REDUCTION OF ALDEHYDES AND KETONES TO THEIR CORRESPONDING ALCOHOLS IN 1-BUTYL-3-METHYLIMIDAZOLIUM TETRAFLUOROBORATE

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Abstract

The use and release of volatile organic solvents (VOS) to the atmosphere have become detrimental to both human health and his environment. In addition, the non-recyclability and the excessive consumption of these solvents in chemical industry influence their high costs. This has incited the growing need towards the design of new processes and benign solvents, helping in minimizing these raised issues. Ionic liquids (ILs) which are acknowledged as green and environmentally friendly solvents, are assigned as promising alternatives for replacing these VOS. The review of some ILs aspects such as structure, synthesis methods, physicochemical properties, solvent applications in reduction reactions, and their recyclability gave an impressive trend and a motivation towards our work. Synthesis of 1-butyl-3-methylimidazolium tetrafluoroborate ([BMIM][BF_4]), as typical IL and investigation of its solvent efficiency, in the reduction of aldehydes and ketones to their corresponding alcohols, were the core objectives of this research.

[BMIM][BF_4] was synthesized *via* microwave (MW) and conventional methods. The characterization of the synthesized [BMIM][BF_4] was done by means of Fourrier transform infrared (FTIR), nuclear magnetic resonance (^{1}H- and ^{13}C-NMR,) and liquid chromatograph-mass spectroscopy (LC-MS) techniques. Physicochemical properties of [BMIM][BF_4] related to its solvent application, such as water content, density, viscosity and thermal stability, were explored. It was observed that synthesis method impacted on the purity and yield of the products, as well as the reaction times. ^{1}H-NMR spectrum of [BMIM][BF_4] showed the high resonance peak of hydrogen atom on carbon at position-two, (C2)-H, around 8.66 ppm, implying the high polarity of this hydrogen atom towards reduction reactions.

[BMIM][BF_4] solvent property, in comparison with normal organic solvent *viz.* ethanol, was investigated through the reduction reactions. The reduced aldehydes and ketones were benzaldehyde (Ph-CHO), acetophenone (Ph-$COCH_3$), ferrocenecarboxyaldehyde (Fc-CHO), and acetylferrocene (Fc-$COCH_3$). Two different methods *viz.* conventional or ultrasound (US) were also employed in aldehydes and ketones reduction by $NaBH_4$, as reducing agent, in either synthesized [BMIM][BF_4] or dry ethanol as solvent. Further to this, similar reduction reaction was carried out under solvent-free conditions for a better investigation of solvent effect. Additionally, reduction reaction of similar substrates under H_2 gas with 10% palladium supported on activated charcoal (10% Pd/C), as catalyst, was also investigated.

The obtained alcohols were characterized by FTIR and NMR. The recyclability of [BMIM][BF_4] was studied by use of both reducing agents, in the reduction of Ph-CHO, as typical example.

Under similar reaction conditions, [BMIM][BF_4] provided higher product yields than dry ethanol. This showed that during reduction process, [BMIM][BF_4] was fast proton donor than dry ethanol, as correlating with ^{1}H-NMR spectrum of [BMIM][BF_4]. This observation together with its efficient recyclability make [BMIM][BF_4] more efficient and cost effective. Furthermore, green approaches such as MW and US examined in this study showed high potential in terms of better product yields and short reaction times.

Preface

The experimental work presented in this dissertation was conducted in the School of Chemistry and Physics, Westville campus, University of KwaZulu-Natal, Durban, South Africa. This work was carried out from February 2015 to October 2017 and was supervised by Prof Vincent O. Nyamori.

The presented studies compiles original work by the author and have not been submitted in any form for a completion of any degree or diploma to any tertiary institution. Where use has been made of the others‘ work, it is accordingly acknowledged in the text.

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Declarations

Declaration 1 - Plagiarism

I, **Josiane Ayingeneye**, declare that:

1. The research reported in this thesis, except where otherwise indicated, is my original research.
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Declaration 2 - Scientific contributions

Oral presentation

Josiane Ayingeneye and Vincent O. Nyamori, "Reduction reactions in ionic liquids: Reduction of aldehydes and ketones by $NABH_4$ in [BMIM][BF_4] to their corresponding alcohols", at the 42nd National Convention of the South African Chemical Institute, Southern Sun Elangeni Hotel, Durban, South Africa, 29 November – 4th December 2015.

Poster presentation

Josiane Ayingeneye and Vincent O. Nyamori, "Synthesis and application of 1-butyl-3-methylimidazolium tetrafluoroborate in reduction of aldehydes and ketones using ultrasound method", at the College of Agriculture, Engineering and Science Postgraduate Research and Innovation Day 2017, Westville campus, University of KwaZulu-Natal, Durban, South Africa, 26 October 2017.

Workshops

1. South Africa Chemical Institute (SACI), "Green chemistry workshop", Southern Sun Elangeni Hotel, Durban, South Africa, 29 November 2015.
2. PerkinElmer, "Innovation Tour-South Africa", Olive Convention Centre, Durban, South Africa, 23 June 2015.

Publication

Josiane Ayingeneye and Vincent O. Nyamori, "Reduction of aldehydes and ketones to their corresponding alcohols in 1-butyl-3-methylimidazolium tetrafluoroborate: A comparison between sodium borohydride reduction and catalytic hydrogenation approaches" (manuscript in preparation).

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Josiane Ayingeneye Date

Dedication

This dissertation is dedicated to my beloved husband Antoine Ayinkamiye and my daughter Dorcas Ishimwe Ayinkamiye. I am so blessed to have them as the most highly important persons in my life. This achieved success is the recompense of their huge sacrifice in so many different ways.

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Table of Contents

Chapter Three

Synthesis and characterization of 1-butyl-3-methylimidazolium tetrafluoroborate

Chapter Four

Reduction of aldehydes and ketones in 1-butyl-3-methylimidazolium tetrafluoroborate to their corresponding alcohols

Chapter Five

Dissertation summary, conclusions and future work

Appendices

List of Figures

Chapter One

Chapter Two

Chapter Three

Chapter Four

List of Tables

Chapter Two

Chapter Three

Chapter Four

List of Schemes

Chapter Two

Chapter Three

Chapter Four

List of Abbreviations and Symbols

Abbreviations / Symbols	Full names
$[CH_3COO]^-$	Acetate
$Ph\text{-}COCH_3$	Acetophenone
$Fc\text{-}COCH_3$	Acetylferrocene
$[RMIM]^+$	Alkyl methylimidazolium
$[RSO_3]^-$	Alkyl sulfonates
$[RSO_4]^-$	Alkyl sulphates
$[RBF_3]^-$	Alkyl trifluoroborate
$AlCl_3$	Aluminium(III) chloride
Amps	Amperes
AR	Analytical reagent
Å	Ångström
$MgSO_4$	Anhydrous magnesium sulphate
a.u	Arbitrary unity
ATR	Attenuated total reflectance
$[(RSO_2)_2N]^-$	Bis(alkyl sulfonyl)amide
[BES]	2-{Bis(2-hydroxoethyl)amino}ethanesulfonate
$[(CF_3SO_2)_2N]^-$ or $[NTf_2]^-$	Bis(trifluoromethylsulfonyl)amide
b.p	Boiling point
$[Br]^-$	Bromide anion
$C_4H_9\text{-}Br$	1-Bromobutane
[BMIM][Br]	1-Butyl-3-methylimidazolium bromide
[BMIM][Cl]	1-Butyl-3-methylimidazolium chloride
$[BMIM][BF_4]$	1-Butyl-3-methylimidazolium tetrafluoroborate
^{13}C-NMR	Carbon thirteen nuclear magnetic resonance
Cm	Centimetre
cP	Centipoise
CRC	Chemical rubber company
Δ	Chemical shift
$[Cl]^-$	Chloride
$H[AuCl_4]$	Chloroauric acid

ca.	Circa (approximately)
J	Coupling constant
[CHES]	2-(Cyclohexylamino)ethanesulfonate
$[Al_3Cl_{10}]^-$	Decachlorotrialuminate
°C	Degree Celsius
$CDCl_3$	Deuterated chloroform
D_2O	Deuterated water
$[N(CN)_2]^-$	Dicyanamide
ϵ_r	Dielectric constant
$[(CH_3)_2PO_4]^-$	Dimethyl phosphate
π^*	Dipolarity/polarizability
d	Doublet
E_{NR}	Electronic transition energy
E-factor	Environmental factor
EPA	Environmental Protection Agency
et al.	Et alia (and others)
$[EtNH_3]^+[NO_3]^-$	Ethylammonium nitrate
[EMIM][Cl]	1-Ethyl-3-methylimidazolium chloride
Fc-CHO	Ferrocenecarboxyaldehyde
Fc	Ferrocenyl
$Fc\text{-}CHOHCH_3$	1-Ferrocenylethanol
$Fc\text{-}CH_2OH$	Ferrocenylmethanol
^{19}F-NMR	Fluorine nineteen nuclear magnetic resonance
FTIR	Fourier transform infrared
GC-FID	Gas chromatograph with flame ionization detector
T_g	Glass formation temperature
g	Grams
GCI	Green Chemistry Institute
$[Al_2Cl_7]^-$	Heptachlorodialuminate
Hz	Hertz
$[SbF_6]^-$	Hexafluoroantimonate(V)
$[PF_6]^-$	Hexafluorophosphate
HCl	Hydrogen chloride

HF	Hydrogen fluoride
H_2	Hydrogen molecule
HBA	Hydrogen bond accepting
α	Hydrogen bond acidity
β	Hydrogen bond basicity
HBD	Hydrogen bond donation
[MOPSO]	2-Hydroxo-4-morpholinepropanesulfonate
i.e.	Id est (that is)
IUPAC	International Union of Pure and Applied Chemistry
$[I]^-$	Iodide
ILs	Ionic liquids
LSER	Linear solvation energy relationship
LC-MS	Liquid chromatography-mass spectroscopy
$LiAlH_4$	Lithium aluminium hydride
m/z	Mass-to-charge ratio
m.p.	Melting point
μm	Micrometre
MW	Microwave
mg	Milligram
mL	Millilitre
mm	Millimetre
mmol	Millimole
min	Minute
M	Mole per decimetre cube
m	Multiplet
NPCS	National industrial research of India Project Consultancy Services
$[C_4F_9SO_3]^-$	Nonafluorobutylsulfonate
NMR	Nuclear magnetic resonance
10% Pd/C	10% palladium supported on activated charcoal
ppm	Parts per million
$Ph\text{-}CHOHCH_3$	1-Phenylethanol
$Ph\text{-}CH_2OH$	Phenylmethanol

π	Pi
PTFE	Polytetrafluoroethylene
$K[CF_3(CF_2)_3CO_2]$	Potassium nonafluoropentanoate
pH	Potential of hydrogen
^{1}H-NMR	Proton nuclear magnetic resonance
RBF	Round-bottom flask
$Ag[CB_{11}H_{12}]$	Silver carborane
s	Singlet
$NaBH_4$	Sodium borohydride
NaBr	Sodium bromide
$NaBF_4$	Sodium tetrafluoroborate
SA	South Africa
$[AlCl_4]^-$	Tetrachloroaluminate
$[B(CN)_4]^-$	Tetracyanoborate
$[BF_4]^-$	Tetrafluoroborate anion
TGA	Thermogravimetric analysis
TLC	Thin-layer chromatography
$[C(CN)_3]^-$	Tricyanomethanide
$[CF_3CO_2]$	Trifluoroacetate
$[CF_3SO_3]^-$ or $[OTf]^-$	Trifluoromethylsulfonate or Triflate
$[(CH_3)_3S][Br\text{-}AlBr_3]$	Trimethylsulfonium bromide-aluminium bromide
t	Triplet
$[CH(CF_3SO_2)_3]^-$	Tris(trifluoromethylsulfonyl)methanide
US	Ultrasound
UK	United kingdom
$	United states dollars
USA	United States of America
VOC	Volatile organic compounds
VOS	Volatile organic solvent
v/v	Volume per volume
wt.%	Weight percentage

Chapter One

Introduction

This chapter gives an overview on the reduction of aldehydes and ketones in the production of alcohols by use of ionic liquids as solvents. It presents background of the project, problem statement, motivation, research hypothesis, aim and objectives of the dissertation and its layout.

1.1 Research background

Alcohols are an important class of compounds since they are used as beverages, laboratory solvents as well as intermediates in the production of many compounds which are crucial for society's everyday life. These products include pharmaceuticals,[1-4,9,10] veterinary medicines,[5,6] plasticizers,[7-9] surfactants,[9,10] lubricants,[9-11] ore floatation agents,[10] pesticides,[10] hydraulic fluids,[9-11] perfumes,[9,10,12] cosmetics, [9,10,13] and detergents. [9,10,14] Among the synthetic routes of producing alcohols, reduction of aldehydes and ketones is one of the frequently used reactions, and a vast variety of reducing agents have been developed.[15-18] Currently, the most common reducing agents for the reduction of aldehydes and ketones are lithium aluminium hydride ($LiAlH_4$) and sodium borohydride ($NaBH_4$). $LiAlH_4$ is one of the most powerful reducing agent, that can reduce practically almost all organic functional groups except some functional groups such as nitro and nitrile groups.[15,19] On the other hand, $NaBH_4$ shows selective reduction of aldehyde and ketone groups to their corresponding alcohols.[20-22] Another important method of producing alcohols is the catalytic hydrogenation of aldehydes and ketones.[23,24] In all these reactions, solvents play a critical role as they not only modify both reaction kinetics and equilibrium of the reaction,[25] but also in some cases they influence selectivity of products.

Mostly and traditionally, the conversion of aldehydes and ketones to their corresponding alcohols takes place in organic solvents. The commonly employed solvents are volatile, thus are detrimental to human health and the environment, especially once released into the atmosphere. Use of organic solvents is among the major contributors of volatile organic compounds (VOC) into the environment (Figure 1.1).

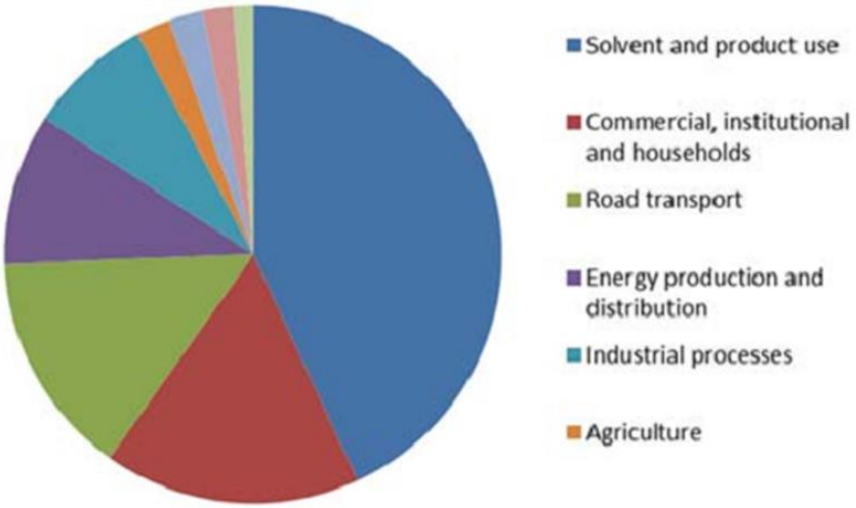

Figure 1.1: Non-methane VOC emission shares from different source categories[26]

Many studies have been performed to minimize the use of these organic solvents and consequently the health and environmental issues which are negatively associated with their usage. Among the viable options is the use of solvent-free reactions or replacing hazardous solvents with ones that pose no, or minimum, harm to health and the environment.

In search of solution, ionic liquids (ILs) have been recognized as environmentally benign solvent and a better alternative to the volatile organic solvents (VOS), especially in the synthesis of alcohols.[27,28] ILs are organic salts which are liquids below 100 °C, usually consisting of an organic cation and a polyatomic inorganic anion (discussed in Chapter Two).

This project was designed to investigate the use of ILs as solvents in the conversion of aldehydes or ketones to their corresponding alcohols. In particular, 1-butyl-3-methyl-imidazolium tetrafluoroborate ([BMIM][BF_4]) was the choice of IL and it has been used as solvent in reduction of aldehydes and ketones to their corresponding alcohols. Two reducing agents, namely $NaBH_4$ and hydrogen gas in presence of 10% palladium supported on activated charcoal (H_2, 10% Pd/C), were used as the reducing agents.

1.2 Problem statement

In organic synthesis, most of the reactions are conducted in volatile organic solvents which are toxic and more often non-recyclable.[29,30] There is also an inevitable and excessive consumption of solvents during reactions, posing a pronounced economical challenge in terms of solvent costs.

Furthermore, due to the toxic nature of the VOS, they are associated with human health problems, such as eye and throat irritation, headaches, and damage to the liver and nervous system.[31] In addition, they exhibit carcinogenic effects.[31]

These solvents contaminate the environment because they are a principal source of ground-level ozone, which is harmful air and main ingredient in smog. On the other hand, at tropospheric level, the destruction of ozone by VOS can lead to changes on the climate, over exposure of the sun light to the earth and destruction of plants. This ozone shows a corrosive effect on certain synthetic materials such as deterioration and fading of certain paints. In addition, when disposed on impermeable surfaces, these solvents can find their way into the water supply through industrial overflow and discharge.[31] Thus, the VOS waste disposal methods are extremely sophisticated and very expensive.[32]

Therefore, this demands the development and the design of new processes, capable to minimize the high cost and toxicity of these solvents and thereby protect the environment by performing chemical reactions using ecologically safe reagents.

1.3 Motivation

The world is currently facing serious problems related to environmental pollution[33] and these have detrimental effects on human health.[34] These problems are directly or indirectly linked to the use of the VOS. Many industrial and commercial activities require these solvents for producing different materials such as food, medicines, paints, chemicals and other consumables, useful in day to day activities in the society. To circumvent all these raised problems, reliable basic strategies have to be implemented for clean and safe environment sake. These strategies consist of initiating pollution prevention across all aspects, establishing root cause of the waste, identifying and implementing changes that reduce or eliminate the waste.[35]

Green chemistry,[36] which is defined a set of principles that reduces or eliminates the use and generation of hazardous substances in the design, manufacture and application of chemical products, catches an increasing attention. ILs were qualified as green solvents. The attractive properties of ILs, such as non-volatility, non-flammability, high thermal stability, high polarity, recyclability, less toxicity and ability to dissolve a wide range of polar and non-polar materials, make them efficient and environmentally friendly benign media in organic synthesis.[37-44]

Unlike conventional organic solvents, the structures of ILs can be modulated by modifying anions and cations scaffolds and this provides additional benefits for 'tuning them for a variety of processes.[45]

The individual combination of cations and anions determines the properties of the ILs for optimization of a specific application[27,42] (discussed in Chapter Two). Also, products separation is very easy because they are immiscible with a number of organic solvents and provide a non-aqueous, polar alternative for two-phase systems.[46]

For instance, alcohols produced from reduction of aldehydes and ketones are not easily extracted from the VOS. These require additional reagents, time and energy consumption for purification because they are produced as crude ones. This poses a challenge in the synthesis of alcohols and their derivatives. Recyclability of ILs significantly decreases the cost of solvents, the solvent waste, and have clean disposal.

1.4 Research problem statement and hypotheses

- Is it possible to synthesize [BMIM][Br] and to use it as a precursor for [BMIM][BF_4] synthesis?
- Is [BMIM][BF_4] an efficient solvent for the reduction of aldehydes and ketones to their corresponding alcohols in comparison with polar solvents such as ethanol?
- Is [BMIM][BF_4] recyclable?
- Which is a better method for reducing aldehydes and ketones; $NaBH_4$ reduction, solvent-free reduction or catalytic hydrogenation over 10% palladium supported on activated charcoal (10% Pd/C)?

1.5 Research aim and objectives

The aim of this work was to synthesize [BMIM][BF_4] and investigate its solvent efficiency in the reduction of aldehydes and ketones to their corresponding alcohols.

This was achieved through specific objectives such as:

- Synthesis and characterization of [BMIM][Br] and [BMIM][BF_4].
- Application of the synthesized [BMIM][BF_4] in different methods of reducing aldehydes and ketones to their corresponding alcohols in comparison with ethanol.
- Comparison of the solvent effect of [BMIM][BF_4] and ethanol in terms of product yields and efficiency.
- Recyclability investigation of [BMIM][BF_4] from different approaches of these reduction reactions.
- Comparative study of different methods involved in these reduction reactions based on the used reducing agent.

1.6 Dissertation layout

Chapter One

This chapter comprises general introduction of the work performed. It presents background, problem statement, motivation of the study, aim and objectives of the research. The dissertation overview is also briefly presented in this chapter.

Chapter Two

This chapter provides a literature review. The trends of green chemistry and current reviews on the subject are provided. A background to ILs, their synthesis, properties, application and recycling are given in this chapter. Different methods of reducing aldehydes and ketones to the corresponding alcohols in both conventional solvent (ethanol) and ILs ([BMIM][BF_4]) are presented in details. Also, some findings, extracted from similar work carried out elsewhere, are presented herein.

Chapter Three

This chapter focuses on the synthesis and characterization of [BMIM][BF_4]. Results and discussion for [BMIM][BF_4] synthesis are presented in this chapter in comparison with reported findings from the literature.

Chapter Four

This chapter provides the application of synthesized [BMIM][BF_4] as solvent in different methods of reducing aldehydes and ketones to their corresponding alcohols. Results for these reduction reactions of aldehydes and ketones through different methods are thoroughly discussed in comparison with existing findings from the literature.

Chapter Five

A summary of the findings and general conclusion of the research are given as well as recommendations for future work.

Appendices

Supplementary information is provided at the end of this dissertation.

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Chapter Two

Literature review

This chapter provides an overview of green chemistry. The role of ionic liquids (ILs) as green solvents in the achievement of sustainable technologies and sustainable development of green chemistry are discussed, with respect to their synthesis, properties, applications and recycling capabilities. Reduction reactions of aldehydes and ketones to their corresponding alcohols are overviewed as typical examples of reactions carried out in ILs.

2.1 Green chemistry

2.1.1 Background

The chemical industry helps in producing many products which play a crucial role in our lives. These products include human medicines; agricultural inputs such as fertilizers, veterinary medicines, fungicides, herbicides and pesticides; plastics, synthetic fuels and other assorted materials. Products used in water purification are also obtained from the chemical industry.

However, the effects of waste in the chemical industry and the meaning of efficiency in organic synthesis are great challenges to the environment and human health. The sustainable solution to these problems consists in replacing undesirable chemical products and processes by cleaner, safer and environmentally friendlier alternatives. Green chemistry has been identified as one of the main approaches of tackling these challenges.[1]

Basically, green chemistry is defined as the design of manufacture and application of chemical products and processes that eliminate waste and reduce or avoids the use of toxic or hazardous reagents and solvents by employing the renewable raw materials.[2-5] Mainly, it focuses on the chemical synthesis, process chemistry and chemical engineering, in industrial applications. Two main ideologies embraced in green chemistry are (i) the efficient utilization of resources and minimization of the waste, and (ii) the health, ecological, and safety issues coming from the manufacture, use, re-use or disposal of chemical products.[6]

The term ‘green chemistry’ was originally used by the United States (U.S.) Environmental Protection Agency (EPA) during the early 1990s.[7] In 1995, this U.S. EPA, under the funding of President Bill Clinton, launched the annual Presidential Green Chemistry Challenge (PGCC)

Awards program underlining scientific innovations in both academia and industry that promoted green chemistry.[8,9]

In 1997, Green Chemistry Institute (GCI) was founded in the USA as the principal change agent that had the knowledge, expertise and abilities to catalyse the movement of the chemical enterprise toward sustainability through the application of green chemistry principles.[10,11] In 1999, the first volume of the now well-established green chemistry journal of the Royal Society of Chemistry was published.[12] Two years later, the GCI became a part of the American Chemical Society, the largest professional scientific society and membership organization for chemists in the world. The Nobel Prize in green chemistry was won in both 2001 (Knowles, Noyori, and Sharpless)[13] and 2005 (Chauvin, Grubbs, and Schrock).[14] These Nobel Prizes upraised the importance of research in green chemistry and helped scientists to be aware that the future of chemistry should be greener.

2.1.2 Twelve principles of green chemistry

In 1998, a set of twelve principles was published by Paul Anastas and John C. Warner, to guide the practice of green chemistry.[15] Briefly, these principles helped in: (i) avoiding the production of waste, which is viewed as the ideal form of waste management, (ii) the design of processes to maximize the amount of raw materials that end up in the products, (iii) the use of renewable material feedstocks and energy sources, (iv) the use of safe, environmentally benign substances, including solvents, whenever possible, (v) the design of energy efficient processes and (vi) avoiding the use of auxiliary substances and the unnecessary derivatization. Furthermore, they include guidelines for professional chemists helping with the implementation of new chemical compounds, new technological processes and new syntheses for actual time, in-process control and monitoring before the formation of hazardous substances. Poliakoff *et al.*[16] captured all these twelve principles of green chemistry in a mnemonic, PRODUCTIVELY:

P – Prevent wastes

R – Renewable materials

O – Omit derivatization steps

D – Degradable chemical products

U – Use of safe synthetic methods

C – Catalytic reagents

T – Temperature, Pressure ambient

I – In-Process monitoring

V – Very few auxiliary substrates

E – E-factor, maximize feed in product

L – Low toxicity of chemical products

Y – Yes, it is safe

2.1.3 Green chemistry benefits

The demand of reducing health and environmental harm caused by man-made materials such as plant foods, pesticides, pigments, dyes, plastics, electronics, medicines, dry cleaning, energy generation, and water purification materials and reagents including the processes used to produce them, was growing rapidly. Daily, millions of tons of harmful chemicals are hidden underground, dumped into rivers, lakes and oceans or emitted into the air.[17] Furthermore, the heavy reliance on increasingly expensive petroleum and the persistence in the environment of toxic substances, with comprehensive negative impacts on human and animal growth, are also highlighted. Based on the new report from Pike research, green chemistry has contributed as a response to these challenges listed above, mapping a market prospect that will grow from $2.8 billion in 2011 to $98.5 billion by 2020.[18]

Green chemistry has tremendous benefits, [19,20] firstly, on human health like cleaner air, cleaner water, improved safety and protective equipment needed for people working in the chemical industry; less use of poisonous materials, less probability of accidents, safer consumer products of all types, safer food, and less exposure to such toxic chemicals taken as endocrine disruptors.

Secondly, on the environment, where many chemicals, intentionally released into the environment during use (case of pesticides) and unintentionally released (emissions during manufacturing) or disposed, are either recovered for further use or degraded to inoffensive products. Plants and animals benefit from these harmless chemicals in the environment. Also, there is a less manifestation of global warming, ozone depletion and smog formation. Ecosystems are less disrupted by chemicals and usage of hazardous waste landfills.

Lastly, in terms of economy and business, green chemistry benefits are pronounced in better yields for chemical reactions, using up smaller amounts of feedstock to obtain the same quantity of product and fewer synthetic steps, for faster manufacturing of desired products, developing plant capacity and saving of water and energy.

Also, waste reduction removes costly remediation, unsafe waste disposal, and end-of-the-pipe treatments. Reduced usage of petroleum products decreases their reservoir depletion and avoids their hazards and price increments. Green chemistry expanded consumer sales by creating and displaying a safer product label and improved affordability of chemical manufactures and their clients.

2.1.4 Green chemistry to sustainable development

Sustainable development is defined as the development that meets the demands of the present and reserves the ability of future generations to satisfy their own needs.[21] Green chemistry helps to attain the sustainable development at the molecular level by designing and using the methods producing new materials and products with less using up of processed natural raw materials. In further, rational use of energy sources, elimination of hazardous solid, liquid and gaseous wastes and the introduction of safety products for man are also considered and contribute to sustainable development.[2,22-24] The application and extension of green chemistry principles through synthesis, processing and using of chemical compounds are facilitating this sustainability (Figure 2.1).

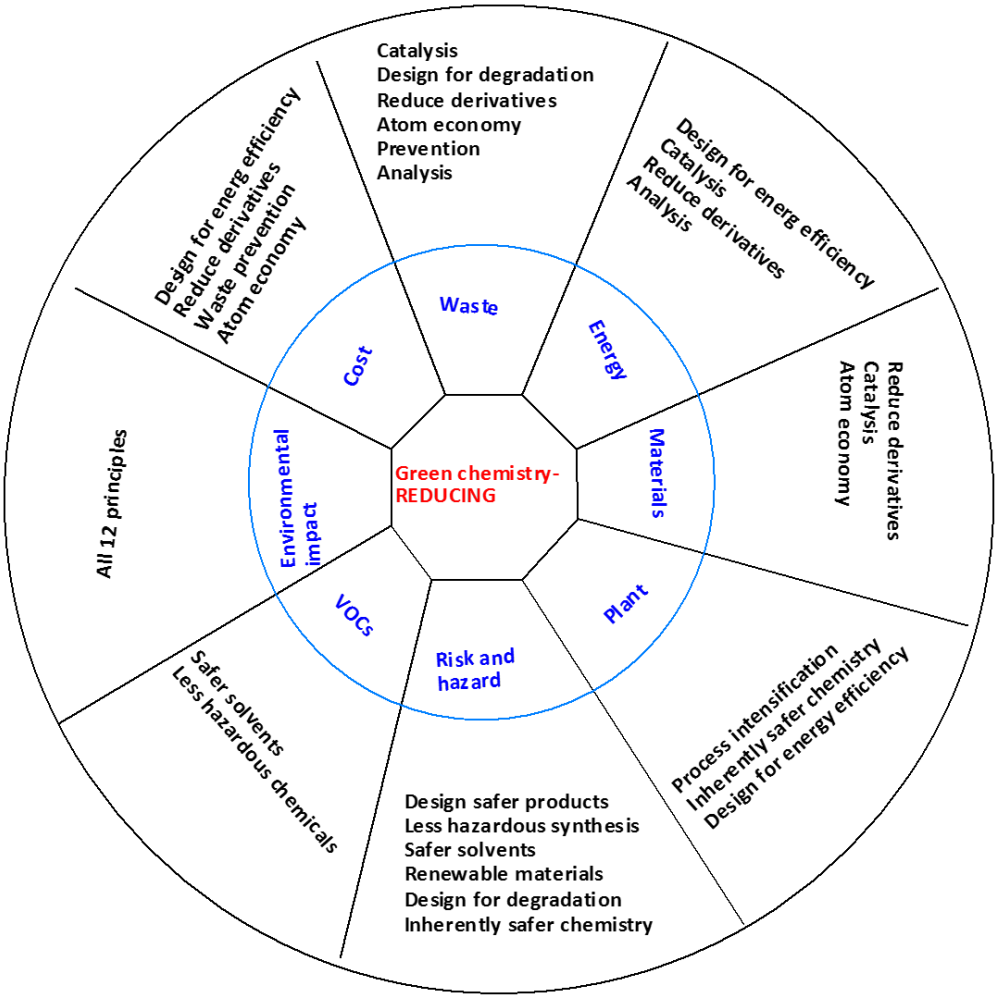


Figure 2.1: Green chemistry as a reduction process[22]

A high number of new analytical methodologies including solid phase microextraction techniques, reported by Spietelun *et al.*,[25] have also been discovered on basis of green chemistry rules. They are convenient in conducting the analytical procedure through all steps by allowing accurate and precise results of analysis. In addition, large attempts are still commenced to design an ideal process that begins from non-polluting initial materials to no secondary products and requires no solvents to carry out the chemical conversion or to isolate and purify the product.

However, the implementation of the environmentally friendly technologies at the research level could not be compared to an industrial scale. Implementation of environmentally benign methods may be helped by higher flexibility in regulations, new programs to enable and accelerate the technology transfer among academic institutions, government and industry and tax incentives for implementing cleaner technologies.

2.1.5 Green chemistry metrics

The assessment of environmental impacts resulting in chemical reactions, chemical processes and chemical products is done by means of mathematical parameters called chemistry metrics. These latter metrics describe the sustainability and the efficiency of both chemical reactions and processes. Factors such as mass, cost, safety and energy are taken into account. Green chemistry has adopted these metrics to evaluate the undesirable environmental consequences caused by the use and the processing of the toxic and harmful chemicals.

Green chemistry metrics are the metrics that measure the greenness of a chemical reaction based on the principles of green chemistry.[26-28] Basically, a chemical process or chemical technology is qualified as green one if there is a reduction in the use of reagents and auxiliaries, waste, hazards, toxicity, negative environmental impact, energy and cost. Briefly, few of these green chemistry metrics are outlined hereafter:

- *Environmental factor* (E-factor): Defined as the mass ratio of all total waste generated in industrial or technological process (in kilograms) per kilogram of desired product. The lowest values of E-factor (E-factor close to zero) shows that less waste is generated and the process is both more suitable and green.[29]
- *Atom economy* (AE): This is calculated by dividing the molecular weight of the desired product by the sum of the molecular weights of all substances reacted in the stoichiometric equation, expressed as a percentage.[30,31] It provides how much of the reactants is converted into the final products.
- *Reaction mass efficiency* (RME): Defined as the mass of the product obtained divided by total mass of the reactants in the stoichiometric equation, expressed as a percentage. This metric considers atom economy, chemical yield and stoichiometry. It shows the cleanness of the reaction and improve the reduction of waste at the basic and global level.[32,33]
- *Carbon efficiency* (CE): Similar to RME but focus mainly on carbon *i.e.* the mass of carbon present in the product obtained divided by total mass of the carbon present in the reactants.
- *Mass intensity* (MI): Defined as the total mass of the materials used in process (reagents, solvents and auxiliary substances) divided by the mass of the product obtained expressed as percentage, *i.e.* MI = E- factor +1. For the ideal synthesis, MI = 1 compared with zero for the E-factor.[33]

- *Effective mass yield* (EMY): Defined as the mass of the desired product divided by the total mass of non-benign reactants (hazardous and toxic reagents) used in its preparation, excluding NaCl and acetic acid.[34]
- *Environmental quotient*, (EQ): This is the product of E-factor and the arbitrarily assigned unfriendliness quotient, Q, where Q is dependent to disposal or recycling of a particular waste.[35] It helps in the assessment of ecotoxicity of the waste generated during the industrial process or organic synthesis.
- *Life cycle assessment* (LCA): This is evaluated in defined domains like cradle-to gate, cradle-to-gate and gate-to gate, based on quantifiable environmental impact indicators such as energy usage, global warming, ozone depletion, acidification, eutrophication, smog formation, and ecotoxicity, in addition to waste generated.[36]

The E-factor, AE and RME have been known as the most common used metrics, since they are simple and fast in evaluating the sustainability of manufacturing process and measure the greenness of chemical synthesis.[26,28]

2.1.6 Green solvents

Solvents are required to facilitate processing and transport of materials in chemical, industrial and pharmaceutical processes. Owing to the high volatility of organic solvents, once released into the environment, these solvents result in leakage and consequently, they become the major source of environmental pollution. The sustainable management of volatile organic compounds (VOC) derived by these solvents, is hampered by their excessive consumption and their disposal techniques costs. However, their best strategy lies on avoiding using them, or if needed, use inoffensive ones, so-called green solvents.

Green solvents are described as a class of solvents that are harmless to the environment damage.[37,38] They are obtained from renewable resources and their biodegradation yields safe products. Their applications are widely found in diverse areas like organic synthesis, polymer chemistry, biocatalysis, nanochemistry and analytical chemistry.[38] Figure 2.2 presents the common green solvents depending on their publication rate. It is noteworthy that the proportion of papers describing particular class of solvents does not make that solvent greener than others.

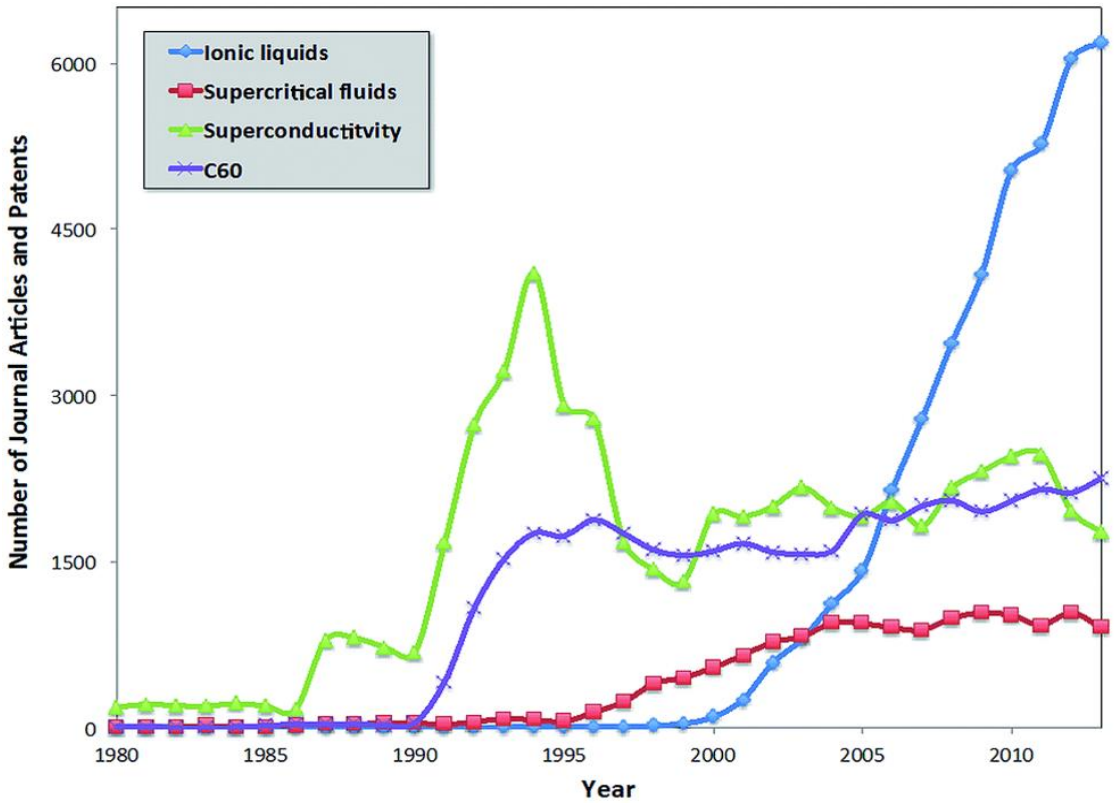


Figure 2.2: The proportion of papers describing each class of solvent (1980-2013)[39]

The greenness of the solvent depends on different parameters such as:

- Availability of replacing non-green-solvent of any kind
- Use and finding the adequate methods to assess the environmental effects of these solvents through their synthesis, use and disposal
- Finding an easier and cheaper way of extraction of products from these solvents by which avoids high energy activities such as distillation
- Recyclability
- Biodegradability and nontoxicity
- Low prices
- Simple preparation

2.2 Ionic liquids

As previously reviewed in Section 2.1.6, the new strategies for practical chemical synthesis consist of a complete elimination of volatile organic solvents or to substitute the compounds belonging to VOC by cheap technological media, harmless to both humans and the environment. The target is to minimize the chemical waste and environmental pollution. Numerous methodologies based on water reaction medium, ILs, supercritical fluids, microwave, and sonochemical treatment have been developed. However, it will not be possible to discuss all these methodologies highlighted above. In this work the focus is limited to ILs which have been assigned as promising alternative solvents to traditional organic solvents.

