NOVEL SYNTHETIC METHODOLOGIES: STUDY OF UNIT PROCESSES FOR PREPARATION OF INDUSTRIALLY IMPORTANT ORGANIC CHEMICALS

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By

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CERTIFICATE

It is certified that the research work presented in this thesis titled **"NOVEL SYNTHETIC METHODOLOGIES : STUDY OF UNIT PROCESSES FOR PREPARATION OF INDUSTRIALLY IMPORTANT ORGANIC CHEMICALS"** submitted by **Mr. Ramavarma Rajagopal** has been carried out by the candidate under my supervision. This work is original and has not been submitted in part or full for any other degree or diploma to this or any other University or Institution. Such material as has been obtained from other sources has been duly acknowledged in the thesis.

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DECLARATION STATEMENT UNDER O.771

The work presented in the thesis has been carried out by me under the guidance of Dr. B. D. Kulkarni, Head and Deputy Director, Division of Chemical Engineering, National Chemical Laboratory, Pune. The experimental work, observations and interpretation of the data in connection with the studies are entirely my own. This work is original and has not been submitted in part or full for any other degree or diploma to this or any other University or Institution.

Research Guide	Candidate
(B. D. Kulkarni)	(Ramavarma Rajagopal)

Dedicated

To

MOTHER

One touch of nature makes the whole world kin

- William Shakespeare

CONTENTS

Page No.

CHAPTER – 1

Section – 1

Introduction to Room Temperature Ionic Liquids

Section- 2

1.2.0. Synthesis and Characterization of Dialkylimidazolium based ILs

Section- 3

1.3.0. Bromination of Arenes Using N-bromosuccinimide (NBS) in Ionic Liquids

Section- 4

1.4.0. Nitration of Phenols Using Hydrated Ferric Nitrate in Ionic Liquids

Section- 5

1.5.1. Ultrasound Promoted C-C bond Formations in Ionic Liquids

1.5.2. Ultrasound Promoted Heck Coupling in Ionic Liquid

1.5.3. Ultrasound Promoted Suzuki Coupling in Ionic Liquid

CHAPTER – 2

Section-1

Section-2

2.2.0. Synthesis and Characterization of modified zirconia catalyst

Section-3

2.3.1. Phenol acylation

2.3.2. Benzoylation of Aromatics

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ABSTRACT

This thesis is divided into two parts viz. the chemistry in ionic liquids and Freidel-Crafts acylation reactions under heterogeneous catalysis.

1.0.0. Chemistry in Ionic Liquids

The past few years has witnessed the evolution of a new era in chemical research by the entry of ionic liquids as potential 'Green Designer Solvents' as novel replacements for volatile organic compounds traditionally used as industrial solvents.

1.1.0. Introduction to ionic liquids

Ionic liquids are systems consisting of salts that are liquid at ambient conditions. A brief history of ionic liquids and their emergence as environmentally benign solvents have been discussed in this section. Various types of I.Ls and their nomenclature are covered. The unique property of this ionic species, which gives liquid character to it, has been discussed in detail. A wide variety of reactions performed in ionic liquids have been summarized.

1.2.0. Synthesis and characterization of dialkylimidazolium based ionic liquids

A series of N,N-dialkyl substituted imidazolium based I.Ls have been synthesized (Fig. 1)

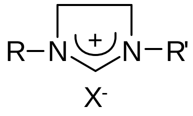
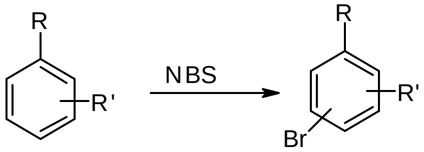


Fig. 1

The alkyl chain length (R and R') and the anionic part (X) are altered. All compounds were characterized by NMR, IR and Mass spectrometry and elemental analysis. Density and viscosity of all compounds were measured. The variation of both density and viscosity has been correlated to the increase in the alkyl chain length and the change of the anion. Melting and decomposition temperatures were measured using TG-DTA techniques.

1.3.0. Bromination of Arenes using NBS in ionic liquids

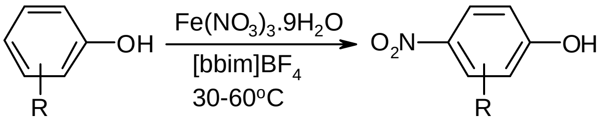
Bromination of arenes is an important unit process for the preparation of a variety of commercially important products such as pharmaceuticals, colorants, photographic chemicals, agrochemicals, speciality and fine chemicals. Apart from bromine in presence of Lewis acid catalysts, a popular and versatile reagent commonly used for aromatic bromination is N-bromosuccinimide (NBS). NBS has been used under a variety of conditions such as NBS-H_2SO_4, NBS-SiO_2, NBS-p-TSA, NBS-Amberlyst, NBS-NaOH, NBS-HZSM-5 and NBS-HBF_4 conferring good regio-selectivity in a number of solvents such as CCl_4, CH_3CN, propylene carbonate and DMF.



This section describes the remarkable increase in the reaction rate in the bromination of activated arenes in the I.L, di-n-butylimidazolium tetraflouroborate [bbim][BF_4] as solvent with complete conversions and high regio-selectivity in the absence of any added catalysts using NBS as the brominating agent. The highly exothermic reaction was completed in less than one minute to give monobrominated product in high para selectivity for the o- and m- substituted substrates. For the p-substituted substrates the ortho bromo compound was the only product. The present conditions also gave exclusive nuclear monobromination even in substituted toluenes.

1.4.0. Nitration of phenols using hydrated ferric nitrate in ionic liquids

Nitration of aromatics has been an immensely important industrial process and the nitro compounds find wide use in dyes, pharmaceuticals, perfumes and plastics. Conventional nitration process required concentrated acids, which make downstream process expensive and tedious. Survey of literature provides light to various eco-friendly processes and researchers came up with different nitrating species and conditions. A wide variety of homogeneous and heterogeneous catalysts were invented in last decade to clean up the process. Nitration of phenols has always been challenging as it lacks selectivity in the conventional processes. Among the nitrating agents employed, metal nitrates either alone or supported on solid



matrices enjoyed considerable importance. This chapter describes a new methodology for the nitration of phenol using hydrated ferric nitrate as nitrating agent in the I.L [bbim][BF_4]. Excellent regio-selectivities were obtained obtained when the reaction was carried out at ambient conditions with the added advantage that I.L. could be completely recovered and recycled making this an environment friendly process.

1.5.0. Ultrasound promoted C-C bond formations in ionic liquids

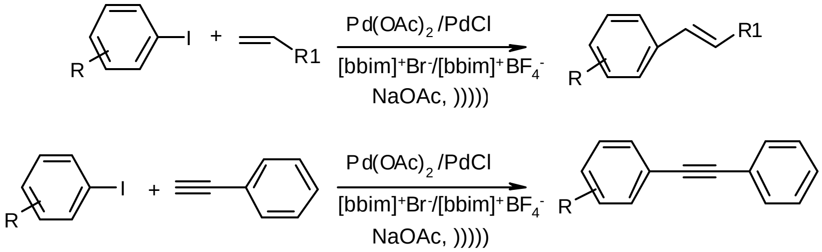
Chemistry is the interaction of energy and matter and chemical reactions require energy to proceed. Ultrasonic irradiation in recent times has developed as an unconventional source of energy in chemical transformations with its property of ‘cavitation’, which produces “hot spots” in the reaction medium. As a result of this cavitation phenomena, “micro bombs” with high temperature and pressure are generated for a very short period of time facilitating the reactions at ambient conditions. Ultrasound has potentially important applications in both homogeneous and heterogeneous catalysis. The inherent advantages of sonocatalysis include i) the use of low/ambient temperature to preserve thermally sensitive substrates and to enhance selectivity ii) the ability to generate high energy species difficult to obtain from photolysis or simple pyrolysis iii) the mimicry of high temperature and pressure conditions on a microscopic scale and iv) cleaning and increasing surface area of solid catalysts thereby increasing their activities. The present study deals with the ultrasound promoted palladium catalyzed C-C bond formation reactions such as Heck and Suzuki cross coupling reactions in room temperature ionic liquids as solvents at ambient temperature. This work is presented in three sections.

1.5.1. Introduction to Sonochemistry

First section covers the introduction to sonochemistry. The phenomenon of cavitation and ultrasound mediated reactions are reviewed.

1.5.2. Ultrasound promoted Heck coupling in ionic liquid at ambient conditions

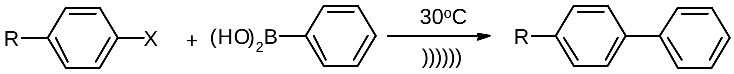
This section starts with an introduction to Heck reaction. Methods, types of ligands, conditions and mechanism are discussed. In the present work, palladium catalyzed Heck reaction was carried out with aryl halide and olefin in I.Ls under ultrasound irradiation at ambient conditions. The formation of Palladium bis carbene complex [A] in catalyzing the reaction and the generation of palladium nanoparticles under the ultrasound irradiation have been proved by the NMR and transmission electron microscope (TEM) studies.



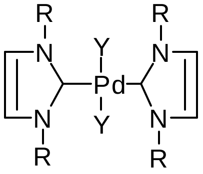
R = H, 4-OMe, 4-Cl
R1 = COOMe, COOEt, Ph

1.5.3. Sonocatalyzed ambient temperature Suzuki coupling reactions

An introduction to Suzuki cross-coupling covers the recent developments. Ambient temperature Suzuki coupling reaction in ionic liquid with methanol as co-solvent under ultrasonic irradiation was achieved in the absence of any added phosphine ligands. The role of co-solvent and the palladium bis carbene complex [A] have been studied in detail.



X = I, Br, Cl
R = H, OCH_3, CH_3, Cl, NO_2



[A]

R = n-butyl
Y = Br, BF_4

2.0.0 Heterogeneous Catalysts for Friedel-Crafts reactions

This part is sub-divided into three sections.

2.1.0. Introduction to heterogeneous catalysis

Catalyst is one of the fundamental pillars of 'Green Chemistry', the design of chemical products and processes that reduce or eliminate the use and generation of hazardous substances. Heterogeneous catalysis in particular addresses the goals of Green Chemistry by providing the ease of separation of products and catalyst, thereby eliminating the need for separation through distillation or extraction or other unit operations. Acid catalysis is of fundamental industrial importance, which plays a vital role in petroleum industry for cracking, isomerization and alkylation to upgrade the oil. Also they are used for large-scale polymerization processes and some organic transformations. Some metal oxides when sulphated develop super acidity, which can bring about the lowering of reaction temperatures thereby saving energy and also improving selectivity in many cases. In this chapter, the theory of heterogeneous catalysis, sulphated metal oxide catalysts and Friedel Crafts acylation reactions are discussed.

2.2.0. Synthesis and characterization of phosphotungstic acid modified sulphated/phosphated zirconia

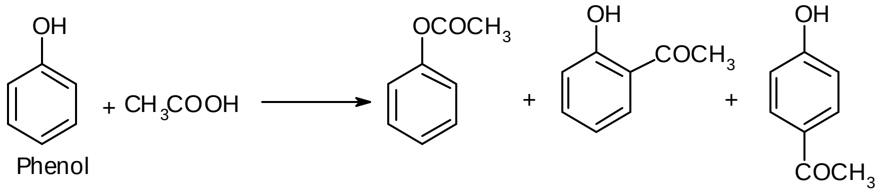
Heteropoly acids are crystalline solids and possess strong acid properties both in solid and in solution. Main drawback is its low surface area. One of the methods to increase the surface area without losing its inherent acidity is to support it in suitable amorphous metal oxides.

A super acidic system was synthesized in which phosphotungstic acid impregnated on zirconia in presence of mineral acids. The impregnation was carried out in water as well as in methanol in presence of sulphuric acid and phosphoric acid. Different loadings of phosphotungstic acid were prepared. The catalysts were calcined at different temperatures ranging from 550-950^{o}C. All catalysts were characterized by X-ray diffraction, surface area measurements, thermogravimetric analysis, transmission electron microscope and acidity measurements. X-ray diffraction studies were carried out and crystalline structural changes were assessed with respect to change in phosphotungstic acid loading and calcination temperature.

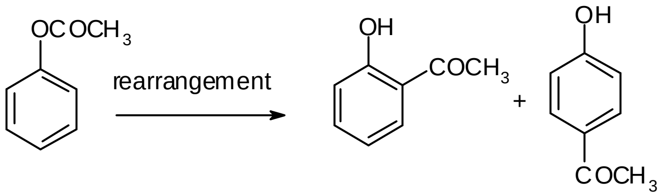
2.2.0. Application of catalysts in Friedel-Crafts acylation reactions

Friedel-Crafts acylation reactions have always been an attractive unit process in the Industry for C-C bond formation. Stoichiometric metal halide Lewis-acid catalysts used in conventional methods result in heavy metal sludge in effluent downstream. Recyclable solid acid catalysts synthesized in the present work are appropriate substitutes for the metal halide Lewis catalysts for pollution free processes.

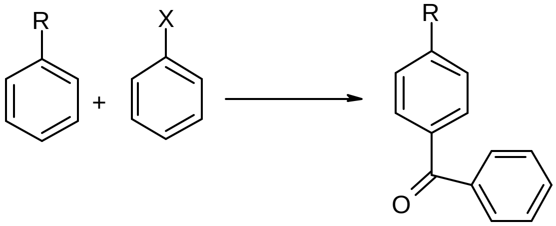
2.3.1. Studies in acetylation of phenol with acetic acid



This section describes the application of phosphotungstic acid modified zirconia catalysts in the acylation of phenol using acetic acid as acylating agent. A detailed study by varying different parameters was carried out to optimize the conditions. Also a detailed study on Fries rearrangement of phenyl acetate over the catalysts was carried out.



2.3.2. Benzoylation of aromatics



R = Cl, OCH_3, Br
X = COCl, CCl_3

In this section, benzoylation of aromatics using both benzotrichloride and benzoyl chloride as benzoylating agents in the presence of above catalysts has been discussed. Excellent yields were obtained in the case of activated arenes affording the benzophenones in high para selectivity.

Preamble

The new millennium started with the inheritance of the problems of industrial revolution of the previous era, which progressed in a rampant pace without due appreciation and proper consideration of the interactive phenomena of ecology, economy and society. The recognition of the problems generated, dictated some basic rules for sustainable development to achieve healthier societal, economic and environmental objectives. These rules are now accepted by the governments, industry and the general public. Applied chemistry while playing a significant role in maintaining and improving the quality of life behind the scenes, is often scandalized for its visible deleterious effect on nature. In this context fine chemical industry is less favorably viewed compared to the petroleum, gas, electricity, lumber and paper industries. The range of chemical products is enormous and these products make an invaluable contribution to the quality of our lives with manufacturing plants having capacities ranging from a few tonnes per year in the fine chemicals area to 500,000 tonnes per year in the petrochemicals area. However, these manufacturing processes also lead to millions of tonnes of waste, and the reduction or elimination of this waste is now a central issue for the industry, the authorities, and the general public.

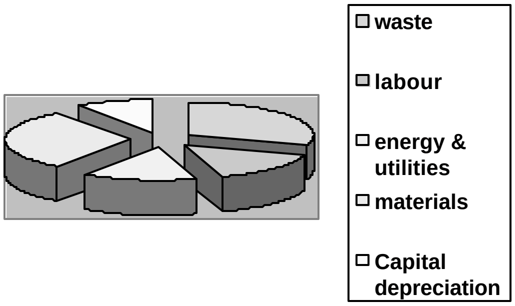


Fig. 1. Breakdown of typical Speciality Chemical Manufacturing Cost

The challenge for chemists and others is to develop new products, processes and services that achieve the societal, economic and environmental benefits that are now required. Table 1 describes the E-factor, which is defined as the ratio (by weight) of the by-products to the desired product(s).

Table 1

Industry	Production / tones pa	E-Factor
Oil refining	10^6-10^8	0.1
Bulk Chemicals	10^4-10^6	1-5
Fine Chemicals	10^2-10^4	5-50
Pharmaceuticals	10^1-10^3	25-100

This requires a new approach which sets out to reduce the materials and energy intensity of chemical processes and products, minimize or eliminate the dispersion of harmful chemicals in the environment, maximize the use of renewable resources and extend the durability and recyclability of products—in a way which increases industrial competitiveness. Clean technology concerns the reduction of waste from an industrial process to minimum and high improvisation is necessary from the current status In chemical synthesis the ideal will be somewhat like an octagonal Chakra/wheel representing the combination of a number of environmental, health and safety, and economic targets Fig 2.

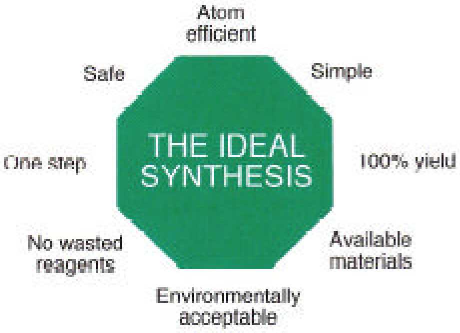


Fig. 2

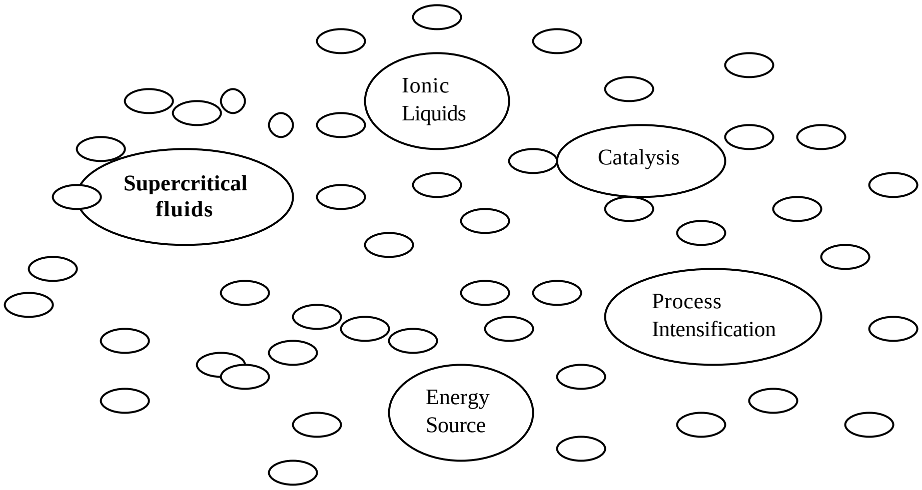
The green chemistry revolution is providing an enormous number of challenges to those who practice chemistry in industry, education and research.

The practice of green chemistry is defined as the utilization of a set of principles (like atom economy in synthesis, catalysis of reactions, use of renewable feedstocks, safe, energy cum material efficient, wasteless processes etc, in design, manufacture and application of chemical products.

THE TWELVE POINTS OF GREEN CHEMISTRY

- Prevention
- Atom Economy
- Less Hazardous Chemical Syntheses
- Designing Safer Chemicals
- Safer Solvents and Auxiliaries
- Design for Energy Efficiency
- Use of Renewable Feedstocks
- Reduce Derivatives
- Catalysis
- Design for Degradation
- Real-time analysis for Pollution Prevention
- Inherently Safer Chemistry for Accident Prevention

The above green chemistry revolution is providing enormous challenges to chemists in industry, education and research. Their effort is to contribute different ingredients to make up the Clean Technology Pool shown below. One of the recent entrants is Ionic Liquids as reaction media, which is investigated for green application among a few other things in this thesis.



The Clean Technology Pool

1.1.0. Ambient Temperature Ionic Liquids

The present day challenge for chemists is to develop new products, processes and services that achieve the societal, economic and environmental benefits. This requires a new approach which sets out to reduce the materials and energy intensity of chemical processes and products, minimize or eliminate the dispersion of harmful chemicals in the environment, maximize the use of renewable resources and extend the durability and recyclability of products. The drive towards clean technology in the chemical industry with an increasing emphasis on the reduction of waste at source will require a high level of innovation and new technology. Solvents constitute a major factor in deciding the efficacy of an environmental friendly technology. There are unavoidable species/side products in various organic reactions, requiring elaborate and expensive separation technologies to get pure products. The ideal solvent should have a very low volatility, it should be chemically and physically stable, recyclable and reusable, and eventually easy to handle. In addition, solvents that allow more selective and rapid transformations will have a significant impact.

1.1.1. Innovations in Solvents

- ***Water as solvent***

Water[1] has been successfully used as a solvent in some biphasic industrial metal catalyzed reactions.[2,3] However, its application is still limited due to low miscibility of organic substrates in water, giving rise to low reaction rates. Water is protic coordinating solvent and so it can react with haloorganics and more vigorously with organometallic complexes by halide-carbon or metal-carbon bond hydrolysis.

- ***Perflourinated solvents***

More recently, perfluorinated solvents have proven their utility for many organic and catalytic reactions.[4,5] Nevertheless, specific ligands must be designed to solubilize catalyst in the perfluorinated phase. Moreover, the decomposition of fluorous solvents at high temperature leads to formation of toxic compounds. Moreover, fluorous compounds are often detected in the organic phase.

- ***Supercritical fluids***

Supercritical fluids have also been used described as new solvents for organic and catalytic reactions.[6] Their physical properties and chemical stability make them eligible to be called as green solvents. Unfortunately, critical conditions needed for their handling is still a limitation.

- ***Ionic Liquids***

Last ten years, Ionic liquids have seen come up as a novel class of solvents.[7] Initially developed by electrochemists, who were looking for ideal electrolytes for batteries. Because they offer an ionic environment on chemical reactions, they may change their course, and so one could expect to see a general ionic liquid effect. These are now used in a lot of applications, which continue to expand such as electrolytes for electrochemical devices and processes, solvents for organic and catalytic processes, new material production, solvents for separation and extraction processes. They also find additional use in enzyme catalysis or in multiphase bio-process operations. In the present work, emphasis will be given to second generation ionic liquids i.e. dialkylimidazolium salts rather than the air and moisture sensitive first generation ones (chloroaluminates). Processes based on these stable ionic liquids have been stressed and a brief account of the various features of ionic liquids as designer solvents are presented.

1.1.2. Introduction to ionic liquids

Generally IL refers to molten salts, which contain ions. To use “molten salts” to describe these systems is as archaic as describing a car as a horseless carriage.[9] Only those liquids, which are non-corrosive, and have low viscocity, are chosen to be called as Ionic Liquids (I.Ls). So classes belonging to molten inorganic salts viz. molten sodium chloride will not be considered under the heading I.L.

Room temperature Ionic Liquids (I.L) are emerging as novel replacements for volatile organic compounds (VOCs) traditionally used as industrial solvents.

Room Temperature Ionic Liquids have no measurable vapour pressure.
Compared to the 300 organic solvents widely used in Chemical Industry,
there are over “trillion” possible ionic liquids!!!!

The above lines by Kenneth R. Seddon, pioneer in I.L, provides the vivid picture of these species as potential “Green Designer Solvents” for various chemical processes. These are termed as “Neoteric Solvents” as they have remarkable new properties that can break new ground and have capacity to clean up the modern Chemical Industry.[8] These solvents are often liquids at room temperature and consist entirely of ionic species. They have many fascinating properties since both the thermodynamics and kinetics of reactions in I.L are different to those in conventional molecular solvents. These “Designer Solvents” –aptly named- consists of an anionic and a cationic part, which can be varied for a particular end use or to possess a particular set of properties.

1.1.3. Classification

I.Ls are classified into two categories.

i. Binary ionic liquids – salts where an equillibrium is involved.
ii. Simple salts – made of single anion and cation.

The first category, the first generation I.Ls, contains a mixture of metal halide and an ionic liquid belonging to first class e.g. mixture of aluminium chloride and dialkylimidazolium chloride. These contain several ionic species and their melting point and properties depend on the mole fractions of the individual components. The second class, generally termed as second generation I.Ls, consists of simple cation and anion e.g. ethylammoniumnitrate $C_2H_5NH_3^+NO_3^-$, dialkylimidazolium ILs [bmim][Br].

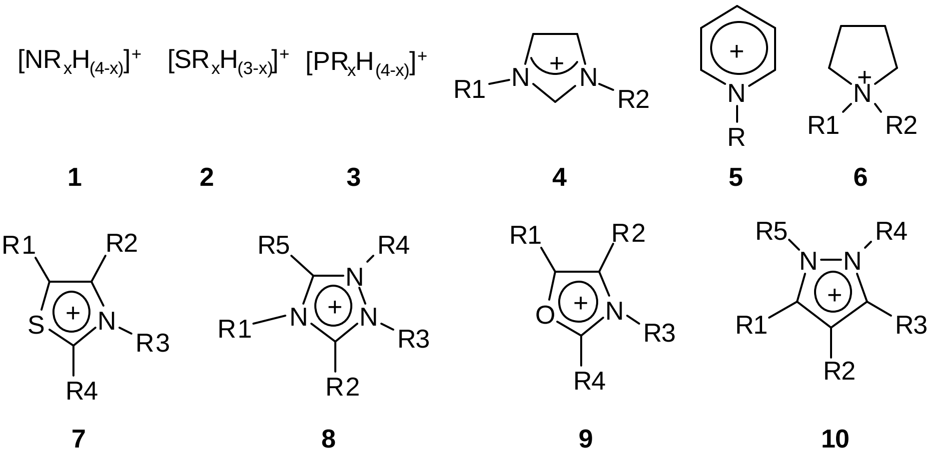
I.Ls generally are composed of relatively large organic cations and inorganic or organic anions and have a melting range of –96°C to 100°C. Cations are mainly quarternary ammonium or phosphonium moiety.

1.1.4. Recent developments in cations and anions

In the literature, it has been mentioned a large number of cation–anion associations are able to yield room temperature ionic liquid, unlike the inorganic salts. They are composed solely of ions (cations and anions) but they are liquid at low temperature (melting point typically below 100°C). Different cation-anion combinations are developed and studied for their suitability to be used as I.Ls.

Cations

The cations are generally bulk in size and organic components with low symmetry. Those described until now are based on ammonium **1,**[10-12] sulfonium **2,**[13] phosphonium **3,**[14] imidazolium **4,**[16-19] pyridinium **5,**[20-22] pyrrolidinium **6,**[23] thiazolium **7,**[24] triazolium **8,**[25] oxazolium **9,**[26] and pyrazolium **10**[27] differently substituted (**Scheme 1**). Of particular interest are the salts based on the *N*,*N*-dialkylimidazolium cation **4** because of the wide spectrum of physico-chemical properties available in that class. Liquid imidazolium salts are generally obtained by anion exchange from imidazolium halide precursors. Reported preparations of those precursors involve long reaction times. Recently, improved synthetic methods for the preparation of 1-alkyl(aralkyl)-3-methyl(ethyl)imidazolium halides have been described.[28] In this paper, the synthesis of 1-alkyl-3-methylimidazolium bromides is described with advantage of short reaction time giving high yields (94–99%) without purification step.

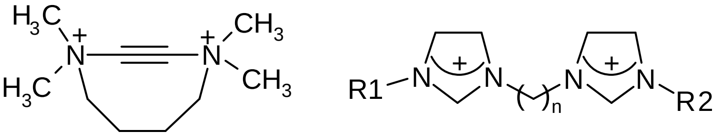


Scheme 1. Examples of cations described in ionic liquids.

The availability of such precursors will provide easier access to room temperature ionic liquids with widely varying structures. It has very often been assumed that non-symmetrical *N*,*N* -dialkylimidazolium cations give lower melting point salts. Very surprisingly, however, 1,3-dialkylimidazolium hexafluorophosphates with dibutyl, dipentyl, dioctyl, dinonyl and didecyl substituents are found to be liquid at room temperature.[29]

The alkyl chain on the imidazolium can also bring a fluorocarbon tail.[30] In that way, the fluorinated salts, when added to a conventional ionic liquid, can act as surfactants and facilitate the emulsification of per-fluorocarbons in ionic liquids. It can also include task-specific functional groups.[31] Such imidazolium derivatives when used as part of the solvent or doped into less expensive ionic liquids, can be used to extract metal ions from water phases. Free amine groups have also been incorporated on the imidazolium cation and have been used to sweeten natural gas by sequestration of H_2S or CO_2.[32]

Alkoxy groups have also been attached to the imidazolium cation giving a large number of new ionic liquids which display particularly excellent antielectrostatic effect.[33] Besides the *N*,*N*-dialkylimidazolium cations, pyrrolidinium cations **6** have gained attention first as plastic crystal former with anions such as BF_4 or NTf_2. These low melting salts exhibit interesting ionic conductivity and, therefore, have received attention for use as electrolytes in a range of applications including solar cells and batteries.[23,34] Other recently developed cations are the planar trialkylsulfonium ones such as **2**. When combined with the NTf_2 anion, they give low melting salts with very high conductivity and the lowest viscosity of all the NTf_2 based room temperature ionic liquids ($[SEt_3][NTf_2]$: m.p. = 35°C and 30mPas at 25°C). Their high conductivity can be ascribed to a little stronger degree of association between SEt_3^+ and NTf_2. than that of 1-ethyl-3-methylimidazolium (EMI^+) and NTf_2 salt.[35] Organic polycations such as **11** and **12**, have also been envisioned (**Scheme 2**). Associated with bromide anions, the dication **12** *(m* = 4*,*R1 = R2 = methyl*)* gives a salt melting at 67–69°C.[36]



11 **12**

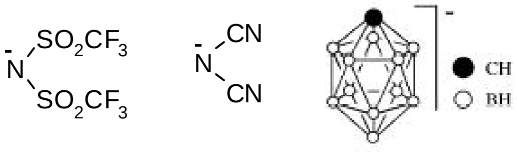
Scheme 2. Examples of polycations.

Based on these polycations, a new category of phosphate ionic liquids was described and presented as good candidates for organic electrochemical processes.[37]

Besides organic cation based ionic liquids, lithium salts are increasingly being developed particularly for secondary batteries and storage of energy. They often have lower lattice energy and, therefore, lower melting points than their neighboring elements in the periodic table. As an example, the mixture of LiCl and $EtAlCl_2$ gives a liquid, on a large range of composition, at temperatures lower than 0°C.[38] In most chemical applications of ionic liquids, cations influence the physical properties of the medium. However, a chemical effect of the cation is also possible. For example, for the hydrovinylation of styrene catalyzed by Ni organometallic complexes, 4-methylpyridinium salts proved to give higher enantioselectivity than their 1-ethyl-3-butylimidazolium homologue.[39] On the other hand, when used as solvents for the regioselective alkylation of indole, 1,3-dialkyl or 1,2,3-trialkylimidazolium based salts proved to be superior to the alkylpyridinium ones.[40,41]

Anions

Concerning the anions, they can be classified in two parts: those which give polynuclear anions, e.g. Al_2Cl_7., Al_3Cl_{10}., Au_2Cl_7., Fe_2Cl_7., Sb_2F_{11}. These anions are formed by the reaction of the corresponding Lewis acid, e.g. $AlCl_3$ with the mononuclear anion, e.g. $AlCl_4$. They are particularly air and water sensitive. The second class of anions corresponds to mononuclear anions which lead to neutral, stoichiometric ionic liquids, e.g. BF_4, PF_6, SbF_6, $ZnCl_3$, $CuCl_2$, $SnCl_3$, $N(CF_3SO_2)_2$, $N(C_2F_5SO_2)_2$, $N(FSO_2)_2$, $C(CF_3SO_2)_3$, CF_3CO_2, CF_3SO_3, CH_3SO_3, etc. Of particular interest is the trifluoromethylsufonylamide anion [NTf_2] **13,**[42,43] which gives particularly thermally stable salts (up to 400°C) (**Scheme 3**).



13 **14** **15**

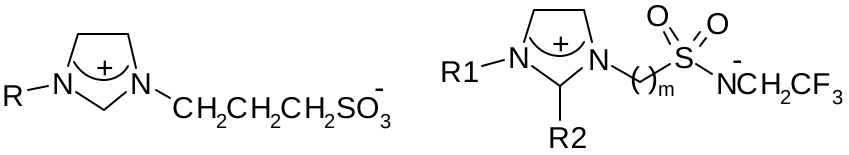
Scheme 3. Examples of anions.

Salts based on this anion can be easily prepared by anion exchange reactions using the commercially available lithium trifluoromethylsufonylamide. Because of the delocalization of the negative charge, the anion is probably less associated with the cation and then more mobile than the triflate one. For reasons that are not completely elucidated, this imide anion strongly lower the melting points of salts such as quarternary ammonium such as Et_4N^+ ([Et_4N][NTf_2]: m.p. = 105°C). $LiNTf_2$ and $LiCTf_3$ salts are considered as attractive alternatives to $LiPF_6$ in high voltage ion cells due to the hydrolytic instability of $LiPF_6$.[44]

The last innovation in the ionic liquid repertoire is the carborane-based salts.[45,46] Carborane anions **15** ($CB_{11}H_{12}$, Scheme 3) are one of the most inert anions in modern chemistry. Nevertheless, despite their great stability, the position 1 of the $CB_{11}H_{12}$ ion can be alkylated leading to new derivatives having melting points just above room temperature. An example is the [1-ethyl-3-methylimidazolium][1-C_3H_7-$CB_{11}H_{11}$] salt, which melts at 45°C. It appears also feasible to substitute the B–H bond with strong electrophiles which allows a systematic variation of the properties of the anion which is unavailable in most traditional anions. Moreover, their very weak nucleophilicity and redox inertness allowed the exploration of new extreme cation reactivity and the isolation of new superacids. Their incorporation in ionic liquids should enhance these properties. Ionic liquids developed until now often present higher viscosities than the common organic solvents used in synthesis. Driven by the need to find materials with lower viscosity, dicyanamide anions **14** have recently been described. [47] This anion associated with *N*-butyl-*N* methylpyrrolidinium, tetra-alkylammonium, or with 1-ethyl-3-methylimidazolium, gives ionic salts with melting point below 10°C. Viscosity for the [EMI][N(CN$_2$)] liquid salt is only 21mPas at 25°C with respect to 34mPas for [EMI][NTf$_2$] at 20°C.

Zwitterionic-type ionic liquids

A series of zwitterionic-type ionic liquids consisting of an imidazolium cations containing a covalently bound counter anionic sites, such as a sulfonate **16** or a sulfonamide **17** group have been prepared (**Scheme 4**).



R=Et, CH_2=CH-

R1 = Et, R2 = H, m = 3
R1 = Me, R2 = Me, m=2

16 **17a, 17b**

Scheme 4. Examples of zwitterionic salts.

Compound **16** is a white powder, which melts at 150°C. However, by adding equimolar amounts of LiNTf$_2$, the mixture presents a glass transition temperature of 16°C. These zwitterionic imidazolium salts (**17a**: *T*g = 61°C; **17b**: *T*g = 23°C) show unique characteristics.[48] For example they present very high ion density but their component ions cannot migrate. They act as an excellent ion conductive matrix, in which only added ions can migrate.

1.1.5. What features make ionic liquids so attractive?

The versatility of their chemical and physical properties

Besides their very low vapor pressure, which makes ionic liquids good alternatives to volatile organic solvents, they display a large operating range (typically from -40 to 200°C), a good thermal stability,[49] high ionic conductivity,[50] and large electrochemical window.[51] However, the key property of these solvents is the possibility to tune their physical and chemical properties by varying the nature of the cations and anions.[52, 53] The spectrum of their physical and chemical properties is much larger than that of organic solvents. Some typical physical characteristics of the more currently used salts are given in **Table 1**.

Table 1. Physical characteristics of 1-butyl-3-methylimidazolium ionic liquids.

Anion	M.P ^{o}C	Density (g/cm^3)	Viscocity (mPas)	Conductivity (Sm^{-1})
BF_4^-	-82/-83	1.17(30^{o}C)	233 (30^{o}C)	0.173 (25^{o}C)
PF_6^-	-61	1.37 (30^{o}C)	312 (30^{o}C)	0.146 (25^{o}C)
$CF_3SO_3^-$	16	1.29 (20^{o}C)	90 (20^{o}C)	0.37 (20^{o}C)
$CF_3CO_2^-$	-50/-30	1.209 (21^{o}C)	73 (20^{o}C)	0.32 (20^{o}C)
NTf_2^-	-4	1.429 (19^{o}C)	52 (20^{o}C)	0.39 (20^{o}C)

It has recently been demonstrated that the viscosity of 1-alkyl-3-methylimidazolium salts can be decreased by using highly branched and compact alkyl chain but more importantly by changing the nature of the anion.[54] For the same cation the viscosity decreases as follows: Cl > PF_6 > BF_4 > NO_3 > NTf_2.

An illustration of their versatility is given by their exceptional solubility characteristics,[55] which make them good candidates for multiphasic catalysis. For example, their solubility with water depends on the nature of the anions, on the temperature and on the length of the alkyl chain on the dialkylimidazolium cation. For the same 1-butyl-3-methylimidazolium cation, the BF_4, CF_3SO_3, CF_3CO_2, NO_3, and halide salts display a complete miscibility with water at 25^{o}C. However, upon cooling the [BMI][BF_4]/water solution to 4^{o}C, a water-rich phase separates. In a similar way, changing the [BMI] cation for the longer chain [HMI] (1-hexyl-3-methylimidazolium) leads to a BF_4 salt, which presents a low co-miscibility with water at room temperature. On the other hand, the PF_6, SbF_6, NTf_2, BR_4 show a very low miscibility with water. But for the PF_6 based melt, the shorter symmetric substituted 1,3-dimethylimidazolium PF_6 salt becomes water-soluble. Salts based on 1,3-dialkylimidazolium cation remain preferred as they generally interact weakly with the anions and are more thermally stable than other quaternary ammonium cations. Recently, Huddleston et al.[56] have examined physical properties (rarely systematically explored in the literature) of different hydrophobic and hydrophilic 1-alkyl-3-methylimidazolium room temperature ionic liquids. It is demonstrated that water content, density, viscosity, surface tension, melting point, and thermal stability were affected by changes in alkyl chain length of the imidazolium cations and by the nature of the anion. As expected, the anion mainly determines water miscibility and has the most dramatic effect on the properties. For a series of 1-alkyl-3-methylimidazolium cations, increasing the alkyl chain length from butyl to octyl increases the hydrophobicity and the viscosity of the ionic liquid, whereas densities and surface tension values decrease. As a result, one could expect that modifications of alkyl substituents of the imidazolium ring yields to different and very tunable solvent properties. The solubility of 1-hexene in different *N*,*N* -dialkylimidazolium and *N*,*N*-methylethylpyrrolidinium salts has been measured. Interestingly, not only increasing the length of the alkyl chain on the cation but also by tuning the nature of the anion can increase the solubility of 1-hexene in the melt.

How do ionic liquids compare with conventional solvents?

At the present time, there is still an empirical knowledge of these media mainly developed on the basis of their solvent effect on organic reactions compared to that of well-known conventional solvents. The challenge would be to be able to predict their properties in order to optimize the choice for a given application.[52]

Solvent polarity has often a strong influence on the outcome of reactions. However, the exact meaning of polarity is already complex, but becomes even more complicated in the case of ionic liquids, as many varied interactions can be involved. Different investigations of solvent–solute interactions in ionic liquids using solvatochromic dyes have been reported.[57,58] The data indicate that polarities of 1,3-dialkylimidazolium salts based on the PF_6, BF_4, CF_3SO_3 and NTf_2 anions can be compared to that of short chain primary alcohol with a little lower polarity for the NTf_2 anion. This is in agreement with the ionic liquid solvent effect described in the Diels–Alder reactions of cyclopentadiene with methyl acrylate.[59] The endo/exo selectivity, which may be viewed as being dependent on the polarity of the solvent, is high (6.1:1) when using [BMI][BF_4] and compare quite well to that obtained with methanol (6.7:1). These selectivities are characteristic of hydrogen-bonded polar organic solvents. The ionic liquid nucleophilicity is dependant on the anions and is much lower than that of polar solvents which makes ionic liquids unique.

Following properties make Ils an attractive substitute for molecular solvents in chemical processes.

1. They are salts which are molten at room temperature- due to the presence of larger cations, as a result of which the ions find it difficult to arrange themselves in the lattice so as to form solid.

2. They have no measurable vapour pressure – the attraction between the ions is sufficiently strong to prevent them from coming apart and evaporating. The IL do not give off any dangerous fumes. Consequently the loss during their recycling will be a minimum.
3. They are non-flammable and have high thermal stability.
4. Although ionic in nature, they can dissolve covalent compounds as well as inorganic salts at or near room temperature, which avoids huge energy costs related to many industrial processes.
5. They can be tailored to needs of the reaction – the variety of ionic liquids allow one to choose the desired outcome and subtly adjust the solvent/structure to achieve it. The ability to manipulate the ions used and the ratio between them provides a significant control over reaction pathway.

The versatility of the IL as potential industrial solvents has to be thoroughly explored. Also the engineering and basic scientific data of these compounds should be well studied and documented which will widely open up the gate towards the use of ILs as green solvents in industrial processes.

1.1.6. Fundamental principles of the formation and development of room-temperature ionic liquids

The purpose of this section is to provide light into the nature and properties of the ionic liquids, which will be useful in defining the ionic liquids as solvents and applications for industrially important catalytic reactions leading to clean technology.

The primary question in this context is how ionic compounds are liquid at ambient or near ambient conditions. We look back at some fundamentals. The melting point of a salt is related to its lattice energy. For e.g. a plot of lattice energy of group 1 halides against the melting point in Kelvin will give a straight line. The relationship was first studied by Kapustinskii, who coined the equation popularly known as Kapustinskii equation.[61] (Equation 1)

$$U = \frac{287.2vZ^+Z^-}{r_0}\left(1 - \frac{0.345}{r_0}\right) \quad \text{-----------} \quad \textbf{Equation 1}$$

U = lattice energy
v = number of ions per molecule
r_0 = sum of the ionic radii
Z^+, $Z-$ = charge of the ionic species

It can be seen that by increasing the value of r_0 (ionic radii), i.e., by using larger anionic and cationic components in the salt, it is possible to lower this energy and therefore reduce the melting point.

From this one can clearly see that as we increase both size of the anion and the cation, the melting point decreases. From the Kapustinskii equation one must also note that an increase in the ionic charge will tend to increase the lattice energy of the crystal. However, the effect on melting point is complicated by the fact that according to Fajan's rules an increasing charge also results in increasing covalency particularly for small cations and large anions.

For a given cation, the above equation demonstrates that the lattice energy will become only be a function of r_0, and since r_0 is the sum of r^+ and r^-, then the lattice energy is only dependent on anion size. For simple anions the radius is well documented,[60,62] but for complex ones, it becomes more difficult to assign the values for radii. For non-spherical anions these radii are of limited use. However for tetrahedral ions the symmetry is sufficiently high for comparison purposes. It is also possible to reduce lattice energy by increasing the size of cation. In the case of organic cations, the length of alkyl chain can be considered as the basis of the size of particular cation. So to decrease the lattice energy, the alkyl chain length should be increased thereby increasing the number of ionic liquids.

One can observe that there is a maximum chain length allowed before other forms of bonding begin to dominate and the melting point increases. The melting point below 0°C can be glass transition temperature rather than the true melting point. The significant variation in melting point which can be induced by simply changing the anion from [$C_n$mim][Cl] to the [$C_n$mim][PF_6] and [$C_n$mim][BF_4] ionic liquids have been well documented. For e.g. [C_4mim][PF_6] melts at 5°C whereas [C_4mim][Cl] has a melting point of 84°C.[66] These lower melting point liquids with shorter alkyl chain length lead to much more fluid and easily managed liquid.[63-65]

An interesting feature in this study is the appearance of liquid crystalline phases with longer alkyl chains, and this is confirmed when their optical textures are examined.[66] Also from this it can be seen that those salts with shorter alkyl chain length (n=2-10) are isotropic ionic liquids at room temperature and exhibit a wide liquid range, whereas the longer chain analogues are low melting mesomorphic crystalline solids which display an enantiotropic smectic A mesophase. The thermal range of the mesophase increases with increasing chain length and in the case of the longest chain salt prepared, $[C_{18}mim][BF_4]$, the mesophase range is ca. 150°C.

