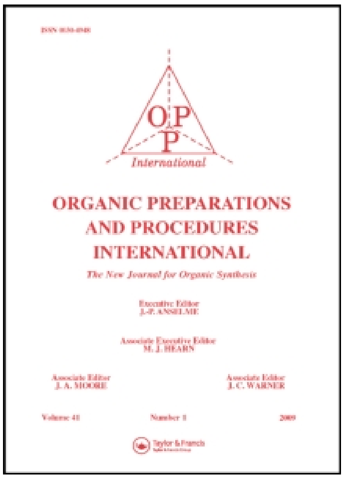

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Introduction

One of the important principles of green chemistry is the elimination of hazardous solvents in chemical synthesis, by which the use of expensive toxic solvents and the generation of wastes can be avoided.[1] In recent years, ionic liquids (ILs) have attracted increasing interest and been successfully used in a variety of reactions as environmentally benign solvents and catalysts due to their relatively low viscosities, low vapor pressure, and high thermal and chemical stability.[2–5] Much attention has currently been focused on the organic reactions with ILs as catalysts or solvents, and many organic reactions have been performed in ILs with excellent outcomes.

Recently, the synthesis of task-specific ionic liquids (TSILs) with special functions according to the requirement of a particular reaction has become an attractive field. All these studies offer the possibility of designing suitable catalysts for a given reaction.[6]An increasing interest in TSILs focuses on designing acidic TSILs to replace traditional liquid acids, such as sulfuric acid and hydrochloric acid, in chemical processes.[7] The conventional Lewis and Bronsted catalysts are often toxic, corrosive, and difficult to separate and recover from products despite their high catalytic activity.[8–9] Utilization of solid acids may be a solution to the problem. However, the shortcomings of rapid deactivation and decrease of activity sites *per* area limit their application to some degree. The design of a catalyst with high activity and selectivity, which is benign to the environment and easily recovered, is an interesting and rapidly developing area in chemistry.[10–12]

Acidic ILs have potential as dual solvents-catalysts in organic reactions. It is well known that ILs with metal halide anions manifest Lewis acidity, especially those based on chloroaluminate anions.[7] Acidic Bronsted ionic liquids (ABILs) are of special importance

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because they possess simultaneously the proton acidity and the characteristic properties of an ionic liquid.[13]

Acidic Bronsted or Lewis ionic liquids, environmental-friendly catalysts, now have the attention of researchers, and many organic reactions, such as esterification, polymerization, alkylation, acylation, carbonylation, aldol condensation, and pinacol rearrangement, nitration and Koch reaction, oxidation of alcohols, alcohol dehydrodimerization, Mannich reaction, cleavage of ethers, and Beckmann rearrangement, have been reported with excellent selectivity, and the ILs used were of outstanding recyclability.[14]

Cole first synthesized acidic Bronsted functionalized ILs and used them as solvent-catalysts in esterifications; the results showed that acidic functionalized ILs could be reused for at least five times without significant loss of activity in the synthesis of ethyl acetate.[15] The introduction of acidic Bronsted functional groups into cations or anions of the ILs, especially SO_3H-functional groups, has obviously enhanced their acidities and water solubilities, and gives great promise for using ILs as green catalysts in many typical acid-catalyzed organic reactions with good catalytic activities.[16–17]

Recently, alkanesulfonic acid-functionalized ionic liquids were reported, offering a new possibility for the development of environmentally friendly acidic catalysts, due to the combination of the advantages of liquid acids and solid acids, such as uniform acid sites, stability in water and air, easy separation and reusability. These $-SO_3H$ functionalized strong acidic Bronsted ionic liquids exhibited great potential in replacement of conventional homogenous/heterogeneous acidic catalysts because they are nonvolatile, non-corrosive, and immiscible with many organic solvents and could be used as dual solvents and catalysts.[1]

Acidic Bronsted ionic liquids containing an alkanesulfonic acid group attached to an imidazole, triphenylphosphine, pyridinium cation, or quaternary amine have been considered as promising new reaction media and found wide use in organic reactions.[10,18] Acidic Bronsted ionic liquids bearing acid counteranions ($[HSO_4^-]$ and $[H_2PO_4^-]$) have been used in many typical acid-catalyzed organic reactions.[19]

This review article provides an overview of the most recent and exciting developments in this fast-growing field. The procedures in this review were extracted from the given References (1–119) in the years between 1999 to the beginning of 2009. Interested readers are invited to consult the original literature for the unique and productive details.

I. Acidity and Characterization of Acidic Bronsted ILs

Many chemical transformations are sensitive to the presence of protons. Therefore, knowledge of the pK_a value, especially of the liquid salts, was important in order to decide about their possible application as reaction media. A common and effective way to evaluate the acidity of Bronsted acids was the Hammett method, first proposed by Gilbert *et al.* in 2003 on the basis of the Hammett acidity function, wherein a basic indicator was used to trap the acidic proton. In reported papers, authors used different methods and techniques for the determination of the acidity of ionic liquids. The measurement of the acidic scale of these acidic Bronsted ILs was conducted on a UV-Vis spectrophotometer with a basic indicator. Increasing the acidic scale of the acidic IL, the absorbance of the unprotonated form of the basic indicator was decreased, whereas the protonated form of the indicator was not observed because of its small molar absorptivity and its wavelength. Thus [I]/[IH] (I represents the indicator) ratio was determined from the measured absorbance differences after

Table 1

Calculation and Comparison of H_0 of Different ILs in CH_2Cl_2

Entry	IL	A_{max}	[I]%	$[IH^{]}]$%	H_0
1		2.582	100.0	0	—
2	[Hmim]Tsa	2.497	96.7	3.3	2.45
3	[Hmim]BF_4	1.703	66.0	34.0	1.28
4	[Bmim]HSO_4	1.012	39.2	60.8	0.80
5	[Bmim]H_2PO_4	2.200	85.2	14.8	1.75
6	[Amim]HSO_4	1.445	56.0	44.0	1.09
7	[Amim]H_2PO_4	2.312	89.5	10.5	1.92
8	[SPmim]HSO_4	0.236	9.1	90.9	−0.01

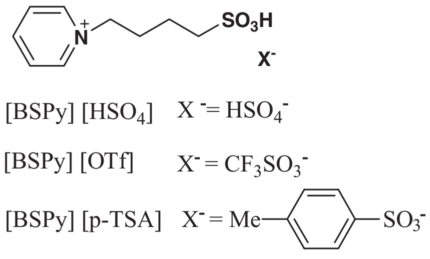
addition of an acidic Bronsted IL, and then the Hammett function, H_0, was calculated by using *Equation 1*. This value was regarded as the relative acidity of the IL.[18] Where $pK(I)_{aq}$ was the pK_a value of the indicator, [I] and $[IH^+]$ were, respectively, the molar concentrations of the unprotonated and protonated forms of the indicator, determined by UV–visible spectroscopy. When an acidic IL was added, the absorbance of the unprotonated form of the indicator decreased.

$$H_0 = pK(I)_{aq} + \log([I]/[IH^+])$$

Equation 1

The authors obtained the acidity order of several ILs with the H_0 values that are shown in *Table 1*: [SPmim]HSO_4 (1-(3-sulfopropyl)-3-methylimidazolium hydrogen sulfate)> [Bmim]HSO_4 (1-butyl-3-methylimidazolium dihydrogen phosphate)> [Amim]HSO_4 (1-amyl-3-methylimidazolium hydrogen sulfate)> [Hmim]BF_4 (1-methylimidazolium tetrafluoroboric acid)> [Bmim]H_2PO_4 (1-butyl-3-methylimidazolium dihydrogen phosphate)> [Amim]H_2PO_4 (1-amyl-3-methylimidazolium dihydrogen phosphate)> [Hmim]Tsa (1-methylimidazolium *p*-toluenesulfonic acid). The data suggested that the Bronsted acidity of [SPmim]HSO_4 was relatively stronger than the other ILs.

The acidities of the three ionic liquids containing [BSPy][OTf] (*N*-butane sulfone pyridinium (BSPy) triflate), [BSPy][HSO_4] (*N*-butane sulfone pyridinium (BSPy) hydrogen sulfate), [BSPy][p-TSA] (*N*-butanesulfonepyridinium (BSPy) *p*-toluenesulfonate) (*Scheme 1*)



Scheme 1

Table 2

H_0 Values of Ionic Liquid in CH_2Cl_2 at Room Temperature

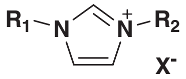
Entry	IL	A_{max}	[I]%	$[IH^{]}]$%	H_0
1		1.134	100.0	0	—
2	[BSPy][HSO_4]	0.709	62.5	37.5	1.21
3	[BSPy][OTf]	0.615	54.2	45.8	1.06
4	[BSPy][p-TSA]	1.007	88.8	11.2	3.98

were examined using 4-nitroaniline as indicator in dichloromethane. Dichloromethane was chosen as the test solvent, because it was an aprotic polar solvent, stable under acidic conditions and had considerable solubility for all tested ionic liquids. The maximal absorbance of the unprotonated form of 4-nitroaniline was observed at 349 nm in CH_2Cl_2. As the acidic ionic liquid was added, the absorbance of the indicator decreased.

The [I]/$[IH^+]$ ratio was determined by measuring the absorbance when each ionic liquids was added and then the Hammett function (H_0) was calculated. The results are shown in *Table 2*.

The experiments showed that the acidity order was: [BSPy][OTf] > [BSPy][HSO_4] > [BSPy][*p*-TSA]. It was clear that acidities of the ionic liquid depend on the anions. In a determination of minimum energy geometries of these ionic liquids, the results manifested that anions had strong interactions with the sulfonic acid proton. It was considered that in addition to the alkylsulfonic acid group, the conjugate acid of the corresponding anion was likely to serve as a potential catalytic acid. Therefore, the acidities and catalytic activities of the ionic liquids depended on the nature of the anion as well.[20]

The acidic strength of carboxylic acids was subjected to extensive experimental and theoretical studies. Imidazolium salts with carboxylic acid groups were regarded as nonclassical acids due to the presence of the positively charged imidazolium ring and of a counter anion (*Scheme 2*).



Scheme 2

The pK_a values of the carboxylic acid groups of compounds were determined by titration with KOH, and the results are shown in *Table 3*. The dicarboxylic acid with the shortest alkyl chain, was the strongest acid in the series ($pK_a = 1.33$); its acidity was comparable with the first deprotonation step in oxalic acid. The other diacids all had a lower first pK_a value (1.40–2.03) than the corresponding halogen-substituted acetic acids (XCH_2COOH, X = F, Cl, Br, I, 2.66–3.13) implying that the positively charged imidazolium ring was more strongly electron-withdrawing than the halides. As was known from aliphatic carboxylic acids, increasing the alkyl chain length led to a decrease in acidity. Interestingly, the presence of the positive charge on the imidazolium ring had only a minor effect on the acidity once the aliphatic spacer was sufficiently long. The stronger acids had higher

Table 3

pK$_a$ Values of Carboxylic Acids at 25°C

Entry	R$_1$	R$_2$	X$^-$	pK$_a$
1	CH_3	CH_2COOH	Cl	1.90
2	CH_3	CH_2COOH	BF_4	2.00
3	CH_3	CH_2COOH	SO_3CF_3	2.03
4	CH_3	$(CH_2)_3COOH$	Cl	3.83
5	CH_3	$(CH_2)_3COOH$	BF_4	3.95
6	CH_3	$(CH_2)_3COOH$	SO_3CF_3	4.11
7	CH_2COOH	CH_2COOH	Cl	1.33
8	CH_2COOH	CH_2COOH	BF_4	1.40
9	CH_2COOH	CH_2COOH	SO_3CF_3	1.44
10	$(CH_2)_3COOH$	$(CH_2)_3COOH$	Cl	3.46
11	$(CH_2)_3COOH$	$(CH_2)_3COOH$	BF_4	3.60
12	$(CH_2)_3COOH$	$(CH_2)_3COOH$	SO_3CF_3	3.65
13[a]	CH_3	$(CH_2)_3COOH$	Cl	4.59
14	CH_2COOH	CH_2COO^-	—	2.92
15	$(CH_2)_3COOH$	$(CH_2)_3COO^-$	—	4.47

[a] One proton is shared by two imidazolium molecules: [CH_3-Im-$(CH_2)_3$COO. . .H. . .OOC$(CH_2)_3$-Im-CH_3]Cl.

melting points than the weaker acids, and this was attributed to increased hydrogen-bonding interactions.[21]

II. Procedures for the Synthesis of Acidic Bronsted Ils Based on Acidic Cations and Acidic Anions

There are two basic methods for the preparation of ionic liquids: metathesis of a halide salt with the desired anion, and acid-base neutralization reactions. Acidic ionic liquids were synthesized by direct neutralization of imidazoles, alkylimidazoles, pyridine and other amines that may have acidic groups in the cation, with acids that formed ionic liquids with an acidic cation or acidic anion.[19]

1. Based on Quaternary Ammonium Cations

a) Triethylammonium Dihydrogen Phosphate ([Et_3NH]H_2PO_4)

The synthesis of ionic liquid was carried out in a round-bottomed flask, which was immersed in a recirculating heated water-bath and fitted with a reflux condenser. Phosphoric acid (85%) was added dropwise into triethylamine in 1:1 molar ratio (1.0 mol) at 60°C for 1 h. After the addition, the reaction mixture was stirred for an addition at period of 2 h at 70°C to ensure the reaction had proceeded to completion. Water was removed by heating the residue at 80°C in high vacuum (5 mm Hg) until the weight of the residue remained constant. The yield of [Et_3NH][H_2PO_4] was 99%.[22]

b) Triethylammonium Hydrogen Sulfate ([Et_3NH]HSO_4)

Triethylamine was dissolved in dichloromethane (10 ml), and concentrated H_2SO_4 *in 1:1 molar ratio (0.02 mol) was added slowly at 0°C. The reaction mixture was stirred at room temperature for 30 min. The resulting ionic liquid was washed by diethyl ether and dried in a vacuum at 80°C. The yield of* [Et_3NH][HSO_4] *was 100%.*[23]

c) 2-Hydroxyethylammonium Formate

*2-Aminoethanol (0.2 mol) was placed in a two necked flask equipped with a reflux condenser and a dropping funnel. The flask was mounted in an ice bath. Formic acid (0.2 mol) was added dropwise to the flask for about 45 min and stirring was continued for 24 h at room temperature, to obtain a clear viscous liquid. No crystallization or solidification was observed when the liquid sample was stored at 20°C for over 1 month. The freezing point of the liquid was found to be −82°C (*Scheme 3*).*[24]

$$\mathrm{HO\text{-}CH_2\text{-}CH_2\text{-}NH_2 + HCOOH \longrightarrow HO\text{-}CH_2\text{-}CH_2\text{-}NH_3^+\ HCOO^-}$$

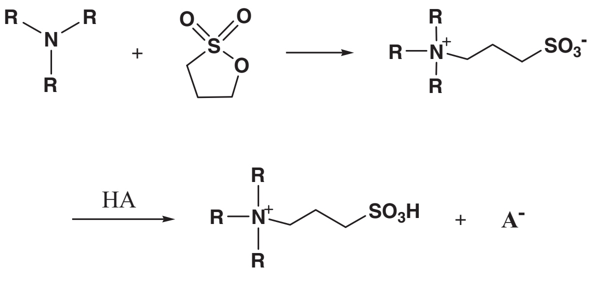
Scheme 3

d) Ionic Liquids Based on $Et_3NHCl{\cdot}xAlCl_3$

The cation and anion of the ionic liquid were provided by amine hydrochloride and anhydrous $AlCl_3$*, respectively. The ionic liquid is known as* $Et_3NHCl.xAlCl_3$*, where x is the appropriate mole fraction of* $AlCl_3$*. Triethylamine hydrochloride (*Et_3NHCl*) and anhydrous* $AlCl_3$ *was added in 1:0.67 molar ratio to a three-neck flask under the protection of dry nitrogen in stages forming a liquid. The mixture was stirred at room temperature for 30 min and then was heated to 80°C. The chloroaluminate ionic liquid was required to be kept in a desiccator because it easily reacts with moisture.*[3]

e) tri-n-Butylammonium Propanesulfonate (TBAPS)

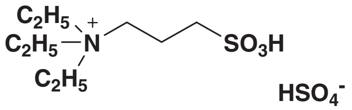
*Tributylamine and 1,3-propanesulfone in a 1:1 molar ratio (0.1 mol) were dissolved in 1,2-dichloroethane (20 ml) and stirred under nitrogen for 24 h at 35–40°C. The white precipitate formed, was collected and washed with petroleum ether. The product was recrystallized from a mixture of chloroform, petroleum ether, and acetone. A 97% yield of white solid was obtained, mp. 172–173°C (*Scheme 4*).*[10]



Scheme 4

f) Triethylammonium Propanesulfonate (TEAPS)

*The same process used for TBAPS was performed, except the reaction was carried out for 12 h at 35–40°C. A 95% yield of white solid was obtained, mp. 290–292°C (*Scheme 5*).*[10]



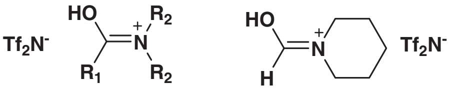
Scheme 5

g) Trimethylammonium Propanesulfonate (TMAPS)

The same process used for TBAPS was performed, except that the reaction was carried out for 2 h at 55–60°C. A 92% yield of white solid was obtained, mp. 344–346°C.[10]

h) Acidic Bronsted Ionic Liquids derived from N,N-Dimethylformamide and N-Formylpiperidine

*The essence of this methodology is simply neutralization of a given amide with a strong Bronsted acid followed by metathesis with an appropriate anion donor in aqueous media. For anion exchange, the lithium salt of bis(trifluoromethylsulfonyl)imide ($LiTf_2N$) was selected for its low melting point. This feature is attributed to the low lattice energy of Tf_2N salts and the negative charge of the anion being delocalized on the nitrogen and four oxygen atoms, generally resulting in weak coordinating strength (*Scheme 6*).*



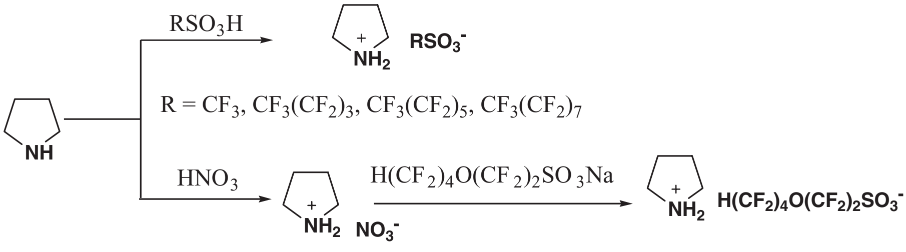
1) R_1 = H; R_2 = Me 2) R_1 = H; R_2 = Et
3) R_1 = H; R_2 = i-pr 4) R_1 = H; R_2 = Bu
5) R_1 = Me; R_2 = Me 6) R_1 = Me; R_2 = Et
7) R_1 = Et; R_2 = Me 8) R_1 = ph; R_2 = Me

Scheme 6

$DMFH^+\ NO_3^-$ was obtained by neutralization of DMF in an iced 1:1 (v/v) mixture with water by careful titration with HNO_3 (2.0 mol), followed by slow dropwise addition of a further equivalent of acid. In the second step, formation of the corresponding RTIL was accomplished by a metathesis reaction of $DMFH^+\ NO_3^-$ with a molar equivalent of $LiTf_2N$ (predissolved in water). Phase separation of the hydrophobic $DMFH^+\ Tf_2N^-$ occurred readily to form two layers on stirring. In order to drive phase separation, the two-phase system was further washed with HNO_3 (2.0 mol). After recovery of the lower RTIL phase, brief rotary evaporation effectively removed minor DMF and HNO_3 residues, leaving behind the desired RTIL as a nearly colorless free-flowing liquid in very high yield.[25]

i) Pyrrolidinium-based Ionic Liquid

*To a stirred solution of pyrrolidine (0.06 mol) in water (10 ml), trifluoromethanesulfonic acid (0.05 mol) was added slowly at room temperature. The reaction mixture was warmed to 60°C, stirred overnight, and then washed with diethyl ether. Removal of the solvent at reduced pressure afforded a white solid. A pure product was obtained after recrystallization from ethanol/diethyl ether. To a stirred solution of pyrrolidine (0.55 mol) in water (60 ml), nitric acid (47 g, 65–68%) was added slowly at room temperature. Then the reaction mixture was warmed to 60°C and stirred overnight. The solution was washed by diethyl ether. Removal of water at reduced pressure gave pyrrolidinium nitrate as a yellow solid. The solution of pyrrolidinium nitrate (0.194 mol) in methanol (50 ml) was added slowly to the solution of sodium 1,1,2,2-tetrafluoro-2-(1,1,2,2-tetrafluoroethoxy)ethanesulfonate (0.208 mol) in methanol (70 ml) and stirred for 12 h at room temperature. After filtration, the filtrate was concentrated to give a pale yellow liquid (*Scheme 7*).*[26]



Scheme 7

j) Lactam-based Ionic Liquids

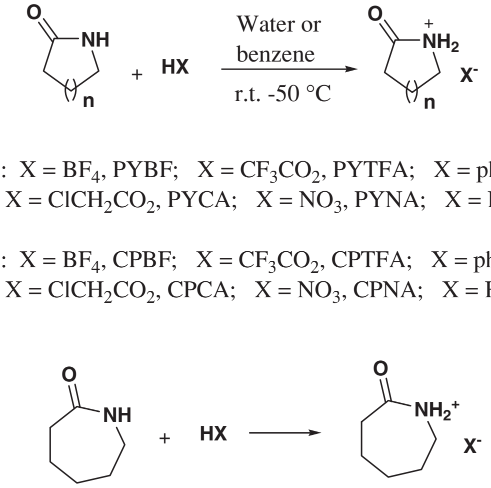
*Caprolactam was dissolved in aqueous 40% fluoroboric acid solution in 1:1 molar ratio (0.1 mol) and stirred for 30 min at room temperature, and then the water evaporated on a rotary evaporator. The residual traces of water were removed under vacuum (5–10 mmHg) for 4 h at 90°C, and a clear light yellow liquid caprolactam cation (abbreviated as [NHC])-based acidic Bronsted ILs [NHC][BF$_4$] was obtained in 99% yield. [NHC][NO3] and [NHC][CF$_3$COO] were also prepared with the same procedure as for [NHC][BF$_4$] (*Scheme 8*).*[27]

k) Guanidine-based Ionic Liquids

*Guanidine-based ILs, 1,1,3,3-tetramethylguanidinium (TMG) trifluoroacetate ([TMG][F$_3$Ac]) and TMG lactate ([TMG][Lac]) were prepared by neutralizing TMG with trifluoroacetic acid or lactic acid in 1:1 molar ratio (*Scheme 9*).*[28]

l) Novel Multi-SO$_3$H Functional Ionic Liquid

Triethylenediamine (0.1 mol) and 1,4-butanesulfonate (0.4 mol) were mixed in toluene and stirred magnetically for 72 h at 80°C. The white solid zwitterion that was formed was collected and washed repeatedly with ether. After drying in vacuum, the white solid was

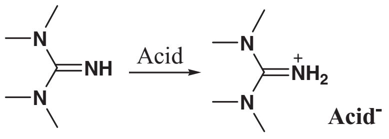


n = 1: X = BF_4, PYBF; X = CF_3CO_2, PYTFA; X = phCOO, PYBA;
X = $ClCH_2CO_2$, PYCA; X = NO_3, PYNA; X = H_2PO_4, PYBA

n = 3: X = BF_4, CPBF; X = CF_3CO_2, CPTFA; X = phCOO, CPBA;
X = $ClCH_2CO_2$, CPCA; X = NO_3, CPNA; X = H_2PO_4, CPPA

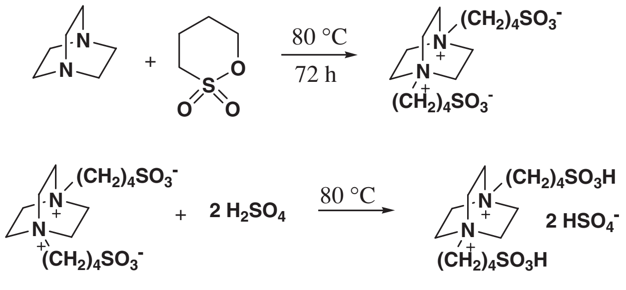
X = BF_4, NO_3, CF_3COO

Scheme 8



Scheme 9

*obtained in good yield (>90%). A stoichiometric amount of sulfuric acid was added to the above obtained zwitterion and the mixture was stirred for 6 h at 80°C to form the ionic liquid. The IL phase was washed repeatedly with toluene and ether to remove non-ionic residues, and dried in vacuum. The product was formed in 90% yield or better and in high purity (*Scheme 10*).*[29]



Scheme 10

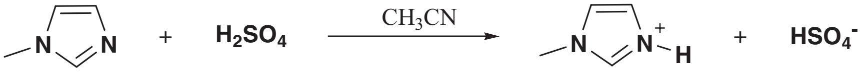
2. Based on Quaternary Imidazolium Cations

a) 1-Methylimidazolium Tetrafluoroborate ([Hmim]BF_4)

1-Methylimidazole (0.75 mol) was placed in a three necked flask, which was fitted with a magnetic stirrer and cooled to 0°C. Tetrafluoroboric acid (0.75 mol) (40% solution in water) was added slowly over a period of 30 min while stirring and cooling to maintain the temperature at 0–5°C. The reaction mixture was stirred for an additional period of 2 h at room temperature. Water was removed in vacuum to give the product as a colorless liquid, which solidified on cooling.[30]

b) 1-Methylimidazolium Hydrogen Sulfate ([Hmim]HSO_4)

