Ionic liquid as a Green Catalyst and Solvent Media for Friedel-Craft Acylation Reaction

Dinesh D. Thakare

Nikhil N. Gharat

1st yr M.Tech. Green Technology

Abstract:

Ionic liquids, being composed entirely of ions, their lack of measurable vapor pressure characterizes them as green solvents, and that a wide range of chemical reactions can be performed in them. Friedel–Crafts acylation reactions are of great importance in both laboratory work and industry processes to synthesize aromatic ketones. $AlCl_3$, H_2SO_4, HF or other Lewis acid can be used as catalyst in Friedel–Crafts reactions. However, these catalysts can cause a serious environmental problem during purification, and are very difficult to reuse. Therefore, it is important to replace these highly corrosive and hazardous acid catalysts with environmentally friendly catalysts which are active under mild conditions and can be easily regenerated after reaction. In recent years, ionic liquids have shown great promise as an attractive alternative to conventional catalysts and solvents for synthesizing organic chemicals. The Friedel–Crafts acylation using ionic liquids have been reviewed in this article.

Key-Words: Ionic Liquids, $[bmim]Cl/AlCl_3$, [bmIm][dca], [emIm][dca], ($[bmim][BF_4]^-$) , ($[bmim][PF_6]^-$) , Friedel–Crafts Acylation.

1. INTRODUCTION:

From the viewpoint of today's environmental consciousness, there is a growing need for greener and more sustainable processes in the chemical industry. Replacement or elimination of some toxic reagents or volatile organic solvents in chemical processes is one of the main goals of green chemistry.

It is well known that, Friedel-Crafts acylation of aromatic compounds has been an important reaction in the production of aryl ketones, which are important intermediates in the production of pharmaceuticals and fine chemicals. Friedel-Crafts acylation of aromatics is usually conducted in volatile organic solvents with acyl halide and acid anhydride being used as acylating agents. The conventional catalysts are Lewis acids ($AlCl_3$, $FeCl_3$, $TiCl_4$, and BF_3) and Bronsted acids (HF, H_2SO_4, and HCl). Until now, $AlCl_3$ or HF was still used as catalysts in many of the industrial processes, producing a high amount of contaminated waste. Moreover, the FC acylation using these Lewis acids are associated with ecological and economic problems including toxicity, corrosion, generation of large amounts of waste, and difficulty in the purification of the final product. Consequently, there remains a strong need for developing a green, moisture-insensitive, simple and cost-effective catalytic system for Friedel–Crafts acylation[1].

Ionic liquid is actually just a liquid salts consisting of ions and ion pairs[2]. Ionic liquids (ILs) have attracted growing academic and industrial interest because of their special properties including excellent thermal and chemical stability, no measurable vapor pressure, non-explosive, good tuneable solubility and it provides the reusability of `green' solvent and catalyst for chemical reactions. In F. C. acylation reaction, ionic liquids have been applied successfully as a way of avoiding corrosive and polluting catalyst system such as HF or $AlCl_3$ in chloroform or benzene[3].

Ionic liquids offer numerous advantages over conventional organic solvents for carrying out organic reactions. Such as, easy product recovery, catalyst can be reused, favourable thermodynamic and kinetic behaviour, enhanced rate of reaction and high selectivity. Ionic liquids usually show the properties summarised in Table No.1.

A salt	Cation and/or anion quite large
Freezing point	Preferably below 100°C

Liquidus range	Often > 200°C
Thermal stability	Usually high
Viscosity	Normally < 100 cP, workable
Dielectric constant	Implied < 30
Polarity	Moderate
Specific conductivity	Usually < 10 $mScm^{-1}$, "Good"
Molar conductivity	< 10 $Scm^2\ mol^{-1}$
Electrochemical window	> 2V, even 4.5 V, except for Bronsted acidic systems
Solvent and/or catalyst	Excellent for many organic reactions
Vapour pressure	Usually negligible

Table 1: Properties of ionic liquids[4]-

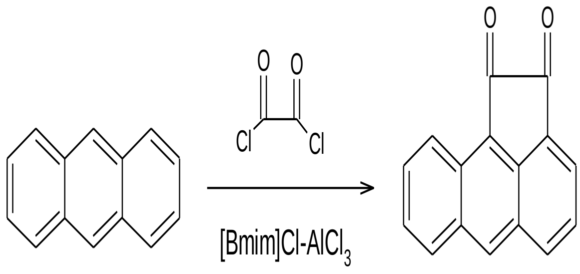
Source: - Ref. 4

2. APPLICATIONS:

Boon et al., firstly reported the acylation of benzene with the ionic liquid of [emim] $Cl/AlCl_3$ ($[emim]^+$ = 1-methyl-3-ethylimidazolium cation) to produce acetophenone. There is only mono-substitution, when benzene and acetyl chloride were reacted in acidic [emim]$Cl/AlCl_3$ ionic liquid. Ionic liquid provided an excellent medium for Friedel–Crafts reaction[5].

