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IONIC LIQUID AS GREEN CATALYST & SOLVENT MEDIA FOR FRIEDEL CRAFT ACYLATION REACTION

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Abstract

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. Many clean solvents like water, ionic liquids, supercritical fluid, polyglycol, fluorine-containing solvents, and so on are employed to replace the conventional organic solvents. Among these, ionic liquids have attracted considerable attention as the clean designable solvents. Ionic liquids received global attention not only in the academic fields but also in the industrial circles. So far, the normal ionic liquids as the clean solvents, and the functional ionic liquids as the special clean solvents (e.g., chiral solvents), the catalysts, and the supports for reagents as well, have been applied extensively in many organic reactions, such as the alkylation, acylation, esterification, rearrangement, hydroformylation, coupling reactions, Diels–Alder reactions, asymmetric synthesis, and so on. This paper mainly reviews the role of the ionic liquids as the green solvent and catalyst for Friedel-Crafts acylation reactions.

Keywords: Acylation, Ionic liquids, Green solvent, Catalyst

I. 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 Brønsted 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 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 reusable '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 [2].

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 1.

II. APPLICATIONS

As this article aims to provide information on application of ionic liquids as a novel reaction media and catalyst as given bellow-

Wikes 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

Table 1: Properties of Ionic Liquid

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
Dielectric constant	Implied < 30
Polarity	Moderate
Specific conductivity	Usually < 10 $mScm^{-1}$
Molar conductivity	< 10 Scm2 mol^{-1}
Electrochemical window	> 2V, even 4.5 V, except for Brønsted acidic systems
Solvent and/or catalyst Excellent for many organic reactions	Excellent for many organic reactions
Vapor pressure	Usually negligible

[emim]Cl/$AlCl_3$ ionic liquid. Ionic liquid provided an excellent medium for this simplest Friedel–Crafts reaction [4].

A. The acylation reaction of anthracene with oxalyl chloride

Yuan 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 [5]. The reaction process is displayed in Fig.1.

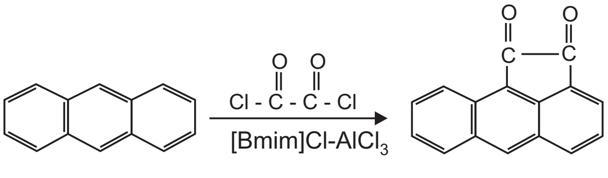


Fig. 1. Acylation of anthracene with oxalyl chloride

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 dropwise 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°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 value of 88.2% of yield and 98.2% of selectivity is observed.

1. 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. Recycle of Ionic Liquid

The reusing performance of [bmim]/$AlCl_3$ 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°C for 30 min. The acylation results which catalyzed by the recycled [bmim]/$AlCl_3$ are summarized in Table

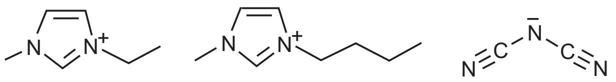
Table 2. Acylation of reused Ionic liquid

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

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 Yuan et al., showed that [bmim]Cl/$AlCl_3$ can be used as a novel environmentally friendly catalyst and solvent for anthracene's acylation reaction.

B. O-acetylation of alcohols and carbohydrates

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 [6]. The ionic liquids investigated were butylmethylimidazolium dicyanamide [bmIm][dca] and ethylmethylimidazolium dicyanamide [emIm][dca] (Fig.2).



[1a] [1b] [2]

Fig. 2. Imidazolium cation [1a] or [1b] and dicyanamide anion [2]

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.

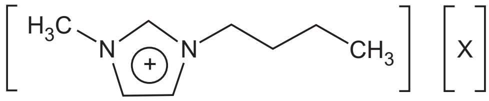
The acetylation reaction for range of alcohols and saccharides (such α -D-Glucose, β -Me-Glucose, Raffinose, 2-Naphthol, *t*-BuOH, and Cyclohexanol) by using dicyanamide ionic liquid and acetic anhydride and no added catalyst is carried out. In a typical reaction procedure, acetic anhydride (1.42 g, 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°C 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 in 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; a similar reaction time was required for complete acetylation.

C. Gadolinium triflate immobilized in imidazolium based ionic liquids for acetylation of alcohols and amines

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. [7], have explored the recyclability of Gd(OTf)$_3$ catalyst in RTILs, 1-butyl-3-methylimidazolium tetrafluoroborate ([bmim][BF$_4$]$^-$, and 1-butyl-3-methylimidazolium hexafluorophosphate ([bmim][PF$_6$]$^-$. as shown in Fig. 3.



