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Study of the Interactions of Ionic Liquids in IC by QSRR

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Abstract The nature of ionic liquids (ILs) facilitates their analysis by ion chromatography which, unlike conventional high-performance liquid chromatography, enables analysis both of cations and anions. This paper describes a pioneering ion-chromatographic investigation of IL cations and statistical evaluation of quantitative structure–retention relationships with the objective of predicting the molecular mechanism responsible for retention. Eleven ionic liquid imidazolium and pyridinium cations were analyzed on a CS15 cation-exchange column by isocratic elution with acetonitrile–methanesulfonic acid mixtures. Structural descriptors of the cations obtained from molecular modeling were used to describe their hydrophobicity as determined by chromatography. The most statistically significant were three-term QSRR regression equations relating log k_w to analyte n-octanol–water partition coefficient (log P), dipole moment (μ), solvent accessible surface area (A_{SAS}), and hydration energy (HE). They indicate the important role of both hydrophobic and polar the retention of ILs on the CS15 column.

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Introduction

Ionic liquids (ILs) are salts comprising molecular ions, organic cations, and organic or inorganic anions. Frequently used cations are pyridinium or imidazolium derivatives, depicted in Fig. 1; tetrafluoroborate, hexafluorophosphate, chloride, and bromide are frequently used as inorganic counterions. The IL term is generally associated with salts in which the ions are poorly coordinated and thus have relatively low melting points (<100 °C). ILs have unusual physical and chemical properties, because of the combination of cations and anions; these are non-volatility, a non-flammability, excellent chemical and thermal stability, and selective solubility. Such properties make them essential in biotechnological applications and in the pharmaceutical and chemical industry [1–4].

Despite the ionic character of ILs, separation and analysis of their cations reported so far are generally based on high-performance liquid chromatographic methods employing a variety of column packings and mobile phases [5, 6]. Ion chromatography (IC) is a new approach to analysis of ILs, but few papers on this subject have been published [7–11]. According to the results presented in all of these, IC is an appropriate technique and useful method for analysis of chloride, bromide or iodine impurities in ionic liquids and for quantitative analysis of IL cations [7–11]. The newest approach in the field of IL analysis by IC is simultaneous analysis of cations and anions. A tandem of columns containing cation and anion exchangers
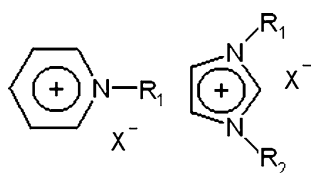
Fig. 1 Schematic diagram of structures of pyridinium and imidazolium IL cations, where R_1 and R_2 represent alkyl or aryl substituents and X^- an anion

followed by conductometric detection has been successfully [11]. IC can be used not only for analysis of IL cations but also to furnish information about retention mechanism, and to enable prediction of retention by use of quantitative structure–retention relationships (QSRRs).

The QSRRs, developed by Kaliszan [12], are statistically derived relationships between chromatographic properties and descriptors characterizing the molecular structure of the analytes. A typical QSRR study comprises the following steps:

1 acquisition of the experimental data set;
2 molecular structure entry;
3 structure descriptor calculation; and
4 regression analysis relating the experimental data with the structural descriptors.

Usually, these relationships are developed by software and are based on the linear or multilinear regression methods. The simplest QSRR model eded for retention prediction is represented by Eq. 1:

$$\log k_w = k_1 + k_2 \log P \tag{1}$$

where k_w is retention factor extrapolated to a pure water as mobile phase; k_1 and k_2 are regression coefficients, characteristic of the separation systems used, representing differences in individual physicochemical properties between the mobile and the stationary phases; and log P is the logarithm of n-octanol–water partition coefficient which can serve as a measure of hydrophobicity [13, 14]. Eq. 1 may be, however, applied only of compounds with very similar structure and the same functional groups.

This model can be used for chromatographic determination of log P. For ILs there are few reports of estimation of this property by the shake flask method. The pioneering work on partition of ILs between n-octanol and water was that of Kaar et al. [15]. In later studies the same method was used for imidazolium cations [16–18]. log P values increase with increasing alkyl chain length of the cation and increasing ILs concentration. The shake flask experimental method is, however, poorly reproducible, and for ILs is also complicated because of their dissociation [14]. For this reason new methods are required for measurement or calculation of log P. One of these utilizes of QSRR

equations. There is one report of the use of QSRR for determination of the hydrophobicity of ILs by reversed-phase high-performance liquid chromatography [19]. There are, however, no reports of the use of IC.

In this investigation, we used the IC of IL cations with QSRR to predict the main interactions responsible for retention of the analytes. Eleven IL imidazolium and pyridinium cations were analyzed by use of a cation-exchange column and isocratic elution with acetonitrile–methanesulfonic acid mixtures. Retention data for the IL cations were used to derive QSRR for logarithms of retention factors normalized to a hypothetical zero percent organic modifier mobile phase treated as a dependent variable. This value was also compared with log P and structural data calculated for IL cations.

Experimental

Materials and Reagents

Ionic liquids selected for the investigation were obtained from Merck (Darmstadt, Germany) and from Professor B. Jastorff's collection (University of Bremen, Germany) synthesized in the laboratory of Professor B. Ondruschka (University of Jena, Germany). Their names, molecular formulas, and main properties are listed in Table 1.