1.1.7. Preparation of I.L

Until recently room-temperature ionic liquids were considered to be rare, but it is now known that many salts form liquids at or close to room temperature. Invariably, these ionic liquids are either organic salts or mixtures consisting of at least one organic component. The most common salts in use are those with alkylammonium, alkylphosphonium, N-alkylpyridinium, and N,N'-dialkylimidazolium cations. There is no reliable way to predict the precise melting point of organic salts, and identification of new room-temperature ionic liquids is a somewhat hit and miss affair.

There are two basic methods for the preparation of ionic liquids: metathesis of a halide salt with, for instance, a silver, group 1 metal or ammonium salt of the desired anion and acid-base neutralization reactions. Many alkylammonium halides are commercially available or they can be prepared simply by the reaction of the appropriate halogenoalkane and amine. Preparation of the pyridinium and imidazolium halides can be achieved similarly.[67,68] For volatile halogenoalkanes, the low boiling points lead to preparations requiring either a sealed tube, such as in the synthesis of [emim]Cl (where $[emim]^+$ is the 1-ethyl-3-methylimidazolium cation), or an elaborate reaction still. Hence, the use of salts with longer chain substituents, such as [bmim]Cl (where $[bmim]^+$ is the 1-butyl-3-methylimidazolium cation),[69] that can be prepared in conventional glassware by heating under reflux has become popular.[70]

In 1992 the first of the new ionic liquids, $[emim][BF_4]$, was prepared via metathesis of [emim]I with $Ag[BF_4]$ in methanol.[71] This salt also has a melting point of 12°C and may be prepared considerably more cheaply using $[NH_4][BF_4]$ in acetone.[72] This ease of preparation, together with its relative moisture stability and its immiscibility with a number of organic solvents is leading to its increasing use in biphasic catalysis. The preparation of $[emim][PF_6]$ shortly followed; this time it was prepared by reaction of [emim]Cl with HPF_6.[73] This salt has a melting point of 60°C, which makes it slightly less attractive than the $[BF_4]^-$ salt, if room temperature working is desired. Since then, thiocyanate, nonafluorobutanesulfonate, bis((trifluoromethyl)sulfonyl)imide, tris((trifluoromethyl)-sulfonyl)methide, trifluoroacetate, and heptafluorobutanoate salts have all been prepared by metathesis reactions. [74,75,19] However, they can leave the ionic liquids contaminated with a small amount of halide ions that may react with solute materials.[76]

Tetraalkylammonium tetraalkylborides are usually prepared by the metathesis reaction of the tetraalkylammonium bromide and the lithium tetraalkylboride.[77] Since both the ammonium cation and the boride anion are asymmetrically substituted, the starting materials are usually made rather than purchased. Reaction of a trialkylborane with the appropriate alkyllithium reagent in dry hexane yields the required lithium tetraalkylboride.[78]

Other ionic liquids are made by the quarternerization of the appropriate amine. This has been used to prepare a number of 1-alkyl-3-methylimidazolium trifluoromethanesulfonate salts.[19] Methyl triflate is reacted with a stoichiometric amount of the 1-alkylimidazole in 1,1,1-trichloromethane. Since the methyl triflate is sensitive to moisture, the reaction must be carried out under anhydrous conditions.

Monoalkylammonium nitrate salts are best prepared by the neutralization of aqueous solutions of the amine with nitric acid.[74, 79] The ionic liquids are isolated by removing excess water in vacuo. In a similar reaction, tetraalkylammonium sulfonates have been prepared by mixing equimolar amounts of the sufonic acid and the tetraalkylammonium hydroxide.[80] Again, excess water was removed in vacuo. To ensure the purity of the ionic liquids, they were dissolved in either acetonitrile or tetrahydrofuran and treated with activated charcoal for at least 24 h, and finally the organic solvent was removed in vacuo.

The final method for the synthesis of ionic liquids is direct combination of a halide salt with a metal halide. This is how the halogenoaluminate(III) and the chlorocuprate(I) ionic liquids are prepared.[81] The chlorocuprate(I) ionic liquids are particularly sensitive to oxygen and have not found widespread use in synthesis.[82]

1.1.8. The importance of the purity of ionic liquids

The physical and chemical properties of ionic liquids can be altered by the presence of impurities arising from their preparation.[83] Purification of the ionic liquids is then essential. The main contaminants are halide anions or organic base that generally emanate from unreacted starting material and water.[84] A colorimetric method has been recently developed to determine the level of unreacted alkylimidazole (<0.2 mol%) in the ionic liquid.[84] As halide impurities can have a detrimental effect on transition metal catalyzed reactions, alternative methods of preparations have been proposed to avoid the use of halide containing starting materials. Examples are given by the direct alkylation of alkylimidazole derivatives.[85-87] Even hydrophobic ionic liquids can accommodate water.[88] Ionic liquids are usually dried by heating under vacuum. However, water is difficult to remove completely probably due to the existence of hydrogen bonding. The presence of water can reduce the density and the viscosity but can also modify the chemical properties. In some cases, e.g. PF_6 based salts, traces of water can generate the decomposition of the anion and the formation of HF.

1.1.9. Properties

The special structural make up of IL is that the physical and chemical properties can be tuned by the careful selection of cations and anions.

Melting point

The most interesting and most debated property of the IL is the melting point. Recent literature reveals the complexity in correlating structure and chemical composition with melting points. Table 1 provides M.Ps of some salts with chloride anion.[89]

Table 2. Melting points of various chlorides

Salt	M.P. ^oC
NaCl	803
KCl	772
$[MMIM]^+Cl^-$	125
$[EMIM]^+Cl^-$	87
$[BMIM]^+Cl^-$	65

In comparison with inorganic salts these have a low symmetry,[90] weak intermolecular interactions[19,92] and good charge distribution in both cations and anions.[93] Increase the size of anions also decreases the MPs. Larsen et.al[45] studied in detail the low melting character of imidazolium salts. They used a weakly coordinating anion i.e carborane and varied the alkyl chain length in the imidazolium moiety. They concluded that the positional disorder of the cations in the crystal structures, which is a direct indicator of packing inefficiency is the reason behind the low melting of these I.Ls having larger anions. If the cation/anion interactions are reduced to the level of van der Waals or very weak hydrogen bonding type forces, then the disorder reflects packing inefficiency.

Vapour Pressure and Thermal Stability

I.Ls have no measurable vapor pressure. This feature is advantageous from engineering point of view as the reactants and products can be easily distilled off from the reaction mixture, which makes more effective method for isolation. Moreover azeotrope formation between the solvent and the products does not arise.

Thermal stability of I.Ls is higher than other molecular solvents. It depends on the strength of heteroatom-carbon and heteroatom-hydrogen bonds. I.Ls synthesized by direct protonation of an amine or a phosphane show restricted thermal stability. I.Ls obtained by alkylation of an amine or phosphane have a tendency to undergo thermally induced transalkylation or dealkylation which will depend on the nature of anion. Dialkylimidazolium based I.Ls have been shown to exhibit very high thermal stability upto $400^{o}C$[19] and in some cases it may be more than $450^{o}C$.

Density

Density is an important property particularly used in fluid flow calculations and the design of liquid/liquid two phase mixer-settler units. It can be generalized that the density of I.Ls depend on the bulkiness of anion.[19] It has been observed that changes in the structure of cation also can have slight changes in the density of I.L.

Viscosity

The viscosity of I.Ls is essentially governed by their tendency to form hydrogen bonding and by the strength of their van der Waals interactions.[19] Comparison of the viscosity of different dialkylimidazolium based I.Ls emphasizes the interplay between van der Waals interactions and hydrogen bonding. For e.g.[19] an increase in viscosity was observed for butylmethylimidazolium I.L when triflate anion is displaced with $n\text{-}C_4F_9SO_3^-$ ion and from the trifluoroacetate ion to $n\text{-}C_3H_7COO^-$ ion. This is due to increased van der Waals interactions in the case of $n\text{-}C_4F_9SO_3^-$ and $n\text{-}C_3F_7COO^-$ ions. Comparison of the viscosities of $[bmim]CF_3SO_3$ with $[bmim](CF_3SO_2)_2N$, reveals a lower viscosity despite stronger van der Waals interactions for I.Ls with $(CF_3SO_2)_2N^-$ ion. In this case, the almost complete suppression of hydrogen bonding overcompensates for the expected increase in viscosity.

The structure of cation also influences viscosity of I.Ls. Increasing the chain length or with fluorinated alkyl chains will result in higher viscosity.

The viscosity of I.Ls can be lowered drastically in some cases, by only slight increase in temperature [93] or by the addition of small amounts of organic cosolvents.[94]

Polarity and Solvent properties

Solvent polarity is the most commonly used criterion for solvent classification. Even when considering molecular solvents it is poorly understood and often confused. Terms such as polar, apolar, and nonpolar are used indiscriminately to apply to values of dielectric constants, dipole moments, and polarizabilities, even though none of these are directly correlated in a simple way. The simplest qualitative definition is that a polar solvent is one that will dissolve and stabilize dipolar or charged solutes. It is widely thought, though yet to be generally demonstrated, that under this definition, ionic liquids will be highly polar solvents. The longest wavelength absorption band of Reichardt's dye (2,4,6-triphenylpyridinium *N*-4-(2,6-diphenylphenoxide) betaine shows one of the largest solvatochromic shifts known (375 nm between diphenylether and water).[95] It can register effects arising from the solvent dipolarity, hydrogen bonding, and Lewis acidity and is considered to be a good general polarity scale. The E_T^N values of a small number of alkylammonium nitrate,[96] thiocyanate,[96] and sulfonate[97] salts have been recorded. Values of ca. 0.95-1.01 for monoalkylammonium nitrates and thiocyanates are close to that of water (1.00, by definition), whereas quaternary ammonium sulfonates give lower values of ca. 0.45-0.65 which are more typical of polar organic solvents such as DMSO. An attempt was also made to separate dipole-dipole polarizability effects from hydrogen-bonding effects by using the $p*$ scale of dipolarity/polarizability, the R scale of hydrogen-bond-donor acidity, and the , scale of hydrogen-bond basicity.[97] Although some difference was seen between the $p*$ values for monalkylammonium salts and the quaternary ammonium salts, the difference in the hydrogen-bond acidities and basicities was far more marked.

The solvent properties of these ionic liquids have also been investigated using chromatographic techniques.[96,97,98] It was generally found that the ionic liquids could be considered to be polar phases with the solvent properties being largely determined by the ability of the salt to act as a hydrogen-bond donor and/or acceptor and the degree of localization of the charge on the anions. However, the ammonium and phosphonium salts that were used would not exhibit large differences in the delocalization of charge on the cation, and this may be an important effect for other salts, such as the pyridinium- and imidazolium based ionic liquids. Furthermore, it was found that increasing the chain length of alkyl substituents on both cations and anions leads to greater lipophilicity of the ionic liquids.[97,99] Also, the influence of hydrogen bonding can be diminished by fluorinating the ionic liquids.[100]

Handling and availability

The handling of ionic liquids depends essentially on the stability of the anion towards hydrolysis. Whereas ionic liquids with nitrate, benzenesulfonate, and [bis(trifluormethylsulfonyl]amide ions, for example, are air and water stable and can even be synthesized in water, systems with chloroaluminate anions must be classified as extremely hygroscopic and labile towards hydrolysis. More difficulties arise when traces of water in chloroaluminate melts react with the anions of the melt to release superacid protons. These cause unwanted side reactions and possess a considerable potential for corrosion. To sum up: the handling and stability of ionic liquids cannot be easily assessed, but it is mainly dependent on the nature of the anion. The commercial availability of ionic liquids was very limited until recently. Only a small number of systems could be purchased from chemical distributors in small quantities (up to 25 g).[101] Since the end of 1999, a large variety of ionic liquids is now commercially available in up to 5 liter scale.[102] If demand for ionic liquids grows further, it is supposed that in the near future particularly producers of ionic liquid precursor compounds (such as amines) will enter the market. In this case it is expected a drastic decrease in prices for ionic liquids. It should be specifically noted here that after most applications the used ionic liquid can be easily recovered, cleaned up - if necessary - and reused repeatedly. In an ideal case the cost for the ionic liquid can be therefore regarded as a one-time investment.

Environmental aspects

Recently ionic liquids have often been discussed as promising solvents for clean processes and green chemistry.[8] These two catchwords represent current efforts to reduce drastically the amounts of side and coupling products and also the solvent and catalyst consumption in chemical processes. The use of ionic liquids could make a contribution in this area, particularly with regard to solvent and catalyst usage. In contrast to volatile organic solvents and extraction media, ionic liquids have no measurable vapor pressure. Therefore there is no loss of solvent through evaporation. Environmental and safety problems arising through the use of volatile organic solvents can also be avoided by the use of a nonvolatile ionic reaction medium. Specifically, the ecotoxicity and ecological impact of most of the ILs are not well documented. Since I.Ls are non-volatile, it is clear that most likely medium for their introduction into environment will be aqueous streams. Uptil now no detailed toxicity study have been conducted for the I.Ls. Very recently Pernak's studies on mammalian toxicity for imidazolium based I.Ls indicates relatively very low toxicity.[116]

1.1.10. Applications of I.Ls

Commercial utility of I.Ls are yet to be established. The main constraint for the commercialization will be the cost of I.Ls. Future research and the utilization of I.L.s in various applications will definitely bring down the prices. All the potential uses of I.Ls have not yet been exploited. Nevertheless some of the important applications for which the unique properties of I.Ls will be advantageous are described below.

Reactions

A wide variety of reactions have been reported in I.Ls. Many reactions resulted in higher rates and better selectivity as compared with molecular solvents. Indeed these solvent systems suit well for catalysis as[7j]

- Monophasic systems in which catalysts and substrates are dissolved in I.Ls.
- Monophasic systems in which the IL acts as both the solvent and the catalyst.
- Biphasic systems in which the catalysts resides in the IL and the substrate and product in the second phase.
- Mono- or biphasic systems in which the anion of the IL acts as a ligand for homogeneous catalyst
- Triphasic systems comprising, for example, an ionic liquid, water and an organic phase in which the catalyst resides in IL, the substrate/product in organic phase and salts formed are extracted into aqueous phase.

I.Ls have been successfully used in a variety of reactions. Hydrogenations,[103,104] oxidations,[105] hydroformylations,[103,106,107] Heck reaction,[108,109] dimerizations,[110] alkylations, [111,112] Diels-Alder reactions[113, 114] are some of the few in the long list of successful reactions in ILs. Homogeneous catalysis imparts greater selectivity than their heterogeneous counterpart, but separation of the catalyst from the product system is difficult. It has been found that the partition coefficient of the most common metal-centered homogeneous catalysts greatly favors I.L phase over immiscible organic phase. This property essentially can be utilized for easy recovery of catalysts and recycling. Recently biotransformations in I.L have been reported.

The ionic nature of the I.Ls can be utilized to control the reaction chemistry either by participating in the reaction or stabilizing highly polar ionic transition state. The unique property of I.L.s to dissolve a number of polar as well as non-polar substrates including some inorganic compounds opens the scope of replacing multi-phase systems to single phase.[115]

Gas Separations

The hygroscopic nature of many I.Ls are utilized to remove water vapour from gas mixtures. Recently Blanchard et.al. demonstrated the solubility of carbon dioxide in I.Ls. At 40 °C and just at 50 bar pressure, $[bbim]PF_6$ dissolves 0.5 mol fraction of CO_2.[115] Even the dissolution of large amount of CO_2 in I.Ls there will be only 10% increase in bulk volume. A recent study by Anthony et.al.[117] showed that the I.Ls can be tailor made by choice of cation, anion and substituents to increase the gas solubility. On account of the difference in the solubilities of gases in I.Ls, they can be used for gas separations. I.Ls, with their non-volatility, are suited for gas separations using supported liquid membrane since conventional liquid membranes suffer a major disadvantage of liquid loss due to evaporation.[117]

Other separations

Fadeev et.al[118] introduced the concept of using I.Ls for liquid separations, when he demonstrated the separation of alcohols from fermentation broth. Metals can be effectively extracted in an I.L/aqueous biphasic systems with some added chelates. Naphthalene is soluble in $[bmim]PF_6$ at room temperature, which is more than its solubility in n-hexane. At the same time, ethanol is freely soluble in I.L but immiscible with n-hexane. This property can be used in selective extraction processes.

Lubricants

I.Ls are good candidates for lubricants with their wetting property on metal, polymers and inorganic surfaces and also have a wider liquidus range and high thermal stability. Very little literature is available on this topic and can be investigated further.

Heat Transfer Fluids

The good liquidus range and high thermal stability makes I.L potential species as good heat transfer fluids.[7c] Some studies reveal that heat capacities of I.L are comparable with heavy hydrocarbon oils and conventional organic solvents.

Electrolyte/Fuel cells

Wide electrochemical window, high conductivity, wide operating temperature range and low dielectric constant make them attractive candidates for applications in batteries and fuel cells.[19] Moreover low inflammability and non-volatile nature provides robustness and safety. Several research papers are available describing the use of I.Ls in polymer gel-ionic liquid electrolytes, lithium-ionic liquid batteries and its use in photovoltaic cells.

1.1.11. Summary and Conclusion

Ionic liquid chemistry is at an incredibly and exciting area of development. The unique properties of these liquids and the possibility to tailor properties by choice of cation, anion and substituents, open the door to a variety of many processing options. In many applications ionic liquids with weakly coordinating anions and suitable substituted cations are attractive alternative "solutions" to commonly used solvents. They give rise to increased solubility of reactants/products, increase in rate and selectivity of reactions, biphasic catalysis, homogeneous catalysis etc. The liquid crystalline properties of some ionic liquids can result in a very highly ordered solvent environment for various end uses such as transition metal catalysis.

The following points are to be addressed in the future for their effective utilization towards the evolution of cost effective green technologies.

1. Fundamental knowledge for the design of ionic liquids – effect of cation, anion and substituents on its physical and chemical properties.
2. Quantitative Structure-Property Relationship (QSPR) modeling, which make use of the statistical link between the physicochemical properties of a compound and a set of molecular descriptors, can be used in the correlation of toxicity and corrosivity.
3. Detailed study on toxicology of ILs.
4. Ease of separation in their pure form and recyclability.
5. Cost of ionic liquids.

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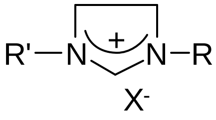
1.2.0. Synthesis and characterization of dialkylimidazolium based ionic liquids

The previous section provided an insight into the importance of the peculiar character and some of the applications of ionic liquids. Ionic liquids are organic salts, invariably possessing a high degree of asymmetry that frustrates packing and thus inhibits crystallization. The permutation and combination of anions and cations can result in numerous ILs with varied chemical and physical properties. Only very few papers[1-5] have appeared in literature with detailed study on physical and chemical properties of ILs with respect to changing anions and cations. A search for a substitute for expensive butylmethylimidazolium hexaflourophosphate [bmim][PF_6], which should have similar physical and chemical characteristics was inevitable.

This section deals with the synthesis, physical and chemical characterization of ionic liquids based on structure **1**.



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1.2.1. Introduction

Very few detailed studies have been reported on the physical and chemical properties of imidazolium based ionic liquids with respect to their changing alkyl chain length and anions. Mainly, the structure of I.L.s with respect to the change in alkyl chain length and the anions and their properties have been stressed in detail. Holbrey et.al.[3] prepared a series of ionic liquids keeping R=Methyl and R'=C_0-C_{18} in the cation and tetraflouroborate as anion. They have measured the melting points and the thermal properties with DSC and TG to establish the stability and also they predicted some liquid crystallinity when the alkyl chain length is increased. Larsen et.al.[2] conducted a detailed examination of the liquidus character of the highly ionic compounds, by single crystal XRD studies of dialkylimidazolium salts with the very weakly coordinating and inert Carborane anion. They concluded that the positional disorder, which induces packing inefficiency in the crystal lattice is the main cause of the low melting point of these species despite presence of large anions. Cation/anion interactions are decreased essentially to the level of van der Waals or very weak hydrogen bonding-type forces leading to packing inefficiency resulting in disorder.

1.2.2. Present Work

The ionic liquids based on structure **1** were synthesized by reported method.[1] The ionic liquids were purified by column chromatography. Density, viscosity, thermal stability, refractive index, NMR, I.R are recorded. The properties are correlated with the change in structure of cation and anion of I.L.s. All the alkyl groups are straight chain. For convenience hydrogen atoms are not shown.

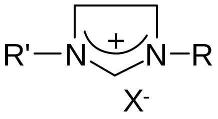

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Table 1. List of I.Ls synthesized.

Compd No.	R	R'	X	Compd No.	R	R'	X
1.	n-C_4	n-C_4	Br	9.	n-C_4	n-C_8	Br
2.	n-C_4	n-C_4	BF_4	10.	n-C_4	n-C_8	BF_4
3.	n-C_4	n-C_5	Br	11.	n-C_4	n-C_{10}	Br
4.	n-C_4	n-C_5	BF_4	12.	n-C_4	n-C_{10}	BF_4
5.	n-C_4	n-C_6	Br	13.	n-C_4	n-C_{12}	Br
6.	n-C_4	n-C_6	BF_4	14.	n-C_4	n-C_{12}	BF_4
7.	n-C_4	n-C_7	Br	15.	n-C_4	n-C_{18}	Br
8.	n-C_4	n-C_7	BF_4	16.	n-C_4	n-C_{18}	BF_4

1.2.3. Methods of Characterization

- ***NMR***

NMR spectra were recorded on Bruker AC 200 spectrometer. 2D- correlation spectroscopy (COSY) and concentration studies are done in Bruker 500 spectrometer.

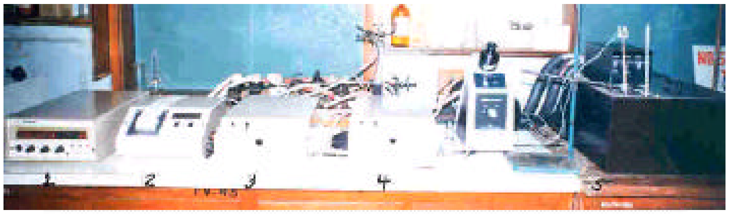
- ***Infrared Spectroscopy***

Infrared spectra were recorded on ATI MATTSON RS-1 FT-IR spectrometer.

- ***Single Crystal X-Ray Diffraction studies***

The single crystal X-ray diffraction data were collected on a Bruker SMART APEX CCD Area detector at –120°C. SHELX-97 was used for structure refinement and solution.

- ***Density measurements***



1- DENSIMETER PROCESSING UNIT (DMA- 60)
2- DENSIMETER PRINTER.
3- DENSIMETER REFERENCE CELL (DMA- 602)
4- DENSIMETER MEASURING CELL (DMA- 602)
5- CIRCULATING THERMOSTAT (HETOFRIG)

Fig 1. Densimeter

Densities were determined using an Anton Paar vibrating tube densimeter (DMA 602/60), which is shown in the Fig. 1. It consists of i) a processing unit (DMA 60) and ii) two external cells (DMA602) (one is measuring cell and other is reference cell) and iii) a thermostat (Heatofrig). Density determination is based on measuring the period of oscillation T of a vibrating U – shaped sample tube (2mm i.d) which is filled with the sample liquid. The introduction of liquid or gas in the tube changes the frequency of oscillation and hence the density. The following relationship exists between the period T and density d where ρw is he density of calibrating substance (water), $T\rho$ is the period of oscillation of calibrating substance (water), $T\rho x$ is the period of oscillation for unknown sample and To is the period for vacuum.

$$d = \left(\frac{\rho_w}{\left(T_\rho / To \right)^2 - 1} \right) \left(\left(\frac{T_{\rho x}}{T_o} \right) - 1 \right) \qquad \text{---------------- } \textbf{Equation 1}$$

Air and distilled water were used as standard fluids. Temperature of the cells was controlled within ± 0.01 K by thermostat water circulated around the cells. The density of an unknown liquid sample was obtained by introducing the sample in one cell and water as reference into the other cell. After measuring T, d was calculated using equation **1**.

- ***Viscosity***

Viscocity was measured in Brookfield Digital viscometer, Model DV-I at room temperature (30^oC).

- ***Dielectric Constant***

Dielectric Constant was measured using Microwave Microstrip Ring Resonator. When a Microwave Microstrip Resonator is perturbed by a dielectric overlay, the effective dielectric constant of the system changes. The change in effective dielectric constant results in change in resonating frequency. Measuring the change in resonating frequency, the dielectric constant of the overlay material can be found out as documented elsewhere.

- ***Refractive Index***

Refractive index measurements were performed using AVVE refractometer, MARK II PLUS, LEICA made.

- ***Thermogravimetric analysis***

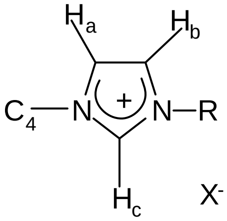
TG-DTA was done using machine MODEL No. PG-320, Seiko, Japan. Argon is used as carrier gas. Weight of sample = 20mg.

1.2.4. Results and Discussions

- **Synthesis**

The different I.Ls are prepared by the quarternization of previously prepared 1-n-butylimidazole with the respective alkyl bromide resulting in the bromo I.L. This is converted into BF_4 salt by the metathesis reaction with sodium tetraflouroborate. Br salt is obtained quanitatively in a neat reaction of alkyl bromide with 1-n-butylimidazole at 70^oC under inert atmosphere. A very viscous liquid (consistency of honey) was obtained with a yellowish to brown colour. The colour can be removed to a certain extent by charcoal treatment. The metathesis reaction is carried out in water. Almost all bromo I.L.s upto C_{10} are soluble in water. To the aqueous solution, sodium tetraflouroborate solution in water is added with stirring. The solution turns milky immediately due to the precipitation of water insoluble BF_4 salt. After 10h of stirring, the BF_4 salt layer was extracted with ethyl acetate. The organic layer was washed with water, dilute hydrochloric acid, sodium bicarbonate solution, finally with brine and removal of solvent furnished the BF_4 salt in high purity.

- **NMR studies**



From the 1H-NMR values of various I.Ls it is clear that chemical shifts of imidazolium protons (i.e. H_a, H_b and H_c) depend on anion and concentration. This effect is strong for H_c proton and weaker for Ha and Hb. This effect can be explained by two phenomena i) H-bonding and ii) ring stacking.

Table 1 ^{1}H NMR values of protons of imidazolium cation

No.	I.L.s		Ha	Hb	Hc
	R	X			
1.	C_4	Br	7.5(s)	7.5(s)	10.43(s)
2.	C_4	BF_4	7.38(s)	7.38(s)	8.87(s)
3.	C_5	Br	7.54(t,2Hz)	7.54(t,2Hz)	10.43(s)
4.	C_5	BF_4	7.4(s)	7.4(s)	8.88(s)
5.	C_6	Br	7.52(t,2Hz)	7.52(t,2Hz)	10.43(s)
6.	C_6	BF_4	7.38(t,1.6Hz)	7.38(t,1.6Hz)	8.89(s)
7.	C_7	Br	7.48(t,2Hz)	7.53(t,2Hz)	10.41(s)
8.	C_7	BF_4	7.38(t,1.6Hz)	7.41(t,1.6Hz)	8.93(s)
9.	C_8	Br	7.48(t,2Hz)	7.53(t,2Hz)	10.43(s)
10.	C_8	BF_4	7.39(t,1.6Hz)	7.42(t,1.6Hz)	8.87(s)
11.	C_{10}	Br	7.47(t,2Hz)	7.54(t,2Hz)	10.37(s)
12.	C_{10}	BF_4	7.33(t,1.6Hz)	7.36(t,1.6Hz)	8.90(s)
13.	C_{12}	Br	7.48(t,2Hz)	7.53(t,2Hz)	10.41(s)
14.	C_{12}	BF_4	7.38(t,2Hz)	7.38(t,2Hz)	8.89(s)
15.	C_{18}	Br	7.48(t,2Hz)	7.53(t,2Hz)	10.41(s)
16.	C_{18}	BF_4	7.38(t,2Hz)	7.38(t,2Hz)	8.89(s)

It is well known that the formation of H-bonds causes a downfield chemical shift of proton. H-bonding in imidazolium ring depends on the basicity of anion. It is logical to assume that H_c proton is less electron rich than H_a and H_b because it is attached to carbon in between two electronegative nitrogen atoms. So H_c proton is more prone for H-bonding with counter anion than others. This is so the case as evidenced from NMR shifts of H_c proton. In the case of more electronegative and basic Br^-, the shift is at 10. But in the case of less electronegative and basic anion BF_4^- the shift is at 8.8 ppm. From this it can be proved that BF_4 salts are more covalently bonded than its Br counterpart. This is also agreeing with the solubility of these salts in water. BF_4 salts are hydrophobic and Br salts are hydrophilic in nature. This characteristic property can be made use of in designing I.Ls of different polarities and solubilities in water.

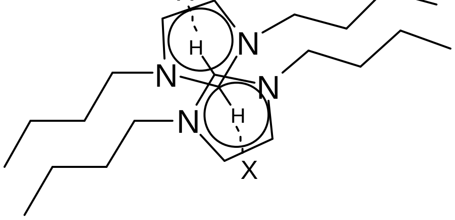
Table 2. ^{1}H-NMR chemical shifts of $C_{18}C_4$IMBr as a function of molar concentration (I.L/m) in $CDCl_3$

I.L./m	H_a	H_b	H_c
0.022	10.83	7.26	7.24
0.066	10.62	7.46	7.41
0.132	10.53	7.50	7.44

Chemical shifts also depend on concentration of solution as shown in Table 2. It is expected that a concentration increase will displace the equilibrium

$$(RR'Im^+)_{solv} + (X^-)_{solv} \rightleftarrows RR'Im^+.....X^-$$

to the right and thus lead to a chemical shift increase. This is observed in compounds with more basic Br^- anion. In BF_4^- salts, this is not prominent. H_c proton shifts downfield and H_a and H_b protons shift upfield when solution is dilute. When solution is concentrated, the H_c proton



2

has an upfield shift and H_a and H_b protons have downfield shifts. A similar effect was noticed by Welton et. al. They explained this phenomena due to crystal stacking of I.L.s. The imidazolium cation generates two magnetically shielding cones above and below its molecular plane which is caused by an electronic current circulating around the π-orbitals, on both sides of aromatic ring. It can be explained that with concentration increase, the imidazolium cations progressively form ion pairs with the anions, which stack as neutral aromatic systems do.

This can be rationalized based on the top-to-bottom structure, **2**, proposed by Welton et. al.[6] When concentration is more, the H_c proton enters into the shielding cone of neighbouring imidazolium and exhibits an upfield shift. While H_a and H_b protons, pointing outside, are only influenced by H-bonding. In a weakly basic anion, this H-bonding is negligible and the shift also will be negligible. In dilute solution there will not be any top-to-bottom structural packing.

- ***COSY NMR studies***

In the 1H NMR spectrum of I.L.s it was observed that the imidazolium protons are split in a peculiar way. It was found from splitting pattern, the H_a and H_b protons were split into a triplet with J = 2Hz for Br^- series and J = 1.6Hz for BF_4^- series. Increase in length of alkyl chain on one side resulted in the increased shift between Ha and Hb protons. To get a clear picture of the coupling of the imidazolium protons, a 2-d correlation spectroscopy (COSY) study was carried out. COSY spectrum revealed that all the three protons are interacting with each other and this resulted in the triplet of H_a and H_b. Both these protons were engaged in a long range coupling with H_c. Although splitting of H_c was not clear from 1H NMR spectra, there is a small hump, from which it can be concluded that both H_a and H_b protons influence H_c proton by long range coupling.

- **Infrared Spectra**

C-H stretching vibrations are observed in the region 4000-2000cm^{-1}. Evidence for the presence of hydrogen bonding can be obtained from the band in the region 3050-3080 cm^{-1} which is regarded as diagnostic of the presence of a strong discrete C_2 proton – X- hydrogen bond. Weak absorption from 2500-2850cm^{-1} may be attributed to the formation of hydrogen bonds between imidazolium protons and the halide ion in the case of Br salt.

BF_4 is a weakly complexing anion and is not expected to participate in strong hydrogen bonding. This indeed is the case with BF_4 salt where very weak bands are observed in 3000-

3100 cm^{-1} region. Therefore IR results are consistent with a lack of hydrogen bonding in salts containing weakly complexing anions.

In conclusion, the cation-anion coulombic attraction is the driving force behind the overall structure of I.L., with local steric effects influencing the final orientation of ions. It is also possible that the orientation of alkyl groups plays a role in hydrophobic effects.

Single Crystal X-ray diffraction studies

Crystal structure of [(C$_{12}$)$_2$IM]$^+$Br$^-$ have been determined. The crystallization was carried out in cold condition (-4^{o}C) by dissolving IL in minimum amount of dichloromethane and adding n-hexane to the solution. The crystal structure showed occluded dichloromethane. As illustrated in the figures, the imidazolium cation seems to be arranged in order. These well ordered structure resulted in high melting point (82^{o}C) of this IL. The Br- lies in close proximity to imidazolium cation. It is not clear from the structure as well as packing diagram, the interaction of Br$^-$ with the cation. Also the interaction between H atoms and Br$^-$ is also speculative.

Table 1. Crystal data and structure refinement

Temperature - 153(2) K

Wavelength - 0.71073 Å

Crystal system, space group - Monoclinic, C2/c

Unit cell dimensions - a = 11.476(5) Å alpha = 90 deg.
b = 13.362(6) Å beta = 97.027(10) deg.
c = 40.878(17) Å gamma = 90 deg.

Volume - 6221(5) Å^3

Z, Calculated density - 8, 1.125 Mg/m^3

Absorption coefficient - 1.423 mm^{-1}

F(000) - 2272

Crystal size - 0.67 x 0.42 x 0.15 mm

Theta range for data collection - 2.01 to 28.00 deg.

Limiting indices - -15<=h<=7, -15<=k<=16, -44<=l<=51

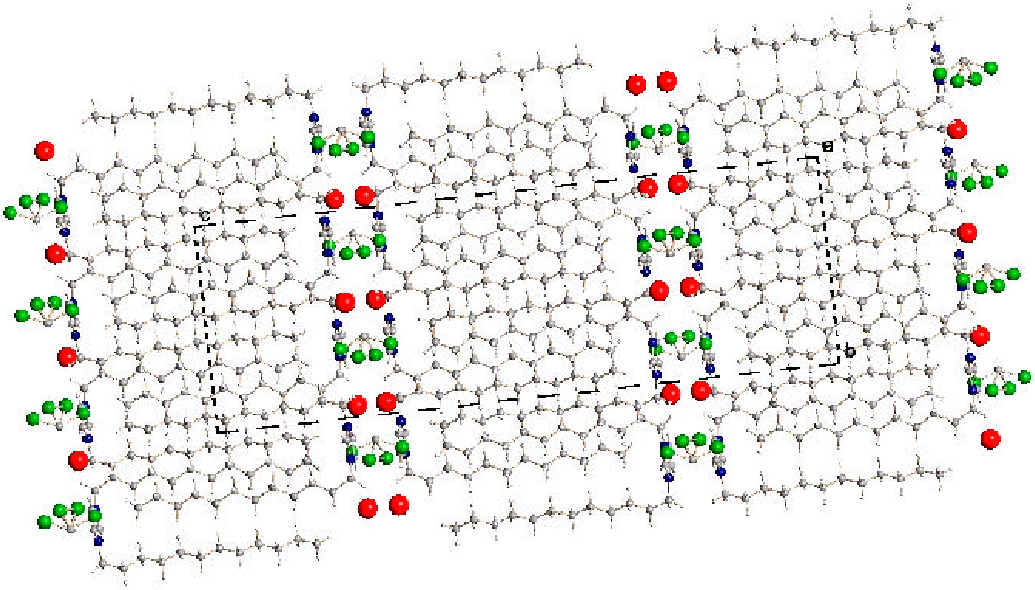
Reflections collected / unique - 14337 / 6678 [R (int) = 0.0524]

Completeness to theta = 28.00 - 88.7 %

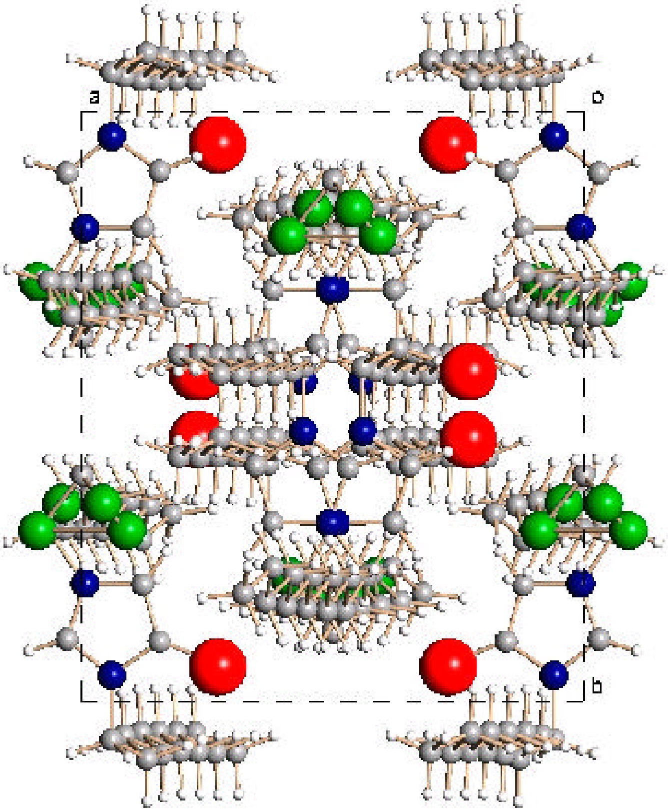
Data / restraints / parameters - 6678 / 0 / 296

Final R indices [I>2sigma(I)] R1 = 0.0653, wR2 = 0.1416

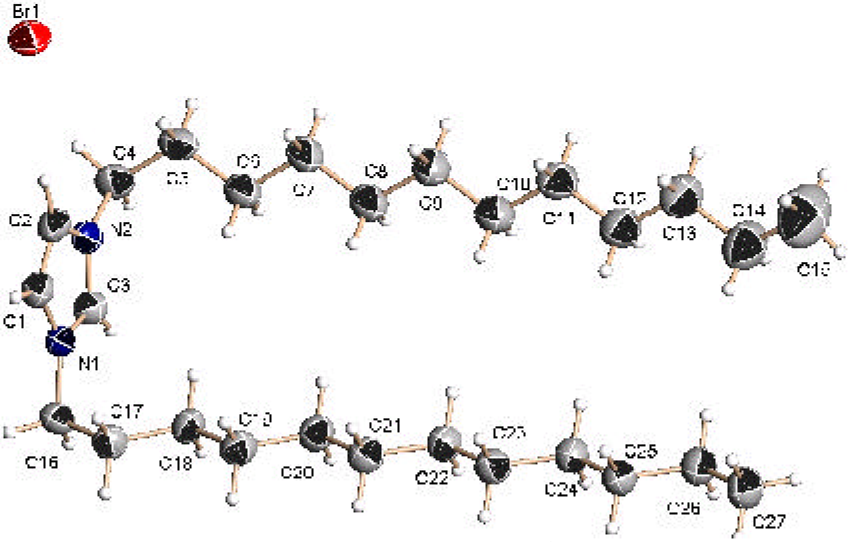
R indices (all data) R1 = 0.1109, wR2 = 0.1597
Largest diff. peak and hole - 0.618 and -0.375 e. Å^{-3}



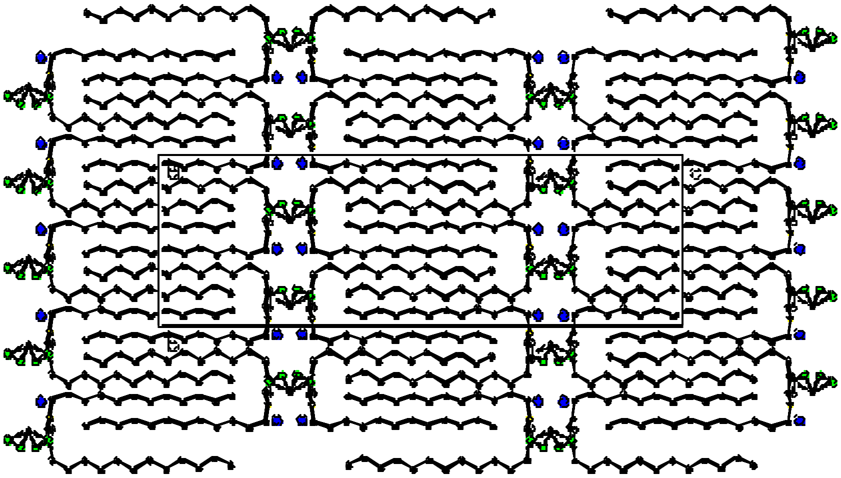
Packing of molecules down b-axis



Packing of molecules down c-axis



ORTEP diagram of $[(C_{12})_2IM]^+Br$



Packing of molecules down a-axis

1.2.5. Physical Properties

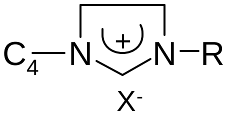


Table 3. Physical properties of ILs.

No.	I.L		Refractive Index	Density g/cc
	R	X		
1.	C_4	Br	1.5123	1.228
2.	C_4	BF_4	1.4284	1.152
3.	C_5	Br	1.5094	1.231
4.	C_5	BF_4	1.4307	1.101
5.	C_6	Br	1.5075	1.208
6.	C_6	BF_4	1.4345	1.098
7.	C_7	Br	1.5103	1.141
8.	C_7	BF_4	1.4467	1.07
9.	C_8	Br	1.5054	1.109
10.	C_8	BF_4	1.4381	1.054
11.	C_{10}	Br	1.5029	1.094
12.	C_{10}	BF_4	1.4423	1.035
13.	C_{12}	Br	1.4945	1.054
14.	C_{12}	BF_4	1.4449	1.02

- **Density**

The overall density of I.L. heavily depends on the molar mass of anion. In the case of imidazolium based I.L.s, addition of $–CH_2$- groups to the alkyl chain decreases the density. The contribution of the larger hydrophobic anions also decreases the density of the I.L. This may be due to weaker molecular attraction and weak hydrogen bonding which decreases molecular agglomeration.

- **Viscosity**

Viscosity is probably the most important physical property for initially determining the processability of a solvent. Ideally one would like the viscosity of a fluid to be as low as

Table 4. Viscosity of I.Ls at room temperature

No.	I.L		Viscosity cP
	R	X	
1.	C_4	Br	383.37
2.	C_4	BF_4	39.32
3.	C_8	Br	154.04
4.	C_8	BF_4	39.26

possible allowing the fluid to be pumped easily. In addition it is desired for the fluid to have only small changes in viscosity in the normal operating temperature range.

Previous studies show that the viscosity of I.L.s is mainly controlled by hydrogen bonding, van der Waals forces, molecular weight and mobility. In respect to the cation structure, alkyl chain lengthening by fluoroalkyl groups make the salt more viscous. Also reduction of freedom of rotation or ramification of alkyl chain length (n-butyl to iso-butyl) increases the viscosity.

Viscosity is on a higher side for I.L.s with more basic anion. This is clearly demonstrated from the data recorded as shown in table . In BF_4 based I.Ls because of less basic anion, the van der Waals forces dominates over the H-bonding due to better charge delocalization. This will reduce the viscosity of the I.L.

