Chapter 2

Exploration of multifaceted acidic 1, 3-disulfoimidazolium chlorometallates as heterogeneous catalysts for preparation of β-amino carbonyl compounds *via* Mannich-type reaction

Published with modification

Saikia, S., Gogoi, P., Dutta, A. K., Sarma, P. and Borah, R. Design of multifaceted acidic 1, 3-disulfoimidazolium chlorometallate ionic systems as heterogeneous catalysts for the preparation of β-amino carbonyl compounds. *Journal of Molecular Catalysis A: Chemical*, 416:63-72, 2016.

32A.1 Importance of chlorometallates as functional material

The recent reviews on halometallates ionic liquids by Estager *et al.* in 2014 and Kore *et al.* in 2017 clearly defined characteristic properties of chlorometallates ionic liquids in presence of anionic equilibria of complex metal halide speciation depending on the type and concentration of metal content that directly determine their individual tunable properties such as Lewis acidity, paramagnetism and electrochemical behavior *etc.* Most of the reported works on chlorometallates are concerned on group IIIA metal (Al^{3+}, Ga^{3+}, In^{3+}), transition elements (Fe^{3+}, Co^{2+}, Mn^{2+}, Ni^{2+}, Zn^{2+}, Sn^{2+} and Sn^{4+}) and some rare earth elements (Hf^{4+}, Gd^{3+}, Eu^{3+} and Dy^{3+}). The development of chloroaluminate ionic liquid reflects its mature stage with lots of applications in catalysis and electrochemistry in spite of their air and water sensitive stability. Some of the transition metal chloride anions eliminate these stability problems of ammonium, pyridinium and imidazolium ionic liquids as compared to the respective chloroaluminates. Based on their melting points, they can be utilized as heterogeneous or homogeneous catalyst in organic reactions. Hydrolytically stable mild Lewis acidic chloroindate (III) ionic liquids were prepared with formation of $[InCl_6]^{3-}$, $[InCl_5]^{2-}$ and $[InCl_4]^{-}$ anions as per the following equations (**2A.1-2A.3**) at $\chi_{InCl3} = 0.25$, $\chi_{InCl3} = 0.33$ and $\chi_{InCl3} = 0.5$ mole fractions [1-4].

$$[\text{cation}]\text{Cl} + 3\text{InCl}_3 \xrightarrow{\chi_{\text{InCl3}} = 0.25} [\text{cation}]_3[\text{InCl}_6] \tag{2A.1}$$

$$4\text{Cl} + 2\text{InCl}_3 \xrightarrow{\chi_{\text{InCl3}} = 0.33} 2[\text{InCl}_5]^{2-} \rightleftharpoons [\text{InCl}_6]^{3-} + [\text{InCl}_4]^{-} \tag{2A.2}$$

$$[\text{cation}]\text{Cl} + \text{InCl}_3 \overset{\chi_{\text{InCl3}} = 0.50}{\rightleftharpoons} [\text{cation}][[\text{InCl}_4] \tag{2A.3}$$

They were employed as reusable catalysts in transesterification (biodiesel synthesis) [5], alkylation of phenols or catechols with alcohols [4], protection of alcohols as acetates and trimethylsilyl ethers [6].

Plethora of Lewis acidic chlorometallates have been synthesized and captured attention of researchers by their multifunctional tunable behavior for potential utilization as reusable heterogeneous or homogeneous ionic liquid catalysts [7]. **Fig.2A.1** summarizes the characteristic factors of halometallates that make them as appropriate alternative of conventional catalysts [8].

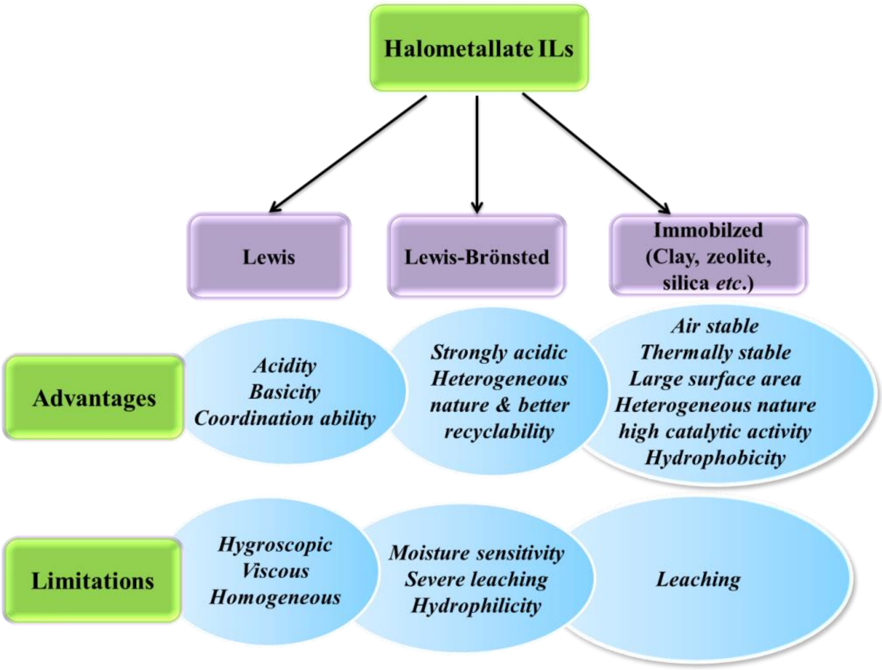


Fig.2A.1: Summarized presentation of halometallate ILs as catalyst

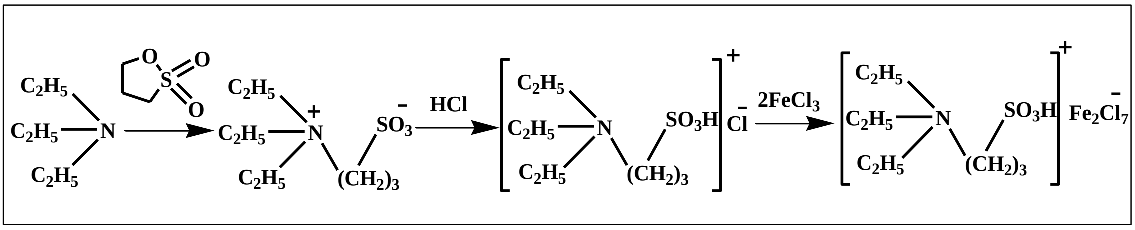
Fig.1.6 of '**Introduction**' chapter (subunit **1.2.2**) displays all the functions related to halometallate ionic liquids in different application fields. It is very interesting to explore fascinating properties of chlorometallates as controllable Lewis acidic or dual functionalized Brönsted-Lewis acidic ionic liquids particularly for catalysis through variation of the metal complex anion and also attachment of -COOH, -SO_3H functionality with the organic cation. Till date the speciation of anion is the key determining factor for variation of physicochemical properties of the Lewis acidic halometallates such as strength of Lewis acidity, semi-conductor nature, electrochemical behavior, viscosity, melting points, moisture and water sensitivity, thermal stability *etc*. The presence of acidic functionality with the cation of Brönsted-Lewis acidic halometallates may contribute significant change of their acidic strength, hydrophilicity, thermal stability and other related physical characteristics. Various chain length of alkyl substituent also affects the hydrophobic character of these halometallate systems. They can be isolated in molten state, semi-solid or in solid phase depending on their strength of intermolecular interactions.

2A.2 Literature review of chlorometallates of Fe(+3), Ni(+2) and Zn(+2) metal chloride

This section discusses a brief review of Lewis and Brönsted-Lewis acidic chlorometallates of Fe(+3), Ni(+2) and Zn(+2) containing ammonium, imidazolium, pyridinium and phosphonium cations and their catalytic uses till 2018.

Physicochemical and spectroscopic behaviors of chloroferrate ionic liquids offer many conclusions regarding their anionic speciation, tunable behavior of Lewis acidity and moisture sensitivity based on the mole fraction of $FeCl_2$ or $FeCl_3$. A detail study on speciation in halometallate ionic liquids by Kore *et al.* in their review clearly distinguish the existence of different chloroaluminate anions at different molar ratios of $AlCl_3$ to 1-alkyl-3-methylimidazolium chloride ($[C_n\text{mim}]Cl$, where n = 2 or 4). At mole fractions of $AlCl_3<0.5$, the melt becomes basic and the dominant complex is neutral $[AlCl_4]^-$ ($\chi AlCl_3 = 0.5$) along with basic $[Cl]^-$ anions. At higher mole fractions, ($\chi AlCl_3 > 0.5$) acidic $[Al_2Cl_7]^-$ start to form whereas $[AlCl_4]^-$, $[Al_3Cl_{10}]^-$, and other anions with higher acidity are also present. Similarly, Sitze *et al.* in 2001 identified the formation of neutral $FeCl_4^-$ species at $\chi_{FeCl3/FeCl2} = 0.50$, $FeCl_4^-$ and Lewis acidic $Fe_2Cl_7^{2-}$ at $\chi_{FeCl_3} = 0.60$ after mixing either iron(II) chloride or iron(III) chloride with 1-butyl-3-methyl imidazolium chloride [9]. These anionic speciations were confirmed using Raman scattering and ab initio calculations. It was observed that for $\chi_{FeCl_3>}0.6$, additional $FeCl_3$ doesn't dissolve and the ionic liquids containing pure $Fe_2Cl_7^{2-}$ never form. Li *et al.* (2016) [10] studied the variation of conductivities and densities of $FeCl_3/[C_4\text{mim}][Cl]$ (Fe(III) chloride with 1-butyl-3-methylimidazolium chloride) ionic liquids from a mole composition ratio of 1/1.7 to 1.5/1 in the temperature range of 293.15 to 343.15K. The extreme increase of ionic conductivity of the tested mixture is found at mole fraction, $\chi_{FeCl3}<0.5$ while the conductivity smoothly decreases above that mole fraction. Bica *et al.* in 2011 reviewed general synthesis and uses of Lewis acidic chloroferrates(III) ionic liquids as solvent, catalyst or catalytic system for a variety of chemical processes involving synthesis of pharmaceutically active compounds or intermediates [11]. They mentioned efficient dual solvent-catalysts function of the chloroferrates(III) ionic liquids for Friedel-Crafts acylation and alkylation [12, 13], sulfonylation [14], Kharash reaction [15], oxidations [16], cycloaddition and dimerization [17], reactions of 1, 3-dicarbonyls [18], polymerization and depolymerization [19] *etc.* Hydrophobicity of chloroferrate ionic liquids was proposed as the outcome of nephelauxetic effects which may contribute to the hydrophobic nature of chloroferrate(III) systems. This explanation was predicted for the behavioral difference of structurally similar anions such as $InCl_4^-$ and $FeCl_4^-$. Also, Xie *et al.* [20] studied the thermomorphic behavior of $[C_4mim][FeCl_4]$ and $[C_{12}mim][FeCl_4]$ which are the first examples of thermomorphism in a metal-containing IL.

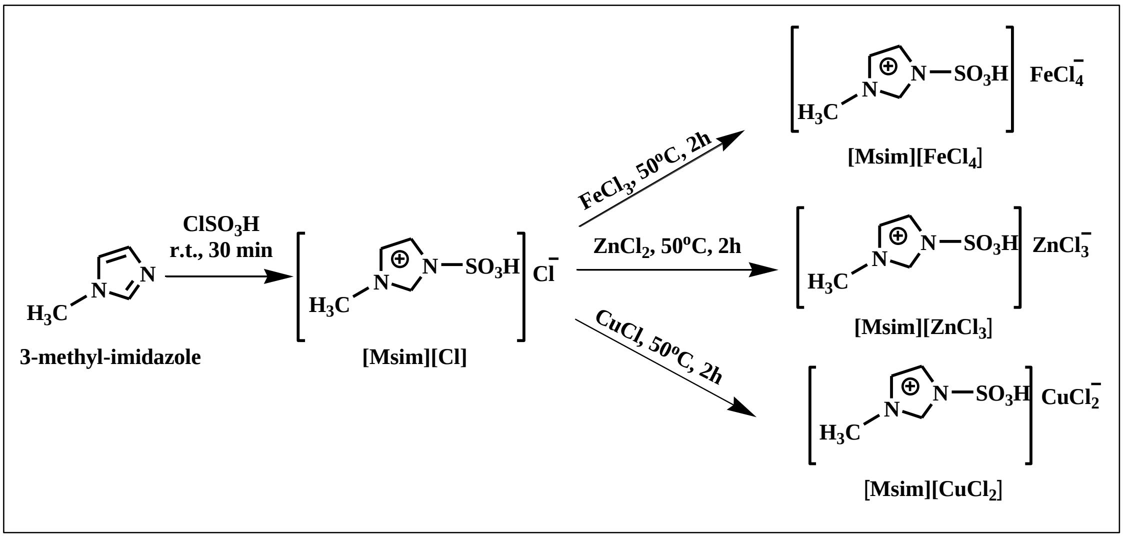
In 2013, Liu *et al.* synthesized the first Brönsted-Lewis acidic chloroferrate ILs by the reaction of $[HO_3S–(CH_2)_3–NEt_3]Cl$ with $FeCl_3$ (**Scheme 2A.1**). Lewis acidity was attributed by $Fe_2Cl_7^-$ anion when molar fraction of $FeCl_3$ was x = 0.67 [21]. This IL was efficiently utilized as reusable catalyst up to seven times for production of biodiesel from waste oil as feedstock at 120°C for 4 h with high acid value by “one-pot” method.



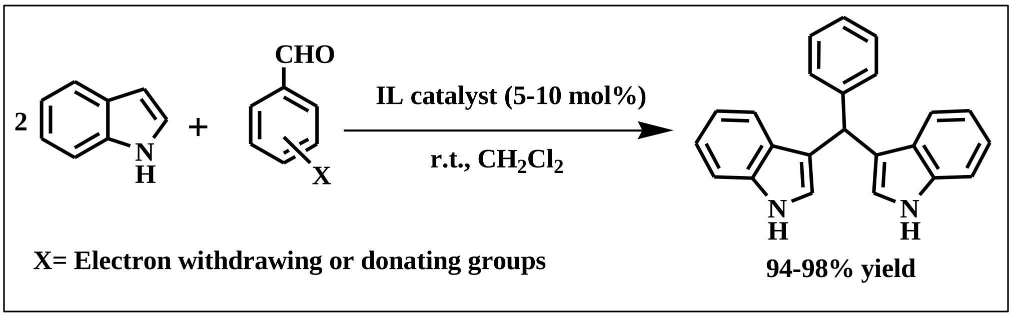
Scheme 2A.1: Synthesis of $[HO_3S–(CH_2)_3–NEt_3]Cl\text{-}FeCl_3$ (x = 0.67)

They also employed this IL as reusable catalyst for esterification of glycerol to glycerol triacetate with yield greater than 98% under reflux for 4 h [22].

In 2015, Gogoi *et al.* prepared three ionic salts of $FeCl_4^-$, $CuCl_2^-$ and $ZnCl_3^-$ anions with 2-methyl-1-sulfoimidazolium cation as the Brönsted-Lewis acidic solid material. It was the first report of direct N-sulfonation of ionic liquid cation in chlorometallate ILs (**Scheme 2A.2**) [23]. Their structures were confirmed with various analytical techniques including FT-IR, Raman, ^{1}H NMR, ^{13}C NMR, SEM-EDX, TGA, Powder XRD, AAS, BET, UV-Vis and elemental analysis. The catalytic activity was studied with 5-10 mol% of these ionic salt as recyclable heterogeneous catalyst for selective synthesis of *bis*(indolyl)methane derivatives (**Scheme 2A.3**) in dichloromethane at room temperature. The Fe(III) based ionic salt required 10-30 min reaction time to give excellent results.

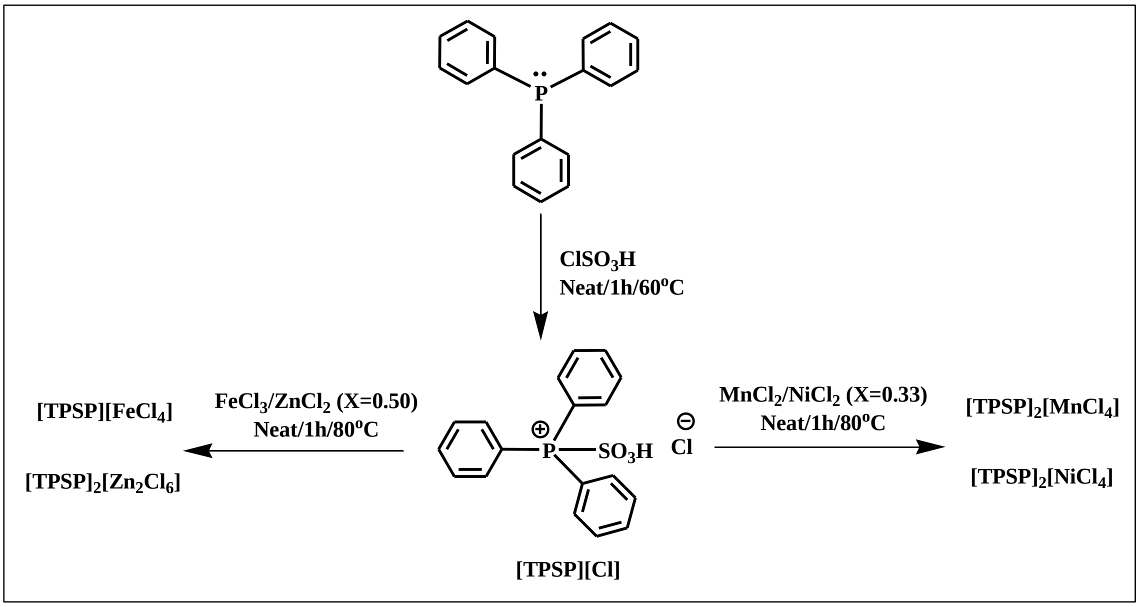


Scheme 2A.2: Synthesis of 3-methyl-1-sulfonic acid imidazolium metal chlorides

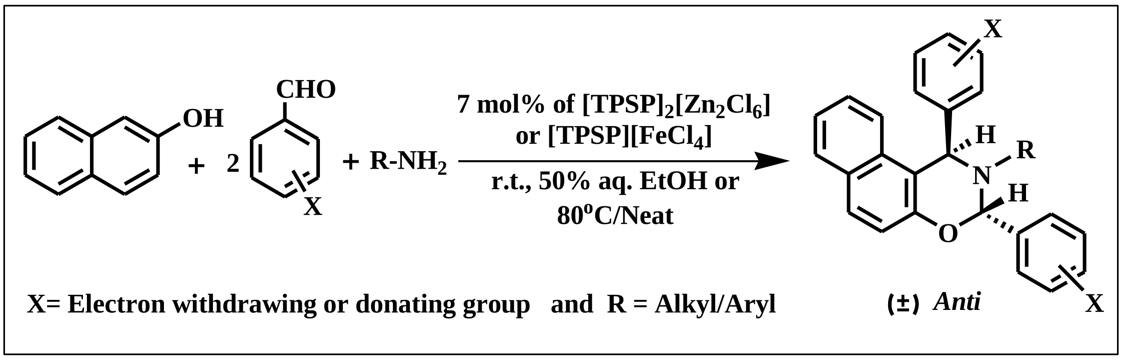


Scheme 2A.3: Synthesis of *bis(*indolyl) methane derivative

The direct -SO_3H functionalized Brönsted-Lewis acidic triphenyl sulphophosphonium chloroferrate(III) [TPSP][$FeCl_4$] was first designed and reported by Dutta *et al.* in 2017 [24]. In this work, they also successfully synthesized three other chlrometallates of transition metal $[TPSP]_n[X]$, where n = 2 and X = $Zn_2Cl_6^{2-}$, $NiCl_4^{2-}$, $MnCl_4^{2-}$ (**Scheme 2A.4**). These stable acidic solids were employed in multi-component synthesis of 2, 3-dihydro-1, 2, 3-trisubstituted-1*H*-naphth [1, 2-e] [1, 3] oxazines (**Scheme 2A.5**) and displayed satisfactory catalytic performance as heterogeneous catalysts.



Scheme 2A.4: Synthesis of triphenyl sulfo phosphonium chlorometallates [TPSP]$_n$[X] where n = 1 or 2; X = $FeCl_4^-$, $Zn_2Cl_6^{2-}$, $NiCl_4^{2-}$, $MnCl_4^{2-}$



Scheme 2A.5: Three component synthesis of 2, 3-dihydro-1, 2, 3-trisubstituted-1*H*-naphth [1, 2-e] [1, 3] oxazines

The same group in 2018 reported two more Brönsted–Lewis acidic ionic salts diethyl disulfoammonium chlorometallates, [DEDSA][$FeCl_4$] and [DEDSA]$_2$[Zn_2Cl_6] as solid material by the reaction of [$(Et)_2N(SO_3H)_2$][Cl] ionic liquid with transition metal chlorides ($FeCl_3$ and $ZnCl_2$) (**Fig. 2A.2**) [25]. These ammonium based chlorometallates were tested as reusable heterogeneous catalysts for the three-component synthesis of novel 14-aryl-7-(N-phenyl)-14H-dibenzo[a, j] acridines (**Scheme 2A.6**) and found to be very effective.