*1-Methylimidazole (0.02 mol) in acetonitrile (5 ml) was charged into a round-bottom flask and the mixture was stirred at 0°C for 1 min. Then, a stoichiometric amount of concentrated sulfuric acid (1.03 ml) was added dropwise and the mixture stirred for 1 h at 0°C and then stirred for 2 h at room temperature. The acidic Bronsted ionic liquid was washed repeatedly with ether to remove non-ionic residues and dried in vacuum (*Scheme 11*).*[31]



Scheme 11

c) 3-Methylimidazolium Nitrate

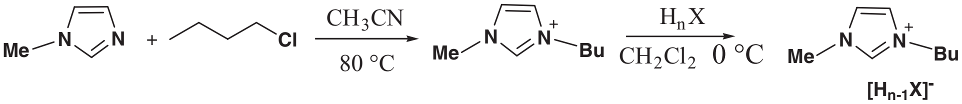
Acidic Bronsted [Hmim][NO_3] and [Hmim][Cl] could be obtained simply by neutralization. The combination of 1-methylimidazole with HNO_3 (67%) in a 1:1 molar ratio produces, after water removal, a white solid (mp. 67°C) identified as 3-methylimidazolium nitrate ([Hmim][NO_3]), whereas the same reaction with conc. HCl gave 3-methylimidazolium chloride ([Hmim][Cl]), a liquid at room temperature.[32]

d) 1-Butyl-3-methylimidazolium Hydrogen Sulfate ([Bmim] HSO_4)

A stoichiometric amount of conc. sulfuric acid was added to 1-butyl-3-methylimidazolium sulfate in 1:1 molar ratio and stirred for at least 2 h at 50°C to obtain a nearly colorless, viscous melt which crystallized after few hours (mp. 29–32°C).[33]

e) l-Butyl-3-methylimidazolium Dihydrogen Phosphate ([Bmim][H_2PO_4])

*[Bmim][H_2PO_4] and [Bmim][HSO_4] derived from chloride salts were obtained by the dropwise addition of one equivalent of conc. sulfuric acid (98%) or phosphoric acid (85%) to a cooled solution of l-butyl-3-methylimidazolium chloride in anhydrous dichloromethane. The mixture was refluxed for 48 h, and the HCl formed as a by-product was carried out of the condenser under a stream of dry nitrogen and dissolved in deionized water at 0°C. When the formed HCl had been completely removed, CH_2Cl_2 was evaporated on a rotary evaporator. The IL was dried under vacuum at 70°C for 6 h and stored in a desiccator (*Scheme 12*).*[8]



Scheme 12

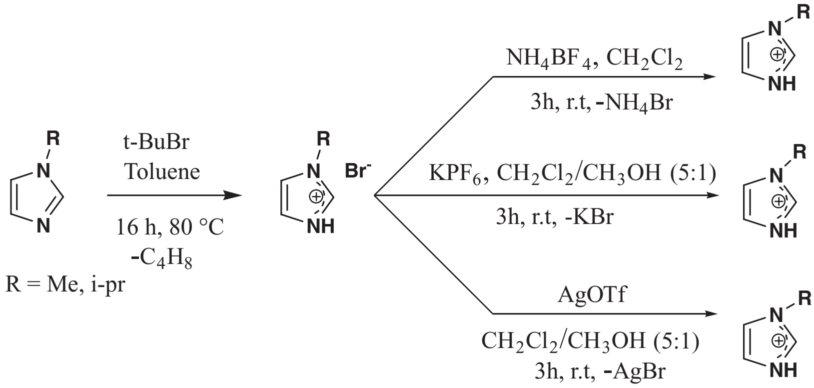
f) 1-Methylimidazolium Trifluoroacetate ([Hmim]Tfa) and 1-Methylimidazolium p-Toluenesulfonate ([Hmim]Tsa)

1-Methylimidazole was placed in a two-necked flask equipped with a magnetic stirrer and cooled in an ice water bath. A small amount of water was added and then the acid (trifluoroacetic acid or p-toluenesulfonic acid) in 1:1 molar ratio was added slowly with stirring. The reaction mixture was stirred for an additional period of 2 h. Water in the crude product was evaporated with a rotary evaporator at 70°C to afford a colorless liquid.[8]

g) N-Methyl- or N-Isopropylimidazolium Cations with Contain BF_4^-, PF_6^-, OTf^- *as Counteranions*

In a two-necked flask, tert-butyl bromide (0.05 mol) was added to a toluene (100 ml) solution of N-isopropylimidazole (0.04 mol). The resulting mixture was heated to 80°C for 16 h. The immiscible layers were separated by decanting the toluene and the sticky N-isopropylimidazolium bromide was washed with hexane and dried under vacuum.

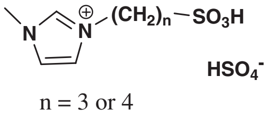
Ammonium tetrafluoroborate, potassium hexafluorophosphate, or silver triflate (0.015 mol) was added to a solution of N-isopropylimidazolium bromide in 1:1 molar ratio in CH_2Cl_2 *(25 ml)/*CH_3OH *(5 ml). The resulting mixture was stirred at room temperature for 3 h. The solution was cooled to −20°C, filtered and the volatiles were removed from the filtrate under vacuum to afford the respective ionic liquids (*Scheme 13*).*[34]



Scheme 13

h) 1-Methyl-3-(3-sulfopropyl)imidazolium and 1-Methyl-3-(3-sulfobutyl)imidazolium Hydrogen Sulfate

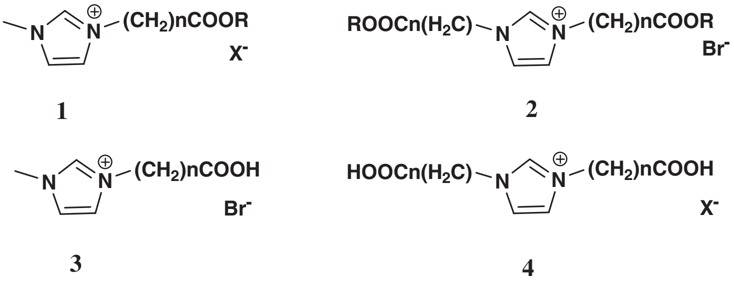
N-*Methylimidazole was stirred with 1,3-propane- or 1,4-butanesultone, respectively, at 40°C for 24 h. The zwitterions produced, all of which were white solids, were washed three* *times with toluene to remove unreacted material and dried in a vacuum. A stoichiometric amount of conc. sulfuric acid was added dropwise to the zwitterions, and the mixture was stirred at 40° C for 2–3 days until it liquefied, resulting in the formation of the ionic liquids. The ionic liquids were washed repeatedly with toluene and ether to remove unreacted material and dried under vacuum (*Scheme 14*).*[35]



Scheme 14

i) Imidazolium Cations with Carboxylic Ester or Acid Groups

*Cations with carboxylic ester groups have been prepared by quarternization of 1-methylimidazole with chloroalkylcarboxylic acid esters. Related imidazolium salts functionalized with 1,3-dicarboxylic esters were obtained from reaction of imidazole potassium salt with two equivalents of bromoalkylcarboxylic acid esters. Imidazolium salts containing carboxylic acid groups have been used as precursors for benzimidazolate zwitterions (*Scheme 15*).*[21]



Scheme 15

*Under an inert atmosphere of dry nitrogen a mixture of 1-methylimidazole (0.01 mol) and $Cl(CH_2)_nCOOCH_3$ ($n = 1$) (0.01 mol) was stirred at room temperature for 1 h, during which time the reaction mixture turned to a solid. The solid was washed with diethyl ether and dried under vacuum for 24 h to give **1**.*

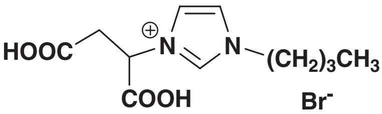
*A mixture of trimethylsilylimidazole (0.01 mol) and $Cl(CH_2)_nCOOCH_3$ ($n = 1$ or $n = 3$) (0.02 mol) was refluxed at 60° C for 24 h under an inert atmosphere of dry nitrogen. The reaction mixture was washed with diethyl ether and dried under vacuum for 24 h to give **2**.*

*A mixture of **1** (0.01 mol) and HCl (37% H_2O solution; 0.011 mol) was refluxed for 30 min. The solvent was removed under reduced pressure and the remaining solid was washed with acetone and diethyl ether to give the product **3** as a white powder.*

*A mixture of **2** (0.01 mol) and HCl (37% H_2O solution; 0.022 mol) was refluxed for 30 min. The solvent was removed under reduced pressure and the remaining solid was washed with acetone and diethyl ether to give the product **4** as a white powder.*

j) 1-(Double-2-methylbutyrate)-3-butylimidazole Bromide [(Ac)$_2$Bim]Br

A mixture of imidazole and dimethylmaleate in 1:1 molar ratio (0.22 mol) and acetone (40 ml) was charged into a three-necked flask equipped with a condenser. The reaction was performed for 24 h under reflux. The mixture was evaporated on a rotary evaporator at 80°C for 2 h in vacuo to remove the volatile materials to yield 1-(double-2-methylbutyrate)imidazole. Then, a mixture of 1-bromobutane (0.26 mol), certain amount of methanol and 1-(double-2-methylbutyrate)imidazole was charged into the three-necked flask at room temperature and stirred at 80°C for 12 h. Evaporation in vacuo *to remove methanol led to 1-(double-2-methylbutyrate)-3-butylimidazolium bromide. Then, concentrated HCl was added and the mixture stirred at 100°C for 2 h. The hydrolyzed mixture was evaporated on a rotary evaporator in vacuum over 2 h to remove the residual HCl. The product was cooled to room temperature to get [(Ac)$_2$Bim]Br as a clear viscous liquid (*Scheme 16*).*[6]



Scheme 16

k) 1-Ethylimidazolium Trifluoroacetate (HeimTA)

1-Ethylimidazole (0.20 mol) and water (10 ml) were placed in a two-necked round-bottomed flask equipped with a mechanical stirrer and cooled to −20°C with an ice-salt bath; under vigorous stirring, trifluoroacetic acid (1 mol) was introduced dropwise under the protection of a nitrogen atmosphere during a period of 10 min and then the mixture was further stirred at room temperature for another 1 h. Water and the low boiling impurities were removed under vacuum on a rotary evaporator at 70°C to afford a slightly yellowish liquid in 95% yield.[36]

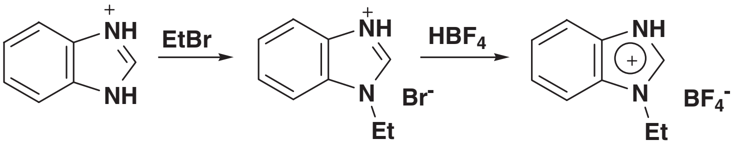
l) 1-Ethylbenzimidazolium Tetrafluoroborate ([Hebim]BF$_4$)

Benzimidazole (0.1 mol) and tetrabutylammonium bromide (0.3 g) as phase-transfer catalyst were dissolved in 30% aqueous solution of sodium hydroxide (100 ml). Bromoethane (0.1 mol) was added dropwise and the solution was stirred overnight at 45°C until two phases formed. The organic phase was separated and then was washed with deionized water and ethyl acetate. Finally, the remaining ethyl acetate was removed under vacuum (1.33 Pa) at 50°C for 3 h to give 1-ethylbenzimidazole (ebim) in 88% yield.

*Tetrafluoroboric acid (40% solution in water) was slowly added to a precooled solution (0–5°C) of 1-ethylbenzimidazole in 1:1 molar ratio (0.1 mol) in a three-necked flask with a magnetic stirrer. The reaction mixture was stirred for an additional period of 2 h at 0°C. Water was removed in vacuum to give the product as a colorless solid (*Scheme 17*).*[37]

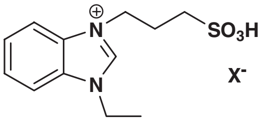
m) 1-Ethyl-3-(3-sulfopropyl)benzimidazolium Tetrafluoroborate and 1-Ethyl-3-(3-sulfopropyl)-benzimidazolium Hydrogen Sulfate

Under vigorous stirring, to 1,3-propanesulfone dissolved in toluene, was added an equaimolar amounts of ethylbenzimidazole and cooling to maintain the temperature at 0–5°C.



Scheme 17

*After the addition was complete, the mixture was slowly heated to room temperature and stirred for 2 h, and then the reaction mixture filtered by suction to remove the white precipitate which was then washed with diethyl ether and dried at 100°C for 5 h to give 3-(1-ethylbenzimidazolium-3-yl)propane-1-sulfonate (Ebim-PS) as white powder. Under vigorous stirring, Ebim-PS was dissolved in water, and equaimolar amount of tetrafluoroboric acid or sulfuric acid was added slowly at room temperature. After the addition was complete, the mixture was slowly heated up to 90°C and stirred for 2 h. Water was removed under vacuum at 70°C for 3 h affording [PSebim]HSO_4 and [PSebim]BF_4 as colorless solids (*Scheme 18*).*[38]



$X^- = BF_4^-, HSO_4^-$

Scheme 18

n) Preparation of [bis-BsImM][OTf]$_2$

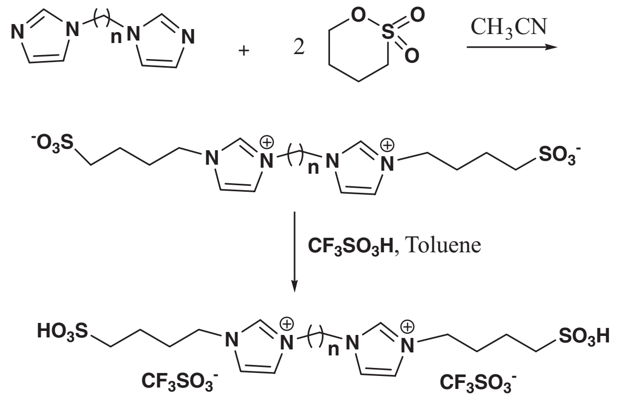
Bis-*(imidazolyl)methane and 1,4-butanesultone were mixed in a molar ratio of 1:2 at 80°C in anhydrous acetonitrile for 24 h. The resulting white powder was pulverized, washed with ethanol and dried in vacuum. The white powder and CF_3SO_3H were mixed in a molar ratio of 1:2 in anhydrous toluene, and heated at 80°C for 24 h, followed by washing with acetonitrile and ether and drying in vacuum to obtain the final IL as a yellow viscous liquid (*Scheme 19*).*[39]

o) 2,3-Dimethyl-1-alkylimidazolium Bromide (DmRimBr)

2,3-Dimethyl-1-alkylimidazolium bromide (DMRImBr, where R = ethyl, butyl, octyl) was prepared by the reaction of 1,2-dimethylimidazole with 1-bromoalkane and then the 2,3-dimethyl-1-alkylimidazolium bromide was washed with dry ethyl acetate to remove any starting material left in the reaction. Ethyl acetate was then removed by evaporation under reduced pressure.[40]

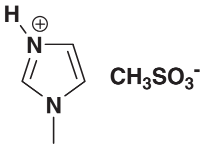
p) 3-Methylimidazolinium Methanesulfonate ([Hmim]CH_3SO_3)

1-Methylimidazole was placed in a round-bottom flask and cooled to 0°C. Methanesulfonic acid in 1:1 molar ratio (0.01 mol) was added slowly with stirring. The mixture was



1) n = 1, [bis-BSImM][OTf]$_2$; 2) n = 6, [bis-BSImH][OTf]$_2$;
3) n = 10, [bis-BSImD][OTf]$_2$

Scheme 19



Scheme 20

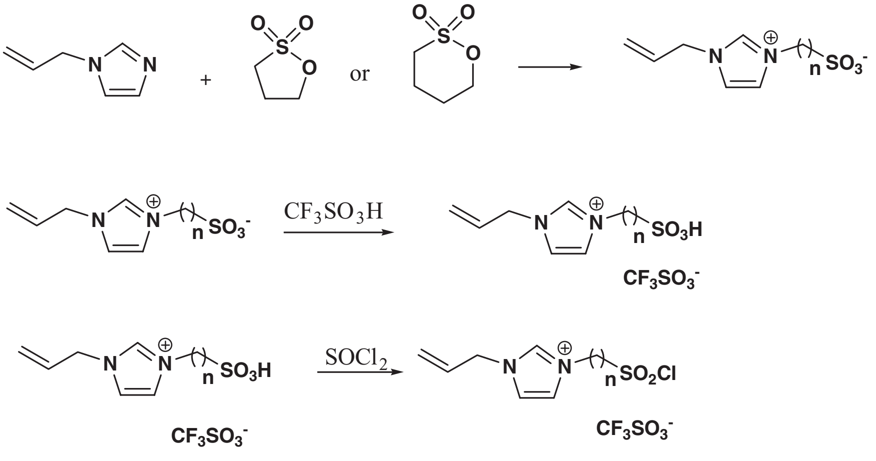
*stirred for 5 min at room temperature to give 3-methylimidazoliniummethane sulfonate (*Scheme 20*).*[41]

q) 1-Allylimidazolium Containing Zwitterionic Salts

1-Allyimidazole in 1:1 molar ratio (0.1 mol) was added to 1,3-propane- or 1,4-butanesultone slowly at 0°C. Then the mixture was stirred at room temperature for about 24 h until it turned into solid. The formed solid was collected, washed with ether, and dried in vacuum at room temperature.

For preparation of acidic Bronsted ionic liquids, CF_3SO_3H *(0.166 mol) was added to equimolar amount of 1-allyimidazolium zwitterionic salt slowly at 0°C. The contents of the flask were then stirred in an oil bath at 60°C for 12 h. The liquid product was washed with diethyl ether and dried in vacuum at 50°C for 2 h.*

*For preparation of Lewis acidic ionic liquids thionyl chloride (0.12 mol) was charged into a two-necked flask with a magnetic stirrer. Under reflux conditions, the acidic Bronsted ionic liquid was slowly added into the flask and then the reaction was allowed to proceed for 8 h. The unreacted thionyl chloride was removed by distillation to give the residual liquid as product. Then the product was washed by diethyl ether and dried in vacuum at 50°C for 2 h (*Scheme 21*).*[42]

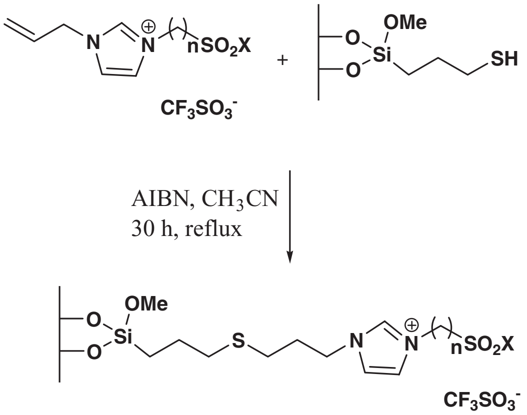


n = 3 or 4

Scheme 21

r) Acidic Ionic Liquids Modified Silica Gel

*To a round bottom flask with a magnetic stirrer above acidic ionic liquid (0.01 mol) (*Scheme 21*), 3-mercaptopropyltrimethoxysilane (MPS) modified silica gel (2 g), acetonitrile (50 ml) and 5% mol (to ionic liquid) azobiisobutyronitrile (AIBN) was added in sequence. Then the reaction mixture was heated under reflux for 30 h. The precipitate was collected and washed successively with acetonitrile, acetone and diethyl ether, and then dried in vacuum at 50°C for 6 h. (*Scheme 22*).*[42]

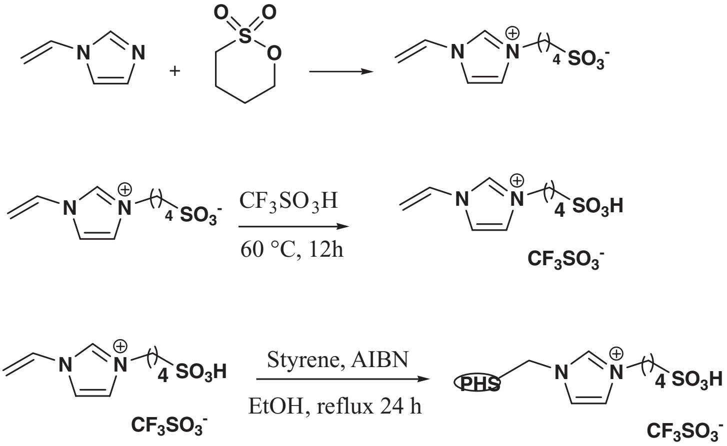


n = 3;   X=Cl, OH
n = 4;   X=Cl, OH

Scheme 22

s) Ionic Liquid Supported Polystyrene

*1-Vinylimidazolium bearing acidic Bronsted ionic liquid such as 3-vinyl-1-(4-sulfobutyl) imidazolium trifluoromethanesulfonate, was synthesized using the method described in the preparation of 1-allyimidazolium containing zwitterionic salts above. To co-polymerize the above acidic ionic liquid with styrene, purified styrene (0.03 mol), the ionic liquid (3.5–10% eq.) and AIBN (5% of vinyl group) were added to the solution of ethanol (50 mL), and then the mixture was stirred at reflux temperature for 24 h. After cooling, the precipitate was collected and washed with ethanol three times. After drying in vacuum at room temperature to remove ethanol, the precipitate was ground in a mortar to afford the ionic liquid immobilized polystyrene in the form of white powder (denoted as PS-IL), which was further washed with ethanol and finally dried in vacuum at room temperature (*Scheme 23*).*[13]

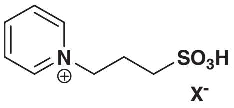


Scheme 23

3. Based on Quaternary Pyridinum Cations

a) N-Propanesulfonepyridinium (PSPy) with Different Anions

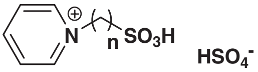
The synthesis of SO_3H-functional ionic liquids with different anions is conveniently performed. The corresponding acid as an aqueous solution, equimolar N-*propanesulfonepyridinium (PSPy) and solutions of acids (*e. g., *HBF_4 is 40% aqueous) were mixed and stirred for 24 h at 40–60°C. The combined solution was then dried in a vacuum at 100°C to remove the water. The produced ionic liquids were washed repeatedly with diethyl ether to remove unreacted material and dried in a vacuum again. If the corresponding acid was solid, such as* p-*toluenesulfonic acid hydrate (*p-*TSA.H_2O), the reaction required a higher temperature. In this case, equimolar PSPy and* p-*TSA.H_2O were mixed and heated to 80°C for 12 h; meanwhile, solid PSPy and* p-*TSA.H_2O were liquefied, resulting in the formation of [PSPy][p-TSA]. The resulting liquid was washed repeatedly with diethyl ether to remove unreacted material and dried* in vacuo *(*Scheme 24*).*[7]



$X^- = BF_4^-, H_2PO_4^-, HSO_4^-, p\text{-}CH_3C_6H_4SO_3^-$

Scheme 24

*Pyridine was stirred solvent free with 1,3-propane- or 1,4-butanesultone, respectively, at 40°C for 24 h. The zwitterions produced, all white solids, were washed with toluene to remove unreacted material and dried in a vacuum. A stoichiometric amount of concentrated sulfuric acid was added dropwise to the zwitterions, and the mixture was stirred at 40°C for 2–3 days until liquefied, resulting in the formation of the ionic liquids. The ionic liquids were washed repeatedly with toluene and ether to remove unreacted material and dried under vacuum (*Scheme 25*).*[7]



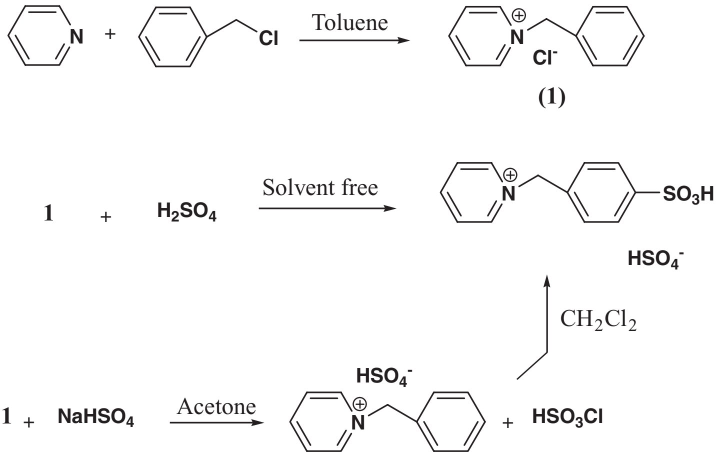
n = 3 or 4

Scheme 25

b) Benzylsulfonepyridinium Hydrogen Sulfate

Pyridine (0.0627 mol) was dissolved in toluene (25 ml) and cooled to 0–5°C, and an equimolar amount of benzyl chloride added slowly over a period of 30 min. The reaction was continued overnight at 0–5°C. After 24 h at room temperature, the reaction mixture was heated to 65–70°C for 24 h to afford the target compound in 92% yield (highly hygroscopic white crystal, mp. 125–128°C). N-*Benzylpyridinium chloride was added to* H_2SO_4 *(97%) in small portions at −5–0°C. Addition of the total amount of the* N-*benzylpyridinium chloride (about 1 h), gave* N-*benzylsulfonepyridinium hydrogen sulfate as yellowish oily liquid in 85% yield.*

