CHARACTERIZATION OF IONIC LIQUID AS A CHARGE CARRIER FOR THE
DETECTION OF NEUTRAL ORGANOMETALLIC COMPLEXES USING
ELECTROSPRAY IONIZATION MASS SPECTROMETRY

Ubisha Joshi, B.S.

Thesis Prepared for the Degree of
MASTER OF SCIENCE

UNIVERSITY OF NORTH TEXAS

August 2012

APPROVED:

Guido F. Verbeck, Major Professor
Teresa Golden, Committee Member
Justin Youngblood, Committee Member
William E. Acree, Chair of the Department of Chemistry
Mark Wardell, Dean of the Toulouse Graduate School
Joshi, Ubisha, *Characterization of ionic liquid as a charge carrier for the detection of neutral organometallic complexes using electrospray ionization mass spectrometry*. Master of Science (Chemistry), August 2012, 57 pp., 2 tables, illustrations, references, 56 titles.

A novel application of ionic liquid as a charge carrier for the analysis and detection of neutral organometallic complexes using a mass spectrometer has been presented. The mass spectrometer detects only charged compounds which raise a difficulty in analyzing a neutral molecule that lacks a basic site to associate with charge. Therefore, an effective way of providing charge has always been an area of keen interest in the field of mass spectrometry. Ionic liquids have a very fascinating property of forming a cation-π interaction with other molecules to give a charged complex. In order to take advantage of this, it is important to know the geometric structure of the complex. Advanced methodologies like hydrogen-deuterium exchange and computational calculations have been used assisting in better understanding of the structure of the ionic liquid complexes.
Copyright 2012

By

Ubisha Joshi
ACKNOWLEDGEMENTS

I would like to thank to my research advisor Dr. Guido F. Verbeck for his assistance and support throughout my studies and research, also entire Verbeck research group for their support and assistance.

I would like to acknowledge Dr. Sergei V. Dzyuba from Texas Christian University, Forth Worth, Texas for providing the ionic liquids. Dr. Justin Youngblood from University of North Texas, Denton, Texas for providing the organometallic complexes. William Hoffman and Barbara Walton from Dr. Verbeck’s research group for assisting with H-D exchange experiment.
# TABLE OF CONTENTS

<table>
<thead>
<tr>
<th>Chapters</th>
<th>Page</th>
</tr>
</thead>
<tbody>
<tr>
<td>ACKNOWLEDGEMENTS</td>
<td>iii</td>
</tr>
<tr>
<td>LIST OF TABLES</td>
<td>vi</td>
</tr>
<tr>
<td>LIST OF FIGURES</td>
<td>vii</td>
</tr>
<tr>
<td>1. INTRODUCTION</td>
<td>1</td>
</tr>
<tr>
<td>1.1. Introduction to Mass Spectrometry</td>
<td>1</td>
</tr>
<tr>
<td>1.2. Introduction to Electrospray Ionization Source</td>
<td>2</td>
</tr>
<tr>
<td>1.3. Introduction to Quadrupole Ion Trap and Triplequad MS</td>
<td>5</td>
</tr>
<tr>
<td>1.4. Introduction to Ionic Liquid</td>
<td>14</td>
</tr>
<tr>
<td>2. IONIC LIQUID FOR INORGANIC CARRIERS</td>
<td>17</td>
</tr>
<tr>
<td>2.1. Introduction</td>
<td>17</td>
</tr>
<tr>
<td>2.2. Experiment</td>
<td>21</td>
</tr>
<tr>
<td>2.2.1. Instrumentation and Materials</td>
<td>21</td>
</tr>
<tr>
<td>2.2.2. Method for Ionic Liquid Analysis</td>
<td>22</td>
</tr>
<tr>
<td>2.2.3. Result and Discussion</td>
<td>23</td>
</tr>
<tr>
<td>2.2.4. Method for Palladium Complex Analysis</td>
<td>29</td>
</tr>
<tr>
<td>2.2.5. Result and Discussion</td>
<td>29</td>
</tr>
<tr>
<td>3. CONCEPT OF H-D EXCHANGE TO ELUCIDATE GAS-PHASE STRUCTURE OF IONIC LIQUID</td>
<td>36</td>
</tr>
<tr>
<td>3.1. Introduction</td>
<td>36</td>
</tr>
<tr>
<td>3.2. Experiment</td>
<td>38</td>
</tr>
<tr>
<td>3.2.1. Materials and Method</td>
<td>38</td>
</tr>
<tr>
<td>3.2.2. Result and Discussion</td>
<td>41</td>
</tr>
<tr>
<td>3.3 Computational Calculation</td>
<td>47</td>
</tr>
</tbody>
</table>
4. CONCLUSION AND FUTURE WORK ..................................................50

REFERENCES ..................................................................................................................53
**LIST OF TABLES**

<table>
<thead>
<tr>
<th>Table</th>
<th>Description</th>
<th>Page</th>
</tr>
</thead>
<tbody>
<tr>
<td>2.1</td>
<td>Aggregation behavior of 13 ionic liquids showing the highest intensity of</td>
<td>28</td>
</tr>
<tr>
<td></td>
<td>respective aggregation in positive and negative mode</td>
<td></td>
</tr>
<tr>
<td>3.1</td>
<td>Distance and angle between two 2-position H atom of cation and boron atom of</td>
<td>47</td>
</tr>
<tr>
<td></td>
<td>anion of ([C+M]^+) complex for ([C_4\text{-mim}]\text{Br}) ionic liquid</td>
<td></td>
</tr>
</tbody>
</table>
LIST OF FIGURES