2.2.1 History of ionic liquids

ILs have been defined differently according to the understanding of various researchers. However, all converged on the same view that ILs are low-melting salts, thus forming liquids under the boiling point of water (100 °C). In the mid-19th century, the earliest material reported as IL was observed in Friedel-Crafts reactions as a red-oil liquid and this has been characterized and confirmed recently after the development of nuclear magnetic resonance (NMR) spectroscopy and found to be heptachlorodialuminate salt shown in Figure 2.3

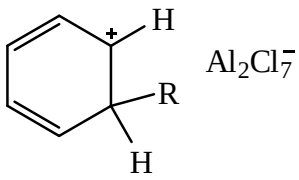
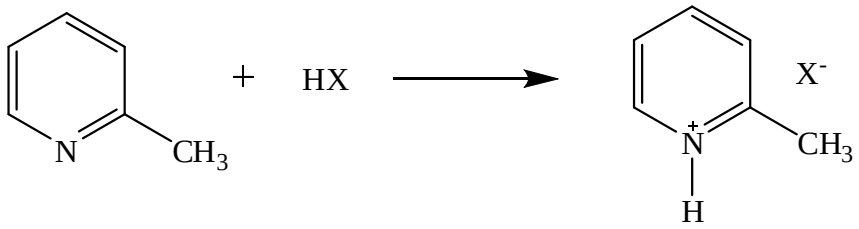


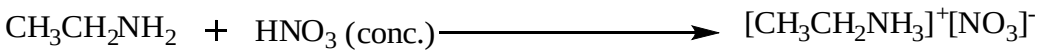
Figure 2.3: Heptachlorodialuminate salt (red-oil liquid) obtained from the mixture of alkyl benzyl chloride in excess and aluminium trichloride in liquid hydrogen chloride[40]

The ILs field started with Humphrey Davy's work on the electrolytic decomposition of simple molten salts under the influence of an applied direct current electric field, to yield the elements that initially had been chemically combined in the salt under study.[41] However, Davy's work focused primarily on high melting simple salts. Ramsay, reported by Schottenberger and co-workers,[42] was the first person to use an ambient temperature IL for scientific purposes. The later IL was prepared by combinations of acids and picoline as shown on Scheme 2.1. Surprisingly, these early reports are disregarded.



Scheme 2.1: Preparation of ambient temperature IL by combinations of picoline and acids[43]

The acknowledged ILs story started in 1914 with the preparation of ethylammonium nitrate ($[EtNH_3]^+[NO_3]^-$) with melting point (m.p.) of 12 °C as firstly reported by Paul Walden.[44] This compound results in the addition of concentrated nitric acid to ethylamine, after which the water was removed by distillation to give the pure salt that was liquid at room temperature and detailed for more purpose than any other IL, as shown on Scheme 2.2.



Scheme 2.2: Preparation of ethylammonium nitrate[44]

In 1982, Wilkes *et al.*[45] reported a new class of ILs based on dialkylimidazolium chloroaluminate. However, these chloroaluminate were very reactive to moisture and many chemicals. Ten years later, Wilkes and Zaworoto [46] synthesized air- and moisture-stable imidazolium salts containing weakly complexing anions such as tetrafluoroborate ($[BF_4]^-$) which developed a great growth till today (Detailed in Chapter Three).

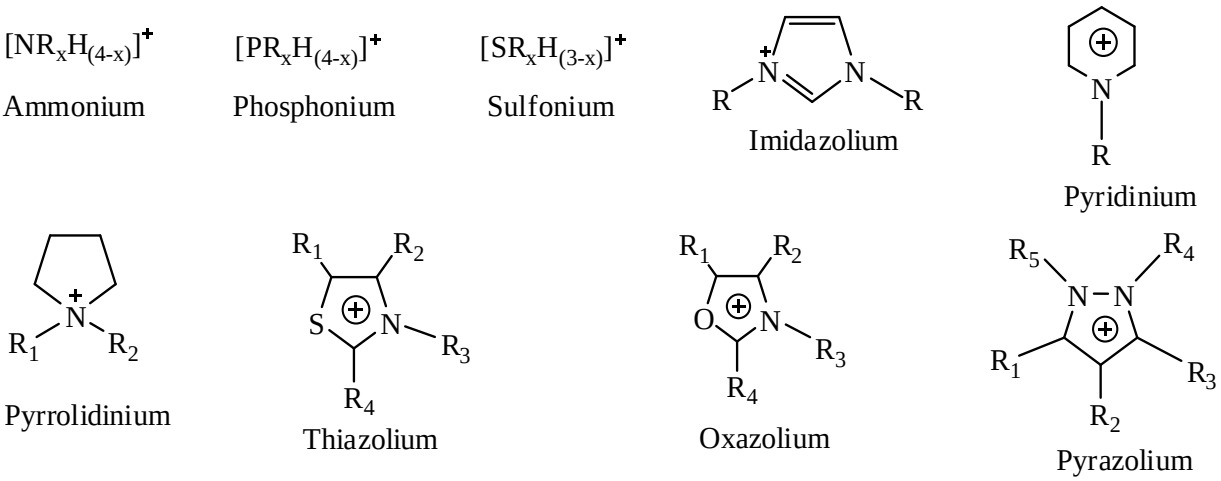
Some names have been given to ILs and this includes room temperature ILs, molten salts, ambient ILs, among other names, based on the context in which the authors need to appropriate them. Nevertheless, there is a significant difference between molten salt and ILs. ILs contain organic rather than inorganic cations. A molten salt is generally thought to refer to a high melting, highly viscous and very corrosive medium while ILs refer to molten phase below 100 °C. Despite both have the wide liquidus range, they differ just in the scale of temperature. For example, sodium chloride (NaCl) is a molten salt with a m.p. of 801 °C while 1-butyl-3-methylimidazolium chloride ([BMIM][Cl]) is an IL with a m.p. around 70 °C.

This feature makes ILs to be handled as ordinary solvents and more used as solvents in applications than higher temperature molten salts.

2.2.2 Structure of ionic liquids

ILs are composed entirely by organic cations and polyatomic inorganic or organic anions as shown on Figure 2.4. Their unique ionic character differentiate them from molecular solvents. Also, their fine-tune capabilities of their structure and organization, can lead to specific applications.

Cations



Anions

inorganic:

$[Cl]^-$, $[Br]^-$, $[I]^-$, $[BF_4]^-$, $[PF_6]^-$, $[NO_3]^-$, $[N(CN)_2]^-$

$[C(CN)_3]^-$, $[B(CN)_4]^-$, $[AlCl_4]^-$, $[Al_2Cl_7]^-$, $[SbF_6]^-$

organic:

$[RSO_3]^-$, $[RSO_4]^-$, $[RCO_2]^-$,

$[(RSO_2)_2N]^-$, $[RBF_3]^-$

Figure 2.4: Different cations and anions frequently used for the formation of ILs[40,47,48]

The interactions existing between cations and anions are coulombic in nature but their solvent and other physicochemical properties are dependent on other forces such as hydrogen bonding, π-π interactions, Van der Waals interactions and dispersive forces within ILs. Krossing *et al.*[49] showed that ILs are salts which are liquid at room temperature because of weak interactions between ions resulting from voluminous cations with delocalized charge and anions with delocalized charge. 1-Butyl-2,3-dimethylimidazolium bis(trifluoromethylsulphonyl)amide has been taken as an example in Figure 2.5.

However, ILs with halides anions (iodide, bromide, chloride) are solid at room temperature due to the smallest of the anion sizes, but very hygroscopic.

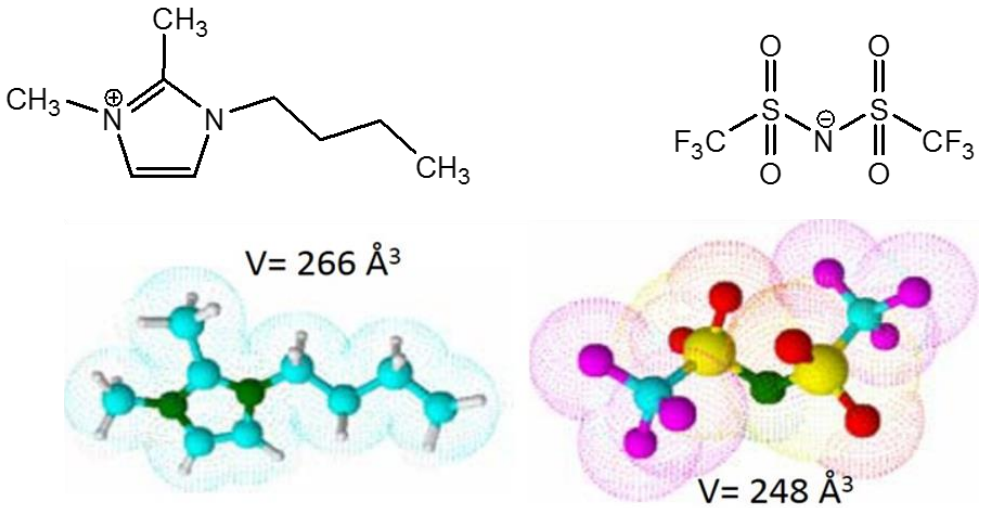


Figure 2.5: Weak interactions within ILs[49]

The field of ILs continues to develop beyond the idea of their interesting structure and properties.[50] They have been greatly researched in academia and industries, and hence the growth in publication rate has become exponential as an indication of their economic importance and their strong environmental impact (Figure 2.2).

2.2.3 Classification of ionic liquids

ILs have been classified according to many criteria such as discovery time, chemical behaviour or functional addition as compiled in Table 2.1.

Table 2.1: Different classes of ILs

Criteria	ILs categories/ Classes	Description	Examples	References
Discovery time	*1st Generation*: Chloroaluminates salts	They are obtained by the mixture of halide salts with $AlCl_3$ and they are water-unstable.	R-Cl–$AlCl_3$, R = cation	51
	2nd Generation: Room temperature ILs	They are air- and water-stable.	$[PF_6]^-$, $[CH_3COO]^-$. $[CF_3COO]^-$, $[NO_3]^-$, $[N(CN)_2]^-$, $[CF_3SO_3]^-$, $[(CF_3SO_2)_2N]^-$, $[CH(CF_3SO_2)_3]^-$ anions-based ILs	46
	3rd Generation	They are non-toxic and biodegradable.	ILs with $[(CH_3)_2PO_4]^-$ and $[CF_3SO_4]^-$ anions	52
Chemical behaviour	*Protic ILs (PILs)*	They are formed by proton transfer from a Brönsted acid to a Brönsted base. They display free available proton ready for hydrogen bonding.	Dialkylimidazolium-based ILs	50, 53, 54
	Aprotic ILs (APILs)	They contain substituents other than a proton (typically an alkyl group) at the site occupied by the labile proton in an analogous PIL.	Nitrogen-substituted alkyl , tetraalkylammonium-based ILs	50, 53, 54
Functional group (FG) addition	*Task-specific ILs (TSILs)*, also called functionalized-ILs	They are modified with the introduction of a particular organic function either on cation, anions or on both to gain a particular function.	ILs-FG, FG: Alkene; alkyne; ether; alcohol; silicon, nitrogen and transitional metal constituents	55-58

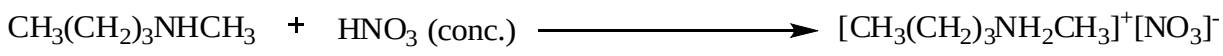
2.2.4 Synthesis of ionic liquids

Since ILs are structurally composed of cations and anions, their synthesis can be split into two steps; *i.e.* (1) the formation of desired cation and (2) the anion exchange reaction.

2.2.4.1 Formation of desired cations

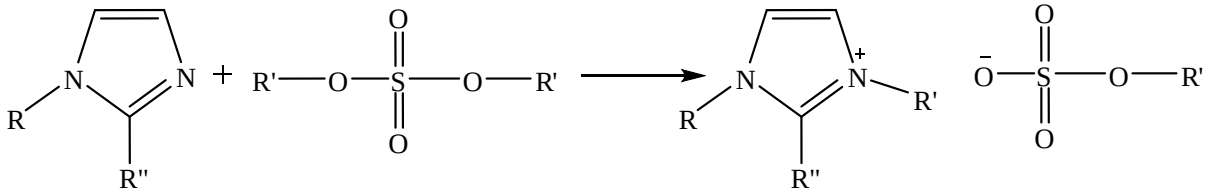
Common commercially desired cations available are halide salts such as 1-butyl-3-methyl-imidazolium chloride, the symmetrical tetraalkylammonium and tetraalkylphosphonium salts as well as trialkylsulphonium iodide.

The cation may be formed, firstly, by *protonation with a free acids* where the aqueous solution of the amine, phosphine or sulphide is neutralized with acids such as nitric acid, phosphoric acid, sulphuric acid, and hydrogen halides. This method ends by having the mixture of organic base, the acid and salt formed through neutralization. However, this equilibrium mixtures are thermally unstable, due to the vapour pressure of the two neutral components.[59] The preparation of $[CH_3(CH_2)_3NH_2CH_3]^+[NO_3]^-$ was the typical example as shown on Scheme 2.3.



Scheme 2.3: Protonation of 1-methylbutylamine with concentrated nitric acid

Secondly, *quaternization* of an amine, phosphine or sulphide using haloalkanes or dialkylsulphates leads to the formation of cations.[55,58] For example, in the case of amine, the organic groups (alkyl or aryl) from haloalkanes or any other alkylating agent is added to the central atom, nitrogen atom, of an amine, and this atom becomes positively charged with four bonds around it as shown in Scheme 2.4.



Scheme 2.4: Quaternization of dialkylimidazole (amine) with dialkylsulfates[60]

The amines and the phosphines are the most common starting materials for the quaternization reactions. In the latter reactions, haloalkanes are predominantly used as alkylating agents due to: (i) the availability of cheap haloalkanes, (ii) the substitution reactions occur at reasonable temperatures, and (iii) the conversion of formed halide salts to salts with others other anions is done smoothly. The most common used haloalkanes are chloroalkanes, bromoalkanes and iodoalkanes, with consideration of reaction conditions required increasingly in the following order Cl → Br → I, as has been likely for nucleophilic substitution reactions. Fluoride salts cannot be formed in this manner due to the poor leaving-group qualities of fluoride anions.

Basically during quaternization process, the amines and the phosphines are mixed with the alkylating agent, and then the mixture is stirred and heated. The reaction conditions such as time and temperature strongly depend on the alkylating agent employed. For instance, chloroalkanes are the least reactive while iodoalkanes are the most. Wasserscheid and Welton[55] point out an illustration example within the quaternization reaction of 1-methylimidazole with chloroalkanes was carried out at 80 °C for 2 to 3 days whereas the same reaction with bromoalkanes was complete at low temperatures (50 to 60 °C) for 24 hours. The reaction with iodoalkanes or dialkylsulphates are carried out at room temperature but shielding of the reaction vessel is required for the formation of iodide salts because they are very light sensitive. Also, there is a relative decrease of haloalkanes' reactivity when their alkyl chain length increases. Regarding the use of dialkylsulphates as alkylating agents, Holbrey *et al.*[60] and Gallagher, Simon, *et al.*[61] reported the preparation of many imidazolium-based ILs that were liquids at room temperature. The latter are non-toxic.

Moreover, other alkylating agents used in quaternization reactions are methyl or ethyl triflate, methyltrifuoroacetate, methyl tosylates, and octyl tosylates given in Figure 2.6.

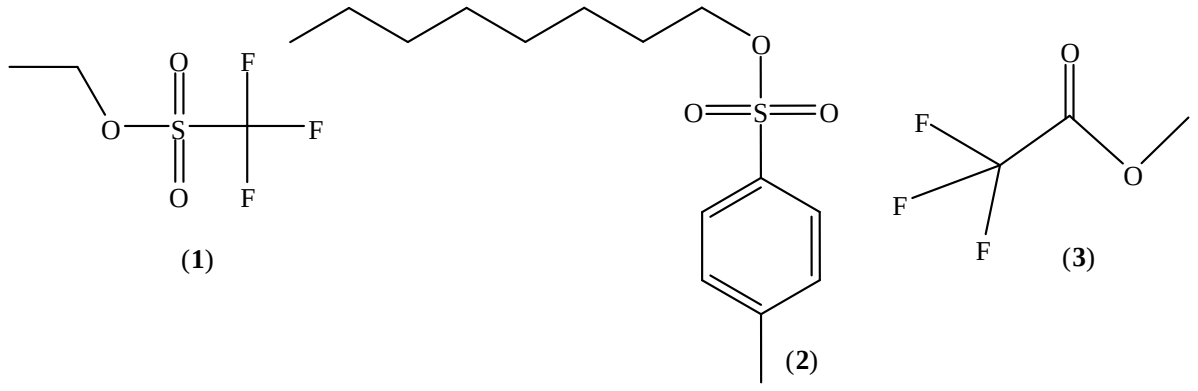


Figure 2.6: Examples of particular alkylating agents: (**1**) ethyl triflate, (**2**) octyl tosylates and (**3**) methyltrifluoroacetate[55]

Besides *n*-alkylpyridinium or 1,3-dialkylimidazolium cations, ILs containing other organic cations like quaternary ammonium,[62] phosphonium,[63] pyrrolidinium,[64] sulphonium [65] and thiazolium [66] have been reported (see Figure 2.4).

Requirements for these quaternization reactions include:

- Gentle heating to avoid the discoloration of the final product.
- Carrying the reactions under secured inert atmosphere by using a glove box, given that the products are very hygroscopic.

2.2.4.2 Anion exchange

The ILs obtained from either protonation or quaternization processes may be modified by replacing the counter anions with other anions of interest for a specific application. This process is described as "anion exchange". The anion exchange reactions can be reviewed in two categories: (i) direct reaction of halide salts with Lewis acids to form Lewis acid-based ILs and (ii) anion metathesis.

2.2.4.2.1 Lewis acid-based ionic liquids

Basically, there is an anion exchange between halide salts generated from previous step (Section 2.2.4.1) and Lewis acid. The most commonly used Lewis acid is aluminium(III) chloride ($AlCl_3$). In 1951, Hurley and Weir[51] reported the IL formed by the combination of 1-butylpyridinium with $AlCl_3$ in mole ratio of 1 : 2 (1-butylpyridinium : $AlCl_3$). Later on, Osteryoung *et al.*[67] and Wilkers'group[40] discovered the technology of synthesizing room temperature chloroaluminate salts from the mixture of $AlCl_3$ and *n*-alkylpyridinium or 1,3-dialkylimidazolium chloride. Depending on the molar proportions of quaternary halide salt (Q^+X^-) and Lewis acid (MX_n), the reaction generates more than one anion species, as illustrated by a series of equilibria on Scheme 2.5. 1-Ethyl-3-methylimidazolium chloride ([EMIM][Cl]), depicted in Figure 2.7, was taken as quaternary halide salt.

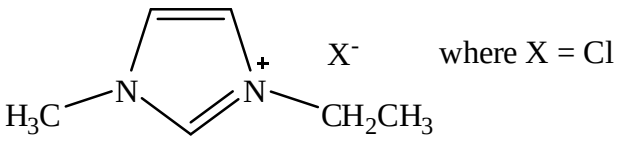


Figure 2.7: Structural representation of 1-ethyl-3-methylimidazolium chloride

It is worth mentioning that owing to high water-sensitivity of both starting materials and IL products, this reaction is carried out in a dry box and the formed ILs have to be stored in a dry box under inert atmosphere.

$$[EMIM]^+[Cl]^- + AlCl_3 \rightleftharpoons [EMIM]^+[AlCl_4]^- \quad (1)$$

$$[EMIM]^+[AlCl_4]^- + AlCl_3 \rightleftharpoons [EMIM]^+[Al_2Cl_7]^- \quad (2)$$

$$[EMIM]^+[Al_2Cl_7]^- + AlCl_3 \rightleftharpoons [EMIM]^+[Al_3Cl_{10}]^- \quad (3)$$

Scheme 2.5: Series of equilibria in the reaction between [EMIM][Cl] and $AlCl_3$[55,58]

This type of reaction is strongly dependent on the Lewis acid constituent and all Lewis acids follow the same reaction route as $AlCl_3$.

Considering the above equilibria, when [EMIM][Cl] predominates in molar excess over $AlCl_3$, the basic IL is formed (1). Conversely, the molar excess of $AlCl_3$ leads to the formation of an acidic ionic liquid (2 and 3). Neutral ILs are formed once both reactants are present in equimolar quantities. Besides $AlCl_3$, other Lewis acids used include ethyl aluminium dichloride ($AlEtCl_2$),[68] boron trichloride (BCl_3),[69] copper(I) chloride (CuCl),[70] tin(II) chloride ($SnCl_2$),[71] and iron(III) chloride ($FeCl_3$).[72]

This reaction is generally exothermic, hence it must be carried out with more attention. Lewis acid-based ILs have been widely applied in electrochemistry, electrodeposition, transition metal coordination chemistry, and as Lewis acid catalysts in organic synthesis. However, most of the Lewis acid-based ILs are air- and water-unstable ILs. This makes them less extensively used due to their handling challenges.

2.2.4.2.2 Anion metathesis

With anion metathesis, a new anion is introduced in halogen-based ILs. At this step, there is an anion exchange between anion from halide salts and the desired anion metal salts.

In 1992, Wilkes and Zaworoto[46] reported the air- and water-stable ILs based on 1,3-dialkylmethylimidazolium cations prepared via metathesis reaction between halide salts and a range of silver, alkali metal and ammonium salts or the free acid of the appropriate anion as given in Table 2.2.

Table 2.2: Examples of ILs prepared by anion metathesis

IL salts	Anion source	Reference
[Cation][PF_6]	HPF_6, $NaPF_6$	48, 73, 74, 79
[Cation][BF_4]	HBF_4, NH_4BF_4, $NaBF_4$	46, 77
[Cation][$(CF_3SO_2)_2N$]	Li[$(CF_3SO_2)_2N$]	73, 76
[Cation][CF_3SO_3]	[CF_3SO_3]CH_3, NH_4[CF_3SO_3]	75, 76
[Cation][CH_3CO_2]	Ag[CH_3CO_2]	46
[Cation][CF_3CO_2]	Ag[CF_3CO_2]	46
[Cation][$CF_3(CF_2)_3CO_2$]	K[$CF_3(CF_2)_3CO_2$]	67
[Cation][NO_3]	Ag[NO_3], Na[NO_3]	73, 76
[Cation][$N(CN)_2$]	Ag[$N(CN)_2$]	78
[Cation][$CB_{11}H_{12}$]	Ag[$CB_{11}H_{12}$]	80
[Cation][$AuCl_4$]	H[$AuCl_4$]	81

The silver salts are predominantly used in anion metathesis due to the high ability of silver ion to precipitate halide ions and then the silver halide salts formed within these reactions are very low soluble in most of the solvents used. This allows its ease separation by filtration and ILs are isolated in high yield and purity. Nevertheless, the efficiency of this method is controverted by the high cost of silver salts and the large quantities of the solid by-products produced.[55]

The use of the free acid and alkali metal or ammonium salts of the appropriate anion salt seems to be probably the most favorable method as the produced by-products are easily removed by washing with water. The drawback of this method becomes extremely pronounced in the preparation of water-miscible ILs where the separation of produced ILs and the by-products will be complex. The additional solvents (sometimes not green) to extract the ILs, the detection of halide ions in the washing solutions, the concentration of the extracts by removing the solvent *in vacuo*, and further purification processes to obtain the pure ILs will lower cost effectiveness. Furthermore, the yield of the final product will be low due to some product loss through all these steps.

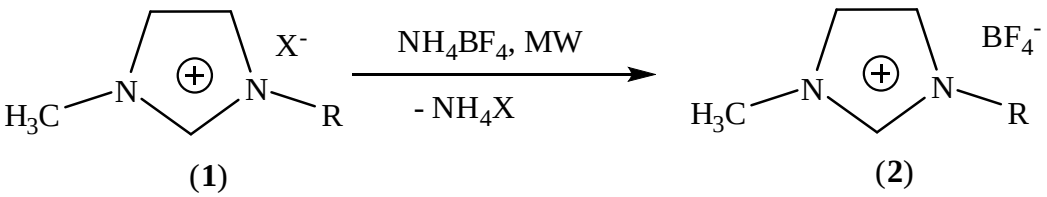
2.2.5 Microwaves assisted ionic liquids synthesis

Microwave (MW) irradiations lie in the region of the electromagnetic spectrum, between radio waves and infrared waves. Their wavelengths are between 0.01 and 1 m, which correspond to frequencies between 0.3 and 30 x 10^9 Hertz.

In chemical perspective, heating with a MW becomes an efficient process leading to a fast increase of temperature with fast reactions occurring and the relatively higher yields. This is due to the effective coupling of the MW energy with the molecules that have the mobile electric charges such as polar molecules and ionic compounds in the reaction media. The MW energy is transferred to the compound via two mechanisms, namely dipole rotation and ionic conduction.[82,83] By dipole rotation mechanism, polar molecules are heated and forced to rotate and same time aligned themselves in the direction of the MW electric field. Therefore, the energy is lost when they are colliding with other molecules. In ionic conduction mechanism, the MW electric field generates the ionic motion of the ionic compounds and the immediate superheating is produced as a result of lost energy due to the electric resistance of the ionic substance.

Owing to their ionic character, ILs can easily absorb MW irradiations and the fast energy transfer is facilitated by ionic conduction mechanism. This feature has raised the interest of synthesizing the ILs using MW technology.[84-88]

In 2001, Varma and Namboodiri[84] firstly reported the use of MW irradiation in ILs preparation. They synthesized 1-alkyl-3-methylimidazolium halides by alkylating 3-methylimidazole with alkyl halides and terminal dihalides under solvent-free conditions. The ILs were produced in less than 2 min with yields of > 70%. Later on, the same group[89] described how to introduce the alternate anion in halogen-based ILs by an anion exchange step under MW irradiation conditions. They illustrated this by the synthesis of ILs containing $[BF_4]^-$ anion as shown on Scheme 2.6.



Scheme 2.6: Preparation of 1-alky-3-methylimidazolium tetrafluoroborates ([RMIM][BF_4]) using MW[89]

This approach has been adopted to synthesize tetrachloroaluminate,[90] tetrachloroindates[91] and tetrachlorogalates[92] anions-based ILs. Palou in his reviews, tried to cover the basics on the use of MW irradiation in synthesis and ILs.[82,83]

The application of MW in ILs synthesis has known a huge success over the conventional method by being eco-friendly approach, cutting down the time required for this synthesis, providing high yields of products with high purity, enhancements in conversion, and the reaction can be completed under solvent-free conditions. It is also noteworthy that the efficient conversion of electric energy into MW energy promotes energy savings and the use of safe heating source. The laboratory MW equipment possesses the selected continuous power supply unlike the household MW.

Lévêque *et al.*[93-95] showed that MW can be used alone or in combination with a power ultrasound (US) and this has been agreed by Roshan *et al.*[96] This method has known a significant application in ILs synthesis like pyridazinium-based ILs,[97] picolinium-based ILs,[98,99] imidazolium and pyridinium-based ILs,[48,100] and monodisperse poly (ionic liquid) particles,[101] among others.

When using MW in synthesis, working factors such as the nature of the reactor (reaction volume per vessel, temperature sensor and pressure sensor, agitation mode, flow rate), the amount of the reaction mixture and the capability of the reaction components to absorb MW energy have to be highly considered. Further to this, reaction parameters such as time, temperature, pressure, power, agitation and flow, must be chosen for an accurate control of a given reaction.[102]

2.2.6 Purification of ionic liquids

The main impurities sources reside in production of by-products or degradation products, incomplete reactions and unreacted species during synthesis. Moreover, the starting materials and the solvents intended to be used in this synthesis, also could contain some impurities.

Based on one of green chemistry principles, which states that "it is better to prevent waste than to treat or clean up waste after it is formed", it is extremely valuable to work with pure starting reagents than purifying the synthesized ILs with impurities from starting materials.[55] Armarego and Perrin[103] described the suitable methods for the purification of the starting materials including 1-methylimidazole.

For instance, in preparation of 1,3-dialkylimidazolium salts, 1-methylimidazole is distilled under vacuum from sodium hydroxide between temperature of 210 and 212 °C. The haloalkanes or other alkylating agents and all solvents have to be dried and distilled prior to use. For all synthesized ILs, any volatile impurities such as unreacted species and solvents can be removed from ILs by distillation.

The traces of oxide ions in $AlCl_3$-based ILs, mostly aluminium dichloride oxide are removed by bubbling triphosgene through the ILs where carbon dioxide gas as by-product is easily evaporated under vacuum.[104] Water as the impurity present in highest concentrations in most of ILs is removed by leaving the ILs at 60 to 80 °C under vacuum for several hours, preferably overnight. The amount of water is determined by use of Karl-Fisher titration while infrared spectroscopy can be used as an indicator. Recently, Ferraz *et al.*[105] reported the use of imidazole carbenes as new method improving the minimization of halide ions and metal ions impurities in imidazolium-based ILs synthesis.

Concerning the workspace and the apparatus used, the system has to be under nitrogen, or other inert gas such as argon, to minimize side reactions which may occur and the glassware has to be dried and kept free of acetone to avoid any discoloration of the product.

2.2.7 Physicochemical properties of ionic liquids

ILs have been declared as "green solvents" compared to conventional organic solvents based on the greenness of their preparation,[106] their specific properties including negligible vapour pressure,[107] non-flammability,[108] excellent thermal stability,[109] fine-tune ability of their ionic constituents for a specific application[110] and possibly lower (eco) toxicity.[111,112] All these aspects make them improved media over traditional solvents in terms of reactivity, selectivity, and recyclability.

Generalization of physicochemical properties of ILs is so ambiguous owing to their huge diversity in anion-cation combinations, preparation and purification modes, nature of impurities and applications. Despite various theories given by researchers, they all agree that the physicochemical properties of ILs vary as function of cation, anion, side chain length on the cation and the introduction of functionalized group on both anions and cations,[55,113,114] as detailed in this section. In many cases, temperature and impurities such as water, halide ions and cosolvents can also alter these physicochemical properties.[115,116]

The 1,3-dialkylimidazolium-based ILs have been highly reviewed because of their wide synthetic applications.[53,55,117-119]

2.2.7.1 Liquid range behaviour and melting points

2.2.7.1.1 Liquid range behaviour

ILs manifest a wide liquid range than common molecular solvents as reported by Villanueva *et al.*[120] The lower temperature limit corresponds to glass formation temperature, (T_g), and varies with the structure and the interactions between ions. For example, T_g of 1-alkyl-3-methylimidazolium ([RMIM]$^+$) salts are in the range of - 70 to - 90 °C.[55] Given that ILs are entirely ionized compounds and having weak ion-ion pairing interactions, they have a little measurable vapour pressure. Hence, ILs upper limit phase is referred to their thermal decomposition rather than vaporization. Most of the ILs are stable at and above 400 °C.[121] The thermal decomposition varies largely with the anions rather than cations and increases with the hydrophobicity of anions as seen on Figure 2.8.

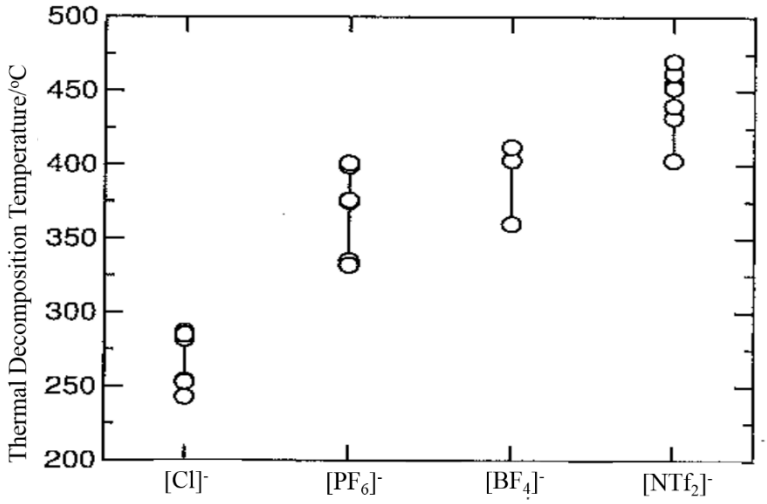


Figure 2.8: Thermal decomposition temperature ranges for a series of RMIM$^+$-based ILs with different anions[122]

From Figure 2.8, the thermal stability increases when the nucleophilicity of the anion decreases. This means that ILs having weakly coordinating anions are most resistant to thermal decomposition. This observation has to be taken as guideline for a selection of maximum operating temperature of any reactions in a given ILs.

The thermal stability of ILs varies with many facts such as impurities which will reduce it, and exposition time to thermal stress as shown by Baranyai and his coworkers.[123] Conversely, Earle *et al.*[107] showed that some thermally stable ILs should evaporate under harsh temperatures and vacuum conditions.

2.2.7.1.2 Melting points

The coulombic interactions existing between ions of ILs, given by equation 2.1, are reduced because of a relative weak ion-ion pairing due to non-coordination of their ions.[55]

$$E_c = MZ^+Z^-/4\pi\varepsilon_0 r \qquad (2.1)$$

Where M is the Madelung constant, Z^+ and Z^- are the ion charges, and r is the inter-ion separation distance.

The melting points (m.p.) of ILs strongly depend on the size of cation and anions. By increasing the size of ions, the inter-ion separation distance will also increase and the large ions enable charge delocalisation which will in turn, reduce the overall charge density. As result, this will reduce the magnitude of the coulombic interactions, disrupt the packing efficiency and reflect the decrease in m.p. Therefore, ILs containing large organic cations or anions have lower m.p. than their analogous inorganic salts. In addition, hydrogen bonding interactions observed in the crystal structures of halide anions-based ILs and absent in the structure of other large anions, can increase the m.p. as compiled in Table 2.3.

Table 2.3: Melting points (m.p.) and thermochemical radii (r) of the anions (X) for Na^+ and $[EMIM]^+$ salts[55]

X^-	**r (Å)**	**m.p. (°C)**	
		NaX	[EMIM][X]
Cl^-	1.7	801	87
$[BF_4]^-$	2.2	384	6
$[PF_6]^-$	2.4	>200	60
$[AlCl_4]^-$	2.8	185	7

In addition, the length of alkyl chain on the cation implicates major changes on m.p. of ILs as shown on Figure 2.9.

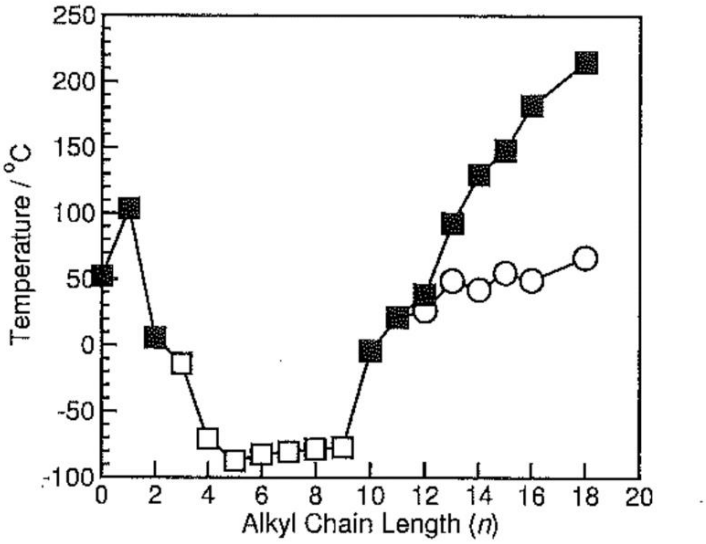


Figure 2.9: Changes in m.p. of [RMIM][BF_4] as a function of chain length, with true m.p. (■) and glass transitions (□), followed by formation of a smetic liquid crystal phase (○)[76]

From Figure 2.9, it is clear that, for $[RMIM]^+$-based ILs, increasing the substituent length (n = 1-4 carbons) reduces the m.p. of ILs through destabilisation of coulombic packing, and this leads to glass formation on cooling for n = 4-8 carbons. The m.p. start to increase again on extending the alkyl chain length (n = 8-10 carbons) as Van der Waals forces between the long hydrocarbon chains increase and impact on the local structure by separating the covalent, hydrophobic alkyl chains with the charged ionic regions of the molecules. This leads to the increased structural ordering which can be observed through the re-emergence of higher m.p. together with the formation of structured liquid crystalline materials.

Moreover, the m.p. increase with the extent of branching within the alkyl chain owing to the changes in crystal packing efficiency due to the decrease of free-rotation volume and the increase of atom density as presented in Table 2.4.

Table 2.4: Melting points (m.p.) and heats of fusion (ΔH_{fusion}) for [BMIM][PF_6] and [PMIM][PF_6] as function of branching in the alkyl substituent[53,122]

N(1)-substitution	m.p. (°C)	ΔH_{fusion} (kJ.mol^{-1})
n-Butyl	6.4	31
sec-Butyl	83.3	72
tert-Butyl	159.7	83
n-Propyl	40	
*Iso*propyl	102	

N(1)-substitution: Substitution on the nitrogen atom at position one of the imidazolium ring.

2.2.7.2 Viscosity

For the ILs to be used as solvent during a chemical reaction or any other applications, their viscosity has to be known. For instance, ILs with high viscosities are disadvantageous to the progress of a reaction and less appropriate as solvent media but they are suitable for applications as lubricants. In comparison with the most common molecular solvents, having room temperature viscosities between 0.2 and 10 cP,[124] ILs are highly viscous and their viscosities range is around 10 to 10^5 cP.

Viscosity of an IL is governed by a combination of a set of interactions, namely, electrostatics interactions, hydrogen bonding, Van der Waals interactions, ion size and also polarizability within ILs constituents (cation and anion). As mentioned early in Section 2.2.2, cations and anions are held together by electrostatic forces which become weak with the increase of ion size due to the delocalization of charges on either cation or anion. More the ions are voluminous, less the Van der Waals interactions become significant and less hydrogen bonding interactions are prominent. Therefore, viscosity of ILs depends strongly on the size and nature of both cations and anions. as shown in Table 2.5 and Table 2.6.

Table 2.5: Viscosity and density data for alkylimidazolium-based ILs for non-haloaluminate ILs at 25 °C

Cation	Anion	Viscosity (cP)	Density ($g.cm^{-3}$)	Reference
$[EMIM]^+$	$[BF_4]^-$	34	1.240	125
$[EMIM]^+$	$[CF_3SO_3]^-$	45	1.390	76
$[EMIM]^+$	$[CF_3SO_3]^-$	43	1.380	126
$[EMIM]^+$	$[(CF_3SO_2)_2N]^-$	34	1.510	127
$[BMIM]^+$	$[BF_4]^-$	115	1.140	128
$[BMIM]^+$	$[(CF_3SO_2)_2N]^-$	69	1.430	129

Table 2.6: Viscosity and density data for alkylimidazolium-based ILs for haloaluminate ILs at 25 °C[45]

IL system	Cation	Anion	Viscosity (cP)	Density ($g.cm^{-3}$)
34-66 mol% [EMIM][Cl-$AlCl_3$]	$[EMIM]^+$	$[Al_2Cl_7]^-$	14	1.389
50-50 mol% [EMIM][Cl-$AlCl_3$]	$[EMIM]^+$	$[AlCl_4]^-$	18	1.294
60-40 mol% [EMIM][Cl-$AlCl_3$]	$[EMIM]^+$	$[Cl]^-$, $[AlCl_4]^-$	47	1.256
50-50 mol% [BMIM][Cl-$AlCl_3$]	$[BMIM]^+$	$[AlCl_4]^-$	27	1.238

Sánchez and co-workers[130] as well as other different researchers[131-133] reported that the viscosities of ILs decrease rapidly when the temperature is increased. It is worth to note that the viscosities of ILs do not follow Arrhenius behaviour but they fit with the Vogel-Tammann-Fulcher equation as shown in equation 2.2.

$$\eta = \eta_0 \exp\left[\frac{B}{T - T_0}\right] \qquad (2.2)$$

Where η_0, B and T_0 are adjustable parameters.

The presence of chloride (Cl^-) impurities or other halide ions impurities obtained from the preparation of these ILs, increase viscosity intensely.

The high concentration of these halide ions lead to the strong hydrogen bonding between these ions and the cation, especially for $[RMIM]^+$-based ILs.

Furthermore, the addition of co-solvent in the ILs reduces its viscosity in respect to the high co-solvent dielectric constant. The magnitude of changes in viscosity is great for polar solvents like water, ethanol, methanol, butanone, ethyl acetate, and less for benzene.[55,115,134] The introduction of other functional groups such as oligoether on the cation, the presence of bis(trifluoromethylsulfonyl)amide ($[NTf_2]^-$ or $[(CF_3SO_2)_2N]^-$) and dicyanamide ($[N(CN)_2]^-$) anions, also reduce the viscosity of ILs.

For non-haloaluminate ILs having the same cation, the viscosity increases with respect to the change of anion in the following order: $[(CF_3SO_2)_2N]^-$, $[BF_4]^-$, $[CF_3CO_2]^-$, $[C_2F_7SO_3]^-$, $[C_3F_7CO_2]^-$, $[CH_3CO_2]^-$, $[C_4F_9SO_3]^-$. This order is not a function of anion size, though other anion properties such as their aptitude to form weak hydrogen bonding with the cations. The presence of polyfluor unit in anion provides reductions in viscosity since the Van der Waals interactions are also reduced.[55] Regarding the cation within ILs having the same anion, higher values of viscosity are observed due to the hydrophobicity of cation resulting in the increase of a length of substituted alkyl unit on cation unit.[55,135]

For haloaluminate ILs, described as ILs with single cation and a mix of anions, the viscosity is directly proportional to the anionic composition. The viscosity of [EMIM][Cl-$AlCl_3$] as typical example has been reported by Mantz and his co-worker[136] at 30 °C over a range of compositions. The viscosity remains relatively constant, changing from 14 to 18 cP for [EMIM][Cl] below 50% and starts increasing when [EMIM][Cl] exceeds 50% over 190 cP as shown on Figure 2.10.