Another method for preparation of this ionic liquid follows. A mixture of N-*benzylpyridinium hydrogen sulfate (0.0405 mol) and anhydrous dichloromethane (15 ml) was added dropwise into chlorosulfonic acid (0.425 mol) at 0–5°C over a period of 1.5 h under stirring. Stirring was continued at this temperature for 8 h, and then heated to 60–65°C for 4 h. Upon completion, dichloromethane was evaporated on a rotary evaporator. The reaction mixture was dried under high vacuum at 70°C for 4.5–6.5 h. The residue was purified by flash column chromatography using silica gel (methanol: ethyl acetate: 95:5),* N-*benzylsulfonepyridinium hydrogen sulfate was obtained as yellowish oil liquid in 87% yield (density (g/cm*^{3}*, 25°C): 1.44; viscosity (cP, 28°C): 197) (*Scheme 26*).*[16]



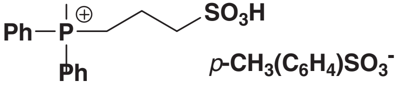
Scheme 26

4. *Based on Quaternary Phosphonium Cations*

a) Ionic Liquid Based on Triphenylphosphine

Reaction of the neutral nucleophiles triphenylphosphine with 1,4-butane- or 1,3-propanesultone, respectively, produced the requisite zwitterions in excellent yields. In a second step, addition of p-*toluenesulfonic acid converted the zwitterions into ionic liquids. The yields for both the zwitterion formation and acidification steps were essentially quantitative.*

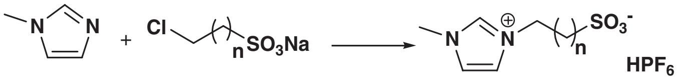
*The zwitterion acidification was accomplished by combining 1:1 molar quantities of the zwitterions with an acid possessing a pK_a sufficiently low to convert the pendant sulfonate group into an alkanesulfonic acid. The result was the transformation of the zwitterion into an ionic liquid cation bearing an appended sulfonic acid group, with the conjugate base of the exogenous acid becoming the IL anion (*Scheme 27*).*[43]



Scheme 27

5. *Based on Quaternary Hexafluorophosphate*

*The sulfonated imidazolium salts artificially modified by HPF_6 were prepared from a mixture of 3-ethylsulfonate-1-methylimidazolium ([Esmim]) or l-methyl-3-propylsulfonate imidazolium. ([Mpsim]) and one equivalent of HPF_6 (60%) solution under vigorous stirring at room temperature. It was estimated that the former reaction of [Esmim] [HPF_6] and [Mpsim] [HPF_6] were complete after a reaction time of 48 h (*Scheme 28*).*[44]



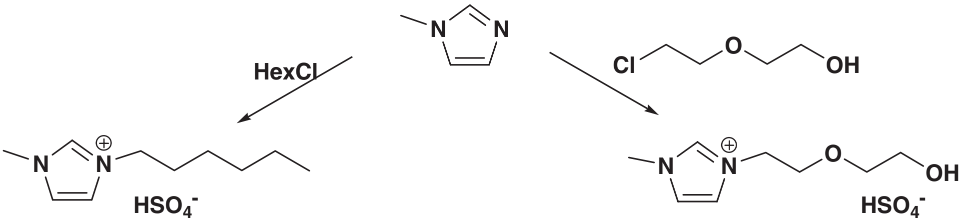
n = 1 [esmim][HPF_6]
n = 2 [mpsim][HPF_6]

Scheme 28

6. Based on Hydrogen sulfate

a) 1-Hexyl-3-methylimidazolium Hydrogen Sulfate ([Hmim]HSO_4) and 1-[2-(2-Hydroxyethoxy)ethyl]-3-methylimidazolium Hydrogen Sulfate ([Heemim]HSO_4)

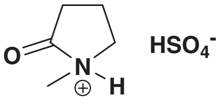
[Hmim][HSO_4] and [Heemim][HSO_4] derived from chloride salts were obtained by a dropwise addition of one equivalent of concentrated sulfuric acid (97%) to a cooled solution of the corresponding l-alkyl-3-methylimidazolium chloride (one equivalent) in anhydrous methylene chloride. The mixture was refluxed for 48 h and the HCl by-product formed in the reaction was distilled out under a stream of dry nitrogen and was dissolved in deionized water at 0°C. (The acid aqueous solution was monitored by titration with NaOH.) When the formed HCl was completely removed, the solution was cooled to room temperature and CH_2Cl_2 was evaporated on a rotary evaporator. The ionic liquid was dried under high vacuum (10^{-2} Torr) at 70°C for 6 h or by azeotropic distillation with benzene (Scheme 29*).*[44]



Scheme 29

b) 1-Methyl-2-pyrrolidinonium Hydrogen Sulfate [NMP][HSO_4]

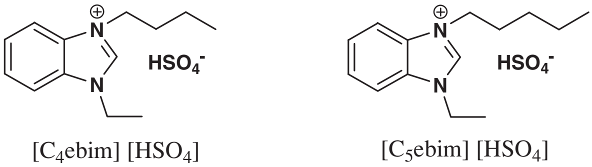
*1-Methyl-2-pyrrolidinone (0.2 mol) was charged into a three-necked flask with magnetic stirrer. Then equimolar concentrated sulfuric acid (98 wt%) was added dropwise slowly at 80°C for 12 h. The mixture was washed with ether three times to remove non-ionic residues and dried in vacuum using a rotary evaporator to obtain the viscous clear [NMP][HSO_4] (*Scheme 30*).*[6]



Scheme 30

c) 1-Butyl-3-ethylbenzimidazolium Hydrogen Sulfate ([C_4ebim]HSO_4) and 1-Amyl-3-ethylbenzimidazolium Hydrogen Sulfate ([C_5ebim]HSO_4)

*These were prepared by the dropwise addition of one equivalent of concentrated sulfuric acid to a cooled solution of [$C_n$ebim]Cl in anhydrous dichloromethane. The mixture was refluxed for 48 h; the by-product HCl formed in the reaction was carried out of the condenser under a stream of dry nitrogen and was dissolved in deionized water at 0°C. When HCl had been completely removed, CH_2Cl_2 was evaporated on a rotary evaporator. The ionic liquids were dried under vacuum at 70°C for 6 h and stored in a desiccator (*Scheme 31*).*[38]



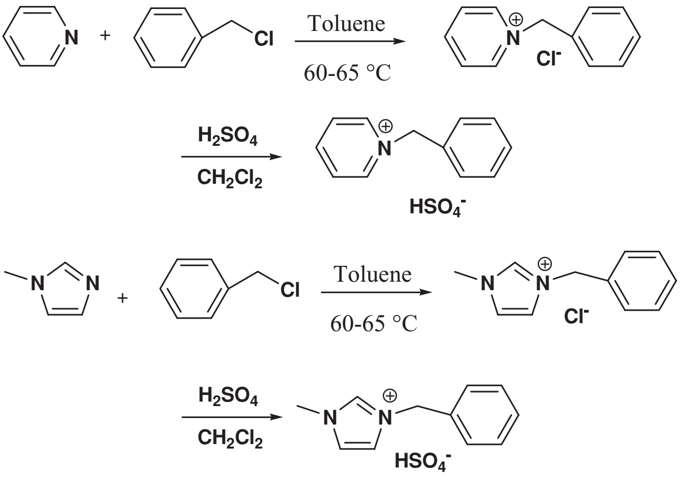
Scheme 31

d) 3-Benzyl-1-methylimidazolium and N-Benzylpyridinium Hydrogen Sulfate

N-*Methylimidazole and pyridine were separately alkylated by using benzyl chloride in the first step, and the resulting quaternary halides were finally transformed into the target compounds by using concentrated sulfuric acid as anion exchange agent. The resulting water-soluble acidic Bronsted ionic liquids were isolated as somewhat viscous oils with good mobility at room temperature. Their viscosities are 3630, 2650 (cP, 28°C), respectively.*

N-*Methylimidazole (0.03 mol) (or freshly distilled pyridine (0.314 mol)) was dissolved in toluene (25 ml) and equimolar amounts of benzyl chloride was added dropwise under stirring at 0–5°C over a period of 30 min. Stirring continued for 24 h at this temperature, then the mixture was heated to 65–70°C for 24 h. Upon completion, the solvent was evaporated under vacuum. The residual liquid was washed with ethyl acetate and then dried under vacuum at 70°C for 8 h to afford 3-benzyl-1-methylimidazolium chloride (off-white viscous oil liquid) in yield 97% and* N-*benzylpyridinium chloride (highly hygroscopic white crystal mp. 25–128°C) in yield 95%.*

The compounds 3-benzyl-1-methylimidazolium chloride (0.0231mol) or N-*benzylpyridinium chloride (0.0231 mol) were dissolved in anhydrous dichloromethane (25 ml). On cooling to −5–0°C, an equimolar amount of concentrated sulfuric acid (97%) or phosphoric acid (85%) was added dropwise over a period of 1.5 h under stirring. Stirring was continued at this temperature for 8 h, and the mixture then refluxed for 24 h under a stream of dry nitrogen (reaction progress monitored by titration of the HCl with 2 M NaOH solution). When the evolved form HCl had been completely removed, the solution was cooled to room temperature and CH_2Cl_2 was evaporated by rotary evaporation. The resulting ionic liquids were dried under high vacuum (10^{-2} Torr) at 70°C for 6–10 h to obtain the desired ionic liquids (*Scheme 32*).*[45]

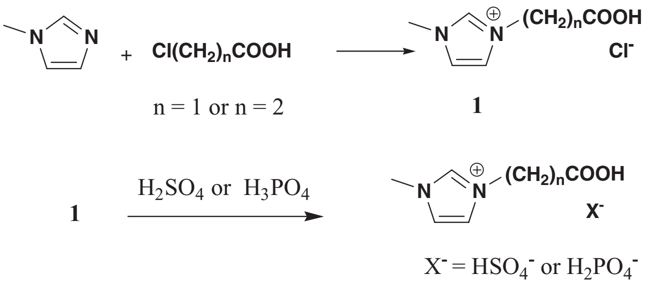


Scheme 32

e) Imidazolium Cations with Carboxylic Acid Groups

These ionic liquids were prepared by a two-step synthesis through initial combination of 1-methylimidazole with chloroacetic acid or 3-chloropropionic acid to form zwitterionic salts, followed by addition of concentrated sulfuric acid (97%) or phosphoric acid (85%). To a solution of chloroacetic acid (0.001 mol) in anhydrous chloroform (80 ml) at room temperature, 1-methylimidazole (0.001 mol) was added. The resulting mixture was stirred for 50 h at reflux. After the reaction, the solid produced was collected and washed with anhydrous ethanol to remove any unreacted starting materials. Then it was dried in vacuum, and zwitterionic salt (1) was obtained.

The acidic ionic liquids were obtained by dropwise addition of one equivalent of concentrated sulfuric acid (97%) to a cooled solution of the corresponding (1, one equivalent) in anhydrous methylene chloride. The mixture was stirred for 48 h at reflux. The HCl formed in the reaction as a by-product, was expelled out under a stream of dry nitrogen and dissolved in deionized water at 0°C. After the CH_2Cl_2 *was evaporated on a rotary evaporator, the ionic liquid was dried under vacuum (*10^{-2} *Torr) at 70°C for 6 h (*Scheme 33*).*[46]



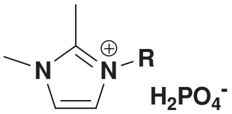
Scheme 33

7. Based on Dihydrogen Phosphate

a) 2,3-Dimethyl-1-alkylimidazolium Dihydrogen Phosphate ([DmRim]H_2PO_4)

2,3-Dimethyl-1-alkylimidazolium bromide (DMRImBr, where R = ethyl, butyl, octyl) was prepared by the reaction of 1,2-dimethylimidazole with 1-bromoalkane, and then 2,3-dimethyl-1-alkylimidazolium bromide was washed with dry ethyl acetate to remove any starting material left in the reaction. Ethyl acetate was then removed by evaporation under reduced pressure.

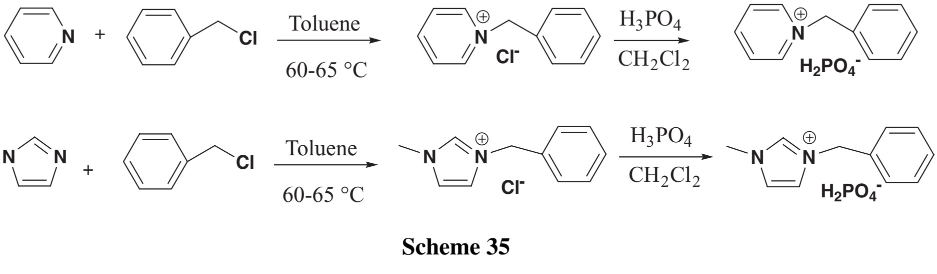
The anion exchange reaction of 2,3-dimethyl-1-alkylimidazolium bromide with potassium dihydrogen phosphate (KH_2PO_4*) was carried out in acetonitrile and the solution was stirred for 48 h at room temperature; precipitate of potassium bromide alkylimidazolium dihydrogenphosphate ([DmRim]*H_2PO_4*) was obtained after evaporating acetonitrile under reduced pressure (*Scheme 34*).*[40]



Scheme 34

b) 3-Benzyl-1-methylimidazolium Dihydrogen Phosphate and N-Benzylpyridinium Dihydrogen Phosphate

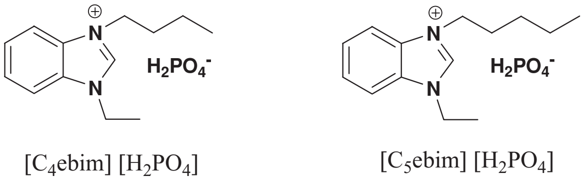
3-Benzyl-1-methylimidazolium chloride (0.0231 mol) or N-*benzylpyridinium chloride (0.0231 mol) was dissolved in anhydrous dichloromethane (25 ml). On cooling to −5–0°C, an equimolar amount of phosphoric acid (85%) was added dropwise over a period of 1.5 h under stirring conditions. Stirring continued at this temperature for 8 h, and the mixture then refluxed for 24 h under a stream of dry nitrogen (reaction progress monitored by titration with 2 M NaOH solution). When the formed HCl had been completely removed, the solution was cooled to room temperature and* CH_2Cl_2 *evaporated by rotary evaporation. The resulting ionic liquids were dried under high vacuum (*10^{-2} *Torr) at 70°C for 6–10 h to obtain the desired ionic liquids (*Scheme 35*).*[45]



Scheme 35

c) 1-Butyl-3-ethylbenzimidazolium Dihydrogen Phosphate ([C_4ebim]) and 1-Amyl-3-ethylbenzimidazolium Dihydrogen Phosphate ([C_5ebim]H_2PO_4)

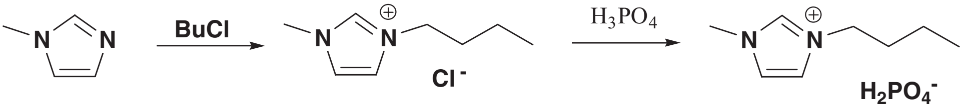
*These ionic liquids were prepared by dropwise addition of one equivalent of concentrated phosphoric acid to a cooled solution of [$C_n$ebim]Cl in anhydrous dichloromethane. The mixture was refluxed for 48 h; the by-product HCl formed in the reaction was carried out of the condenser under a stream of dry nitrogen and was dissolved in deionized water at 0°C. When HCl had been completely removed, CH_2Cl_2 was evaporated on a rotary evaporator. The ionic liquids were dried under vacuum at 70°C for 6 h and stored in a desiccator (*Scheme 36*).*[38]



Scheme 36

d) l-Butyl-3-methylimidazolium Dihydrogen Phosphate ([Hmim][H_2PO_4)

*[Bmim][H_2PO_4] derived from chloride salts were obtained by a dropwise addition of one equivalent of concentrated phosphoric acid (85%) to a cooled solution of the corresponding l-alkyl-3-methylimidazolium chloride (1 equivalent) in anhydrous methylene chloride. The mixture was refluxed 48 h and the HCl byproduct formed in the reaction distilled out of the condenser under a stream of dry nitrogen and dissolved in deionized water at 0°C (the acid aqueous solution was monitored by titration with NaOH.) When the formed HCl had been completely removed, the solution was cooled to room temperature, and CH_2Cl_2 evaporated with a rotary evaporator. The ionic liquid was dried under high vacuum (10^{-2} Torr) at 70°C for 6 h or by azeotropic distillation with benzene (*Scheme 37*).*[44]

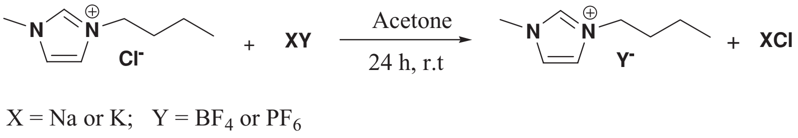


Scheme 37

8. Based on p-Toluenesulfonic Acid

a) 1-Butyl-3-methylimidazolium p-Toluenesulfonic Acid ([Bmim]PTSA)

*1-Butyl 3-methylimidazolium chloride (0.01 mol) was placed in a two-necked flask with stirrer and cooled to 0°C. Water (5 ml) was added to it, and then paratoluenesulfonic acid in 1:1 molar ratio (0.01 mol) added slowly under stirring. The mixture was stirred for 2 h and the water removed on a rotary evaporator at 60°C to obtain a green colored liquid (*Scheme 38*).*[47]



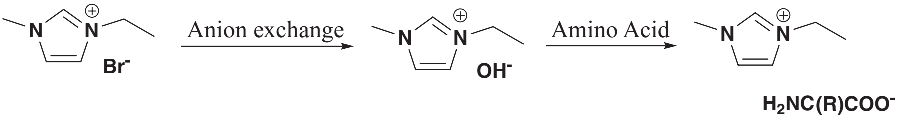
Scheme 38

9. Based on Amino Acids

a) 1-Ethyl-3-methylimidazolium Amino Acid

Preparation of amino acid ionic liquids (AAILs) was first undertaken by the present authors with 1-ethyl-3-methylimidazolium cation, [emim], which is a cation commonly used in preparing many ionic liquids. In the initial stage, we aimed to prepare [emim][AA] salts by anion exchange. Anion exchange reactions were effective when the target salts were water insoluble, whereas the byproducts (generally inorganic salts) are water soluble. Hydrophobic target salts then were obtained by simple washing with water. In the case of water soluble products, purification was not carried out by simple washing. While this was in principle a good method of preparing silver salts such as AgBr or AgCl, there was some concern over these silver salts dissolving into the ionic liquids formed. Since halogen anion content was a major issue in the preparation of ionic liquids, these methods were not recommended for the preparation of halogen-free ionic liquids.

*AAILs were prepared by a neutralization method. This method was also simple, involving the mixing of anion hydroxide and free acid. For this neutralization, [emim]OH was mixed with acid (HY) to prepare salts and water as a byproduct. To prepare [emim]OH aqueous solution, an anion exchange resin was used. An aqueous solution of [emim]OH prepared in this way was added to a slight excess of an equimolar amino acid aqueous solution so as to prepare [emim]AA. The product was dried in vacuum for 24 h at 80°C (*Scheme 39*).*[48]

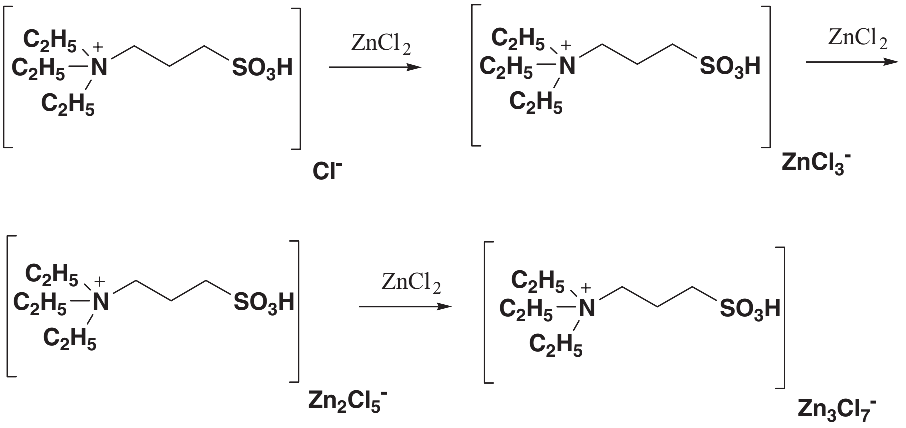


Scheme 39

10. Based on Lewis Acids

a) Ionic liquids Based on Trichlorozincinate Anions

The Bronsted–Lewis acidic ionic liquids were prepared by the reaction of [HSO_3—$(CH_2)_3$—NEt_3]Cl with different amounts of $ZnCl_2$. Under vigorous stirring, $ZnCl_2$ was added to [HSO_3—$(CH_2)_3$—NEt_3]Cl, then the mixture was reacted for 4 h at 100°C, giving Bronsted–Lewis acidic IL as viscous liquid at room temperature. With the increasing of the $ZnCl_2$ mass, the viscosity of the obtained IL also increased. The Lewis acidity of IL varied depending on the $ZnCl_2$ mass. When the molar fraction of $ZnCl_2$ was less than 0.5, the

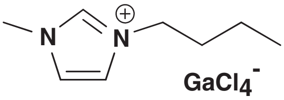


Scheme 40

*ILs only processed Bronsted acidity and no Lewis acidity, otherwise, the obtained ILs were Bronsted–Lewis acidic (*Scheme 40*).*[14]

b) [1-Butyl-3-methylimidazolium] [$GaCl_4$]

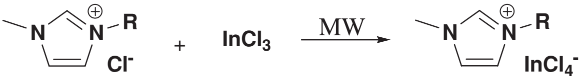
*Gallium trichloride (0.005 mol) and 1-butyl-3-methylimidazolium chloride (0.0051 mol) were placed in a glass test tube and mixed on a vortex mixer. The mixture was subjected to microwave (MW) irradiation at 600 W (twice for 15 s irradiation) in a Panasonic household MW oven until a crude mixture of the liquid and a small quantity of unreacted $GaCl_3$ remained, which was filtered using a syringe filter to afford colorless single phased liquid (Yield 94%) (*Scheme 41*).*[49]



Scheme 41

c) Imidazolium Based Tetrachloroindate(III)

*Admixing equimolar amounts of indium trichloride and solid 1-butyl-3-methylimidazolium chloride (0.005 mol), followed by MW irradiation for 30 s without any solvent afforded a crude mixture of liquid and small quantity of unreacted $InCl_3$, which was removed by filtration to afford colorless single phased liquid (mp. −6°C) (*Scheme 42*).*[50]

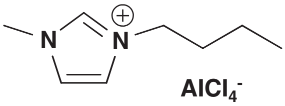


R = Methyl, Ethyl, Hexyl, Octyl

Scheme 42

d) Chloroaluminate Ionic Liquid

*1-Butyl-3-methylimidazolium tetrachloroaluminate was prepared by slowly adding equivalent aluminium(III)chloride (1.1 mol) to equivalent of 1-butyl-3-methylimidazolium chloride (1.0 mol) over a period of 8 h in toluene (*Scheme 43*).*[51]



Scheme 43

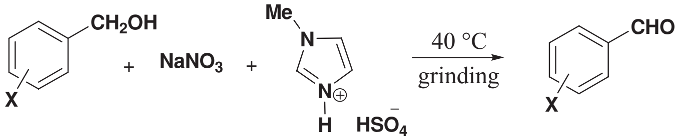
III. Application of Acidic Bronsted ILs in Organic Reactions

1. Oxidation

a) Oxidation of Alcohols

The transformation of alcohols to the corresponding carbonyl compounds is one of the most fundamental reactions in organic synthesis. Various methods have been developed for the oxidation of alcohols to the corresponding carbonyl compounds. Among other oxidation agents, nitric acid attracted much attention for the conversion of alcohols to the carbonyl compounds mainly due to its ready availability and strong oxidizing power. However, all of the oxidative methods suffered from one or more drawbacks, such as use of toxic heavy metal reagents, long reaction times, low yields, and inconvenient work-up procedures. Moreover, most of the oxidation reactions were conducted in volatile and toxic organic solvents.

