Investigation on Aggregate Formation of Ionic Liquids

Sandra Dorbritz, Wolfgang Ruth, Udo Kragl*

Institute of Chemistry, University of Rostock, Albert-Einstein-Strasse 3a, 18059 Rostock, Germany
Fax: (+49)-381-498-6452, e-mail: udo.kragl@uni-rostock.de

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Abstract: Understanding the behavior of ionic liquids on the molecular level is essential for explaining solubilizing or reaction processes, including catalytic reactions in ionic liquids or with ionic liquids as co-solvent. Using mass spectrometry techniques it is possible to characterize their aggregate formation behavior, which depends on the used solvent. With increasing polarity of the solvent and decreasing ionic liquid concentration, the size of the formed aggregates decreases. From conductivity measurement curves "critical aggregate concentrations" were calculated, which confirm the results of mass spectrometry measurements. Addition of ionic liquids increases the solubility of acetophenone in water. This effect can be explained by the aggregate formation ability of ionic liquids. The findings can be used to explain the outstanding solubility and solvation properties of ionic liquids.

Keywords: aggregates; biocatalysis; conductivity; ionic liquids; mass spectrometry

Introduction

The interest in ionic liquids (IL) is increasing from year to year. There exists nearly no field in chemistry or biochemistry that is not involved in ionic liquid research and progress. Ionic liquids serve as solvent or co-solvent for enzyme reactions[1] or whole cell processes,[2] common organic reactions like Friedel–Crafts alkylation and acylation,[3] and as reaction media for transition metal catalysis.[4] They are also successfully applied as medium for electrochemical purposes.[5] As extraction medium they are suited for the recovery of biofuels[6] and deep desulfurization processes of oils.[7] With this article we want to characterize selected ionic liquids on the molecular level. We also try to explain some of the effects observed when they are used in practical applications.

Hydrotropes are often used in catalytic reaction processes.[8] Hydrotropes induce a characteristic steep increase in aqueous solubilities of hydrophobic compounds around a certain characteristic concentration. ILs can be assigned to some extent to this group. For organic synthesis hydrotropes are used in the microwave-enhanced Hantzsch dihydropyridine ester synthesis and the Claisen–Schmidt reaction in aqueous solution. Hydrotropes enhance rates of reactions in multiphase transformations, which can lead to autocatalysis in the biphasic alkaline hydrolysis of aromatic esters. In addition, hydrotropes also find application in formulations of pharmaceuticals and especially in extraction and separation processes.[8]

As an example for solubility-increasing effects, we describe the assistance of the IL 1-butyl-3-methylimidazolium tetrafluoroborate [BMIM][BF$_4$] or 1,3-dimethylimidazolium methyl sulfate [MMIM][MeSO$_4$] in the dissolubility process of acetophenone in water. Like some hydrotropes ionic liquids form small aggregates. Here we show that ionic liquids form solvent-dependent aggregates. Indeed, hydrotropes do not form such large aggregates as surfactants do. But ILs show, for instance, a positive test on surfactant behavior using PAN-dye [1-(2-pyridylazo)-2-naphthol].

As described by other research groups it is possible to prove and characterize the existence of aggregates in solutions by electrospray ionization mass spectrometry (ESI-MS).[9] We used this technique to determine the solvent dependence of aggregate formation. From conductivity measurements it is possible to determine the "critical aggregate concentration" (CAC). The CAC is comparable to the "critical micelle concentration" (CMC) of surfactants.

Results and Discussion

Mass Spectrometry Measurements

When injecting IL solutions into the mass spectrometer, spectra with signals in regular distances corresponding to the molar mass of the ionic liquid appear. Displayed are actually distances in mass to charge ratio. Indeed it could be shown, by high resolution scans, that all conglomerates are singly charged. Using these kinds of scans the $^{12}C/^{13}C$ isotopic separation is evaluated accurately. It is either possible to determine positive or negative ions in the ESI-modus (Figure 1).