- **Refractive Index**

From experimental data, it is clear that the more ‘ionic’ I.L.s have higher values of refractive index. The refractive index is related to the polarizability/dipolarity of the medium. So this data gives direct correlation of refractive index and polar nature of I.L.s. The more the value of R.I the more polar is the liquid.

- **Dielectric Constant**

The dielectric constant values of I.Ls are comparable with chloroform as shown in Table 5.

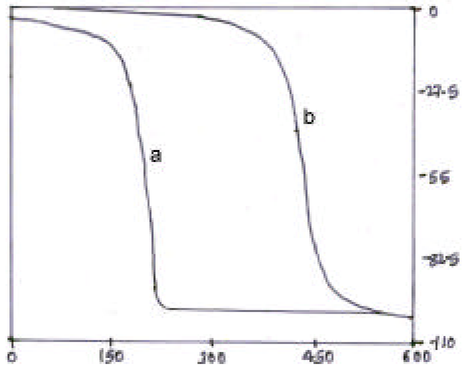
Table 5. Dielectric constants of different solvents

Solvent	Dielectric Constant
Water	78.54
Acetonitrile	37.5
Methanol	32.7
Dichloromethane	8.93
Tetrahydrofuran	7.58
Chloroform	4.81
[bbim]Br	**4.43**
[bbim]BF$_4$	**3.68**
Benzene	2.28

- **Thermal Analysis**

The I.L.s have no distinguishable vapour pressure and as a result it decomposes on heating. In general the I.L.s hitherto reported are thermally stable upto 400°C after which it tends to decompose and at around 480°C it completely decomposes.

From our experiments, it was clear that halide ions dramatically decrease the thermal stability by almost 100°C. Decomposition started at around 220°C and the IL fully decomposed at around 330°C.

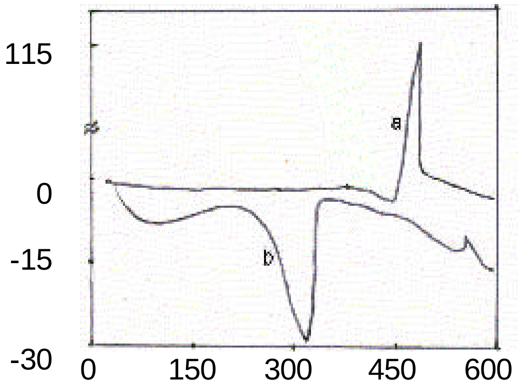


TG curves of a. $[bbim]^+Br^-$ and b. $[bbim]^+BF_4^-$

In the case of BF_4 salts, decomposition started at 335°C and at 480°C complete weight loss was observed. Increasing the cation size from $C_4C_4Im^+$ to $C_8C_4Im^+$ does not appear to have a significant effect on thermal stability.

Differential thermal Analysis (DTA) curves revealed a unique feature. Br^- salts resulted in an endotherm and BF_4^- salts gave an exotherm.

Usually the complete weight loss should occur with the absorption of heat, which will result in an endotherm. In the case of BF_4^- salts, there may be some side reaction, which can result in a more thermodynamically stable product. From the weight loss calculated from the exact decomposition temperature, it can be concluded that the decomposition of BF_4^- species into more stable BF_3 and F^- may have resulted in the endotherm.



DTA image of a. $[bbim]^+BF_4^-$ and b. $[bbim]^+Br^-$

1.2.6. Experimental

Preparation of $[bbim]^+Br^-$

1-Butylimidazole (10g) was heated with 1-bromobutane (12ml) at 70°C with good stirring for 2h. Excess 1-bromobutane was distilled off under high vacuum. The resulting thick brownish yellow liquid was dissolved in methanol and treated with activated charcoal at 60°C for 15 minutes, filtered and solvent evaporated to afford the product as a pale yellow viscous liquid.

Preparation of $[bbim]^+ BF_4^-$

This is obtained by the metathesis of $[bbim]^+ Br^-$ with sodium tetraflouroborate in water. $[bbim]^+Br^-$ (10g) was dissolved in water (50ml). To this solution, $NaBF_4$ (6g) dissolved in water (20ml) was added with good stirring. After the reaction, the bottom layer of the product was separated and the aqueous layer was extracted with dichloromethane (3x10ml). The combined product and dichloromethane extracts were washed with water, dried over sodium sulphate and solvent evaporated to furnish the product $[bbim]^+ BF_4^-$ as pale yellow free flowing liquid.

Compound 1

^{1}H NMR ($CDCl_3$, 200MHz): δ = 0.94 (t, J=7.0Hz, 6H, CH_3), 1.36 (sept, J=7.6Hz, 4H, $CH_3CH_2(CH_2)_2N$), 1.86 (pent, J=7.5Hz, 4H, NCH_2CH_2), 4.20 (t, J=7.0Hz, 4H, NCH_2), 7.50 (s, 2H, NCHCHN), 10.43 (s, 1H, NCHN).

^{13}C NMR ($CDCl_3$, 50MHz): δ = 13.18 ($NCH_2CH_2CH_2CH_3$), 19.21 ($NCH_2CH_2CH_2CH_3$), 31.89 ($NCH_2CH_2CH_2CH_3$), 49.57 ($NCH_2CH_2CH_2CH_3$), 122.61 (NCHCHN), 135.29 (NCHN).

Anal cald for $C_{11}H_{21}N_2Br$ (261): C=50.57%, H=8.05%, N=10.73%; found C=50.24%, H=7.91, N=10.54.

Compound 2

^{1}H NMR ($CDCl_3$, 200MHz): δ = 0.94 (t, J=7.0Hz, 6H, CH_3), 1.36 (sept, J=7.6Hz, 4H, $CH_3CH_2(CH_2)_2N$), 1.86 (pent, J=7.5Hz, 4H, NCH_2CH_2), 4.20 (t, J=7.0Hz, 4H, NCH_2), 7.38 (s, 2H, NCHCHN), 8.87 (s, 1H, NCHN).

^{13}C NMR (CDCl$_3$, 50MHz): δ = 13.18 ($\mathrm{NCH_2CH_2CH_2}\mathit{C}\mathrm{H_3}$), 19.21 ($\mathrm{NCH_2CH_2}\mathit{C}\mathrm{H_2CH_3}$), 31.89 ($\mathrm{NCH_2}\mathit{C}\mathrm{H_2CH_2CH_3}$), 49.57 ($\mathrm{N}\mathit{C}\mathrm{H_2CH_2CH_2CH_3}$), 122.61 ($\mathrm{N}\mathit{C}\mathrm{H}\mathit{C}\mathrm{HN}$), 135.29 ($\mathrm{N}\mathit{C}\mathrm{HN}$).

Anal cald for $C_{11}H_{21}N_2BF_4$ (268): C=49.25%, H=7.84%, N=10.45%; found C=49.08%, H=7.59, N=10.25.

Compound 3

^{1}H NMR (CDCl$_3$, 200MHz): δ = 0.84 (t, J=7.0Hz, 3H, CH$_3$), 0.91 (t, J=7.0Hz, 3H, CH$_3$), 1.29 (m, 6H), 1.88 (pent, J=7.5Hz, 4H, $\mathrm{NCH_2C}\mathit{H}_2$), 4.33 (t, J=7.0Hz, 4H, $\mathrm{NC}\mathit{H}_2$), 7.54 (t, J=2Hz, 2H, $\mathrm{NC}\mathit{H}\mathrm{C}\mathit{H}\mathrm{N}$), 10.43 (s, 1H, NCHN).

^{13}C NMR (CDCl$_3$, 50MHz): δ = 12.68, 13.05, 19.21, 31.89, 49.57, 121.89, 135.71.

Compound 4

^{1}H NMR (CDCl$_3$, 200MHz): δ = 0.89-0.95 (m, 6H, CH$_3$), 1.34 (m, 6H), 1.87 (m, 4H), 4.22 (t, J=7.0Hz, 4H, $\mathrm{NC}\mathit{H}_2$), 7.40 (s, 2H, $\mathrm{NC}\mathit{H}\mathrm{C}\mathit{H}\mathrm{N}$), 8.88 (s, 1H, NCHN).

^{13}C NMR (CDCl$_3$, 50MHz): δ = 12.76, 13.20, 18.82, 21.43, 27.64, 29.23, 31.50 49.52, 122.19, 135.01.

Compound 5

^{1}H NMR (CDCl$_3$, 200MHz): δ = 0.84-0.94 (m, 6H, CH$_3$), 1.38 (m, 6H, $\mathrm{CH_3C}\mathit{H}_2\mathrm{(CH_2)_2N}$), 1.86 (m, 6H, $\mathrm{NCH_2C}\mathit{H}_2$), 4.20 (t, J=7.0Hz, 4H, $\mathrm{NC}\mathit{H}_2$), 7.52 (d, J=2Hz, 2H, $\mathrm{NC}\mathit{H}\mathrm{C}\mathit{H}\mathrm{N}$), 10.43 (s, 1H, NCHN).

^{13}C NMR (CDCl$_3$, 50MHz): δ = 12.93,13.18, 18.92, 21.42, 26.57, 27.56, 29.42, 31.72, 49.30, 49.57, 122.57, 135.32.

Compound 6

^{1}H NMR (CDCl$_3$, 200MHz): δ = 0.84-0.94 (m, 6H, CH$_3$), 1.36 (m, 6H, $\mathrm{CH_3C}\mathit{H}_2\mathrm{(CH_2)_2N}$), 1.92 (m, 6H, $\mathrm{NCH_2C}\mathit{H}_2$), 4.18 (t, J=7.0Hz, 4H, $\mathrm{NC}\mathit{H}_2$), 7.38 (t, J=2Hz, 2H, $\mathrm{NC}\mathit{H}\mathrm{C}\mathit{H}\mathrm{N}$), 8.89 (s, 1H, NCHN).

^{13}C NMR (CDCl$_3$, 50MHz): δ = 12.93,13.18, 18.90, 21.32, 26.85, 27.53, 29.41, 31.89, 49.18, 49.57, 122.32, 135.51.

Compound 7

^{1}H NMR (CDCl$_3$, 200MHz): δ = 0.87-0.94 (m, 6H, CH$_3$), 1.27 (m,10H, $\mathrm{CH_3C}\mathit{H}_2\mathrm{(CH_2)_2N}$), 1.86 (pent, J=7.5Hz, 4H, $\mathrm{NCH_2C}\mathit{H}_2$), 4.32 (m, 4H, $\mathrm{NC}\mathit{H}_2$), 7.48 (t, J=2Hz, 1H, $\mathrm{NCHC}\mathit{H}\mathrm{N}$), 7.53 (t, J=2Hz, 1H, $\mathrm{NCHC}\mathit{H}\mathrm{N}$), 10.41 (s, 1H, NCHN).

^{13}C NMR (CDCl$_3$, 50MHz) : δ = 12.16, 12.87, 18.08, 21.09, 24.77, 27.27, 29.03, 30.17, 30.90, 48.33, 48.59, 121.29, 135.15.

Compound 8

^{1}H NMR ($CDCl_3$, 200MHz) : δ = 0.82-0.94 (m, 6H, CH_3), 1.26 (m, 10H, $CH_3C\mathit{H}_2(CH_2)_2N$), 1.83 (m, 4H, $NCH_2C\mathit{H}_2$), 4.19 (t, J=7.0Hz, 4H, $NC\mathit{H}_2$), 7.38 (t, J=1.8Hz, 1H, NC*H*C*H*N), 7.41 (t, J=1.8Hz, 1H, NC*H*C*H*N), 8.93 (s, 1H, NCHN).

^{13}C NMR ($CDCl_3$, 50MHz) : δ = 12.38, 13.04, 18.41, 21.57, 25.13, 27.67, 29.21, 30.65, 31.13, 48.33, 48.99, 121.77, 134.64.

Compound 9

^{1}H NMR ($CDCl_3$, 200MHz) : δ = 0.82-0.92 (m, 6H, CH_3), 1.21 (m,12H, $CH_3C\mathit{H}_2(CH_2)_2N$), 1.88 (pent, J=7.5Hz, 4H, $NCH_2C\mathit{H}_2$), 4.34 (m, 4H, $NC\mathit{H}_2$), 7.48 (t, J=2Hz, 1H, NCHC*H*N), 7.53 (t, J=2Hz, 1H, NCHC*H*N), 10.43 (s, 1H, NCHN).

^{13}C NMR ($CDCl_3$, 50MHz) : δ = 12.34, 12.89, 18.26, 21.38, 25.02, 27.82, 29.03, 30.46, 31.09, 48.33, 48.59, 121.29, 135.15.

Compound 10

^{1}H NMR ($CDCl_3$, 200MHz) : δ = 0.84-0.94 (m, 6H, CH_3), 1.29 (m, 12H, $CH_3C\mathit{H}_2(CH_2)_2N$), 1.86 (m, 4H, $NCH_2C\mathit{H}_2$), 4.21 (m, 4H, $NC\mathit{H}_2$), 7.39 (t, J=1.6Hz, 1H, NC*H*C*H*N), 7.42 (t, J=1.6Hz, 1H, NC*H*C*H*N), 8.87 (s, 1H, NCHN).

^{13}C NMR ($CDCl_3$, 50MHz) : δ = 12.93,13.18, 18.90, 21.32, 26.85, 27.53, 29.41, 30.57, 31.89, 49.18, 49.57, 122.32, 135.51.

Compound 11

^{1}H NMR ($CDCl_3$, 200MHz) : δ = 0.80-0.90 (m, 6H, CH_3), 1.18 (m,16H, $CH_3C\mathit{H}_2(CH_2)_2N$), 1.86 (pent, J=7.5Hz, 4H, $NCH_2C\mathit{H}_2$), 4.32 (m, 4H, $NC\mathit{H}_2$), 7.47 (t, J=2Hz, 1H, NCHC*H*N), 7.54 (t, J=2Hz, 1H, NCHC*H*N), 10.37 (s, 1H, NCHN).

^{13}C NMR ($CDCl_3$, 50MHz) : δ = 12.20, 12.89, 18.15, 21.14, 24.79, 27.29, 29.11, 30.21, 30.92, 48.35, 48.57, 121.32, 135.21.

Compound 12

^{1}H NMR ($CDCl_3$, 200MHz) : δ = 0.84-0.94 (m, 6H, CH_3), 1.24 (m, 16H, $CH_3C\mathit{H}_2(CH_2)_2N$), 1.87 (m, 4H, $NCH_2C\mathit{H}_2$), 4.20 (t, J=7.0Hz, 4H, $NC\mathit{H}_2$), 7.33 (t, J=1.6Hz, 1H, NC*H*C*H*N), 7.36 (t, J=1.6Hz, 1H, NC*H*C*H*N), 8.90 (s, 1H, NCHN).

^{13}C NMR ($CDCl_3$, 50MHz) : δ = 12.95,13.20, 18.97, 21.41, 26.87, 27.59, 29.48, 31.89, 49.18, 49.58, 122.24, 135.42.

Compound 13

^{1}H NMR ($CDCl_3$, 200MHz) : δ = 0.87-0.94 (m, 6H, CH_3), 1.22 (m,20H, $CH_3C\mathit{H}_2(CH_2)_2N$), 1.86 (pent, J=7.5Hz, 4H, $NCH_2C\mathit{H}_2$), 4.32 (m, 4H, $NC\mathit{H}_2$), 7.48 (t, J=2Hz, 1H, NCHC*H*N), 7.53 (t, J=2Hz, 1H, NCHC*H*N), 10.41 (s, 1H, NCHN).

^{13}C NMR ($CDCl_3$, 50MHz) : δ = 12.16, 12.87, 18.08, 21.09, 24.77, 27.27, 29.03, 30.17, 30.90, 48.33, 48.59, 121.29, 135.15.

Compound 14

^{1}H NMR ($CDCl_3$, 200MHz): δ = 0.84-0.94 (m, 6H, CH_3), 1.36 (m, 20H, $CH_3CH_2(CH_2)_2N$), 1.92 (m, 4H, NCH_2CH_2), 4.18 (t, J=7.0Hz, 4H, NCH_2), 7.38 (t, J=2Hz, 2H, NC*H*C*H*N), 8.89 (s, 1H, NCHN).

^{13}C NMR ($CDCl_3$, 50MHz): δ = 12.93,13.18, 18.90, 21.32, 26.85, 27.53, 29.41, 31.89, 49.18, 49.57, 122.32, 135.51.

Compound 15

^{1}H NMR ($CDCl_3$, 200MHz): δ = 0.87-0.94 (m, 6H, CH_3), 1.27 (m,32H, $CH_3CH_2(CH_2)_2N$), 1.86 (pent, J=7.5Hz, 4H, NCH_2CH_2), 4.32 (m, 4H, NCH_2), 7.48 (t, J=2Hz, 1H, NCHC*H*N), 7.53 (t, J=2Hz, 1H, NCHC*H*N), 10.41 (s, 1H, NCHN).

^{13}C NMR ($CDCl_3$, 50MHz): δ = 12.16, 12.87, 18.08, 21.09, 24.77, 27.27, 29.03, 30.17, 30.90, 48.33, 48.59, 121.29, 135.15.

Compound 16

^{1}H NMR ($CDCl_3$, 200MHz): δ = 0.84-0.94 (m, 6H, CH_3), 1.36 (m, 32H, $CH_3CH_2(CH_2)_2N$), 1.92 (m, 4H, NCH_2CH_2), 4.18 (t, J=7.0Hz, 4H, NCH_2), 7.38 (t, J=2Hz, 2H, NC*H*C*H*N), 8.89 (s, 1H, NCHN).

^{13}C NMR ($CDCl_3$, 50MHz): δ = 12.93,13.18, 18.90, 21.32, 26.85, 27.53, 29.41, 31.89, 49.18, 49.57, 122.32, 135.51.

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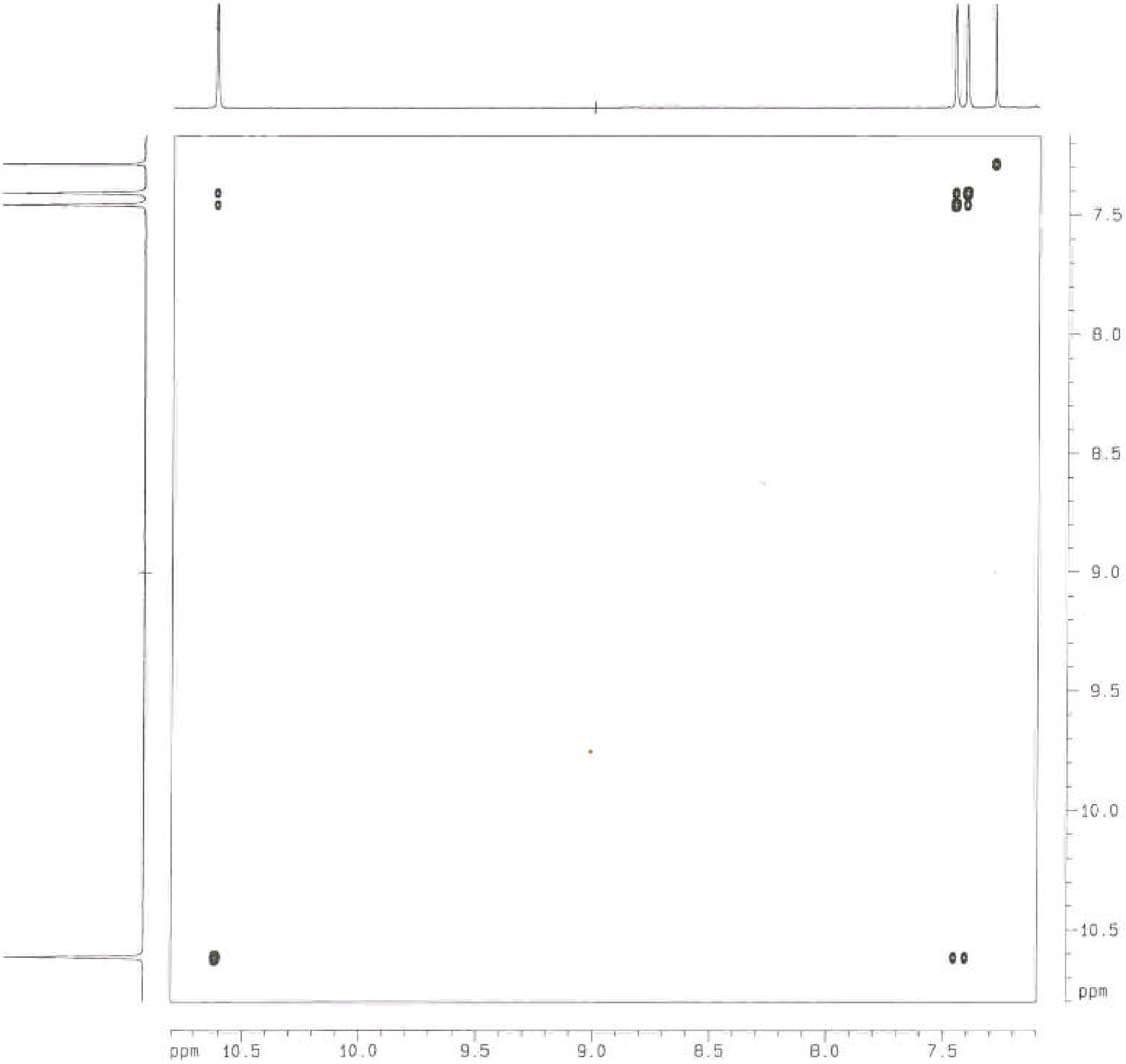
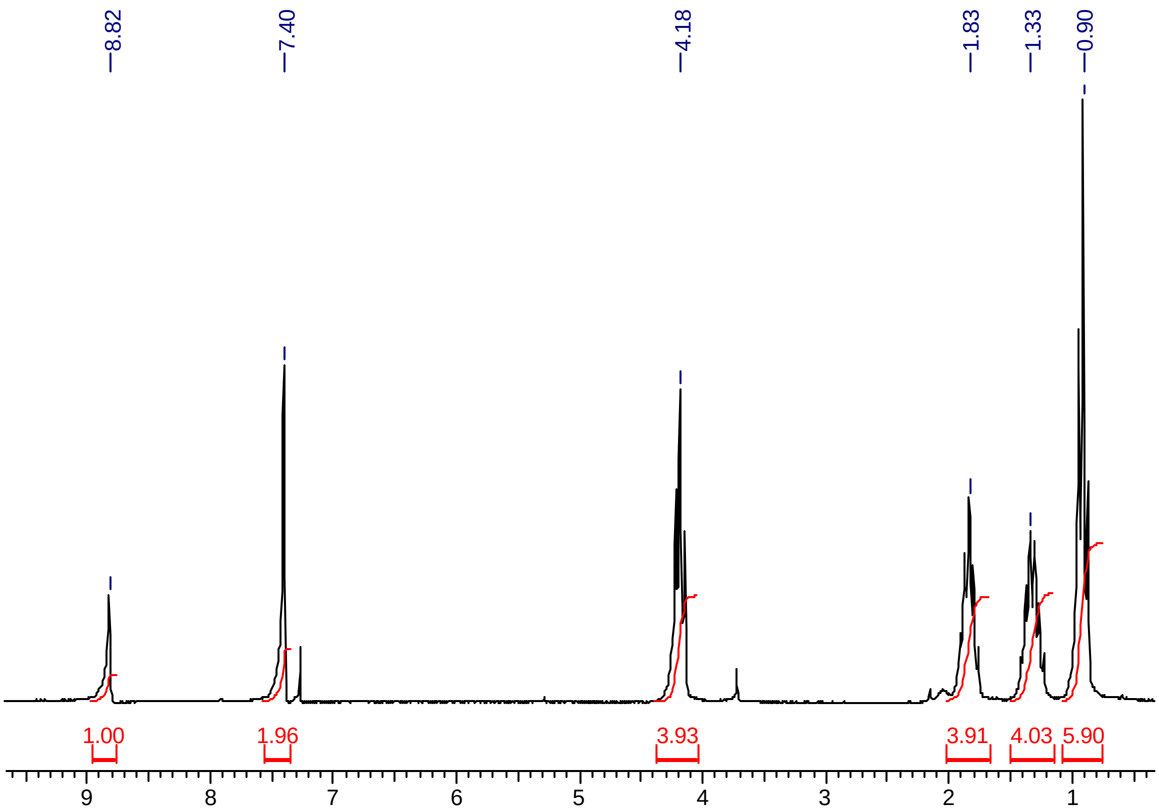
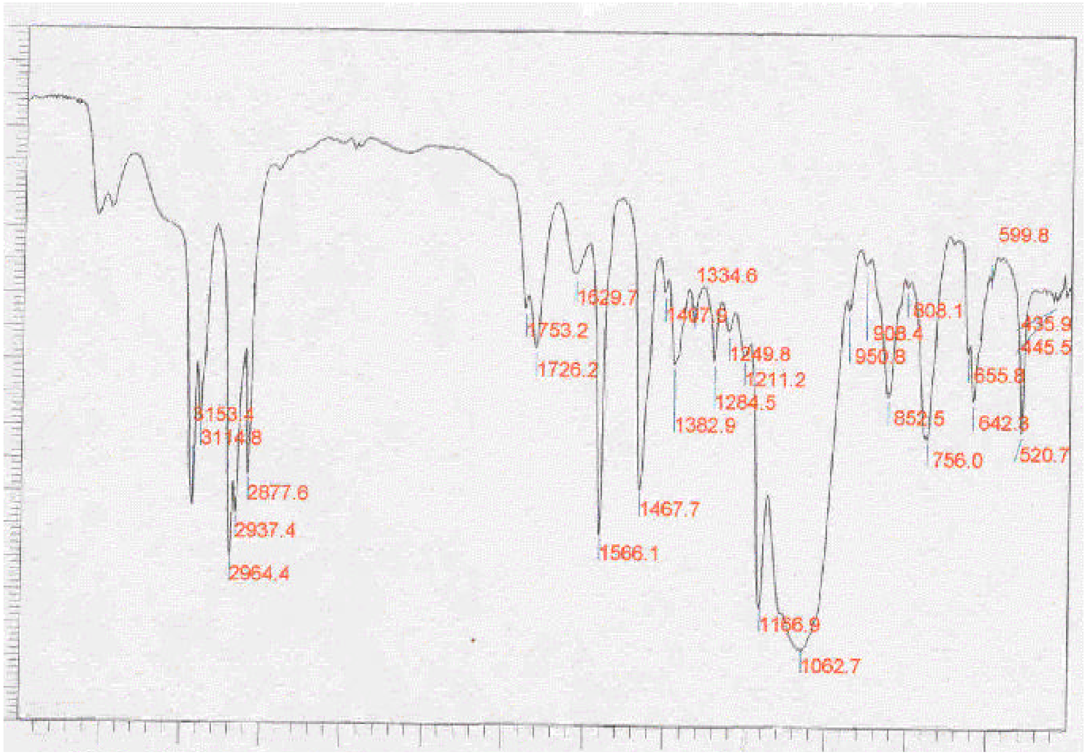


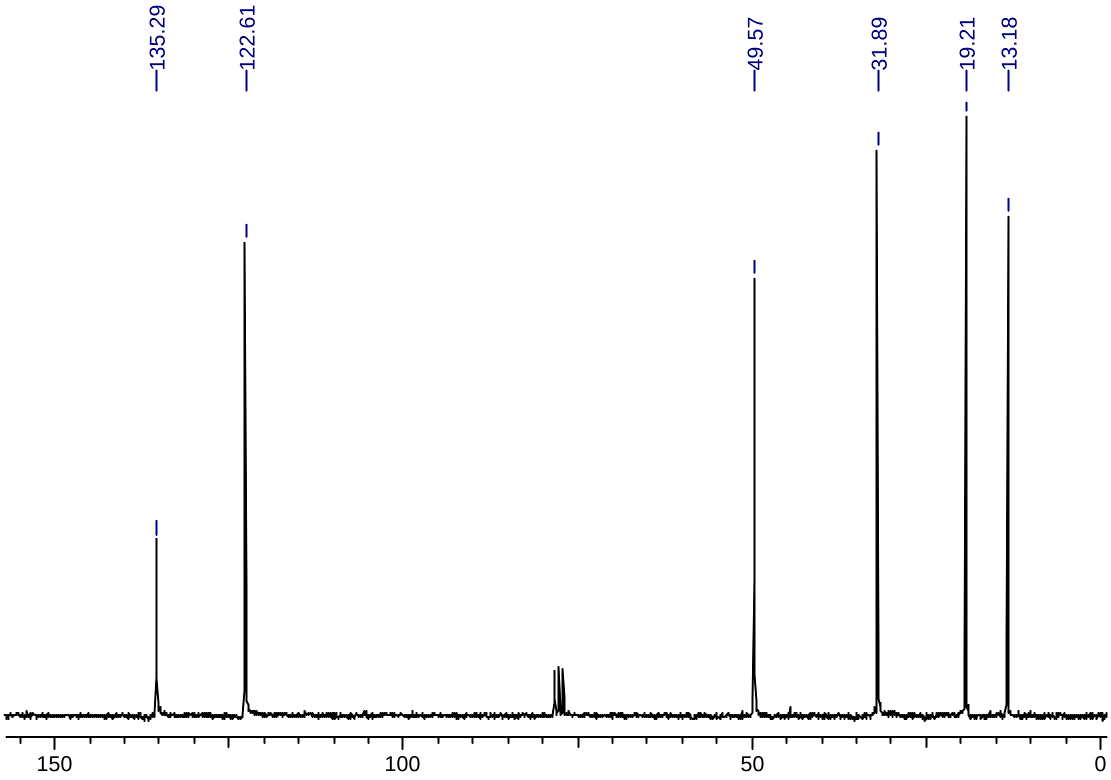
COSY of $[C_{18}C_4IM]^+Br^-$



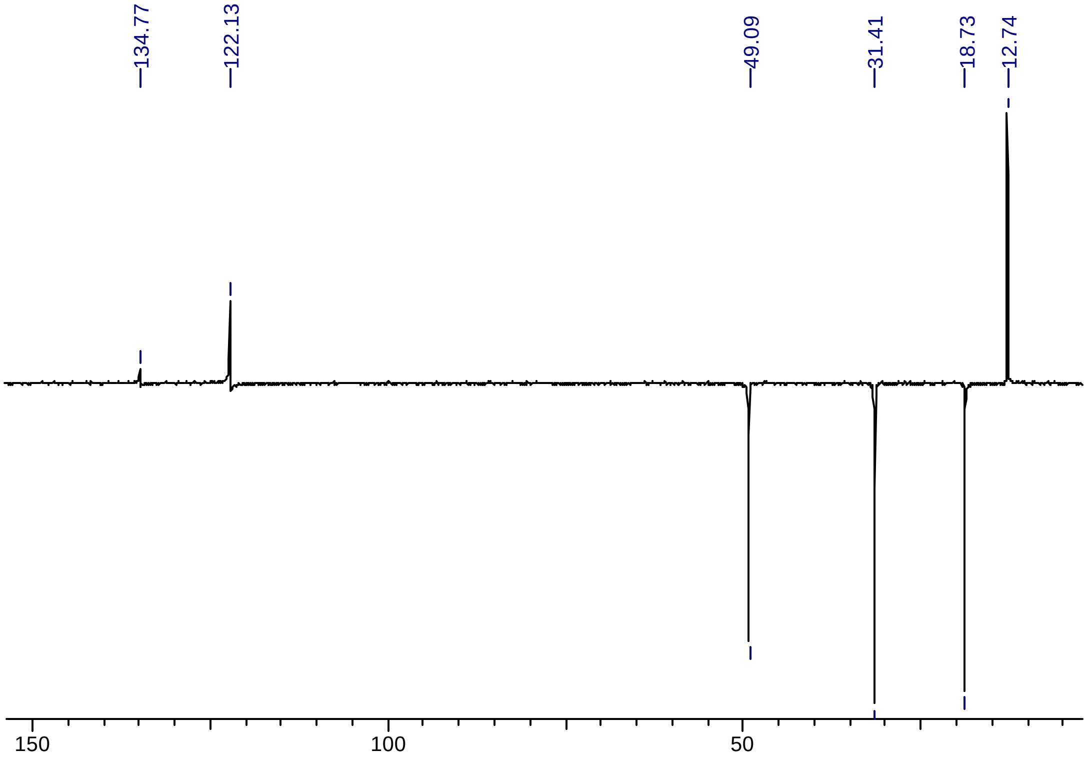
1H NMR of [$C_4C_4IM]^+BF_4^-$



IR spectrum of [$C_4C_4IM]^+BF_4^-$



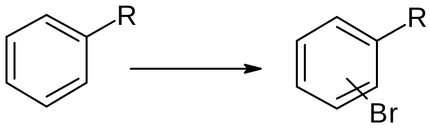
13C NMR of $[C_4C_4IM]^+BF_4^-$



DEPT of $[C_4C_4IM]^+BF_4^-$

1.3.0. Bromination of arenes using N-bromosuccinimide (NBS) in ionic liquids

Bromination chemistry is a relatively small area of organic chemistry but one with many useful applications (including photographic chemicals, pharmaceutical and agrochemical intermediates), and an international speciality chemical industry is based on it. The chemistry is largely based on the use of elemental bromine and the problems associated with the use of traditional acid catalysts are compounded by the low atom utilisation of bromine. The most important bromination reactions include aromatic bromination, bromodehydroxylation and the α-bromination of carboxylic acids.



$$ROH \longrightarrow RBr$$

$$RCH_2COOH \longrightarrow RCHBrCOOH$$

Aromatic bromination reactions are typically catalysed by Lewis acids such as $FeCl_3$ and $AlCl_3$ which present the familiar environmental problems of separation difficulties usually leading to HCl emissions and the production of large volumes of aqueous and salt waste. In the case of the aliphatic brominations phosphorus and sulfur reagents are commonly used. The α-bromination of carboxylic acids is carried out using red phosphorus, in some cases in near stoichiometric quantities. The phosphorus ends up as a cake of phosphates and other phosphorus species containing bromine and organic contaminants. Additionally, all of the above reactions usefully employ no more than 50% of the bromine with an equivalent amount being converted to HBr which needs to be scrubbed from the off gases and removed as NaBr. In reactions using stoichiometric levels of phosphorus and with a substrate molecular weight of 100, even 100% efficient organic chemistry only gives 40% of the final mass as product, with 60% being waste. At a more likely level of 80% efficient organic chemistry, the figures change to 31% product and 69% waste. A clean synthesis approach to bromination reactions should be able to greatly improve their environmental performance and atom efficiency. It is now known for example, that aromatic brominations, at least for other than strongly deactivated substrates, can be effectively catalysed by solid acids (including supported mild Lewis acids that are easily recovered and can be reused many times). It should also prove possible to replace the phosphorus in aliphatic brominations. Furthermore, it should be possible to devise economical methods for oxidatively regenerating the bromide side-product to bromine ideally using oxygen, which will lead to water only as a side product.

1.3.1. Introduction

Brominated arenes are versatile intermediates in the synthesis of a wide variety of biologically active compounds.[1] They are widely used for the preparation of products of commercial importance such as pharmaceuticals, agrochemicals, synthetic colorants and performance chemicals. Unlike chlorination, bromination reaction in general is milder, does not proceed so rapidly or to great degree. With lower permissible operating temperature, the formation of polybromo compounds are formed to a lesser extent. A lot of variations in the brominating methodology with respect to the conditions, reagents and solvents for regioselective brominations have been tried which are well documented in the literature.[2]

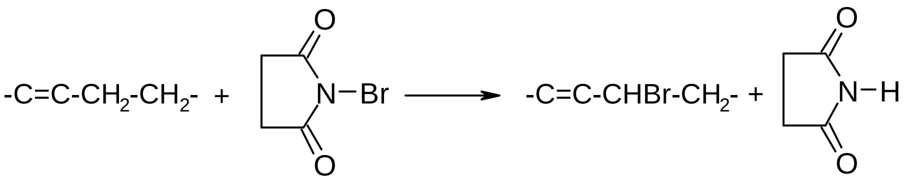
Since the present work is focused on the bromination of aromatics with N-bromosuccinimide (NBS) as brominating species, a brief survey of literature has been included.

In contrast to the well known addition of halogen to the double bond, it was only in 1919 that the first report by Wohl[3] appeared on an apparently general method for the direct introduction of a bromine atom in the “allyl position” of an olefin as shown below Scheme 1.

$$\text{-C=C-CH}_2\text{-CH}_2\text{-} \longrightarrow \text{-C=C-CHX-CH}_2\text{-}$$

Scheme 1

The direct introduction of a halogen atom (usually bromine) by means of N-haloamine (generally N-bromosuccinimide) in the allyl position is known as the “Wohl-Ziegler” reaction as shown in Scheme 2.



Scheme 2

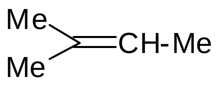
Wohl used N-bromoacetamide, which was not easily available and hence got very little attention. Later Ziegler[4] introduced N-bromosuccinimide as a unique brominating agent in his papers. Subsequently various other N-haloamines viz. N-bromophthalimide, N-chlorosuccinimide, N-bromoglutarimide and N-bromohexahydrophthalimide were used but found inferior to N-bromosuccinimide.

- **NBS as brominating agent**

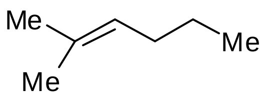
NBS is an important reagent not only for bromination but also for host of other reactions. Depending upon the nature of the reactants and conditions, in solution, NBS reacts differently with many aromatic compounds. Because of its ability to provide brominating species at very low concentrations, it is used extensively in bromination reactions involving radical substitution, electrophilic addition and substitution pathways.

- ***Monoolefins***

Ziegler found that with few exceptions NBS reacted much more readily with a methylene than a methyl group and that tertiary hydrogen atoms in general are more attacked. Thus 2-methyl-2-butene (**1**) required 16h for completion of the reaction, whereas with 2-methyl-2-hexene (**2**) the reaction was finished after only 10min.



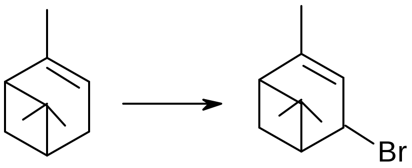
1



2

- ***Isoprenoids***

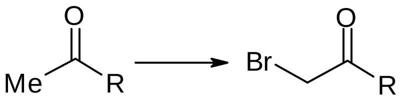
Apparently, this reaction follows Ziegler's rule in that a methylene group is attacked in preference to a methyl group as shown in Scheme 3.



Scheme 3

- ***Carbonyl Compounds***

Carbonyl compounds were brominated to their corresponding α-bromoketones[5] as shown in scheme 4.



Scheme 4

- **Aromatic Compounds**

- *Nuclear bromination*

Aromatic compounds undergo nuclear bromination[6] under Wohl-Ziegler conditions in presence of an equimolar amounts of acid catalyst like metal chloride (aluminium, zinc and ferric) or sulphuric acid.

- *Side Chain Bromination*

Toluene was not affected by NBS in the absence of a catalyst, but benzyl bromide was formed in 64% yield in presence of peroxide[5]. In the presence of electronegative groups, side chain substitution occurs without catalyst.[7,8]

- **NBS Reagent**

NBS can be prepared in 75-81% yield by brominating quickly an ice-cold, alkaline solution of succinimide.[7] It is desirable to employ NBS of 97% purity or better, for which purpose, the reagent is best crystallized quickly from hot water. In the absence of light and moisture, the reagent is stable for many months. NBS is also available commercially.

- **Reaction Parameters**

- *Solvents*

By far the most widely used solvent has been carbon tetrachloride. In certain cases benzene has certain advantages,particularly since NBS is appreciably more soluble in benzene than CCl_4. Petroleum ether[9] and heptane[10] are also used occasionally. Chloroform[11] has given excellent results particularly in large scale runs, since it is a more general solvent for organic compounds than carbon tetrachloride and succinimide is soluble in hot chloroform, thus yielding a homogeneous solution. Ethanol has been employed with NBS as solvent.[11] Acetic anhydride[12] seems to be a good solvent but NBS seems to be unstable in it. Also ethyl acetate and dioxan also degrades NBS. Ether[12] has been proved to be a good solvent in bromination of very reactive methylene group.

Bromination of arenes in polar aprotic solvents is reported to be very facile and regioselective without any addition of catalyst. NBS in DMF results in facile bromination of aromatic compounds.[14] Recently the bromination of phenols and naphthols by NBS in acetonitrile and carbon disulphide has been reported.[13] Reaction in acetonitrile resulted in para selectivity whereas ortho selectivity was achieved with CS_2 as solvent under mild conditions.

In a recent publication, the solid state reaction of NBS with number of substituted anilines, phenols and other aromatic compounds has been studied. The excellent regioselectivity obtained was correlated to the intrinsic reactivity of the molecular system and the crystallinity of solid phase. They concluded that the reaction proceeds through an electrophilic substitution rather than by free-radical pathway.

- *Molar proportions*

Generally, excess of NBS is used in the bromination of aromatic compounds. No definite rule can be established as optimum proportions often vary with the specific substrate.

- *Temperature*

In most instances, the reactions are carried out at the boiling point of the solvent. For certain unusually reactive compounds, the temperature may be lowered by using a solvent such as ether or by cooling. On the other hand, it has sometimes been found advantageous to operate at higher temperature. Reactions of higher temperatures generally are carried out in the absence of a solvent.

- **Catalysts for bromination**

- *NBS/Thallium (III) Acetate*

Thallium (III) acetate has been used as catalyst for bromination of aromatic compounds in low yields. The inefficiency of the catalyst may be due to its thermal instability.[14]

- *NBS/Silica Gel*

NBS in combination with silica gel[15] resulted in an efficient bromination of aromatics. This reagent system was especially suited for 2-methoxy naphthalene but took longer time for reaction (18h).

- *NBS/Peroxide*

The bromination of methylbenzenes with NBS in the presence of peroxide gave side chain brominated product.[16]

- *NBS/Lewis acids*

Lewis acids such as aluminium, zinc or ferric chloride have been used in equimolar amounts to effect the nuclear bromination of aromatic hydrocarbons.[17] These processes generate large amounts of toxic metal wastes giving rise to ecological problems.

- *NBS/H_2SO_4-H_2O*

Bromination using NBS in sulphuric acid-water medium, afforded only the ring bromination.[18]

- *NBS/HTIB or PTSA*

Ring bromination of polyalkylbenzenes with NBS and organic acidic catalysts such as HTIB (hydroxy(tosyloxy)iodo)benzene or p-toluenesulphonic acid have been reported.[19] Longer reaction times were required in both cases.

- *NBS/Amberlyst*

Strongly acidic macroreticular cation exchange resin Amberlyst 15 (A15) with sulphonic acid functionality and weakly acidic carboxylic acid resin Amberlite IRP-64 (A64) were effectively used as catalyst for electrophilic brominations.[20] Again the main disadvantage is the longer reaction time for both the catalysts.

- *NBS/NaOH*

NBS or Dibromodimethylhydantoin in aqueous base is used for bromination of activated benzoic acids.[21] Atleast one activating group is required on benzoic acid moiety for the reaction to occur; reaction with benzoic acid itself resulted in poor yields. Bromination occurred in para position to activating group. If para position is substituted by activating group, then the reaction tends to slow down considerably.

- *NBS/H-ZSM-5*

NBS bromination proceeded with high regioselectivity on both nuclear and side chain of aromatics using zeolite H-ZSM-5 as acid catalyst.[22]

1.3.2. Present Work

A perusal of literature revealed that bromination of aromatics was very facile in polar aprotic solvents like DMF, acetonitrile. In section 2, the hydrogen bonding ability and the polarity of ionic liquids have been studied and described in detail. In this section the efficacy of ionic liquids as solvents in bromination of aromatics has been studied.