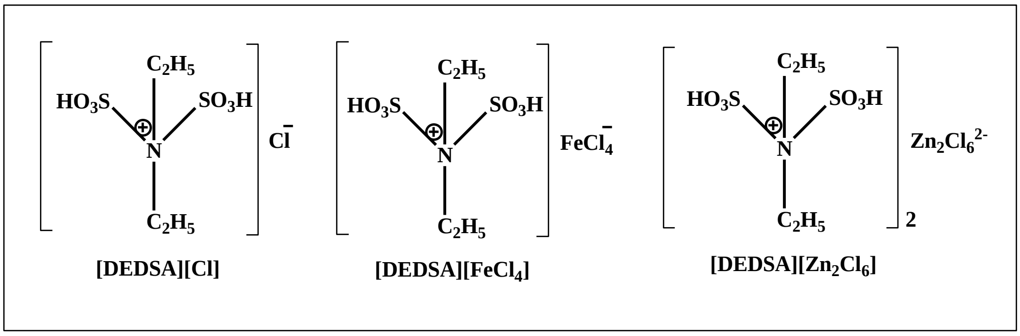
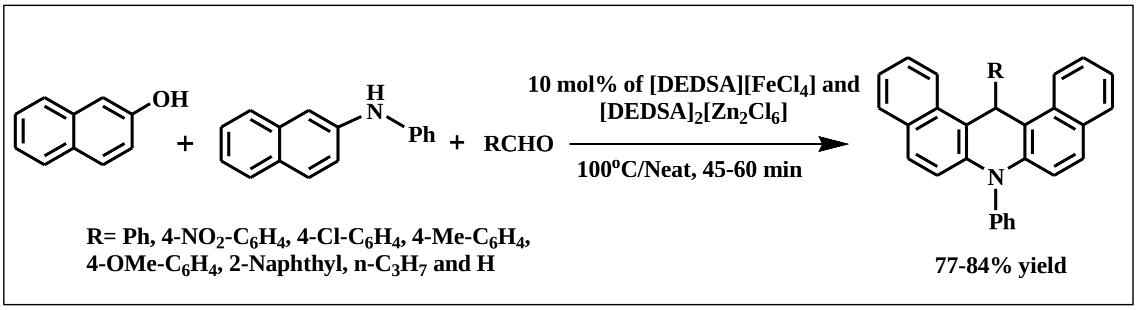


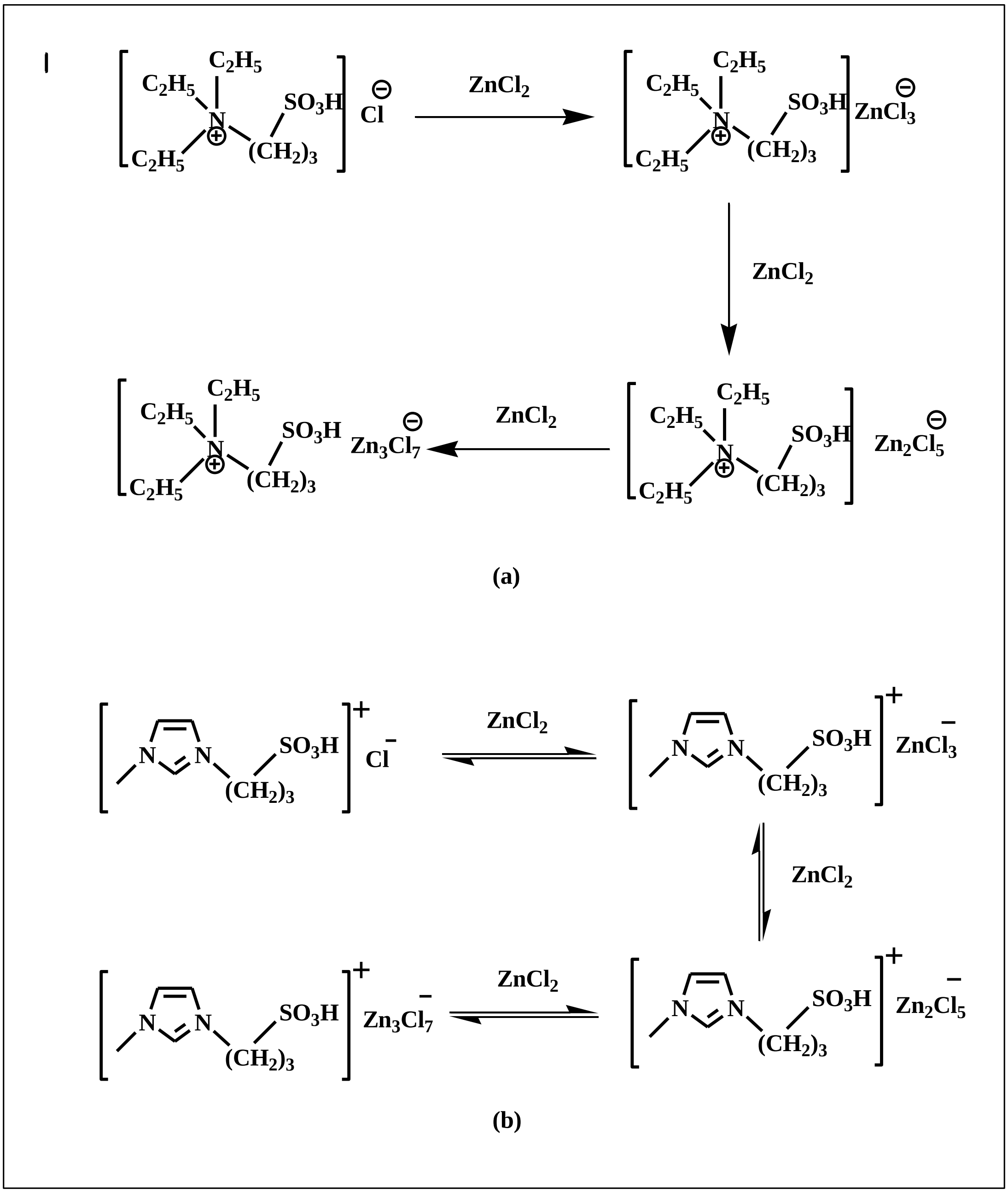
Fig. 2A.2: Structures of diethyl disulfoammonium chlorometallates



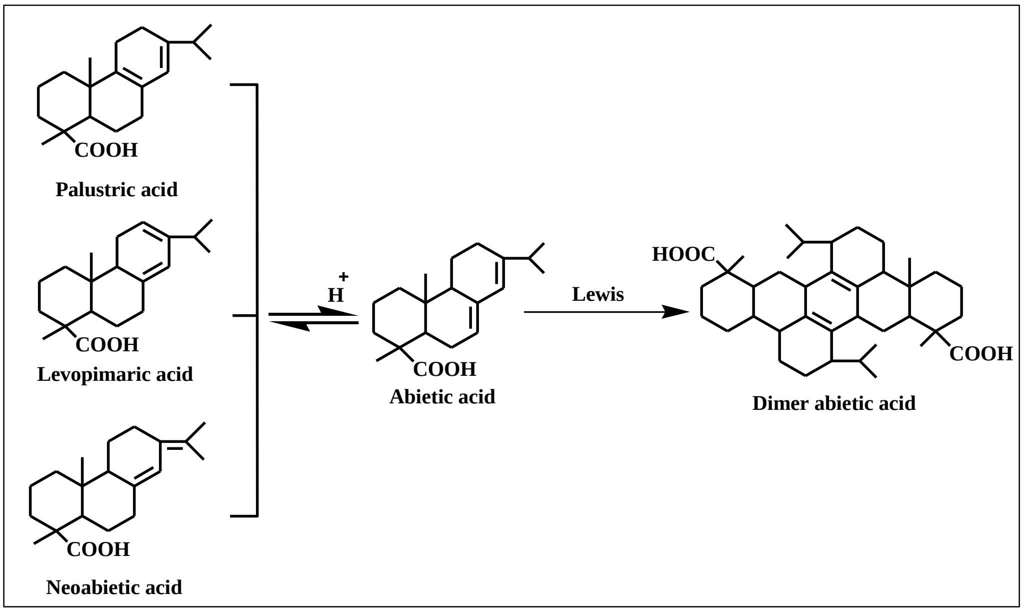
Scheme 2A.6: Synthesis of acridines using [DEDSA][$FeCl_4$] and $[DEDSA]_2[Zn_2Cl_6]$ catalysts

An extensive study of chlorozincate (II) was done by Estager *et al.* which described various molar ratios of zinc(II) chloride mixed with 1-octyl-3-methylimidazolium chloride and was investigated using Raman spectroscopy, differential scanning calorimetry as well as Gutmann acceptor number [26, 27]. The chlorozincate (II) ionic liquids were observed as neutral compound of $[ZnCl_4]^{2-}$ species or in equilibrium with Lewis basic chloride if the mole fraction of χ_{ZnCl2} = 0.3-0.33 [28], otherwise with χ_{ZnCl_2}>0.33, the chloride anion was entirely consumed to form Lewis acidic dimer $[Zn_2Cl_6]^{2-}$. The two Lewis acidic oligomeric polynuclear species $[Zn_3Cl_8]^{2-}$ and $[Zn_4Cl_{10}]^{2-}$ appeared at χ_{ZnCl_2}>0.50. Molar composition of χ_{ZnCl_2} = 0.20 was found to be basic. The formation of oligomeric $[Zn_2Cl_6]^{2-}$ and $[Zn_4Cl_{10}]^{2-}$ species are observed analogous to that of chloroaluminate (III) through dimerization of $[ZnCl_3]^-$ or $[Zn_2Cl_5]^-$ anions. The less moisture sensitivity of chlorozincate(II) ionic liquids finds many uses in organic reactions as recyclable catalysts such as O-acylation of cellulose, chemoselective reduction of heteroarenes and many others [29-32].

In 2008, Liu *et al.* explored the first synthesis of Brönsted-Lewis acidic chlorometallates of Zn(II) cation (3-sulfonic acid)-propyl triethyl ammonium chlorozincinates $[HSO_3–(CH_2)_3–NEt_3]Cl–ZnCl_2$ (**Scheme 2A.7(a)**) as efficient reusable catalyst for dimerization of rosin (**Scheme 2A.8**) [33]. The same group in 2009 also developed 1-(3-sulfonic acid)-propyl-3-methylimidazole chlorozincinates ([HO$_3$S-(CH$_2$)$_3$-mim]Cl-ZnCl$_2$) as reusable catalyst for the same dimerization reaction (**Scheme 2A.7(b)**) [34]. Both the catalysts showed Brönsted-Lewis acidity at molar fraction of $\chi_{ZnCl_2}>0.5$ and behaved as good catalyst at $\chi_{ZnCl_2} = 0.64$.



Scheme 2A.7: Synthesis of (a) (3-sulfonic acid)-propyltriethyl ammonium chlorozincinates [HSO$_3$–(CH$_2$)$_3$–NEt$_3$]Cl–ZnCl$_2$ and (b) 1-(3-sulfonic acid)-propyl-3-methylimidazole chlorozincinates ([HO$_3$S-(CH$_2$)$_3$-mim]Cl-ZnCl$_2$)



Scheme 2A.8: Dimerization of rosin

They also employed (3-sulfonic acid)-propyltriethylammonium chlorozincinate as an efficient catalyst for the alkylation of isobutane/isobutene using 0.83 mole fraction of [35].

Apart from Liu there were researchers Kore *et al.* in 2013 designed different -SO_3H based chlorometallates of Zn(II) cation by direct combination of ionic liquids and $ZnCl_2$. Among them N-alkylsulfonic IL imidazolium chlorozincate (**Fig.2A.3**) was used as suitable catalyst for Beckmann rearrangement [36].

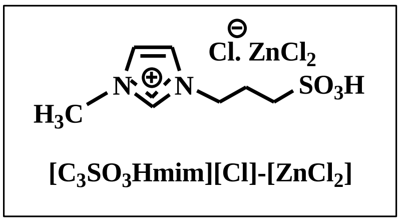


Fig.2A.3: Structure of $[C_3SO_3Hmim][Cl]-[ZnCl_2]$

The formation of Brönsted–Lewis acidic chlorozincate(II) ionic salts of imidazolium and phosphonium cations are already mentioned in the reaction **Scheme 2A.2** and **Scheme 2A.4**. They were utilized as reusable heterogeneous acid catalysts in organic reactions [23, 24].

The extensive study of chloronickellate (II) ionic liquid systems are not observed in literature unlike Fe(III) and Zn(II) based chlorometallates. However, the limited study clearly identified the existence of $NiCl_4^{2-}$ as anionic speciation in most of the chloronikellate(II) ionic liquids.

In 1979, Gale *et al.* investigated electrochemical and spectral behavior of Ni(II) ion in chloride-rich basic ionic liquid $AlCl_3$-1-butylpyridinium chloride with large organic cation at room temperature. The electrochemical study supported the presence of $NiCl_4^{2-}$ complex in basic media of ionic liquids [37].

A potentiometric titration method was utilized by Hussey *et al.* in 1982 to study the coordination complexes of Ni(II), Fe(II) and Fe (III) in $AlCl_3$-*N*-*n*-butylpyridinium chloride ($AlCl_3$-BPC) melt at 40°C containing excess amount of chloride anion (basic melt) which evidenced the formation of $FeCl_4^{2-}$, $FeCl_4^-$ and $NiCl_4^{2-}$ anions [38, 39].

Dent and his co-workers in 1990 performed EXAFS (extended X-ray absorption fine structure) analysis to detect tetrahedral complex $[MCl_4]^{2-}$ of transition metal cations, M = Mn^{2+}, Co^{2+}, Ni^{2+} in 1-methyl-3-ethylimidazolium salts $[MeEtim]_2[MCl_4]$ dissolved in [MeEtim]Cl-$AlCl_3$ basic ionic liquids [40].

Hitchcock and his group [41] synthesized two ionic salts $[emim]_2[CoCl_4]$ and $[emim]_2[NiC_4]$ (emim = 1-ethyl-3-methylimidazolium cation) and determined their structure using infrared spectra, electronic absorption spectra and crystal structure analysis. The crystal structures clearly demonstrated involvement of all three imidazolium ring protons and Cl atoms of tetrachlorometallate(II) anions in an extended three-dimensional hydrogen-bonded network.

Bowlas (1996) observed liquid crystalline behavior of tetrachloronickellate (II) salts of 1-alkyl-3-methylimidazolium $[C_n\text{-min}]^+$ and N-alkylpyridinium $(C_n\text{-py}]^+$ cations, where the alkyl chain length was varied from C_{12} to C_{18} [42].

The structures of low melting ionic salt $[C_2mim]_2[NiCl_4]$ was also studied in solid and liquid state by XAFS (X-ray absorption fine structure) using supported disks of boron nitride, graphite, and lithium fluoride matrixes [43].

Roeper *et al.* also (2011) observed tetrahedral arrangement of four chloride anions around Ni(+2) cation of anhydrous $NiCl_2$ in basic solution of 1-ethyl-3-methyl imidazolium chloride and $AlCl_3$ with extended X-ray absorption fine structure [44].

Zhong *et al.* [45] synthesized bis(1-n-butyl-3-methyl-imidazolium) tetrachloronickelate ($[Bmim]_2[NiCl_4]$) and immobilized nickel ion-containing ionic liquid ($ImmNi^{2+}$-IL) on silica surface based on 1-methyl-3-(3-trimethoxysilylpropyl) imidazole chloride (**Fig.2A.4**). They were applied as new catalysts for Suzuki cross-coupling reactions between aryl chlorides and arylboronic acids giving maximum of 100% yield. Both the catalytic systems needed pretreatment before use. Addition of triphenylphosphine acted as promoter for the reaction. The structure of ($[Bmim]_2[NiCl_4]$) was again established by X-ray crystallographic analysis [46].

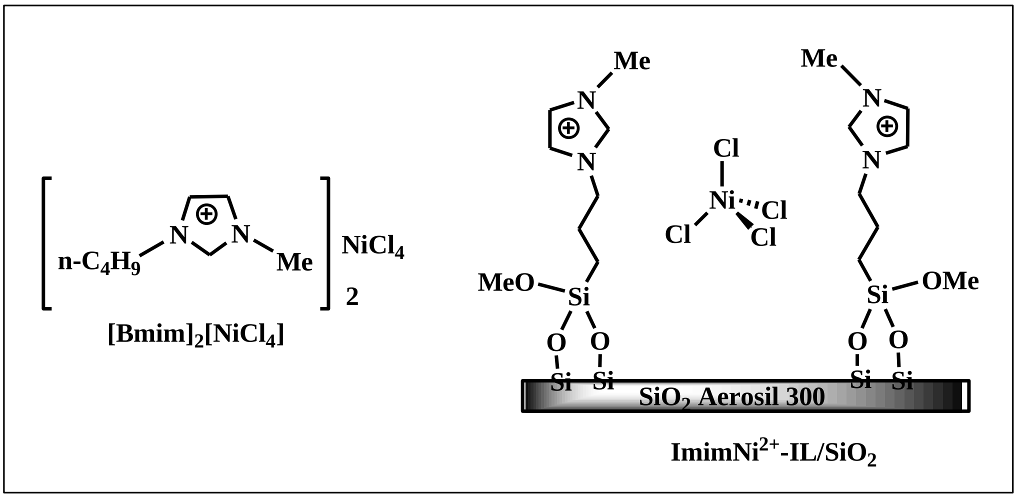
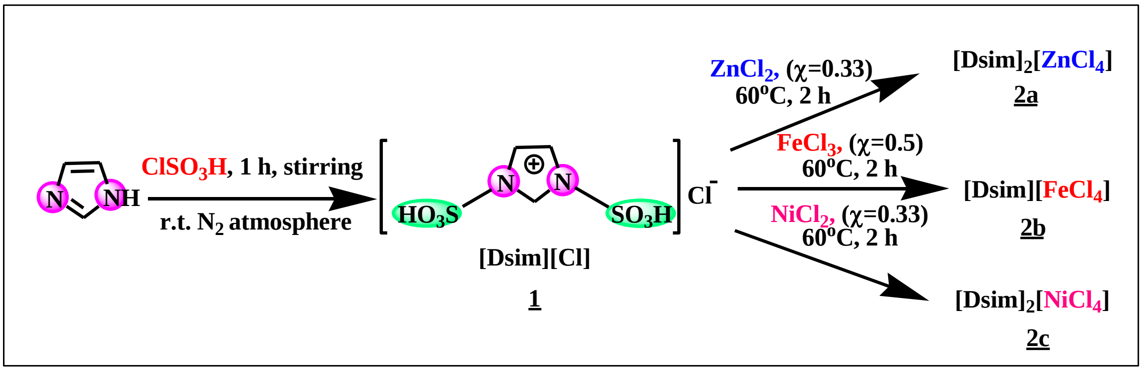


Fig.2A.4: Structures of $[Bmim]_2[NiCl_4]$ and $ImimNi^{2+}$-IL/SiO_2

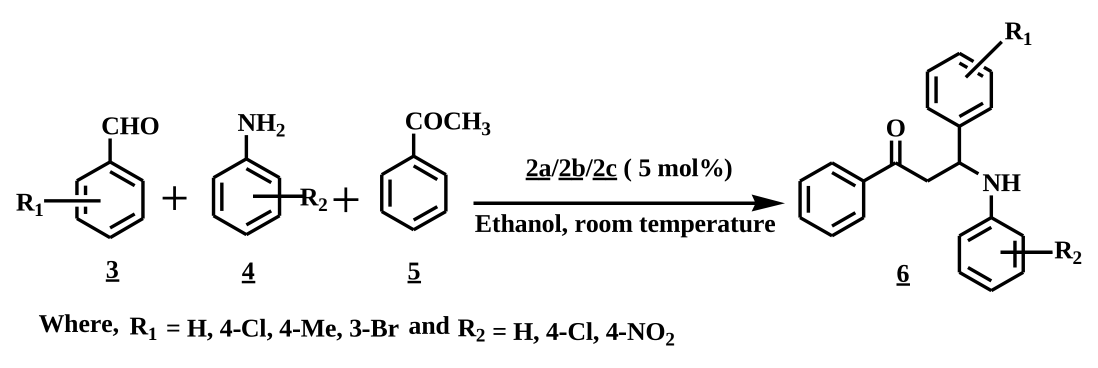
Again the same concept of immobilization was applied by Sasaki *et al.* [47] for immobilization of Ni^{2+} cation bearing IL on silica surfaces using 1-methyl-3-(3-trimethoxysilylpropyl) imidazole chloride and Aerosil 300. The authors tested their catalytic activity in Kharasch addition reaction and Suzuki cross-coupling reactions.

Also Taylor *et al.* [48] analyzed X-ray photoelectron spectra (XPS) of a series of 1-octyl-3-methylimidazolium halometallate ionic liquids of general formula $(1-\chi)[C_8C_1Im]Cl–\chi MCl_y$ (where χ is the mole fraction of metal halide and $y = 2$ or 3) which involved the use of metal chlorides such as $Fe^{III}Cl_3$ ($\chi FeCl_3 = 0.5$), $Fe^{II}Cl_2$ ($\chi FeCl_2 = 0.33$), $Co^{II}Cl_2$ ($\chi CoCl_2 = 0.33$), $Ni^{II}Cl_2$ ($\chi NiCl_2 = 0.33$) and $Zn^{II}Cl_2$ ($\chi ZnCl_2$ = 0.25, 0.33, 0.5, 0.6). Investigation of XPS data has allowed the prediction of trends in solvent parameters for these ionic liquids, including hydrogen bond basicity and Lewis acidity.

From the brief literature review of acidic chlorometalltes of Fe(III), Zn(II) and Ni(II) cation, it was observed that most of the reported chloroferrate(III), chlorozincate(II) and chloronickellate(II) are Lewis acidic due to the absence of Brönsted acidic functional groups attached to the organic cation. In this situation, their catalytic efficiency mainly depends on the composition of chlorometallate species. Few reports only described the modification of Lewis-acidity of these chlorometallates to Brönsted-Lewis acidic by incorporation of direct N-SO_3H and N-alkylsulfonic groups with the organic cation and they worked as efficient reusable homogeneous or heterogeneous catalysts in organic reaction. The general concept of water sensitive stability of chlorometalltes can't be applicable for all those materials which are readily recyclable for several runs at atmospheric condition. The scope for development of water stable acidic chlorometallates of the three transition metals was implemented by treatment of 1, 3-disulfoimidazolium chloride with each metal chloride ($FeCl_3$, $NiCl_2$, $ZnCl_2$) in different molar ratios (1:1 and 2:1) (**Scheme 2A.9**) to get respective 1, 3-disulfoimidazolium chlorometallates as solid ionic salts. The detail experimental procedure, characterization techniques of the ionic salts and also their catalytic studies for Mannich-type reaction (**Scheme 2A.10**) of acetophenone, aromatic aldehydes and substituted aniline are described in **Section 2B**.



Scheme 2A.9: Synthesis of 1, 3-disulfoimidazolium chlorometallates



Scheme 2A.10: Synthesis of β-amino carbonyl compounds

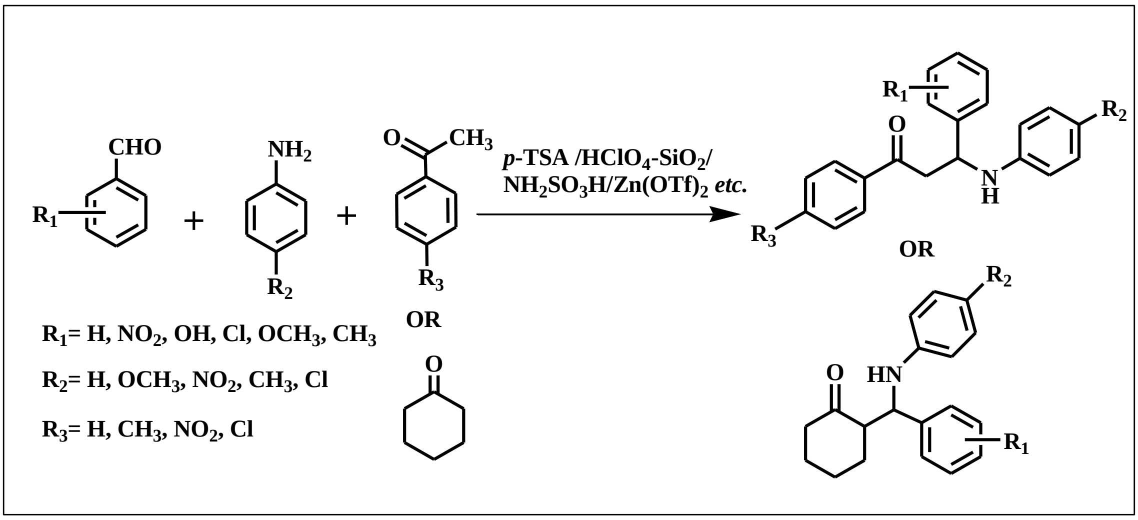
2A.3 Uses of β-amino carbonyl compounds

Construction of nitrogenous molecules has been always one of the most important tasks in organic synthesis. Among all the synthetic methodologies available, Mannich reaction produces β-amino carbonyl compounds which are also known as Mannich bases through C-C bond forming reaction [49-51]. These are precursors of β-lactams [52], α- and γ-amino alcohol [53-55], α- and β-amino acid derivatives [56], peroxyacetylenic alcohol or ethers [57] and other medicinal products.

Clinically important some Mannich bases are cocaine, fluoxetine, atropine, ethacrynic acid, trihexyphenidyl, procyclidine, ranitidine, biperiden *etc.* [58-60]. The literature search revealed that Mannich bases are very reactive and can be easily converted to other compounds and thus play key role in pharmaceuticals [61]. A variety of biological activities are identified for β-amino carbonyl compounds including anti-inflammatory [62, 63], anticancer [64, 65], antifilarial [62], antibacterial [66-68], antifungal [67, 69], anticonvulsant [70], anthelmintic [71], antitubercular [72, 73], analgesic [74], anti-HIV [72], antimalarial [75], antipsychotic [76], antiviral [77] activities *etc.* In addition to that Mannich bases have been used as detergent additives [78], resins, polymers, surface active agents [79], and so on. Some of them are employed for enantioselective C-C bond formation reaction [80, 81] and also preparation of agrochemicals use for plant growth regulators [82]. Thus multifaceted activities of Mannich bases set a valuable position in synthetic organic chemistry.

2A.4 Review of ionic liquid mediated/catalyzed Mannich reaction

Mannich reaction is an acid catalyzed three-component reaction of non-enolisable aldehyde, primary or secondary amine and enolisable carbonyl compound to afford β-amino carbonyl compounds (**Scheme 2A.11**) [83]. The most common catalysts used in the Mannich reaction are $HClO_4$-SiO_2 [84], bromo dimethylsulfonium bromide (BDMS) [85], TMSCl [86], *p*-TSA [87], $SmCl_3$ [88], Amberlyst-15 [89], $AuCl_3$-PPh_3 [90], silica supported sulfuric acid [91], carbon-based solid acid [92], $InCl_3$ [93], $NbCl_5$ [94], sulfamic acid [95], Fe_3O_4-cysteine MNP [96], $BiCl_3$ [97], sucrose char sulfonic acid [98], boric acid [99], $Zn(OTf)_2$ [100] and many other Brönsted/Lewis acidic catalysts [101-113]. Some of them utilize drastic reaction condition, toxic solvent, non-recyclable catalyst, longer reaction time, expensive catalyst and also laborious work-up step for isolation of product [113-115]. Different catalytic systems have been found in the literature to eliminate the above limitations of classical Mannich reaction [97] within Green Chemistry principles.

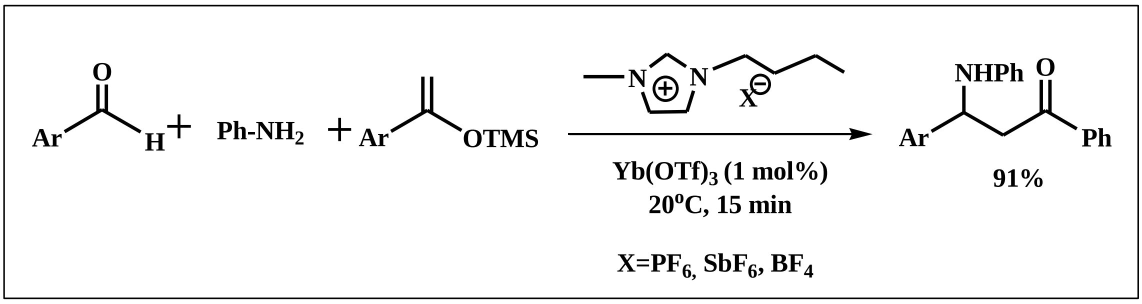


Scheme 2A.11: Three component Mannich reaction

Arend *et al*. (1998) in his review discussed modified versions of this Mannich reaction which allows a distinctly simpler entry into β-amino carbonyl compounds involving preformed electrophiles (e.g. iminium salts or imines) or nucleophiles (enolates, enol ethers, and enamines) [114].

