Scientific paper

Chromatographic and Chemometric Methods for Evaluation of Properties of Ionic Liquids

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Abstract

The interest in ionic liquids is in constant increase due to their popularity in various applications. The wide applicability of these compounds is the main reason of their use on industrial scale, especially in organic synthesis. This leads to the presence of ionic liquids in water and soils. Therefore, there is a need to study their toxicology and to better understand the basis of it.

The main aim of the contribution is to review the existing knowledge about the influence of ionic liquids on living organisms and to provide information about the use of chromatographic and chemometric methods in evaluation of properties of ionic liquids.

Keywords: ionic liquids, chromatography, stationary phase, chemometric, QSAR

1. Introduction

The interest in properties of room-temperature-ionic liquids is rapidly expanding. In an ionic liquid, the cation is generally large and the anion is either large or small, resulting in poorer packing of the larger ions with weaker attraction, so the compound tends to remain liquid. Figure 1 presents the schematic structure of the most commonly used imidazolium ionic liquids. It is this liquid state that is the key to ionic liquids' useful properties, which include high thermal stability, negligible vapour pressure and good electrochemical stability – making them attractive to any industry using solvents.[1–4] Due to their non-volatile feature, the most attractive application of ionic liquids is to replace the traditional volatile organic solvents, which are harmful to the environment. Other features, such as reusability, low viscosity, better reactivity and selectivity, also ensure ionic liquids to be a good candidate for "green chemistry".[1–4] There have been numerous studies concerning their preparation, their use as a reaction medium and their physical properties. Therefore, this subject has become especially interesting, because of the possibility of migration of ionic liquids to the environment. The wide applicability of these compounds is the main reason of their use on industrial scale.

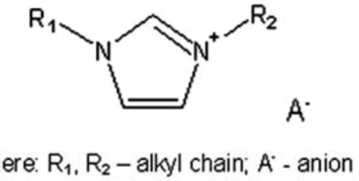


Figure 1. Schematic structure of imidazolium ionic liquids.

As ionic liquids are non-volatile, their presence in air is not probable, in comparison with the possibility of their occurrence in water and soil.[5–7] This is the main reason why estimation of ionic liquids properties is so important and is the subject of many works. In other words: the migration of these substances in the environment will depend on the interactions between the compounds and water or soil. It is important to know these interactions, because this will give us a possibility to understand mechanisms responsible for ionic liquids activity in the environment.

In an attempt to understand the nature of interactions of room-temperature-ionic liquids, high performance liquid chromatography may be used. One of the way of changing and optimizing the chromatographic results is to change the column type. This means a change in the stationary phase. Such alterations may be also used to study the interactions between stationary phase ligands and the analyzed compound. Ionic liquids may interact with other compounds in several different ways: van der Waals forces, electrostatic, π…π. However, there is little knowledge about what interaction is the strongest. The main aim of the present contribution was to provide information about the usefulness of chromatographic and chemometric methods to estimate the properties of ionic liquids.

2. Experimental

2.1. Materials and Reagents

Standards of 1-*n*-propyl-3-methyl-imidazolium tetrafluoroborate (PMIM), 1-*n*-butyl-3-methyl-imidazolium tetrafluoroborate (BMIM), 1-*n*-amyl-3-methyl-imidazolium tetrafluoroborate (AMIM), 1-*n*-hexyl-3-methyl-imidazolium tetrafluoroborate (HMIM) were obtained from E. Merck (Darmstadt, Germany) and also supplied by professor Bernd Jastorff (University of Bremen, Germany). Schematic structures of analyzed ionic liquids and their main properties are given in Table 1.

For the preparation of the mobile phase, methanol of “for HPLC” purity (S. Witko, Łódź, Poland) was used, as well as deionized water purified using a Milli-Q system (Millipore, El Passo, TX, USA), KH_2PO_4 (POCh, Gliwice, Poland), 85% solution of HPLC grade orthophosphoric acid (J. T. Baker, Deventer, The Netherlands).

In the current studies a series of homemade packing materials with different surface ligands have been utilized: cholesterol (SG-CHOL); n-acylamide (SG-CHOL, SG-AP); aminopropyl (SG-CHOL, SG-AP, SG-MIX); cyanopropyl, phenyl, octadecyl, octyl, butyl (SG-MIX, SG-Ph), naphthalene (SG-Ar) and residual silanols locali-

Table 1. Structure and basic properties of ionic liquids used.