<table>
<thead>
<tr>
<th>Figure</th>
<th>Description</th>
<th>Page</th>
</tr>
</thead>
<tbody>
<tr>
<td>1.1</td>
<td>Schematic diagram of ESI process showing the formation of gas-phase ions</td>
<td>4</td>
</tr>
<tr>
<td>1.2</td>
<td>Schematic of a quadrupole showing four electrodes</td>
<td>6</td>
</tr>
<tr>
<td>1.3</td>
<td>The stability region of the quadrupole ion trap defined by the Mathieu</td>
<td>10</td>
</tr>
<tr>
<td></td>
<td>coordinates</td>
<td></td>
</tr>
<tr>
<td>1.4</td>
<td>A segment of the stability diagram of quadrupole ion trap</td>
<td>11</td>
</tr>
<tr>
<td>1.5</td>
<td>Stability diagram of different mass with ac and dc voltage and a mass scan</td>
<td>12</td>
</tr>
<tr>
<td></td>
<td>line</td>
<td></td>
</tr>
<tr>
<td>1.6</td>
<td>Schematic diagram of three quadrupoles in normal in MS/MS scan modes</td>
<td>13</td>
</tr>
<tr>
<td>2.1</td>
<td>Mass spectra of positively charged species generated from (a) DMF and (b)</td>
<td>18</td>
</tr>
<tr>
<td></td>
<td>MeOH solution and ([\text{C}_4\text{mim}]\text{PF}_6)</td>
<td></td>
</tr>
<tr>
<td>2.2</td>
<td>Cation-(\pi) stacking in guanine and arginine proteins</td>
<td>20</td>
</tr>
<tr>
<td>2.3</td>
<td>A spectrum of ([\text{Py-CH}_2\text{CH}_2\text{OH}]\text{BF}_4) showing</td>
<td>24</td>
</tr>
<tr>
<td></td>
<td>aggregation in negative ion</td>
<td></td>
</tr>
<tr>
<td>2.4</td>
<td>Mass spectrum of 1-ethyl-3-methylimidazolium bromide, ([\text{C}_2\text{mim}]\text{Br}) in positive</td>
<td>25</td>
</tr>
<tr>
<td></td>
<td>mode</td>
<td></td>
</tr>
<tr>
<td>2.5</td>
<td>Mass spectrum of 1-ethyl-3-methylimidazolium bromide, ([\text{C}_2\text{mim}]\text{Br}) in negative</td>
<td>26</td>
</tr>
<tr>
<td></td>
<td>mode</td>
<td></td>
</tr>
<tr>
<td>2.6</td>
<td>Molecular representation of the Pd (II) complex on ([\text{C}_4\text{mim}]^+) cation showing</td>
<td>30</td>
</tr>
<tr>
<td></td>
<td>cation-(\pi) interaction</td>
<td></td>
</tr>
<tr>
<td>2.7</td>
<td>Mass spectra showing the presence of the complex ([\text{PdCl}_2(\text{PPh}_3)_2+(\text{C}_4\text{mim})^+]) with different IL giving diverse relative intensity of the complex</td>
<td>33</td>
</tr>
<tr>
<td>2.8</td>
<td>Comparison between the aggregation of IL studied from ESI-MS and RLS</td>
<td>35</td>
</tr>
<tr>
<td>3.1</td>
<td>Reaction showing the 2-position H-D exchange in imidazolium cation</td>
<td>38</td>
</tr>
</tbody>
</table>
3.2 A schematic showing electrospray ionization source modification for H-D exchange experiment. H-D exchange taking place in the 2-position hydrogen of [C₄mim]⁺ cation .................................................................40

3.3 A mass spectrum of [C₄mim]OTf in methanol solvent in positive mode. The inset is a spectrum of [C₄mim]OTf in d-methanol solvent in positive mode ..............42

3.4 A mass spectrum showing H-D exchange in [C₄mim]⁺ ........................................44

3.5 A mass spectrum showing H-D exchange in [[C₄mim]⁺+[ C₄mim]BF₄] complex ..................................................................................................................................45

3.6 The geometry of aggregation of ionic liquid with labeled atoms for measurements .................................................................................................................................46

3.7 The geometry of aggregation of ionic liquid with labeled atoms for measurements .................................................................................................................................48

1.1 Introduction to Mass Spectrometry

Mass spectrometry (MS) is a very powerful analytical technique traditionally used for mass determination and structural characterization of species. The fundamental operation of MS is comprised of three modules, (i) an ion source, which converts introduced sample to gas-phase ions, (ii) a mass analyzer, which separates the generated ions according to their mass-to-charge ($m/z$) ratio using electric field in an evacuated chamber or vacuum, and (iii) a detector, which detects the ions electronically and measures the quantity and provides data for calculating the abundance of each ion present. MS has both qualitative uses like identifying unknown compounds, determining isotopic composition and determining the compound structure by studying fragments, as well as quantitative uses like determining the amount of compound in a sample and studying the structure and geometry of gas-phase ions. Since the ions are very reactive and short lived, their manipulation should be conducted in vacuum maintained between $10^{-4}$ to $10^{-8}$ Torr. Vacuum is also important in order to control the collision of ions with the wall of the chamber and also with other molecules and among themselves as well. The gas-phase ions are sorted and distributed according to their $m/z$ ratio by a mass analyzer where a value of certain potential is applied. Only the ions that have suitable trajectory for the applied potential will travel through the vacuum chamber making their way to the detector. By varying the strength of the potential, ions of different mass can be
selected, manipulated and detected progressively. Mass spectrometers are designed to detect singly or multiply-charged ions according to their $m/z$ ratio, hence, the conversion of the sample to its respective ion phase is a very critical part during analysis. Some ionization sources fragment the sample producing ions whereas in some cases, the mass analyzer is capable of trapping and fragmenting the samples or even coupling the two systems together to trap and fragment the ions. MS runs in two modes, positive mode to detect positively charged ions and negative mode to detect negatively charged ions. However, both ions cannot be viewed at the same time since the potential applied needs to be altered during the analysis. Depending on the type of analyte and requirement of the experiment being performed, different types of ionization source, mass analyzer and detectors can be selected.

1.2 Introduction to Electrospray Ionization Source

Electrospray ionization (ESI) has been widely used as a source for production of gas-phase ions through a solvated charged molecule. ESI was initially developed for the analysis of large and complex bimolecular structures like peptides, amino acids and proteins because the ionization technique is soft with little to no fragmentation. The advantage of this is that the analysis is performed on the parent ion peak, typically \([M+H]^+\) ion, allowing for the lateral structure determination through the mechanism of collision-induced dissociation or hydrogen/deuterium (H-D) exchange for labile protons. The proton transfer is the common reaction for the production of ions in solution phase. Generally polar solvents are used due to the fact that they form charged droplets easily. When a neutral molecule is dissolved in solvent, the ions are formed through the
adduction of proton to the neutral molecule forming [M+H]^+ ion. In some cases, the neutral molecule is dissolved in an acidic solution to promote the ionization. The process of protonation or deprotonation yields positively or negatively charged ions. The solvated ions are then introduced to the capillary of an ESI source through a syringe where desolvation process occurs through a series of mechanisms and singly charged ions are produced for further manipulation.

The electrospray consists of a metallic capillary maintained at a voltage of 2-4 kV. As the solution filled with charged droplets enters the capillary, the spraying of the charged droplets from the end of the capillary takes place along with the formation of a Taylor cone. The Taylor cone is comprised of aerosol droplets which contain many solvated ion species. As the droplet traverses from the source to the sampling cone, solvent evaporation takes place due to the high vacuum environment. As the solvent evaporation occurs, the droplet size decreases until columbic repulsion from the ions exceeds the surface tension of the solvent. At this point, an event called columbic fission occurs resulting in production of several smaller droplets which contain fewer ions. The process of columbic fission repeats until the solvent evaporation process has been completed. A schematic of the process of formation of ions is shown in Figure 1.1. The primary driving force in the conversion of charged droplets into gas-phase ion is the presence of excess charge in the droplet. However, there are number of molecules and compounds known which do not interact with the charged species or do not possess basic
Figure 1.1: Schematic diagram of ESI process showing the formation of gas-phase ions.
site as they lack the place to associate the charge like proton (H+) or alkali metals (Na+). Hence, a different and effective way of providing charge to these molecules is necessary for analysis by MS. Due to the soft ionization technique of ESI, it has been extensively used in studying non-covalent interaction. The process is mild enough to maintain the weak, non-covalent interaction between molecules when they are transferred from the solution phase into the gas-phase ions allowing the detection and characterization of these complexes through the mass spectrometry. Numerous research involving biomolecules like protein-protein, protein-DNA, DNA-DNA, protein-drug, and protein-ligand interactions have been studied using ESI-MS for the study of potential new drugs. Weak non-covalent interactions such as in nagolamycin and DNA complexes or neutral sugar and protein complexes have been successfully detected using ESI-MS.