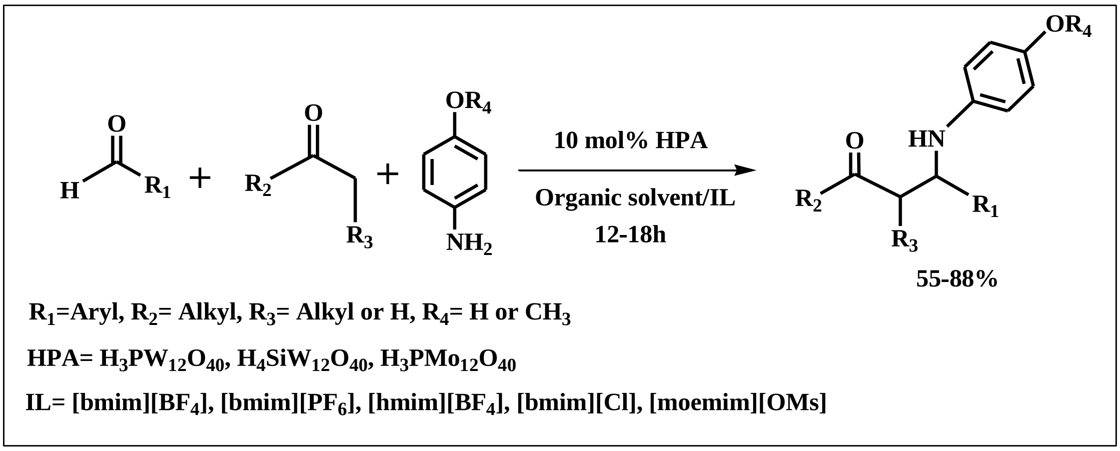
In 2014 Sreevalli *et al*. [83] reviewed greener routes of the Mannich/Mannich type reactions using solvent free method, water, supercritical CO_2, surfactant as media, ionic liquids, ultrasonication, microwave irradiation *etc.*

In concern with the use of ionic liquids as medium or catalyst, many publications have been found with incorporation of several greener components to this synthetic method [116]. As a reaction medium, some of the ionic liquids require use of additional catalyst to increase the productivity of desired compound as the ionic liquid itself is not enough to enhance the yield or it acts as solvent only. Most of them are neutral ionic liquids as they lack any acidic functionality and can be better used as medium than catalyst. Lee *et al.* [117] in 2002 reported the Mannich-type reaction of benzaldehyde, aniline and acetophenone trimethylsilyl enolate at 20^oC using 1 mol% of $Yb(OTf)_3$ in [bmim][PF_6] (**Scheme 2A.12**) with benzene as co-solvent.



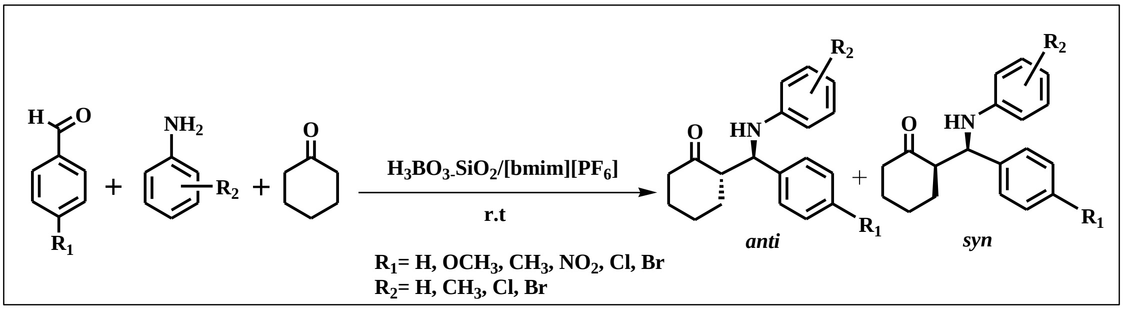
Scheme 2A.12: One-pot Mannich-type reaction catalyzed by Yb(OTf)$_3$ in ionic liquid

Use of solid heteropolyacids (HPAs) catalyst in ionic liquid for preparation of β-amino ketones was first reported by Rasalkar *et al.* in 2007 (**Scheme 2A.13**). The study was extended to various substrates using this optimized condition. The reaction was conducted for 12-18 h at room temperature [118].



Scheme 2A.13: HPA catalyzed Mannich reaction in ionic liquid

Kumar and his group in 2011, performed the Mannich reaction of aryl aldehydes using silica-supported boric acid as catalyst in 1-butyl-3-methylimidazolium hexafluorophosphate ([bmim][PF$_6$]) at mild condition for short reaction time (0.41-1 h) with excellent yields of diastereomeric mixture of β -amino carbonyl compounds (**Scheme 2A.14**) [119].



Scheme 2A.14: H$_3$BO$_3$–SiO$_2$/ionic liquid ([bmim][PF$_6$]) catalyzed Mannich reaction

Zhao *et.al* (2004) examined three Brönsted acidic ionic liquids (**Fig.2A.5a**) as reusable catalyst for preparation of Mannich base as shown in **Fig.2A.5b** at 25°C for 12 h to give moderate yield of the product [120].

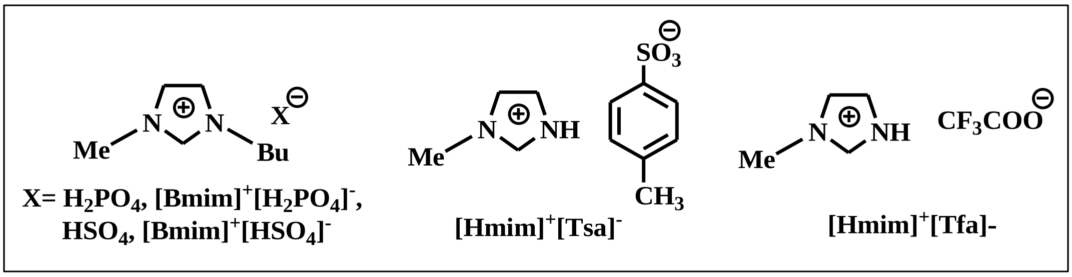


Fig.2A.5a: Structures of Brönsted acidic ionic liquids

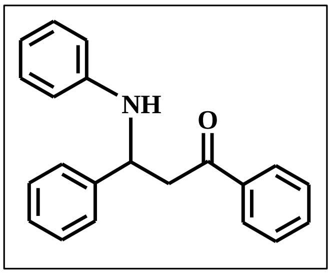


Fig.2A.5b: Structure of Mannich base

In the same year five ionic liquids 1, 1, 3, 3-tetramethylguanidinium-trifluoroacetate/perchlorate/trifluoromethylsulfonate/formate/lactate (**Fig.2A.6**) were examined as reaction media by Gao *et al.* in the Mannich reaction of benzaldehyde, aniline and acetophenone [121].

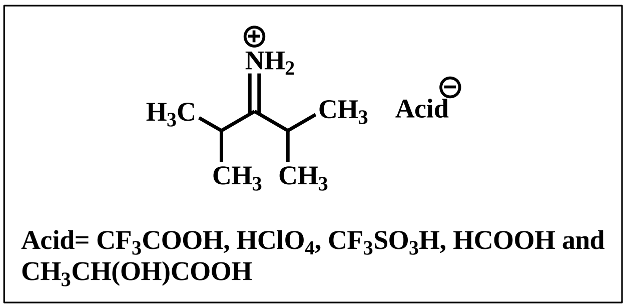


Fig.2A.6: Structure of 1, 1, 3, 3-tetramethylguanidinium based ILs

Li *et al.* (2005) used carboxyl-functionalized ionic liquid ([cmmim][BF_4]) (**Fig.2A.7**) in aqueous solution of [bmim][BF_4] for the three-component Mannich reaction of aromatic aldehyde, acetophenone and aniline for 10-15 h reaction at mild condition to give 77-92 % yield of product [122].

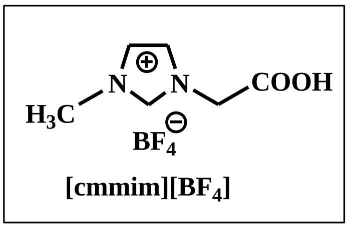


Fig.2A.7: Structure of Carboxyl functionalized IL

The use of -N alkylsulfonic functionalized imidazolium and phosphonium ILs (**Fig.2A.8**) as dual specific solvent/catalyst system in the preparation of Mannich base was studied by Sahoo and his co-workers in the year 2006 at room temperature within less time [123]. These two ILs were recycled for four runs.

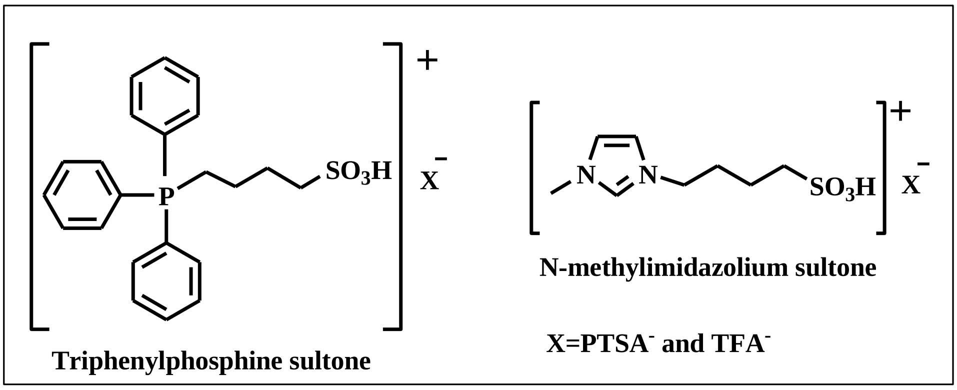


Fig.2A.8: Structures of –N alkylsulfonic functionalized imidazolium and phosphonium ILs

In the year 2007, Dong and his group conducted the Mannich reaction in water using catalytic amount of reusable N, N, N-trimethyl-N-butanesulfonic acid ammonium hydrogen sulfate [TMBSA][HSO_4] at normal temperature for 6-12 h to produce 71-93% of the β-amino carbonyl compound (**Fig.2A.9**) (**Scheme 2A.11**) [124].

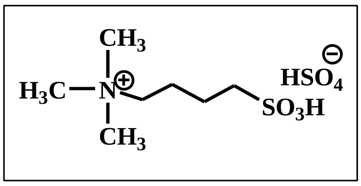


Fig.2A.9: Structure of [TMBSA][HSO_4] IL

They also used another Brönsted acidic IL catalyst 3-(N, N-dimethyldodecylammonium) propanesulfonic acid hydrogensulfate ([DDPA][HSO_4]) for the same reaction in water [125] (**Fig.2A.10**).

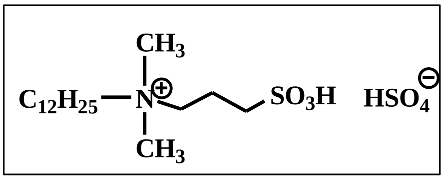
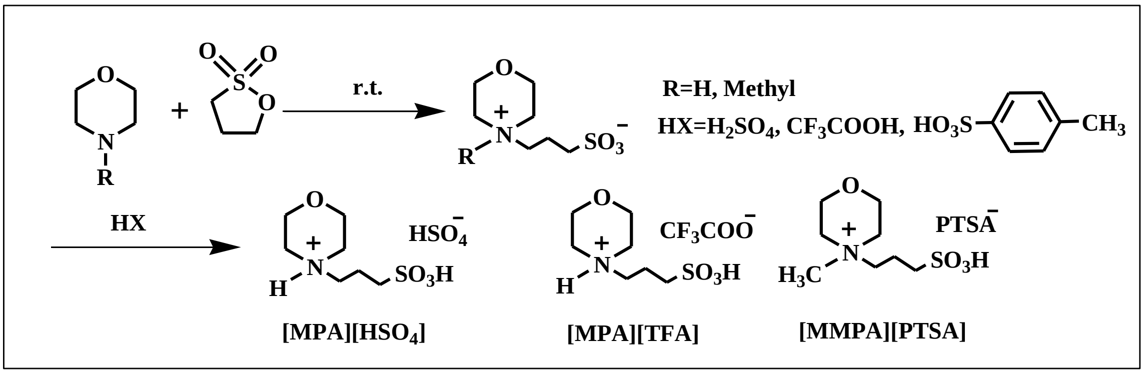


Fig.2A.10: Structure of [DDPA][HSO_4] IL

The first use of basic IL catalyst 1-butyl-3-methylimidazolium hydroxide ([bmim][OH] was reported by Gong *et al.* (2007) with a mixture of cyclohexanone, aromatic aldehydes, and aromatic amines in ethanol for 10 hour with high yields [126].

Yue (2010) utilized three recyclable N-alkanesulfonic acid functionalized morpholinium IL catalysts obtained from **Scheme 2A.15** for the Mannich reaction at room temperature stirring (**Scheme 2A.11**) within 1-6 h to give 62-93% yield of the Mannich product [127].



Scheme 2A.15: -SO_3H functionalized morpholinium ILs synthesized by Yue *et al.*

He *et al.* in 2014 [128] synthesized several geminal Brönsted acidic ILs (GBAILs) of quaternary ammonium cations of different chain length of alkyl substituents (**Fig.2A.11**) in combination with *p*-toluene sulfonate anion. Among them, GBAIL-C_{14} showed excellent catalytic activity for the water mediated Mannich reaction at 25°C and was reused for seven runs with retention of identical catalytic efficiencies.

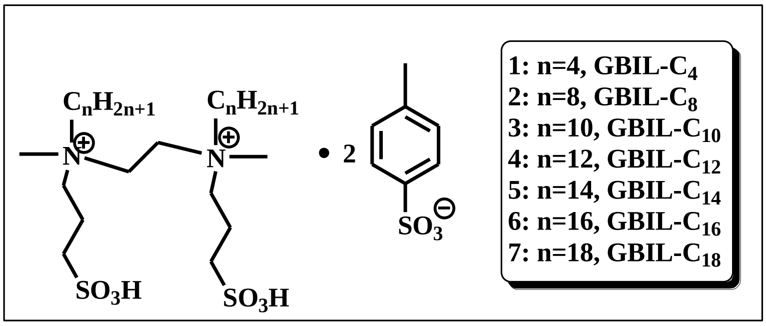


Fig.2A.11: Structure of geminal Brönsted acidic ILs (GBAILs)

Porkodi and his group in 2015 applied 1-propylimidazolium trifluroacetoacetate IL as reusable protic acidic catalyst for the title reaction at mild temperature in ethanol [129].

In the year 2017, Sardar *et al.* [130] employed four Brönsted acidic ionic liquids comprising of iodide and borate at room temperature (**Fig.2A.12**).

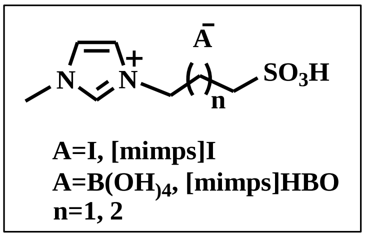


Fig.2A.12: 1-methyl-3-(3-sulfopropyl)-imidazolium ionic liquids

In 2014, Chang *et al.* synthesized Brönsted acid-surfactant combined catalysts (BASCs) functionalized (**Fig.2A.13**) with different acids which were applied in the three-component Mannich reaction of aldehyde, acetone and amine at 25°C in water. They studied the effect of cation length, recyclability and the acidity of the catalysts. Results indicated 3-(N, N-dimethyloctylammonium) propanesulfonic acid toluene sulfate ([DOPA][Tos]) as best catalyst due to formation of emulsion during reaction. They also synthesized [MPSIM][X] (where, X^- = Br, HSO_4, H_2PO_4, $C_7H_7SO_3$, CH_3SO_3), [BPSIM][Tos], [DOPA][Tos], [DOPA][HSO_4] and [DDPA][Tos] ionic liquids and assessed their catalytic ability in the reaction of benzaldehyde (1.0 mmol), aniline (1.0 mmol), cyclohexanone (1.0 mmol) in 1.5 mL water (**Scheme 2A.16**). Among the ionic liquids, [DOPA][Tos] displayed greater catalytic efficiency with 75-89% yield within 3-4.5 h reaction time [131].

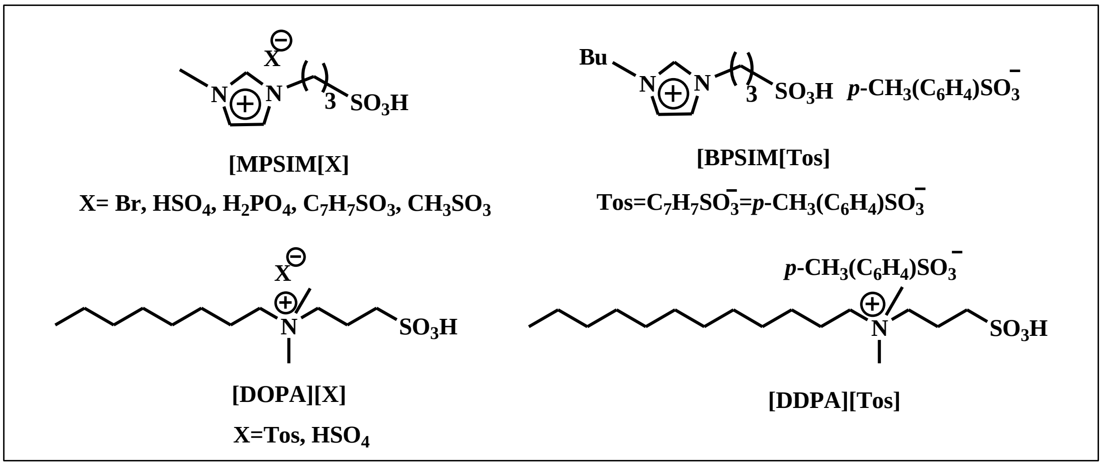
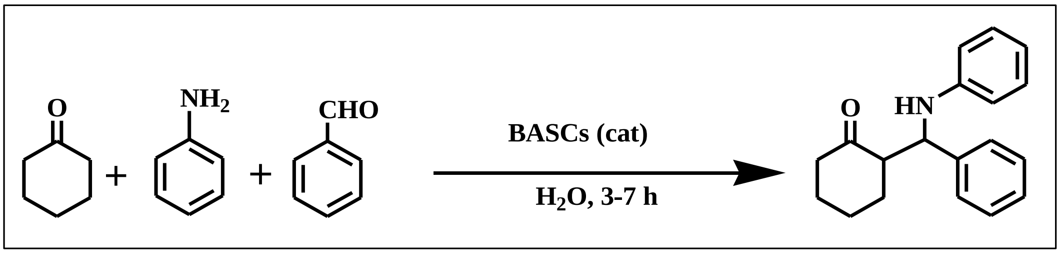


Fig.2A.13: Structures of –SO_3H functionalized surfactant based ionic liquids



Scheme 2A.16: Mannich reaction catalyzed by BASCs

A known task-specific Brönsted acidic catalytic system of 1-(3-sulfopropyl)-3-methylimidazolium hydrogen sulfate bearing an anion of heteropolyacid derivative ($[PW_{12}O_{40}]_3$) (**Fig.2A.14**) in $[BMI][NTf_2]$ ionic liquid was efficiently utilized by Alvim *et al.* (2014) for the three-component Mannich reaction of aryl aldehyde, aryl amine, and ketone at 30°C in 20 h (**Scheme 2A.17**) [132].

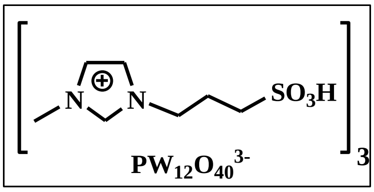
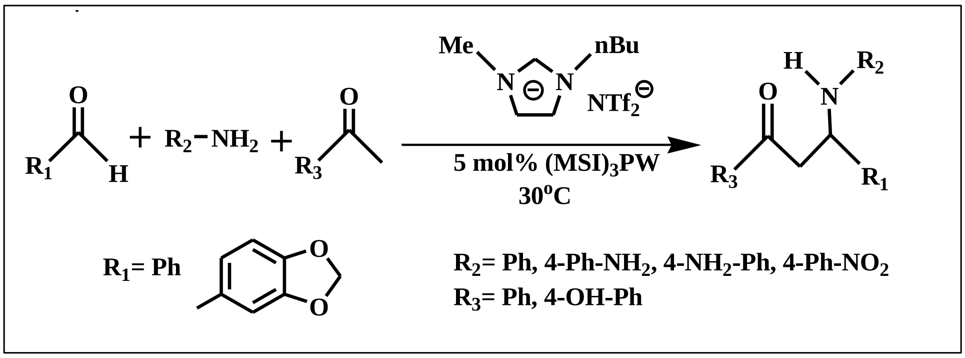


Fig.2A.14: Structure of MSI_3PW



Scheme 2A.17: Mannich reaction catalyzed by $(MSI)_3PW$ in $[BMI][NTf_2]$

Huan *et al.* (2016) designed a water tolerant Lewis-Brönsted dual acidic choline-based ionic liquid $[Ch\text{-}OSO_3H]Cl\cdot 2ZnCl_2$ and used as catalyst for the synthesis of (**Fig.2A.15**) β-amino carbonyl compounds. This biodegradable ionic liquid was easily recyclable up to 5 times with satisfactory yield [133].

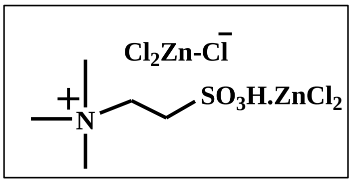


Fig.2A.15: Structure of $[Ch\text{-}OSO_3H]Cl\cdot 2ZnCl_2$

A large number of Brönsted-Lewis dual acidic ILs immobilized mesoporous silica material containing complex transition metal halide anions of Fe, Co, Sn and Ti metals were prepared by Wang *et al.* (2017). They investigated their catalytic performances as heterogeneous catalyst for direct Mannich reaction of aromatic aldehyde, aniline and substituted acetophenone in ethanol at room temperature within 1-4 h with 81-99% yields. Among them ILSO$_3$H-TiCl$_5$@Sn-MCM-41 was proved to be more stable and efficient recyclable catalyst for this reaction (**Fig.2A.16**) [134].

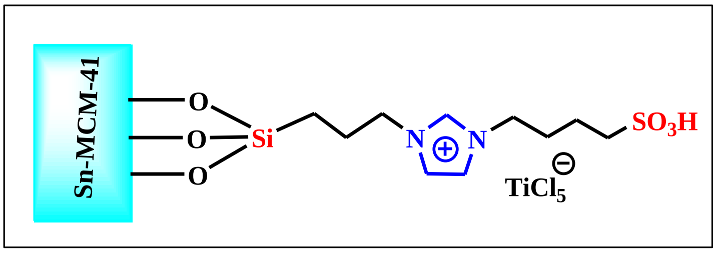


Fig.2A.16: Structure of ILSO$_3$H-TiCl$_5$@Sn-MCM-41 catalyst

Most of the Brönsted or Brönsted-Lewis acidic ionic liquids contain alkyl sulfonic groups in cation which contribute Brönsted acidity to the ionic liquids and serves as better catalyst or reaction media for the synthesis of β-amino carbonyl compounds. Above discussion clearly mentioned lack of report on the Mannich reaction using direct N-SO$_3$H functionalized chlorometallate as catalyst.

2B.1 Synthesis and characterization of the catalyst

The formation of three -SO_3H functionalized chlorometallates $[Dsim]_2[ZnCl_4]$, $[Dsim][FeCl_4]$, $[Dsim]_2[NiCl_4]$ was completed according to the reaction **Scheme 2A.9** included in **Section 2A**. The following characterization methods were utilized to determine their structures, thermal stability and Hammett acidity of the ionic salts to explore as efficient reusable heterogeneous catalysts for the Mannich-type reaction in ethanol at atmospheric condition (**Scheme 2A.10**).