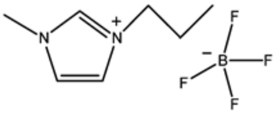
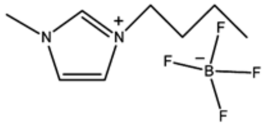
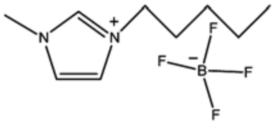
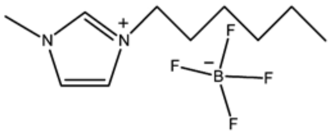
Name	**Abbreviation**	**Structure**	**Molar mass (g mol^{-1})**
1-*n*-propyl-3-methyl-imidazolium tetrafluoroborate	PMIM		212
1-*n*-butyl-3-methyl-imidazolium tetrafluoroborate	BMIM		226
1-*n*-amyl-3-methyl-imidazolium tetrafluoroborate	AMIM		240
1-*n*-hexyl-3-methyl-imidazolium tetrafluoroborate	HMIM		254

Table 2. Characteristics of HPLC columns used in the study.

Stationary phase type	**Column**	**Abbreviation**	**Column dimensions (mm)**	**Silica particle size (µm)**	**Pore diameter (Å)**
octadecyl	Gemini 5µ C18 110 Å	Gemini	250 × 4.6	5	110
octadecyl, end-capped	RP-18e Purospher^{TM} Star	Star	250 × 4.6	5	120
octyl	Macrosphere 300 C8 5µm	SG-C8	250 × 4.6	5	300
butyl	Macrosphere 300 C4 5µm	SG-C4	250 × 4.6	5	300
alkylamide	alkylamide	SG-AP	250 × 4.6	5	100
cholesterolic	cholesterolic	SG-CHOL	250 × 4.6	5	100
mixed	mixed	SG-MIX	250 × 4.6	7	-
phenyl	phenyl	SG-Ph	125 × 4.6	4.6	-
aryl	aryl	SG-Ar	125 × 4.6	4.6	-

zed on the silica gel surface of all packings. The reaction mechanism and the conditions for synthesis of alkylamide, cholesterolic, mixed, phenyl and aryl stationary phases synthesis are given in the literature for: SG-AP,[8] SG-CHOL,[9] SG-MIX,[10] SG-Ph,[11] SG-Ar.[11] A commercial Macrosphere 300 C4 5 (Alltech, Deerfield, IL, USA; SG-C4); Macrosphere 300 C8 5 (Alltech, Deerfield, IL, USA; SG-C8); Gemini 5μ C18 110 Å (Phenomenex, Torrance, CA, USA) (Gemini); RP-18e Purospher^{TM} Star (E. Merck, Darmstadt, Germany; Purospher) columns have also been applied in the study (Table 2).

2.2. Instrument and Chromatographic Conditions

A LC-10Avp (Shimadzu, Kyoto, Japan) high performance liquid chromatographic system equipped with a diode-array detector DAD (Shimadzu, Kyoto, Japan), a Rheodyne 7125 manual injection valve (Rheodyne, Berkeley, CA, USA) with a 20-(micro)L loop were selected for chromatographic measurements. CLASS-VP program was used for the data collection.

The elution was carried out with isocratic conditions of: 95% v/v 40 mmol L^{-1} potassium phosphate buffer (adjusted with orthophosphoric acid to pH = 4) and 5% v/v methanol in case of all packings except SG-Ar and SG-Ph for which conditions were: 50% v/v 40 mmol L^{-1} potassium phosphate buffer (adjusted with orthophosphoric acid to pH = 4) and 50% v/v methanol. In case of log $k_{\mathrm{W,SG\text{-}CHOL}}$ determination 40 mmol L^{-1} potassium phosphate buffer adjusted to pH = 7 was used. The flow rate was 1 ml/min.

In the interpretation of the results, the HyperChem v.5.1 package with the ChemPlus extension (HyperCube, Waterloo, Canada) was used.

3. Results and Discussion

Chromatographic analysis of ionic liquids on various column packing types allows for prediction of principal interactions responsible for their retention. Results obtained for 1-butyl-3-methylimidazolium cation are presented in Figure 2 together with a schematic illustration of stationary phase structures and interactions.