1. X = BF_4^-
2. X = PF_6^-

Fig. 3. Room temperature ionic liquid

$Gd(OTf)_3$ 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 Ac_2O 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 Ac_2O was chosen initially as a model reaction. Benzyl alcohol reacted with Ac_2O 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% 1^{st} run), whereas in $[bmim][PF_6]$ relatively lower yields (76% 1^{st} run) were obtained. When the solvent–catalyst system is recycled and reused, the catalytic activity was slightly decreased in the case of $[bmim][BF_4]$ (72%, 3^{rd} run), whereas a drastic decrease of yield (40% 3^{rd} run) was observed in the case of $[bmim][PF_6]$.

After having optimized the reaction conditions for benzyl alcohol, acetylations of various alcohols with Ac_2O 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 (Fig.4). The reactions of a variety of alcohols, phenols, diols as well as allylic alcohols proceeded in excellent yields, e.g. Phenol (88% yield), α Napthol (92% yield), β -Naphthol (90% yield), Write here the substrate names and there corresponding yield form the Ref.7, you can get the names of structure form structure drawing software or internet.

$$R-OH+Ac_2O \xrightarrow[\text{[bmim] [BF}_4\text{], RT}]{\text{Gd (OTf)}_3\text{(0.5 mol \%)}} R-OAc$$

Fig. 4: $Gd(OTf)_3$–$[bmim][BF_4]$ catalyzed acetylation of alcohols

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 and have obtained high yields of N-acetylated products (Fig. 5). $Gd(OTf)_3$ 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. The excellent yield of acylated product obtained for various substrate such as Benzyl amine (90% yield), Aniline (96% yield), N-methyl aniline (86% yield) and O-methyl aniline (89% yield).

$$R-OH+Ac_2O \xrightarrow[\text{[bmim] [BF}_4\text{], RT}]{\text{Gd (OTY)}_3\text{(0.2 mol\%)}} R-NHAc$$

Fig. 5. $Gd(OTf)_3$ catalyzed acetylation of amines in $[bmim][BF_4]$

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 (Table 3). Moderate to high yields of the products were obtained in second and third runs.

Table 3: Recyclability and reuse of $Gd(OTf)_3$–$[bmim][BF_4]$ for representative acetylation reactions

S.No.	Substrate	Yield (%)
1.	α- naphthol	92 (1st run) 83 (2nd run) 46 (3rd run)
2.	Cyclohexanol	92 (1st run) 87 (2nd run) 82 (3rd run)
3.	N-Methyl aniline	86 (1st run) 78 (2nd run) 72 (3rd run)

In order to gain insight into the mechanism of these acetylation reaction Alleti et al., have recorded a broad–band 1H decoupled 13C NMR spectrum for a solution of $Gd(OTf)_3$, Ac_2O and $[bmim][BF_4]$ (1 : 30 : 7 mol ratio). A weak absorption at δ ^{13}C 183.9 (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 Fig. 6.

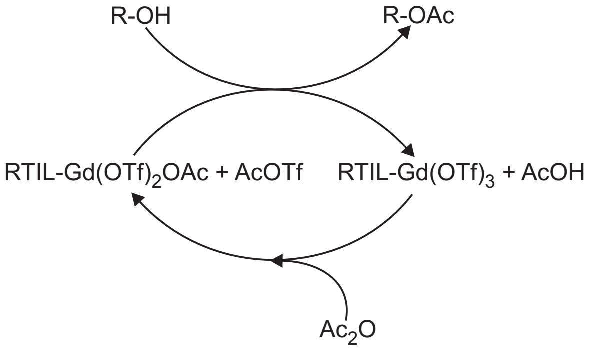


Fig. 6. Schematic representation of the catalytic cycle for RTIL– Gd(OTf)$_3$ catalyzed acetylations

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.

III. CONCLUSION

The application of ionic liquids in Friedel-Crafts acylation reactions is reviewed. Ionic liquids can be used as catalyst and solvents. Lewis acidic ionic liquids can be used as catalyst solvents, giving high reaction rate, conversion and selectivity, and catalyze both activated and deactivated aromatic compounds. Catalysts in ionic liquid solvents can enhance reaction rates, conversion and selectivity, but they are usually used to catalyze the activated aromatics.

Further study is needed in this aspect for Friedel-Crafts acylation of aromatic compounds in ionic liquids. This method offers a good catalyst system in the context of "green" chemistry.

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