1.3.3. Result and Discussion

A variety of aromatic substrates such as phenols, anisoles, toluene, xylenes, aniline, acetanilide, 2-naphthol and 2-methoxynaphthalene (nerolin) were subjected to bromination. As soon as the reactants were mixed in the I.L., the substrates were converted to the corresponding mono bromo derivatives in just 5 min in high regioselectivity and isolated yields with the temperature shooting up from ambient 30°C to ~ 40°C. The results are summarized in Table 1. All the bromoarenes isolated are known compounds reported in literature. Their identities were confirmed by I.R., ^{1}H NMR and mass spectral analyses. Their melting points were in conformity with those reported in literature. The purities of bromoarenes which are liquids were further confirmed by GC analysis. The bromoarenes could be selectively extracted with solvent ether leaving the I.L. and succinimide behind as residue. This residue on further extraction with DCM furnished the I.L. in its pure form which could be recycled. With a view to control the exothermicity, a scale up batch with anisole (25g) was performed by the slow addition of a slurry of NBS in the I.L. to the solution of anisole in the I.L. over 30 min maintaining the reaction temperature at 30°C making the methodology amenable for commercial use.

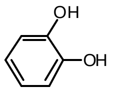
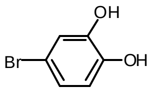
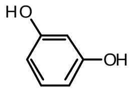
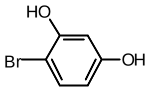
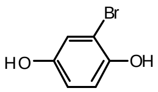
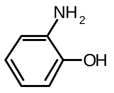
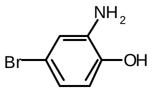
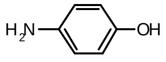
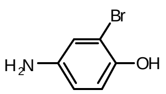
Under the conditions of the reaction, phenol and aniline gave rise to a mixture of products at conversions of 51.7% and 58.9% respectively. For phenol, the p-isomer (60%) was the major product together with o-isomer (14.9%) and 2,4-dibromo phenol (25%). For aniline, the 2,4-dibromoaniline (48.9% was the major product together with o-isomer (37.9%) and p-isomer (13.2%). In both the cases, the yields and conversions were determined by GC analysis. For o- and m-cresols, the conversions stabilized at 25% giving rise to a mixture of products difficult to resolve by TLC or GC.

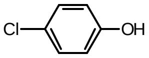
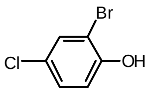
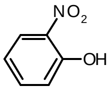
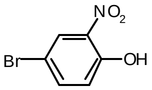
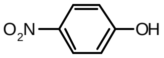
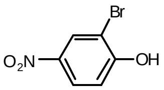
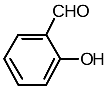
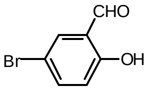
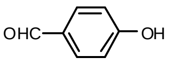
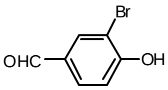
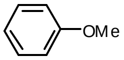
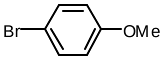
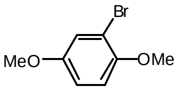
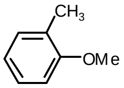
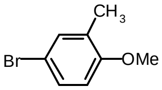
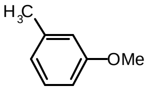
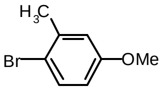
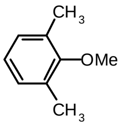
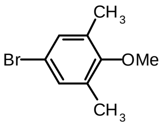
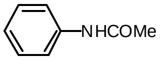
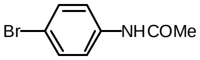
In the case of substituted phenols, the methodology gave equivalent high yields of p-isomer for both electron donating and electron withdrawing substituents (Entry 1-4). Anisole, o- and m- substituted anisoles exclusively afforded the para bromo compound with no trace of the ortho isomer as established by GC analysis (Entry 5-8). All xylenes and methyl anisoles afforded the ring brominated mono bromo compounds in excellent yields. In the case of xylenes and methyl anisoles, the identity of the products was particularly confirmed by ^{1}H NMR spectra which indicated no side chain bromination. Whereas m- and p- xylenes afforded the 4-bromo and 2-bromo isomer respectively as the only product in excellent isolated yields, it was found that o-xylene on the basis of ^{1}H NMR (Fig. 4 and 5 NMR) gave rise to a mixture of isomeric ring brominated products difficult to resolve by TLC and isolate by chromatography. In this case the conversion of o-xylene stabilized at 50% and the selectivities to the 4-bromo (72%) and 3-bromo (28%) were estimated from ^{1}H NMR. Curiously, however, toluene got brominated exclusively in the side chain to an extent of 35% with no trace of ring brominated product. 2-Naphthol and nerolin afforded 1-bromo derivative exclusively to an extent of 65% and 81% respectively. Cyclohexene was regioselectively brominated at the C3 alicyclic carbon with the olefinic bond remaining intact. Benzene, naphthalene, nitrobenzene and chlorobenzene did not react under these conditions.

The nuclear bromination observed in almost in all the cases with the exception of toluene strongly indicates that an electrophilic aromatic substitution mechanism operates predominantly in this bromination methodology using the I.L. [bbim]BF_4. The remarkable enhancement in reaction rates could possibly be explained by the enhancement of the reactivity of NBS as a result of increased polarization of –N-Br bond in the polar I.L.medium. This indeed was found to be the case by recording the ^{13}C-NMR of NBS in the I.L., acetonitrile and DMF as solvents respectively.[24] The ^{13}C chemical shifts for the carbonyl group of NBS in the various solvents are recorded in Table 2. As is evident, the polarization of the carbonyl group increases progressively from the non-polar CCl_4 through the dipolar aprotic CH_3CN and

DMF, and reaches a maximum in the I.L [bbim]BF$_4$. This increase in the chemical shift by an order of 10.68ppm and 3.34ppm in comparison to non-polar and dipolar aprotic solvents commonly used in NBS bromination results in greater polarization of the N-Br bond to generate the bromo cation. This observation can to a large extent explain the enhanced reactivity of NBS in the I.L. as also the ring brominations observed through a predominantly electrophilic reaction mechanism. The inherent Bronsted and Lewis acidities of ring protons H2, H4 and H5 of the imidazolium cation in [bbim]BF$_4$ may have contributed to the enhanced polarization of NBS in the I.L. Previous studies involving multi-nuclear NMR spectroscopy and conductivity measurements for the imidazolium ions correlating their acidity characteristics substantiate the above observations. Further evidence came forth when we conducted the bromination of anisole with NBS in the I.L., N-n-octylpyridinium tetrafluoroborate, which does not exhibit such acidity characteristics. Indeed this reaction was quite sluggish taking 5h at 30^{o}C as compared to 5 min in [bbim]BF$_4$ for complete conversion.

Table 1 : Bromination of aromatic substrates with NBS in [bbim]BF$_4$

Entry	Substrate	Isolated Product^{a}	M.P ^{o}C	Lit. M.P ^{o}C	Yield (%)
1.			85-87	87	86
2.			98-100	97-100	95
3.			109	110-111	90
4.			176-177	177-179	84
5.			164-165	165	86

6.			33	34-36	90
7.			91	92	82
8.			112	114	88
9.			105-106	105-108	84
10.			125	125-126	86
11.			90/8mm	223 (B.P)	98
12.					96
13.			-		92
14.			-		94
15.					82
16.			165-166	164-165	96

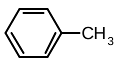
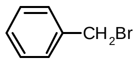
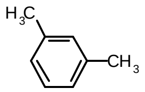
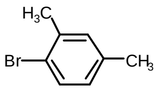
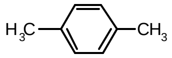
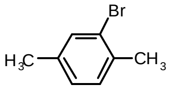
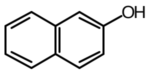
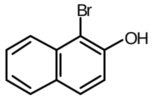
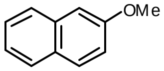
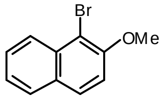
17.					35^{c}
18.					90
19.				199-201	90
20.			82-84	84	65
21.			83-84	85	81

Table 2 : ^{13}C-NMR study of NBS in different solvents.

No.	System	C=O δ- value
1.	NBS-[bbim]BF_4	183.09
2.	NBS-DMF	179.75
3.	NBS-Acetonitrile	179.38
4.	NBS-CCl_4	172.41

1.3.4. Experimental

- *Bromination of aromatics*

To a stirred solution of aromatic substrate (0.018mol) in [bbim]BF_4 (4g) at 28°C, NBS (0.018mol) was added in one lot when temperature shot upto 36°C. A clear solution resulted immediately. The reaction was monitored by TLC and complete conversions were achieved after 5 min. At this stage, the reaction mixture turned turbid due to the precipitation of succinimide. The mixture was extracted with solvent ether (3x10ml) when all the products were extracted into it leaving behind an immiscible layer of succinimide in I.L. The ether layer was separated, washed with water, brine, dried over sodium sulphate and solvent evaporated to furnish the products which were further purified by chromatography through a column of silica-gel (60-120 mesh) or by distillation under reduced pressure.

The remaining mixture of I.L. with succinimide was extracted with DCM (3x10ml) to dissolve I.L. leaving behind the insoluble succinimide. The DCM layer was washed with water, brine, dried over sodium sulphate and the solvent evaporated to recover the I.L quantitatively for reuse.

- *Scaled up batch operation with controlled addition of NBS*

To a stirred solution of anisole (25g, 0.23mol) in [bbim]BF_4 (50g) at 28°C, a slurry of NBS (41.25g, 0.23mol) in [bbim]BF_4 (50g) was introduced slowly over 30min such a way as to maintain the temperature of the reaction below 30°C. After the complete addition, the mixture was stirred further for 15min. at 28-30°C. The completion of the reaction was monitored by GC. The reaction mixture was subjected to distillation under reduced pressure when 4-bromo anisole distilled out at 90°C/8mmHg in 98% yield. The distillation bottoms was washed with water (3x20ml) to remove succinimide. The remaining I.L. was dried under reduced pressure (10mm Hg) and used again twice for the bromination of anisole successfully.

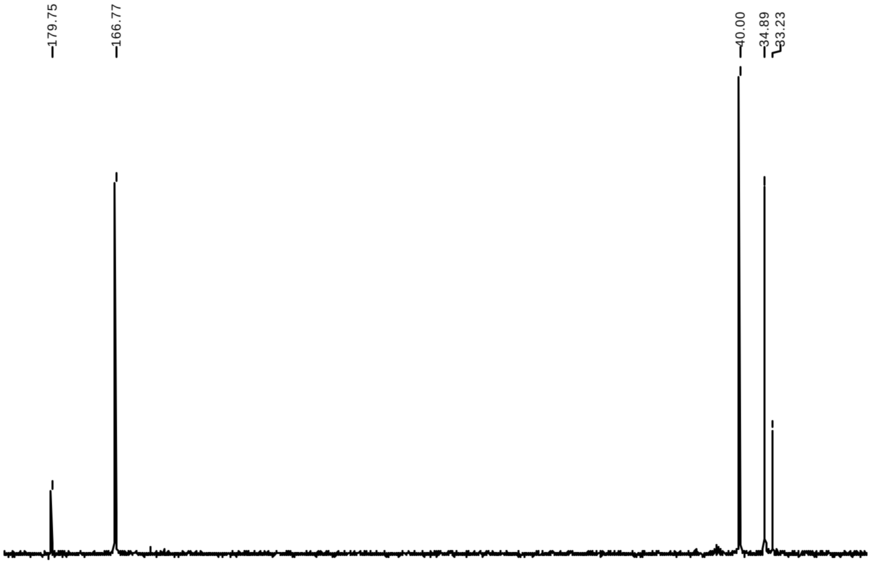


Fig. 1 ^{13}C NMR of NBS+DMF mixture

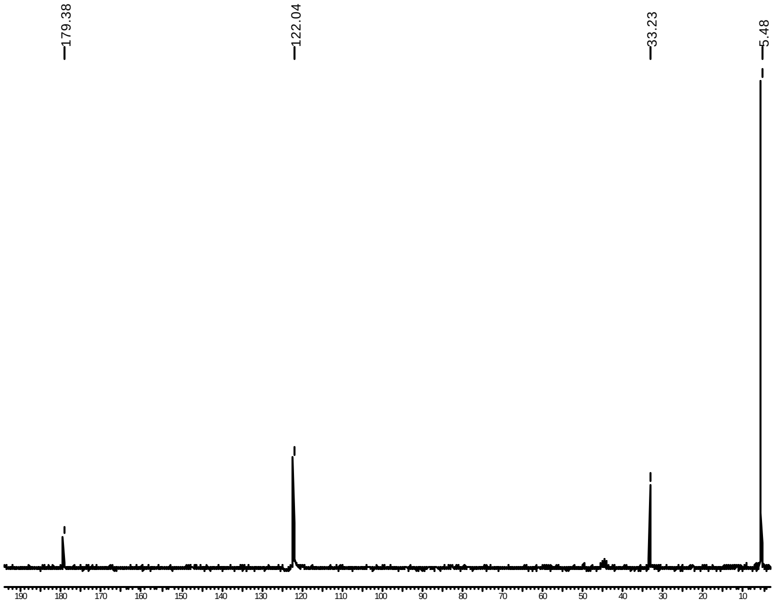


Fig. 2 ^{13}C NMR of NBS+Acetonitrile mixture

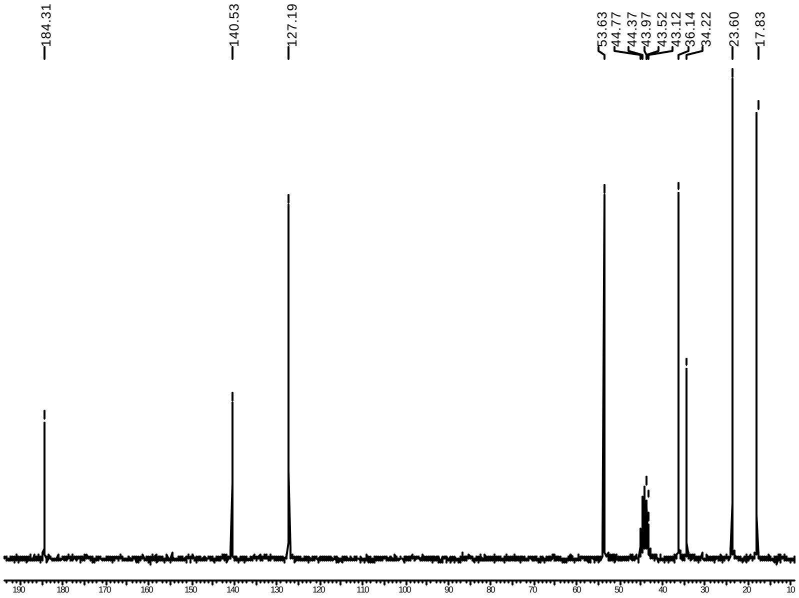


Fig. 3. ^{13}C NMR of NBS+bbimBF$_4$ mixture

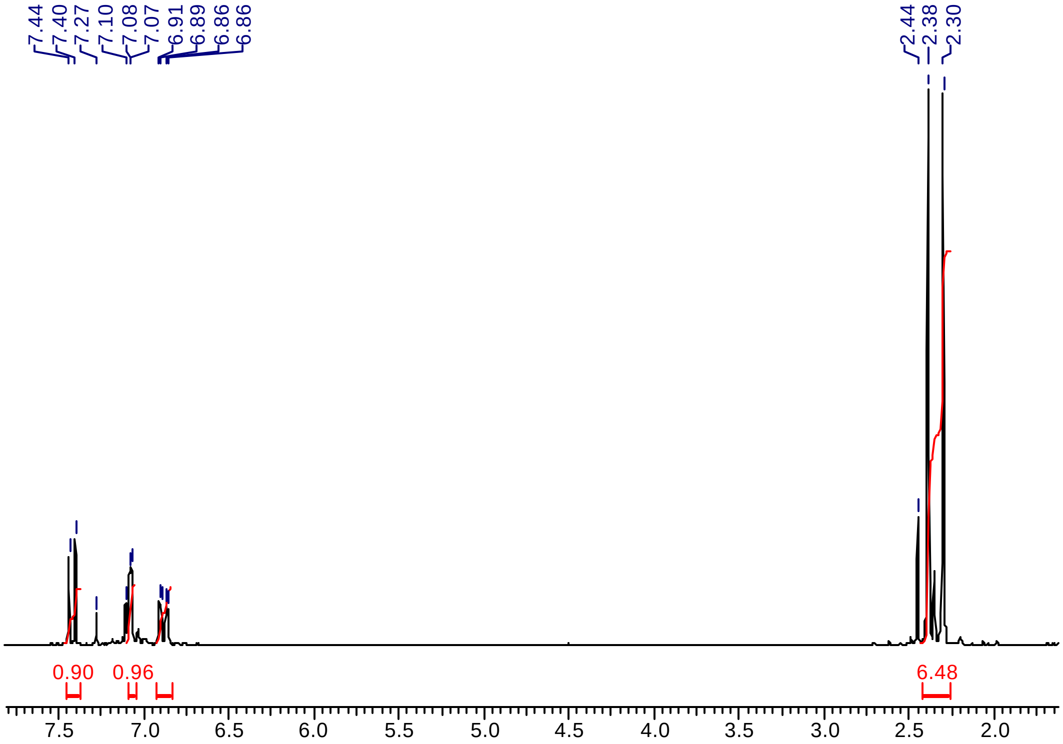


Fig. 4. ^{1}H-NMR of 4-bromo-m-xylene

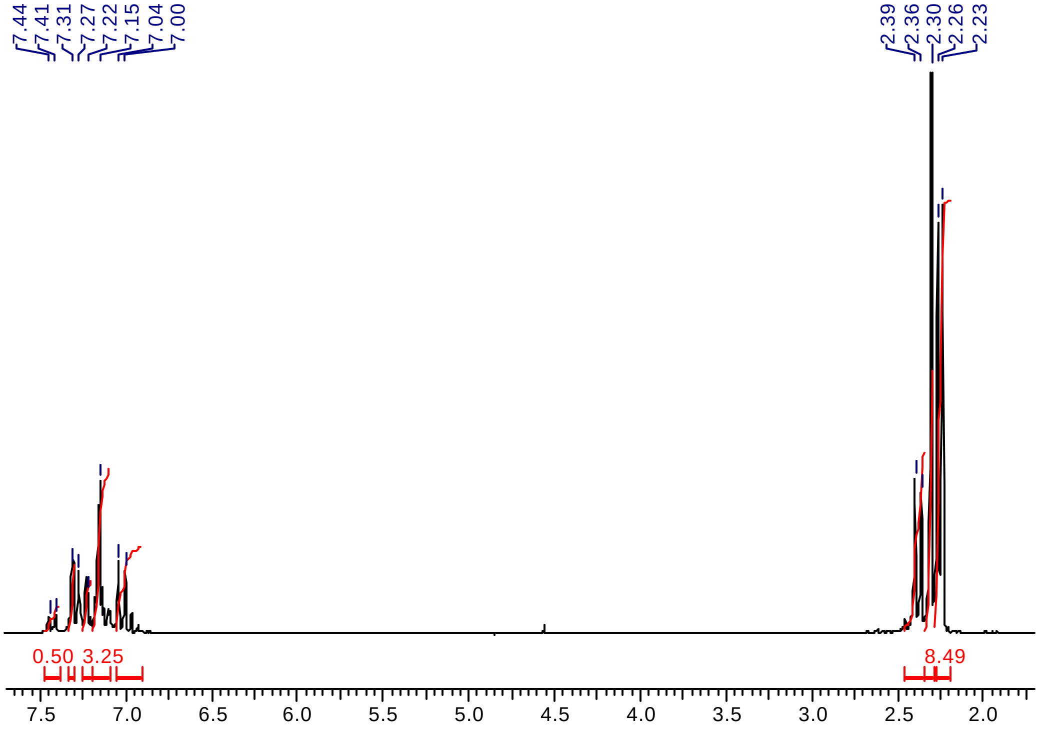


Fig. 5. ^{1}H-NMR of bromination product of o-xylene

1.3.5. Reference

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1.4.0. Nitration of phenols using hydrated ferric nitrate in ionic liquids

Nitration of aromatic compounds is an extremely important industrial process. Even after 150 years of its discovery, nitration as a unit process poses major challenges. The nitroaromatic compounds are widely utilized and act as chemical feedstocks for a wide range of useful end products such as dyes, pharmaceuticals, perfumes and plastics. Unfortunately nitrations typically require the use of potent mixtures of concentrated or fuming nitric acid with sulfuric acid leading to excessive acid waste streams and added expense. Alternatively, nitric acid may be used in conjunction with strong Lewis acids such as boron trifluoride. The Lewis acid is used at or above stoichiometric quantities and is destroyed in the aqueous quench liberating large amounts of strongly acidic by-products. With chemists under increasing pressure to perform atom economic processes, creating minimal or no environmentally hazardous by-products, development of novel catalyst systems that facilitate aromatic nitrations in this manner should be of great importance.

1.4.1. Introduction

The nitration of phenols is a fundamental unit process of great industrial importance generating commercially valuable intermediates and there is a great need for regioselective, pollution free processes. A survey of literature shows nitration of phenol lacks positional selectivity for *para* isomer with majority of processes giving rise to *o*-isomer (~67%) as the major product along with minor amounts of p-isomer (~33%).[1] Among several nitrating agents employed which include mixed acid, super acids, acyl nitrates and a variety of metal nitrates under different conditions,[2] ferric nitrate in particular either alone or supported on solid matrices such as clays has enjoyed considerable importance.[3] Indeed, a very recent publication reports the electrophilic nitration of aromatics *other than phenols* using ethylmethylimidazolium salts as ionic liquid solvents. In all cases reported in this recent work, the isomer distribution in the products was in keeping with those reported for conventional systems with *ortho* product being the major isomer.

1.4.1.1. Nitration of phenols

Phenol can be nitrated with aqueous nitric acid in the presence of catalytic nitrous acid to give a mixture mainly consisting of 2- and 4- nitrophenol.[4] Although these can be separated (*ortho* isomer is steam volatile), the economics of the route compares unfavorably with hydrolysis of 2- and 4- nitrochlorobenzene. Nitrocresols are more frequently obtained by nitrosation or nitration, although mixture of isomers often result. A survey of literature shows nitration of phenol lacks positional selectivity for *para* isomer with majority of processes giving rise to *o*-isomer (~67%) as the major product along with minor amounts of *p*-isomer (~33%).[5-7] Not much success have been achieved for desired *p*-isomer. A variety of nitrating agents under different conditions have been reported recently for the nitration of phenols. Indeed metal nitrates and supported metal nitrates on various supports are reported to achieve *para* selectivity. Very recently, Rodrigues et. al.[6] reported that phenol can be nitrated by silica-gel supported acetyl nitrate with excellent ortho selectivity. A large volume of literature is available for ortho selective nitration of phenols. Nitration of phenol with N_2O_4[7] and pyridine derivatives carrying transferable nitro group or silica gel supported acetyl nitrate gave exclusively ortho product. Poierier et. al.[8] compared the nitrating effect of various commercially available metal nitrates in the nitration of phenol. They found that ferric nitrate in ethanol gave a 1:1 mixture of *o*- and *p*- isomer. The same reaction in chloroform resulted in a slight increase in para selectivity. Chromium nitrate gave very high para selectivity. Various reagents and conditions have been reported recently in the nitration of phenol and the results are summarized in the Table 1.

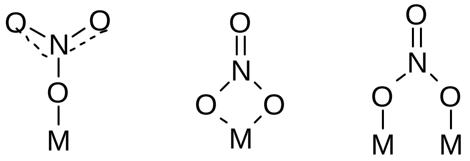
Table 1. Nitration of phenol by reported methods.

No.	Reagent/solvent/conditions	Ortho %	Para %
1.	HNO_3/H_2SO_4[2]	36	25
2.	CLAYFEN/THF/room temp./ 20hrs[3]	40	50
3.	$HNO_3/SiO_2/CH_2Cl_2$[4]	40	42
4.	CLAYCOP/acetic anhydride/CCl_4[5]	86	6
5.	$Fe(NO_3)_3.9H_2O$/EtOH/50°C/3hrs[6]	50	50
6.	$Fe(NO_3)_3.9H_2O/CHCl_3$/50°C/3hrs[6]	49	47
7.	$Cr(NO_3)_3.9H_2O$/EtOH/65°C/4hrs[6]	24	76
8.	$Cr(NO_3)_3.9H_2O$/THF/room temp./24hrs[7]	37	60
9.	$Cr(NO_3)_3.2N_2O_4$/THF/room temp./immediately[8]	40	59

1.4.1.2. Metal Nitrates in nitration of phenols

Metal nitrates have been extensively used in the nitration of phenol as can be seen from the literature available. In this transition metal nitrates supported on suitable supports have enjoyed more attention being more selective and eco-friendly.[9] Mechanistically, the classical Hughes-Ingold (ionic) and Perrin (radical) pathways compete.[10] The latter gives a product distribution stemming from unpaired spin density in the radical cation intermediate.[11] This unpaired spin density is greater in the para than in the ortho position. So for more para selectivity, the logical way is to make the reaction proceed through radical instead of ionic pathway.

It is well documented that many (anhydrous) transition metal nitrates,[12,13] the bond between the metal and the nitrate group is covalent and hence they can be considered as coordination complexes.[14,15] Examples are bivalent metals like $Mn(NO_3)_2$, $Ni(NO_3)_2$, $Cu(NO_3)_2$, trivalent metals like $Cr(NO_3)_3$ and tetravalent metals like $Ti(NO_3)_4$ and $Sn(NO_3)_4$. The nitrato group is unique as its chemical reactivity varies widely with the multiplicity of the metal-nitrate bond; also the more multiple the bond becomes, the more reactive is the nitrate group. Three types of covalent bond are possible as shown in Fig 1.



Unidentate Bidentate Bridging

Fig. 1

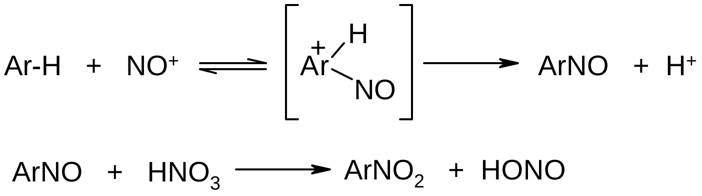
It has been found that the unidentate nitrates are not reactive whereas bidenatate species possess strong oxidizing powers towards many organic substances.[15]

Depending on the strength of the sigma bond by which oxygen atom is bonded to the metal, either a nitrate ion is produced or the NO_2 radical. The metallic center then achieves abnormally large coordination numbers:8 with tetranitrato derivatives of titanium (IV), manganese (II), iron (III), cobalt (II), tin (IV) and up to 12 with hexanitrato derivatives of cerium (III), cerium (IV), thorium (IV). The exceptional reactivity of these substances, coupled with their inter-relationship with other oxygenated derivatives of nitrogen,[14] allows one to direct formation of either neutral or charged, radical, or electrophilic or nucleophilic species, depending upon the substrate. The dual condition for the reactivity of a metallic nitrate is the coexostence of a bidentate covalent coordination by the nitrato group to the metal, with the availability of lower intermediate oxidation states for the metal.[15] Laszlo et al.[16] took up the work on the study of activity of the cheap and non-toxic ferric nitrate nonahydrate towards organic substrates.

Apparently, this ionic mode of existence precludes the required covalent bonding of the nitrato group. They obtained a dark red oil when an acetone solution of ferric nitrate nonahydrate was subjected to high vacuum which was confirmed by I.R spectral data to be a bidentate nitrate group on iron.

1.4.1.3. Mechanism

There are a number of aspects in the mechanistic study in general nitration reaction, which will be beyond the scope of this discussion. Here the discussion will be confined only to the recent developments in nitration of phenols.



The classical nitration of phenol is the nitrous acid catalyzed nitration.[17] The electrophilic attack was prompted by the nitrosonium ion (NO^+), arising from a catalytic amount of nitrous acid, forms an intermediate nitroso compound, which is oxidized by nitric acid to the nitro derivative with the regeneration of nitrous acid. The nitrosonium ion (NO^+) is an interesting chemical species. As a Lewis acid, it is unique. Other acids either have a very high electron affinity (H^+) or a very low electron affinity (alkali ions), relative to the standard bases. Hence, location of the charge in acid-base salts or complexes is not in doubt. For the nitrosonium

$$C_6H_6 \; + \; NO^+ \longrightarrow C_6H_6^{+\cdot} \; + \; NO^\cdot$$

ion, however, its electron affinity (9.2eV) is of comparable magnitude as for typical bases. To give an example, which will be further elaborated upon in the section on nitration of phenols, the reaction leads to the formation of an aromatic radical cation, with an equilibrium constant K=119 in the gas phase. This is due to the matching between the ionization potentials of benzene (9.24eV) and the electron affinity of NO^+ (9.26). This mid-range electron affinity makes nitrosonium ions highly reactive species because of their charge and, at the same time, renders them relatively mild and finely tunable oxidants.

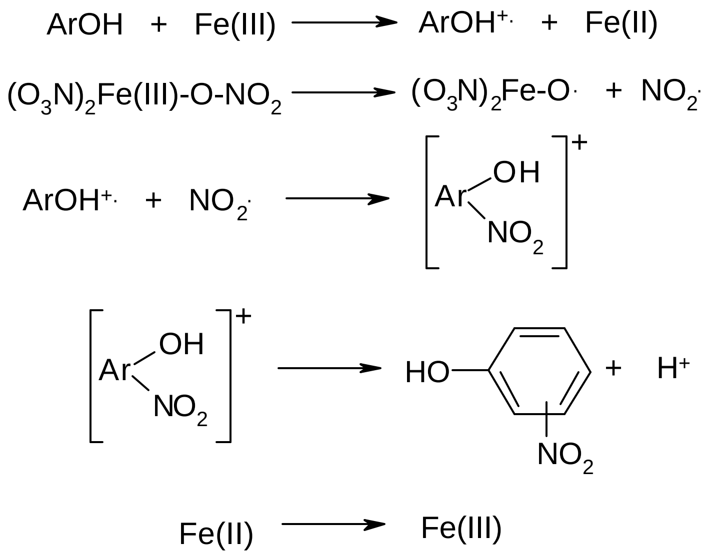
The classical Hughes-Ingold mechanism for aromatic substitution is a two-step sequence. The Wheland intermediate formed in the first step deprotonates to the final product in the second step.[10] Kenner[18] proposed transfer of a single π electron form the aromatic substrate to the electrophile, as the initial step. Nagakira[19] showed operation of strong driving force for such single electron transfer (SET) whenever the electron affinity of electrophiles exceeds the ionization potential of the aromatic substrate. The intervention of charge-transfer complexes as intermediates have been postulated by Brown.[20] But it was Perrin [21] who threw light into actual SET mechanism. The initial SET between aromatic donor and the nitronium or nitrosonium ion acceptors leads to an ion radical pair, $[ArH^{+\cdot}, NO_2^{\cdot}]$ or $[ArH^{+\cdot}, NO^{\cdot}]$, which collapses in a fast step to Wheland intermediate. Accordingly, nitration occurs preferentially at the sites of the $ArH^{+\cdot}$, radical cation, with the greatest potential for new bond formation. Since collapse of a radical pair is involved, positions with the greatest unpaired spin density will be attacked preferably. This unpaired spin density is greater in para than in ortho position. This can be summarized as shown in scheme 1.

$$ArH \longrightarrow ArH^{+\cdot}$$

$$ArH^{+\cdot} + NO_2^{\cdot} \longrightarrow [ArHNO2]^{+} \longrightarrow ArNO_2 + H^{+}$$

Scheme 1

Another plausible mechanism suggested for nitration by ferric nitrate is as shown in scheme 2.[22]



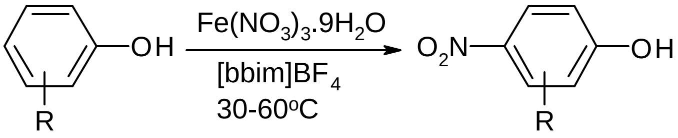
Scheme 2

1.4.2. Present Work

The use of room temperature ionic liquids (I.Ls) as “green” solvents in organic synthetic processes has gained considerable importance in recent years due to their negligible vapour pressures, easy recoverability and reusability.[24] Indeed, a very recent publication reports the electrophilic nitration of aromatics other than phenols using ethylmethylimidazolium salts as ionic liquid solvents. In all cases reported in this recent work, the isomer distribution in the products was in keeping with those reported for conventional systems with ortho product being the major isomer. In sharp contrast, the present work describes the para selective nitration of phenols in the I.L. [bbim]BF_4 using hydrated ferric nitrate as the nitrating agent. A comparative study of the reaction in other I.Ls has also been undertaken.

1.4.3. Results and Discussions

Phenol and substituted phenols were nitrated with $Fe(NO_3)_3.9H_2O$ in I.L. as shown in scheme 3.



Scheme 3.

The results are summarized in Table 1. The reaction mixtures were homogeneous and the reactions were monitored by TLC. All the reactions went to complete conversion except that for p-nitrophenol (entry 12) wherein the conversion stabilized at 92% even after much longer reaction time (6h). The I.L. [bbim]BF_4 could be selectively and completely extracted with chloroform from the reaction mixture after it has been made alkaline. The solvent thus recovered could be used at least 3 times for the nitration of phenol. Phenol and activated phenols could be completely nitrated at 30°C (1-1.5h) whereas the deactivated phenols required elevated temperature (60°C) and marginally longer reaction times (2-3h).

As is evident from Table 1, phenol, ortho/meta substituted phenols afforded the p-nitrophenols in very high selectivity (68-86%) whereas the para substituted phenols afforded selectively the o-isomer (82-92%). All of the isolated nitrophenols are known compounds and their melting points are reported in literature.[23] No dinitro products or the *m*-isomer could be detected. The other products formed in this reaction constitute a complex mixture of polymeric/oxidized products difficult to separate and identify.

Table – 1: Nitration of phenol and substituted phenols by $Fe(NO_3)_3.9H_2O$ in [bbim][BF_4]

No.	Substrate/phenol	Time h.	Conversion %	Yields %		
				Nitrophenols		Others
				Ortho	Para	
1.	H	1.5	100	9	80.2	-
2.	*o*-CH_3	1.0	100	10	79	11
3.	*o*-OCH_3	1.0	100	23	68	9
4.	*m*-CH_3	1.5	100	8	76	16
5.	*o*-Cl	1.0	100	15	78	7
6.	*o*-NO_2	2.0	100	-	82	18
7.	*o*-$COCH_3$	2.0	100	-	83	17
8.	*o*-COOMe	2.0	100	-	86	14
9.	*p*-CH_3	1.0	100	82	-	18
10.	*p*-OCH_3	1.0	100	86	-	14
11.	*p*-Cl	1.0	100	92	-	8
12.	*p*-NO_2	6.0	92	84	-	08
13.	*p*-$COCH_3$	3.0	100	88	-	12
14.	*p*-COOMe	2.0	100	88	-	12

Table –2. Nitration of phenol with $Fe(NO_3)_3.9H_2O$ in various I.L.s as solvents at 30^oC.

No.	Solvent	Time h.	Conversion %	Yield %		
				Nitrophenol		others
				o-	p-	
1	$bbimBF_4$	1	100	9.0	80.2	10.8
2	bbimBr	15	0	-	-	-
3	$bmimBF_4$	1	100	28.0	63.0	9.0
4	bmimBr	15	60	---complex mixture---		
5	$EtNH_3^+NO_3^-$	10	100	12.0	75.0	13.0

It was interesting to study the nitration of phenol with $Fe(NO_3)_3.9H_2O$ in other ionic liquids under similar conditions. The ionic liquids used for the investigation are known and were prepared following methods reported in literature.[24] The results are summarized in Table 2. The analogous [bmim]BF_4 showed reduced para selectivity. The I.L [bbim]Br showed no conversion and analogous [bmim]Br gave rise to a complex mixture of products difficult to separate. The I.L. $EtNH_3^+NO_3^-$ showed good para selectivity but the reaction was sluggish.

A probable mechanistic pathway favoured in the I.L medium will be the homolytic cleavage of the initially formed phenol-Fe(III) complex leading to the formation of a phenoxy radical cation intermediate followed by the reaction with NO_2 radicals generated by the splitting of the $(O_2N)_2Fe(III)\text{-}O\text{-}NO_2$ before collapsing to the Wheland intermediate.[25] The deprotonation of the Wheland intermediate in a fast step results in the final nitrophenols. Para regio-selectivity for the reaction of the radical cation with NO_2 as the reaction intermediates has been well documented. Theoretical studies have also shown that the unpaired spin density for such intermediates is greater in the para than in the ortho positions. That the nitration in [bbim][BF_4] is in all probability proceeds through such radical ion pathways is given further credibility in a very recent paper which reports that I.Ls particularly alkyl imidazolium salts are excellent media for the generation of radical ions of solute molecules.

1.4.4. Experimental

Nitration of phenol

A solution of the phenol (2mmol) and $Fe(NO_3)_3.9H_2O$ (1.2mmol) in $[bbim]BF_4$ (1g) was strirred vigorously under argon atmosphere. After completion of reaction (monitored by T.L.C.), sodium carbonate solution (10% w/v, 5ml.) was added. The I.L layer was separated and extracted with dichloromethane (DCM). The DCM layer was separated, washed with 10% sodium carbonate solution (5ml. x 2) and brine. The DCM was evaporated under reduced pressure to afford the pure I.L for recycle. The combined aqueous alkaline layer was filtered, acidified and extracted with ethyl acetate (10ml x 3). The ethyl acetate layer was dried over sodium sulphate and the solvent evaporated under reduced pressure to furnish crude product. The crude product was subjected to column chromatography, to isolate pure products.

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1.5.1. Ultrasound promoted C-C bond formations in ionic liquids.

1.5.1.1 Introduction to Ultrasound

When ultrasonic energy at high power is applied to a liquid, a phenomenon called 'cavitation' occurs. Cavitation is the formation, growth and collapse of bubbles in the liquid.[1,2] This results in the 'cold boiling' of liquid. Ultrasonic vibration reduces the thickness of liquid films, enhances gas transfer and reduces bubble coalescence, which increases the interfacial area of gas transfer.[3-6] This can be used to separate gases as lighter molecules in an ultrasonic field will travel further than heavier ones. Ultrasonic energy can also be used to remove contaminants from air and to break down toxic components in soil and water. The role of ultrasound in homogeneous and heterogeneous chemistry has been well documented in the literature.

Ultrasounds are waves at frequencies above those within the hearing range of the average person, i.e., at frequencies above 16 kHz. Ultrasonic energy (high frequency sound waves) produces an alternating adiabatic compression and rarefaction of the liquid media being irradiated. In the rarefaction part of the ultrasonic wave (when the liquid is unduly stretched or "torn apart"), microbubbles form because of reduced pressure (i.e. sufficiently large negative pressures). These microbubbles contain vaporized liquid or gas that was previously dissolved in the liquid. The microbubble can be either stable about their average size for many cycles (stable cavitation) or transient when they grow to certain size and violently collapse or implode during the compression part of the wave (transition cavitation). The critical size depends on the liquid and the frequency of the sound; at 20kHz, for example, it is roughly 100-170 µm. The energy put into the liquid to create microvoids is released during implosion creating high local pressures upto 1000 atm and high transitory temperatures up to 5000K.[7-11] This energy-releasing phenomena of the bubble formation and collapse is termed as acoustic cavitation.[12-14]

Cavitation can also be achieved by throttling a valve downstream from a pump. When the pressure at an orifice or any other mechanical constriction falls below the vapour pressure of the liquid, cavitations are generated which then collapse downstream with a recovery of pressure, giving rise to high temperature and pressure pulses. This cavitation is termed as hydrodynamic cavitation.[15]

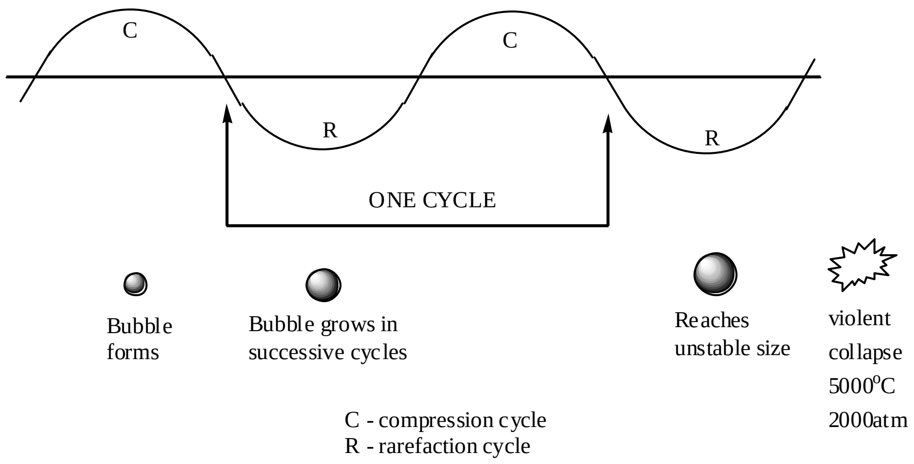


Fig. 1 Sound propagation in a liquid showing cavitation bubble formation and collapse

1.5.1.2 Factors influencing Sonochemical processes

Application of ultrasound to chemical transformations may be termed as Sonochemistry. Sonochemistry depends on the nature or physicochemical properties of the solvent, solute or gas in the bubble which have dramatic effect on the cavitational collapse.[14]

Effect of solvent

Cavities are readily formed when using solvents with high vapour pressure, low viscosity and low surface tension. The intermolecular forces in the liquid must be overcome in order to form the bubbles. Thus, solvents with high densities, surface tensions and viscosities generally have higher threshold for cavitation but more harsh condition when cavitation begins.[12]

Effect of ambient gas

There are several properties of gases that can affect sonochemical activities.[5] The heat capacity ratio C_p/C_v or polytropic ratio of the gas in the bubble affects the amount of heat released and, hence the final temperature produced in an adiabatic compression and the cause of reaction. Higher temperatures and pressures are generated with monoatomic gases with higher polytropic ratio than those with polyatomic gases with lower polytropic ratio.[5] Another parameter that affects cavitational collapse is the thermal conductivity of gases. A gas with low thermal conductivity reduces heat dissipation from cavitation site following adiabatic collapse and should favour higher collapse temperature compared with high thermal conductivity gas.[1] The solubility of gas is also an important aspect. The more soluble the gas, the more likely it is to diffuse in to the cavitation bubble. Soluble gases should result in the formation of larger number of cavitation nuclei and extensive bubble collapse since these gases are readily forced back to the bulk phase.[1]

Effect of temperture

Unlike most of the reaction systems, lowering of reaction temperature increases the rate of reaction. This is attributed to the lowering of the solvent vapor pressure, which increases the intensity of cavitation. At low vapor pressure, less vapor has an opportunity to diffuse into the bubble and making the implosion more violent. Also, as liquid temperature decreases, the amount of gas dissolved increases and the vapor pressure of the liquid decreases. Very volatile solvents lead to relatively high pressures in the bubble and also ‘cushion’ the collapse.[16]

Effect of pressure

Effect of pressure in reaction can cause some increase in the rate of sonochemical reaction due to the magnified effect of cavitation implosions. Too much pressure reduces the rate of reaction by decreasing the frequency or efficiency of bubble formations.[14]

Effect of acoustic intensity

An increase in ultrasound intensity implies an increase in the acoustic amplitude. The collapse time, the temperature and the pressure of collapse are all dependent on the acoustic amplitude. The cavitation bubble collapse will be more violent at higher acoustic amplitudes. So an increase in intensity will result in greater sonochemical effects in the collapsing bubble.[5,17]

Effect of acoustic power

Power delivered to the system can increase the sonochemical activity to an optimum level after which it falls.[18,19] When acoustic power increases and simultaneously increases amplitude of vibration, the maximum radius of the cavity bubble also increases as well as its time of collapse and this bubble is not able to collapse within time equal half of the period i.e. before the sound field reverses itself, the rarefaction phase begins acting on the collapsing bubble.[20,21]

Frequency of ultrasonic irradiation

Frequency has significant effect on the cavitation process because it alters the critical size of the cavitational bubble.[22-27] At high frequencies, the cavitational effect is reduced because either i) the rarefaction cycle of the sound wave produces a negative pressure which is insufficient in its duration and/or intensity to initiate cavitation or ii) the compression cycle occurs faster than the time for the microbubble to collapse. Lower frequency ultrasound produces more violent cavitation, leading to higher localized temperature and pressure.