An example for [BMIM][BF$_4$] (structure is given in Figure 1) in methanol, measured in the positive ion mode, is represented in Figure 2. Brackets clarify aggregate signals and m/z distances. As can be seen, the smallest signal detected belongs to the single [BMIM] ion. Following in regular distances are signals with the composition $C_nA_{(n-1)}$. Highest in intensity is an aggregate formed of two cations and one anion. Due to their low intensity the following signals are hard to recognize. Therefore, the interesting area is amplified and shown as insert. Again, we could prove that the aggregates belonging to the signals are singly charged. So in addition to MS/MS measurements the origin of the signals is well defined. Small deviations of the signal mass, compared to the calculated mass of the aggregate, are due to isotope effects. As the abundance for the ^{10}B isotope is 19.9% and for the ^{11}B isotope 80.1%,[10] there is a shift to smaller m/z values for larger aggregates, containing more boron atoms. When amplifying a signal, the isotope pattern can be recognized easily (Figure 2).

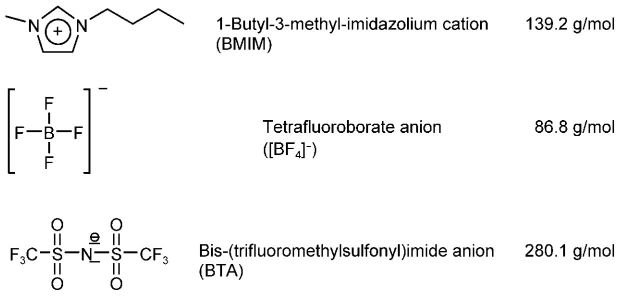

Figure 1. Structures of (**a**) [BMIM][BF$_4$] and (**b**) [BMIM][BTA].

In Figure 3 are shown the spectra of methanolic [BMIM][BF$_4$] solutions with different concentrations of ionic liquid, measured in the positive ion mode. As can be recognized by the brackets, size and distribution of the aggregates change with concentration. Signal intensity of larger aggregates increases with increasing concentration. For the 10^{-4} mol/L mixture only the single cation and the aggregate built of two cations and one anion can be found. For the 10^{-1} mol/L mixture a complete series of aggregates within the measurable range is detectable. In addition the signals (in the amplified region) are easier to recognize as the signal to noise ratio improves (Figure 3).

In Figure 4 are presented spectra for 10^{-1} mol/L [BMIM][BF$_4$] solutions in different solvents, measured in the negative ion mode. Differences in aggregate formation behavior are easily seen. In water, only small aggregates like CA_2 und C_2A_3 are formed. They are only partly detectable within the noise. Of course, the single anion can be found as well (at $m/z = 86.8$). It is not displayed in order to show larger aggregates clearly. In the spectrum obtained for methanol larger aggregates can be found compared to the spectrum obtained for water. The intensive signals for the smaller aggregates can be distinguished from the noise easily. With decreasing polarity of the solvent the formation of higher aggregates is facilitated, giving evidence for all possible aggregates within the range of measurement (2-propanol). The spectra are clear, and nearly no noise is detectable.

