 0.7079[46]
[emim ⁺][NTf ₂ ⁻]	0.0607 ± 0.0039	0.0642 ± 0.0142	0.1407 ± 0.0124	0.0661 [48]	0.0891-0.1096 [3], 0.0070 [32],	925[45], 0.4467[46]
[bmim ⁺][NTf ₂ ⁻]	0.1193 ± 0.0063	0.1076 ± 0.0038 [30]	0.3350 ± 0.0190	0.0229 [9], 0.3162 [48], 1.2882 [34]	0.1096-0.6166 [3], 0.4266-0.6607 [49], 0.0210 [32],	925[45], 0.4467[46]
[hmim ⁺][NTf ₂ ⁻]	0.0352 ± 0.0127	0.1336 ± 0.0679	0.7827 ± 0.1734	1.4454 [48]	1.4125-1.6596 [3],	925[45], 0.4467[46]
[omim ⁺][NTf ₂ ⁻]	3.6141 ± 1.0810	3.6567 ± 0.1912 [30]	9.8147 ± 0.1258	11.2202 [48]	6.3095-11.2202 [3],	925[45], 0.4467[46]
[bdmim ⁺][NTf ₂ ⁻]	0.0326 ± 0.0107	0.7252 ± 0.0591	0.7327 ± 0.2768		0.6095-1.1587 [49]	925[45], 0.4467[46]
[emim ⁺][TfO]	0.0084 ± 0.0016	0.0322 ± 0.0021	0.1150 ± 0.0987			0.0008[45], 0.0005[46]
[emim ⁺][EtSO ₄ ⁻]	0.0069 ± 0.0033	0.0226 ± 0.0093	0.0127 ± 0.0015			0.0008[45], 0.0005[46]
[emim ⁺][CH ₃ COO ⁻]	0.0098 ± 0.0008	0.0092 ± 0.0008	0.539 ± 0.0712	0.0030 [34]		0.0008[45], 0.0005[46]
[bmim ⁺][MeSO ₄ ⁻]	0.0072 ± 0.0007	0.0111 ± 0.0002	0.0038 ± 0.0038			0.0091[45], 0.0054[46]
[bmim ⁺][MDEGSO ₄ ⁻]	0.0476 ± 0.0363	0.0191 ± 0.0036	0.0111 ± 0.0006			0.0001[45], 1.95x10 ⁻⁶ [46]
[mim ⁺][Cl ⁻]	0.0643 ± 0.0230	0.0354 ± 0.0138	0.1539 ± 0.0953			0.0005[45], 2.24x10 ⁻⁶ [46]
[emim ⁺][Cl ⁻]	0.0849 ± 0.0049	0.096 ± 0.0242	0.1612 ± 0.0278			0.0008[45], 0.0005[46]
[hemim ⁺][Cl ⁻]	0.0111 ± 0.0036	0.0058 ± 0.0001	0.0125 ± 0.0047			7.85x10 ⁻⁵ [45], 0.0001[46]
[dmim ⁺][Cl ⁻]	0.0140 ± 0.0026	0.0242 ± 0.0022	0.0227 ± 0.0032			0.0003[45], 0.0001[46]
[eim ⁺][Cl ⁻]	0.0445 ± 0.0042	0.0699 ± 0.0013	0.0764 ± 0.0014			0.0013[45], 3.1623[46]
[hmim ⁺][Cl ⁻]	0.0213 ± 0.0064	0.0221 ± 0.0010	0.1246 ± 0.0041	0.0186 [48]		0.0931[45], 0.0617[46]
[empy ⁺][EtSO ₄ ⁻]	0.0049 ± 0.0011	0.0203 ± 0.0057	0.0313 ± 0.0100			0.0019[45], 0.0007[46]
[bmpy ⁺][BF ₄ ⁻]	0.0082 ± 0.0009	0.0105 ± 0.0004	0.0170 ± 0.0049			0.0215[45], 0.0076[46]
ETAN	0.0028 ± 0.0008	0.0017 ± 0.0004	0.0026 ± 0.0008			0.0005[45], 0.0003[46]

Table 4: Octanol-water partition coefficients (K_{ow}) of ILs measured with shake-flask method, combined method and slow-stirring method at 30°C. Literature values are also shown, classified into those obtained by shake-flask or slow-stirring method. Estimated K_{ow} values obtained by molinspiration.com and Bio-Loom Software are also shown.