1.3 Introduction to Quadrupole Ion Trap and Triplequad-MS

Quadrupole has been extensively used as a mass analyzer due to its promising characteristic like moderate resolution in compact devices, light weight and absence of any heavy magnet and likelihood of trading off sensitivity against resolution by simply adjusting the electronics. The quadrupole consist of four electrodes set parallel to each other. Identical potential is applied in the opposing electrode pair, as shown in the Figure. The quadrupole is responsible for filtering the ions based on their mass to charge ratio (m/z). The ions enter and travel in z direction and oscillate in x and y directions. The potential applied controls the oscillation of the ions and only the ions that have suitable
Figure 1.2: Schematic of a quadrupole showing four electrodes.
trajectory for the selected potential will travel through the length of the electrode and finally to the detector. 9 Whereas the other ions will have an unstable trajectory and will collide with the electrodes. There is a limited stability region for ions trapped giving the mass range of the trap 2000 amu which can be shifted. The Mathieu equation is used to locate the stability region of the quadrupole ion trap. The generalized Mathieu equation and Mathieu coordinates that describes the quadrupole stability region as shown in Figure 1.3 and Figure 1.4 are given by

\[
\frac{d^2u}{dz^2} + (a_u - 2q_z \cos 2\zeta)u = 0 \tag{i}
\]

\[
a_u = a_z = -2a_r = \frac{-8\varepsilon U}{m\omega^2 r_0^2} \tag{ii}
\]

\[
q_u = q_z = 2q_r = \frac{4\varepsilon V}{m\omega^2 r_0^2} \tag{iii}
\]

Where,

- \(a_z\) = Mathieu coordinate
- \(q_z\) = Mathieu coordinate
- \(\zeta = \omega t/2\)
- \(t = \) time
- \(u = \) Transverse displacement in x and y direction
- \(\omega = \) angular frequency
- \(U = \) dc potential
- \(V = \) rf potential
- \(z = \) charge
- \(m = \) mass
The generalized behavior of solutions to the Equation (i) is usually sufficient to understand most of the features of quadrupole operation. In particular the solution to the equation is either bounded or unbounded. Physically, a bounded solution correspond to a case where displacement along X and Y axis gives a stable trajectory for the ions to reach the detector. An extended analysis of Equation (i) reveals that the stable trajectory depends on only two parameters of the equation which are au and qu. This fact allows plotting a region in au-qu space where collection of the stable trajectory can be obtained.

The stability diagram provides a powerful visual method for understanding the operation of the quadrupole mass filter. In a mass spectrometer, a tunable mass filter is used capable of producing mass spectra. A quadrupole can be operated where both au and qu parameters are independent of each other at all times. However, the values of au and qu are related by a simple ratio. It is established by applying dc (U) which is always some fraction of the applied ac (V) potential such that the ratio U/V is held constant. Holding a U/V ratio constant is equivalent to operating a mass filter to a set of operating points which lie on a straight line with zero intercept. This line is known as mass scan line as shown in Figure 1.5. The mass scan line can be adjusted by adjusting the appropriate U/V ratio. To select a specific mass, the scan line is adjusted in such a manner that only small portion of line falls anywhere within the stability diagram. In this situation, only the ions whose mass lies in the area between the peak and the scan line will pass through the electrode. By simply altering the slope of mass scan line (changing U/V ratio), a sharp tip of au-qu diagram may be obtained and used to create a narrow pass mass filter.
When a series of three such quadrupoles are put together in a mass spectrometer, it is known as triple quadrupole mass spectrometer. A schematic diagram of such kind of mass spectrometer is shown in Figure 1.6. The three quadrupoles are labeled as Q1, Q2 and Q3 as shown in the diagram. In a normal scan mode, Q1 and Q2 behave like a capillary for ion transmission and Q3 as a mass analyzer. On the contrary, the practical use of the triple quadrupole comes handy while doing the collision induced dissociation experiments. It is a very useful tool in order to discover the structural conformation of the parent ions. In this mode, the quadrupoles Q1 and Q2 acts like a mass transfer whereas the middle quadrupole Q2 is a collision chamber. In this chamber, the selected ions that pass through Q1 collide with inert gases, usually helium or argon, and fragments are produced. Such produced fragments are then pass through Q3 where they are either fully scanned or may be filtered and then finally to the detector. This process allows for the detection of the daughter ions and hence the structural conformation of the original analyte ion can be deduced. Q1 and Q2 can be even set for more than a single mass and this type of setting is called multiple reaction monitoring.
Figure 1.3: The stability region of the quadrupole ion trap defined by the Mathieu coordinates.
Figure 1.4: A segment of the stability diagram of quadrupole ion trap.
Figure 1.5: Stability diagram of different mass with ac and dc voltage showing a mass scan line.
Figure 1.6: Schematic diagram of three quadrupoles in normal and MS/MS scan modes.
1.4 Introduction to Ionic Liquid

Ionic liquid is a term described for an organic salt with their melting point at or below 100°C. Ionic liquids contain two parts, a positively charged cation and a negatively charged anion. They usually contain bulky nitrogen or phosphorus based asymmetrical, organic cation like alkylimidazolium, pyridinium, and pyrrolidinium. The anion can be either organic or inorganic like bromide, chloride, tetrafluoroborate, hexafluorophosphate, trifluoromethylsulfonate, trifluoroethanoate etc. One of the most important features of ionic liquid is being able to alter the cation or anion in the particular ionic liquid. With the large number of possible cation and anion, the estimated number is in the order of $10^{18}$, making this class of compound one of the largest group in chemistry. Because of this property of being able to alter the cation and anion part, it is also known as “Designer Solvent”. By altering the cation or anion, the physical and chemical property of the ionic liquid can be changed or improved.12

Historically, ethanolammonium nitrate was the first formed compound by Gabriel and Weiner in 1883 whose melting point was between 52-55°C. The preparation of ethylammonium nitrate by Paul Walden in 1914 was the first discovered ionic liquid with melting point 12°C. In 1982, Wilkies et al. discovered dialkylimidazolium chloroaluminate but they were air and moisture reactive. The main revolution occurred after the invention of alkylimidazolium salts in 1992.13 These air and moisture stable liquids were invented using weakly complexing anion like $\text{BF}_4^-$ in the imidazolium compound.14
Ionic liquid possess fascinating properties, including low volatility, tunable viscosity, wide range of miscibility and solvent properties, electrolytic conductivity, thermal stability, liquid over a wide range of temperature, transport properties, etc. Because of this diverse and tunable property, they have been widely used in different aspect of research. In the field of analytical chemistry, they have been used in extractions, liquid chromatography, capillary electrophoresis, mass spectrometry, electrochemistry, spectroscopy etc. The low vapor pressure, low volatility and wide range of solubility with different compounds make them suitable for MALDI matrices. Ionic liquid has also been used as biosensors, in biomedical application, and nuclear fuel processing.\textsuperscript{15, 16}