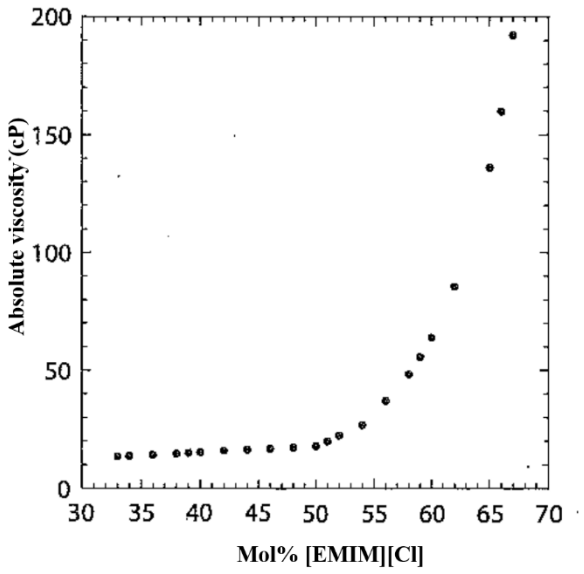


Figure 2.10: Variation in absolute viscosity in [EMIM][Cl-$AlCl_3$] as a function of the [EMIM][Cl] mol% at 30 °C[136]

This viscosity's increase is due to the increase in $[Cl]^-$ concentration and significantly confirms the hydrogen bonding between $[Cl]^-$ anions and the hydrogen atoms on the $[RMIM]^+$ ring. Similarly to non-haloaluminate ILs, the larger size cation generates greater viscosity and high asymmetric substitution on the cations reduces the viscosity of the IL.

Transport properties of ILs such as diffusion and mass transfer as well as reaction rate can be improved by decreasing the viscosity of the ILs for a good practical catalytic applications.

2.2.7.3 Density

Generally, densities of ILs are higher than those of water and organic solvents,[134,137] varying between 1.030 $g.cm^{-3}$ for 1-hexyl-3-methylimidazolium chloride ([HMIM][Cl]) and 2.4 $g.cm^{-3}$ for a 34-66 mol% trimethylsulphonium bromide-aluminium bromide ($[(CH_3)_3S][Br\text{-}AlBr_3]$).[55] Exceptions are observed for alkyl pyrrolidinium dicyanamide ($[RPY][(CN)_2N]$) with density ranging from 0.92 to 0.97 $g.cm^{-3}$ at 25 °C.[55]

The density of ILs depends upon its constituents as shown in Table 2.5 and Table 2.6. The density decreases by increasing the size of the cations. Basically, the increase of the alkyl chain length on the cation leads to the constant extend of the molar volume per each two $-CH_2-$ groups.[138]

However, it increases with the increase of anion mass in this order $[CH_3SO_3]^-$ ≈ $[BF_4]^-$ < $[CF_3CO_2]^-$ < $[CF_3SO_3]^-$ < $[PF_6]^-$ <$[NTf_2]^-$ for ILs having same cation. In addition, density increases with the presence of fluorine (in cation or anion) slowly,[139] other halogens (iodine and bromine),[140] pentafluorosulphane,[141] aromatic cations rather than aliphatic due to their π-π interactions within their structure which can reduce the inter-molecular distances,[128] nitriles[129] and hydroxyl groups[142] in the cation structure of the IL. The presence of alkyl ether functional groups for imidazolium-based ILs exhibits higher densities than n-alkyl substituted equivalents.[143] Regarding the anion, the presence of heavy elements on it such as oxypentafluorotungstate anion, ($[WOF_5]^-$) increases significantly the density.[144]

The dependence of ILs densities on the temperature is less significant than on viscosity but they still decrease with the increase of temperature.[132,135,145] In addition, impurities such as water and halide ions decreases the density, where, for instance, the presence of 25 wt.% water in [BMIM][BF_4] results in only a 4% decrease in density.[55]

2.2.7.4 Solubility in ionic liquids

Solubility of compounds in ILs depends on the constituents of the ILs and the degree of cation substitution. For example, water is soluble in ILs with halide anions ($[Cl]^-$, $[Br]^-$) but becomes completely immiscible in ILs with $[PF_6]^-$ anions. In chemical synthesis, especially in catalytic process, a knowledge of differential solubilities of reagents, catalysts and products in ILs is needed for effective isolation, extraction of the product and the recyclability of catalysts and ILs.

The efficient solute solubility in ILs is related to the IL properties such as the ability of hydrogen bond donation (HBD) from the cation, the hydrogen bond accepting (HBA) in the anion and the π-π or C-H…π interactions which enhance aromatic solubility.[55]

In general, solubility of organic compounds and metal ions in ILs is the most evaluated. Solubilisation of metal ions, especially those that are used as catalysts, involves dissolution either of simple metals or metal coordination complexes. This solubility must be sufficient and selective in order to allow the immobilisation of the catalysts in the reacting phase and the product separation in the extraction phase. Simple metal salts are poorly soluble in non-coordinating ILs while metal complexes are more soluble. From this point, complexation and addition of lipophilic ligands on metal ions increase their solubility in ILs as reported by Liu *et al.*[146] and Abbot *et al.*[147]

Davis initiated another approach helping in metal ions solubility in ILs, which rises in integration of the complexing functionality as an integral part of the IL.[148] The knowledge of solubility of metal salts in ILs enhance the metal finishing technologies by providing a framework for the design of metal extraction processes based on the use of ILs as solvents.[149]

Solubility of organic compounds in ILs depends on their solubilizing interactions with IL components. This enables reaction and easy extraction processes to be maximized according to the liquid-liquid extraction systems used.[74] Hydrocarbons are poorly soluble in most ILs and their solubility increases by increasing the alkyl-chain length of ILs. Polar solutes and those with strong proton-donor groups (carboxylic acids, phenols and diols) interact strongly with ILs. Compounds like aliphatic and aromatic ketones, aldehydes and esters interact with ILs via weak Van der Waals interactions.[55] Solubility of water in ILs changes with both cation substitution and anion types, where coordination anions generate water soluble ILs and large, non-coordinating anions lead to hydrophobic ILs.

Complex organic compounds such as cyclodextrins, glycolipids,[150] antibiotics[151] and monosaccharides[152] can be dissolved in ILs. Their solubility is more significant into polar ILs with hydrogen bond acceptor capability like Cl^--containing ILs.

Solubility and partition studies of organic compounds in ILs have extended the ILs applications in chromatography and analytical chemistry. Based on this, the green-sample preparation methods of organic compounds for the chromatographic analysis,[153] analytical sample preparation of organic compounds from food and environmental samples,[154] and both experimental and theoretical studies of interaction between organic compounds and ILs,[155] have been reported.

2.2.7.5 Polarity

For all chemical reactions, the choice of solvents impacts intensely on the reaction rate and chemical equilibria. However, the efficiency of the solvent in the reaction must be examined prior to use.

Besides the solvent's molecular-macroscopic properties stated in previous sections (Section 2.2.7.1 to Section 2.2.7.4), the microscopic individual and mutual intermolecular interactions such as dipole moment, electronic polarizability, HBD and HBA capability, electron-pair donor and electron-pair acceptor capability, have to be considered.[156] The assumption of forces of interactions between solvent and solute molecules lead to the rule "like dissolves like".

The sum of all these possible (specific and non-specific) intermolecular interactions between solvent and solute molecules, except for those that lead to a definite chemical reaction, are related to polarity.[55,156] By definition, the polarity of solvent is referred to its ability to dissolve a solute by interacting with the solute molecules.

Polarity of ILs have to be investigated for their selective uses in chemical processes, *i.e.* understanding the solvation process in ILs, the relationship between IL structure and solvent polarity.[157] Like other properties, polarity of ILs also is dictated by different combinations of cations and anions, the length of the alkyl chain and the functional group attached to the cation and the type of anion. Solvent polarity of ILs is investigated using several methods including: (i) microwave dielectric spectroscopy,[55,158,159] (ii) chromatographic measurements using Abraham's solvation parameters model,[55,160,161] (iii) solvatochromic method using empirical Kamlett-Taft solvent parameters,[55,162] (iv) fluorescence spectra,[55,163] and (v) electron paramagnetic resonance spectroscopy.[55,164]

In details, *microwave dielectric spectroscopy* helps to determine the dielectric constant (ϵ_r) as the most measure of solvent polarity used by chemists. High ϵ_r shows higher polar solvent. For a series of $[RMIM]^+$-based ILs, the polarity decreases as the alkyl chain on the cation increases and in the order $[OTf]^- > [BF_4]^- > [PF_6]^-$ as shown in the Table 2.7.

Table 2.7: Static dielectric constants (ϵ_r) for ILs[158]

Ionic liquid	ϵ_r
[EMIM][OTf]	15.2
$[EMIM][BF_4]$	12.8
$[BMIM][BF_4]$	11.7
$[BMIM][PF_6]$	11.4
$[HMIM][PF_6]$	8.9

Regarding chromatographic method, alkylammonium and phosphonium-based ILs have been employed as stationary phases in gas chromatography to study the retention of variable compounds through Abraham's solvation parameter model given by the equation 2.3.

$$\text{Log } K_{\text{L}} = c + r\,\text{R}_2 + s\,\pi_2^{\text{H}} + a\,\alpha_2^{\text{H}} + b\,\beta_2^{\text{H}} + l\,\text{log}\,L^{16} \qquad (2.3)$$

Where,

K_{L}: Solute-solvent partition coefficient.

$\text{R}_2, \pi_2^{\text{H}}, \alpha_2^{\text{H}}, \beta_2^{\text{H}}, \text{log}\,L^{16}$: Describe solute properties in the solvent where the first four terms deal with the ability of the solute to contribute in the solute-solvent interactions.

c, r, s, a, b, l : Solvent coefficients that explain solvent properties; where *c* is a constant, *r* is the tendency of the solvent to interact through σ- and π-electron pairs (Lewis basicity), *s* describes solvent's contribution from dipole-dipole and dipole-induced dipole interactions (polarizability/dipolarity), *a* and *b* denote the hydrogen bond basicity of the solvent and its hydrogen bond acidity respectively, *l* indicates how the solvent will separate homologous series (hydrophobicity of the solvent) and has idea of solvent cavity formation and dispersion interactions.

This model describes solute behaviour such as basicity, shows solute-solvent interaction and explains the solvent properties. Basically, solvation process involves three steps.

In step (1), the self-association of the solvent is altered by the creation of the cavity of proportional size to the volume of the solute, within the solvent. In step (2), the solute is introduced in the cavity and then in step (3), solute-solvent interaction occurs (Van der Waals, the intermolecular attractive forces) where the solvent molecules are polarized by the solute, reorganizing from their original positions and orientations around the solute itself as depicted on Figure 2.11. This model is based on the linear free energy relationship (LFER).[165-167]

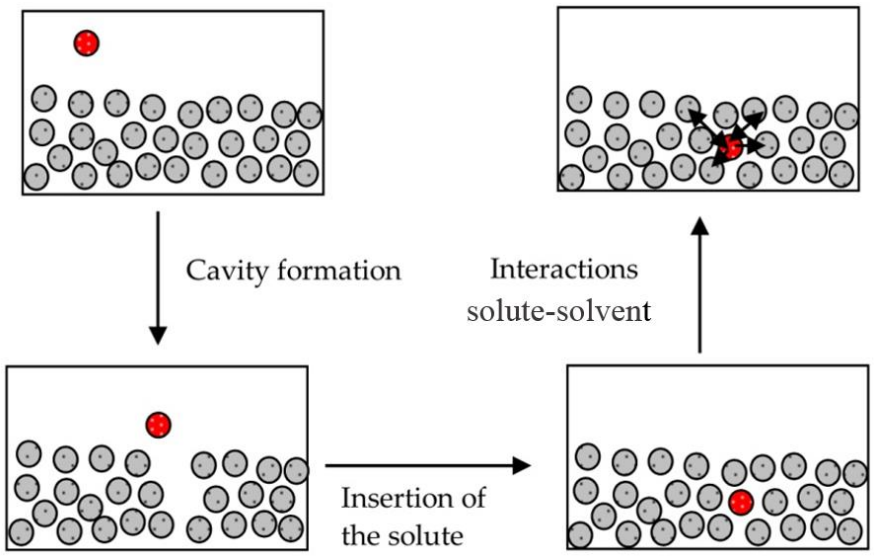


Figure 2.11: Model of the solvation process[168]

The general observation drawn from this model once applied on ILs, is that ILs such as tetraalkylammonium halides, nitriles and substituted alkane sulfonates are strong hydrogen bond bases and this basicity is a function of the anion. This basicity decreases for penta-cyanopropionide, picrate ($[C_6H_2(NO_2)_3O]^-$), triflate ($[CF_3SO_3]^-$), perfluorobenzenesulfonate ($[C_6F_5SO_3]^-$) salts, and this is due to weak coulombic interactions by delocalization of the charge on the anions.[55]

In fact, ILs with poor associating anions exhibit high solvent's ability to form a cavity and its dispersion interactions in comparison to molecular polar solvents and this increases with the size of the cation. More the cavity is big, less the solvent is polar. This ability weakens with higher hydrogen bond base anions. The ILs with electron-rich aromatic rings interact with solutes via π-π and n-π interactions. It is noteworthy that, in general, hydrogen bond basicity (***a***) is generally high and depends mainly on the anion, hydrogen bond acidity (***b***) is generally low and depends on both cation and anion, dipolarity/polarizability (***s***) are high, reflecting the influence of coulombic interactions and dispersion forcers (***l***) are constant for all ILs.

With *solvatochromic dyes*, the values of the energy of the electronic transition, E_{NR}, and solvent properties parameters such as π^*, α and β have been explored based on Kamlett–Taft linear solvation energy relationship (LSER) equation (equation 2.4) as compiled in Table 2.7.

$$(XYZ) = (XYZ)_0 + \mathrm{a}\,\alpha + \mathrm{b}\,\beta + \mathrm{s}\,\pi^* \qquad (2.4)$$

Where π^* is for dipolarity/polarizability, α is for hydrogen bond acidity and β is for hydrogen bond basicity.

Table 2.8: Solvent polarity measurements of some ILs and few organic solvents[55,169-171]

Salt	E_{NR}	π^*	α	β	Ω
$[Pr_2NH_2][SCN]$	1.006	1.16	0.97	0.39	
[*sec*-$BuNH_3$][SCN]	1.006	1.28	0.91		0.87
Water	1.000	1.09	1.17	0.47	0.82
$[EtNH_3][NO_3]$	0.954	1.24	0.85	0.46	
$[BuNH_3][SCN]$	0.948	1.23	0.92		
$[PrNH_3][NO_3]$	0.923	1.17	0.88	0.52	
$[Bu_3NH][NO_3]$	0.802	0.97	0.84		
$[BMIM][ClO_4]$	0.684				0.67
$[BMIM][BF_4]$	0.673	1.09	0.73	0.72	0.66
[BMIM][TfO]	0.667				0.65
$[BMIM][PF_6]$	0.667	0.91	0.77	0.41	0.68
Ethanol	0.654	0.54	0.75	0.75	0.72
$[BMIM][Tf_2N]$	0.642				
[BMIM]Cl		1.17	0.41	0.95	
$[EtNH_3]Cl$	0.636				
$[OMIM][PF_6]$	0.633	0.88	0.58	0.46	
$[OMIM][Tf_2N]$	0.630				
[OMIM]Cl		1.09	0.33	0.90	
$[Pr_4N][CHES]$	0.62	1.08	0.34	0.80	
$[BMIM][CF_3CO_2]$	0.620				
$[Bu_4N][CHES]$	0.62	1.01	0.34	0.98	
$[Pe_4N][CHES]$	0.58	1.00	0.15	0.91	
$[Bu_4N][BES]$	0.53	1.07	0.14	0.81	
$[BMMIM][Tf_2N]$	0.525				
$[Bu_4N][MOPSO]$	0.49	1.07	0.03	0.74	
$[OMMIM][BF_4]$	0.543				
$[OMMIM][Tf_2N]$	0.525				
$[Et_4N][NO_3]$	0.460				
Acetonitrile	0.460	0.75	0.19	0.31	0.69
$[Et_4N]Cl$	0.454				
$[Hx_4N][PhCO_2]$	0.420				
Diethyl ether	0.117	0.27	0.00	0.47	0.47
Cyclohexanone	0.009	0.00	0.00	0.00	0.60

The most used solvatochromic dyes are Nile red[55] and Reichardt's dye.[55,159] Recently, three solvatochromic dyes[162] such as $Fe(phen)_2(CN)_2$ (**Fe**), 3-(4-amino-3-methyl-phenyl)-7-phenyl-benzo-[1,2-b:4,5-b′]-difuran-2,6-dione(**ABF**) and 4-tert-butyl-2-(dicyanomethylene)-5-[4-(diethylamino)benzylidene]-Δ^3-thiazoline (**Th**), have been used to determine the polarity of imidazolium-based ILs (Figure 2.12).

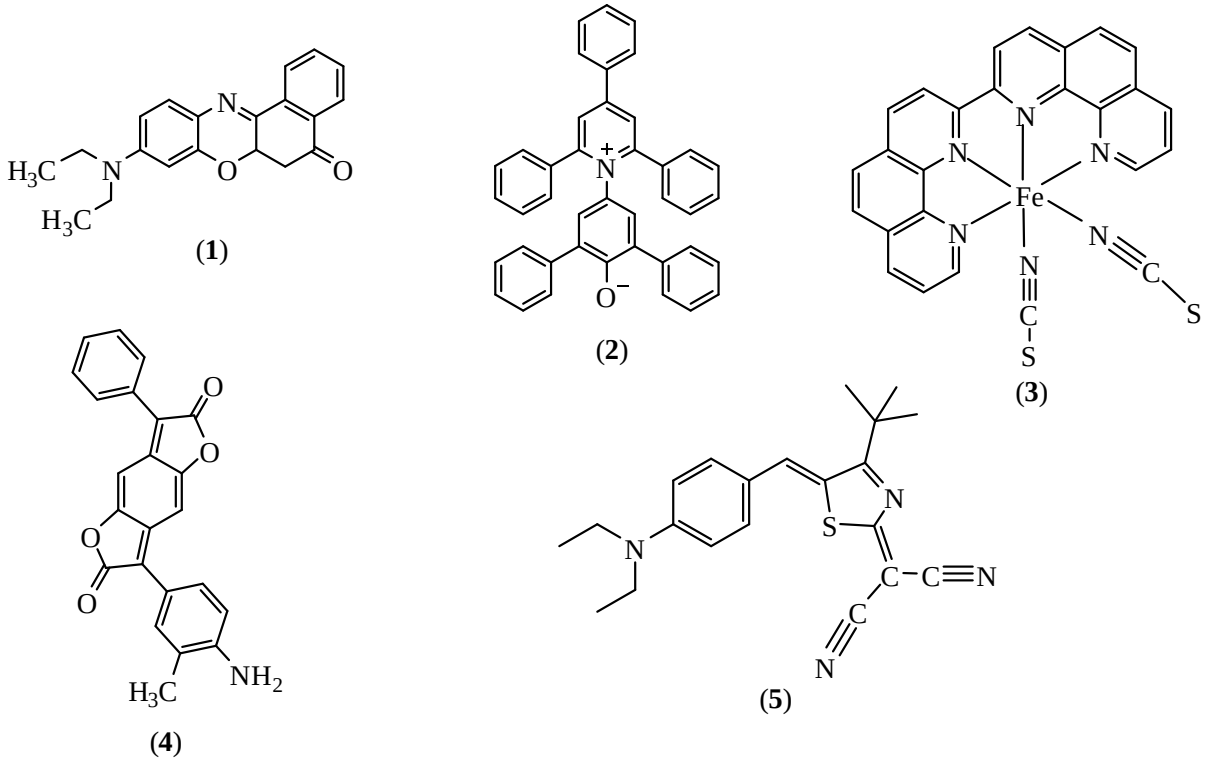


Figure 2.12: Solvatochromic dyes used in ILs'polarity determination: (**1**) Nile red, (**2**) Reichardt's dye, (**3**) $Fe(phen)_2(CN)_2$ (**Fe**), (**4**) 3-(4-amino-3-methyl-phenyl)-7-phenyl-benzo-[1,2-b:4,5-b′]-difuran-2,6-dione(**ABF**) and (**5**) 4-tert-butyl-2-(dicyanomethylene)-5-[4-(diethylamino)benzylidene]-Δ^3-thiazoline (**Th**)

One interesting point is that there is an antagonistic behaviour of cation and anion towards the hydrogen bonding properties.[55,172] For instance, E_{NR} for $[BMIM][BF_4]$ = 217.2 kJ mol^{-1} and E_{NR} for $[BIM][BF_4]$ = 212.5 kJ mol^{-1}. This shows that more acidic cations lead to higher E_{NR} and are highly polar whereas more basic anions lead to higher E_{NR} and are less polar.

It has found that π^*-values for ILs, defined as the measure of solvent's ability to induce a dipole in the solute and polarizability effects, are significantly higher due to their ionic character than those of molecular solvents and are dependent on both anion and cation.[171,173]

This confirms that ILs can interact with a big variety of solutes when compared to molecular solvents. The exceptions are observed on quaternary ammonium salts seeing that the charge centre on the cation is more closely the solute unlike monoalkylammonium salts and imidazolium salts. The presence of both large permanent dipoles from functional groups and delocalized bonds which generate greater polarizabilities, increase the π^*-values. However, these values are reduced when the alkyl chain length on the cations increases.

The α-values determine the availability of the HBD sites on the cation and describes the ability of a solvent to donate a proton to the solute in a solvent-solute hydrogen bonds.[55,171] These values are governed by the nature of the cation, with the anion showing secondary effect. The highest α-values are observed on the cations with hydrogen bond substituents such as –OH. $[RMIM]^+$-based ILs possess high α-values and these can decrease by introducing an alkyl group substituent at the 2-position of the imidazolium ring. ILs based on alkylpyridinium, pyrrolidinium and ammonium cations have lesser α-values and phosphonium ionic liquids having the lowest of all.[171]

The β-values represent the HBA sites on the anion and describe the ability of the solvent to donate electron density in order to form hydrogen bonds with protons of the solute.[55,171] The β-values are controlled by anions, and cation have no clear effect. Spange *et al.*[162] showed that the strength of HBD ability of the cation is inversely related with the HBA ability of the corresponding anion. This was in agreement with Ab Rani *et al.*[171] study as shown on Figure 2.13.

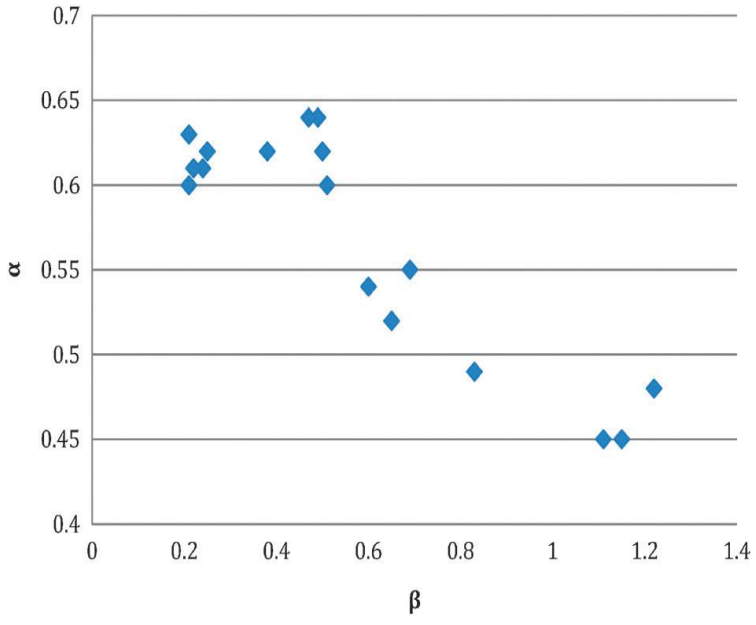


Figure 2.13: α-Values for a range of [BMIM][X] as a function of β-values[171]

A large β of the anion excludes the HBD ability of the cation independent of the nature of cation. However, the larger the β is, the larger the π^* is because strong coordination strength of the anion involves dipolarity/polarizability to increase.

In conclusion, based on ϵ_r values of many ILs, these latter are classified as solvents of moderate-low polarity. However, this is in disagreement with what arising from solvatochromic dyes. Basically, the dipole-dipole interactions in molecular liquids cannot be compared to those in ILs because their net charges of the ions produce a different environment with the surrounding ions. In addition, the strong ion-ion interactions in ILs make them highly structured materials and lead to peculiar polymeric networks of anions and cations connected by hydrogen bonds and coulombic interactions.[170] For a simple comparison of polarity scales using both Kamlet-Taft and Abraham parameters, *a* and β values are high in both models and are mainly function of anion. In contrast, *b* is low (Abraham) whereas α is high (Kamlet-Taft).[55,173]

Another interesting aspect on the ILs'polarity is their linear temperature dependence as reported by Prausnitz *et al.*,[174] Baker *et al.*[175] and Tokuda *et al.*[135] They reported that the E_{NR} values decrease with temperature for pyridinium and pyrrolidinium-based ILs, but increase with temperature for phosphonium-based ILs. This explains the significance attributed to the choice of the cation as response of polarity regarding a change in temperature.

2.2.8 Applications of ionic liquids

The ability to tune ILs properties by suitable selection of ions offer a wide range of ILs' applications. Also, the introduction of structural functionalities on the cationic or anionic part has made it possible to design new ILs with targeted properties according to the structure-property relationship.[176,177] ILs have been the pioneering perspective of widespread academic study[178] and have been involved in enormous commercial and industrial processes[53,179] as shown on Figure 2.14. This has brought them into being used as solvents and catalysts in organic synthesis,[55] in the design of environmentally friendly media for excellent extraction and separation technologies,[74] electrochemistry,[180-182] dye-sensitized solar cells,[183] lubricants or lubrication additives,[184] pharmacy,[185,186] nanotechnology,[187] heat exchangers, distillation columns and reactors,[188] for energy, materials and medicine,[189] clean energy and environment,[190] electrofinishing of metals,[147] polymer science and technology[191] to mention few.

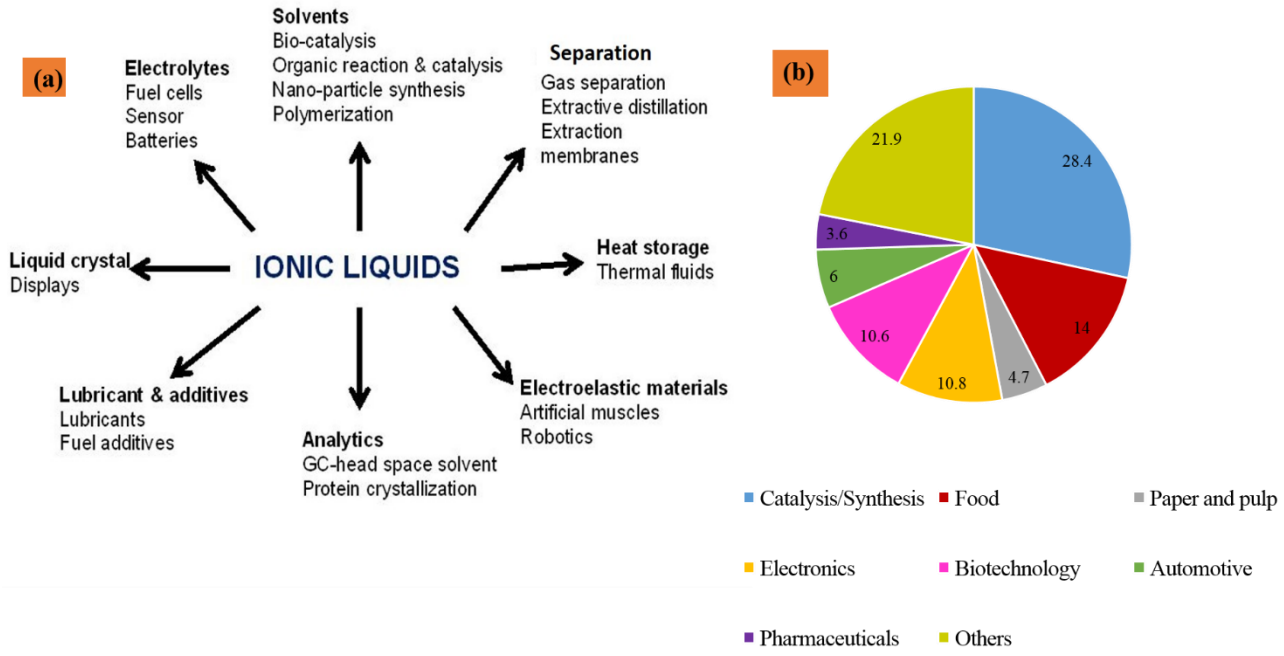


Figure 2.14: (a) Applications of ILs[192] and (b) ILs market size by application[193]

2.2.9 Recovery of ionic liquids

As seen in Section 2.2.8, ILs have shown a growth interests in both academics and industries as promising solvents for a variety of applications. In contrast to conventional organic solvents, their unique properties such as less volatility, thermal stability, wide liquid range, biphasic systems, inflammability and efficient separation provide technological, environmental and economic benefits. Their reusability and recovery reduce the amount of waste generated during the chemical processes and reduce their cost expenses given that they are still relatively expensive.

Many methods have been proposed by different researchers, according to the structure of the ILs.[107,196-197] Mainly, these methods are distillation, extraction, adsorption, induced phase separation, and membrane-based separations. Distillation method is highly used and consists in removing only volatile compounds in ILs due to the trivial vapour pressure of ILs. Extraction and membrane-based separations such as nanofiltration and evaporation are applied in separations of non-volatile compounds with ILs. Water as the major contaminant of ILs can be removed from ILs through three different mechanisms.

First mechanism involves the phase addition whereby an electrolyte or other saturated aqueous solution is added to the IL aqueous solution. Then, that electrolyte extracts some of the water and forms a second phase that can be easily removed by decantation.[198]

Second mechanism consists in using a force field by creating a gravity settling. The magnetic field is then induced on a biphasic system composed by an IL-rich phase and water-rich phase, which can be separated easily according to the magnetic response of each phase.[199] The third mechanism uses a barrier which is a membrane filtration able to retain the IL from aqueous solution and water is collected as filtrate.[200]

2.3 Reduction of aldehydes and ketones to their corresponding alcohols in ionic liquid

2.3.1 Structure of aldehydes, ketones and alcohols

Aldehydes and ketones are both organic compounds having the carbonyl (C=O) group in their structure. However, aldehydes have one alkyl substituent whereas ketones have two alkyl substituents. The carbonyl carbon atom is sp^2 hybridized and bonded to three other atoms through coplanar sigma bonds oriented about 120^o apart. The unhybridized p-orbital overlaps with p-orbital of oxygen to form a π-bond. The C=O double bond is shorter, stronger and polarized than C=C double bond.

On the other hand, alcohols are organic compounds containing hydroxyl groups (O-H). They are synthesized by a variety of methods and the O-H group can be converted to other functional groups. This enlarges the usages of alcohols in nature, in industry, around the house, and in organic chemistry as reagents, solvents, and synthetic intermediates. According to the type of carbon atom attached to O-H group, alcohols are classified as primary, secondary or tertiary alcohol, respectively. Reduction of aldehydes and ketones is the fast and efficient route of synthesizing alcohols. The structure of aldehydes, ketones and alcohols is illustrated on Figure 2.15.

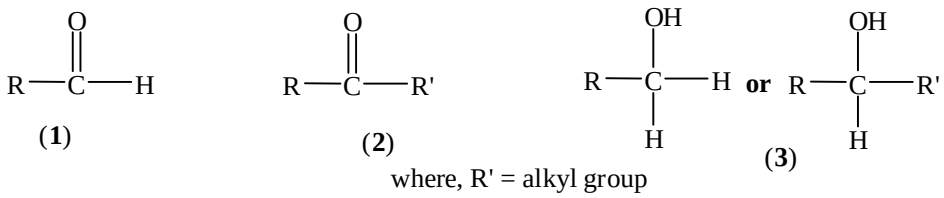


Figure 2.15: Structural representation of (**1**) aldehydes, (**2**) ketones and (**3**) alcohols

2.3.2 Reducing agents for aldehydes and ketones

Electrochemically, a reducing agent is an element or compound able to donate its electron to the neighbouring chemical species in a redox chemical reaction. In organic synthesis, a reducing agent is defined as the donor of hydrogen to another species having any unsaturated group within its structure.[201] As described in Section 2.3.1, aldehydes and ketones also have carbonyl group which can be reduced by addition of hydrogen on it to generate alcohols group. Some reducing agents have been reviewed in the subsequent sections for this type of reaction.

2.3.2.1 Metal hydrides

Metal hydrides such as lithium aluminium hydride ($LiAlH_4$), sodium borohydride ($NaBH_4$) and their derivatives, are the most commonly used reducing agents.[202] Regardless the usefulness and versatility of these metal hydrides, they are moisture and air sensitive and show incompatibility with certain functional groups which have limited their use in certain cases. $LiAlH_4$ can reduce almost all organic functional groups and shows a tolerance to few functional groups such as nitro and nitrile groups.[203,204] Furthermore, boranes and their derivatives, despite their pyrophoricity and inconvenient handle, are also used as reducing agents. The substituted boranes and some aminoboranes are the most used.[205-207]

For example, scheme illustrating the reduction mechanism of aldehydes and ketones, using $NaBH_4$, is explained in Section 2.3.3.1, Scheme 2.7.

$NaBH_4$, discovered in 1940 by H. I. Schlesinger, has been seen in details owing to its low price, ease to handle and high chemoselectivity for the reduction of aldehyde and ketone group to their corresponding alcohols.[208] It is soluble in protic solvents like water and lower alcohols, decomposes in neutral or acidic aqueous solutions and is stable at pH equal to 14.[209] In any given conditions, it can also reduce acyl chlorides, thiol esters and imines. The reactivity of $NaBH_4$ can be modified by addition of other compounds such as transition metal salts and other reagents, changing solvent systems, and using polymer support reagents[210]. For instance, oxidation with iodine in tetrahydrofuran (THF) to form borane-tetrahydrofuran complex able to reduce carboxylic acids,[211] addition of methanol (MeOH) in refluxing THF to form $NaBH_4$-MeOH system able to reduce esters[212] to the corresponding alcohols. Recently, Rayati and his group[213] reported the $NaBH_4$ reduction of aldehydes catalysed by an oxovanadium (IV) Schiff base complex encapsulated in the nanocavity of zeolite-Y.

2.3.2.2 Hydrogen gas on metal catalysts

Hydrogen (H_2) gas is the lightest and most abundant element in the universe and occupies about 70%-75% of the universe by mass.[214] H_2 gas shows a lot of different advantages as reducing agent for catalytic purposes because it is all consumed and does not generate any by-product. H_2 gas has to be activated on catalyst before behaving as reducing agent. The utmost used catalysts are transitional metal catalysts such as nickel, palladium, copper, rhodium, ruthenium, platinum and iridium.

For all metal catalysts, metal centre typically needs to have an empty coordination site in order to bind the H_2 first, prior to the hydrogenation as shown and explained in details in Section 2.3.3.3, Scheme 2.10. All these catalysts can be used either alone or supported on different substrates according to the reaction conditions.

The common supports are carbon, barium sulphate, calcium carbonate and aluminium oxide. Yan *et al.*[215] reported the use of transition metal nanoparticle catalysts. Recently, Monguchi *et al.*[216] highlighted different Pd-supported catalysts for the chemoselective hydrogenation.

Great interests have been placed on activated carbons based on their properties as catalysts and catalyst support in the catalysis in the last decade. They are relatively inexpensive, have a high surface area and allow easy recovery of supported metal by simple combustion of the support. In addition, they are chemically inert both in acidic and basic media and do not present very acidic centres on their surface which, in turn, could favour unwanted side reactions during the catalytic run.[217]

Actually, palladium metal supported on activated carbon (Pd/C) has been widely used owing to their great surface area and activity. Palladium loading is typically between 5% and 10%. This catalyst has been used in carbonyl reduction, nitro compound reduction, reduction of imines and Schiff bases.[218,219] Also, it has application in coupling reactions like Suzuki reaction[220] and Stille reaction.[221] The literature on the application of this catalyst in the reduction of aldehydes and ketones to their corresponding alcohols is limited.[222-224]

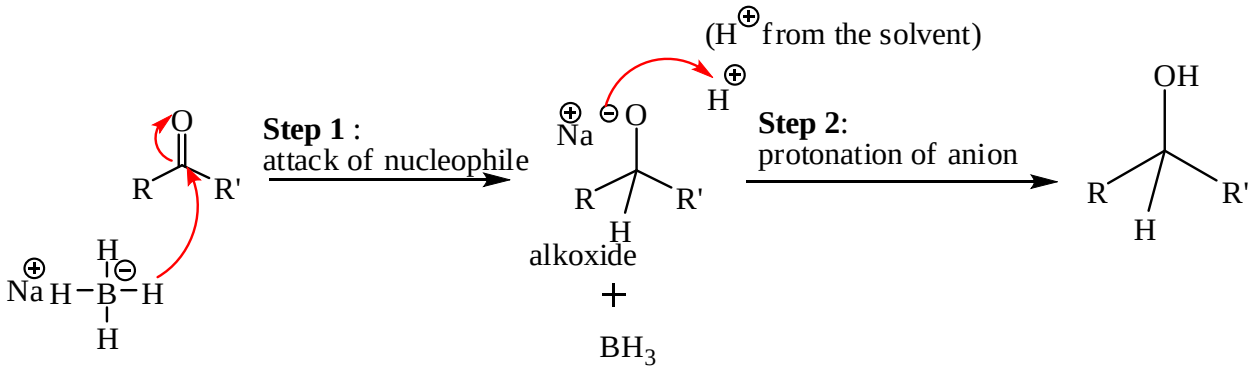
2.3.3 Modes of reduction of aldehydes and ketones

In C=O double bond, oxygen is more electronegative than carbon and thus the bonding electrons and the π electrons are pulled towards the oxygen atom. As a result, C=O double bond has a large dipole moment and this polarization contributes to the reactivity of aldehydes

and ketones whereby the positively polarized carbon atom acts as an electrophile and the negatively polarized oxygen atom acts as a nucleophile towards the nucleophilic addition reactions and alcohols are obtained as the products. There is a wide variety of methods used for the reduction of aldehydes and ketones to their corresponding alcohols but this work limits to three of them as detailed in the subsequent sections

2.3.3.1 Sodium borohydride reduction under solvent

$NaBH_4$ reduction of aldehydes and ketones consists of two mechanistic steps: Addition of hydride ions (H^-) on the carbonyl group and protonation of the anion that results, as shown on Scheme 2.7.



Scheme 2.7: Synthetic pathway of $NaBH_4$ reduction reaction of aldehyde and ketone

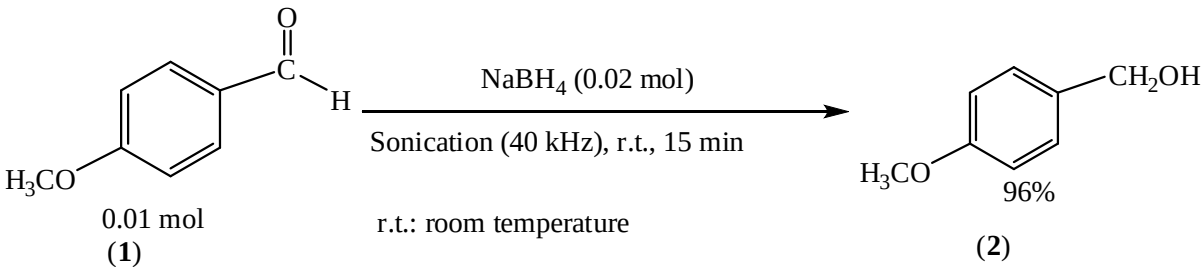
In step1, when the nucleophile $(BH_4)^-$ attacks the carbonyl group, it donates H^- to this carbonyl and the carbon atom changes from sp^2 to sp^3. Thus, a transfer of electron to the O atom and the C-H bond formation take place. This implies that the electrons of the π-bond are donated to the oxygen, thereafter, an alkoxide anion is generated.