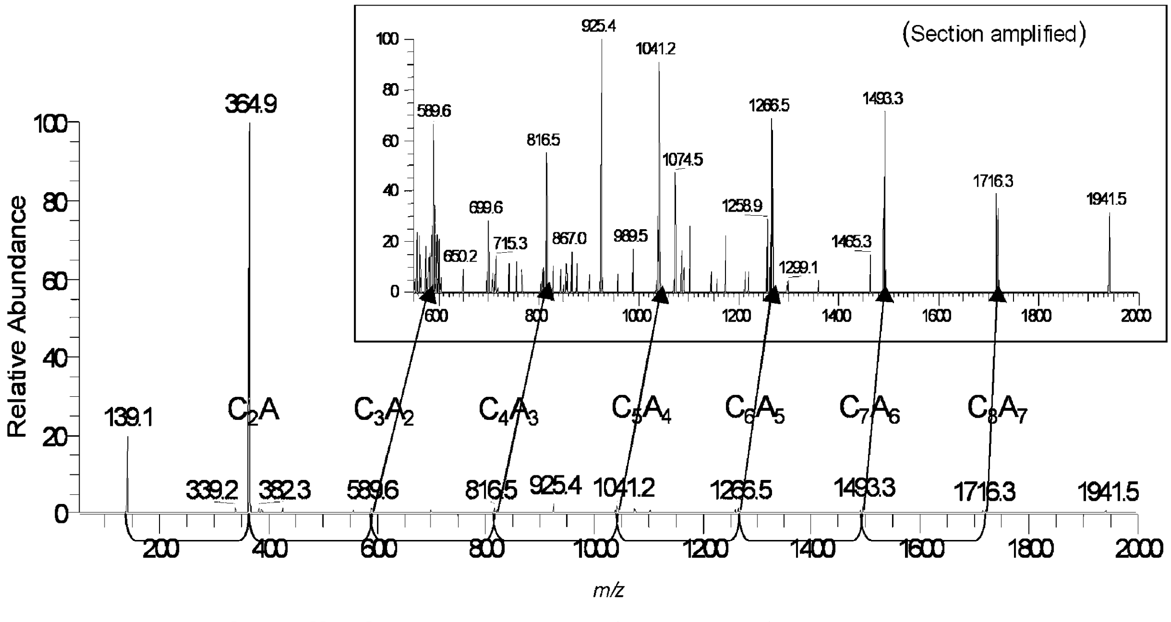

Figure 2. Spectrum of 0.1 M [BMIM][BF$_4$] solution in methanol (positive mode).