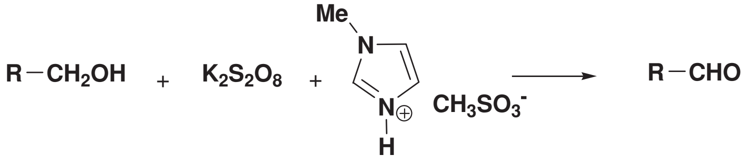
Acidic Bronsted ionic liquid 3-methylimidazolinium hydrogensulfate have been used as both a reagent and a reaction medium for the oxidation of benzylic alcohols with $NaNO_3$. This acidic Bronsted ionic liquid afforded good to excellent yields for conversion of benzylic alcohols to the corresponding carbonyl compounds (*Scheme 44*).[5]



Scheme 44

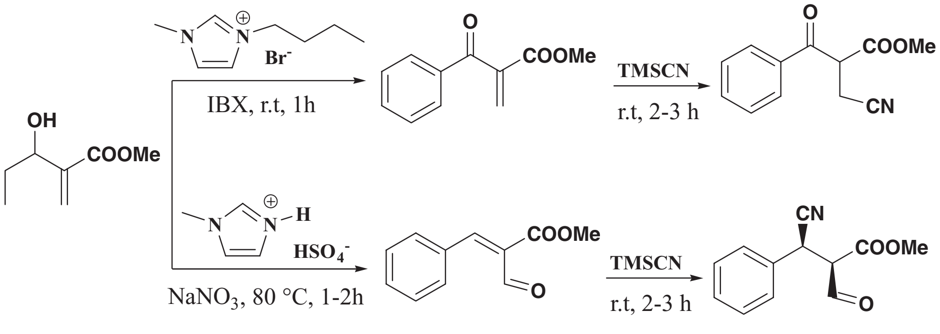
An efficient conversion of alcohols to aldehydes was achieved using potassium persulfate and 3-methylimidazolinium methanesulfonate ([Hmim]CH_3SO_3) (*Scheme 45*). Relatively short reaction times, utilization of cheap and recyclable reagent, and high yield of products are some advantages of the present protocol.[41]

The oxidation of Baylis–Hillman adducts with 2-iodoxybenzoic acid (IBX)/[Bmim]Br or isomerization-oxidation with $NaNO_3$/[Hmim]HSO_4 systems afforded β-ketomethylene compounds or E-cinnamaldehydes, respectively. These α,β-unsaturated carbonyl compounds underwent Michael addition with TMSCN in the same vessel to afford the



Scheme 45

corresponding thermodynamically more stable β-cyano products (*Scheme 46*). [Hmim]HSO_4 plays the dual role of acid catalyst and solvent for both oxidation and hydrocyanation.[52]



Scheme 46

b) Oxidative Aromatic Chlorination

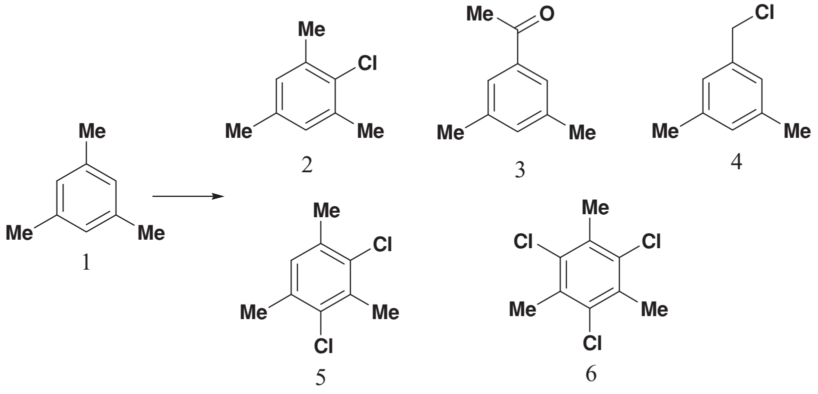
Halogenated organic compounds constitute an important class of intermediates as they can be converted into other functionalities by simple chemical transformation. Aryl halides are the starting materials for the preparation of organometallic reagents, numerous bulk and fine chemicals, and pharmaceuticals.

Acidic Bronsted ionic liquid [Hmim][NO_3] was used as a co-solvent and promoter for oxidative halogenation of aromatic compounds from non-activated or sterically hindered arenes with aqueous halohydric acids (*Scheme 47*). This ionic liquid is air stable, easy to prepare and handle, and is able to oxidize hydrohalic acids (HX), being at the same time re-oxidized by oxygen. Aromatic chlorination in [Hmim][NO_3]—HCl could therefore be considered a green oxidative process, characterized by a very high atom economy (99%).[32]

2. Protection of Organic Compounds

a) Protection of Carbonyl Compounds

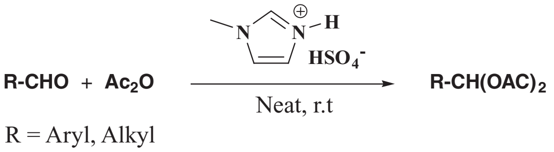
Selective protection and deprotection of carbonyl groups are often essential steps in organic chemistry. 1,1-Diacetates are one of the most useful carbonyl protecting groups due to their stability under both neutral and basic media as well as under acidic conditions. The diacetates of α,β-unsaturated aldehydes are important starting materials for Diels–Alder reactions and also useful intermediates in industry. Some of the reported methods for the preparation of 1,1-diacetates from aldehydes and acetic anhydride include sulfuric acid,



Scheme 47

triflic acid, CAN, H_2NSO_3H, $ZrCl_4$, Wells–Dawson acid ($H_6P_2W_{18}O_{62}\cdot 24H_2O$), and silica sulfuric acid. Although some of these methods have been used for protection of aldehydes to the corresponding diacetates with good to high yields, the majority of these methods suffer disadvantages, such as reaction under oxidizing conditions, use of strong acid, high temperature, long reaction times, and moisture sensitivity of the reagent, high cost, and high toxicity.

An efficient, convenient, mild and highly chemoselective procedure for conversion of aldehydes to the corresponding acylals in the presence of acetic anhydride and a catalytic amount of acidic Bronsted ionic liquid ([Hmim]HSO_4) was reported. The reaction was easily carried out at room temperature under solvent-free conditions (*Scheme 48*).

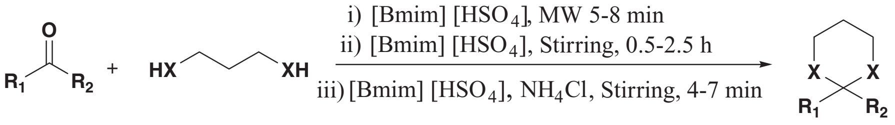


Scheme 48

This method is highly selective for the synthesis of acylals from aldehydes in the presence of ketones. The use of an inexpensive and relatively non-toxic acidic catalyst is another advantage of this method. In contrast to other acids, storage and handling of this compound does not require special precautions and it maybe stored on the bench top for weeks without losing its catalytic activity.[31]

Acetalization and thioacetalization of carbonyl compounds, under solvent-free conditions, was described using the acidic ionic liquid 1-butyl-3-methylimidazolium hydrogen sulfate ([Bmim]HSO_4) at room temperature, in conjunction with microwave energy and ammonium chloride (*Scheme 49*).

It has been observed that ionic liquids are not recycled in microwave-assisted reactions while reactions performed by simple stirring at room temperature and/or in the presence of ammonium chloride proceed well and allow the recovery of the ionic liquid. The catalyst retained its acidity, catalytic activity, and recyclability in ammonium chloride, whereas

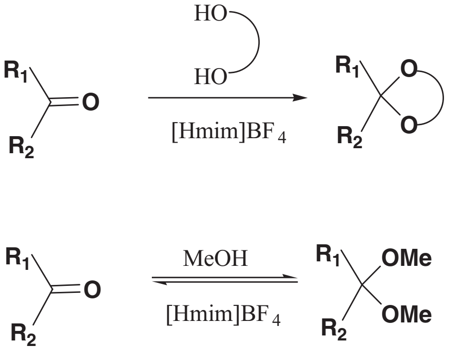


R_1 = Aryl, Alkyl; R_2 = H, Alkyl
X = S, O

Scheme 49

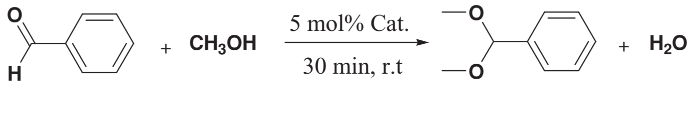
decomposition occurred under microwave irradiation. Microwave irradiation caused charring and decrease in acidity of highly ionic [Bmim]HSO_4. This, apparently, could be the reason for the non-recyclability of [Bmim]HSO_4 under microwave irradiation. Increase in reaction rates with ammonium chloride, probably, is due to enhancement in the acidity of the reaction medium. The same catalyst was also used for the deprotection of acetals, thioacetals as well as for transthioacetalization under microwave irradiation. The protection of carbonyl groups was simply accomplished by stirring the reactants at room temperature (~25°C) for 0.5–2.5 h. Use of microwave energy reduced the reaction time greatly from 2.5 h to 8 min. Combination of ammonium chloride along with [Bmim]HSO_4 greatly increased the reaction rate without the use of microwave energy.[53]

Protection of carbonyl groups as acetals or ketals using acidic Bronsted ionic liquid [Hmim]BF_4 as catalyst as well as solvent was investigated (*Scheme 50*). Satisfactory results were obtained for the protection of carbonyls as cycloacetals or ketals with diols. The product was conveniently separated from the reaction mixture, and the ionic liquid was re-used after removal of water.[54]



Scheme 50

1-Butyl-3-methylimidazolium tetrachlorogallate, [Bmim][$GaCl_4$], was found to be an active catalyst for the efficient acetalization of aldehydes under mild conditions (*Scheme 51*).



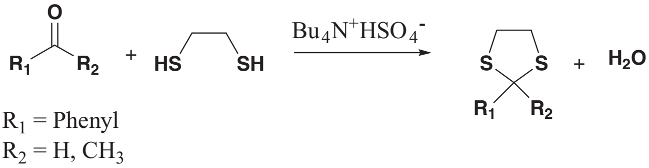
Scheme 51

The incorporation of imidazolium into the indium(III) or gallium(III) chlorides facilitated the transformation since the imidazolium cation acted as an intermediate–stabilizer during catalysis and indeed, the yields increased from 40% to 70% and from 55% to 81%, respectively, when [Bmim][$InCl_4$] and [Bmim][$GaCl_4$] were used as catalyst.[49]

Acidic Bronsted ionic liquids based on the benzimidazolium cation (*Schemes 18, 31, 36*) were efficient and recyclable catalysts for the acetalization of aromatic aldehydes with diols. In comparison to the other ionic liquids used in acetalization, this catalyzed system offered substantial advantages: (i) aromatic aldehydes had good solubility in these ionic liquids; (ii) catalytic amounts of ionic liquid achieved high conversion and selectivity for acetalization; (iii) the use of large amount of diols was avoided.

The reactants had good solubility in benzimidazolium ionic liquids, while the acetals were nearly immiscible with ILs, which facilitated the shift of the equilibrium of the acetalization reaction. The acetalization started as a homogeneous process and ended as biphasic. All the ionic liquids gave very good conversions and excellent product selectivities for acetalization. [PSebim]HSO_4 ((1-ethylbenzimidazolium-3-yl)propane-1-sulfonate hydrogen sulfate) was the best for the acetalization in all ILs, leading to 98% conversion of *p*-nitrobenzaldehyde to its acetal. Increasing the anion's Bronsted acidity of ILs improved the catalytic activity of the acidic ILs.[38]

A variety of carbonyl containing compounds successfully reacted with 1,2-ethanedithiol in a thioacetalization reaction using tetrabutylammonium hydrogen sulfate as a mild and efficient acid catalyst (*Scheme 52*). Aldehydes and ketones gave good to excellent yields under mild conditions.[55]



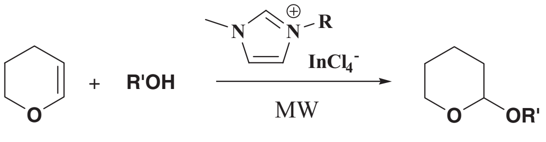
Scheme 52

A novel method to immobilize acidic Bronsted ionic liquid on solid support was described by the co-polymerization of 1-vinylimidazolium based ionic liquid with styrene in the presence of azo*bis*isobutyronitrile (*Scheme 23*). The polymeric support immobilized acidic ionic liquid was used as an effective and reusable catalyst for acetalization reaction under mild reaction conditions.[13]

b) *Tetrahydropyranylation of Alcohols*

Protection of the hydroxy group by 3,4-dihydro-2H-pyran is frequently used for natural products in synthesis. Because tetrahydropyan ethers are stable to strong bases or nucleophiles such as Grignard reagents, organolithium compounds, metal hydrides, alkylating and acylating reagents, and oxidizing compounds, tetrahydropyranylation is used to protect hydroxy groups in multi-step syntheses.[19] There are several processes available in the literature for the preparation of THP-ethers but the majority of them require long reaction times and involve the use of volatile organic solvents or large amounts of solid supports, which eventually leads to generation of a large amount of toxic waste. Therefore, there is a need for a solvent-free and efficient alternative for the protection of hydroxyl compounds.

A solvent-free MW-assisted protocol was developed for the synthesis of 1-alkyl-3-methylimidazolium tetrachloroindate(III) using an unmodified household microwave oven. Imidazolium-based room temperature ionic liquids containing chloroindate(III) exhibit Lewis acid properties similar to those of chloroaluminate ILs without being reactive toward air and water, which was generally considered to be a main limitation. The use of these ionic liquids in the MW-assisted protection of alcohols was demonstrated in the tetrahydropyranylation that precludes the use of volatile organic solvents (*Scheme 53*). Furthermore, the ionic liquid catalysts were effectively recycled.[50]



R = Methyl, Ethyl, Hexyl, Octyl

Scheme 53

c) Acylation of Amines

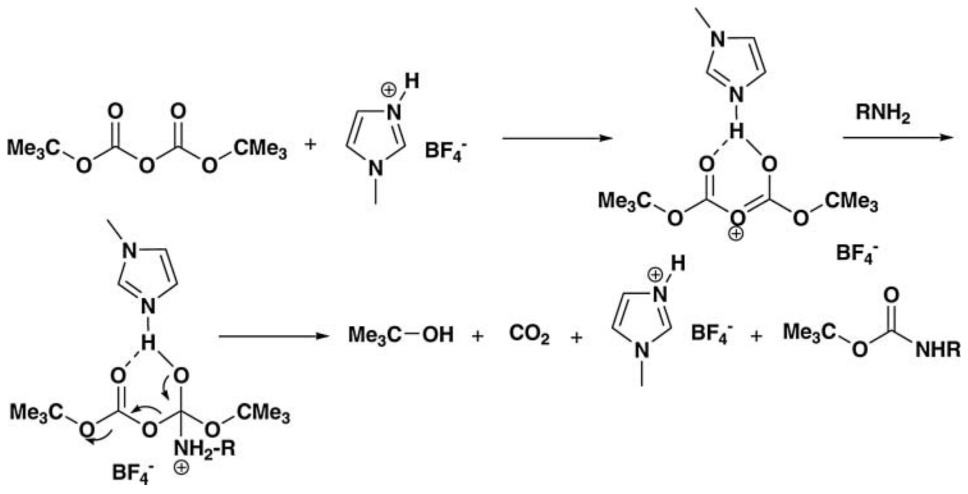
Sequential protection and deprotection of any polyfunctional molecule often requires a selective and efficient protecting reagent together with mild reaction conditions. The protection of an amine is an important step in synthetic organic chemistry. There are a variety of N-Boc protection strategies. However, these methods have several drawbacks such as long reaction times, formation of side-products during base-catalyzed reaction, the need of excess reagents in the case of Lewis acid-catalyzed reactions, and difficulty in the preparation of solid acid catalysts in some cases during solid acid-catalyzed reactions. The challenge of designing a protocol for efficient Boc protection of amines, which is mild as well as environmentally-friendly and has the advantages of solid catalysts, continues to draw attention. An acidic Bronsted ionic liquid could be an ideal alternate system, which has all the characteristics of solid catalysts and a greener outlook at the same time.

Acidic Bronsted ionic liquid, 1-methylimidazolium tetrafluoroborate ([(Hmin)]BF_4) catalyzed efficient and chemoselective N-Boc protection of various amines using $(Boc)_2O$ (*Scheme 54*).

The reported protocol was efficient, inexpensive, chemoselective, and the IL was reusable. The advantages of the present method were (i) the use of a green and easy to handle catalyst; (ii) the ease of preparation of ionic liquid; (iii) mild and solvent-free reaction conditions; (iv) the ease of extraction of the product/substrate from ionic liquid; (v) ionic liquid was directly reused after drying without any significant loss of activity; and (vii) excellent chemoselectivity.[56]

Organic carbamates are valuable synthetic intermediates and are widely used for drug synthesis, production of agrochemicals, and polyurethane based polymers and as protecting groups of amines function.

An efficient approach for the synthesis of carbamates from primary aliphatic amines and dimethyl carbonate (DMC) was developed using acid functional ionic liquids as catalysts



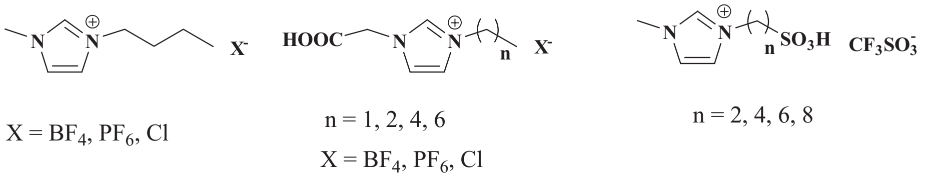
Scheme 54

(*Scheme 55*). This catalytic system was stable, easily separable, and reusable. Furthermore, this series of acid functional ionic liquids had higher catalytic activity under mild reaction conditions without addition of any organic solvents or catalysts.

$$\mathrm{H_2N(CH_2)_nNH_2} + 2\,\mathrm{DMC} \xrightarrow[\text{80 °C, 4h}]{\text{Acidic ionic liquid}} \mathrm{CH_3CO_2CHN(CH_2)_nNHCO_2CH_3} + 2\,\mathrm{CH_3OH}$$

n = 6 or 8

$$\mathrm{RNH_2} + \mathrm{DMC} \xrightarrow[\text{80 °C, 4h}]{\text{Acidic ionic liquid}} \mathrm{RNHCO_2CH_3} + \mathrm{CH_3OH}$$



Scheme 55

The $-\mathrm{CO_2H}$ functionalized ionic liquid had higher activity for the reaction. The anion also played an important role in the reaction. Selectivity of corresponding carbamate went up sharply when using −SO3H functionalized ionic liquids, $\mathrm{Mim(CH_2)_2SO_3HTfO}$, $\mathrm{Mim(CH_2)_4SO_3HTfO}$, or $\mathrm{Mim(CH_2)_8SO_3HOTf}$ as catalysts, and 95% selectivity was achieved with $\mathrm{MIm(CH_2)_8SO_3HOTf}$ with $\mathrm{Cl^-}$ or $\mathrm{OTf^-}$ as anion. The selectivity of hexamethylene dicarbamates (HDC) increased with the chain length of N-substituted alkyl of imidazole cations.[57]

3. *Esterification*

Aliphatic, aryl, and heterocyclic esters are valuable intermediates in chemical and pharmaceutical industries. Esterification of alcohols, particularly unbranched alcohols, carboxylic acids using a small amount of homogeneous acid catalyst (sulfuric acid, hydrogen chloride, phosphoric acid and boric acid or metal salts on solid supports) are well known. The esterification reaction is an equilibrium reaction and can be displaced toward the product by removal of water, or by the use of an excess of one of the reactants. For the preparation of esters, the major drawbacks of these common methods are the final neutralization of the homogeneous acid catalyst, or separation of the metal catalyst supported on solid support. Moreover, the removal of adsorbed products from the catalyst is quite difficult and requires a large excess of volatile organic solvents, the elimination of the excess of one of the reactants or contamination by homogeneous catalyst from the crude reaction mixture.

l-Butyl-3-methylimidazolium hydrogen sulfate ([Bmim]HSO_4), l-hexyl-3-methylimidazolium hydrogen sulfate ([Hmim][HSO_4]), l-butyl-3-methylimidazolium dihydrogen phosphate ([Bmim][H_2PO_4]) and l-[2-(2-hydroxyethoxy)ethyl]-3-methylimidazolium hydrogen sulfate ([Heemim][HSO_4]) were used as catalysts for esterification reactions (*Scheme 56*).

$$\mathbf{RCOOH} + \mathbf{R'OH} \xrightarrow{\text{ABILs}} \mathbf{RCOOR'}$$

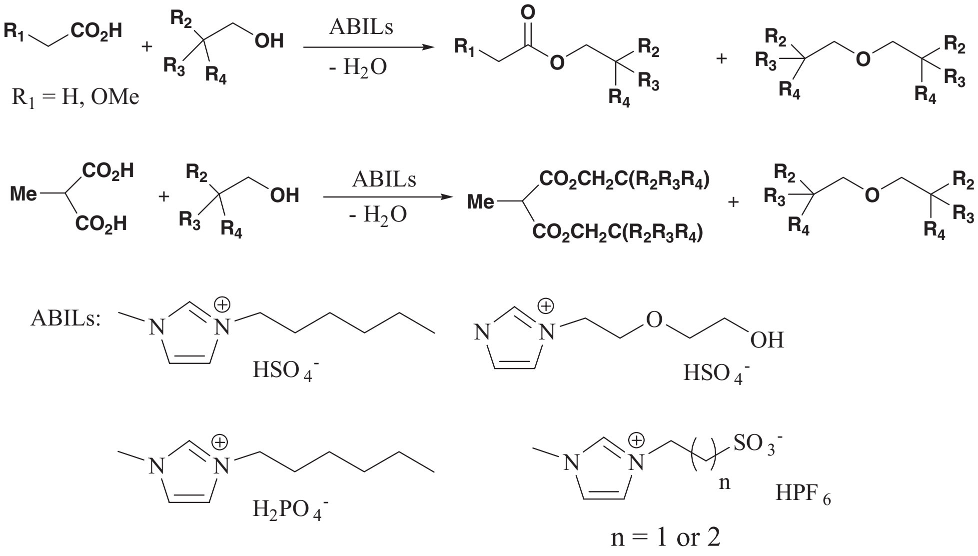
Scheme 56

The yield and the reaction time for esterification with [Bmim][HSO_4] and [Heemim][HSO_4] as catalyst were better than from [Hmim][HSO_4], and these results suggested that the performance of the ionic liquid was dependent upon the character of the side-chain of the cation (low lipophilic character of the [Bmim] cation and high polarity of the [Heemim] cation) indicating the small impact of the cation on the catalytic performance. It was also possible that the immiscibility of the ester products with the ionic liquid facilitated the reaction equilibrium shifting to the product side.[44]

Esterification reactions of acetic acid, methoxyacetic acid, and methylmalonic acid with neopentanol, hexanol, heptanol, and decanol were investigated in three ionic liquids with hydrogen sulfate, dihydrogen phosphate as counter anions, and also with two ionic liquids modified with HPF_6 as catalyst (*Scheme 57*). The nature of both the counteranion and cation influenced the activity of the catalyst. Good yields (99–80%) and high selectivities were obtained, and all the produced esters were easily recovered due to their immiscibility with the ionic liquid as green reaction medium.

Aryl esters are important products or intermediates in the chemical and pharmaceutical industries. Mineral acids (sulfuric acid, hydrochloric acid, phosphoric acid) and Lewis acids (boric acid, $AlCl_3$) are popular catalysts in the manufacturing industries. Corrosion caused by acidic media, contamination of water with acids, and difficulties with recycling acid catalysts are the main problems associated with using such acids as catalysts in esterification. For economic and ecological reasons, there is a need to develop an environmentally benign method for the esterification of aryl esters.