In step 2, the alkoxide anion is protonated by H^+ from the solvent to give the final alcohol product. This acid-base reaction forms a new O-H bond. The protonation of an alkoxide strongly depends on the polarity of the solvent in which the reaction is carried out. Reason why protic solvents are required for this reduction. ILs have been used as solvents in these type of reductions.[225] The addition of immobilized baker's yeast[226] and enzyme[227] enhances the reaction yields.

2.3.3.2 Sodium borohydride reduction under solvent-free

Nowadays, with the increasing research in green chemistry, working without solvents provides incredible advantages such as simple process, small plants and free-energy costs of removal, recycling and disposal of waste solvents. Basically, reagents are inserted in a dry material, rather than dissolved in a solvent under these solventless conditions.

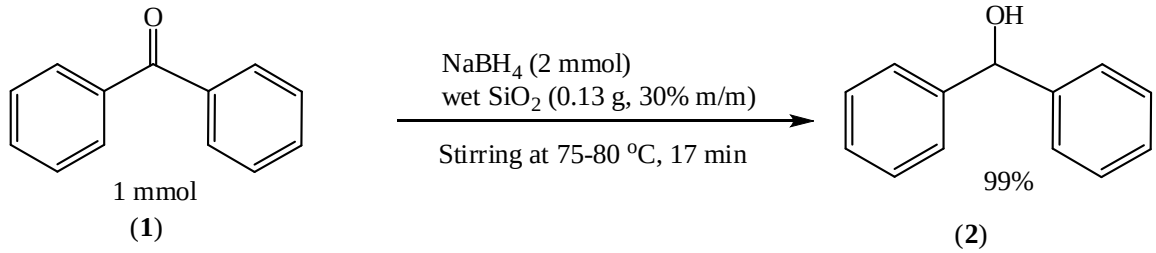
Reduction of aldehydes and ketones with $NaBH_4$ to their corresponding alcohols under solvent-free conditions are feasible. To improve this type of reaction, $NaBH_4$ can be activated by solid acids,[228] or other supporters such as Fontainebleau sand,[210] wet silica gel[229] and wet alumina.[230] In addition, this reduction can be carried out using ball- milling method[231] or under ultrasonic irradiation.[232] Few examples are given in Scheme 2.8 and Scheme 2.9.



0.01 mol
(**1**)

(**2**)

Scheme 2.8: Ultrasound assisted reduction of p-anisaldehyde using $NaBH_4$ under solvent-free conditions[232]



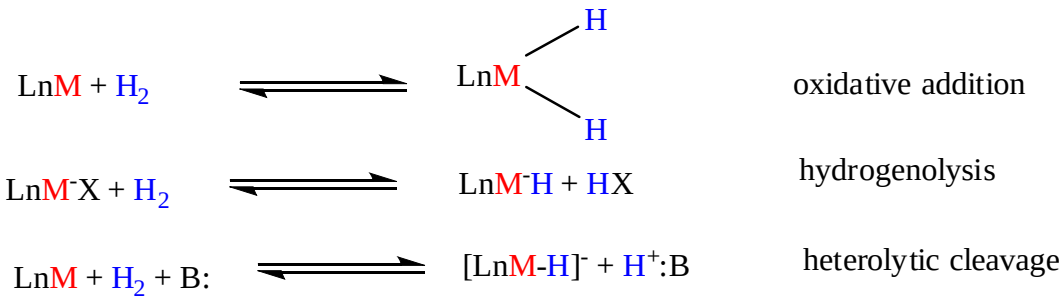
1 mmol
(**1**)

(**2**)

Scheme 2.9: Reduction of benzophenone with $NaBH_4$ in the presence of wet silica (SiO_2) under solvent-free conditions[229]

2.3.3.3 Catalytic hydrogenation

Catalytic hydrogenation is the addition of H_2 to a multiple bond (C=C, C≡C, C=O, C=N, C≡N, N=O, N=N, N≡N) to reduce it to a lower bond order, in presence of a catalyst. To perform catalytic hydrogenation, transition metal catalysts can activate H_2 in three different ways as shown on Scheme 2.10.



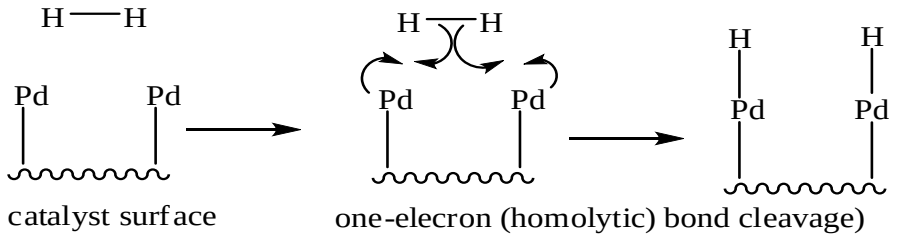
Scheme 2.10: Three different ways of activating H_2 on the metal catalyst

Catalytic hydrogenation reactions of aldehydes and ketones to their corresponding alcohols are not chemoselective reactions. Different side reactions, such as aromatic ring hydrogenation and hydrogenolysis of the produced alcohol to the hydrocarbon derivatives, can take place.[233,234] Addition of ethylenediamine can solve some of these problems, but isolation of the product and the catalyst recycling will still problematic.[235]

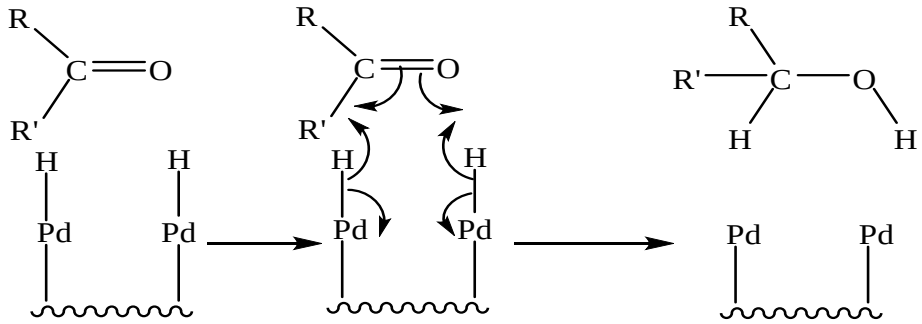
In this research, catalytic hydrogenation of aldehydes and ketones to their corresponding alcohols using Pd/C comes in our attention.

Basically, in the presence of catalyst, homolytic bond cleavage occurs within the H_2, resulting in very active hydrogen bound loosely to the palladium atoms (see oxidative addition above in Scheme 2.10) and then catalytic hydrogenation occurs in the presence of carbonyl group as shown on Scheme 2.11. Catalytic hydrogenation reactions in ILs have been performed with excellence owing to the ability of ILs acting as solvents ligands, catalysts and as stabilizing agents for the catalysts.[236-238]

Step 1. Adsorption of hydrogen



Step 2. Catalytic hydrogenation



Scheme 2.11: Catalytic hydrogenation of aldehydes and ketones

2.3.4 Reduction of aldehydes and ketones in 1-butyl-3-methylimidazolium tetrafluoroborate

[BMIM][BF_4], has been widely used in many organic chemical reactions as a green solvent due to its negligible vapour pressure.[107,239] Despite the many applications of this IL in synthetic processes, less consideration has been taken on its use as solvent in reduction of aldehydes and ketones to their corresponding alcohols.

Based on its structure, [BMIM][BF_4] can interact differently with other molecules depending on the type of reaction it is used in. For the reduction of aldehydes and ketones to their corresponding alcohols, it acts as hydrogen donor particularly the hydrogen at the position carbon-2 {(C2)-H} as shown on Figure 2.16.

Under literature, [BMIM][PF_6] exhibits itself as a promising solvent to replace the classical volatile organic solvents.[225] The produced alcohols were in good yields (55% - 70%). Further to this, the volatile alcohols were directly distilled from the [BMIM][PF_6] layer without using other volatile organic solvents.

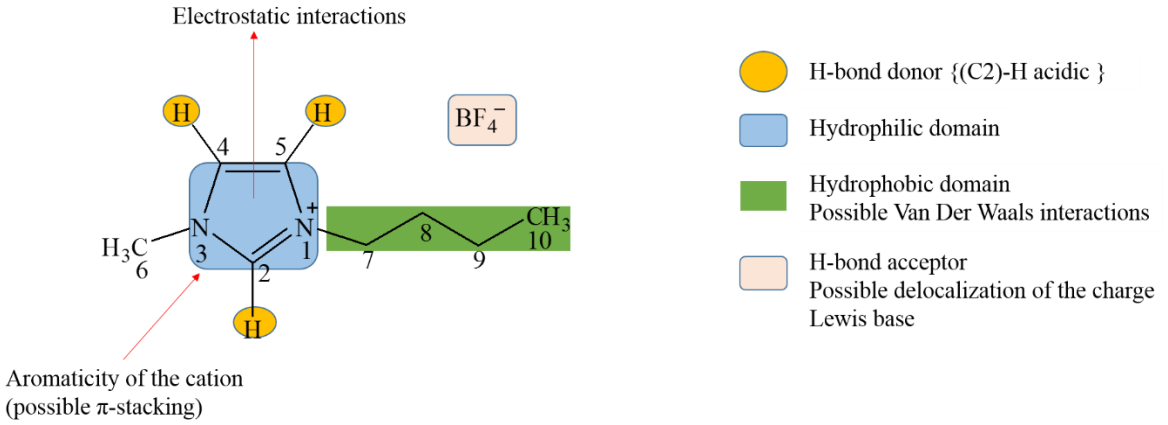


Figure 2.16: Schematic picture illustrating the different interactions present in [BMIM][BF_4]

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Chapter Three

Synthesis and characterization of 1-butyl-3-methylimidazolium tetrafluoroborate

This chapter presents details on the reagents, equipment, and all experimental procedures involved in the synthesis of 1-butyl-3-methylimidazolium bromide ([BMIM][Br]), used as the precursor for the synthesis of 1-butyl-3-methylimidazolium tetrafluoroborate ([BMIM][BF_4]). The instrumentation techniques used for characterization of the synthesized [BMIM][Br] and [BMIM][BF_4] are also provided herein. The physicochemical properties of both [BMIM][Br] and [BMIM][BF_4] were determined and all the obtained results are discussed in this chapter.

3.1 Introduction

The negligible volatility of ILs and their fine-tune ability of their properties make them promising solvents for replacing volatile organic solvents as detailed in Chapter Two. In addition, the non-coordination of their ionic constituents allow them to dissolve a wide range of organic compounds.[1,2] Based on the cation structure, the most reported classes of ILs are imidazolium, ammonium, pyridinium, pyrrolidinium, sulfonium, piperidinium, benzotriazolium, and pyrazolium-based ILs.[3] The imidazolium-based ILs are the most studied and used class owing to their medium range ordering.[4]

In this research, the choice of synthesizing [BMIM][BF_4] as typical IL was based on the commercial availability and affordability of the starting materials involved in its synthesis. Also, the mild reaction conditions, such as temperature, for synthesis makes them favourable. [BMIM][BF_4] has been synthesized using two synthesis methods, *i.e.* conventional and microwave methods. A comparison of these two methods is discussed as well as the effect of each method on the physicochemical properties. The synthesized IL was then used as solvent for the reduction of aldehydes and ketones to their corresponding alcohols (discussed in details in Chapter Four). Howarth et al.[5] reported the similar reduction reactions carried out in 1-butyl-3-methylimidazolium hexafluorophosphate ([BMIM][PF_6]). The latter IL is immiscible with water whereas [BMIM][BF_4] is miscible with water. The investigation of [BMIM][BF_4] solvent behaviour was of great interest in this study.

3.2 Chemicals, gases and solvents

Commercially available chemicals, gases and solvents used in the synthesis and characterization of [BMIM][BF_4] were fairly pure and used as received unless otherwise stated. Sources or suppliers and purity of all the chemicals used are listed in Table 3.1.

Table 3.1: Chemicals, gases and solvents used in both synthesis and characterization of [BMIM][BF_4] and its precursor

Chemicals/gases/solvents	Sources/Suppliers	Purity (wt.%)	State of usage
Acetone	Protea Chemicals, SA	AR/100	Dried before use*
Anhydrous magnesium sulphate	Thembane chemicals, SA	99	Used as received
Argon gas	Afrox, SA	Ultra high purity	Used as received
1-Bromobutane	Merck, German	≥ 99	Used as received
Deuterated chloform-D1	Merck, German	99.8	Used as received
Deuterated water	Merck, German	99.9	Used as received
Diethyl ether	Innovative Technology, USA	Ultra high purity	Used as received
Hydranal®-Composite 5	Fluka, New German	-	Used as received
Kieselguhr	Capital Lab Supplies, SA	-	Used as received
Methanol (analytical grade, AR)	Capital Lab Supplies, SA	99.9	Used as received
1-Methylimidazole	Merck, German	≥ 99	Purified before use*
Nitrogen gas	Afrox, SA	Ultra high purity	Used as received
Sodium tetrafluoroborate	Capital Lab Supplies, SA	98	Used as received

*: Purification/drying is done as described in Section 3.6.2.

3.3 Equipment and apparatus

This section describes the equipment and the instrument used for the synthesis of [BMIM][BF_4].

- All the reagents and samples were weighed using Ohaus PA214 analytical balance with 0.1 mg precision weighing.
- Heating and stirring of the reagents in synthesis of [BMIM][BF_4] through conventional synthesis method were done on a Lab Smart MS-H-Pro$^+$ model hot plate.
- Due to the high hygroscopicity of the samples, washing and other manipulations were done in Aldrich$^{(R)}$ AtmosBag, 51''x 58'' with two hands (from Sigma-Aldrich, USA).
- Used diethyl ether solvent was dried by Innovative Technology (PS-MD-3, Amesbury, MA, USA) pure solvent unit.

3.3.1 Microwave synthesizer reactor

The CEM Discover SP Microwave Synthesizer, A/N 372874 model (purchased from Trilab Support Company, Pinetown, SA), shown in Figure 3.1, was used for the synthesis of both [BMIM][Br] and [BMIM][BF_4].

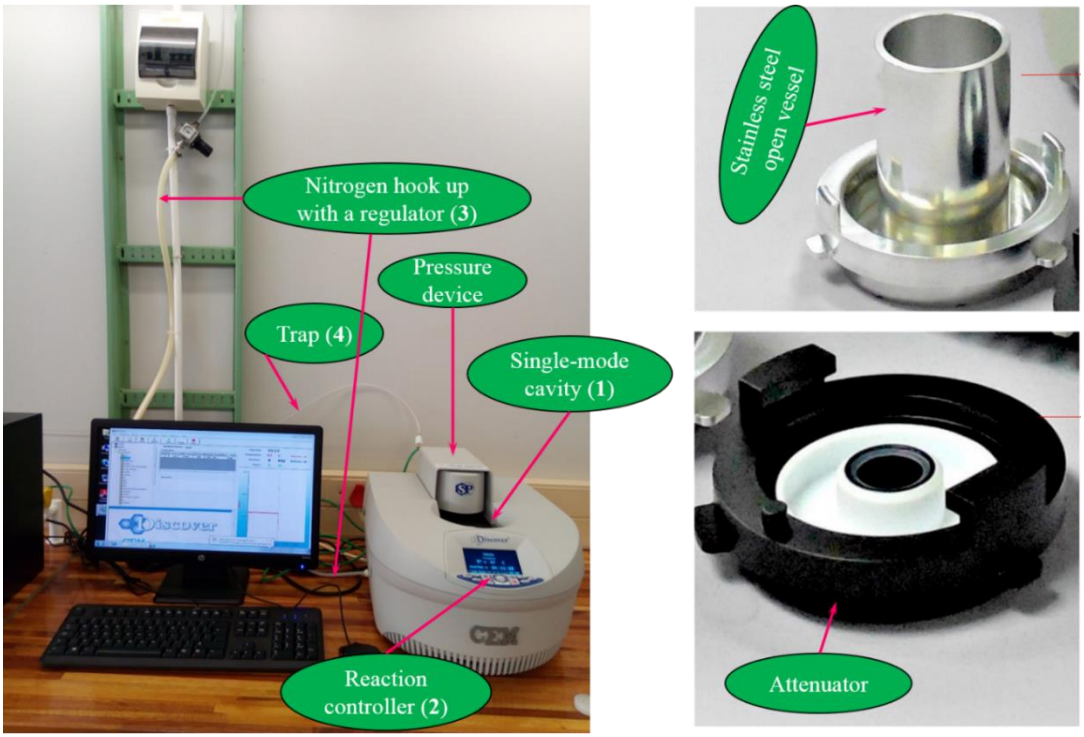


Figure 3.1: Compartments of the CEM Discover SP microwave reactor used in the synthesis of [BMIM][Br] and [BMIM][BF_4]

The microwave (MW) consists of four main components including the single-mode cavity (**1**) where the open vessel and the attenuator are inserted at the heart of the MW. At the bottom of the cavity, there is a plastic clear piece of infrared which helps in reading the temperature from the bottom of the vial.

The reactions were performed in the glass vessels, (vials of 35 mL), placed in the attenuator. The vial was equipped with a magnetic stirrer bar and capped with a silicone/polytetrafluoroethylene (PTFE), 35mL, Activent vial cap (from Trilab Support Company, Pinetown, SA). The loaded volumes for each sample were 20 to 25 mL in 35 mL vial. The cavity is designed to facilitate the coupling of the MW energy to the ionic components of the sample. The reaction parameters such as power, temperature, pressure, time and agitation mode, were set and controlled by a computer connected to the MW using Intuitive Synergy ^{TM} software system and Dynamic version. The manual set up can also be done using a touch pad (**2**) acting as reaction controller on the MW itself. The maximum operating pressure of this reactor is 20 bar, the power range is 15-300 watts and the temperature range is 60-250 °C. In this synthesis, the choice of these parameters was set depending on the IL to be synthesized.

After the completion of the reaction, the vessel was quickly cooled by nitrogen gas from the nitrogen pipe hooked up with the regulator (**3**) set at 30 psi. The overflow chemicals were drained into the trap (**4**) at the back of the MW.

3.4 Characterization instruments

Different instruments, software versions and the techniques by which the data were collected for the characterization of the synthesized ([BMIM][Br] and [BMIM][BF_4] are outlined and presented in the subsequent sections.

3.4.1 Fourier transform infrared spectroscopy

Perkin Elmer Universal ATR Spectrum 100 FTIR Spectrometer, coupled to spectrum version 6.1.0. Software was used to record the infrared spectra of the samples. Samples were analysed and the absorption peaks were reported in wavenumbers (cm^{-1}) in a spectral range of 4,000-380 cm^{-1}.

3.4.2 Nuclear magnetic resonance spectroscopy

The ^{1}H-, ^{13}C- and ^{19}F-NMR spectra were recorded on a 400 MHz Bruker Ultrashield at room temperature using Bruker TOPSPIN 2.1 software. For NMR spectroscopic analysis, samples were dissolved in deuterated water (D_2O) and deuterated chloroform ($CDCl_3$) for [BMIM][Br] and [BMIM][BF_4], respectively. The chemical shifts (δ) were reported in parts per million (ppm), to a scale calibrated by tetramethylsilane (TMS, δ = 0.00 ppm) as reference.

Peaks and integrals are given as ppm while the coupling constants (*J*) are given in Hertz and the multiplicity of the chemical shifts (s = singlet, d = doublet, t = triplet, m = multiplet) are also reported.

3.4.3 Liquid chromatography-mass spectroscopy

The LC-MS spectra were obtained with Shimadzu, LC-2030C-3D, *Prominence-i,* (Shimadzu South Africa Pty Ltd) spectrometer using a loop instead of column at room temperature. Samples were dissolved in methanol (AR, grade) up to 5 ppm. A mobile phase of methanol : water (95 : 5, v/v) and 0.1% formic acid was used under a flow rate of 0.2 $mL.min^{-1}$. Eluent peaks were analysed with electrospray ionization mass spectrometry and were reported in mass-to-charge ratios (m/z). Positive-ion and negative-ion modes were used to identify ILs.

3.5 Physicochemical properties of the synthesized ionic liquids

This section describes different equipment and instruments used to determine the physicochemical properties of both [BMIM][Br] and [BMIM][BF_4] as listed in the following subsections.

3.5.1 Water content

The water content of synthesized [BMIM][Br] and [BMIM][BF_4] was determined by volumetric Karl-Fischer titration using Karl-Fischer Moisture Titrator MKS-500 model (supplied by Kyoto Electronics Manufacturer Co. Ltd. (KEM), Japan) with Hydranal®-Composite 5 solution as the titrant and anhydrous methanol (AR, 99.9%) as the solvent. For each sample, at least 100 mg (10 drops) and 30 mg of [BMIM][BF_4] and [BMIM][Br],

respectively, were used and the measurements were replicated three times. The uncertainty of the water content measurements on each sample was less than ± 0.005%.

3.5.2 Density measurements

The densities of synthesized [BMIM][Br] and [BMIM][BF_4] were determined gravimetrically at room temperature by weighing the volume of the samples with Ohaus PA214 analytical balance in AtmosBag saturated with argon. Under inert atmosphere of argon, 5 g of each synthesised IL were weighed correctly into a 50 cm^3 graduated measuring cylinder and the volume determined. For the case of [BMIM][Br], which is a solid, dry acetone was used as medium, where the initial volume was maintained at 10 cm^3. Upon transferring [BMIM][Br] into the measuring cylinder, the final volume was recorded, and then the volume of [BMIM][Br] was deduced by difference. For certainty aspect, each sample has been measured five times and the absolute uncertainty in density was ± 10^{-3} $g.cm^{-3}$.

3.5.3 Viscosity measurements

The dynamic viscosity of synthesized [BMIM][BF_4] was measured using BS/U-Tube viscometer (from Paragon Scientific Ltd, UK), with the calibration constant of 0.3307 $mm^2.s^{-1}$ at 40 °C, based on a capillary viscometer principle. This capillary viscometer was calibrated using olive oil with a viscosity of 84 cP at 25 °C. The time taken by [BMIM]BF_4 to fall a given distance, between two bulbs in a capillary tube of a calibrated diameter, was measured by means of a stopwatch. The sample temperature was fixed at a constant temperature of 25 °C and controlled within ± 0.1 °C by use of a water bath (Grant instruments, Cambridge, UK) equipped with a thermometer. Each sample was measured five times and the relative uncertainty in the dynamic viscosity measurements was less than ± 1%.

3.5.4 Thermal stability

The TA Instrument Q series ™ Thermal Analyser TGA (Q600) was used to determine their upper decomposition temperature limit. A sample (10-30 mg) was placed in an aluminium pan and heated from 40 to 600 °C under nitrogen flow at a heating rate of 10 $°C.min^{-1}$. The acquisition and analysis of data were done using a TA instrument Universal Analysis 2000 software package.

3.6 Experimental procedures

This section outlines the procedures and precautions followed during the synthesis of both [BMIM][Br] and [BMIM][BF_4] in two different methods.

3.6.1 General procedures

All glassware was cleaned with warm soapy water and brush, thereafter was thoroughly rinsed with warm water and acetone, and then dried in a Scientific Oven (purchased from Shalom Laboratory Suppliers, Durban, SA) set at 110 °C for 1 hour to remove all traces of water.

Due to the hygroscopicity of the reagents, all manipulations were done in AtmosBag saturated with argon. In addition, these reagents were flushed with a stream of dry argon prior to use using standard Schlenk techniques in a fume hood.

3.6.2 Purification/drying of reagents and solvents

3.6.2.1 Purification of 1-methylimidazole[6]

Potassium hydroxide pellets (4 g) were added to 1-methylimidazole (200 mL) in a 250 mL round-bottom flask (RBF) equipped with a magnetic stirrer bar. The mixture was allowed to reflux and stir at 198 °C for 3 hours under argon with five porcelain granules added into the mixture to assure homogeneous heating. Thereafter, the mixture was distilled between 210 to 212 °C. The dried 1-methylimidazole was collected and kept under argon until when needed.

3.6.2.2 Purification of 1-bromobutane

1-Bromobutane (200 mL) was washed with small portions of concentrated sulfuric acid (20 mL), by use of separating funnel, until no further colour was removed into the acid layer. Aqueous solution of sodium bicarbonate (2 M) was added to neutralize the remaining traces of sulfuric acid. The obtained 1-bromobutane was dried under reduced pressure at 60 °C for 8 hours and thereafter, distilled before use.[6]

3.6.2.3 Drying of acetone

The acetone was dried by adding activated molecular sieves (4 Å, bead diameter 1.7-2.4 mm) for 4 days before use. The used molecular sieves were activated by leaving them overnight in a furnace at 300-450 °C.

3.6.2.4 Drying of diethyl ether

Dry diethyl ether was dispensed by PS-MD-3 Innovative Technology solvent purification system. This pure solvent unit comprises two stainless steel low-pressure columns containing activated alumina and copper per request. The purification grade solvent is pushed from its storage container under low nitrogen pressure through these columns whereby trace amounts of water and oxygen are removed producing dry and deoxygenated solvent. Thereafter, the purified solvent is drained into a storage flask where it is dispensed, under nitrogen, by means of standard syringe techniques.

3.6.3 Synthesis of 1-butyl-3-methylimidazolium bromide and 1-butyl-3-methylimidazolium tetrafluoroborate

The structure of [BMIM][Br] and [BMIM][BF_4] is shown in Figure 3.2. Based on the heating mode used for the reaction, this synthesis has been done in two different methods, namely conventional method and microwave (MW) assisted ILs synthesis method. Each method is described in details in the subsequent sections.

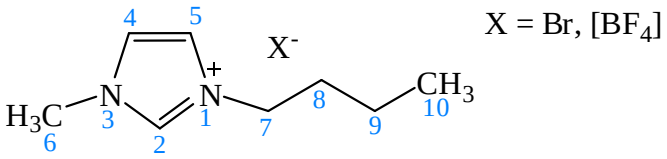


Figure 3.2: Chemical structure of the synthesized [BMIM][X]

3.6.3.1 Conventional method

This method utilizes the normal heating set-up, where the sample mixture is heated using an oil bath placed on the hot plate. Basically, the sample mixture is refluxed in a RBF equipped with a condenser under argon atmosphere. The temperature and time of refluxing differ from one ionic liquid to another.

3.6.3.1.1 Synthesis of 1-butyl-3-methylimidazolium bromide

Dried 1-methylimidazole (5.003 g, 60.95 mmol) and 1-bromobutane (9.648 g, 73.08 mmol) were added in a 250 mL three-necked RBF. The reaction mixture was refluxed at 78 °C under argon atmosphere for 5 hours. Two layers were formed and were separated by decantation. The yellow denser layer was washed with dried diethyl ether (3 x 30 mL) and allowed to crystalize for 48 hours at room temperature in a glove bag full of argon. The crystals were dried overnight under reduced pressure to give white solid crystals of [BMIM][Br] (10.414 g, 78%).

IR (ATR, cm^{-1}) 3416, 3126, 3081, 2961, 2867, 1701, 1558, 1456, 1163, 892, 808, 754, 655, 630, 412

^{1}H NMR (D_2O, ppm) δ_H = 8.64 (1H, s, N-(C2)H-N), 7.41 (1H, s, N-C(4)-H), 7.36 (1H, s, N-C(5)-H), 4.12 (2H, t, J=7.16 Hz, N-CH_2), 3.82 (3H, s, N-CH_3), 1.75 (2H, m, N-CH_2-CH_2), 1.23 (2H, m, N-CH_2-CH_2-CH_2), 0.84 (3H, t, J=7.40 Hz, CH_2-CH_3)

^{13}C NMR (D_2O, ppm) δ_C = 135.82, 123.46, 122.20, 49.28, 35.66, 31.25, 18.74, 12.64.

LC-MS (ESI, m/z) ($[BMIM]^+$- Br) 139 (100), ($[BMIM]_2$ $Br)^+$ 357 (32)

3.6.3.1.2 Synthesis of 1-butyl-3-methylimidazolium tetrafluoroborate

A solution of [BMIM][Br] (5.006 g, 22.85 mmol) in a dry acetone (25 mL) was stirred with sodium tetrafluoroborate (2.508 g, 22.85 mmol) in a three-necked RBF for 24 hours at room temperature under argon atmosphere. The reaction mixture was filtered through a pad of kieselguhr to remove sodium bromide (NaBr) formed as by-product. The filtrate was dried over anhydrous magnesium sulphate ($MgSO_4$), and then the solvent was removed under reduced pressure. The obtained yellow oily solution of [BMIM][BF_4] was dried under high vacuum at 80 °C for 12 hours. (3.631 g, 70%).
IR (ATR, cm^{-1}) 3638, 3162, 3121, 2964, 2878, 1574, 1466, 1169, 1034, 1017, 847, 753, 651, 623, 520.

^{1}H NMR ($CDCl_3$, ppm) δ_H = 8.73 (1H, s, N-(C2)H-N), 7.44 (2H, d, N-C(4,5)-H), 4.15 (2H, d, J=5.32 Hz, N-CH_2), 3.89 (3H, s, N-CH_3), 1.79 (2H, d, N-CH_2-CH_2), 1.29 (2H, d, N-CH_2-CH_2-CH_2), 0.85 (3H, t, J=6.04 Hz, CH_2-CH_3).

^{13}C NMR ($CDCl_3$, ppm) δ_C = 135.94, 123.71, 122.38, 49.50, 35.98, 31.77, 19.16, 13.18.

^{19}F NMR ($CDCl_3$, ppm) δ_F = -151.56

LC-MS (ESI, m/z) ($[BMIM]^+$- BF_4) 139 (100), ($[BMIM]_2 BF_4)^+$ 365 (80)

3.6.3.2 Microwave method

This method involves the use of MW energy as the heating source. The studied ILs were synthesized based on the modified procedure originally developed by Namboodiri *et al.*[7]

3.6.3.2.1 Synthesis of 1-butyl-3-methylimidazolium bromide

Dried 1-methylimidazole (5.003 g, 60.95 mmol) and 1-bromobutane (9.648 g, 73.08 mmol), under argon purged conditions, were introduced into 35 mL cylindrical vial equipped with Teflon magnetic stirrer bar and this latter was capped with silicone/PTFE cap. This vial was inserted in the cavity of the MW reactor through the attenuator. A pressure gauge and a release bulb were located to the cover of the reactor. The reaction parameters for this reaction were set using a computer with Intuitive Synergy ™ software system connected to the reactor. The reaction temperature was 78 °C, the MW power and pressure were 150 watts and 200 psi, respectively.

The reaction mixture was continually stirred with high stirring mode for 12 min to give two layers, yellow dense layer and the upper colourless layer which was the unreacted bromobutane. These two layers were separated by decantation and the yellow one was washed with dried diethyl ether (3 x 30 mL) and allowed to crystalize for 48 hours at room temperature in a glove bag full of argon. The crystals were dried overnight under reduced pressure to give white solid crystals of [BMIM][Br] (13.074 g, 98%).
IR (ATR, cm^{-1}) 3375, 3126, 3081, 2961, 2867, 1702, 1568, 1456, 1163, 892, 809, 754, 655, 630, 412

^1H NMR (D_2O, ppm) δ_H = 8.65 (1H, s, N-(C2)H-N), 7.41 (1H, s, N-C(4)-H), 7.36 (1H, s, N-C(5)-H), 4.10 (2H, t, J=7.16 Hz, NCH_2), 3.82 (3H, s, N-CH_3), 1.78 (2H, m, N-CH_2-CH_2), 1.22 (2H, m, N-CH_2-CH_2-CH_2), 0.80 (3H, t, J=7.40 Hz, CH_2-CH_3).

^{13}C NMR (D_2O, ppm) δ_C = 135.81, 123.46, 122.21, 49.24, 35.63, 31.25, 18.74, 12.65.

LC-MS (ESI, m/z) ($[BMIM]^+$- Br) 139 (100), ($[BMIM]_2$ Br)$^+$ 357 (34)

3.6.3.2.2 Synthesis of 1-butyl-3-methylimidazolium tetrafluoroborate

The same experimental MW set-up was used as for the synthesis of [BMIM][Br]. A solution of [BMIM][Br] (5.006 g, 22.85 mmol) in a dry acetone (25 mL) and sodium tetrafluoroborate (2.508 g, 22.85 mmol) were stirred at high stirring mode for 20 min at 80 °C in the MW reactor. The reaction mixture was filtered through a pad of kieselguhr to remove NaBr formed as by-product. The filtrate was dried over $MgSO_4$, and thereafter the solvent was removed under reduced pressure. The obtained yellow oily solution was dried under high vacuum at 80 °C for 12 hours to give [BMIM][BF_4] (4.796 g, 93%).
IR (ATR, cm^{-1}) 3160, 3122, 2964, 2877, 1574, 1466, 1169, 1034, 1017, 847, 753, 651, 623, 520.

^{1}H NMR ($CDCl_3$, ppm) δ_H = 8.66 (1H, s, N-(C2)H-N), 7.44 (2H, d, N-C(4,5)-H), 4.15 (2H, t, J=7.38 Hz, N-CH_2), 3.90 (3H, s, N-CH_3), 1.82 (2H, m, N-CH_2-CH_2), 1.32 (2H, m, N-CH_2-CH_2-CH_2), 0.87 (3H, t, J=7.36 Hz, CH_2-CH_3).

^{13}C NMR ($CDCl_3$, ppm) δ_C = 135.96, 123.76, 122.46, 49.58, 36.03, 31.82, 19.22, 13.23.

^{19}F NMR ($CDCl_3$, ppm) δ_F = -150.67

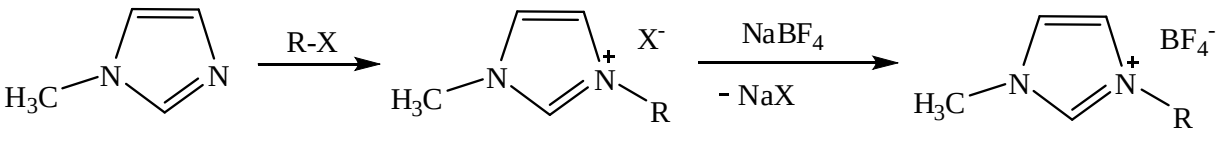
LC-MS (ESI, m/z) ([BMIM]$^+$- BF_4) 139 (100), ([BMIM]$_2$ BF_4)$^+$ 365 (72).

3.7 Results and discussion

This section compiles the results obtained from the synthesis and characterization of [BMIM][BF_4] in two different methods (MW and conventional). In addition, the results for some physicochemical properties' determination are also presented. All the experimental data reported here are compared and referenced to those reported in literature.

3.7.1 Synthesis of 1-butyl-3-methylimidazolium tetrafluoroborate

The starting materials used in synthesis of [BMIM][BF_4] were all commercially available. The ILs were synthesized by modifying the procedure originally described by Wilkes and Zaworoto[8] shown in Scheme 3.1.



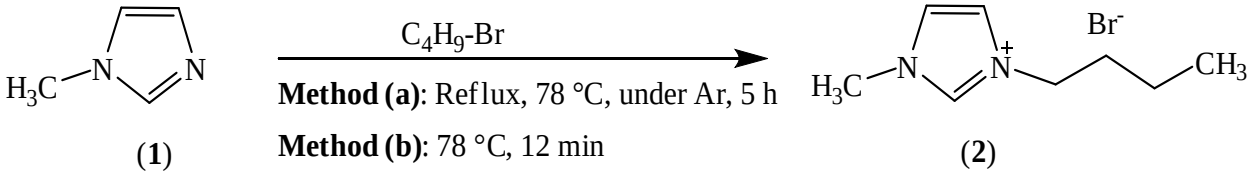
(**1**) (**2**) (**3**)

Scheme 3.1: Synthetic pathway of 1-butyl-3-methylimidazolium tetrafluoroborate[7]

Generally, synthesis of ILs involved two main steps: (i) the formation of the cation where the bases like amine, phosphine, sulphide and pyridine are alkylated, mostly with haloalkanes (R-X). The second step (ii) is the anion exchange between halides and non-coordinating anions either by double displacement anion metathesis or acid-base neutralization reactions.[3,9]

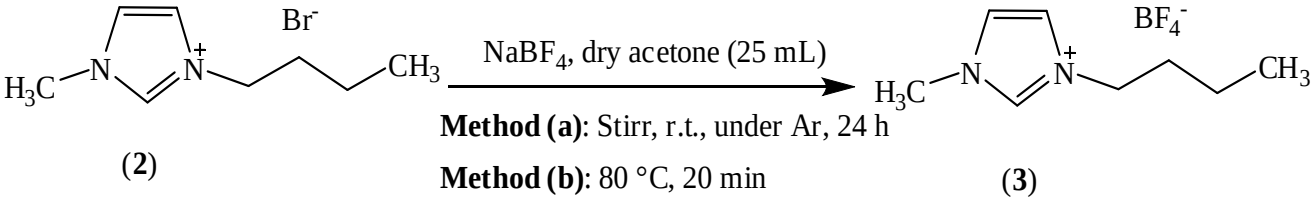
Similarly in this work, the synthesis of [BMIM][BF_4] involved two synthetic steps as depicted in Scheme 3.2.

Step 1: Formation of cation



(**1**) (**2**)

Step 2: Anion exchange via metathesis



(**2**) (**3**)

where Ar: Argon, h: Hours and r.t.: Room temperature
Method (a): Conventional , Method (b): Microwave

Scheme 3.2: Synthetic pathway of [BMIM][BF_4] by (a) conventional method and (b)MW method

Firstly, 1-methylimidazole was alkylated by 1-bromobutane in mole ratio of 1 : 1.2 (1-methyimidazole : 1-bromobutane), under inert atmosphere of argon, to give [BMIM][Br] as

yellow viscous liquid which was washed with dry diethyl ether and allowed to crystallize for 48 hours. This step was done under solvent-free conditions. The obtained crystals were crushed in inert glove bag. In this synthesis, 1-methylimidazole was the limiting reagent and 1-bromobutane was in excess in order to ensure full alkylation for all the 1-methylimidazole.

Dry diethyl ether was used to wash the unreacted 1-bromobutane and thereafter the residual ether solvent was removed under vacuum to obtain crystals which were dried overnight under reduced pressure to give white solid crystals of [BMIM][Br].[10,11]

Secondly, [BMIM][Br] reacted with sodium tetrafluoroborate in a mole ratio of 1 : 1 ([BMIM][Br] : sodium tetrafluoroborate) in dry acetone where anion exchange took place between bromide ($[Br]^-$) and tetrafluoroborate ($[BF_4]^-$) anions. NaBr was formed as by-product and precipitated at the bottom and thereafter was removed by filtration through the kieselguhr pad. The filtrate was concentrated under reduced pressure to produce a yellowish viscous liquid [BMIM][BF_4].[12,13]

The Schlenk line apparatus was used for both of these two steps to maintain inert atmosphere (under argon) given that in general ILs are hygroscopic.[14-16] The reaction conditions were dependent on the synthesis method. Conventional method consisted of refluxing the reaction at 78 °C for 5 hours (step 1) using oil bath as a heating source and stirring the reaction at room temperature for 24 hours (step 2). With MW method, all the reactions were done using CEM Discover single mode microwave. MW energy was applied to the reaction at 78 °C for 12 min and 80 °C for 20 min for step 1 and step 2, respectively. Other reaction parameters such as pressure, power and stirring mode were maintained constant for both steps and were strictly controlled. The isolated yields, calculated based on 1-methylimidazole and [BMIM][Br] for step 1 and step 2, respectively, are compiled in Table 3.2.

Table 3.2: Isolated yields of synthesized [BMIM][X]

X	Synthesis method	Time (hours)	Yield (%)
$[B]r^-$	Conventional	5	78[a]
$[BF_4]^-$	Conventional	24	70[b]
$[Br]^-$	MW	0.2	98[a]
$[BF_4]^-$	MW	0.33	90[b]

[a] Isolated yields based on 1-methylimidazole for step 1
[b] Isolated yields based on [BMIM][Br] for step 2

Product yields and reaction time showed strong dependence on the heating mode for this synthesis. As typical example, for step 1 in both methods, reactions were carried out at the same temperature (78 °C).