Isocratic-grade acetonitrile (J.T. Baker, Deventer, The Netherlands), methanesulfonic acid (MSA; Fluka, Buchs, Switzerland) for ion chromatography, and deionized water prepared with a Milli-Q purification system (Millipore, Bedford, MA, USA) were used for mobile phase preparation. The pH of the MSA was measured before mixing with the organic modifier. The potassium hydroxide for suppressor regeneration was obtained from POCh (Gliwice, Poland).

Instrumentation

A Dionex model ICS-3000 ion chromatograph consisting of an autosampler, a degasser, pumps, a thermostat, a conductometric detector, and a personal computer with Chromeleon 6.8 software was used for all the chromatographic measurement of the retention data of IL cations (Dionex Corporation, Sunnyvale, CA, USA). The Dionex micromembrane suppressor CMMS 300 (4 mm) for chemical suppression was installed between the conductometric detector and the Dionex IonPac CS15 analytical column (4 × 250 mm, 8.5 μm). The column consists of a macroporous polymer of ethylvinylbenzene crosslinked with 55% divinylbenzene and functionalized with carboxyl and phosphonate cation-exchange sites and crown-ether groups. The crown ethers are attached

Table 1 Basic characteristics and molecular descriptors of the IL cations used in this investigation

Systematic name	Abbreviation	Molecular formula	Molecular mass (g mol^{-1})	Structural descriptor					
				log P	A_{SAS} (Å^2)	μ (D)	PO (Å^3)	HE (kcal mol^{-1})	TE (kcal mol^{-1})
1-Ethyl-3-ethylimidazolium bromide	[EEIM][Br]	C$_7$H$_{13}$N$_2$Br	205	0.15	336.91	1.913	15.39	−0.43	−34078.33
1-n-Propyl-3-methylimidazolium tetrafluoroborate	[PMIM][BF$_4$]	C$_7$H$_{13}$N$_2$BF$_4$	212	0.28	351.55	5.098	15.39	−0.55	−34078.31
1-n-Butyl-3-methylimidazolium tetrafluoroborate	[BMIM][BF$_4$]	C$_8$H$_{15}$N$_2$BF$_4$	226	0.68	387.67	7.212	17.22	−0.08	−37671.22
1-n-Butyl-3-ethylimidazolium tetrafluoroborate	[BEIM][BF$_4$]	C$_9$H$_{17}$N$_2$BF$_4$	240	1.02	410.26	5.819	19.05	0.60	−41264.22
1-Butyl-4-methylpyridinium tetrafluoroborate	[MBPy][BF$_4$]	C$_{10}$H$_{16}$NBF$_4$	237	1.68	389.57	3.187	19.35	0.88	−39143.10
1-n-Amyl-3-methylimidazolium tetrafluoroborate	[AMIM][BF$_4$]	C$_9$H$_{17}$N$_2$BF$_4$	240	1.07	425.18	9.664	19.05	0.31	−41264.02
1-Benzyl-3-methylimidazolium tetrafluoroborate	[BzMIM][BF$_4$]	C$_{11}$H$_{13}$N$_2$BF$_4$	260	0.48	350.96	9.502	21.37	−2.76	−45860.68
1-(p-Ethylbenzyl)-3-methylimidazolium tetrafluoroborate	[EBzMIM][BF$_4$]	C$_{13}$H$_{17}$N$_2$BF$_4$	288	1.03	411.23	11.453	25.04	-1.19	−53045.82
1-Hexyl-4-methylpyridinium tetrafluoroborate	[HMPy][BF$_4$]	C$_{12}$H$_{20}$NBF$_4$	265	2.47	468.11	10.124	23.02	1.68	−46315.01
1-n-Hexyl-3-methylimidazolium tetrafluoroborate	[HMIM][BF$_4$]	C$_{10}$H$_{19}$N$_2$BF$_4$	254	1.47	461.01	12.094	20.89	0.68	−44856.80
1-n-Octyl-3-methylimidazolium tetrafluoroborate	[OMIM][BF$_4$]	C$_{12}$H$_{23}$N$_2$BF$_4$	282	2.26	532.23	17.314	24.56	1.42	−52042.31
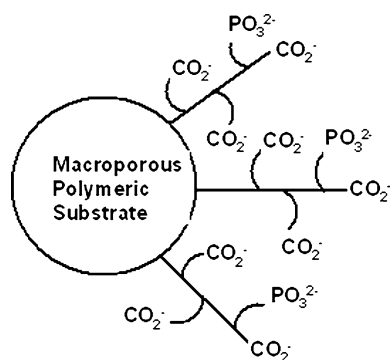
Fig. 2 Schematic representation of organic chains carrying ion-exchange sites of CS15 column

covalently to the core whereas the phosphonic and the carboxyl groups are connected to aliphatic chains, which are themselves bonded covalently to the core. These chains can represent "tentacles" on which the carboxyl and phosphonate groups have been placed (Fig. 2) [20]. A Dionex IonPac CG15 (4 × 50 mm) guard column was also used. pH was measured with a CP-505 (Elmetron, Zabrze, Poland) pH meter. PTFE membrane filters (0.2 μm; BGB Analytik, Boeckten, Switzerland) were used for filtration.