Esterification of carboxylic acids with alcohols was carried out in an acidic Bronsted ionic liquid 1-methylimidazolium tetrafluoroborate ([Hmim]BF_4) (*Scheme 58*). Good yields



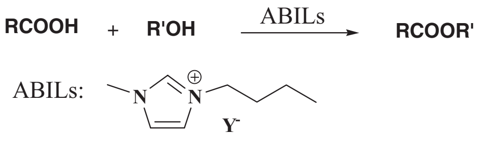
Scheme 57

$$RCOOH + R'OH \xrightarrow[110\ °C]{ABIL} RCOOR'$$

Scheme 58

were obtained, and the esters produced were easily separated from the reaction mixture without the use of any volatile organic solvents. The ionic liquid [Hmim]BF_4 was reused after removal of water.[30]

Acidic Bronsted ionic liquid containing nitrogen-based organic cations 1-methylimidazole and 1-butyl-3-methylimidazolium and inorganic anions of the type BF_4^-, PF_6^- and $PTSA^-$ were used as a catalyst and reaction medium for Fischer esterification of alcohols with acids (*Scheme 59*). Ionic liquids as catalyst afforded good alcohol conversion and excellent ester selectivity. Fischer esterification of acetic acid with benzyl alcohol with various acidic Bronsted ionic liquids was carried out. Maximum substrate conversion and product selectivity were observed on using [Bmim]PTSA as catalyst. The ester was easily separated from the reaction mixture and the ionic liquid reused four times after removal of water. No significant loss in catalytic activity was observed on recycling.[47]



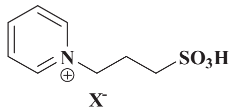
Y = BF_4 or PF_6

Scheme 59

Several water-stable acidic Bronsted ionic liquids with an alkanesulfonic acid group in a pyridinium cation have shown good catalytic activity in esterification reactions of benzoic acid with methanol, ethanol, and butanol (*Scheme 60*).

$$\mathrm{RCOOH} + \mathrm{R'OH} \xrightarrow{\text{ABILs}} \mathrm{RCOOR'}$$

ABILs:



$X^- = BF_4^-, H_2PO_4^-, HSO_4^-, p\text{-}CH_3C_6H_4SO_3^-$

Scheme 60

The catalytic activity of each ionic liquid was dependent on its anion. The experimental results indicated that increasing of the anion's Bronsted acidity improved the catalytic activity of the ionic liquid. Furthermore, the immisciblity of ILs with the esters produced facilitated the esterification reaction equilibrium. The ionic liquid with $[HSO_4]^-$ as the anion has shown the best catalytic activity and biphasic behavior between the IL and the produced esters. The produced esters were separated by decantation, and the ILs were reused after the removal of water.[7]

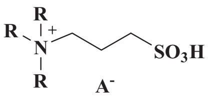
Some novel SO_3H-functional acidic Bronsted ILs that bear an alkanesulfonic acid group in an acyclic trialkanylammonium cation, containing *tri-n*-butylammonium-propanesulfonate (TBAPS), triethylammonium propanesulfonate (TEAPS), trimethylammonium propanesulfonate (TMAPS), were used both as solvents and catalysts for Fischer esterification reactions of aliphatic and aryl acids with aliphatic alcohols and phenols (*Scheme 61*). The reaction rate in ionic liquids was depend upon the ionic liquid chosen. $[TMPSA][HSO_4]$ gave a higher rate enhancement than the others. The solubility of the starting material in ILs, the higher Bronsted acidity, and the better immiscibility of the ester product with the ionic liquid $[TMPSA][HSO_4]$ facilitated the shift of the equilibrium of the Fischer esterification reaction; the resulting ester was not soluble in the IL catalyst. The produced ester was separated by decantation after the reaction and the ILs reused without noticeable decrease in catalytic activity.[10]

Fischer esterification of long-chain aliphatic acids with methanol and ethanol was promoted by two novel acidic Bronsted ionic liquids that bear an aromatic sulfonic acid

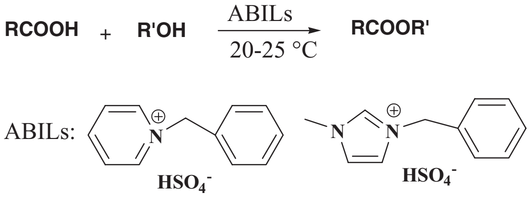
$$\mathrm{RCOOH} + \mathrm{R'OH} \xrightarrow[\text{r. t. 110 °C}]{\text{ABILs}} \mathrm{RCOOR'}$$

$R = Me, Et, C_6H_5;\quad R' = Et, n\text{-}Bu, C_6H_5CH_2$

ABILs:



Scheme 61

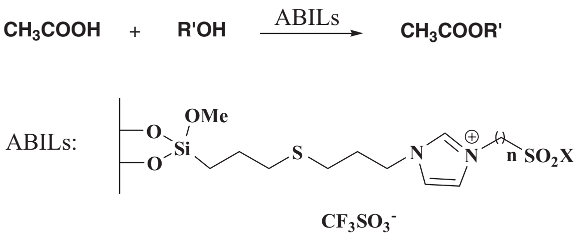


R = $CH_3(CH_2)_n$- n = 2, 3, 4, 6, 10, 14
or R = - $CH_3(CH_2)_7CH{=}CH^-(CH_2)_7^-$
R' = Me, Et

Scheme 62

group on the imidazolium or pyridinium cation (*Scheme 62*). The reactions proceeded smoothly at room temperature in good to excellent isolated yields (85–99%) under solvent-free conditions in the presence of 10 mol% ionic liquids. This reaction system had several noteworthy features: (i) the reaction was carried out at room temperature with shorter reaction time; (ii) the produced esters were separated easily by decantation in high yields and purity; (iii) the acidic Bronsted ILs were reused three times without significant loss of catalytic activity and (iv) the acidic Bronsted ILs were inexpensive, environmentally benign and safe.[16]

1-Allylimidazolium-containing acidic ionic liquids were immobilized by a covalent bond on 3-mercaptopropyltrimethoxysilane modified silica gel. The ionic liquids modified silica gel thus formed behaved as recyclable solid catalysts for esterification of alcohol with acetic acid (*Scheme 63*).[42]



n = 3 X = Cl, OH
n = 4 X = Cl, OH

Scheme 63

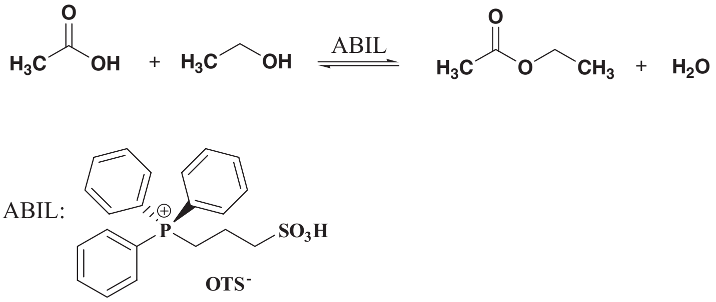
A series of salts containing trialkylammonium, dialkylammonium, and alkylammonium cations with different anions, including $[Et_3NH][HSO_4]$, $[Et_3NH][H_2PO_4]$, $[Et_3NH][BF_4]$, $[Et_3NH][p\text{-}CH_3C_6H_4SO_3]$, $[Et_2(PhCH_2)NH][HSO_4]$, $[n\text{-}Bu_3NH][HSO_4]$, $[n\text{-}Oct_3NH][HSO_4]$, $[Et_2NH_2][HSO4]$, $[Et_2NH_2][H_2PO_4]$, $[Et_2NH_2][BF_4]$, $[i\text{-}Pr_2NH_2][HSO_4]$, $[EtNH_3][HSO_4]$, $[EtNH_3][H_2PO_4]$, and $[EtNH_3][BF_4]$, were prepared and used as catalysts and media in esterification reactions (*Scheme 64*). Higher acidity of the anion in the ionic liquid resulted in high yield of the ester. Among the anions used, HSO_4^- dominated the activity by providing the desired Bronsted acidity for the catalysis of the esterification reaction. The ionic liquids containing anions $p\text{-}CH_3C_6H_4SO_3^-$, $H_2PO_4^-$, and BF_4^- could

$$CH_3COOH + CH_3(CH_2)_6CH_2OH \xrightarrow[90\ °C,\ 4h]{ABILs} CH_3COOCH_2(CH_2)_6CH_3 + H_2O$$

Scheme 64

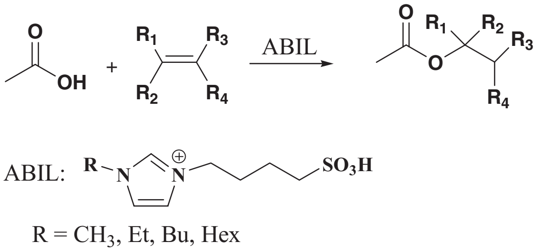
be weaker acids and therefore showed lower activity. However, they were supplemented with a Bronsted acid catalyst such as *p*-toluenesulfonic acid hydrate to make up for the acidity to give high yields of the ester. For a given anion, the yield of the ester increased with decrease in the size of the cation. Better solvation by the water of the smaller cations was probably responsible for their higher activity. There was no phase separation in the reactions where the size of anion and or cation was longer.[58]

The functionalized ionic liquids were prepared by reaction of triphenylphosphine with cyclic sultones. The resulting zwitterions were then converted into ionic liquids upon reaction with *p*-toluenesulfonic acid. Acidic Bronsted IL (*Scheme 64*) was found to be a useful medium to catalyze processes such as the Fischer esterification. Yields varied from moderate to high. The ionic liquid medium combined the low volatility and ease of separation from product normally associated with solid acid catalysts (*Scheme 65*).[59]



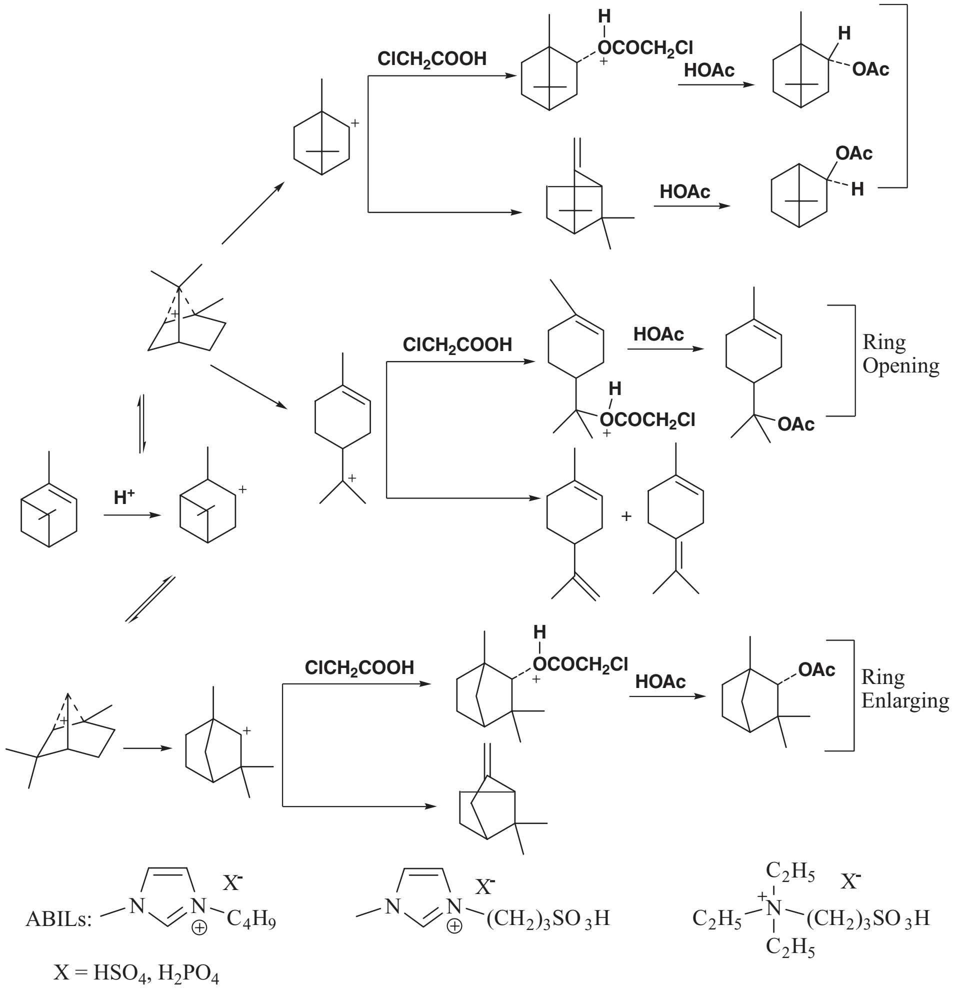
Scheme 65

An efficient and environmentally friendly addition of aliphatic acids to olefins using SO_3H-functionalized ionic liquids as a substitute for conventional homogenous and heterogeneous acidic catalysts was reported (*Scheme 66*).[60]



Scheme 66

The direct esterification of α-pinene with acetic acid to produce bornyl acetate and α-terpinyl acetate was investigated in the presence of acidic ILs (*Scheme 67*). The results indicated that the cation of IL determined the catalytic activity of IL and the anion



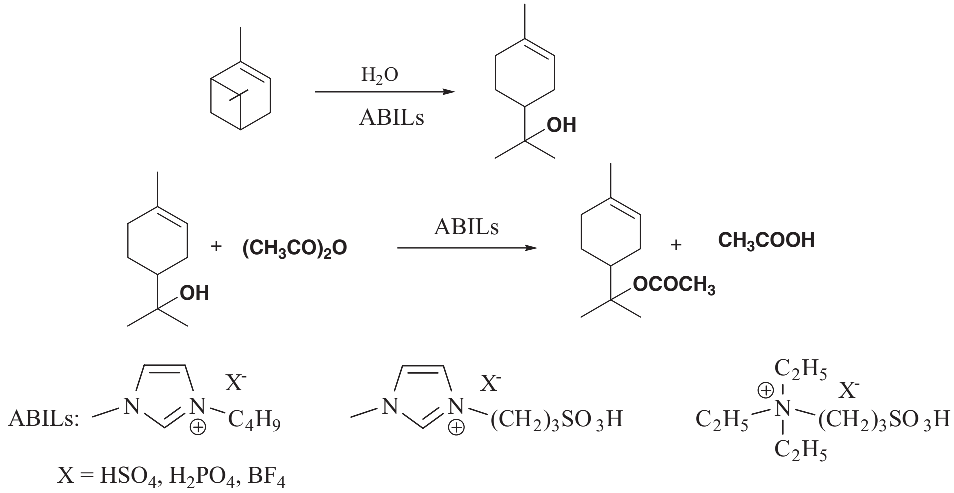
Scheme 67

could obviously affect the selectivity of the esterification products. Compared with the current two-stage process using H_2SO_4 or H_3PO_4 as catalyst, the direct process using $[HSO_3{-}(CH_2)_3{-}NEt_3]HSO_4$ or $[HSO_3{-}(CH_2)_3{-}NEt_3]H_2PO_4$ was simple and highly selective. The product was easily separated from the reaction mixture and the IL catalyst was of good reusability.

Comparison of the catalytic performance of ILs with the same cations made it clear that the anions of ILs had an obvious affect on the selectivity of the esterification products. When the anion was $[HSO_4]^-$, the total selectivity of the rearrangement products was lower than that of $[H_2PO_4]^-$, and the esterification product was mainly bornyl acetate. However when $[H_2PO_4]^-$ was the anion, the esterification product was mainly α-terpinyl acetate. The different selectivities of the esterification products could be due to the different ability of $[HSO_4]^-$ and $[H_2PO_4]^-$ to stabilize the non-classical carbonium ion. Compared with $[H_2PO_4]^-$, $[HSO_4]^-$ was suitable to stabilize the non-classical carbonium ion, which offered more opportunities for chloroacetic acid to attack the carbonium ion to yield bornyl acetate. Thus, selectivity toward bornyl acetate was high. Although the ability of $[H_2PO_4]^-$ to stabilize the non-classical carbonium ion was poor, it was a good catalytist for the rearrangement of the intermediate to yield the carbonium ion, thus favoring selectivity toward α-terpinyl acetate composed to bornyl acetate.[15]

α-Pinene is the main constituent of turpentine oil. When treated with water in the presence of acidic catalyst, α-pinene is mainly hydrated to α-terpineol which may be used as perfume, mixed essence, foaming agent, cleaning agent, fungicide and ore dressing agent. α-terpineol can be esterified with acetic anhydride to α-terpinyl acetate which is an important and widely used synthetic perfume of citric and lavender scents. α-terpineol and α-terpinyl acetate are traditionally manufactured in the presence of the liquid inorganic acid catalysts. The drawbacks of such a process include serious corrosive and environmental problems, troublesome product separation and purification, and non-recyclability of the catalysts.

Hydration of α-pinene and esterification of α-terpineol was investigated in the presence of various acidic ionic liquids (*Scheme 68*). It was found that the cations of ionic liquids determined the catalytic performance of acidic ionic liquids, and the anions had an obvious effect on the selectivity of desired products.



Scheme 68

It was also found that ionic liquid 1-methyl-3-(3-sulfopropyl)-imidazolium dihydrogen phosphate ($[HSO_3\text{-pmim}]H_2PO_4$) exhibited outstanding catalytic properties in both reactions. Furthermore, the efficient product isolation combined with the recyclablity of the catalyst was expected to contribute to the development of a clean and environmentally friendly strategy for the synthesis of α-terpineol and α-terpinyl acetate.[61]

4. Ether Cleavage

The common methods for the cleavage of non-activated ethers have employed strong acids. Milder conditions using boron trihalides (or diborane or sodium borohydride plus iodine) have been extended recently and found to give cleavage at room temperature or below in most cases.[62]

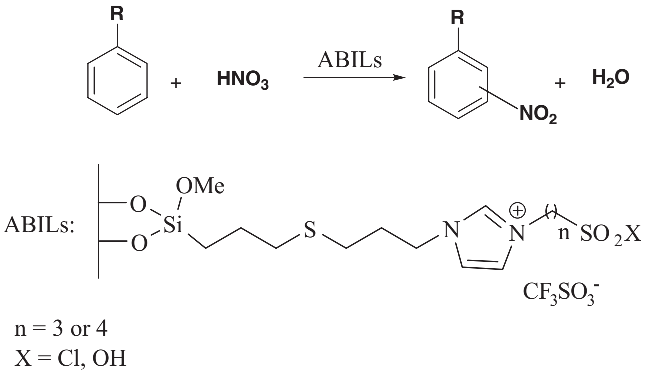
The combination of 1-methylimidazole with anhydrous hydrogen bromide, in a 1:2 mol ratio has produced the 3-methylimidazolium hydrobromide (HmimBr–HBr) at room temperature. This acidic ionic liquid cleaved ethers efficiently and produced the corresponding bromides and alcohols from cyclic and straight-chain dialkyl ethers and phenols and alkyl bromides from aryl alkyl ethers.[63]

5. Nitration Reactions

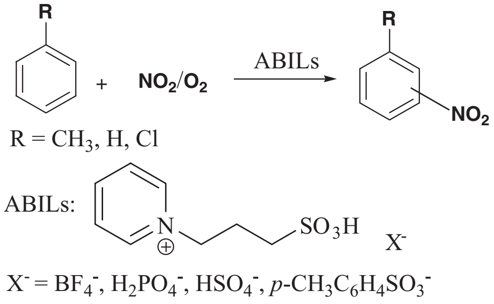
Nitration of aromatic compounds with nitric acid are among the most important reactions in the chemical industries whose products are key organic intermediates or energetic materials. From either an industrial or environmental standpoint, the ideal nitration agent is aqueous nitric acid, which is inexpensive and generates only water as waste. Unfortunately, few catalytic systems using aqueous nitric acid as nitration agent are reported up to now.

In comparison with chloroaluminate based acidic ionic liquids, acidic Bronsted ionic liquids that contain trifluoromethanesulfonic acid (CF_3SO_3H) had shown higher stability toward air and water. Trifluoromethanesulfonic acid contained in the acidic Bronsted ionic liquids was further converted to the sulfonyl chloride as Lewis acidic ionic liquids. Although these acidic ionic liquids were employed successfully as catalysts for reactions such as alkylation, nitration and Beckmann rearrangement, the separation of products or of the ionic liquids themselves remained a problem when they were used in some homogenous reaction systems such as esterification of alcohols with acetic acid or nitration of aromatic compounds with aqueous nitric acid, due to the miscibility of these ionic liquids with products or reagents.

1-Allylimidazolium containing acidic ionic liquids were immobilized on modified silica gel by a covalent bond and used as recyclable heterogeneous catalysts for nitration reaction (*Scheme 69*). Acidic Bronsted ionic liquid catalyzed the nitration of aromatic compounds with aqueous nitric acid of 62% concentration. This method offers a more practical and convenient separation of products over pure ionic liquid system.[42]



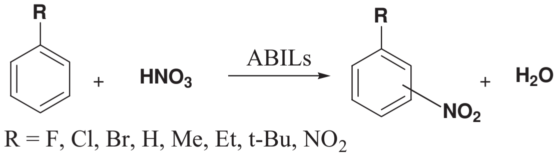
Scheme 69



Scheme 70

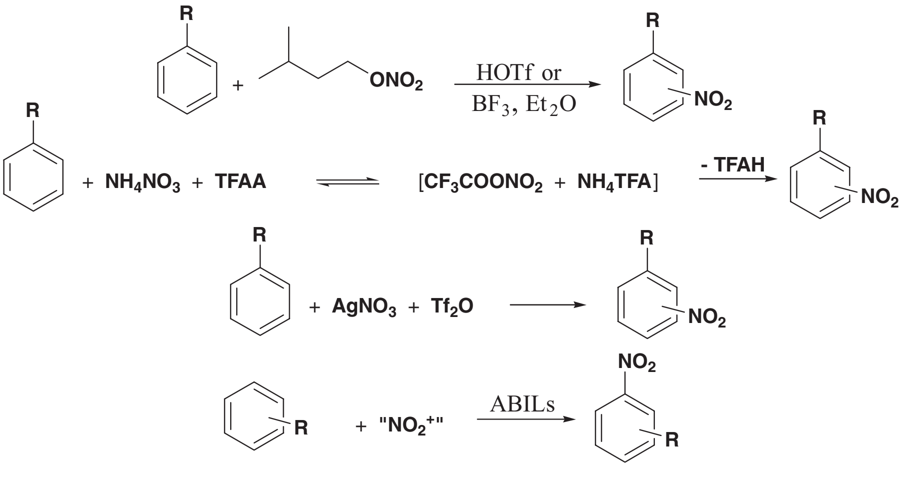
Nitration of simple aromatic compounds in the presence of sulfonic acid-functionalized ionic liquid containing [BSPy][HSO_4], [BSPy][OTf], and [BSPy][pTSA] ([BSPy] has been studied. *N*-(4-Hydroxsulfonylbutyl)pyridinium) with NO_2/air had shown higher *para*-selectivity in moderate yield (*Scheme 70*). Furthermore, the use of NO_2/air was clean, very inexpensive and facile. The acidic ionic liquid was easily separated from the products and recycled with only 9.4% loss in the yield during five cycles. This methodology offered significant improvements for the nitration of aromatic compounds with regard to yield of products, simplicity in operation, mild reaction conditions and avoidance of toxic catalysts and solvents.[20]

Some novel acyclic acidic Bronsted ionic liquids that bear an alkanesulfonic acid group in an acyclic trialkanylammonium cation were synthesized and their uses as halogen-free catalysts for regioselective mononitration of aromatic compounds investigated (*Scheme 71*). The reactions were carried out at 60–80°C and gave reasonable to good yields and improved *para*-selectivities for halogenobenzenes compared to those in the absence of the catalysts. In addition, the ILs were recovered and reused without noticeably decreasing the catalytic activity.[64]



Scheme 71

Ionic liquid nitration was a useful alternative to classical nitration routes due to easier product isolation and recovery of the ionic liquid solvent, and also avoided problems associated with neutralization of large quantities of strong acid. The potential utility of a series of 1-ethyl-3-methylimidazolium salts [Emim][X] with X = OTf^-, CF_3COO^-, and NO_3^- as well as [$HNEtiPr_2$][CF_3COO] ionic liquids were explored as solvents for electrophilic nitration of aromatics using a variety of nitrating systems, namely NH_4NO_3/TFAA, isoamyl nitrate/BF_3/Et_2O, isoamyl nitrate/TfOH, $Cu(NO_3)$/TFAA, and $AgNO_3$/Tf_2O (*Scheme 72*).[65]



Scheme 72

6. Prins Reaction

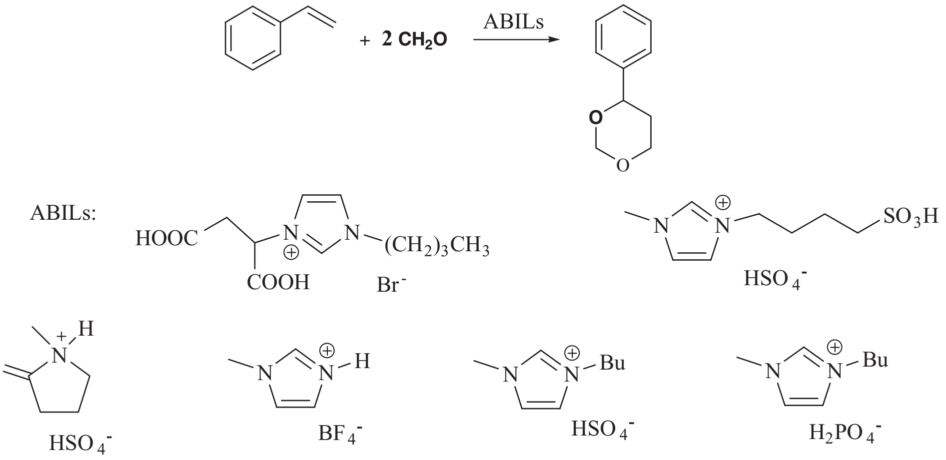
The Prins reaction involving the acid-catalyzed reaction of olefins with aldehydes is an important carbon—carbon bond forming reaction and usually leads to the formation of dioxanes as common major products. The conventional approaches of the Prins reaction use strong protic acid catalysts, such as sulfuric acid, hydrochloric acid, or *p*-toluenesulfonic acid. However, the application of these homogeneous catalysts is limited due to their toxicity and corrosiveness. Moreover, a major disadvantage is that the use of these homogeneous catalysts results in a tedious work-up procedure and the requirement for neutralization of the catalysts with strong acids which produces undesirable wastes.

Acidic Bronsted ILs were synthesized and used to catalyze the Prins reaction of styrene with formaldehyde under reflux conditions (*Scheme 73*). The reaction proceeded smoothly and therefore the purification of products was fairly simple. Furthermore, [Bmim][HSO$_4$] was conveniently separated from the products and easily recycled for another round of reaction.[6]

7. Heck Reaction

The palladium-catalyzed coupling of olefins with aryl or vinyl halides, known as the Heck reaction, has attracted increased attention due to its synthetic versatility. Chemists have seen the recent development of many efficient procedures involving Pd catalyst. However, most of them are homogeneous systems and share common drawbacks; namely, catalyst/product separation and catalyst reuse are difficult. This problem has been solved by the immobilization of the Pd catalysts and by using heterogeneous catalysts. However, these systems do not reach the high activities of homogeneous catalysts and often suffer from substantial Pd leaching. Therefore, finding simpler, more efficient and reusable catalytic systems for the Heck reaction is of practical importance and is still in demand.

Ionic liquids had recently been used in the Heck reaction under the catalysis of palladium with or without a phosphine ligand. ILs served as an excellent medium and as a

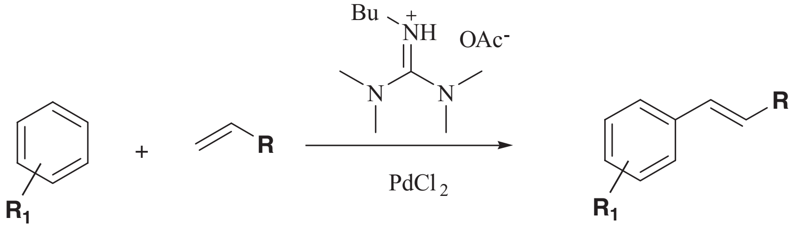


Scheme 73

mobile support for Pd catalysts. To avoid catalyst leaching in IL systems, some efforts have been made to introduce functional groups into the ionic liquid which could complex with metal centers. The introduction of imidazolium tags into a metal complex enhanced the solubility of the catalyst in ionic liquids. The Heck reaction was performed in a number of low melting *N,N*-dialkylimidazolium or *N*-alkylpyridinium ionic liquids with halide, hexafluorophosphate, or tetrafluoroborate anions.[66] However, the syntheses of functionalized ionic liquids or ionic metal complexes were rather complicated and multi-step procedures had been used. The essential requirement for the Heck reaction includes a base, a ligand-stabilized active Pd species, and a reaction medium. Guanidine is a strong organic base and able to form a complex with a Pd(II) salt. It is also known that ionic liquids based on guanidinium salts are excellent reaction media for organic reactions.