1.5.1.3 Fundamentals of sonochemical reactions

The influence of ultrasonic energy on chemical activity may involve any of the following:[2,3,28,29]

1. production of heat
2. promotion of mixing (stirring) or mass transfer
3. promotion of intimate contact between materials
4. production of free radicals

The physical effects of ultrasound can enhance the reactivity of a catalyst by enlarging its surface area or accelerate a reaction by proper mixing of reagents. The chemical effects of ultrasound enhance reaction rates because of the formation of highly reactive radical species formed during cavitation.[4,11] Homogeneous sonochemistry examines, mainly in the liquid phase, the activity of radicals or excited species formed in the bubble gas phase during the violent implosion and their possible release into the liquid.[17] The cavitation event also gives rise to acoustic microstreaming or formation of miniature eddie current that enhances the mass and heat transfer in the liquid, and also causes velocity gradients that results in shear forces. In heterogeneous sonochemistry, the mechanical effects of cavitation resulting from the erosion action of microjets formed during the asymmetric collapse of bubbles at the vicinity of interfaces are also important.[17]

The following theories have been proposed to explain the sonochemical events.

1. hot-spot theory
2. electrical theory
3. plasma discharge theory
4. super-critical theory

The hot-spot theory suggests that a pressure of the order of 1000atm is generated and a temperature of about 5000K results during violent collapse of the bubble.[7-9]
The electrical theory suggested by Margulis[30] says that during bubble formation and collapse, enormous electrical field gradients are generated and these are sufficiently high to cause bond breakage and chemical activity.

The plasma theory by Lepoint and Mullie[31] also suggests that the extreme conditions associated with the fragmentative collapse is due to intense electrical fields and seems to involve a true implosion which is related to corona-like discharges caused by fragmentation process and the formation of microplasmas inside the bubbles.

Hoffmann[32] proposed super-critical theory, in which the existence of a layer in the bubble-solution interface where temperature and pressure may be beyond the critical conditions of water and which may have physical properties intermediate between those of a gas and a liquid. They also proved that supercritical water is obtained during the collapse of cavitation bubbles generated sonolytically.

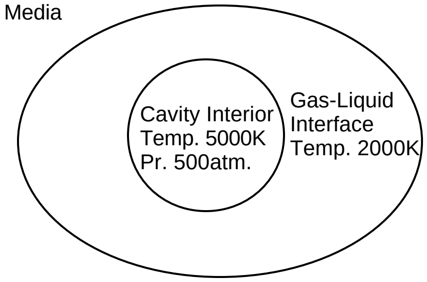


Fig. 2 Schematic diagram of Cavitation Bubble

In general, most studies have adopted 'hot spot' concept for experimental result interpretation.

Hot spot theory suggests a sonochemical reaction as a highly heterogeneous reaction in which reactive species and heat are produced from a well defined microreactor i.e. 'cavitation bubble'.[11,33] In the figure, three regions for occurrence of reactions are postulated
i) a hot gaseous nucleus; ii) an interfacial region and radial gradient in temperature and local radical density; iii) the bulk solution at ambient temperature.

Reactions involving free radicals can occur within the collapsing bubble, at the interface of the bubble and in the surrounding liquid. Within the center of the bubble, harsh conditions generated on bubble collapse cause bond breakage and/or dissociation of the water and other vapors and gases, leading to the formation of free radicals to the formation of excited states. Solvent and/or substrates suffer homolytic bond breakage to produce reactive species. High temperatures and pressures created during cavitation provide the activation energy required for the bond cleavage. The radicals generated either react with each other to form new molecules and radicals or diffuse into the bulk liquid to serve as oxidants. The second reaction site is the liquid shell immediately surrounding the imploding cavity, which has been estimated to heat up to approximately 2000K during cavitation implosion. In this solvent layer surrounding the hot bubble, both combustion and free-radical reactions (involving $^{\cdot}OH$ derived from decomposition of water) occur. Pyrolysis in the interfacial region is predominant at high solute concentrations, while at low solute concentrations, free-radical reactions are likely to predominate. At the interface between bubble and bulk liquid, surface-active reagents also accumulate and species produced in the bubble first react with chemicals in the bulk liquid. It has been shown that the majority of degradation takes place in the bubble-bulk interface region.[34,35]

1.5.1.4 Equipment

The first requirement for sonochemistry is a source of ultrasound energy. This is usually generated via an ultrasonic transducer. This is a device which converts mechanical or electrical energy to sound energy. There are three main types of transducers used in sonochemistry : Liquid-driven (effective liquid whistling), magnetostrictive (reduction of size of metal when placed in magnetic field e.g. Ni) and piezoelectric. Most of the current equipments utilize piezoelectric ceramic tranducers. Two piezoelectric ceramic plates are clamped between metallic plates to form a piezoelectric sandwich, which provides an added mechanical motion. Piezoelectric transducers are very efficient and depending on their dimensions, can be made to operate over the whole ultrasonic range. The two commonly used sources of ultrasound in laboratory are ultrasonic cleaning bath and the ultrasonic horn or probe system.[36] These generally operate at frequencies of around 40 and 20 kHz, respectively.

- ***Ultrasonic cleaning bath***

A simple ultrasonic cleaning bath is the simple and cheapest source of ultrasound. It usually consist of a tank fitted with transducers at the bottom. The reaction flask can be immersed into the tank filled with some liquid mostly water. The amount of energy, which reaches the reaction through the vessel walls is low – normally between 1 and 5 W cm^{-2}. Temperature control in the commercial cleaning bath is very poor and may require additional thermostatic control.

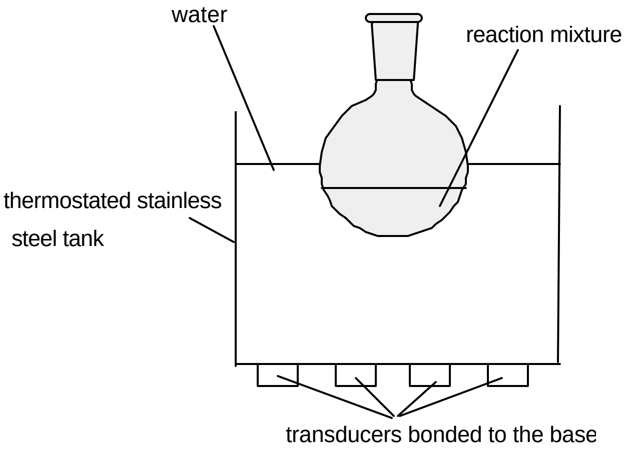


Fig. 3 Ultrasonic cleaning bath

- ***Ultrasonic probe***

This apparatus allows acoustic energy to be introduced directly into the system rather than rely on its transfer through water in the tank and through the walls of the tank. It is more

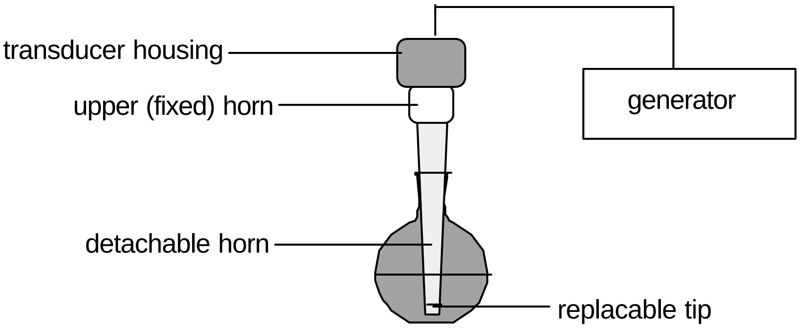


Fig. 4 Ultrasonic Probe

expensive and less convenient because of the requirement of special seals for the closed reaction vessels which carry inert atmospheres or pressures above ambient or reflux temperatures. The maximum power out put can be as high as several hundreds W cm^{-2} and is tunable.

1.5.1.4 Rules of sonochemistry

As mentioned in earlier section, the sonochemistry involves mainly the cavitation phenomena, which results in hot spots and micro reactors. With this theory many conclusions are derived by many workers to generalize the reactions, which are activated by ultrasound. Considering all possibilities in the formation and collapse of cavitation bubble as main mechanism, the sonochemical reactions can be classified into three groups.[37]

a. Homogeneous systems which proceed via radical or radical-ion intermediates – this implies that sonication is able to effect reactions proceeding through radicals and further it is unlikely to effect ionic reactions.
b. Heterogeneous systems proceeding via ionic intermediates – the reaction is influenced primarily through mechanical effects of cavitation such as surface cleaning, particle size reduction and improved mass transfer.
c. Heterogeneous reactions, which include a radical pathway or a mixed mechanism i.e. radical and ionic – radical reactions will be chemically enhanced by sonication but the general mechanical effect referred to above in b may still apply. If the radical and ionic mechanisms lead to different products ultrasound should favour the radical pathway and this could lead to a switch in the nature of the reaction products.

A look-back into literature on the development of sonochemistry is essential to exemplify the above rules.

Homogeneous liquid-phase reactions

Studies in sonochemical synthesis in homogeneous conditions suggest that cavitation is less effective in promoting the reactions. The sonochemical effects generally occur either inside the collapsing bubble where extreme conditions are produced, at the interface between the cavity and the bulk liquid where the conditions are far less extreme or in the bulk liquid immediately surrounding the bubble where the predominant effects will be mechanical. In order for a chemical to experience the actual effect of sonication, it should volatalize and enter into the cavitation bubble. The conventional laboratory equipments give very little concentration of cavitation bubbles and the yields of reaction in that case will be low. Sonication in water can cause the formation of $HO^{\cdot}$, which is an highly oxidizing species and can cause side reaction with reactants.[38] Organic solvents will also slowly decompose on sonication but it is only a minor contribution to any sonochemical reaction taking place in the medium.

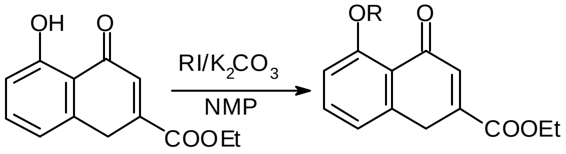
A typical reaction which proves the cavitation effects and the collapsing bubble is the production of amorphous iron form sonolysis of $Fe(CO)_5$ (0.4M) in decane under argon.[39] Volatile iron carbonyl enters the bubble and the very fact that amorphous iron results confirms that very high temperatures are generated and extreme cooling rates are involved. In the case of molybdenum hexacarbonyl the product is nanostructured molybdenum carbide which has proved to be an excellent dehydrogenation catalyst.[40]

Even if the reactants are not volatile in some cases, it cannot be concluded that the sonochemistry has no effect on such species. Bubble collapse produces a very large shear forces in the surrounding liquid capable of breaking the chemical bonds. This phenomena has been made use of in radical polymerization recently.

Accelerations in the range of 4-15% are observed in the acid catalyzed hydrolysis of esters. This can be attributed to the increased molecular motion induced by the pressure gradients associated with bubble collapse.

Heterogeneous systems

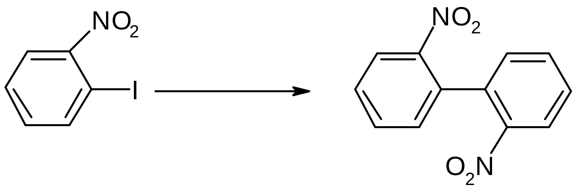
This system differs from the homogeneous system only in the phase at which the bubble collapse takes place. In the case of the cavitation bubble formed at or near to any large solid surface the bubble collapse will no longer be symmetrical. The large solid surface hinders liquid movement from that side and so the major liquid flow into the collapsing bubble will be from other side of the bubble. As a result the liquid jet will be formed which is targeted at the surface with the speed in excess of $100 ms^{-1}$. The mechanical effect of this is equivalent to high pressure jetting and very effective in cleaning. Depending upon the conditions used this powerful jet can activate surface catalytic material into porous supports and generally increase mass and heat transfer to the surface by disruption of interfacial boundary layers.



Scheme 1

The O-alkylation of 5-hydroxychromones is a difficult process probably as a result to ionization caused by hydrogen bonding between the carbonyl and OH group coupled with some dispersion of the resulting phenoxide O- charge (Scheme 1). The yield can be greatly improved by sonication (probe 20kHz). Power ultrasound will be very effective by the reduction of particle size of potassium carbonate.[36]

Conventional Ullmann coupling methodology of 2-iodonitrobenzene to give dinitrodiphenyl requires 48h with ten fold excess of copper powder where as power ultrasound affords similar yield in 1.5h using only 4 fold excess of copper (Scheme 2).[36] It was observed that the average particle size of the copper fell from 87 to 25 μm but this increase is insufficient to explain the large enhancement of reaction rate. Sonication assisted in breaking down of intermediates and/or desorption of products from the surface. Also an additional practical advantage is that sonication prevented the sticking of copper powder to the vessel walls which is a common problem in conventional process.



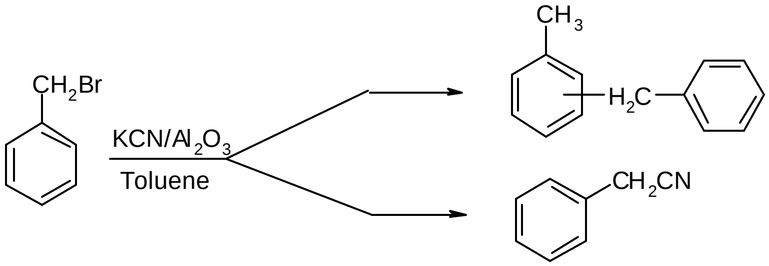
Scheme 2

The saponification of benzoate esters using 10% sodium hydroxide results in low yields under reflux after 90 minutes. Sonication results in the formation of fine emulsion of two immiscible liquids and this mechanical effect facilitates the complete conversion of ester in just 1h at room temperature.[42]

Other applications of sonochemically induced emulsification are in phase transfer catalysis, emulsion polymerization and two phae enzymatic syntheses.

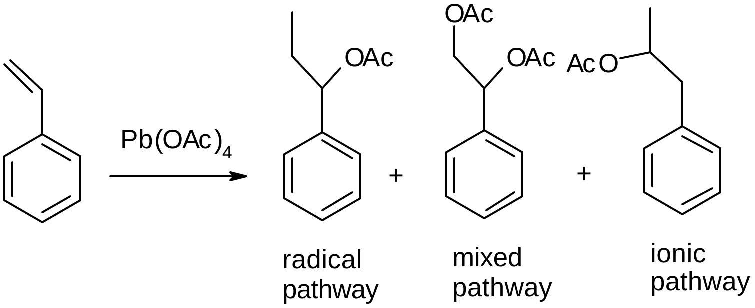
Reactions switched by ultrasound

Ando et.al[43] demonstrated for he first time the sonochemical switching when a suspension of benzyl bromide and alumina supported potassium cyanide in toluene as solvent resulted in benzyl cyanide in 77% yield under sonication. The room temperature stirring results in 75% of diphenyl methane products via Friedel-Crafts reaction of benzyl bromide with solvent toluene. The explanation is based upon the structural change to tha catalytic sites of the solid support under sonication, possibly by masking them through cavitationally induced cyanide absorption (Scheme 3).



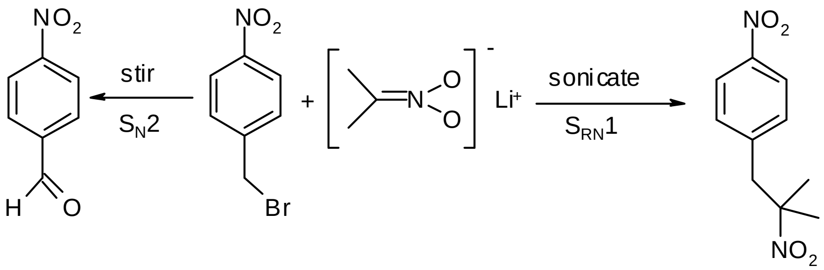
Scheme 3

The decomposition of lead tetraacetate in acetic acid in the presence of styrene at 50oC generates small quantity of diacetate via ionic mechanism. Under otherwise identical conditions sonication of the mixture gives 1-phenylpropyl acetate predominantly through an intermediate methyl radical, which adds to the double bond (Scheme 4). This clearly depicts the favouring of radical pathway under sonochemical conditions.[44]



Scheme 4

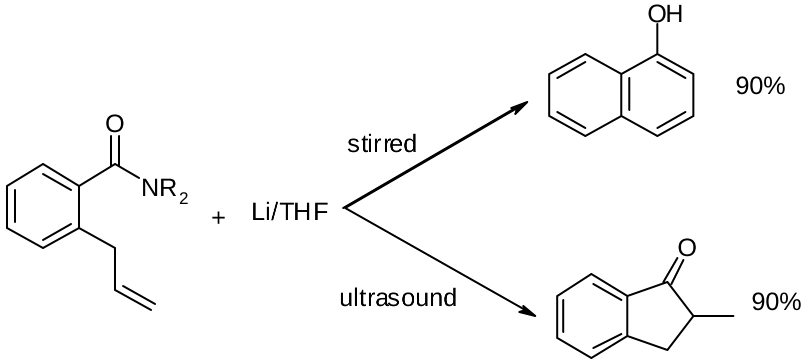
A sonochemical switching was observed in the reaction of 4-nitrobenzyl bromide with 2-lithio-2-nitro propane when 4-nitro benzaldehyde was the sole product via polar mechanism



Scheme 5

(scheme 5). An alternative SET pathway exists in this reaction leading to the formation of dinitro compounds. Sonication changes normal course of reaction and gives preferentially the latter compound.[45]

Another example of sonochemical switching is observed in the formation of the indanone nucleus from o-allyl benzamides.[46] Under sonication the formation of the ketyl radical anion is accelerated and cyclization to 2-methylindanone occurs (Scheme 6).



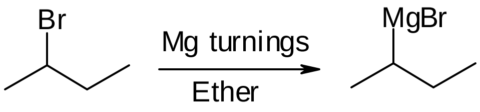
Scheme 6

1.5.1.5 Applications of ultrasound in synthesis

Activation of metals

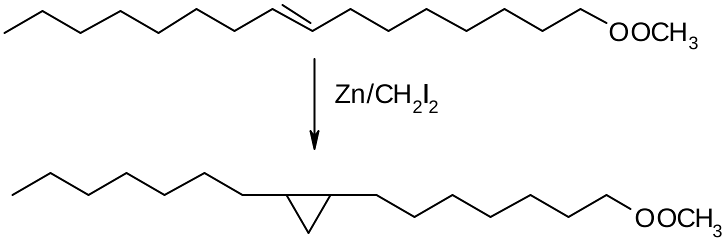
Ultrasound can be used to accelerate reactions involving metals through surface activation which can be achieved in three ways a) by sonication during the reaction b) as a pre-treatment before the metal is used in a conventional reaction or c) to generate metals in a different and more reactive form.

A remarkable achievement in this area is the ultrasound promoted Grignard reaction.[42] The reaction is very simple and can be carried out without much precaution. Damp technical grade ether can be used as solvent. Ultrasound effectively initiates the reaction without any help of other chemical initiators. The periodic crushing of magnesium metal to initiate the reaction can be avoided by the use of ultrasound (Scheme 7).



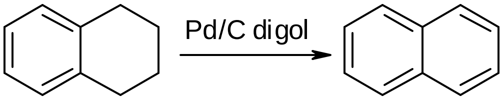
Scheme 7

Zinc is particularly activated by sonication. Simmons-Smith reaction involving the formation of cyclopropane rings with zinc dust, diiodomethane and an alkene suffers several experimental drawbacks like sudden exothermicity, foaming and difficulties in removing finely dispersed metal particles. Conventional method uses modification in Zn metal by using zinc-silver or zinc-copper couple and/or iodine or lithium in conjuction with metal. These can be avoided using sonochemical method (Scheme 8).[48]



Scheme 8

The dehydrogenation of tetrahydronaphthalene to naphthalene using 3% Pd/C under digol as solvent is facilitated by sonication (Scheme 9).[49] In conventional method, at 200°C yield is only 55% after 6 h and then become stabilized.



Scheme 9

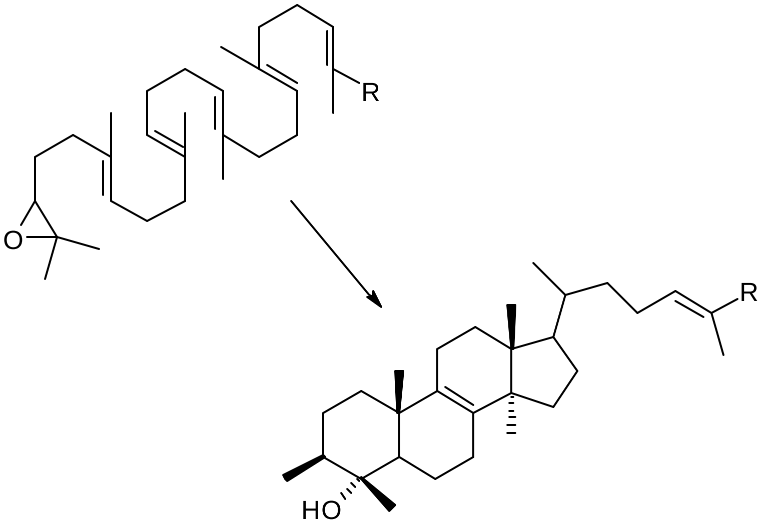
A novel method of generating finely divided zinc metal is by the use of pulsed sonoelectrochemistry using an ultrasonic horn as cathode.[50] Normal electrolysis of zinc chloride and ammonium chloride solution with ultrasonic horn as cathode results in the zinc depositions on horn (cathode) as fine powder. This has been proved more active catalyst than commercial zinc for Michael addition.

A very active Rieke metal powders can be prepared by the application of ultrasound at ambient conditions. Nickel can be surface activated using sonication which will be more effective in the hydrogenation catalyst Raney Nickel.[51]

Enzymatic synthesis

Enzyme or whole cell reactivity under ultrasound irradiation is an emerging field. High power ultrasound will break biological cell walls releasing the contents but it can also denature enzymes. So it is very important that conditions of sonication must be carefully regulated to tolerate the biological cell.

Controlled sonication has been used to stimulate a suspension of Baker's yeast to produce an inexpensive source of sterol cyclase.[52] Significantly, sonication has no effect on the activity of the isolated cell-free cyclase system, a result which demonstrates how cell membrane disruption can occur without damage of the contents. Sonication is very effective in solvent combinations in peptide synthesis where two immiscible solvents when sonicated forms an emulsion which facilitates the reaction.[53]

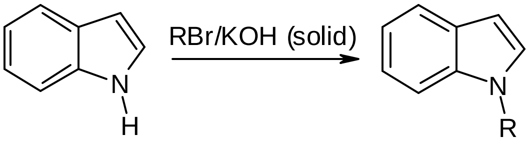


Scheme 10

Another example of pulse sonication is the converion of cholesterol to cholestenone, optimum conditions being a pulsed ultrasound of 2.8W power applied for 5s interval for 10min gave 40% increase in the yield (Scheme 10).

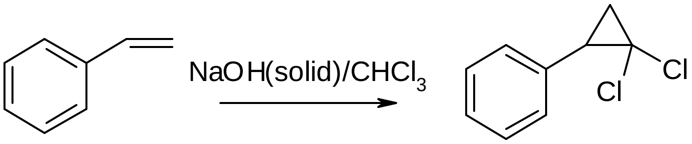
Phase transfer and related reactions

The effect of cavitation in suspended solids are explained in above section which forms the basis of reactions involving solid-liquid phase transfer catalysis. N-alkylation of indole with alkyl bromide in toluene with KOH as base at 25^{o}C using tetrabutylammonium nitrate as PTC results in 19% yield after 3h of stirring (Scheme 11).



Scheme 11

The yield increased to 80% after sonication for just 80min.[27] Sonochemistry sometimes completely eliminated the use of PTC as in the case of the generation of dichlorocarbene by direct reaction of chloroform and NaOH solution (Scheme 12).



Scheme 12

1.5.1.6 References

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1.5.2. Ultrasound promoted Heck coupling in ionic liquid at ambient conditions

1.5.2.1. Preamble

One of the major problems in transition metal catalyzed reactions is the recycle of expensive catalysts and ligands. Ionic liquids are able to dissolve organometallic compounds and are therefore possible solvents for reactions with homogeneous catalysts. The possibility to adjust solubility properties by different cation/anion combinations in I.L.s allows a systematic optimization of the biphasic reaction. Also ILs will be superior solvents for ionic metal complex catalysts. The use of ultrasound as non-conventional form of energy, for carrying out organic reactions has already been detailed in the previous section. A phenomenon called 'cavitation' provides the driving force for the reaction. Solvents play a very important role in the production of cavitation when ultrasound is passed through a medium. Solvents with very low vapour pressure are considered as good solvents for ultrasound promoted chemical transformations. In the next two sections, the use of ultrasound in promoting C-C bond formation reactions in ionic liquids are demonstrated.

1.5.2.2. Introduction

The synthesis of arylated and vinylated olefins is of fundamental importance in Organic chemistry. In this C-C coupling of haloalkenes and haloarenes with alkenes is known as Heck coupling reaction.[1] Styrenes and dienes can be prepared directly from corresponding alkene and aryl or vinyl compounds substituted with a leaving group X such as Cl, Br, I, N_2BF_4, OTf, COCl. Owing to the possibility of preparing not only simple terminal or 1,2-disubstituted olefins but also numerous complex molecular frame-works, e.g. tertiary and quarternary stereogenic centers via Heck reactions, this methodology has become one of the most important transition-metal catalyzed transformations in organic synthesis.[2]

- **Catalytic cycle**

The mechanism of Heck reaction is illustrated in Fig. 1. Palladium salts alone can be used, although the addition of ligands is often found to improve the efficiency of the reaction. The palladium catalyst precursor has been postulated as a coordinatively unsaturated 14-electron species (PdL_2). Oxidative addition of R'X occurs to generate a cis-$RPdXL_2$ species, which consequently isomerizes to the thermodynamically more stable trans configuration. In order for alkene to insert into the complex, free coordination site is necessary and creation of this has generally been accepted as involving the delegation of an uncharged ligand to give a neutral Pd complex to which the alkene coordinates.

The C-C bond forming step, where the alkene inserts into the Pd-R' bond, results in the formation of unstable σ-bond. Rotation about the C-C bond and β-hydride elimination produces the new substituted alkene, which is then eliminated from the system. In order for the cycle to continue, regeneration of the active PdL_2 complex is effected by the addition of a base to remove HX from the inactive $HPdXL_2$ complex.

There are a lot of literatures available for the mechanism of the Heck reaction with stress on some theoretical study on the key alkene insertion step.[4] The reaction conditions and reagents are carefully selected as they add to the sensitivity of reaction. Amatore et.al.[3] proposed the formation of initial complex on mixing $Pd(OAc)_2$ with n equivalents of PPh_3 (where n≥2). The resulting complex $Pd(PPh_3)_2(OAc)_2$ is unstable. A ligated PPh_3 causes the complex to undergo an intramolecular reduction, generating a short lived palladium(0) species. Coordination of another molecule of PPh_3 results in the formation of $[Pd(0)(PPh_3)_2(OAc)]^-$, 2, the active catalytic species that initiates the Heck cycle. The reducing PPh_3 forms a phosphonium salt and the adventitious presence of water results in the formation of acetic acid, triphenylphosphine oxide and protons. The anionic species, $[Pd(0)(PPh_3)_2(OAc)]^-$, 2, is therefore recommended as the active catalyst that initiates the catalytic cycle, which agrees

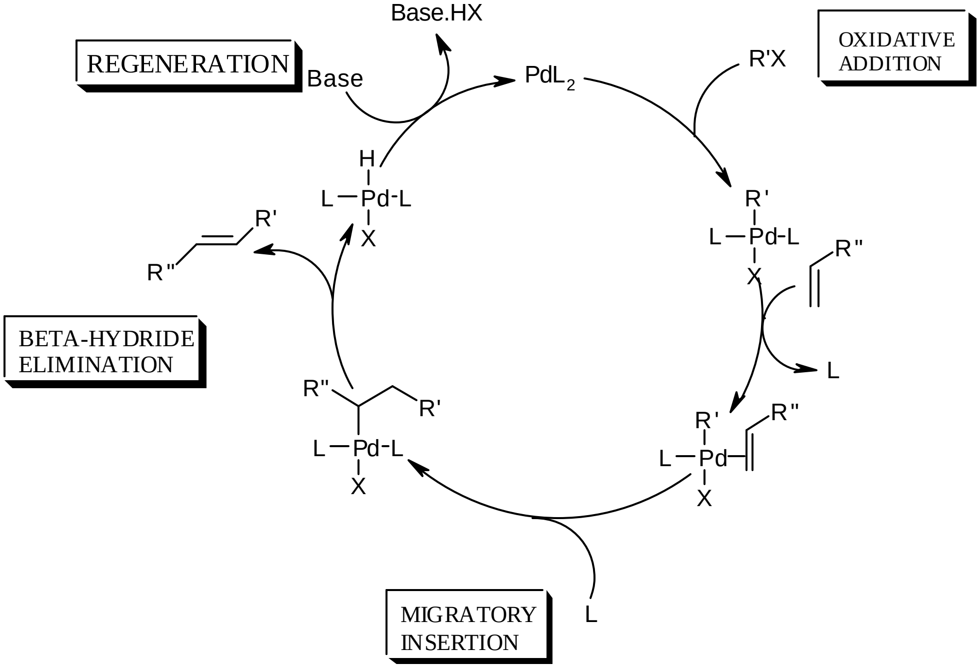


Fig. 1

with an earlier postulation by Spencer,[15] of possibility of acetate containing palladium intermediates in the catalytic cycle of aryl chlorides. Oxidative addition of R'X to the anionic complex proceeds rapidly to give a transitory anionic pentacoordinated complex. After the loss of halide ion X-, the neutral trans-R'Pd(OAc)$(PPh_3)_2$ species is found to be the key reaction intermediate. In the Heck reaction of aryl bromides and aryl chlorides the anion X- involves in determining the real structure and reactivity of resulting reactive intermediates. Catalyst precursors are also an integral part in defining the reaction path way. So it is very clear that the reaction intermediates and their associated reactivities are intimately associated with the chosen catalyst, substrates, additives and reaction conditions.

- **Catalysts**

A variety of catalysts are reported for Heck reaction.[1,2,5] Apart from the traditional Pd (0) phosphine complexes, a good number of improvements and modifications are reported. Pd(II) salts in the presence of ligands are reported to be very effective catalysts. Jeffrey[6] showed that the addition of tetralkylammonium salts can increase the reactivity and selectivity of the reaction. Resier reported an increase in catalytic efficiency by employing high pressure conditions. Recently microwave assisted Heck reaction have been reported.

General problem of Heck reaction to be carried out in industry is the separation and the reusability of expensive palladium catalyst. A solution to this problem is to support palladium species on a suitable solid support by which the catalyst can be easily filtered and recycled after the completion of reaction. Many supports such as carbon, silica magnesia etc. are reported.[9] Palladium deposited on porous glass,[10] palladium clusters[11] and palladium/nickel clusters[12] are also very effective heterogeneous catalyst. Drawbacks of these catalytic systems are their high reaction temperatures, need of activated haloarenes or diazonium salts and also the effective reusability is yet to be established. Dendritic diphosphine metal complexes are structurally well defined catalysts for Heck reaction which can be easily recycled.[12]

Another methodology is the two-phase catalysis.[13] In this the catalyst is sequestered in a hydrophilic phase in which organic products are insoluble. Water soluble catalytic systems utilizing sulphonated phosphines (TPPTS) have been successfully employed in Heck reaction. Also a carbohydrate substituted moiety is reported to render water solubility for the catalyst. Heck coupling in aqueous media is also reported in the presence of phase transfer catalysts. [14]

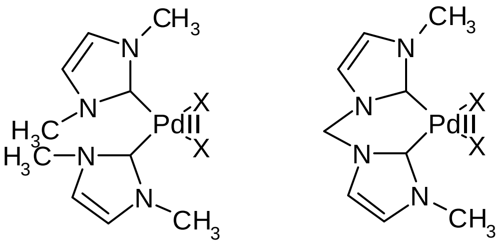
In a quest for active and productive catalyst for large scale applications of Heck reaction, Hermann et.al and Beller[16] came up with a novel air and moisture stable phosphapalladacycles which resulted in high turn over number and turn over frequency.

Importantly, some of the chloro compounds are also activated with modified palladacycle. The increased catalyst productivity of palladacycles is due, in part, to heir pronounced thermal stability in solution. Conventional adducts such as $Pd(PPH_3)_2(OAc)_2$ and $Pd_2(PPh_3)_2(\mu\text{-}OAc)_2$ are deactivated at temperature above 120°C causes depletion of catalytic activity by the precipitation of elemental palladium resulting in the breaking of catalytic cycle. Palladacycles are very stable upto 130°C which makes them advantageous catalyst for less reactive substrates.

Some new types of catalysts are developed by Milstein et.al and Reetz[17] which consist of Pd(II) species with a tridentate PCP-ligand system which are air and moisture stable. No catalyst degradation was observed after heating to 140°C and a turn over number of 132900 is achieved. Also they has shown activity for chloro and bromo compounds.

- *Palladium bis carbene complexes*

Pd-Carbene complexes are another class of highly stable and active catalysts. N-heterocyclic carbenes (NHC) derived from imidazole and pyrazole synthesized by Hermann et.al[18] exhibited remarkable stability towards heat and oxygen. Spectroscopic studies revealed the close relationship of NHCs and organophosphanes. They are both pronounced σ-donor ligands with only backbonding character. Regarding the theory of their bonding, the NHCs are best treated as "diaza-allyl systems", with little π aromaticity being present in the C-C and CN unsaturated species. The typical σ-donor ligand character can substitute classical 2e- donor ligands such as amines, ethers and phosphanes.



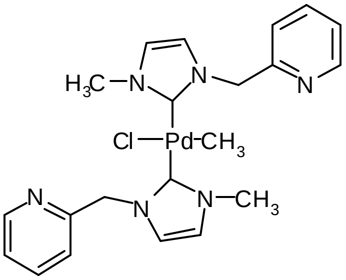
1 **2**

X = Cl, Br, I

Complexes 1 and 2 are very active after reduction to Pd[0] species with formate or hydrazine for the Heck reaction of bromides and chlorides. These catalyst have following advantages over phosphine based catalysts.

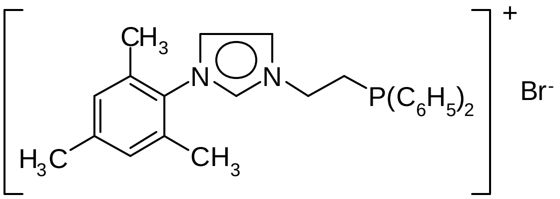
a. high thermal and hydrolytic durability resulting from exceptionally stable M-C bonds (long shelf-life, stability to oxidation)

b. easy accessibility
c. no need for an excess of ligand
d. the prospects for derivatization to water-soluble catalysts (two-phase catalysis), immobilization, and chiral modification seem promising because of the constitution of ligands.



3

Catalysts like proved to be very active for Heck coupling reaction with turn over number 1.7 x 10^6. High efficiencies in Heck reactions of aryl bromides were reported by Nolan group who used palladium in presence of C,P-chelating N-heterocyclic carbene ligands derived from the sterically demanding imidazolium salt.



4

Exceptionally stable nickel and palladium complexes derive from imidazolium linked orthocyclophanes catalyzes Heck coupling of aryl bromides and iodides with remarkable activity.

A number of metals other than Pd, are reported to be active for Heck coupling. These include Co, Rh, Ir and Pt. A number of Ni salts are also employed for this reaction but with limited success.[19,20,21]

- **Limitations in Heck reaction**

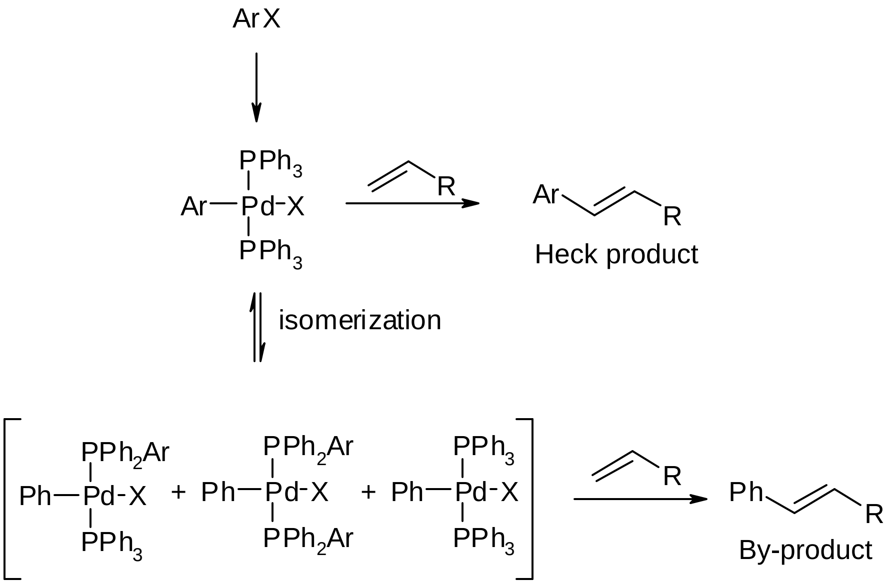
    - *C-X bond strength*

The oxidative addition of Ar-X to a palladium (0) species is considered as key step and has been debated elaborately in the literature. This is the initiating step for almost all Pd-catalyzed reactions involving R-X species as one of the reactant. The order of bond strengths for halides is: Ar-Cl>Ar-Br>Ar-I, which corresponds to the experimentally found bond dissociation energies of 96, 81 and 65 kcal/mol, respectively.[4a] This trend is also reflected in the ability of aryl halides to undergo the oxidative coupling with Pd(0) species: Ar-Cl<Ar-Br<<Ar-I. Electron donating substituents on the aryl group make the oxidative addition more difficult, as a result, electron-poor aryl halides are often referred to as 'activated', and electron-rich aryl groups as 'deactivated'.

The challenging task for synthetic chemists is to activate chloroarenes for the Heck reaction for the following reasons. i. Aryl iodides are more expensive than aryl chlorides and aryl bromides. ii. Aryl chlorides are more widely available. iii. Aryl chlorides are inherently more robust and can tolerate a wider range of reaction protocols.

- *By-products and catalyst decomposition*

Deactivated halides are unreactive to oxidative addition with Pd(0) under mild conditions, reaction proceeds at much higher temperature.



5 6 7

Scheme 2. Mechanism of by-product formation

This leads to the decomposition of catalyst and other side-reactions, through the cleavage of P-C bond in the case of a phosphine ligand. Oxidative addition of Ar-X gives trans-$ArPdX(PPh_3)_2$ intermediate which can react with olefin to form expected Heck product. The complex may undergo P-C bond cleavage and aryl scrambling to give isomerised intermediate. There can be a maximum of two phenyl group cleaved. Subsequent intermolecular phosphine scrambling of

5 accounts for the formation of 6 and 7, and 5-7 can react with the olefin to furnish undesired by-products. In a study on thermal stability of complexes of the type $(Ph_3P)_2Pd(Ph)(X)$ (where X=F,Cl,Br and I) revealed that aryl scrambling of aryl iodide complex is much more facile than their chloride and bromide counter-part and also electron-withdrawing groups on both phosphine ligand and the palladium-bound aryl groups was found to suppress aryl scrambling. Some other mechanisms for P-C bond cleavage suggest the nucleophilic 1,2-migration of phenyl group from phosphine to Pd atom and an oxidative addition of a P-Ph bond to a palladium (0) species. P-C bond cleavage also contributes to the decomposition of catalytic species by creating unstable subcoordinated palladium complexes that eventually precipitated out of solution as palladium black.

- **Recent Advances in Heck reactions**

Recent advances in the innovations in Heck reaction with respect to different reaction parameters is discussed briefly.

- *External energy*

Improvements in Heck procedures have been demonstrated with different forms of energy inputs other than traditional heating by means of ultrafast heating and pressure effects.

Very fast heating by means of microwaves leads to shortening of the reaction times, while the yields and selectivity do not greatly differ from the same reactions carried out using conventional heating.[8] Heck reactions are facilitated by higher temperature, naturally if reagents, products and catalyst can survive harsh treatments. In conventional heating the heat is transferred to the reaction bulk through the walls of the container by convection which can result in non-uniform heating and local heating. This can be overcome to an extend with microwave heating which uniformly deploy heat directly to the reacting molecules by microwave energy absorption by polar solvent.

High pressure can also have a beneficial effect on Heck reaction. The key steps of the Heck cycle – oxidative addition and migratory insertion- have a negative activation volume and thus are likely to be accelerated by pressure.[2a] An increase in stability of the catalyst has been observed by the increase in pressure by the inhibition of deligation of palladium catalyst, so that lower amounts of ligand can sustain the Pd(0) state. The increase of oxidative addition with pressure makes it possible to perform reactions with substrates, practically unreactive under normal conditions such as chloride and bromide leaving groups.

- *Media*

Virtually all solvents have been used for Heck reactions but the most suitable are polar solvents having an ability to additionally support palladium complexes by weak coordination such as acetonitrile, DMF, DMA, NMP etc. The search for alternative media is targeted at he development of highly productive, environmentally safe, recyclable techniques which can be promoted to large scale applications.

- *Aqueous Media*

The use of aqueous solvents pursues such utilitarian goals as the development of environmentally and technologically safe processes. Water, the most polar solvent promotes the migratory insertion which have pronounced effect on underligated and phosphine free systems. But presence of water can have a negative effect on oxidative addition step. The reactions of aryl chlorides and unactivated aryl bromides are benefited by aqueous medium.

Water is a good ligand for palladium – strongly bonded but kinetically labile. When added in large quantities, water is able to displace other labile ligands from the coordination shell of palladium, particularly iodide which poisons the catalyst and blocks the cationic path. But at the same time water can wash out useful ligands such as acetate. Moreover, the aqueous environment has an effect similar to the effect of high pressure discussed above, as hydrophobic interactions make more compact transition states more favorable.