Methods

Chromatographic Procedure

The analytes were eluted by isocratic elution with acetonitrile–MSA mixtures at a flow rate of 1 mL min^{-1}. Both mobile phase components were chosen as recommended by the manufacturer for the CS15 column [20]. Acetonitrile is the only organic solvent up to 100% compatible with this column. The concentration of the ILs was 0.1 mM in aqueous solution and the injection volume was 20 μL. Each analysis was performed in three replication. During chromatographic investigations both the guard and the analytical columns were thermostated at 35 °C, and the suppressor and conductometric detector at 30 °C. Those temperatures were chosen because of the specification and manufacturer recommendation. The micromembrane suppressor was continuously regenerated by use of 40 mM KOH solution at a flow rate of 7 mL min^{-1}.

The concentration of MSA in the mobile phase varied from 1 to 9 mM and in the volume concentration of acetonitrile from 20 to 75% (v/v). The column hold-up volume, V_M, necessary for calculation of retention factors $k = V_R/V_M - 1$, was measured by use of the mobile phase system peak.

QSRR Procedure

The retention factors of the ILs were used for determination of log k_w, by use of the Snyder–Soczewinski equation (Eq. 2) of the linear solvent strength (LSS) model [21]:

$$\log k = \log k_w - S\varphi \qquad (2)$$

where k is the retention factor, the meaning of k_w is the same as in in Eq. 1, S is a constant for a given analyte or congeneric group of analytes, and φ is the volume fraction of the organic component of the mobile phase.

All the structural descriptors were derived by use of HyperChem software with the ChemPlus extension (Hypercube, Waterloo, Canada). They are summarized in Table 1 and were obtained after modeling of the structures of the molecules and optimization their geometry. The calculation procedure used was the semi-empirical quantum-chemical AM1 method. All calculations were performed under simulated vacuum conditions, as this is most typical for the HyperChem software. For the QSRR analysis the multiple regression procedure was executed and QSRR equations derived in this study contained the following molecular structural descriptors of the analytes: logarithm of the n-octanol–water partition coefficient (log P), solvent (water) accessible surface area (A_{SAS}), total dipole moment (μ) polarizability (PO), hydration energy (HE), and total energy (TE).

Statistical evaluation was performed on a personal computer with the Statistica package (StatSoft, Tulsa, USA) and graphs were plotted by use of OriginPro software (OriginLab, MA, USA).

Results and Discussion

IC Analysis of ILs

The k values measured for all mobile phase compositions are summarized in Table 2. Figure 3 shows a typical chromatogram obtained from separation of IL cations with 20% (v/v) acetonitrile and 5 mM MSA. In general, as acetonitrile concentration increases from 20 to 60%, retention decreases. IL had the same retention behavior as on the reversed-phase stationary phases commonly used in HPLC. If up to 65% of acetonitrile was used the IL cations were eluted on the basis of their hydrophobicity (Tables 1, 2). This can be justified by the structure of the packing material used in the investigation. On the surface of the stationary phase there are short alkyl chains, crown ether groups, and cation-exchange sites. It seems that the mechanism of retention of IL cations is predominantly dependent not only on electrostatic forces but also on hydrophobic interactions between the non-polar parts of the stationary phase surface, i.e. the crown-ether and aliphatic chains, with the alkyl chains of the imidazolium and pyridinium cations.

The opposite retention behavior occurred when acetonitrile was used in excess of 65% (v/v). The analytes showed normal phase HPLC retention behavior and the most hydrophobic cation OMIM was eluted before the hydrophilic EEIM (Table 2). This behavior was observed only for use of 1 mM MSA, because of its low eluent strength.

Nevertheless, in some cases similar k were observed for IL cations of different hydrophobicity, i.e., having different log P values (Tables 1, 2). The reason for this effect was explained in detail in our earlier study [22].

Elution of IL cations is, however, affected by both the amount of acetonitrile and the concentration of MSA. k values are reduced when the concentration of MSA is increased.

Chromatographic Behavior of ILs in the IC system

Chromatographic retention of ILs may be explained by another phenomenon. It has been proved that ILs form heterogeneous solutions or ion pairs when they are dissolved in water or other solvents [23, 24]. When ILs enter the chromatographic system they become dissociated salts. Therefore, IL cation and anion can form ion-pairs with ions of the mobile phase (in our case MSA). Although this effect seems to have a rather slight effect on IL retention behavior (because the concentrations and volumes of IL used are low) it is worth discussing.

Ruiz-Angel et al. [24] showed that, depending on the type of salt used as mobile phase component, retention of ILs increased with increasing affinity of the inorganic anions for the apolar stationary phases (chaotropicity). Retention of an imidazolium or pyridinium cation may be a consequence of hydrophobic interactions of the ion-pair, and ion-exchange with the anion-covered stationary phase surface or with the cation exchange sites [23, 24].

The conditions used in our study also promote ion pair formation between IL cations or anions and MSA. First MSA anions can be adsorbed by the stationary phase surface and change its properties [24]. BF_4 is an chaotropic anion, which may be adsorbed by the packing material more strongly than the MSA anion [24]. Therefore, the observed retention differences for high or low concentrations of MSA are meaningful. For concentrations >2.5 mM, MSA forms ion pairs with imidazolium and pyridinium cations, and BF_4 covers the surface of the packing. The retention of IL cations will be mainly differentiated by their hydrophobicity. On the other hand reducing the amount of MSA (1 mM) in the mobile phase will, consequently, lead to a change in the mechanism of

Table 2 Retention factors, k, of the test analytes, with their relative standard deviations (RSD, %), for all the mobile phase compositions investigated