Mass spectrometry has been a very valuable tool for obtaining the detailed structural information and characterization of various ionic liquid. Another important use of MS is the quality control of ionic liquid during their synthesis and monitoring the unwanted side reaction occurring in these liquids. The usage of ionic liquid in MS has opened the new horizon for the analysis of compounds dissolved in ionic liquid and enabling the usage of nonpolar solvents during electrospray ionization. A major emphasis has been on the utilization of these ionic liquid as matrices for MALDI which has been gaining emerging interest in last few years.\textsuperscript{12} Ionic liquids has also been used as matrix substances for fast atom bombardment analysis of the analytes dissolved within.\textsuperscript{17} Ionic liquids has also been used in an undiluted state in ESI-MS,\textsuperscript{18} the advantage is being able to avoid unwanted side reaction between solvent and components of ionic liquid. MS can be used for the theoretical studies to elucidate the physiochemical properties of IL such as the acidity of components of IL\textsuperscript{19}, the determination of the water solubility\textsuperscript{20}, and analysis
of supramolecular structures in ionic liquids. Ionic liquid has been an excellent additive in electrospray ionization mass spectrometry. The most commonly used solvents are methanol, water, acetonitrile or their mixture which are capable of dissolving analyte and has properties for the formation of a stable spray. Whereas, the use of apolar solvents like alkenes and hexane are restricted. On the contrary, the addition of ionic liquid makes the usage of these solvents possible. For example, the addition of 10-5 M of phosphonium IL to hexane leads to the formation of stable spray. Small amount of IL added to solvents like benzene, toluene and diethyl ether gives a satisfactory results and pentene and cyclohexane needs relatively high concentration of IL. Beside, the addition of IL can also improve the solubility of certain analytes facilitating the analysis.

The MALDI matrices should possess some characteristic property like capability of solubility with analyte, absorption behavior at the applied laser wavelength, inertness and vacuum stability. IL shows most of these characters and has been consequently used as potential matrix. IL have low vapor pressure and thus stable under vacuum condition. One of the most interesting fields for application of IL as matrix is during the analysis of low molecular weight compounds due to significant reduction of matrix signal. The viscous liquid surface of ionic liquid is very homogeneous which reduces a common problem caused by traditional matrix called hot-spot formation, causing inhomogeneities in sample and variation in signal intensity. A number of compounds like peptides, proteins have been successfully analyzed using IL as MALDI matrixes.
CHAPTER 2

IONIC LIQUIDS FOR INORGANIC CARRIERS

2.1 Introduction

One of the most captivating properties of ionic liquid which has been recently studied is its ability of aggregation forming a \( \pi-\pi \) stacking complexes. Such type of aggregation is found to be present between the cation and anion, cation and solvent or ionic liquid itself, anion and solvent or ionic liquid itself.\textsuperscript{26} However, the aggregation is not limited to only one molecule of solvent or compound but can be seen for several molecules depending on the type of ionic liquid used. Imidazolium cation is one of the heavily studied cation. Imidazolium with halide anion forms clusters with numerous molecule of methanol in both imidazolium and halide ions.\textsuperscript{27} Similarly, with hexafluorophosphate anion, up to three molecules of dimethylformamide solvent have formed cluster with imidazolium cation along with methanol.\textsuperscript{26} Figure 2.1 shows the mass spectra where such kinds of clusters are detected in two of the solvents. Several other polar solvents including dimethyl sulfoxide, acetonitrile, tetrahydrofuran have also been studied.

Aromatic cation such as imidazolium and triazolium and their derivatives has delocalized charge and are often used for the synthesis of ionic liquid. These aromatic cations also shows the ability to form a \( \pi-\pi \) stacking structures with other imidazolium salts and some
Figure 2.1: Mass spectra of positively charged species generated from (a) DMF and (b) MeOH solution and [C₄-mim]PF₆.
organometallic crystals. In addition to columbic and hydrophobic interaction, hydrogen bond plays a vital role in the formation of the stacking. Cation-cation $\pi$-$\pi$ stacking has also been reported recently. The triazolium and dinitramide ions form small ionic clusters via the hydrogen bonds$^{28}$. The H on the nitrogen atom of triazolium forms a bond to the oxygen atom of the dinitramide ions. The cation-$\pi$ interaction has also been extensively studied in the aspect of molecular biology. Attention has been given in the study of interaction of cation with aromatic rings including the cation-$\pi$ interaction.$^{29}$ Figure 2.2 represents a schematic of such kind of interaction between two biomolecules guanine and arginine. These interactions have shown unusual stability in the aqueous environment.$^{30,31}$

Aromatic nitrogen containing ligands have also been proven to form such $\pi$ stacking with metal complexes$^{32}$. In this type of interaction, hydrogen bond as well as $n$-$n$ interaction has played the important role in stacking or assembly of compounds. The stacking can be either face-to-face type or an edge- or point-to-face or T-conformational. However, the face-to-face stacking does not have to be perfect; it can be offset or slipped packing. There are many metal-ligands that have been studied where only the edge of the ring interact giving point-to-face interaction, known as C-H…$\pi$ attraction. $[\text{C}_n\text{mim}]^+\text{X}^-$ has an amphiphilic cation and hence possesses self-aggregation property. Here, n is the number of carbon atom in the alkyl chain and long alkyl chain is advantageous for H-aggregation.
Figure 2.2: Cation-π stacking in guanine and arginine proteins
As mentioned earlier, one of the limitations of MS is detection of neutral complexes and invention of an effective charge delivery system is always on the run. Hence, ionic liquid can be considered as a potential candidate for this process. They not only possess charge but also has tendency to form a $\pi$-stacking with metal complexes. This has opened a new window for the usage of ionic liquid in the field of mass spectrometry. Research shows that addition of ionic liquid not only act as a charge provider to the neutral complex but opens the new window in the usage of non polar solvents like hexane for the characterization of organometallic complexes. Some studies even show the undiluted direct usage of low viscous ionic liquids as a spraying solvent.

2.2 Experiment

2.2.1 Instrumentation and Materials

The mass spectrometer used for analysis was an LCQ DECA XP Plus (Thermo Finnigan; San Jose, CA) with an electrospray ionization source attached to the front end. The transfer of analyte solution was made by a 500µL glass syringe (Hamilton; Reno, NV). The ionic liquids for analysis were synthesized by Dr. Sergei V. Dzyuba from Texas Christian University, Ft. Worth, Texas. The solvents methanol and Tetrahydrofuran were purchased from Sigma Aldrich.

Thirteen different liquids were studied using ESI-MS. These were chosen so as to give different types of cation and anions. The list of Ionic liquid (IL) studied is shown below:

1. 1-butyl-3-methylimidazolium bromide ,$[\text{C}_4\text{-mim}]\text{Br}$
2. 1-butyl-3-methylimidazolium nitrate ,$[\text{C}_4\text{-mim}]\text{NO}_3$
3. 1-butyl-3-methylimidazolium thiocyanate, [C₄-mim]SCN
4. 1-butyl-3-methylimidazolium tetrafluoroborate, [C₄-mim]BF₄
5. 1-butyl-3-methylimidazolium trifluoromethanesulfonate, [C₄-mim]CF₃SO₃
6. 1-butyl-3-methylimidazolium heptafluorobutanoate, [C₄-mim]C₃F₇CO₂
7. 1-ethyl-3-methylimidazolium bromide, [C₂-mim]Br
8. 1-benzyl-3-methylimidazolium bromide, [mim-Bn]Br
9. 1-ethanol-3-methylimidazolium bromide, [mim-CH₂CH₂OH]Br
10. 1-ethanol-3-methylimidazolium tetrafluoroborate, [mim-CH₂CH₂OH]BF₄
11. 1-pentyl-1-methylpyrrolidinium 1,1,1-trifluoro-N-
    [(trifluoromethyl)sulfonyl]methanesulfonamide [Et₃NCH₂CH=CHCH₃]NTf₂
12. 1-ethylpyridinium tetrafluoroborate, [Py-CH₂CH₂OH]BF₄
13. 1-ethylpyridinium bromide, [Py-CH₂CH₂OH]Br