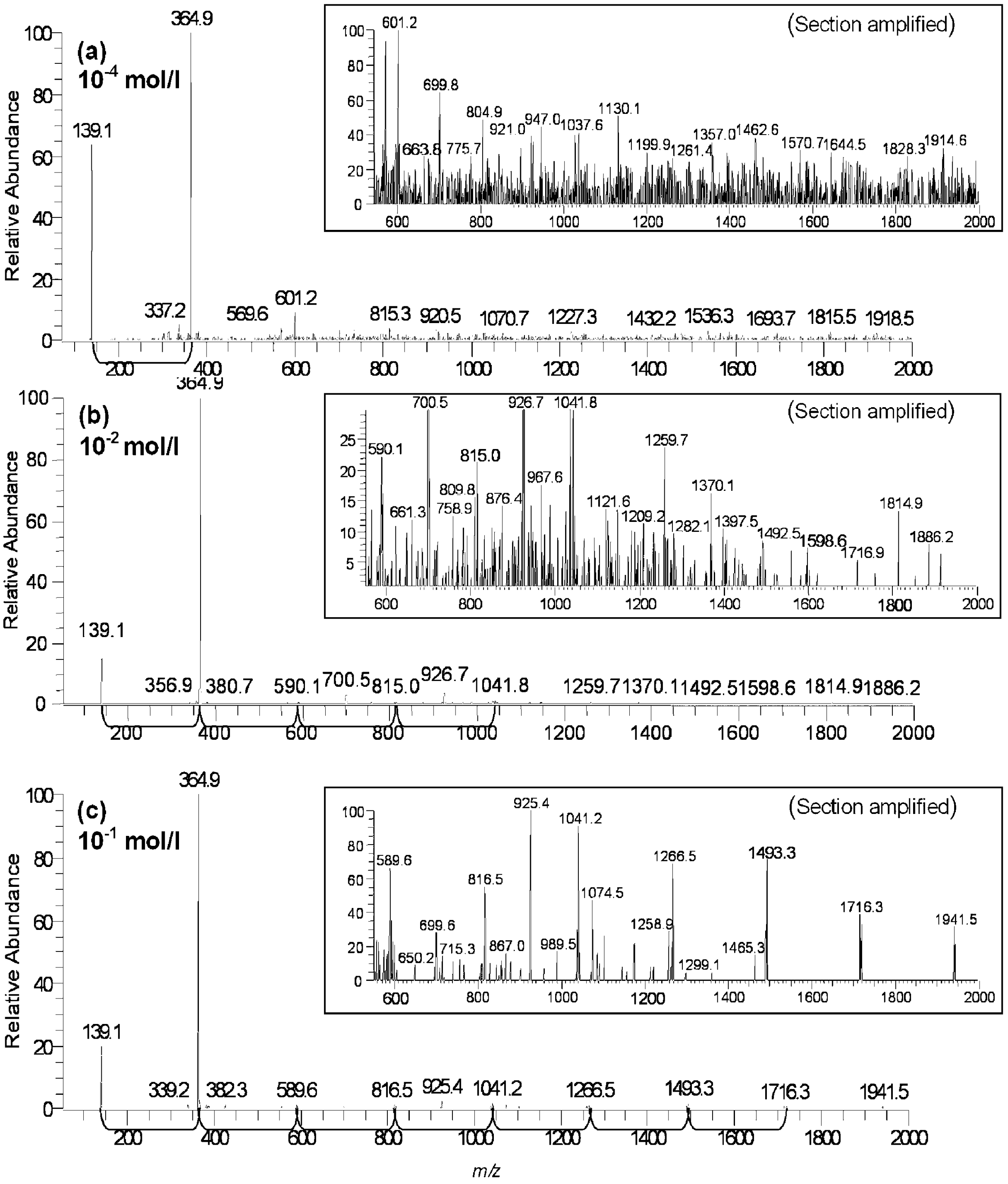

Figure 3. Spectra of [BMIM][BF$_4$] solutions in methanol, (**a**) 10^{-4} mol/L, (**b**) 10^{-2} mol/L, (**c**) 10^{-1} mol/L (positive mode).

Similar results can be found for [BMIM][BF$_4$] in ethyl acetate. The small CA$_2$ aggregate is not even formed here. All in all, it can be observed that the ionic liquid adapts to its environment. The smaller the E$_T$(30) values (according to Reichardt)[11] of the used solvent, the larger are the formed aggregates and the more distinct the signals from the noise (see Table 1). We believe that the aggregate formation, especially in less polar solvents, is probably necessary to minimize the charge density within the ions (Figure 4).

Similar observations can be made for spectra of the water non-miscible 1-butyl-3-methyl-imidazolium bis-(trifluoromethanesulfonyl)imide [BMIM][BTA] solvent mixtures (see Supporting Information). Admittedly, differences are not as obvious here as for spectra of the water-miscible [BMIM][BF$_4$]. We assume that the existence of the larger anion minimizes the need of charge delocalization by forming aggregates.