1 mM MSA

ACN	50%	55%	60%	65%	70%	75%
EEIM	16.39 ± 0.27	15.72 ± 0.41	14.62 ± 0.19	14.10 ± 0.25	13.16 ± 0.11	12.64 ± 0.38
PMIM	16.39 ± 0.14	16.10 ± 0.18	15.34 ± 0.17	14.74 ± 0.23	13.60 ± 0.10	13.10 ± 0.05
BMIM	17.32 ± 0.19	16.02 ± 0.12	15.28 ± 0.27	14.56 ± 0.19	12.24 ± 0.07	11.87 ± 0.36
BEIM	17.43 ± 0.12	15.38 ± 0.06	14.54 ± 0.29	13.41 ± 0.20	11.90 ± 0.11	10.33 ± 0.41
MBPyr	19.04 ± 0.17	17.03 ± 0.28	15.41 ± 0.22	15.07 ± 0.08	12.58 ± 0.12	12.17 ± 0.00
AMIM	18.50 ± 0.02	16.11 ± 0.31	15.16 ± 0.27	14.56 ± 0.49	12.39 ± 0.02	10.98 ± 0.35
BzMIM	20.84 ± 0.17	20.58 ± 0.20	17.23 ± 0.13	16.69 ± 0.19	14.04 ± 0.02	13.12 ± 0.09
EBzMIM	22.37 ± 0.17	20.65 ± 0.10	18.21 ± 0.22	16.07 ± 0.20	13.51 ± 0.00	12.30 ± 0.11
HMPyr	21.73 ± 0.28	19.64 ± 0.13	18.64 ± 0.12	14.49 ± 0.05	12.23 ± 0.05	10.51 ± 0.38
HMIM	21.29 ± 0.12	19.32 ± 0.10	16.27 ± 0.27	14.09 ± 0.1	12.03 ± 0.02	10.40 ± 0.12
OMIM	25.87 ± 0.17	21.90 ± 0.04	17.42 ± 0.04	14.45 ± 0.50	12.15 ± 0.08	9.88 ± 0.36

2.5 mM MSA

ACN	20%	30%	40%	45%	50%	60%
EEIM	10.93 ± 0.28	8.59 ± 0.25	6.95 ± 0.42	6.51 ± 0.43	6.01 ± 0.19	5.60 ± 0.37
PMIM	11.95 ± 0.08	9.26 ± 0.30	7.35 ± 0.29	6.87 ± 0.31	6.35 ± 0.35	5.90 ± 0.32
BMIM	16.23 ± 0.15	11.44 ± 0.41	8.43 ± 0.26	7.70 ± 0.12	6.74 ± 0.27	5.84 ± 0.21
BEIM	19.15 ± 0.13	12.66 ± 0.35	8.89 ± 0.23	8.39 ± 0.17	6.76 ± 0.12	5.52 ± 0.26
MBPyr	20.54 ± 0.43	13.46 ± 0.34	9.95 ± 0.40	9.20 ± 0.40	7.46 ± 0.13	6.20 ± 0.23
AMIM	25.19 ± 0.11	14.78 ± 0.19	9.91 ± 0.10	9.12 ± 0.10	7.26 ± 0.31	5.85 ± 0.16
BzMIM	30.23 ± 0.14	17.33 ± 0.12	11.36 ± 0.22	10.44 ± 0.14	8.41 ± 0.29	6.86 ± 0.09
EBzMIM	31.70 ± 0.13	19.32 ± 0.13	12.36 ± 0.33	10.81 ± 0.38	8.54 ± 0.27	6.70 ± 0.30
HMPyr	–	20.11 ± 0.21	12.20 ± 0.20	10.68 ± 0.17	8.21 ± 0.18	6.07 ± 0.34
HMIM	–	20.38 ± 0.26	12.59 ± 0.22	10.44 ± 0.14	7.88 ± 0.11	5.76 ± 0.40
OMIM	–	33.72 ± 0.14	19.32 ± 0.20	14.73 ± 0.19	10.19 ± 0.16	6.44 ± 0.30

5 mM MSA

ACN	20%	25%	30%	35%	40%	45%
EEIM	5.50 ± 0.07	4.87 ± 0.14	3.97 ± 0.11	3.93 ± 0.20	3.49 ± 0.15	3.32 ± 0.15
PMIM	6.03 ± 0.19	5.30 ± 0.11	4.28 ± 0.17	4.23 ± 0.06	3.75 ± 0.10	3.59 ± 0.16
BMIM	8.26 ± 0.12	6.80 ± 0.15	5.31 ± 0.04	5.06 ± 0.15	4.28 ± 0.10	3.99 ± 0.07
BEIM	9.72 ± 0.03	7.71 ± 0.05	5.88 ± 0.11	5.48 ± 0.16	4.54 ± 0.09	4.11 ± 0.10
MBPyr	10.35 ± 0.09	8.21 ± 0.17	6.32 ± 0.09	5.92 ± 0.13	4.84 ± 0.08	4.54 ± 0.10
AMIM	12.78 ± 0.10	9.48 ± 0.07	6.96 ± 0.05	6.23 ± 0.14	5.02 ± 0.04	4.53 ± 0.02
BzMIM	14.54 ± 0.16	11.24 ± 0.02	8.13 ± 0.17	7.22 ± 0.03	5.82 ± 0.04	5.22 ± 0.11
EBzMIM	18.97 ± 0.12	13.05 ± 0.05	9.10 ± 0.17	7.88 ± 0.06	6.16 ± 0.13	5.43 ± 0.04
HMPyr	19.61 ± 0.07	13.92 ± 0.09	9.53 ± 0.14	7.99 ± 0.06	6.13 ± 0.05	5.37 ± 0.04
HMIM	22.71 ± 0.8	14.48 ± 0.11	11.56 ± 0.02	8.01 ± 0.14	5.92 ± 0.10	5.22 ± 0.01
OMIM	–	–	22.30 ± 0.02	15.08 ± 0.06	10.56 ± 0.03	7.41 ± 0.07