- *Molten Salts*

The use of molten salts or nonaqueous ionic liquids allows for both easy recycling of catalytic system (due to temperature-dependent miscibility with non-polar solvents and water) and the possible activation of catalyst. Molten salts are highly polar, thus facilitating the cationic mechanism of Heck reactions, and can contribute to the stabilization of underligated Pd(0) species by forming anionic complexes with halide ions. This is exemplified by the enhanced reactivity of aryl chlorides. Usually quaternary ammonium salts are used as catalyst. n-Bu_4NBr is reported to be the effective catalyst in this system. The recycling of catalyst is usually been done by evaporating the reactants and products from the mixture, leaving behind ionic liquid and catalyst. The ionic liquids 1-butyl-3-methyl imidazolium (bmim), 1-pentyl-3-methylimidazolium (pmim) and 1-hexylpyridinium (C_6py) cations and chloride, BF_4 or PF_6 as counteractions have been effective in Heck reactions. The reaction between iodobenzene and ethylacrylate proceeds smoothly in C_6pyCl at 40^{o}C with Et_3N or Na_2CO_3 as base to give quantitative yields of ethylcinnamate with phosphine-free $Pd(OAc)_2$ as catalyst. Ionic liquid process for Heck reaction has been considered as one of the cleanest recyclable procedures so far described, because of the catalyst holding capacity for ionic liquid phase and the complete purging of other reagents is possible. Literature suggest the inefficiency of ionic liquid to catalyse chloroarenes, but it is proven very effective for bromoarenes including 4-bromoanisole. The formation of carbene formation in imidazolium based ionic liquids is proven very recently. Xiao et.al. reported the facile formation of Pd-carbene complex with [bmim]Br but failed to form complex with its BF_4 counterpart i.e [bmim]BF_4. This complex is proved to be effective for Heck reaction for less reactive substrates also. It can be concluded that carbene complex serves as a temporary storage for palladium, keeping it from deactivation through reduction to Pd(0) and nucleation of inactive metal particles.

- *Super critical fluids and subcritical fluids*

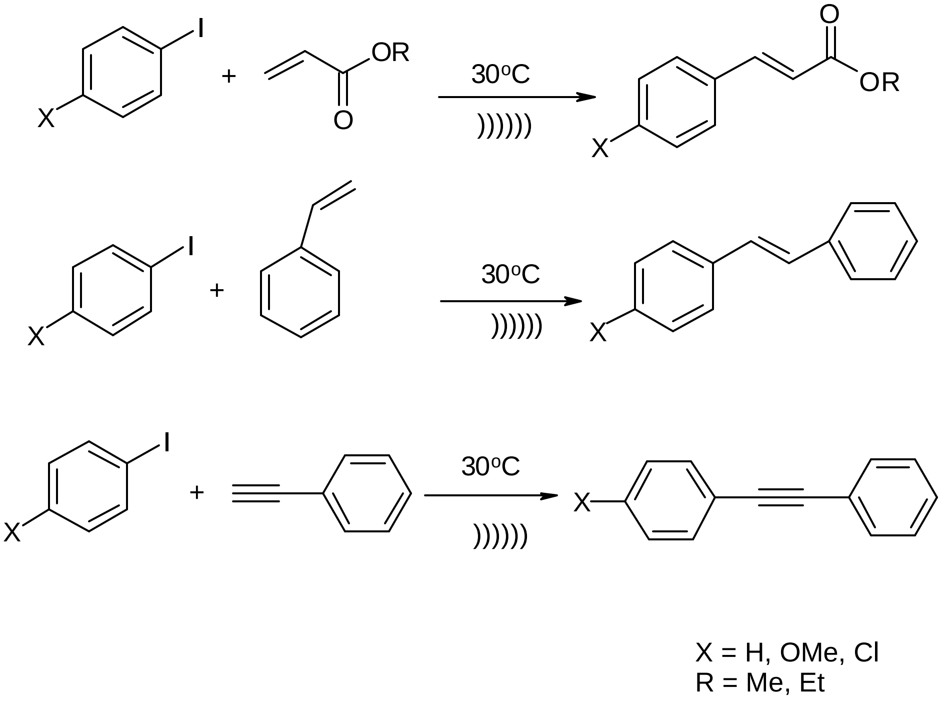
These years supercritical fluids have come-up as promising media for organic reactions. Supercritical carbondioxide is considered as most perfect environmentally friendly solvents. Liquid CO_2 is a good solvent for organic compounds but very poor solvent for inorganic salts. Solvent properties of CO_2 can be compared with those of fluorinated solvents. Solubility of palladium species is the main concern in this system. This can be overcome by using fluorine containing precatalyst such as palladium trifluoroacetate. The use of palladium on charcoal is demonstrated in the Heck reaction of aryl iodide to give a very moderate yield. Supercritical water is also a good choice as a solvent. Near critical point (373^{o}C, 221 bar), water loses its structure and turns into a nonpolar liquid with dielectric constant close to 6, which leads to a dramatic increase of he solubility of organic compounds and makes it a good solvent even for reactions with hydrophobic substrates. Several reports on over heated water (260^{o}C) as solvent for Heck reaction have been published.

- *Fluorous systems*

The success of aqueous biphasic catalysis brought about several limitations, of which the most famous and ambitious is the so-called fluorous (fluorine+aqueous) catalysis employing a specific affinity of fluorinated compounds for perfluorinated solvents. The solubilization of the catalyst requires the use of fluorinated ligands with high fluorine content. Such solvents are immiscible mostly with organic solvents which makes the separation of the catalyst easy. Heck reaction with fluorine substituted triphenylphosphine ligands have been reported to be active catalyst in fluorous solvents. The main drawback is the loss of activity of palladium due to the formation of inactive palladium black.

1.5.2.3. Present Work

Heck reaction between substituted iodobenzenes with various olefins/phenyl acetylene was carried out under ambient temperature under ultrasound irradiation. The reaction went to completion with good selectivity to trans product with out any added phosphine ligand.



Scheme 3. Ultrasound promoted Heck reaction

1.5.2.4. Results and Discussions

The products could be easily separated from the catalyst by extraction with 10% ethylacetate in petroleum ether leaving behind the palladium catalyst in the dissolved state in the immiscible ionic liquid. The catalyst thus recovered as a solution in the ionic liquid could be reused at least three times without any loss of activity. Pure products were isolated by column chromatography.

As is evident, the ultrasound assisted Heck reaction of the iodobenzenes with alkenes/alkynes proceeded smoothly at ambient temperature (30°C) with complete conversion of iodobenzenes in just 1.5-3h to afford the *trans* products in excellent isolated yields (73-87%). No reaction under similar sonication condition was observed when the ionic liquid was replaced by molecular solvents such as DMF and NMP even in the presence of a ligand such as PPh_3.

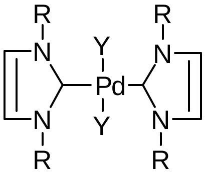
Table 1. Heck reaction of iodobenzenes with activated alkenes/alkyne under sonication in $[bbim]^+ Br^-/[bbim]^+ BF_4$

No.	Aryl Halide	Olefin/alkyne	Time (h)	Product	% Yield (Isolated)
1.	Iodobenzene	Methyl acrylate	2.0	Methyl Cinnamate	81
		Ethyl acrylate	1.5	Ethyl Cinnamate	87
		Styrene	1.5	Stilbene	82
		Phenyl acetylene	2.0	Diphenylacetylene	78
2.	p-methoxy iodobenzene	Methyl acrylate	3.0	4-methoxymethyl cinnamate	82
		Ethyl acrylate	3.0	4-methoxyethyl cinnamate	79
		Styrene	3.0	4-methoxy stilbene	80
		Phenyl acetylene	2.0	4-methoxy Diphenylacetylene	77
3.	p-chloro iodobenzene	Methyl acrylate	1.5	4-chloromethyl cinnamate	79
		Ethyl acrylate	1.5	4-chloroethyl cinnamate	77
		Styrene	1.5	4-chloro stilbene	73
		Phenyl acetylene	2.0	4-chloro Diphenylacetylene	78

The reaction also did not proceed with the less reactive aryl chlorides (chlorobenzene, p-nitrochlorobenzene and 2,4-dinitrochlorobenzene) and aryl bromides (bromobenzene) under the sonochemical conditions of the present work. Obviously, no reaction even in traces could be observed under ambient conditions in the absence of ultrasound.

Phosphine ligands, ammonium and phosphonium halides and quarternary ammonium salts have been found to stabilize the Pd-catalysts probably via formation of zero valent Pd species and accelerate the olefination reaction. In the case of imidazolium ionic liquids, the 2-H proton is acidic and in presence of a base can be deprotonated to form a carbene. These carbenes readily coordinate with metals especially with Pd(II) resulting in an imidazolylidine-palladium carbenoid species. These Pd-carbene complexes with alkylimidazo-2-ylidenes have been reported very recently to be active in the Heck reaction. In the present work, the formation of such complex was studied by subjecting a mixture of $Pd(OAc)_2$/ $PdCl_2$ and NaOAc in $[bbim]^+Br^-$ and $[bbim]^+BF_4^-$ respectively to ultrasound irradiation for 1h. The complex was extracted into chloroform from the ionic liquid, the chloroform evaporated and the resulting crude product purified by column chromatography [Petroleum ether/EtOAc, 1:1].

Indeed, the formation of the complex A was established and characterized by ^1H-NMR by the appearance of N-CH vinylic protons at 6.85d as a singlet in the complex similar to the value reported by Xiao et.al. and by the conspicuous absence of the N_2CH protons which appears as a singlet at 8.82d in the parent ionic liquid. The complexes were also characterized by Mass Spectrometry which showed the respective molecular ion peaks (Fig. 3-5, NMR). It is highly probable that complex A can be the immediate precursor for the likely active catalyst which could lead to a zero-valent Pd-species whose *in situ* generation by reduction of the divalent Pd-carbene complex is accelerated by electron transfer reactions under the sonochemical conditions primarily through the phenomenon of cavitation. It is well known that sonochemical processes proceed through SET mechanistic pathway by means of formation of transient cavitation bubbles. Adiabatic collapse of such cavitation bubbles are reported to generate temperatures of the order of 5000^0 K, pressure of ~1000 atm and high electrostatic potentials in the form of hot spots of very short lifetimes (~10^{-8} sec). It is also highly probable, the Pd- complexes form in-situ will experience secondary reactions in the liquid phase after the bubble collapse. Moreover such Pd-carbene complexes have been shown to be the precursors for active catalysts for the Heck and related C-C bond forming reactions in both molecular solvents and ionic liquids.



[A]

R = n-butyl
Y = Br, BF_4

Scheme 3. Pd-biscarbene complex A

It has long been known that chemical or electrochemical reduction of transition metal salts in the presence of ammonium salts leads to $R_4N^+X^-$ stabilized colloids. A recent study points to the involvement of intermediary colloidal Pd-nanoparticles generated under thermolytic conditions for the catalysis of the Heck reaction. The formation of such Pd-nanoparticles was investigated in the present work by subjecting the reaction mixture after a successful Heck reaction under sonochemical condition for the reaction of iodobenzene with ethylacrylate in $[\mathrm{bbim}]^+\mathrm{BF}_4^-$ for "*in situ*" TEM analysis.

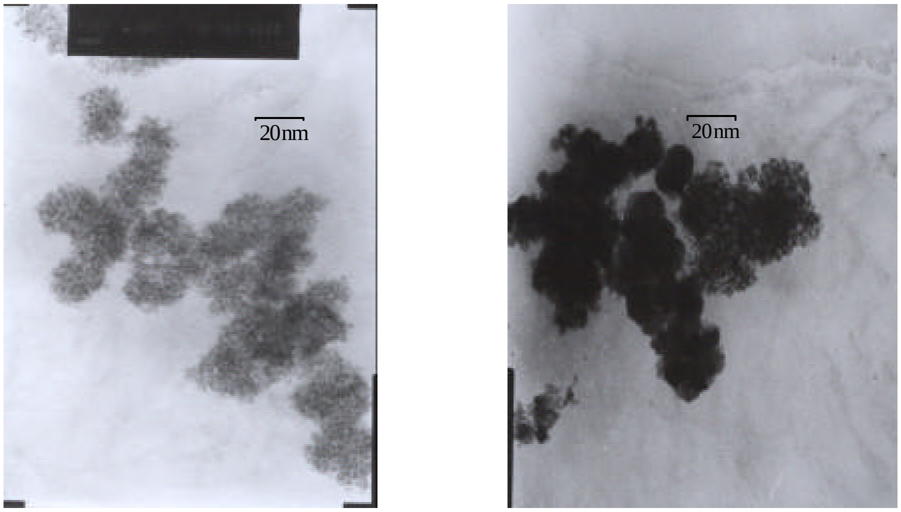


Fig. 2. TEM images of Pd-nanoparticles after Heck reaction

TEM analysis was carried out in Transmission Electron Microscope Model JEOL-1200 EX operated at 100KV with a magnification of 200K. The sample after appropriate dilution with isopropanol was directly deposited on carbon film coated TEM grids forming a thin film of colloidon. The TEM image (Figure-2) shows the presence of monodispersed grains nearly spherical in shape. The average size of the grains obtained from the TEM picture is about 20nm. The porous grains show that they are composed of dispersed particles of approximately 1nm size. The clusters of Pd^0 nanoparticles in ionic liquids were found to be stable even after storage for a week since no change in TEM picture was observed after this period, the ionic liquid obviously contributing to the stability.

Reactions with preformed catalyst was carried out to prove the exact catalytic species. It was found that Pd-biscarbene complex catalyzed the reaction between iodobenzene and ethyl acrylate resulting in comparable yields with that of $\mathrm{Pd(OAc)_2}$.

1.5.2.5. Experimental

- *Heck reaction*

In a 25 mL. two-neck flask fitted with a septum and two-way stop-cock with an argon balloon, ionic liquid (0.75 ml.), aryl halide (1.0 mmol), sodium acetate (0.1g) and $Pd(OAc)_2$ or $PdCl_2$ (1mol% with respect to aryl halide) were taken and thoroughly degassed and flushed with argon simultaneously. Acrylate or styrene (1.2mmol) was then introduced into the system through septum and the mixture was sonicated for the specified time. The reaction was monitored by TLC. After the completion of reaction, water and dichloromethane were added to the mixture. The DCM layer was washed with dil.HCl, water and brine, dried over sodium sulphate and solvent evaporated to afford the crude product. This was subjected to column chromatography (EtOAc/pet.ether 0.02:1) which furnished the pure product. The pure products were characterized by NMR, IR, Mass spectral and elemental analysis.

- *Preparation of complex [A]*

A mixture of $Pd(OAc)_2$ (50mg), NaOAc (500mg) and $[bbim]^+BF_4^-$ (1ml) was sonicated for 1h under inert atmosphere. Water (20mL.) and CH_2Cl_2 (10 mL.) were added. The organic layer was separated, washed with water (3x10ml) and brine (15 ml), dried over sodium sulphate and solvent evaporated under reduced pressure to afford crude product. The crude mixture was purified by column chromatography (petroleum ether/EtOAc, 1:0.4) to give the complex 45mg(45%) as offwhite fluffy powder.

M.P = 105-106°C

^1H NMR (200MHz, $CDCl_3$) : δ = 6.81(s, 4H), 4.82 (t, 8H NCH_2), 2.08 (m, 8H NCH_2CH_2), 1.50 (m, 8H $NCH_2CH_2CH_2$), 1.01 (t, 12H $NCH_2CH_2CH_2CH_3$).

^{13}C NMR (50MHz, $CDCl_3$) : 169.63, 120.28, 50.54, 33.11, 20.11, 13.73.

MS: m/z 466[M^+ - BF_4].

1. Methyl cinnamate

IR : 2980, 1721, 1643, 1587, 1479, 1267, 1169, 880

1H NMR ($CDCl_3$, 200MHz, δ) : 3.9 (s, 3H), 6.4 (d, J=14Hz, 1H), 7.4-7.6 (m, 5H), 7.65 (d, J=14Hz, 1H).

MS m/e: 162

2. Ethyl cinnmate

IR : 2988, 1721, 1643, 1587, 1479, 1267, 1164, 887

1H NMR ($CDCl_3$, 200MHz, δ) : 1.3 (t, J=8.0Hz, 3H), 4.2 (q, J=8.0Hz, 2H), 6.4 (d, J=12Hz, 1H), 7.4-7.5 (m, 5H), 7.65 (d, J=12Hz, 1H).

MS m/e: 176

3. Stilbene

IR : 2923, 1599, 1251, 814.

1H NMR ($CDCl_3$, 200MHz, δ) : 7.1 (d, J=17Hz, 1H), 7.4-7.6 (m, 11H).

MS m/e: 180

4. Diphenylacetylene

IR : 3069, 2108, 1592, 1487, 1242, 876.

1H NMR ($CDCl_3$, 200MHz, δ) : 7.1-7.3 (m, 10H).

MS m/e: 178

5. 4-methoxy ethyl cinnamate

IR : 2980, 1721, 1643, 1587, 1479, 1267, 1169, 880

1H NMR ($CDCl_3$, 200MHz, δ) : 1.3 (t, J=8.0Hz, 3H), 3.84 (s, 3H), 4.2 (q, J=8.0Hz, 2H), 6.4 (d, J=17Hz, 1H), 6.9 (d, J=8.2Hz, 2H), 7.5 (d, J=8.2Hz, 2H), 7.65 (d, J=17Hz, 1H).

MS m/e: 206

6. 4-Methoxy methyl cinnamate

IR : 2980, 1721, 1643, 1587, 1479, 1267, 1169, 880

1H NMR ($CDCl_3$, 200MHz, δ) : 3.82 (s, 3H), 3.9 (s, 3H), 6.4 (d, J=17Hz, 1H), 7.02 (d, J=8.0Hz, 2H), 7.54 (d, J=8.0Hz, 2H), 7.65 (d, J=17Hz, 1H).

MS m/e: 192

7. 4-Methoxy stilbene

IR : 2923, 1599, 1375, 1251, 814.

1H NMR ($CDCl_3$, 200MHz, δ) : 3.85 (s, 3H), 6.9 (d, J=8.4Hz, 2H), 7.1 (d, J=17Hz, 1H), 7.4-7.6 (m, 8H).

MS m/e: 210

8. 4-Methoxy diphenyl acetylene

IR : 3057, 2108, 1597, 1487, 1443, 1242, 882.

1H NMR ($CDCl_3$, 200MHz, δ) : 3.84 (s, 3H), 6.9 (d, J=8Hz, 2H), 7.1-7.5 (m, 7H).

MS m/e: 208

9. 4-Chloro methyl cinnamate

IR : 2980, 1721, 1643, 1587, 1479, 1267, 1169, 880

1H NMR ($CDCl_3$, 200MHz, δ) : 3.88 (s, 3H), 6.4 (d, J=17Hz, 1H), 7.4-7.5 (m, 4H), 7.65 (d, J=17Hz, 1H).

MS m/e: 196

10. 4-Chloro ethyl cinnamate

IR cm^{-1}: 2980, 1721, 1643, 1587, 1479, 1267, 1169, 880.

1H NMR ($CDCl_3$, 200MHz, δ) : 1.3 (t, J=8.0Hz, 3H), 4.2 (q, J=8.0Hz, 2H), 6.4 (d, J=17Hz, 1H), 7.4 (d, J=8.2Hz, 2H), 7.5 (d, J=8.2Hz, 2H), 7.65 (d, J=17Hz, 1H).

MS m/e: 210

11. 4-Chloro stilbene

IR : 2930, 1599, 1469, 1254, 832.

1H NMR ($CDCl_3$, 200MHz, δ) : 7.1 (d, J=17Hz, 1H), 7.4-7.6 (m, 10H).

MS m/e: 214

12. 4-Chloro diphenylacetylene

IR : 3036, 2108, 1592, 1490, 1248, 872.

1H NMR ($CDCl_3$, 200MHz, δ) : 7.1-7.5 (m, 9H).

MS m/e: 212

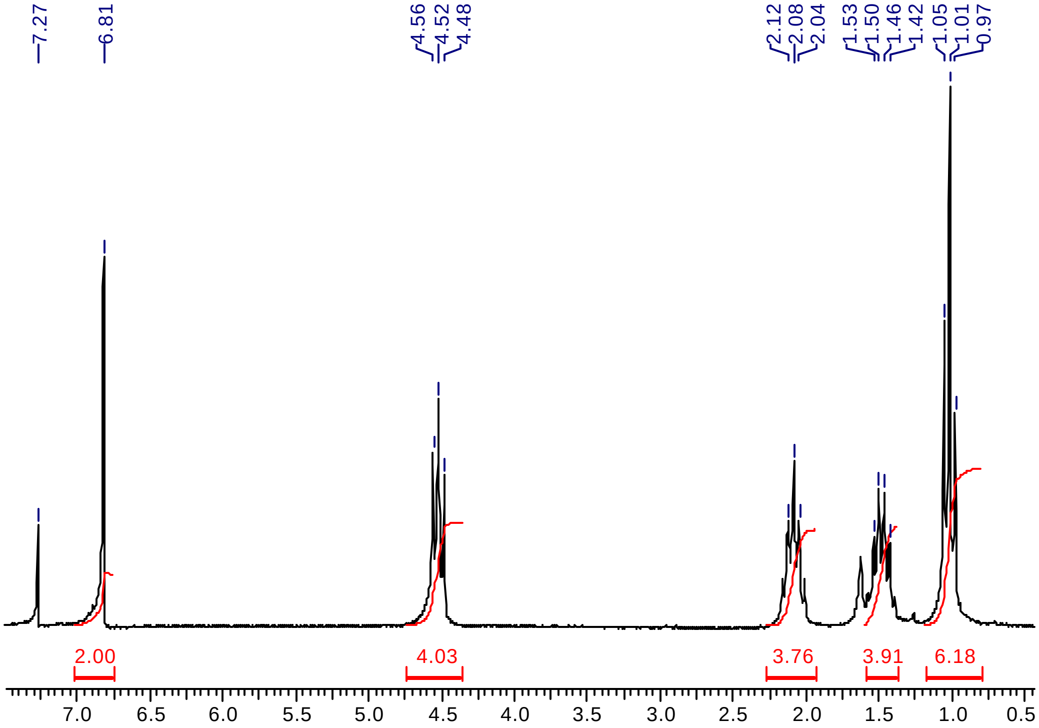


Fig. 3. ^{1}H NMR of Pd-biscarbene complex

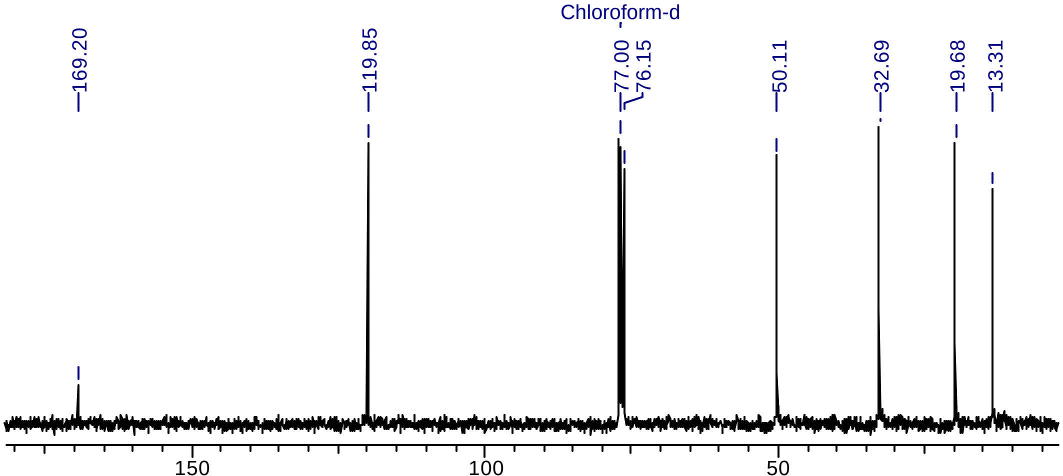


Fig. 4. ^{13}C NMR of Pd-biscarbene complex

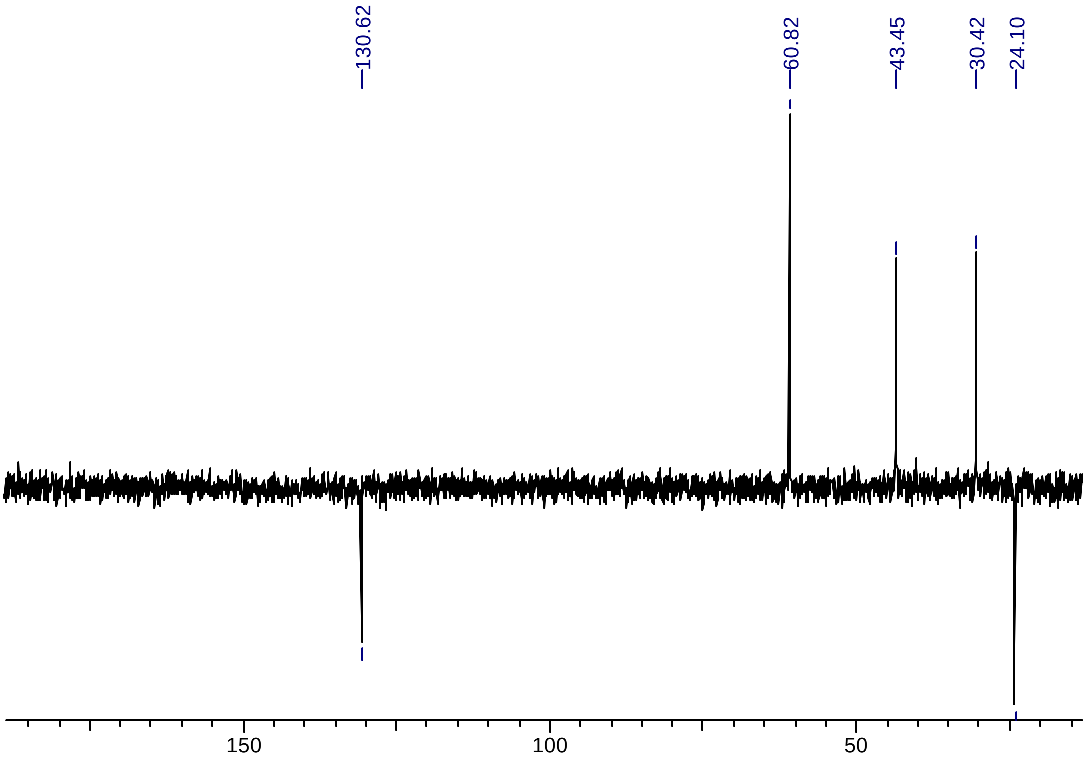


Fig. 5. DEPT of Pd-biscarbene complex

1.5.2.6. References

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1.5.3. Ultrasound promoted Suzuki Coupling in Ionic Liquid

1.5.3.1. Introduction

The palladium catalyzed cross coupling of organoboranes, organoboronic acids and esters with organic halides is called as Suzuki coupling.[1] This methodology has become very popular in past decade, which is demonstrated by the appearance of a number of publications and reviews.[2]

$$R'{-}M + R''{-}X \longrightarrow R'{-}R'' + M{-}X$$

$$M = \text{-9-BBN, -B(cyclohexyl)}_2\text{, -B(OR)}_2$$

The cross coupling reaction of organoboron compounds, which involves transmetalation to palladium(II) halides as key step, was found to proceed smoothly in the presence of aqueous base. The protocol has been proved to be quite a general reaction for a wide range of selective carbon-carbon bond formations, in addition to previous studies for related coupling reactions of organomagnesiums, -zincs, -stannanes and –silicones.[1] Now, many organometallic reagents undergo similar cross coupling reactions, but much attention has recently been focused on the use of organoboronic acids in laboratories and industries since they are convenient reagents, generally thermally stable and inert to water and oxygen, thus allowing handling without special precautions. A detailed account of catalytic cycle, catalysts, bases, solvents, conditions and side reactions are presented.

Catalytic cycle

The cross coupling of organoboron compounds follow an analogous catalytic cycle to main metal reagents involving following steps (Fig. 1).

- oxidative addition of organic halides or other electrophiles to a palladium(0) complex yielding R-Pd-X (1).
- transmetalation between Pd-X and R'-B
- Reductive elimination of R-R' to regenrate the palladium (0) complex.

The oxidative addition and reductive elimination are reasonably well understood, very less information is available for the transmetallation step in presence of a base. The addition of sodium hydroxide or other base exerts a remarkable accelerating effect on the transmetallation. Organoboronic acids do not react with R-Pd-X (X=halogen).[3-8] The quarternization of the boron atom with a negatively charged base enhances the nucleophilicity of the organic group on the boron atom for alkylation of R-Pd-X.[9] The

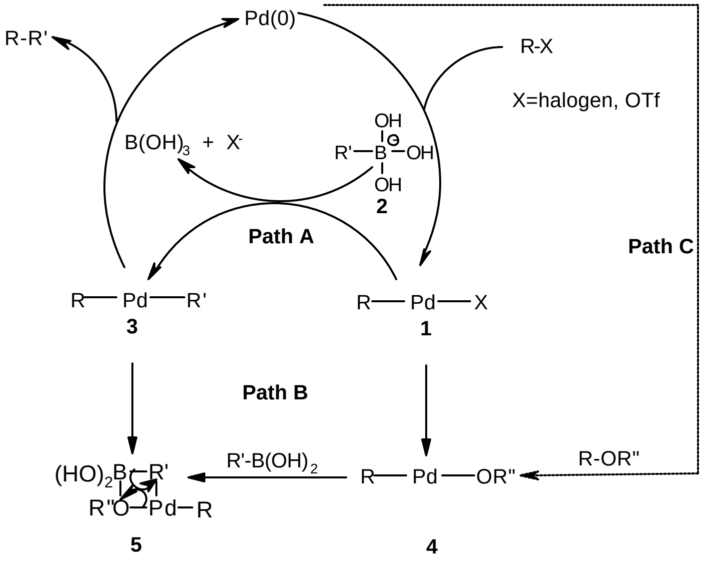


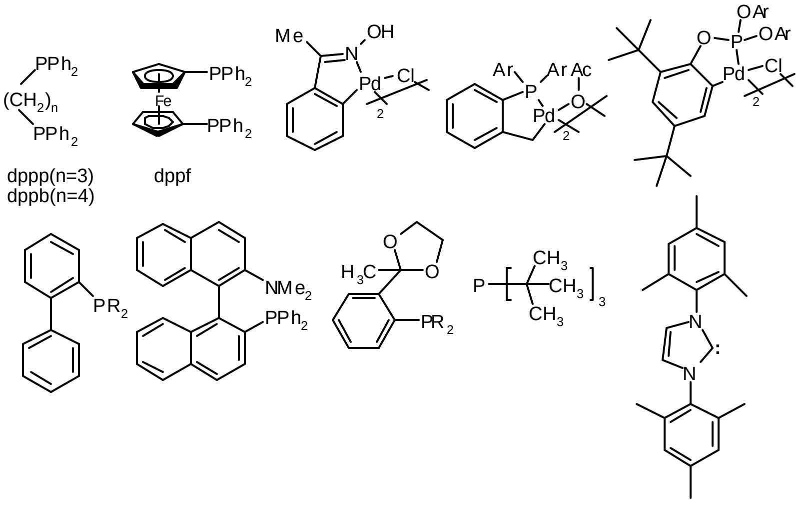
Fig. 1. Catalytic cycle for Suzuki coupling

transmetallation to 1 decreases in the order of Cl>Br>I.[9] This is in reverse of oxidative addition of organic halides to palladium (0) complexes and is highly dependent on the added base. An alternative process is transmetallation to an (alkoxo)-, (hydroxo)-, (acetoxo)-, or (acetylacetoxo)palladium (II) complex (4) in situ generated by the ligand exchange between R-Pd-X and a base (R"O^-). There are two transmetallation processes Path A and Path B for the cross coupling reaction in alkaline solution; however, it is not yet obvious in many reactions which process is predominant. The experimental results and other studies clearly reveal that transmetallation process and the rate-determninig step are highly dependent on organoboron reagents, presumably also organic electrophiles and the functionality therein.

Reaction Conditions

- **Catalysts**

The reaction is feasible with various catalysts, bass and solvents, however, the combinations will significantly affect the yields and the selectivity of products. $Pd(PPh_3)_4$ is the most common, but $Pd_2(dba)_3$ itself or plus a phosphine ligand are convenient for preparing the desired palladium(0)/phosphine complexes. $Pd(OAc)_2$ and $PdCl_2$/phosphines or plus an additional ligand are also good precursors to generate an analogous palladium(0) species because they are easily reduced in situ to the corresponding palladium(0) complexes.[10] The reduction of $Pd(OAc)_2$ with phosphine[11] is instantaneous but $PdCl_2$/phosphines can be reduced with the aid of a base.[12,13] $NiCl_2$/phosphine systems are also reported as active catalysts, but BuLi or DIBAL-h is recommended for its reduction to Ni(0) complex because their reduction is slow[14] or leads to inactive nickel hydroxide in presence of an aqueous base.[15] Various phosphine ligands are effective in stabilizing the palladium(0) species, but the stoichiometry of phosphine to palladium and the bulkiness or donating ability of phosphine ligands change the reactivity of catalysts toward oxidative addition and transmetallation.[16,17]



Scheme 2. Various ligands for Suzuki reaction.

The palladium complexes having fewer than four phosphines, weakly coordinating $AsPh_3$, or a bulky phosphine provide highly reactive catalysts because of the ready formation of the coordinatively unsaturated species. The inhibitory effect of phosphine ligand can be mainly attributed to its large steric hindrance during oxidative addition and transmetalation.[18] In the coupling reaction involving chloro arenes, a bulky ligand which can supply electrons to metal center is preferred. The electron pumping into metal center can cause the ready dissociation of ligand to generate a coordinatively unsaturated species. Also bulkier ligands like $P(Cy)_3$,[17] (dicyclohexylphosphino)aryl phosphines[19,20,21] and N-heterocyclic carbenes[22,23] are more practical ligands yielding stable catalysts at higher temperature. Palladacycles[24-36] exhibited exceptionally high catalytic efficiency in the biaryl coupling.

Nickel catalysts have demonstrated high catalytic activity for chloroarenes[14] and mesylates.[29] $NiCl_2$(dppf) with $K_3PO_4.nH_2O$[14] in dioxan solvent showed promising activity in biaryl coupling of chlorobenzenes. The reduced nickel catalyst supported on charcoal[30] and $NiCl_2$(bipyridine)[31] were also studied.

Phosphine free palladium generated in situ from $Pd(OAc)_2$ is an excellent catalyst for biaryl coupling in water or in aqueous organic solvents.[32] The advantage of such ligandless catalyst is that it eliminates phosphine related side reactions such as aryl-aryl exchange and phosphonium salt formation and achieves high catalyst efficiency allowing shorter reaction times and high turnover of the catalyst. Although ligandless catalyst often achieve significant increase in reaction rates in aqueous media, complete conversion cannot be possible in several cases. Various water soluble ligands are now available. Sulfonated phosphines such as triphenylphosphine monosulponic acid (TPPMS) and triphenylphosphine trisulphonic acid (TPPTS) are traditional ligands for homogeneous palladium and rhodium catalysts in aqueous media which are now utilized for several industrial processes.[33]

The basic problems of homogeneous catalysts incurred at separation and recycling of expensive metals can be solved by using a supported metal catalyst or by carrying reactions in a liquid-liquid two-phase system.[38] Palladium supported on charcoal (Pd/C)[34] or clay[35] and a reduced nickel on charcoal ($Ni(NO_3)_2$/C/BuLi)[30] have been used for biaryl coupling of arylboronic acids. Palladium phosphine complex supported on polystyrene resin,[36,37] deloxan[38] a crosslinked macroporous siloxane resin and amphiphilic polyethyleneglycol graft resin are reported as air stable, reusable catalysts.[39]

- **Bases and Solvents**

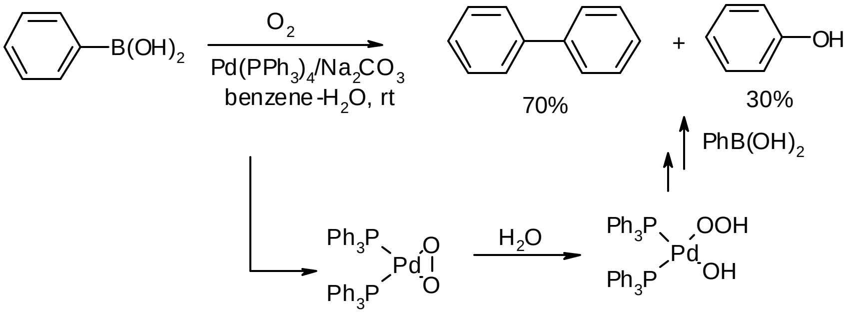
The cross-coupling reaction of organoboronic acids, in general, require a negatively charged base, such as sodium or potassium carbonate, phosphate and hydroxide (1.5-2.0 equivalents). They can be used in an aqueous solution or with phase transfer catalysts such as Bu_4NX. Aqueous Na_2CO_3 is a mild and effective base for the biaryl coupling reaction of arylboronic acids. In a recent report, the coupling of mesitylboronic acid with iodobenzene revealed the activity of base as $TlOH>Tl_2CO_3\sim Ba(OH)_2>NaOH>K_3PO_4>Na_2CO_3>NaHCO_3$.[40,41] $Ba(OH)_2$ has been recognized as effective base for the synthesis of sterically crowded 2,6,2'-trisubstituted biaryls. Since transmetalation involves nucleophilic substitution of Pd-X, a strong base is recommended when several ortho substituents are in the halides or the boronic acids. The substitution of metal halides with thallium, barium or silver nucleophiles is significantly faster than that of sodium or potassium due to the irreversible formation of highly insoluble metal salts. Fluoride salts[42] such as CsF and Bu_4NF (2-3equivs) are mild bases in which substrates are sensitive to other bases. Although reaction is slow for sterically crowded halides, a wide range of functional groups is tolerated. The usual side reactions encountered in coupling reaction due to basic solutions are saponification of esters, racemization of optically active compounds, Aldol condensation of carbonyl compounds or hydrolytic B-C bond cleavage. This can be overcome by using bases as heterogeneous phase.

- **Side reactions**

- *Participation of Phosphine-bound Aryls*

Triarylphosphines are excellent ligands to stabilize palladium species; however, the undesirable side reaction of the aryl-aryl interchange between palladium and phosphine-bound aryls leading to the coupling product of phosphine-bound aryls.[43,44] This is more in the electron rich haloarenes. The presence of ortho substituents can considerably decrease the side reaction. The aryl-aryl interchange is very sensitive to electronic and steric effects of a phosphine ligand and haloarenes.[45-47] An electron donating group in either phosphine or haloarenes increased the aryl-aryl interchange whereas both withdrawing groups and steric hindrance of ortho-substituent reversely slowed down the equilibration. The experimental results indicate that the donating phosphines having large steric hindrance are generally recommended for fast oxidative addition of organic halides to the coordinatively unsaturated and electron rich complexes.

- *Oxygen induced homocoupling*



Scheme 3.

The coupling reactions exposed to air may result in the homocoupling of arylboronic acid to biaryl. (Scheme 3) The reaction is slow under neutral conditions, but very fast in the presence of an aqueous base. It is probable that such dimerization takes place during the workup operation in air when there is unreacted aryl boronic acid. This may be due to the formation of peroxopalladium(II) complex in the catalytic cycle.[48]

- *Dehalogenation*

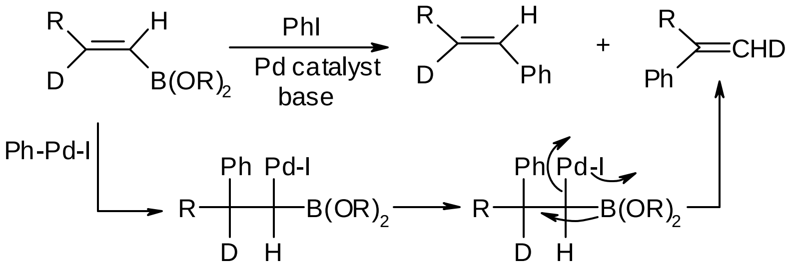
The coupling reaction is often accompanied with dehalogenation of organic halides (RX to RH), particularly when alchohols were used as the solvent. Such products can be derived from β-hydride elimination from Ar-Pd-OCH$_2$R giving Ar-Pd-H and RCHO[49] or the reduction of Ar-Pd-OH with PPh$_3$ affording Ar-Pd-H and Ph$_3$P=O.[27]

- *Protodeboronation*

The reaction under aqueous conditions gives undesirable results due to competitive hydrolytic B-C bond cleavage.

- *Head to Tail Coupling*

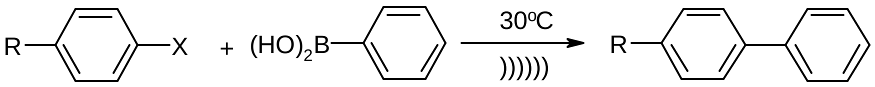
The coupling reaction of 1-alkenylboronic esters in the formation of a head-to-tail coupling product when ligandless palladium catalyst and a weak base such as triethylamine are used. (Scheme 4) The formation of such abnormal coupling product can be best understood by the mechanism of the Heck reaction for vinylic metal compounds. A deuterium labeling study proved the addition-elimination mechanism where as β-hydrogen transfers to the terminal carbon.[50]



Scheme 4

1.5.3.2. Present Work

The Suzuki coupling reaction of halobenzenes with phenyl boronic acid was carried out at ambient temperature under ultrasonic irradiation. The reaction proceeded without the addition of any phosphine ligands. The reaction was first tried in I.L $[bbim]^+BF_4^-$ as solvent.



X = I, Br, Cl
R = H, OCH_3, CH_3, Cl, NO_2

1.5.3.3. Results and Discussions

The results of Suzuki coupling reaction carried out using different haloarenes and phenyl boronic acid are shown in table. Initial reactions of haloarenes and phenyl boronic acid with $PdCl_2$/$Pd(OAc)_2$ as catalyst using different bases in ionic liquid $[bbim]BF_4$ under sonication condition failed to proceed. The main reason was found to be the poor solubility of reactant species. This was overcome by the addition of equal quantity of that of I.L., methanol to the reaction mixture. This resulted in a considerable rate acceleration with almost quantitative reaction. In air as the ambient gas, the reaction of 4-methoxyiodobenzene with phenyl boronic acid showed significant formation of unsubstituted biaryl (20%) due to the homo coupling of phenyl boronic acid, which however was not formed in the presence of the inert argon as ambient gas.

The reaction gave very good to moderate yields for different haloarenes. Iodobenzene gave quantitative yields in 20-30min., bromobenzene resulted in 82-85% yields in 10-45min. and chlorobenzenes yielded 42-52% yields in 1-1.5h. Normally less or non-reactive chlorobenzenes showed significant conversions without the addition of any phosphine ligands. However they required stronger base like sodium methoxide.

Although reaction went to completion, the catalyst species got destroyed as evidenced by the black solid in reaction mixture. With the reaction successfully proceeding, the next step is to make the expensive palladium catalyst reusable. After the reaction, thin layer chromatography of the reaction medium revealed a iodine developing spot at R_f 0.5 (Pet.Ether : Ethyl Acetate 0.6:0.4). This was isolated by column chromatography and characterized using NMR.

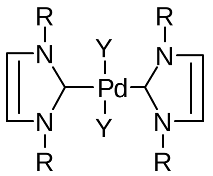
Table 1. Suzuki cross-coupling reaction of halobenzenes with phenylboronic acid in [bbim][BF_4]/MeOH under ultrasonic irradiation.

No.	Substrate	Time (min)	Yield of biaryls (%)^c	Mp of biaryls ^oC
1	Iodobenzene	20	92^a (92)	69-71
2	4-Methoxy iodobenzene	20	93^b (92)	91-93
3	4-Chloro iodobenzene	30	85^a (82)	75
4	4-Nitro iodobenzene	30	82^b (83)	113-115
5	Bromobenzene	45	82^a (82)	68
6	4-Methoxy bromobenzene	10	85^b (88)	92-93
7	4-Nitro bromobenzene	20	90^b (88)	112
8	Chlorobenzene	60	42^a (43)	70
9	4-Nitro chlorobenzene	30	65^b (66)	113
10	4-Chloro toluene	60	52^a (50)	44-46
11	2,4-dinitro chlorobenzene	90	42^b (39)	109

[a] based on gc analysis with external standards.