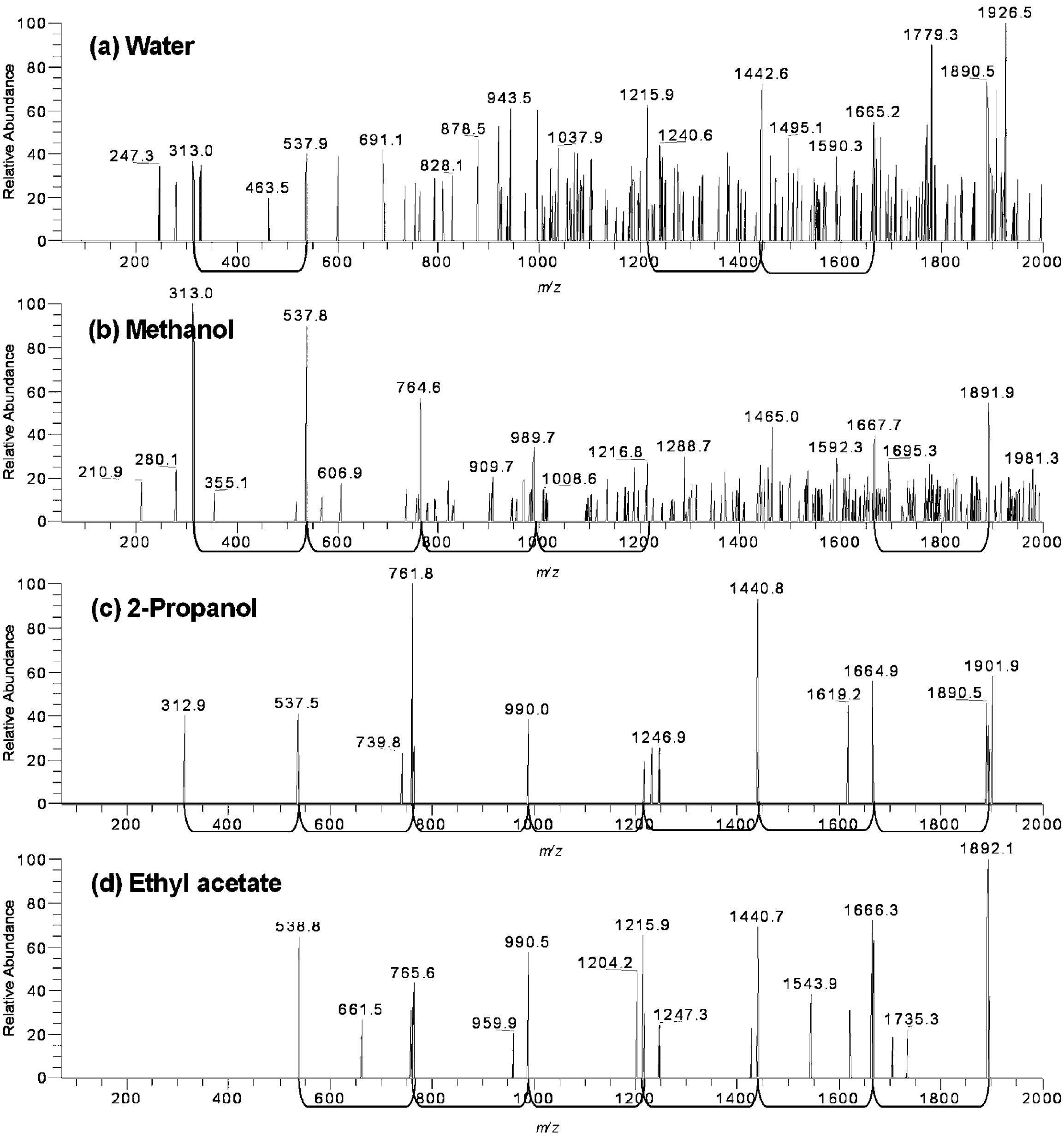

Figure 4. Spectra of 0.1 M [BMIM][BF_4] solutions in (**a**) water, (**b**) methanol, (**c**) 2-propanol, (**d**) ethyl acetate (negative mode).

Conductivity Measurements

In order to gain further evidence for the aggregate formation and to make sure that there are no artefacts formed during MS measurements, the conductivity of ionic liquid solutions in some solvents was measured as a function of concentration. From these conductivity-concentration graphs the "critical aggregate concentration" (CAC) of the ionic liquid can be determined. The CAC is comparable to the "critical micelle concentration" (CMC) of surfactants. Admittedly, agglomerates built of ionic liquids are much smaller than the ones built of surfactants. An example for a complete graph is shown in Figure 5a. Similar graphs were obtained by Hussey and co-workers, but by adding a non-soluble organic solvent (benzene, CH_2Cl_2) to an ionic liquid.[12] The graph is divided into a part of increasing and one of decreasing conductivity, depending on the added amount of solvent. This graph is a result of several effects influencing the measured conductivity. With increasing ionic liquid concentration the conductivity increases as expected. However, there is a deviation from the expected linear behavior, which can be ascribed to two effects: i) increase of viscosity and therefore reduction of the mobility of the charge carriers; ii) reduction of the number of the charge carriers due to the

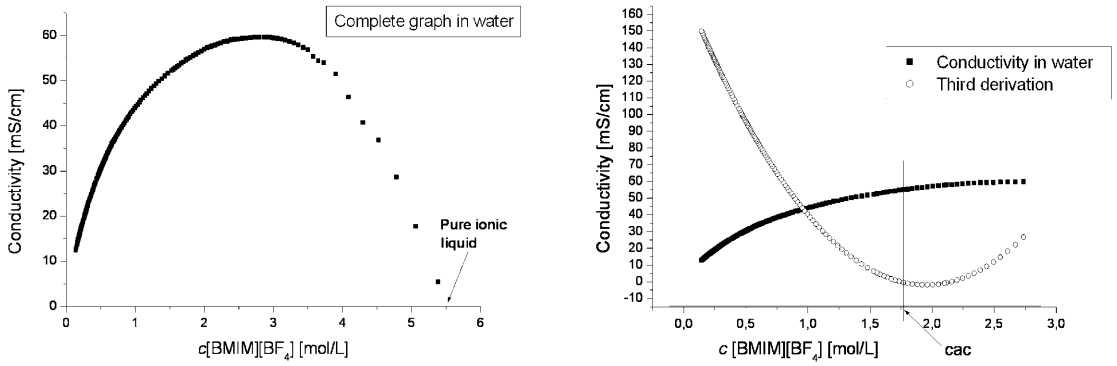

Figure 5. Conductivity graphs for [BMIM][BF_4] in water at 30 °C. (**a**) Complete graph, (**b**) Increasing part of the conductivity graph with its third derivation for CAC determination.

aggregate formation. These latter effects become dominant at higher concentrations, thus leading to a strong decrease of conductivity (Figure 5).