2.2.2 Method for Ionic Liquid Analysis

All IL were made 0.5% (v:v) solution in methanol which is 1µL of ionic liquid added to 1mL of methanol and vortexed for 10 seconds. The solution was then injected directly to a MS through the ESI port with the help of a glass syringe. The analysis was carried out at the flow rate of 5µL/min, 4 kV of spray voltage and 200°C capillary temperature. Both positive and negative spectra were obtained. The peaks of aggregation were reported in the spectra as long as there was window available (for the instrument used, the mass-to-charge ratio (m/z) was 50-2000) and collected for a time period of 2 minutes for each run.
2.2.3 Result and Discussion

All of the IL investigated showed the self-aggregation property in both cation and anion component. Listed below in Figure 2.3 is one of the spectra of IL 1-ethylpyridinium tetrafluoroborate collected in negative mode where the aggregation behavior of charged ion with the molecule itself can be seen. The behavior is not limited to one molecule but aggregation of several molecules can be seen in the spectrum. The relative intensity for the complex \([\text{Anion}^{-} + n(\text{molecule})]\), where \(n\) is the integer is found to be decreasing with the increasing value for \(n\) as can be seen from the spectrum.

Unexpectedly, this was the only spectrum which showed such kind of aggregation behavior where the relative intensity decreases as the number of molecules in the complex increased. Among the other 25 spectra, the relative intensity fluctuates according to the type of IL used and whether the aggregation is on cation or anion. Listed below in Figures 2.4 and 2.5, are two of the spectra of IL which showed interestingly different aggregation behavior.
Figure 2.3: A spectrum of $[\text{Py-CH}_2\text{CH}_2\text{OH}]\text{BF}_4$ showing aggregation in negative ion.
Figure 2.4: Mass spectrum of 1-ethyl-3-methylimidazolium bromide, [C$_2$-mim]Br, in positive mode.
Figure 2.5: Mass spectrum of 1-ethyl-3-methylimidazolium bromide, \([C_2\text{-mim}]\text{Br}\), in negative mode.
As seen above in the spectrum of 1-Ethyl-3-methylimidazolium bromide in positive mode, the highest intensity of peak 112 at \( m/z \) is due to the positive ion \([\text{C}_2\text{-mim}]^+\), at \( m/z \) 303 is due to the complex \([([\text{C}_2\text{-mim}]^+)[\text{C}_2\text{-mim}]\text{Br}]\). However, the next highest intensity at \( m/z \) 875 is given by the complex \([([\text{C}_2\text{-mim}]^+4[\text{C}_2\text{-mim}]\text{Br}]\). Similarly, in the negative mode of the same IL, the highest intensity at \( m/z \) 462 is given by the complex \([\text{Br}^+2[\text{C}_2\text{-mim}]\text{Br}]\). Some of the IL gives the respective cation or anion at highest intensity while some shows the aggregated complex at the highest intensity. This way different IL shows different aggregation behavior in terms of the relative intensity which is summarized Table 2.1.

In the summary of the table, we can conclude that among 13 different ILs, 9 ILs give cation at highest intensity, confirming more dissociation than aggregation whereas, remaining 4 IL gives \([\text{C}+\text{M}]^+\) ion at highest intensity in positive mode, confirming more aggregation than dissociation. Similarly, in negative mode, 8 IL give anion at highest intensity and 4 IL gives highest intensity of complex \([\text{A}+2\text{M}]^-\) whereas one IL gives the highest intensity of the complex \([\text{A}+\text{M}]^-\).
Table 2.1: Aggregation behavior of 13 ionic liquids showing the highest intensity of respective aggregation in positive and negative mode.

<table>
<thead>
<tr>
<th>Ionic Liquids</th>
<th>Positive mode(Highest Intensity)</th>
<th>Negative mode(Highest Intensity)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Overall Among Aggregated Peaks</td>
<td>Overall Among aggregated peaks</td>
</tr>
<tr>
<td></td>
<td>[C\textsuperscript{2}-mim]Br</td>
<td>[C\textsuperscript{+}]\textsuperscript{+}</td>
</tr>
<tr>
<td></td>
<td>[C\textsuperscript{4}-mim]Br</td>
<td>[C\textsuperscript{+}]\textsuperscript{+}</td>
</tr>
<tr>
<td></td>
<td>[C\textsuperscript{4}-mim]NO\textsubscript{3}</td>
<td>[C\textsuperscript{+}]\textsuperscript{+}</td>
</tr>
<tr>
<td></td>
<td>[C\textsuperscript{4}-mim]SCN</td>
<td>[C\textsuperscript{+}]\textsuperscript{+}</td>
</tr>
<tr>
<td></td>
<td>[C\textsuperscript{4}-mim]BF\textsubscript{4}</td>
<td>[C+M\textsuperscript{+}]\textsuperscript{+}</td>
</tr>
<tr>
<td></td>
<td>[C\textsuperscript{4}-mim]OTf</td>
<td>[C+M\textsuperscript{+}]\textsuperscript{+}</td>
</tr>
<tr>
<td></td>
<td>[C\textsuperscript{4}-mim]C\textsubscript{3}F\textsubscript{7}CO\textsubscript{2}</td>
<td>[C+M\textsuperscript{+}]\textsuperscript{+}</td>
</tr>
<tr>
<td></td>
<td>[mim-Bn]Br</td>
<td>[C\textsuperscript{+}]\textsuperscript{+}</td>
</tr>
<tr>
<td></td>
<td>[mim-CH\textsubscript{2}CH\textsubscript{2}OH]BF\textsubscript{4}</td>
<td>[C\textsuperscript{+}]\textsuperscript{+}</td>
</tr>
<tr>
<td></td>
<td>[mim-CH\textsubscript{2}CH\textsubscript{2}OH]Br</td>
<td>[C\textsuperscript{+}]\textsuperscript{+}</td>
</tr>
<tr>
<td></td>
<td>[Py-CH\textsubscript{2}CH\textsubscript{2}OH]Br</td>
<td>[C\textsuperscript{+}]\textsuperscript{+}</td>
</tr>
<tr>
<td></td>
<td>[Et\textsubscript{3}NCH\textsubscript{2}CH=CHCH\textsubscript{3}]NTf\textsubscript{2}</td>
<td>[C+M\textsuperscript{+}]\textsuperscript{+}</td>
</tr>
<tr>
<td></td>
<td>[Py-CH\textsubscript{2}CH\textsubscript{2}OH]BF\textsubscript{4}</td>
<td>[C\textsuperscript{+}]\textsuperscript{+}</td>
</tr>
</tbody>
</table>

M: Molar mass of resp. molecule; C: Resp. Cation; A: Resp. Anion
2.2.4 Method for Ionic Liquid and Palladium Complex Analysis

For the organometallic complex, an extensively studied cation, 1-butyl-3-methylimidazolium (C₄-mim)⁺ was chosen for IL and Bis(triphenylphosphine)Palladium Chloride [PdCl₂(PPh₃)₂] was chosen for the organometallic complex. Six different counter ions, Bromide [Br⁻], Nitrate [NO₃⁻], Thiocyanate [SCN⁻], Tetrafluoroborate [BF₄⁻], Trifluoromethanesulfonate [CF₃SO₃⁻], and Heptafluorobutanoate [C₃F₇CO₂⁻] were used in order to do investigate the effect of different counter ions on the aggregation property of the IL. Since both the Palladium (II) complex and all of the ILs dissolve readily in Tetrahydrofuran (THF), it was used as the solvent of analysis. 0.0008 g of PdCl₂(PPh₃)₂ dissolved in 1000 µL of Tetrahydrofuran (THF) and 0.1µL of ionic liquid was dissolved in 100µL of THF. 50:50 (v:v) of the Palladium (II) solution and IL solution was mixed and analyzed using ESI-MS.