2.1.1 The acylation reaction of anthracene with oxalyl chloride[6]:

Xin-hua et al., reported an efficient preparation method of 1,2-aceanthrylenedione through acylation of anthracene with oxalyl chloride in the presence of [bmim]$Cl/AlCl_3$ ($[bmin]^+$ = 1-butyl-3-methylimidazolium cation) ionic liquid, which was demonstrated to be efficient and reusable catalyst and can be used as solvent for the acylation (See Scheme 1).



Scheme 1: Acylation of anthracene with oxalyl chloride.

Source: - Ref. 6

The acylation carried out as, anthracene and oxalyl chloride were put into a 100-mL three-neck flask equipped with a stirrer, a reflux condenser with drying pipe and a thermometer, then certain amount of [bmim]$Cl/AlCl_3$ was added to the flask in 10 min with continuous stirring. The acylation reaction was conducted for certain time with continuous stirring under atmospheric pressure at 45^0 C. Then the reaction mixture was cooled to room temperature, and induced into two liquid phases (organic phase and ionic liquid phase) by extracting with chloroform. Ionic liquid could be reused after the organic phase was extracted out with trichloromethane. Quantitative analysis was conducted according to the GC spectrum of organic phase accompanying with a correction factor. The organic phase was rinsed with acetonitrile and toluene after vacuum distillation, then red acicular 1,2-aceanthrylenedione was obtained after recrystallizing with ethanol. The maximum yield 88.2% and selectivity 98.2% of 1,2-aceanthrylenedione was obtained.

2.1.2 Comparison of [bmim]Cl/$AlCl_3$ ionic liquid with $AlCl_3$:

Friedel–Crafts acylation can be catalyzed by some other inorganic lewis acidic catalysts, of which $AlCl_3$ has the highest catalytic activity. In order to compare, the acylation of anthracene with oxalyl chloride was also carried out with equivalent $AlCl_3$ as catalyst, and CS_2 was used as solvent. The results show that [bmim]Cl/$AlCl_3$ is an environmentally friendly catalyst, and the catalytic efficiency of [bmim]Cl/$AlCl_3$ is better than that of $AlCl_3$. The yields of 1,2-aceanthrylenedione when using [bmim]Cl/$AlCl_3$ and $AlCl_3$ were 88.2% and 83.8%, respectively, and the selectivity of 1,2-aceanthrylenedione were 98.2% and 92.3%, respectively. Furthermore, in the presence of [bmim]Cl/$AlCl_3$ ionic liquid, the isolation and purification for the target products was more easy and the acylation is free of any volatile organic solvent since the ionic liquid plays dual roles of Lewis acid catalyst and solvent. However, for $AlCl_3$ catalyst system, some problems were caused, such as heavy environmental pollution, troublesome recovery and purification of product, and difficult recovering of catalyst.

2.1.3 Recycle of Ionic Liquid:

The reusing performance of [bmim]/$AlCl_3$ was investigated with the recycle experiments. After extracting the reaction mixture with chloroform, the reaction mixture became two liquid phases, organic phase (unreaction reactants and products phase) and [bmim]Cl/$AlCl_3$ ionic liquid phase. [Bmim]Cl/$AlCl_3$ was reused as catalyst after extracting out the organic phase with ether and vacuum drying at 80–100^0C for 30 min. The acylation results which catalyzed by the recycled [bmim]/$AlCl_3$ are summarized in Table 2.

Reusing times	Yield (%)	Selectivity (%)

1	88.2	98.2
2	88.0	98.2
3	88.1	97.5
4	87.9	96.4
5	87.3	96.1

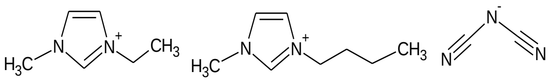
Table 2: Reusing performance of [bmim]/$AlCl_3$ in the acylation reaction

Source: Ref. 6

Thus the pure 1,2-aceanthryenedione was successfully prepared by acylation reaction of anthracene with oxalyl chloride in the presence of [bmim]Cl/$AlCl_3$ ionic liquid and Xin-hua et al., showed that [bmim]Cl/$AlCl_3$ can be used as a novel environmentally friendly catalyst and solvent for anthracene acylation reaction.