7.5 mM MSA

ACN	20%	25%	30%	35%	40%	45%
EEIM	3.65 ± 0.00	3.59 ± 0.03	2.95 ± 0.15	2.74 ± 0.15	2.51 ± 0.30	2.17 ± 0.00
PMIM	4.01 ± 0.04	3.87 ± 0.12	3.17 ± 0.11	3.01 ± 0.24	2.69 ± 0.02	2.30 ± 0.07
BMIM	5.47 ± 0.08	4.88 ± 0.00	3.89 ± 0.09	3.41 ± 0.10	3.25 ± 0.10	2.56 ± 0.13
BEIM	6.45 ± 0.03	5.52 ± 0.05	4.28 ± 0.09	3.57 ± 0.08	3.53 ± 0.06	2.63 ± 0.09
MBPyr	6.86 ± 0.02	5.84 ± 0.00	4.59 ± 0.07	4.31 ± 0.20	3.81 ± 0.10	2.93 ± 0.11
AMIM	8.45 ± 0.02	6.68 ± 0.08	5.02 ± 0.19	4.06 ± 0.22	3.91 ± 0.017	2.91 ± 0.16
BzMIM	10.18 ± 0.00	7.89 ± 0.02	5.88 ± 0.05	4.74 ± 0.08	4.42 ± 0.03	3.39 ± 0.11
EBzMIM	12.54 ± 0.01	9.17 ± 0.06	6.62 ± 0.12	5.17 ± 0.22	4.65 ± 0.12	3.52 ± 0.05
HMPyr	13.85 ± 0.02	9.82 ± 0.04	6.88 ± 0.18	5.34 ± 0.21	4.70 ± 0.04	3.49 ± 0.10
HMIM	14.84 ± 0.01	10.08 ± 0.08	6.93 ± 0.12	5.30 ± 0.04	4.62 ± 0.04	3.40 ± 0.02
OMIM	–	–	15.40 ± 0.04	10.08 ± 0.14	7.06 ± 0.14	4.87 ± 0.05

9 mM MSA

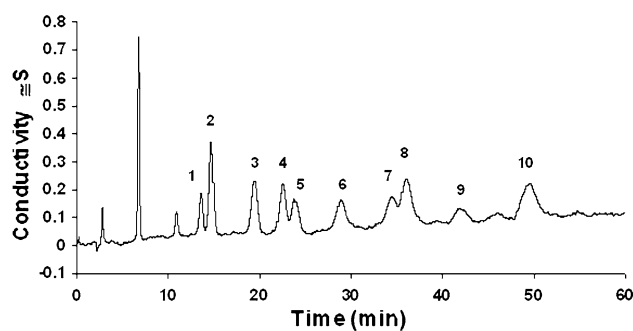| ACN	15%	20%	25%	30%	35%	40%
EEIM	3.60 ± 0.31	3.05 ± 0.51	2.66 ± 0.22	2.29 ± 0.10	2.13 ± 0.48	1.98 ± 0.46
PMIM	4.07 ± 0.22	3.36 ± 0.36	2.90 ± 0.37	2.48 ± 0.09	2.30 ± 0.53	2.11 ± 0.29
BMIM	6.28 ± 0.41	4.69 ± 0.22	3.81 ± 0.31	3.12 ± 0.07	2.77 ± 0.56	2.45 ± 0.46
BEIM	7.98 ± 0.33	5.61 ± 0.02	4.37 ± 0.57	3.49 ± 0.13	3.02 ± 0.33	2.54 ± 0.30
MBPyr	8.24 ± 0.26	5.88 ± 0.11	4.67 ± 0.37	3.74 ± 0.06	3.28 ± 0.42	2.85 ± 0.40
AMIM	11.46 ± 0.35	7.27 ± 0.46	5.43 ± 0.54	4.14 ± 0.05	3.47 ± 0.54	2.92 ± 0.29

Fig. 3 Chromatogram obtained from separation of a mixture of ionic liquid cations by isocratic elution with mobile phase consisting of 20% (*v/v*) acetonitrile and 80% (*v/v*) 5 mM MSA. *1* EEIM, *2* PMIM, *3* BMIM, *4* BEIM, *5* MBPy, *6* AMIM, *7* BzMIM, *8* EBzMIM, *9* HMPy, *10* HMIM

retention. BF_4 anions must form ion-pairs with IL cations, because the quantity of MSA anions has been reduced. IL cations are then retained inside the column, mostly by cation-exchange and polar interactions.

Determination of log k_w by IC

The retention times of all the IL cations eluted isocratically by acetonitrile–MSA mixtures were used for estimation of log k_w of the Snyder–Soczewinski equation (Eq. 2) (Table 2). log k_w characterizes the relative hydrophobicity of ILs and can serve as an alternative to the log P.