FT-IR analysis

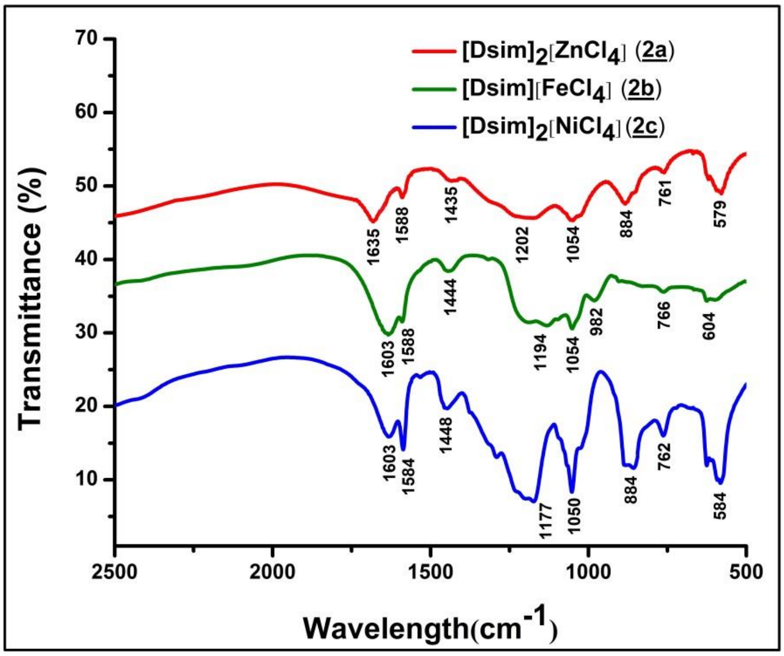


Fig.2B.1: FT-IR spectra of 1, 3- disulfoimidazolium chlorometallates

The assignments of various FT-IR bands of the acidic chlorometallates (**Fig.2B.1**) are summarized in **Table 2B.1**.

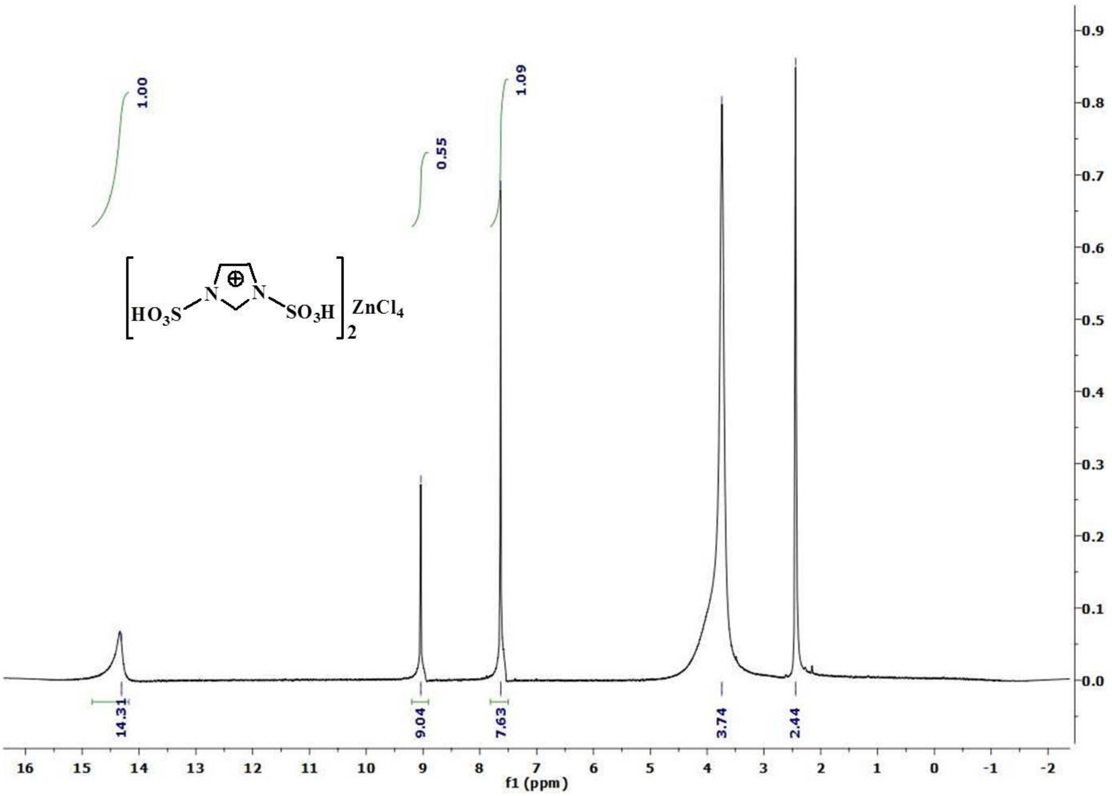
Table 2B.1: FT-IR assignments of the three ionic salts

FT-IR bands (cm^{-1})	Assignments
1603-1635	-C=C- stretching of imidazole unit
1584-1588	-C=N- stretching of imidazole unit
1177-1202	S-O symmetric vibration
1050-1054	S-O antisymmetric vibration
884-982	N-S stretching and in plane ring vibration
761-766	Out of plane ring bending of C-H bond
579-604	Bending vibration of –SO_3H groups

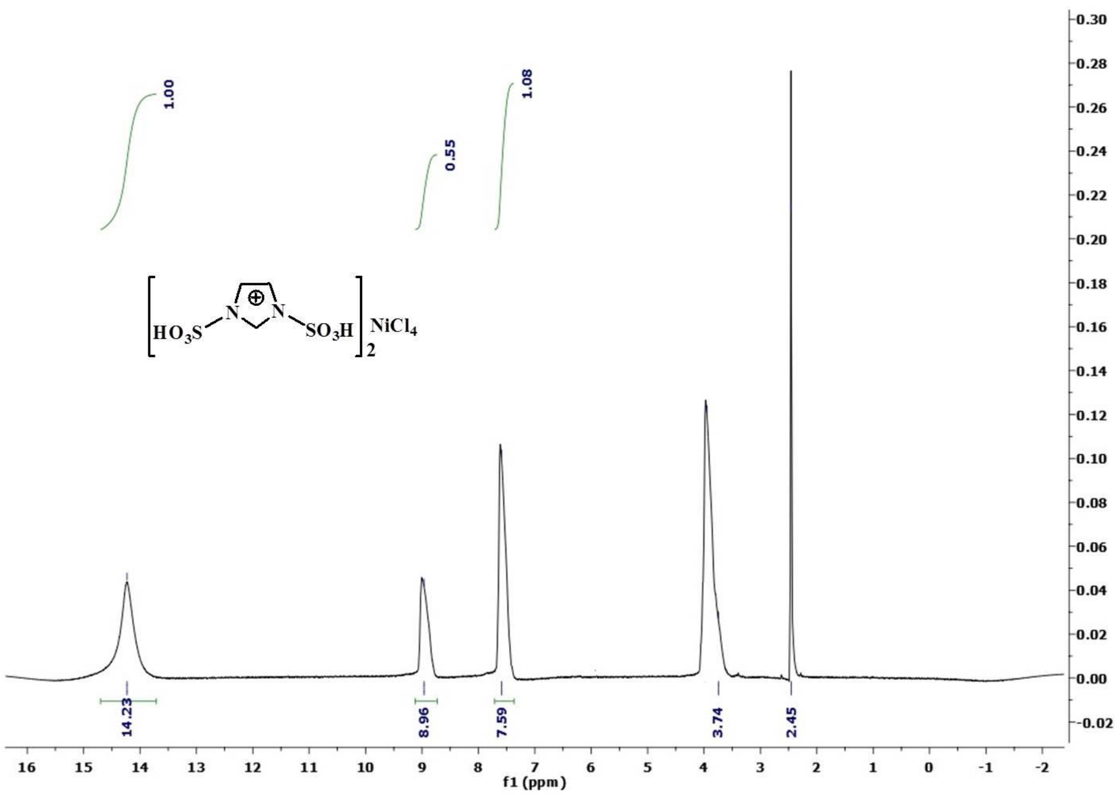
Beside these main assignments, the broad -OH peak of the three solids at 3386-3438 cm^{-1} expressed the involvement of two SO_3H groups in H-bonding [135, 136]. According to the reported literature the IR spectra of **2b** and **2c** in the region 400-200 cm^{-1} were characterized by the distinct metal-chloride vibration of $FeCl_4^-$ at 380 cm^{-1} and around 285 cm^{-1} for $NiCl_4^{2-}$ [41, 137]. **2a** did not display any characteristic absorption in this region.

NMR analysis

Presence of two $-SO_3H$ groups in imidazole unit was designated by the two proton singlet at 14.0-14.3 ppm in ^1H NMR spectra of 1, 3-disulfoimidazolium chlorometallates **2a** and **2c** (**Fig.2B.2**). Analysis of ^1H and ^{13}C NMR spectra of [Dsim][$FeCl_4$] were restricted due to the lower solubility of **2b** in DMSO-d_6. The characteristic signals of imidazole ring carbons were also present in the ^{13}C NMR spectra of **2a** and **2c** (**Fig.2B.3**).

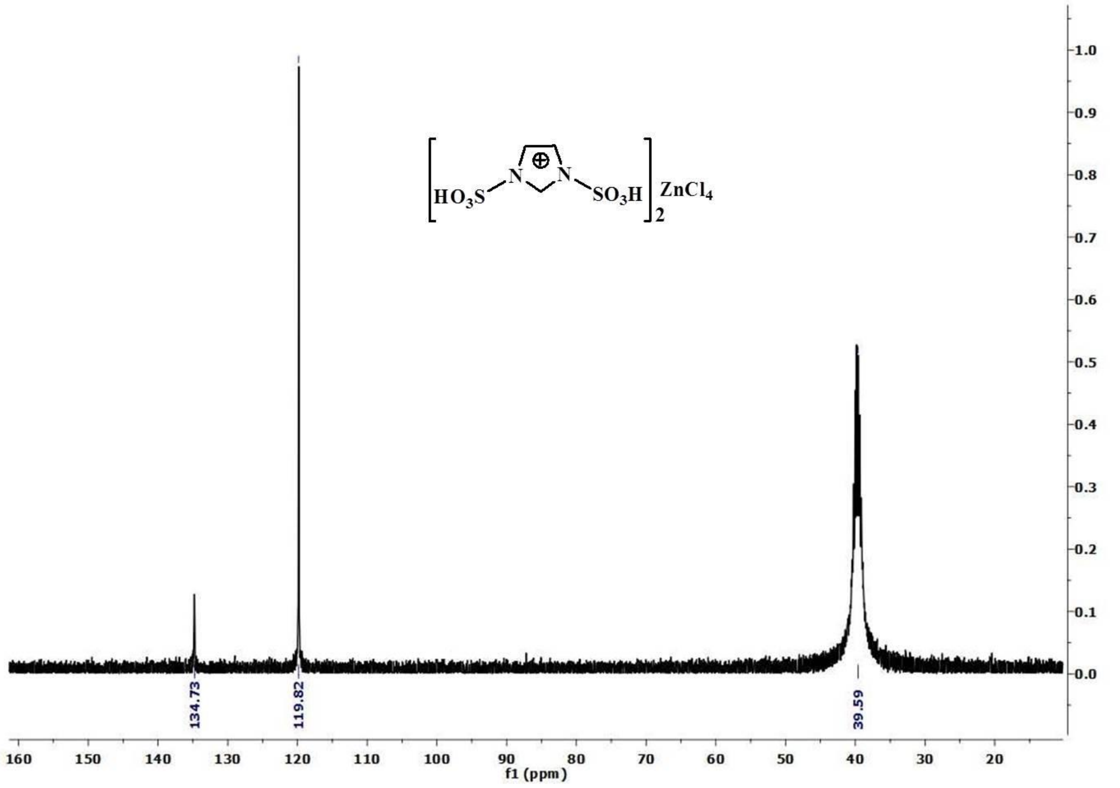


(a)

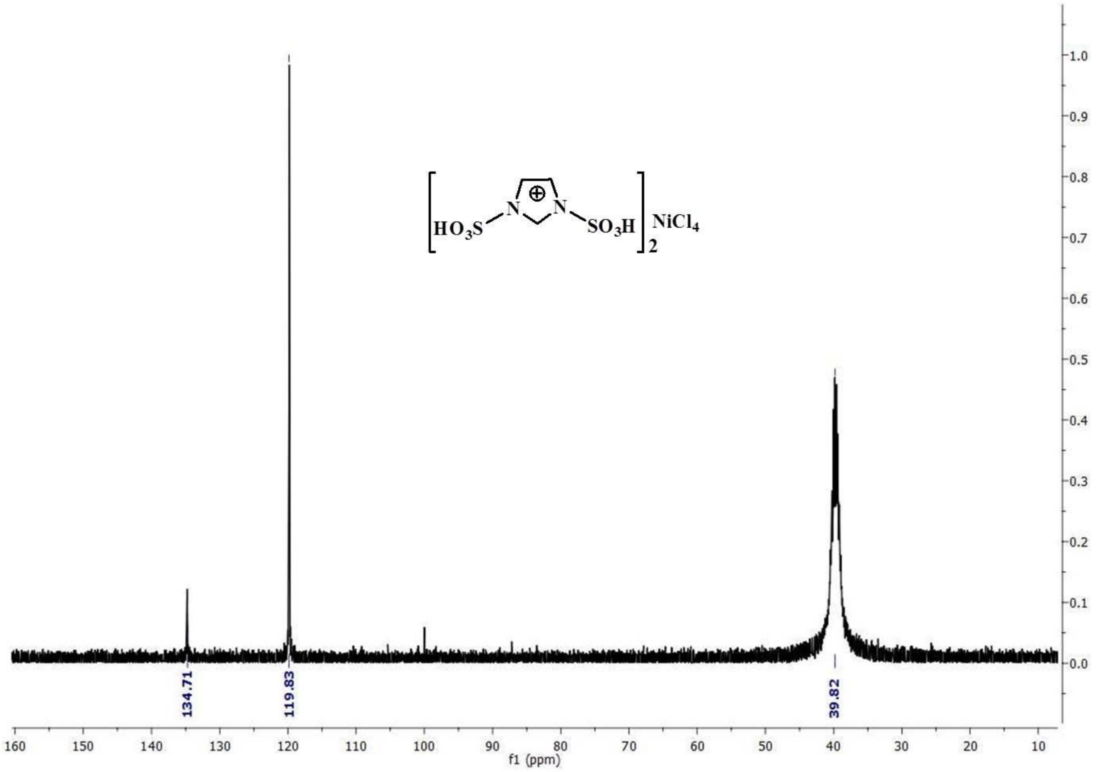


(b)

Fig.2B.2: ^{1}H NMR spectra of (a) **2a** and (b) **2c**



(a)



(b)

Fig.2B.3: ^{13}C NMR spectra of (a) <u>**2a**</u> and (b) <u>**2c**</u>

Elemental analysis

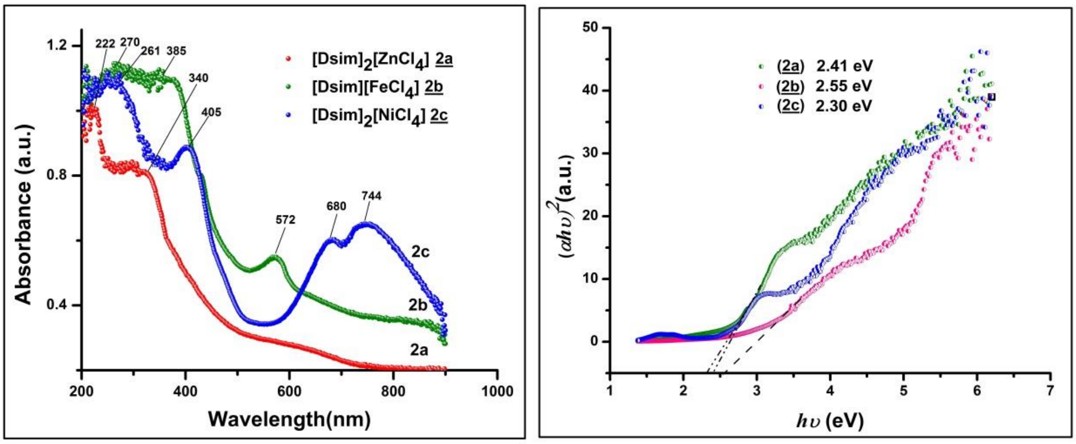
These solids were subjected to CHN analyses to determine the percentages of C, H and N present in 1, 3-disulfoimidazolium chlorometallates after treatment at 90^{o}C in vacuum oven for 3 h for removal of physisorbed water. 30 ppm solution of aqua regia was used to estimate the amount of metal content in each solid using Inductive Coupled Plasma (ICP) analysis. The obtained values were comparable with the original metal content in the respective ionic solid (**Table 2B.2**).

Table 2B.2: ICP analyses of the three disulfoimidazolium chlorometallates (<u>**2a**</u>-<u>**2c**</u>)

Entry	Catalysts	Metal analyzed	Metal amount (mg/L)		
			calculated	Experimental	
				Fresh	Used[a]
1	[Dsim]$_2$[ZnCl$_4$]	Zn	2.92	2.88	2.86
2	[Dsim][FeCl$_4$]	Fe	3.92	3.95	3.88
3	[Dsim]$_2$[NiCl$_4$]	Ni	2.65	2. 55	2.52

[a] Estimated after 3rd cycle of the catalytic Mannich-type reaction

UV-Visible diffuse reflectance spectra



(a) (b)

Fig.2B.4: (a) UV-visible absorbance spectra and (b) TAUC plot of **2a**, **2b** and **2c**

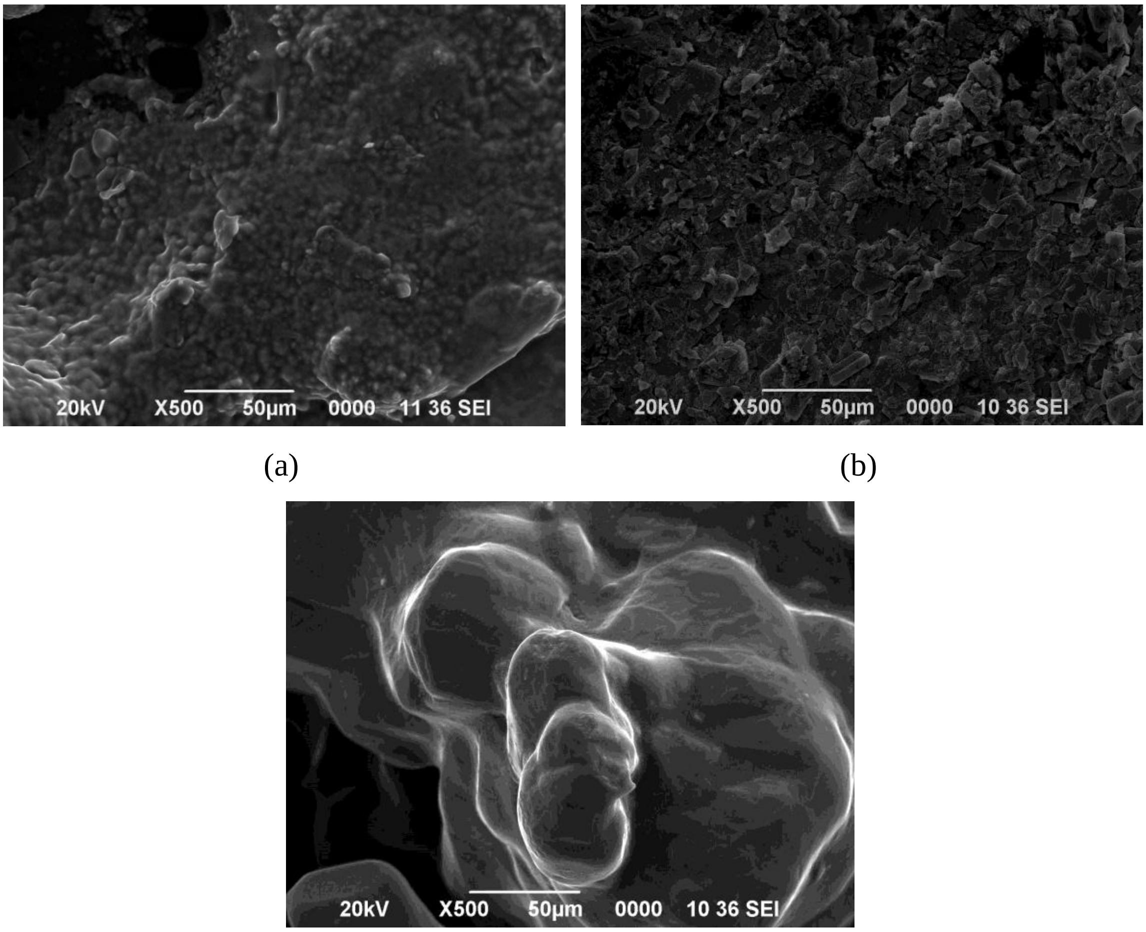
Fig.2B.4 showed different absorbance peaks for different chlorometallate anions of disulfoimidazolium ionic liquids. Intra-ligand charge transfer transition can be attributed to the absorbance at 222 nm and 340 nm in **2a** [138, 139]. For **2b**, peaks at 270 nm and 385 nm designate the ligand to metal charge (L → Fe (+3)) transfer transitions whereas other absorption band at 572 nm can be assumed as d-d characteristic transition of $FeCl_4^-$ [140-142]. The absorbance spectrum of **2c** exhibits two bands of almost equal intensity at 680 nm and 744 nm which can be considered as the tetrahedral moiety of $NiCl_4^{2-}$ as revealed by literature data [143]. On the basis of ligand field theory the band at 261 nm can also be assigned as L → M charge transfer transition for tetrahedral complexes. Also presence of the equilibrium mixture of a little mono and dichloro nickel species along with the $NiCl_4^{2-}$ complex can be established by the peak at 405 nm [144]. The UV-visible analysis gave us a clarified anionic speciation of the three materials which further provided a chance to evaluate semiconducting properties of these materials by calculation of optical band gaps using Tauc plot (**Equation 2B.1**). The Tauc relation (**Equation 2B.1**) can estimate optical band gap of systems under investigation validating the usual meaning of the symbols [145].

$$\alpha h\nu \propto (h\nu - Eg)^n$$ (**Equation 2B.1**)

Where, α is the absorption coefficient, $h\nu$ is the photon energy and Eg is the optical band gap for indirect transitions ($n = 2$) or direct transitions ($n = 1/2$). Considering all transitions are direct, and allowed type ($n = 1/2$), the estimated Eg values from the intercepts of plot **Fig.2B.4(b)** $h\nu$ vs $(\alpha h\nu)^2$ are found to be 2.55, 2.41 and 2.30 eV for **2a**,

2b and **2c** respectively. Thus the three solid compounds bearing significant band gap values similar to that of semiconductors firmly indicate their importance.

SEM analysis



(a) (b)

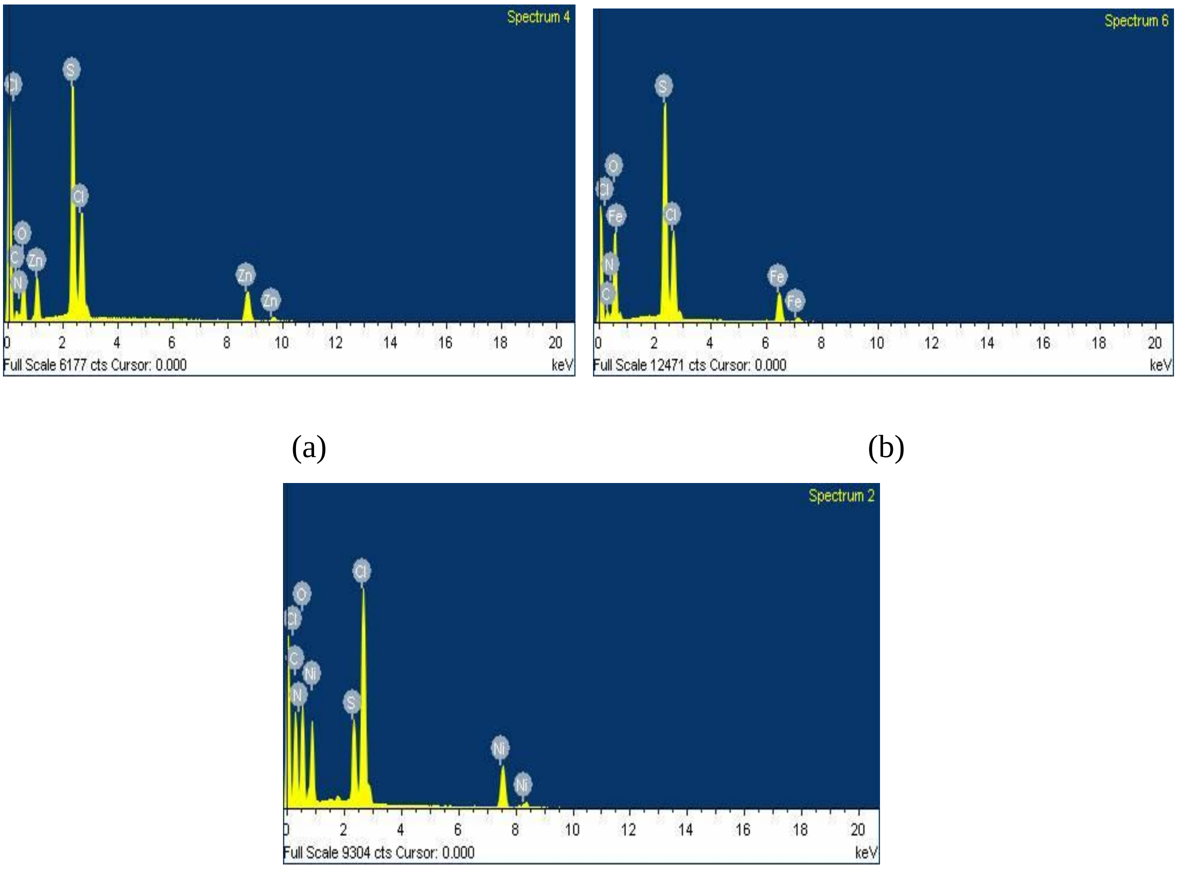
(c)

Fig.2B.5: SEM images of (a) $[Dsim]_2[ZnCl_4]$, (b) $[Dsim][FeCl_4]$ and (c) $[Dsim]_2[NiCl_4]$

Fig.2B.5 indicated some cracks and deformities on the surfaces of the three organochlorometallates. The surface morphology analysis portrayed the variations of structural arrangement in **2a**-**2c** based on the nature of transition metal chlorides. The gloomy surface of **2a** in **(a)** expresses the poor particle visibility while **(b)** displays contorted surface with existence of some solid particles. **2c** demonstrates a surface **(c)** with fused particles. These discontinuities in surface behavior may be accounted for the moisture sensitivity of the catalysts.