2.2 *O*-acetylation of alcohols and carbohydrates[7]:

Forsyth et al., reported that dicyanamide based ionic liquids are not only effective solvents for alcohols and saccharides but also active base catalysts for their *O*-acetylation. The ionic liquids investigated were butylmethylimidazolium dicyanamide [bmIm][dca] and ethylmethylimidazolium dicyanamide [emIm][dca] (See Figure 1).



1a 1b 2

Figure 1: (**1a** or **1b)** Imidazolium cation and (**2)** dicyanamide anion**.**

Source: - Ref.7

Glucose is soluble in these liquids to greater than 10 weight percent at room temperature. The solubility of disaccharides (*e.g.* sucrose) and trisaccharides (*e.g.* raffinose) is less than glucose, although solubility of all saccharides increases with rising temperature. The dicyanamide ionic liquids appear to be unique, thus far, among families of ionic liquids in presenting high solubility to saccharides.

The acetylation reaction for range of alcohols and saccharides (such α-D-Glucose, β-Me-Glucose, Raffinose, 2-Naphthol, *t*-BuOH, and Cyclohexanol) by using dicyanamide ionic liquid and acetic anhydride and no added catalyst is carried out. In a typical reaction procedure, acetic anhydride (1.42 g, 13.9 mmol) was added to α-D-glucose (0.5 g, 2.78 mmol) and [bmIm][dca] ionic liquid (1.14 g, 5.56 mmol). The mixture was stirred at room temperature until completion of reaction. Water was added to precipitate penta-*O*-acetyl-D-glucopyranose (isolated yield 89%), whereas the reaction at 50^0C gives the 98% isolated yield. The extent of acetylation and the anomeric ratio were determined using ^{1}H NMR for samples of crude reaction mixture and isolated product. The acylation reactions of all the substrate using the dicyanamide ionic liquid yielded the completely acetylated product with more than 85% yield.

Forsyth et al., observe that the reactions proceed just as rapidly, in the absence of catalyst, whereas the catalysed reaction indicates that the ionic liquid has a more crucial role than simply as an inert solvent. This suggests that the ionic liquid is acting as a regenerating catalyst. The mechanism of this catalysis is currently under investigation, but it is most likely related to the basicity of the dicyanamide anion. The absence of any reaction in the case of the butylmethylimidazolium bis(trifluoromethanesulfonyl) amide [bmIm][tfsa] ionic liquid further supports this proposition. The recovered [emIm][dca] was re-used in an acetylation reaction and a similar reaction time was required for complete acetylation.

2.3 Gadolinium triflate immobilized in imidazolium based ionic liquids; recyclable catalyst and green solvent [8]:

Room temperature ionic liquids (RTILs) that are air and moisture stable have recently been found to be excellent environmentally benign solvents for a variety of reactions. Alleti et al., have explored the recyclability of $Gd(OTf)_3$ catalyst in RTILs, 1-butyl-3-methylimidazolium tetrafluoroborate ($[bmim][BF_4]^-$) **3,** and 1-butyl-3-methylimidazolium hexafluorophosphate ($[bmim][PF_6]^-$) **4,** (See Figure 2).

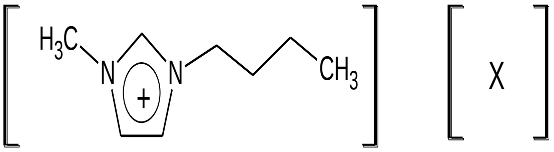


Figure 2: Room temperature ionic liquids.

3; $X = BF_4^-$

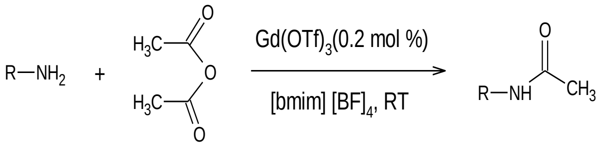
4; $X = PF_6^-$

Source: - Ref. 8

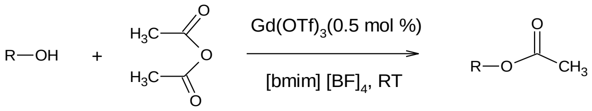
$Gd(OTf)_3$ is relatively more water tolerant than other lanthanide based metal triflates. Thus strictly anhydrous reaction conditions that have been used with other Lewis acid catalysts can be avoided in the case of this catalyst. In addition, it is a relatively inexpensive reagent. Alletic et al., have recently used this catalyst for efficient and convenient acetylations of alcohols and amines using acetic anhydride as the reagent in conventional organic solvents. A variety of primary, secondary and tertiary alcohols as well as phenols and amines can be acylated readily using this water-tolerant Lewis acid.