2.2.5 Result and Discussion

The molecular weight of PdCl₂(PPh₃)₂ is 701.90 g/mol and the chosen cation 1-butyl-3-methylimidazolium (C₄-mim)⁺ gives a peak at $m/z$ 139.00. Hence, our prediction of the complex [PdCl₂(PPh₃)₂ + (C₄-mim)⁺] should give a peak around the $m/z$ 840.90 (=701.90+139.00) in the positive mode and similarly in the respective negative mode, if any complex is formed. Figure 2.6 shows the schematic of the complex that is expected to form due to the cation-π interaction between the cation and the Palladium (II) complex.
Figure 2.6: Molecular representation of the Pd (II) complex on [C₄-mim]⁺ cation showing cation-π interaction.
The spectra obtained from the analysis of different IL and palladium (II) complex used are shown in Figure 2.7. All of the spectra are collected in the positive mode as the complex possess overall positive charge. The Y-axis in all spectra is at 5.5 million ion count scale to keep the spectra uniform. The complex \([\text{PdCl}_2(\text{PPh}_3)_2 + (\text{C}_4\text{-mim})^+]\) can be observed at \(m/z\) 840.73 at different intensity depending on IL used. \([\text{C}_4\text{-mim}]\text{SCN}\) gave ion count for the complex of around \(0.1 \times 10^6\), \([\text{C}_4\text{-mim}]\text{Br}\) gave ion count of around \(0.5 \times 10^6\), \([\text{C}_4\text{-mim}]\text{NO}_3\) gave ion count of around \(1.5 \times 10^6\). Whereas, the ILs \([\text{C}_4\text{-mim}]\text{BF}_4\), \([\text{C}_4\text{-mim}]\text{CF}_3\text{SO}_3\), and \([\text{C}_4\text{-mim}]\text{C}_3\text{F}_7\text{CO}_2\) gave the maximum ion count of approximately 5 million. However, the expected peak was not present in the negative mode with the different counter ions.

Despite the fact that the aggregated complex is present in all of the IL studied, the absolute intensity of the peak changes in each of the IL used. The only variable in each of the investigation is estimated to be the counter ion. Hence, it would be legitimate to predict that the counter ions have some consequence in the formation of the complex as can be clearly seen in the spectra.

Among the six different counter ions were studied and the relative intensity of the complex formed was found to decrease according to the following trend of the counter ion:

\[\text{SCN}^- < \text{Br}^- < \text{NO}_3^- < \text{BF}_4^- < \text{CF}_3\text{SO}_3^- < \text{C}_3\text{F}_7\text{CO}_2^-\]

From the above trend, it can be predicted that the IL with fluorine-containing anion exhibits higher aggregation as compared to non-fluorinated IL. One of the possible reasons for this type of behavior can be predicted that fluorinated anions are weakly
coordinated with the cation. In the electrospray ionization source during the formation of gas-phase ions, when positive voltage is applied to the capillary, the anions are left behind in the walls of capillary and the cations along with the palladium complex are sprayed out from the Taylor cone. Since fluorinated anions are weakly coordinated with cation, more counts of the cation (C₄-mim)⁺ are available from the fluorinated ILs. These available cation forms the cation-π stacking with the palladium complex PdCl₂(PPh₃)₂ giving relatively more ion counts for the complex [PdCl₂(PPh₃)₂ + (C₄-mim)⁺]. Also BF₄⁻, CF₃SO₃⁻, and C₃F₇CO₂⁻ are the conjugate base of very strong acid.

Resonance light scattering (RLS) is a technique that could be used to measure the presence of aggregates in the solution. The studies done using resonance light scattering on pure IL shows similar kind of results. A novel fluorine-containing amphiphilic cation was synthesized and its aggregation with DNA was studied using RLS.33 Figure 2.8 compares the relative intensity of the aggregation formed using the ESI-MS and the RLS which demonstrates that the fluorine-containing IL has more aggregation. One of the reasons that can be predicted is the stability of the ions and aggregates are retained once they are placed in solvent. Since ESI is a soft ionization technique, the stability is further assisted or there is no possibility of destruction to the aggregated complex. Investigation of the alkyl chain length on the imidazolium-based IL has also been done which shows that the longer the alkyl chain in IL, the more advantageous it is for the formation of H-aggregation. This H-aggregation aids in the formation of additional complex.34
Figure 2.7: Mass spectra showing the presence of the complex \([\text{PdCl}_2(\text{PPh}_3)_2 + (\text{C}_4\text{-mim})]^{+}\) with different IL giving diverse relative intensity of the complex.
As the proof of concept of using ionic liquid as a charge carrier for detection of neutral organometallic complexes using ESI-MS has been verified, further investigation using different complexes was also investigated. Two different platinum complexes [(pz)₂Pt(qdt)] and [(4,4 bpy)₂Pt(qdt)] were investigated in the [C₄-mim]PF₆ ionic liquid. In order to cover wide range of information, four different solvents were used, which were chloroform, dimethyl sulphoxide, tetrahydrofuran and dichloromethane. However the predicted peak was not observed in neither of the complexes.

From the data above, it can be concluded that ionic liquid can be effectively used as a charge carrier for the detection of neutral complexes using MS. However, one particular ionic liquid does not work for all the complexes and with the vast range of ionic liquids and organometallic complexes available, it is practically not possible to run experiment in all combination so as to find out which ionic liquid can be used as a best carrier for which type of organometallic complexes. For this reason, more detail information regarding the structural conformation of the ionic liquid aggregates in gas phase is required. Hence, further studies using the concept of H-D exchange along with computation experiments were performed in order to elucidate the gas phase structure of ionic liquid.
Figure 2.8: Comparison between the Aggregation of IL studied from ESI-MS and RLS.
CHAPTER 3

CONCEPT OF H-D EXCHANGE TO ELUCIDATE GAS-PHASE STRUCTURE OF IONIC LIQUID

3.1 Introduction

Hydrogen/deuterium (H-D) exchange is one of the most powerful and versatile techniques for determining the conformational dynamic. Over the last few decades, H-D exchanges have been extensively studied and have yielded valuable information regarding protein structures and conformations\textsuperscript{35-40} and physiochemical properties of metallic complexes.\textsuperscript{41-44} The H-D exchange technique is based on the actuality that hydrogen atoms from O-H, N-H and S-H, and other liable protons groups can exchange with hydrogen from surrounding solvent. However, H-H exchange cannot be monitored or measured.\textsuperscript{38} In contrast, exposure of compounds to deuterated solution causes the rapid exchange of H to D in the regions that lack stable hydrogen bonds. When the compound is exposed to deuterium containing solvent, the H-D exchange in such environment can be monitored using a mass spectrometer.