A better yield and purer [BMIM][Br] product was obtained in short reaction time using the MW method, similar to what has been reported in literature.[17,18]

The difference in heating time and the product yields is attributed to the energy transfer facility from the energy source to the reaction as shown on Figure 3.3.

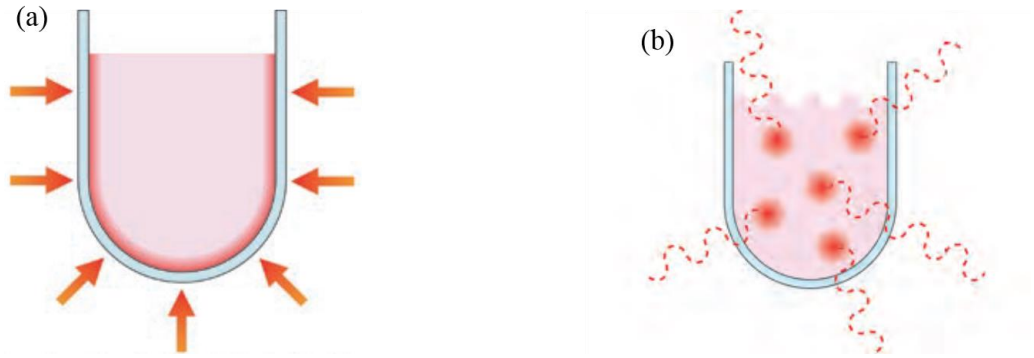


Figure 3.3: Heating modes in synthesis of [BMIM][BF_4]: (a) conventional heating and (b) MW heating[19]

With conventional method, which is extensively used and reported,[8,9,12,16,20-22] the energy is transferred indirectly to the reaction by convective heating mechanism. Basically, the vessel is heated first and the energy is transferred from outside of the vessel to inside the reaction. This type of heating slows the reaction and shows itself inefficient because it continues even after the energy source has been taken away. Prolonged heating can provide coloured products, some side reactions and unexpected product decomposition.

In contrast, while heating with MW, the energy is transferred to the reaction by ionic conduction mechanism owing to the ionic character of ILs which enhances their excellent coupling capability with the MW energy.[7,19,23-25] The energy is directly absorbed by the reaction and fast activation of the molecules in reaction is observed. This activation raises the reaction to the desired temperature immediately and thus limits side reactions and endorses a fast and efficient heating mode. Furthermore, for the required time, controlled MW heating provides more accurate and precise reaction temperature. Hence, the probability of overheating or underheating the reaction is virtually minimal.

3.7.2 Characterization of 1-butyl-3-methylimidazolium tetrafluoroborate

The spectral analyses and the determination of some physicochemical properties were used as adequate ways to confirm the formation of [BMIM][BF_4] and to also assess its purity.

3.7.2.1 Fourier transform infrared analysis

The ILs constituents absorb electromagnetic energy in the infrared region of the spectrum. This energy causes the fast stretching and bending vibrational frequencies of the bonds in the ILs.[26] The FTIR technique was used to examine the functional groups and the interactions between constituents in IL.

FTIR spectrum of synthesized [BMIM][BF_4] is shown on Figure 3.4 and the peak assignments data are summarized in Table 3.3. The synthesized [BMIM][BF_4], using both conventional and MW methods, exhibited similar IR spectra that were in good agreement with the data reported in literature.[10,12,27] For comparison purpose, 1-methylimidazole spectrum was also recorded.

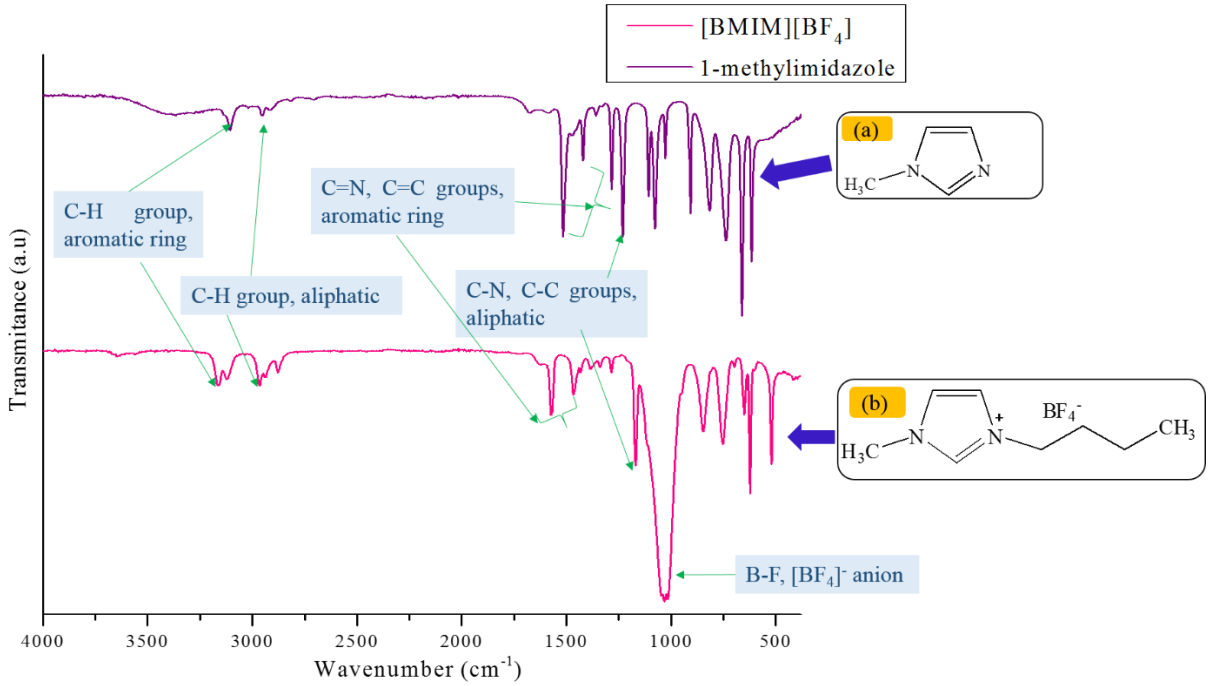


Figure 3.4: FTIR spectra for (a) 1-methylimidazole and (b) [BMIM][BF_4] synthesized by MW method

Table 3.3: Selected FTIR frequency bands for 1-methylimidazole and synthesized [BMIM][BF_4]

Peak wavenumbers (cm^{-1})	Assignment	Functional group
3159, 3115, 3108*	=C-H, stretching	=C-H, on the ring (sp^2), aromatic ring
2961, 2873, 2954*	-C-H, symmetric and asymmetric stretching	-CH_3 terminal, -CH_2 aliphatic
1572, 1462, 1513*, 1417*	C=C, C=N stretching	C=C, C=N on the aromatic ring
1169, 1230*	N-C, C-C, stretching	N-Me, N-Bu, C-C aliphatic
1021	B-F, stretching	$[BF_4]^-$ anion

*: Absorption peak on 1-methylimidazole spectrum
Me: Methyl group (CH_3), Bu: Butyl group (C_4H_9)

Figure 3.4 and Table 3.3 showed that there was a slight absorption peak shift to upper wavenumbers for chemical bonds in [BMIM][BF_4] compared to their analogues in 1-methylimidazole. This is mainly due to the introduction of butyl chain and $[BF_4]^-$ anion, which is coupled with the strong interactions with the cation. [26-28] The characteristic broad peak observed at 1021 cm^{-1}, which was absent in the 1-methylimidazole, was assigned to B-F bond, confirming the presence of $[BF_4]^-$ anion.[29] [BMIM][Br] spectrum is attached in appendix, Figure A1 as supportive information.

3.7.2.2 Nuclear magnetic resonance analysis

The NMR (^{1}H-, ^{13}C- and ^{19}F-NMR) spectroscopy was used to confirm the formation of the product. This analysis helped to investigate the electronic structure of the synthesized [BMIM][BF_4] and their reactivity as solvent medium based on the chemical shifts value of each hydrogen atom on the imidazolium ring (discussed in Chapter Four).

For comparison purpose, the ^{1}H-NMR spectra of 1-methylimidazole was also recorded. ^{1}H-NMR spectra of 1-methylimidazole and [BMIM][BF_4] is presented in Figure 3.5 and all NMR data are summarized in Table 3.4.

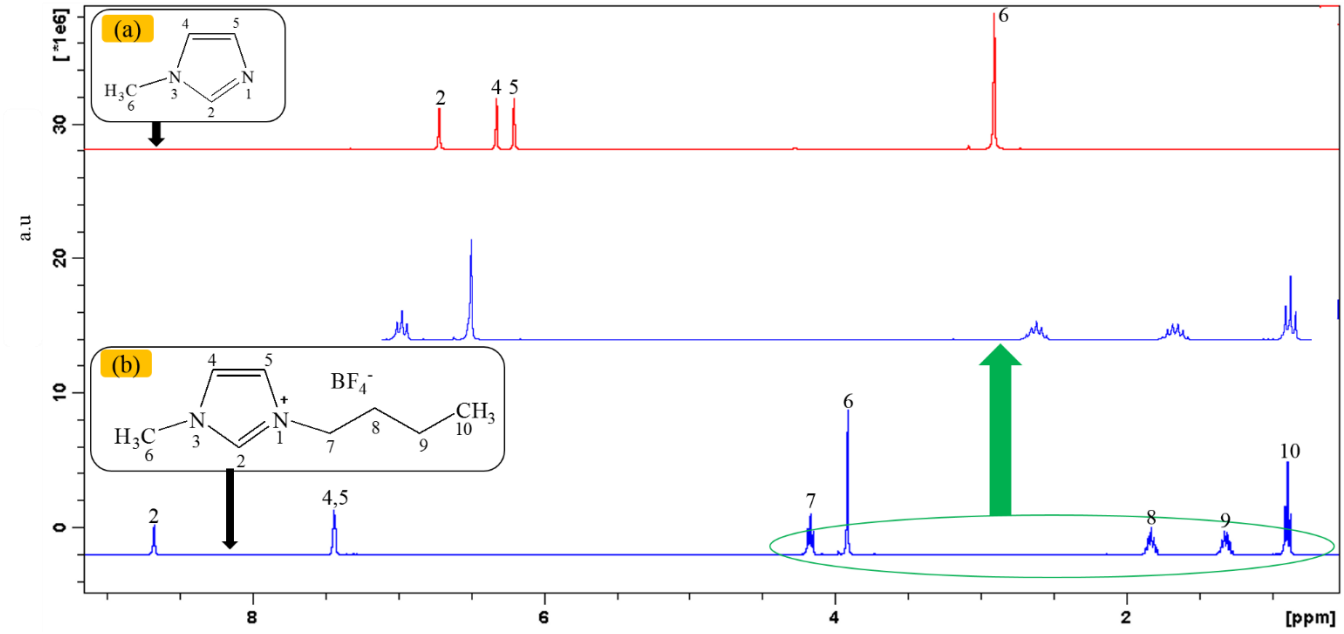


Figure 3.5: ^{1}H-NMR spectra for (a) 1-methylimidazole (red) and (b) [BMIM][BF_4] (blue) synthesized by MW method, using $CDCl_3$ as NMR solvent

The ^{1}H-NMR spectrum of [BMIM][BF_4] showed the downfield migrations of chemical shifts of imidazolium ring to downfield region and the appearance of new chemical shifts in upfield region compared to 1-methylimidazole spectrum. These were good evidences for both the introduction of butyl chain on 1- methylimidazole skeleton and the hydrogen bonding between imidazolium ring and $[BF_4]^-$ anion. In our case, this hydrogen bonding effect is less pronounced for these chemical shifts migration due to large size and weak coordinating ability of $[BF_4]^-$ anion with a delocalized charge distribution.[30]

The quaternization of one nitrogen atom of the imidazolium ring, diminishes the electron density of that nitrogen. This destabilization is propagated within entire imidazolium ring and creates asymmetric electron distribution, thereby reduces significantly the electron density at the hydrogen atoms in the imidazolium ring. Therefore, these hydrogen atoms resonate at higher frequencies (deshielded) comparable to similar atoms in 1-methylimidazole. In agreement with the qualitative picture of diamagnetic shielding in NMR, lower electron density at the place of the ^{1}H nucleus involves weak local shielding of the external magnetic field, which leads to higher ppm shifts.[30]

Table 3.4: ^{1}H-NMR peaks and assignments for 1-methylimidazole and synthesized [BMIM][BF_4]

Resonance peaks	**1-methylimidazole**			**[BMIM][BF_4]**			
	δ (ppm)	Integrated protons	Multiplicity	δ (ppm)	Integrated protons	Multiplicity	*J* (Hertz)
N-C<u>H</u>-N	6.67	1	s	8.66	1	s	-
N-C<u>H</u>-CH-N	6.28	1	s	7.44	1	s	-
N-CH-C<u>H</u>-N	6.16	1	s	7.44	1	s	-
N-C<u>H_2</u>	-	-	-	4.15	2	t	7.38
N-C<u>H_3</u>	2.88	3	s	3.90	3	s	-
N-CH_2-C<u>H_2</u>	-	-	-	1.82	2	q	4.94
C<u>H_2</u>-CH_3	-	-	-	1.32	2	m	7.52
CH_2-C<u>H_3</u>	-	-	-	0.87	3	t	7.36

The hydrogen atoms, at the imidazolium ring in [BMIM][BF_4], chemically resonated at different frequencies depending on how far they are attached to nitrogen atoms. Therefore, (C4)-H and (C5)-H are almost chemically equivalent, neutral and appeared as an overlapped doublet peak at 7.44 ppm from both methods.[27,31]

The (C2)-H resonated further in high frequency region and this is due to higher electron deficit imposed on this (C2) atom by the two nitrogen atoms which are more electronegative (electron withdrawing) than carbon atoms. The electrons of (C2) atom are inductively pulled by nitrogen atoms through C=N bond causing the (C2) atom to remain more electron deficient and this enhances the polarity of hydrogen atom attached at this carbon centre.[10,32] The upfield chemical shift of the butyl chain protons is a function of the distance of the studied proton from the imidazolium ring. The protons on the methyl and methylene groups attached to nitrogen atoms are highly attracted due to electron withdrawing effect of these nitrogen atoms.

^{13}C-NMR of [BMIM][BF_4] was 135.96, 123.76, 122.46, 49.58, 36.03, 31.82, 19.22, 13.23. ^{13}C-NMR of 1-methylimidazole was 136.14, 125.04, 119.61, 32.37. ^{13}C-NMR spectrum of [BMIM][BF_4] showed insignificant chemical shifts of carbon atoms on the imidazolium ring compared to 1-methylimidazole. This was explaining the least sensitivity of ^{13}C-NMR as reported by Grishina *et al.*[31]

The presence of one peak at -150.67 ppm in ^{19}F-NMR spectrum of [BMIM][BF_4], absent in ^{19}F-NMR spectrum of 1-methylimidazole, confirmed the presence of $[BF_4]^-$ anion.

^{13}C-NMR and ^{19}F-NMR spectra of [BMIM][BF_4] are annexed in appendices section for more information (see Figure B1-2). [BMIM][Br] spectra (^{1}H- and ^{13}C-NMR) are also attached as Figure B3-4 in appendix.

3.7.2.3 Liquid chromatography-mass spectroscopy analysis

Different aggregates of synthesized [BMIM][BF_4] (mass/charge) were obtained by LC-MS analysis in positive-ion-mode as shown on Figure 3.6. The obtained results showed a good agreement with the literature data from other ionization techniques such as direct analysis in real time mass spectrometry (DART-MS)[33] and extractive electrospray ionization mass spectrometry (EESI-MS).[34]

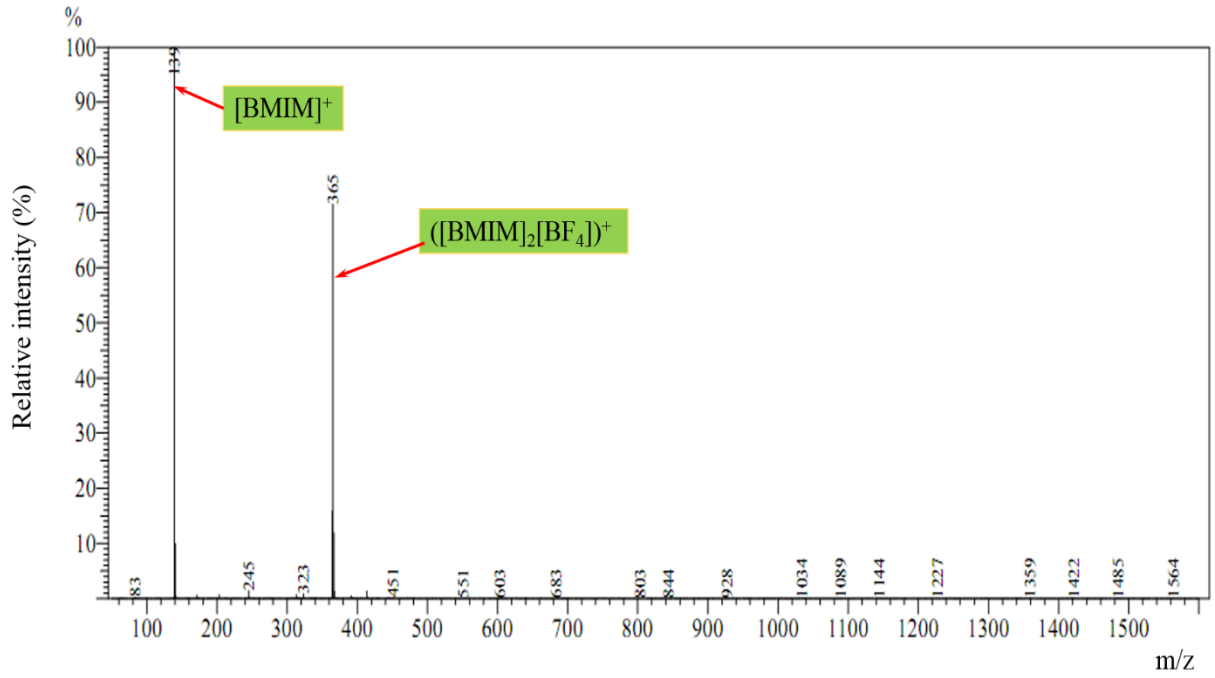


Figure 3.6: LC-MS spectrum for [BMIM][BF_4] synthesized by MW method

The base peak at *m/z* 139 was assigned to $[BMIM]^+$ ion with the relative ion abundance derived from the relative intensity of 100% and this is the supporting evidence of the [BMIM][BF_4] formation.

High dilution of the sample submitted at LC-MS analysis up to 5 ppm (2.22×10^{-5} mol.l^{-1}) generated other species called IL cluster ions. IL cluster ions are defined as the ions formed by grouping of more ions of same species often in association with a second species. They exist as positive $[C_nA_{n-1}]^+$ and negative $[C_{n-1}A_n]^-$ IL cluster ions depending on the combination between cation (C) and anion (A) species within an IL and the used ionization modes.[33-37] The peak at 365 m/z, with the relative intensity of 72%, was identified as positive IL cluster ion standing for $([BMIM]_2[BF_4])^+$ with a neat state charge of +1. However, with negative-ionization mode, no results were obtained due to variation in the sensitivity of ions. LC-MS spectrum of [BMIM][Br] from both methods is also annexed as Figure C1, in appendix.

3.7.3 Physicochemical properties of the synthesized ionic liquids

The water content, density, viscosity and thermal stability properties were determined and used as qualitative gears to ascertain the purity of synthesized ILs from both methods as summarized in Table 3.5. The strong influence of impurities on physicochemical properties was reported.[3,38]

3.7.3.1 Water content

Both [BMIM][BF_4] and its precursor, [BMIM][Br] were investigated for water content. The variations in properties were attributed to differences in the moisture content, depending on the method used in synthesis, given that they have the same cation and ILs are generally very hygroscopic.[3] Hence, it was important to determine the water content within the synthesized ILs which helps in investigating their purity given that water is seen as major impurity. For example, the presence of water within [BMIM][BF_4] diminishes its stability and leads to its decomposition to hydrogen fluoride (HF) and other by-products.[39,40] Furthermore, water content has also effect on other physicochemical properties of [BMIM][BF_4] as recently reported by Grishina *et al.*[31] which is also in agreement with Cammarata *et al.* findings.[41] Water interacts with ILs by changing the local ordering of ILs constituents, hence disrupting the existing weak hydrogen bonds between cation and anion. The water molecules and the cation of ILs exhibit a certain competition towards direct hydrogen bonds interactions to the anion as reported by Mele *et al*.[42] On the other hand, water molecules can also interact with the cation through the bonding with three hydrogen atoms found on the imidazolium ring.[43] These interactions depend on the length of the alkyl chains present on imidazolium ring cation[43] and the anion nature.[44,45]

During the synthesis of [BMIM][Br] and [BMIM][BF_4], water could be absorbed from either work-up process or moisture-air and even after thorough drying, trace amounts of water may still be present.[45,46] The water fractions (wt.%) absorbed by [BMIM][Br] and [BMIM][BF_4], determined using volumetric Karl-Fischer titration, are indicated on Figure 3.7 and in Table 3.5.

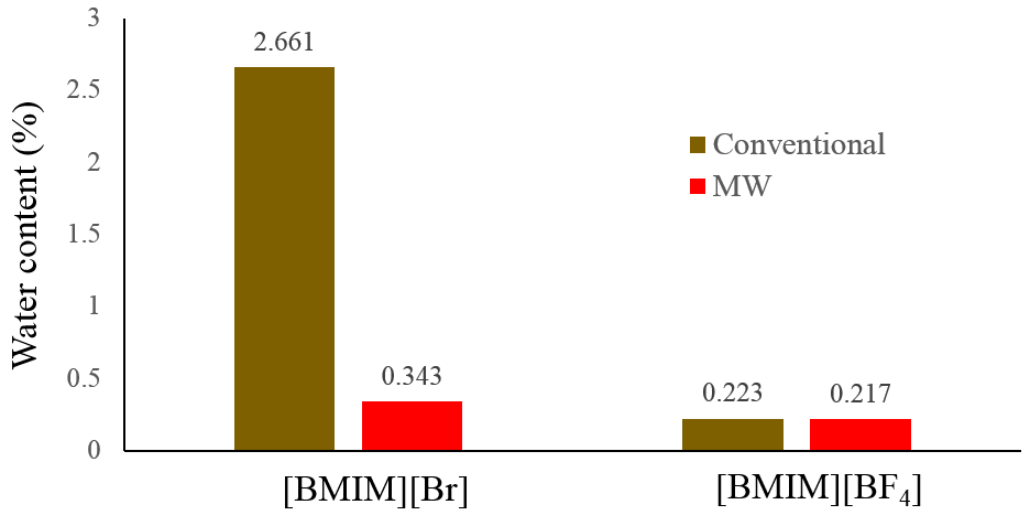


Figure 3.7: Water content for [BMIM][Br] and [BMIM][BF_4] synthesized by MW and conventional methods, respectively

[BMIM][Br] showed higher water content than [BMIM][BF_4] from both synthesis methods. The water content difference range between the two synthesis methods were 2.318% for [BMIM][Br] while that for [BMIM][BF_4] it was 0.006%. Comparing these water content difference ranges, it is clear that the water uptake decreased from $[Br]^-$ anion to $[BF_4]^-$ anion-based ILs as reported by Cammarata *et al.*[41] This could be explained by the strength of hydrogen bonding interactions between anions and water molecules, where small and strong coordinated anion like $[Br]^-$ interacts with hydrogen atoms from water, speedily and strongly than large asymmetric and weak coordinated anion like $[BF_4]^-$.[15,44,45]

The higher content values were observed in the ILs synthesized with conventional method. These results were confirmed by the appearance of a significant band at 3638 cm^{-1} in [BMIM][BF_4] FTIR spectrum, synthesized conventionally (Figure A2 in appendix). [BMIM][BF_4], synthesized using MW method, was showing trivial OH stretching band of water (see Figure 3.4).

3.7.3.2 Density

The density property determination is helpful in liquid-liquid biphasic separation, extraction process or catalysis. Density values of both [BMIM][Br] and [BMIM][BF_4], were determined at 25 ± 1 °C as presented on Figure 3.8 and in Table 3.5.

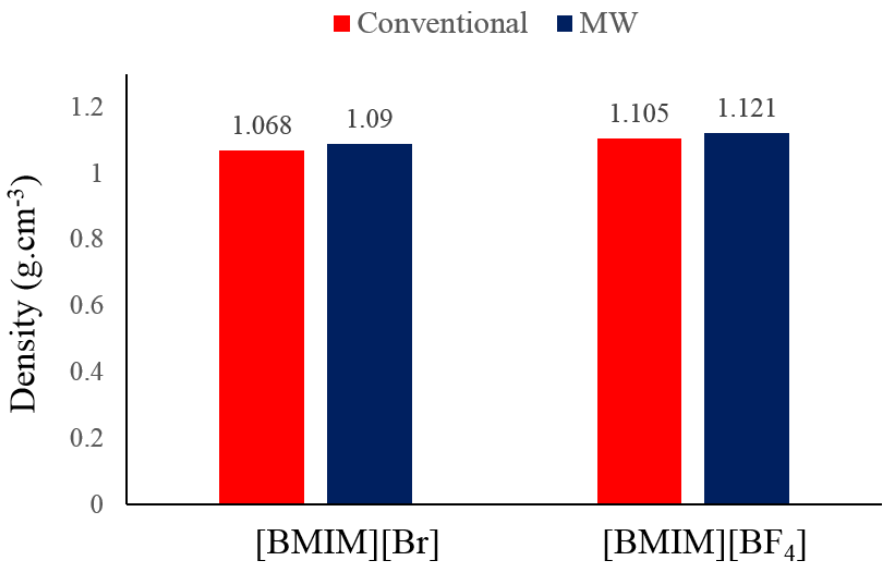


Figure 3.8: Density for [BMIM][Br] and [BMIM][BF_4] synthesized by MW and conventional methods, respectively

[BMIM][Br] showed lower density than [BMIM][BF_4] from both synthesis methods. The remarked differences are attributed to the water presence and the anion nature. Torrecilla *et al.*[47] reported that the lower density values are observed in ILs with high water content. This support the observed trend in this work where for example [BMIM][BF_4] density decreases from 1.121 g.cm^{-3} to 1.105g.cm^{-3} when the water content increases from 0.217% to 0.223% for MW and conventional methods, respectively. Basically, the hydrogen bond network between cation and anion is disrupted and weakened by the introduction of water molecules. Hence, ions are more spread apart, less closely packed, thus lower density.[48] Similar trend was reported by Martins *et al.*[49] for a series of imidazolium-based ILs with bis(trifluoromethylsulfonyl)imide.

On the other side, it appeared that the density increased with the molar mass of the anion for the ILs synthesized using similar synthesis method.[31,50] Therefore, lower density was found for [BMIM][Br] compared to that for [BMIM][BF_4] in both methods. The similar anion effect on the density was found for a series of phosphonium-based ILs reported by Bhattacharjee *et al.*[51] The obtained [BMIM][BF_4] densities were beneficial to the phase separation of immiscible liquids mixtures during the product extraction and the [BMIM][BF_4] recycling as detailed in Chapter Four

Table 3.5: Physicochemical properties of synthesized [BMIM][X]

X	Synthesis method	Water content (%)		Density (g.cm^{-3}) at 25 °C		Viscosity (cP) at 25 °C		Thermal stability (°C)	
		Exp.	*Lit.*	*Exp.*	*Lit.*	*Exp.*	*Lit.*	*Exp.*	*Lit.*
$[Br]^-$	Conv.	2.661	-	1.068	-	-	-	269	273[50]
$[Br]^-$	MW	0.343		1.090		-		272	
$[BF_4]^-$	Conv.	0.223	0.21[31], 0.453[45]	1.105	1.120[45], 1.2014[47]	200	219[45]	400	430[31], 403[45], 445[22]
$[BF_4]^-$	MW	0.217		1.120		220		401	

Conv.: Conventional method
MW: Microwave method

3.7.3.3 Viscosity

Viscosity known as transport property, has a significant impact on the rate of mass transport and has to be measured accurately. The solvent dynamic viscosities obtained for synthesized [BMIM][BF_4] at 25 ± 1 °C were 220 cP and 200 cP from MW and conventional methods, respectively (Table 3.5). The dynamic viscosity of [BMIM][Br] was not determined given that firstly, it was a solid and secondly, the viscosity measurement was done using capillary viscometer type qualified for fluids only.

The lower dynamic viscosity values were obtained for [BMIM][BF_4] synthesized conventionally compared to the one synthesized with MW. This could imply that the viscosity decreases when the water content increases.[31,51,52]

The obtained viscosity values were not matching exactly with the literature data owing to a significant variability in viscosity data reported by different researchers. For example, for [BMIM][BF_4], the reported viscosity at 25 °C was 219 cP by Huddleston,[45] 115 cP by Zhao[53] and 153.78 cP by Liu *et al.*[54]

3.7.3.4 Thermal stability

The application of IL as solvent, especially at elevated temperatures requires the determination of its thermal stability. The TGA technique was used to investigate the thermal stability of synthesized ILs[55,56] as well as the presence of residual impurities. An onset decomposition temperature, defined as the intersection of the mass base line (at 100%) with the tangent on the gravimetric reduction point of TG curve, was used to evaluate the starting decomposition temperature of each synthesized IL, considered as the thermal stability. This method involves the changes in weight when the sample is heated. Recently, quantitative structure-property relationship method has been adopted to determine the thermal stability of ILs.[57]

The TGA plots of all synthesized ILs, generated under nitrogen flow and temperature range of 40 to 600 °C, are stacked on Figure 3.9.

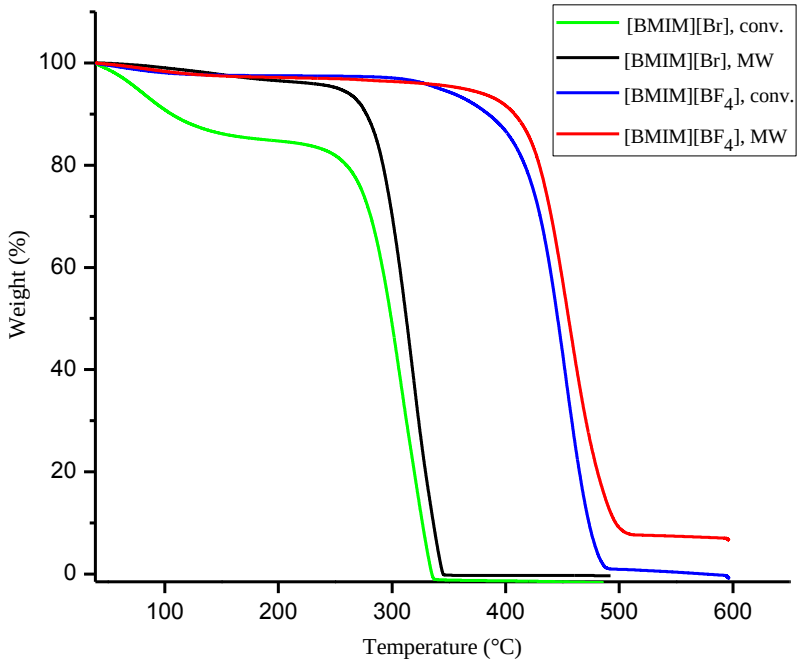


Figure 3.9: Thermogravimetric profiles for [BMIM][Br] and [BMIM][BF_4] synthesized by MW and conventional (conv.) methods, respectively

The starting decomposition temperature values of [BMIM][Br] were 272 ^oC and 269 °C, in MW and conventional methods, respectively, against 273 ^oC reported by Fredlake *et al.*[50] The starting decomposition temperature values of [BMIM][BF_4] were 401 ^oC and 400 ^oC, in MW and conventional methods, respectively, and were in agreement with the literature.[45]

From Figure 3.9, it is shown that the TGA curves of all the synthesized ILs had one step except [BMIM][Br], synthesized conventionally, which showed two different steps. On heating, from 40 to 600 °C, the weight loss shown below 150 °C was assigned to the loss of water absorbed from moisture.[57] This loss of water was highly significant in [BMIM][Br] at *ca.* 6 wt.% and 1 wt.% from conventional and MW synthesis methods, respectively. By changing the anion from $[Br]^-$ to $[BF_4]^-$, the loss of water was less than 1 wt.% in [BMIM][BF_4] from both methods. This was explaining the affinity of the water molecules and the anion as reported by Huddleston *et al.*.[45]

The thermograms reveal that [BMIM][Br] synthesized conventionally contains more water than the one synthesized using MW. This variation in moisture content could be possibly arise

from absorption of moisture from the atmosphere as consequence of prolonged reaction time, together with exposing human errors. The slightly high thermal stability was observed to the ILs synthesized by MW method and this was showing the high purity of these ILs.

The weight loss observed in the temperature range of 150 °C and the onset decomposition temperature was attributed to the slow thermal decomposition of both the anion and the cation.[31]

The thermal stability showed a strong dependence on the anion structure given the cation was the same.[55,56] This correlates with the anion hydrophobicity, expressed as a measure for hydrogen bonding capacity, and the nucleophilicity.[45] ILs with halide anions exhibit lower thermal stability owing to their significantly high nucleophilicity and basicity. This was shown by the first derivative plot, (Figure 3.10), which gives the exact decomposition temperatures for each IL.

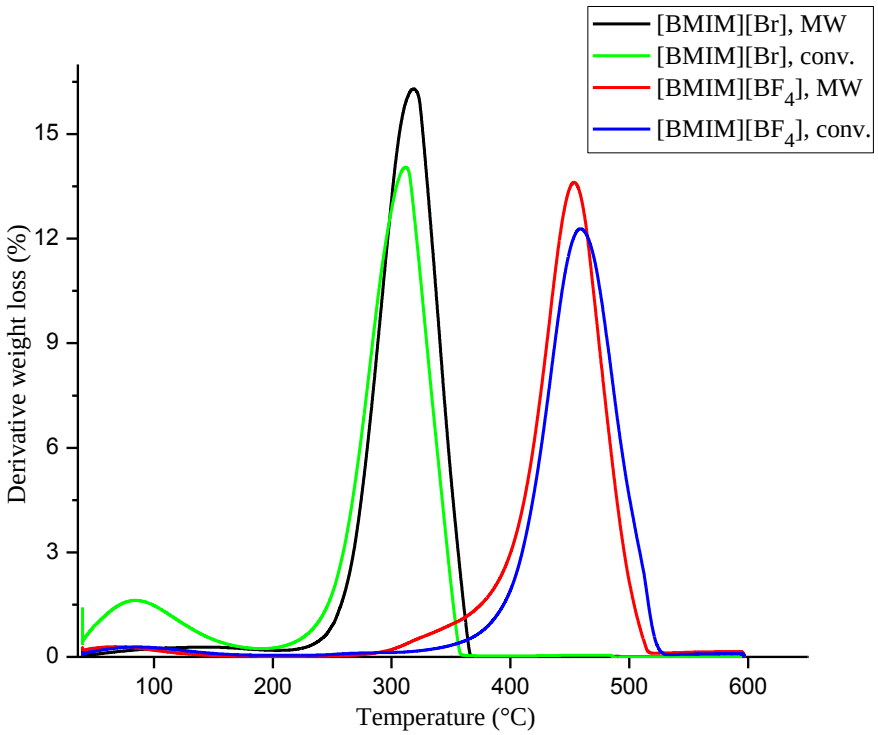


Figure 3.10: First derivative of the thermograms obtained for [BMIM][Br] and [BMIM][BF_4] synthesized by MW and conventional (conv.) methods, respectively

The exact decomposition temperatures for [BMIM][Br] were 318 °C and 313 °C from MW and conventional synthesis methods, respectively. Similarly, [BMIM][BF_4] decomposed exactly at 458 °C and 454 °C.

A trend was observed whereby [BMIM][BF_4] showed high thermal stability than its precursor where $[Br]^-$ anion is thermally less stable than $[BF_4]^-$ anion. This could be explained by the coordinating ability of the anion as reported by Ngo *et al.*[55] where ILs with weakly coordinating anions are the most resistant to thermal decomposition. $[BF_4]^-$ anion exhibits a pronounced charge delocalization across its constituent atoms which are held together by intermolecular Van der Waals interactions. These interactions make $[BF_4]^-$ more voluminous compared to singly charged $[Br]^-$ anion and the thermal stability increases as function of anion size increase[50] as well as the hydrophobic character of that anion.

[BMIM][Br] thermograms showed minimal weight residue, confirming the fast decomposition of halides-based ILs.[56] However, a weight residue of 5 to 10% was observed at the [BMIM][BF_4] thermograms. This was arisen from the production of charred residue post degradation materials which could probably be assigned as the decomposed carbonaceous polymeric materials.[58]

3.8 Conclusion

[BMIM][Br] was successfully synthesized and used as precursor for the synthesis of ([BMIM][BF_4]. This synthesis was done successfully through two different methods, *i.e.* conventional and MW methods. Excellent yields were produced from MW method and within a short time, owing to the excellent coupling ability of the MW energy and ILs constituents. The conventional method gave lower yields of the ILs, attributable to the slow and inefficient energy transfer encountered in this method. Therefore, this inefficient heating source offered the longer reaction times which consequently generated impurity such as water.

All the synthesized products were characterized by spectroscopic analyses such as FTIR, NMR (^{1}H-, ^{13}C- and ^{19}F-NMR) and LC-MS. Furthermore, some physicochemical properties including water content, density, viscosity and thermal stability were determined with intention of investigating the purity of synthesized [BMIM][Br] and [BMIM][BF_4].

The strong dependence of these properties on the anion structure were explained through the hydrogen bonding interactions, *i.e.* between anion and imidazolium ring, where smaller anion interacts stronger than larger anion. Also, water content and viscosity properties were found higher in [BMIM][Br] than in [BMIM][BF_4]. In addition, density and thermal stability properties increased with the large and non-coordinating anion such as $[BF_4]^-$. The presence of water, as impurity, decreased drastically the density, viscosity and thermal stability properties.

Comparing the results obtained, from spectral characterization and physicochemical properties of the synthesized ILs, with the data extracted from the literature, a clear comparison of the synthesis methods was shown. MW method exhibited more preferences in terms of short reaction times and higher pure product yields than conventional method for the synthesis of [BMIM][BF_4].

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Chapter Four

Reduction of aldehydes and ketones in 1-butyl-3-methylimidazolium tetrafluoroborate to their corresponding alcohols

Chapter Four investigates 1-butyl-3-methylimidazolium tetrafluoroborate ([BMIM][BF_4]), as a solvent, in the reduction reactions of aldehydes and ketones to their corresponding alcohols. The main focus of this study was to investigate the solvent efficiency of [BMIM][BF_4] in the reduction reactions. Also, the [BMIM][BF_4] was compared to ethanol, which is one of the common molecular volatile organic solvents. Also, the different reducing agents and different reduction modes used for typical reactions are discussed herein. This chapter also includes a brief background on specific reactors used and related procedures generally followed during these reactions.

4.1 Introduction

Reduction of aldehydes and ketones to their corresponding alcohols has been acknowledged as an important reaction in several areas such as in pharmaceuticals,[1] bio-catalysis,[2] and fine chemical industries.[3] Different reducing agents such as metal hydrides[4] and hydrogen (H_2) gas in presence of catalysts[5,6] are used for these reactions. The solvent impact for this reduction reaction is highly evaluated. For example, using sodium borohydride ($NaBH_4$) as a reducing agent requires a protic solvent which, in this case, acts a as proton generator as shown in Chapter Two, Scheme 2.5. However, the drawback on the common used, organic solvents, is based on their high volatility, which leads to the environmental pollution in so many different ways. To circumvent this challenge, ionic liquids (ILs) have been known as promising solvents to replace volatile organic solvents (detailed in Chapter Two, Section 2.2).

Besides the use of ILs, as greener solvent, ultrasound (US) irradiation process was also identified as one among the green approaches towards reduction of aldehydes and ketones to their corresponding alcohols. In this dissertation, it is important to note that the terms ultrasound and ultrasonic (US) are used interchangeably throughout the manuscript.