Hydrophobicity is important because of its effect on most of the important processes occurring in biological systems [25]. The shake flask experimental method, normally used for log P determination is time-consuming, expensive, poorly reproducible, and not suitable for ILs, because of their ionic character [14]. Therefore, other methods are needed for measuring the hydrophobicity of ILs. One of the possibilities are calculation methods. However, they are also more difficult for ionic compounds than for non-polar molecules, especially with independent atom coefficients or the presence of charge [26]. Also the manner in which a positive charge is delocalized in the IL cation is still not fully understood and is left for manual estimation [27].

The log P values calculated by use of HyperChem software are presented in Table 1. The calculation process performed with this software is based on an atom fragment method developed by Ghose et al. [28]. log P is estimated as a sum of atom-based fragment values and the charge of the analyzed cations is not considered. The molecules are treated as neutral species, therefore this method does not seem to be precise for ionic substances, especially ILs.

A more accurate method is estimation of log P for IL cations by other experimental technique, for example IC, used for the first time in this work. This technique enables

Table 2 continued

9 mM MSA

ACN	15%	20%	25%	30%	35%	40%
BzMIM	14.25 ± 0.07	8.86 ± 0.18	6.48 ± 0.39	4.86 ± 0.11	4.05 ± 0.52	3.39 ± 0.27
EBzMIM	19.10 ± 0.07	11.05 ± 0.21	7.61 ± 0.34	5.46 ± 0.06	4.42 ± 0.38	3.61 ± 0.23
HMPyr	22.15 ± 0.50	12.53 ± 0.26	8.19 ± 0.17	5.76 ± 0.04	4.55 ± 0.41	3.65 ± 0.25
HMIM	24.55 ± 0.43	13.49 ± 0.31	8.50 ± 0.15	5.82 ± 0.04	4.53 ± 0.35	3.57 ± 0.30
OMIM	–	–	26.18 ± 0.24	13.70 ± 0.03	8.64 ± 0.30	5.82 ± 0.26

Table 3 Correlation matrix of log k_w values for different concentration of MSA

log k_w (mM MSA)	1 (mM MSA)	2.5 (mM MSA)	5 (mM MSA)	7.5 (mM MSA)	9 (mM MSA)
1	1.00	1.00	0.97	0.96	0.97
2.5		1.00	0.97	0.96	0.97
5			1.00	1.00	1.00
7.5				1.00	1.00
9					1.00

Table 4 Slopes (*S*), intercepts (log k_w), numbers of data points used to derive the regression (*n*), and squares of correlation coefficient (R^2) of the Snyder–Soczewinski equation (Eq. 2)

IL cation	S	log k_w	R^2	n
EEIM	−0.9286	0.7616	0.9702	6
PMIM	−0.9732	0.8100	0.9730	6
BMIM	−1.2767	0.9932	0.9766	6
BEIM	−1.4904	1.1016	0.9672	6
MBPy	−1.3873	1.1088	0.9747	6
AMIM	−1.7747	1.2628	0.9726	6
BzMIM	−1.8489	1.3551	0.9774	6
EBzMIM	−2.1431	1.4980	0.9801	6
HMPy	−2.3211	1.5733	0.9807	6
HMIM	−2.4773	1.6277	0.9784	6
OMIM	−3.3113	2.1735	0.9986	4

determination of hydrophobicity in a more complex manner, because the log k_w value includes not only the ability to participate in hydrophobic interactions but also the ion-exchange potential of IL cations.

Considering that five different concentration of MSA were used, five values of log k_w were obtained for each IL cation. However, all the values of log k_w correlate significantly with each other as shown in the Table 3. Therefore, for further QSRR studies the log k_w corresponding to the retention factor in pure 7.5 mM MSA were selected, because these had the highest correlation coefficients between log k and φ. Table 4 summarizes regression data for determination of log k_w of the Snyder–Soczewinski equation (Eq. 2). This value increases with increasing molar mass for a series of imidazolium ILs and for arylimidazolium and pyridinium cations. Nevertheless, concluding that log k_w increase with increasing molecular mass for all ILs is wrong. The observed trend is valid only for series of cations with the same essential building units.

The highest correlation between log k and φ (Table 4) was achieved for IL cations of the highest hydrophobicity (Table 1). This effect is indicative of different retention mechanisms for polar and hydrophobic ILs in IC. All of studied cations interact with the stationary phase surface by an ion-exchange mechanism, but each of them with different strength. Moreover, low correlation for polar IL cations is probably the consequence of their stronger (in comparison with AMIM, HMIM, and OMIM) ability to interact by hydrogen bonding or other hydrophilic

interactions. For HMPy, EBzMIM, HMIM, and OMIM the correlation coefficients are approximately 0.98 (Table 4). The presence of long alkyl chains in the structure of the IL cations increases their hydrophobicity which probably determines their retention. It seems that the main interaction types are cation-exchange and hydrophobic, and that the participation of all polar bonds is slender.

Comparison of Calculated log P with log k_w

log k_w determined chromatographically and log P calculated by HyperChem software were both linearly regressed (Eq. 1). The coefficients characterizing this dependence are summarized in Table 5. The observed correlations were statistically significant, but very poor when log k_w and log P values for all cations (i.e., alkylimidazolium, arylimidazolium, and pyridinium) were used for calculations ($R^2 = 0.5911$). A significant improvement occurred if only data for *n*-alkylimidazolium cations were subjected to linear regression ($R^2 = 0.9689$).