Hydrogen/deuterium exchange mass spectrometry (HDXMS) has been a very popular technique for determining the structural conformation and dynamic aspect of protein in solution phase \textsuperscript{35, 36}. When the protein is exposed to deuterium containing environment, H-D exchange takes place resulting in the increase of mass of protein. The exchange results increase in mass of one unit per exchange event. This shift allows the exchange to be monitored using a mass spectrometric technique. The first demonstration
of the technique of utilization of H-D exchange along with combination of mass spectrometry was done by Katt and Chait in 1991.\textsuperscript{45} The key concept in this approach is that hydrogen bonding between amino acid side chains and protein backbone amides hinders exchange whereas the amides that are not stabilized by hydrogen bonding will exchange more readily. Also the amides that are located in the core or that have limited solvent accessibility will have slower rate of H-D exchange. The increase in the mass of the protein can be related to the number of H-D exchange that took place. However, studies have reviled that in most cases, the H-D exchange is time and pH dependent.\textsuperscript{46} As the protein is exposed to deuterated solvent for longer time, the more H-D exchange takes place. Hence, H-D exchange primarily implies the structural dynamic of the protein rather than the actual structure which is tightly folded protein are less dynamic for exchange than that are distorted.\textsuperscript{38}

Extensive research that is being done in ionic liquid is not deprived from this concept of HDXMS.\textsuperscript{47-49} Several studies have been done in order to understand the behavior of ionic liquid in deuterated solvent as well as many deuterated ionic liquids have also been synthesized\textsuperscript{50, 51} and used as solvents for NMR studies. Imidazolium cation is widely used as building block for the synthesis of numerous ionic liquids. The ionic liquid also shows similar kind of H-D exchange with deuterium predominately at NCHN position which is also known as 2-position of imidazolium ring.\textsuperscript{52, 53} Ionic liquids with imidazolium cation when dissolved in deuterated methanol, the H-D exchange takes place without the need of any external agents. The reaction is shown in Figure 3.1 below.
The ease of extraction of proton at 2-position determines numerous electrochemical properties and chemical stability of the ionic liquid. All the protons on the imidazolium ring are prone for H-D exchange and the 2-position exchange was repeatedly reported with several solvents and variety of ionic liquids. However, exchange in all hydrogen position was possible with the addition of external agents like bases, Lewis acid or metal clusters were required. Few contradictory cases have also been reported on the exchange behavior. The exchange of 2-position was observed in deuterated methanol and water with imidazolium bromide but not with other anions.

3.2 Experiment

3.2.1 Materials and Method

The mass spectrometer used for the analysis was triple quadrupole mass spectrometry, TSQ7000 (Thermo Finnigan; San Jose, CA) with an electrospray ionization source attached to the front end. The sample was transferred to the MS with a 500µL glass syringe (Hamilton; Reno, NV). The ionic liquids used for the study was provided by Dr. Sergei from TCU. Methanol and Deuterated methanol (D-methanol) were purchased from Sigma Aldrich.

Figure 3.1: Reaction showing the 2-position H-D exchange in imidazolium cation.
Six of the ionic liquids were selected for study in D-methanol, which were \([C_4\text{-mim}]\text{Br}, [C_4\text{-mim}]\text{NO}_3, [C_4\text{-mim}]\text{BF}_4, [C_4\text{-mim}]\text{CF}_3\text{SO}_3, [C_4\text{-mim}]\text{SCN}, \) and \([C_4\text{-mim}]\text{C}_3\text{F}_7\text{CO}_2\). The samples of ionic liquid for run were made in the dilution of 1µL in 1mL of D-methanol and vortexed for 10 seconds to obtain uniform mixture. The instrumental parameters were set at 4.5 kV spray voltage, 250° C transfer capillary temperature, 5µL/ min of flow rate, collected in positive mode for a total run time of 1 minute. The spectra were collected from \(m/z\) 100 to 2000.

For an H-D exchange experiment in gas-phase, a modification was made in the front end of the electrospray ionization source. D-methanol vapors were used as a source of deuterium molecules for the exchange. A small vial with two holes on the cap was filled halfway with D-methanol. The sheath gas (nitrogen) was bubbled into the deuterated methanol to get vapors of D-methanol. Mixtures of nitrogen gas and D-methanol vapors were introduced through the sheath gas inlet of the electrospray ionization source. As the ionic liquid solution gets discharged from the capillary tip, the D-methanol vapor comes in contact with the droplets and the ionic liquid complexes for H-D exchange. A schematic of the modification is shown in Figure 3.2. The spectra were collected from \(m/z\) 125 to 150 and from \(m/z\) 365 to 380 to view the peaks from \([C_4\text{-mim}]^+\) and \([C_4\text{-mim}]^+ + [C_4\text{-mim}]\text{BF}_4\) complex.
Figure 3.2: A schematic showing electrospray ionization source modification for H-D exchange experiment.

H-D exchange taking place in the 2-position hydrogen of \([\text{C}_4\text{-mim}]^+\) cation.
3.2.2 Results and Discussion

Comparing the \( m/z \) values of the peak of the cation and their aggregates from six ionic liquids in methanol and d-methanol, a trend was seen. Figure 3.3 shows spectra of \([\text{C}_4\text{-mim}]\text{CF}_3\text{SO}_3\) in methanol and d-methanol solvents. The peak at \( m/z \) 138.68 was from cation \([\text{C}_4\text{-mim}]^+\) in methanol whereas the cation peak in d-methanol solvent was seen at \( m/z \) 139.78. This shift of 1 unit was due to the deuteration of the 2-position hydrogen in cation. The aggregation peak of \( [\text{[C}_4\text{-mim}]^+ +\text{[C}_4\text{-mim}]\text{CF}_3\text{SO}_3] \) was shifted by 2 units, the aggregation peak of \( [\text{[C}_4\text{-mim}]^+ +2\text{[C}_4\text{-mim}]\text{CF}_3\text{SO}_3] \) was shifted by 3 units, the aggregation peak of \( [\text{[C}_4\text{-mim}]^+ +3\text{[C}_4\text{-mim}]\text{CF}_3\text{SO}_3] \) shows a shift by 4 units. However, due to the high noise, the further aggregation peaks were not identified in the spectrum obtained from d-methanol.