Bronsted guanidine acid-base ionic liquids (GILs) are efficient media for the Heck reaction. The guanidine acid-base ionic liquid is one of the simplest catalyst systems, which was used as a solvent, and also as a ligand and a base and offered the advantage of high activity and reusability without the need of a phosphine ligand. GILs were prepared by neutralizing guanidine with acetic acid or HPF_6.

The basic guanidine-based room-temperature ionic liquid was successfully used in the palladium catalytic Heck reaction (*Scheme 74*). GIL played multiple roles in this system. First, it provided ligands to stabilize the activated Pd-(0) during the reaction. Second, it



Scheme 74

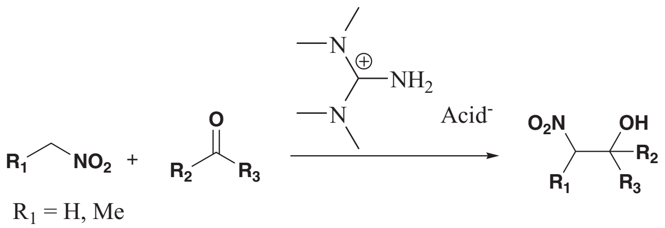
offered a strong base to favor the competitive β-hydride elimination, and finally, acted a highly polar solvent to increase the reaction rate. The catalyst and the GIL were recycled at least five times without the loss of catalytic activity.[67]

8. Henry Reaction

The Henry reaction in which 2-nitroalcohols are formed on treatment of nitroalkanes and carbonyl compounds with a basic catalyst is one of the most useful carbon—carbon bond forming reactions and has wide synthetic applications in organic synthesis. Nitroalcohols are useful intermediates in the preparation of nitroalkenes, α-nitroketones, and β–aminoalcohols derivatives, such as ephedrine and norephedrine.

Henry reactions can be catalyzed by organic and inorganic bases. 1,1,3,3-tetra-Methylguanidine (TMG) and its cyclic analogs were utilized as efficient catalysts. The protocol was thought to have significant advantages to achieve milder reaction conditions and shorter reaction times.

Guanidine-based ILs, 1,1,3,3-tetramethylguanidinium trifluoroacetate ([TMG][F_3Ac]) and TMG lactate ([TMG][Lac]) were prepared by neutralizing TMG with trifluoroacetic acid or lactic acid. The TMG-based IL was shown to catalyze the Henry reactions of nitroalkanes and carbonyl compounds including aliphatic and aromatic aldehydes and cycloalkanones effectively (*Scheme 75*). The reactions proceeded smoothly at room temperature to produce 2-nitroalcohols in good yields. The catalyst was reused repeatedly.[28]

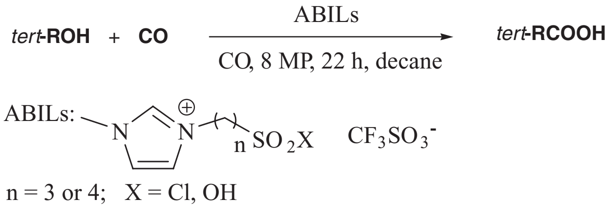


Scheme 75

9. Koch Carbonylation

The carbonylation of alcohols or olefins with carbon monoxide and water to form carboxylic acids, known as the Koch reaction, is one of the most important synthetic routes to manufacture tertiary acids. Generally, this reaction is carried out in a homogenous system in the presence of excess strong acids such as H_2SO_4, BF_3 or HF at high pressure of CO. From the environmental point of view, the use of strong acids on a large scale will cause a series of problems such as the need for corrosion resistant equipments, a complicated wash and separation step to isolate the tertiary acid from the strong acids, and the disposal of large amount of waste acids. To overcome these disadvantages, an alternative method is to perform this reaction in a heterogeneous system by using solid catalyst. A variety of solid acids, such as Nafion-H, silver trifluoromethanesulfonate, H-zeolites, sulfated zirconia and Amberlyst 36, have been examined as catalysts for the Koch reaction.

The Koch carbonylation of tertiary alcohol with CO was carried out in decane in the presence of acidic ionic liquid (*Scheme 76*), which represents a novel application of acidic ionic liquid as well as a novel reaction system for the Koch reaction that led to good reusability and easy separation of product.[68]



Scheme 76

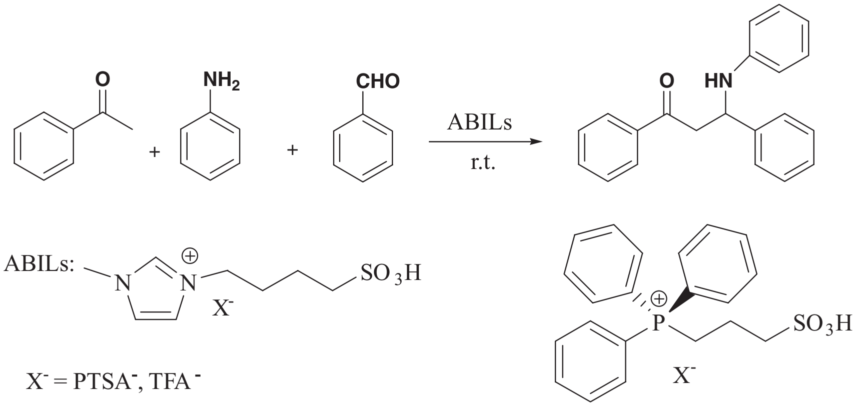
10. Mannich Reaction

The Mannich reaction is one of the most important C=C bond forming reactions in organic synthesis for the preparation of secondary and tertiary amine derivatives. These amines are further used for the synthesis of many intermediates, biologically active and natural products such as alkaloids and polyketides. The products of Mannich reaction are mainly β-aminocarbonyl compounds and derivatives that are used for the synthesis of amino alcohols, peptides, and lactams, and as precursors to optically active amino acids. The conventional catalysts for classical Mannich reaction of aldehydes, ketones and amines involve mainly organic and mineral acids like proline, acetic acid, *p*-dodecylbenzenesulfonic acid and some Lewis acids. They often suffer from the drawbacks of long reaction times and harsh reaction conditions, toxicity and difficulty in product separation, which limit use in the synthesis of complex molecules. Bronsted acid catalysts and Lewis base catalysts have been reported to catalyze the Mannich reaction.The use of ionic liquids as reaction medium may offer a convenient solution to both the solvent emission and catalytic recycling problem.

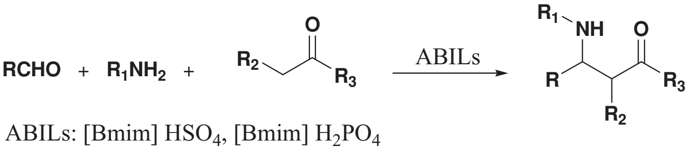
Acidic Bronsted ionic liquids containing nucleophile 1-methylimidazole and triphenylphosphine with 1,4-butanesultone and *p*-toluenesulfonic acid and trifluoroacetic acid as anions catalyzed Mannich reaction smoothly to afford β-aminocarbonyl compounds in excellent yields and less time (*Scheme 77*).

This method avoided the use of acid catalysts and environmentally unfavorable volatile organic solvents. The simple experimental procedure, rapid reaction, easy product separation and reuse of ionic liquids made the use of the ionic liquid a greener and economically viable catalyst for the synthesis of β-aminocarbonyl compounds compared with the traditional protocols.[69]

Acidic Bronsted ionic liquids, including l-butyl-3-methylimidazolium hydrogen sulfate ([Bmim][HSO_4]), l-butyl-3-methylimidazolium dihydrogen phosphate ([Bmim][H_2PO_4]), 1-methylimidazolium *p*-toluenesulfonic acid ([Hmim]Tsa) and 1-methylimidazolium trifluoroacetic acid ([Hmim]Tfa), were successfully used as catalysts and solvents for Mannich reactions using aldehydes, amines, and ketones (*Scheme 78*). Utilization of acidic ILs as catalysts and solvents had several advantages: (i) high yield and high reaction rate were achieved; (ii) the preparation of acidic ILs was simple; (iii) the ILs were easily recycled



Scheme 77



Scheme 78

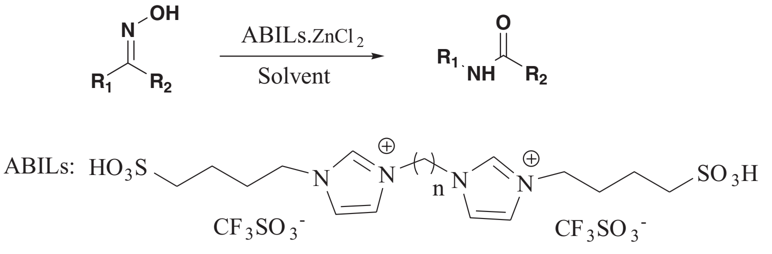
and reused; higher yields were obtained in the presence of [Hmim]Tfa in comparison with the other acidic Bronsted ionic liquids. The [Hmim]Tfa was reused four times without considerable loss of activity.[8]

11. Beckmann Rearrangement

Beckmann rearrangement, the conversion of an oxime into an amide, has long been an important subject for catalyst researchers. It accomplishes both the cleavage of a carbon–carbon bond and the formation of a carbon–nitrogen bond, and represents a powerful method in organic synthesis and chemical manufacturing, particularly for the preparation of ε-caprolactam from cyclohexanone oxime in industry. This reaction, however, generally requires high temperature, strong Bronsted acid and dehydrating media, conditions that will produce large numbers of by-products and lead to serious corrosion problems.

Acidic Bronsted ILs, which possesses the advantageous characteristics of solid acids and mineral acids, are designed to replace traditional mineral liquid acids, such as sulfuric acid and hydrochloric acid. In recent years, the use of ILs as media or catalysts in Beckmann rearrangement have been reported, affording a new approach for catalytic Beckmann rearrangement.

A series of acidic Bronsted ILs–$ZnCl_2$ with double SO_3H functional groups in ILs, [bis-BsImM]$[OTf]_2$ (Bs: butyl-sulfonyl, Im: imidazolium, M: methane, OTf: triflic acid), [bis-BsImH]$[OTf]_2$ (H: hexane) and [bis-BsImD]$[OTf]_2$ (D: decane), were synthesized as clean, highly efficient catalyst systems for the Beckmann rearrangement (*Scheme 79*). Due



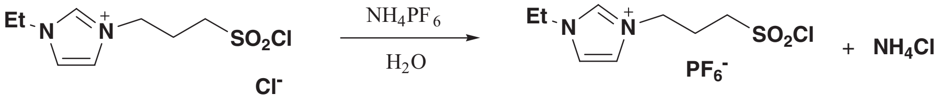
1) n =1, [bis-BSImM] $[OTf]_2$ 2) n =6, [bis-BSImH] $[OTf]_2$ 3) n =10, [bis-BSImD] $[OTf]_2$

Scheme 79

to their unique structures, they are quite strongly acidic and have very poor solubility in common organic solvents except for ethanol and methanol.

Excellent yields of amides were obtained for the reaction when these novel acidic ILs were used together with $ZnCl_2$ as catalysts without producing any waste. Moreover, the immiscibility of the novel acidic ILs with organic solvents made the separation of catalysts very easy. Ionic liquids with triflic acid anions had better catalytic activities than those of other acidic ionic liquids.[39]

Under mild conditions and without any additional organic solvents, the Beckmann rearrangement of ketoximes was performed in a novel task-specific ionic liquid consisting of a sulfonyl chloride group (*Scheme 80*), especially for the conversion of cyclohexanone oxime to ε-caprolactam. ε-Caprolactam has good solubility in water while the task-specific ionic liquid is immiscible with water and therefore, ε-caprolactam was easily separated from the reaction system by aqueous extraction.[70]



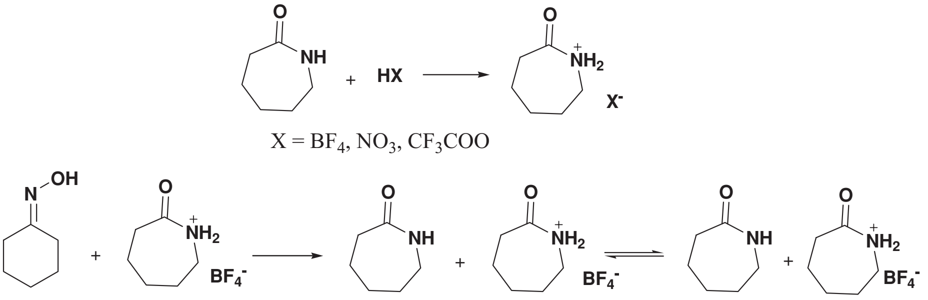
Scheme 80

The Beckmann rearrangement of cyclohexanone oxime afforded ε-caprolactam with the use of a novel caprolactam tetrafluoroborate. Use of the acidic Bronsted IL as catalyst and reaction medium resulted in high conversion and selectivity under mild reaction conditions (*Scheme 81*). The strong chemical combination between caprolactam product and acidic ionic liquid was avoided. Product recovery without neutralization was possible.[27]

Catalytic amounts of ionic liquids containing *N*-methyl- or *N*-isopropylimidazolium cations with counteranions, such as BF_4^-, PF_6^-, and OTf^-were used as the reaction medium for the Beckmann rearrangement of oximes to amides in the presence of PCl_5 (*Scheme 82*). Moderate to good conversions of oximes to amides in all the ILs were obtained.[34]

12. Reductive Amination of Carbonyl Compounds

Functionalized amines are important organic intermediates and have wide applications in synthetic and combinatorial chemistry because of their versatile utility as intermediates for

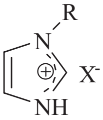


$X = BF_4, NO_3, CF_3COO$

Scheme 81

$$\text{Oxime} \xrightarrow[20\%\text{PCl}_5,\ 80\ °\text{C, 3h}]{20\%\text{mmol ABIL}} \text{Amide}$$

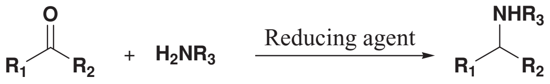
ABIL:



$X^- = BF_4^-, PF_6^-, OTF^-$

Scheme 82

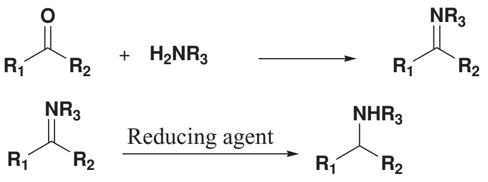
synthesis of pharmaceuticals and agrochemicals. For preparation, two synthetic methods are commonly used. One is the reductive amination, which is termed as a direct reaction. This method allows the conversion of carbonyl functionality to an amine by direct treatment of a mixture of the carbonyl compound and the amine with suitable reducing agents in a single operation without preformation of an intermediate imine or iminium salt (*Scheme 83*).



R_1, R_3 = Alkyl, Aryl or Heterocyclic; R_2 = H, Alkyl, Aryl or Heterocyclic

Scheme 83

The other is a stepwise or indirect reaction, which involves the conversion of amine from the reduction of the imine derivatives isolated in a separate step (*Scheme 84*).[71] There are several reagents and catalysts reported in the literature for reductive amination,

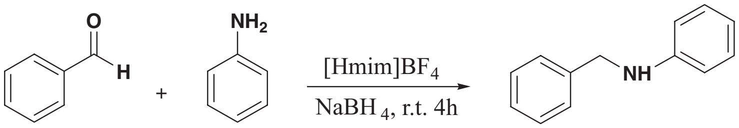


R_1, R_3 = Alkyl, Aryl or Heterocyclic; R_2 = H, Alkyl, Aryl or Heterocyclic

Scheme 84

following direct as well as indirect approaches. Most are associated with expensive and flammable reagents, utilization of complex catalysts and low product yield even though conversion of the aldehyde is high in some cases. In many instances, a large excess of amine was used to improve the yield and also to prevent reduction of the aldehydes to alcohols.

$NaBH_4$ was utilized with various Bronsted acids to facilitate initial formation of the imine leading to successful reductive amination. Most of these acidic Bronsted catalysts are toxic, corrosive and difficult to separate from the reaction mixture. Acidic Bronsted IL, 1-methylimidazolium tetrafluoroborate [(Hmim)BF_4] as a recyclable medium was used for efficient conversion of carbonyl compounds to imines followed by reduction using $NaBH_4$ for the synthesis of functionalized amines (*Scheme 85*).[9]



Scheme 85

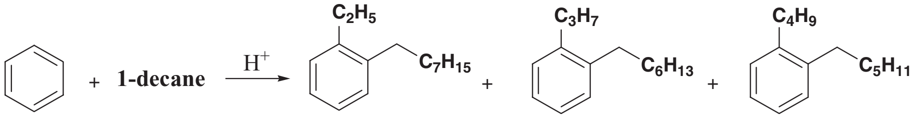
13. Friedel–Crafts Alkylation

Transformations catalyzed by highly acidic and superacidic catalysts are among the most important reactions in industrial chemistry. However, many of these reactions using mineral acids or classical superacidic systems cannot be regarded as environmentally benign. Often, hazardous volatile acids are involved (*e. g.* HF). In other cases, the acid has to be used in stoichiometric or even in longer than stoichiometric ratio to the feedstock. Therefore, much waste is produced during the hydrolysis for product isolation. Other restrictions originate from the physico-chemical properties of the commonly used acidic systems. Insufficient solubility of the substrates in the liquid acid is an especially common limitation. The use of ionic liquids in highly Bronsted-acidic (stronger Brønsted-acidic than 100% sulfuric acid) catalysts has so far been limited to chloroaluminate systems. However, chloroaluminate ionic liquids have a number of serious limitations, namely their irreversible destruction by moisture and their lack of tolerance to functionalities in the substrates.

Hydrogensulfate and tetrakis(hydrogensulfato)borate ionic liquids (1-butyl-3-methyl-imidazolium hydrogensulfate [Bmim][HSO_4], 1-butyl-3-methylimidazolium tetrakis(hydrogen-sulfato) borate [Bmim][$B(HSO_4)_4$)], 1-octyl-3-methylimidazolium tetrakis(hydrogensulfato) borate [Omim][$B(HSO_4)_4$)) are highly interesting additives to mineral acids to form new, highly Bronsted-acidic catalysts.

They were used as additives to sulfuric acid in the Friedel–Crafts alkylation of benzene with 1-decene (*Scheme 86*).

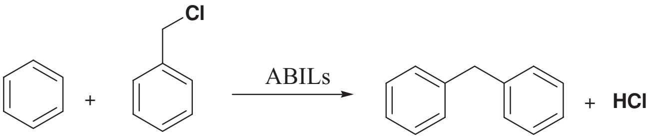
In some cases, low amounts of ionic liquid additive resulted in a dramatic improvement of product yield. Mixtures of sulfuric acid with only 2.2 mol% of [Omim][$B(HSO_4)_4$] ionic liquid yielded 90% more monoalkylbenzene product than the neat sulfuric acid catalyst under identical reaction conditions. This and related results were explained by an interplay of solubility and acidity effects caused by the ionic liquid additive.[33]



Scheme 86

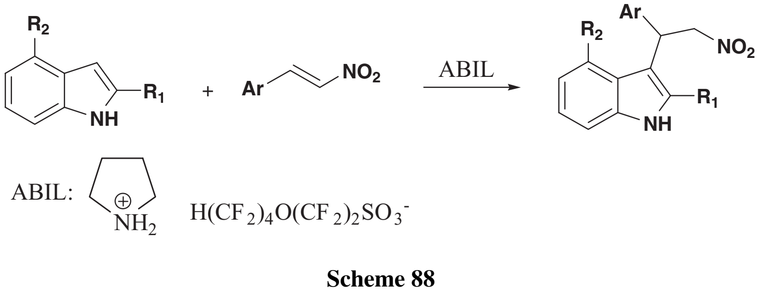
Diphenylmethane (DPM) and substituted diphenylmethanes are important chemicals used as pharmaceutical intermediates and other fine chemicals. DPM has been synthesized industrially by Friedel-Crafts reaction of benzene with benzyl chloride in the liquid phase, using homogeneous acids, such as $AlCl_3$, $FeCl_3$, and H_2SO_4, as catalysts. There are several problems in the application of these catalysts, such as high toxicity, corrosion, difficulties in separation or recovery, and disposal problems due to a large number of acidic effluents. Therefore, some solid acids such as, HY zeolite, sulfated ZrO_2, and ion-exchanged clays have been developed in this reaction as alternatives. Although these solid acidic catalysts are harmless to the environment and health, they showed a poor activity or higher performing temperature in the benzylation reaction.

The synthesis of diphenylmethane (DPM) from benzene and benzyl chloride with acidic ionic liquids, such as $(C_2H_5)_3NHCl.AlCl_3$, $(C_2H_5)_3NHCl.ZnCl_2$, $(C_2H_5)_3NHCl.FeCl_3$, and $(C_2H_5)_3NHCl.CuCl_2$, as catalysts was investigated (*Scheme 87*). The results showed that $(C_2H_5)_3NHCl.AlCl_3$ is a highly efficient catalyst. Both the yield and the selectivity of DPM reached 100% in the presence of $(C_2H_5)_3NHCl.AlCl_3$ as catalyst, when the reaction was carried out under ambient conditions.[11]



Scheme 87

Ionic liquid $[C_4H_8NH_2][(H(CF_2)_4O(CF_2)_2SO_3]$ was highly fluid even below room temperature. It was used both as the recyclable solvent and efficient catalyst for Friedel–Crafts alkylations of indoles with nitroalkenes (*Scheme 88*).[26]

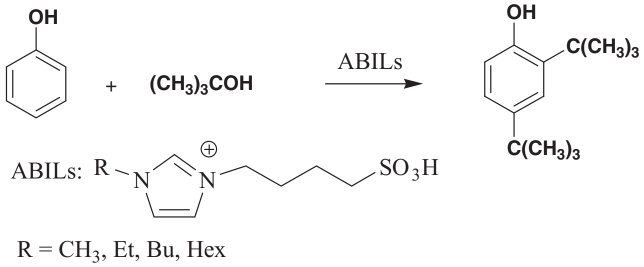


Scheme 88

14. Alkylation of Phenol

The alkylation reaction of phenol with *tert*-butyl alcohol (TBA) is an important reaction both in organic synthesis and chemical manufacturing. The alkylated phenol products are used as raw materials for the manufacture of a variety of resins, durable surface coatings, varnishes, wire enamels, printing inks, surface-active agents, rubber chemicals, antioxidants, fungicides, petroleum additives, ultraviolet absorbers, and heat stabilizers for polymeric materials. Investigation of both homogeneous and heterogeneous catalysts for this typical Friedel–Crafts alkylation reaction results in different selectivity and activities based mainly on the acidity of the catalysts used. Catalysts used for this reaction include Lewis acids such as $AlCl_3$ and BF_3, Bronsted acids such as H_3PO_4, H_2SO_4, HF, $HClO_4$, cation-exchange resin, mesoporous materials, zeolites, molecular sieves, and finally supercritical and near-supercritical water. Liquid acid catalysts cause equipment corrosion and environmental pollution, while solid acids deactivate rapidly due to the build-up of coke. Although cation-exchange resins show a good performance, thermal stability and fouling of the resins are also major problems. SO_3H-functionalized ionic liquids have exhibited great potential in replacement of conventional homogenous and heterogeneous acidic catalysts because they are non-volatile, non-corrosive and immiscible with many organic solvents.

The alkylation of phenol with TBA catalyzed by acidic Bronsted ionic liquid was successful (*Scheme 89*). The ionic liquid was utilized repeatedly over three times without any apparent loss of the conversion and selectivity. The results showed that acidic Bronsted ionic liquid had a potential application in the production of 2,4-di-t-butylphenol with good activity and selectivity.[72]



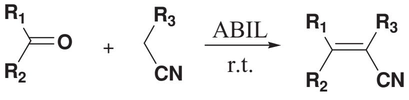
Scheme 89

15. Knoevenagel Reaction

The Knoevenagel condensation is one of the most useful C=C bond forming reactions in organic synthesis. It is employed in the synthesis of therapeutic drugs, natural products, herbicides, insecticides, functional polymers and fine chemicals.[73]

Traditionally, it has been carried out in the presence of a base such as piperidine, pyridine, or their corresponding salts, acid, or surfactant catalyst in organic solvents. To now, a wide variety of new catalysts, such as Lewis acids, inorganic solids with special structure and amines immobilized on polymers and some of the ionic liquids have been developed for this reaction.