EDX analysis

Energy dispersion X-ray (EDX) analysis confirmed the presence of respective metal chloride along with other constituent elements of disulfoimidazolium metal chlorides as shown in **Fig.2B.6**.



(a) (b)

(c)

Fig.2B.6: EDX images of (a) $[Dsim]_2[ZnCl_4]$, (b) $[Dsim][FeCl_4]$ and (c) $[Dsim]_2[NiCl_4]$

TGA analysis

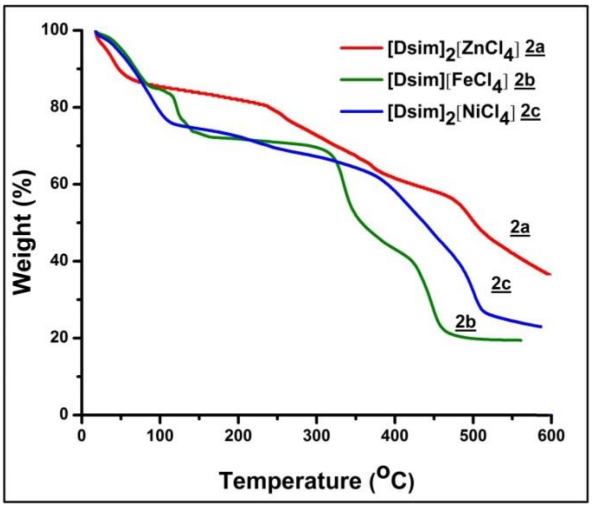


Fig.2B.7: TGA curves of the three ionic solids

Thermo gravimetric analysis of the three materials depicted stepwise decomposition of the chlorometallates (**Fig.2B.7**). The TGA curve for $[Dsim]_2[ZnCl_4]$ showed two step decomposition involving initial 12% weight loss below 100^oC which can be assigned for physisorbed water followed by another decomposition at 250^oC. The TGA analysis of $[Dsim][FeCl_4]$ salt expressed 14% weight loss due to absorbed moisture at 90^oC and a total of 25% weight loss producing two breaks around 125^oC and 310^oC respectively. Three step decomposition was observed for $[Dsim]_2[NiCl_4]$ around 100^oC, 220^oC and 400^oC with total weight loss of 45% which includes 25% of moisture from the ionic salt. The TGA graph displayed decomposition of each material above 100^oC which can be attributed to stepwise losing of two SO_3H groups present in the imidazolium cation by interaction with chlorometallate anion. Analysis of the curves also indicates the presence of certain amount of non-volatile residue which may be accounted for metal chlorides of the respective salts. Among the three metal salts, $[Dsim]_2[ZnCl_4]$ was found to be more thermally stable (up to 250^oC) than other two.

Powder X-ray diffraction analysis

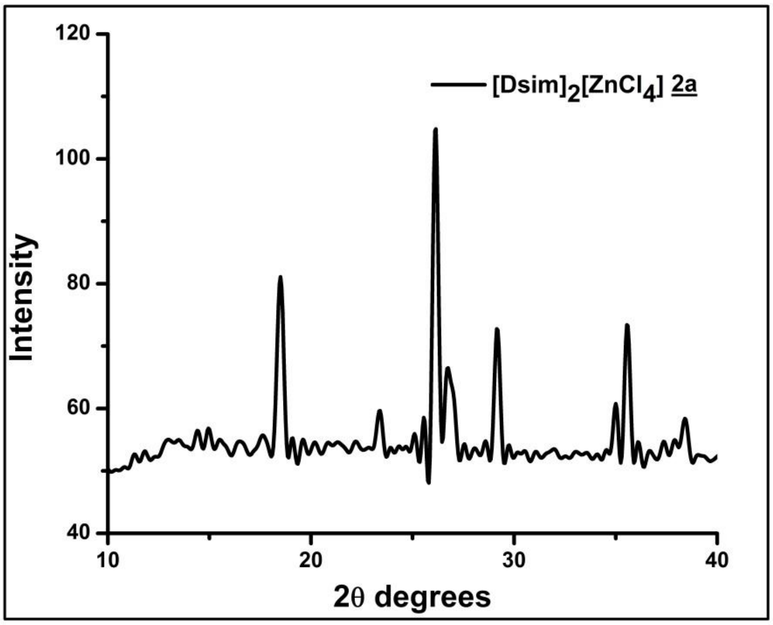


Fig.2B.8: Powder XRD pattern of **2a**

Fig.2B.8 represents the powder XRD pattern of **2a**. The peaks observed at 2θ = 16.6, 25.5, 29.4 and 34.9^o were defined as the characteristic XRD diffraction peaks of $ZnCl_2$ in $[Dsim]_2[ZnCl_4]$ and the XRD database (JCPDS card no. 74-0517) corresponding to (0 0 2), (1 0 1), (1 0 2) and (1 0 3) reflection planes matched the same. On the other hand, powder XRD analyses of $[Dsim][FeCl_4]$ and $[Dsim]_2[NiCl_4]$ could not produce the actual pattern which may be reasoned as the strong hygroscopic character of these two solids as observed from the TGA graph (**Fig.2B.7**).

Raman analysis

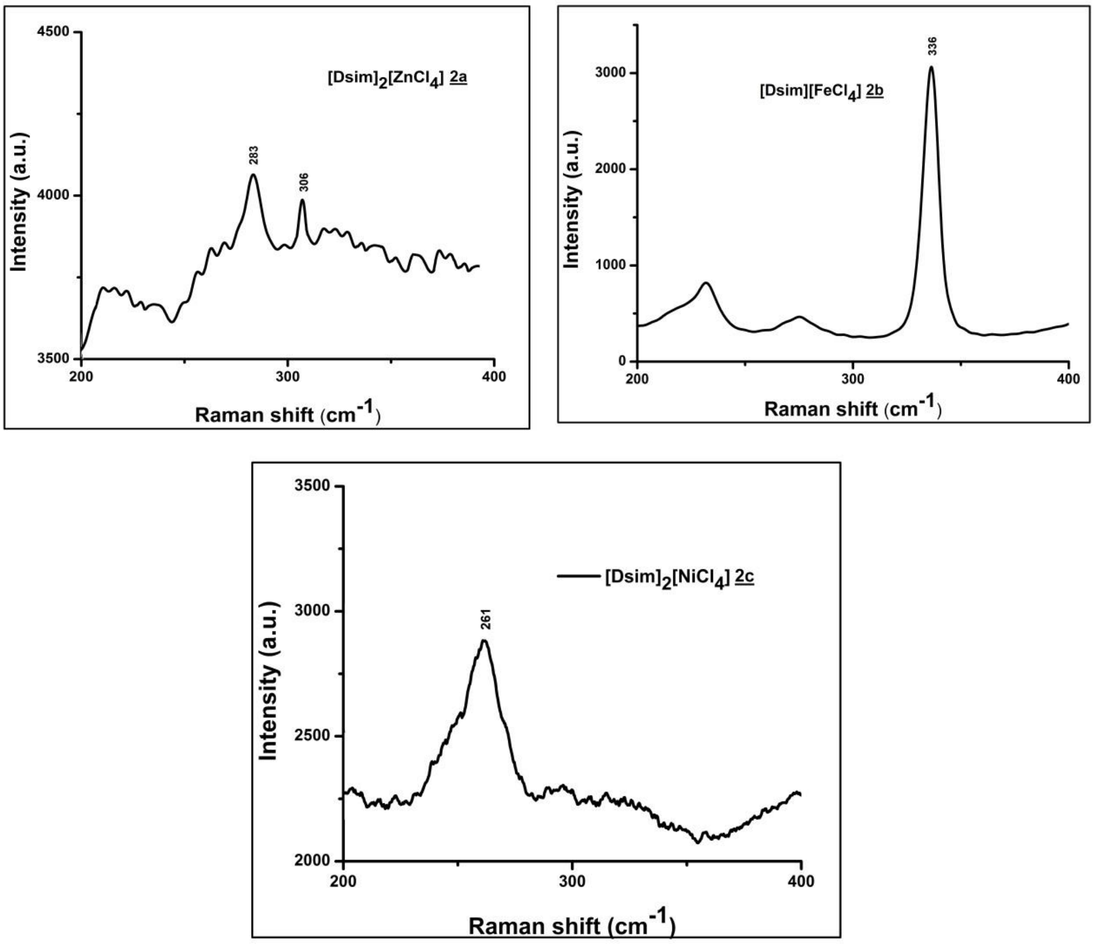


Fig.2B.9: Raman spectra of **2a**, **2b** and **2c**

The strong peak at 283 cm^{-1} and the medium peak at 306 cm^{-1} in the Raman spectra (**Fig.2B.9**) of **2a** can be assigned to the mixture of major amount of $ZnCl_4^{2-}$ and minor amount of dimeric $Zn_3Cl_6^{2-}$ unit [26, 146]. There is no experimental evidence found till date in support of the existence of $ZnCl_3^{-}$ in either solid or liquid state. A strong peak at 336 cm^{-1} in Raman spectrum of **2b** can be referred to the literature value for tetrahedral $FeCl_4^{-}$ species which confirmed the presence of this chlorometallate anion [147]. Also, the characteristic peak at 261 cm^{-1} for $NiCl_4^{2-}$ justifies the presence of chloronickellate species in the Raman spectrum of **2c** (**Fig.2B.9**) [148].

Hammett acidity measurement

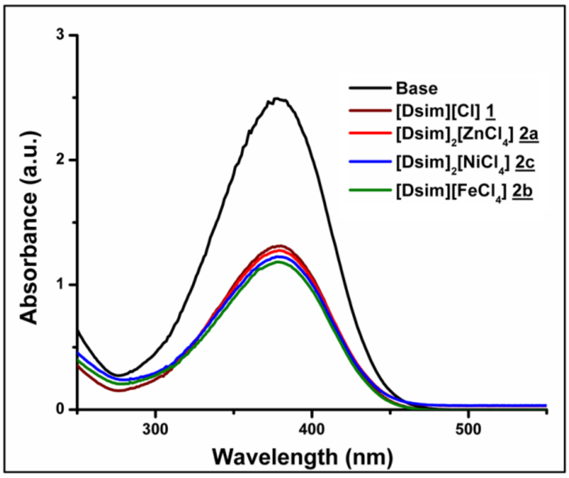


Fig.2B.10: Hammett plot for three ionic salts in ethanol

Hammett acidity function H◦ was obtained from the Hammett plot (**Fig.2B.10**) by measuring the absorbance of the three ionic chlorometallates with respect to the parent ionic liquid [Dsim][Cl] in ethanol on a UV-visible spectrophotometer using 4-nitroaniline as basic indicator (λ_{max} = 378 nm) [149, 150]. The decreasing Brönsted acidity order of the three solid acids with respect to their observed H◦ (**Table 2B.3**) values was as: [Dsim][$FeCl_4$]>[Dsim]$_2$[$NiCl_4$]>[Dsim]$_2$[$ZnCl_4$]>[Dsim][Cl]. This acidity order was further confirmed from the catalytic behavior of these acidic salts as heterogeneous catalyst in the synthesis of β-amino carbonyl compounds.

Table 2B.3: Hammett acidity function H◦ of **2a**-**2c**

Entry	IL	Amax	[I]%	[IH$^+$]%	H^o
1	-	2.493	100	0	-
2	[Dsim][Cl]	1.325	53.1	46.9	1.0439
3	[Dsim]$_2$[$ZnCl_4$]	1.276	51.2	48.8	1.0107
4	[Dsim][$FeCl_4$]	1.183	47.4	52.6	0.9447
5	[Dsim]$_2$[$NiCl_4$]	1.225	49.1	50.9	0.9741

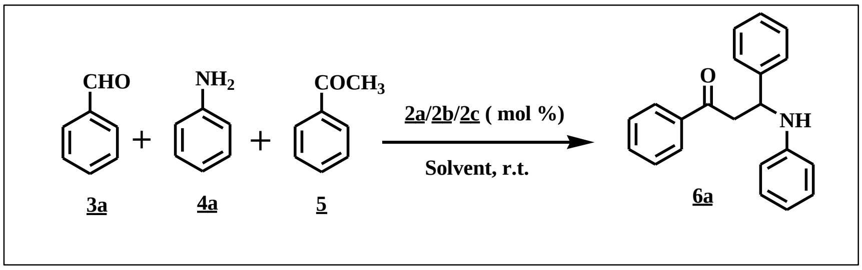
Leaching test

The leaching test of the three salts was performed in various solvents such as absolute EtOH, H_2O, CH_2Cl_2 and EtOAc *etc*. Equal amount of **2a**, **2b** and **2c** (20 mg) was stirred separately in 5 mL solvent for 2.5 h at room temperature and then filtered to measure the pH of the filtrate. This test results neutral character of EtOH, CH_2Cl_2 and EtOAc solution except in case of H_2O (pH = 1-2).

2B.2 Catalytic study

The three multi-functionalized acidic salts were investigated as heterogeneous catalyst for the three component Mannich-type synthesis of β-amino ketones involving room temperature stirring of acetophenone (1 mmol), benzaldehyde (1 mmol) and aniline (1 mmol) in ethanol. Optimization of the catalyst amount utilizing 5, 10 and 20 mol% of each solid acid (**Table 2B.4**, entries 1-3) perceived that only 5 mol% of the each solid catalyst could be preferable to produce 85-94% yield of **6a** within 45-80 min under mild condition. The acidity order of three catalysts as observed from the Hammett plot strictly followed the same order in terms of activity for the preparation of **6a** in **Table 2B.4** using 5 mol% of each catalyst in ethanol in terms of reaction time (**Table 2B.4**, entries 1-3). Apart from EtOH, 5 mol% of each of the catalysts showed similar type of catalytic activity in dichloromethane and ethyl acetate at room temperature stirring (**Table 2B.4**, entries 4-5). Literature mentioned some quick disadvantages of this one pot reaction as its sensitivity towards temperature led to further decomposition of β-amino ketones into side products in presence of acid catalyst [132, 151, 152]. Therefore, low temperature methodology is highly desirable for this reaction and hence we optimized the reaction condition at ambient temperature to achieve the same. The model reaction was extended to one -SO_3H group bearing 3-methyl-1-sulfonic acid imidazolium transition metal chlorides [Msim][X] (where X = $[ZnCl_3]^-$, $[FeCl_4]^-$) by using 5 mol% of these solid acid in ethanol at ambient condition which proved the better catalytic efficiency of disulfonic analogues **2a** and **2b** (**Table 2B.4**, entry-6) [23]. The enhancement in activity of three catalytic systems bearing two –SO_3H groups attached to imidazolium cation (**2a**, **2b** and **2c**) was also clearly understood by performing the above synthesis with 5 mol% of 1-butyl-3-methylimidazolium chlorometallates $[BMIm]_n[X]$ (n = 2 and 1; [X] = $[ZnCl_4]^{2-}$, $[FeCl_4]^-$, $[NiCl_4]^{2-}$) at room temperature stirring for 3-4 h to afford 65-75% yields of **6a** (**Table 2B.4**, entry 7) [143, 153, 154]. Also catalytic activity of other disulfonic analogues such as 1, 3-disulfoimidazolium chloride and carboxylate ILs without metal center [Dsim][X] ([X] = Cl^-, CF_3COO^-, CCl_3COO^-) were tested for comparison with the disulfonic chlorometallates **2a**, **2b** and **2c** (**Table 2B.4**, entry 8) [155]. Optimization study concluded that the hygroscopic nature of **2b** and **2c** didn't affect the overall efficacy of the catalysts. After that the optimized condition was successfully utilized in substrate scope study to synthesize various β-amino ketone derivatives (**Table 2B.5**).

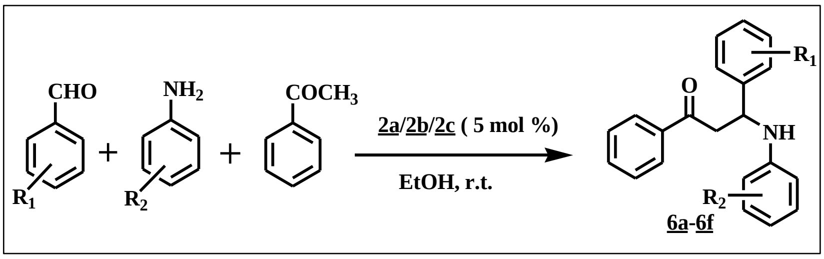
Table 2B.4: Optimization of the catalyst amount for the preparation of β-amino ketone derivative at room temperature

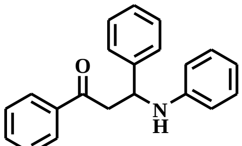
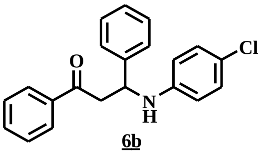
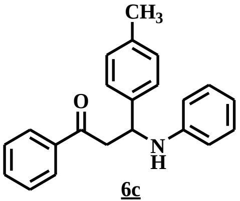
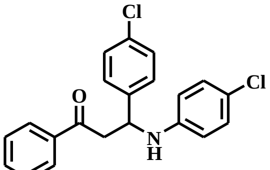
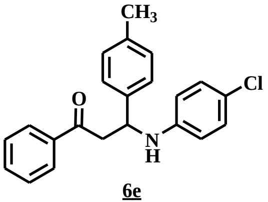


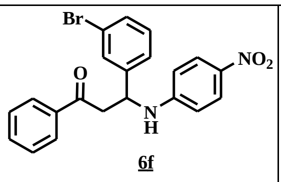
Entry	Catalyst	Amount (mol%)	Time (min)	Yield %[a] **6a**
1	$[Dsim]_2[ZnCl_4]$ **2a**	5/10/20[a]	80/60/45	85/91/90
2	$[Dsim][FeCl_4]$ **2b**	5/10/20[a]	45/30/15	94/95/97
3	$[Dsim]_2[NiCl_4]$ **2c**	5/10/20[a]	60/45/30	90/91/95
4	**2a**/**2b**/**2c**	5[b]	1.5h/50/60	83/92/87
5	**2a**/**2b**/**2c**	5[c]	1.5h/50/60	84/90/85
6	$[Msim][ZnCl_3]/[Msim][FeCl_4]$	5[a]	2h/80	80/86
7	$[BMIm]_2[ZnCl_4]/[BMIm][FeCl_4]$ $/[BMIm]_2[NiCl_4]$	5[a,d]	4 h/3 h/3.5 h	65/75/73
8	$[Dsim][Cl]/[Dsim][CF_3COO]/$ $[Dsim][CCl_3COO]/$	5[a,e]	2.5 h/80/2 h	82/87/85

[a] Using 1 mmol of acetophenone, 1 mmol of benzaldehyde and 1 mmol of aniline in ethanol; [b] Reaction was performed in CH_2Cl_2; [c] Reaction was conducted in EtOAc; [d] The three catalysts (entry 7) were prepared using the standard literature procedure [143, 153, 154]; [e] Other three 1, 3-disulfoimidazolium catalysts (entry 8) were synthesized by the reported procedure [155].

Table 2B.5: Substrate scope study using **2a**, **2b** and **2c** as catalysts

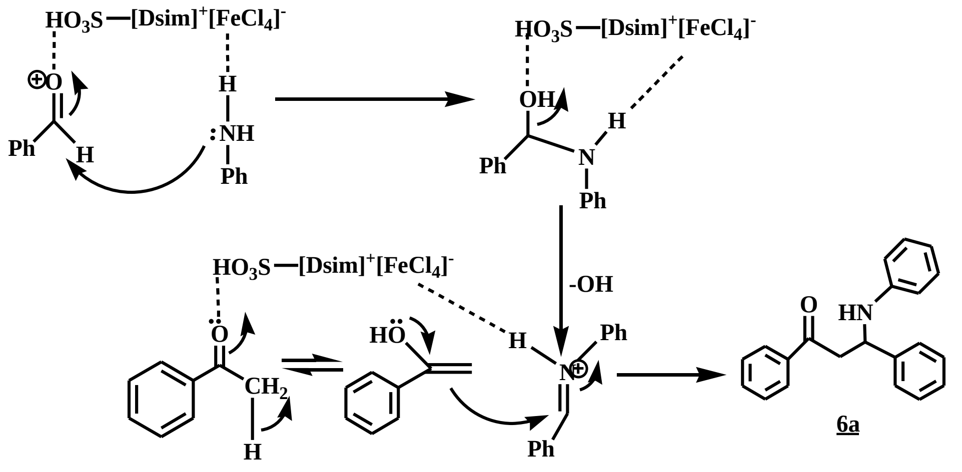


Entry	R_1	R_2	Product	Time [a] (min) **2a/2b/2c**	Yield[b] % **6(a-f)**	Mp. (°C) found	Mp. (°C) reported
1	H	H	 **6a**	80/45/60	85/94/90	159-161.8	165-167 [129]
2	H	4-Cl	 **6b**	70/45/55	88/95/92	161.1-165.7	170-171 [92]
3	4-CH_3	H	 **6c**	1.5h/1h/1.5	82/85/85	127.2-132.5	134-135 [92]
4	4-Cl	4-Cl	 **6d**	70/30/50	90/96/91	121.4-122.8	114-119 [92]
5	4-CH_3	4-Cl	 **6e**	80/50/60	84/95/90	159.2-160.9	163-165 [129]

6	3-Br	4-NO_2	 **6f**	1.5h/50/1h	82/88/85	130.5-134.3	130-132 [129]

^{a}Method using 5 mol% of **2a**/**2b**/**2c** as catalyst in ethanol (5 mL); ^{b} Isolated yields

Plausible mechanism



Scheme 2B.1: Plausible mechanism of -SO_3H bearing IL catalyzed Mannich-type reaction

The possible mechanism of $[Dsim][FeCl_4]$ catalyzed three component synthesis of β-amino ketone derivative can be described as the interaction of aldehyde functionality with -SO_3H group of chlorometallate catalyst followed by nucleophilic attack with $[FeCl_4]^-$ activated amino group of aniline according to **Scheme 2B.1**.

Reusability test of catalysts

Reusability of the three catalysts was determined by performing the model reaction taken for optimization study in 5 mmol scale in ethanol. Dichloromethane was added to the reaction mixture after evaporation of ethanol upon completion of the reaction. Catalysts can be easily recycled as solid residue from the organic layer of reaction mixture in CH_2Cl_2 by filtration which was suitable for further use. **Fig.2B.11** represents the reusability profile of each catalyst for three consecutive runs. Retention of appreciable catalytic activity is noted for all the three catalysts after recycle. Finally, ICP-OES analysis was done for the spent catalysts to describe the catalytic activity up to three runs (**Table 2B.2**) which presented the similar amount of metal content as the fresh ones.