The rest of results are gathered in Figure 3. The obtained data clearly indicate a decrease of the ionic liquid cation retention with a larger alkyl ligand. It was found that the analyzed cations interact stronger with surface of the packing by hydrophobic van der Waals forces. On the other hand, the investigations performed with the use of phenyl and aryl stationary phase showed intense interactions between ionic liquids cations and chemically bonded aromatic molecules. The retention values of ionic liquids analyzed on these two packings in mobile phase consist of only 5% MeOH v/v were so high, that the analytical conditions had to be changed. Methanol in the mobile phase was increased to 50% v/v. This indicates stronger $\pi\ldots\pi$ interaction types in comparison with van der Waals interactions. It can be concluded that main interactions in ionic liquids retention mechanism are: dispersive and $\pi\ldots\pi$ type.

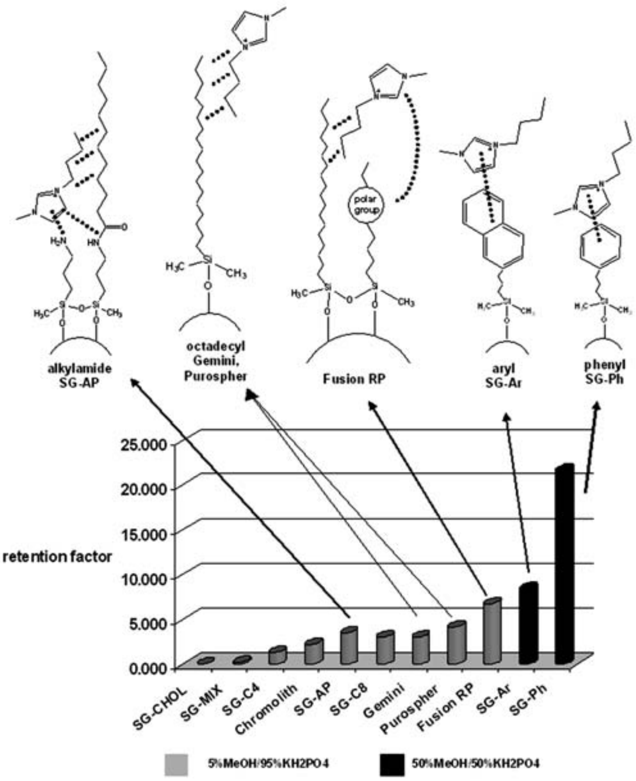


Figure 2. Dependence 1-butyl-3-methylimidazolium cation retention factor values as a function of different stationary phases. Conditions: 95% v/v 40 mM KH$_2$PO$_4$ (pH = 4) and 5% v/v MeOH, except of SG-Ar and SG-Ph, where conditions are: 50% v/v 40mM KH$_2$PO$_4$ (pH = 4) and 50% v/v MeOH.

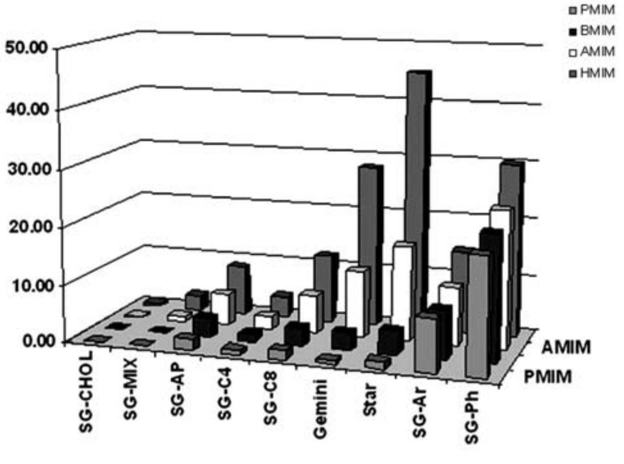


Figure 3. Dependence of ionic-liquid cations retention as a function of different packing materials. Eluents: 40 mM KH$_2$PO$_4$ (pH = 4) and 5% v/v MeOH, or 50% v/v MeOH.

We compared the experimentally determined values of logk_W obtained for ionic liquid cations on the packing materials with the standard hydrophobicity measure log*P*. The log*P* and log$k_{W,IAM}$ values were determined according to Stepnowski et al.,[6] who have reported the experimentally (with the use of HPLC) measured and theoretically estimated lipophilicity coefficients obtained for representatives of imidazolium ionic liquid cations. Results of these studies are presented in Table 3 and Figure 4.

Table 3. Comparison of the obtained measure of lipophobicity.