The US irradiation reduction method was firstly reported by Robert Williams Wood (1868–1955) and Alfred Lee Loomis (1887–1975) in 1927[7,8] In general, the US waves provide a non-thermal energy which activates the chemical reactions in solution.[9] This US energy is too low to alter electronic, vibrational and rotational molecular states of the liquid through which it passes. Basically, this specific activation is experienced throughout the formation and destruction of acoustic cavitation within reaction liquid phase.[10]

By applying US irradiation, there is a creation of waves which are compressed and expanded alternatively along their propagation inside the molecules of the liquid reaction through it they are passing. These US waves are of longer wavelength than the one found between atoms in the molecule. Hence, the expansion of US waves exceeds the intermolecular forces of the molecules subjected to the sonication and subsequently the acoustic cavitation with small and oscillating bubbles of gaseous compounds is formed within the liquid molecule. This bubble cavitation grows according to the applied US energy until they attain an unstable size where they can collide and violently collapse. This collapse results in the significant build-up of energy which mechanically disrupts the attractive forces holding atoms together in the molecules of a compound subjected to sonication. This occurs by allowing them to react quickly in a liquid phase.[10] This cavitational process is affected by solvent parameters such volatility, viscosity, density, surface tension, and dissolved gas of the liquid molecule, which is sonicated.[11] Although the ILs have the negligible vapor pressure, higher viscosity and density, which exclude them to be qualified as the solvents providing the ease formation of bubble cavitation, they have been extensively used in US application and the better yields were reported.[12,13]

In this work, reduction reactions of aldehydes and ketones was chosen as model reaction. The carbonyl functional group contained by these compounds was targeted in order to investigate the solvent ability of [BMIM][BF_4]. The targeted aldehydes and ketones for reduction were benzaldehyde (Ph-CHO), acetophenone (Ph-$COCH_3$), ferrocenecarboxyaldehyde (Fc-CHO), and acetylferrocene (Fc-$COCH_3$). The choice of reducing aldehydes and ketones was motivated by the enormous demand of their corresponding alcohols by the industrial sector and medical field. For example, phenylmethanol (Ph-CH_2OH), obtained from Ph-CHO, is used as a solvent for ink and paints, in cosmetics and personal care products.[14]

1-Phenylethanol (Ph-$CHOHCH_3$), produced from Ph-$COCH_3$, is used in the synthesis of optically active products.[15] Ferrocenylmethanol (Fc-CH_2OH), a product of Fc-CHO reduction, is applied as an oxidant in the fabrication of screen printed electrode (β-hydroxybutyrate biosensor).[16] Also, 1-ferrocenylethanol (Fc-$CHOHCH_3$), a derivative of Fc-$COCH_3$ reduction process, is a reactant for preparation of ferrocene-modified thiopyrimidines, which are used as an anticancer agent.[17]

Two different reducing agents namely, H_2 gas and $NaBH_4$, in two different solvents, *viz.* dry ethanol and [BMIM][BF_4], synthesized in Chapter Three, were employed. Conventional and US irradiation approaches were involved in $NaBH_4$ reduction reactions. Additionally, with $NaBH_4$, the reduction reaction was also carried out under solvent-free conditions.

4.2 Chemicals, solvents and gases

All chemicals, solvents and gases used for the reduction reactions of aldehydes and ketones to their corresponding alcohols as well as the characterization of the obtained alcohols are summarized in Table 4.1.

Table 4.1: Chemicals, solvents and gases used for the production and characterization of alcohols

Chemicals/solvents/gases	Suppliers	Grade/Purity (%)
Absolute ethanol	Fisher Scientific supplies, USA	100
Acetone	Protea Chemicals, SA	AR/100
Acetophenone	Merck, German	≥ 99
Acetylferrocene	Capital Lab Supplies, SA	≥ 95
Anhydrous magnesium sulphate	Thembane chemicals, SA	99
Argon	Afrox, SA	Ultra high purity
Benzaldehyde	Merck, German	> 99
1-Butyl-3-methylimidazolium tetrafluoroborate	Synthesized in our laboratory, SA	--
Deuterated chloform-D1	Merck, German	99.8
Diethyl ether	Sigma–Aldrich, USA	≥ 99.8
Ferrocenecarboxyaldehyde	Sigma–Aldrich, German	98
Hexane	Capital Lab Supplies, SA	99
Hydrogen	Afrox, SA	Ultra high purity
Molecular sieves, type 4 (4Å)	Capital Lab Supplies, SA	--
Palladium on activated charcoal	Sigma–Aldrich, German	10 wt.%
Silica gel 60 (0.063-0.2 mm)	Fluka, New German	100
Sodium borohydride	Merck, German	98
Sodium wires	Merck, German	99.95

4.3 Instrumentation

This section gives details of equipment, instruments and software versions used in the reduction reactions and characterization of products. Brief description on the usage of some particular instruments is also provided.

4.3.1 General instruments

- Ohaus PA214 analytical balance with 0.1 mg precision
- MS-H-Pro^{+} Lab Smart hot plate was used to stir the reaction mixture.
- Aluminium thin-layer chromatography (TLC) silica gel 60 F_{254} plates, (supplied by Merck, German), were used to monitor the product formation.
- Spectroline fluorescence ENF-240 C/FE with 230 volts, 50 Hz, 0.17 amps model ultraviolet lamp was used to detect or visualize the TLC spots of the sample (supplied by Spectronics Corporation, Westbury, New York, USA).
- Whatman^{TM} filter papers were used to filter the reaction mixture.
- Rotary vapour system for solvent distillation.

4.3.2 Specific instruments involved in reduction reactions

4.3.2.1 Ultrasonic water bath

For the US irradiation method, a UD150SH-6L Digital Ultrasonic Cleaner (supplied by Shalom laboratories, SA) was used for the reduction reactions. This reactor had 6 L of maximum volume, 40 KHz of frequency, 150 watts of power, 220/50 Hz of voltage and 327 x 176 x 150 mm as tank dimension. A representative diagram and the current picture of the ultrasonic reactor are shown in Figure 4.1.

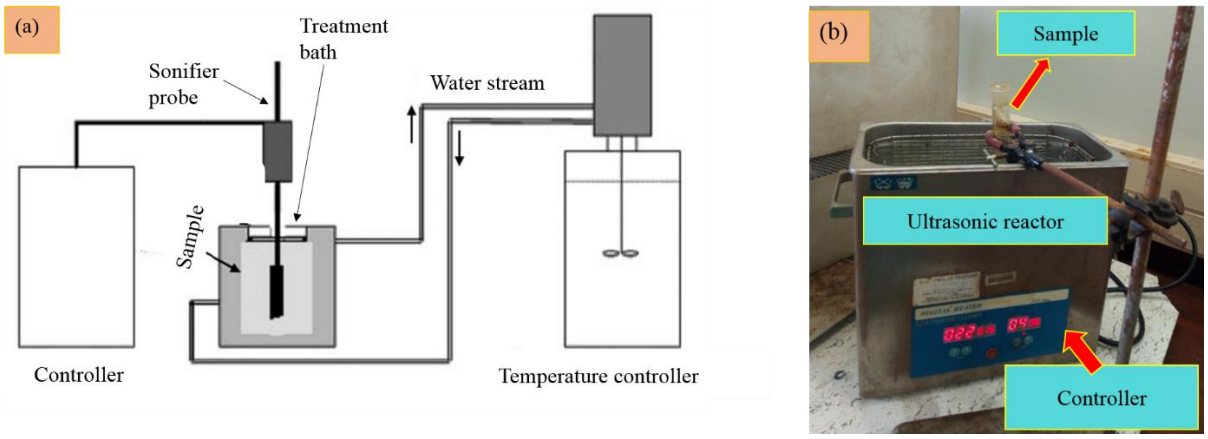


Figure 4.1: (a) Sketch illustrating ultrasonic reactor composition[18] and (b) the photograph of the actual ultrasonic reactor used in the laboratory for the reduction process

4.3.2.2 Parr hydrogenation reactor

Reduction of aldehydes and ketones to their corresponding alcohols using H_2 gas as reducing agent and 10% palladium supported on activated charcoal (10% Pd/C), as catalyst, was carried out in a 4575/76 HP/HT Parr hydrogenation reactor (Figure 4.2).

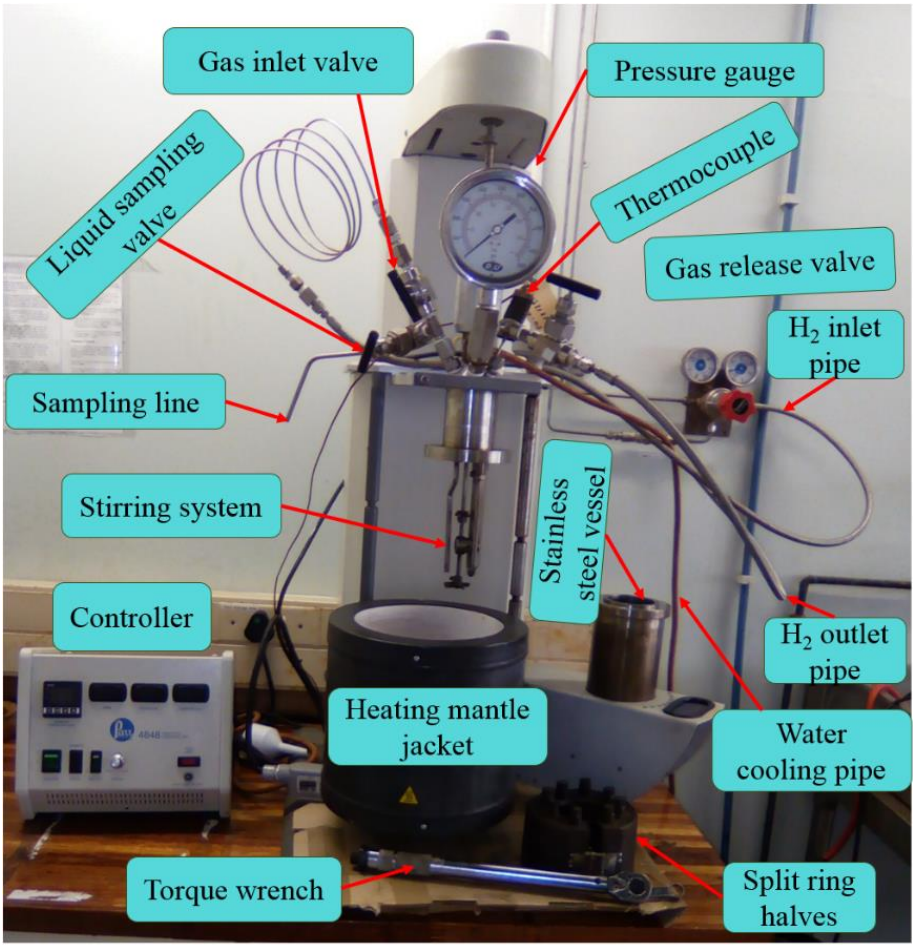


Figure 4.2: Picture of the actual Parr reactor instrument used in the catalytic hydrogenation of aldehydes and ketones

The reactor comprises of a stirring system plunged into type 316 stainless steel vessel which is well sealed and airtight during the reaction. Two valves, namely, gas inlet valve and liquid sampling valve are connected to a dip tube extended to the bottom of the cylinder. H_2 gas is introduced into the reaction mixture system through the gas inlet valve, whereas sampling at different time intervals for reaction monitoring is done through the liquid sampling valve. The gas release valve, located on the gauge adapter, is used to control pressure in the reaction vessel.

The pressure gauge with a T316 stainless steel bourdon tube, connected to the Parr reactor, was used to set the H_2 gas. A type J thermocouple in a 1/8'' diameter stainless steel sheath is inserted into the thermowell and is connected on both the reactor and the controller, to indicate the reaction temperature. The 4848 reactor controller was connected to this reactor and helped in setting temperature, reaction time and stirring speed, as needed.

4.3.3 Characterization instruments

The characterization of alcohols products was done by means of melting points (m.p.) or boiling points (b.p.) and spectroscopic analyses.

The m.p. were determined using a Bibby Stuart scientific model SMP10 apparatus (supplied by Shalom laboratory supplies, Durban, SA). The b.p. were determined by following the micro scale boiling point procedure. FTIR and NMR (^{1}H- and ^{13}C-NMR) characterization were done using same instruments described in Chapter Three.

The catalytic hydrogenation products were characterized and analysed off-line by Shimadzu 2010 gas chromatograph with flame ionization detector (GC-FID) fitted with DB-5 column (length = 30 m , inner diameter = 0.25 mm and thickness = 0.25 μm).

4.4 Experimental procedures

4.4.1 Cleaning of the equipment and drying of solvents

The cleaning of glassware was done as described in Chapter Three, Section 3.6.1. The inner part of Parr reactor vessel and liquid sampling line were washed with warm soapy water followed by rinsing sequentially with warm water and acetone, and thereafter dried in open air at room temperature.

Dry diethyl ether was obtained from Innovative Technology pure solvent unit as described in Chapter Three, Section 3.6.2.4. Ethanol, which was used as solvent, was dried by means of 4 Å molecular sieves, which were activated in the furnace overnight prior to use, and then distilled.[19] Hexane was dried by introducing sodium wire in its container and keeping it airtight for at least three days before use.

4.4.2 Reduction of aldehydes and ketones by use of sodium borohydride under solvent conditions

4.4.2.1 Conventional method

Equimolar amounts of aldehyde or ketone (3.79 mmol) was dissolved in 20 mL of dry ethanol in 100 mL Schlenk tube. $NaBH_4$ (0.227 g, 6 mmol) was added in one portion to the solution and mixture was stirred for 1 hour in the case of aldehyde, and for 24 hours in the case of ketone. This was carried out using a magnetic stirrer, at room temperature until the colour change appeared. Thereafter, the reaction was quenched by adding one to three drops of hydrogen chloride (HCl). Similar procedure was followed in 20 mL of [BMIM][BF_4], except that $NaBH_4$ was added slowly, with stirring, within 30 min at room temperature. Further to this, the product was extracted with dry diethyl ether (20 mL x 4) and the combined extracts were concentrated to give the crude product.

In both solvents, the formation of the product was checked by preparative TLC plates using hexane : diethyl ether (2 : 1) as eluent. The crude product was purified by means of a column chromatography packed with silica gel using the same eluent as for TLC, dried over anhydrous magnesium sulphate ($MgSO_4$) and the solvent was removed under reduced vacuum pressure to yield the pure alcohol.

4.4.2.2 Ultrasound irradiation method

Aldehyde or ketone (3.79 mmol) and $NaBH_4$ (0.227 g, 6 mmol) were dissolved in 20 mL of either ethanol or [BMIM][BF_4] in 100 mL round-bottom flask (RBF) and stirred for 5 min at room temperature. The reaction mixture was then taken to the rectangular open stainless steel reaction tank filled with water up to two-third of its capacity for sonication in 15 min. The formation of the product was checked by preparative TLC plates using hexane : diethyl ether (2 : 1) as eluent. One to three drops of HCl was added to quench the reaction. The extraction and the purification of the crude products were carried out as described in Section 4.4.2.1.

4.4.3 Reduction of aldehydes and ketones by use of sodium borohydride under solvent-free conditions

4.4.3.1 Mechanochemical method

Aldehyde or ketone (3.79 mmol) and $NaBH_4$ were mixed in a Pyrex tube fitted with a ground-glass joint. Two different amounts of $NaBH_4$ were used, *i.e.* 6 mmol (0.227 g) and 18 mmol (0.681 g), respectively. The compounds were ground with glass rod at room temperature for 30 min and one to three drops of HCl was added to quench the reaction. The formation of the product was checked by preparative TLC plates using hexane : diethyl ether (2 : 1) as eluent. For solid compounds such as Fc-CHO and Fc-$COCH_3$, minimal amount of dry ethanol (2 mL) was added to dissolve the respective compounds. The purification of the obtained crude alcohol was done as described in Section 4.4.2.1.

4.4.3.2 Ultrasound irradiation method

A mixture of aldehyde or ketone (3.79 mmol) and $NaBH_4$ (0.227 g, 6 mmol) was sonicated in an ultrasonic water bath for 15 min at room temperature and one to three drops of HCl was added to quench the reaction. The rest of experiment followed the same procedure as in Section 4.4.3.1.

4.4.4 Catalytic hydrogenation of aldehydes and ketones with 10% palladium supported on activated charcoal

A mixture of aldehyde or ketone (3.79 mmol), 10% Pd/C (100 mg) and either dry ethanol or [BMIM][BF_4] (100 mL) was placed into the Parr hydrogenation stainless steel vessel. The vessel and mixture were hermetically sealed. The reaction conditions were set at 6 bar of H_2 gas and 24 hours of stirring at room temperature.

For ethanol solvent, the catalyst was removed from the mixture by two consecutive filtrations *viz.* filtration through Whatman filter papers (diameter of 55 mm), followed by filtration through a simple pure polytetrafluoroethylene (PTFE) 0.45 μm membrane syringe filter. In the case of [BMIM][BF_4], the reaction mixture was extracted from the [BMIM][BF_4]-Pd/C system by use of dry diethyl ether through a decanting funnel (4 x 40 mL). The extract was filtered as described in the case of filtration for ethanol, mentioned at the start of this paragraph, and

concentrated to give the crude alcohol. The product formation was checked and the crude alcohols were purified following the procedure outlined in Section 4.4.2.1.

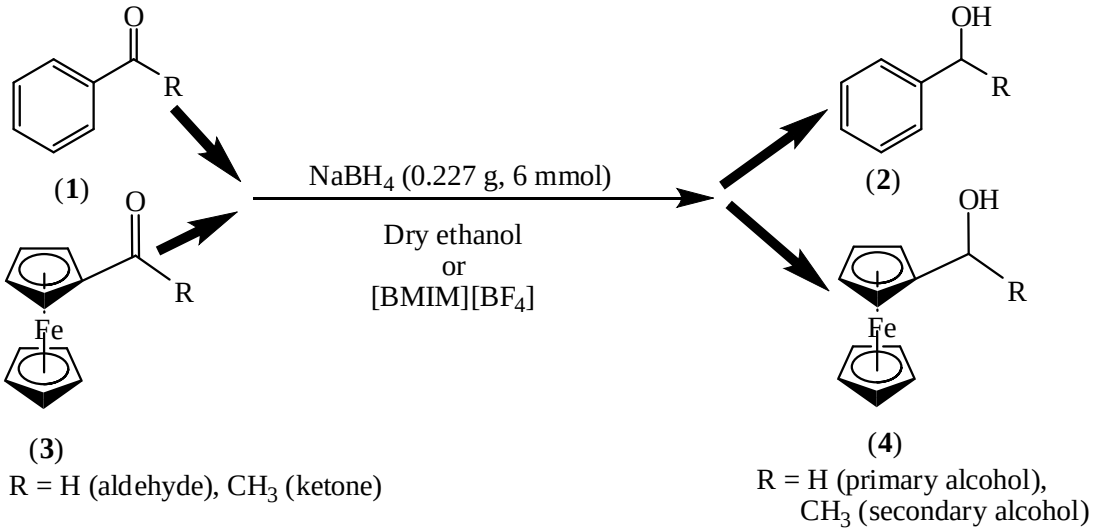
4.4.5 Recyclability of 1-butyl-3-methylimidazolium tetrafluoroborate

Ph-CHO (0.402 g, 3.79 mmol) was reduced to Ph-CH_2OH in [BMIM][BF_4], following the procedure outlined in Section 4.4.2.1. After extraction of the crude Ph-CH_2OH, [BMIM][BF_4] was further washed with dry diethyl ether, dried under reduced pressure at 80 °C for 5 hours and thereafter purged with argon gas. The same experiment was repeated and the recycled [BMIM][BF_4] was reused up to five runs. In each case, spectroscopic characterization (mentioned in Section 4.3.3) of both Ph-CH_2OH and [BMIM][BF_4] was done. A minimal loss of IL was observed after each run but this did not affect the process.

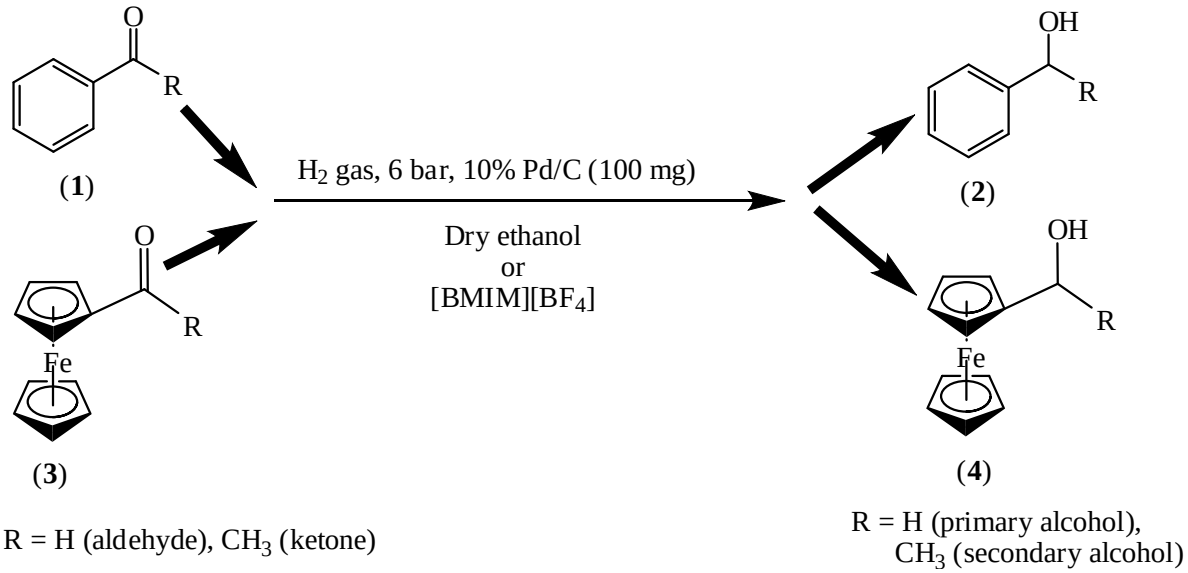
Same compound was reduced with H_2 gas, at 6 bar using 10% Pd/C in [BMIM][BF_4] as described in Section 4.4.4. In this case, after extraction of the crude Ph-CH_2OH, [BMIM][BF_4]-Pd/C system was further washed with dry diethyl ether, dried under reduced pressure at 80 °C for 5 hours and thereafter degassed with argon gas. In addition, this system was stirred for 1 hour at 6 bar of H_2 gas, before being reused for subsequent run. Five runs were performed on the same compound without changing [BMIM][BF_4]-Pd/C system, and in each case the obtained Ph-CH_2OH was characterized as stated above.

4.5 Results and discussion

Aldehydes and ketones were reduced to their corresponding alcohols *via* two different methods namely, $NaBH_4$ reduction (under solvent and under solvent-free) and catalytic hydrogenation. as depicted in Scheme 4.1 and Scheme 4.2, respectively. In the case of in-solvent, the main focus was to investigate the role of solvent in terms of efficiency with respect to each reduction method. Two solvents, *viz.* ethanol, which is a volatile organic solvent, and [BMIM][BF_4], which is an IL, were used. From all the investigated methods, the reduction reaction involved monitoring the reaction by use of IR spectroscopy with the appearance of C-H and O-H bonds upon product formation. Further to this, the disappearance of the C=O moieties on the aldehydes and ketones was an indication of the formation of the product (detailed in Chapter Two, Section 2.3.3). This was also confirmed by use of NMR spectroscopy techniques.



Scheme 4.1: $NaBH_4$ reduction process of phenyl (Ph) and ferrocenyl (Fc) aldehydes and ketones to their corresponding alcohols in 20 mL of solvent



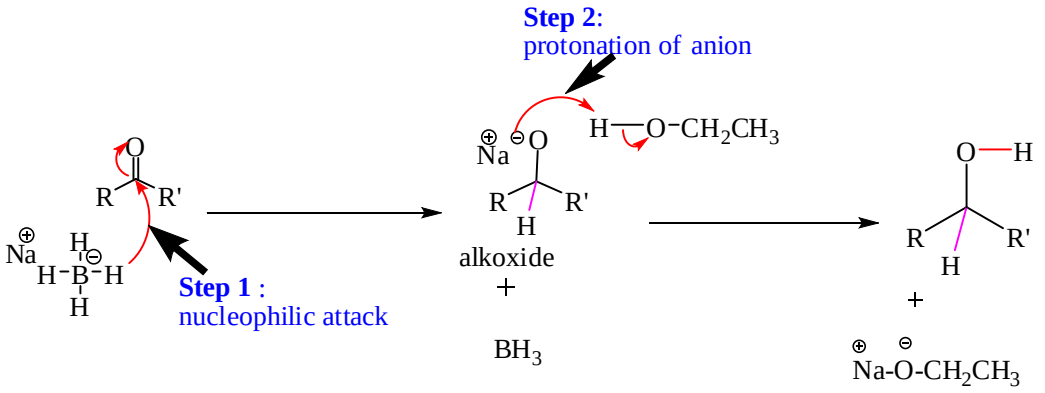
Scheme 4.2: Catalytic hydrogenation process of phenyl (Ph) and ferrocenyl (Fc) aldehydes and ketones to their corresponding alcohols in 100 mL of solvent

4.5.1 Reduction of aldehydes and ketones by use of sodium borohydride under solvent conditions

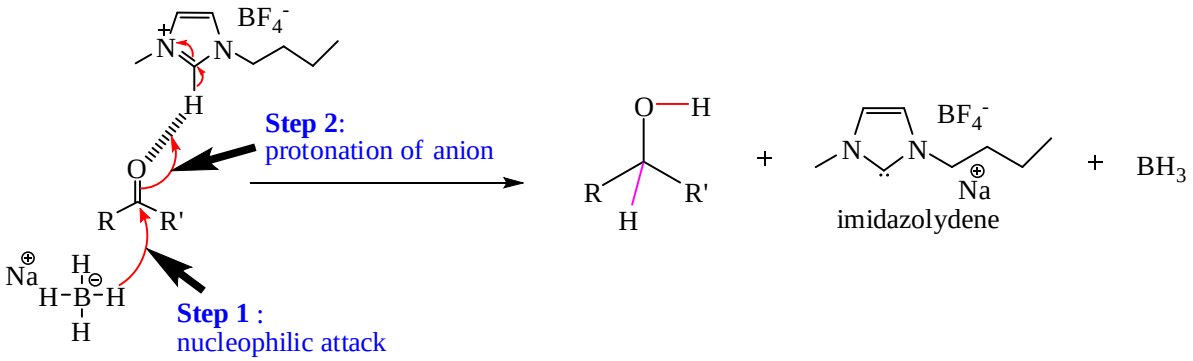
Mixing selected aldehyde or ketone with $NaBH_4$ powder in either dry ethanol or $[BMIM][BF_4]$ yielded corresponding alcohols as shown on Scheme 4.1. In-solvent conditions, the reduction of aldehyde and ketone to their alcohols involved two consecutive steps (Scheme 4.3).

Firstly, the unsaturated carbonyl carbon is protonated by the hydride (H^-) from $NaBH_4$ and an alkoxide is formed. Secondly, the alkoxide is hydrogenated by a proton generated from the solvent. From the second step, it is clear that the presence of protic solvent is a requirement for this reduction process.[20]

(a) Dry ethanol as solvent



(b) [BMIM][BF_4] as solvent



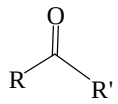
Scheme 4.3: Plausible mechanism of $NaBH_4$ reduction reaction of aldehyde and ketone in (a) dry ethanol and (b) [BMIM][BF_4]

This reduction reaction was carried out at room temperature using two different approaches, namely conventional and ultrasound (US). The mole ratio used for both approaches was 1 : 1.59 (aldehyde or ketone : $NaBH_4$).

Starting with conventional approach, which consists of stirring the mixture using a magnetic stirrer hot plate, the reaction conditions were optimized using different time periods, *i.e.* 1 hour, 8 hours and 24 hours. Given that the alcohols obtained from reduction of Ph-CHO and Ph-$COCH_3$ are well known and can be easily identified, their reduction was used as model reaction. At set interval period, the formation of the product was monitored by TLC plates.

The results for this reduction reaction are presented in Table 4.2 and graphically in Figure 4.3. The yields were isolated based on starting materials, *i.e.* Ph-CHO and Ph-$COCH_3$.

Table 4.2: The reduction reactions of Ph-CHO and Ph-$COCH_3$ with $NaBH_4$ to their corresponding alcohols at room temperature in either ethanol or [BMIM][BF_4] as a solvent

Entry	**Starting material**		**Time (hours)**	**Yield (%)**	
	R	R’		Ethanol	[BMIM][BF_4]
1	Ph	H	1	67	89
2	Ph	H	8	67	89
3	Ph	H	24	67	89
4	Ph	CH_3	1	7	18
5	Ph	CH_3	8	38	59
6	Ph	CH_3	24	52	78

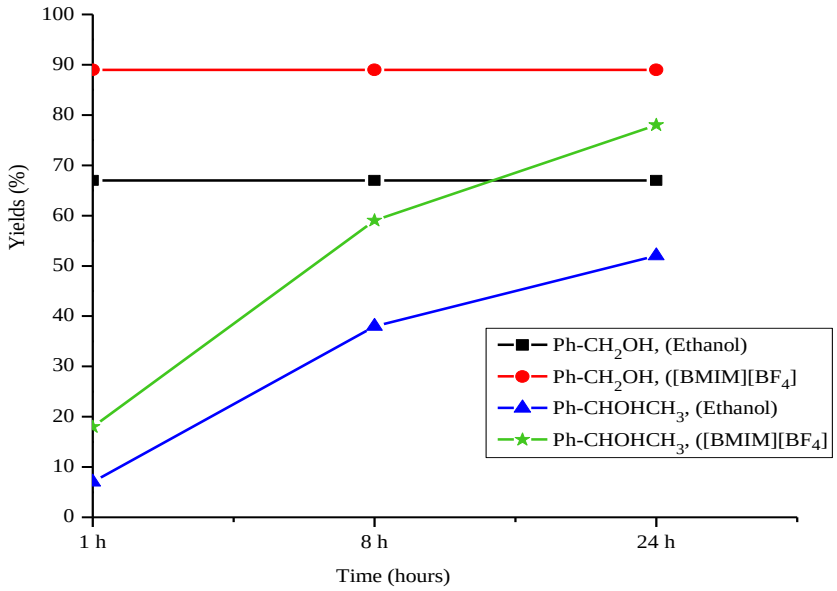


Figure 4.3: The reduction of Ph-CHO and Ph-$COCH_3$ with $NaBH_4$ to their corresponding alcohols at room temperature

A significant structural effect on the reduction of aldehyde and ketone was noted in both solvents. For example, higher isolated yields from Ph-CHO reduction were obtained in 1 hour relative to those from Ph-$COCH_3$ within the same period (entry 1 *vs.* entry 4). Also, the Ph-$COCH_3$ was reduced in high yields only after 24 hours (entry 6).

This showed that aldehydes are more easily reduced than ketones. This could be due to both electronic effect and steric hindrance of the second substituent (R').[20,21] Based on the structure of carbonyl functional group (C=O), the polarization of this C=O bond leads to partial positive charge on carbon atom (as electrophilic) and partial negative charge on oxygen atom. From this notion, it is clear that the nucleophile attack on the carbonyl occurs at that electrophilic carbon. Therefore, in the ketone case, the alkyl substituent attached to this C=O reduces the electrophilicity of the carbonyl carbon by pushing their electrons towards that carbon (electronic factor). For aldehyde, hydrogen atom attached to the carbonyl carbon does not show any effect on the electrophilic carbon.

Additionally, the two alkyl substituents found in ketones create more steric resistance towards nucleophilic attack at the electrophilic carbon than the single substituent shown by aldehydes (steric factor). The same reaction conditions were applied to Fc-CHO and Fc-$COCH_3$ reduction.

Also, in this research, the ultrasound (US) irradiation approach was applied. This involved sonicating the mixture for 15 min at room temperature using a 40 kHz ultrasonic water bath reactor. The same mole ratio and solvents were used as in conventional method described above (see Section 4.4.2.2). The obtained results are compared to those from conventional method, summarized and presented in Table 4.3 and Figure 4.4.

It is worth noting that the formed by-products, namely sodium ethanoate and imidazolydene from the reduction done in ethanol and [BMIM][BF_4], respectively, were removed by silica gel column chromatography during purification of the obtained crude alcohols.

Table 4.3: Comparison of ultrasound and conventional methods for the reduction of aldehydes and ketones to their corresponding alcohols in either ethanol or [BMIM][BF_4] at room temperature

Entry	Alcohols	Ultrasonic irradiation[a]			Conventional method[b]		
		Time (hours)	Yield* (%)		Time (hours)	Yield* (%)	
			Ethanol	[BMIM][BF_4]		Ethanol	[BMIM][BF_4]
1	Ph-CH_2OH	0.25	74	96	1	67	89
2	Ph-$CHOHCH_3$	0.25	60	82	24	52	78
3	Fc-CH_2OH	0.25	61	85	1	56	70
4	Fc-$CHOHCH_3$	0.25	40	73	24	33	50

*: Isolated yields were based on starting materials
[a]: Ultrasonic method (sonicating the reaction mixture for 0.25 hour at room temperature)
[b]: Conventional method (stirring the reaction mixture with a stirring plate using a magnetic stirrer bar at room temperature)

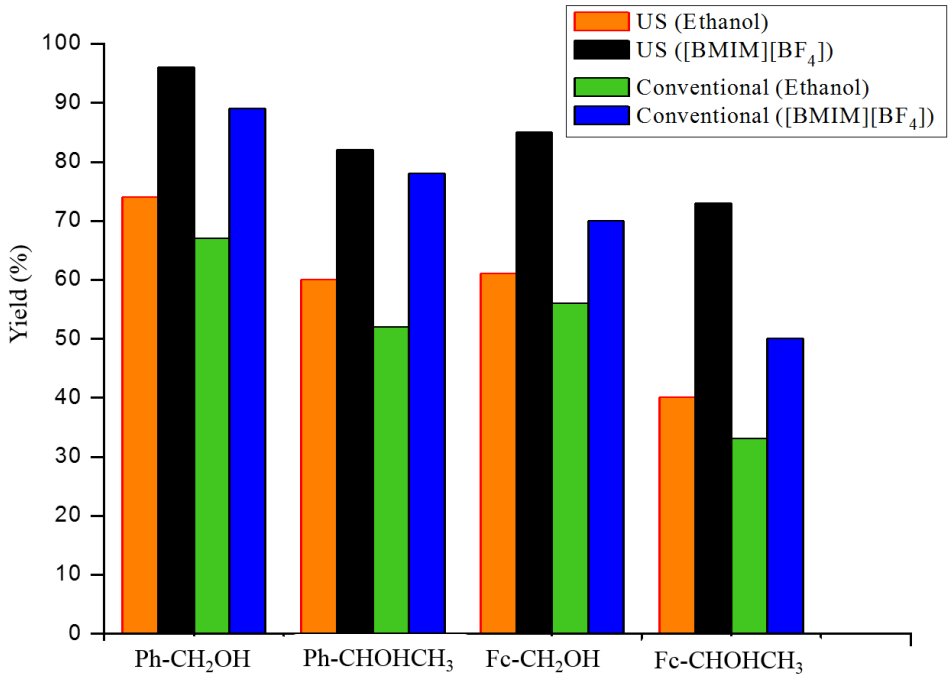


Figure 4.4: Isolated yields from $NaBH_4$ reduction of aldehydes and ketones in-solvent conditions (either in ethanol or [BMIM][BF_4]) at room temperature

Table 4.3 showed that alcohols from US method were obtained within a short reaction time and were relatively in good to excellent yields as reported in the literature.[22-24] For the sake of comparison, US irradiation method is simpler, greener, more efficient, faster and energy-saver than conventional method.

From those two approaches, *i.e.* ethanol or [BMIM][BF_4]as a solvent, alcohol formation showed a strong dependence on the solvent in which the reaction took place. Based on Scheme 4.3, both solvents on step two of the reaction (protonation of alkoxide) have to donate their proton to the formed alkoxide anion in order to produce an alcohol. Considering Figure 4.4, the relatively higher yields of Ph-CH_2OH were obtained from [BMIM][BF_4], *i.e.* 96% and 89% for US irradiation and conventional methods, respectively, in comparison with 74% and 67% from ethanol. This could be explained by the polarity effect of those two solvents in terms of proton generation ability. Based on [BMIM][BF_4] structure, hydrogen atom attached at carbon on position two, (C2)-H, showed poor-electron density induced by electronegativity dipole of the two nitrogen atoms which pull this carbon electrons to themselves.[25] Therefore, this implies the high acidity to this IL hydrogen atom (pH = 4.27)[26] compared to hydrogen atom (pH = 7.33)[27] released by hydroxyl part of ethanol. Consequently, [BMIM][BF_4] behaves as a faster proton donor than ethanol. Under the same reaction conditions, in the presence of a nucleophile, [BMIM][BF_4] is more reactive than ethanol. Therefore, the quickest reduction is attained in [BMIM][BF_4], which is in agreement with the literature.[28] The isolated yields, from $NaBH_4$ reduction of aldehydes and ketones to their alcohols in [BMIM][BF_4] were higher compared to those isolated from [BMIM][PF_6] reported by Howarth *et al*.[29]

4.5.2 Reduction of aldehydes and ketones by use of sodium borohydride under solvent-free conditions

The same aldehydes and ketones (3.79 mmol) reduced in Section 4.5.1 were reduced with $NaBH_4$ in the absence of solvent. Two reduction approaches, *viz.* mechanochemical and ultrasonic irradiation, were employed. In mechanochemical approach, aldehyde or ketone and $NaBH_4$ were ground together for 30 min whereas in the US irradiation approach, the same reaction mixture was sonicated for 15 min, all at room temperature. Initially, for both approaches, the used mole ratio was 1 : 1.59 (aldehyde or ketone : $NaBH_4$).

However, for mechanochemical approach, due to low reactivity, $NaBH_4$ was increased from 6 mmol to 18 mmol and the new mole ratios became 1 : 1.59 and 1 : 4.75.

Dry ethanol (2 mL) was added to the solid Fc-CHO and Fc-$COCH_3$, to dissolve them. The obtained results are shown on Figure 4.5.

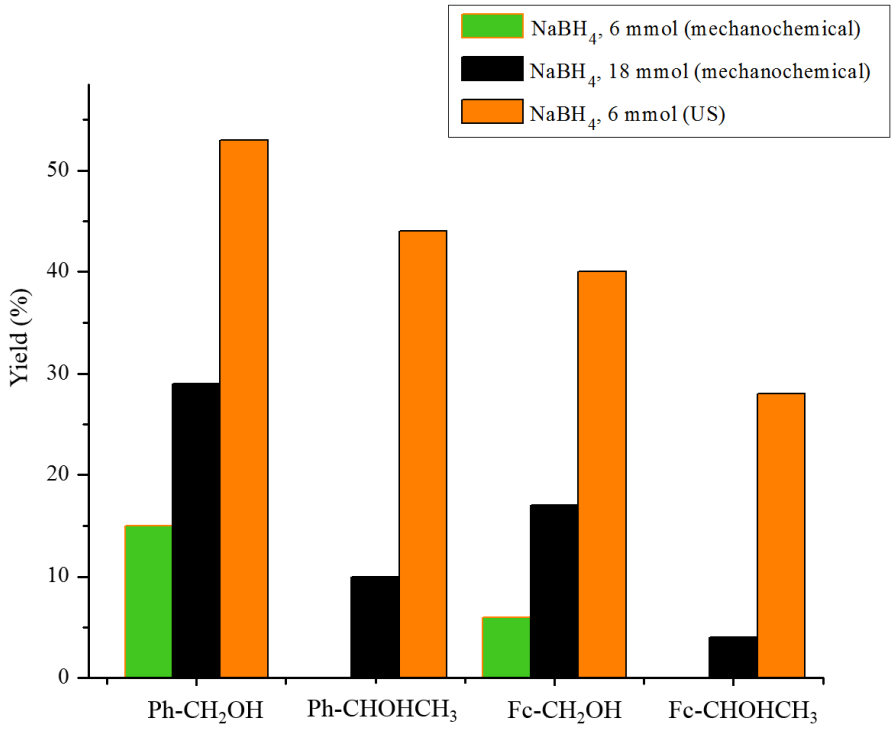


Figure 4.5: Isolated yields from $NaBH_4$ reduction of aldehydes and ketones under solvent-free conditions at room temperature

Figure 4.5 showed that by using the mole ratio of 1 : 1.59 under mechanochemical grinding, lower yields of Ph-CH_2OH and Fc-CH_2OH (15% and 6%, respectively) were formed. Under the same conditions, Ph-$CHOHCH_3$ and Fc-$CHOHCH_3$ were not formed at all. This was confirmed by TLC analysis, where upon reaction the TLC spots showed the similar retention factor with only one single spot as the substrates (ketones).