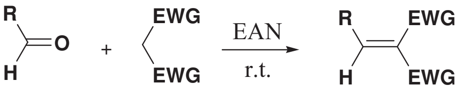
The Knoevenagel condensation between malononitrile or ethyl cyanoacetate and carbonyl compounds was effectively promoted by 1,1,3,3-tetramethylguanidium lactate under mild conditions (*Scheme 90*). Good to high isolated yields were obtained. The ionic liquid enhanced the reaction rates significantly even though it was used in catalytic amount. The ionic liquid was prepared simply and reused efficiently.[74]



R_1, R_2 = Aryl, Alkyl, H; R_3 = CN, COOEt

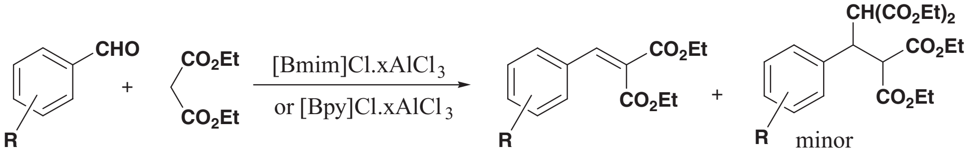
Scheme 90

The Knoevenagel condensation of aromatic aldehydes with active methylene compounds proceeded efficiently in a reusable ionic liquid, ethylammonium nitrate (EAN), at room temperature in the absence of any catalyst in high yields (*Scheme 91*).[75]



Scheme 91

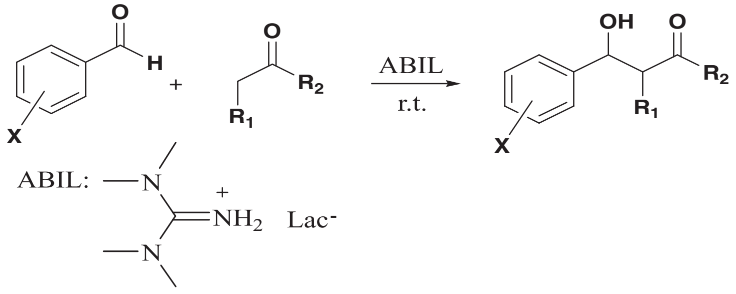
1-Butyl-3-methylimidazolium chloroaluminate, [Bmim]Cl.AlCl$_3$, and 1-butylpyridinium chloroaluminate, [Bpy]Cl.AlCl$_3$, ionic liquids were found to work well as the Lewis acid catalyst and solvent in the Knoevenagel condensations of benzaldehyde and substituted benzaldehydes with diethyl malonate to give benzylidene malonates (*Scheme 92*).[76]



Scheme 92

16. *Aldol and Claisen-Schmidt Reactions*

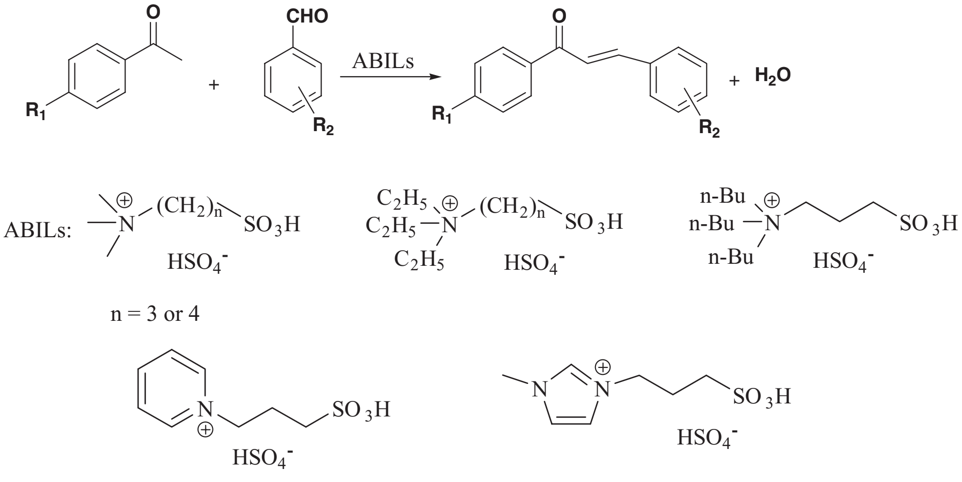
Aldol reactions are effective C—C bond forming reactions and the product β-hydroxy ketones are frequently found in complex polyol architectures of natural products. These reactions have been studied extensively. The classical aldol reactions are highly atom-economic but suffer from problems of low selectivity. Aldol reactions can be catalyzed by organic or inorganic bases. The reactions catalyzed by inorganic bases are not easily controlled and dehydration of the product is often unavoidable. Organic molecules such as proline and guanidines have also been used as the catalysts. The ionic liquid, 1,1,3,3-tetramethylguanidine lactate ([TMG][Lac]), was used as a recyclable catalyst for the direct aldol reaction at room temperature without any solvent (*Scheme 93*). The results demonstrated that good chemo- and regioselectivity was achieved, and the ionic liquid was easily recovered and recycled without major decrease of activity.[77]



Scheme 93

Chalcones have attracted increased attention due to numerous pharmacological applications. They are main precursors for the biosynthesis of flavonoids and exhibit various biological activities such as anti-cancer, anti-inflammatory, nitric oxide regulation and anti-hyperglycemic agents. Traditionally, chalcones are obtained *via* the Claisen–Schmidt condensation carried out in basic or acidic media under homogeneous conditions. Heterogeneous catalysts such as Lewis acids, Bronsted acids, solid acids, solid bases, and other catalysts have been used with varying success.

Some recyclable acyclic SO_3H-functionalized ionic liquids were utilized as catalysts for the synthesis of chalcones by Claisen–Schmidt condensation (*Scheme 94*). The chalcone was simply separated from the catalyst by decantation. After removal of the water from the reaction mixture the catalysts were recycled and reused for several times without noticeable decrease in catalytic activity.[78]

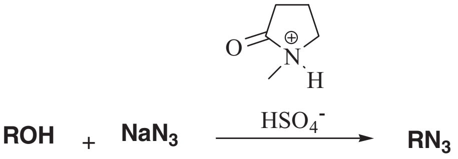


Scheme 94

17. Preparation of Azides from Alcohols

Conversions of alcohols to the corresponding azides are essential in functional group transformation. Alkyl azides have frequently been used for the synthesis of amino groups and for the construction of N-heterocycles. Azides have been used for preparation of medicines such as azidopyrimidines and purines due to their anti HIV-1 biological activity. 5-azido-5-deoxyxylofuranose has been employed for synthesis of sugar triazole derivatives as anti-tuberculosis agents.

Acidic ionic liquid pyrrolidinium bisulfate, [HNMP]HSO_4, was used as a highly chemoselective, inexpensive, and efficient catalyst and also as a solvent for conversion of alcohols to the corresponding azides using NaN_3 (*Scheme 95*).[79]

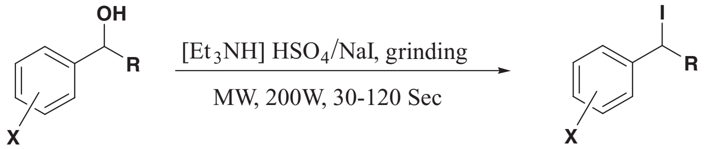


Scheme 95

18. Halogenation of Alcohols

Alkyl halides are very versatile intermediates in organic synthesis. They react with nucleophiles such as amines or alkoxides to give the corresponding amines or ethers, and can be lithiated to introduce electrophiles *via* a halogen–lithium exchange reaction. The most common precursors for preparation of alkyl halides are alcohols, and their conversion into halides is one of the most frequently used functional group transformation reactions. Although alkyl iodides are less stable and more expensive than other alkyl halides, they are more reactive than the other alkyl halides, and in some cases iodides are the only reactive halides.

The iodination of alcohols with KI in the presence of a catalytic amount of triethylammonium hydrogensulfate ([Et_3NH]HSO_4) as a novel and inexpensive ionic liquid under microwave irradiation was investigated (*Scheme 96*).[23]



Scheme 96

Acidic Bronsted ionic liquid 1-butyl-3-methylimidazolium hydrogen sulfate [Bmim]HSO_4 was demonstrated as an efficient reusable catalyst and solvent, for the halogenation of aromatic and aliphatic alcohols in conjunction with microwave and thermal heating (*Scheme 97*).[80]

$$\mathbf{RCH_2OH} \xrightarrow{\text{NaX, [Bmim] } HSO_4^-} \mathbf{RCH_2X}$$

R = Alkyl, Aryl; X = Br, I

Scheme 97

19. Isomerization

The earlier industrial catalysts for the isomerization processes are Friedel-Crafts catalysts, such as $AlCl_3$ with additives such as HCl. The processes utilizing these catalysts can be operated at low temperature, which is favorable for the formation of multibranched isomers due to thermodynamic considerations. Industrial isomerization catalysts are bifunctional catalysts, which are solid acids loaded with transition metals. The industrial isomerization processes utilize bifunctional catalysts, and are operated under moderate reaction temperature and high pressure of hydrogen. These processes are referred to as hydroisomerization because of the presence of hydrogen.

The bifunctional catalysts have the advantage of a low extent of side-reactions and good selectivity. However, they also have some disadvantages, such as high cost of catalysts due to the utilization of noble metals, high investment and operating cost because of the presence of hydrogen, high reaction temperature for the Pt-supported zeolite catalysts, and environmental concern for the Pt-supported chlorinated-alumina catalysts.

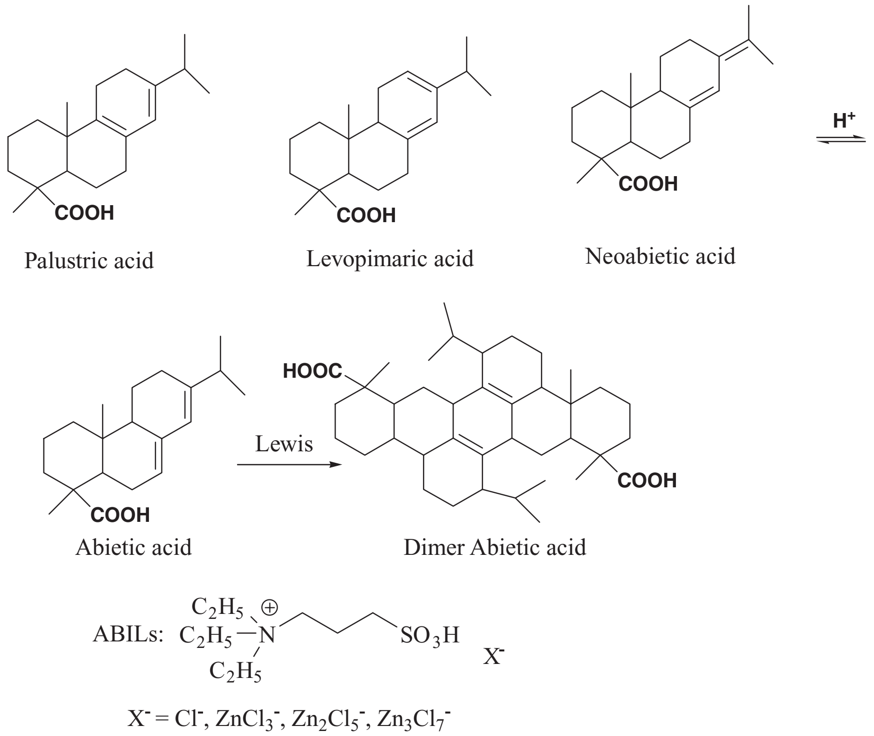
An ionic liquid catalyst combined with a metal salt additive, which provides a catalytic composition with improved acidity, favors the formation of paraffin hydrocarbons with a higher octane number. The isomerization of normal paraffins into corresponding branched isomers is an important process in petroleum refining. The isomerization oil of low carbon number has a high octane number, low sensibility, and low sulfur content.

The ionic liquid $Et_3NHCl.AlCl_3$ (mole fraction of $AlCl_3$ was 0.67) has shown good catalytic performance for the isomerization of *n*-pentane. The conversion of *n*-pentane increased with enhanced reaction temperature, reaction time, and catalyst/oil volume ratio, while the yield of isomerization oil (isoparaffin fractions of low carbon number) and the selectivity of isoparaffins decreased. The octane number of pentane is 61.7, while octane number of isopentane is 92.3.[81]

Rosin is a mixture of several rosin acids, such as levopimaric acid, neoabietic acid, palustric acid, and abietic acid. Due to the conjugated double bonds and carboxyl group, they are chemically active substances and easily oxidized by air. Therefore, rosin is modified to improve its application. Polymerized rosin, produced by dimerization of abietic acid, is one of the most important modified rosin products.

Ionic liquids $[HSO_3{-}(CH_2)_3{-}NEt_3]Cl.xZnCl_2$ with $x>0.5$ (x: molar fraction of $ZnCl_2$) are both Bronsted and Lewis acidic. The catalytic properties of these ionic liquids were investigated in the dimerization of rosin (*Scheme 98*).

It was found that ionic liquid $[HSO_3{-}(CH_2)_3{-}NEt_3]Cl{-}xZnCl_2$ ($x = 0.64$) had good catalytic properties. The product was easily separated from the reaction mixture and the ionic liquid catalyst was of good reusability. The cation contributed to Bronsted acidity of IL and catalyzed the isomerization of non-abietic acids. The anion determined Lewis acidity of IL and played a decisive role for the dimerization of abietic acid. $[HSO_3\ (CH_2)_3$



Scheme 98

$NEt_3]Cl.xZnCl_2$ ($x = 0.64$) was of good catalytic performance for the dimerization of rosin.[14]

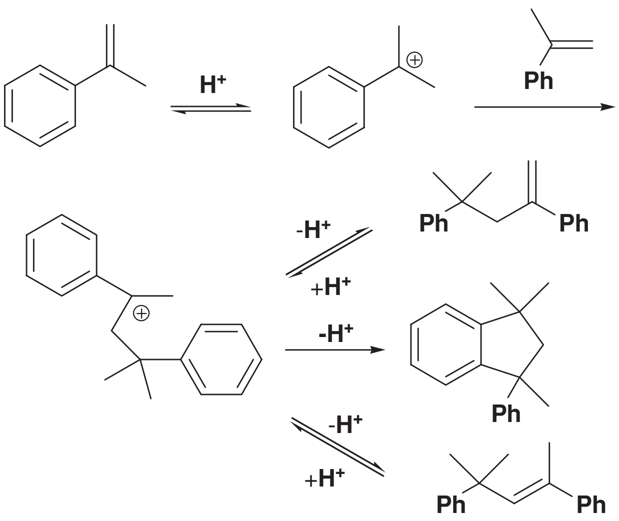
Acidic Bronsted ionic liquid catalyzed and temperature-controlled highly selective dimerization of α-methylstyrene to produce widely used chemicals for polymer application contain 2,4-diphenyl-4-methyl-1-pentene and the saturated cyclic isomer, 1,1,3-trimethyl-3-phenylindan (*Scheme 99*).

At low temperature, such as 60°C, 2,4-diphenyl-4-methyl-1-pentene was formed in 93% selectivity with >92% conversion using a catalytic amount of $[Hmim]BF_4$ under solvent-free conditions while indan was obtained in 100% selectivity when the temperature was increased to 170°C. The ionic liquid $[Hmim]BF_4$ was recycled six times showing no decrease of activity of the ionic liquid during work-up procedure.[82]

20. Polymerization

Ionic liquids have been used as solvents for polymerization reactions. Free radical, atom transfer radical polymerization, cationic, cationic ring-opening, and metathesis polymerizations have been performed. However, there is only one example of polycondensation in ionic liquids.

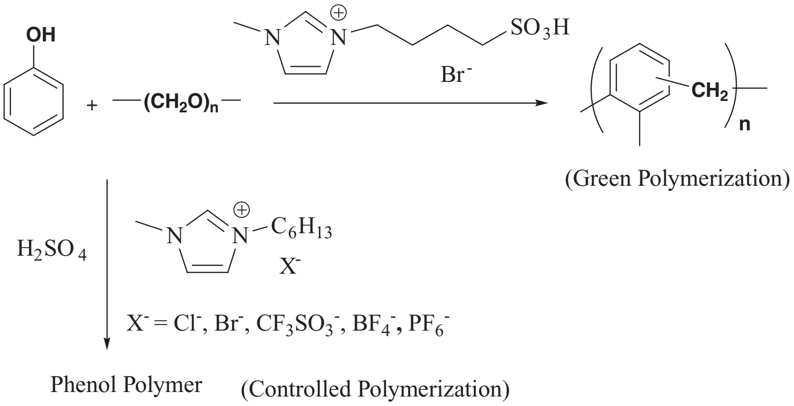
Polymerization of phenol with paraformaldehyde and catalytic amounts of sulfuric acid was carried out in room temperature ionic liquids based on imidazolium salts. The properties of ionic liquids were systematically varied by employing the six different anions chloride,



Scheme 99

bromide, iodide, tetrafluoroborate, trifluoromethanesulfonate, and hexafluorophosphate. In case of hydrophilic ionic liquids having chloride or bromide anion, phenol polymers with low molecular weight and narrow polydispersity were obtained.

In contrast, using hydrophobic ionic liquids such as tetrafluoroborate and trifluoromethanesulfonate anions, high molecular weight phenol polymers were prepared because interaction of the hydrophilic ionic liquids with phenol is stronger than that of the hydrophobic ionic liquids. Moreover, by using Bronsted acid ionic liquid carrying a sulfuric acid moiety as a solvent, catalytic acid-free green polymerization of phenol with paraformaldehyde was accomplished (*Scheme 100*). The ionic liquid was efficiently recovered and reused in new polymerization process of phenol. This little-known synthesis of resins in ionic liquids is very simple and thus will be industrially applicable.[83]



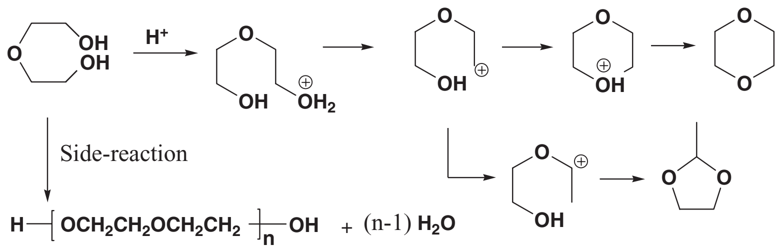
Scheme 100

21. Heterocyclic Synthesis

Heterocycles form by far the largest of the classical divisions of organic chemistry. Moreover, they are of immense importance not only both biologically and industrially, but to the function of any developed human society as well. Their participation in a wide range of areas cannot be underestimated. The majority of pharmaceuticals that mimic natural products with biological activity are heterocycles. Most of the significant advances against infectious disease have been made by designing and testing new structures that are often heteroaromatic derivatives. In addition, a number of pesticides, alkaloids, and cardiac glycosides are heterocyclic natural products of significance for both human and animal health.

a) 1,4-Dioxane

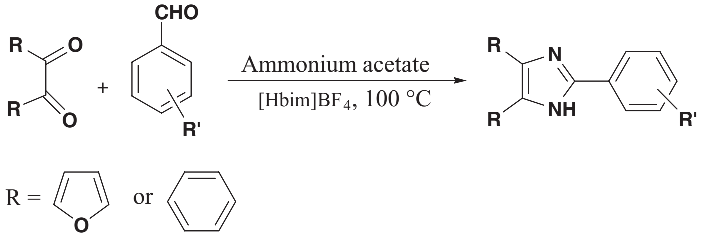
Cyclodehydration of diols is an important reaction to synthesize heterocycles in the chemical industry. As we all know, 1,4-dioxane, which is the main product of cyclodehydration of diethylene glycol (DEG), is an excellent solvent with high volatility and solubility and widely used in manufacture of specialty chemicals, pesticides and bulk drug intermediates. Traditionally, cyclodehydration of DEG is carried out by employing mineral acids such as sulfuric acid or phosphorus acid, heteropoly acid, cation exchange resin, or zeolites. However, these catalysts have some disadvantages for cyclodehydration of DEG. Mineral acids would either corrode the reaction equipment or cause pollution to the environment; heteropoly acid is too expensive to use; the use of cation exchange resins would be massive, and zeolites would be deactivated in the process. The use of acidic Bronsted ionic liquids as novel reaction media may offer a convenient solution to both solvent emission and the catalyst recycling problem. Indeed, cyclodehydration of diethylene glycol using various acidic Bronsted ionic liquids as dual solvent-catalysts was studied (*Scheme 101*).[18] The main advantage of this procedure was high conversion of DEG, easy preparation and reuse of IL, avoiding toxic catalysts and solvents.



Scheme 101

b) Imidazoles

Compounds with an imidazole ring system have many pharmacological properties and can play important roles in biochemical processes. An improved and rapid one-pot synthesis of 2,4,5-triarylimidazoles *via* the condensation of 1,2-diketones and α-hydroxy ketones such as benzoin with aromatic aldehydes and ammonium acetate in a room temperature ionic liquid was described and does not need any added catalyst (*Scheme 102*). Different



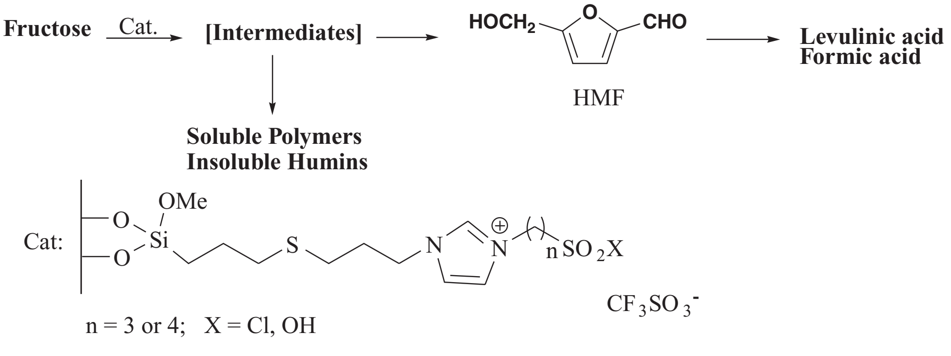
Scheme 102

ionic liquids based on 1-*n*-butyl and 1,3-di-(*n*-butyl) imidazolium salts were screened and their efficacy in terms of acidity and polarity were correlated with yields and reaction time. [Hbim][BF_4] promoted this reaction by virtue of the inherent Bronsted acidity conferred by its most acidic hydrogen. This would make the ionic liquids capable of bonding with carbonyl oxygen, increasing the reactivity of the parent carbonyl compounds. The one-pot methodology resulted in excellent isolated yields in short reaction times, and was characterized by simple work up procedures and efficient recovery and recycling of the ionic liquid, which acted as a promoter.[84]

c) Furfural

The preparation of 5-hydroxymethylfurfural (HMF) through the dehydration reaction of sugars is one of the most important approaches to transform biomass to useful chemicals, as HMF and its derivatives have been recognized as promising surrogates for petroleum-based chemicals. For example, HMF is known as a potential biofuel and one of its oxidative derivatives, 2,5-furandicarboxylic acid, may replace terephthalic acid as a monomer in the production of plastics.

Preparations of 5-hydroxymethylfurfural (HMF) by the dehydration of fructose in the presence of the acidic Bronsted ionic liquid, 3-allyl-1-(4-sulfobutyl)imidazolium trifluoromethanesulfonate, as well as its Lewis acid derivative, 3-allyl-1-(4-sulfuryl chloride butyl)imidazolium trifluoromethanesulfonate, were investigated (*Scheme 103*). It was concluded that the type of acidic ionic liquid used played a significant role in the reaction, and the Lewis acidic ionic liquid acted more effectively than its acidic Bronsted counterpart.



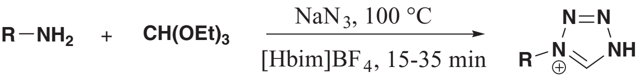
Scheme 103

When these acidic ionic liquids were immobilized on silica gel, they were as effective and reusable solid catalysts for the dehydration reaction of fructose to HMF, offering much better performances for the title reaction than sulfuric acid and sulfonyl chloride modified silica gels in terms of activity and reusability.[85]

d) Tetrazole

Tetrazoles are an increasingly popular functional group with wide ranging applications. This functional group has roles in coordination chemistry as a ligand, in medicinal chemistry as a metabolically stable surrogate for a carboxylic acid group, and in various materials science applications including propellants and explosives.

An efficient synthesis led directly to 1-substituted-1H-1,2,3,4-tetrazoles from easily available amines and sodium azide in stoichiometric proportions using ionic liquid 1-n-butylimidazolium tetrafluoroborate in excellent yields (*Scheme 104*). The inherent Bronsted acidity and high polarity of the IL resulted in a significant enhancement in the reaction rate.[86]

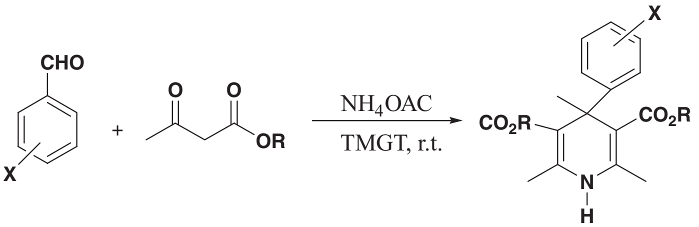


Scheme 104

e) Synthesis of Six-membered Heterocycles

1,4-Dihydropyridines (DHPs) exhibit a wide range of biological activities, acting as potent vasodilators, antihypertensives, bronchodilators, antiatherosclerotics, hepatoprotective, antitumor, antimutagenic, geroprotective, and antidiabetic agents. DHPs are commercially used as calcium channel blockers for treatment of cardiovascular disease.

The combination of 1,1,3,3-tetramethylguanidinium trifluoroacetate (TMGT) as ionic liquid and ultrasound irradiation was a rapid and efficient method for the three-component condensation synthesis of 1,4-dihydropyridines at room temperature (*Scheme 105*).