	Experimentally measured ionic liquid cations logkW vaule			
Stationary phase	PMIM	BMIM	AMIM	HMIM
Imobilozed IAM artificial membrane	0.92	1.32	1.52	1.70
Cholesterolic SG-CHOL	1.2	2.63	3.63	5.39
	Theoretically estimated log*P* values			
	–1.74	–1.44	–1.09	–0.71

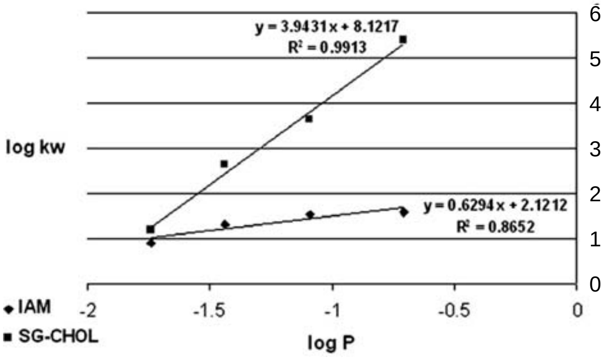


Figure 4. Correlation between the theoretically estimated logP values and experimentally determined logkw for IAM and SG-CHOL stationary phases.

An interesting dependence in the case of cholesterolic stationary phase was found. The correlation coefficient is higher than in the case of IAM packing, which mimics biological membranes and should give better results in this investigation. Such an effect is probably a consequence of possible combination of hydrophobic, donor-acceptor, π…π, hydrogen bonding interactions on SG-CHOL stationary phase. All of the mentioned interactions are expected to be important in membrane transport, which is probably the reason for such a good correlation between the retention of ionic liquids and hydrophobicity measure in case of cholesterolic packing. Furthermore, the high correlation values indicate that log*P* for ionic liquid correlates well with their partitioning into a given stationary phase.

Another way of estimating the log*P* values is the use of chemometric approach. The HyperChem software allows for estimation of a variety of molecular descriptors commonly used in Quantitative Structure Activity Relationships (QSAR) studies, e.g. van der Waals surface area, solvent accessible area, which can be used to draw conclusions regarding the lipophilicity of analysed molecules. The imidazolium-based ionic liquid cations used in this study are built on the same skeleton containing an imidazolium ring with one methyl group bonded to both nitrogen atoms. The main QSAR properties were determined for all compounds. Then, the 'selectivity' parameter was determined, as follows:

α_S = ionic liquid solvent accessible area / skeleton solvent accessible area,

α_W = ionic liquid van der Waals surface area / skeleton van der Waals surface area.

The obtained values were compared with log*P* values and are presented in Figure 5. As it can be seen, the QSAR parameters correlate well with the log*P* value. In the case of ionic liquid cation the structure differs only in the number and position of methyl groups and the main interactions in which they can take part are van der Waals (dispersion) force, similar as in the case of interactions taking part when log*P* determined. These investigations show that with the use of chemometric approach it is possible to predict hydrophobicity of ionic liquids cations.

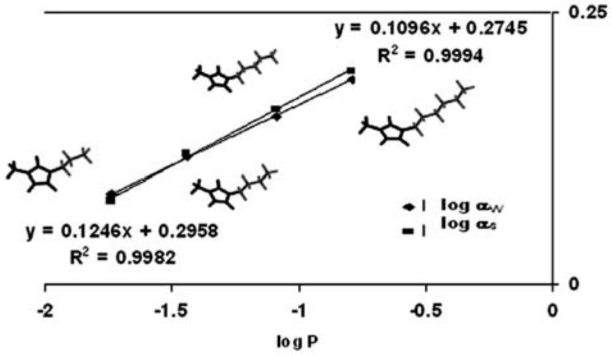


Figure 5. Correlation between log α_W and log α_S with log*P* values for the studied imidazolium-based-ionic liquids.

4. Conclusions

The studies of ionic liquids interactions are still scarce and in this contribution, liquid chromatography provided interesting results. HPLC allowed for the descriptions of the main interactions, which were found to be π…π type and van der Waals dispersive forces. The use of different chemometric approaches allows for further conclusions regarding the interactions. The present work proved the usefulness of HPLC and chemometric methods in the preliminary studies of ionic liquids properties.

5. Acknowledgements

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6. References

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Povzetek

Zanimanje za ionske tekočine narašča zaradi široke uporabnosti v industrijskih procesih, še posebej v organski sintezi, kar je vodilo do njihove prisotnosti v okolju, zlasti v vodi in prsti. Zato so se pokazale potrebe, da bolje razumemo njihove toksične lastnosti.

Glavni cilj tega prispevka je, da poda pregled obstoječe literature o vplivu ionskih tekočin na žive organizme in da oceni uporabnost kromatografskih in kemometrijskih metod za oceno lastnosti ionskih tekočin.