This effect is closely connected with the structure of the IL cations and, as a consequence, with interactions in which those salts can participate. MBPy, HMPy, BzMIM, and EBzMIM contain several double bonds (delocalized electrons), which can interact strongly through π–π interactions. The structures of the other IL cations differ only in the number and position of methyl groups on the imidazolium rings. Alkyl chains participate in hydrophobic interactions, therefore the presented correlation is high,

Table 5 Regression coefficients (±SE), numbers of data points used to derive the regression (n), square of correlation coefficients (R^2), standard errors of the estimate (s), and F test values (F) of regression equations log $k_w = k_1 + k_2$ log P determined for IL cations

	k_1	k_2	n	s	F	R^2
7.5 mM MSA for all studied cations	0.8230 (±0.1557)	0.4141 (±0.1148)	11	0.2770	13	0.5911
7.5 mM MSA for n-alkylimidazolium cations	0.5719 (±0.0654)	0.6821 (±0.0547)	7	0.0971	156	0.9689

because the log P values also indicate the ability of compound to interact through hydrophobic forces. The high R^2 values for IL with the same building unit are also connected with the nature of Eq. 1, which works well only for analytes with similar structure, not differing in functional groups. Chromatographic retention (expressed as log k_w) and log P have different sensitivity to different interactions, especially hydrogen bonding.

Despite the low correlation for whole group of IL cations (Table 5), the column used in this study is suitable for prediction of log P for ILs with the same skeleton and alkyl substituents.

It does not seem to be very difficult to find a significant correlation for cations of a similar structure, where the differences in the retention are mainly because of one type of interaction. The major problem is to find such a good correlation for a mixture of substances of different structure, because competition among different types of interaction affects retention. However, more detailed study of a larger group of IL cations is needed. Such experiments are currently of interest to us.

Correlation of log k_w Determined by IC with log P Determined by the Shake-Flask Method

Comparison of log k_w data presented in this study with results obtained in several other investigations is complicated. First, there is little information about determination of log P for ILs by the shake-flask method, which is complicated for ionic compounds [29–31]. However, log P has been determined for [C$_4$MIM][Cl] (−0.31), [C$_8$MIM][Cl] (−0.27), [C$_{10}$MIM][Cl] (−0.20), [C$_{12}$MIM][Cl] (−0.14) [29], [C$_2$MIM][PF$_6$] (−1.82), [C$_4$MIM][PF$_6$] (−1.70) [30], [C$_4$MIM][BF$_4$] (0.003), [C$_4$MIM][NO$_3$] (0.0038), [C$_4$MIM][PF$_6$] (0.0220), [C$_4$MIM][Cl] (0.004), [C$_4$MIM][Br] (0.0033), [C$_2$MIM][Tf$_2$N] (0.09), [C$_4$MIM][Tf$_2$N] (0.11), [C$_6$MIM][Tf$_2$N] (1.42), and [C$_8$MIM][Tf$_2$N] (6.3) [31]. Only [BMIM][BF$_4$] was also the subject of our study. Another difficulty in comparison those two hydrophobicity measures (log k_w and log P) is concerned with differentiation of the IL cation and anion. In our investigation only cations were detected by the IC system, therefore log k_w are characteristic for these species. Results obtained by use of the shake-flask method represent the hydrophobicity of the whole molecule, and, as was proved in earlier studies,

the anion has a large effect on log P values [30, 31]. Although direct comparison of log P and log k_w is not appropriate, some trends are obvious. Chromatographic hydrophobicity measured by use of IC is higher than that determined by use of the conventional method.

Retention Data for QSRR

In QSRRs studies, two kinds of input data are needed: chromatographic retention data for a number of analytes and analyte-related properties. One QSRR approach was described in an earlier paragraph: relating log k_w to the logarithm of the n-octanol–water partition coefficient (log P). QSRR may be, however, performed in other ways, regressing log k_w against structural descriptors obtained by calculation chemistry. Therefore, to achieve a QSRRs model, compounds must be represented by a molecular descriptor (Table 1).

Multiple linear regression was used to generate QSRR equations for the eleven ILs. Several structural descriptors were chosen for the studies, namely log P, A_{SAS}, μ, PO, HE, and TE. Other descriptors were also considered and tested, but the equations derived using these were not statistically significant. Those descriptors were: net minimal charge (δ_{min}), net maximum charge (δ_{max}), binding energy, isolated atomic energy, electronic energy, heat of formation, molecular mass. Low correlation coefficients for log k_w and δ_{min}, δ_{max} were especially unexpected as it was assumed that charge would have an important effect on retention. On the other hand such descriptors as PO, A_{SAS}, and HE may be used for estimation of the ability of the analyte to undergo polar interactions.

Two-term QSRR equations using structural properties of IL cations obtained from molecular modeling calculations were found to describe isocratic retention in terms of log k_w; these are presented in Table 6. The calculations were performed to determine the hydrophobicity of IL in a more complex manner. Use of the most statistically significant equations enable estimation of log k_w, and, at the same time, log P (as it correlates well with log k_w) (Table 5).