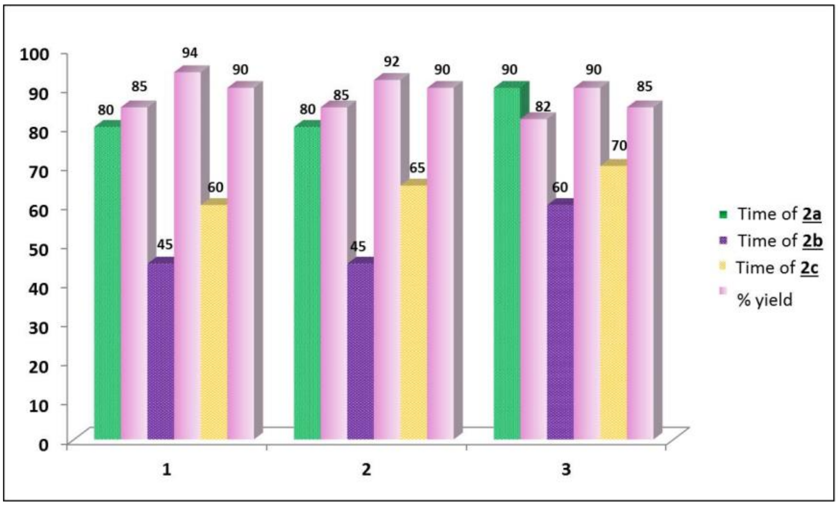


Fig.2B.11: Bar diagram for recyclability of catalysts

2B.3 Conclusion

In this study, a new series of -SO_3H functionalized imidazolium chlorometallate ionic salt systems: [Dsim][$FeCl_4$] and [Dsim]$_2$[X], where X = $ZnCl_4^{2-}$ and $NiCl_4^{2-}$ was developed and fully characterized by various analytical techniques such as NMR, FT-IR, Raman, UV-visible, PXRD, SEM-EDX, ICP-OES, TGA, CHN *etc.* The solid ionic systems were screened for their anionic speciation *via* electronic spectroscopy and Raman analysis. Band gap values calculated from the Tauc plot established all the three systems as semiconductor material with low band gap energies. Enhanced acidity and the thermal stability of these systems satisfactorily employed them as catalysts for the synthesis of β-amino carbonyl compounds. Besides this, easy recyclability and reusability of the catalysts up to three consecutive cycles make it relevant for further consideration. This study summarized that the presence of functionalized imidazolium cation in imidazolium chlorometallate systems played a major role in determining the behavior of these solids in conjunction to the chlorometallate anions. Both the -SO_3H functionalized cation and the transition metal chloride anionic part of the systems open the possibility of an easy and considerable tunability of these materials for future prospects.

2B.4 Experimental section

General techniques

All the reagents were purchased from Merck and used without any further treatment. The known 3-methyl-1-sulfonic acid imidazolium transition metal chlorides [Msim][X] (where X = $[ZnCl_3]^-$, $[FeCl_4]^-$) and 1-butyl-3-methylimidazolium chlorometallates [BMIm]$_n$[X] (n = 2 and 1; [X] = $[ZnCl_4]^{2-}$, $[FeCl_4]^-$, $[NiCl_4]^{2-}$) were synthesized using the standard procedure available in literature [13, 22-24]. All the analytical procedures and the instruments related to them are summarized in **Table 2B.6**.

Table 2B.6: Analysis and instruments

Analysis	Instrument and specification
FTIR	Nicolet Impact-410 spectrophotometer
^{1}H and ^{13}C NMR	JEOL 400 MHz spectrophotometer (δ in ppm) in DMSO-d_6 and $CDCl_3$
Hammett acidity	UV 2550 spectrophotometer
TGA	Shimadzu TGA-50
Scanning electron microscopy & EDX	JEOL JSM–6390LV SEM, equipped with energy dispersive X–ray analyzer (EDX)
Raman	Horiba LabRAM HR spectrophotometer equipped with a He-Ne laser of excitation wavelength of 514.5 nm
Powder X-ray diffraction	Rigaku Multiflex instruments using a nickel filtered CuKα (0.15418 nm) radiation source and scintillation counter detector
UV-Vis diffuse reflectance	UV 2450, Shimadzu spectrophotometer
ICP-OES	ICP-OES Perkin Elmer Optima 2100DV
Melting point	Büchi–560

Preparation of 1, 3-disulfoimidazolium chlorometallates [Dsim][$FeCl_4$] and [Dsim]$_2$[X] (2a-2c), where X^- = [$ZnCl_4$]$^{2-}$, [$NiCl_4$]$^{2-}$

The synthesis of three 1, 3-disulfoimidazolium chlorometallates utilized two step reaction procedure (**Scheme 2A.9**, **Section 2A**). The first step involved dropwise addition of chlorosulfonic acid (20 mmol) to a stirred solution of imidazole (10 mmol) in dry CH_2Cl_2 (30 mL) at 0°C within a period of 5 min under nitrogen atmosphere in a 100 mL round bottom flask. After one hour of stirring formation of 1, 3-disulfoimidazolium chloride [Dsim][Cl] was observed as appearance of viscous ionic liquid layer insoluble in dichloromethane. The viscous layer was then washed three times with dry CH_2Cl_2 (3×20 mL) by decantation of dichloromethane solution. The liquid residue was dried under vacuum which produced 98% pale yellow viscous oil of [Dsim][Cl]. The 2nd step was performed by mixing of certain mole fractions of respective metal chlorides with the [Dsim][Cl]. Calculated mole fractions of $ZnCl_2$, $FeCl_3$, and $NiCl_2$ in their respective reaction mixture with [Dsim]Cl were 0.33 for $ZnCl_2$ (**2a**), 0.5 for $FeCl_3$ (**2b**) and 0.33 for $NiCl_2$ (**2c**) [27]. As for example, 0.5 mol fraction of $FeCl_3$ (1.62 g, 10 mmol) was added into [Dsim][Cl] (2.67 g, 10 mmol) and stirred at 60°C in an oil bath for 2 hour to synthesize **2b**. The solid chlorometallate salts were washed with dry CH_2Cl_2 (2x5 mL) and then dried in vacuum oven at 80°C to get 96-97% yields of **2a**-**2c**. Finally they were kept in vacuum desiccator to prevent any decomposition due to moisture sensitivity. Observation of melting point up to 400°C in Büchi-560 melting point apparatus did not show the complete melting to liquid state but displayed a colour change in to black or brown from their initial colour. It can be interpreted as breaking of their composition at high temperature as shown by TGA analysis (**Fig.2B.7**).

Procedure for Hammett acidity calculation

The procedure for Hammett acidity calculation involved mixing of equal concentration of 4-nitroaniline (5 mg/L, p*K*a = 0.99) and the solid acid (5 mmol/L) in ethanol solution. The absorbance of 4-nitroaniline decreases as the acidity of ionic salts increases due to protonation of the indicator $[HI]^+$ in ethanol solution. The ratio of $[I]/[IH^+]$ can be obtained from the absorption differences and $pK(I)_{aq}$ represents the p*K*a value of the indicator referred to an aqueous solution. **Equation 2B.2** gives us the H◦ values of respective chlorometallates.

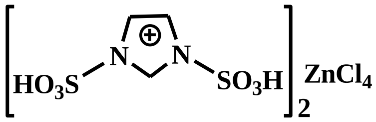
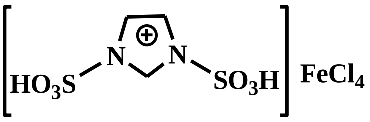
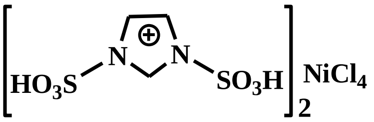
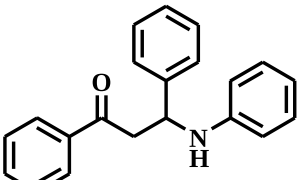
$$H_\circ = pK(I)aq + \log[I]/[IH^+] \qquad (\textbf{Equation 2B.2})$$

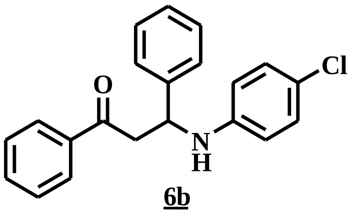
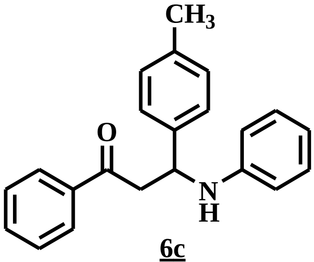
Typical procedure for the synthesis of β-amino carbonyl compounds (6)

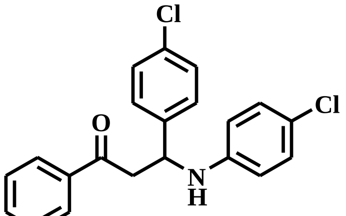
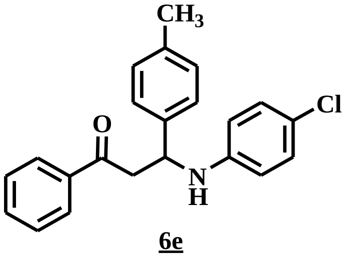
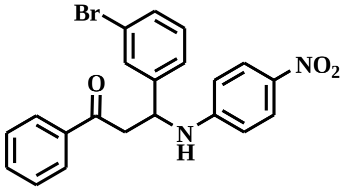
To synthesize β-amino carbonyl compounds a three component reaction of acetophenone (1 mmol), aromatic aldehyde (1 mmol) and aromatic amine (1 mmol) in absolute ethanol (5 mL) was conducted in a 50 mL round bottom flask at ambient temperature with continuous stirring in presence of 5 mol% of 1, 3-disulfoimidazolium chlorometallates $[Dsim]_2[X]$ or $[Dsim][FeCl_4]$ where X = $[ZnCl_4]^{2-}$, $[NiCl_4]^{2-}$ respectively. After completion of the reaction monitored by thin layer chromatography using a mixture of EtOAc and petroleum ether (1:5) as solvent system, ethanol was eliminated under reduced pressure in rotary evaporator. Then dichloromethane was added to the reaction mixture and the solid acidic catalyst was recovered from the dichloromethane solution (5 mL) by filtration which was remaining as insoluble residue. The recycled catalyst was reactivated after washing with CH_2Cl_2 solvent (5 mL) and then dried in vacuum oven at

80°C for 2 hour for next run. The product was precipitated from saturated solution of dichloromethane using distilled hexane. The solid product was then filtered and again recrystallized from ethanol solution to get analytically pure product.

2A.5 Spectral data

Entry	Spectral data
 **2a**	[Dsim]$_2$[ZnCl$_4$] **2a**: Off white solid; 96% yield; FT-IR (KBr): 3438, 1635, 1588, 1435, 1202, 1054, 884, 761 and 579 cm^{-1}; ^{1}H NMR (400 MHz, DMSO-d$_6$): δ 14.3 (s, 4H), 9.04 (s, 2H), 7.63 (s, 4H); ^{13}C NMR (100 MHz, DMSO-d$_6$): δ 134.7, 119.8; CHN analysis for $C_6H_{16}Cl_4N_4O_{12}S_4Zn$: Calcd. C, 10.73; H, 2.40; N, 8.34; Found: C, 10.66; H, 2.36; N, 8.22.
 **2b**	[Dsim][FeCl$_4$] **2b**: Yellow solid; 97% yield; FT-IR (KBr): 3405, 1635, 1588, 1444, 1194, 1054, 982, 766 and 604 cm^{-1}; CHN analysis for $C_3H_8Cl_4N_2O_6S_2Fe$: Calcd.: C, 8.38; H, 1.88; N, 6.52; Found: C, 8.31; H, 1.80; N 6.48.
 **2c**	[Dsim]$_2$[NiCl$_4$] **2c**: Yellow solid; 96% yield; FT-IR (KBr): 3386, 1603, 1584, 1448, 1177, 1050, 884, 762 and 584 cm^{-1}; ^{1}H NMR (400 MHz, DMSO-d$_6$): δ 14.23 (s, 4H), 8.96 (s, 2H), 7.59 (s, 4H); ^{13}C NMR (100 MHz, DMSO-d$_6$): δ 134.7, 119.8; CHN analysis for $C_6H_{16}Cl_4N_4O_{12}S_4Ni$: Calcd. C, 10.84; H, 2.43; N, 8.43; Found: C, 10.81; H, 2.40; N, 8.35.
 **6a** **1,3-diphenyl-3-(phenylamino)propan-1-one**	White solid, Mp.: 159-161.8°C (165-167°C) [41]; FT-IR (KBr) cm^{-1}: 3382, 3020, 1668, 1597, 1506, 1291, 1218, 993, 746, 689; ^{1}H NMR: (CDCl$_3$, 400 Hz): δ 7.89 (d, J = 6.7 Hz, 2H), 7.54 (t, J = 7.4 Hz, 1H), 7.41–7.45 (m, 3H), 7.31 (t, J = 7.6 Hz, 2H), 7.19–7.25 (m, 2H), 7.07 (t, J = 7.8 Hz, 2H), 6.65 (t, J = 7.3 Hz, 1H), 6.55 (d, J = 7.6 Hz, 2H), 4.99 (t, J = 5 Hz, 1H), 3.50 (dd, J = 5.3 Hz, J = 16.1 Hz, 1H), 3.41 (dd, J = 7.5 Hz, J = 16 Hz, 1H); ^{13}C NMR (100

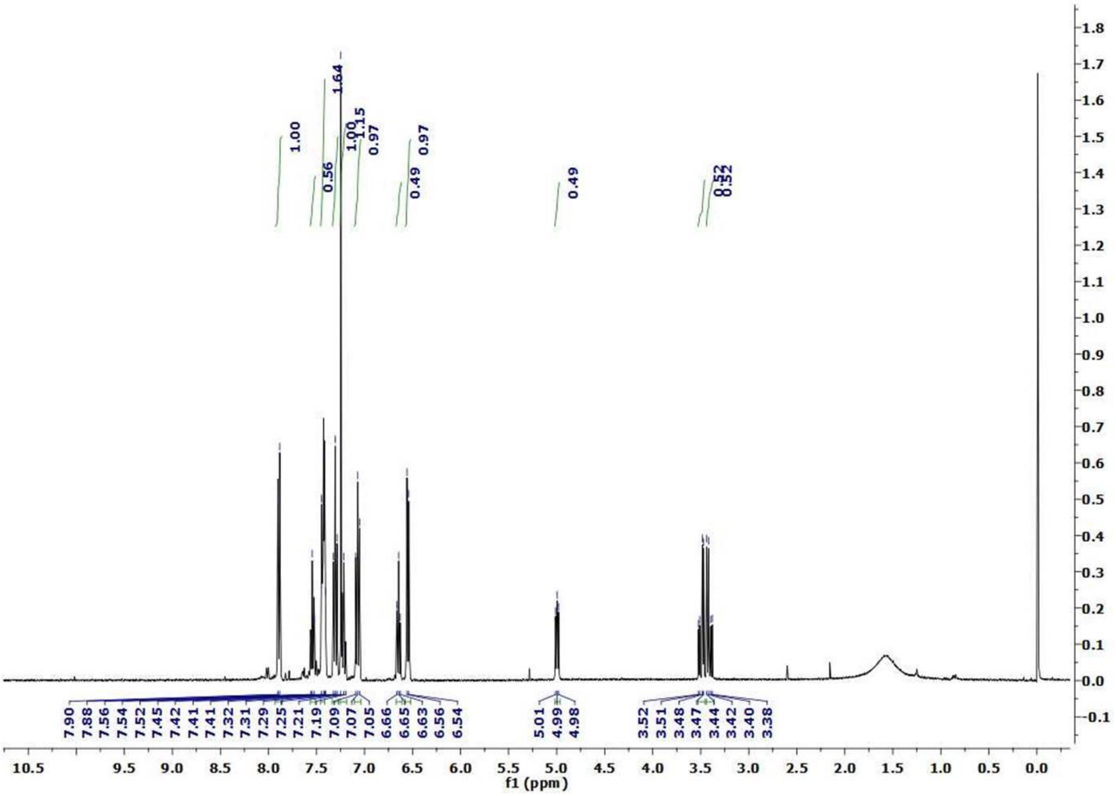
	MHz, $CDCl_3$): δ 198.3, 147.0, 143.0, 136.8, 133.4, 129.1, 128.8, 128.7, 128.2, 126.4, 117.8, 113.5, 54.9, 46.3; CHN analysis for $C_{21}H_{19}NO$: Calcd. C, 83.69; H, 6.35; N, 4.65; Found: C, 83.58; H, 6.31; N, 4.63.
 **6b** **3-(4-chlorophenylamino)-1,3-diphenylpropan-1-one**	Off white solid, Mp.: 161.1-165.7°C (170-171°C) [42]; FT-IR (KBr) cm^{-1}: 3371, 3021, 1667, 1597, 1495, 1279, 1000, 911, 802, 745, 688; δ ^1H NMR (400 MHz, $CDCl_3$): δ 7.88 (d, *J*=7.4 Hz, 2H), 7.55 (t, *J* = 7.4 Hz, 1H), 7.39-7.45 (m, 5H), 7.31 (t, *J* = 7.6 Hz, 2H), 7.21-7.25 (m, 1H), 7.02 (d, *J* = 8.7 Hz, 2H), 6.50 (d, *J* = 8.7 Hz, 2H), 4.94 (t, *J* = 5.5 Hz, 1H), 3.52 (dd, *J* = 5.1 Hz, *J* = 16.3 Hz, 1H), 3.44 (dd, *J* = 7.5 Hz, *J* = 16.3 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 198.2, 145.8, 142.1, 136.5, 133.5, 129.1, 129.0, 128.8, 128.2, 127.7, 126.5, 115.3, 54.9, 45.7; CHN analysis for $C_{21}H_{18}ClNO$: Calcd. C, 75.11; H, 5.40; N, 4.17; Found C, 75.08; H, 5.35; N, 4.14.
 **6c** **1-Phenyl-3-(phenylamino)-3-p-tolylpropane-1-one**	Off white solid, Mp.: 127.2-132.5°C (134-135°C) [42]; FT-IR (KBr) cm^{-1}: 3383, 3034, 1667, 1597, 1502, 1445, 1286, 1063, 987, 815, 745, 682; ^1H NMR (400 MHz, $CDCl_3$): δ 7.90 (d, *J* = 6.6 Hz, 2H), 7.55 (t, *J* = 7.4 Hz, 1H), 7.43 (t, *J* = 7.6 Hz, 2H), 7.32 (t, *J* = 8.0 Hz, 2H), 7.06-7.13 (m, 4H), 6.66 (t, *J* = 7.3Hz, 1H), 6.57 (d, *J* = 8.3 Hz, 2H), 4.98 (t, *J* = 6.4 Hz, 1H), 3.50 (dd, *J* = 5.4 Hz, *J* = 16.1 Hz, 1H), 3.41 (dd, *J* = 7.5 Hz, *J* = 16.1 Hz, 1H), 2.3 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 198.4, 146.9, 139.9, 137.1, 136.8, 133.4, 129.5, 129.1, 128.7, 128.2, 126.3, 117.9, 114, 54.7, 46.3, 21.1; CHN analysis for $C_{22}H_{21}NO$: Calcd. C, 83.78; H, 6.71; N, 4.44; Found: C, 83.72; H, 6.75; N, 4.42.

 **6d** **3-(4-chlorophenylamino)-3-(4-chlorophenyl)-1-phenylpropan-1-one**	White solid, Mp.: 121.4-122.8°C (114-119°C) [42]; FT-IR (KBr) cm^{-1}: 3326, 3085, 1661, 1591, 1489, 1299, 1000, 809, 745, 682; ^{1}H NMR (400 MHz, $CDCl_3$): 8.02(d, *J* = 8.6 Hz, 1H),7.88 (d, *J* = 7.1 Hz, 2H), 7.56(t, *J* = 7.4 Hz, 1H), 7.44 (t, *J* = 7.7 Hz, 2H), 7.34 (d, *J* = 8.5 Hz, 2H), 7.25-7.28 (m, 2H), 7.02 (d, *J* = 8.8 Hz, 2H), 6.44 (d, *J* = 8.8 Hz, 2H), 4.91 (t, *J* = 4.84 Hz, 1H), 3.45 (dd, *J* = 5.4 Hz, *J* = 16.5 Hz, 1H), 3.39 (dd, *J* = 7.5 Hz, *J* = 16.6 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$):δ 197.7, 145.3, 141.0, 136.5, 133.7, 133.2, 129.1, 129, 128.8, 128.2, 127.8, 122.8, 115.3, 54.0, 45.7; CHN analysis for $C_{21}H_{17}Cl_2NO$: Calcd. C, 68.12; H, 4.63; N, 3.78; Found: C, 68.08; H, 4.68; N, 3.72.
 **6e** **3-(4-Chlorophenylamino)-1-phenyl-3-p-tolylpropan-1-one**	White solid, Mp.: 159.2-160.9°C (163-165°C) [41]; FT-IR (KBr) cm^{-1}: 3410, 3090, 1587, 1511, 1335, 1091, 824, 748, 687; ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.89 (d, *J* = 7.4 Hz, 2H), 7.55 (t, *J* = 7.3 Hz, 1H), 7.43 (t, *J* = 7.7 Hz, 2H), 7.28 (d, *J* = 8.0 Hz, 2H), 7.12 (d, *J* = 7.9 Hz, 2H), 7.00 (d, *J* = 8.8 Hz, 2H), 6.46 (d, *J* = 8.8 Hz, 2H), 4.90 (t, *J* = 5.1 Hz, 1H), 3.47 (dd, *J* = 5 Hz, *J* = 16.3 Hz, 1H), 3.37 (dd, *J* = 7.8Hz, *J* = 16.2 Hz, 1H), 2.30 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 198.3, 145.6, 139.5, 137.2, 136.7, 133.5, 129.6, 128.9, 128.8, 128.2, 126.2, 115.0, 54.7, 46.2, 21.1; CHN analysis for $C_{22}H_{20}ClNO$: Calcd. C, 75.53; H, 5.76; N, 4.00; Found: C, 75.50; H, 5.73; N, 3.95.
 **6f**	Yellow solid, Mp.:130.5-134.3°C (130-132°C) [41]; FT-IR (KBr) cm^{-1}: 3363, 3062, 1686, 1593, 1532, 1458, 1286, 991, 831, 751, 682, 599; ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.00 (d, *J* = 8.6 Hz, 2H), 7.88 (d, *J* = 7.7 Hz, 2H), 7.58 (t, *J* = 7.3 Hz, 1H), 7.53 (s, 1H),

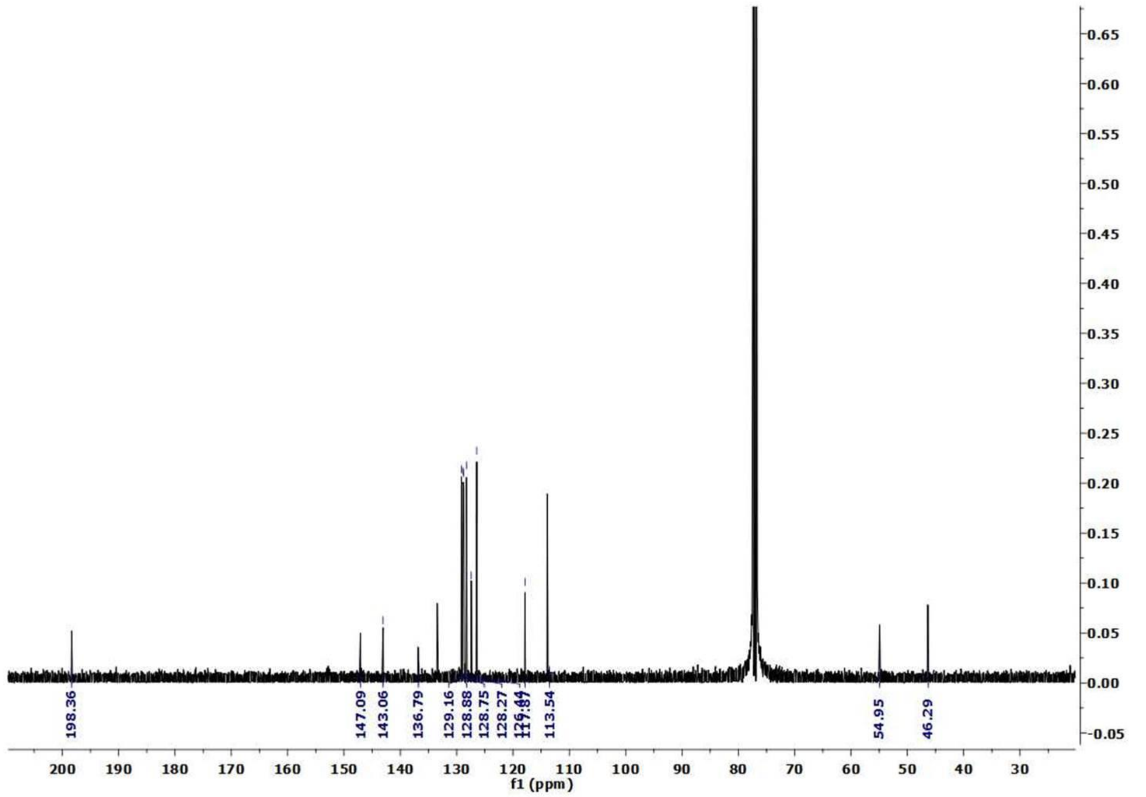
3-(4-nitrophenylamino)-3-(3-bromophenyl)-1-phenylpropan-1-one	7.45 (t, *J* = 7.3 Hz, 2H), 7.39 (d, *J* = 7.7 Hz, 1H), 7.32 (d, *J* = 7.4Hz, 1H), 7.20 (t, *J* = 7.7 Hz, 1H), 6.50 (d, *J* = 8.8 Hz, 2H), 5.06 (s, 1H) , 3.55 (dd, *J* = 5.1 Hz, *J* = 16.1 Hz, 1H), 3.50 (dd, *J* = 7.2 Hz, *J* = 16.1 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 197.4, 151.7, 138.7, 135.9, 133.6, 131.2, 130.8, 129.3, 129.0, 128.3, 126.3, 125.0, 112.4, 53.8, 45.4; CHN analysis for $C_{21}H_{17}BrN_2O_3$: Calcd. C, 59.31; H, 4.03; N, 6.59; Found: C, 59.25; H, 4.10; N, 6.54.

