Contents lists available at ScienceDirect

International Journal of Mass Spectrometry

Solvent effects on surface activity of aggregate ions in electrospray ionization

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A B S T R A C T

A principal feature of electrospray ionization (ESI) is the transfer of ions in solution into the gas-phase for analysis by mass spectrometry. The electrospray process is intricate and therefore each stage of the process must be well-characterized in order to optimize the quality of the data obtained. The surface activity of a given ion is a substantial factor in its likelihood of evaporating from droplets formed by the electrospray, and leads to a differential response of one ion over another. Consequently, investigation of the response of a variety of ions in multiple solvents lends insight toward both desolvation processes and the surface activity of the ions studied in the chosen solvent. In the present work, a cationic ionic liquid, butyl methylimidazolium (BMIM), was paired with a counterion and mixed in various solvents. Subsequently, BMIM paired with a different counterion was added to the solution and analyzed by ESI mass spectrometry to determine the relative response ratio between two observable aggregates. The findings assist in the elucidation of differential surface activity of chemically distinct ions in ESI, with respect to changes in solvent. Furthermore, the results obtained suggest acetonitrile is an optimal solvent for the analysis of ions of this type due to a reduction in differential effects, whereas other common ESI solvents prove to enhance the surface activity of specific aggregate ions.

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1. Introduction

Surface activity is a broad term used in many fields of chemistry including catalysis [1], adsorption [2], host–guest interactions [3,4] and nanoparticles [5,6]. In electrospray ionization mass spectrometry (ESI-MS), surface activity is intricately involved with the mechanism by which charged ions are produced [7–11]. Consider the case where two ions, A^+ and B^+, are present in a solution. If the solvent selected is most different in nature from A, this ion will prefer to be present at an interface which minimizes its overall solvation [7]. If the container in question is a semi-spherical electrospray droplet, the ion A will partition as much as possible to the outer layer becoming surface active, while ion B resides preferentially in the core of the droplet due to its better solvation [7,12]. Essentially, ions that are the least well solvated and/or ion paired are most likely to be found on the surface of a droplet rather than buried in the interior, and so are over-represented in the

spectrum because they are the ions most likely to evaporate from the droplet first [13]. For ions with similar properties, ESI provides a good match between concentration and abundance but, for ions that differ greatly in size or polarity, the results obtained may become distorted from those of the original solution analyzed [12,14]. The nature of the solvent will affect the absolute instrumental response of the ions as well, so we might expect water to have quite different effects compared to dichloromethane, and we would expect methanol and acetonitrile to have effects somewhere between the two extremes [12,14]. The situations in which bias occurs must be understood and accounted for to insure that any ESI-MS data have real quantitative meaning [15].

We wanted to compare the effects of different solvents on the relative propensity of particular ions to appear in the spectrum. Aggregate ions are a common feature of ESI mass spectra, and are even exploited for calibration purposes. The aggregates are of the form $[(\text{cation}_{n+1}(\text{anion})_n]^+$ in the positive ion mode and $[(\text{cation})_n(\text{anion})_{n+1}]^-$ in the negative ion mode. For example, a solution of potassium iodide produces aggregates of the form $[(K)_{n+1}(I)_n]^+$ which are used for mass spectrometer calibration in the positive ion mode. Ionic liquids [16] display this property quite strongly [16], and these "gaseous supramolecules" have been studied in detail [17]. Concentrated solutions (10^{-4} mol L^{-1}) are dominated

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by the aggregates, which become less prominent as the concentration diminishes. ESI-MS of dications with mixed counterions of the form [dication][I][NTf$_2$] exhibit positive ions of the type [dication + NTf$_2$]$^+$ preferentially over [dication + I]$^+$, but most markedly in water > methanol > acetone > acetonitrile [18]. However, there are no competitive experiments that we know of that have compared the relative propensity of aggregate ions to appear depending on their nature, nor have such experiments been conducted in different solvents.

We chose five butylimidazolium (BMIM) salts for the investigation (see Table 1 for their physical properties, along with those of water for comparison), with anions ranging from the small and hydrophilic chloride ion to the large and hydrophobic bis (trifluoromethanesulfonyl) imide ion, [N(SO$_2$CF$_3$)$_2$]$^-$ (also known as bistriflimide and abbreviated [NTf$_2$]$^-$). Table 2 details the size, surface area and volume of these anions, along with the standard molar Gibbs transfer energy for anions from water to 60:40 methanol/water (a measure of hydrophilicity).

2. Materials and methods

All salts were purchased from Sigma–Aldrich and used as received, except for [BMIM][NTf$_2$] whose preparation was based on a literature procedure [28]. Lithium bis(trifluoromethanesulfonyl) imide (0.8 g, 0.003 mol, Aldrich) and 1-butyl-3-methylimidazolium chloride (0.5 g, 0.003 mol, TCI America) were each dissolved separately in 50 mL of deionized water. The lithium solution was added to the [BMIM]Cl solution with stirring. The solution became milky immediately and was allowed to sit for 45 min. The solution was heated at 55 °C for 15 min after which point small oily droplets could be observed in the bottom of the flask. This material was extracted with dichloromethane (3 × 15 mL). The organic layer was washed with deionized water (5 × 10 mL) to remove any residual lithium chloride and starting material. The dichloromethane was removed via rotary evaporation resulting in 1.0 mL of liquid. The material was dried under vacuum for 48 h prior to use.