The CAC can be determined using the first part of the graph. The CAC is the concentration at which the change in conductivity has its highest value. This point can be easily recognized using a higher deviation. Thus, the measured data were fitted using Microcal Origin from Microcol Software, Inc., Northampton, MA, USA. The concentration at which the third derivation becomes zero, is the "critical aggregate concentration" (CAC). The CAC estimated for various solvents are listed in Table 1.

In accordance with the aggregate formation observed by mass spectrometry, the CAC of the water-miscible [BMIM][BF_4] decreases with increasing hydrophobicity of the solvent, which is also indicated by decreasing E_T (30) value. The larger the formed aggregates are, the earlier (in concentration) the critical point is reached. As also expected, conductivities decrease at a given concentration with the E_T(30) values of the used solvent. In water or methanol the formed aggregates are smaller. Thus the mobility of the charge carriers is larger than it is for larger aggregates. In addition, when forming smaller aggregates a higher number in free carriers is available at a given concentration.

Bowers and co-worker determined for [BMIM][BF_4] in water a CAC of 0.82 mol/L (*T* 25 °C).[13] Our result of 1.81 mol/L (*T* 30 °C) is much higher but within the same order of magnitude. We analyzed our ionic liquid using ion chromatography for traces of chloride and fluoride and Karl–Fischer titration for traces of water. These three compounds are the most common impurities. The level of impurity was negligible for all compounds. The difference to the results of Bowers might to a certain extent be ascribed to different measuring temperatures. For our measurements we used two different batches of the ionic liquid with the same result, respectively. The water-non-miscible [BMIM][BTA] is difficult to analyze directly. Attempts to extract chloride, which is the main impurity from synthesis, and analyzing the aqueous extract did not show impurities.

For [BMIM][BTA] in methanol a CAC of 0.99 mol/L could be determined, which is slightly smaller than the value for [BMIM][BF_4] in the same solvent. The result is not astonishing when comparing the spectra for both compounds. As already mentioned, it is possible that due to the larger anion a charge delocalization by aggregate formation is not necessary at such high level as for the tetrafluoroborate-anion.

Acetophenone Solubility

As can be seen from Figure 6, it is possible to increase the solubility of acetophenone in water by adding an ionic liquid – in our case [BMIM][BF_4]. The same effect can be observed by adding [MMIM][$MeSO_4$].[14] Acetophenone is very often used in enzyme catalysis as substrate, especially when comparing novel enzymes such as alcohol dehydrogenases with respect to their catalytic activity against aromatic or hydrophobic ketones. Also the conversion of hydrophobic ketones such as octanone either in one- or two-phase systems is of high interest.[15]

Table 1. Results of conductivity measurements for [BMIM][BF_4] at 30 °C.

Solvent	CAC [mol/L]	E_T(30)[11] [kcal/mol]	Conductivity at CAC [mS/cm]
Water	1.81	63.1	55
Methanol	1.62	55.4	41
2-Propanol	0.09	48.4	0.4
Ethyl acetate	0.03	38.1	0.01

Ionic liquids, which have a stabilizing effect on many enzymes, might be an interesting opportunity. We attribute the observed solubility-increasing effect to the formation of aggregates of IL– and acetophenone – molecules. Due to concentration effects, it was not possible to analyze the formation by mass spectrometry. Similar experiments, concerning attempts to increase the solubility of acetophenone by adding conventional salts with small cation and anion, were not successful (Figure 6).