2A.6 NMR spectra of some selected compounds

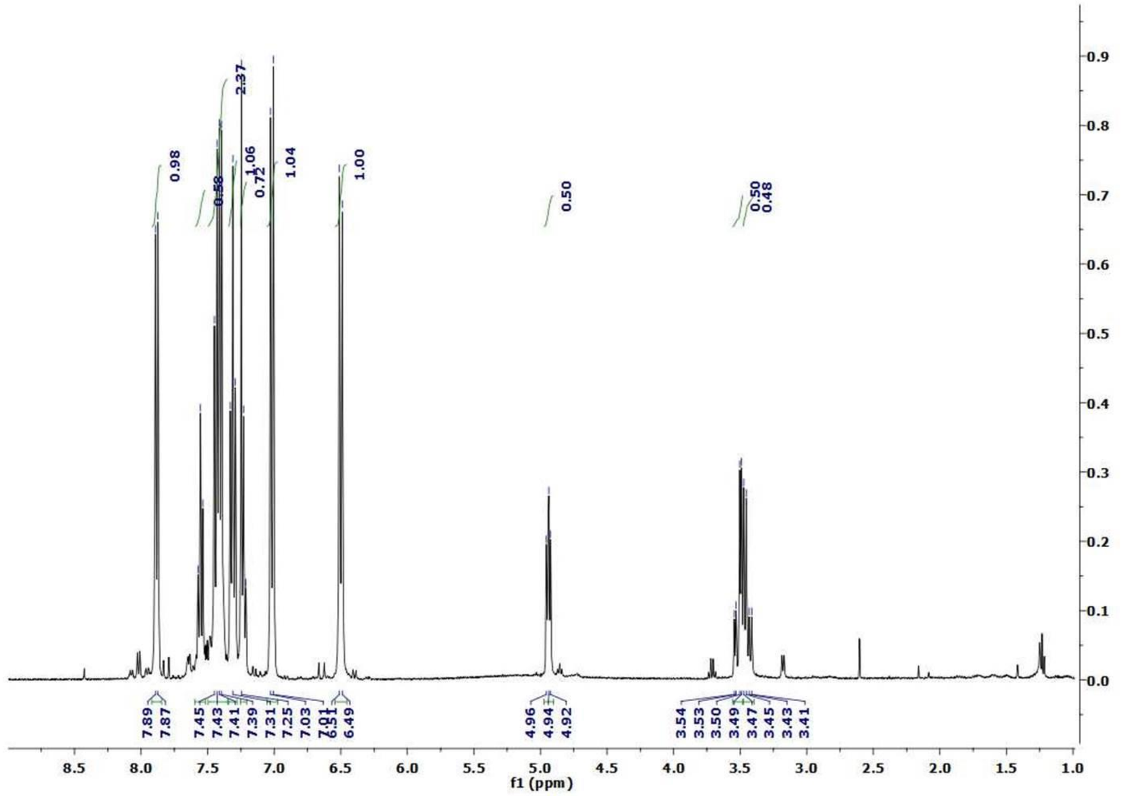
1. ^{1}H NMR of **<u>6a</u>**



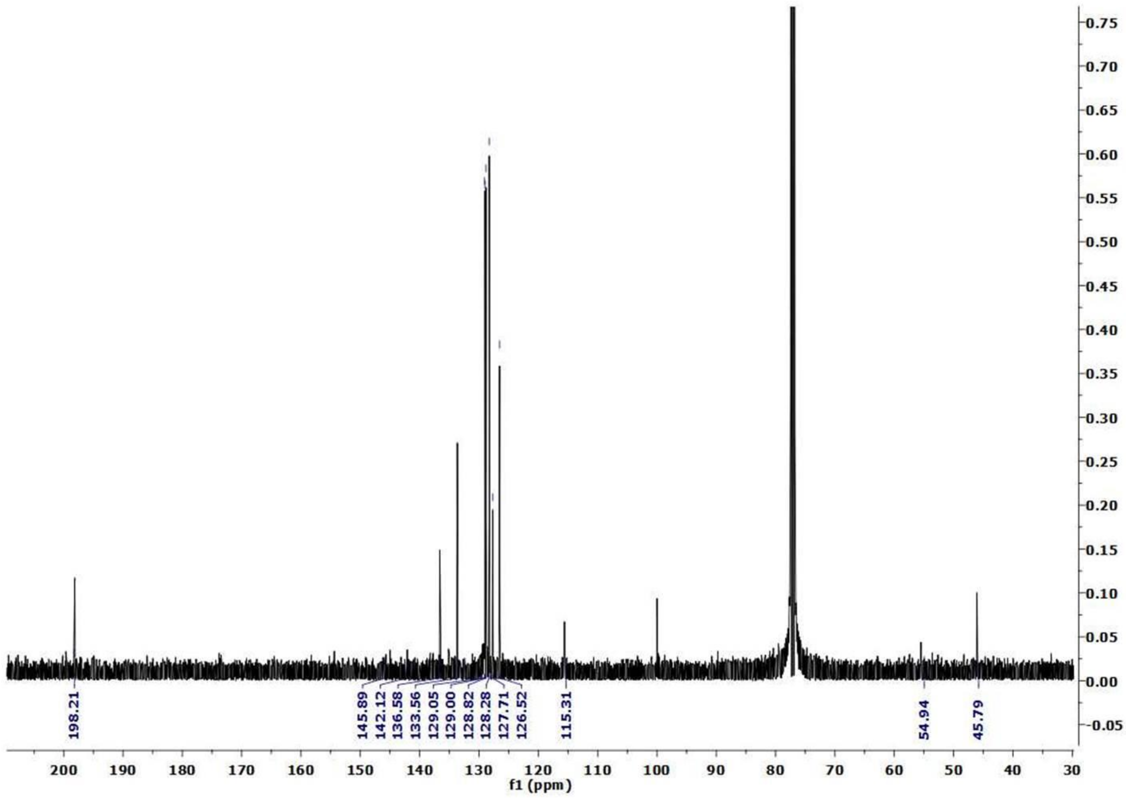
^{13}C NMR spectra of **6a**



2. ^{1}H NMR of **6b**



^{13}C NMR of **6b**



References

1. Hardacre, C., Murphy, R. W., Seddon, K. R., Srinivasan, G. and Swadźba-Kwaśny, M. Speciation of chlorometallate ionic liquids based on Gallium (III) and Indium (III). *Australian journal of chemistry*, 63(5):845-848, 2010.
2. Yang, J. Z., Tian, P., He, L. L. and Xu, W. G. Studies on room temperature ionic liquid $InCl_3$-EMIC. *Fluid Phase Equilibria*, 204(2):295-302, 2003.
3. Apperley, D. C., Hardacre, C., Licence, P., Murphy, R. W., Plechkova, N. V., Seddon, K. R., Srinivasan, G., Swadźba-Kwaśny, M. and Villar-Garcia, I. J. Speciation of chloroindate (III) ionic liquids. *Dalton Transactions*, 39(37):8679-8687, 2010.
4. Gunaratne, H. N., Lotz, T. J. and Seddon, K. R. Chloroindate (III) ionic liquids as catalysts for alkylation of phenols and catechol with alkenes. *New Journal of Chemistry*, 34(9):1821-1824, 2010.
5. Neto, B. A. D., Alves, M. B., Lapis, A. A., Nachtigall, F. M., Eberlin, M. N., Dupont, J. and Suarez, P. A. 1-n-Butyl-3-methylimidazolium tetrachloro-indate ($BMI{\cdot}InCl_4$) as a media for the synthesis of biodiesel from vegetable oils. *Journal of Catalysis*, 249(2):154-161, 2007.

6. Mohammadpoor-Baltork, I., Moghadam, M., Tangestaninejad, S., Mirkhani, V., Khosropour, A. R. and Mirjafari, A. [C_4mim][$InCl_4$]: An efficient catalyst-medium for alkoxymethylation of alcohols and their interconversion to acetates and TMS-ethers. *Comptes Rendus Chimie,* 14(6):568-579, 2011.
7. Estager, J., Holbrey, J. D. and Swadźba-Kwaśny, M. Halometallate ionic liquids-revisited. *Chemical Society Reviews*, 43(3):847-886, 2014.
8. Kore, R., Berton, P., Kelley, S. P., Aduri, P., Katti, S. S. and Rogers, R. D. Group IIIA halometallate ionic liquids: Speciation and applications in catalysis. *ACS Catalysis*, 7(10):7014-7028, 2017.
9. Sitze, M. S., Schreiter, E. R., Patterson, E. V. and Freeman, R. G. Ionic liquids based on $FeCl_3$ and $FeCl_2$. Raman scattering and ab initio calculations. *Inorganic Chemistry*, 40(10):2298-2304, 2001.
10. Li, J. G., Hu, Y. F., Peng, X. M. and Zhang, X. M. Study on physicochemical properties of $FeCl_3$/[C_4mim][Cl] ionic liquids. The *Journal of Chemical Thermodynamics*, 97:277-281, 2016.
11. Bica, K., Leder, S. and Gaertner, P. From solvent to sustainable catalysis-chloroferrate ionic liquids in synthesis. *Current Organic Synthesis*, 8(6):824-839, 2011.
12. Valkenberg, M. H. and Hölderich, W. F. Friedel-Crafts acylation of aromatics catalysed by supported ionic liquids. *Applied Catalysis A: General*, 215(1-2):185-190, 2001.
13. Xuewen, S. U. N., Suoqi, Z. H. A. O. and Hui, L. I. Alkylation of benzene with propylene catalyzed by $FeCl_3$-chloropyridine ionic liquid. *Frontiers of Chemical Science and Engineering*, 1(3):292-295, 2007.
14. Padwa, A., Bullock, W. H. and Dyszlewski, A. D. Studies dealing with the alkylation-[1, 3]-rearrangement reaction of some phenylthio-substituted allylic sulfones. *The Journal of Organic Chemistry,* 55(3):955-964, 1990.
15. Sasaki, T., Tada, M., Zhong, C., Kume, T. and Iwasawa, Y. Immobilized metal ion-containing ionic liquids: Preparation, structure and catalytic performances in Kharasch addition reaction and Suzuki cross-coupling reactions. *Journal of Molecular Catalysis A: Chemical*, 279(2):200-209, 2008.

16. Hu, Y. L., Liu, Q. F., Lu, T. T. and Lu, M. Highly efficient oxidation of organic halides to aldehydes and ketones with H_5IO_6 in ionic liquid [C_{12}mim][$FeCl_4$]. *Catalysis Communications*, 11(10):923-927, 2010.
17. Nguyen, M. D., Nguyen, L. V., Jeon, E. H., Kim, J. H., Cheong, M., Kim, H. S. and Lee, J. S. Fe-containing ionic liquids as catalysts for the dimerization of bicyclo [2.2.1] hepta-2, 5-diene. *Journal of Catalysis*, 258(1):5-13, 2008.
18. Vasiloiu, M., Gaertner, P. and Bica, K. Iron catalyzed Michael addition: chloroferrate ionic liquids as efficient catalysts under microwave conditions. *Science China Chemistry*, 55(8):1614-1619, 2012.
19. Kim, J. Y., Kim, J. T., Song, E. A., Min, Y. K. and Hamaguchi, H. O. Polypyrrole nanostructures self-assembled in magnetic ionic liquid as a template. *Macromolecules*, 41(8):2886-2889, 2008.
20. Xie, Z. L. and Taubert, A. Thermomorphic behavior of the ionic liquids [C_4mim][$FeCl_4$] and [C_{12}mim][$FeCl_4$]. *ChemPhysChem*, 12(2):364-368, 2011.
21. Liu, S., Wang, Z., Li, K., Li, L., Yu, S., Liu, F. and Song, Z. Brønsted-Lewis acidic ionic liquid for the “one-pot” synthesis of biodiesel from waste oil. *Journal of Renewable and Sustainable Energy*, 5(2):023111, 2013.
22. Liu, S., Wang, A., Liu, Z., Li, L., Yu, S., Xie, C. and Liu, F. Synthesis of glycerol triacetate using a Brønsted–Lewis acidic ionic liquid as the catalyst. *Journal of the American Oil Chemists' Society*, 92(9):1253-1258, 2015.
23. Gogoi, P., Dutta, A. K., Sarma, P. and Borah, R. Development of Brönsted–Lewis acidic solid catalytic system of 3-methyl-1-sulfonic acid imidazolium transition metal chlorides for the preparation of bis (indolyl) methanes. *Applied Catalysis A: General*, 492:133-139, 2015.
24. Dutta, A. K., Gogoi, P. and Borah, R. Triphenylsulfophosphonium chlorometallates as efficient heterogeneous catalysts for the three-component synthesis of 2, 3-dihydro-1, 2, 3-trisubstituted-1H-naphth [1, 2-e][1, 3] oxazines. *Polyhedron*, 123:184-191, 2017.
25. Dutta, A. K., Gogoi, P. and Borah, R. Diethyldisulfoammonium chlorometallates as heterogeneous Brønsted–Lewis acidic catalysts for one-pot synthesis of 14-aryl-7-(N-phenyl)-14H-dibenzo[a, j] acridines. *Applied Organometallic Chemistry*, 32(1):3900, 2018.

26. Estager, J., Nockemann, P., Seddon, K. R., Swadźba-Kwaśny, M. and Tyrrell, S. Validation of speciation techniques: A study of chlorozincate (II) ionic liquids. *Inorganic Chemistry*, 50(11):5258-5271, 2011.
27. Lecocq, V., Graille, A., Santini, C. C., Baudouin, A., Chauvin, Y., Basset, J. M., Arzel, L., Bouchu, D. and Fenet, B. Synthesis and characterization of ionic liquids based upon 1-butyl-2, 3-dimethylimidazolium chloride/$ZnCl_2$. *New journal of chemistry*, 29(5):700-706, 2005.
28. Taylor, A. W., Men, S., Clarke, C. J. and Licence, P. Acidity and basicity of halometallate-based ionic liquids from X-ray photoelectron spectroscopy. *RSC Advances*, 3(24):9436-9445, 2013.
29. Abbott, A. P., Capper, G., Davies, D. L., Munro, H. L., Rasheed, R. K. and Tambyrajah, V. Preparation of novel, moisture-stable, Lewis-acidic ionic liquids containing quaternary ammonium salts with functional side chains. *Chemical Communications*, (19):2010-2011, 2001.
30. Abbott, A. P., Capper, G., Davies, D. L., Rasheed, R. K. and Tambyrajah, V. Quaternary ammonium zinc-or tin-containing ionic liquids: water insensitive, recyclable catalysts for Diels-Alder reactions. *Green Chemistry*, 4(1):24-26, 2002.
31. Abbott, A. P., Bell, T. J., Handa, S. and Stoddart, B. O-Acetylation of cellulose and monosaccharides using a zinc based ionic liquid. *Green Chemistry*, 7(10):705-707, 2005.
32. Karakulina, A., Gopakumar, A., Akçok, İ., Roulier, B. L., LaGrange, T., Katsyuba, S. A., Das, S. and Dyson, P. J. A rhodium nanoparticle-Lewis acidic ionic liquid catalyst for the chemoselective reduction of heteroarenes. *Angewandte Chemie*, 128(1):300-304, 2016.
33. Liu, S., Xie, C., Yu, S. and Liu, F. Dimerization of rosin using Brønsted–Lewis acidic ionic liquid as catalyst. *Catalysis Communications*, 9(10):2030-2034, 2008.
34. Shiwei, L. I. U., Congxia, X. I. E., Shitao, Y. U., Mo, X. I. A. N. and Fusheng, L. I. U. A Brønsted-Lewis acidic ionic liquid: Its synthesis and use as the catalyst in rosin dimerization. *Chinese Journal of Catalysis*, 30(5):401-406, 2009.

35. Liu, S., Chen, C., Yu, F., Li, L., Liu, Z., Yu, S., Xie, C. and Liu, F. Alkylation of isobutane/isobutene using Brønsted–Lewis acidic ionic liquids as catalysts. *Fuel*, 159:803-809, 2015.
36. Kore, R. and Srivastava, R. A simple, eco-friendly, and recyclable bi-functional acidic ionic liquid catalysts for Beckmann rearrangement. *Journal of Molecular Catalysis A: Chemical*, 376:90-97, 2013.
37. Gale, R. J., Gilbert, B. and Osteryoung, R. A. Electrochemical and spectral investigations of nickel (II) ion equilibriums in room-temperature chloroaluminate solvents. *Inorganic Chemistry*, 18(10):2723-2725, 1979.
38. Laher, T. M. and Hussey, C. L. Electrochemical studies of chloro complex formation in low-temperature chloroaluminate melts. 1. Iron (II), iron (III), and nickel (II). *Inorganic Chemistry*, 21(11):4079-4083, 1982.
39. Laher, T. M. and Hussey, C. L. Electrochemical studies of chloro complex formation in low temperature chloroaluminate melts. 2. Silver (I). *Inorganic Chemistry*, 22(9):1279-1283, 1983.
40. Dent, A. J., Seddon, K. R. and Welton, T. The structure of halogenometallate complexes dissolved in both basic and acidic room-temperature halogenoaluminate (III) ionic liquids, as determined by EXAFS. *Journal of the Chemical Society, Chemical Communications*, (4):315-316, 1990.
41. Hitchcock, P. B., Seddon, K. R. and Welton, T. Hydrogen-bond acceptor abilities of tetrachlorometalate (II) complexes in ionic liquids. *Journal of the Chemical Society, Dalton Transactions*, (17):2639-2643, 1993.
42. Bowlas, C. J., Bruce, D. W. and Seddon, K. R. Liquid-crystalline ionic liquids. *Chemical Communications*, (14):1625-1626, 1996.
43. Carmichael, A. J., Hardacre, C., Holbrey, J. D., Nieuwenhuyzen, M. and Seddon, K. R. A method for studying the structure of low-temperature ionic liquids by XAFS. *Analytical Chemistry*, 71(20):4572-4574, 1999.
44. Roeper, D. F., Pandya, K. I., Cheek, G. T. and O'Grady, W. E. The structure of nickel chloride in the ionic liquid 1-ethyl-3-methyl imidazolium chloride/aluminum chloride: X-ray absorption spectroscopy. *Journal of the Electrochemical Society*, 158(3):F21-F28, 2011.
45. Zhong, C., Sasaki, T., Tada, M. and Iwasawa, Y. Ni ion-containing ionic liquid salt and Ni ion-containing immobilized ionic liquid on silica: Application to

Suzuki cross-coupling reactions between chloroarenes and arylboronic acids. *Journal of Catalysis*, 242(2):357-364, 2006.

46. Zhong, C., Sasaki, T., Jimbo-Kobayashi, A., Fujiwara, E., Kobayashi, A., Tada, M. and Iwasawa, Y. Syntheses, structures, and properties of a series of metal ion-containing dialkylimidazolium ionic liquids. *Bulletin of the Chemical Society of Japan*, 80(12):2365-2374, 2007.
47. Sasaki, T., Tada, M., Zhong, C., Kume, T. and Iwasawa, Y. Immobilized metal ion-containing ionic liquids: Preparation, structure and catalytic performances in Kharasch addition reaction and Suzuki cross-coupling reactions. *Journal of Molecular Catalysis A: Chemical*, 279(2):200-209, 2008.
48. Taylor, A. W., Men, S., Clarke, C. J. and Licence, P. Acidity and basicity of halometallate-based ionic liquids from X-ray photoelectron spectroscopy. *RSC Advances*, 3(24):9436-9445, 2013.
49. March. J. *Advanced Organic Chemistry: Reactions, Mechanisms, and Structure*, John Wiley & Sons, New York, NY, USA, 3rd edition, 1985.
50. Belinelo, V. J., Reis, G. T, Stefani, G. M., Ferreira-Alves, D. L and Pil´o-Veloso, D. Synthesis of 6α, 7β-dihydroxyvouacapan- 17β-oic acid derivatives. Part IV: mannich base derivatives and its activities on the electrically stimulated guinea-pig ileum preparation. *Journal of the Brazilian Chemical Society*, 13(6):830-837, 2002.
51. Joshi, S., Khosla, N. and Tiwari, P. In vitro study of some medicinally important Mannich bases derived from antitubercular agent. *Bioorganic & medicinal chemistry*, 12(3):571-576, 2004.
52. Hayashi, Y., Tsuboi, W., Ashimine, I., Urushima, T., Shoji, M. and Sakai, K. The direct and enantioselective, one-pot, three-component, cross-Mannich reaction of aldehydes. *Angewandte Chemie*, 115(31):3805-3808, 2003.
53. Kobayashi, S., Hamada, T. and Manabe, K. The catalytic asymmetric Mannich-type reactions in aqueous media. *Journal of the American Chemical Society*, 124(20):5640-5641, 2002.
54. Matsunaga, S., Kumagai, N., Harada, S. and Shibasaki, M. Anti-selective direct catalytic asymmetric Mannich-type reaction of hydroxyketone providing β-amino alcohols. *Journal of the American Chemical Society*, 125(16):4712-4713, 2003.

55. Trost, B. M. and Terrell, L. R. A direct catalytic asymmetric Mannich-type reaction to syn-amino alcohols. *Journal of the American Chemical Society*, 125(2):338-339, 2003.
56. Zhang, H., Mifsud, M., Tanaka, F. and Barbas, C. F. 3-Pyrrolidinecarboxylic acid for direct catalytic asymmetric anti-Mannich-type reactions of unmodified ketones. *Journal of the American Chemical Society*, 128(30):9630-9631, 2006.
57. Córdova, A. The direct catalytic asymmetric Mannich reaction. *Accounts of Chemical Research*, 37(2):102-112, 2004.
58. Racane, L., Tralic-Kulenovic, V. and Fiser-Jakic, L. Synthesis of bis-substituted amidinobenzothiazoles as potential anti-HIV agents. *Heterocycles*, 55(11):2085-2098, 2001.
59. Kashiyama, E., Hutchinson, I., Chua, M. S., Stinson, S. F., Phillips, L. R., Kaur, G., Sausville, E. A., Bradshaw, T. D., Westwell, A. D. and Stevens, M. F. Antitumor benzothiazoles. 8. Synthesis, metabolic formation, and biological properties of the C-and N-oxidation products of antitumor 2-(4-aminophenyl) benzothiazoles. *Journal of Medicinal Chemistry*, 42(20):4172-4184, 1999.
60. Bhusare, S. R., Pawar, R. P. and Vibhute, Y. B. Synthesis and antibacterial activity of some new 2-(substituted phenyl sulfonamido)-6-substituted benzothiazoles. *Indian Journal of Heterocyclic Chemistry*, 11(1):79-80, 2001.
61. Raman, N., Esthar, S. and Thangaraja, C. A new Mannich base and its transition metal (II) complexes-synthesis, structural characterization and electrochemical study. *Journal of Chemical Sciences*, 116(4):209-213, 2004.
62. Kalluraya, B., Chimbalkar, R. M. and Hegde, J. C. Anticonvulsant activity of nicotinyl/isonicotinyl substituted 1, 2, 4-triazol-5-thione Mannich bases. *Indian Journal of Heterocyclic Chemistry*, 15(1):15-18, 2005.
63. Köksal, M., Gökhan, N., Küpeli, E., Yesilada, E. and Erdogan, H. Analgesic and antiinflammatory activities of some new Mannich bases of 5-nitro-2-benzoxazolinones. *Archives of Pharmacal Research*, 30(4):419-424, 2007.
64. Ivanova, Y., Momekov, G., Petrov, O., Karaivanova, M. and Kalcheva, V. Cytotoxic Mannich bases of 6-(3-aryl-2-propenoyl)-2 (3H)-benzoxazolones. *European Journal of Medicinal Chemistry*, 42(11-12):1382-1387, 2007.