These results clearly show that the number of mass shift due to deuterated methanol is directly correlated with the number of cation or liable proton present in the aggregated complex. During the analysis, additional external agents were not used and so it will be legitimate to predict that the H-D exchange took place in the 2-position hydrogen of the cation. As per this prediction, the 2-position hydrogen(s) present in the aggregation should be readily available for the exchange, which will contribute an important platform for the prediction of the structure of the ionic liquid and its aggregation.
Figure 3.3: A mass spectrum of $[C_4\text{-mim}]\text{OTf}$ in methanol solvent in positive mode. The inset is a spectrum of $[C_4\text{-mim}]\text{OTf}$ in d-methanol solvent in positive mode.
The H-D exchange in gas-phase was studied in the cation peak $[\text{C}_4\text{-mim}]^+$ and the aggregation peak of $[[\text{C}_4\text{-mim}]^+][\text{C}_4\text{-mim}]\text{BF}_4$. Since the mass of deuterium is one unit more than the mass of hydrogen, one H-D exchange will result in one unit shift of the peak. A peak at $m/z$ 139.28 is due to the cation $[\text{C}_4\text{-mim}]^+$ and a peak is present at $m/z$ 140.38 which is due to the deuteration of the 2-position hydrogen of the cation. The deuteration causes the mass shift of the cation by one unit as seen in Figure 3.5.

A peak at $m/z$ 364.96 is due to the aggregated $[[\text{C}_4\text{-mim}]^+][\text{C}_4\text{-mim}]\text{BF}_4$ complex. Two peaks are observed in the vicinity of the complex at $m/z$ 365.96 and 366.96. The peak at $m/z$ 365.96 signifies presence of a complex with one deuterated proton and the peak at $m/z$ 366.96 signifies the presence of a complex with two deuterated proton since there is two mass unit shift compared to the parent complex.

From the spectra, it can be concluded that the H-D exchange takes place not only in the cation but also in the complex. The process of H-D exchange in cation can be explained using a theory of formation of a relatively stable carbene. It is also known as persistent carbene or stable carbene. Carbenes are reactive, short lived molecules that could not be isolated. In 1970, Wanzlick’s group prepared first imidazol-2-ylidene carbene by deprotonation of an imidazolium salt. The deprotonation occurs in the 2-position hydrogen of the imidazolium cation forming a carbene molecule. During a deuterium exchange experiment performed by Breslow, it was demonstrated that under standard reaction conditions, in deuterated water, the 2-position hydrogen was rapidly exchanged for a deuteron in a statistical equilibrium.
In \([\text{[C}_4\text{-mim}]^+ + \text{[C}_4\text{-mim}]\text{BF}_4]\) complex, the fluorine atoms from anion pulls the 2-
position hydrogen atoms from the cation towards them forming a partial H-F bond and
giving an imidazol carbene. At this short lived carbene phase, the deuteron from the
solvent gets added to the 2-carbon position of the cation since addition of deuteron is
more favorable. This way, the 2-position proton of the cation gets deuterated in the
complex.

![imidazol-2-ylidene](image)

Figure 3.4: imidazol-2-ylidene.

For detailed information regarding the geometry of the ionic liquid complex,
some computational calculations were made using Gaussian03.
Figure 3.5: A mass spectrum showing H-D exchange in [C4-mim]^+.
Figure 3.6: A mass spectrum showing H-D exchange in [[C4-mim]$^+$+[C4-mim]BF$_4$] complex.
3.3 Computational Calculation

In order to further assist in understanding the structural properties of ionic liquid, the structure of most stable aggregation form of ionic liquid which is \([\text{C+M}]^+\), was optimized using Density Functional Theory (DFT). \([	ext{C}_4\text{-mim}]\text{BF}_4\) was chosen as the ionic liquid for computational findings so as to obtain polyatomic anion. The calculations were performed with Gaussian03. To compare the energy level, distance and angle between the anion and 2-position hydrogen atoms of cations, and to determine the most stable geometry, the conformational analysis was carried out at four different levels of theory B3LYP/6-31G(d), MO5/6-31G(d), MO6/6-31G(d) and MP2/6-31G(d). Figure 3.7 shows the output structures from the calculations performed at different theory levels. The angle and the distance between two of the 2-position hydrogen from cation labeled as H1 and H2 and boron atom labeled as B in anion is mentioned in Table 3.1.

Table 3.1: Distance and angle between two 2-position H atom of cation and boron atom of anion of \([\text{C+M}]^+\) complex for \([	ext{C}_4\text{-mim}]\text{Br}\) ionic liquid.

<table>
<thead>
<tr>
<th>Theory Level</th>
<th>Distance H1-B (Å)</th>
<th>Distance H2-B (Å)</th>
<th>Angle H1-B-H2 (°)</th>
</tr>
</thead>
<tbody>
<tr>
<td>MO5/6-31G(d)</td>
<td>2.459</td>
<td>2.858</td>
<td>128.5</td>
</tr>
<tr>
<td>MO6/6-31G(d)</td>
<td>3.135</td>
<td>2.389</td>
<td>149.6</td>
</tr>
<tr>
<td>MP2/6-31G(d)</td>
<td>2.481</td>
<td>2.646</td>
<td>103.9</td>
</tr>
<tr>
<td>B3LYP/6-31G(d)</td>
<td>3.039</td>
<td>2.419</td>
<td>139.4</td>
</tr>
</tbody>
</table>
Figure 3.7: The geometry of aggregation of ionic liquid with labeled atoms for measurements.
By comparing the calculated values of angle and bond distance, it was found that among the four basis sets used, the output result from the basis set MO6/6-31G(d) gave the most wide angle between the atoms and greater distance between two hydrogen and boron atoms. Through visual confirmation of the output as well, it can be understood that the hydrogen was conformationally more available for the H-D exchange.
CHAPTER 4
CONCLUSION AND FUTURE WORK

The mass spectrometrists are always on the hunt for the effective charge deliver system, and the success of this project will open a new window. The concept has been proven to be successful to certain extent as shown by the preliminary data. The neutral Palladium complex, PdCl₂(PPh₃)₂, which has not been reported to be detected by MS was successfully detected with the usage of ionic liquid as a charge carrier and Tetrahydrofuran as solvent, though not considered as a MS friendly solvent. Among the several ionic liquids considered, for detection of the Palladium complex, the most effective ionic liquid was found to be the one which has fluorine ion present in the anion. Hence, fluorinated ionic liquid has some advantage over the other ionic liquids, when used as a charge carrier. In addition, studies done through resonance light scattering reveals that fluorinated ionic liquid exhibit higher aggregation.

To completely understand the property of ionic liquid as charge carrier, it is vital to understand the geometric structure of the aggregation. Analyzing the data obtained from the computational calculation, information regarding the structure of the complex has been determined to certain extent. However, more studies need to be done to understand the precise geometric structure of all of the aggregated complexes of ionic liquid. Once the geometric structure has been confirmed, there will be a better understanding on the property of ionic liquid being used as a charge carrier for neutral organometallic complexes.
The H-D exchange was also detected in the higher aggregated complexes of the ionic liquid shown in Figure 4.1. This provides excellent information regarding the geometric structure of higher aggregated complexes. Once the structure of smaller aggregation has been confirmed, the structure of higher aggregates can also be determined which will better assist in understanding the usage of ionic liquid as charge carrier.

The information mentioned above provides proof of the ability of the ionic liquid being able to be effectively used as a charge carrier for analysis of neutral complexes and has opened a new world for the usage of ionic liquid where analytical, organic and computational chemists can work together in a common platform.
REFERENCES


47. Yasaka, Y.; Wakai, C.; Matubayasi, N.; Nakahara, M., Slowdown of H/D Exchange Reaction Rate and Water Dynamics in Ionic Liquids:â€‰% Deactivation of