Conclusions

Using mass spectrometry or conductivity measurements, it is possible to explain the outstanding solubility and solvation properties of several ionic liquids to a certain extent. Ionic liquid solutions can be characterized on the molecular level, which is very important for finding novel applications either in (bio)catalysis or, e.g., extraction. Both of the tested ionic liquids, the water-miscible [BMIM][BF_4] as well as the water-non-miscible [BMIM][BTA], form aggregates. Their size depends on the solvent used and the IL concentration. The formation of aggregates is also affected by the anion structure of the IL. Ionic liquids can also be used to improve the solubility of hydrophobic compounds. The solubility of acetophenone solubility, which is very important especially in the field of enzyme catalysis, can be increased by [BMIM][BF_4] by a factor of 10. The increase in the solubility of acetophenone is only one example for the very advantageous solvation properties of ionic liquids, which can be explained mainly by their aggregate formation ability and therewith by their ability to adapt to their environment. Information about this behavior is also of importance when dealing with the behavior of ionic liquids in the environment and, e.g., their biotic degradation.

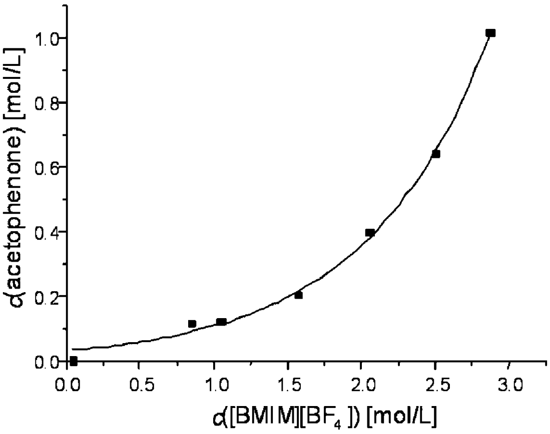

Figure 6. Solubility of acetophenone in aqueous [BMIM][BF_4] solutions.

Experimental Section

Materials

[BMIM][BTA] was synthesized in our laboratory.[16] [BMIM][BF_4] was purchased from Solvent Innovation, Cologne, Germany. For quality control of the ionic liquids we used Karl–Fischer titrations for residual water analysis. Determinations were carried out in a 756 KF Coulometer from Metrohm AG, Herisau, Switzerland. For the determination of chloride and fluoride impurities in [BMIM][BF_4] we used ion chromatography [column: Phenomenex Star-Ion-A300 (Metrohm AG), eluent: Na_2CO_3 (1.3 mmol/L)/$NaHCO_3$ (2 mmol/L), flow: 0.6 mL/min, room temperature). [BMIM][BF_4] could be used without further reconditioning. [BMIM][BTA] was of similar purity.

Used organic solvents (methanol, 2-propanol, ethyl acetate) were all HPLC Gradient Grade and purchased from T. J. Baker, Deventer, The Netherlands. The used water was deionized, and organic residues were removed (0.055 μS/cm). Acetophenone (p.a., > 98%) was obtained from Merck-Schuchardt, Hohenbrunn, Germany.

Conductivity Measurements

Conductivity measurements were all carried out at 30 °C in closed, thoroughly cleaned, and dried glassware. The used conductivity sensor SE 204 is integrated in the Portamess 910 from KNICK, Berlin, Germany.

Mass Spectrometry Measurements

All mass spectrometry measurements were carried out using an LCQ Advantage HPLC/MS from ThermoFinnigan, San Jose, Ca, USA. All solutions were directly introduced into the MS *via* a syringe pump (ESI as ionization method, sheet gas: nitrogen, flow: 10, no auxiliary gas). The HPLC device was not in use. The applied software was Xcalibur 1.3 from ThermoFinnigan.

Determination of Solubility of Acetophenone

Solubilizing experiments were carried out at 25 °C. To aqueous [BMIM][BF_4] solutions of different concentrations different amounts of acetophenone were added. The two-phase system was shaken for 6 hours with a speed of 1200 rpm. After settling of the phases the aqueous phase was separated, diluted and analyzed by HPLC [column: Nucleosil 100C18 (Knauer, Berlin, Germany), eluent: $MeOH/H_2O = 1/1$, flow: 0.8 mL/min, *T* 25 °C, UV detector: $\lambda = 242$ nm for acetophenone).

PAN Test

PAN dye was dissolved in pentane. 10 μL of this mixture were added to 500 μL of an aqueous [BMIM][BF_4] solution (40 vol %) and shaken.

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