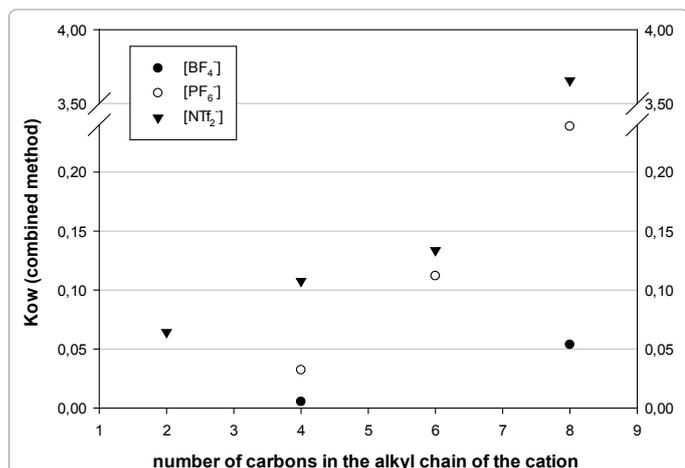


Figure 2: Octanol-water partition coefficients (K_{ow}) obtained by the combined method of ILs with different anions as a function of the alkyl chain length of the cation.

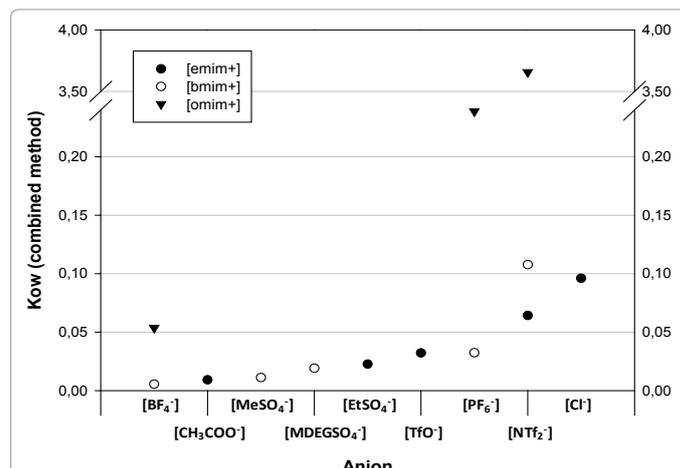


Figure 3: Octanol-water partition coefficients (K_{ow}) obtained by the combined method of ILs with three different alkyl chains ([emim⁺], [bmim⁺] y [omim⁺]) and different anions.

environmental effects, liquid/liquid solute partitioning and miscibility with other solvents. However, the values of the K_{ow} of ILs differ very much according to the experimental method used for their determination. It is possible that the differences in K_{ow} values obtained by different authors for the same ionic liquid might be also due to differences in ionic liquid concentrations.

The K_{ow} of ILs used in this study range between 0.0017 (ETAN)

and 3.6567 ([omim⁺][NTf₂⁻]) at 30°C. The ILs studied here are fairly hydrophilic, and their K_{ow} are lower than in commonly used industrial solvents.

The values of K_{ow} are lowest for the most hydrophilic ILs and increase with the cation alkyl chain length. Since all of the K_{ow} values are very small, we conclude that none of the ILs studied will accumulate or concentrate in the biota.

Acknowledgements

This work has been partially supported from the European Commission (FEDER/ERDF) and the Spanish MINECO (Ref. CTQ2011-25613 and Ref. CTQ2014-57467-R). Mercedes G. Montalbán acknowledges support from Spanish MINECO (FPI grant, BES-2012-053267).