QSRR Analysis

The two most statistically significant equations with high coefficients of determination (R^2) used log P, μ, A_{SAS}, and

Table 6 Regression coefficients (±SE), numbers of data points used to derive the regression (n), square of the correlation coefficients (R^2), standard errors of the estimate (s), and F test values (F) of regression equations determined for IL cations

	k_1	k_2	k_3	s	F	n	R^2
$\log k_w = k_1 + k_2 \log P + k_3 \mu$	0.5049 (±0.0676)	0.1822 (±0.0496)	0.0687 (±0.0085)	0.0916	85	11	0.9545
$\log k_w = k_1 + k_2 A_{SAS} + k_3 HE$	−2.3954 (±0.3065)	0.0090 (±0.0007)	−0.1813 (±0.0344)	0.0922	83	11	0.9540
$\log k_w = k_1 + k_2 A_{SAS} + k_3 TE$	−1.6697 (±0.2653)	0.0037 (±0.0008)	−0.00003 (±0.0000)	0.1067	64	11	0.9409
$\log k_w = k_1 + k_2 A_{SAS} + k_3 PO$	−1.5053 (±0.2818)	0.0037 (±0.0009)	0.0637 (±0.0165)	0.1196	52	11	0.9284

HE (Table 6). The first descriptor represents the ability of the IL cation to interact by hydrophobic forces. The dipole moment accounts for dipole–dipole and dipole-induced dipole attractive interactions of the analyte with the components of the competing mobile and stationary phase. A_{SAS} and HE are connected with polar interactions. The first is the molecular surface area accessible to water. It represents hydrophilic interactions which occur between water and other molecules in such a way that the other molecules are attracted to water. HE is the energy released when IL cations undergo complete hydration in aqueous solution. The contributions of those four descriptors to $\log k_w$ are dominant in the interaction of the IL cation and stationary phase molecules. Furthermore, R^2 for both equations is almost equal, which may suggest that those interactions, although varied in nature, have similar effects on $\log k_w$ (Table 6).

However, the main purpose of this contribution is to determine which interaction is dominant and, consequently, to find the optimum properties for chromatographic determination of $\log k_w$. For this reason other statistically significant equations were calculated (Table 6).

A high coefficient of determination was also obtained when A_{SAS} and the total energy of the IL cations were taken into consideration ($R^2 = 0.9409$) (Table 6). It seemed that both types of energy (TE and HE) affect the chromatographic retention of IL cations to a great extent, although the effect of TE is lower. On the other hand, when TE and HE are used in QSRR calculations together, they do not correlate well with $\log k_w$ ($R^2 = 0.8788$).

Interesting are results presented for QSRR calculations with descriptors which refer to hydrophobic and polar interactions. The last equation in Table 6 combines A_{SAS} and PO. PO gives information about molecular shape, the electronic charge distribution in the molecule. PO is the relative tendency of charge distribution by an external electric field, which may be caused by the presence of a nearby ion or dipole. The strength of the dispersive interactions of a substance containing no dipoles is related to its polarizability. The high R^2 value for this equation may suggest that for $\log k_w$ of ILs hydrophilic and dispersive interactions are equally important. However, cation exchange is also important.
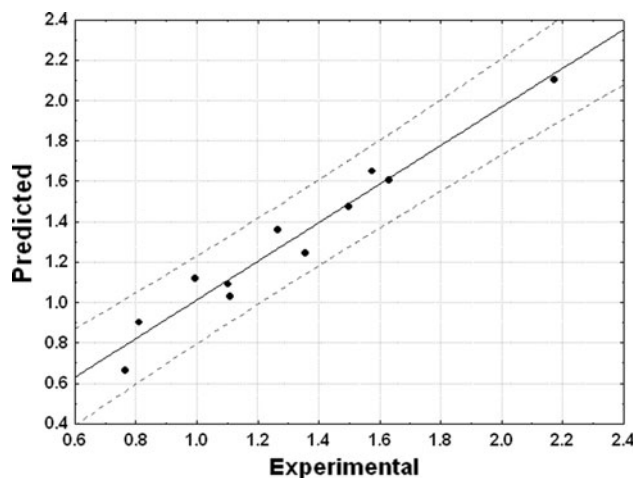
Fig. 4 Relationship between $\log k_w$ determined experimentally (Table 5) and calculated theoretically with first equation presented in Table 6

Use of QSRR for investigation of IL cations in IC enables evaluation of $\log k_w$ by use of suitable descriptors. Figure 4 presents the correlation between experimentally determined $\log k_w$ and the same property calculated by use of the equation with the highest correlation coefficient ($R^2 = 0.9545$).

Conclusion

The retention of IL cations strongly depends on the stationary phase surface and on mobile phase composition. If IL cations are eluted from a weak cation-exchange column with carboxylate and phosphonate cation-exchange sites and crown ether groups with acetonitrile–methanesulfonic acid as mobile phase, their retention mostly depends on their hydrophobic properties and they are eluted in reversed-phase order if the amount of ACN is <60% (v/v). However, the cations follow normal-phase elution when the amount of ACN is increased to 65% (v/v).

IC enables determination of chromatographic hydrophobicity $\log k_w$. Its values are higher than $\log P$ estimated by the shake-flask method, but they include many more interactions in which ILs participate during the partition

process. The QSRR equations confirm the importance of hydrophobic interactions, dispersion interactions, and dipole–dipole and dipole-induced dipole attractive interactions in retention, as a result of their relationship with $\log k_w$.

This paper reports the first work describing use of data from ion chromatography of IL cations in QSRR. Further investigations should be undertaken, in particular to investigate the importance of stationary phase and mobile phase's composition, and investigation of more ILs.

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