Scheme 105

In this approach, the use of large volumes of organic solvents was avoided; the work-up was simplified, and reaction times were considerably decreased.[87]

A facile enamination of 1,3-dicarbonyl compounds was developed that afforded good to excellent yields of β-enamino esters and β-enaminones using acidic Bronsted ionic liquid 1-methylimidazolium trifluoroacetate ([Hmim]Tfa) at room temperature (*Scheme 106*).

R_1 = OMe, OEt, Me; R_2 = Me, Ph; R_3 = H, Ph, $SiMe_3$

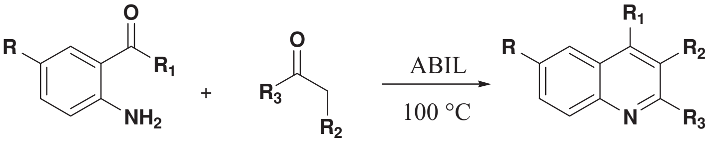
Scheme 106

This methodology was extended for the synthesis of substituted pyridines in excellent yield by a one-pot, three-component reaction of 1,3-dicarbonyl compounds, ammonium acetate, and alkynone in the presence of [Hmim]Tfa.[88]

f) Quinolines

The quinoline nucleus occurs in several natural compounds (cincona alkaloids) and pharmacologically active substances displaying a broad range of biological activity. The biological activity of quinoline compounds has been found in the form of antiasthmatic, antibacterial, anti-inflammatory, and antihypertensive properties. In addition to the medicinal applications, quinolines have been employed in the study of bioorganic and bioorganometallic processes. They are also known for their formation of conjugated molecules and polymers that combine enhanced electronic, optoelectronic, or non-linear optical properties with excellent mechanical properties.

1-*n*-Butylimidazolium tetrafluoroborate [Hbim]BF_4 was evaluated for the preparation of biologically active substituted quinolines and fused polycyclic quinolines using the Friedlander heteroannulation reaction (*Scheme 107*). The reactions proceeded very well under relatively mild conditions without any added catalyst. The IL acted as a promoter for this regiospecific synthesis in 90–98% yield and was recycled.[89]



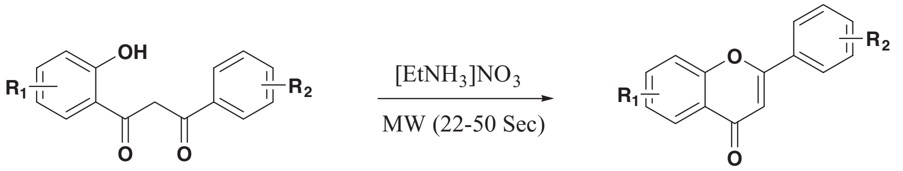
R = H, R_1 = CH_3 or R = Cl, R_1 = Ph

Scheme 107

g) Flavones and Coumarins

Flavones are important naturally occurring organic compounds possessing a wide range of biological activities used in the treatment of various diseases. A high yielding and rapid method for the smooth conversion of substituted 1-(2-hydroxyphenyl)-3-phenyl-1,3-propanediones to the corresponding 2-phenyl-4H-chromen-4-ones under microwave irradiations using ionic liquid [$EtNH_3$]NO_3 was reported (*Scheme 108*).[90]

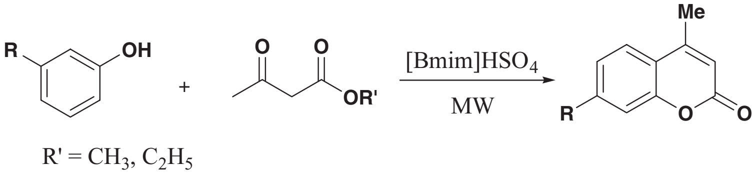
Coumarin derivatives are natural products widely distributed in the plant kingdom and are mainly used as fragrances, pharmaceuticals, and agrochemicals. The synthesis of coumarins has been carried out by the Pechmann reaction by condensation of phenols with



Scheme 108

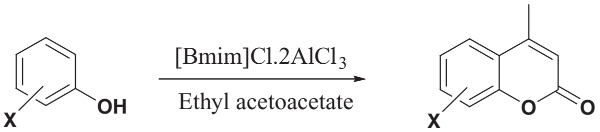
β-ketoesters in acidic medium. A large number of catalysts have been used for this reaction, such as. H_2SO_4, $HClO_4$, P_2O_5 and chloroaluminate ionic liquids; however, these reagents are required in excess and their corrosive nature makes them difficult to handle, in addition to the formation of several side products.

The use of acidic room temperature ionic liquid 1-butyl-3-methylimidazolium hydrogen sulfate was exploited for the synthesis of coumarins under microwave irradiation and solventless conditions in short duration of time with quantitative yields (*Scheme 109*).[91]



Scheme 109

1-Butyl-3-methylimidazolium chloroaluminate, [Bmim]Cl.2AlCl$_3$ ionic liquid was utilized as an alternative to conventional acid catalysts in the Pechmann condensation of phenols with ethyl acetoacetate and led to the formation of coumarin derivatives (*Scheme 110*). The reaction time was reduced drastically even under ambient conditions. The ionic liquid played the dual role of solvent and Lewis acid catalyst and provided a quick and efficient route to the syntheses of coumarins.[92]

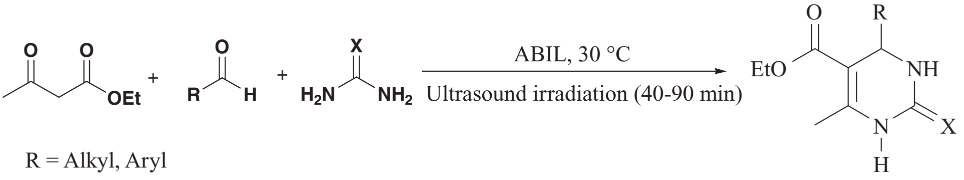


Scheme 110

h) Pyrimidines

In recent years, 3,4-dihydropyrimidin-2-(1H)-ones (DHPMs) and their derivatives have attracted considerable interest because of their therapeutic and pharmacological properties. They have emerged as integral backbones of several channel blockers, antihypertensive agents and neuropeptide Y (NPY) antagonists. Moreover, several alkaloids containing the DHPM unit have been isolated from marine sources, which also exhibit interesting biological properties.

3,4-Dihydropyrimidin-2-(1H)-ones were synthesized in excellent yields in short reaction time at ambient temperature in the absence of any added catalyst by the reaction of aromatic or aliphatic aldehydes with ethyl acetoacetate (EAA) and urea (or thiourea) in ionic liquid [Hbim]BF_4 under ultrasound irradiation (*Scheme 111*).



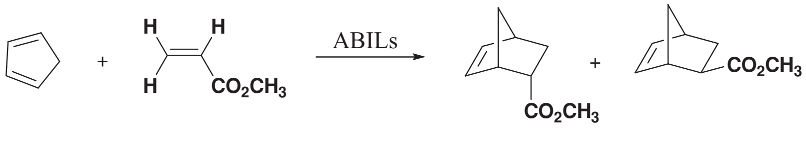
Scheme 111

The ionic liquid [Hbim]BF_4 acted as a favorable medium with improved energetics of cavitation for the sonochemical process and also promoted the reaction with its inherent Bronsted acidity, thus obviating the necessity of using additional acid catalyst. The Bronsted acidity was conferred by the −NH proton of [Hbim]BF_4 capable of bonding with the carbonyl oxygen of the aldehydes as well as that of the β-keto ester EAA.[93]

22. Diels-Alder Reaction

The Diels-Alder reaction is a powerful tool in organic synthesis and in the chemical industry. Ionic liquids have been used as solvents and as acid catalysts for Diels-Alder reactions. More recently, a number of Diels-Alder cycloadditions were reported in aprotic, imidazolium ILs, as well as a carbohydrate IL based on fructose. Chloroaluminate ILs with Al_2Cl_7 and Al_3Cl_{10} anions were also used as both solvents and Lewis catalysts. ILs have been employed to further increase the yield of endo products in the Diels-Alder reaction.[94]

The Diels-Alder cycloaddition reaction between methyl acrylate and cyclopentadiene was investigated in a number of air and moisture stable ionic liquids (*Scheme 112*). Ionic liquids [Bmim][BF_4], [Bmim][ClO_4], [Emim][CF_3SO_3], [Emim][NO_3], and [Emim][PF_6], and [$EtNH_3$] [NO_3] were used as solvents for this reaction. Hence, they are potentially useful solvents for Diels-Alder cycloadditions, and related reactions, particularly for moisture and oxygen sensitive reagents.

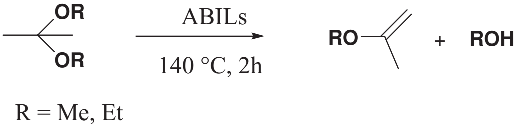


Scheme 112

Reaction of cyclopentadiene with methyl acrylate leads to a mixture of *exo* and *endo* products. The use of room-temperature ionic liquids, lead to substantial *endo* selectivity enhancements when compared to non-polar solvents. Polarity of the solvent leading to the stabilization of the more polar (*endo*) activated complex. The ionic liquids showed selectivities that were characteristic of hydrogen-bonding, polar organic solvents. In ethylammonium nitrate *endo*/*exo* ratios were higher. It is possible that this was a consequence of a more highly ordered structure of the transition state with the ethylammonium salt, which was held together by N—H hydrogen bonds rather than the weaker C—H hydrogen bonds that dominate in imidazolium salts.[95]

23. Cracking Reaction of Dialkoxypropanes

Alkoxypropenes are a highly valuable class of fine chemicals with applications in polymer formulations, surfactants and drug delivery systems as well as general organic syntheses. They are important intermediates in the synthesis of clarithromycin, β-ionone, vitamin A, and vitamin E. Simple ammonium ionic liquids such as ([Et_3NH][H_2PO_4]), [Me_3NH] [H_2PO_4], [Et_2NH_2][H_2PO_4], [Et_3NH][HSO_4], [Me_3NH][HSO_4], [Et_2NH_2][HSO_4], [Pr_3NH][HSO_4], [Bu_3NH][HSO_4], [Et_3NH][BF_4], and [Et_3NH][CH_3COO] have been used in the cracking reaction of dialkoxypropanes to alkoxypropenes without the use of traditional volatile organic compounds and additional catalysts (*Scheme 113*). The reactions proceeded well in sulfated ionic liquids and alkoxypropenes were obtained with high conversion and selectivity, especially in the [Et_3NH][HSO_4] ionic liquids.[22]

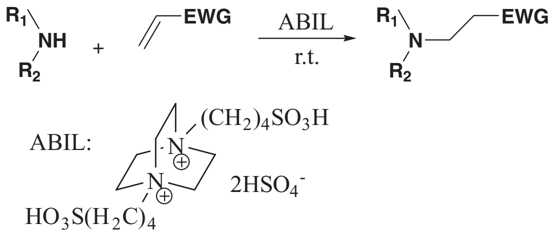


Scheme 113

24. Conjugate Addition of Amines to Electron-deficient Alkenes

The addition of nitrogen compounds across carbon–carbon multiple bonds is an unsolved synthetically important problem for both basic research and for the chemical industry. An alternative method for preparing these compounds is *via* the Michael addition. It is a very straightforward approach for the synthesis of substituted amines and their derivatives with 100% atom efficiency and without any by-product formation. A number of alternative procedures have been reported recently using a variety of reagents such as Pd compounds, $InCl_3$, $CeCl_3$, $Yb(OTf)_3$, $Bi(NO_3)_3$, $Bi(OTf)_3$, $Cu(OAc)_2$, $LiClO_4$, clay, silica gel, SmI_2, $FeCl_3$, $CrCl_3$, $SnCl_4$, and base ionic liquids. Many suffer from limitations such as the requirement for a large excess of reagents, long reaction times, harsh reaction conditions and also involvement of toxic solvents such as acetonitrile or 1,2-dichloroethane. Hence, the development of less expensive, simpler, greener catalysts for the reactions is highly desirable.

An efficient procedure was developed for the conjugate addition of amines to electron-deficient alkenes by using multi-SO_3H functional ionic liquid (*Scheme 114*). Operational simplicity, without need of any solvent, low cost of the catalyst used, high yields, excellent chemoselectivity, applicability to large-scale reactions were the key features of this methodology.[29]

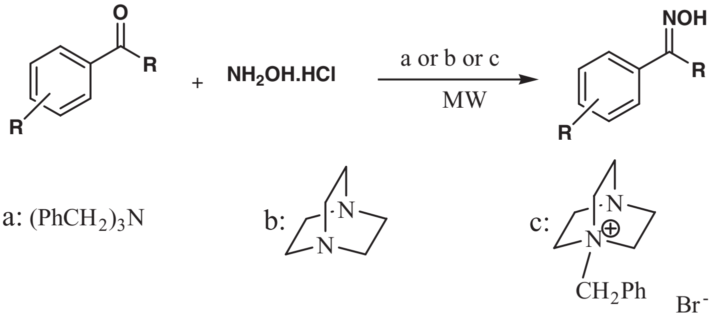


Scheme 114

25. Oximation

Oximes are highly crystalline materials and oximation is a very efficient method for the characterization and purification of carbonyl compound. These compounds not only represent a useful series of derivatives of carbonyl compounds, but also may be used as intermediates for the preparation of amides by the Beckmann rearrangement, nitrones, hydroximinoyl chlorides, nitrile oxide, and chiral α-sulfinyl oximes. The usual method for preparation of oximes involves treatment of carbonyl compounds with hydroxylamine hydrochlorides in a basic aqueous medium.

Tribenzylamine (TBA) or 1,4-diazabicyclo[2.2.2]octane (DABCO) or 1-Benzyl-4-aza-1-azoniabicyclo[2.2.2]octane bromide (BDABCO) can serve as base and as precursors of ionic liquids for the preparation of aldoximes under microwave irradiation. This method was friendly to the environment (*Scheme 115*).[96] Protonation of these organic bases during the reaction makes them ionic liquids which thereby enhance the reaction rate under microwave irradiation.



Scheme 115

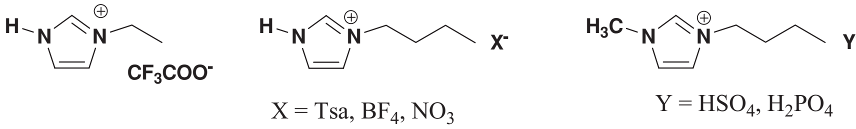
IV. Electrochemical Applications

In the field of electrochemistry, ILs were expected to be key materials to provide a solution to the safety problems of batteries because of to their non-flammable property.[97] Ionic liquids, with good thermal and electrochemical stability, non-flammability, high ionic conductivity, negligible pressure, and wide electrochemical potential windows at ambient temperature, are promising media for electrochemical synthesis and a real potential for use in rechargeable Li-ion batteries, biosensors,[98–101] actuators,[102] solvents for electrochemical devices, super capacitors fuel cells, dye-sensitized solar cells,[103] and polymer electrolytes.[104]

Molten salt ILs at ambient temperature are attracting increasing interest due to their specific properties, which make them appealing alternative electrolytes in advanced electrochemical devices. In this respect, attention had been paid mostly to imidazolium salts because of their high ionic conductivity and high electrochemical stability. Protic ILs for example, Bronsted acid–base molten salts derived from the combination of organic amines and *N,N-bis*(trifluoromethanesulfonyl)imide (HTFSI) behaved as good electrolytes in cells designed for hydrogen oxidation and oxygen reduction at platinum electrodes at relatively high temperatures (130°C and above).

Acidic Bronsted ionic liquids were successfully applied to the electrochemical synthesis of polyaniline films on platinum electrode surfaces by using cyclic voltammetry. The films exhibited quite dense packing and good ordering of polymer dendrite as compared with those prepared using conventional hydrochloric acid, indicated that Bronsting acid ionic liquids were as promising alternatives to dual medium-dopants in the synthesis of conducting polymers. Bronsted acids such as HCl or H_2SO_4, were extensively used in the electrochemical oxidative polymerization of PAN (polyacrylonitrile) and ABILs acted as the supporting electrolyte in the synthesis of PAN.

The ABILs applied were 1-ethylimidazolium trifluoroacetate ([Heim][Tfa]), 1-butylimidazolium tetrafluoroborate ([Hbim][BF_4]), 1-butylimidazolium nitrate ([Hbim] [NO_3]), 1-butylimidazolium *p*-toluenesulfonate ([Hbim][Tsa]), 3-butyl-1-methyl-imidazolium dihydrogen phosphate ([Bmim][H_2PO_4]) and 3-butyl-1-methylimidazolium hydrogen sulfate ([Bmim][HSO_4]) (*Scheme 116*).[36]

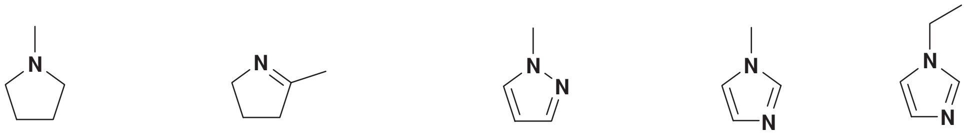


X = Tsa, BF_4, NO_3

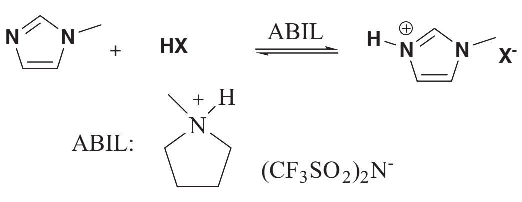
Y = HSO_4, H_2PO_4

Scheme 116

A series of ionic liquids (ILs) were prepared by neutralizing tertiary amines (*Scheme 117*) with N,N-bis(trifluoromethanesulfonyl)imide (HTFSI) (*Scheme 118*).



Scheme 117

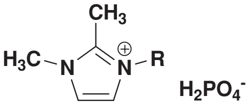


Scheme 118

These ILs had very good temperature stability and a high ionic conductivity (10^{-2} Scm^{-1}). By incorporating these ILs into a poly(vinylidenfluoride-co-hexafluoropropylene) polymer matrix, membranes with a high melting temperature, high decomposition point, and an ionic conductivity of about 10^{-2} Scm^{-1} at 140°C, were obtained. These IL-based, proton-conducting membranes were proposed as new polymer electrolytes for high-temperature polymer electrolyte membrane fuel cells (PEMFCs).[105]

Ionic liquids comprising imidazolium cations and acidic counteranions were important due to their ability of proton conduction. Polymer electrolytes containing ionic liquids with dihydrogenphosphate ($H_2PO_4^-$) and bisulfate (HSO_4^-) anions received much attention due to their suitability as potential candidates for high temperature membranes for use in polymer electrolyte membrane fuel cells (PEMFCs).

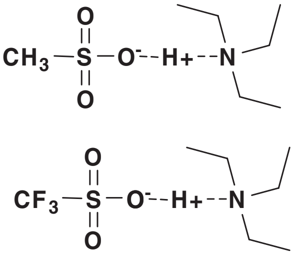
The conductivity and viscosity of ionic liquids containing acidic counteranion, such as 2,3-dimethyl-1-alkylimidazolium dihydrogenphosphate ($DMRImH_2PO_4$), were found to depend upon the chain length of alkyl (R) group, and ionic liquid with ethyl group ($DmEtImH_2PO_4$) showed maximum conductivity of 0.07 Scm^{-1} at 120°C (*Scheme 119*). The conductivity of polymer electrolytes containing ($DmEtImH_2PO_4$) in a polymer matrix was found to depend upon the concentration of ionic liquid, phosphoric acid and temperature. Polymer electrolytes containing different ionic liquids were thermally stable up to 225°C and were suitable as high temperature membranes in proton exchange membrane fuel cells under non-humid conditions.[40]



R = Ethyl, Butyl, Octyl

Scheme 119

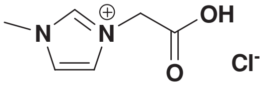
The performance of anhydrous proton-conducting polymers obtained by blending modified Nafion membranes with proton conducting ionic liquids (PILs) was investigated. The results emphasized the importance of the PIL uptake by the functional polymer (*Scheme 120*). The best PIL did not necessary result in the more conducting membrane. Optimization of the membrane conductivities therefore required adapting the ionic liquid (anion and ammonium) in order to get the suitable PIL uptake. Nafion was present in the electrode



Scheme 120

active layers and therefore these electrodes were used after blending Nafion with PIL in high-temperature proton exchange membrane fuel cells (PEMFCs).[79]

The high ionic conductivity of carboxylic acid functionalized room temperature ionic liquid appears to be decisive for its successful application as electrolyte in a Leclanché battery with benzoquinone as manganese dioxide substitute (*Scheme 121*).[106]



Scheme 121

V. Cost and Life Cycle of Acidic Bronsted ILs

The development of a catalytic system that may be green, cost-effective, mild, easily separable, and reusable has long been awaited. Acidic ionic liquids have been successfully used in organic reactions due to their unique properties such as very low vapor pressure and reusability.[107]

The demonstrated ability of the ionic liquid to be reused indefinitely will enable production of large quantities of product per unit ionic liquid catalyst. This will provide a substantial increase in the ratio of product value to cost of production. Additionally, since catalyst is not lost or consumed during the process, addition of fresh catalyst is not necessary. The ability to indefinitely reuse catalyst will also substantially reduce the amount of waste generated and will substantially lower the cost of disposal and environmental impact of the process.

To extend the scope and decrease the cost of ILs, a new and inexpensive class of ILs as acidic ILs was synthesized by simple protonation of amines with protic acids. Acidic Bronsted ionic liquids have the useful characteristics of solid acids and mineral liquid acids and are designed to replace traditional mineral liquid acids like sulfuric acid and hydrochloric acid in chemical procedures.[108]

However, for practical utilization, imidazolium-based ionic liquids still suffer from a relatively expensive cost. Non-imidazolium-based ILs should be of particular interest due to their availability in technical quantities and lower cost compared to their imidazolium-based counterparts.[107]

VI. Toxicity of Acidic Bronsted ILs

Although the information about physical, thermodynamic, kinetic or engineering data had been extended continuously, up to now only limited data with regard to the toxicity and ecotoxicity of ionic liquids have been available. The green character of ionic liquids has usually been justified with their negligible vapor pressure, but even if ionic liquids will not evaporate and not contribute to air pollution, most of them are water soluble and might enter the environment by this path (*e. g.* accidental spills, effluents).

Experimental studies have been helpful in establishing general guidelines for the selection of ILs with low potential for toxicity. However, relatively little is still known about the toxicity of these materials as a class, especially when compared to conventional organic solvents. Several recent toxicity studies of IL effects on organisms have been documented and the following results obtained. Polymeric materials with pyridinium functionality can exhibit significant toxicity to bacteria.

Antimicrobial activity increased as the alkyl chain length increased on pyridinium, imidazolium, and quaternary ammonium salts.[109]

Many ILs are similar to cationic surfactants, which are known to induce polar narcosis due to their ability to be incorporated into biological membranes. Therefore, longer alkyl chains may be incorporated into the polar headgroups of the phospholipid bi-layer, which are the major structural components of membranes. Narcosis then results because membrane-bound proteins are disrupted by the toxicant. Many of the imidazolium and pyridinium compounds were more toxic than common high-volume solvents such as acetonitrile, acetone and methanol. Some exceptions include low alkyl chain length quaternary ammonium ILs and those ILs containing choline as the cation, which were relatively nontoxic. The data suggest that choline or quaternary ammonium solvents may be more environmentally friendly alternatives than both aromatic ILs and some traditional industrial solvents.

Varying the anion has a minimal effect on the toxicity of pyridinium and imidazolium salts, which suggests that toxicity is largely derived by the cation, although recent studies indicate that the anion can play a role in toxicity.

Toxicity was predicted to increase slightly with the number of nitrogen atoms having two aromatic bonds and one single bond. Thus, ammonium cations are less toxic than pyridinium cations, which are slightly less toxic than imidazolium cations. If true, this would mean that triazolium-based ILs would be even more toxic than imidazolium-based compounds. The IL toxicity should decrease as the number of negatively charges atoms on the cation increases.

Although anions play a secondary role in determining toxicity, the results indicate that the presence of positively charged atoms in the anion leads to higher toxicity than those systems with a single negative anion atom. The correlations also indicate that methylating the aromatic ring of the cation should reduce toxicity.[110–112]

VII. Summary

Acidic Bronsted ionic liquids as environmental-friendly solvents and catalysts with high activity and selectivity and easily recovered were used to replace traditional liquid acids, such as sulfuric acid and hydrochloric acid, in chemical processes, especially acid catalyzed reactions, in which using traditional liquid acids and solid acids had problems, such as high toxicity, corrosion, difficulties in separation or recovery, and disposal problems due to a large number of acidic effluents. The acidity of Bronsted acids was calculated by the Hammett method. Acidic ionic liquids were synthesized by direct neutralization of amines and phosphines that usually had acidic groups in the cation, with traditional acids that formed ionic liquids with acidic cation or acidic anion.

Acidic Bronsted ionic liquids with acidic cation or acidic anion had special importance because they had simultaneously the proton acidity and the characteristic properties of ionic liquid.

Bronsted or Lewis acidic ionic liquids were used as solvents and catalysts in many organic reactions such as esterification, polymerization, alkylation, acylation, carbonylation, aldol condensation, pinacol rearrangement, nitration, Koch reaction, oxidation of alcohols, alcohol dehydrodimerization, Mannich reactions, cleavage of ethers, Beckmann rearrangement, oximation, halogenation, Diels-Alder reaction, heterocyclic synthesis, nitration, and the Prins reaction; and they also were successfully applied to the electrochemical process.[113–119]

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