[b] isolated yields by column chromatography; products fully characterized by M.P., MS and elemental analysis.

[c] Figures in parentheses are yields obtained using modified procedure.



[A]

R = n-butyl
Y = Br, BF_4

Fig. 5. Pd-biscarbene complex A

This was found to be Pd-biscarbene complex (Fig 5). The 1H NMR showed the absence of –N-CH-N- proton and the peak corresponding to –N-CH-CH-N- shifted from 7.4 to 6.83. These are characteristic peaks of complexed carbene systems. The 13C NMR showed the shift of –N-C-N- carbon from 139 to 168, which confirms the Pd complexation. Further it was confirmed by mass spectra where M+466.

The next step was to synthesize Pd-biscarbene complex in large scale for carrying out reactions. From literature,[51] the Pd-biscarbene complex was synthesized by refluxing a THF solution of I.L, Pd source and a base (triethyl amine or sodium acetate) for 2h. We found that the same reaction proceeds under ultrasonic irradiation in 15 min. in 50% yield. Column chromatography yielded an off-white to yellow amorphous powder. It was fully characterized. The reaction of haloarene and phenyl boronic acid was carried out in methanol as solvent with Pd-biscarbene complex using sodium acetate as base. The reaction was monitored by GC. The reactions resulted in good conversions. After the reaction was over, methanol was evaporated, the residue extracted with solvent ether in which all reactants and products except catalyst, inorganic salts and base got extracted. The residue after extraction with ether was again extracted with dichloromethane when complex gets extracted. Evaporation of DCM furnished the catalyst almost quantitatively for reuse. The reusability of catalyst was studied two times. There was a marginal decrease in the yields of biphenyls in each case and also some decomposition of catalyst was observed. There was no formation of inactive palladium black. The reaction with preformed complex tolerated both air and argon as the ambient gases without formation of palladium black or any homocoupled product.

With a view to make the recycling step easier, the Suzuki cross-coupling reaction of 4-methoxy bromobenzene was performed using complex A as the catalyst in a mixture of I.L and methanol under the ultrasound irradiation conditions. However, the reaction was found to be quite sluggish (20% conversion after 1h) with complete decomposition of the complex A as seen on TLC.

In our previous investigation of ultrasound promoted Heck reaction in I.L. at ambient temperature we have shown the *in situ* formation of clusters of Pd nanoparticles. In an analogous manner, the reaction mixture after a successful Suzuki coupling reaction of iodobenzene with phenylboronic acid was subjected to *in situ* TEM analysis. The TEM image (Fig. 2) did not show the presence of any colloidal Pd nanoparticles.

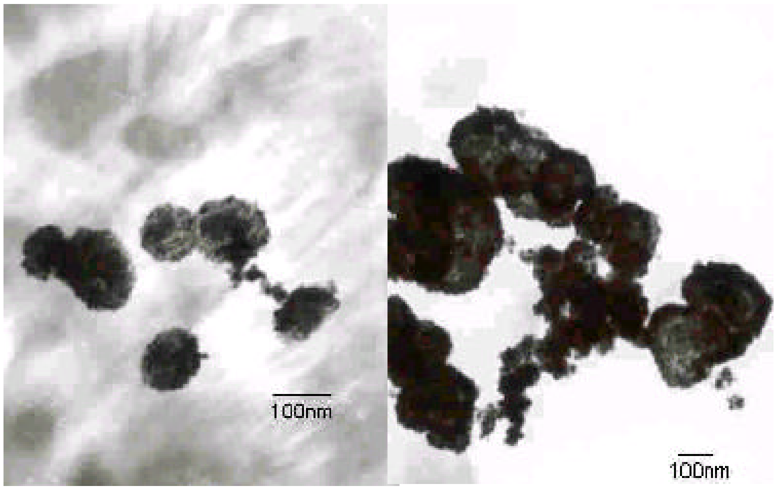


Fig. 2. TEM image of Pd-black formed after Suzuki coupling.

1.5.3.4. Conclusion

The use of ultrasound has not only accelerated the formation of Pd-biscarbene complex A in methanol as co-solvent but also in all probability brought about the in situ generation of a zero-valent Pd-species as the active catalyst from [A] in enhanced rates by electron transfer reactions primarily through the phenomenon of acoustic cavitation. It is well known that sonochemical processes proceed through SET mechanistic pathway by means of formation and adiabatic collapse of the transient cavitation bubbles. It is also highly likely ultrasound induced secondary reactions in the liquid phase after bubble collapse could be responsible for promoting the oxidative addition, transmetallation and reductive elimination of the catalytic cycle proposed for the Suzuki reaction.

1.5.3.5. Experimental

- ***Suzuki Reaction***

A mixture of aryl halide (0.5mmol), phenylboronic acid (0.5mmol), bbimBF$_4$ (0.5g), Pd(OAc)$_2$ (0.001g) and NaOAc (0.045g) [NaOMe (0.035g) for chlorobenzenes] in MeOH (1.0ml) was sonicated under argon for the specified time. The reactions were monitored by TLC/GC. After completion, water (2ml) was added and the mixture extracted with ether (2x5ml). The ether layer was separated, dried and the solvent evaporated to leave behind the products and reactants. The amenable product mixtures were subjected to column chromatography to isolate pure products. The rest were subjected to GC analysis using external standards for quantification. The pure I.L. could be quantitatively recovered from aqueous layer by extraction with DCM and recycled.

- ***Pd-carbene complex***

A mixture of [bbim]BF4 (0.268g, 1mmol), Pd(OAc)2 (0.056g, 0.25mmol), NaOAc (0.02g) and dry methanol (5ml) was sonicated for 10 min under argon atmosphere. Time should be adjusted to minimize the formation of palladium black. The reaction mixture was directly subjected to column chromatography. The fraction corresponding to the spot at Rf 0.6 in Thin layer chromatography (ethyl acetate : pet. Ether 0.3:0.7) was collected. Evaporation of solvent furnished an amorphous off-white fluffy powder (0.060g, yield 40%).

Pd-Complex [A] – Offwhite fluffy powder

^{1}H NMR (200MHz, CDCl$_3$) : δ = 6.81(s, 4H), 4.82 (t, 8H NCH_2), 2.08 (m, 8H NCH$_2$CH_2), 1.50 (m, 8H NCH$_2$CH$_2$CH_2), 1.01 (t, 12H NCH$_2$CH$_2$CH$_2$CH_3).

^{13}C NMR (50MHz, CDCl$_3$, 25^{o}C, TMS): 169.63, 120.28, 50.54, 33.11, 20.11, 13.73. MS: m/z 466[M$^+$ - BF$_4$].

- ***Suzuki reaction with Pd-carbene complex***

A mixture of aryl halide (0.5mmol), phenylboronic acid (0.5mmol), NaOAc (0.045g) [NaOMe (0.035g) for chlorobenzenes] and Pd-biscarbene complex A (5mg) in MeOH (1ml) was sonicated under argon for the specified time. The reactions were monitored by TLC/GC. After completion of reaction, methanol was evaporated under reduced pressure and residue extracted with ether (2x5ml). Ether layer was separated, dried and the solvent evaporated to furnish products, which were worked up for quantification as mentioned in the first procedure. The residue remaining after the ether extraction was then extracted with EtOAc (2x2ml), washed with water and the solvent evaporated to recover complex A quantitatively for recycle.

1.5.3.6. References

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2.1.1. General Introduction

In the drive towards cleaner technologies, catalysis constitutes a powerful arsenal along with others in the fleet. The trend towards 'Green' chemistry or sustainable technology necessitates a paradigm shift from traditional concepts of process efficiency, that focus exclusively on chemical yields, to one that assigns economic value for eliminating wastes and avoiding the use of toxic and/or hazardous chemicals. Berzelius[1] coined the word catalysis way back in 1835 and defined the term as…

This is a new power to produce chemical activity belonging to both inorganic and organic nature, which is surely more widespread than have hitherto believed and the nature of which is still concealed from us. When I call it a new power, I do not mean to imply that it is a new capacity independent of the electrochemical properties of the substance. On the contrary, I am unable to suppose that this is anything other than a kind of special manifestation of these, but as long as we are unable to discover their mutual relationship, it will simplify our researchers to regard it as a separate power for the time being. It will also make it easier for us to refer to it if it possesses a name of its own. I shall therefore, using a derivation well-known in chemistry, call it the catalytic power of the substances, and the decomposition by means of this power catalysis, just as we use the word analysis to denote the separation of the component parts of bodies by means of ordinary chemical forces. Catalytic power actually means that substances are able to awaken affinities which are asleep at this temperature by their presence and by their own affinity.

Since then it took quite some time to establish its identity and at present they tend to become an integral part of a chemical process. The three approaches in catalysis viz. homogeneous, heterogeneous and enzymatic, have their advantages and limitations. Homogeneous catalysis mainly make use of organometallic complexes finds wide applications in both bulk and fine chemicals. Biocatalysts or enzymatic catalysis have advantages of mild reaction conditions, high chemo, regio and enantioselectivity towards the products. Solid, heterogeneous catalysts have advantages of easy recovery and recycleability and are readily amenable for continuous processes.

2.1.2. Introduction to Heterogeneous catalysis

Heterogeneous catalysts provide a definite advantage over other catalysts by virtue of their easy recovery and reusability. Solid catalysts are already used in oil refining and bulk chemicals. The experience and understanding gleaned from these applications form a sound foundation for their use in organic synthesis.

The catalytic reactions of interest in fine chemical synthesis can be divided into 5 categories.

1. Solid-acid catalysis
2. Solid-base catalysis
3. Catalytic Hydrogenation and dehydrogenation
4. Catalytic Oxidation
5. Catalytic C-C bond formation

An introduction to solid acid catalysts, which forms the theme of this chapter will be presented in this section.

2.1.3. General classification of heterogeneous catalysts

Class of catalysts	Examples
Metals (supported, bimetallic,alloy)	Pt, Pd, Rh, Ni, Cu, Ag
Metal oxides (amorphous, crystalline, mixed)	SiO_2, Al_2O_3, MgO, CaO, SiO_2- Al_2O_3, Fe-Mo,V-Mo.
Metal Sulphides (supported)	Co-Mo, Ni-Mo, Ni-W.
Metal Salts	$Zr_3(PO_4)_4$, ZnS
Zeolites	Faujasites, ZSM-5, MCM
Molecular sieves	AlPO, SAPO, HMS families
Ion-Exchange resins	Nafion-H or Br-form of resins
Heteropoly acids	$H_3PMo_{12}O_{40}$, $H_4SiW_{12}O_{40}$
Clay minerals	Kaolinite, montmorillonite.

2.1.4. Solid acid Catalysis

A corrosive and high heavy metal effluents obviates the need of solid recyclable catalysts in acid catalyzed reactions. High efficient and useful catalysts should possess following characteristics.[2]

1. High catalytic activity
2. No corroding of reaction vessels or reactors
3. Recyclability
4. Easy separation of catalysts.
5. No problem of disposal of catalysts

Three characteristics are decisive in preparation of solid catalysts for organic transformations.

1. Catalytically active sites
    - a sufficiently large active surface area per unit weight or unit volume of catalyst is required.
    - The catalytically active surface must be stable at the temperatures of pretreatment and the intended catalytic reaction.
    - The catalytically active surface must have the desired structure and chemical composition.
2. transport properties
    - the transport of the reactant molecules to the catalytically active surface, and of the reaction products from the surface, must proceed sufficiently rapidly.
    - the transport of thermal energy to and from the catalyst particles must occur smoothly.
3. the mechanical strength
    - for technical applications the mechanical strength of catalyst particles is important.

2.1.5. Principle of Measurement of Acidic properties

A complete description of acidic properties on solid surfaces requires the determination of acid strength and of amount and nature (Bronsted or Lewis type) of acidic sites.

2.1.5.1. Acidic property

- *Strength and amount of solid acid*

The acid strength of a solid is defined as the ability of the surface to convert an adsorbed neutral base into its conjugate acid. If the reaction proceeds by means of proton transfer from the surface to the adsorbate, the acid strength is expressed by the Hammet acidity function,[3]

$Ho = pKa + \log [B]/[BH+]$,

Where [B] and [BH+] are respectively the concentrations of the neutral base (basic indicator) and its conjugate acid and pKa is $pK_{BH}{}^{+}$. If the reaction takes place by means of electron pair transfer from the adsorbate to the surface, Ho is expressed by

$Ho = pKa + \log[B]/[AB]$,

Where [AB] is the concentration of the neutral base which reacted with the Lewis acid or electron pair acceptor, A.

The amount of acid on a solid, which is called the acidity, is usually expressed as the number or mmol of acid sites per unit weight or per unit surface area of the solid, and is obtained by measuring the amount of a base, which reacts with the solid acids. For the determination of strength and amount of a solid acid, there are two main methods; amine titration method using indicators and gaseous base adsorption method.

a. *Amine titration method using indicators*

The colour of suitable indicators adsorbed on a surface will give a measure of its acid strength.[4,5,6] If the colour is that of the acid form of the indicator, then the value of the Ho function of the surface is equal to or lower than the pKa of the conjugate acid of the indicator. Lower the value of Ho correspond to greater acid strength. For e.g. a solid which gives a yellow coloration with benzalacetophenone (pKa = -5.6) but is colorless with anthraquinone (pKa = -8.2), has an acid strength Ho which lies between –5.6 and –8.2.

b. Gaseous base adsorption method

When gaseous bases are adsorbed on acid sites, a base adsorbed on a strong acid site is more stable than one adsorbed on a weak acid site, and is more difficult to desorb. As elevated temperatures stimulate desorption of the adsorbed bases from acid sites, those at weaker sites will be evacuated preferentially. Thus, the proportion of adsorbed base evacuated at various temperatures can give a measure of acid strength. The amount of a gaseous base which a solid acid can adsorb chemically from the gaseous phase is a measure of the amount of acid on its surface.[7] Ammonia, n-butyl amine and pyridine have been extensively used as gaseous bases for the determination of strength and amount of a solid acid. The drawback of ammonia and n-butyl amine is their tendency to dissociate due to the hydrogen atoms attached to nitrogen. Triethylamine is used to overcome this drawback.[8] Also pyridine now-a-days have become popular. The main drawback of pyridine is that it can be adsorbed into strong basic sites to form an anion radical of pyridine.[9] The heat of adsorption of various bases is also a clearly a measure of the acid strength on the solid surface. Differential thermal analysis and thermogravimetry of desorption of basic molecules is available for theh estimation of acid amount together with the acid strength of a solid acid.

c. Estimation of acidity from catalytic activity

Catalytic activity has been used as a measure of acidity and acid strength. The activity for dehydration of isopropyl alcohol or the isomerization of butene in the presence of excess air is reported to be a good measure of acidity.[10,11,12,13]

- *Bronsted and Lewis acid sites*

The methods mentioned above for determining the strength and amount of acidity are unsuitable for distinguishing between Bronsted and Lewis acidity. The acid amount which is measured is the sum of the amounts of Bronsted and Lewis acid at a certain acid strength.
Infrared spectroscopic studies of ammonia and pyridine adsorbed on solid surfaces make it possible to distinguish between Bronsted and Lewis acid and to assess the amounts of Bronsted and Lewis acid independently.[14,15]

2.1.6. Zirconia based solid acid catalysts

Acid catalysis has played a vital role in petroleum industry for various isomerization, cracking and alkylation reactions used to upgrade oil. Also acids are used as catalysts for large-scale polymerization processes and they have shown promising results in hydration/dehydration reactions such as interconversion of ethanol to ethylene.[16] Supported metal oxides have recently come into lime-light as a very potential acid catalysts for various reactions. In this some metal oxides when sulfated develop the ability to catalyze reactions characteristic of very strong acid catalysts at low temperature. Isomerization of straight chain alkanes to more highly branched isomers, which not only have higher octane numbers but are more useful intermediates for further synthesis, is more favourable at lower temperature. Arata[17,18] has identified a range of active sulfated oxides including those based on SO_4^{2-}/ZrO_2, SO_4^{2-}/Fe_2O_3, SO_4^{2-}/SnO_2, SO_4^{2-}/TiO_2, SO_4^{2-}/SiO_2, SO_4^{2-}/Al_2O_3 and SO_4^{2-}/HfO_2. Sulfation must be performed on the amorphous precursors such as hydroxides or oxyhydroxides for better activity except for Al_2O_3. The breakthrough cam when the same author reported that the zirconia treated with sulfuric acid or ammonium sulfate, exhibits extremely strong acidity and is capable of catalyzing the isomerization of n-butane to isobutene ate room temperature. The catalytic performance is unique compared to typical solid acid catalysts, such as zeolites, which show no activity for the reaction at such low temperature. Using Hammet inidicators they claimed that sulfated zirconia is an acid 10^4 times stronger than 100% sulfuric acid. They are referred to as super acids. These features attracted sulfated zirconia as a potential replacement of strong corrosive acids resulting in environmentally benign catalyst.

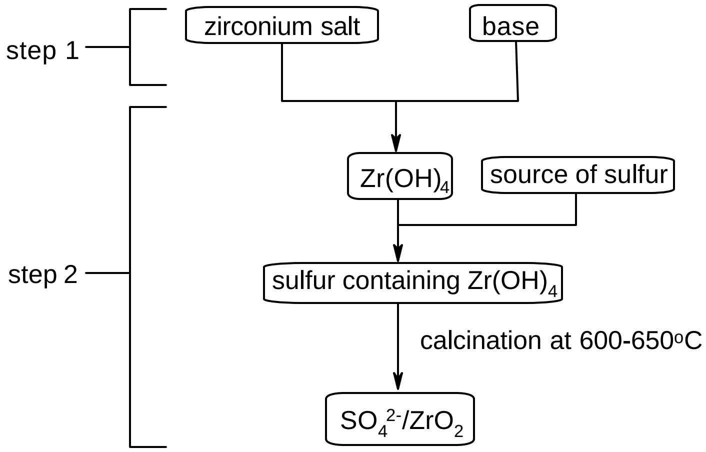
The major process in which the catalyst is used is the alkylation of isobutene with butanes to produce gasoline alkylates.[19] Current technology uses HF or H_2SO_4 as catalyst which suffer many drawbacks such as high toxicity and extreme corrosivity in addition to inherent risk of handling large amounts of hazardous acids. Another important process is the use of sulfated zirconia fro gasoline reformulation. Currently, there is a worldwide protocol toward decreasing the aromatic contents in gasoline because of their toxicity. The loss of octane number as a result of removal of aromatics could be mitigated by the addition of other high-octane compounds such as multi-branched hydrocarbons. The strong acidity and the exceptionally high activity of sulfated zirconia made it attractive as a catalyst in isomeric hydrocarbon-producing processes such as hydroisomerization, hydrocracking, alkylation and oligomerization.

Numerous studies have been devoted to the preparation of sulfated zirconia and to the characterization of its physicochemical properties and catalytic performance in various chemical reactions. But still a number of issues like the nature of acid sites, the role of Lewis and Bronsted acid sites in these catalysts are controversial.[20-27]

2.1.7. General methods of preparation of sulfated zirconia

- *2-step method*

These are the methods used often which is represented in scheme 1. The classical route proposed by Arata[17] is to prepare sulfated zirconia by first hydrolyzing zirconium salt such as $ZrOCl_2$ or $ZrO(NO_3)_2$, with aqueous ammonia to produce zirconium hydroxide and then to sulphate the zirconium hydroxide with H_2SO_4 or $(NH_4)_2SO_4$ solution. The resultant sulphated zirconium hydroxide was calcined in air at 550°C-650°C to generate acidity.



Scheme 1. Illustration of the two-step method for the preparation of sulfated zirconia.

In addition to $ZrOCl_2$ and $ZrO(NO_3)_2$, several other zirconium salts such as $ZrCl_4$, $Zr(NO_3)_4$, Zrpropoxide [$Zr(OC_3H_7)_4$] etc. were also used as the zirconium source.[28-34] Both ammonia and urea were used for hydrolysis.[35] Zr propoxide was hydrolyzed by water.[32-34] Some studies suggested that salts used to prepare the Zr hydroxide have a significant impact on crystal structure of resulting zirconia catalyst.[26]

Authors suggested that the final pH of the solution after precipitation and the rate of addition of base have profound influence on the structure and catalytic activity of resulting species.[30,36-39]

The preparation of $Zr(OH)_4$ was also achieved by the sol-gel method. This method results in zirconia having very high surface area.[40]

Sulfation of zirconia has been reported by different methods. Usually it was done by immersing the hydrated zirconia into 1N H_2SO_4 solution keeping material/liquor ratio 2-10ml/g. Sulfation by incipient wetness method was also reported. Sulfation by dry-kneading method and subsequent calcinations has been reported recently by Arata.

Besides H_2SO_4 and $(NH_4)_2SO_4$, other sources of sulfur such as SO_2, H_2S, CS_2, SO_2Cl_2 etc. were also used.[32,33,36] Ultimately all the sulfur-containing species are transformed into the form of sulfate (SO_4^{2-}) during catalyst calcinations.

Calcination temperature is very important for imparting maximum acidity for the catalyst.[38] The sulfur content in the catalyst also depends on the calcinations temperature. The most common calcinations temperature is 550° to 650°C. The typical sulfur content of calcined sulfated zirconia is 0.8-3wt%.

In general, amorphous $Zr(OH)_4$ must be used as the precursor for sulfation. Sulfation of crystallized zirconium oxide does not produce strong acidity.[20,23,38]

- *1-step method*

This method makes use of sol-gel method. Zirconium propoxide was mixed with n-propanol, nitric acid and sulfuric acid. This solution was then mixed with another solution containing n-propanol and water, and the mixture was vigorously stirred for gelation. The alchohol was removed by supercritical CO_2 after aging for 2h at room temperature. During calcinations and crystallization of the zirconia, sulfate is expelled onto the surface and transformed into catalytically active species.

2.1.8. Heteropoly acids as catalysts

Catalysis by heteropoly acids (HPA) and related compounds is a field of growing importance.[41] HPAs are polyoxometalates incorporating anions (heteropolyanions) having metal-oxygen octahedral as the basic structural unit.[42-44] Among a wide variety of HPAs those belonging to the so-called Keggin series are the most importance for catalysis. They have an anionic structure

$XM_{12}O_{40}^{x-8}$

Where X is the central atom (Si^{4+}, P^{5+} etc.), x is its oxidation state and M is the metal ion (Mo^{6+}, W^{6+}, V^{5+} etc.). These anions have a well-defined Keggin structure which is composed of a central tetrahedron XO_4 surrounded by 12 edge-sharing metal-oxygen octahedral MO_6.[45] The Keggin HPAs are the most stable and easily available. In addition to their well defined structure,[43,44] HPAs have special properties which are of great value for catalysis, such as strong Bronsted acidity,[41d] ability to catalyze reversible redox reactions under mild conditions,[41a,41c] high solubility in water and oxygenated organic solvents, fairly high stability in solid state. These properties render HPAs potentially promising acid, redox and bifunctional catalysts in homogeneous as well as in heterogeneous systems.

Recently HPAs were found to be an active catalyst for oxidation reactions in various synthetically useful organic transformations. Another field not well documented is the capability of HPAs in catalyzing liquid phase reactions. A variety of quite efficient HPA based synthesis of antioxidants, medicines, vitamins etc. have been recently reported.

2.1.9. Preparation of HPA

Most of the HPAs are commercially available as crystalline hydrates. They are usually prepared by acidifying an aqueous solution containing the salt of the heteroelement and alkali metal molybdate or tungstate, with subsequent isolation of the HPA by extracting with ether or by ion exchange.[42,44] Electrodialysis provides a potential method for its preparation. An efficient membrane has been invented for its efficient synthesis.[46,47] The HPA is formed at the anode compartment of dializer from Na_2WO_4 and H_3PO_4 in an aqueous solution. The acidification needed is provided by the electrolysis of water. Na^+ ions are transferred by the electric potential from the anode to cathode through the cation exchange membrane. As a result, pure phosphotungstic acid at the anode and NaOH at the cathode are formed. The HPA is isolated by crystallization in an almost 100% yield.

2.1.10. Characterization

- *Proton sites*

HPAs are strong Bronsted acids.[41b,41d] Structural charcterization with respect to proton structure, bond length-bond strength correlation, Keggin structure and its catalytic activity is well documented.[41d,41g,48] Bond length-bond strength correlations[49] as well as ^{17}O MAS-NMR data[50] indicate that in the free polyanions in solution, the bridging oxygen atoms, having a higher electron density than terminal oxygen atoms, are protonated. In the free Keggin anion, edge-bridging M-O-M oxygens are assumed to be predominant protonation sites. In solid HPAs, the protons take parting the formation of the HPA crystal structure, linking the neighboring HPA anions. In this case the more accessible terminal oxygens can be protonated. From single-crystal X-ray and neutron diffraction data,[51] the proton sites in the crystalline phosphotungstic acid hexahydrate are represented as diaquahydrogen ions, $H_5O_2^+$, each of which links four neighboring heteropolyanions by forming hydrogen bonds with the terminal W=O oxygens. In the dehydrated phosphotungstic acid, according to ^{17}O NMR data,[52] the protons are also predominantly localized on the terminal oxygens. This structure is assumed to be directly formed from the proton structure of the phosphotungstic acid hydrate upon dehydration. Stoichiometrically, each proton is shared by four terminal oxygens like in phosphotungstic acid hexahydrate, since all the terminal oxygens in the crystal lattice are apparently equivalent in ^{17}O MAS NMR. It is suggested that the proton migrates between four equivalent oxygens, $W{=}O\ldots H^+\ldots O{=}W$, and thus links four HPA anions together, as does the

$H_5O_2^+$ ion in phosphotungstic acid hexahydrate. The same structure was suggested for the structurally similar HPA salts, e.g., $Cs_3PW_{12}O_{40}$, in which the Cs^+ ions each have four equivalent terminal oxygens as the closest neighbors.[51]

- *Acid strength*

Hammet acidity function and the dissociation constants are used to define acid properties of HPAs in solutions.[41d] The dissociation constants of HPAs were measured in solvents H_2O, Me_2CO, EtOH amd AcOH and Hammet acidity function was determined in H_2O[53] and H_2O-AcOH, H_2O-dioxan, H_2O-EtOH and H_2O-Me_2CO mixtures.[54] HPAs in solution are stronger than the usual mineral acids such as H_2SO_4, HCl, HNO_3 etc. The strongest and most stable acid in Keggin series is phosphotungstic acid. The acidity of HPA concentrated solutions in terms of the Hammet acidity function also weakly depends on their composition and is higher than that of H_2SO_4. Solid HPAs possess purely Bronsted acidity and are stronger than such conventional solid acids as SiO_2-Al_2O_3, H_3PO_4/SiO_2 and HX and HY zeolites.[55,56] The acid strength of crystalline HPAs decrease in the series:

$$PW > SiW \geq PMo > SiMo$$

Which is identical with that in solutions. Usually, relative catalytic activities of HPAs are consistent with this order both in homogeneous and in heterogeneous systems.

HPAs have moderately high thermal stability. The Keggin-type PW, SiW, PMo and SiMo decompose at 465°, 445°, 375° and 350° respectively.[57] The decomposition causes loss of activity. However thermally decomposed molybdenum HPAs become reconstructed under exposure to water vapor.[58,59] Under wet conditions, HPAs can hence be used as solid acid catalysts in vapor-phase reactions operated at relatively high temperatures.

Microcalorimetry experiments[60] reveal a uniform distribution of proton sites in dehydrated phosphotungstic acid. There are some strong proton sites which can be attributed to surface protons localized at the bridging O atoms in the Keggin unit. The order of acid strengths of solid HPAs, as determined by microcalorimetry at a sorption temperature of 50°C after pretreatment at 150°C, is $PW \geq SiW >> PMo \geq SiMo$.[61]

2.1.11. Supported Heteropoly acids

Supported HPA catalysts are important for applications because bulk HPAs have a low specific surface (1-5m2g-1).[41b,d,g,i] The catalytic activity of supported HPAs depends on the type of the carrier, the HPA loading, conditions of pretreatment etc. Acidic and neutral substances such as SiO_2,[62] active carbon,[63,64] acidic ion-exchange resin[65] etc. are suitable supports, the most often being SiO_2. Basic solids such as Al_2O_3 and MgO tend to decompose HPA.[41g,66] In some cases the supporting inhibits the formation of coke.[67]

SiO_2 is relatively inert towards HPAs, at least above a certain loading level, although some kind of chemical interaction takes place between HPA and SiO_2.[68] Microcalorimetric data shows that the phosphotungstic acid loading over 20wt% on SiO_2, results in weaker and non-uniform proton sites. Only 20% of the total number of proton sites remain as strong as in bulk PW. According to ammonia thermal desorption data, the acid strength of supported PW decreases in the series of carriers: SiO_2 > α-Al_2O_3 > activated carbon. At low loadings, the PW and SiW form finely dispersed species on SiO_2 surface.

SiO_2 supported molybdenum HPAs retain the Keggin structure at high loadings but decompose at very low loadings due to their strong interactions with surface silanol groups.

Solid acid catalysts having strong acid sites, regular structure, and a very narrow pore size distribution- e.g. zeolites and modified layered materials- have been most desirable because they are can induce size and shape selectivity. Recently, HPAs (HPW) supported on a mesoporoous pure-silica molecular sieve MCM-41[69] (BET surface area $1200m^2g^{-1}$, uniform pores 32A in size) were prepared and characterized. HPA retains the Keggin structure on the MCM-41 surface at an HPA loading above 20wt%; at lower loadings a partial decomposition of PW with basic impurities in MCM-41. HPA forms finely dispersed species on MCM-41 surface.

Pillared layered double hydroxides[70] (anionic clays) were prepared by ion-exchange reaction of $[Zn_2Al(OH)_6]NO_3xH_2O$ with Keggin-type heteropoly anions. Complete replacement of NO_3^- was achieved for Keggin anions, such as $PW_9V_3O_{40}^{6-}$, $H_2W_{12}O_{40}^{6-}$, $SiW_9V_3O_{40}^{7-}$, etc., with a charge of –6 or lower. No exchange was observed for anions such as $PW_{12}O_40_3$- and $SiW_{12}O_{40}^{4-}$. The intercalated anions below 200°C were accessible for catalytic chemical conversions, e.g., for photocatalytic oxidation of isopropanol to acetone.

2.1.12. Salts of HPAs

Water-insoluble HPA salts with certain monovalent cations, such as NH^{4+}, K^+, Cs^+, etc., have high surface areas and microporous/mesoporous structures.[71] Even these solids are prepared (by precpitation from aqueous solutions) to be stoichiometric, residual quantities of protons still remain, which are apparently responsible for the catalytic activity of these salts. Acidic Cs salt, $Cs_{2.5}H_{0.5}PW$, due to its strong acid sites and high surface area ($100\text{-}200m^2g^{-1}$), is a remarkably efficient solid acid catalyst fro a variety of organic transformations, especially for liquid-phase reaction.[41g,72]

2.1.13. References

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2.2.0. Synthesis and Characterization of Phosphotungstic acid modified phosphated zirconia catalyst

2.2.1. Introduction

The main reason of the use of hydrated zirconia as a precursor of a catalyst carrier is because the surface OH groups are able to undergo a chemical reaction or strong interaction with incorporated second components.[1-3] Upon thermal activation, hydrated zirconia yields catalysts with very different properties. Extensive studies of Arata et. al[4-8] showed that sulphate addition to freshly precipitated metal oxides such as Fe_2O_3, TiO_2, ZrO_2 and HfO_2, yielded solids with very strong acid properties. In this group sulphated zirconia has been studied extensively.

Other oxo-anions like tungstate and molybdate anions impregnated on hydrated zirconia also produced solid super acids.[9] Addition of Fe and Mn to sulphated zirconia has a promoting effect on its acid strength.[10,11] A recent report on the synthesis of B_2O_3/ZrO_2 obtained by impregnation of boric acid, which has low acidity, has confirmed that the interaction of oxo-anions with hydrated zirconia indeed results in the formation of stronger acid sites than those of the algebraic sum of single components.[12] As explained in previous section, heteropoly acids have been proved as efficient catalysts for various reactions in liquid phase.[13] Because of limited surface area,[14] they are commonly supported on SiO_2, SiO_2-Al_2O_3, TiO_2 or activated carbon when used as catalysts for gas-solid phase reactions.[15] Due to the low acidity and its potential interaction with HPAs, their addition to hydrated ZrO_2 could yield strong solid acids.

In a recent work, an active catalyst was obtained by supporting heteropoly acids on amorphous oxides in presence of low amount of a mineral acid, sulphuric acid. This system also gets deactivated quickly.[16]

In the present work it was proposed to synthesize phosphotungstic acid supported on amorphous zirconia in the presence of low amount of phosphoric acid (PTZ).

2.2.2. Synthesis

- *Synthesis of Zirconium hydroxide $Zr(OH)_4$*

28% aqueous ammonia (100ml.) was added dropwise into a clear solution of zirconyl oxy chloride ($ZrOCl_2$. $8H_2O$) (100g) dissolved in 1000 ml distilled water. The white precipitate (pH 10) was stirred at room temperature for 2h. The precipitate is filtered and washed with distilled water until chloride free (silver nitrate test). The solid was dried a 100^{o}C under static air for 12h obtaining 40g of pure and amorphous zirconium hydroxide (surface area 140 m^2/g).

- *Synthesis of PTZ ($H_3PW_{12}O_{40}/H_3PO_4/ZrO_2$)*

Methanolic solutions of 5%, 10%, 12% and 15% phosphotungstic acid calculated with respect to zirconia were prepared in which 1wt% of concentrated phosphoric acid was added. To this mixture dried hydrated zirconia powder was added, keeping Methanol : Zirconium hydroxide ratio 10:1 and stirred for 1h. The flask is transferred to a rotary evaporator and methanol evaporated at 35^{o}C under reduced pressure. The resulting white powder was calcined. The details of solids are given in Table 1.

Table 1. Summary of PTZ samples prepared.

No.	Name	% PTA loading	Calcination Temperature ^{o}C
1.	5PTZ550	5	550
2.	5PTZ650	5	650
3.	5PTZ750	5	750
4.	5PTZ950	5	950
5.	10PTZ550	10	550
6.	10PTZ650	10	650
7.	10PTZ750	10	750
8.	10PTZ950	10	950
9.	12PTZ750	12	750
10.	15PTZ550	15	550
11.	15PTZ650	15	650
12.	15PTZ750	15	750

2.2.3. Methods of Characterization

- *X-ray diffraction*

X-ray diffraction (Rigaku, Model D/MAX III VC, Japan, Ni filtered Cu Kα radiation, with a graphite crystal monochromator and, computed assisted automated diffractometer) was used to identify the zirconia catalysts activated at different temperatures. The patterns were recorded in the region, 10^o to 80^o 2θ at a scanning rate of 4^o min^{-1}. All the peak positions were corrected with respect to Silicon ($2\theta = 28.4^o$), which was used as internal standard.

- *Surface area measurements*

A high vacuum adsorption unit (NOVA) was used for the measurement of nitrogen adsorption isotherms to determine the surface areas. The unit works on continuous flow method. The samples were activated at 573 K for 3 h in high vacuum (10^{-5} mm). After the treatment, the anhydrous weights of the samples were recorded. The samples were then cooled to 77 K in liquid nitrogen and allowed to adsorb nitrogen gas. Finally, by knowing the amount of N_2 adsorbed at different equilibrium pressures, the BET surface area was calculated using the equation

$$S_{BET} = V_m N A_m$$

Where, V_m is the monolayer volume, N is the Avagadro's number and Am is the cross sectional area of the adsorbate. For nitrogen, the value of A_m is 16.2 $Å^2$.

- *Thermal Analysis*

Thermal (TG/DTA) analysis of uncalcined zirconia samples was performed on an automatic. The thermograms for the samples (20mg) were recorded under the followig conditions.

Weight of sample = 20mg.
Heating rate = 10^oC/min.
Atmosphere = flowing dry nitrogen.

The temperature range studied was from room temperature to 950^oC.

2.2.4. Results and Discussion

- *XRD*

Catalysts with different PTA loading calcined at different temperatures are shown in Fig 1 to Fig 3. In all the cases the crystallization of zirconia occurred when the calcinations temperature was 750°C. At 550°C, crystallization started, but at 750°C it was complete

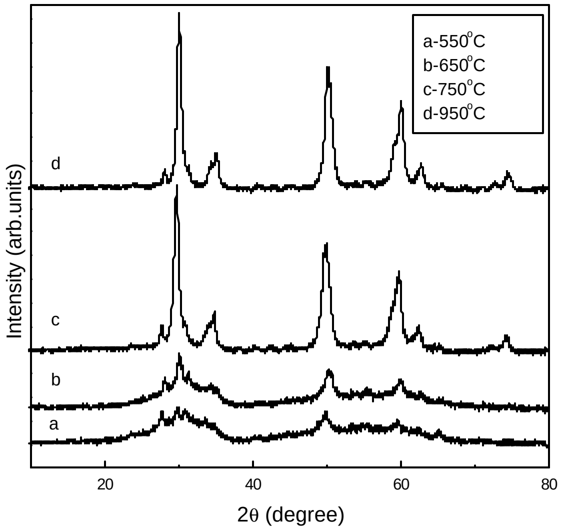

Fig. 1. 5% PTA loading

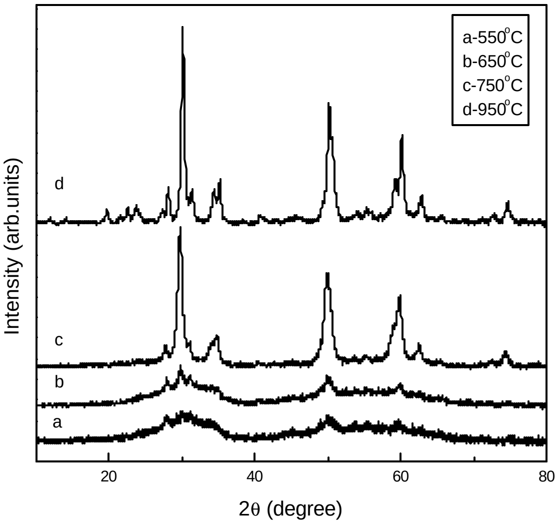

Fig.2. 10% PTA loading

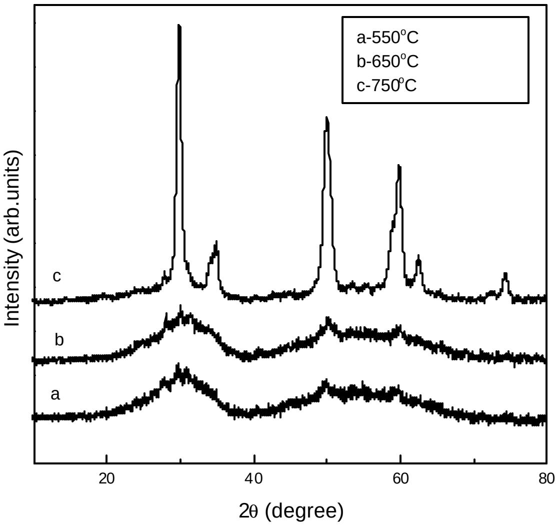

Fig. 3. 15% PTA loading

and almost pure tetragonal phase resulted as indicated by the peak at $2\theta = 30^{o}$. When the calcination temperature was 950°C, monoclinic phase begins to appear but in a very low percentage.

There is no indication of crystalline phase related to bulk PTA which comes as a very strong peak at $2\theta = 10^{o}$ and small peaks at 2θ = 15, 17 and 22 even at a PTA loading of 15%. The reason may be that PTA particles are too small and/or too well dispersed on zirconia surface, which may be undetectable by XRD. It is well documented that the XRD pattern of PTA impregnated on freshly prepared SiO_2 and calcined at 400°C showed characteristic peaks of PTA.[17] Hence it can be concluded that PTA is well dispersed on zirconia surface. Moreover, PTA may have strong interaction with zirconia on the surface. Small peaks of monoclinic WO_3 were observed in 10% sample activated at 950°C. These may be due to the breaking up of Keggin heteropoly anion. From the calcinations temperature required for crystallization of zirconia, it can be concluded that PTA and phosphoric acid helps to stabilize the catalytically active tetragonal phase of zirconia and also it retards the formation of monoclinic phase.

- *Surface area*

Table 2 shows the BET surface area of PTZ750 series catalysts. First entry, i.e. simple zirconia calcined at 750°C showed a surface area of 32m^2/g. At 12% loading of PTA, the surface area increased by almost 3 times. It has been reported that the addition of sulfate anions to freshly precipitated zirconia results in solids with much higher surface areas when calcined at 773-873K in comparison with unsulfated zirconia, thus showing a stabilizing effect on the structure of the final calcined zirconia.[18] Here also it is observed that phosphating and impregnation of PTA on amorphous zirconia and the subsequent activation resulted in a monolayer of PTA on zirconia surface which stabilizes the bulk zirconia.

Table 2. Surface area of PTZ750 series with different PTA loading

%PTA loading	Surface area m^2/g
0	32
5	65
10	78
12	91
15	84

- *Scanning Electron Microscopy*

Fig. 4 shows the SEM image of zirconia calcined at 750°C. It shows crystalline particles having average size of 10nm of monoclinic zirconia. The PTA impregnated sample calcined at 750°C resulted in some voids in the structure morphology (Fig.5). The tetragonal zirconia (confirmed by XRD) has been seen as particles of 10nm. These voids may have resulted from the phosphation and dehydration of PTA at high calcination temperature.

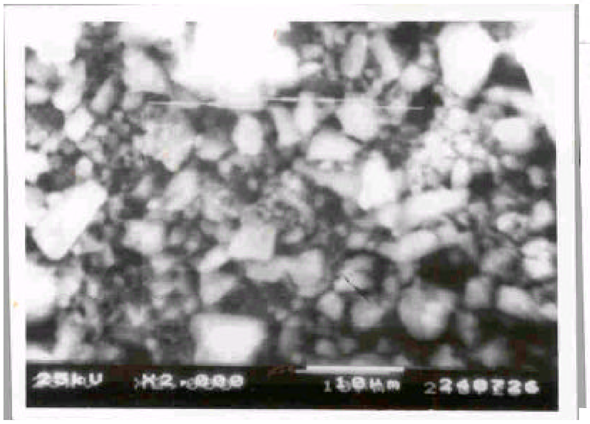

Fig. 4. SEM image of ZrO_2 calcined at 750°C

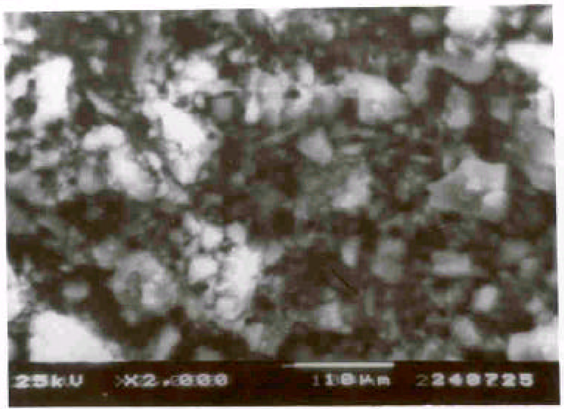

Fig. 5. SEM image of 12PTZ750

- *Acidity*

The acidity of catalysts is measured using Hammet indicator method. This was carried out by exposing previously evacuated samples (0.1g) at 120°C for 4h to a benzene solution of selected Hammet indicators. A colour change was observed when catalysts were exposed to anthraquinone solution. It can be concluded that the acidity range of catalyst series is at pK_a range equal to –8.2.