65. Gul, H. I., Vepsalainen, J., Gul, M., Erciyas, E. and Hanninen, O. Cytotoxic activities of mono and bis Mannich bases derived from acetophenone against Renca and Jurkat cells. *Pharmaceutica Acta Helvetiae*, 74(4):393-398, 2000.
66. Ashok, M., Holla, B. S. and Poojary, B. Convenient one pot synthesis and antimicrobial evaluation of some new Mannich bases carrying 4-methylthiobenzyl moiety. *European Journal of Medicinal Chemistry*, 42(8):1095-1101, 2007.
67. Pandeya, S. N., Sriram, D., Nath, G. and De Clercq, E. Synthesis, antibacterial, antifungal and anti-HIV activities of norfloxacin Mannich bases. *European Journal of Medicinal Chemistry*, 35(2):249-255, 2000.
68. Holla, B. S., Shivananda, M. K., Shenoy, M. S. and Antony, G. Studies on arylfuran derivatives: part VII. Synthesis and characterization of some Mannich bases carrying halophenylfuryl moieties as promising antibacterial agents, *IL Farmaco*, 53(8-9):531-535, 1998.
69. Singh, B. N., Shukla, S. K. and Singh, M. Synthesis and biological activity of Sulphadiazine Schiff's bases of Isatin and their N-Mannich bases. *Asian Journal of Chemistry*, 19(7):5013, 2007.
70. Vashishtha, S. C., Zello, G. A., Nienaber, K. H., Balzarini, J., De Clercq, E., Stables, J. P. and Dimmock, J. R. Cytotoxic and anticonvulsant aryloxyaryl Mannich bases and related compounds. *European Journal of Medicinal Chemistry*, 39(1):27-35, 2004.
71. Bennet-Jenkins, E. and Bryant, C. Novel sources of anthelmintics. *International Journal for Parasitology*, 26(8-9):937-947, 1996.
72. Sriram, D., Banerjee, D. and Yogeeswari, P. Efavirenz Mannich bases: Synthesis, anti-HIV and antitubercular activities. *Journal of Enzyme Inhibition and Medicinal Chemistry*, 24(1):1-5, 2009.
73. Mulla, J. S., Khan, A. Y., Panchamukhi, S. I., Khazi, M. A., Kalashetti, M. B. and Khazi, I. M. Synthesis and antitubercular activity of Mannich bases of imidazo [2, 1-b][1, 3, 4] thiadiazoles. *Indian Journal of Novel Drug Delivery*, 3(4):289-295, 2011.
74. Malinka, W., Świątek, P., Filipek, B., Sapa, J., Jezierska, A. and Koll, A. Synthesis, analgesic activity and computational study of new

isothiazolopyridines of Mannich base type. *IL Farmaco*, 60(11-12):961-968, 2005.

75. Barlin, G. B. and Jiravinyu, C. Potential antimalarials. X. Di-Mannich bases of 4-(7'-Trifluoromethyl-1', 5'-naphthyridin-4'-ylamino) phenol and N-(4'-Diethylamino-1'-methylbutyl)-7-trifluoromethyl-1, 5-naphthyridin-4-amine. *Australian Journal of Chemistry*, 43(7):1175-1181, 1990.
76. Scott, M. K., Martin, G. E., DiStefano, D. L., Fedde, C. L., Kukla, M. J., Barrett, D. L., Baldy, W. J., Elgin Jr, R. J. and Kesslick, J. M. Pyrrole Mannich bases as potential antipsychotic agents. *Journal of Medicinal chemistry*, 35(3):552-558, 1992.
77. Edwards, M. L., Ritter, H. W., Stemerick, D. M. and Stewart, K. T. Mannich bases of 4-phenyl-3-buten-2-one. A new class of antiherpes agent. *Journal of Medicinal Chemistry*, 26(3):431-436, 1983.
78. Karll, R. E. and Lee, R. J., BP Corporation North America Inc. *Process and Compositions*. US Patent 4, 384, 138, 1983.
79. Otto, F. P. US Patent, US 3 649 229, 1972.
80. Ji, J. X., Qiu, L. Q., Yip, C. W. and Chan, A. S. A convenient, one-step synthesis of optically active tertiary aminonaphthol and its applications in the highly enantioselective alkenylations of aldehydes. *The Journal of Organic Chemistry*, 68(4):1589-1590, 2003.
81. Huang, P. J. J., Youssef, D., Cameron, T. S. and Jha, A. Microwave-assisted synthesis of novel 2-naphthol bis-Mannich bases. *Arkivoc*, 2008(16):165-177, 2008.
82. da Rosa, F. A., Rebelo, R. A. and Nascimento, M. G. Synthesis of new indolecarboxylic acids related to the plant hormone indoleacetic acid IAA. *Journal of the Brazilian Chemical Society*, 14(1):11-15, 2003.
83. Sreevalli, W., Ramachandran, G., Madhuri, W. and Sathiyanarayanan, K. I. Green trends in Mannich reaction. *Mini-Reviews in Organic Chemistry*, 11(1):97-115, 2014.
84. Shaterian, H. R., Yarahmadi, H. and Ghashang, M. Silica supported perchloric acid ($HClO_4$-SiO_2): An efficient and recyclable heterogeneous catalyst for the one-pot synthesis of amidoalkyl naphthols. *Tetrahedron*, 64(7):1263-1269, 2008.

85. Khan, A. T., Parvin, T. and Choudhury, L. H. Effects of substituents in the β-position of 1, 3-dicarbonyl compounds in bromodimethylsulfonium bromide-catalyzed multicomponent reactions: A facile access to functionalized piperidines. *The Journal of Organic Chemistry*, 73(21):8398-8402, 2008.
86. Heravi, M. M., Ranjbar, L., Derikvand, F. and Bamoharram, F. F. A modified and green Dakin-West reaction: An efficient and convenient method for a one-pot synthesis of β-acetamido carbonyl compounds. *Journal of Molecular Catalysis A: Chemical*, 271(1-2):28-31, 2007.
87. Das, B., Reddy, K. R., Srinivas, Y. and Kumar, R. A. One-pot multicomponent synthesis of β-acetamidoketones catalysed by *p*TSA. *Canadian Journal of Chemistry*, 85(7-8):479-482, 2007.
88. Wang, X., Mao, H., Yu, Y., Zhu, X. and Zhu, C. Samarium triiodide-catalyzed formation of Mannich-type products by amidoalkylation of 1, 3-dicarbonyl compounds. *Synthetic Communications*, 37(21):3751-3758, 2007.
89. Das, B. and Reddy, K. R. Facile One-pot multicomponent synthesis of β-acetamido ketones with amberlyst-15 as heterogeneous catalyst. *Helvetica Chimica Acta*, 89(12):3109-3111, 2006.
90. Xu, L. W., Xia, C. G. and Li, L. Transition metal salt-catalyzed direct three-component Mannich reactions of aldehydes, ketones, and carbamates: efficient synthesis of N-protected β-aryl-β-amino ketone compounds. *The Journal of Organic Chemistry*, 69(24):8482-8484, 2004.
91. Khodaei, M. M., Khosropour, A. R. and Fattahpour, P. A modified procedure for the Dakin–West reaction: an efficient and convenient method for a one-pot synthesis of β-acetamido ketones using silica sulfuric acid as catalyst. *Tetrahedron letters*, 46(12):2105-2108, 2005.
92. Davoodnia, A., Tavakoli-Nishaburi, A. and Niloofar, T. H. Carbon-based solid acid catalyzed one-pot mannich reaction: A facile synthesis of β-amino carbonyl compounds. *Bulletin of the Korean Chemical Society*, 32(2):635-638, 2011.
93. Loh, T. P., Liung, S. B., Tan, K. L. and Wei, L. L. Three component synthesis of β-amino carbonyl compounds using indium trichloride-catalyzed one-pot Mannich-type reaction in water. *Tetrahedron*, 56(20):3227-3237, 2000.

94. Wang, R., Li, B. G., Huang, T.K., Shi, L. and Lu, X. X. $NbCl_5$-Catalyzed one-pot Mannich-type reaction: three component synthesis of β-amino carbonyl compounds. *Tetrahedron letters*, 48(12):2071-2073, 2007.
95. Xia, M. and Lu, Y. D. A novel direct and one-pot Mannich synthesis of fluorinated β-aminobutanones with sulfamic acid as a green catalyst. *Journal of Fluorine Chemistry*, 127(8):1119-1124, 2006.
96. Gawande, M. B., Velhinho, A., Nogueira, I. D., Ghumman, C. A. A., Teodoro, O. M. N. D. and Branco, P. S. A facile synthesis of cysteine–ferrite magnetic nanoparticles for application in multicomponent reactions-a sustainable protocol. *RSC Advances*, 2(15):6144-6149, 2012.
97. Li, H., Zeng, H. Y. and Shao, H. W. Bismuth (III) chloride-catalyzed one-pot Mannich reaction: three-component synthesis of β-amino carbonyl compounds. *Tetrahedron Letters*, 50(49):6858-6860, 2009.
98. Xu, Q., Yang, Z., Yin, D. and Wang, J. One-pot three-component Mannich reaction catalyzed by sucrose char sulfonic acid. *Frontiers of Chemical Engineering in China*, 3(2):201-205, 2009.
99. Mukhopadhyay, C., Datta, A. and Butcher, R. J. Highly efficient one-pot, three-component Mannich reaction catalysed by boric acid and glycerol in water with major 'syn'diastereoselectivity. *Tetrahedron Letters*, 50(29):4246-4250, 2009.
100. Shou, W. G., Yang, Y. Y. and Wang, Y. G. An efficient synthesis of β-amino esters via $Zn(OTf)_2$-catalyzed Mannich-type reaction. *Tetrahedron Letters*, 47(11):1845-1847, 2006.
101. Kobayashi, S., Matsubara, R. and Kitagawa, H. Catalytic, asymmetric Mannich-type reactions of N-acylimino esters for direct formation of N-acylated amino acid derivatives. Efficient synthesis of a novel inhibitor of ceramide trafficking, HPA-12. *Organic Letters*, 4(1):143-145, 2002.
102. Ueno, M., Ishitani, H. and Kobayashi, S. Air-stable, storable, and highly selective chiral Lewis acid catalyst. *Organic Letters*, 4(20):3395-3397, 2002.
103. Badorrey, R., Cativiela, C., Díaz-de-Villegas, M. D. and Gálvez, J. A. Study of the Lewis acid-promoted addition of silylenol ethers to imines derived from glyceraldehyde. *Tetrahedron Letters*, 44(51):9189-9192, 2003.

104. Periasamy, M., Suresh, S. and Ganesan, S. S. Stereoselective synthesis of syn-β-amino esters using the $TiCl_4/R_3N$ reagent system. *Tetrahedron Letters*, 46(33):5521-5524, 2005.
105. Jacobsen, M. F., Ionita, L. and Skrydstrup, T. Highly diastereoselective Mannich-type reactions of chiral N-acylhydrazones. *The Journal of Organic Chemistry*, 69(14):4792-4796, 2004.
106. Komoto, I. and Kobayashi, S. Lewis acid catalysis in supercritical carbon dioxide. Use of poly (ethylene glycol) derivatives and perfluoroalkylbenzenes as surfactant molecules which enable efficient catalysis in $ScCO_2$. *The Journal of Organic Chemistry*, 69(3):680-688, 2004.
107. Chung, W. J., Omote, M. and Welch, J. T. The catalytic mannich reaction of 1, 1-difluoro-2-trialkyl (aryl) silyl-2-trimethyl-silyloxyethenes: Preparation of β-amino acid derivatives. *The Journal of Organic Chemistry*, 70(19):7784-7787, 2005.
108. Pandey, G., Singh, R. P., Garg, A. and Singh, V. K. Synthesis of Mannich type products via a three-component coupling reaction. *Tetrahedron Letters*, 46(12):2137-2140, 2005.
109. Yi, W. B. and Cai, C. Mannich-type reactions of aromatic aldehydes, anilines, and methyl ketones in fluorous biphase systems created by rare earth (III) perfluorooctane sulfonates catalysts in fluorous media. *Journal of Fluorine Chemistry*, 127(11):1515-1521, 2006.
110. Wang, L., Han, J., Sheng, J., Tian, H. and Fan, Z. Rare earth perfluorooctanoate $[RE(PFO)_3]$ catalyzed one-pot Mannich reaction: Three component synthesis of β-amino carbonyl compounds. *Catalysis Communications*, 6(3):201-204, 2005.
111. Wang, L. M., Han, J. W., Sheng, J., Fan, Z. Y. and Tian, H. $Yb(OTf)_3$ catalyzed Mannich reaction of acetophenone with aromatic aldehydes and aromatic amines: Three component one-pot synthesis of beta-amino ketone derivatives. *Chinese Journal of Organic Chemistry*, 25(5):591-594, 2005.
112. Akiyama, T., Takaya, J. and Kagoshima, H. One-pot Mannich-type reaction in water: HBF_4 catalyzed condensation of aldehydes, amines, and silyl enolates for the synthesis of β-amino carbonyl compounds. *Synlett*, 1999(09):1426-1428, 1999.

113. Manabe, K., Mori, Y. and Kobayashi, S. Three-component carbon–carbon bond-forming reactions catalyzed by a Brønsted acid–surfactant-combined catalyst in water. *Tetrahedron*, 57(13):2537-2544, 2001.
114. Arend, M., Westermann, B. and Risch, N. Modern variants of the Mannich reaction. *Angewandte Chemie International Edition*, 37(8):1044-1070, 1998.
115. Sobczak, J. W., Sobczak, E., Kosiński, A. and Biliński, A. XANES investigations of Pd-doped polyaniline. *Journal of Alloys and Compounds*, 328(1-2):132-134, 2001.
116. Wasserscheid, P. and Welton, T. *Ionic liquids in synthesis*. John Wiley & Sons, volume 1, pages 1-721, 2nd edition, 2008.
117. Lee, S. G. and Park, J. H. Ytterbium (III) triflate-catalyzed one-pot Mannich-type reaction in ionic liquid. *Bulletin of the Korean Chemical Society*, 23(10):1367-1368, 2002.
118. Rasalkar, M. S., Bhilare, S. V., Deorukhkar, A. R., Darvatkar, N. B. and Salunkhe, M. M. Heteropoly acid in ionic liquid-an efficient and recyclable system for one-pot three-component Mannich reaction. *Canadian Journal of Chemistry*, 85(1):77-80, 2007.
119. Kumar, V., Sharma, U., Verma, P. K., Kumar, N. and Singh, B. Silica-supported boric acid with ionic liquid: A novel recyclable catalytic system for one-pot three-component Mannich reaction. *Chemical and Pharmaceutical Bulletin*, 59(5):639-645, 2011.
120. Zhao, G., Jiang, T., Gao, H., Han, B., Huang, J. and Sun, D. Mannich reaction using acidic ionic liquids as catalysts and solvents. *Green Chemistry*, 6(2):75-77, 2004.
121. Gao, H., Han, B., Li, J., Jiang, T., Liu, Z., Wu, W., Chang, Y. and Zhang, J. Preparation of room-temperature ionic liquids by neutralization of 1, 1, 3, 3-tetramethylguanidine with acids and their use as media for Mannich reaction. *Synthetic Communications*, 34(17):3083-3089, 2004.
122. Li, J., Peng, Y. and Song, G. Mannich reaction catalyzed by carboxyl-functionalized ionic liquid in aqueous media. *Catalysis Letters*, 102(3-4):159-162, 2005.

123. Sahoo, S., Joseph, T. and Halligudi, S. B. Mannich reaction in Brønsted acidic ionic liquid: A facile synthesis of β-amino carbonyl compounds. *Journal of Molecular Catalysis A: Chemical*, 244(1-2):179-182, 2006.

124. Dong, F., Jun, L., Xin-Li, Z. and Zu-Liang, L. Mannich reaction in water using acidic ionic liquid as recoverable and reusable catalyst. *Catalysis Letters*, 116(1-2):76-80, 2007.

125. Dong, F., Zhenghao, F. and Zuliang, L. Functionalized ionic liquid as the recyclable catalyst for Mannich-type reaction in aqueous media. *Catalysis Communications*, 10(8):1267-1270, 2009.

126. Gong, K., Fang, D., Wang, H. L. and Liu, Z. L. Basic functionalized ionic liquid catalyzed one-pot Mannich-type reaction: Three component synthesis of β-amino carbonyl compounds. *Monatshefte für Chemie-Chemical Monthly*, 138(11):1195-1198, 2007.

127. Yue, C. Aromatic compounds Mannich reaction using economical acidic ionic liquids based on Morpholinium salts as dual solvent-catalysts. *Synthetic Communications*, 40(24):3640-3647, 2010.

128. He, L., Qin, S., Chang, T., Sun, Y. and Zhao, J. Geminal Brønsted acid ionic liquids as catalysts for the mannich reaction in water. *International Journal of Molecular Sciences*, 15(5):8656-8666, 2014.

129. Porkodi, J., Nagarajan, S., Selvam, S. and Kandasamy, E. Synthesis of β-aminocarbonyl compounds catalyzed by 1-propylimidazolium trifluroacetoacetate. *Der Pharma Chemica*, 7:260-264, 2015.

130. Sardar, S., Wilfred, C. D. and Leveque, J. M. One-pot Mannich base synthesis using task specific protic ionic liquids. *Malaysian Journal of Analytical Sciences*, 21(5):1203-1209, 2017.

131. Chang, T., He, L., Bian, L., Han, H., Yuan, M. and Gao, X. Brønsted acid-surfactant-combined catalyst for the mannich reaction in water. *RSC Advances*, 4(2):727-731, 2014.

132. Alvim, H. G., Bataglion, G. A., Ramos, L. M., de Oliveira, A. L., de Oliveira, H. C., Eberlin, M. N., de Macedo, J. L., da Silva, W. A. and Neto, B. A. Task-specific ionic liquid incorporating anionic heteropolyacid-catalyzed Hantzsch and Mannich multicomponent reactions. Ionic liquid effect probed by ESI-MS (/MS). *Tetrahedron*, 70(20):3306-3313, 2014.

133. Huan, P., Yulin, H., Rong, X. and Dong, F. Choline-based biodegradable ionic liquid catalyst for Mannich-type reaction. *Journal of Chemical Sciences*, 128(12):1855-1860, 2016.

134. Wang, H. B., Yao, N., Wang, L. and Hu, Y. L. Brønsted-Lewis dual acidic ionic liquid immobilized on mesoporous silica materials as an efficient cooperative catalyst for Mannich reactions. *New Journal of Chemistry*, 41(19):10528-10531, 2017.

135. Shirini, F., Khaligh, N. G. and Akbari-Dadamahaleh, S. Preparation, characterization and use of 1, 3-disulfonic acid imidazolium hydrogen sulfate as an efficient, halogen-free and reusable ionic liquid catalyst for the trimethylsilyl protection of hydroxyl groups and deprotection of the obtained trimethylsilanes. *Journal of Molecular Catalysis A: Chemical*, 365:15-23, 2012.

136. Ramasamy, R. Vibrational spectroscopic studies of imidazole. *Armenian Journal of Physics*, 8(1):51-55, 2015.

137. Smith, M. C., Xiao, Y., Wang, H., George, S. J., Coucouvanis, D., Koutmos, M., Sturhahn, W., Alp, E. E., Zhao, J. and Cramer, S. P. Normal-mode analysis of $FeCl_4^-$ and $Fe_2S_2Cl_4^{2-}$ via vibrational Mössbauer, resonance Raman, and FT-IR spectroscopies. *Inorganic chemistry*, 44(16):5562-5570, 2005.

138. Devashankar, S., Mariappan, L., Sureshkumar, P. and Rathnakumari, M. Growth and characterization of tetramethyl ammonium tetrachloro zincate II: A ferroic crystal. *Journal of Crystal Growth*, 311(17):4207-4212, 2009.

139. Kumar, A., Kumar, M., Verma, S. K., Alvi, P. A. and Jasrotia, D. S. Single crystal growth, x-ray structure analysis, optical band gap, raman spectra, strain tensor and photoluminscence properties in $[HgCl_4]^-[R]^+$ and $[ZnCl_4]^-[R]^+$ (R = 2-amino-5-chloropyridine) hybrid materials. *Journal of Fundamental and Applied Sciences*, 7(3):422-435, 2015.

140. M. Bartkowska, M. Regel-Rosocka, J. Szymanowski. Extraction of zinc (II), iron (III) and iron (II) with binary mixtures containing tributyl phosphate and di (2-ethylhexyl) phosphoric acid or Cyanex 302. *Physicochemical Problems of Mineral Processing*, 36:217-224, 2002.

141. Bäcker, T., Breunig, O., Valldor, M., Merz, K., Vasylyeva, V. and Mudring, A. V. In-situ crystal growth and properties of the magnetic ionic liquid $[C_2mim][FeCl_4]$. *Crystal Growth & Design*, 11(6):2564-2571, 2011.

142. Kogelnig, D., Stojanovic, A., vd Kammer, F., Terzieff, P., Galanski, M., Jirsa, F., Krachler, R., Hofmann, T. and Keppler, B. K. Tetrachloroferrate containing ionic liquids: Magnetic-and aggregation behavior. *Inorganic Chemistry Communications*, 13(12):1485-1488, 2010.
143. Wei, X., Yu, L., Wang, D., Jin, X. and Chen, G. Z. Thermo-solvatochromism of chloro-nickel complexes in 1-hydroxyalkyl-3-methyl-imidazolium cation based ionic liquids. *Green Chemistry*, 10(3):296-305, 2008.
144. Khokhryakov, A. A., Mikhaleva, M. V. and Paivin, A. S. Electronic absorption spectra of nickel dichloride and nickel oxide solutions in the 2CsCl-NaCl and KCl-NaCl melts. *Russian Journal of Inorganic Chemistry*, 51(8):1311-1314, 2006.
145. Narayanan, R., Deepa, M. and Srivastava, A. K. Nanoscale connectivity in a TiO_2/CdSe quantum dots/functionalized graphene oxide nanosheets/Au nanoparticles composite for enhanced photoelectrochemical solar cell performance. *Physical Chemistry Chemical Physics*, 14(2):767-778, 2012.
146. Quicksall, C. O. and Spiro, T. G. Raman spectra of tetrahalozincates and the structure of aqueous $ZnCl_4^{2-}$. *Inorganic Chemistry*, 5(12):2232-2233, 1966.
147. ChunHui, Y., LinLin, W., HuanHuan, G., HongMei, S. and Qi, S. An efficient and recyclable iron (III)-containing imidazolium salt catalyst for cross-coupling of aryl Grignard reagents with alkyl halides. *Chinese Science Bulletin*, 57(16):1953-1958, 2012.
148. Yatsimirskii, K. B. Spectroscopic studies on coordination compounds formed in molten salts. *Pure and Applied Chemistry*, 49(1):115-124, 1977.
149. Thomazeau, C., Olivier-Bourbigou, H., Magna, L., Luts, S. and Gilbert, B. Determination of an acidic scale in room temperature ionic liquids. *Journal of the American Chemical Society*, 125(18):5264-5265, 2003.
150. Wang, Y. Y., Li, W. and Dai, L. Y. Brønsted acidic ionic liquids as efficient reaction medium for cyclodehydration of diethylene glycol. *Chinese Journal of Chemistry*, 26(8):1390-1394, 2008.
151. Wynands, L., Delacroix, S., Van Nhien, A. N., Soriano, E., Marco-Contelles, J. and Postel, D. New glycosyl-α-aminotetrazole-based catalysts for highly enantioselective aldol reactions. *Tetrahedron*, 69(24):4899-4907, 2013.

152. Eftekhari-Sis, B., Abdollahifar, A., Hashemi, M. M. and Zirak, M. Stereoselective synthesis of β-Amino Ketones via Direct Mannich-type reactions, catalyzed with $ZrOCl_2$ $8H_2O$ under solvent-free conditions. *European Journal of Organic Chemistry*, 2006(22):5152-5157, 2006.
153. Wang, Q., Geng, Y., Lu, X. and Zhang, S. First-row transition metal-containing ionic liquids as highly active catalysts for the glycolysis of poly (ethylene terephthalate) (PET). *ACS Sustainable Chemistry & Engineering*, 3(2):340-348, 2015.
154. Sakal, S. A., Lu, Y. Z., Jiang, X. C., Shen, C. and Li, C. X. A promising ionic liquid [BMIM][$FeCl_4$] for the extractive separation of aromatic and aliphatic hydrocarbons. *Journal of Chemical & Engineering Data*, 59(3):533-539, 2014.
155. Dutta, A. K., Gogoi, P. and Borah, R. Synthesis of dibenzoxanthene and acridine derivatives catalyzed by 1, 3-disulfonic acid imidazolium carboxylate ionic liquids. *RSC Advances*, 4(78):41287-41291, 2014.