To examine the catalytic activity of $Gd(OTf)_3$ in RTILs, acetylation of benzyl alcohol with acetic anhydride was chosen initially as a model reaction. Benzyl alcohol reacted with acetic anhydride at room temperature in [bmim][BF_4] and [bmim][PF_6] in the presence of 0.5 mol percent of the catalyst. In [bmim][BF_4] the yields are good to excellent (92% 1st run), whereas in [bmim][PF_6] relatively lower yields (76% 1st run). When the solvent–catalyst system is recycled and reused, the catalytic activity was slightly decreased in the case of [bmim][BF_4] (72%, 3rd run), whereas a drastic decrease of yield (40% 3rd run) was observed in the case of [bmim][PF_6].

After having optimized the reaction conditions for benzyl alcohol, acetylations of various alcohols with acetic anhydride have been carried out in [bmim][BF_4] in the presence of 0.5 mol% of Gd$(OTf)_3$ as a catalyst at room temperature (See Scheme 2). The reactions of a variety of alcohols, Excellent yields of acylated products obtained for various substrates are as shown in Table 3 (Entry 10-13).



phenols, diols as well as allylic alcohols proceeded in excellent yields as shown in Table 3 (Entry 1-9).



Scheme 2: Gd$(OTf)_3$–[bmim][BF_4] catalyzed acetylation of alcohols.

Source: - Ref. 8

Alleti et al., have also investigated the acetylation of amines using Gd$(OTf)_3$ as the catalyst in [bmim][BF_4]. Using as low as 0.2 mol% of the catalyst, high yields of N-acetylated products have been obtained (Scheme 3). Gd$(OTf)_3$ catalyzed acetylation of amines proceeded in relatively shorter times as compared to acetylation alcohols as was also observed in case of CH_3CN as the solvent.

Scheme 3: $Gd(OTf)_3$ catalyzed acetylation of amines in $[bmim][BF_4]$.

Source: - Ref. 8

Entry	Substrate	Product	Yield (%)
1	phenol	phenyl acetate	88
2	naphthalen-1-ol	naphthalen-1-yl acetate	92
3	naphthalen-2-ol	naphthalen-2-yl acetate	90
4	4-nitrophenol	(4-nitrophenyl) acetate	76
5	benzene-1,4-diol	(4-acetyloxyphenyl) acetate	99
6	benzene-1,3-diol	(3-acetyloxyphenyl) acetate	93
7	benzene-1,2-diol	(2-acetyloxyphenyl) acetate	95
8	cyclohexanol	cyclohexyl acetate	92
9	3,7-dimethylocta-2,6-dien-1- ol	3,7-dimethylocta-2,6-dienyl acetate	86
10	phenylmethanamine	N-benzylacetamide	90
11	aniline	N-phenylacetamide	96
12	N-methylaniline	N-methyl-N-phenylacetamide	86
13	2-methylaniline	N-(2-methylphenyl)acetamide	89

Table 3: Acetylation of alcohols using $Gd(OTf)_3$–[bmim][BF4] (Entry 1-9), and Acetylation of amines using $Gd(OTf)_3$ catalyst in$[bmim][BF_4]$ (Entry 10-13)

Source: - Ref. 8

For selected compounds of alcohol and amines, Alleti et al. have demonstrated recyclability and reuse of the $Gd(OTf)_3$–$[bmim][BF_4]$ catalyst system (See Table 4). Moderate to high yields of the products were obtained in second and third runs.

Sr. No.	Substrate	Product	Yield (%)
1.	naphthalen-1-ol	naphthalen-1-yl acetate	92 (1st run)
			83 (2nd run)
			46 (3rd run)
2.	cyclohexanol	cyclohexyl acetate	92 (1st run)
			87 (2nd run)
			82 (3rd run)
3.	N-methyl aniline	N-methyl-N-phenylacetamide	86 (1st run)
			78 (2nd run)
			72 (3rd run)

Table 4: Reuse of $Gd(OTf)_3$–[bmim][BF_4] for representative acetylation reactions.

Source: - Ref. 8

In order to gain insight into the mechanism of these acetylation reactions, Alleti et al. have recorded a broad–band ^1H decoupled ^{13}C NMR spectrum for a solution of $Gd(OTf)_3$, Ac_2O and [bmim][BF_4] (1:30:7 mol ratio).A weak absorption at $\delta^{13}C$ 183.9 was (CD_2Cl_2 solvent) was observed indicating the formation of AcOTf as the reactive acylating agent. Based on this observation, a schematic representation of the proposed mechanism is shown in Figure 3.