For each test a stable MS signal of a diluted ionic liquid (IL) was obtained (concentrations were 40 μM, 4 × 10^{-5} M). A second solution containing a different IL (in the same solvent) was then added in equal volume. The peaks monitored in this experiment were those representing the [(BMIM)$_2$ + anion]$^+$ cations. For comparison of IL signal intensity a response ratio, defined as the peak area of the IL of interest divided by the second IL peak area, was calculated. In the absence of any signal response discrimination this procedure was expected to result in halving of the signal for the initial IL ions present while a secondary peak should also be observed at equal intensity for the IL added. If one signal is obviously favored, it can be surmised that the ion-solvent interaction for that ion is less favorable resulting in surface enrichment and suppression of the other ion. The clusters were examined in the positive ionization mode using the full scan MS function on a Micromass Q-Tof micro™ mass spectrometer. Cone

voltage was set low to minimize fragmentation of the aggregate ions.

Mass spectra were collected on a Micromass Q-ToF micro™ mass spectrometer using pneumatically-assisted electrospray ionization. Capillary voltage: 2900 V. Cone voltage: 10 V. Extraction voltage: 0.5 V. Source temperature: 80 °C. Desolvation temperature: 150 °C. Cone gas flow: 100 L/h. Desolvation gas flow: 200 L/h. Scan time was 3 s and the inter scan time was 0.1 s.

3. Results

Each of the possible combinations of anions were mixed as their BMIM salts in a 1:1 ratio and the relative ratio of the peak areas of the two different aggregate ions [(BMIM)$_2$ + anion]$^+$ measured in four different solvents: equal parts water/acetonitrile, methanol, acetonitrile, and dichloromethane (Table 3). [BMIM]Cl was not soluble in solvents less polar than dichloromethane, and [BMIM][NTf$_2$] was not soluble in pure water, so these salts set the boundaries of what solvents we could reliably study.

Chloride is the smallest of the anions examined and most likely to be strongly solvated by polar solvents, but is least well solvated by non-polar solvents. The degree to which an analyte's hydrophobicity influences ESI response may be estimated, and because of this, it is expected that more hydrophobic analytes will produce a greater ion count in a mass spectrum [27]. As such, chloride aggregates should be under-represented compared to large, hydrophobic anions in polar solvents, but the reverse should be true in non-polar solvents. This effect is indeed observed; most dramatically in matchups against [PF$_6$]$^-$ and [NTf$_2$]$^-$. Response factors between the BMIM aggregates of chloride and the other anions are similar in acetonitrile, but the [(BMIM)$_2$ + Cl]$^+$ aggregate ion is barely detectable in water/acetonitrile and methanol. Conversely, the [(BMIM)$_2$ + Cl]$^+$ aggregate ion is over-represented against all others in dichloromethane, suggesting that the droplet partitions the chloride ions preferentially at the surface. Fig. 1(a–d) shows the relative intensity comparison between Cl$^-$ and [NTf$_2$]$^-$ aggregate ions in water/acetonitrile, methanol, acetonitrile, and dichloromethane.

It is worth noting that the values observed above were subject to significant variation depending on exact instrumental conditions. The position of the spray head, desolvation, cone gas flow rates, cone voltage, source, desolvation gas temperature, sample concentration etc, all affected the exact ratios obtained. However, the general trends were reproducible.

Iodide is overrepresented with respect to chloride in water/acetonitrile, but underrepresented in other solvents. When iodide is matched up against the other counterions, the only dramatic difference is seen in the acetonitrile/water and methanol against [PF$_6$]$^-$ and [NTf$_2$]$^-$, where iodide is strongly underrepresented. The iodide aggregate is consistently less abundant than the [BF$_4$]$^-$ aggregate in all solvents, but the difference is least marked in the less polar solvents. The similarity between [BF$_4$]$^-$ and iodide is borne out when it is matched up against the larger anions. The

Table 1
Physical properties of water and five butylimidazolium salts [19–22].

Substance	Surface tension (dyn cm^{-1} at 25 °C)	Melting point (°C)	Density (g mL^{-1} at 25 °C)	Dipolarity/polarizability (40 °C)	Molar mass (g/mol)
Water	73	0.0	0.997	n/a	18.0
[BMIM]Cl	n/a (solid)	41	1.08	2.247	174.7
[BMIM]I	54.7	−72	1.44	n/a	266.1
[BMIM][BF$_4$]	46.6	−81[a]	1.12	1.647	226.0
[BMIM][PF$_6$]	48.8	10[a]	1.368	1.914	284.2
[BMIM][Tf$_2$N]	37.5	−25[b]	1.436	1.889	419.4

[a] Dried.
[b] Water equilibrated.