References

1. Keskin S, Kayrak-Talay D, Akman U, Hortaçsu O (2007) A review of ionic liquids towards supercritical fluid applications. J Supercrit Fluids 43: 150-180.
2. Kabo GJ, Blokhin AV, Paulechka YU, Kabo AG, Shymanovich MP, et al. (2004) Thermodynamic Properties of 1-Butyl-3-methylimidazolium Hexafluorophosphate in the Condensed State. J Chem Eng Data 49: 453-461.
3. Ropel L, Belveze LS, Aki SN, Stadtherr MA, Brennecke JF (2005) Octanol-water partition coefficients of imidazolium-based ionic liquids. Green Chem 7: 83-90.
4. Freire MG, Carvalho PJ, Silva AM, Santos LM, Rebelo LP, et al. (2009) Ion specific effects on the mutual solubilities of water and hydrophobic ionic liquids. J Phys Chem B 113: 202-211.
5. Domanska U, Rekawek A, Marciniak A (2008) Solubility of 1-Alkyl-3-ethylimidazolium-Based Ionic Liquids in Water and 1-Octanol. J Chem Eng Data 53: 1126-1132.
6. Danielsson LG, Zhang YH (1996) Methods for determining n-octanol-water partition constants. TrAC 15: 188-196.
7. Deng Y, Besse-Hoggan P, Sancelme M, Delort AM, Husson P, et al. (2011) Influence of oxygen functionalities on the environmental impact of imidazolium based ionic liquids. J Hazard Mater 198: 165-174.
8. Han SY, Qiao JQ, Zhang YY, Lian HZ, Ge X (2012) Determination of n-octanol/water partition coefficients of weak ionizable solutes by RP-HPLC with neutral model compounds. Talanta 97: 355-361.
9. Lee SH, Lee SB (2009) Octanol/water partition coefficients of ionic liquids. J Chem Technol Biotechnol 84: 202-207.
10. Mackay D (1982) Correlation of bioconcentration factors. Environ Sci Technol 16: 274-278.
11. Mackay D, Fraser A (2000) Kenneth Mellanby Review Award. Bioaccumulation of persistent organic chemicals: mechanisms and models. Environ Pollut 110: 375-391.
12. Wang X, Ma Y, Yu W, Geyer HJ (1997) Two-compartment thermodynamic model for bioconcentration of hydrophobic organic chemicals by algae: Quantitative relationship between bioconcentration factor and surface area of marine algae or octanol/water partition coefficient. Chemosphere 35: 1781-1797.
13. Meylan WM, Howard PH, Boethling RS, Aronson D, Printup H, et al. (1999) Improved method for estimating bioconcentration/bioaccumulation factor from octanol/water partition coefficient. Environ Toxicol Chem 18: 664-672.
14. Raevsky OA, Grigor'ev VY, Weber EE, Dearden JC (2008) Classification and Quantification of the Toxicity of Chemicals to Guppy, Fathead Minnow and Rainbow Trout: Part 1. Nonpolar Narcosis Mode of Action. QSAR Comb Sci 27: 1274-1281.
15. Su LM, Liu X, Wang Y, Li JJ, Wang XH, et al. (2014) The discrimination of excess toxicity from baseline effect: effect of bioconcentration. Sci Total Environ 484: 137-145.
16. Lyman WJ, Reehl WF, Rosenblatt DH (1990) Handbook of chemical property estimation methods: environmental behavior of organic compounds. American Chemical Society.
17. Karickhoff SW (1981) Semi-empirical estimation of sorption of hydrophobic pollutants on natural sediments and soils. Chemosphere 10: 833-846.
18. Gerstl Z (1990) Estimation of organic chemical sorption by soils. J Contam Hydrol 6: 357-375.
19. Chiou CT (2003) Partition and Adsorption of Organic Contaminants in Environmental Systems. John Wiley & Sons.
20. Voutsas E, Magoulas K, Tassios D (2002) Prediction of the bioaccumulation of persistent organic pollutants in aquatic food webs. Chemosphere 48: 645-651.
21. Thomann RV (1989) Bioaccumulation model of organic chemical distribution in aquatic food chains. Environ Sci Technol 23: 699-707.
22. Allen DT, Shonnard DR (2001) Green Engineering: Environmentally Conscious Design of Chemical Processes. Pearson Education.
23. NSCEP (1975) Modeling dynamics of biological and chemical components of aquatic ecosystems. National Service Center for Environmental Publications.
24. Veith GD, Kosian P (1983) Estimating bioconcentration potential from octanol/water partition coefficients. Phys Behav PCBs Gt, Lakes Ann Arbor Sci, Ann Arbor MI 269-282.
25. Marcus Y (1990) Structural aspects of water in 1-octanol. J Solut Chem 19: 507-517.
26. NSCEP (1996) Product Properties Test Guidelines: Partition Coefficient (n-Octanol/Water), Shake Flask Method. US Environmental Protection Agency, Washington DC, USA.
27. OECD (1995) Test No. 107: Partition Coefficient (n-octanol/water): Shake Flask Method. Organisation for Economic Co-operation and Development, Paris.
28. Berthod A, Carda-Broch S (2004) Determination of liquid-liquid partition coefficients by separation methods. J Chromatogr A 1037: 3-14.
29. OECD (2006) Test No. 123: Partition Coefficient (1-Octanol/Water): Slow-Stirring Method. Organisation for Economic Co-operation and Development, Paris.
30. de los Rios AP, Hernández-Fernández FJ, Tomas-Alonso F, Rubio M, Gomez D, et al., (2008) On the importance of the nature of the ionic liquids in the selective simultaneous separation of the substrates and products of a transesterification reaction through supported ionic liquid membranes. J Membr Sci 307: 233-238.
31. Deng Y, Besse-Hoggan P, Husson P, Sancelme M, Delort AM, et al. (2012) Relevant parameters for assessing the environmental impact of some pyridinium, ammonium and pyrrolidinium based ionic liquids. Chemosphere 89: 327-333.
32. Ventura SPM, Gardas RL, Gonçalves F, Coutinho JAP (2011) Ecotoxicological risk profile of ionic liquids: octanol-water distribution coefficients and toxicological data. J Chem Technol Biotechnol 86: 957-963.
33. Kaar JL, Jesionowski AM, Berberich JA, Moulton R, Russell AJ (2003) Impact of ionic liquid physical properties on lipase activity and stability. J Am Chem Soc 125: 4125-4131.
34. Zhao H, Baker GA, Song Z, Olubajo O, Zanders L, et al. (2009) Effect of ionic liquid properties on lipase stabilization under microwave irradiation. J Mol Catal B Enzym 57: 149-157.
35. Chapeaux A, Simoni LD, Stadtherr MA, Brennecke JF (2007) Liquid Phase Behavior of Ionic Liquids with Water and 1-Octanol and Modeling of 1-Octanol/Water Partition Coefficients. J Chem Eng Data 52: 2462-2467.
36. Domanska U, Bogel-Lukasik E, Bogel-Lukasik R (2003) 1-Octanol/Water Partition Coefficients of 1-Alkyl-3-methylimidazolium Chloride. Chem Eur J 9: 3033-3041.
37. Kamath G, Bhatnagar N, Baker GA, Baker SN, Potoff JJ (2012) Computational prediction of ionic liquid 1-octanol/water partition coefficients. Phys Chem Chem Phys 14: 4339-4342.
38. Lee BS, Lin ST (2014) A priori prediction of the octanol-water partition coefficient (K_{ow}) of ionic liquids. Fluid Phase Equilibria 363: 233-238.
39. Cho CW, Preiss U, Jungnickel C, Stolte S, Arning J, et al. (2011) Ionic liquids: predictions of physicochemical properties with experimental and/or DFT-calculated LFER parameters to understand molecular interactions in solution. J Phys Chem B 115: 6040-6050.
40. Wattanasin P, Saetear P, Wilairat P, Nacapricha D, Teerasong S (2015) Zone fluidics for measurement of octanol-water partition coefficient of drugs. Anal Chim Acta 860: 1-7.
41. Heynderickx PM, Spael P, Van Langenhove H (2014) Quantification of Octanol-water partition coefficients of several aldehydes in a bubble column using selected ion flow tube mass spectrometry. Fluid Phase Equilibria. 367: 22-28.
42. Stepnowski P, Storonik P (2005) Lipophilicity and metabolic route prediction of imidazolium ionic liquids. Environ Sci Pollut Res Int 12: 199-204.
43. Ranke J, Müller A, Bottin-Weber U, Stock F, Stolte S, et al. (2007) Lipophilicity parameters for ionic liquid cations and their correlation to *in vitro* cytotoxicity. Ecotoxicol Environ Saf 67: 430-438.