However, increasing the quantity of $NaBH_4$ to 18 mmol (mole ratio of 1 : 4.75) led to the reduction of ketones, where slightly lower yields of 10% and 4% for Ph-$CHOHCH_3$ and Fc-$CHOHCH_3$, respectively, were obtained. The TLC analysis showed two spots as an indication that the product was formed but needed to be separated from the unreacted starting material. The purification was done by silica gel chromatography using hexane : diethyl ether (2 : 1) as eluent. In addition, the yields of Ph-CH_2OH and Fc-CH_2OH were improved to 29% and 17%,

respectively. The observed reducing agent effect emphasized that aldehydes are easily and quickly reduced than ketones as mentioned previously.[20,21]

The application of US irradiation method to this reduction reactions using the mole ratio of 1 : 1.59 improved both product yields and reaction times. The obtained yields were 53%, 44%, 40% and 28% for Ph-CH_2OH, Ph-$CHOHCH_3$, Fc-CH_2OH and Fc-$CHOHCH_3$, respectively, within 15 min. The mechanism associated with US that accelerates the chemical reaction (Section 4.5.1) was also applicable herein.[10] However, the obtained results were relatively lower compared to the ones reported by Firdaus *et al*.[30] As typical example, for the reduction of Ph-CHO, Firdaus reported 96% of Ph-CH_2OH obtained by using 1 : 2 as mole ratio within 15 min. The increase in yields was attributed to the large amount of $NaBH_4$ involved. The same trend was also observed previously in the current study for mechanochemical approach.

On the other hand, with intention of emphasizing on the role of solvent in a typical chemical reaction, three different yields of Ph-CH_2OH, obtained with a mole ratio of 1 : 1.59 and by sonication for 15 min, were compared. These yields were 96%, 74% and 53%, obtained from [BMIM][BF_4], dry ethanol (in-solvent process) and solvent-free reduction process, respectively. It was shown that the higher isolated yields, *i.e.* 96% and 74%, respectively, (Table 4.3, entry1) were identified from the reduction done in presence of solvent while the lower yield, 53% (Figure 4.3), was observed from the reduction under solvent-free conditions. The solvent acts as conveyor and hence favours the collisions of reactants by offering enough contact surface to them and altering their interactions towards the formation of the desired products.[31]

4.5.3 Catalytic hydrogenation of aldehydes and ketones with 10% palladium supported on activated charcoal

Reduction reactions were also done in the presence of 10% Pd/C as catalyst using H_2 gas as the reducing agent. The plausible reaction mechanism for this reaction was given in Chapter Two, Section 2.3.3.3, Scheme 2.7.

To optimize the reaction conditions, hydrogenation of Ph-CHO (3.79 mmol) was taken as model reaction. The same amount of solvents (100 mL), *viz.* dry ethanol or [BMIM][BF_4] were used. The reaction was carried out at room temperature for 24 hours and H_2 gas was at 6 bar. Sampling was done by collecting 1 mL aliquots after every 2 hours and analysing using a GC-FID. The retention time of the peaks were compared to those of commercial Ph-CH_2OH.

Samples from dried ethanol were analysed directly whereas those from [BMIM]BF_4 were extracted first with diethyl ether in the volume ratio [BMIM]BF_4 : diethyl ether of 1 : 5. This was repeated four times and the combined extract were then analysed. The obtained results for Ph-CHO conversion and selectivity towards Ph-CH_2OH formation are graphically shown in Figure 4.6.

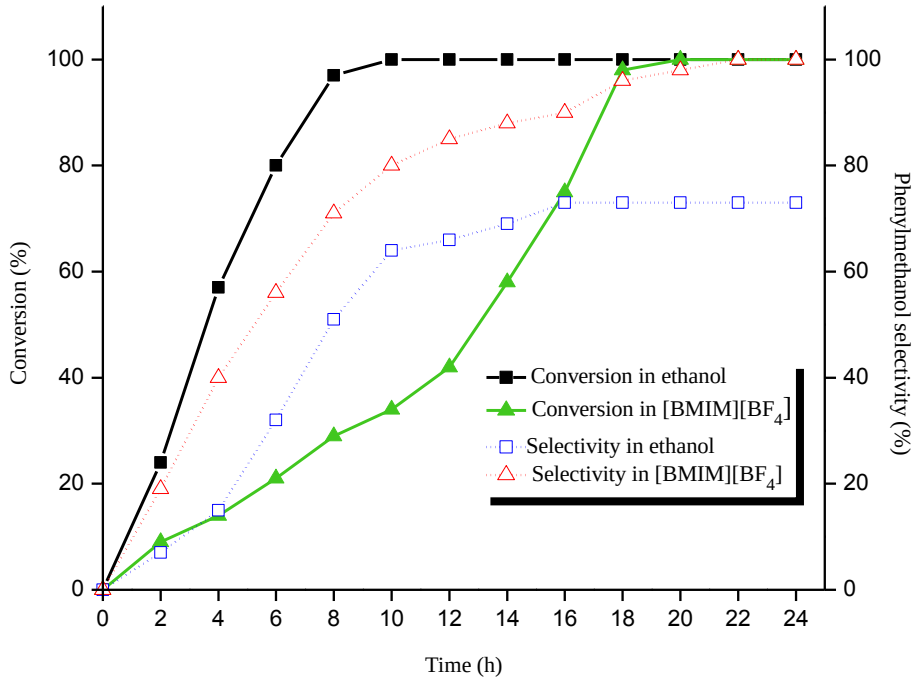


Figure 4.6: Ph-CHO conversion (solid line and closed symbols) and selectivity to Ph-CH_2OH (dot line and open symbols) in dry ethanol (squares) and in [BMIM][BF_4] (triangles) determined from GC-FID analysis

The conversion of Ph-CHO to products and the selectivity towards Ph-CH_2OH were defined by equation 4.1 and 4.2, respectively.

$$\text{Conversion} = \frac{n\,(t=0) - n\,(t)}{n\,(t=0)} \times 100 \qquad (4.1)$$

$$\text{Selectivity} = \frac{n}{\Sigma \text{ products formed}} \times 100 \qquad (4.2)$$

Where n (t = 0): The initial concentration of Ph-CHO as starting material, measured in $mg.L^{-1}$.

n (t): The sum of concentration of unreacted Ph-CHO, formed Ph-CH_2OH and other products at different time intervals from GC-FID analysis, in $mg.L^{-1}$.

n: Converted Ph-CH_2OH.

The catalytic performance of 10% Pd/C catalyst was correlated with the solvent nature. The conversion of Ph-CHO was slower in [BMIM][BF_4] than in ethanol (Figure 4.6**)** as agreed with Anderson *et al*.[32] As typical example, 100% conversion was attained within 10 hours in ethanol against 20 hours in [BMIM][BF_4] under the same reaction conditions. The lower conversion in [BMIM][BF_4] was due to the higher viscosity of the solvent (1.120 cP, measured in Chapter Three) compared to that of ethanol (1.074 cP at 25 °C).[33] The elevated viscosity could favour the slow molecular diffusion and solubility of H_2 gas in [BMIM][BF_4], which resulted in the decrease of reaction rate.[34-37] Consequently, the mass transfer of Ph-CHO to 10% Pd/C surface for hydrogenation was slow in [BMIM][BF_4].

However, in terms of selectivity towards the formation of Ph-CH_2OH, [BMIM][BF_4] was more selective than ethanol as shown by the 80% and 64%, respectively, after 10 hours of reaction. The selectivity was influenced by interactions of catalyst and [BMIM][BF_4]. This later was easily deprotonated and then coordinated to the metal centre. Therefore, Ph-CHO was quickly reduced. The weak pairing of cation-anion interactions in [BMIM][BF_4] also lead to the formation of large cavities within it capable of accommodating the substrate molecules. The modification of enthalpy and entropy of the reactants by this differential solvation leads to the activation of their transition-states and, hence, the reaction is driven towards higher selective yields.[32] Hence, one would suggest that [BMIM][BF_4] was acting as a promoter.[37] Similar high selectivity of ILs was also reported for hydrogenation of nitroarenes in [BMIM][BF_4].[38]

The same reaction conditions were applied to the reduction of other aldehydes and ketones (3.79 mmol), *i.e.* Fc-CHO, Ph-$COCH_3$ and Fc-$COCH_3$, respectively, and the results are compiled in Table 4.4.

Table 4.4: Catalytic hydrogenation of aldehydes and ketones to their corresponding alcohols with 10% Pd/C for 24 hours

Entry	Substrate	Product (Alcohols)	Yields (%)	
			Ethanol	[BMIM][BF_4]
1	Ph-CHO	Ph-CH_2OH	78	83
2	Ph-$COCH_3$	Ph-$CHOHCH_3$	55	74
3	Fc-CHO	Fc-CH_2OH	59	62
4	Fc-$COCH_3$	Fc-$CHOHCH_3$	28	47

The 10% Pd/C catalyst showed a lower tendency towards hydrogenation of the aromatic ring[39] under these reaction conditions. The reported product yields were isolated based on the starting material rather than being calculated from GC-FID analysis owing to the unavailability of their commercial standards.

4.5.4 Characterization of produced alcohols

The obtained alcohols were characterized by means of FTIR and ^{1}H-NMR spectroscopies, m.p. and b.p. determination, respectively. Furthermore, the colour change from starting materials to products was used to confirm formation of the product. The m.p. and b.p. of the produced alcohols were in close agreement with the literature data[33] and this indicates the high purity of these synthesized alcohols (Table 4.5).

Table 4.5: Physical appearance, melting and boiling points of the produced alcohols

Starting materials		**Produced alcohols**			
Formula	Colour	Formula	Colour	m.p./b.p. (°C)	
				Exp.	*Lit.*[33]
Ph-CHO	colourless	Ph-CH_2OH	slightly yellow	205-207[l]	203-205[l]
Ph-$COCH_3$	colourless	Ph-$CHOHCH_3$	slightly yellow	202-204[l]	204[l]
Fc-CHO	red	Fc-CH_2OH	golden yellow	79-81[s]	79-81[s]
Fc-$COCH_3$	orange	Fc-$CHOHCH_3$	orange-yellow	75-78[s]	76-79[s]

[l]: Liquid, [s]: Solid
Exp.: Experimental, *Lit.*: Literature

From FTIR analysis, different functional groups were identified in comparison to the starting material. The disappearance of a strong sharp carbonyl absorption band (*ca.* 1689 $cm^{-1}$and 1653 cm^{-1} for Ph-CHO and Fc-CHO, respectively) and the appearance of a broad hydroxyl absorption band (*ca.* 3321 cm^{-1} and 3226 cm^{-1} for Ph-CH_2OH and Fc-CH_2OH) confirmed the formation of the product as shown in Figure 4.7. The stacked image combining all the FTIR spectra of Ph-CHO, Fc-CHO, and their produced alcohols is given and the peak assignments data are summarized in Table 4.6. FTIR spectra of Ph-$COCH_3$, Fc-$COCH_3$, and their corresponding alcohols is shown in appendix, Figure A3 for supplementary information.

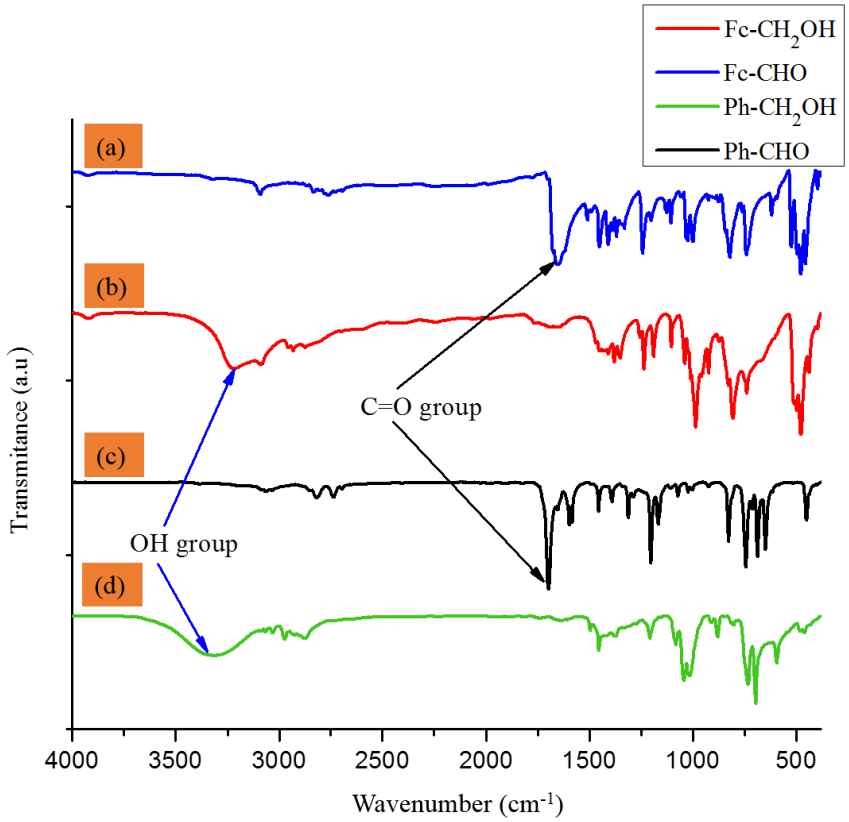


Figure 4.7: FTIR spectra for (a) Fc-CHO (blue), (b) Fc-CH_2OH (red), (c) Ph-CHO (black) and (d) Ph-CH_2OH (green)

Table 4.6: Main FTIR absorption bands observed in Ph-CHO, Ph-CH_2OH, Fc-CHO, and Fc-CH_2OH

Peak wavenumber (cm^{-1})	**Assignment**	**Functional group**
3321,3226	O-H, stretching	Alcohol
3064, 3078, 3086	=C-H, stretching	Aromatic ring
2873, 2799, 2917, 2762	-C-H, stretching	Aliphatic chain
1689, 1653	C=O, stretching	Carbonyl group
1454, 1447, 1417	-C=C, stretching	Aromatic ring
12121, 1197, 1242, 1234	-C-O, -C-C, stretching	Aliphatic chain

From the ^{1}H-NMR analysis, the formation of the alcohols was exhibited by the disappearance of carbonyl proton resonance peak at *ca.*10 ppm (for Ph-CHO and Fc-CHO, Figure B5 in appendix) and the appearance of two new resonance peaks. These new peaks are standing for proton attached to the carbonyl carbon after being attacked by a reducing agent in the region of 4.65-4.26 ppm and proton found on the hydroxyl group in the region of 4.27-1.52 ppm as shown on Figure 4.8.

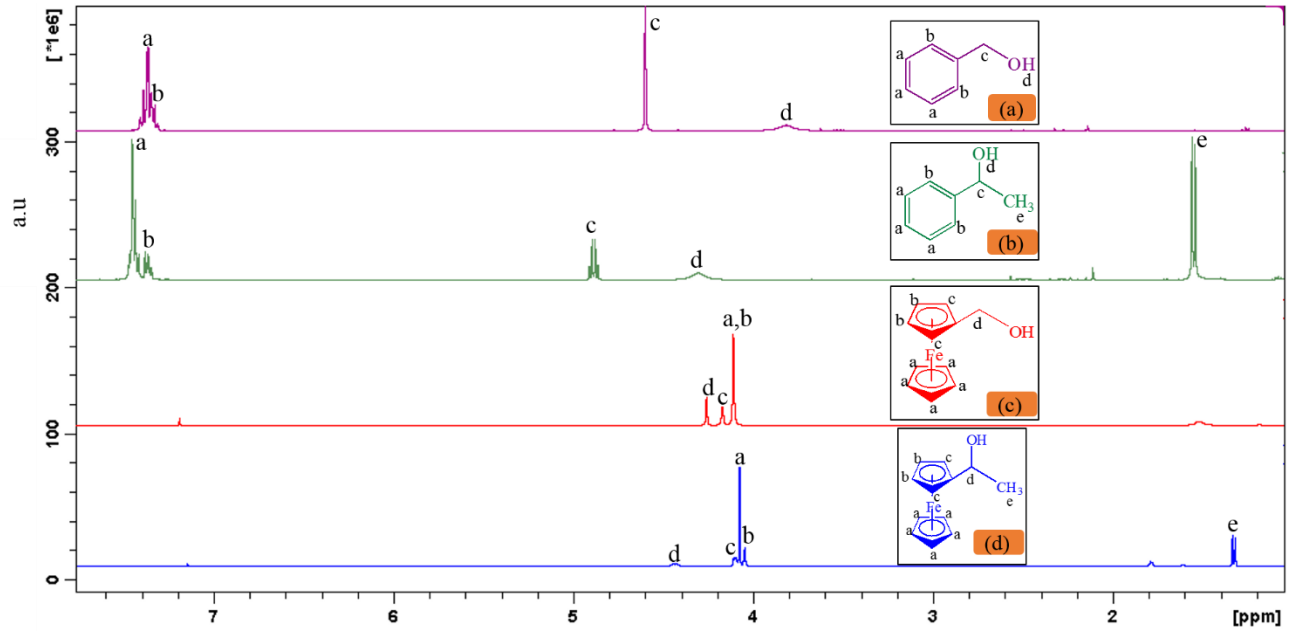


Figure 4.8: ^{1}H-NMR spectra for (a) Ph-CH_2OH (purple), (b) Ph-$CHOHCH_3$ (green), (c) Fc-CH_2OH (red) and (d) Fc-$CHOHCH_3$ (blue), using $CDCl_3$ as NMR solvent

Phenyl (Ph) ring protons were presented by a set of two resonance peaks labelled as 'a and b', integrating to three and two protons, respectively. Ph-CH_2OH peaks were at 7.39 ppm, as multiplet peak, and at 7.33 ppm, as doublet peak. Similarly, Ph-$CHOHCH_3$ peaks were at 7.42 ppm, as multiplet peak, and at 7.34 ppm, as doublet peak. The peaks observed at 4.56 ppm and 4.80 ppm integrated to two protons as singlet peak and to one proton as quartet peak for Ph-CH_2OH and Ph-$CHOHCH_3$, respectively, were assigned to proton added to the carbonyl carbon from reducing agent. This showed that C-H bond was formed. The one singlet peak attributed to one proton from OH group was shown at 3.78 ppm and 4.25 ppm for Ph-CH_2OH and Ph-$CHOHCH_3$, respectively. This was a good evidence for alcohol formation. The doublet peak at 1.51 ppm integrating to three protons was attributed to methyl group in Ph-$CHOHCH_3$.

The ^{13}C NMR spectra of Ph-CH_2OH and Ph-$CHOHCH_3$ were also provided, respectively. ^{13}C NMR ($CDCl_3$, ppm) δ_C = 141.08, 128.50, 127.47, 127.08, 64.72, (Figure B6, in appendix) and ^{13}C-NMR (($CDCl_3$, ppm) δ_C = 146.30, 128.44, 127.26, 125.66, 69.97, 25.35 (Figure B7, in appendix).

Similar trends were observed at the ferrocenyl-based alcohols. The ferrocenyl (Fc) ring shows three set of resonance peaks labelled as '*b, a* and *c'* integrating to two, five and two protons respectively. Fc-CH_2OH peaks were at 4.11 and 4.17 ppm while Fc-$CHOHCH_3$ were at 4.14, 4.11 and 4.09 ppm. In addition, the peaks at 4.26 ppm and 4.47 ppm integrating to two protons as singlet peak for Fc-CH_2OH and to one proton as quartet peak for Fc-$CHOHCH_3$, respectively was due to proton attached to the carbonyl carbon after attack of nucleophile on that carbon. The doublet peak at 1.37 ppm integrating to three protons was attributed to methyl group in Fc-$CHOHCH_3$.

The ^{13}C NMR spectra of Fc-CH_2OH and Fc-$CHOHCH_3$ are also given hereafter, respectively. ^{13}C-NMR ($CDCl_3$, ppm) δ_C = 88.58, 68.56, 68.37, 67.94, 60.76 (Figure B8, in appendix) and ^{13}C-NMR ($CDCl_3$, ppm) δ_C = 94.78, 68.29, 67.87, 66.10, 65.59, 23.71 (Figure B9, in appendix).

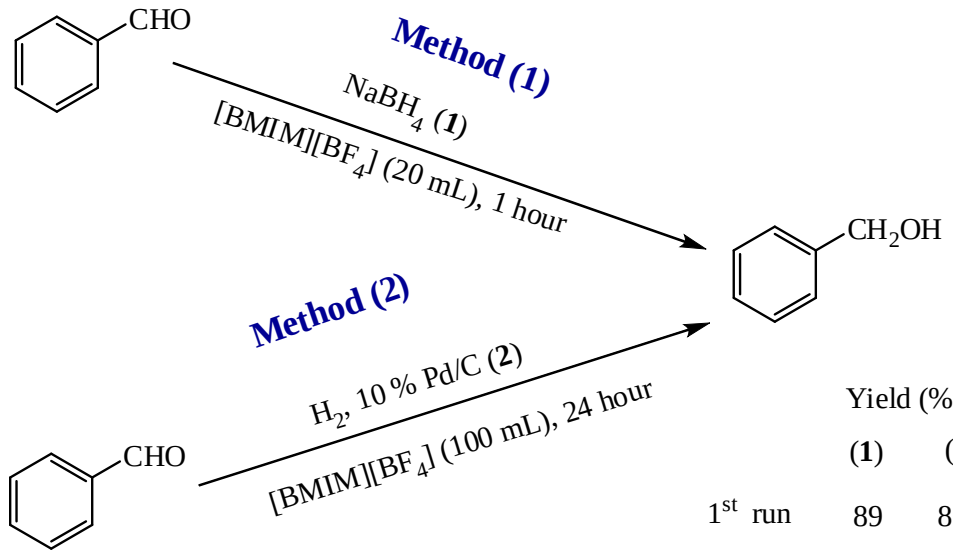
From all these observations, it is clear that protons from Ph-based alcohols resonate slightly in downfield region compared to their analogous in Fc-based alcohols. As a typical example, the same protons labelled '*b*' in Ph-$CHOHCH_3$ at 4.80 ppm and the one labelled '*d*' in Fc-$CHOHCH_3$ at 4.47 ppm were compared. Due to the electron-withdrawing character of Ph ring,[40] the electrons of the rest of the molecule ($CHOHCH_3$) are inductively pulled towards Ph ring. Thus, the remaining protons are deshielded and resonate at high frequencies. Conversely, Fc ring, acting as electron rich group[41] due to the pronounced electropositivity of iron (Fe), donates its electrons to the rest of the molecule. This creates a strong shielding to the remaining protons and hence they shift upfield in lower frequency region. The similar observation was noted from the ^{13}C-NMR analysis. For instance, the substituted carbon on the ring resonates at 146.30 ppm and 94.78 ppm for Ph-$CHOHCH_3$ and Fc-$CHOHCH_3$, respectively. This supports the FTIR analysis results (Figure A5 in appendix) where for OH functional group, Ph-$CHOHCH_3$ vibrates at higher frequency (3318 cm^{-1}) than Fc-$CHOHCH_3$ (3202 cm^{-1}).

4.5.5 Recyclability of 1-butyl-3-methylimidazolium tetrafluoroborate

The recovery and the reusability of ILs provide at first glance their environmental and economic benefits compared to conventional volatile organic solvents.[42,43] In this section, the recyclability and the reusability of [BMIM][BF_4], as solvent, was investigated through the reduction of Ph-CHO at room temperature. Two reducing agents, namely $NaBH_4$ and H_2 gas in presence of 10% Pd/C, were involved in this reduction reaction.

The formed Ph-CH_2OH was extracted with dry diethyl ether. The recycled [BMIM][BF_4] or [BMIM][BF_4]-Pd/C system was washed with dry diethyl ether. The recovery efficiency of [BMIM][BF_4] was assessed based on the isolated yields of Ph-CH_2OH from five repeated consecutive runs. These yields were calculated based on Ph-CHO, as the limiting agent.

The intactness and the contamination of the recycled [BMIM][BF_4] was analysed using FTIR and ^{1}H-NMR spectroscopy at the end of each run. The obtained results are given in Scheme 4.4. Nevertheless they are showing slight small effects on the isolated yields, but they are quite promising.



	Yield (%)	
	(**1**)	(**2**)
1st run	89	83
2nd run	87	83
3rd run	87	80
4th run	86	73
5th run	80	65

Scheme 4.4: Recovery and reusability of [BMIM][BF_4] for the reduction of Ph-CHO using $NaBH_4$ (**1**) or H_2, 10% Pd/C (**2**) as the reducing agent

For $NaBH_4$ reduction, the isolated Ph-CH_2OH yields remained high up to the fourth run. The slight drop in yield observed at the fifth run was attributed to the presence of reagent residuals in [BMIM][BF_4] which reduced this IL activity.

This was confirmed by the appearance of unusual peaks at 3626 cm^{-1} from FTIR analysis (appendix, Figure A4) and two peaks, at 2.18 ppm and 1.63 ppm, from ^{1}H-NMR analysis (appendix, Figure B10) when compared to the [BMIM][BF_4] spectra (FTIR and ^{1}H-NMR) for the four previous runs. This could refer that the activity of [BMIM][BF_4] was decreased by the presence of the contaminants[44] whereby water from moisture accumulation, during sample preparation and reaction set-up, was suspected to be the main one, despite an extensive drying of this IL. Here, the hygroscopicity of the ILs, in general, is noticed. The above observed peaks were associated to the presence of OH group showing the presence of water within [BMIM][BF_4]. The presence of water was also confirmed by the decrease in viscosity from 1.120 cP up to 1.094 cP, showing the distortion of [BMIM][BF_4] ordered structure and the strong hydrogen bonding of water molecules to $[BF_4]^-$ anion.[45]

On the other hand, where H_2 gas over 10% Pd/C was used, the isolated yield of Ph-CH_2OH started declining on the fourth run. As done at the end of each run, FTIR and ^{1}H-NMR analysis of [BMIM][BF_4] showed that it remained uncontaminated. Therefore, the noticed drop in yields was attributed to the decrease in catalyst activity.[38]

The transferal inaccuracies of [BMIM][BF_4] from the reaction flask/vessel contributed to some loss in yield, but was minimized as much as possible. It is important to note that, this loss did not affect the activity of this IL.

4.6 Conclusion

FTIR and NMR (^{1}H- and ^{13}C-) analyses of the produced alcohols by different methods confirmed that aldehydes and ketones were reduced successfully and the products obtained were in good isolated yields.

Under the same reaction conditions, Ph-based aldehydes or ketones were found to be fairly more favourable in reduction relatively to their corresponding Fc-based aldehydes or ketones. This trend correlated with the inductive electronic effect of Ph and Fc ring at the electrophilic site of the carbonyl carbon.

The electron-withdrawing ability of Ph increased the electrophilicity of that carbonyl carbon by reducing its electronic density, whereas Fc-ring, as an electron-donating group enriched that electrophilic carbon by pumping their electrons to the carbonyl carbon centre. Also, the bulky Fc-ring would have caused unfavourable steric effects.

It is also important to note that the reduction by $NaBH_4$ in-solvent provided better product yields than the one done under solvent-free conditions. This highlights the crucial role of the solvent in this particular reactions. On the other hand, under the defined reaction conditions, US irradiations method promoted the $NaBH_4$ reduction of aldehydes and ketones, with impressive product yields and short reaction times. US irradiation method showed itself as simple, fast, selective comparable to both conventional and mechanochemical methods.

Also, the hydrogenation of aldehydes and ketones in presence of 10% Pd/C as a catalyst was also done successfully, whereby ethanol showed more conversion attributes of the starting materials than [BMIM][BF_4] in terms of reaction time. However, [BMIM][BF_4] showed higher selectivity towards the formation of the desired product.

Although $NaBH_4$ reduction method generates some by-products such as sodium ethanoate and imidazolydene, from the use of ethanol and [BMIM][BF_4] as solvent, respectively, at the end of reaction, compared to catalytic hydrogenation, its chemoselectivity towards the reduction of aldehydes and ketones to their corresponding alcohols together with the short reaction time makes it a suitable and more efficient approach.

In terms of solvent efficiency, [BMIM][BF_4] was found to be more attractive solvent compared to ethanol since higher yields of alcohols, as the desired product, was obtained. This was due to favourable solvent hydrogen-bond donating ability (proticity) of [BMIM][BF_4] towards both $NaBH_4$ and catalytic hydrogenation reduction reactions.

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Chapter Five

Dissertation summary, conclusions and future work

This chapter compiles the summary of the previous covered chapters and the overall conclusion of the project. The suggestions for ongoing development of this work are also provided herein.

5.1 Dissertation summary

Chapter One highlights the importance of producing alcohols by reduction of aldehydes and ketones using ionic liquids (ILs) as the green solvents. This has been shown through a brief background highlighting the applications of alcohols and different synthetic routes for the reduction of aldehydes and ketones. It was noted that the common solvent used in this process involves the use of volatile organic solvents (VOS). However, the major challenges, associated with the use of VOS, with respect to human health, environment and particularly those related to synthesis of alcohols were discussed. The choice of ILs both as a sustainable response and promising alternative to VOS was justified. Additionally, within this chapter, the research aim, objectives and hypothesis linked to the practical approach of this work were stated. Also, the thesis outline was provided at the end of this chapter.

Chapter Two gives the literature review of different aspects explored in this study as detailed hereafter. The contributions of green chemistry towards efficient management of resources and waste, ecological, health and safety issues from users and the re-use of chemical products were explained in detail in this chapter. ILs, known as green solvents owing to their less volatility and their easier recyclability, are described in details within this chapter. Their history, structure, classification, synthesis, purification, physicochemical properties, application and recovery methods were discussed herein. This chapter further explained different methods involved in the reduction of aldehydes and ketones to their corresponding alcohols. This was done firstly by identifying and describing the reducing agents, *i.e.* sodium borohydride ($NaBH_4$) and hydrogen (H_2) gas in presence of 10% palladium supported on activated charcoal (10% Pd/C) as catalyst. Secondly, reaction mechanisms used for this reduction were also shown and explained.

Chapter Three emphasizes on the synthesis and characterization of IL namely 1-butyl-3-methylimidazolium tetrafluoroborate ([BMIM][BF_4]). Chemicals, reagents, solvents, and various instruments involved in the synthesis and physicochemical characterization of this IL are presented in detail. The chapter also outlined and explained different synthesis methods used in this study, *viz.* conventional and microwave (MW). This included the details of the followed experimental procedures. All the obtained results from the two synthesis methods and the descriptive study of [BMIM][BF_4] were discussed.

Chapter Four compared the application of [BMIM][BF_4] with ethanol (as an example of a VOS) as solvents for the reduction of aldehydes and ketones to their corresponding alcohols. Details of chemicals, reagents, solvents, and instruments used in the reduction processes and data collection, are provided. Two different reduction approaches, based on the reducing agent stated above, *i.e.* $NaBH_4$ reduction and catalytic hydrogenation, were presented. The obtained results showing the solvent efficiency of [BMIM][BF_4] in comparison to ethanol, are presented and discussed in this chapter.

Chapter Five is a summary of the current work, overall conclusion and the future ways of developing this study.

5.2 Overall conclusion

Synthesis of [BMIM][BF_4] and investigation of its solvent efficiency were the core objectives of this research work. The reduction of aldehydes and ketones to their corresponding alcohols was taken as model reactions.

Two synthetic steps required for this synthesis were successfully performed. These steps were; (i) the synthesis of [BMIM]Br, used as precursor for the synthesis of [BMIM][BF_4] (Chapter Three, Scheme 3.2, step 1), and (ii) the anion exchange between bromide anion and tetrafluoroborate anion by anion metathesis(Chapter Three, Scheme 3.2, step 2).

Two synthesis methods, *i.e.* (MW) and conventional, were employed. In conventional method, the oil bath was used as heating source, (in step 1, mentioned in the above paragraph). Given that the reaction flask was firstly heated before the reaction mixture, this reaction was slow and took a long time to attain the required reaction temperature. The inefficiency of this method was not only inhered in long reaction time, but also in occurrence of other side reactions and

decomposition due to the prolonged heating even after reaction. Therefore, lower yields were obtained.

In MW method, there was localized heating inside the reaction mixture coming from the direct coupling of MW energy and the IL constituents. Thus, the desired reaction temperature was quickly achieved and this enhanced the product yields.

Comparing the results of the performed work with literature data, MW showed superiority over conventional approaches, in terms of short reaction times, higher yields and better purity of products.

The synthesis of [BMIM][BF_4] was fully confirmed by FTIR, NMR (^{1}H- and ^{13}C- NMR), and LC-MS spectroscopy. In addition, the physicochemical properties including water content, density, viscosity and thermal stability, were successfully determined and helped in evaluating the purity of the synthesized ILs. The synthesized [BMIM][BF_4] was water-stable, denser, viscous and thermally stable. Hence, [BMIM][BF_4] was a suitable solvent for liquid-liquid extraction, catalytic and lubrication processes.

The synthesized [BMIM]BF_4 was used as reaction medium in the reduction of aldehydes and ketones to their corresponding alcohols at room temperature. Similar reactions and conditions were done in ethanol. Reduction reactions were performed by use of two reducing agents *viz.* $NaBH_4$ and H_2 gas, 10% Pd/C. The reduced compounds were benzaldehyde, acetophenone, ferrocenecarboxyaldehyde and acetylferrocene.

With $NaBH_4$, normal stirring on a cold plate (conventional) and ultrasonic irradiation (US) techniques, were employed, respectively. Independently on the used technique, alcohols produced from [BMIM][BF_4] were more pure and in satisfactory yields compared to those from ethanol. The solvating ability of [BMIM][BF_4] was more pronounced than ethanol. [BMIM][BF_4] acted as faster proton donor, owing to high acidity of hydrogen atom located at carbon in position two of this IL (Chapter Two, Figure 2.14). Therefore, in presence of a nucleophile, [BMIM][BF_4] was more reactive than ethanol and this improved efficiency of the reaction and the product yields.

This reduction was also done under solvent-free conditions with a purpose of investigating the solvent effects. Synthesis approaches used were US irradiation and mechanochemical grinding. However, the obtained product yields were extremely low and this observation highlighted the role played by a solvent on the mass transfer of the reactants within a chemical process. From these $NaBH_4$ reduction processes, US method was found dominant over the

conventional and mechanochemical, *i.e.* in terms of short reaction times and better product yields.

With H_2 gas as the reducing agent and 10% Pd/C as a catalyst, the reduction reactions in [BMIM][BF_4]were observed to be slower than in ethanol and this is due to high viscosity of [BMIM][BF_4]. This could be thought as a drawback of [BMIM][BF_4] for a catalytic hydrogenation, however its high selectivity towards formation of the desired alcohols was of great consideration. [BMIM][BF_4] acted as a co-catalyst, which favoured the alcohol selectivity.

The [BMIM][BF_4] recyclability was investigated for both $NaBH_4$ reduction and catalytic hydrogenation reactions. It was noted that from five consecutive runs done using [BMIM][BF_4] without any replacement, the isolated products were in relatively good yields.

The remarked non-volatility and recyclability of [BMIM][BF_4] met the pivotal goal of green chemistry that seeks to design products capable of reducing the use and generation of harmful substances. Furthermore, green approaches such as MW irradiation and US irradiations, in combination with ILs, provide a huge contribution towards sustainable chemistry.

5.3 Future work

Based on the findings from the current work, several horizons can be explored for further study of ILs, with [BMIM][BF_4] in particular. The following prospects are proposed:

- Synthesis of [BMIM][BF_4] by use of ultrasound irradiation method.
- Synthesis of modified [BMIM][BF_4]-based ILs for several applications such as pharmaceutical process, fabrication of energy storage and conversion devices and biomass biorefinery.
- Investigation of [BMIM][BF_4] toxicity for a better environmental sustainability.
- Synthesis of other ILs by use of alternative greener approach.
- Investigations of the new/novel ILs in point (4) for other applications other than reduction processes.