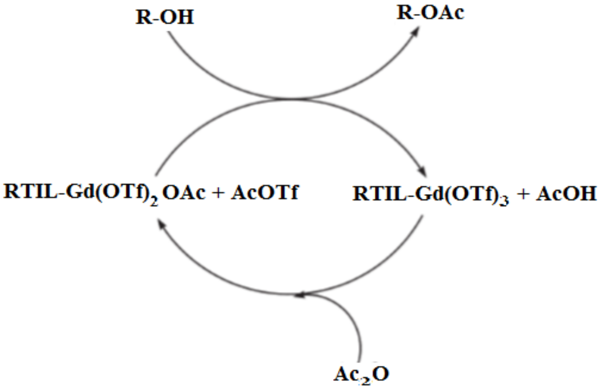


Figure 3: Schematic representation of the catalytic cycle for RTIL– $Gd(OTf)_3$ catalyzed acetylation mechanism.

Source: - Ref. 8

Thus, Gd $(OTf)_3$ immobilized in RTILs is an efficient recyclable catalyst system for acetylation of aliphatic and aromatic alcohols and amines. A variety of alcohols, phenols, diols as well as allylic alcohols and amines have been acetylated using 0.2 mol percent of the catalyst in these environmentally benign solvents.

3. CONCLUSION:

The application of ionic liquids in Friedel-Crafts acylation reactions is reviewed in present paper. Ionic liquids can be used as catalyst and solvents giving high reaction rate, conversion and selectivity, and catalyze both activated and deactivated aromatic compounds. The 88.2% yield and 98.2% selectivity of 1,2-Aceanthrylenedione was obtained by acylation of anthracene using [bmim]Cl/$AlCl_3$ and oxalyl chloride with 5 times reuse of the IL catalyst gives about similar results, and it was found to be better method than the Lewis acid catalyst. Similarly, the acylation of alcohols, carbohydrates and amines has been discussed and excellent results were obtained using ionic liquids. By choosing the correct ionic liquid, high product yields can be obtained and a reduced amount of waste can be produced in a given reaction. This method offers a good catalyst system in the context of ‘‘green’’ chemistry.

Reference:

1. Guenadil, F.; Aichaoui, H.; Lambert, D. M.; McCurdy C. R.; and Poupaert, J. H.; ‘Highly Selective Catalytic Friedel–Crafts Acylation of Activated Highly Selective Catalytic Friedel–Crafts Acylation of Activated Aromatic Compounds Using the I_2.DMF Complex as Catalyst’, *Letters in Organic Chemistry*, 5 (2008) 665-668.
2. Earle, M. J. and Seddon, K. R.; ‘Ionic liquids. Green solvents for the future’, *Pure and Applied Chemistry*, 72 (7) (2000) 1391–1398.
3. Chen, Y.; Zu, Y.; Fu, Y.; Zhang, X.; Yu, P.; Sun, G.; and Efferth, T.; ‘Efficient Lewis Acid Ionic Liquid-Catalyzed Synthesis of the Key Intermediate of Coenzyme Q10 under Microwave Irradiation’, *Molecules*, **15,** (2010), 9486-9495.
4. Johnson, K. E.; ‘What’s an Ionic Liquid?’ , *The Electrochemical Society Interface*, 16 (1) (2007) 38-41.
5. Boon, J. A.; Levisky, J. A.; Pflug, J. L.; and Wilkes J. S.; ‘Friedel–Crafts reactions in ambient temperature molten salts’, *Journal of Organic Chemistry*, 51 (1986) 480–483.
6. Xin-hua, Y.; Min, C.; Qi-xun, D.; and Xiao-nong, C.; ‘Friedel–Crafts acylation of anthracene with oxalyl chloride catalyzed by ionic liquid of [bmim]Cl/$AlCl_3$’, *Chemical*

Engineering Journal, 146 (2009) 266–269.

7. Forsyth, S. A.; MacFarlane, D. R.; Thomson, R. J.; and Itzstein, M. V.; ‘Rapid, clean, and mild O-acetylation of alcohols and carbohydrates in an ionic liquid’, *Chemical Communication*, (2002), 714–715.
8. Alleti, R.; Oh, W. S.; Perambuduru, M.; Afrasiabi, Z.; Sinn, E.; and Reddy, V. P.; ‘Gadolinium triflate immobilized in imidazolium based ionic liquids: a recyclable catalyst and green solvent for acetylation of alcohols and amines’, *Green Chemistry*, 7 (2005) 203–206.
9. Sanghi, R.; and Srivastava, M. M.; *Green Chemistry Environmental friendly alternatives*, Narosa Publication, New Delhi, 2007.