-
44. Studzinska S, Stepnowski P, Buszewski B (2007) Application of Chromatography and Chemometrics to Estimate Lipophilicity of Ionic Liquid Cations. *QSAR Comb Sci* 26: 963-972.
45. <http://www.molinspiration.com/services/logp.html>
46. <http://www.biobyte.com>
47. Choua CH, Perng FS, Wong DSH, Su WC (2003) 1-Octanol/Water Partition Coefficient of Ionic Liquids. Boulder, CO, USA.
48. Lee SH (2005) Biocatalysis in Ionic Liquids: Influence of Physicochemical Properties of Ionic Liquids on Enzyme Activity and Enantioselectivity. Pohang University of Science and Technology, Pohang, Korea.
49. Gardas RL, Freire MG, Marrucho IM, Coutinho JAP (2006) Octanol-water partition coefficients of (imidazolium-based) ionic liquids. In: The 2nd National Conference on Thermodynamics of Chemical & Biological Systems, The Indian Thermodynamics Society, Veer Narmad South Gujarat University, Surat, India.
50. Leo A, Hansch C, Elkins D (1971) Partition coefficients and their uses. *Chem Rev* 71: 525-616.
51. Ruelle P (2000) The n-octanol and n-hexane/water partition coefficient of environmentally relevant chemicals predicted from the mobile order and disorder (MOD) thermodynamics. *Chemosphere* 40: 457-512.
52. Hsieh CM, Lin ST (2009) Prediction of 1-octanol-water partition coefficient and infinite dilution activity coefficient in water from the PR + COSMOSAC model. *Fluid Phase Equilibria* 285: 8-14.