Appendix A - FTIR spectra

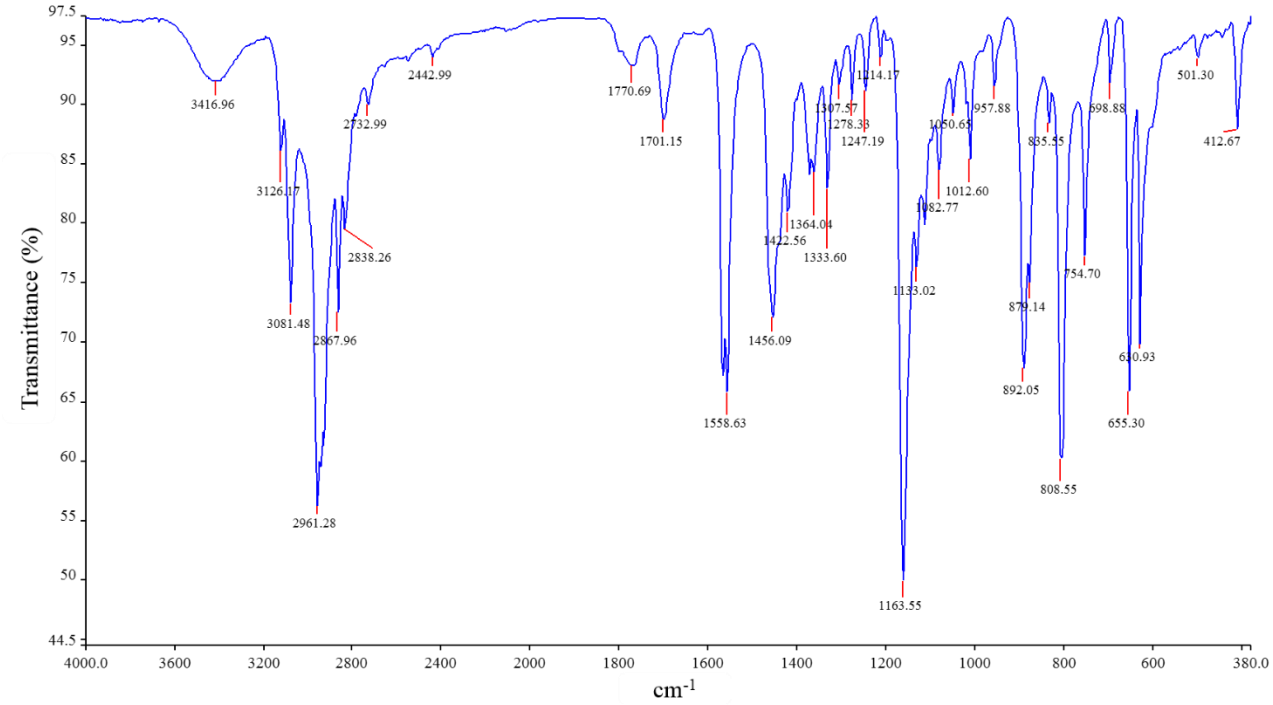

Figure A1: FTIR spectrum for synthesized [BMIM][Br] by conventional method

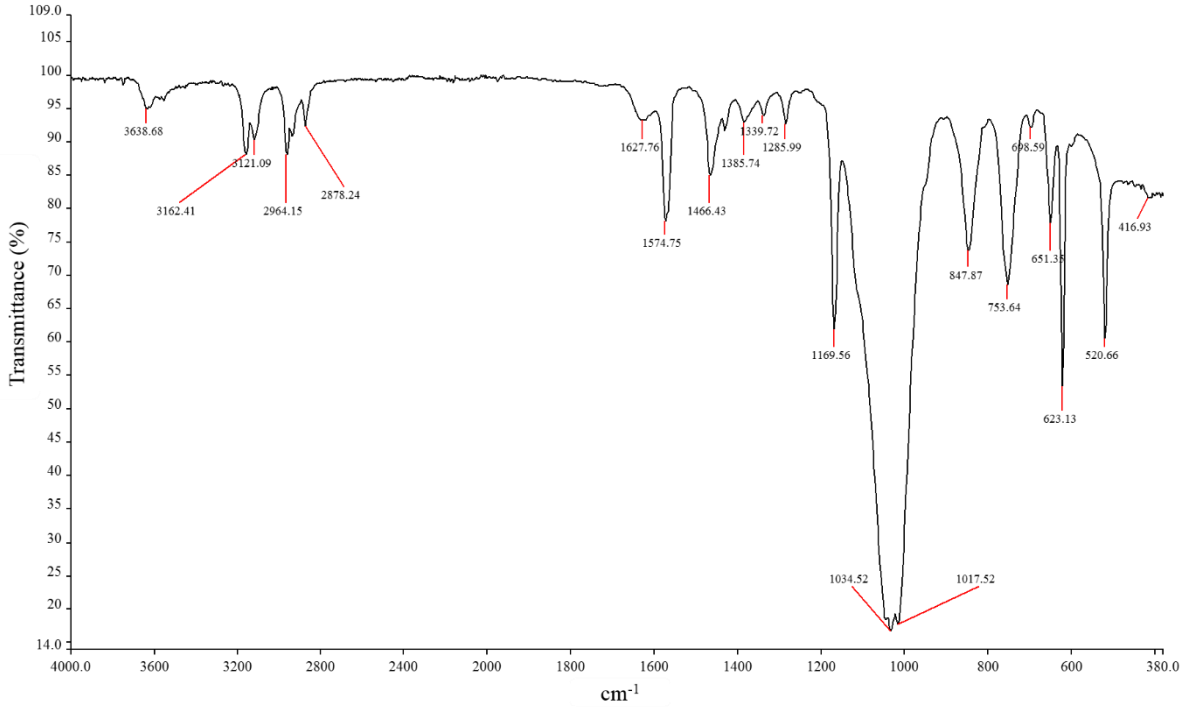

Figure A2: FTIR spectrum for synthesized [BMIM][BF_4] by conventional method

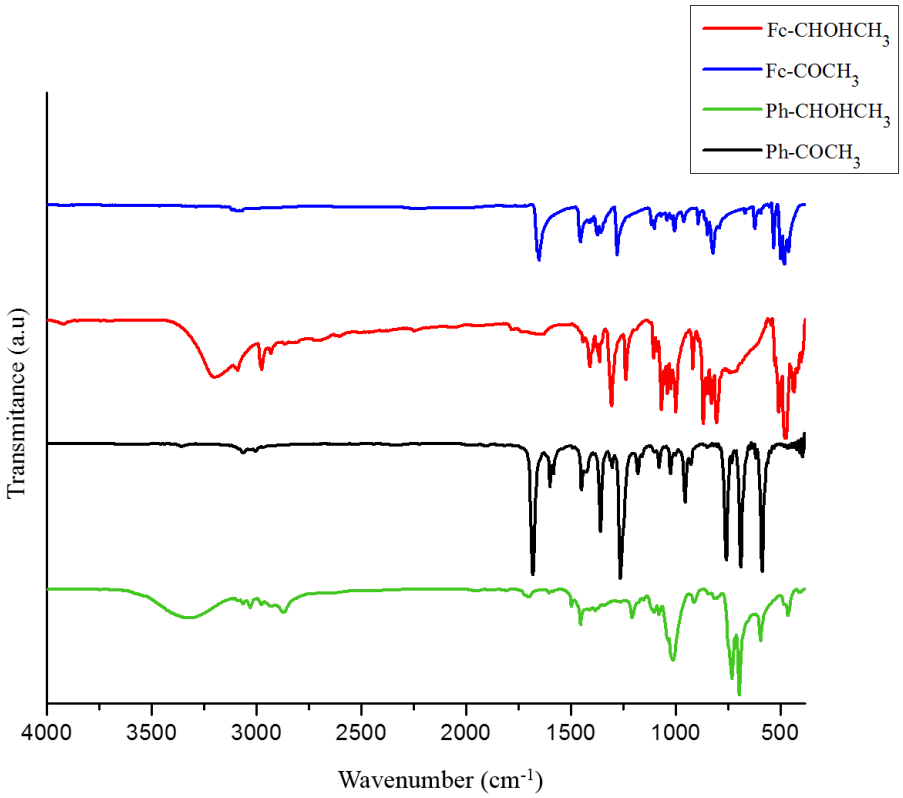

Figure A3: FTIR spectra of Fc-$COCH_3$ (blue), Fc-$CHOHCH_3$ (red), Ph-$COCH_3$ (black) and Ph-$CHOHCH_3$ (green)

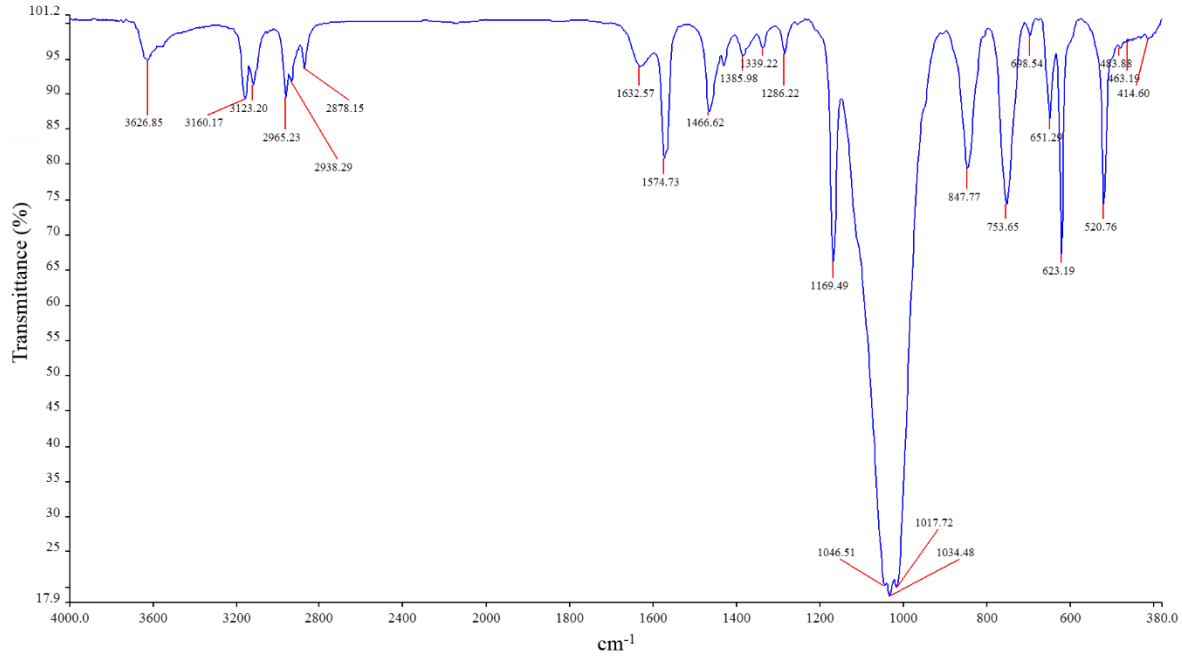

Figure A4: FTIR spectrum for [BMIM][BF_4] recycled at the end of fifth run for the $NaBH_4$ reduction of Ph-CHO

Appendix B – NMR spectra

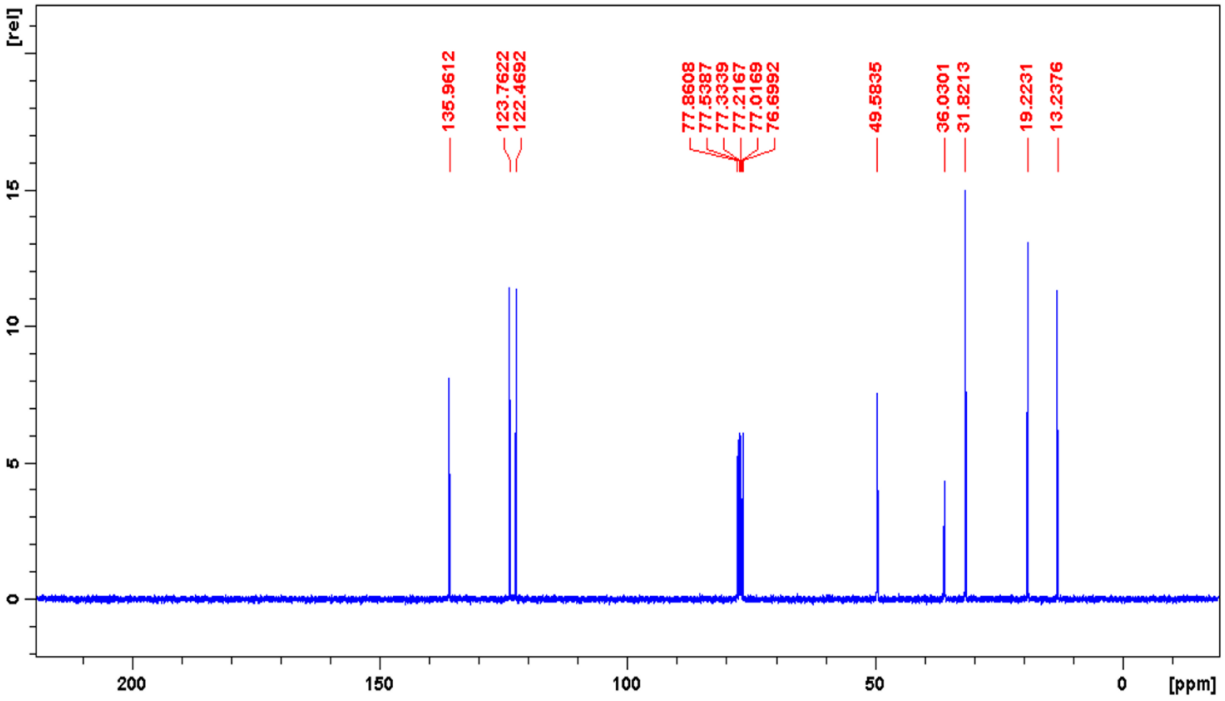

Figure B1: ^{13}C-NMR spectrum for [BMIM][BF_4] synthesized by MW, similar to the one synthesized by conventional method

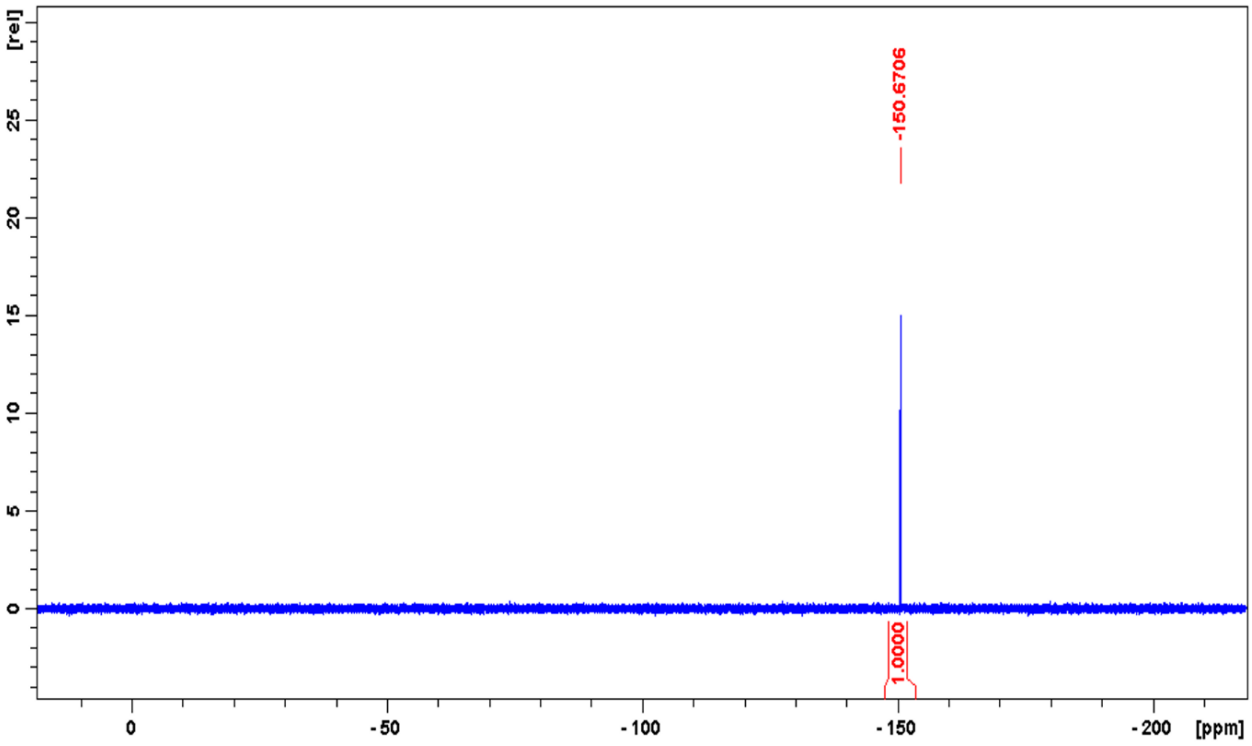

Figure B2: ^{19}F-NMR spectrum for [BMIM][BF_4] synthesized by MW, similar to the one synthesized by conventional method

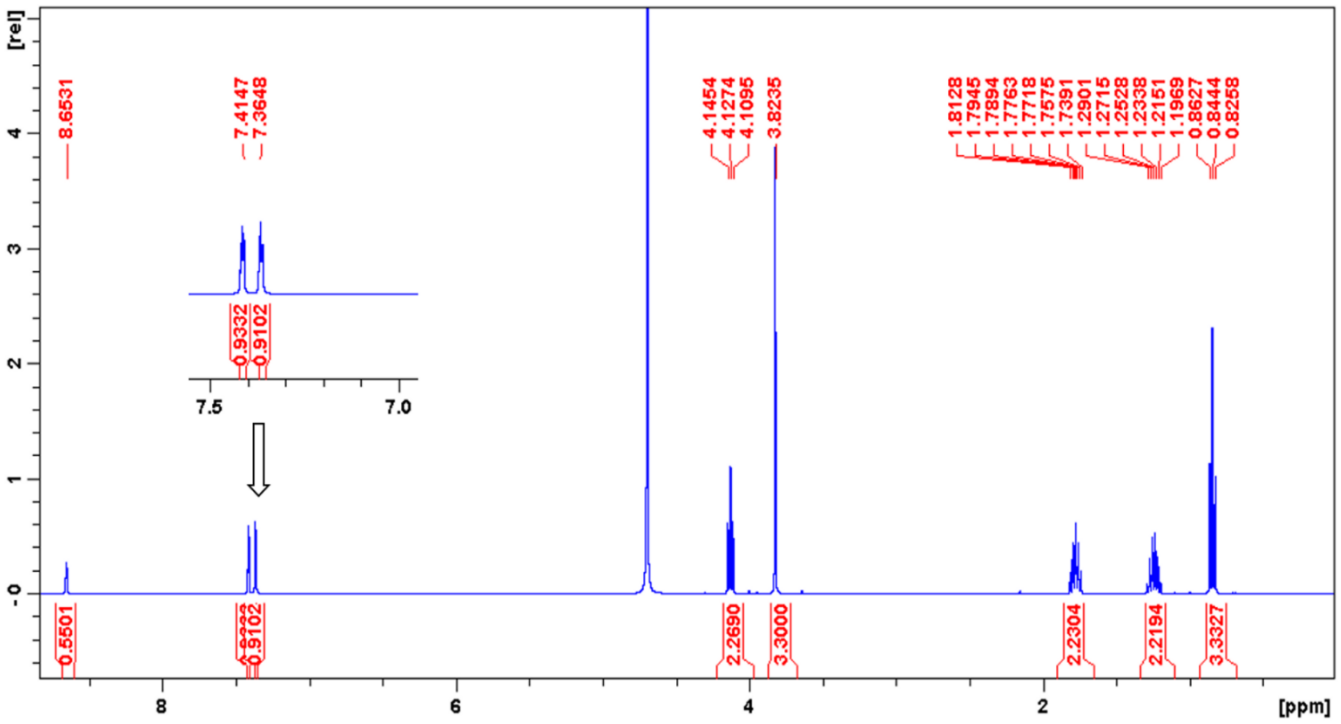

Figure B3: ^{1}H-NMR spectrum for [BMIM][Br] synthesized by MW, similar to the one synthesized by conventional method

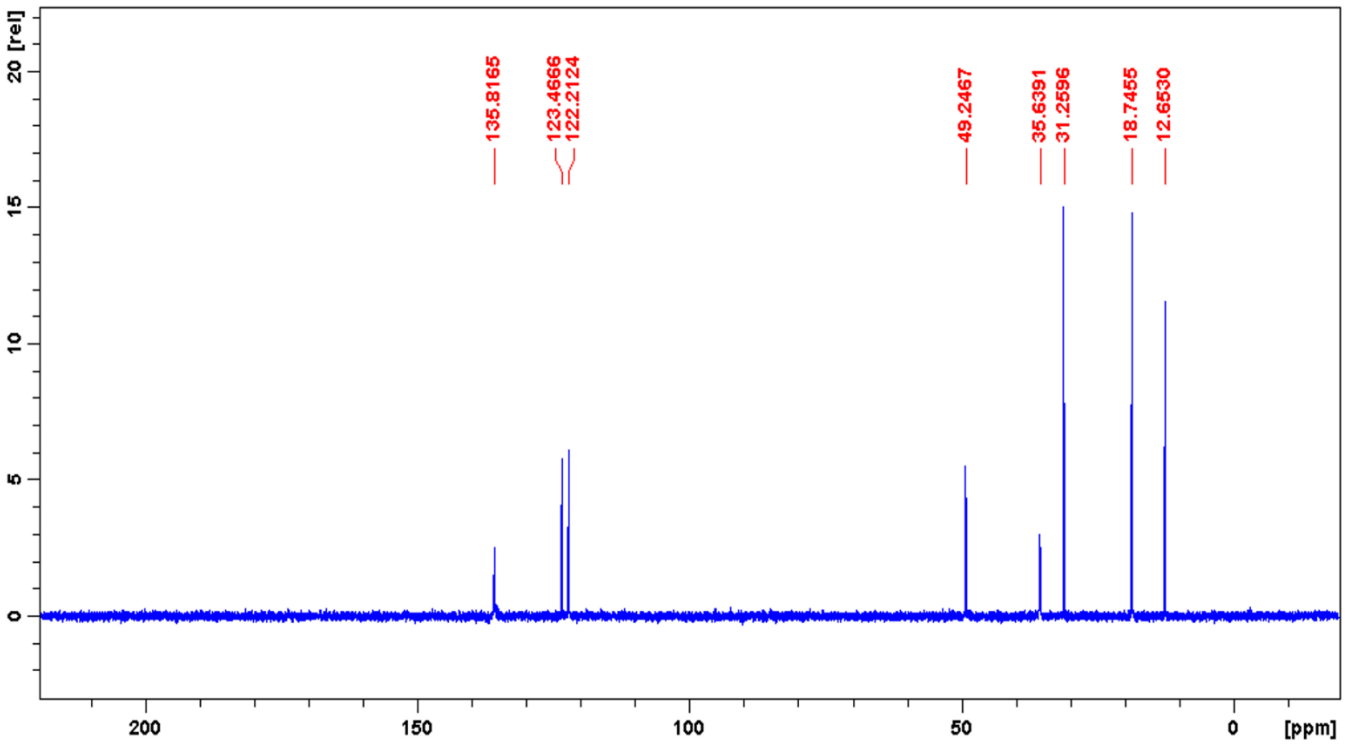

Figure B4: ^{13}C-NMR spectrum for [BMIM][Br] synthesized by MW, similar to the one synthesized by conventional method

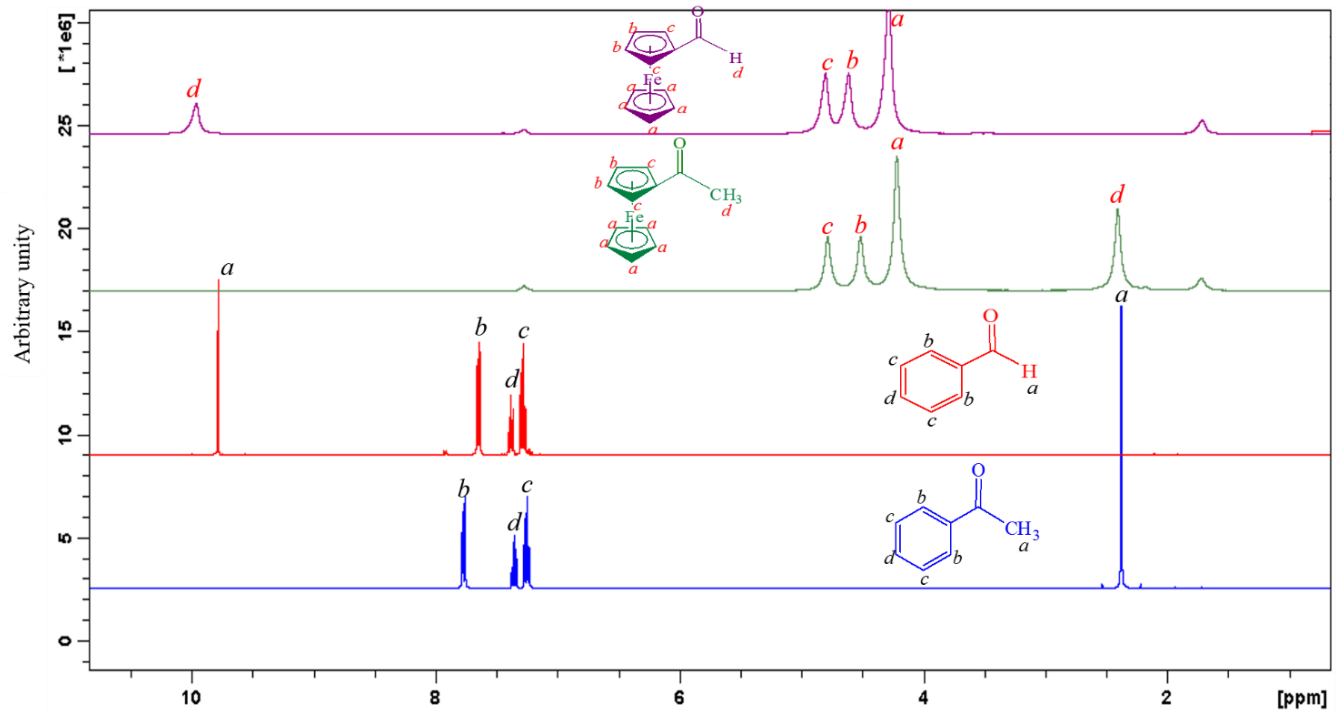

Figure B5: ^{1}H-NMR spectra for Fc-CHO (purple), Fc-$COCH_3$ (green), Ph-CHO (red) and Ph-$COCH_3$ (blue)

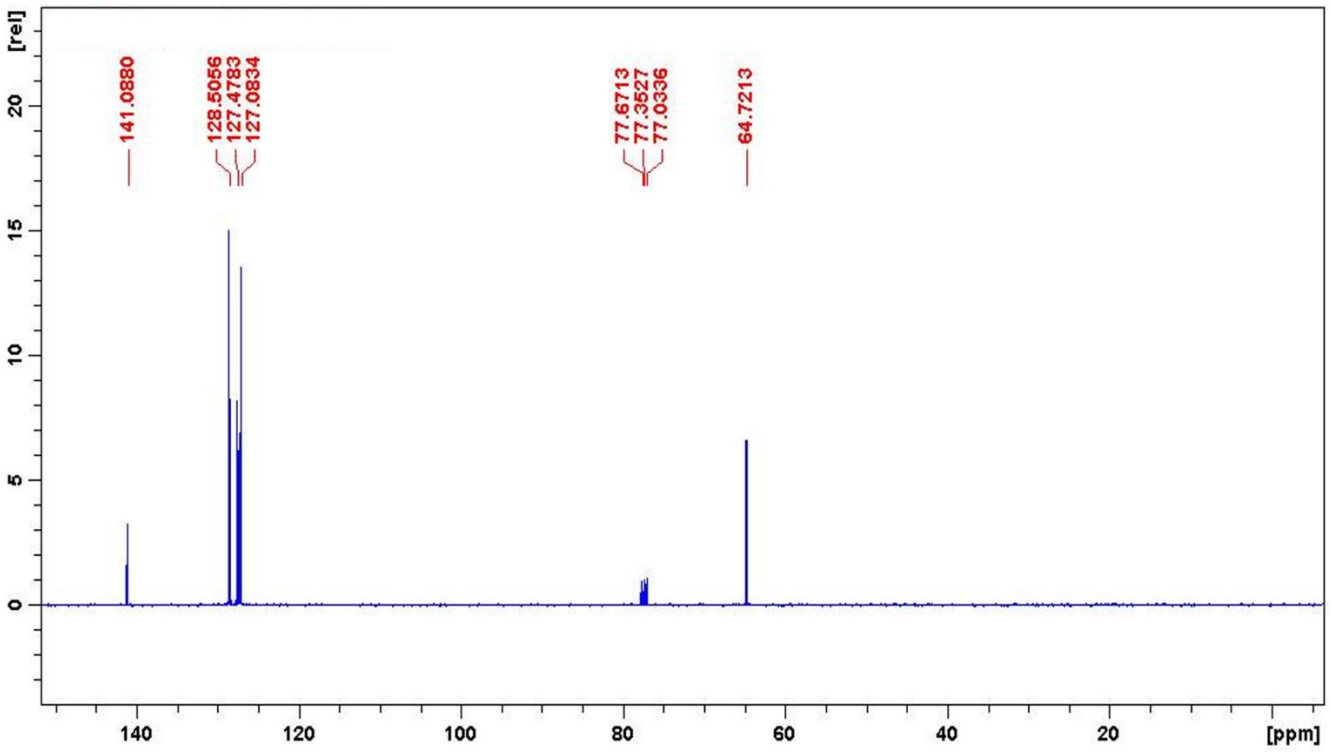

Figure B6: ^{13}C-NMR spectrum for Ph-CH_2OH

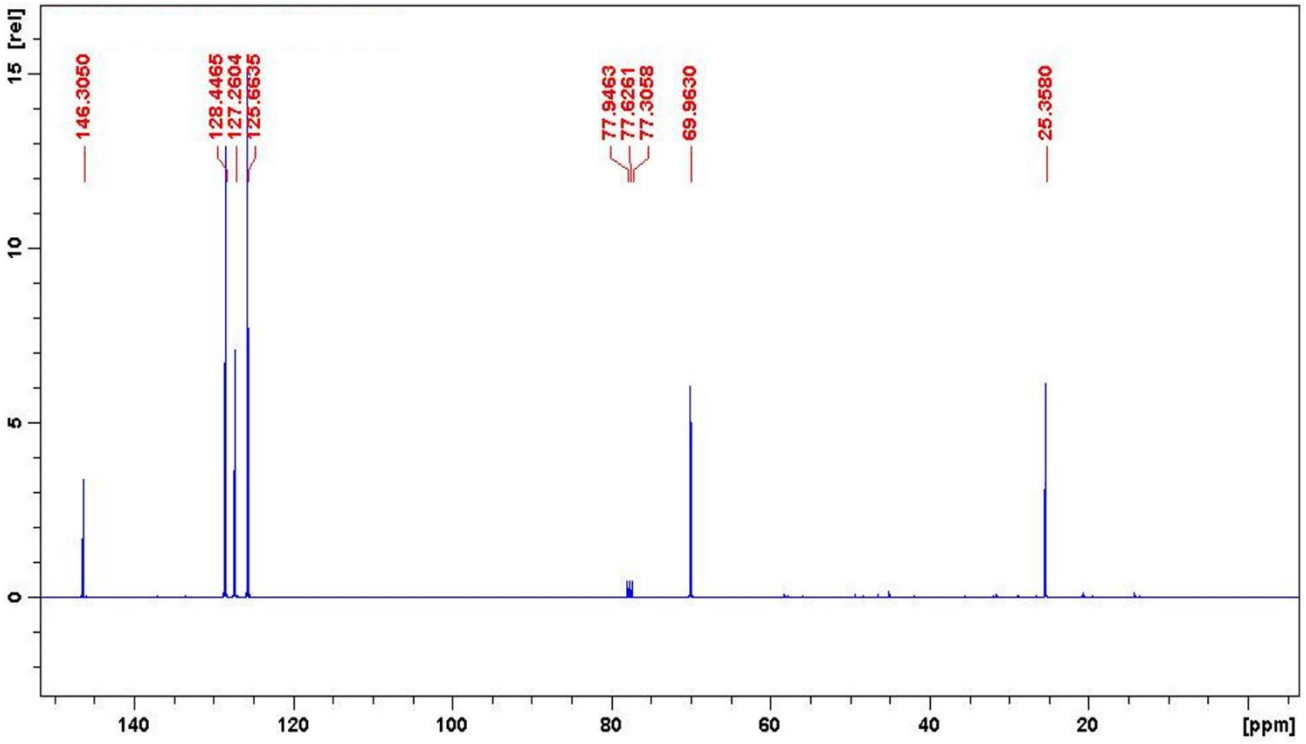

Figure B7: ^{13}C-NMR spectrum for Ph-CHOHCH$_3$

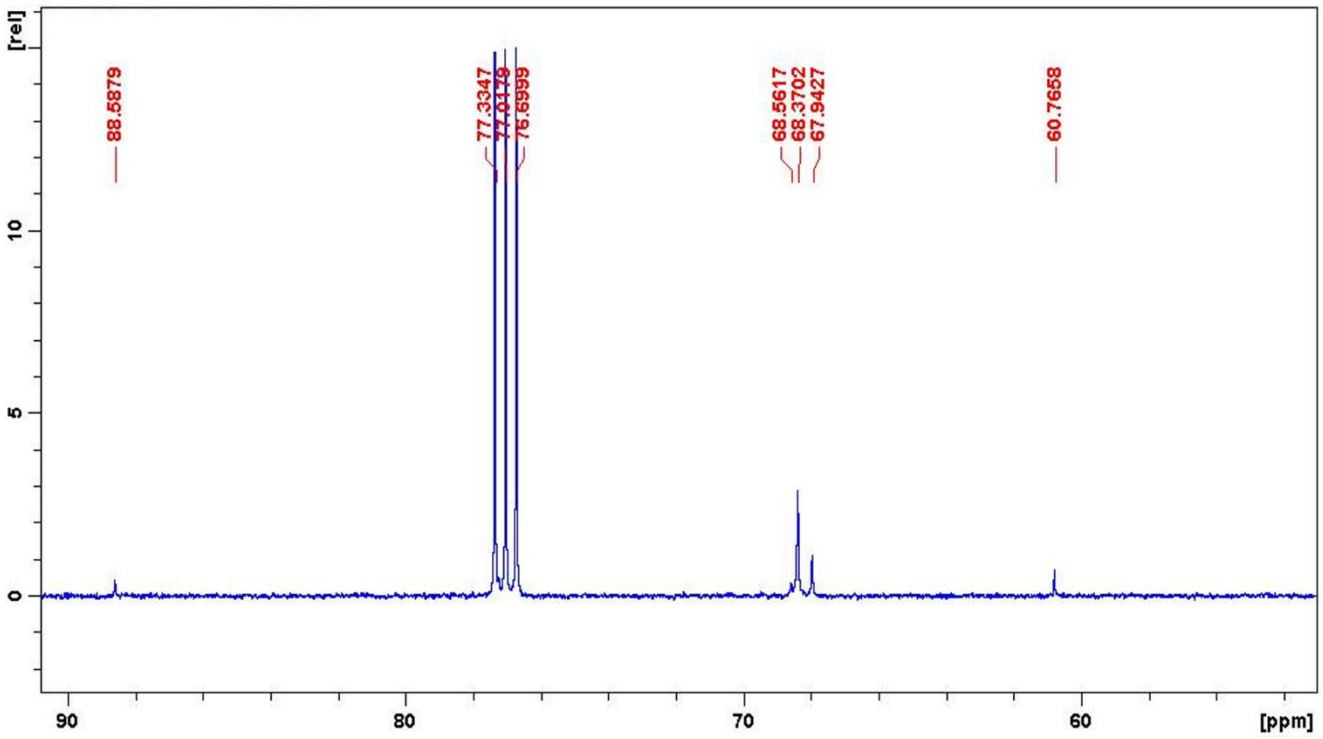

Figure B8: ^{13}C-NMR spectrum for Fc-CH$_2$OH

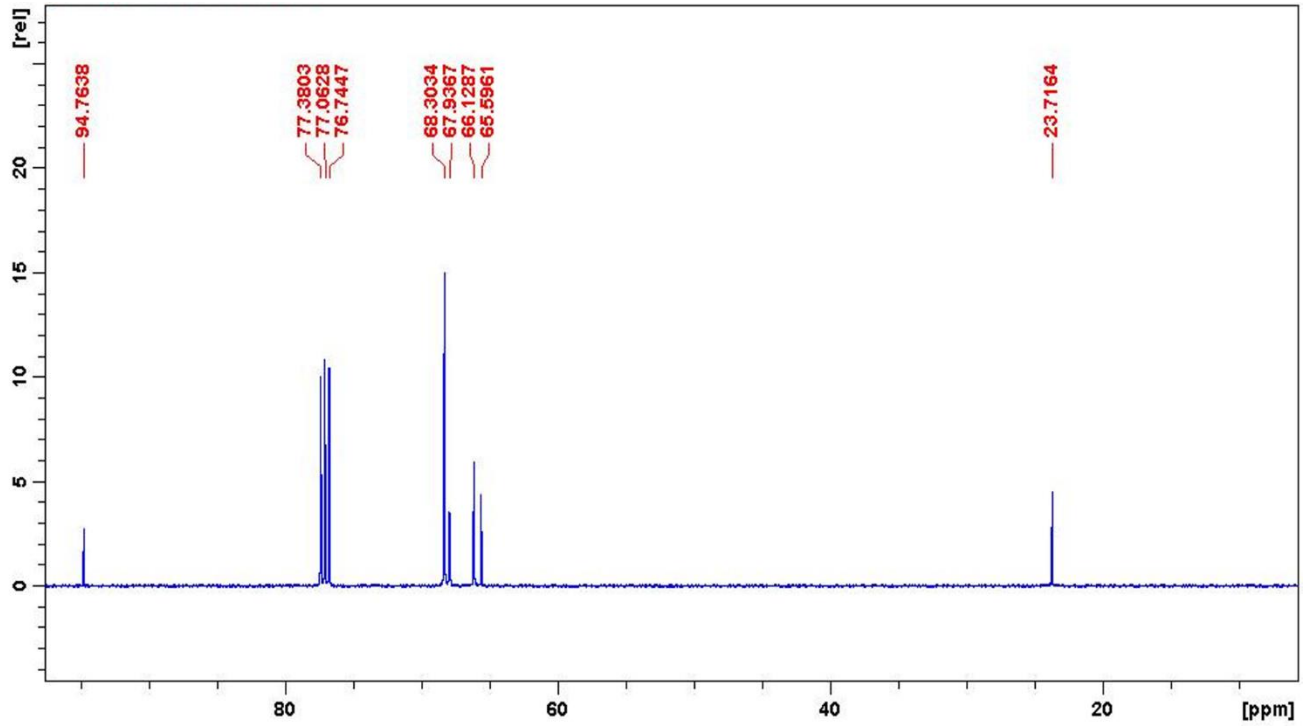

Figure B9: ^{13}C-NMR spectrum for Fc-CHOHCH$_3$

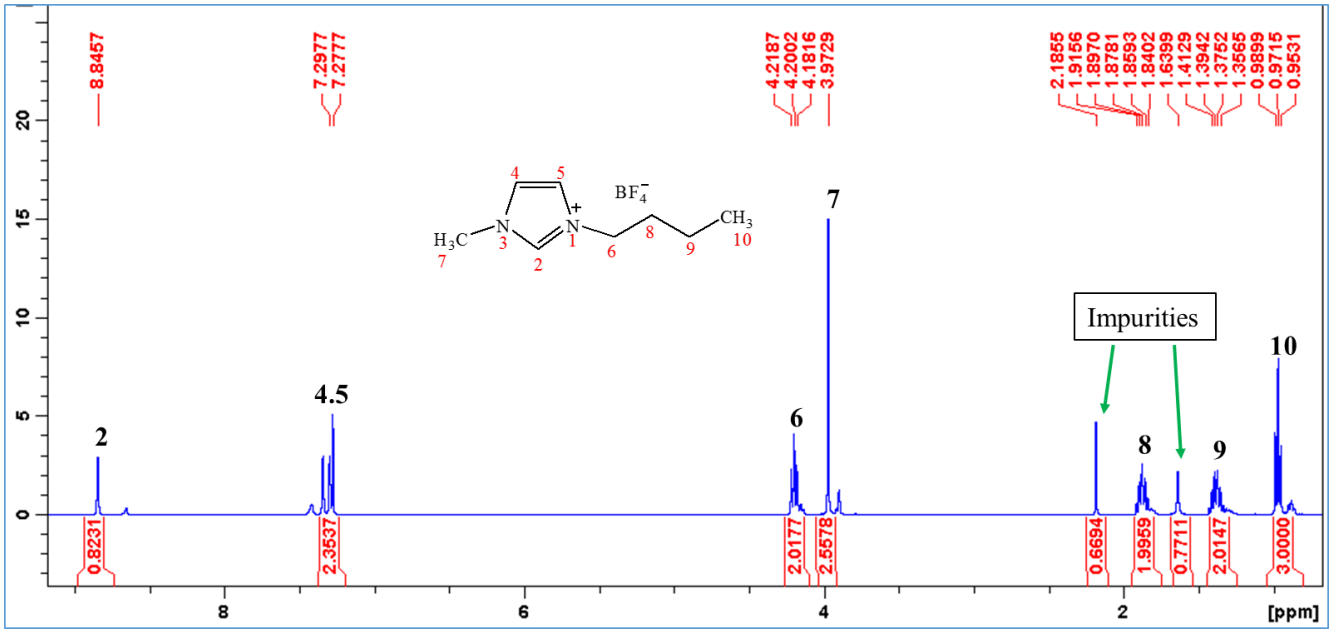

Figure B10: ^{1}H-NMR spectrum for [BMIM][BF$_4$] recycled at the end of 5th run for the NaBH$_4$ reduction of Ph-CHO

Appendix C – LC-MS spectra

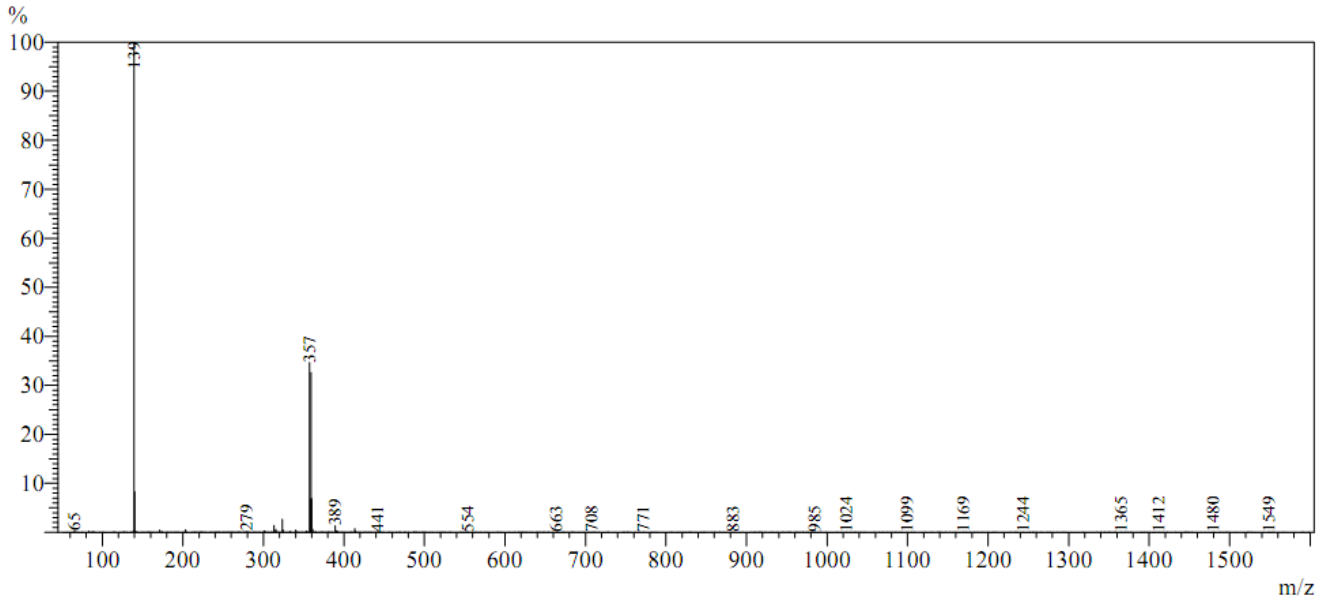

Figure C1: LC-MS spectrum for [BMIM][Br] synthesized by MW, similar to the one synthesized by conventional method