- *Thermal analysis*

Differential Thermal Analysis of 5, 10, 12 and 15% PTA loaded on unactivated amorphous zirconia shows exotherms at 430°C and 540°C. The 430°c peak results from the crystallization of zirconia. The 540°C peak shows the delayed crystallization of zirconia due to TPA. This may be due to the Zr-O-W formation between PTA's terminal W=O oxygen atoms and surface Zr+ species. At 790°C, the endotherm may have resulted from the decomposition of TPA species on the surface. TG-DTG curves showed a weight loss of about 4%. This can be a Keggin structural destruction of PTA, which was confirmed by XRD pattern (peaks at $2\theta = 24$ and 26° corresponding to monoclinic tungsten when activated at 950°C).

2.2.5. References

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2.3.1. Phenol Acylation

2.3.1.1. Preamble

Friedel–Crafts acylations (including benzoylations and sulfonylations) are real and alarming examples of very widely used acid-catalysed reactions, which are based on 100 year old chemistry and are extremely wasteful. The reaction of an acid chloride with an aromatic substrate requires a greater than stoichiometric quantity of aluminium chloride as the 'catalyst' (>2 mole equivalents in sulfonylations). Every molecule of the ketone product forms a complex with one molecule of the catalyst, effectively removing it from the reaction. The organic product is released by using a water quench with the resulting emission of about 3 equivalents of HCl which need to be scrubbed from the off gases leading to the production of 3 equivalents of salt waste. Once the organic product has been recovered, aluminous water remains, which must be disposed of. The overall process generates considerably more waste than product. Many other industrial processes are catalysed by $AlCl_3$. These include alkylations and the production of resins *via* cationic polymerisation. While these reactions do not require the use of stoichiometric quantities of the Lewis acid, none of the catalyst is recovered and all such processes show the same atom accounts (Table 1).

Table 1: Atom accounts in a typical $AlCl_3$-catalyzed Friedel-Crafts acylation.

Element	Fate	Atom Utilization
Carbon	Products and by-products	Up to 100%
Hydrogen	Products, by-products and waste (from quench)	<<100%
Aluminium	Aluminous water/Aluminous salts	0%
Chlorine	Waste water (from quench) and salt (from HCl scrubbing)	0%
Oxygen	Waste water	0%

The green chemistry goal for such reactions should be to remove all elements from the accounts other than those involved in the organic chemistry and, of course, to push the organic chemistry towards 100% selectivity to the desired product. A number of new, more environmentally friendly acids for liquid phase organic reactions, notably solid acids (which are generally easier and less energy and resource consuming to recover than soluble acids), have been discussed and are beginning to find their way into industrial usage. These include zeolites, clays and other mixed metal oxides, inorganic–organic composite materials, functionalised polymers and supported reagents as well as lanthanide triflates. Other interesting 'green' solutions to the problem include the use of ionic liquids.

2.3.1.2. Introduction

- **General Introduction to Friedel-Crafts Acylation reaction**

Friedel-Crafts acylation reaction is considered as the most popular transformation for the formation of aromatic ketones. The reaction follows the scheme in which an aromatic substrate is reacted with an acyl chloride or anhydride or acid in presence of Lewis acid catalyst. It is a very versatile reaction, leading to a variety of products that include aromatic aldehydes, alkyl aryl ketones, symmetric and unsymmetric diaryl ketones and cyclized products.[1,2,3]

Generally acylating agents react more readily than alkylating agents, and therefore acylations can be carried out usually under mild conditions. Electron releasing substituents enhances the rate of reaction. The introduction of first acyl group hinders the entry of second, and disubstitution in the same ring is therefore rare.

Although acylation has much in common with alkylation, there are characteristic differences. Consumption of acidic catalyst is stoichiometric or more and the course of reaction is more uniform, leading to higher regioselectivity. Also isomerizations and other side reactions are rare.

- **Catalysts**

Friedel-Crafts catalysts are electron acceptors ie. Lewis acids.$AlCl_3$ is most commonly used catalyst for acylation reactions. (Table 2) Impurities in $AlCl_3$, such as $FeCl_3$ or traces of water, enhance yields and reactivity of some systems.[4,5,6] The activity of $AlCl_3$ can be moderated by the addition of solvents like nitrobenzene, which forms 1:1, adducts. BF_3 and $SnCl_4$ are also suitable catalysts for sensitive heterocycles. If anhydrides, esters or carboxylic acids are used as acylating agents, strong proton acids such as sulphuric acid, perchloric acid, orthophosphoric acid and polyphosphoric acid can be applied.[7]

Table 2. Various Lewis acid Catalysts for Acylation reaction

Group	Characteristic	Examples
A	Very active, high yields but extensive intra- and intermolecular isomerizations	$AlCl_3$, $AlBr_3$, AlI_3, $GaCl_3$, $GaCl_2$, $GaBr_3$, GaI_3, $ZrCl_4$, $HfCl_4$, $HfBr_4$, HfI_4, SbF_5, NbF_5, $NbCl_5$, TaF_5, $TaCl_5$, $TaBr_5$, MoF_6, $MoCl_5$
B	Moderately active, high yields without significant side reactions	$InCl_3$, $InBr_3$, $SbCl_5$, WCl_6, $ReCl_5$, $FeCl_3$, $AlCl_3$-$ArNO_2$, $AlBr_3$-$ArNO_2$, $GaCl_3$-RNO_2, SbF_5-RNO_2 and $ZnCl_2$
C	Weak, low yields without side reactions	BCl_3, BBr_3, BI_3, $SnCl_4$, $TiCl_4$, $TiBr_4$, $ReCl_3$, $FeCl_2$ and $PtCl_4$
D	Very weak or inactive	Many metal, alkaline-earth and rare-earth element halides

- *Acidic oxides and Sulfides (Acidic Chalcogenides)*

Chalcogenide catalysts include a great variety of solid oxides and sulfides; most widely used are alumina or silica (either natural or synthetic), in which other oxides such as chromia, magnesia, molybdena, thoria, tungsten oxide and zirconia may also be present.

- *Acidic Cation-Exchange Resins*

Bronsted acid catalytic activity is responsible for the successful use of acidic cation-exchange resins. They are used in esterification, acetal synthesis, ester alchoholysis etc. The solid acid type permits simplified procedures when high boiling and viscous compounds are involved because the catalyst can be separated from the products by simple filtration. Sulfonated styrene-divinylbenzene cross-linked polymers have been used as common acidic resins.

- *Superacids*

Superacids are acids which are stronger than 100% sulfuric acid. Fluorosulfuric acid is one of the strongest Bronsted super acid. Perfluoroalkane sulphonic acids also show high acidity. Magic acid (HSO_3F-SbF_5) is the most acidic acid which has both Lewis and Bronsted acidity. Fluoroantimonic acid, HF-SbF_5 even surpasses Magic acid acidity.

Solid super acidic systems have been developed for large scale petrochemical and other chemical transformations. Sulphated metla oxides are the strong candidates in this class.

- *Solvents*

The aromatic substrate itself, non-polar solvents such as CCl_4 or CS_2 or solvents of medium polarity such as dchloromethane or dichlorethane may be used. If $AlCl_3$ is used as catalyst nitromethane or nitrobenzene can result in homogeneous mixture. This can result in reduced reactivity due to complexation with catalyst. The choice of solvent can influence the regioselectivity of the acylation.[8]

- **Procedures for acylations**

Acylations using an acyl halide-Lewis acid catalyst system usually are carried out according to following procedures.

1. Acylating agent is added to a cooled solution or suspension of he catalyst in a solvent, followed by the addition of aromatic substrate – Perrier method.[9]
2. All reactants are mixed and cooled, and catalyst added slowly – Elbs method.[10]
3. The aromatic substrate is used as the solvent for the catalyst and the acylating agent is then added slowly – Bouveault method.[11]

The Perrier method often is preferred, because a constant ratio of catalyst to acylating agent is maintained throughout the reaction.

- **Acylating agents**

The great versatility of Friedel-Crafts acylations is based on the fact that both the acylating agent and the aromatic substrate can be varied systematically and through a wide range. The reactivity of acylating agents follows roughly the following order:

$[RCO^+][BF_4]^- \sim [RCO]^+[ClO_4]^- > RCOO^-SO_3H > RCOX > (RCO)_2O > RCOOR' > RCONR_2'$.

The reactivity of acyl halides decreases as follows:

RCOI>RCOBr>RCOCl>RCOF.

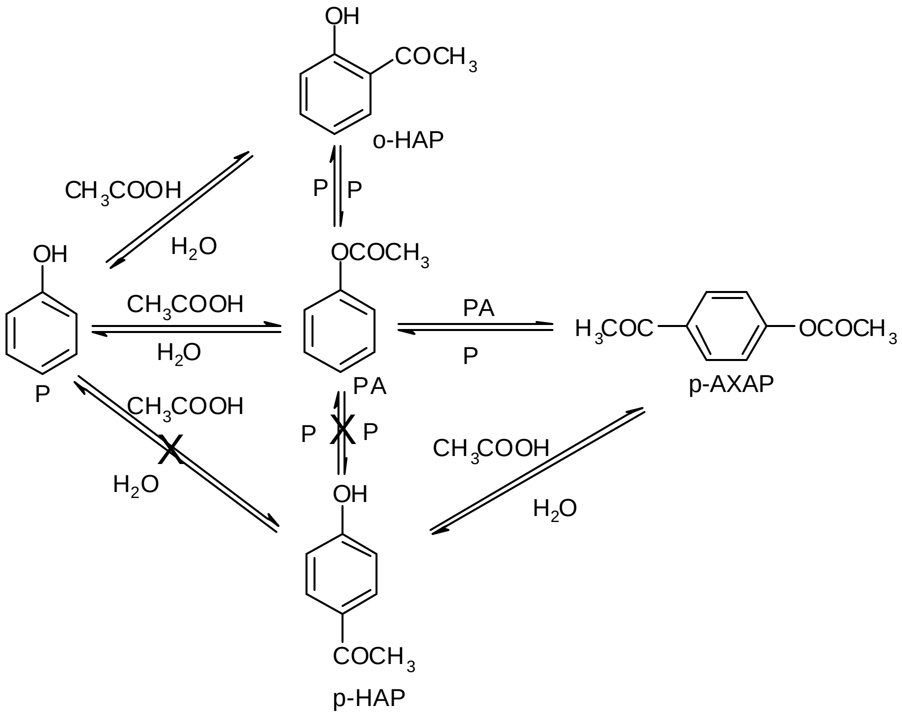
The reactivity of acyl halides depends also on R, which may be alkyl or aryl and which can be substituted by halogen as well as by an alkyl, alkoxy or a nitro group. The aromatic substrate and the type of catalyst also affect the reactivity.[12,13]

- **Introduction to Phenol acylation**

Hydroxyacetophenones are very useful intermediates for the manufacture of pharmaceuticals.[14,15] They are usually synthesized by catalytic rearrangement of phenyl acetate or direct acylation of phenol using acetic acid. Stoichiometric quantity of $AlCl_3$ is the "catalyst" of choice in the phenylacetate rearrangement, which is the method of choice. This results in highly toxic downstreams, which will be of great concern to ecology. To circumvent this problem many solid acid catalysts are reported. Mainly acid zeolites have been reported to catalyze the reaction at high temperature in a gas phase fixed bed down flow reactors.[16-24] Many kinetic models have been developed for the reaction.[20-22]

- **Reaction Scheme**

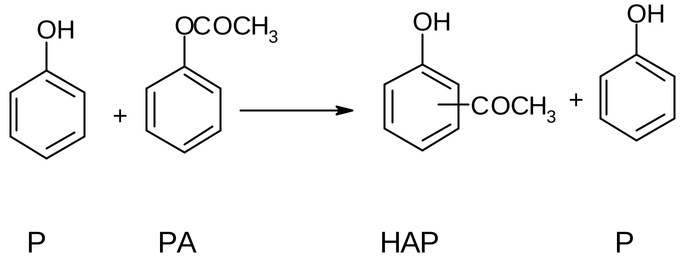
Neves et. al.[20] proposed the reaction scheme 1, which allows to explain qualitatively the main



Scheme 1. Possible reaction pathway.

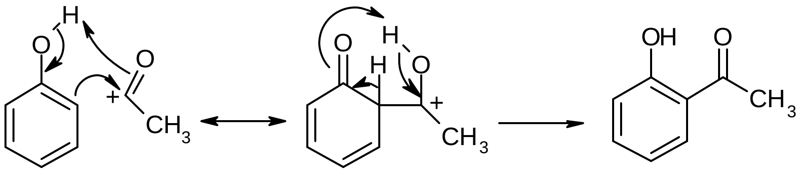
features of the phenol acylation with acetic acid, including the difference in the formation of o- and p-hydroxyacetophenones.

Same group reported that phenyl acetate can act as acylating agent for the acylation of phenol as per scheme 2.[22]



Scheme 2

They have proposed that o-HAP can either be formed by direct C-acylation of phenol or by Fries rearrangement of phenyl acetate PA. p-HAP is formed by the hydrolysis of p-AXAP. They postulated that the C-acylation of phenol with acetic acid (as well as phenyl acetate) resulting in o-HAP can be due to the pronounced stabilization of the transition state as shown in scheme 3.[20]

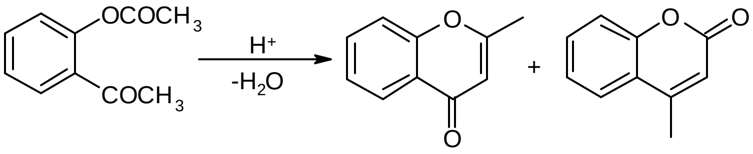


Scheme 3

This stabilization exists neither for transition state of phenol acylation in the para position nor for the transition state involved in the formation of AXAP.

- **Side reactions**

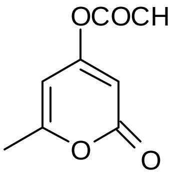
Jayat et.al[25] observed the extensive coke formation in the phenol acylation reactions at high temperatures using MFI aluminosilicates and gallosilicates. They have found out that the main ingredients of coke are methyl naphthols, 2-methylchromone and 4-methylchromone. Methyl naphthol resulted from a series of transformations invoving acetic acid and phenol. 2-Metylchromone and 4-methyl coumarin resulted from the transformation of orthoacetoxyacetophenone (o-AXAP) (scheme 4).



o-AXAP 2MC 4MC

Scheme 4

Neves et.al[20] found some traces of 4-acetoxy-6-methyl-α-pyrone (AXMP) resulted from the auto-condensation of ketene or of acetic acid.



AXMP

Recently Kozhevnikov et. al[26] reported that heteropoly acids are effective catalysts for Fries rearrangement. Silica supported heteropoly acids have been studied previously as a catalyst for Fries migration, but the conversions are poor.

2.3.1.3. Present work

With the importance of hydroxy acetophenones in pharmaceutical industry, we planned to take up one step procedure for hydroxy acetophenones by the direct acylation of phenol using acetic acid. Sulphated zirconia has been proved to be a good super acidic catalyst for the acylation reaction. The main drawback is the sulphate leaching during high temperature operations and in high acidic medium. Supported heteropoly acids have been proven to be a good substitute for sulphated zirconia. We have prepared phosphotungstic acid supported on zirconia inpresence of small quantity of phosphoric acid and well characterized (previous section). This section describes the activity of PZW catalyst on acylation of phenol using acetic acid as acylating agent. Reactions are performed in gas-phase down-flow reactor.

2.3.1.4. Experimental

- **Apparatus**

- *Atmospheric pressure reactor*

The reaction was carried out in gas-phase down-flow reactor. The microreactor, used to carry out catalytic reactions at atmospheric pressure, was made up of silica tube. The inner diameter of the tube was 15mm and was 57cm long fitted with a B-19 ground silica socket and side limb with a stop cock to it at the top. Schematic diagram is as shown in Fig.1. The temperature of the reactor furnace and the catalyst bed was monitored and controlled using digital temperature controllers. 2g of PZW12-750 catalyst was loaded in the middle of the reactor, which was filled with porcelain beads on top and bottom. The catalyst was pelletized and cut into uniform sized beads of 10-20 mesh before loading to reactor. Length of catalyst bed was 15mm and the volume 2.6cm^3. An infusion pump (Sage Instruments, Model 352, USA) was used to deliver the feed to the reactor. The reaction was carried out with different temperature, phenol : acetic acid mole ratio and feed flow rate. The reactants with desired mole ratio was mixed and pumped into reactor with a syringe pump. Carrier gas (N_2) was allowed to flow through a mass flow controller. After the reaction the product mixture was passed through a cold water condenser to collect the liquid products. The products were analyzed with Shimadzu GC-14B gas chromatography using SE-30 packed column. All experiments were performed with PZW12-750 catalyst. The side products were identified by GC-MS.

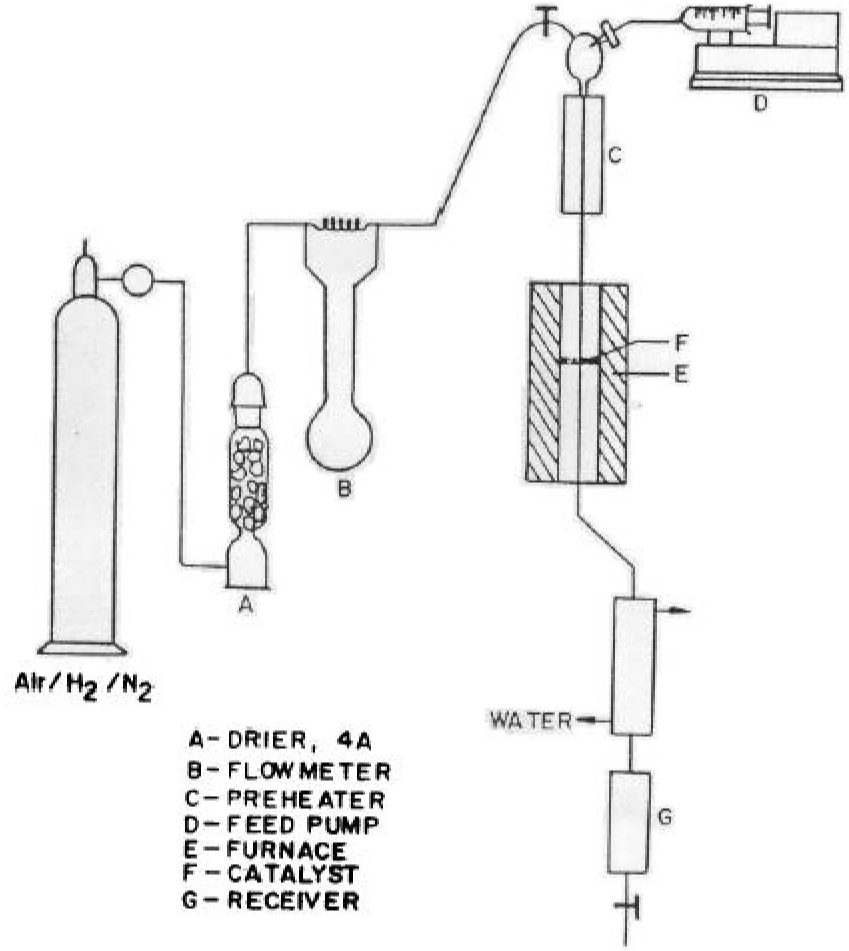


Fig. 1. Fixed bed down flow atmospheric pressure reactor.

2.3.1.5. Results and Discussion

Effect of temperature, mole ratio and feed flow rate on the reaction course was studied in detail. The reaction prominently yielded phenyl acetate (PA), the O-acylated product and o-hydroxyacetophenone (o-HAP) resulted from C-acylation. Also acetone was formed by decomposition of acetic acid. Formation of phenyl acetate was much faster than C-acylation.

- *Effect of Temperature*

The reaction was carried out at three different temperatures 250°C, 300°C and 350°C to evaluate the temperature dependence of product distribution.

- *Temperature Vs Mole Ratio*

Fig 2 shows the phenol conversion and product distribution with temperature for three different phenol : acetic acid mole ratio at feed flow rate 2.7 ml/h. Conditions are optimized for this contact time.

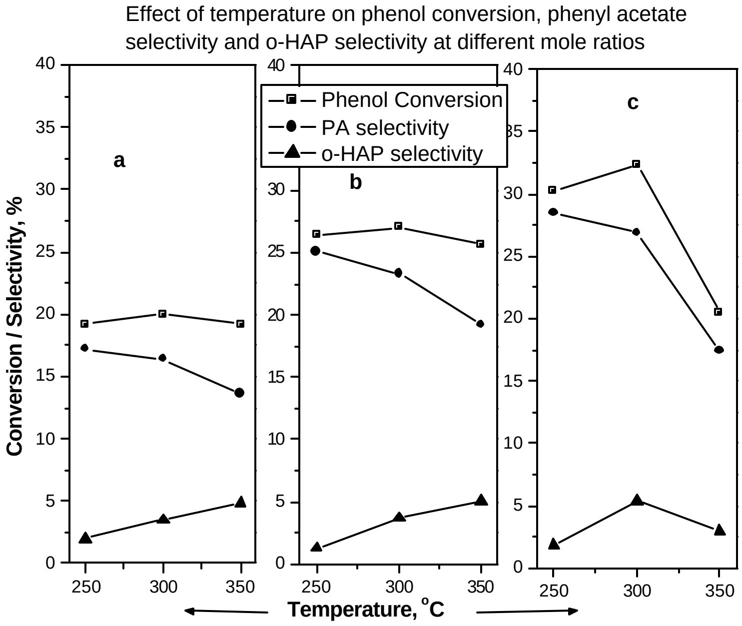
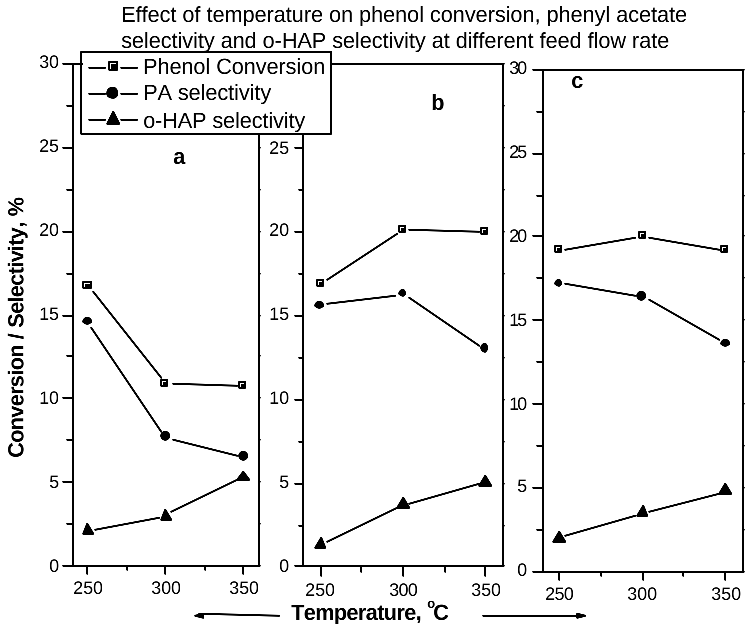


Fig.2: a – AA/P = 1.5; b – AA/P = 2.5; c – AA/P = 3.5

An increase in conversion and selectivity was observed when the temperature was raised from 250 to 300°C. But it decreased when the temperature is increased further to 350°C. Selectivity of o-HAP increased with increase in temperature. Also increase in mole ratio tends to increase the conversion/selectivities. Maximum conversion and selectivities of products were obtained at temperature 300°C and mole ratio 3.5.

- *Temperature Vs feed flow rate*

Fig. 2 shows the influence of temperature on the conversion/selectivity at different feed flow rate with constant mole ratio 2.5.



Effect of temperature on phenol conversion, phenyl acetate selectivity and o-HAP selectivity at different feed flow rate

Fig. 3: a-1.5ml/h; b-2.7ml/h; c-3.9ml/h

Maximum selectivity towards O-HAP was obtained by limiting the conversion of phenol by decreasing the contact time.

- *Influence of mole ratio and feed flow rate*

Increase in phenol to acetic acid ratio, increased the conversion of phenol. Also O-HAP selectivity was maximum when A.A/P mole ratio was 3.5. When feed flow rate was increased, the contact time decreases. The o-HAP selectivity decreased and an increase in PA selectivity was observed with the increase in feed flow rate.

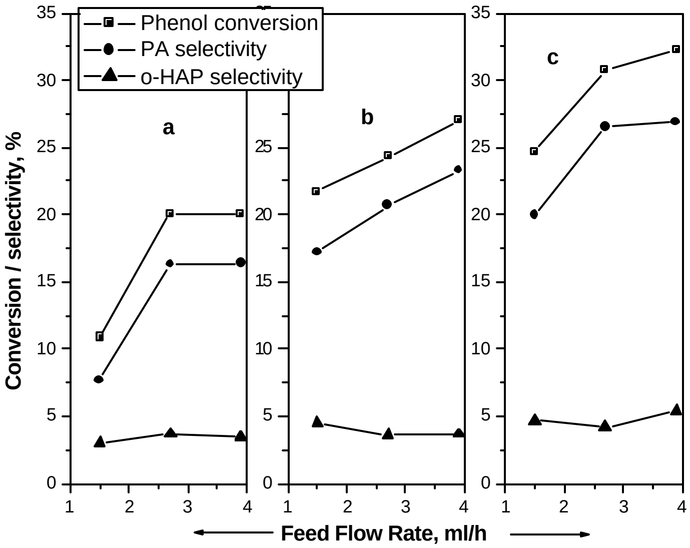


Fig.4: a – AA/P = 1.5; b – AA/P = 2.5; c – AA/P = 3.5

Phenol gets acylated in two ways. i) O-acylation to give PA and ii) C-acylation to give hydroxy acetophenones. In this, O-acylation has been proven 100 times faster than C-acylation. So at low contact time values i.e. higher feed flow rates, phenol is acylated by acetic acid mainly to PA. A moderate and high contact time i.e. low feed flow rate resulted in other reactions at a given phenol conversion. This leads to the redistribution of the products in favour of o-HAP formation.

2.3.1.6. Conclusion

Phenol acylation with acetic acid carried out over phosphotungstic acid modified phosphated zirconia resulted in moderate conversion of phenol. The major products were phenyl acetate and o-HAP. At higher temperature, side products are formed. The exact mechanistic pathway is still not conclusively established. The results obtained in these experiments can be compared with highly acidic zeolite catalysts, proving that zirconia based solid acid catalysts are potential candidates for various acid catalyst organic transformations.

2.3.1.7. Phenyl acetate rearrangement

2.3.1.7a. Introduction

Fries rearrangement serves as valuable step in the production of a spectrum of industrial pharmaceuticals, dyes and agriculture. Classical Fries rearrangement involves the migration of acyl group from an ester resulting in a ketone. Fries rearrangements are generally catalyzed by acids like hydrofluoric acid (HF), the most frequently used $AlCl_3$, BF_3, $TiCl_4$ or $SnCl_4$. HF, which acts as solvent and catalyst, is very toxic, corrosive and very volatile. Metal chlorides are corrosive and react violently with water. Furthermore, the reaction mixture has to undergo a hydrolysis step generating corrosive gases and contaminated salts, which destroys the homogenous catalysts and unable to recycle.

There are lot of substitutes reported for these homogeneous catalysts in the form of zeolites, clays, nafion silica composites and BEA zeolites.

Recently, methane sulfonic acid has been reported to be an active homogeneous catalyst for Fries rearrangement. A high conversion of phenyl acetate was obtained with selectivity towards para-hydroxy acetophenone.

Phosphotungstic acid has been demonstrated to be an active solid acid catalyst for the Fires rearrangement of phenyl acetate recently.

In all solid acid catalysts reported shows fast deactivation at high reaction temperatures making it difficult for reuse.

2.3.1.7b. Present Work

With some success achieved for the acylation of phenol with acetic acid over PTZ catalyst, it was planned to conduct Fries rearrangement of phenyl acetate under identical conditions. It was expected that this study may give some clues to the exact reaction pathway of phenol acylation.

2.3.1.7c. Results and Discussion

Fries rearrangement of penyl acetate (PA) was carried out in gas phase reactor as mentioned in the phenol acylation. The PA feed was pumped from top using a syringe pump.

The flow of N_2 carrier gas was kept constant at 25ml/min. Catalyst loading was 2g wit bed length 15mm and volume 2.6 cm^3. The catalyst was activated in a flow of nitrogen at 500°C before the start of reaction. Results are tabulated in the Table 3.

Table 3. Phenyl acetate rearrangement over PZW12-750 catalyst.

No.	Temp. °C	Feed Flow Rate ml/hr	Conv. Phenyl Acetate %	Phenol %	OHAP %	PHAP %	PXAP %	Others %
1	300	1.5	38.8	34.9	2.8	0.7	0.4	-
2	250	1.5	10	9.6	-	-	-	0.4
3	350	1.5	44.7	37.1	3.5	1.0	0.8	2.3
4	300	3.9	42.3	35.9	1.4	0.7	0.4	3.9

The main products are phenol, o-HAP, p-HAP and o-AXAP. As can be seen from the results the course of reaction heavily depends on temperature. At 250°C, very small conversion was observed. But increase in the temperature to 300oC causes an increase in conversion of PA to 38.8% with acetophenone selectivity 5%. Further increase in temperature to 350°C increased the conversion as well as selectivity but resulted in considerable amount of unidentified products. Increasing the feed flow rate, which reduces the contact time, resulted in increase in PA conversion, also the undesired products increased.

It is well documented that o-HAP was formed by direct C-acylation of phenol. p-HAP was formed in much complex pathway which involves 3 steps.

i. O-acylation of phenol
ii. Autoacylation of phenyl acetate
iii. Hydrolysis of p-acetoxy acetophenone (p-AXAP).

The selectivity towards o-isomer in this experiment may be due to a pronounced stabilization of transition state. The traces of p- product and p-AXAP would have resulted from the autoacylation of phenol, which is formed by the decomposition of phenyl acetate, and phenyl actetate respectively.

2.3.1.7d. Conclusion

In conclusion, Fries migration of phenyl acetate over phosphotungstic acid modified phosphated zirconia catalyst resulted in a conversion of 45%. Phenol was the major product followed by o-HAP and p-HAP with traces of p-AXAP. It is inconclusive the exact pathway of the reaction whether it is intermolecular or intramolecular. The results obtained with the present catalyst system are superior to other zeolite systems hitherto reported in literature, proving the efficacy of the zirconia based solid acid catalyst for the efficient acylation reactions.

2.3.1.8. Reference

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2.3.2. Benzoylation of Aromatics

2.3.2.1. Introduction

Friedel-Crafts acylation constitutes the most important unit process for the preparation of aryl ketones. A wide range of homogeneous catalysts like $FeCl_3$, $AlCl_3$, BF_3 and protic acids like HF and H_2SO_4 have been used for the reaction.[1,2] These catalysts, however, suffer from the inherent drawback of extreme corrosivity, high susceptibility to water and difficulty in catalyst recovery. The stoichiometric amounts of catalyst with respect ot acylating agent required for the reaction makes the work-up procedure tedious. The high Lewis acidity of these homogeneous catalysts also results in several undesired side reactions leading to multiple acylated products. The rampant use of acid catalysts in chemical and refinery industries has resulted in extensive environmental pollution during the past. Growing ecological concern demands the replacement of highly corrosive, hazardous and polluting liquid acids by eco-friendly solid acids. A wide range of solid acids from zeolites[3,4] and clays[5] to Nafion-H[6] has been screened for the applicability towards this reaction.

Recently much attention has been centered on the sulphate doped metal oxide catalysts, the superacidity of which has been a subject of debate. These systems have been reported to be active for benzoylation of toluene with benzoyl chloride and benzoic anhydride at temperatures below the reflux temperature of the mixture.[7,8] However, sulphur leaching during the reaction, coke deposition at higher temperatures, changes in sulphur oxidation state and crystalline phase changes from tetragonal to monoclinic limit the industrial use of these catalyst. Constant efforts are on the way to improve the stability and reusability of the systems.[9] Incorporation of transition metal oxides has been reported to enhance the thermal stability and the stability of the surface sulphate species.[10-12]

Zeolites are known for their shape selective properties and they have been used widely in a variety of acid and base catalyzed shape selective reactions. H-beta zeolite has been successful in catalyzing the benzoylation reaction of naphthalene with benzoyl chloride with high selectivity towards 2-benzoyl naphthalene.[13] Also toluene was benzoylated with good selectivity with H-BETA and H-ZSM-12.[14] Re^{3+} exchanged Y-zeolites enhances the activity of the parent Y-zeolite in the benzoylation reaction of toluene with benzoyl chloride.[15] An increase in Si/Al ratio decreases the activity of these zeolites catalysts. H-ZSM-5 was found to be efficient catalyst for the benzoylation reaction for a variety of aromatic substrates including heterocycles.[16]

Large pore zeolites like H-Y and H-BEA have been successfully demonstrated to catalyze dimethoxybenzene with benzoic anhydride and substituted benzoyl chloride leading to the selective formation of dimethoxybenzophenones.[14]

Silica-Gel supported ferric chloride benzoylated both activated and deactivated substrates with benzotrichloride in ethylene dichloride as solvent at reflux temperature.[18]

Recently transition metal triflates came into lime light as potential Lewis acid catalysts for a variety of reactions. Singh et. al.[17] demonstrated the efficacy of copper and tin triflates in alkylation, acylation, benzoylation and sulfonylation reaction. Copper triflate gave the best yields for the benzoylation reactions of anisole, dimethoxybenzene and toluene.

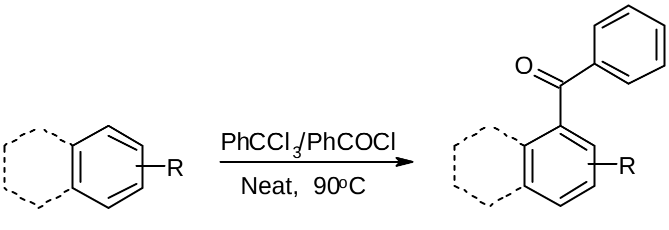
Aluminium promoted sulphated zirconia and titania have been shown to catalyze the benzoylation of toluene efficiently. The aluminium metal doping increases the super acidity of catalysts.[19]

Also iron supported sulphated zirconia was found recently to be a very efficient catalyst for the benzoylation of arenes.[20]

2.3.2.2. Present Work

As can be seen from literature, the metal doped sulphated solid super acids are efficient catalysts for the benzoylation reactions. The main disadvantage of these systems is the leaching out of the catalystically active species from the catalyst matrix, e.g. sulphate leaching from sulphated zirconia at high temperature and highly acidic corrosive conditions. To circumvent this problem there is a need for highly stable and active catalyst. It has been shown in previous sections, the phosphotungstic acid modified phosphated zirconia has been found to be very stable catalyst for the acylation and Fries migration reactions. This section investigates the efficiency of the PTZ catalyst in catalyzing the benzoylation reaction of various aromatic substrates with both benzo trichloride and benzoyl chloride as benzoylating agents respectively.

2.3.2.3. Results and Discussions



Scheme 1. Benzoylation of Aromatics

Benzoylation of aromatics was performed with 12PTZ-750 using both benzotrichloride and benzoyl chloride as benzoylating agents. The reaction was carried out in neat at 90°C for 5h. Reactions were monitored by TLC and GC. Corresponding benzophenones were obtained as sole product in good yields and with good para selectivity in all the cases.

Table 1. 12PTZ-750 catalyzed benzoylation of aromatic substrates

No	Substrate	Product	Yields (%)	
			$PhCCl_3$	PhCOCl
1.	Phenol	4-Hydroxybenzophenone	58	52
2.	Anisole	2-methoxybenzophenone	66	54
3.	Resorcinol	2,4-dihydroxybenzophenone	72	50
4.	2-Naphthol	1-benzoyl-2-naphthol	58	47
5.	2-methoxy naphthalene	1-benzoyl-2-methoxynaphthalene	62	48

Notably activated arenes underwent benzoylation efficiently and the reactions were essentially regiospecific. All products were characterized by melting points, I.R and mass spectral analysis. All activated aromatics such as phenol, anisole and resorcinol yielded the para isomer regiospecifically in good yields. The activated naphthalenes viz. 2-naphthol and 2-methoxynaphthalene afforded the 1-benzoyl isomers. However, benzene, halobenzene itself failed to undergo benzoylation under the reaction conditions. They did not react even at 160°C and even with catalyst proportions as high as 100% w/w.

The temperature of reaction was standardized at 90°C with the benzoylation of anisole. No reaction was observed at temperatures below 80°C. At 90°C optimum yields of benzoylated product was obtained. Above 90°C, side products were observed and the catalyst got deactivated faster. The dependence of the extent of benzoylation of anisole on temperature was studied (Fig. 1). It was observed that the optimum yield of benzoylated product was obtained at 90°C beyond which there was a gradual decrease in the yield.

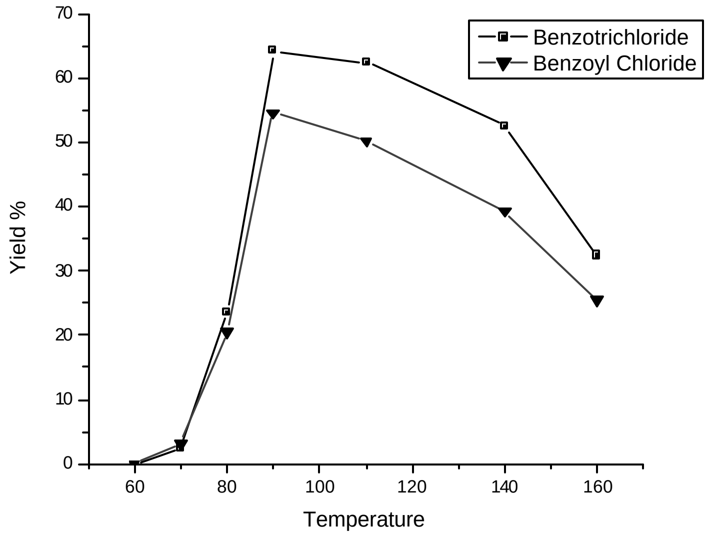
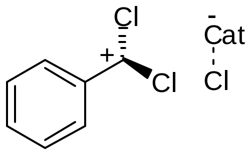


Fig. 1. Dependence of temperature on Benzoylation of Anisole

The yields obtained with the use of benzotrichloride were generally higher than those obtained using benzoylchloride. This can be attributed to the enhanced activation of benzotrichloride by the Lewis acid sites on the catalyst surface. Sulphated zirconia has been reported to have high Lewis acidity because of the sulphate groups dispersed on the surface of the tetragonal zirconia.[21] In this system, addition of phosphoric acid increases the surface acidity. Also impregnation of phosphotungstic acid resulted in an increase in Bronsted acidity. On calcinations at high temperature, the water molecule and the surface –OH groups gets dehydrated, leaving behind phosphotungstic acid layer on phosphated zirconia.[22] This dehydration produces some anionic vacancies with some trapped electrons on the surface.[23] Mechanistically, it may be presumed that Lewis acid sites on catalyst can form coordinate



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bonds with benzoyl chloride and benzotrichloride thereby increasing their electrophilicity. It has been proved by earlier work[24] conducted in our laboratory that benzoyl chloride form a weaker coordination complex with the Lewis acid sites on the catalyst. The benzotrichloride forms a more electrophilic phenyldichlorocarbenium charge transfer complex **1**. It can be presumed that the trapped electrons in the anionic voids (vide supra) can stabilize the carbocation thereby facilitating the benzoylation reaction.

The catalyst was recovered after the reaction by filtration, washed with benzene and acetone and dried at 100°C for 6h. No deactivation of catalyst was observed after 2 recycles. In the third recycle, the reaction gave very low yields due to extensive deactivation of catalyst. The catalyst was further calcined at 750°C and tested for activity. Benzoylation of anisole resulted in almost same yield as that of original catalyst. From this it can be concluded that there was no leaching of phophate or phosphotungstic acid from the zirconia matrix in the harsh reaction conditions. Also there was no change in XRD pattern of the spent catalyst, which shows the intactness of the crystalline nature.

2.3.2.4. Experimental

12PTZ-750 catalyst was prepared as described in the section 2. The catalyst was activated at 750°C for 4h before use.

In a typical reaction, a mixture of benzotrichloride (0.98g, 0.005mol) was mixed with anisole (0.54g, 0.005mol) and to this 12PTZ-750 (0.1g) added. The mixture was heated at 90°C with good stirring for 5h. Reaction was monitored by TLC/GC. After reaction was over, ice-cold water was added, catalyst filtered off and the mixture was made alkaline with aqueous alkali solution to remove excess of benzotrichloride. It was then extracted with dichloromethane (10mlx3). The organic layer separated, washed with brine, dried over sodium sulphate and the solvent distilled off under reduced pressure to obtain crude product. The crude product was purified by column chromatography.

The melting points, IR, 1H-NMR spectral data of benzophenones are summarized below.

1. **4-Hydroxybenzophenone.**

Mp. : 132-133°C. (Lit. Mp. 134°C)
IR (Nujol,cm-1) : 3420, 3010, 1630, 1560, 1275, 1155, 790, 710.
1H NMR (200 MHz, CDCl3, δ) : 6.8 (2H, d, J=8Hz, Ar-H), 7.2-7.8 (5H, m, Ar-H), 8.0 (2H, d, J=8Hz, Ar-H).
MS m/e (relative intensity %) : 198 (M+, 25), 138 (15), 122 (58), 115 (8), 105, (100), 94 (50), 77 (42).

2. **2-Methoxybenzophenone.**

Mp. : 60-62°C. (Lit. Mp. 61-62°C).
IR (Nujol, cm-1): 1650, 1510, 1440, 1325, 1250, 1180, 1150, 1030, 940.
1H NMR (200 MHz, CDCl3, δ) : 3.8 (3H, s, OCH3), 6.9 (2H, d, J=8Hz, Ar-H), 7.3-7.5 (5H, m, Ar-H), 7.6-7.8 (2H, m, Ar-H).
MS m/e (relative intensity %) : 212 (M+, 24), 198 (8), 135 (72), 122 (22), 105 (100), 92 (15), 77 (80).

3. **2,4-Dihydroxybenzophenone**.

Mp. : 131-133°C. (Lit. Mp. 134°C).

IR (Nujol, cm^{-1}) : 3460, 1710, 1600, 1540, 1475, 1280, 1180, 1110, 770.
1H NMR (200 MHz, $CDCl_3$, δ) : 5.7 (1H, s, OH), 6.8-7.1 (3H, m, Ar-H), 7.2-7.5 (3H, m, Ar-H), 7.9-8.2 (2H, m, Ar-H).
MS m/e (relative intensity %) : 214 (M+, 12), 136 (10), 122 (70), 105 (100), 77 (45).

4. **1-Benzoyl-2-naphthol**.

Mp.: 135-136°C. (Lit. Mp. 135-137°C).
IR (Nujol, cm^{-1}) : 3350, 1740, 1640, 1600, 1460, 1270, 1170, 1030, 1030, 830, 750.
1H NMR (200 MHz, $CDCl_3$, δ) : 7.2-8.0 (m, 11H, Ar-H), 8.3 (1H, broad, OH).
MS m/e (relative intensity %) :248 (M+, 15), 171 (14), 143 (65), 126 (20), 105 (100), 92 (22), 77 (75).

5. **1-Benzoyl-2-methoxynaphthalene**.

Mp.: 132°C
IR (Nujol, cm^{-1}) : 1710, 1640, 1600, 1510, 1450, 1320, 1260, 1180, 1150, 1030, 930, 750.
1H NMR (200 MHz, $CDCl_3$, δ) : 3.8 (s, 3H, OCH3), 7.1-8.0(m, 11H, Ar-H).
MS m/e (relative intensity %) : 262 (M+, 24), 248 (42), 158 (100), 143 (33), 128 (40), 115 (87), 101 (8), 89 (20), 75 (12).

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